Jennifer Zallen: Decoding the developmental dance

Jennifer Zallen wants to know how cells coordinate their movements during fly embryogenesis.

Like choreographed dancers on a stage, cells must coordinate their movements during embryogenesis to build the body shape. In her laboratory at the Sloan Kettering Institute in New York City, Jennifer Zallen is figuring out the dance steps of a particularly dramatic coordinated cell movement called convergent extension.

"After several conversations over family vacations, we ended up publishing a paper together."

During convergent extension, the fly embryo narrows in width and more than doubles in length to create the basic layout for the body plan. Zallen has discovered that extension occurs by local cell movements. Some cells simply wedge between their neighbors, and other cells come together in groups from across the width of the embryo, forming arrangements called "rosettes." The rosettes then disassemble as the cells arrange themselves into an approximate line, thereby elongating the embryo (1).

Zallen, who set up her lab three years ago, is now investigating candidate cellular choreographers using mutant screens. She has also recently started measuring cell shapes and movements to detect patterns within populations that might give clues to the underlying order of convergent extension.

Zallen moved to Sloan Kettering after completing her postdoctoral work on fly morphogenesis in the lab of Nobel prize-winning developmental biologist, Eric Wieschaus (2, 3). Before that she earned her Ph.D. with esteemed neuroscientist Cori Bargmann by working on neuronal migration during worm development (4, 5, 6). And before that she studied biology at Harvard.

It could be argued that Zallen has the text-book career of a developmental biologist. Her recent foray into measuring cell shapes and movements, however, has taken her not just into a different chapter, but into an entirely different book—that of condensed matter physics (7).

SCIENTIFIC CERTAINTY

What was life like growing up in the Zallen household?

Both of my parents are professors at Virginia Tech; my mother is a biologist, and my father is a physicist. So I was surrounded by science from a very early age, and I feel like it's something I've always been interested in.

You never dreamed of one day becoming a truck driver or an artist or something?

If I did, those ideas were quickly beaten out of me. No, I'm joking! Don't quote me on that!

I think, as a child, science just captivated my interest, and I never got bored with it. It's what we talked about at the dinner table. It was the pictures we had up on the walls in our house.

Oh? No regular landscape paintings?

We had those too. [*Laughs.*] But we also had sketches from my dad's textbook of different crystal structures and the organization of atoms. When my dad retired, he had an art exhibit of all the sketches he made throughout his career.

I was always fascinated by these pictures. In fact, it was one of my dad's sketches of the arrangement of atoms in an amorphous metal that more recently got us talking about how these arrangements look like epithelial cells in the embryo.

After several conversations over family vacations, we ended up publishing a paper together on this topic in the *Journal of Physics: Condensed Matter*.

GEOMETRY OF DEVELOPMENT

What was the paper about, in nonphysics terminology?

It's very simple. Basically, we used the same type of measurements that the condensed matter physics community has been using to study two-dimensional foams to study how epithelial cell sheets change over time in living embryos.

Jennifer Zallen

What are these foams?

Soap foams. They're like a bunch of 3D bubbles, but compressed almost into 2D between, for example, two glass plates. Physicists study these as a model for the way that atoms pack together in disordered solids. Foams are known for being highly disordered—as we all know from beer foam. So you have a range of shapes and sizes of bubbles and also a range of topologies—the number of other bubbles that a single bubble is in contact with.

Fly epithelial cells can have a range of cell topologies. If a cell layer was totally ordered, like a honeycomb, you'd see that every cell was touching six other cells. But this is something that we almost never see in nature.

What did you find from doing the measurements?

We've found that as fly embryos elongate, the disorder in cell sheets—the range of different topologies that we see—increases. To begin with, we mostly see five-, six-, and seven-sided cells, and then as convergent extension progresses, we start to see three- and four-sided cells and eight-sided cells.

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We can use this measure of disorder as a precise indicator of what stage the embryo is at. But the very fact that disorder occurs presents us with a paradox: why do we get this wide range of behaviors at the cellular level, when the tissue is always elongating in a systematic, reproducible way?

What are your thoughts?

We figure that, although it looks disordered to us, there must be some sort of underlying logic that allows the embryo to translate these disordered behaviors into elongation in a specific axis. By watching cells move, we saw that groups of cells form rosette arrangements and then resolve in a directional way. These rosettes help explain both the increase in disorder and how this disorder leads to elongation.

The number of cells in rosettes is consistent from embryo to embryo, but right now it's difficult for us to predict what a given cell will do during rosette formation and disassembly: whether it will go on to become a triangle or an octagon, how far it will move, and exactly which cells it will end up next to. So now we're using quantitative computational approaches to help us look for morphological trends at the population level that aren't obvious from looking at single cells.

Is it possible that a cell in contact with eight other cells might be more influential than one in contact with three?

We don't have any evidence yet, but I think that's a really interesting idea. It's quite possible that besides elongation, rosettes might also provide a way for a key signaling cell to increase its range of action by bringing it into contact with a greater number of neighbors.

It would be interesting to look in mutants where the rosettes don't form to see what the consequences are for signaling.

THE NEXT DIMENSION

What else are you working on?

Up until now we've been thinking about this process in two dimensions, approximating the epithelial sheet as something we can draw on paper, because this is easier for us to wrap our heads around. But these cells are obviously three-dimensional, and we're missing out on what's going on beneath the surface by focusing solely on a view from the top.

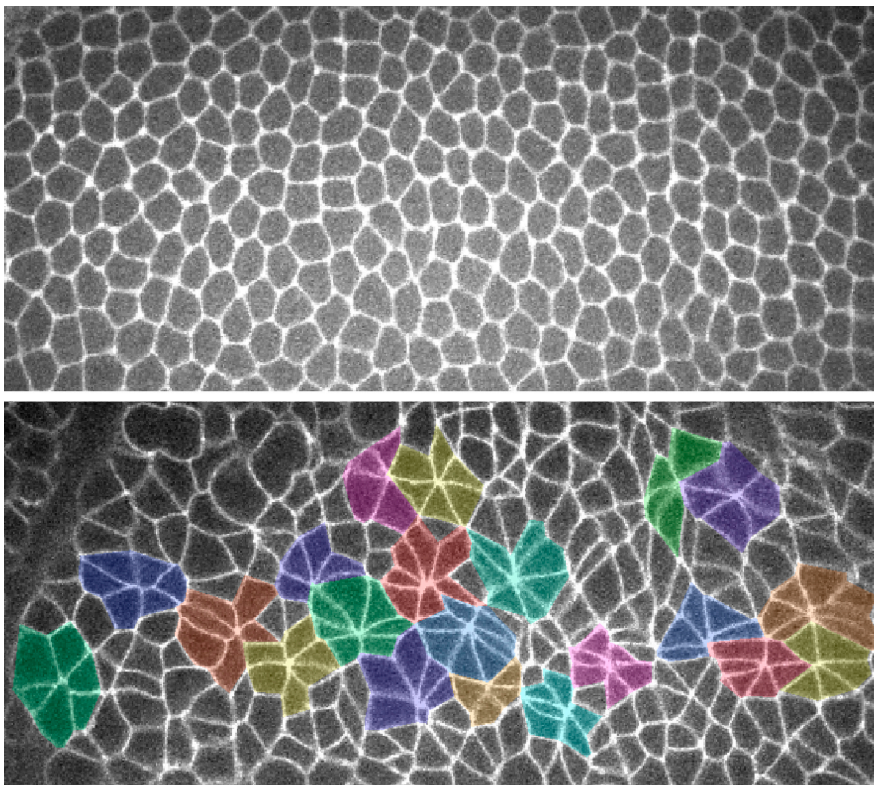
"Although it looks disordered to us, there must be some sort of underlying logic."

We know by looking at the 3D cell morphology that a cell can encounter different neighbors along its height. These contacts could also be influencing the signals received by the cells as well as the forces acting on them. So what we're now doing is analyzing cell behavior throughout the entire depth of the cell sheet over time in 4D movies. We think this is an important step toward understanding how more complex tissues develop.

That sounds like a lot of data to get your head around.

This analysis wouldn't be possible without computer algorithms that can analyze hundreds of cells in many embryos over time. Actually, this is a new direction for the lab. We're developing computational approaches that will allow us to analyze cell behavior in the embryo quantitatively, not just qualitatively.

I was really lucky. Two computational people found out about my lab and decided to join after stumbling across the paper in the *Journal of Physics: Condensed Matter*. Their expertise has really helped us to think about cell shape and behavior in a new way. JCB



A fly epithelium has an ordered arrangement of cells before embryonic elongation (top). Disorder increases (bottom) as rosettes (colors) form during elongation.

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