EFFECTS OF CARDIOLIPIN OXIDATION ON THE CYTOCHROME BC_1 COMPLEX

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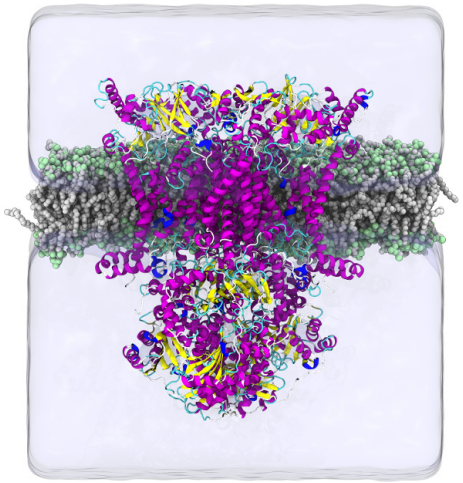

Cytochrome bc_1, also known as complex III, is the third component of the electron transfer chain in the respiratory system, which is the main source of energy in living cells. The complex catalyzes the transport of electrons in the inner mitochondrial membrane and releases protons to the intermembrane space. Cardiolipins (CL) constituting up to 20 mol% of the phospholipids in the inner mitochondrial membrane affect the structure and dynamics of the membrane. They have been found to be vital for the stability and proper function of the complex [1]. Oxidation of CLs as a result of oxidative stress is closely related to aging, programmed cell death, and Barth's syndrome [2].

In this study, we use atomistic molecular dynamics simulations to deepen the understanding of the role of CLs in the cytochrome bc_1 properties and the effects of cardiolipin oxidation on the structure and function of complex III. To this end, we embedded the protein complex in a multi-component membrane whose lipid composition largely matches mitochondrial conditions. In the simulations, we used the CHARMM36 force field to perform 1 μs all-atom simulations in a constant pressure (1 bar) and temperature (310 K). Validation of the simulated model included comparison to previous simulation studies and experiments. Further work is being done to explore effects of the oxidized lipids on cytochrome bc_1. In the presentation, we discuss the results of these studies and their biological relevance.

[1] S. Pöyry, O. Cramariuc, P. A. Postila K. Kaszuba, M. Sarewicz, A. Osyczka, I. Vattulainen, T. Róg, Biochimica et Biophysica Acta (BBA), 1827(6):769-778, 2013.
[2] T. Eisenberg, S. Büttner, Fems Yeast Research, 14(1):179-197, 2014.