Individual blood cells flying through capillaries can now be viewed in real time. The technique, called stimulated Raman scattering (SRS) microscopy, generates videos of moving cells deep inside tissue and could replace biopsies in the diagnosis of cancers.

The technique works by shining laser beams at the sample, which causes atoms within the molecules to vibrate. Different molecules vibrate at characteristic frequencies and therefore interact with beams tuned to specific frequencies. Software built into the microscope can pick up these differences. This means cells can be imaged without using dyes, which can be toxic or interfere with biological processes.

Until now, however, SRS microscopy was only accurate enough for use on thin tissue samples that can transmit light. It was difficult to capture an image through thicker samples, such as a human arm, because too much light was scattered back from the tissue. This also made the imaging process too slow to use on moving, living organisms.

To get around these problems, Brian Saar, now at the Massachusetts Institute of Technology, and colleagues at Harvard University designed a new system for collecting the light. To do so they made the atoms in the sample vibrate by shining a laser beam through a small hole in the photodetector, which was placed right on top of the sample. This increased the collection efficiency of the scattered light, producing a clearer image.

**Clear signal**

"It allowed us to go from imaging at one frame per minute to 30 frames per second with a good signal to noise ratio," says Saar. The team also developed a new signal processing system, to read out the signal sufficiently quickly for video imaging.
These faster imaging times mean the team can now look inside tissues in living organisms, which is useful for a number of reasons, says Saar. Firstly it means that dynamic processes, such as blood flow can be studied in real time.

"Second, it means we can start to think about clinical diagnostics since a living animal or human cannot hold still enough to obtain good quality images at low scan speeds."

With tumour diagnosis, for example, surgeons usually remove a sample for analysis while the patient waits on the operating table. SRS could be used to look at the same tissues, without using dyes and without a biopsy.

In the immediate future, Saar is using the system to study how drugs are absorbed and processed in the body.


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