Graduate School Event

# Thesis Defense: Effect propagation in biological networks

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Host: Lisa Bugnet

This thesis comprises two separate pieces of work, both of which revolve around the importance of interaction networks for biological function and how we can utilise them in mathematical modelling to deepen our understanding of biological systems.In Part I, we focus on large intracellular networks of interacting genes, introducing a method for predicting gene expression levels by integrating information about genotype and gene regulatory network topology. The novelty lies in combining classical statistical genomics approaches with the knowledge of regulatory networks from systems biology, thereby creating a model which is not only predictive but also interpretable. The broader goal of developing such interpretable predictive models is to understand the biological mechanisms underlying complex traits, including diseases. Complex traits are encoded by hundreds to thousands of genetic variants all across the genome, making it challenging to uncover their causal biological mechanisms. Simultaneously, complex trait predictions by purely statistical models are hugely overparametrised, posing technical challenges in statistical inference. Structuring predictive models by existing biological knowledge addresses both these challenges. Our Quantitative Omnigenic Model (QOM) is a first step in this direction: the QOM has hundreds of times fewer parameters than classical statistical genomics models, while its predictive performance remains comparable to that of standard methods. Simultaneously, the QOM extracts candidate causal and quantitative chains of effect propagation through the regulatory network for every individual gene, making it interpretable.In Part II, we study smaller networks of cell-cell interactions in the pancreatic islets of Langerhans, which release hormones that regulate blood glucose levels. In collaboration with the experimental physiology group of Prof. Rupnik at the Medical University of Vienna, we analyse the strong synchronous behaviour of pancreatic cells observed in experiments. These include waves of activity spreading across the islet on the timescale of 1 second, as well as long pulses on the timescale of several minutes. This collective behaviour can be observed thanks to our collaborators' novel approach of imaging intact pancreatic slices rather than isolated islets or islet cells, as is a common practice in the field. Combined with quantitative analysis and biophysical modelling, this presents a unique opportunity to address systems-level questions. First, in chapter 8 we analyse a set of experiments where islets were exposed to different types of glucose stimulation. Then, in Chapter 9, we utilise insights gained from these observations to construct a simple cell-resolved biophysical model of the islet, which reproduces the collective dynamics observed in experiments. A key ingredient of the

model is the strong positive coupling between neighbouring cells, as well as the antagonistic interaction between two distinct cell types in the islet, α- and β-cells. Understanding the implications of collective behaviour on healthy glucose regulation is key, since disrupted synchrony is a hallmark of diabetes. The novelty in our approach is taking a systems-level perspective and focusing on the connection between cell-cell interactions and the biological function of the islet as a whole.

## Monday, September 8, 2025 03:00pm - 04:00pm

I22 Lakeside View and Zoom

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This invitation is valid as a ticket for the ISTA Shuttle from and to Heiligenstadt Station. Please find a schedule of the ISTA Shuttle on our webpage: https://ista.ac.at/en/campus/how-to-get-here/ The ISTA Shuttle bus is marked ISTA Shuttle (#142) and has the Institute Logo printed on the side.