Poster L-34

Modeling Transcription Kinetics with Differential Equations

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Short Abstract: In this work, we propose a model for recovering the time-series expression of a given transcription network. The only input data needed is the time-series expression from global regulators. To test our methodology, we performed simulation and real data cross-validation on a literature-based transcription network.

Long Abstract:
The advent of time-course microarray experiments has created a new framework for modeling transcription kinetics. It is now possible to evaluate transcription dynamics directly from the mRNA level variation. However, the mathematical models proposed so far for this biological process depends on organism-specific experimental parameters.

In this work, we propose a mathematical model based on differential equations that recovers the time-series expression from a given transcription network. The only input data needed is the expression of global regulators. Transcription delay and mRNA decay are assumed to be global, which eliminates the need for specific experimental data. All parameters are obtained by a genetic algorithm optimization. We have also compared the use of organism-specific experimental parameters instead of global parameters.

A simulation study showed that the algorithm converges to same results, independent of the initial parameter's set. Besides, cross-validation analysis was performed on a literature-based transcription network from Saccharomyces cerevisiae with 192 genes. The estimation error was about 10% on the training set and 20% on the testing set. The use of organism-specific experimental parameters has not significantly reduced the estimation error. This feature enables this model to be used with almost every kind of organism, not being restricted by availability of experimental data.

Poster L-34

Molecular Computation with Virtual Gene Circuits

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Short Abstract: Gene circuits represent a biological counterpart for silicon-based Boolean ports and have awaked research interests due to their computational power. This work proposes a novel gene circuit architecture, called Virtual Gene Circuit (VGC), which allows a circuit to exhibit different behaviors in the same plasmid.

Long Abstract:

One important goal of postgenomic research will be to understand how cellular phenomena arise from the connectivity of genes and transcriptome. This connectivity generates molecular network diagrams and a systematic understanding will require the development of a mathematical framework for describing them.

A molecular network diagram resembles an electric circuit, which is formed by simple units called Boolean ports. Gene circuits represent a biological counterpart for silicon-based Boolean ports and have awaked research interests due to their computational power. The concept of engineered gene circuit as a computational environment was proposed by R. Weiss (Princeton University) in 2001 and focuses on programming new cellular behaviors by designing and embedding synthetic gene circuits that perform Boolean functions in single cells like bacteria, yeast and mammalian steam cells. Gene circuits represent an alternative way to perform molecular computations in vivo and hold promise for a wide range of applications in biotechnology, computation, environmental engineering and medicine. For instance, a "suicide" gene circuit could potentially be programmed into bacteria used to clean up pollution, making the microbes die off once their job was done. Synthetic gene circuits could also be engineered into bacteria to enable them to react to the presence of cancer cells by killing or disabling the tumor.

The initial work proposed by R.Weiss was concentrated in the lac operon, a well-known regulatory circuit which arises naturally in E. Coli bacteria. In this environment, some important Boolean biological gates were built: NOT, NAND and IMPLIES. These gates can be organized into intracellular networks to evaluate Boolean functions. Furthermore, an intercellular communication schema was proposed and it enables a programming environment for cell behavior in a complex, predictable and reliable fashion. Recent researches show that noise is an important component in engineered gene circuit regulation and there is transcription plasticity depending on environment conditions.

The single behavior of actual engineered gene circuits represents their major disadvantage, even in the noise presence. This work proposes a novel gene circuit architecture, called Virtual Gene Circuit (VGC), which allows a circuit to exhibit different behaviors in the same plasmid. Our proposal resembles the polymorphism mechanism encountered in the computational object-oriented paradigm where a same object can activate a specific behavior depending on environment conditions.

A VGC is a virtually connected plasmid network which allow us evaluate several Boolean functions over the same support in vivo. This plasticity comes from the fact we can regulate linear, parallel, auto-regulation and hybrid behaviors in a single VGC. Each plasmid acts an entangled quantum state whose decoherence is controlled by specific transcription signals depending on desired Boolean function. The work will show in silico gene networks that simulate complex VGCs and discuss some biochemical alternatives to map them in vivo environments.