Correspondence Between Discrete and Continuous Models of Gene Regulatory Network

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Abstract

We know that some proteins can regulate the expression of genes in a living organism. The regulation of gene expression occurs through networks of regulatory interactions in a non linear way between DNA, RNA, Proteins and some molecules, called genetic regulatory networks. It is becoming clear that mathematical models and tools are required to analyse these complex systems.

In the course of his study on gene regulatory networks R. Thomas proposed a discrete framework that mimics the qualitative evolution of such systems. Such discrete models are of great importance because kinetic parameters are often non measurable *in vivo* and because available data are often of qualitative nature. Then Snoussi proved consistency between the discrete approach of R. Thomas and Piecewise Linear Differential Equation Systems, which are easy to construct from interaction graph and thresholds of interactions. There exists a transition between two qualitative states (in the discrete model) if and only if there exists a trajectory of the differential model that goes from a point of the domain corresponding to the first qualitative state to the boundary separating this domain to the one corresponding to the second qualitative state.

Our work focuses also on the relationships between both approaches: we would like to extend the result due to Snoussi. Can we give some conditions on the model or on the trace of the qualitative state space which ensures that it is possible to construct a trajectory of the differential model that passes through the same sequence of domains ?

Our main result consists in a theorem stating that, considering a continuous model, for which the associated discrete model has a finite path $s_0 \rightarrow s_1 \rightarrow ... \rightarrow s_n$ such that for all $i \in [1, ..., n-1]$, $s_{i-1} \neq s_{i+1}$, then, under some hypotheses, trajectories of the differential system starting from the domain associated with s_0 pass successively through each domain associated with the states of the path. The used hypotheses have been introduced by Jean-Luc Gouze and Farcot in a previous work concerning limit cycles. The proof is done by induction and sketch of the proof is given.

Finally, several well chosen examples will illustrate the use of the theorem as well as its limitations due to the stated hypotheses.