Dynamics of complex bio-systems

Hydrogen-bond dynamics at protein interfaces

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In Short

- Characterize the dynamics of protein/water hydrogen-bond networks at the interface between SecA monomers in *E. coli* dimer and probe the response of these interactions to long-distance conformational coupling
- Analysis of dynamic hydrogen-bond networks requires development of new efficient algorithms for complex system such as SecA and photosystem II
- Characterization of proton release pathways by analyzing protein water hydrogen bond networks in photosystem II

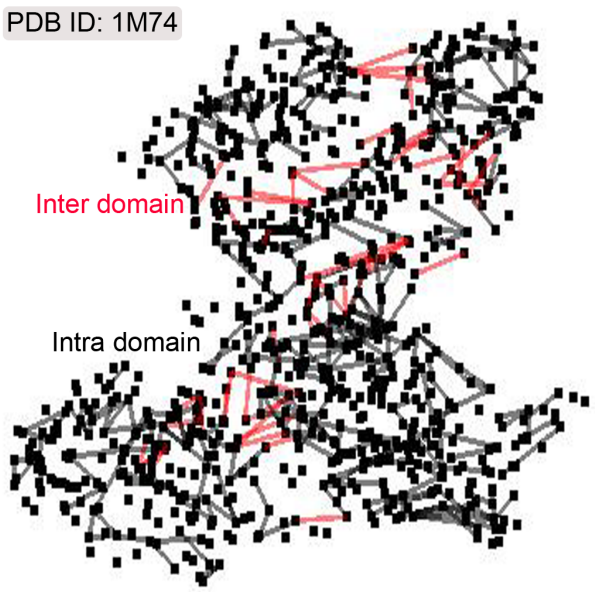

Figure 1: *Illustration of H bonding interactions in B. subtilis ADP-bound SecA (PDB ID: 1M74). Protein amino-acids are represented as nodes and hydrogen bonds as edges in the graph. Intra and inter hydrogen bonds are represented as black and red lines, respectively. Image presents data available in [2].*

Newly-synthesized soluble proteins in bacteria are secreted across the outer cell membrane via the Sec machinery. That machinery includes soluble and membrane-bound components. The soluble SecA protein recognizes the signal peptide of the secretory protein [1] and by multiple cycles of binding and hydrolysis of adenosine triphosphate (ATP), conducts the protein across the membrane and the SecY translocon.

An open question is how the reaction coordinate of the ATP-powered protein secretion evolves large-scale conformational changes in SecA protein. To this aim, we performed atomistic simulations on *B. subtilis* SecA distinguished by the starting crystal structure coordinate, mutant vs. wild-type, and by the nucleotide-binding state (ADP vs. ATP). We have developed new algorithms to identify hydrogen-bond networks in proteins. We used concepts from graph theory, whereby we represent protein groups as nodes and the protein-water interactions as edges in the graph (Fig. 1). By finding paths of connected nodes, we searched for connections between distant regions of the protein and we connected our findings with the conformational dynamics of the protein. Additionally, we calculated the lifetime of water molecules in the first hydration shell of the protein groups and we observed that SecA surface is highly heterogeneous with respect to the dynamics of water.

Simulations performed in *E. coli* SecA showed a rapid conformational change at the domain where the pre-protein binds (PBD). In solution, SecA is mostly found as a dimer. We aim to model a reliable crystal structure of the E. coli SecA dimer based on the crystal structure [3] (Fig. 2). To this direction, we plan to perform extensive atomistic simulations of wild-type and mutations of *E. coli* SecA, address the impact of the dimeric structure to the movement of PBD and investigate the role of water between the two interfaces to the large conformational change observed.

Significant water-mediated intrinsic processes also occur in photosystem II (PSII), which is a protein found in the thylakoid membrane of plants, cyanobacteria and algae. It is a bio-nanomachine that uses the energy of the light to split the water molecules into protons electrons and molecular oxygen. We aim to understand the mechanism of long-distance proton transfer in PSII subunits PsbU and PsbO a well as hydrogen-bond interfaces between the mentioned subunits and the entire protein with the thylakoid membrane specific lipids present in the crystal structure.

The simulations of photosystem II (PSII) (Fig. 3) subunits were carried out to find out whether the potential proton-binding site on the surface of PsbO subunit of PSII connects to PsbU subunit via hydrogen-bonded water, we studied the dynamics of a simplified model system consisting of PsbO and PsbU in water. Coordinates for the complex were

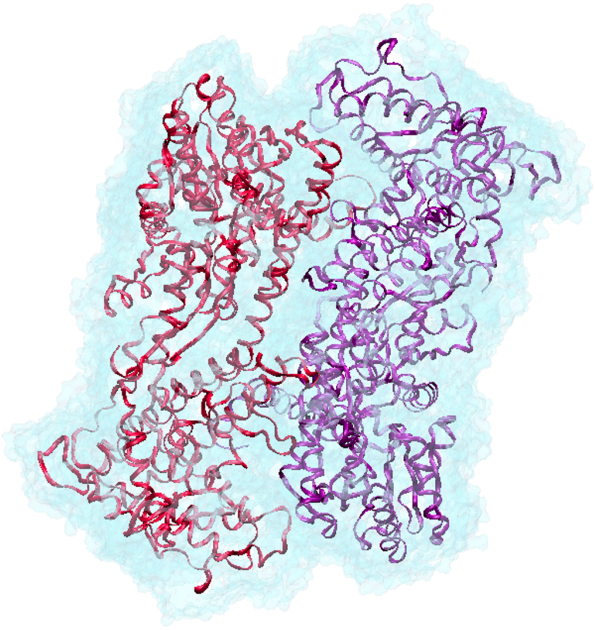

Figure 2: *SecA dimer interface (PDB id: 1M6N) representation in VMD. Monomers A and B are represented as ribbons and they are distinguished by different coloring, red and purple, respectively. The first hydration shell of the protein is shown in light blue. [4]*

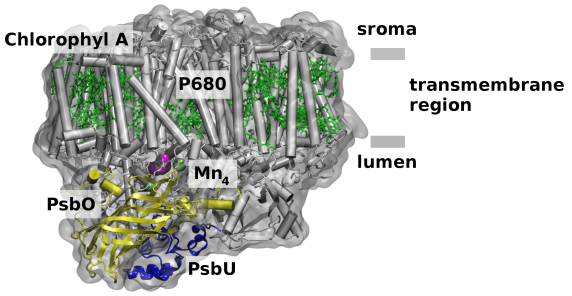

Figure 3: *The structure of PSII monomer with the indicated manganese cluster of the oxygen evolution centre and highlighted PsbO chain in yellow and PsbU in blue. [3]*

extracted from the crystal structure of photosystem II (PDB ID: 3WU2) [5]. To this aim we have performed three independent simulations of the PsbO-PsbU complex, 185ns each and analyzed the dynamics of hydrogen bonds between protein groups and water at the interface between PsbO and PsbU. Our further aim is to probe the conformational dynamics and water interactions of a whole photosystem II monomer. During the 2018-2019 HLRN allocation we performed a preliminary 50ns simulation of the photosystem II monomer in a hydrated POPC lipid membrane, and initiated analyses of hydrogen-bond networks using algorithms developed in our group [6].

The preliminary analyses illustrate the extensive protein-water hydrogen-bond networks that span the solvent-exposed regions of photosystem II (Fig. 4). With the use of HLRN resources we will prolong the simulation by 200ns. Data analyses will focus on identifying protein-water hydrogen-bond networks that could serve as proton-transfer pathways, and characterizing their dynamics.

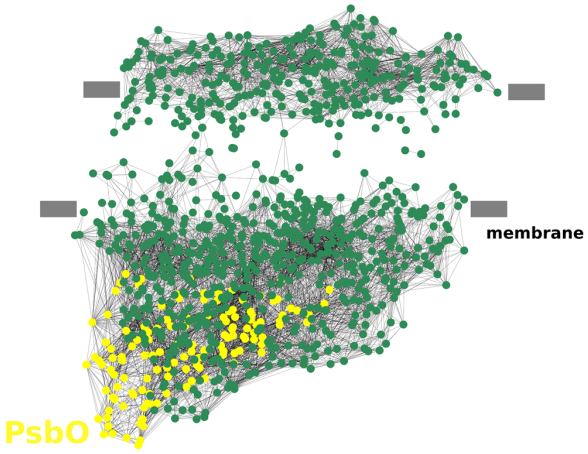

Figure 4: *Illustration of protein-water hydrogen bonds in photosystem II. We show hydrogen bonds present at least 1% of the trajectory segment used for analysis.*

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

More Information

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Funding

Work was supported in part by the DFG Collaborative Research Center SFB 1078 "Protonation dynamics in Protein Function" (Project C4), Excellence Initiative of the German Federal and State Governments provided via the Freie Universität Berlin.