Decoding network dynamics in cancer

Biological systems are composed of highly dynamic and interconnected molecular networks that drive biological decision processes. The goal of network biology is to describe, quantify and predict the information flow and functional behaviour of living systems in a formal language and with an accuracy that parallels our characterisation of other physical systems such as Jumbo-jets. Decades of targeted molecular and biological studies have led to numerous pathway models of developmental and disease related processes. However, so far no global models have been derived from pathways, capable of predicting cellular trajectories in time, space or disease. The development of high-throughput methodologies has further enhanced our ability to obtain quantitative genomic, proteomic and phenotypic readouts for many genes/proteins simultaneously. Here, I will discuss how it is now possible to derive network models through computational integration of systematic, large-scale, high-dimensional quantitative data sets. I will review our latest advances in methods for exploring phosphorylation networks. In particular I will discuss how the combination of quantitative mass-spectrometry, systems-genetics and computational algorithms (NetworKIN [Linding et al. Cell 2007] and NetPhorest [Miller et al. Science Signaling 2008]) made it possible for us to derive systems-level models of JNK and EphR signalling networks [Bakal et al. Science 2008, Jørgensen et al. Science 2009]. I shall discuss work we have done in comparative phoso-proteomics and network evolution [Tan et al. Science Signaling 2009, Tan et al. Science 2009, Tan et al. Science 2011]. Finally, I will discuss our most recent work in analyzing genomic sequencing data from NGS studies and how we have developed new powerful algorithms to predict the impact of disease mutations on cellular signaling networks [Creixell et al. Nature Biotechnology 2012, Erler & Linding Cell 2012, Horn et al. Nature Methods 2014].