Synthetic Nanopores for DNA Sequencing

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Human Genome Project

- Completed in April 2003 a 3-billion base pair human genome reference DNA sequence
- Disorders Cystic Fibrosis and Sickle Cell Anemia
- DNA sequence affects responses medicines, resistance to infections and toxins.

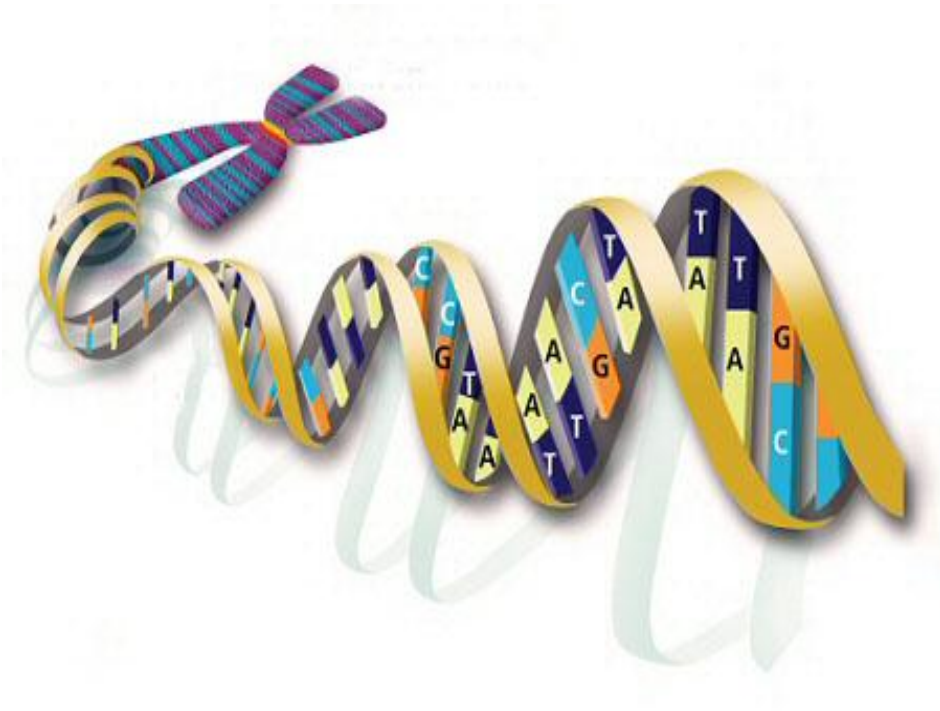


Image: www.ornl.gov

Why Nanopores?

- Low Cost
- Fast
- Versatile
- Improve human life:

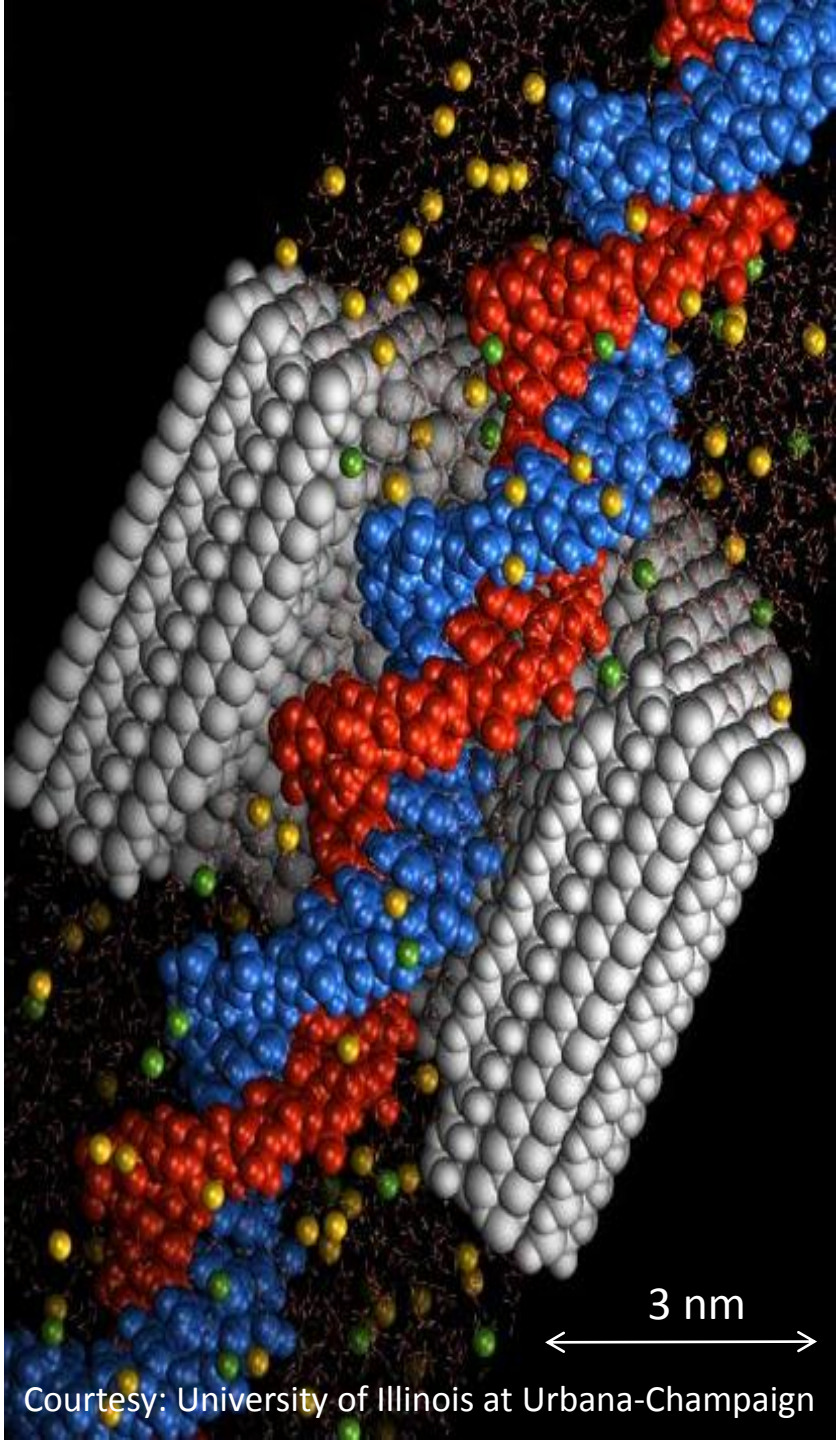
Directly

✓ Early detection of potential threats

Indirectly

✓ Correcting harmful mutations

✓ Individualized medical approach to genetic diseases.



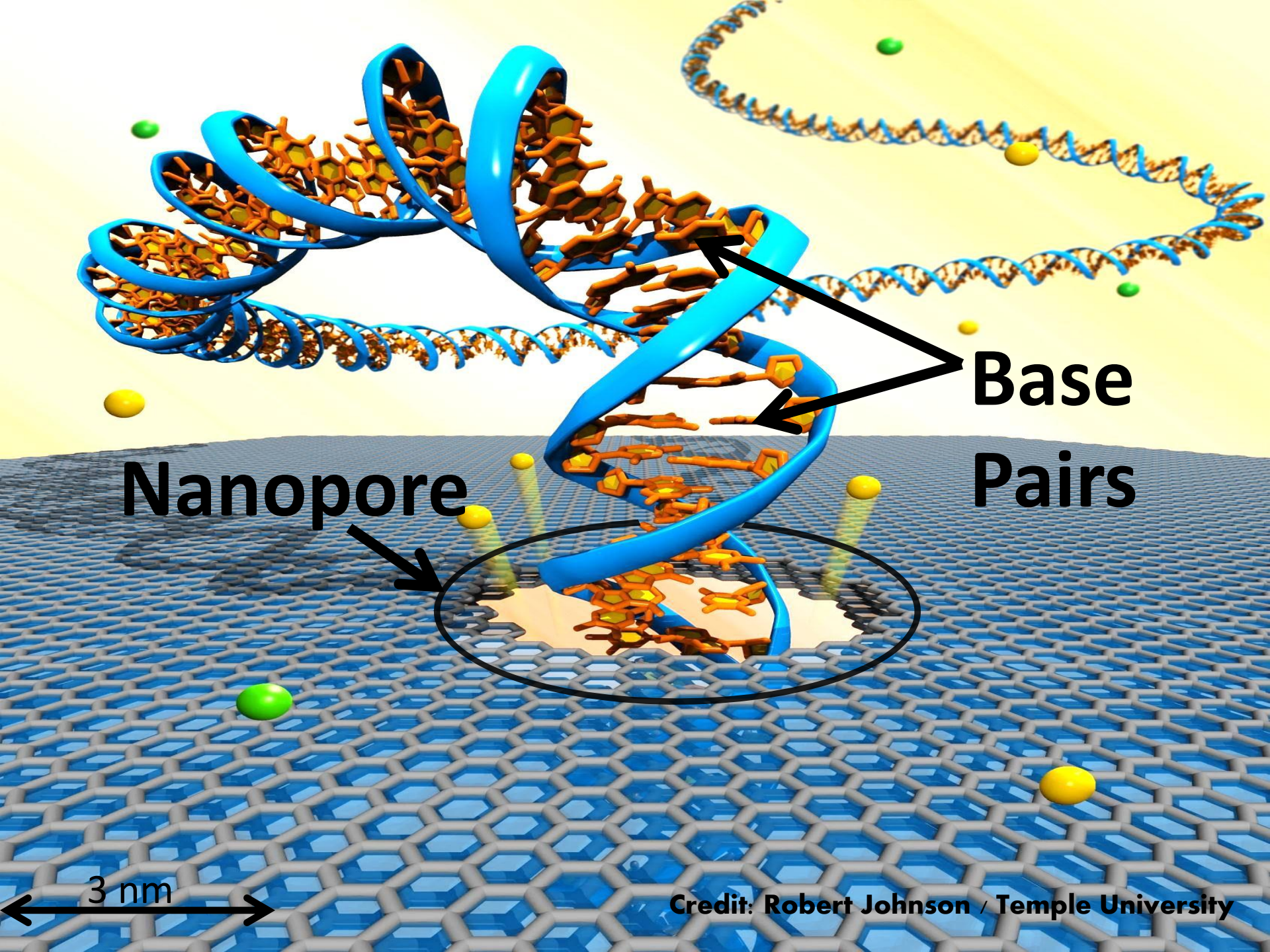
Courtesy: University of Illinois at Urbana-Champaign

Why Synthetic Nanopores?

- Compared to Biological Pores Synthetic Nanopores have:
  - Higher Stability
  - Better resistance to chemicals
  - Ruggedness to environmental conditions
  - Superior engineering capabilities
  - Wide selection of material possibilities

How do Nanopores Work?

“Thread a Needle”



Credit: Robert Johnson / Temple University

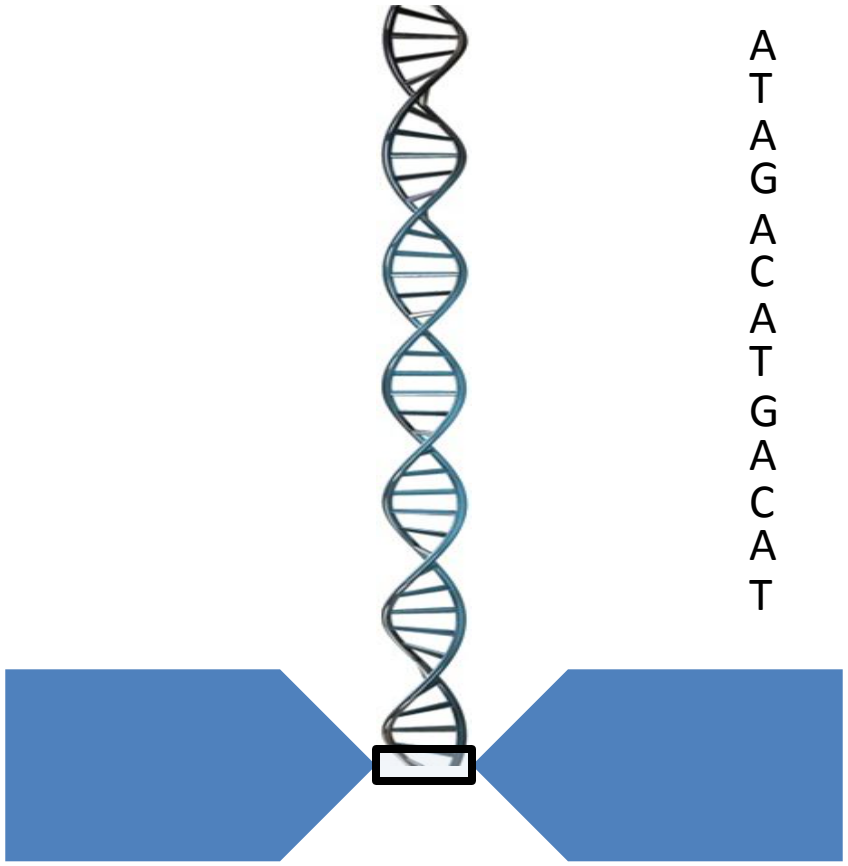
Research Goals for Summer 2012

Research Goals for Summer 2012

One of the problems with current configuration:

Rate of Translocation.

- Slow down DNA strand passage through nanopore by chemical and electrical manipulation.
- Expected result is the capacity to achieve a translocation rate with lower bandwidth.

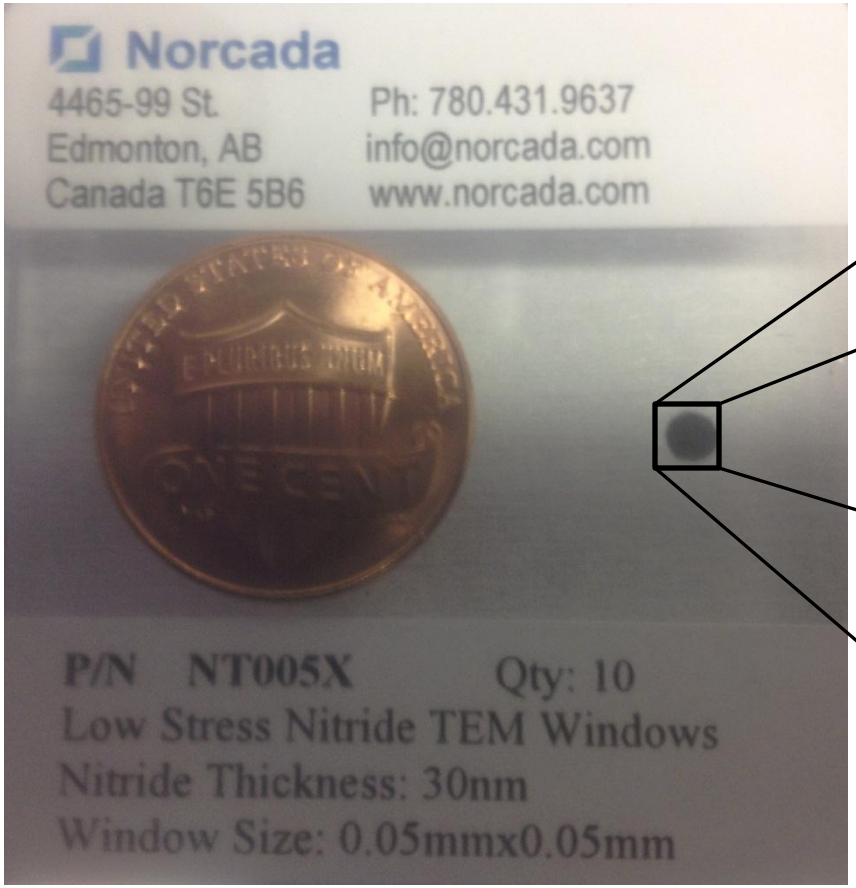


Drilling a Nanopore

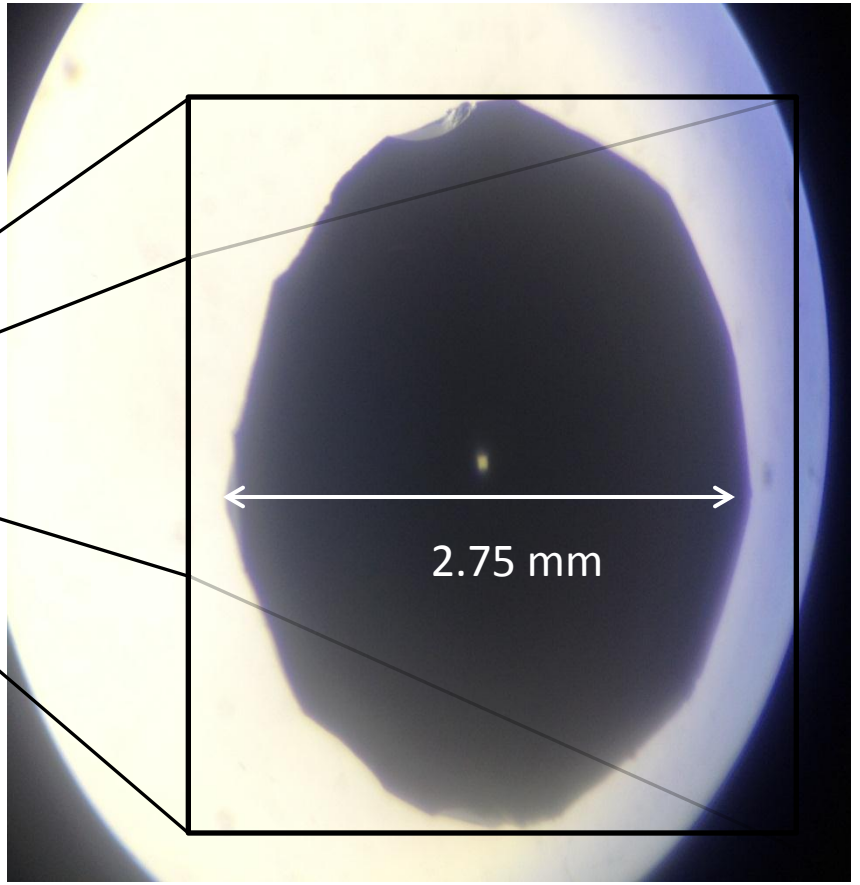
Metalizing the Nanopore

Membrane Set up

Drilling a Nanopore



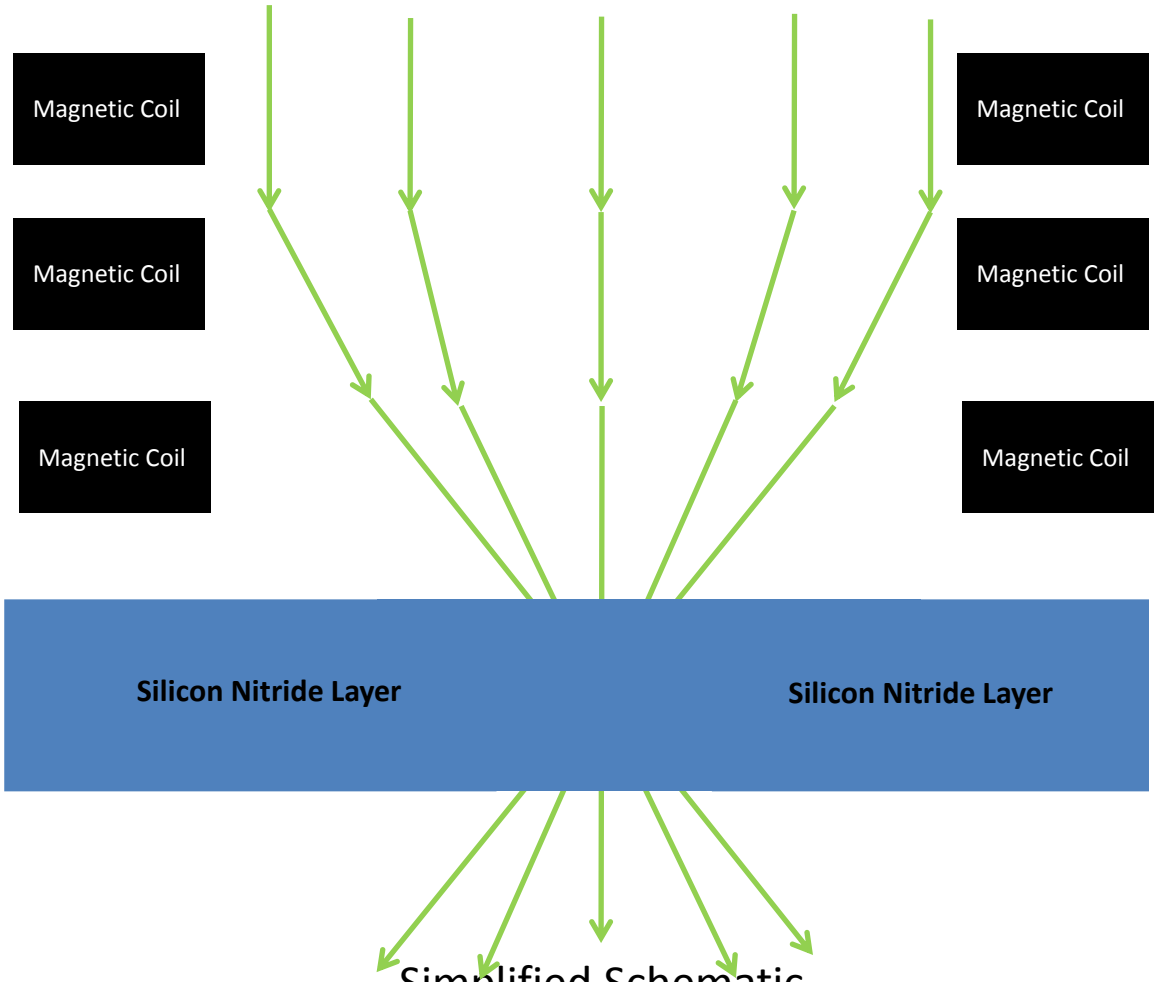
Norcada Silicon Nitride Chip



Norcada Chip at 56x

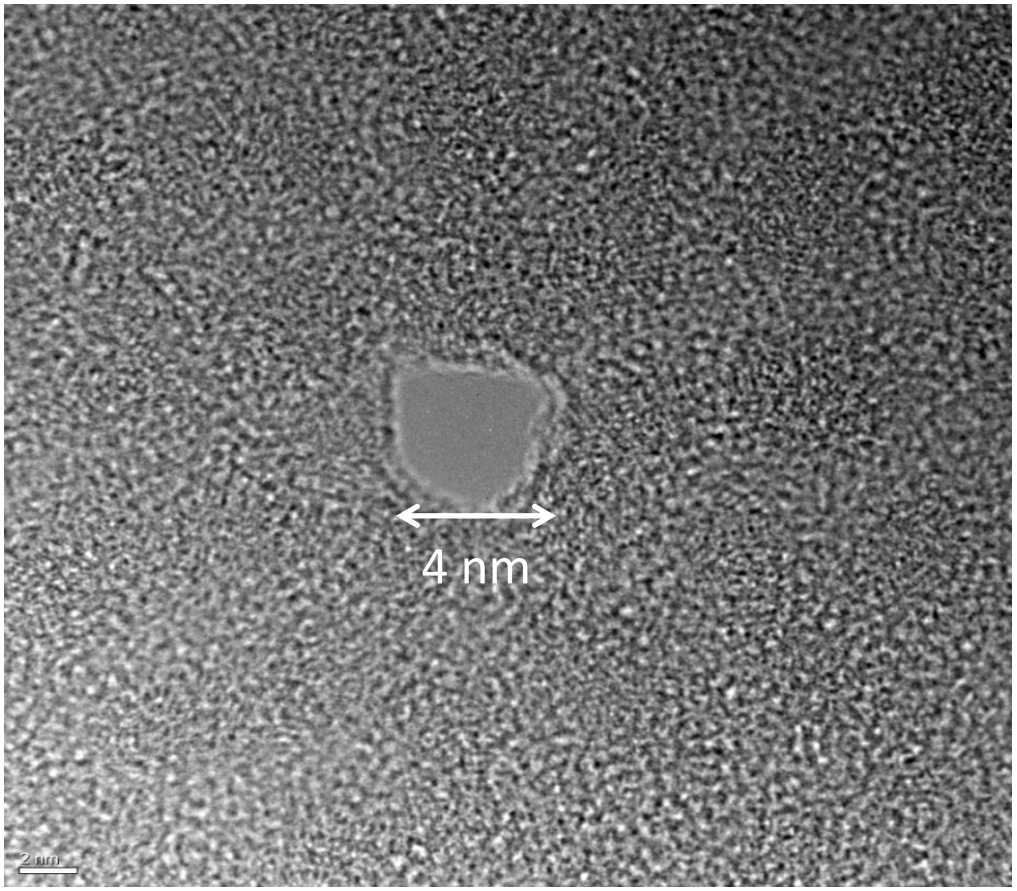
How TEM creates the pore

Transmission Electron Microscope (TEM)



Simplified Schematic Representation of Membrane in TEM

Finalized Pore



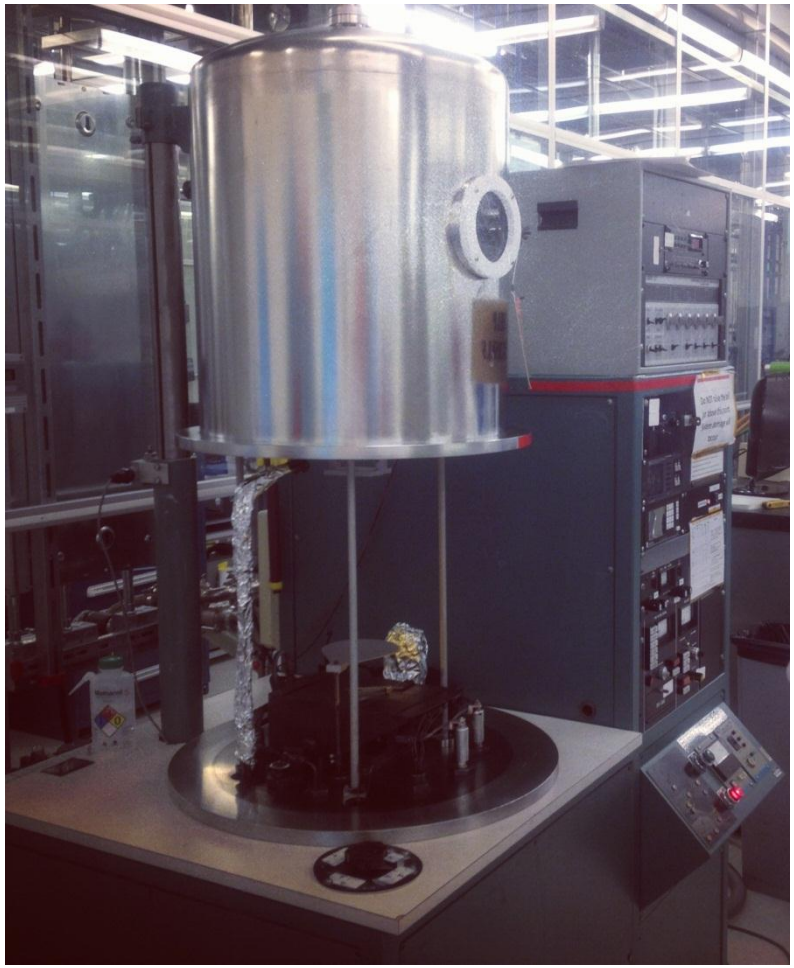
Nanopore at 690 kx

Drilling a Nanopore

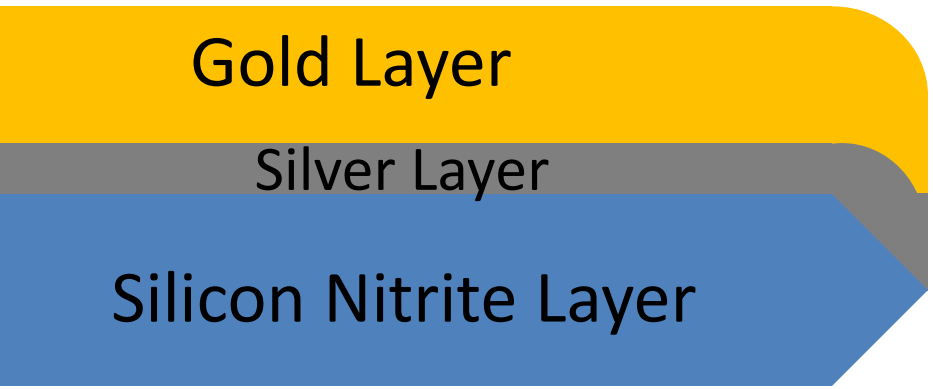
Metalizing the Nanopore

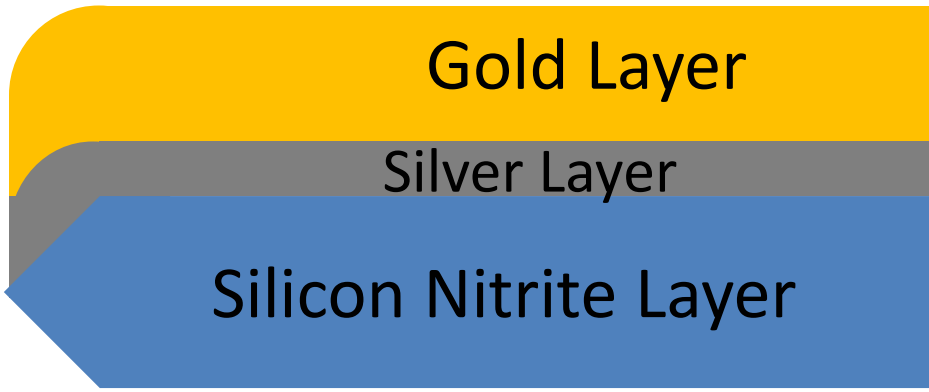
Membrane Set up

Metalizing the Nanopore



Electron Beam Evaporator


Gold Layer
Silver Layer
Silicon Nitrite Layer


Gold Layer
Silver Layer
Silicon Nitrite Layer

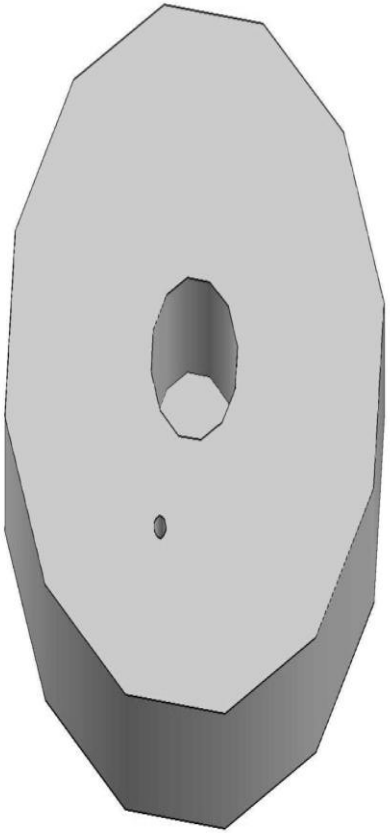
Drilling a Nanopore

Metalizing the Nanopore

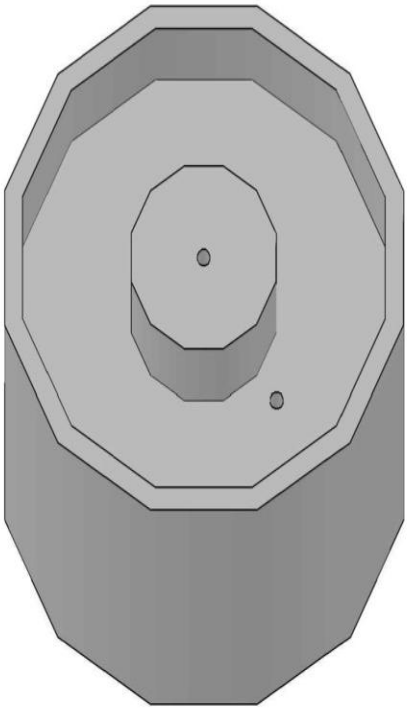
Membrane Set up

Membrane Set up

Teflon Structure

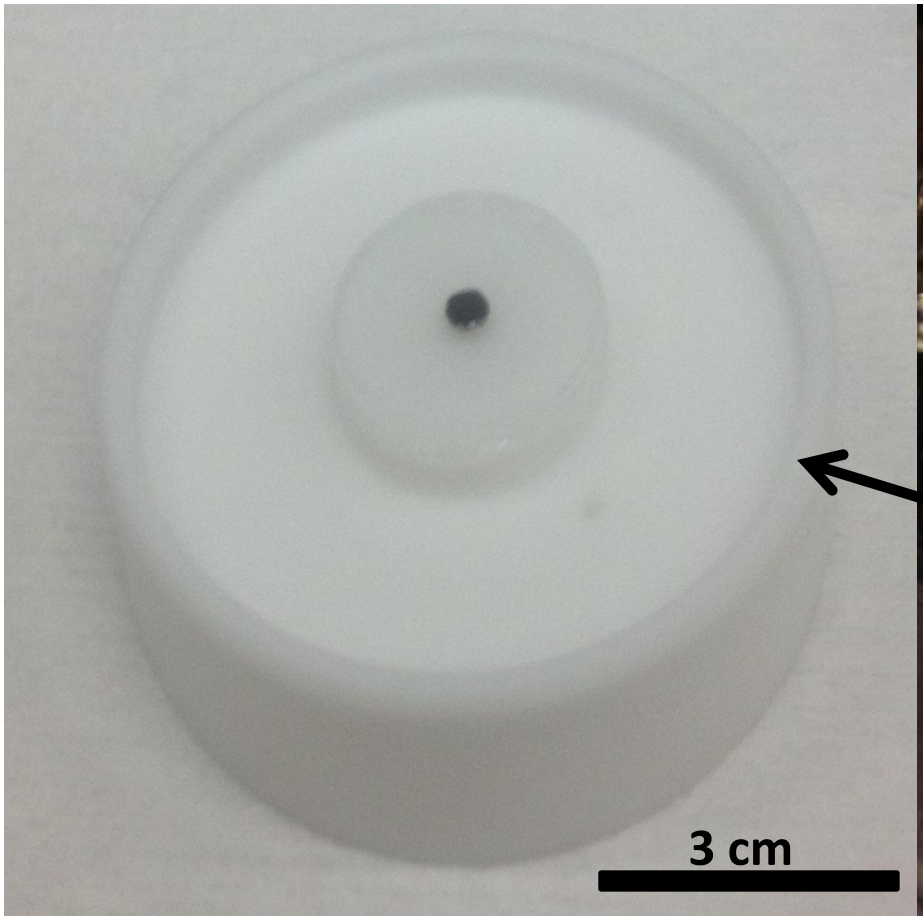


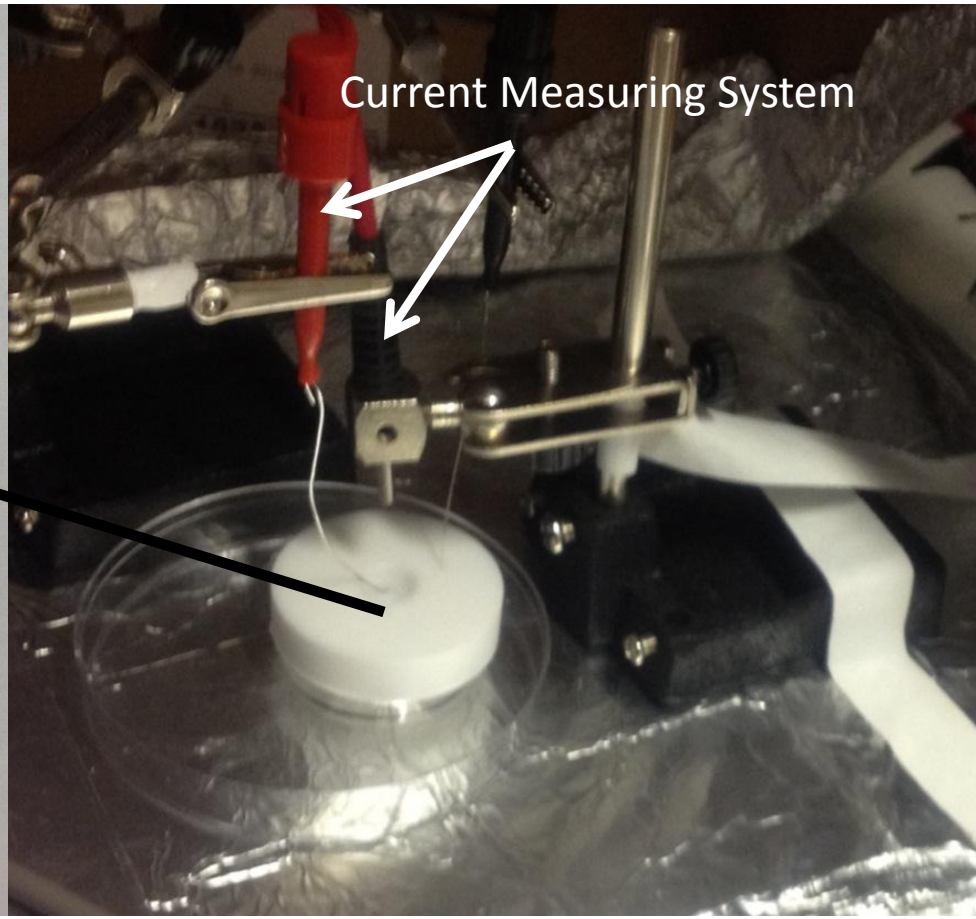
Top View

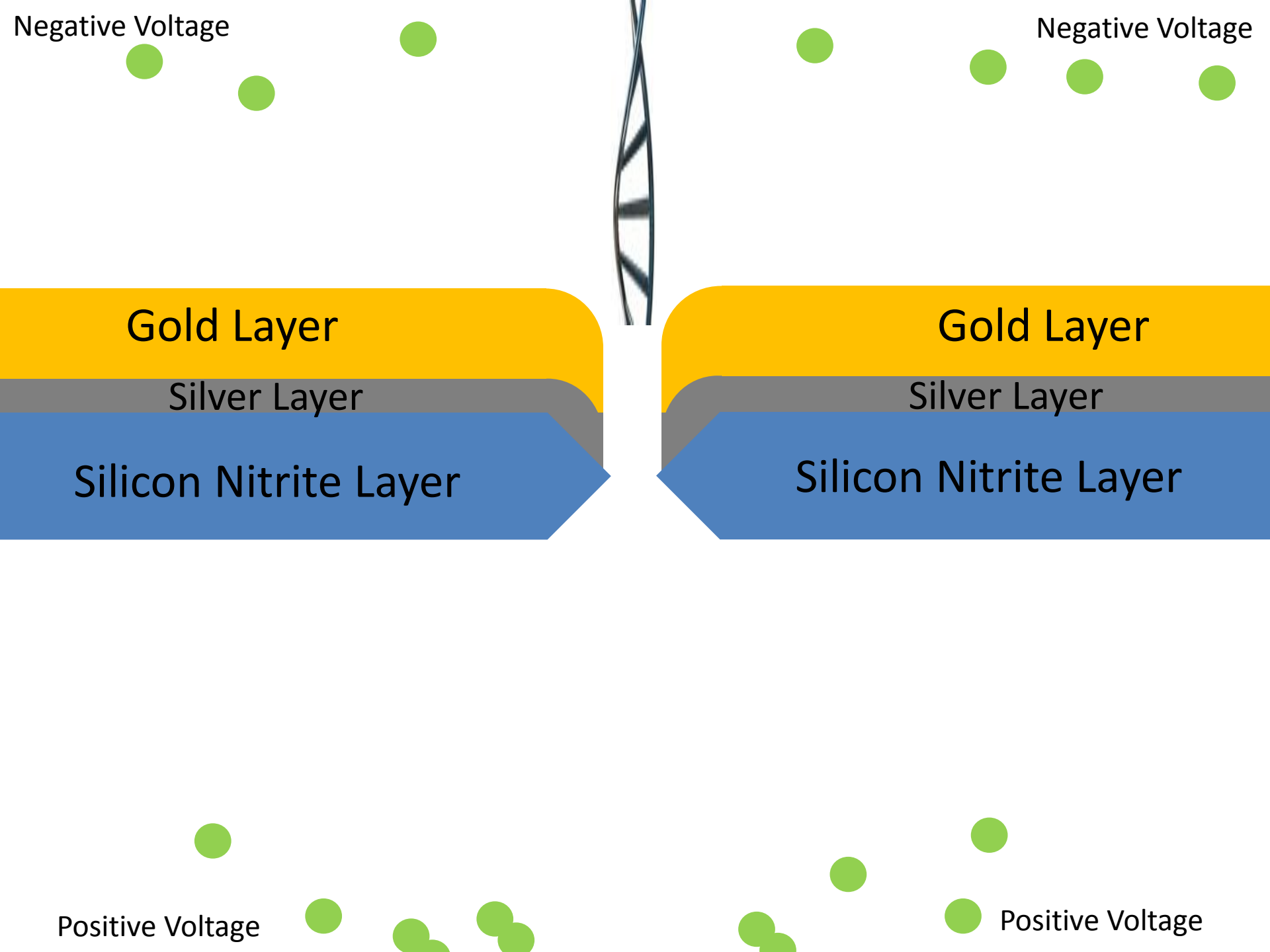


Bottom View

Membrane Set up





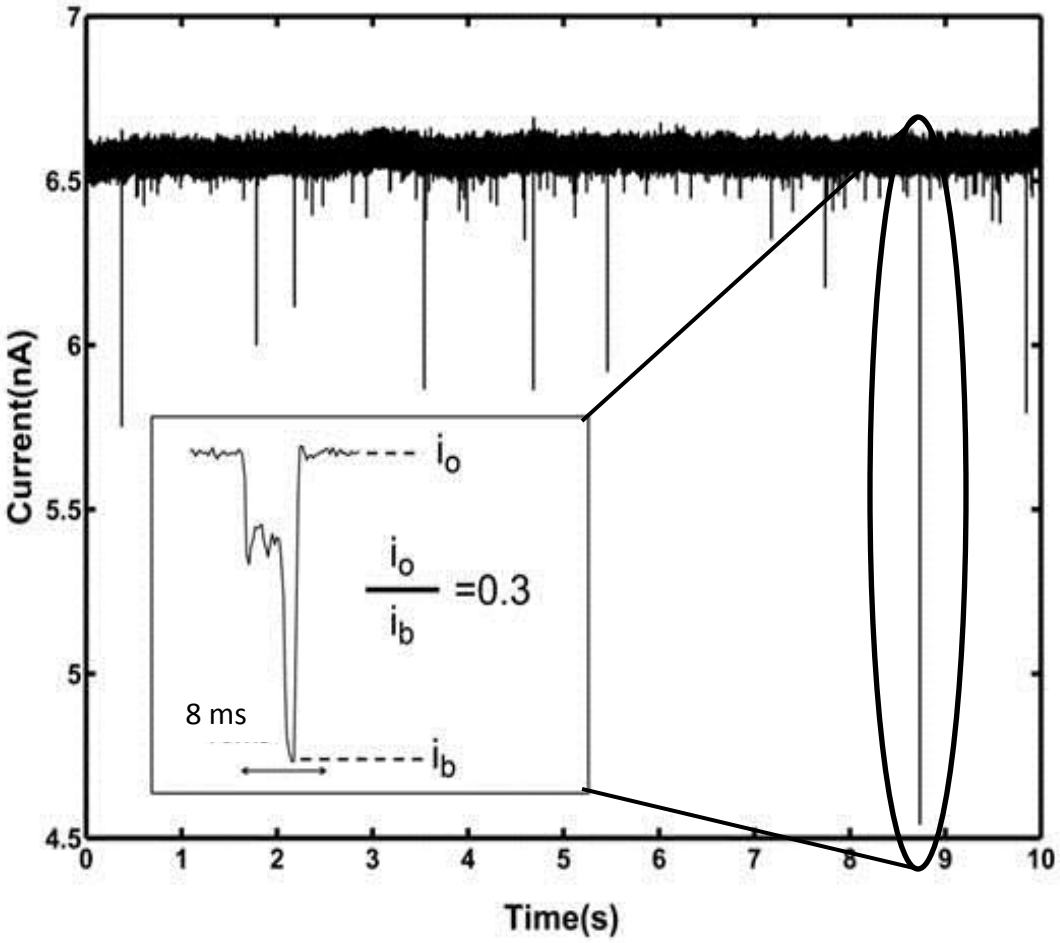

Negative Voltage
Negative Voltage
Gold Layer
Gold Layer
Silver Layer
Silver Layer
Silicon Nitrite Layer
Silicon Nitrite Layer
Positive Voltage
Positive Voltage

Results

Silicon Nitride Membrane

- E. coli 5700 base pair DNA
- A 4.6 nm pore total translocation took 8 ms.
- Blockage levels 30% of open pore current value.
- Single base pair translocation time 1.75µs

Current Across Membrane at 300 mV



Future of Research

- Many common diseases such as diabetes, hypertension, deafness, and cancers have more complex causes that may be a combination of sequence variations in several genes on different chromosomes, in addition to environmental factors

- Some disorders, such as cystic fibrosis (chr. 7) and sickle cell anemia (chr. 11), are caused by base sequence changes in a single gene.

Acknowledgments

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