HYDRA: PUBLISHABLE SUMMARY

The ubiquitous presence and versatile role of water in biological processes rely primarily on two peculiar properties of the water molecule, i.e., its sizeable dipole moment, and its propensity to form hydrogen bonds. The first property endows water with its large dielectric constant, that screens electrostatic interactions, and favours the solvation of electrolytes. The second property, instead, plays a crucial role at the molecular scale, since it provides the flexible and directional force able to drive the self assembly of complex structures.

Because of their impact on a surprisingly wide rage of biological processes, the HYDRA project targeted precisely the equilibrium properties and short-time dynamics of hydrogen bonding at water/biomolecule interfaces. Two techniques, i.e., neutron scattering experiments, and computer simulation, have been identified as the most powerful probes of this aspect of biological systems, and have been extensively used in our investigations.

Three paradigmatic systems have been proposed for detailed investigation, consisting of tubulin and actin self-assembling into functional supra-molecular structures (microtubules and fibrils, respectively), of phospholipid bilayers in water, and of proteins aggregating into amyloid fibres.
The original scope of these investigations has been enlarged to explore the effect of novel organic ionic compounds (room temperature ionic liquids, RTIL's) on these systems and related processes, that concern the formation of microtubules and actin fibres by tubulin and actin, respectively; the mechanical properties and dynamical processes at biomembranes, made primarily of phospholipids bilayers, and the formation of amyloid fibres, that is widely seen as the crucial stage in the development of neurodegenerative conditions such as Alzheimer and Parkinson's disease. RTIL's affect these processes through changes of the structure and dynamics of interfacial water, that is, in turn, the unifying motif of our research.

These considerations have motivated the large interest of the community towards our work, that has been reflected in generous allocations of neutron beam time and computational resources.

The backbone of the activity has been represented by neutron scattering experiments, whose role has been expanded with respect to the original plan to match the overwhelming interest received from the community working around experimental facilities.
During the two years of the HYDRA project, elastic and quasi-elastic neutron scattering, neutron reflectometry and spectroscopy, and neutron diffraction have been used in concert to investigate the systems listed in our proposal.
Experiments have been carried out at three European facilities (Institute Laue Langevin, Grenoble, France; Heinz-Maier-Leibnitz Zentrum, Germany; and ISIS, UK) and two in the Unites States (Oak Ridge National Lab; and National Institute of Standards and Technology), accounting for a total of about eighty days of beam time.
Simulations have been carried out at supercomputers in Dublin (Stokes and Fionn), in Bologna (Fermi) and in Paris (Curie), using both empirical models and first-principle methods to investigate the same systems considered in our experiments.

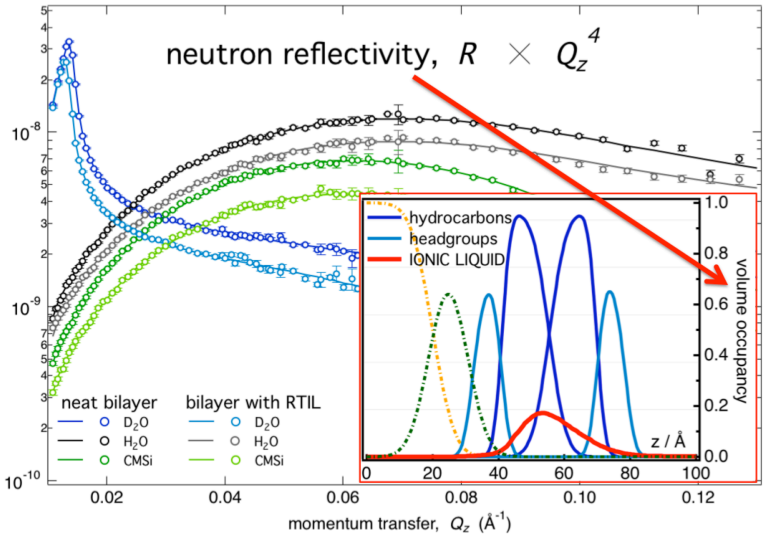

Fig. 1 - Reflectivity *R* as a function of the momentum transfer Q_z measured on d_{67}-DMPC after incubation with a 0.5 M [bmim][Cl] water solution. (Insert) Volume occupancy profile as a function of height *z* from the surface obtained by best fitting the reflectivity data. RTIL absorption accounts for 10% of the lipid bilayer volume.

Several neutron scattering experiments, in particular, have been carried out to investigate the interaction of RTIL on phospholipid bilayers, analysing their effect of the lipid and water structure and dynamics. The addition of RTIL's, for instance, changes the reflection coefficient of lipid bilayers with respect to neutrons (see Fig. 1). Neutron reflectometry measurements, therefore, allowed us to map the distribution of RTIL ions within the phospholipid bilayers, while quasi-elastic neutron scattering experiments have provided a wealth of results on the dynamics of water and lipids hydrated by RTIL solutions. Up to date, these represent the most detailed information available on these systems, and provide the experimental basis for using RTILs in modifying and controlling properties of phospholipid bilayers in view of electrochemistry, pharmacology and nanotechnology applications.

Extensive computer simulation studies have been devoted to the investigation of the hydrogen bond dynamics at the phospholipid/water for the same systems studied by our experiments. These represent large scale simulations (see Fig. 2), whose result provide invaluable insight into the experimental data, and offer a real-space, real-time view that complement the Fourier-space, frequency domain information provided by neutron scattering.

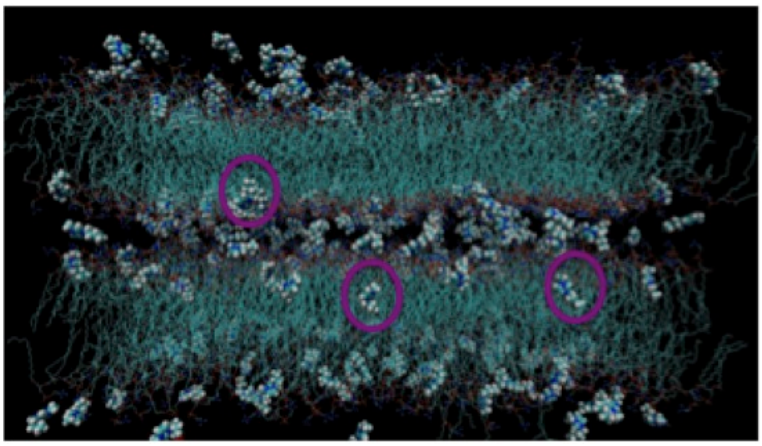

Fig. 2 – Screenshot of the molecular dynamics simulation at 70ns of POPC+[bmim][Cl] at 0.5M, FIONN, ICHEC: water and [Cl] are not shown, some of the incorporated [bmim] ions are highlighted into violet circles.

In a second stage of our plan, neutron spectroscopy has been used to investigate the fibrillation kinetics of peptides and proteins in water and in water solutions of RTIL's. The results are being analysed to investigate the origin of the opposite effect of selected RTILs on the degree and kinetics of fibrillation, with obvious implications on possible pharmaceutical applications of RTIL's.

For reasons of immediate interest, and opportunities to obtain high quality samples, the investigation on tubulin and actin polymerization has been replaced by the analysis of DNA interaction with RTIL solutions, that represents the basic science background for the long term preservation of nucleic acid samples at ambient conditions. Also in this case, results are being readied for publication.

Besides the reports in peer reviewed journals that have been or will be published during the next few months, the major outcome of our activity are: (i) the acquisition of a leadership role for our group in the experimental and computational investigation of biological effects of RTIL's; (ii) the nucleation of several international collaborations that concern Ireland, UK, France, Italy, Switzerland and the US, actively engaged in the continuation of our activity.
Developing result (i) into techniques to control the properties of water at bio-interfaces through the addition of organic ionic compounds would provide European science with an important advantage in biochemistry, pharmacology and nanotechnology.

Our activity will continue through a partnership between University College Dublin and the Paul Scherrer Institute in Switzerland, that has offered a PSI Fellowship to the expert investigator of this Marie Curie project, as a tangible sign of interest and success for our project.