

## 論文の内容の要旨

### Control Theoretic Approaches to Analysis and Identification of Biochemical Networks

(制御理論的アプローチによる生化学ネットワークの解析と同定)

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This thesis is concerned with the theoretic analysis and identification of complex dynamical behaviors of biochemical networks. Focusing on a characteristic feedback control structure of biochemical systems, we first propose a unified control theoretic formalism of biochemical dynamics. We then develop analysis and identification methods to investigate the dynamics of biochemical networks in a mathematically tractable way. Applying the proposed methods to existing biological examples, we further explore universal characteristics that govern a variety of dynamical behaviors in biochemical systems.

Specifically, we here focus on the following four topics: (i) oscillatory behavior analysis, (ii) robust stability analysis, (iii) analysis of spatial patterns induced by intrinsic noise and (iv) parameter identification. These four topics range from temporal to spatial dynamics and from qualitative to quantitative analysis, and they cover important issues in biology.

(i) Oscillatory behavior and (ii) robust stability are analyzed based on a unified deterministic feedback model of biochemical networks. We propose mathematically tractable ways to analyzing the shape profiles of oscillatory chemical concentrations and the robustness of

equilibrium states. With these tools in hand, we reveal the dimensionless parameters that essentially govern the oscillations and the robustness in biochemical networks.

We then turn our attention to (iii) the spatial and stochastic dynamics in a cell. Extending the deterministic formalism, we first propose a control theoretic framework to model the stochastic reaction-diffusion systems. We then develop an efficient computational tool to compute the spatial power spectrum of intrinsic noise. The developed method is useful to discover underlying spatial dynamics of biochemical networks induced by intrinsic noise.

The advancements of theories hinge upon the construction of reliable dynamical models. Thus, the last topic is devoted to (iv) the development of a parameter identification method. Specifically, we propose a computationally efficient and mathematically tractable parameter identification method using flow cytometry measurements. The developed method has a rich mathematical background associated with classical identification methods considered in control systems community for a long time. Using this property, we mathematically guarantee the performance of the method.