Graphene membranes and DNA fingerprinting on Graphene

Alexander V. Balatsky
Towfiq Ahmed

Carbonhagen 2013

Copenhagen, Aug 19 2013

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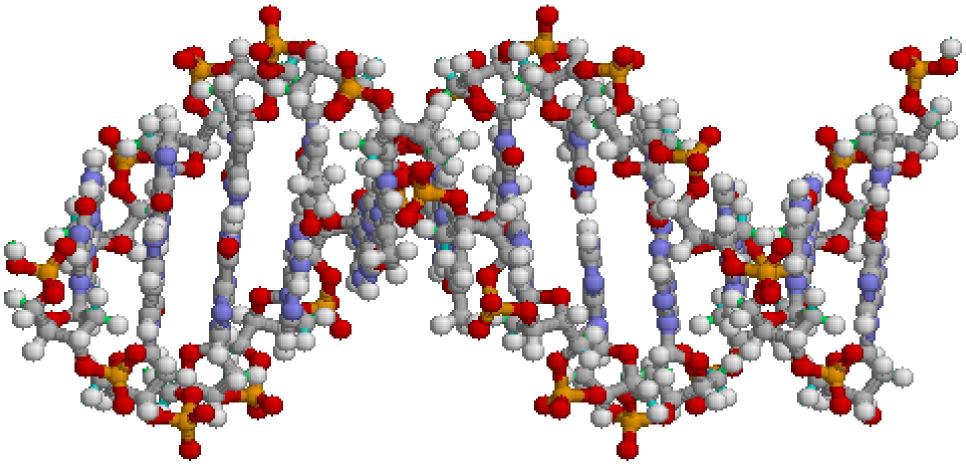
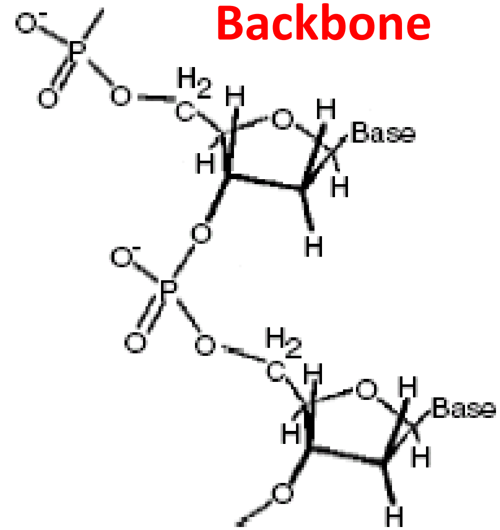
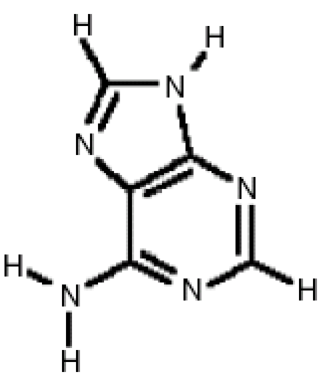


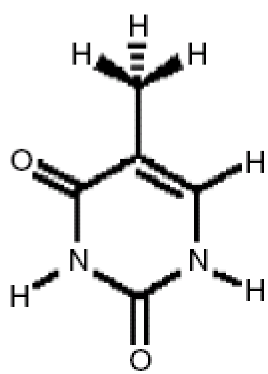
Backbone



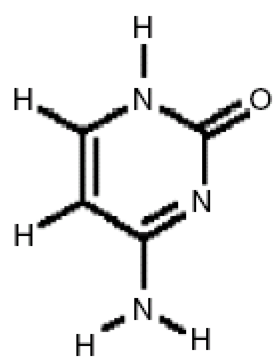
Adenine



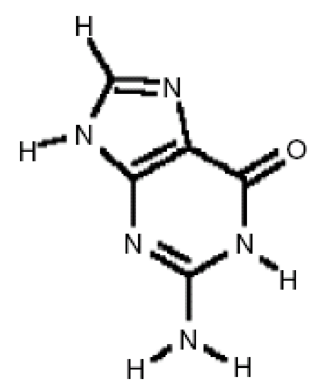
Thymine



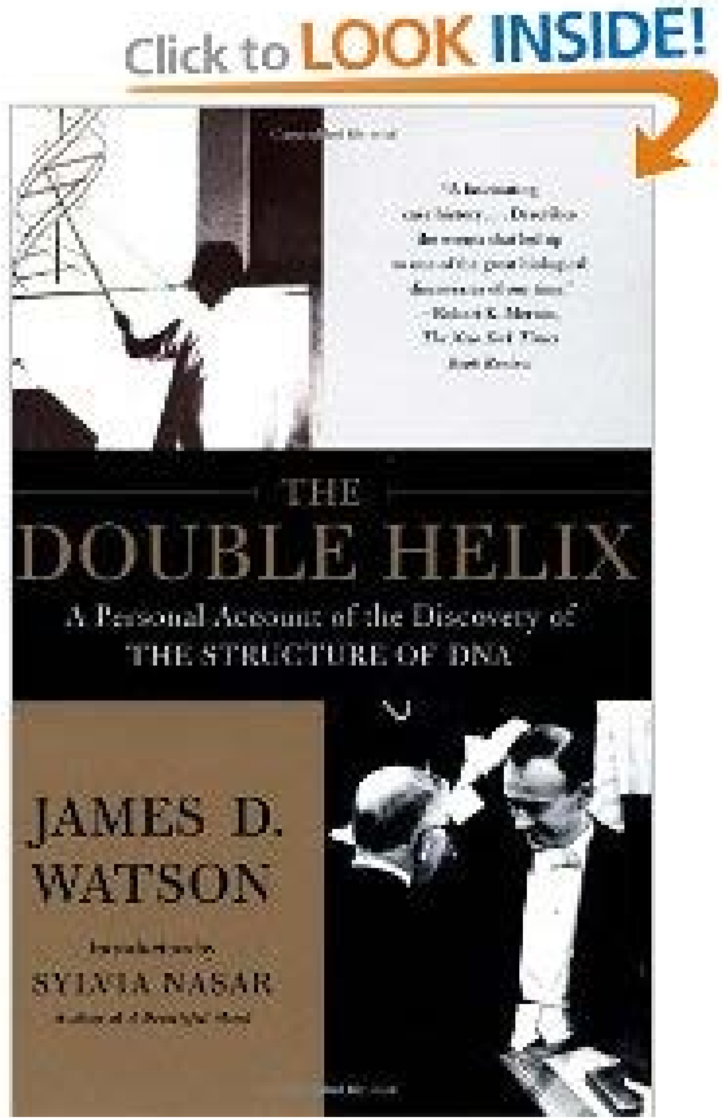
Cytosine



Guanine



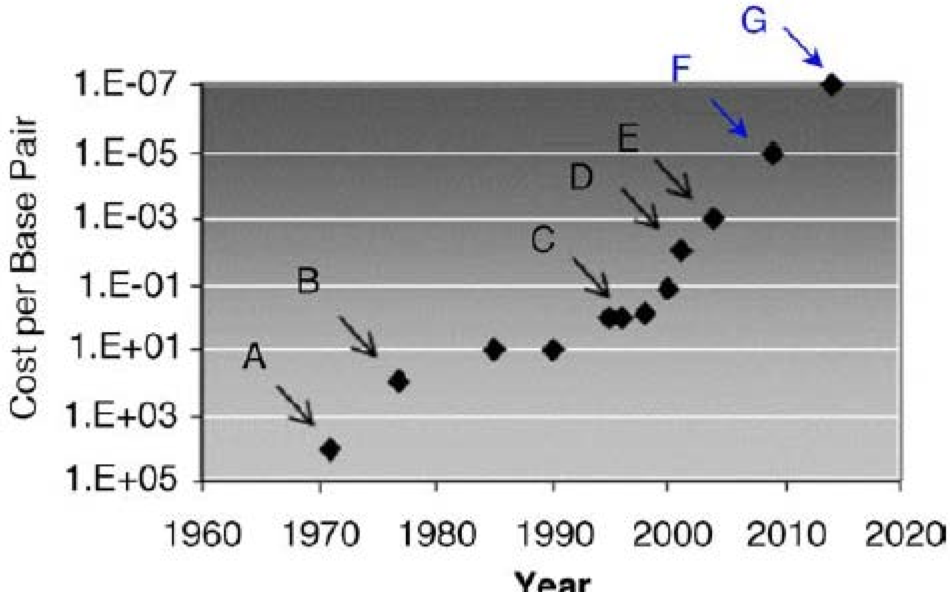
Humans ~ 3 Billion base pairs

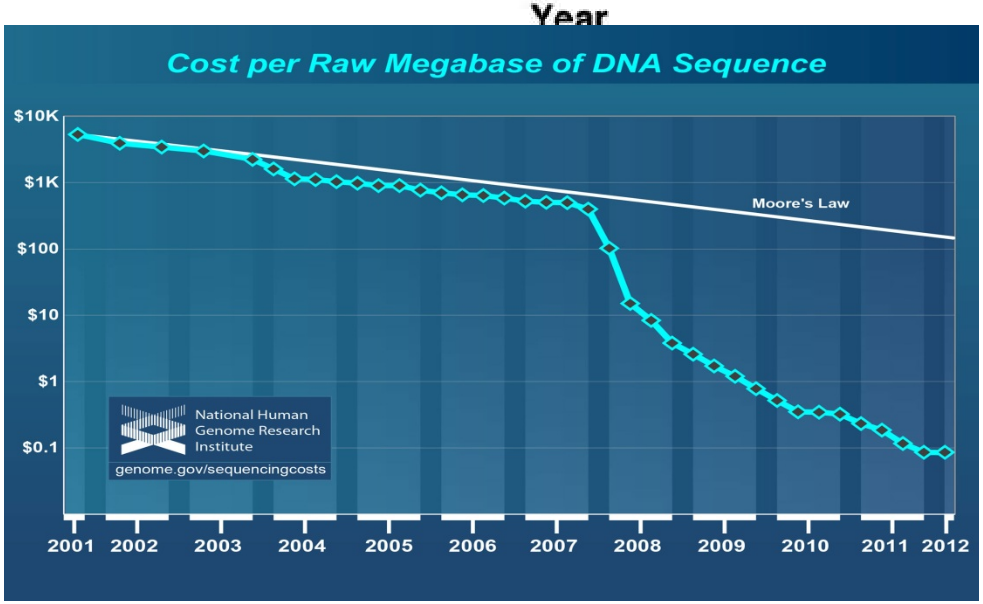


Click to LOOK INSIDE!
THE
DOUBLE HELIX
A Personal Account of the Discovery of
THE STRUCTURE OF DNA
JAMES D.
WATSON
SYLVIA NASAR

F: ~$100,000

G: ~$1,000





A: Sequenced 12 bp for a total cost of $120,000

…

E: Current Cost

F: Near term goal

G = Genomic Revolution

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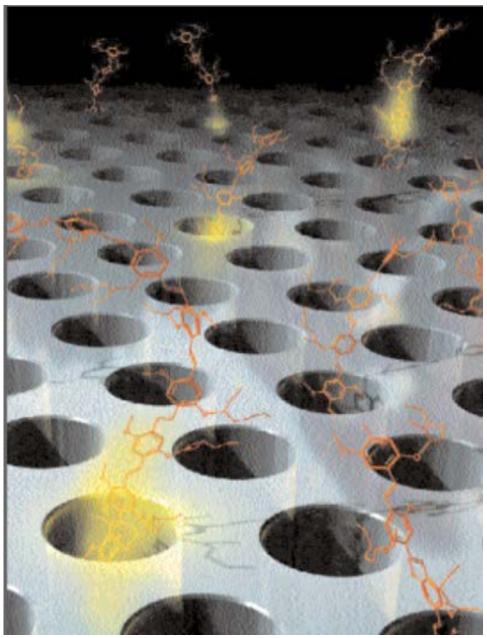
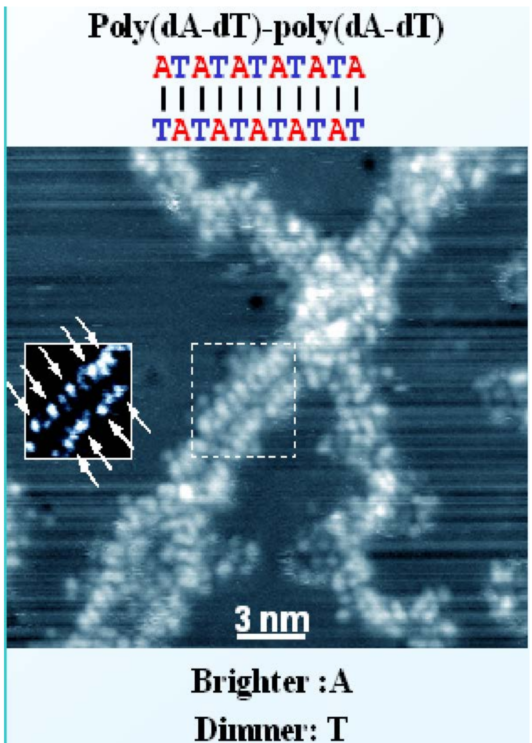
Alternative Methods of DNA Sequencing Inexpensive and Fast

The use of personal genetic information to predict disease susceptibility and guide proactive care has the power to transform entire healthcare system.





Ref: H. Tanaka, Surf Science,(2003)

Scanning Tunneling Microscopy (STM) and gated nano-pores for DNA sequencing

- It's based on the electronic differentiation of DNA bases

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Motivation

DNA Sequencing:

Accurate **STM** and **Nanopore** based **DNA fingerprinting**.

Nanotechnology

Applications in medicine and nano-electronics with DNA-functionalized Graphene.

GOALs

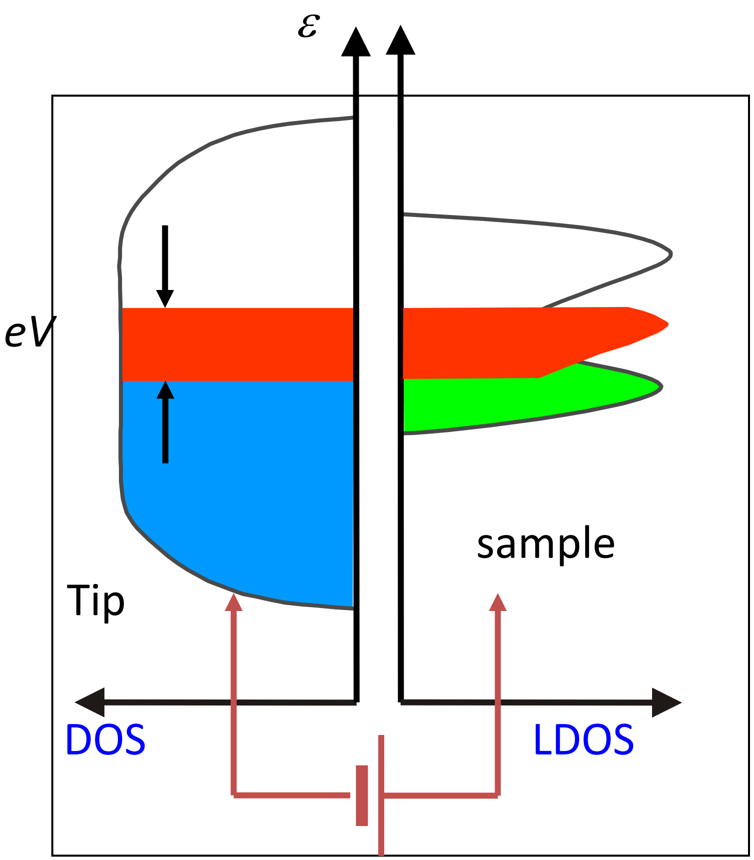
Part-1

- **Simulate dI/dV STM spectrum of DNA/graphene hybrid by *ab initio* calculation.**
- **Identify DNA bases from the differences of local density of states (LDOS) near E_F.**

Part-2

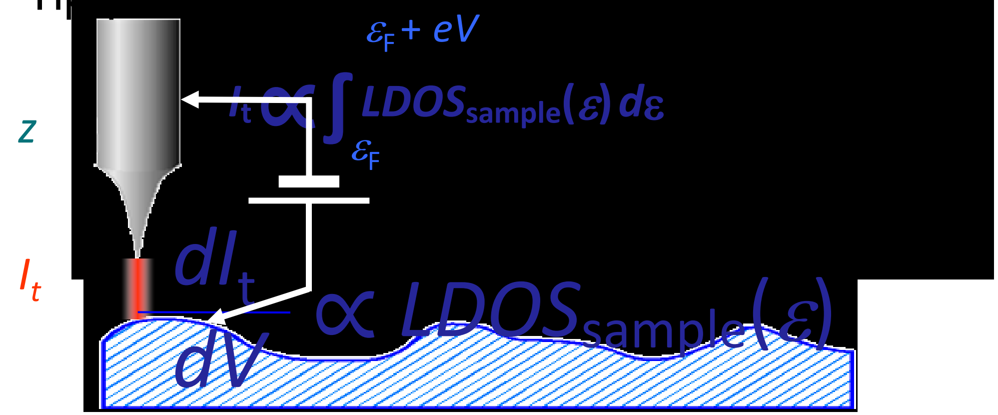
- **Calculate transport current properties from first principles**

Local probes: Scanning tunnelling microscopy, Nobel prize 1986



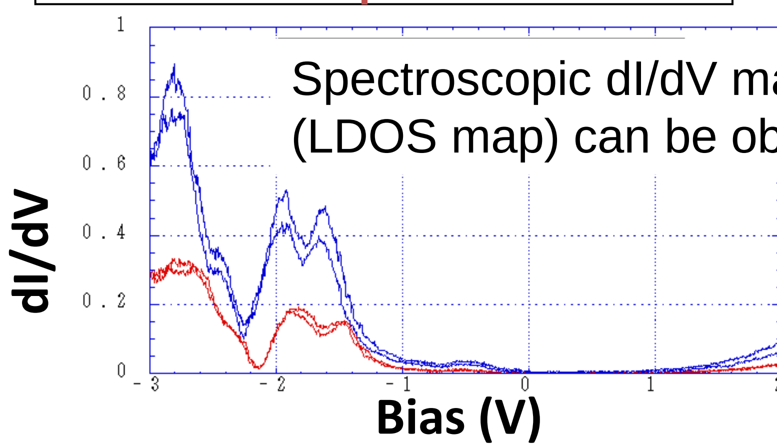
dI/dV c[redacted]

Ti[redacted]

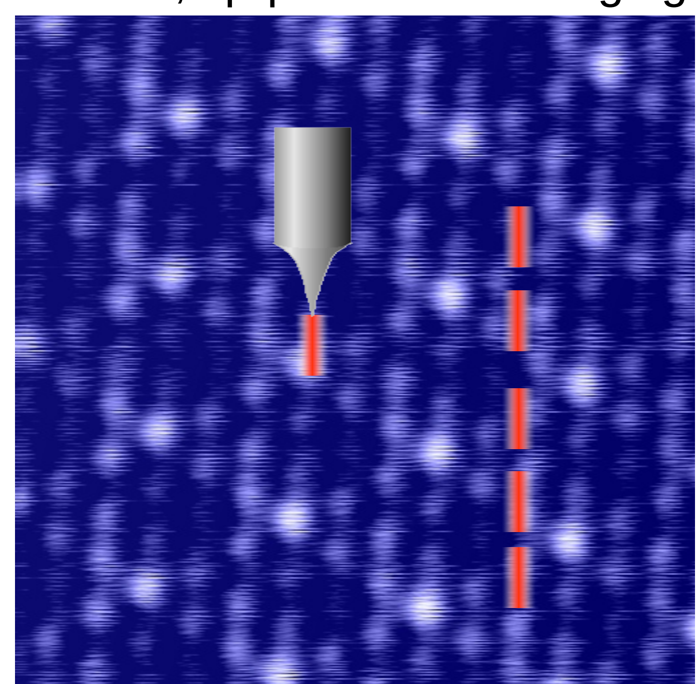


Topo image

bias=const; tip-position is changing

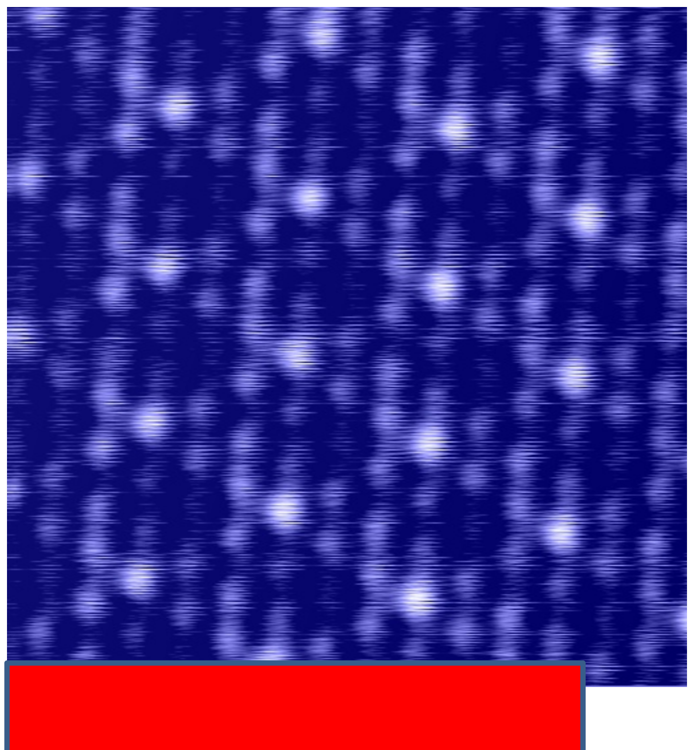


Spectroscopic dI/dV map (LDOS map) can be obtained

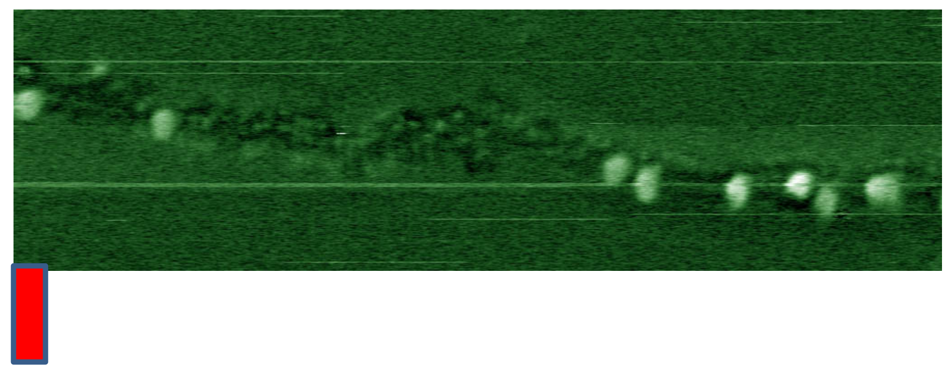


Sequencing without Amplification with Tunneling Currents

We can image matter at atomic resolution ->
Single atom, single chanrge, single spin
->**we can image and fingeprint a single base**
NB Electronics is not very good at telling chemistry

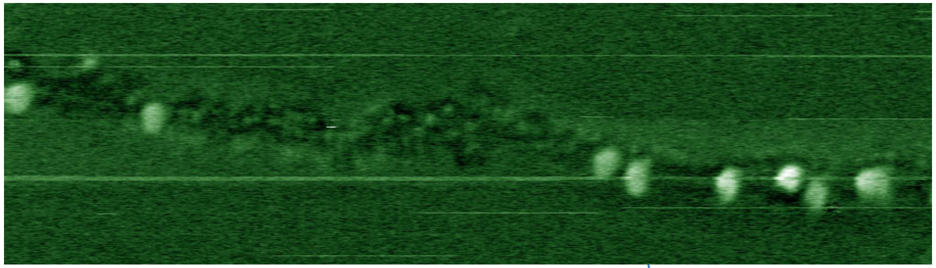


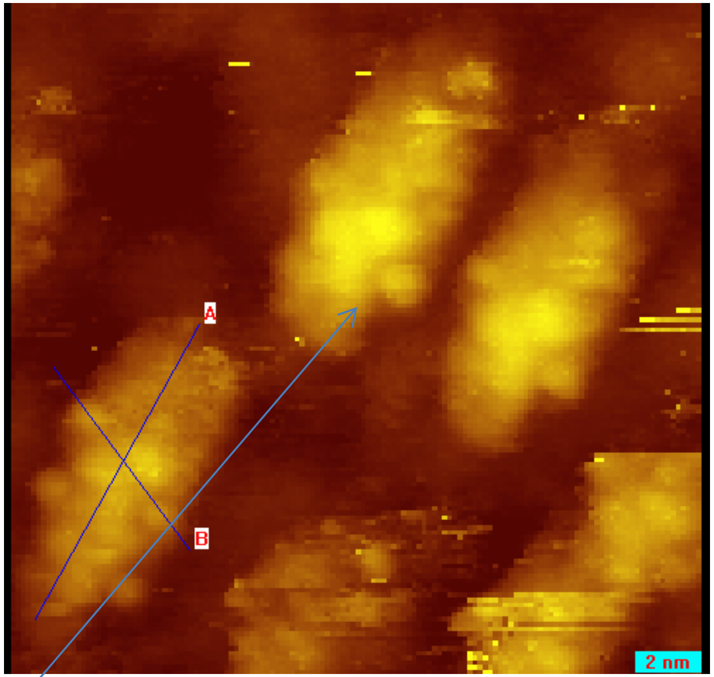
Nb Se2 surface, atoms shown



ssDNA , Guanine molecules shown

DNA as a robust molecule in a harsh environment





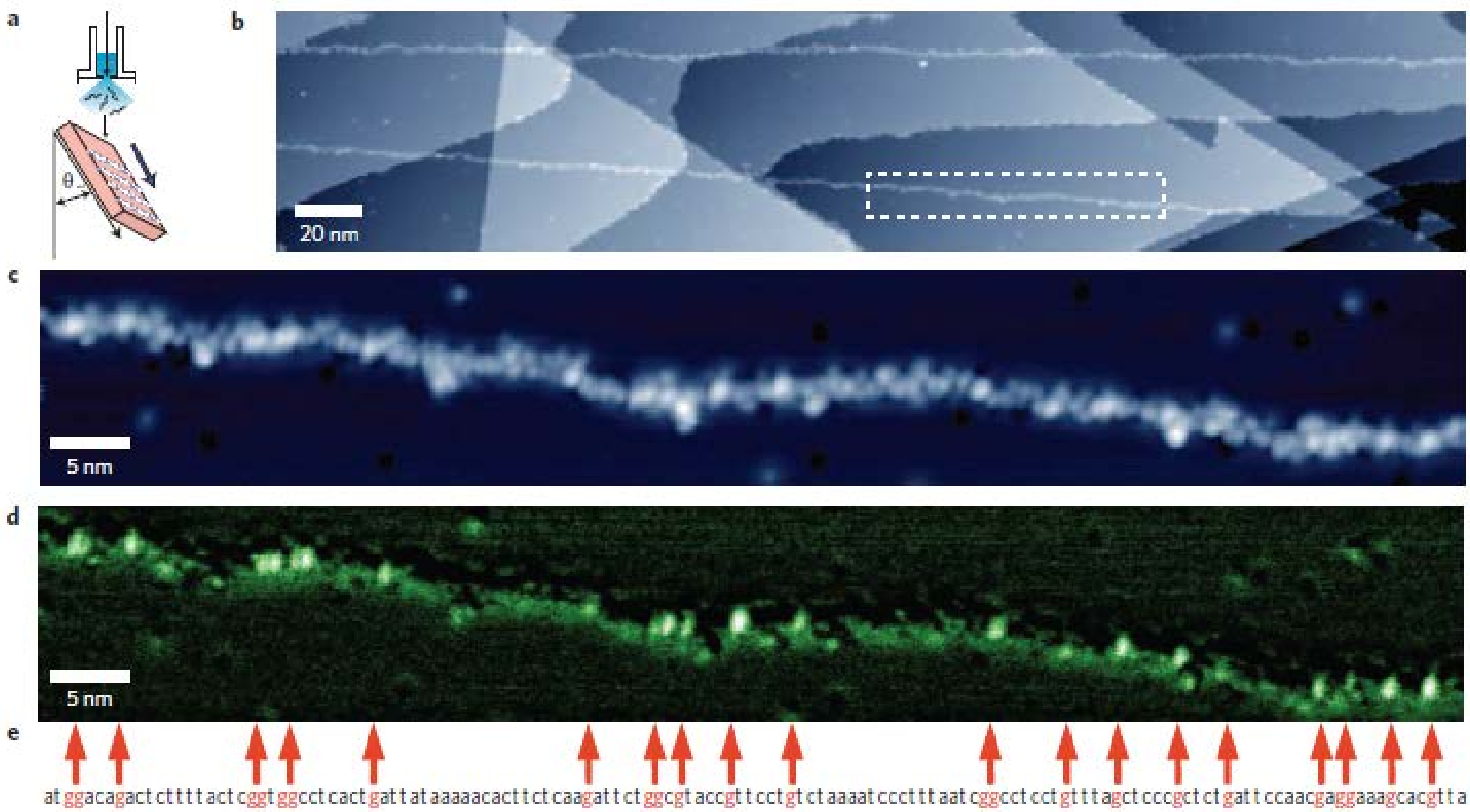
Ref: H. Tanaka, Surf Science,(2003)
H. Tanaka et al. Nature
Nanotech. v 4, p 518 (2009)

D. Yarotski et al, Nano. Lett v9, p 12 (2009)

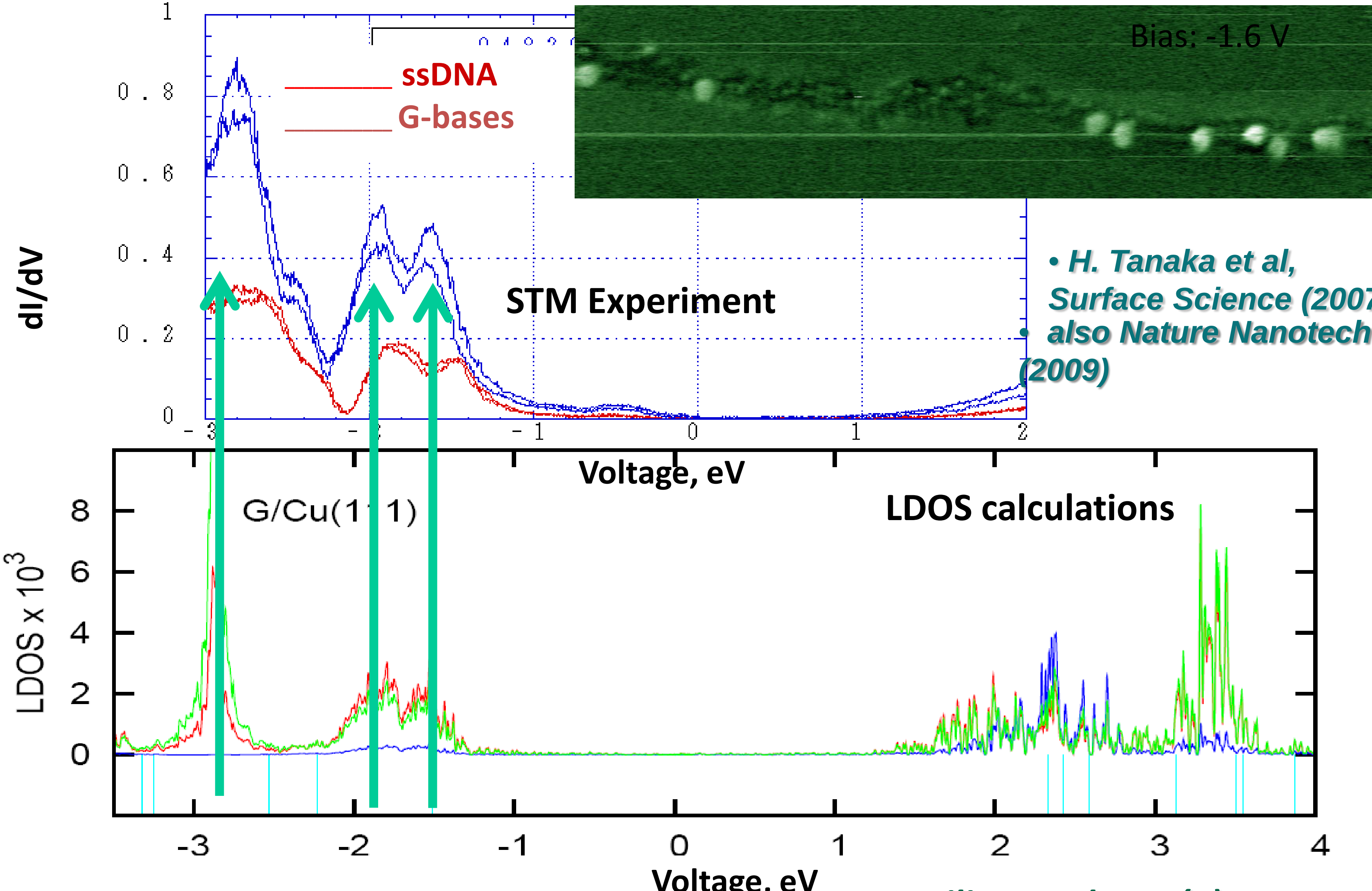
SINGLE BASE STABILIZED,VSUALIZED, NOT AMPLIFIED

- *H. Tanaka et al. Nature Nanotech. v 4, p 518 (2009)*

NATURE NANOTECHNOLOGY | VOL 4 | AUGUST 2009 | www.nature.com/naturenanotechnology



STM spectra: comparison with experiment



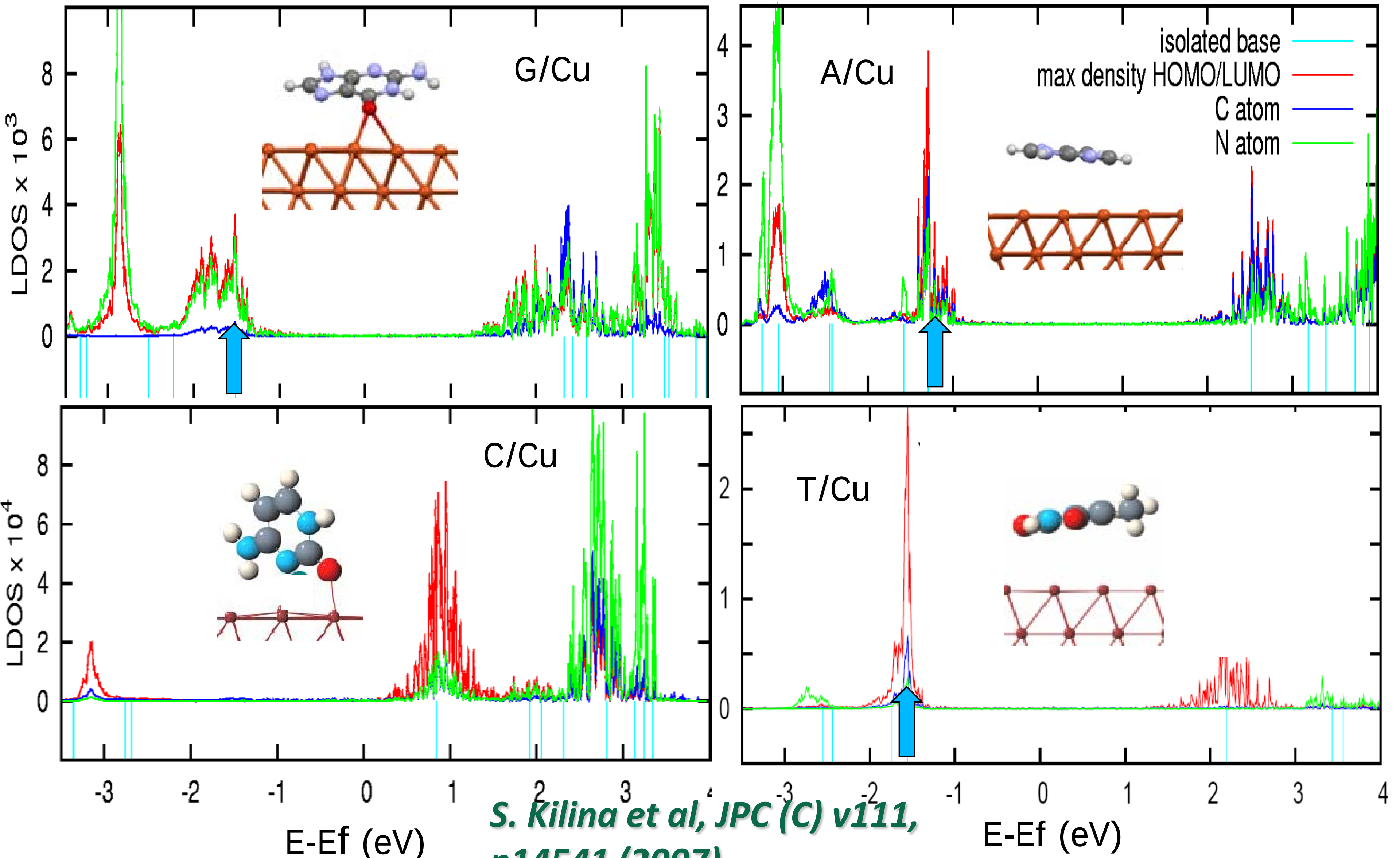
- *H. Tanaka et al, Surface Science (2007)*
- *also Nature Nanotech. (2009)*

S. Kilina et al, JPC (C) v111, p14541 (2007)

Simulated STM spectra of absorbed DNA bases

Chemisorbed bases

Physisorbed bases



S. Kilina et al, JPC (C) v111, p14541 (2007)

Part-1:

Single Base DNA Finger Printing on Graphene with

Scanning Tunneling Spectroscopy (STS)

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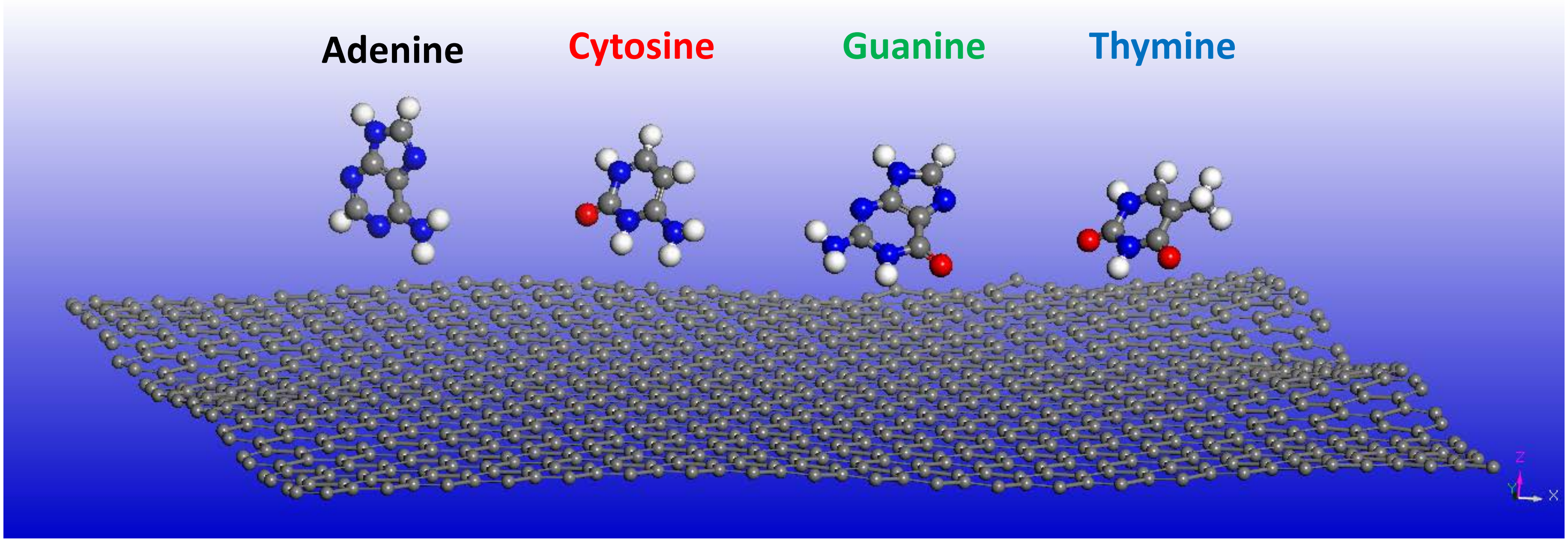
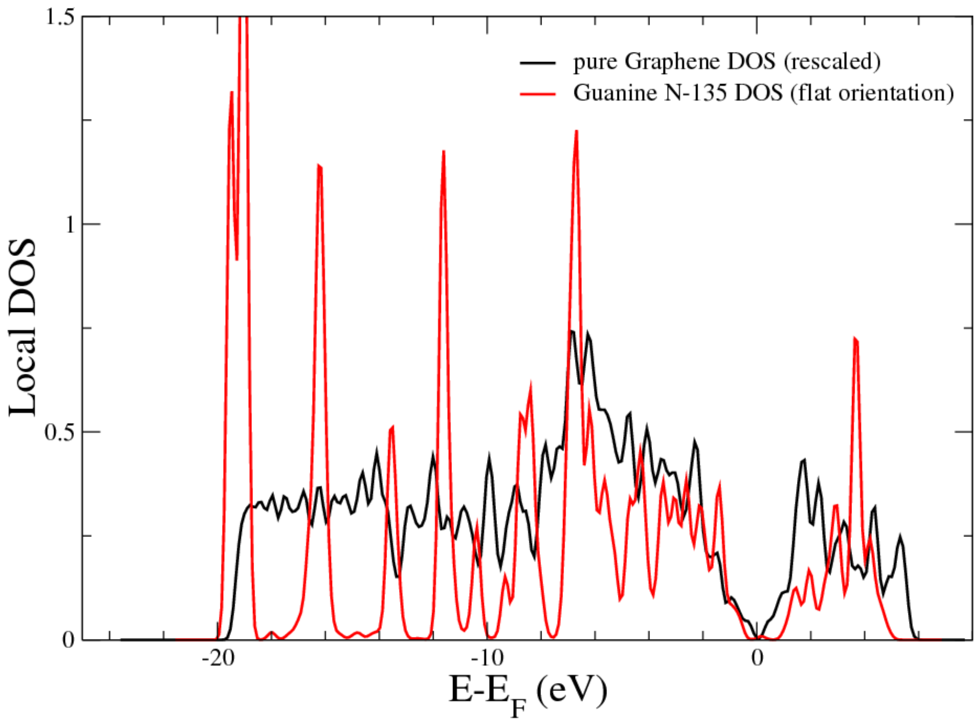
System: DNA base + Graphene



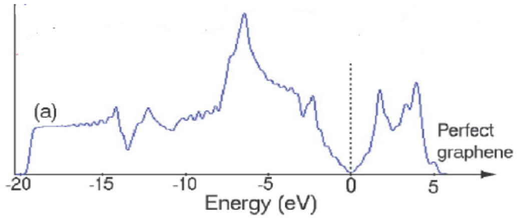
Why Graphene

1. Linear Dispersion (Dirac Cone) near E_F .
2. Robust Electromechanical Properties.

Scuseria *et al* .
Nano Letters, 2009



Ref:
Phys. Rev. Lett. 92, 225502 (2004)



Computational Detail:

- VASP code.
- Supercell with ~ 135 – 600 atoms
- Gamma point calculation

Nano Letters, DOI: 10.1021/nl2039315 January 18, 2012

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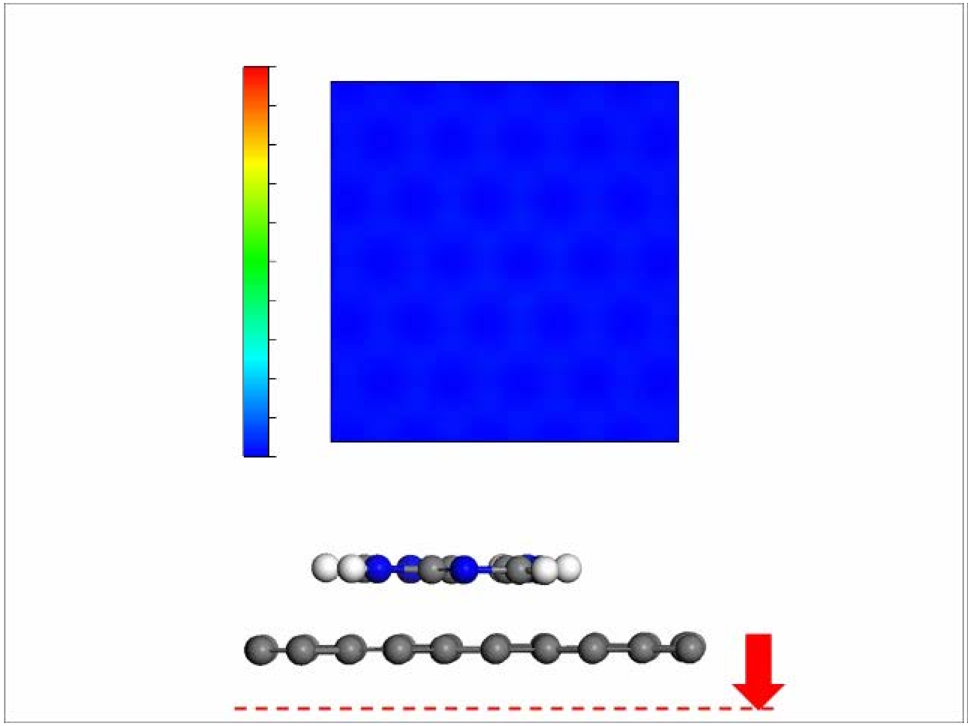
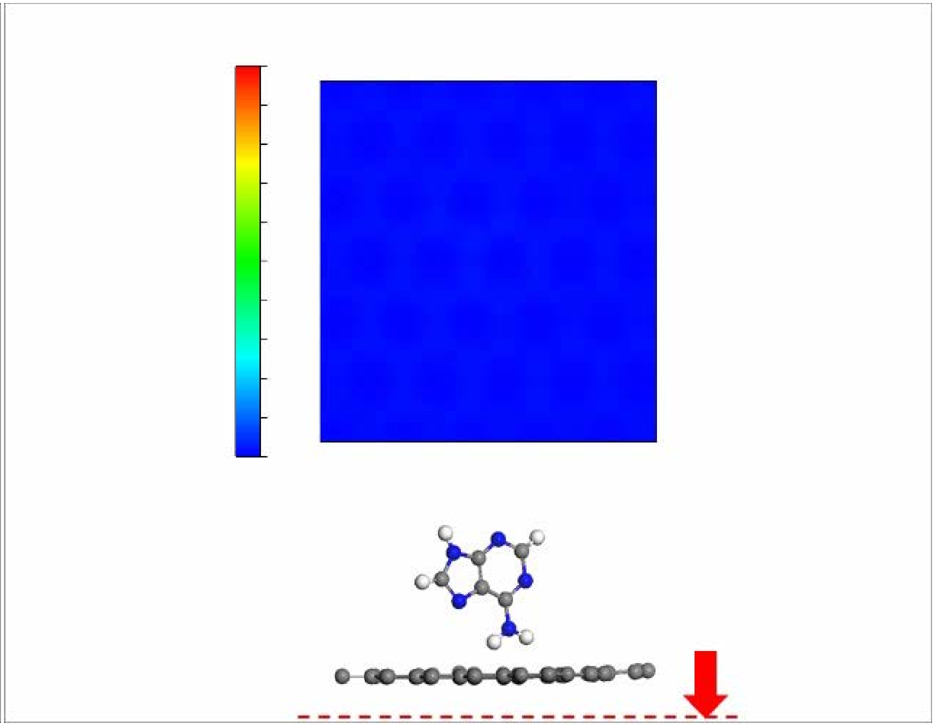
STM Calculation:

Partial Charge Density xy - Slices in z direction

(-3.0 eV Bias Voltage)



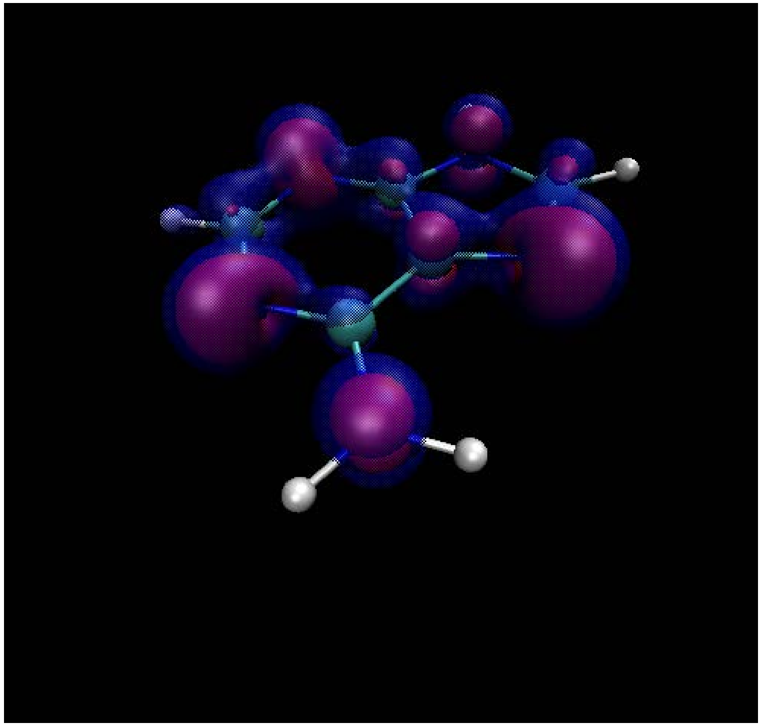


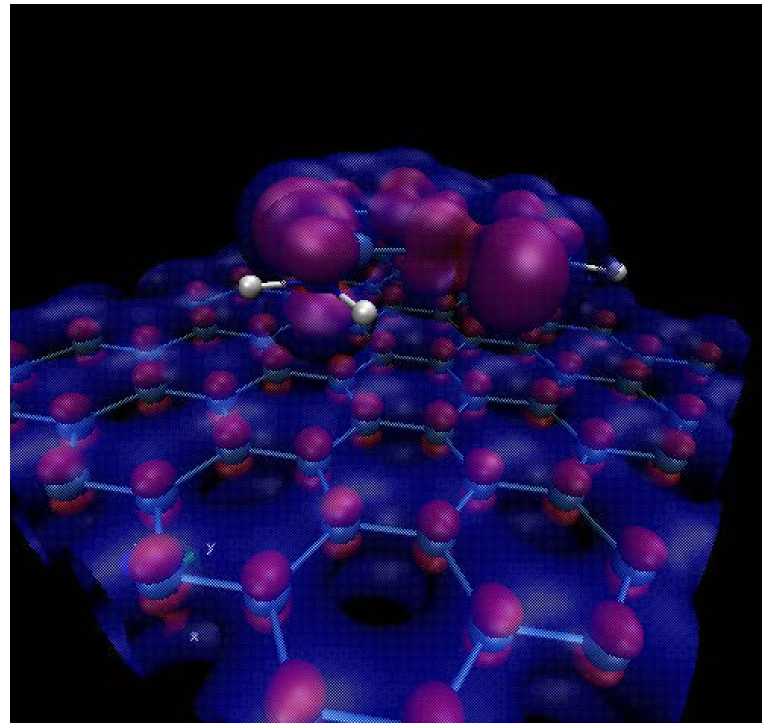
A$_0$

$$\rho(x,y,z) = \int_{-3\ eV}^{E_F} \rho(x,y,z;E)\,dE$$

A$_1$

Adenine



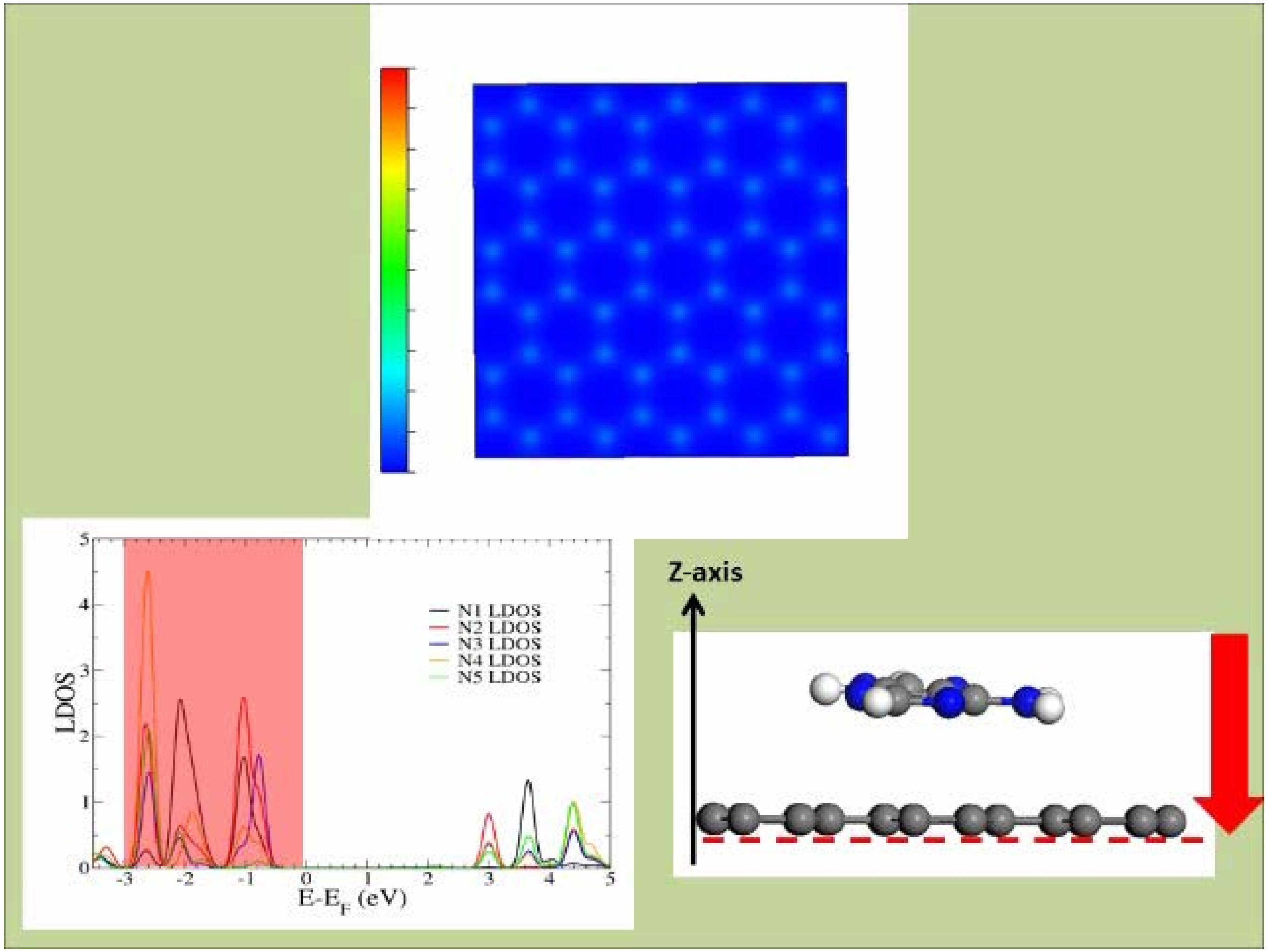


Purple Blob: **-3.0 eV to E_F Integrated Charge Density**

Blue Blob: **-5.0 eV to E_F Integrated Charge Density**

$$\rho(x,y,z) = \int_{-3\,eV}^{E_F} \rho(x,y,z;E)\,dE$$

Bias Voltage and z-dependent PCD
(A_0 Configuration)



STS (Scanning tunneling spectroscopy) Calculation:

LDOS (dI/dV)

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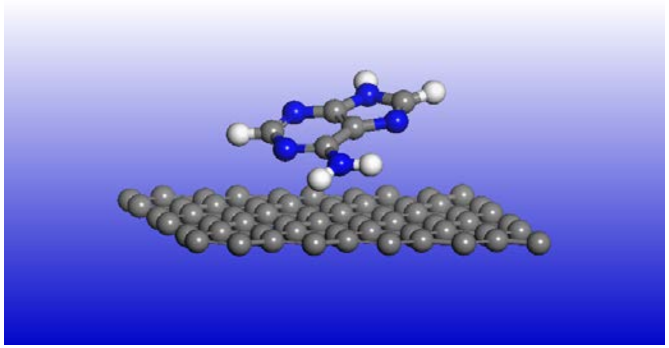
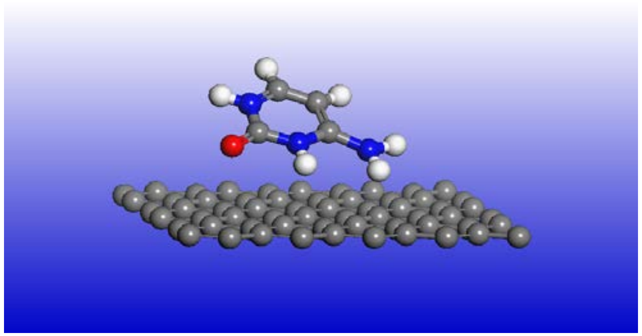
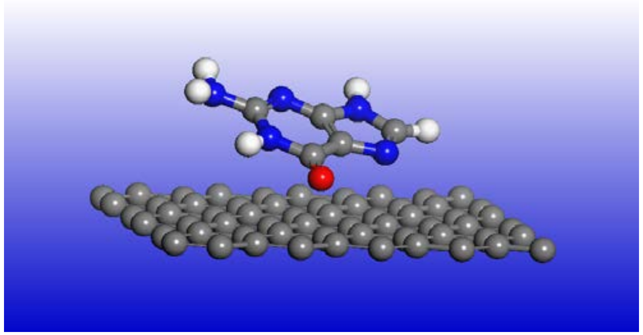
Geometry and Topography



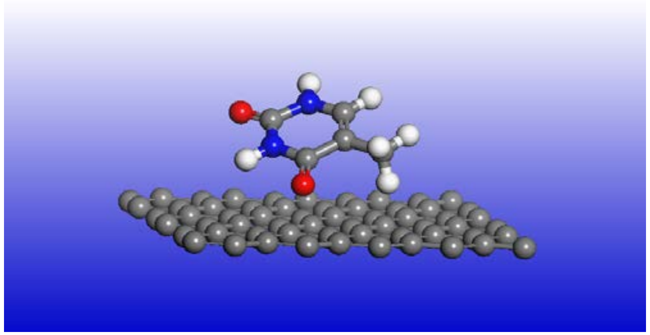
Adenine



Cytosine



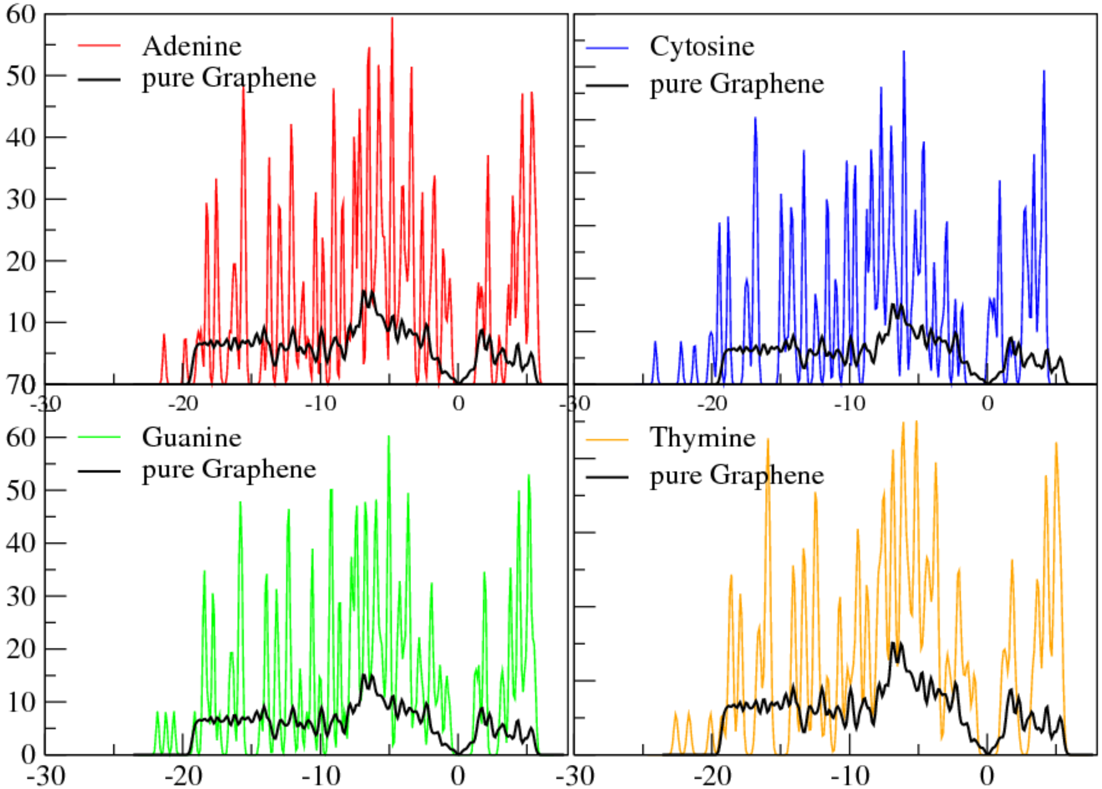
Guanine

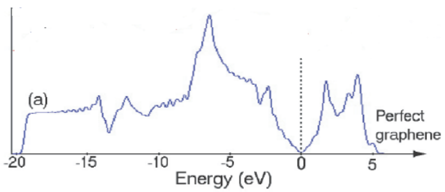


Thymine

Total Density of States

(flat Orientation of **Base** on **Graphene**)

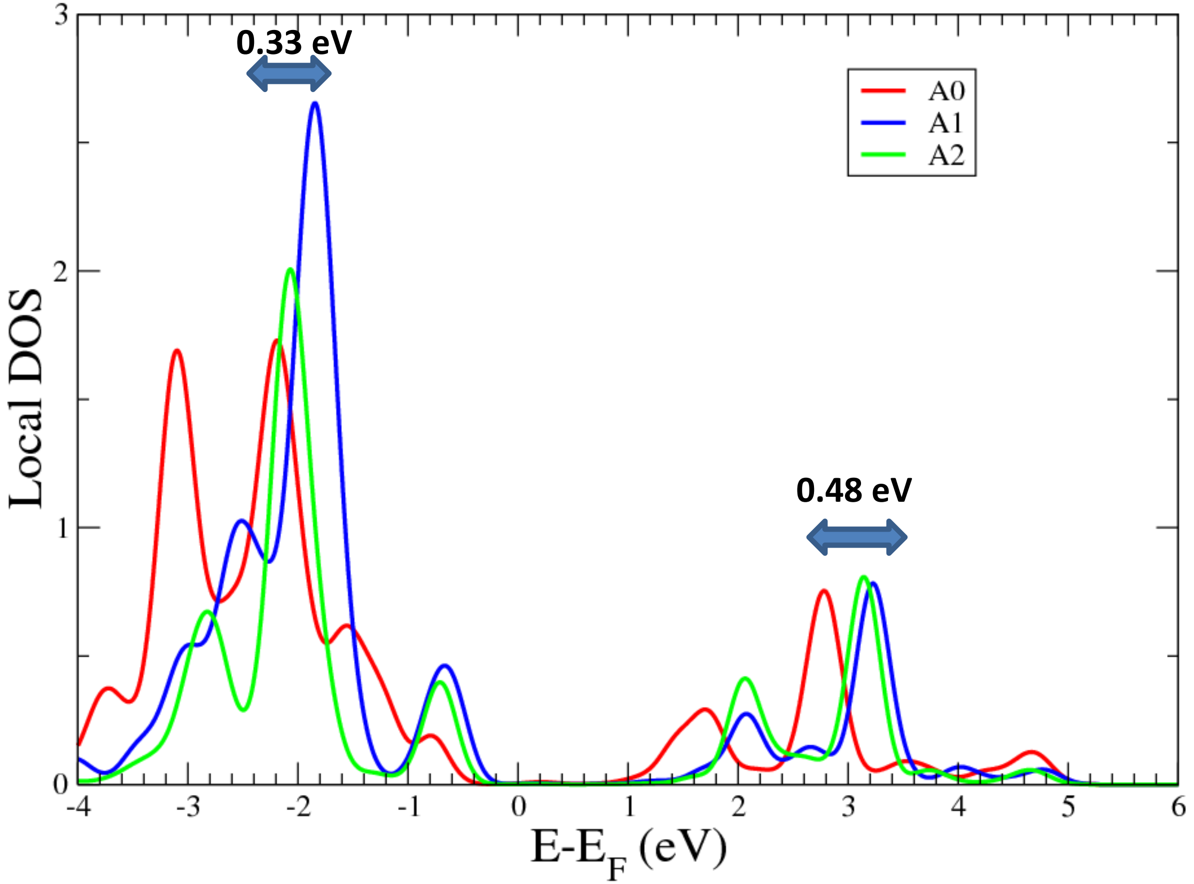




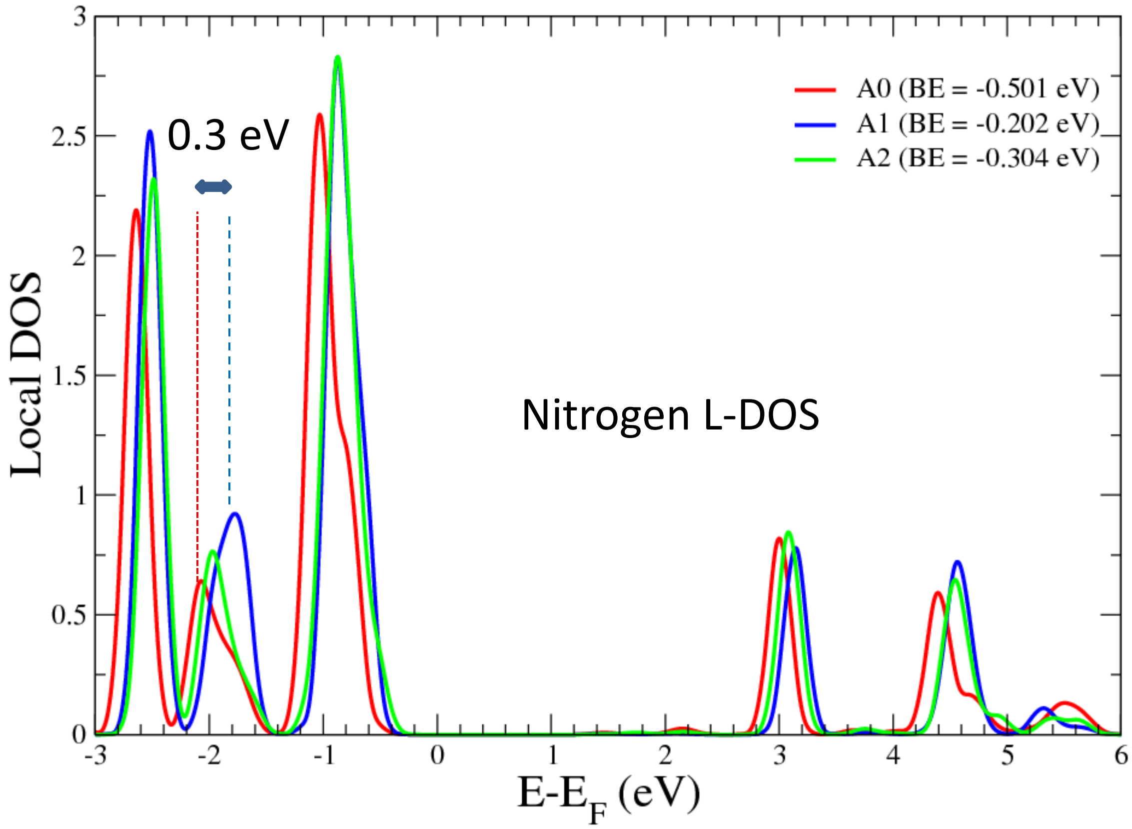
Ref:

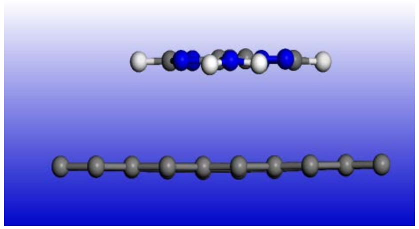
Phys. Rev. Lett. 92, 225502 (2004)
E. J. Duplock, M. Scheer, P. J. D. Lindan

Nitrogen LDOS in **Adenine** (Large Graphene)

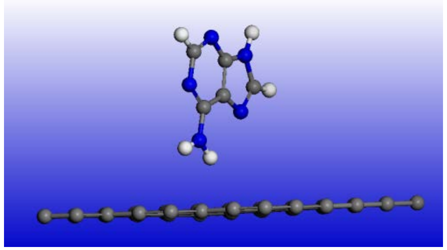


L-DOS Shift for Adenine Orientation

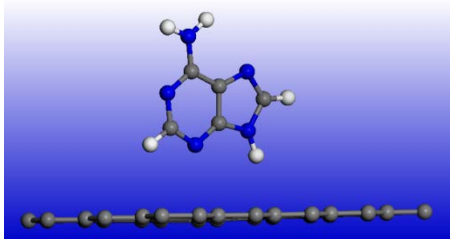




A0



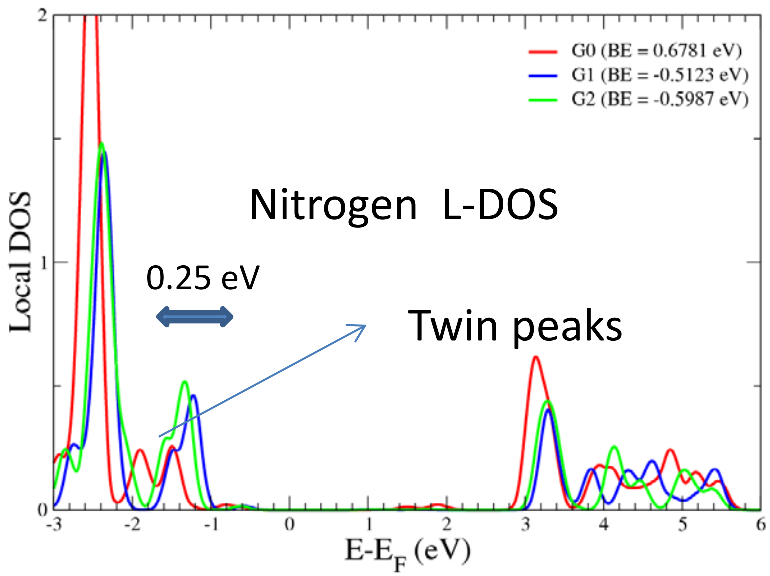
A1

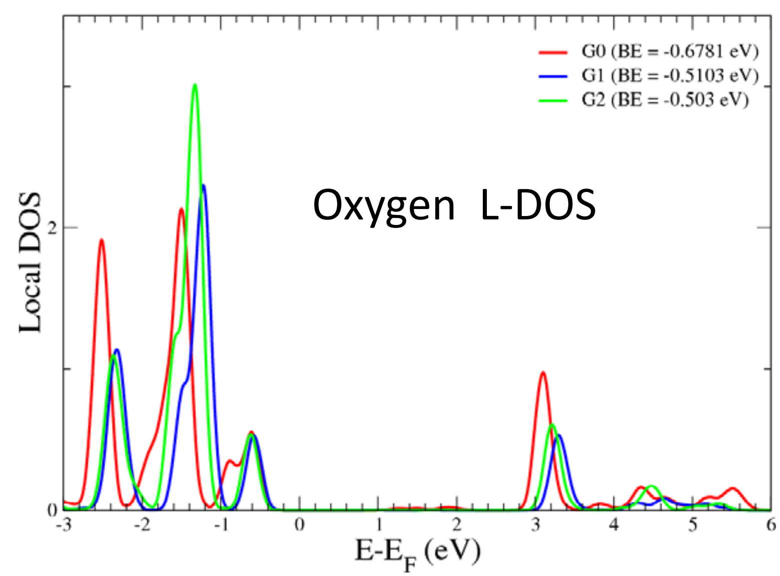


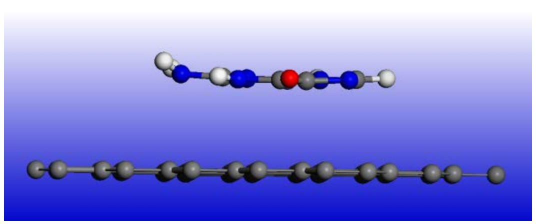
A2

$$\Delta = E_{Tot} - (E_{Base} + E_{Graphene})$$

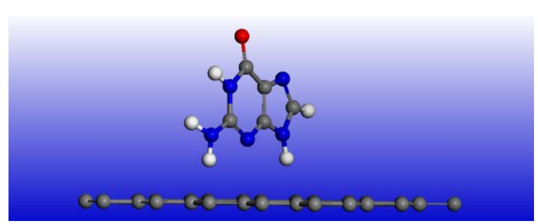
L-DOS Shift for Guanine Orientation



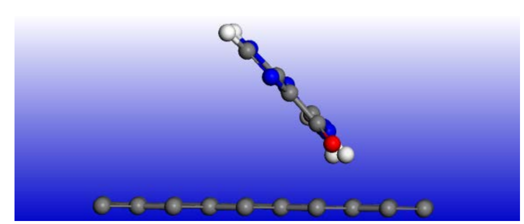




G0

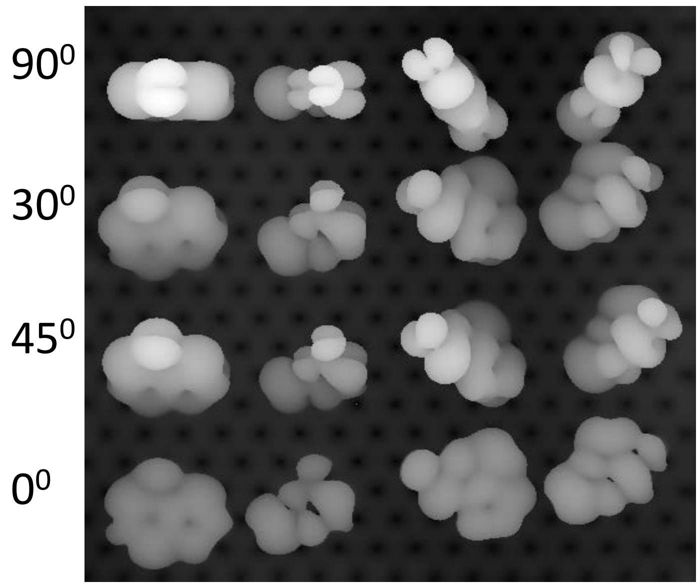


G1

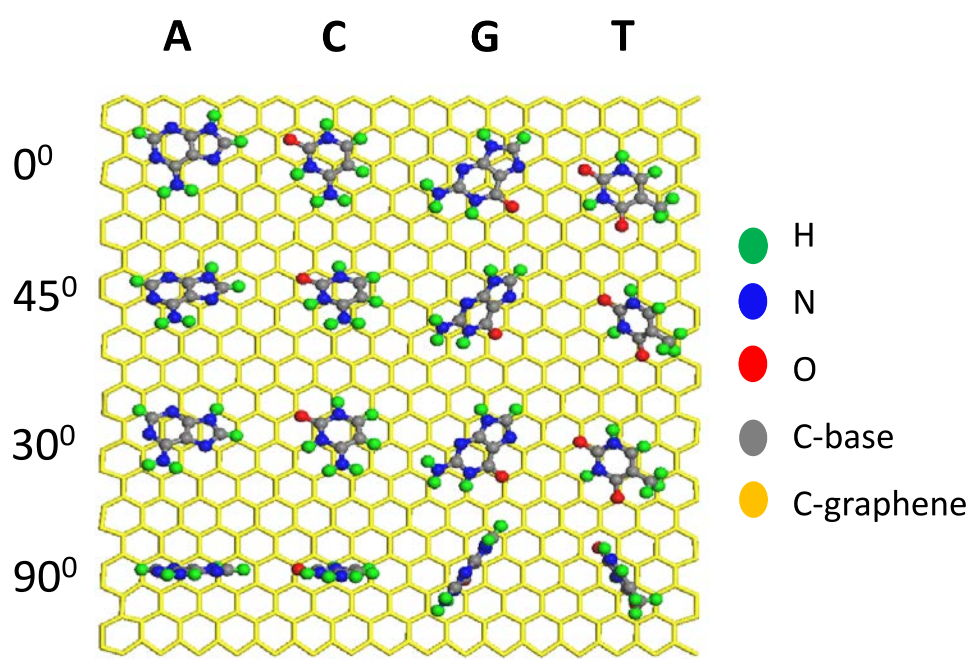


G2

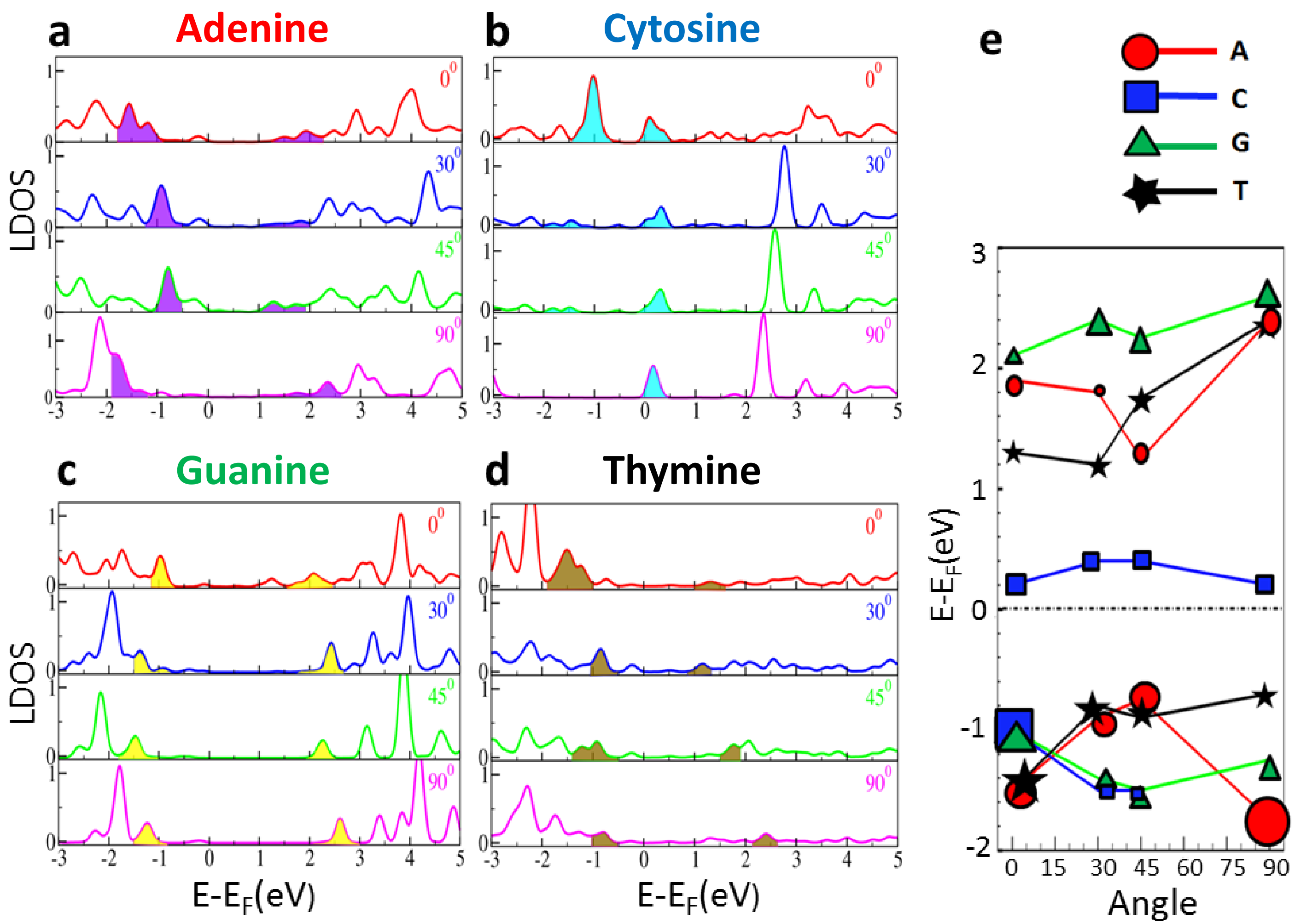
STM Simulation
(ab initio)



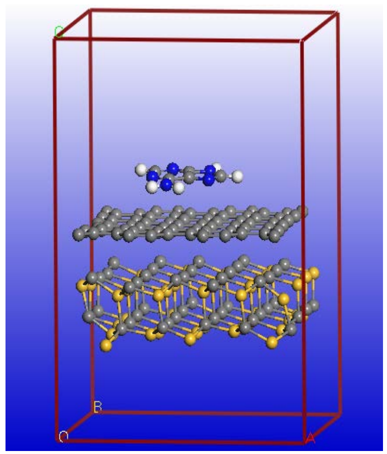
HIVE –STM
Vanpoucke, PRB 241308, 2008

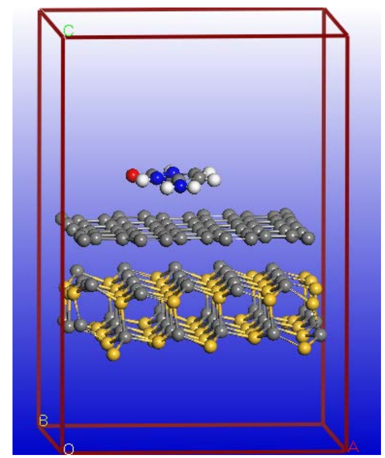


DNA Fingerprinting on Graphene: N LDOS

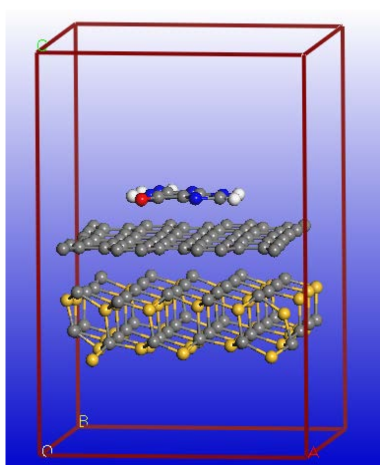


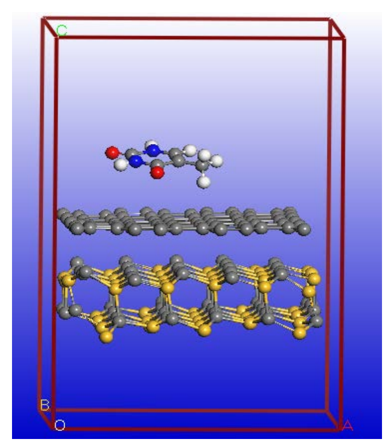
More Realistic Setup:
See Through Effect of the Substrate



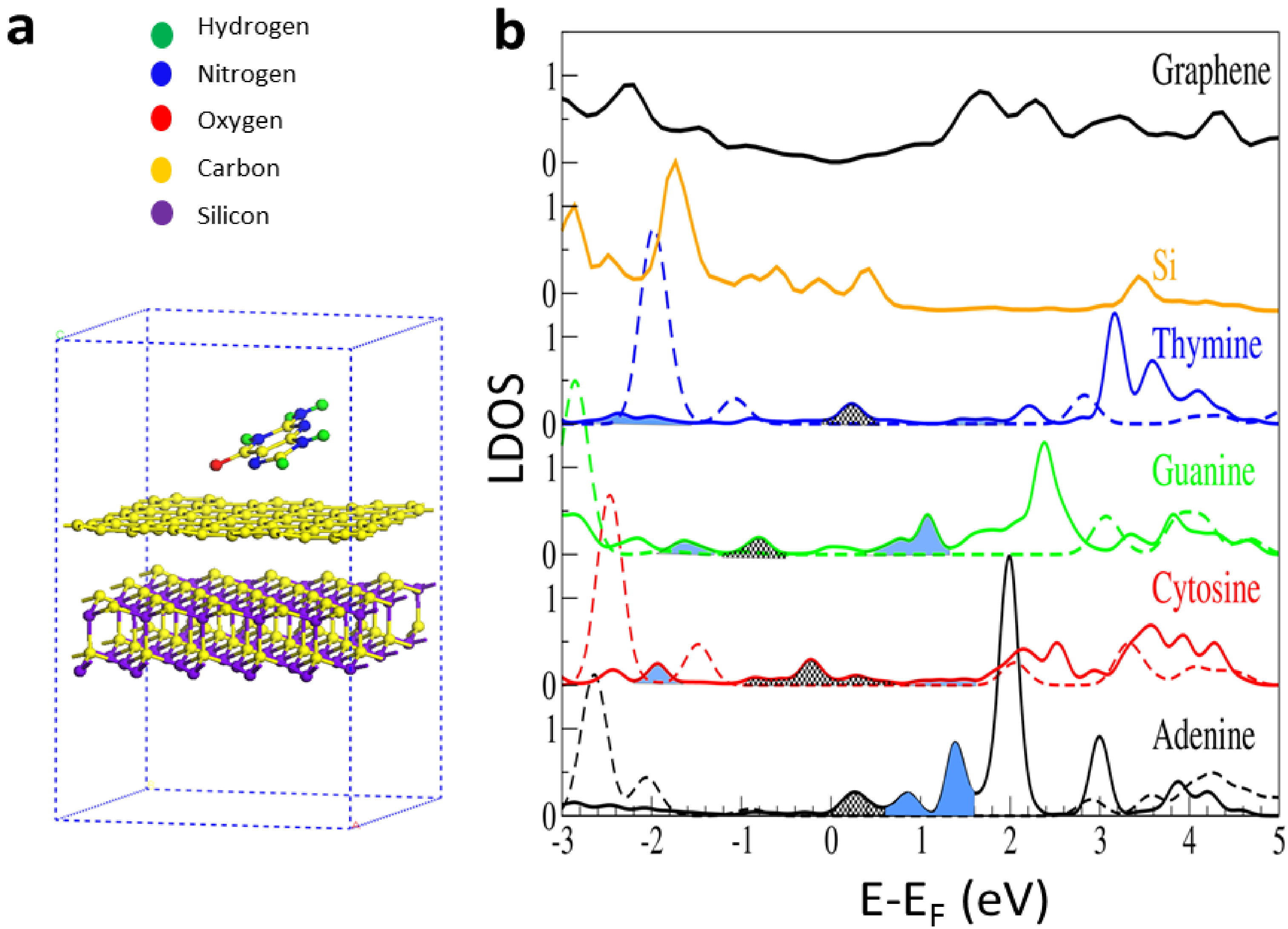


Single Layer SiC

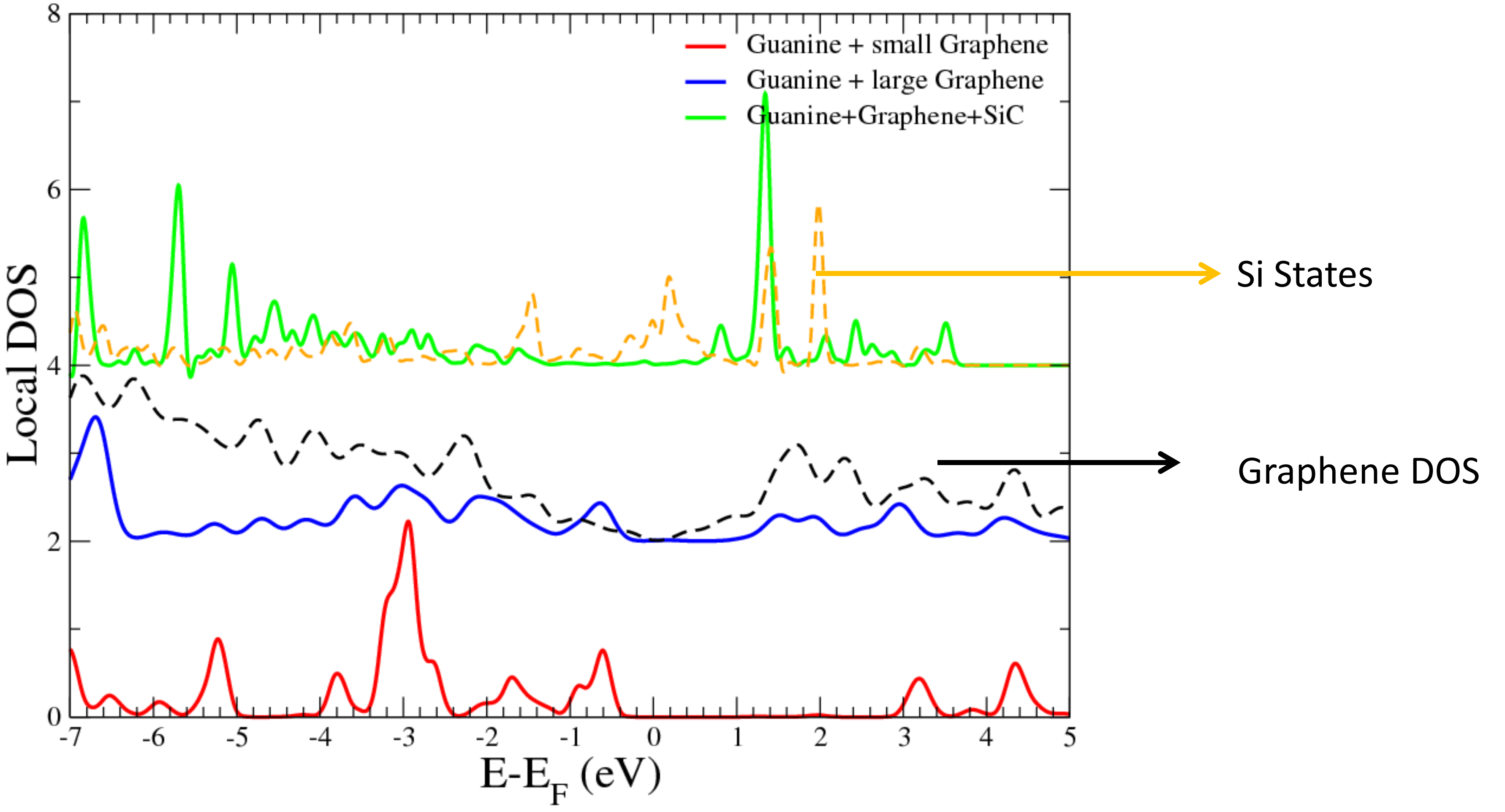




DNA/graphene with SiC Substrate



Nitrogen L-DOS on Guanine



Summary (Part 1):

The calculated **LDOS** fingerprints can help guide **STS** as an approach to identify DNA bases, and likely other biomolecules on graphene surfaces.

NANO LETTERS

Letter

pubs.acs.org/NanoLett

Electronic Fingerprints of DNA Bases on Graphene

Towfiq Ahmed,[*,†] Svetlana Kilina,[‡] Tanmoy Das,[§] Jason T. Haraldsen,[§,∥] John J. Rehr,[†] and Alexander V. Balatsky[*,§,∥]

[†]Department of Physics, University of Washington, Seattle Washington 98195, United States

[‡]Department of Chemistry and Biochemistry, North Dakota State University, Fargo, North Dakota 58108, United States

[§]Theoretical Division and [∥]Center for Integrated Nanotechnologies, Los Alamos National Laboratory, Los Alamos, New Mexico 87545, United States

S *Supporting Information*

Part-2:

Single base DNA Finger Printing with Graphene Nanopores using Transverse current Spectroscopy

Why Graphene Nanopore?

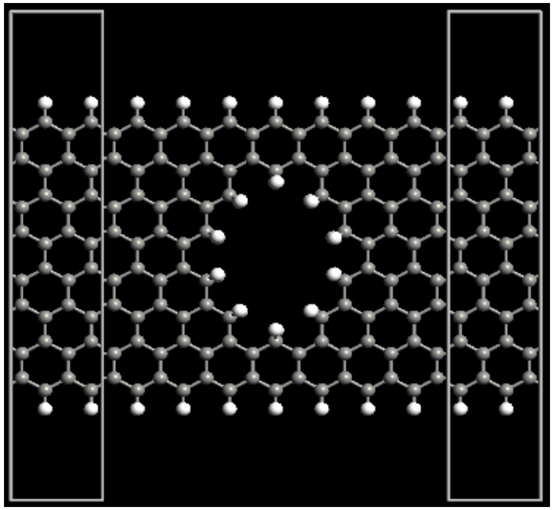
- **Robust Electro Mechanical Properties**

  150 Million psi tensile modulus

  (Lee C *et al.* Science 321 2008)

- **Single Atomic Thickness**

- **Commercial availability and reproducibility of High Quality Graphene Membranes**



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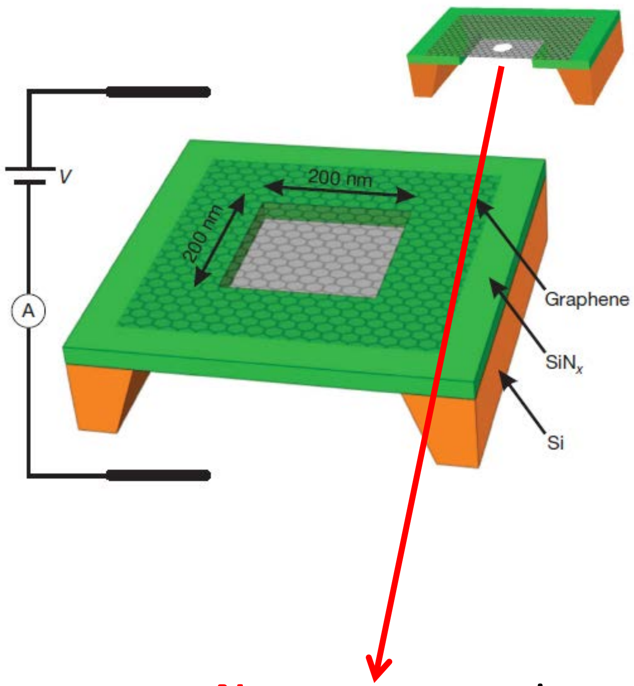
Graphene: A Nano-scale Trans-electrode Membrane



Nanopore experimental preperation by Branton Lab

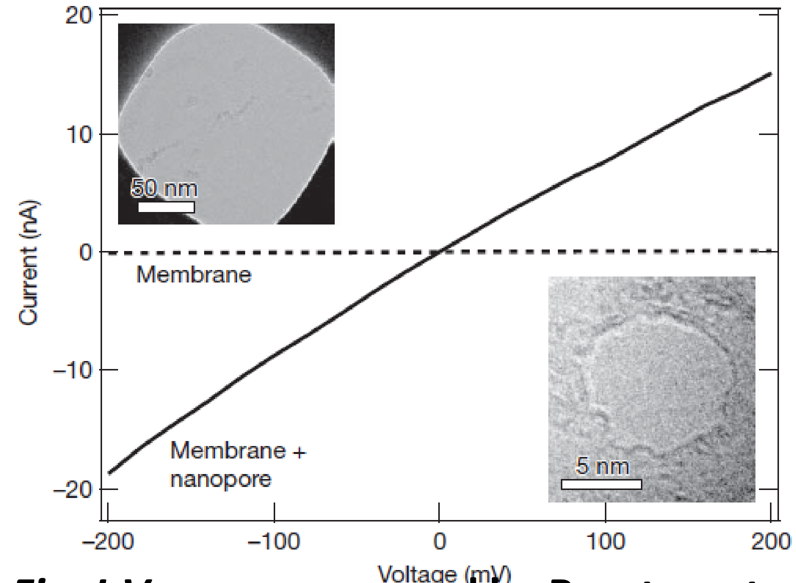


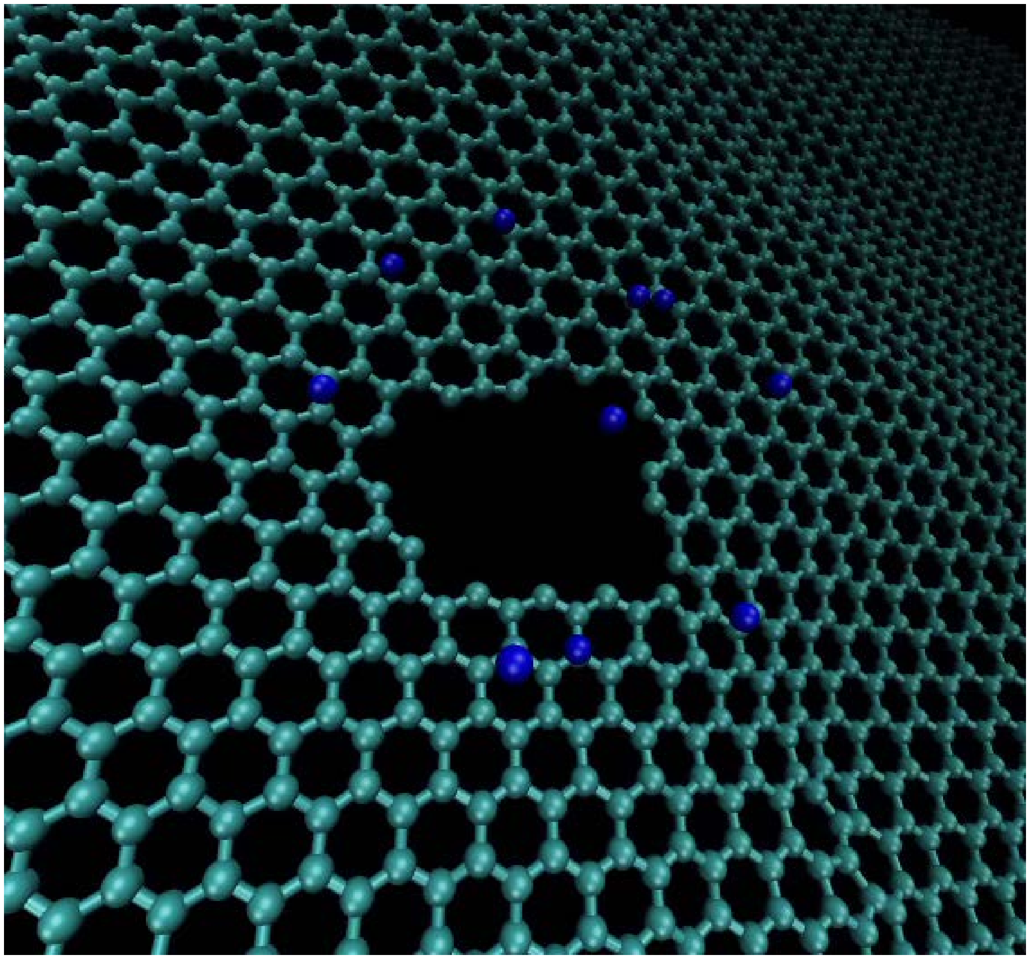
Fig. I-V **curve measured by Branton *et al.* Nanopore on graphene shows conducting behavior in contrast with pure membrane (dashed line)[1]**

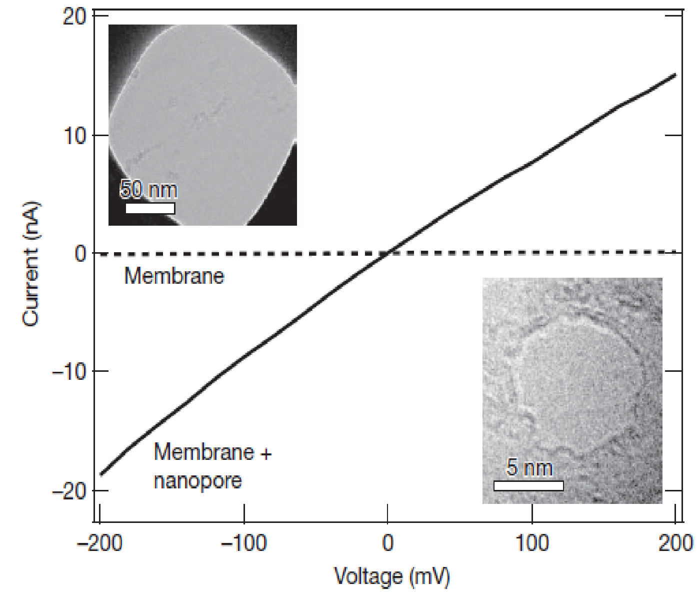
REF: [1] Garaj, S., et al, Graphene as a sub-nanometre transelectrode membrane. ***Nature*** **467: 190-194 (2010).**

M. Drndic Nature Nano 2012

Healing of the Nanopore,

K Zakharchenko, Nordita





Computational Details

- *Ab initio (LDA)* calculation of ***T(E)*** **and Current** using NEGF method.

$$I = \frac{e}{h}\int_{-\infty}^{\infty} T(E)[n_F(E-\mu_L) - n_F(E-\mu_R)]dE$$

- k_x=1, k_y=1, k_z=100
- Approx. ~ 200 atoms per unit cell

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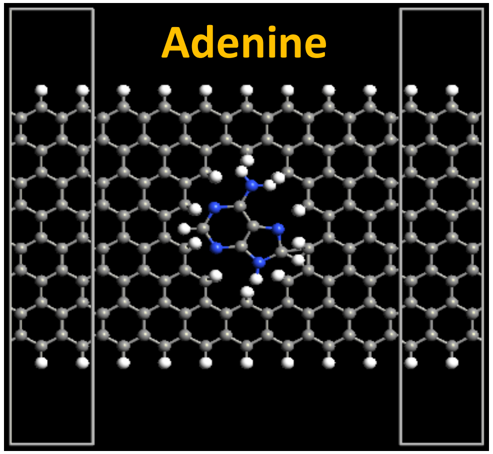
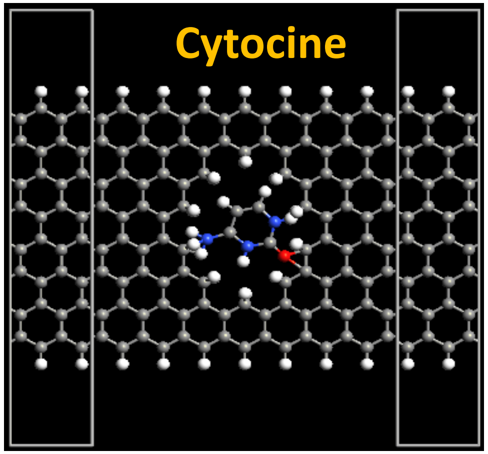
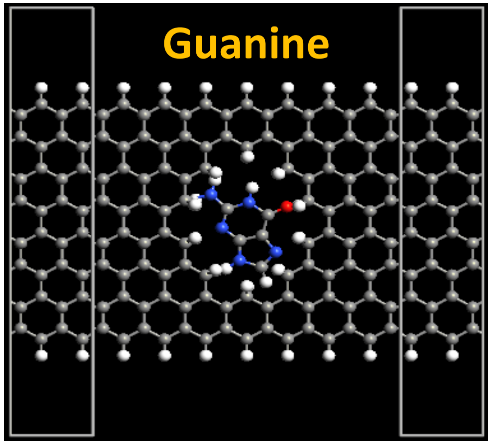
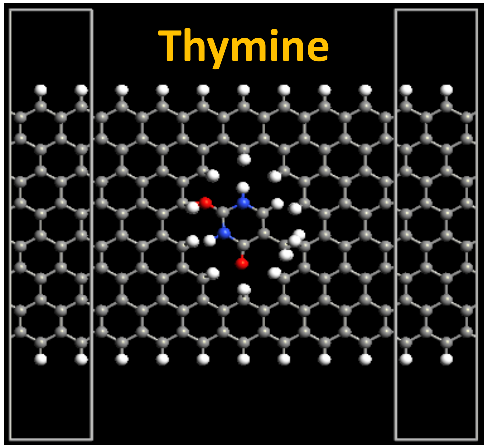
Single DNA Base in Nanopore









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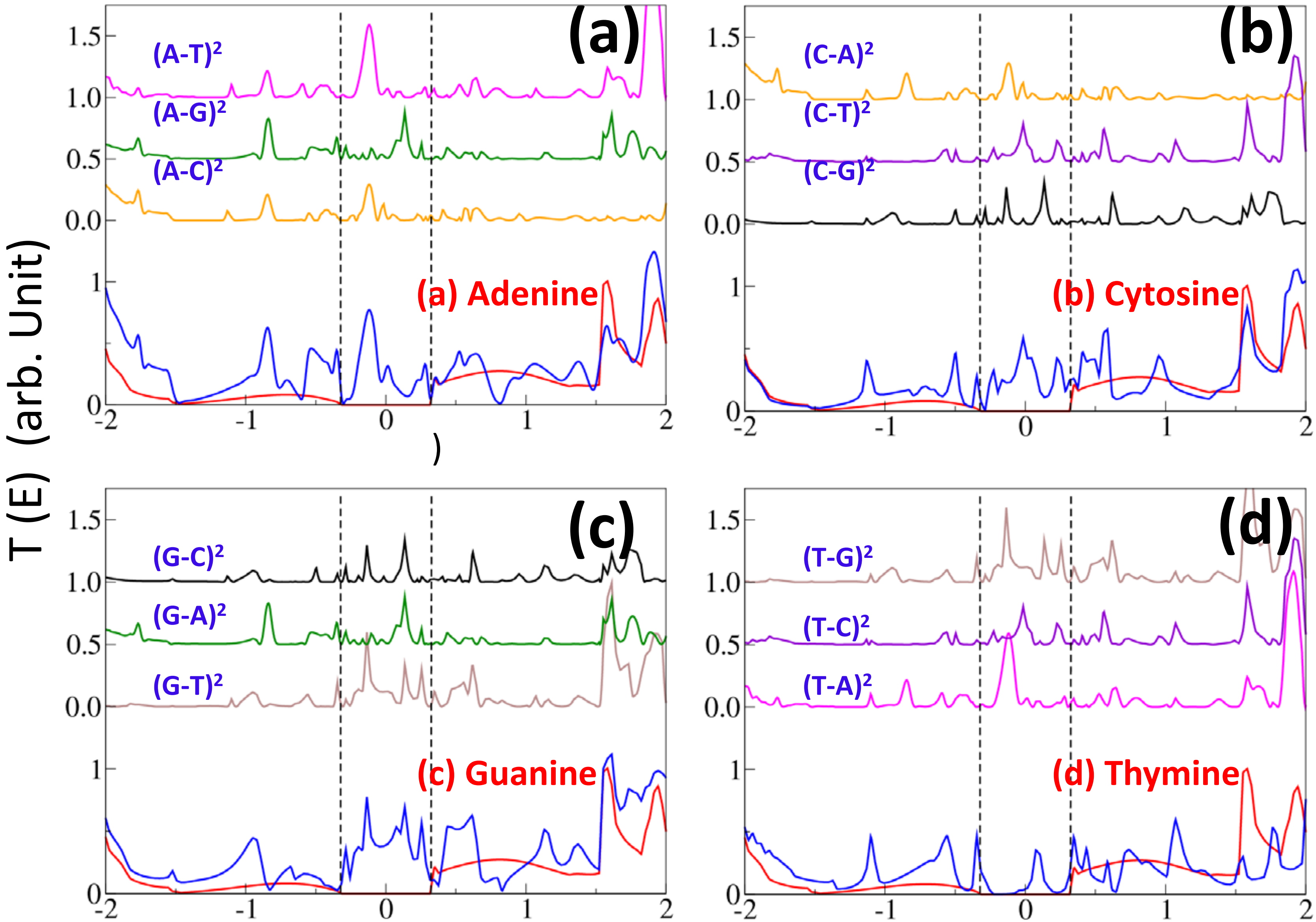
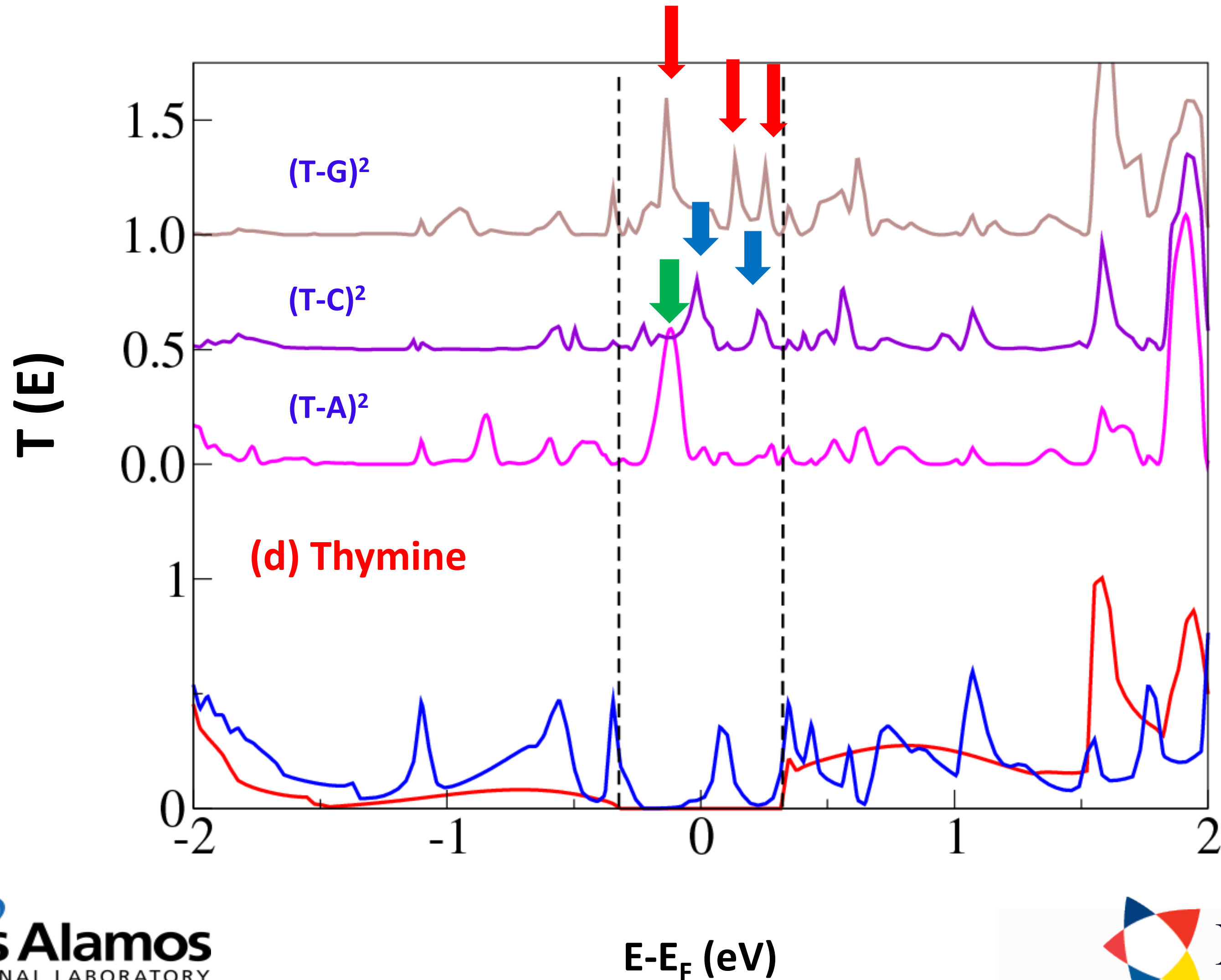
Tranmission Coefficient for Differentiating DNA bases



Transmission Coefficient for Thymine



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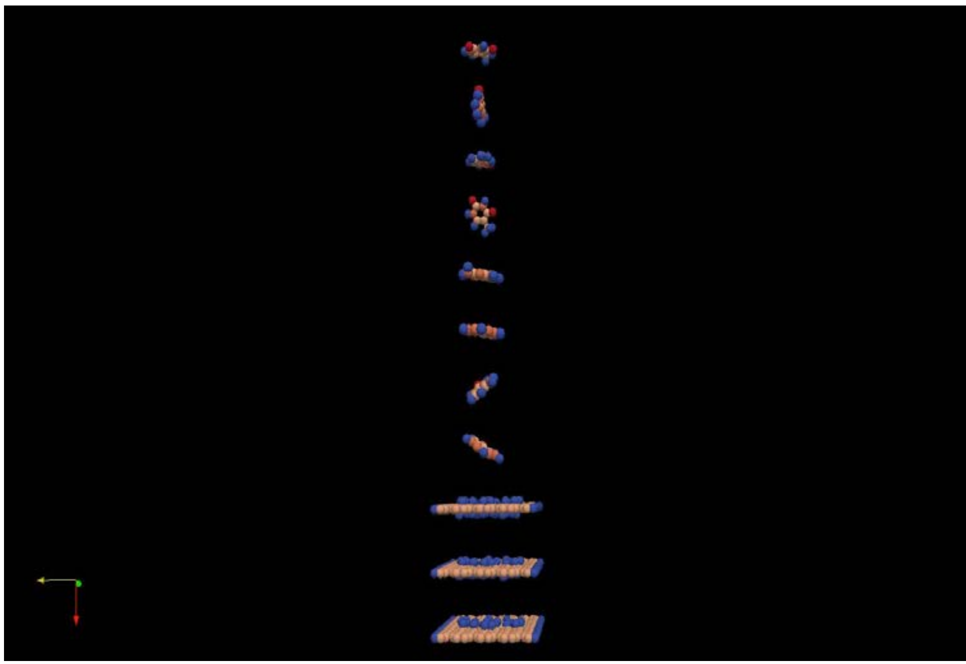
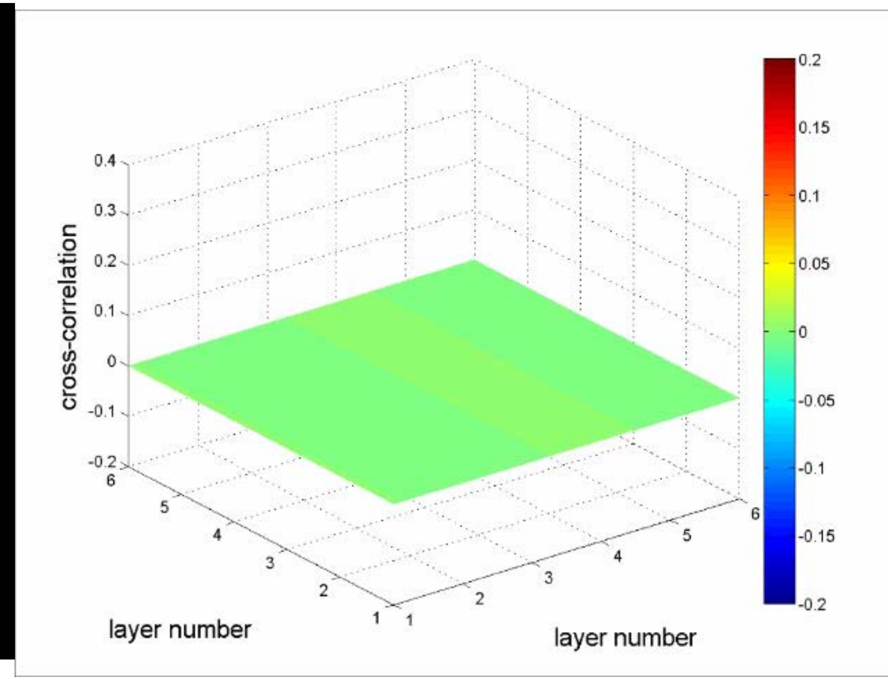
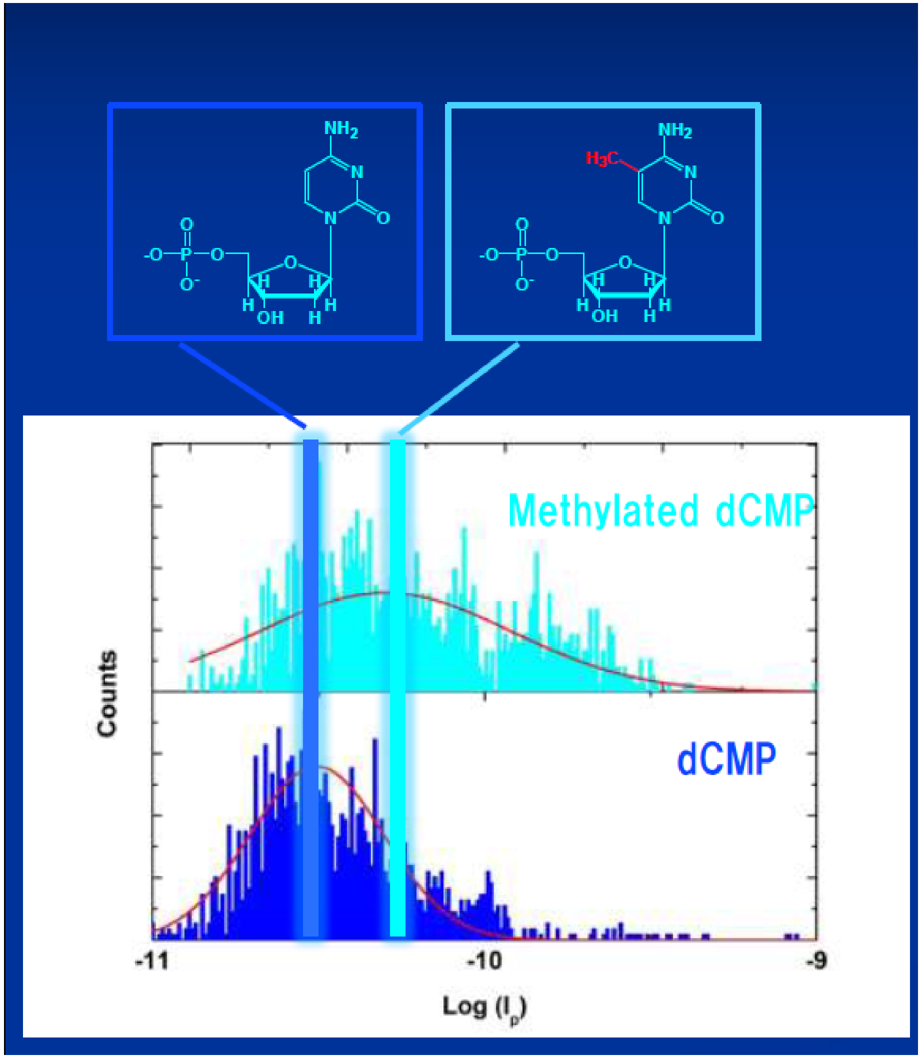
Whats Next ?

Correlation Dynamics of 6 graphene layers:
A QUALITATIVE ANALYSIS





Future plans:Detection of methylated bases ?



Taniguchi, Kawai
Osaka Univ
Nature Asia review 2012

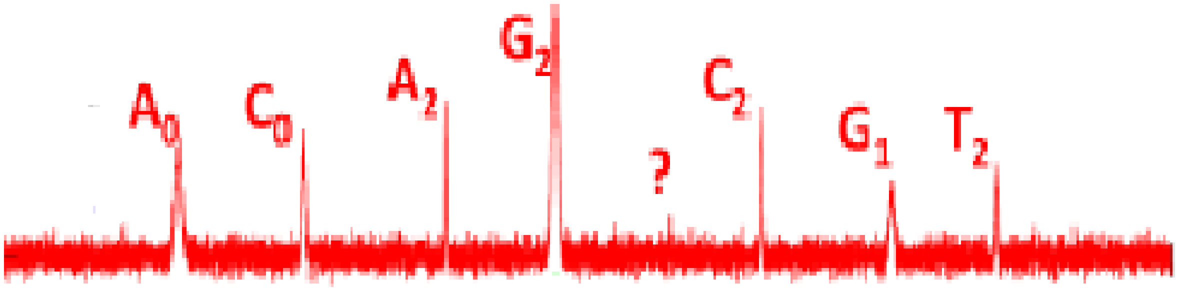
How to increase Signal-to-Noise ?

Measurable in EXPERIMENTS

Current Spectrum:

$$I = \frac{e}{h}\int_{-\infty}^{\infty} T(E)[n_F(E-\mu_L) - n_F(E-\mu_R)]dE.$$

Test Sequence: $A_0C_0A_2G_2T_1C_2G_1T_2$



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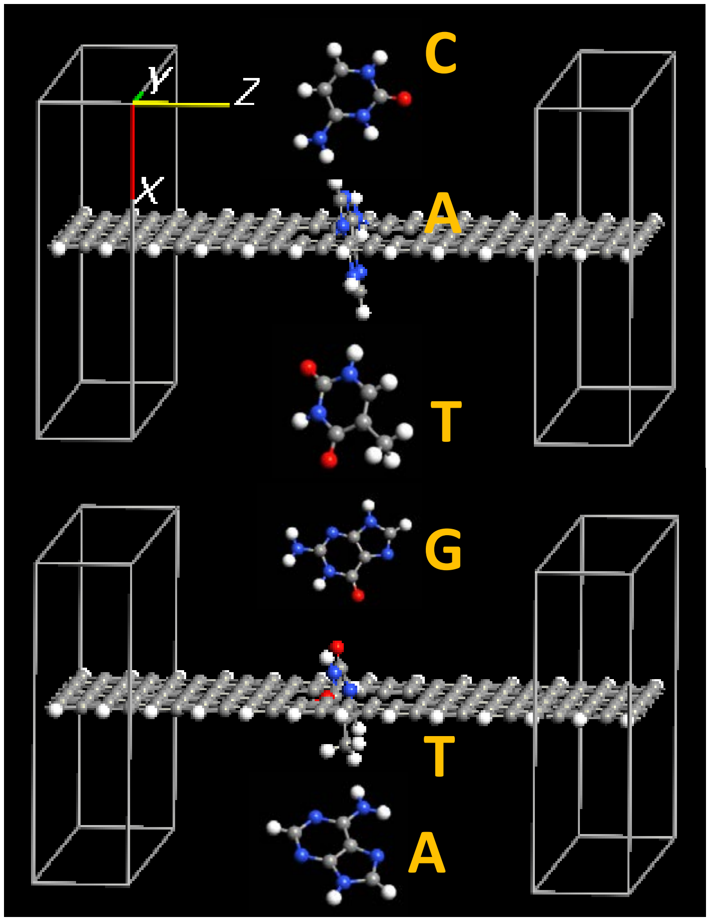
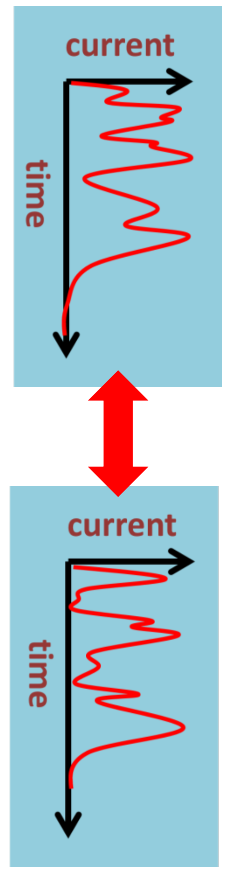
What are the sources of noise ?





Source of NOISE:

Configuration Noise:

- **Fluctuation in backbone Configuration**

Apparatus Noise:

- **Johnson-Nyquist Type Noise**

H. Nyquist Phys. Rev. 32, 110 (1928)

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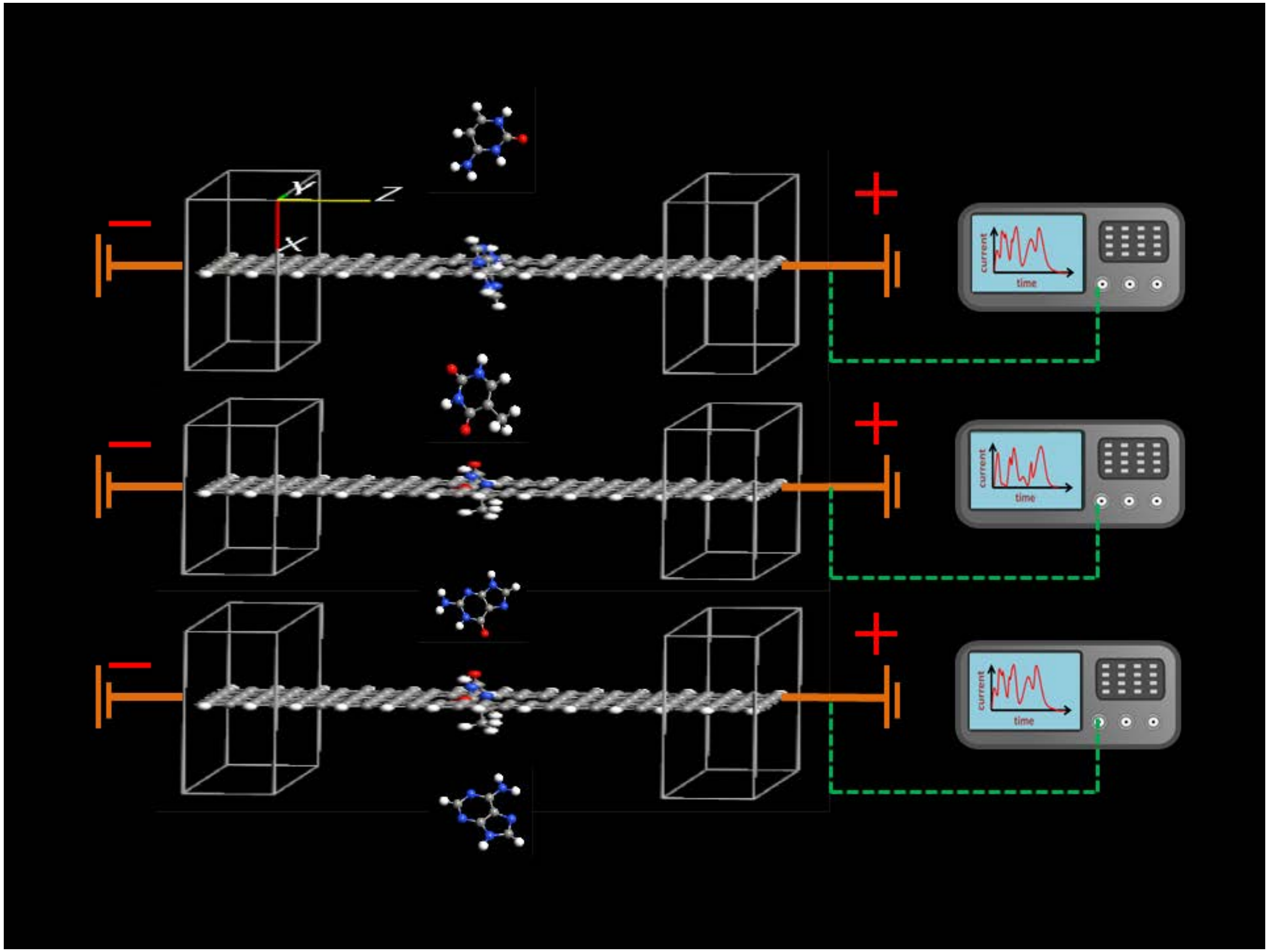
Proposed Device Configuration (Schematic):



Cross-correlation of Signals

Layer-1: $I^1(t) = I_S^1(t) + I_N^1(t)$

Layer-2: $I^2(t) = I_S^2(t) + I_N^2(t)$

$$\langle I^1 \otimes I^2 \rangle = \langle I_S^1 \otimes I_S^2 \rangle + \underbrace{\langle I_S^1 \otimes I_N^2 \rangle + \langle I_N^1 \otimes I_S^2 \rangle + \langle I_N^1 \otimes I_N^2 \rangle}_{\text{small}}$$

small

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Simulation Parameters:

- $I_N(t)$ = Gaussian White Noise
- Average time Interval between Bases = 1 ms
- Average travel time between Membranes = 0.2 ms

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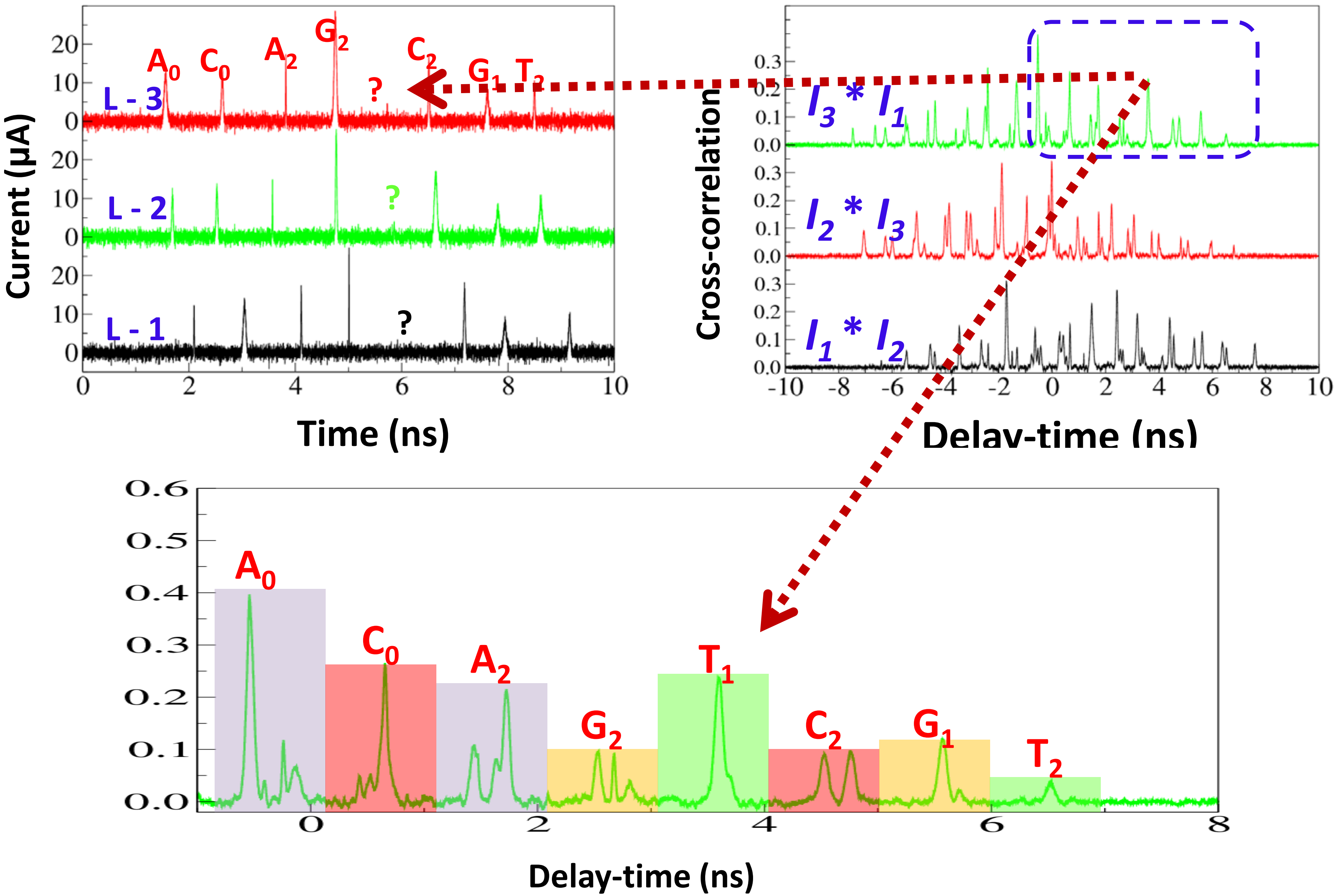
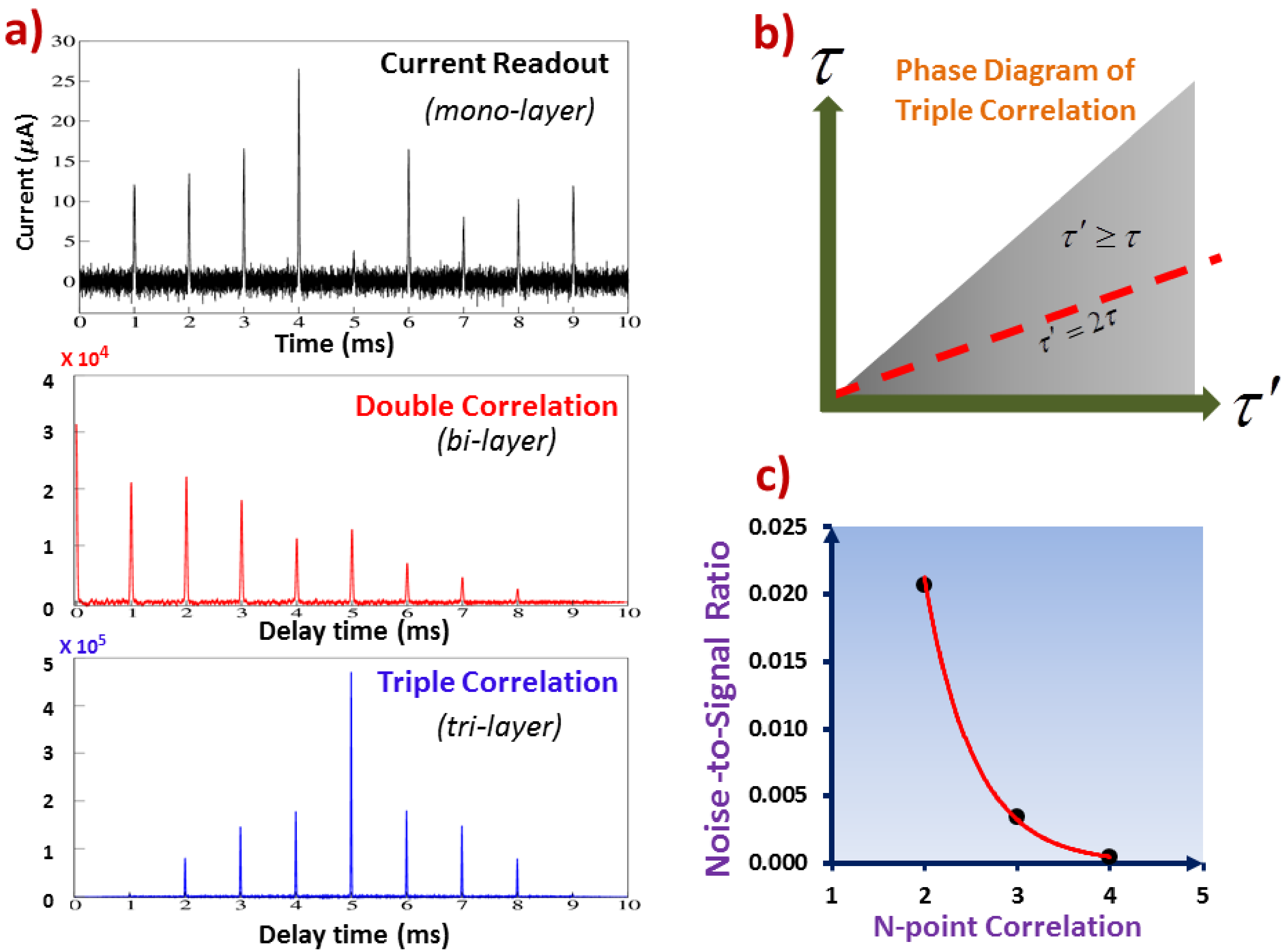
Cross-correlation Recovers Signals



Multipoint Cross-correlation



References

- S. Kilina et al, JPC (C) v111, p14541 (2007)
- D. Yarotski et al, Nano. Lett v9, p 12 (2009)
- T. Ahmed et al, Electronic fingeprints of DNA bases on Graphene, Nano Lett. 12, 927-931 (2012) DOI: 10.1021/nl2039315
- T. Ahmed et al, in preparation
- K. Zacharchenko, in preparation

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U.S. DEPARTMENT OF ENERGY
NORDITA
UNIVERSITY OF CALIFORNIA SAN DIEGO

Conclusions

- ***STM combined with modelling offers a potential for DNA sequencing and *visualization* of nano-bio interfaces***

- ***If we can handle single photon, electron charge and single spin ->***

we can handle single quantum of bio information: DNA and other molecules imaging and sequencing, ultimately imaging "functionality"

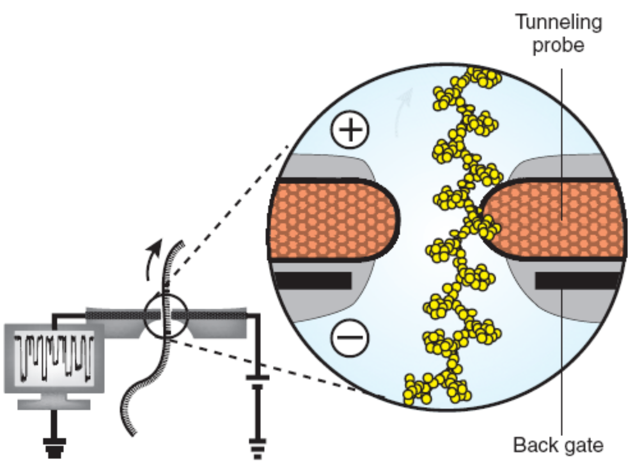
- ***Field is at the exponential growth of physics based sequencing methods (Moore 2.0)***

- ***Due to: computational power exponential scale up, proliferation of accessible local probes that extract very local information***
- ***Interaction between the DNA-base and Cu(111), Graphene surface:***
  - Reliable prediction of electronic signatures of DNA bases *physisorbed* (weak interaction) or *chemisorbed* (strong interaction through dipole) on the metal surface
  - LDOS of Guanine is unique enough to allow DNA partial sequencing with STM
  - Next: multipore electronics, direct imaging gene defects.

Thank You

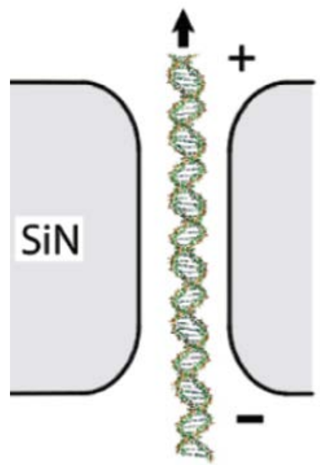
Electrical DNA Sequencing in Nanopores

idea

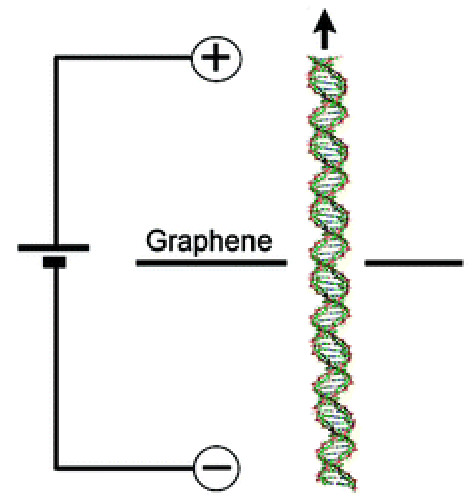


adapted from D. Branton *et al.*,
Nature Biotechnology 10, 1146 (2008)

problem



solution?



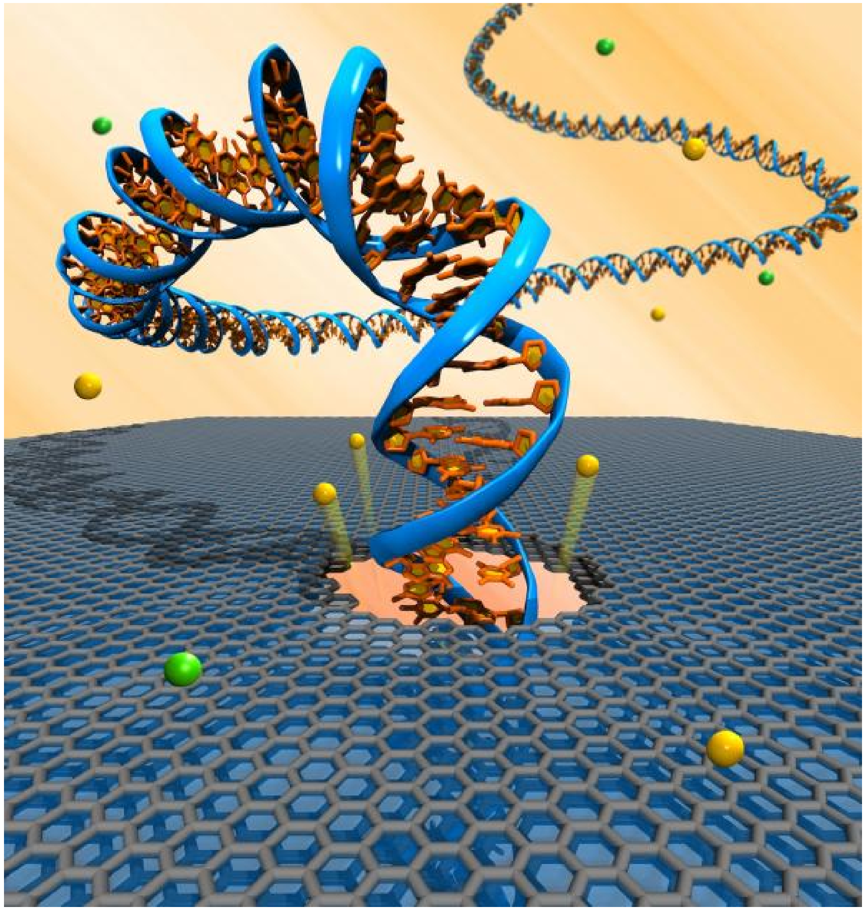
adapted from G. F. Schneider *et al.*,
Nano Letters 10, 3163 (2010)

pull DNA through a nanopore and read sequence as tunneling current signal from embedded electrodes

deep nanopore channels make it hard to achieve single-nucleobase resolution

graphene is as thin as it gets and nanopores can be fabricated by removing carbon atoms with an electron beam

DNA Translocation through Graphene Nanopore



University of Pennsylvania researchers developed a carbon-based, nanoscale platform to electrically detect single DNA molecules. Electric fields push tiny DNA strands through atomically-thin graphene nanopores that ultimately may sequence DNA bases by their unique electrical signature. (Credit: Robert Johnson)

http://www.sciencedaily.com/releases/2010/07/100726124418.htm

Summary (Part-2)

- Cross-correlation analysis for multilayered graphene nanopores enhances signal-to-noise ratio and therefore increases the **accuracy** of DNA fingerprinting techniques in fast nanopore devices.

Correlation dynamics for DNA sequencing in multi-layer graphene nanopores

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