mantle filtering theory used in these analyses assumes that the conductivity varies only in the radial direction. Yet magnetotelluric and other geomagnetic induction studies have shown that there are significant three-dimensional variations in electrical conductivity in the upper mantle. The magnetic field diffuses much more slowly through a good electrical conductor than a poor one. Could such structures distort an initially slowly varying field of core origin in such a way that changes at the surface occur much more rapidly? Calculations will be necessary to see if this speculation has any substance.

Regardless of one's point of view, one can but admire the care with which Coe *et al.* have done their experimental work. Eventually, the consequences should be profound. □

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DEVELOPMENTAL NEUROBIOLOGY

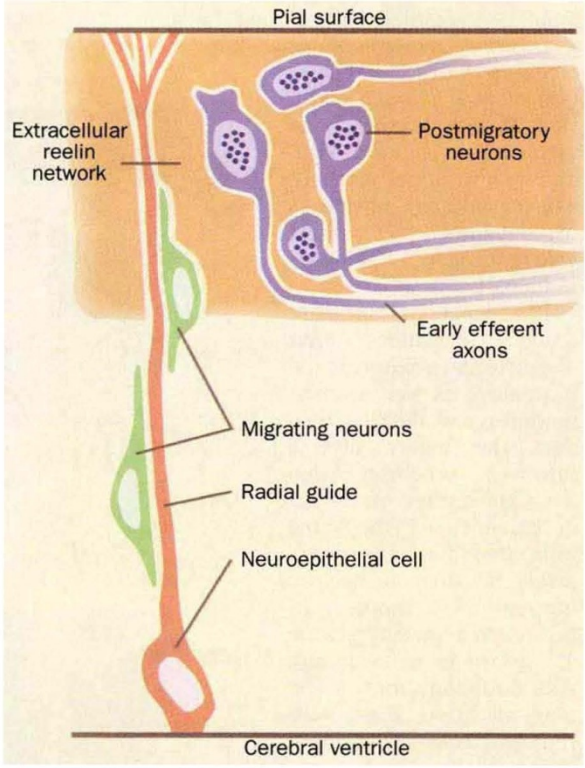
A real gene for *reeler*

André M. Goffinet

EVERY so often a paper comes along which shows we are indeed making significant progress towards understanding the sheer complexity of the mammalian brain, with its billions of neurons and connections, and how it develops in the embryo. One such appears on page 719 of this issue[1], where D'Arcangelo and colleagues report the cloning of the mouse *reeler* gene. It is a gem of a paper — although the authors say that the evidence is not entirely definitive, I find it compelling.

The *reeler* mutation has puzzled developmental neurobiologists for nearly 50 years, the long-lasting interest stemming from the unique phenotype that results (reviewed in refs 2 and 3). Briefly, in homozygous *reeler* embryos, neurons are generated in normal numbers, at the normal time. Initial neuronal migration occurs normally, as does differentiation of the various cell types, axonal and dendritic deployment, and formation of connections. However, from embryonic day 13–14, when the first migrating neurons reach their destination, cell patterning goes awry. This selective architectonic defect is most obvious in the cerebellar and cerebral cortices, but it occurs almost everywhere in the central nervous system.

Although the *reeler* mouse has been used successfully as a model of abnormal corticogenesis, the mutation's mechanism of action has remained unknown. Some investigators favoured the idea that aberrant *reeler* protein disturbs cell interactions between radial glial cells and migrating neurons[4], whereas others, including myself, thought it more likely that it affects homotypic adhesion between early postmigratory neurons[2,3]. Interestingly, Derer and Nakanishi[5] have proposed that extracellular, matrix-mediated cell interactions are disrupted by the defect. No satisfactory experimental approach could be found to progress along any of those lines, and the field has been relatively stagnant for the past few years.



A model for reelin action in cortical development. Neurons are generated in ventricular zones, along the cerebral ventricles, and migrate radially along the extensions of neuroepithelial (later glial) cells. Postmigratory neurons express the *reelin* gene as part of their differentiation programme. Reelin protein is incorporated in the extracellular matrix where it helps to stabilize cortical architectonic patterns.

Now *reeler* is back with a vengeance, with the appearance of the paper in this issue and the impending publication of three others. D'Arcangelo *et al.*[1] report the full-length *reeler* complementary DNA and present a first analysis of the deduced protein, dubbed reelin. Two other studies using positional cloning strategies[6,7] provide incomplete sequence data that confirm the more complete work[1] (although the length of the messenger RNA and size of the protein deduced by Hirotsune *et al.*[7] turn out to be wrong). A fourth paper[8] describes the characterization of an epitope that is specifically absent in *reeler* mice.

The results of D'Arcangelo *et al.* are highly impressive. The *reeler* gene encodes a long mRNA of about 12 kilobases. Reelin is a huge protein of 3,461 residues (relative molecular mass, 388K), with features that are highly indicative of a secreted extracellular protein. It shows homology to F-spondin, a protein secreted by the floor plate of the developing spinal cord that may contribute to the growth and guidance of axons in both the spinal cord and the peripheral nervous system[9], and to tenascin, a large, hexameric, extracellular matrix protein[10].

The *reelin* RNA is first detected in the embryonic brain on day 11.5. It then increases in concentration up to birth, remains high during the postnatal period and then declines progressively to adult levels; it is brain-specific. *In situ* hybridization studies detect the *reelin* RNA in postmigratory neurons in the external zone of the hemisphere at embryonic day 13.5, just before the *reeler* phenotype can be detected. The *reelin* transcript is also seen in early postmigratory neurons in other telencephalic fields. In external granule cells of the cerebellum, expression seems to be initiated at the end of tangential migration. Most strikingly, no *reelin* expression is found in the ventricular zones where the cell bodies of radial neuroepithelial cells are located. At the level of the cerebral cortex, early expressing cells could correspond to Cajal–Retzius cells, transient neurons that may act as 'pathfinder' neurons and be involved in the primordial organization of the cortex. It is worth noting that the epitope described by Ogawa *et al.*[8] is apparently also specific to Cajal–Retzius cells.

These results suggest a simple model of matrix-mediated radial corticogenesis, shown in the figure, which complements radial guidance of migrating neurons by glial cells. Reelin would be secreted locally by early postmigratory neurons to act as a neuron–matrix adhesion molecule and help stabilize early architectonic cell patterns[2,3]. The term 'stabilization' should not be taken in a restrictive, purely mechanical sense; indeed, for neuron–matrix–neuron interactions to influence

cell patterns, they must be relayed to the interior of the cell, to the cytoskeleton and signalling machineries[11,12]. In accord with previous studies of chimaeric mice (see for example ref. 13), the structure of reelin implies that it functions outside cells. To act as an architectonic-stabilization factor, reelin could interact with a cell-surface receptor, although the available data certainly do not rule out homophilic binding. To risk an educated guess, a reelin receptor might be analogous to the receptor-type protein phosphatase-β, the extracellular domain of which is similar to chondroitin sulphate proteoglycan and is able to bind to tenascin[14].

The new data provide a basis to address this matter and many others. The function of reelin in the developing brain can be analysed in structural and cell biological studies. If the expression of reelin is an integral part of early neuronal differentiation, how is it controlled, particularly at the transcriptional level? If reelin is indeed an adhesion protein necessary for architectonic development, what would happen in transgenic mice that overexpress it? From comparative embryological studies[3], it seems that the *reeler* gene participated in cortical evolution in the lineage leading from stem reptiles to mammals, and the cloning of *reelin* provides the opportunity to pursue this idea further.

Finally, the *reelin* gene is present in humans and maps to region 22 on the long arm of chromosome 7 (ref. 1). As yet, no human brain disorder has been mapped to this interval, and it could be that the *reeler* malformation is lethal in human embryos. Nevertheless, the possible role of the gene in human brain malformations and polygenic diseases such as schizophrenia will undoubtedly come under scrutiny.

The news of the cloning of *reeler* will be widely applauded by the neurobiological community. But — as ever — much work remains to be done, and it will keep several postdocs busy for several years. □

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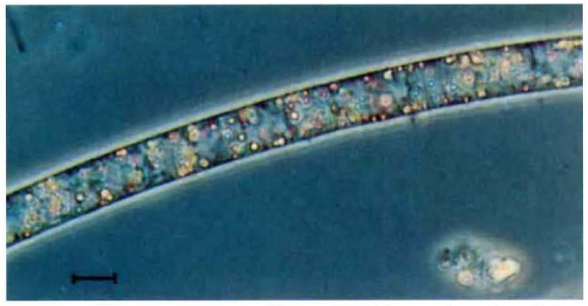
MICROBIAL ECOLOGY

Life at the sea floor

Holger W. Jannasch

THE microbial world continues to deliver surprises, the latest being announced by Fossing *et al.* on page 713 of this issue[1]. Seemingly defying their typical dependence on diffusion for their supply of nutrients, certain microorganisms grow in massive mats on the sea floor along the west coast of South America; such is their density that they wreak havoc with the local Peruvian and Chilean fisheries by clogging up nets with what is known locally as *estopa* (the Spanish for uncleansed wool)[2]. The principal constituent of these mats is a filamentous bacterium called *Thioploca* (Fig. 1), and its metabolic characteristics have long been a puzzle. Fossing and colleagues have now come up with the explanation of how *Thioploca* can exist at such densities, one involving a hitherto unknown nutritional mechanism for bringing nitrate as oxidant into direct contact with hydrogen sulphide as reductant.



M Hüttel

FIG. 1 Single *Thioploca* filament with enclosed sulphur globules. Scale bar, 40 μm.

The smallness of microbes guarantees their dispersal and ubiquity in the biosphere, as well as their readiness and ability to conduct the highly diverse turnover processes that keep the cycles of matter in balance. At the same time, their tiny size is necessary for them to acquire nutrients by simple diffusion. Whenever bacteria are grown in mass culture with doubling times of less than an hour, heavy stirring and constant nutrient supply are required. How, in principle, can things be different in nature?

Having been around at the time — 1977 — when the strange mats off the Peruvian and Chilean coast were discussed here at Woods Hole[3], I am only too aware of how little further information about them has been obtained since then. *Thioploca* has been known about for some time but data on the mats, which occur for a stretch of 3,000 kilometres, have been fragmentary and posed more questions than answers. Fossing and colleagues have now pulled the pieces together.

In a nutshell, their results are these: identification of particular nutrient concentrations below a very rich upwelling zone, with unusually high levels of nitrate and near-zero oxygen; characterization of the ability of the *Thioploca* cells to accumulate nitrate to even higher concentrations within large liquid vacuoles, and of the highly efficient gliding mobility of the nitrate-laden cell filaments within large slime sheaths; and elucidation of the unique metabolic role of this transport system, as depicted in Fig. 2*a*.

Thioploca, then, makes a living by bridging the nitrate-rich zone near the sediment surface, using nitrate as the

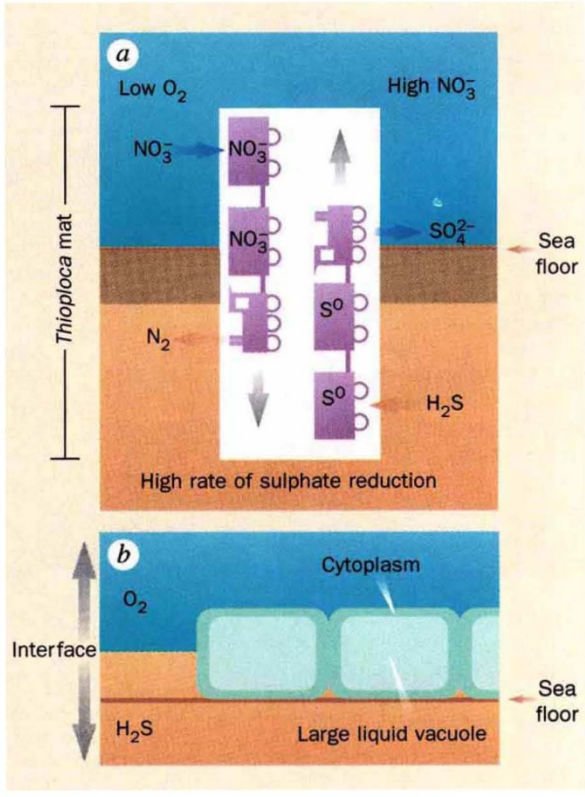


FIG. 2 *a*, Stationary interface and moving *Thioploca* filaments. *b*, Moving interface and stationary *Beggiatoa* filaments.