Tuesday Minisymposium

Organisers: Buttenschoen & Fletcher

Steffen Rulands

Max Planck Institute

"Setting up the epigenome: a collective phenomenon"

Methods from single-cell multi-omics allow measuring several layers of regulation along the one- dimensional sequence of the DNA. The biological function of these processes relies, however, on emergent processes in the three-dimensional space of the nucleus, such as droplet formation through phase sepa- ration. How can measurements along the sequence of the DNA be translated into an understanding of emergent dynamics in nuclear space? Here, we combine single-cell NMT-sequencing experiments with a theoretical and computational approach to rigorously map measurements along the DNA sequence to a description of the emergent spatial dynamics in the nucleus. Drawing on scNMT-seq experiments in vitro and in vivo we demonstrate our approach in the context of early development. We show how epigenetic modifications of the DNA, DNA methylation, are established through the interplay between chemical and topological modifications of the DNA, leading to the formation of condensates of methylated DNA in the nucleus. Using this theoretical framework, we finally identify epigenetic processes that precede lineage decisions in the early embryo. Our work sheds new light on epigenetic mechanisms involved in cellular decision making. It also provides a general framework of how mechanistic insights into the spatio-temporal processes governing cell-fate decisions can be gained by the combination of methods from single-cell multi-genomics, computational biology and theoretical physics.

Alessandra Bonfanti

University of Cambridge

"Characterising the rheology of soft tissues using Fractional Viscoelastic models"

When subjected to external mechanical loading, many biological materials, such as ligaments, lung tissue, endothelial cells, or collagen fibrils, exhibit a viscoelastic power-law behaviour. Using standard viscoelastic models involving combinations of spring and dashpot elements to capture this behaviour oversimplifies the response; this limits our ability to adequately quantify the characteristics of these materials. Alternatively, empirical expressions designed to fit the power-law behaviour may provide effective means to describe experimental measurements, but the use of such ad-hoc models without a proper constitutive relationship limits the scope of the measurements and restricts their predictive capability. Fractional calculus provides a convenient framework to accurately capture power-law behaviours. Various empirical expressions introduced to fit experimental data can be derived or approximated with simple fractional models, often using fewer parameters. Furthermore, this approach seems to be well suited to extract material properties. As we demonstrated in the context of single cells and simple tissues, fitting a model on one set of experiments, can be used to predict the response of the same material to a broad range of external stimuli. Furthermore, using consistent models accross various experimental measurement methods enables us to compare material parameters that could not be easily compared otherwise. This allows us to shed new light on behaviour previously reported in the literature. Fractional calculus is a niche area of mathematics that has been available for a long time in the literature. It has to date attracted limited attention in the biological field, or any other area due to the mathematical complexity. To promote the use of such generalised fractional viscoelastic models, we provide an open source library RHEOS for numerical analysis of experimental data. The occurrence of such power-law behaviour also in non-living tissues, e.g. gels, casein, plants; implies that fractional viscoelastic models can have a great impact on.

Mathias Sonja

Uppsala University

"Impact of force function formulations on the numerical simulation of center-based models"

Center-based models are a framework for the computational study of multicellular systems with widespread use in cancer modeling and computational developmental biology. At the core of these models are the numerical scheme used to update cell positions and the force functions that encode the pairwise mechanical interactions of cells. For the latter there are multiple choices that could potentially affect both the biological behavior captured, and the robustness and efficiency of simulation. For example, available open-source software implementations of center-based models rely on different force functions for their default behavior and it is not straightforward for a modeler to know if these are interchangeable. Our study addresses this problem and contributes to the understanding of the potential and limitations of three popular force functions from a numerical perspective. We show empirically that choosing the force parameters such that the relaxation time for two cells after cell division is consistent between the different force functions results in good agreement of the population radius of a growing monolayer. Furthermore, we report that numerical stability is not sufficient to prevent unphysical cell trajectories following cell division, and consequently, that too large time steps can cause geometrical differences at the population level. We illustrate that the different force functions show varying sensitivity to this issue.

Clinton Durney

UBC

"Quantifying cellular contributions to salivary gland tubulogenesis"

Epithelial cells organize themselves into tubes for the necessary functions of gas and nutrient transport, and the production and secretion of hormones and enzymes. The tubes of the Drosophila salivary gland result from the organization and collective motion of a flat sheet of polarized epithelial cells through a budding process. Through orchestrated cell movements and cell rearrangements, the nascent tube begins to form. In this talk, we develop a novel 3D-vertex model that allows for the investigation and quantification of the role that cellular mechanics and cellular rearrangements play during this vital morphogenetic process. The novel 3D model is able to quantify cell mechanical behavior and analyze the effect of different forces during invagination. Using this biophysical model, we investigate how patterning of forces on the apical surface cause cell shape changes that lead to invagination. Specifically, we investigate the roles of apicomedial induced cellular constriction, junctional actomyosin, a supracellular actomyosin cable and cellular intercalations have during gland morphogenesis.