directly. In a few instances it was possible to identify the location of coupling as the axon of the coupled neuron. In these cases, the axonal coupling distance was 50–120 μm from the soma, which is before the myelin sheath usually begins.

What is the function of this axo–axonal coupling? It would certainly enable very fast communication between hippocampal neurons. The authors suggest that axonal coupling might underlie high-frequency oscillations and the synchronization of neuronal activity across networks, and could contribute to the abnormal discharges seen in epilepsy. They also comment that neuromodulators could open and close the gap junctions, thereby altering the network connectivity under different conditions, which would provide the system with great flexibility.

Rachel Jones

References and links

ORIGINAL RESEARCH PAPER Schmitz, D. *et al*. Axo–axonal coupling: a novel mechanism for ultrafast neuronal communication. *Neuron* **31**, 831–840 (2001)

FURTHER READING Galaretta, M. & Hestrin, S. Electrical synapses between GABA-releasing interneurons. *Nature Rev. Neurosci.* **2**, 425–433 (2001)

the involvement of the UPS system in synaptic development. Furthermore, the deficits in transmitter release, but not the morphological abnormalities, were partly rescued in loss-of-function *hiw;faf* double mutants. This observation indicates that the two phenotypes can be genetically dissociated, and that a balance between negative and positive regulators of the UPS controls synaptic function.

What are the synaptic substrates that are regulated by the UPS? Does a similar mechanism operate in other synapses and in other organisms? Is UPS function important for short-term synaptic plasticity? Like every groundbreaking article, this paper poses more questions than it answers.

Juan Carlos López

References and links

ORIGINAL RESEARCH PAPER DiAntonio, A. *et al.* Ubiquitination-dependent mechanisms regulate synaptic growth and function. *Nature* **412**, 449–452 (2001)

FURTHER READING Weismann, A. M. Themes and variations on ubiquitylation. *Nature Rev. Mol. Cell. Biol.* **2**, 169–178 (2001)

DEVELOPMENT

Ear see rescue

The vertebrate otocyst, which gives rise to the structures of the inner ear, invaginates from the hindbrain surface epithelium adjacent to rhombomeres 5 and 6 (r5 and r6). Induction of the otocyst requires signals from the hindbrain neuroepithelium, so it is not surprising to find that mutations that affect the patterning of the r4–r6 region can cause profound defects in inner ear development. *Hoxa1* is activated in r4–r6 around the time that the otocyst begins to develop, and its targeted disruption in the mouse leads to malformation of the vestibular apparatus and the cochlea. However, as reported in *Nature Genetics*, Pasqualetti *et al.* have now shown that these defects can be rescued by a sub-teratogenic dose of the vitamin A derivative retinoic acid (RA).

Although excess RA can severely disrupt hindbrain development, Pasqualetti *et al.* showed that a dose of 5 mg kg^{-1} was not teratogenic to wild-type embryos when administered from 8.0 days post coitum (dpc) onwards. Using this dose, they showed that vestibular and cochlear structures could be partially or fully rescued in *Hoxa1*$^{-/-}$ embryos if RA was administered between 8.0 and 8.75 dpc. Treatment outside this time period did not rescue the inner ear phenotype, indicating that there is a limited time window during which the RA response can compensate for the loss of *Hoxa1* function.

The authors then analysed changes in gene expression in response to RA treatment. *Hoxb1*, *kreisler* and *Fgf3* are usually expressed within the r4–r6 region, but they are all downregulated in *Hoxa1*$^{-/-}$ embryos. In embryos treated with RA at 8.0 dpc + 2 h, the expression of all three genes was transiently restored. However, in embryos exposed to RA at 8.75 dpc, only *Fgf3* was upregulated, yet inner ear development could still be rescued. This implies that *Fgf3* expression might be sufficient to rescue inner ear structures in *Hoxa1*$^{-/-}$ embryos, and that RA can replace the function of *Hoxa1* in activating the *Fgf3* signalling pathway.

So, this study points to a molecular mechanism through which *Hoxa1* might exert its effect on inner ear development, but Pasqualetti *et al.* argue that it could also have wider implications. The use of vitamin supplements during pregnancy is controversial, and its benefits are unclear, but there is no evidence that the amount of vitamin A in commercially available vitamin preparations is harmful to the fetus, and the authors suggest that there might be certain circumstances when it could even be beneficial.

Heather Wood

References and links

ORIGINAL RESEARCH PAPER Pasqualetti, M. *et al*. Retinoic acid rescues inner ear defects in *Hoxa1* deficient mice. *Nature Genet.* **29**, 34–39 (2001)

FURTHER READING Fekete, D. M. Development of the vertebrate ear: insights from knockouts and mutants. *Trends Neurosci*. **22**, 263–269 (1999)

NEUROELECTRONICS

Silicon neurons

The idea of developing neuroelectronic systems to use as neuroprosthetics has been around for a long while … in science-fiction books. Few neuroscientists have focused their attention on this very real challenge, despite the fact that it is becoming increasingly approachable. A recent study by Zeck and Fromherz should stimulate progress in this field, as they provide evidence that it is possible to transmit signals through a silicon–neuron–neuron–silicon circuit.

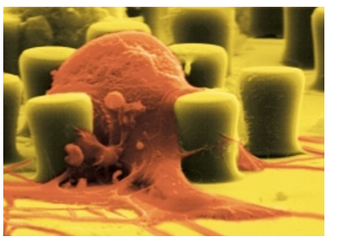
The authors cultured individual snail neurons on top of a stimulator and a transistor in a silicon chip. As these neurons form electrical synapses with neighbouring cells, the authors could trigger presynaptic action potentials by delivering voltage pulses to the stimulator, and record a spike in the postsynaptic neuron and a concomitant voltage change in the transistor under this cell. It is therefore feasible to form 'synaptic contacts' between electronic circuits and nerve cells. Although there are still many technological limitations to the development of more complex and efficient circuits, this proof-of-principle experiment is a fundamental step in a neglected field.

Juan Carlos López

References and links

ORIGINAL RESEARCH PAPER Zeck, G. & Fromherz, P. Noninvasive neuroelectronic interfacing with synaptically connected snail neurons immobilized on a semiconductor chip. *Proc. Natl Acad. Sci. USA* **98**, 10457–10462 (2001)

FURTHER READING Jenkner, M. *et al.* Interfacing a silicon chip to pairs of snail neurons connected by electrical synapses. *Biol. Cybern.* **84**, 239–249 (2001) | Ulbrich, M. & Fromherz, P. Neuron–silicon selfexcitation: a prototype of iono-electronics. *Adv. Materials* **13**, 344–347 (2001)



Snail neuron cultured on a silicon chip and surrounded by polyimide pickets. © 2000 National Academy of Science, USA.