# What makes them what they are?

## Structural determinants of rhodopsin protein function

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### In Short

- Retinal Proteins
- Internal Water Dynamics
- Structural Analysis
- Network Analysis

Microbial rhodopsins are retinal-binding proteins that function as ion pums, ion channels, or signaling receptors. A fascinating aspect about microbial rhodopsins is functional interconversion, that is, the nature of the functioning of the protein can be altered by appropriately chosen mutations. For example, three amino acid mutations suffice to convert the bacteriorhodopsin proton pump into a sensor protein 1. Functional interconversions are important to study because they provide insight into the key structural elements that govern functionality, and for protein engineering.

It was recently reported by Innoue and co-workers that 4 mutations can convert the sodium pump KR2 into a proton pump, albeit an inefficient one; by contrast, the proton pump GR could not be converted into a sodium pump even with 6 mutations 2. We will model wild-type and mutant GR, and KR2, to find out which interactions could be modified in GR to establish sodium pumping activity.

Antother fundamental between signaling receptors, ion pumps and ion channels is their internal water dynamics and its coupling to protein dynamics. Water molecules are often staly bound in intenal cavities or can visit the protein transiently. The importance of such water molecules is very significant because they shape internal dynamics of the protein since they can contribute of long-distance coupling of amino acid residues via extended hydrogen-bond networks. In order to characterise those networks we have developed a graph-based algorithm that enables efficient analyses of hydrogen-bond networks in complex biosystems. We called the algorithm Bridge3.

Bridge is set of algorithms that rely on concepts from graph theory to compute complex H-bond networks. Using geometrical criteria, we compute H bonds that can interconnect different parts of the bio-system we study. These H bonds can be directly between two protein sidechains, they can be mediated by chains of H-bonded water molecules (i.e., water wires), or they can be mediated by H-bonded lipid headgroups.

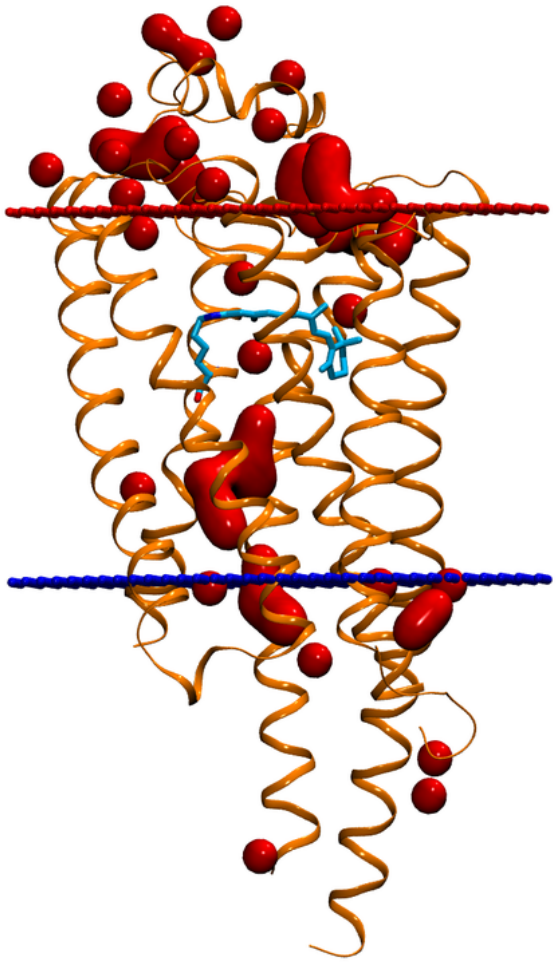

***Figure 1:*** *Crystal structure of Jumping spider rhodopsin 1 4, oriented along the membrane normal. Protein is depicted in cartoon representation (orange). The retinal chromophore is shown as cyan sticks. Crystallized water molecules are shown as a surface representation in red color. Dummy atoms representing the positions of the lipid bilayer are shown in red and blue spheres for the cytoplasmic and extracellular sides, respectively. Molecular graphics were prepared with VMD5*

We used Bridge to analyze molecular dynamics trajectories of C1C2 6. For C1C2 Bridge identified extensive networks of protein-water H bonds, and an unanticipated network that can bridge transiently the retinal Schiff bases of the two C1C2 monomers; that is, the primary proton donors of C1C2 are part of a transient H-bond network across a distance of 20Ã. The functional implications of this extended H-bond network are not entirely clear at the moment; we speculate that it might lead to cooperativity in the

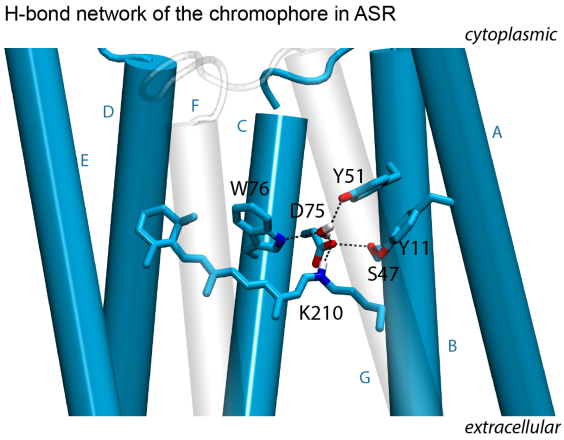


***Figure 2:*** *Molecular graphics of the internal hydrogen-ond network found in Anabaena Sensory Rhodopsin after analyzing the last 100ns of an MD simulation at 300K. The presence of a staly bound water molecule allows for very stable interractions in the chromophore vicinity. Molecular graphics of the path shown in panel A. Molcular graphics were prepared with VMD5*

functioning of the C1C2 monomers 6.

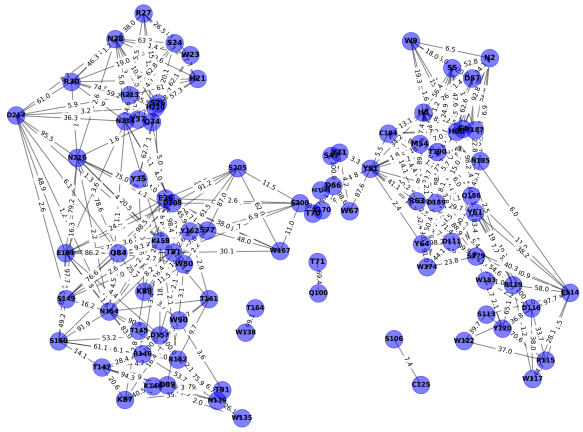

***Figure 3:*** *Graphs of ASR water wires obtained with Bridge. Water-mediated H-bond networks identified in simulations of ASR at 300K.*

## WWW

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

## More Information


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## Project Partners

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