

# CONTROLLED ELECTROPHORETIC FILTERING OF BIO SAMPLES USING PI FLOW FETS

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## ABSTRACT

The control of electro-osmotic flows (EOF) in microfluidic devices has been achieved by using a new generation of Flow Field Effect Transistors (FFETs) with integrated Polarisable Interfaces (PI). This new type of microfluidic devices was compared to more conventional Metal-Insulator-Electrolyte FFETs. By using a Fluidic Wheatstone Bridge configuration, a precise control of the liquid flow rate was obtained with very small voltages (<500mV). By controlling the EOF independently from the external electric field, electrophoretic filter effects could be observed. Our capability to integrate such fluidic transistors in serial or parallel architectures opens new routes for high selectivity biomolecules sorting using programmable chips.

**KEYWORDS:** Electro-osmotic Flow, Flow Field Effect Transistors, Biomolecules, Separation Device, Glass-PDMS-Glass Sandwich Microchip, Polarisable Interfaces

## INTRODUCTION

The concept of microfluidic Flow Field Effect Transistor (FFET) has been proposed more than 10 years ago [1], and then studied for bio-separation [2] and nanofluidics [3]. The principle of such flow transistors is based on the variation of inner surface potential of microchannels using a lateral gate voltage, so that the amplitude of the electrically induced liquid flow (electro-osmotic flow) can be controlled independently from the lateral electric field.

The previously proposed systems relied on a metal/insulator/electrolyte (MIE) configuration (Figure 1). Such a device configuration is relatively simple but not applicable to samples exhibiting neutral and basic pH or high ionic strengths. This is mainly due to the surface charge that naturally develops at the liquid-solid interface between the insulator and the electrolyte, which requires very large tuning voltages to ensure surface potential modulation. When the initial surface charge is too important (at high pH), the dielectric barrier cannot sustain sufficient electric field and a dielectric breakdown of the insulating layer occurs.

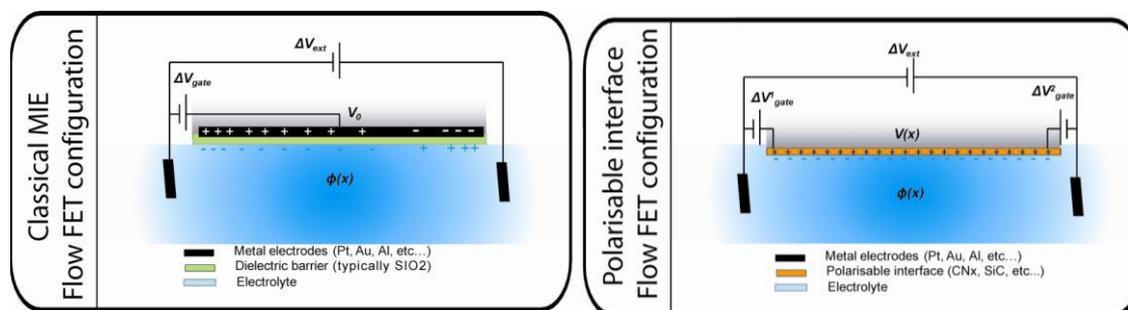


Figure 1: Schematic of MIE Flow FET (left) and PI Flow FET (right) configurations

More recently, we proposed a new type of device based on Polarisable Interfaces (PI) [4] that theoretically bypass these MIE FFET limitations. In this device configuration, the electric potential of a conducting layer in direct contact with the electrolyte is controlled at both ends of the microchannel. With this dual gate configuration, the potential of the liquid to solid interface can be modulated using very low gate voltages (below 1V), independently of the electrolyte composition.

## EXPERIMENTAL

Experimentally, a Glass-PDMS-Glass [5] has been used for the fabrication of our FFET devices. MIE as well as PI FFETs were integrated in a microfluidic Wheatstone Bridge ( $\mu$ FWB) to accurately monitor the electro-osmotic flow variation as a function of the gate voltage. The  $\mu$ FWB configuration enables accurate determination of EOF as a function of applied gate voltage [6].

The geometry of the FWB could be different, depending on the specificity of the experiments (Figure 2), which did not affect the comparability of the results. The height of the microfluidic channels varied from 4 to 10  $\mu$ m, so that the contribution of the lateral PDMS wall to EOF could be negligible. Both inferior and superior channel surfaces were patterned with either MIE or PI structures.

KCl solutions with concentration ranging from  $10\mu\text{M}$  to  $1\text{M}$  were used as electrolyte. The pH was measured between 6 and 7 for all measurements. The lateral voltage was generally set to  $10\text{V}$  to minimize electrochemical effects in the FWB as well as the Joule effects.

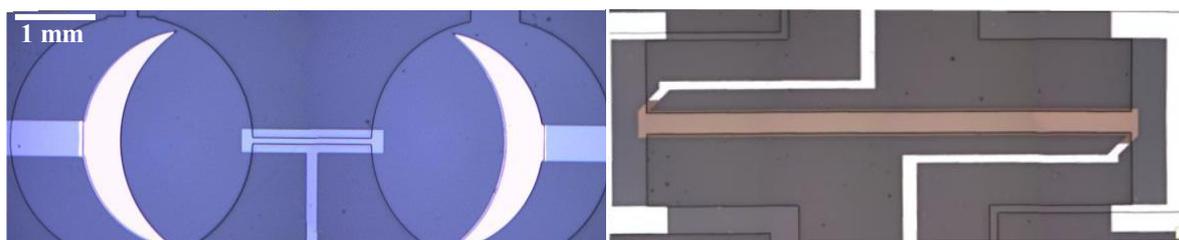


Figure 2: Central channel of the  $\mu\text{FWB}$  device. (left) Cr-SU8 based MIE Flow FET (single gate configuration); (right) SiC based PI Flow FET (dual gate configuration). The scales are the same for both pictures. The geometry of the central channel of the FWB was larger during PI-FFETs studies than during MIE-FFETs studies.

## RESULTS

Several MIE configurations were tested. While good EOF control could be achieved with Cr- $\text{Si}_3\text{N}_4$  or Cr- $\text{SiO}_2$  MIE interfaces, a severe erosion of the underlying Cr layer suggested that leakage currents occurred at the MIE interface. These deteriorations could be limited using SU8 resist based isolating layers of  $2\mu\text{m}$  thick. In the same time, the EOF control dramatically decreased, which suggested that the previously obtained FFETs did not rely on the surface potential control, but rather on the modification of the transverse electric field. This hypothesis was confirmed by the analysis of the electrical current that was varying in the same amplitude as the EOF velocity when “porous” isolating layers were used.

On the other hand, we demonstrated that the EOF control factors of PI-FFETs could be several orders of magnitude larger than that of more conventional MIE-FFETs, without significant variation of transverse electric fields. More interestingly, the EOF control could be achieved with neutral pH buffers as shown in Figure 3. In addition, we demonstrated that the EOF control increased with buffer ionic strength, which makes this technology compatible with real bio-samples.

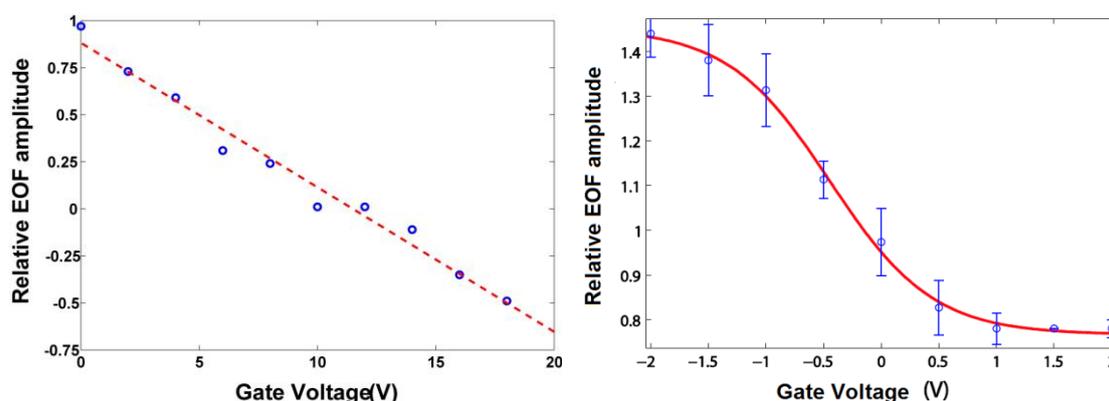


Figure 3: Electro-Osmotic Flow (EOF) control obtained with a  $1\text{mM}$  KCl buffer for (left) CR-SI $3\text{N}_4$  based MIE-FFETs and (right) SiC based PI-FFETs.

## DISCUSSION

The Glass-PDMS-Glass technology can be used to integrate PI-FFETs into electrophoretic separation devices in order to tune their separation efficiency. Moreover, as the total velocity of the biomolecules can be finely tuned by varying the EOF independently from the electric field, the PI-FFET can be used either as a high pass or low pass electrophoretic filter (Figure 4a). If the EOF velocity is increased until the liquid velocity is equal to biomolecule electrophoretic velocity, the transport of these species can be stopped.

Multiple PI-FFETs can then be mounted in series or in parallel in order to generate more complex filtering functions (Figure 4b and 4c). If mounted in a series with opposing electric fields, the device is able to extract a given electrophoretic window from a sample continuously. This band pass filtering can be used to isolate proteins or particles from a complex mixture or even to real time monitor the presence of a given agent in biosamples. When PI-FFETs are placed in a parallel configuration, an electrophoretic band rejection filter can be designed so that well defined electrophoretic species (like albumin) can be suppressed from a sample.

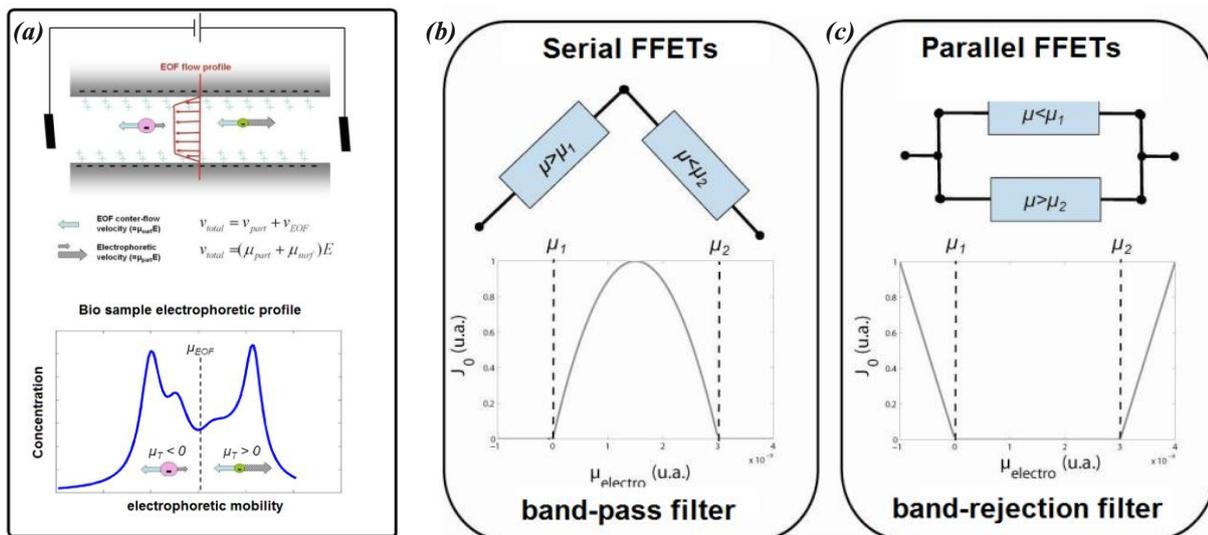


Figure 4: (a) Concept of the electrophoretic gate. The total velocity of a charged molecule is the sum of the electrophoretic velocity that depends on the transverse electric field  $E$  and the EOF fluid velocity that depends on the surface mobility  $\mu_{EOF}$ . By varying the gate voltage of the PI-FFET,  $\mu_{EOF}$  can be increased so that the Flow FET acts as a cut off for bio molecule mobility (only high mobility molecules with a positive total mobility can cross the gated channel). (b and c) Two examples of combined Flow FETs for generating electrophoretic band-pass or band-rejection filters.

These simple architectures can also be coupled to the immunological detection of biothreats. When a labeled monoclonal antibody binds to its target, a shift in its electrophoretic mobility is expected. As a consequence, the labeled dyes can change from an electrophoretic window to another, which can be monitored by a simple band rejection filter. More importantly, there is a high probability that unspecific bindings would result in random electrophoretic mobilities of the complexes. As a consequence, a narrow band pass filter could be applied to monitor only specific antibody bindings having a given electrophoretic mobility, which would dramatically increase the specificity of single step immunological detection devices.

## CONCLUSION

The applicative potential of PI-FFETs as tunable electrophoretic filtering devices is not limited to the electrophoretic band pass or band rejection functions, but can be extended to the wide variety of filters developed for signal processing applications. We expect that the development of programmable biosample analysis system coupled with real time detection will result in a significant breakthrough for both biomedical and defense applications.

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