The F-ATP synthase: what advantages might the rotary mechanism confer?

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***Short Abstract* — F-ATP synthase is an enzyme complex that synthesizes ATP using energy from the passage of protons down their electrochemical gradient across the membrane. People are familiar with its rotary mechanism and the complex structure. However, no literature has addressed what the advantages the rotary mechanism may have over the more common "transporter" mechanism. Two simplified model was made using BioNetGen to compare effectiveness of rotary and the alternating-access mechanisms. We found that (i) the peak operating conditions for both mechanisms, (ii) the superior performance of the rotary mechanism in two regimes, and (iii) the requirement for locally enhanced proton concentration near the FOF1 complex.**

***Keywords* — F-ATP synthase, rotary mechanism, quantitative modeling, elastic coupling, BioNetGen**

I. Introduction

F-ATP synthase, or F-ATPase, is found in bacterial plasma membranes, in mitochondrial inner membranes and in chloroplast thylakoid membranes. It uses a proton gradient to drive ATP synthesis by allowing the passive flux of protons across the membrane down their electrochemical gradient [1]. In 1997, a Japanese group first observed how this protein works. It uses a rotary mechanism to carry out its cellular function of manufacturing ATP. After that FOF1 is well known for its intricate rotary mechanism and the complex dual-ring structure [2-3]. F type is the only type that could both works as an ATP synthase and a proton pump that utilize the energy from ATP to maintain the proper pH difference across the membrane.

Many investigations have studied the rotation details, and advanced techniques allow people to observe how this machine works in a higher resolution [4-6]. But these experimental studies of necessity take the mechanism and structure for granted. However, the literature does not appear to have addressed to what significant extent the basic advantage of a rotary mechanism over the more common alternating-access mechanism coupled to ATP hydrolysis/synthesis. In principle, an ATP-coupled alternating-access transporter should be reversible under the same conditions that reverse the FOF1.

Here we use BioNetGen, a rule based modeling method to make two simple quantitative models to compare the effectiveness of rotary and alternating-access mechanisms for ATP synthesis [7]. Our approach allows the models to be identically matched in a thermodynamic sense, with only mechanistic differences.

II. Results and Conclusions

A 180 mV potential across the membrane was set in all the system. The parameters were referenced from published literatures [8-10]. Although the simplicity of the models makes the results highly speculative, some findings appear to be robust:

(i) The existence of peak operating conditions for both mechanisms.

(ii) The superior performance of the rotary mechanism in two regimes.

(iii) The requirement for locally enhanced proton concentrations near the FOF1 complex compared to bulk values implied by pH measurements.

These simple models are the first steps toward a longer-term goal of building a comprehensive modeling framework for both F and V-type ATPases with an arbitrary number of c subunits and with elastic coupling between FO and F1 sub-complexes.

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