

ferentiate precociously (1, 7). Conversely, cells with extra copies of *hetR* differentiate supernumerary heterocysts, whereas cells with extra copies of *patS* cannot differentiate at all. The two proteins, HetR and PatS, therefore represent two sides of the coin, one positively encouraging differentiation and the other suppressing it.

The HetR protein has remarkable properties. If the NtcA control of *hetR* transcription is bypassed, by using the copper-regulated *petE* promoter (also used by Yoon and Golden to drive *patS* expression), the resulting level of HetR can be so high that 30% of the cells differentiate, even in the presence of the usually inhibitory nitrate or ammonia (8). HetR can, therefore, drive differentiation even under normally repressing conditions. Second, there is a critical serine residue in HetR (7). When a strain carrying a Ser→Asn mutation, which does not differentiate, was forced to revert, five of five revertants had the wild-type serine restored. Third, HetR appears to be a serine protease, capable of digesting itself, inhibited by DFP, and probably phosphorylated on a serine (9).

This information suggests a simple hypothesis: A PatS peptide cleavage product is an inhibitor of the HetR protease activity. Because both of the genes are expressed in developing heterocysts (compare figure 4 of Yoon and Golden with the figure above), we need to explain how HetR is able to promote its own synthesis in the presence of PatS, which it is known to do (8). One possibility is that PatS is an inactive precursor substrate for the HetR protease and that the active cleaved peptide, Arg-Gly-Ser-Gly-Arg, is released into the periplasm and transported to vegetative cells, where it is indeed active against HetR. All of the elements of this proposal are testable by using recombinant HetR and synthetic peptides. Other models are equally plausible and testable in the same way. For example, HetR could cleave the PatS peptide to yield an inhibitor of PatA, a kinase required for HetR's positive activity (8, 10).

The *hetR* gene has at least four promoters, several of which are activated after nitrogen is decreased. None of these contains the canonical sequence to which NtcA binds, so there must be intermediate signaling molecules (protein kinases?) between NtcA and *hetR* transcription; these could be targets of PatS control. It will of course be interesting to determine where the *patS* transcript starts and what its promoter sequence looks like. HetR, directly or indirectly, promotes its own gene transcription in heterocysts and represses it in vegetative cells. These activities require phosphorylation, because they are affected by mutations in the kinase PatA (10). In a *patA* mutant, all but the terminal cells in

the majority of filaments fail to activate transcription of the *hetR* gene. In the *hetR* Ser→Asn mutant, however, transcription of *hetR* increases in all the cells after nitrogen has been reduced. We conclude that wild-type HetR has two activities: enhancement of *hetR* transcription in heterocysts and repression of *hetR* transcription in vegetative cells. The first of these requires the PatA kinase, whereas the second does not. These considerations suggest another possible site of action of the PatS peptide: inhibition of the PatA kinase.

No matter what mechanism is found to apply ultimately, the remarkable discovery of peptide control of differentiation in

such a simple experimental system should lead to insights applicable to a wide range of more complex problems in eukaryotes.

References

1. H.-S. Yoon and J. W. Golden, *Science* **282**, 935 (1998).
2. J. W. Golden *et al.*, *Nature* **314**, 419 (1985).
3. C.-C. Zhang, *Proc. Natl. Acad. Sci. U.S.A.* **90**, 11840 (1993); *Mol. Microbiol.* **20**, 9 (1996).
4. M. J. Fath, E. Koshy, R. Haselkorn, unpublished results.
5. B. McCartney *et al.*, *J. Bacteriol.* **179**, 2314 (1997).
6. T.-F. Wei, R. Ramasubramanian, J. W. Golden, *ibid.* **176**, 4473 (1994); J. E. Frias, E. Flores, A. Herrero, *Mol. Microbiol.* **14**, 823 (1994).
7. W. J. Buikema and R. Haselkorn, *Genes Dev.* **5**, 321 (1991).
8. ———, in preparation.
9. R. Zhou *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **95**, 4959 (1998).
10. J. Liang *et al.*, *ibid.* **89**, 5655 (1992).

NOTA BENE: PHYSICS

Just a Light Squeeze

Quantum mechanics is a rigorous taskmaster, but occasionally it will let you get away with magic. An example has recently been reported by Schmitt *et al.* (1) of the University of Erlangen-Nurnberg, who used fiber optics to create unusual pulses — solitons — marked by even more unusual behavior called a “squeezed state.”

Solitons are isolated waves on the verge of both creation and destruction. A typical pulse of light propagating in a glass fiber wants to spread out, smearing its energy over broader and broader regions. Yet in a nonlinear material, which glass becomes at very high optical intensity, the energetic pulse modifies the fiber's index of refraction in a way that leads to sharpening and narrowing. If these two tendencies are in balance, the pulse becomes a soliton (solitary wave) and can propagate without loss for very long distances. This has made optical solitons attractive to builders of long-haul communication networks.

Schmitt *et al.* have used soliton pulses of 126 femtoseconds duration to explore the strange phenomenon of quantum mechanical squeezing. Heisenberg's uncertainty principle says that if one knows the position of a particle to high accuracy, then one's knowledge of momentum must suffer. More rigorously, the product of the uncertainties of position and momentum must be greater than or equal to $\hbar$, the Planck constant. Position and momentum are called “conjugate” variables, wedded as they are in quantum mechanical bliss and blessed by Heisenberg. But there are other conjugate variables, such as energy and time, or the number of photons in an optical pulse and their phase relations. Here is where tricks can be played: If the quantum fluctuations in one variable are allowed to be large, the uncertainty in the conjugate variable can be reduced, or “squeezed.” For this reason, squeezed states are of considerable interest to researchers developing ultraprecision measurements.

Squeezed solitons from fibers have been observed before (2), but Schmitt *et al.* achieved a direct observation of reduced fluctuations in the photon number, in contrast to the earlier measurements, which measured aggregate optical amplitude. Their apparatus consisted of a Sagnac interferometer, made from a 6.4-meter loop of highly precise optical fiber, a pulsed laser, beam splitters, and photodetectors. The Sagnac loop allows two counterpropagating pulses to interfere with each other and trade off quantum fluctuations, and if the relative amplitude of the two pulses is carefully adjusted, the loop becomes a factory for squeezed solitons. The direct photon number squeezing reflects the quantum behavior of individual frequency components in the pulse, rather than some average, and hence provides a more detailed picture of the squeezing process. Taken together, these results offer a better understanding of the nature of optical quantum processes and the possibility of a ready source of squeezed pulses for measurement and communications.

—DAVID VOSS

References

1. S. Schmitt *et al.*, *Phys. Rev. Lett.* **81**, 2446 (1998).
2. R. Rosenbluth and R. M. Shelby, *ibid.* **66**, 153 (1991); S. R. Friberg *et al.*, *ibid.* **77**, 3775 (1996); S. Spälter *et al.*, *Opt. Express* **2**, 77 (1998).