

# Push and Pull

*What appears chaotic is actually a well-orchestrated process for embryonic head-to-tail elongation.*

FEW SIGHTS ARE AS CAPTIVATING AS THE MOVEMENTS OF A DEVELOPING embryo. Shapeless tissue remodels itself as cells migrate en masse to form elongated structures that, depending on the species, will become a frog spinal cord, a human gut, or the main body of a fly. ¶ Jennifer Zallen, an HHMI early career scientist at Memorial Sloan-Kettering Cancer Center, studies how embryonic tissues stretch along an anterior-posterior axis using the fruit fly *Drosophila melanogaster* as a

model system. Shortly after formation of the embryo, the mass of fruit fly cells dramatically elongates over about a two-hour period and establishes a head at one end and a tail at the other, a process known as convergent extension.

Over the past seven years, Zallen's lab has used high-resolution, time-lapse imaging to track embryonic cell migration during that two-hour window. She has found that what looks like chaotic pushing and shoving between neighboring cells in elongating tissue is actually a highly cooperative and orderly process.

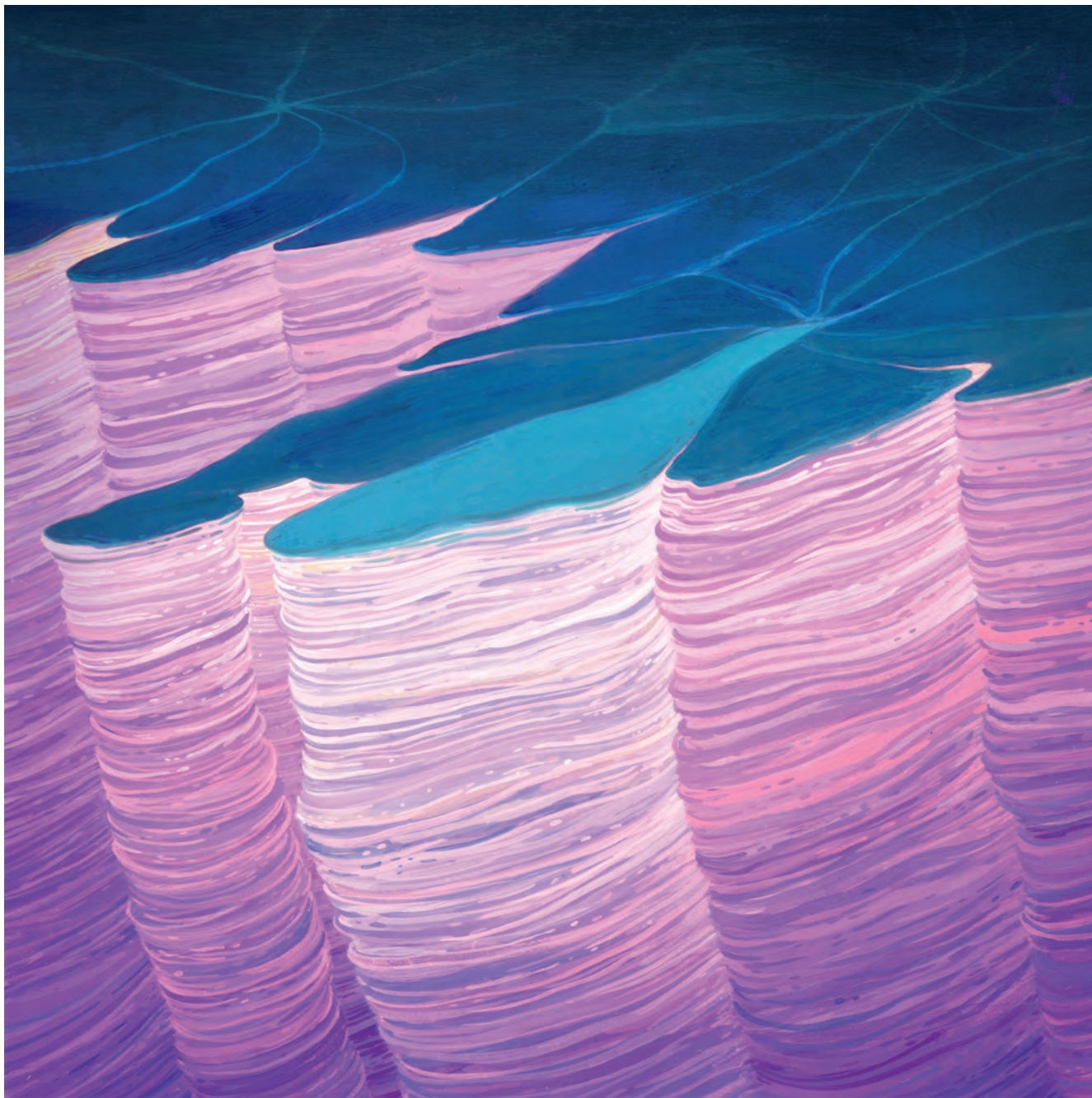
Zallen's group established the ground rules of the game in a 2006 *Developmental Cell* paper. Tracking single cells in a living embryo, they showed that cells consistently join and then exit pinwheel-like structures

known as rosettes as a fly embryo becomes longer and thinner. Computational analysis indicated that most cells repeatedly move in and out of multiple 5-8 cell clusters as the embryo stretches outward. Each group of cells reorganizes to become longer and narrower, suggesting that rosette formation could drive morphological change.

Since then, her laboratory has focused on understanding the multiple signals that encourage cells to move in and out of transient groups. "It is forces generated at the contacts between cells that cause the cells to rearrange and the tissue to elongate," says Zallen. "These forces place special demands on the cell junctions, which must be dynamic enough to dismantle individual contacts but strong enough to prevent the group from ripping apart under tension."

Zallen's lab group recently combined molecular techniques with *Drosophila* genetics to characterize one facet of that junctional regulation. In work published February 14, 2012, in *Developmental Cell*, they identified a biochemical cue that allows cells to disengage from some neighbors in a rosette so they can find new ones. They found that a signaling factor, the tyrosine kinase protein Abl, makes the contact points (known as adherens junctions) between cells in a rosette more dynamic or fluid—in other words, it allows cells to glide more smoothly against one another. Fruit fly embryos genetically engineered to lack Abl show poor rosette formation and impaired elongation. Surprisingly, the more dynamic junctions in normal embryos are also stronger, resisting apparent breaks or tears seen in embryos lacking Abl.

Equally essential for axis formation are mechanical signals that rope cells into a rosette. In work published in *Developmental Cell* in 2009, Zallen reported that cells perceive physical tension exerted by their



neighbors. These mechanical signals promote rosette cohesion by prompting the motor protein myosin to join long cables that extend across multiple cells and contract like a drawstring, pulling cells together to form a rosette.

One way her group showed this experimentally was by literally tugging on a *Drosophila* embryo with a glass needle and then using live imaging to watch as fluorescently labeled myosin was recruited to the needle. This experiment helped explain one purpose that mechanical forces serve, namely, to bring cells together into multicellular gatherings.

Whether the same mechanisms that push and pull cells in a simple organism like *Drosophila* drive convergent extension in vertebrate embryos remains unknown. “Right now, people have seen snapshots of something that looks like rosettes in other animals,” she says, noting that the vertebrate neural tube (the embryonic structure that gives rise to the central nervous system) exhibits pinwheel-like swirls of cells. “But rosette formation is a dynamic behavior that is difficult to assess in a static picture. Live imaging of vertebrate cells is needed to see if these cells move in a way that leads to elongation.”

Even if she and others discover that vertebrates evolved a different way to form tubular organs, Zallen has an ambitious long-term goal: to figure out how large populations of cells act collectively. “Over the past 20 years, people have learned a lot about factors that determine cell identity,” she says. “But we know much less about how cells get to the right place to build a three-dimensional animal. This is the big unsolved question in developmental biology.” ■ – ELISE LAMAR



WEB EXTRA: See a video of rosette formation in *Drosophila* at [www.hhmi.org/bulletin/Fall2012](http://www.hhmi.org/bulletin/Fall2012).