

clusions can be used to calculate past moisture budgets (7, 10). Recent analyses of fluid inclusions in halite from Permian lakes have even shown that pH dropped below 1 partly as a result of aridity and low buffering capacity (11).

Fluid inclusions may also provide information about water table elevation, lake level, or sea level. As minerals precipitate near Earth's surface, they may entrap bubbles of immiscible gas. Those gases may preserve information on the pressure at the time of entrapment and may be used to reconstruct water depth (12, 13).

When minerals grow in Earth-surface environments, microbes and organic material may be sealed within fluid inclusions. Recently, researchers have revived

dormant microbes believed to have been entrapped in fluid inclusions in 250-million-year-old halite (14). The potential for preservation and the timing of entrapment of these microbes have been questioned (15), but the possibility of finding degraded or even viable organisms in fluid inclusions opens up many exciting (and likely controversial) possibilities in paleobiology.

Lowenstein *et al.*'s study exemplifies the potential of fluid inclusions to elucidate environmental conditions in the geologic past. Studies of fluid inclusions are likely to play an important role in future reconstructions of Earth's paleoenvironment, from the composition of sea and atmosphere to biology and climate.

## References

1. T. K. Lowenstein, M. N. Timofeeff, S. T. Brennan, L. A. Hardie, R. V. Demicco, *Science* **294**, 1086 (2001).
2. C. E. Harvie, N. Moller, J. H. Weare, *Geochim. Cosmochim. Acta* **48**, 723 (1984).
3. L. A. Hardie, *Geology* **24**, 279 (1996).
4. W. J. Johnson, R. H. Goldstein, *Nature* **362**, 335 (1993).
5. D. Raynaud *et al.*, *Science* **259**, 926 (1993).
6. R. A. Berner, G. P. Landis, *Science* **239**, 1406 (1988).
7. T. K. Lowenstein *et al.*, *Geol. Soc. Am. Spec. Pap.* **289**, 19 (1994).
8. T. K. Lowenstein, J. Li, C. B. Brown, *Chem. Geol.* **150**, 223 (1998).
9. K. C. Benison, R. H. Goldstein, *Chem. Geol.* **154**, 113 (1999).
10. Y. Wenbo *et al.*, *Paleogeogr. Paleoclimatol. Paleocool.* **117**, 279 (1995).
11. K. C. Benison *et al.*, *Nature* **392**, 911 (1998).
12. K. D. Newell, R. H. Goldstein, *Chem. Geol.* **154**, 97 (1999).
13. G. Mallarino, P. Di Stefano, R. H. Goldstein, *Int. Assoc. Sedimentol. Annu. Meeting Abstr.* **21** (2001).
14. R. H. Vreeland, W. D. Rosenzweig, D. W. Powers, *Nature* **407**, 897 (2000).
15. R. M. Hazen, E. Roedder, *Nature* **411**, 155 (2001).

## PERSPECTIVES: NEUROBIOLOGY

# Neurocreationism—Making New Cortical Maps

Pasko Rakic

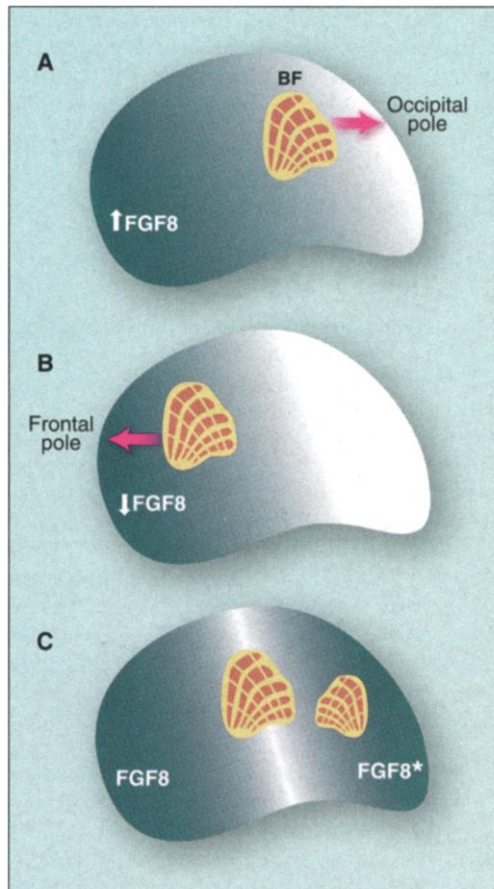
**T**he brain can be thought of as a map in which the position of its constituent neurons indicates what they do. Nowhere is this more evident than in a brain region called the cerebral cortex, which consists of structurally distinct cellular (cytoarchitectonic) areas responsible for functions as diverse as sensory perception, motor control, and cognition.

As the cerebral cortex evolved, the number of cytoarchitectonic areas increased and the number of sensory representations was duplicated (1). Interest in how the map of the cerebral cortex develops in the embryo has

cerebral vesicle themselves carry intrinsic programs for species-specific cortical regionalization (protomap model) (4). According to this hypothesis, some region-

specific cytoarchitectonic features can develop independently of input (5, 6). Indeed, the word "proto" emphasizes the malleable nature of this primordial map. Within this primordial map, it is envisaged that cues generated within cortical neurons attract appropriate input and cooperatively create a final area-specific, three-dimensional organization. Support for the intrinsic specification of cortical maps has accumulated steadily with reports that a number of genes whose products regulate development are expressed in discrete gradients within cortical regions before (or independently of) the incoming input (7–11). The protomap hypothesis has been bolstered by evidence that abolition of thalamic input by genetic manipulation does not prevent cortical compartmentalization (12–14). These dramatic findings prompt the question of how a well-defined cortical area can be established by proteins secreted far from their targets. Fukuchi-Shimogori and Grove (2) now reveal that a change in the concentration gradient of a single growth factor across the cerebral wall may have a dramatic effect on the organization of the cortical map in developing mouse embryos.

**Developmental cartography.** A concentration gradient of FGF8 (blue) with the source situated in the frontal pole affects the position of the whisker barrel field (BF) in the cerebral cortex of developing mouse embryos. An increase (A) or decrease (B) in the production of FGF8 causes a shift of the BF toward the frontal or occipital pole, respectively. (C) Insertion of another source of FGF8 at the occipital pole (\*) induces formation of an extra BF with mirror-image whisker representation.



Enhanced online at [www.sciencemag.org/cgi/content/full/294/5544/1011](http://www.sciencemag.org/cgi/content/full/294/5544/1011) belief that it can explain the emergence of human mental capacity during evolution. The research article by Fukuchi-Shimogori and Grove on page 1071 of this issue (2) now identifies a molecule that is involved in defining areas within the telencephalon of the developing mouse brain.

Traditionally, it has been presumed that the embryonic telencephalon first forms an equipotential sheet of cells that then becomes specified by input from subcortical centers (tabula rasa model) (3). An alternative view—derived from experimental manipulations of cortical input in primate embryos—is that cells of the embryonic

The author is in the Department of Neurobiology, Yale University School of Medicine, New Haven, CT 06520, USA. E-mail: pasko.rakic@yale.edu

These investigators report that perturbing the expression and site of production of FGF8, a member of the fibroblast growth factor family, can profoundly alter the map of the mouse cerebral cortex. FGF8 is normally expressed at the anterior pole of the telencephalic vesicles and is suspected of influencing neocortical patterning of the telencephalon as it does in the developing hindbrain. To test this hypothesis, the authors used an elegant gene transfer technique—in utero microelectroporation—to alter production of FGF8 in the developing neocortex on embryonic day 11, well before the formation of thalamo-cortical connections. In this way, the authors avoided the early embryonic lethality that occurs in mice engineered to completely lack FGF8 (15). Their strategy paid off as the mice survived and displayed a dramatic reorganization of their cortical maps. This reorganization included a shift in boundaries among the frontal, parietal, and occipital areas with no visible disturbances in other brain regions. An increase in FGF8 in the frontal pole displaces the representation of the facial whiskers, the familiar “barrel field,” more posteriorly (see the figure). In contrast, blocking FGF8 activity with a soluble FGF8 receptor moved the fields in the opposite direction. Remarkably, introduction of an extra source of FGF8 into the occipital pole produced an extra barrel field situated in the occipital lobe of the cerebral cortex (see the figure). Histological stain-

ing clearly revealed the presence and morphology of the barrel fields, leaving little doubt as to the validity of the results.

The ability to rearrange and create new cortical maps at will in a laboratory setting is a great achievement. The results of the Fukuchi-Shimogori and Grove study have important implications for understanding how cytoarchitectonic areas could have been duplicated or added during evolution of the cerebral cortex. It is especially intriguing that the misplaced extra barrel field has a reverse (mirror image) representation of the whiskers, as would be predicted for an area that was duplicated during evolution (1). Given that it is now possible to duplicate the sensory representations of the periphery and to create a new functional area in the cerebral cortex, we have an unprecedented opportunity to study how cortical maps develop. For example, it will be important to determine whether the misplaced area induced by the investigators attracts the appropriate thalamic input. Although input from the thalamus appears to have little influence on the initial regionalization of the cortex, it is essential for its appropriate maturation (4). Intriguingly, the overall size of the cerebrum in the experimental animals was reduced, prompting speculation about the status of other cortical areas. It is likely that many other competing signaling pathways besides the FGF8 signaling pathway are also involved in cortical map formation (7–14). Most important, the new work

illustrates how a single mutation in a growth factor could have a sudden and profound effect during evolution on the pattern of cortical map formation. Recent evidence indicates that FGF8 affects cellular proliferation, apoptosis, and differentiation in the mammalian forebrain through modulation of Otx2 and Emx2 expression (16). But this is far from the end of the story. As a next step, it will be important to search for additional genes and morphoregulatory molecules that may be involved in cortical specification. It will also be necessary to develop rodent and possibly primate models of cortical dysgenesis that mimic specific genetic or acquired cortical disorders of development (17).

#### References

1. J. M. Allman, J. H. Kaas, *Brain Res.* **31**, 85 (1971).
2. T. Fukuchi-Shimogori, E. A. Grove, *Science* **294**, 1071 (2001); published online 20 September 2001 (10.1126/science.1064252).
3. O. D. Creutzfeldt, *Naturwissenschaften* **64**, 507 (1977).
4. P. Rakic, *Science* **241**, 170 (1988).
5. P. Rakic et al., *Proc. Natl. Acad. Sci. U.S.A.* **88**, 2083 (1991).
6. R. O. Kuljis, P. Rakic, *Proc. Natl. Acad. Sci. U.S.A.* **87**, 5303 (1990).
7. M. F. Barbe, P. Levitt, *J. Neurosci.* **11**, 519 (1991).
8. Y. Arimatsu et al., *Proc. Natl. Acad. Sci. U.S.A.* **89**, 8879 (1992).
9. A. Simeone et al., *Nature* **358**, 687 (1992).
10. N. Sestan et al., *Curr. Biol.* **11**, 39 (2001).
11. Y. Gitton et al., *J. Neurosci.* **19**, 4889 (1999).
12. E. M. Miyashita-Lin et al., *Science* **285**, 906 (1999).
13. A. Mallamaci et al., *Nature Neurosci.* **3**, 679 (2000).
14. K. M. Bishop et al., *Science* **288**, 344 (2000).
15. X. Sun et al., *Genes Dev.* **13**, 1834 (1999).
16. P. H. Crossley, S. Martinez, Y. Ohkubo, J. L. R. Rubenstein, *Neuroscience*, in press.
17. J. L. R. Rubenstein, P. Rakic, *Cereb. Cortex* **9**, 521 (1999).

#### PERSPECTIVES: CLIMATE CHANGE

## Storing Carbon on Land

R. J. Scholes and I. R. Noble

**T**he negotiations over the Kyoto Protocol have swung from imminent collapse in The Hague to unexpected advances at Bonn. But terrestrial sinks of carbon continue to be problematic. How important are they in the global carbon cycle? How may they change in the future? And what use might nations make of land management to reduce greenhouse gases in the atmosphere in compliance with the Kyoto Protocol?

Each year, about 120 PgC (1 PgC =  $10^{15}$  g of carbon) is exchanged in each direction between terrestrial ecosystems and the atmosphere; another 90 PgC is ex-

changed between ocean and atmosphere. For comparison, 6.3 PgC is emitted by burning fossil fuels, about half of which is taken up again by the biosphere within years to a decade (1). This net uptake, or “sink,” is currently fairly evenly split between land and ocean, but the uptake processes are different, as are projected future behaviors of the two sinks.

The ocean sink is projected to increase from the current  $1.7 \pm 0.5$  PgC/year to around 5 PgC/year by 2100 (2). The land, believed to have been a net carbon source before 1950, is currently a net sink of  $1.4 \pm 0.7$  PgC/year. Given that deforestation is thought to be a source of 1.6 PgC/year, the land not undergoing deforestation must be a sink of 2 to 4 PgC/year (3). Models project that the land sink excluding deforestation will increase to around 5 PgC/year by 2050 and then level off or decline, possi-

bly steeply (4). Whatever decisions are made about sinks in the Kyoto compliance mechanisms, it is essential that these carbon fluxes continue to be monitored.

Several processes may contribute to the net land sink, including the stimulation of plant growth by the rising atmospheric CO<sub>2</sub> concentration, fertilization of ecosystems by airborne nitrogen pollutants, early effects of climate change, recent and historical changes in land management, and time delays between carbon uptake by plants and its eventual release. The relative proportions of these contributions remain uncertain, as does their geographic distribution (3). Forest inventory data from North America reveal little evidence of enhanced growth rates (5), suggesting that virtually the entire North American sink can be explained by changes in land management. Neither this mechanism nor nitrogen fertilization may be adequate to explain the large tropical sink. The experimentally confirmed increase in plant productivity resulting from increased CO<sub>2</sub> concentrations is theoretically sufficient to account for a large part of the global sink,

R. J. Scholes is at the CSIR Division of Water, Environment and Forest Technology, Box 395, Pretoria, South Africa. E-mail: bscholes@csir.co.za. I. R. Noble is at the Cooperative Research Centre for Greenhouse Accounting, Canberra, Australia. E-mail: ian.noble@greenhouse.crc.org.au