

# Research Roundup

## Bugs get decrepit too

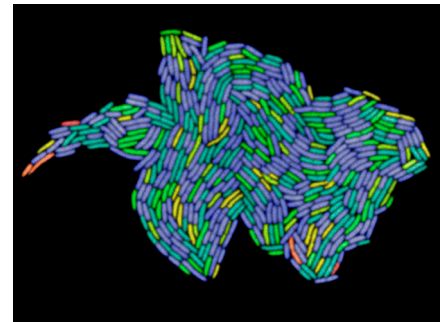
There is no escape. Even the lowly *Escherichia coli*, which at first glance seems to go on dividing symmetrically and forever, ages over time, according to Eric Stewart, François Taddei (Inserm, Paris, France), and colleagues.

There was hope for *E. coli* immortality because the bug lacked obvious asymmetries. Organisms that age tend to segregate damaged molecules preferentially into a compromised parent, and that segregation often shows up as a morphological asymmetry. Furthermore, the uncompromised offspring often turns up as a juvenile form that must undergo further development or growth before being competent for reproduction. Signs of such a progression were also lacking in the case of *E. coli*.

Stewart and colleagues undertook a more comprehensive examination of *E. coli* division dynamics, using a custom-

made, computerized tracking system that followed *E. coli* divisions as they generated 35,049 cells. Cleavage sites in the middle of the bacterium were defined as “new poles” and those at the distal ends as “old poles.” Thus, as cells divided to form a chain, cells at either end of the chain had particularly “old” poles. These cells had a growth rate 2.2% slower than that of “new pole” cells; they also divided later, produced less biomass, and were more likely to die. The differences increased as poles got increasingly “older” or “younger” (via repeated formation of “new” poles in consecutive divisions).

Stewart says he went into the study an agnostic on whether *E. coli* would show its age. “I couldn’t decide myself, in the beginning,” he says. One reason is that “people don’t know to what extent damage can be fixed,” he says. “Perfect repair could be possible but the cost that would be involved would be high.” *E. coli* may



STEWART/TIMMERMANN

***E. coli* that are young (blue) and old (red) have distinct properties.**

instead attempt the kind of sorting of damaged contents that is seen during the generation of everything from budding yeast daughter cells to human germline cells. Stewart hopes to visualize any such sorting in *E. coli*; he is also screening for mutants that age (and thus produce dead cells) more slowly. **JCB**

Reference: Stewart, E.J., et al. 2005. *PLoS Biol.* doi:10.1371/journal.pbio.0030045.

## Chemotaxis by local steering

Chemotaxing cells have a defined front and back. Thus, movement models have always included explanations of how a single cell can integrate information about its surroundings and come up with a single answer about where the “front” is located. But now Cécile Arriemerlou and Tobias Meyer (Stanford University, Stanford, CA) claim that it is local decisions about lamellar extension that matter.

Meyer says this idea “was really from watching cells in the microscope and seeing how they make direction changes. It was more consistent with stochastic, small turns than the cell knowing

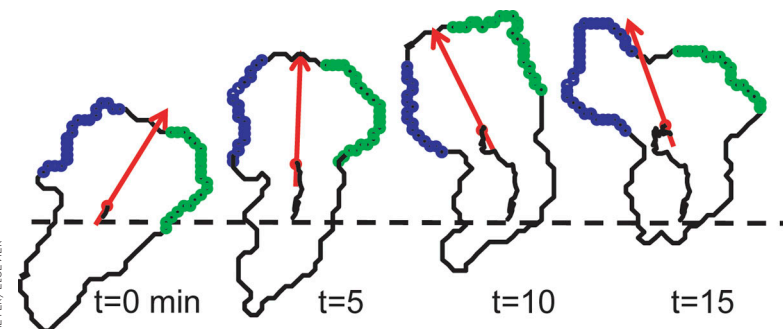
where the signal is located.” The biased random walk was driven by local lamellipod extensions, correlated with PI3P pulses, that spanned only a fraction of the total leading edge. Furthermore, the actions of the left and right of the leading edge were not correlated.

The decision to protrude, Meyer believes, is based only on local chemoattractant binding, so that each receptor ligation triggers a local lamellipod that turns the cell by ~2 degrees. The steering, then, is just the stochastic difference between multiple small turns toward the left and right. This system “is running on the top of self-polarization at the front of the cell and helping to guide it,” says Meyer.

The distinct self-polarization process is important, however, in defining the front of the cell as the part of the cell that is responsive to turning and extension signals, and in allowing random walking in the absence of a chemotactic gradient. Such random walking increases the range of cells, so that they can reach the areas where chemotactic signals are present to guide their continued travels.

Meyer believes that the self-polarization does involve a global process, and also involves PIP3, but that the process is distinct from steering. He hopes to isolate components that are necessary locally for chemotactic steering but not globally for self-polarization and random migration. **JCB**

Reference: Arriemerlou, C., and T. Meyer. 2005. *Dev. Cell.* 8:215–227.

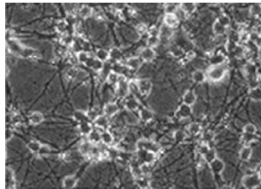
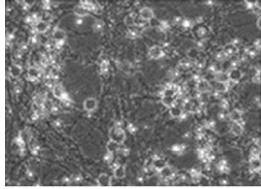


MEYER/EELSEVIER

**Left and right turns are driven by independent lamellipod extensions (blue and green).**

## No exit for Ca<sup>2+</sup>

Overexcited neurons go to their death because of a Ca<sup>2+</sup> overdose, say Daniele Bano, Pierlugi Nicotera (University of Leicester, UK), and colleagues. The overdose is induced by a calpain protease, which chops up the exchanger that normally ferries Ca<sup>2+</sup> out of the cell.



NICOTERA/ELSEVIER

Glutamate-induced death (top) is rescued by inhibiting calpain.

Neurons that are cut off from a blood supply and thus from oxygen fail to clear the neurotransmitter glutamate from their synapses. The result is overstimulation, including an excessive dose of intracellular calcium. Nicotera and colleagues show that this initial increase can subsequently be translated into a larger and potentially deadly overdose of Ca<sup>2+</sup>. The overdose occurs downstream of a calpain cleavage of the Na<sup>+</sup>/Ca<sup>2+</sup> exchanger NCX3. The Ca<sup>2+</sup> overload is blocked and necrotic cell death is reduced after inhibition of calpain or expression of the alternative NCX2 exchanger. Reduction of NCX3 function by siRNA results, however, in the opposite effect: treated neurons are sensitized to Ca<sup>2+</sup>-induced necrotic death.

NCX3 is a low affinity but high capacity exchanger, and thus is well suited to ferrying large amounts of Ca<sup>2+</sup> out of the cell. It is not clear whether calpain's action to stop this restorative function is a form of deliberate suicide or of pathology. The calpain may be acting to eliminate defective cells and thus save the organism from potential damage, or it may be overdoing a normal calpain function, such as regulation of membrane protein turnover, resulting in an accidental pathology. **JCB**

Reference: Bano, D., et al. 2005. *Cell*. 120:275–285.

## Diet affects DNA

Mitochondria apparently adjust their DNA inheritance strategies when faced with different metabolic conditions, based on results from Xin Jie Chen, Ronald Butow, and colleagues (UTSW, Dallas, TX). The key to the change is a metabolic protein called aconitase.

When grown in glucose, budding yeast rely on glycolytic fermentation, but on other carbon sources the Krebs cycle and oxidative fermentation kick in. Aconitase, one element in the Krebs cycle, is turned on when glucose is absent.

The Texas team now shows that this induction helps out not only with the Krebs cycle, but also with the inheritance of mitochondrial DNA (mtDNA). Aconitase turned up as a protein associated with mtDNA; its absence resulted in spores lacking mtDNA. The enzymatic activity of aconitase was not required for mtDNA-stabilizing action. Aconitase could, however, substitute for another mtDNA nucleoid protein, Abf2p, which is thought to package mtDNA under fermentative conditions.

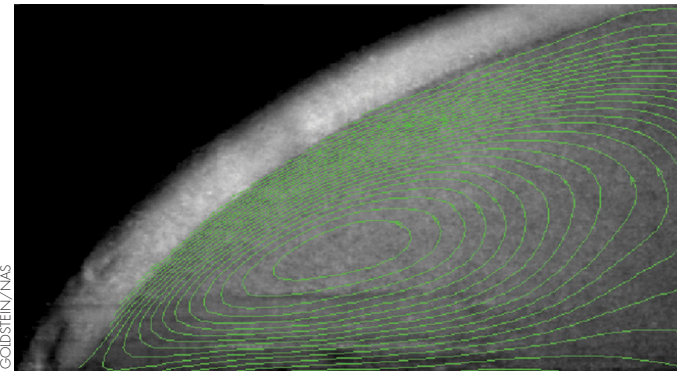
"Cells go to some trouble to ensure inheritance under different conditions," says Butow. Although Abf2p is required in fermentative conditions, it seems that aconitase is needed under both fermentative and aerobic, oxidative conditions. Aconitase protects cells lacking Abf2p from ethidium bromide hypersensitivity, but its exact function in packaging, and whether that function helps protect mtDNA from oxidative mutation, remains to be determined. **JCB**

Reference: Chen, X.J., et al. 2005. *Science*. 307:714–717.

## Bacteria keep oxygen flowing

A combination of bacterial chemotaxis and gravitational falling creates vortices in water droplets, according to Idan Tuval (Universitat de Les Illes Balears, Spain), Raymond Goldstein (University of Arizona, Tucson, AZ), and colleagues. The vortices improve harvesting of oxygen from the surrounding atmosphere and mixing of the oxygen into the droplet.

By conventional thinking, bacterial swimming results in negligible flows, and thus diffusion effects dominate over stirring. But Goldstein and colleagues took advantage of the well-known phenomenon of bioconvection in which, in a drop lying



GOLDSTEIN/NAS

Bacteria-induced flow helps oxygenate a droplet.

on a surface, bacteria are moving cooperatively toward the more oxygenated upper layer. After concentrating in this layer they are subject to gravity and stochastically form downward plumes. Once started, these plumes feed themselves: the incompressibility of water means that falling bacteria draw in more bacteria behind themselves.

The researchers discovered a new phenomenon near the corner of the drop, where the fluid meets the supporting solid. Here, the curved drop surface coincides more and more with the direction of gravitational pull, so falling bacteria are channeled along the surface of the drop, driving a circulating vortex. These parcels of liquid thus spend considerable time by the surface, where they pick up hefty doses of oxygen before diving back toward the deoxygenated center of the drop. "It's a little conveyor belt," says Goldstein. "It's a very efficient mixer."

The team visualized the flows both in vitro and in silico, although the oxygen measurements are yet to be made in vitro. The flows would be expected to affect the spreading of other metabolites, including quorum signals that prompt biofilm formation. **JCB**

Reference: Tuval, I., et al. 2005. *Proc. Natl. Acad. Sci. USA*. 102:2277–2282.