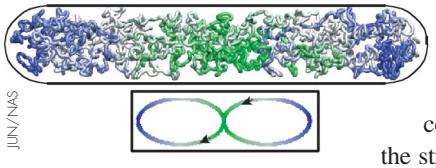
Text by William A. Wells
wellsw@rockefeller.edu

Segregation by entropy

Entropy may be sufficient to drive bacterial chromosome segregation, say Suckjoon Jun and Bela Mulder (FOM Institute for Atomic and Molecular Physics, Amsterdam, Netherlands).

The rapid and abrupt nature of chromosome segregation in bacteria has led researchers to suspect eukaryotic-like mechanisms based on active cytoskeletal proteins. Jun approached the problem from a very different viewpoint: that of a polymer physicist. Polymers tend to repel each other because of the greater conformational freedom, and thus higher entropy that results if they untangle and separate. It is this tendency, which is much stronger in confined spaces such as the cell, that the Dutch group believes is the driver for chromosome segregation.

They devised a mathematical model of bacterial chromosome replication and segregation. In this model, the existing DNA is constrained within a nucleoid, and newly replicated DNA is ejected by entropic forces into a peripheral region. Based purely on a consideration of entropic states, the bacterial chromosomes segregated rapidly after replication. Supercoiling and DNA condensation are expected to increase the structure of a given chromosome and increase the entropic effects.



JUN/NAS

Modeling (top) shows how bacterial chromosome separation can be driven by entropy alone.

To test the model, better visualization of bacterial chromosome segregation is needed. Past studies have suggested that segregation may not occur until much of the chromosome is replicated, but uncertainties remain. Meanwhile, Jun hopes to create an approximation of two segregating chromosomes under controlled conditions in a microchamber. JCB

Reference: Jun, S., and B. Mulder. 2006. *Proc. Natl. Acad. Sci. USA.* 103:12388–12393.

Killers aid a pregnancy

From a mother's perspective, a fetus is a bag full of foreign antigens—invaders against which an immune system might be expected to protect. But, according to Jacob Hanna, Ofer Mandelboim (Hebrew University, Jerusalem, Israel), and colleagues, certain immune cells actually help fetal cells to invade the uterus and ensure an adequate blood supply. Their success is essential to avoid the often fatal condition of preeclampsia.

All this cellular action takes place in the decidua, the outer lining of the uterus during pregnancy. Up to 40% of the cells in this tissue are maternal natural killer (NK) cells—but specifically the NK cells rich in CD56. Unlike the majority of circulating NK cells, these dNK cells are good at excreting proinflammatory cytokines and bad at killing infected cells.

The Israeli group found that dNK cells produce chemokines that can attract embryonic cells called trophoblasts. These trophoblasts form the placenta, in part by invading the decidua and tapping into the underlying blood vessels. Blood vessel growth and remodelling appears to be further aided by the VEGF now found to be secreted by dNK cells.

If this invasion is insufficient, the result is preeclampsia: blood vessels that do not fully penetrate the myometrium result in high blood pressure in the mother and fetus, which can only be relieved by delivering the fetus. In a recent genetic study, preeclampsia risk was greatest for parental gene combinations that inhibited dNK cell activation. Thus, when fetal cells are looking for a foothold, a pacifist subset of killer cells is the critical collaborator. JCB

Reference: Hanna, J., et al. 2006. *Nat. Med.* doi:10.1038/nm1452.

Automatic cell topology

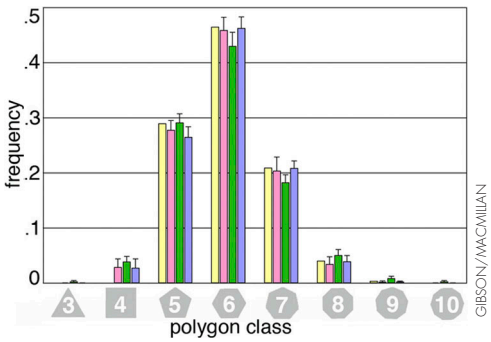
Soap bubbles (and coins pushed together on a tabletop) shift around until they reach an optimal packing state. But epithelial cells are not free to shift, because they maintain a constant grip on their neighbors. Instead, their predictable packing state simply emerges as a consequence of a random cell division process, according to Matthew Gibson and Norbert Perrimon (Harvard Medical School, Boston, MA), and Ankit Patel and Radhika Nagpal (Harvard University, Cambridge, MA).

The Harvard group first confirmed that epithelial neighbors did not easily reassort their contacts, even during a cell division. They then constructed a model that predicted the probability that a daughter cell would have a particular number of sides after assigning a cell division plane randomly.

Where the division plane hit the side of a neighboring cell, that neighboring cell gained an extra side. This gain was balanced in the dividing cell: typically its two progeny had less than twice the number of sides than the parent. This to-and-fro of sides drives the system to an equilibrium with a very specific distribution of cells, with hexagons the most abundant. The relative numbers of these shapes as predicted by the model was matched almost precisely by the shapes seen in real epithelia.

"If it didn't [emerge this way], maybe it would be very difficult for the cell to proliferate rapidly," says Nagpal, because the cells would have to reassort to regain stable topologies. The Harvard group now plans to add assumptions about cell volume and side lengths to the model, which will allow predictions about how changes in cell proliferation can change the shape of a tissue. JCB

Reference: Gibson, M.C., et al. 2006. *Nature.* doi:10.1038/nature05014.



Predicted (yellow) topologies match those seen in various species.