Quantitative Methods for Genetic Programming

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GENETIC programs are getting more sophisticated in the functions that they encode. I will describe the work that we are doing to increase the size and complexity of genetic programs. One problem is that there is a lack of fundamental simple genetic circuits that can easily be combined to construct programs. We have developed a simple genetic NOR gate that integrates multiple promoter inputs and turns on a promoter output. The gate is robust and can be layered by having the output promoter of one gate serve as the input promoter to the next gate. We have demonstrated that the inputs are outputs are modular and have used this gate to program colonies of *E. coli* to communicate to produce higher-order logic operations. We are applying directed evolution and synthetic metagenomics to identify orthogonal repressor-DNA operator pairs that can be used as the basis of multiple gates that can be used simultaneously as part of a design. Computational methods to optimize and connect genetic circuits are being developed based on biophysical methods that can map the DNA sequence of a genetic part to its function. Methods to apply models of ribosome binding sites, terminators, and promoters will be described in the context of the automated optimization of genetic programs. Finally, I will describe how we are retooling algorithms from asynchronous logic minimization to problems in the automated design of genetic programs.