A graphene field-effect transistor as a molecule-specific probe of DNA nucleobases

Nikolai Dontschuk, Alastair Stacey, Anton Tadich, Kevin J. Rietwyk, Alex Schenk, Mark T. Edmonds, Olga Shimoni, Chris I. Pakes, Steven Prawer,& Jiri Cervenka

•The School of Physics, The University of Melbourne, Australia.
•Australian Synchrotron, Victoria 3168, Australia.
•Department of Physics, La Trobe University, Australia

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by,

S.Vidhya
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Introduction

- Fast and reliable DNA sequencing is a long-standing target in biomedical research.
- Electrical sequencing using graphene and nanopore technologies has recently attracted great attention due to the possibility to provide real-time sequencing of a whole single DNA molecule
- These methods are based on the use of graphene as an electrical readout-based chemical sensor while a strand of DNA is fed through a nanopore.
- Graphene-based sequencing technologies are fundamentally reliant on detecting molecular-specific interactions of individual nucleobases with a graphene surface or its defects
- In this paper, they have experimentally demonstrated the use of graphene field-effect transistors (GFETs) as probes of the presence of a layer of individual DNA nucleobases adsorbed on the graphene surface.
- They also show that GFETs are able to measure distinct coverage-dependent conductance signatures upon adsorption of the four different DNA nucleobases; a result that can be attributed to the formation of an interface dipole field

Background

DNA Sequencing

- Process of determining the precise order of nucleotides within a DNA molecule
- It includes any method or technology that is used to determine the order of the four bases -adenine, guanine, cytosine, and thymine - in a strand of DNA.
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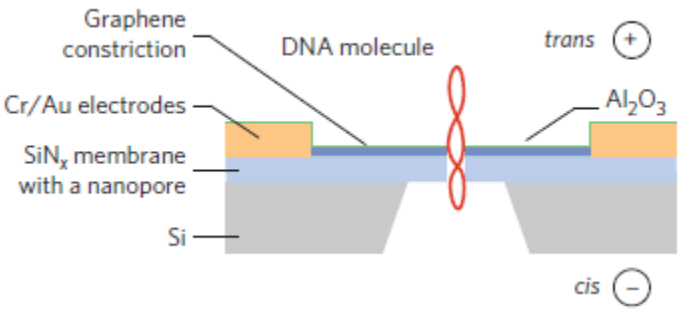
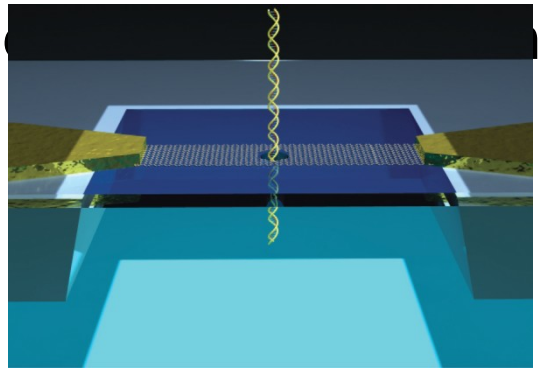




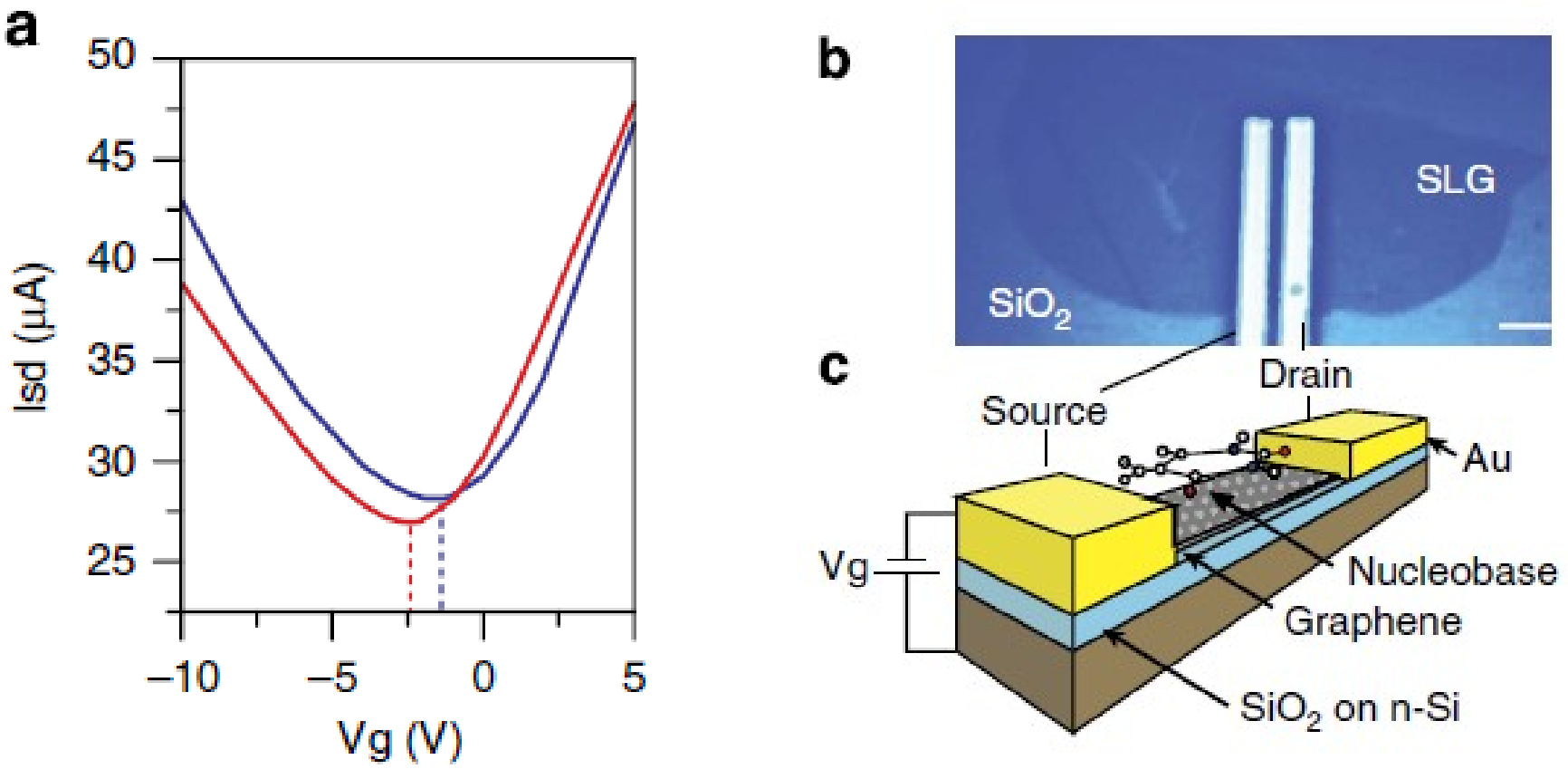
Background

- Graphene-based electrical sensors have already demonstrated exceptional sensor characteristics by being capable of detection of adsorption and desorption of individual gas molecules from the graphene surface
- This sensitivity is a direct consequence of the two-dimensional crystal structure, unique electronic properties and exceptionally low-noise intrinsic characteristics of graphene based devices
- A key practical aspect of any chemical sensor is their ability to distinguish between target analytes. To attain which in certain devices utilised graphene chemically functionalized with specific chemical binding groups to achieve analyte specificity.
- Chemical functionalization, however, comes at the cost of decreased graphene mobility and increased distance between the sensor and analytes, potentially hampering sensitivity.
- For these reasons a direct analyte–sensor interaction may be favourable for chemical sensing of individual DNA nucleobases.

Device Fabrication & Measurements

- GFET sensors were constructed from single-layer graphene (SLG) channels 50 μm wide and 50–200 μm long sitting on top of a SiO2 on doped Si transistor gate. Graphene grain size > (5–10 mm2) was used to ensure that results reflect the bulk properties of these polycrystalline graphene sheets, averaging out the effects of a range of defects present in the layers.
- XPS measurements were made on large area graphene samples (25mm2) fabricated identically to GFET devices but without evaporated electrical contacts.
- All measurements were conducted in an ultra-high vacuum (UHV) setup with base pressure <1 x 10-9 mbar to suppress the influence of contaminating molecules adsorbed on the surface. Samples were thoroughly annealed after insertion into UHV.
- Deposition of the molecules on graphene utilized in situ low-temperature effusion cells loaded with pure powders of the DNA nucleobases.
- Electric transport measurements were obtained by setting a constant voltage between the source and drain contacts (VSD) and monitoring the source drain current (ISD), while the gate

Device Fabrication & Measurements



Two terminal graphene devices used to monitor molecule induced graphene properties.

(a) Source drain current at a constant source drain voltage (10 mV) with varying gate voltage for clean (blue) graphene and 0.1ML guanine (G) covered (red) graphene.

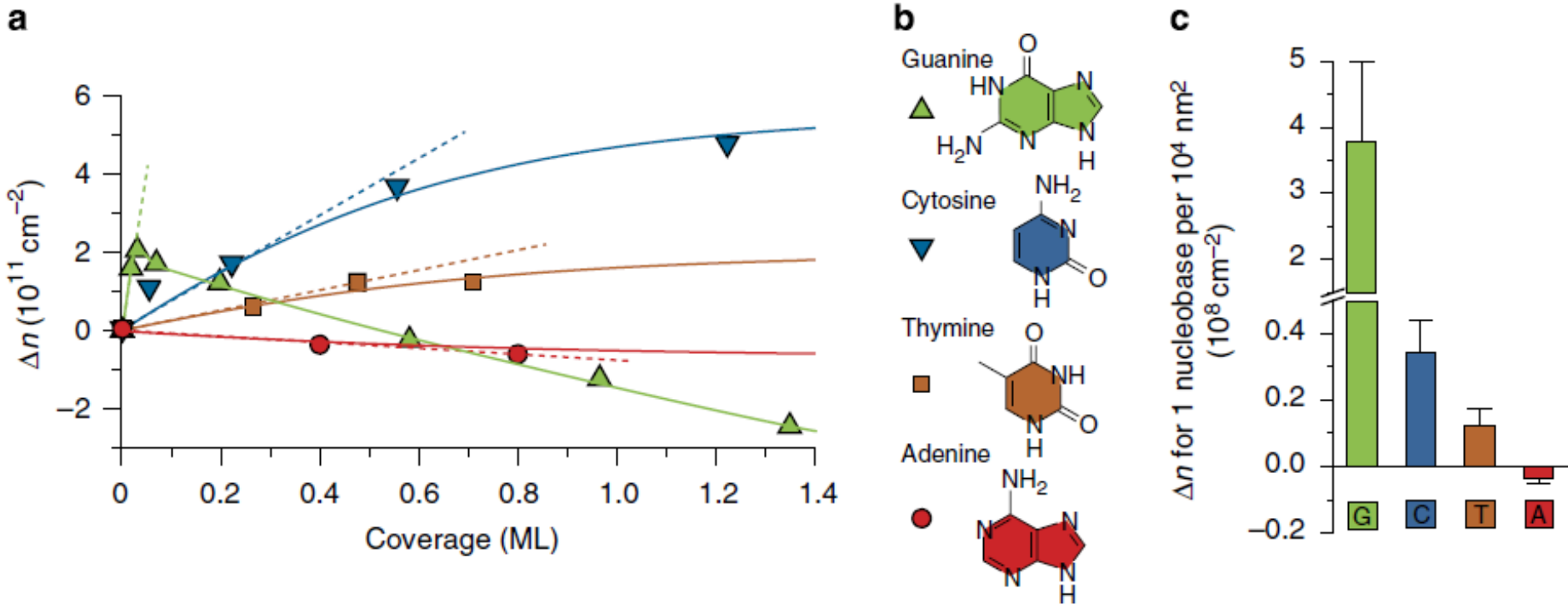
(b) Optical and

(c) schematic images of a GFET device used for electrical experiments and

Probing molecule-specific interactions

- The figure demonstrates the high sensitivity of GFETs to adsorption of a small number of molecules, in this case ~0.1 monolayer (~ 109 molecules) of guanine.
- The conductivity spectrum of graphene shifts to the left after guanine adsorption, indicating an effective n-type doping of graphene in response to adsorption of the molecules.
- The voltage shift of the spectra can be determined by the position of the current minima (marked by the dashed lines).
- The gate voltage corresponding to the minimum in ISD, known as the charge neutrality point (CNP), represents the Dirac point in the graphene band structure.
- The number of charge carriers in graphene is calculated using a parallel plate capacitor approximation of the doped Si/Si02/graphene stack.
- For the case of G in Fig. 1, a 0.7V shift indicates a relative increase of 1.7 x 1011 electrons cm-2 in the conduction band of graphene.

Adsorbed nucleobase dependence of induced GFET CNP shifts



(a) Charge carrier density change (n) of GFETs induced by adsorption of guanine (G), cytosine (C), adenine (A) and thymine (T). The dashed lines represent linear fits to the low coverage regime used to calculate the expected single-molecule-induced shifts in (b). The solid lines are fits to C, A and T data using the electrostatic depolarization model, which attributes the observed shifts to the interface electric field formation from molecular dipoles. The solid line for G is a guide to the eye only. (c) Calculated charge

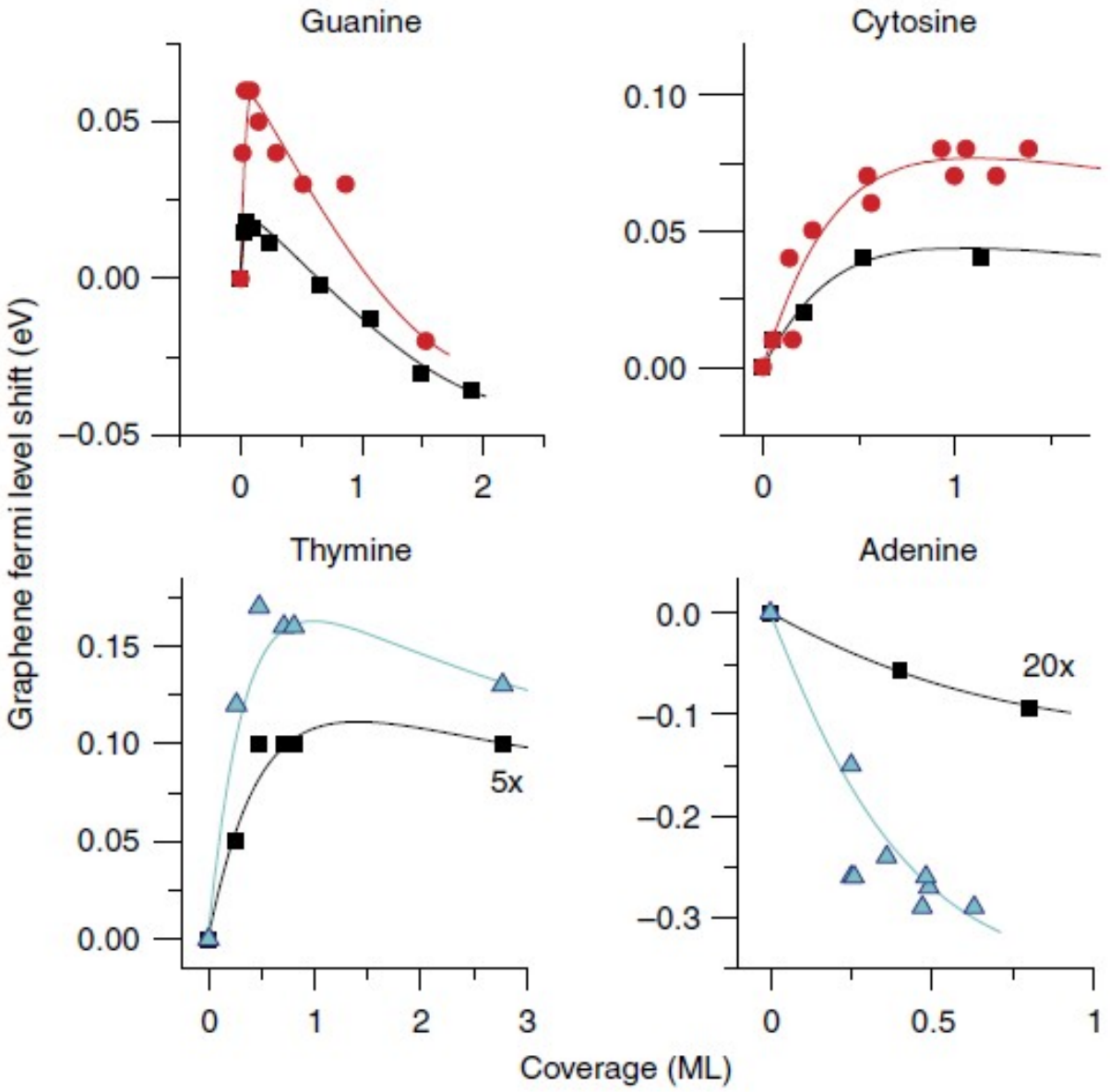
Probing molecule-specific interactions

- The predicted induced charge carrier density in the scaled-down GFETs by the individual nucleobases is of the order of Δn=106–108 e, with the largest signal for adsorbed guanine showing an increase of Δn=3.8 x 108 e.
- An option to improve GFET sensitivity to single nucleobases is to further scale down to the graphene nanoribbon regime.
- Shrinking the channel area, however, increases the expected low frequency device noise, making nucleobase signal detection more challenging.
- Another way to achieve single molecule resolution is to improve the sensitivity of GFET devices by using a different detection method or mechanism. For instance, monitoring changes in ISD at a fixed VG is expected to significantly improve the device sensitivity in high-mobility graphene devices.
- To sense adenine, however, an additional enhancement of the sensitivity would be required.

Comparison between electric transport and XPS

- To get a more detailed insight into the sensing mechanism of GFETs and the related molecule–graphene interactions, synchrotron-based XPS and NEXAFS measurements were conducted simultaneously with the electrical transport measurements.
- XPS analysis allows to directly corroborate the measured changes in electrical data with respect to the changes in binding energy of the core level C 1s XPS peak of graphene, and thus changes in its Fermi level.
- A comparison of the differences in the magnitude of the two measurement techniques shows the measured binding energy shifts to be consistently larger than measured CNP shifts.
- Unlike electrical CNP measurements of GFETs, its expected that the measured C 1s shifts to be independent of any graphene contact work function alignment. This would indicate that the choice of Ti/Au contacts is limiting the GFET sensitivity to adsorbed nucleobases.
- Carbon and nitrogen angle-resolved NEXAFS measurements

Comparison of nucleobase-induced Fermi level shifts



Graphene Fermi level shifts of SLG GFETs (black squares) are calculated from CNP measurements using the tight binding model dispersion equation (1). XPS measurements of Fermi level shifts a determined by changes in the C 1s position of SLG (blue triangles) and BLG (red circles). The two techniques confirm the structure observed molecular coverage dependence of shifts in the graphene's Fermi level. The error for electrical measurements was 0.005 eV, the fitting error of XPS

Discussion

• The observed changes in graphene's electronic structure on the adsorption of four individual DNA nucleobases indicate molecule-specific interactions with a strong coverage dependency.

• It is commonly accepted that the adsorption of molecules onto a metal surface gives rise to the formation of molecular dipoles in the adsorbate layer. The effect of the electric field generated by such a dipole layer is a modulation of the surface potential of the metal, which can be measured as a change in the surface work function of the metal.

• DFT modelling predicts that nucleobase adsorption onto graphene will induce interfacial dipole formation, giving rise to a shift in graphene's work function by 0.22, 0.15, 0.13 and 0.01 eV for G, A, C and T. But whats observed was in the lower coverage regime (below 0.1 ML) the order of magnitude of Fermi level shift was G > C > T > A, which gradually changed to a molecular sequence of C > T > A > G at coverages greater than a monolayer. The magnitude of the shifts was in the range of 0–0.2 and 0–0.06 eV for C 1s and CNP shifts, respectively.

• The strong coverage dependence of DNA nucleobases induced CNP shifts in graphene can be partly explained by the molecular

Conclusion

• They have shown that the electric transport measurements using GFETs fabricated on SiO2 can probe distinct conductance signatures upon adsorption of four different DNA nucleobases.
• By decreasing the size of the graphene channel in these devices and taking advantage of recent improvements in graphene mobility and noise reduction techniques, its predicted that single-molecule sensing of guanine, cytosine and thymine by bulk graphene devices can be achieved.
• They have also established that the different nucleobases have different magnitudes of interaction with graphene that strongly depend on molecular coverage.
•. While these results confirm the fundamental sensitivity of graphene for DNA sensing, the task of implementing this design of graphene sensor into any realizable DNA sequencing technology presents even further challenges not yet discussed. Further research into device design may enable this molecule discriminability to be exploited for selective nucleobase sensing


Thank
you...
Don't Fear Moving Slowly Forward,
Fear Standing Still.....