

Preface

Synthetic biology is an engineering discipline that builds on our mechanistic understanding of molecular biology to program microbes or mammalian cells to carry new functions. In the past decade of development, significant progress has been made in designing biological parts and assembling them into genetic circuits to achieve basic functionalities. Synthetic biology currently focuses on the rational construction of biological systems based on engineering principles. Such predictable manipulation of a cell for these biological systems requires modeling, systems analysis and design as well as experimental techniques to work together. The modeling component of synthetic biology allows one to design genetic network and analyze its expected behavior, and the experimental component merges model with real systems by providing quantitative data and sets of available biological 'parts' to construct genetic networks. Since there are several intrinsic kinetic fluctuations such as splicing and mutation as well as extrinsic disturbances such as thermal noise and upstream interference, stochastic dynamic models are introduced for genetic networks *in vivo*.

Based on stochastic dynamic model, kinetic activities are identified for biological parts to redefine the libraries by least square parameter estimation method via experimental data. Then according to the gene network topology and design specifications, several robust design algorithms are systematically developed to select adequate biological parts from their corresponding libraries for the synthetic gene network to satisfy the prescribed design specifications under intrinsic fluctuations and extrinsic disturbances *in vivo*. When the volume of libraries becomes very large, the genetic algorithm (GA)-based and evolutionary algorithm (EA)-based methods are also developed to efficiently search for adequate biological parts from the corresponding libraries to engineer a desired synthetic gene network.

In order to achieve a desired behavior or function under intrinsic and extrinsic molecular noises, the H_2 optimal tracking and H_∞ robust disturbance attenuation have been provided as two design specifications for synthetic gene networks in this book. In order to solve robust synthetic gene network design problem in H_2 optimal tracking, H_∞ robust filtering

or mixed H_2/H_∞ robust tracking design, we need to solve a corresponding Hamilton-Jacobi inequality (HJI)-constrained optimization problem. Therefore, the global linearization technique or fuzzy interpolation method is employed to interpolate several local linear systems to approximate the nonlinear stochastic synthetic gene networks. In this situation, a set of linear matrix inequalities (LMIs)-constrained optimization problem can replace a HJI-constrained optimization problem so that it can be easily solved by using the LMI toolbox in Matlab in the design procedure of robust synthetic gene network.

In the IC industry, due to high complexity and difficulty in very large scale integrated (VLSI) circuits, which can not be imaged about 2 or 3 decades ago, system design companies (like Intel) and system implementation companies (like Taiwan Semiconductor Manufacturing Company, TSMC) perform the products of VLSI circuits by division of labor. In the future, systems designers should cooperate with implementation companies to produce complex synthetic gene networks. If this is the case, the development of systematic design tools is an important topic for synthetic gene networks. Therefore, the proposed robust optimal tracking design methods have potential applications to synthetic gene network design in the near future.

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