Parameter estimation of a neuronal fate decision simulation model in C. elegans using online model checker: a high-level Petri net approach

Keywords: Model – Parameter estimation – Modeling and simulation – Biopathway – Petri net – fozi-1 –

Abstract: This poster presents a systematic framework to automatically estimate kinetic parameters of a given model or a model starting from scratch by applying online model checking technique supported by Probabilistic Linear Temporal Logic with Statistic (PLTLs), and a simple yet sufficient parameter estimation method to a well-founded Petri net class (i.e., HFPNe). Firstly, we built a quantitative ASE fate model in C. elegans containing 3,327 components emulating nine genetic conditions. This model extends a previous model by taking into account a newly identified transcription factor fozi-1. Secondly, we have extracted 45 biological properties in total underlying dynamic behaviors about ASE fate determination from observed known data which are later translated into temporal logic formulas for the formal verification. Thirdly, we have conducted a large number of simulations (20 million-runs) to estimate 23 kinetic parameters contributing to the regulation of forming alternative cell fates, and obtained 57 parameter sets whose models can conform to the entire 45 properties for further simulation analysis. Finally, we have evaluated the correctness and robustness of these 57 models by means of adding different magnitude of noise in to the model. One simulation model is concluded to be the most reasonable and robust owing to the high stability against the noises. We also have discussed the results and summarized several plausible explanations.

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