Greening R. Thomas' Framework: a Divide and Conquer Approach

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When we model a complex biological system, we often try to understand the causality chains that explain the different behaviours observed. Qualitative models based on discrete mathematics tend to be powerfull to give this type of answer: A reason why the extended R.Thomas formalism completed by formal methods, has become a classic for regulatory networks [1,2].

However, observed behaviours often depend on environmental conditions (like nutrient availability in cell culture experimentation). Therefore, the construction of a right modelisation depends on our ability to take into account all this environemental information in a single modelling framework.

Moreover, even in a given modelisation framework, several modelling choices are possible. This is due to different instantiations of dynamical parameters piloting the behaviour of the model, that can lead to traces consistent with all observations. If the modeller chooses a particular setting, when new biological information is known about the system, the parameter identification step must be restarted from the beginning. The systematic approach would then consist in characterizing, at each step, all of the parameter settings consistent with current knowledge: when a new observation becomes available, the modeller just refines the previous set of consistent parameter settings by selecting only those that are also consistent with this new information.

The use of artefacts enables the simulations of successive environmental situations in a unique global network with the R. Thomas modelling framework. However, we recommend another option based on a "divide and conquer" approach: the green extension of R. Thomas' framework with the notion of environments. This approach has several steps. First, a specific (and thus smaller) regulatory network is built for each environment. Then, for each regulatory network, a consistent set of parameter settings compatible with the associated biological properties is searched. Finally, all consistent sets are intersected to obtained the settings which satisfy the properties for all environments[3].

This poster will show you that the addition of a new environmental context (calcium addition) in a running example of the *Pseudomonas aeruginosas* virulence regulation model. Pseudomonas is an opportunistic bacteria which can cause serious infections in the lung of cystic fibrosis patients with the production of thick mucus [4].

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References

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