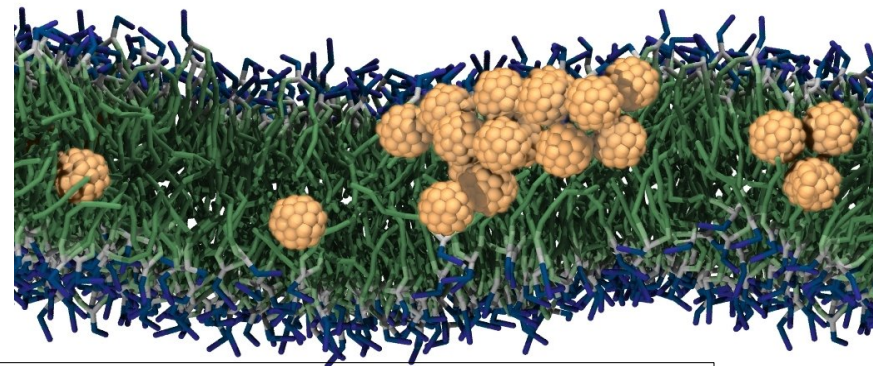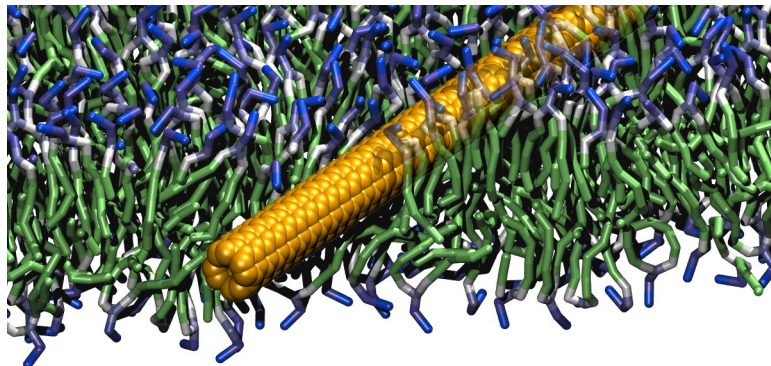# Computer Simulations of the Interaction between Carbon Based Nanoparticles and Biological Systems

Chi-cheng Chiu
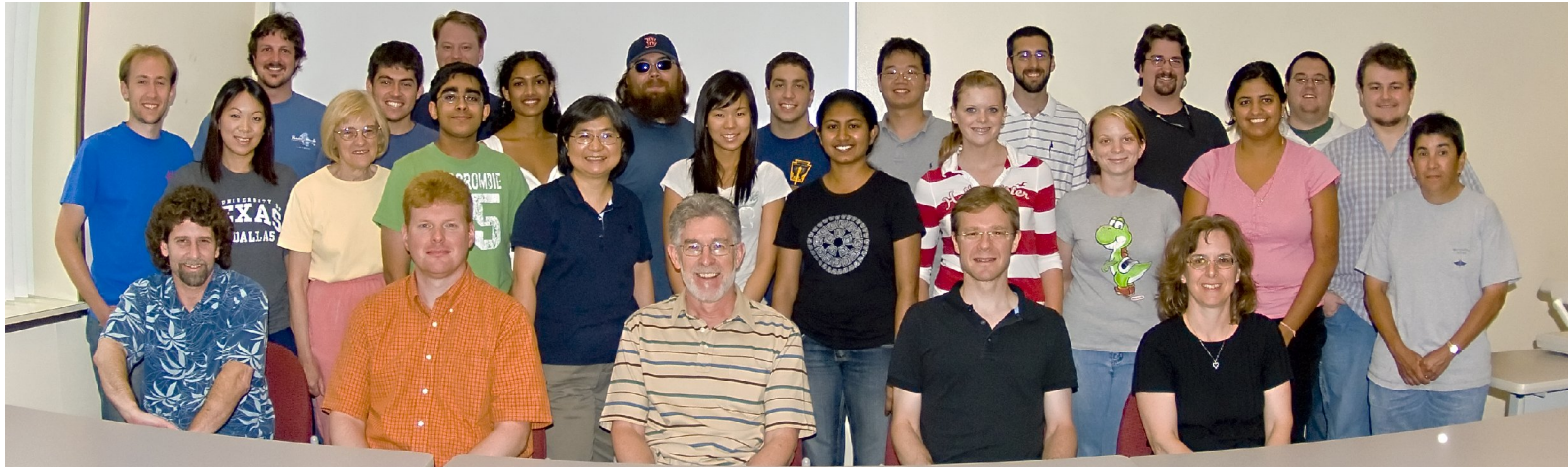The University of Texas at Dallas
12/11/2009

BioNanoSciences Group
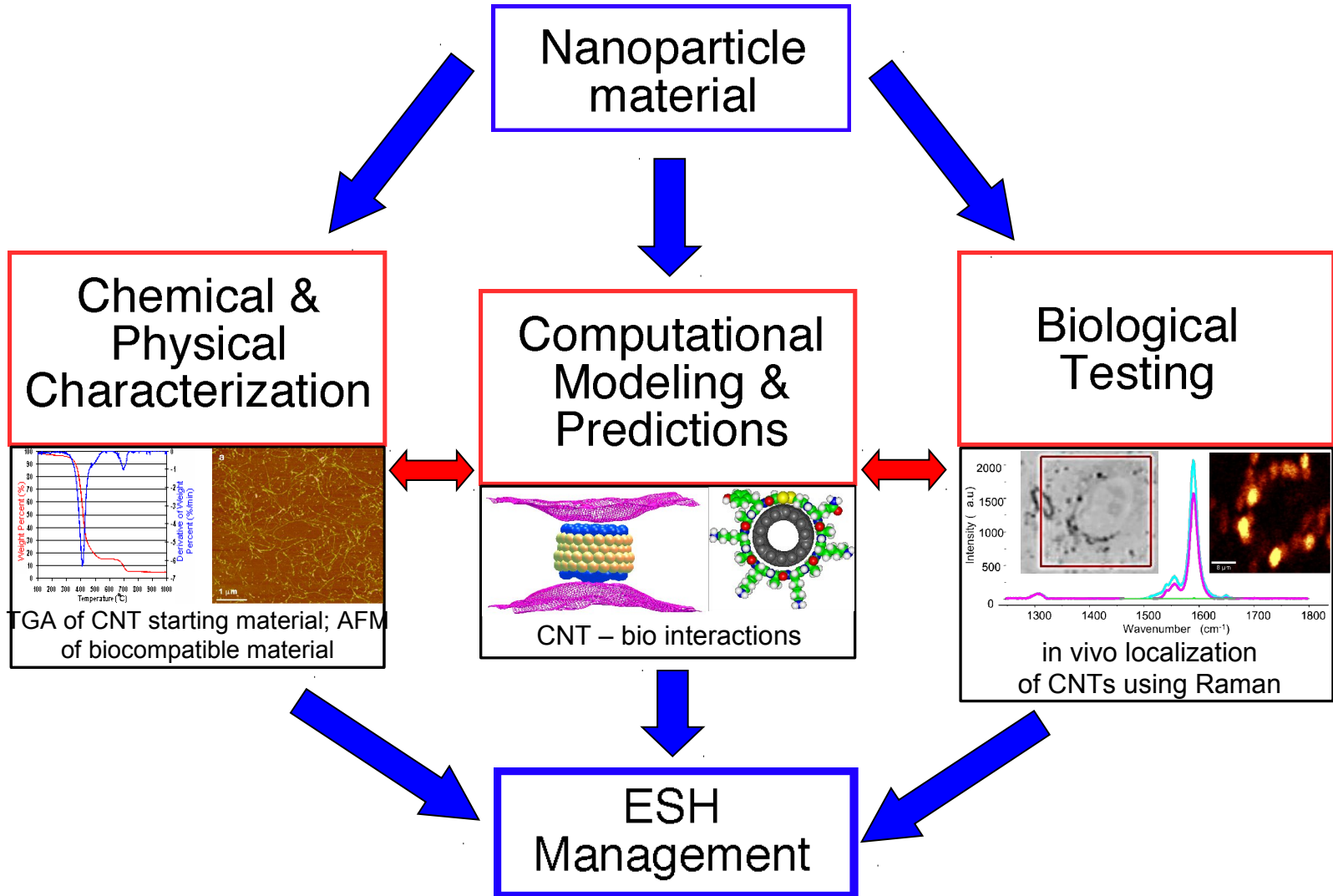# The University of Texas at Dallas

- PI: Pantano, Dieckmann, Draper, Nielsen, Musselman

- Wide range of expertise : analytical chemistry, cell biology, surface chemistry, computational chemistry, etc.

Accelerating the next technology revolution.

SRC/SEMATECH Engineering Research Center for Environmentally Benign Semiconductor Manufacturing

Predicting, Testing, and Neutralizing Nanoparticle Toxicity

Nanoparticle material

Chemical & Physical Characterization

TGA of CNT starting material; AFM of biocompatible material

Computational Modeling & Predictions

CNT – bio interactions

Biological Testing

in vivo localization of CNTs using Raman

ESH Management

Outline

- Introduction
    - Background
    - Simulation Method
- C_{60} with lipid bilayer
- Carbon Nanotube with lipid bilayer
    - Carboxylation
    - Diameter dependence
    - Multi-walled vs Single-walled
- Conclusion
- Future plan

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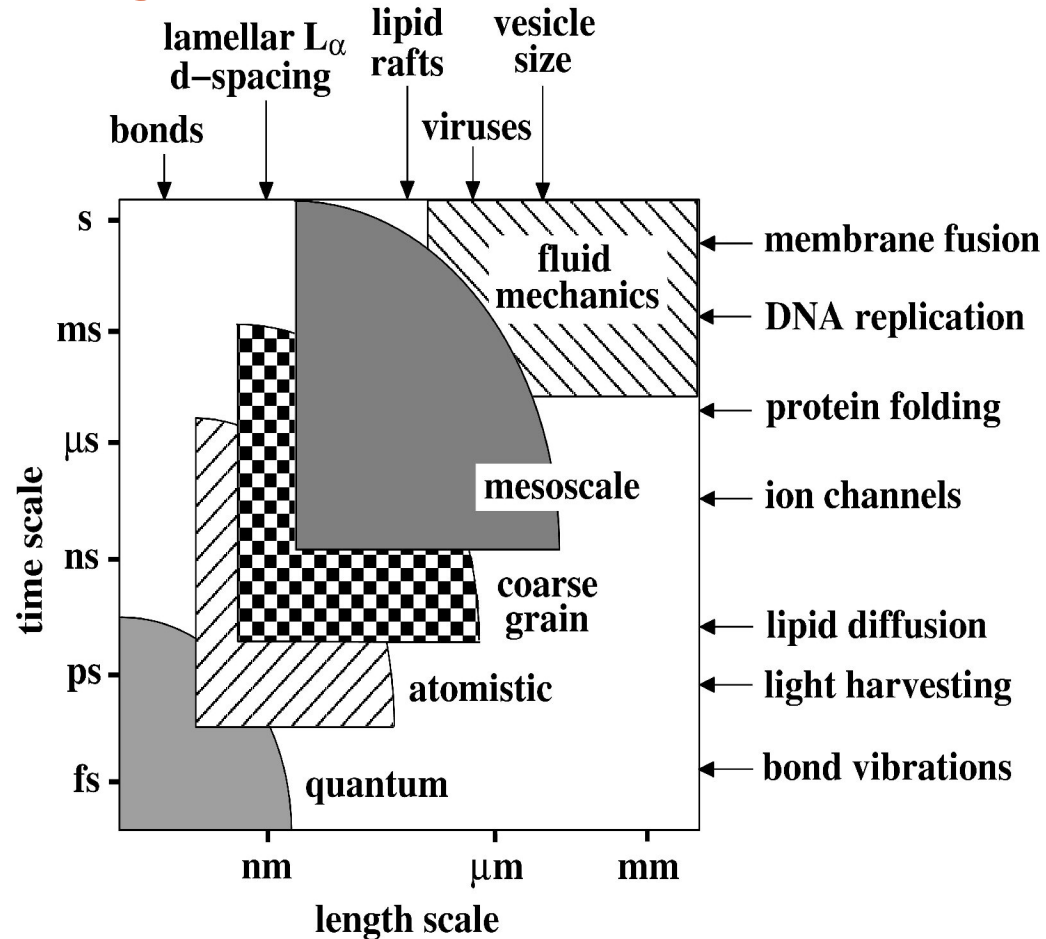
Introduction

- Increased attention about the environmental, health, and safety implications of nanomaterials.

- Carbon based nanoparticles (CNPs) :

    - C_{60} (buckyball)

    - single / multi walled carbon nanotubes (SWNT/MWNT)

    - graphene

    - enormous potential applications in nanoelectronics

- To interact with living organism, CNPs may cross a membrane barrier
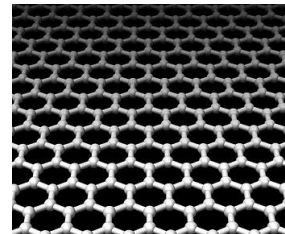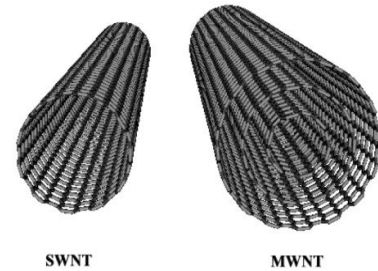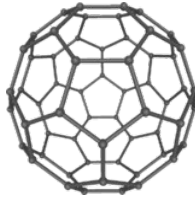
Study the interaction between CNPs and a biological membrane

- Difficult to study biological membranes at molecular level

- Experimental problem :
  - easily perturbed heterogeneous system
  - i.e. membrane proteins

- Computational problem :
  - ***time and size scales***
  - ***realistic models*** for biological systems
  - Recent review: Monticelli et al. Soft Matter, 2009, 5, 4433-4445

S. O. Nielsen et. al., J. Phys.: Condensed Matter 16, R481 (2004)

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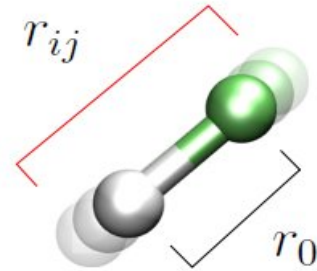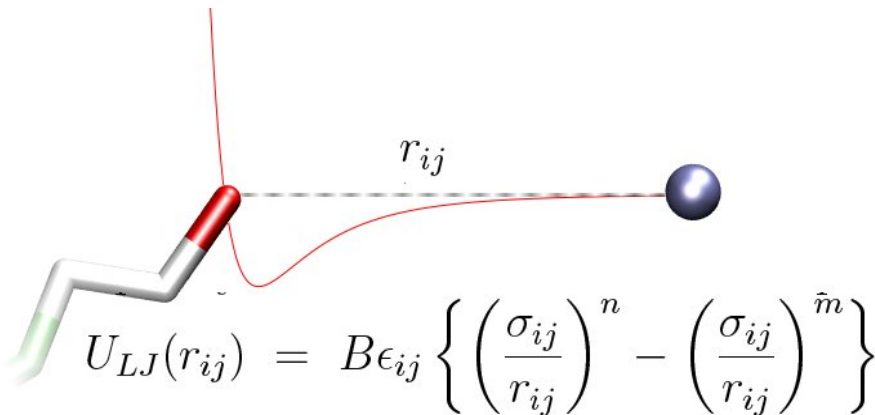
Computer Simulations
– Molecular Dynamics (MD)

- The energy of chemical structures, in combination with statistical mechanics, allows for, in principle, all properties of a system to be calculated.

- Calculate intermolecular forces → microscopic dynamics → macroscopic properties

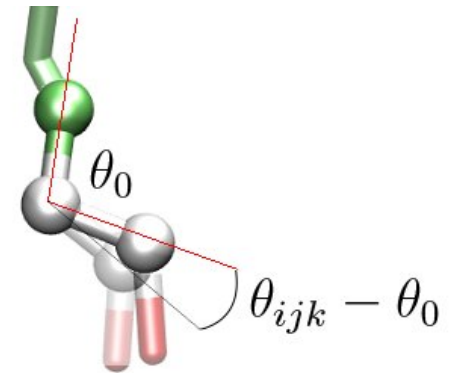- Used in drug design, atomic layer etching, FIB processing

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Force Field

$$U = U_{bonded} + U_{non-bonded}$$

$$U_{bonded} = U_{bond} + U_{bend} + ...$$

$$U_{non-bonded} = U_{LJ} + U_{elec}$$

$$U_{LJ}(r_{ij}) = B\epsilon_{ij}\left\{\left(\frac{\sigma_{ij}}{r_{ij}}\right)^n - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{\tilde{m}}\right\}$$

$$U_{bonds}(r_{ij}) = k_b(r_{ij} - r_0)^2$$

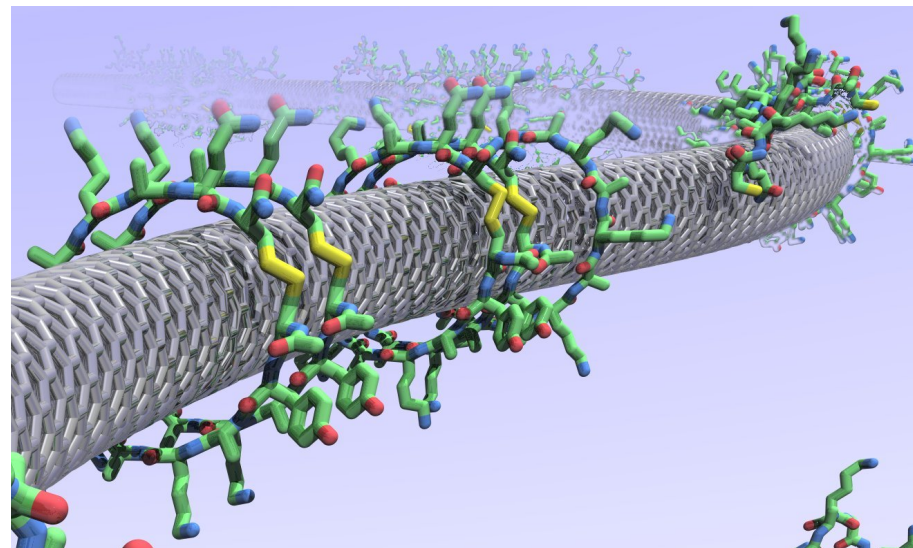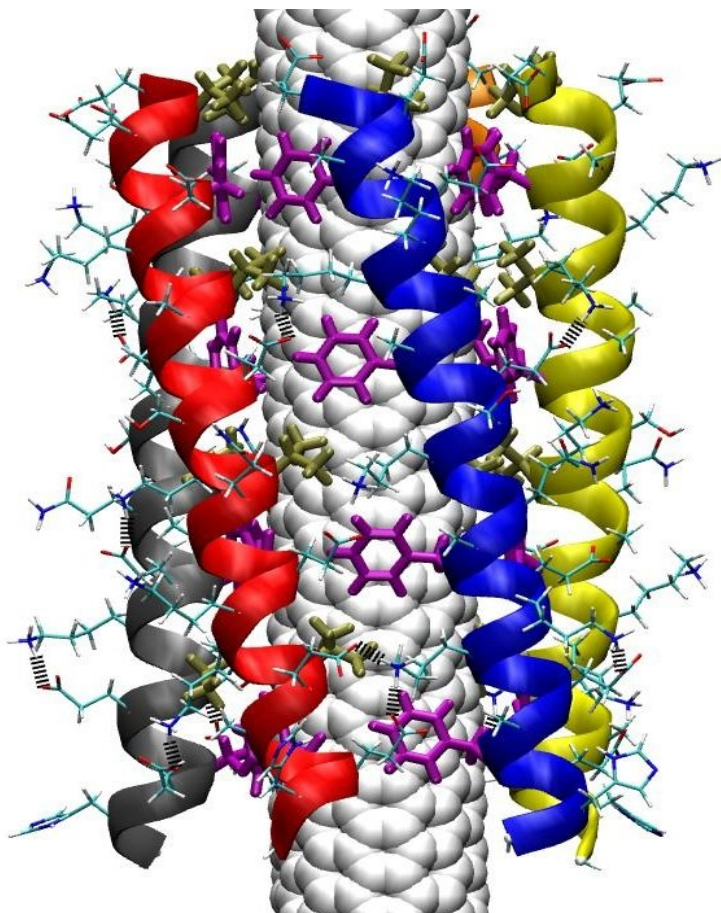$$U_{bends}(r_{ijk}) = k_\theta(\theta_{ijk} - \theta_0)^2$$

- Force field (FF) :
  - uses simple mathematical functions to treat the structure-energy relationship
  - validated against physical properties

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Previous BioNano MD Studies
Carbon Nanotube
Non-covalent Functionalization

- CNT functionalization
- CNT surface modification
- Atomistic MD
- No membrane involved

Chiu et al. J Phys Chem B 2008, 112, 16326
Chiu et al. Biopolymers: Peptide Science 2009, 92, 156   Chiu et al. AcsNano submitted

Coarse-Grain Molecular Dynamics

- Coarse-Grain (CG) MD :
  - reduced number of particles
  - larger system, longer simulation time
- CG force field developed by Shinoda et al. (AIST, Japan)
- Parameterized against experimental and atomistic simulation data
  - Surface tension
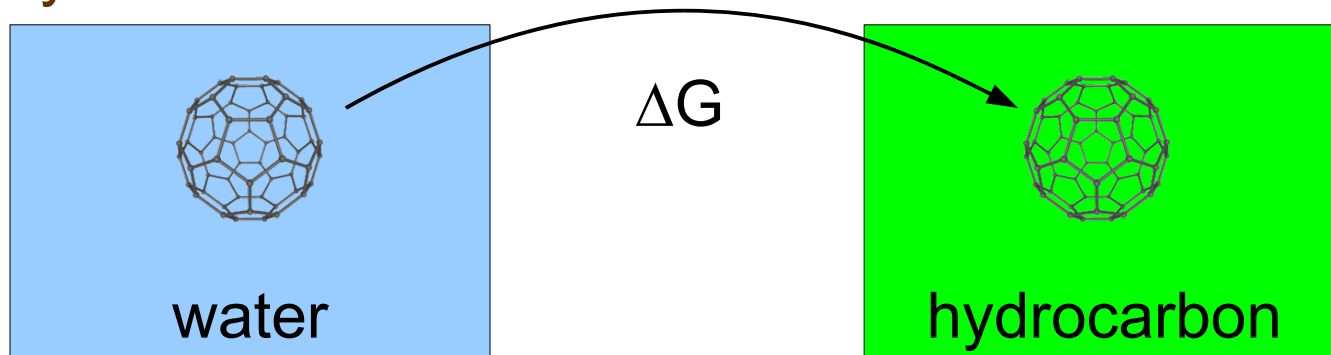 - Transfer free energy
  - Membrane structural data

Shinoda et al. Mol Simul. 2007, 33, 27
Devane et al. J. Chem. Theory Comput. 2009, 5, 2115
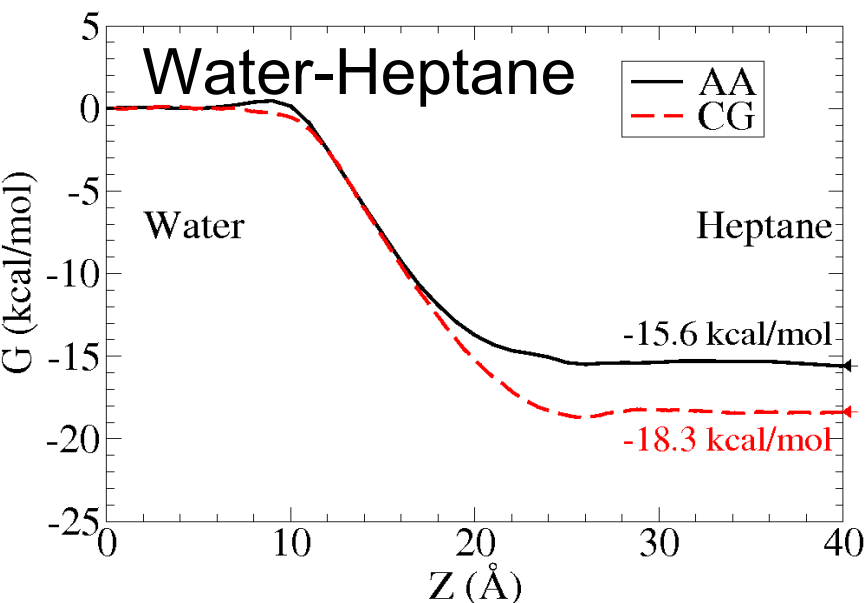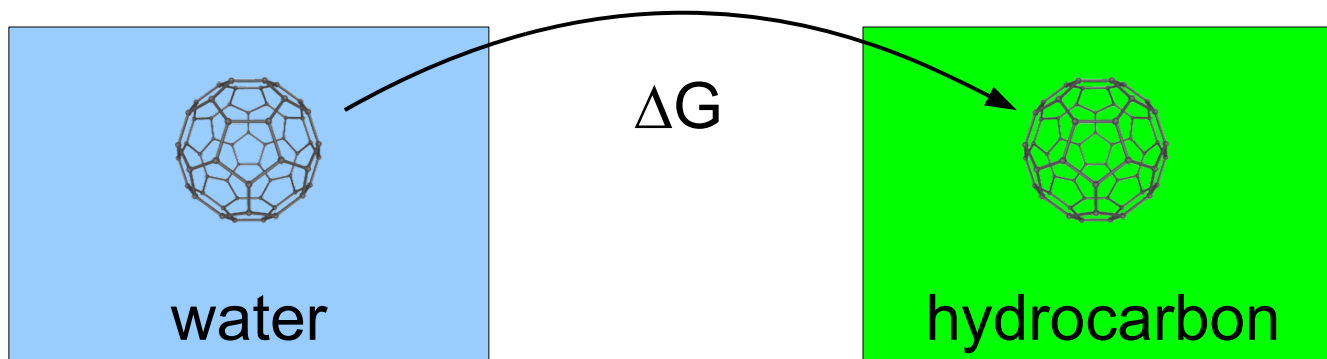Shinoda et al. Soft Matter 2008, 2454, 4

head

tail
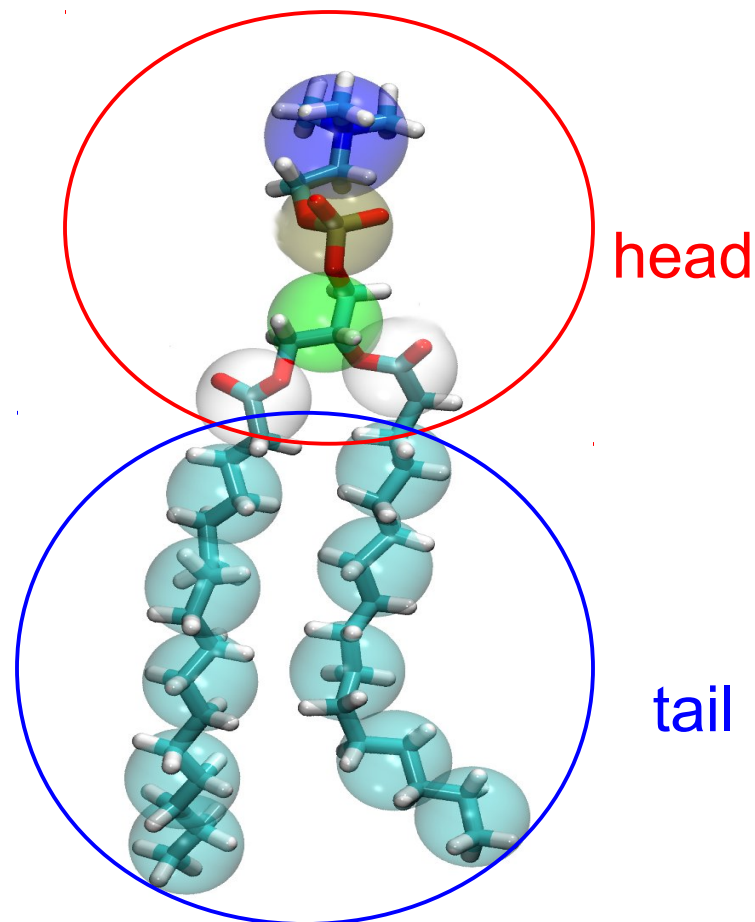
Dipalmitoylphosphatidylcholine (DPPC)

CG model for C_{60}

- Based on the CG force field, we developed a CG model for C_{60}

- Validate the model against experimental and atomistic simulation data

- Transfer free energy

- Aggregation behavior

- Simple model for the membrane system:
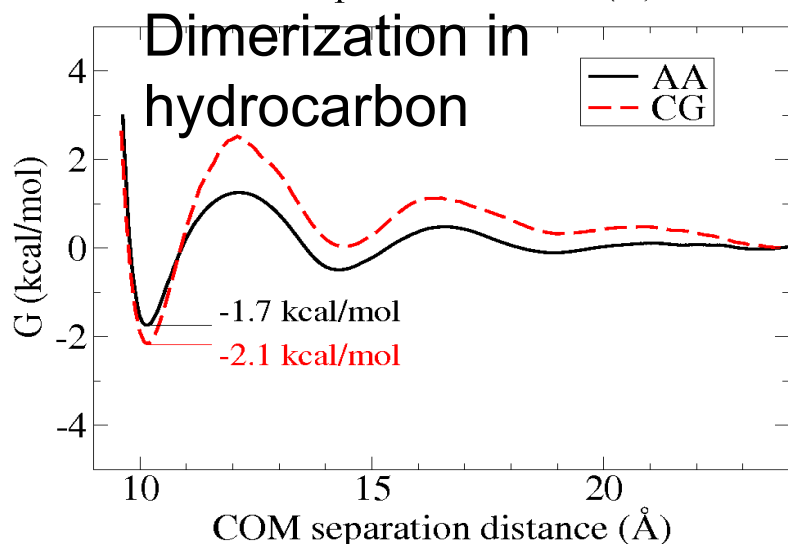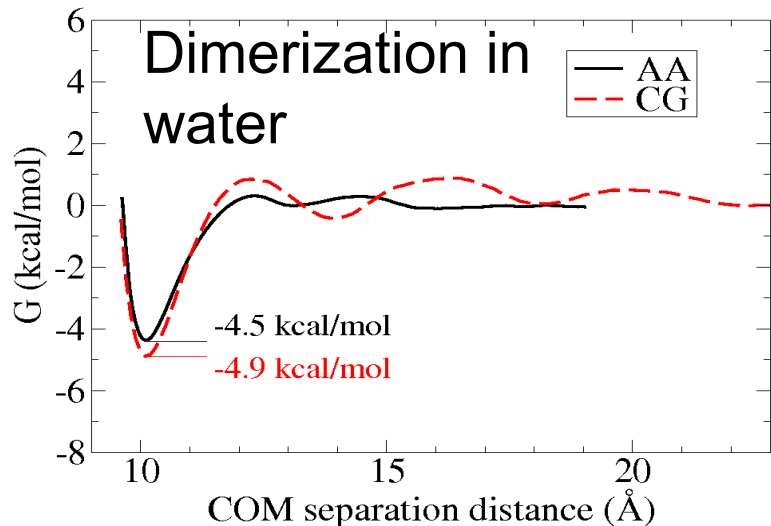   - Water
    - Hydrocarbon

ΔG

water

hydrocarbon

C$_{60}$ CG model validation (individual C$_{60}$)

water

hydrocarbon

ΔG

Water-Heptane

- AA
- - - CG
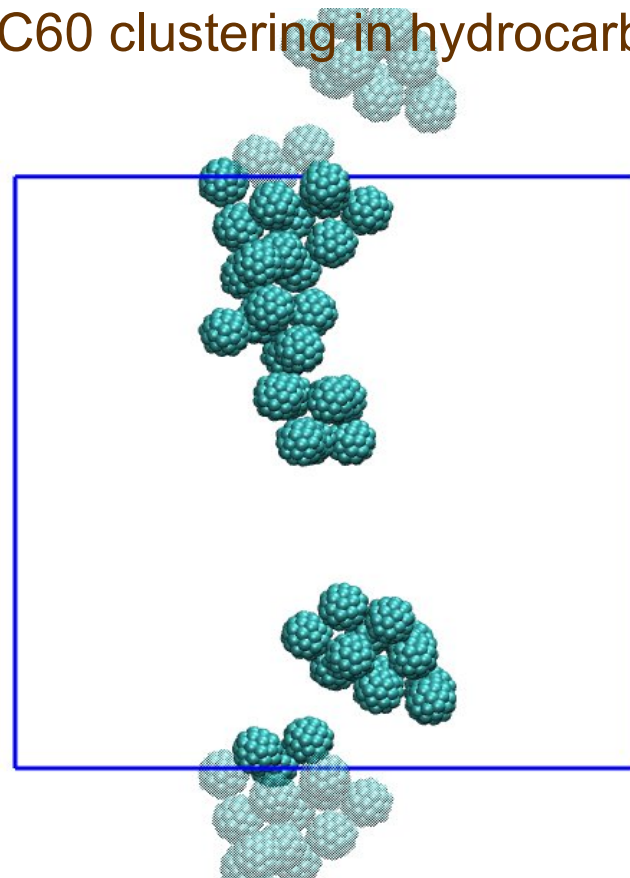
Water

Heptane

-15.6 kcal/mol

-18.3 kcal/mol

- **Water - Heptane transfer free energy**
  - No reliable experimental data on C$_{60}$ solubility in water
  - Compared with atomic simulations (AA)
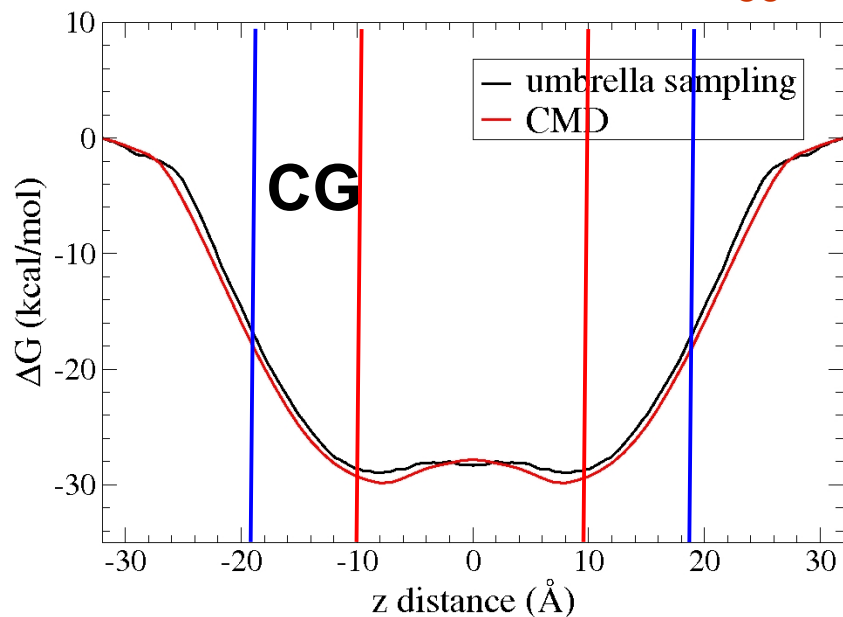
Validation of C_{60} aggregation

Dimerization in water

Dimerization in hydrocarbon

-4.5 kcal/mol
-4.9 kcal/mol

-1.7 kcal/mol
-2.1 kcal/mol

- C60 dimerization free energy in water and in hydrocarbon

- Compare with atomistic simulation

- C60 clustering in hydrocarbon

Li, L. et al Physical Review E 2005, 71, 011502
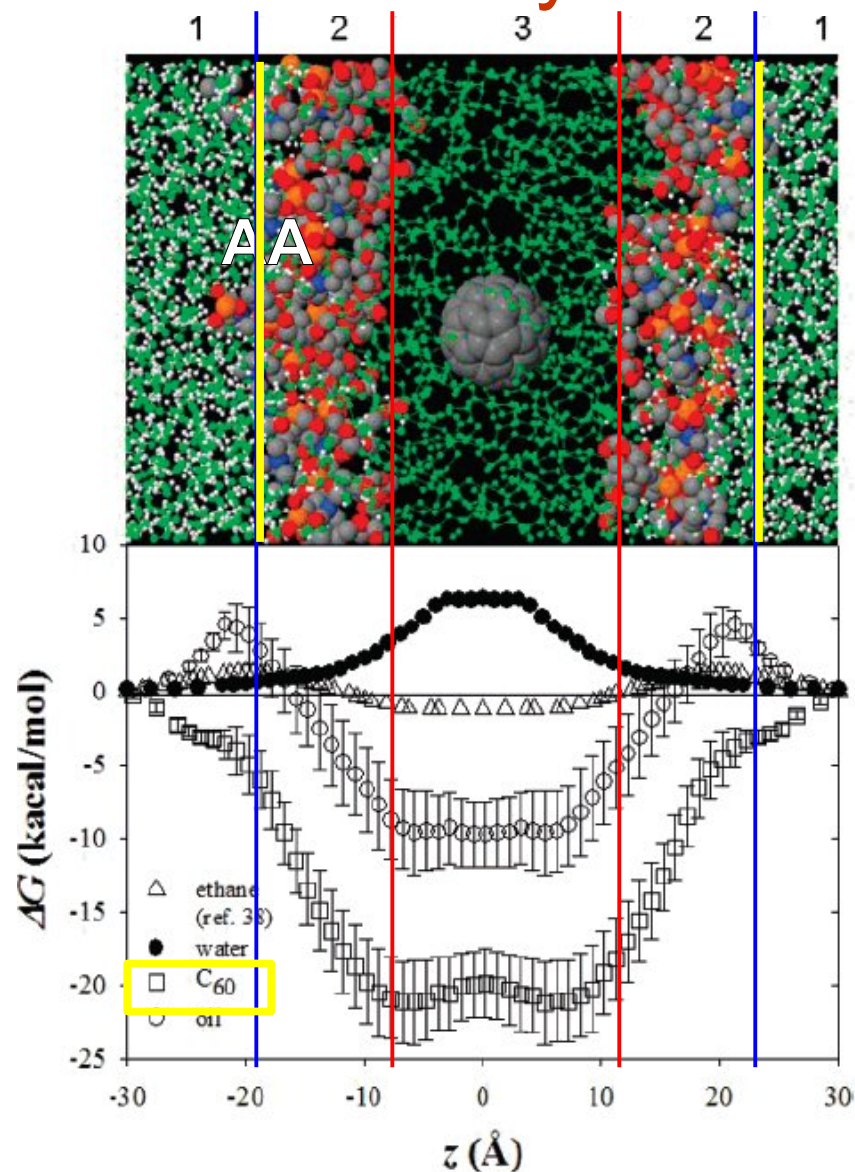Li et al J Phys Chem B 2007, 111, 4067

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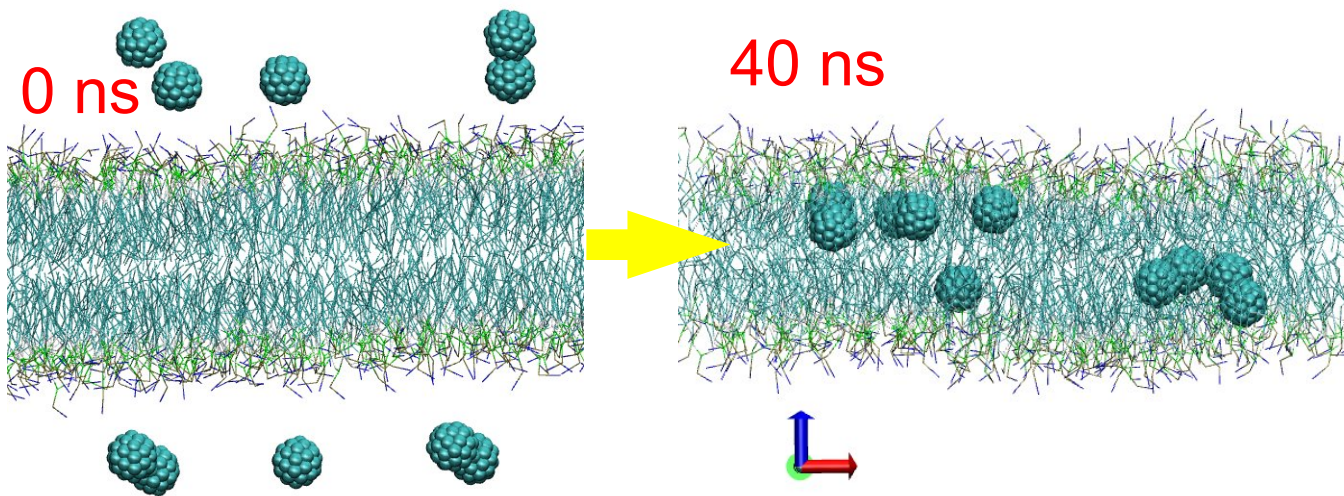
Individual C_{60} with DPPC bilayer

- The free energy profile is similar to the reported all-atom result

Li et al J Phys Chem B 2008, 112, 2078
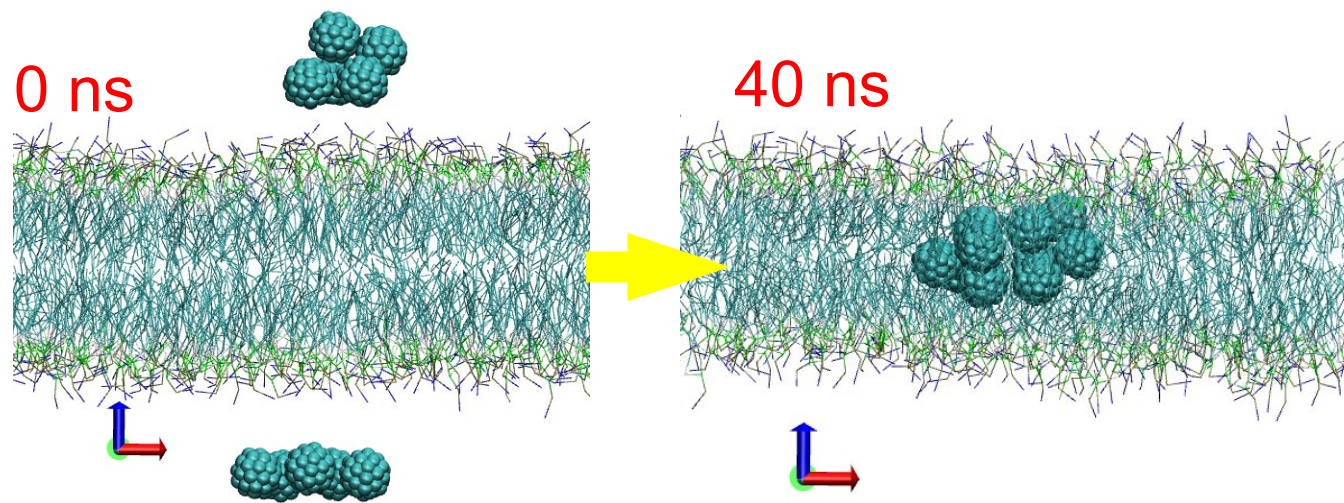
Aggregation of C_{60} in DPPC Lipid Bilayer

0 ns

40 ns

- Two different initial conditions
- C_{60} form clusters inside a bilayer
- Aggregation may affect toxicity

0 ns

40 ns

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CG model for carbon nanotube

- Given the validation of the C_{60} CG model, we applied the model to CNTs

- Aggregation / bundling behavior in water

- Aggregation may affect toxicity

- Different degree of carboxylation

- Dimerization free energy
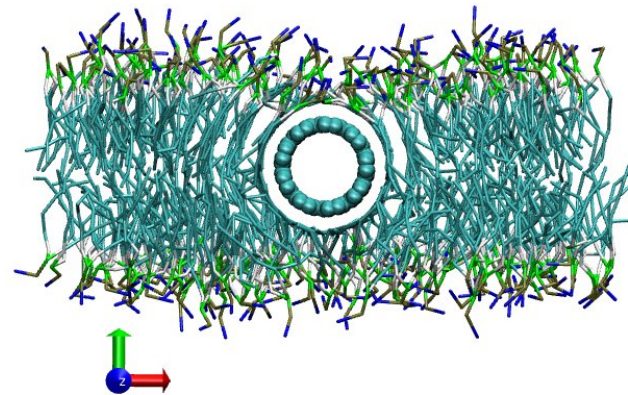
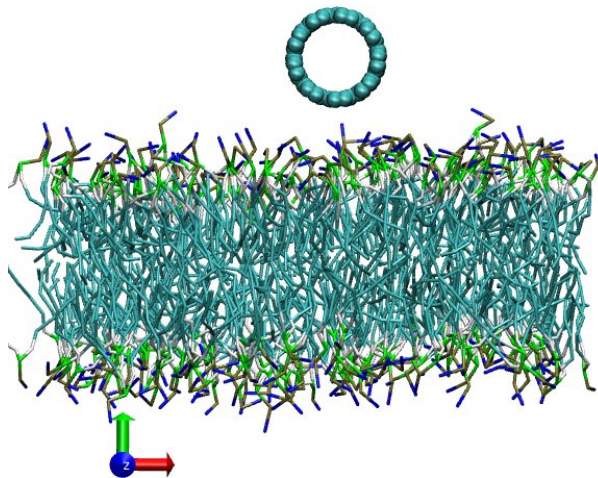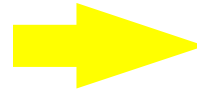$$\Delta G_{dimer}$$
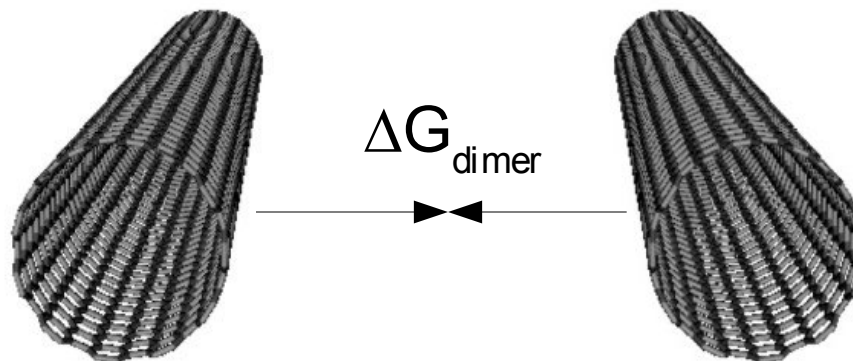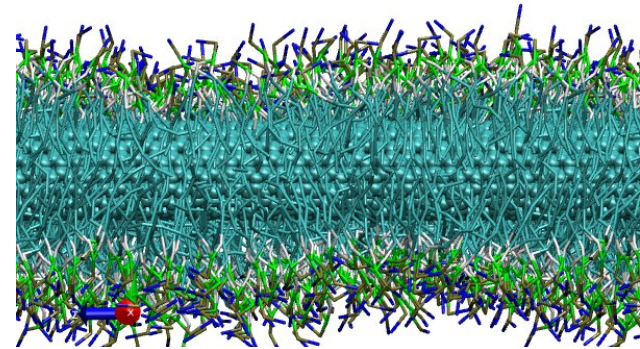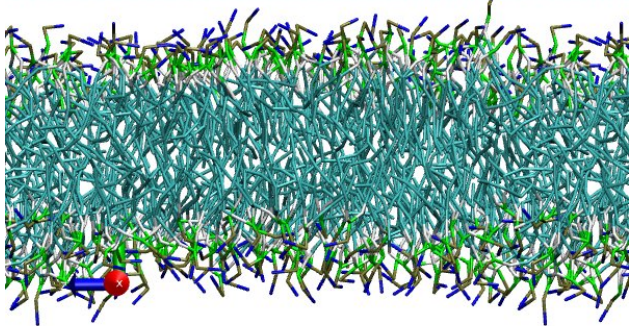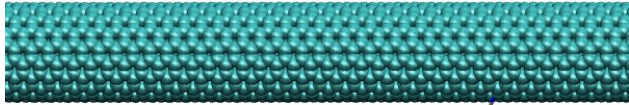
Carboxylated SWNT Bundling in Water
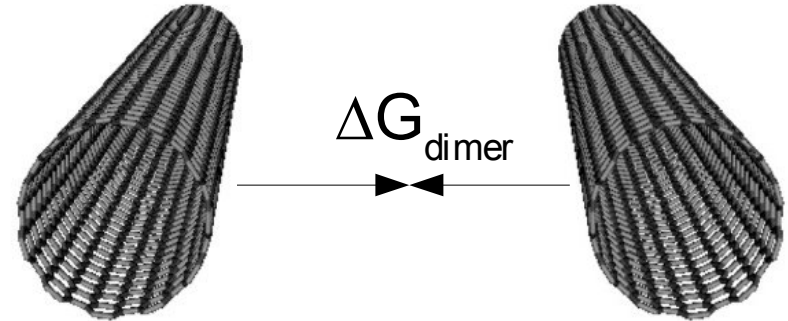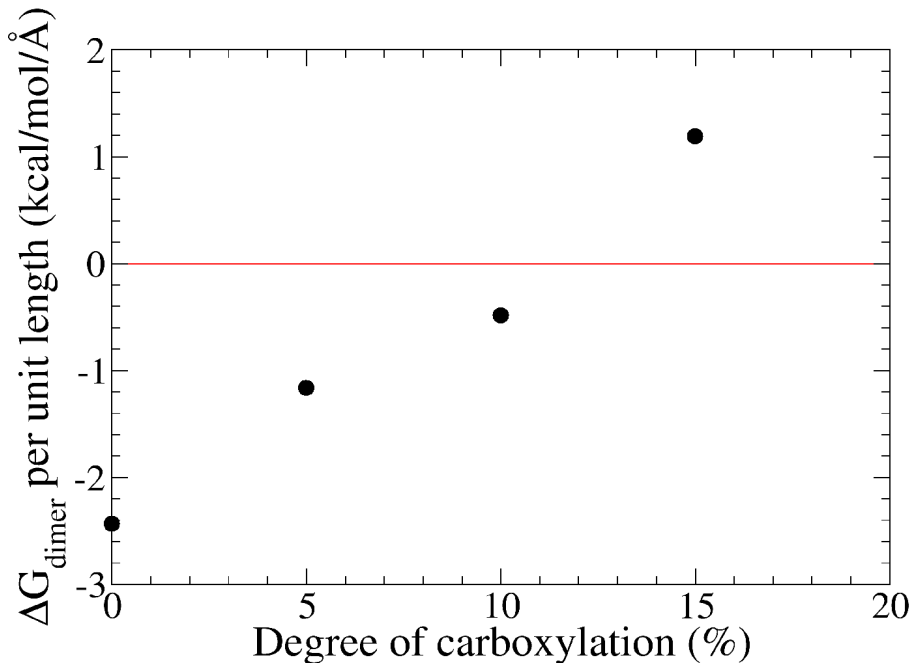
- Use aspartic acid (ASP) or glutamic acid parameters to functionalize the SWNT to represent carboxylated SWNT

- 5%, 10%, 15% functionalize SWNT
- Agrees with experimental data (from PI Dr. Musselman)

Bajaj, P. M.S. Thesis, The University of Texas at Dallas, Richardson, TX, 2008

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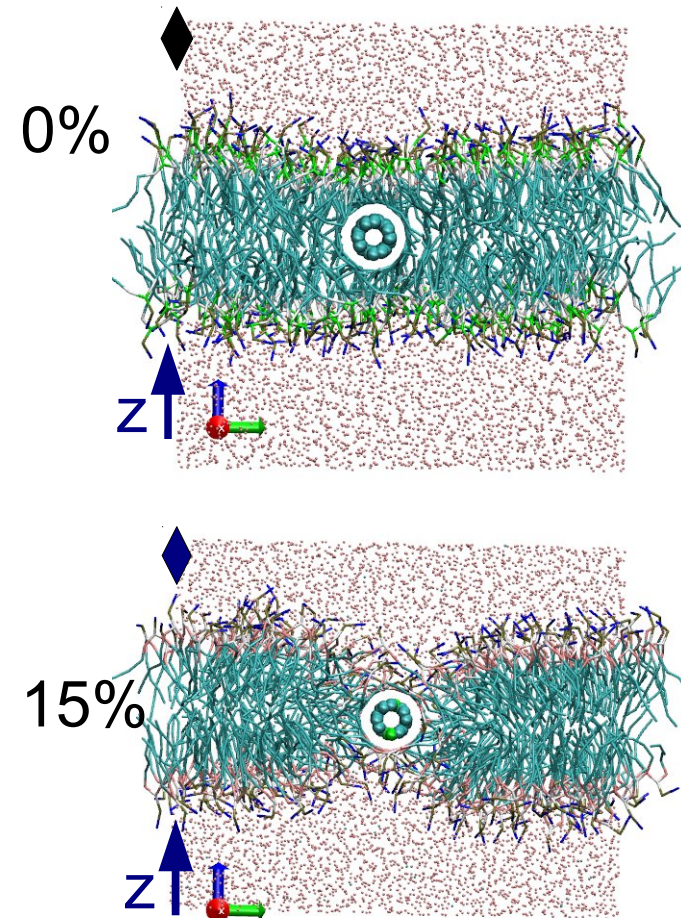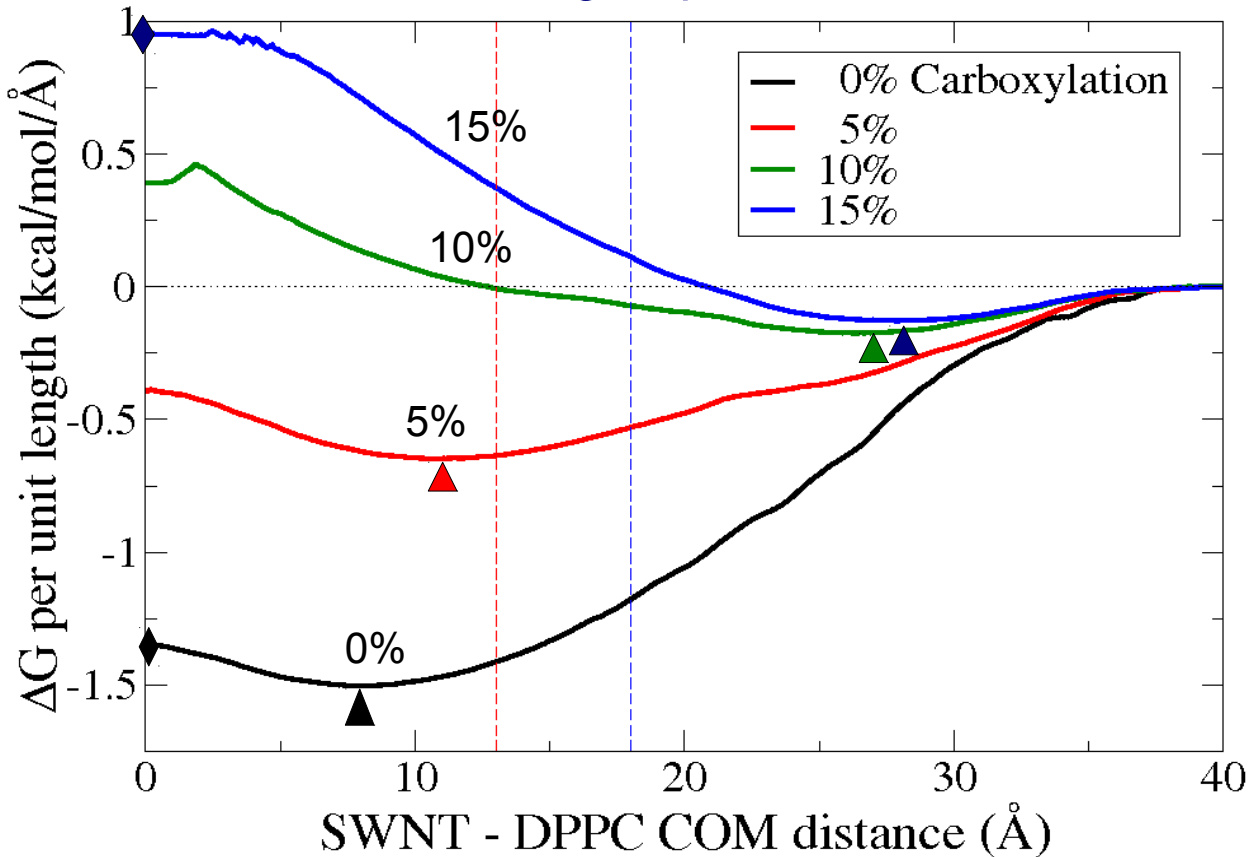
CNT interacting with DPPC bilayer

- NT radius = 7.48Å

- 10 ns simulation

SWNT/DPPC Lipid Bilayer

- Water – bilayer transfer free energy
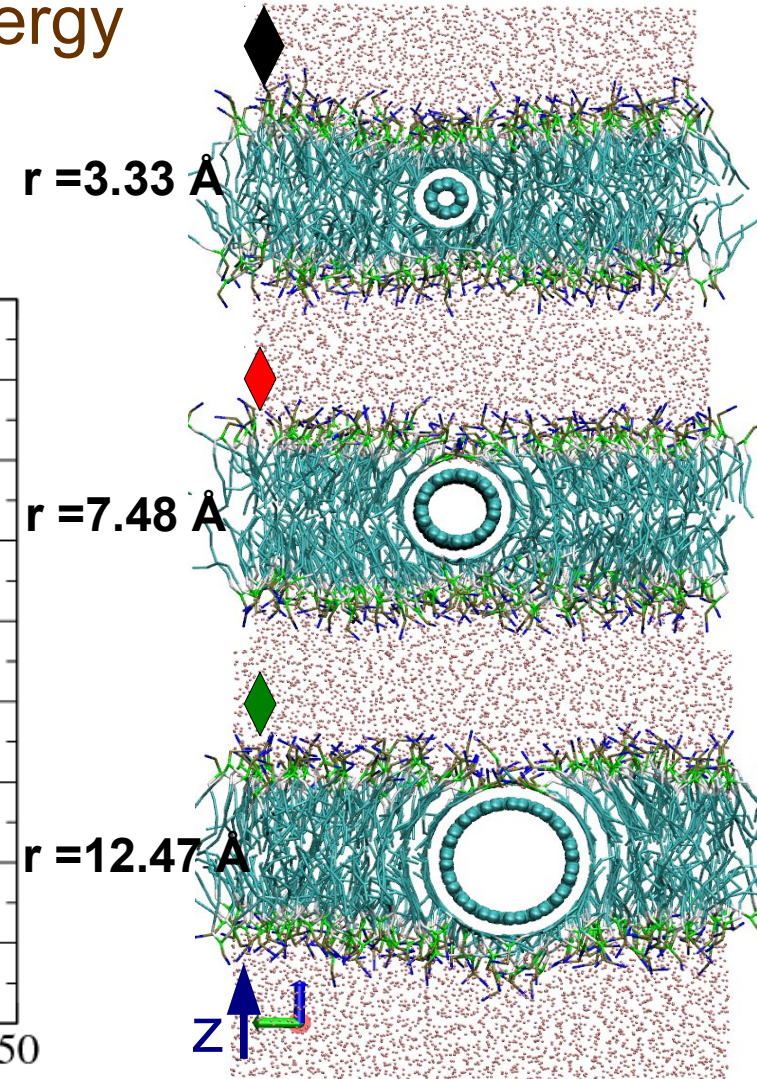
- Different degree of carboxylation

- r = 3.33 Å

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SWNT/DPPC Lipid Bilayer

- Water – bilayer transfer free energy
- Different NT diameter

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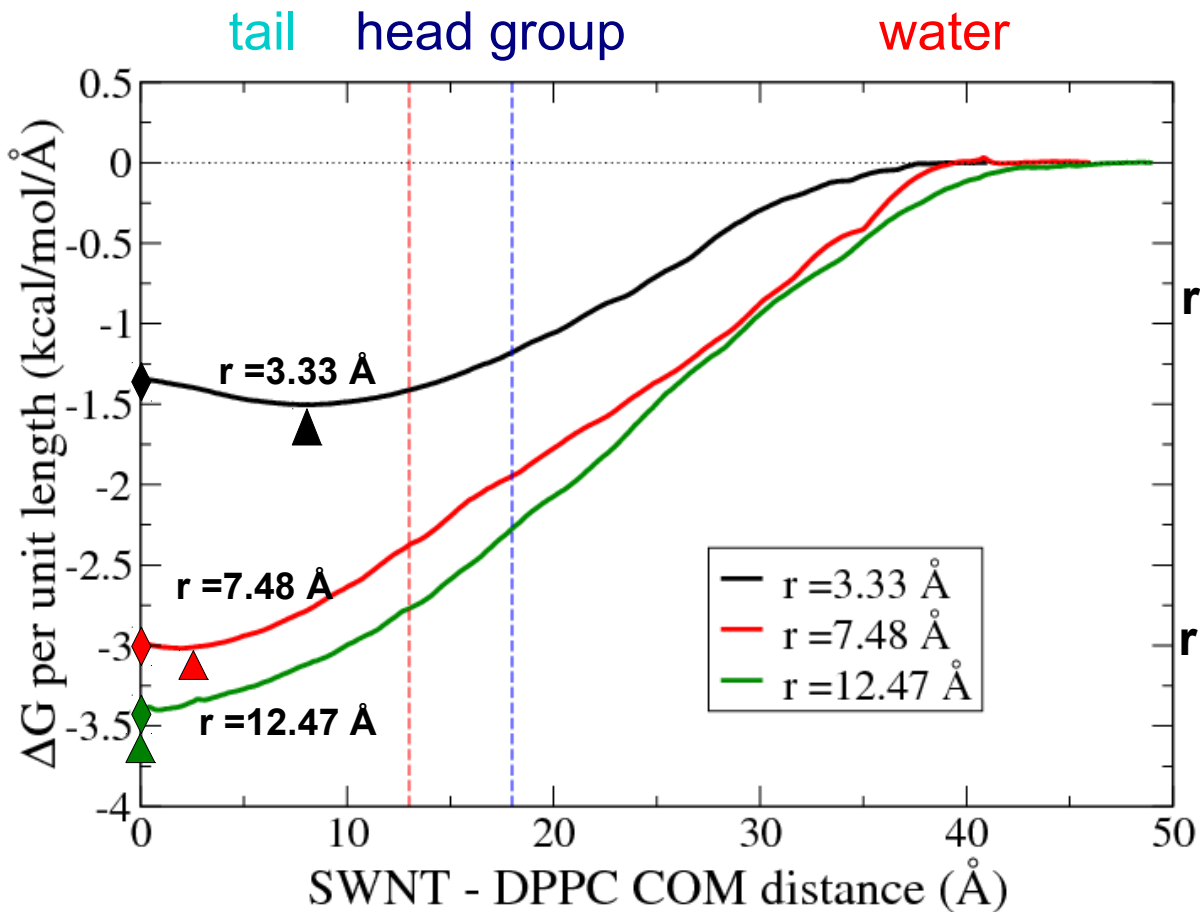
CNT/DPPC Lipid Bilayer

- Water – bilayer transfer free energy
- SWNT vs DWNT
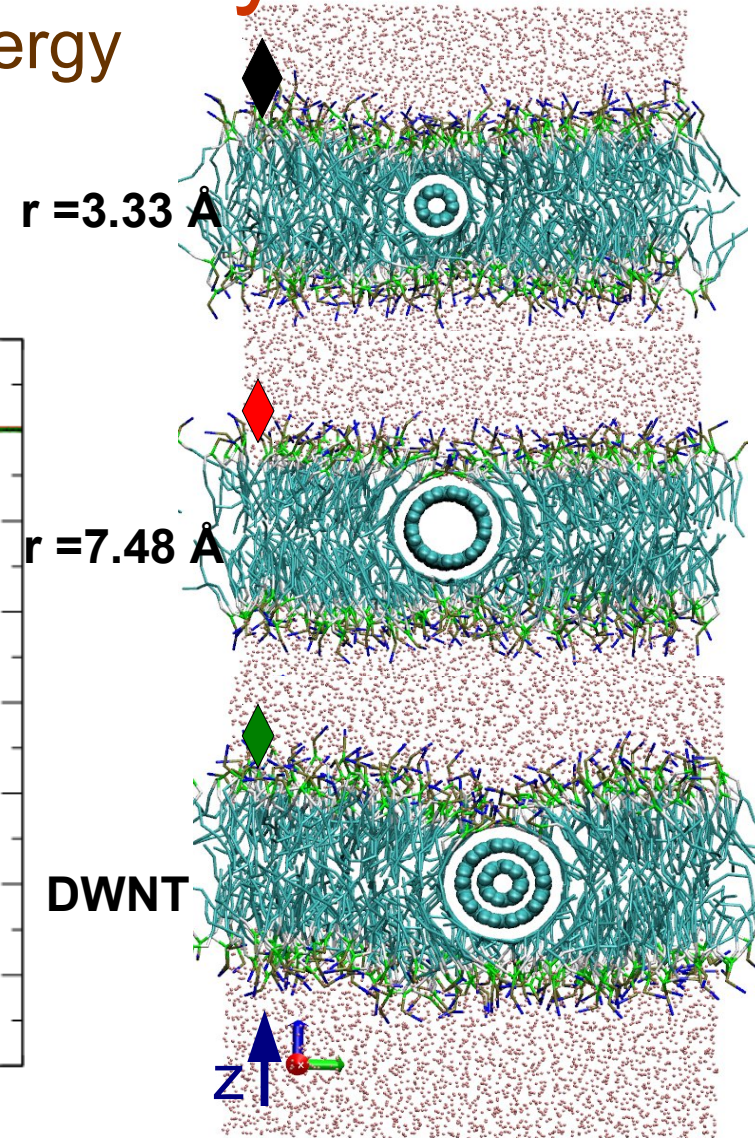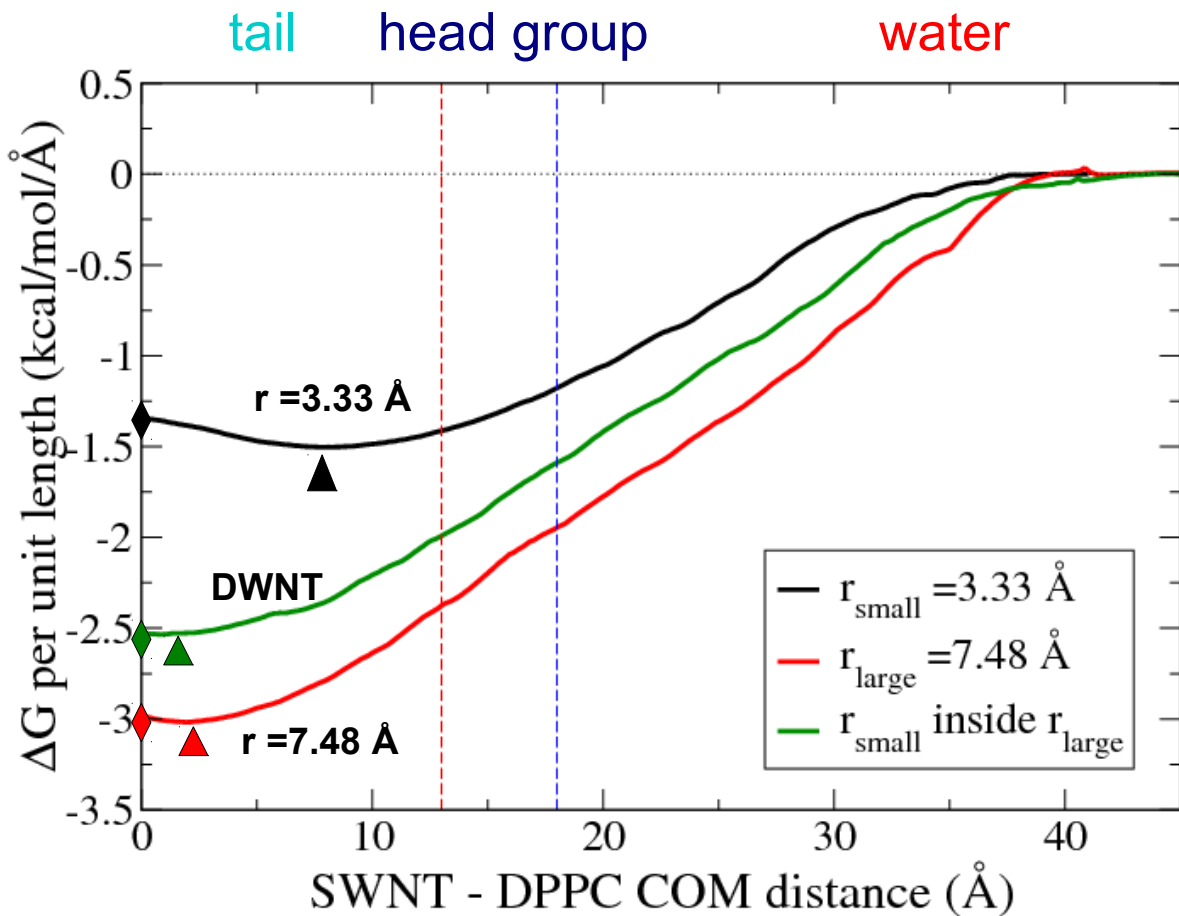
Conclusion

- Developed and validated CG molecular simulation force field for carbon based nanoparticles (fullerenes)

- C_{60} form clusters in a lipid bilayer

- Pristine CNTs spontaneously diffuse into the membrane

- 5% carboxylated SWNTs locate near the lipid head group region; above 10% carboxylation, it is no longer thermodynamically favorable for SWNTs to penetrate the bilayer.

- Larger diameter SWNTs locate deeper inside the bilayer and induce lipid tail structuring.

- DWNTs have stronger interactions with both lipid and water molecules.

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Future Plan

- Protein coated CNTs

- Different membrane systems

  - Monolayer systems in lung alveoli (model for CNP inhalation in lung)

- CNT/C60 effect on membrane mechanical properties

  - Effect on cellular processes

- Correlate with cytotoxicity data