ACS Chemical Neuroscience

In This Issue

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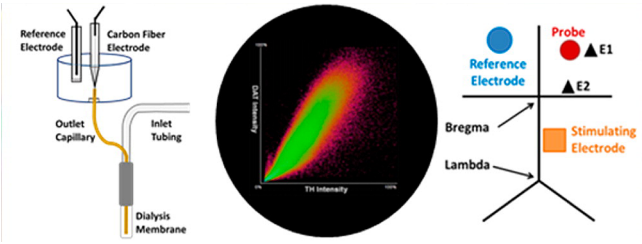
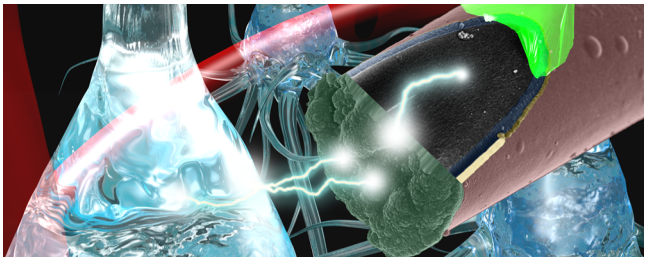
## REFINING INTRACRANIAL MICRODIALYSIS




The benefits of microdialysis for chemical monitoring are well documented. However, the implanting of microdialysis probes into the brain causes tissue damage, which consequently causes neurochemical instability. In an effort to overcome this problem, Nesbitt et al. (DOI: 10.1021/cn500257x) resort to an anti-inflammatory drug, dexamethasone, to mitigate the effects of tissue disruption.

The authors use fast-scan cyclic voltammetry to measure evoked dopamine responses in tissue surrounding microdialysis probes. These are compared to dopamine responses recovered by microdialysis probes. They highlight the ability of dexamethasone to stabilize dopamine recovery over 24 h without altering the actual responses. The anti-inflammatory actions of dexamethasone are confined to the local vicinity of the probe. Immunohistochemistry showed that dexamethasone had little effect on the dopamine terminal markers, tyrosine hydroxylase, and the dopamine transporter. These results indicate that dexamethasone works to stabilize evoked dopamine responses by suppressing inflammation as opposed to having a neurochemical effect on dopamine terminals themselves.

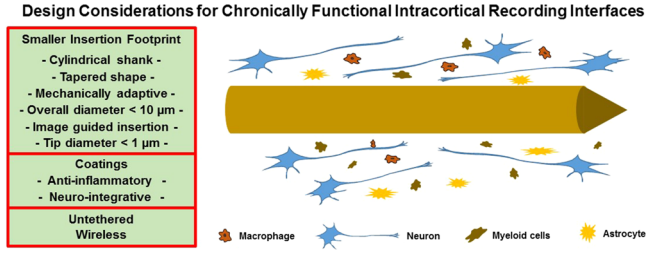
## BRAIN TISSUE RESPONSES TO NEURAL IMPLANTS



Implantable neural electrical and chemical recording devices have greatly enhanced our understanding of brain function and the pathology of brain injuries and disorders. While several significant advances have been made in the field, work remains to be done to prolong long-term function of these devices as well as to improve and refine these technologies. In this review, Kozai et al. (DOI: 10.1021/cn500256e) focus on implantable devices, namely, microdialysis probes, microfabricated biosensors, and carbon-fiber electrodes, and their impact on brain function and chemical environment.

The authors briefly describe common performance issues and then discuss the sources of variability and potential mitigation strategies. These intervention strategies hold great promise for improving both the long- and short-term stability of implants and further facilitating the study of memory, plasticity, and behavior, or monitoring patient condition.

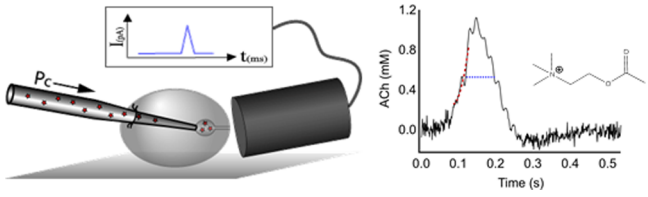
## BRAIN MACHINE INTERFACES AND THE FOREIGN BODY RESPONSE




Spinal cord injuries and neurodegenerative diseases can lead to adverse outcomes such as paraplegia or tetraplegia. A number of methods are used to rehabilitate patients suffering from these conditions with the ultimate goal of returning volitional movement. In the current issue, Gunasekera et al. (DOI: 10.1021/cn5002864) discuss the recent design and technological innovations in brain–computer interface function and their role in facilitating control of external assistive devices such as a prosthetic limb.

The authors review the recent advances in the field of intracortical neural interfacing by providing details on the different types of neural interfaces currently available, their applications, and materials used in fabrication. Additionally, the authors offer up-to-date information on mechanisms that contribute to intracortical recording interface failure. The recent advances in this field are noteworthy, and issues related to recording failure will be of interest to scientists using other intracortical neural implants to study a wide range of other brain disorders such as epilepsy, Parkinson's disease, mood disorders, and pain management.

## DETECTING RELEASE EVENTS FOR ACETYLCHOLINE AT THE MILLISECOND TIME SCALE




Electrochemical methods such as amperometry and cyclic voltammetry that provide high temporal resolution and quantitative information on neurotransmitter release have been widely used in single cell studies and in vivo recordings to gain a better understanding of the fundamental aspects of the exocytosis machinery at secretory cells and the dynamics of neuronal activity. However, these electrochemical techniques are limited to measurements of electroactive molecules. For non-electroactive signaling molecules such as acetylcholine, there are optical and electrochemical detection schemes to detect acetylcholine indirectly using a two-enzyme system comprising acetylcholinesterase and choline oxidase. Here, hydrogen peroxide is produced as a secondary detectable catalytic product.

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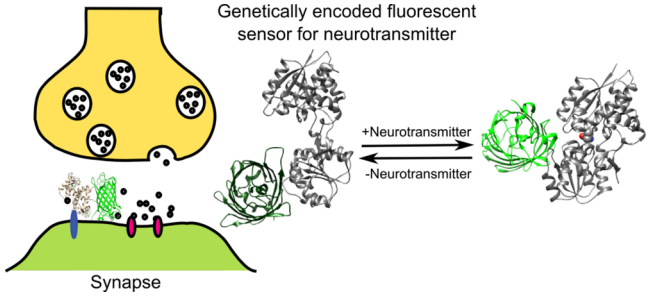
However, there is currently no biosensor sensitive enough to detect release of nonelectroactive neurotransmitters, such as acetylcholine from single cells. In the current issue, Keighron et al. (DOI: 10.1021/cn5002667) report a new approach for an acetylcholine biosensor design to overcome this drawback.

It is known that using nanoparticles on sensor surfaces reduces enzyme denaturation while increasing sensor surface areas. The authors used an optimized enzyme stoichiometry of acetylcholine esterase and choline oxidase for placement onto gold nanoparticles on electrode surfaces to achieve the highest sequential enzymatic activity. Importantly, by carefully controlling the thickness of the enzyme layer placed onto the electrode surface (close to a monolayer coverage of enzyme), the authors minimized the loss in time response by diffusion of analytes from enzymes to the electrode surface. This resulted in improved temporal resolution by more than 100 compared to other existing enzyme-based electrochemical sensors.

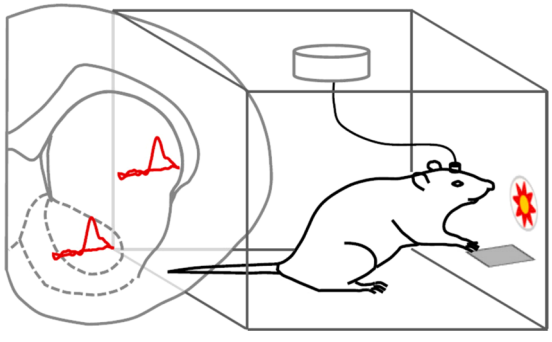
## GENETICALLY ENCODED PROBES FOR NEUROTRANSMITTER DYNAMICS




More than 100 neurotransmitters and neuromodulators exist in the brain. Alterations in the dynamics of these molecules have been linked to neurological and psychiatric diseases. In the current issue, Liang et al. (DOI: 10.1021/cn500280k) review approaches and probes to track neurotransmitters that will provide much-needed insight into the mechanisms underlying the dynamics of these molecules in the brain.

The authors discuss approaches and probes to determine the spatial and temporal extent of neurotransmitter dynamics in the brain, including voltammetry, microdialysis, PET, MRI, and fluorescent microscopy. The methods are compared to several genetically encoded fusion protein constructs that are capable of reporting glutamate release in live cells. The advantages of genetically encoded sensors are delineated, and future design strategies for making sensors for other neurotransmitters are discussed.

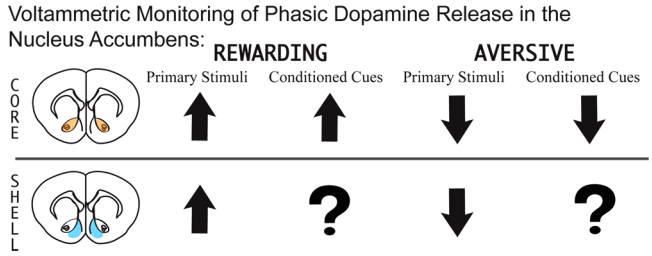
## VARIATION IN PHASIC DOPAMINE RELEASE DURING ALCOHOL AND SUCROSE SELF-ADMINISTRATION



Alcohol use disorder (AUD) affects approximately 7.2% of the adult population in the United States. While the exact mechanisms leading to excessive alcohol intake remain unknown, it has been suggested that control over alcohol consumption shifts from the prefrontal cortex and ventral region of the striatum to the dorsal/dorsolateral striatum, with increased drinking. Here, Shnitko and Robinson (DOI: 10.1021/cn500251j) investigate the neurochemical mechanisms of AUD, focusing on how phasic dopamine release in the dorsal and ventral striatum encodes alcohol seeking.

The authors evaluate dopamine signaling in the dorsal striatum during alcohol-seeking behavior based on a habit-promoting schedule of reinforcement that models cognitively inflexible behavior driven by alcohol-related stimuli. Using fast-scan cyclic voltammetry, they measured real-time, phasic dopamine release in the dorsomedial and dorsolateral striatum, and the nucleus accumbens core during alcohol and sucrose self-administration in rats. The results of the study suggest that phasic dopamine release in the dorsolateral striatum encodes reward-predictive cues, as those stimuli would trigger the response to consume reward. Additionally, it is seen that dopamine transients in dorsal striatum are amplified in rats drinking alcohol compared to those drinking sucrose.

## A ROLE FOR PHASIC DOPAMINE RELEASE IN ENCODING AVERSION




Mesolimbic dopamine has long been shown to underlie reward-seeking and appetitive behavior in vertebrates. However, its role in aversion and avoidance behavior remains unclear. In this review, Wenzel et al. (DOI: 10.1021/cn500255p) describe how advances in electrochemistry are providing otherwise invisible details regarding the role of mesolimbic dopamine in the process of aversion.

The authors attempt to clarify the issue of dopamine involvement in the coding of aversive stimuli by reconciling evidence from different studies. They review existing electrophysiological and electrochemical literature and report an alternative view of dopamine neuron function, one where both positive and negative stimuli modulate accumbal dopamine release and promote adaptive behaviors.



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