

ELECTROCHEMICAL NANOFLUIDICS: THE MESOSCOPIC LIMIT

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ABSTRACT

We have developed a lithography-based nanofluidic device for sensitive electrochemical detection applications. The device consists of a solution-filled channel bounded by parallel electrodes that are separated by ~ 50 nm. Redox cycling at the two electrodes is used to amplify the electrochemical signals from molecules in the volume between the electrodes, and can lead to dramatic improvements in sensitivity and/or selectivity. Interestingly, an important limit to sensitivity is placed by statistical fluctuations in the number of molecules present in the device, a consequence of its extremely small volume (a few femtolitres). In this Proceedings article, we focus on the consequences of these statistical fluctuations on the signal-to-noise ratio of electrochemical sensors based on redox cycling.

KEYWORDS: Nanofluidics, electrochemistry, sensing, number fluctuations, mesoscopic.

INTRODUCTION

Electrochemical detection is a method for transducing chemical information (the concentration of an analyte in solution) into an electrical signal (a current resulting from the transfer of electrons between molecules in solution and an electrode). This detection strategy is particularly well suited for integration into complex analytical fluidic systems since (1) it directly yields an electrical signal without the need for optical components, (2) it can easily be miniaturized using standard lithography technology, and (3) it has inherently low power consumption. Compared to competing approaches, however, it suffers from limited sensitivity and, most importantly, from very limited selectivity. The latter is particularly constraining in biomedical applications, where a typical sample contains a plethora of electrochemically active species: the desired signal is thus often masked by contributions from interfering species present at higher concentrations.

We have been exploring the use of nanofluidic devices for boosting both the sensitivity [1,2] and the selectivity [3,4] of electrochemical detection. Our approach is based on so-called redox cycling. As illustrated in Figure 1, we fabricate two planar electrodes separated by a thin (50 nm) layer of liquid. The electrodes are electrically biased such that one electrode donates electrons to the target molecules in solution, while the other electrode withdraws electrons. Randomly diffusing molecules in the layer of liquid thus shuttle electrons from one electrode to the other. Through this molecular ping-pong game, each target molecule can contribute on average $>10^4$ electrons [2] to the electrical current instead of a single electron as would be the case in conventional systems.

At sufficiently small volumes and analyte concentrations, the absolute number of target molecules present in the active region of the devices becomes sufficiently small that conventional mean-field formalisms start to break down. In particular, statistical fluctuations resulting from the discrete nature of molecules become significant. We refer to this intermediate regime between the conventional macroscopic behavior and the molecular limit as the mesoscopic regime. We will see below that these statistical fluctuations can become the dominant source of noise in nanofluidic sensors [1,5]. With such applications in mind, we present in this Proceedings article an analysis of the fluctuations and their consequences for the signal-to-noise ratio (SNR) of the sensor.

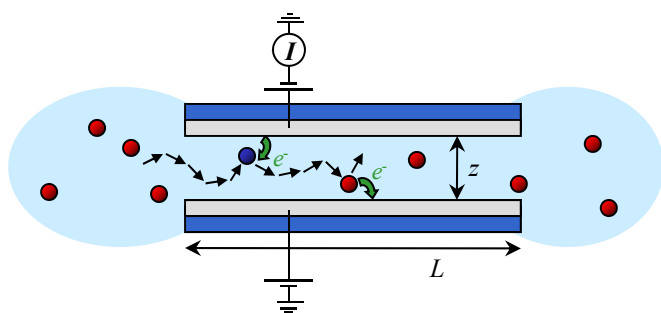


Figure 1: Device concept. Two macroscopic, fluid-filled reservoirs are connected by a nanochannel of length L and height z whose floor and ceiling consist of independently addressable metal electrodes. Electrochemically active molecules are reduced (pick up electrons) at the top electrode and are oxidized (give up electrons) at the bottom electrode. Each molecule undergoing a diffusive random walk inside the channel thus shuttles multiple electrons from one electrode to the other, leading to a dramatic amplification of the current signal $I(t)$.

THEORY

Background. Consider a device as sketched in Figure 1 connected to a large reservoir. The average number of analyte molecules present in the active region between the electrodes, $\langle N \rangle$, is simply given by $\langle N \rangle = N_A V C$, where N_A is Avogadro's number, V is the volume of the active region of the device, and C is the concentration of analyte in solution. Each analyte molecule in the active region undergoes redox cycling, contributing a current of magnitude i_p to the total average current $\langle I \rangle$ flowing between the electrodes. The sensor signal $\langle I \rangle$ is therefore simply given by $\langle I \rangle = \langle N \rangle i_p$.

If one were to take an instantaneous snapshot of the system at some arbitrary time t , however, the instantaneous number of molecules in the active region, $N(t)$, would not necessarily be (or even be likely to be) exactly equal to $\langle N \rangle$. Elementary statistics tells us that the probability of finding exactly N analyte molecules in the active region, P_N , is given by the Poisson distribution, $P_N = \langle N \rangle^N e^{-\langle N \rangle} / N!$. The standard deviation of the Poisson distribution, ΔN , is simply equal to $\langle N \rangle^{1/2}$. The relative size of the deviations is therefore $\Delta N / \langle N \rangle = \langle N \rangle^{-1/2}$. This indicates that the fluctuations in $N(t)$ are utterly negligible in macroscopic systems where $\langle N \rangle$ is very large. Scaling down the dimensions of the system however causes a corresponding decrease in the value of $\langle N \rangle$ and a corresponding increase in the relative size of the fluctuations. Can these fundamental fluctuations impact the performance of nanofluidic sensors?

The noise spectrum. Poisson statistics universally describe the magnitude of the fluctuations in $N(t)$, but this says nothing about their time evolution. The latter is however extremely relevant for a sensor design since fluctuations that occur on a time scale much faster than the response time of the detection system are simply averaged over and are therefore irrelevant. We are thus interested in the spectral density of the fluctuations as well as their amplitudes. For simplicity, we focus here on a device with parallel planar electrodes of length L and separated by a distance $z \ll L$. The electrodes are assumed to span the whole width of a rectangular channel; motion along the width direction is thus irrelevant and the width does not enter explicitly into the problem.

Describing the time evolution of the fluctuations in $N(t)$ requires knowledge of the relevant mass transport equations. We concentrate on the case of no convection and assume a high enough salt concentrations that electrostatics do not influence mass transport (i.e. Debye length much smaller than z). Mass transport is then controlled solely by diffusion and fluctuations in $N(t)$ result from the Brownian motion of independently moving molecules. In this case, $i_p = eD/z^2$, where $-e$ is the charge of the electron and D is the diffusion constant of the molecules, also holds.

The spectrum of number fluctuations for diffusion in an open one-dimensional channel was described in detail by Bezrukov *et al.* [6] and those results can be directly applied here. The only additional approximation is that we take the instantaneous current, $I(t)$, to be simply related to the instantaneous number of particles, $N(t)$, by $I(t) = N(t)i_p$. This is made possible by the fact that $z \ll L$, and thus that the time scale for electron shuttling is a factor of $(L/z)^2 \gg 1$ shorter than for diffusion along the length of the channel. The approximation is valid so long as we are only interested by time scales that are much longer than the shuttling time, z^2/D .

Following [5], the power spectral density for our simple system in the frequency range of interest takes the approximate form

$$S(f) = \frac{S_0}{1 + (f/f_0)^{3/2}}, \quad (1)$$

where S_0 is given by [6]

$$S_0 = \frac{i_p^2 L^2}{3D} \langle N \rangle \quad (2)$$

and f_0 by

$$f_0 = \frac{3^{2/3} D}{\pi L^2}. \quad (3)$$

The noise is thus white at low frequencies and decreases as $f^{-3/2}$ above a crossover frequency f_0 . The value of f_0 is directly related to the typical residence time of a particle in the channel, and therefore decreases for longer channel lengths as expected from intuition.

Comparison with shot noise. To underline the importance of this source of noise, particularly at low frequencies, it is useful to compare the power density given by Eq. (2) with that expected for shot noise for the same average current. The power density for shot noise is given by $S_{\text{shot}} = 2e \langle I \rangle = 2e i_p \langle N \rangle$, yielding $S_0/S_{\text{shot}} = L^2/6z^2$ [1]. For a device with typical dimensions $L = 50 \mu\text{m}$ and $z = 50 \text{nm}$, this means that noise caused by number fluctuations has a power density that is a factor $>10^5$ times larger than the corresponding shot noise.

DISCUSSION

In a typical sensing experiment, the current $I(t)$ is measured and used to determine the concentration of redox molecules in solution using $C = \langle N \rangle / N_A V = \langle I \rangle / N_A V i_p$. Statistical noise in the measured current therefore leads to error in the measured concentration. We define the signal-to-noise ratio as $\text{SNR} = \langle I \rangle / \Delta I_m$, ΔI_m being the measured rms amplitude of the current noise taking into account any filtering by the detection electronics:

$$\Delta I_m = \sqrt{\int S(f) |T(f)|^2 df}. \quad (4)$$

Here $T(f)$ is the transfer function of the electronics. For simplicity, we consider an idealized measurement system with a sharp step-function cutoff at f_m . Additional noise contributions from, e.g., the measurement electronics are ignored here, a reasonable simplification since statistical noise is usually the dominant source of noise in these systems. We are interested in how varying the dimensions of the system impacts the SNR.

Case 1: $f_m > f_0$. In this case the measurement electronics are fast enough to be integrated over the full bandwidth of the statistical noise. In this case ΔI_m is just the general result from Poisson statistics, $\Delta I_m = i_p \langle N \rangle^{1/2}$, and $\text{SNR} = \langle N \rangle^{1/2}$, independently of device geometry. Note however that the sensor response speed is intrinsically limited by the speed at which molecules can diffuse between the device and the external reservoir, a process which occurs on a time scale $\sim L^2/8D$. Increasing f_m much above f_0 therefore does not yield an advantage.

Case 2: $f_m < f_0$. Here the measurement takes place in the frequency range where statistical noise has a constant spectral density given by Eq. (2), and higher frequency fluctuations are filtered out. In this case,

$$\text{SNR} = \frac{1}{L} \left(\frac{3D \langle N \rangle}{f_m} \right)^{1/2}. \quad (5)$$

This is a somewhat counterintuitive result: increasing the length of the channel, L , by a factor of 2 causes the signal $\langle I \rangle$ to double but the SNR to *decrease* by a factor $2^{1/2}$ (taking into account that $\langle N \rangle$ depends on L in Eq. (5)). Conversely, reducing L while keeping the device volume constant (e.g. by increasing the width of the device to compensate) leads to an improvement in the SNR. In the same manner, several short devices in parallel yield a higher SNR than a corresponding monolithic device with a length equal to the cumulative length of the short devices.

CONCLUSION

Redox cycling between electrodes separated by nanometer-scale dimensions can result in dramatic gains in electrochemical signals and selectivity. However, one penalty for using devices with such small volumes is that the absolute number of molecules contributing to the signal can become very small. When this occurs, statistical fluctuations in molecule numbers become the dominant source of noise in the sensor. In these cases, a proper choice of device geometry can greatly mitigate the influence of statistical fluctuations on the signal-to-noise ratio.

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REFERENCES

- [1] M.A.G. Zevenbergen, D. Krapf, M.R. Zuiddam, S.G. Lemay, "Mesoscopic concentration fluctuations in a fluidic nanocavity detected by redox cycling," *Nano Letters*, **8**, 497 (2007).
- [2] M. A. G. Zevenbergen, B.L. Wolfrum, E.D. Goluch, P.S. Singh, S.G. Lemay, "Fast electron-transfer kinetics probed in nanofluidic channels," *Journal of the American Chemical Society*, **394**, 447 (2009).
- [3] B.L. Wolfrum, M.A.G. Zevenbergen, S.G. Lemay, "Nanofluidic redox cycling amplification for the selective detection of catechol," *Analytical Chemistry*, **36**, 3342 (2008).
- [4] E.D. Goluch, B.L. Wolfrum, P.S. Singh, M.A.G. Zevenbergen, S.G. Lemay, "Redox cycling in nanofluidic channels using interdigitated electrodes," *Analytical and Bioanalytical Chemistry*, **22**, 1036 (2009).
- [5] M. A. G. Zevenbergen, P.S. Singh, E.D. Goluch, B.L. Wolfrum, S.G. Lemay, "Electrochemical correlation spectroscopy in nanofluidic cavities," *Analytical Chemistry*, **81**, 8203 (2009).
- [6] S. M. Bezrukov, A. M. Berezhkovskii, M. A. Pustovoit, A. Szabo, "Particle number fluctuations in a membrane channel," *J. Chem. Phys.* **113**, 8206 (2000).

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