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How inter-subunit contacts in the membrane domain of complex I affect proton transfer energetics

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Abstract

The respiratory complex I is a redox-driven proton pump that employs the free energy released from quinone reduction to pump protons across its complete *ca*. 200 Å wide membrane domain. Despite recently resolved structures and molecular simulations, the exact mechanism for the proton transport process remains unclear. Here we combine large-scale molecular simulations with quantum chemical density functional theory (DFT) models to study how contacts between neighboring antiporter-like subunits in the membrane domain of complex I affect the proton transfer energetics. Our combined results suggest that opening of conserved Lys/Glu ion pairs within each antiporter-like subunit modulates the barrier for the lateral proton transfer reactions. Our work provides a mechanistic suggestion for key coupling effects in the long-range force propagation process of complex I.

***Keywords*: bioenergetics • proton transfer • NADH:ubiquinone oxidoreductase • enzyme dynamics**