Review

The basic repeating modules of the cerebral cortical circuit

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Abstract: The fundamental organization of the cerebral cortical circuit is still poorly understood. In particular, it is unclear whether the diverse cell types form modular units that are repeated across the cortex. We discovered that the major cell types in cortical layer 5 form a lattice structure. Distinct types of excitatory and inhibitory neurons form cell type-specific radial clusters termed microcolumns. Microcolumns are present in diverse cortical areas, such as the visual, motor, and language areas, and are organized into periodic hexagonal lattice structures. Individual microcolumns have modular synaptic circuits and exhibit modular neuronal activity, suggesting that each of them functions as an information processing unit. Microcolumn development is suggested to be independent of cell lineage but coordinated by gap junctions. Thus, neurons in cortical layer 5 organize into a brainwide lattice structure of functional microcolumns, suggesting that parallel processing by massively repeated microcolumns underlie diverse cortical functions, such as sensory perception, motor control, and language processing.

Keywords: cerebral cortex, neocortex, neurons, sensory processing, motor control, language

1. Introduction: The hypothesis of repeating cortical modules

The cerebral cortex is composed of various types of excitatory and inhibitory neurons. Each of these cell types possesses specific cellular and molecular properties, synaptic connections, and different functions in information processing. Therefore, the organization of these diverse cell types in the cortical circuit shapes the basic architecture of information processing in the brain.

Despite the critical importance of cortical circuit organization, many basic structural characteristics remain unclear due to the extreme complexity involved. A hypothesis is that a small group of neurons of diverse types constitutes a single unit circuit that is further repeated across the cortex.1–3 This hypothesis is believed to be in accordance with the evolution of the cerebral cortex. Although the surface area of the cortex has changed several thousand times during mammalian evolution, the thickness has changed only by a few times, and the basic six-layer structure has been largely conserved.4,5 If the cortex is composed of repeating units, the surface area could thus be adaptively changed by adjusting the number of repeats.6

In addition, although different cortical areas have different functions, the primary classes of neurons and their physiological properties are generally similar among cortical areas.7,8 In addition, individual cortical areas can at least partly carry out the functions of other cortical areas.9–11 These observations suggest the possibility that the essential information processing architectures in different cortical areas are similar.6,12–15 Thus, the above considerations raise the hypothesis that diverse types of neurons constitute a single basic unit circuit, which is then repeated across different cortical areas. If such a structure does indeed exist, it would suggest that a large number of homologous unit circuits serve to process diverse cortical functions. Accordingly, the unit circuits would be expected to define the basic logic of cortical information processing.

Abbreviations: CPN: cortical/callosal projection neuron; EGFP: enhanced green fluorescent protein; PV: parvalbumin; SCPN: subcerebral projection neuron; SOM: somatostatin.
Although many theories have been proposed for the hypothesis of repeating circuits, there is currently no consensus. In the visual cortex of several mammalian species, including cats and monkeys, neurons responding to similar visual stimuli form radial clusters called cortical columns. However, the functions of these cortical columns remain unclear, and they are unlikely to represent universal unit circuits because they are limited to specific cortical areas of specific mammalian species. Thus, after more than 80 years since the original hypothesis was proposed, the existence of repeating units in the cortex remains unclear. Below we review the repeated cortical structures that have been reported recently by groups including ours.

2. Layer 5 is composed of repeating modules

If the cerebral cortex does have a repeating structure, certain types of neurons would be expected to form a periodic arrangement. Therefore, we attempted to detect repeating organizations of specific cell types. We analyzed cortical layer 5 because the neuronal types in this layer have been relatively well described. Previous studies have observed that layer 5 neurons that express the transcription repressor id2 form clusters consisting of several cells. We found that id2 expression labels subcerebral projection neurons (SCPNs), which are one of the two major types of excitatory neurons in layer 5. SCPNs are present in layer 5 of diverse cortical areas and extend long axons to the spinal cord, superior colliculus, pons, and other subcortical regions, which constitute the major output pathway from the cerebral cortex. In particular, axons of motor cortical SCPNs form the corticospinal tract. By examining the SCPN distribution in brain slices, we found that SCPNs form radial clusters (SCPN microcolumns). SCPN microcolumns have a width of 1–2 cells and are several cells in height (Fig. 1). Fourier analysis of the SCPN density revealed that the organization of SCPN microcolumns was periodic. Similar microcolumns of SCPNs have also been reported in the human language area. Next, we conducted three-dimensional analyses to further evaluate the repeating structure in more detail. To this end, various cell types in mouse layer 5 were labeled using fluorescent dye injection, antibody staining, and marker gene expression in transgenic mice. After fixation, brain samples were made transparent and scanned using two-photon microscopy. We determined the 3-D coordinates of tens of thousands of SCPNs per hemisphere and found SCPN microcolumns in multiple cortical areas such as the visual, somatosensory, and motor cortices (Fig. 2a). Moreover, SCPN microcolumns in different areas had a very similar structure with a width of approximately 1–2 cells and a modular structure characterized by a discrete arrangement (Fig. 2b). Furthermore, SCPN microcolumns were observed to have a honeycomb-like hexagonal lattice periodic arrangement along the cortex (Figs. 2c and 2d).

The other major type of layer 5 excitatory neurons is cortical/callosal projection neurons (CPNs) projecting to the ipsilateral and contralateral cerebral cortex. These neurons also formed microcolumns (CPN microcolumns), which are interdigitated with SCPN microcolumns. The two major classes of inhibitory neurons, parvalbumin-expressing and somatostatin-expressing cells aligned with SCPN microcolumns, but not with CPN microcolumns. Therefore, all the major cell types in layer 5 organize into cell type-specific microcolumns with lattice structures (Fig. 3).

3. Modular circuit and modular neuronal activity of microcolumns

We next analyzed the neural activity of SCPNs to investigate the function of these microcolumns. SCPNs were labeled with a Ca²⁺ indicator protein to detect intracellular Ca²⁺ increases that accompany action potentials. In vivo brain imaging revealed that SCPNs in the same microcolumn exhibit synchronized neuronal activity and thus have similar temporal patterns of activity (Figs. 4 and 5a). This synchronous activity was common for SCPN microcolumns in the visual, somatosensory, and motor cortices (Fig. 4c). In order to further characterize information processing in microcolumns, we examined SCPN
responses to visual inputs. In the primary visual cortex, individual neurons exhibit various selectivity to visual pattern orientations (orientation selectivity), and also show various selectivity to the left and right eyes (ocular dominance). We found that SCPNs in the same microcolumn respond to a similar orientation (Figs. 5b and 6) and have similar ocular dominance\(^{24}\) (Fig. 5c). Moreover, electrophysiological...

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### Fig. 2. Microcolumns are present in multiple cortical areas and organize into a hexagonal lattice structure. (a) SCPNs labeled by injecting fluorescent dyes into the pons in the adult mouse brain. L4, L5, and L6: layer 4, 5, and 6, respectively. SCPNs are arranged into microcolumns. (b) Structural analysis of microcolumns in the visual, somatosensory, and motor areas. Inset: SCPN density was measured at various tangential distances from other SCPNs (black dot). The density was normalized to the average density in the analyzed region. Black line and shading indicate the average and standard error of mean (S.E.M.) determined by analyzing independent data, respectively. The values at <10 µm and ~20 µm are higher and lower than the average, respectively, indicating that SCPNs form discrete microcolumns with a radius of ~10 µm. (c) Top view of microcolumns. The vertical axis is parallel to the anterior–posterior orientation. Cyan dots: the centers of microcolumns. Colored lines: estimated hexagonal lattice. (d) Two-dimensional power spectrum of the density of SCPNs. The horizontal and vertical axes represent spatial frequencies in the lateral–medial and anterior–posterior orientations, respectively. Colored dots indicate the peaks corresponding to the lattice orientation shown in the same color in (c). Adapted from Ref. 24.
4. The development of microcolumns

In the development of the cerebral cortex, excitatory neurons are generated in the deep cortical regions and migrate radially toward the brain surface. Because excitatory neurons that are derived from the same mother cells (“clonally related”

**Fig. 3.** Schematic drawing of the layer 5 lattice organization. SCPN and CPN microcolumns interdigitate with each other. Parvalbumin (PV)-expressing cells and somatostatin (SOM)-expressing cells align with SCPN microcolumns but not with CPN microcolumns. Microcolumns organize into a hexagonal lattice arrangement. Adapted from Ref. 24.

**Fig. 4.** Neurons in the same microcolumns exhibit synchronized activity. (a) *In vivo* Ca$^{2+}$ imaging. SCPNs were labeled with a Ca$^{2+}$ indicator protein G-CaMP6. (b) (Left) Four SCPNs labeled with G-CaMP6. (Middle) Ca$^{2+}$ signals. Cells 1–3 (tangential distance <15 µm) exhibited synchronized activity (gray vertical lines). Cell 4 (tangential distance to other 3 cells >25 µm) exhibited no synchronization with other cells. (Right) Ca$^{2+}$ signals of cells 1–3 exhibited high correlation (gray), whereas cell 4 showed no correlation with other cells. (c) Dependence of the average Ca$^{2+}$ signal correlation on the tangential distance between SCPNs, which is measured perpendicular to the orientation of microcolumns. (Thick black line) Actual data. (Gray shading) Data from 1000 surrogates generated by random shuffling of Ca$^{2+}$ signals among SCPNs. (Dashed line and thin black line) Highest 5% and median of the surrogate data, respectively. Correlations are found for SCPN pairs that are closer than ~10 µm. Adapted from Ref. 24.

*Fig. 5.* Neurons in the same microcolumns exhibit synchronized activity. (a) *In vivo* Ca$^{2+}$ imaging. SCPNs were labeled with a Ca$^{2+}$ indicator protein G-CaMP6. (b) (Left) Four SCPNs labeled with G-CaMP6. (Middle) Ca$^{2+}$ signals. Cells 1–3 (tangential distance <15 µm) exhibited synchronized activity (gray vertical lines). Cell 4 (tangential distance to other 3 cells >25 µm) exhibited no synchronization with other cells. (Right) Ca$^{2+}$ signals of cells 1–3 exhibited high correlation (gray), whereas cell 4 showed no correlation with other cells. (c) Dependence of the average Ca$^{2+}$ signal correlation on the tangential distance between SCPNs, which is measured perpendicular to the orientation of microcolumns. (Thick black line) Actual data. (Gray shading) Data from 1000 surrogates generated by random shuffling of Ca$^{2+}$ signals among SCPNs. (Dashed line and thin black line) Highest 5% and median of the surrogate data, respectively. Correlations are found for SCPN pairs that are closer than ~10 µm. Adapted from Ref. 24.
neurons) tend to align radially, a hypothesis has been proposed that clonally related neurons form a functional module and constitutes a cortical column\(^{29}\). However, the labeling of sister neurons revealed that SCPNs in individual microcolumns are generally not clonally related (Fig. 7), thus indicating that microcolumns are not clusters of clonally related neurons\(^{22}\) (Fig. 8a).

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**Fig. 5.** Schematic diagram of microcolumn activity. (a) SCPNs in the same microcolumn receive common synaptic inputs and exhibit synchronized activity. (b) SCPNs in the same microcolumn have similar orientation preference. (c) Analysis of ocular dominance. SCPNs in the same microcolumns have similar selectivity for the left and right eyes. Adapted from Ref. 24.

**Fig. 6.** Neurons in individual microcolumns respond to similar orientation. (a) Visual patterns with various orientations were presented to mice, and responses of visual cortex SCPNs were recorded using in vivo Ca\(^{2+}\) imaging. The gray lines show responses in single trials and the black line is the average. (b) For each pair of SCPNs, the difference in the optimal stimulus orientation was determined. The average difference is plotted against the tangential distance between SCPNs, which is measured perpendicular to the microcolumn direction. (Thick black line) Actual data. (Gray shading) Data from 1000 random surrogates generated by random shuffling of the preferred orientation among SCPNs. (Thin black line and dashed line) Median and bottom 5% of random surrogates, respectively. The optimal orientation is similar for SCPNs closer than 10 µm. Adapted from Ref. 24.

**Fig. 7.** Microcolumns are composed of clonally unrelated neurons. Green shows enhanced green fluorescent protein (EGFP)-labeling of clonally related excitatory neurons. (a) Brain slice at postnatal day 4. Three radial clusters of EGFP-labeled neurons are present. (b) SCPN microcolumns are labeled for id2 mRNA expression (magenta). Clonally unrelated neurons labeled with EGFP are dispersed among multiple microcolumns (arrowheads). Adapted from Ref. 22.

**Fig. 8.** Schematic diagram of microcolumn development. (a) Individual microcolumns are composed of clonally unrelated neurons. (b) Microcolumn neurons have cell type-specific gap junctions in the neonatal stage. (c) Gap junctions are absent at the adult stage. Adapted from Ref. 24.
Microcolumns are present in the mouse cortex at the latest around 6–7 days after birth (P6–7). At this stage, formation of chemical synapses has been initiated, but they are still infrequent. Therefore, we hypothesized that microcolumn neurons have cellular interactions other than chemical synaptic connections, and we examined electrical coupling mediated by gap junctions. We found that at P6–7, SCPNs, and CPNs are specifically coupled to neighboring neurons of the same type (Figs. 8b, 9a, and 9b). This coupling was found to be biased to radially aligned neurons (Figs. 8b and 9c), suggesting that neurons in the same microcolumn are preferentially coupled (Fig. 8b). This electrical coupling of SCPNs and CPNs disappears by P14 when visual cortical neurons exhibit visual pattern selectivity (Figs. 8c and 9b).

These findings indicated that neurons in individual microcolumns are generally not clonally related and are temporarily coupled by gap junctions (22) (Fig. 8). This electrical coupling is present at the stage of cortical circuit formation, suggesting that it is involved in the formation of microcolumn neural circuits.

5. Implications for cortical computation

The above anatomical studies indicate that in a wide region of the cerebral cortex, layer 5 is composed of repeating microcolumns. The functional modularity revealed by in vivo Ca²⁺ imaging suggests that each microcolumn functions as an information processing module, thus raising the hypothesis that parallel processing by a large array of microcolumns is responsible for information processing in layer 5. Because microcolumns are present in various different cortical areas, they may serve to process basic computations common to diverse cortical functions, such as sensory processing, motion control, and language processing.

In the brains of blind and deaf individuals, the visual and auditory cortex, respectively, are recruited by other sensory modalities in a compensatory manner. Surgical rerouting of the retinal axons to the auditory pathway generates functional structures similar to visual cortical columns in the auditory cortex, which are suggested to provide visual functions. These phenomena are consistent with the idea that information processing in different cortical areas is similar and consists of a columnar...
architecture. Microcolumns may be the structural elements of such an architecture.

6. Relationship with other cortical structures and disease

Microcolumns are generally composed of clonally unrelated neurons. On the other hand, clonally related excitatory neurons in mice have been shown to transiently form gap junctions. These gap junctions largely disappear by the end of the first postnatal week, a stage when microcolumn neurons frequently exhibit gap junction coupling. Clonally related excitatory neurons later develop mutual synaptic connections and show similar visual responses. These observations suggested that both clonally related neurons and clonally unrelated microcolumn neurons form their own specific circuits.

The visual cortex of several mammalian species, such as cats and monkeys, has columnar clusters consisting of cells with similar ocular dominance and orientation selectivity termed ocular dominance columns and orientation columns, respectively. The width of ocular dominance columns is approximately several tens of cells, which is much larger than microcolumns. In addition, neurons in neighboring orientation columns in species such as cats and monkeys generally respond to similar orientations, whereas those in adjacent microcolumns in mice generally respond to different orientations (Fig. 6b). This difference can be explained by assuming that in certain species, including cats and monkeys, microcolumns with similar ocular dominance and orientation selectivity are located close to each other, constituting ocular dominance and orientation columns, respectively. Consistent with this idea, orientation columns have been suggested to have a hexagonal arrangement.

Previous studies have suggested that during development, cortical neurons form columnar clusters coupled by gap junctions called “neuronal domains” which may be structurally related to microcolumns. Because neuronal domains are not limited to layer 5 but rather span multiple cortical layers, other cortical layers may also have neuronal clusters similar to microcolumns. In addition, various modular arrangements have been reported previously for cell bodies, dendrites, and axons of cortical neurons. Cell-type-based analyses similar to the present study may reveal microcolumn-like functional organizations among those structures.

Our study revealed that cortical cell types constitute a three-dimensional circuit that is organized at single-cell precision. Structural or functional defects in this precisely organized circuit may lead to deterioration of the brain. Previous studies have reported differences in the columnar arrangement of cortical neurons between individuals with and without diseases, such as autism. Thus, further studies of potential defects in the microcolumn lattice organization may contribute to the characterization of psychiatric and neurological diseases.

7. Conclusions

Major cell types in cortical layer 5 organize into a hexagonal lattice structure of cell type-specific microcolumns. These microcolumns are present in diverse cortical areas, including the sensory, motor, and language areas. Individual microcolumns have modular synaptic circuits and exhibit modular neuronal activity, suggesting that each functions as an information processing unit. Microcolumns develop from clonally unrelated neurons that are transiently coupled by gap junctions. These observations suggest that parallel processing by massively repeated microcolumns underlie diverse cortical functions, such as sensory perception, motor control, and language processing.

References

1. Lorente de Nó, R. (1938) Architectonics and structure of the cerebral cortex. In Physiology of the Nervous System (ed. Fulton, J.F.). Oxford University Press, Oxford, pp. 291–330.
2. Larriva-Sahd, J.A. (2014) Some predictions of Rafael Lorente de Nó 80 years later. Front. Neuroanat. 8, 1–8.
3. Mountcastle, V.B. (1997) The columnar organization of the neocortex. Brain 120, 701–722.
4. Hofman, M.A. (1989) On the evolution and geometry of the brain in mammals. Prog. Neurobiol. 32, 137–158.
5. DeFelipe, J. (2011) The evolution of the brain, the human nature of cortical circuits, and intellectual creativity. Front. Neuroanat. 5, 1–17.
6. Miller, K.D. (2016) Canonical computations of cerebral cortex. Curr. Opin. Neurobiol. 37, 75–84.
7. Greig, L.C., Woodworth, M.B., Galazo, M.J., Padmanabhan, H. and Macklis, J.D. (2013) Molecular logic of neocortical projection neuron specification, development and diversity. Nat. Rev. Neurosci. 14, 755–769.
8. Tasic, B., Yao, Z., Graybuck, L., Smith, K.A., Nguyen, T.N., Bertagnoll, D. et al. (2018) Shared and distinct transcriptomic cell types across neocortical areas. Nature 563, 72–78.
9. Sharma, J., Angelucci, A. and Sur, M. (2000)
Induction of visual orientation modules in auditory cortex. *Nature* **404**, 841–847.

10) von Melchner, L., Pallas S.L. and Sur, M. (2000) Visual behaviour mediated by retinal projections directed to the auditory pathway. *Nature* **404**, 871–876.

11) Merabet, L.B. and Pascual-Leone, A. (2010) Neural reorganization following sensory loss: The opportunity of change. *Nat. Rev. Neurosci.* **11**, 44–52.

12) Creutzfeldt, O.D. (1977) Generality of the functional structure of the neocortex. *Naturwissenschaften* **64**, 507–517.

13) Douglas, R.J., Martin, K.A.C. and Whitteridge, D. (1989) A canonical microcircuit for neocortex. *Neural Comput.* **1**, 480–488.

14) Pack, C.C. and Bensmaia, S.J. (2015) Seeing and feeling motion: Canonical computations in vision and touch. *PLoS Biol.* **13**, 1–11.

15) Carandini, M. and Heeger, D.J. (2012) Normalization as a canonical neural computation. *Nat. Rev. Neurosci.* **13**, 51–62.

16) da Costa, N.M. and Martin, K.A.C. (2010) Whose cortical column would that be? *Front. Neuroanat.* **4**, 1–10.

17) Rockland, K.S. and Ichinohe, N. (2004) Some thoughts on cortical minicolumns. *Exp. Brain Res.* **158**, 265–277.

18) Horton, J.G. and Adams, D.L. (2005) The cortical column: A structure without a function. *Philos. Trans. R. Soc. B Biol. Sci.* **360**, 837–862.

19) Rakic, P. (2008) Confusing cortical columns. *Proc. Natl. Acad. Sci. U.S.A.* **105**, 12099–12100.

20) Marcus, G., Marblestone, A. and Dean, T. (2014) The atoms of neural computation. *Science* **346**, 551–552.

21) Plebe, A. (2018) The search of “canonical” explanations for the cerebral cortex. *Hist. Philos. Life Sci.* **40**, 1–36.

22) Maruoka, H., Kubota, K., Kurokawa, R., Tsuruno, S. and Hosoya, T. (2011) Periodic organization of a major subtype of pyramidal neurons in neocortical layer V. *J. Neurosci.* **31**, 18522–18542.

23) Kwan, R.Y., Lam, M.M.S., Johnson, M.B., Dube, U., Shim, S., Rašín, M.-R. et al. (2012) Species-dependent posttranscriptional regulation of NOS1 by FMRP in the developing cerebral cortex. *Cell* **149**, 899–911.

24) Maruoka, H., Nakagawa, N., Tsuruno, S., Sakai, S., Yoneda, T. and Hosoya, T. (2017) Lattice system of functionally distinct cell types in the neocortex. *Science* **358**, 610–615.

25) Rubenstein, J.L.R., Anderson, S., Shi, L., Miyashita-Lin, E., Bullone, A. and Hevner, R. (1999) Genetic control of cortical regionalization and connectivity. *Cereb. Cortex* **9**, 524–532.

26) Yoneda, T., Sakai, S., Maruoka, H. and Hosoya, T. (2018) Large-scale three-dimensional imaging of cellular organization in the mouse neocortex. *J. Vis. Exp.* **139**, e58027.

27) Hama, H., Hikili, H., Namiki, K., Hoshida, T., Kurokawa, H., Ishidate, F. et al. (2015) Scale: An optical clearing palette for biological imaging. *Nat. Neurosci.* **18**, 1518–1529.

28) Ohkura, M., Sasaki, T., Sadakari, J., Gengyo-Ando, K., Kagawa-Nagamura, Y., Kobayashi, C. et al. (2012) Genetically encoded green fluorescent Ca2+ indicators with improved detectability for neuronal Ca2+ signals. *PLoS One* **7**, 1–10.

29) Pasko, R. (1988) Specification of cerebral cortical areas. *Science* **241**, 170–176.

30) Ashby, M.C. and Isaac, J.T.R. (2011) Maturation of a recurrent excitatory neocortical circuit by experience-dependent unsilencing of newly formed dendritic spines. *Neuron* **70**, 510–521.

31) Li, M., Cui, Z., Niu, Y., Liu, B., Fan, W., Yu, D. et al. (2010) Synaptogenesis in the developing mouse visual cortex. *Brain Res. Bull.* **81**, 107–113.

32) Yu, Y.C., He, S., Chen, S., Fu, Y., Brown, K.N., Yao, X.H. et al. (2012) Preferential electrical coupling regulates neocortical lineage-dependent microcircuit assembly. *Nature* **486**, 113–117.

33) Yu, Y.C., Bulโรงแรม, R.S., Wang, X. and Shi, S.H. (2009) Species synapses develop preferentially among sister excitatory neurons in the neocortex. *Nature* **458**, 501–504.

34) Ohtsuki, G., Nishiyama, M., Yoshida, T., Murakami, T., Histed, M., Lois, C. et al. (2012) Similarity of visual selectivity among clonally related neurons in visual cortex. *Neuron* **75**, 65–72.

35) Li, Y., Lu, H., Cheng, P.L., Ge, S., Xu, H., Shi, S.H. et al. (2012) Clonally related visual cortical neurons show similar stimulus feature selectivity. *Nature* **486**, 118–121.

36) Paik, S.B. and Ringach, D.L. (2011) Retinal origin of orientation maps in visual cortex. *Nat. Neurosci.* **14**, 919–925.

37) Yuste, R., Peinado, A. and Katz, L.C. (1992) Neuronal domains in developing neocortex. *Science* **257**, 665–669.

38) Peinado, A., Yuste, R. and Katz, L. (1993) Extensive dye coupling between rat neocortical neurons during the period of circuit formation. *Neuron* **10**, 103–114.

39) Casanova, M.F. and Casanova, E.L. (2018) The modular organization of the cerebral cortex: Evolutionary significance and possible links to neurodevelopmental conditions. *J. Comp. Neurol.* **530**, 1–11.

40) Kondo, S., Yoshida, T. and Ohki, K. (2016) Mixed functional microarchitectures for orientation selectivity in the mouse primary visual cortex. *Nat. Commun.* **7**, 1–16.

41) Ichinohe, N., Fujiyama, F., Kaneko, T. and Rockland, K.S. (2003) Honeycomb-like mosaic at the border of layers 1 and 2 in the cerebral cortex. *J. Neurosci.* **23**, 1372–1382.

42) Ray, S., Naumann, R., Bargaki, A., Tang, Q., Schmidt, H. and Brecht, M. (2014) Grid-layout and theta-modulation of layer 2 pyramidal neurons in medial entorhinal cortex. *Science* **343**, 891–896.

43) Ji, W., Gămainț, R., Bista, P., D’Souza, R.D., Wang, Q. and Burkhalter, A. (2015) Modularity in
the organization of mouse primary visual cortex. Neuron 87, 633–644.
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Profile

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