Part I
Computer Modeling of Pluronic:CNT Composites
R. J. K. Udayana Ranatunga

Part II
Sonication of Pluronic Polymers Induces Toxic Degradation Products
Ruhung Wang
Nanoparticle (NP) Material: Varying shapes and surface chemistries

- Spherical C$_{60}$
- Faceted Ceria
- Planar Graphene Oxide
- Cylindrical MWCNTs

Focuses
1. Dispersant mechanism/effectiveness
2. Correlation of NP aggregation state and toxicity
3. Tracking cellular uptake and concentration of NPs

Characterization ↔ Modeling ↔ Biological Testing
Carbon nanotubes (CNTs) aggregate in water
- Hinders processing, controlled assembly
- Aggregation implicated in toxicity

Dispersion strategies

- Noncovalent functionalization with polymers/peptides
- Defect-group functionalization
- Noncovalent functionalization with surfactants
- Covalent sidewall functionalization
- Endohedral functionalization

Dispersing agents promote separation of particle aggregates / clumps
- Improve processability, handling of material
- Aid in nanomaterial remediation

Pluronics are an amphiphilic tri-block copolymer which can be used as a nanotube dispersant

**Pluronics®**
- Commercially available
- FDA approved
- Block lengths vary

**naming convention**

- **F68**
  - Physical state
  - Hydrophilic block mass
  - Hydrophobic block mass
  - $x10 = \%$ hydrophilic
Interested in modeling Pluronic:CNT composites

- **Existing Pluronic models**
  - All atom representation
  - Too detailed!
  - Cannot simulate adequate sizes

- **Need to create a coarse grained (CG) model**
  - All atom simulations used to set bonded interactions
  - Experiment data (density, surface energies) used to tune non-bonded interactions
**Bonded Parameters**

- **Bonded parameters**
  - Dictate the vibrations and flexibility of a molecule

- **Parametrization strategy**
  - Carry out all atom simulations to obtain target data for CG model
  - Iteratively tune CG model parameters to arrive at target data
Bonded Parameters

Bond stretching

\[ U(r) = \frac{1}{2} k_r (r - r_0)^2 \]

Bond bending

\[ U(\theta) = \frac{1}{2} k_\theta (\theta - \theta_0)^2 \]
Non-bonded Parameters

\[ U_{ij}(r) = \frac{27}{7} \varepsilon \left\{ \left( \frac{\sigma}{r_{ij}} \right)^9 - \left( \frac{\sigma}{r_{ij}} \right)^6 \right\} \]

\[ \sigma = 4.875 \, \text{Å} \]

\[ \varepsilon = 0.415 \, \text{kcal/mol} \]

- Density depends mostly on \( \sigma \)
- Surface tension depends mostly on \( \varepsilon \)

\[ \rho(M) = \left( \frac{1}{\rho_\infty + \frac{2V_e}{M}} \right)^{-1} \]

\[ \gamma = \gamma_\infty - \frac{k_0}{M_n} \]
Focus on three specific Pluronics,

- **L62**: \((EO)_6(PO)_{35}(EO)_6\)

- **P65**: \((EO)_{19}(PO)_{29}(EO)_{19}\)

- **F68**: \((EO)_{77}(PO)_{29}(EO)_{77}\)

Hydrophobic length remains constant, hydrophilic length increases:
L62, P65, F68
Pluronic: Nanotube in Water

- Study Pluronics coating Multi-Walled CNT
  - Outer radius = 2.9 nm
  - Length = 7.0 nm

- For each Pluronic species study 4 different mass loadings
  - L62
    - 50%
    - 100%
    - 200%
    - 400%
  - P65
  - F68
Interaction of CNT:PLN with Lipid Bilayer

- Insertion of CNTs into lipid bilayers → biological implications
- Bare nanotube spontaneously enters lipid bilayer
- Most Pluronic coated CNTs require external force
- Qualitatively, F68 > P65 > L62 in raising insertion energy barrier
Simulating Pluronic: MWCNTs

- Simulations are too CPU intensive
  - Diameter of experimentally used MWNT ~10-20 nm
  - Too many atoms to simulate!
  - Developing a new approach

- Phenomenological model:
  - Explicitly include free energy terms involved in formation of Pluronic: MWNT composite structures
Conclusions from Simulation Studies

• Successfully constructed a coarse grained model of Pluronics

• Pluronics with higher % hydrophilic mass are suitable for dispersing carbon nanotubes
  • Larger corona → barrier towards aggregation
  • Higher barrier towards membrane insertion

• Simulating experimentally relevant Pluronic-functionalized MWNTs leads to the development of new computational methodology
Pluronics and CNTs: Modeling and Toxicity

SRC-ERC Teleseminar Series,
July 26th 2012

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Sonication of Pluronic Polymers
Induces Toxic Degradation Products
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Generation of Toxic Degradation Products by Sonication of Pluronic® Dispersants: Implications for Nanotoxicity Testing

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MWNTs and Bio-compatible Dispersants

- MWNTs

- Three dispersants
  BSA : 67 kDa protein
    
    \[(8 \text{ nm} \times 8 \text{ nm} \times 8 \text{ nm}) \times 4 \text{ nm}\]

  F-68 : 8.4 kDa tri-block copolymer
    
    \[(EO)_{77}(PO)_{29}(EO)_{77}\]

  F-127 : 12.6 kDa tri-block copolymer
    
    \[(EO)_{101}(PO)_{56}(EO)_{101}\]
Effectiveness of F-68, F-127, or BSA in dispersing MWNTs using bath sonication at 37 kHz and 120 W.

- Pluronic® F-68 and F-127 are better dispersants than BSA for MWNTs.
Cytotoxicity of MWNTs suspended in F-68, F-127, or BSA as a function of bath sonication time.

- MWNT-F-68 and MWNT-F-127 suspensions become toxic after sonication.

- MWNT-BSA suspensions are not toxic to NRK cells.
Cytotoxicity of F-68, F-127, and BSA as a function of bath sonication time in the absence of MWNTs.

- Pluronic® F-68 and F-127 solutions become highly toxic after sonication.
- BSA solutions are not toxic.
Cell death was apparent after 12 h exposure to sonicated F-68.

No morphological changes were observed in cells exposed to non-sonicated F-68.
IC\textsubscript{50} of sonicated F-68 and F-127 for NRK cells after 24 h exposure.

<table>
<thead>
<tr>
<th>Pluronic\textsuperscript{®}</th>
<th>F-68</th>
<th>F-127</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sonication Time (h)</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>IC\textsubscript{50} (µM)</td>
<td>53.2</td>
<td>16.5</td>
</tr>
</tbody>
</table>

- The longer the sonication time, the more toxic the Pluronic polymers become.

* IC\textsubscript{50}: The half maximal inhibitory concentration
Sonication induces degradation in F-68 and F-127

Sonication is known to degrade various polymers

- Sonication $\Rightarrow$ cavitation bubbles $\Rightarrow$ heat, pressure, and shear forces

- Sonication $\Rightarrow$ $H_2O_2$ $\Rightarrow$ free radical attacks

Many degradation products of polymers are toxic to cells

- free radicals
- reactive oxygen species (ROS)
- organic acids
- alcohols
- aldehydes

Does sonication induce polymer degradation?

Monitor changes in polymer size as a function of sonication time by

- Dynamic Light Scattering (DLS)
- SDS-PAGE
Degradation of F-68 polymers were detected in $\text{BaI}_2$ stained SDS-PAGE gels as a function of sonication time.

Similar results were found in F127.

Established the correlation between polymer degradation and toxicity; both are sonication dependent.
Removing toxic degradation products in MWNT-F-68 and MWNT-F-127 suspensions by dialysis.

MWNTs
- Non-sonicated F-68
- F-68 degradation products

Dialysis
Degradation products of F-68 and F-127 polymers in MWNT suspensions were removed by dialysis.

MWNTs remained in high concentrations and stable in suspension after dialysis against intact non-sonicated F-68 or F-127.
Conclusions from MWNT-Pluronic Suspension Toxicity Studies

- Pluronic® tri-block copolymers F-68 and F-127 are better dispersants compared to BSA in suspending MWNTs in biocompatible solutions.

- F-68 and F-127 become highly toxic after sonication in the presence or absence of MWNTs; polymer toxicity correlate with degradation, both are sonication time dependent.

- Caution should be used in interpreting the results of nanotoxicity studies where the sonolytic degradation of dispersants has not been controlled.

- Dialyzing MWNT-F-68 or MWNT-F-127 suspensions against non-sonicated F-68 or F-127 replaced the degraded materials and eliminated toxicity while retaining the MWNTs in suspension at high concentration.
Thank You