



Single-entity electrochemistry of collision in sensing applications

Alina Sekretareva

Department of Chemistry-Ångström, Uppsala University, Uppsala 75120, Sweden



ARTICLE INFO

Keywords:

Electroanalysis
Nanoimpacts
Impact electrochemistry
Nanoparticle coulometry
Electrocatalytic amplification

ABSTRACT

Single entity electrochemistry of collision (SEEC) is an emerging electrochemical method with the great potential for ultra-sensitive analysis applications. Here, the possibilities and challenges of SEEC in sensing are discussed. The analytical characteristics of the collision-based detection method, such as sensitivity, detection range, the limit of detection, signal-to-noise ratio, and selectivity, are examined. Factors affecting these parameters and strategies to improve them are discussed. Potential target analytes in environmental and bioanalytical applications are overviewed based on the reported up to date literature. Finally, challenges and limitations currently preventing real-life applications of the method are highlighted.

1. Introduction

The ultimate challenge of modern electroanalytical chemistry is to reach a single-molecule level of detection. The fascination of the scientific community with prospects of single-molecule methods for fundamental understanding of stochastic processes and ultra-sensitive analysis resulted in the rapid development of single-entity electrochemistry of collision (SEEC, also referred to as impact or nanoimpact electrochemistry) in the last decade [1]. The collision electrochemistry approach is based on measuring an electrochemical signal arising when a single entity (a cell, a particle, or a single molecule) freely moving in solution collides with an electrode. Since the frequency of collisions is proportional to the concentration of colliding entities, SEEC can be applied for quantitative detection of the entities.

The first collision experiments were reported by Heyrovsky and co-workers in 1995 on suspensions of colloidal semiconducting particles colliding with a drop mercury electrode [2–5]. While the authors did not observe signals from individual particles, they have shown that the voltammograms of a polydisperse nanoparticles suspension could be obtained as a sum of the voltammetric signals of a series of homodisperse nanoparticles. Later Scholz et al. observed signals from collisions of individual liposomes, which produced current transients upon bursting and spreading on the surface of a mercury electrode. They showed that the current signals were capacitive in nature and could be used to determine the number of molecules inside each liposome [6]. Subsequently, several more works were published on collisions of hard particles producing capacitive signals upon contact with an electrode by Scholz's and Compton's groups [7–9]. In 2004 Lemay and co-workers detected Faradic signals due to adsorption of individual nonconductive micro- and nanospheres on the surface of an ultramicroelectrode in a solution of a redox probe [10]. In 2006 Heyrovsky et al. published

results of collision experiments with metal powder suspensions demonstrating the possibility to measure Faradaic currents from reactions taking place on the surface of the individual colliding particles [11]. The last two works demonstrated a proof-of-principle of SEEC.

While several electrochemical techniques, such as voltammetry and potentiometry [12,13], have been applied in collision experiments, the amperometric sensing approach dominates the field. In an amperometric experiment, the collision of a particle with a potentially-biased microelectrode produces a discrete change in the current-time response, which depending on the experimental conditions, can be observed either as a spike- or step-like transient (Fig. 1a,b). The spike-like signal is observed if the particle deactivates on the electrode surface or departs from the surface after the collision. The staircase response indicates that the particle sticks to the electrode following the collision. In this case, particles build up on the electrode surface in subsequent collisions, either increasing background current in the case of redox-active particles or decreasing it in blocking experiments with insulating particles. Changes in the background signal affect signal-to-noise ratio and the surface area of the electrode, all of which complicate data analysis. The spike-like signal is, therefore, desirable for sensing applications [14].

All SEEC methods based on Faradaic current measurements can be divided into two broad categories according to the electrochemical process utilised for detection: indirect (or mediated) and direct (Fig. 1c,d and e) [15]. Indirect (mediated) collision electrochemistry is a non-destructive method based on measuring changes in the current in the presence of a redox couple in the solution. Current changes occur either due to amplification or blocking of the Faradaic current by the colliding nanoparticle (Fig. 1c, d) [10,16,17]. Current increase upon collisions of NPs can be detected as a result of catalytic or area amplification (Fig. 1c) [16,17]. Catalytic amplification, first demonstrated by Bard and co-workers in 2007, [17] is observed when a catalytic reaction

E-mail address: alina.sekretareva@kemi.uu.se

<https://doi.org/10.1016/j.snr.2021.100037>

Received 14 December 2020; Revised 15 February 2021; Accepted 14 March 2021

Available online 20 March 2021

2666-0539/© 2021 The Author. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

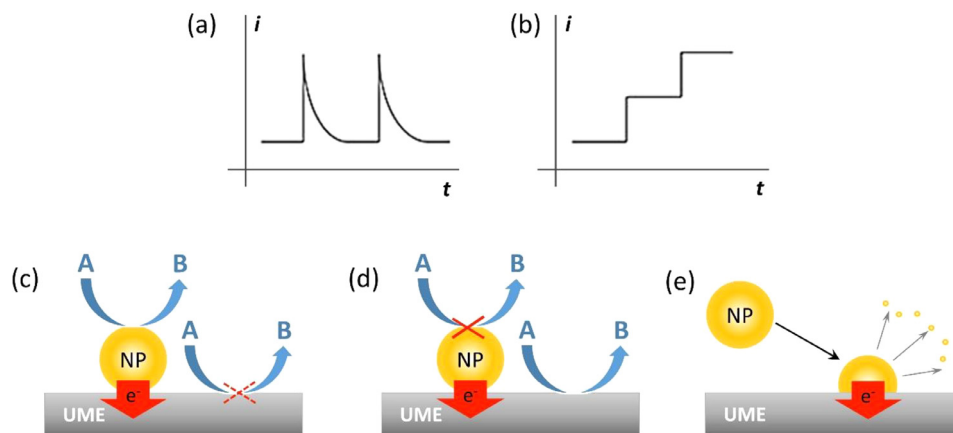


Fig. 1. Schematic drawing of (a) spike- and (b) step-like current responses in SEEC: Schematics of indirect collision electrochemistry based on (c) current amplification and (d) current blocking experiments. The reaction $A \rightarrow B$ generates a detectable signal. In catalytic amplification-based experiments, the reaction occurs only on the surface of NP. In area amplification-based experiments, the reaction can occur on both the NP and UME. In blocking-based experiments, the reaction does not occur on the NP. The NP blocks are of the UME active towards the reaction. (e) Schematics of direct collision electrochemistry. The colliding NP oxidises upon collision.

occurs only on the nanoparticle in contact with the electrode and not on the electrode itself at the applied potential. In this setup, the particle acts as a nanoelectrode, and the electrode only provides electrical contact to the NP. Signal amplification is provided by multiple catalytic turnovers on the surface of the nanoparticle [17,18]. Area amplification takes place when a conductive NP collides and attaches to the electrode surface, increasing the active electrode area for the redox reaction to happen and, thus, resulting in a current increase. The surface area of the particle should be comparable with the size of the electrode [16]. In blocking-based experiments, the microelectrode is dipped in a redox mediator solution, and the steady-state current of the mediator redox reaction is monitored. When a nonconductive particle collides with the electrode, the mediator's diffusion to the surface is blocked (Fig. 1d), leading to a decrease in the current.

Direct collision electrochemistry is a destructive technique that relies on measuring currents from direct oxidation or reduction of the colliding nanoparticle due to electron transfer between the particle and the electrode (Fig. 1e). The method was first demonstrated in 2011 by Compton's group for characterisation of silver nanoparticles (AgNPs) oxidising on the surface of an ultramicroelectrode (UME) [19]. The colliding entity itself should be redox-active at the applied potential for detection via direct collision electrochemistry. Direct SEEC is mostly used to detect and characterise metallic nanoparticles but has also been demonstrated for organic nanoparticles [20]. Analysis of colliding vesicles and micelles through oxidation or reduction of their redox content upon bursting on the electrode surface can also be considered as direct collision electrochemistry [21,22].

In this review, possibilities and challenges associated with applications of SEEC for sensing are discussed. First, the standard analytical performance of the method characterised by the limit of detection, signal-to-noise ratio, detection range, sensitivity, and selectivity, and factors affecting these parameters are examined. For each of the parameters, limitations of the state-of-the-art collision-based detection approaches and ways to overcome these limitations are considered. The most promising examples of SEEC applications in environmental and bioanalytical sensing are overviewed in the second part.

2. Analytical characteristics of collision-based detection

When colliding entities represent the target analyte and produce a detectable signal upon collisions with an electrode either through direct or indirect electrochemistry, the sensing can be realised using a label-free approach [19,23]. For sensing of analytes not able to bring about an electrochemical signal, labelling with nanoparticles or enzymes generating current response when in contact with the electrode is required

[24,25]. Independent of the detection approach used, the standard analytical characteristics can be extracted from collision experiments as discussed below.

2.1. Calibration curve

The frequency with which single entities arrive at the electrode surface is determined by mass transfer. In the general case, the mass transfer in an electrochemical experiment occurs through diffusion, convection, and migration [26,27]:

$$J = J_{diff} + J_{conv} + J_{mig} = -D\nabla C + Cv + \mu CE \quad (1)$$

where J is the flux, C is the concentration, D is the diffusion coefficient, and μ is the electrophoretic mobility of the entities. E is the electric field, and v is the electrolyte flow velocity. Stochastic modelling of the mass transfer equation allows predicting the average frequency of collisions in the experiment [28]. The average frequency of collision in an optimised system is proportional to the concentration of colliding entities and can be used for the method calibration. Alternatively, the average time of first arrival (TFA) can be utilised as an analytical signal for ultra-low concentrations of analyte in solution [29,30]. TFA is a time from the beginning of the collision experiment until the moment when the first signal from a colliding entity is observed.

Let us consider the detection of Co^{2+} ions by the catalytic amplification approach reported by Bard's group as an example (Fig. 2) [30]. In this example flow of ions to the electrode is governed only by diffusion, which is a common situation in SEEC experiments. Metal ions diffuse to the electrode and are electrodeposited on the surface as cobalt oxide. The oxidation of single ions does not produce a measurable signal since only few electrons are transferred in the reaction. However, when enough oxidised atoms nucleate into an active cluster, the electrocatalytic reaction occurs on this cluster generating a current response. The frequency of diffusion-controlled collisions with the electrode (f) can be approximated as follows [30]:

$$f = 4DCrN_A \quad (2)$$

where r is the radius of the electrode, and N_A is Avogadro's Number, and the diffusion coefficient D calculated using the Stokes-Einstein equation [31]:

$$D = \frac{k_B T}{6\pi\eta r_{entity}} \quad (3)$$

where k_B is Boltzmann's constant, T is temperature, η is the kinematic viscosity of the solution, and r_{entity} is the radius of the entity. By plotting the experimental frequency of collisions (Fig. 2b) at different

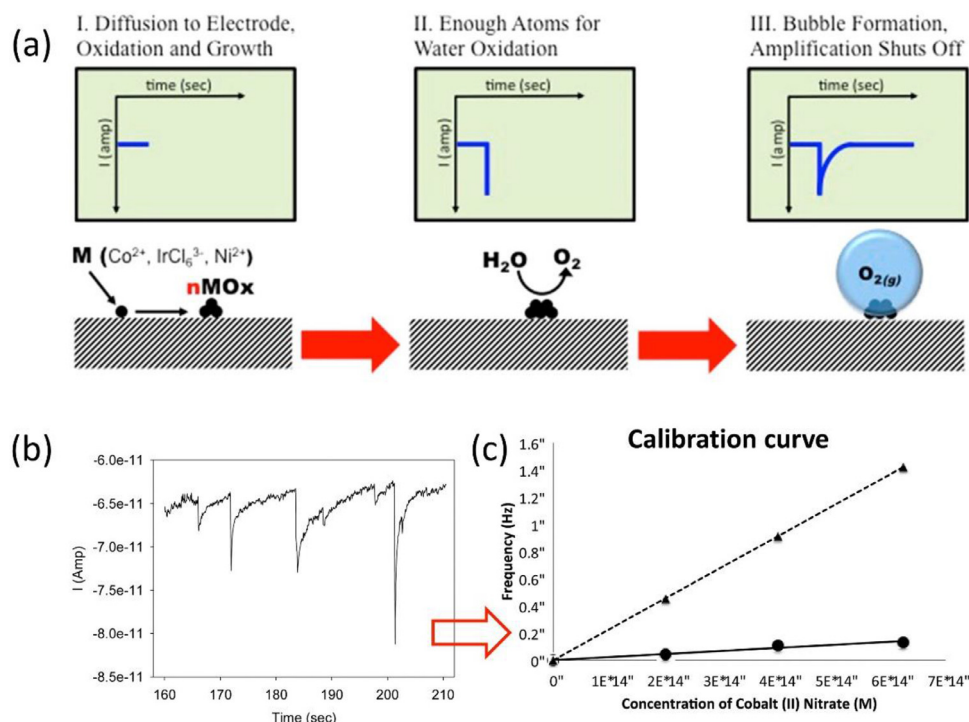


Fig. 2. (a) Schematic of the detection method. (b) Experimentally observed current transients recorded in 62.5 μM cobalt nitrate solution. (c) Calibration curves obtained by plotting experimental (solid line) and theoretical (dashed line) frequencies of collisions vs Co^{2+} concentration in solution. Reprinted with modifications from [30]. Copyright © 2016, American Chemical Society.

concentrations of Co^{2+} in the solution, **the calibration curve** shown in Fig. 2c is obtained. Comparing the experimental and theoretical frequency of collisions (Eq. (2)) provides additional information allowing to estimate the average number of metal atoms in the active cluster.

It should be noted that **sensitivity** defined as the slope of the calibration curve in conventional ensemble measurements [32], is independent of the magnitude of each collision's current response in the case of SEEC detection method (Eq. (4)):

$$\text{Slope} = 4DN_A r \quad (4)$$

This definition of sensitivity implies that the limit of detection (LOD) is also independent of the magnitude of the current response generated by each collision and signal-to-noise ratio (S/N). However, each single collision event should produce a measurable signal to be detected. The ability to register the individual signal is determined by the magnitude of the current response and S/N. We believe that the term sensitivity defined as the slope of the calibration curve can still be applied to characterise SEEC-based assays and provide valuable information on analytical performance, as long as the sensitivity value is not connected to LOD. For the simplest case of the diffusion-controlled flux of the analyte (or the reporting label for the label-based detection method), the slope of the calibration curve depends on the radius of the detection electrode and the diffusion coefficient of the analyte/label.

Thus, in general, sensitivity can be increased either by increasing the size of the electrode or facilitating the mass transfer of the analyte/label to the electrode surface. Increasing the electrode/electrolyte interface area leads to higher background currents, which contribute to the shot noise [29], thus decreasing S/N and eventually preventing reliable detection of current transients of collisions. Several strategies to increase the mass transfer to the electrode surface have been reported in the literature, which are discussed further in detail with regards to LOD in collision experiments.

While the majority of effort is focused on pushing down the lowest amount of analyte that can be quantified in SEEC, for some applications wide **linear range** is required. The upper limit of the linear range in

SEEC is determined by the ability to resolve two consecutive collisions as separate events, which depends on the duration of the signal and data acquisition parameters. Resolution of two closely spaced events increases when recording data with higher bandwidths. For the high flux of colliding entities to the electrode surface, closely spaced individual collisions become merged into single events when filtering at low frequency [33]. Once two separate collision events could not be distinguished, the calibration curve starts to deviate from linearity.

2.2. Signal-to-noise ratio and limit of detection

Signal-to-noise ratio (S/N) ratio in collision experiments is determined by the current transient responses upon collisions of single entities and the background noise of the detection electrode. For the direct detection method, the charge corresponding to each spike due to the full electrochemical oxidation or reduction of a spherical metallic nanoparticle can be determined as follows [19]:

$$Q_{max} = \frac{4nF\pi\rho r_{entity}^3}{3A_r} \quad (5)$$

where Q_{max} is the maximum transferred charge, n is the number of electrons per the redox reaction of one atom of the particle, ρ is the mass density of the entity, A_r is the relative atomic mass, and F is the Faraday constant. However, Eq. (5) is valid only for small NPs, whereas for larger particles, dissolution happens in consecutive steps, resulting in multiple current transients [34,35]. Thus, the size of single spikes will be smaller than predicted by Eq. (5). Typically, the current signals on the order of hundreds of pA to several nA are observed in direct SEEC [19,36].

The maximum size of a current response in detection methods based on catalytic amplification in the conditions of diffusion-controlled mass transfer for a single spherical nanoparticle can be estimated as follows [17,18]:

$$i = 4\pi(\ln 2)nFDCr_{entity} \quad (6)$$

where n is the number of electrons transferred in the catalytic reaction, C is the concentration, and D is the diffusion coefficient of the redox species. The typically observed signals are on the order of tens to hundreds of pA [17,18]. The response might be much smaller if catalysis controls the reaction rate, as for example, in enzymatic reactions [37,38].

Noise in SEEC is mainly determined by statistics of counting electrons, i.e., shot noise in the current. Background current contributes to the shot noise and, consequently, to the measurement error [39]:

$$\sigma^2 = q_e(i_{\text{baseline}} + \Delta i)/\Delta t \quad (7)$$

where σ is the variance of the total measured signal, q_e is the elementary charge, i_{baseline} is the background current, Δi and Δt are the size and duration of the current transient, respectively. Thus, for collision experiments, the viable approach for increasing S/N is to reduce background currents. Decreasing the detection electrode's size leads to lower background currents but increases the lowest detectable concentration per unit of time. For commonly utilised disk electrodes, the S/N increases slower than the decrease in the lowest detectable concentration per unit of time, and overall sensitivity decreases with decreasing the size of the detection electrode [40]. The detection electrode material affects the background current and can be optimised to improve the S/N ratio. For example, Stevenson's group showed that S/N for detection of PtNPs by electrocatalytic amplification can be improved on mercury electrodes compared to gold electrodes due to the lower faradaic background of mercury electrodes [14,41]. Besides improved S/N, the signal is spike-shaped on the mercury electrodes compared to the step-shaped response on gold, which is desirable for sensing applications. Boron-doped diamond electrodes have much lower background currents than commonly applied detection electrodes and have been successfully applied to record collisions with improved S/N ratios [42,43].

The limit of detection (LOD) is defined as the lowest concentration level that can be determined to be statistically different from an analytical blank [32]. SEEC allows measuring an individual signal from one entity, so it can reach a single-entity level of detection. However, to register one entity driven by diffusion to the electrode surface in typical collision experiment conditions (microdisk electrode, $r = 10 \mu\text{m}$, $D = 10^{-10} \text{m}^2 \text{s}^{-1}$, 10 ml solution volume), $2.5 \times 10^9 \text{s}$ (~ 80 years) are required (Eq. (2)), which practically is not achievable. Thus, the practical LOD in SEEC experiments depends on the ability to detect a signal from a single entity with statistical significance and is determined by the signal-to-noise ratio (S/N) and the frequency of collisions of the analyte/label with the electrode. Thus, it might be more informative to separately define the lowest detectable concentration per unit of time LDC/ Δt , [27,40] controlled by the frequency of collisions.

For the diffusion-controlled flux of the analyte/label to the electrode surface, the collision frequency is determined by the electrode's size and the time of the measurements (Fig. 3a) [44]. Fig. 3b shows an estimation of LDC/ Δt for collision experiments on a micrometre electrode. As can be seen, it is difficult to achieve detection limits lower than $\sim \text{fM}$ range for assays performed in minutes on micrometre-sized detection electrodes. For particles moving by electrophoretic migration, the LOD of $\sim 0.01 \text{fM}$ can be achieved [29].

Several strategies have been reported in the literature to increase the frequency of collisions by facilitating the mass transfer to the electrode surface. Boika and co-workers demonstrated that electrokinetic phenomena, such as dielectrophoresis and electrothermal fluid flow, induced by applying a high-frequency alternating current, increase mass transfer of AgNPs to the electrode surface [45]. The ac heating allowed increasing the collision frequencies by up to three orders of magnitude. A magnetic field was applied to increase the flow of magnetic nanoparticles to the electrode surface and control the frequency of collisions [46–50]. Stevenson and co-workers demonstrated a 6-times increase in collision frequency of magnetic nanoparticles driven to the electrode surface by the magnetic field [49]. Crooks and co-workers reported decreased by four orders of magnitude LDC/ Δt in a microfluidic channel with incorporated magnets upon collisions of insulating magnetic beads with a gold UME.

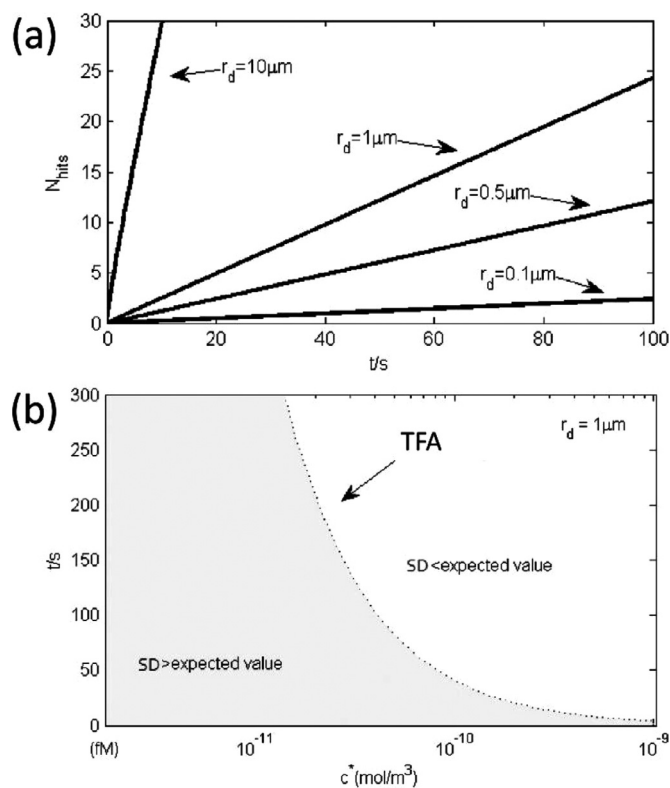


Fig. 3. (a) The average number of collisions per time on a microdisk calculated for various electrode radii. The nanoparticle concentration and the diffusion coefficient are $c^* = 1 \text{pM}$ and $10^{-10} \text{m}^2 \text{s}^{-1}$, respectively. (b) LOD dependence on the concentration calculated via TFA for a microdisk radius of $1 \mu\text{m}$. The areas where the standard deviation (SD) is larger than the expected TFA value are coloured in grey. Reprinted from [44]. Copyright © 2015 Elsevier B.V.

The approach allowed to detect magnetic beads in the concentration of 500zM in 300s [48].

Another approach to facilitate mass transfer is to introduce a fluid flow [50,51]. Stevenson, Crooks et al. showed a decrease of the LDC/ Δt by eight times for the detection of platinum nanoparticles (PtNPs) on mercury electrodes in a microfluidic system with the flow-over configuration compared to systems without flow [51]. The authors noted that the distribution of PtNPs in the flow is irregular, and the frequency of collisions decreases with increasing the flow rate after passing the optimal flow rate value. In the flow-over configuration systems, the analyte is not directed to the electrode surface and has to travel to the electrode by diffusion. This leads to counterintuitive dependence of the collision frequency on the flow rate at high flow rates: the frequency scales as the $1/3$ power of the flow rate [27,52]. The scaling can be improved if the flow is directed towards the surface of the electrode, as, for example, in a wall-jet configuration system [36,53,54]. With increasing the flow rate until moderate flows, collision frequency is enhanced both due to increased mass transfer and increased kinetic energy of colliding particles, which allows overcoming repulsive force preventing collision with the electrode. The decrease of the collision frequency with the increasing flow rate after passing the maximum was observed in wall-jet systems and was explained by insufficient time of contact between the nanoparticle and the electrode at high flow rates [53].

Increasing the electrode area while maintaining high S/N is another viable approach towards lower LODs [27,36,55]. Compton and co-workers showed the advantage of using microwire electrodes over microdisk electrodes for the detection of ultralow concentrations [32]. The same group demonstrated two orders of magnitude lower LOD for direct detection of AgNPs on the microelectrode array (MEA) in a wall-jet configuration system compared to analysis on a single UME under

stationary conditions [36]. The LOD enhancement was achieved both due to higher surface area for collisions and facilitation of mass transfer by the flow. Lemay et al. argued that the SEEC approach can be applied for reliable and practical detection of analytes in ultralow concentrations only on electrode arrays with a large number of individually addressable electrodes and readout systems [27].

2.3. Selectivity

Selectivity refers to the extent to which the method can be used to determine particular analytes in mixtures or matrices without interferences from other components with similar behaviour. The ability to measure individual entities in mixtures of similar entities with statistical significance represents a great challenge for SEEC in real-life sensing applications. Arguably, the most promising approach to improve selectivity of collision experiments is by introducing selective labelling chemistries. Additional current amplification that might be inserted through labelling is desirable for increasing the ability to detect individual entities. For example, Dick et al. demonstrated selective detection of murine cytomegalovirus in urine of an infected mouse through collision electrochemistry coupled to enzymatic labelling (Fig. 4a) [56]. A sample containing the virus was incubated with an antibody specific for the virion surface proteins labelled with glucose oxidase (GOx). One virus binds many labelled antibodies, concentrating GOx molecules on its surface and providing current amplification. When the virus comes close to the electrode surface, ferrocene methanol mediated oxidation of glucose by GOx generates a detectable currents signal. Zhang et al. reported selective detection of a protein, platelet-derived growth factor, in cerebrospinal fluid of a rat brain by labelling colliding PtNPs with aptamers specific to platelet-derived growth factor [57]. PtNPs were modified

with aptamers specific to the targeted protein, which blocked catalytic hydrazine oxidation on the surface of the colliding NPs. In the presence of the platelet-derived growth factor, due to interactions with the protein, aptamers were displaced from the PtNPs surface, regenerating current response.

Direct label-free collision electrochemistry can be potentially adapted for selective detection of metallic nanoparticles in mixtures [58]. Compton's group demonstrated a proof-of-principle strategy for selective detection and quantification of AgNPs and nickel nanoparticles (NiNPs) of unknown concentrations in a mixed solution (Fig. 4b). The particles were distinguished by performing measurements at two different potentials, corresponding to the direct oxidation of only AgNPs and both AgNPs and NiNPs. The data set at each potential was fitted by the time-dependent function with the concentration, diffusion coefficient of the NPs, and radius of the electrode as only parameters (Fig. 4c). The diffusion coefficient of the NPs was determined experimentally using the Stokes-Einstein equation (Eq. (3)) and the radius of the NPs derived from the charge per spike distribution (Eq. (5)). The demonstrated approach can be potentially applied for analysis of more complex mixtures of nanoparticles by utilising electronic tongue-like systems coupled with pattern recognition methods for data analysis [59,60]. However, use of direct collision electrochemistry for reliable detection of NPs in mixtures is complicated by the fact that larger particles are not always fully converted on the electrode surface in a single collision event [35,61] and small particles produce signals below the detectable current values. Additionally, for polydisperse mixtures of NPs under diffusion-controlled conditions, the detection is biased towards smaller nanoparticles since they move faster to the electrode surface [33].

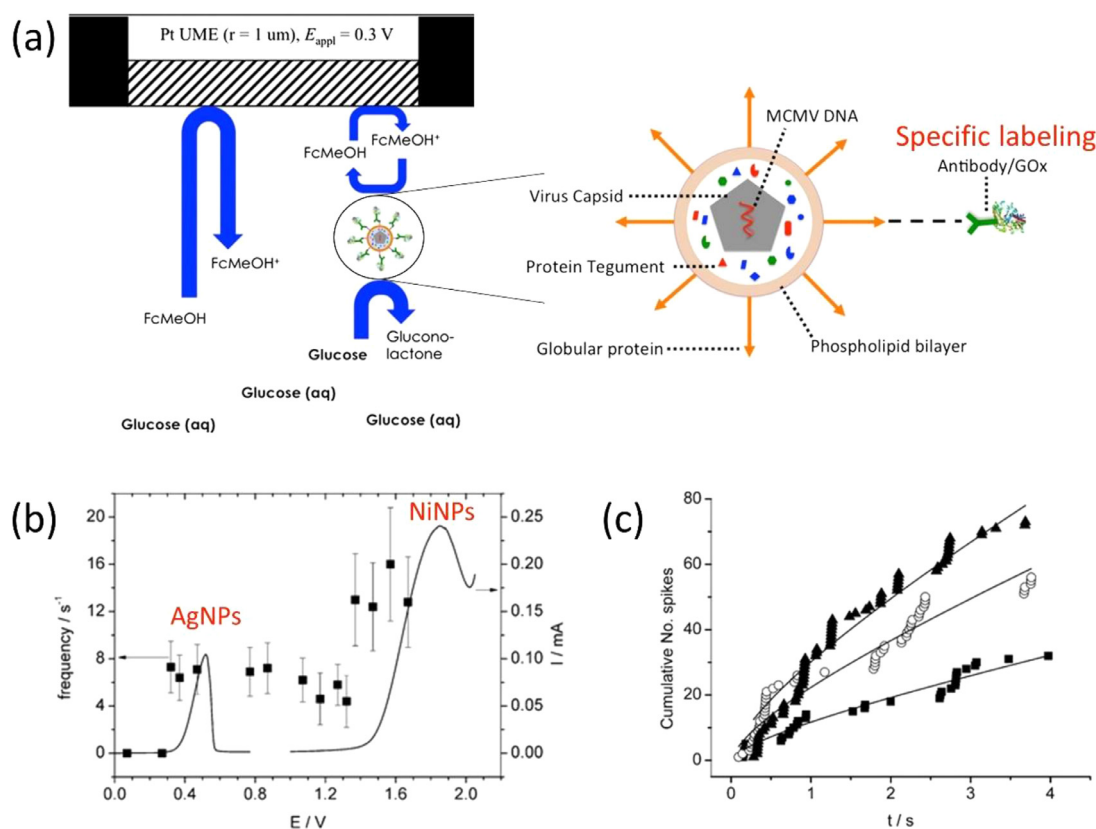


Fig. 4. (a) Schematic representation of the detection method. The specific interaction of the virus with GOx-labelled antibody is highlighted. Reprinted with modifications from [56]. Copyright © 2016. National Academy of Sciences. (b) The plot of the average frequency at various applied potentials. Stripping voltammograms for AgNP-modified and NiNP-modified electrodes are overlaid. (c) The fit of the accumulative number of spikes vs time at varying NiNPs concentrations. Dots show experimental data, solid lines theoretical fitting curves. Reproduced from [58] with permission from The Royal Society of Chemistry.

3. Potential sensing applications

Several reports on SEEC applications for sensing environmental pollutants and biomolecules at ultralow concentrations have been published. In this section, a brief overview of these works is provided.

3.1. Environmental sensing

Metallic nanoparticles are widely used in various industrial applications, and tones of them are released to the environment yearly. Due to possible nanotoxicity concerns, reliable methods for detection and characterisation of nanoparticles in the environment are required. Sensing low concentrations of nanoparticles in environmental samples is one of the target applications for collision electrochemistry. The reported detection schemes are primarily based on the direct collision electrochemistry approach (Fig. 1e). This approach allows detecting nanoparticles and potentially eliminating them at the point of release by full electrolysis. Compton and co-workers reported sensing of picomolar concentrations of AgNPs in potable and seawater samples by direct oxidation at a carbon fibre UME at an applied potential of 0.8 V vs Ag/AgCl [62,63]. Krause et al. using a similar detection method were able to measure AgNPs in sub-picomolar concentrations on an MEA (Fig. 5) [64]. The MEA system consisted of 62 individually-addressable platinum working electrodes, eight μm in diameter each (Fig. 5a). Utilisation of the MEA and parallel recording allowed to decrease LDC/ Δt . Pumera and co-workers demonstrated a possibility to use cheap, disposable screen-printed electrodes with a carbon-based working electrode of 3 mm diameter to detect and quantify AgNPs by direct oxidation at 0.15 V vs Ag/AgCl [65]. However, the method is not applicable for nanoparticles smaller than 100 nm since the signal generated by smaller particles is lower than the background noise. Detection of various metal-based nanoparticles, such as Ni, Au, Cu, CuO, and CeO₂ NPs by the direct collision electrochemistry approach, was reported [58,66–69].

Another important potential application of SEEC is detection of heavy metal contaminations in environmental samples. Bard's group developed a sensing strategy to quantify metal ions at the femtomolar level with a 10 s detection time (Fig. 2) [14,30]. The detection is based on the electrodeposition of metal ions on the electrode surface, where, upon reaching the critical number of atoms, they start to generate detectable current due to catalytic amplification. Sensing of cobalt, iridium, nickel, and iron via catalytic water oxidation and lead via catalytic methanol oxidation in the femtomolar range has been demonstrated. Andreescu and co-workers investigated interactions between heavy metal contaminants, such as As³⁺, and nanoparticles [70,71]. The detection was performed through direct oxidation or reduction of As³⁺ adsorbed on the surface of the NP. For adsorption on CeO₂ NPs, current

transients were recorded for the oxidation of As³⁺ to As⁵⁺ and the reduction of As³⁺ to As⁰. For As³⁺ adsorbed on Fe₃O₄ particles, only oxidation signals were observed. In both cases, the amount of the As³⁺ adsorbed per NP correlated with the concentration of As³⁺ in the solution. However, only relatively high concentrations of As³⁺ in solution, 0.001–10 μM , were used, which can be detected by stripping voltammetry [72].

3.2. Bioanalytical applications

One of the promising bioanalytical applications of collision electrochemistry is analysis of low DNA and RNA concentrations for diagnostic purposes. The reported up to date sensing schemes employ labelling of the target molecules with PtNPs and detection of colliding PtNPs via electrocatalytic amplification [24,25,73,74]. Bard's group first demonstrated that PtNPs modified with single-strand DNA (ssDNA) can be applied for sensing of the target DNA in a sandwich-type sensor [24]. Crooks and co-workers applied a similar strategy for microRNA detection [25]. The PtNPs were modified with ssDNA, and after incubation with the target microRNA, collision experiments were performed before and after exposure of the conjugates to a duplex-specific nuclease (DSN). DSN cuts ssDNA hybridised to complementary microRNA, exposing a catalytic surface of the PtNPs and enabling detection of current transients upon collisions of the exposed PtNPs with a UME. The detection approach can be adopted for various targets, such as peptides or proteins, using specific combinations of nucleic acids and enzymes to identify the analyte. The detection limit of the method, however, is too high for diagnostic purposes. Bai et al. modified the method lowering the detection limit by six orders of magnitude down to aM level (Fig. 6a) [73]. Magnetic nanoparticles were modified with ssDNA, which were then functionalised with PtNPs. After hybridisation with target microRNA and DSN, conjugates with magnetic nanoparticles were magnetically separated and the remained solution with freed PtNPs was used for collision experiments. Applicability of the method for analysis of cancer cells was demonstrated. Andreescu and co-workers extended the detection strategy proposed by Bard and Crooks to sense ochratoxin B [74]. AgNPs were modified with target-specific ssDNA aptamers blocking electron transfer between the colliding NP and the electrode. Binding of the ochratoxin B to the surface resulted in conformational changes of the aptamer, opening electron transfer to the NP and producing current transient due to direct oxidation of the NP.

Detection of viruses and bacteria is another attractive target for SEEC. Reported detection strategies for bacteria are mostly based on blocking collision electrochemistry (Fig. 1d). The approach was demonstrated for *Escherichia coli* (*E.coli*), *Bacillus subtilis*, and *Shewanella oneidensis* [75–78]. The method is not selective since any nonconductive

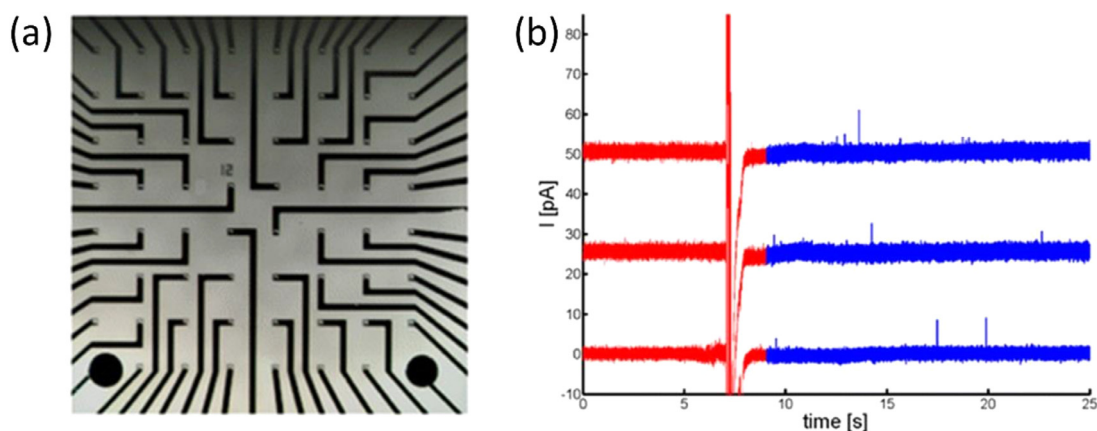


Fig. 5. SEEC in environmental sensing. (a) Light microscope image of the microelectrode array. (b) Example of the parallel recording of AgNPs collisions on three individual electrodes of the array. Reprinted with modifications from [64]. Copyright © 2015, American Chemical Society.

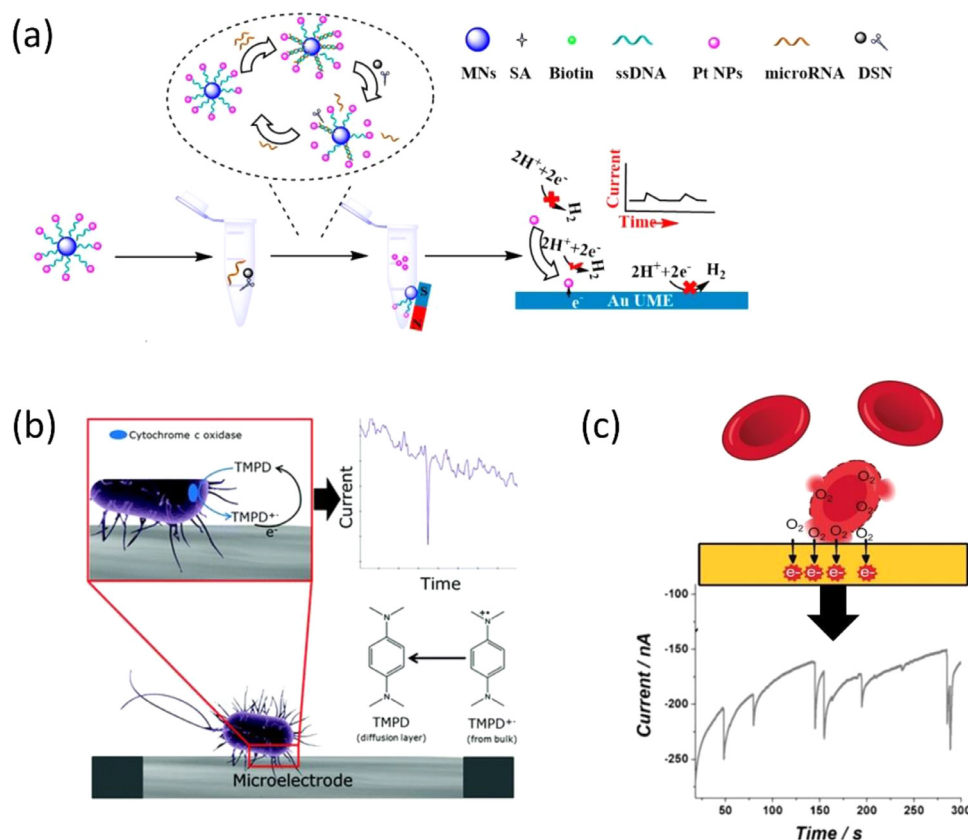


Fig. 6. SEEC in bioanalytical applications. (a) Schematic of the detection scheme for ultrasensitive microRNA detection. Adapted with permission from [73]. Copyright © 2020, American Chemical Society. (b) Schematic drawing of *E. coli* detection through the mediated reaction of *N,N,N',N'*-tetramethyl-*para*-phenylene-diamine (TMDP). Reproduced from [79] with permission from The Royal Society of Chemistry. (c) Schematic drawing of SEEC application for counting red blood cells in diluted blood. Adapted with permission from [95] and [84]. Copyright © 2016 WILEY–VCH Verlag GmbH & Co. KGaA, Weinheim.

particles present in the solution will produce a signal. Strategies using intrinsic redox activity of bacterial cells or specific labelling approaches are desirable for practical applications. Compton's group demonstrated detection of *E. coli* bacteria colliding with the ultramicroelectrode through the mediated reaction of *N,N,N',N'*-tetramethyl-*para*-phenylene-diamine (TMDP) (Fig. 6b) [79]. TMDP radical cation is reduced on the electrode surface, generating TMDP in the diffusion layer, which can be oxidised back by bacterial cytochrome C oxidases, amplifying the current signal. This approach allowed to quantify bacteria in the range of 3×10^8 to 1.8×10^9 cells per mL. Mirkin and co-workers applied a similar approach for sensing of *E. coli* and *Stenotrophomonas maltophilia* through ferricyanide reduction and oxidation of $\text{Ru}(\text{NH}_3)_6^{2+}$, respectively [78]. Moreover, the authors demonstrated the possibility of differentiating positively and negatively charged bacteria by observing different sticking patterns at various UME potentials. Labelling of *E. coli* with AgNPs and detection via direct oxidation of colliding NPs on the electrode has been reported [80,81]. Boika and co-workers achieved the limit of quantification of 2.5 fM in 3 min for AgNPs-labelled *E. coli* through preconcentration of bacteria by a high frequency alternating current waveform [81]. Bacteria cells were labelled with AgNPs non-specifically, and, thus, the method is not selective but can be potentially modified for selective detection of target bacteria through the introduction of specific labelling chemistries. Detection of labelled viruses using SEEC has been shown [23,56,82]. Sepunaru et al. reported measurements of sub-picomolar concentrations of influenza virus non-specifically labelled with AgNPs [82]. For the practical sensing of viruses, virus-specific labelling chemistries should be introduced. Dick et al. achieved selective detection of murine cytomegalovirus with LOD of 30 fM by applying antibodies specific to the virus for enzymatic labelling (Fig. 4a) [56].

Another exciting target for SEEC is sensing of mammalian cells [83–85]. Dick reported a proof-of-principle study demonstrating a possibility to use collision experiments to elucidate electrochemistry of cancerous cells and monitor the difference between the cancerous and healthy cells [83]. The redox-active content of individual cancer cells was monitored during collisions of cells with the electrode in surfactant presence. The current transient recorded upon collisions of lymphoblastic lymphoma T-cells were two orders of magnitude higher than those of healthy cells. Compton and co-workers showed that SEEC can be applied for counting red blood cells in diluted blood (Fig. 6c) [84]. In the presence of hydrogen peroxide, current transients attributed to the surface-induced haemolysis of the cells upon collisions with the electrode were observed. Collision experiments allowed quantifying red blood cells in sub-picomolar concentrations, which covers the range of physiological concentrations.

4. Outlook

SEEC is a promising analytical method with the potential for future applications in environmental and bioanalytical sensing at ultra-low concentrations. However, several technical and fundamental challenges should be addressed before it can be used for analysis of real-life samples. SEEC is extremely sensitive to experimental conditions, including electrolyte composition and concentration [86,87], surface chemistry at the detecting electrode [88,89], and geometry of the cell [90,91]. Moreover, data acquisition parameters and electronics might significantly affect signals recorded in collision experiments [92,93]. These factors should be carefully investigated and considered when designing a sensing platform based on collision electrochemistry. Selectivity and stability of the signal remain an issue for collision-based detection. While

selective detection of the target analyte in complex matrixes using SEEC has been achieved [56,57,73], most sensing strategies reported in the literature are not selective. Practical application of the label-free direct collision electrochemistry for analysis of particle mixtures is particularly challenging. Aggregation [94] and only partial dissolution of particles upon collisions [34,35] seriously limit prospects of the direct detection method in quantitative analysis. Development of selective labelling approaches and ways to stabilise NPs can bring SEEC closer to practical applications. Another challenge that should be tackled is the accurate detection of analytes in ultralow concentrations within reasonable times. A large number of individual collision events should be collected for statistically reliable quantification of the target analyte. Multiplexed data recording on electrode arrays coupled with advanced statistical data processing to increase the amount of data collected is desirable for future high-throughput applications [1,27]. Providing all the issues resolved, SEEC can facilitate development of the most sensitive electrochemical sensors and biosensors ever known.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- [1] L.A. Baker, Perspective and Prospectus on Single-Entity Electrochemistry, *J. Am. Chem. Soc.* 140 (2018) 15549–15559.
- [2] M. Heyrovsky, J. Jirkovsky, B.R. Mueller, Polarography and Voltammetry of Aqueous Colloidal SnO₂ Solutions, *Langmuir* 11 (1995) 4293–4299.
- [3] M. Heyrovsky, J. Jirkovsky, M. Struplova-Bartackova, Polarography and Voltammetry of Aqueous Colloidal TiO₂ Solutions, *Langmuir* 11 (1995) 4300–4308.
- [4] M. Heyrovsky, J. Jirkovsky, M. Struplova-Bartackova, Polarography and Voltammetry of Mixed Titanium(IV) Oxide/Iron(III) Oxide Colloids, *Langmuir* 11 (1995) 4309–4312.
- [5] M. Heyrovsky, J. Jirkovsky, Polarography and Voltammetry of Ultrasmall Colloids: Introduction to a New Field, *Langmuir* 11 (1995) 4288–4292.
- [6] D. Hellberg, F. Scholz, F. Schauer, W. Weitschies, Bursting and spreading of liposomes on the surface of a static mercury drop electrode, *Electrochem. Commun.* 4 (2002) 305–309.
- [7] C.E. Banks, N.V. Rees, R.G. Compton, Sono-electrochemistry in acoustically emulsified media, *J. Electroanal. Chem.* 535 (2002) 41–47.
- [8] N.V. Rees, C.E. Banks, R.G. Compton, Ultrafast Chronoamperometry of Acoustically Agitated Solid Particulate Suspensions: Nonfaradaic and Faradaic Processes at a Polycrystalline Gold Electrode, *J. Phys. Chem. B* 108 (2004) 18391–18394.
- [9] F. Scholz, D. Hellberg, F. Harnisch, A. Hummel, U. Hasse, Detection of the adhesion events of dispersed single montmorillonite particles at a static mercury drop electrode, *Electrochem. Commun.* 6 (2004) 929–933.
- [10] B.M. Quinn, P.G. van't Hof, S.G. Lemay, Time-Resolved Electrochemical Detection of Discrete Adsorption Events, *J. Am. Chem. Soc.* 126 (2004) 8360–8361.
- [11] A.V. Korshunov, M. Heyrovsky, Voltammetry of Metallic Powder Suspensions on Mercury Electrodes, *Electroanalysis* 18 (2006) 423–426.
- [12] S.J. Percival, B. Zhang, Fast-Scan Cyclic Voltammetry Allows Determination of Electron-Transfer Kinetic Constants in Single Nanoparticle Collision, *J. Phys. Chem. C* 120 (2016) 20536–20546.
- [13] H. Zhou, J.H. Park, F.-R.F. Fan, A.J. Bard, Observation of Single Metal Nanoparticle Collisions by Open Circuit (Mixed) Potential Changes at an Ultramicroelectrode, *J. Am. Chem. Soc.* 134 (2012) 13212–13215.
- [14] R. Dasari, D.A. Robinson, K.J. Stevenson, Ultrasensitive Electroanalytical Tool for Detecting, Sizing, and Evaluating the Catalytic Activity of Platinum Nanoparticles, *J. Am. Chem. Soc.* 135 (2013) 570–573.
- [15] S.V. Sokolov, S. Eloul, E. Kätelhön, C. Batchelor-McAuley, R.G. Compton, Electrode-particle impacts: a users guide, *Phys. Chem. Chem. Phys.* 19 (2017) 28–43.
- [16] J.H. Park, S.N. Thorgaard, B. Zhang, A.J. Bard, Single Particle Detection by Area Amplification: Single Wall Carbon Nanotube Attachment to a Nanoelectrode, *J. Am. Chem. Soc.* 135 (2013) 5258–5261.
- [17] X. Xiao, A.J. Bard, Observing Single Nanoparticle Collisions at an Ultramicroelectrode by Electrocatalytic Amplification, *J. Am. Chem. Soc.* 129 (2007) 9610–9612.
- [18] X. Xiao, F.-R.F. Fan, J. Zhou, A.J. Bard, Current Transients in Single Nanoparticle Collision Events, *J. Am. Chem. Soc.* 130 (2008) 16669–16677.
- [19] Y.-G. Zhou, N.V. Rees, R.G. Compton, The Electrochemical Detection and Characterization of Silver Nanoparticles in Aqueous Solution, *Angew. Chem.* 123 (2011) 4305–4307.
- [20] W. Cheng, E.J.E. Stuart, K. Tschulik, J.T. Cullen, R.G. Compton, A disposable sticky electrode for the detection of commercial silver NPs in seawater, *Nanotechnology* 24 (2013) 505501.
- [21] W. Cheng, R.G. Compton, Investigation of Single-Drug-Encapsulating Liposomes using the Nano-Impact Method, *Angew. Chem. Int. Ed.* 53 (2014) 13928–13930.
- [22] J. Dunevall, H. Fathali, N. Najafinobar, J. Lovric, J. Wigström, A.-S. Cans, A.G. Ewing, Characterizing the Catecholamine Content of Single Mammalian Vesicles by Collision-Adsorption Events at an Electrode, *J. Am. Chem. Soc.* 137 (2015) 4344–4346.
- [23] J.E. Dick, A.T. Hiltnerbrand, A. Boika, J.W. Upton, A.J. Bard, Electrochemical detection of a single cytomegalovirus at an ultramicroelectrode and its antibody anchoring, *Proc. Natl. Acad. Sci.* 112 (2015) 5303–5308.
- [24] S.J. Kwon, A.J. Bard, DNA Analysis by Application of Pt Nanoparticle Electrochemical Amplification with Single Label Response, *J. Am. Chem. Soc.* 134 (2012) 10777–10779.
- [25] A.D. Castañeda, N.J. Brenes, A. Kondajji, R.M. Crooks, Detection of microRNA by Electrocatalytic Amplification: A General Approach for Single-Particle Biosensing, *J. Am. Chem. Soc.* 139 (2017) 7657–7664.
- [26] A.J. Bard, L.R. Faulkner, *Electrochemical Methods: Fundamentals and Applications*, 2nd edition, Wiley, 2000.
- [27] T. Moazzenzade, J. Huskens, S.G. Lemay, Stochastic electrochemistry at ultralow concentrations: the case for digital sensors, *Analyst* 145 (2020) 750–758.
- [28] E. Kätelhön, R.G. Compton, Understanding nano-impacts: impact times and near-wall hindered diffusion, *Chem. Sci.* 5 (2014) 4592–4598.
- [29] A. Boika, A.J. Bard, Time of First Arrival in Electrochemical Collision Experiments as a Measure of Ultralow Concentrations of Analytes in Solution, *Anal. Chem.* 87 (2015) 4341–4346.
- [30] J.E. Dick, A.J. Bard, Toward the Digital Electrochemical Recognition of Cobalt, Iridium, Nickel, and Iron Ion Collisions by Catalytic Amplification, *J. Am. Chem. Soc.* 138 (2016) 8446–8452.
- [31] A. Einstein, Über die von der molekularkinetischen Theorie der Wärme geforderte Bewegung von in ruhenden Flüssigkeiten suspendierten Teilchen, *Ann. Phys.* 322 (1905) 549–560.
- [32] IUPAC Compendium of Analytical Nomenclature, http://media.iupac.org/publications/analytical_compendium/
- [33] C.A. Little, R. Xie, C. Batchelor-McAuley, E. Kätelhön, X. Li, N.P. Young, R.G. Compton, A quantitative methodology for the study of particle-electrode impacts, *Phys. Chem. Chem. Phys.* 20 (2018) 13537–13546.
- [34] S.M. Oja, D.A. Robinson, N.J. Vitti, M.A. Edwards, Y. Liu, H.S. White, B. Zhang, Observation of Multipeak Collision Behavior during the Electro-Oxidation of Single Ag Nanoparticles, *J. Am. Chem. Soc.* 139 (2017) 708–718.
- [35] J. Ustarroz, M. Kang, E. Bullions, P.R. Unwin, Impact and oxidation of single silver nanoparticles at electrode surfaces: one shot versus multiple events, *Chem. Sci.* 8 (2017) 1841–1853.
- [36] S.V. Sokolov, T.R. Bartlett, P. Fair, S. Fletcher, R.G. Compton, Femtomolar Detection of Silver Nanoparticles by Flow-Enhanced Direct-Impact Voltammetry at a Microelectrode Array, *Anal. Chem.* 88 (2016) 8908–8912.
- [37] A.N. Sekretaryova, M.Yu. Vagin, A.P.F. Turner, M. Eriksson, Electrocatalytic Currents from Single Enzyme Molecules, *J. Am. Chem. Soc.* 138 (2016) 2504–2507.
- [38] C. Chan, L. Sepunaru, S.V. Sokolov, E. Kätelhön, N.P. Young, R.G. Compton, Catalytic activity of catalase-silica nanoparticle hybrids: from ensemble to individual entity activity, *Chem. Sci.* 8 (2017) 2303–2308.
- [39] R. Gao, M.A. Edwards, J.M. Harris, H.S. White, Shot noise sets the limit of quantification in electrochemical measurements, *Curr. Opin. Electrochem.* 22 (2020) 170–177.
- [40] P.E. Sheehan, L.J. Whitman, Detection Limits for Nanoscale Biosensors, *Nano Lett* 5 (2005) 803–807.
- [41] R. Dasari, K. Tai, D.A. Robinson, K.J. Stevenson, Electrochemical Monitoring of Single Nanoparticle Collisions at Mercury-Modified Platinum Ultramicroelectrodes, *ACS Nano* 8 (2014) 4539–4546.
- [42] D. Wakerley, A.G. Güell, L.A. Hutton, T.S. Miller, A.J. Bard, J.V. Macpherson, Boron doped diamond ultramicroelectrodes: a generic platform for sensing single nanoparticle electrocatalytic collisions, *Chem. Commun.* 49 (2013) 5657–5659.
- [43] L. Jiang, I. Santiago, J. Foord, Observation of nanoparticle events of catalase on diamond ultramicroelectrodes by direct electron transfer, *Chem. Commun.* 53 (2017) 8332–8335.
- [44] S. Eloul, E. Kätelhön, C. Batchelor-McAuley, K. Tschulik, R.G. Compton, Diffusional impacts of nanoparticles on microdisc and microwire electrodes: The limit of detection and first passage statistics, *J. Electroanal. Chem.* 755 (2015) 136–142.
- [45] J. Bonezzi, T. Luitel, A. Boika, Elektrokinetic Manipulation of Silver and Platinum Nanoparticles and Their Stochastic Electrochemical Detection, *Anal. Chem.* 89 (2017) 8614–8619.
- [46] K. Tschulik, R.G. Compton, Nanoparticle impacts reveal magnetic field induced agglomeration and reduced dissolution rates, *Phys. Chem. Chem. Phys.* 16 (2014) 13909–13913.
- [47] G.P. Santos, A.F.A.A. Melo, F.N. Crespihlo, Magnetically controlled single-nanoparticle detection via particle-electrode collisions, *Phys. Chem. Chem. Phys.* 16 (2014) 8012–8018.
- [48] J.J. Yoo, M.J. Anderson, T.M. Alligant, R.M. Crooks, Electrochemical Detection of Insulating Beads at Subattomolar Concentration via Magnetic Enrichment in a Microfluidic Device, *Anal. Chem.* 86 (2014) 4302–4307.
- [49] D.A. Robinson, J.J. Yoo, A.D. Castañeda, B. Gu, R. Dasari, R.M. Crooks, K.J. Stevenson, Increasing the Collision Rate of Particle Impact Electroanalysis with Magnetically Guided Pt-Decorated Iron Oxide Nanoparticles, *ACS Nano* 9 (2015) 7583–7595.
- [50] J.J. Yoo, J. Kim, R.M. Crooks, Direct electrochemical detection of individual collisions between magnetic microbead/silver nanoparticle conjugates and a magnetized ultramicroelectrode, *Chem. Sci.* 6 (2015) 6665–6671.
- [51] T.M. Alligant, M.J. Anderson, R. Dasari, K.J. Stevenson, R.M. Crooks, Single Nanoparticle Collisions at Microfluidic Microband Electrodes: The Effect of Electrode Material and Mass Transfer, *Langmuir* 30 (2014) 13462–13469.
- [52] T.M. Squires, R.J. Messinger, S.R. Manalis, Making it stick: convection, reaction and diffusion in surface-based biosensors, *Nat. Biotechnol.* 26 (2008) 417–426.

- [53] J. Jiang, X. Huang, L. Wang, Effect of forced convection on the collision and interaction between nanoparticles and ultramicroelectrode, *J. Colloid Interface Sci.* 467 (2016) 158–164.
- [54] Y. Bunga, R. Katakya, Silver nanoparticle impacts on gold electrode surfaces in flow-injection configuration, *Sens. Actuators B Chem.* 290 (2019) 140–146.
- [55] J. Ellison, C. Batchelor-McAuley, K. Tschulik, R.G. Compton, The use of cylindrical micro-wire electrodes for nano-impact experiments; facilitating the sub-picomolar detection of single nanoparticles, *Sens. Actuators B Chem.* 200 (2014) 47–52.
- [56] J.E. Dick, A.T. Hilterbrand, L.M. Strawsine, J.W. Upton, A.J. Bard, Enzymatically enhanced collisions on ultramicroelectrodes for specific and rapid detection of individual viruses, *Proc. Natl. Acad. Sci.* 113 (2016) 6403–6408.
- [57] Y. Zhang, J. Mao, W. Ji, T. Feng, Z. Fu, M. Zhang, L. Mao, Collision of Aptamer/Pt Nanoparticles Enables Label-Free Amperometric Detection of Protein in Rat Brain, *Anal. Chem.* 91 (2019) 5654–5659.
- [58] E.J.E. Stuart, Y.-G. Zhou, N.V. Rees, R.G. Compton, Determining unknown concentrations of nanoparticles: the particle-impact electrochemistry of nickel and silver, *RSC Adv* 2 (2012) 6879–6884.
- [59] A.R. Jr, C.A. R. Dantas, C.M. Miyazaki, O.N.O. Jr, Recent advances in electronic tongues, *Analyst* 135 (2010) 2481–2495.
- [60] P. Ciosek, W. Wróblewski, Sensor arrays for liquid sensing – electronic tongue systems, *Analyst* 132 (2007) 963–978.
- [61] C.A. Little, X. Li, C. Batchelor-McAuley, N.P. Young, R.G. Compton, Particle-electrode impacts: Evidencing partial versus complete oxidation via variable temperature studies, *J. Electroanal. Chem.* 823 (2018) 492–498.
- [62] E.J.E. Stuart, N.V. Rees, J.T. Cullen, R.G. Compton, Direct electrochemical detection and sizing of silver nanoparticles in seawater media, *Nanoscale* 5 (2013) 174–177.
- [63] X. Li, C. Batchelor-McAuley, R.G. Compton, Silver Nanoparticle Detection in Real-World Environments via Particle Impact Electrochemistry, *ACS Sens* 4 (2019) 464–470.
- [64] K.J. Krause, A. Yakushenko, B. Wolfrum, Stochastic On-Chip Detection of Subpicomolar Concentrations of Silver Nanoparticles, *Anal. Chem.* 87 (2015) 7321–7325.
- [65] M.Z. Mohamad Nasir, M. Pumera, Impact electrochemistry on screen-printed electrodes for the detection of monodispersed silver nanoparticles of sizes 10–107 nm, *Phys. Chem. Chem. Phys.* 18 (2016) 28183–28188.
- [66] Y.-G. Zhou, N.V. Rees, J. Pillay, R. Tshikhudo, S. Vilakazi, R.G. Compton, Gold nanoparticles show electroactivity: counting and sorting nanoparticles upon impact with electrodes, *Chem. Commun.* 48 (2012) 224–226.
- [67] B. Haddou, N.V. Rees, R.G. Compton, Nanoparticle – electrode impacts: the oxidation of copper nanoparticles has slow kinetics, *Phys. Chem. Chem. Phys.* 14 (2012) 13612–13617.
- [68] N.P. Sardesai, D. Andreescu, S. Andreescu, Electroanalytical Evaluation of Antioxidant Activity of Cerium Oxide Nanoparticles by Nanoparticle Collisions at Microelectrodes, *J. Am. Chem. Soc.* 135 (2013) 16770–16773.
- [69] G. Zampardi, J. Thöming, H. Naatz, H.M.A. Amin, S. Pokhrel, L. Mädler, R.G. Compton, Electrochemical Behavior of Single CuO Nanoparticles: Implications for the Assessment of their Environmental Fate, *Small* 14 (2018) 1801765.
- [70] A. Karimi, S. Andreescu, D. Andreescu, Single-Particle Investigation of Environmental Redox Processes of Arsenic on Cerium Oxide Nanoparticles by Collision Electrochemistry, *ACS Appl. Mater. Interfaces.* 11 (2019) 24725–24734.
- [71] F.H. Narouei, D. Andreescu, S. Andreescu, Rapid characterization of arsenic adsorption on single magnetite nanoparticles by collisions at microelectrodes, *Environ. Sci. Nano.* 7 (2020) 1999–2009.
- [72] D. Yamada, T.A. Ivandini, M. Komatsu, A. Fujishima, Y. Einaga, Anodic stripping voltammetry of inorganic species of As³⁺ and As⁵⁺ at gold-modified boron doped diamond electrodes, *J. Electroanal. Chem.* 615 (2008) 145–153.
- [73] Y.-Y. Bai, Z. Wu, C.-M. Xu, L. Zhang, J. Feng, D.-W. Pang, Z.-L. Zhang, One-to-Many Single Entity Electrochemistry Biosensing for Ultrasensitive Detection of microRNA, *Anal. Chem.* 92 (2020) 853–858.
- [74] A. Karimi, A. Hayat, S. Andreescu, Biomolecular detection at ssDNA-conjugated nanoparticles by nano-impact electrochemistry, *Biosens. Bioelectron.* 87 (2017) 501–507.
- [75] J.Y. Lee, B.-K. Kim, M. Kang, J.H. Park, Label-Free Detection of Single Living Bacteria via Electrochemical Collision Event, *Sci. Rep.* 6 (2016) 30022.
- [76] A.T. Ronspees, S.N. Thorgaard, Blocking electrochemical collisions of single *E. coli* and *B. subtilis* bacteria at ultramicroelectrodes elucidated using simultaneous fluorescence microscopy, *Electrochimica Acta* 278 (2018) 412–420.
- [77] E. Lebègue, N.L. Costa, R.O. Louro, F. Barrière, Communication—Electrochemical Single Nano-Impacts of Electroactive *Shewanella Oneidensis* Bacteria onto Carbon Ultramicroelectrode, *J. Electrochem. Soc.* 167 (2020) 105501.
- [78] G. Gao, D. Wang, R. Brocenschi, J. Zhi, M.V. Mirkin, Toward the Detection and Identification of Single Bacteria by Electrochemical Collision Technique, *Anal. Chem.* 90 (2018) 12123–12130.
- [79] R.A.S. Couto, L. Chen, S. Kuss, R.G. Compton, Detection of *Escherichia coli* bacteria by impact electrochemistry, *Analyst* 143 (2018) 4840–4843.
- [80] L. Sepunaru, K. Tschulik, C. Batchelor-McAuley, R. Gavish, R.G. Compton, Electrochemical detection of single *E. coli* bacteria labeled with silver nanoparticles, *Biomater. Sci.* 3 (2015) 816–820.
- [81] A. Frkonja-Kuczyn, L. Ray, Z. Zhao, M.C. Konopka, A. Boika, Electrokinetic preconcentration and electrochemical detection of *Escherichia coli* at a microelectrode, *Electrochimica Acta* 280 (2018) 191–196.
- [82] L. Sepunaru, B.J. Plowman, S.V. Sokolov, N.P. Young, R.G. Compton, Rapid electrochemical detection of single influenza viruses tagged with silver nanoparticles, *Chem. Sci.* 7 (2016) 3892–3899.
- [83] J.E. Dick, Electrochemical detection of single cancer and healthy cell collisions on a microelectrode, *Chem. Commun.* 52 (2016) 10906–10909.
- [84] L. Sepunaru, S.V. Sokolov, J. Holter, N.P. Young, R.G. Compton, Electrochemical Red Blood Cell Counting: One at a Time, *Angew. Chem. Int. Ed.* 55 (2016) 9768–9771.
- [85] T.L.T. Ho, N.T.T. Hoang, J. Lee, J.H. Park, B.-K. Kim, Determining mean corpuscular volume and red blood cell count using electrochemical collision events, *Biosens. Bioelectron.* 110 (2018) 155–159.
- [86] K. Ngamchuea, R.O.D. Clark, S.V. Sokolov, N.P. Young, C. Batchelor-McAuley, R.G. Compton, Single Oxidative Collision Events of Silver Nanoparticles: Understanding the Rate-Determining Chemistry, *Chem. – Eur. J.* 23 (2017) 16085–16096.
- [87] K.J. Krause, F. Brings, J. Schnitker, E. Kätelhön, P. Rinklin, D. Mayer, R.G. Compton, S.G. Lemay, A. Offenhäuser, B. Wolfrum, The Influence of Supporting Ions on the Electrochemical Detection of Individual Silver Nanoparticles: Understanding the Shape and Frequency of Current Transients in Nano-impacts, *Chem. – Eur. J.* 23 (2017) 4638–4643.
- [88] C.-H. Chen, E.R. Ravenhill, D. Momotenko, Y.-R. Kim, S.C.S. Lai, P.R. Unwin, Impact of Surface Chemistry on Nanoparticle–Electrode Interactions in the Electrochemical Detection of Nanoparticle Collisions, *Langmuir* 31 (2015) 11932–11942.
- [89] H. Ma, J.-F. Chen, H.-F. Wang, P.-J. Hu, W. Ma, Y.-T. Long, Exploring dynamic interactions of single nanoparticles at interfaces for surface-confined electrochemical behavior and size measurement, *Nat. Commun.* 11 (2020) 2307.
- [90] S. Eloul, R.G. Compton, Shielding of a Microdisc Electrode Surrounded by an Adsorbing Surface, *ChemElectroChem* 1 (2014) 917–924.
- [91] S. Eloul, E. Kätelhön, R.G. Compton, When does near-wall hindered diffusion influence mass transport towards targets? *Phys. Chem. Chem. Phys.* 18 (2016) 26539–26549.
- [92] D.A. Robinson, M.A. Edwards, H. Ren, H.S. White, Effects of Instrumental Filters on Electrochemical Measurement of Single-Nanoparticle Collision Dynamics, *ChemElectroChem* 5 (2018) 3059–3067.
- [93] K. Kanokkanchana, E.N. Saw, K. Tschulik, Nano Impact Electrochemistry: Effects of Electronic Filtering on Peak Height, Duration and Area, *ChemElectroChem* 5 (2018) 3000–3005.
- [94] D.A. Robinson, A.M. Kondajji, A.D. Castañeda, R. Dasari, R.M. Crooks, K.J. Stevenson, Addressing Colloidal Stability for Unambiguous Electroanalysis of Single Nanoparticle Impacts, *J. Phys. Chem. Lett.* 7 (2016) 2512–2517.
- [95] J.J. Gooding, Single Entity Electrochemistry Progresses to Cell Counting, *Angew. Chem. Int. Ed.* 55 (2016) 12956–12958.