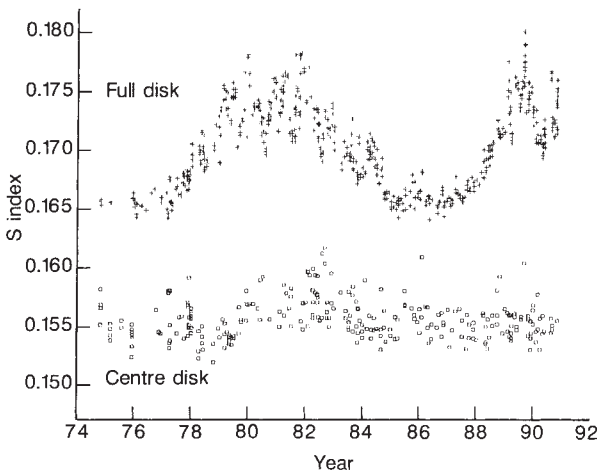subtle global effects. Further-more, the K-index for the centre of the disk is systemat-ically weaker than the full-disk measurement at solar minimum. Evidently, the disk-centre observations cor-respond closely to the non-magnetic component of the quiet Sun. Hence, the level of emission in quiet regions at disk's centre must be representative of the degree of activity (actually, 'inactivity' would be more appropriate) that would be expected during a Maunder minimum phase. In fact, an approximate conversion between the Mount Wilson 'S-index' used by Baliunas and Jastrow and the K-index measured by Livingston and White indicates that the quiescent disk-centre obser-vations are very similar to the mean value of the S-index for the magnetically flat stars in the sample considered in the current work.

The strength of the Ca II K line as measured by W. C. Livingston and O. R. White using the McMath telescope of the National Solar Observatory. The measurements have been approxi-mately converted to the 'S-index' used at Mount Wilson. The full disk data denoted by (+) clearly show the solar cycle. The disk-centre observations are represented by boxes. The data obtained before 1984 are observations of the geometrical centre of the disk. Following 1984, the data are nominal disk-centre observations — that is, the 2 arcminute aperture was moved around slightly to isolate the K index for the most quiet area, uncontaminated by magnetic active regions, in the neighbourhood of disk centre.

Other crucial solar parameters, such as the effective temperature, may also vary. Observations[8] of the temperature-sensitive neutral carbon line at 538.0 nm, which is formed in the solar photosphere, show that this feature has been getting steadily stronger over the past 12 years. The increase seems to be unmodulated by the activity cycle, and indicates a tem-perature rise of 4.6 K. This value, in turn, implies an increment in the solar constant (about 0.3 per cent) which is greater than that seen by the ACRIM experiment (about 0.1 per cent). The photospheric model used for the carbon line may be wrong, of course, or the change in the strength of this feature may be due to other factors, such as microturbulent velo-city fields, in addition to variations in effective temperature.

By contrast, other investigations[9] based on sensitive measurements of the limb brightness suggest that a substantial frac-tion of the variation in the solar irradiance during the cycle can be attributed to tem-poral changes in the latitude-dependent surface temperature of the Sun. This approach depends upon the application of a model-dependent correction for the con-tributions by spot complexes and faculae to the observed flux variability.

On stellar evolutionary timescales, we know that young stars are characterized by enhanced levels of magnetic-field-related chromospheric and coronal emission with X-ray and extreme-ultraviolet fluxes 100–1,000 times the present solar values[10]. These enhanced levels of activity decay with time accord-ing to an exponential or a power-law dependence[11]. If the Sun followed the same path of evolution, then its irradiance in the ultraviolet was once substantially greater than today. These results have been used in exploring the atmosphere of the young Earth, especially with respect to the formation of free oxygen and a pro-tective ozone layer in advance of biologic-al activity[12]. Among the key questions that arise, however, is whether the Sun actual-ly passed through this 'T Tauri' stage of evolution and what the state of the Earth might have been at the time. Stellar obser-vations provide circumstantial evidence that the young Sun did experience a T Tauri phase; certainly, the very existence of our Solar System is consistent with the formation of a disk around a pre-main sequence Sun, as observed in many T Tauri stars. Irradiation records locked within meteorites contain evidence for an enhanced level of flare activity in the solar past though the question still remains open[13].

Because ultraviolet variability con-tributes significantly to solar, and prob-ably stellar, total irradiance variations[14], and because energy at these wavelengths is screened from us by the ozone layer, any further elucidation of the cycles will require space-based observations. Indeed solar ultraviolet variations may have important consequences for the terrestrial climate and, if for that reason alone, the solar–stellar connection will continue to be explored. □

Mark S. Giampapa is in the National Solar Observatory, National Optical Astronomy Observatories, PO Box 26732, Tucson, Arizona 85726, USA.

8. Livingston, W. C. in Climate Impact of Solar Variability (eds Schatten, K. H. & Arking, A.) 336–340 (NASA CP 3086, Washington DC, 1990).
9. Kuhn, J. R., Libbrecht, K. G. & Dicke, R. H. Science 242, 908–910 (1988).
10. Giampapa, M. S. in Solar Radiactive Output Variations (ed. Foukal, P.) 241–249 (CRI, Cambridge, Massa-chusetts, 1987).
11. Walter, F. M. & Barry, D. C. in The Sun in Time (eds Sonett, C. P., Giampapa, M. S. & Matthews, M. S.) (University of Arizona Press, Tucson, in the press).
12. Canuto, V. M. et al. Nature 305, 281–286 (1983).
13. Caffee, M. W. et al. in The Sun in Time (eds Sonett, C. P., Giampapa, M. S. & Matthews, M. S.) (University of Arizo-na Press, Tucson, in the press).
14. Lean, J. Science 244, 197–200 (1989).

ANION TRANSPORT

Revelations of a chloride channel

Harvey F. Lodish

THE cloning and sequencing of the first voltage-gated chloride channel, reported by Jentsch and colleagues on page 510 of this issue[1], is notable for several reasons. The electroplax channel of the electric ray (*Torpedo*) defines a new class of mem-brane channel proteins; in particular, its sequence is unrelated to that of glycine- or GABA-triggered Cl⁻ channels or to vol-tage-gated sodium or potassium channels. The report illustrates the power of strate-gies based on functional expression for cloning rare messenger RNAs whose pro-tein products are not purified or even identified. And the channel's complemen-tary DNA may provide an entrée into identification and cloning of other Cl⁻ channels, particularly the one(s) in airway epithelial and other cells whose regulation is altered in cystic fibrosis.

Why is the electric organ of *Torpedo* so rich in Cl⁻ channels? Jentsch et al. esti-mate that one mRNA per 1,000 in the cells codes for the cloned channel. The organs consist of stacks of modified muscle cells that have lost contractile fibres. The 'top' surface of each cell is innervated by cholinergic neurons, whose stimulation activates nicotinic acetylcholine receptors, causing Na⁺ entry and depolarization of (mainly) the 'top' plasma membrane. The 'bottom', or contra-innervated, plasma membrane, in contrast, is abundant in Cl⁻ channels. The increased permeability of this membrane to Cl⁻ balances the entry of Na⁺, and 'clamps' the potential of the 'bottom' membrane close to its resting potential of 90 mV, inside negative.

The combination of depolarization of the 'top' membrane (becoming slightly

inside-positive) and normal polarization of the bottom (inside-negative) results in a voltage gradient across each cell, top-to-bottom, of about 90–100 mV ('bottom-positive'). The stacking of hundreds of such cells, like batteries in a series, generates the stunning potential of about a hundred volts characteristic of these organs. The abundance of acetylcholine receptors in the cells was essential to their cloning[2], and similarly Jentsch took advantage of the abundance of Cl⁻ channels in using them as the source of mRNA.

The electroplax Cl channel, like the erythrocyte anion exchange protein, band 3, is inhibited by the drugs based on modified stilbene disulphonates such as DIDS. However, a relatively high concentration — in the micromolecular range — is required for inhibition. Surprisingly, the two main DIDS-binding proteins in electroplax membranes are the α subunit of the $(\text{Na}^+ + \text{K}^+)$ ATPase and a second protein Jentsch and colleagues cloned a few years ago but which is not a subunit of a Cl⁻ channel[3]. This highlights the potential hazards in using an inhibitor of relatively low affinity and specificity to purify a channel (or any other) protein.

The cloning strategy that was ultimately successful involved functional expression of the protein in *Xenopus* oocytes. Injection of total electroplax mRNA induces expression of a voltage-sensitive Cl channel, and Jentsch *et al.* selected cDNAs that, when hybridized to total mRNA, removed (hybrid-depleted) the channel-inducing activity. Moreover, an RNA transcript of the full-length cDNA *in vitro* induced expression of Cl⁻ channel activity. The encoded protein of 805 amino acids, has 12 (or 13) presumed membrane-spanning α helices and in sequence does not resemble any known protein.

The cloned channel protein is voltage-sensitive; that is, it is slowly activated when the membrane is hyperpolarized. Perhaps surprisingly, the channel does not contain a sequence resembling the presumed 'voltage gating helix' (helix 4) in voltage-dependent K^+ and Na^+ channels, where every third residue is arginine or lysine[4]. However, these cation channels open when the membrane is depolarized.

The cloned channel protein has many properties in common with the major electroplax Cl⁻ channel studied in detail by Miller and his associates in reconstituted lipid bilayers[5]. In particular, once the channel is opened the flux of Cl⁻ ions increases with membrane depolarization. Single-channel recording will be required to determine whether the two are identical (there may be a regulatory subunit). Both the electroplax Cl channel and one from kidney have two Cl⁻ diffusion pathways, and the electroplax channel is thought to be a homodimer. The opening and inactivation of the two Cl⁻ 'proto-channels' are coupled to the chloride transmembrane electrochemical gradient — a novel mechanism of channel gating[6] — and it will be of some interest to see whether this property is intrinsic to the cloned Cl⁻ channel protein.

An important question is the relationship of this channel to the apical Cl chan-nel in airway and sweat duct (and other) epithelial cells which is defective in cystic fibrosis (CF)[7,8]. The cloned 'CF gene' product is almost certainly not a Cl⁻ channel, but a protein that regulates channel activity, even though expression of a wild-type gene in a CF epithelial cell reverses the defect in Cl⁻ transport[9,10].

Can one use molecular hybridization with the electroplax channel cDNA to clone the mammalian 'CF Cl⁻ channel'? Can it be used to clone other interesting Cl channels, such as those in coated vesicles[11] or in the apical membrane of the gastric oxyntic cell[12] that, together with an ATP-driven H^+ pump, are required to establish a pH gradient? Attempts of this sort with other ion transport proteins might be instructive. When Kopito and I cloned the erythrocyte anion exchange protein[13], we thought we could use the cDNA as the probe to isolate clones for anion channel proteins. This approach did yield two other cDNAs encoding anion exchangers but no anion channels[14]. The cDNA encoding the *Drosophila Shaker* voltage-sensitive K^+ channel has been used to clone a large number of insect and mammalian K^+ channel proteins[15]. But this large 'superfamily' does not include two key types of K^+ channel proteins, those activated by ATP or by Ca^{2+} ions. Thus, once one clones a new type of channel protein or transporter, one can rather quickly clone its close relatives, yet increasingly sophisticated expression cloning strategies will be needed to clone entirely new types of membrane proteins. How many families of anion channels exist is an open and pressing question. □

Harvey F. Lodish is in the Whitehead Institute and Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts 02142, USA.

1. Jentsch, T.J., Steinmeyer, K. & Schwartz, G. *Nature* **348**, 510–514 (1990).
2. Noda, M. *et al. Nature* **302**, 528–532 (1983).
3. Jentsch, T.J., Garcia, A.M. & Lodish, H.F. *Biochem. J.* **261**, 155–166 (1989).
4. Jan, L.Y. & Jan, Y.N. *Cell* **56**, 13–25 (1989).
5. Miller, C. & Richard, E.A. in *Chloride Channels and Carriers in Nerve. Muscle. and Glial Cells* (eds Alvarez-Leefsmans, F.J. & Russel, J.M.) 383–405 (Plenum, New York, 1990).
6. Richard, E.A. & Miller, C. *Science* **247**, 1208–1210 (1990).
7. Quinton, P.M. *FASEB J.* **4**, 2709–2717 (1990).
8. Welsh, M.J. *FASEB J.* **4**, 2718–2725 (1990).
9. Rich, D.P. *et al. Nature* **347**, 358–364 (1990).
10. Drumm, M.L. *et al. Cell* **62**, 1227–1233 (1990).
11. Xie, X.-S., Crider, B.P. & Stone, D.K. *J. biol. Chem.* **264**, 18870–18873 (1989).
12. Demarest, J.R., Loo, D. & Sachs, G. *Science* **245**, 402–404 (1989).
13. Kopito, R.R. & Lodish, H.F. *Nature* **316**, 234 (1985).
14. Lindsey, A.E. *et al. Proc. natn. Acad. Sci. U.S.A.* **87**, 5278–5282 (1990).
15. Jan, L.Y. & Jan, Y.N. *Trends Neurosci.* **13**, 415–419 (1990).

DAEDALUS

Only connect

BRITAIN, like many other countries, suffers chronically from road congestion. Existing roads can be upgraded and new ones built, but every stretch of extra road is jam-packed from the moment it is opened. Daedalus now proposes to double or triple our road capacity almost at a stroke.

He points out that in a fast stream of traffic, each car is separated from the next by at least ten car-lengths of empty road. This gap gives each driver the chance to see and react to the brake lights of the car ahead, should it decelerate unexpectedly. Simply by halving the reaction time of the drivers, the cars could pack twice as tightly, and road capacity would double.

The obvious technology for this job is the short-range infrared link used to control television sets. An infrared brake light, coded not merely to say that the brake was on, but to relay the changing speed and deceleration of the vehicle, could easily be detected by the car behind. Faster than any human driver, it could apply the appropriate brake force to avoid collision. In the process, of course, it would transmit its actions to the car behind it, and the message would pass down the traffic stream. A forward-shining infrared 'acceleration light', telling each car the speed and acceleration of the one behind, would complete the system. The stream of traffic would become a virtual train, its cars coupled tightly by invisible elastic couplings.

The technology should be quite simple. Many modern cars have power brakes and electronic engine management systems that lend themselves to remote control; the new fittings would be mainly cheap electronics with few expensive mechanics. Two vehicles equipped with the system would establish communication by a 'handshake' of the sort used by fax machines, and would then close up to their safe distance. A dashboard light would warn each driver of the connection, and his instinctive alarm at the tight spacing should soon wear off. Drivers should soon learn to switch rapidly between normal and 'automatic' safe distance perception, just as they switch rapidly between the different safe driving rules for single and multiple carriageways.

Once brought to market, the new system should spread fast. Drivers without it, painfully aware that their car was being shunned by those around, will be shamed by this continuous public demonstration of their disregard for safety, wasteful use of road space, and lack of the latest motoring gadget. All over our newly capacious motorway network, the 'trains' of self-satisfied, tight-packed motorists will increase in length and frequency. Soon only the odd unmodified banger will stagger along in enforced isolation, a pariah of the roads. David Jones