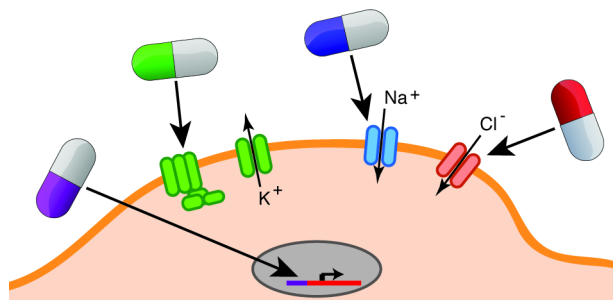


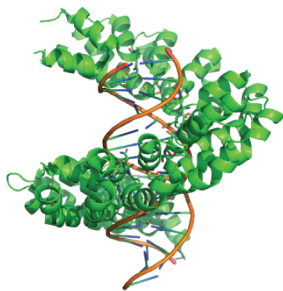
NEW APPROACHES TO CONTROLLING NEURAL ACTIVITY



The control of neural activity with spatial and molecular precision poses a great technological challenge. Previous methodologies modulated neural activity using pharmacology or electrical stimulation which lacked either spatial or molecular control. In this issue, Shapiro et al. (DOI: 10.1021/cn300053q) review some of the latest technological advances in the pursuit of accurately regulating neural activity.

The authors critically assess contemporary approaches which utilize the genetic alteration of neurons that are then controlled via specific small molecules. Importantly, these small molecules do not hinder normal central nervous system function. The authors weigh the pros and cons of using these “orthogonal pharmacogenetic” tools for studying brain function.

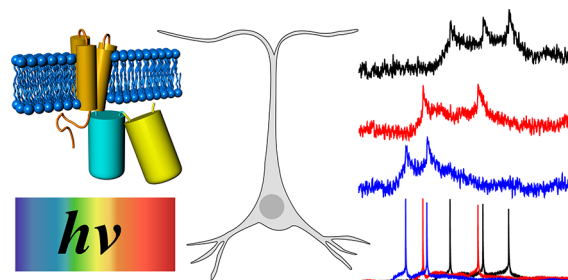
EXAMINING EPIGENETIC DYNAMICS UNDERLYING NEURONAL FUNCTION



Advances in analyzing patient genomes have led to the discovery of genetic mutations implicated in neurological disease. However, understanding the genetic basis of these diseases is difficult. Hsu and Zhang (DOI: 10.1021/cn300089k) summarize some of the latest developments in genome engineering technologies and their application to examining epigenetic dynamics underlying neuronal function.

The authors describe the use of designer DNA-binding proteins based on transcriptional activator-like effectors and zinc finger proteins that are engineered to precisely mutate a specific gene. In the future, designer nucleases may be used for direct gene correction in cases of neurodegenerative genetic disorders that are caused by a small set of mutations.

GENETICALLY ENCODED FLUORESCENT VOLTAGE INDICATORS



The brain contains an intricate network of neurons. To understand nervous system function and underlying complex behaviors, it is important to understand electrical signal fluctuations within neuronal circuits and their larger structures. In this issue, Mutoh et al. (DOI: 10.1021/cn300041b) provide an overview of a newer, superior class of reporters designed to study the dynamics of electric signaling in the brain.

The authors focus their review on the reasons for developing genetically encoded fluorescent voltage indicators (GEVIs) while pointing out the drawbacks of the classic voltage-sensitive dyes. The review summarizes four general approaches for GEVI design and critically evaluates each methodology. Finally, existing and emerging applications of GEVIs are discussed.

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