SCIENCE • BIOLOGY

The expansion microscopy revolution

This new technique, based on a series of biochemical preparations, makes it possible to increase the size of the samples to be examined by twenty times.

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A team from the Massachusetts Institute of Technology (MIT), which in 2015 invented a revolutionary imaging technology for biology, published a new recipe that makes its deployment even easier in *Nature Methods* on October 11. Expansion microscopy does not consist of "zooming in" with the instrument, but of magnifying the sample that we want to observe. A series of biochemical preparations swell the size of objects by twenty times, which allows us to see details larger than 20 billionths of a meter. That is, below the limit of traditional optical microscopes. For their demonstration, the researchers showed images of microtubules, the "skeleton" of the cell, and synapses, the junctions between neurons. This impressive magnification was achieved by changing the absorbing polymer used until then.

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"Expansion microscopy is revolutionary. It has changed our field. We have been able to study what we could not see ," enthuses Virginie Hamel, co-manager, with Paul Guichard, of the Centriole laboratory at the University of Geneva , about the method invented by Edward Boyden of MIT in 2015. This cutting-edge laboratory in Europe spends part of its time training colleagues in these techniques. *"It works brilliantly. It is easy, quick to learn and use, accessible to all,"* adds Paul Guichard, who also has contacts with countries in Africa wishing to develop this protocol. Although Edward Boyden, winner of the Breakthrough Prize in 2016, patented the technique and created a company, Expansion Technologies, to promote the invention, all researchers can use it without a license.

Frozen sample

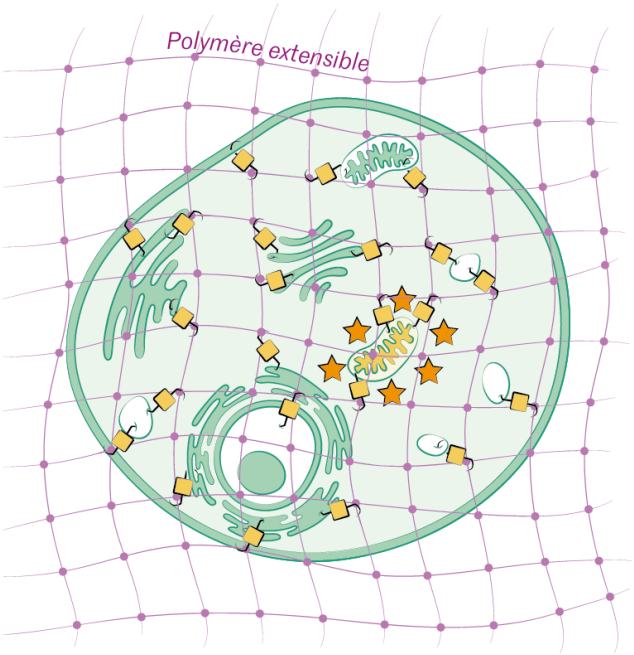
The Swiss team studies the structure of the centriole, a microscopic element that intervenes at the time of cell division. Or is interested in ocular pathologies linked to structures inside photoreceptor cells. Or describes the forms of plankton collected during the missions of the *Tara schooner.*

Anchoring

Gelation
An acrylamide-based polymer is added to form a gel.

Grossir l'échantillon

★ *Molécule lumineuse*



Expansion
An injection of water causes the absorbent gel (as in diapers) to swell up to twenty times, without changing the arrangement of the organelles.

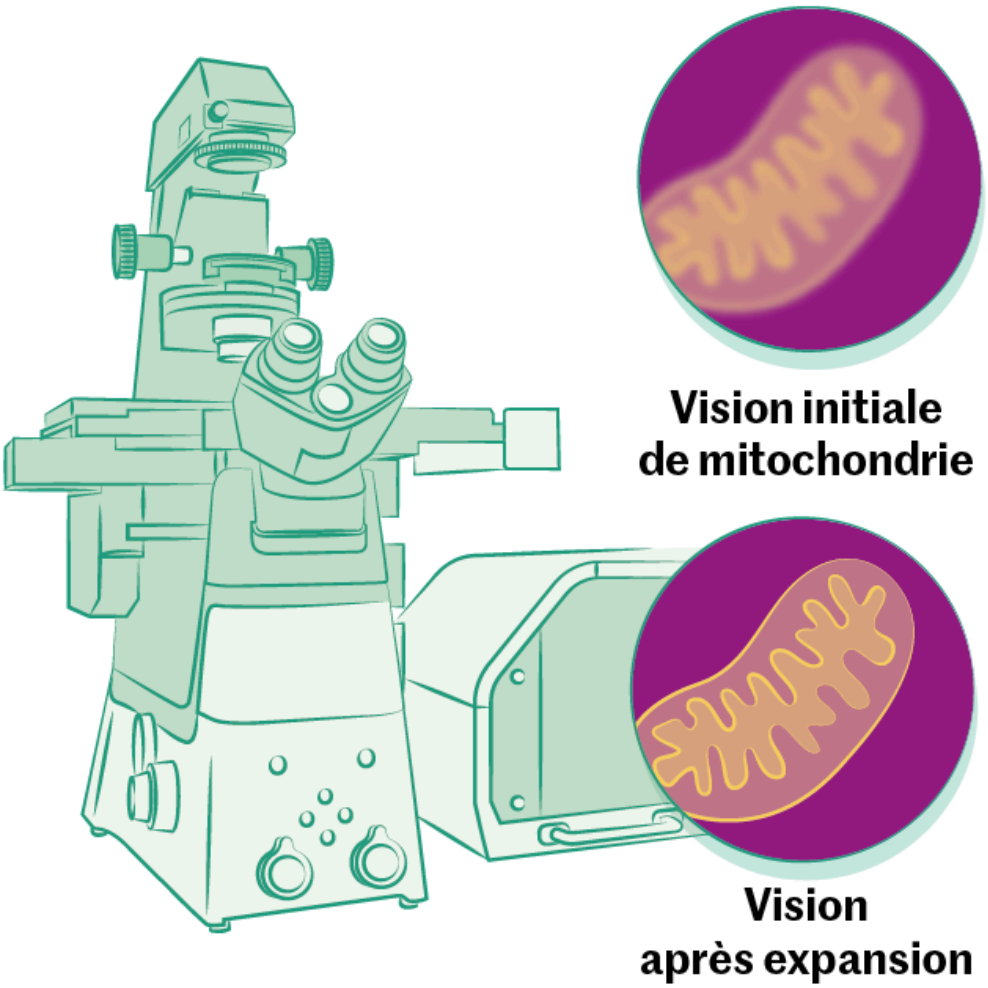
Spotting
Light molecules that bind to the organelle of interest are introduced to be observed under a microscope. This preparation can take two days.

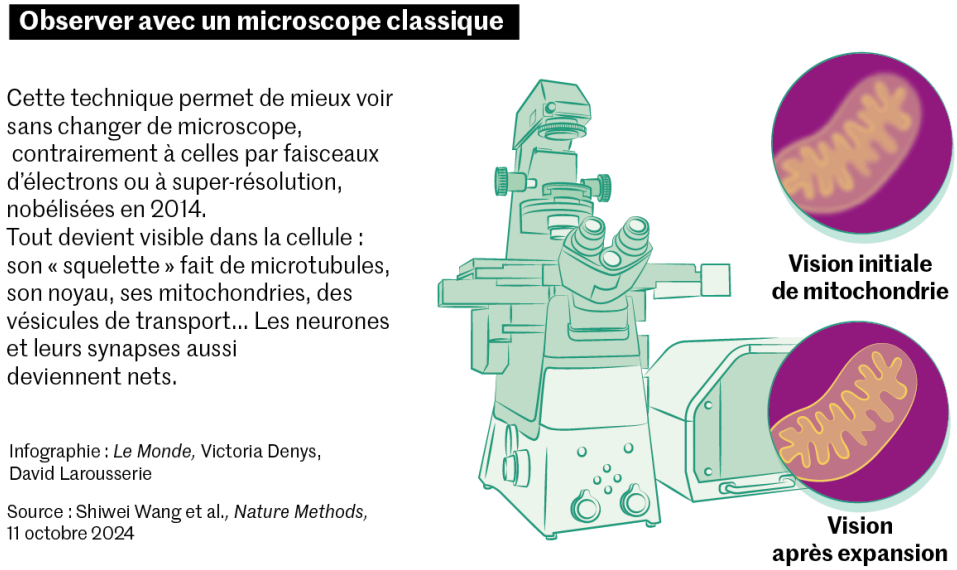
Source: Shiwei Wang et al., *Nature Methods* , October 11, 2024
Infographic *Le Monde*

Paul Guichard acknowledges that some remain skeptical about the method because they fear that swelling will deform the structures and therefore create artifacts. *"The deformation is isotropic and the protocols are designed to verify this* ," reassures Virginie Hamel. The other limitation is that, like other techniques, the sample is necessarily frozen and therefore no dynamics are observed, which is a shame for living phenomena.

Observer avec un microscope classique

Cette technique permet de mieux voir sans changer de microscope, contrairement à celles par faisceaux d'électrons ou à super-résolution, nobélisées en 2014.
Tout devient visible dans la cellule : son « squelette » fait de microtubules, son noyau, ses mitochondries, des vésicules de transport... Les neurones et leurs synapses aussi deviennent nets.





The twenty-fold magnification obtained will probably be beaten. In fact, it already is, because protocols have been developed that involve several expansion steps, but they are therefore less practical than the one presented in *Nature Methods* . The limit to the expansion in size is in fact physical. The gel to be observed can quickly exceed a centimeter and can no longer pass under the microscope...

David Larousserie