

## Gating of an organic transistor through a bilayer lipid membrane with ion channels

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The authors use bilayer lipid membranes (BLMs) as a means to control the gating of organic electrochemical transistors (OECTs). Upon formation of a high quality BLM, the gating of an OECT can be fully suppressed. Gating is restored when gramicidin ion channels are incorporated into the BLM. The valence-dependent permeability of gramicidin enables these devices to discriminate between monovalent and divalent ions. This work shows that ion channels can be effectively employed to control the selectivity of organic transistor-based sensors. © 2006 American Institute of Physics. [DOI: 10.1063/1.2266250]

Over several decades, extensive studies have been undertaken to understand the nature of bilayer lipid membranes (BLMs) due to their importance in biological systems.<sup>1</sup> While normally blocking to ions, the ionic permeability of a BLM can be altered with the addition of ion channels, which have been shown to have a wide range of complexity and functionality.<sup>2,3</sup> Laboratory techniques, such as patch clamp, have provided a means to understand the behavior of individual ion channels present in BLMs.<sup>4</sup> Due to their inherent relevance to biological systems, methods to utilize BLMs for sensing applications have been explored with some urgency; this has given rise to a range of systems engineered for this purpose, including mechanically stabilized BLMs via solid,<sup>5</sup> gel,<sup>6</sup> or porous<sup>7</sup> supports, chemically stabilized BLMs reinforced by cross-linking<sup>8</sup> or polymeric stabilizers,<sup>9</sup> and sensor arrays that are a precursor to lab-on-a-chip-type technologies.<sup>10,11</sup> These BLM-based systems demonstrate adequate sensitivity and selectivity towards a wide range of analytes. However, interfacing BLMs with electronics to yield a high throughput and low cost design remains a challenging issue.<sup>10</sup>

In recent years, organic electronic materials have been explored for their use in sensing applications.<sup>12</sup> This class of materials is particularly interesting due to their low cost, ease of processing, and tunable properties. To date, organic field effect transistors have been explored as gas sensors,<sup>13–16</sup> and organic electrochemical transistors (OECTs) have shown promise for sensing in aqueous systems.<sup>17</sup> In particular, OECTs based on poly(3,4-ethylenedioxythiophene) doped with poly(styrene sulfonate) (PEDOT:PSS) have been integrated into microfluidic systems,<sup>18</sup> used for logic circuits,<sup>19</sup> and utilized effectively for sensing water vapor,<sup>20</sup> glucose,<sup>21</sup> and deoxyribonucleic acid.<sup>22</sup> These devices act as ion to electron converters, providing a facile route for interfacing the worlds of biology and electronics.<sup>18,23</sup> One key advantage is that a relatively small ionic current can cause large changes in the electronic current.<sup>18</sup> For this reason, coupling

OECTs with BLMs provides an interesting route to amplify normally small ionic currents observed in BLM-based sensors. Given the wide selection of ion channels and the flexibility to modify them chemically, many types of analytes can be sensed.<sup>1</sup>

In this letter, we used a bilayer lipid membrane to control the gating of an organic electrochemical transistor. Complete suppression of gating was observed when a BLM was formed between the conducting polymer and the gate electrode. Gating was restored once the BLM was ruptured. In addition, gramicidin ion channels<sup>24</sup> were incorporated into BLMs, demonstrating that varied levels of gating can be obtained by modulating the ion permeability of a BLM. Also, given the dependence of permeability of gramicidin channels on ion valence,<sup>24</sup> we fabricated sensors that can differentiate between monovalent and divalent cations.

Figure 1 shows a schematic of an OECT that is gated through a BLM. The active material used in these OECTs was Baytron P, a commercial formulation of PEDOT:PSS. A

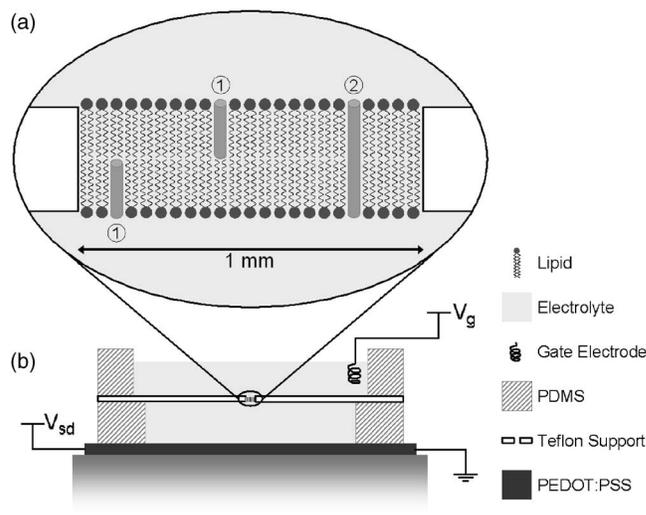


FIG. 1. Schematic of PEDOT:PSS electrochemical transistor gated through a bilayer lipid membrane (not drawn to scale). (a) Representation of BLM formed on a Teflon support with gramicidin, shown as ion blocking monomers (1) and an ion permeable dimer (2). (b) Layout for overall device design (some device details omitted for clarity).

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mixture of 80% Baytron P and 20% ethylene glycol, used to enhance conductivity,<sup>25</sup> was spun onto clean glass substrates to yield films which were approximately 50 nm thick. Substrates were cleaned mechanically with liquid detergent and primed with a water-isopropanol mixture to allow for uniform film formation. Strips of PEDOT:PSS, approximately 6 mm wide, were patterned with adhesive tape. 100 nm thick films of gold were evaporated on top of the PEDOT:PSS films (omitted from Fig. 1 for clarity) to reduce background resistance and define an active region of 3 mm<sup>2</sup>. Devices were exposed to three sequential de-ionized water baths and then dried with nitrogen to remove contaminants that might leach out of the device during operation. An elastomeric polymer, polydimethylsiloxane (PDMS), was used to define electrolyte wells. PDMS was prepared by mixing Sylgard 184 with a 10:1 base:curing agent ratio, casting the mixture on a silicon wafer, and curing at 60 °C for 1 h. Desired mold shapes were formed by cutting the PDMS. The gate electrode (Ag/AgCl) was soaked in a bleach solution (6 wt % sodium hypochlorite) for approximately 10 min followed by a thorough de-ionized water rinse just prior to device assembly. A stereoscope was mounted above the device to monitor BLM formation on the Teflon support.

Lipid solutions were prepared from 1,2-diphytanoyl-*n*-glycero-3-phosphocholine (4ME 16:0 PC) powder obtained from Avanti Polar Lipids. A 25 mg/ml solution of lipid in chloroform was prepared as a stock solution. Chloroform solutions were then dried under nitrogen and lipids were dissolved in *n*-decane to yield concentrations of 25 mg/ml. The ion channel gramicidin D (a mixture of gramicidins A, B, and C) was obtained from Sigma-Aldrich. A stock solution of gramicidin was prepared by dissolving gramicidin in ethanol at a concentration of 0.15 mg/ml. Gramicidin was either stirred into the electrolyte solution or mixed directly with a lipid solution to achieve higher degrees of incorporation.

A 1 mm diameter hole was machined in a 500  $\mu$ m thick Teflon support, which was utilized for bilayer lipid membrane formation. The Teflon component was cleaned thoroughly by rubbing with liquid detergent and was allowed to sit for approximately 10 min in detergent prior to being rinsed extensively with de-ionized water. Prior to submersing in electrolyte, a small amount of lipid-decane solution was applied to the support in order to prime the Teflon surface.

Once dried, the Teflon was assembled along with the PDMS components to define a well for electrolyte solution. A small amount of vacuum grease was applied to Teflon-PDMS interfaces to prevent leakage. Electrolyte solution (either 1M KCl or 0.5M CaCl<sub>2</sub>) was then added until the Teflon support was fully submersed. To form a BLM, a small amount of lipid solution (<1  $\mu$ l) was applied to the Teflon support with a glass pipet by the painting method.<sup>26</sup> The evolution of this process was observed optically with a stereoscope to verify realistic BLM formation.

To increase the ionic permeability of the BLM, gramicidin stock solution was added to the electrolyte (in the range from 1 to 20  $\mu$ l of stock solution), which then consequently incorporated in to the BLM. Because gramicidin must be present on both sides of a BLM to form ion transporting channels,<sup>24</sup> the electrolyte was stirred prior to BLM formation to ensure good dispersion of the gramicidin monomers. If after sufficient time no significant gate currents were observed with a particular gramicidin addition, the BLM was

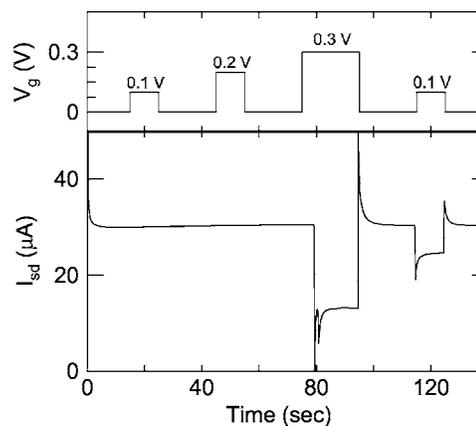


FIG. 2. Transient response of a PEDOT:PSS electrochemical transistor gated through a BLM ( $V_{sd}=0.1$  V). The BLM was formed at  $t < 0$  s. When a BLM is intact, gating of the source-drain current is completely suppressed ( $t < 80$  s). With extended application of larger gate voltages ( $V_g \geq 0.3$  V), rupture of the BLM is observed ( $t \sim 80$  s). Once the BLM ruptures, gating of the PEDOT:PSS film can be observed.

ruptured, the electrolyte was stirred and the BLM was reformed. If a reformed BLM still lacked the desired ion conductivity, additional gramicidin was added to solution and the process was repeated. To obtain the highest degree of gramicidin incorporation in BLMs, gramicidin solution was mixed directly with lipid solution (up to a 4:1 lipid to gramicidin ratio) prior to applying the BLM.

Figure 2 shows typical source-drain current ( $I_{sd}$ ) for a device probed with various gate voltages (the BLM was formed at  $t < 0$  s). It can be clearly observed that with an intact BLM ( $t < 80$  s) no modulation of  $I_{sd}$  is observed. This is consistent with the absence of significant gate current: in the case of a high quality BLM, the gate current shows a small transient response that decays below the noise threshold within 100 ms. If sufficiently high voltages are applied for extended times, rupture of the BLM occurs ( $t \sim 80$  s). At this point, a substantial gate current (100  $\mu$ A initially) results, and a large modulation of the source-drain current is clearly observed. The decrease of  $I_{sd}$  observed here is the result of ion drift into the PEDOT:PSS film and the subsequent dedoping of the conducting polymer.<sup>23</sup> For identical voltage pulses of 0.1 V, it is clear that there is no modulation when the BLM is intact ( $t < 80$  s), while there is significant modulation after the BLM is ruptured ( $t > 80$  s).

Figure 3 shows how the incorporation of gramicidin ion channels impacts gating through a BLM. In the case of a pristine BLM, no gating is observed until after a gate pulse is applied to rupture the membrane. When gramicidin is added to the BLM, gating is reintroduced. Depending on the amount of gramicidin added, initial gate currents can be modulated from 10 pA (pristine BLM) to 50  $\mu$ A (nearly equivalent to the absence of a BLM). Equivalent experiments performed on a device with CaCl<sub>2</sub> electrolyte show some gate current is reintroduced; however, due to the much lower permeability of gramicidin to divalent species,<sup>24</sup> gating currents can only be modulated in the range of 10 pA–1 nA. Currents in this range are not sufficient to gate OECTs of this geometry on a reasonable time scale. The modulation of  $I_{sd}$  with CaCl<sub>2</sub> is equivalent to a device with a pristine BLM only. This selectivity arises from the valence-dependent permeability of gramicidin channels, and it is reflected by the difference in the gate currents mentioned above. Hence,

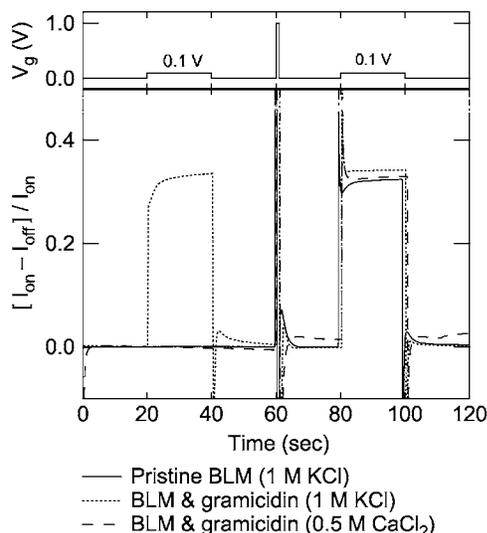


FIG. 3. Transient response of a PEDOT:PSS electrochemical transistor gated through a BLM with the introduction of gramicidin ( $V_{sd}=0.1$  V). The response with  $\text{CaCl}_2$  electrolyte in the absence of gramicidin is equivalent to that of a pristine BLM in KCl electrolyte and is omitted for clarity. [ $I_{on}=I_{sd}$  ( $V_g=0$  V) and  $I_{off}=I_{sd}$  ( $V_g=0.1$  V)].

gramicidin channels present a simple route to enable OECTs to differentiate ionic valence. It should be noted that the temporal response of  $I_{sd}$  depends on the permeability of the membrane and the device geometry. Faster response can be obtained by decreasing the area of the PEDOT:PSS channel.

Significant work has been done to modify gramicidin to introduce additional functionality,<sup>27</sup> which can be easily integrated into this device structure. Beyond simple channels such as gramicidin, there are a multitude of ion channels available with various stimulus-dependent responses.<sup>3</sup> While the long term stability of the BLMs is not addressed in this letter, several methods have been established to improve the long term stability of BLMs,<sup>5-9</sup> which can be incorporated into this type of device in a straightforward manner. Biosensors based on ion to electron conversion in OECTs offer great promise, particularly when coupled with BLMs. In these devices, biological recognition elements can be incorporated into a BLM, providing both transduction elements for biological analytes as well as segregating analytic solutions from electronic components. This is a significant opportunity, as properly designed BLMs can essentially isolate and conceal electronic components from the biological world: to an analyte, these sensors appear to be cell membranes. Finally, given the ease of processing and simple electronic readout, these devices represent a step toward a new generation of disposable, high-sensitivity sensors.

In summary, this work shows that bilayer lipid membranes can be utilized to control the gating of organic electrochemical transistors. Using ion channels, such as gramicidin, the magnitude of gating can be controlled. Capitalizing on the valence-dependent permeability of gramicidin ion channels, it is also possible to distinguish between solutions of monovalent and divalent ions.

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<sup>1</sup>Planar Lipid Bilayers (BLMs) and Their Applications, edited by H. T. Tien and A. Ottova-Leitmannova (Elsevier, Amsterdam, 2003).

<sup>2</sup>L. Stryer, *Biochemistry*, 3rd ed. (Freeman, New York, 1988).

<sup>3</sup>B. Hille, *Ion Channels of Excitable Membranes*, 3rd ed. (Sinauer, Sunderland, MA, 2001).

<sup>4</sup>M. Mayer, S. Terrettaz, L. Giovangrandl, T. Stora, and H. Vogel, in *Biosensors*, edited by J. Cooper and T. Cass (Oxford University Press, Oxford, UK, 2003).

<sup>5</sup>E. Sackmann, *Science* **271**, 43 (1996).

<sup>6</sup>M. Uto, M. Araki, T. Taniguchi, S. Hoshi, and S. Inoue, *Anal. Sci.* **10**, 943 (1994).

<sup>7</sup>D. P. Nikolelis, C. G. Siontorou, V. G. Andreou, and U. J. Krull, *Electroanalysis* **7**, 531 (1995).

<sup>8</sup>R. Benz, W. Prass, and H. Ringsdorf, *Angew. Chem., Int. Ed.* **21**, 368 (1982).

<sup>9</sup>W. Meier, A. Graff, A. Diederich, and M. Winterhalter, *Phys. Chem. Chem. Phys.* **2**, 4559 (2000).

<sup>10</sup>J. Xu, X. B. Wang, B. Ensign, M. Li, L. Wu, A. Guia, and J. Q. Xu, *Drug Discovery Today* **6**, 1278 (2001).

<sup>11</sup>F. J. Sigworth and K. G. Klemic, *Biophys. J.* **82**, 2831 (2002).

<sup>12</sup>J. T. Mabeck and G. G. Malliaras, *Anal. Bioanal. Chem.* **384**, 343 (2006).

<sup>13</sup>B. Crone, A. Dodabalapur, A. Gelperin, L. Torsi, H. E. Katz, A. J. Lovinger, and Z. Bao, *Appl. Phys. Lett.* **78**, 2229 (2001).

<sup>14</sup>Z. T. Zhu, J. T. Mason, R. Dieckmann, and G. G. Malliaras, *Appl. Phys. Lett.* **81**, 4643 (2002).

<sup>15</sup>L. Torsi, A. Tafuri, N. Cioffi, M. C. Gallazzi, A. Sassella, L. Sabbatini, and P. G. Zambonin, *Sens. Actuators B* **93**, 257 (2003).

<sup>16</sup>L. Wang, D. Fine, and A. Dodabalapur, *Appl. Phys. Lett.* **85**, 6386 (2004).

<sup>17</sup>H. S. White, G. P. Kittleson, and M. S. Wrighton, *J. Am. Chem. Soc.* **106**, 5375 (1984).

<sup>18</sup>J. T. Mabeck, J. A. DeFranco, D. A. Bernards, G. G. Malliaras, S. Hocde, and C. J. Chase, *Appl. Phys. Lett.* **87**, 013503 (2005).

<sup>19</sup>D. Nilsson, N. Robinson, M. Berggren, and R. Forchheimer, *Adv. Mater. (Weinheim, Ger.)* **17**, 353 (2005).

<sup>20</sup>D. Nilsson, T. Kugler, P. O. Svensson, and M. Berggren, *Sens. Actuators B* **86**, 193 (2002).

<sup>21</sup>Z. T. Zhu, J. T. Mabeck, C. C. Zhu, N. C. Cady, C. A. Batt, and G. G. Malliaras, *Chem. Commun. (Cambridge)* **2004**, 1556.

<sup>22</sup>K. Krishnamoorthy, R. S. Gokhale, A. Q. Contractor, and A. Kumar, *Chem. Commun. (Cambridge)* **2004**, 820.

<sup>23</sup>D. Nilsson, M. X. Chen, T. Kugler, T. Remonen, M. Armgarth, and M. Berggren, *Adv. Mater. (Weinheim, Ger.)* **14**, 51 (2002).

<sup>24</sup>O. S. Andersen, *Annu. Rev. Physiol.* **46**, 531 (1984).

<sup>25</sup>B. Y. Ouyang, C. W. Chu, F. C. Chen, Q. F. Xi, and Y. Yang, *Adv. Funct. Mater.* **15**, 203 (2005).

<sup>26</sup>P. Mueller, W. C. Wescott, D. O. Rudin, and H. T. Tien, *J. Phys. Chem.* **67**, 534 (1963).

<sup>27</sup>R. E. Koeppe and O. S. Andersen, *Annu. Rev. Biophys. Biomol. Struct.* **25**, 231 (1996).