

Predictive logical modelling of cell fate decision networks

Denis Thieffry¹

Institut de Biologie de l'Ecole Normale Supérieure (IBENS), UMR CNRS 8197 - INSERM 1024, 46 rue d'Ulm, 75005 Paris, France¹

Logical modelling constitutes a flexible framework to design predictive qualitative models, which can be readily analysed or simulated as such, and potentially used as scaffolds to build more quantitative (continuous or stochastic) models.

We use multi-valued decision diagrams to implement (multi-level) logical updating rules in the modelling software *GINsim*. This representation enabled the development of efficient algorithms for the identification of stable states, as well as to identify specific (positive or negative) regulatory circuits involved in specific dynamical properties (e.g., multiple attractors or sustained oscillations).

To cope with large molecular regulatory networks, we have further implemented a flexible reduction method, which preserves the dynamical attractors representing alternative cellular states.

This reduction method is complemented with a novel algorithm enabling the compression of state transition graphs into hierarchical graphs, yet emphasising the most important transitions associated with attractor reachability.

This approach will be illustrated through the modelling of regulatory networks controlling cell fate decisions in human cancer cells. In particular, I will show how it can be used to predict the effects of single and multiple drug applications, and thereby delineating synergistic drug effects.