



**University of Stuttgart**

Stuttgart Research Center Systems Biology



## Systems Biology Seminar Talk

# Frequency encoding regulates cell type composition in the small intestine

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**11:00 CET**

**Host:**

**Prof. Michael Heymann**

**Room 1.177, UG**

**Allmandring 31**

**Stuttgart**

### Abstract:

Multicellular tissues maintain remarkably precise architectures, requiring mechanisms that robustly coordinate proliferation, differentiation, and self-organisation. In the small intestine, this process is especially demanding: stem cells must continuously replenish multiple specialised cell types while preserving a regular spatial pattern. Although the molecular components of intestinal signalling pathways are well established, the dynamical principles by which these pathways regulate tissue organisation remain unclear. Recent work in cell lines has shown that signalling pathways can use dynamic signal encoding—where features such as pulse duration, wave propagation, or oscillation frequency (e.g., in calcium, NF- $\kappa$ B, or ERK signalling) transmit information beyond static activity levels. Whether tissues exploit such temporal codes to regulate composition has remained an open question.

Here, we investigate Notch signalling, a canonical pathway that governs the choice between absorptive and secretory fates. Using a fluorescent Notch activity reporter in a transgenic mouse model, we performed live-cell imaging of intestinal organoids combined with single-cell tracking. We discovered that Notch signalling in progenitor cells does not operate as a static on/off switch, but rather exhibits oscillatory dynamics.

To test whether these dynamics are functional, we developed a microfluidic system enabling the external modulation of Notch activity in real time. By tuning the oscillation frequency, we found that specific dynamic regimes biased cell fate outcomes—shaping the proportion of progenitor versus differentiated secretory cells. Thus, the encoding of information in the temporal frequency of signalling directly determines tissue composition.

This research reveals a new mechanism of how Notch regulates cell fate decisions in the intestine. It also establishes a new in vitro platform technology to control signalling processes in multicellular systems.

### CV:

He studied physics at the University of Cambridge for my Bachelor and Master's degrees. During his PhD at the Max Planck Institute of Biochemistry (near Munich), he applied biophysical methods as well as microfabrication tools to study in vitro reconstitution of self-organising protein systems. As a postdoc in the Sonnen Lab, he is interested in applying microfluidics to study signalling dynamics in the small intestine.