nature neuroscience

Focus on neurotechniques

***Nature Neuroscience* presents a focus highlighting recent technical advances in neuroscience.**

In the past five years, the number of abstracts describing new methods or technology development that were presented at the annual Society for Neuroscience meeting increased by nearly 50 percent. As neuroscientists capitalize on recent technological innovations, they stand poised to make unprecedented progress. In this issue, we present an array of review articles sampling some of the most exciting recent advances in techniques used across the field of neuroscience.

One area in which a technological advance has opened new avenues has been the application of pluripotent stem cells to study neurodegenerative disease. Recent work has made it possible to produce human neurons of the types most susceptible to disease and traumatic injury, and, using source material from patients, researchers can potentially examine neurons with predisposing mutations. On page 780, Jackson Sandoe and Kevin Eggan discuss the opportunities and challenges that arise from the use of pluripotent stem cell neurodegenerative disease models and suggest potential strategies for avoiding these caveats.

Microscopy has historically provided substantial insight into the nervous system and recent advances have extended its power, allowing scientists to observe circuits, neurons and molecules at ever-greater resolution. Light microscopy has many advantages, but, until recently, the resolution has not been sufficient to characterize the substructures of neurons. In their Review on page 790, Stephan Sigrist and Marta Maglione discuss the recent emergence of super-resolution light microscopy, which allows for high-resolution dynamic imaging in the 10–100-nm range. Sigrist and Maglione focus on the advances in our understanding of neuronal compartments these techniques have provided in recent years. Before there was super-resolution light microscopy, however, electron microscopy was the go-to technique and for some applications it remains the gold standard. In particular, the ability to determine the subcellular localization of proteins with immunogold cytochemistry and electron microscopy continues to provide valuable insights. On page 798, Ole Petter Ottersen and Mahmood Amiry-Moghaddam discuss immunogold techniques, including their limitations and possible pitfalls. The combination of these different types of microscopy promises to be particularly powerful in the future.

However, neuroscientists are no longer limited to observing neurons, as techniques for manipulating neuronal activity have arrived. Early applications of optogenetics were relatively imprecise, but in a Review on page 805, Adam Packer, Botond Roska and Michael Häusser discuss the myriad combinations of optical, anatomical and genetic strategies that can currently be used to more specifically manipulate neuronal activity with light. The authors discuss the challenges and opportunities provided by these techniques to achieve spatially selective and temporally precise control of electrical activity in specific neural circuits, individual cells or subcellular compartments. They also offer their perspective on how harnessing the full potential of optogenetics will help us master functional circuit mapping and yield new insights into the nature of the neural code.

The advances in optical neuroscience are not confined to just optogenetics. Chemical tools for optopharmacology enable manipulation of endogenous signaling proteins. On page 816, Richard Kramer, Alexandre Mourot and Hillel Adensik discuss advances in developing new tools in optopharmacology or photosensitive reagents that act on receptors on channels that allow precise control. The authors also discuss advances in optogenetic pharmacology, combining optics, chemistry and genetics to attach a synthetic photosensitive ligand onto a genetically engineered protein to allow activation or inhibition of only that specific protein with light, discussing the limitations, challenges and advantages of these technologies.

Optical techniques for manipulating neuronal activity rely on genetic and pharmacological interventions that are well matched to the life cycle of the rodent. As a result, mice and rats have become the animal model of choice for many laboratories studying the neural basis of perception and behavior. Traditionally, rodent behavioral tasks have been far simpler than those used for primates, but on page 824, Matteo Carandini and Anne Churchland discuss the potential for doing more sophisticated studies in mice and rats. The authors provide an overview of rodent sensory capabilities and review the methods of psychophysics that can be used to explore perceptual decisions, focusing on the technical issues that arise in their implementation in rodents.

Recent technology also offers the opportunity to manipulate human brain activity non-invasively, using transcranial magnetic stimulation and transcranial direct current stimulation. On page 838, Leonardo Cohen, Eran Dayan, Nitzan Censor, Ethan Buch and Marco Sandrini provide a thorough overview of the mechanisms and limitations of these techniques. They also discuss ways to move the field forward, by combining various techniques to uncover global brain dynamics.

Although functional magnetic resonance imaging (fMRI) has long been used to examine changes in brain activity, it has more recently been applied to make inferences about the underlying neuronal networks. On page 832, Randy Buckner, Fenna Krienen and B.T. Thomas Yeo critique the use of functional connectivity data to derive measures of anatomical connectivity and changing brain dynamics. They discuss what information these analysis techniques can and cannot provide, what constrains the interpretation of such studies, and their potential uses.

The techniques described in this focus represent some of the newest approaches that are currently available for exploring the nervous system. However, this is likely to be only the beginning of a technological transformation in neuroscience. With the recent announcement of the BRAIN project (Brain Research through Advancing Innovative Neurotechnologies), more innovation surely lies ahead. We look forward to the exciting new results to come, as researchers push the frontiers of neuroscience. ■