of the Solar System's formation, after which it was either pulled into the Sun or blasted out of the Solar System when the Sun ignited. By contrast, the noble gases in the upper mantle came from meteorites[4,5]. Mukhopadhyay's findings, together with those of others, allow us to appreciate the true complexity of gas delivery to our planet from different sources at different stages of Earth's infancy[1,4,5,8].

But the questions of how gas from the solar nebula was trapped in the solid parts of growing planets, and how the gas was preserved through early accretionary events, will certainly test our models of accretion. Some of the noble-gas isotopes from the Icelandic deep mantle came from long-dead radioactive isotopes of iodine and plutonium that were present in the early Solar System. Mukhopadhyay[1] compared these noble-gas isotopes with those in the convecting mantle[9], and concluded that the Iceland deep mantle formed in a drier environment, and preserved a higher proportion of its plutonium-decay gases, than did the convecting mantle. This chimes with the idea of a process or location in the deep mantle that has preserved the earliest geochemical signals of accretion exceptionally well. Mukhopadyay's findings may also help to connect theories of how a planet starts to obtain its gas with evidence[10] from other isotope systems that also points to the very early formation of reservoirs hidden in the deep mantle.

Although many geochemists have argued that Earth contains a deep, gas-rich reservoir, they have struggled to pinpoint where it should be. Ever since it became apparent from seismic tomography that Earth's mantle was not nicely layered[11], the location or processes that could prevent such a deep reservoir from mixing into the convecting mantle and disappearing completely have remained enigmatic. Wherever this reservoir might be, it has survived the cataclysmic Moon-forming event (in which Earth was struck by a Mars-sized body)[12]; avoided mixing with volatile compounds brought to Earth by meteorites; and withstood continual removal of material by mantle plumes.

One result from Mukhopadhyay's work is touched on only lightly by the author, but might have the greatest impact on how we think the mantle behaves. If the isotopic composition of the basalt analysed by Mukhopadhyay — and therefore of the Iceland plume from which this hotspot rock is derived — is indeed representative of a deep mantle reservoir, then this reservoir cannot also be the source of ^{3}He needed to explain the ^{4}He/^{3}He ratio in the upper mantle, because the heavy noble gases in the basalt don't match those in the upper mantle. The two-reservoir mantle model must therefore be modified. Mukhopadhyay's data about the cocktail of mantle noble gases, however, will endure. ■

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1. Mukhopadhyay, S. *Nature* **486,** 101–104 (2012).
2. Kurz, M. D., Jenkins, W. J. & Hart, S. R. *Nature* **297,** 43–47 (1982).
3. Moreira, M., Kunz, J. & Allegre, C. J. *Science* **279,** 1178–1181 (1998).
4. Ballentine, C. J., Marty, B., Sherwood Lollar, B. & Cassidy, M. *Nature* **433,** 33–38 (2005).
5. Holland, G., Cassidy, M. & Ballentine, C. J. *Science* **326,** 1522–1525 (2009).
6. Gonnermann, H. M. & Mukhopadhyay, S. *Nature* **449,** 1037–1040 (2007).
7. Harrison, D., Burnard, P. & Turner, G. *Earth Planet. Sci. Lett.* **171,** 199–207 (1999).
8. Marty, B. *Earth Planet. Sci. Lett.* **313,** 56–66 (2012).
9. Pepin, R. O. & Porcelli, D. *Earth Planet. Sci. Lett.* **250,** 470–485 (2006).
10. Boyet, M. & Carlson, R. W. *Science* **309,** 576–581 (2005).
11. van der Hilst, R. D., Widiyantoro, S. & Engdahl, E. R. *Nature* **386,** 578–584 (1997).
12. Canup, R. M. & Asphaug, E. *Nature* **412,** 708–712 (2001).
13. Kellogg, L. H. & Wasserburg, G. J. *Earth Planet. Sci. Lett.* **99,** 276–289 (1990).

NEUROSCIENCE

Sibling neurons bond to share sensations

Two studies show how electrical coupling between sister neurons in the developing cerebral cortex might help them to link up into columnar microcircuits that process related sensory information. SEE LETTERS P.113 & P.118

THOMAS D. MRSIC-FLOGEL & TOBIAS BONHOEFFER

A pioneering set of experiments in the 1950s and 1960s inspired generations of neuroscientists to explore how the anatomy of the brain gives rise to its function[1–3]. When researchers lowered electrodes into the cerebral cortices of cats and monkeys, they found that neurons lying above and below each other form functional columns — that is, they respond in a similar way to certain stimuli, such as touch on specific areas of the skin or the orientation of an elongated visual stimulus.

Even though such cortical columns have long been considered to be exemplars of basic computational units of cortical organization, the precise relationship between their anatomy and function has been difficult to define and remains the subject of debate[4–5]. This is particularly true in rodents, in which the cortex seems to lack functional columns almost entirely. What is common to rodents and other mammals, however, is a highly specific organization of cortical connections that link neurons across layers in the cortex to relay and process related sensory information[6–8]. Reporting in this issue, Yu *et al.*[9] (page 113) and Li *et al.*[10] (page 118) reveal some of the developmental events that could give rise to such precisely arranged functional circuits.

It has long been known that, during embryonic development of the cortex, neuronal progenitor cells give birth to daughter cells that migrate towards the brain surface to form strings of 'sibling' neurons that span the cortical layers (Fig. 1a). These radially aligned clones, referred to as radial units or ontogenetic columns, have been proposed to constitute the basis of the functional columns in the mature brain[11]. However, a direct link between cellular lineage, microcircuit development and the sensory preference of neurons had not been demonstrated.

Yu and colleagues[9] used viruses to label sibling neurons in the developing cortex of mouse embryos with a fluorescent protein, and then recorded the cells' electrical activity in brain slices prepared shortly after birth. The authors showed that gap junctions — small pores that couple adjacent cells electrically by bridging their membranes — formed transiently between sibling neurons in the same radial unit, very early in development (Fig. 1b). Gap junctions had previously been observed between clusters of excitatory neurons in the developing cortex and had been proposed to contribute to the establishment of neuronal assemblies[12], but the ancestry and significance of such cell clusters were unknown. Moreover, other work had revealed that, later in development, neurons in radial clones mostly connect to one another through chemical synapses[13] mediated by neurotransmitter molecules (Fig. 1c). Yu *et al.* showed that gap-junction inactivation abolished the formation of such synapses, and report that transient electrical coupling is thus essential for the establishment of chemical synapses between sibling neurons.

Li and colleagues[10] used the same method to label radial clones, and then used a microscopy technique known as two-photon calcium imaging[14] to monitor the activity of sibling neurons in the cortex of live mice in response to visual stimuli. The authors observed that clonally related neurons, when compared with a random subset of neighbouring cells,

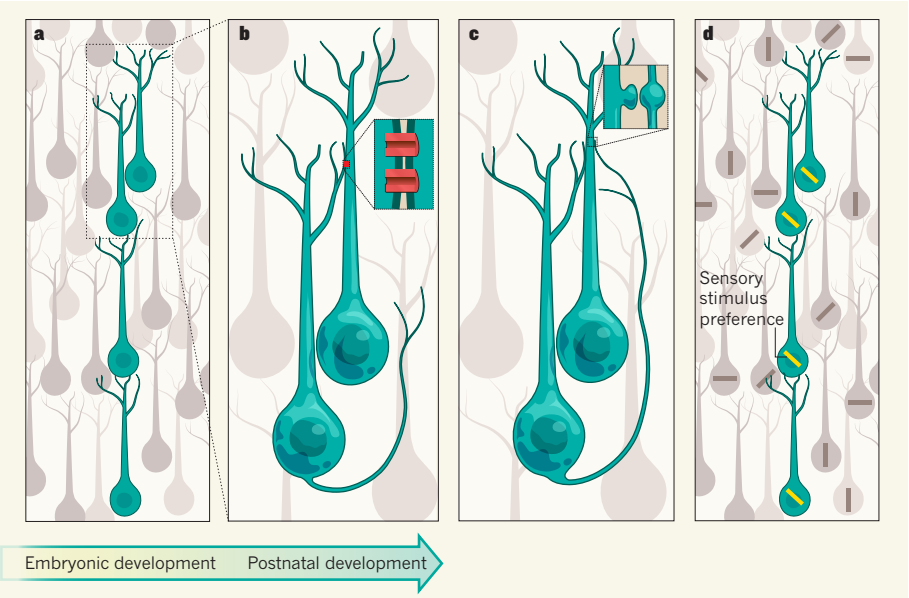

Figure 1 | A link between neuronal lineage, connectivity and sensory preference. **a**, During embryonic development, newly born neurons migrate towards the surface of the cortex and form strings of sibling neurons that span the cortical layers. Yu *et al.*[9] and Li *et al.*[10] used viruses that express a green fluorescent protein to label neurons derived from a single progenitor cell. **b**, Yu *et al.* show that, early in development, sibling neurons are preferentially connected by small pores called gap junctions (inset) that enable electrical currents to pass directly between them. **c**, As development proceeds, gap junctions disappear and chemical synapses (inset) are preferentially established between sibling neurons. **d**, Li *et al.* describe how, in a later developmental phase, sibling neurons respond to similar sensory features, such as the orientation of visual stimuli.

were more likely to respond to stimuli of the same orientation in the animals' visual field (Fig. 1d). Moreover, the blockade of gap junctions eliminated the shared preference for stimulus orientation, which further supports the idea that electrical coupling between sibling neurons plays a part in influencing the functional organization of the cortex.

The two studies are intriguing because they lend support to the involvement of genetic lineage in the assembly of precise columnar circuits in the cortex. An extreme interpretation of the results is that ontogenetic columns constitute an elementary unit of functional organization in the cortex; that is, a basic, repeating circuit comprising excitatory neurons that process related sensory information. However, the relevance of ontogenetic columns for sensory processing is still unclear; an excitatory neuron in the mammalian cortex receives inputs from at least 1,000 others, but only a handful of these connections are with sibling neurons. It will be important to assess how much the connections between siblings actually contribute to shaping their sensory responses.

The small size of mouse ontogenetic columns, as reported by Li *et al.* and Yu *et al.*, might explain why functional columns have not previously been described in the visual cortex of rodents, in which neurons with different sensory preferences seem to be locally intermixed[15,16]. But the authors' findings also raise the question of whether there is any relationship between ontogenetic columns and the much larger functional columns in the cortices of other mammals such as cats or primates. Large functional columns could form as aggregates of multiple ontogenetic mini-columns, or from larger radial clones containing many more neurons than those of rodents, or by a different mechanism altogether.

Regardless, the two studies demonstrate that at least some of the connection specificity in cortical microcircuits is established intrinsically by clonal lineage. The studies also show that cellular lineage could influence neurons' development of a similar sensory preference during early postnatal life — but how might this be achieved? Yu and colleagues' results suggest a close interplay between clonal lineage and early neuronal activity. Electrical coupling is likely to influence the formation and/or stabilization of chemical synapses between neurons that share gap junctions, because it is known that synapses can grow stronger or weaker if the cells' electrical activities are correlated or uncorrelated, respectively — a process known as synaptic plasticity. It is tempting to speculate that the sensory preference of these sub-networks might then be developed by similar mechanisms: electrically coupled neurons could select and stabilize a common set of sensory inputs, which would endow these cells with a shared preference for certain sensory features. Future experiments are required to determine the developmental events that define how non-sibling neurons with similar stimulus preferences become connected to each other in the cortical circuit.

Other important questions remain unanswered. To what extent is the electrical coupling between cortical neurons necessary for the establishment of stimulus selectivity? In other words, did the early blockade of gap junctions between sibling neurons result in a fundamentally altered visual cortex? Li and colleagues' results indicate that gap-junction blockade does not prevent the emergence of orientation preference, but more subtle features — such as the range of orientations that a neuron detects — could depend on gap-junction connectivity.

Another issue relates to the fact that, during embryonic development, clonally related neurons not only migrate radially towards the cortical surface — some are also distributed tangentially. The connectivity and functional fate of these displaced sibling neurons remains undetermined. Do they also establish functional sub-networks with their siblings, or do they form local connections with non-sibling neighbours? How does the interplay between sensory input and synapse plasticity link up neurons from different ontogenetic columns with similar sensory preferences to form larger functional assemblies? And do displaced sibling neurons have a role in this process? Whatever the answers to these questions, the two studies reveal the fascinating way in which neurons emerging from the same progenitor cell are destined to share functional properties, and thus show how the earliest developmental events influence the elaborate functional circuitry of the brain. ■

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1. Mountcastle, V. B. *J. Neurophysiol.* **20,** 408–434 (1957).
2. Hubel, D. H. & Wiesel, T. N. *J. Physiol.* **165,** 559–568 (1963).
3. Hubel, D. H. & Wiesel, T. N. *J. Physiol.* **195,** 215–243 (1968).
4. da Costa, N. M. & Martin, K. A. *Front. Neuroanat.* **4,** 16 (2010).
5. Horton, J. C. & Adams, D. L. *Phil. Trans. R. Soc. Lond. B* **360,** 837–862 (2005).
6. Binzegger, T., Douglas, R. J. & Martin, K. A. *J. Neurosci.* **24,** 8441–8453 (2004).
7. Yoshimura, Y., Dantzker, J. L. M. & Callaway, E. M. *Nature* **433**, 868–873 (2005).
8. Ko, H. *et al. Nature* **473,** 87–91 (2011).
9. Yu, Y. C. *et al. Nature* **486,** 113–117 (2012).
10. Li, Y. *et al. Nature* **486,** 118–121 (2012).
11. Rakic, P. *Science* **241,** 170–176 (1988).
12. Yuste, R., Nelson, D. A., Rubin, W. W. & Katz, L. C. *Neuron* **14,** 7–17 (1995).
13. Yu, Y. C., Bultje, R. S., Wang, X. & Shi, S. H. *Nature* **458,** 501–504 (2009).
14. Stosiek, C., Garaschuk, O., Holthoff, K. & Konnerth, A. *Proc. Natl Acad. Sci. USA* **100,** 7319–7324 (2003).
15. Ohki, K. *et al. Nature* **433,** 597–603 (2005).
16. Mrsic-Flogel, T. D. *et al. Neuron* **54,** 961–972 (2007).