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Nanoelectrodes: Applications in electrocatalysis, single-cell analysis and high-resolution electrochemical imaging

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A B S T R A C T

High sensitivity and high spatial resolution in localized electrochemical measurements are the key advantages of electroanalysis using nanometer-sized electrodes. Due to recent progress in nanoelectrode fabrication and electrochemical instrument development, nanoelectrochemical methods are becoming more widespread. We summarize different protocols for the fabrication of needle-type nanoelectrodes and discuss their properties with regard to various applications. We discuss the limits of conventional theory to describe electrochemistry at the nanoscale and point out technical aspects for characterization and handling of nanometric electrodes. Different applications are highlighted: i) Nanoelectrodes are powerful tools for non-ensemble studies of electrocatalysis at single nanoparticles at high mass transport rates. ii) Electrochemical nanosensors are employed for highly localized non-invasive analysis of single living cells and intracellular detection of neurotransmitters and metabolites. iii) Used in scanning electrochemical probe techniques, nanoprobes afford topographical and truly chemical imaging of samples with high spatial resolution.

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1. Introduction

From the metabolism and communication mechanisms of biological cells to current industrial technologies for energy conversion and storage, electrochemistry governs many processes relevant to our past, present and future existence. We need innovative analytical techniques to understand life's principles and to identify underlying concepts that will help to design more powerful catalyst materials which will finally contribute to create sustainable strategies to cover our high energy demand. Many of these principles and concepts are based on the rules of chemistry at the micro- and nanoscale and often the very entities of study, *e.g.* biological cells or nanostructured materials are very small [1–3]. Analytical methods based on nanoelectrodes and electrochemical nanosensors are promising tools to address these questions [4,5]. For instance,

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the physiology of single cells can be studied or catalytic reactions occurring at single nanoparticles can be investigated. In addition, highly resolved electrochemical imaging [6,7] yields information concerning the heterogeneous electrochemical activity in biological systems [8,9] and energy materials [10].These techniques aim at obtaining information that is difficult to acquire using conventional analytical methodologies.

A nanoelectrode is a solid electrochemical interface whose size in at least two dimensions is substantially below 1 µm. This review critically discusses the recent progress in using nanoelectrodes in various electroanalytical applications and highlights crucial concepts and considerations that are relevant to the successful implementation of such tools into modern analytical chemistry. We summarize the most important fabrication schemes to produce nanoelectrodes with a focus on low-cost fabrication and easy experimental applicability. Geometric, electrochemical and mechanic properties of the resulting electrodes are discussed with regard to special applications of these electrodes. We only discuss those fabrication schemes producing pointy, needle-type electrodes as their high aspect ratio is the prerequisite for most applications. This feature is of particular importance for the use of nanoelectrodes for high-resolution electrochemical imaging using scanning probe techniques and electrochemical analysis in small confined volumes [11].

The small size of nanoelectrodes dictates their specific electrochemical properties that substantially deviate from the electrochemical behavior observed at macroscopic electrodes. These features of nanoelectrodes are exploited in their electroanalytical applications. However, there is still a lack in understanding size-dependent effects on the electrochemical behavior of very small nanoelectrodes. As the electrode dimensions approach those of molecules and atoms, classical theory to describe electrochemical processes does no longer hold true [12]. We briefly discuss the most important of these effects and their implications on the interpretation of results obtained from experiments at nanoelectrodes. Also, we highlight technical aspects and measures that are necessary to assess and preserve the size and quality of such delicate electrodes.

The use of nanometric electrochemical sensors is motivated by the small dimensions of samples that require the sensor to be of smaller or at most equal size compared to the entity of interest. Nanoelectrodes allow the study of electrochemical processes at single nanoparticles. Investigating individual particles rather than whole statistical ensembles helps in elucidating the relationship between particle size and catalytic activity. In addition, electrocatalytic turnover at single particles exhibits high mass transport rates which allows to investigate reaction kinetics without mass transport limitation. This review is also a survey of the studies that recognize the merits of these non-classical analytical methods and use electrochemical nanoprobes for the electrocatalyst characterization.

In biological systems, microelectrochemical techniques have been used to study cell metabolism, factors leading to pathogenic conditions as well as intercellular communication via the release of neurotransmitters [8,13–15]. These techniques allow to detect metabolites and messenger molecules released from individual cells to study cell function at the single-cell level. Individual cell fates can be monitored and often analytical information complementary to standard optical methods is obtained. Thus, exploiting nanoelectrodes for the life sciences brings about a deeper understanding of physiological processes occurring inside living cells. We discuss the state of the art and future perspectives of electrochemical nanoprobes for chemical analysis in and around cells.

Nanoelectrodes were also increasingly implemented in scanning probe techniques to achieve electrochemical mapping of analytes with unprecedented spatial resolution. In biological and non-biological systems, electrochemical imaging reveals inhomogeneous reactivity of samples. As the size of the detecting probe decreases, not only the spatial resolution is improved but also the technique becomes increasingly non-invasive. This review highlights the challenges associated with employing nanoelectrodes for high-resolution chemical imaging and summarizes the remarkable progress made in recent years.

2. Electrode fabrication

2.1. Insulated STM tips and fibers

Even though small metal electrodes originally designed for neurophysiology measurements and exhibiting dimensions smaller than 1 µm are known since the 1960s [16] it was the success of Scanning Tunneling Microscopy (STM) that initially boosted the progress in nanoelectrochemistry and in particular the fabrication of nanometric electrodes [17]. For a useful electrochemical interpretation of experimental data, nanoelectrodes have to be fabricated with a defined geometry that allows to model electrode processes and mass transport. The first electrodes used in an electrochemical context were Pt/Ir rods that were, just like STM tips, etched in acidic solution by applying an AC voltage and then later insulated using various coating materials to leave only the apex of the electrode exposed. The electrode is moved through hot wax [18] or molten glass [17] to cast the insulating sheath. Excavating the very tip of the electrode can be achieved by elaborate procedures, for instance mounting the electrode in an STM instrument, applying a voltage between the electrode and the sample and approaching the tip towards the sample until an electric discharge between the two electrodes ruptures the insulating cap and leaves the tip exposed [19]. Alternatively, as insulating material, electrodeposition paints have been commonly used for carbon fiber microelectrodes in neurophysiological studies [20] and have been adapted to the fabrication of nanoelectrodes [21–23]. Upon heat curing, the insulating sheath shrinks and retracts to leave the nanometric tip protruding from the insulator. Alternatively, “inverted deposition”, where the electrode tip just bulges out of the deposition paint solution was proposed [24]. The electrochemically active parts of electrodes produced according to these methods are typically sphere segments or cones. Mirkin et al. developed analytical expressions to describe the behavior of these electrodes in Scanning Electrochemical Microscopy (SECM, see section 4.3) [19], however, for most applications disk geometry is desirable to make the nanometric electrode most sensitive to electrochemical processes occurring only at the very tip. Moreover, the nature of electrodes derived from STM tips or carbon microfibers precludes later polishing steps which is often necessary to obtain defined electrode geometries and to regenerate electrodes between experiments. On the other hand, the very pointy shape allows to insert these electrodes into small volumes while maintaining high sensitivity. Especially flame-etched carbon fibers are promising probes for measurements in small volumes [25,26]. After etching micrometric carbon fibers to create nanotips, the fibers are inserted into glass capillaries for handling and electrical connection. Their conical shape is characterized by a small diameter at the tip while maintaining a relatively large surface area which ensures still high sensitivity.

2.2. Metals fused in capillaries

Another widespread method to produce nanoelectrodes with good control of the electrode geometry and high reproducibility is to pull nanopipettes together with an incorporated metal wire using a laser-assisted pipette puller (Fig. 1a). This route is based on early