Understanding Biocompatibility Through Molecular Dynamics Simulations

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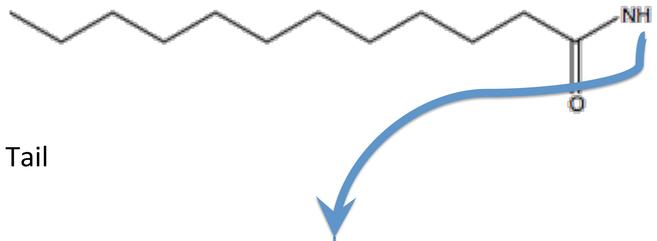
1 - Introduction

A group of amine-oxides was selected as being of interest for the following reasons:

- They form monolayers, bilayers and micelles just as lipids do
- Surfaces made from such molecules are protein resistant, making these molecules biocompatible.
- They could be potential drug delivery systems, since molecules contained within would be protected.

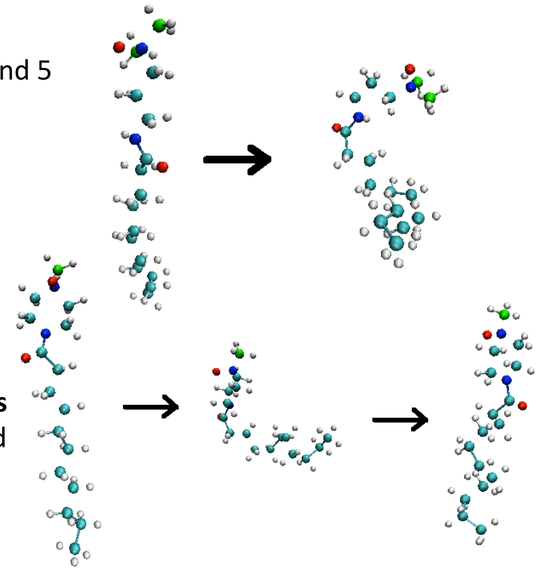


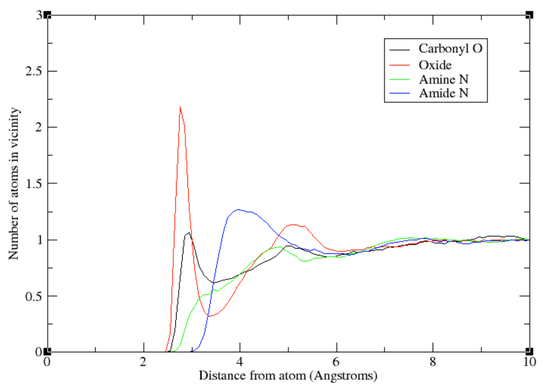
2 – Single Molecule Studies

0.5 ns equilibration, 1 ns simulation. NPT ensemble.

Molecules 2 and 5 **curl** to reduce hydrophobic surface area

Molecules 1, 4 and 3 curl, then uncurl and **chains compress** instead





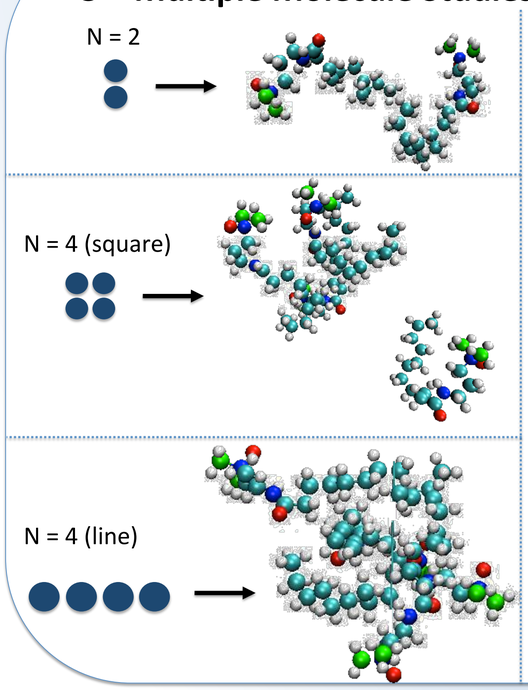
Solvation distances (distribution of water as function of distance) differ only slightly between oxide 3 and the other molecules – the nitrogen atoms have different constraints.

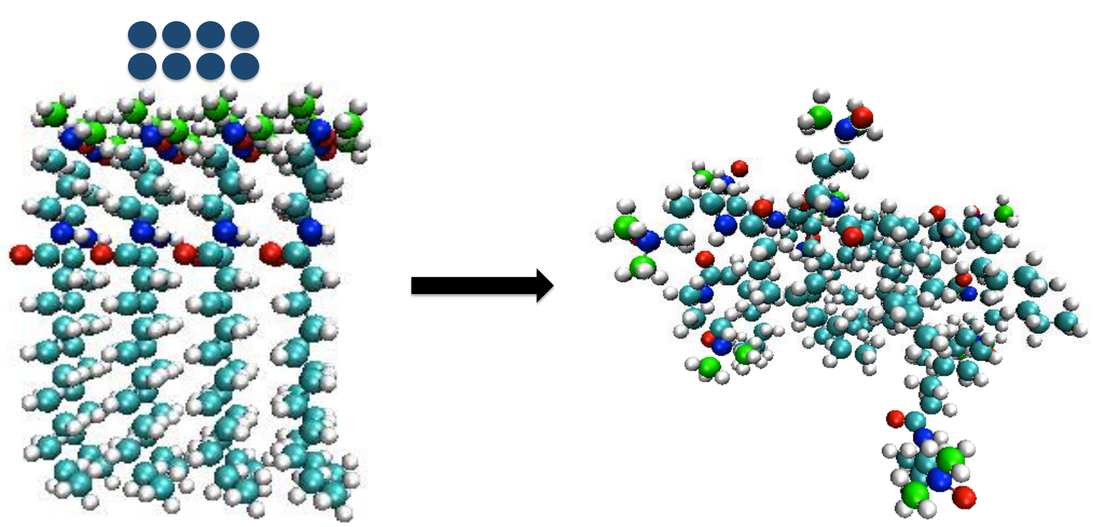
Average **Hydrogen bonding** during simulation is similar for most molecules, but not oxide 3: less affinity at oxide site so water moves to carbonyl?

	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

3 – Multiple Molecule Studies

Same conditions as for single molecules, using N = 2, 4 and 8, spaced 4 Å apart.
Still 0.5 ns equilibration and 1 ns simulation.
Aggregation not always seen in this length of simulation.
In N = 8 studies a single, but disordered, mass of molecules formed.





4 – Conclusions and Further Work

Aggregation was seen in these simulations, as was normal amphiphilic behaviour in single molecules. Formation into any kind of **micelle was not seen**.

Simulations using **many more molecules** may show better formation of structures.
Simulations using **molecules bound to a surface** (Au or Si) should also be attempted.

5 - 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