Proton Transfer in the Membrane Domain of Respiratory Complex I

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Abstract

Respiratory complex I (NADH:ubiquinone reductase) is the largest enzyme of aerobic respiratory chain and it functions as a redox-driven proton pump, employing the energy from quinone reduction to pump protons across the mitochondrial membrane. Recently resolved crystal structures [1,2] show a long chain of conserved polar and charged residues that span the entire length of the the membrane domain (*ca.* 200 Å), linking the quinone reduction chamber to the other end of the enzyme. Recent molecular dynamics (MD) simulations have clarified the roles of some of these residues [3,4], but the overall molecular mechamism by which it catalyses this long range proton-electron transfer process is still unclear. We perform large-scale classical MD on a microsecond time scale and QM/MM simulations to study hydration effects and proton transfer (pT) in the membrane domain of this gigantic proton pump.

References

1. R. Baradaran, J.M. Berrisford, G.S. Minhas, L.A. Sazanov, Nature 494(2013) 443-450
2. V. Zickermann, C. Wirth, H. Nasiri. K. Siegmund, H. Schwalbe, C. Hunte, U. Brandt, Science 347 (2015) 44-49
3. V.R.I. Kaila, M. Wikström, G. Hummer, PNAS 111 (2014) 6988-6993
4. V. Sharma, G. Belevich, A.P. Gamiz-Hernandez, T. Ròg, I. Vattulainen, M.L. Verkhovskaya, M. Wikström, G. Hummer, V.R.I. Kaila, PNAS 112 (2015) 11571-11576