Poster I-69

Embedding Properties of Biological Regulatory Network

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Biological regulatory networks (BRN) allow us to capture the main behaviours of interactions between genes. Current studies are led on small BRN, corresponding to a specific biological problem, with interactions between few genes. These networks are necessarily parts of more global networks; it leads to the following question: does a network keep its pre-studied behaviour when it is embedded into a more global network? Here we focus on René Thomas' formalism for BRN.

Let G be a BRN whose behaviour is known. Let R be a bigger regulatory network which contains the underlying graph of G. Let E be this sub-graph of R: we cannot say that G is directly embedded into R as BRN. Some thresholds on E interactions can be different, as the additional edges from G surrounding variables create new thresholds and increase their ranking. We have developed an algorithm which computes a canonical BRN G' from E (by calibrating the thresholds after removing the additional edges mentioned above). G' allows us to compare E and G. This algorithm computes new threshold values, where the maximum range decreases from the variable old out-degree to its new one. Accordingly, parameters and expression levels have to change: the folding algorithm gets a new ranking for these values.

The folded state transition graph of G' gives the "self-contained" behaviour of E extracted from R and can be formally compared with the G state transition graph. This mathematical work allows us to prove sufficient conditions to preserve behaviours by embedding.

After formally defining the notion of conservative in-edge (in-edge whose parameters K locally keeps the dynamics of its variable), we have proved the following theorem:

Theorem 1 *If a BRN G is embedded into a BRN R, then G keeps its behaviour if all in-edges are conservative.*
From this theorem, we can deduce easily two usable corollaries:

Corollary 1 *If there are no in-edges from R to G, then G keeps its behaviour into R.*

Corollary 2 *If K(v,W□Z)=K(v,W) for any variable v in G, any set of predecessors W of v in G and any set of predecessors Z of v in R, then G keeps its behaviour into R.*

Notice that Theorem 1 proves formally that out-edges never modify the behaviour of *G*. This simple remark already gives in practice a widely usable method to analyse BRN in a modular way.