Measuring the Mechanical Properties of a Cell

Goal: Use your finger to measure the stiffness of a water bead, just like a biophysicist would use a sharp tip to measure the stiffness of a cell.

Background

One of the most exciting discoveries in biophysics today is that the physical properties of a cell, like a cell's stiffness, is extremely important. For many years scientists have focused on the chemical signalling of cells, the biological makeup of the cell, or the electrical properties of the cell. Now we are finding that the physical attributes of the cell are important in cancer research, disease studies, and even in the immune system.

Your immune system is incredibly complex with many types of cells that protect you from foreign invaders by mounting an attack against these invaders. One type of cell, the T cell, is used to determine which bodies are foreign so that they can be removed. To do this, the T cell makes contact with another cell that has a molecule of the foreign invader, called an antigen, on its cell membrane. During this contact, the T cell tries to bind a series of different molecules on its cell membrane, called antibodies, to the antigen. If an antibody binds to the antigen, then the T cell is activated and the antibody that bound to the foreign invader's antigen is eventually used to tag the invaders for destruction. What is interesting about this process is that biophysicists recently discovered that the stiffness or rigidity of the T cells themselves changes once they have been activated. These activated T cells become softer or less stiff and are therefore able to have a larger contact area with the cell that carries the antigen. Thus, targeting the stiffness of a T cell, rather than its chemical makeup, may be a method of future immune therapies.

The question that we will look at in this experiment is how biophysicists are able to measure the stiffness of cells. To look at this question, we will do two things. First, we will make a model for the cell so you will have some intuition about a cell's physical properties. Second, we will show you how biophysicists measure the stiffness of cells using our model cell.

To make a model of a cell we are going to use a toy you can buy at the store, water beads (Orbeez). Water beads are a good model for a cell because they contain both a solid and a liquid phase, just like a cell! Inside a cell there is not only water (the liquid phase), but there is also a cytoskeleton (the solid phase). The cytoskeleton consists of a network of long, filament-like molecules that give the cell its shape. Water beads are made out of a network of long, filament-like molecules too. When these molecules absorb water, the water beads expand and start to behave somewhat like a solid and somewhat like a liquid, just like a cell.

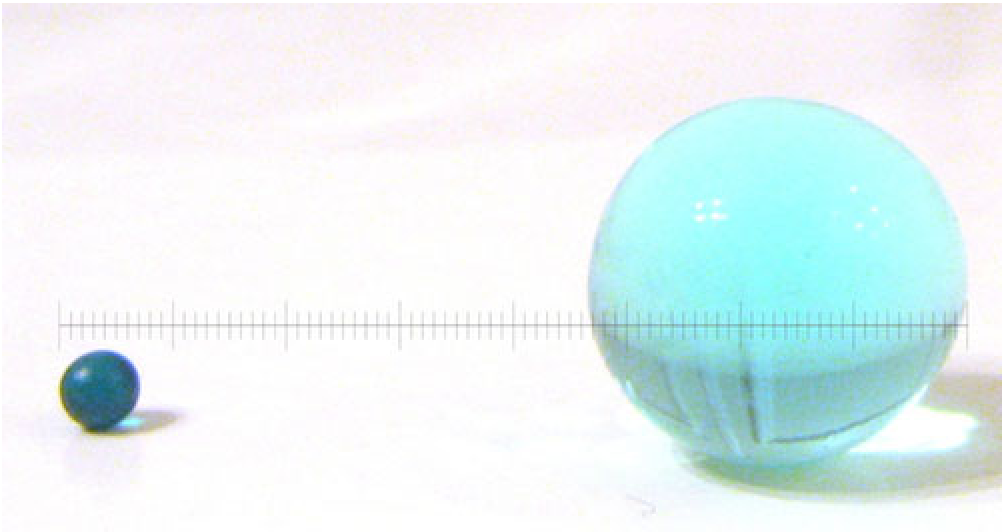
To measure the stiffness of cells, biophysicists poke the cell with a sharp probe smaller than the cell. (This probe is a part of an atomic force microscope or AFM.) When the cell is poked with the sharp probe, it indents. The more it indents at a given force, the softer the cell is. In this experiment your finger will act as the sharp probe and the water bead will be the cell. Measuring the amount the water bead indents will tell you about the stiffness of your water bead.

Parts List
Water beads (Orbeez)
Bowl with water

How to

1) Open up your package of water beads (10-20 per package) and place a third of the package into a large bowl filled with water.
2) After 2 hours, put another third of the package into the bowl of water.
3) After another 2 hours, you should have two different sized water beads and water beads that haven't been placed in water. Let sit even longer or change the wait times if you want the water beads to be even bigger. You may have to change to larger bowls depending on how large you want the water beads to get.
4) Now take your finger and poke a water bead. Do the water beads indent differently based on how much you push on them? You should notice that the harder you press, the more the water beads indent. This is because the water beads are elastic and so they deform more as you press harder. The cell is similar in that if you press harder, the cell indents more. So just by pressing on a cell, you can measure the stiffness of the cell!
5) Ask your audience if they can think of other ways to measure the mechanical properties? Have your audience play with the water beads and see what they come up with. They could bounce the water beads, they could burst the water beads, they could apply pressure with the whole palm of the hand by squeezing the water beads, they could apply a shear force (twist them), or they could come up with other methods. You could talk about which methods might be usefully applied to cells.
6) You could also tell your audience that the activated T cells are both softer and *bigger* than the normal cells. Ask your audience, if they would they have predicted this after playing with the water beads. Why or why not?
7) Finally, the main take-home message is that biophysicists can measure a cell's stiffness just by pressing on the cell. This allows us to start to make progress about how that cellular stiffness affects cancer, diseases, and the immune system.

What it should look like



http://blog.mrmeyer.com/2011/wcydwt-orbeez/

Extras

This experiment is a great way to demonstrate how to measure the stiffness of a cell. But there are some important differences between this experiment and the ones biophysicists perform on cells.

One difference is that the measurement of cell stiffness is much more complicated than this. When you press on an elastic material like a water bead or a cell it will deform based on the material's elastic properties. The simplest model for deformation of an elastic material considers a rod of length L being compressed a distance ΔL. The stiffness or the elastic modulus, E, for the material of the rod is then just a ratio of the stress, σ, on the rod to the strain, ε, on the rod:

$$E=\sigma/\varepsilon.$$

Here, the stress is the force per area applied to the rod, while the strain is the ΔL per L of the rod. Stepping back you can see that this simple model is just a form of Hooke's Law, $F=kx$. So thinking about the force with which you press and the amount that the cell/water bead indents is a good place to start in this experiment. However, a cell has a slightly more complicated geometry than a rod and it scales as an exponential rather than a line. Still, the basic premise for how to measure the elastic modulus or stiffness is the same. You essentially measure the stress and strain on the cell to get the modulus.

Another difference is that the cell or water bead is not just an elastic solid or a viscous liquid. It has both solid and liquid phases so it is viscoelastic. You can see this in two ways. The first way is that when you apply a stress to the cell/water bead it will take a while to reform after you remove the stress. The second way is that the cell/water bead will deform different amounts (have different amounts of strain) depending on how fast you apply a particular stress. So the same amount of stress can produce different amounts of strain! This is because it takes time for the cell/water bead to deform or reform. If you apply the stress too quickly, the cell/waterbead doesn't have time to respond. See if you can see these differences in a single water bead and then test the viscoelastic differences in water beads of different sizes.

So, we have seen how to measure the stiffness of cells, but biophysicists are also working to figure out why the stiffness of cells varies. Why are T cells that are activated softer? Perhaps the increased contact area by the softer cell allows for an increase in the immune response? Do you have ideas? If you have ideas that you would like to test, maybe you should be a biophysicist.

The science in this experiment is from "Cytoskeletal adaptivity regulates T cell receptor signaling" by Thauland et al. which appeared in *Science Signaling* in 2017. A useful article is: https://www.eurekalert.org/pub_releases/2017-03/uoc--uss030617.php.

More on water beads and physics you can do with them:
https://www.youtube.com/watch?v=MFVXsnq230c
https://learning-center.homesciencetools.com/article/water-beads-superabsorbent-polymer-science/