

## **Perspectives on Engineering Life**

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### **Background**

My research involves the design and construction of synthetic living systems, re-engineered organisms, and engineered parts for existing organisms. My group focuses on applications of synthetic biology ranging from cell-based diagnostics to microbial consortia that produce biofuels. Our particular emphasis is on designing gene circuits and cell-cell communication systems that enable novel multicellular behaviors in bacteria or yeast. In recent work<sup>1,2</sup>, we *ported* an entire signaling pathway from the plant *Arabidopsis* to the yeast *S. cerevisiae* making new parts and pathways available to synthetic biologists. We are currently building on this work to coerce yeast to behave cooperatively in a multicellular manner, with the aim to perform simple distributed computation. In other work<sup>3</sup>, we developed a method for tuning the spontaneous switching rate of a genetic switch, and are now building that work to develop sequential logic systems in cells<sup>4</sup> that could control them to divide the labor of digesting complex feedstock among specialized, synthetically differentiated cells.

### **The Industrialization of Biology**

Attempting to build on scientific results in the life sciences, synthetic biologists often find that even when a scientific result is valid, the methods are poorly explained, purposefully not explained, or simply buried in some researcher's head. My lab's Aquarium Project<sup>5</sup> aims to fix this problem by providing the means to specify, as precisely as possible, how to obtain a result. Researchers encode protocols as computer programs specifying how to manipulate items in the Aquarium inventory. Protocols are scheduled and presented to technicians on touchscreen monitors placed throughout the lab. Every step is logged: who performed the step, which items were used, and so on. The data can be used to debug and improve the experiment. More importantly it provides a complete, executable description of the results obtained -- one that could be used by any lab running Aquarium to reproduce the result. Systems such as Aquarium, for example embodied in companies such as *Emerald Cloud*, *Transcriptic*, and *Synthego*, clearly point toward a future in which the design and construction of new synthetic life is almost as routine as computer programming. The repercussions are staggering. What living programs will we write? Which ones should we avoid writing?

## The Ethics of Funding and the Principle of First Use

Coming from an engineering background (I was trained in computer engineering, robotics, and control systems), I have plenty of experience with the usual funding agencies that support engineering such as DARPA, AFOSR, and ONR. In fact, some of my early funding came from them. Since I started working on synthetic biology, however, I have become increasingly wary of DOD funding in this realm<sup>6</sup>. Synthetic biology will someday develop into an incredibly powerful technology that has obvious *dual-use* concerns. A common argument among researchers is that they do not care from whom their funding comes as long as it is out in the open. However, I have seen first hand that the context in which a new technology is first explored often determines its first use. For example, unmanned aerial vehicles were first explored in earnest by DOD programs with intense interest from the military, and their first successful use was in war. It is only later that drone technologies have started to become useful in other fields. The dangers of drones should not be understated, but they pale in comparison to a first use of synthetic biology in a warfare situation. Thus, it makes sense to first explore peaceful (for example therapeutic) applications of synthetic biology so that the discipline has a chance to mature before potentially dangerous applications are explored. I am intensely interested, then, in exploring first uses of synthetic biology in biofuels, diagnostics, global health, therapeutics, and the like.

## References

1. E. Pierre-Jerome, S. S. Jang, K. A. Havens, J. L. Nemhauser and E. Klavins, "Recapitulation of the forward nuclear auxin response pathway in yeast", *Proceedings of the National Academy of Science*. 2014.
2. K. Havens\*, E. Pierre-Jerome\*, S. Jang\*, J. Guseman\*, N. Bolten, E. Klavins, and J. Nemhauser, "A synthetic approach reveals extensive tunability of auxin perception", *Plant Physiology*. pp. 112.202184. July 2012.
3. R.G. Egbert and E. Klavins, "Fine-tuning gene networks using simple sequence repeats", *Proceedings of the National Academy of Science*. Vol. 109, No. 42. pp. 16817-16822. Oct 2012.
4. K. Oishi and E. Klavins, "A Framework for Implementing Finite State Machines in Gene Regulatory Networks", *ACS Synthetic Biology*. 3 (9), pp 652–665. 2014.
5. Aquarium. <http://klavinslab.org/aquarium.html>.
6. Hayden, E.C., "Bioengineers debate use of military money", *Nature*. Vol. 479. p. 458. Nov. 22, 2011.