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INVITED REVIEW

# Advanced real-time recordings of neuronal activity with tailored patch pipettes, diamond multi-electrode arrays and electrochromic voltage-sensitive dyes

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## Abstract

To understand the working principles of the nervous system is key to figure out its electrical activity and how this activity spreads along the neuronal network. It is therefore crucial to develop advanced techniques aimed to record in real time the electrical activity, from compartments of single neurons to populations of neurons, to understand how higher functions emerge from coordinated activity. To record from single neurons, a technique will be presented to fabricate patch pipettes able to seal on any membrane with a single glass type and whose shanks can be widened as desired. This dramatically reduces access resistance during whole-cell recording allowing fast intracellular and, if required, extracellular perfusion. To simultaneously record from many neurons, biocompatible probes will be described employing multi-electrodes made with novel technologies, based on diamond substrates. These probes also allow to synchronously record exocytosis and neuronal excitability and to stimulate neurons. Finally, to achieve even higher spatial resolution, it will be shown how voltage imaging, employing fast voltage-sensitive dyes and two-photon microscopy, is able to sample voltage oscillations in the brain spatially resolved and voltage changes in dendrites of single neurons at millisecond and micrometre resolution in awake animals.

**Keywords** Patch clamp · Fast cellular perfusion · Multi-electrode recording · Diamond sensors · Voltage-sensitive dyes · Two-photon microscopy

## Introduction

One of the outstanding features of the nervous system is the electrical activity of its neurons and how this activity spreads along the neuronal network. The recording of this activity allows, on the one hand, the detailed study of the mechanisms generating and modulating it, and on the other hand, to have clues on how the coordinated activity of neuronal populations generates internal brain states and behaviour. This paper reviews some recent and promising innovations of techniques able to record the real-time neuronal activity, from the synaptic transmission to single cells to brain slices to in vivo mammalian preparations, all with maximal biocompatibility. This review focuses on improved patch techniques, extracellular multi-electrode systems, the detection of oxidizable neurotransmitter release and voltage imaging.

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## Advanced patch-clamp recordings

Patch-clamp recording, originally developed in the late 1970s for measuring single ion channel currents, rapidly became the gold standard for the measurement of cellular electrical activity with high temporal resolution and precision [41, 89]. This prompted an exceptional knowledge advancement in almost every biological field such as the structure-function relationship of membrane proteins, cell signalling, hormone and neurotransmitter secretion, nuclear membrane trafficking and

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