con nitride is part of a wider search in which the array of classical ceramic compounds is being expanded.

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1. Zerr, A. *et al. Nature* **400,** 340–342 (1999).
2. Hampshire, S. *Mater. Sci. Technol.* **11,** 119–171 (VCH, Weinheim, 1994).
3. Jack, K. H. in *New Oxide Technical and Engineering Ceramics* (ed. Hampshire, S.) 1–30 (Elsevier, London, 1986).
4. Segal, D. *Mater. Sci. Technol.* **17A,** 70–98 (VCH, Weinheim, 1996).
5. Riedel, R. *Mater. Sci. Technol.* **17B,** 1–50 (VCH, Weinheim, 1996).

Neurobiology

Discriminating migrations

Pasko Rakic

Many brain structures, like some frontier countries, are composed exclusively of immigrants. In the mammalian brain, for example, virtually all neurons migrate from their origin, near the cerebral ventricles, to the distant territories where they establish permanent residence. Although the mechanisms that attract neurons to their final destinations are not well understood, we know that certain brain structures discriminate between cell populations by discouraging specific classes of neuron from invading their territories. On page 331 of this issue, Wu *et al.*[1] reveal a molecular cue that guides neurons as they migrate from the postnatal rodent forebrain into the olfactory bulb. They show that this guidance mechanism depends on the brain structures that surround the migratory pathway — structures that repel migrating neurons from their borders, while leaving invasion of the olfactory bulb as an option.

In the developing nervous system, most neurons are generated at different sites from those in which they permanently reside[2]. The intervening process, termed neuronal migration, denotes the displacement of a neuronal cell body from its origin in the proliferative zones to its final destination in the mature brain. After they have finished dividing, cells dislodge from adjacent progenitors, extend a 'leading process', then move along specific pathways[2]. Interactions between the migrating neurons and the surfaces of neighbouring cells are crucial for the selection of migratory pathways, as well as for orientating, conducting and stopping neuronal movement at the appropriate site[3].

The main difference between neuronal migration and axonal navigation is movement of the cell body. Whereas it undergoes a unidirectional translocation in neuronal migration, the cell body remains stationary in axonal movement. Translocation is regulated by specific ion channels/receptors, which cooperatively regulate the calcium influx that is essential for the cytoskeletal rearrangements affecting the rate at which the neuron moves[4]. With regard to pathway selection, migrating neurons fall into two main categories — gliophilic cells, which show an affinity for the elongated radial glial fibres that guide their movement, and neurophilic cells, which preferentially stick to the

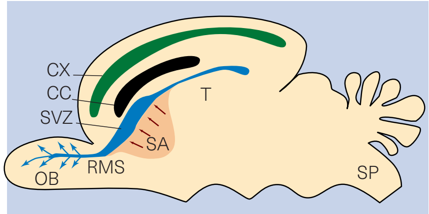

Figure 1 **Possible function of Slit in directing neuronal migration in the postnatal mouse brain. The blue colour indicates migration of neurons from their origin in the subventricular zone (SVZ), situated at the surface of anterior cerebral ventricles, to the olfactory bulb (OB) via the rostral migratory stream (RMS). Red arrows indicate the presence and direction of repulsive influences — one of which has been identified by Wu *et al.*[1] as Slit — that emanate from the surrounding structures of the forebrain such as the septal area (SA). CX, cortex; CB, cerebellum; CC corpus callosum; T, thalamus; SP, spinal cord.**

surface of other neurons. The neurophilic cells usually move tangentially, bypassing radial glial shafts[2], and a good example of this is translocation of cells from the anterior portion of the telencephalic subventricular zone to the olfactory bulb[5]. The olfactory bulb is unique in that it continues to import these neurons even in the mature brain[6], and the newly generated neurons move tangentially as a cohort of closely apposed cells called the rostral migratory stream.

Why do neurons generated in the telencephalic subventricular zone migrate to the relatively distant olfactory bulb, rather than to nearby structures such as the septum or anterior forebrain? The reason was suspected to be selective recognition of a particular substrate by the migratory neurons. Hu and Rutishauser[7] initially suggested that a repulsive molecule in the septum could prevent neurons from the subventricular zone from entering septal territory. Wu *et al.*[1] now propose a specific protein that does this job.

This protein turns out to be a member of the Slit family of proteins, which were initially identified in the fruitfly *Drosophila melanogaster*[8] and have since been found in the brains of amphibians, birds, rodents and primates — including humans. These proteins rose to prominence when they were found to be important in controlling axon guidance. Then, earlier this year, four papers (reviewed in ref. 9) showed that an interaction between the Slit proteins and a cell-surface receptor called Roundabout (Robo) is involved in preventing axons from crossing the embryonic midline.

Wu *et al.* now suggest a previously unsuspected function for Slit in directing neuronal migration, well before the initiation of axonal connections (Fig. 1). By co-culturing tissue explants from various brain structures, the authors confirmed that a repulsive activity acts on migrating neurons in the brain. They also showed that Slit is expressed in the postnatal septum, and that it is chemorepulsive for migration of subventricular-zone neurons from explants, as well as for migration of these neurons within the rostral migratory stream. Although this effect seems to be repulsive, it does not inhibit the migration, and it depends on a concentration gradient of the Slit protein. By blocking endogenous Slit using the extracellular domain of Robo, which is a receptor for Slit, Wu *et al.* showed that Slit contributes to the repulsive activity of the septum for neurons of the subventricular zone.

The novelty of Wu and colleagues' findings lies in the fact that the Slit molecules are diffusible, distributed as a concentration gradient that can be read by migrating cells with the appropriate receptor. In a parallel study in *Neuron*[10], the same group shows that Slit also acts as a guidance cue for neurons migrating from the ganglionic eminence to the neocortex in the embryonic brain. Anderson *et al.*[11] previously found that a selective class of neurons from the ganglionic eminence does not migrate radially, but, rather, that these neurons invade the subventricular zone tangentially on their way to different cortical areas. Now it seems that Slit, which is present in the ventricular zone of the ganglionic eminence, directs the migration of cells from this region to the cortex[10].

So, although repulsive molecules were thought to guide the formation of axonal connections, Wu *et al.* provide the first experimental evidence that a similar mechanism directs neuronal cell migration. Their study is also an example of how new approaches in experimental biology allow us to examine the roles of individual genes and their products in complex, multicellular developmental events, and to look at their involvement in congenital malformations. The findings also provoke new ideas for therapeutic strategies. For instance, repulsive molecules might be used to prevent metastasis in the brain, or to streamline transplanted cells into parts of the brain affected by neurodegenerative disorders.

Motility is one of the primordial features of prokaryotic and eukaryotic cells. From the beginning of animal evolution, mobile cells were adapted to move within the environment — either towards positive chemical stimuli or away from negative ones. This basic strategy seems to be preserved even in nerve cells. It is not, of course, enough to place neurons in their final position in the brain, because this process also requires surface-mediated interactions between migrating neurons and adjacent cells[3,12]. But amplification of the ancient strategies that operate in the most primitive single-celled organisms may be combined with the newer developmental mechanisms in a cooperative attempt to build a complex nervous system.

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1. Wu, W. *et al. Nature* **400,** 331–336 (1999).
2. Rakic, P. *Experientia* **46,** 882–891 (1990).
3. Pearlman, A. L. *et al. Curr. Opin. Neurobiol.* **8,** 44–54 (1998).
4. Komuro, H. & Rakic, P. *J. Neurobiol.* **37,** 110–130 (1998).
5. Lois, C., Garcia-Verdugo, J. M. & Alvarez-Buylla, A. *Science* **271,** 978–981 (1996).
6. Luskin, M. B. *J. Neurobiol.* **36,** 221–233 (1998).
7. Hu, H. & Rutishauser, U. *Neuron* **16,** 933–940 (1996).
8. Nüsslein-Vollhard, C., Wieschaus, E. & Kluding, H. *Wilhelm Roux Arch. Dev. Biol.* **193,** 267–283 (1988).
9. Harris, W. A. & Holt, C. E. *Nature* **398,** 462–463 (1999).
10. Zhu, Y., Li, H., Zhou, L., Wu, J. Y. & Rao, Y. *Neuron* **23,** 473–485 (1999).
11. Anderson, S. A., Eisenstat, D. D., Shi, L. & Rubenstein, J. L. R. *Science* **278,** 474–476 (1997).
12. Rakic, P., Cameron, R. S. & Komuro, H. *Curr. Opin. Neurobiol.* **4,** 63–69 (1994).

Astronomy

Big planets and little stars

James Liebert and William B. Hubbard

The unambiguous discoveries of giant, extrasolar planets and very cool 'brown dwarf' stars have only been made in the past few years. Perhaps it was the dramatic detection of the companion brown dwarf star, Gliese 229B — which had methane in its spectrum and evidence for dust and cloud formation — that has most linked the communities of astronomers interested in giant planets and cool stars, who met together for the first time last month*. If Gliese 229B were a true star, then its atmosphere would be so much hotter that neither methane nor most types of clouds could form. Astronomers have always categorized stars according to their temperature: the brightest and hottest are O stars, followed by B, A, F, G stars (which include our Sun), K and, at the bottom of the scale, M stars, which rarely reach a cool 2,500 K.

These are exciting times, with fresh discoveries of new classes of cool astrophysical objects, many of which have masses too low to fuse hydrogen into helium — the definition of a star. The detection of stand-alone brown dwarf stars with temperatures similar to Gliese 229B near 1,000 K led to a new category of 'methane' or 'T dwarf' stars. These have infrared spectra dominated by methane and gaseous water, more like Jupiter than a small M dwarf star. The Sloan Digital Sky Survey (SDSS) reported the discovery of the first such object without a companion star the week before this meeting[1]. Stunning infrared and optical spectra of this and a second SDSS discovery were shown at the meeting (J. Pier, US Naval Observatory, Arizona). Hot on the heels of Sloan, however, is the brown dwarf group working on infrared sources found in the Two Micron All Sky Survey (2MASS), which have spectra of four T dwarfs (A. Burgasser, Caltech).

The 2MASS group has discovered nearly one hundred of the warmer 'L dwarf' stars, another category of substellar objects that are still below M dwarf temperatures. They have modelled the observed L dwarf properties using a theory of stellar evolution calculated by A. Burrows and colleagues (Univ. Arizona). Using this model of the L dwarf data it is possible to estimate the likely spatial density and luminosities of substellar objects (N. Reid, Caltech). The 2MASS group predicts that most L dwarf stars are cooler and less luminous than Gliese 229B, with temperatures down to several hundred degrees kelvin (or less). It is possible that these cool dwarfs are as numerous as all the stars in our local neighbourhood. In contrast, a low-resolution infrared spectrum of a possible planetary-mass object, previously reported elsewhere[2], now appears to show evidence for carbon monoxide, which indicates a temperature closer to 3,000 K (in the range of cool stars) rather than 1,600 K.

Many L dwarfs appear to be rotating, with velocities up to 80 km s^{-1} (E. Martin and G. Basri, Univ. California, Berkeley). The rapid rotation of these objects means that they could be very young, which would explain why a substellar object is still a fairly luminous infrared source. Alternatively, they may be old (and therefore stellar) objects, implying that such low-temperature stars are more like Jupiter, which has a short rotation period of about ten hours, than the Sun — a slow rotator that loses its angular momentum because of an internal magnetic dynamo. Substellar objects in the Pleiades cluster and the very young (2–7 Myr) Sigma Orionis cluster have masses lower than 0.075–0.08 of the solar mass, below which theoretical calculations predict hydrogen fusion cannot take place (R. Rebolo, Instituto de Astrofísica de Canarias). The objects in Pleiades extend down to 40 Jupiter masses (0.04 solar mass) or less; in Orion, substellar objects may have been found near 15 Jupiter masses (0.015 solar). The discovery of such low-mass objects indicates that the formation of a cluster of stars can also produce objects truly intermediate between the lowest-mass stars and the mass of Jupiter, that is not very close in mass to either. This narrows further the distinction between giant planets and cool stars.

The prospects of finding many more extrasolar planets and brown dwarf stars are looking good with a dedicated 1.2-metre telescope at the European Southern Observatory in Chile (D. Queloz, Jet Propulsion Lab., Pasadena). Michel Mayor's group at the Observatoire de Genève is measuring radial velocities of some 1,500 G–K dwarf stars. Although the results to date should be heavily biased in favour of finding massive, close companions, it appears nonetheless that planetary companions less massive than about ten Jupiters are much more common than substellar companions above this mass. That is, brown dwarfs may be more common as stand-alone objects than as companions.

It is not yet clear whether extrasolar planets and brown dwarfs would have a banded appearance similar to Jupiter's (G. Schubert, Univ. California, Los Angeles). According to theory and numerical simulations, these rapidly rotating objects should transport energy to their atmospheres by means of thermal convection from the cooling interior. The style of convection is influenced by the rapid rotation, which leads to cells forming columnar rolls parallel to the rotation axis. The ends of the cells form bands that vary in time, similar to the bands of clouds on Jupiter. The critical parameter is the Rayleigh number, which determines the character of the convection and increases by about seven orders of magnitude from Jupiter to the most massive brown dwarfs. Schubert predicts that brown dwarfs might also have bands, but that the banded structure will be much more chaotic and time-variable than in Jupiter.

Astronomers are beginning to understand the importance of planet-like processes such as meteorology and cloud formation in cool atmospheres. According to thermochemical models, 'clouds' of silicate are buried at high pressures deep below Jupiter's visible atmosphere. These theoretical clouds have now been detected in the atmospheres of L dwarfs at temperatures above 1,000 K, where they absorb more strongly at shorter wavelengths and so redden the emitted near-infrared light. The clouds suddenly disappear in methane dwarfs at effective temperatures cooler than 1,000 K, as predicted by theory. But a sobering account of the complexity of cloud microphysics highlights a basic need

* *From Giant Planets to Cool Stars,* Flagstaff, Arizona, USA, 8–11 June 1999.