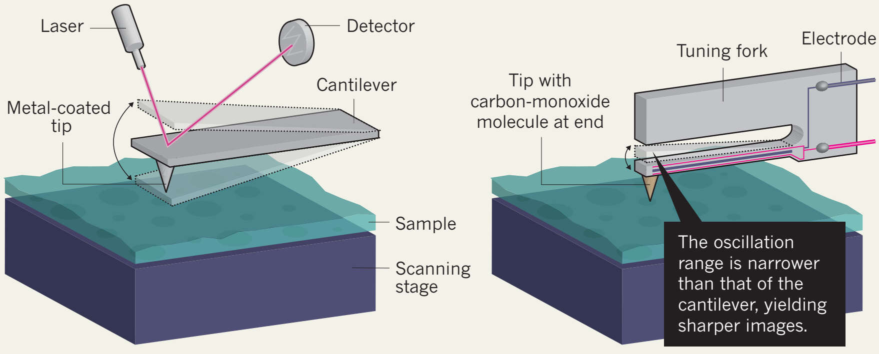
SOURCE: ANDY EXTANCE/FRANZ GIESSIBL/CLAIRE WELSH/NATURE

ANATOMY OF AN ATOMIC FORCE MICROSCOPE

Atomic force microscopy (AFM) images the topography of a material by dragging an atomically sharp vibrating probe across its surface. Advances in probe design are sharpening the method's resolution.

CONVENTIONAL AFM
The probe tip is affixed to a flexible silicon cantilever, the deflection of which is tracked using a laser.

SUBNANOMETRE-RESOLUTION AFM
A vibrating quartz tuning fork is used in place of a cantilever. Changes in its oscillation frequency are detected as electrical signals.



Liljeroth's team has used carbon-monoxide tips to study electronic components embedded in graphene nanoribbons. Yet current approaches cannot simulate non-flat structures well enough to help in their interpretation. Together with his Aalto colleague Adam Foster, Liljeroth is developing machine-learning algorithms and artificial-intelligence programs to predict images of objects of any size, configuration or orientation. The pair have assembled a network of collaborators, and are seeking funding to support the effort.

Ultimately, this approach could lead to fully automated data interpretation, Liljeroth says. But Philip Moriarty, a physicist at the University of Nottingham, UK, suggests that this is unlikely to work in all cases, because even experienced researchers disagree on what atomic force microscopy data show. Moriarty cites the results of a recognition test in which his team was asked to classify images into categories — such as whether they showed atoms assembling individually, in rows or as pairs. The highest scoring participant succeeded only about 70% of the time. "If humans can't recognize one image from another, we've got a bit of a problem," Moriarty warns, because researchers' judgement provides the benchmark by which algorithms are trained. Yet by participating in Liljeroth's network, Moriarty hopes to explore the possibility that, with access to appropriate image data, artificial-intelligence-based classification systems could outperform people.

But there's little image data available on which to train such systems, Gross says. Only about 100 known molecules have been resolved to atomic resolution using carbon-monoxide-tip atomic force microscopy, he estimates. Although automated classification should be tried "at some point", Gross thinks that it's too early, at present.

Simulations such as Jelinek's could provide a suitable training set, Liljeroth suggests. "The question is whether these synthetic images are close enough to experiments."

SOUL-DESTROYING REPETITION

If nothing else, automation could help to mitigate the arduous practical challenges faced by researchers who use atomic force microscopy (see 'High-speed image collection'). Filipe Junqueira, a PhD student in Moriaty's lab, is studying how to produce arrays of thin columns of gallium arsenide. Each column, known as a nanowire, has a diameter of 10 nanometres or greater and is grown inside a stainless steel ultrahigh-vacuum chamber. To image the nanowires, Junqueira must overcome practical obstacles such as experimental noise and sample manipulation using a metal arm known as a wobble stick. His measurements contain interference that might be related to construction work being carried out several hundred metres away, even though the atomic force microscope he uses is housed in a basement and is supported by a table that can dampen vibration.

Other labs have taken more drastic steps to minimize the effects of noise. At Vienna University of Technology, Ulrike Diebold's team suspends its microscope from 36 vibration-damping elastic cords. When combined with an automated system that keeps the system level, this enables carbon-monoxide-tip atomic force microscopy that provides "beautiful images", according to team member Martin Setvin.

And there are further challenges. To mount a carbon-monoxide molecule on a tip, researchers must push the microscope's probe up to a surface coated with carbon monoxide, and then pass an electric current through the probe. It can take hours to get the process right, Setvin says. "If you lose the carbon-monoxide molecule, you have lost a day of work."

For a PhD student with little experience of scanning-probe techniques, it can take "a couple of months to start getting very nice atomic force microscopy images", Liljeroth says. Although some level of expertise will always be necessary, he hopes that machine-learning algorithms and automation will help to reduce the time that is needed for tip preparation.

Moriarty echoes this sentiment, as preparing a good tip can require a lot of trial and error. The only way of knowing whether a researcher has attached the correct molecule or atom is to record a clear image. The researcher must then repeat the image-collection process with fresh tips, to gather enough observations to be confident in his or her interpretation. Moriarty admits that scientists can find this a "soul-destroying" practice. "Automating that process is the way to go," he says.

Moriarty and others have already taken a step in this direction by developing an automated process for using tips to move hydrogen atoms[5].

Despite slow progress, Moriarty finds cause for optimism in astronomy, a field in which machine learning is helping researchers to judge when data might be meaningful. The Laser Interferometer Gravitational-Wave Observatory (LIGO) collaboration, for instance, successfully applied computational algorithms to distinguish possible gravitational waves from artefacts.

But limitations remain, Moriarty admits, because even LIGO needs scientists to confirm manually whether potential detections are real. Tip preparation at the push of a button would require a system to be able to accurately judge the quality of the images that it gathers, he says. "The only way to automate is to train the blasted machine to recognize when it's got a good image," Moriarty says. "If a machine could do that, those astronomers would be out of a job." ■

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CORRECTIONS

The Toolbox article 'The future of scientific figures' (*Nature* **554,** 133–135; 2018) implied that Benjamin Delory developed the persistence barcode method. In fact, he and his colleagues developed an analysis pipeline that relied on and adapted an existing method.

The Technology Feature 'Deep learning for biology' (*Nature* **554,** 555–557; 2018) erroneously affiliated Mark DePristo at Verily Life Sciences. He is, in fact, at Google. Also, the DeepVariant tool was developed jointly by Verily and Google.