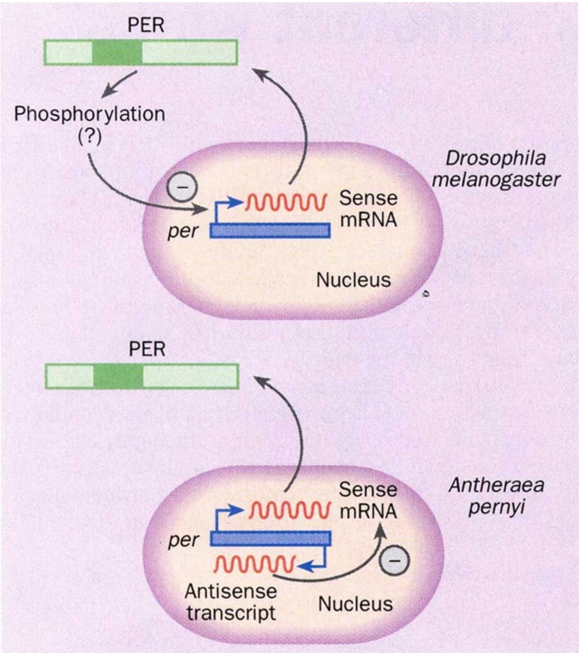

Two distinct mechanisms regulate the circadian clock in the fruitfly and in the silkmoth. Reppert and colleagues[3,4] have shown that the protagonist is the same, but the way in which it acts is different. Whereas in the fruitfly, *per* expression is regulated by a negative-feedback loop, in the silkmoth, regulation of the *per* mRNA transcript is achieved by dynamic hybridization with antisense RNA.

'doughnut', which indicates that the protein does not leave the cytoplasm. Levels of PER also oscillate in the axonal projections that originate from the eight neurosecretory cells, and PER levels correlate with the cyclic output of neuropeptide secretion. So the clock function of the PER–TIM dimer must operate without entering the nucleus and, therefore, independently of transcriptional autoregulatory loops. Then the question is: how does the *per* transcript oscillate without the transcriptional feedback loop?

The surprise came from *in situ* hybridization studies. Analysis with the *per* sense strand, which is classically used as an experimental control, showed a bright signal that also oscillated with a circadian periodicity. Although the exact structure of the silkmoth *per* gene is not yet known, Reppert and colleagues believe that an antisense *per* transcript may be generated by an intronic promoter (see figure). The antisense transcript can hybridize with the sense messenger RNA and block its function. In this way, the oscillating levels of PER protein can be determined.

But how can the oscillating PER modulate levels of TIM in the absence of a nuclear feedback loop? This is still not clear, although it could be argued that *tim* transcripts are regulated in a similar fashion. It has been proposed that, in the fruitfly, the PER–TIM dimer acts directly on the transcription of target genes, resulting in the regulation of output rhythms[2]. This is clearly not the case in silkmoth neurons, because the two proteins do not enter the nucleus. So if the PER–TIM complex is truly a key clock component, there must be alternative pathways for the regulation of overt rhythms.

Notably, the cytoplasmic localization of PER in the silkmoth is seen only in the eight neurosecretory cells in the brain — in other silkmoth cells, such as in the embryonic gut epithelium, PER is, in fact, nuclear, and functions in the same way as the fly protein. Moreover, translation of PER protein in silkmoth brain cells is synchronous with transcription of the *per* gene. So the transcription-to-translation event provides no delay in this circadian timing system. This is in contrast to the delay in translation of four to six hours that has been observed in the fruitfly[5,12]. On the other hand, the pattern of *per* transcription–translation in the silkmoth eye shows the same temporal delay as transcription–translation of the *Drosophila per* gene. So two completely different regulatory pathways are acting in the same organism and on the same gene — in ocular photoreceptors and neurons — to generate an apparent equivalent rhythmicity.

The challenge is to understand the molecular features of the clock. The finding by Reppert and colleagues that *per* oscillation in the *A. pernyi* brain is due to a dynamic synthesis and pairing of sense and antisense transcripts is a tantalizing new twist to the story. The relative half-lives of these mRNAs may be a key determinant of the circadian behaviour of the silkmoth, and experiments aimed at modifying this behaviour should prove to be exciting. □

Paolo Sassone-Corsi is at the Institut de Génétique et de Biologie Moléculaire et Cellulaire, BP 163, 67404 Illkirch, Strasbourg, France (e-mail: paolosc@titus.u-strasbg.fr).

1. Konopka, R. J. & Benzer, S. *Proc. Natl Acad. Sci. USA* **68,** 2112–2116 (1971).
2. Hall, J. C. *Trends Neurosci.* **18,** 230–240 (1995).
3. Sauman, I. & Reppert, S. M. *Neuron* **17,** 889–900 (1996).
4. Sauman, I., Tsai, T., Roca, A. L. & Reppert, S. M. *Neuron* **17,** 901–909 (1996).
5. Hardin, P. E., Hall, J. C. & Rosbash, M. *Proc. Natl Acad. Sci. USA* **89,** 11711–11715 (1992).
6. Sassone-Corsi, P. *Cell* **78,** 361–364 (1994).
7. Aaronson, B. D., Johnson, K. A., Loros, J. J. & Dunlap, J. D. *Science* **263,** 1578–1584 (1994).
8. Molina, C. A., Foulkes, N. S., Lalli, E. & Sassone-Corsi, P. *Cell* **75,** 875–886 (1993).
9. Myers, M. P., Wager-Smith, K., Wesley, C. S., Young, M. W. & Seghal, A. *Science* **270,** 805–808 (1995).
10. Seghal, A. *et al. Science* **207,** 808–810 (1995).
11. Levine, J. D., Sauman, I., Imbalzano, M., Reppert, S. M. & Jackson, F. R. *Neuron* **15,** 147–157 (1995).
12. Curin, K. D., Huang, Z. J. & Rosbash, M. *Neuron* **14,** 365–372 (1995).

DAEDALUS

Winter's icy grip

Ice and snow are very slippery, a fact exploited to the full in skating and skiing, but a major hazard on ice-bound roads. One explanation is that ice contracts on melting. Its melting-point therefore decreases with pressure. Press on it with a skate or a tyre, and it finds itself above its melting-point. It promptly melts to a thin film of lubricating water. Such light pressure may seem inadequate; but only a tiny fraction of a solid surface can ever make true molecular contact with another, so the local pressures are enormous.

Musing on this problem, Daedalus began to invent a refrigerated tyre. It would be so much colder than ambient that even the highest pressure could not melt the ice to water. But he soon realized that if the tyre happened to hit a patch of wet ice, or a puddle of slush, it would solidify the water instantly and freeze in place. The vehicle would jerk to an immovable halt.

He then recalled the intriguing fact that stretched rubber cools when it is allowed to contract, and warms up again when stretched. A normal tyre is too inextensible to exploit this effect. What is needed is a pneumatic tyre that stretches markedly on being inflated. Where it hits the road, it will be compressed by the weight of the vehicle, and will cool down. On a wet road it will freeze in place, secure against all skidding. Yet the stretching of the trailing edge as it lifts away from the road will warm it up again, and release the grip. This cunning tyre will freeze firmly to a wet road, and yet roll freely. Sadly, practical tyre rubbers may not cool strongly enough for the job.

So Daedalus is turning his attention to the wet road surface itself. What is needed, he says, is a tyre coating that under pressure reacts reversibly with water or snow, forming a solid hydrate. Many such hydrates are known, mainly of small molecules such as bromine or butane. He is now devising tyre-coatings loaded with hydratable groupings. When the 'Hydratyre' hits a wet or icy road, the huge local pressure will form solid hydrate, binding it to the road. As it lifts away, the pressure will be released, and the hydrate will decompose again. In wet or frost, the Hydratyre will be utterly skid-proof. In the dry, however, its non-rubbery coating may be a trifle slippery.

This paradoxical property may pose novel hazards. Amazed at how surely they can drive in wet and snow, drivers may be tempted into still more frightful risks on dry roads. Until all drivers have adjusted to their new Hydratyres, road authorities may have to minimize the danger by spraying water or ice on the roads in hot weather. David Jones