A versatile silicon platform for electrical recording of ion channels activity

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Abstract

Ions channels are membrane proteins which allow specific ions to go through biological membrane. They play a key role in physiological mechanisms as diverse as action potential propagation, kidney function and muscle contraction. For this reason they are very valuable targets for pharmaceutical industry. Yet, high throughput drug screening on ion channels with an electrical monitoring of the channel activity – the more informative monitoring - is limited by the lack of a system having both the flexibility and high data quality of manual patch clamp, and the high throughput of automated patch clamp [1].

Attempts have been made to develop integrated *in vitro* platforms to fulfil these requirements on extracted or synthetized ion channels embedded in an artificial lipid bilayer [2]. However, to our knowledge, none of these platforms allow electrical activity recordings of ion channels in a solvent-free bilayer self-formed from small unilamellar lipid vesicles containing already the ion channel of interest, which would make possible automation and high speed of these measurements.

We are developing a silicon platform with an array of nanopores with a well-controlled diameter (20 nm – 100 nm) between two electrically addressable compartments. The fabrication of silicon chip requires only a processing of the front face, and a PDMS fluidic interface allows fast integration for liquid handling, optical monitoring and electrical recordings (fig. 1) [3]. FRAP (fluorescence recovery after photobleaching) experiments have shown (fig. 3) that incubation of small unilamellar vesicles without ion channels (as a reference) on the surface of the silicon chip leads to the formation of a supported lipid bilayer, whereas electrical characterization (fig. 2) suggests that the so-formed lipid bilayer spans and seals the nanopores, leading to a lower recorded current value. These results are a first step toward ion channel monitoring with this platform. The influence of the nanopores diameter on their sealing by the bilayer together with the feasibility of ion channel electrical activity monitoring on the platform will be discussed at the conference.

References

[1] Yajuan, X. and al., Current Chemical Genomics, vol. **6** (2012) p. 87-92
[2] Zagnoni, M., Lab on a Chip, vol. **12** (6) (2012) p. 1026
[3] Marchand, R. and al., Microelectronic Engineering, vol. **144** (2015) p. 57-60

Figures

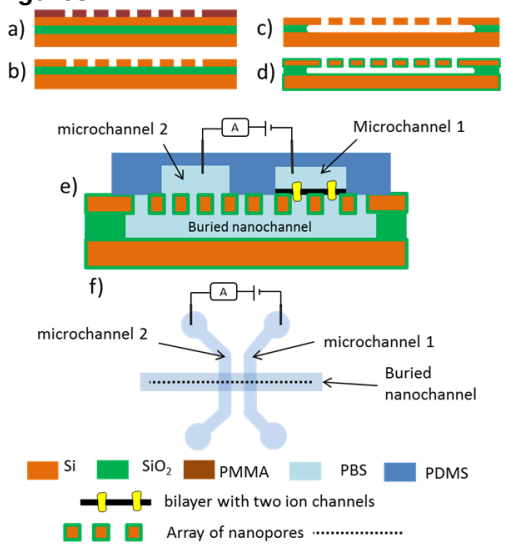

Figure 1 : Fabrication and integration of the silicon platform
a) Nanopore patterning by ebeam lithography, **b)** Reactive ion etching, **c)** Burried oxide etching, **d)** Thermal oxydation, **e)** Side view of the platform, **f)** Top view of the platform

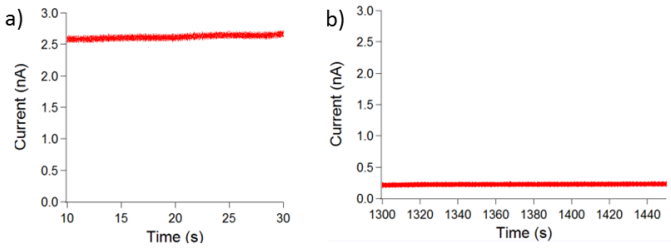

Figure 2 : Electrical recordings on a silicon platform with 20 nm diameter nanopore at 100 mV applied potential a) Before lipid vesicles insertion. **b)** After a 15 min incubation of a 700 µg/mL suspension of POPC (99% mol) – NBD-PC (1% mol) 80 nm average diameter vesicles

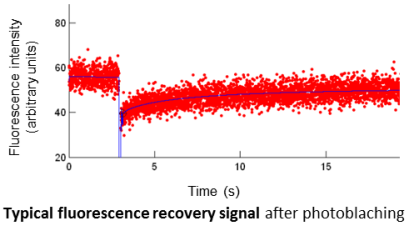

Figure 3 : Typical fluorescence recovery signal after photoblaching of a 3,3 µm diameter spot on a supported lipid bilayer obtained after 15 min incubation of a suspension of POPC (99% mol) – NBD-PC (1% mol) 80 nm average diameter vesicles on the silicon chip surface Average diffusion coefficient : 2µm²/s. Average mobile fraction 70 %