Hydration and Protonation Dynamics in Cytochrome C Oxidase

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Kurzgefasst

- Membranprotein Cytochrom-c-Oxidase “veratmet” Sauerstoff mit Hilfe von Protonen zu Wasser
- Protonen gelangen durch zwei wechselwirkende Kanäle in das Zentrum des Proteins
- Welchen genauen Weg (Transferpfad) nehmen die Protonen in den Kanälen?
- Wie ist der Prtontransport reguliert?

Cytochrom c-Oxidase is a protein of the respiratory chain which reduces oxygen to water with the help of protons. The energy gained by this reaction is udes to transport further protons through the membrane. How do these protons get from outside the protein to the redox reaction centre?

According to crystal structres and other experiments, two proton conducting channels are responsible for the proton uptake. The order of redox chemsitry and proton uptake through the two channels, however, has to be highly regulated. The protein is thus supposed to “communicate” its protonatiom state. In other words, the exact position of the protons has an impact on the dynamics within the protein. Previous work shows that the water dynamics, the connection between water molecules and protein residues via hydrogen bonds as well as the conformational dynamics is affected by the proton movement [1,2].

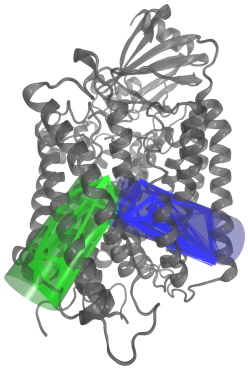

Abbildung 1: *The D and K channel in Cytochrome-c-Oxidase.*

An important ingredient in the regulation of the proton uptake through the two channels is a “gate” fromed by two asparagine residues in the D channel. This “asparagine gate” shows an open conformation, allowing water and ths prtons to pass through, only in cases in which the proton still has to be transported. This is further coupled to the hydrogen bond dynamics within the channels. As an additional means for control, the two channels likely “communicate” with each other. Our Simulations show that, for example, the life times of hydrogen bonds between residues of the “asparagine gate” and water in the D channel (2) depends on the protonation state of the K channel [1,2].

Channel hydration is highly regulated by the presence of local charges. Accordingly via a proton transfer mechanism in particular the D-channel gets hydrated if an access proton is near the entrance. When the proton has passed the asparagine gate the channel gets dehy- drated. Due to the correlation of hydrogen bond communication and channel hydration the inter channel communication is indirectly affected by proton transfer. Within the D-channel itself dihedral conformations and hydrogen bonds play an important role just like the presence and location of an access proton at the entrance. They interplay with different protonations of the key residues of the D-channel and regulate the gating zone. Hydrogen bonds formed close to the asparagin gate are highly influenced by the local present of charges (short-range interaction) as well as the protonation of E286 (long-range interaction). But also the spatial fluctuations of water molecules ready to enter the channel as well as those already contained in the channel are strongly mediated by these means.

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Weitere Informationen

[1] M. Bagherpoor Helabad, T. Ghane, M. Reidelbach, A. L. Woelke, E. W. Knapp, P. Imhof, iProtonation-state dependent communication in Cytochrome c Oxidase. *Biophys. J.* **113**, 817–828 (2017).

[2] T. Ghane, R. F. Gorriz, S. Wrzalek, S. Volkenandt, F. Delatieh, M. Reidelbach, P. Imhof, Hydrogen-Bonded Network and Water Dynamics in the D-channel of Cytochrome c Oxidase *J. Membrane Biol* , 1–16 (2018).

Projektpartner

AG Knapp, FU Berlin

Förderung

DFG Sonderforschungsbereich (SFB) 1078

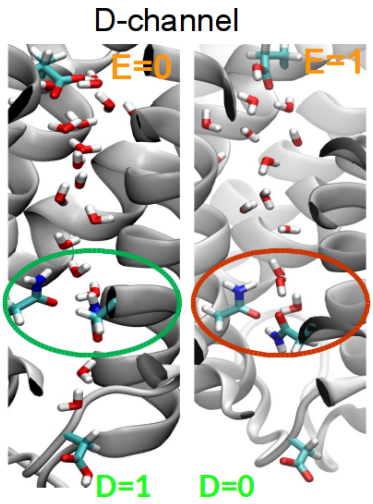

Abbildung 2: *The conformation in the channels depends on the protonation state.*

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