DETECTION OF SUB-PICOLITER-PER-MINUTE FLOWS BY ELECTROCHEMICAL AUTOCORRELATION SPECTROSCOPY

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ABSTRACT

This paper reports on electrochemical autocorrelation spectroscopy as a technique to detect ultra-low liquid flow rates as well as to generally study transport of small amounts of molecules in a nanofluidic channel. The molecules undergo pronounced number fluctuations due to Brownian motion. We measure these fluctuations electrically using nanogap transducers embedded in the walls of a nanochannel. When liquid is driven through the channel, also the fluctuations are transported at the same velocity, which we detect by performing an autocorrelation analysis of current-time traces obtained at the detector. Thereby we are able to determine record-low flow rates below 1 pL/min.

KEYWORDS

Nanofluidics, flow detection, electrochemical sensor, autocorrelation, redox cycling

INTRODUCTION

A sensitive flow measurement would be desirable for, e.g., the investigation of slip at liquid-solid boundaries [1], the transport of macromolecules through nanochannels [2] or mixing in nanofluidic chemical reactors [3]. However, the low flow rates that are encountered in nanofluidic systems are challenging to measure since only minuscule amounts of liquid are transported. For example, at a flow rate of 10 pL/min it would take over five years for a drop of water (30 µL) to pass through a nanochannel. The lower limit for flow rates measured with a commercially available system is 500 pL/min based on on-chip detection of heat transfer (SLG1430 Liquid Mass Flow Meter, Sensirion AG, Switzerland). Lower flow rates have been determined by optical detection of a moving liquid-air meniscus, either using a laser distance meter [4] or by direct observation of the filling of a channel. Liang *et al.* monitored the displacement of a water-air boundary in a microchannel downstream of a nanochannel down to a record low rate of 30 pL/min [5].

THEORY

Our method is based on the detection of number fluctuations of solute molecules in a nanochannel. We measure these fluctuations by using electrochemical nanogap transducers consisting of two electrodes embedded in opposing nanochannel walls [6] (see Figure 1). The electrodes are biased to allow for redox-cycling to take place, i.e. the repeated oxidation and reduction of electrochemical active molecules. The molecules shuttle in between the electrodes by diffusion and transport several thousand electrons per second across the channel, thereby generating a highly amplified electrical current that is directly proportional to the number of analyte molecules present in the device. This number N and the corresponding current I fluctuate considerably in time due to random Brownian motion undergone by the molecules. The number density follows a Poisson distribution, and the ratio of noise to average number scales as $\sqrt{\langle(\Delta N)^2\rangle}/\langle N\rangle = 1/\sqrt{N}$. These fluctuations can therefore only be detected in nanoscale volumes and/or in strongly diluted solutions.

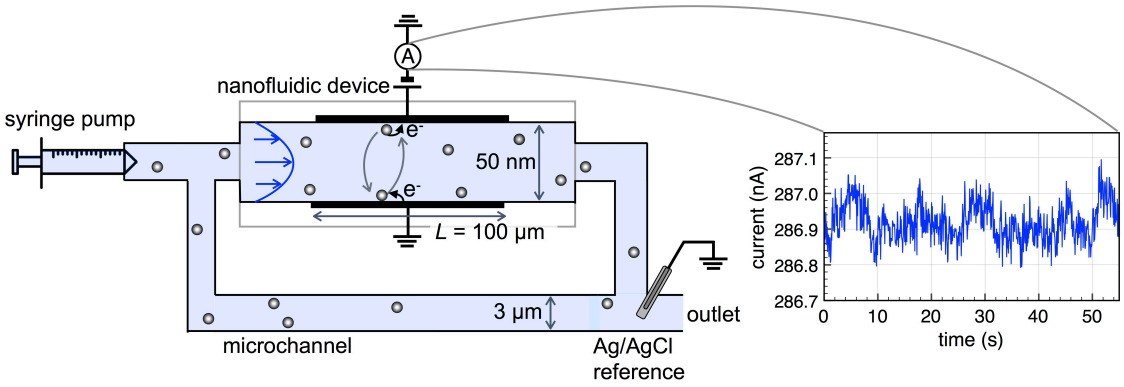

Figure 1. Schematic of the measurement concept (not to scale). Low flow rates are generated by using a syringe pump in a parallel flow configuration, in which a micro- and nanochannel run in parallel to reduce the nanochannel flow by the ratio of both channels' hydraulic resistances. Electrochemically active molecules undergo redox cycling at electrodes embedded in the nanochannel walls. This allows for a sensitive detection of the absolute number as well as number fluctuations of molecules present in the nanochannel. Flow velocities are determined by autocorrelation analysis of the detected current-time traces.

The change of the number density of molecules in the channel over time is reflected in the autocorrelation function $G(\tau)$ of current fluctuations $\delta I(t) = I(t) - \langle I(t) \rangle$:

$$G(\tau) = \langle \delta I(t) \delta I(t+\tau) \rangle$$

$G(\tau)$ is a function of the diffusion coefficient of the molecules and the channel geometry and approximately decays exponentially in the time that it takes for one molecule to diffuse along the detection volume [7].

When liquid is driven through the device, also the molecular number fluctuations are pushed through the nanochannel. Therefore, the residence times are reduced and the correlation of the current-time traces is lost at shorter times as the flow rate is increased. (Note that due to the high-aspect-ratio geometry leading to low Péclet numbers Pé < 0.1, the flow does not influence the number density and is strictly superpositioned to the diffusive transport.) We detect liquid flow by determining the average velocity of molecules $v = L/\tau_0$, where L is the length of the detection area and τ_0 denotes the time at which the correlation is lost, $G(\tau_0) = 0$. I.e. if the molecules are transported at 50 µm/s in a 100 µm long device, all molecules in the detection volume are replaced after 2 s and the autocorrelation is then lost entirely.

DEVICE FABRICATION AND FLOW GENERATION

100 µm long, 5 µm wide and 50 nm high nanogap devices were fabricated on an oxidized silicon wafer as described previously [8]. A 20 nm thick Pt bottom electrode, a 50 nm sacrificial Cr layer defining the nanochannel volume and a 100 nm thick Pt top electrode were defined by optical lithography and deposited by consecutive electron-beam evaporation and lift-off steps. The channels were covered in a 500 nm thick SiN passivation layer, which was opened up at both ends of the nanochannel by reactive-ion etching to form access holes.

Liquid was driven through the nanodevice by a syringe pump, which however cannot deliver ultra-low flow rates directly. We therefore used the pump in in a parallel flow configuration [5] as sketched in Figure 1: a microfluidic layer in polydimethylsiloxane was bonded to the device so that a 100 µm long, 5 µm wide and 3 µm high microchannel connected both access holes of the nanochannel. The flow was then divided in between the parallel nano- and microchannel according to the ratio of their hydraulic resistances. These resistances depend cubically on the channel height [9], and the nanochannel flow rate was reduced by a factor of approximately 270 000 with respect to the pump flow rate.

EXPERIMENTAL

Ferrocenedimethanol ($Fc(MeOH)_2$ from Acros, diffusion coefficient $D = 6.7 \cdot 10^{-10}$ m^2/s) as redox-active species was prepared as a 1 mM solution in Milli-Q water with 1 M KCl (Sigma-Aldrich) added as background electrolyte together with 5 mM H_2SO_4 (Sigma-Aldrich) to prevent electrode degradation. Prior to measurements, the Cr sacrificial layer was removed and the nanochannel was released by filling the microchannels with a chromium etchant solution (Selectipur, BASF). The $Fc(MeOH)_2$ containing solution was then driven through the channel with varying syringe pump flow rates of up to 100 µL/h.

Both the bottom and top electrode of the device were connected to a CH Instruments 842B bipotentiostat and biased at 0 V and 0.5 V, respectively, to allow for redox cycling to take place. A Ag/AgCl reference electrode was connected downstream of the nanochannel. The whole setup was shielded from interference in a Faraday cage. 300 s long current-time traces were recorded with 10 ms sampling intervals at the top electrode. High-pass filtering was applied to remove low frequency drift.

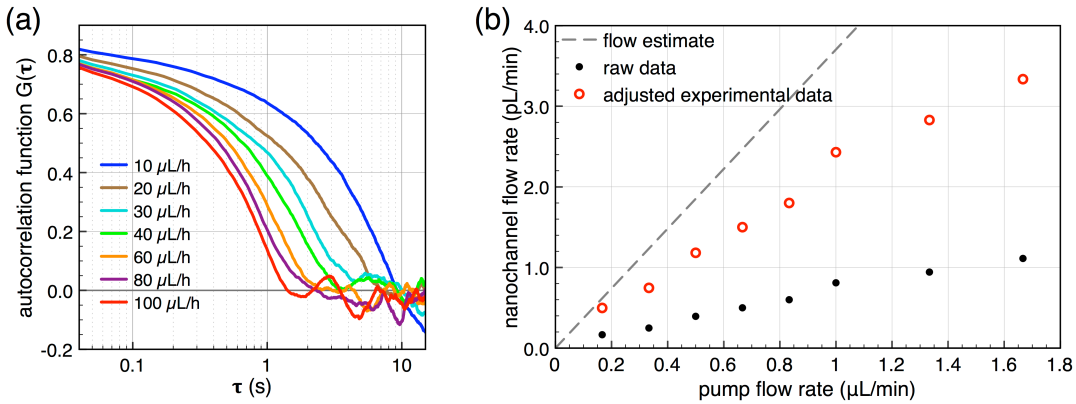

Figure 2. (a) Autocorrelation functions for different syringe pump flow rates determined from current-time traces recorded in a 100 µm long, 5 µm wide and 50 nm high nanochannel. (b) Nanofluidic flow rates as a function of the pump flow rate. Red circles denote experimental data that has been corrected for dynamic adsorption of analyte molecules at the nanochannel walls. The slope of the dashed line is an estimate of the ratio of the hydraulic resistances of the nano- and microchannel.

RESULTS AND DISCUSSION

Figure 2a shows autocorrelation functions of the current-time traces as a function of the pump flow rate. The correlation is lost at shorter times τ_0 with an increasing pump flow rate reflecting the shorter residence times of molecules in the device. We determine liquid flow rates by dividing the detection volume by the times τ_0, which we extrapolate from the autocorrelation function. Nanochannel flow rates obtained in this way are shown in Figure 2b as a function of the syringe pump flow rate (black dots). However, these rates do not reflect the actual liquid flow. Due to the high surface-to-volume ratio of the channel of $2 \cdot 10^7$ m^{-1}, reversible dynamic adsorption of the molecules at the channel walls is a pronounced effect. Molecules can only move while in solution, and therefore adsorption effectively leads to retardation of the molecules' average velocity with respect to the liquid flow. The fraction of the number of adsorbed molecules is readily extracted from the ratio of the current noise and current amplitude [10]. On average it amounts to $N_{\mathrm{ads}}/N_{\mathrm{tot}} = 0.66$, i.e. the molecules are slowed down to 33% of the average liquid flow speed. Adjusted flow rates are shown as red circles in Figure 2b. They are in agreement with the expected rates (dashed line), which can be estimated only with a large error margin because they depend cubically on both channels' height and the PDMS bulges at higher pressures [11], thus reducing the nanochannel flow nonlinearly.

We are able to detect nanofluidic flow rates below 1 pL/min, which is well below the lowest values of approximately 30 pL/min reported for optical detection.

CONCLUSION AND OUTLOOK

We have used all-electric autocorrelation spectroscopy of mesoscopic number fluctuations to detect record-low liquid flow rates in electrochemical nanogap sensors. This method is the direct analogue to fluorescence correlation spectroscopy [12] and can also be used to investigate a wider range of properties such as adsorption, concentration, diffusion or reaction kinetics. Our measurement was performed with a comparatively high concentration of 1 mM, but the sensitivity of the nanogap allows the detection of concentrations well below 1 nM [13] and we envision studying transport of single molecules.

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