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ORIGINAL PAPER

Modelling the influence of thermal effects induced by radio frequency electric field on the dynamics of the ATPase nano-biomolecular motors

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Abstract We model the dynamics of the F_0 component of the F_0F_1-ATPase mitochondrion-based nano-motor operating in a stochastically-fluctuating medium that represents the intracellular environment. The stochastic dynamics are modeled via Langevin equation of motion wherein fluctuations are treated as white noise. We have investigated the influence of an applied alternating electric field on the rotary motion of the F_0 rotor in such an environment. The exposure to the field *induces* a temperature rise in the mitochondrion's membrane, within which the F_0 is embedded. The external field also induces an electric potential that promotes a change in the mitochondrion's transmembrane potential (TMP). Both the induced temperature and the change in TMP contribute to a change in the dynamics of the F_0. We have found that for external fields in the radio frequency (RF) range, normally present in the environment and encountered by biological systems, the contribution of the induced thermal effects, relative to that of the induced TMP, to the dynamics of the F_0 is more significant. The changes in the dynamics of the F_0 part affect the frequency of the rotary motion of the F_0F_1-ATPase protein motor which, in turn, affects the production rate of the ATP molecules.

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Introduction

The F_0F_1-ATP synthase, denoted as ATPase, is a rotary protein-based molecular motor whose F_0 part is located in the inner membrane of mitochondrion (IMM) which is itself surrounded by the intermediate space separating inner and outer membranes (OMM). This molecular motor is responsible for synthesizing adenosine triphosphate (ATP) molecules from adenosine diphosphate (ADP) and inorganic phosphate (Pi). The ATP molecules are used, as common fuel, by intracellular molecular motors in performing their biological functions. The ATPase motor consists of two main components [1,2], as shown schematically in Fig. 1. The F_0 rotor is composed of three sub-units, namely; the γ-shaft that transmits the torque between the F_0 and F_1 parts, the rotor (C_n), and the stator (ab_2) which is situated near the rotor and acts as the entrance and exit channels. The C_n, with $n = 10$—14, is composed of a ring-shaped array of n identical double-helix sub-units connecting to the shaft at their centers, and generates the rotary motion as a result of ion flow across the membrane. The F_1 component also consists of three sub-units, namely; the γ-shaft that is shared with the F_0, three coupled $\alpha\beta$ proteins that provide the binding sites at which the ATP molecule is synthesized, and the δ subunit, attached to the b_2, that couples to the $\alpha\beta$ proteins.

In this paper, we compute the effects of an external *alternating* electric field, in the frequency range 10 kHz to 10 GHz, which corresponds to the RF range in the electromagnetic field spectrum, on the function of the F_0 component. We see that the exposure of the mitochondrion's membrane, modeled in this paper as a *continuum tissue* without the consideration of its molecular structure, to this field promotes thermal effects in the membrane, as well as inducing a change in its TMP, and that the induced temperature plays a more significant role in the dynamics of the ATPase vis-a-vis the induced TMP. In our previous work [3], we modeled the influence of both an external constant electric field and electric current on the dynamics of the F_0. It was shown that the ATP production was affected because of the change in the transmembrane potential as well as the change in the elasticity properties of the membrane (change in surface tension). We found that at low values of the field (less than 5000 V/m), the transmembrane potential played a more significant role in the change in the production rate of the ATP molecules, whereas at high values, the induced change in the surface tension of the membrane also contributed to the change in the production rate.

The organization of this paper is as follows. In the Section 2, we give a brief summary of the previous results on the influence of electric field-induced thermal effects in the body and in the cell. In Section 3, we explain how an alternating electric field penetrates the tissue and causes an increase in the local temperature. Furthermore, we also consider the effect of the field on the change in the transmembrane potential and how its corresponding power dissipation in the membrane also contributes to the rise in the temperature. We then perform a computational modeling of the dynamics of the F_0 rotor located in a membrane within which power is dissipated as a result of its exposure to the field. Section 4 reports the results of our computations and their discussion.

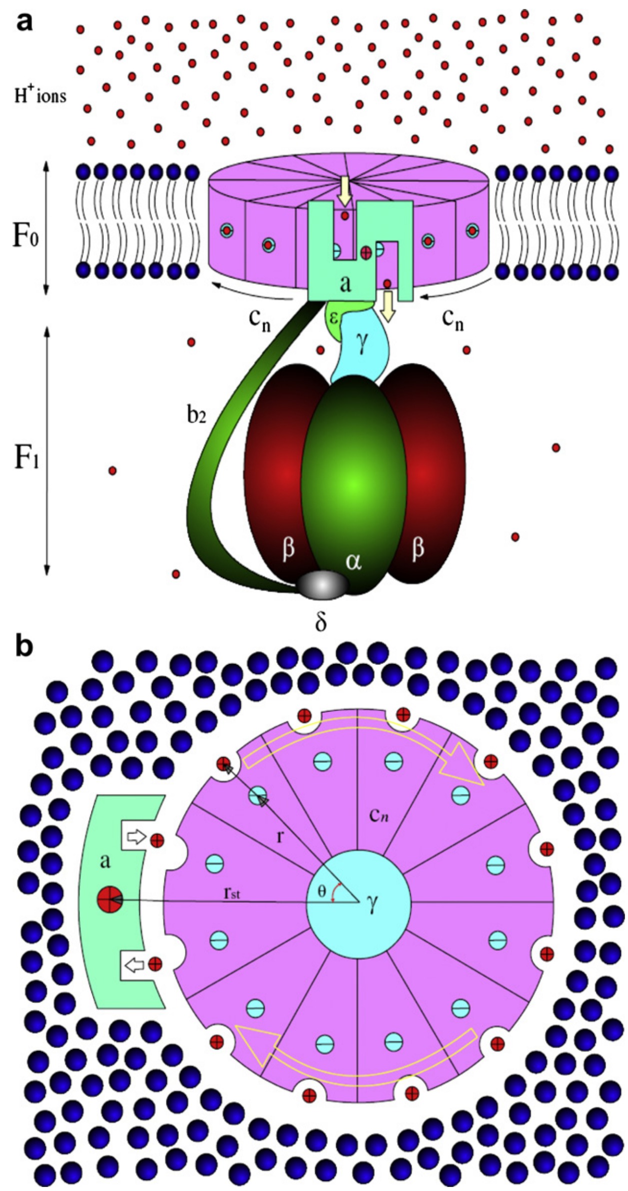

Figure 1 a) The schematic structure of the F_0F_1-ATPase motor located inside the membrane, showing the details of the two main components and the mechanism of the ion flow through the F_0 rotor; b) the schematic representation of the top-view of the F_0, showing the rotor C_n, the stator *a*, the charge on the stator, shown by, the positive ions, shown by ⊕, the negative-charge sites on the rotor, shown by ⊖. The filled circles represent the membrane phospholipid molecules.

A brief summary of previous results

In a numerical modeling of the induced electric field, and the specific absorption rate (SAR) of microwave radiation near tissue [4], it was shown that the temperature increased for both the transient and steady-state cases. Finite-difference-time-domain (FDTD) method was employed to perform the electromagnetic calculations, for half-wave dipoles radiating at 900 and 1900 MHz. The resulting temperature rise was computed via finite-element