air pressure, than moving around fluid that clogs a partially collapsed airway.

However, the researchers acknowledge shortcomings in their model. Airways are not infinitely long tubes, as Heil and Hazel assumed. "The airway branches are relatively short before they branch again," says Heil. "You have this tree structure, and that is something we do not take into account."

Oliver Jensen, **PhD**, professor of applied mathematics at the University of Nottingham, United Kingdom, says the new model is a step forward compared to older ones. "They've developed an absolutely wonderful tool," says Jensen. He notes the model also should apply to other systems with fluid-lined tubes, such as blood vessels.

For doctors who treat collapsed airways, Heil and Hazel's work eventually could lead to fine-tuned air pressure for different patients. For now, when doctors sit down to use a ventilator, says Jensen, "It's nice if they can at least understand what is happening in the airways."

—Sarah CP Williams

New Algorithm Finds Stories in Biomedical Literature

A good story ties up all the loose ends. A new data-mining tool takes a stab at doing the same. Dubbed *storytelling*, the algorithm may make it easier to unearth unexpected connections in the avalanche of freshly published research, or among high-throughput datasets. For example, *storytelling* can sift through tens of thousands of PubMed abstracts to discover scientific links between two apparently unrelated topics; or draw connections across a knowledge structure such as the Gene Ontology.

"What we are trying to do is link data sets very far apart," says **Richard Helm**, **PhD**, associate professor of biochemistry at Virginia Polytechnic Institute. "In the end, we link data set A with data set Z in the form of a story." The work was presented at the Twelfth ACM SIGKDD International Conference on Knowledge Discovery and Data Mining (KDD 2006), in August 2006.

Researchers might not have time to find complex relationships waiting for discovery in the literature, but *storytelling* does. It finds key documents bridging from one research publication (the starting point) to another (the end point). Using System X, a Virginia Tech supercomputer, the algorithm first classifies each PubMed article's abstract into an organized branched set of terms. It can then make thousands of comparisons and join related publications into a chain connecting start to finish.

For example, Helm and his colleagues, used *storytelling* to dig through the literature seeking ties between two remotely related papers: one on tomato genes expressed in yeast and another on how chemical stress affects yeast gene expression. The supercomputer boiled down 140,000 yeast publications to nine abstracts—stepping stones from paper one to paper two. The results included a paper that identified a novel protein, expressed only when yeast cells are exposed to cadmium, which researchers might not have immediately connected with the first two papers. Although the paper might have surfaced in an ordinary PubMed search, it would have required much sifting to find it. While not every search will yield treasures, hopefully most results from *storytelling* will provide new insights and hypotheses that researchers can test at the bench, Helm says.

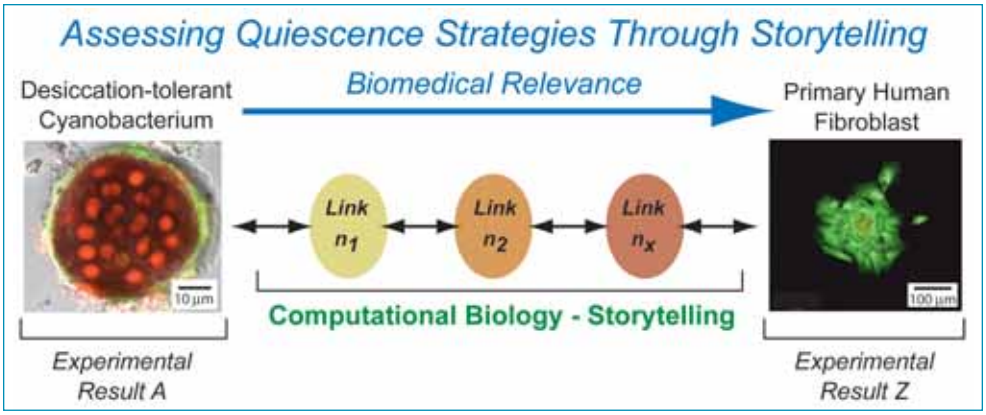
Bud Mishra, **PhD**, professor of computer science and cell biology at New York University, thinks *storytelling* can help biologists make new connections. "In some sense it closely resembles what biologists do, and it works in the same way that biologists think," says Mishra.

—Brian Lee

A Fast Lane Through the Stomach

What goes into the stomach must come out, but perhaps not in the same order in which it entered, as gastroenterologists have long assumed. A two-dimensional computer model of human stomach digestion reveals a previously unknown narrow pathway that can funnel liquids from the top of the stomach to the intestines within 10 minutes.

"There are very few times you discover something that you weren't expecting to find when you designed the experiment," says **James G. Brasseur**, **PhD**, professor of mechanical engineering, bioengineering and mathematics at Penn State University and one of the researchers

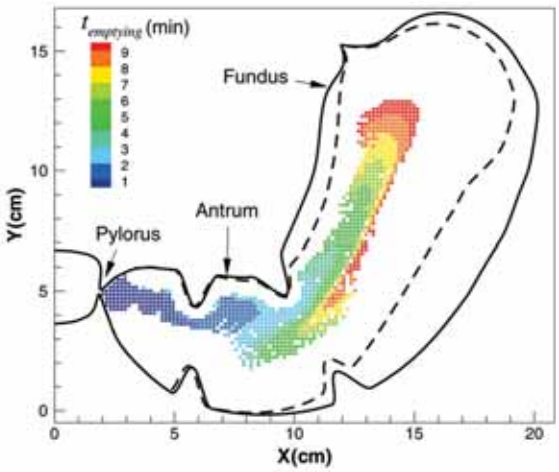


As shown here, one might use* storytelling *to understand the pathways into and out of a quiescent state. Datasets evaluating desiccation-tolerant cyanobacteria (left, coccoid cells stained red and encased in an extracellular matrix, the exterior of which is stained green) could potentially be linked to studies involving the metabolic arrest and recovery of primary human fibroblasts (right, Live/Dead stain; image taken 72 hours after a two week metabolic arrest).* Storytelling *allows the biologist to link disparate datasets, allowing for the development of new hypotheses that can be tested at the bench and re-evaluated within the algorithm, ultimately resulting in new insights into the process of interest. Courtesy of Richard Helm.

who created the model for studying drug delivery. But this was one such time.

The curious finding could help explain the wide variability in drug activation time: A drug might get swept along in this fast digestive current one time, and not another. The work appeared online in the *Journal of Biomechanics* in August 2006.

In 2004, Brasseur and research associate **Anupam Pal**, **PhD**, had published a computer simulation of gastric flow and mixing. In the current work, they used the same basic simulation, but studied gastric emptying. They gave unique numbers to thousands of points (fluid particles) uniformly distributed around the stomach. They then watched the order in which these particles left the stomach during a 10 minute simulation, while keeping track of each particle's position at each time-step. When they then ran the simulation in reverse, they could watch the particles' changing positions. After color-coding the points by time of leaving, they observed a ribbon-like path of gastric emptying that originates in the top of the stomach and passes along its side of least curvature. The entire animated sequence can be seen at http://mne.psu.edu/Brasseurlab/gastric/.



This image of Brasseur's two-dimensional stomach model shows the initial locations of all particles that left the stomach over the course of 10 minutes. The pattern of gastric emptying suggests the existence of a Magenstrasse in the stomach. The dashed line shows the shape of the stomach after 10 minutes. Courtesy of James Brasseur.

The researchers dubbed their discovery the "Magenstrasse," which means "stomach road" in German. It is a sort of passing lane, where digested matter reaches the intestines more quickly than food and liquids outside the road. "We do not know if the Magenstrasse has a physiological function or if it is only a byproduct of the contraction waves in the distant stomach," says Brasseur. The team showed that when the simulation excluded contractions known to exist at the bottom of the stomach, the Magenstrasse didn't form.

"Brasseur's modeling has revealed a potential new mechanism of liquid emptying that can explain why some patients take a very short time to absorb drugs in their bloodstream," says **Michael Fried**, **MD**, director of the division of gastroenterology and hepatology at the University Hospital Zurich, Switzerland. He says pharmaceutical companies who wish to achieve constant and reproducible patterns of absorption of drugs must take this study into account. However, Fried notes, the model "has to be validated in animals or in humans."

Brasseur agrees more research is necessary. "We would need further studies that checked how the path works with nutrients and drugs of different densities," he says. He believes the Magenstrasse would still exist if the stomach contents are thicker than the viscous liquid used in his team's simulations, but it may assume a different shape.

—Maria José Viñas

Stem Cells' Existential Crisis Explained

To differentiate or not to differentiate? That is the question constantly faced by embryonic stem cells. And they seem to answer it decisively at the behest of a molecular trio of transcription factors. A new computational model shows how it is possible for three proteins to control the switch in the observed, clear-cut manner. The model also gives researchers a hypothesis they can test in the lab.

"We've shown that these three players are able to define the embryonic stem cell switch," says **Carsten Peterson**, **PhD**, professor of computational biology at Lund University in Sweden and lead author of the study. By explaining this either/or molecular circuitry, the model could eventually help scientists harness stem cells for treatments. The work appears in the September 2006 issue of *PLoS Computational Biology*.

Embryonic stem cells have two defining traits: They can divide forever to remain stem cells, and they are pluripotent, meaning they have the potential to become any type of somatic cell in the body—gut, muscle, skin, blood or nerve. But whether in a Petri dish or the body, stem cells receive a barrage of molecular signals that they must interpret and respond to with a binary decision. "Either you are a stem cell or you commit yourself," says Peterson.

Over the last few years, biologists have discovered that a handful of proteins determine an embryonic stem cell's fate. Three in particular—named OCT4, SOX2 and NANOG—seem to coordinate the decision by cueing the actions of hundreds of target genes.

Peterson's team derived mathematical equations governing the rate at which these three transcription factors bind and unbind to DNA, thereby regulating the expression of differentiation genes and stem cell genes. The team then used the Systems Biology Workbench to simulate how this trio controls other genes to engineer opposing outcomes: self-renewal or differentiation. They infer that the proteins reinforce one another's actions through a positive feedback mechanism, creating a bistable switch: either on or off, with no middle ground. When all three proteins are active, stems cells remain stem cells; when the trio is inactive, the cells differentiate, with no middle ground. Peterson and others hypothesize that stem cells receive external signals to control the switch. Because of the positive cascade of interactions, the cells effectively ignore slight changes in those signals and respond with a single outcome every time.

The model was based on previous work by **Laurie Boyer**, **PhD**, a postdoctoral fellow at the Whitehead Institute in