shown that a phosphate anion of type **1** (the same as that used by Hamilton *et al.*; see the figure) can modulate the enantioselective transfer hydrogenation of α,β-unsaturated aldehydes, with an ee of up to 98% (*8*).

However, no chiral-anion–mediated metal catalysis with high enantioselectivity was reported, despite the fact that transition metal–based systems are usually cationic. Most researchers considering the strategy of a metal center surrounded directly by one or more bound enantiopure ligands more efficient (see the figure, left panel); the use of chiral anionic counterions residing in the second coordination sphere of the metal ion (see the figure, right panel) was deemed less effective and predictable.

An opportunity arose in the burgeoning area of homogenous gold catalysis (*9, 10*). Many reactions—including intramolecular nucleophilic additions of alcohols, tosylamines, and carboxylic acids to allenic fragments—are effectively promoted by catalytic amounts of Au(I) ions and phosphine ligands (L). However, highly stereoselective reactions with broad substrate scope have been hard to achieve with the traditional chiral ligand/metal ion strategy (*11*).

Capitalizing on their recent observation that some Au(I)-catalyzed reactions are sensitive to the nature of the anionic counterion (*11*), Hamilton *et al.* hypothesized that an enantiopure counterion of type **1** could be the key to an effective asymmetric transformation of these reactions. Using this approach, they achieved very high level of stereoinduction (ee up to 99%). The protocol can be used for various allenic alcohols and tosylamines. In the case of substrates that lack sterically demanding substituents and for which high enantioselectivity is therefore difficult to achieve, the chiral anion strategy remains efficient (ee 80%); when a chiral phosphine ligand acts in synergy with the anionic counterion, a higher proportion of the major enantiomer is produced (ee 92%). Hamilton *et al.* show that this dual approach of combining chiral ligands and anionic counterions is also effective in the hydroxycarboxylation of allenes, for which the use of either chiral ligands or chiral anions alone fails to succeed.

The work of Hamilton *et al.* may open a new chapter in asymmetric homogenous metal catalysis. There is much to gain from this modular and supramolecular approach, because it may, in some cases, be sufficient to exchange traditional achiral anionic counterions for chiral versions at the last step of the catalyst preparation. However, it remains to be seen how broadly applicable this approach will be. Deep understanding of the mechanisms at play in chiral ion pairing situations may prove to be necessary, possibly requiring the use of modern nuclear magnetic resonance techniques and computational studies (*2, 12, 13*).

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MICROBIOLOGY

Necessary Noise

The randomness of a switch between two alternative bacterial states has been traced to the variable expression of a single protein.

Jerome T. Mettetal and Alexander van Oudenaarden

In the classic view of cellular biology, cells are simply a product of genetic and environmental conditions, and all differences between individual cells can be attributed to one or both of these factors. Recent work, however, suggests that when grown in the same environment, cells from genetically identical populations can exhibit very different behaviors. Even simple attributes, such as the number of proteins produced from a constitutively expressed gene, can vary greatly from cell to cell. In other cases, individual cells will make vastly different phenotypic choices seemingly at random (*1–4*). Why some cells remain in one phenotypic state whereas others switch to a different one, and what the molecular processes are that cause cells to "play dice" when determining their fate, remain open questions.

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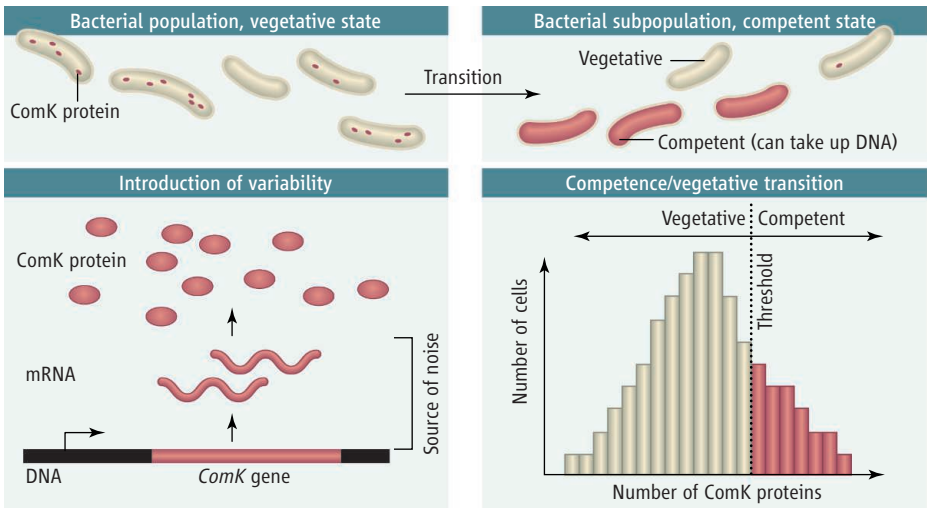
On page 526 in this issue, Maamar *et al.* (*5*) tackle these questions using the soil bacterium *Bacillus subtilis*. They find that the random nature of the phenotypic choice made by these bacteria to remain vegetative (dormant) or become "competent" (able to take up DNA from the environment) can be traced to variable expression of a single protein. Although many organisms exhibit phenotypic variability driven by stochastic gene expression, the *B. subtilis* system is of particular interest because variation ("noise") in protein expression is thought to play a key role in the natural behavior of a population.

Under certain conditions, only some bacteria exit a vegetative state and become competent. The key protein orchestrating this process, ComK, also spurs its own expression by acting as a transcription factor. This autoregulatory positive-feedback loop enables cells to stably reside at either a low or a high level of ComK expression, corresponding to vegetative and competent states respectively. In the vegetative state, cells have too few ComK proteins to activate further *comK* gene expression, ensuring that the concentration of this protein remains low. By contrast, in the competent state, ComK is produced in large quantities, ensuring that the gene remains highly expressed. Further, there is a critical quantity of ComK that separates the two states; cells with a ComK protein concentration above this threshold will become competent (see the figure). It is thought that in vegetative cells, rare fluctuations in protein concentrations can cause cells to cross this threshold.

To determine the source of the fluctuations that drive this transition, Maamar *et al.*, use a fluorescent probe that binds to messenger RNA (mRNA) in situ to measure individual mRNAs produced from the endogenous *comK* gene and from a synthetic gene with an identical upstream promoter region. By measuring correlations in mRNA expression, they



Randomly flipping a cell-fate switch. A population of bacteria can express variable amounts of ComK protein. Only cells that express greater than a threshold concentration of ComK become competent. Cell-to-cell variation in ComK protein expression ("noise") arises from variations in comK mRNA concentration across the cell population.

find that noise in ComK protein expression comes mainly from random production and/or degradation of *comK* mRNA, rather than from external factors (such as variability in ribosome numbers from cell to cell).

To demonstrate that noise in *comK* gene expression is the key factor causing cells to transition to competence, Maamar *et al*. modifed a strain (which has an increased basal *comK* mRNA production) by decreasing the rate of translation initiation. This reduces noise (*6*) while keeping the average comK protein concentration fixed. In the modified strain, low noise levels caused cells to transition into the competent state less frequently than wild-type cells. In other words, the reduced-noise strain produces more mRNA, but less protein from each mRNA. This reduces the amount of variability in mRNA expression levels, and thus variability in protein concentration.

In a complementary study, Süel *et al.* (*7*) create a strain in which bacteria cannot complete cell division, causing multiple cells to share cytoplasm. In this strain, cell-to-cell variability is reduced because connected cells share proteins, averaging away differences in protein concentrations between cells. Like Maamar *et al*., they find that a decrease in cell-to-cell variability leads to a decrease in transitions to the competent state.

Maamar *et al*. and Süel *et al.* provide a comprehensive microscopic view of how stochastic fluctuations in gene expression can cause cells to change their phenotype. An even clearer picture of such cell decision-making might be attained by coupling real-time measurements of mRNA and protein concentrations (*8*, *9*) with switching events in single living cells. There remains the nagging question of why the population only allows a fraction of its cells to become competent. By splitting the population into two phenotypes, *B. subtilis* may use naturally occurring noise to increase population diversity and enhance survival in the face of environmental uncertainty (*10*–*12*). It is possible that evolution has been using a strategy of modifying transcription and translation rates to fine-tune the noise levels (*5*, *6*) of key genes that underlie phenotypic diversity in a population.

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ECONOMICS

Spying on Others Evolves

Watchful eyes induce altruistic behavior and an "arms race" of signals between observers and the observed.

Manfred Milinski and Bettina Rockenbach

When reputation is at stake, animals as well as humans switch from selfish to altruistic behavior, because only the latter is socially rewarded (*1, 2*). But how do they assess whether their actions are observed? Recent investigations into human behavior have shown that subtle cues of being watched such as two stylized eye-like shapes on a computer screen background suffice to change behavior (*3*). A picture showing a pair of eyes attached to a cafeteria collection box significantly raises the donated amount compared to a flower symbol; in fact, the eyes were most effective when looking directly at the observer (*4*).

Although just ink on paper, these eye-shaped cues seem to elicit unconscious hard-wired reactions. Indeed, electrophysiological responses recorded from the scalp of normal subjects showed responses to isolated eyes that are even larger than the responses to full faces (*5*). Brain imaging studies in humans have also highlighted a role for the superior temporal sulcus (STS) and amygdala in gaze processing; the STS is likely to be essential for recognizing the eyes, head, and body as stimuli used in social communication, whereas the amygdala is likely to be essential for attaching social and emotional significance to these stimuli (*6*). Interestingly, even birds respond strongly to eye-like shapes, especially when two eyes are staring at them (*7*).

What is the benefit of watching someone? Spying on others seems widespread in animals and humans (*8*). By snooping on one another's social life, animals and humans can work out how to behave when they meet in the future. Recent experiments

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