Laboratory of Single Molecule Biology

Graduate School of Frontier Biosciences

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Cells are complex systems composed of various biomolecules. These biomolecules spontaneously self-organize into systems with functions such as motility, information processing, and proliferation, allowing cells to flexibly adapt to dynamic environments. With recent advancements in high-resolution microscopy, it has become possible to observe and manipulate individual biomolecules working within living cells (single-molecule imaging and force manipulation techniques). Our laboratory applies these cutting-edge imaging and force manipulation techniques, along with mathematical modeling, to investigate intracellular signaling systems and molecular motors. We aim to elucidate how biological functions emerge from these molecular systems at single-molecule resolution.

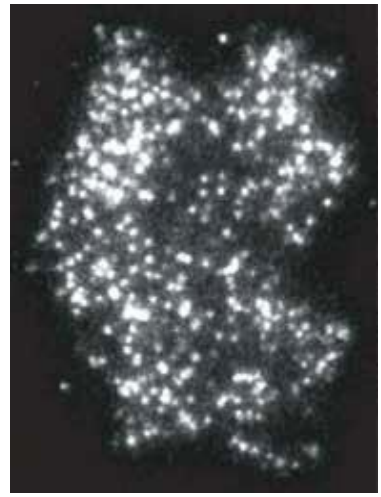
Single-Molecule Biology of Chemotaxis Signaling Systems

Cells recognize chemical gradients in their environment and move directionally toward or away from these cues, a phenomenon known as chemotaxis. This process is not only crucial for environmental exploration in unicellular organisms but also plays key roles in neural circuit formation, morphogenesis, and immune responses in multicellular organisms. Our laboratory investigates the molecular mechanisms underlying chemotaxis signaling, from gradient sensing to motility regulation, using the cellular slime mold *Dictyostelium discoideum*, a widely studied model organism, and advanced single-molecule imaging techniques. We have developed a high-throughput automated analysis system for intracellular single-molecule imaging, transforming traditionally artisanal single-molecule measurements into a practical and scalable analytical technique. Through these studies, we aim to elucidate, at single-molecule resolution, how intracellular biomolecules collectively give rise to cellular motility and information processing. Additionally, we are working to purify and reconstitute key signaling molecules *in vitro* to reconstruct specific signaling functions under controlled conditions. This "build-to-understand" approach is expected to open new frontiers in life sciences.

Single-Molecule Force Manipulation of Molecular Motors and Intracellular Fluctuations

We investigate the motility mechanism and efficiency of the molecular motor kinesin, which is responsible for intracellular vesicle transport, using optical tweezers-based single-molecule force manipulation microscopy. Traditionally, molecular motors were thought to generate directional motion by utilizing thermal fluctuations (collisions with water molecules). However, recent findings indicate that in the cellular environment, where these motors naturally operate, nonthermal fluctuations are actively generated through metabolic energy consumption. By implementing high-speed feedback control, we have enabled precise and arbitrary force application to working kinesin at single-molecule level and discovered that artificially introduced force fluctuations accelerate kinesin movement. Currently, we are refining our experimental conditions to more closely mimic the intracellular environment while incorporating information-theoretic approaches and mathematical modeling to investigate how intracellular fluctuations affect individual molecules in detail. Through these studies, we aim to reveal how living systems optimize the conversion of chemical energy into mechanical work.

Amoeboid cells of the cellular slime mold Dicyostelium showing chemotaxis to a concentration gradient of an attractant



Intracellular single molecule imaging of molecules that comprise the chemotaxis signaling system. Each white dot is a molecule of a molecule called PTEN.

Let's study it together!

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