Talk abstracts for Monday 28th October

Becca Asquith: The "stemness" of immune memory

Our immune system remembers previously encountered pathogens and mounts a quicker, more efficient response upon meeting the same pathogen for a second time. How this immune memory is maintained for decades is unknown. It has been hypothesised that there is a dedicated population of stem cells that maintain memory. A recently identified population, named TSCM cells, is a leading candidate for this stem cell-like population. Whether TSCM cells have the dynamic characteristics of stem cells has never been addressed in humans. We use mathematical modelling of experimental data from healthy human volunteers to address this question.

Patrick Kemmeren: Understanding regulatory systems and mechanisms of genetic interactions by exploiting expression profiles of large scale gene deletions

To understand regulatory systems, it is useful to systematically determine how individual genes contribute to the expression of all other genes. We have therefore monitored genome-wide mRNA expression for individual deletions of one-quarter of yeast genes. The resulting genetic perturbations reflect the architecture of protein complexes and pathways and can be exploited to investigate regulatory systems properties. Systematic classification of transcription factors shows a high abundance of repressors, suggesting that chromatin is not as restrictive as previously assumed. By including gene expression profiles of double deletions, we could also investigate genetic interactions, a phenomenon where combinations of mutations lead to unexpected effects. Understanding mechanisms of genetic interactions is important for deciphering pathway architecture as well as understanding the relationship between genetic variation and disease. To decipher potential mechanisms we have employed modelling approaches using Boolean networks and Petri Net modeling where genes are represented as nodes and relationships between genes as edges. This allowed over 9 million possible models to be enumerated and exposed that a quantitative edge difference is a strict requirement to explain inversion, a previously uncharacterized genetic interaction pattern. Taken together, these examples show how systematic investigation and modelling of gene expression profiles of individual single and double deletions can increase our understanding of regulatory systems.

Andela Šarić: How to build a biological nanomachine

The molecular machinery of life is largely created via self-organisation of individual molecules into functional assemblies. Such processes are multi-scale in nature and constantly driven far from thermodynamic equilibrium. Our group develops minimal coarse-grained computer models to help understand how the assembly of a large number of macromolecules results in a functional nanomachine.

Here I will discuss the physical mechanisms behind two key biological nanomachines that operate via protein assembly – active elastic ESCRT-III filaments that remodel cell membranes and split cells in two, and bacterial mechanisensitive protein channels that convert mechanical signals into chemical. I will discuss the model development, simulation results, and the mapping of the simulation data to in vivo experiments. Beyond their biological context, our findings can also guide the design of artificial structures that are able to perform work at the nanoscale.

Dora Tang: Bottom up synthetic cellularity

Living cells are well equipped in exploiting a large number of out of equilibrium processes to support life. A complete understanding of these mechanisms is still in its infancy due to the complexity and number of the individual components involved in the reactions. These reactions are spatially localized within membrane bound or membrane less compartments.

Creating artificial, cell-like structures which have the features of compartmentalization and the ability to contain reactions is an important route to designing, building and engineering synthetic cellular systems with specific complexity and function. This bottom up approach allows excellent control over the components and represents an interesting alternative to generating cellular models.

In this talk I will discuss strategies for the design and synthesis of membrane bound and membrane free compartments such as lipid vesicles, proteinosomes and coacervates and describe how these compartments may be used as platforms for implementing dynamical behaviours including: enzyme catalysis, intercellular communication or autocatalysis.

Boyan Yordanov: TBA

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