

THE AUTHOR FILE

David Kleinfeld

Measuring neurotransmitter concentration, letting lab meetings run free, and why biology does not own neuroscience.

Just a few failures could send him back to Brooklyn, likely its unhip section, where he would be a server at



David Kleinfeld

the local ice cream parlor, jests David Kleinfeld from the University of California at San Diego (UCSD). He holds appointments in the physics, neurobiology, and electrical and computer engineering departments.

In their newest work, Kleinfeld and his colleagues address how to better measure learning-related neurotransmitter release in the brain *in vivo*.

Cyclic voltammetry, which translates the loss or addition of an electron into a voltammetric readout, was an option. But dopamine and norepinephrine release, which are both connected to learning, have the same voltammetric signatures.

Instead, the scientists expanded the range of neurotransmitters that their implantable engineered cell lines could sense, tweaking these cell-based neurotransmitter fluorescent engineered reporters (CNiFERs) to detect dopamine and norepinephrine. The team hopes to grow the CNiFER family for many neurotransmitters.

Here, they conditioned mice to associate a task with a reward of sweetened water. Classic experiments have shown that conditioned animals have heightened neuronal firing rates and dopamine release in the cortex. The researchers could measure how much dopamine is secreted and found that the release lasts for ten seconds. Dopamine levels vary as learning progresses and with the mouse's anticipation of reward. More experiments will reveal whether learning involves, as reinforcement theory suggests, an analog type of neurotransmitter release or whether it is more sudden and digital, as Gestalt psychologists believe.

For a physicist, Kleinfeld says, research on the brain is the most interesting possible activity. "I think the notion that biology 'owns' neuroscience is wrong," he says. Neuroscience is about behavior, communication and control. New techniques to study the circuitry underlying behavior link the field back to early neuroethology and control theory.

Kleinfeld received his PhD in physics at UCSD. His postdoctoral fellowship at AT&T Bell Laboratories led

to a decade there as a staff researcher. "There were some great discoveries when I was there," he says, mentioning the first single-molecule measurements and the bending of light as evidence for dark matter.

He enjoys teaching at UCSD, Cold Spring Harbor Laboratory (CSHL) and the Marine Biological Laboratory (MBL). He took the summer MBL neurobiology course and later taught it with colleague Partha Mitra, a CSHL researcher, for more than a decade. "I think David has helped educate a whole generation of neuroscientists in quantitative thinking and has always been generous with his time," says Mitra. When a technical question pops up about neuronal biophysics or recording or imaging methods, Kleinfeld is the person Mitra turns to. He trusts Kleinfeld's judgment and scholarship and the way he reasons rather than argues from authority.

Kleinfeld values and fosters close friendships with colleagues. "The best ideas come out of discussions," he says. "Sometimes I think that I get an idea on my own," he says, but fears that he may be free-associating from a past conversation and forgetting to give someone credit. Weekly, he lunches with UCSD colleagues who study condensed matter physics. "Not that I want to work on rocks—but there are bizarre quantum materials out there, and keeping abreast of this stuff is a good counterbalance to neuroscience," he says.

In the electrical and computer engineering department, he is helping to set up a new program on bioelectric signals. In the neurobiology department, he never misses the weekly faculty presentations.

He styles his own lab meetings as "free-running" events in which the discussion after a presentation can last a few hours. The approach, which lets everyone ask questions or add ideas, is inspired by George Feher, Kleinfeld's thesis advisor.

Beyond teaching, running a lab, writing grants, reviewing papers, and building and fixing equipment, Kleinfeld likes to swim and hike. He voraciously reads the news and, he says, everything by Tom Wolfe. "My wife and I try to get out to plays," he says. "San Diego has some great theater."

Feher also suggested publishing either the first paper or the definitive paper on a topic. "It does not always happen, but it is a goal," says Kleinfeld. Papers should contain impeccable data, he says, but researchers should remember that discussions and models may prove to be wrong. "And write well," he says. "Consider each manuscript as a piece of art—it is a record of your career."

Vivien Marx

Muller, A. *et al.* Cell-based reporters reveal *in vivo* dynamics of dopamine and norepinephrine release in murine cortex. *Nat. Methods* **11**, 1245–1252 (2014).

"Consider each manuscript as a piece of art..."