Physics in Ramen and cellular organelles

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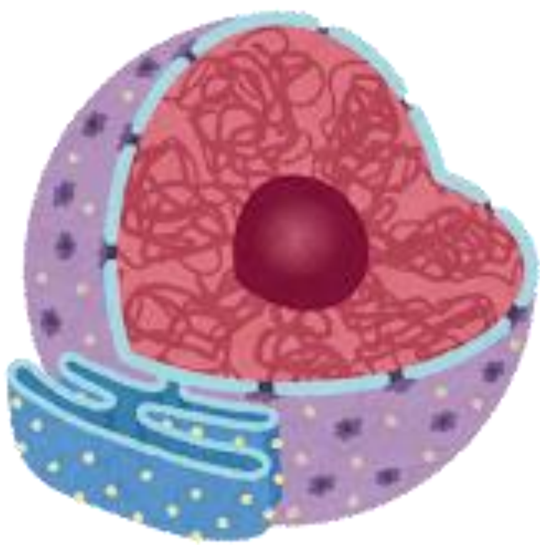
I am strongly inspired to understand biological phenomena using physics. Let me explain my research project and what I find fascinating about it. Our body is composed of many cells. We have acquired various functions through the cooperation of many cells. While the interaction between cells is an interesting topic, let's focus on what happens inside a cell. Each cell has many types of organelles, such as the nucleus, nucleolus, and endoplasmic reticulum. Let's think of your house. Your house has several rooms, each with furniture for a different purpose. The beds are in the bedrooms, and cooking tools are in the kitchen. If all the furniture and your stuff were put together in one room, you would have to search through the room every day. The same thing occurs in a cell. The cell is efficiently working on tasks by using compartmentalization. Various chemical reaction processes are happening in a cell, and many reactions keep going on at the same time. For the success of these simultaneous reactions, the cell needs a "test tube" in which it can concentrate what it needs locally. So how do cells establish compartmentalization? For example, nuclei and mitochondria are separated inside and outside by membranes. On the other hand, some organelles do not have membranes. For example, nucleoli in the nucleus and stress granules in the cytoplasm do not have membranes [1)]. These membrane-less organelles (MLOs) are thought to be able to take up and expel specific molecules quickly. Let us consider the nucleolus, which is found in the nucleus. The nucleolus is a type of MLO with at least three layers. Let us consider a factory that makes cars. Cars are put on a line in the factory and processed and made at each location. The nucleolus is thought to efficiently synthesize ribosomes by using its layered structure in the same way [2, 3)]. Ribosomes are machines in the cells that read mRNA to make proteins. This process is called translation. Ribosomes are extremely important complexes for translation. So nucleoli, which are responsible for ribosome synthesis, are important organelles that are essential for our life. MLOs exist in the cell and contribute to maintaining vital activities. How do membrane-less organelles form? The fact is that MLOs are made through phase separation. And these facts are confirmed by MLOs' properties, spherical shapes, their fusion with each other, and so on. A familiar example of phase separation is the Ramen soup. When you had Ramen, you might have noticed that the oil in Ramen soup is floating. Ramen soup spontaneously separates into a solution with less oil and a solution with more oil. When you look at the surface of the Ramen, you can see the oil droplets and phase separation of the soup. Thus, phase separation phenomena are very familiar to us. Phase separation is one of the phase transition phenomena, in which the solution separates into a solute-rich solution and a solute-dilute solution due to the temperature decreasing. In addition to temperature, the strength of the solvent-solute interaction is also an important parameter that determines whether phase separation occurs or not.



In MLOs, proteins, which are their main component, contribute greatly to phase separation. Proteins are long chains of various types of amino acids connected by peptide bonds, and they take on various three-dimensional structures in the body. In short, they are like accessories made by connecting colorful beads. The sequences of the proteins and the degrees of protein modification are thought to be important for MLO formation.

Understanding the phase separation occurring inside the cells involves biological difficulties. Polymers can be classified into two main categories, homopolymer, accessories connected by the same type of beads, and heteropolymer, accessories connected by various types of beads. Proteins are heteropolymers composed of varieties of amino acids. In addition to this difficulty, MLOs are multicomponent droplets containing multiple types of proteins. Furthermore, it is known that not only proteins but also RNAs are working for the phase separation of MLOs as essential components for phase separation [4)]. There is no theory that completely describes the phase separation phenomena of multi-component heteropolymers. In other words, studying heteropolymers provides not only new insights into biology but also opens new vistas of physics. My research goal is to contribute to both biology and physics by working on phase separation phenomena. Intracellular phase separation is also known to be related to multiple diseases. Therefore, understanding phase separation in cells may promote the elucidation of these disease mechanisms and the development of treatments. I believe that the findings of physics save patients and contribute to healthier living for humanity in the future. I was strongly inspired by this research project approaching biological phenomena from the viewpoint of physics. The fusion of biology and physics is very exciting for me. I am passionate about biophysics research.

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3) Riback, J.A., *et al.* (2020) Nature 581, 209–214. doi: 10.1038/s41586-020-2256-2.

4) Yamazaki T., *et al.* (2018) Mol Cell 70, 1038-1053. doi: 10.1016/j.molcel.2018.05.019.

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