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Editorial

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The BRAIN Initiative: Toward a Chemical Connectome

On April 2, 2013, I had the honor of visiting the White House for President Obama's announcement of the BRAIN Initiative (Brain Research through Advancing Innovative Neurotechnologies; http://www.whitehouse.gov/infographics/brain-initiative). Earlier dubbed the BAM (Brain Activity Map) Project, this multiyear nationwide effort has been renamed to reflect its emphasis on technology, and particularly nanotechnology.[1] Developing advanced technologies is expected to lead to new ways of investigating complex problems associated with understanding brain function. As it was originally conceived, the BAM Project was focused on creating large-scale functional maps of brain activity in the form of simultaneously measuring action potentials or intracellular Ca^{2+} concentrations from large numbers of interconnected neurons.[2] The development and use of recording and imaging technologies for massively parallel measurements was envisioned to lead to large data sets that could be used by neuroscientists and computational scientists to uncover emergent properties associated with neuronal circuitry. The objective was to advance fundamental understanding of how information is encoded in brains.

Focusing solely on neuronal electrical activity is shortsighted if the goal is to understand information processing in brains. Brain function integrally entails complex synaptic chemistries. These chemistries are maintained at enormous costs in terms of protein synthesis, for example, neurotransmitter synthetic and degrading enzymes, synaptic machinery for exocytosis, and diverse receptor proteins. Energy requirements needed to maintain membrane potentials, which drive reuptake of synaptic transmitters, in addition to action potentials, are also costly from a biological perspective. The trade-off is a chemical diversity that provides for tremendous richness in terms of the information content inherent in interneuronal signaling. Chemical signaling underlies G-protein-coupled receptors (GPCRs) and their effects on circuitry remodeling but also ligand-gated ion channels and direct effects of GPCRs on membrane excitability. Thus, a BRAIN Initiative that envisions that emergent properties will be uncovered simply by measuring action potentials of ever increasing numbers of neurons without taking into consideration information inherent (and currently unknown) in complex chemical signaling is grossly oversimplified.

Information processing in brains ultimately also resides in dynamic changes in neurotransmitter diffusion gradients combined with spatially complex and tightly controlled patterns of receptor protein expression. This special issue of *ACS Chemical Neuroscience* arises from the biennial International Society of Monitoring Molecules in Neuroscience Meeting (http://www.monitoringmolecules.org/), which was most recently held in September 2012 in London. The issue provides timely and poignant reminders of the central roles played by chemical neurotransmission in brain function, dysfunction, and the treatment of disorders. On the whole, the issue highlights how far we have come in terms of our understanding of chemical signaling but also how far we have yet to go.

New tools fuel fundamentally new conceptualizations. By and large, today's approaches for sensing neurotransmitters are not able to approach chemical neurotransmission at the scales that will ultimately be important for uncovering emergent properties. Likewise, most methods are not highly multiplexed such that the interplay of multiple chemical transmitters can be unraveled. In addition to measuring electrical activity at hundreds or thousands of neurons simultaneously, we need to advocate for a large-scale multidisciplinary effort aimed at in vivo nanoscale chemical sensing.[3] This vision entails developing chemical sensors that are small (recording at the level of synapses), fast (on par with time frames of release/reuptake), chemically selective (can readily distinguish among closely related neurotransmitters), and multiplexed (record changes in multiple neurotransmitters simultaneously). As we celebrate our current accomplishments in elucidating molecular mechanisms of chemical neurotransmission featured in this month's issue of *ACS Chemical Neuroscience*, I invite you to look toward the future. The editors at *ACS Chemical Neuroscience* welcome your views on developing a vision for a chemical connectome. We look forward to publishing your advances in understanding chemical transmission. The International Society for Monitoring Molecules in Neuroscience Meeting similarly welcomes your input and participation regarding programming for its upcoming meeting, which will be held at the University of California, Los Angeles in the summer of 2014.

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AUTHOR INFORMATION

Notes

Views expressed in this editorial are those of the author and not necessarily the views of the ACS.

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