ERICE 23-27 May 2017

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V Course of the International School of Statistical Physics
ETTORE MAJORANA FOUNDATION AND CENTRE FOR SCIENTIFIC CULTURE
http://www.ccsem.infn.it/
Directors: Peter Hanggi, Fabio Marchesoni

Welcome

We address a very warm welcome to all the participants and contributors to this fourth 2017 Conference on “Frontiers in Water Biophysics”.

The Conference is placed for the second time in the superb location of Erice, hosted by the Ettore Majorana Foundation and Centre for Scientific Culture. As in the mirable book “Air and Water” by Mark Denny, Erice is suspended between air and water at the interface of biophysics with other sciences. Ideas merged from previous meetings consolidated the scientific program of 2017 conference, with the water properties in the focus of pharmaceutical, food and biological processes. Once again, an enthusiastic “melting pot” of science has been slowly and carefully cooked to respect the original mission of Frontiers in Water Biophysics: “Fostering mixing, learning and empathy between science cultures was and remains the main purpose of any project”.

As for the past editions, many peoples contributed in theory and in practice to the preparation and the organization of this 2017 event. The continuous advice of the Ettore Majorana Center and of the colleagues involved in the previous events has been highly appreciated, and some special thanks are deserved to the members of the Scientific Committee for their present and future suggestions.

We believe that our scientific endeavor in setting down the Frontiers in Water Biophysics Conference will generate new contacts and collaboration, new ideas and new relevant results. This objective supported and will support us in pursuing ahead with the strongest consideration of achieving a fantastic socio-scientific goal.

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Programme

	MON 22	TUE 23	WED 24	THU 25	FRI 26	SAT 27
9:00- 10:30		*Opening* (10:30-10:45)	**R. WINTER**	**K. DAWSON**	**V. VLACHY**	**A. PACIARONI**
10:30-11:00		S. McLAIN	**Coffee Break**	**Coffee Break**	**Coffee Break**	**Coffee Break**
11:00-11:45			C. Calero	P. Gallo	F. Bruni	B. Bagchi
11:45-12:15		R. Ludescher (11:45-12:30)	F. Martelli	A. Bittner	J. Zubeltzu	**A. DE SIMONE**
12:15-12:45		S. Di Fonzo (12:30-13:00)	M. Faieta	S. Acosta-Gutierrez	G. D'Angelo	
12:45-13:00			M. S. Paes	M. Lauricella	G. Magi Meconi	***Closing***
13:00-15:00		**LUNCH**	**LUNCH**	**LUNCH**	**LUNCH**	**LUNCH**
15:00-15:30	**ARRIVAL**	B. Rossi	Organized Discussion	**I. COLUZZA**	Organized Discussion	
15:30-16:00		P. Pittia				
16:00-16.45		A. Hassanali	**S. ROKE**	G. Graziano	**J-E. SHEA**	**DEPART**
16:45-17:00		C. Bottari		V. Bianco **(16:45-17:15)**		
17:00-17:30		**Coffee Break**	**Coffee Break**	**Coffee Break**	**Coffee Break**	
17:30-18:00		**POSTER SESSION***	F. Librizzi	**EXCURSION to ERICE ART&FOOD (includ. DINNER)**	M. Paolantoni **(17:30-18:15)**	
18:00-18:30			D. Matyushov			
18:30-19:00			A. Benedetto		L. Chiodo **(18:15-18:45)**	
	DINNER	**DINNER**	**DINNER**		**DINNER**	

*Poster Session continues at Coffee Breaks

Color Code: Tutorials - MiniSymposium - Coffee Break and "social events"

TUESDAY 23

10:45 PL1

S. McLain *"The essential role of water in biomolecular function"*

11:45 IL1

R. D. Ludescher *"Multiple solvent-slaved dynamic processes in human serum albumin monitored by phosphorescence spectroscopy"*

12:30 OP1

S. Di Fonzo *"The role of water in G-quadruplexes DNA stability and dynamics by UP-RRS"*

15:00 OP2

B. Rossi *"Water adsorption and responsive behaviour in polysaccharide pH-sensitive hydrogels"*

15:30 OP3

P. Pittia *"Thermal properties and molecular mobility of low-moisture amorphous trehalose-limonene matrices obtained by different glass-forming approaches"*

16:00 IL2

A. A. Hassanali *"Aqueous solutions: proteins, protons, holes and other interfaces"*

16:45 OP4

C. Bottari *"Hydrogen-bond rearrangement in cyclodextrin aqueous solutions probed by UV Raman and Brillouin scattering*

POSTER SESSION

WEDNESDAY 24

09:00 TU1

R. Winter *"Exploring the conformational space and dynamics of biomolecular systems using pressure perturbation*

11:00 IL3

C. Calero *"Water at biomembranes: structure, dynamics and influence on ion adsorpion"*

11:45 OP5

F. Martelli *"Structural properties of water confined by phospholipid membranes"*

12:15 OP6

M. Faieta *"Degradation kinetics of phycocyanin under isothermal and dynamic heating"*

12:45 OP7

M. Schincariol Paes *"Cambuci osmotic dehydration: determination of the first thermodynamic pseudo equilibrium using solid-liquid equilibrium diagram"*

15:00 DISCUSSION

16:00 PL2

S. Roke *"Aqueous nanoscale systems: from long range interactions in water to membrane hydration and water droplets"*

17:30 OP8

F. Librizzi *"Pressure effects on the protein dynamical transition"*

18:00 OP9

D. Matyushov *"Water dynamics determine how enzyme function"*

18:30 OP10

A. Benedetto *"The effect of room-temperature ionic liquids on bio-membranes, proteins, and their hydration water: a neutron scattering, afm, and computer simulation study"*

THURSDAY 25

09:00 TU2
K. A. Dawson *"Microscopic understanding of the biomolecular corona"*
11:00 IL4
P. Gallo *"Insights on the mechanism of slowing down of hydration water and effect of trehalose on protein cryoprotection"*
11:45 OP11
A. M. Bittner *"Water and viruses: reciprocal control"*
12:15 OP12
S. Acosta-Gutierrez *"Water-based screening of antibiotics permeability in gram-negative bacteria"*
12:45 OP13
M. Lauricella *"Probing methane-hydrate nucleation by metadynamics simulations"*

16:00 PL3
I. Coluzza *"A multi-scale approach to the study of protein design, folding, and aggregation. Is explicit water relevant?"*
17:30 IL5
G. Graziano *"Conformational stability of globular proteins in water as a function of temperature"*
18:00 OP14
V. Bianco *"Contribution of water on the selection and stability of proteins at ambient and extreme thermodynamic conditions"*
EXCURSION TO ERICE ART&FOOD (INCLUD. DINNER)

FRIDAY 26

09:00 TU3
V. Vlacky *"Toward better understanding of aqueous polyelectrolyte solutions"*
11:00 IL6
F. Bruni *"The putative liquid-liquid transition is a liquid-solid transition in water confined in MCM"*
11:45 OP15
J. Zubeltzu *"Simulations of nanoconfined water between planar and corrugated planes"*
12:15 OP16
G. D'Angelo *"Probing intermolecular interactions in phospholipid bilayers by far-infrared spectroscopy"*
12:45 OP17
G. Magi Meconi *"Adsorption and desorption behavior of ionic and nonionic sufractants on polymer surfaces"*

15:00 DISCUSSION
16:00 PL4
J.-E. Shea "*Effect of surfaces and osmolytes in modulating peptide assembly*"
17:30 IL7
M. Paolantoni *"Structural dynamics in the protein hydration shell as revealed by extended depolarized light scattering (EDLS) experiments"*
18:15 OP18
L. Chiodo *"Role of water in the open and closed-locked structures of the human alpha7 nicotinic receptor: a full atomistic computational study of native and mutated forms"*

SATURDAY 27

09:00 TU4
A. Paciaroni*"Fast internal dynamics of biomolecules and their hydration water. A neutron scattering spectroscopy based view"*
11:00 IL8
B. Bagchi *"Protein hydration and hydrophobic force law in neat water and aqueous binary mixtures"*
11:45 PL5
A. De Simone *"Biophysics of waters at protein surfaces and proteins at water interfaces"*

12:45 CLOSING

TUTORIAL

EXPLORING THE CONFORMATIONAL SPACE AND DYNAMICS OF BIOMOLECULAR SYSTEMS USING PRESSURE PERTURBATION

Roland Winter

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Pressure perturbation serves as an important tool to mechanistically explore the conformational and free-energy landscape of biomolecular systems and to reveal the effects of pressure on biosystems exposed to high-pressure stress [1], including organisms thriving in the deep sea where pressures up to the kbar-level are encountered. We report on the principal action of pressure on biomolecules with emphasis on membranes, proteins, nucleic acids, and their assemblies [1,2]. By combining X-ray and neutron scattering, spectroscopies, and liquid-state theoretical approaches, the effects of molecular crowding, cosolvents, temperature and pressure on the intermolecular interaction, solvational properties and dynamics of proteins will be discussed [3]. Using single-molecule Förster resonance energy transfer and fluorescence correlation spectroscopy, we delineate the thermodynamics and kinetics of nucleic acid folding processes in the absence and presence of osmolytes at both ambient and extreme environmental conditions. The osmolyte trimethylamine-N-oxide has been found to stabilize the folded conformation not only at high temperatures, but also at high pressures, i.e., serves as both, "thermolyte" and "piezolyte". We then discuss the wide potential of the pressure perturbation approach to uncover high-energy conformational and functional substates of proteins, for example, to dissect protein aggregation and polymerization reactions [4]. This approach reveals new insights into the pre-aggregated regime as well as mechanistic details about concurrent polymerization pathways and the differential stability of the protein filaments formed. Finally, we present some recent results using pressure perturbation to explore membrane-associated biomolecular assemblies and uncover membrane-mediated conformational substates of proteins, furnishing unprecedented information on proteo-lipid interactions [5], and to modulate enzymatic conversions [6].

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MICROSCOPIC UNDERSTANDING OF THE BIOMOLECULAR CORONA

Kenneth. A. Dawson

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In essence we argue that a more complete understanding of how nanoparticles interact with living organisms requires an appreciation of the molecular arrangements of recognition motifs and architecture at the nanoscale (biomolecular corona) surface. We consider that it is now necessary to develop away from current phenomenological to more microscopic understanding of these biological interactions.

The concept of biological identity (including 'biomolecular corona') of nanoparticles is first summarized in terms of the approach to the cellular membrane (1-3), and then within cells (4). Besides laying some of the foundations for biological recognition at the nanoscale, we also argue (5) that this level of understanding is necessary (system by system) before making any broad conclusions about the efficacy or value of classes of nanoscale therapeutics, and avoid unwarranted elimination of many useful directions simply because they were poorly implemented.

We stress the unique opportunity to control (based on such molecular underpinning) biological interactions provided by the nanoscale, and the potential to support a strong and vibrant nano-therapeutics platform.

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TOWARD BETTER UNDERSTANDING OF AQUEOUS POLYELECTROLYTE SOLUTIONS

Vojko Vlachy

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Properties of polyelectrolytes in solution differ qualitatively from both the uncharged polymers as also from the low−molecular weight salts. The multi−faceted applications to technological processes make the understanding of these systems important. In addition, studies of aqueous solutions of nucleic acids, as also other molecules with polyelectrolyte character (proteins), are important for biology. In the simplest case such a solution contains large, often highly charged, polyions and the related number of counterions to render the system electroneutral. Strong attractive interaction between polyions and small ions of the opposite sign (counterions) leads to the accumulation of counterions in the vicinity of a polyion. As a consequence, the activity and the mobility of the counterions are reduced well below their bulk values. In polyelectrolyte−electrolyte mixtures small ions having the same sign of charge as that for the macroions (coions) are pushed away from the polyions. These properties can be fairly well accounted for by the traditional electrostatic theories[1−3]. Such theories treat water as dielectric continuum and cannot account for the solvation and salt−specific effects. Biologically important molecules contain besides charges as also the hydrophobic groups. The presence of such groups may modify the solvation of charges and influence the potential of the mean force between the polyion and ions in the solution. We review the properties of partially hydrophobic polyelectrolytes (aliphatic *x,y*−ionenes of varying hydrophobicity) in aqueous−salt environment. We present the results obtained by the following experimental methods[4−9] : osmometric, conductometric and transference number measurements (ion−binding determinations), isothermal titration calorimetry, apparent heat capacities and molar volumes measurements, dielectric relaxation spectroscopy, nuclear magnetic resonance, and small angle neutron scattering. We discuss the experimental and molecular dynamics results[6,10] in light of the polyion−ion interaction, affected by hydration and presence of hydrophobic groups. Emphasize is on the salt−specific effects.

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FAST INTERNAL DYNAMICS OF BIOMOLECULES AND THEIR HYDRATION WATER. A NEUTRON SCATTERING SPECTROSCOPY BASED VIEW.

Alessandro Paciaroni

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Until the middle of the twentieth century, proteins have been perceived by scientists as rigid entities, like the beautiful and colorful structures flooding the covers of modern journals. However, a scenario with a unique protein structure, the 'folded state', can be deceptive. Ironically, the dynamic nature of biology seems to have been forgotten at this microscopic level. Actually, a number of experimental techniques have confirmed that proteins are much more like soft materials that sample a large ensemble of conformations around the average structure as a result of thermal energy.

A complete description of proteins requires a multidimensional energy landscape that defines the relative probabilities of the conformational states (thermodynamics) and the energy barriers between them (kinetics). To understand biomolecules in action, the fourth dimension, time, must be added to the snapshots of proteins frozen in crystal structures. This concept leads to an extension of the structure–function paradigm to include dynamics. In fact, the picture is even more complex than that, because the biomolecule dynamics is critically coupled to that of the surrounding solvent, which in turn plays a key role for the onset of the very biological functionality.

While a direct link between micro- to milli-second domain motions ("slow motions") and enzymatic function has been established, very little is understood about the connection of these functionally relevant, collective movements with the local pico- to nano-second timescale thermal fluctuations. Such "fast motions", correspond to jumps among conformational substates over energy barriers of less than 1 kT at physiological temperature.

Neutron scattering spectroscopy is one of the most powerful experimental technique to investigate the features of fast fluctuations of biomolecules. By exploiting intrinsic properties of the neutron probe interacting with the biological matter (coherent/incoherent cross section, isotopic contrast) it is possible to single out the single particle or the collective dynamics of a labeled part of the system, and even isolate the solvent contribution.

Elastic, inelastic, quasielastic, and spin echo neutron scattering cover a time window from about 10^{-13}s to 10^{-7}s, thus allowing to carefully follow the profile of different tiers of the biomolecule-water potential energy hypersurface, and selectively track the H-bond fluctuations at the protein-solvent interface and the protein side-chains and domain reorientational motions.

In this tutorial lecture, we will illustrate how neutron scattering experiments gave a fundamental contribution to the discovery of some key phenomena related to the functionally relevant fast dynamics of biomolecules and their solvent and helped clarifying the intimate link among motions occurring in very different timescales.

PLENARY LECTURES

PL1

THE ESSENTIAL ROLE OF WATER IN BIOMOLECULAR FUNCTION

Sylvia McLain

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Understanding how biological molecules interact with physiologically relevant environments is crucial for understanding their function. From proteins folding into their functional forms to ligand-protein binding and membrane formation, understanding how nature engineers self-assembled biomolecules is fundamental to understanding the development of life itself. Water is the physical milieu in which these interactions occur, yet there is relatively little understanding of the role that water plays, especially on the atomic scale where an interplay between hydrophilic and hydrophobic motifs gives rise to more complex functions.

Using experimental techniques that probe on the atomic scale - predominately neutron scattering and NMR - in combination with computational techniques, we have investigated the interactions between a variety of naturally-occuring and synthetic biomolecules and water in solution. This research has provided insights into a variety of phenomenon, where specifically hydration in both protein folding and psycho-active drug-delivery will be discussed. In both of these systems, water has been found to play a more active role than it has previously been thought, where protein folding appears to be actively initiated by site speicific hydration around the protein backbone. Similarly, drug-conformation has also been linked to hydration, where specifically understanding water-mediated drug interactions appear to be the key to understanding both their delivery and function in vivo.

AQUEOUS NANOSCALE SYSTEMS: FROM LONG RANGE INTERACTIONS IN WATER TO MEMBRANE HYDRATION AND WATER DROPLETS

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Water is important for many processes on earth. In living organisms, membrane formation and functioning, protein folding and activity are driven by hydration. In our environment, water shapes our landscape and determines our climate. To obtain molecular level knowledge on multiple length scales of aqueous solutions and nano- and micron scale curved interfaces in solution, we develop and use nonlinear light scattering and imaging tools. With those methods, we study the interaction of ions and water, the structure of confined water droplets and the formation and functioning of membranes.

By probing the interaction of ions with water with fs elastic second harmonic scattering, a background-free method sensitive to ordering effects on the nanoscale, we find universal long-range effects that can be observed already at an ionic strength of 10 micromolar (~70 hydration shells). 20 different electrolytes all increase the orientational order of bulk water in the same way. This modification of the hydrogen bond network of water is due to the interaction of the total electric field of all the ions with the water network, leading to a modulation of the water-water interactions. This entails a change in the energy stored in bulk water and manifests itself macroscopically as a small amplitude minimum in the surface tension. Light and heavy water show a remarkably different behavior, pointing to the importance of nuclear quantum effects [1-3].

Nanoscale water droplets with a radius of 100 nm embedded in a hydrophobic liquid environment are exemplary of (marine) aerosols. We have determined the surface water structure of these small droplets at room temperature, under supercooled conditions and in frozen form and find that the hydrogen bond network at the interface exhibits more order than an equivalent extended planar interface made of the same chemical. The increased amount of order is equivalent o a reduction of the surface temperature by 50 K [4].

Liposome interfaces are highly curved and thus for a 100 nm liposome some 15% of additional lipid is expected in the outer leaflet. We find from our experiments that are exceptionally sensitive to transmembrane asymmetry that the number of lipids in the outer and inner membrane is the same. The difference in area between the leaflets is determined by the number of hydrating water molecules. In addition curvature effects are discussed leading to unexpected consequence [5].

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PL3

A MULTI-SCALE APPROACH TO THE STUDY OF PROTEIN DESIGN, FOLDING, AND AGGREGATION. IS EXPLICIT WATER RELEVANT?

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In nature, proteins are dissolved in water, which has a profound impact on proteins folding and aggregation properties.
In order to study such effect at a fundamental level, we employ a multiscale coarse-grained approach. First, we demonstrate with a multiscale approach that a simple design procedure[1] can produce proteins that fold into their target structure both at a simple representation level (lattice model[2–4]) as well as at a realistic representation level (caterpillar model[5,6]). In fact, we show that, for a large set of real protein structures, the caterpillar protein model produces designed sequences with similar physical properties to the corresponding natural occurring sequences. For an independent set of proteins, previously used as a benchmark, the correct folded structure of both the designed and the natural sequences is also demonstrated. Within the lattice model, we introduce an explicit solvent[7,8] and we show that fundamental features of natural proteins can be reproduced on large populations of artificial sequences designed taking into account the properties of water at different temperatures and pressures. Finally, we push our model to solutions of proteins studying their aggregation properties.

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EFFECT OF SURFACES AND OSMOLYTES IN MODULATING PEPTIDE ASSEMBLY

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Intrinsically disordered peptides (IDP) do not fold into well-defined globular structures, but rather populate a disparate ensemble of conformations with transient secondary structures. These peptides can perform a variety of functions, from cell signaling to structural scaffolding. Under pathological conditions, a number of IDPs can self-assembled into aggregate structures that have been linked to disease. Using a combination of coarse-grained and atomistic simulations, I will discuss the effect of surfaces and the osmolytes urea and TMAO in regulating the structure and assembly of intrinsically disordered peptides. I will focus on two model systems, the mussel foot protein implicated in underwater adhesion of mussels to rocks, and the Tau peptide implicated in Alzheimer's Disease.

BIOPHYSICS OF WATERS AT PROTEIN SURFACES AND PROTEINS AT WATER INTERFACES

Alfonso De Simone

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Understanding the many roles of waters in biology is a top scientific challenge that requires crossing the disciplinary boundaries between structural biology and statistical mechanics. Water is not only the solvent of life, but indeed has specific roles in relevant biomolecular mechanisms in the cell, including protein-protein interactions, protein folding and macromolecular assembly. The physical properties of the active waters in these processes can be extremely different from those of the bulk solvent. In this context, we employ molecular dynamics simulations intertwined with experiments of biomolecular NMR [1] to dissect the balance between entropic and enthalpic terms in the hydration of macromolecules [2] and to ultimately address the dynamical and structural properties of waters at the protein surfaces [3-6] and of proteins at water interfaces [7-8].

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INVITED LECTURES

MULTIPLE SOLVENT-SLAVED DYNAMIC PROCESSES IN HUMAN SERUM ALBUMIN MONITORED BY PHOSPHORESCENCE SPECTROSCOPY

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Despite extensive experimental and computational efforts to understand the nature of the hierarchy of protein fluctuations and the modulating role of the protein hydration shell, a detailed microscopic description of the dynamics of the protein-solvent system has yet to be achieved. By using single tryptophan protein phosphorescence, we follow site-specific internal protein dynamics over a broad temperature range and demonstrate three independent dynamic processes. Process I is seen at temperatures below the bulk solvent T_g, has low activation energy, and is likely due to fast vibrations that may be enabled by water mobility on the protein surface. Process II is observed above 170 K with activation energy typical of β relaxations in a glass; it has the same temperature dependence as fluctuations of hydration shell waters. Process III is observed at T > 200 K; it has super-Arrhenius temperature dependence and closely follows the primary relaxation of the bulk. The fluorescence of pyranine bound to the protein reports on the mobility of water in the hydration shell; it reveals a shift in emission spectra with increasing temperature indicative of a changing H-bond network at the surface of the protein. These results support a model of solvent-slaved protein dynamics.

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IL2

AQUEOUS SOLUTIONS: PROTEINS, PROTONS, HOLES AND OTHER INTERFACES

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Water is one of the most ubiquitous substances in the universe. Despite long study from both experimental and theoretical approaches, phenomena in liquid water and its coupling to other systems continues to be a source of rather rich and interesting physics. In this talk, I will discuss work over the last several years aimed at using atomistic molecular dynamics simulations to understand the structural and dynamical properties of water in various contexts. I will first tackle the question of `biological water' and whether it really exists. This will then lead into describing our efforts in quantifying and understanding topological properties of the hydrogen bond network of water and how it couples with protein conformational changes. I will then briefly discuss more recent work on understanding the electronic properties of water at interfaces such as the air-water interface and near amino acids and end with some new findings on density fluctuations in water.

WATER AT BIOMEMBRANES: STRUCTURE, DYNAMICS AND INFLUENCE ON ION ADSORPTION

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Biological membranes provide a limiting structure which separates the interior and exterior of cells and organelles. Being selectively permeable, they control the flow of substances in and out of the cell, which permits to regulate its composition and the communication between cells through signaling with ions. In the fulfillment of these functions, interfacial water plays a fundamental role, since it mediates in the interaction of the membrane with other biomolecules (such as proteins, sugars or other membranes), and it determines the electrostatic properties of the membrane.
In this contribution we discuss the properties and role of interfacial water in both membrane functions. First, we investigate using all-atom molecular dynamics simulations the properties of confined water in between interacting phospholipid membranes [1]. We show that both the translational and rotational dynamics of water molecules exhibit a monotonic dependence with the distance between the confining membranes. We interpret the results using a layering model of water molecules with the help of a local definition of distance to the membrane. Second, we study the effect of water in the interaction of phospholipid membranes with metallic ions. Using metadynamics simulations we quantify the free energy of adsorption of biologically relevant metallic ions and water to the membrane, providing a full characterization of ion adsorption [2]. Using the same technique we ascertain the effect of cholesterol in the adsorption of metallic ions to the membrane [3].

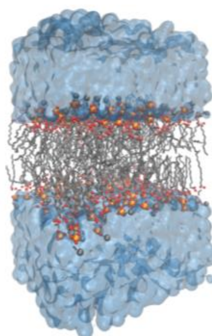

Figure: representation of model of hydrated membrane

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INSIGHTS ON THE MECHANISM OF SLOWING DOWN OF HYDRATION WATER AND EFFECT OF TREHALOSE ON PROTEIN CRYOPROTECTION

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In the first part of the talk I will show results from a molecular dynamics simulation study that has evidenced that protein hydration water has two well distinct slow structural relaxations. The [illegible]-relaxation typical of glassy dynamics and a second, slower, relaxation caused by the coupling with protein motions and importantly connected to the protein dynamical transition. I will then show a further simulation study along this line of a lysozyme protein immersed in a water-trehalose solution. The aim of this research is to understand in detail the cryoprotectant role played by this disaccharide through the modifications of both the slow relaxations. The most important finding is that the long relaxation coupled to protein dynamics appears enormously slowed down in the cryoprotectant solution with respect to pure hydration water.

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IL5

CONFORMATIONAL STABILITY OF GLOBULAR PROTEINS IN WATER AS A FUNCTION OF TEMPERATURE

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It is well established that globular proteins in water undergo two denaturation transitions, the so-called cold denaturation and hot denaturation [1]. It has been shown that this special feature can be rationalized by means of a model [2,3], grounded in statistical mechanics, that takes into account: (a) the increase in solvent-excluded volume effect associated with denaturation (it is the difference in the Gibbs energy cost to create a cavity in water suitable to host the denatured state and the native state, respectively); (b) the increase in conformational entropy of the polypeptide chain associated with denaturation [4]; (c) the balance existing between the energetic attractions of the denatured state with water, those of the native state with water and the intramolecular ones. The native state is thermodynamically stable in the temperature range where the gain in translational entropy of water molecules (due to the decrease in the solvent-excluded volume effect) overwhelms the loss in conformational entropy of the chain. The first contribution has a parabola-like temperature dependence in water, whereas the second one has a linear temperature dependence [2,3].
According to the model and the assumed energy balance, the denaturation enthalpy change should originate solely from the reorganization of water-water H-bonds upon the conformational transition and should be zero at the temperature of maximum density of water, T_H = TMD. Analysis of thermodynamic data for a large set of globular proteins [5] has shown that $\langle T_H \rangle = 277.5 \pm 25$ K, close to the experimental TMD value of water. This heuristic finding has strengthened the validity of the model and has suggested its application to rationalize the extra thermal stability of globular proteins from thermophilic microorganisms [6], and the effect of heavy water.

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THE PUTATIVE LIQUID-LIQUID TRANSITION IS A LIQUID-SOLID TRANSITION IN WATER CONFINED IN MCM

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Neutron diffraction experiment have been performed on water confined in MCM-41/C10 (pore size 2.8 nm) as a function of temperature, in the range 165 - 300 K. The NIMROD diffractometer used allows to investigate a wide *Q* range, extending from 10^{-2} to 30 $Å^{-1}$; this is of particular relevance, as it is possible to look at the same time at the peak (around 0.21 $Å^{-1}$) resulting from the (10) plane of the 2D hexagonal arrangement of the water cylinders in the silica matrix and at water peak (around 1.7 $Å^{-1}$). The intensity of the first peak has been taken as an indicator of the average mass density of water in the pores, and the observed intensity changes as a function of temperature as an indication of a liquid-liquid transition below 210 K. The shape of the water peak, at around 1.7 $Å^{-1}$, suggests the formation of hexagonal ice below 240 K, as shown by the characteristic structure factor features typically present in crystalline water. Based on these observations the proposed liquid-liquid transition, determined with small angle neutron scattering technique , is really a crystallization transition of at least a fraction of water molecules confined in the MCM material.

IL7

STRUCTURAL DYNAMICS IN THE PROTEIN HYDRATION SHELL AS REVEALED BY EXTENDED DEPOLARIZED LIGHT SCATTERING (EDLS) EXPERIMENTS

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The hydration dynamics of a model protein (lysozyme) in water-rich aqueous solutions has been investigated by Extended Depolarized Light Scattering (EDLS) experiments at different concentrations and temperatures [1,2]. This technique has proved to be suitable for the study of dynamical processes in the broad frequency range going from fractions of GHz to tens of THz, corresponding to molecular dynamics on a time scale ranging from fractions to hundreds of picoseconds [3-7].
A detailed analysis of the EDLS spectral profiles provides evidence of the existence of two distinct relaxation processes on a picosecond time scale ascribed to hydration and bulk water. Under the influence of the protein, the structural dynamics of water is found to slow down by a factor 7-8, with a characteristic relaxation time going from *ca.* 0.6 ps for bulk water to *ca.* 4-5 ps for hydrating water molecules [1,4,7]. This retardation accounts for the effect induced by the protein on the local density fluctuations of water, which are basically related to the fast rearrangement of hydrogen bonds within the shell. It has been estimated that, in diluted conditions, this perturbation extends over large distances (>10 Å) from the protein surface, affecting the dynamics of more than three water layers. Moreover, our experiments evidence a strong reduction of the population of perturbed water with the increasing of lysozyme concentration. This behavior cannot be explained considering the random superposition among the solute hydration layers, but is instead consistent with the formation of protein clusters [2,7].
The overall picture has been confirmed by comparative EDLS investigation performed employing deuterated water as solvent. Interestingly, these experiments reveal a non-negligible isotopic effect on the retardation dynamics. Indeed, passing from light to deuterated water, a relatively greater slowing down effect is found. On the other hand, the spatial extent of the perturbation is found to be comparable for both solvation environments.

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PROTEIN HYDRATION AND HYDROPHOBIC FORCE LAW IN NEAT WATER AND AQUEOUS BINARY MIXTURES

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Dynamics of the hydration layer surrounding a protein has drawn intense attention in the last few years, even giving rise to considerable controversies and debates. The central issue seems to be the time scale of relaxation [1-3]. The estimates vary from protein to protein and also depend on the technique used to measure relaxation of the hydration layer. For example, dielectric relaxation provides a time scale of the order of 40-100 ps while solvation dynamics gives time scales as long as ns, and NMR finds no slow down. Similarly, uncertainties exist about the width of hydration layer. We shall combine simulations performed on different proteins to interrogate these issues. Particular attention shall be paid to the role of amino acid side chains in hydration layer dynamics [4]. We shall also discuss the nature of hydrophobic force experienced by two parallel plates immersed inside water [5]. We find a sharp cross-over in the distance dependence of the hydrophobic force law [5]. We shall also present initial results of protein hydration and hydrophobic force law in water-DMSO and water-Ethanol binary mixtures.

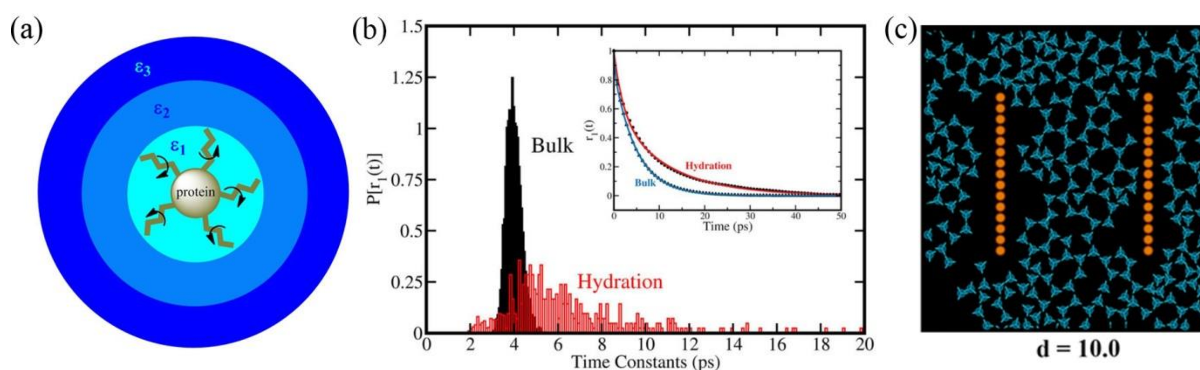

Figure 1: *(a) Schematic illustration of the conformational motion of protein side chains in an aqueous solution. Shell-wise decomposition of dielectric constant of protein hydration layers are shown in different shades of blue colour, (b) distribution of average orientational timescales and normalised time correlation functions (inset) of bulk and hydration layer of lysozyme and (c) hydrophobicity induced drying transition and solvent ordering in 2D Mercedes-Benz water confined between two hydrophobic plates.*

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ORAL PRESENTATIONS

THE ROLE OF WATER IN G-QUADRUPLEXES DNA STABILITY AND DYNAMICS BY UP-RRS

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Guanine-rich DNA strand can fold, in the presence of Na+ or K+ cations, into unique four-stranded structures called G-quadruplexes [1]. These structures are involved in several relevant biological processes such as aging, cancer and, more generally, in the regulation of gene expression [2-4]. Studying the factors governing the quadruplex folding is a key-step to understand their biological role.
Several investigations, involving molecular dynamics simulations and spectroscopic studies, have been dedicated in the last years on the effects of several co-solutes on conformation and stability of G-quadruplex DNA structure in an attempt to clarify the G-quadruplex behavior under cell-mimicking conditions. Despite the large number of studies, the elucidation of the interplay between the living environment and the G-4 biophysics at molecular level is still elusive.
Ultraviolet Polarized Resonant Raman Spectroscopy (UP-RRS) can be a valuable tool, thanks to the Raman cross section selective enhancement of the vibrational signals associated with some specific electronic transitions (e.g., those of purine rings in guanine rich DNA). This methodological approach allows to emphasize the perturbation at different temperatures due to the presence of co-solutes and to investigate even extremely diluted DNA samples. Indeed by combining the results obtained by UP-RRS, circular dichroism spectroscopy and microcalorimetry, it is possible to obtain novel information, at molecular level, not only on the nucleoside conformation (including sugar rings), structure and aggregation properties in crowded environments, but also on the hydration changes and local dynamics in the hydrogen bonding in the conformational transitions as a function of temperatures.

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OP2

WATER ADSORPTION AND RESPONSIVE BEHAVIOUR IN POLYSACCHARIDE PH-SENSITIVE HYDROGELS

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Hydrogels are a unique class of cross-linked polymers that are able to adsorb a large amount of water while preserving their three-dimensional structure. Among the wide range of polymeric formulation that gives rise to biocompatible hydrogels, an attractive class of 'intelligent gels' is represented by stimuli-responsive hydrogels. They are hydrogels whose swelling behaviour, network structure, permeability or mechanical strength can be triggered in response to different stimuli, such as temperature, pH and ionic strength. Particular effort has been devoted to the systematic exploration of the applications and development of pH-responsive hydrogels. The recently growing use of hydrogels especially in technological fields of high social impact has led to the need of the elucidation of the strict relationship between the molecular properties and the macroscopic behaviours observed in pH-responsive hydrogels. For example, for optimizing the loading and release of drugs in, it appears very important to be able to drive the diffusion of small and large molecules into the gel matrix. This mechanism can be efficiently controlled through the suitable tuning of i) the mesh size of the gel network and ii) of the hydrophobic/hydrophilic interactions established between the polymer matrix, the solvent and the drug. The understanding of the fundamental properties of these systems can benefit from a joint use of different experimental techniques that provides a multi-scale view -from molecular to macroscopic length scale- of the pH-sensitive gelling behaviour exhibited by hydrogels. In this contribution, we show how the combination of Small Angle Neutron Scattering (SANS), UV Raman and Brillouin light scattering (BLS) measurements can be successfully used to link the static and dynamical features of polysaccharide hydrogels with their water-retaining ability and with their chemical-physical response to pH variations. Moreover, we discuss how the chemical and physical interactions between the drug and the hydrophobic/hydrophilic moieties of polymer matrix can change the hydrogel characteristics influencing the release performances. As prototype case study, the water adsorption properties and the pH-responsive behaviour exhibited by natural and biodegradable cyclodextrin-based hydrogels, namely cyclodextrin nanosponges (NS) will be explored.

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THERMAL PROPERTIES AND MOLECULAR MOBILITY OF LOW-MOISTURE AMORPHOUS TREHALOSE-LIMONENE MATRICES OBTAINED BY DIFFERENT GLASS-FORMING APPROACHES

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The achievement of a glassy state is critical to encapsulate bioactives and flavour compounds that become entrapped in the system during vitrification. Process factors, thermal history and composition affect the retention ability and the physical properties of the low moisture/dry encapsulated amorphous materials.
Spray drying is a widely applied technology to encapsulated flavour into low moisture, carbohydrate-based powders, but new technologies exist or are under development to improve quality and stability of the final products. Milling is a technology largely used in the pharmaceutical sector for processing purposes, while in recent times it received a growing interest due to their ability to induce crystal-to-glass transformations at temperature below Tg and to modify the physical properties and functionality of the materials exploitable in innovative applications.[1] With comilling two components are simultaneously subjected to the same mechanical milling stress, producing co-crystals or alloys,[2] as well as inclusion complexes and solid dispersions. Volatile aroma compounds are small molecules that can be entrapped in the glassy matrix. Although various theories support their retention in the glassy state, however, so far, scarce information are available about the role of the aroma molecules in affecting the physical properties and mobility of the carbohydrate glassy matrices and how different processes procedures affect aroma retention.
This study aimed to investigate the physical properties and molecular mobility of low moisture, microencapsulated limonene-trehalose amorphous matrices obtained by two different glass-forming technologies, namely, spray drying (as an example of desolvation technique) and comilling. Thermal analysis (DSC) evidence a significant difference in the structural properties of the low moisture products obtained by spray-drying and comilling procedures. The content of limonene in the comilled systems (GC-MS) did not affect the Tg of the glassy dispersion, while it significantly modified the kinetics of cold-crystallisation and melting. TD-NMR analysis highlighted a significant increase of the relaxation time T2 related to the presence of limonene not interacting with the trehalose matrix. The overall view consistently supports the use of milling as a better technology for aroma encapsulation.

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HYDROGEN-BOND REARRANGEMENT IN CYCLODEXTRIN AQUEOUS SOLUTIONS PROBED BY UV RAMAN AND BRILLOUIN SCATTERING

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Cyclodextrins (CDs) are natural cyclic oligosaccharides composed by a variable number of glucose units. Their characteristic truncated-cone shape permits to the CDs to behave as a molecular host able to encapsulate a wide variety of guest molecules which are poorly soluble in water systems. CDs have found different applications in pharmaceutical and food industries.
Since most of the CD's applications take place in aqueous media, the understanding of the role played by water in activating the CD as host system is of fundamental importance. The hydrogen-bond (H-bond) interactions between the groups of CD and the surrounding water molecules are expected to play a key role in determining the performance of this oligosaccharide as solubilizing, stabilizing, and complexing agents. Consequently, the investigation of hydration properties of CD molecules represents a very important topic and it is crucial for their application in biological system.
In this work, the hydration shell behavior in cyclodextrin aqueous solutions was investigated by a joint combination of UV Raman and Brillouin scattering. The measurements have been performed on water solutions of native and chemically modified cyclodextrins as function of both temperature and solute concentration. In the analysis of Raman spectra, the attention was focused on the changes occurring in the O-H stretching band of water. These temperature- and concentration-dependent modifications have been related to the structural rearrangement occurring in the H-bonding network of water molecules under different experimental conditions. At the same time, information on the collective dynamics of the cyclodextrin-water solutions were provided by UV Brillouin scattering experiments. This technique allows us to probe relaxation processes occurring at the characteristic timescale 0.1–10 ps, which is associated to the average timescale of the intermolecular bonds lifetime, typically observed in liquid H-bond systems. Summarizing, in this contribution we will show the potentiality of the joint use of UV Raman and Brillouin scattering to investigate the solute-solvent interactions and hydration shall behaviour in cyclodextrin aqueous solutions.

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STRUCTURAL PROPERTIES OF WATER CONFINED BY PHOSPHOLIPID MEMBRANES

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Biological membranes are essential for the cell life and hydration water provides the driving force for their assembly and stability. Here we study the structural properties of water in a phospholipid membrane. We characterize local structures inspecting the intermediate range order (IRO) adopting a sensitive local order metric, recently proposed by Martelli et al. (1), which measures and grades the degree of overlap of local environments with structures of perfect ice. Close to the membrane, water acquires high IRO and changes its dynamical properties, e.g., slowing down its translational and rotational degrees of freedom in a region that extends over ~1 nm from the membrane interface. Surprisingly, we show that at a distance as far as ~2.5 nm from the interface, although the bulk-like dynamics is recovered, water's IRO is still slightly higher than in bulk at the same thermodynamic conditions.
Therefore, the water-membrane interface has a structural effect at ambient conditions that propagates further than the often-invoked 1 nm-length scale, a results that should be taken carefully into account when analyzing experimental data of water conned by membranes and could help us understanding the role of water in biological systems (2).

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DEGRADATION KINETICS OF PHYCOCYANIN UNDER ISOTHERMAL AND DYNAMIC HEATING

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Justification: Increasing public concern about the addition of synthetic colors to foods has generated the necessity to identify adequate food colorant replacements and characterize their stability under common processing conditions such as temperature. Phycocyanin (PC) is a natural color derived from the cyanobacteria *Arthrospira platensis* that can replace Fast Green FCF (FD&C Green No. 3) and Brilliant Blue (FD&C Blue No.1) in food products. PC has been approved for its use as a colorant and functional ingredient in foods by the FDA in 2013.

Objective: This study aims to characterize the stability of PC during isothermal heating and provide an adequate model to estimate its degradation under non-isothermal conditions.
Methods: Solutions of phycocyanin in double distilled water (0.3 μM) were heated isothermically in a water bath kept at 55, 60, 70, and 80°C. The stability of the phycocyanin's was monitored in terms of its fluorescence emission intensity (λ_{exc}: 370nm; $\lambda_{em:}$ 643nm) at set time intervals. The isothermal degradation curves of PC were fit with a Weibullian model (i.e., $\frac{C(t)}{C_0} = e^{-bt^n}$). The temperature dependence of the models parameters (b and n) was characterized by adequate secondary models. The stability of the PC under non-isothermal conditions (3 different temperature profiles) was recorded and used to validate the derived model.

Results: Fluorescence emission provided a robust measure of PC stability. PC exhibit a prominent peak at 643nm when excited at 370nm. Based on the selected goodness of fit measures (mean squared error and residuals), the isothermal degradation kinetics was adequately characterized using the Weibullian model. The values of the rate (b) and scale (n) parameters increased as temperature increased (0.02 to 0.35min^{-1} and 0.5 to 1.5, respectively). The temperature dependence of both parameters was characterized by logarithmic exponential models. The solution of the respective rate equation appropriately estimated the degradation under the three non-isothermal profiles. Deviations between the estimated and experimental values were lower than 8%.

Significance: A better understanding of stability of PC during thermal treatments can expand the use of PC as a food color and functional ingredient. Adequate modelling approaches can help optimize heat treatments of foods containing PC.

CAMBUCI OSMOTIC DEHYDRATION: DETERMINATION OF THE FIRST THERMODYNAMIC PSEUDO EQUILIBRIUM USING SOLID-LIQUID EQUILIBRIUM DIAGRAM

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Cambuci (*Campomanesia phaea* O. Berg) is a Brazilian Atlantic Coastal Forest plant and, according to Gonçalves et al. (2010), it is rich in nutraceutic compounds and is also able to enhibit α-amilase and α-glucosidase enzymes, which contributes to diabetes mellitus control. Donado-Pestana et al. (2015) verified that the cambuci fruit extract increased HDL and lowered the LDL cholesterol levels in the blood plasma of mices. Although this fruit has nutritional benefits, its consumption is restricted to areas next to the harvest locations, as the product is perishable mainly because of the high moisture level (over 80 g/100 g w.b.). To guarantee a longer shelf life to the fruit, it was studied the osmotic dehydration using non-caloric solutes (glycerol and sorbitol) at concentrations varying from (40 to 60) g/100 g for up to 6 h. The composition changes in the fruit (solid-liquid system) were represented in a three-component diagram according to Fito and Chiralt (1996) methodology, which enables to define the first pseudo equilibrium period. To construct the equilibrium diagram, cambuci fruits were selected from the same producer and crops and, after the sanitation, it was manually peeled and sliced to the thickness of 4 mm and diameter of 30 mm, approximately. The process temperature was kept at 25 °C and the fruit/osmotic solution ratio was 1:10. Moisture and soluble solids analyses were carried out each 30 min in the first hour and then each one hour until the end of the process. After 1 h of dehydration, the solution containing glycerol at the lowest concentration (40 g/100 g) reached the pseudo equilibrium and the solution containing sorbitol at the same concentration needed 6 h to reach the same solutes and water mass fraction. The results observed can be explained due to the different molecular weight of the solutes, as sorbitol has higher molecular weight than glycerol (182.17 and 92) g/ mol, respectively, and therefore a longer period for diffusion of the solute in the fruit matrix was necessary to reach the pseudo equibrium. Lower water mass fraction (0.35 g/100 g of fruit) was enabled by the glycerol solution with the highest concentration (60 g/100 g) and it was required three hours to reach the pseudo equilibrium. It was concluded that the use of solutes with different molecular weights affect the time to reach the pseudo equilibrium and that highest osmotic solution concentration provides lower water mass fraction and higher solid mass fraction, but it requires a longer time to reach the pseudo equilibrium.

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PRESSURE EFFECTS ON THE PROTEIN DYNAMICAL TRANSITION

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The Protein Dynamical Transition (PDT) consists in a steep increase in the temperature dependence of the flexibility of proteins occurring at about 200K. One of the most powerful techniques for its investigation is incoherent neutron scattering, which can give a measure of the Mean Square Displacements (MSD) of the non-exchangeable protein hydrogen atoms, as firstly shown by Doster and co-workers in 1989 [1]. The biological relevance of PDT has been pointed out and its physical origin has raised debates in the literature, still being an open question [2-6]. Studies of protein structural dynamics in general, and of the PDT in particular, as a function of pressure would be highly desirable both to help clarifying its physical origin and from a more biological point of view, since many biological systems live at high hydrostatic pressure.
Very few studies have addressed the problem of the pressure dependence of protein dynamics as studied with neutron scattering, and most of them have been concerned with samples in solution investigated near room temperature [7,8]. Studies on the pressure dependence of the PDT on protein systems are lacking, probably because of the relevant experimental challenges.
We report here on the temperature dependence of the MSD of Myoglobin (Mb) in an ultraviscous mixture of protein/D8-Glycerol/D_2O [9], in the temperature range 20-300K, and at different pressure values, from ambient pressure to 5 kbar. Data have been analysed within a double well potential model and show a significant reduction of protein dynamics with increasing pressure up to 2 kbar; a sudden MSD increase is observed between 2 and 3 kbar, likely related to protein pressure induced denaturation. However, the pressure effect decreases the MSD amplitude without altering the PDT onset temperature. Implications of these findings to the Mb energy landscape will be discussed.

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OP9

WATER DYNAMICS DETERMINE HOW ENZYME FUNCTION

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Many enzymes, such as those operating in respiratory chains of biology, have to operate at nearly zero reaction free energy and yet to sufficiently lower the reaction barrier. Water plays a vital roles in the mechanistic solutions for this challenge and in design principles of physiological energy chains of biology. These large protein complexes, located in membranes of mitochondria, have to provide a unidirectional electron flow avoiding damaging side reactions. Electrowetting of the active site following electron transfer is universally used to trap the charge and to avoid backward transitions (a diode-type unidirectional current [1]). A more general design principle involves non-ergodic sampling of the enzyme's phase space [2]. Proteins are generally unable to sample the entire space of their configurations, leading to the breakdown of the fluctuation-dissipation relation. The result is a significant lowering of the activation barrier in redox enzymes [2] due to an effectively higher temperature of enzyme's operation. In some cases, this non-ergodic sampling is combined with the multiplicity of quantum states of the active sites coupled to the fluctuations of the hydration layers [3]. All these different strategies of accelerating chemical reactivity by natural enzymes take advantage of large-amplitude electrostatic noise produced by electro-elastic fluctuations of the protein-water interface [4].

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OP10

THE EFFECT OF ROOM-TEMPERATURE IONIC LIQUIDS ON BIO-MEMBRANES, PROTEINS, AND THEIR HYDRATION WATER: A NEUTRON SCATTERING, AFM, AND COMPUTER SIMULATION STUDY

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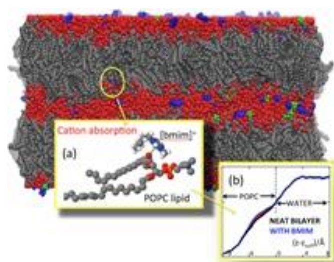
The molecularly thin layer of water in direct contact with bio-molecules in a physiological environment plays a major role in determining their properties and functions. In this context, water is a shorthand notation for “water electrolyte solution”, since almost without exception a variety of ions dissolved in water are needed to ensure the stability of bio-systems, greatly contributing to their complex behaviours.

In recent years, the development of compounds of the so-called room-temperature ionic liquid (RTIL) family has enormously expanded the number of ionic systems that could be used to modify the properties of the interfacial water, and thus to affect the behaviour of bio-systems.



My study concerns the microscopic mechanisms underlying RTIL effects on biosystems (e.g. phospholipid bilayers, proteins, and nucleic acids) through their hydration water, and relies on the combination of neutron scattering, molecular dynamics (MD) simulations, and complementary techniques as Atomic Force Microscopy (AFM), Raman scattering, and infrared spectroscopy.

In my contribution I will briefly review the state of the art in this topic [1]. Then I will focus on two specific cases. The first one concerns their interaction with biomembranes: I will show how RTILs diffuse into the hydrophobic portion of lipid biomembranes, enhancing the penetration of water into the bilayer (fig. 1) [2,3]. The second one concerns the RTIL interaction with proteins [4,5]. I will show how these organic salts can either help or prevent amyloidogenesis. Implications in bio-medicine, sensing technology, and material science will be presented.

Fig. 1 – Schematic view of one of the sample configurations used in my MD simulations [3]. POPC domains in grey, water layers in red, $[bmim]^+$ in blue, and $[PF6]^-$ in green. Inset (a): Representative configuration of POPC and $[bmim]^+$. Inset (b): water density profiles: the difference (area in red) points to a water excess in the POPC doped with $[bmim]^+$.

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OP11

WATER AND VIRUSES: RECIPROCAL CONTROL

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It is not likely you will catch influenza in Erice at 30ºC and 70% humidity - generally, the interaction of water with the coat proteins of viruses influences the transmission. We started our investigations with a textbook virus example, Tobacco Mosaic Virus (TMV) [1-3]. TMV retains its tubular shape in vacuum, and in contact with air or solvents [4]. However, the highly regular helical coat was as yet probed by methods that average over many particles at very high humidity (X-ray diffraction, cryo-electron microscopy) [1]. We achieved local probing of single virus particles, without averaging, by multifrequency AFM [5] and low voltage SEM. TMV in the dry state shows unexpected nanoscale surface features at irregular axial spacings. We are developing a model that can explain how drying brings about new structural features. The stepwise and reversible wetting by water can be studied by AFM in a humidity chamber, and by environmental electron microscopy in up to 10 mbar water. We observed scenarios such as wet wedges (around TMV), layers (on TMV), and water pools (confined by TMV) [6]. Except for ultrathin layers (≥1 nm), the water topography is completely compatible with macroscale wetting scenarios. The Tomato Mosaic Virus (nearly identical to TMV) can be transported by clouds and in fog [7]. This prompted us to ask whether viruses can in turn initiate cloud formation by nucleation of ice - this is known from bacterial ice nucleation proteins (INPs), but not generally from other proteins. We tested a protein cage, apoferritin, as model for a small spherical virus, in supercooling scenarios. Indeed, apoferritin induces rapid freezing already at -6.5ºC, similar to INPs. Although apoferritin probably plays a minor role in nature, viruses of similar composition and shape are abundant even in seawater, and could indeed supplement the standard nucleation route at mineral dust particles [8].

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OP12

WATER-BASED SCREENING OF ANTIBIOTICS PERMEABILITY IN GRAM-NEGATIVE BACTERIA

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Bacteria multi-drug resistance is a challenging problem of contemporary medicine. A new molecular framework is needed for identifying and developing new antinfectives. This is especially true for Gram-negative bacteria where the presence of the additional outer membrane (OM) hinders the access to internal targets[1]. General diffusion porins are expressed to facilitate the entry of polar molecules, and they are the main pathway for polar antibiotics to overcome the OM. Bacteria can develop resistance by changing the rate with which these compounds permeate the OM, either by modulating the expression of porins, or by altering porins permeability through mutations[2]. The discovery of new effective polar antibiotics passes through the determination of the electrostatic interactions controlling translocation through porins[3].

Aiming to reveal the electrostatic field inside bacterial porins, we have developed an all-atom water polarization based method to explore the electrostatics of solvated protein[4,5]. This method allows us not only to analyze protein's electrostatics but also to investigate the effects caused by media conditions, e.g., pH and ion concentration, with full atom resolution. By using the electrostatic profile of the channel and simple physicochemical properties of antibiotics, we have implemented a simple theoretical model to score drugs for their permeability[6]. These results may have important implications for the formulation of a general model for antibiotics translocation, and can be taken into account for screening molecules with improved permeation properties in rational drug designing.

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PROBING METHANE-HYDRATE NUCLEATION BY METADYNAMICS SIMULATIONS

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Methane clathrate hydrate is matter of great technological interest as a potential gas source (especially from marine hydrates) or as a medium for the storage and transport of methane. Despite this interest, very little is known about its kinetics and mechanism of formation, which is also very important as it aids in the development of additives to control the nucleation process. Indeed, experimental investigation of this topic is very difficult. An alternative approach to elucidate the nucleation mechanism is provided by molecular simulation. Recent studies have shown that the typical time scale of this phenomenon, even when the system is kept in supercritical conditions, is very large, of the order of microseconds. We, therefore, present a study of methane-hydrate nucleation by advanced atomistic simulation using the metadynamics approach. A set of collective observables is employed to describe the nucleation process. Thus, the free-energy as function of these observables is calculated by using the Landau approach.

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OP14

CONTRIBUTION OF WATER ON THE SELECTION AND STABILITY OF PROTEINS AT AMBIENT AND EXTREME THERMODYNAMIC CONDITIONS

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Proteins that are functional at ambient conditions do not necessarily work at extreme conditions of temperature *T* and pressure *P*. Furthermore, there are limits of *T* and *P* above which no protein has a stable functional state. Here we show that these limits and the selection mechanisms for working proteins depend on how the properties of the surrounding water change with *T* and *P*. We find that proteins selected at high *T* are super-stable and are characterized by an optimal segregation of a hydrophilic surface and a hydrophobic core. Surprisingly, a larger segregation reduces the stability range in *T* and *P*. Our computer simulations, based on a new protein design protocol, explain the hydropathy profile of proteins as a consequence of a selection process influenced by water, offering an alternative rationale to the evolutionary action exerted by the environment in extreme conditions. Our results are potentially useful for engineering proteins and drugs working at extreme conditions.

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OP15

SIMULATIONS OF NANOCONFINED WATER BETWEEN PLANAR AND CORRUGATED PLANES

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We study the response of water to the imposition of a planar and rougous potential for a film of water ~1nm thickness by computer simulations, using both empirical potentials and first-principles calculations. With no rugosity, we observe a continuous melting at high densities, related to the phase change of the oxygens only, with the hydrogens remaining liquid-like throughout. Moreover, we find an intermediate hexatic phase for the oxygens between the liquid and a triangular solid ice phase, following the Kosterlitz-Thouless-Halperin-Nelson-Young theory for two-dimensional melting. The decoupling in the behavior of the oxygens and hydrogens gives rise to a regime in which the complexity of water seems to disappear, resulting in what resembles a simple monoatomic liquid. The characterization of the liquid shows that it maintains the local structure of triangular ice independently of the density. For the rougous potential, we use a periodic confining potential emulating the atomistic oscillation of the confining walls, which allows varying the lattice parameter and amplitude of the oscillation. We do it for a triangular lattice, with several values of the lattice parameter: one which is ideal for commensuration with layers of Ih ice, and other values that would correspond to more realistic substrates. For the former, the phase diagrams show an overall rise of the melting temperature. However, before the melting, the triangular structure of the liquid is maintained despite the fact that it is not favoured by the external periodicity. For the latter, the liquid does not freeze, but a clear inhomogeneity is observed in the liquid as the strength of the rugousity increases. Although the first principles calculations give a more triangular-like liquid than the one observed with empirical potentials (TIP4P/2005), both agree surprisingly well in the main conclusions of the study.

OP16

PROBING INTERMOLECULAR INTERACTIONS IN PHOSPHOLIPID BILAYERS BY FAR-INFRARED SPECTROSCOPY

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Fast thermal fluctuations and low frequency phonon modes are believed to play a part in the dynamic mechanisms of many important biological functions in cell membranes.
Recently we have investigated the vibrational collective dynamics of lipid bilayers by MD simulations[1] and showed that these molecules support several low energy optical-like phonon modes in a spectral region below 300 cm^{-1}.
These optical vibrational modes are potentially involved in the vibrational energy transfer and in the hydrogen-bond dynamics at the membrane-water interfaces.
Here we report the results of a detailed far-infrared study of the molecular subpicosecond motions of phospholipid bilayers at various hydrations.
We show that these systems have a rich spectrum of low frequency collective modes and confirm the MD predictions. We deduce that these low frequency modes arise from vibrations of different lipids interacting through intermolecular van der Waals forces.
Furthermore we observe that the low frequency vibrations of lipid membrane have strong similarities with the subpicosecond motions of liquid water and suggest that resonance mechanisms are an key element to the dynamics coupling between membranes and their hydration water.

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ADSORPTION AND DESORPTION BEHAVIOR OF IONIC AND NONIONIC SURFACTANTS ON POLYMER SURFACES

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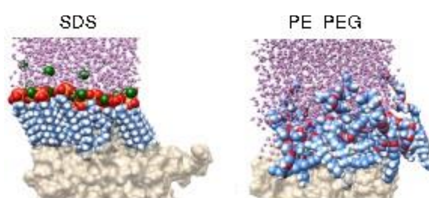
Experimental and computational studies are combined to elucidate the adsorption proprieties of ionic and nonionic surfactants on hydrophobic polymer surface such us poly(styrene). To present these two types of surfactants, sodium dodecyl sulfate and poly(ethylene glycol)-block-poly(ethylene), commonly utilized in emulsion polymerization, are chosen. By applying quartz crystal microbalance with dissipation monitoring it is found that, at low surfactant concentrations, it is easier to desorb (as measured by rate) ionic surfactants than nonionic surfactants. From molecular dynamics simulations, the effective attractive force of these nonionic surfactants to the surface increases with the decrease of their concentration, whereas, the ionic surfactant exhibits mildly the opposite trend. The contrasting behavior of ionic and nonionic surfactants, critically relies on two observations obtained from the simulations. The first is that there is a large degree of interweavement between head and tails groups in the adsorbed layer formed by the no-ionic surfactant (PEO/PE systems). The second is that water molecules penetrate this layer. In the disordered layer these nonionic surfactants generate at the surface, only oxygens of the head groups present at the interface with the water phase or oxygens next to the penetrating waters can form hydrogen bonds. Oxygens inside this layer lose this favorable energy, with a magnitude that increases with the surfactants density at the interface. This reduced stability of the surfactants diminishes their driving force for adsorption. All that is shown to be in accordance with experimental results on the dynamics of surfactants desorption. Ionic surfactants assemble into an ordered structure and the attraction to the surface was even slightly augmented at higher surfactant concentration, in agreement with the experimentally determined adsorption isotherm. The reason these two types of surfactants behave differently is because the ionic surfactant has a small head group that is strongly hydrophilic, whereas the head groups of the nonionic surfactants are large and only weakly attracted to water [1].



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OP18

ROLE OF WATER IN THE OPEN AND CLOSED-LOCKED STRUCTURES OF THE HUMAN ALPHA7 NICOTINIC RECEPTOR: A FULL ATOMISTIC COMPUTATIONAL STUDY OF NATIVE AND MUTATED FORMS

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Nicotinic acetylcholine receptors (nAChRs) are ligand-gated ion channels that regulate signal transmission at the neuromuscular junction [1]. Knowing their active and inactive structures, and the gating transition induced by ligand binding, is of crucial importance to understand the basis of the ligand-receptor interactions, and to develop new pharmacological approaches to influence the receptor function. Experimental structures of human *open-pore* and *closed-locked* conformations of nAChRs are still scarcely available [2]. In this respect, homology modeling and MD simulations are valuable tools to predict and refine structures of transmembrane proteins; however, they have been unsuccessful in providing stable open and closed structures of human nAChRs so far.

We recently provided an all-atom model of the human α7 full-length receptor complexed with epibatidine in a stably *open* conformation, obtained via homology modeling of a chimera based on high resolution structures, and extensive MD with minimal restraints [3]. Following the same route, we built and extensively refined a model of the human α7 *closed-locked* receptor bound to alpha-conotoxin. Indeed, the lack of a reference state for the human closed-locked conformation led so far to a quite difficult definition of the variables defining the intermediate resting and desensitized states [2].

Our analysis of the size and profile of the pore, of its hydration level, and of other structural descriptors supports the characterization of the active and inactive states both in the extracellular and transmembrane regions. In particular, we discuss the role of water in stabilizing the pore opening and in the ions permeation mechanism in the active state.

Furthermore, it is know that the amino acid composition at specific pore positions has a key role on ionic selectivity and permeation rate. Of particular relevance is the highly conserved pore-facing GLU residues at position -1': the effect of this GLU ring on the amplitude of the single-channel current is larger than other rings of pore-lining charged side chains. We built and extensively simulated a model of the open channel complexed with epibatidine in this mutant form. Effects of mutation on the structural descriptors and in particular on the pore hydration level are discussed.

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POSTER PRESENTATIONS

STRUCTURAL MODIFICATIONS OF HUMAN TELOMERIC QUADRUPLEX COMPLEXED WITH ANTI-CANCER DRUG DURING THERMAL MELTING: A SAXS STUDY

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The behavior of the intramolecular G-quadruplex formed by the human telomeric DNA sequence $AG_3(TTAGGG)_3$ during thermal melting has been investigated. Two diluted solutions (150µmol/L) of G-quadruplex with and without complexation with the well known anti-cancer drug D-Actinomycin [1], were measured by small angle x-ray scattering (SAXS) at various temperatures crossing the melting point. Ab initio modelling of the samples was calculated using the ATSAS package [2]. The first SAXS structural characterization of the free G-quadruplex changes in the path toward unfolding is provided. We show that complexation with the drug confer the G-quadruplex a quite compact structure in the whole investigated temperature range, at variance with free G-quadruplex that tends to lose its secondary structure after melting [3].

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SPECTROSCOPIC STUDY OF THE UNFOLDING AND AGGREGATION PROCESSES OF LYSOZYME UNDER DENATURING CONDITIONS: TOWARDS THE FORMATION OF PROTEIN HYDROGELS

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The complex structure of a protein is the result of interplay among different types of interactions that are strongly affected by the solvent; the balance between intramolecular and protein-solvent attractions determines the equilibrium between folded and unfolded state of the macromolecule [1, 2]. Protein conformation is strictly connected to its activity and, at the same time, a degree of structural flexibility is also requested for the protein in order to be active, the solvent playing a crucial role in this biological asset. This action, usually investigated under physiologic conditions, can be explored in more depth by studying the solvating properties of proteins as a function of pH, ionic strength and solvent composition [3]. In general, protein systems rearrange to minimize the interaction between hydrophobic residues and the polar solvent [4]. Depending on solvating conditions, the stabilization driving force can favor the folding of the protein system toward its native structure or can lead to misfolding and/or aggregation of protein molecules [5]. Such an aggregation process is characterized by different steps in which the protein undergoes conformational rearrangements and intermolecular association to form stable structures of increasing complexity, going from small clusters to amyloid fibrils, possibly passing through intermediate species. These species are involved in many neurodegenerative diseases [6, 7]. The formation of ordered aggregates is also interesting in biomaterial science since they can originate biocompatible hydrogels whose proprieties can be modulated by changing the aggregation condition [8]. Often transparent thermoreversible gels, suitable for spectroscopic investigations, can be easily produced. Due to its relative small size and simple structure, hen egg white lysozyme (HEWL) is one of the most suitable models to investigate protein denaturation. In this work, we have investigated the unfolding, aggregation and gelation processes of highly concentrated solution of lysozyme in denaturing conditions at different temperatures. The selected concentrated conditions have the double benefit of favoring the gelation process and mimicking the situation of crowding of the cytoplasm in living cells. Infrared (IR) and UV Resonant Raman (UVRR) spectroscopy have been used to probe structural properties of both protein and aqueous environment, in concentrated samples during the phase transformations. This study has allowed to develop a methodology for the preparation and characterization of transparent protein hydrogels with different physical characteristics.

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DSC ISOTHERMAL DEHYDRATION OF THIN FILMS OF SOLUTIONS, GELS AND COMPLEX REAL SYSTEMS: A RESEARCH SUMMARY[1]

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The isothermal dehydration of aqueous biosystems is a relevant topic in food, pharmaceutical and cosmetic industry. The process has been recently investigated in our laboratory for the assessment of a model calorimetric set-up and for the characterization of the parameters featuring the experimental calorimetric curve. The development of a theoretical model, which provides information regarding the water activity, was supported by investigating the effect of the several parameters involved in the isothermal dehydration, such as sample mass and temperature.[2,3]
In a series of studies, the experimental Differential Scanning Calorimetry (DSC) data obtained under controlled conditions in isothermal mode have been collected on the dehydration of thin films consisting of aqueous solutions,[2,3] polysaccharide solutions and gels,[4] living cell monolayers[5] and vegetable thin slices[6]. The results of these experiments are here summarized showing a set of common features and peculiarities, ascribed to the component behavior in the aqueous system.
Based on the assessed proportionality between the calorimetric heat flow, HF(t), and water activity (a_w) of solutions of known a_w, the values calculated from calorimetry have been compared to those obtained with classic hygrometric measurements revealing a good consistency between the two methods. The experimental data of HF(t) were mathematically turned into desorption isotherms, providing a continuous description of the water activity vs water content down to the low water activity limit.
This experimental method represents an innovative approach to support other consolidated analytical techniques in the physico-chemical characterization of aqueous systems and, more importantly, a step forward in the determination of water activity as a continuous measurement in a timeframe far shorter than that necessary with other instruments.

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INTERPLAY OF HYDRATION AND ATROPISOMERISM FOR THE STABILITY OF CONCENTRATED AQUEOUS SOLUTION OF CONTRAST MEDIA

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A relevant issue in drug development concerns the behavior of atropisomeric molecules in aqueous solution. The hampered flexibility of such molecules is responsible for the presence of different stable or meta-stable conformations in solution. As a consequence, they can show seemingly stable solutions at concentration of supersaturation, with a direct outcome on the phase separation phenomena such as crystallization. The objective of a wide-range research is towards elucidating the mechanism of aggregation in aqueous solution when different conformations are present and the driving force that rules the selection of one conformation as the most suitable to give rise to crystals in the solid state. This objective has been pursued by using a combination of time-resolved Raman spectroscopy and SWAXS.
Iopamidol is taken as model, being characterized by two conformations in solution with interconversion rate of few minutes and an energy barrier of rotation of about 20 kcal/mol. UV Resonant Raman experiments have been carried out in solution to find out the molecular interactions and the effect of hydration water on the conformation. SWAXS studies have been carried out as a function of concentration to elucidate the effect of water on the nature of the aggregates. Then, both Raman and SWAXS experiments have been carried out as a function of time to elucidate the kinetic of aggregation and crystallization, in order to identify the conformations involved in the aggregates and the structure of the incipient crystalline forms. The data are used to clarify whether the aggregation involves only the so-called “Right Conformer” or the aggregation is initially non-specific and in a second moment the conformation is forced to change. This aspect affects both the species in solution and the nature of the polymorphs that can be obtained in the solid state.

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ROLE OF WATERS IN THE BINDING AND REGULATION OF SYNAPTIC VESICLES BY α-SYNUCLEIN

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α-synuclein (αS) is a 140-residue pre-synaptic protein involved in neuronal communication and whose aberrant aggregation is associated with Parkinson's disease. In dopaminergic neurons, αS exists in a tightly regulated equilibrium between water-soluble and membrane-associated forms. Understanding the molecular and structural details of this equilibrium is essential to characterise both physiological and pathological roles of this protein. There is currently a significant gap in this context as the dynamic nature of αS in both its cytosolic and membrane-bound forms prevents the successful application of standard methods of structural biology. To overcome these limitations, we defined a hybrid approach of solution and solid-state nuclear magnetic resonance (NMR) in combination with biophysical tools such as single molecule FRET, cryoEM and STED imaging to reveal the nature of the interactions of αS with synaptic vesicles and provide insights into their roles into functional and pathological processes at the synapses. The availability of NMR data on the membrane-bound state of αS enabled to refine structural ensembles of this protein at the surface of synaptic vesicles. The ensembles provided key indication of the role of water in defining the nature of the equilibrium between membrane-bound and water-soluble conformations of the protein in these processes.

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SLOW DYNAMICS OF SUPERCOOLED AQUEOUS SOLUTIONS OF TREHALOSE

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Water is one of the most prominent complex liquid that shows anomalies when cooled.
It is thought that such a behaviour stems from the fundamental role played by the hydrogen bonds between water molecules [1].
From a dynamical point of view the most prominent microscopic theory that is able to partially explain water glassy dynamics upon supercooling is the Mode Coupling Theory (MCT). MCT was initially developed in the framework of simple liquids but its predictions are remarkably good also in explaining the slow dynamic of supercooled water [2].
Of particular interest is the dynamical behaviour of aqueous solutions of different disaccharides. These solutions are very common in nature and their interesting properties may help to understand the anomalies of supercooled water, e.g. how the disruption of water hydrogen bonds due to the presence of other molecules may affect the dynamic of supercooled water. Moreover aqueous solutions of this kind are relevant in many technological applications, such as cryopreservation of organic molecules [3, 4]. In this context, trehalose has been proven to be especially effective, when added to a solutions of water, to slow down the dynamics of water.
In this work we study the dynamics of aqueous solutions of trehalose at different concentrations using molecular dynamics simulations. Analysis of dynamic quantities, such as density-density autocorrelation functions and diffusion coefficients, is carried out in the MCT framework. This allows us to extract important quantities that are able to describe the behaviour of the system (e.g. relaxation times τ and critical temperature T_C).

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STATE DIAGRAM OF NON-STARCH POLYSACCHARIDES EXTRACTED FROM RIPE BANANAS (*MUSA CAVENDISHII*)

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Dietary fiber is a group of carbohydrates, which undergoes little degradation when digested, increasing the satiety sensation, benefits the intestinal microbiota, and makes lipids harder to absorb. Therefore, the dietary fiber is considered a healthy food component and the non-starch polysaccharides (NSP) are part of this group. Even when ripe, bananas have NSP in their cell walls, becoming them possible as dietary fiber source from overripe bananas, which would be discarded otherwise. The aim of this work is to characterize NSP obtained from overripe banana puree, using thermal analysis (DSC) under several moisture contents and vapor sorption isotherms. The data obtained allow the construction of state diagram, useful for understanding the interactions between the solids and the water in the samples. This information is important for estimating the best storage and usage conditions.
The sugars of overripe bananas were extracted using ethanol, resulting in an insoluble fraction, rich in NSP. This process was carried out under six different combinations of temperature (25 °C or 65 °C) and extraction time (30, 60 or 90) min. For comparison, pure arabinoxylan and galacturonan, common components of banana, were also analyzed. Thermal analysis was carried out in a DSC Q2000 (TA Instruments, Pullman, USA), with aluminium pans, under nitrogen atmosphere . Samples were cooled up to -60 °C, then heated up to 90 °C, at a 5 °C/min rate. The samples with low moisture contents showed no crystallization peaks, but fusion peaks and glass transitions occurred at different temperatures, depending on the moisture content. The Gordon-Taylor and Chen models were, respectively, adjusted to glass transition and crystallization data ($r^2 \geq 0{,}96$). Sorption isotherms were obtained by Dynamic Dewpoint Isotherm (DDI) method using a VSA 1055 (Decagon Devices, New Castle, USA) ; type III isotherms were obtained.
Additionally, thermogravimetric analyses were performed under nitrogen or air atmosphere, up to 800 °C. Decomposition began around 250 °C for all samples.

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EFFECTIVE SPECIFIC HEAT AND DIELECTRIC CONSTANT OF WATER AROUND PROTEIN: DISTINCT THERMODYNAMIC PROPERTIES OF PROTEIN HYDRATION LAYER

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The first hydration layer in protein and DNA plays an extremely important role in not only stabilizing the biomolecules, but also in maintaining their biological functions essential for life. In biomolecules, surfaces are highly charged and polar. At the same time they also have certain exposure for the hydrophobic residues. Due to this inherent heterogeneity the structure and dynamics of the hydration layer can be different from those of bulk water. Recent calculations have shown that residence time of water molecules in hydration layer can have a wide distribution ranging from much smaller to much larger values as compared to the bulk [2]. It has also been pointed out that the effective dielectric constant can be considerably lower than the bulk, which indeed has been shown in solvochromatic experiments by spectroscopists [1]. Another important response function is specific heat, which determines the thermodynamic properties of the system in terms of energy fluctuations. We use statistical mechanical expressions combined with molecular dynamics simulation to obtain the shell wise effective specific heat and dielectric constant using linear response theory. These effective response functions could have utility in having an intuitive look into different thermodynamic features of the protein hydration layer. Although somewhat approximate, these values can be useful in understanding the mechanism behind energy transfer and heat conduction among different regions of the system, such as protein, hydration layer and bulk solvent. Our calculations show that the effective dielectric constant of first hydration shell can be as small as half [1] and the specific heat of hydration layer can be as high as twice that of the bulk solvent. Thus our study provides an evidence for the uniqueness of protein hydration layer by means of well-known response functions.

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DESIGNING HIGHLY SPECIFIC PROBES WITH TUNABLE AFFINITY

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Finding ligands able to bind with high specificity to a target protein is one of the major challenges in medical research, especially for the development of anti-cancer drugs [1]. Recently it was shown that therapies based on nanoparticles are ineffective [2] due to the difficulty of designing a particle coating which specifically recognizes cancerous cells. We aim at developing a novel computational protocol, based on the recently developed caterpillar [3] coarse grained model, to design proteins that can be used as effective coatings for novel cancer targeting nanoparticles. Key to the success of the targeting are proteins, which are highly selective towards the receptors on the cell membrane but with tunable binding affinity to reduce binding to healthy cells [4]. According to previous studies [5], performed with lattice protein models, such special protein sequences can be obtained by introducing destabilizing mutations in proteins designed to strongly bind to a target substrate. Since such control has not been attempted before on real proteins, we test the feasibility of our approach on a reference system first. We present results of our preliminary studies for a “protein like” pocket. First we design the sequences of both protein and pocket at the same time, in order to optimize the protein-ligand interactions. Then we monitor the binding affinity as a function of the percentage of destabilizing mutations in the amino-acids sequence of the protein.

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INVESTIGATING THE ROLE OF HYDRATION IN THE AGGREGATION PATHWAY OF AcPDro2

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The formation of amyloid fibrils due to protein aggregation is linked to a large number of diseases including the most common neurodegenerative disorders. In the past many efforts have focused on studying the structural rearrangements that proteins undergo during aggregation, trying to decipher the pathway they follow from their native globular conformations into large self-assembled insoluble fibrils[1].

Water has been shown to be an important player in amyloidogenesis, and aggregation-prone proteins often show characteristic hydration patterns on their surfaces[2,3]. In this study we used molecular dynamics simulations to investigate the influence of water in the aggregation mechanism of the acylphosphatase AcPDro2, often used as a model system in protein aggregation studies. We compared the hydration of the native structure to that of a previously characterized partially unfolded intermediate on its aggregation pathway[4], evaluating the specific role of water molecules during the two different stages of the process.

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HEAVY METALS IN SURFACE WATER: A RISK ASSESSMENT OF ITS USE FOR IRRIGATION

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Introduction. The toxicity of heavy metals (HM) is expressed in their ability to accumulate, and subsequently react actively with organics in the course of metabolism, forming new compounds dangerous for the organism. Techno genesis provokes the entry of HM into aquatic ecosystem mainly in the purification of industrial wastewater systems, contributing to uncontrolled contamination of surface water, which is used for irrigation purposes [1, 2]. In this context, the relevance of research on the identification of changes in the ecosystem caused by the concentration changes of HM is dictated by the peculiarities of the geological and climatic conditions of the southern regions of Armenia, in particular the Ararat region. Here, the main sources of HM are industry, local incineration plants and boiler houses, vehicles. In the region's infrastructure a special place is occupied by a ramified network of arable soils, for irrigation of which the local population uses the surface waters of the Araks River basin. The purpose of the work is to evaluate the pollution of the soil-plant ecosystem by using the surface waters of basin the Araks River for irrigation of arable soil located in the vicinity of Artashat.
Materials and methods. Maize of the armenian population (Zea mays), grown in the Armavir region in the village of Artashat and as a control plant the inbred line B73 maize (Iowa Stiff Stalk Synthetic) was used in the experiments. For the instrumental determination of the concentration of chemical elements, the prepared samples water, soil and the incinerated corn grains were placed in standard XRF plates of the Thermo Scientific™ Niton™ XRF Portable Analyzer with a diameter of 32 mm, then closed with a lavsan film and carry out a direct measurement of the X-rays to the samples for a total of 210 seconds.
Results and discussion. According to the results obtained, the value of the elongation of the fifth leaf of maize the Artashat sample is almost the same as for sample B73 in case of moderate stress. It means the plant grows in the field, changes are observed in the physiological parameters of growth, which are close in terms of indicators for a severe drought in the laboratory. Thus, the background (natural) adaptation of the plant is quite consistent with the results of drought modelling. In next cycle of experiments, the change in the concentration of a number of chemical elements in soil and plant samples before and after irrigating with irrigation water was investigated. According to the results obtained, the maize samples under study demonstrate a accumulate activity with respect to HMs . So, after harvesting the plants in its ripe grains, an increase in the concentration of zinc and iron was almost three times, and in the case of copper and manganese - a weakly expressed accumulation. The cumulative capacity of corn is also indicated by the fact that, after harvesting, the content of the HM in the soil was unambiguously reduced. It is obvious that soil pollution due to the use of contaminated irrigation water poses a serious threat to the environment and biota, for food safety, and therefore for the human health.

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THE MPEMBA EFFECT

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Water molecules are dipoles positioned and oriented joined by hydrogen bonds. When water is heated this structure collapses (increasing entropy). After the water is recooled to a lower temperature the structure is not reconstructed immediately but needed some time. This time is sometimes not enough inside a freezer because the cooling process is fast. Entropy reduction curves function of temperature S=f(T) appear retardation (lagging) relative to entropy growth curves. The water after was heated and recooled at the starting temperature, has more entropy than before it was heated. Means that molecules have now the same kinetic energy, but thermal motion before heating was more oriented by the structure mentioned above. Recooling random collisions are more possible leading to faster temperature's reduction.

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STUDY OF WATER TIP4P/2005 DIFFUSION IN NANOTUBES

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Studying water behaviour in confinement is a topic of general interest in order to understand how water flows in biological enviroments.
TIP4P/2005 [1] is considered one of the most accurate water potentials to simulate water properties both in equilibrium and metastable conditions. Water diffusion inside nanotubes has been already studied using water models such as TIP3P[2] or SPC/E [3] whereas few studies are available with TIP4P/2005 [4-6]. In this work we propose to study the diffusivity of water when confined in rigid hydrofobic nanotubes of different sizes comparing the results to the bulk ones and to experiments.

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Alberto Zaragoza de Lorite, Ana Laura Benavides, Chantal Valeriani

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