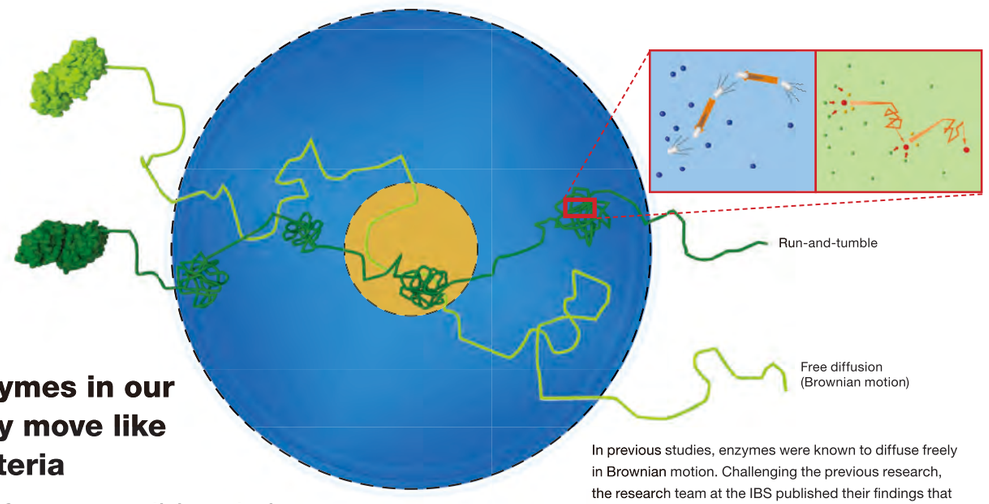


Enzymes in our body move like bacteria

Proof for enzyme antichemotaxis overturns previous results

In previous studies, enzymes were known to diffuse freely in Brownian motion. Challenging the previous research, the research team at the IBS published their findings that enzymes display antichemotaxis and demonstrate the motion of "run-and-tumble."

Enzymes are proteins that catalyze a wide variety of chemical reactions within living organisms. There are over 70,000 enzymes in the human body, each of which plays a key role in the metabolic functions. Enzymes regulate chemical reactions by acting as catalysts by directly binding with chemical reactants called substrates. To do so, enzymes and substrates have to meet. It was believed that enzymes move in Brownian motion, which refers to a random movement of microscopic particles suspended in liquids or gases.

Recently, however, there has been growing evidence that enzymes move directionally. A research team at the Center for Soft and Living Matter (Director Steve Granick), observed that enzymes exhibit antichemotaxis, the tendency to move away from substrates. This finding is contrary to the existing theory that enzymes diffuse more quickly in areas with more substrates. Moreover, the research team's experiment found that this tendency intensifies with higher substrate concentration.

It was only recently that the movement of enzymes began to receive attention from academia. With mounting evidence that enzyme diffusivity is enhanced at high substrate concentration, the concept of enzymes displaying chemotaxis has emerged as one of the leading theories on the subject. Chemotaxis is the movement of organic matter toward a higher concentration of a particular chemical, and can be found in the motion of bacteria swimming toward food supply or in the movement of sperm towards the egg during fertilization.

Used for this research, the Fluorescence Correction Spectroscopy (FCS) method is an analytical technique in which a laser beam is applied to a solution containing fluorescent molecules with the aim to obtain information on the molecules passing through the beam zone. Director Granick employed the technology that combined FCS with Stimulated Emission Depletion (STED), which is a microscopy technology designed to overcome the diffraction limit of light, and a specialty of the research team.

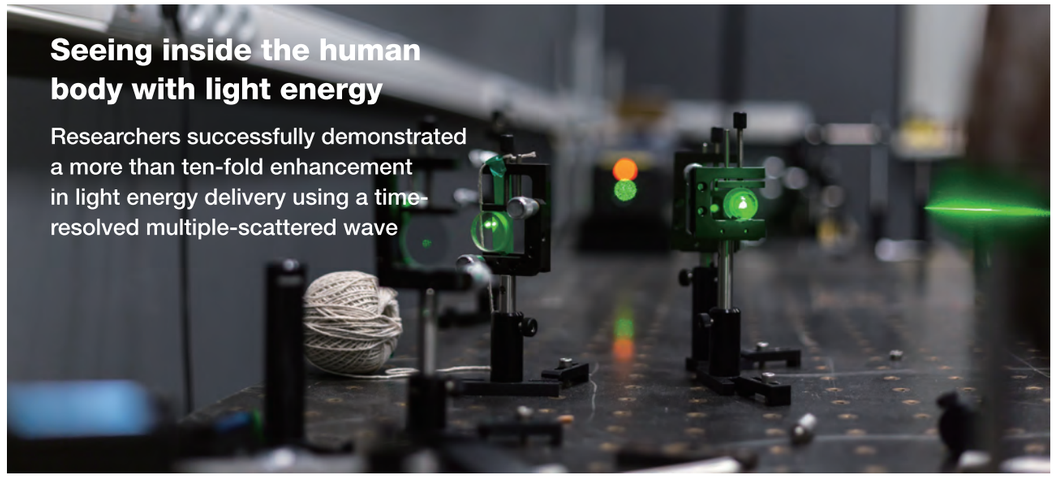
To verify the interactions between substrates and enzymes, the research team designed a chip with varying substrate concentrations and observed the movement of urease enzyme by using FCS. In the first experiment, researchers found that the enzymes moved towards the area with lower substrate concentration. The enzyme concentration was low in the area with higher substrate concentration, while it was high in the area with lower substrate concentration. Therefore, it was verified that enzymes exhibit antichemotaxis rather than chemotaxis.

In the second experiment, the researchers utilized STED-FCS, which can reduce the beam diameter to 50 nanometers, to observe the movement of enzymes. As the result, they observed the phenomenon known as "run-and-tumble," where the enzyme repeats the process of moving in one direction before shifting toward a random direction. The run-and-tumble process is known as the movement of bacteria that repeat linear movements and random tumbles in an attempt to find a food source effectively. While bacteria oriented towards the food supply, enzymes moved towards the area of lower substrate concentration. The reason behind this is that the enzymes are expelled in the opposite direction of substrates, while catalyzing. The research team noted, "Although the result that enzymes avoid substrates may seem counter-intuitive, it might be a sort of control mechanism to keep multiple reactions from occurring at once under a strong enzymatic catalysis."

This research showed that enzymes, which are merely protein molecules, nonetheless move directionally like microorganisms such as bacteria and cells. This discovery is expected to make a significant contribution to the future study on metabolism including the reaction between various enzymes.

Paper published

Jee Ah-Young et al., "Enzyme leaps fuel antichemotaxis," *PNAS*, 2018, DOI:0.1073/pnas.1717844115

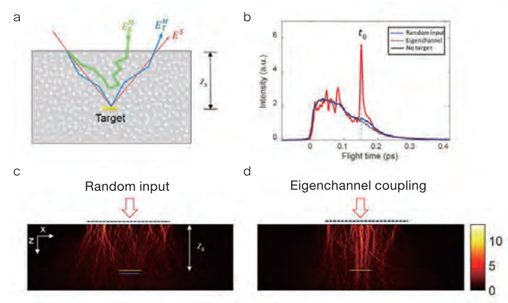


Seeing inside the human body with light energy

Researchers successfully demonstrated a more than ten-fold enhancement in light energy delivery using a time-resolved multiple-scattered wave

Can light be used to diagnose or treat diseases? If enough light energy can be delivered deep inside the human body, it can observe and destroy cancer tissues. However, the human body is a complex medium consisting of countless molecules. When light enters into this medium, the pattern of the light is diffused randomly due to multiple scattering that takes place after the light comes into contact with the countless molecules within the body and becomes drastically diminished depending on the depth.

Based on this idea, researchers led by associate director CHOI Wonshik from the Center for Molecular Spectroscopy and Dynamics (Director CHO Minhaeng), found a method to collect light energy by employing multiple scattering waves that reflect off of objects. The research team developed a strategy to amplify the intensity of light signals by filtering out multiple-scattered waves reflecting off objects through time-resolved measurement. Time-resolved measurement is a method of selectively obtaining only multiple-scattered waves that mainly interact with target objects, by identifying reflection signals produced by the medium at specific periods. If the selected multiple-scattered waves are reinjected into the medium, light energy enhanced by more than ten-fold of existing methods can be delivered to target objects.



The technique of enhancing the delivery of light energy to targets embedded within a complex medium was verified by a computer simulation developed by the researchers.

The experiment was conducted by inserting the target object of a silver (Ag) disk into the medium, which was created to be similar to human tissue, and observing it through a microscope. When the target object is deeply imbedded in the medium, reflection signals can be distinguished as the single-scattering wave (red), multiple-scattered waves reflected from the target object (blue) and multiple-scattered waves that fail to reach the target object (green) (Fig a).

Most of the reflected signals measured at the specific time (t_0), which corresponds to the depth of the target object by utilizing time-resolved measurement, were multiple-scattered waves that reflect from objects. Identifying the eigenchannel of incident light that maximizes the intensity of the multiple-scattered waves and reinjecting it into the medium, the light energy is reflected in a very strong intensity (red) only at the specific time of t_0 (Fig b). In addition, when light is injected in a pattern that maximizes the intensity of multiple-scattered waves (Fig. d), the result showed that the intensity of light transmission in the direction of the target object is enhanced, compared to the cases of injecting light in a random pattern (Fig c). Applying the abovementioned method to a target object embedded within a rat's skull, researchers demonstrated a more than ten-fold improvement of light energy delivery to the target without damaging the skull.

The light energy collection technique developed by the research team is a breakthrough technology that allows the effective delivery of light energy to targets that are too deeply embedded to visualize in a scattering medium like a human or animal body. This technology can not only be utilized in the research fields of optogenetics and light stimulation, but also can be applied to a variety of biotechnological fields including phototherapy and photovoltaic charging for implanted medical devices.

Paper published

Jeong Seungwon et al., "Focusing of light energy inside a scattering medium by controlling the time-gated multiple light scattering", *Nature Photonics*, 2018, DOI:10.1038/s41566-018-0120-9