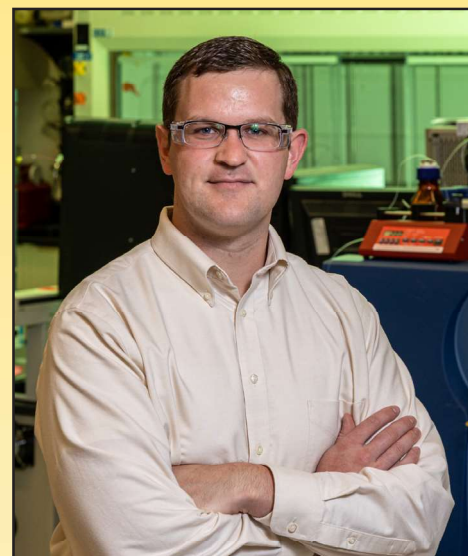
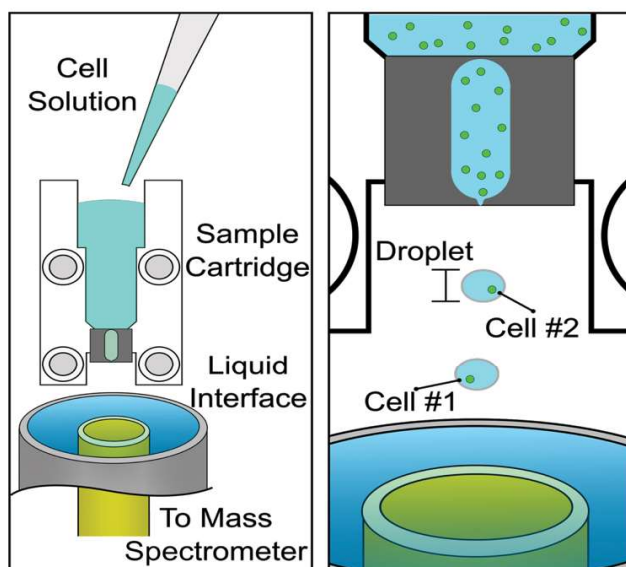


CellSight — Rapid, Native Single Cell Mass Spectrometry

Problem: Cells are naturally heterogeneous, exhibiting differences in chemistry due to their history, age, and microenvironment, among other factors. Tumors, for example, are heterogeneous mixtures that include epithelial, mesenchymal, stromal, and immune cells. Even when they start from a single genetic precursor, natural stochastic cellular processes create variation in cell chemistries over time. Conventional measurements of cell chemistry fail to identify cellular variations by providing only an average picture of the cell. New technologies that offer single cell resolution are needed to understand cellular heterogeneity.

Solution: CellSight enables untargeted chemical analysis of cell suspensions with single-cell resolution. The system utilizes single-cell droplet ejection and liquid extraction mass spectrometry to measure cellular chemistry quantitatively, with high throughput, in an untargeted manner and without any sample preparation or molecular staining required. Droplet ejection isolates individual cells that are captured in a continuously flowing liquid solvent via an extraction–mass spectrometry technology pioneered and patented at ORNL. Upon being exposed to the solvent, the cell ruptures due to the change in osmotic pressure. The analyte molecules are then measured using mass spectrometry in an untargeted or targeted manner. The CellSight system measures cellular chemistry quickly (1 s/cell) and can process thousands of molecules simultaneously. These unprecedented capabilities will provide critical insights into cell chemistry.

Impact: Knowledge of the chemical constituents in single cells, including lipids, metabolites, and proteins, is valuable for applications such as determining cellular function, understanding molecular mechanisms inside cells, and designing targeted therapies. Most studies measure cellular chemistry in aggregate, and, thus, information on cellular variations is lost and understanding of cellular function impeded. Research related to disease treatment, pharmaceutical drug development, cell signaling, and cell function will be aided by rapid characterization and quantitation of a cell's molecular components, with detail provided by resolving single cells.



John "Jack" F. Cahill, PhD Chemical Sciences Directorate

Dr. Cahill is an associate research scientist in the Chemical Sciences Directorate at ORNL. His research focuses on the development and application of novel surface sampling and high-throughput mass spectrometry techniques to chemically characterize tissues, plant systems, bacterial colonies, and materials at small spatial scales. Dr. Cahill's work on elucidating metabolic chemistry with cellular resolution led to the CellSight system.

Intellectual Property

CellSight—Rapid, Native Single Cell Mass Spectrometry, ID-201804255

Publications

- J. F. Cahill, J. Riba, and V. Kertesz, "Rapid, Untargeted Chemical Profiling of Single Cells in Their Native Environment," *Anal. Chem.* 2019; 91 (9): 6118–5126. DOI: 10.1021/acs.analchem.9b00680.

For more information, please contact
Jennifer Tonzello Caldwell, Ph.D.
Group Leader, Technology Commercialization
caldwelljt@ornl.gov
865-574-4180