

This thesis addresses the principles underlying two biological issues: the spatial separation of molecular domains observed in membrane trafficking compartments and the frequency preference of epigenetic circuits.

In the first project, competition between two molecules of the Rab family is proposed as mechanism generating their observed spatial segregation. Multiple mathematical models are developed using ODEs. Models are screened for experimentally measurable observables such as mean molecule amounts and correlations between molecular species. Subsequently, experimental validation is performed by imaging the two molecules on the surface of trafficking compartments with fluorescence microscopy. The obtained imaging data are analyzed by quantifying mean values and correlations to verify model predictions. Eventually, based on experimental results, a single competition model is selected.

The second project concerns band-pass filtering in epigenetic regulation by microRNAs, well-known repressors of gene activity. First, a minimal ODE model for describing the interaction between microRNAs and their target genes is developed and tested under periodic miRNA synthesis by measuring the so-called Fold Repression – an index that quantifies the strength of gene activity repression. We predict that Fold Repression can display maximal values for a narrow range of input frequencies, thus exhibiting band-pass filtering properties. Moreover, we screen a model with an additional target gene to investigate how competition between targets affects the frequency-dependent repression. In this way we show that competing targets can be repressed by distinct frequencies, making periodic miRNA synthesis a potential way of selective target regulation.

For experimental validation, an optogenetic system is used to generate periodic miRNA synthesis of desired frequency. RNA quantification and fluorescence microscopy techniques are employed to measure the resulting fold-repression to be compared with theoretical predictions.