Simple forces, complex shapes

Form follows physics in the fly eye, say Sascha Hilgenfeldt, Sinem Erisken, and Richard Carthew (Northwestern University, Evanston, IL). The idea that a small set of physical forces governs the shape of tissues goes back at least a hundred years, but there has been little evidence to support it. Now, Hilgenfeldt et al. show that just two parameters—cell elasticity and adhesion strength—can account for the arrangement of cells in the ommatidium, the 20-cell subunit of the fly’s compound eye.

The geometry of the cone cells in the center of the ommatidium resembles groups of soap bubbles, says Hilgenfeldt, who studies the physics of bubbles, foams, and other “soft solids.” This arrangement suggested that, as in bubble aggregates, adhesion and elasticity might help determine shape. And like bubbles, the cells might be minimizing the surface energy at their interface.

To test this theory, the authors created a computer-simulated model of ommatidium geometry. Adhesion in these structures is supplied by cadherins at the cells’ apicolateral surfaces. The elasticity of the cell membrane arises from a number of complex interactions between the lipid bilayer and the cytoskeleton but can be characterized by its resistance to deformation. The team found that beginning with cells of random shapes, and then adjusting the relative strengths of cadherin binding and membrane elasticity to minimize the total surface energy of all the cells, they could precisely reproduce the observed geometries of the eye.

The model also predicted the abnormal cellular arrangements that are found in various cadherin mutants. “Even a small variation in adhesion can alter cell packing dramatically,” Carthew says.

Can other tissue geometries be explained as simply? “We think these results stand as an example for less-ordered epithelia,” Carthew says, though some element of random variation may be needed in the mix to account for these structures. They also hope to model developmental changes with the same principles.

“You could imagine that tissues undergoing morphogenesis go through a series of minimal energetic states, dictated by changes in a few factors that regulate cell interactions,” Carthew says, such as placement and number of adhesion molecules or cytoskeletal alterations.

Reference: Hilgenfeldt, S., et al. 2008. Proc. Natl. Acad. Sci. USA. doi:10.1073/pnas.0711077105.

Histone chaperone regulates replication

Histone supply and demand are tightly coupled at the replication fork by a chaperone, according to Genevieve Almouzni (Curie Institute, Paris, France) and colleagues. The chaperone, Asf1, passes histones from parental to daughter DNA strands and unwinds just enough DNA to match its transfer activities.

While investigating histone dynamics during replication, the authors found Asf1 in complex with a helicase and two histones. When the group knocked down Asf1, the cells stalled in S phase. Finding no defect in replication initiation and no activated checkpoint to halt replication, the authors suspected that the absence of Asf1 decreased the activity of the helicase, which must first unwind DNA for it to be replicated. They found very little helicase-formed ssDNA at replication sites in cells lacking Asf1, indicating that helicase progression was disabled.

With functional Asf1, but with replication halted by a chemical inhibitor, the number of Asf1/histone/helicase complexes increased. The authors concluded that Asf1 was picking up histones from the parental DNA strand but was unable to offload them in the absence of new daughter strand synthesis. Replication was also stopped by flooding the cell with histones; since Asf1 was loaded with the new histones, it could not remove any more from the parental DNA strand, thus stopping unwinding.

“This system coordinates replication with the packaging of DNA into chromatin,” Almouzni says. It also ensures that the charged and sticky histones are chaperoned and prevents DNA from unwinding in the absence of replication. The movements of histone-laden Asf1 during replication are still unclear. Given the large distances involved, Almouzni envisages Asf1 shuttling back and forth from parent to daughter strands, rather than straddling the gap.

Reference: Groth, A., et al. 2007. Science. 318:1928–1931.