Project Title: Robotic Automation of DNA Assembly
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The emerging field of synthetic biology is immensely exciting in that it gives us the power to arbitrarily reprogram biology with our own instructions and desires. Being able to load our own code into a living organism is not only cool, but gives us new tools for medicine, new platforms for computation, and interesting insight into our own living heritage. Synthetic biology however is still in its infancy – in order to realize such a futuristic dream of programmable biology, there are a few basic difficulties that need to be dealt with.

One of the biggest challenges facing the field is the issue of construction. That is, how do we physically assemble the DNA encoding genetic circuits that others have designed through computational simulation and rational analysis? The current techniques available are either not powerful enough or too expensive. DNA synthesis costs roughly half a dollar per base – this means that a small 1kb gene is on the order of $500 to order. While this may be reasonable for synthesizing single genes, ordering entire genetic circuits, which may involve ten or more genes, rapidly becomes cost prohibitive. Other techniques available to researchers, such as traditional cloning or even newer Gibson assembly approaches, are extremely time-consuming and require weeks to months of work for the assembly of a single construct.

This fall I plan on working in Dr. Weiss's lab on tackling this foundational problem of DNA construction. The proposed project is the design of a novel synthesis technique. Instead of standard cloning procedures, DNA is assembled through repeated ligation on top of magnetic beads. This removes the need for a lengthy purification step and shaves assembly time down from several weeks to a single day. Preliminary results show its effectiveness and in early fall we applied for a provisional patent on the technique through the TLO. Reliability of the technique however is still an issue, and we hope to improve consistency through repeated experimentation and protocol tweaking.

The other major aspect of this project is the complete automation of the assembly technique on a liquid handling robot. We hope to program the entire workflow onto the robot such that every step can happen autonomously. The dream is that a researcher can go from design straight to final DNA construct all without even leaving home – one click assembly from DNA design software sends all the necessary parameters to the robot, which then immediately begins all the lengthy and tedious steps necessary to build the final construct. Automation provides three major benefits: 1) speed – a robot can work around the clock unlike a human, which means that constructs are built in less time, 2) consistency – humans are prone to error in long tedious protocols whereas robots are not, and 3) yield – because a robot is both better performing and more consistent, longer and more complex genetic circuits can be assembled in a single run.

The potential in such an automated platform is enormous – if it works reliably, it helps bioengineering take a step in the direction of the more established engineering disciplines; the focus is on design, rather than the actual specifics of construction. The most complex biological circuit constructed to date involve only eight genes – this is an insignificant fraction compared to the billions of components in any modern electrical engineering design. Automation will hopefully allow us to build constructs up to tens or hundreds of genes

long, allowing us to construct more complex circuits and explore the vast potential offered by synthetic biology.

In addition to the main project, I will also be continuing in my supervisory and mentoring role over the MIT iGEM team as they prepare for their upcoming competition in November. The team conceptualized, designed, and built a novel bacterial touch screen over the summer, and have been frantically collecting results and characterizing the system over the fall. Helping to teach the team and watch their progress has been particularly rewarding, and I hope to see them succeed at the final competition.

The opportunity to work in Weiss lab on new DNA assembly techniques is very exciting – very rarely do students have the opportunity to define the foundational techniques and direction of an entire field. I hope to receive credit as part of my work on this radical redefining of how synthetic biology is performed. And regardless of the project outcome, working on this project will teach me a great deal in the design of complex genetic circuits and the construction of end-to-end integrated systems.