Joint Lecture of UniSysCat and SFB1078

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Room C 264 at TU Berlin

Exploring the mechanism of respiratory chain enzymes by multi-scale simulations

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Cell respiration forms one of the most important energy conversion processes in nature and these reactions are catalyzed by membrane bound enzymes that convert chemical energy into an electrochemical ion gradient stored across the biological membrane. In higher cell systems these processes take place in the respiratory chains formed by complexes I-V, however, recently alternative modular adaptations have been discovered. Membrane-bound hydrogenase (Mbh) of Pyrococcus furiosus is an ancient enzyme that couples proton pumping and Na^+/H^+ exchange with redox coupled hydrogen-gas (H_2) production across the archaeal cytoplasmic membrane. Mbh couples redox-catalysis with ion-transport with a unique Ni-Fe active site that evolved into the quinone-binding site of modern Complex Is. Here we use atomistic molecular-dynamics (MD) simulations in combination with data clustering methods, and quantum chemical calculations to probe principles underlying proton reduction, as well as proton- and sodium-transport in Mbh. We identify putative Na^+ binding sites and proton pathways leading across the membrane and to the Ni-Fe active center, as well as conformational changes that could regulate the proton uptake. We suggest that Na^+-binding and protonation changes at a putative ion-binding site couple to proton transfer across the antiporter-like MbhH subunit by modulating the conformational state of a conserved ion-pair at the subunit interface. Our findings illustrate conserved coupling principles within the Complex I superfamily and provide functional insight into archaeal energy transduction mechanisms.

References

[1] M.E. Mühlbauer, A.P. Gamiz-Hernandez, V.R.I. Kaila, Functional Dynamics of an Ancient Membrane-Bound Hydrogenase, J Am Chem Soc 143(49) (2021) 20873-20883.

[2] A. P. Gamiz-Hernandez, A. Jussupow, M. P. Johansson, V. R. I. Kaila, Terminal Electron-Proton Transfer Dynamics in the Quinone Reduction of Respiratory Complex I. J Am Chem Soc 139, 16282-16288 (2017)

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