

# When simple systems do complex things

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Sometimes, even the seemingly simplest of systems can exhibit surprisingly complex and subtle behaviour. This article describes recent computational work within the School of Physics at the University of Edinburgh, looking at the structure and dynamics of simple aqueous alcohols.

We like to think that, as computational scientists, we understand the simple things and can devote our attention, and CPU cycles, to thinking about the more complex problems in science. Sometimes though, even the simplest of systems can exhibit beguiling complexity. Take water as a classic example: the simplest inorganic liquid, the most abundant molecule on Earth and over two-thirds of you and me. It exhibits no less than 41 anomalous properties [1] and some say these anomalies are the basis of its ability to support life. After a long history – over thirty years – of performing computer simulations of water, we are still a long way from being able to say that we understand it. As Guillot has stated in a recent review [2] ‘One has a sense of incompleteness if one considers that not a water model in the literature is able to reproduce with a great accuracy all the water properties.’

Small surprise then, that simple molecules in solution do strange things as well. Methanol,  $\text{CH}_3\text{OH}$ , is the smallest member of the alcohol family. It is also just about the simplest molecule that displays amphiphilic behaviour; that is, it comprises both hydrophobic (the water-hating  $\text{CH}_3$  group) and hydrophilic (the water-loving OH) entities within the same molecule. It exhibits, like all amphiphiles, molecular schizophrenia towards water. Amphiphiles are everywhere in physics, chemistry and biology. Larger amphiphiles self-organise themselves into solution forming spheres (micelles), cylinders (columnar phases) and sheets (lamellae), depending on concentration and temperature.

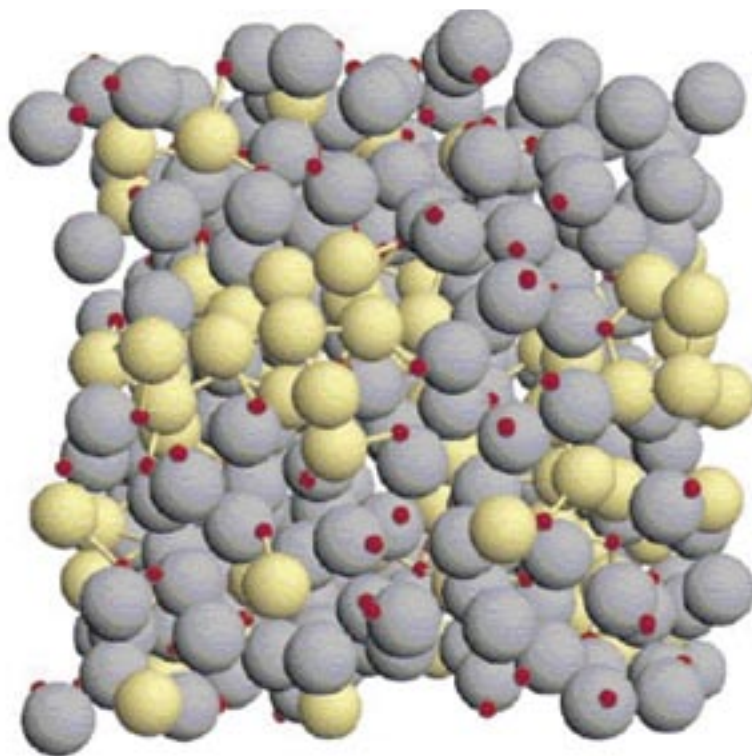


Figure 1: A configuration from the EPSR fit to the ND data illustrating incomplete mixing. The grey spheres denoted hydrophobic methyl groups, the small red spheres the methanol oxygens and the yellow spheres the oxygen atoms of water molecules.

Biologically, amphiphiles are ubiquitous; they comprise the fundamental structural units of cell membranes (phospholipids); DNA forms strong hydrogen-bonds to water and hydrophobic effects are believed to play an important role in protein folding.

It is not immediately obvious that methanol should behave as a ‘typical’ amphiphile in solution, yet it does. Its solutions exhibit the same thermodynamic non-ideality; it shows a tendency to self-organise in water (as I will discuss) and this organisation is consistent with hydrophobic-like structures where the non-polar hydrophobic groups are in contact. This has led to it being used as a prototypical amphiphilic system, studied using both state-of-the-art experimental and computational techniques in a combined research programme at Edinburgh.

In 2002, the experimental group at Edinburgh and RAL published an article suggesting that the anomalous thermodynamics in a methanol-rich solution (methanol mole fraction = 0.7) could possibly be attributed to the micro-heterogeneity that the system exhibited [3]. In other words, despite being fully miscible in all proportions on a macroscopic scale, methanol and water seemed not to want to fully mix on a microscopic scale, and this ‘micro-immiscibility’ could explain some of the strange thermodynamic properties that had for a long, long time been attributed to the enhanced structure of the water around the hydrophobic group. Their analysis (based on Empirical Potential Structure Refinement (EPSR) of their Neutron Diffraction (ND) results) convincingly showed that the system was far from homogeneously mixed (see Figure 1).

This micro-immiscibility has recently been confirmed by simulation. My group have performed classical molecular dynamics

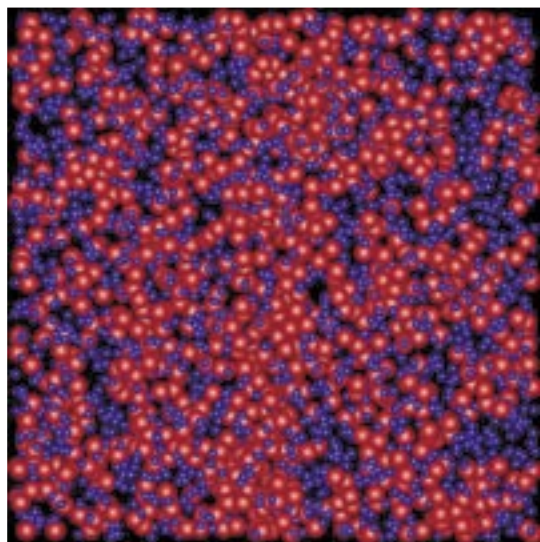


Figure 2: a snapshot of the front face of the MD simulation box for the methanol-rich solution. Water oxygens are red, methyl carbons are blue. The entire box comprises ~20000 atoms. A very large water 'super-cluster', containing over 400 molecules, can be seen running top to bottom of the middle of the box.

simulations using the DL\_POLY code that predict the presence of large clusters of water, up to hundreds of atoms. The water molecules break up the structure of pure liquid methanol, which is itself extensively hydrogen-bonded. The methanol molecules re-orient themselves such that their hydrophobic methyl groups come into contact with each other and the hydrophilic hydroxyl groups point at the pockets of water [4]. We were also able to say something about the dynamics of the water clusters, by calculating their average lifetimes. What we found was that large water clusters, such as the one shown in the simulation snapshot in Figure 2, could live for almost the entire duration of the simulation (in some cases several nanoseconds). These 'super-clusters' were far from static though, as they rapidly shed and re-absorbed peripheral water molecules and smaller clusters from their outer surfaces. The average lifetime of the small fraction (about 10%, aggregated over the entire simulation) of water molecules not part of a cluster was only a few picoseconds.

In analysing the MD trajectories, we faced a significant data challenge: thousands of particles running for millions of time steps generate multiple gigabytes of trajectory data. But that is just one composition at one state point. Visualisations such as Figure 2 help a lot, as do movies, but there is still too much information to digest. By coding our own analysis tools, we were able to distil the essential information from gigabytes of data. This allowed us to capture cluster size distributions, calculate their lifetimes and even to partition the members of water clusters to be on either the external or the internal surfaces of the cluster and to investigate the properties of these types of molecules separately.

This micro-segregation was not unique to a single composition. Using interchangeable data formats and the same analysis tools, a combined experimental and computational study [5] showed that the clustering of water persists across a wide composition range (see Figure 3). The similarity of the cluster distributions obtained from two completely independent datasets, one derived from experimental data, the other from MD simulations, is remarkable. Furthermore, both water and methanol (data not shown) are found to cross the theoretical percolation threshold for a range of compositions, making aqueous methanol a bi-percolating liquid mixture. Interestingly, the composition range for which this occurs is in the same region in which the anomalous thermodynamic properties have extreme values.

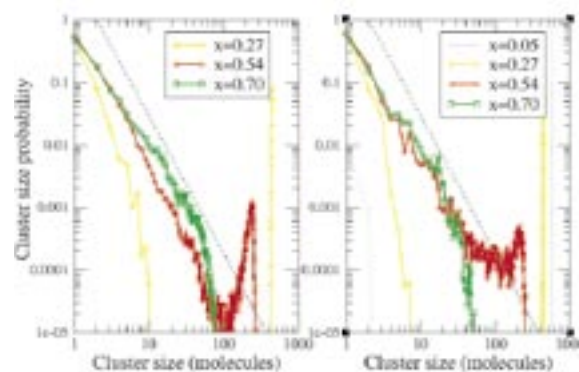


Figure 3: distributions of water cluster sizes, from both experimental data (left) and MD simulations (right) for different mole fractions of methanol ( $x$ ). The dashed line indicates the theoretical percolation threshold.

So if this is how water behaves around just about the simplest of amphiphiles, what does this mean for the structure and dynamics of water around even slightly more complex amphiphiles? We don't yet know the answer, but the current programme of both experimental and computational research in this area certainly aims to try to find out. Work is just getting underway on this and related systems on HPCx. Obvious questions that we would like to answer include: what happens to these water clusters at far from ambient conditions, at higher pressures or lower temperatures? Do these classical simulations predict the same things as quantum mechanical simulations (our own simulations on very small systems suggest that they do)? Another interesting question is just how big do these water clusters get? There is an obvious upper limit to their size since solutions of methanol are clear, but there is a long way between the lengthscale of where we have looked so far and that ceiling. More important than 'how big?' is simply 'why?' What is the energetic basis for the formation of these structures?

While it might be plausible to think that methanol is a good prototypical amphiphile, it may be taking it too far to consider it a realistic model of a biomolecule. So what do we observe for a simple biomolecule? In a collaboration with IBM Research at the T.J. Watson Research Center, classical and quantum mechanical MD simulations of N-methylacetamide (NMA,  $\text{CH}_3\text{N}(\text{H})\text{C}=\text{OCH}_3$ ) solutions are underway. The hydrophobic methyl groups are there once again, but this time the hydrogen-bond acceptor and donor characteristics are spread across the NHCO linkage, a signature protaceous element. We don't know what the structure and dynamics of the water surrounding this molecule will be, but we're fairly sure it will be anything but simple.

## References

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