Review on Modeling Molecular Motor*

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Abstract: The structure and function of three kinds of motor proteins are introduced. The fundamental importance on studying molecular motor in living systems is also discribed. With detailed review on several archetype theoretical models, the progress and application on modeling molecule motor are presented.

Keywords: models of molecular motor; muscl' s motion; review of research status
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1 Introduction

With the electron microscope, computer, x-ray, microneedles, optical traps, and nanometry such modern techniques application have been made to the biological realm that the structure and function of subcellular have become more clearly understood. More and more biologists and theoretical biophysicists concentrate on studying the mechanism of living systems and mimicking the biological structure to invent subtle artificial instrument. Molecular motor systems of proteins or protein complexes have lately become the topic intensively studied because of their key role in many important fundamental biological processes involved in translating chemical energy into mechanical work at a molecular scale. Recent reviews have covered different aspects of molecular motor such as mitosis, meiosis, biochemistry and kinetics, micro—mechanics, sub-unit composition and evolution. In addition, many theoretical models have been proposed to interpret the mechanism of the molecular motor.

A perfect theoretical model will play a key role in disclosing the work mechanism of the molecular motor systems. Not only can we use the model to explain the essence of relative living phenomena, to show the causation of some disease, and to design feasible experiments, but also can we design new drugs and new vaccine for cancers and Aids, propose scientific theory for modern biological technique, and make artificial molecular motor tracks for controlling some biological processes. On the other hand, molecular motor systems have already experienced such a billion-year-long evolution that they can run in the most perfect way. If we apply such mechanism to macro-machine, it should become the most attractive approach on reducing the engines fuel consuming to increase the efficiency and improving the stability. Therefore it will be of magnificent prospect to study molecular motor systems in living systems by physical means.

2 Structure of Molecular Motor Systems

The great progress have been made on the observations of molecular motor systems since H. E Huxley proposed the rotating cross—bridge model to study the muscular contraction in 1954. The atomic structure of the motor domain and the basic elements of kinetic cycle have been known now. Several x-ray crystal structure of kinesin motor domain have recently been showed at high resolution (0.2 ~ 0.3 nm) in both their monomeric and dimeric states. According to these experimental observation, there are three different families of motor[1] proteins in cellular, the myosins moving along actin filaments, the kinesins and dynesins moving along tubulin filaments. Mandelkow[2] have presented the kinesine's common features: kinesins are made up of three parts: the 40 000 globular motor domain which generates force and binds ATP and microtubles, the α-helical stalk domain that severs as a spacer and force transducer, and the globular tail domain that binds the light chains and connects the complex to the cargo (eg., vesicles, organelles, chromosomes). Usually, kinesins hydrolyze 1 ATP in one step whose distance is 8 nm long. To some special kinesins the rate of ATP hydrolyzing is 20 per second. The ordinary velocity of kinesin moving is about 0.5 ~ 1 um/s, but some is slow to 0.01 um/s and some can add up to 2 ~ 3 um/s. The structure of dynesins is similar to that of kinesins.

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The myosin actin systems consist of myosin proteins and actin filaments. The myosins are composed of a head and filamentous proteins tail. Actin filaments are composed of actin monomers winding into (right helix, the distance of per helix is 36nm and the width of the spiral is about 7 nm. The myosin have ATPase active sites, the active sites can't be found without actin, but if the pure actin are put into myosin, the ATPase active sites can be rapidly activated, the rate of ATP hydrolysis can add up to 200 times than that of it usually does.

Although the three kind of molecular motor have different structure, they still have common basic functions, such as hydrolyzing ATP and translating the chemical energy into mechanical energy by which the cargo can be sent to the destination. Because the actual biological environment and processes are very complicated it is difficult to mimic them in experiment. Only a few parameters and features can be surveyed through experiments. So a great many researchers have resorted to theoretical model to explain the mechanism. Up to date there have been three kind of archetype models proposed to study the molecular motor systems: namely the fluctuation models, the phase transition models, and the resonance models. In the following we will focus on reviewing these models.

3 Review on Theoretical Models

One typical kind of fluctuation model is ratchets models. This kind of models treats molecular motor as heavily damped Brownian particles, and by a single Brownian particle to study the molecular motor motion. Using a potential inspired by Feynman's ratchet, Magnasco showed that fluctuations of the force around a zero average can be rectified provided that the fluctuations are slow enough (ie. non-"white" noise). According to Magnasco's model, the fluctuating forces cause potential symmetry breaking of the system. The system absorbs energy from the source of the fluctuations, the molecular motor undergo similar Brownian motion and produce net transport as the fluctuation continues. Another typical fluctuation driven ratchets model is proposed by Asturmian et al.[3]. They show that nonequilibrium fluctuations brought about by an energy releasing process can be "absorbed" and used to do chemical or mechanical work. Although the fluctuation models have discussed different aspects of molecular motors, there still exist a matter of debate on the mechanism of its motion.

The typical phase transition model is two-state model proposed by Julicher[1]. Using the basic idea of the Ising model for phase transitions, he studied a single motor and a large of such motor movement in asymmetric periodic potential. In his model the microtuble and molecular motor are regarded as periodic polar railway tracks and carnot engines with cargoes. The motor consumes chemical energy and cause system conformation change, the phase transition occurred between two states. This model of molecular motor systems has three typical features. A striking feature is that: thermal equilibrium is a singular limit in the biological process. Along some paths approaching equilibrium, the deficiency is strictly zero, while along some others it is constant. It is worth remarking that a departure from reversibility may lead to an increase in efficiency in contrast to what is sometimes assumed. In an almost symmetric system close to equilibrium, efficiency may be made as close to zero, whereas beyond the spontaneous dynamical transition, the efficiency easily reaches values as high as 50% to 60%. The second feature is that: the time scales play a very important role for given interaction potential, the efficiency of the operation of molecular motor depends on how lifetimes, drift times and diffusion times are matched. Even the motor's direction of motion can depend on this matching. The third feature is that: a large collection of such motor might involve dynamic phase transitions which is similar to paramagnetic-ferromagnetic and liquid-vapor transitions. In this phase transition model, the asymmetric potential involving times and spatial dependence of the motor's chemical activity is used very reasonably. This analysis of treating molecular motor as a carnot engine is very inspiring. But the biological structure and environments can't be deliberately considered, and the explanation on the molecular motor how to work is some what abstract from the viewpoint of biology.

The newly type resonance model is named stochastic inclined rods model proposed by Matura et al.[4] which studied the actin myosin system in a symmetric periodic potentials. Stochastic inclined rods model includes three parts: myosin head, myosin rods (spring) and myosin bundle. The myosin head interacts with thermal noise, the resonance occurs between the myosin head and the noise, when stochastic resonance occurs, the energy transfers from the random noise to the myosin head, then the myosin head and spring are made keeping the vibration, while the

myosin head vibrates, it collides with a G-actin and obliquely kicks the G-actin sphere because the direction of the vibration is inclined against the line of the actin fibers, In this way the myosin molecule obtain the propellant force along the direction of the actin fibers: the perpendicular component to the fibers is canceled out in the average of the total force, the level component is gathered by the myosin bundle making myosin move along one direction. Although this kind resonance model presented a perfect sliding mechanism of the actin myosin system, the explanation on the breaking symmetry is very simple compared with other models. Nevertheless, the interaction potential is chosen too simply the time factor hasn' t been considered in the interaction processes.

With micromachine to mimic the movement of the molecular is another kind study method. Entropic ratchets devices, physical barries device geometrical sieve device and the silicon-chip device all belong to this micromachine, and among those instruments the silicon-chip device is the newest one which uses charge-charge interaction to generate the ratchet potential mimicking Brownian ratchet transporting. The mechanism of such devices can be summarize like this: the ratchets like wells that trap DNA generated by charging a series of patterned electrodes, when the electrodes are discharged, the traps vanish and the molecules undergo Brownian motion. Next, when the potential is reapplied, and the particles again collected in the traps. A spatial asymmetry in the shape of each ratchet-shaped well rectifies the Brownian motion and produces net transport as the on-off cycle is repeated. Each molecule' s transport rate depends on its diffusion constant allowing the possibility of size-based separations.

Despite the study of molecule motor has make some successes, however, many key elements are still missing from our understanding of its mechanisms. Besides, there are continuously new finding presented. For example, Noji[5] has observed a single molecule of F-ATPase acts as a rotary motor, whose central rotor of radius is about 1 nm, the filament rotated for more than 100 revolutions in an anticlockwise direction when viewed from the ' membrane' side, the rotary torque produced reached more than 40 PN/nm under high load. Another example is that a marine natural product inhibitor of kinesin motor is isolated by Roman[6]. Such product can inhibit kinesin activity by targeting its motor domain and mimicking the activity of the microtubule. The development of techniques for manipulating a single actin filament using microneedles, optical traps, and nanometry has made it possible to measure displacement directly from single molecules of myosin and its subfrangments *in vitro*. Yanagida et al.[7] have reported a myosin displacement of about 15 nm to about 30 nm which is significantly larger than would be expected from the ever models. Therefore, with the biological computer application on biology, using period asymmetry potential involving time, space and temperature to study molecule motor systems dynamics and to design micromachine according to the mechanism of molecular motor, will become the intensive topic research in the near future.

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分子马达模型综述

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摘 要: 介绍三类马达酶的结构, 功能和生命体内分子马达的研究状况, 并详细介绍几类典型分子马达的理论模型, 同时展望了分子马达的发展前景和应用.

关键词: 分子马达模型; 肌肉运动; 研究现状综述