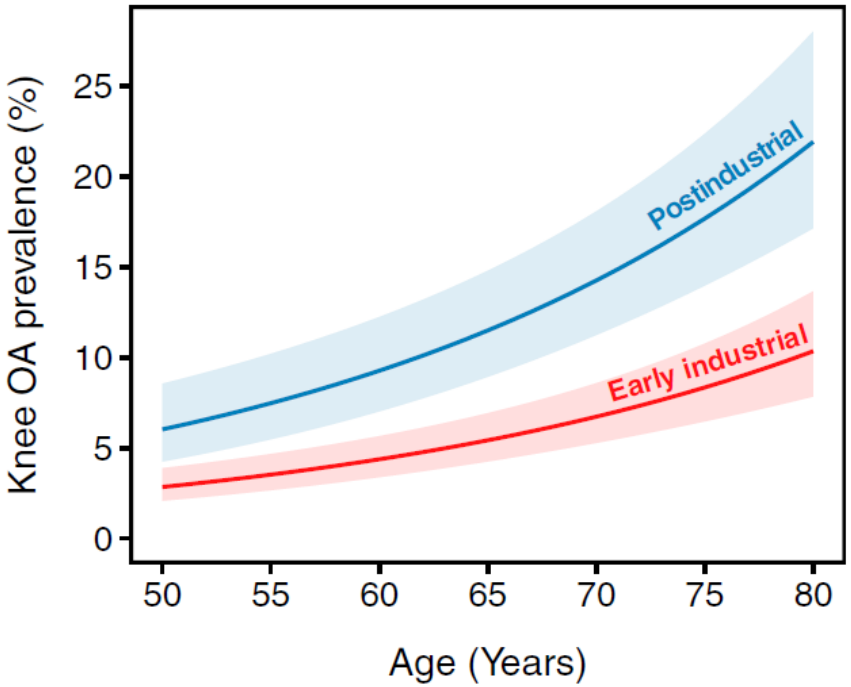
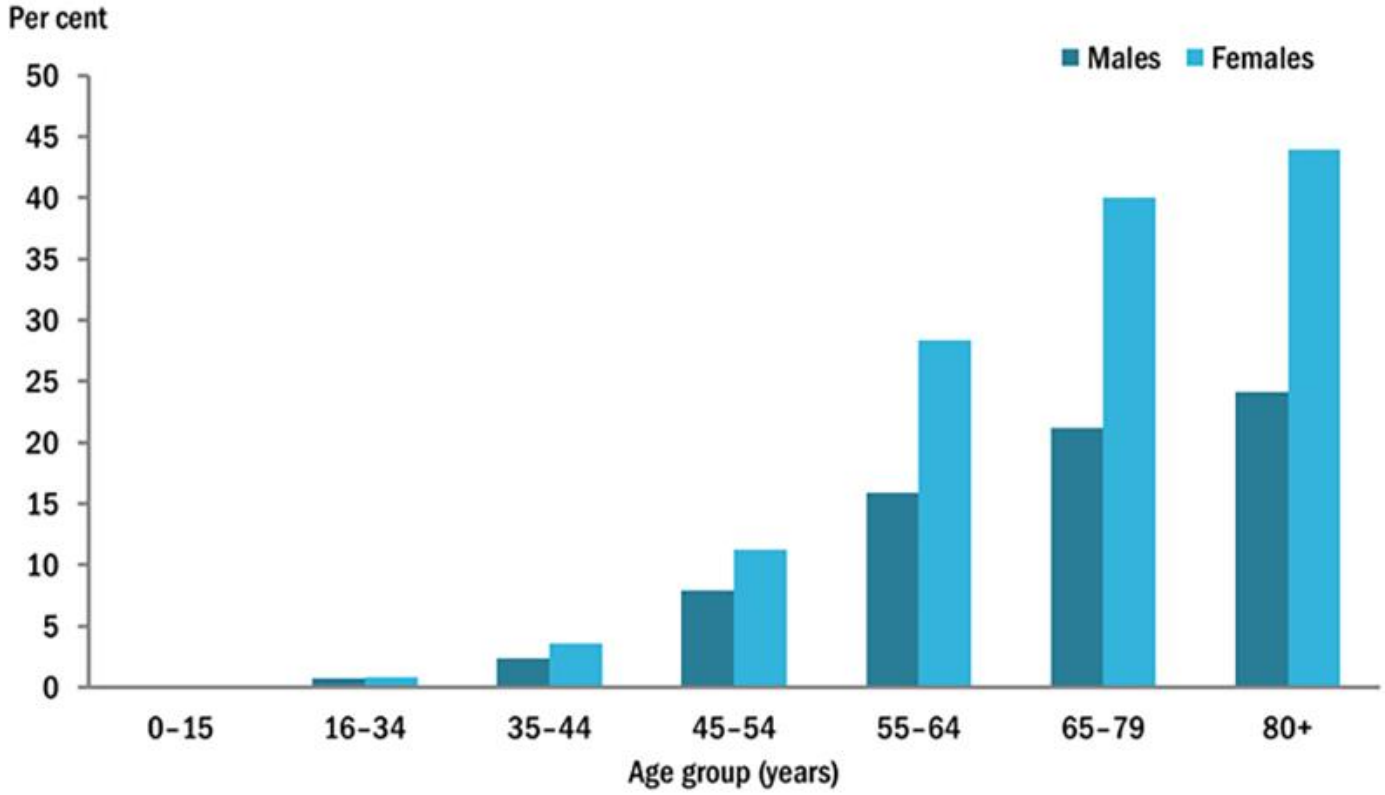
Albumin-water interactions: molecular dynamics study

Piotr Bełdowski, Krzysztof Domino, Robert Dobosz

Relevance of the problem





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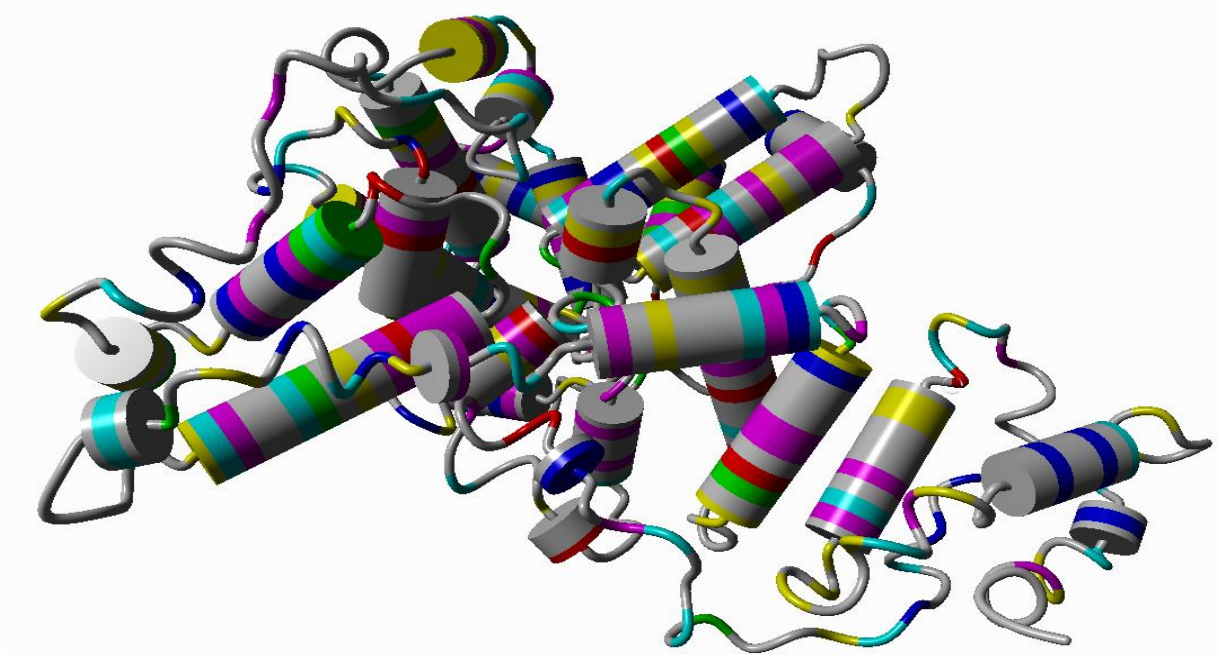
Albumin

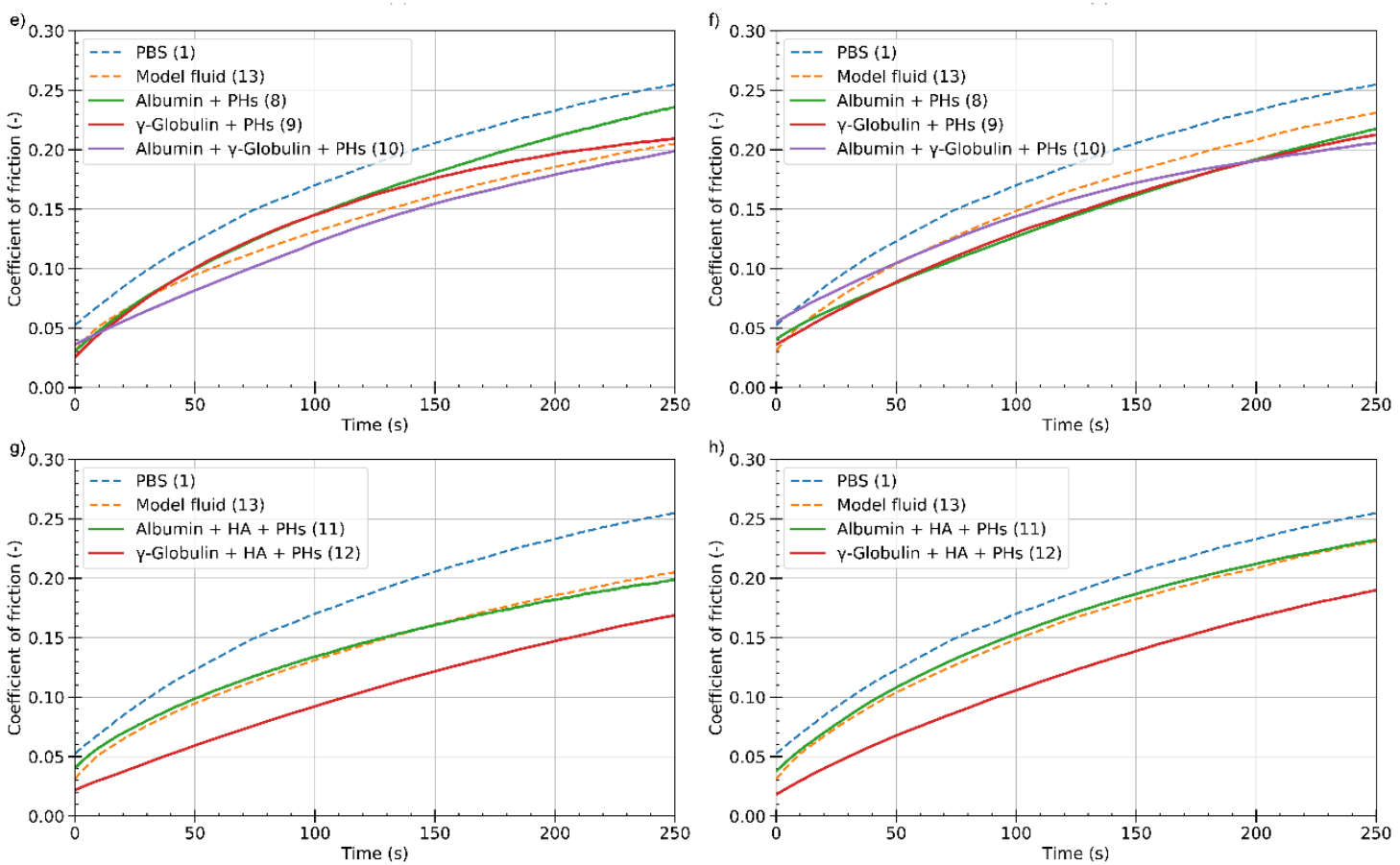


Visualization of albumin molecule in a cartoon form. Several amino-acids have been colored to show their position in the molecule. Colors read as follows: pink-LEU, yellow-LYS, green-TYR, cyan-GLU, blue-PHE, red-ARG. Tubes reflects alpha helices.

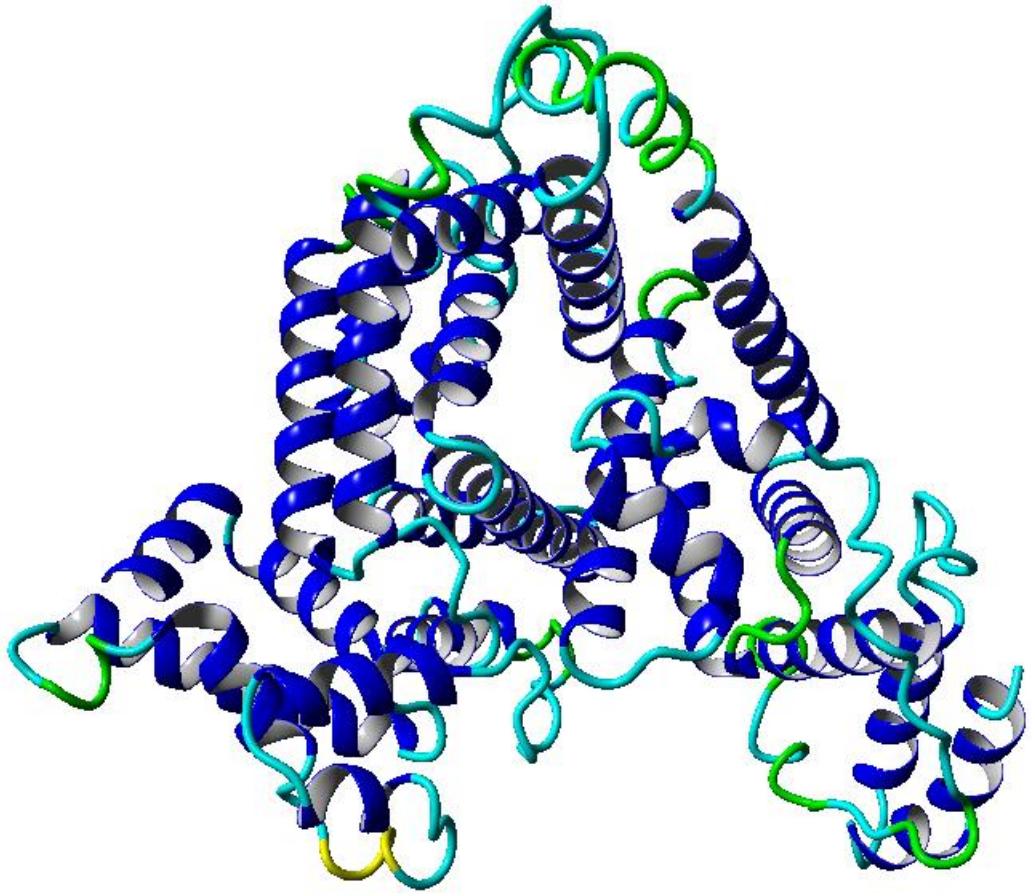
Functions

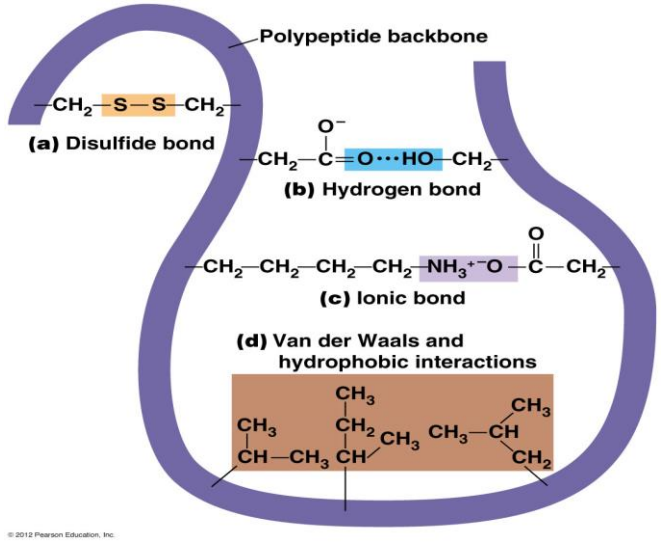
- Maintains oncotic pressure
- Transports thyroid hormones
- Transports other hormones, in particular, ones that are fat-soluble
- Transports fatty acids ("free" fatty acids) to the liver and to myocytes for utilization of energy
- Transports unconjugated bilirubin
- Transports many drugs; serum albumin levels can affect the half-life of drugs. Competition between drugs for albumin binding sites may cause drug interaction by increasing the free fraction of one of the drugs, thereby affecting potency.
- Competitively binds calcium ions (Ca^{2+})

Synergy in Lubrication



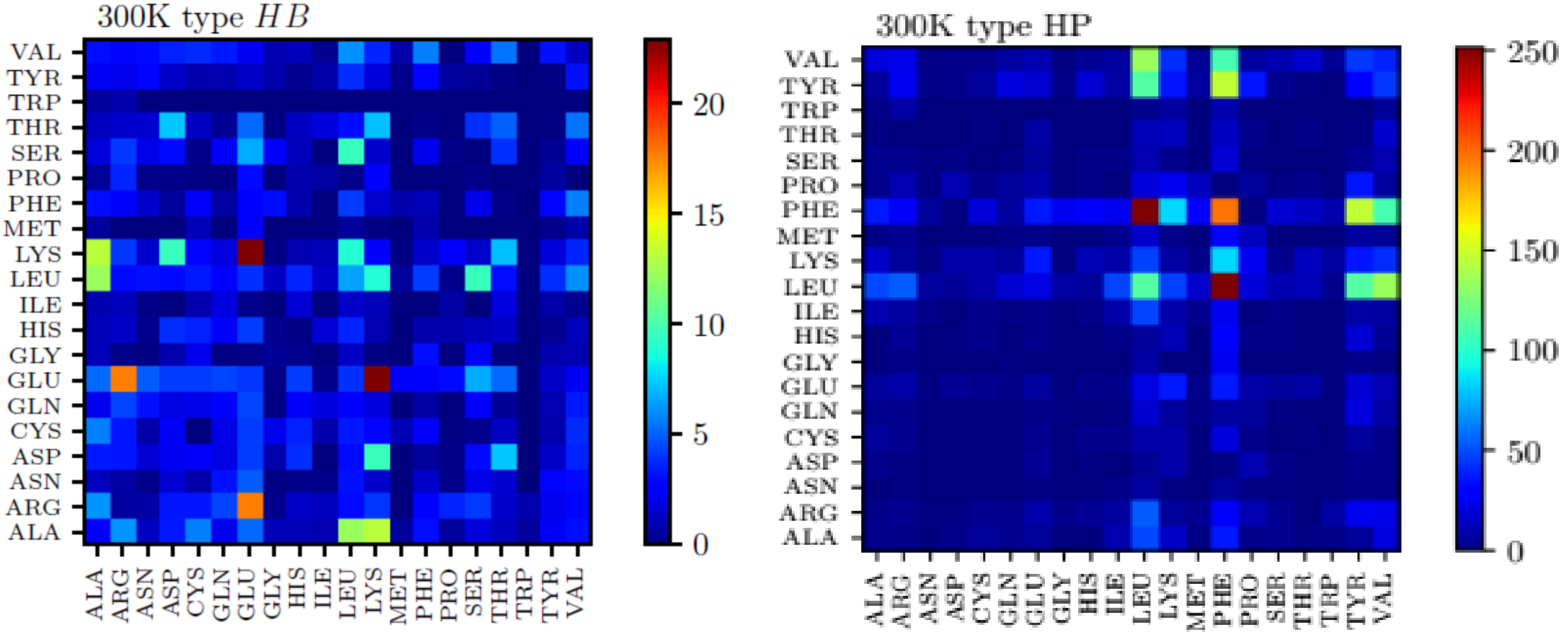
Molecular Dynamics





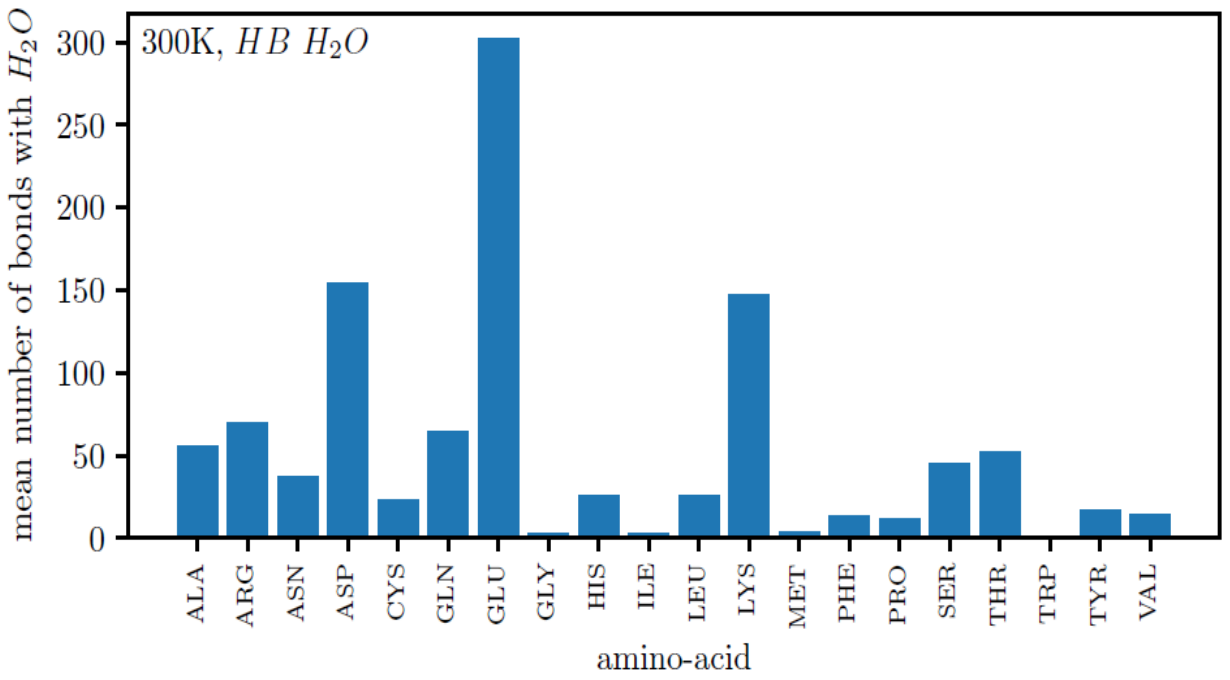
$$E_{total} = \sum_{bonds} k_b(R-R_{eq})^2 + \sum_{angle} k_\theta(\theta-\theta_{eq})^2 + \sum_{dihedrals} \frac{V_n}{2}[1+\cos(n\varphi-\gamma)] + \sum_{i<j}\left[\frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^{6}} + \frac{q_i q_j}{\varepsilon R_{ij}}\right]$$

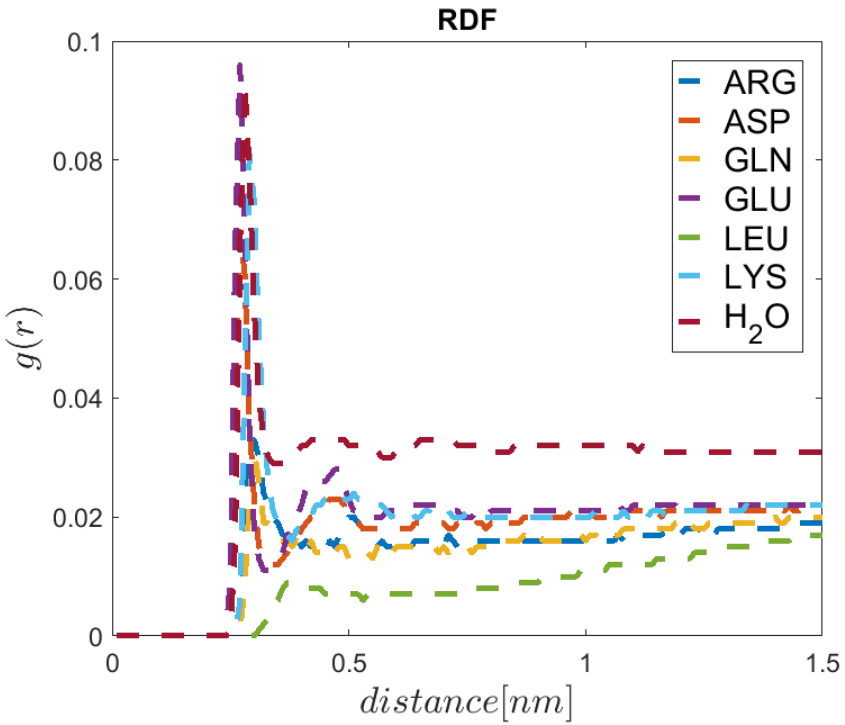
Results



Maps of HB hydrogen bonds (left panel) and HP contacts (right panel) between particular amino-acids. For HB bonds there are much more combinations than in the case of contacts, here most bonds are formed with Lysine (LYS). In case of NP contacts Phenylalanine (PHE) and Leucine (LEU) plays a major role, T = 300K.

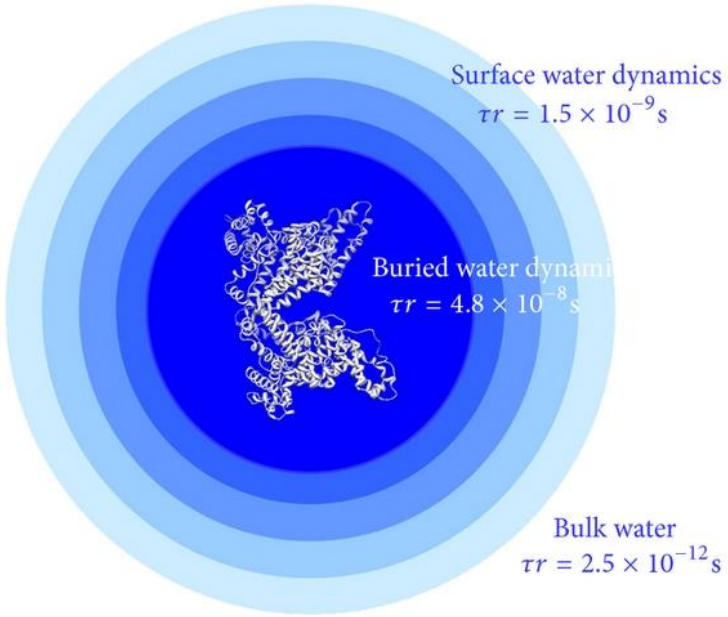
Water organisation





Histograms of HB H_2O contacts with water particles, it appears that Glutamine (GLU) plays an important role, T = 300K.

Water-protein interactions



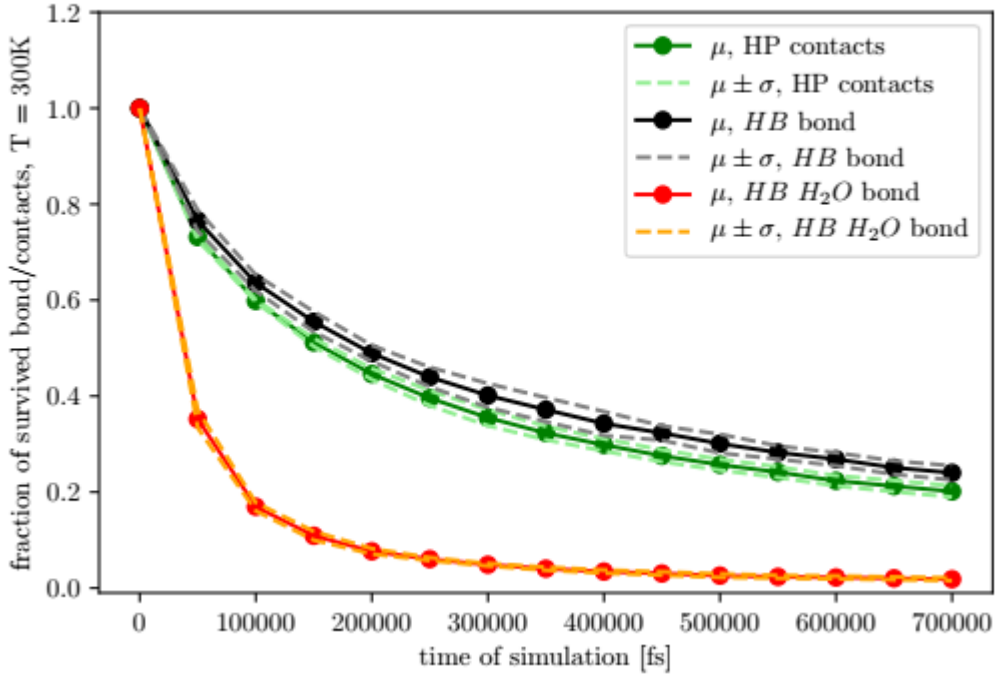
In binary system (water-protein and/or polymer) we assume the distribution of water molecules as schematically represented by the model showed in Figure. Water molecules can be classified into three different categories according to their dynamical properties:

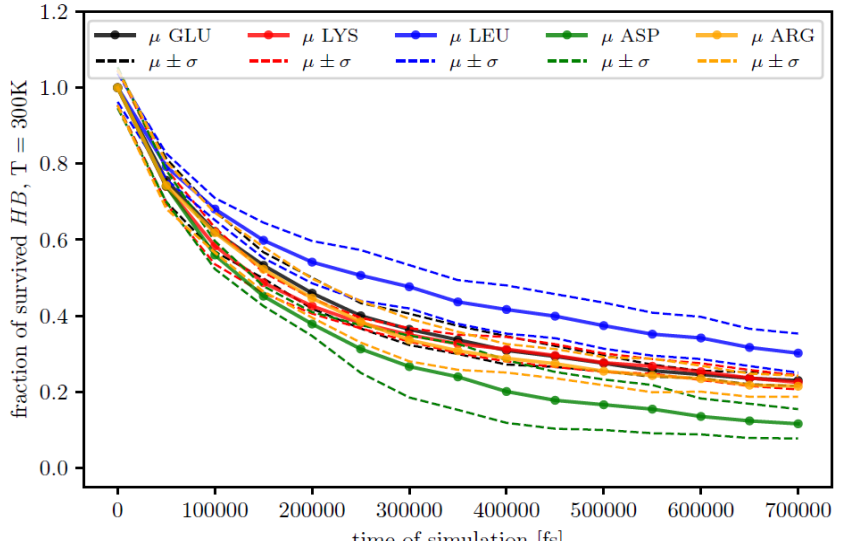
(i) bulk water with a typical reorientational correlation time of the order of picoseconds;

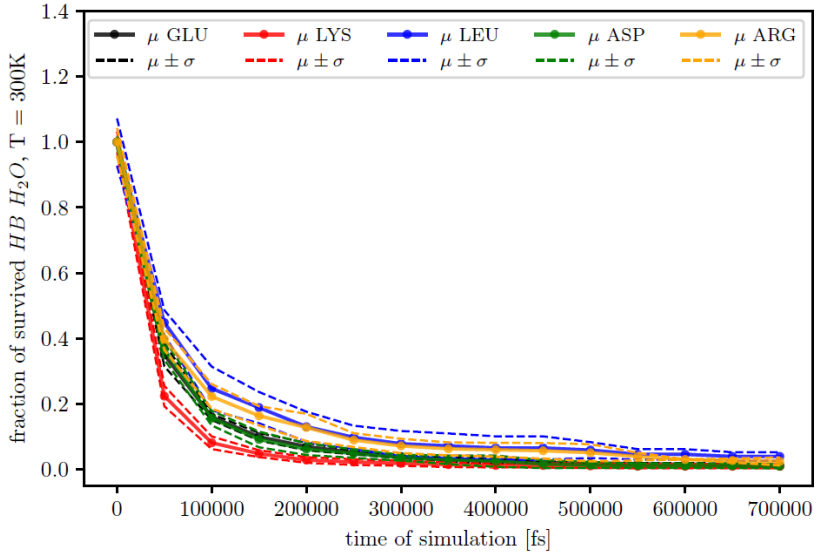
(ii) water present at the macromolecular surface which exhibits a partially restricted reorientational motion;

(iii) buried water molecules. The dynamical properties of the water molecules in these conditions can be well represented by a distribution of correlation time values.

Decay curve for various types of bonds interactions and contacts







Conclussions

- Polar amino acids form shorter lived H-bonds with water that hydrophobic,
- Water-Albumin H-bonds are several orders of magnitude more stable than Albumine’s intramolecular bonding, yet much longer than water-water bonding,
- More accurate water models can give more accurate results on bond stability.

Future plans

- Hyaluronan-albumin docking (implicit and explicit solvent)
- Hyaluronan-albumin-phospholipid docking (implicit and explicit solvent)
- MD simulations (equilibrium and nonequilibrium) toward understanding dynamics of bonding

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Thank you for attention