Review Article
Nanopipettes as a tool for single nanoparticle electrochemistry
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Nanopipettes provide a tool to reduce sample volumes to an extent that the behavior of single entities becomes apparent and, as we discuss here, enable measurement of the electrochemical behavior of single nanoparticles. For example, nanopipettes allow the electrocatalytic activity of individual nanoparticles to be measured in isolation and they also allow the dynamic motion of single nanoparticles near interfaces to be measured. This review highlights exemplar works from the previous 2 years on the different ways in which nanopipettes have been used to probe single nanoparticle electrochemistry.

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Current Opinion in Electrochemistry 2017, XX:XX-XX
This review comes from a themed issue on Innovative Methods in Electrochemistry
Edited by Frederic Kanouni
For a complete overview see the Issue and the Editorial
Available online XX XXXX 2017
http://dx.doi.org/10.1016/j.coecel.2017.06.006
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Introduction
In the field of nanoelectrochemistry [1,2], nanopipettes are a powerful tool for the measurement and manipulation of entities possessing at least one dimension <100 nm. Fabrication of nanopipettes with apertures of this size follows a rapid and inexpensive bench-top process, whereby a glass or quartz capillary is heated (melted) and pulled into two near-identical conical pipettes. Pipette geometry (cone angle/diameter) can be tailored by changing the parameters of the heat-pull cycle using a programmable puller [3,4,5].

A key motivation for using nanopipettes is a reduced sample volume that can reveal the behavior of single entities, either through resistive pulses [6], nanoparticle collisions [7] or by creating a nanoscale/microscale electrode surface. Additionally, the opening of a highly tapered nanopipette can be positioned close to an interface, which can then be exploited for on-demand delivery [1,8,9**]. This review highlights such uses of nanopipettes for electrochemical investigations of single nanoparticles in the ~2 years prior to 2017. Our focus excludes other important applications of nanopipettes in electrochemistry. Specifically, readers interested in learning about the use of nanopipettes as imaging probes are directed to reviews of scanning electrochemical cell microscopy (SECCM) [10,11], scanning ion conductance microscopy (SICM) [12], and scanning electrochemical microscopy (SECM) with an interface between two immiscible electrolyte solutions (ITIES) probe [13]. For a review of the use of pipettes to study of interfacial ion transfer we direct the reader to reference [14].

Nanoparticles are important as electrocatalysts in energy technologies. While methods for controlling their composition and structure continue to progress, tools are still needed to evaluate the structure–activity relationship and help direct these efforts. Ensemble methods for studying catalytic activity are confounded by polydispersity in the nanoparticle synthesis, which can be avoided by studying single particles.

In a typical nanopipette measurement (Figure 1) a potential is applied between two electrodes, one inside the electrolyte-filled pipette and the other in the external solution. An ionic current must pass through the narrow opening of the nanopipette which acts as a nanoscale sensing zone. A range of physical phenomena, related to the coupling of fluid flow with the ionic and electric field distributions [15,16], are key to single nanoparticle electrochemical measurements: (1) The ionic current diminishes as the pipette approaches a surface, allowing nanopipettes to be positioned at a precise distance from a substrate [12]; (2) The ionic current drops momentarily when an entity passes through the pipette orifice, in a so-called ‘resistive pulse’ (see inset), the magnitude, shape and duration of which can be used to measure size, charge, shape, and deformability of single nanoparticles and biomolecules [6,17]; (3) The application of a potential and/or pressure differential can be used to controllably deliver/collection particles or molecules, though a combination of electrophoresis with pressure and/or electroosmotically driven flows [18*].

The volume of the nanopipette near the orifice is small enough that it stochastically contains zero or one nanopar-
The use of the nanoparticle collision method to study the electrocatalytic activity of single nanoparticles [7,19]. Briefly, a small electrode that displays slow electron transfer kinetics for an electrocatalytic reaction is poised at a potential such that no redox reaction occurs until the collision of a particle that catalyzes the reaction, and whose activity can be ascertained from the enhanced redox current (Figure 1, inset).

**Multifunctional nanopipettes**

Coating the inner surface of nanopipettes with electrode materials, in particular a nanometer-thick layer of carbon, has facilitated new single nanoparticle electrochemical measurements. Carbon-coated nanopipettes (CNPs) are fabricated by chemical vapor deposition (CVD). A carbon source (methane) mixed with a carrier gas (argon) is flowed through the nanopipette contained in a furnace (875 °C). Short deposition times (~30 min) maintain a continuous channel in the CNP, allowing manipulation of fluid flow and ionic current sensing. At longer deposition times (≥90 min), the carbon closes off the nanopipette near its tip but leaves a small open volume creating the so-called “nanosampler” [20].

Michael Mirkin’s laboratory has recently used open and closed CNP geometries for electroanalysis of small volumes via exhaustive electrolysis of attoliter to picoliter samples [21,22,23,24,25,26]. Importantly, the confinement of the sample volume within the nanopipette confers high capture efficiency of redox molecules at moderate scan rates where charging currents are not too large. The possibility of performing voltammetric studies upon the contents of individual vesicles or the products of single nanoparticle catalysis is intriguing. The authors also demonstrated the suitability of CNPs as SECM probes [24]. Hu et al. extended the range of electrochemical phenomena studied with open CNPs [27]. They used an electrical connection to the carbon coating to adjust its potential. This gave control over the internal surface charge and consequently, control of ion transport through the pipette. These studies are exciting because they suggest that ICR and electroosmotic flows, important to controlling nanoparticle velocities in nanopores, are tunable in CNPs. Interestingly, when the carbon electrode was floating (not under potentiostatic control), bipolar electrochemistry of a redox molecule and resistive pulse sensing of gold nanoparticles were simultaneously observed.
The utility of CNPs to probe new electrochemical phenomena was displayed recently in the study of single electrocatalytic nanoparticle collisions. Such measurements are often confounded by deactivation of the particles and by the large numbers of nanoparticles present, which complicates experimental interpretation. Zhou et al. [28**] employed open CNPs as the current collector, although they deliberately did not fill the entire CNP with electrolyte as illustrated in Figure 2A. Instead, they were able to control the volume of fluid within the CNP by dipping its open end into electrolyte and balancing the capillary forces pulling fluid in with an internally applied positive pressure. After placing the CNP into a dilute solution containing 30 nm diameter iridium oxide (IrO₂) particles and H₂O₂, nearly a minute passed before a single particle entered the CNP and elastically collided with the carbon electrode producing a current spike. The authors subsequently transferred the CNP containing a single nanoparticle into a particle-free solution containing electrolyte and H₂O₂. Individual current transients continued to be recorded as the IrO₂ particle underwent random motion inside the CNP, stochastically colliding with the carbon wall for ~100 s as shown in Figure 2B. Based upon the unchanging distribution of peak heights, these measurements support the resistance of IrO₂ nanoparticles to deactivation. Puzzling aspects of these observations, which the authors acknowledge, are the duration of current transients (plotted in Figure 2C), the time interval between them, and the length of time spent within the CNP. The diffusive rate of the nanoparticle is expected to be quite fast such that collisions should occur on the microsecond timescale and that the particle would escape the CNP within milliseconds.

Jin He’s group recently deposited a protruding carbon electrode in one of the barrels of a dual-barrel nanopipette to study single nanoparticles [29*]. In their experiments, the open barrel was used for resistive pulse sensing while the open circuit potential (OCP) of the adjoining carbon electrode was monitored. Interestingly, translocation of 40 nm Au nanoparticles through the open barrel resulted in increases in the OCP of the carbon electrode that exactly coincided with resistive pulses in the open nanopipette. The authors attributed the OCP changes to two distinct sensing mechanisms, supported by finite element modeling. First, the influence of double layer interactions between the particle and electrode as particles accumulate near the nanopipette orifice, and second, that the electrode serves as a point probe within the potential drop of the open nanopipette’s access resistance, which changes during a particle translocation. These studies offer new insights into the dynamic motion of nanoparticles under the influence of electric fields as well as their charge interactions.

Clausmeyer et al. studied O₂ reduction at Ag nanoclusters using a dual-barreled nanopipette as an analogue to a gas-diffusion electrode [30*]. A carbon electrode in one
barrel, functionalized with Ag nanoclusters, served as the electrode, while a gas-filled barrel delivered O₂ across the gas/liquid interface. The high transport rates, due to the close proximity between the barrels, allowed the authors to perform Tafel analysis beyond the regime conventionally accessible.

Nanopipette-based delivery of nanoparticles to electrified interfaces

Using a nanopipette to deliver a nanoparticle to a small electrode allows resistive pulse and nanoparticle collision measurements of the same nanoparticle [9**,21]. The resistive pulse measurement gives the nanoparticle size [17], while the electrochemical activity is obtained through the nanoparticle collision measurement [7,19], allowing determination of single nanoparticle size/activity relationships.

In the experiment from McKelvey et al. [9**], shown in Figure 3, nanoparticles are loaded inside the nanopipette, which is precisely positioned above an underlying electrode using computer controlled piezoelectric positioners and ionic current feedback. A small positive pressure then drives nanoparticles from the nanopipette. Parts B and C show simultaneously recorded ionic and redox currents with the pipette positioned 3 and 5 μm above the electrode, respectively. The passage of nanoparticles through the orifice is indicated by resistive pulses, which are followed by a drop in redox current, 1.5 and 12 ms later, respectively, as the polystyrene nanoparticle collides with the electrode and partially blocks FcMeOH transport to its surface. Particles released further from the electrode not only take longer to reach it (the time to reach the surface is proportional to the cube of the distance traveled), they also interact differently with the electrode. When the pipette was far from the electrode, particles irreversibly stuck to the electrode (part C), while the fluid flow when the pipette was close to the electrode was sufficient to prevent particle adhesion, giving a temporary drop in the redox current (part B). Similarly, a microfluidics platform might be used to combine resistive pulse sensing [6] and convective delivery of nanoparticles to nanoelectrodes [31], although in this case the experimental geometry could not be altered. This technological advancement is exciting, but needs to be expanded to work with electrochemically active nanoparticles, an approach we are currently pursuing. The use of a similar set-up for delivering a quantified number of nanoparticles to cells, where they function as drug delivery vectors [32], might also be envisaged.

Nanopipette-based droplet cells for nanoparticle delivery

In SECCM, the meniscus at the end of an electrolyte-filled micro/nanopipette is contacted with a larger electrode surface to define an electrode with dimensions similar to the pipette opening [10]. As shown in Figure 4a, the electrode formed is small enough that single nanoparticle collisions can be observed. Using the meniscus to define the electrode bypasses the need to insulate off a portion of the electrode surface, as in constructing conventional microelectrodes, and broadens the range of substrates on which microelectrodes can easily be fabricated [10]. When using double-barreled nanopipettes, the ionic current between the barrels provides a feedback signal for positioning the nanopipette, which is independent of the underlying surface. NB: The nanopipette is typically much larger than the nanoparticles, precluding the use of the resistive pulse method.

Using SECCM, Unwin’s group has delivered [33,34**,35*,36,37] and grown [38,39] nanoparticles on specific locations on various electrodes in a controllable fashion. Kleijn et al. first demonstrated the landing of individual Au nanoparticles on highly oriented pyrolytic graphite (HOPG) and a carbon TEM grid using a SECCM-based approach [34**]. In particular, landing a single nanoparticle on the TEM grid allowed both a cyclic voltammogram and high resolution TEM of the same nanoparticle to be reported, as shown in Figure 4B.

Bentley et al. took advantage of the low noise, high bandwidth current capabilities of SECCM, afforded by the
small electrode area, to assess the charge passed when individual Au nanoparticles collided with and were oxidized by an oxidized Au electrode (Figure 4C) [36]. The charge passed (~10 s FC) was shown to correlate with the particle surface area. Similarly, Kang et al. used SECCM to deliver ruthenium oxide nanoparticles to a HOPG surface. Spikes due to H2O2 oxidation were observed at higher frequency than predicted by the single-pass diffusive flux. The discrepancy was attributed to a single nanoparticle undergoing multiple impacts with the electrode surface [37]. Ustarroz also observed multiple peaks from single nanoparticles when delivering Ag nanoparticles to Au and HOPG surfaces, where they were electrodissolved [35], confirming prior results that Ag nanoparticles dissolve through multiple partial oxidation events [40].

Conclusions

Nanopipettes represent a quick, simple and inexpensive tool to study nanoscale systems. We have highlighted some recent developments centered on electrochemical measurements of single nanoparticles that have enabled through the use of nanopipettes. These developments, although interesting and exciting, have largely centered on exemplar measurements. Future work needs to move beyond model systems, for example, using these techniques to quantify the size/activity relationships of electrocatalytic nanoparticles, or quantify the forces for nanoparticle interactions with surfaces.

Acknowledgments

Research on nanopipettes and electrochemistry of single nanoparticles in the White group is funded by Air Force Office of Scientific Research MURI FA9550-14-1-0003.

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

• Paper of special interest
•• Paper of outstanding interest.

6 Innovative Methods in Electrochemistry


This paper illustrates forces acting on a nanoparticle in resistive-pulse sensing and shows how nanoparticle translocation direction/velocity can be controlled by changing these forces.


This paper describes the use of CNPs for capture and monitoring of repeated electrocatalytic collisions of single IrOx nanoparticles.


This paper demonstrates a multimode nanoparticle sensing method using a dual-barrel nanopore/nanoelectrode nanopipette.


The authors describe a dual-barrel nanopipette, in which one barrel contains a carbon nanoelectrode decorated with Ag nanoclusters and the other is gas-filled. Oz is delivered rapidly and locally across the gas/liquid interface at the tip, allowing kinetic studies of ORR in a kinetic regime inaccessible to standard techniques.


This paper reports measurement of the electrocatalytic activity and the geometry of the same single nanoparticles, using a combination of SECCM voltammetry of hydrazine oxidation and TEM.


This paper reports using a nanopipette droplet cell to study the electrochemical dissolution of single Ag nanoparticles, showing that this process proceeds through multiple partial oxidation events.


