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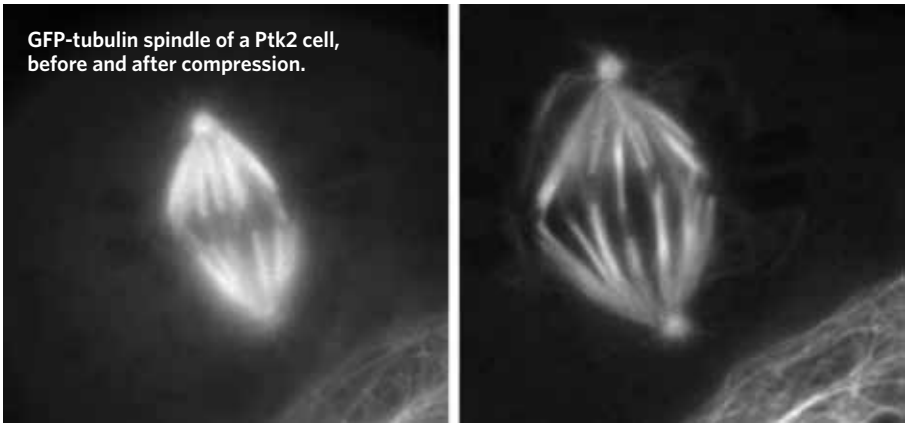
The successful squish

It was the last week of her summer of research at Woods Hole Marine Biological Laboratory on the coast of Massachusetts in 2007, and biophysicist Sophie Dumont decided to try one final experiment. With the state-of-the-art microscopes that had been loaned to the research station, Dumont started pressing on mammalian cells and watching what happened. She was hoping to see the effects of such mechanical distortion on the mitotic spindle, the apparatus responsible for divvying up the chromosomes during cell division. It was an important experiment, since mechanical forces may direct the length of the spindle, which varies greatly during development and between cell types, so understanding how the spindle responds to those forces could help illuminate that process. However, like so many of her attempts earlier that year, she succeeded only in killing the cells. Until, that is, the very last night.

It was already dark outside, but Dumont's eyes were still glued to the microscope in front of her. She gently laid down a tiny pad of agarose gel atop the cells. Then, using a joystick not too dissimilar from an old video-game system, she navigated a hydraulics-controlled needle down to the surface of the agarose pad, then just a few microns farther, compressing the cells below. This time, to her relief, the cells didn't die. Instead, as the cells flattened out, Dumont could see a healthy—and dramatically longer—mitotic spindle.

"It took me maybe 5 or 10 minutes to realize it's not just a random chance event—that it was a directed elongation," Dumont recalls. What convinced her was the fact that she saw three cells in mitosis, all responding the same way. The spindle—a spidery collection of microfilaments that stretch from the chromosomes at the center of the cell to the poles at the edges during mitosis—grew in response to the pressure. "It was very lucky for me that on that particular day there were three" dividing cells in view, she says. "It's hard enough to find one. If you're really lucky, you get two."

When Dumont excitedly showed the results to her advisor, cell biologist Timothy Mitchison of Harvard Medical School, who was also spending the summer at Woods Hole, he was pleased. "It was very clear something interesting was going on," Mitchison says of the initial discovery. "The spindle elongated spectacularly."



GFP-tubulin spindle of a Ptk2 cell, before and after compression.

Dumont was eager to dig her heels in, but alas, she was out of time. The next day, she packed up and headed back to Boston, where she didn't have the necessary equipment to continue the experiment. She spent the next few months setting up the lab and trying to recreate the exciting phenomenon she had witnessed back at Woods Hole. Finally, in December, she succeeded: She once again flattened dividing cells without killing them, and saw the spindle double in length (*Current Biology* 19, 1086–95, 2009).

"It wasn't hit or miss," says cell biologist and mitosis researcher Ted Salmon of UNC Chapel Hill, who shares lab space with Mitchison at Woods Hole during the summer months. "[Dumont] figured out a way to flatten the cells reliably and reproducibly and record the response"—something previous scientists had failed to do in mammalian cells.

Now that Dumont seemed to be able to lengthen spindles by simply pressing on the cells, the big question was how.

One thing she noticed in these initial experiments was the relative timing of everything: The spindle widened quickly upon compression, but lengthening took an average of 12 minutes—about four times as long as widening. This slower speed suggested that elongation was not merely a passive response to the lengthening of the cell itself, as previously thought. Indeed, further experiments revealed that compression switched off the microtubule disassembly process that occurs during microtubule renewal, causing the microtubules to lengthen.

"[The] identification of this mechanical regulation of spindle fiber was a really important contribution to the mitosis field," Salmon says, "[but] I think this is just the start of things." The next step, he says, is to learn about the nanometer-scale properties of the connections between chromosomes and spindles, "and the technology that she developed is going to provide the opportunity to do that." —Jef Akst