Proceedings of BIO2006
2006 Summer Bioengineering Conference
June 21-25, Amelia Island Plantation, Amelia Island, Florida, USA

BIO2006-155757

NANO THERMAL HYDRODYNAMICS IN THE GAP OF A CELL MEMBRANE

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INTRODUCTION

As a barrier to compartmentalize the cells, membrane forms the interface between a cell and its surroundings (Fig. 1). The essential function of a membrane is to maintain a relatively stable environment in the cell, exchange substances selectively and transfer energy and information continually with the outside [1]. Among various events occurring in the cell membrane, fluidity has been a major scientific focus from which many life mysteries can be revealed. Up to now, various methods have been developed to investigate, monitor and measure the fluidity of the fatty acid chain of phospholipids in the cell membrane [2]. Particularly, Singer and Nicolson unveiled their well known fluid mosaic model for the membrane, which incorporates the ideas that the basic structure of the membrane is a fluid lipid bilayer, and that intrinsic membrane proteins just “float” in this “sea” of lipid, while the extrinsic membrane proteins are located on both surfaces of the membrane [3]. It is intriguing that when above the phase transition temperature, the membrane lipid molecular will have three modes of motion like: lateral diffusion, rotational movement and flip-flop activity [1-4]. These thermodynamic processes are vital to cell existence, growth, division, differentiation and also are responsible for hundreds of thousands of life phenomenon. Previously, the species transport across the membrane is interpreted mainly from a phenomenological way using lumped system model. Therefore, detailed flow processes occurred in the membrane domain and their clues related to life mechanism were not sufficiently tackled. In fact, such important issues can be clarified through modeling the nano scale thermal hydrodynamics over the gap space of a cell membrane. Here, we show that many complex events observed in the membrane can be explained by the thermally induced flow convections inside the membrane. It sets up correlations between nano scale hydrodynamics, non-equilibrium thermodynamics and cell membrane activities. The disclosed mechanisms are expected to provide a new viewpoint on the interaction between intracellular and extracellular processes through the membrane.

THEORY AND METHOD

The analysis starts from calculating the three-dimensional fluid mechanics over the space of a cell membrane gap within an area of 40nm $\times$ 40nm $\times$ 10nm or more different configurations. It was surprising to find that, an extremely small temperature difference ΔT across the cell membrane such as 0.0001K~0.1K would induce rather complex flow inside the cell membrane, which clarifies many important mechanisms in a living system.

For a conceptual investigation, we had adopted the classical Navier-Stokes equation and the corresponding continuity and energy equations to characterize the three-dimensional thermal flow inside the membrane. As is widely accepted, the continuum description is acceptable for length scales of a few times the mean free path of molecules [5]. In water, this is of the order of the molecular diameter, i.e. 0.2-0.3 nm. Unless the membrane gap thickness is below 1 nm like that of a virus, the continuum description of the “solvent” (water) may break down. Therefore, for the present membrane thickness of 10nm, the above modeling on the fluid is very useful. Compared with the typical diameter of a spherical cell at around 10 μm, the flow space between the two lipid bilayers can be treated as in a three-dimensional rectangular domain with size of 40nm$\times$40nm$\times$10nm (see Fig. 1, 2). Besides, to guarantee the universality of this study, various typical membrane configurations as shown in Fig. 1 have been tested, which was to represent the cases with or without proteins floating in the lipid bilayer. The density of the membrane liquid was taken as that of water for brief, i.e. $\rho = \rho_0 [1-\alpha (T - T_0)]$, while the liquid viscosity is expressed as $\mu = A \exp (\Delta E / RT)$ to reflect the temperature dependent effect. The base membrane viscosity μ was treated as 0.5 poise. The coefficient of volume expansion α was 5e-4 /K. When considering the temperature fluctuation, unsteady state thermal process in extremely small scale, environmental temperature change and the external field effect on cell, a temperature variation across the cell membrane can fall in a wide range like 0.0001K~0.1K. Therefore the boundary conditions are set as follows. The bottom surface of the cube is set as hot wall and all the other surfaces are as cold at the same temperature. Effects under a variety of temperature difference between the hot and cold wall such as 0.0001, 0.001 K and 0.01 K have therefore been investigated and similar conclusions can be drawn all the time. In these calculations, the base temperature was set as in body temperature 310K and the cell is in gravity. At the surrounding surfaces of the cube or the protein cylinders, flow velocity was assumed as zero or specified at a value such as 1e-20 m/s. Then computational fluid dynamics method was adopted to numerically calculate the flow and temperature field inside the complex bilayer of cell membrane.

RESULTS

Fig. 2 depicted a typical flow circulation inside the cell membrane with multiple protein-cylinders embedded. If subject to different calculation domain, various complex flows can be predicted to arise owing to thermal non-equilibrium over the cell membrane. Generally, such flow spans three dimensional space, which therefore clearly reflects the lateral diffusion, rotational movement and flip-flop activity of lipid molecular. In the eye of classical fluid mechanics, this phenomenon resembles the well known Bernard convection, which previously was mainly observed in a much larger gap space and has been intensively studied. Such phenomenon refers to the instability of a fluid layer confined between two thermally conducting plates heated from below. Our present simulations still reveal that, the velocity vector around the protein cylinder in the lipid bilayer appears as rather asymmetric, which would easily lead to flow and rotation of a floating object nearby. Therefore, the previously observed rotation of protein across the cell membrane can most probably be attributed to this reason. Another important conclusion drawn from a comprehensive study still lies in that the frequently happened thermal fluctuation in fact serves as one major factor to induce time dependent nano scale flow circulation inside the cell membrane. This suggests a basic route to explain why a living system always has a rhythmic activity. Particularly, all the above processes are induced only by the thermal fluctuation and consume no additional energy. This accords perfectly with the well established fact as described in many textbooks.

DISCUSSION

The nano hydrodynamics approach is surprisingly useful in providing a straight forward answer to many puzzling physical and chemical events occurred inside a cell membrane. It is very possible that, quite a few sub-cellular level mysteries can be clarified through this theoretical investigation. For example, existence of the thermally induced flow circulation will prevent the external species from directly entering into the cell interior, which implies that such reciprocating flow in fact serves as a barrier. In clinics, drug resistance is a major mechanism responsible for failure of therapy, especially in advanced cancer. This study reveals that, existence of the circulation may prevent the species from directly transporting inside the cell interior. Further, during an insemination process, when one sperm swim into the oocyte, the membrane of oocyte solidifies immediately in order to prevent other sperms from getting into the oocyte. Clearly, modeling on the nano fluid mechanics over the cell membrane will disclose more details on such process. Finally, more parametric studies can be performed following the theoretical way as proposed in this paper. For example, effect of the membrane lipid composition, content of unsaturated bond and chain length, the ratio between lecithin and sphingomyellin, and molecular interactions between the lipid and protein molecules such as hydrophobic effects, hydrogen bonding or charge interactions, cell surface and lipid structure on membrane fluidity can all be tested. A comprehensive presentation and discussion on some of these interesting results will be given in the conferences.

In recent years, the appearance of micro/nano fabrication allows investigators to realize sophisticated nanofluidic device. This provides possibilities to measure and evaluate the nano flow processes in or outside a cell. The discussed issues as initiated in this study can find experimental quantifications in the near future. In this side, modeling, measurement and implementation of the nano scale fluid mechanics over the cell membrane and the cell interior may possibly open an exciting new frontier in cell physics.

ACKNOWLEDGMENTS

This work is partially supported by the NSFC Grants 50575219 and 50325622.

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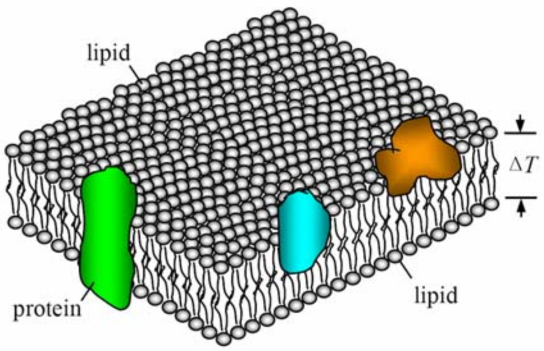

Figure 1. Cell membrane configuration with fluid inside

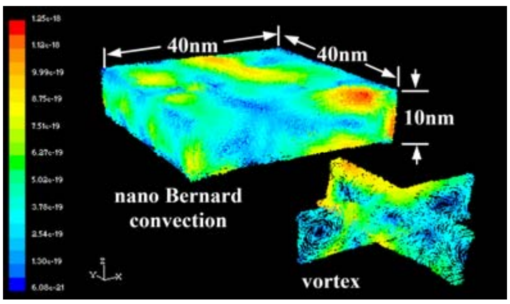

Figure 2. The thermally induced Bernard convection (the left upper part) and its two cross-sectional vortexes (the right lower part) inside the membrane gap