ASU BIODESIGN INSTITUTE
ARIZONA STATE UNIVERSITY

Single-molecule Nanoscience in the Center for Single Molecule Biophysics

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AINE Launch Meeting, April 4, 2008

Single Molecule Measurements

- Get away from ensemble averages
- Cheaper, better, faster at the nanoscale

1. Overview of Center
2. Make anything nano you want with DNA
3. Molecular electronic approach to DNA sequencing

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Center for Single Molecule Biophysics

Hao Yan

Self assembly, DNA nanotechnolgy

- **Make**

Peiming Zhang

Bioconjugate and surface chemistry

Stuart Lindsay

Scanning probe

- **Measure**

Marcia Levitus

Single molecule optics

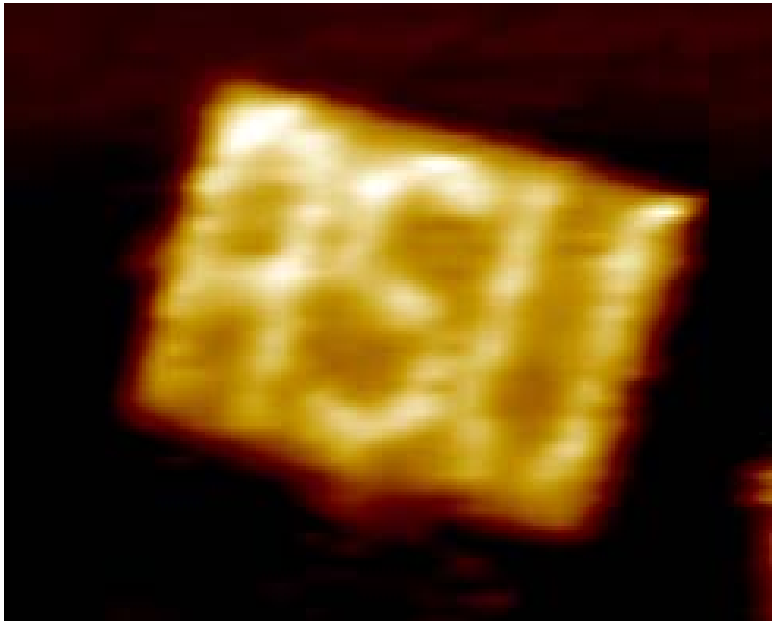
Michael Thorpe

Theory and modeling

- **Model**

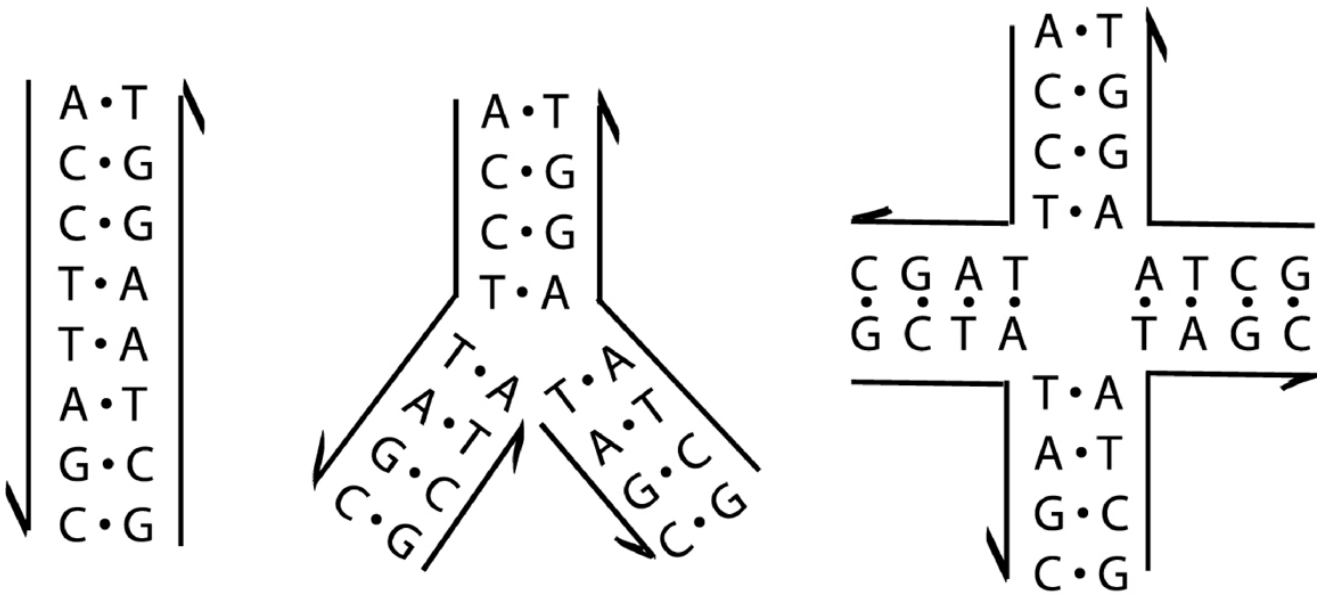
Making Nano things with DNA

Hao Yan (Hao.Yan@asu.edu)

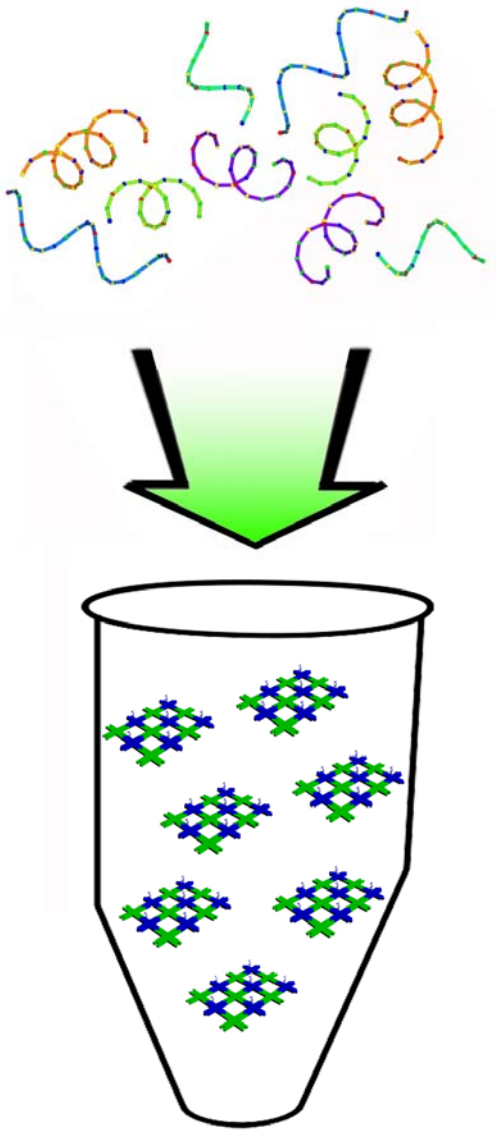


Functional Nanostructures from DNA self-assembly:

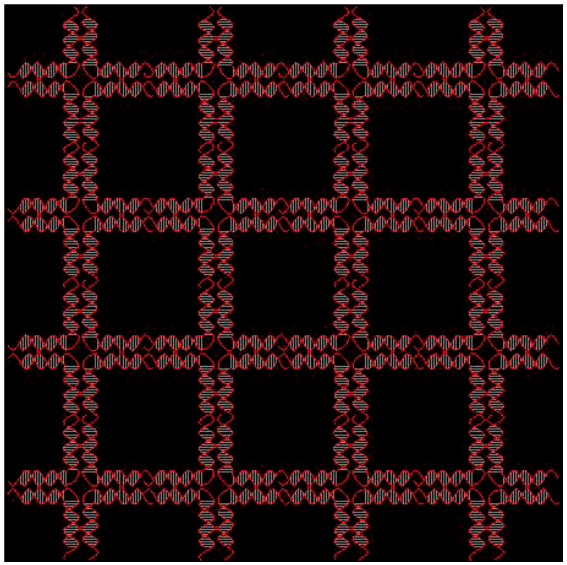
Addressable assembly



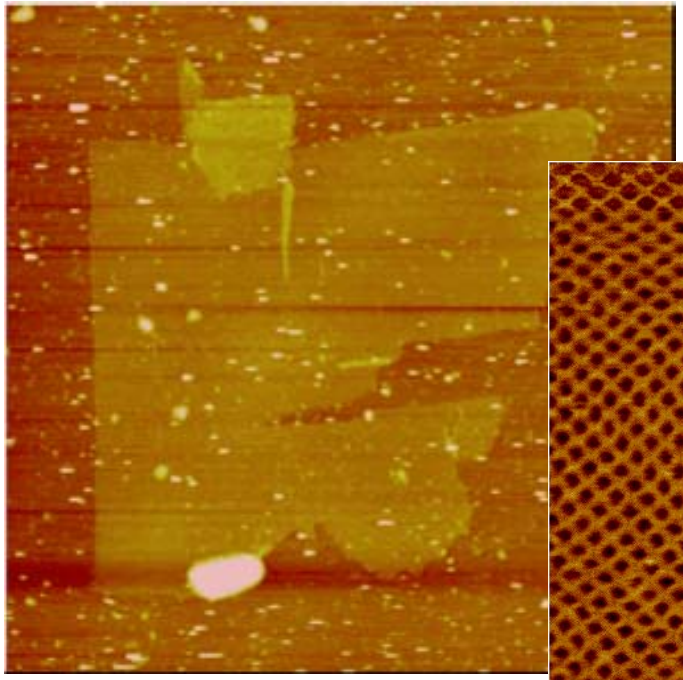
Nanofab in a test tube



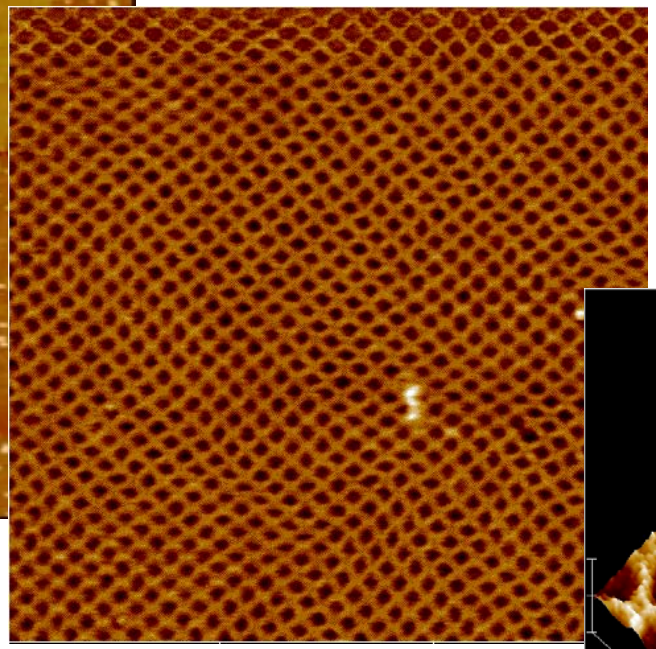
Self-assembly



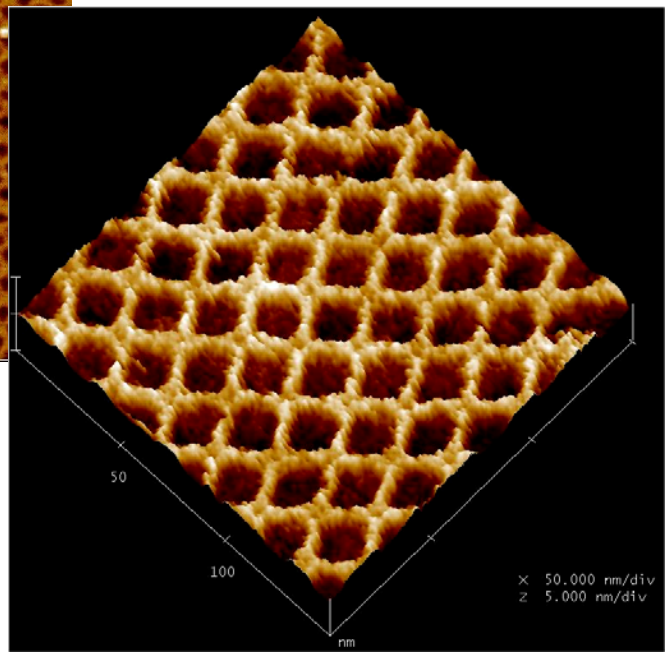
AFM images of the nanoarrays



10x10 um



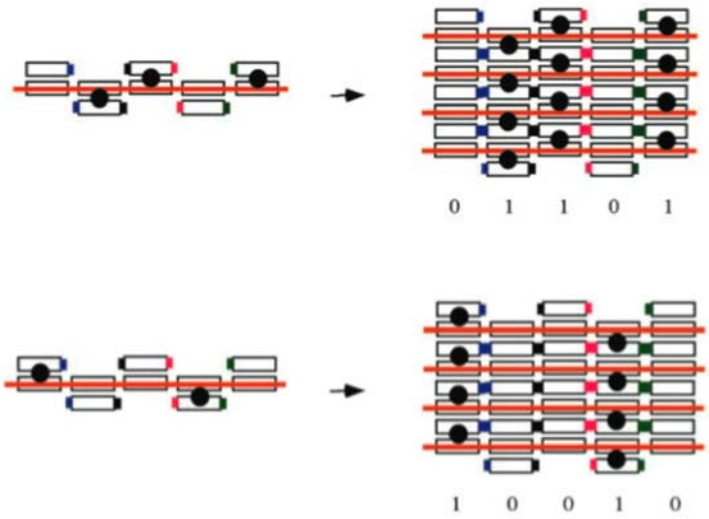
600x600 nm

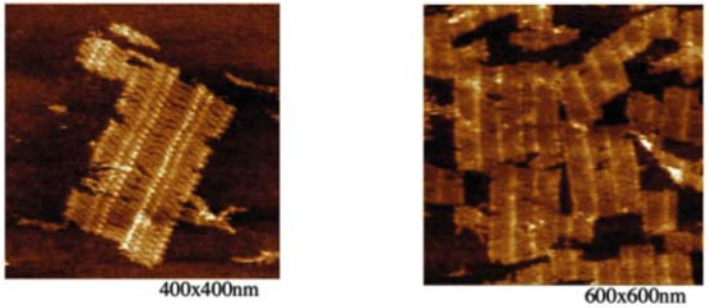


150x150 nm

Yan *et al.* ***Science*** 301, 1882-1884 (2003).

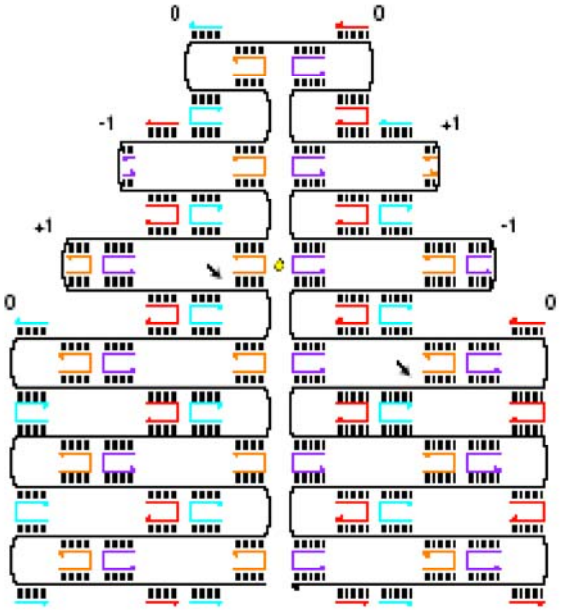
Nucleated self-assembly of Barcode Nanoarrays

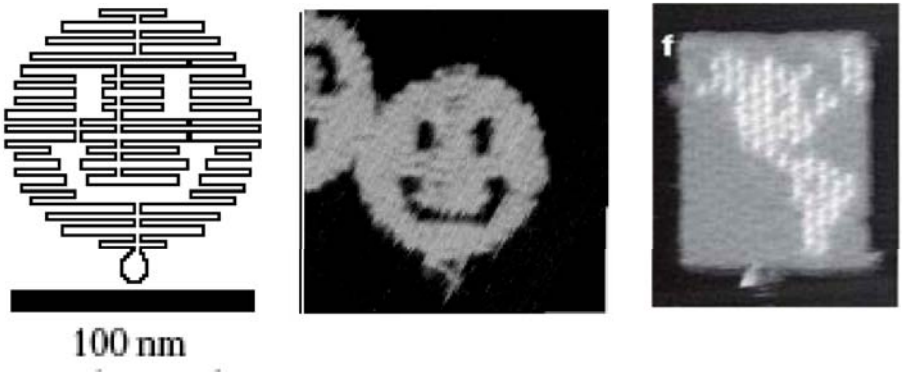




Yan *et al*. ***PNAS*** *100, 8103-8108* (2003).

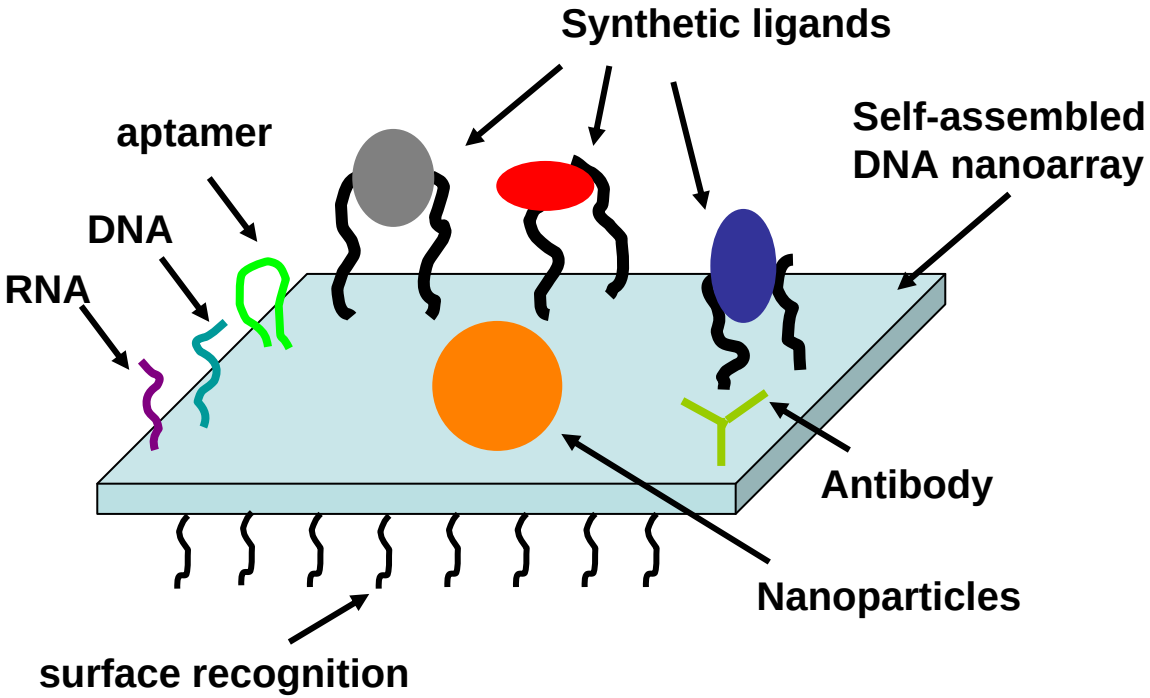
Scaffolded DNA Origami





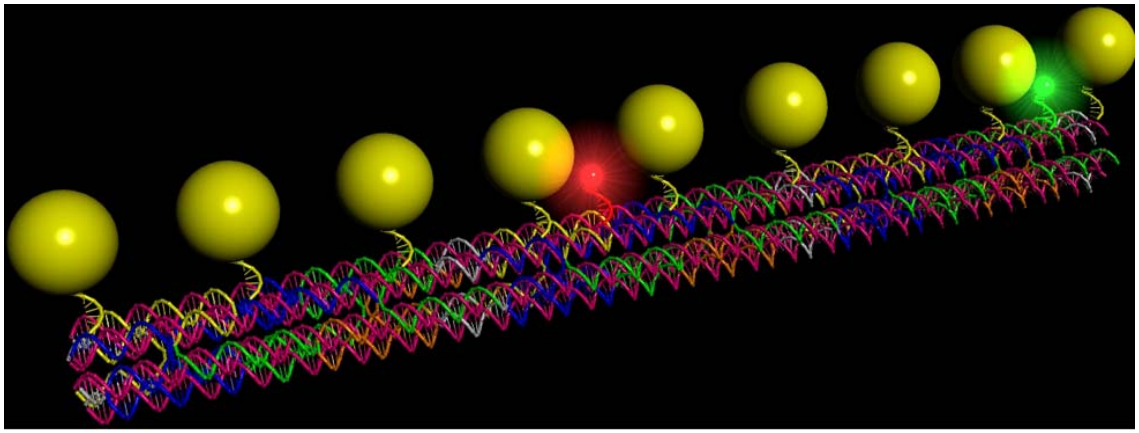
Rothemund, ***Nature,*** 440, 297-302 (2006)

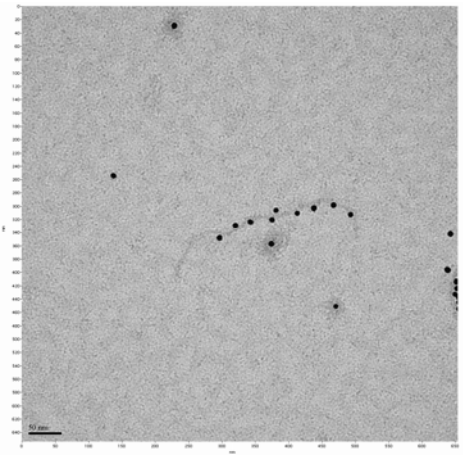
Directed self-assembly: use of self-assembled DNA nanostructures as scaffolds

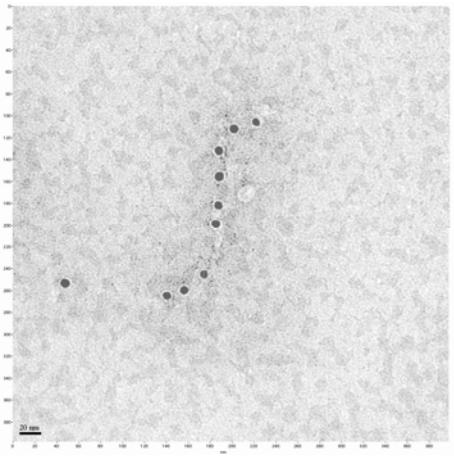


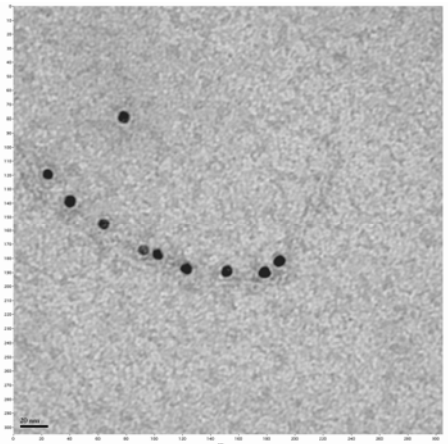
Implication: higher order complex nanostructures through self-assembly

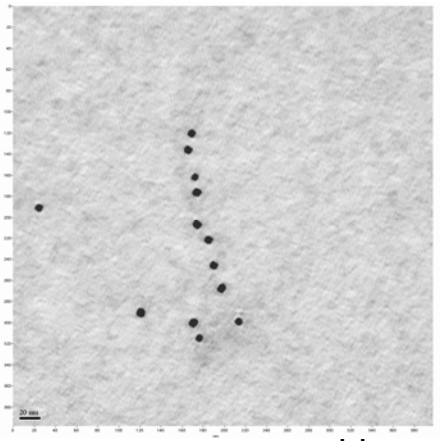
Self-assembled Photonics



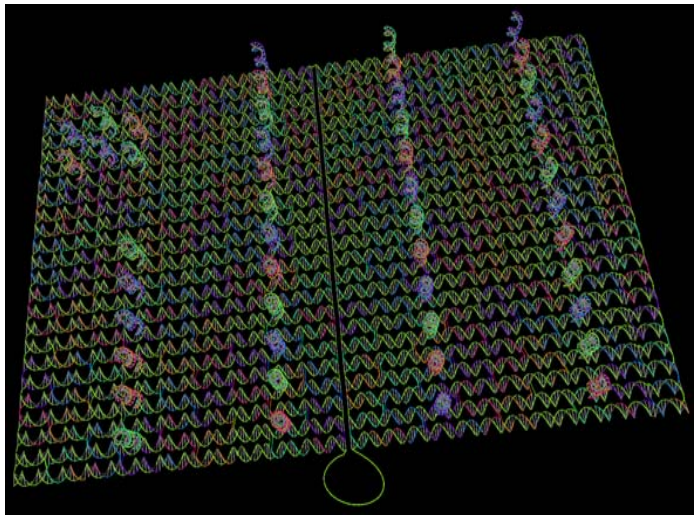


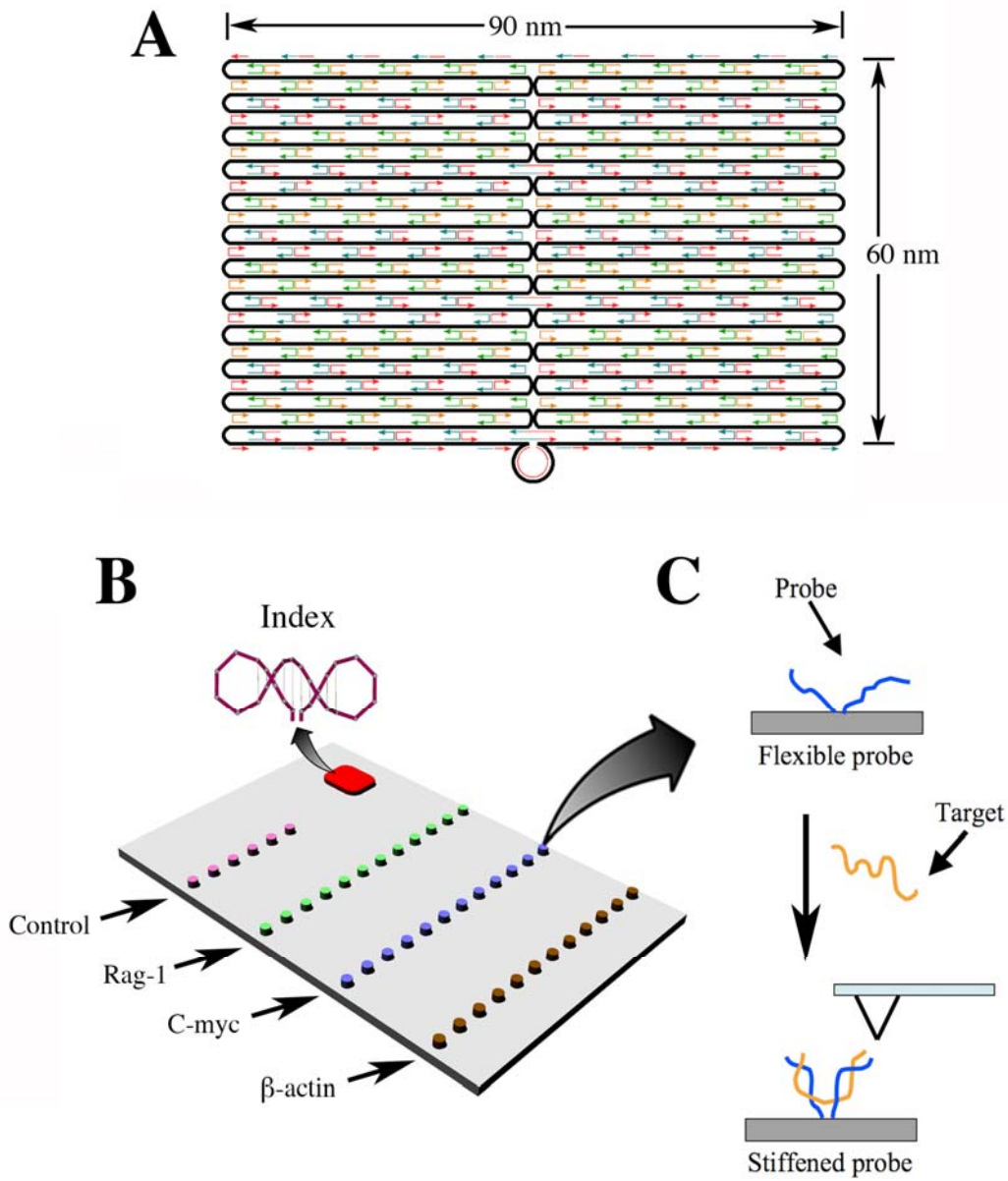






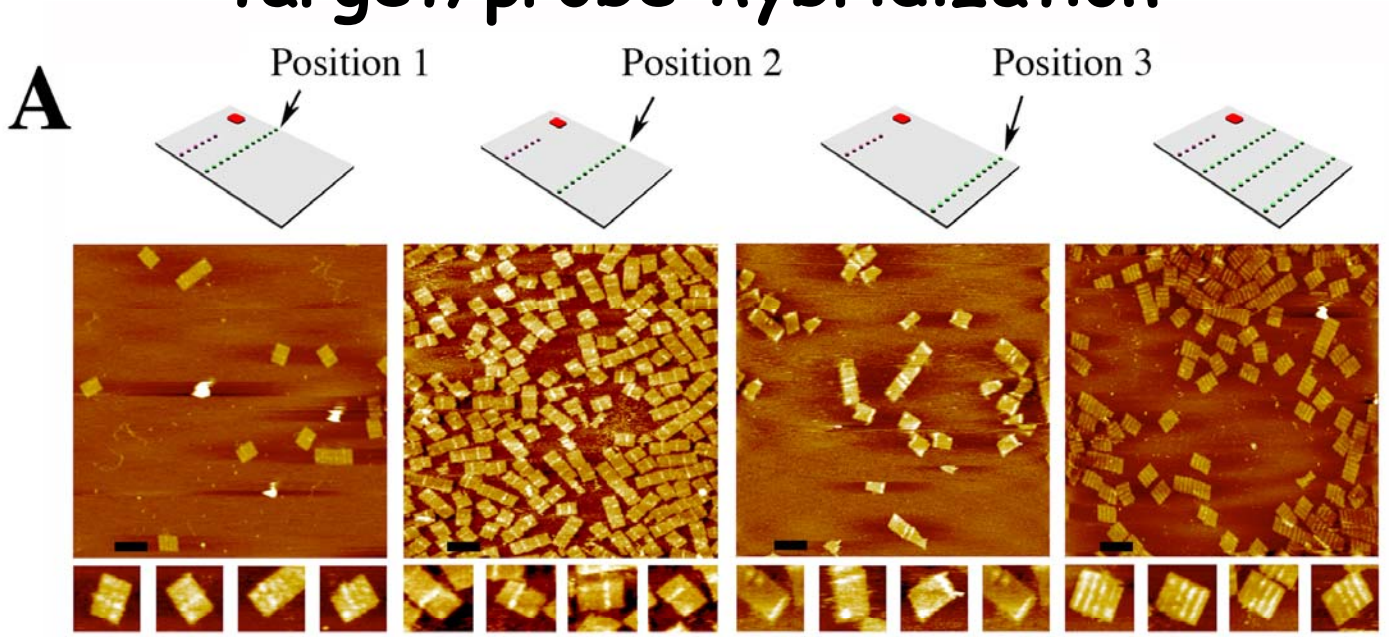
Hybridization arrays for use in solution

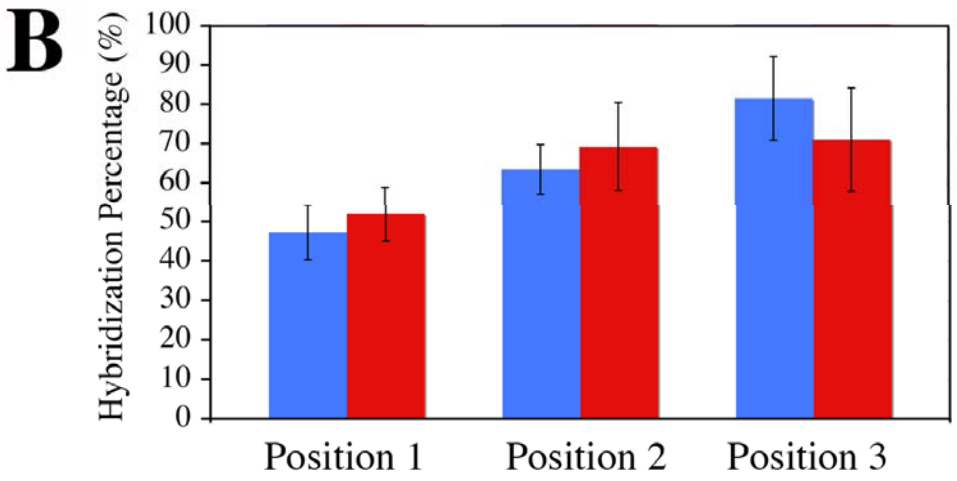




Ke, Lindsay, Chang, Liu & Yan *Science 319 180 2008*

Nanoscale position effect on target/probe hybridization

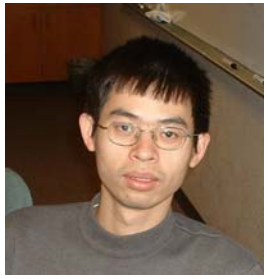




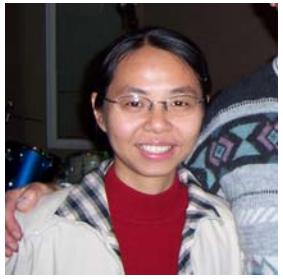
Red – all 3 probes
Blue – one at a time

Science **319** 180-183 (2008)

Molecular Electronic approach to DNA sequencing



Jin He



Lisha Lin

Peiming Zhang

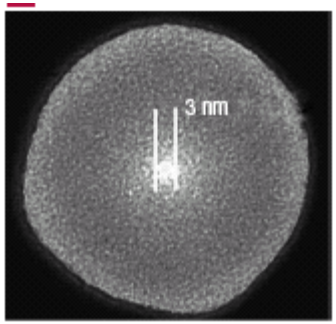
Single Molecule Readout Scheme for a Nanopore

Why limited read lengths are a problem

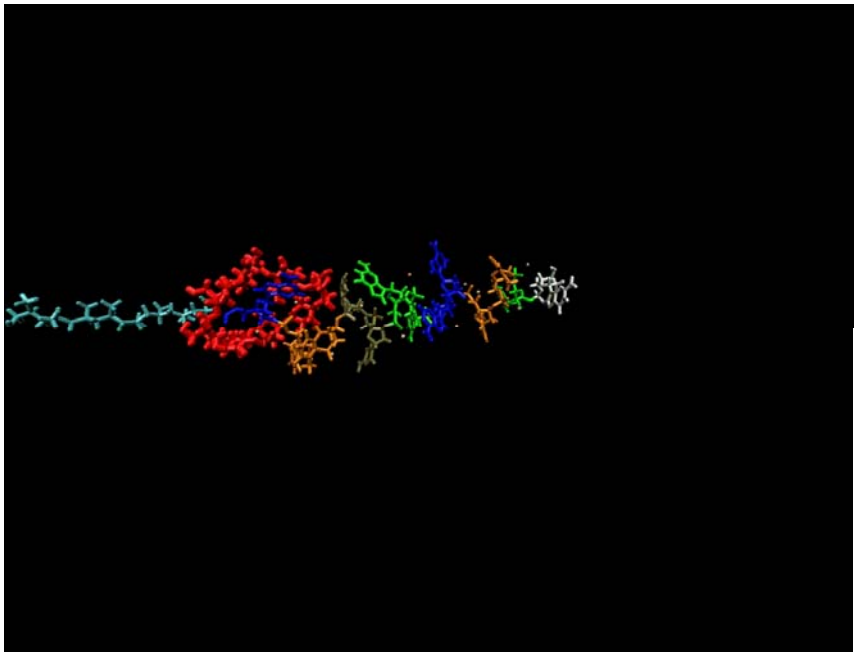
- Copy number variation
- Inversions
- Deletions
- Tandem repeats
- Genomic instability

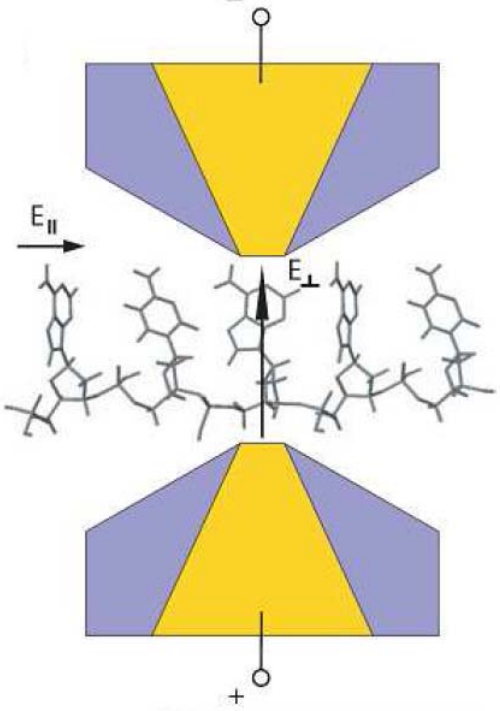
- **Genomic length reads?**
- **Fast, cheap reads?**
- **Single molecule reads?**

The Nanopore



Li et al. Nature Matl. **2** 611, 2003

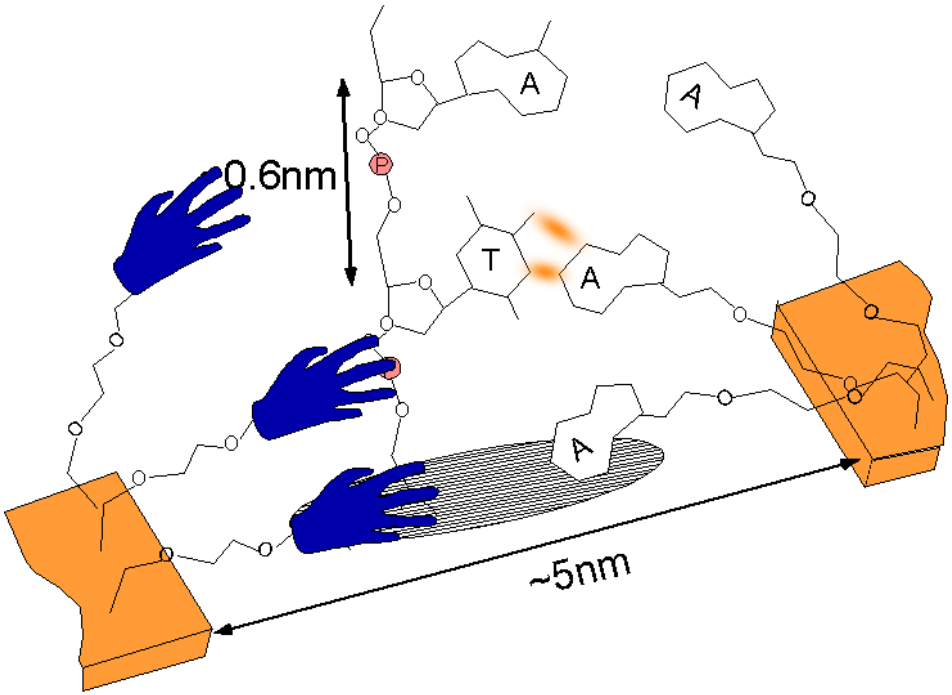




Zwolak and DiVentra, Rev. Mod. Phys. In press

- Ion Blockade readout
- Tunneling readout
- Capacitance readout
- Force readout

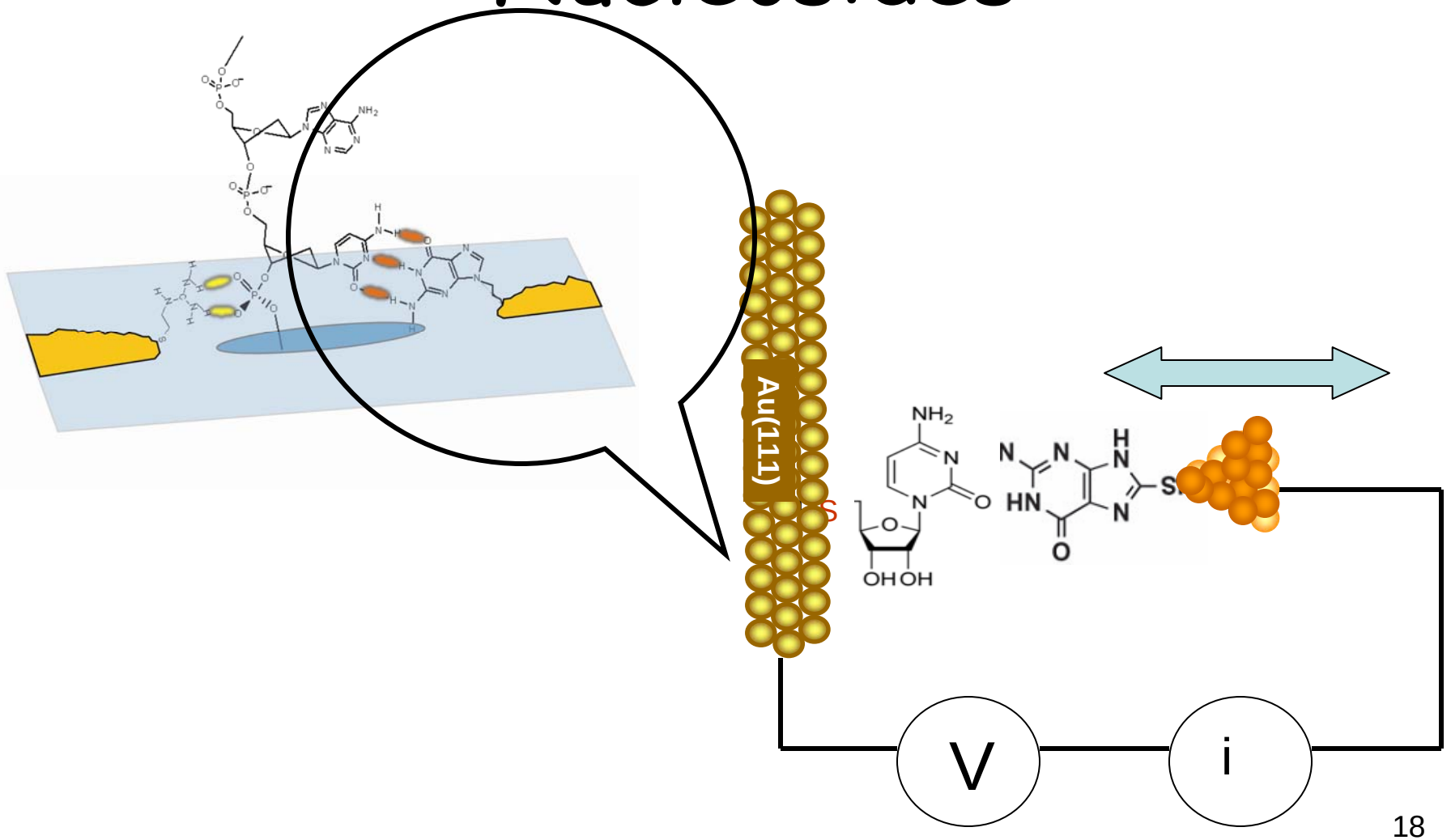
Elements of a Recognition Reader



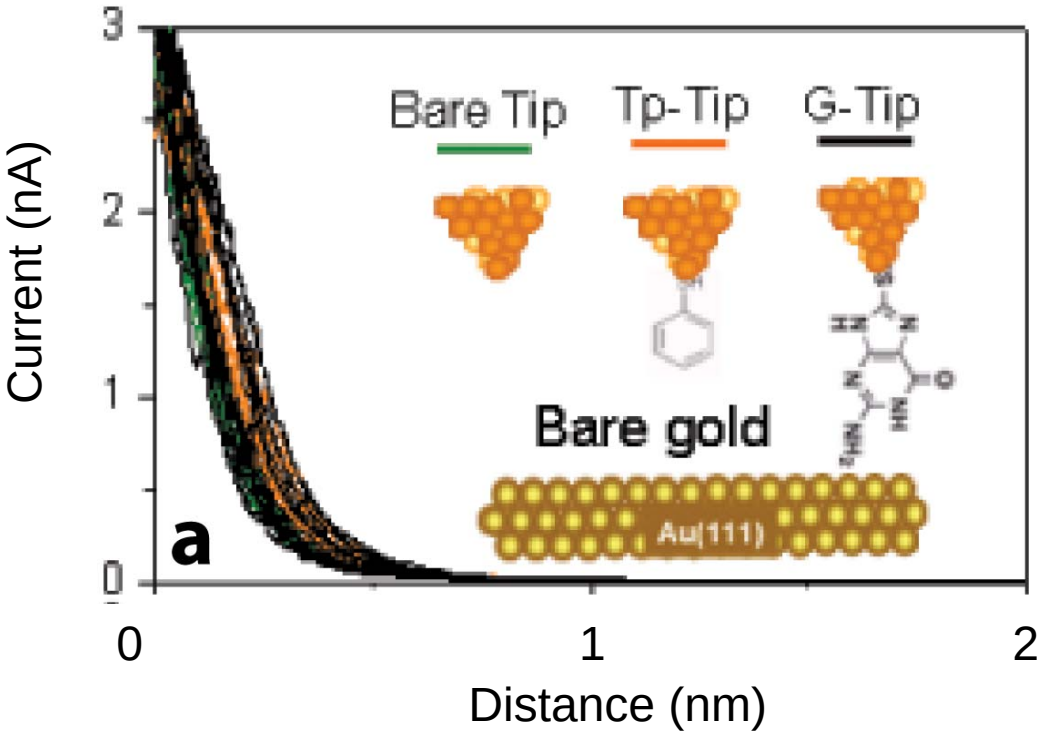
- Nanopore or nanochannel
- Base Reader
- Molecular Wires
- "Phosphate grabber"

- Can get desired S/N with G>0.1nS?
- Parallel read out for enhanced fidelity/ assembly

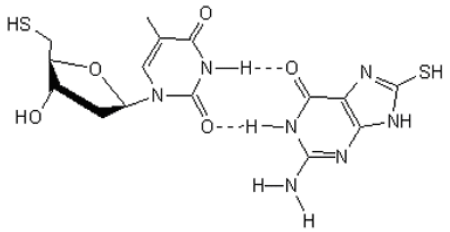
Reading the Bases: STM of Nucleosides

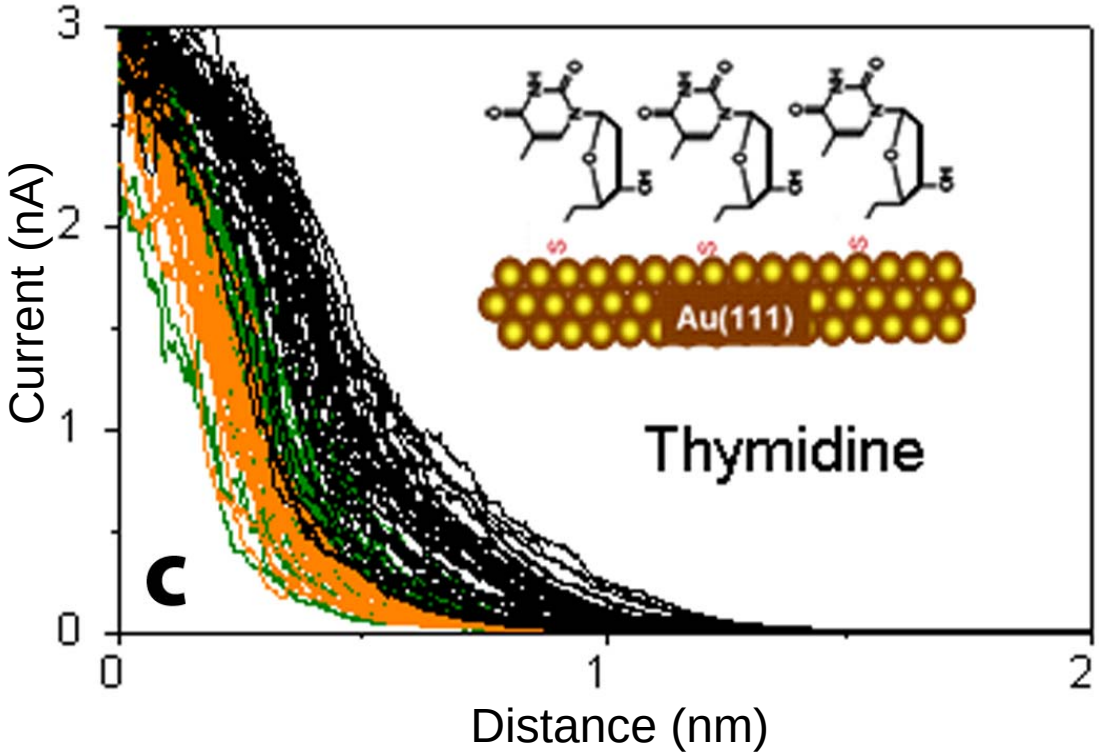


STM of Nucleosides (a) Controls

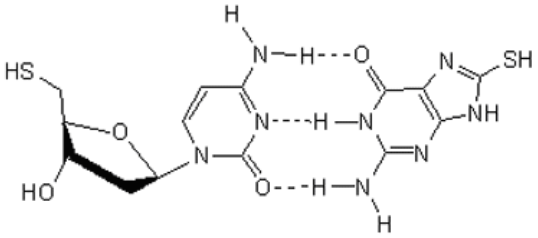


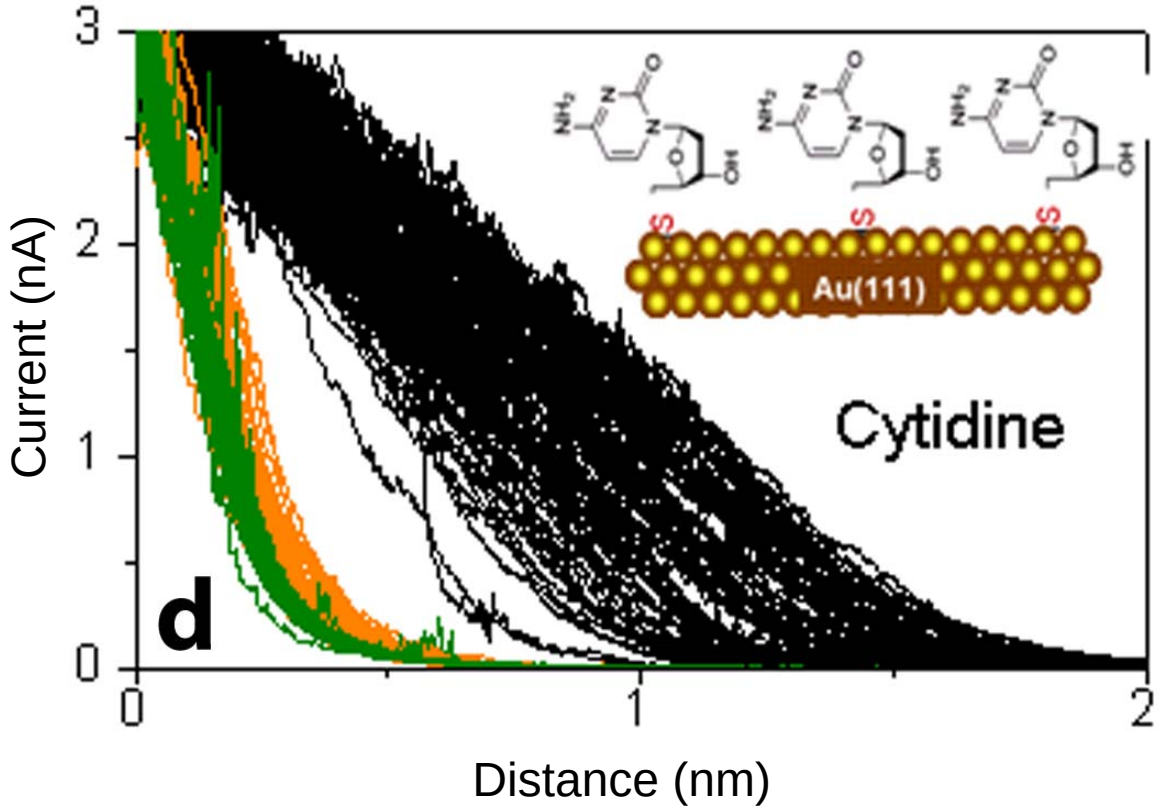
STM of Nucleosides (b) G-T Wobble base-pairing





STM of Nucleosides (b) G-C Watson-Crick base-pairing



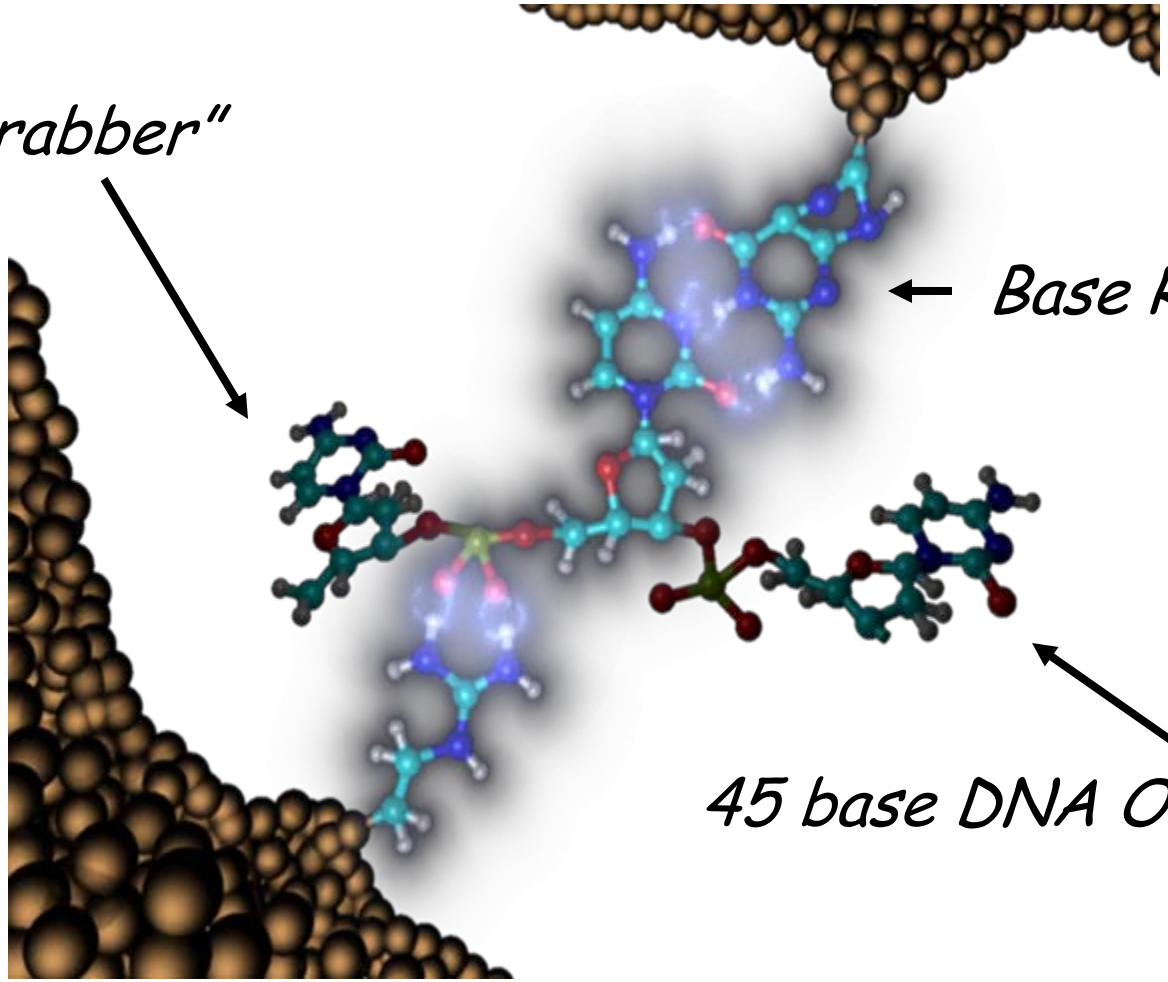


For details see Nano Letters **7** 3854, 2007

Accuracy of H-bond tunneling

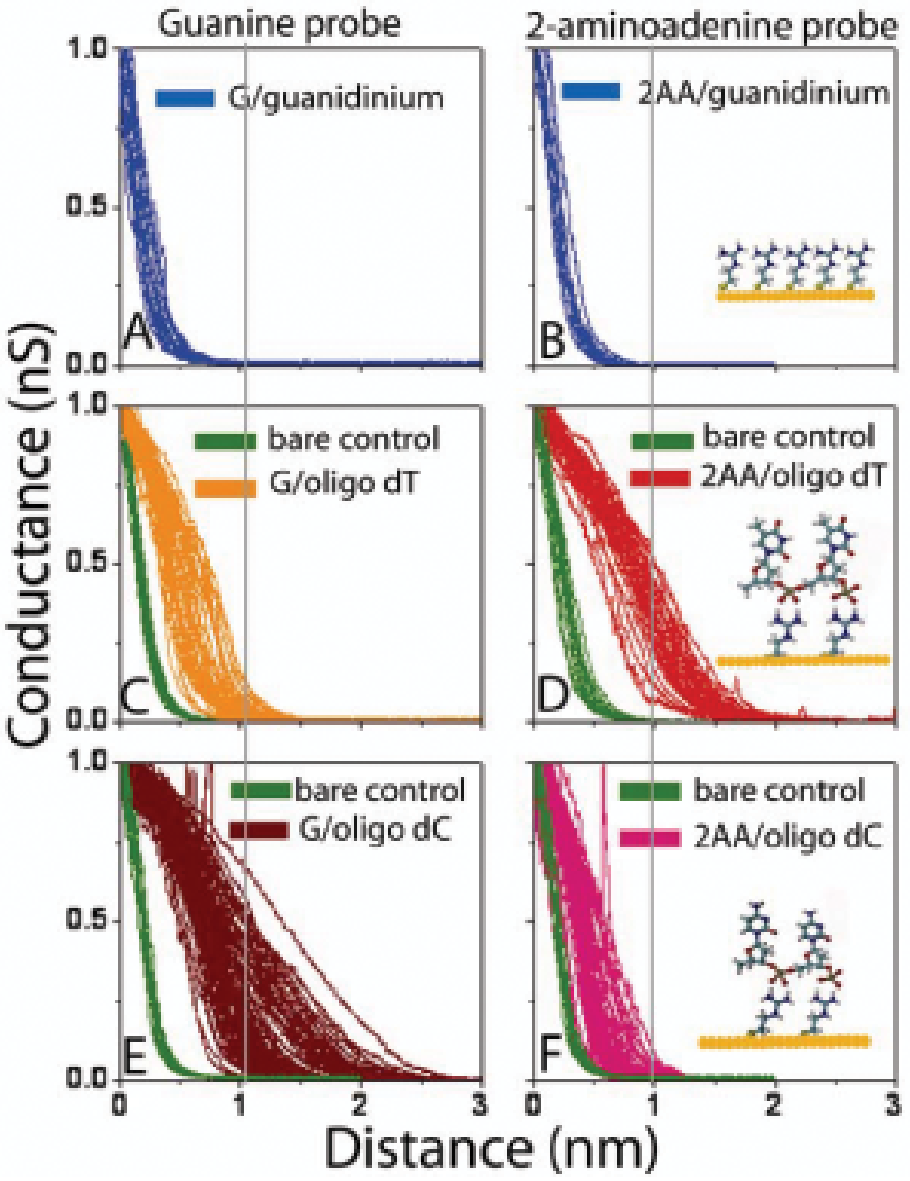
- *No* false positives with 50 threshold
- False negatives in <50% of reads
- $(0.5)^{13} < 10^{-4}$ so 99.99% accuracy with 13 read heads

Tunneling through intact DNA



Decay curves for 45 base DNA Oligos on GD

- Unambiguous reads of C and T
- T reads with 2-aminoadenine



New Class of Sensor

- Self-assembled tunnel junction – binary readout
- Chemical selectivity – product of dissociation constants
- Needle in a haystack – single molecule detection in high background