学 位 論 文 内 容 の 要 旨

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学 位 論 文 題 名

The effects of non-equilibrium angle fluctuation on rotary protein motor kinetics: numerical study with a data driven model
（回転モータータンパク質の反応動力学における角度非平衡揺らぎの効果：データ駆動モデルによる数値解析研究）

F_1-ATPase is a rotary protein motor whose shaft rotates step-wisely along with intermediate reactions under thermal fluctuation. This protein is intensively studied especially with single molecule measurement in order to reveal its chemo-mechanical coupling mechanism to establish remarkably high energy conversion efficiency. Recent experiments revealed that its chemical reaction rate is modulated by the rotation angle during rotary dwells waiting for the reactions, which suggests that the angle fluctuation plays an important role in the reaction process. Meanwhile, effects of conformational fluctuation on enzyme chemical kinetics have been discussed from both experimental and theoretical view points in other proteins and anomalous kinetics are reported such as non-exponential decay and positive correlation in catalytic turn-over time.

The aim of this study is to scrutinize how the rotary angle fluctuation affects the chemical reaction process of the F_1-ATPase as the temperature changes. Because the single molecule observation can be done only around the room temperature, a mathematical model used in previous works was adopted and extended it to be applicable to a wider range of temperature than is attainable in experiments. This is a one-dimensional model of the rotary angle described by Langevin type stochastic differential equation, where the rotation and rotary dwells are manifested by the brownian motion in harmonic a potential whose bottom position switches stochastically. In order to be consistent with the real data, the model parameter inference is based on objective methods applying statistics and information theory.

As a result of the numerical simulation, the rotary angle distribution during the catalytic dwell was found to deviate from the local-equilibrium one as the temperature increases.
This diffusive non-equilibrium property induces two effects which have not been observed in F_1. First, temperature dependence of the rate coefficient of P_i release, one of the fitting exponents of the dwell time distribution, deviates from the Arrhenius law, which has been assumed to hold in experimental estimation of the activation free energy. A modified method is also proposed to calculate the thermodynamic quantities from the static angle dependent rate constant. Second, increasing negative correlation was found as the temperature increases between waiting time for two successive reactions, hydrolysis and P_i release. This breaks the premise of the conventional double-exponential fitting to estimate their rate coefficients and is consistent with the fitting error of simulation data at $60^\circ C > T$, which is close to the physiological temperature of the bacteria from which the protein was originally obtained (~75˚C). This result proposes a caution against the conventional dwell time analysis when single molecule measurement experiment at such a high temperature becomes possible in the future.