The results of the Sgró and Partridge study differ from those of a similar study by Service and colleagues (*7*, *8*). Service's group compared "B" and "O" lines of fruit flies (*9*), which are analogous to the young and old lines, respectively, in the Sgró and Partridge study. The B lines have a steeper increase in mortality rate than O flies early in life and higher mortality rates throughout their lives (*7*) (see the figure, bottom). This is in contrast to the wave of increased mortality among young fly lines at the onset of aging found in the new study (*2*). Service's group (*8*) compared the longevities of mated and unmated B and O lines of fruit flies. They found that unmated, nonreproducing flies lived longer than mated flies, but that the difference in longevity remained the same for both lines whether they were mated or not.

There are three possible explanations for the differences between the B and O and young and old lines. First, the lines themselves were derived from different baseline stocks of *Drosophila*, so the way in which they "evolved" may reflect genetic differences that were there from the start. Second, the flies in Service's experiments (*8*) had normal intact ovaries, whereas those in the new study did not. In fact, many of the unfertilized flies in the Service study still produced some eggs, thus incurring some reproductive cost. Third, there were differences in the mode and intensity of selection for young and old lines. In terms of mode, Sgró and Partridge's selection regime more effectively isolated age-specific egg production as the agent of selection. In terms of intensity, the Service group progressively increased the intensity of selection by increasing the difference in B and O line generation times from two- to fivefold (*9*). In contrast, Sgró and Partridge sustained a steady twofold difference in generation time between young and old lines throughout selection.

The effects of the mode of selection can be evaluated by adopting a selection regime similar to that used by Service and colleagues (*9*), and by selecting for new derivatives from the young and old lines. The effects of the intensity of selection can be evaluated by first increasing the intensity of selection on the derivatives of the young and old lines, and then by repeating the experimental manipulations that abrogate reproduction. If the differences between the two studies can be attributed to the baseline population or selection regime, then this diversity in outcomes may be giving us a glimpse of the true complexity of the genetics of aging and the diverse mechanisms by which a changing life-span evolves. Regardless of whether the disparities between these findings are resolved, the Sgró and Partridge study has provided a new means for understanding the evolutionary relationship between reproduction and mortality.

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PERSPECTIVES: APPLIED PHYSICS

Semiconductor Lasers Lose Their Cool

Richard M. De La Rue

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Semiconductor lasers are used widely in applications ranging from telecommunications to compact disc (CD) players to atmospheric chemistry. A relatively new concept in semiconductor laser technology, the quantum cascade (QC) laser, promises to revolutionize laser technology in the mid- to far-infrared spectrum. Vertical cavity surface emitting lasers (VCSELs) are also promising because the perpendicular beam they emit allows arrays of lasers to be packed closely on a wafer surface, thus enabling large arrays of lasers to be manufactured at low cost. Three recent papers (*1–3*) explain how some of the remaining technical obstacles to the wider applicability of QC and VCSEL lasers may be overcome.

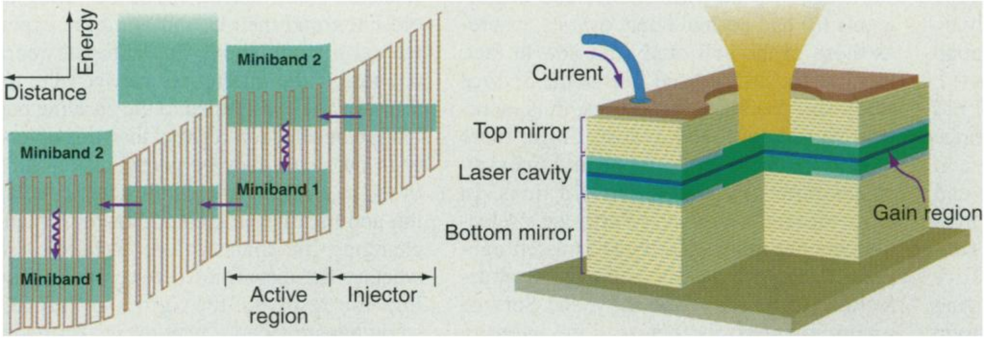
Traditional semiconductor lasers are diodes and can operate at or above room temperature. They are also capable of continuous, as opposed to pulsed, operation. "Pump" power is delivered by an electric current injected into the junction region of the diode. In contrast, QC and VCSEL lasers have until recently been restricted to low temperatures. The three papers (*1–3*) describe QC and VCSEL lasers operating at room temperature, although none demonstrates continuous operation and only one (*1*) describes devices pumped by electrical current injection.

Initial demonstrations of a new type of semiconductor laser typically involve optical rather than electrical pumping. Optical pumping by short excitation pulses avoids substantial heating and bypasses the engineering challenges inherent in delivering high electric current densities into the active region. Such device engineering is a major issue in VCSELs, in blue lasers based on nitrides, and in quantum cascade lasers where the potential drop across the device implies much heat generation. Krestnikov *et al.* (*2*) and Someya *et al.* (*3*) use a vertical cavity device geometry for their blue nitride-based lasers, thus combining two forms of device engineering difficulty when attempts are made to extend them to electrical pumping. Most new semiconductor lasers also do not begin as room temperature devices, their obvious operating regime. The standard approach has been to start with optical pumping at cryogenic temperatures and low duty-cycle excitation by short pulses. Cryogenic cooling has also been used with electrically pumped lasers, because the threshold current for lasing increases exponentially with temperature. Optical pumping is generally much less efficient than electrical pumping, but this is not necessarily a problem because high instantaneous power pulses are readily obtained, for example, from mode-locked titanium-sapphire lasers or, at shorter wavelengths, from nitrogen gas lasers. In (*2*) and (*3*), the instantaneous pump level is about 1 MW cm^{-2}; by contrast, the best semiconductor lasers have threshold power densities of well below 100 W cm^{-2}.

Most semiconductor lasers are based on direct band gap III-V compounds. Active structures are grown epitaxially on single-crystal substrates of gallium arsenide (GaAs) or indium phosphide (InP). A notable exception is the blue semiconductor laser (*4*, *5*), which is usually grown on insulating substrates of single-crystal sapphire. QC lasers (*6*) retain the use of substrates of GaAs or InP but involve the growth of remarkably complex and precise epitaxial structures. QC lasers are unusual in their use of a single type of current carrier (electrons), instead of the traditional *p-n* diode in which light is generated through electron-hole recombination. Traditional laser technology does not easily enable coherent laser emission in the infrared, but the advent of the QC laser is likely to change this situation radically.

The paper by Müller *et al.* on QC

The author is in the Optoelectronics Research Group, Department of Electronics and Electrical Engineering, University of Glasgow, Glasgow G12 8QQ, Scotland, UK. E-mail: R.Delarue@elec.gla.ac.uk



Recent advances in laser technology. The VCSEL laser **(right)** emits light perpendicular to the device; traditional lasers emit light from the edges. The QC laser **(left)** exploits quantum confinement of electrons in ultrathin layers of semiconductors.

lasers (*1*) describes operation at or below room temperature (300 K), and their epitaxial structure was designed for good performance at room temperature. But results were obtained with pulsed operation at a low duty cycle, because the total instantaneous current and power injected into the laser are typically 2 A and 16 W, respectively. Although these values may not seem large, the power density, with an active area of about 0.04 mm^2, is nearly half a gigawatt per square meter.

The electrical power density level in (*1*) is much less than the optical pumping levels involved in (*2*) and (*3*). The provision of an adequate thermal management scheme even for 16 W is nontrivial and not easily justified on cost, weight, and complexity grounds. So it is quite plausible that practical QC lasers either will use low duty-cycle operation at an average drive power level of a few milliwatts, rising to 0.6 W at a maximum duty cycle of 4%, or will operate continuously in more compact device structures with the same threshold current density. Because they were concerned with obtaining electrical tunability, Müller *et al.* used a three–quantum well combination that gives a substantial quantum-confined Stark effect (*1*). By using a two-contact configuration, they could control the emission wavelength and the output power level of the laser independently while avoiding the temperature changes caused by continuous operation.

The "engineering" issues of design, construction, and operation of new semiconductor lasers discussed above are hardly the stuff of revolution, but the devices described are likely to be important for a variety of applications. Both types of lasers allow high power densities. QCs will, for example, allow high-resolution mass spectrometry over much of the IR spectrum, and the blue VCSELs will find application in high density optical storage. A recent paper on quantum dot emitters embedded in high-Q resonant cavities (*7*) may lead to even more sophisticated combinations of light generation and cavity structure. This device, in which a selectively oxidized nanocavity contains a quantum dot, may allow photon emission events to be controlled individually, even at usefully high power levels. Such control is not only of physical interest but also has the potential to radically transform the nature of fiber-optical communications.

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PERSPECTIVES: NEUROBIOLOGY

The CRYs of Flies and Mice

Paul E. Hardin and Nicholas R. J. Glossop

Essentially all organisms (microbes, plants, and animals) use an endogenous timekeeping system, termed the circadian clock, to control daily rhythms in physiology and behavior. In each organism studied thus far, the clock's timekeeping mechanism, or oscillator, is characterized by an intracellular feedback loop in which expression of a group of genes results in production of proteins that then switch off the expression of those genes. The circadian feedback loops of the fruit fly *Drosophila* and mice (see the figure) are similar in that they are controlled by a homologous set of transcriptional activator proteins (CLOCK and BMAL1 in mice; dCLK and CYC/dBMAL1 in *Drosophila*) and inhibitors that block these activators (mPER 1, 2, and 3 and maybe mTIM in mice; PER and TIM in *Drosophila*) (*1*). In addition to keeping circadian time, the feedback loop maintains synchrony with environmental light-dark cycles by shifting phase in response to light. Discovery of the blue light receptor CRYPTOCHROME (CRY) in *Drosophila* and mice fueled speculation that this protein would mediate circadian photoreception in both species (*2*). Although this turned out to be the case in *Drosophila* (*3*), on page 2531 of this issue Okamura and colleagues now provide strong evidence that mouse CRYs (mCRYs) act as transcriptional inhibitors within the circadian feedback loop and not as circadian photoreceptors (*4*).

Although the *Drosophila* and mouse circadian feedback loops have similar components, they function at opposite phases of the circadian cycle and mediate light-dependent phase resetting through different mechanisms. In *Drosophila*, transcription of the *per* and *tim* genes is activated by dCLK-CYC protein dimers late in the day and inhibited by PER and TIM proteins late at night (*1*). In contrast, transcription of *mPer1*, *mPer2*, and *mPer3* is activated by CLOCK-BMAL1 dimers early in the day and repressed by the mPER proteins and perhaps mTIM late in the day (*1*). Despite these phase differences, *Drosophila* and mice show similar responses to light pulses administered during the dark phase. In both, light administered early in the dark phase causes phase delays, whereas light administered late in the dark phase causes phase advances. The mechanisms by which light resets the clock are, however, vastly different in *Drosophila* and mice. In *Drosophila*, light leads to the degradation of TIM protein (*5*). In mice, light causes the rapid induction of *mPer1* and *mPer2* transcription (*6*). Hence, light acting during the early night causes a phase delay due to prolonged high levels of *mPer1* and *mPer2* transcripts, whereas light acting during the late evening prematurely produces *mPer1* and *mPer2* transcripts that advance the clock.

A key issue in both *Drosophila* and mice is the identity of the circadian pho-

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The authors are in the Department of Biology and Biochemistry and Biological Clocks Program, University of Houston, Houston, TX 77204, USA. E-mail: phardin@uh.edu

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