# Speed-snap science: Solving for molecular details in a flash

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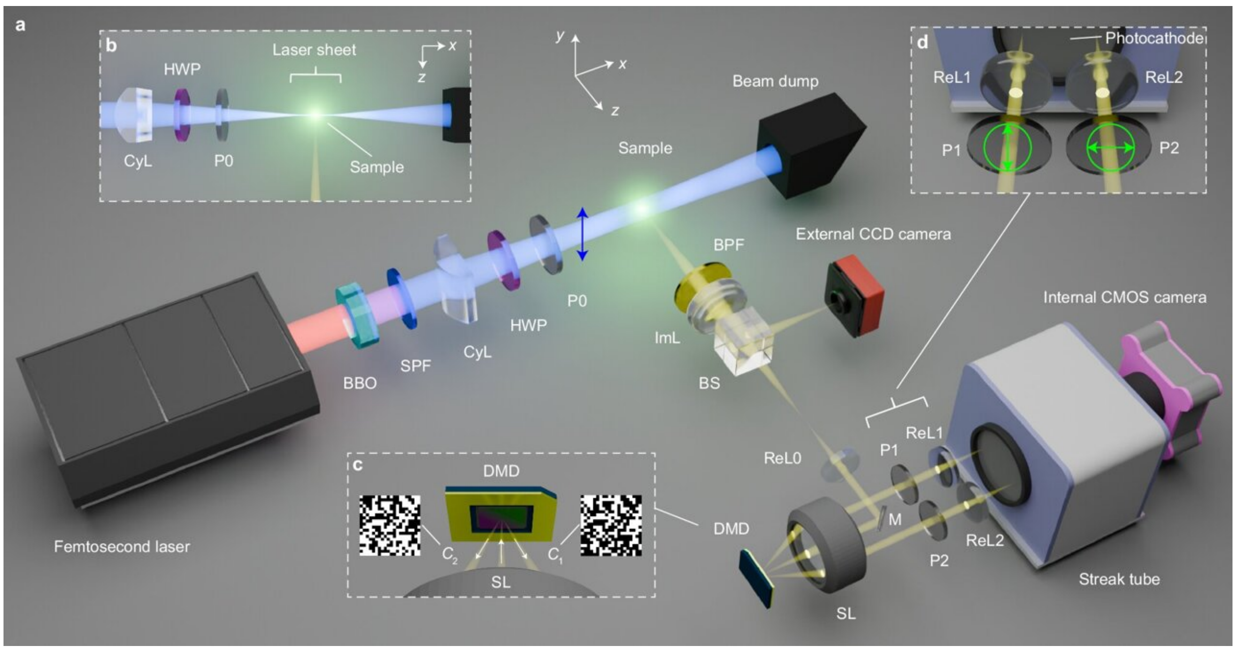


Compressed ultrafast planar-polarization anisotropy imaging (CUP2AI). Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-025-60072-1

How do we know exactly what is happening at a molecular level during extremely fast processes, such as burning during combustion? In less than the blink of an eye, one chemical compound and then another are present in a flame only to disperse and give way to more. Understanding which molecules are present gives scientists a way of understanding the inner workings of the chemical processes taking place.

But traditionally used methods for measuring molecule sizes struggle to capture such fast, transient processes. And conventional optical microscopy not only falls short in speed but also cannot spatially resolve molecules, which typically are no larger than a few nanometers, or billionths of a meter, in size.

Now a Caltech team led by Lihong Wang, the Bren Professor of Medical Engineering and Electrical Engineering, has developed a new tool called Compressed Ultrafast Planar Polarization Anisotropy Imaging (CUP2AI), which delivers insights into dynamic events, with potential applications not only in combustion studies but also in such areas as drug design and nanoparticle formation.

In a paper recently published in the journal *Nature Communications*, Wang and his colleagues present the CUP2AI technique and describe its successful use in imaging carcinogenic chemicals in flames and imaging, in water, a common fluorescent chemical used in biomedical applications.

"When an event is fast, you want to see the whole event dynamically," says Wang, who is also the Andrew and Peggy Cherng Medical Engineering Leadership Chair and executive officer for medical engineering at Caltech. "You want to understand the physical process in both space and time, and that is what our new light-speed imaging technique enables."

Take the example of combustion flames, says Peng Wang, a former postdoctoral scholar from Lihong Wang's group who is a lead author of the new paper along with Yogeshwar Nath Mishra of Caltech, JPL, and the Indian Institute of Technology in Jodhpur, and Florian J. Bauer of the Friedrich-Alexander University of Erlangen-Nuremberg in Germany.

To fully understand what is happening, scientists need to study flames using a variety of fuels, which means that the chemical reactions will happen differently. Then there are altered conditions to consider, and in each case, modified chemical reactions will take place producing a unique subset of molecules.

"If we are able to probe the molecule size, we can understand how these reactions happen for different fuels under different conditions. Because combustion is used in cars, airplanes, and even rockets, we need to understand these chemical reactions. Then we can make more efficient combustion engines. We can also potentially help reduce the pollutants produced through combustion."

## A new technique built on the foundation laid by the world's fastest camera

CUP2AI builds upon previous work in Wang's lab that resulted in the invention of the world's fastest camera as well as the creation of a series of ultra-fast imaging techniques through the development of a technique called compressed ultrafast photography (CUP).

The new technique relies on the polarization of light. Like wavelength and intensity, polarization is a fundamental property of light and represents the direction in which the electric component of a light wave is oriented with respect to the wave's general direction of travel. And it turns out that the polarization of fluorescent light is linked to the orientation of the molecule that emits it.

To understand this, first consider that molecules are always moving. One of the ways in which they move is translational—that is, from one place to another. A second is rotational, involving spinning around one or more of three axes.

"The characteristics of this second type of motion is determined by the size of the molecule," says Peng Wang. "As you might imagine, the larger the molecule, the harder it is to rotate." Smaller molecules, in contrast, are easier to rotate and thus can rotate faster.

When a laser beam interacts with a molecule, the electrons in the molecule are excited to a higher energy state. As they relax back down to a lower energy state, they emit photons, producing fluorescence emission that decays over some period of time.

For molecules excited by a linearly polarized laser, this fluorescence will have a certain degree of polarization. But that polarization will evolve rapidly on timescales that are measured in billionths or trillionths of a second, and this is what CUP2AI measures.

Specifically, CUP2AI takes two different polarization measurements—one parallel to the direction of the laser beam's polarization and one perpendicular to that direction. Initially, the majority of the fluorescence comes from the parallel polarization, but, over time, rotation increases the amount of polarization in the perpendicular direction, making the difference, or anisotropy, smaller and smaller. How fast this anisotropy changes is determined by molecular size.

"The larger the molecule, the slower this difference will decay, and that allows us to figure out the size of the molecule," says Peng Wang. He adds that other methods that have been used to measure molecular size in dynamic environments have only been able to determine the size at a single point or to average the entire sample. "Ours is the first tool that is able to make a 2D map of fluorescence all in a single shot," he says.

Lihong Wang adds that the relationship between molecular size and the decay of the polarization anisotropy is based on an equation originally derived by the famous scientists Albert Einstein, George Stokes, and Peter Debye. "So we are combining classical physics with modern technology and applying it to a very current problem—combustion efficiency—that has to do with energy," he says. "That's exciting to me."

**More information:** Peng Wang et al, Single-shot two-dimensional nano-size mapping of fluorescent molecules by ultrafast polarization anisotropy imaging, *Nature Communications* (2025). DOI: 10.1038/s41467-025-60072-1

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