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REPORT IN BRIEF

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Visualizing Chemistry: The Progress and Promise of Advanced Chemical Imaging

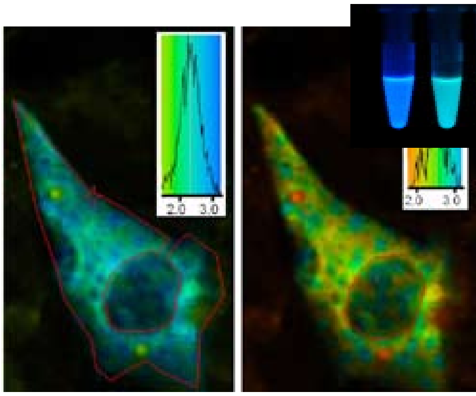
Scientists have long relied on the power of **imaging** techniques to help them see things invisible to the naked eye and advance scientific knowledge. Microscopy, which has been in use since the sixteenth century, is now powerful enough to detect, identify, track, and manipulate single molecules on surfaces, in solutions, and even inside living cells. Advances in **chemical imaging** are being rapidly driven by new applications in medicine, detection needs for national security, materials sciences, and the emerging field of nanotechnology, among others. **There are several specific improvements to chemical imaging techniques that, if developed, could enable fundamental breakthroughs in our basic understanding of molecular structure and most advance our ability to solve critical science and technology problems.**

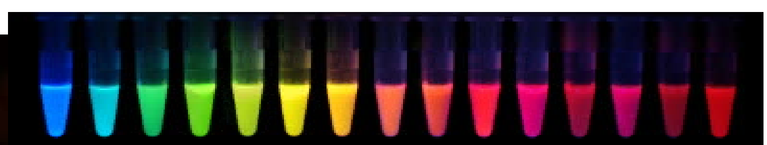
What is chemical imaging?

Chemical imaging is the ability to create a visual image of the composition, structure, and dynamics of any given chemical sample. Chemical imaging takes advantage of a wide range of techniques, all of which rely on the interaction of light or other radiation with the sample. A chemical image is generated from measures of the three dimensions of space, time, and other variables such as wavelength and chemical species. Many of chemical imaging's applications touch our daily lives. For example, imaging has played a key role in the development of organic material devices used in electronics and offers noninvasive methods of diagnosing and understanding diseases such as Alzheimer's.

What is the grand challenge for chemical imaging?

A major goal for chemical imaging is both to 1) gain a fundamental understanding of complex chemical structures and processes, and 2) use that knowledge to control processes and create structures on demand. This report identifies the research needed to advance or combine techniques to best meet this grand challenge. In general, all chemical imaging could benefit from the development of better light sources, improved detectors, new chemical probes and markers, further miniaturization





Recent advances enable chemists to better scale both space and time. For example, the many colors of fluorescent proteins available today (above) can be expressed in almost any cell and used as spectroscopic markers to track changes and movement of proteins. They are incorporated in several techniques such as the fluorescence lifetime imaging (FLIM) shown left being used to investigate molecular interactions in cells. Chemists can use FLM to measure the dynamics of excited states to nanosecond time scales.

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of instrumentation, higher data acquisition speeds; and better data storage and management.

What are the various techniques of chemical imaging and how can they be improved?

The many imaging techniques are used alone or in combination for various applications. They differ in their ability to capture time scales, penetration depths, and ranges of lateral dimensions. The imaging techniques described in this report are divided into the following three main categories.

1) Optical imaging and magnetic resonance techniques interact with samples using low-energy resonance (electronic, vibrational, or nuclear). In contrast to high-energy techniques, they are non-destructive and can therefore be performed in the body (in vivo) or in the sample under study (in situ). Examples include:

- **Nuclear Magnetic Resonance (NMR)** and **Magnetic Resonance Imaging (MRI)** are mature technologies that use magnetic fields to provide detailed spatial information at angstrom (Å) resolution of molecules.
- **Vibrational imaging** techniques produce a vibrational spectrum something like a "fingerprint" of matter that identifies specific molecules by their chemical bonds.
- **Fluorescence techniques** rely on fluorescent proteins that can bind to particular targets or be genetically expressed in biological systems, acting as spectroscopic markers in the body.
- **Ultrafast spectroscopy** is possible with new ultrafast pulsed light sources that provide peak power needed to measure excited states.

Critical advances needed: Optical imaging has high sensitivity, about matched to the human eye, but it is limited in the structural detailed it can provide. New optical probes should be developed for greater spatial control; fluorescence labels need to be more robust and their chemistry better understood; ultrafast optical detectors could measure multiple dimensions in parallel. NMR and MRI are limited by low sensitivity. Better signal to noise ratios could be achieved with improved detector technology; the signals from molecules themselves could be improved by manipulating their nuclear spins; safer contrast agents are needed for use in biological tissues; higher magnetic fields also increase sensitivity.

2) Electron, x-ray, ion, and neutron spectroscopy techniques interact with samples using high-energy radiation much smaller than that of visible light, which provides high-resolution chemical and structural information below surfaces of materials. Examples include:

- **Electron microscopy**, developed nearly 100 years ago, takes advantage of the fact that an electron wavelength is about 1000 times smaller than that of visible light, providing a much higher-resolution probe that can penetrate below the surfaces of materials.
- **X-ray spectroscopy and imaging** use short-wavelength, high-energy photos to penetrate more deeply than electrons.
- **Mass spectrometry** produces images by moving a point of ionization over a sample surface and is used for mapping material and biological samples.

Critical advances needed: Electron microscopy is limited by the quality of the electron beam; X-ray technology would benefit from ultrafast detectors capable of imaging directly onto a chip to improve resolution, range, sensitivity and readout speed; use of x-rays to in biological materials requires probes that can detect and localize chemical signals.

3) Proximal probe techniques use small probes very close to the sample. These methods are especially useful for understanding the chemistry of surfaces.

Critical advances needed: Proximal probes are limited to imaging surfaces, so increasing the penetration depth is critical to look below surfaces; chemically selective proximal probes are needed for the study of chemically heterogeneous systems; near-field optics should be used to reach beyond length scales governed by the wave nature of light.

This brief was prepared by the National Research Council based on the report by the Committee on Revealing Chemistry through Advanced Chemical Imaging. The report was sponsored by the National Science Foundation, U.S. Department of Energy, U.S. Army, and the National Cancer Institute. For more information, contact the Board on Chemical Sciences and Technology at (202) 334-2156 or visit http://dels.nas.edu/bcst. Copies of *Visualizing Chemistry: The Progress and Promise of Advanced Chemical Imaging* are available from the National Academies Press, 500 Fifth Street, NW, Washington, D.C. 20001; (800) 624-6242; www.nap.edu.

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