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## Ed Boyden's blog

Ed Boyden is an assistant professor in the MIT Media Lab. His lab broadly invents new tools to engineer brain circuits, in order to treat intractable disorders, augment cognition, and better understand the nature of existence.

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Tuesday, October 09, 2007

### Synthetic Neurobiology


Toward abstraction layers for neuroengineering.

When you program a computer, you don't have to steer individual electrons around manually; if you did, the complexity of performing even the simplest calculation would be daunting. It's clear that building or fixing a complex thing requires a layer of abstraction, so you can solve the specific problem at hand while ignoring the underlying complexity. Problems of the brain must also be addressed at appropriate levels of abstraction. During the last week of September, I participated in a [neurotechnology panel at MIT](#). One theme quietly emerged: different neurological and psychiatric problems demand neural control technologies that operate over different spatial and temporal scales. Critical design choices must be made: do you go for an invasive, spatially focal neural stimulator or for a noninvasive but spatially cruder one?

Consider the question of how you might augment cognition and mood by stimulating selected neural circuits. You'd probably want maximum flexibility--the ability to tune mood, decision-making, judgment, and so on, independent of one another. Researchers have attempted to alter cognitive functions by noninvasive stimulation of cortical brain regions, each a few cubic centimeters in volume. It's become clear, however, that these brain regions are not the most elementary of brain circuit elements. For example, manipulation of one specific brain region can change many cognitive and emotional functions, in parallel. Consider the concrete example of [transcranial magnetic stimulation](#) (TMS) of the right prefrontal cortex. In the last few years, studies have shown that TMS of this brain region with a standard protocol (one pulse per second for 10 to 30 minutes) can [alter decision-making in the face of unfairness](#), [improve the symptoms of depression](#), and [increase risk-taking behavior](#). Thus, it may be difficult to induce a specific, desired brain state, without inducing other (perhaps undesired) brain states, when the primitives under consideration are all "brain regions." Clearly, this convenient abstraction layer, which has been prominent across centuries of neuroscience, will need to be refined in order to develop a fully flexible architecture for cognitive augmentation.

The hard part of neuroengineering is the "neuro" part. Our job is to sculpt neural-circuit activity so that it accomplishes a desired computation or behavior, without inducing alterations that are non-optimal. A few weeks back, Biological Engineering department chair Doug Lauffenburger declared to me, "What you're doing is synthetic neurobiology," drawing parallels

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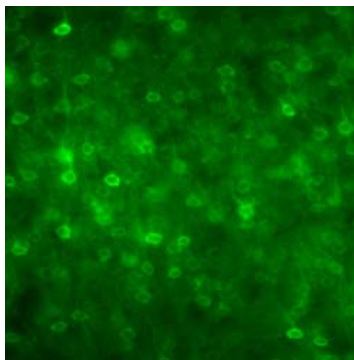
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between my lab's work and the work of labs that do synthetic biology. If you've been following the field of synthetic biology, you'll know that a major premise is the creation of abstraction layers for biological engineering. This agenda includes the development of standardized sets of basic engineering parts (i.e., standard pieces of DNA that encode precisely defined functions), and design rules for building complex systems out of similar ones (i.e., ways of connecting gene networks to accomplish desired organismal outcomes). By following the design rules, and using the standardized parts, biological engineers can create novel biological systems from scratch--systems that make sense and work in a predictable way.

In our lab, we have begun to assemble a toolbox of methods for precisely controlling specific neural-circuit primitives. We are now using these tools to learn how to control behavioral outputs, with great precision and power. Hopefully, in this way we will learn what the neurobiological primitives are for engineering the brain and develop design rules for the optimal control of neural-circuit output, especially in disease states. We're at an early stage. The synthetic biologists started off with the strong hypothesis that genes were the right abstraction layer. After all, the genome is fundamental, and DNA is easy to generate, manipulate, and read. But for neural computation, we don't know what the DNA equivalent is. Are the primitives dendritic elements? Single neurons? Synaptic connections? Cell types? Small networks? Large networks? And at what nervous-system scales should we be reading? Writing?



Light-controllable neurons. Credit: J. Cardin, X. Han, X. Qian, C. Moore, E. Boyden.

Most likely, the abstraction layer for synthetic neurobiology will vary greatly across the different neurological and psychiatric disorders for which we're engineering solutions. A key task in the years to come will be to develop a methodology for assessing the level of description appropriate for solving a specific problem. Although much of my lab's work is focused on controlling very specific neural-circuit elements, using pulses of light to turn individual cell types on or off with high precision, it's clear that very powerful tools can exist at much higher levels of abstraction. For example, [cognitive behavioral therapy](#), in which patients learn how to debug negative thoughts that contribute to depressed feelings, is a profound and powerful neurotechnology. And it is entirely based on language. Language-based neurotechnologies activate sets of neurons, distributed across the whole brain, in very precise patterns--and in ways that can cause changes capable of enduring throughout a lifetime. Language can induce precise changes in the brain that move people to happiness, teach them skills, lead them into war, and make them feel empathy or hatred or exhilaration. As John Hockenberry pointed out to me this past spring, language is the original brain interface. Perhaps the complexity of synthetic neurobiology arises from the fact that brain engineering is, in some ways, what we all do, all the time.

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Hey Ed,

I've been following your work since your days in Karl's lab at Stanford. I've sent my friend Sagar at MIT to talk and hopefully work with you.

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### [The basic elements?](#)

Is the basic unit a physical entity, or could it be a process? Candace Pert, Molecules of Emotion, talks about neurotransmitters and their behaviour as the essential link between brain, conscious processing - language - and physiological functioning, via the immune system. Maybe that is where to look, rather than the physical units of neurology. (When people say it is foolish to think that words can affect physiological functions, I ask them to imagine they are on a plane, hearing a request to prepare for an emergency landing. Just words.)

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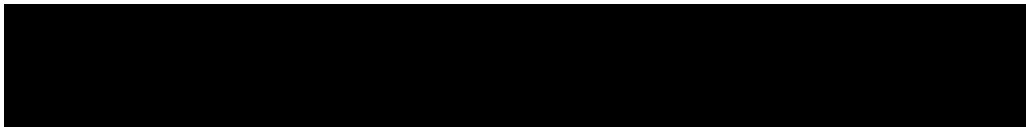
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