Journal of Structural Biology 186 (2014) 95–111

Contents lists available at ScienceDirect

Journal of Structural Biology

journal homepage: www.elsevier.com/locate/yjsbi

Coupling between inter-helical hydrogen bonding and water dynamics in a proton transporter

Coral del Val [a], Luiza Bondar [b], Ana-Nicoleta Bondar [c,*]

[a] Department of Artificial Intelligence, University of Granada, E-18071 Granada, Spain
[b] University Medical Center Utrecht, Department of Radiotherapy, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands
[c] Theoretical Molecular Biophysics, Institute of Theoretical Physics, Department of Physics, Freie Universität Berlin, Arnimallee 14, D-14195 Berlin, Germany

ARTICLE INFO

Article history:
Received 8 November 2013
Received in revised form 13 February 2014
Accepted 15 February 2014
Available online 24 February 2014

Keywords:
Proton transfer
Water dynamics
Hydrogen bonding

ABSTRACT

Long-distance proton transfers by proton pumps occurs in discrete steps that may involve the direct participation of protein sidechains and water molecules, and coupling of protonation changes to structural rearrangements of the protein matrix. Here we explore the role of inter-helical hydrogen bonding in long-distance protein conformational coupling and dynamics of internal water molecules. From molecular dynamics simulations of wild type and nine different bacteriorhodopsin mutants we find that both intra- and inter-helical hydrogen bonds are important determinants of the local protein structure, dynamics, and water interactions. Based on molecular dynamics and bioinformatics analyses, we identify an aspartate/threonine inter-helical hydrogen-bonding motif involved in controlling the local conformational dynamics. Perturbation of inter-helical hydrogen bonds can couple to rapid changes in water dynamics.
© 2014 Published by Elsevier Inc.

1. Introduction

Membrane-embedded proton transporters use titratable protein groups and internal water molecules to transfer protons across cell membranes. The movement of ions is controlled by gates (Gadsby, 2009) – protein structural elements that can sample two conformations, open and closed, thus controlling accessibility of ions to the protein (Gadsby, 2009; Gora et al., 2013). The dynamics of structural elements that may function as gates must couple to the protonation dynamics and to the dynamics at remote regions of the protein, such that the transporter coordinates the sequential steps of proton uptake, movement of protons across the protein, and proton release. To assess the role of inter-helical hydrogen bonding in the conformational dynamics of a proton transporter, we performed extensive molecular dynamics simulations of bacteriorhodopsin trimers embedded in hydrated lipid membranes and explored the response of the protein and water dynamics to mutations that affect hydrogen bonding.

The light-driven proton-pumping cycle of bacteriorhodopsin includes five distinct proton-transfer steps during which a proton is pumped from the cytoplasmic to the extracellular side of the membrane. A complete reaction cycle takes approximately 10–15 ms (Edman et al., 1999; Hatcher et al., 2002; Lanyi, 1999). In the first step the retinal Schiff base proton is transferred to the nearby D85 on the extracellular side (Fig. 1B), then a proton is released from an extracellular proton-release group, followed by reprotonation of the retinal Schiff base from the cytoplasmic D96, proton uptake from the cytoplasm by D96 and, in the fifth and last proton transfer step, transfer of the proton from D85 to the extracellular proton release group (for a review see, e.g., Lanyi, 1999). The distance between D96 and the retinal Schiff base, ∼11 Å, is too large for a direct proton transfer, and the transfer of the proton from D96 to the retinal Schiff base during the millisecond-timescale transition from the M to the N intermediate is thought to couple to the transient assembly of a water wire in the cytoplasmic channel of the pump (Cao et al., 1991; Lanyi, 1999; Sass et al., 2000; Schobert et al., 2003). Though thermodynamically allowed (Roux et al., 1996), a continuous cytoplasmic water wire is not observed in crystal structures of the resting-state of the pump (Belrhali et al., 1999; Luecke et al., 1999); cytoplasmic water molecules are present in some of the crystal structures of bacteriorhodopsin deprotonated retinal states (Kouyama et al., 2004; Sass et al., 2000; Schobert et al., 2003).

Since waters are required for long-distance proton transfers in the cytoplasmic channel, the observation from experiments that specific site-directed mutations alter the kinetics of proton transfers – e.g., Y57F (Govindjee et al., 1995), D85E (Butt et al., 1989; Heberle et al., 1993), or R82A (Balashov et al., 1993; Otto et al., 1990) – raises the important question as to whether the

* Corresponding author.
E-mail address: nbondar@zedat.fu-berlin.de (A.-N. Bondar).

http://dx.doi.org/10.1016/j.jsb.2014.02.010
1047-8477/© 2014 Published by Elsevier Inc.

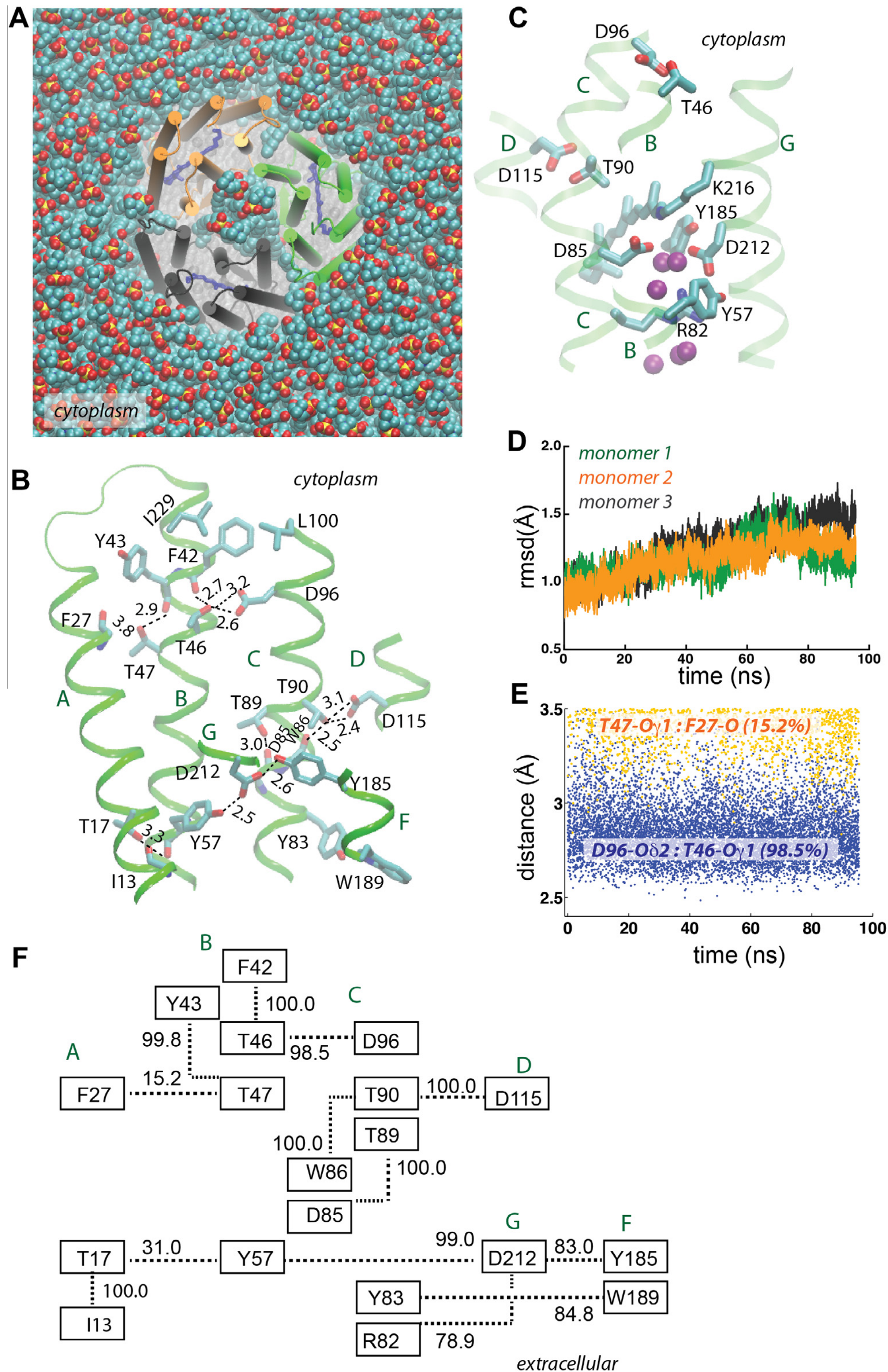

Fig.1. The wild-type bR trimer in a hydrated lipid membrane. (A) System setup: View from the cytoplasmic side. The trimer is shown with the monomers colored in green, orange, and black cartoons; the retinal molecules covalently bound to K216 are shown as blue bonds. Lipid molecules are shown with phosphate atoms in yellow, nitrogen – blue, oxygen – red, and carbon atoms – cyan. Oxygen atoms of water molecules on the extracellular side are shown as transparent silver spheres. (B) Selected hydrogen bonds at the D96 and D212 sites. The image is prepared based on the crystal structure from Luecke et al. (1999). (C) Selected inter-helical hydrogen bonds and water molecules at the end of Sim1. The water oxygen atoms within 3.5 Å of the amino acid residues shown explicitly are depicted as small magenta spheres. Both in the starting crystal structure and at the end of Sim1 there are three water molecules within hydrogen-bonding distance from D85/D212. For clarity, hydrogen atoms are not shown. (D) Root-mean-square-distance (rmsd) profiles for the Cα atoms of the transmembrane helical segments during Sim1. (E) Dynamics of the T46–D96 and T47–F27 hydrogen bonds. The D96 proton resides on the Od2 carboxyl oxygen atom. We plot as time-series the distances that meet the hydrogen-bonding distance criterion of ⩽3.5 Å during Sim1 for one monomer. We give the percentage of the non-constrained simulation during which there is hydrogen bonding. (F) Schematic representation of selected hydrogen bonds and their dynamics in one of the wild-type protein monomers (Sim1). Dotted lines indicate hydrogen-bonding interactions; real numbers along the dotted lines give the percentage of time when a hydrogen-bonding distance is sampled. For additional data on the other two monomers see Fig. S3. For all molecular graphics we used VMD (Humphrey et al., 1996). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Download English Version:

https://daneshyari.com/en/article/5914248

Download Persian Version:

https://daneshyari.com/article/5914248

Daneshyari.com