



## **PREDICTING PANCREAS CELL FATE DECISIONS AND REPROGRAMMING WITH A HIERARCHICAL MULTI-ATTRACTOR MODEL**

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Cell fate reprogramming, such as the generation of insulin-producing beta cells from other pancreas cells can be achieved by external modulation of key transcription factors. However, the known gene regulatory interactions which form a complex network with multiple feedback loops makes it increasingly difficult to view regulatory pathways as schemes of causal influences that serve as basis for predicting the effect of transcriptional perturbation. On the other hand, not sufficient information on regulatory networks is available for detailed formal models. Here we demonstrate that by using the qualitatively described regulatory interaction as basis for a coarse-grained dynamical ODE(ordinary differential equation) model it is possible to recapitulate the observed attractor of the exocrine and beta, alpha, delta endocrine cells types and to predict which gene perturbation can result in desired lineage reprogramming. Our model indicates that the constraints imposed by the incompletely elucidated regulatory network architecture suffice to erect a predictive model for making informed decisions in choosing the set of transcription factors that need to be modulated for fate reprogramming.

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