Understanding Biocompatibility Through Molecular Dynamics Simulations

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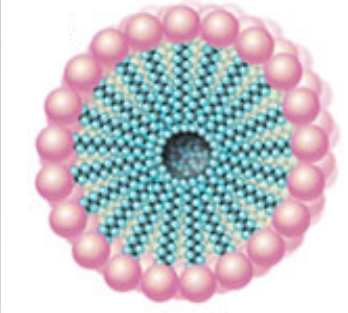
Overview

- Properties of amphiphiles
- Introduction to molecules used here
- Introduction to the problem we're trying to solve
- Simulations performed

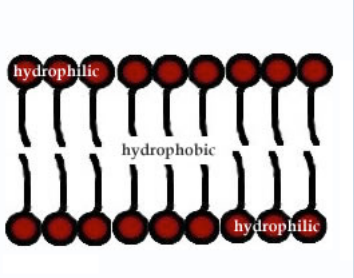
Amphiphiles

- Molecules with hydrophilic heads and long hydrophobic tails, that can form a variety of structures:

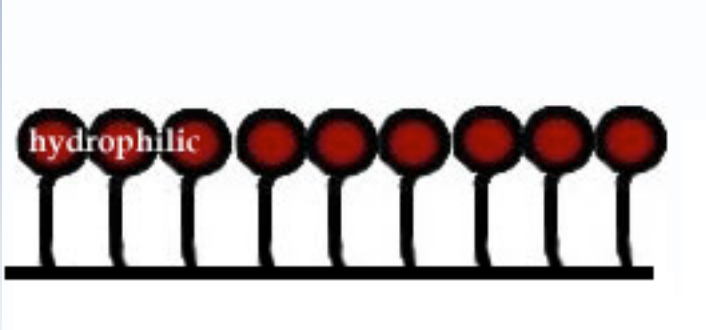
Micelles



Bilayers

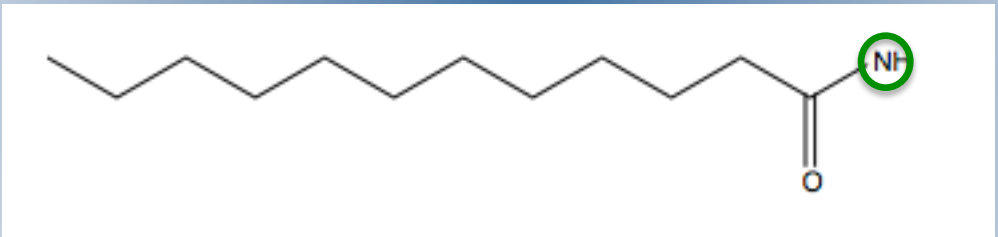


Monolayers from a surface



Our Molecules

- Andrew Marsh's group have long been interested in this type of amine oxide:
  - Protein resistant; drug delivery system?



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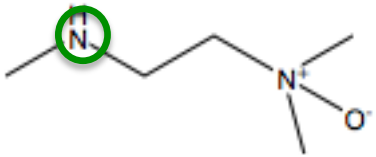

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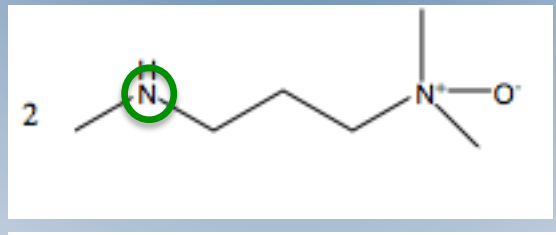

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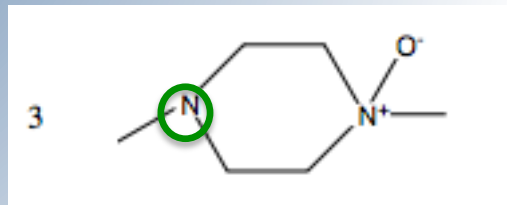

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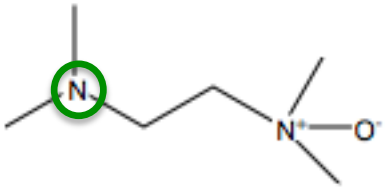

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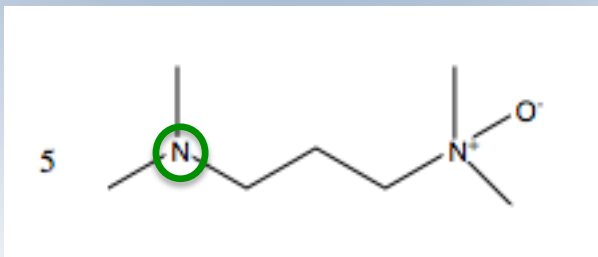


Will MD simulation help us understand the property of biocompatibility?

Our Aims

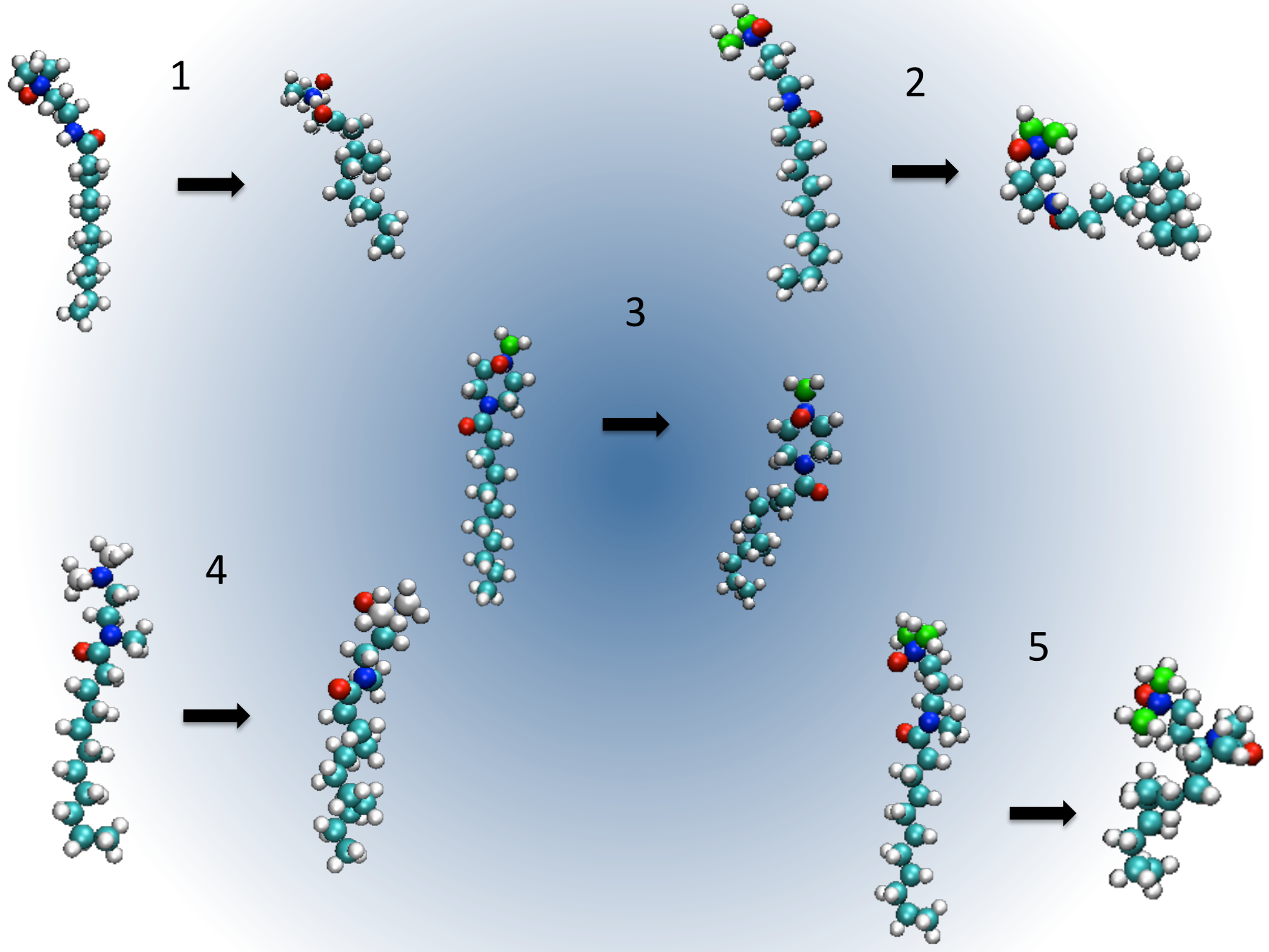
- To observe individual molecules at atomic resolution using molecular dynamics simulations
- To observe groups of molecules and (hopefully) their aggregation

- We know that these molecules can form useful structures:
  - Beneficial to examine behaviour in solution at atomic level
  - Results may be comparable to experimental data


Simulate single molecules. Analyse differences / patterns
Simulate groups of molecules. Analyse aggregation / patterns

Single Molecule Studies

- 1.0 fs time step
- 0.5 ns equilibration
- 1.0 ns simulation
- NPT ensemble
- 298 K and 1 atm
- TIP3P water
- CHARMM force field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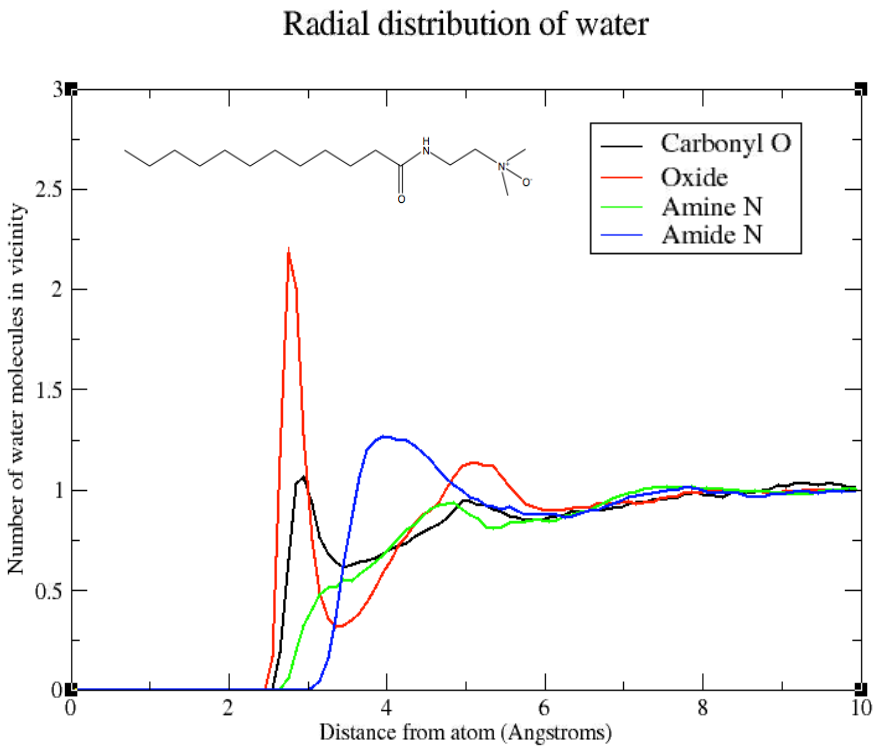
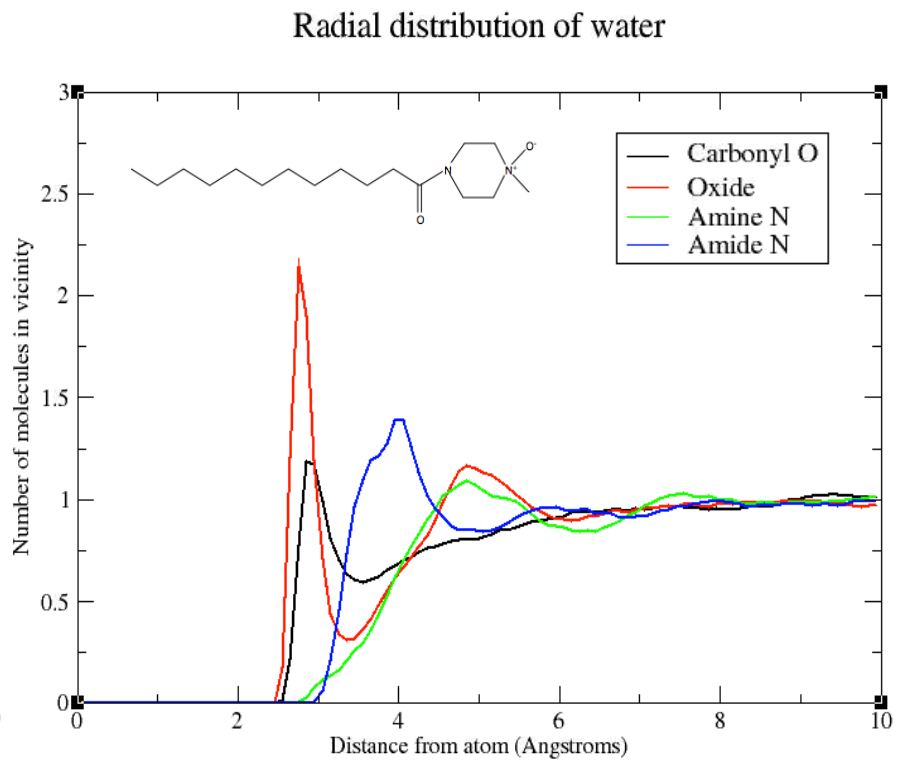




Density of oxygen atoms in water from the atom of interest

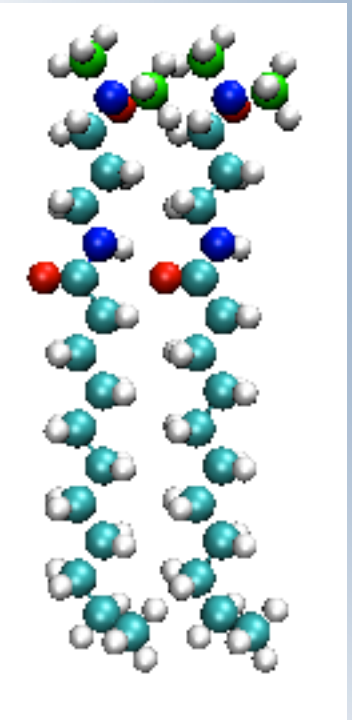
Average hydrogen bonds on atoms during simulation

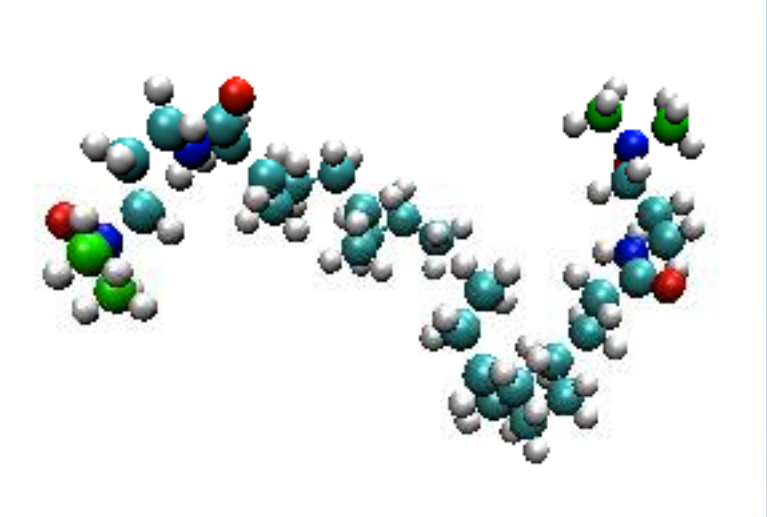
	Oxide 1	Oxide 2	Oxide 3	Oxide 4	Oxide 5
Carbonyl O	0.999	0.991	1.172	1.011	0.954
Oxide O^-	2.073	2.227	1.970	2.145	2.251

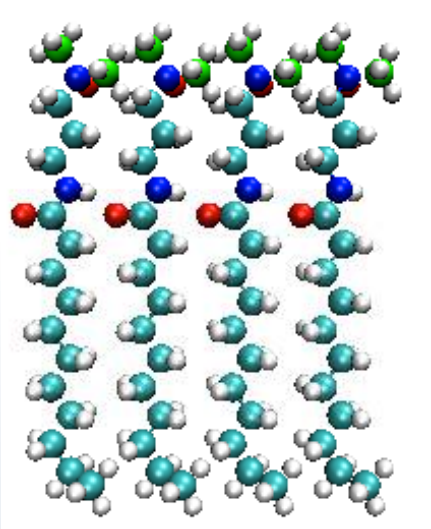
Multiple Molecules

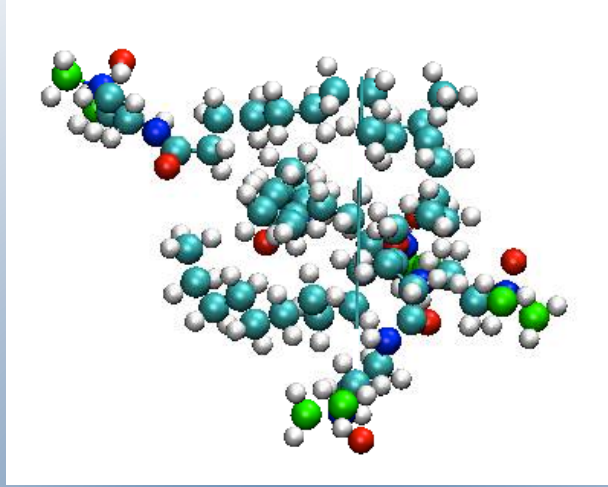
- For each molecule, new simulations of N = 2, N = 4 and N = 8 were set up, in the following configurations:

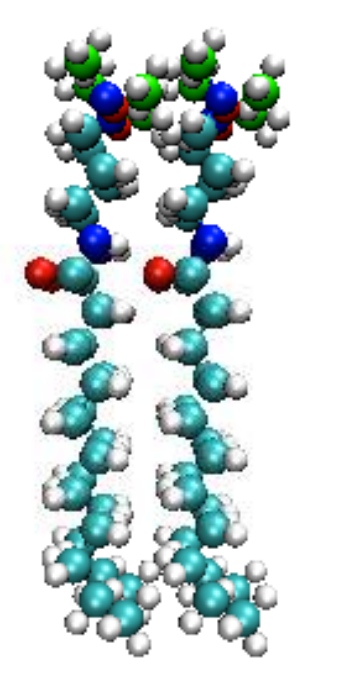
N = 2, oxide 2: hydrophobic ends together, but entire chain not concealed from solution

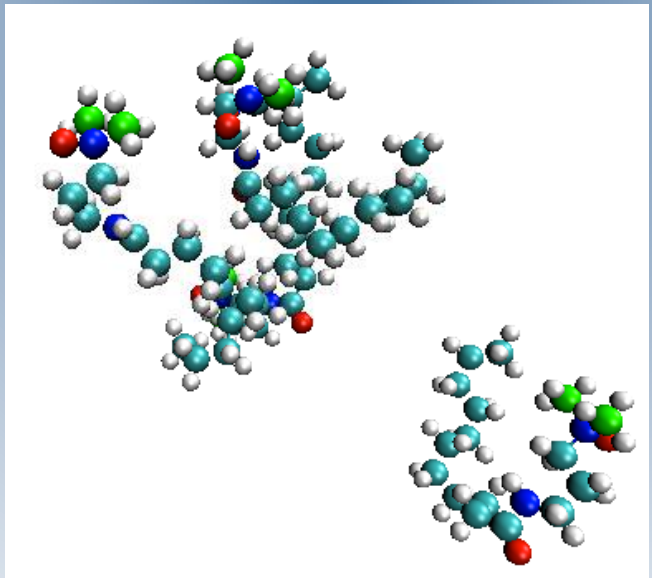












N = 4, 2 configurations: some aggregation, though not as efficient in the second configuration.

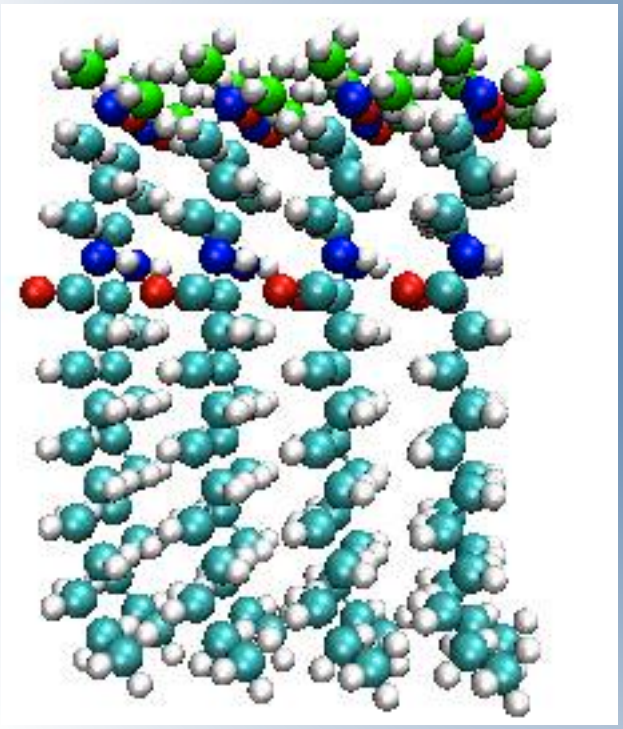
Molecule outside aggregate curls as in single molecule study.

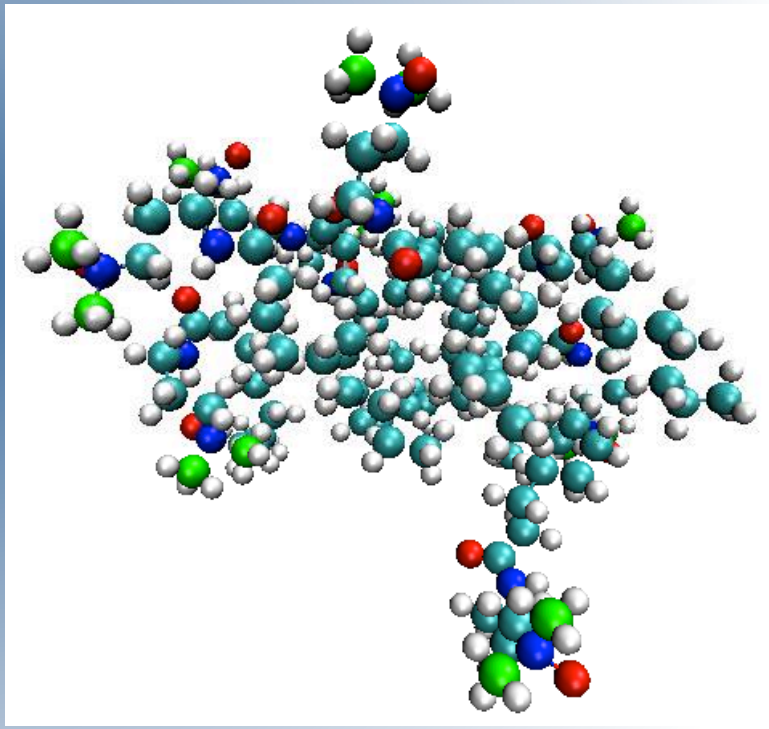
In a longer run these two results would be expected to be the same.

N = 8: Aggregation; head groups all directed into solvent, some tails still exposed.

Not an ordered structure – unsurprising with only N = 8.

Similar results with the other molecules





Further Work

- Different molecules with different properties
- Simulations of monolayers with a surface (Si or Au)
- Simulating bigger combinations to get micells
- Predicting NMR spectra from simulated aggregates for comparison with experimental results

Acknowledgements

- David Cheung in Theoretical Chemistry for supervision and advice
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- MOAC and EPSRC for the opportunity and funding for the project

EPSRC
Pioneering research and skills

References:

1. Kane *et al.* **Langmuir** 19: 2388 – 2391
2. Kast *et al.* **J. Phys Chem** 107: 5342 – 5351
3. M. Beecham, 2004, New Amphiphiles for Refolding Proteins. PhD thesis, University of Warwick (UK), Ch. 6