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EVROPSKÁ UNIE
MINISTERSTVO ŠKOLSTVÍ, MLÁDEŽE A TĚLOVÝCHOVY
OP Vzdělávání pro konkurenceschopnost
INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

Název: Heavy metals and their visualization nanotechnologiskymi instruments for monitoring in living organisms

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Název projektu: Mezinárodní spolupráce v oblasti "in vivo" zobrazovacích technik

Current limitations of in vivo electrochemical measurement

Use of the sensors and biosensors for real time in vivo and/or in vitro monitoring of clinically relevant physiological analytes have been restricted to laboratory use. This is primarily because they suffer from poor selectivity and sensitivity when used in a biological or biomimicking environment. Other factors that restrict their application include:

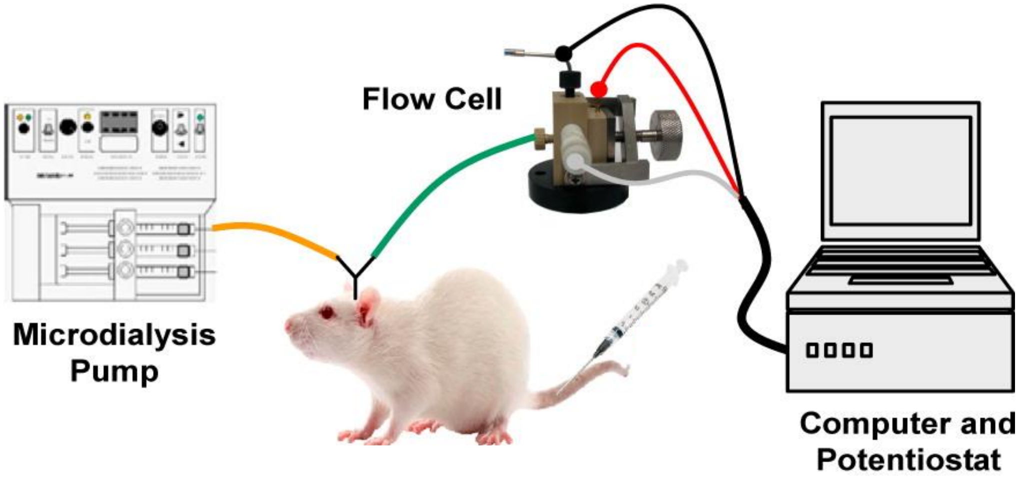
1. most of the sensors developed in laboratories on the bench are too large to be used for implantation because of extensive tissue or cell damage; the same restriction applies to in-vitro extracellular measurements;

2. bio-incompatibility of materials used in their development;

3. long term stability;

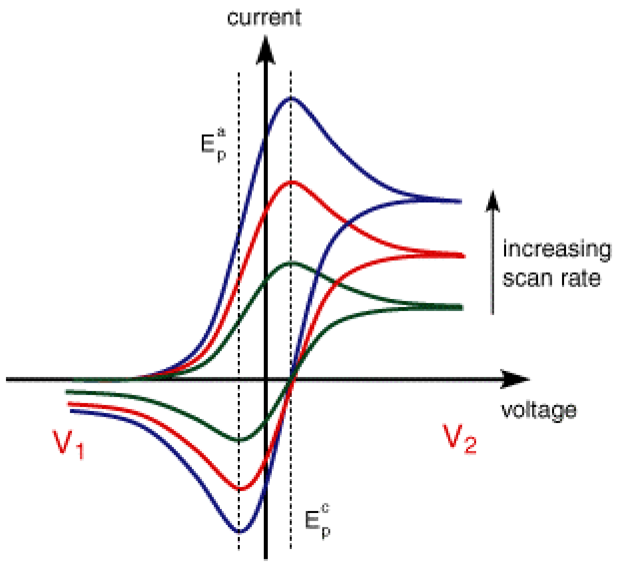
4. frequent fouling compromising their sensitivity;

5. concern about selectivity to the analyte of interest.



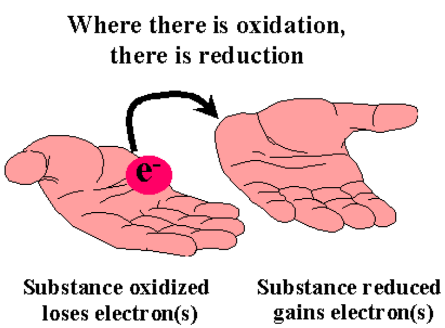
Electrochemical techniques

Fast scan cyclic voltammetry (FSCV) is a particularly powerful technique used to monitor very rapid events in live systems (such as for example neurochemical release).



FSCV has enabled the real-time, in-vivo and/or in-vitro measurements with high spatial and temporal resolution of fluctuations of the target analyte (neurotransmitter) concentration because of its transient release and uptake by living cells.

Due to the small electrode size, both micro- and nanoelectrodes exhibit a small double-layer capacitance which aids the rapid change in electrode potentials and eliminates distortions in the applied voltage waveform that are observed with larger electrodes.



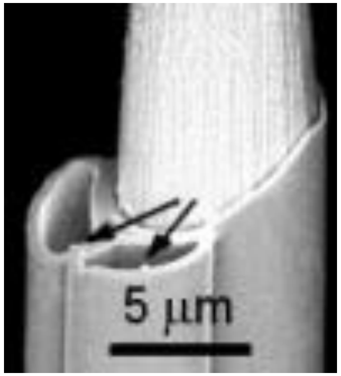
Nano and micro electrodes

The advantages of miniaturized electrodes (whether implantable or not) for electrochemical sensing can be briefly summarized as follows:

1. they have improved signal-to-noise ratios, because analytical Faraday currents are substantially increased by the higher rates of mass transfer of hemispherical diffusion of the electroactive compounds;

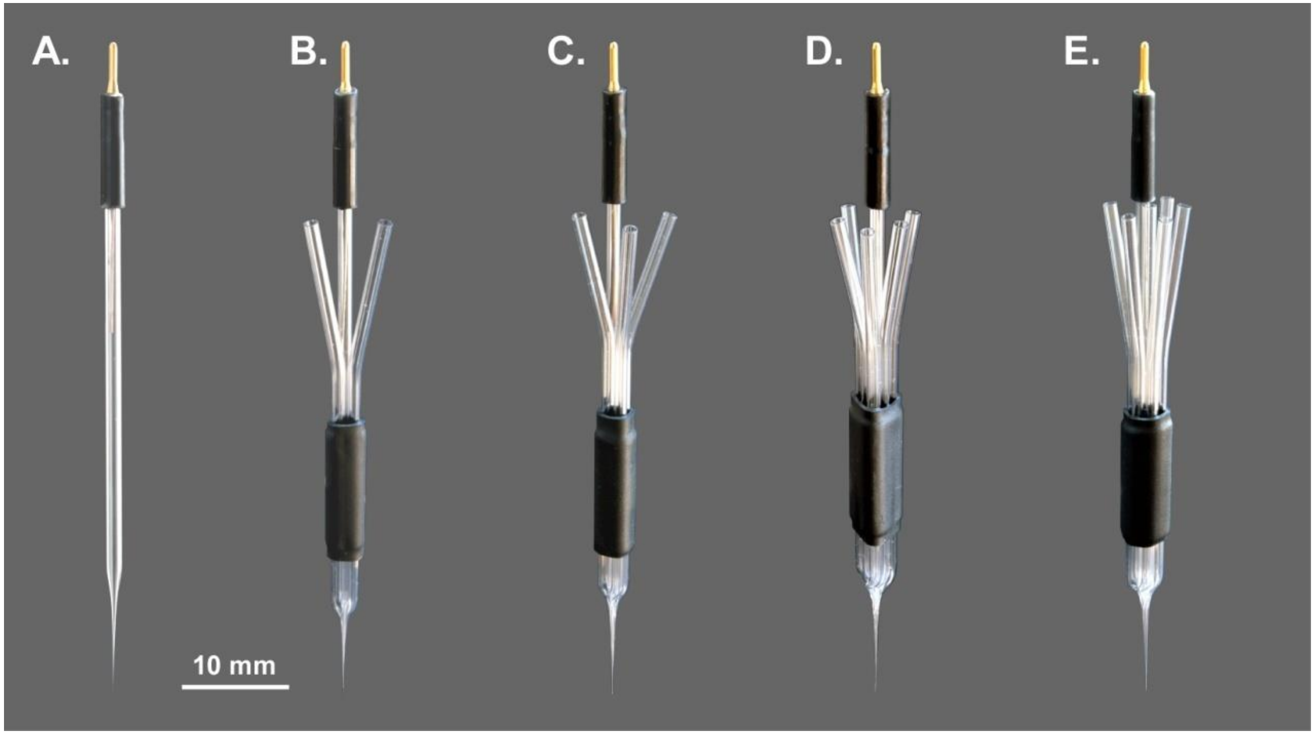
2. their response times are much faster because of the small double-layer capacitance charging currents and time constants, resulting in the capability of high temporal resolution of analyte fluctuations;

3. the so-called iR drop is of less concern because the total analytical currents measured by such electrodes are much smaller than those measured with typical large-scale electrodes.



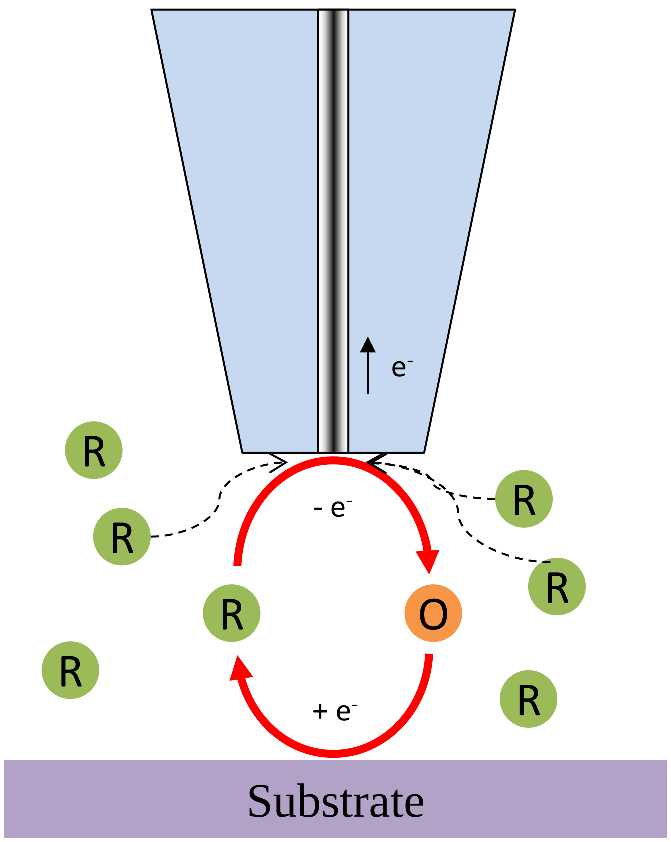
Nano and micro electrodes

Recent developments in nano and microtechnology have enabled the manufacture of electrochemical sensors (electrodes) in the range 1–30 μm in diameter. These are now available with different geometry (disc, rod, band, etc.) and materials (C, Au, Pt, Ag).



integrated capillary-electrodes

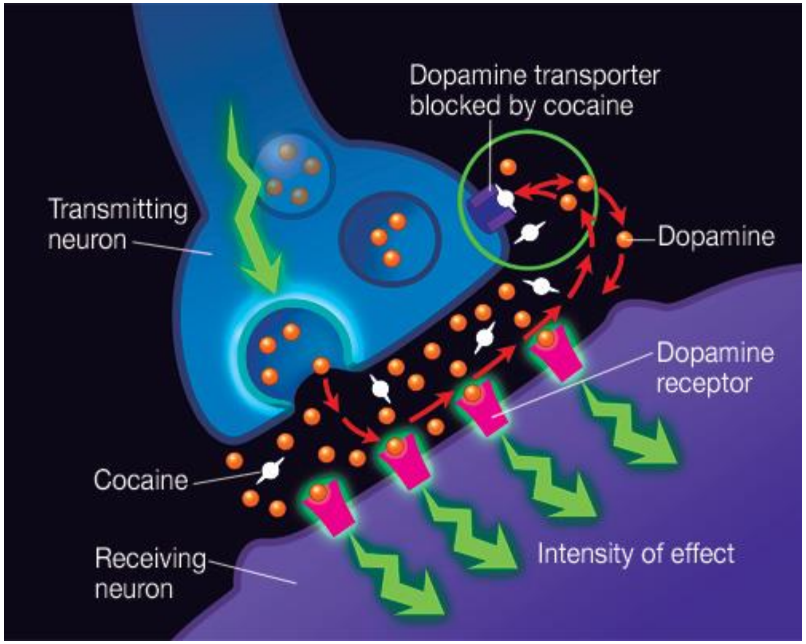
Comparison with SECM



Most research has focused on development of the electrochemical methods. However, for clarity it is necessary to state that not all state-of-the-art electrochemical techniques, for example scanning electrochemical microscopy, SECM, can be applied to in-vivo measurements for awake, moving animals, for obvious "geometric" reasons. Until now SECM has been restricted to cell cultures or (at most) to small anaesthetized animals. Nevertheless, use of micro or ultramicroelectrodes (UMEs) and microfabricated electrode arrays (MEAs) is not restricted by any particular electrochemical technique and can be used both in vivo and in vitro.

Dopamine

Dopamine is an electroactive catecholamine neurotransmitter, abundant in the mammalian central nervous system, affecting both cognitive and behavioral functions of living organisms.



In the normal communication process, dopamine is released by a neuron into the synapse, where it can bind to dopamine receptors on neighboring neurons. Normally, dopamine is then recycled back into the transmitting neuron by a specialized protein called the dopamine transporter. If cocaine is present, it attaches to the dopamine transporter and blocks the normal recycling process, resulting in a buildup of dopamine in the synapse, which contributes to the pleasurable effects of cocaine.

Wilson, G. S. and R. Gifford (2005). "Biosensors for real-time in vivo measurements." Biosensors & Bioelectronics **20**(12): 2388-2403.

Wireless Neurochemical Monitoring

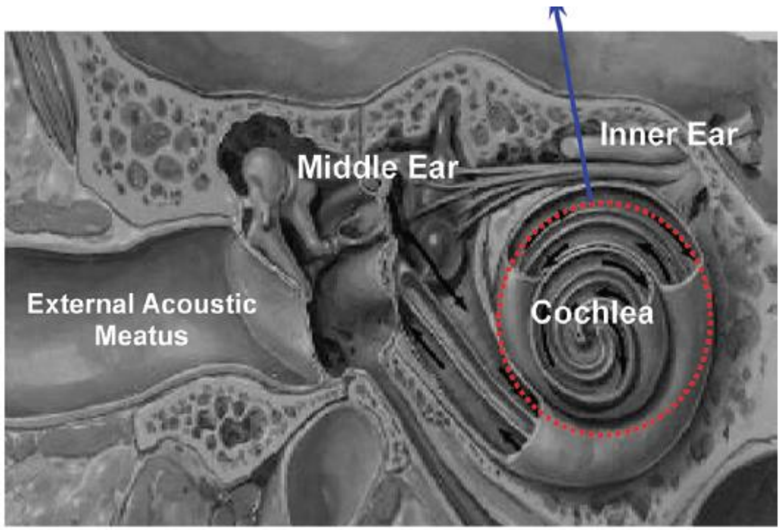
WINCS attached to the neurosurgical stereotactic frame where it is coupled with the WincsTrode implanted in the brain. WINCS is operated at a remote support station laptop computer with custom software.

WINCS (Wireless Instantaneous Neurotransmitter Concentration Sensing) which was developed at Mayo Clinic is system that combines rapid scan voltammetry with wireless telemetry for highly resolved electrochemical recording and analysis.

Kasasbeh, A., K. Lee, et al. (2013). "Wireless Neurochemical Monitoring in Humans." Stereotactic and Functional Neurosurgery **91**(3): 141-147.

Example

In vivo method for real time monitoring of the changes of ascorbate level in the cochlear perilymph during the acute period of tinnitus induced by local microinfusion of salicylate



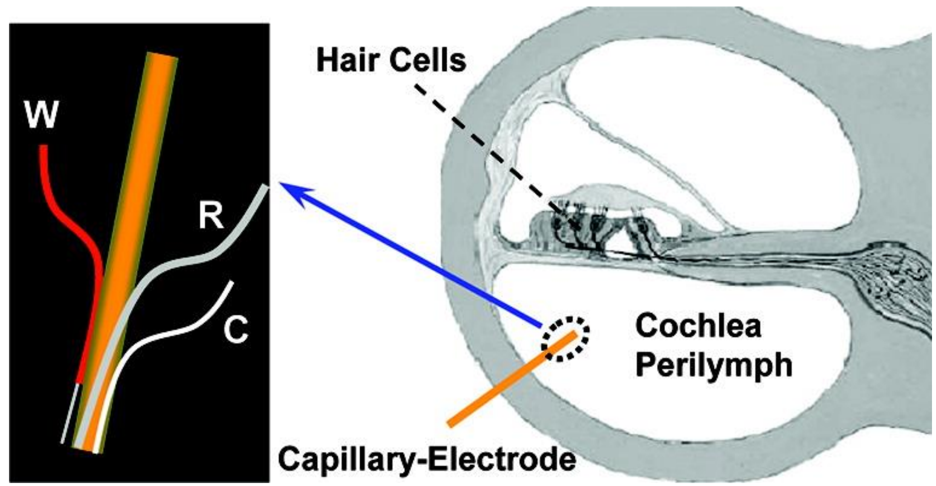
Structure of Ear

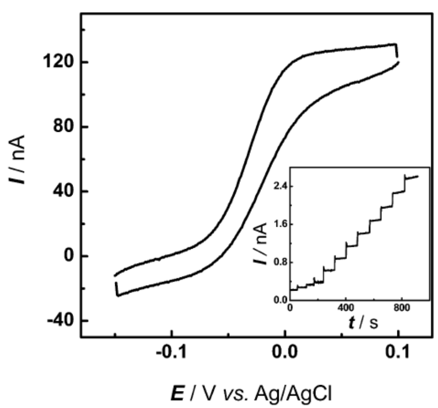
Junxiu Liu; Ping Yu; Yuqing Lin; Na Zhou; Tao Li; Furong Ma; Lanqun Mao; *Anal. Chem.* **2012,** 84, 5433-5438

Example

To accomplish in vivo electrochemical monitoring of ascorbate in the microenvironment of the cochlear perilymph, the MWNT-modified CFME is used as working electrode, a microsized Ag/AgCl is used as reference electrode, and Pt wire is used as counter electrode.

The integrated capillary-electrode is carefully implanted into the cochlear perilymph and used both for externally microinfusing of salicylate into the cochlear perilymph and for real time monitoring of the change of ascorbate levels.





Typical cyclic voltammogram obtained at the integrated capillary-electrode with the MWNT-modified CFME working electrode in artificial perilymph containing 5 mM ascorbate. Scan rate: 10 mV s−1. Inset, current−time response recorded for successive addition of ascorbate into artificial perilymph at the capillary-electrode at 0.05 V. The concentrations of ascorbate used for the first three and other additions were 1 μM and 5 μM, respectively.

Junxiu Liu; Ping Yu; Yuqing Lin; Na Zhou; Tao Li; Furong Ma; Lanqun Mao; *Anal. Chem.* **2012,** 84, 5433-5438

Thank you for your attention.

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