QUANTUM-LIMITED 2D SENSORS FOR PH AND BIOSENSING

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ABSTRACT

We have developed biosensors based on dual-gated field-effect transistors (FETs) that operate at the quantum capacitance limit [1]. The FETs are fabricated with atomically thin MoS_2 semiconducting films and top-gated with a room temperature ionic-liquid (Figure 1). The high ionic liquid polarizability allows strong coupling between the top (ionic liquid) and back-gate (substrate oxide) dielectrics, which enables the amplification of a voltage applied to the ionic liquid gate by 200×, limited only by the channel quantum capacitance. Because the devices operate near their theoretical limits, they enable new applications in biosensing, beyond the reach of traditional FET-based sensors [2].

KEYWORDS: Field-effect transistor (FET), MoS_2, Biosensor, Super-Nernstian, pH, Enzyme activity

INTRODUCTION

Measurements of pH are critical to applications ranging from monitoring oceanic health to ensuring homeostasis in cells. Yet the sensitivity and limit of detection (LOD) of existing pH measurements limit their use in these important application areas. For applications in biotechnology, improving pH LOD would particularly benefit the measurements of enzymes, which play a central role in facilitating virtually every biochemical reaction in our bodies. One important class of enzymes are kinases, which catalyze protein phosphorylation through the hydrolysis of adenosine triphosphate (ATP), thereby facilitating efficient cell signaling. The reaction, which releases protons, causes the pH of the solution to change by less than 0.005 units under normal cell function, about an order of magnitude lower than conventional measurements [3, 4]. Disruptions in the function of enzymes like kinases, in turn, lead to serious illnesses including Alzheimer's disease.

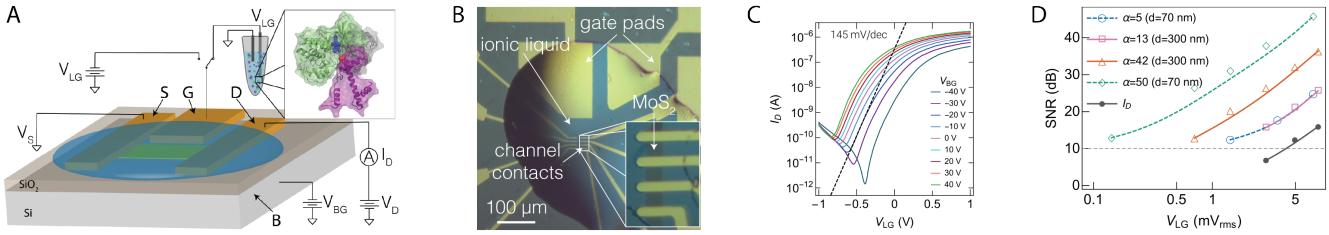

Figure 1: Field-effect Transistors (FETs) with a room temperature ionic liquid gate dielectric for biosensing. (A) Device schematic of an ionic liquid-gated FET. A channel formed between the source [S] and drain [D] terminals is controlled electrostatically by a voltage applied to the silicon substrate [B] or the ionic liquid top-gate [G]. A voltage applied to the ionic liquid-gate (V_{LG}) can be switched between a voltage source for characterization or a biosensing element. (B) An array of ionic liquid dual-gate FETs fabricated using a 2D MoS_2 film on a 300 nm SiO_2 substrate. (C) Transfer characteristics show the drain current (I_D) as a function of V_{LG} for a varying back-gate voltage (V_{BG}) (D) The signal-to-noise ratio (SNR) as a function of V_{LG} for varying gain (α). The channel noise in the ionic liquid gated FETs, was found to be insensitive to increasing α, which in turn allowed an improved SNR.

EXPERIMENTAL

High-performance FETs were fabricated using a technique we recently developed [5]. Large area and high quality monolayer MoS_2 flakes were exfoliated from bulk crystal using a gold-mediated exfoliation method on to oxidized, heavily doped silicon substrates that also served as a global back-gate. After the monolayer MoS_2 flakes were located and inspected using an optical microscope, optical photolithography was used to pattern the source, drain, and gate electrodes followed by electron beam evaporation of metal Ti/Au (2 nm/100 nm) and lift-off. A

second photolithography step was used to define the active channel area, followed by XeF_2 etching to remove excess MoS_2 outside the defined channel area. Next, a small droplet of the DEME-TFSI ionic liquid was applied onto each device using a micromanipulator and an optical microscope. The droplet was sized to cover the MoS_2 monolayer and the gate electrodes (Figure 1).

RESULTS AND DISCUSSION

We leveraged the high performance of the devices to measure pH (Figure 2) with a sensitivity such that the gate voltage changes by 4.4 V when the solution pH changes by 1, exceeding the Nernst value of 59 mV at room temperature by ≈75×. The dramatically improved sensitivity, and high signal-to-noise-ratio (SNR) allowed the detection of pH changes as small as 92×10^{-6} at a bandwidth of 10 Hz. This low LOD, in turn, facilitated the measurements of activity and kinetics during biological processes such as enzyme catalyzed phosphorylation of substrate proteins.

We compared the FET measurements (Figure 2) against enzyme activity measurements obtained from a radioactively labeled γ-^{32}P-ATP assay. The FET-based measurements are in excellent quantitative agreement with the well-established γ-^{32}P-ATP technique. The time-resolved FET measurements allowed the quantification of both the enzyme activity and kinetics from a single assay (Figure 2). Finally, the FET measurements were completed in minutes, representing a drastic improvement in turnaround time relative to γ-^{32}P-ATP assays, which involve handling radioactive materials and are slow to perform.

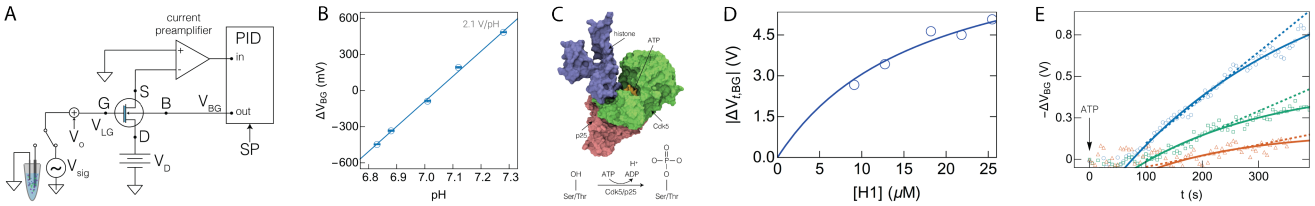

Figure 2: (A) The FETs were used in a constant current mode by using a proportional-integral-derivative (PID) controller. I_D was held constant in response to changes to V_{LG} by varying V_{BG}. (B) Measurements of pH were performed by connecting the ionic liquid-gate [G] to a sensing element. The sensitivity, $dV_{BG}/dpH=2.1$ V ($R^2=0.99$), was extracted from the data and found to exceed the Nernst value of 59 mV. The error bars represent the standard uncertainty with k=2. (C) The proline directed kinase Cdk5 catalyzes the phosphorylation of substrate proteins (e.g., histone H1) in the presence of an activator (e.g., p25) and adenosine triphosphate (ATP). The hydrolysis of ATP results in a change in solution pH. (D) Ionic liquid-gate FETs ($\alpha=159$) were used to measure the change in solution pH as a function of the histone H1 concentration ([H1]). The FET measurements agree quantitatively with an assay that used radioactively labeled γ-^{32}P-ATP as a reporter of Cdk5 activity. (E) Time-series measurements of enzyme catalyzed phosphorylation of [H1] allow the direct estimation of the reaction dynamics and activity from a single assay.

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