

大阪大学臨床医工学融合研究教育センター(MEI)センター
グローバルCOE「医・工・情報学の融合による予測医学基盤創成」
—in silico medicine を指向したオープンプラットフォームの構築—

グローバルCOEプログラム

■ 若手研究者短期留学・滞在 ■

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■ 報告 ■

Two months in Osaka University has passed by very quickly. The work that I proposed for collaboration with Wada lab is to study the biomechanical properties of cell and construct a computational model of a cell. A cell consists of many elements in cytoplasm besides nucleus. Some of the elements are mitochondria, actin filament. However, actin filament network is found to be the most important part of cell which is there to define the shape of the cell, cell motility, and how the cell responds to an environment.

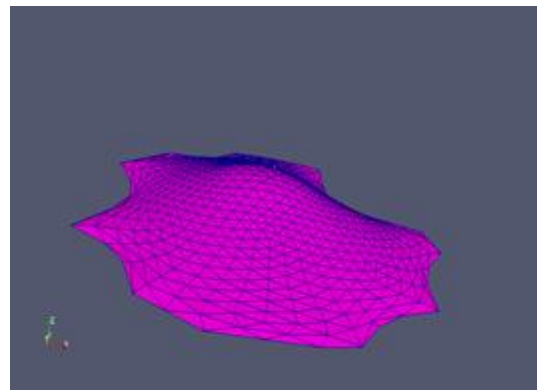
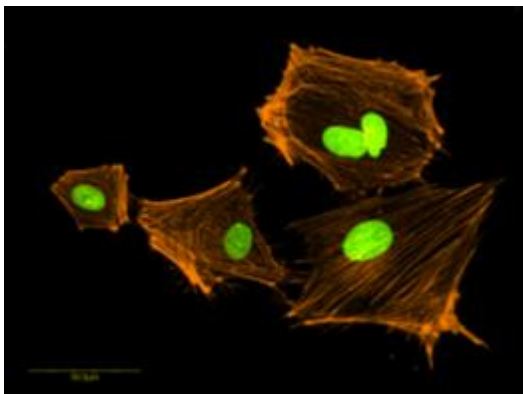
Understanding the cell structure and cell behavior under stimuli is crucial. It creates the path to dive into understanding the motility of cell and the shape of the cell. For example in cancer cell, the uncontrollable spreading of the cancer cell causes difficulty during cancer treatment and damages surrounding organ or tissue. Therefore, understanding how the cell spreads and how it circulates within a closed system will help us understand and leads us to determine the

treatments of the disease.

Cells are interconnected to the surrounding environment through extracellular matrix where the mechanical stimuli can be transferred directly to the cell. The chemical activities inside the cell can be converted into mechanical energy. During cell attachment, cell spreading, and motility of cells, mechanical energy plays an important role. Cells positively respond to mechanical stimuli by changing their own behaviors and by modifying their shape and environment. For example, forces applied to the cell and the consequent cellular deformations induce a variety of processes, including morphological changes, growth, differentiation, secretion, gene expression and altered extracellular matrix production. This response can either lead to cell adaptation to counteract the effect of the applied stimuli or to cell damage or death when the applied stimuli exceed the adaptive capacity of the cell. Understanding the mechanical properties of cells will help to better understand the physical mechanisms responsible for cancer metastasis. With the recent advances in biomechanics and nanotechnology, it has now become possible to experimentally apply mechanical influences on biological structures. A wide variety of experimental biophysical probes have been used to extract the mechanical properties of cancer cells to explore cell mechanics, locomotion of cells or differentiation in cells.

My interests involve a study of how cells respond to external forces. This includes the properties of cells and the deformation of cell shape. In particular, I am interested in applying mechanical theory to cell modeling, characterizing the mechanical properties of the cell, and the change in cell shapes. The experiment that we did at Osaka University during my visit included observation of morphological changes in rabbit fibroblast cells. We stained the cells with Alexa Fluor 546-phalloidin. The cells were observed under a laser scanning microscope to view the actin filament network and the cells' nuclei. The actin filament network observed in this case shows the elongation of the actin

filament while the cell spreads out on a glass surface. Cell is model as a spherical shape due to the surface to volume ratio. The computational model was determined based on strain energy principle. During the spreading mechanism, the actin filaments elongated. This elongation mechanism is modeled based on spring network model. The stiffness of the spring replicates the stiffness of the actin filament. The elongation of the actin filament took place when the cell is contracting and extracting. In our study, we perform a comparison between experimental observation through image analysis of our stained fibroblast and created simultaneously a model based on the spread shape of the cell. The motion of the cell depends on how the actin filament network stretches and contracts. To analyze such motion, one needs to determine the length and the stiffness of the actin filament. The image was taken by laser scanning microscopy was analyzed and then the information was applied to the mathematical model from previous work by Wada lab.



The image shows rabbit fibroblast which was stained with Alexa Fluor 546-phalloidin solution. The stained actin filament was shown in orange and the nucleus was in green. The images of the actin filament stretching and contracting were observed. The cell is modeled based on the minimum strain energy theory. The strain energy stored within a round shape cell is minimum. The stretching of the actin filament increased the internal strain energy. The model is computed based on a minimizing energy principle each time the actin filament contracts or extends.

Most of all, I would like to thank Global COE program for providing me an opportunity to explore this research field in Wada lab. I am excited and hope this will be an initiation of our strong collaboration between my lab at KMUTT and the lab here at Osaka University. I would like to thank Wada sensei, Miyazaki sensei and every lab members for the warm welcome and hospitality all of you have given to me. Special thanks to Nishimura san and Kanemori san who put their effort trying to help me out with programming and cell culture lab with some difficulty communicating in English. Last but not least, I would like to also thank Julien san for advices during my exploration of the Japanese culture here in Osaka. All the lab members, I apologize for my bad Japanese language skill and hope to be better at this next time we meet. Please stay warm for this coming winter.

