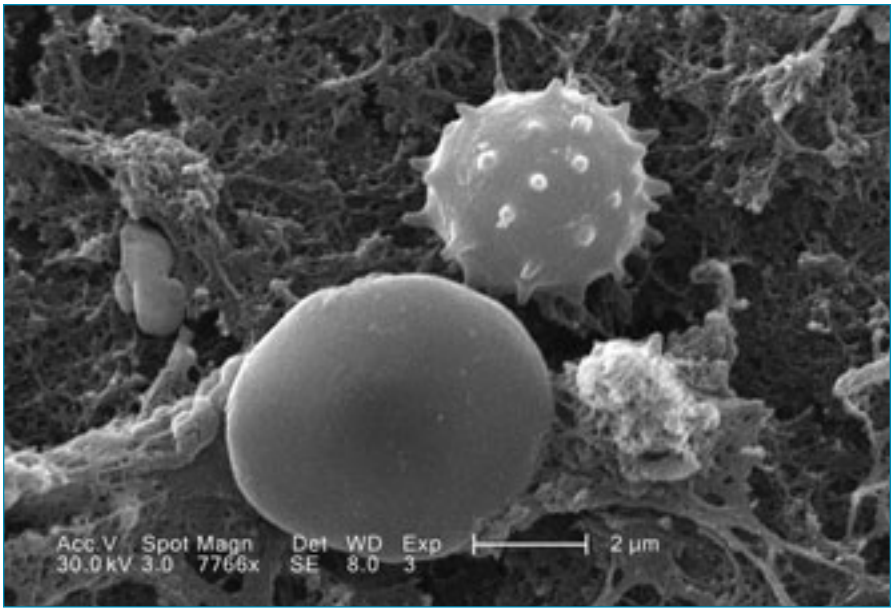


The knobby surface of a white blood cell (top) facilitates sticking, and the smooth surface of a healthy red blood cell (bottom) discourages it. Scanning electron micrograph courtesy of CDC/Janice Carr.

that addresses what geometry makes some cells stickier than others. According to their model, reported in *Physical Review Letters* in September 2006, a cell that efficiently initiates adhesion is dotted with elevated receptor patches–knobby protrusions tipped with receptor molecules. The taller the patches, the better.

"Once you start thinking about it, it's obvious." says **Christian Korn**, a PhD candidate in theoretical physics at the Max Planck Institute of Colloids and Interfaces and one of the authors. "You need these protrusions."

Cell adhesion requires two steps: encounter and docking. Korn and **Ulrich Schwarz, PhD**, a theoretical biophysicist and assistant professor at the University of Heidelberg, modeled the encounter step—to identify the cells that are best at initiating adhesion.

To create the model, the researchers simulated spheres sporting receptor patches and flowing above a flat surface with the corresponding ligands. The stickiness of cells was measured by how long it took for the first receptor-ligand encounter to occur. Korn and Schwarz then varied the number, size, and height of the receptor patches to discover the optimum receptor patch geometry. Plastering the cell with as many receptor patches as possible—akin to fully wrapping a bouncy ball in tape—is not the best strategy, they found. "The cell can have only 1% of the surface covered with receptors, and it works almost as efficiently as if it were 100% covered," Korn says. In addition, increasing the lateral size of the patches –placing bigger bits of tape on the ball—doesn't make much difference. Yet increasing the height of those receptor patches—using raised stickers instead of tape—helps the receptor patches find their target ligands sooner compared to lower receptor patches on a cell of the same size.

The researchers point to similar geometry repeated across vastly different systems in nature. Wrinkled white blood cells, which often need to dock close to an infection, place their receptor patches on the tips of finger-like microvilli. Red blood cells, in contrast, are surfboard smooth. But when a red blood cell becomes infected with malaria, it also grows knobs and new receptors on its surface to slow its progress toward destruction in the spleen. Even sticky pollen grains and wandering diatoms in the ocean, Korn says, display spiky geometry.

For experimentalists now probing such systems, says **Cheng Zhu, PhD**, a professor of biomedical engineering at Georgia Tech, the model is interesting, but only part of the equation. "Their model may explain cases where encounter is the limiting step," he says. "Without the complete equation, it's difficult to say how this might affect data interpretation in cases where docking is limiting."

Korn is now extending the model to include binding as well as encounter. He is optimistic that his model will continue to uncover general characteristics of sticky cells. "The big strength of theoretical modeling," he says, "is that you can get the big picture because you focus on a few essential aspects."

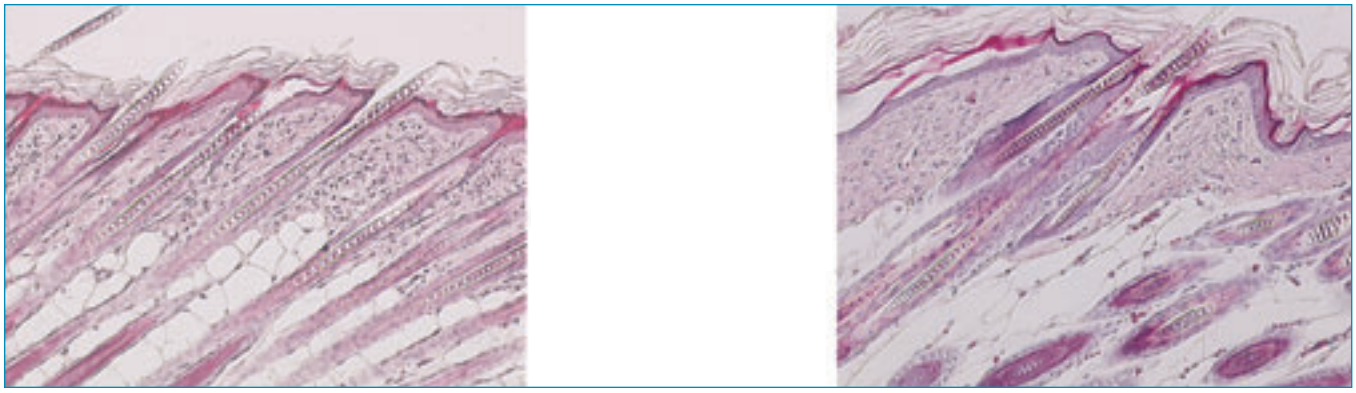
—By Louisa Dalton

Biological Evidence for Turing Patterns

In the 1950s, computer science pioneer Alan Turing suggested an elegantly simple mechanism for how biological patterns such as scales, feathers, and hair might form. Now, more than fifty years later, biologists have used a computer model and transgenic mice to confirm mathematical predictions of the Turing model of pattern formation within a specific biological system: mouse hair development.

"It's the most convincing biological (as contrasted with chemical) experiment to date that claims to support the Turing mechanism," says **Irving Epstein, PhD**, a chemistry professor at Brandeis University. The work appeared online in the journal *Science* in November 2006.

Turing's 1952 proposition goes like this: Two molecules—an activator that enhances its own production, and an inhibitor that slows the production of the activator—diffuse and react. If the inhibitor diffuses sufficiently faster than the activator, repetitive patterns may spontaneously emerge.



Normal mice have well-spaced hair follicles (left). But a moderate suppression of WNT signaling changes the pattern to follicle clumps (right). Courtesy of Thomas Schlake, Max Planck Institute of Immunobiology.

Evenly spaced mouse hair is just the type of pattern that a Turing mechanism might create. That's one reason biologist **Thomas Schlake, PhD**, at the Max Planck Institute of Immunobiology started searching for key molecules involved in mouse hair follicle formation that might fit Turing's predicted pair. He found them in the signaling molecule WNT and its inhibitor DKK.

Schlake and his colleagues created a computer model describing the pair's Turing behavior and then asked the model to predict what would happen if something went wrong—if WNT or DKK appeared in too great or too small a burst. Experiments with transgenic mice verified their computational predictions. Mice that strongly overexpress DKK, suppressing WNT signaling, look like they are balding. And mice that moderately overexpress DKK form clumps of hair instead of regularly spaced follicles.

Schlake thinks it's likely that other inhibitor/activator pairs (Turing called them morphogens) form the base of other natural patterns.

Of course, stripping complex developmental pathways down to the actions of one Turing pair is a strong simplification of the real world, he adds. Mouse hair follicle placement doesn't solely depend on the behavior of two interacting molecules. Leagues of other signaling molecules stabilize and refine the process.

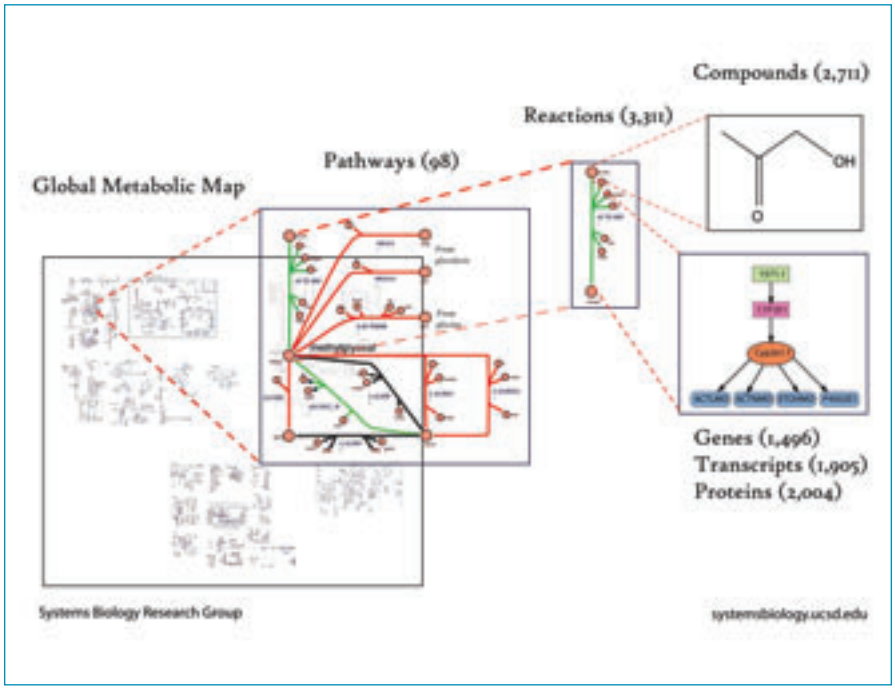
Yet it is that very power to simplify and predict outcomes from a small number of key variables that is the hallmark of a good model, Epstein says. He is not surprised that 50 years after Turing proposed his model, biologists are just now providing detailed molecular evidence for it. "Turing," he says, "was a very smart man."

—By Louisa Dalton

The BiGG Picture

It's hard to imagine a map depicting the daily flow of traffic on water, wheels and foot throughout San Diego—or any large city—over the course of a day. "That map can have many different functional states which are quite different in the middle of the night and during rush hour," says **Bernhard Palsson, PhD**, professor of bioengineering at the University of California, San Diego.

But it's even harder to imagine the map recently assembled by Palsson and his multidisciplinary research team—a virtual metabolic network representing the intracellular traffic catalyzed by more than 2,000 proteins and 3,300 bio-



Overview of the BiGG global human metabolic network. Courtesy of Bernhard Palsson and Neema Jamshidi.