Workshop on acceleration of the validation and regulatory acceptance of alternative methods and implementation of testing strategies

This report describes the proceedings of the BfR-RIVM workshop on validation of alternative methods which was held 23 and 24 March 2017 in Berlin, Germany. Stakeholders from governmental agencies, regulatory authorities, universities, industry and the OECD were invited to discuss current problems concerning the regulatory acceptance and implementation of alternative test methods and testing strategies, with the aim to develop feasible solutions. Classical validation of alternative methods usually involves one to one comparison with the gold standard animal study. This approach suffers from the reductionist nature of an alternative test as compared to the animal study as well as from the animal study being considered as the gold standard. Modern approaches combine individual alternatives into testing strategies, for which integrated and defined approaches are emerging at OECD. Furthermore, progress in mechanistic toxicology, e.g. through the adverse outcome pathway approach, and in computational systems toxicology allows integration of alternative test battery results into toxicity predictions that are more fine-tuned to the human situation. The road towards transition to a mechanistically-based human-focused hazard and risk assessment of chemicals requires an open mind towards stepping away from the animal study as the gold standard and defining human biologically based regulatory requirements for human hazard and risk assessment.
Gaze typing in virtual reality: Impact of keyboard design, selection method, and motion

Gaze tracking in virtual reality (VR) allows for hands-free text entry, but it has not yet been explored. We investigate how the keyboard design, selection method, and motion in the field of view may impact typing performance and user experience. We present two studies of people (n = 32) typing with gaze+dwell and gaze+click inputs in VR. In study 1, the typing keyboard was flat and within-view; in study 2, it was larger-than-view but curved. Both studies included a stationary and a dynamic motion conditions in the user’s field of view. Our findings suggest that 1) gaze typing in VR is viable but constrained, 2) the users perform best (10.15 WPM) when the entire keyboard is within-view; the larger-than-view keyboard (9.15 WPM) induces physical strain due to increased head movements, 3) motion in the field of view impacts the user’s performance: Users perform better while stationary than when in motion, and 4) gaze+click is better than dwell only (fixed at 550 ms) interaction.

General information
State: Published
Organisations: Department of Management Engineering, Technology and Innovation Management, Transport DTU, Copenhagen Center for Health Technology, Texas A and M University
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Aberrant intestinal microbiota in individuals with prediabetes

Aims/hypothesis: Individuals with type 2 diabetes have aberrant intestinal microbiota. However, recent studies suggest that metformin alters the composition and functional potential of gut microbiota, thereby interfering with the diabetes-related microbial signatures. We tested whether specific gut microbiota profiles are associated with prediabetes (defined as fasting plasma glucose of 6.1–7.0 mmol/l or HbA1c of 42–48 mmol/mol [6.0–6.5%]) and a range of clinical biomarkers of poor metabolic health. Methods: In the present case–control study, we analysed the gut microbiota of 134 Danish adults with prediabetes, overweight, insulin resistance, dyslipidaemia and low-grade inflammation and 134 age- and sex-matched individuals with normal glucose regulation. Results: We found that five bacterial genera and 36 operational taxonomic units (OTUs) were differentially abundant between individuals with prediabetes and those with normal glucose regulation. At the genus level, the abundance of Clostridium was decreased (mean log2 fold change −0.64 (SEM 0.23), padj = 0.0497), whereas the abundances of Dorea,[Ruminococcus], Sutterella and Streptococcus were increased (mean log2 fold change 0.51 (SEM 0.12), padj = 5 × 10^{-4}; 0.51 (SEM 0.11), padj = 1 × 10^{-4}; 0.60 (SEM 0.21), padj = 0.0497; and 0.92 (SEM 0.21), padj = 4 × 10^{-4}, respectively). The two OTUs that differed the most were a member of the order Clostridiales (OTU 146564) and Akkermansia muciniphila, which both displayed lower abundance among individuals with prediabetes (mean log2 fold change −1.74 (SEM 0.41), padj = 2 × 10^{-3} and −1.65 (SEM 0.34), padj = 4 × 10^{-4}, respectively). Faecal transfer from donors with prediabetes or screen-detected, drug-naive type 2 diabetes to germfree Swiss Webster or conventional C57BL/6 J mice did not induce impaired glucose regulation in recipient mice. Conclusions/interpretation: Collectively, our data show that individuals with prediabetes have aberrant intestinal microbiota characterised by a decreased abundance of the genus Clostridium and the mucin-degrading bacterium A. muciniphila. Our findings are comparable to observations in overt chronic diseases characterised by low-grade inflammation.
Akkermansia muciniphila, Clostridium, Faecal transfer, Gut microbiota, Hyperglycaemia, Intestinal microbiota, Low-grade inflammation, Prediabetes

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Accelerating the clean energy revolution - perspectives on innovation challenges: DTU International Energy Report 2018

General information
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Number of pages: 111
Publication date: 2018
A modular reconfigurable digital microfluidics platform

Miniaturizing the traditional wet lab processes and realizing the full potential of lab-on-a-chip technology (LOC) has been a great challenge for scientists and engineers in the quest of providing healthcare where such does not exist, or to increase lab efficiency and lower the operational cost. A range of practical LOC fabrication technologies has already been demonstrated, and as a result, the research of real life applications has been steadily increasing. However, due to the variety of used technologies and LOC form factors, it often requires a modification or even a complete redesign of the available instrumentation systems. Standardization and flexible instrumentation has seen limited development in the LOC field even though developing on all application levels has been proven as an effective way to stimulate a growth in a research field. To address this, we present a modular digital microfluidics (DMF) instrumentation platform and a concept of integrated chip-instrument co-design that has the potential to solve a wide range of LOC instrumentation challenges.

Biased Decision Making in Realistic Extra-Procedural Nuclear Control Room Scenarios

In normal operations and emergency situations, operators of nuclear control rooms rely on procedures to guide their decision making. However, in emergency situations, where several interacting problems can cause unpredictable adverse effects, these procedures may be insufficient in guiding operators to safe shutdown of the power plant. Little is known about the decision making strategies that operators employ in these extra-procedural situations. To address this, a realistic simulation study was conducted with five crews of active, licensed nuclear operators to see the behavioural patterns that occur when procedures are not sufficient. This paper, a re-analysis of a dataset collected for a different study, investigates how the design and existence of procedures influence, and possibly bias, decision making strategies. We found evidence that operators were affected by confirmation bias, and that, in some cases, the mismatch between their home power plant and the simulated power plant made them commit errors due to misapplied expertise. We further found that this effect was amplified by the existence and design of the procedures used. Based on these findings, we suggest that designers may improve safety by creating procedures that bear the risks of these biases in mind, or by specifically aiming to debias the users. Avenues for debiasing through design are discussed.
Changes and Sentiment: A Longitudinal E-Mail Analysis of a Large Design Project

Changes are part of any project. Although previous research provides methods to deal with changes, understanding of changes in relation to sentiment is still unclear. This is important as people's mood can affect performance and decisions. We implement an approach to quantify "change language" in emails and study its relation to sentiment. We find that sentiment decreases when problems or changes emerge, and increases when changes are implemented successfully. We discuss the implications of our findings for research and project engineering practice, providing avenues for further work.

General information
State: Published
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Data-Driven Learning in High-Resolution Activity Sampling From Patients With Bipolar Depression: Mixed-Methods Study.

Background: Behavioral activation is a pen and paper-based therapy form for treating depression. The patient registers their activity hourly, and together with the therapist, they agree on a plan to change behavior. However, with the limited clinical personnel, and a growing patient population, new methods are needed to advance behavioral activation.

Objective: The objectives of this paper were to (1) automatically identify behavioral patterns through statistical analysis of the paper-based activity diaries, and (2) determine whether it is feasible to move the behavioral activation therapy format to a digital solution.

Methods: We collected activity diaries from seven patients with bipolar depression, covering in total 2,480 hours of self-reported activities. A pleasure score, on a 1-10 rating scale, was reported for each activity. The activities were digitalized into 6 activity categories, and statistical analyses were conducted.

Results: Across all patients, movement-related activities were associated with the highest pleasure score followed by social activities. On an individual level, through a nonparametric Wilcoxon Signed-Rank test, one patient had a statistically significant larger amount of spare time activities when feeling bad (z=−2.045, P=.041). Through a within-subject analysis of covariance, the patients were found to have a better day than the previous, if that previous day followed their diurnal rhythm (p=.265, P=.029). Furthermore, a second-order trend indicated that two hours of daily social activity was optimal for the patients (β2=−0.08, t (63)=−1.22, P=.23).

Conclusions: The data-driven statistical approach was able to find patterns within the behavioral traits that could assist the therapist in as well as help design future technologies for behavioral activation.

General information
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Design for Health: Towards Collaborative Care

The design of novel healthcare delivery models better suited to address the burden of chronic diseases requires a thorough understanding of the foundational concepts of patient and healthcare provider collaboration. Reviewing the literature, we propose a taxonomy towards collaborative care: a generic term characterising healthcare delivery models that focus on the importance of patient-provider interactions, support safe patient participation in their own care, and redefine the balance of decision-power and accountability between patient and provider in health and care management.

General information
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Organisations: Department of Management Engineering, Engineering Systems, Copenhagen Center for Health Technology, ATAH Aps, University of Copenhagen
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Designing human-robot collaborations in industry 4.0: explorative case studies

We are experiencing an increase in human-robot interactions and the use of collaborative robots (cobots) in industrial work systems. To make full use of cobots, it is essential to understand emerging challenges and opportunities. In this paper, we analyse three successful industrial case studies of cobots' implementation. We highlight the top three challenges and opportunities, from the empirical evidence, relate them to current available literature on the topic, and use them to identify key design factor to consider when designing industrial work system with human-robot collaborations.

General information
State: Published
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Design process robustness: A bi-partite network analysis reveals the central importance of people

Design processes require the joint effort of many people to collaborate and work on multiple activities. Effective techniques to analyse and model design processes are important for understanding organisational dynamics, for improving collaboration, and for planning robust design processes, reducing the risk of rework and delays. Although there has been much progress in modelling and understanding design processes, little is known about the interplay between people and the activities they perform and its influence on design process robustness. To analyse this interplay, we model a large-scale design process of a biomass power plant with people and activities as a bipartite network. Observing that some people act as bridges between activities organised to form nearly independent modules, in order to evaluate process fragility, we simulate random failures and targeted attacks to people and activities. We find that our process is more vulnerable to attacks to people rather than activities. These findings show how the allocation of people to activities can obscure an inherent fragility, making the process highly sensitive and dependent on specific people. More generally, we show that the behaviour of robustness is determined by the degree distributions, the heterogeneity of which can be leveraged to improve robustness and resilience to cascading failures. Overall, we show that it is important to carefully plan the assignment of people to activities.

Differential bacterial capture and transport preferences facilitate co-growth on dietary xylan in the human gut

Metabolism of dietary glycans is pivotal in shaping the human gut microbiota. However, the mechanisms that promote competition for glycans among gut commensals remain unclear. *Roseburia intestinalis*, an abundant butyrate-producing Firmicute, is a key degrader of the major dietary fibre xylan. Despite the association of this taxon to a healthy microbiota, insight is lacking into its glycan utilization machinery. Here, we investigate the apparatus that confers *R. intestinalis* growth on different xylans. *R. intestinalis* displays a large cell-attached modular xylanase that promotes multivalent and dynamic association to xylan via four xylan-binding modules. This xylanase operates in concert with an ATP-binding cassette transporter to mediate breakdown and selective internalization of xylan fragments. The transport protein of *R. intestinalis* prefers oligomers of 4-5 xylosyl units, whereas the counterpart from a model xylan-degrading *Bacteroides* commensal targets larger ligands. Although *R. intestinalis* and the *Bacteroides* competitor co-grew in a mixed culture on xylan, *R. intestinalis* dominated on the preferred transport substrate xylotetraose. These findings highlight the differentiation of capture and transport preferences as a possible strategy to facilitate co-growth on abundant dietary fibres and may offer a unique route to manipulate the microbiota based on glycan transport preferences in therapeutic interventions to boost distinct taxa.
Effects on metabolic parameters in young rats born with low birth weight after exposure to a mixture of pesticides

Pesticide exposure during fetal life can lead to low birth weight and is commonly observed in reproductive toxicology studies. Associations have also been found in low birth weight babies born from pesticide-exposed gardeners. Since low birth weight is also linked to metabolic disorders, it can be speculated that early life exposure to pesticides could increase the risk of becoming obese or developing diabetes later in life. We have analyzed potential long-term effects of gestational and lactational exposure to a low dose mixture of six pesticides that individually can cause low birth weight: Cyromazine, MCPB, Pirimicarb, Quinoclamine, Thiram, and Ziram. Exposed male offspring, who were smaller than controls, displayed some degree of catch-up growth. Insulin and glucagon regulation was not significantly affected, and analyses of liver and pancreas did not reveal obvious histopathological effects. Efforts towards identifying potential biomarkers of metabolic disease-risk did not result in any strong candidates, albeit leptin levels were altered in exposed animals. In fat tissues, the key genes Lep, Nmb and Nmbr were altered in high dosed offspring, and were differentially expressed between sexes. Our results suggest that early-life exposure to pesticides may contribute to the development of metabolic disorders later in life.

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Pesticides are toxic substances that are deliberately released into our environment to kill or control living organisms. They have many beneficial qualities with regards to their intended use, but also carry with them potential harmful side effects for other living organisms that are inadvertently exposed, including humans. In this article, we will discuss some of the possible toxic effects they can have on male reproductive health. Of particular concern are pesticides with endocrine disrupting properties, which have been shown to interfere with male reproductive development. Early life exposure can prevent proper masculinization, having permanent consequences for the offspring.

Environmental toxicology: Pesticides

Plastic is a general term for a diverse group of polymeric materials that are used in a plethora of products. They represent a major source of human exposure to endocrine disrupting chemicals, including phthalates, bisphenols and persistent organic pollutants (POPs). For humans, foods represent the main source of exposure, but common house dust can also be a significant source of exposure in small children.
Phthalates and bisphenol A can interfere with male reproductive development by inducing reproductive organ malformations and impaired sperm production. Also persistent halogenated chemicals may be intentionally or unintentionally present in plastics and migrate/leak to foods or the environment causing concern for male reproductive function.

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**Organisations:** National Food Institute, Research Group for Molecular and Reproductive Toxicology, Research Group for Analytical Food Chemistry, Copenhagen Center for Health Technology  
**Authors:** Boberg, J. (Intern), Granby, K. (Intern), Svingen, T. (Intern), Vinggaard, A. M. (Intern)  
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In the original article wrong unites were quoted in Table 3 (page 508) and Table 4 (page 510) as well as in the paragraph 3.2 Core chemical exposure experiments on page 509. Also in paragraph 2.3 Selection and testing of chemicals the link to the Supplemental Materials (ESM) was missing. The correct versions of the tables and the paragraph as well as the ESM link are provided below.

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**Authors:** Hecker, M. (Ekstern), Hollert, H. (Ekstern), Cooper, R. (Ekstern), Vinggaard, A. M. (Intern), Akahori, Y. (Ekstern), Murphy, M. (Ekstern), Nellermann, C. (Intern), Higley, E. (Ekstern), Newsted, J. (Ekstern), Laskey, J. (Ekstern), Buckalew, A. (Ekstern), Grund, S. (Ekstern), Maletz, S. (Ekstern), Giesy, J. (Ekstern), Timm, G. (Ekstern)  
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Scopus rating (2004): SJR 0.807 SNIP 1.022
Web of Science (2004): Indexed yes
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Executive summary

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Authors: Jørgensen, B. H. (Intern)
Pages: 13-19
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Identifying Disruptive Technologies in Design: Horizon Scanning in the Early Stages of Design

Technology development is accelerating, driving disruption. Design is seen as key differentiator in creating innovative offerings but few design methods consider future technologies explicitly. In this article, we explore how a foresight method, namely horizon scanning, may be applied in a design context to anticipate disruption of construction. By means of a 3-step horizon scan, we identify 133 potentially disruptive technologies from across industries. We find that when preparing for disruption, design may benefit from the future-oriented and technology-focused features of horizon scanning.

Key findings and recommendations

Model-Based Systems Engineering for Life-Sciences Instrumentation Development

General information

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Networked capabilities for sustainable energy solutions

General information
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Organisations: Department of Management Engineering, Engineering Systems, Copenhagen Center for Health Technology
Papery-based sensors for rapid detection of virulence factor produced by Pseudomonas aeruginosa

Pyocyanin is a toxin produced by Pseudomonas aeruginosa. Here we describe a novel paper-based electrochemical sensor for pyocyanin detection, manufactured with a simple and inexpensive approach based on electrode printing on paper. The resulting sensors constitute an effective electrochemical method to quantify pyocyanin in bacterial cultures without the conventional time consuming pretreatment of the samples. The electrochemical properties of the paper-based sensors were evaluated by ferri/ferrocyanide as a redox mediator, and showed reliable sensing performance. The paper-based sensors readily allow for the determination of pyocyanin in bacterial cultures with high reproducibility, achieving a limit of detection of 95 nM and a sensitivity of 4.30 μA/μM in standard culture media. Compared to the similar commercial ceramic based sensors, it is a 2.3-fold enhanced performance. The simple in-house fabrication of sensors for pyocyanin quantification allows researchers to understand in vitro adaptation of P. aeruginosa infections via rapid screenings of bacterial cultures that otherwise are expensive and time-consuming.
We want to implement two-photon excitation fluorescence microscopy (TPEFM) into endoscopes, since TPEFM can provide relevant biomarkers for cancer staging and grading in hollow organs, endoscopically accessible through natural orifices. However, many obstacles must be overcome, among others the delivery of short laser pulses to the distal end of the endoscope. To this avail, we present imaging results using an all-fibre dispersion management scheme in a TPEFM setup. The scheme has been conceived by Jespersen et al. in 2010 and relies on the combination of a single mode fibre with normal and a higher order mode fibre with anomalous dispersion properties, fused in series using a long period grating. We show that using this fibre assembly, a simple and robust pulsed laser delivery system without any free-space optics, which is thus suitable for clinical use, can be realised.
The Hi-Ring Architecture for Data Center Networks
Optical technologies have long been used for standard telecom applications ranging from long haul to metro and access networks. With the rapid expansion of traffic in data center networks, the deployment of optical technologies for computationally intensive short reach networking has attracted a lot of attention. The main interest in photonics comes from the fact that optical technologies are known for providing high bandwidth at low-cost and low power consumption. Unlike electrical switching, optical switching offers bit rate-independent operation; thus, the required processing capacity can greatly be reduced as there is no need to perform operations like electrical demultiplexing of high-speed data streams. Moreover, simultaneous switching of wavelength channels using an optical circuit switch yields energy-efficient operation, which is crucial to data centers.

General information
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Organisations: Department of Photonics Engineering, High-Speed Optical Communication, Centre of Excellence for Silicon Photonics for Optical Communications, Nanophotonic Devices, Networks Technology and Service Platforms, Copenhagen Center for Health Technology
Authors: Kamchevska, V. (Intern), Ding, Y. (Intern), Berger, M. S. (Intern), Dittmann, L. (Intern), Oxenløwe, L. K. (Intern), Galili, M. (Intern)
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2nd International Workshop on Mental Health and Well-being: Sensing and Intervention: sensing and intervention
Mental health issues affect a significant portion of the world's population and can result in debilitating and life-threatening outcomes. To address this increasingly pressing healthcare challenge, there is a need to research novel approaches for early detection and prevention. In particular, ubiquitous systems can play a central role in revealing and tracking clinically relevant behaviors, contexts, and symptoms. Further, such systems can passively detect relapse onset and enable the opportune delivery of effective intervention strategies. However, despite their clear potential, the uptake of ubiquitous technologies into clinical mental healthcare is rare, and a number of challenges still face the overall efficacy of such technology-based solutions. The goal of this workshop is to bring together researchers interested in identifying, articulating, and addressing such issues and opportunities. Following the success of last year's inaugural workshop, we aim to continue facilitating the UbiComp community in developing a holistic approach for sensing and intervention in the context of mental health.

General information
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Organisations: Department of Applied Mathematics and Computer Science, Embedded Systems Engineering, Copenhagen Center for Health Technology, Cornell University, University College London
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Number of pages: 4
Pages: 745-748
3.5 W of diffraction-limited green light at 515 nm from SHG of a single-frequency tapered diode laser

Multi-Watt efficient compact green laser sources are required for a number of applications e.g. within biophotonics, laser pumping and laser displays. We present generation of 3.5 W of diffraction-limited green light at 515 nm by second harmonic generation (SHG) of a tapered diode laser, itself yielding more than 9 W at 1030 nm. SHG is performed in single pass through a cascade of two nonlinear crystals with re-focusing and dispersion compensating optics between the two nonlinear crystals. The laser is single-frequency and the output power is stabilized to better than ±0.4%.

A Combination of Machine Learning and Cerebellar-like Neural Networks for the Motor Control and Motor Learning of the Fable Modular Robot

We scaled up a bio-inspired control architecture for the motor control and motor learning of a real modular robot. In our approach, the Locally Weighted Projection Regression algorithm (LWPR) and a cerebellar microcircuit coexist, in the form of a Unit Learning Machine. The LWPR algorithm optimizes the input space and learns the internal model of a single robot module to command the robot to follow a desired trajectory with its end-effector. The cerebellar-like microcircuit refines the LWPR output delivering corrective commands. We contrasted distinct cerebellar-like
A Combination of Machine Learning and Cerebellar Models for the Motor Control and Learning of a Modular Robot

We scaled up a bio-inspired control architecture for the motor control and motor learning of a real modular robot. In our approach, the Locally Weighted Projection Regression algorithm (LWPR) and a cerebellar microcircuit coexist, forming a Unit Learning Machine. The LWPR optimizes the input space and learns the internal model of a single robot module to command the robot to follow a desired trajectory with its end-effector. The cerebellar microcircuit refines the LWPR output delivering corrective commands. We contrasted distinct cerebellar circuits including analytical models and spiking models implemented on the SpiNNaker platform, showing promising performance and robustness results.

Activity-Based Collaboration for Interactive Spaces

Activity-based computing (ABC) is a conceptual and technological framework for designing interactive systems that offers a better mapping between the activities people conduct and the digital entities they use. In ABC, rather than interacting directly with lower-level technical entities like files, folder, documents, etc., users are able to interact with ‘activities’ which encapsulate files and other low-level resources. In ABC an ‘activity’ can be shared between collaborating users and can be accessed on different devices. As such, ABC is a framework that suits the requirements of designing interactive spaces. This chapter provides an overview of ABC with a special focus on its support for collaboration (‘Activity Sharing’) and multiple devices (‘Activity Roaming’). These ABC concepts are illustrated as implemented in two different interactive spaces technologies; ReticularSpaces [1] and the eLabBench [2, 3]. The chapter discusses the benefits of activity-based collaboration support for these interactive spaces, while also discussing limitations and challenges to be addressed in further research.
Adaptive control in an artificial pancreas for people with type 1 diabetes

In this paper, we discuss overnight blood glucose stabilization in patients with type 1 diabetes using a Model Predictive Controller (MPC). We compute the model parameters in the MPC using a simple and systematic method based on a priori available patient information. We describe and compare 3 different model structures. The first model structure is an autoregressive integrated moving average with exogenous input (ARIMAX) structure. The second model structure is an autoregressive moving average with exogenous input (ARMAX) model, i.e. a model without an integrator. The third model structure is an adaptive ARMAX model in which we use a recursive extended least squares (RELS) method to estimate parameters of the stochastic part. In addition, we describe some safety layers in the control algorithm that improve the controller robustness and reduce the risk of hypoglycemia. We test and compare our control strategies using a virtual clinic of 100 randomly generated patients with a representative inter-subject variability. This virtual clinic is based on the Hovorka model. We consider the case where only half of the meal bolus is administered at mealtime, and the case where the insulin sensitivity increases during the night. The numerical results suggest that the use of an integrator leads to higher occurrence of hypoglycemia than for the controllers without the integrator. Compared to other control strategies, the adaptive MPC reduces both the time spent in hypoglycemia and the time spent in hyperglycemia.
Adaptive Smoothing in fMRI Data Processing Neural Networks

Functional Magnetic Resonance Imaging (fMRI) relies on multi-step data processing pipelines to accurately determine brain activity; among them, the crucial step of spatial smoothing. These pipelines are commonly suboptimal, given the local optimisation strategy they use, treating each step in isolation. With the advent of new tools for deep learning, recent work has proposed to turn these pipelines into end-to-end learning networks. This change of paradigm offers new avenues to improvement as it allows for a global optimisation. The current work aims at benefitting from this paradigm shift by defining a smoothing step as a layer in these networks able to adaptively modulate the degree of smoothing required by each brain volume to better accomplish a given data analysis task. The viability is evaluated on real fMRI data where subjects did alternate between left and right finger tapping tasks.
Administration of two probiotic strains during early childhood does not affect the endogenous gut microbiota composition despite probiotic proliferation

Probiotics are increasingly applied to prevent and treat a range of infectious, immune related and gastrointestinal diseases. Despite this, the mechanisms behind the putative effects of probiotics are poorly understood. One of the suggested modes of probiotic action is modulation of the endogenous gut microbiota, however probiotic intervention studies in adults have failed to show significant effects on gut microbiota composition. The gut microbiota of young children is known to be unstable and more responsive to external factors than that of adults. Therefore, potential effects of probiotic intervention on gut microbiota may be easier detectable in early life. We thus investigated the effects of a 6 month placebo-controlled probiotic intervention with Bifidobacterium animalis subsp. lactis (BB-12®) and Lactobacillus rhamnosus (LGG®) on gut microbiota composition and diversity in more than 200 Danish infants (N = 290 enrolled; N = 201 all samples analyzed), as assessed by 16S rRNA amplicon sequencing. Further, we evaluated probiotic presence and proliferation by use of specific quantitative polymerase chain reaction (qPCR). Probiotic administration did not significantly alter gut microbiota community structure or diversity as compared to placebo. The probiotic strains were detected in 91.3% of the fecal samples from children receiving probiotics and in 1% of the placebo treated children. Baseline gut microbiota was not found to predict the ability of probiotics to establish in the gut after the 6 month intervention. Within the probiotics group, proliferation of the strains LGG® and BB-12® in the gut was detected in 44.7% and 83.5% of the participants, respectively. A sub-analysis of the gut microbiota including only individuals with detected growth of the probiotics LGG® or BB-12® and comparing these to placebo revealed no differences in community structure or diversity. Six months of probiotic administration during early life did not change gut microbiota community structure or diversity, despite active proliferation of the administered probiotic strains. Therefore, alteration of the healthy infant gut microbiota is not likely to be a prominent mechanism by which these specific probiotics works to exert beneficial effects on host health. NCT02180581 . Registered 30 June 2014.

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A framework of knowledge creation processes in participatory simulation of hospital work systems

Participatory simulation (PS) is a method to involve workers in simulating and designing their own future work system. Existing PS studies have focused on analysing the outcome, and minimal attention has been devoted to the process of creating this outcome. In order to study this process, we suggest applying a knowledge creation perspective. The aim of this study was to develop a framework describing the process of how ergonomics knowledge is created in PS. Video recordings from three projects applying PS of hospital work systems constituted the foundation of process mining analysis. The analysis resulted in a framework revealing the sources of ergonomics knowledge creation as sequential relationships between the activities of simulation participants sharing work experiences; experimenting with scenarios; and reflecting on ergonomics consequences. We argue that this framework reveals the hidden steps of PS that are essential when planning and facilitating PS that aims at designing work systems.
A least squares approach for efficient and reliable short-term versus long-term optimization

The uncertainties related to long-term forecasts of oil prices impose significant financial risk on ventures of oil production. To minimize risk, oil companies are inclined to maximize profit over short-term horizons ranging from months to a few years. In contrast, conventional production optimization maximizes long-term profits over horizons that span more than a decade. To address this challenge, the oil literature has introduced short-term versus long-term optimization. Ideally, this problem is solved by a posteriori multi-objective optimization methods that generate an approximation to the Pareto front of optimal short-term and long-term trade-offs. However, such methods rely on a large number of reservoir simulations and scale poorly with the number of objectives subject to optimization. Consequently, the large-scale nature of production optimization severely limits applications to real-life scenarios. More practical alternatives include ad hoc hierarchical switching schemes. As a drawback, such methods lack robustness due to unclear convergence properties and do not naturally generalize to cases of more than two objectives. Also, as this paper shows, the hierarchical formulation may skew the balance between the objectives, leaving an unfulfilled potential to increase profits. To promote efficient and reliable short-term versus long-term optimization, this paper introduces a natural way to characterize desirable Pareto points and proposes a novel least squares (LS) method. Unlike hierarchical approaches, the method is guaranteed to converge to a Pareto optimal point. Also, the LS method is designed to properly balance multiple objectives, independently of Pareto front’s shape. As such, the method poses a practical alternative to a posteriori methods in situations where the frontier is intractable to generate.
Analysis of DDoS-capable IoT malwares

The Internet of Things (IoT) revolution promises to make our lives easier by providing cheap and always connected smart embedded devices, which can interact on the Internet and create added values for human needs. But all that glitters is not gold. Indeed, the other side of the coin is that, from a security perspective, this IoT revolution represents a potential disaster. This plethora of IoT devices that flooded the market were very badly protected, thus an easy prey for several families of malwares that can enslave and incorporate them in very large botnets. This, eventually, brought back to the top Distributed Denial of Service (DDoS) attacks, making them more powerful and easier to achieve than ever. This paper aims at provide an up-to-date picture of DDoS attacks in the specific subject of the IoT, studying how these attacks work and considering the most common families in the IoT context, in terms of their nature and evolution through the years. It also explores the additional offensive capabilities that this arsenal of IoT malwares has available, to mine the security of Internet users and systems. We think that this up-to-date picture will be a valuable reference to the scientific community in order to take a first crucial step to tackle this urgent security issue.

General information

State: Published
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An effect-directed strategy for characterizing emerging chemicals in food contact materials made from paper and board

Food contact materials (FCM) are any type of item intended to come into contact with foods and thus represent a potential source for human exposure to chemicals. Regarding FCMs made of paper and board, information pertaining to their chemical constituents and the potential impacts on human health remains scarce, which hampers safety evaluation. We describe an effect-directed strategy to identify and characterize emerging chemicals in paper and board FCMs. Twenty FCMs were tested in eight reporter gene assays, including assays for the AR, ER, AhR, PPARγ, Nrf2 and p53, as well as mutagenicity. All FCMs exhibited activities in at least one assay. As proof-of-principle, FCM samples obtained from a sandwich wrapper and a pizza box were carried through a complete step-by-step multi-tiered approach. The pizza box exhibited ER activity, likely caused by the presence of bisphenol A, dibutyl phthalate, and benzylbutyl phthalate. The sandwich wrapper exhibited AR antagonism, likely caused by abietic acid and dehydroabietic acid. Migration studies confirmed that the active chemicals can transfer from FCMs to food simulants. In conclusion, we report an effect-directed strategy that can identify hazards posed by FCMs made from paper and board, including the identification of the chemical(s) responsible for the observed activity.

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A New Wavelet-Based ECG Delineator for the Evaluation of the Ventricular Innervation

T-wave amplitude (TWA) has been proposed as a marker of the innervation of the myocardium. Until now, TWA has been calculated manually or with poor algorithms, thus making its use not efficient in a clinical environment. We introduce a new wavelet-based algorithm for the delineation QRS complexes and T-waves, and the automatic calculation of TWA. When validated in the MIT/BIH Arrhythmia database, the QRS detector achieved sensitivity and positive predictive value of 99.84% and 99.87%, respectively. The algorithm was validated also on the QT database and it achieved sensitivity of 99.50% for T-peak detection. In addition, the algorithm achieved delineation accuracy that is similar to the differences in delineation between expert cardiologists. We applied the algorithm for the evaluation of the influence in TWA of anticholinergic and antiadrenergic drugs (i.e., atropine and metoprolol) for healthy subjects. We found that the TWA decreased significantly with atropine and that metoprolol caused a significant increase in TWA, thus confirming the clinical hypothesis that the TWA is a marker of the innervation of the myocardium. The results of this paper show that the proposed algorithm can be used as a useful and efficient tool in clinical practice for the automatic calculation of TWA and its interpretation as a non-invasive marker of the autonomic ventricular innervation.

General information
State: Published
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Publication information
An introduction to Deep learning on biological sequence data - Examples and solutions

Deep neural network architectures such as convolutional and long short-term memory networks have become increasingly popular as machine learning tools during the recent years. The availability of greater computational resources, more data, new algorithms for training deep models and easy to use libraries for implementation and training of neural networks are the drivers of this development. The use of deep learning has been especially successful in image recognition; and the development of tools, applications and code examples are in most cases centered within this field rather than within biology. Here, we aim to further the development of deep learning methods within biology by providing application examples and ready to apply and adapt code templates. Given such examples, we illustrate how architectures consisting of convolutional and long short-term memory neural networks can relatively easily be designed and trained to state-of-the-art performance on three biological sequence problems: prediction of subcellular localization, protein secondary structure and the binding of peptides to MHC Class II molecules. All implementations and datasets are available online to the scientific community at https://github.com/vanessajurtz/lasagne4bio. Supplementary data are available at Bioinformatics online.

General information

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A Riccati-Based Interior Point Method for Efficient Model Predictive Control of SISO Systems

This paper presents an algorithm for Model Predictive Control of SISO systems. Based on a quadratic objective in addition to (hard) input constraints it features soft upper as well as lower constraints on the output and an input rate-of-change penalty term. It keeps the deterministic and stochastic model parts separate. The controller is designed based on the deterministic model, while the Kalman filter results from the stochastic part. The controller is implemented as a primal-dual interior point (IP) method using Riccati recursion and the computational savings possible for SISO systems. In particular the computational complexity scales linearly with the control horizon. No warm-start strategies are considered. Numerical examples are included illustrating applications to Artificial Pancreas technology. We provide typical execution times for a single iteration of the IP algorithm and the number of iterations required for convergence in different situations.

General information
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Organisations: Department of Applied Mathematics and Computer Science, Scientific Computing, Copenhagen Center for Health Technology, Center for Energy Resources Engineering, Lund University
Authors: Hagdrup, M. (Intern), Johansson, R. (Ekstern), Bagterp Jørgensen, J. (Intern)
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A systematic and practical method for selecting systems engineering tools

The complexity of many types of systems has grown considerably over the last decades. Using appropriate systems engineering tools therefore becomes increasingly important. Starting the tool selection process can be intimidating because organizations often only have a vague idea about what they need. The tremendous number of available tools makes it difficult to get an overview and identify the best choice. Selecting wrong tools due to inappropriate analysis can have severe impact on the success of the company. This paper presents a systematic method for selecting systems engineering tools based on thorough analyses of the actual needs and the available tools. Grouping needs into categories, allow us to obtain a comprehensive set of requirements for the tools. The entire model-based systems engineering discipline was categorized for a modeling tool case to enable development of a tool specification. Correlating requirements and tool capabilities, enables us to identify the best tool for single-tool scenarios or the best set of tools for multi-tool scenarios. In both scenarios, we use gap analysis to prevent selection of infeasible tools. We used the method to select a traceability tool that has been in successful operation since 2013 at GN Hearing. We further utilized the method to select a set of tools that we used on pilot cases at GN Hearing for modeling, simulating and formally verifying embedded systems.

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Organisations: Department of Applied Mathematics and Computer Science, Embedded Systems Engineering, Copenhagen Center for Health Technology
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Big Data hvor N=1

Forskningen vedrørende anvendelsen af 'big data' indenfor sundhed er kun lige begyndt, og kan på sigt blive en stor hjælp i forhold til at tilrettelægge en mere personlig og helhedsorienteret sundhedsindsats for multishyge. Personlig sundhedssteknologi, som kort præsenteres i dette kapitel, rummer et stor potentiale for at gennemføre 'big data' analyser for den enkelte person, det vil sige hvor N=1. Der er store teknologiske udfordringer i at få lavet teknologier og metoder til at indsamle og håndtere personlige data, som kan deles, på tværs på en standardiseret, forsvarlig, robust, sikker og ikke mindst anonym facon.

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Authors: Bardram, J. E. (Intern)
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Can smartphone-based electronic markers discriminate between patients with bipolar disorder, healthy first-degree relatives and healthy control individuals

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Commemorating 25 years of optical coherence tomography: A perspective on biomedical applications

This guest editorial introduces the Special Section on 25 Years of OCT

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BFI (2013): BFI-level 1
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Web of Science (2012): Indexed yes
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Comparing three methods for participatory simulation of hospital work systems

Summative Statement: This study compared three participatory simulation methods using different simulation objects: Low resolution table-top setup using Lego figures, full scale mock-ups, and blueprints using Lego figures. It was concluded the three objects by differences in fidelity and affordance addressed different elements of a hospital work system.

Problem statement: Different methods for simulating the future work system for healthcare professionals have been applied in a number of green field and renovation design projects of hospitals in Denmark. The methods differed in the type of simulation objects representing the work system. Hence, this was an opportunity to study if these differences influenced which elements of a work system were in focus when healthcare professionals simulated and evaluated future work. Preliminary observations indicated this was the case but it was not understood how and why this influence took place.

Research Objective / Question: How does the simulation object influence which elements of a work system are being evaluated in participatory simulation events?

Methodology: Observation notes and video recordings of three types of simulation events using different objects were analyzed in respect to which elements of a work system were being targeted. A work system was defined as consisting of human work practices embedded in the three interdependent dimensions: space, organization and technology. All simulation events were based on participants playing clinical scenarios using the objects.

Results: Full scale mock-ups significantly addressed the local space and technology/tool elements of a work system. In contrast, the table-top simulation object addressed the organizational issues of the future work system. The blueprint based simulation addressed the organizational issues in combination with a global space outlook, e.g. the layout of an entire department.

Discussion: It is proposed that the simulation objects influence on work system focus is based on two attributes: Fidelity and affordance. Fidelity concerns the degree of resolution or the level of detail of what are being manifested by the objects.

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simulation object. The affordance is a property of the object concerning how simulation participants will perceive how it may be used. When having a low-resolution model of a work system as in the table-top setup it is much easier to test a number of “what if” scenarios on how to organize the work in different spatial layouts. In addition to the object attributes other factors may play a role in what work system elements are being addressed. An important one seems to be at which point in the hospital design process the simulation is carried out.

Conclusions: Different simulation objects may to a certain degree influence what part of a work system is being addressed in participatory simulation events. For human factors practitioners in hospital design projects it is important to pay attention to this when planning and facilitating simulation events to evaluate different designs.

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Contact activity and dynamics of the social core
Humans interact through numerous communication channels to build and maintain social connections: they meet face-to-face, make phone calls or send text messages, and interact via social media. Although it is known that the network of physical contacts, for example, is distinct from the network arising from communication events via phone calls and instant messages, the extent to which these networks differ is not clear. We show here that the network structure of these channels show large structural variations. The various channels account for diverse relationships between pairs of individuals and the corresponding interaction patterns across channels differ to an extent that social ties cannot easily be reduced to a single layer. Each network of interactions, however, contains both central and peripheral individuals: central members are characterized by higher connectivity and can reach a large fraction of the network within a low number of steps, in contrast to the nodes on the periphery. The origin and purpose of each communication network also determine the role of their respective central members: highly connected individuals in the person-to-person networks interact with their environment in a regular manner, while members central in the social communication networks display irregular behavior with respect to their physical contacts and are more active through irregular social events. Our results suggest that due to the inherently different functions of communication channels, each one favors different social behaviors and different strategies for interacting with the environment. These findings can facilitate the understanding of the varying roles and impact individuals have on the population, which can further shed light on the prediction and prevention of epidemic outbreaks, or information propagation.

General information
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Correlations between human mobility and social interaction reveal general activity patterns
A day in the life of a person involves a broad range of activities which are common across many people. Going beyond diurnal cycles, a central question is: to what extent do individuals act according to patterns shared across an entire population? Here we investigate the interplay between different activity types, namely communication, motion, and physical proximity by analyzing data collected from smartphones distributed among 638 individuals. We explore two central questions: Which underlying principles govern the formation of the activity patterns? Are the patterns specific to each individual or shared across the entire population? We find that statistics of the entire population allows us to successfully predict 71% of the activity and 85% of the inactivity involved in communication, mobility, and physical proximity. Surprisingly, individual level statistics only result in marginally better predictions, indicating that a majority of activity patterns are shared across our sample population. Finally, we predict short-term activity patterns using a generalized linear model, which suggests that a simple linear description might be sufficient to explain a wide range of actions, whether they be of social or of physical character.

General information
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Organisations: Copenhagen Center for Health Technology, Department of Applied Mathematics and Computer Science, Cognitive Systems, University of Copenhagen
Authors: Møller, A. (Ekstern), Jørgensen, S. L. (Intern), Mathiesen, J. (Ekstern)
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.11 SJR 1.236 SNIP 1.101
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BFI (2015): BFI-level 1
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Scopus rating (2014): SJR 1.559 SNIP 1.148 CiteScore 3.54
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.772 SNIP 1.153 CiteScore 3.94
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Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
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ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.425 SNIP 1.233 CiteScore 4.58
ISI indexed (2011): ISI indexed no
Web of Science (2011): Indexed yes
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Scopus rating (2010): SJR 2.705 SNIP 1.178
Creating Ultra Dense Point Correspondence Over the Entire Human Head

While the acquisition and analysis of 3D faces has been an active area of research for decades, it is still a complex and demanding task to accurately model the entire head and ears. Having accurate models would for example enable virtual design of hearing devices. In this paper, we describe a complete framework for surface registration of complete human heads where the result is point correspondence with a very high number of points. The method is based on a volumetric and multi-scale non-rigid registration of signed distance fields. The method is evaluated on a set of 30 human heads and the results are convincing. The output can for example be used to compute statistical shape models. The accuracy of predicted anatomical landmarks is on the level of experienced human operators.

General information

State: Published
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Pages: 438-447
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Surface registration, Signed distance field, Human head modelling

Cross-Validation of a Glucose-Insulin-Glucagon Pharmacodynamics Model for Simulation using Data from Patients with Type 1 Diabetes
Background: 
Currently, no consensus exists on a model describing endogenous glucose production (EGP) as a function of glucagon concentrations. Reliable simulations to determine the glucagon dose preventing or treating hypoglycemia or to tune a dual-hormone artificial pancreas control algorithm need a validated glucoregulatory model including the effect of glucagon.

Methods: 
Eight type 1 diabetes (T1D) patients each received a subcutaneous (SC) bolus of insulin on four study days to induce mild hypoglycemia followed by a SC bolus of saline or 100, 200, or 300 µg of glucagon. Blood samples were analyzed for concentrations of glucagon, insulin, and glucose. We fitted pharmacokinetic (PK) models to insulin and glucagon data using maximum likelihood and maximum a posteriori estimation methods. Similarly, we fitted a pharmacodynamic (PD) model to glucose data. The PD model included multiplicative effects of insulin and glucagon on EGP. Bias and precision of PD model test fits were assessed by mean predictive error (MPE) and mean absolute predictive error (MAPE).

Results: 
Assuming constant variables in a subject across nonoutlier visits and using thresholds of ±15% MPE and 20% MAPE, we accepted at least one and at most three PD model test fits in each of the seven subjects. Thus, we successfully validated the PD model by leave-one-out cross-validation in seven out of eight T1D patients.

Conclusions: 
The PD model accurately simulates glucose excursions based on plasma insulin and glucagon concentrations. The reported PK/PD model including equations and fitted parameters allows for in silico experiments that may help improve diabetes treatment involving glucagon for prevention of hypoglycemia.

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Scientific Computing, Dynamical Systems, Copenhagen Center for Health Technology, Center for Energy Resources Engineering, Copenhagen University Hospital, Zealand Pharma A/S
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.14 SJR 0.875 SNIP 1.078
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.934 SNIP 0.971 CiteScore 1.99
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.882 SNIP 0.955 CiteScore 1.84
BFI (2013): BFI-level 1
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ISI indexed (2013): ISI indexed no
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.711 SNIP 0.976 CiteScore 1.33
ISI indexed (2012): ISI indexed no
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.691 SNIP 0.904 CiteScore 0.6
ISI indexed (2011): ISI indexed no
Data-driven engineering design research: Opportunities using open data
Engineering Design research relies on quantitative and qualitative data to describe design-related phenomena and prescribe improvements for design practice. Given data availability, privacy requirements and other constraints, most empirical data used in Engineering Design research can be described as "closed". Keeping such data closed is in many cases necessary and justifiable. However, this closedness also hinders replicability, and thus, may limit our possibilities to test the validity and reliability of research results in the field. This paper discusses implications and applications of using the already available and continuously growing body of open data sources to create opportunities for research in Engineering Design. Insights are illustrated by an examination of two examples: a study of open source software repositories and an analysis of open business registries in the cleantech industry. We conclude with a discussion about the limitations, challenges and risks of using open data in Engineering Design research and practice.

DeepLoc: prediction of protein subcellular localization using deep learning
The prediction of eukaryotic protein subcellular localization is a well-studied topic in bioinformatics due to its relevance in proteomics research. Many machine learning methods have been successfully applied in this task, but in most of them, predictions rely on annotation of homologues from knowledge databases. For novel proteins where no annotated homologues exist, and for predicting the effects of sequence variants, it is desirable to have methods for predicting protein properties from sequence information only. Here, we present a prediction algorithm using deep neural networks to predict protein subcellular localization relying only on sequence information. At its core, the prediction model uses a recurrent neural network that processes the entire protein sequence and an attention mechanism identifying protein regions important for the subcellular localization. The model was trained and tested on a protein dataset extracted from one of the latest UniProt releases, in which experimentally annotated proteins follow more stringent criteria than previously. We demonstrate that our model achieves a good accuracy (78% for 10 categories; 92% for membrane-bound or soluble), outperforming current state-of-the-art algorithms, including those relying on homology information. The method is available as a web server at http://www.cbs.dtu.dk/services/DeepLoc . Example code is available at https://github.com/JJAlmagro/subcellular_localization . The dataset is available at http://www.cbs.dtu.dk/services/DeepLoc/data.php . jjalma@dtu.dk.
Deep recurrent conditional random field network for protein secondary prediction

Deep learning has become the state-of-the-art method for predicting protein secondary structure from only its amino acid residues and sequence profile. Building upon these results, we propose to combine a bi-directional recurrent neural network (biRNN) with a conditional random field (CRF), which we call the biRNN-CRF. The biRNN-CRF may be seen as an improved alternative to an autoregressive uni-directional RNN where predictions are performed sequentially conditioning on the prediction in the previous timestep. The CRF is instead nearest neighbor-aware and models for the joint distribution of the labels for all time-steps. We condition the CRF on the output of biRNN, which learns a distributed representation based on the entire sequence. The biRNN-CRF is therefore close to ideally suited for the secondary structure task because a high degree of cross-talk between neighboring elements can be expected. We validate the model on several benchmark datasets. For example, on CBS13, a model with 1.7 million parameters, achieves a Q8 accuracy of 69.4 for single model and 70.9 for ensemble, which to our knowledge is state-of-the-art. 1

General information
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Organisations: Department of Applied Mathematics and Computer Science, Copenhagen Center for Health Technology, Cognitive Systems, University of Copenhagen
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Source: FindIt
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Den mikrobielle verden indeni os - En kort introduktion til tarmens mikrobiom

General information
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Organisations: Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology
Authors: Licht, T. R. (Intern)
Pages: 3-5
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Detection of Paroxysms in Long-Term, Single Channel EEG-Monitoring of Patients with Typical Absence Seizures.

Absence seizures are associated with generalized 2.5-5 Hz spike-wave discharges in the EEG. Rarely are patients, parents or physicians aware of duration or incidence of seizures. Six patients were monitored with a portable EEG-device over four times 24 hours to evaluate how easily outpatients are monitored and how well an automatic seizure detection algorithm can identify the absences. Based on patient-specific modeling, we achieved a sensitivity of 98.4% with only 0.23 false detections per hour. This yields a clinically satisfying performance with a positive predictive value of 87.1%. Portable EEG-recorders identifying paroxystic events in epilepsy outpatients are a promising tool for patients and physicians dealing with absence epilepsy. Albeit the small size of the EEG-device, some children still complained about the obtrusive nature of the device. We aim at developing less obtrusive though still very efficient devices e.g. hidden in the ear canal or below the skin.

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Temanummer_Milj_og_Sundhed_2017.pdf
DOIs:
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Diagnostic value of sleep stage dissociation as visualized on a 2-dimensional sleep state space in human narcolepsy

Type 1 narcolepsy (NT1) is characterized by symptoms believed to represent Rapid Eye Movement (REM) sleep stage dissociations, occurrences where features of wake and REM sleep are intermingled, resulting in a mixed state. We hypothesized that sleep stage dissociations can be objectively detected through the analysis of nocturnal Polysomnography (PSG) data, and that those affecting REM sleep can be used as a diagnostic feature for narcolepsy. A Linear Discriminant Analysis (LDA) model using 38 features extracted from EOG, EMG and EEG was used in control subjects to select features differentiating wake, stage N1, N2, N3 and REM sleep. Sleep stage differentiation was next represented in a 2D projection. Features characteristic of sleep stage differences were estimated from the residual sleep stage probability in the 2D space. Using this model we evaluated PSG data from NT1 and non-narcoleptic subjects. An LDA classifier was used to determine the best separation plane. This method replicates the specificity/sensitivity from the training set to the validation set better than many other methods. Eight prominent features could differentiate narcolepsy and controls in the validation dataset. Using a composite measure and a specificity cut off 95% in the training dataset, sensitivity was 43%. Specificity/sensitivity was 94%/38% in the validation set. Using hypersomnolence subjects, specificity/sensitivity was 84%/15%. Analyzing treated narcoleptics the specificity/sensitivity was 94%/10%. Sleep stage dissociation can be used for the diagnosis of narcolepsy. However the use of some medications and presence of undiagnosed hypersomnolence patients impacts the result.
Diagnostic, LDA classifier, Machine learning, Narcolepsy, Sleep stage dissociation
Distributed co-simulation of embedded control software with exhaust gas recirculation water handling system using INTO-CPS

Engineering complex Cyber-Physical Systems, such as emission reduction control systems for large two-stroke engines, require advanced modelling of both the cyber and physical aspects. Different tools are specialised for each of these domains and a combination of tools validating different properties is often desirable. However, it is non-trivial to be able to combine such different models of different constituent elements. In order to reduce the need for expensive tests on the real system it is advantageous to be able to combine such heterogeneous models in a joint co-simulation in order to reduce the overall costs of validation. This paper demonstrates how this can be achieved for a commercial system developed by MAN Diesel & Turbo using a newly developed tool chain based on the Functional Mock-up Interface standard for co-simulation supporting different operating systems. The generality of the suggested approach also enables future scenarios incorporating constituent models supplied by sub-suppliers while protecting their Intellectual Property.
Economy, Movement Dynamics, and Muscle Activity of Human Walking at Different Speeds

The complex behaviour of human walking with respect to movement variability, economy and muscle activity is speed dependent. It is well known that a U-shaped relationship between walking speed and economy exists. However, it is an open question if the movement dynamics of joint angles and centre of mass and muscle activation strategy also exhibit a U-shaped relationship with walking speed. We investigated the dynamics of joint angle trajectories and the centre of mass accelerations at five different speeds ranging from 20 to 180% of the predicted preferred speed (based on Froude speed) in twelve healthy males. The muscle activation strategy and walking economy were also assessed. The movement dynamics was investigated using a combination of the largest Lyapunov exponent and correlation dimension. We observed an intermediate stage of the movement dynamics of the knee joint angle and the anterior-posterior and mediolateral centre of mass accelerations which coincided with the most energy-efficient walking speed. Furthermore, the dynamics of the joint angle trajectories and the muscle activation strategy was closely linked to the functional role and biomechanical constraints of the joints.
Electroencephalography (EEG) provides a measure of brain activity and has improved our understanding of the brain immensely. However, there is still much to be learned and the full potential of EEG is yet to be realized. In this thesis we suggest to improve the information gain of EEG using three different approaches; 1) by recovery of the EEG sources, 2) by representing and inferring the propagation path of EEG sources, and 3) by combining EEG with functional magnetic resonance imaging (fMRI). The common goal of the methods, and thus of this thesis, is to improve the spatial dimension of EEG.

The main topic of this thesis is the localization of the EEG generators. This entails solving both a forward and an inverse problem. The inverse problem maps the EEG signal recorded on the scalp to its origin in the brain. It is a highly ill-posed problem which we tackle by employing a sparsity promoting 'spike and slab' like method augmented with physiologically relevant source priors. The incorporated temporal and spatial priors exploit coherence between neighboring time samples and between neighboring source locations, respectively. We show that these augmentations effectively increase the source recovery ability.

The forward problem describes the propagation of neuronal activity in the brain to the EEG electrodes on the scalp. The geometry and conductivity of the head layers are normally required to model this path. We propose a framework for inferring forward models which is based on the EEG signal and a low dimensional representation of forward models. The representation is built by principal component analysis of a corpus of forward models. The method can be used to recover subject-specific forward models when structural scans and/or conductivity estimations are not available.
Finally we investigate the extraction of EEG components having bandpower dynamics correlated with fMRI components. We show that adding anatomical information to the inference scheme improves the recovery of correlated components compared to only using functional information. The anatomical information is incorporated through the EEG forward model and assumes that the activity of the fMRI component overlaps spatially with the origin of the coupled EEG component.

**General information**
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Cognitive Systems, Copenhagen Center for Health Technology
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**Relations**
Projects:
EEG Based Inference of Spatio-Temporal Brain Dynamics
Publication: Research › Ph.D. thesis – Annual report year: 2017

**EEG in the classroom: Synchronised neural recordings during video presentation**
We performed simultaneous recordings of electroencephalography (EEG) from multiple students in a classroom, and measured the inter-subject correlation (ISC) of activity evoked by a common video stimulus. The neural reliability, as quantified by ISC, has been linked to engagement and attentional modulation in earlier studies that used high-grade equipment in laboratory settings. Here we reproduce many of the results from these studies using portable low-cost equipment, focusing on the robustness of using ISC for subjects experiencing naturalistic stimuli. The present data shows that stimulus-evoked neural responses, known to be modulated by attention, can be tracked for groups of students with synchronized EEG acquisition. This is a step towards real-time inference of engagement in the classroom.

**General information**
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Cognitive Systems, Copenhagen Center for Health Technology, Stanford University, City College of New York
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Number of pages: 9
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Scopus rating (2017): CiteScore 4.36 SJR 1.533 SNIP 1.245
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BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.63 SJR 1.692 SNIP 1.354
Effects of Gliadin consumption on the Intestinal Microbiota and Metabolic Homeostasis in Mice Fed a High-fat Diet

Dietary gluten causes severe disorders like celiac disease in gluten-intolerant humans. However, currently understanding of its impact in tolerant individuals is limited. Our objective was to test whether gliadin, one of the detrimental parts of gluten, would impact the metabolic effects of an obesogenic diet. Mice were fed either a defined high-fat diet (HFD) containing 4% gliadin (n=20), or a gliadin-free, isocaloric HFD (n=20) for 23 weeks. Combined analysis of several parameters including insulin resistance, histology of liver and adipose tissue, intestinal microbiota in three gut compartments, gut barrier function, gene expression, urinary metabolites and immune profiles in intestinal, lymphoid, liver and adipose tissues was performed. Mice fed the gliadin-containing HFD displayed higher glycated hemoglobin and higher insulin resistance as evaluated by the homeostasis model assessment, more hepatic lipid accumulation and smaller adipocytes than mice fed the gliadin-free HFD. This was accompanied by alterations in the composition and activity of the gut microbiota, gut barrier function, urine metabolome, and immune phenotypes within liver and adipose tissue. Our results reveal that gliadin disturbs the intestinal environment and affects metabolic homeostasis in obese mice, suggesting a detrimental effect of gluten intake in gluten-tolerant subjects consuming a high-fat diet.
Efficient generation of 3.5W laser light at 515nm by frequency doubling a single-frequency high power DBR tapered diode laser

More than 3.5 W of green light at 515 nm is generated by frequency doubling a single-frequency high power DBR tapered diode laser. The frequency doubling is performed in a cascade of PPMgLN and PPMgSLT crystals in order to reach high power and avoid thermal effects present in PPMgLN at high power. The green light is diffraction limited (M2 <1.1) and single-frequency operation is demonstrated with a linewidth less than 2 pm.

General information

State: Published
Organisations: Department of Photonics Engineering, Diode Lasers and LED Systems, Copenhagen Center for Health Technology, Leibniz-Institut für Höchstfrequenztechnik
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Pages: 167-170
Publication date: 2017
Main Research Area: Technical/natural sciences

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Web of Science (2018): Indexed yes
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Scopus rating (2017): CiteScore 1.86 SJR 0.614 SNIP 0.95
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Electrophysiological dynamics of covert and overt visual attention.

Attention is a key neural function for choosing certain information to receive more processing than others. Attention is allocated either by directly looking at the target (overt) or without eye movement towards the target (covert). The current study was designed to extract relevant features by using steady-state visual evoked potentials (SSVEP) task. SSVEP task was presented to subjects at the same time that the electroencephalography (EEG) signals were recorded by the scalp electrodes. Subjects were instructed to respond to a certain stimulus by pressing a button. This way attention was measured in continuous manner. Results showed that the amplitude of SSVEP frequencies is higher in overt than covert attention. This indicates that by overt attention events are registered with larger power. However, exploring the harmonics of frequencies showed that covert attention generates larger 2nd harmonic (e.g. 12Hz) than the 1st harmonic (e.g. 6Hz). This pattern was not observed in overt attention. We suggest that covert attention increases the non-linearity in the visual system. Results from the source analysis showed that SSVEP signals are extracted from the primary visual cortex in overt attention. However, when covert attention is allocated to SSVEP, frequencies are extracted from parietal and frontal areas. This shows that covert attention recruits higher cognitive function. To test how SSVEPs are represented in higher brain areas, we conducted an invasive multi-unit recording from rhesus monkeys. Monkeys were trained to perform similar SSVEP task. Recording was done from somatosensory (S1) and motor (M1) cortices. Results showed that the neuronal ring rates in S1 and M1 not only increased selectively to attended icker stimulus, but also they were highly synchronized. Moreover, some SSVEP frequencies was enhanced in single neurons. These results showed, for the rst time, that visual attention to repetitive stimuli is able to regulate neuronal activities in S1 and M1 regions.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Copenhagen Center for Health Technology, Copenhagen University Hospital
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Number of pages: 141
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Relations
Projects:
Electrophysiological dynamics of covert and overt visual attention.
Publication: Research › Ph.D. thesis – Annual report year: 2017

End-to-end information extraction without token-level supervision
Most state-of-the-art information extraction approaches rely on token-level labels to find the areas of interest in text. Unfortunately, these labels are time-consuming and costly to create, and consequently, not available for many real-life IE tasks. To make matters worse, token-level labels are usually not the desired output, but just an intermediary step. End-to-end (E2E) models, which take raw text as input and produce the desired output directly, need not depend on token-level labels. We propose an E2E model based on pointer networks, which can be trained directly on pairs of raw input and output text. We evaluate our model on the ATIS data set, MIT restaurant corpus and the MIT movie corpus and compare to neural baselines that do use token-level labels. We achieve competitive results, within a few percentage points of the baselines, showing the feasibility of E2E information extraction without the need for token-level labels. This opens up new possibilities, as for many tasks currently addressed by human extractors, raw input and output data are available, but not token-level labels.

General information
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Organisations: Department of Applied Mathematics and Computer Science, Cognitive Systems, Copenhagen Center for Health Technology, Tradeshift, Københavns Universitet
Authors: Palm, R. B. (Intern), Hovy, D. (Forskerdatabase), Laws, F. (Ekstern), Winther, O. (Intern)
Number of pages: 5
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Journal: ArXiv
Volume: 2017
Engineering Value-Effective Healthcare Solutions: A Systems Design Perspective

Our modern healthcare systems commonly face an important dilemma. While they depend on innovation to provide continuously greater healthcare value, they also struggle financially with the burden of adopting a continuous flow of new products and services. Although several disruptive healthcare models, i.e. decentralised, personalised, pervasive, connected, and stratified, promise to relieve some of this tension, they do not per se guarantee optimal value generation.

We argue that systems thinking and engineering design can remedy this limitation. We support this claim by making the case of Design for Evolvability and by elaborating on two examples: MRI systems and Point-of-Care in-vitro diagnostics solutions. We specifically argue that Design for Evolvability can realign the agendas of various healthcare stakeholders, serving both individual and national interests. We finally acknowledge the limitations of current engineering design practices and call for new theoretical and empirical research initiatives taking a systems perspective on healthcare product and service design.

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State: Published
Organisations: Copenhagen Center for Health Technology, Department of Management Engineering, Engineering Systems
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Pages: 31-41
Publication date: 2017

Enhancing User Experience in Next Generation Mobile Devices Using Eye Tracking as a Biometric Sensor

A good User Experience is not about just “getting the job done” in the most efficient way. It is also about the subjective elements, providing a positive experience to the user while doing so; emotionally and affectively, having the user engage with the service or product.

Knowing when this takes place means we need ways of measuring concepts like attention. The basis for this should preferably be rooted in our understanding of the anatomically based attention networks of the brain.

This thesis looks at biometric markers of cognitive and affective processes; at the overview level Electroencephalography (EEG), Galvanic Skin Conductance (GSR), Heart Rate and Heart Rate Variability as well as Face Expression Detection – and in much more detail Eye Tracking.

A simple framework for relating eye movements and pupil dilations to the visual processing system and to the attentional networks is suggested. It is demonstrated that it is possible to identify components of attention and cognitive load using low cost eye tracking in conventional office settings. It is also shown that aspects of surprise, similar to negativity feedback error coding, is measurable. Behavioural patterns possibly related to time on target, cognitive load, performance or stimuli are inferred. The existence of possibly unique individual gaze patterns related to visual stimuli or to the brain’s Default Mode Network are shown.

A way of synchronizing EEG and Eye Tracking is also suggested, and in addition, a few software assets (a Python interface to The Eye Tribe tracker and an implementation of the Attention Network Test (ANT)) have been created.

General information
Environmental influences on ovarian dysgenesis - developmental windows sensitive to chemical exposures

A woman's reproductive health and ability to have children directly affect numerous aspects of her life, from personal well-being and socioeconomic standing, to morbidity and lifespan. In turn, reproductive health depends on the development of correctly functioning ovaries, a process that starts early during fetal life. Early disruption to ovarian programming can have long-lasting consequences, potentially manifesting as disease much later in adulthood. A growing body of evidence suggests that exposure to chemicals early in life, including endocrine-disrupting chemicals, can cause a range of disorders later in life, such as those described in the ovarian dysgenesis syndrome hypothesis. In this Review, we discuss four specific time windows during which the ovary is particularly sensitive to disruption by exogenous insults: gonadal sex determination, meiotic division, follicle assembly and the first wave of follicle recruitment. To date, most evidence points towards the germ cell lineage being the most vulnerable to chemical exposure, particularly meiotic division and follicle assembly. Environmental chemicals and pharmaceuticals, such as bisphenols or mild analgesics (including paracetamol), can also affect the somatic cell lineages. This Review summarizes our current knowledge pertaining to environmental chemicals and pharmaceuticals, and their potential contributions to the development of ovarian dysgenesis syndrome. We also highlight knowledge gaps that need addressing to safeguard female reproductive health.
Fatty acid composition and phospholipid types used in infant formulas modifies the establishment of human gut bacteria in germ-free mice

Human milk fat contains high concentrations of medium-chained fatty acids (MCFA) and triacylglycerols emulsified by a sphingomyelin-rich phospholipid membrane (milk phospholipids, MPL). Infant formula comprises mainly long-chained fatty acids (LCFA) emulsified with dairy proteins and soy lecithin (SL) lacking sphingomyelin. Sphingomyelin content and saturation level of phospholipids affect the gut lipase activity, which alters the concentrations of lipid hydrolysis products in ileum and colon, and hereby putatively affects the competitive advantage of specific gut bacteria. Thus, differences in phospholipid and FA composition may modulate the establishment of the gut microbiota. We investigated effects of fatty acid (FA) composition and emulsification (MPL vs SL) ingested during establishment of human gut microbiota in germ-free mice, and found that cecal microbiotas from mice given MCFA-rich emulsions were characterized by high relative abundances of Bacteroidaceae and Desulfovibrionaceae, while LCFA-rich emulsions caused higher abundances of Enterobacteriaceae, Erysipelotrichaceae, Coriobacteriaceae and Enterococcaceae. Consumption of SL-emulsified lipids skewed the community towards more Enterococcaceae and Enterobacteriaceae, while MPL increased Bacteroidaceae, Desulfovibrionaceae, Rikkenellaceae and Porphyromonadaceae. Intake of SL increased cecal concentrations of iso-valeric and iso-butyric acids. This suggests that fat-type and emulsifiers applied in infant formula may have distinct effects on the establishment of the gut microbiota in formula-fed infants.

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First Foods and Gut Microbes
The establishment of the human gut microbiota in early life has been associated with later health and disease. During the first months after birth, the microbial composition in the gut is known to be affected by the mode of delivery, use of antibiotics, geographical location and type of feeding (breast/formula). Consequently, the neonatal period and early infancy have attracted much attention. However, after this first period the gut microbial composition continues to develop until the age of 3 years, and these first years have been designated "a window of opportunity" for microbial modulation. The beginning and end of this window is currently debated, but it likely coincides with the complementary feeding period, marking the gradual transition from milk-based infant feeding to family diet usually occurring between 6 and 24 months. Furthermore, the 'first 1000 days,' i.e., the period from conception until age 2 years, are generally recognized to be of particular importance for the healthy development of children. While dietary changes are known to affect the adult gut microbiota, there is a gap in our knowledge on how the introduction of new dietary components into the diet of infants/young children affects the gut microbiota development. This perspective paper summarizes the currently very few studies addressing the effects of complementary diet on gut microbiota, and highlights the recent finding that transition to family foods greatly impacts the development of gut microbial diversity. Further, we discuss potential impacts on child health and the need for further studies on this important topic.
Flexible Method for the Automated Offline-Detection of Artifacts in Multi-Channel Electroencephalogram Recordings

Electroencephalogram (EEG) signal quality is often compromised by artifacts that corrupt quantitative EEG measurements used in clinical applications and EEG-related studies. Techniques such as filtering, regression analysis and blind source separation are often used to remove these artifacts. However, these preprocessing steps do not allow for complete artifact correction. We propose a method for the automated offline-detection of remaining artifacts after preprocessing in multi-channel EEG recordings. In contrast to existing methods it requires neither adaptive parameters varying between recordings nor a topography template. It is suited for short EEG segments and is flexible with regard to target applications. The algorithm was developed and tested on 60 clinical EEG samples of 20 seconds each that were recorded both in resting state and during cognitive activation to gain a realistic artifact set. Five EEG features were used to quantify temporal and spatial signal variations. Two distance measures for the single-channel and multi-channel variations of these features were defined. The global thresholds were determined by three-fold cross-validation and Youden’s J statistic in conjunction with receiver operating characteristics (ROC curves). We observed high sensitivity of 95.5%±4.8 and specificity of 88.8%±2.1. The method has thus shown great potential and is promising as a possible tool for both EEG-based clinical applications and EEG-related research.

General information
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Foreign object detection in multispectral X-ray images of food items using sparse discriminant analysis

Non-invasive food inspection and quality assurance are becoming viable techniques in food production due to the introduction of fast and accessible multispectral X-ray scanners. However, the novel devices produce massive amounts of data and there is a need for fast and accurate algorithms for processing it. We apply a sparse classifier for foreign object detection and segmentation in multispectral X-ray. Using sparse methods makes it possible to potentially use fewer variables than traditional methods and thereby reduce acquisition time, data volume and classification speed. We report our results on two datasets with foreign objects, one set with spring rolls and one with minced meat. Our results indicate that it is possible to limit the amount of data stored to 50% of the original size without affecting classification accuracy of materials used for training. The method has attractive computational properties, which allows for fast classification of items in new images.

From Raw Data to Social Systems - Separating the Signal from the Noise in Smartphone Sensor Measurements

Digital tools for communication and information exchange have been ingrained in our lives. We google our information and we skype our parents. We use the Internet to shop for groceries, do banking, and study. We play massively multiplayer online games, belong to online communities, and date online. However, this does not mean that our lives have really moved to the digital domain. Even though the Internet makes it possible to exist without ever leaving the confines of our bedrooms, we still choose to meet our friends in person or to travel through physical, rather than virtual, space. There is a richness to personal contact and direct experience that has not yet been replaced by the digital services. Until this shift happens, we continue to analyze and investigate our offline lives in the pursuit for deepening our understanding of human nature. Digital breadcrumbs, which we leave behind with every online action, are relatively easy to collect. Capturing our offline behaviors, on the other hand, is not trivial. Scientist often rely on data that approximates only one aspect of our
lives. For example, mobile operator logs reveal who we call, but not who we meet. An alternative approach is to derive proxies of certain behaviors from smartphone sensor readings. Copenhagen Networks Study (CNS) employs this method, among others, to build the biggest dataset of the kind available to researchers in academia. The thesis shows a path from collecting raw smartphone data for CNS, through extracting increasingly meaningful information, to gaining novel insights into human behavior. Step by step, I turn a cryptic and seemingly uninteresting collection of hardware identifiers and received signal strengths into a detailed record of people’s lives: where they go, who they encounter, who they become friends with. I compare their offline activities and social ties to their online representations and find a surprisingly small overlap. The methods I propose the thesis constitute a more privacy-aware alternative to currently employed social sensing approaches. I show how to track the mobility and interactions of participants without sharing the results with third parties inadvertently. At the same time, the findings presented in this thesis emphasize the fragility of our privacy: the data we today consider as safe to share today, tomorrow might prove to carry rich information about our lives.

General information
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Generative Temporal Modelling of Neuroimaging - Decomposition and Nonparametric Testing
The goal of this thesis is to explore two improvements for functional magnetic resonance imaging (fMRI) analysis; namely our proposed decomposition method and an extension to the non-parametric testing framework. Analysis of fMRI allows researchers to investigate the functional processes of the brain, and provides insight into neuronal coupling during mental processes or tasks.

The decomposition method is a Gaussian process-based independent components analysis (GPICA), which incorporates a temporal dependency in the sources. A hierarchical model specification is used, featuring both instantaneous and convolutive mixing, and the inferred temporal patterns. Spatial maps are seen to capture smooth and localized stimuli-related components, and often identifiable noise components. The implementation is freely available as a GUI/SPM plugin, and we recommend using GPICA as an additional tool when performing ICA on fMRI data to investigate the effect of the temporal source prior.

In fMRI, statistical tests are used to investigate the significance of activation in specific brain regions. By extending the non-parametric testing framework to incorporate functional prior knowledge, an increase in sensitivity can be achieved, entailing better evaluations and conclusions. The functional prior knowledge is incorporated by use of a proposed Graph-Based Cluster Permutation Test (GBCPT), entailing the possibility to expand the use of cluster permutations to multiple applications, wherever a graph-based setup can be used.

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Glyphosate has limited short-term effects on commensal bacterial community composition in the gut environment due to sufficient aromatic amino acid levels

Recently, concerns have been raised that residues of glyphosate-based herbicides may interfere with the homeostasis of the intestinal bacterial community and thereby affect the health of humans or animals. The biochemical pathway for aromatic amino acid synthesis (Shikimate pathway), which is specifically inhibited by glyphosate, is shared by plants and numerous bacterial species. Several in vitro studies have shown that various groups of intestinal bacteria may be differently affected by glyphosate. Here, we present results from an animal exposure trial combining deep 16S rRNA gene sequencing of the bacterial community with liquid chromatography mass spectrometry (LC-MS) based metabolic profiling of aromatic amino acids and their downstream metabolites. We found that glyphosate as well as the commercial formulation Glyfonova®450 PLUS administered at up to fifty times the established European Acceptable Daily Intake (ADI = 0.5 mg/kg body weight) had very limited effects on bacterial community composition in Sprague Dawley rats during a two-week exposure trial. The effect of glyphosate on prototrophic bacterial growth was highly dependent on the availability of aromatic amino acids, suggesting that the observed limited effect on bacterial composition was due to the presence of sufficient amounts of aromatic amino acids in the intestinal environment. A strong correlation was observed between intestinal concentrations of glyphosate and intestinal pH, which may partly be explained by an observed reduction in acetic acid produced by the gut bacteria. We conclude that sufficient intestinal levels of aromatic amino acids provided by the diet alleviates the need for bacterial synthesis of aromatic amino acids and thus prevents an antimicrobial effect of glyphosate in vivo. It is however possible that the situation is different in cases of human malnutrition or in production animals.
High-fat feeding rather than obesity drives taxonomical and functional changes in the gut microbiota in mice

**Background:** It is well known that the microbiota of high-fat (HF) diet-induced obese mice differs from that of lean mice, but to what extent, this difference reflects the obese state or the diet is unclear. To dissociate changes in the gut microbiota associated with high HF feeding from those associated with obesity, we took advantage of the different susceptibility of C57BL/6J(BomTac (BL6) and 129S6/SvEvTac (Sv129) mice to diet-induced obesity and of their different responses to inhibition of cyclooxygenase (COX) activity, where inhibition of COX activity in BL6 mice prevents HF diet-induced obesity, but in Sv129 mice accentuates obesity.

**Results:** Using HiSeq-based whole genome sequencing, we identified taxonomic and functional differences in the gut microbiota of the two mouse strains fed regular low-fat or HF diets with or without supplementation with the COX-inhibitor, indomethacin. HF feeding rather than obesity development led to distinct changes in the gut microbiota. We observed a robust increase in alpha diversity, gene count, abundance of genera known to be butyrate producers, and abundance of genes involved in butyrate production in Sv129 mice compared to BL6 mice fed either a LF or a HF diet. Conversely, the abundance of genes involved in propionate metabolism, associated with increased energy harvest, was higher in BL6 mice than Sv129 mice.

**Conclusions:** The changes in the composition of the gut microbiota were predominantly driven by high-fat feeding rather than reflecting the obese state of the mice. Differences in the abundance of butyrate and propionate producing bacteria in the gut may at least in part contribute to the observed differences in obesity propensity in Sv129 and BL6 mice.
Improved detection of chemical substances from colorimetric sensor data using probabilistic machine learning

We present a data-driven machine learning approach to detect drug- and explosives-precursors using colorimetric sensor technology for air-sampling. The sensing technology has been developed in the context of the CRIM-TRACK project. At present a fully-integrated portable prototype for air sampling with disposable sensing chips and automated data acquisition has been developed. The prototype allows for fast, user-friendly sampling, which has made it possible to produce large datasets of colorimetric data for different target analytes in laboratory and simulated real-world application scenarios. To make use of the highly multi-variate data produced from the colorimetric chip a number of machine learning techniques are employed to provide reliable classification of target analytes from confounders found in the air streams. We demonstrate that a data-driven machine learning method using dimensionality reduction in combination with a probabilistic classifier makes it possible to produce informative features and a high detection rate of analytes. Furthermore, the probabilistic machine learning approach provides a means of automatically identifying unreliable measurements that could produce false predictions. The robustness of the colorimetric sensor has been evaluated in a series of experiments focusing on the amphetamine pre-cursor phenylacetone as well as the improvised explosives pre-cursor hydrogen peroxide. The analysis demonstrates that the system is able to detect analytes in clean air and mixed with substances that occur naturally in real-world sampling scenarios. The technology under development in CRIM-TRACK has the potential as an effective tool to control trafficking of illegal drugs, explosive detection, or in other law enforcement applications.

General information

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Bibliographical note
Inferring human intentions from the brain data

The human brain is a massively complex organ composed of approximately a hundred billion densely interconnected, interacting neural cells. The neurons are not wired randomly - instead, they are organized in local functional assemblies. It is believed that the complex patterns of dynamic electric discharges across the neural tissue are responsible for emergence of high cognitive function, conscious perception and voluntary action. The brain's capacity to exercise free will, or internally generated free choice, has long been investigated by philosophers, psychologists and neuroscientists. Rather than assuming a causal power of conscious will, the neuroscience of volition is based on the premise that "mental states rest on brain processes", and hence by measuring spatial and temporal correlates of volition in carefully controlled experiments we can infer about their underlying mind processes, including concepts as intriguing as "free will", "agency" and "consciousness". Recent developments in electrophysiology and neuroimaging methods allow for increasingly more accurate estimation of spatial and temporal characteristics of decision processes.

The work presented in this thesis is intended to contribute to our understanding of the dynamics of voluntary decision processes about prospective action. In the two presented studies we probe different types of decisions and compare them in terms of behavioral and EEG characteristics. We show that decision processes are manifested by complex, broadband modulation of brain oscillatory patterns, primarily in Alpha (8-12Hz) and Beta (16-30Hz) ranges. Our results suggest that decisions about whether to act or not, what type of action to perform, and about the timing of the action have distinct dynamic representations, and thus are to some extent mediated by different neural components. Furthermore, free action can be partially explained by low level behavioral preferences, especially in contexts where no explicit incentive favors one action over an other.

Apart from the investigation of volition, considerable part of the work presented in this thesis is dedicated to experiment design methodology and efficient EEG processing methods. We have developed a dedicated, flexible Virtual Reality Environment (VRE) platform, suitable for investigation of volition and action preparation processes with range of modalities, including electroencephalography (EEG), functional magnetic resonance (fMRI), eye-tracking (ET) and behavioral measures. By providing ecologically valid, semi-realistic experience we aimed at reinforcing the natural decision processes and minimize the problem of random-sequence generation and fatigue in participants undergoing highly repeatable cognitive experiments. Other methodological contributions presented in the thesis are related to efficient, automatized and highly data-preserving methods for processing of EEG data, based on minimal number of arbitrarily selected parameters.

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Integrated single- and two-photon light sheet microscopy using accelerating beams

We demonstrate the first light sheet microscope using propagation invariant, accelerating Airy beams that operates both in single- and two-photon modes. The use of the Airy beam permits us to develop an ultra compact, high resolution light sheet system without beam scanning. In two-photon mode, an increase in the field of view over the use of a standard Gaussian beam by a factor of six is demonstrated. This implementation for light sheet microscopy opens up new possibilities across a wide range of biomedical applications, especially for the study of neuronal processes.
Integrating experiences from operations into engineering design: modelling knowledge transfer in the offshore oil industry

Summative Statement: Integrating human factors and users’ experiences in design projects is a well-known challenge. This study focuses on the specific challenges for transferring these experiences and how using a knowledge transfer model can help this integration on the design of high-risk productive work systems, such as offshore oil rigs.

Problem statement: Poorly designed workspaces result in adverse effects on occupational health and safety, as well as reduced efficiency and productivity. In large-scale engineering projects and, in special the offshore oil sector that has to face geographical and workwise distance between operations and engineering design teams, integrating human factors and transferring knowledge are key aspects when designing for better performance systems.

Research Objective: Based on an in-depth empirical investigation in an offshore oil company, this study aims to provide a framework for the knowledge transfer process from operations into engineering design that helps identifying and facing the challenges for such a transfer process.

Methodology: The study was carried out as a case study in an offshore oil company. We used the empirical data collected through interviews and surveys to identify the main challenges for the knowledge transfer process based on a pragmatic 4-step framework. At a later stage, we developed a set of requirements to improve the knowledge transfer from operations into design.

Results: Knowledge transfer implies the knowledge to be 1) captured on the operating units, 2) transformed into an engineering design context, 3) transferred to the appropriate project team members, and finally 4) applied throughout the design process of new installations. It is a four-step process involving challenges going from not having specific performance indicators encouraging rig workers to focus on capturing knowledge targeted to design to not having this knowledge available to be applied at the right time in the projects, making it at times impossible to implement in terms of design specifications. Challenges also pass through dealing with the large amount of knowledge registered in the systems without standards to categorise and store this knowledge, to being difficult to access and retrieve the knowledge in the systems.

Discussion: Transferring knowledge and experiences from users brings human factors into play and modelling the knowledge transfer process provides a better idea of what is involved. The entire process requires a continuous flow in order to develop a permanent repository that is continuously updated and is used to optimise the design towards better system performance. Overall, the requirements developed based on the identified challenges point to the need to have clear procedures and standards to capture the operational knowledge, as well as an alignment of the key performance indicators related to the knowledge transfer process, since it will allow for better collaboration and communication between the two divisions. Furthermore, clear methods and resources to systematise and transform the knowledge, together with appropriate methods to make it available to the project teams are paramount.

Conclusions: Using a framework helps to identify challenges is of importance for both practitioners and researchers, since it 1) helps developing practical requirements for improving knowledge transfer and 2) supports framing the knowledge transfer process in a systematic way, allowing for comparison within different cases towards generalising the findings.
been gained within the field of macro-ergonomics. It is suggested that the Participatory Ergonomics Framework (PEF) validated by Haines et al. (2002) needs to be updated based on these experiences and hence more focussed on design activities.

Research Objective / Question: The objective of this study was to update and design-orient the PEF based on experiences with PDPs within the last ten years.

Methodology: Five participatory design projects across different industries were systematically analyzed and compared in order to develop a framework pointing to supportive theory and practical guidance for ergonomics practitioners. The five PDPs were based in the following industries: construction, public service, food processing, and two healthcare projects. The starting point for the analysis was the notion of work systems meeting each other in the intervention into design projects by ergonomists/researchers.

Results: The nine dimensions and categories in the framework by Haines et al. (2002) are still relevant. However, they are not entirely oriented towards design projects and the framework do not include the dynamics between the ergonomist/researcher and the design activities going on in a company. It is suggested to add the following dimensions to the PEF: Involved work systems, type of interaction between the ergonomist work system and the company design work systems, transfer and integration of results from PDPs into the overall design project in the company.

Discussion: The proposed update of the PEF introduces a dynamic understanding of PDPs by the notion that PDP’s may be seen as interactions between different work systems, including those of the ergonomist/researcher, company designers, consultants, and technology suppliers. By an initial mapping the relevant work systems, the intervention by ergonomists may be better planned and better ensure a real impact on the overall design project. This is of importance because many PDPs have an intermittent and temporary character. The notion of interaction between different work systems also allows for theories on how ergonomists/researchers can impact design projects by facilitating participatory schemes.

Conclusions: This study suggested an updating of the PEF in order to include the dynamics between an ergonomist work systems with its own goals and rationale and a number of company work systems involved in design projects and having other goals and rationales. The updated framework are aimed at guidance in planning and conduction PDPs.

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Low Cost and Flexible UAV Deployment of Sensors
This paper presents a platform for airborne sensor applications using low-cost, open-source components carried by an easy-to-fly unmanned aircraft vehicle (UAV). The system, available in open-source, is designed for researchers, students and makers for a broad range of exploration and data-collection needs. The main contribution is the extensible architecture for modularized airborne sensor deployment and real-time data visualisation. Our open-source Android application provides data collection, flight path definition and map tools. Total cost of the system is below 800 dollars. The flexibility of the system is illustrated by mapping the location of Bluetooth beacons (iBeacons) on a ground field and by measuring water temperature in a lake.

General information
State: Published
Organisations: Department of Management Engineering, Technology and Innovation Management, Copenhagen Center for Health Technology, Transport DTU, IT University of Copenhagen
Medial structure generation for registration of anatomical structures

Medial structures (skeletons and medial manifolds) have shown capacity to describe shape in a compact way. In the field of medical imaging, they have been employed to enrich the description of organ anatomy, to improve segmentation, or to describe the organ position in relation to surrounding structures. Methods for generation of medial structures, however, are prone to the generation of medial artifacts (spurious branches) that traditionally need to be pruned before the medial structure can be used for further computations. The act of pruning can affect main sections of the medial surface, hindering its performance as shape descriptor. In this work, we present a method for the computation of medial structures that generates smooth medial surfaces that do not need to be explicitly pruned. Additionally, we present a validation framework for medial surface evaluation. Finally, we apply this method to create a parametric model of the cochlea shape that yields better registration results between cochleae.
Microbiota composition of simultaneously colonized mice housed under either a gnotobiotic isolator or individually ventilated cage regime

Germ-free rodents colonized with microbiotas of interest are used for host-microbiota investigations and for testing microbiota-targeted therapeutic candidates. Traditionally, isolators are used for housing such gnotobiotic rodents due to optimal protection from the environment, but research groups focused on the microbiome are increasingly combining or substituting isolator housing with individually ventilated cage (IVC) systems. We compared the effect of housing systems on the gut microbiota composition of germ-free mice colonized with a complex microbiota and housed in either multiple IVC cages in an IVC facility or in multiple open-top cages in an isolator during three generations and five months. No increase in bacterial diversity as assessed by 16S rRNA gene sequencing was observed in the IVC cages, despite not applying completely aseptic cage changes. The donor bacterial community was equally represented in both housing systems. Time-dependent clustering between generations was observed in both systems, but was strongest in the IVC cages. Different relative abundance of a Rikenellaceae genus contributed to separate clustering of the isolator and IVC communities. Our data suggest that complex microbiotas are protected in IVC systems, but challenges related to temporal dynamics should be addressed.
Modeling Pharmacokinetics and Pharmacodynamics of Glucagon for Simulation of the Glucoregulatory System in Patients with Type 1 Diabetes.

The goal of this thesis was to develop a pharmacokinetics/pharmacodynamics (PK/PD) model for glucagon. The proposed PD model included multiplication of the stimulating glucagon effect and inhibiting insulin effect on the endogenous glucose production (EGP). Moreover, the concentration-response relationship of glucagon and EGP was characterized by a non-linear function, where the response saturated for high concentrations of glucagon. The novel EGP model extended Hovorka's glucoregulatory model to include the effect of glucagon. The PK/PD model described both regular glucagon and a novel glucagon analogue in healthy dogs. The extended glucoregulatory model translated to the human species and described glucose-insulin-glucagon dynamics in healthy subjects and patients with type 1 diabetes (T1D). The extended glucoregulatory model was successfully validated by leave-one-out cross-validation in seven T1D patients which justified its use for simulations. The model replicated a clinical study of the effect of glucagon at varying insulin levels. The simulations also suggested new glucagon doses to be tested in a similar in vivo study to provide new insight to the relationship between insulin, glucagon, and EGP. Finally, the model was used to conduct a large original simulation study investigating an insulin dependent glucagon dosing regimen for treatment of insulin-induced mild hypoglycemia.

General information
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Multi-scale spatio-temporal analysis of human mobility
The recent availability of digital traces generated by phone calls and online logins has significantly increased the scientific understanding of human mobility. Until now, however, limited data resolution and coverage have hindered a coherent description of human displacements across different spatial and temporal scales. Here, we characterise mobility behaviour across several orders of magnitude by analysing similar to 850 individuals’ digital traces sampled every similar to 16 seconds for 25 months with similar to 10 meters spatial resolution. We show that the distributions of distances and waiting times between consecutive locations are best described by log-normal and gamma distributions, respectively, and that natural time-scales emerge from the regularity of human mobility. We point out that log-normal distributions also characterise the patterns of discovery of new places, implying that they are not a simple consequence of the routine of modern life.
Novel Approach for Automatic Detection of Atrial Fibrillation Based on Inter Beat Intervals and Support Vector Machine

Atrial fibrillation (AF) is the most common cardiac arrhythmia associated with a major economic burden for the society. Automatic detection of AF in long term recordings can efficiently assist in early diagnosis and management of comorbidities associated with AF. This study presents a novel approach for AF detection based on Inter Beat Intervals (IBI) extracted from long term electrocardiogram (ECG) recordings. Five time-domain features are extracted from the IBIs and a Support Vector Machine (SVM) is used for classification. The results are compared to a state of the art algorithm based on raw ECG. Both algorithms are evaluated on the MIT-BIH Atrial Fibrillation database resulting in equally high classification performance (Sensitivity ≥ 95%). The proposed approach requires detection of R-peaks in the ECG signal but allows for significantly reduced computation time without loss of performance.

On the Keyhole Hypothesis: High Mutual Information between Ear and Scalp EEG

We propose and test the keyhole hypothesis that measurements from low dimensional EEG, such as ear-EEG reflect a broadly distributed set of neural processes. We formulate the keyhole hypothesis in information theoretical terms. The experimental investigation is based on legacy data consisting of 10 subjects exposed to a battery of stimuli, including alpha-attenuation, auditory onset, and mismatch-negativity responses and a new medium-long EEG experiment involving data acquisition during 13 h. Linear models were estimated to lower bound the scalp-to-ear capacity, i.e., predicting ear-EEG data from simultaneously recorded scalp EEG. A cross-validation procedure was employed to ensure unbiased estimates. We present several pieces of evidence in support of the keyhole hypothesis: There is a high mutual information between data acquired at scalp electrodes and through the ear-EEG "keyhole," furthermore we show that the view represented as a linear mapping is stable across both time and mental states. Specifically, we find that ear-EEG data can be predicted reliably from scalp EEG. We also address the reverse view, and demonstrate that large portions of the scalp EEG can be predicted from ear-EEG, with the highest predictability achieved in the temporal regions and when using ear-EEG electrodes with a common reference electrode.
Open semantic analysis: The case of word level semantics in Danish

The present research is motivated by the need for accessible and efficient tools for automated semantic analysis in Danish. We are interested in tools that are completely open, so they can be used by a critical public, in public administration, non-governmental organizations and businesses. We describe data-driven models for Danish semantic relatedness, word intrusion and sentiment prediction. Open Danish corpora were assembled and unsupervised learning implemented for explicit semantic analysis and with Gensim’s Word2vec model. We evaluate the performance of the two models on three different annotated word datasets. We test the semantic representations’ alignment with single word sentiment using supervised learning. We find that logistic regression and large random forests perform well with Word2vec features.
Optical Coherence Tomography

Optical coherence tomography (OCT) is a technique that is used to peer inside a body noninvasively. Tissue structure defined by tissue absorption and scattering coefficients, and the speed of blood flow, are derived from the characteristics of light remitted by the body. Singly backscattered light detected by partial coherence interferometry (PCI) is used to synthesize the tomographic image coded in false colors. A prerequisite of this technique is a low time-coherent but high space-coherent light source, for example, a superluminescent diode or a supercontinuum source. Alternatively, the imaging technique can be realized by using ultrafast wavelength scanning light sources. For tissue imaging, the light source wavelengths are restricted to the red and near-infrared (NIR) region from about 600 to 1300 nm, the so-called therapeutic window, where absorption ($\mu_a \approx 0.01 \text{ mm}^{-1}$) is small enough. Transverse resolution in OCT is diffraction limited, as in conventional imaging; depth resolution is limited by the coherence length of the light. Both figures are of the order of micrometers. Velocity resolution is of the order of $0.1 \text{ mm s}^{-1}$. Several instruments are commercially available. At present, OCT is mainly used in the medical field, in particular, in ophthalmology. Owing to the high transmissivity of ocular media, the depth penetration is considerable. Corresponding applications in dermatology are somewhat hindered by the strong scattering of epidermic tissue ($\mu_s \approx 10^2 \text{ mm}^{-1}$). As OCT provides images with a resolution comparable to conventional histology, but in real time, it can be used as a biopsy technique in a wide range of biological systems to detect diseases. These include the tomographic imaging of the internal microstructure of in vivo atherosclerotic plaques, the tomographic real-time diagnostics for intraoperative monitoring, and in microsurgical intervention. Optical biopsy based on OCT also provides diagnostic information by differentiating the architectural morphology of urological tissue, gastrointestinal tissue, and respiratory tissue.
Playware ABC: Engineering Play for Everybody
This paper describes the Playware ABC concept, and how it allows anybody, anywhere, anytime to be building bodies and brains, which facilitates users to construct, combine and create. The Playware ABC concept focuses engineering and IT system development on creating solutions that are usable by all kinds of users and contexts. The result becomes solutions, often based on modular technologies that are highly flexible and adaptable to different contexts, users, and applications.

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Pre-treatment microbial Prevotella-to-Bacteroides ratio, determines body fat loss success during a 6-month randomized controlled diet Intervention
Based on the abundance of specific bacterial genera, the human gut microbiota can be divided into two relatively stable groups that might play a role in personalized nutrition. We studied these simplified enterotypes as prognostic markers for successful body fat loss on two different diets. A total of 62 participants with increased waist circumference were randomly assigned to receive an ad libitum New Nordic Diet (NND) high in fiber/wholegrain or an Average Danish Diet (ADD) for 26 weeks. Participants were grouped into two discrete enterotypes by their relative abundance of Prevotella spp. divided by Bacteroides spp. (P/B ratio) obtained by quantitative PCR analysis. Modifications of dietary effects of pre-treatment P/B group were examined by linear mixed models. Among individuals with high P/B the NND resulted in a 3.15 kg (95%CI 1.55;4.76, P<0.001) larger body fat loss compared to ADD whereas no differences was observed among individuals with low P/B (0.88 kg [95% CI −0.61;2.37, P=0.25]). Consequently, a 2.27 kg (95%CI 0.09;4.45, P=0.041) difference in responsiveness to the diets were found between the two groups. In summary, subjects with high P/B-ratio appeared more susceptible to lose body fat on diets high in fiber and wholegrain than subjects with a low P/B-ratio.

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Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology, Gelesis Inc., University of Copenhagen
Reducing the rate and duration of re-admissions among patients with unipolar disorder and bipolar disorder using smartphone-based monitoring and treatment - the RADMIS trials: Study protocol for two randomized controlled trials

Background: Unipolar and bipolar disorder combined account for nearly half of all morbidity and mortality due to mental and substance use disorders, and burden society with the highest health care costs of all psychiatric and neurological disorders. Among these, costs due to psychiatric hospitalization are a major burden. Smartphones comprise an innovative and unique platform for the monitoring and treatment of depression and mania. No prior trial has investigated whether the use of a smartphone-based system can prevent re-admission among patients discharged from hospital. The present RADMIS trials aim to investigate whether using a smartphone-based monitoring and treatment system, including an integrated clinical feedback loop, reduces the rate and duration of re-admissions more than standard treatment in unipolar disorder and bipolar disorder. Methods: The RADMIS trials use a randomized controlled, single-blind, parallel-group design. Patients with unipolar disorder and patients with bipolar disorder are invited to participate in each trial when discharged from psychiatric hospitals in The Capital Region of Denmark following an affective episode and randomized to either (1) a smartphone-based monitoring system including (a) an integrated feedback loop between patients and clinicians and (b) context-aware cognitive behavioral therapy (CBT) modules (intervention group) or (2) standard treatment (control group) for a 6-month trial period. The trial started in May 2017. The outcomes are (1) number and duration of re-admissions (primary), (2) severity of depressive and manic (only for patients with bipolar disorder) symptoms; psychosocial functioning; number of affective episodes (secondary), and (3) perceived stress, quality of life, self-rated depressive symptoms, self-rated manic symptoms (only for patients with bipolar disorder), recovery, empowerment, adherence to medication, wellbeing, ruminations, worrying, and satisfaction (tertiary). A total of 400 patients (200 patients with unipolar disorder and 200 patients with bipolar disorder) will be included in the RADMIS trials. Discussion: If the smartphone-based monitoring system proves effective in reducing the rate and duration of readmissions, there will be basis for using a system of this kind in the treatment of unipolar and bipolar disorder in general and on a larger scale.

General information

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BFI (2010): BFI-level 1
Rethinking Hearing Aid Fitting by Learning From Behavioral Patterns

The recent introduction of Internet connected hearing instruments offers a paradigm shift in hearing instrument fitting. Potentially this makes it possible for devices to adapt their settings to a changing context, inferred from user interactions. In a pilot study we enabled hearing instrument users to remotely enhance auditory focus and attenuate background noise to improve speech intelligibility. N=5, participants changed program settings and adjusted volume on their hearing instruments using their smartphones. We found that individual behavioral patterns affected the usage of the devices. A significant difference between program usage, and weekdays versus weekends, were found. Users not only changed programs to modify aspects of directionality and noise reduction, but also continuously adjusted the volume. Rethinking hearing instruments as devices that adaptively learn behavioral patterns based on user interaction, might provide a degree of personalization that has not been feasible due to lack of audiological resources.

Security And Privacy Issues In Healthcare Monitoring Systems: A Case Study

Security and privacy issues are rarely taken into account in automated systems for monitoring elderly people in their home, exposing inhabitants to a number of threats they are usually not aware of. As a case study to expose the major vulnerabilities these systems are exposed to, this paper reviews a generic example of automated healthcare monitoring system. The security and privacy issues identified in this case study can be easily generalised and regarded as alarm bells for all the pervasive healthcare professionals.
Semi-Supervised Generation with Cluster-aware Generative Models
Deep generative models trained with large amounts of unlabelled data have proven to be powerful within the domain of unsupervised learning. Many real life data sets contain a small amount of labelled data points, that are typically disregarded when training generative models. We propose the Cluster-aware Generative Model, that uses unlabelled information to infer a latent representation that models the natural clustering of the data, and additional labelled data points to refine this clustering. The generative performances of the model significantly improve when labelled information is exploited, obtaining a log-likelihood of −79.38 nats on permutation invariant MNIST, while also achieving competitive semi-supervised classification accuracies. The model can also be trained fully unsupervised, and still improve the log-likelihood performance with respect to related methods.

Sensing behaviour in healthcare design
We are entering an era of distributed healthcare that should fit and respond to individual needs, behaviour and lifestyles. Designing such systems is a challenging task that requires continuous information about human behaviour on a large scale, for which pervasive sensing (e.g. using smartphones and wearables) presents exciting opportunities. While mobile sensing approaches are fuelling research in many areas, their use in engineering design remains limited. In this work, we present a collection of common behavioural measures from literature that can be used for a broad range of applications. We focus specifically on activity and location data that can easily be obtained from smartphones or wearables. We further demonstrate how these are applied in healthcare design using an example from dementia care. Comparing a current and proposed scenario exemplifies how integrating sensor-derived information about user behaviour can support the healthcare design goals of personalisation, adaptability and scalability, while emphasising patient quality of life.
Simulation Approach for Timing Analysis of Genetic Logic Circuits

Constructing genetic logic circuits is an application of synthetic biology in which parts of the DNA of a living cell are engineered to perform a dedicated Boolean function triggered by an appropriate concentration of certain proteins or by different genetic components. These logic circuits work in a manner similar to electronic logic circuits, but they are much more stochastic and hence much harder to characterize. In this article, we introduce an approach to analyze the threshold value and timing of genetic logic circuits. We show how this approach can be used to analyze the timing behavior of single and cascaded genetic logic circuits. We further analyze the timing sensitivity of circuits by varying the degradation rates and concentrations. Our approach can be used not only to characterize the timing behavior but also to analyze the timing constraints of cascaded genetic logic circuits, a capability that we believe will be important for design automation in synthetic biology.
Spatial Filter Feature Extraction Methods for P300 BCI Speller: A Comparison

Brain Computer Interface (BCI) systems enable subjects affected by neuromuscular disorders to interact with the outside world. A P300 speller uses Event Related Potential (ERP) components, generated in the brain in the presence of a target stimulus, to extract information about the user’s intent. Several methods have been proposed for spatial filtering and classification of the P300 components. In this study, xDAWN algorithm, Independent Component Analysis (ICA) and Principal Component Analysis (PCA) methods are used and evaluated based on the classification performance of two different classifiers, namely the Support Vector Machine (SVM) and Fisher’s Linear Discriminant Analysis (FLDA). In addition, it is shown that the incorporation of some prior knowledge regarding the location of P300 elicitation on the scalp can reduce the computational load while maintaining or even improving the classification performance.

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Study protocol: effect of playful training on functional abilities of older adults - a randomized controlled trial

Background: Loss of functional capabilities due to inactivity is one of the most common reasons for fall accidents, and it has been well established that loss of capabilities can be effectively reduced by physical activity. Pilot studies indicate a possible improvement in functional abilities of community dwelling elderly as a result of short-term playing with an exergame system in the form of interactive modular tiles. Such playful training may be motivational to perform and viewed by the subjects to offer life-fulfilling quality, while providing improvement in physical abilities, e.g. related to prevent fall accidents. The RCT will test for a variety of health parameters of community-dwelling elderly playing on interactive modular tiles.

Methods: The study will be a single blinded, randomized controlled trial with 60 community-dwelling adults 70+ years. The trial will consist an intervention group of 30 participants training with the interactive modular tiles, and a control group of 30 participants that will receive the usual care provided to non-patient elderly. The intervention period will be 12 weeks. The intervention group will perform group training (4-5 individuals for 1 h training session with each participant receiving 13 min training) on the interactive tiles twice a week. Follow-up tests include 6-min Walk Test (6MWT), the 8-ft Timed Up & Go Test (TUG), and the Chair-Stand Test (CS) from the Senior Fitness Test, along with balancing tests (static test on Wii Board and Line Walk test). Secondary outcomes related to adherence, motivation and acceptability will be investigated through semi-structured interviews. Data will be collected from pre- and post-tests. Data will be analyzed for statistically significant differences by checking that there is a Gaussian distribution and then using paired t-test, otherwise using Wilcoxon signed-rank test. "Intention to treat" analysis will be done.

Discussion: The trial tests for increased mobility, agility, balancing and general fitness of community-dwelling elderly as a result of playing, in this case on modular interactive tiles. A positive outcome may help preventing loss of functional capabilities due to inactivity.
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System-Level Sensitivity Analysis of SiNW-bioFET-Based Biosensing Using Lockin Amplification

Although Silicon Nanowire biological Field-Effect Transistors (SiNW-bioFETs) have steadily demonstrated their ability to detect biological markers at ultra-low concentration, they have not yet translated into routine diagnostics applications. One of the challenges inherent to the technology is that it requires an instrumentation capable of recovering ultra-low signal variations from sensors usually designed and operated in a highly-resistive configuration. Often overlooked, the SiNWbioFET/instrument interactions are yet critical factors in determining overall system biodetection performances. Here, we carry out for the first time the system-level sensitivity analysis of a generic SiNW-bioFET model coupled to a custom-design instrument based on the lock-in amplifier. By investigating a large parametric space spanning over both sensor and instrumentation specifications, we demonstrate that systemwide investigations can be instrumental in identifying the design trade-offs that will ensure the lowest Limits-of-Detection. The generic character of our analytical model allows us to elaborate on the most general SiNW-bioFET/instrument interactions and their overall implications on detection performances. Our model can be adapted to better match specific sensor or instrument designs to either ensure that ultra-high sensitivity SiNW-bioFETs are coupled with an appropriately sensitive and noise-rejecting instrumentation, or to best tailor SiNW-bioFET design to the specifications of an existing instrument.
Hearing systems have evolved over many years from simple mechanical devices (horns) to electronic units consisting of microphones, amplifiers, analog filters, loudspeakers, batteries, etc. Digital signal processors replaced analog filters to provide better performance and new features. Central processors were added to provide many functions for monitoring and controlling other parts of the devices. Hearing systems have thus evolved into complex embedded systems. Radio systems were added to allow hearing aids to communicate with accessories, auxiliary equipment, third-party products, etc. Many new features are enabled by such radio communication. Monitoring and controlling hearing aids from remote control devices or smart phones have been incorporated into several products. Direct audio streaming between hearing aids and dedicated streaming devices or smart phones is possible with some products. Also emerging are advanced features that are based on interactions with internet services, clouds, etc. Hearing systems are thus evolving into large and complex smart systems. Designing complex embedded systems or large smart systems are notoriously difficult. Many systems are still developed using document-based methods, where requirements and proposed architecture are described textually with the addition of a few figures and tables. Such documents cannot be subjected to testing, so it is impossible to predict the functionality and performance or even feasibility of the intended systems. Replacing documents with models have several advantages. Models can be simulated and analyzed such that functionality and performance can be predicted before any parts have been built. Potential flaws in the specification can therefore be corrected in early phases, which may reduce development effort and costs. This thesis concerns methods for identifying, selecting and implementing tools for various aspects of model-based systems engineering. A comprehensive method was proposed that include several novel steps such as techniques for analyzing the gap between requirements and tool capabilities. The method was verified with good results in two case studies for selection of a traceability tool (single-tool scenario) and a set of modeling tools (multi-tool scenarios). Models must be subjected to testing to allow engineers to predict functionality and performance of systems. Test-first strategies are known to produce good results in software development. This thesis concerns methods for test-driven modeling of hearing systems. A method is proposed for test-driven modeling of embedded systems of medium complexity. It utilizes formal model checking to guarantee functionality and performance. Test-driven design space exploration is enabled by using statistical model checking to obtain estimates that are verified formally at the final stages of the method. The method was applied with good results to a case study, where two solutions to a design problem were developed and verified. Feasible ranges for critical parameters were identified. Both solution conformed to all requirements. Smart systems are typically too large and complex to be verified by formal model checking, and the research showed that statistical model checking in its current form cannot be used for verifying such systems. A new method is therefore proposed for test-driven modeling of smart systems. The method uses formal verification of basic interactions. Simulations are used for verifying the overall system. To predict performance for scenarios that are too large to be simulated, the method uses mathematical forecasting based on simulating series of smaller scenarios, fitting simulation results to estimator functions, and extrapolating beyond the simulated data set. Mathematical forecasting allowed us to predict the performance of system scenarios that were much too large to be simulated. Such performance estimates may be somewhat imprecise but are nevertheless valuable because they provide answers that cannot be
obtained otherwise. The research has thus proposed and verified methods for selecting modeling tools and for test-driven systems modeling for the benefit of GN Hearing and other organizations involved in development of complex embedded systems of large smart systems.

**General information**

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**The Attentional Capture of Colour in Visual Interface Design: A Controlled Environment Study**

The use of colour is an integral component in visual interface design for creating separation between objects and for conveying meaning. It has previously been established that colours can be separated in a hierarchy of primary colours and secondary colours, and that colours are consistently associated with specific mood tones. However, it has thus far not been investigated whether these two factors, which we refer to as the perception-primacy and emotion-conveyance, are associated with attentional capture in a congruent manner. To investigate this, we conducted a visual search task study in a controlled environment, in which 11 participants scanned a 20 item display for a coloured target amongst coloured distractors. We found evidence to support that primary colours capture attention significantly more than secondary colours, and inconclusive evidence that colours convey their meaning at a sufficiently early level of processing to influence attention. We end by discussing implications of our results for design practice and research in psychology.

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**The Internet of Hackable Things**

The Internet of Things makes possible to connect each everyday object to the Internet, making computing pervasive like never before. From a security and privacy perspective, this tsunami of connectivity represents a disaster, which makes each object remotely hackable. We claim that, in order to tackle this issue, we need to address a new challenge in
Towards industry strength mapping of AUTOSAR automotive functionality on multicore architectures: work in progress

The automotive electronic architectures have moved from federated architectures, where one function is implemented in one ECU (Electronic Control Unit), to distributed architectures, consisting of several multicore ECUs. In addition, multicore ECUs are being adopted because of better performance, cost, size, fault-tolerance and power consumption. Automotive manufacturers use AUTomotive Open System ARchitecture (AUTOSAR) as the standardized software architecture for ECUs. With AUTOSAR, the functionality is modeled as a set of software components composed of subtasks, called runnables. In this paper we propose an approach for the automatic software functionality assignment to multicore distributed architectures, implemented as a software tool. The AUTOMAP, decides: the (i) mapping of software components to multicore ECUs, (ii) the assignment of runnables to the ECU cores, (iii) the clustering of runnables into tasks and (iv) the mapping of tasks to “OS-Applications”, such that timing and mapping constraints are satisfied. AUTOMAP has been developed to handle large industrialized use cases, fine-grained realistic mapping and timing constraints, and to produce outputs that support the system engineer in the mapping task. We have successfully evaluated AUTOMAP on several realistic use cases from Volvo Trucks.
Two subgroups of antipsychotic-naive, first-episode schizophrenia patients identified with a Gaussian mixture model on cognition and electrophysiology

Deficits in information processing and cognition are among the most robust findings in schizophrenia patients. Previous efforts to translate group-level deficits into clinically relevant and individualized information have, however, been non-successful, which is possibly explained by biologically different disease subgroups. We applied machine learning algorithms on measures of electrophysiology and cognition to identify potential subgroups of schizophrenia. Next, we explored subgroup differences regarding treatment response. Sixty-six antipsychotic-naive first-episode schizophrenia patients and sixty-five healthy controls underwent extensive electrophysiological and neurocognitive test batteries.

Patients were assessed on the Positive and Negative Syndrome Scale (PANSS) before and after 6 weeks of monotherapy with the relatively selective D2 receptor antagonist, amisulpride (280.3±159 mg per day). A reduced principal component space based on 19 electrophysiological variables and 26 cognitive variables was used as input for a Gaussian mixture model to identify subgroups of patients. With support vector machines, we explored the relation between PANSS subscores and the identified subgroups. We identified two statistically distinct subgroups of patients. We found no significant baseline psychopathological differences between these subgroups, but the effect of treatment in the groups was predicted with an accuracy of 74.3% (P=0.003). In conclusion, electrophysiology and cognition data may be used to classify subgroups of schizophrenia patients. The two distinct subgroups, which we identified, were psychopathologically inseparable before treatment, yet their response to dopaminergic blockade was predicted with significant accuracy. This proof of principle encourages further endeavors to apply data-driven, multivariate and multimodal models to facilitate progress from symptom-based psychiatry toward individualized treatment regimens.
Using data- and network science to reveal iterations and phase-transitions in the design process

Understanding the role of iterations is a prevalent topic in both design research and design practice. Furthermore, the increasing amount of data produced and stored by companies leaves traces and enables the application of data science to learn from past design processes. In this article, we analyse a documentlog to show the temporal evolution of a real design process of a power plant by using exploratory data analysis and network analysis. We show how the iterative nature of the design process is reflected in archival data and how one might re-construct the design process, involving iterations between many parties, including the client, external consultants, suppliers, and designers. We also show how people use different representations during the design process and how this is associated with a design phase transition in the process. Finally, we relate our findings with the literature on iterations and discuss implications for research and practice with application to project management and process modelling.

Validation of a Simulation Model Describing the Glucose-Insulin-Glucagon Pharmacodynamics in Patients with Type 1 Diabetes

Currently, no consensus exists on a model describing endogenous glucose production (EGP) as a function of glucagon concentrations. Reliable simulations to determine the glucagon dose preventing or treating hypoglycemia or to tune a dual-hormone artificial pancreas control algorithm need a validated glucoregulatory model including the effect of glucagon.

Whole grain-rich diet reduces body weight and systemic low-grade inflammation without inducing major changes of the gut microbiome: a randomised cross-over trial
Objective To investigate whether a whole grain diet alters the gut microbiome and insulin sensitivity, as well as biomarkers of metabolic health and gut functionality. Design 60 Danish adults at risk of developing metabolic syndrome were included in a randomised cross-over trial with two 8-week dietary intervention periods comprising whole grain diet and refined grain diet, separated by a washout period of ≥6 weeks. The response to the interventions on the gut microbiome composition and insulin sensitivity as well on measures of glucose and lipid metabolism, gut functionality, inflammatory markers, anthropometry and urine metabolomics were assessed. Results 50 participants completed both periods with a whole grain intake of 179±50 g/day and 13±10 g/day in the whole grain and refined grain period, respectively. Compliance was confirmed by a difference in plasma alkylresorcinols (p<0.0001). Compared with refined grain, whole grain did not significantly alter glucose homeostasis and did not induce major changes in the faecal microbiome. Also, breath hydrogen levels, plasma short-chain fatty acids, intestinal integrity and intestinal transit time were not affected. The whole grain diet did, however, compared with the refined grain diet, decrease body weight (p<0.0001), serum inflammatory markers, interleukin (IL)-6 (p=0.009) and C-reactive protein (p=0.003). The reduction in body weight was consistent with a reduction in energy intake, and IL-6 reduction was associated with the amount of whole grain consumed, in particular with intake of rye. Conclusion Compared with refined grain diet, whole grain diet did not alter insulin sensitivity and gut microbiome but reduced body weight and systemic low-grade inflammation.

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Workspace experiments: a journey on planning participatory design

Summative Statement: This paper presents a resource material in planning and performing participatory workspace design processes. This material brings up design dialogues into focus and gives insights on how to stage them, bridging the gap of merging user involvement with the well-defined design work-practice. Problem statement: There is a widespread interest in implementing user involvement in major building and construction projects. Nevertheless, it is also often difficult to translate the contributions from users to workspace design that seriously take on board the employees’ specific work practices as a platform for a desired change. There is a need of a tool that manages to travel into a well-defined design work-practice and merge with it. Research Objective: We developed a resource material to merge user involvement within current designers’ practices when designing new workspaces. The aim was to test how a participatory prototyping process can help developing such a material aimed at architects and other participants on workspace design projects. Methodology: We developed the resource material through a participatory “prototyping process”, that is through a mutual learning process taking place in a cooperative design setting. The material was gradually built during a research project, including three workshops emphasizing joint exploration by architects, consulting engineers and health & safety consultants. This method was used because we could discuss, explore, and try out various aspects of the new resource material with its prototypes and thus mediate communication among the different participants of the process, content and format being gradually developed through participation. Results: The result was a flexible resource material for designers as a tool to help building a participatory process specifically for each project. The material consists of a toolbox containing: 1) three booklets, 2) “playing” cards, 3) a game board, and 4) a leaflet explaining the main process the tool aims at bringing participants through. The booklets are the core of the toolbox and they aim at giving ideas and inspiration on methods and activities that can be part of the participatory process. The cards and the game board aim at making the use of the resource material a participatory and interactive activity in itself. The leaflet provides some guidance the participatory planning. Discussion: As we see it, the resource material was well accepted during a training session and some participants were happy they in fact used the time during the session to solve some planning issues for their projects. The material became an asset that streamlined the planning of a participatory process while putting the key themes within user involvement and workspace design on the agenda. It still has room for improvements, but it is a good starting to introduce participatory methods into the design practices and to facilitate the planning for such activities. Conclusions: The task of involving users in design processes is not easy and it can be a challenge to merge these activities. The resource material helps staging the interventions and activities and preparing the materials to be used. On a long term, we see the resource material as an open source, where new methods and inspiring ideas can always be added.

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A comparative study of pseudorandom sequences used in a c-VEP based BCI for online wheelchair control

In this study, a c-VEP based BCI system was developed to run on three distinctive pseudorandom sequences, namely the m-code, the Gold-code, and the Barker-code. The Visual Evoked Potentials (VEPs) were provoked using these codes. In the online session, subjects controlled a LEGO® Mindstorms® robot around a fixed track. Choosing the optimal code proved a significant increase in accuracy (p

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Organisations: Copenhagen Center for Health Technology, Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, University of Copenhagen
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Publication date: 2016

A comprehensive performance analysis of EEMD-BLMS and DWT-NN hybrid algorithms for ECG denoising

Electrocardiogram (ECG) is a widely used non-invasive method to study the rhythmic activity of the heart. These signals, however, are often obscured by artifacts/noises from various sources and mini-mization of these artifacts is of paramount importance for detecting anomalies. This paper presents a thorough analysis of the performance of two hybrid signal processing schemes ((i) Ensemble Empirical Mode Decomposition (EEMD) based method in conjunction with the Block Least Mean Square (BLMS) adaptive algorithm (EEMD-BLMS), and (ii) Discrete Wavelet Transform (DWT) combined with the Neural Network (NN), named the Wavelet NN (WNN)) for denoising the ECG signals. These methods are compared to the conventional EMD (C-EMD), C-EEMD, EEMD-LMS as well as the DWT thresholding (DWT-Th) based methods through extensive simulation studies on real as well as noise corrupted ECG signals. Results clearly show the superiority of the proposed methods.

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Organisations: Copenhagen Center for Health Technology, Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark
Adaptive gaze stabilization through cerebellar internal models in a humanoid robot

Two main classes of reflexes relying on the vestibular system are involved in the stabilization of the human gaze: The vestibulocollic reflex (VCR), which stabilizes the head in space and the vestibulo-ocular reflex (VOR), which stabilizes the visual axis to minimize retinal image motion. The VOR works in conjunction with the opto-kinetic reflex (OKR), which is a visual feedback mechanism for moving the eye at the same speed as the observed scene. Together they keep the image stationary on the retina. In this work we present the first complete model of gaze stabilization based on the coordination of VCR and VOR and OKR. The model, inspired on neuroscientific cerebellar theories, is provided with learning and adaptation capabilities based on internal models. Tests on a simulated humanoid platform confirm the effectiveness of our approach.

General information
A framework for geometry acquisition, 3-D printing, simulation, and measurement of head-related transfer functions with a focus on hearing-assistive devices

Individual head-related transfer functions (HRTFs) are essential in applications like fitting hearing-assistive devices (HADs) for providing accurate sound localization performance. Individual HRTFs are usually obtained through intricate acoustic measurements. This paper investigates the use of a three-dimensional (3D) head model for acquisition of individual HRTFs. Two aspects were investigated: whether a 3D-printed model can replace measurements on a human listener and whether numerical simulations can replace acoustic measurements. For this purpose, HRTFs were acoustically measured for four human listeners and for a 3D printed head model of one of these listeners. Further, HRTFs were simulated by applying the finite element method to the 3D head model. The monaural spectral features and spectral distortions were very similar between re-measurements and between human and printed measurements, however larger deviations were observed between measurement and simulation. The binaural cues were in agreement among all HRTFs of the same listener, indicating that the 3D model is able to provide localization cues potentially accessible to HAD users. Hence, the pipeline of geometry acquisition, printing, and acoustic measurements or simulations, seems to be a promising step forward towards in-silico design of HADs.
Algorithms and Methods for High-Performance Model Predictive Control

The goal of this thesis is to investigate algorithms and methods to reduce the solution time of solvers for Model Predictive Control (MPC). The thesis is accompanied with an open-source toolbox for High-Performance implementation of solvers for MPC (HPMPC), that contains the source code of all routines employed in the numerical tests. The main focus of this thesis is on linear MPC problems.

In this thesis, both the algorithms and their implementation are equally important. About the implementation, a novel implementation strategy for the dense linear algebra routines in embedded optimization is proposed, aiming at improving the computational performance in case of small matrices. About the algorithms, they are built on top of the proposed linear algebra, and they are tailored to exploit the high-level structure of the MPC problems, with special care on reducing the
Analog Gradient Beamformer for a Wireless Ultrasound Scanner.

This paper presents a novel beamformer architecture for a low-cost receiver front-end, and investigates if the image quality can be maintained. The system is oriented to the development of a hand-held wireless ultrasound probe based on Synthetic Aperture Sequential Beamforming, and has the advantage of effectively reducing circuit complexity and power dissipation. The array of transducers is divided into sub-apertures, in which the signals from the single channels are aligned through a network of cascaded gradient delays, and summed in the analog domain before A/D conversion. The delay values are quantized to simplify the shifting unit, and a single A/D converter is needed for each sub-aperture yielding a compact, low-power architecture that can be integrated in a single chip. A simulation study was performed using a 3.75 MHz convex array, and the point spread function (PSF) for different configurations was evaluated in terms of lateral full-width-at-half-maximum (FWHM) and -20 dB cystic resolution (CR). Several setups were simulated varying the sub-aperture size N and the quantization step, and design constraints were obtained comparing the PSF to that of an ideal non-quantized system. The PSF is shown for N = 32 with a quantization step of 12 ns. For this configuration, the FWHM is degraded by 0.25% and the CR is 8.70% lower compared to the ideal situation. The results demonstrate that the gradient beamformer provides an adequate image quality, and open the way to a fully-integrated chip for a compact, low-cost, wireless ultrasound probe.
A Noise-Assisted Data Analysis Method for Automatic EOG-Based Sleep Stage Classification Using Ensemble Learning

Reducing the number of recording modalities for sleep staging research can benefit both researchers and patients, under the condition that they provide as accurate results as conventional systems. This paper investigates the possibility of exploiting the multisource nature of the electrooculography (EOG) signals by presenting a method for automatic sleep staging using the complete ensemble empirical mode decomposition with adaptive noise algorithm, and a random forest classifier. It achieves a high overall accuracy of 82% and a Cohen’s kappa of 0.74 indicating substantial agreement between automatic and manual scoring.

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Application of a New Robust ECG T-Wave Delineation Algorithm for the Evaluation of the Autonomic Innervation of the Myocardium

T-wave amplitude (TWA) is a well-known index of the autonomic innervation of the myocardium. However, until now it has been evaluated only manually or with simple and inefficient algorithms. In this paper, we developed a new robust single-lead electrocardiogram (ECG) T-wave delineation algorithm that is able to detect the T-wave with a wavelet-based method and automatically calculate the TWA. We evaluated the algorithm on the QT database, achieving a sensitivity of 99.92% for the T wave peak and 99.38% for the T wave end. In addition, the percentage of records automatically delineated with high precision was higher than previous published works. Finally, the algorithm was applied to study the influence of anticholinergic and antiadrenergic drugs (i.e. atropine and metoprolol) on the TWA. It was observed that atropine significantly decreased the TWA when compared to baseline level, that head-up tilt caused a decrease of TWA and that metoprolol blunted this decrease. Through the development of a robust algorithm, this study opens the way for further research on the T-wave analysis for the assessment of the autonomic innervation of the ventricular myocardium.

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Architecture Synthesis for Cost-Constrained Fault-Tolerant Flow-based Biochips
In this paper, we are interested in the synthesis of fault-tolerant architectures for flow-based microfluidic biochips, which use microvalves and channels to run biochemical applications. The growth rate of device integration in flow-based microfluidic biochips is scaling faster than Moore's law. This increase in fabrication complexity has led to an increase in defect rates during the manufacturing, thereby motivating the need to improve the yield, by designing these biochips such that they are fault tolerant. We propose an approach based on a Greedy Randomized Adaptive Search Procedure (GRASP) for the synthesis of fault-tolerant biochip architectures. Our approach optimizes the introduction of redundancy within a given unit cost budget, such that, the biochemical application can successfully complete its execution within its deadline, even in the presence of faults, and the yield is maximized. The proposed algorithm has been evaluated using several benchmarks and compared to the results of a Simulated Annealing metaheuristic.

A roadmap for evolving towards optical intra-data-center networks
The first part of this paper focuses on presenting an updated view on the state of the art in data center networks. The European project COSIGN has provided industrial optical data center network roadmaps, strategies and a techno-economic analysis of the involved industrial partners’ value proposition. The conclusions and technology timeline is summarised in this paper.

Assemblages of Patient Safety: Bringing together matters of concern between design and multiple knowledge practices in healthcare
This thesis identifies how design processes emerge during the use of devices in healthcare, by attending to assemblages where contingencies of risk and harm co-exist with the contribution of healthcare professionals to the safe care of patients.
With support from the field of Science and Technology Studies, the thesis approaches such assemblages as heterogeneous in nature comprising of human and non-human entities that share capacities for action. The multi-sited ethnography of specific healthcare settings formed the basis of an analysis of how the nonhuman, as an actor, enters into emergent practices of interdisciplinary care.

General information
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Assessing Levels of Attention Using Low Cost Eye Tracking
The emergence of mobile eye trackers embedded in next generation smartphones or VR displays will make it possible to trace not only what objects we look at but also the level of attention in a given situation. Exploring whether we can quantify the engagement of a user interacting with a laptop, we apply mobile eye tracking in an in-depth study over 2 weeks with nearly 10,000 observations to assess pupil size changes, related to attentional aspects of alertness, orientation and conflict resolution. Visually presenting conflicting cues and targets we hypothesize that it’s feasible to measure the allocated effort when responding to confusing stimuli. Although such experiments are normally carried out in a lab, we have initial indications that we are able to differentiate between sustained alertness and complex decision making even with low cost eye tracking “in the wild”. From a quantified self perspective of individual behavioural adaptation, the correlations between the pupil size and the task dependent reaction time and error rates may longer term provide a foundation for modifying smartphone content and interaction to the users perceived level of attention.

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A Survey of Man in the Middle Attacks
The Man-In-The-Middle (MITM) attack is one of the most well known attacks in computer security, representing one of the biggest concerns for security professionals. MITM targets the actual data that flows between endpoints, and the
confidentiality and integrity of the data itself. In this paper, we extensively review the literature on MITM to analyse and categorize the scope of MITM attacks, considering both a reference model, such as the open systems interconnection (OSI) model, as well as two specific widely used network technologies, i.e., GSM and UMTS. In particular, we classify MITM attacks based on several parameters, like location of an attacker in the network, nature of a communication channel, and impersonation techniques. Based on an impersonation techniques classification, we then provide execution steps for each MITM class. We survey existing countermeasures and discuss the comparison among them. Finally, based on our analysis, we propose a categorisation of MITM prevention mechanisms, and we identify some possible directions for future research.

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Automatic Functionality Assignment to AUTOSAR Multicore Distributed Architectures

The automotive electronic architectures have moved from federated architectures, where one function is implemented in one ECU (Electronic Control Unit), to distributed architectures, where several functions may share resources on an ECU. In addition, multicore ECUs are being adopted because of better performance, cost, size, fault-tolerance and power consumption. In this paper we present an approach for the automatic software functionality assignment to multicore distributed architectures. We consider that the systems use the AUTomotive Open System ARchitecture (AUTOSAR). The functionality is modeled as a set of software components composed of subtasks, called runnables, in AUTOSAR terminology. We have proposed a Simulated Annealing metaheuristic optimization that decides: the (i) mapping of software components to multicore ECUs, (ii) the assignment of runnables to the ECU cores, (iii) the clustering of runnables into tasks and (iv) the mapping of tasks to “OS-Applications” (used to isolate mixed safety-criticality functions). We are interested to determine an implementation such that (1) the mapping constraints are satisfied, (2) the runnables are schedulable and (3) they are spatially and temporally isolated if they have different safety-criticality levels, (4) the overall communication bandwidth is minimized and (5) the utilization of the cores and ECUs is balanced. The proposed approach was evaluated on three realistic case studies.

Automatic Model Generation Framework for Computational Simulation of Cochlear Implantation

Recent developments in computational modeling of cochlear implantation are promising to study in silico the performance of the implant before surgery. However, creating a complete computational model of the patient's anatomy while including an external device geometry remains challenging. To address such a challenge, we propose an automatic framework for the generation of patient-specific meshes for finite element modeling of the implanted cochlea. First, a statistical shape model is constructed from high-resolution anatomical μCT images. Then, by fitting the statistical model to a patient's CT image, an accurate model of the patient-specific cochlea anatomy is obtained. An algorithm based on the parallel transport frame is employed to perform the virtual insertion of the cochlear implant. Our automatic framework also incorporates the surrounding bone and nerve fibers and assigns constitutive parameters to all components of the finite element model. This model can then be used to study in silico the effects of the electrical stimulation of the cochlear implant. Results are shown on a total of 25 models of patients. In all cases, a final mesh suitable for finite element simulations was obtained, in an average time of 94 s. The framework has proven to be fast and robust, and is promising for a detailed prognosis of the cochlear implantation surgery.
Behavioral activities collected through smartphones and the association with illness activity in bipolar disorder

Smartphones are useful in symptom-monitoring in bipolar disorder (BD). Objective smartphone data reflecting illness activity could facilitate early treatment and act as outcome in efficacy trials. A total of 29 patients with BD presenting with moderate to severe levels of depressive and manic symptoms used a smartphone-based self-monitoring system during 12 weeks. Objective smartphone data on behavioral activities were collected. Symptoms were clinically assessed every second week using the Hamilton Depression Rating Scale and the Young Mania Rating Scale. Objective smartphone data correlated with symptom severity. The more severe the depressive symptoms (1) the longer the smartphone’s screen was “on”/day, (2) more received incoming calls/day, (3) fewer outgoing calls/day were made, (4) less answered incoming calls/day, (5) the patients moved less between cell towers IDs/day. Conversely, the more severe the manic symptoms (1) more outgoing text messages/day sent, (2) the phone calls/day were longer, (3) the fewer number of characters in incoming text messages/day, (4) the lower duration of outgoing calls/day, (5) the patients moved more between cell towers IDs/day. Further, objective smartphone data were able to discriminate between affective states. Objective smartphone data reflect illness severity, discriminates between affective states in BD and may facilitate the cooperation between patient and clinician.

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Scopus rating (2003): SJR 0.682 SNIP 0.551
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Scopus rating (2000): SJR 0.94 SNIP 0.668
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Characterizing Design Process Interfaces as Organization Networks: Insights for Engineering Systems Management

The engineering design literature has provided guidance on how to identify and analyze design activities and their information dependencies. However, a systematic characterization of process interfaces between engineering design activities is missing, and the impact of structural and compositional aspects of interfaces on process performance is unclear. To fill these gaps, we propose a new approach that characterizes process interfaces as organization networks consisting of people and their interactions when performing interfacing activities. Furthermore, we provide guidance on how to test and interpret the effect of those characteristics on interface problems. As a result, we show how structural and compositional aspects of the organization networks between information-dependent activities provide valuable insights to better manage complex engineering design processes. The proposed approach is applied to the development of a power plant, analyzing 79 process interfaces. The study reveals a relationship between the structure and composition of the process interfaces and reported interface problems. Implications of this approach include the integration of information about process and organization architectures, the systematic identification of key performance metrics associated with interface problems, and improved support for engineering managers by means of a better overview of information flows between activities.

General information
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Scopus rating (2010): SJR 0.403 SNIP 1.444
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Cloud Radio Access Network (C-RAN) is a novel mobile network architecture which can address a number of challenges that mobile operators face while trying to support ever-growing end-users' needs towards 5th generation of mobile networks (5G). The main idea behind C-RAN is to split the base stations into radio and baseband parts, and pool the Baseband Units (BBUs) from multiple base stations into a centralized and virtualized BBU Pool. This gives a number of benefits in terms of cost and capacity. However, the challenge is then to find an optimal functionality splitting point as well as to design the so-called fronthaul network, interconnecting those parts. This thesis focuses on quantifying those benefits and proposing a flexible and capacity-optimized fronthaul network. It is shown that a C-RAN with a functional split resulting in a variable bit rate on the fronthaul links brings cost savings due to the multiplexing gains in the BBU pool and the fronthaul network. The cost of a fronthaul network deployment and operation can be further reduced by sharing infrastructure between fronthaul and other services. The origins of multiplexing gains in terms of traffic burstiness, the tidal effect and various possible functional splits are analyzed and quantified. Sharing baseband resources between many cells is possible for traditional C-RANs. However, in order to further benefit from multiplexing gains on fronthaul, it is recommended to implement a functional split yielding variable bit rate in the fronthaul. For the analyzed data sets, in deployments where diverse traffic types are mixed (bursty, e.g., web browsing and constant bit rate, e.g., video streaming) and cells from various geographical areas (e.g., office and residential) are connected to the BBU pool, the multiplexing gain value reaches six. Using packet-based fronthaul has the potential to utilize fronthaul resources efficiently. However, meeting synchronization and delay requirements is a challenge. As a possible solution, the use of IEEE Precision Time Protocol (PTP) (also known as 1588v2) has been evaluated, and for the analyzed scenario it can assure synchronization on the nanosecond level, fulfilling mobile network requirements. Furthermore, mechanisms to lower delay and jitter have been identified, namely: source scheduling and preemption. An innovative source scheduling scheme which can minimize jitter has been proposed. The scheme is optimized for symmetric downlink and uplink traffic, but can also be used when downlink traffic exceeds uplink. Moreover, a demonstrator of a Software Defined Networking (SDN) controlled Ethernet fronthaul has been built.

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Cochlear implant electrode localization in post-operative CT using a spherical measure

When implanting cochlear implants the positions of electrodes have a large impact on the quality of the restored hearing. Due to metal artifacts it is difficult to estimate the precise location in post-operative scans. In this paper we present a method for automatically locating and determining the ordering of electrode contacts on implanted electrode arrays from post-operative CT images. Our method applies a specialized filter chain to the images based on a threshold and spherical measure, and selects contact positions at local maxima in the filtered image. Two datasets of 13 temporal bone specimens scanned in CBCT are used to validate the method, which successfully locates the electrode array in every image.

Colonic transit time is related to bacterial metabolism and mucosal turnover in the human gut

Little is known about how colonic transit time relates to human colonic metabolism, and its importance for host health, although stool consistency, a proxy for colonic transit time, has recently been negatively associated with gut microbial richness. To address the relationships between colonic transit time and the gut microbial composition and metabolism, we assessed the colonic transit time of 98 subjects using radiopaque markers, and profiled their gut microbiota by 16S rRNA gene sequencing and their urine metabolome by ultra performance liquid chromatography mass spectrometry. Based on correlation analyses, we show that colonic transit time is associated with overall gut microbial composition, diversity and metabolism. A relatively prolonged colonic transit time associates with high microbial species richness and a shift in colonic metabolism from carbohydrate fermentation to protein catabolism as reflected by higher urinary levels of potentially deleterious protein-derived metabolites. Additionally, shorter colonic transit time correlates with metabolites likely reflecting increased renewal of the colonic mucosa. Together, this suggests that a high gut microbial richness does not per se imply a healthy gut microbial ecosystem and points at colonic transit time as a highly important factor to consider in microbiome and metabolomics studies.

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Colonic transit time relates to bacterial metabolism and mucosal turnover in the human gut

Little is known about how colonic transit time relates to human colonic metabolism, and its importance for host health, although stool consistency, a proxy for colonic transit time, has recently been negatively associated with gut microbial richness. To address the relationships between colonic transit time and the gut microbial composition and metabolism, we assessed the colonic transit time of 98 subjects using radiopaque markers, and profiled their gut microbiota by 16S rRNA gene sequencing and their urine metabolome by ultra performance liquid chromatography mass spectrometry. Based on correlation analyses, we show that colonic transit time is associated with overall gut microbial composition, diversity and metabolism. A relatively prolonged colonic transit time associates with high microbial species richness and a shift in colonic metabolism from carbohydrate fermentation to protein catabolism as reflected by microbial metabolites in urine. This results in a number of potentially deleterious protein-derived metabolites. Additionally, longer colonic transit time correlates with metabolites likely reflecting reduced renewal of the colonic mucosa. Together, this suggests that a high gut microbial richness does not per se imply a healthy gut microbiota, and contributes to the understanding of the pathophysiology of diseases where increased transit time is a risk factor. Finally, our findings highlight the colonic transit time as an important physiological variable, which should be considered in gut microbiota and metabolomics studies.

Controllability and flexibility analysis of CO2 post-combustion capture using piperazine and MEA

In this study, we developed a decentralized control scheme and investigate the performance of the piperazine (PZ) and monoethanolamine (MEA) CO2 capture process for industrially-relevant operation scenarios. The base for the design of the control schemes is Relative Gain Array (RGA) analysis combined with open-loop dynamic sensitivity analysis. This study suggests that controllers with smaller time integrals and larger gains are required to maintain the PZ plant within reasonable short closed-loop settling times when compared to MEA. It also shows that the offset from the designated set-points in the presence of disturbances in the flue gas flow and heat duty is larger using PZ compared to MEA. The settling time for the PZ plant is generally larger than for MEA. However, the PZ plant rejects the disturbances faster and with less variability in the load of the power plant. Furthermore, this study indicates that the proposed PI-based control structure can handle large changes in the load provided that the manipulated variables, i.e. lean solvent flow or reboiler duty, do not reach their saturation limit. Additionally, we observed that shortage in the steam supply (reboiler duty) may represent a critical operational bottleneck, especially when PZ is being used. The MEA plant controllers drive the system towards drying out/flooding while the CO2 capture rate performance of the PZ plant reduces drastically in the presence of constraints in the availability of steam. These findings suggest the need for advanced control structures, e.g. MPC, which can explicitly account for constraints in the process variables.
Designing Context-Aware Cognitive Behavioral Therapy for Unipolar and Bipolar Disorders
This position paper presents our preliminary design of context-aware cognitive behavioral therapy for unipolar and bipolar disorders. We report on the background for this study and the methods applied in the ongoing design process. The paper ends by presenting and discussing different design options. We hope this will be useful input for further discussion at the workshop.

General information
State: Published
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Developing a framework to transfer knowledge from operations into engineering design projects: understanding the knowledge management challenge

General information
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Diffusion Retardation by Binding of Tobramycin in an Alginate Biofilm Model.
Microbial cells embedded in a self-produced extracellular biofilm matrix cause chronic infections, e.g., by Pseudomonas aeruginosa in the lungs of cystic fibrosis patients. The antibiotic killing of bacteria in biofilms is generally known to be reduced by 100–1000 times relative to planktonic bacteria. This makes such infections difficult to treat. We have therefore proposed that biofilms can be regarded as an independent compartment with distinct pharmacokinetics. To elucidate this pharmacokinetics we have measured the penetration of the tobramycin into seaweed alginate beads which serve as a model of the extracellular polysaccharide matrix in P. aeruginosa biofilm. We find that, rather than a normal first order saturation curve, the concentration of tobramycin in the alginate beads follows a power-law as a function of the external concentration. Further, the tobramycin is observed to be uniformly distributed throughout the volume of the alginate bead. The power-law appears to be a consequence of binding to a multitude of different binding sites. In a diffusion model these results are shown to produce pronounced retardation of the penetration of tobramycin into the biofilm. This filtering of the free tobramycin concentration inside biofilm beads is expected to aid in augmenting the survival probability of bacteria residing in the biofilm.

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Distributed Model Predictive Control for Smart Energy Systems
Integration of a large number of flexible consumers in a smart grid requires a scalable power balancing strategy. We formulate the control problem as an optimization problem to be solved repeatedly by the aggregator in a model predictive control framework. To solve the large-scale control problem in real-time requires decomposition methods. We propose a decomposition method based on Douglas–Rachford splitting to solve this large-scale control problem. The method decomposes the problem into smaller subproblems that can be solved in parallel, e.g., locally by each unit connected to an aggregator. The total power consumption is controlled through a negotiation procedure between all cooperating units and an aggregator that coordinates the overall objective. For large-scale systems, this method is faster than solving the original problem and can be distributed to include an arbitrary number of units. We show how different aggregator objectives are implemented and provide simulations of the controller including the computational performance.

General information
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Dynamic Operation and Simulation of Post-Combustion CO2 Capture

Thermal power need to operate, on a daily basis, with frequent and fast load changes to balance the large variations of intermittent energy sources, such as wind and solar energy. To make the integration of carbon capture to power plants economically and technically feasible, the carbon capture process has to be able to follow these fast and large load changes without decreasing the overall performance of the carbon capture plant. Therefore, dynamic models for simulation, optimization and control system design are essential. In this work, we compare the transient behavior of the model against dynamic pilot data for CO2 absorption and desorption for step-changes in the flue gas flow rate. In addition we investigate the dynamic behavior of a full-scale post-combustion capture plant using monoethanolamine (MEA) and piperazine (PZ). This analysis demonstrates the good agreement between the developed model (dCAPCO2) and the pilot measurements at both, transient and steady-state conditions. It outlines how the time needed to reach a new steady-state varies with respect to amine type and concentration. The simulation study reveals that it is essential to control the lean solvent flow to avoid sudden changes in the CO2 removal rate and to avoid increased heat demand of solvent regeneration. In addition, it shows how storage tanks (liquid hold-up of the system) can be designed to accommodate significant upstream changes in the power plant management. This flexibility is especially needed for operation in future mixed green energy market. [All rights reserved Elsevier].
Economic Model Predictive Control for Spray Drying Plants

The main challenge in cost optimal operation of a spray dryer, is to maximize the production rate while minimizing the energy consumption, keeping the residual moisture content of the powder below a maximum limit and avoiding that the powder sticks to the chamber walls. The conventional PI control strategy is simple, but known to be insufficient at providing optimal operation in the presence of variations in the feed and the ambient air humidity. This motivates our investigation of Model Predictive Control (MPC) strategies.

In this thesis, we consider the development and application of new models and MPC strategies to optimize the operation of four-stage spray dryers. The models are first-principle dynamic models with parameters identified from dryer specific experiments and powder properties identified from laboratory tests. A simulation model is used for detailed closed-loop simulations and a complexity reduced control model is used for state estimation and prediction in the controllers. These models facilitate development and comparison of control strategies. We develop two MPC strategies; a linear tracking MPC with a Real-Time Optimization layer (MPC with RTO) and an Economic Nonlinear MPC (E-MPC). We tailor these for the spray drying process to optimize the cost of operation by adjustments to the inputs of the dryer according to the present disturbances and process constraints. Simulations show that MPC strategies improve the profit of operation by up to 9.69%, the production of powder by up to 9.6%, the residual moisture content by up to 0.114 p.p. and the energy efficiency by up to 6.06% while the produced powder is within the given quality specifications and sticky powder on the walls of the chamber is avoided. Thus, we are able to improve the cost of operation significantly compared to the conventional PI control strategy.

The proposed MPC strategies are based on a feedback control algorithm that explicitly handles constrained control inputs and uses a model to predict and optimize the future behavior of the dryer. The solution of the control problem results in a sequence of inputs for a finite horizon, out of which only the first input is applied to the dryer. This procedure is repeated at each sample instant and is solved numerically in real-time. The MPC with RTO tracks a target that optimizes the cost of operation at steady-state. The E-MPC optimizes the cost of operation directly by having this objective directly in the controller. The need for the RTO layer is then eliminated.

We demonstrate the application of the proposed MPC with RTO to control an industrial GEA MSDTM-1250 spray dryer, which produces approximately 7500 kg/hr of enriched milk powder. Compared to the conventional PI controller, our first results shows that the MPC improves the profit of operation by approximately 228,000 €/year, the product rate by 322 kg/hr, the residual moisture content by 0.166 p.p. and the energy efficiency by 1% at comparable ambient air humidity conditions. The demonstrated MPC with RTO is fully integrated in the daily operation of the spray dryer today.

Our primary objectives in the thesis are: 1) Spray dryer modeling of a smallscale four-stage spray dryer. The purpose of the models are to enable simulations of the spray drying process at different operating points, such that the models facilitate development and comparison of control strategies; 2) Development of MPC strategies that automatically adjust the dryer to variations in the feed and the ambient air humidity, such that the energy consumption is minimized, the residual moisture content in the powder is controlled within the specifications and sticky powder is avoided from building up on the dryer walls; 3) Demonstrate the industrial application of an MPC strategy to a full-scale industrial four-stage spray dryer.

The main scientific contributions can be summarized to:

- Modeling of a four-stage spray dryer. We develop new first-principles engineering models for simulation of a four-stage spray dryer. These models enables simulations of the spray dryer at different operating points with high accuracy.
- Development and simulation of control strategies. We develop two control strategies, the MPC with RTO and the E-MPC strategy. The performance of the controllers is studied and evaluated by simulation.
- Industrial application of MPC to a spray dryer. We demonstrate that our proposed MPC with RTO is applicable to an industrial GEA MSDTM-1250 spray dryer, that produces enriched milk powder.
Effect of administration of antibiotics peripartum to wistar rats on bile acid profiles in offspring

Vertical transmission of the maternal microbiota is assumed to be crucial for the offspring's development. A disrupted microbiota composition leading to an altered metabolic activity of the microbiota can affect bile acid profiles, which are known to influence host metabolism. Here, we examined whether perturbation of the maternal gut microbiota during pregnancy, induced by administration of either amoxicillin or vancomycin to pregnant rats, influenced bile acid profiles in the offspring. The dams were treated with antibiotics from 8 days before the dams gave birth and continued until weaning (4 weeks later). Blood samples were collected from offspring at ages 2, 4 and 14 weeks, and from dams at the end of treatment. From these blood samples, bile acids were extracted and 22 bile acids were quantified by targeted liquid chromatography mass spectrometry. Comparing the serum bile acid profiles of antibiotic-treated rat dams with non-treated dams, we found that the antibiotic treatments significantly changed the bile acid profiles. However, no effect was seen in the offspring of the antibiotic-treated dams at any age. The bile acid profiles of the offspring did however change significantly with age, where the largest amounts of bile acids were found in the 4-weeks old pups. Future work will involve integrating the bile acid data with physiology and microbiota data of both pups and dams.

Electronic self-monitoring of mood using IT platforms in adult patients with bipolar disorder: A systematic review of the validity and evidence

Background: Various paper-based mood charting instruments are used in the monitoring of symptoms in bipolar disorder. During recent years an increasing number of electronic self-monitoring tools have been developed. The objectives of this systematic review were 1) to evaluate the validity of electronic self-monitoring tools as a method of evaluating mood compared to clinical rating scales for depression and mania and 2) to investigate the effect of electronic self-monitoring tools on clinically relevant outcomes in bipolar disorder.

Methods: A systematic review of the scientific literature, reported according to the Preferred Reporting items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines was conducted. MEDLINE, Embase, PsycINFO and The Cochrane Library were searched and supplemented by hand search of reference lists. Databases were searched for 1) studies on electronic self-monitoring tools in patients with bipolar disorder reporting on validity of electronically self-reported mood ratings compared to clinical rating scales for depression and mania and 2) randomized controlled trials (RCT) evaluating electronic mood self-monitoring tools in patients with bipolar disorder.
Results: A total of 13 published articles were included. Seven articles were RCTs and six were longitudinal studies. Electronic self-monitoring of mood was considered valid compared to clinical rating scales for depression in six out of six studies, and in two out of seven studies compared to clinical rating scales for mania. The included RCTs primarily investigated the effect of heterogeneous electronically delivered interventions; none of the RCTs investigated the sole effect of electronic mood self-monitoring tools. Methodological issues with risk of bias at different levels limited the evidence in the majority of studies.

Conclusions: Electronic self-monitoring of mood in depression appears to be a valid measure of mood in contrast to self-monitoring of mood in mania. There are yet few studies on the effect of electronic self-monitoring of mood in bipolar disorder. The evidence of electronic self-monitoring is limited by methodological issues and by a lack of RCTs. Although the idea of electronic self-monitoring of mood seems appealing, studies using rigorous methodology investigating the beneficial as well as possible harmful effects of electronic self-monitoring are needed.

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Scopus rating (2012): SJR 6.452 SNIP 2.714 CiteScore 9.34
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Scopus rating (2011): SJR 5.954 SNIP 2.533 CiteScore 9.18
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Scopus rating (2010): SJR 6.533 SNIP 2.642
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Emergency Management involving Critical Infrastructure Disruptions: operationalizing the deployment of resilience capabilities

Recent developments nurturing the importance of Emergency Management (EM) of Critical Infrastructure (CI) brought a shift of emphasis from protecting the systems to building resilience. Resilience approach is required to cope with inevitable events, ensuring ability to anticipate, absorb, adapt to, and/or rapidly recover from a potentially disruptive event. The study proposes a novel approach to integrating the resilience capacities of CI into the EM cycle, which facilitates emergency services and CI operators to collaborate in addressing resilience improvement measures, while planning to cope with CI disruptions. It grounds on a previously published comprehensive framework which reflects the main characteristics of such emergencies (e.g. interdependent, multi-sectoral, multi-stakeholder) and supports the identification, assessment and development of specific technical and organizational capabilities. A pilot application is provided on a real case involving the public and private actors engaged in the Regional Programme on Critical Infrastructure Protection and Resilience (CIP-R) in Lombardy (Italy).

Enhancing Security and Privacy in Video Surveillance through Role-Oriented Access Control Mechanism

Use of video surveillance has significantly increased in the last few decades. Modern video surveillance systems are equipped with techniques that automatically extract information about the objects and events from the video streams and allow traversal of data in an effective and efficient manner. Pervasive usage of such systems gives substantial powers to those monitoring the videos and poses a threat to the privacy of anyone observed by the system. Aside from protecting
privacy from the outside attackers, it is equally important to protect the privacy of individuals from the inside personnel involved in monitoring surveillance data to minimize the chances of misuse of the system, e.g. voyeurism. In this context, several techniques to protect the privacy of individuals, called privacy enhancing techniques (PET) have therefore been proposed in the literature which detect and mask the privacy sensitive regions, e.g. faces, from the videos. However, very few research efforts have focused on addressing the security aspects of video surveillance data and on authorizing access to this data. Interestingly, while PETs help protect the privacy of individuals, they may also hinder the usefulness of video surveillance systems resulting in compromising the very purpose of such systems, i.e. public safety. Thus the challenge is to provide sufficient need-specific data to those monitoring the surveillance systems yet preserving the privacy of people as much as possible. This can be achieved through a dynamic access control mechanism that may provide proportionate access to data while allowing reversing the PETs whenever required. In this context, a summary of thesis contributions is given below.

In this thesis, we present an abstract model of video surveillance systems that helps identify the major security and privacy requirements in a video surveillance system. We study existing solutions against these requirements and point out practical challenges in ensuring the security of video surveillance data in all stages (in transit and at storage). Our study shows a gap, between the security requirements that we identified and the proposed security solutions, where future research efforts may focus in this domain. From the challenges that we outline regarding security in video surveillance, we focus on development of a dynamic access control mechanism.

We develop a general-purpose access control model that is suitable for video surveillance systems as well as other domains sharing similar requirements. As the currently dominant access control models – the role-based access control (RBAC) and the attribute-based access control (ABAC) – suffer from limitations while offering features complementary to each other, their integration has become an important area of research. Our access control model combines the two models in a novel way in order to unify their benefits while avoiding their limitations. Our approach provides a mechanism that not only takes information about the current circumstances into account during access control decision making, but is also suitable for applications where access to resources is controlled by exploiting the contents of resources in the access control policy. We evaluate our model against RBAC and ABAC and demonstrate that our model brings together the benefits offered by RBAC and ABAC while addressing the role- and permission-explosion issues faced in RBAC.

Based on our access control model, we then present an access control mechanism for video surveillance systems. Contrary to the existing approaches, the proposed access control mechanism is role-oriented and retains advantages associated with role-based access control, yet it allows specification of policies using the metadata associated with the objects as well as the attributes of users and environment. In addition to role hierarchies, the content-based permissions in our model allow derivation of several permissions from the explicitly stated ones due to the hierarchical relations between the attributes of different entities. We implement a prototype of the proposed mechanism and demonstrate that the access control policies using our approach may be specified via eXtensible Access Control Markup Language (XACML).

### General information

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### Environmental chemicals and their effects on female reproductive health: Searching for molecular mechanisms and effect biomarkers

Incorrect developmental programming of the female reproductive tract can lead to compromised reproductive fitness later in life. It has been suggested that exposure to endocrine disrupting chemicals (EDCs) in utero can disrupt ovarian programming in humans, which is supported by several animal studies. However, it remains unclear which specific processes during development are affected, and if there are particular sensitive developmental windows. Most of the etiological evidence derives from rodent studies, whereas cause-effect relationships in humans are extremely difficult to obtain, not least due to the fact that there is a significant lag time between exposure during fetal life and disease symptoms in adulthood. Furthermore, humans are typically exposed to chemicals at a much lower dose than those of
experimental studies, but exposed to a large number of different chemicals. This may lead to combination or mixture effects, where chemicals present at doses that would not cause effects on their own, can add up and cause an effect. The aim of the PhD project was to identify early biomarkers and sensitive windows for late life effects on the ovary after chemical exposure to mixtures of EDCs during early development.

A comprehensive literature review was synthesized to obtain an overview over current knowledge on the effects environmental chemicals can have on the developing ovary. This work identified four potentially sensitive windows of reproductive programming in females; i) primordial germ cell migration and gonadal sex determination, ii) meiosis, iii) follicle assembly, and iv) early folliculogenesis. For the experimental work, which aimed at identifying potential early biomarkers for late life diseases, two general approaches were adopted; a targeted approach looking at specific endpoints and a selection of effect biomarkers, and a more open-ended screening approach looking for potentially novel biomarkers. In the targeted approach, endpoints known to be important for reproductive function and ovary health were investigated at the molecular and morphological levels in neonatal, pre-pubertal and adult rat ovaries exposed to mixtures of EDCs during development. In the screening approach, a proteomics screen was performed to investigate differentially expressed proteins in the rat ovary after developmental exposure to mixtures of EDCs.

In the initial targeted approach, rat dams were exposed to a mixture of phthalates, pesticides, UV-filters, bisphenol A, butyl-paraben, as well as the mild analgesic paracetamol (PM). The compounds were tested all together (Totalmix) or in subgroups with anti-androgenic (AAmix) or estrogenic (Emix) properties. PM was tested separately. Reproductive endpoints were investigated in offspring at pre-puberty (PD22) and adulthood (approx. 1 year of age). In pre-pubertal animals a significant reduction in primordial follicle numbers was seen after AAmix and PM exposure, whereas in the 1 year old animals reduced ovary weights were seen in Totalmix-, AAmix-, and PM-groups. Finally, animals in the Totalmix group showed a higher incidence rate of irregular estrous cycles than control animals.

The reduction in primordial follicles after AAmix exposure was suspected to be caused by interruption to follicle assembly. Thus, a small pilot study, exposing explanted neonatal ovaries to AAmix, submixtures (pesticide mix (PEmix), phthalate mix (Phmix)), and mono(2-ethylhexyl)phthalate (MEHP), was conducted. No significant effects were seen on gene expression, but histological evaluation showed that primordial follicles were reduced in the PEmix exposed ovaries. For the proteomics screening study, a shotgun proteomics approach was performed on PD17 ovaries from offspring corresponding to those of the initial targeted study. Protein extracts were analyzed by LC-MS/MS, and evaluation of the data for potential effect biomarkers showed that three proteins, Trimethyllysine dioxygenase (TMLH), Keratin, type II cytoskeletal 8 (KRT8), and anti-Müllerian hormone (AMH) were dysregulated in all exposure groups. Also, ingenuity pathway analysis revealed canonical pathways known to be involved in ovary function, such as mTOR and HIPPO signaling, to be affected in all exposure groups.

In conclusion, the studies conducted for this PhD revealed that follicle count in pre-pubertal rats can potentially be used as a marker for early life affected ovary development caused by EDC mixture exposure, leading to reproductive senescence later in life. Furthermore, three proteins were identified as possible biomarkers for effects on the developing ovary, and potentially for late life adverse effects.
"playware", which is defined as hardware or software that aims to initiate play and playful experiences among its users. The thesis evaluates MOTO tiles as an example of a relatively new area of research, Games for Health, where digital games are seen as tools for the creation of health-promoting activities. The thesis starts with a presentation of the results of two different pilot trials done with the MOTO tiles technology which showed remarkable development among the elderly, particularly regarding balance. It further contextualizes MOTO tiles in the research area of "games for health" by an account of research done in this area, including the sub-area of "exergames", which are games that require the user to be physically active in order to play. This account points out that the research hitherto completed is inadequate with regards to scientific validity. The review of randomized controlled trials (RCT) done in the area of exergames shows that there is a need for more studies, and for studies with a higher methodological quality. Based on the knowledge gained in the pilot studies and the review of the area of exergames, the author of this thesis analyzes and presents how RCTs are done, as well as exploring how to secure studies of high methodological quality. The knowledge gained from this analysis is then used to plan and conduct an RCT on the MOTO tiles with elderly people in the age range from 70 years and above. The findings from the RCT show that it is possible to do a study of high methodological quality, but it also points out problems that are partly to do with the age group, including the problem of missing data due to, for example, sudden illness, which is more common among elderly. None the less, the findings of the study showed one primary outcome that was significant (an increase of 22% in score in the test "Chair Stand") and another that had indications that there could be an important clinical finding (a decrease of 12% in score in the test "Timed Up & Go"), while one was unaffected (no difference in the test "6 Minutes Walking Test"). The author concludes that more studies are still needed and that higher power of the studies should be considered or meta-analysis on several trials combined. The trial additionally confirms the findings from the pilot tests and shows that the participants saw statistically significant improvements on the balance score ("Line Walk" or "Tandem Walk") with an impressive increase of 149% in score after adjusting for the outlier. Besides the physical tests, the participants answered a questionnaire, and here the findings showed that the vast majority of the participants enjoyed the training and wanted to continue using the MOTO tiles. Over half also indicated that they felt better and 75% indicated that they had improved physically. This shows that playware such as the MOTO tiles can promote health and, not least, that this can be done in a playful and thus, motivational manner. Taking these findings as the point of departure, the thesis further investigates how the MOTO tiles as an example of playware and exergames created play among the users. This investigation begins with a presentation of the concept of play, based on the philosophy of play that is the foundation of modern game research. Play is here understood as something we humans engage in for nothing else than the sake of the enjoyment it brings, or, as it is formulated: The purpose of play is play itself. From this understanding, the thesis goes on to present we in play we have a special attitude towards the world, and this frames our understanding of actions done, when we are in what we call the "state of play". Further, the thesis gives an account of an important finding in playware research, that in order to get into the state of play we use "play tools", such as games, toys etc. This finding is further developed in the thesis by applying the Actor Network Theory (ANT) as a framework for analysis, by which the author reaches a new understanding of games as "actors" which encourage their players to act in certain prescribed ways, with the goal of bringing them into the state of play. This brings a new perspective on games and gives a framework to understand how play tools work. Developing on these findings, the thesis then presents the notion of "play dynamics" that is, dynamics, which play tools make use of to bring players into the state of play. Examples of such dynamics are presented, and the thesis points to the need to further develop our understanding of play dynamics, the different types of dynamics and how they work together to create new dynamics and effects.

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State: Published
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Relations
Projects:
Evaluation and understanding of Playware Technology – trials with playful balance training.

Evolvable Smartphone-Based Platforms for Point-Of-Care In-Vitro Diagnostics Applications
The association of smart mobile devices and lab-on-chip technologies offers unprecedented opportunities for the emergence of direct-to-consumer in vitro medical diagnostics applications. Despite their clear transformative potential, obstacles remain to the large-scale disruption and long-lasting success of these systems in the consumer market. For instance, the increasing level of complexity of instrumented lab-on-chip devices, coupled to the sporadic nature of point-of-
care testing, threatens the viability of a business model mainly relying on disposable/consumable lab-on-chips. We argued recently that system evolvability, defined as the design characteristic that facilitates more manageable transitions between system generations via the modification of an inherited design, can help remedy these limitations. In this paper, we discuss how platform-based design can constitute a formal entry point to the design and implementation of evolvable smart device/lab-on-chip systems. We present both a hardware/software design framework and the implementation details of a platform prototype enabling at this stage the interfacing of several lab-on-chip variants relying on current- or impedance-based biosensors. Our findings suggest that several change-enabling mechanisms implemented in the higher abstraction software layers of the system can promote evolvability, together with the design of change-absorbing hardware/software interfaces. Our platform architecture is based on a mobile software application programming interface coupled to a modular hardware accessory. It allows the specification of lab-on-chip operation and post-analytic functions at the mobile software layer. We demonstrate its potential by operating a simple lab-on-chip to carry out the detection of dopamine using various electroanalytical methods.

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**Experimental Demonstration of Multidimensional Switching Nodes for All-Optical Data Center Networks**
This paper reports on a novel ring-based data center architecture composed of multidimensional switching nodes. The nodes are interconnected with multicore fibers and can provide switching in three different physical, hierarchically overlaid dimensions (space, wavelength, and time). The proposed architecture allows for scaling in different dimensions while at the same time providing support for connections with different granularity. The ring topology reduces the number of different physical links required, leading to simplified cabling and easier link management, while optical bypass holds the prospect of low latency and low-power consumption. The performance of the multidimensional switching nodes has been investigated in an experimental demonstration comprising three network nodes connected with multicore fibers. Both high capacity wavelength connections and time-shared subwavelength connections have been established for connecting different nodes by switching in different physical dimensions. Error-free performance (BER < 10−9) has been achieved for all the connections with various granularity in all the investigated switching scenarios. The scalability of the system has
been studied by increasing the transmission capacity to 1 Tbit/s/core equivalent to 7 Tbit/s total throughput in a single seven-core multicore fiber. The error-free performance (BER < 10−9) for all the connections confirms that the proposed architecture can meet the existing demands in data centers and accommodate the future traffic growth.
Eye-head stabilization mechanism for a humanoid robot tested on human inertial data

Two main classes of reflexes relying on the vestibular system are involved in the stabilization of the human gaze: the vestibulocollic reflex (VCR), which stabilizes the head in space and the vestibulo-ocular reflex (VOR), which stabilizes the visual axis to minimize retinal image motion. Together they keep the image stationary on the retina. In this work we present the first complete model of eye-head stabilization based on the coordination of VCR and VOR. The model is provided with learning and adaptation capabilities based on internal models. Tests on a simulated humanoid platform replicating torso disturbance acquired on human subject performing various locomotion tasks confirm the effectiveness of our approach.
Mobile robots, Stability in control theory, humanoid robots, stability, eye-head stabilization mechanism, humanoid robot, human inertial data, VCR, VOR, torso disturbance, locomotion tasks, vestibulocollic reflex, vestibulo-ocular reflex, Theoretical Computer Science, Computer Science (all), Eye-head coordination, Head stabilization, Humanoid robotics, Aldehydes, Anthropomorphic robots, Biomimetics, Videocassette recorders, Humanoid robot, Internal models, Learning and adaptation, Vestibular system, Vestibulo-ocular reflex, Stabilization

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Fluorinated alkyl substances and technical mixtures used in food paper-packaging exhibit endocrine-related activity in vitro

Migration of chemicals from packaging materials to foods may lead to human exposure. Polyfluoroalkyl substances (PFAS) can be used in technical mixtures (TMs) for use in food packaging of paper and board, and PFAS have been detected in human serum and umbilical cord blood. The specific structures of the PFAS in TMs are often unknown, but polyfluorinated alkyl phosphate esters (PAPs) have been characterized in TMs, food packaging, and in food. PAPs can be metabolized into fluorotelomer alcohols (FTOHs) and perfluoroalkyl carboxylic acids (PFCAs). Some PFAS have endocrine activities, highlighting the need to investigate these effects. Herein, we studied the endocrine activity of less characterized PFAS, including short-chain PFCAs and FTOHs, PAPs, and TMs of unknown chemical composition. Long-chain PFCAs were also included. We applied seven assays covering effects on estrogen, glucocorticoid, androgen, and peroxisome proliferator-activated receptor (PPAR) activity, as well as steroidogenesis in vitro and ex vivo. In general, PAPs, FTOHs, TMs, and long-chain PFCAs showed estrogenic activity through receptor activation and/or increasing 17β-estradiol levels. Furthermore, short- and long-chain PFCAs activated PPARα and PPARγ. Collectively, this means that (i) PAPs, FTOHs, and PFCAs exhibit endocrine activity through distinct and sometimes different mechanisms, (ii) two out of three tested TMs exhibited estrogenic activity, and (iii) short-chain FTOHs showed estrogenic activity and short-chain PFCAs generally activate both PPARα and PPARγ with similar potency and efficacy as long-chain PFCAs. In conclusion, several new and divergent toxicological targets were identified for different groups of PFAS.

General information
State: Published
Organisations: National Food Institute, Research Group for Molecular Toxicology, Research Group for Analytical Food Chemistry, Copenhagen Center for Health Technology, Université de Rennes, BioDetection Systems b.v.
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Scopus rating (2015): SJR 1.015 SNIP 1.273 CiteScore 2.54
Scopus rating (2014): SJR 0.836 SNIP 1.055 CiteScore 2.47
Scopus rating (2013): SJR 0.664 SNIP 1.24
Scopus rating (2012): SJR 0.917 SNIP 1.297
Scopus rating (2011): SJR 0.979 SNIP 1.303
Scopus rating (2010): SJR 0.901 SNIP 1.196
Scopus rating (2009): SJR 0.931 SNIP 1.281
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Scopus rating (2005): SJR 0.856 SNIP 0.947
Scopus rating (2004): SJR 0.918 SNIP 1.049
Scopus rating (2003): SJR 0.875 SNIP 1.064
Scopus rating (2002): SJR 0.923 SNIP 0.935
Scopus rating (2001): SJR 0.743 SNIP 0.906
Scopus rating (2000): SJR 0.793 SNIP 0.966
Forward Models can be Inferred from EEG Data

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Cognitive Systems, Copenhagen Center for Health Technology
Authors: Hansen, S. T. (Intern), Hauberg, S. (Intern), Hansen, L. K. (Intern)
Number of pages: 3
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Fundamental structures of dynamic social networks
Social systems are in a constant state of flux, with dynamics spanning from minute-by-minute changes to patterns present on the timescale of years. Accurate models of social dynamics are important for understanding the spreading of influence or diseases, formation of friendships, and the productivity of teams. Although there has been much progress on understanding complex networks over the past decade, little is known about the regularities governing the microdynamics of social networks. Here, we explore the dynamic social network of a densely-connected population of ~1,000 individuals and their interactions in the network of real-world person-to-person proximity measured via Bluetooth, as well as their telecommunication networks, online social media contacts, geolocation, and demographic data. These high-resolution data allow us to observe social groups directly, rendering community detection unnecessary. Starting from 5-min time slices, we uncover dynamic social structures expressed on multiple timescales. On the hourly timescale, we find that gatherings are fluid, with members coming and going, but organized via a stable core of individuals. Each core represents a social context. Cores exhibit a pattern of recurring meetings across weeks and months, each with varying degrees of regularity. Taken together, these findings provide a powerful simplification of the social network, where cores represent fundamental structures expressed with strong temporal and spatial regularity. Using this framework, we explore the complex interplay between social and geospatial behavior, documenting how the formation of cores is preceded by coordination behavior in the communication networks and demonstrating that social behavior can be predicted with high precision.

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Cognitive Systems, Copenhagen Center for Health Technology, University of Copenhagen, Massachusetts Institute of Technology
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Scopus rating (2017): CitScore 8.59 SJR 6.092 SNIP 2.626
High-resolution kinetics and modeling of hydrogen peroxide degradation in live cells

Although the role of oxidative stress factors and their regulation is well studied, the temporal dynamics of stress recovery is still poorly understood. In particular, measuring the kinetics of stress recovery in the first minutes after acute exposure provides a powerful technique for assessing the role of regulatory proteins or enzymes through the use of mutant backgrounds. This project endeavors to screen the temporal dynamics of intracellular oxidant levels in live cells as a function of gene deletion in the budding yeast, Saccharomyces cerevisiae. Using the detailed time dynamics of extra- and intra-cellular peroxide we have developed a mathematical model that describes two distinct kinetic processes, an initial rapid degradation in the first 10–20 min followed by a slower process. Using this model, a qualitative comparison allowed us to assign the dependence of temporal events to genetic factors. Surprisingly, we found that the deletion of transcription factors Yap1p or Skn7p was sufficient to disrupt the establishment of the second degradation phase but not the initial phase. A better fundamental understanding of the role protective factors play in the recovery from oxidative stress may lead to strategies for protecting or sensitizing cell to this stress.

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Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Regulatory Genomics, Eucaryotic Molecular Cell Biology, Department of Electrical Engineering, Copenhagen Center for Health Technology, Biomedical Engineering
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Scopus rating (2015): SJR 2.518 SNIP 1.623 CiteScore 5.89
BFI (2014): BFI-level 1
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Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
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ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
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Scopus rating (2011): SJR 2.198 SNIP 1.73 CiteScore 5.66
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 2.357 SNIP 1.676
Infant Gut Microbiota Development Is Driven by Transition to Family Foods Independent of Maternal Obesity

The first years of life are paramount in establishing our endogenous gut microbiota, which is strongly affected by diet and has repeatedly been linked with obesity. However, very few studies have addressed the influence of maternal obesity on infant gut microbiota, which may occur either through vertically transmitted microbes or through the dietary habits of the family. Additionally, very little is known about the effect of diet during the complementary feeding period, which is potentially important for gut microbiota development. Here, the gut microbiotas of two different cohorts of infants, born either of a random sample of healthy mothers (n = 114), or of obese mothers (n = 113), were profiled by 16S rRNA amplicon sequencing. Gut microbiota data were compared to breastfeeding patterns and detailed individual dietary recordings to assess effects of the complementary diet. We found that maternal obesity did not influence microbial diversity or specific taxon abundances during the complementary feeding period. Across cohorts, breastfeeding duration and composition of the complementary diet were found to be the major determinants of gut microbiota development. In both cohorts, gut microbial composition and alpha diversity were thus strongly affected by introduction of family foods with high protein and fiber contents. Specifically, intake of meats, cheeses and Danish rye bread, rich in protein and fiber, were associated with increased alpha diversity. Our results reveal that the transition from early infant feeding to family foods is a major determinant for gut microbiota development.

General information
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Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, Division of Risk Assessment and Nutrition, Copenhagen Center for Health Technology, University of Copenhagen
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Integrating ergonomics knowledge into business-driven design projects: The shaping of resource constraints in engineering consultancy

BACKGROUND:
The integration of ergonomics knowledge into engineering projects leads to both healthier and more efficient workplaces. There is a lack of knowledge about integrating ergonomic knowledge into the design practice in engineering consultancies.

OBJECTIVES:
This study explores how organizational resources can pose constraints for the integration of ergonomics knowledge into engineering design projects in a business-driven setting, and how ergonomists cope with these resource constraints.
PARTICIPANTS:
An exploratory case study in an engineering consultancy was conducted. A total of 27 participants were interviewed.

METHODS:

Data were collected applying semi-structured interviews, observations, and documentary studies. Interviews were transcribed, coded, and categorized into themes.

RESULTS:

From the analysis five overall themes emerged as major constituents of resource constraints: 1) maximizing project revenue, 2) payment for ergonomics services, 3) value of ergonomic services, 4) role of the client, and 5) coping strategies to overcome resource constraints.

CONCLUSION:

We hypothesize that resource constraints were shaped due to sub-optimization of costs in design projects. The economical contribution of ergonomics measures was not evaluated in the entire life cycle of a designed workplace. Coping strategies included teaming up with engineering designers in the sales process or creating an alliance with ergonomists in the client organization.
Ladder Variational Autoencoder

Variational autoencoders are powerful models for unsupervised learning. However deep models with several layers of dependent stochastic variables are difficult to train which limits the improvements obtained using these highly expressive models. We propose a new inference model, the Ladder Variational Autoencoder, that recursively corrects the generative distribution by a data dependent approximate likelihood in a process resembling the recently proposed Ladder Network. We show that this model provides state of the art predictive log-likelihood and tighter log-likelihood lower bound compared to the purely bottom-up inference in layered Variational Autoencoders and other generative models. We provide a detailed analysis of the learned hierarchical latent representation and show that our new inference model is qualitatively different and utilizes a deeper more distributed hierarchy of latent variables. Finally, we observe that batch normalization and deterministic warm-up (gradually turning on the KL-term) are crucial for training variational models with many stochastic layers.

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Cognitive Systems, Copenhagen Center for Health Technology, University of Copenhagen, Aalto University
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Number of pages: 12
Measure of Node Similarity in Multilayer Networks

The weight of links in a network is often related to the similarity of the nodes. Here, we introduce a simple tunable measure for analysing the similarity of nodes across different link weights. In particular, we use the measure to analyse homophily in a group of 659 freshman students at a large university. Our analysis is based on data obtained using smartphones equipped with custom data collection software, complemented by questionnaire-based data. The network of social contacts is represented as a weighted multilayer network constructed from different channels of telecommunication as well as data on face-to-face contacts. We find that even strongly connected individuals are not more similar with respect to basic personality traits than randomly chosen pairs of individuals. In contrast, several socio-demographics variables have a significant degree of similarity. We further observe that similarity might be present in one layer of the multilayer network and simultaneously be absent in the other layers. For a variable such as gender, our measure reveals a transition from similarity between nodes connected with links of relatively low weight to dissimilarity for the nodes connected by the strongest links. We finally analyze the overlap between layers in the network for different levels of acquaintanceships.
Mechanisms behind cancer risks associated with consumption of red and processed meat

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Modeling and Prediction Using Stochastic Differential Equations
Pharmacokinetic/pharmacodynamic (PK/PD) modeling for a single subject is most often performed using nonlinear models based on deterministic ordinary differential equations (ODEs), and the variation between subjects in a population of subjects is described using a population (mixed effects) setup that describes the variation between subjects. The ODE setup implies that the variation for a single subject is described by a single parameter (or vector), namely the variance (covariance) of the residuals. Furthermore the prediction of the states is given as the solution to the ODEs and hence
assumed deterministic and can predict the future perfectly. A more realistic approach would be to allow for randomness in the model due to e.g., the model be too simple or errors in input. We describe a modeling and prediction setup which better reflects reality and suggests stochastic differential equations (SDEs) for modeling and forecasting. It is argued that this gives models and predictions which better reflect reality. The SDE approach also offers a more adequate framework for modeling and a number of efficient tools for model building. A software package (CTSM-R) for SDE-based modeling is briefly described.

General information
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Organisations: Department of Applied Mathematics and Computer Science, Dynamical Systems, Copenhagen Center for Health Technology, Center for Energy Resources Engineering, Scientific Computing
Authors: Juhl, R. (Intern), Møller, J. K. (Intern), Jørgensen, J. B. (Intern), Madsen, H. (Intern)
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Modelling the glucose-insulin-glucagon dynamics after subcutaneous administration of native glucagon and a novel glucagon analogue in dogs
Zealand Pharma has invented a glucagon analogue, ZP-GA-1, with increased stability in liquid formulation for treatment of hypoglycemia. A pharmacodynamic (PD) model is needed to compare ZP-GA-1 with marketed glucagon. We aim to develop a model of the complex glucose-insulin-glucagon dynamics based on physiology and data.

General information
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Organisations: Department of Applied Mathematics and Computer Science, Scientific Computing, Copenhagen Center for Health Technology, Center for Energy Resources Engineering, Dynamical Systems, Zealand Pharma A/S, McGill University
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Modelling the glucose-insulin-glucagon dynamics after subcutaneous administration of native glucagon and a novel glucagon analogue in dogs

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Scientific Computing, Copenhagen Center for Health Technology, Center for Energy Resources Engineering, Dynamical Systems, Zealand Pharma A/S, McGill
In healthy individuals, insulin and glucagon work in a complex fashion to maintain blood glucose levels within a narrow range. This regulation is distorted in patients with diabetes. The hepatic glucose response due to an elevated glucagon level depends on the current insulin concentration and thus endogenous glucose production (EGP) cannot be modeled without knowledge of the concentration of both hormones in plasma. Furthermore, literature suggests an upper limit to EGP irrespective of glucagon levels. We build a simulation model of the glucose-insulin-glucagon dynamics in man including saturation effect of EGP.

Ten healthy subjects received a 1 mg subcutaneous (SC) glucagon bolus (GlucaGen®). Plasma samples were collected until 300 minutes post dose for analysis for glucagon, insulin, and glucose concentrations. All observations were used to fit a physiological model of the glucose-insulin-glucagon dynamics using the Hovorka model with a novel multiplicative description of the effects of insulin and of glucagon on EGP.

Bayesian estimation by Maximum a Posteriori using prior knowledge reported in literature was used to estimate the model parameters for each subject. Profile likelihood plots were used to investigate parameter identifiability. Unidentifiable parameters were fixed at their prior mean values.

The new model enables simulations of the glucose-insulin-glucagon dynamics in humans at both low and high glucagon concentrations (180-8000 pg/mL) and physiologic insulin concentrations (1.2-81.9 mIU/L). The model can be used for simulation of glucagon bolus strategies for treatment of hypoglycemia and for in silico simulation of dual-hormone artificial pancreas algorithms.

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glucose production (EGP) can not be modelled without knowledge of the concentration of both hormones in plasma. Furthermore, literature suggests an upper limit to EGP irrespective of glucagon levels. We build a simulation model of the glucose-insulin-glucagon dynamics in man including saturation effect of EGP.

Ten healthy subjects received a 1 mg subcutaneous (SC) glucagon bolus (GlucaGen®). Plasma samples were collected until 300 minutes post dose and analyzed for glucagon, insulin, and glucose concentrations. All observations were used to fit a physiological model of the glucose-insulin-glucagon dynamics using the Hovorka model with a novel multiplicative description of the effects of insulin and of glucagon on EGP.

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The new model enables simulations of the glucose-insulin-glucagon dynamics in humans at both low and high glucagon concentrations (180-8000 pg/mL) and physiologic insulin concentrations (1.2-81.9 mIU/L). The model can be used for simulation of glucagon bolus strategies for treatment of hypoglycemia and for in silico simulation of dual-hormone artificial pancreas algorithms.
Multiple endocrine disrupting effects in rats perinatally exposed to butylparaben

Parabens comprise a group of preservatives commonly added to cosmetics, lotions and other consumer products. Butylparaben has estrogenic and anti-androgenic properties and is known to reduce sperm counts in rats following perinatal exposure. Whether butylparaben exposure can affect other endocrine sensitive endpoints, however, remains largely unknown. In this study, time-mated Wistar rats (n=18) were orally exposed to 0, 10, 100 or 500 mg/kg bw/day of butylparaben from gestation day 7 to pup day 22. Several endocrine-sensitive endpoints were adversely affected. In the two highest dose groups, the anogenital distance of newborn male and female offspring was significantly reduced, and in prepubertal females, ovary weights were reduced and mammary gland outgrowth was increased. In male offspring, sperm count was significantly reduced at all doses from 10 mg/kg bw/day. Testicular CYP19a1 (aromatase) expression was reduced in prepubertal, but not adult animals exposed to butylparaben. In adult testes, Nr5a1 expression was reduced at all doses, indicating persistent disruption of steroidogenesis. Prostate histology was altered at prepuberty and adult prostate weights were reduced in the high dose group. Thus, butylparaben exerted endocrine disrupting effects on both male and female offspring. The observed adverse developmental effect on sperm count at the lowest dose is highly relevant to risk assessment, as this is the lowest observed adverse effect level in a study on perinatal exposure to butylparaben.
Net-Sights: A Practical Guide: Network insights for collaborative sustainable production

General information
State: Published
Organisations: Department of Management Engineering, Engineering Systems, Copenhagen Center for Health Technology
Authors: Andersen, J. W. (Intern), Parraguez Ruiz, P. (Intern), Maier, A. (Intern)
Number of pages: 52
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Electronic versions:
Neural Markers of Responsiveness to the Environment in Human Sleep

Sleep is characterized by a loss of behavioral responsiveness. However, recent research has shown that the sleeping brain is not completely disconnected from its environment. How neural activity constrains the ability to process sensory information while asleep is yet unclear. Here, we instructed human volunteers to classify words with lateralized hand responses while falling asleep. Using an electroencephalographic (EEG) marker of motor preparation, we show how responsiveness is modulated across sleep. These modulations are tracked using classic event-related potential analyses complemented by Lempel-Ziv complexity (LZc), a measure shown to track arousal in sleep and anesthesia. Neural activity related to the semantic content of stimuli was conserved in light non-rapid eye movement (NREM) sleep. However, these processes were suppressed in deep NREM sleep and, importantly, also in REM sleep, despite the recovery of wake-like neural activity in the latter. In NREM sleep, sensory activations were counterbalanced by evoked down states, which, when present, blocked further processing of external information. In addition, responsiveness markers correlated positively with baseline complexity, which could be related to modulation in sleep depth. In REM sleep, however, this relationship was reversed. We therefore propose that, in REM sleep, endogenously generated processes compete with the processing of external input. Sleep can thus be seen as a self-regulated process in which external information can be processed in lighter stages but suppressed in deeper stages. Last, our results suggest drastically different gating mechanisms in NREM and REM sleep.

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Web of Science (2017): Indexed Yes
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Scopus rating (2016): CiteScore 5.96 SJR 4.849 SNIP 1.617
Web of Science (2016): Indexed yes
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Scopus rating (2015): SJR 5.042 SNIP 1.694 CiteScore 6.33
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 5.305 SNIP 1.761 CiteScore 6.66
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 5.742 SNIP 1.863 CiteScore 7.22
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BFI (2012): BFI-level 2
Scopus rating (2012): SJR 5.743 SNIP 1.963 CiteScore 7.6
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Neurofeedback Therapy for Enhancing Visual Attention: State-of-the-Art and Challenges

We have witnessed a rapid development of brain-computer interfaces (BCIs) linking the brain to external devices. BCIs can be utilized to treat neurological conditions and even to augment brain functions. BCIs offer a promising treatment for mental disorders, including disorders of attention. Here we review the current state of the art and challenges of attention-based BCIs, with a focus on visual attention. Attention-based BCIs utilize electroencephalograms (EEGs) or other recording techniques to generate neurofeedback, which patients use to improve their attention, a complex cognitive function. Although progress has been made in the studies of neural mechanisms of attention, extraction of attention-related neural signals needed for BCI operations is a difficult problem. To attain good BCI performance, it is important to select the features of neural activity that represent attentional signals. BCI decoding of attention-related activity may be hindered by the presence of different neural signals. Therefore, BCI accuracy can be improved by signal processing algorithms that dissociate signals of interest from irrelevant activities. Notwithstanding recent progress, optimal processing of attentional neural signals remains a fundamental challenge for the development of efficient therapies for disorders of attention.

General information
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Novel Automatic Detection of Pleura and B-lines (Comet-Tail Artifacts) on In-Vivo Lung Ultrasound Scans.

This paper presents a novel automatic method for detection of B-lines (comet-tail artifacts) in lung ultrasound scans. B-lines are the most commonly used artifacts for analyzing the pulmonary edema. They appear as laser-like vertical beams, which arise from the pleural line and spread down without fading to the edge of the screen. An increase in their number is associated with presence of edema. All the scans used in this study were acquired using a BK3000 ultrasound scanner (BK Ultrasound, Denmark) driving a 192-element 5.5 MHz wide linear transducer (10L2W, BK Ultrasound). The dynamic received focus technique was employed to generate the sequences. Six subjects, among those three patients after major surgery and three normal subjects, were scanned once and six ultrasound sequences each containing 50 frames were acquired. The proposed algorithm was applied to all 300 in-vivo lung ultrasound images. The pleural line is first segmented on each image and then the B-line artifacts spreading down from the pleural line are detected and overlayed on the image. The resulting 300 images showed that the mean lateral distance between B-lines detected on images acquired from patients decreased by 20% in compare with that of normal subjects. Therefore, the method can be used as the basis of a method of automatically and qualitatively characterizing the distribution of B-lines.

General information
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Number of pages: 7
Publication date: 2016

Host publication information
Optimal uplink power control for dual connected users in LTE heterogeneous networks

In Dual Connectivity (DC), a User Equipment (UE) can be configured with two radio access nodes in order to aggregate the available resources at both nodes. As with dual connectivity each node has independent radio resource management, the maximum power allocation at the UE can be easily exceeded and the interference can be increased. Hence, the power distribution among the carriers needs to be optimized and has to minimize the required coordination among the nodes. In this paper we propose an optimal power allocation based on the load of the cells and cell effective interference. Additionally, we determine criteria for configuration of UEs with dual connectivity. The simulation results show performance improvement by the proposed algorithm with respect to the achieved user throughput. Performance gains (threelfold gain in median user throughput) are evident in low as well as high loads in the cell.

General information
State: Published
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Number of pages: 5
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Participatory simulation in hospital work system design

When ergonomic considerations are integrated into the design of work systems, both overall system performance and employee well-being improve. A central part of integrating ergonomics in work system design is to benefit from employees’ knowledge of existing work systems. Participatory simulation (PS) is a method to access employee knowledge; namely employees are involved in the simulation and design of their own future work systems through the exploration of models representing work system designs. However, only a few studies have investigated PS and the elements of the method. Yet understanding the elements is essential when analyzing and planning PS in research and practice.

This PhD study investigates PS and the method elements in the context of the Danish hospital sector, where PS is applied in the renewal and design of public hospitals and the work systems within the hospitals. The investigation was guided by three research questions focusing on: 1) the influence of simulation media on ergonomic evaluation in PS, 2) the creation of ergonomic knowledge in PS, and 3) the transfer and integration of the ergonomic knowledge into work system design. The investigation was based on three PS cases in the Danish hospital sector. The cases were analyzed from an ergonomics system perspective combined with theories on knowledge creation, transfer, and integration. The results are presented in six scientific papers from which three core findings are extracted: 1) simulation media attributes influence the type of ergonomic conditions that can be evaluated in PS, 2) sequences and overlaps of knowledge creation activities are sources of ergonomic knowledge creation in PS, and 3) intermediaries are means of knowledge transfer, and interpretation and transformation are means of knowledge integration.

Perturbation of neonatal microbial gut community by peripartum antibiotics in wistar rats lead to decreased weight gain

General information
State: Published
Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology, Technical University of Denmark
Authors: Tulstrup, M. V. (Intern), Bahl, M. I. (Intern), Roager, H. M. (Intern), Licht, T. R. (Intern), Clement Thaarup, I. (Ekstern)
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Perturbation of Neonatal Microbial Gut Community by Peripartum Antibiotics in Wistar Rats Lead to Decreased Weight Gain

Cross talk between a mammalian host and its intestinal microbiota plays a role in immune mediated diseases such as allergies, asthma, type 1 diabetes, as well as in obesity and auto immune diseases. Over the past decades, a significant increase of these diseases in young children in the developed world has been documented. In Western countries the pattern of initial colonization of the gut during the first days of life has changed dramatically. Among factors potentially modulating initial colonization, the use of antibiotics is particularly important. Antibiotics are frequently administered orally to either mothers or young children to treat or prevent bacterial infections not necessarily related to the gastrointestinal system. This has adverse effects on the commensal gut microbial community, as it disrupts the intricate balance between specific bacterial groups within this ecosystem, potentially leading to dysbiosis.

We hypothesized that modulation of community composition and function induced by peripartum antibiotics affects intestinal microbial composition and general health of the offspring.

To address this, 33 pregnant Wistar rats were dosed by oral gavage with either amoxicillin (AMX), vancomycin (VAN) or water (CON) daily from 8 days before delivery until weaning of the offspring. Significant lower weight gain of the offspring of antibiotic treated dams compared to the control were observed. The antibiotic treated dams had significantly larger caecum size and higher caecal pH as well as spleen size than control animals. Offspring were dissected at different time points and significant changes in liver, spleen and epididymal fat were measured between groups. Composition of the gut microbiota, alpha diversity, caecum short chain fatty acid levels, caloric contents of faeces, bile salt levels, acute phase protein haptoglobin in blood, social and locomotive behavior as well as gene expression of tight junction proteins are currently being analyzed.
Perturbation of Neonatal Microbial Gut Community by Peripartum Antibiotics in Wistar Rats Lead to Decreased Weight Gain

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PK/PD modelling of glucose-insulin-glucagon dynamics in healthy dogs after a subcutaneous bolus administration of native glucagon or a novel glucagon analogue
Objective We aim to develop a simulation model of the complex glucose-insulin-glucagon dynamics based on physiology and data. Furthermore, we compare pharmacokinetic (PK) and pharmacodynamic (PD) characteristics of marketed

Perturbation of Neonatal Microbial Gut Community by Peripartum Antibiotics in Wistar Rats Lead to Decreased Weight Gain

General information
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Organisations: National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology, Technical University of Denmark
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Perturbation of Neonatal Microbial Gut Community by Peripartum Antibiotics in Wistar Rats Lead to Decreased Weight Gain

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reconstituted glucagon with a stable liquid glucagon analogue invented by Zealand Pharma A/S.

**Research Design and Methods** We expanded a physiological model of endogenous glucose production with multiplicative effects of insulin and glucagon and combined it with the Hovorka glucoregulatory model. We used a Bayesian framework to perform multidimensional MAP estimation of model parameters given priors reported in the literature. We used profile likelihood analysis to investigate parameter identifiability and reduce the number of model variables. We estimated model parameters in pre-clinical data from one cross-over study with a total of 20 experiments in five dogs. The dogs received two subcutaneous (SC) bolus injections of low and high doses of glucagon and ZP-GA-1 (20 and 120 nmol/kg).

**Results** We report posterior probability distributions and correlations for all identifiable model parameters. Based on visual inspection and residual analysis, the PD model described data satisfactorily for both glucagon and the analogue. Parameter estimates of the PD model were not significantly different between the two compounds.

**Conclusions** The new PK/PD model enables simulations of the glucose-insulin-glucagon dynamics after a SC bolus of glucagon or glucagon analogue. The novel glucagon analogue by Zealand Pharma A/S shows PK and PD characteristics similar to marketed glucagon.

**General information**
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Organisations: Department of Applied Mathematics and Computer Science, Scientific Computing, Dynamical Systems, Copenhagen Center for Health Technology, Center for Energy Resources Engineering, Zealand Pharma A/S, McGill University
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**Portable Prescreening System for Sleep Apnea**
Obstructive sleep apnea (OSA) occurs in more than 4 % of the adult population. Diagnoses for OSA in sleep clinics are costly and more than half of those submitted to a sleep clinic do not have OSA. A simple, easy, and portable homebased monitoring system to evaluate who are in high- or low risk of suffering from OSA would be beneficial. The system must be able to identify individuals with a high pre-test reliability regarding OSA with the aim of referral and further investigation. We aimed to develop a portable, smartphone, and homebased monitoring system to classify whether a patient screened for sleep apnea is at high risk or low risk of having OSA. A new test setup was developed containing an Android based smartphone, the built in accelerometer, and a microphone. To ease the clinical analysis of the data a MATLAB based graphical user interface has been developed visualizing the data allowing the user to navigate through the data and the detected apnea events. The events are classified using both features from the audio and the signal from the accelerometer placed on sternum. Furthermore using the accelerometer data the sleep position is estimated and the morphology from the respiratory pattern is available describing the events and making it possible to distinguish between OSA and central sleep apnea (CSA).

**General information**
State: Published
Organisations: Copenhagen Center for Health Technology, Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, University of Copenhagen
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Pages: 4917-4920
Predicting the emotions expressed in music

With the ever-growing popularity and availability of digital music through streaming services and digital download, making sense of the millions of songs, is ever more pertinent. However the traditional approach of creating music systems has treated songs like items in a store, like books and movies. However music is special, having origins in a number of evolutionary adaptations. The fundamental needs and goals of a user's use of music, was investigated to create the next generation of music systems. People listen to music to regulate their mood and emotions was found to be the most important fundamental reason. (Mis)matching people's mood with the emotions expressed in music was found to be an essential underlying mechanism, people use to regulate their emotions. This formed the basis and overall goal of this thesis, to investigate how to create a predictive model of emotions expressed in music. To use in the next generation of music systems.

The thesis was divided into three main topics involved in creating a predictive model 1) Elicitation of emotion, 2) Audio representation and 3) Modelling framework, associating the emotion and audio representation, allowing to predict the emotions expressed in music.

The traditional approach of quantifying musical stimuli on the valence and arousal representation of emotions using continuous or Likert scales was questioned. An outline of a number of biases and the so-called confidence effect when using bipolar scales led to the use of relative scales in the form of pairwise comparisons. One issue with pairwise comparisons is the scaling, this was solved using an active learning approach through a Gaussian Process model.

Traditional audio representation disregards all temporal information in audio features used for modelling the emotions expressed in music. Therefore a probabilistic feature representation framework was introduced enabling both temporal and non-temporal aspects to be coded in discrete and continuous features. Generative models are estimated for each feature time-series and used in a discriminative setting using the Probability Product Kernel (PPK) allowing the use of this approach in any kernel machine.

To model the pairwise comparisons directly, a Generalized Linear Model, a kernel extension and a Gaussian Process model were used. These models can predict the ranking of songs on the valence and arousal dimensions directly. Furthermore use of the PPK allowed to find optimal combinations of both feature and feature representation using Multiple Kernel Learning.
Prediction Methods for Blood Glucose Concentration: Design, Use and Evaluation

Standard diabetes insulin therapy for type 1 diabetes and late stages of type 2 is based on the expected development of blood glucose (BG) both as a consequence of the metabolic glucose consumption as well as of meals and exogenous insulin intake. Traditionally, this is not done explicitly, but the insulin amount is chosen using factors that account for this expectation.

The increasing availability of more accurate continuous blood glucose measurement (CGM) systems is attracting much interest to the possibilities of explicit prediction of future BG values. Against this background, in 2014 a two-day workshop on the design, use and evaluation of prediction methods for blood glucose concentration was held at the Johannes Kepler University Linz, Austria. One intention of the workshop was to bring together experts working in various fields on the same topic, in order to shed light from different angles on the underlying problem of modeling the glucose insulin dynamics of type 1 diabetes patients. Among the international participants were continuous glucose monitoring developers, diabetologists, mathematicians and control engineers, both, from academia and industry. In total 18 talks were given followed by panel discussions which allowed to receive direct feedback from the point of view of different disciplines.

This book is based on the contributions of that workshop and is intended to convey an overview of the different aspects involved in the prediction. The individual chapters are based on the presentations given by the authors at the workshop but were written afterward which allowed to include the findings and conclusions of the various discussions and of course updates.

The chapter “Alternative Frameworks for Personalized Insulin-Glucose Models” by Harald Kirchsteiger et al. asks the question whether more and more detailed physiological descriptions of the glucose metabolism with an ever-increasing degree of sophistication and number of modeled phenomena are really what is needed for pushing the boundaries in glucose prediction for control. As an alternative, the chapter introduces two data-based approaches that focus not on the prediction of exact future blood glucose values, but rather on the prediction of changes in the patients’ blood glucose range.

The chapter “Accuracy of BG Meters and CGM Systems: Possible Influence Factors for the Glucose Prediction Based on Tissue Glucose Concentrations” by Guido Freckmann et al. discusses performance metrics used to characterize the accuracy of continuous glucose measurement devices. This topic is highly relevant for prediction models since many of them rely on the data given by the continuous sensors which are previously calibrated with blood glucose meter measurements which are also subject to measurement errors. Inaccurate measurements will directly affect the performance of the corresponding predictions.

The chapter “CGM — How Good Is Good Enough?” by Michael Schoemaker and Christopher G. Parkin also tackles the problem of continuous glucose monitor performance evaluation. Several performance metrics used in different published studies are compared and their individual characteristics analyzed. The chapter reveals why the comparison of a sensor evaluated in two different clinical studies is not always straightforward.

The chapter “Can We Use Measurements to Classify Patients Suffering from Type 1 Diabetes into Subcategories and Does It Make Sense?” by Florian Reiterer et al. makes use of continuous time prediction models to describe the interaction between ingested carbohydrates, subcutaneously injected insulin, and continuously measured glucose concentration. The identified model parameters of 12 subjects were analyzed and statistically significant correlations between the parameters and patient characteristics such as weight and age could be found.

The chapter “Prevention of Severe Hypoglycemia by Continuous EEG Monitoring” by Claus Borg Juhl et al. shows how to use EEG signals to predict upcoming hypoglycemic situations in real-time by employing artificial neural networks. The results of a 30-day long clinical study with the implanted device and the developed algorithm are presented.

The chapter “Meta-Learning Based Blood Glucose Predictor for Diabetic Smartphone App” by Valeriya Naumova et al. demonstrates how a highly sophisticated glucose prediction model can be ported from a development language running on a PC to a format such that it can be used conveniently by the patients. A unique feature of the algorithm is its independence of any user input other than historic CGM data which is automatically transmitted from a CGM device. No parameter estimation nor prediction model individualization is required.

The chapter “Predicting Glycemia in Type 1 Diabetes Mellitus with Subspace-Based Linear Multistep Predictors” by Marzia Cescon et al. uses data-based methods to precompute the rate of appearance of injected insulin and ingested carbohydrates in the bloodstream and of data-based models to combine this information and compute predictions up to 120 min in the future. The results show the performance on data from 14 type 1 diabetes patients in a clinical trial.

shows a modeling technique designed to extract the information on the net effect of meals on the blood glucose concentration. By assuming that all major unexplained glycemic excursions can be attributed to oral glucose ingestion, a meal vector is estimated which significantly improves the mathematical model. Results are shown on three patients during a clinical trial and on virtual patients where it is shown how the method can be used for adjustments of the basal insulin rate.

The chapter "Physiology-Based Interval Models: A Framework for Glucose Prediction Under Intra-patient Variability" by Jorge Bondia and Josep Vehi tries to cope with the large intrasubject variability by using the concept of interval predictions. Instead of predicting a single blood glucose value in the future, a whole solution envelope is determined. With the presented theory it can be guaranteed that the real value is always inside of the envelope and moreover the envelope is not conservative. The method is evaluated on a physiological diabetes model.

The chapter "Modeling and Prediction Using Stochastic Differential Equations" by Rune Juhl et al. considers uncertainty in the dynamics between different patients as well as within a patient by making use of stochastic differential equations. It is shown how the mixed effects modeling methodology can be applied such that the underlying information of several datasets from different patients is extracted to form the model.

The chapter "Uncertainties and Modeling Errors of Type 1 Diabetes Models" by Levente Kovács and Péter Szalay analyzes the effect of prediction model uncertainties on the control system during a design procedure involving the steps model reduction by elimination of state variables, state estimation using extended Kalman Filters and Sigma Point filters and linear parameter-varying control synthesis.

The chapter "Recent Results on Glucose–Insulin Predictions by Means of a State Observer for Time-Delay Systems" by Pasquale Palumbo et al. introduces a prediction model which in real time predicts the insulin concentration in blood which in turn is used in a control system. The method is tested in simulation on a time-delay system representing the glucose–insulin system.

The chapter "Performance Assessment of Model-Based Artificial Pancreas Control Systems" by Jianyuan Feng et al. makes use of prediction models to compute treatment advice. The novelty of the proposed algorithm consists in explicitly considering (among others) the model prediction error and model error elimination speed. A retuning of the advisory system is done in case the prediction model does not perform well. Results on 30 virtual patients show the performance of the control system.

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in a vast amount of new applications and methods. However, such low-cost sensors are generally limited in their accuracy and precision, making them unsuitable for e.g. accurate tracking and pose estimation.

With recent improvements in projector technology, increased processing power, and methods presented in this thesis, it is possible to perform structured light scans in real time with 20 depth measurements per second. This offers new opportunities for studying dynamic scenes, quality control, human-computer interaction and more.

This thesis discusses several aspects of real time structured light systems and presents contributions within calibration, scene coding and motion correction aspects. The problem of reliable and fast calibration of such systems is addressed with a novel calibration scheme utilising radial basis functions [Contribution B]. A high performance flexible open source software toolkit is presented [Contribution C], which makes real time scanning possible on commodity hardware. Further, an approach is presented to correct for motion artifacts in dynamic scenes [Contribution E].

An application for such systems is presented with a head tracking approach for medical motion correction [Contribution A, F]. This aims to solve the important problem of motion artifacts, which occur due to head movement during long acquisition times in MRI and PET scans. In contrast to existing methods, the one presented here is MRI compatible [Contribution D], not dependent on fiducial markers, and suitable for prospective correction.

Factors contributing to accuracy and precision of structured light systems are investigated with a study of performance factors [Contribution G]. This is also done in the context of biological tissue, which exhibit subsurface effects and other undesirable effects [Contribution H], and it is shown that this error is to a large extent deterministic and can be corrected.

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Organisations: Department of Applied Mathematics and Computer Science, Image Analysis & Computer Graphics, Copenhagen Center for Health Technology
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Sequential neural models with stochastic layers
How can we efficiently propagate uncertainty in a latent state representation with recurrent neural networks? This paper introduces stochastic recurrent neural networks which glue a deterministic recurrent neural network and a state space model together to form a stochastic and sequential neural generative model. The clear separation of deterministic and stochastic layers allows a structured variational inference network to track the factorization of the model's posterior distribution. By retaining both the nonlinear recursive structure of a recurrent neural network and averaging over the uncertainty in a latent path, like a state space model, we improve the state of the art results on the Blizzard and TIMIT speech modeling data sets by a large margin, while achieving comparable performances to competing methods on polyphonic music modeling.

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Software Defined Networking: Applicability and Service Possibilities

Network Service Providers (NSP) often choose to overprovision their networks instead of deploying proper Quality of Services (QoS) mechanisms that allow for traffic differentiation and predictable quality. This tendency of overprovisioning is not sustainable for the simple reason that network resources are limited. Hence, to counteract this trend, current QoS mechanisms must become simpler to deploy and operate, in order to motivate NSPs to employ QoS techniques instead of overprovisioning. Software Defined Networking (SDN) represents a paradigm shift in the way telecommunication and data networks are designed and managed. This thesis argues that SDN can greatly simplify QoS provisioning in communication networks, and even improve QoS in various ways. To this end, the impact of SDN on QoS is assessed from both a network performance perspective (e.g. bandwidth, delay), and also from a more generic perspective (e.g. service provisioning speed, resources availability). As a result, new mechanisms for providing QoS are proposed, solutions for SDN-specific QoS challenges are designed and tested, and new network management concepts are prototyped, all aiming to improve QoS for network services, from this extended point of view. Specifically, the challenge of SDN based QoS provisioning is addressed by considering every layer of the SDN architecture. In chapter 2, a short introduction to SDN is given, following that a complete architecture for QoS aware service provisioning in SDN is introduced in chapter 3. The following three chapters (4, 5 and 6) focus on each logical plane of the SDN architecture and identify the major challenges with respect to QoS, in relation to that specific plane (i.e. data, control and management). Further, each chapter proposes solutions to address the identified challenges, and demonstrates these solutions by testing them in various network scenarios. The last chapter of the thesis concentrates on applying SDN to improve QoS and increase the network utilization in a novel data center environment. This environment comprises a hybrid packet-circuit architecture, on top of which intelligent algorithms are applied in order to selectively offload traffic from the capacity constrained packet based network onto optical circuits. Overall, the research work presented in this thesis identifies and addresses the critical aspects of SDN based QoS provisioning. Moreover, several tests and demonstrations have been performed by using virtualization techniques. These tests aim to support the proposed ideas, and also to create a better picture of practical SDN deployments and the difficulties that arise in such virtualized environments.

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Steady State Visual Evoked Potential Based Brain-Computer Interface for Cognitive Assessment

Cognitive assessment is of growing importance, with the general population getting older and a rapidly growing incidence of dementia, which is a major public health issue. Treatment of dementia must, to be most effective, start early in the disease process. Thus, early detection of cognitive decline is important. Cognitive decline may be detected using fully automated computerized assessment. Such systems will provide inexpensive and widely available screenings of cognitive ability. The aim of this pilot study is to develop a real time steady state visual evoked potential (SSVEP) based brain-computer interface (BCI) for neurological cognitive assessment. It is intended for use by patients who suffer from diseases impairing their motor skills, but are still able to control their gaze. Results are based on 11 healthy test subjects. The system performance have an average accuracy of 100% ± 0%. The test subjects achieved an information transfer rate (ITR) of 14.64 bits/min ± 7.63 bits=min and a subject test performance of 47.22% ± 34.10%. This study suggests that BCI may be applicable in practice as a computerized cognitive assessment tool. However, many improvements are required for the system to be fully valid and of clinical use.
Studielederudfordringer ved tværfaglige uddannelser

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Surface-enhanced Raman spectroscopic study of DNA and 6-mercapto-1-hexanol interactions using large area mapping

The emergence of 2D SERS substrates with large areas of hot spots has enabled data to be gathered at large scale. This work presents a statistical tool for analysing large amounts of SERS data by utilizing a peak-fitting model in a specific spectral range. By analysing the distributions of Raman intensities and peak positions it is possible to directly inspect the interplay between DNA and 6-mercapto-1-hexanol on gold covered nanopillars. It is demonstrated that optimised functionalization parameters can be extracted from the Raman spectra directly. Using the peak-fitting approach it is possible to avoid miss-interpretation of intensity histograms, where contamination might contribute with an enhanced background and not a peak.

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Authors: Frøhling, K. B. (Intern), Alstrøm, T. S. (Intern), Bache, M. (Intern), Schmidt, M. S. (Intern), Schmidt, M. N. (Intern), Larsen, J. (Intern), Jakobsen, M. H. (Intern), Boisen, A. (Intern)
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Scopus rating (2016): CiteScore 1.76
Web of Science (2016): Indexed yes
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BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 2.1
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Synchronization Algorithm for SDN-controlled All-Optical TDM Switching in a Random Length Ring Network

We propose and demonstrate an algorithm that allows for automatic synchronization of SDN-controlled all-optical TDM switching nodes connected in a ring network. We experimentally show successful WDM-SDM transmission of data bursts between all ring nodes.

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Authors: Kamchevska, V. (Intern), Cristofori, V. (Intern), Da Ros, F. (Intern), Guo, B. (Ekstern), Jackson, C. (Ekstern), Fagertun, A. M. (Intern), Ruepp, S. R. (Intern), Nejabati, R. (Ekstern), Simeonidou, D. (Ekstern), Dittmann, L. (Intern), Berger, M. S. (Intern), Oxenløwe, L. K. (Intern), Galili, M. (Intern)
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Synchronization in a Random Length Ring Network for SDN-Controlled Optical TDM Switching

In this paper we focus on optical time division multiplexed (TDM) switching and its main distinguishing characteristics compared with other optical subwavelength switching technologies. We review and discuss in detail the synchronization requirements that allow for proper switching operation. In addition, we propose a novel synchronization algorithm that enables automatic synchronization of software defined networking controlled all-optical TDM switching nodes connected in a ring network. Besides providing synchronization, the algorithm also can facilitate dynamic slot size change and failure detection. We experimentally validate the algorithm behavior and achieve correct operation for three different ring lengths. Moreover, we experimentally demonstrate data plane connectivity in a ring network composed of three nodes and show successful wavelength division multiplexing space division multiplexing transmission and switching of data bursts when using the proposed algorithm to provide synchronization.

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Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.814 SNIP 1.708 CiteScore 3.39
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.782 SNIP 1.784 CiteScore 3.24
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.557 SNIP 1.654 CiteScore 2.51
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.795 SNIP 1.882 CiteScore 2.71
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.819 SNIP 3.904 CiteScore 2.99
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BFI (2010): BFI-level 1
The Center for Integrated Molecular Brain Imaging (Cimbi) database

We here describe a multimodality neuroimaging containing data from healthy volunteers and patients, acquired within the Lundbeck Foundation Center for Integrated Molecular Brain Imaging (Cimbi) in Copenhagen, Denmark. The data is of particular relevance for neurobiological research questions related to the serotonergic transmitter system with its normative data on the serotonergic subtype receptors 5-HT_{1A}, 5-HT_{1B}, 5-HT_{2A}, and 5-HT_{4} and the 5-HT transporter (5-HTT), but can easily serve other purposes.

The Cimbi database and Cimbi biobank were formally established in 2008 with the purpose to store the wealth of Cimbi-acquired data in a highly structured and standardized manner in accordance with the regulations issued by the Danish Data Protection Agency as well as to provide a quality-controlled resource for future hypothesis-generating and hypothesis-driven studies. The Cimbi database currently comprises a total of 1100 PET and 1000 structural and functional MRI scans and it holds a multitude of additional data, such as genetic and biochemical data, and scores from 17 self-reported questionnaires and from 11 neuropsychological paper/computer tests.

The database associated Cimbi biobank currently contains blood and in some instances saliva samples from about 500 healthy volunteers and 300 patients with e.g., major depression, dementia, substance abuse, obesity, and impulsive aggression. Data continue to be added to the Cimbi database and biobank.

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Scopus rating (2016): CiteScore 6.31 SJR 3.967 SNIP 1.759
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 4.583 SNIP 1.852 CiteScore 6.71
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 4.323 SNIP 2.03 CiteScore 6.9
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 4.489 SNIP 2.028 CiteScore 7.06
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 4.026 SNIP 1.972 CiteScore 6.86
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 3.728 SNIP 1.818 CiteScore 6.31
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 3.654 SNIP 1.869
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 3.954 SNIP 1.899
Web of Science (2009): Indexed yes
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Scopus rating (2008): SJR 4.196 SNIP 1.771
Web of Science (2008): Indexed yes
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 3.467 SNIP 1.94
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 3.78 SNIP 1.921
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 3.481 SNIP 1.803
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 2.003 SNIP 1
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 0.696 SNIP 0.404
Web of Science (2002): Indexed yes
The Personal Health Technology Design Space

Interest is increasing in personal health technologies that utilize mobile platforms for improved health and well-being. However, although a wide variety of these systems exist, each is designed quite differently and materializes many different and more or less explicit design assumptions. To enable designers to make informed and well-articulated design decisions, the authors propose a design space for personal health technologies. This space consists of 10 dimensions related to the design of data sampling strategies, visualization and feedback approaches, treatment models, and regulatory constraints.
Timing Analysis of Genetic Logic Circuits using D-VASim

A genetic logic circuit is a gene regulator network implemented by re-engineering the DNA of a cell, in order to control gene expression or metabolic pathways, through a logic combination of external signals, such as chemicals or proteins. As for electronic logic circuits, timing and propagation delay analysis may play a very significant role in the designing of genetic logic circuits. In this demonstration, we present the capability of D-VASim (Dynamic Virtual Analyzer and Simulator) to perform the timing and propagation delay analysis of genetic logic circuits. Using D-VASim, the timing and propagation delay analysis of single as well as cascaded genetic logic circuits can be performed. D-VASim allows user to change the circuit parameters during runtime simulation to observe its effect on circuit's timing behavior. The results obtained from D-VASim can be used not only to characterize the timing behavior of genetic logic circuits but also to analyze the timing constraints of cascaded genetic logic circuits.

Transferring in vivo exposure into in vitro assays using silicone to assess the endocrine activity of POPs accumulated in human breast implants

Transferring in vivo exposure into in vitro assays using silicone to assess the endocrine activity of POPs accumulated in human breast implants
Using Network Science to Support Design Research: From Counting to Connecting

A network-based perspective on designing permits research on the complexity of product, process, and people interactions. Strengthened by the latest advances in information technologies and accessibility of data, a network-based perspective and use of appropriate network analysis metrics, theories, and tools allow us to explore new data-driven research approaches in design. These approaches allow us to move from counting to connecting, meaning to explicitly link disconnected pieces of data, information, and knowledge, and thus to answer far-reaching research questions with strong industrial and societal impact. This chapter contributes to the use of network science in empirical studies of design organisations. It focuses on introducing a network-based perspective on the design process and in particular on making use of network science to support design research and practice. The main contribution of this chapter is an overview of the methodological challenges and core decision points when embarking on network-based design research, namely defining the overall research purpose and selecting network features. We furthermore highlight the potential for using archival data, the opportunities for navigating different levels of the design process that network analysis permits, what we here call zooming in and out, and the use of network visualisations. We illustrate the main points with a case from our own research on engineering communication networks. In this case, we have used more than three years of archival data, including design activity logs and work-related email exchanges from a recently completed large-scale engineering systems project of designing and developing a renewable power plant.

Visualizing Patient Journals by Combining Vital Signs Monitoring and Natural Language Processing

This paper presents a data-driven approach to graphically presenting text-based patient journals while still maintaining all textual information. The system first creates a timeline representation of a patients’ physiological condition during an admission, which is assessed by electronically monitoring vital signs and then combining these into Early Warning Scores (EWS). Hereafter, techniques from Natural Language Processing (NLP) are applied on the existing patient journal to extract all entries. Finally, the two methods are combined into an interactive timeline featuring the ability to see drastic changes in the patients’ health, and thereby enabling staff to see where in the journal critical events have taken place.
Voice analysis as an objective state marker in bipolar disorder

Changes in speech have been suggested as sensitive and valid measures of depression and mania in bipolar disorder. The present study aimed at investigating (1) voice features collected during phone calls as objective markers of affective states in bipolar disorder and (2) if combining voice features with automatically generated objective smartphone data on behavioral activities (for example, number of text messages and phone calls per day) and electronic self-monitored data (mood) on illness activity would increase the accuracy as a marker of affective states. Using smartphones, voice features, automatically generated objective smartphone data on behavioral activities and electronic self-monitored data were collected from 28 outpatients with bipolar disorder in naturalistic settings on a daily basis during a period of 12 weeks. Depressive and manic symptoms were assessed using the Hamilton Depression Rating Scale 17-item and the Young Mania Rating Scale, respectively, by a researcher blinded to smartphone data. Data were analyzed using random forest algorithms. Affective states were classified using voice features extracted during everyday life phone calls. Voice features were found to be more accurate, sensitive and specific in the classification of manic or mixed states with an area under the curve (AUC)=0.89 compared with an AUC=0.78 for the classification of depressive states. Combining voice features with automatically generated objective smartphone data on behavioral activities and electronic self-monitored data increased the accuracy, sensitivity and specificity of classification of affective states slightly. Voice features collected in naturalistic settings using smartphones may be used as objective state markers in patients with bipolar disorder.

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Web of Science (2016): Indexed yes
Scopus rating (2015): SJR 3.169 SNIP 1.273 CiteScore 5.61
Web of Science (2015): Indexed yes
Scopus rating (2014): SJR 3.189 SNIP 1.31 CiteScore 5.74
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Voice analysis as an objective state marker in bipolar disorder

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Scopus rating (2013): SJR 2.618 SNIP 1.509 CiteScore 4.8
Scopus rating (2012): SJR 3.084 SNIP 1.753 CiteScore 5.42
Scopus rating (2011): SJR 2.743 SNIP 1.625 CiteScore 4.84
Scopus rating (2010): SJR 2.711 SNIP 1.474
Scopus rating (2009): SJR 3.041 SNIP 1.566
Scopus rating (2008): SJR 2.764 SNIP 1.218
Scopus rating (2007): SJR 2.834 SNIP 1.368
Scopus rating (2006): SJR 2.228 SNIP 1.328
Scopus rating (2005): SJR 2.283 SNIP 1.128
Scopus rating (2004): SJR 2.23 SNIP 1.262
Scopus rating (2003): SJR 2.197 SNIP 0.988
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Wrist-worn pervasive gaze interaction
This paper addresses gaze interaction for smart home control, conducted from a wrist-worn unit. First we asked ten people to enact the gaze movements they would propose for e.g. opening a door or adjusting the room temperature. On
basis of their suggestions we built and tested different versions of a prototype applying off-screen stroke input. Command prompts were given to twenty participants by text or arrow displays. The success rate achieved by the end of their first encounter with the system was 46% in average; it took them 1.28 seconds to connect with the system and 1.29 seconds to make a correct selection. Their subjective evaluations were positive with regard to the speed of the interaction. We conclude that gaze gesture input seems feasible for fast and brief remote control of smart home technology provided that robustness of tracking is improved.

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A Bolus Calculator Based on Continuous-Discrete Unscented Kalman Filtering for Type 1 Diabetics
In patients with type 1 diabetes, the effects of meals intake on blood glucose level are usually mitigated by administering a large amount of insulin (bolus) at mealtime or even slightly before. This strategy assumes, among other things, a prior knowledge of the meal size and the postprandial glucose dynamics. On the other hand, administering the meal bolus during or after mealtime could benefit from the information provided by the postprandial meal dynamics at the expense of a delayed meal bolus. The present paper investigates different bolus administration strategies (at mealtime, 15 minutes after or 30 minutes after the beginning of the meal). We implement a continuous-discrete unscented Kalman filter to estimate the states and insulin sensitivity. These estimates are used in a bolus calculator. The numerical results demonstrate that administering the meal bolus 15 minutes after mealtime both reduces the risk of hypoglycemia in case of an overestimated meal and the time spent in hyperglycemia if the meal size is underestimated. Faster insulin and the use of glucagon will have the potential to encourage postprandial meal bolus administration and hence will not require to accurately estimate the meal size.

General information
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Organisations: Department of Applied Mathematics and Computer Science , Scientific Computing, Dynamical Systems, Copenhagen Center for Health Technology, Center for Energy Resources Engineering, Technical University of Denmark
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Advanced automated gain adjustments for in-vivo ultrasound imaging

Automatic gain adjustments are necessary on the state-of-the-art ultrasound scanners to obtain optimal scan quality, while reducing the unnecessary user interactions with the scanner. However, when large anechoic regions exist in the scan plane, the sudden and drastic variation of attenuations in the scanned media complicates the gain compensation. This paper presents an advanced and automated gain adjustment method that precisely compensate for the gains on scans and dynamically adapts to the drastic attenuation variations between different media. The proposed algorithm makes use of several ultrasonic physical estimates such as scattering strength, focus gain, acoustic attenuation, and noise level to gain a more quantitative understanding of the scanned media and to provide an intuitive adjustment of gains on the scan. The proposed algorithm was applied to a set of 45 in-vivo movie sequences each containing 50 frames. The scans are acquired using a recently commercialized BK3000 ultrasound scanner (BK Ultrasound, Denmark). Matching pairs of in-vivo sequences, unprocessed and processed with the proposed method were visualized side by side and evaluated by 4 radiologists for image quality. Wilcoxon signed-rank test was then applied to the ratings provided by radiologists. The average VAS score was highly positive 12.16 (p-value: 2.09 x 10-23) favoring the gain-adjusted scans with the proposed algorithm.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Copenhagen Center for Health Technology, Center for Fast Ultrasound Imaging, Copenhagen University Hospital, BK Medical Aps
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Number of pages: 4
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A Networked Perspective on the Engineering Design Process: At the Intersection of Process and Organisation Architectures

The design process of engineering systems frequently involves hundreds of activities and people over long periods of time and is implemented through complex networks of information exchanges. Such socio-technical complexity makes design processes hard to manage, and as a result, engineering design projects often fail to be on time, on budget, and meeting specifications. Despite the wealth of process models available, previous approaches have been insufficient to provide a networked perspective that allows the challenging combination of organisational and process complexity to unfold. The lack of a networked perspective also has limited the study of the relationships between process complexity and process performance. This thesis argues that to understand and improve design processes, we must look beyond the planned process and unfold the network structure and composition that actually implement the process. This combination of process structure—how people and activities are connected—and composition—the functional diversity of the groups participating in the process—is referred to as the actual design process architecture. This thesis reports on research undertaken to develop, apply and test a framework that characterises the actual design process architecture of engineering systems as a networked process. Research described in this thesis involved literature reviews in Engineering Design, Engineering Systems, Complexity and applied Network Science, and two case studies at engineering design companies with the objective of iteratively developing the framework and providing a proof-of-concept of its use in a large engineering design project. The developed Networked Process (NPr) Framework is composed of a conceptual model of the actual design process architecture, and an analytical method that allows the model and datadriven support to be quantified. The framework provides a networked perspective on three fundamental levels of analysis: 1) the activity-level, characterised as a network of people performing each activity, 2) the interface-level, characterised as a network of people interfacing between two interdependent activities, and 3) the whole process-level, characterised as a dynamic network of people and activities. The aim of the framework is to improve the design process of engineering systems through a more detailed overview of the actual design process, to support data-driven reflection of the relationship between process architecture and performance, and to provide the means to compare process plans against the actual process. The framework is based on a multi-domain network approach to process architecture and draws on previous research using matrix-based and graph-based process models. The results of the NPr Framework’s application in two case studies showed that decision makers in engineering design projects were able to gain new insights into their complex design processes through the framework. Such insights allowed them to better support and manage design activities, process interfaces and the whole design process. The framework also was used to enrich project debriefing and lessons-learned sessions, to spot process anomalies, to improve design process planning, to examine process progress, and to identify relationships between process architecture and performance. Contributions to knowledge include: First, the development of a more complete model of the actual process architecture and concrete analytical methods to quantify the developed model. Second, the identification of key structural and compositional variables as well as tests to identify the relationship between those variables and performance metrics. Third, the creation of a platform for further research on the relationships between actual design process architecture, behaviour and performance.
Automatic Generation of a Computational Model for Monopolar Stimulation of Cochlear Implants

General information
State: Published
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Bihormonal control of blood glucose in people with type 1 diabetes
This paper presents a bihormonal artificial pancreas (AP) for people with type 1 diabetes (T1D) designed to provide a safe blood glucose control with minimal use of glucagon. The control algorithm uses insulin as well as glucagon to prevent hyper- and hypoglycemia. We employ a novel prediction-based activation of glucagon administration. The control algorithm consists of a Kalman filter, an insulin infusion model predictive controller (MPC), a proportional-derivative (PD) controller for glucagon infusion, and a meal time insulin bolus calculator. The PD controller is activated if the Kalman filter predicts hypoglycemia. Predictions utilize an ARMAX model describing glucose-insulin and glucose-glucagon dynamics. The model parameters are estimated from basic patient-specific data. A continuous glucose monitor provides feedback. We test the control algorithm using a simulation model with time-varying parameters available for 3 patients. We consider a simulation scenario where meals are estimated correctly as well as overestimated by 30%. The simulation results demonstrate that during normal operation, the controller only needs insulin and does not need glucagon. During unexpected events, such as insulin overdose due to an overestimated meal, the control algorithm uses glucagon efficiently to avoid severe hypoglycemia.
Characterization of early and mature electrophysiological biomarkers of patients with Parkinson's disease

Cochlear Implant Planning, Selection and Simulation with Patient Specific Data

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Organisations: Department of Applied Mathematics and Computer Science, Image Analysis & Computer Graphics, Copenhagen Center for Health Technology, Alma IT Systems, MED-EL GMBH, UPF/ICREA
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Cochlear Implant Planning, Selection and Simulation with Patient Specific Data

Cochlear electrodes, Insertion simulation, Surgical planning, Hearing restoration

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Comparison of Prediction Models for a Dual-Hormone Artificial Pancreas

In this paper we compare the performance of five different continuous time transfer function models used in closed-loop model predictive control (MPC). These models describe the glucose-insulin and glucose-glucagon dynamics. They are discretized into a state-space description and used as prediction models in the MPC algorithm. We simulate a scenario including meals and daily variations in the model parameters. The numerical results do not show significant changes in the glucose traces for any of the models, excepted for the first order model. From the present study, we can conclude that the second order model without delay should provide the best trade-off between sensitivity to uncertainties and practical usability for in vivo clinical studies.

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Scopus rating (2007): SJR 0.107 SNIP 0.021
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Control of a post-combustion CO\textsubscript{2} capture plant during process start-up and load variations

Dynamic and flexible operation of a carbon capture plant is important as thermal power plants must be operated very flexibly to accommodate large shares of intermittent energy sources such as wind and solar energy. To facilitate such operation, dynamic models for simulation, optimization and control system design are crucial. In this paper, we present a dynamic mathematical model for the absorption and desorption columns in a carbon capture plant. Moreover, we implement a decentralized proportional-integral (PI) based control scheme and we evaluate the performance of the control structure for various operational procedures, e.g. start-up, load changes, noise on the flue gas flow rate and composition. Note that the carbon capture plant is based on the solvent storage configuration. To the authors' knowledge, this is the first paper addressing the issue of start-up operation and control of carbon capture. The study demonstrates that the implemented control structure keeps the carbon capture process at 90% CO\textsubscript{2} removal rate with a deviation up to 8% during load variations. In addition, it reveals that the control structure brings the process to the desired set point in approximately 10 min during process start-up.

General information
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Control Plane Strategies for Elastic Optical Networks

The goal of this Ph.d. project is to present and address selected challenges related to the increasing traffic demand and limited available capacity in core optical fiber infrastructure in parallel with tighter requirements of reducing energy consumption and operational costs. Elastic Optical Networks (EONs) concept is proposed as a solution to enable a more flexible handling of the optical capacity and allows an increase of available capacity over the existing optical infrastructure. One main requirement for enabling EONs is to have a flexible spectrum structure (i.e. Flex-Grid) which allows the spectrum to be used as an on-demand resource. Flex-Grid raises new challenges for controlling the dynamic spectrum slots environment. This thesis addresses, as part of the Celtic project “Elastic Optical Networks” (EONet), the control of Flex-Grid architectures by extending the capabilities of a GMPLS (Generalized Multi-Protocol Label Switching)-based control framework in accordance with existing IETF standards and recommendations. The usual approach of extending capacity in transport networks by incrementally adding more optical resources results in a very inefficient usage and determines a high power consumption. EONs offer the opportunity of deploying energy efficiency strategies, which benefit from the flexible nature of elastic optoelectronic devices. This thesis proposes and investigates different approaches for reducing power consumption based on EONs in realistic dynamic traffic scenarios.
Design of Low Power Algorithms for Automatic Embedded Analysis of Patch ECG Signals

The diagnosis of cardiac arrhythmias often depends on information from long-term ambulatory electrocardiographic (ECG) monitoring. For several decades, these recordings have been obtained by wired Holter recorders. However, to overcome some of the known disadvantages of the old technologies, several different cable-free wireless patch-type ECG recorders have recently reached the market. One of these recorders is the ePatch designed by the Danish company DELTA. The extended monitoring period available with the patch recorders has demonstrated to increase the diagnostic yield of outpatient ECG monitoring. Furthermore, the patch recorders facilitate the possibility of outpatient ECG monitoring in new clinically relevant areas, e.g. telemedicine monitoring of cardiac patients in their homes. Some of these new applications could benefit from real-time embedded interpretation of the recorded ECGs. Such algorithms could allow the real-time transmission of clinically relevant information to a central monitoring station. The first step in embedded ECG interpretation is the automatic detection of each individual heartbeat. An important part of this project was therefore to design a novel algorithm that was optimized for heartbeat detection in ePatch ECGs and embed the algorithm in the ePatch sensor for real-time analysis. We designed the algorithm based on a novel cascade of computational efficient filters and adaptive thresholds. We evaluated the algorithm on both standard databases and three different manually annotated ePatch databases. We found a very high detection performance with respect to both normal and abnormal beats as well as different types of artifacts arising from different daily life activities (average detection performance on 952,632 manually annotated beats obtained from 198 different patients: Se = 99.86% and P+ = 99.74%). This shows the possibilities for the embedded analysis of the ePatch ECGs, and the designed algorithm thus provides a platform for further research in this area. The expected advantages of the patch recorders are, however, unconditionally limited by their ability to record high-quality diagnostic ECGs throughout the recording period. Another main focus of this thesis was therefore to investigate different important clinical aspects of the novel ePatch recorder. To achieve this, we designed two pilot studies that were intended to provide information about the clinical usability of the ePatch ECGs for heart rhythm analysis. In the first pilot study, two medical doctors were asked to provide an individual assessment of the usefulness of 200 ePatch ECG segments for heart rhythm analysis. They found that more than 98% of the segments were useful. The second pilot study was designed as a high level comparison between the diagnostic information that could be extracted from simultaneous recordings obtained with the ePatch recorder and the traditional telemetry equipment. This comparison was conducted by a cardiologist on 11 admitted patients. He found no clinically relevant differences between the information extracted from the two systems. Both pilot studies thus indicate a high potential for the clinical application of ECGs recorded with the ePatch system. To further investigate the general signal quality obtained by the ePatch, we designed a novel algorithm for the automatic estimation of the overall percentage of analyzable time (PAT) in ECGs. The algorithm obtained very high classification performance and is therefore expected to provide a reliable estimation of the overall PAT. We then applied the algorithm to investigate the PAT in 250 different ePatch recordings. We found that 10% of the recordings obtained less than 10% analyzable time, and they were considered as incorrect measurements. For the remaining 90% of the recordings, we found a very high PAT (median: 100% (interquartile range: 97.9% to 100%); mean: (92.4 ± 18.8)%). We therefore didn’t find indications of problems related to the general signal quality obtained by the ePatch recorder. Overall, we thus find a high potential for the application of the ePatch recorder in many different clinical settings in the future.
D-VASim: Dynamic Virtual Analyzer and Simulator for Genetic Circuits

A genetic circuit represents a gene regulator network that is triggered by a combination of external signals, such as chemicals, proteins, light or temperature, to emit signals to control gene expression or metabolic pathways accordingly. In order to match the intended behaviour, genetic circuits are either assembled from a standard library of well-defined genetic gates or from parts of an available library, for instance, BioBricks. The obtained behavior can be validated through in-silico analysis, solving reaction kinetics using ordinary differential equations (ODEs) or by stochastic simulation, with the aim to reduce the number of required in-vitro experiments.

We present a behavioural simulation and analysis tool that allows the biologist to carry out virtual lab experiments as an interactive process during simulation of the genetic circuit, rather than a batch process, which is current practice. We believe that this increases the insights gained from the analysis and allows for exploring more parameters in an intuitive manner.

Fault-Tolerant Digital Microfluidic Biochips: Compilation and Synthesis
How Many Separable Sources? Model Selection In Independent Components Analysis
Unlike mixtures consisting solely of non-Gaussian sources, mixtures including two or more Gaussian components cannot
be separated using standard independent components analysis methods that are based on higher order statistics and
independent observations. The mixed Independent Components Analysis/Principal Components Analysis (mixed
ICA/PCA) model described here accommodates one or more Gaussian components in the independent components
analysis model and uses principal components analysis to characterize contributions from this inseparable Gaussian
subspace. Information theory can then be used to select from among potential model categories with differing numbers
of Gaussian components. Based on simulation studies, the assumptions and approximations underlying the Akaike
Information Criterion do not hold in this setting, even with a very large number of observations. Cross-validation is a
suitable, though computationally intensive alternative for model selection. Application of the algorithm is illustrated using
Fisher's iris data set and Howells' craniometric data set. Mixed ICA/PCA is of potential interest in any field of scientific
investigation where the authenticity of blindly separated non-Gaussian sources might otherwise be questionable. Failure of
the Akaike Information Criterion in model selection also has relevance in traditional independent components analysis
where all sources are assumed non-Gaussian.
Implementation of real-time duplex synthetic aperture ultrasonography

This paper presents a real-time duplex synthetic aperture imaging system, implemented on a commercially available tablet. This includes real-time wireless reception of ultrasound signals and GPU processing for B-mode and Color Flow Imaging (CFM). The objective of the work is to investigate the implementation complexity and processing demands. The image processing is performed using the principle of Synthetic Aperture Sequential Beamforming (SASB) and the flow estimator is implemented using the cross-correlation estimator. Results are evaluated using a HTC Nexus 9 tablet and a BK Medical BK3000 ultrasound scanner emulating a wireless probe. The duplex imaging setup consists of interleaved B-mode and CFM frames. The required data throughput for real-time imaging is 36.1 MB/s. The measured data throughput peaked at 39.562 MB/s, covering the requirement for real-time data transfer and overhead in the TCP/IP protocol. Benchmarking of real-time imaging showed a total processing time of 25.7 ms (39 frames/s) which is less than the acquisition time (29.4 ms). In conclusion, the proposed implementation demonstrates that both B-mode and CFM can be executed in-time for real-time ultrasound imaging and that the required bandwidth between the probe and processing unit is within the current Wi-Fi standards.
Investigation of the Minimum Conditions for Reliable Estimation of Clinically Relevant HRV Measures: Introducing a Novel Approach to the Validation of HRV Measurement Systems

The R-peak localization error (jitter) of a heart rate variability (HRV) system has a great impact on the values of the HRV measures. Only a few studies have analyzed this subject and purely done so from the aspect of choice of sampling frequency. In this study we provide an overview of the various factors that comprise the jitter of a system. We propose a method inspired by the field of signal averaged electrocardiography (SAECG) that allows for a quantification of the jitter of any HRV system that records and stores the raw ECG signal. Furthermore, with this method the differences between the HRV measures of the system and HRV measures corresponding to the physiological truth can be quantified. The method is used to obtain the physiologically true R-peak locations of subjects from Physionet’s ‘Normal Sinus Rhythm Database’. The effects of jitter are then analyzed via mathematical modelling for short-term and long-term HRV for various HRV measures. The effects of abnormal beats and missed and false detections are analyzed as well.

General information
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Organisations: Copenhagen Center for Health Technology, Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, DELTA, University of Copenhagen
Authors: Ahrens, E. (Ekstern), Sørensen, H. B. D. (Intern), Langberg, H. (Ekstern), Hoppe, K. (Ekstern), Bodholt Saadi, D. (Ekstern)
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**Smartphone data as an electronic biomarker of illness activity in bipolar disorder**

**Objectives**

Objective methods are lacking for continuous monitoring of illness activity in bipolar disorder. Smartphones offer unique opportunities for continuous monitoring and automatic collection of real-time data. The objectives of the paper were to test the hypotheses that (i) daily electronic self-monitored data and (ii) automatically generated objective data collected using smartphones correlate with clinical ratings of depressive and manic symptoms in patients with bipolar disorder.

**Methods**

Software for smartphones (the MONARCA I system) that collects automatically generated objective data and self-monitored data on illness activity in patients with bipolar disorder was developed by the authors. A total of 61 patients aged 18–60 years and with a diagnosis of bipolar disorder according to ICD-10 used the MONARCA I system for six months. Depressive and manic symptoms were assessed monthly using the Hamilton Depression Rating Scale 17-item (HDRS-17) and the Young Mania Rating Scale (YMRS), respectively. Data are representative of over 400 clinical ratings. Analyses were computed using linear mixed-effect regression models allowing for both between individual variation and within individual variation over time.

**Results**

Analyses showed significant positive correlations between the duration of incoming and outgoing calls/day and scores on the HDRS-17, and significant positive correlations between the number and duration of incoming calls/day and scores on the YMRS; the number of and duration of outgoing calls/day and scores on the YMRS; and the number of outgoing text messages/day and scores on the YMRS. Analyses showed significant negative correlations between self-monitored data (i.e., mood and activity) and scores on the HDRS-17, and significant positive correlations between self-monitored data (i.e., mood and activity) and scores on the YMRS. Finally, the automatically generated objective data were able to discriminate between affective states.

**Conclusions**

Automatically generated objective data and self-monitored data collected using smartphones correlate with clinically rated depressive and manic symptoms and differ between affective states in patients with bipolar disorder. Smartphone apps represent an easy and objective way to monitor illness activity with real-time data in bipolar disorder and may serve as an electronic biomarker of illness activity.

**General information**

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Organisations: Copenhagen Center for Health Technology, Rigshospitalet, IT University of Copenhagen
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Towards droplet size-aware biochemical application compilation for AM-EWOD biochips

Microfluidic-based biochips are replacing the conventional biochemical analyzers, and are able to integrate on-chip all the necessary functions for biochemical analysis using microfluidics. The digital microfluidic biochips are based on the manipulation of liquids not as a continuous flow, but as discrete droplets on an array of electrodes. Microfluidic operations, such as transport, mixing, split, are performed on this array by routing the corresponding droplets on a series of electrodes. Several approaches have been proposed for the compilation of digital microfluidic biochips, which, starting from a biochemical application and a given biochip architecture, determine the allocation, resource binding, scheduling, placement and routing of the operations in the application. To simplify the compilation problem, researchers have assumed an abstract droplet size of one electrode. However, the droplet size abstraction is not realistic and it impacts negatively the execution of the biochemical application, leading in most cases to its failure. Hence the existing compilation approaches have to be revisited to consider the size of the droplets. In this paper we take the first step towards a droplet size-aware compilation by proposing a routing algorithm that considers the droplet size. Our routing algorithm is developed for a novel digital microfluidic biochip architecture based on Active Matrix Electrowetting on Dielectric, which uses a thin film transistor array for the electrodes. We also implement a simulator that allows us to perform the needed adaptations and to validate the proposed routing algorithm.

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Towards Quasi-continuous Heart Rate Variability Estimation using a Patch Type Electrocardiogram Recorder

Changes in different heart rate variability (HRV) measures have been found to possess predictive information in patients with many different diseases, e.g. myocardial infarction, diabetic neuropathy, and patients at risk of developing sepsis. At the same time, the emerging of patch type electrocardiogram recorders facilitates new possibilities for long-term monitoring, real-time data analysis, and wireless transmission of clinically relevant parameters, e.g. short-term HRV measures. This information might in the future assist the healthcare professionals in timely notification of changes in the risk stratification profile obtained from the HRV measures. The purpose of this study is therefore to investigate the possibilities for quasi-continuous estimation of reliable HRV measures using the ePatch heart monitor. We compared the physiologically true values of 11 selected HRV measures with the values obtained using automatically generated RR series from electrocardiograms recorded with the ePatch using four different sampling frequencies (128 Hz, 256 Hz, 512 Hz, and 1024 Hz). We found no significant differences between neither the mean nor the median values of the obtained HRV measures for any of the sampling frequencies. This is very promising for the future application of the ePatch for quasi-continuous monitoring of HRV measures.

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Centre for Playware

Copenhagen Center for Health Technology
Period: 02/04/2018 → 01/04/2020
Number of participants: 4
Acronym: HBP SGA2
Number of related Ph.D. students: 1
Project participant:
Capolei, Marie Claire (Intern)
Corchado Miralles, Carlos (Intern)
Cyber Resilience for the Shipping Industry (CyberShip)
The shipping industry has become more vulnerable to cyber-attacks in recent years, because of its dependence on information technology and increasingly complex networks. Cyber systems are incorporated into almost every facet of maritime operations, such as financial and human resources management, security systems, navigation (Global Navigation Satellite Systems (GNSS), Automatic Identification System (AIS), Electronic Chart Display Systems (ECDIS), etc.), communications, electronic certificates, cargo tracking, pre-arrival processing and other key systems and equipment. All maritime structures (including ships and offshore facilities) as well as the connected infrastructure (e.g. offices of shipping companies, ports etc) are vulnerable. Currently, the awareness regarding cyber security aspects is either at a very low level or completely disregarded. The issue of cyber security has been brought into the attention of the International Maritime Organization (IMO), and industry associations such as BIMCO and others. As a result of this guidelines for tackling cyber security problems have been developed.
This project is aimed at providing shipping companies and regulators with a reference framework and decision support model to better cope with disruptions originating from a cyber-attack.

Department of Management Engineering
Management Science
Transport DTU
Department of Applied Mathematics and Computer Science
Cyber Security
Copenhagen Center for Health Technology
Period: 01/09/2017 → 31/08/2019
Number of participants: 5
Acronym: CyberShip
Project participant:
Psaraftis, Harilaos N. (Intern)
Jensen, Christian D. (Intern)
Sepúlveda Estay, Daniel Alberto (Intern)
Sahay, Rishikesh (Intern)
Project Manager, organisational:
Barfod, Michael Bruhn (Intern)

Relations
Publications:
Work Package 2 Report - Cyber resilience for the shipping industry

Future risk assessment of chemicals (MiracluX)
Development of Physiologically Based Kinetic (PBK) models for risk assessment of chemicals.
National Food Institute
Copenhagen Center for Health Technology
Research Group for Molecular Toxicology
Research Group for Reproductive Toxicology
Brunel University
Period: 02/01/2017 → 31/12/2018
Number of participants: 5
PBK modeling, Risk assessment
Project participant:
Bonomo, Silvia (Intern)
Project Manager, academic:
Taxvig, Camilla (Intern)
Svingen, Terje (Intern)
Boberg, Julie (Intern)
Project Coordinator:
Vinggaard, Anne Marie (Intern)

Relations
Activities:
Copenhagen Workshop on Endocrine Disrupters
Project

GazeIT – Accessibility by Gaze Trackning
Copenhagen Center for Health Technology
Department of Management Engineering
Technology and Innovation Management
Period: 01/04/2016 → 31/03/2021
Number of participants: 1
Acronym: GazeIT
Project participant:
Hansen, John Paulin (Intern)

Human Brain Project. Subproject 10 Neurorobotics Platform - SGA1
The Neurorobotics Platform (NRP) developed in the Human Brain Project (HBP) is an Internet-accessible simulation system that allows the simulation of robots controlled by spiking neural networks. It targets researchers of multiple fields. Prospected users include but are not limited to neuroscientists wanting to validate brain models in the context of closed action-perception loops as well as robotics researchers wanting to develop new neuro-inspired controllers.

Department of Electrical Engineering
Automation and Control
Centre for Playware

Reducing the rate and duration of re-admission among patients with unipolar and bipolar disorder using smartphone-based monitoring and treatment
According to WHO, depression is becoming a leading cause of disability. The RADMIS project seeks to design smartphone-based monitoring and treatment technology for depressive patients. The goal is to establish the efficacy of this technology by measuring re-admission and clinical outcome.

Department of Applied Mathematics and Computer Science
Embedded Systems Engineering
Cognitive Systems
Psychiatric Center Copenhagen, Rigshospitalet
Period: 01/03/2016 → 01/09/2019
Number of participants: 2
Acronym: RADMIS
Number of related Ph.D. students: 2
Project participant:
Bardram, Jakob Eyvind (Intern)
Winther, Ole (Intern)

Financing sources
Source: Public research programme (public)
Name of research programme: Innovation Fund Denmark
Web address: http://innovationsfonden.dk/en
Amount: 11,000,000.00 Danish Kroner
Year of approval: 2016

Activities:

**Characterizing molecular mechanisms for short anogenital distance**
Period: 4 Jun 2018 → 6 Jun 2018
Camilla Victoria Lindgren Schwartz (Speaker)
Anne Marie Vinggaard (Other)
Terje Svingen (Other)
National Food Institute
Research Group for Molecular and Reproductive Toxicology
Copenhagen Center for Health Technology

**Related event**
5th European Doctoral College on Environment and Health (EDCEH): Endocrine Disruptors: an update
04/06/2018 → 06/06/2018
Activity: Talks and presentations › Conference presentations

**Characterizing novel molecular mechanisms for short AGD – a biomarker of fetal testicular function**
Period: 23 May 2018 → 27 May 2018
Camilla Victoria Lindgren Schwartz (Speaker)
Anne Marie Vinggaard (Other)
Sofie Christiansen (Other)
Frederic Chalmel (Other)
Terje Svingen (Other)
National Food Institute
Research Group for Molecular and Reproductive Toxicology
Copenhagen Center for Health Technology

**Related event**
20th European Testis Workshop
23/05/2018 → 27/05/2018
Obedos, Portugal
Activity: Talks and presentations › Conference presentations

**Glyphosate alone does not adversely affect testicular androgen function in mature rats**
Period: 23 May 2018 → 27 May 2018
Hanna Katarina Lilith Johansson (Other)
Lene Narby Nielsen (Other)
Anne Marie Vinggaard (Other)
Martin Iain Bahl (Other)
Terje Svingen (Speaker)

National Food Institute
Research Group for Molecular and Reproductive Toxicology
Copenhagen Center for Health Technology
Research Group for Gut Microbiology and Immunology
Degree of recognition: International

Related event

20th European Testis Workshop
23/05/2018 → 27/05/2018
Obedos, Portugal
Activity: Talks and presentations › Conference presentations

Invited Speaker Design Debate at 15th International Design Conference (DESIGN2018)
Period: 21 May 2018 → 24 May 2018
Anja Maier (Invited speaker)

Department of Management Engineering
Engineering Systems
Copenhagen Center for Health Technology
Degree of recognition: International
Links:
http://www.designconference.org/ (15th International Design Conference (DESIGN2018))
https://www.designsociety.org/ (The Design Society)

Related event

The International Design Conference - DESIGN 2018
21/05/2018 → 24/05/2018
Dubrovnik, Croatia
Activity: Talks and presentations › Conference presentations

Concerns and tradeoff in privacy and safety of sensor-based monitoring of older people living at home
Period: 9 May 2018
Humira Ehrari (Other)
Henning Boje Andersen (Other)
Carl Johan Langberg (Other)

Department of Management Engineering
Technology and Innovation Management
Copenhagen Center for Health Technology
Documents:
Sensors and monitoring

Related event

11th World Conference of Gerontechnology
07/05/2018 → 11/06/2018
St. petersburg, United States
Activity: Talks and presentations › Conference presentations
Combination effects of pesticides on birth weight and metabolic programming in rat offspring
Period: 24 Jan 2018 → 25 Jan 2018
Terje Svingen (Invited speaker)
Louise Ramhøj (Other)
Marta Axelstad Petersen (Other)
Sofie Christiansen (Other)
Martin Scholze (Other)
Julie Boberg (Other)
Anne Marie Vinggaard (Other)
Ulla Hass (Other)
National Food Institute
Research Group for Molecular and Reproductive Toxicology
Copenhagen Center for Health Technology
Degree of recognition: National

Related event
Miljøstyrelsens Bekæmpelsesmiddelforkningskonference
24/01/2018 → 25/01/2018
Vejle, Denmark
Activity: Talks and presentations › Conference presentations

Journal of Engineering Design (Journal)
Period: 1 Jan 2018 → …
Anja Maier (Editor)
Department of Management Engineering
Engineering Systems
Copenhagen Center for Health Technology
Links:
https://www.tandfonline.com/loi/cjen20 (Journal of Engineering Design)

Related journal
Journal of Engineering Design
0954-4828
BFI (2018): BFI-level 1, Scopus rating (2017): CiteScore 2.39 SJR 0.727 SNIP 1.379, ISI indexed (2013): ISI indexed yes,
Web of Science (2018): Indexed yes
Central database
Activity: Research › Journal editor

Towards New Affect Integrated Interaction Design (Event)
Period: 23 Oct 2017
Anja Maier (External examiner)
Department of Management Engineering
Engineering Systems
Copenhagen Center for Health Technology
Description
Norwegian University of Science and Technology, Department of Engineering Design and Materials, TrollLabs
Censor for PhD project
Body type: PhD Assessment Committee
23 October 2017
Degree of recognition: International
Activity: Examinations and supervision › External examination
High power diode lasers converted to the visible
Period: 11 Oct 2017
Ole Bjarlin Jensen (Invited speaker)
Anders Kragh Hansen (Invited speaker)
Peter E. Andersen (Guest lecturer)
Mathias Christensen (Guest lecturer)
André Müller (Invited speaker)
Mahmoud Tawfieq (Invited speaker)
Bernd Sumpf (Invited speaker)
Paul Michael Petersen (Invited speaker)
Department of Photonics Engineering
Diode Lasers and LED Systems
Copenhagen Center for Health Technology

Description
Invited talk at the conference including 2 page abstract to be published in IEEE Xplore.
Degree of recognition: International

Related event
2017 IEEE High Power Diode Lasers & Systems Conference
11/10/2017 → 12/10/2017
Coventry, United Kingdom
Activity: Talks and presentations › Conference presentations

ICED17: 21st International Conference on Engineering Design
Anja Maier (Chairman)
Department of Management Engineering
Engineering Systems
Copenhagen Center for Health Technology
Degree of recognition: International
Links:
http://www.iced17.org

Related event
ICED17: 21st International Conference on Engineering Design
21/08/2017 → 25/08/2017
Vancouver, Canada
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

Change or be changed: Resilience in socio-technical systems (Event)
Period: 4 Jul 2017
Anja Maier (External examiner)
Department of Management Engineering
Engineering Systems
Copenhagen Center for Health Technology

Description
University of Cambridge, Department of Engineering, Engineering Design Centre
Censor for PhD project

Body type: PhD Assessment Committee
Management Team Copenhagen Center for Health Technology (Event)
Period: 1 Jul 2017 → …
Anja Maier (Member)
Department of Management Engineering
Engineering Systems
Copenhagen Center for Health Technology

Description
Member Management Team for Copenhagen Center for Health Technology
Degree of recognition: International

Related event
Management Team Copenhagen Center for Health Technology
01/07/2017 → …
Copenhagen, Denmark
Activity: Membership › Membership of committees, commissions, boards, councils, associations, organisations, or similar

PhD Assessment Committee Aalborg University (External organisation)
Period: 2 Jun 2017
Ole Broberg (Participant)
Copenhagen Center for Health Technology
Department of Management Engineering
Engineering Systems

Description
Member of assessment committee for PhD thesis by Anne Helbo Jespersen "OHS management systems audits as a regulatory instrument of psychosocial risks - principles and practice"
Degree of recognition: International

Related external organisation
PhD Assessment Committee Aalborg University
Activity: Membership › Membership in review committee

Mechanisms of action involved in chemically induced effects on male reproductive health
Period: 30 Mar 2017 → 31 Mar 2017
Camilla Victoria Lindgren Schwartz (Speaker)
Sofie Christiansen (Other)
Anne Marie Vinggaard (Other)
Terje Svingen (Other)
National Food Institute
Research Group for Molecular and Reproductive Toxicology
Copenhagen Center for Health Technology
Degree of recognition: Regional

Related event
3rd ReproYoung Conference
30/03/2017 → 31/03/2017
Båstad, Sweden
Activity: Talks and presentations › Conference presentations
Annual Design Society Board of Management and Advisory Board Meeting (Event)
Period: 13 Mar 2017 → 17 Mar 2017
Anja Maier (Participant)
Copenhagen Center for Health Technology
Department of Management Engineering
Engineering Systems
Description
Annual Design Society Board of Management and Advisory Board Meeting
Degree of recognition: International
Links:
http://www.designsociety.org (Design Society)
Related event
Annual Design Society Board of Management and Advisory Board Meeting
13/03/2017 → 17/03/2017
Montreal, Canada
Activity: Membership › Membership of committees, commissions, boards, councils, associations, organisations, or similar

ICED17: 21st International Conference on Engineering Design (Event)
Period: Jan 2017 → Aug 2017
Ole Broberg (Participant)
Copenhagen Center for Health Technology
Department of Management Engineering
Engineering Systems
Description
Member of Scientific Committee
Degree of recognition: International
Related event
ICED17: 21st International Conference on Engineering Design
21/08/2017 → 25/08/2017
Vancouver, Canada
Activity: Membership › Membership in review committee

Engineering Systems Design - International Research Seminar at DTU
Period: 12 Jan 2017
Josef Oehmen (Organizer)
Anja Maier (Organizer)
Department of Management Engineering
Engineering Systems
Copenhagen Center for Health Technology
Description
Engineering Systems Design - International Research Seminar at DTU
Filippo Salustri (Ryerson University, Canada): "Three Monsters in design research: defining, formalizing, and visualizing - an overview of 3 very difficult problems that still tax us" Despite tremendous headway in developing a robust science of design, some aspects of "designing" remain beyond our grasp, especially insofar as those aspects overlap significantly with non-engineering design disciplines. This talk will review some of Fil Salustri’s efforts to clarify three of these aspects.

Michael Kokkolaras (McGill, Canada): “Rigorous practical optimization for simulation-based engineering design” Computational models have accelerated the engineering design optimization process. Simulation-related challenges have been mostly addressed by heuristics-based methods. This talk presents alternatives that are supported by convergence properties.
Georges Fadel (Clemson University, United States of America): “Evolving Designs using Affordances” The talk focuses on the adaptation of the theory of “affordances” from the field of perceptual psychology to better capture the perceived positive and negative interactions between the user and the artifact and use optimization to evolve designs.

Degree of recognition: International

Documents:
Research Seminar on Engineering Systems Design - Flyer
Links:
http://www.dtu.dk/english/service/calendar/2017/01/engineering-systems-design-international-research-seminar?id=e364fe90-47c5-4d80-88fc-07f70dc8b733

Related event

Engineering Systems Design - International Research Seminar at DTU
12/01/2017 → 12/01/2017
Copenhagen, Denmark
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

Den Bibliometriske Forskningsindikator: Faggruppe 45 - System- og teknologiudvikling, serviceudvikling og facilities management, entreprenørforskning (External organisation)
Period: 1 Jan 2017 → 31 Dec 2019
Anja Maier (Participant)
Department of Management Engineering
Engineering Systems
Copenhagen Center for Health Technology
Links:
http://ufm.dk/forskning-og-innovation/statistik-og-analyser/den-bibliometriske-forskningsindikator

Related external organisation

Den Bibliometriske Forskningsindikator: Faggruppe 45 - System- og teknologiudvikling, serviceudvikling og facilities management, entreprenørforskning
Activity: Membership › Membership of committees, commissions, boards, councils, associations, organisations, or similar

Design Science Journal (Journal)
Period: 1 Jan 2017 → …
Anja Maier (Editor)
Department of Management Engineering
Engineering Systems
Copenhagen Center for Health Technology

Description
Network-based modeling and analysis in design

Guest editors of thematic collection:
Wei Chen, Northwestern University, USA
Babak Heydari, Stevens Institute of Technology, USA
Anja Maier, Technical University of Denmark, Denmark
Jitesh Panchal, Purdue University, USA

Call for Papers: http://www.designsciencejournal.org/network-based-modeling-analysis-design/

Articles published/to be published in the collection: https://www.cambridge.org/core/journals/design-science/collections/network-based-modeling-and-analysis-in-design-special-collection
Degree of recognition: International
Links:
**Related journal**

*Design Science Journal*

Web of Science (2018): Indexed yes  
Indexed in DOAJ  
Local database  
Activity: Research › Journal editor

**Vice-Chair, ISMRM study group on Detection & Correction of Motion in MRI & MRS (External organisation)**  
Period: 2016 → 2017  
Lars G. Hanson (Participant)  
Copenhagen Center for Health Technology  
Center for Hyperpolarization in Magnetic Resonance  
Department of Electrical Engineering  
Center for Magnetic Resonance

**Description**  
Research Network of the International Society for Magnetic Resonance in Medicine  
Degree of recognition: International

**Related external organisation**

**Vice-Chair, ISMRM study group on Detection & Correction of Motion in MRI & MRS**  
Activity: Membership › Membership of research networks or expert groups

**PhD opponent Chalmers University of Technology (External organisation)**  
Period: 6 Dec 2016  
Ole Broberg (External examiner)  
Copenhagen Center for Health Technology  
Department of Management Engineering  
Engineering Systems

**Description**  
PhD opponent on the thesis by Steven Mallam "Distributed Participatory Design in Multidisciplinary Engineering Projects"  
Degree of recognition: International  
Activity: Examinations and supervision › External examination

**Participatory Simulation in Hospital Work System Design (External organisation)**  
Period: 29 Nov 2016  
Anja Maier (Chairman)  
Department of Management Engineering  
Engineering Systems  
Copenhagen Center for Health Technology

**Description**  
PhD thesis at Technical University of Denmark  
PhD Assessment Committee

Body type: PhD Assessment Committee  
Degree of recognition: International

**Related external organisation**

**Participatory Simulation in Hospital Work System Design**  
Activity: Membership › Membership in review committee
XIIth International Symposium on Human Factors in Organizational Design and Management (ODAM) (External organisation)
Period: Sep 2016 → Aug 2017
Ole Broberg (Participant)
Copenhagen Center for Health Technology
Department of Management Engineering
Engineering Systems

Description
Member of Scientific Committee
Degree of recognition: International

Related external organisation
XIIth International Symposium on Human Factors in Organizational Design and Management (ODAM)
Activity: Membership › Membership in review committee

Mapping of design capacity in Denmark
Period: 21 Sep 2016
Ole Broberg (Participant)
Department of Management Engineering
Engineering Systems
Copenhagen Center for Health Technology

Description
Mapping of design capacity in Denmark

Related event
Mapping of design capacity in Denmark
21/09/2016 → 21/09/2016
Copenhagen, Denmark
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

1st Engineering Systems Design & Data Science: EuroTech Alliance DTU-TUM Workshop in Munich
Period: 19 Sep 2016 → 20 Sep 2016
Anja Maier (Speaker)
Engineering Systems
Department of Management Engineering
Copenhagen Center for Health Technology

Description
Engineering Systems Design & Data Science: EuroTech Alliance DTU-TUM Workshop in Munich

Related event
Engineering Systems Design & Data Science: EuroTech Alliance DTU-TUM Workshop in Munich
19/09/2016 → 20/09/2016
Munich, Germany
Activity: Talks and presentations › Conference presentations

Risks related to static magnetic fields
Period: 1 Sep 2016
Lars G. Hanson (Invited speaker)
Copenhagen Center for Health Technology
Center for Hyperpolarization in Magnetic Resonance
Department of Electrical Engineering
Center for Magnetic Resonance

**Description**
Invited oral presentation
Links:
http://dx.doi.org/10.1016/j.ejmp.2016.07.272

**Related event**

1st European Congress of Medical Physics
01/09/2016 → 04/09/2016
Athens, Greece
Activity: Talks and presentations › Conference presentations

Net-Sights: Data-driven network insights @ Big Data Business Academy
Period: 21 Jun 2016
Anja Maier (Invited speaker)
Engineering Systems
Department of Management Engineering
Copenhagen Center for Health Technology
Links:
http://www.netsights.dk

**Related event**

Big Data Business Academy Kick-Off
21/06/2016 → 21/06/2016
Lyngby, Denmark
Activity: Talks and presentations › Conference presentations

Late-life effects on testosterone production following in utero exposure to the pesticide fludioxonil
Terje Svingen (Speaker)
Camilla Taxvig (Other)
Julie Boberg (Other)
Jorma Toppari (Other)
Ulla Hass (Other)
Anne Marie Vinggaard (Other)
National Food Institute
Research Group for Molecular and Reproductive Toxicology
Copenhagen Center for Health Technology
Degree of recognition: International

**Related event**

19th European Testis Workshop : Molecular and Cellular Endocrinology
11/06/2016 → 15/06/2016
Saint Malo, France
Activity: Talks and presentations › Conference presentations

14th International Design Conference
Period: 16 May 2016 → 19 May 2016
Anja Maier (Participant)
Description
14th International Design Conference (DESIGN16)
Links:
http://www.designconference.org

Related event
14th International Design Conference
16/05/2016 → 19/05/2016
Dubrovnik, Croatia
Activity: Attending an event › Participating in or organising a conference

Future of Design Research @ Workshop Design Research: 10 Years On
Period: 16 May 2016
Anja Maier (Invited speaker)

Related event
14th International Design Conference
16/05/2016 → 19/05/2016
Dubrovnik, Croatia
Activity: Talks and presentations › Conference presentations

CESUN Europe Event
Period: 21 Apr 2016 → 22 Apr 2016
Anja Maier (Participant)

Related event
CESUN Europe Event: Comprehensive Engineering: Systems and Social Science - Humanities - Big data - Complexity
21/04/2016 → 22/04/2016
Delft, Netherlands
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

Annual Design Society Board of Management and Advisory Board Meeting (External organisation)
Anja Maier (Participant)
Description
Body type: Advisory Board
Degree of recognition: International
Links:
http://www.designsociety.org

Related external organisation

Annual Design Society Board of Management and Advisory Board Meeting
Activity: Membership › Membership of committees, commissions, boards, councils, associations, organisations, or similar

Design Science Journal (Journal)
Period: 1 Feb 2016 → …
Anja Maier (Editor)

Engineering Systems
Department of Management Engineering
Copenhagen Center for Health Technology

Description
Editorial board
Links:
http://www.designsciencejournal.org/

Related journal

Design Science Journal
Web of Science (2018): Indexed yes
Indexed in DOAJ
Local database
Activity: Research › Journal editor

advanced NMR spectroscopy
Period: 19 Jan 2016
Lars G. Hanson (Lecturer)

Copenhagen Center for Health Technology
Department of Electrical Engineering

Description
Lecture on Magnetic Resonance Imaging

Related event

Advanced NMR Spectroscopy: PhD course
11/01/2016 → 21/01/2016
Kgs. Lyngby, Denmark
Activity: Talks and presentations › Guest lectures, external teaching and course activities at other universities

A framework for conceptualisation for PSS solutions - On network-based development models (External organisation)
Period: 18 Jan 2016
Anja Maier (Chairman)
Copenhagen Center for Health Technology
PhD Assessment Committee Aalborg University (External organisation)
Period: 2015
Ole Broberg (Participant)
Copenhagen Center for Health Technology
Department of Management Engineering

A framework for conceptualisation for PSS solutions - On network-based development models
Activity: Membership › Membership in committees, commissions, boards, councils, associations, organisations, or similar

PhD Assessment Committee Aalborg University (External organisation)
Period: 2015
Ole Broberg (Participant)
Copenhagen Center for Health Technology
Department of Management Engineering

A framework for conceptualisation for PSS solutions - On network-based development models
Activity: Membership › Membership in committees, commissions, boards, councils, associations, organisations, or similar

PhD Assessment Committee Aalborg University (External organisation)
Period: 2015 → 2016
Lars G. Hanson (Participant)
Biomedical Engineering
Department of Electrical Engineering
Copenhagen Center for Health Technology

Secretary, ISMRM study group on Detection & Correction of Motion in MRI & MRS (External organisation)
Activity: Membership › Membership of research networks or expert groups

PhD Assessment Committee Aalborg University (External organisation)
Period: 2015 → 2016
Lars G. Hanson (Participant)
Biomedical Engineering
Department of Electrical Engineering
Copenhagen Center for Health Technology

Secretary, ISMRM study group on Detection & Correction of Motion in MRI & MRS (External organisation)
Activity: Membership › Membership of research networks or expert groups

Secretary, ISMRM study group on Detection & Correction of Motion in MRI & MRS (External organisation)
Period: 2015 → 2016
Lars G. Hanson (Participant)
Biomedical Engineering
Department of Electrical Engineering
Copenhagen Center for Health Technology

Secretary, ISMRM study group on Detection & Correction of Motion in MRI & MRS (External organisation)
Activity: Membership › Membership of research networks or expert groups

Designing Engineering Systems
Period: 4 Dec 2015
Anja Maier (Keynote speaker)
Department of Management Engineering
Engineering Systems Group
Copenhagen Center for Health Technology

Designing Engineering Systems
Period: 4 Dec 2015
Anja Maier (Keynote speaker)
Department of Management Engineering
Engineering Systems Group
Copenhagen Center for Health Technology

Designing Engineering Systems
Period: 4 Dec 2015
Anja Maier (Keynote speaker)
Department of Management Engineering
Engineering Systems Group
Copenhagen Center for Health Technology
Risk in MRI associated with the static B0 field  
**Period:** 19 Nov 2015  
**Lars G. Hanson (Invited speaker)**  
Copenhagen Center for Health Technology  
Department of Electrical Engineering  

**Description**  
Inaugural Professorship Lecture  
Links:  
https://www.youtube.com/watch?v=YnxJqxiLhDs

**Related external organisation**

**Unknown external organisation**  
Activity: Talks and presentations › Conference presentations

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ESMRMB safety course: ESMRMB School of MRI  
19/11/2015 → 21/11/2015  
Lund, Sweden  
Activity: Talks and presentations › Guest lectures, external teaching and course activities at other universities

**Description**  
Invited lecture  
Links:  

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Engineering Systems: Designing Connections  
**Period:** 30 Oct 2015  
**Anja Maier (Invited speaker)**  
Department of Management Engineering  
Engineering Systems Group  
Production and Service Management  
Copenhagen Center for Health Technology  

**Description**  
Annual DTU PhD Graduation Ceremony 2015  
Links:  
http://www.dtu.dk/english/News/2015/11/Celebrating-this-year%E2%80%99s-new-PhD-graduates?id=0f2fa998-b8d1-4e25-9128-6e1a128222af (DTU PhD Graduation Ceremony 2015)

**Related external organisation**

**Unknown external organisation**  
Activity: Talks and presentations › Conference presentations

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Gaze interaction with textual user interface  
**Period:** 21 Aug 2015  
**John Paulin Hansen (Lecturer)**  
Copenhagen Center for Health Technology  
Department of Management Engineering  
Technology and Innovation Management  

**Description**  
This presentation suggests using rapid serial visual presentation (RSVP) of single Words for prompting command options that may be executed by gaze-strokes. In a study with 27 participants the RSVP commands would engage a near-by display; adjust the speed of Word presentation; and provide a “back” option for text navigation. People readily understood
how to execute RSVP command prompts and a majority of them preferred gaze input to a pen pointer. We present the concept of a smartwatch that can track eye movements and mediate command options whenever in proximity of intelligent devices that it connects with, i.e. a Gaze-Watch. For instance, standing next to a monitor, it may suggest to turn it on, if you look up at the monitor now. Command suggestions are provided in the RSVP-format, but they only stay active for a limited time, in which the gaze should be moved to apply them.

**Related event**

**ECEM2015: European Conference on Eye Movements**

16/08/2015 → 21/08/2015
Vienna, Austria
Activity: Talks and presentations › Conference presentations

**Programme Committee Chair for ICED17 21st International Conference on Engineering Design (External organisation)**

Period: 30 Jul 2015 → 25 Aug 2017
Anja Maier (Chairman)
Department of Management Engineering
Engineering Systems
Copenhagen Center for Health Technology

**Description**

ICED17 21st International Conference on Engineering Design

Body type: Scientific Programme Committee
Degree of recognition: International
Documents:
ICED17 -Call-For-Papers-rev3
Links:
http://iced17.org (ICED17 21st International Conference on Engineering Design)

**Related external organisation**

**Programme Committee Chair for ICED17 21st International Conference on Engineering Design**

Activity: Membership › Membership of committees, commissions, boards, councils, associations, organisations, or similar

**MRI simulation for sequence development, protocol optimisation, and education**

Period: 29 Jun 2015 → 1 Jul 2015
Lars G. Hanson (Organizer)
Department of Electrical Engineering
Biomedical Engineering
Copenhagen Center for Health Technology

**Description**

MRI simulation for sequence development, protocol optimisation, and education

Links:

**Related event**

**MRI simulation for sequence development, protocol optimisation, and education: ESMRMB Lectures on MR**

29/06/2015 → 01/07/2015
Kgs. Lyngby, Denmark
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

**Bisphenol A and five structural analogues induce adipocyte differentiation and other obesity-related endpoints in 3T3-L1 cells**

Period: 27 Apr 2015 → 30 Apr 2015
Cecilie Nethe Ramskov Tetzlaff (Other)
Terje Svingen (Other)
Anne Marie Vinggaard (Other)
Camilla Taxvig (Other)

National Food Institute
Research Group for Molecular and Reproductive Toxicology
Copenhagen Center for Health Technology

Related event

8th Copenhagen Workshop on Endocrine Disrupters
27/04/2015 → 30/04/2015
Copenhagen, Denmark
Activity: Talks and presentations › Conference presentations

Effects of chemical mixtures on female reproductive endpoints
Period: 27 Apr 2015 → 30 Apr 2015
Hanna Katarina Lilith Johansson (Other)
Anne Marie Vinggaard (Other)
Terje Svingen (Other)
Ulla Hass (Other)
Julie Boberg (Other)

National Food Institute
Research Group for Molecular and Reproductive Toxicology
Copenhagen Center for Health Technology
Degree of recognition: International

Related event

8th Copenhagen Workshop on Endocrine Disrupters
27/04/2015 → 30/04/2015
Copenhagen, Denmark
Activity: Talks and presentations › Conference presentations

Emerging Chemicals in food packaging - toxicological profiling of knowns and unknowns
Period: 27 Apr 2015 → 30 Apr 2015
Anna Kjerstine Rosenmai (Other)
Linda Bengtström (Other)
Barbara van Vuig-Lussenburg (Other)
Jens Højslev Petersen (Other)
Camilla Taxvig (Other)
Terje Svingen (Other)
Laurianne Lesnè (Other)
Mona-Lise Binderup (Speaker)
Marianne Dybdahl (Other)
Cecilie Nethe Ramskov Tetzlaff (Other)
Bernard Jégou (Other)
Xenia Trier (Other)
Anne Marie Vinggaard (Speaker)

National Food Institute
Research Group for Molecular and Reproductive Toxicology
Copenhagen Center for Health Technology
Degree of recognition: International

Related event
Mixture effects of twenty-seven environmental contaminants given to rats at doses comparable to human exposure

Period: 27 Apr 2015 → 30 Apr 2015

Niels Hadrup (Other)
Terje Svingen (Other)
Karen Riiber Mandrup (Other)
Hanne Frederiksen (Other)
Kasper Skov (Other)
Henrik Lauritz Frandsen (Other)
Anne Marie Vinggaard (Other)

National Food Institute
Research Group for Molecular and Reproductive Toxicology
Research Group for Analytical Food Chemistry
Copenhagen Center for Health Technology
Degree of recognition: International

Related event

8th Copenhagen Workshop on Endocrine Disrupters
27/04/2015 → 30/04/2015
Copenhagen, Denmark
Activity: Talks and presentations › Conference presentations

Member of the ESMRMB Nomination and Awards Committee (External organisation)
Lars G. Hanson (Participant)
Copenhagen Center for Health Technology
Center for Hyperpolarization in Magnetic Resonance
Department of Electrical Engineering
Center for Magnetic Resonance
Degree of recognition: International

Related external organisation

Member of the ESMRMB Nomination and Awards Committee
Activity: Membership › Membership of committees, commissions, boards, councils, associations, organisations, or similar

PhD Evaluation Committee Luleå University of Technology (External organisation)
Period: 2012
Ole Broberg (Participant)
Copenhagen Center for Health Technology
Department of Management Engineering
Engineering Systems

Description
Member of the evaluation committee for thesis by Åsa Wikberg Nilsson "Re-thinking Designing - Collaborative Probing of Work and Workplace Change"
Degree of recognition: International

Related external organisation
Member of Programme Committee, ENERGIX, Research Council of Norway (External organisation)
Period: Sep 2012 → Sep 2016
Birte Holst Jørgensen (Participant)
Copenhagen Center for Health Technology
Department of Management Engineering

Description
Board member

Body type: Research programme
Degree of recognition: International

Related external organisation

Member of Programme Committee, ENERGIX, Research Council of Norway
Activity: Membership › Membership of committees, commissions, boards, councils, associations, organisations, or similar

PhD opponent Chalmers University of Technology, Sweden (External organisation)
Period: 2011
Ole Broberg (External examiner)
Copenhagen Center for Health Technology
Department of Management Engineering
Engineering Systems

Description
PhD opponent on thesis by Cecilia Berlin "Ergonomics Infrastructure: An Organizational Roadmap to Improved Production Ergonomics"
Degree of recognition: International
Activity: Examinations and supervision › External examination

Design Society Advisory Board (Event)
Period: 15 Aug 2011 → 14 Aug 2022
Anja Maier (Chairman)
Copenhagen Center for Health Technology
Department of Management Engineering
Engineering Systems

Description
Design Society Advisory Board Member (re-elected)
Degree of recognition: International
Links:
https://www.designsociety.org/ (The Design Society - a worldwide community)
https://www.designsociety.org/7/Advisory+Board (Design Society Advisory Board)

Related event

Design Society Advisory Board
15/08/2011 → 14/08/2022
Activity: Membership › Membership of committees, commissions, boards, councils, associations, organisations, or similar

Prizes:
Human Factors Engineering and Systems Design with Federal University of Rio de Janeiro/COPPE: International Network Program
Ole Broberg (Recipient)
Copenhagen Center for Health Technology, Department of Management Engineering, Engineering Systems

Details
Awarded date: Jun 2013
Granting Organisations: Danish Agency for Science, Technology and Innovation
Prize: Prizes, scholarships, distinctions

IEA Fellow
Ole Broberg (Recipient)
Copenhagen Center for Health Technology, Department of Management Engineering, Engineering Systems

Description
The IEA Fellowship is given to recognize extraordinary or sustained, superior accomplishments of an individual within the human factors and ergonomics field.

Details
Awarded date: 2016
Granting Organisations: International Ergonomics Association
Prize: Prizes, scholarships, distinctions

Industrial PhD scholarship with Alectia Consulting: Integration of human factors knowledge into engineering design processes
Ole Broberg (Recipient)
Copenhagen Center for Health Technology, Department of Management Engineering, Engineering Systems

Details
Awarded date: 2009
Granting Organisations: Danish Agency for Science Technology and Innovation
Prize: Prizes, scholarships, distinctions

Method for knowledge transfer from the operations phase of offshore units into design, planning, and optimization
Ole Broberg (Recipient)
Copenhagen Center for Health Technology, Department of Management Engineering, Engineering Systems

Description
Two year research project

Details
Awarded date: 2014
Granting Organisations: The Danish Maritime Fund
Prize: Prizes, scholarships, distinctions

Methods for employee participation in product innovation.
Ole Broberg (Recipient)
Copenhagen Center for Health Technology, Department of Management Engineering, Engineering Systems

Description
Two year research project

Details
Awarded date: 2014
Granting Organisations: The Danish Industry Foundation
Prize: Prizes, scholarships, distinctions

Nordic Ergonomics Society Great Prize
Ole Broberg (Recipient)
Copenhagen Center for Health Technology, Department of Management Engineering, Engineering Systems

Details
Awarded date: 2004
PhD Scholarship: Interactive simulation: A new means for promoting occupational health and safety in the hospital sector.
Ole Broberg (Recipient)
Copenhagen Center for Health Technology, Department of Management Engineering, Engineering Systems

Details
Awarded date: 2013
Granting Organisations: The Working Environment Research Fund
Prize: Prizes, scholarships, distinctions

Promoting the occupational health services efforts in relation to technological changes in companies
Ole Broberg (Recipient)
Copenhagen Center for Health Technology, Department of Management Engineering, Engineering Systems

Description
Research project

Details
Awarded date: 2001
Granting Organisations: The Working Environment Research Fund
Prize: Prizes, scholarships, distinctions

Scholarship awarded by the H-STAR program
Ole Broberg (Recipient)
Copenhagen Center for Health Technology, Department of Management Engineering, Engineering Systems

Description
Visiting Researcher Stanford University: Center for Design Research

Details
Awarded date: 1 Sep 2009
Granting Organisations: Danish Agency for Science, Technology and Innovation
Prize: Prizes, scholarships, distinctions

Vanførefondens Forskerpris 2018
John Paulin Hansen (Recipient)
Department of Management Engineering, Technology and Innovation Management, Transport DTU, Copenhagen Center for Health Technology

Details
Awarded date: 23 May 2018
Degree of recognition: National
Granting Organisations: Vanførefonden
Prize: Prizes, scholarships, distinctions

Workspace Design II: Development of a new dialogue-oriented design practice
Ole Broberg (Recipient)
Copenhagen Center for Health Technology, Department of Management Engineering, Engineering Systems

Description
Three year research project

Details
Awarded date: 2010
Granting Organisations: The Working Environment Research Fund
Prize: Prizes, scholarships, distinctions

Workspace Design I: User involvement and work life integration into technological and organizational change processes.
Ole Broberg (Recipient)
Copenhagen Center for Health Technology, Department of Management Engineering, Engineering Systems
Description
Three year research project

Details
Awarded date: 2005
Granting Organisations: The Working Environment Research Fund
Prize: Prizes, scholarships, distinctions

Press clippings:

Sammenhæng mellem indtag af grønt og bakteriediversitet i tarmen
Tine Rask Licht
15/05/2018
National Food Institute, Copenhagen Center for Health Technology

Media contribution (1)

Sammenhæng mellem indtag af grønt og bakteriediversitet i tarmen
15/05/2018
DR Viden, Denmark
Maria Behrendt
Tine Rask Licht
National Food Institute, Copenhagen Center for Health Technology
Press / Media

Sandt og falsk om tarmens mikrobiota
Tine Rask Licht
12/01/2018
National Food Institute, Copenhagen Center for Health Technology

Media contribution (1)

Sandt og falsk om tarmens mikrobiota
12/01/2018
DYNAMO, Denmark, Print
Lotte Krull
Tine Rask Licht
National Food Institute, Copenhagen Center for Health Technology
Press / Media

Faldende sædkvalitet og stigende forekomst af kryptorkisme i hunde
Anne Marie Vinggaard
16/11/2017
National Food Institute, Copenhagen Center for Health Technology, Research Group for Molecular and Reproductive Toxicology

Media coverage (1)

Faldende sædkvalitet og stigende forekomst af kryptorkisme i hunde
16/11/2017
Videnskab.dk (National), Denmark, Web
Mads Molten
Anne Marie Vinggaard
Copenhagen Center for Health Technology, National Food Institute, Research Group for Molecular and Reproductive Toxicology
Press / Media

Health Innovation: System Design for Behaviour Change
Anja Maier
16/11/2017
Department of Management Engineering, Copenhagen Center for Health Technology, Engineering Systems

Conference on Health Innovation : Innovation som drivfraft for fremtidens sundhedssektor
Event: Conference

Media contribution (1)

Health Innovation: System Design for Behaviour Change
16/11/2017
Video (International), Denmark, Web
Copenhagen Health Innovation
c. 4 minutes
http://copenhagenhealthinnovation.dk/sundhed17/
Anja Maier
Press / Media

Effekterne af en fuldkornskost på sundhed og tarmbakterier
Tine Rask Licht
08/11/2017
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media coverage (1)

Effekterne af en fuldkornskost på sundhed og tarmbakterier
08/11/2017
HealthDay (International), Denmark, Web
Serena Gordon
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media

Effekterne af en fuldkornskost på sundhed og tarmbakterier
Tine Rask Licht
03/11/2017
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media coverage (1)

Effekterne af en fuldkornskost på sundhed og tarmbakterier
03/11/2017
Dagbladet (NO) (National), Denmark, Print
Jenny Mina Rødahl
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media

Effekterne af en fuldkornskost på sundhed og tarmbakterier
Tine Rask Licht
01/11/2017
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media coverage (1)

Effekterne af en fuldkornskost på sundhed og tarmbakterier
01/11/2017
Ritzau (National), Denmark, Other
Ida Meyer
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media
Sundhedsskadelige stoffer i fødevarekontaktmateriale
Anne Marie Vinggaard
19/09/2017
National Food Institute, Copenhagen Center for Health Technology, Research Group for Molecular and Reproductive Toxicology

Media coverage (1)

Strategi til at teste for sundhedsskadelige stoffer i fødevarekontaktmateriale
19/09/2017
Ingeniøren (National), Denmark, Web
Henrik Winther
Anne Marie Vinggaard
Copenhagen Center for Health Technology, National Food Institute, Research Group for Molecular and Reproductive Toxicology

Press / Media

Tarmbakterier og vægttab
Tine Rask Licht
12/09/2017
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media coverage (1)

Tarmbakterier og vægttab
12/09/2017
Politiken (National), Denmark, Print
Lars Dahlager
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology

Press / Media

Sundhedsskadelige stoffer i fødevarekontaktmateriale
Anne Marie Vinggaard
07/09/2017
National Food Institute, Copenhagen Center for Health Technology, Research Group for Molecular and Reproductive Toxicology

Media coverage (1)

Strategi til at teste for sundhedsskadelige stoffer i fødevarekontaktmateriale
07/09/2017
Videnskab.dk (National), Denmark, Web
Kristian Sjøgren
Anne Marie Vinggaard
Copenhagen Center for Health Technology, National Food Institute, Research Group for Molecular and Reproductive Toxicology

Press / Media

Tarmbakterier
Tine Rask Licht
06/09/2017
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media coverage (1)

Tarmbakterier
06/09/2017
Ud&Se (National), Denmark, Print
Kommenteret irsk studie om stress og bifidobakterier  
11/01/2017  
BT, Print  
Sebastian Bjerring Jensen  
Tine Rask Licht  
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology  
Press / Media

Tarmbakterier og sundhed  
Tine Rask Licht  
21/12/2016

Subject  
Tarmbakterier og sundhed  
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

Tarmbakterier og sundhed  
21/12/2016  
Radio24Syv, Radio  
Anders Nedergaard  
Tine Rask Licht  
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology  
Press / Media

Tarmbakterier, fedme, mus  
Tine Rask Licht  
15/12/2016  
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

Tarmbakterier, fedme, mus  
15/12/2016  
DR P1 Videnskabens Verden, Radio  
Stine Blegvad  
Tine Rask Licht  
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology  
Press / Media

Tarmbakterier, fedme, mus  
Tine Rask Licht  
07/12/2016  
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

Tarmbakterier, fedme, mus  
07/12/2016  
EatingWell magazine, Print  
Marissa Donovan  
Tine Rask Licht  
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology  
Press / Media
Tarmbakteriers påvirkning af forbrændingen
Tine Rask Licht
30/11/2016
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

Tarmbakteriers påvirkning af forbrændingen
Tine Rask Licht
28/11/2016
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

Information om brug af fluorstoffer og deres toksicitet
Anne Marie Vinggaard
05/10/2016
National Food Institute, Research Group for Molecular Toxicology, Copenhagen Center for Health Technology

Media contribution (1)

Tarmbakterier
Tine Rask Licht
12/09/2016
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)
24 spørgsmål til professoren
Tine Rask Licht
02/09/2016

Subject
24 spørgsmål til professoren
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

24 spørgsmål til professoren
02/09/2016
Radio 24Syv, Radio
Lone Frank
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology

Cocktail effekter og fødevarekontaktmaterialer
Anne Marie Vinggaard
29/08/2016

Subject
Cocktail effekter og fødevarekontaktmaterialer
National Food Institute, Research Group for Molecular Toxicology, Copenhagen Center for Health Technology

Media contribution (1)

Cocktail effekter og fødevarekontaktmaterialer
29/08/2016
Ritzau, Web
Kristine Dam
Anne Marie Vinggaard
Copenhagen Center for Health Technology, National Food Institute, Research Group for Molecular Toxicology

Transittidsstudiet
Tine Rask Licht
24/08/2016

Subject
Interview (ca. 1 time, klippes ned) i forbindelse med vores studie af sammenhængen mellem tarmens transittid, mikrobiota, og bakterielle metabolitter (Nature Microbiology, Juni 2016)
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

Transittidsstudiet
24/08/2016
DR P1, Radio
Kristoffer Frøkjær
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology

kogebog med 'god mad til tarmens bakterier'
Tine Rask Licht
18/08/2016

Subject
Der skal udkomme en ny kogebog med 'god mad til tarmens bakterier' eller noget i den retning.
Den vil de skrive om, og kombinere det med lidt viden om området
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

kogebog med 'god mad til tarmens bakterier'
18/08/2016
Metroexpress, Print
Maria Cuculiza
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media

mælkesyrebakterier
Tine Rask Licht
04/08/2016

Subject
mælkesyrebakterier
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

mælkesyrebakterier
04/08/2016
Bonnier Publications, Web
Karen Lyager Horve
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media

Transittid
Tine Rask Licht
28/06/2016

Subject
Transittid
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

Transittid
28/06/2016
NutraIngredients | FoodNavigator, Web
Will Chu, Science editor
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media
Transittid
Tine Rask Licht
27/06/2016

Subject
Transittid
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

Transittid
Tine Rask Licht
27/06/2016
videnskab.dk, Web
Malene Sommer Christiansen
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media

Transittid
Tine Rask Licht
27/06/2016

Subject
Transittid
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

Transittid
Tine Rask Licht
27/06/2016
DR Lev Nu, Web
Susanne Vigsø Grøn
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media

Transittid
Tine Rask Licht
27/06/2016

Subject
Transittid
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

Transittid
Tine Rask Licht
27/06/2016
Ritzau, Web
Jan Bjerre Lauridsen
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media

Farmakonomen
Tine Rask Licht
02/05/2016
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology


Media contribution (1)

Farmakonomen
02/05/2016
Farmakonomen (fagblad), Print
Karoline Lawætz
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media

bakteriesamfund
Tine Rask Licht
30/03/2016

Subject
Det korte svar er nej. Har elaboreret omkring bakteriesamfund, resistensspredning, konkurrence mellem bakterier i forskellige miljøer.
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

bakteriesamfund
30/03/2016
DR, P1, Videnskabens Verden, Radio
Anne Mette Simonsen
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media

Ny undersøgelse vedr. Round Up og hjælpestoffers effekt på aromatase aktivitet
Anne Marie Vinggaard
03/03/2016
National Food Institute, Research Group for Molecular Toxicology, Copenhagen Center for Health Technology

Media contribution (1)

Ny undersøgelse vedr. Round Up og hjælpestoffers effekt på aromatase aktivitet
03/03/2016
Ingeniører, Web
Mia Stage
Anne Marie Vinggaard
Copenhagen Center for Health Technology, National Food Institute, Research Group for Molecular Toxicology
Press / Media

Kost, tarmflora, småbørn
Tine Rask Licht
18/02/2016
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

Kost, tarmflora, småbørn
18/02/2016
DR1, Sundhedsmagasinet, Television
Lasse Lindhardt Jensen
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media
Smartphones and watches under the researcher's microscope
Julia Rosemary Thorpe
20/11/2015
Department of Management Engineering, Production and Service Management, Engineering Systems Group, Copenhagen Center for Health Technology

Media contribution (1)

Smartphones and watches under the researcher's microscope
20/11/2015
Magasinet Pleje, Print
http://www.magasinetpleje.dk/article/view/229623/smarte_ure_under_forskernes_lup#.VnpcAv6FNes
Smarte telefoner og ure under forskernes lup, af Lotte Brochmann
Julia Rosemary Thorpe
Copenhagen Center for Health Technology, Department of Management Engineering, Production and Service Management, Engineering Systems Group
Press / Media

Tarmbakteriers betydning for sundheden
Tine Rask Licht
21/12/1800
National Food Institute, Research Group for Gut Microbiology and Immunology, Copenhagen Center for Health Technology

Media contribution (1)

Tarmbakteriers betydning for sundheden
21/12/1800
Radio24Syv - Fitness M/K, Radio
Anders Nedergaard
Tine Rask Licht
Copenhagen Center for Health Technology, National Food Institute, Research Group for Gut Microbiology and Immunology
Press / Media