"Seeing inside without coloring cells": GIST and KAIST develop technology for real-time observation of living cell interiors

- Joint research team from GIST and KAIST develops plasmonic metasurface-based stain-free cell imaging technology

- Applies 'oligomer structures' composed of clustered gold nanoparticles... Detects internal structures beyond the cell membrane

- Enables real-time observation and quantitative analysis without cell damage... Expected to be utilized in pathology diagnosis and new drug development

- Published online in the international materials science journal ***Small***

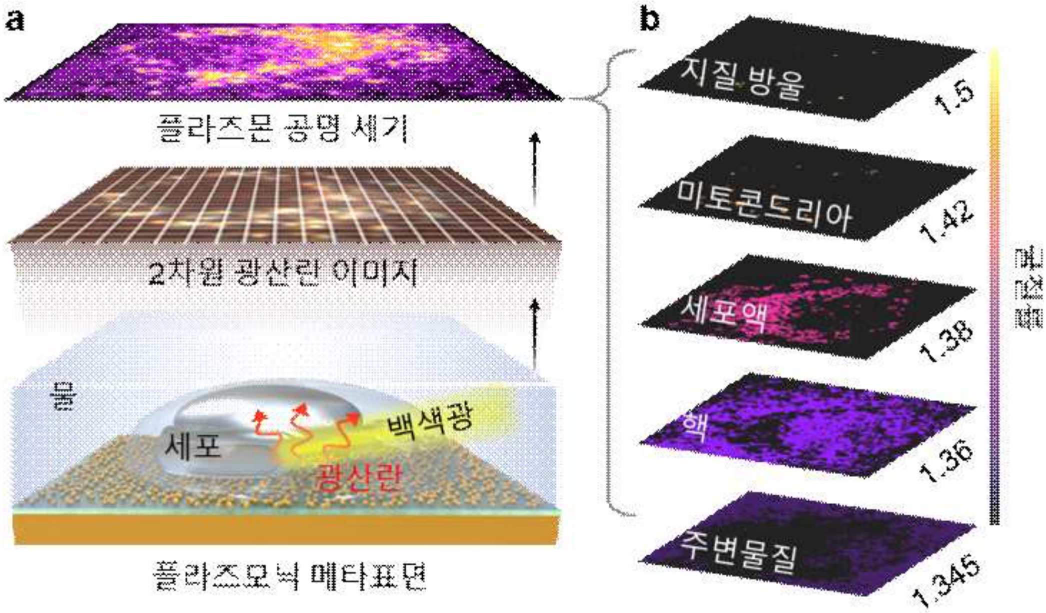
▲ Group photo of the GIST-KAIST joint research team. (Top row from left) Doeun Kim, postdoctoral researcher (first author) from the Department of Electrical Engineering and Computer Science at GIST; Juhwan Kim, integrated master's and Ph.D. student (first author); Jiyeong Ma, master's student; Gyurin Kim, integrated master's and Ph.D. student; (Bottom row from left) JuHyeong Lee, integrated master's and Ph.D. student; So Young Yoon, researcher from the Department of Life Sciences; Professor Youngsoo Jun; Professor Young Min Song, School of Electrical Engineering at KAIST (corresponding author); Professor Hyeon-Ho Jeong, Department of Electrical Engineering and Computer Science at GIST (corresponding author).

The Gwangju Institute of Science and Technology (GIST, President Kichul Lim) announced that a joint research team led by Professor Hyeon-Ho Jeong of the Department of Electrical Engineering and Computer Science and Professor Young Min

Song of the School of Electrical Engineering at KAIST has developed a nano-optical imaging technology capable of observing the internal structure of living cells in real time without the need for separate staining treatments.

This technology is significant in that it allows for the quantitative analysis of internal cell structure and movement without damaging the cells.

Accurately understanding the distribution and changes of internal cellular components is essential for understanding life phenomena and the causes of diseases.

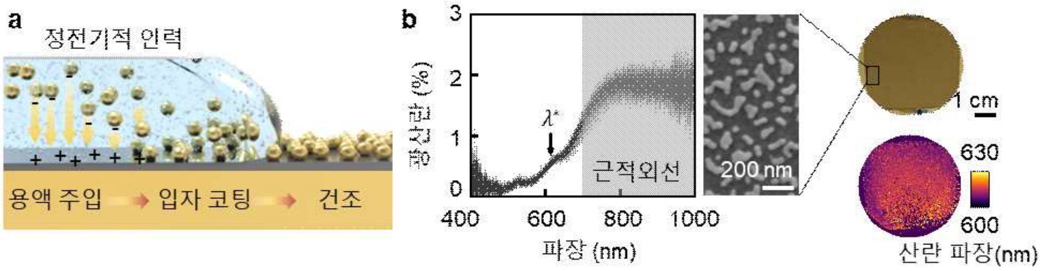


▲ ***Principles of cell imaging. (a) A schematic diagram showing the observation of internal cell structures using light scattering signals, and (b) the refractive index distribution for each intracellular organelle. By utilizing the differences in light scattering signals caused by different refractive indices, the interior of the cell can be observed and analyzed without staining.***

However, since most living cells are transparent, it is difficult to distinguish their internal structures using a standard optical microscope. For this reason, staining techniques that attach fluorescent substances to specific structures for observation have been widely used; however, this method requires a separate preparation process to treat the cells with fluorescent substances, and there are limitations to real-time observation as the fluorescent signal may weaken or the cells may be damaged during the observation process.

Recently, nano-optics-based stain-free cell imaging technology utilizing plasmonic metasurfaces* has been attracting attention, but there are limitations in observing internal cell structures as the range in which light can be detected is limited to the vicinity of the cell surface.

** Plasmonic metasurface: An ultrathin optical material that artificially controls the movement of light by regularly arranging metal structures much smaller than a hair on a thin surface.*



▲ Fabrication of a plasmonic metasurface. (a) the fabrication process of a plasmonic metasurface using an electrostatic coating process and (b) the light scattering characteristics of the fabricated metasurface and the results of large-area fabrication. By utilizing the electrostatic coating method, large-area metasurfaces can be realized without a lithography process.

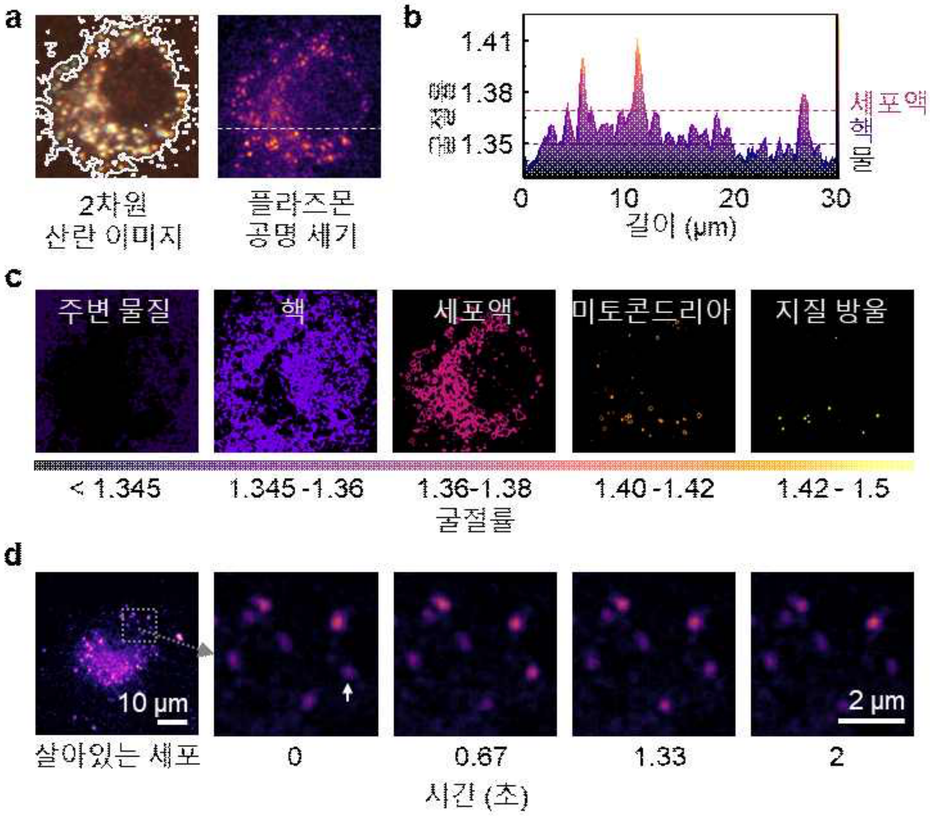
To overcome this, the joint research team developed a new plasmonic metasurface incorporating an "oligomer structure," based on the observation that intracellular organelles possess different optical properties.

By applying the oligomer structure, the light-sensing range was significantly expanded compared to existing methods, enabling the detection of internal cellular structures beyond the cell membrane, which were previously difficult to observe with conventional techniques. The detected structures appear as distinct color changes, allowing for the intuitive and quantitative analysis of intracellular information without the need for separate staining processes.

** oligomer structure: A structure formed by the aggregation of multiple gold nanoparticles, utilized to enhance interactions with light.*

Using the plasmonic metasurface with the oligomer structure, the joint research team observed animal cells (COS-7) without separate chemical treatment and confirmed the validity of the technology for observing internal cellular structures through comparison with fluorescently stained images.

Furthermore, they succeeded in visualizing the movement of organelles inside living cells in real time through millisecond (ms) imaging, which is one-thousandth of a second. This confirmed that real-time observation is possible without damaging the cells.



▲ ***Imaging of living cells. (a) Light scattering image and plasmon resonance intensity distribution, (b) refractive index by location inside the cell, (c) image of intracellular organelles, and (d) results of observing the movement of organelles inside living cells in real time. This demonstrates that internal cell structures and dynamic changes can be observed without a separate staining process.***

This nano-optical imaging technology allows for the observation of living cells in their natural state and is expected to be utilized in various fields of life science and biomedical science, such as pathology diagnosis, new drug development, and cell metabolism research.

Professor Hyeon-Ho Jeong stated, "The key advantage is the ability to observe the inside of cells in real-time and quantitatively without labels or staining." He added, "Since it allows us to obtain dynamic information about living cells while significantly reducing complex staining processes, we expect it to be applied in diverse bio research fields."

Young Min Song stated, "In the future, when combined with machine learning-based automated analysis technology, this could expand into high-speed, high-precision cell imaging as well as precision medicine technology."

This research, supervised by Professor Hyeon-Ho Jeong of the Department of Electrical Engineering and Computer Science and Professor Youngsoo Jun of the Department of Life Sciences at GIST, and Professor Young Min Song of the School of Electrical Engineering at KAIST, with postdoctoral researcher Doeun Kim and integrated master's and Ph.D. student Juhwan Kim as first authors, was supported by the Ministry of Science and ICT and the National Research Foundation of Korea's Excellent Young Researcher Program, the Sejong Science Fellowship, the GIST-CNUH Cooperation Program, and the national research talent development program 'InnoCORE.'

The research results — Virtual Overlay Staining With Plasmonic Oligomer Metasurface — were published online on May 24, 2026, in the international academic journal *Small* in the field of materials science.

Meanwhile, GIST stated that this research achievement was considered to have both academic significance and potential for industrial application, and that discussions regarding technology transfer can be conducted through the Technology Commercialization Center (hgmoon@gist.ac.kr).