Measuring the strength needed to move chromosomes

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(PhysOrg.com) -- It's about as long as the width of a human hair and only half that length across. So it's tiny — measured in millionths of a meter — and extremely tricky to manipulate. But the meiotic spindle plays so irresistibly important a role in separating our chromosomes during cell division that scientists are compelled to try to study it.

Now researchers at The Rockefeller University and colleagues in Japan have devised a contraption sensitive enough to probe and ply these microscopic spindles and have used it to measure for the first time the structure's stiffness and deformability. The findings, published last month in Nature Methods, are the culmination of four and a half years of refinements.

"It's a bit of a trick, but it works out. You can catch the spindles," says Tarun Kapoor, head of the Laboratory of Chemistry and Cell Biology at Rockefeller. "Now we've probed the mechanical architecture of the structure as a whole." To capture and manipulate the spindles, Kapoor and colleagues developed a system of two tiny, plate-like cantilevers mounted underneath the lens of a microscope that can be maneuvered with micromanipulators to sandwich the elusive structures. One of the cantilevers is stiff; the other is an ultra-thin sensor (called a piezo-resistive strain sensor) that measures the spindle's response to forces when the distance between the two cantilevers is reduced to compress the spindle.

During cell division, meiotic spindles tease apart chromosomes to opposite ends of a cell and ensure that each daughter cell inherits the correct genetic information. Scientists have studied many biochemical interactions required for chromosome segregation but know much less about its mechanical properties — the actual forces exerted on and by the players involved. Kapoor and colleagues determined that the forces strong enough to bend but not break meiotic spindles were in the nanoNewton range (about one billionth of the force of Earth's gravity on an average-sized apple).

Applying these minute forces to meiotic spindles assembled in extracts prepared from eggs of African clawed frogs (a model system for this kind of research), Kapoor found to his surprise that the size of the spindles was not fixed. After a series of compressions, they readjusted, becoming smaller, but keeping both the same ratio of length to width (roughly two to one) and the same strength constant. "Our immediate goal now is to find out how and why the structure can maintain different sizes."

This force-measuring system could be applied to study cellular organelles and structures, Kapoor says. This new method of mechanical testing, along with other biochemical methods, could allow scientists to ultimately explain mechanisms that ensure the fidelity of the replication of our genome.

More information: *Nature Methods* 6(2): 167-172 (February 2009), Probing the mechanical architecture of the vertebrate meiotic spindle; Takeshi Itabashi, Jun Takagi, Yuta Shimamoto, Hiroaki Onoe, Kenta Kuwana, Isao Shimoyama, Jedidiah Gaetz, Tarun M. Kapoor and Shin'ichi Ishiwata

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