ACS Chemical Neuroscience

IN THIS ISSUE

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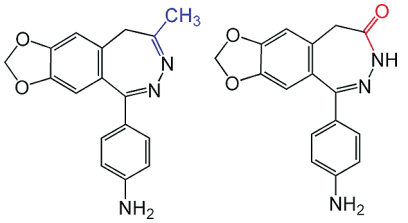
Mechanism of AMPA Receptor Inhibition



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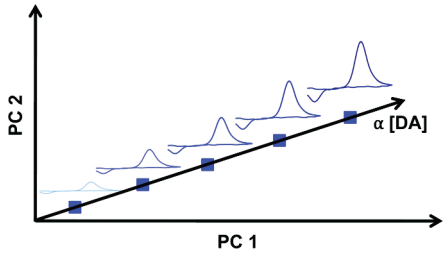
The α-amino-3-hydroxy-5-methyl-4-isoazolepropionic acid (AMPA) receptors are a class of ionotropic glutamate receptors. Malfunction of these receptors can lead to neurological disorders such as amyotrophic lateral sclerosis, epilepsy, and stroke. Targeting unusually high AMPA receptor activity is a vigorous area of research in treating these disorders. In this issue, Ritz et al. (DOI: 10.1021/cn200033j) provide important mechanistic insight into the mechanism of the best known class of AMPA receptor inhibitors.

To date, 2,3-benzodiazepines are considered to be the most potent and selective inhibitors of AMPA receptors. How these compounds act on AMPA receptor channel opening, however, is unclear. To address this lack of mechanistic insight, the authors studied the structure−activity relationships of two 2,3-benzodiazepines that differed by a carbonyl substitution for a 4-methyl group in the diazepine ring. The effect of these two compounds was characterized on the GluA2Q_{flip} AMPA receptor. Each compound was found to bind to its own independent noncompetitive site and inhibited different conformational states of the receptor. The mechanistic insight gained from this study has significant broader implications in designing new and more potent drugs targeting AMPA receptors.

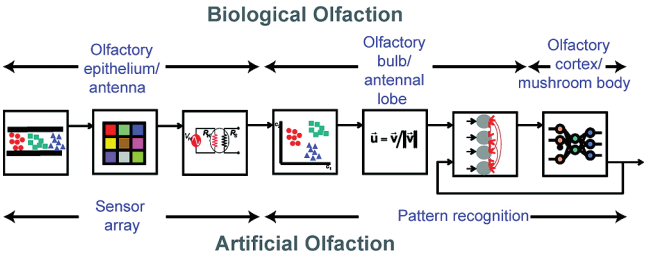
Predicting Concentration Flux for Neuromodulators



Fast-scan cyclic voltammetry (FSCV) is a widely used method of determining electroactive neuromodulator concentrations in vivo. Since this technique produces unique signature cyclic voltammograms for an individual neurochemical analyte, FSCV can also be used to identify and study concentration changes of specific neuromodulators with high spatiotemporal resolution. The analysis of these data is typically conducted via principal component regression (PCR), a chemometric technique for predicting concentration flux in FSCV experimental data sets. In this issue, Keithley and Wightman (DOI: 10.1021/cn200035u) assess calibration methodology associated with PCR and provide tools to improve this approach for neuromodulator concentration prediction in FSCV experimental data sets.

The authors provide examples of concentration prediction errors arising from PCR data analysis for FSCV experiments conducted in vivo that may limit the use of this approach. They also provide several tools to improve this methodology such as improved graphical representation of calculated regression vectors and the use of Cook's distance for removal of outliers in data sets. Additionally, the authors address electrode drift, which can result in significant concentration prediction errors. Thus, this article provides tools and guidelines for more accurate prediction of concentration changes of neurochemical signals.

Recent Advances in Artificial Olfaction



The olfactory system helps organisms detect and respond to volatile environmental chemical stimuli. Given the importance of scent in society, culture, and everyday life inherent in activities ranging from appetite stimulation to sensing potential threats, the development of artificial olfaction has received significant interest. However, creating an artificial device to mimic the natural perception of odor remains elusive. In the current issue, Raman et al. (DOI: 10.1021/cn200027r) summarize some of the latest developments in developing an artificial olfaction system.

The creation of an "electronic nose" has derived much of its inspiration from closely related chemosensory systems in place for most mammals and insects. Artificial identification of different odors relies upon an array of detectors that recognize separate chemicals. These data are fed into a recognition module that identifies the chemical signatures of the stimulus. Engineering a system to solve such a complex puzzle is fraught with technical challenges. In this article, the authors assess the latest biological advances and computational principles that may lead to a breakthrough in artificial olfaction.

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