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The Phylogenetic Signature Underlying ATP Synthase c-ring Compliance

Alessandro Pandini,[1] Jens Kleinjung,[2] Willie R. Taylor,[2] Wolfgang Junge,[3] and Shahid Khan[2,4,*]

[1]Department of Computer Science and Synthetic Biology Theme, Brunel University London, Uxbridge, United Kingdom; [2]Mathematical
Biology, The Francis Crick Institute (formerly the National Institute for Medical Research), London, United Kingdom; [3]Department of Biophysics, University of Osnabrück, Osnabrück, Germany; and [4]Molecular Biology Consortium, Lawrence Berkeley National Laboratory,
Berkeley, California

ABSTRACT
The proton-driven ATP synthase (FOF1) is comprised of two rotary, stepping motors (FO and F1) coupled by an elastic power transmission. The elastic compliance resides in the rotor module that includes the membrane-embedded FO c-ring. Proton transport by FO is firmly coupled to the rotation of the c-ring relative to other FO subunits (ab2). It drives ATP synthesis. We used a computational method to investigate the contribution of the c-ring to the total elastic compliance. We performed principal component analysis of conformational ensembles built using distance constraints from the bovine mitochondrial c-ring x-ray structure. Angular rotary twist, the dominant ring motion, was estimated to show that the c-ring accounted in part for the measured compliance. Ring rotation was entrained to rotation of the external helix within each hairpin-shaped c-subunit in the ring. Ensembles of monomer and dimers extracted from complete c-rings showed that the coupling between collective ring and the individual subunit motions was independent of the size of the c-ring, which varies between organisms. Molecular determinants were identified by covariance analysis of residue coevolution and structural-alphabet-based local dynamics correlations. The residue coevolution gave a readout of subunit architecture. The dynamic couplings revealed that the hinge for both ring and subunit helix rotations was constructed from the proton-binding site and the adjacent glycine motif (IB-GGGG) in the midmembrane plane. IB-GGGG motifs were linked by long-range couplings across the ring, while intrasubunit couplings connected the motif to the conserved cytoplasmic loop and adjacent segments. The correlation with principal collective motions shows that the couplings underlie both ring rotary and bending motions. Noncontact couplings between IB-GGGG motifs matched the coevolution signal as well as contact couplings. The residue coevolution reflects the physiological importance of the dynamics that may link proton transfer to ring compliance.