Tuning retinal circuits

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While studying the retina more than 100 years ago, Santiago Ramón y Cajal noted that deposits of silver dichromate completely filled the arborization of a single neuron but stopped at the cell boundary. He concluded that contiguous neurons are discrete and that signals between them must cross an extracellular gap, now known as a chemical synapse. He vigorously defended this idea against 'reticularism', the view that neurons form continuous networks, with his penetrating observations and towering polemics, and by 1935 reticularism was apparently crushed.

But we now know that the reticulartists were also right: retinal neurons can couple with one another by means of clusters of fine intercellular channels called gap junctions and it seems that this coupling is crucial for retinal function. New results described on page 734 of this issue by Mills and Massey offer a deeper insight into reticularism with the demonstration that these gap junctions differ in pore size at different points in a circuit and that they are regulated by different second messengers.

The authors injected tracers of different molecular weights into an AII amacrine cell of the rabbit retina (maintained in vitro) and followed their spread into adjacent neurons to which the AII is known to be coupled. As expected, the smaller tracer spread into the neighbouring AII cells and cone bipolar cells. A larger tracer with the same charge also spread readily into AII cells, but penetrated poorly into cone bipolars (see Figs 2 and 3 of Mills and Massey's paper). High concentrations of cyclic AMP were already known to curtail tracer spread to AII cells, and the authors found that cyclic GMP had a similar effect on tracer spread to cone bipolar cells (see their Fig. 4).

This discovery of a difference in pore size and in second messengers raises a host of questions that may eventually link the architecture of microcircuits to that of their computationally important molecules. To grasp the key issues requires some knowledge of the overall circuitry in which the AII cell is a critical link (see figure).

Neural signals for daylight and starlight are transduced by different photoreceptors (cones and rods respectively) and traverse the retina over different circuits — until the last stage, which is transmission to the ganglion cell. This stage requires 10-10 chemical synapses (because each synapse operates stochastically), and these occupy most of the ganglion cell's dendritic surface. So, to provide separate sets of synapses would require either fewer synapses per circuit (compromising signal quality) or more space.

An alternative design has been adopted universally by mammals: cone bipolar cells contribute one full set of excitatory chemical synapses to the ganglion cell, and rod bipolar cells 'borrow' them at night by chemically exciting the AII cell, which through extensive gap junctions passes depolarizing (excitatory) ionic currents into the cone bipolar synapses.

Direct coupling avoids both delay and additional stochastic fluctuation and functions as a simple manoeuvre to transfer the starlight signal to the ganglion cell.

But there is a catch. In daylight, cone-evoked depolarizations should spread backwards from the cone bipolar synapse into the AII cell and then laterally, as a result of coupling between neighbouring AIIIs. This would expand the summation area of the individual ganglion cell well beyond its dendritic field and thus degrade the spatial detail carried by the ganglion cell array. So, once the neural connections were recognized as a 'circuit', it was predicted that the AII-cone bipolar junction should uncouple in daylight. The demonstration by Mills and Massey that coupling at this junction is indeed reversible is gratifying and strengthens our interpretation of retinal circuitry.

The coupling between AII cells addresses an entirely different problem. In one second of starlight, fewer than one rod in a thousand transduces a photon. Therefore the several thousand rods wired to a ganglion cell carry mostly noise, which potentially obscures the rare light events. But photons reflected from an object in the visual scene, although thinly spread, are correlated. Coupling spreads the correlated signal to many AIIIs, reducing signal amplitude but reducing the uncorrelated noise even more. This manoeuvre improves the signal-to-noise ratio in the AII cell, which can then remove residual noise by using voltage-sensitive sodium channels to set a threshold. Coupling in the AII network may increase gradually with nightfall in order to optimize spatial averaging to the cone terminals and thus the rest of the cone bipolar circuit. In starlight, only one rod per thousand transduces a photon over one second, so the rod-cone junction conveys mostly noise. Consequently, this junction uncouples, and rod terminals excite rod bipolar cells to excite AII amacrine cells chemically. The AII cell couples to the cone bipolar axon, in effect parasitizing the cone bipolar-to-ganglion cell synapses. Gap junctions couple AII cells strongly enough to spread current widely and thus enlarge the ganglion cell's summation area well beyond its dendritic tree. This would improve signal-to-noise ratio in the dimmest light, but degrade acuity in brighter light, so this junction is also regulated.

To convey the full range of environmental intensities requires three different but partially overlapping neural circuits. The mammalian retina accomplishes this at no extra cost in space or noise by using four sets of gap junctions (red), at least three of which are regulated. In daylight, cone terminals excite (depolarize) cone bipolar cells that chemically excite the ganglion cell. This last excitatory stage occupies most of the ganglion cell's dendritic surface (some space is reserved for inhibitory synapses). Gap junctions couple the cone terminals strongly enough to improve signal-to-noise ratio, but not so much as to degrade acuity. In twilight, cones are less active, but the 50 rods surrounding each cone couple to it via their terminals. In effect, rods 'parasitize' the cone terminals and thus the rest of the cone bipolar circuit. In starlight, only one rod per thousand transduces a photon over one second, so the rod-cone junction conveys mostly noise. Consequently, this junction uncouples, and rod terminals excite rod bipolar cells to excite AII amacrine cells chemically. The AII cell couples to the cone bipolar axon, in effect parasitizing the cone bipolar-to-ganglion cell synapses. Gap junctions couple AII cells strongly enough to spread current widely and thus enlarge the ganglion cell's summation area well beyond its dendritic tree. This would improve signal-to-noise ratio in the dimmest light, but degrade acuity in brighter light, so this junction is also regulated.

NATURE VOL 377 26 OCTOBER 1995
676
SEMICONDUCTOR HETEROSTRUCTURES

Magnetic grains in GaAs

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As the fabrication of structures such as quantum wells in semiconductors has become commonplace, a whole world of new ultra-compact electronic devices has been opened up. If discrete magnetic components could be incorporated into such structures, their technological potential would be increased still further; but, so far, combining magnetic compounds with semiconducting matrices to produce sizeable magnetic effects has proved difficult. Now, as they describe on page 707 of this issue, Jing Shi and colleagues1 have developed a new method of incorporating minute ferromagnetic grains into a semiconducting matrix.

The host material, a thin film of gallium arsenide, is first implanted with high-energy Mn ions. Subsequent thermal treatment activates a crystallization process, resulting in situ formation of submicrometric GaMn grains. From sophisticated techniques that allow one to examine individual grains, Shi et al. found that the crystallographic structure of the insets was different from all other known bulk GaMn modifications. In particular, the data revealed fivefold symmetry, the signature of quasicrystallinity. This is intriguing in itself, but the more important point is that the grains were ferromagnetic—good news indeed for semiconductor physicists.

Artificially structured systems prepared by ‘atomic engineering’ methods are currently much in vogue with condensed matter physicists and material scientists. These systems may be granular solids of various forms (grains embedded in a solid matrix or contained in ‘nushells’ made of another material) or multilayers prepared on flat surfaces by depositing layers of two or more different materials in combination. Such heterostructures show physical effects not seen in bulk solids, many of which may prove useful for building new generations of miniature electronic or optoelectronic devices. Perhaps the best-known example is that multilayers composed of different semiconducting materials are practical realizations of quantum-mechanical potential wells. By changing layer thicknesses and compositions, one can control well characteristics such as depth and shape, and thus manipulate the quantum states of entrapped electrons to obtain desired patterns of energy levels. The principle has been used for the design of a blue-green solid state laser2 which could quadruple the capacity of compact discs.

Systems fabricated from combinations of magnetic and non-magnetic materials are an important class of artificially structured solids. The mobile and valence electrons that determine the electronic properties of such systems interact with the magnetic atoms, further modifying their quantum states. This gives rise to a variety of new effects, many of which seem to be strongly sensitive to external magnetic fields, and might therefore be exploited for constructing new field-tunable electronic sensors and devices. One effect that is currently attracting much attention is giant magnetoresistance, an unusually strong dependence of the electric conductivity on external magnetic field, which is seen in certain metallic granular solids as well as in multilayered structures.

Strong interest in semiconducting systems containing magnetic implants was first aroused in the mid-1970s following the discovery that substituting magnetic ions for a small fraction (say, 5 per cent) of the metallic cations in a semiconducting material leads to profound changes in the material’s optical, magneto-optical and conducting properties. For example, such alloys (usually referred to as ‘semimagnetic semiconductors’) show an unusually strong Faraday effect—in a magnetic field, they rotate the polarization vector of transmitted light by an amount proportional to the applied field intensity. This effect can be used for building light modulators as well as ‘light valves’ for fibre-optic technology.

Currently, research on epitaxial multi-