Interactions of Chemical Mechanical Planarization Nanoparticles with Model Cell Membranes: Implications for Nanoparticle Toxicity (425.041)

PI:

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Graduate Students:

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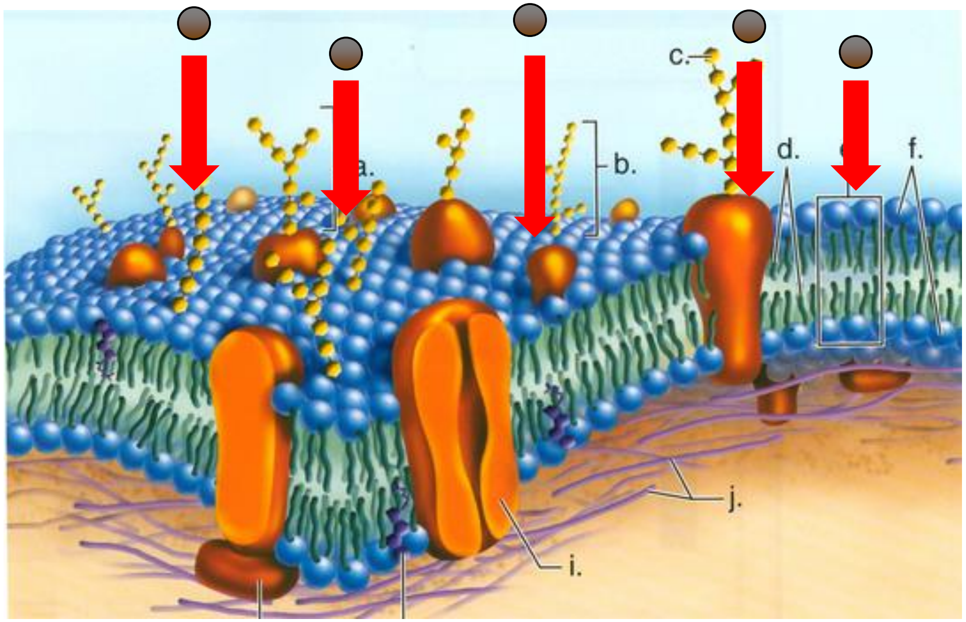
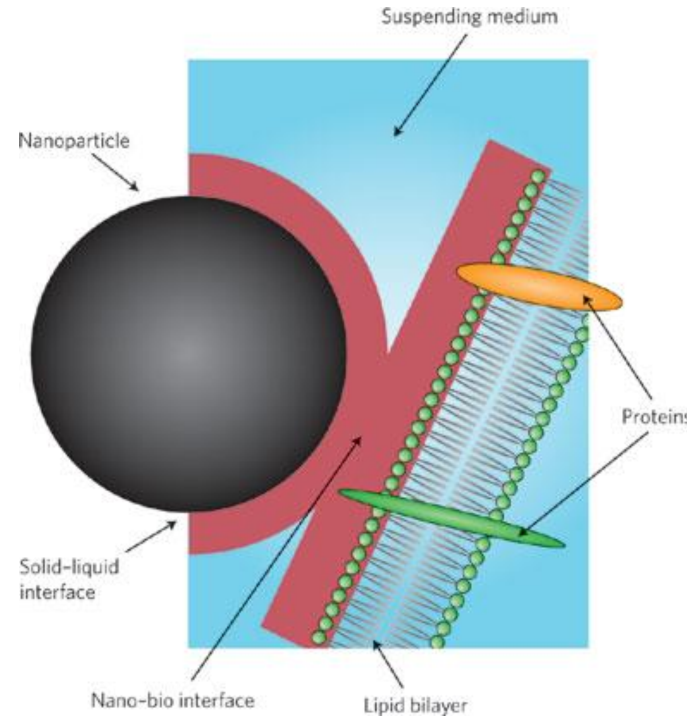
- **Xitong Liu, second-year PhD student, DoGEE, JHU**
- **Wenyu Gu, MSE, DoGEE, JHU – currently PhD student at University of Michigan**

Cost Share (other than core ERC funding):

- **$101,472 from Johns Hopkins University in the form of 80% of tuition for 3 years**

Objectives





- **To investigate the propensity of chemical mechanical planarization nanoparticles (silica, ceria, and alumina) to attach to model biological membranes**
- **To develop a rapid assay to assess the propensity of nanomaterials to absorb on biological membranes**

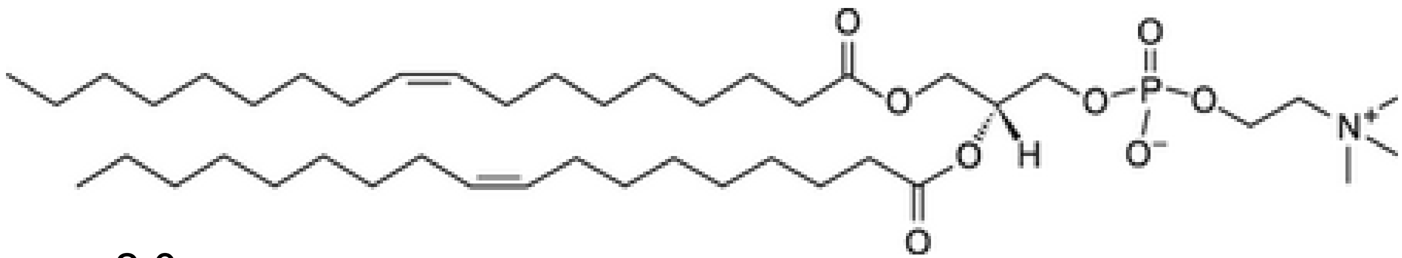
Sylvia S. Mader, *Biology,* 9th ed., 2007, McGraw-Hill.   Nel et al., *Nature Materials* 2009, 8, 543–557.

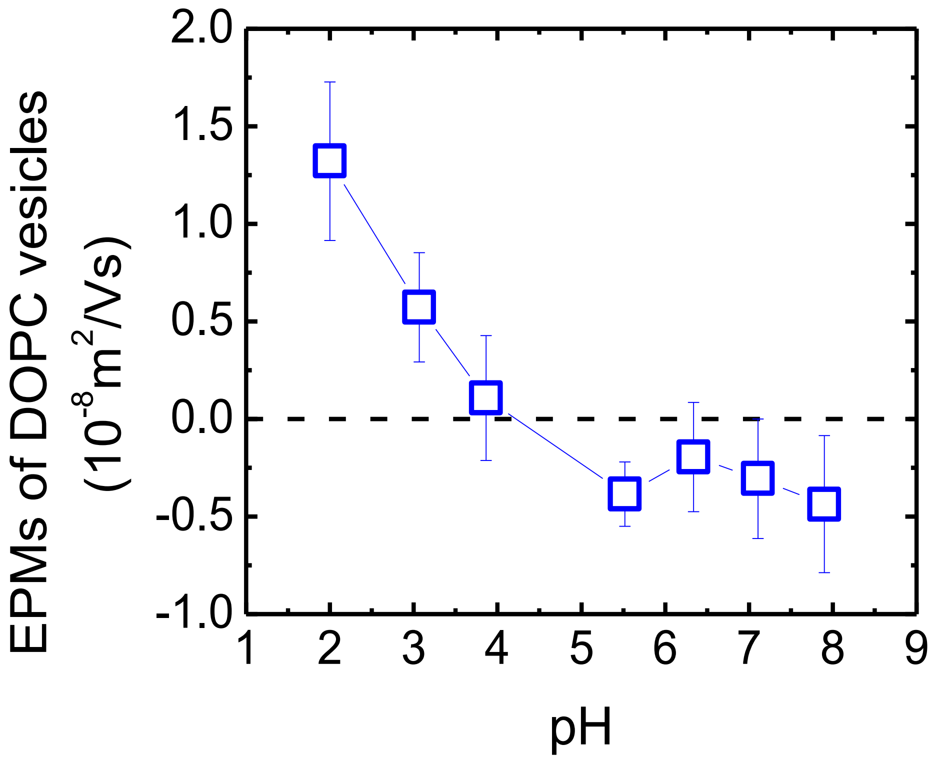
ESH Metrics and Impact

1. **Rapid assay for propensity of CMP particles to bind to cell membranes**
   - **Use of sensitive quartz crystal microbalance (QCM-D)**
2. **Reduction in the use of CMP particles that bind strongly to membranes**
   - **CMP particles will be tested with binding assay before being employed in semiconductor fabrication plants**
3. **Reduction in emission of CMP particles that bind strongly to membranes to environment**
   - **CMP nanoparticles may be replaced with other alternative materials/particles that do not strongly interact with biological membranes**

DOPC Supported Lipid Bilayers (SLBs) as Model Cell Membranes

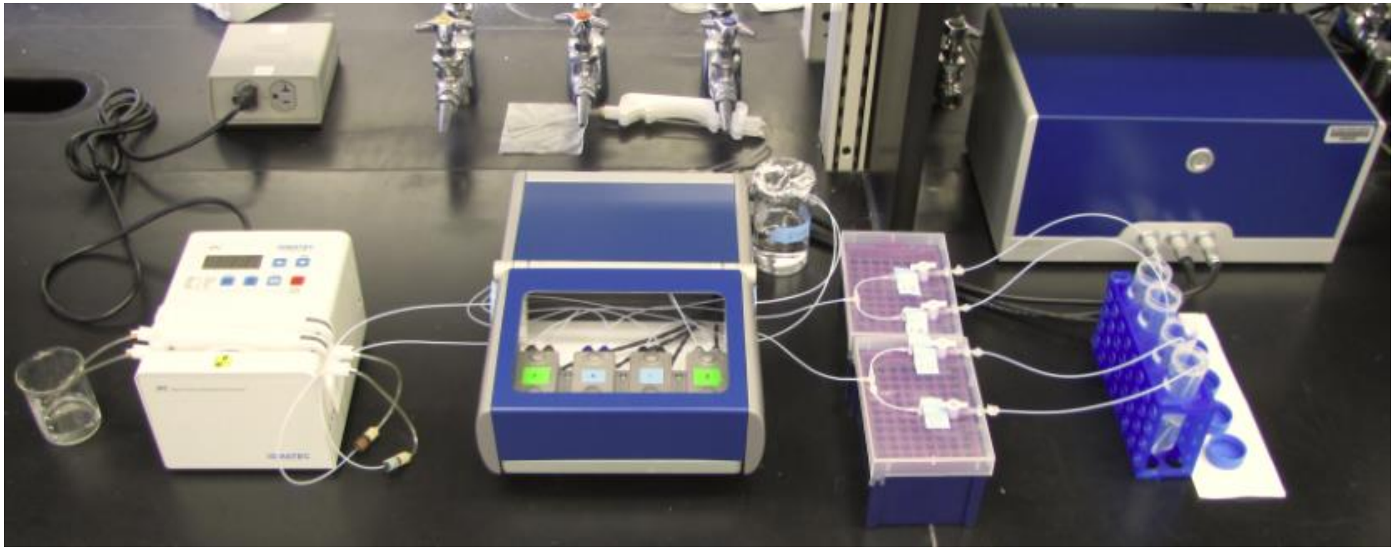
DOPC (1,2-dioleoyl-*sn*-glycero-3-phosphocholine)

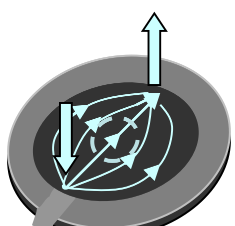




- **DOPC vesicles prepared by extrusion with 50-nm membranes**
- **pH_{ZPC} of DOPC is about 4**

Quartz Crystal Microbalance with Dissipation Monitoring (QCM-D)



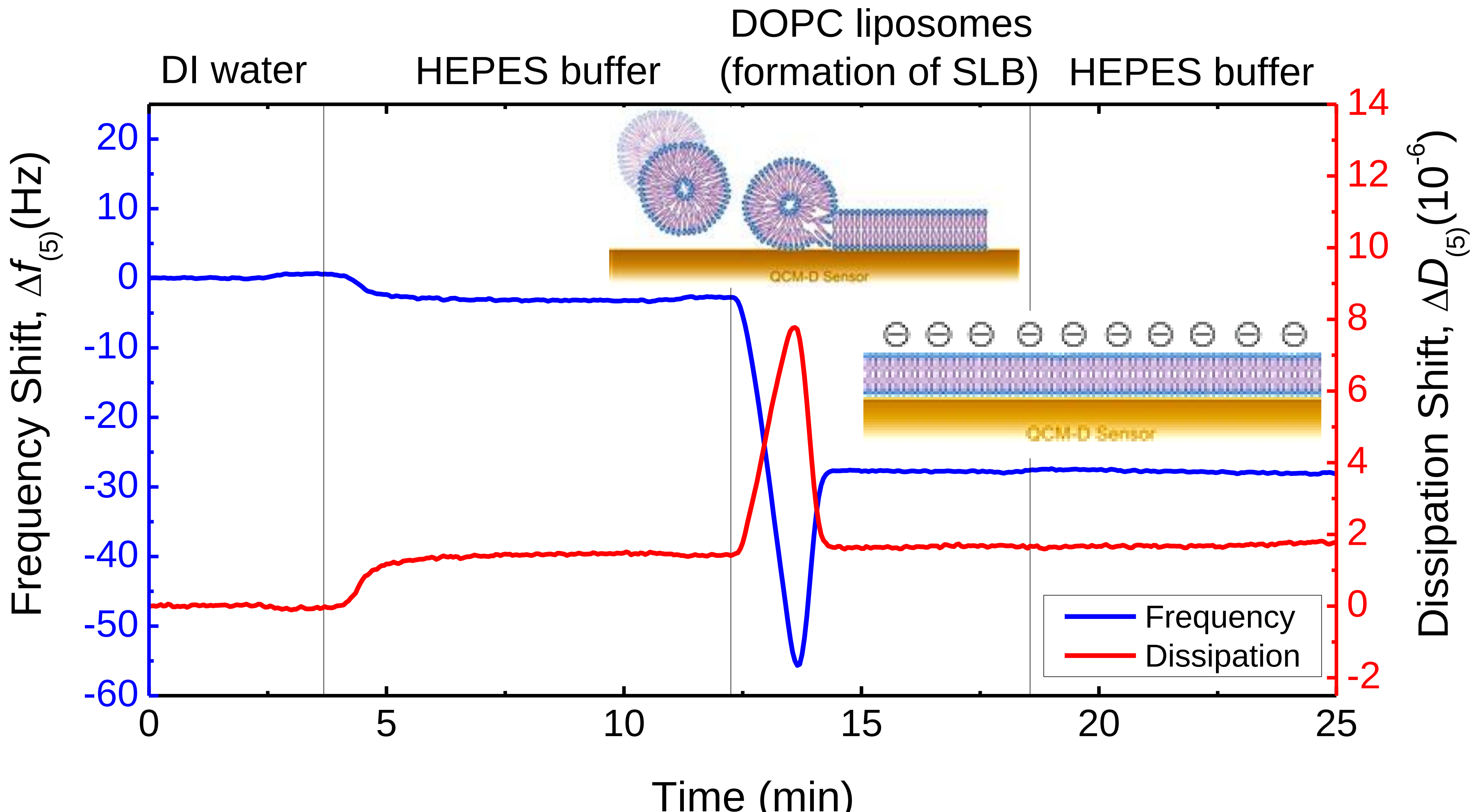


- **Sensitivity of ca. 10 ng/cm^2**
- **Frequency, Δ*f* – deposited mass**
- **Dissipation, Δ*D* – "softness" of deposited constituents**
- **Laminar flow at 0.1 mL/min**
- **T = 25 ºC, pH = 2–8**

Picture of crystal is from qsense http://www.qsense.com/

Formation of Supported Lipid Bilayers on Silica-Coated QCM-D Crystals

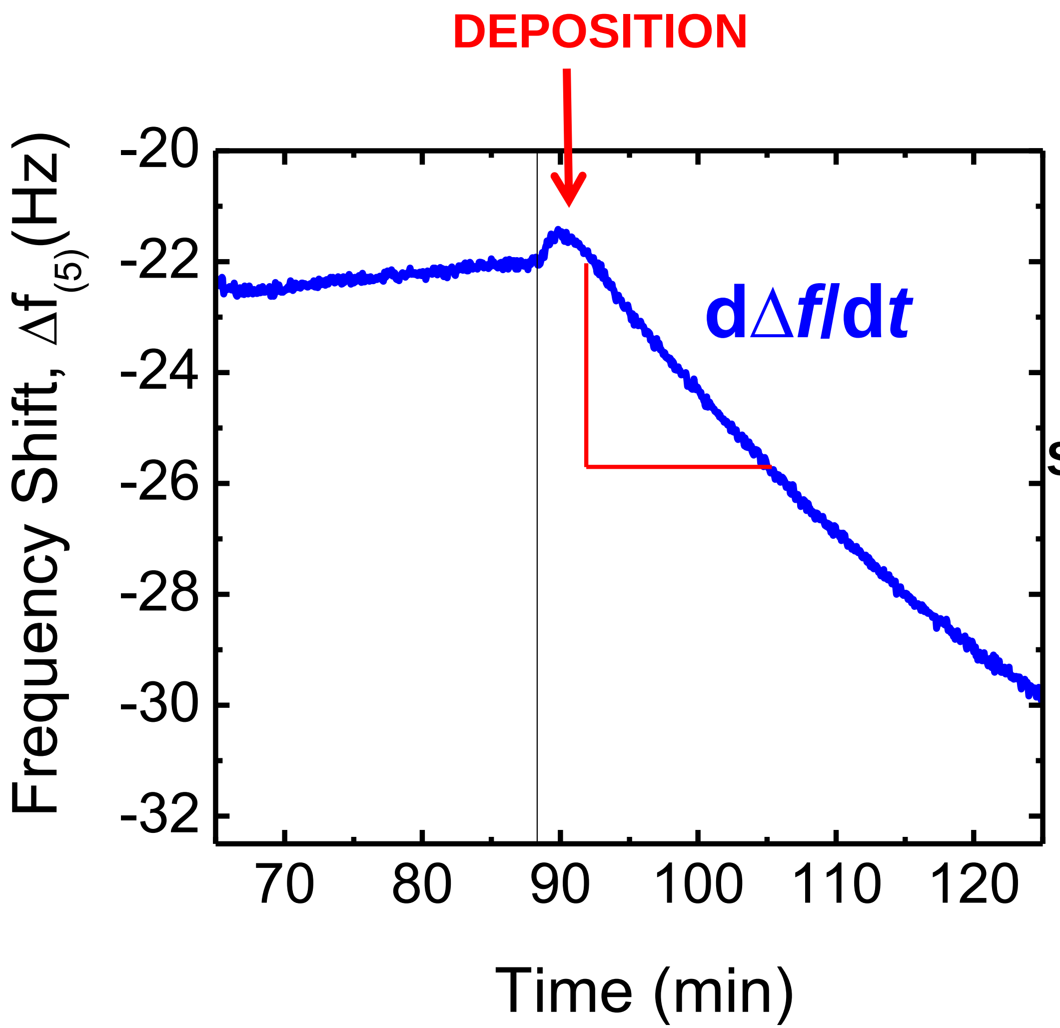
- **Approach of Keller and Kasemo, 1998**

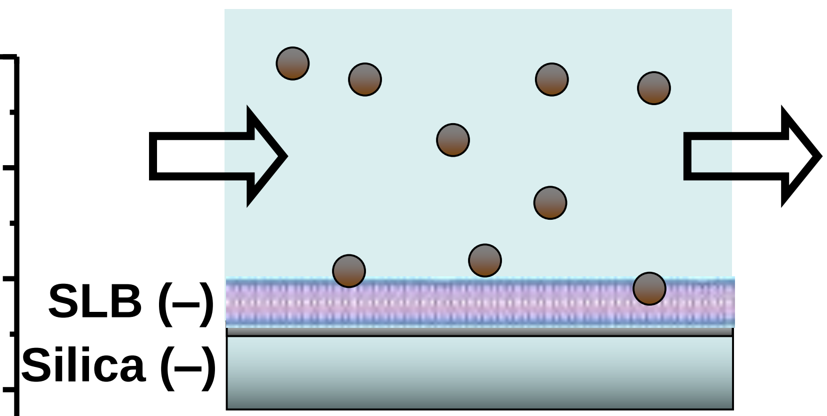


SRC Engineering Research Center for Environmentally Benign Semiconductor Manufacturing

Cartoons are from qsense http://www.qsense.com/

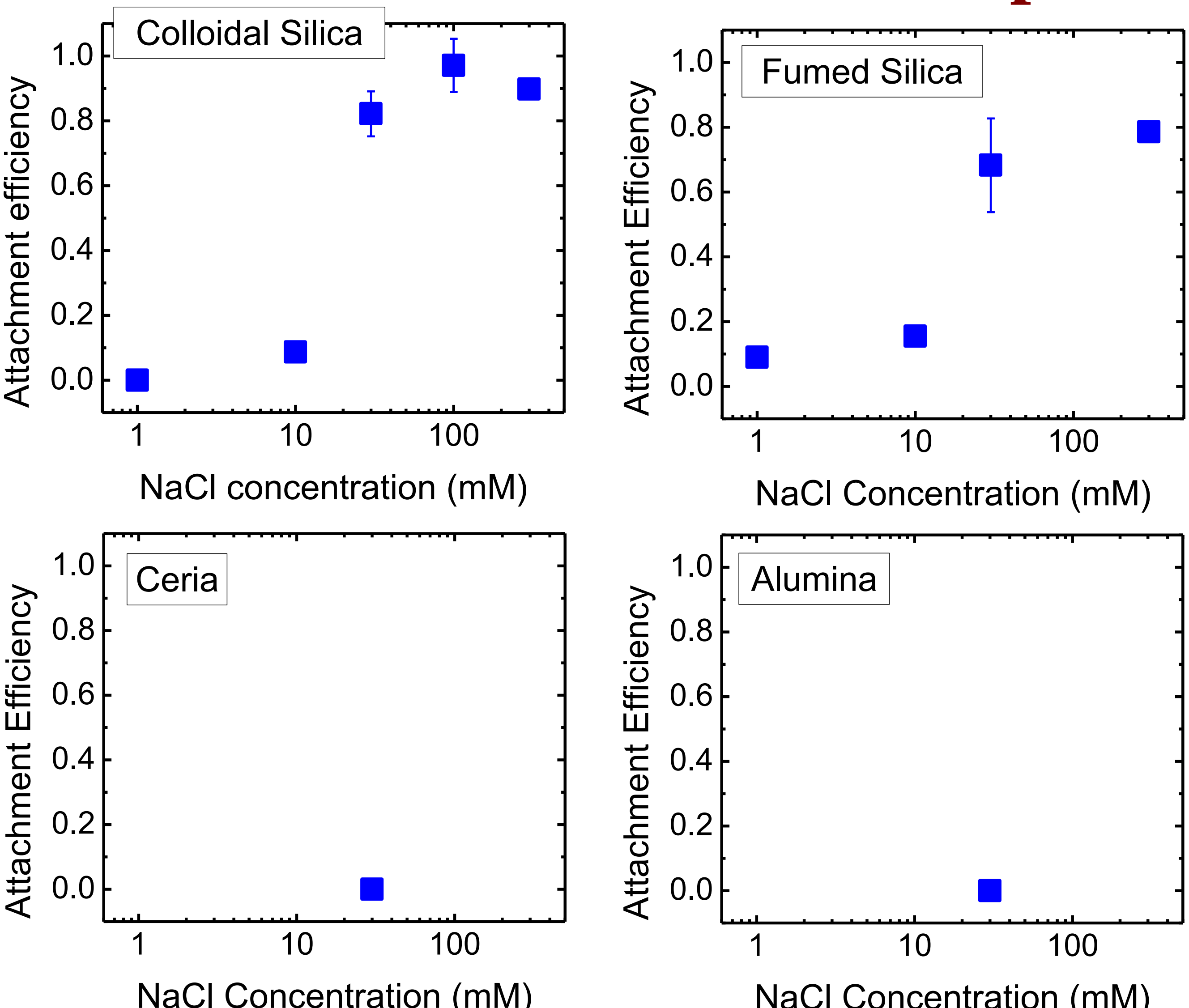
Deposition of CMP NPs on SLBs





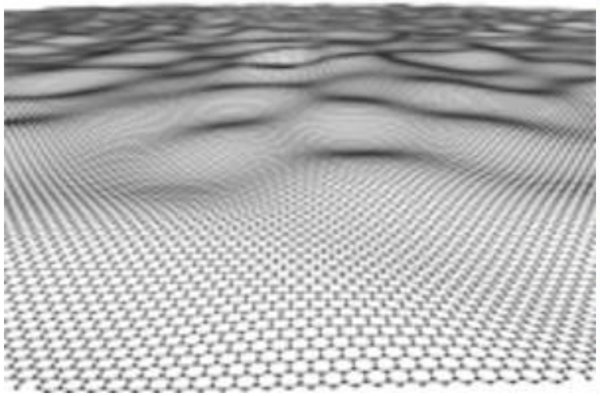
- **dΔf/dt is proportional to rate of nanoparticle deposition**

Comparing Deposition Kinetics of Cabot CMP NPs on SLBs at pH 7.4

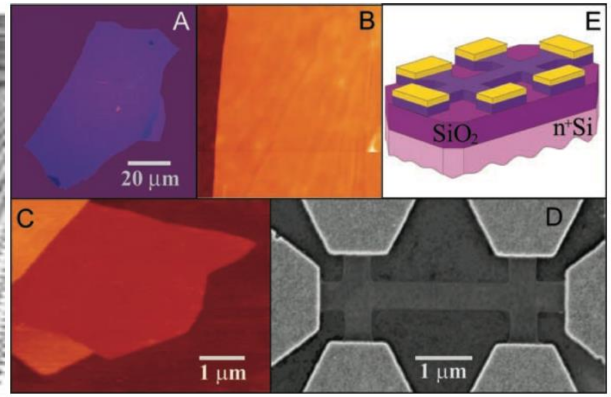


- **At pH 7.4, all CMP NPs are negatively charged**
- **For both silica NPs, deposition kinetics increases as NaCl concentration increases**
- **Ceria and alumina NPs have low propensity to attach to membranes**

Graphene and Graphene Oxide

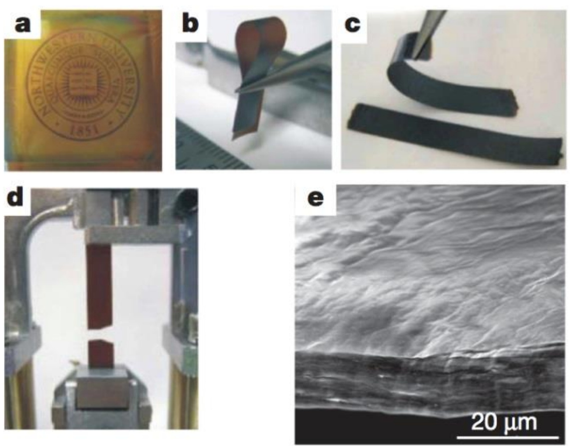


phys.org

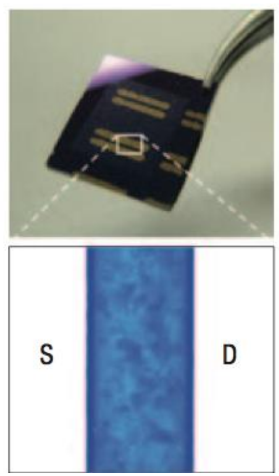


Novoselov et al., *Science,* 2004, 666-669

- **Graphene**
  - One layer of C atoms
  - High electrical conductivity



Dikin et al.,*Nat*ure, 2007, 457-460

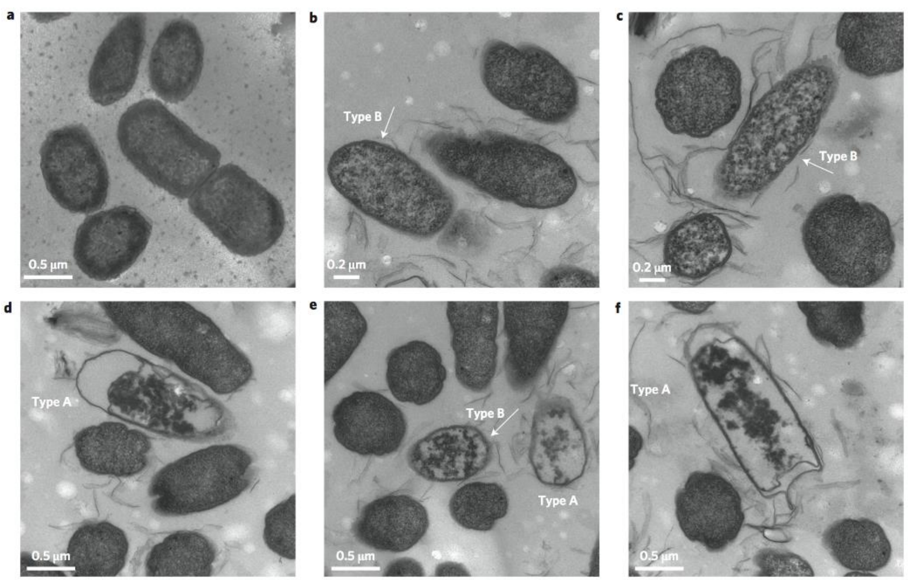


Eda et al. *Nat. Nanotechnol*, 2008, 270-274

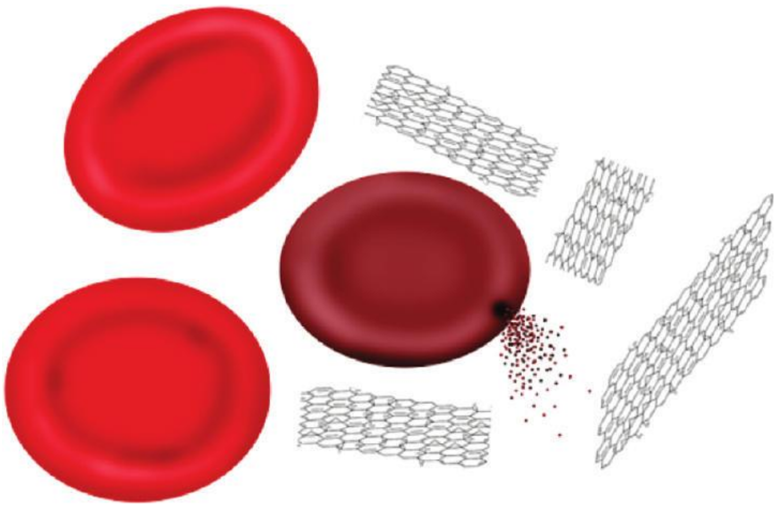
- **Graphene oxide (GO)**
  - Reduced to form rGO
  - Can be dispersed in water

Toxicity of Graphene Oxide

- **Destructive extraction of phospholipids from membranes of *Escherichia coli* cells**
- **Hemolysis of red blood cells**

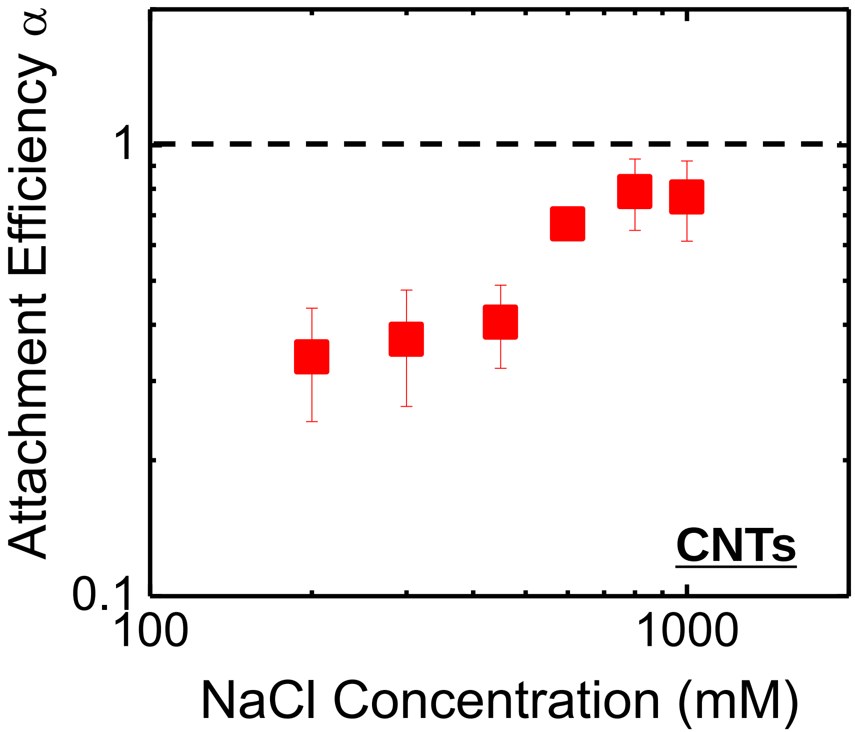


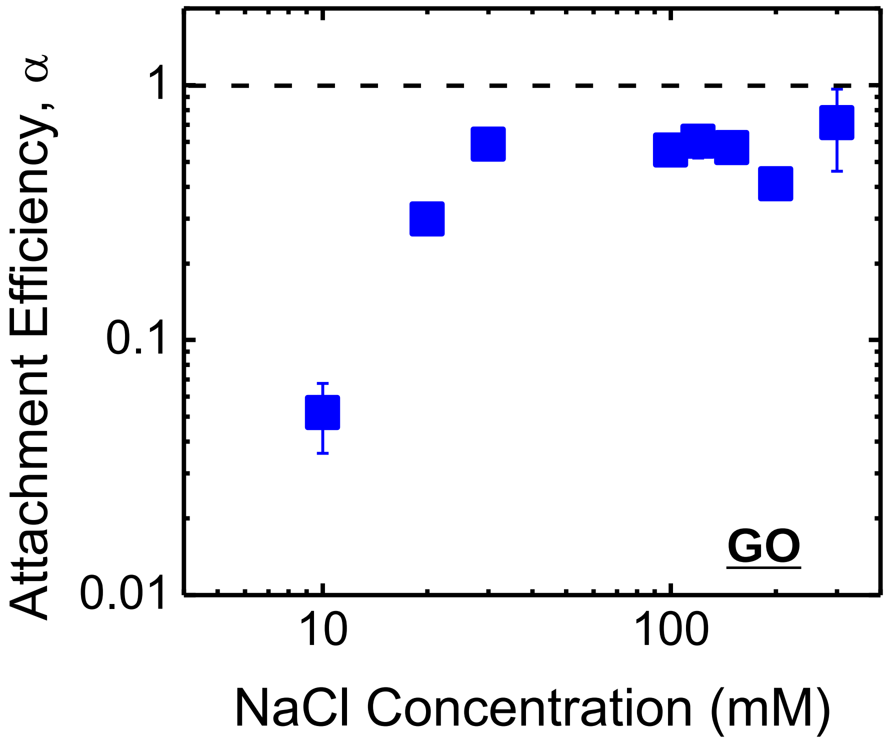
Tu et al. *Nat. Nanotechnol*, 2013, 594-601



Liao et al., *ACS Appl. Mat. Interfaces*, 2011, 2607-2615

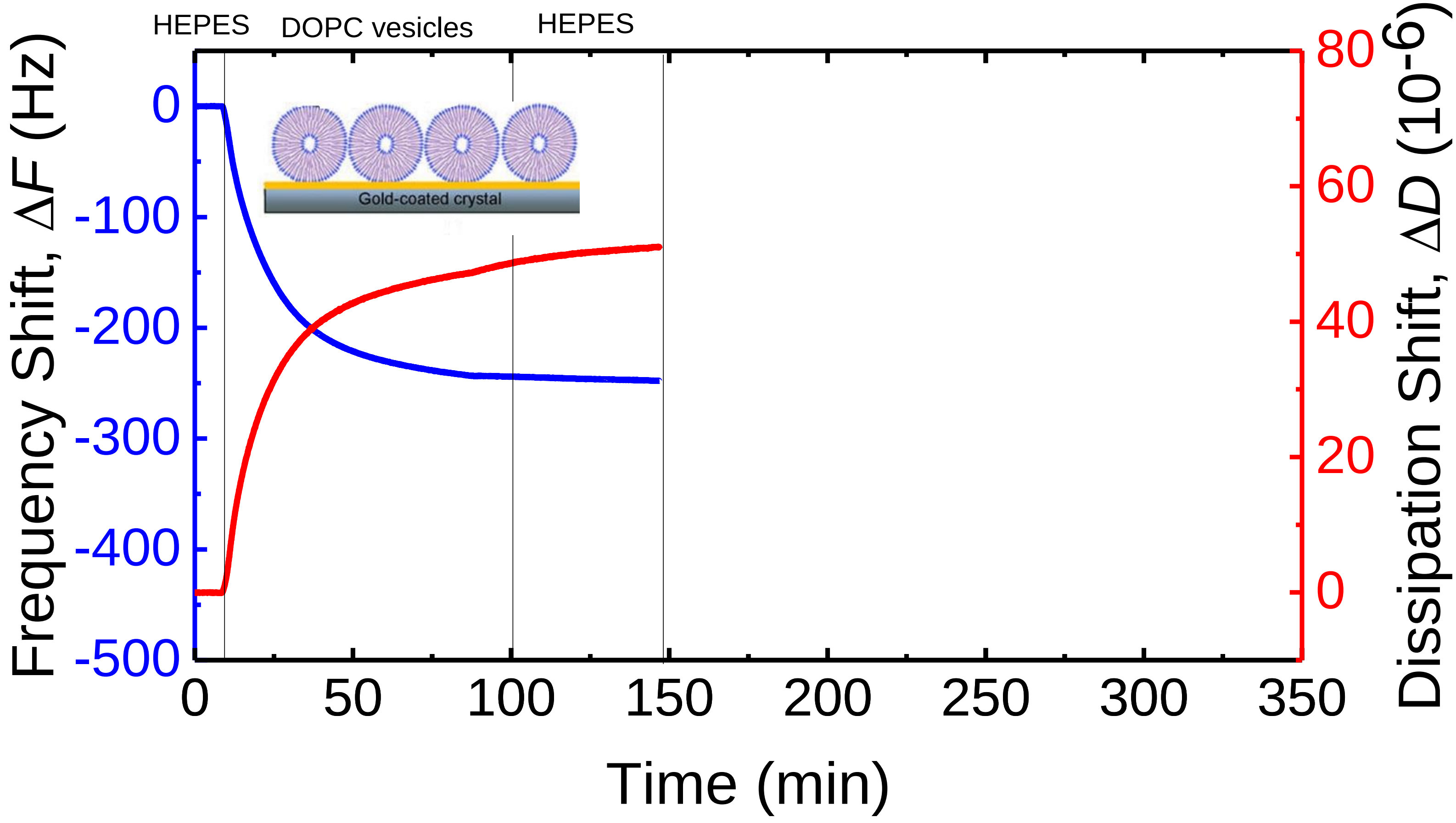
Deposition Kinetics of CNTs and GO on SLBs in NaCl



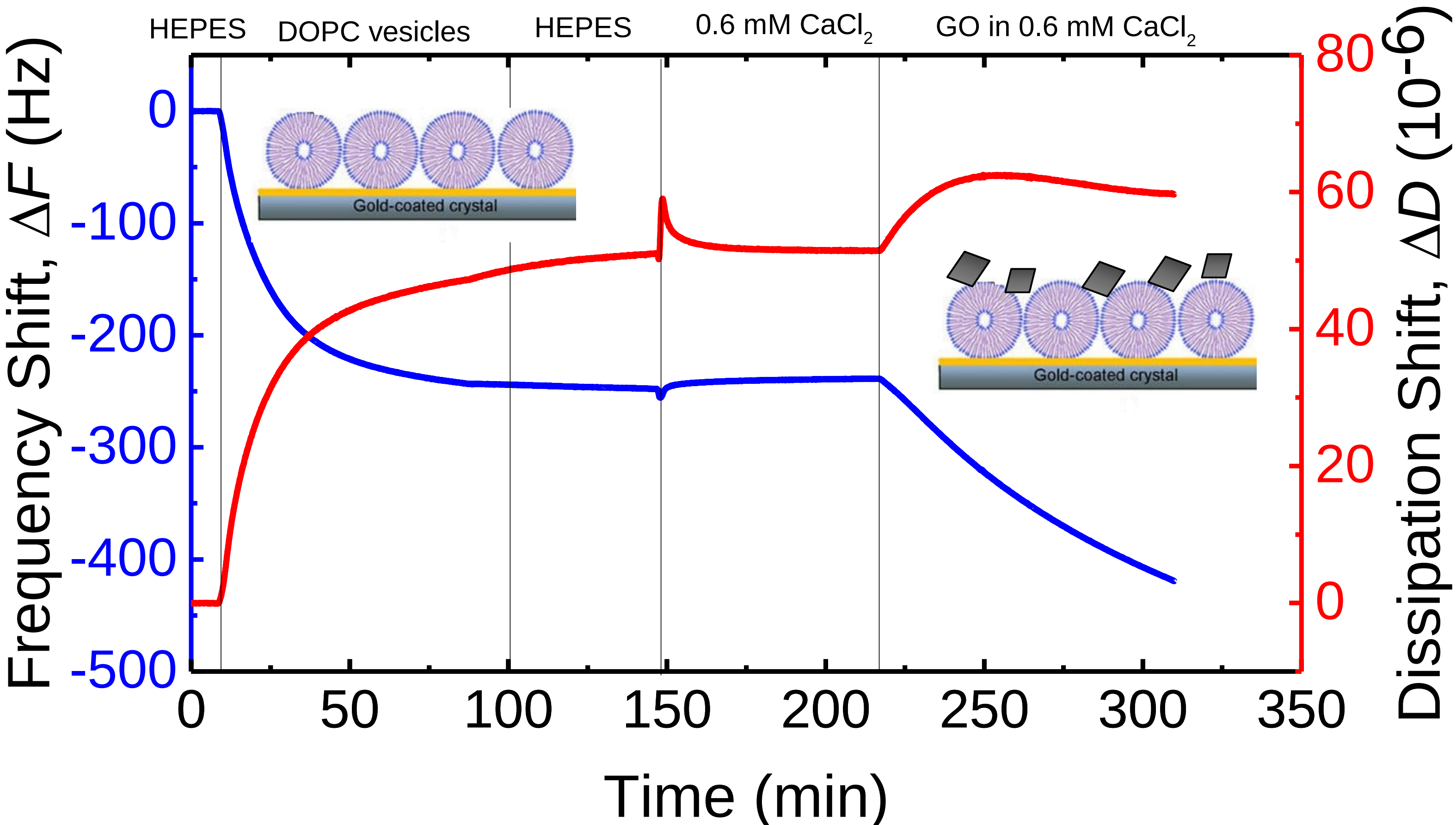


- **Attachment efficiencies of CNTs and GO lower than 1.0 even at high NaCl concentrations**

Interactions of GO with Supported Vesicular Layer



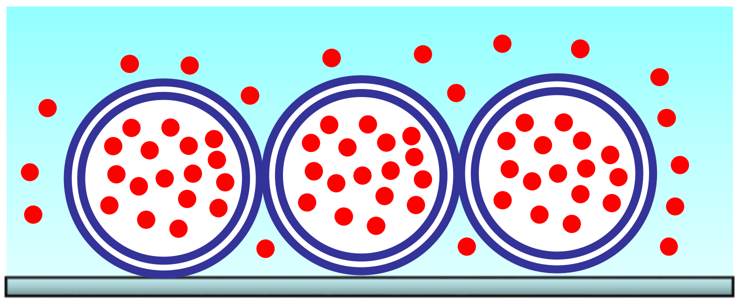
Interactions of GO with Supported Vesicular Layer



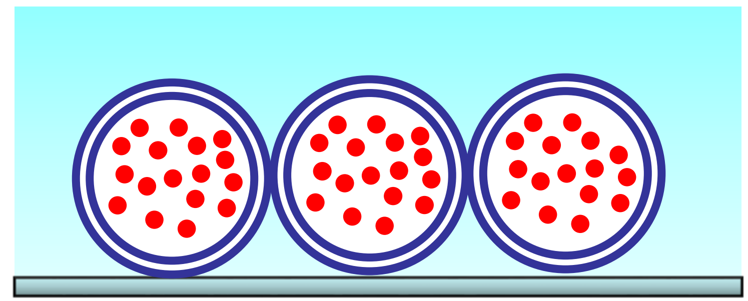
- **GO deposited on supported vesicles; no significant rupture of vesicles**

Fluorescent Dye-Encapsulated Vesicles Deposited on QCM-D Crystals

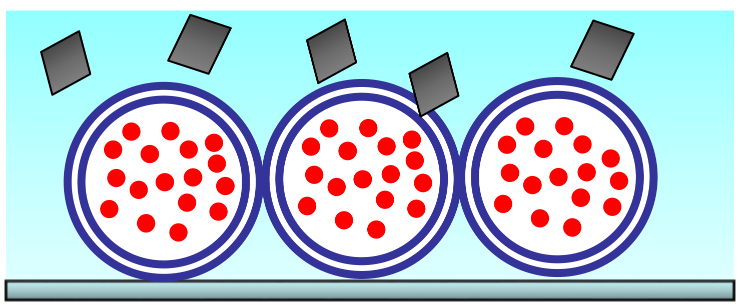
(A) **Supported vesicular layers on Au**



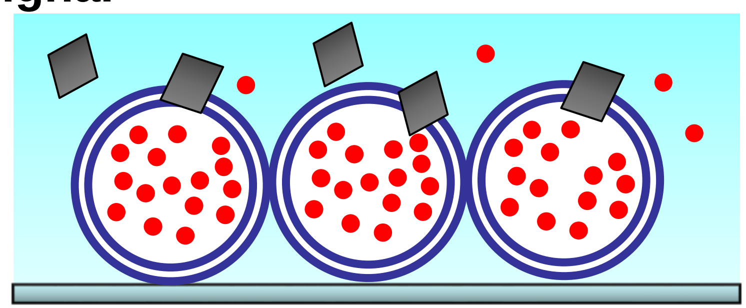
(B) **Buffer rinse to remove external dye**



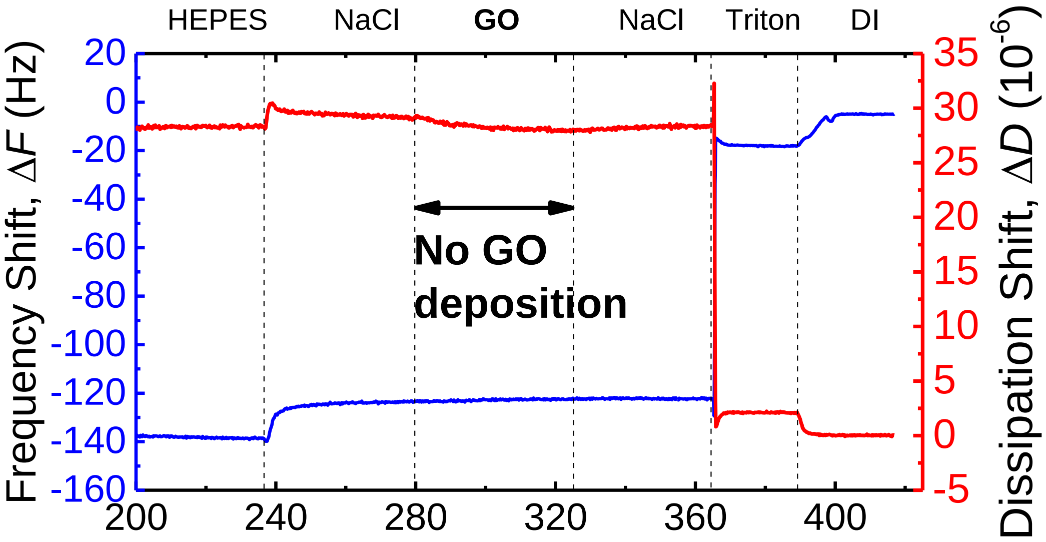
(C) **Introduce GO**



(D) **Monitor dye leakage and QCM-D signal**

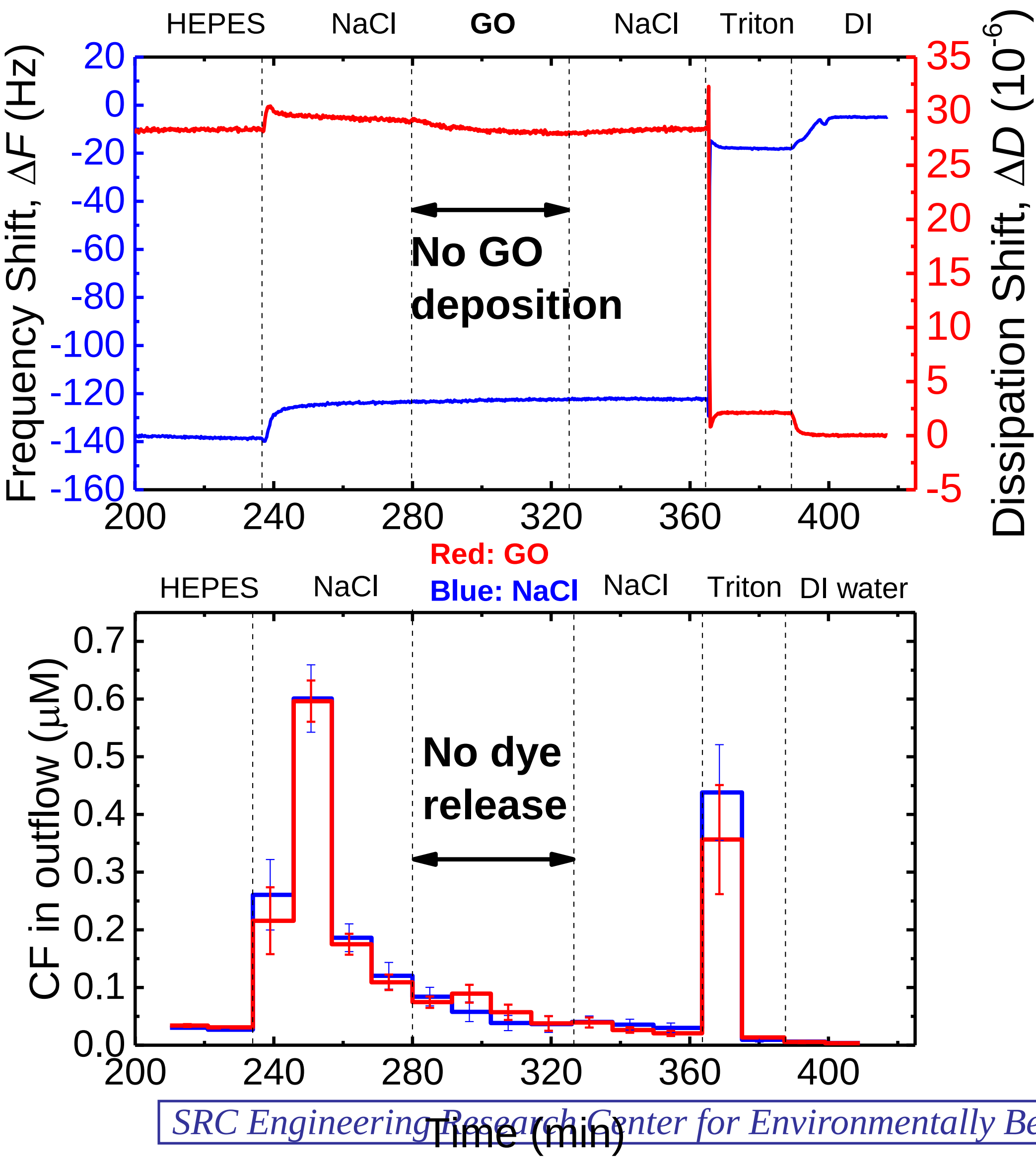


Exposure of Supported Vesicles to GO under Unfavorable Deposition Conditions



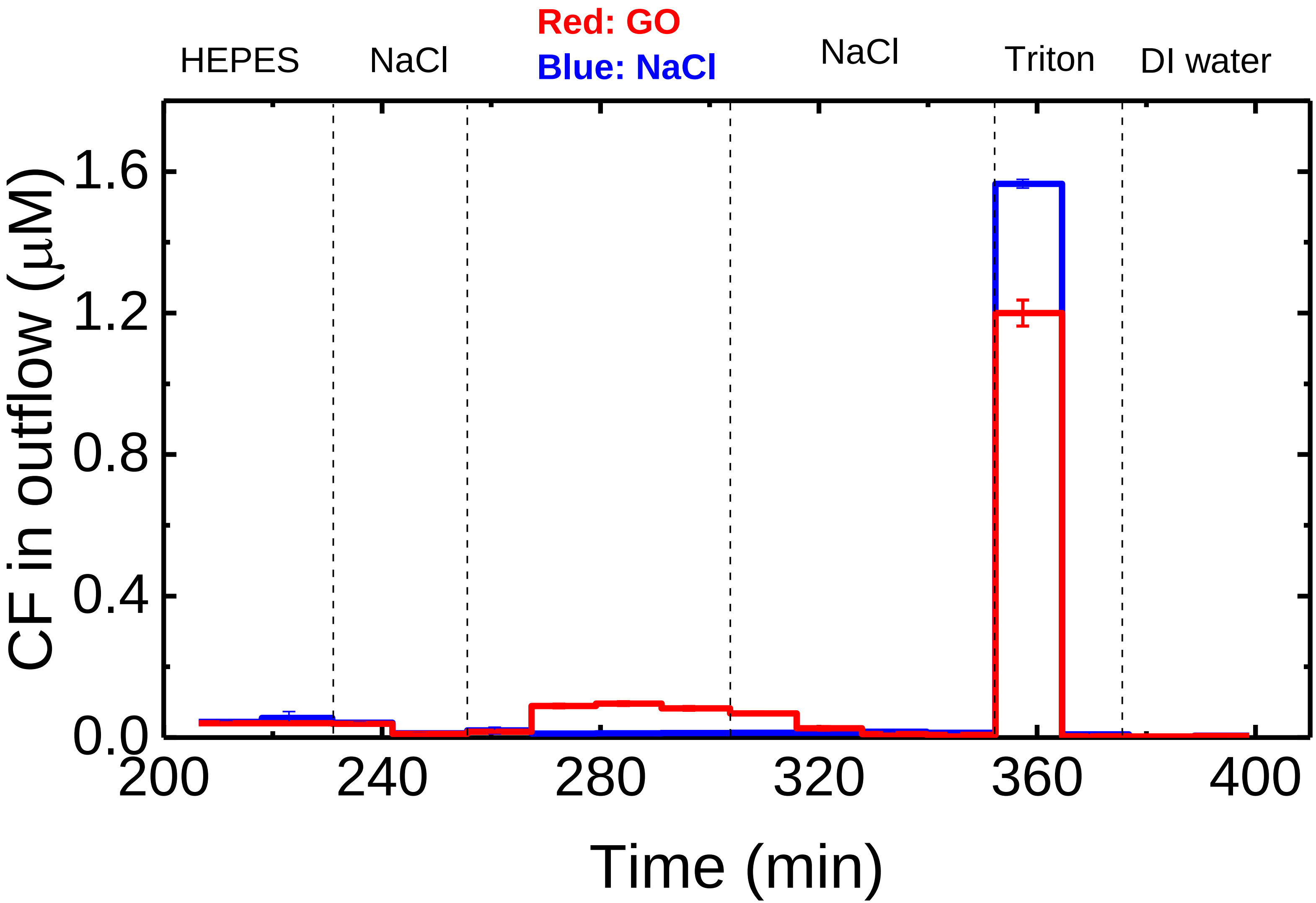
- **GO does not deposit on vesicles at 1 mM NaCl**

Exposure of Supported Vesicles to GO under Unfavorable Deposition Conditions



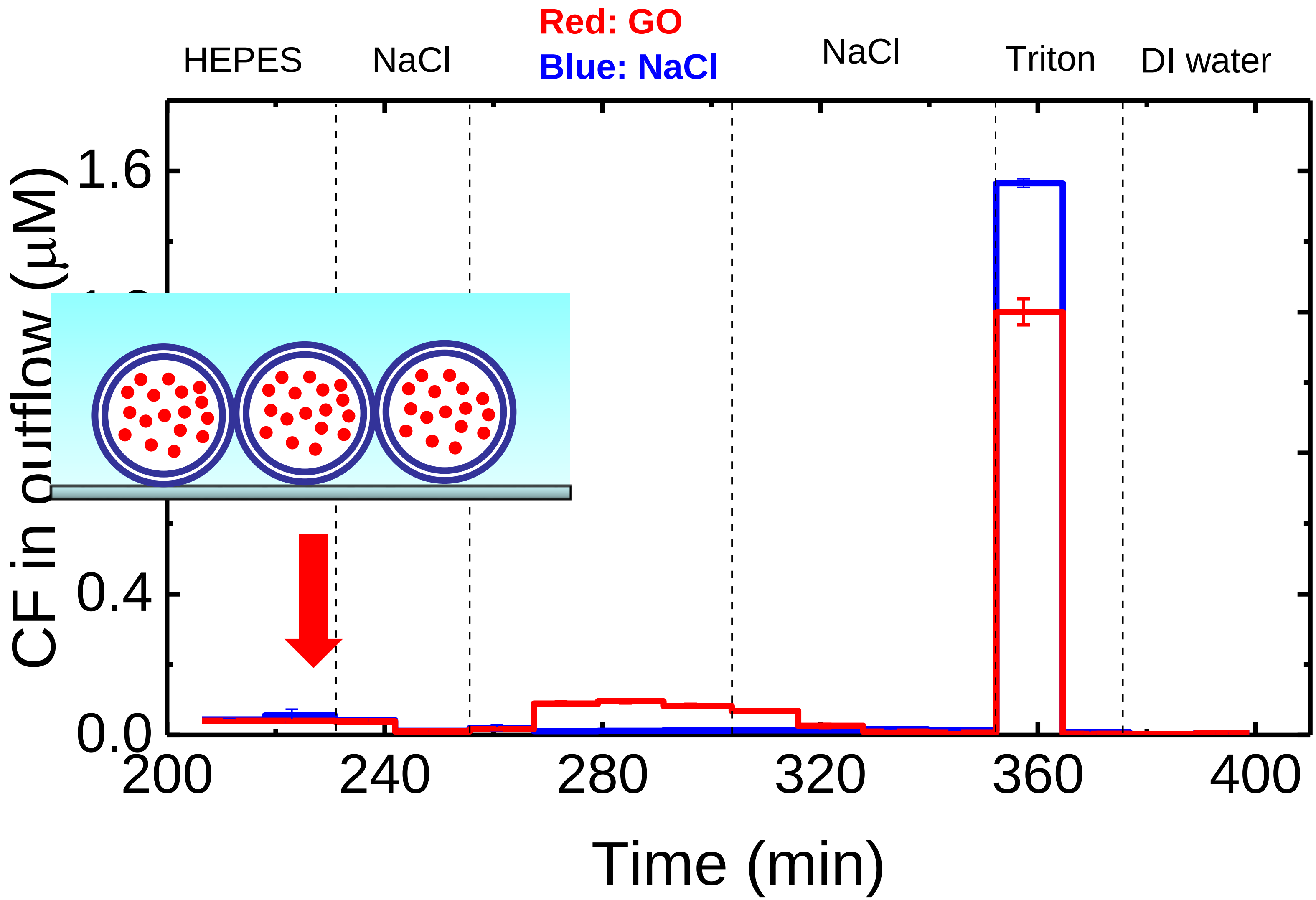
- GO does not deposit on vesicles at 1 mM NaCl
- Carboxyfluoresceine (CF)
- Emission at 517 nm
- No significant dye release when vesicles are exposed to GO

Exposure of Vesicles to GO at 150 mM NaCl

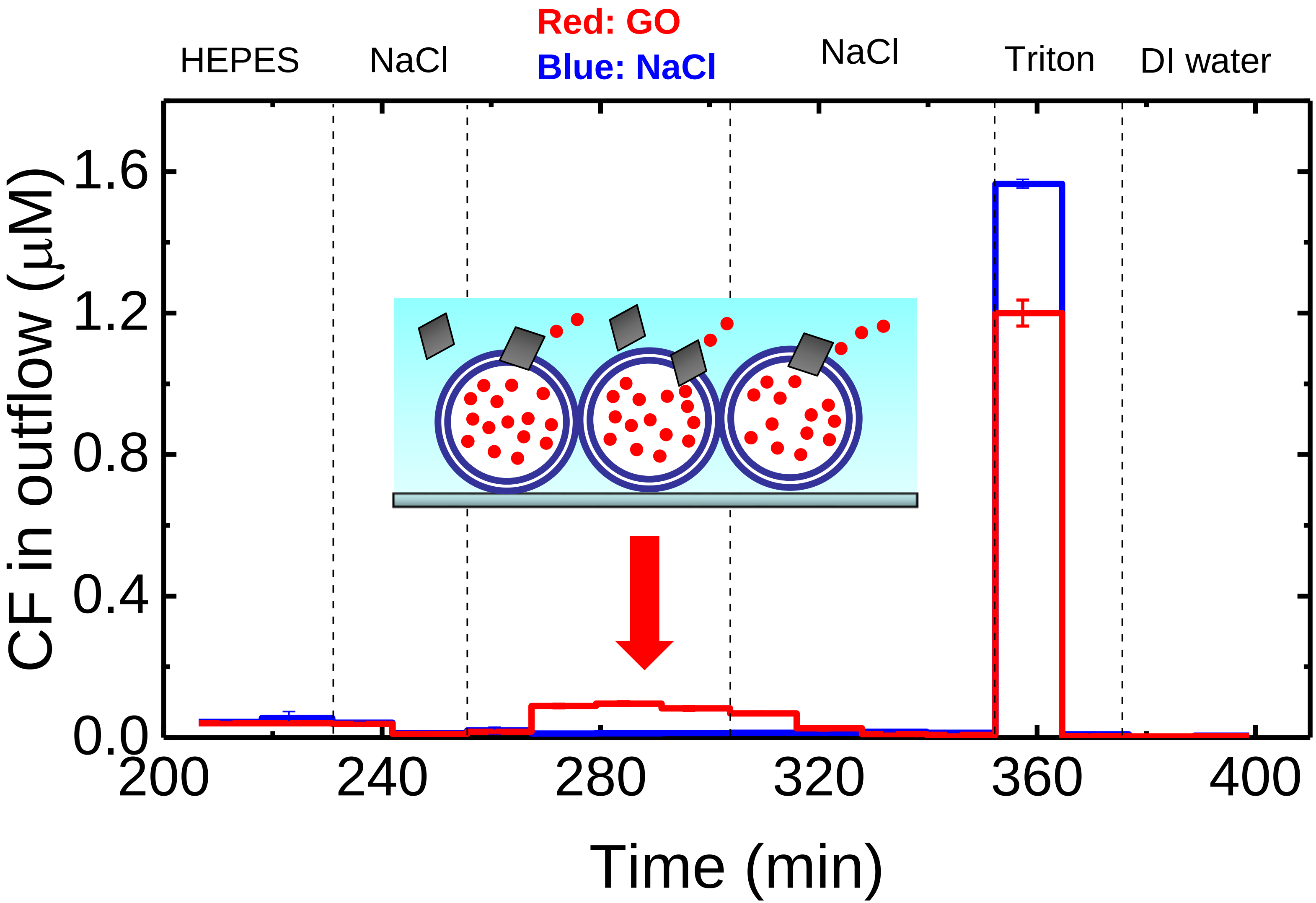


- **GO undergoes favorable deposition at 150 mM NaCl**

Exposure of Vesicles to GO at 150 mM NaCl

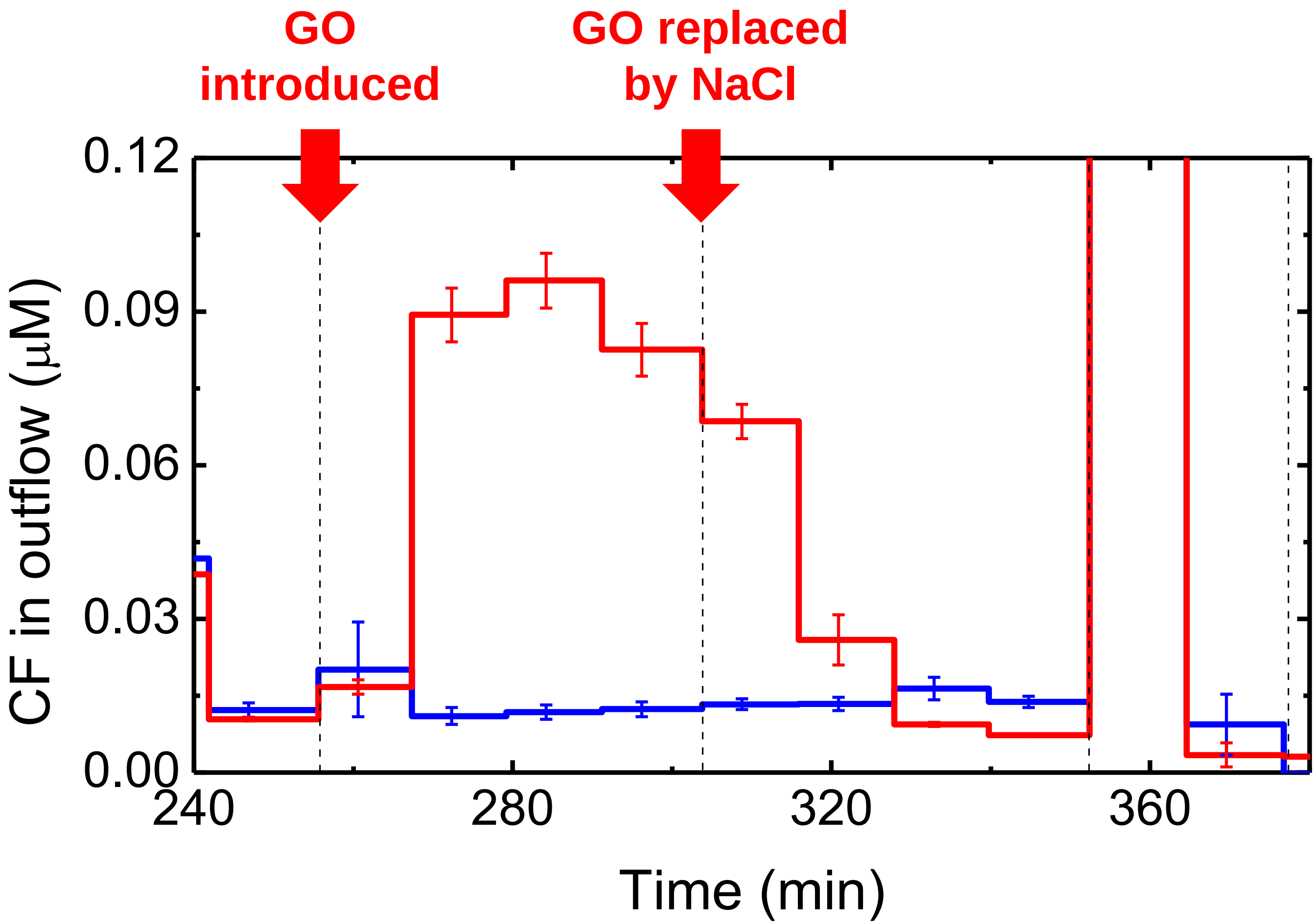


Exposure of Vesicles to GO at 150 mM NaCl



- Dye release upon exposure to GO at 150 mM NaCl

Exposure of Vesicles to GO at 150 mM NaCl



- **Dye release decreases when GO is replaced by NaCl solution, indicative of hole healing**

Summary of Current Findings

- **Deposition of carbon-based nanomaterials on model biological membranes is controlled by electric double layer interactions**
- **Nanoparticle–membrane interactions are strongly influenced by pH and electrolyte concentrations**
- **Favorable attachment is not observed at high NaCl concentrations possibly due to repulsive hydration forces**
- **GO resulted in some dye release from vesicles, likely due to hole formation on vesicles**
- **Holes on vesicles seem to heal in the absence of GO**

Industrial Interactions and Technology Transfer

- **Dr. Chen, together with the other PIs from the SRC ERC, have obtained representative CMP NPs from Cabot Microelectronics in order to investigate their propensity to attach to biological membranes**
- **Dr. Chen, together with the other PIs, have closely interacted with SRC industrial members (David Speed from IBM and Mansour Moinpour from Intel) regarding research progress**
- **SRC industrial members will be updated on the development of the QCM-D as a rapid and online binding assay for nanomaterials**
- **SRC industrial members will be informed of the types of CMP NPs that have a strong propensity to bind to cell membranes based on the research findings in Dr. Chen's lab**
- **Dr. Chen's group presented 3 ERC/SRC teleseminars**

Future Plans

Next Year Plans

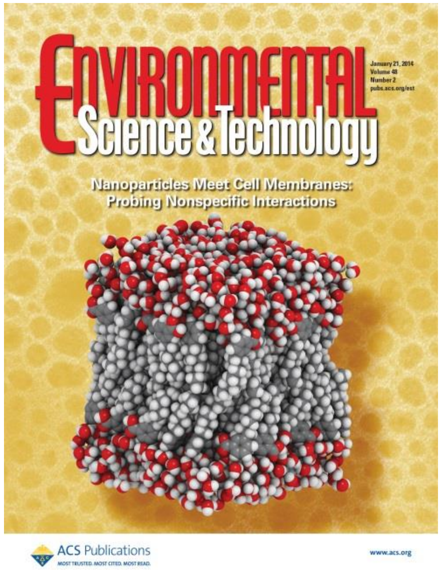
- Continue to investigate the propensity of GO and CMP NPs to penetrate or disrupt model biological membranes
- Develop a rapid assay using the QCM-D to evaluate the propensity of nanomaterials to disrupt biological membranes

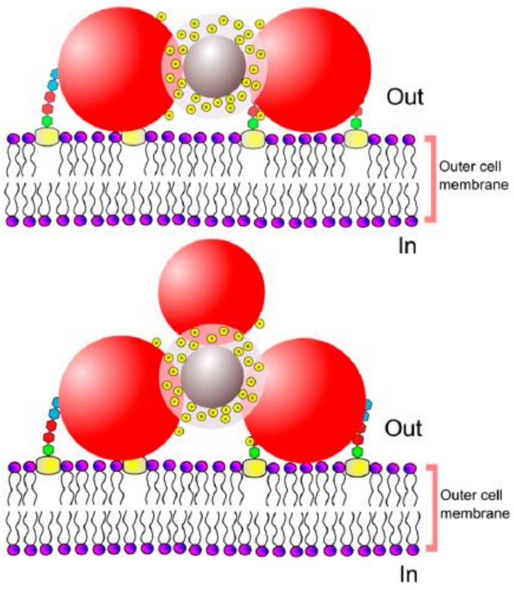
Long-Term Plans

- Examine the interactions of GO and CMP NPs with proteins and the effects of protein corona on NP interactions with model cell membranes

Publications, Presentations, and Recognitions/Awards

- **Publications**
  - **Four papers published in *Environmental Science & Technology*, including a feature article featured on the cover of *ES&T* , one paper published in *ES&T Letters*, and one in *Environmental Science: Processes and Impacts***
  - **One other manuscript just submitted**
- **Presentations**
  - **Dr. Chen has been invited to give talks at seven universities, IBM, ACS Meeting at San Francisco, and US Environmental Protection Agency**
  - **9 oral presentations at conferences**



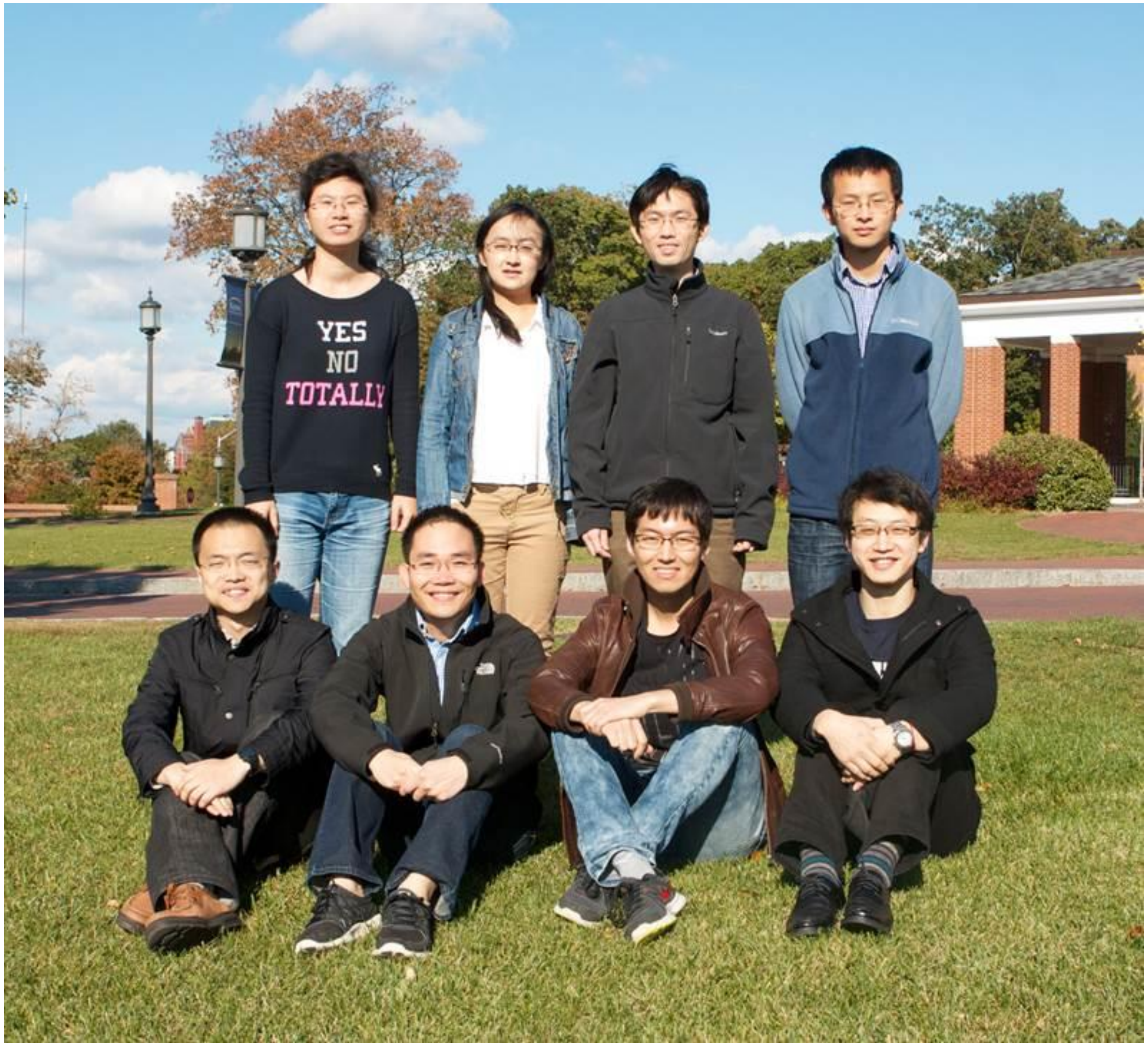


Huynh et al. *ES&T Letters,* 2014, 1, 361-366

Publications, Presentations, and Recognitions/Awards

- **Recognitions/Awards**
  - **Dr. Chen was invited to give a keynote talk at the International Water Association (IWA) Symposium on Environmental Nanotechnology in Nanjing, China**
  - **Peng Yi and Khanh An Huynh received the prestigious C. Ellen Gonter Environmental Chemistry Awards from the American Chemical Society Division of Environmental Chemistry**
  - **Khanh An Huynh and Xitong Liu received student awards from the Sustainable Nanotechnology Organization**
- **Students**
  - **2 Ph.D. students graduated: Peng Yi (2013) and Khanh An Huynh (2014)**
  - **1 MSE student graduated: Wenyu Gu (2013)**

Thank you!



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