ACS SyntheticBiology

In This Issue

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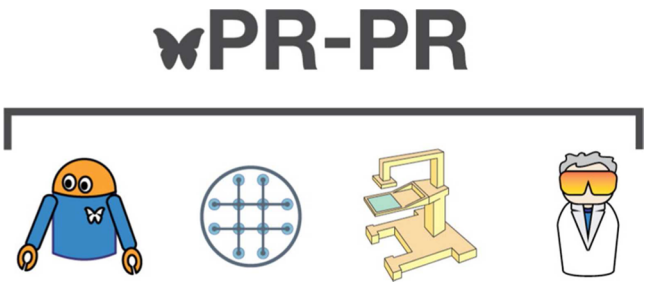
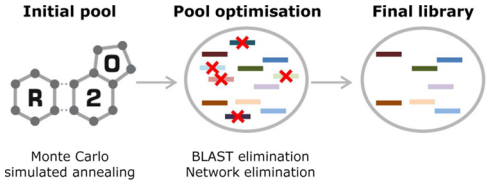
PR−PR: CROSS-PLATFORM LABORATORY AUTOMATION SYSTEM



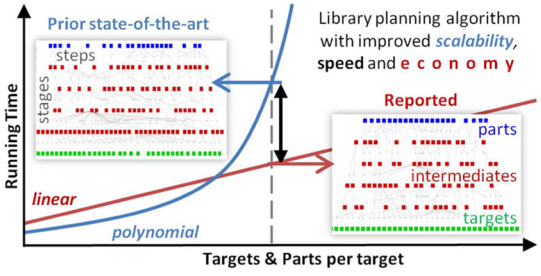
Research increasingly requires collaborative efforts between multiple teams. By eliminating the "human factor", laboratory automation devices, such as robotics, can contribute to reliable and reproducible experimental data. However, since experiments can only be performed using the equipment available, and because any two laboratories rarely have the same equipment, it can be very challenging for one laboratory to reproduce the experimental results of another. In this Technical Note, Linshiz *et al.*, (DOI: 10.1021/sb4001728) report research and development efforts that enable protocol transferability between automation platforms, toward empowering laboratories to use the same complex protocols despite automation equipment differences.

R2oDNA DESIGNER: COMPUTATIONAL DESIGN OF BIOLOGICALLY NEUTRAL SYNTHETIC DNA SEQUENCES



In this Technical Note, Casini et al., (DOI: 10.1021/sb4001323) have developed a novel computational algorithm (and accompanying web server: www.r2odna.com) for designing orthogonal biologically neutral synthetic DNA sequences. The method, which works by stochastically mutating random sequences, has a number of uses in synthetic biology such as spacer sequences to insulate biological parts from local context, barcodes, linkers for efficient directed DNA assembly, and as negative controls for functional sequences. These sequences are free from known functional motifs, secondary structures, and repeats.

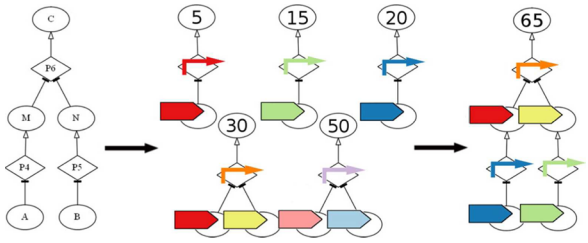
HEURISTIC FOR MAXIMIZING DNA REUSE IN SYNTHETIC DNA LIBRARY ASSEMBLY



Increasing production rates and reducing associated costs remain challenges in *de novo* DNA synthesis. One possible solution is the reuse of DNA in combinatorial library construction. Here, Blakes, Raz *et al.* (DOI: 10.1021/sb400161v) provide an algorithm for planning multistage assemblies of DNA libraries with shared intermediates that attempt to maximize DNA reuse.

The authors show that their algorithm provides DNA assembly graphs of equivalent quality to those produced by the current best approach, but significantly beats its runtime. The algorithm presented here can thus be used as a metric of "manufacturability" to guide DNA library design.

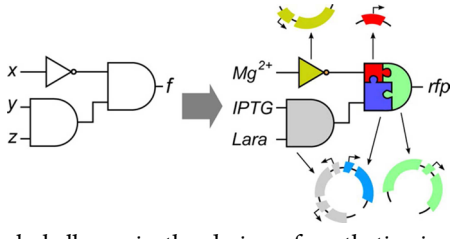
DIRECTED ACYCLIC GRAPH-BASED TECHNOLOGY MAPPING



As engineering foundations such as standards and abstraction begin to mature within synthetic biology, one limiting factor for the realization of more complex genetic circuits could be the availability and effectiveness of genetic design automation (GDA) tools that use these foundations to separate the design of genetic circuits from their physical construction. Here, Roehner and Myers (DOI: 10.1021/sb400135t) demonstrate the use of an algorithm in their GDA tool, iBioSim, to map from standardized specifications for three different genetic circuits against four randomly generated libraries of increasing size.

The authors not only evaluate the performance of their algorithm against computationally exhaustive and greedy approaches but also demonstrate how their tool can be used in the future to generate a genetic circuit design that includes functional and structural information on DNA components that can inform subsequent optimization steps and eventually physical construction of the design.

OPTIMAL PART AND MODULE SELECTION FOR CIRCUIT DESIGN AUTOMATION



An integral challenge in the design of synthetic circuits is the selection of optimal parts such that the resulting circuit behavior

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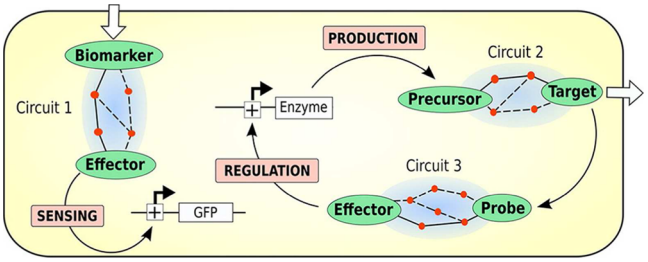
best mimics the desired circuit behavior. In this effort, efficient part and module selection algorithms are essential. Now, Huynh and Tagkopoulos (DOI: 10.1021/sb400139h) introduce a structured abstraction methodology and a dynamic programming-based algorithm that guarantees optimal part selection.

The authors reduce running time and space requirements by providing three extensions based on symmetry check, information look-ahead, and branch-and-bound techniques. They evaluated the proposed methodology with a benchmark of 11 circuits, a database of 73 parts, and 304 experimentally constructed modules and report encouraging results, suggesting a step toward increased efficiency in synthetic circuit design and construction.

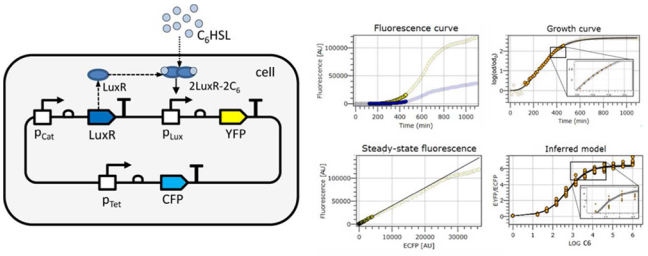
RETROPATH: AUTOMATED PIPELINE FOR EMBEDDED METABOLIC CIRCUITS



Metabolic circuits are a promising alternative to other genetic circuits as modular parts implementing functionality for synthetic biology applications. In this work, Carbonell *et al.*, (DOI: 10.1021/sb4001273) present RetroPath, an automated design tool for metabolic circuits.

The authors demonstrate how their proposed techniques can be used to design advanced circuits such as biosensors connecting biomarkers to effectors or devices that are able to sense and regulate the production of chemicals in a host or chassis organism. Such automated techniques allow for the exploration of how metabolic space can be efficiently exploited for novel synthetic biology applications.

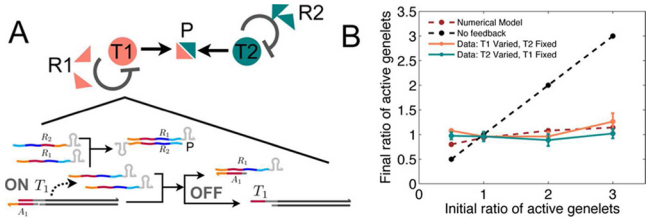
COMPUTATIONAL METHOD FOR AUTOMATED CHARACTERIZATION OF GENETIC COMPONENTS



The use of engineering principles in the design and construction of biological systems with predictable behavior is a primary focus of synthetic biology. In order to design a reliable system using biological components, experimental and computational techniques that allow robust characterization of these components are necessary. In this study, Yordanov *et al.*, (DOI: 10.1021/sb400152n) describe a computational method for the automated characterization of genetic components.

The methods developed by the authors uses a recently developed multichannel experimental protocol together with Bayesian parameter inference and model selection, all integrated within a convenient computational tool. While the current approach helps streamline the characterization of devices, further development will enable the establishment of new standards for robust characterization within the broader scientific community.

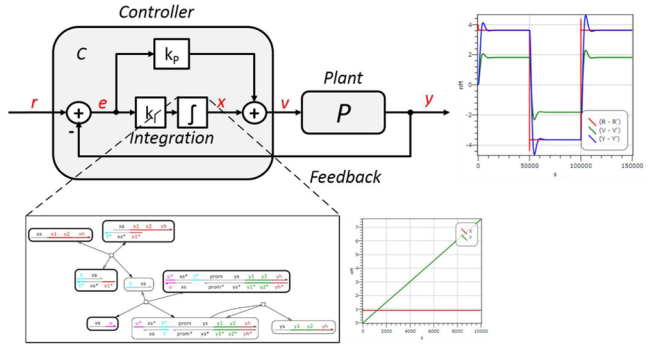
NEGATIVE AUTOREGULATION MATCHES PRODUCTION AND DEMAND IN SYNTHETIC TRANSCRIPTIONAL NETWORKS



In fields such as *in vitro* cell-free synthetic biology, systematic implementation of feedback is needed to guarantee scalability and modularity of large scale systems. In this paper, Franco *et al.* (DOI: 10.1021/sb400157z) describe the advantages of using negative feedback in the context of synthetic gene networks.

The authors show that similar to negative feedback in conventional engineered systems, negative autoregulation allows a synthetic gene to modulate its activity and output concentration to match the "demand" of its environment. Using a minimal, two-gene network, where each gene has the ability to self-inhibit, the authors demonstrate that activity levels of the genes reach the same equilibrium, matching production and demand despite variability in gene concentration.

COMPUTATIONAL DESIGN OF NUCLEIC ACID FEEDBACK CONTROL CIRCUITS



The use of synthetic circuits for controlling molecular-scale processes has potential applications in future *in vitro* and *in vivo* biotechnology. In this study, Yordanov *et al.*, (DOI: 10.1021/sb400169s) describe a computational approach for designing feedback control circuits constructed from nucleic acids.

The authors adapted an existing methodology for expressing signal processing and control circuits as biomolecular reactions. They implemented these reactions in three different classes of nucleic acid circuits and compared different approaches. Results indicated that the three molecular programming strategies offered different advantages. The work presented here is a step toward the engineering of devices with potential applications in biotechnology and medicine and also provides a computational tool for the design, simulation and analysis of such biological circuits.

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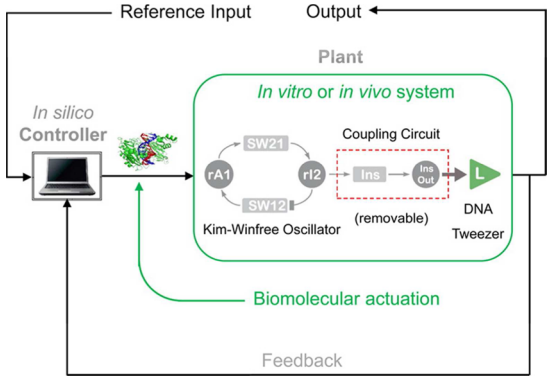
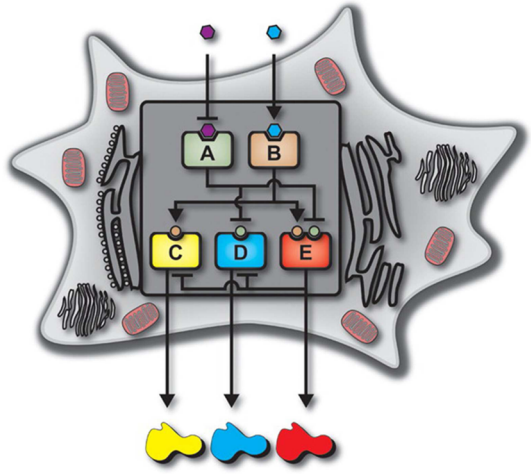
LOAD CAPACITY IMPROVEMENTS IN NUCLEIC ACID BASED SYSTEMS



A much touted application of synthetic biology is that of *in situ* monitoring-and-control. Here, in order to minimize the steady-state/tracking error, the control mechanism of the synthetic biological device must be dynamic; that is, it should produce time-varying output in response to a constant-valued input. Additionally, the sensory mechanism of the device must be dynamic so as to reject the noise and disturbance inherent in the underlying cellular processes. In this study, Kulkarni *et al.*, (DOI: 10.1021/sb5000675) demonstrate how such systems can be realized using basic biomolecular material such as DNA, RNA, and enzymes.

The authors describe methods to speed up these constructs and also integrate their algorithms into Visual DSD. Their approach can be easily adapted to improve the robustness, tunability, and loading capacity of a wide range of synthetic biological devices.

BIOLOGICAL 2-INPUT DECODER CIRCUIT IN HUMAN CELLS



While multioutput systems are just as important as multi-input circuits in the effort toward advanced computing applications, the former remain an unsolved problem. Here, Guinn and Bleris (DOI: 10.1021/sb4001596), as a means of enabling the control of multiple outputs with a few inputs, introduce a genetic architecture that behaves as a biological decoder.

The authors built and characterized a genetic circuit capable of converting two chemical inputs into four unique outputs. The circuit consists of a five node system and utilizes a network of transcription factors and synthetic microRNAs to receive the inputs, process them and transduce the information into four measurable responses. The work presented here is the first implementation of a genetic decoder.

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