Title: A Tool-Chain to Accelerate Synthetic Biological Engineering

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There is a pressing need for design automation tools for synthetic
biological systems. Compared to electronic circuits, cellular
information processing has more complex elementary components with a
much greater complexity of interactions between components. Moreover,
chemical computation within a cell is strongly affected both by other
computations taking place within the cell and by the cell's native
metabolic processes and its external environment. All this adds up to
a design flow that is currently highly iterative, error-prone, and
extremely slow: critical problems that must all be addressed in order
to realize the potential of synthetic biology.

We have been developing a tool-chain approach to decomposing the
problems of design and assembly into automatable fragments.
Practitioners using our tool-chain will be able to design organisms
using higher level descriptions, which are automatically transformed
into genetic regulatory network designs, then assembled into DNA
samples ready for in vivo execution. At the same time, the tool-chain
is free and open software that will allow researchers to incorporate
their own design tools, thereby disseminating their results to the
community and enhancing the capabilities of the tool-chain.

The current prototype begins, at the top end, with the Proto spatial
computing language (Beal & Bachrach, 2006), which has a dataflow model
of parallelism that maps well onto the continuous parallel flow of
information through a genetic regulatory network (Beal & Bachrach,
2008). The biological compiler extension of Proto uses a motif-based
compilation system to translate high-level programs into an abstract
design for a genetic regulatory network for a boolean transcriptional
logic circuit (Beal et al., in review). Preliminary results with this
system show that it can translate compact representations of complex
information processing programs into genetic regulatory network
designs that perform correctly in ODE chemical simulation using a Hill
equation model.

These designs are then translated into DNA parts by the MatchMaker
system (Yaman et al., in review), which is integrated with Clotho, an

extensible framework for biological data integration and exchange (Densmore et al., '10). MatchMaker maps the design onto a set of available DNA parts using a constraint-based search for an equivalent interaction subgraph. The set of implementing DNA parts is then serialized into a final design, which is then fed to an assembly planner and will be able to be constructed from laboratory samples of DNA with the aid of a laboratory automation robot.

Preliminary end-to-end results from our prototype tool-chain are promising: the designs generated are equivalent to ones already being constructed in the laboratory to implement the same functionality. These results show the promise of a tool-chain approach to design automation for synthetic biology systems: design may be potentially accelerated by orders of magnitude through early fault detection (by simulation or verification analysis at each stage of the tool-chain), reduction of human error (by abstracting away details and routinizing more aspects of design), and application of AI techniques to automate exploration of the design space.