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## ANALYSING MAMMALIAN SIGNAL TRANSDUCTION AND GENE REGULATION USING COMPUTATIONAL MODELS

## ABSTRACT

Signal transduction and gene regulation play critical roles in the regulation of fundamental cellular processes. We develop and analyse computational models that allow an understanding of regulatory properties and dynamical aspects of these processes. Here, I will concentrate on two examples. The first is the transcription factor MYC that plays a major role in the regulation of cell proliferation and is often upregulated in cancer. Several hypotheses have been proposed to explain cell type specific MYC target gene expression despite genome wide DNA binding. We suggest that specific gene expression profiles arise since target gene promoters differ in their affinity for MYC. Our computational modelling approach in combination with extensive experimental data demonstrates that differences in MYC-DNA-binding affinity are sufficient to explain the distinct promoter occupancies observed in ChIP-sequencing experiments.

Moreover, I will focus on the NF-kB pathway and analyse the regulation of pathway readouts and target gene expression by addressing the dependency of the pathway dynamics on extracellular and intracellular parameters, the role of feedbacks and the modulatory effect of the RNA-binding protein RC3H1.

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