REACTION DYNAMICS ANALYSIS OF AN *E. COLI* PROTEIN TRANSLATION SYSTEM BY COMPUTATIONAL MODELING

Tomoaki Matsuura, Department of Biotechnology, Graduate School of Engineering, Osaka University
Matsuura_tomoaki@bio.eng.osaka-u.ac.jp
Naoki Tanimura, Mizuho Information & Research Institute, Inc.
Kazufumi Hosoda, Osaka University
Tetsuya Yomo, Osaka University
Yoshihiro Shimizu, Quantitative Biology Center, Riken

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A single enzymatic reaction can often be described by Michaelis-Menten kinetics, but once reactions are connected to one other, it becomes difficult to understand and capture a complete description of the reaction dynamics due to its high dimensionality. To elucidate the dynamic features of a biologically relevant large-scale reaction network, we constructed a computational model of minimal protein synthesis consisting of 241 components and 968 reactions that synthesize the Met-Gly-Gly (MGG) peptide based on an *Escherichia coli*-based reconstituted *in vitro* translation (IVT) system [1]. We performed a simulation using parameters collected primarily from the literature and found that the rate of MGG peptide synthesis becomes nearly constant in minutes, thus achieving a steady-state similar to experimental observations. In addition, concentration changes to 70% of the components, including intermediates, reached a plateau in a few minutes. However, the concentration change of each component exhibits several temporal plateaus, or a quasi-stationary state (QSS), before reaching the final plateau. To understand the complex dynamics, we focused on whether the components reached a QSS, mapped the arrangement of components in a QSS in the entire reaction network structure and investigated time-dependent changes. We found that components in a QSS form clusters that grow over time but not in a linear fashion and that this process involves the collapse and regrowth of clusters before the formation of a final large single cluster. These observations might commonly occur in other large-scale biological reaction networks. This developed analysis might be useful for understanding large-scale enzymatic reactions, thereby extracting the characteristics of the reaction network, including phase transitions. As the reconstituted IVT has been used for various applications inducing directed evolution of membrane proteins [2,3], the developed computational model might be useful in further enhancement of the yield of synthesized proteins using the reconstituted IVT.

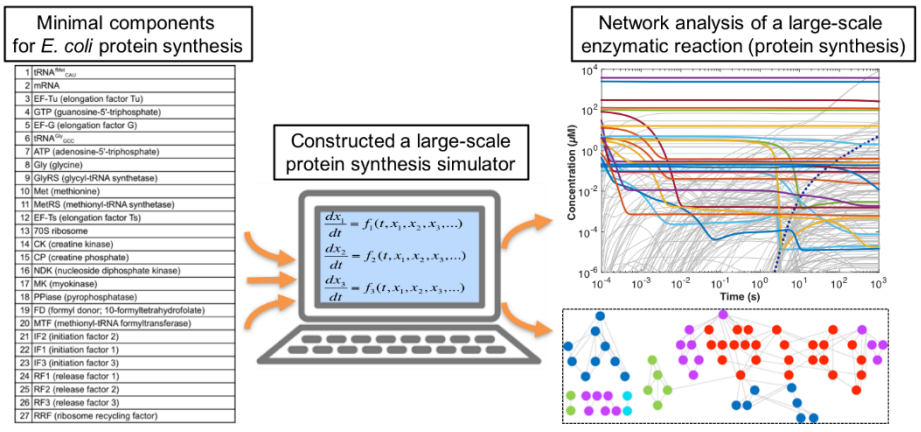

Figure 1: Schematic of the protein synthesis simulator construction and analysis of a biologically relevant large-scale reaction network. The computational model was constructed based on the E. coli-based reconstituted in vitro translation (IVT) system (Shimizu Y et al., Nat Biotechnol. 2001)

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