

Large-scale network reconstruction using logical modeling

ULRIKE MÜNZNER^{1,a)} EDDA KLIPP² MARCUS KRANTZ² TATSUYA AKUTSU^{1,b)}

Abstract: Signal transduction networks are prone to the combinatorial complexity. In such a network, the number of microstates increases exponentially, while the empirical data describing these states tends to be scarce. These two characteristics challenge mathematical descriptions in terms of scalability and data congruence. We developed a workflow to establish large-scale, mechanistically detailed and simulatable signal transduction networks. Our approach uses the reaction-contingency (rxncon) language which captures measured elemental states and their biological context. A network reconstructed in rxncon language allows translation into a Boolean format and hence, analysis of the information flow without the requirement of kinetic or quantitative parameters. We used this workflow to reconstruct a mechanistically detailed network of the cell division cycle in *Saccharomyces cerevisiae*. The corresponding Boolean network reproduces the wildtype behavior of a yeast cell on the level of bud morphology, DNA replication and nuclear division. Furthermore, this network correctly predicts the phenotypes of 62 out of 85 tested mutants. In the future, new analysis methods may allow a more thorough investigation of large Boolean networks in terms of attractor calculation.

¹ Bioinformatics Center, Institute for Chemical Research, Kyoto University, Gokasho, Uji 611-0011, Japan

² Theoretical Biophysics, Institute of Biology, Humboldt-Universität zu Berlin, 10115 Berlin, Germany

a) ulrike@kuicr.kyoto-u.ac.jp

b) takutsu@kuicr.kyoto-u.ac.jp