Optical monitoring of micro fluidic flow conditions, employing surface plasmon resonance sensing

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Abstract. Near surface flow conditions in micro / nano channels are difficult to assess by experiment. Associated flow and materials transport properties yet are poorly understood, and inconclusive. A novel optical tool for determination of the near wall transport parameters in a micro channel, utilizing the evanescent field of a surface plasmon resonance (SPR) set-up as the sensing probe, is presented. The method is based on the transient flow response due to convective diffusion, in absence of specific adsorption. An approximately step-function type temporal solute concentration variation serves as the input signal. The time varying optical response of a surface plasmon resonance sensor, acting as an integral part of a micro channel, has been taken as the output signal. It provides the flow dependent change of the solute concentration in the channel within the optical detection and near wall distance interval $0 < d < 0.5 \, \mu m$. The temporal signal evolution and response time, until an initially plain aqueous solution is replaced by the solute, varies inversely with solute concentration and flow rate. In the asymptotic limits, the near wall forced convective and diffusive channel transit times, along with the associated velocities, can be extracted and separated. The validity of the scaling relation for Fickian diffusive transport has been confirmed by experiment. Furthermore, solute diffusion coefficients in the solution can be determined with high precision. Convective near wall flow reveals a distorted parabolic flow profile and indicates relaxation of the no-slip condition, and presence of slip flow. Comparison with Poiseuille flow conditions, calculated for the same channel geometry, reveals a threshold characteristic. The experimental data allow estimations of the slip length / slip velocity that varies non-linearly with the macroscopic flow rate in the channel.
1. Introduction

Recent developments of sensitive and compact instrumentation for life science and environmental analytical applications, also known as lab-on-chip or micro total analysis systems (μ-TAS), have attracted considerable technological and economic attention [2, 5]. The technology crucially relies on and comprises controlled fluid transport of liquid analytes to and from a sensing transducer, using integrated micro fluidic devices. Particle transport within fluids, containing dissolved solutes, is appropriately treated by a combination of convective diffusion (CDE) with hydrodynamic Navier-Stokes (NSE) equations. This covers the interplay of two different, superimposed and perpendicular transport mechanisms: molecular diffusion of the solute out of the bulk fluid towards the channel walls, mainly driven by local concentration gradients, and forced convective, hydrodynamic transport of the solute within the solution along the channel. The CDE and NSE represent non-linear second order partial equations, with variable coefficients. The solutions shall provide both, the temporal development and spatial distribution of solute concentration \( c(x, y, z, t) \), along with its velocity profile. Solving of the CDE and the NSE is mathematically demanding, largely related to difficult boundary and initial conditions. Both, boundary and initial conditions depend critically on the nature of physico-chemical processes of the solute(s) in solution and their interaction at or on bioactive interfaces, acting as sensing or functionalized elements.

Under certain conditions, micro- and macrofluidic conduits reveal substantially different, yet not fully understood hydrodynamic properties [3]. The reduced geometric dimensions of micro channels account for more complex flow pattern, particularly near wall boundaries, where the high surface to volume ratio supports increased influence of surface effects. They may originate from micro surface roughness and friction, micro air bubble and / or boundary layer formation, local electric fields by adsorbed charges and impurities, and interfacial potential gradients. A further important and related, but rarely considered issue addresses the wetting properties at the wall surface, whether behaving hydrophilic or hydrophobic and, eventually, the influence and magnitude of capillary forces. Under these conditions, the no-slip flow condition commonly holds in a modified form, but is insufficiently treated by conventional theory. At very small dimensions, reliable flow profile measurements are difficult to perform.

Presently, only a limited number of experimental micro flow investigations have been reported. High-resolution velocity profiles in micro channels, recorded by image velocimetry (PIV), revealed significant deviations from ideal flow behavior, particularly at flow boundaries and interfaces, and in close vicinity to channel walls. At distances < 5\( \mu \)m, boundary layer effects, flow oscillations, as well as vortex like fluid motions have been resolved [9, 10], while at larger wall distances the parabolic profile was largely maintained. The PIV technique, however, is not suited to reliably probe the near surface region at distances at or below the \( \mu \)m range. In this work, an attempt has been made, to evaluate near wall fluid transport parameters with high spatial resolution by experiment. Quantitative data are important, since they determine the sensing characteristics and adsorption efficiency of the flow cell, but also affect and distort measurements of kinetic binding constants. The transient response of surface plasmon resonance (SPR) recordings in absence of surface adsorption has been used to extract quantitative solute transport data, with the optical instrument serving as an integral part of the micro flow channel. The optical sensing range of the SPR phenomenon comprises a precisely defined wall distance interval, at which flow parameters are extracted. It is placed at approximately 0.5\( \mu \)m, or about half of the operating wavelength of the SPR spectrometer. The associated physical function and operation conditions of the surface plasmon resonance spectrometer [7], and instrument employed in this work have been reported in detail elsewhere [6]. Both, convective and diffusive flow velocities superimpose, and differ substantially. This difference can be explained and elaborated on bases of the above mentionned convective diffusion equation that applies to the flow system under investigation. By varying solute concentration and flow velocity / flow rate both, diffusive and convective transport parameters can be explored directly.

2. Theoretical aspects and data extraction

The general dynamic vector form of the differential convective diffusion equation follows ultimately from the continuity equation

\[
\frac{\partial c}{\partial t} = - \text{div } j
\]  

(1)
where \( j \) is the mass flow and describes the motion of an ionic or macromolecular solute particle in a solvent stream:

\[
\frac{\partial c}{\partial t} = D \Delta c - (v \cdot \text{grad}) \cdot c \quad (2)
\]

\( c \) represents the temporal and spatial concentration distribution of the solute in the solvent. \( D \) is the diffusion coefficient of the solute, and \( v \) the temporal and spatial velocity profile of the solution. Source and sink terms are not included, since specific solute adsorption is absent.

Under stationary conditions, \( \frac{\partial c}{\partial t} = 0 \), the CDE reduces to:

\[
D \Delta c = (v \cdot \text{grad}) \cdot c \quad (3)
\]

which can be solved analytically for simple geometries. Subtraction of the stationary form from the dynamic CDE, yields the temporal variation \( \frac{\Delta c}{\Delta t} \). Tracking of the temporal evolution \( \Delta t \) resp, until stationary conditions and chemical equilibrium are established, provides an experimental exploration method of the CDE. Defined initial conditions are required to numerically extract the transient response. Consequently, the application of a solute concentration variation step \( \Delta c \) as an input quantity is providing \( \Delta c \Delta t \) resp, which varies with \( c, v, D, \) and temperature as well as the channel geometry.

In the asymptotic limit, for \( v \to 0 \), at finite \( c \), the CDE transforms into the molecular diffusion equation:

\[
\frac{\partial c}{\partial t} = D \Delta c \quad (4)
\]

The NSE can be related to the CDE in absence of a dissolved solute, i.e., at \( D = 0 \), and replacement of the solute (analyte) concentration \( c \) by the solvent density \( \rho \). In absence of the diffusive term, for \( c \to 0 \) at finite \( v \), (2) transforms into the first Navier-Stokes equation, to compute the velocity profile:

\[
\frac{\partial \rho}{\partial t} = - \text{grad} (\rho v) \quad (5)
\]

Thus, evaluation of the dynamic flow response \( \Delta c \Delta t \) in the asymptotic limits, for \( v \to 0 \) and \( c \to 0 \), shall provide information on the diffusive and convective flow properties in the channel.

The Poiseuille equation represents a simple analytical solution to the NSE for tubular and rectangular channel with low aspect ratios. The ideal velocity profile across the channel cross section is parabolic, with \( v_t(z) = 0 \) at the wall surface \( (z = \frac{h}{2}) \), comprising the no-slip condition:

\[
v_t(z) = (z^2 - \frac{h^2}{4}) \cdot \frac{1}{2} \frac{\partial \rho}{\partial x} \quad (6)
\]

\( v_t \) is the tangential velocity component in the flow direction \( z \), \( \frac{\partial \rho}{\partial x} \) is the pressure gradient along the cell length, \( h \) the cell height. The total mass flux \( j \) of the solute out of the solution onto the active sensing area is given by two contributions

\[
j = cv - D \cdot (\text{grad} c) \quad (7)
\]

Calculation of \( j \) requires solving of the CDE for both \( c(x, y, z, t) \) and the solution velocity \( v(x, y, z, t) \).

Transient response analysis also has been used to study diffusion through membranes [8]. The transient SPR signal, taken in this work in close vicinity to the wall surface within the distance interval \(< 0.5 \mu m \), exploits local flow properties via its solute concentration dependent temporal refractive index variations \( \Delta c(\Delta n(t)) \).

3. Experimental aspects

A sketch of the experimental set-up, comprising a SPR sensor with angular interrogation, is illustrated in Fig. 1a. The optical sensor with its attached semi-transparent gold film and sensing surface is placed at the lower base plate of the channel. The counter plate is made from Teflon, and comprises the flow in- and outlet. The local optical SPR probing range into the flow channel is indicated in the lower, cut-out magnified figure. It corresponds to the decay length and extension of the evanescent optical wave
Figure 1. a) Schematic arrangement of the flow cell with its integrated SPR-sensor. Flow and solute transport conditions are indicated in the figure. The magnified bottom section illustrates the near wall optical sensing range, defined by the penetration of the SPR-evanescent wave field into the solution, up to 0.5\(\mu\)m. Approximately 70% of the signal originate within a distance interval of 0.2\(\mu\)m from the gold surface b) Black box schematics of the input-output relation. The step function type flow input signal applies at the left flow cell entrance, the (optical) output signal is taken at the SPR sensor c) Cross-sectional high resolution transmission electron microscope (TEM) image of the channel wall forming gold surface, depicting rms roughness modulations around 3 – 5nm.
state condition is reached.

Both, diffusive and convective transport of solute ions out of the bulk solution flow towards, and along the sensing surface superimpose, and cause a temporal change of the ion concentration within the SPR sensing volume $\Delta c(t)$. Over a time period $\Delta \tau$, a stable uniform ion concentration distribution and chemical equilibrium is established within the channel. The transient output signal, provided by the SPR spectrometer, delivers the temporal variation of the concentration dependent refractive index within the sensing volume $\Delta n(t)$, either governed by diffusive or convective transport, $\tau_{\text{Diff}}$ and $\tau_{\text{Conv}}$, or a combination thereof. For moderately high solute concentrations, the associated refractive index variation scales strictly linear, thus providing a direct measure for the concentration within the near wall region.

The SPR cell response time, taken as the output signal, was determined as function of solute concentration variations $\Delta c$ and volume flow rate $f$, using the 10% to 90% SPR signal variation criterion, as well as their asymptotic values at $f \rightarrow 0$ and $c \rightarrow 0$, respectively. As mentioned before, in the former case, the diffusive transit time and associated diffusion length are explored, at which solute particles are traveling perpendicular to the sensing surface, until the sensing volume (in front of the sensing surface) is filled. In the latter case, the forced convective response can be extracted, where the solute particles travel preferably lateral, in close vicinity of the sensing surface, until the sensing volume is filled, while the diffusive flow contribution can be neglected.

Experiments have been performed at ambient temperature (25°C), using the SPREET A surface plasmon resonance evaluation kit, and attached flow cell, described in detail elsewhere [6]. Due to its robust and stable design, the device is easy to operate. Supplying suited peripheral instrumentation and optimized operation conditions both, noise level and sensor drift can be maintained at very low levels, utilizing a temporal resolution of 2s.

4. Results and discussion
Figs. 2a and b depict representative variations of SPR signals (in RIU values), as a function of time for 0.1m and 0.006m NaOH solutions, respectively. Note that the SPR-output signal variation $\Delta n$ (in RIU) is proportional to the input concentration variation, $\Delta c$. While the former data set at large $c$ reveals a single, sharp temporal SPR response variation, and rapid signal increase over a time scale of 30 – 40s, at very low concentration two different, superimposed response features at similar magnitude, but substantially different time scales are resolved: an initial, fast response of around 20s, followed by a much slower temporal variation, extending up to 300s.

Fig. 3(a) outlines the recorded 10% – 90% response times $\Delta \tau_{\text{resp}}$, as a function of NaOH solute concentration $c$, depicted in a log-log representation. Data have been taken at constant volume flow rate of 444µL/min. For comparison, the originally recorded linear plots are included in the insets for both, NaOH and NaCl solutions.

There are three different flow regions resolved for the NaOH solution: a region of constant SPR response $\Delta \tau_{\text{resp}} = 34 + / - 4.1s$ at high NaOH concentrations, with $c > 0.1$; a transition region, with
the molar concentration varying at \( 0.1 < c < 0.01 \), featuring a steady increase of the response time and, eventually, a stable region at very low concentrations. At \( c < 0.01 \), the response time remains stable at \( \tau_{\text{RESP}} = 234 +/- 41 \) s, independent of the solute concentration. Considering the channel length of \( 11 \text{mm} \), the associated (averaged) near wall hydrodynamic flow speed within the wall distance from 0 to 0.5 \( \mu \text{m} \) at the given flow rate is determined to \( v_{HD} = 0.047 \text{mm/s} \).

The near wall flow speed squares with the applied flow rate, and associated uniform flow velocity \( v_u \), respectively. This is illustrated in Fig. 3(b), where the experimentally determined \( v_{HD} \) is plotted against the applied \( v_u \) in the channel. \( v_u \) is obtained from the applied volume flow rate, taking into account channel length and volume. Fig. 4 shows the estimated slip velocity \( v_{slip} \) and slip length \( \delta_{slip} \) obtained at an uniform flow velocity of \( 9 \text{mm/s (540\mu l/min)} \) determined to \( 0.07 \text{mm/s} \) and \( 0.73 \mu \text{m} \). For this estimate it was considered that the experimental flow profile is also parabolic, and obeys the same slope near the surface. For the uniform flow velocity \( < 5 \text{mm/s} \) as threshold value it has been found, below which slippage disappears. For higher uniform flow speeds the slip length increases non-linearly.

The related, convective response time \( \Delta \tau_{HD} \) scales inversely with \( v_u \), following a power law, as indicated in the Fig. 5(a). For comparison, the inset reveals the estimated hydrodynamic transit time, calculated on bases of the Poiseuille equation for a wall distance of 0.5 \( \mu \text{m} \). Distinct differences exist between both data sets: the estimated transit / response times for the purely parabolic flow profile are about a factor 2 higher than the experimentally determined \( \tau_{HD} \)-values. In other words, the ideal parabolic flow profile yields about a factor 2 lower near wall flow speed, compared to the experimentally determined quantity.

The temporal concentration variation \( \Delta c/\Delta \tau \) in the high concentration limit for a \( 0.1 \text{m NaOH} \) solution, as function of volume flow rate is depicted in Fig. 5(b). The inset reveals the original data set, where the response time reveals a clearly non-linear increase with decreasing flow rate, along with an associated exponent of \(-0.69 \). The large difference to the exponent of \(-1.21 \) in Fig. 5(a), recorded at very low solute concentrations, illustrates the different dominating transport mechanisms. It is important to note that \( \Delta c/\Delta \tau \) scales linearly with \( f \), thus establishing easy extrapolation towards \( f = 0 \) (or \( u = 0 \)), to extract the value of the (aforementioned concentration independent) diffusive transit time. In accord with the solution to (4), for the given flow cell geometry, the diffusive transit time until the (concentration) equilibrium is established, is determined from \( \Delta c/\Delta \tau_0 = 0.0029 \), to \( \tau_{Diff} = 172.4 \) s. Considering the channel height and diffusion length of 0.75 mm, the associated diffusion velocity across the channel is obtained to \( v_{Diff} = 0.0043 \text{mm/s} \), independent of the applied flow rate.

The present experimental findings concern several different critical transport issues, related to
Figure 4. Estimated slip velocity and slip length at an uniform flow velocity of 9 mm/s (540 µl/min).

Solute diffusion and forced convective flow. A theoretical approach, addressing the diffusive transit time, has been used before [11], and based on the Fickian diffusion scaling relation. The expression originates from statistical mechanics considerations, and is given as $\tau_{\text{Diff}} = \frac{h^2}{D}$, where $h$ is the cell height, or mean square particle displacement, and $D$ the diffusivity of the solute. High fraction of the output signal originates from the presence of $OH^-$ ions in the solution. Also, $OH^-$ ion diffusivity and mobility values are approximately a factor 3 higher, compared to their $Na^+$- counter ions, thus implying faster transport into the near surface sensing volume. It is therefore reasonable, to select the associated transport coefficient [12] with $D_{OH^-} = 3.12 \times 10^{-5} \text{cm}^2/\text{s}$, and not the about 30% lower combined ion pair diffusivity. With this approximation, and using the cell height $h = 0.75 \text{mm}$, the diffusive transit time calculates to $\tau_{\text{Diff}} = 180.3 \text{s}$. Within an error margin of 5%, this value agrees with the experimentally determined $\tau_{\text{Diff}} = 172.4 \text{s}$.

The experimental results directly confirm the presence of convective flow conditions in the near wall regime $\leq 0.5 \mu m$, along with the absence of a boundary layer. Experimental evidence for the possibility of such a stable boundary layer in a micro channel, where the tangential velocity component drops

Figure 5. (a) Variation of SPR response time as function of applied uniform flow velocity, associated to the data set of Fig. 3(b). The solid line corresponds to the best fit, employing a power law at an exponent of $-1.21$. Inset reveals the variation, obtained for the ideal parabolic flow profile from the Pouseille equation for a wall distance of $0.5 \mu m$, revealing an exponent of $-1$. (b) Experimentally determined variation and shape of the dynamic part of the CDE, $\Delta c/\Delta \tau$, as function of volume flow rate for determination of the diffusive transport parameter for 0.1 molar NaOH solution. The broken line indicates extrapolation to $f = 0$, which provides the diffusive transit time. Inset reveals the associated original data set of the SPR response time as function of flow rate.
to zero within wall distances up to 5µm, was given in the PIV data of Fig. 8 of [9]. On the other hand, shortly outside of this no-slip region, below and at µm ranges, the tangential flow velocity reveals comparable magnitudes under conditions, pertaining to and displayed in Fig. 3(b). The agreement with the results of independent experimental micro flow observations, obtained with a different technical set-up, thus confirms the present findings and associated data extraction method.

At present, there is no full understanding, regarding the origin of scaling effects and deviations from the ideal parabolic hydrodynamic flow profile near channel walls. Variations of viscosity along the flow direction have been considered recently [4]. Also, surface effects have been invoked to play a crucial role, and the relaxation of the no-slip condition has been attributed to the presence of hydrophilic or hydrophobic surfaces [1], and surface roughness or intermolecular interactions for very smooth surfaces [13]. Direct evidence for the existence of rate dependent slip flow has been reported recently [14]. The recorded slip length, which is proportional to the slip velocity [1] was shown to scale non-linearly with the applied flow rate / flow velocity, similar to the results presented in Fig. 3(b) of this work. Therefore, we attribute the observed high near wall velocity primarily to the presence of slip flow at the wall surface, which distorts the ideal low velocity parabolic profile within the SPR-sensing volume.

5. Conclusions
The transient flow of an aqueous solution has been exploited, towards analysing flow conditions in a microchannel. Flow properties are ascribed to the convective diffusion equation, transforming into the Navier-Stokes equation at low solute concentration and the diffusion equation at low flow speed. The evanescent wave of a surface plasmon resonance set-up has been used as the sensing probe, penetrating approximately 0.5µm into the channel. From the temporal signal evolution, the near wall forced convective and diffusive channel transit times have been extracted. Analysis of the data reveals validity of the Fickian scaling law. The method allows precise determination of solute diffusion coefficients in aqueous solution. Above a critical flow rate, near wall convective flow speed substantially exceeds Pouseuille flow for an ideal parabolic profile, and is indirectly attributed to the presence of slip flow.

6. References
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