Dynamics on complex bio-systems

Water and proton binding at membrane interfaces with negatively charged lipids

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In Short

- Simulations of photosystem II (PSII)to determine the response of dynamic internal H-bond networks and changes in local structure for different S-states of the light driven water splitting reaction
- Constructing and analysing PSII in thylacoid membrane system to determine the behaviour of its negatively charged lipids that could bind protons
- Characterize the dynamics of water hydrogen bonding at negatively charged membrane models
- Implement efficient computational tools for the analysis of dynamic hydrogen-bond networks in complex biomolecules

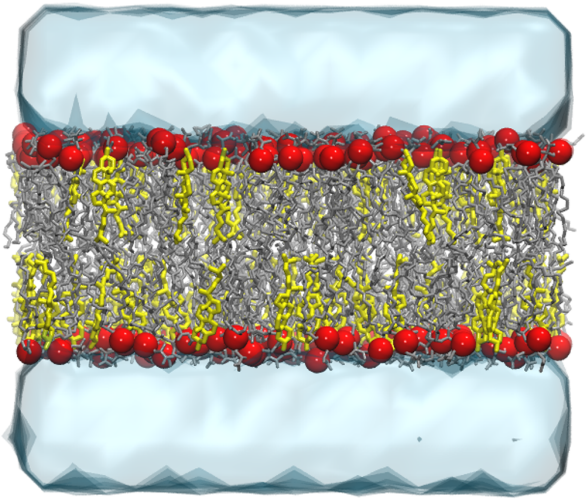

***Figure 1:** Surface representation of POPS anionic lipid membrane. Lipids are shown as grey licorice representation while lipid headgroups are colored as red van der Waals spheres. Cholesterol molecules are shown as yellow licorice and water as surface representation. All molecular graphics were prepared with VMD. [5].*

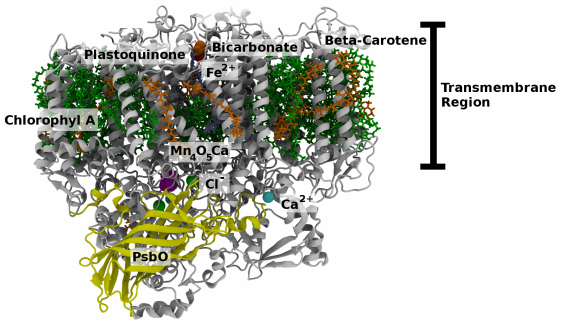

***Figure 2:** PSII monomer structure (PDB id: 3WU2) [6] representation in VMD. Embedded in the structure is visible labeled manganese cluster and its stabilising subunit PsbO in yellow. The reaction centres has 2 neighbouring chlorine ions. In onrage representation are beta-carotene moieties often exchenged with the lipid bilayer. [4]*

Lipid membrane interfaces host a variety of reactions essential for the cell physiology. Negatively charged lipids are of particular interest as model systems as they are related with a number of human diseases, including cancer [1]. Anionic membranes can provide a potential target for positively charged proteins or drug molecules and promote new therapeutics [2].

We plan to characterize the dynamics of protein and anionic lipids by water/lipid headgroup vs. water/protein hydrogen-bond networks. We aim to associate our findings with the potential binding of protons to membrane systems investigating the dynamics of water-mediated lipid clusters and perceive the impact of cholesterol in anionic membranes (Fig. 1). We plan to use algorithms and concepts from graph theory to visualize and analyze complex hydrogen bond networks at membrane interfaces. We have analyzed hydrogen bond networks in membranes including phosphocholine (POPC) and phosphatidylglycerol (POPG) [3], and most recently, we performed molecular dynamics simulations of membranes composed of phosphatidylcholine (POPE) and phosphatidylglycerol (POPG), phosphoserine (POPS), and an E. coli membrane model consisting of 6 different lipid types [4].

Light driven water splitting reaction is the most important function of PSII (Fig. 2). As the first protein in photosynthesis, its role is to produce protons that gather on the lumental side of the thylacoid membrane, hgh energy electrons used in energy creation chain and molecular oxygen released into the atmosphere. The intriguing path of protons start at the manganese cluster, the reaction centre consisting four manganese atoms, five oxygens and an calcium ion coordinated by ten aminoacid residues deep within the structure of PSII.

We intend to perform atomistinc molecular dynamics for all the stages of water splitting reaction to investigate the influence of the electronic state of the manganese cluster onto its first hydration shell. With applications of graph theory to efficiently in-

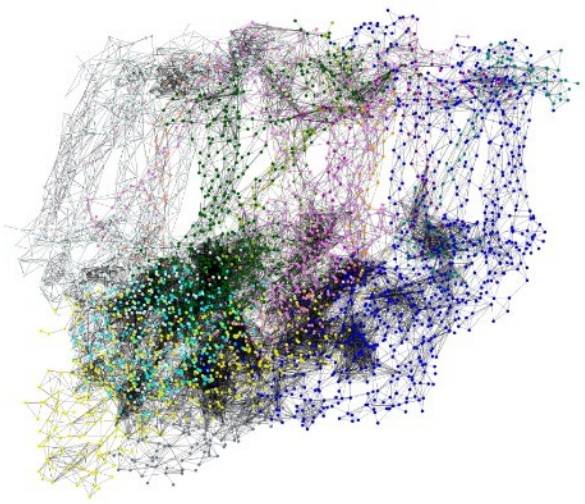

Figure 3: *PSII representation constructed with the use of the Bridge algorithm [7] developed in our lab (Fig. 3). All dots symbolize an amino acid residue, and lines are direct or water mediated hydrogen bonds that may be capable of transporting a proton. With the use of algorithms filtering functions we intend to investigate this vast and deep network to uncover more facts about intrinsic proton dynamics of PSII and their influence of the negativevely charged lipids of the thylacoid membrane. [3]*

terpret the data, we will be able to investigate the influence the reaction stages have on proton release pathways that start at the oxygen evolution centre. Additionally simulating PSII in cyanobacterial thylacoid membrane will give us insight into the influence of released protons stored on the lumenal side of the thylacoid membrane as well as the dynamics of proton sharing between the negatively charged lipids of the lipid bilayer.

WWW

http://www.physik.fu-berlin.de/en/einrichtungen/ag/ag-bondar/

More Information

[1] Zwaal, R.F.A., Comfurius P., Bevers E.M. *Cell. Mol. Life Sci.* **62**, 971-88 (2005). doi:10.1007/s00018-005-4527-3

[2] Escriba, PV., Busquets X., Inokuchi J., Balogh G., Torok Z., Horvath I., Harwood J.L., Vigh L. *Prog. Lipid Res.* **59**, 38-53 (2015). doi:10.1016/j.plipres.2015.04.003

[3] Karathanou K., Bondar A.N. *J Membr Biol.* **3**, 461:473 (2018). doi:10.1007/s00232-018-0023-1

[4] Pandit K.R., Klauda J.B. *Biochim Biophys Acta.* **5**, 1205-10 (2012). doi:10.1016/j.bbamem.2012.01.009

[5] Humphrey W., Dalke A., Schulten K. *J. Molec.Graphics* **14**, 33 (1996).

[6] Umena, Y., et al. *Nature* **473.7345**, 50-60 (2011).

[7] Siemers, M., Lazaratos, M., et al. *Journal of chemical theory and computation* **15.12**, 6781-6798 (2019).

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