A Robust Statistical Model to Predict the Future Value of the Milk Production of Dairy Cows Using Herd Recording Data

The future value of an individual dairy cow depends greatly on its projected milk yield. In developed countries with developed dairy industry infrastructures, facilities exist to record individual cow production and reproduction outcomes consistently and accurately. Accurate prediction of the future value of a dairy cow requires further detailed knowledge of the costs associated with feed, management practices, production systems, and disease. Here, we present a method to predict the future value of the milk production of a dairy cow based on herd recording data only. The method consists of several steps to evaluate lifetime milk production and individual cow somatic cell counts and to finally predict the average production for each day that the cow is alive. Herd recording data from 610 Danish Holstein herds were used to train and test a model predicting milk production (including factors associated with milk yield, somatic cell count, and the survival of individual cows). All estimated parameters were either herd- or cow-specific. The model prediction deviated, on average, less than 0.5 kg from the future average milk production of dairy cows in multiple herds after adjusting for the effect of somatic cell count. We conclude that estimates of future average production can be used on a day-to-day basis to rank cows for culling, or can be implemented in simulation models of within-herd disease spread to make operational decisions, such as culling versus treatment. An advantage of the approach presented in this paper is that it requires no specific knowledge of disease status or any other information beyond herd recorded milk yields, somatic cell counts, and reproductive status.

General information
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Organisations: Department of Applied Mathematics and Computer Science, National Veterinary Institute, Epidemiology, Dynamical Systems, University of Copenhagen
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Number of pages: 9
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Dynamics of a railway vehicle on a laterally disturbed track
In this article a theoretical investigation of the dynamics of a railway bogie running on a tangent track with a periodic disturbance of the lateral track geometry is presented. The dynamics is computed for two values of the speed of the vehicle in combination with different values of the wavelength and amplitude of the disturbance. Depending on the combinations of the speed, the wavelength and the amplitude, straight line forward motion, different modes of symmetric or asymmetric periodic oscillations or aperiodic motions, which are presumably chaotic, are found. Statistical methods are applied for the investigation. In the case of sinusoidal oscillations they provide information about the phase shift between the different variables and the amplitudes of the oscillations. In the case of an aperiodic motion the statistical measures indicate some non-smooth transitions.
Effect of different oral oxytetracycline treatment regimes on selection of antimicrobial resistant coliforms in nursery pigs

A major concern derived from using antimicrobials in pig production is the development of resistance. This study aimed to assess the impact of selected combinations of oral dose and duration of treatment with oxytetracycline (OTC) on selection of tetracycline resistant (TET-R) coliforms recovered from swine feces. The work encompassed two studies: 1) OTC 5 mg/kg and 20 mg/kg were administered to nursery pigs for 3 and 10 days, respectively, under controlled experimental conditions, and 2) 10 mg/kg, 20 mg/kg and 30 mg/kg OTC were given to a higher number of pigs for 6, 3 and 2 days, respectively, under field conditions. Statistical modeling was applied to analyze trends in the proportion of TET-R coliforms. In the experimental study, no statistical difference in proportion of TET-R coliforms was observed between treatments at the end of the trial (day 18) and compared to day 0. In the field study, treatment had a significant effect on the proportion of TET-R bacteria two days after the end of treatment (2dAT) with the regimes "low dose-six days" and "medium dose-three days" yielding the highest and lowest proportions of TET-R strains, respectively. No indication of co-selection for ampicillin- and sulphonamide-R bacteria was observed for any treatment at 2dAT. By the end of the nursery period, the proportion of TET-R bacteria was not significantly different between treatments and compared to day 0. Our results suggest that similar resistance levels might be obtained by using different treatment regimes regardless of the combinations of oral dose-duration of treatment.
Ratings:
BFI (2018): BFI-level 2
BFI (2017): BFI-level 2
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BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 2.65 SJR 1.326 SNIP 1.208
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.393 SNIP 1.21 CiteScore 2.56
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.281 SNIP 1.262 CiteScore 2.54
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.438 SNIP 1.484 CiteScore 3
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.437 SNIP 1.579 CiteScore 3.18
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 1.562 SNIP 1.738 CiteScore 3.27
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 1.371 SNIP 1.476
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 1.29 SNIP 1.472
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 1.169 SNIP 1.3
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 1.043 SNIP 1.322
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.022 SNIP 1.401
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 1.078 SNIP 1.262
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 0.869 SNIP 1.259
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 0.913 SNIP 1.186
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 0.84 SNIP 1.112
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 0.833 SNIP 1.058
Web of Science (2001): Indexed yes
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Web of Science (2000): Indexed yes
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DOIs:
Effect of tetracycline dose and treatment-mode on selection of resistant coliform bacteria in nursery pigs

This study describes results of a randomized clinical trial investigating the effect of oxytetracycline treatment dose and mode of administration on selection of antibiotic resistant coliform bacteria in fecal samples from nursery pigs. Nursery pigs (pigs of 4-7 weeks of age) were treated with oxytetracycline against Lawsonia intracellularis induced diarrhea in five pig herds. Each group was randomly allocated to one of five treatment groups: oral flock treatment with (i) high (20 mg/kg), (ii) medium (10 mg/kg) and (iii) low (5 mg/kg) dosage, (iv) oral-pen-wise (small group) treatment (10 mg/kg), and (v) individual intramuscular injection treatment (10 mg/kg). All groups were treated once a day for five days. In all groups, treatment caused a rise in numbers and proportion of tetracycline resistant coliform bacteria right after treatment, followed by a significant drop by the time where pigs left the nursery unit. Counts and proportion of tetracycline-resistant coliforms did not vary significantly between treatment groups, except immediately after treatment, where the highest treatment dose resulted in the highest number of resistant coliforms. A control group treated with tiamuline did not show significant changes in number or proportion of tetracycline resistant coliforms. Selection for tetracycline-resistant coliforms was significantly correlated to selection for ampicillin- and sulfonamide-resistant, but not to cefotaxime-resistant strains. In conclusion, difference in dose of oxytetracycline and the way the drug was applied did not cause significantly different selection of tetracycline resistant coliform bacteria, under the conditions tested.

IMPORTANCE Antimicrobial resistance is a global treat to human health. Treatment of livestock with antimicrobials has a direct impact on this problem, and there is a need to improve the ways that we use antimicrobial in livestock production. We hypothesized that antibiotic resistance development following treatment of diarrhea in nursery pigs could be reduced by either lowering the dose of oxytetracycline or by replacing the commonly used practice of flock treatment with individual or small group treatments, since this would reduce the number of pigs treated. However, the study showed no significant difference between treatment-groups with respect to the number or proportion of tetracycline resistant coliforms selected. The most important conclusion is that under the practical field conditions, there will be no added value in terms of lowering resistance development by exchanging flock treatment with individual or small group treatment of nursery pigs. The reason for lack of effect of single animal treatment is probably that such animals share the environment with treated animals and take up resistant bacteria from the environment.

General information
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BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 4.08
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.891 SNIP 1.308 CiteScore 4.14
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.857 SNIP 1.384 CiteScore 4.02
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.899 SNIP 1.414 CiteScore 4.25
Estimation of the transmission dynamics of African swine fever virus within a swine house

The spread of African swine fever virus (ASFV) threatens to reach further parts of Europe. In countries with a large swine production, an outbreak of ASF may result in devastating economic consequences for the swine industry. Simulation models can assist decision makers setting up contingency plans. This creates a need for estimation of parameters. This study presents a new analysis of a previously published study. A full likelihood framework is presented including the impact of model assumptions on the estimated transmission parameters. As animals were only tested every other day, an interpretation was introduced to cover the weighted infectiousness on unobserved days for the individual animals (WIU). Based on our model and the set of assumptions, the within- and between-pen transmission parameters were estimated to $\beta_w = 1.05$ (95% CI 0.62-1.72), $\beta_b = 0.46$ (95% CI 0.17-1.00), respectively, and the WIU = 1.00 (95% CI 0-1). Furthermore, we simulated the spread of ASFV within a pig house using a modified SEIR-model to establish the time from infection of one animal until ASFV is detected in the herd. Based on a chosen detection limit of 2.55% equivalent to 10 dead pigs out
of 360, the disease would be detected 13-19 days after introduction.

**General information**

State: Published
Organisations: National Veterinary Institute, Epidemiology, Office for Study Programmes and Student Affairs, Department of Applied Mathematics and Computer Science, Dynamical Systems, Technical University of Denmark
Authors: Nielsen, J. P. (Ekstern), Larsen, T. S. (Ekstern), Hisham Beshara Halasa, T. (Intern), Christiansen, L. E. (Intern)
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Main Research Area: Technical/natural sciences

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Journal: Epidemiology and Infection
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BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
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Scopus rating (2016): CiteScore 1.98 SJR 1.134 SNIP 0.865
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.341 SNIP 1.079 CiteScore 2.29
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.288 SNIP 1.026 CiteScore 2.19
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.313 SNIP 1.126 CiteScore 2.57
ISI indexed (2013): ISI indexed yes
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BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.42 SNIP 1.175 CiteScore 2.69
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Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.327 SNIP 1.223 CiteScore 2.71
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.034 SNIP 1.045
Web of Science (2010): Indexed yes
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Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.051 SNIP 1.052
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 0.928 SNIP 1.059
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.994 SNIP 1.228
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.855 SNIP 0.954
Web of Science (2005): Indexed yes
From vision to operation - Smart real-time control of water systems in Aarhus, Denmark

General information
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Organisations: Department of Environmental Engineering, Urban Water Systems, Department of Applied Mathematics and Computer Science, Dynamical Systems, DHI Denmark, Technical University of Denmark, Aarhus Water
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Warum ist es so schwierig, die lateralen Gleisstörungen durch Messungen der Fahrzeugdynamik zu bestimmen

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Dynamical Systems
Authors: Christiansen, L. E. (Intern), True, H. (Intern)
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Source-ID: 139204720
Publication: Research - peer-review › Conference article – Annual report year: 2017
Why is it so difficult to determine the lateral Position of the Rails by a Measurement of the Motion of an Axle on a moving Vehicle?

Several attempts of measuring the exact location of the rails by the use of ordinary vehicles have been made. While the method works reasonably well in the vertical direction, the results of the lateral measurements made with different vehicles are so widely scattered that it is virtually impossible to draw any conclusions. We may therefore ask: does a wheel set follow the track disturbances exactly? In this article we investigate the lateral dynamics of a half-car vehicle model with two-axle bogies running on a rigid tangent track with sinusoidal lateral disturbances of the rails. The wavelength, the amplitude and the phase between the rail disturbances are varied. Two different vehicle speeds are investigated. One speed is under and the other above the vehicle critical speed. In the article we show examples of axle motions that do not follow the track disturbances in phase, amplitude or period or several of these together. The results are discussed, and we must conclude that it is in general impossible to determine the track geometry from the motion of a wheel set.

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Authors: True, H. (Intern), Christiansen, L. E. (Intern)
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Train-Track Interaction, Railway Vehicle Dynamics, Vehicle-Track coupled Dynamics
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A Comparison of Dynamics in Two Models for the Spread of a Vector-Borne Disease

In 2007, bluetongue virus (BTV) was introduced to both Denmark (DK) and the United Kingdom (UK). For this reason, simulation models were built to predict scenarios for future incursions. The DK and UK models have a common description of within-herd dynamics, but differ greatly in their descriptions of between-herd spread, one using an explicit representation of vector dispersal, the other a transmission kernel. Here, we compare model predictions for the dynamics of bluetongue in the UK, based on the 2007 incursion and vaccination rollout in 2008. We demonstrate how an agent-based model shows greater sensitivity to the level of vaccine uptake and has lower variability compared with a kernel-based model. However, a model using a transmission kernel requires less detailed data and is often faster.

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Organisations: Department of Applied Mathematics and Computer Science, Dynamical Systems, National Veterinary Institute, The Pirbright Institute
Authors: Græsbøll, K. (Intern), Sumner, T. (Ekstern), Enøe, C. (Intern), Christiansen, L. E. (Intern), Gubbins, S. (Ekstern)
Pages: 215-223
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Main Research Area: Technical/natural sciences

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Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.258 SNIP 1.262 CiteScore 2.29
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.038 SNIP 1.19 CiteScore 2.23
Adaptive Test Schemes for Control of Paratuberculosis in Dairy Cows

Paratuberculosis is a chronic infection that in dairy cattle causes reduced milk yield, weight loss, and ultimately fatal diarrhea. Subclinical animals can excrete bacteria (Mycobacterium avium ssp. paratuberculosis, MAP) in feces and infect other animals. Farmers identify the infectious animals through a variety of test-strategies, but are challenged by the lack of perfect tests. Frequent testing increases the sensitivity but the costs of testing are a cause of concern for farmers. Here, we used a herd simulation model using milk ELISA tests to evaluate the epidemiological and economic consequences of continuously adapting the sampling interval in response to the estimated true prevalence in the herd. The key results were that the true prevalence was greatly affected by the hygiene level and to some extent by the test-frequency. Furthermore, the choice of prevalence that will be tolerated in a control scenario had a major impact on the true prevalence in the normal hygiene setting, but less so when the hygiene was poor. The net revenue is not greatly affected by the test-strategy, because of the general variation in net revenues between farms. An exception to this is the low hygiene herd, where frequent testing results in lower revenue. When we look at the probability of eradication, then it is correlated with the testing frequency and the target prevalence during the control phase. The probability of eradication is low in the low hygiene herd, and a test-and-cull strategy should probably not be the primary strategy in this herd. Based on this study we suggest that, in order to control MAP, the standard Danish dairy farm should use an adaptive strategy where a short sampling interval of three months is used when the estimated true prevalence is above 1%, and otherwise use a long sampling interval of one year.

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Organisations: National Veterinary Institute, Section for Epidemiology, Department of Applied Mathematics and Computer Science, Dynamical Systems, University of Copenhagen
A herd- and cow-specific decision support tool for control of mastitis

General information
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Organisations: National Veterinary Institute, Section for Epidemiology, Department of Applied Mathematics and Computer Science, Dynamical Systems, University of Copenhagen
Authors: Gussmann, M. K. (Intern), Kirkeby, C. T. (Intern), Græsbøll, K. (Intern), Christiansen, L. E. (Intern), Nielsen, S. S. (Ekstern), Toft, N. (Intern), Hisham Beshara Halasa, T. (Intern)
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Associations between health, management and antimicrobial use in Danish swine and veal calves

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Organisations: National Veterinary Institute, Section for Epidemiology, Department of Applied Mathematics and Computer Science, Dynamical Systems, University of Copenhagen
Authors: Fertner, M. E. (Intern), Toft, N. (Intern), Boklund, A. (Intern), Stege, H. (Ekstern), Christiansen, L. E. (Intern)
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Methodologies for managing the Energy-Water-Food nexus at different scales

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Publisher: Technical University of Denmark (DTU)
Editors: Sønderberg Petersen, L., Hvidtfeldt Larsen, H.
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Main Research Area: Technical/natural sciences
Modeling the growth dynamics of multiple Escherichia coli strains in the pig intestine following intramuscular ampicillin treatment

**Background:** This study evaluated how dosing regimen for intramuscularly-administered ampicillin, composition of Escherichia coli strains with regard to ampicillin susceptibility, and excretion of bacteria from the intestine affected the level of resistance among Escherichia coli strains in the intestine of nursery pigs. It also examined the dynamics of the composition of bacterial strains during and after the treatment. The growth responses of strains to ampicillin concentrations were determined using in vitro growth curves. Using these results as input data, growth predictions were generated using a mathematical model to simulate the competitive growth of E. coli strains in a pig intestine under specified plasma concentration profiles of ampicillin.

**Results:** In vitro growth results demonstrated that the resistant strains did not carry a fitness cost for their resistance, and that the most susceptible strains were more affected by increasing concentrations of antibiotics that the rest of the strains. The modeling revealed that short treatment duration resulted in lower levels of resistance and that dosing frequency did not substantially influence the growth of resistant strains. Resistance levels were found to be sensitive to the number of competing strains, and this effect was enhanced by longer duration of treatment. High excretion of bacteria from the intestine favored resistant strains over sensitive strains, but at the same time it resulted in a faster return to pre-treatment levels after the treatment ended. When the duration of high excretion was set to be limited to the treatment time (i.e. the treatment was assumed to result in a cure of diarrhea) resistant strains required longer time to reach the previous level.

**Conclusion:** No fitness cost was found to be associated with ampicillin resistance in E. coli. Besides dosing factors, epidemiological factors (such as number of competing strains and bacterial excretion) influenced resistance development and need to be considered further in relation to optimal treatment strategies. The modeling approach used in the study is generic, and could be used for prediction of the effect of treatment with other drugs and other administration routes for effect on resistance development in the intestine of pigs.

**General information**

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*Organisations: Department of Applied Mathematics and Computer Science, Dynamical Systems, National Veterinary Institute, Section for Epidemiology, University of Copenhagen, University of Glasgow*

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*Web of Science (2017): Indexed yes*

*BFI (2016): BFI-level 1*

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*Web of Science (2016): Indexed yes*

*BFI (2015): BFI-level 1*

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*Web of Science (2015): Indexed yes*

*BFI (2014): BFI-level 1*

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*Web of Science (2013): Indexed yes*
Models to Estimate Lactation Curves of Milk Yield and Somatic Cell Count in Dairy Cows at the Herd Level for the Use in Simulations and Predictive Models

Typically, central milk recording data from dairy herds are recorded less than monthly. Over-fitting early in lactation periods is a challenge, which we explored in different ways by reducing the number of parameters needed to describe the milk yield and somatic cell count of individual cows. Furthermore, we investigated how the parameters of lactation models correlate between parities and from dam to offspring. The aim of the study was to provide simple and robust models for cow level milk yield and somatic cell count for fitting to sparse data to parameterize herd- and cow-specific simulation of dairy herds. Data from 610 Danish Holstein herds were used to determine parity traits in milk production regarding milk yield and somatic cell count of individual cows. Parity was stratified in first, second, and third and higher for milk, and first to sixth and higher for somatic cell count. Fitting of herd level parameters allowed for cow level lactation curves with three, two, or one parameters per lactation. Correlations of milk yield and somatic cell count were estimated between lactations and between dam and offspring. The shape of the lactation curves varied markedly between farms. The correlation between lactations for milk yield and somatic cell count was 0.2–0.6 and significant on more than 95% of farms. The variation in the daily milk yield was observed to be a source of variation to the somatic cell count, and the total somatic cell count was less correlated with the milk production than somatic cells per milliliter. A positive correlation was found between relative levels of the total somatic cell count and the milk yield. The variation of lactation and somatic cell count curves between farms highlights the importance of a herd level approach. The one-parameter per cow model using a herd level curve allows for estimating the cow production level from first the recording in the parity, while a two-parameter
Multistrain models predict sequential multidrug treatment strategies to result in less antimicrobial resistance than combination treatment

Background: Combination treatment is increasingly used to fight infections caused by bacteria resistant to two or more antimicrobials. While multiple studies have evaluated treatment strategies to minimize the emergence of resistant strains for single antimicrobial treatment, fewer studies have considered combination treatments. The current study modeled bacterial growth in the intestine of pigs after intramuscular combination treatment (i.e. using two antibiotics simultaneously) and sequential treatments (i.e. alternating between two antibiotics) in order to identify the factors that favor the sensitive fraction of the commensal flora. Growth parameters for competing bacterial strains were estimated from the combined in vitro pharmacodynamic effect of two antimicrobials using the relationship between concentration and net bacterial growth rate. Predictions of in vivo bacterial growth were generated by a mathematical model of the competitive growth of multiple strains of Escherichia coli. Results: Simulation studies showed that sequential use of tetracycline and ampicillin reduced the level of double resistance, when compared to the combination treatment. The effect of the cycling frequency (how frequently antibiotics are alternated in a sequential treatment) of the two drugs was dependent upon the order in which the two drugs were used. Conclusion: Sequential treatment was more effective in preventing the growth of resistant strains when compared to the combination treatment. The cycling frequency did not play a role in suppressing the growth of resistant strains, but the specific order of the two antimicrobials did. Predictions made from the study could be used to redesign multidrug treatment strategies not only for intramuscular treatment in pigs, but also for other dosing routes.
Non-parametric method for separating domestic hot water heating spikes and space heating

In this paper a method for separating spikes from a noisy data series, where the data change and evolve over time, is presented. The method is applied on measurements of the total heat load for a single family house. It relies on the fact that the domestic hot water heating is a process generating short-lived spikes in the time series, while the space heating changes in slower patterns during the day dependent on the climate and user behavior. The challenge is to separate the domestic hot water heating spikes from the space heating without affecting the natural noise in the space heating measurements. The assumption behind the developed method is that the space heating can be estimated by a non-parametric kernel smoother, such that every value significantly above this kernel smoother estimate is identified as a domestic hot water heating spike. First, it is showed how a basic kernel smoothing approach is too simple to deliver reliable results. Therefore the problem is generalized to a local least squares problem, which makes it possible to design a robust kernel smoother, which estimate is not affected by the spikes. Furthermore, the generalized model makes it possible to estimate higher order local polynomials. Finally, the results are evaluated and it is found that the method is capable of calculating a reliable separation of the total heat load into the two components.

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Dynamical Systems
Authors: Bacher, P. (Intern), de Saint-Aubain, P. A. (Intern), Christiansen, L. E. (Intern), Madsen, H. (Intern)
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Main Research Area: Technical/natural sciences

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BFI (2018): BFI-level 2
BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 4.64 SJR 2.093 SNIP 1.965
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 2.088 SNIP 2.174 CiteScore 4.07
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 2.123 SNIP 2.936 CiteScore 4.21
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.897 SNIP 2.433 CiteScore 3.79
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.816 SNIP 2.737 CiteScore 3.36
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 1.506 SNIP 2.536 CiteScore 3.23
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 1.631 SNIP 2.081
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 1.564 SNIP 1.79
Web of Science (2009): Indexed yes
Simulating the Epidemiological and Economic Impact of Paratuberculosis Control Actions in Dairy Cattle

We describe a new mechanistic bioeconomic model for simulating the spread of Mycobacterium avium subsp. paratuberculosis (MAP) within a dairy cattle herd. The model includes age-dependent susceptibility for infection; age-dependent sensitivity for detection; environmental MAP build up in five separate areas of the farm; in utero infection; infection via colostrum and waste milk, and it allows for realistic culling (i.e., due to other diseases) by including a ranking system. We calibrated the model using a unique dataset from Denmark, including 102 random farms with no control actions against spread of MAP. Likewise, four control actions recommended in the Danish MAP control program were implemented in the model based on reported management strategies in Danish dairy herds in a MAP control scheme. We tested the model parameterization in a sensitivity analysis. We show that a test-and-cull strategy is on average the most cost-effective solution to decrease the prevalence and increase the total net revenue on a farm with low hygiene, but not more profitable than no control strategy on a farm with average hygiene. Although it is possible to eradicate MAP from the farm by implementing all four control actions from the Danish MAP control program, it was not economically attractive since the expenses for the control actions outweigh the benefits. Furthermore, the three most popular control actions against the spread of MAP on the farm were found to be costly and inefficient in lowering the prevalence when used independently.

General information
State: Published
Organisations: National Veterinary Institute, Section for Epidemiology, Department of Applied Mathematics and Computer Science, Dynamical Systems, University of Copenhagen, SEGES Cattle
Authors: Kirkeby, C. T. (Intern), Græsbøll, K. (Intern), Nielsen, S. S. (Ekstern), Christiansen, L. E. (Intern), Toft, N. (Intern), Rattenborg, E. (Ekstern), Hisham Beshara Halasa, T. (Intern)
Number of pages: 13
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information
Journal: Frontiers in Veterinary Science
Volume: 3
ISSN (Print): 2297-1769
Ratings:
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BFI (2017): BFI-level 1
Danish holsteins favor bull offspring: Biased Milk Production as a Function of Fetal Sex, and Calving Difficulty
In a previous study from 2014 it was found that US Holstein cows that gave birth to heifer calves produced more milk than cows having bull calves. We wanted to assess whether this is also true for Danish cattle. Data from 578 Danish Holstein herds were analysed with a mixed effect model and contrary to the findings in the US, we found that cows produced higher volumes of milk if they had a bull calf compared to a heifer calf. We found a significantly higher milk production of 0.28% in the first lactation period for cows giving birth to a bull calf, compared to a heifer calf. This difference was even higher when cows gave birth to another bull calf, so having two bull calves resulted in a difference of 0.52% in milk production compared to any other combination of sex of the offspring. Furthermore, we found that farmer assisted calvings were associated with a higher milk yield. Cows with no farmer assistance or with veterinary assistance during the most recent calving produced less milk. There were also indications that dams would favor a bull fetus by decreasing milk production during the second pregnancy if the calf born in the first parity was a heifer. We hypothesize that size of calves is a confounding factor for milk production. However, calving weight was not available in the present data set to test this hypothesis.

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, National Veterinary Institute, Section for Epidemiology, Dynamical Systems, University of Copenhagen
Authors: Græsbøll, K. (Intern), Kirkeby, C. (Intern), Nielsen, S. S. (Ekstern), Christiansen, L. E. (Intern)
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BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.11 SJR 1.201 SNIP 1.092
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Scopus rating (2015): SJR 1.414 SNIP 1.131 CiteScore 3.32
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.545 SNIP 1.141 CiteScore 3.54
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.74 SNIP 1.147 CiteScore 3.94
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.945 SNIP 1.142 CiteScore 4.15
ISI indexed (2012): ISI indexed yes
Diversity of metabolic profiles of cystic fibrosis *Pseudomonas aeruginosa* during the early stages of lung infection

*Pseudomonas aeruginosa* is the dominant pathogen infecting the airways of cystic fibrosis (CF) patients. During the intermittent colonization phase, *P. aeruginosa* resembles environmental strains but later evolves to the chronic adapted phenotype characterized by resistance to antibiotics and mutations in the global regulator genes mucA, lasR and rpoN. Our aim was to understand the metabolic changes occurring over time and between niches of the CF airways. By applying Phenotype MicroArrays, we investigated changes in the carbon and nitrogen catabolism of subsequently clonally related mucoid and non-mucoid (NM) lung and sinus *P. aeruginosa* isolates from 10 CF patients (five intermittently colonized/five chronically infected). We found the most pronounced catabolic changes for the early/late NM isolate comparisons, with respiratory reduction seen for all chronically infecting isolates and two intermittently colonizing isolates. Fewer differences were observed between sinus and lung isolates, showing a higher degree of isolate similarity between these two niches. Modest respiratory changes were seen for the early isolate/PAO1 comparisons, indicating colonization with environmental isolates. Assignment of metabolic pathways via the KEGG database showed a prevalence of substrates involved in the metabolism of Ala, Asp and Glu, d-Ala, and Arg and Pro. In conclusion, extensive heterogeneity in the metabolic profiles of the *P. aeruginosa* isolates was observed from the initial stages of the infection, showing a rapid diversification of the bacteria in the heterogeneous environment of the lung. Metabolic reduction seems to be a common trait and therefore an adaptive phenotype, though it can be reached via multiple metabolic pathways.

**General information**

State: Published
Organisations: Department of Systems Biology, Bacterial Cell Factories, Novo Nordisk Foundation Center for Biosustainability, Department of Informatics and Mathematical Modeling, Infection Microbiology, University of Copenhagen, Rigshospitalet
Authors: Jørgensen, K. M. (Ekstern), Wassermann, T. (Ekstern), Johansen, H. K. (Intern), Christiansen, L. E. (Intern), Molin, S. (Intern), Høiby, N. (Ekstern), Ciofu, O. (Ekstern)
Number of pages: 16
Pages: 1447-1462
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Main Research Area: Technical/natural sciences

**Publication information**

Journal: Microbiology
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iCull – A bioeconomic model for herd management and disease control

General information
State: Published
Organisations: National Veterinary Institute, Section for Epidemiology, Department of Applied Mathematics and Computer Science, Dynamical Systems, University of Copenhagen
Authors: Kirkeby, C. (Intern), Græsbøll, K. (Intern), Nielsen, S. S. (Ekstern), Christiansen, L. E. (Intern), Toft, N. (Intern), Hisham Beshara Halasa, T. (Intern)
Number of pages: 1
Publication date: 2015

Introduction to Statistics - eNotes
Online textbook used in the introductory statistics courses at DTU. It provides a basic introduction to applied statistics for engineers. The necessary elements from probability theory are introduced (stochastic variable, density and distribution function, mean and variance, etc.) and thereafter the most basic statistical analysis methods are presented: Confidence band, hypothesis testing, simulation, simple and multiple regression, ANOVA and analysis of contingency tables. Examples with the software R are included for all presented theory and methods.

Kommentarer til Modeller for Danske Fjorde og Kystnære Havområder

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Dynamical Systems
Authors: Møller, J. K. (Intern), Christiansen, L. E. (Intern)
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Delrapport som produkt af rekruteret arbejde for Landbrug & Fødevarer. Formålet er at kommentere og diskutere resultaterne præsenteret i den tredelte rapport "Modeller for Danske Fjorde og Kystnære Havområder", som er udarbejdet af DHI og Aarhus Universitet, DCE. Der er desuden udgivet en opfølgning til denne delrapport: "Kommentarer til Modeller
Pharmacodynamic modelling of in vitro activity of tetracycline against a representative, naturally occurring population of porcine Escherichia coli

The complex relationship between drug concentrations and bacterial growth rates require not only the minimum inhibitory concentration but also other parameters to capture the dynamic nature of the relationship. To analyse this relationship between tetracycline concentration and growth of Escherichia coli representative of those found in the Danish pig population, we compared the growth of 50 randomly selected strains. The observed net growth rates were used to describe the in vitro pharmacodynamic relationship between drug concentration and net growth rate based on E max model with three parameters: maximum net growth rate ($\alpha_{\text{max}}$); concentration for a half-maximal response ($E_{\text{max}}$); and the Hill coefficient ($\gamma$). The net growth rate in the absence of antibiotic did not differ between susceptible and resistant isolates ($P = 0.97$). The net growth rate decreased with increasing tetracycline concentrations, and this decline was greater in susceptible strains than resistant strains. The lag phase, defined as the time needed for the strain to reach an OD600 value of 0.01, increased exponentially with increasing tetracycline concentration. The pharmacodynamic parameters confirmed that the in vitro pharmacodynamic relationship between drug concentration and net growth rate based on E max model with three parameters: maximum net growth rate ($\alpha_{\text{max}}$); concentration for a half-maximal response ($E_{\text{max}}$); and the Hill coefficient ($\gamma$). The net growth rate in the absence of antibiotic did not differ between susceptible and resistant isolates ($P = 0.97$). The net growth rate decreased with increasing tetracycline concentrations, and this decline was greater in susceptible strains than resistant strains. The lag phase, defined as the time needed for the strain to reach an OD600 value of 0.01, increased exponentially with increasing tetracycline concentration. The pharmacodynamic parameters confirmed that the in vitro pharmacodynamic relationship between drug concentration and net growth rate based on E max model with three parameters: maximum net growth rate ($\alpha_{\text{max}}$); concentration for a half-maximal response ($E_{\text{max}}$); and the Hill coefficient ($\gamma$). The net growth rate in the absence of antibiotic did not differ between susceptible and resistant isolates ($P = 0.97$). The net growth rate decreased with increasing tetracycline concentrations, and this decline was greater in susceptible strains than resistant strains. The lag phase, defined as the time needed for the strain to reach an OD600 value of 0.01, increased exponentially with increasing tetracycline concentration. The pharmacodynamic parameters confirmed that the in vitro pharmacodynamic relationship between drug concentration and net growth rate based on E max model with three parameters: maximum net growth rate ($\alpha_{\text{max}}$); concentration for a half-maximal response ($E_{\text{max}}$); and the Hill coefficient ($\gamma$). The net growth rate in the absence of antibiotic did not differ between susceptible and resistant isolates ($P = 0.97$). The net growth rate decreased with increasing tetracycline concentrations, and this decline was greater in susceptible strains than resistant strains. The lag phase, defined as the time needed for the strain to reach an OD600 value of 0.01, increased exponentially with increasing tetracycline concentration. The pharmacodynamic parameters confirmed that the in vitro pharmacodynamic relationship between drug concentration and net growth rate based on E max model with three parameters: maximum net growth rate ($\alpha_{\text{max}}$); concentration for a half-maximal response ($E_{\text{max}}$); and the Hill coefficient ($\gamma$). The net growth rate in the absence of antibiotic did not differ between susceptible and resistant isolates ($P = 0.97$). The net growth rate decreased with increasing tetracycline concentrations, and this decline was greater in susceptible strains than resistant strains. The lag phase, defined as the time needed for the strain to reach an OD600 value of 0.01, increased exponentially with increasing tetracycline concentration. The pharmacodynamic parameters confirmed that the in vitro pharmacodynamic relationship between drug concentration and net growth rate based on E max model with three parameters: maximum net growth rate ($\alpha_{\text{max}}$); concentration for a half-maximal response ($E_{\text{max}}$); and the Hill coefficient ($\gamma$). The net growth rate in the absence of antibiotic did not differ between susceptible and resistant isolates ($P = 0.97$). The net growth rate decreased with increasing tetracycline concentrations, and this decline was greater in susceptible strains than resistant strains. The lag phase, defined as the time needed for the strain to reach an OD600 value of 0.01, increased exponentially with increasing tetracycline concentration. The pharmacodynamic parameters confirmed that the in vitro pharmacodynamic relationship between drug concentration and net growth rate based on E max model with three parameters: maximum net growth rate ($\alpha_{\text{max}}$); concentration for a half-maximal response ($E_{\text{max}}$); and the Hill coefficient ($\gamma$). The net growth rate in the absence of antibiotic did not differ between susceptible and resistant isolates ($P = 0.97$). The net growth rate decreased with increasing tetracycline concentrations, and this decline was greater in susceptible strains than resistant strains. The lag phase, defined as the time needed for the strain to reach an OD600 value of 0.01, increased exponentially with increasing tetracycline concentration.
Pharmacokinetic-Pharmacodynamic Model To Evaluate Intramuscular Tetracycline Treatment Protocols To Prevent Antimicrobial Resistance in Pigs

High instances of antimicrobial resistance are linked to both routine and excessive antimicrobial use, but excessive or inappropriate use represents an unnecessary risk. The competitive growth advantages of resistant bacteria may be amplified by the strain dynamics; in particular, the extent to which resistant strains outcompete susceptible strains under
antimicrobial pressure may depend not only on the antimicrobial treatment strategies but also on the epidemiological parameters, such as the composition of the bacterial strains in a pig. This study evaluated how variation in the dosing protocol for intramuscular administration of tetracycline and the composition of bacterial strains in a pig affect the level of resistance in the intestine of a pig. Predictions were generated by a mathematical model of competitive growth of Escherichia coli strains in pigs under specified plasma concentration profiles of tetracycline. All dosing regimens result in a clear growth advantage for resistant strains. Short treatment duration was found to be preferable, since it allowed less time for resistant strains to outcompete the susceptible ones. Dosing frequency appeared to be ineffective at reducing the resistance levels. The number of competing strains had no apparent effect on the resistance level during treatment, but possession of fewer strains reduced the time to reach equilibrium after the end of treatment. To sum up, epidemiological parameters may have more profound influence on growth dynamics than dosing regimens and should be considered when designing improved treatment protocols.
Sampling and Pooling Methods for Capturing Herd Level Antibiotic Resistance in Swine Feces using qPCR and CFU Approaches

The aim of this article was to define the sampling level and method combination that captures antibiotic resistance at pig herd level utilizing qPCR antibiotic resistance gene quantification and culture-based quantification of antibiotic resistant coliform indicator bacteria. Fourteen qPCR assays for commonly detected antibiotic resistance genes were developed, and used to quantify antibiotic resistance genes in total DNA from swine fecal samples that were obtained using different sampling and pooling methods. In parallel, the number of antibiotic resistant coliform indicator bacteria was determined in the same swine fecal samples. The results showed that the qPCR assays were capable of detecting differences in antibiotic resistance levels in individual animals that the coliform bacteria colony forming units (CFU) could not. Also, the qPCR assays more accurately quantified antibiotic resistance genes when comparing individual sampling and pooling methods. qPCR on pooled samples was found to be a good representative for the general resistance level in a pig herd compared to the coliform CFU counts. It had significantly reduced relative standard deviations compared to coliform CFU counts in the same samples, and therefore differences in antibiotic resistance levels between samples were more readily detected. To our knowledge, this is the first study to describe sampling and pooling methods for qPCR quantification of antibiotic resistance genes in total DNA extracted from swine feces.

General information
State: Published
Organisations: National Veterinary Institute, Section for Bacteriology, Pathology and Parasitology, Department of Applied Mathematics and Computer Science, Dynamical Systems, University of Copenhagen
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Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: PLoS One
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Simulating Spread of Antimicrobial Resistant Bacteria in the Pig Pen: try our online tool

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, National Veterinary Institute, Section for Epidemiology, Dynamical Systems, University of Copenhagen
Authors: Græsbøll, K. (Intern), Nielsen, S. S. (Ekstern), Toft, N. (Intern), Christiansen, L. E. (Intern)
Number of pages: 1
Publication date: 2015
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Simulating Spread of Antimicrobial Resistant Bacteria in the Pig Pen: try our online tool

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, National Veterinary Institute, Section for Epidemiology, Dynamical Systems, University of Copenhagen
Authors: Græsbøll, K. (Intern), Nielsen, S. S. (Ekstern), Toft, N. (Intern), Christiansen, L. E. (Intern)
Number of pages: 1
Publication date: 2015
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Main Research Area: Technical/natural sciences
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Stochastic modelling of Listeria monocytogenes single cell growth in cottage cheese with mesophilic lactic acid bacteria from aroma producing cultures

A stochastic model was developed for simultaneous growth of low numbers of Listeria monocytogenes and populations of lactic acid bacteria from the aroma producing cultures applied in cottage cheese. During more than two years, different batches of cottage cheese with aroma culture were analysed for pH, lactic acid concentration and initial concentration of lactic acid bacteria. These data and bootstrap sampling were used to represent product variability in the stochastic model. Lag time data were estimated from observed growth data (lactic acid bacteria) and from literature on L. monocytogenes single cells. These lag time data were expressed as relative lag times and included in growth models. A stochastic model was developed from an existing deterministic growth model including the effect of five environmental factors and inter-bacterial interaction [Østergaard, N.B, Eklöw, A and Dalgaard, P. 2014. Modelling the effect of lactic acid bacteria from starter- and aroma culture on growth of Listeria monocytogenes in cottage cheese. International Journal of Food Microbiology. 188, 15-25]. Growth of L. monocytogenes single cells, using lag time distributions corresponding to three different stress levels, was simulated. The simulated growth was subsequently compared to growth of low concentrations (0.4-1.0CFU/g) of L. monocytogenes in cottage cheese, exposed to similar stresses, and in general a good agreement was observed. In addition, growth simulations were performed using population relative lag time distributions for L. monocytogenes as reported in literature. Comparably good predictions were obtained as for the simulations performed using lag time data for individual cells of L. monocytogenes. Therefore, when lag time data for individual cells are not available, it was suggested that relative lag time distributions for L. monocytogenes can be used as a qualified default assumption when simulating growth of low concentrations of L. monocytogenes.

General information
State: Published
Organisations: National Food Institute, Division of Industrial Food Research, Department of Applied Mathematics and Computer Science, Dynamical Systems, Research Group for Microbial Food Safety and Quality
Authors: Østergaard, N. B. (Intern), Christiansen, L. E. (Intern), Dalgaard, P. (Intern)
Number of pages: 11
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Main Research Area: Technical/natural sciences

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BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 3.97 SJR 1.462 SNIP 1.554
A Comparison between Two Simulation Models for Spread of Foot-and-Mouth Disease

Two widely used simulation models of foot-and-mouth disease (FMD) were used in order to compare the models’ predictions in term of disease spread, consequence, and the ranking of the applied control strategies, and to discuss the effect of the way disease spread is modeled on the predicted outcomes of each model. The DTU-DADS (version 0.100), and ISP (version 2.001.11) were used to simulate a hypothetical spread of FMD in Denmark. Actual herd type, movements, and location data in the period 1st October 2006 and 30th September 2007 was used. The models simulated the spread of FMD using 3 different control scenarios: 1) A basic scenario representing EU and Danish control strategies, 2) pre-emptive depopulation of susceptible herds within a 500 meters radius around the detected herds, and 3) suppressive vaccination of susceptible herds within a 1,000 meters radius around the detected herds. Depopulation and vaccination started 14 days following the detection of the first infected herd. Five thousand index herds were selected randomly, of which there were 1,000 cattle herds located in high density cattle areas and 1,000 in low density cattle areas, 1,000 swine herds located in high density swine areas and 1,000 in low density swine areas, and 1,000 sheep herds. Generally, DTU-DADS predicted larger, longer duration and costlier epidemics than ISP, except when epidemics started in cattle herds located in high density cattle areas. ISP supported suppressive vaccination rather than pre-emptive depopulation, while DTU-DADS was indifferent to the alternative control strategies. Nonetheless, the absolute differences between control strategies were small making the choice of control strategy during an outbreak to be most likely based on practical reasons.
Association of MAP specific ELISA-responses and productive parameters in 314 Danish dairy farms

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science , Dynamical Systems, National Veterinary Institute, Section for Epidemiology, University of Copenhagen
Authors: Græsbøll, K. (Intern), Nielsen, S. S. (Ekstern), Hisham Beshara Halasa, T. (Intern), Kirkeby, C. (Intern), Toft, N. (Intern), Christiansen, L. E. (Intern)
Number of pages: 1
Publication date: 2014
Event: Poster session presented at 12th International Colloquium on Paratuberculosis, Parma, Italy.
Main Research Area: Technical/natural sciences
Electronic versions:
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Source-ID: 97569852
Publication: Research - peer-review → Poster – Annual report year: 2014

Association of map specific ELISA-responses and productive parameters in 367 danish dairy farms

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science , Dynamical Systems, National Veterinary Institute, Section for Epidemiology, University of Copenhagen
Authors: Græsbøll, K. (Intern), Nielsen, S. S. (Ekstern), Hisham Beshara Halasa, T. (Intern), Kirkeby, C. (Intern), Toft, N. (Intern), Christiansen, L. E. (Intern)
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Main Research Area: Technical/natural sciences
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How Fitness Reduced, Antimicrobial Resistant Bacteria Survive and Spread: A Multiple Pig - Multiple Bacterial Strain Model

More than 30% of E. coli strains sampled from pig farms in Denmark over the last five years were resistant to the commonly used antimicrobial tetracycline. This raises a number of questions: How is this high level sustained if resistant bacteria have reduced growth rates? Given that there are multiple susceptible and resistant bacterial strains in the pig intestines, how can we describe their coexistence? To what extent does the composition of these multiple strains in individual pigs influence the total bacterial population of the pig pen? What happens to a complex population when antimicrobials are used? To investigate these questions, we created a model where multiple strains of bacteria coexist in the intestines of pigs sharing a pen, and explored the parameter limits of a stable system; both with and without an antimicrobial treatment. The approach taken is a deterministic bacterial population model with stochastic elements of bacterial distributions and transmission. The rates that govern the model are process-oriented to represent growth, excretion, and uptake from environment, independent of herd and meta-population structures. Furthermore, an entry barrier and elimination process for the individual strains in each pig were implemented. We demonstrate how competitive growth between multiple bacterial strains in individual pigs, and the transmission between pigs in a pen allow for strains of antimicrobial resistant bacteria to persist in a pig population to different extents, and how quickly they can become dominant if antimicrobial treatment is initiated. The level of spread depends in a non-linear way of the parameters that govern excretion and uptake. Furthermore, the sampling of initial distributions of strains and stochastic transmission events give rise to large variation in how homogenous and how resistant the bacterial population becomes. Most important: resistant bacteria are demonstrated to survive with a disadvantage in growth rate of well over 10%.
Optimal vaccination strategies against vector-borne diseases

Using a process oriented semi-agent based model, we simulated the spread of Bluetongue virus by Culicoides, biting midges, between cattle in Denmark. We evaluated the minimum vaccination cover and minimum cost for eight different preventive vaccination strategies in Denmark.

The simulation model replicates both a passive and active flight of midges between cattle distributed on pastures and cattle farms in Denmark. A seasonal abundance of midges and temperature dependence of biological processes were included in the model. The eight vaccination strategies were investigated under four different grazing conditions. Furthermore, scenarios were tested with three different index locations stratified for cattle density. The cheapest way to vaccinate cattle with a medium risk profile (less than 1000 total affected cattle) was to vaccinate cattle on pasture. Regional vaccination displayed better results when index cases were in the vaccinated areas. However, given that the long-range spread of midge borne disease is still poorly quantified, more robust national vaccination schemes seem preferable.

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Dynamical Systems, National Veterinary Institute, Section for Epidemiology
Authors: Græsbøll, K. (Intern), Enøe, C. (Intern), Bødker, R. (Intern), Christiansen, L. E. (Intern)
Number of pages: 10
Pages: 153-162
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Main Research Area: Technical/natural sciences

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Scopus rating (2015): SJR 0.768 SNIP 0.699 CiteScore 1.6
Listeria monocytogenes is a well-known foodborne pathogen that potentially causes listeriosis. No outbreaks or cases of listeriosis have been associated with cottage cheese, but several confirmed cases and outbreaks in the EU and the US have been related to dairy products made from raw or pasteurised milk. This, in combination with the fact that cottage cheese support growth of Listeria monocytogenes, induces a documentation requirement on the food producer. In the EU regulatory framework, mathematical models are recognised as a suitable supplement to traditional microbiological methods. The models can be used for documentation of compliance with microbiological criteria for Listeria monocytogenes under reasonably foreseeable conditions. Cottage cheese is a fresh, fermented dairy product. It consists of a fermented cheese curd mixed with a fresh or cultured cream dressing. The product contains considerable concentrations of lactic acid bacteria from the added starter or aroma cultures. The presence of these microorganisms induces some complexity to the product, since the lactic acid bacteria metabolites and e.g. bacteriocins exhibit an inhibitory effect towards co-culture microorganisms such as Listeria monocytogenes. During storage at temperatures allowing the mesophilic lactic acid bacteria to grow (> 8-10°C), a pronounced inter-bacterial interaction and growth inhibition of co-culture Listeria monocytogenes was observed. These observations emphasised the need for inter-bacterial interaction models when predicting the growth response of Listeria monocytogenes in fermented dairy products. The objective of the PhD-project was to develop new, or extend existing mathematical models to be used for risk assessment and product development. When the project was initiated, none of the existing predictive models were found to appropriately describe the simultaneous growth of lactic acid bacteria from the added starter or aroma culture and Listeria monocytogenes in cottage cheese. New, deterministic growth models were developed for Listeria monocytogenes, starter lactic acid bacteria and aroma lactic acid bacteria. The new cardinal parameter type growth models included the effect of temperature, pH, NaCl, lactic and sorbic acid. The models were developed based on growth data obtained from absorbance measurements in liquid laboratory media and growth data obtained in cottage cheese with fresh or cultured cream dressing. An important step in the modelling procedure was the calibration of the reference growth rate (µref, h⁻¹ at 25°C) which was strongly affected by the dominating lactic acid bacteria culture. By combining the developed secondary growth models with the empirical Jameson approach, good predictions of the simultaneous growth of Listeria monocytogenes and lactic acid bacteria were obtained. Both growth rate and maximum population densities of Listeria monocytogenes was accurately described under constant and dynamic storage temperatures (between 5°C and 15°C). The inter-bacterial interaction was clearly important to include when predicting growth response of Listeria monocytogenes in fermented dairy products. Alternative, semi-mechanistic, iimodelling approaches were evaluated based on methods applied in the fermentation technology. The dynamics of lactic acid concentration and product pH was related to growth of lactic acid bacteria by the yield factor concept. The ability to predict the maximum population density of Listeria monocytogenes in cottage cheese based on dynamic lactic acid and pH was evaluated. For cottage cheese with fresh cream dressing, the semi-mechanistic interaction model successfully predicted the maximum population density. Lactic acid and pH was, however, insufficient to describe the growth inhibition of Listeria monocytogenes observed in cottage cheese with cultured cream dressing. Improved, mechanistic, prediction of Listeria monocytogenes in cottage cheese with cultured cream dressing would require that additional mechanisms were included in the model, such as other metabolites or bacteriocins. Finally, the semi-mechanistic and the empirical Jameson approach to inter-bacterial interaction modelling were compared. The empirical Jameson model consistently performed equally well or better than the more complex semi-mechanistic model. In order to evaluate the growth response of more realistic concentrations of Listeria monocytogenes and to take variability into account, a stochastic approach was applied. The deterministic growth models were used in combination with stochastic input values for bacterial concentration; lag time duration and product characteristics. Good agreement between predicted and observed growth was obtained, when applying broth based lag time distributions for Listeria monocytogenes single cells in combination with the relative lag time concept. Furthermore, application of relative lag time distributions from Listeria monocytogenes population data provided good predictions of the growth response of only a few Listeria monocytogenes cells in cottage cheese at chilled temperatures. From the results of the present PhD-project it was found that once solid, deterministic, secondary growth models have been developed and validated, they can be modified and/or extended to a range of other modelling procedures. Furthermore, inclusion of inter-bacterial interaction was considered to be an inevitable part when modelling and predicting growth of L. monocytogenes in fermented dairy products.
products. In general, simple approaches to describe interaction and growth inhibition (empirical approach), lag time prediction of individual cells (variability in population RLT-values) and representation of e.g. variable product characteristics (bootstrapping from empirical distributions) were advocated. It is believed that it is necessary to define some applicable methodologies for the development of growth models for complex products such as fermented dairy products. Model development is a comprehensive process with an almost infinite data requirement and the findings of the present PhD-project is thought to be important in relation to the development of predictive models that are valuable for, and readily applicable in the food industry.

### Comparing control strategies against foot-and-mouth disease: Will vaccination be cost-effective in Denmark?

Recent outbreaks of foot-and-mouth disease (FMD) in Europe have highlighted the need for assessment of control strategies to optimise control of the spread of FMD. Our objectives were to assess the epidemiological and financial impact of simulated FMD outbreaks in Denmark and the effect of using ring depopulation or emergency vaccination to control these outbreaks. Two stochastic simulation models (InterSpreadPlus (ISP) and the modified Davis Animal Disease Simulation model (DTU-DADS)) were used to simulate the spread of FMD in Denmark using different control strategies. Each epidemic was initiated in one herd (index herd), and a total of 5000 index herds were used. Four types of control measures were investigated: (1) a basic scenario including depopulation of detected herds, 3km protection and 10km surveillance zones, movement tracing and a three-day national standstill, (2) the basic scenario plus depopulation in ring zones around detected herds (Depop), (3) the basic scenario plus protective vaccination within ring zones around detected herds, and (4) the basic scenario plus protective vaccination within ring zones around detected herds. Disease spread was simulated through direct animal movements, medium-risk contacts (veterinarians, artificial inseminators or milk controllers), low-risk contacts (animal feed and rendering trucks, technicians or visitors), market contacts, abattoir trucks, milk tanks, or local spread. The two simulation models showed different results in terms of the estimated numbers. However, the tendencies in terms of recommendations of strategies were similar for both models. Comparison of the different control strategies showed that, from an epidemiological point of view, protective vaccination would be preferable if the epidemic started in a cattle herd in an area with a high density of cattle, whereas if the epidemic started in an area with a low density of cattle or in other species, protective vaccination or depopulation would have almost the same preventive effect. Implementing additional control measures either 14 days after detection of the first infected herd or when 10 herds have been diagnosed would be more efficient than implementing additional control measures when more herds have been diagnosed. Protective vaccination scenarios would never be cost-effective, whereas depopulation or suppressive vaccination scenarios would most often be recommended. Looking at the median estimates of the cost-benefit analysis, depopulation in zones would most often be recommended, although, in extreme epidemics, suppressive vaccination scenarios could be less expensive. The vast majority of the costs and losses associated with a Danish epidemic could be attributed to export losses.

### General information

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Decisions on control of foot-and-mouth disease informed using model predictions

The decision on whether or not to change the control strategy, such as introducing emergency vaccination, is perhaps one of the most difficult decisions faced by the veterinary authorities during a foot-and-mouth disease (FMD) epidemic. A simple tool that may predict the epidemic outcome and consequences would be useful to assist the veterinary authorities in the decision-making process. A previously proposed simple quantitative tool based on the first 14 days outbreaks (FFO) of FMD was used with results from an FMD simulation exercise. Epidemic outcomes included the number of affected herds, epidemic duration, geographical size and costs. The first 14 days spatial spread (FFS) was also included to further support the prediction. The epidemic data was obtained from a Danish version (DTU-DADS) of a pre-existing FMD simulation model (Davis Animal Disease Spread – DADS) adapted to model the spread of FMD in Denmark. The European Union (EU) and Danish regulations for FMD control were used in the simulation. The correlations between FFO and FFS and the additional number of affected herds after day 14 following detection of the first infected herd were 0.66 and 0.82, respectively. The variation explained by the FFO at day 14 following detection was high (P-value < 0.001). This indicates that the FFO may take a part in the decision of whether or not to intensify FMD control, for instance by introducing emergency vaccination and/or pre-emptive depopulation, which might prevent a “catastrophic situation”. A significant part of the variation was explained by supplementing the model with the FFS (P-value < 0.001). Furthermore, the type of the index-herd was also a significant predictor of the epidemic outcomes (P-value < 0.05). The results of the current study suggest that national veterinary authorities should consider to model their national situation and to use FFO and FFS to help planning and updating their contingency plans and FMD emergency control strategies.

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Decisions on foot-and-mouth disease control informed by model prediction

The predictive capability of the first fortnight incidence (FFI), which is the number of detected herds within the first 14 days following detection of the disease, of the course of a foot-and-mouth disease (FMD) epidemic and its outcomes were investigated. Epidemic outcomes included the number of affected herds, epidemic duration, geographical size, and costs. The first fourteen days spatial spread (FFS) was also included to support the prediction. The epidemic data were obtained from a Danish version (DTU-DADS) of the Davis Animal Disease Spread simulation model.

The FFI and FFS showed good correlations with the epidemic outcomes. The predictive capability of the FFI was high. This indicates that the FFI may take a part in the decision of whether or not to boost FMD control, which might prevent occurrence of a large epidemic in the face of an FMD incursion. The prediction power was improved by supplementing the models with information on FFS and characteristics of the index-herd. Results presented here will contribute to improve preparedness of Denmark to early control of a hypothetical FMD epidemic.

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Optimal vaccination scenarios against vector-borne diseases
Using a process oriented semi-agent based model we simulated the spread of Bluetongue virus in Denmark. We evaluated the efficiency and minimum vaccination cover for eight different preventive vaccination strategies in Denmark. The simulation model replicates both passive and active flight of Culicoides between hosts on pasture and stables in Denmark. Seasonal abundance of midges and temperature dependence on biological processes were included in the model. The eight vaccination scenarios comprised of: All holdings vaccinated to a given percentage, random holdings selected for vaccination, two scenarios based on the size of holdings, mosaic vaccination of nearest neighbor farms, vaccination of hosts on pasture, regional vaccination, and trench vaccination from the border to Germany. These eight scenarios were investigated under normal grazing conditions and under a forced housing scenario.

The most robust vaccination scenarios were all holdings vaccinated and the mandatory vaccination of hosts on pasture. Regional vaccination and trench vaccination display better results under some conditions, but are very sensitive to the incursion route.

With this study we intended to test scenarios that would increase distance between infectious and susceptible hosts. This can be done very efficiently on a regional scale if the incursion route is well specified. However as the long-range spread of midge borne disease is still poorly quantified, more robust national vaccination schemes seems preferable.

Results in this presentation were obtained building upon the model presented in: Simulating spread of Bluetongue Virus by flying vectors between hosts on pasture. Kaare Græsbøll et al. Scientific Reports. 2:863 (2012).

Scheduling sampling to maximize information about time dependence in experiments with limited resources
Looking for periodicity in sampled data requires that periods (lags) of different length are represented in the sampling plan. We here present a method to assist in planning of temporal studies with sparse resources, which optimizes the number of observed time lags for a fixed amount of samples within a fixed time window given a maximum time lag of interest. The method can also optimize the temporal sampling specifically for situations where samples are at risk of being rescheduled due to otherwise unpredictable events such as weather, faulty equipment, etc. The method is based on the framework of simulated annealing in which we have defined an energy function to be minimized. We compare the calculated sampling plan with a random plan and a cyclic design and demonstrate how our calculated plan provides the most information about temporal autocorrelation.
Simulated effects of changes in herd sizes and densities with regard to FMD outbreaks in Denmark

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Simulation of Listeria monocytogenes single cell colonial growth

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The range of attraction for light traps catching Culicoides biting midges (Diptera: Ceratopogonidae)

Background
Culicoides are vectors of e.g. bluetongue virus and Schmallenberg virus in northern Europe. Light trapping is an important tool for detecting the presence and quantifying the abundance of vectors in the field. Until now, few studies have investigated the range of attraction of light traps.

Methods
Here we test a previously described mathematical model (Model I) and two novel models for the attraction of vectors to light traps (Model II and III). In Model I, Culicoides fly to the nearest trap from within a fixed range of attraction. In Model II Culicoides fly towards areas with greater light intensity, and in Model III Culicoides evaluate light sources in the field of view and fly towards the strongest. Model II and III incorporated the directionally dependent light field created around light traps with fluorescent light tubes. All three models were fitted to light trap collections obtained from two novel experimental setups in the field where traps were placed in different configurations.

Results
Results showed that overlapping ranges of attraction of neighboring traps extended the shared range of attraction. Model I did not fit data from any of the experimental setups. Model II could only fit data from one of the setups, while Model III fitted data from both experimental setups.

Conclusions
The model with the best fit, Model III, indicates that Culicoides continuously evaluate the light source direction and intensity. The maximum range of attraction of a single 4W CDC light trap was estimated to be approximately 15.25 meters. The attraction towards light traps is different from the attraction to host animals and thus light trap catches may not represent the vector species and numbers attracted to hosts.
Comparison of different control strategies on FMD in Denmark

The purpose of this study was to compare different control strategies that could be used in Denmark during an outbreak of FMD, based on epidemiological, ethical and economic parameters. Nearly a hundred different control strategies and more than 30 sensitivity analyses were run, changing between depopulation (Depop), suppressive (VacToKill) and protective (VacToLive) vaccination with different times for implementation and different zone sizes. It is therefore obvious that not all results can be included here; neither will all results be presented at the seminar. However, we have done our best to extract the essence of the results. All results will be presented in the final project report, which will be available on request to the authors.

Comparing epidemiological outputs showed that extra control measures will always reduce the average duration and size of an epidemic. However, the variations in duration and size of epidemics are large, and if epidemics are small, extra control measures may not always be necessary. Comparing depopulation to suppressive and protective vaccination shows that from an epidemiologic point of view, vaccination will be beneficial. However, comparing the economy of the epidemics, it is shown that vaccination is more expensive compared to depopulation.

Results from 1000 epidemics starting in cattle herds in cattle dense areas. Epidemiological results from ISP presented as medians and 5-95 percentiles (brackets), economical as means.

The size, duration and costs of epidemics vary much with the type of index herd (starting points). Furthermore, not only economy, but also ethical and political issues will also play an important role in decision making. Therefore, it is important to keep in mind that this work will not give the answer as to which strategy to use during an epidemic, but can be used as a decision support tool. Sometimes, even though one strategy will be predicted to be cheaper, the second cheapest strategy might reduce the number of killed animals so much that it will become a better option.

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Consequence of changes in herd size and densities for the contingency planning

The objective of the current work was to evaluate whether the effects and control of foot-and-mouth disease (FMD) spread would differ following the structural changes to the Danish agricultural sector from now until 2030. Following the predicted structural changes, a new farm file was created, representing active farms in 2030. Index herds were randomly selected from the created farm file. The farm file contains information about the herd ID, coordinates, number of animals and movement rates. DTU-DADS and ISP were used to simulate the spread of FMD in Denmark in 2030. Following discussions with the industry, low risk contacts are assumed to increase with increasing herd size, and thus the number of low risk contacts was increased by 50%. All other input values were assumed to stay the same.

Four different control scenarios were run: 1) A basic scenario representing current EU and Danish control strategies, 2) pre-emptive depopulation of susceptible herds in a radius of 0.5, 1, 1.5 and 3 km around the detected herds, 3) suppressive vaccination in a radius of 1, 2, 3, and 5 km around the detected herds 4) protective vaccination in similar radiuses to suppressive vaccination. Depopulation and vaccination started after detecting 10 infected herds.

Compared to the current situation, future FMD outbreaks are, based on median values, predicted to be shorter and cheaper. Nonetheless, we also predicted that extreme epidemics would be larger and more expensive. Epidemiologic results predict that pre-emptive depopulation and protective vaccination are good choices to control the disease in future populations. However, economically, protective vaccination is predicted to be too expensive in Denmark, and thus pre-emptive depopulation and suppressive vaccination are better options to control FMD in the future.

It is also important to mention that enlarging the depopulation and vaccination zones might not be a good option, because direct costs would increase and resources problems might arise leading to larger economic damage.

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Development of a restricted state space stochastic differential equation model for bacterial growth in rich media

In the present study, bacterial growth in a rich media is analysed in a Stochastic Differential Equation (SDE) framework. It is demonstrated that the SDE formulation and smoothened state estimates provide a systematic framework for data driven model improvements, using random walk hidden states. Bacterial growth is limited by the available substrate and the inclusion of diffusion must obey this natural restriction. By inclusion of a modified logistic diffusion term it is possible to introduce a diffusion term flexible enough to capture both the growth phase and the stationary phase, while concentration is restricted to the natural state space (substrate and bacteria non-negative). The case considered is the growth of Salmonella and Enterococcus in a rich media. It is found that a hidden state is necessary to capture the lag phase of growth, and that a flexible logistic diffusion term is needed to capture the random behaviour of the growth model. Further, it is concluded that the Monod effect is not needed to capture the dynamics of bacterial growth in the data presented.

General information
Influence of livestock markets on the spread of FMD

The purpose of this study was to investigate, whether cattle markets would influence the duration, size and economic consequences of a potential FMD epidemic in Denmark.

The spread of FMD was simulated using the InterSpread Plus. For movements of cattle to and from markets, we modeled the frequency of movements to markets for the individual herd and categorized herds that could receive contacts from markets. The epidemics were initiated in herds with market contacts. In a basic market scenario, we used the individual herds’ probability of moving animals to markets, while in a control scenario we reduced all probabilities of movements to markets to zero, to reflect a situation with no markets. Each scenario was initiated in 386 different herds (index), and for each index herd, the model was run 100 times. The number of extra contacts generated through a market was set to 3.5 and the probability of transmission from markets was modeled as a normal distribution with a mean of 0.415 and a standard deviation of 0.06. This probability was a combination of the risk from purchase of animals from markets and the indirect contact from visitors on markets. Danish markets would be closed as soon as FMD is detected. Therefore, markets were only active during the first three weeks of the epidemic, as time from infection to first detection was assumed to be 21 days.

The results show an effect of markets on the size, duration and costs of a FMD epidemic (Table 1); the median duration of epidemics is 1 week longer, and 28 more herds are detected with FMD. In the scenarios with markets, the epidemics included a larger area compared to scenarios without markets. It is also shown that epidemics with markets are more expensive compared to epidemics without markets.

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Modelling spread of Bluetongue and other vector borne diseases in Denmark and evaluation of intervention strategies

The main outcome of this PhD project is a generic model for non-contagious infectious vector-borne disease spread by one vector species between up to two species of hosts distributed on farms and pasture. The model features a within-herd model of disease, combined with a triple movement kernel that describes spread of disease using vectors or hosts as agents of the spread.

The model is run with bluetongue as the primary case study, and it is demonstrated how an epidemic outbreak of bluetongue 8 in Denmark is sensitive to the use of pasture, climate, vaccination, vector abundance, and flying parameters.

In constructing a more process oriented agent-based approach to spread modeling new parameters describing vector behavior were introduced. When these vector flying parameters have been quantified by experiments, this model can be implemented on areas naïve to the modeled disease with a high predictive power.

Furthermore this PhD has provided a new method of estimating the effect of light traps, which can estimate the additive effect of closely placed traps, and determine trap range of individual traps based on emitted light intensity. Moreover there has been devised a method to sample in time which maximizes information about time dependence and is robust to changes.

Model's comparison

Three popular disease spread simulation models were used to simulate the spread of foot-and-mouth disease (FMD) in Denmark. The models’ predictions in term of disease spread, consequence, and the ranking of the applied control...
strategies were compared. The original Davis Animal Disease Spread (DADS version 0.05) was adapted to DTU-DADS, and this model as well as InterSpread Plus (ISP version 2.001.11) and the North American Animal Disease Spread Model (NAADSM version 3.0.81) were all used to simulate hypothetical spread of FMD in Denmark. Data on Danish herds were used including herd type, movements, and location in the period 1st October 2006 to 30th September 2007. The three models to the highest possible extend set up to simulate the same epidemics in 3 different control scenarios: 1) A basic scenario representing EU and Danish control strategies, 2) pre-emptive depopulation of susceptible herds in a 500 meters radius around the detected herds, and 3) suppressive vaccination of susceptible herds in a 1,000 meters radius around the detected herds. Depopulation and vaccination started either 14 days following the detection of the first infected herd or following detection of 50 infected herds. Five thousand index herds were selected randomly in which there were 1,000 cattle herds located in high density cattle area and 1,000 in low density cattle area, 1,000 swine herds located in high density swine area and 1,000 in low density swine area, and 1,000 sheep herds. Generally, NAADSM predicted the largest, longest duration and costliest epidemics. DTU-DADS predicted larger, longer duration and costlier epidemics than ISP, except when epidemics started in cattle herds located in high density cattle area. ISP predicted suppressive vaccination to be less costly than depopulation, while the least costly control strategy predicted by DTU-DADS differed depending on the species and density area of the index herd. It was not possible to run the depopulation scenarios in the NAADSM due to limitations in the model. Running several models in parallel gives better insight in disease spread, limits typing and coding errors and improves understanding of modeled processes. The chosen control strategy might depend on the chosen model.

General information
State: Published
Organisations: National Veterinary Institute, Section for Epidemiology, Department of Informatics and Mathematical Modeling, DTU Data Analysis, Mathematical Statistics
Authors: Hisham Beshara Halasa, T. (Intern), Boklund, A. (Intern), Stockmarr, A. (Intern), Enøe, C. (Intern), Christiansen, L. E. (Intern)
Pages: 17-20
Publication date: 2012

Host publication information
Title of host publication: Optimizing the control of foot-and-mouth disease in Denmark by simulation : Final report
Place of publication: Kgs. Lyngby
Publisher: Technical University of Denmark (DTU)
Main Research Area: Technical/natural sciences
Seminar: Closing seminar for Optimizing the control of foot-and-mouth disease in Denmark by simulation, Copenhagen, Denmark, 09/05/2012
Electronic versions:
Pages_from_prod21357306600747.ClosingSeminar_Abstracts_updated_7.pdf
Links:
Publication: Research - peer-review › Article in proceedings – Annual report year: 2012

Optimizing the control of foot-and-mouth disease in Denmark by simulation: Comparison of foot-and-mouth disease simulation models

General information
State: Published
Organisations: National Veterinary Institute, Section for Epidemiology, Department of Informatics and Mathematical Modeling, DTU Data Analysis, Mathematical Statistics
Authors: Hisham Beshara Halasa, T. (Intern), Boklund, A. (Intern), Stockmarr, A. (Intern), Enøe, C. (Intern), Christiansen, L. E. (Intern)
Number of pages: 35
Publication date: 2012

Publication information
Media of output: Power Point presentation
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions:
3c_comparison_of_three_different_simulation_models.pdf
Publication: Research - peer-review › Sound/Visual production (digital) – Annual report year: 2012

Optimizing the control of foot-and-mouth disease in Denmark by simulation: Comparison of different control strategies on FMD in Denmark
Optimizing the control of foot-and-mouth disease in Denmark by simulation: Influence of livestock markets on spread of FMD

Predicting the structural development in Danish livestock and how it affects control strategies against FMD

The purpose of this study was to assess if the optimal control strategy against foot-and-mouth disease (FMD) spread is invariant to structural development in Danish livestock until 2030. The DTU-DADS model as presented by Halasa et al. uses demographic information of all farms including their location, size, and production type. The main challenge was to predict the demographic data.

Based on data for all herds with animals susceptible to FMD in the Central Husbandry Registry from 1999 to 2010 and supplementary data for swine herds from Danish Agriculture & Food Council (2002 to 2009), all farms were classified by production type and size each year. A total of 88 classes were used. For each species group (cattle, swine, and sheep and goat) a transition probability matrix (TPM) was estimated based on the ten year to year transitions. It was hypothesized that there might be regional differences. This was assessed by dividing Denmark into 7 regions,
counting all transitions per region, and comparing these counts to the country wide counts using a Chisq test. Due to the regionalization, some of the less populated size categories were merged to reduce noise. All regions were found to have significantly different TPMs. These TPMs were used in a Markov chain to predict the distribution of farms in year 2030. However, the predictions were unrealistic as far too many farms opened – since all closed farms were allowed to reopen. It was decided to make the closed state a terminal state and make an independent prediction of how many farms should open each year. The best model was a log-linear model for each region. The combined result is a reduction from 51,031 herds in 2007 to 14,126 farms in 2030 with larger average size.

General information
State: Published
Organisations: National Veterinary Institute, Section for Epidemiology, Department of Informatics and Mathematical Modeling, Mathematical Statistics
Authors: Christiansen, L. E. (Intern), Hisham Beshara Halasa, T. (Intern), Boklund, A. (Intern), Enøe, C. (Intern)
Pages: 37
Publication date: 2012

Host publication information
Title of host publication: Optimizing the control of foot-and-mouth disease in Denmark by simulation : Final report
Place of publication: Kgs. Lyngby
Publisher: Technical University of Denmark (DTU)
Main Research Area: Technical/natural sciences
Seminar: Closing seminar for Optimizing the control of foot-and-mouth disease in Denmark by simulation, Copenhagen, Denmark, 09/05/2012
Electronic versions:
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Links:
Publication: Research - peer-review › Article in proceedings – Annual report year: 2012

Simulated Effects of Introducing Emergency Vaccination or Depopulation During FMD Outbreaks in Denmark
The purpose of this study was to explore the effects of modifying FMD control 14 days following detection of the first infected herd in a simulated FMD epidemic in Denmark. The spread of FMD was simulated using an adapted version of the well described DADS simulation model, called DTU-DADS, using Danish herd locations and movements data. The epidemics were initiated in 1000 randomly chosen cattle herds located in cattle-dense areas.

The basic scenario consisted of: the minimum EU control measures, culling of forward-traced herds and a 3-day national stand-still on animal movements. Alternative scenarios included depopulation, suppressive or preventive vaccination within 1 km.

The results show that there may be positive effects of applying additional control measures on the size, duration and costs of the epidemics. The median duration decreased from 56 days in the basic scenario to 45-47 days in the vaccination scenarios, and to 40 days in the depopulation scenarios. Furthermore, the number of infected herds decreased, but with fewer infected herds in the protective vaccination scenario. The total costs of an epidemic, including export losses, changed from €562 million in the basic scenario to €515, €535 and €610 million in the depopulation, suppressive and protective vaccination scenarios, respectively.

These results suggest that vaccination will often be a more expensive strategy in a country with a large export, like Denmark. Furthermore, the simulated results show that from an economic point of view depopulation in zones is often preferable.

General information
State: Published
Organisations: National Veterinary Institute, Section for Epidemiology, Department of Informatics and Mathematical Modeling, Mathematical Statistics
Authors: Boklund, A. (Intern), Hisham Beshara Halasa, T. (Intern), Christiansen, L. E. (Intern), Willeberg, P. (Intern), Enøe, C. (Intern)
Number of pages: 1
Publication date: 2012
Event: Abstract from EuFMD meeting 2012, Jerez de la Frontera, Spain.
Main Research Area: Technical/natural sciences
Electronic versions:
prod21357306137969.Eufmd_Open_Session_2012_ANB.pdf
Source: dtu
Source-ID: u::6561
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2012
Simulating spread of Bluetongue Virus by flying vectors between hosts on pasture

Bluetongue is a disease of ruminants which reached Denmark in 2007. We present a process-based stochastic simulation model of vector-borne diseases, where host animals are not confined to a central geographic farm coordinate, but can be distributed onto pasture areas. Furthermore vectors fly freely and display search behavior to locate areas with hosts. We also include wind spread of vectors, host movements, and vector seasonality. Results show that temperature and seasonality of vectors determines the period in which an incursion of Bluetongue may lead to epidemic spread in Denmark. Within this period of risk the number of infected hosts is affected by temperature, vector abundance, vector behavior, vectors’ ability to locate hosts, and use of pasture. These results indicate that restricted grazing during outbreaks can reduce the number of infected hosts and the size of the affected area. The model can be implemented on other vector-borne diseases of grazing animals.

General information
State: Published
Organisations: Department of Informatics and Mathematical Modeling, Mathematical Statistics, National Veterinary Institute, Section for Epidemiology
Authors: Græsbøll, K. (Intern), Bødker, R. (Intern), Enøe, C. (Intern), Christiansen, L. E. (Intern)
Number of pages: 8
Pages: 863
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Main Research Area: Technical/natural sciences

Publication information
Journal: Scientific Reports
Volume: 2
ISSN (Print): 2045-2322
Ratings:
BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.63 SJR 1.625 SNIP 1.401
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.057 SNIP 1.684 CiteScore 5.3
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.103 SNIP 1.544 CiteScore 4.75
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.886 SNIP 1.51 CiteScore 4.06
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.458 SNIP 0.896 CiteScore 2.44
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
ISI indexed (2011): ISI indexed no
Original language: English
Computational models, Biological models, Diseases
DOIs:
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Links:
http://www.nature.com/srep/2012/121115/srep00863/full/srep00863.html

Relations
Projects:
Simulating spread of Bluetongue Virus by flying vectors between hosts on pasture
Source: dtu
Source-ID: n:oai:DTIC-ART:pubmed/374300512::21337
Publication: Research - peer-review › Journal article – Annual report year: 2012
Development of antibiotic resistance and up-regulation of the antimutator gene pfpI in mutator Pseudomonas aeruginosa due to inactivation of two DNA oxidative repair genes (mutY, mutM)

Prevention and correction of oxidative DNA lesions in Pseudomonas aeruginosa is ensured by the DNA oxidative repair system (GO). Single inactivation of mutT, mutY and mutM involved in GO led to elevated mutation rates (MRs) that correlated to increased development of resistance to antibiotics. In this study, we constructed a double mutant in mutY and mutM (PAOMY-Mgm) and characterized the phenotype and the gene expression profile using microarray and RT-PCR. PAOMY-Mgm presented 28-fold increases in MR compared with wild-type reference strain PAO1. In comparison, the PAOMYgm (mutY) single mutant showed only a fivefold increase, whereas the single mutant PAOMMgm (mutM) showed a nonsignificant increase in MR compared with PAO1 and the single mutants. Mutations in the regulator nfxB leading to hyperexpression of MexCD-OprJ efflux pump were found as the mechanism of resistance to ciprofloxacin in the double mutant. A better fitness of the mutator compared with PAO1 was found in growth competition experiments in the presence of ciprofloxacin at concentrations just below minimal inhibitory concentration. Up-regulation of the antimutator gene pfpI, that has been shown to provide protection to oxidative stress, was found in PAOMYMgm compared with PAO1. In conclusion, we showed that MutY and MutM are cooperating in the GO of P. aeruginosa, and that oxidative DNA lesions might represent an oxidative stress for the bacteria.

General information
State: Published
Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling, Hospital Universitario Son Espases, Technical University of Denmark, Copenhagen University Hospital, University of Copenhagen
Authors: Mandsberg, L. F. (Ekstern), Macia, M. D. (Ekstern), Bergmann, K. R. (Ekstern), Christiansen, L. E. (Intern), Alhede, M. (Ekstern), Kirkby, N. (Ekstern), Hoiby, N. (Ekstern), Oliver, A. (Ekstern), Ciofu, O. (Ekstern)
Pages: 28-37
Publication date: 2011
Main Research Area: Technical/natural sciences

Publication information
Journal: F E M S Microbiology Letters
Volume: 324
Issue number: 1
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Ratings:
BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.76 SJR 0.747 SNIP 0.597
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.131 SNIP 0.752 CiteScore 2.08
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.122 SNIP 0.767 CiteScore 2.17
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.043 SNIP 0.72 CiteScore 2.25
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.069 SNIP 0.817 CiteScore 2.25
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.096 SNIP 0.761 CiteScore 2.26
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.07 SNIP 0.756
How does increasing immunity change spread kernel parameters in subsequent outbreaks? – A simulation study on Bluetongue Virus

Modelling the spatial spread of vector borne diseases, one may choose methods ranging from statistic to process oriented. One often used statistic tool is the empirical spread kernel. An empiric spread kernel fitted to outbreak data provides hints on the spread mechanisms, and may provide a good estimate on how future epidemics could proceed under similar conditions. However, a number of variables influence the spread of vector borne diseases. If one of these changes significantly after an outbreak, it needs to be incorporated into the model to improve the prediction on future outbreaks. Examples of such changes are: vaccinations, acquired immunity, vector density and control, meteorological variations, wind pattern, and so on. Including more and more variables leads to a more process oriented model. A full process oriented approach simulates the movement of virus between vectors and host, describing density and motion of vectors/hosts, climatic variables, and so on will theoretically be able to describe an outbreak under any circumstances. It will most likely contain parameters not very well established, and is also very heavy in computer time. Nevertheless, we have tried to create a relatively detailed simulation spread model. And by using empirical spread kernels from past outbreaks we have fitted some of the more uncertain parameters for this case study. A stochastic simulation model was developed for the spread of bluetongue virus. In the model hosts (cattle) and vectors (Culicoides) are distributed onto a grid representing farm/field quadrants of 1 hectare. Each quadrant has a host SEIR model (Susceptible Exposed Infectious Recovered) and a vector SEI model attached. Transmission of virus between hosts and vectors depend on many parameters most of which are temperature dependent. Spatial movement of virus between quadrants is modelled by local flight and wind spread of vectors. The simulated spatial spread rate of virus is very dependent on movement parameters, but also the distribution and total numbers of hosts and vectors influenced the spread of virus. With empirical spread kernels from past outbreaks and known distributions of host animals, it was possible to fit parameter values of vector movement. The final model including the fitted process based movement parameters is used to simulate e.g. 50% of cattle protected by acquired immunity after a first epidemic outbreak. We can then demonstrate how this changes the spread kernel for future outbreaks.

General information
State: Published
Organisations: Section for Veterinary Epidemiology and public sector consultancy, Mathematical Statistics, Department of Informatics and Mathematical Modeling, Division of Veterinary Diagnostics and Research, National Veterinary Institute
Authors: Græsbøll, K. (Intern), Bødker, R. (Intern), Enøe, C. (Intern), Christiansen, L. E. (Intern)
The Universal Primer - An open source solution for archiving, organizing and streaming live lectures

Many disparate projects providing open access to educational videos are currently available or under development. These projects lack a unifying interface for accessing content, employ differing content licenses, and provide little or no infrastructure for user-contribution or live teaching. The goal of the Universal Primer is to address these problems, and allow anyone, anywhere, to teach or learn anything that can be reasonably taught or learned through a computer. The Universal Primer is 1: A fully open source solution for streaming live lectures. And 2: A Wikipedia-like website for uploading and organizing open-licensed community contributed educational material.

Nonlinear Stochastic Modelling of Antimicrobial resistance in Bacterial Populations
Geo-locating cattle using EU databases

General information
State: Published
Organisations: Section for Veterinary Epidemiology and public sector consultancy, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Mathematical Statistics, Department of Informatics and Mathematical Modeling
Authors: Græsbøll, K. (Intern), Bødker, R. (Intern), Enøe, C. (Intern), Christiansen, L. E. (Intern)
Publication date: 2010
Event: Poster session presented at NKVet Symposium, Databases in veterinary medicine – Validation, harmonisation and application, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 272161
Publication: Research - peer-review › Poster – Annual report year: 2010

Increasing the resolution of Bluetongue spatial modelling - from cattle farms to cattle in fields

General information
State: Published
Organisations: Section for Veterinary Epidemiology and public sector consultancy, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Mathematical Statistics, Department of Informatics and Mathematical Modeling
Authors: Græsbøll, K. (Intern), Bødker, R. (Intern), Christiansen, L. E. (Intern), Enøe, C. (Intern)
Publication date: 2010
Event: Abstract from GEOVET 2010, Sydney, Australia.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 272256
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2010

Modelling conjugation with stochastic differential equations

Conjugation is an important mechanism involved in the transfer of resistance between bacteria. In this article a stochastic differential equation based model consisting of a continuous time state equation and a discrete time measurement equation is introduced to model growth and conjugation of two Enterococcus faecium strains in a rich exhaustible media. The model contains a new expression for a substrate dependent conjugation rate. A maximum likelihood based method is used to estimate the model parameters. Different models including different noise structure for the system and observations are compared using a likelihood-ratio test and Akaike's information criterion. Experiments indicating conjugation on the agar plates selecting for transconjugants motivates the introduction of an extended model, for which conjugation on the agar plate is described in the measurement equation. This model is compared to the model without plate conjugation. The modelling approach described in this article can be applied generally when modelling dynamical systems.

General information
State: Published
Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling, Division of Microbiology and Risk Assessment, National Food Institute
Authors: Philipsen, K. R. (Intern), Christiansen, L. E. (Intern), Hasman, H. (Intern), Madsen, H. (Intern)
Pages: 134-142
Publication date: 2010
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Theoretical Biology
Volume: 263
Issue number: 1
ISSN (Print): 0022-5193
Ratings:
BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.918 SNIP 0.932 CiteScore 2.16
Quantification of the spatial variability of rainfall based on a dense network of rain gauges

The spatial variability of rainfall within a single Local Area Weather Radar (LAWR) pixel of 500 x 500 m is quantified based on data from two locations. The work was motivated by the need to quantify the variability on this scale in order to provide an estimate of the uncertainty of using a single rain gauge for calibrating the LAWR. A total of nine rain gauges were used, each representing one-ninth of the 500 x 500 m area. The analysis was carried out based on a dataset obtained using tipping bucket gauges during the summer and fall of 2007 and 2008, and the results were compared with results from an earlier campaign in 2003. The fact that the 2007-2008 dataset was almost four times larger than the original dataset from 2003 motivated this extended study. Two methods were used to describe the variability: the coefficient of variation and the spatial correlation structure of the rainfall field. Despite the small area of 0.25 km(2), accumulated rainfall was found to
vary significantly within individual events with durations ranging from 5 min to 13 h. The coefficient of variation was found to range from 1-26% in the 2007-2008 dataset and in some special cases even higher. The 95% prediction interval for a given rainfall depth is estimated and can be used to address the uncertainty of using a single rain gauge to represent the rainfall within a 500 x 500 m area. (C) 2009 Elsevier B.V. All rights reserved.
Simulating the spread of Bluetongue virus – Focused on the effects of spatial distribution of cattle

General information
State: Published
Organisations: Section for Veterinary Epidemiology and public sector consultancy, Division of Veterinary Diagnostics and Research, National Veterinary Institute, Mathematical Statistics, Department of Informatics and Mathematical Modeling
Authors: Græsbøll, K. (Intern), Bødker, R. (Intern), Christiansen, L. E. (Intern), Enøe, C. (Intern), Kirkeby, C. (Intern)
Publication date: 2010
Event: Abstract from Bluetongue in the Nordic countries, Oslo, Norway.
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 263623
Publication: Research - peer-review › Journal article – Annual report year: 2010

Antibiotic resistance in Pseudomonas aeruginosa strains with increased mutation frequency due to inactivation of the DNA oxidative repair system

The chronic Pseudomonas aeruginosa infection of the lungs of cystic fibrosis (CF) patients is characterized by the biofilm mode of growth and chronic inflammation dominated by polymorphonuclear leukocytes (PMNs). A high percentage of P. aeruginosa strains show high frequencies of mutations (hypermutators [HP]). P. aeruginosa is exposed to oxygen radicals, both those generated by its own metabolism and especially those released by a large number of PMNs in response to the chronic CF lung infection. Our work therefore focused on the role of the DNA oxidative repair system in the development of HP and antibiotic resistance. We have constructed and characterized mutT, mutY, and mutM mutants in P. aeruginosa strain PAO1. The mutT and mutY mutants showed 28- and 7.5-fold increases in mutation frequencies, respectively, over that for PAO1. These mutants had more oxidative DNA damage (higher levels of 7,8-dihydro-8-oxodeoxyguanosine) than PAO1 after exposure to PMNs, and they developed resistance to antibiotics more frequently. The mechanisms of resistance were increased β-lactamase production and overexpression of the MexCD-OprJ efflux-pump. Mutations in either the mutT or the mutY gene were found in resistant HP clinical isolates from patients with CF, and complementation with wild-type genes reverted the phenotype. In conclusion, oxidative stress might be involved in the development of resistance to antibiotics. We therefore suggest the possible use of antioxidants for CF patients to prevent the development of antibiotic resistance.

General information
State: Published
Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling, Copenhagen University Hospital, University of Copenhagen
Authors: Mandsberg, L. F. (Ekstern), Ciofu, O. (Ekstern), Kirkby, N. (Ekstern), Christiansen, L. E. (Intern), Poulsen, H. E. (Ekstern), Højby, N. (Ekstern)
Pages: 2483-2491
Publication date: 2009
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 272269
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2010

Publication information
Journal: Antimicrobial Agents and Chemotherapy
Volume: 53
Issue number: 6
ISSN (Print): 0066-4804
Ratings:
BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.21 SJR 2.21 SNIP 1.312
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.322 SNIP 1.365 CiteScore 4.28
Modelling bacterial growth in rich media with a non-parametric extension to an SDE based Model

General information
State: Submitted
Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling
Authors: Philipsen, K. R. (Intern), Christiansen, L. E. (Intern), Madsen, H. (Intern)
Publication date: 2009
The effect of pH and storage on copper speciation and bacterial growth in complex growth media

In this paper we examine how the bacterial growth is influenced by the availability of copper ions in complex Mueller Hinton growth media. The data shows that the free copper concentration is seven to eight orders of magnitude lower the total copper concentration and that there seems to be a better correlation between the free copper concentration and bacterial growth, than for the total copper concentration and growth. Furthermore, it is shown that the initial pH influences the amount of free copper ions in the media and that this has a direct effect on the ability of bacterial cultures to grow. However, there still remains an effect of pH on bacterial growth which cannot be attributed to the influence of the Cu2+ concentration alone. The study also shows that the sterilization treatment can have some effect on the availability of copper ions in the media over time. Freshly autoclaved and sterile filtered media contain the same level of free copper...
ions and perform equally well in the biological assay. However, storage in the refrigerator influences the free copper contents in media, which have been autoclaved, but not in media, which were sterile filtered. Therefore, the latter method is to be recommended, when working with bacterial copper testing.

**General information**
State: Published
Organisations: Division of Microbiology and Risk Assessment, National Food Institute, Mathematical Statistics, Department of Informatics and Mathematical Modeling, University of Copenhagen
Authors: Hasman, H. (Intern), Bjerrum, M. J. (Ekstern), Christiansen, L. E. (Intern), Hansen, H. C. B. (Ekstern), Aarestrup, F. M. (Intern)
Pages: 20-24
Publication date: 2009
Main Research Area: Technical/natural sciences

**Publication information**
Journal: Journal of Microbiological Methods
Volume: 78
Issue number: 1
ISSN (Print): 0167-7012
Ratings:
BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.05 SJR 0.723 SNIP 0.8
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.816 SNIP 0.873 CiteScore 2.04
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.903 SNIP 1.037 CiteScore 2.28
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.917 SNIP 1.019 CiteScore 2.5
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.87 SNIP 1.004 CiteScore 2.32
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.9 SNIP 0.972 CiteScore 2.29
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.945 SNIP 1.05
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.993 SNIP 1.156
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.926 SNIP 1.031
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 0.942 SNIP 1.111
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.138 SNIP 1.251
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.964 SNIP 1.141
A new spatial aggregation algorithm that improves performance of spatial cluster detection

General information
State: Published
Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling, University of California at Davis
Authors: Christiansen, L. E. (Intern), Van Meter, K. (Ekstern)
Publication date: 2008
Event: Poster session presented at International Biometric Conference, Dublin, Ireland.
Main Research Area: Technical/natural sciences

A procedure to characterize geographic distributions of rare disorders in cohorts

Background Individual point data can be analyzed against an entire cohort instead of only sampled controls to accurately picture the geographic distribution of populations at risk for low prevalence diseases. Analyzed as individual points, many smaller clusters with high relative risks (RR) and low empirical p values are indistinguishable from a random distribution. When points are aggregated into areal units, small clusters may result in a larger cluster with a low RR or be lost if divided into pieces included in units of larger populations that show no increased prevalence. Previous simulation studies showed lowered validity of spatial scan tests for true clusters with low RR. Using simulations, this study explored the effects of low cluster RR and areal unit size on local area clustering test (LACT) results, proposing a procedure to improve accuracy of cohort spatial analysis for rare events. Results Our simulations demonstrated the relationship of true RR to observed RR and p values with various, randomly located, cluster shapes, areal unit sizes and scanning window shapes in a diverse population distribution. Clusters with RR

General information
State: Published
Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling, University of California at Davis
Authors: Meter, K. C. V. (Ekstern), Christiansen, L. E. (Intern), Hertz-Picciotto, I. (Ekstern), Azari, R. (Ekstern), Carpenter, T. E. (Ekstern)
Pages: 26
Publication date: 2008
Main Research Area: Technical/natural sciences

Publication information
Journal: International Journal of Health Geographics
Volume: 7
ISSN (Print): 1476-072X
Ratings:
Estimating the parameters of a stochastic differential equation model of bacterial growth

General information
State: Submitted
Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling
Authors: Christiansen, L. E. (Intern), Andersen, J. S. (Intern), Wegener, H. C. (Ekstern), Madsen, H. (Intern)
Publication date: 2008
Main Research Area: Technical/natural sciences

Publication information
Journal: Biometrics
ISSN (Print): 0006-341X
Ratings:
BFI (2018): BFI-level 2
BFI (2017): BFI-level 2
Web of Science (2017): Indexed Yes
Mathematical model for the growth of P. aeruginosa and four mutator strains in sub-MIC concentration of Ciprofloxacin

P. aeruginosa causes very critical and complicated infections, for which treatment is strongly dependent on successful antibiotic treatment. Therefore the evolution of antibiotic resistant P. aeruginosa does have serious consequences. Cystic fibrosis (CF) is characterized by the chronic P. aeruginosa lung infection. Intensive antibiotic treatment has improved the survival and clinical condition of CF patients, but development of resistance to antibiotics makes these infections difficult to treat efficiently. Ciprofloxacin is commonly used in the early and aggressive treatment. A hypothesis is that the presence of antibiotic results in selection of mutators in the lungs of CF patients, as these bacteria has a higher fitness under the presence of antibiotics. The goal of this study is to model the growth of P. aeruginosa and four different mutator strains (PA01 mutT, mutY, mutM and mutM-mutY mutants) when growing under sub-MIC Ciprofloxacin concentration (0.1 μg/ml), in order to describe the growth pattern under the presence of antibiotic. Data available for the modelling process is bioscreen measurements of the bacterial content as a function of time for each bacteria strain growing in LB media with and without the presence of Ciprofloxacin. The growth of the bacteria strains is modelled with a continuous-discrete time stochastic state space model consisting of a continuous time state equation expressed as a system of stochastic differential equations and a discrete time measurement equation. The model parameters are estimated from data using a Maximum Likelihood approach. We introduce a new expression for multiple substrate dependent growth in LB media, which is identified by a method first introducing the growth as a random walk in the model. From the bioscreen measurement we found a change in the growth pattern under the presence of Ciprofloxacin. In most cases the presence
of Ciprofloxacin resulted in a longer lag phase, a period of growth followed by a transition phase and then a second period of growth. We have developed a new mathematical model using a multi substrate approach, which will be able to describe this change in growth as a function of the Ciprofloxacin concentration. Following the determination of the growth pattern we wish to continue this study by modelling a competition experiment between PA01 and each of the four mutator strains. The goal is to determine whether the mutator strain has an advantage in an environment with sub-MIC concentrate of Ciprofloxacin.

**General information**

State: Published

Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling, University of Copenhagen

Authors: Philipsen, K. R. (Intern), Christiansen, L. E. (Intern), Madsen, H. (Intern), Mandsberg, L. F. (Ekstern)

Publication date: 2008

Event: Poster session presented at 1st ASM Conference on Antimicrobial Resistance in Zoonotic Bacteria and Foodborne Pathogens, Copenhagen, Denmark.

Main Research Area: Technical/natural sciences

Links:

http://www.asm.org/Meetings/index.asp?bid=59071

Source: orbit

Source-ID: 228082

Publication: Research - peer-review › Poster – Annual report year: 2008

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**Maximum Likelihood based comparison of the specific growth rates for P. aeruginosa and four mutator strains**

The specific growth rate for P. aeruginosa and four mutator strains mutT, mutY, mutM and mutY–mutM is estimated by a suggested Maximum Likelihood, ML, method which takes the autocorrelation of the observation into account. For each bacteria strain, six wells of optical density, OD, measurements are used for parameter estimation. The data is log-transformed such that a linear model can be applied. The transformation changes the variance structure, and hence an OD-dependent variance is implemented in the model. The autocorrelation in the data is demonstrated, and a correlation model with an exponentially decaying function of the time between observations is suggested. A model with a full covariance structure containing OD-dependent variance and an autocorrelation structure is compared to a model with variance only and with no variance or correlation implemented. It is shown that the model that best describes data is a model taking into account the full covariance structure. An inference study is made in order to determine whether the growth rate of the five bacteria strains is the same. After applying a likelihood-ratio test to models with a full covariance structure, it is concluded that the specific growth rate is the same for all bacteria strains. This study highlights the importance of carrying out an explorative examination of residuals in order to make a correct parametrization of a model including the covariance structure. The ML method is shown to be a strong tool as it enables estimation of covariance parameters along with the other model parameters and it makes way for strong statistical tools for inference studies.

**General information**

State: Published

Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling, University of Copenhagen

Authors: Philipsen, K. R. (Intern), Christiansen, L. E. (Intern), Mandsberg, L. F. (Ekstern), Ciufo, O. (Ekstern), Madsen, H. (Intern)

Pages: 551-557

Publication date: 2008

Main Research Area: Technical/natural sciences

**Publication information**

Journal: Journal of Microbiological Methods

Volume: 75

Issue number: 3

ISSN (Print): 0167-7012

Ratings:

BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.05 SJR 0.723 SNIP 0.8
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.816 SNIP 0.873 CiteScore 2.04
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Simulation Study for Transfer of Antibiotic Resistance via Mutator Subpopulation

Evolution of antibiotic resistance in bacterial populations is an increasing problem having fatal consequences for treatment of diseases. Therefore it is very important to understand this evolution. Traditionally evolution is considered to happen by single point mutations, where each mutant must have a growth advantage over the parent strain and grow to a sufficient number before a second mutation can occur. However, when multiple mutations are necessary for development of resistance, single mutations occurring with a normal mutation rate can not always explain the observed resistance. We
introduce an alternative hypothesis by which a subpopulation of mutators drives the evolution process. Resistance is acquired by a subpopulation of mutators, for which the mutation rate is much higher than the wild-type. If the resistance is located on a transferable plasmid it can subsequently be transferred to the wild-type population by conjugation. To examine whether this pathway will in fact speed up evolution, we perform a simulation study, where bacteria are simulated to grow in a chemostat environment, such as the intestine of a human. Since mutation events are stochastic processes, we model the system by a discrete Markov process with the possibility of changes in each state given by a Poisson distribution. Parameters for growth, mutation and conjugation rates used in the simulation study resemble those of E.coli with a mutator obtained with the XL1-red mutator strain having a 5000 times higher mutation rate than the wild-type. We simulate the process for 24 hours and perform 1000 repetitions, which correspond to considering 1000 people with the same initial bacterial population in the intestine. In none of the repetitions a double mutation occurs in the wild-type population, but in almost 300 cases a double mutated strain has been conjugated to the wild-type bacterial population. To confirm these results future work should include an experimental study of the hypothesis.
Using random walk in models specified by stochastic differential equations to determine the best expression for the bacterial growth rate

In this presentation we consider a new method first introduced by Kristensen et al. [1] to improve the model for bacterial growth. Traditionally the substrate dependent growth rate \( \mu(S) \) is modeled using the Monod expression, however it fails to describe the growth of bacteria in rich media. For \( P. \) aeruginosa we observe a growth pattern far from Monod growth. Therefore a reformulation of the growth expression is necessary. Without any pre-knowledge about the functional dependence between the growth rate and the substrate content and with only limited experimental resources necessary, the proposed method allows us to develop a new expression for the growth rate. The method is based on the stochastic continuous-discrete time state-space model, with a continuous-time state equation (a stochastic differential equation, SDE) combined with a discrete-time measurement equation. In our study the SDE contains two state variables, the bacterial and substrate densities. To improve the growth model we initially allow the growth rate \( \mu(S) \) to vary as a random walk, i.e. we reformulate the SDE model to include \( \mu(S) \) as an extra state variable which change is described by the Wiener process. We use data from Optical Density bioscreen measurements of \( P. \) aeruginosa to perform a Maximum Likelihood estimation of the model parameters and subsequently obtain a smoothing estimate for the model state variables by means of a nonlinear smoothing algorithm based on the extended Kalman filter, using an implementation described by Kristensen et. al [2]. The resulting time series allows us graphically to inspect the functional dependence of the growth rate on the substrate content. From the method described above we find three new plausible expressions for \( \mu(S) \). Therefore we apply the likelihood-ratio test to compare the expressions which are nested. Additional inference concerning the best expression is performed by considering the incremental variance \( \sigma^2 \) of the Wiener process. The best expression is found to be \( S(a/(1 + b(1 − S)^2) + c) \) with \( \sigma^2 = 3.46 \cdot 10^{-4} \), which is one order of magnitude lower than the incremental variance for the Monod expression. Thus, the method was applied to successfully determine a significant better expression for the substrate dependent growth expression, and we find the method generally applicable for model development. References [1] Kristensen NR, Madsen H, Jørgensen, SB (2004) A method for systematic improvement of stochastic grey-box models. Computers and Chemical Engineering 28:1431-1449. [2] Kristensen NR, Madsen H, Jørgensen, SB (2004) Parameter estimation in stochastic greybox models. Automatica 40:225-237.
Improvement and automation of tools for short term wind power forecasting

General information
State: Published
Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling
Authors: Nielsen, H. A. (Intern), Pinson, P. (Intern), Christiansen, L. E. (Intern), Nielsen, T. S. (Intern), Madsen, H. (Intern), Badger, J. (Ekstern), Giebel, G. (Ekstern), Ravn, H. F. (Ekstern)
Publication date: 2007

Host publication information
Title of host publication: EWEC 2007, 'European Wind Energy Conference', Scientific Track, Milan, Italy
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 200241
Publication: Research - peer-review › Article in proceedings – Annual report year: 2007

Intelligent wind power prediction systems: Final report

General information
State: Published
Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling, Meteorology, Wind Energy Division, Risø National Laboratory for Sustainable Energy
Authors: Nielsen, H. A. (Intern), Pinson, P. (Intern), Nielsen, T. S. (Intern), Christiansen, L. E. (Intern), Madsen, H. (Intern), Giebel, G. (Intern), Badger, J. (Intern), Larsen, X. G. (Intern), Ravn, H. V. (Intern), Tøfting, J. (Ekstern), Voulund, L. (Ekstern)
Publication date: 2007

Publication information
Publisher: Informatics and Mathematical Modelling, Technical University of Denmark, DTU
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions: tr07_14.pdf
Links:
http://www2.imm.dtu.dk/pubdb/views/publication_details.php?id=5328
Source: orbit
Source-ID: 201571
Publication: Research › Report – Annual report year: 2007

Spatial scan statistics using elliptic windows
The spatial scan statistic is widely used to search for clusters in epidemiologic data. This paper shows that the usually applied elimination of secondary clusters as implemented in SatScan is sensitive to smooth changes in the shape of the clusters. We present an algorithm for generation of set of confocal elliptic windows and propose a new way to present the information when a spatial point process is considered. This method gives smooth changes for smooth expansions of the set of clusters. A simulation study is used to show how the elliptic windows outperforms the usual circular windows. The proposed method for graphical representation of the information in a set of clusters contain more information than just presenting non-overlapping clusters. The authors suggest that more than one graphical representation of a set of clusters should be used to easily extract more information and to avoid pitfalls of the selected method.

General information
State: Published
Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling, National Food Institute
Authors: Christiansen, L. E. (Intern), Andersen, J. S. (Intern), Wegener, H. C. (Intern), Madsen, H. (Intern)
Publication date: 2007
Event: Abstract from 1st Nordic-Baltic Biometric Conference 2007, Foulum, Denmark.
Stochastic differential equations used to model conjugation

Stochastic differential equations (SDEs) are used to model horizontal transfer of antibiotic resistance by conjugation. The model describes the concentration of donor, recipient, transconjugants and substrate. The strength of the SDE model over the traditional ODE models is that the noise can be split into measurement noise and system noise. The system noise is used to compensate for those biological processes not explicitly described by the model. Many authors model conjugation by a simple mass action model first proposed by Levin et al. (1979). Also Michaelis-Menten dependence on the recipient concentration has been used to mathematically describe conjugation (Andrup et al. 1998). We find that it is important to include substrate depletion to model conjugation for a system with exhaustible media and implement the substrate dependence as a Michaelis-Menten expression. This is supported by an experiment conducted with E. faecium. In addition, we suggest that a 3rd order time-delay must be included in the model to account for the delay before a newly conjugated plasmid is expressed. A ML estimate of the parameters based on experimental data is found using the software CTSM. The conjugation rate is estimated to $1.4 \times 10^{-9} \pm 0.38 \times 10^{-9}$ 1/h.

Spatial scan statistics using elliptic windows

The spatial scan statistic is widely used to search for clusters. This article shows that the usually applied elimination of secondary clusters as implemented in SatScan is sensitive to smooth changes in the shape of the clusters. We present an algorithm for generation of a set of confocal elliptic windows and propose a new way to present the information when a spatial point process is considered. This method gives smooth changes for smooth expansions of the set of clusters. A simulation study is used to show how the elliptic windows outperforms the usual circular windows. The proposed method for graphical representation of the information in a set of clusters contain more information than just presenting nonoverlapping clusters. We suggest that more than one graphical representation of a set of clusters should be used to easily extract more information and to avoid pitfalls of the selected method.
Comparing effectiveness of regional and circular intervention zones in case of a foot-and-mouth disease outbreak

In case of a foot-and-mouth disease (FMD) or other exotic disease outbreak, surveillance zones and infected areas are conventionally created as circles with their centroids at the known infected premises. Given the availability of geographic information systems (GIS), it is no longer difficult to identify relevant zonal or area boundaries. However, it is not clear if from a disease control standpoint this is the optimal strategy. An alternative approach is to define regions using ZIP codes, counties, states, major roads, or natural barriers. We used an updated version of an epidemic simulation model originally applied to a 3-county area in California and the available information about the state’s livestock demographics to compare these two control strategies. The comparisons included the simulated duration of outbreaks, number of herds and animals affected, and manpower issues. These findings will be useful for state, national and international regulatory veterinarians in designing optimal disease control programs.

General information
State: Published
Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling, University of California at Davis
Authors: Christiansen, L. E. (Intern), Dickey, B. F. (Ekstem), Carpenter, T. E. (Ekstem)
Publication date: 2005
Event: Abstract from Conference of Research of Workers in Animal Diseases, St. Louis, US,
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 191388
Publication: Research - peer-review › Journal article – Annual report year: 2006
Effects of Climate on Incidence of Campylobacter spp. in Humans and Prevalence in Broiler Flocks in Denmark

Campylobacter infections are increasing and pose a serious public health problem in Denmark. Infections in humans and broiler flocks show similar seasonality, suggesting that climate may play a role in infection. We examined the effects of temperature, precipitation, relative humidity, and hours of sunlight on Campylobacter incidence in humans and broiler flocks by using lag dependence functions, locally fitted linear models, and cross validation methods. For humans, the best model included average temperature and sunlight 4 weeks prior to infection; the maximum temperature lagged at 4 weeks was the best single predictor. For broilers, the average and maximum temperatures 3 weeks prior to slaughter gave the best estimate; the average temperature lagged at 3 weeks was the best single predictor. The combined effects of temperature and sunlight or the combined effects of temperature and relative humidity predicted the incidence in humans equally well. For broiler flock incidence these factors explained considerably less. Future research should focus on elements within the broiler environment that may be affected by climate, as well as the interaction of microclimatic factors on and around broiler farms. There is a need to quantify the contribution of broilers as a source of campylobacteriosis in humans and to further examine the effect of temperature on human incidence after this contribution is accounted for.

Investigations should be conducted into food consumption and preparation practices and poultry sales that may vary by season.

General information
State: Published
Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling, Communications and Management Secretariat, National Food Institute
Authors: Patrick, M. E. (Ekstern), Christiansen, L. E. (Intern), Wainø, M. (Ekstern), Ethelberg, S. (Ekstern), Madsen, H. (Intern), Wegener, H. C. (Intern)
Pages: 7474-7480
Publication date: 2004
Main Research Area: Technical/natural sciences

Publication information
Journal: Applied and Environmental Microbiology
Volume: 70
Issue number: 12
ISSN (Print): 0099-2240
Ratings:
BFI (2018): BFI-level 2
BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 4.08
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.891 SNIP 1.308 CiteScore 4.14
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.857 SNIP 1.384 CiteScore 4.02
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.899 SNIP 1.414 CiteScore 4.25
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.975 SNIP 1.429 CiteScore 4.29
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 1.914 SNIP 1.455 CiteScore 4.12
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 1.887 SNIP 1.436
Nonlinear time series analysis of zoonoses

General information
State: Published
Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling
Authors: Christiansen, L. E. (Intern), Madsen, H. (Intern)
Publication date: 2004

Publication information
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions: imm3361.ps
Links:
Source: orbit
Source-ID: 154838
Publication: Research › Ph.D. thesis – Annual report year: 2004

Spatial Scan Statistic: Selecting clusters and generating elliptic clusters
The spatial scan statistic is widely used to search for clusters. This paper shows that the usually applied elimination of overlapping clusters to find secondary clusters is sensitive to smooth changes in the shape of the clusters. We present an algorithm for generation of set of confocal elliptic clusters. In addition, we propose a new way to present the information in a given set of clusters based on the significance of the clusters.

General information
State: Published
Climate as a predictor of prevalence of campylobacter spp. in humans and broilers in Denmark

General information
State: Published
Organisations: Mathematical Statistics, Department of Informatics and Mathematical Modeling
Authors: Christiansen, L. E. (Intern), Evans, M. C. (Ekstern), Waino, M. (Ekstern), Ethelberg, S. (Ekstern), Madsen, H. (Intern), Wegener, H. C. (Ekstern)
Publication date: 2003

Host publication information
Title of host publication: Conference on Campylobacter, Helecobacter and Related Organisms, Aarhus, Denmark, October, 01/01/2003
Main Research Area: Technical/natural sciences
Links:
Source: orbit
Source-ID: 58511
Publication: Research - peer-review › Article in proceedings – Annual report year: 2003

Nonlinear Characteristics of Randomly Excited Transonic Flutter

The paper describes the effects of random external excitations on the onset and dynamical characteristics of transonic flutter (i.e. large-amplitude, self-sustained oscillations) for a high aspect ratio wing. Wind tunnel experiments performed at the National Aerospace Laboratory (NAL) in Japan have shown that the self-sustained oscillations arise in a subcritical Hopf bifurcation. However, analysis of the experimental data also reveals that this bifurcation is modified in various ways. We present an outline of the construction of a 6 DOF model of the aeroelastic behavior of the wing structure. When this model is extended by the introduction of nonlinear terms, it can reproduce the subcritical Hopf bifurcation. We hereafter consider the effects of subjecting simplified versions of the model to random external excitations representing the fluctuations present in the airflow. These models can reproduce several of the experimentally observed modifications of the flutter transition. In particular, the models display the characteristic phenomena of coherence resonance.

General information
State: Published
Organisations: Department of Physics, Department of Informatics and Mathematical Modeling
Authors: Christiansen, L. E. (Intern), Lehn-Schiøler, T. (Intern), Mosekilde, E. (Intern), Granasy, P. (Ekstern), Matsushita, H. (Ekstern)
Pages: 385-405
Publication date: 2002
Main Research Area: Technical/natural sciences

Publication information
Journal: Mathematics and Computers in Simulation
Volume: 58
Issue number: 4-6
ISSN (Print): 0378-4754
Ratings:
BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Nonlinear dynamics approach of modeling the bifurcation for aircraft wing flutter in transonic speed

The procedure of obtaining the two-degrees-of-freedom, finite dimensional, nonlinear mathematical model, which models the nonlinear features of aircraft flutter in transonic speed is reported. The model enables to explain every feature of the transonic flutter data of the wind tunnel tests conducted at National Aerospace Laboratory in Japan for a high aspect ratio wing. It explains the nonlinear features of the transonic flutter such as the subcritical Hopf bifurcation of a limit cycle oscillation (LCO), a saddle-node bifurcation, and an unstable limit cycle as well as a normal (linear) flutter condition with its linear pan. At a final procedure of improve a quantitative matching with the test data, the continuation method for analyzing the bifurcation is extensively used.
The Dynamics of a Railway Vehicle on a Disturbed Track: Modelling of lateral irregularities

This work studies a mathematical model of a bogie, the aim being to investigate the correlation between the lateral motion of the bogie and lateral irregularities of the track that the bogie is running along. When modelling the wheel-rail forces real wheel and rail profiles are used. One of the main differences between this work and previous ones is that the vertical degrees of freedom are included making the model very realistic as this allows a dynamic calculation of the penetration depth in the contact area.

In chapter two the model of the bogie is described, this is followed by a chapter describing how the wheel-rail interaction is modelled. The fourth chapter gives a presentation of the numerical algorithms used in this work.

The fifth chapter presents the results obtained during this work, it begins with an brief investigation of the dynamics when running on a straight track. The second section introduces some statistical measures and treats centerline irregularities when running with a fixed speed of 30 m/s. The following section investigates the behaviour of the model when the track possesses gauge irregularities. The fourth and fifth sections describe the changes observed when changing the velocity of the railway vehicle and the phase between the sinusoidal irregularities of the rails. In the final section the eigenfrequencies of the bogie are found and the most important modes are described. Chapter six is a discussion of the obtained results, and these are related to the possibility of measuring track irregularities using accelerometers mounted on the bogie. Finally, some appendixes are included bringing some details of the derivations related to the wheel-rail interaction and details about the used pro files.
Period: 01/12/2017 → 30/11/2020
Number of participants: 4
Phd Student:
Bjerregård, Mathias Blicher (Intern)
Supervisor:
Borup, Morten (Intern)
Niyato, Dusit (Ekstern)
Main Supervisor:
Christiansen, Lasse Engbo (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)
Project: PhD

Stochastic grey-box models for marine ecosystems
Department of Applied Mathematics and Computer Science
Period: 01/08/2017 → 31/07/2020
Number of participants: 4
Phd Student:
Moazzami, Hamidreza (Intern)
Supervisor:
Carstensen, Niels Jacob (Intern)
Møller, Jan Kloppenborg (Intern)
Main Supervisor:
Christiansen, Lasse Engbo (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Samfinansieret - Andet
Project: PhD

Development of a herd- and cow-specific decision support tool for control of mastitis
National Veterinary Institute
Period: 01/07/2015 → 30/06/2018
Number of participants: 5
Phd Student:
Gussmann, Maya Katrin (Intern)
Supervisor:
Christiansen, Lasse Engbo (Intern)
Nielsen, Søren Saxmose (Ekstern)
Toft, Nils (Intern)
Main Supervisor:
Hisham Beshara Halasa, Tariq (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Samfinansieret - Andet
Project: PhD

Benchmarking and extending models of real estate price prediction, under financial regulation requirements
Department of Applied Mathematics and Computer Science
Period: 01/08/2014 → 22/02/2016
Number of participants: 5
Phd Student:
Katossky, Arthur (Intern)
Supervisor:
Nielsen, Mads Stenbo (Ekstern)
Rasmussen, Kourosh Marjani (Intern)
Thygesen, Uffe Høgsbro (Intern)
Main Supervisor:
Christiansen, Lasse Engbo (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: ErhvervsPhD-ordningen VTU
Project: PhD

Scenario Optimization Models for Individual Life-cycle Asset Allocation
Department of Management Engineering
Period: 15/12/2013 → 20/04/2017
Number of participants: 6
Phd Student:
Bjerring, Thomas Trier (Intern)
Supervisor:
Weissensteiner, Alex (Intern)
Main Supervisor:
Rasmussen, Kourosh Marjani (Intern)
Examiner:
Christiansen, Lasse Engbo (Intern)
Hanke, Michael (Ekstern)
Poulsen, Rolf (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)
Project: PhD

iCull
Herd-specific economic decision tool for farmers.
National Veterinary Institute
Section for Epidemiology
Section for Veterinary Epidemiology and public sector consultancy
Department of Applied Mathematics and Computer Science
Dynamical Systems
Period: 01/11/2013 → 31/10/2015
Number of participants: 6
Acronym: iCull
Project ID: 23176
Project participant:
Kirkeby, Carsten Thure (Intern)
Græsbøll, Kaare (Intern)
Project Manager, organisational:
Toft, Nils (Intern)
Project Manager, academic:
Hisham Beshara Halasa, Tariq (Intern)
Christiansen, Lasse Engbo (Intern)
Saxmose, Søren (Ekstern)

Relations
Activities:
Simulation modelling of paratuberculosis within herds
iCULL – A herd-specific tool for financial evaluation of the impact of paratuberculosis
14th international symposium on veterinary epidemiology and economics
Undersøgelse af sammenhænge mellem sundhed, velfærd og antibiotikaforbrug hos danske husdyr

National Veterinary Institute
Period: 15/12/2011 → 17/11/2016
Number of participants: 8
Phd Student:
Fertner, Mette Ely (Intern)
Supervisor:
Boklund, Anette (Intern)
Christiansen, Lasse Engbo (Intern)
Stege, Helle (Ekstern)
Main Supervisor:
Toft, Niels (Intern)
Examiner:
Jensen, Vibeke Frøkjær (Intern)
Dewulf, Jeroen (Ekstern)
Pedersen, Ken Steen (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)

Relations
Publications:
Associations between health, management and antimicrobial use in Danish swine and veal calves
Project: PhD

Predictive food microbiology - new tools for risk assessment and dairy product development

National Food Institute
Period: 15/08/2011 → 05/11/2014
Number of participants: 6
Phd Student:
Østergaard, Nina Bjerre (Intern)
Supervisor:
Christiansen, Lasse Engbo (Intern)
Main Supervisor:
Dalgaard, Paw (Intern)
Examiner:
Nauta, Maarten (Intern)
Larsen, Marianne Halberg (Ekstern)
Skandamis, Panagiotis N. (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU) Samf.
Project: PhD

Analysis of Pattern Formation on Networks

Department of Applied Mathematics and Computer Science
Period: 01/08/2011 → 21/11/2014
Number of participants: 5
Phd Student:
Marschler, Christian (Intern)
Main Supervisor:
Starke, Jens (Intern)
Examiner:
Christiansen, Lasse Engbo (Intern)
Barkley, Dwight (Ekstern)
Sugiyama, Yuki (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU) Samf.
Project: PhD

Non-stationary time series models of hydrologic extremes
Department of Environmental Engineering
Period: 01/05/2010 → 29/04/2015
Number of participants: 7
Phd Student:
Gregersen, Ida Bülow (Intern)
Supervisor:
Madsen, Henrik (Intern)
Rosbjerg, Dan (Intern)
Main Supervisor:
Ambjerg-Nielsen, Karsten (Intern)
Examiner:
Christiansen, Lasse Engbo (Intern)
Berndtsson, Ronny (Ekstern)
Rauch, Wolfgang (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: DTU, Samfinansiering
Project: PhD

Modelling spread of Bluetongue and other vector borne diseases in Denmark and evakuation of intervention strategies
Department of Informatics and Mathematical Modeling
Period: 01/01/2010 → 22/03/2013
Number of participants: 6
Phd Student:
Græsbøll, Kaare (Intern)
Supervisor:
Enøe, Claes (Intern)
Main Supervisor:
Christiansen, Lasse Engbo (Intern)
Examiner:
Thygesen, Uffe Høgsbro (Intern)
Konradsen, Flemming (Ekstern)
de Koeijer, Aline A. (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: 1/3 DTU-stip, 2/3 FUR/andet
Project: PhD

Stokastisk dynamisk modellering til kort-tidsregulering af glukose/insulin-metabolismen
Department of Informatics and Mathematical Modeling
Period: 01/06/2009 → 12/12/2013
Number of participants: 6
Phd Student:
Duun-Henriksen, Anne Katrine (Intern)
Supervisor:
Jensen, Peter Ruhdal (Intern)
Main Supervisor:
Madsen, Henrik (Intern)
Examiner:
Christiansen, Lasse Engbo (Intern)
Andreasen, Steen (Ekstern)
Gabrielsson, Johan (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Forskningsrådsfinansiering
Project: PhD

Models for efficient integration of solar energy
Department of Informatics and Mathematical Modeling
Period: 01/10/2008 → 24/08/2012
Number of participants: 6
PhD Student:
Bacher, Peder (Intern)
Supervisor:
Nielsen, Henrik Aalborg (Intern)
Main Supervisor:
Madsen, Henrik (Intern)
Examiner:
Christiansen, Lasse Engbo (Intern)
Palsson, Olafur Petur (Intern)
Taboada, Maria Jose Jimenez (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU) Samf.
Project: PhD

Optimizing the control of foot-and-mouth disease in Denmark by simulation
Section for Veterinary Epidemiology and public sector consultancy
Division of Veterinary Diagnostics and Research
National Veterinary Institute
DTU Data Analysis
Department of Informatics and Mathematical Modeling
University of Copenhagen
University of California at Davis
Danish Veterinary and Food Administration
United States Department of Agriculture
Danish Meat Association
Danish Cattle Federation
Period: 01/01/2008 → 31/12/2011
Number of participants: 12
Project ID: 22314
Contact person:
Christiansen, Lasse Engbo (Intern)
Lund, Mogens (Ekstern)
Willeberg, Preben (Ekstern)
Evolution and adaptation of antimicrobial resistance in bacterial populations

It is generally believed that evolution of resistance occurs as a series of random single point mutations. However, we believe that emergence of new characters occurs as multiple mutations probably in sub-populations as a consequence of fluctuating stresses caused by lethal substances, such as antibiotics, and that these populations are so limited in size that the selection process is greatly affected by chance (stochastic). We will combine expertise in bacteriology, molecular biology, microbial epidemiology, mathematical modelling and phylogeny to study the evolution and adaptation of antimicrobial resistance in bacterial populations. Focus will be on resistance in staphylococci and Pseudomonas because of the major clinical problems with resistance in these bacteria. The results are expected to be useful in predicting appearance of new antimicrobial resistance problems, guide intervention strategies for the future, lead to new treatment strategies and possible also lead to industrial development of new biotechnologies based on evolutionary concepts.

Division of Microbiology and Risk Assessment

National Food Institute

Department of Informatics and Mathematical Modeling

University of Copenhagen

Period: 30/04/2006 → 31/03/2010

Number of participants: 11

Project participant:

Ingmer, Hanne (Ekstern)

Christensen, Henrik (Ekstern)
Antigiotika anvendelse og tidlig og rumlig spredning af antibiotikaresistens

Department of Informatics and Mathematical Modeling
Period: 15/08/2001 → 27/04/2005
Number of participants: 7
Phd Student:
Christiansen, Lasse Engbo (Intern)
Supervisor:
Andersen, Jens Strodl (Intern)
Main Supervisor:
Madsen, Henrik (Intern)
Examiner:
Thyregod, Poul (Intern)
Agger, Jens (Ekstern)
Guttorp, Peter (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: DTU-lønnet stipendie
Project: PhD

Minimizing antibiotic resistance development MINIRESIST
The overall objective is to minimize resistance development in the intestinal flora of pigs following antibiotic treatment. The project has the following specific objectives: - To investigate the influence of antibiotic treatment regimes on the efficacy of treatment, the development and spread of resistant bacteria and on the load of resistant bacteria in the intestine at the point of slaughter. - To investigate the underlying kinetics of selection of resistant bacteria and the spread of resistance genes between bacteria in the intestine. - To investigate the association between the load of resistant bacteria in the intestine at the time of slaughter and the load on the carcasses after slaughter. - To develop and validate a comprehensive mathematical model for resistance development associated with the use of antibiotics in pig production. - To formulate improved treatment regimes using the mathematical model.

Division of Veterinary Diagnostics and Research
National Veterinary Institute
University of Copenhagen
Danish Agriculture and Food Council
University of Glasgow
Institute of Farm Animal Genetics
Period: 11/01/2001 → 14/12/2013
Number of participants: 13
Acronym: MINIRESIST
Project ID: 22481
Project participant:
Hansen, Axel Jacob Kornerup (Ekstern)
Guardabassi, Luca (Ekstern)
Nielsen, Jens Peter (Ekstern)
Nielsen, Søren Saxmose (Ekstern)
Toft, Nils (Ekstern)
Angen, Øystein (Intern)
Madsen, Henrik (Intern)
Christiansen, Lasse Engbo (Intern)
Bækbo, Poul (Ekstern)
Andreasen, Margit (Ekstern)
Matthews, Louise (Ekstern)
Schwarz, Stefan (Ekstern)
Project Manager, organisational:
Olsen, John Elmerdahl (Ekstern)

Financing sources
Source: Forskningsprojekter - Andre ministerier og styrelser
Name of research programme: Forskningsprojekter - Andre ministerier og styrelser
Amount: 3,726,720.00 Danish Kroner
Project

Activities:

**Effects of Climate on Prevalence of Campylobacter spp. in Humans and Broilers in Denmark**

Period: 1 Jan 2002 → …

Lasse Engbo Christiansen (Speaker)
National Food Institute
Division of Microbiology and Risk Assessment

Description
Place: International Conference on Emerging Infectious Diseases, Atlanta

Related external organisation

Unknown external organisation
Activity: Talks and presentations › Conference presentations