One *E. coli* cell (yellow) switches lactose metabolism phenotypes, whereas nearby cells do not.

A stochastic single-molecule event is enough to switch a bacterial cell from one phenotype to another. By monitoring fluorescently labeled lactose permease with single-molecule live-cell imaging, Harvard University chemistry professor X. Sunney Xie and coworkers investigated how *Escherichia coli* cells switch lactose metabolism phenotypes (*Science* 2008, 322, 442). At intermediate concentrations of the inducer compound methyl-β-D-thiogalactoside (a lactose analog), a population of genetically identical cells stably coexists in two phenotypes. Uninduced cells, which can't metabolize lactose, have a small number of membrane-bound permeases, whereas induced cells, which can metabolize lactose, have many membrane-bound permeases and fluoresce brightly. A cell expresses a large burst of permease only if the transcription factor *lac* repressor completely dissociates—an infrequent occurrence—from the DNA. The much more frequent partial dissociation of the repressor from the DNA leads to small bursts of permease expression that aren't sufficient to switch the cell's phenotype. "We show that a single-molecule stochastic event solely determines a cell's phenotype," Xie says. "This argues for why single-molecule live-cell studies are important for biology."
Researchers have designed a hybrid protein in which the activity of one protein is controlled by that of another.

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