ACHIEVEMENTS

Atomic Force Microscopy Reveals Nanoscopic Raft Dynamics on Cell Membranes: From Hypothesis to Visualization

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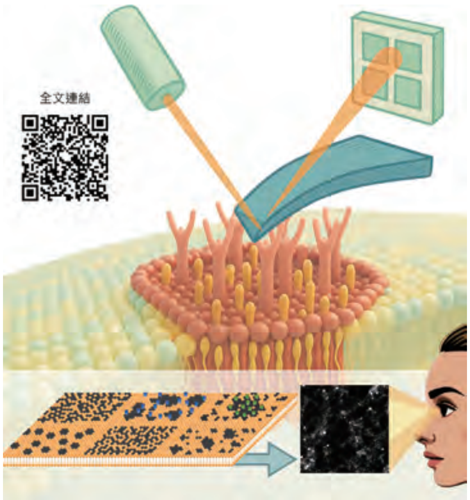
A collaborative research team of four professors and several graduate students, including Prof. Richard P. Cheng, Prof. Ja-an Annie Ho, Prof. Chun-hsien Chen of the Departments of Chemistry and Biochemical Science and Technology at National Taiwan University, and Prof. Li-Chen Wu of the Department of Applied Chemistry at National Chi Nan University, has made a long-sought breakthrough. By combining atomic force microscopy (AFM) with a Hadamard product–based image reconstruction algorithm, the researchers successfully achieved visualization, for the first time, of the nanoscopic dynamics of membrane rafts in live cells, making visible these subtle dynamics that had long remained invisible on the cell membrane.



Observing submicrometer-scale membrane rafts on living cells.

Click or Scan the QR code to read the full article published in the *Science Advances*.

Membrane rafts are nanometer-scale structures rich in cholesterol and sphingolipids, thought to serve as vital platforms for cell signaling, viral entry, and cancer metastasis. Since the conception emerged in the 1990s, the existence and behavior of these lipid domains have been intensely debated. Conventional fluorescence microscopy, usually performed on fixed and stained cells, could not capture the key features that are only tens of nanometers wide and change within seconds. Consequently, even the question of whether such rafts exist on live membranes remained unanswered for decades.

Led by PhD candidates Ms. Hsiang-Ling Chuang and Ms. Yu-Chen Fa, the research team employed high-resolution AFM together with Hadamard product–based image processing to record, in real time, the formation, fusion, and dissolution of membrane rafts on live cell surfaces. Using C-Laurdan phase-sensitive dyes and integrin co-localization imaging, they demonstrated that the nanoscale domains observed by AFM indeed correspond to membrane raft structures. This groundbreaking discovery, published in *Science Advances*, marks the first direct visualization of lipid raft dynamics in live cells.

The study revealed that these rafts are highly dynamic liquid-ordered (Lo) regions, usually 10 to 200 nanometers in diameter, continuously reorganizing through interactions among lipids, proteins, and the cytoskeleton. According to Prof. Chun-hsien Chen, AFM provides nanoscale measurements of surface height and stiffness on live cells, while Hadamard product analysis effectively suppresses irrelevant background signals, enhancing the visibility of the raft-related features. “This combination allows us to identify subtle, transient signals that conventional optical techniques could never resolve,” Prof. Chen explained.

Building on the current understanding of membrane rafts, Prof. Ja-an Annie Ho noted, “This technology, which enables the visualization of membrane dynamics in real time, could become a rapid screening platform for drug discovery.”

Integrating chemistry, biophysics, and biochemical technology, this interdisciplinary research opens a new window into the nanoscale organization of live membranes, offering powerful new tools for drug development and disease mechanism research.

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