Protein Nanopore-gated Bio-transistor for Membrane Ionic Current Recording

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Although naturally occurring biological nanopores have shortcomings such as a relatively weak structural durability and a limited life-time, they are still intriguing candidates for nanobiosensing applications due to their sensitivity and specificity to analytes as well as various choices of ion channels depending on functionalities. In order to overcome limitations of biological nanopores, man-made solid-state nanopores have been explored. The fabricated solid-state nanopore is structurally durable and suitable for nanofabrication process yet it is still challenging to construct and a low throughput process, and lacks the chemical specificity of natural ion channels[1]. Can bionanotechnology be applied to improve this situation? Recent work has shown that nanomaterials (nanotubes, nanowires) can be gated by electrolyte, and even coated with lipid bilayers allowing charges of either the bilayer themselves[2]. These reports focus on time average changes in source/drain current due to gating by charges near the nanowire/nanotube. Thus, to date, no nanowire/nanotube device has been able to measure the time-dependent single ion channel recording.

Here we show direct interrogation of the dynamical opening and closing of ion channel pores with an integrated nano-bio system in a controlled microfluidic environment. Randomly oriented semiconducting CNT network transistors are covered by biomembranes (lipid bilayers) incorporated with transmembrane proteins (ion channels). This forms a robust and direct probe of ion channel currents with millisecond temporal resolution and sub-pico amp current resolution. The effect of both biomembranes and ionic current through transmembrane proteins on the electrical characteristic of transistors has been evaluated. We also demonstrate for the first time electrophysiological recording of single ion channel events from individual ion pores using our CNT transistors. The device developed here could offer a nano-electrophysiology system to study interactions between biomolecules and bionanoelectronics and bioelectrical activities of the cellular membrane.

Fig. 1(a) shows schematics of experimental set up of CNT device showing p-type I-V curves depending on source-drain bias. The continuous and defect-free supported lipid bilayers were formed on top of fabricated CNT FET as shown in Fig.1(b,c). Electrical characteristic modulations of CNT FETs were clearly observed by introduction of biomembranes and reconstitution of ion channel into biomembranes (Fig. 1(d)). This result indicates that CNT FETs can be gated by tiny ionic current flowing into local environment of CNTs in which the type of ions can be selected and controlled by the ion channel used. For ion channel recording with CNT electrophysiological system, time-dependent ionic current flow of specific ions was recorded (Fig. 1(e)). I-V responses of devices were measured to obtain the conductivity of devices and the ability of the biomembranes to isolate CNT device from the medium solution Fig 1(f). For the first time, single ion channel recordings using a CNT device were successfully recorded with high signal to noise ratio. Each current spike with the range of 0.5 -10 pA indicates ionic current flow when an individual ion channel is open.

This approach, significantly different than any prior approach to the study of ion channel trans-membrane currents, will find broad applications in electrophysiology, nanopore based sequencing, and membrane protein studies.

This work was supported by NIH National Cancer Institute Grant (CA143351-01).

[1] D. Branton, et al., "The potential and challenges of nanopore sequencing," Nature Biotechnology, vol. 26, pp. 1146-1153, 2008.
[2] X. Zhou, et al., "Supported lipid bilayer/carbon nanotube hybrids," Nat Nanotechnology, vol. 2, pp. 185-90, Mar 2007.

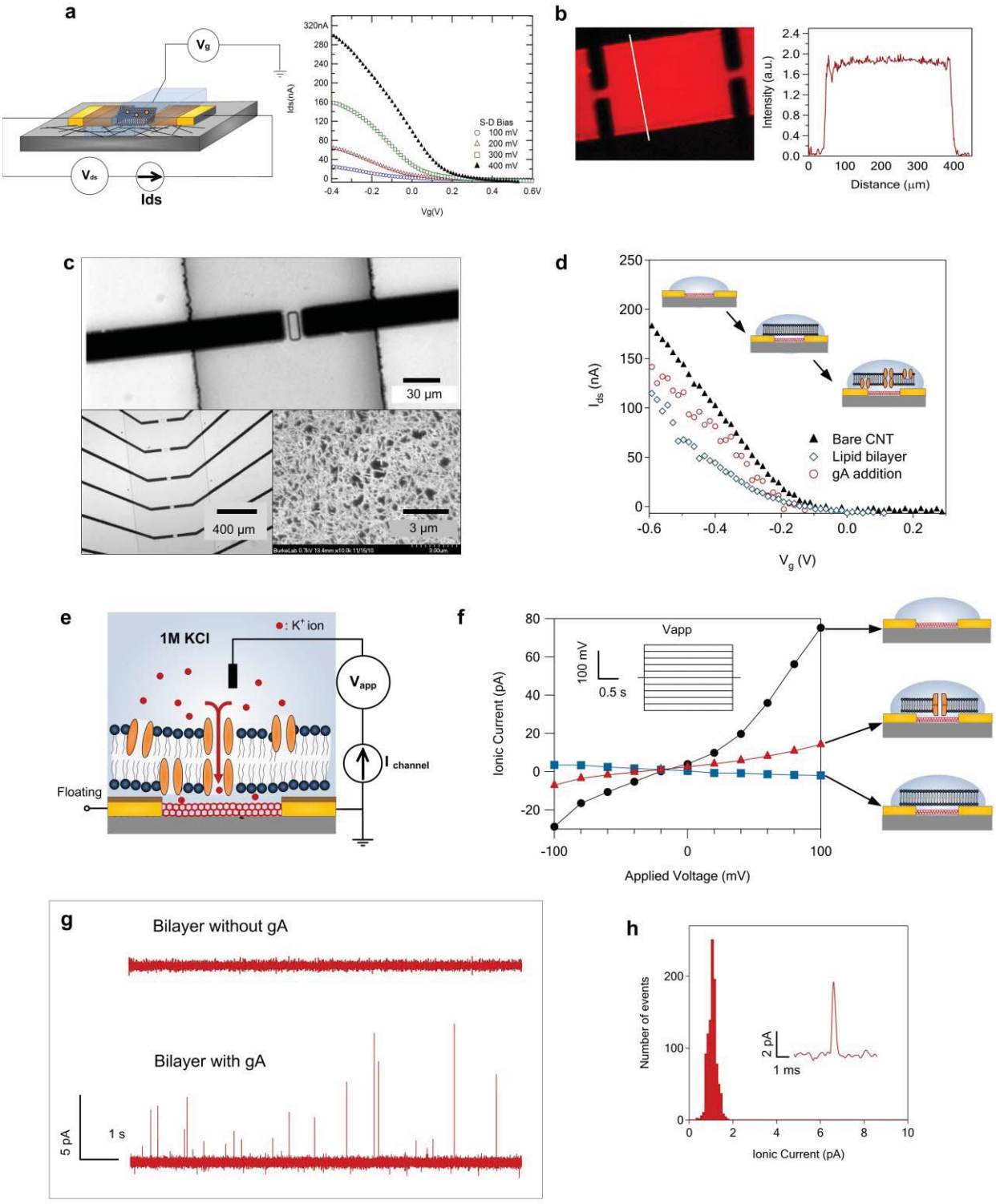

Figure 1 (a) Experimental set-up of CNT FET and typical p-type depletion curves (b) Fluorescence image of lipid bilayer and intensity profile (c) Micrograph of fabricated device and a SEM of CNT networks (d) Depletion curves after introduction of biomembranes (blue) and ion channels(red) (e) Cartoon of ion channel recording showing ionic current flow (f) I-V responses of CNT device of bare(black), biomembrane(blue), ion channel(red) (g) Individual ion channel current trace (h) Histogram of single ion channel events and typical event dwell-time.