

# Optimal control protocols for the $F_1$ -ATPase motor

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A biomolecular motor composed of protein complexes exchanges energy, matter, and information with its surroundings. Despite being in contact with a fluctuating environment, it performs (on average) a directed motion in accordance with the second law by transducing chemical energy stored in the surrounding environment<sup>1</sup>. Among several biomolecular motors the  $F_0F_1$ -ATP synthase has gained much attention due to its high efficiency<sup>2</sup>. It produces ~95% of the cellular ATP (adenosine triphosphate) from ADP (adenosine diphosphate) and  $P_i$  (inorganic phosphate). The membrane-embedded  $F_0$ -unit utilizes energy from proton flux to rotate the  $F_1$ -unit's  $\gamma$ -crankshaft and synthesizes ATP molecules. Since the  $\gamma$ -crankshaft rotates as fast as ~350 revolutions per second, it remains a puzzle how  $F_0F_1$  transduces free energy in a highly efficient manner. One possible way to investigate this is to uncover the functional principle of that particular unit where ATP is synthesized, i.e., the  $F_1$ -ATPase. To this end, we focus on an isolated  $F_1$ -ATPase, which can also be controlled in an experimental setup<sup>3</sup>. We design a control protocol (mimicking  $F_0$  operation) by which the  $F_1$  unit's  $\gamma$ -crankshaft can be rotated to synthesize ATP at low dissipation. We follow a near-equilibrium framework to construct a non-trivial designed protocol<sup>4</sup>. Then, we rotate the crankshaft with this designed protocol to compute dissipation. Our analysis reveals that the designed protocol dissipates less energy than a constant velocity protocol for a wide range of protocol durations<sup>5</sup>.

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<sup>1</sup> Mugnai, M. L., Hyeon, C., Hinczewski, M. & Thirumalai, D. Theoretical perspectives on biological machines. Rev. Mod. Phys. 92, 025001 (2020).

<sup>2</sup> Soga, N., Kimura, K., Kinoshita, K., Yoshida, M. & Suzuki, T. Perfect chemomechanical coupling of FOF1-ATP synthase 114, 4960–4965 (2017).

<sup>3</sup> Toyabe, S. et al. Nonequilibrium energetics of a single  $F_1$ -ATPase molecule. Phys. Rev. Lett. 104, 198103 (2010).

<sup>4</sup> Sivak, D. A. & Crooks, G. E. Thermodynamic metrics and optimal paths. Phys. Rev. Lett. 108, 190602 (2012).

<sup>5</sup> Gupta, D. et al. Optimal control of the  $F_1$ -ATPase molecular motor, The Journal of Physical Chemistry Letters 13 (51), 11844-11849 (2022).