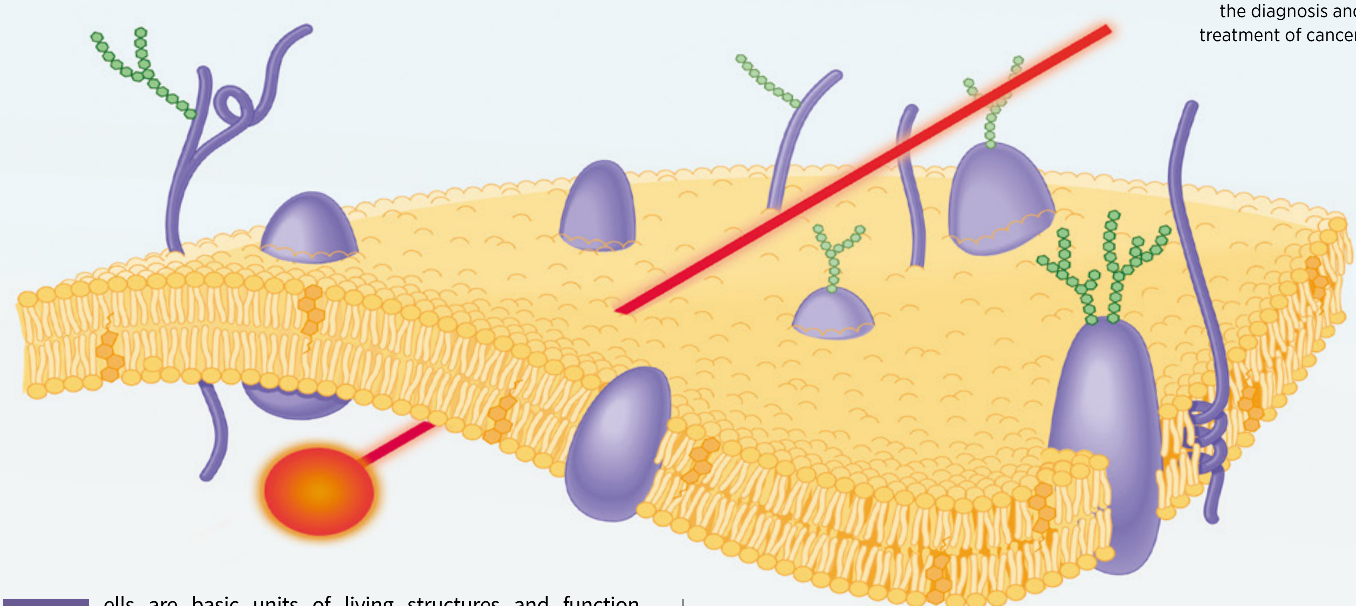
PUSHING THE LIMITS OF CHEMICAL MEASUREMENT

Researchers at Nanjing University work to improve tools for chemical measurement, allowing unprecedented identification of molecular events inside cells.



By measuring molecular events in cells, NJU scientists aim to contribute to the diagnosis and treatment of cancer.

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Cells are basic units of living structures and function. Their order and complexity resembles a small universe. Understanding how matter and energy move and convert within the 'single cell universe' will extend our knowledge about the origin and evolution of life, the mechanics of diseases and more. The precision and depth of knowledge about the chemical world is improved by analytical chemistry, which provides experimental data obtained via measurement.

Improving such tools for chemical measurement defines the research goal of a multidisciplinary team at Nanjing University (NJU). Led by Hong-Yuan Chen, a member of the Chinese Academy of Sciences (CAS) and a fellow of the American Chemical Society (ACS), and Jing-Juan Xu, a Changjiang Professor at NJU, the team has developed an unprecedented 'cell-insight system', to decipher molecular events inside a single living cell. "We have integrated our strengths in electrochemistry, optical spectroscopy and mass spectrometry," Chen says.

Dechen Jiang, a member of Chen's team, developed a 'nano-kit' for single-cell electrochemistry analysis, enabling the measurement of biomolecule activity within single cells and subcellular organelles. Another team member, Bin Kang, is the first to measure the heat transfer within a single living cell, and revealed the thermodynamic rules driving molecule movement in living systems. Chen has also won the 2015 Nature Awards for Mentoring in Science for his life-time achievements in research and inspiring young researchers.

These results are backed by single-cell imaging mass spectrometry with ultra-high spatial resolution, developed by Xu and others.

Developing *in situ* analytical methods for measuring biological and molecular events in cells is the main goal of a group led by Huangxian Ju, a Changjiang Professor at NJU. With decades of work in electroanalysis, nanobiosensing, bioimaging, bioanalytical chemistry, and design of signal amplification strategies, Ju now focuses on *in situ* analysis of cellular functional molecules to improve cancer diagnosis and treatment.

Ju and his colleagues have developed a series of methods to quantify, *in situ*, glycans on the cell surface, along with genes and enzymes in cells. These molecules mediate a variety of biological processes. Combining local remodelling and hierarchical coding strategies, they created living cell images of multiple protein-specific glycoforms, essential for understanding physiological or pathological processes.

An expert in single-molecule analysis, Yi-Tao Long, an electrochemist at NJU, is dedicated to nanopore electrochemistry, focusing on the electrochemical measurement of single molecules. "Single biomolecule interface allows for designable electrochemical nanoconfinement with atomic precision for identifying single molecules," Long says. After many trials, his team created unique sensing interfaces of Aerolysin nanopores with controllable regions for quickly realizing high-spatial and high-temporal resolutions. Through these pore-forming interfaces, with innovative nanopore-based sensing mechanisms and advanced electrochemical instrumentation, direct detection, identification, and location of biologically important molecules are possible. Long and his colleagues also found exciting new experimental possibilities in electro-optical single molecule sensing and sequencing.

Technology to measure electron transfer at single-molecule level is critical to the *in situ* study of biological processes. Junjie Zhu's team developed an ultrasensitive electrochemical microscopy to reduce the detection limit, enabling measuring electron transfer at single-molecule level. ■