

## REVERSE ENGINEERING AND SYNTHESIS OF BIOMOLECULAR SYSTEMS

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### 1. Introduction

Synthetic biology is the new frontier of biological engineering. Instead of incrementally altering living organisms, synthetic biologists propose to use biological knowledge, modular biological parts, and computer-aided design to quickly develop systems capable of unprecedented biochemical feats. Synthetic biology therefore promises dramatic improvements in green chemistry<sup>1</sup>, alternative energy<sup>2</sup>, drug manufacture<sup>3,4</sup>, and therapeutics<sup>5</sup>.

There have been numerous recent advancements in synthetic biology. The need for accuracy at the design and simulation stage have inspired dialogue on how to add functional characterizations to parts documentation in the Registry of Standard Biological parts<sup>6,7</sup>. In addition, a design strategy - constructing networks from quantitatively characterized libraries of diversified components -- has been proposed<sup>8</sup>. A synthetic network must be integrated into an engineering chassis. To this end the development of evolved ribosome-mRNA pairs may be the first step towards an orthogonal cellular network<sup>9 10 11 12</sup>.

Although scientists have made significant progress in synthetic biology, the field must still overcome a number of challenges. To this end, this session offers novel methodologies in three general areas: namely, in designing synthetic systems, in developing novel biological parts, and in analyzing complex networks.

### 2. Session Papers

Design principles and development strategies from other engineering disciplines must be adjusted to the peculiarities of biological systems. **Ball et al.** propose to approach synthetic biology with heterogeneous design strategies that are common in other engineering fields. **Shea et al.** propose and demonstrate a compilation strategy for building iterative arithmetic computers based on biochemical reactions. **Ceroni et al.** propose a tool to predict the response of circuits, such as a synthetic circuit with inducible gene expression. **Tari et al.** have developed an automated pathway synthesis method that uses knowledge bases and Medline abstracts to automatically synthesize pharmacokinetic pathways.

The design of synthetic systems, of course, is dependent on the availability of well-characterized biological parts. **Davidson et al.** use an emulsion approach in the development of a

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library of T7 promoters of varying strength. **Corradin *et al.*** explore the potential of a retrovirus HTLV-1 gene circuit as a relaxation oscillator that is deliverable into eukaryotes.

The complexity inherent in synthetic biology implies the need for sophisticated analytical tools. **Ramesh *et al.*** employ graph clustering techniques to detect modularity in highly complex gene regulatory networks. **Biasiolo *et al.*** study transcriptional and post-transcriptional networks of multiple myeloma samples by measuring the drop in network performance caused by deactivation of putative regulatory elements.

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