

expertise to thousands of scientists worldwide. He was elected to the Institute of Medicine in 2010 and to the National Academy of Sciences in 2012, and selected as a Howard Hughes Medical Institute Investigator in 2013. For developing and applying optogenetics and CLARITY, Deisseroth has received the NIH Director's Pioneer Award (2005), the Zuelch Prize (2012), the BRAIN prize (2013), the Pasarow Prize (2013), and the Perl Prize (2012), and among other awards, was the sole recipient of the 2010 Koetser Prize, the 2010 Nakasone Prize, the 2011 Alden Spencer Prize, the 2013 Richard Lounsbery Prize, and the 2014 Dickson Prize in Science.

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**KARL DEISSEROTH, M.D. Ph.D.**

OPTICAL DECONSTRUCTION OF  
FULLY-ASSEMBLED BIOLOGICAL SYSTEMS

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FEBRUARY 20, 2014  
4:00 P.M.  
208 LIGHT HALL

Upcoming Discovery Lecture:

RICHARD LIFTON, M.D., Ph.D.  
*Yale University*

*March 6, 2014*  
*208 Light Hall / 4:00 P.M.*

VANDERBILT  UNIVERSITY  
MEDICAL CENTER

## OPTICAL DECONSTRUCTION OF FULLY-ASSEMBLED BIOLOGICAL SYSTEMS

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Karl Deisseroth's research group develops optical tools for precise, high-resolution investigation of intact biological systems, and applies these tools to study the neural circuit underpinnings of adaptive and maladaptive behavior; he also continues to practice psychiatry and direct undergraduate education in Bioengineering at Stanford University. Over the past decade his laboratory created and developed both optogenetics (a technology for precisely controlling millisecond-scale activity patterns in specific cell types using microbial opsin genes and fiberoptic-based neural interfaces<sup>1,2</sup>) and CLARITY (a technology to optically resolve high-resolution structural and molecular detail within intact tissues without disassembly). Most recently in optogenetics, his team has developed strategies for targeting microbial opsins and light to meet the challenging constraints of the freely-behaving mammal, engineered a panel of microbial opsin genes spanning a range of optical and kinetic properties, built high-speed behavioral and neural activity-readout tools compatible with real-time optogenetic control, disseminated the tools to thousands of investigators, and applied these optogenetic tools to develop circuit-based insight into anxiety, depression, and motivated behaviors<sup>3,4</sup>. Distinct from optogenetics, his CLARITY technology<sup>5</sup> can be used to transform intact biological tissue into a hybrid form in which components are removed and replaced with exogenous elements, resulting in a transparent tissue-hydrogel that both preserves, and makes accessible, structural and molecular information for visualization and analysis. With CLARITY, whole mouse brains have now been labeled and imaged, and molecular markers have been used to identify individual structures and projections in banked human brain tissue, thereby unlocking rich sources of information for probing disease mechanisms as well as the native structure and complexity of the nervous system<sup>5</sup>, in a manner complementary to optogenetic approaches<sup>6</sup>.

<sup>1</sup> Deisseroth K (2010). Optogenetics: controlling the brain with light. *Scientific American* 303(5): 48-55.

<sup>2</sup> Deisseroth K (2011). Optogenetics. *Nature Methods*, 8:26-9.

<sup>3</sup> Kim SY, Adhikari A, Lee SY, Marshal JH, Kim CK, Mallory CS, Lo M, Pak S, Mattis J, Lim BK, Malenka RC, Warden MR, Neve R, Tye KM & Deisseroth K (2013). Assembling behavioral states: divergent neural pathways recruit separable anxiety features. *Nature* 496:219-23.

<sup>4</sup> Warden M, Selimbeyoglu A, Mirzabekov J, Lo, M, Thompson K, Kim S, Adhikari A, Tye K, Frank L & Deisseroth K (2012). A prefrontal cortex-brainstem projection controlling response to behavioral challenge. *Nature* 492:428-32.

<sup>5</sup> Chung K, Wallace J, Kim S, Kalyanasundaram S, Andalman A, Davidson T, Mirzabekov J, Zalocusky K, Mattis J, Denisin A, Pak S, Bernstein H, Ramakrishnan C, Grosenick L, Gradinaru V & Deisseroth K (2013). Structural and molecular interrogation of intact biological systems. *Nature* 497:332-7.

<sup>6</sup> Deisseroth K (2014). Circuit dynamics of adaptive and maladaptive behaviour. *Nature* 505:309-17.

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### **KARL DEISSEROTH, M.D. Ph.D.**

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**INVESTIGATOR, HOWARD HUGHES MEDICAL  
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Karl Deisseroth is the D.H. Chen Professor in the Bioengineering and Psychiatry Departments at Stanford, and is a practicing inpatient and outpatient psychiatrist, employing medications and interventional brain stimulation techniques (VNS, TMS and others) to treat patients with psychiatric disease. He received his bachelor's degree from Harvard in 1992, his PhD from Stanford in 1998, and his MD from Stanford in 2000. He completed postdoctoral training, medical internship, and adult psychiatry residency at Stanford, and he was board-certified in 2006 by the American Board of Psychiatry and Neurology. Deisseroth led the development and application of optogenetics: the integration of genetics and optics to achieve gain- or loss-of-function of well-defined events (such as action potential patterns) in defined cell types within intact biological systems. He also led the development of CLARITY, a chemical engineering-based method for transforming biological systems by creating a tissue-hydrogel hybrid, to allow full transparency and accessibility to molecular labels without slicing or sectioning; CLARITY enables high-throughput whole brain analysis of wiring and fine structure without disassembly. He has also led both basic science and disease-focused work employing optogenetics and CLARITY, with investigations into aspects of Parkinsonism, anxiety, social dysfunction, depression, and other neuropsychiatric disease symptoms. Deisseroth also serves as Director of Undergraduate Education in Bioengineering at Stanford, teaches yearly courses in the graduate and undergraduate curricula, and provides education and training in optogenetics and CLARITY as well as freely distributing and supporting tools and

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