NEURAL FIELD DYNAMICS AND THE DEVELOPMENT OF THE CEREBRAL CORTEX.

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Abstract.
As neuron precursors divide and generate action potentials, they concurrently undergo apoptosis. We propose that the ensemble on neurons competitively selected is that which generates the maximum synchrony of action potentials. Consequently, local intracortical neurons and patchy connections emerge in "ultra-small" world configurations, forming clearly defined macrocolumns and patch connections in hexagonal array, where patch connections have relatively long axons, and less defined structures elsewhere in the cortex. Extension of the competitive principle to local synaptic level explains antenatal organisation of response properties in primary visual cortex, including effects of stimulus orientation, angle relative to motion, length, and speed on apparent orientation preference. Post-natal Hebbian consolidation of connections leads to the mature configuration. By implication, superimposed spatio-temporal images, rather than categorical feature responses, form the substrate of cortical information processing.

Keywords

Macrocolumns, Cortical patch connections, Cortical embryogenesis, Cortical apoptosis, Synchronous oscillation, Neural small worlds, V1 Organization, Cortical Visual responses, Cortical feature responses, Spatio-temporal neural images.

1. Introduction

During embryogenesis cells that become the neurons of the cerebral cortex divide and migrate to their mature positions while undergoing apotosis –the cell death of a substantial fraction of their number - ultimately forming minicolumns in their radial disposition, while in their surface disposition they are said to form macrocolumns – periodic structures that are most apparent in the primary visual (V1) and somatosensory (S1) cortices, are each about 300 microns across, and are roughly delineated by superficial patchy connections on the perimeter of each column. Within each column, individual cells in V1 respond with an orientation preference (OP) to visual lines of differing orientation [1]. The surface organization of OP exhibits significant hexagonal rotational periodicity, in which each roughly delineated macro- columnar unit exhibits all values of OP arrayed around a pinwheel [2,3]. Varying chirality and orientation of the pinwheels achieves continuity of OP at the columnar margins, and patchy connections link areas of similar OP together, "like to like" (Figure 1.)

Hubel [4], in his Nobel address, hailed Mountcastle's original proposal that columns formed fundamental building blocks of cortex as "Surely the most important contribution to understanding of cerebral cortex since Ramon y Cajal". Enthusiasm for the explanatory power of the concept has since waned. Horton and Adams [5] described the cortical column as "a structure without a function", and terminology describing them has become confused [6].

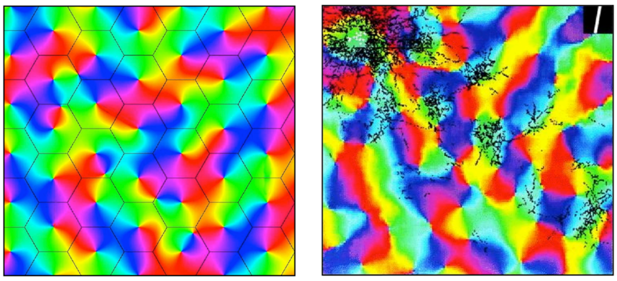

Figure 1 Left: idealized diagram of organization in V1 of OP, 0-180 degrees, about singularities, and with marginal continuity, within an hexagonal framework composed of superficial patch connections. Right: experimental data [18]. The black areas are patchy synaptic connections.

Difficulties arise partly because columnar structure is not clearly apparent outside V1 and S1, and because there is marked interspecies variation in definition of columns even in V1, to the point of apparent absence in small animals. Attempts to model the emergence of columnar organization of OP have also struck considerable difficulty. In some species there is clear emergence of structure ante-natally, rather than post-natally, yet models of the macrocolumn are generally dependent on response to visual features [7]. Which "features" are regarded as fundamental is also controversial, and how this relates to signal processing is problematic.

We have proposed a theory of emergence of cortical columns and their functional significance [8], which differs considerably from all other explanations. We base our explnation on two findings: (1) in vitro, embryonic neurons fire synchronously and self-organize into "small worlds" [9] and (2) synchronous firing of neurons prevents their apoptosis [10].

We assume synchrony and cell survival are causally linked - perhaps because some collective pumping action allows a synchronously coupled assembly of cells to increase their uptake of one or more vital metabolic substances. Therefore the emergent cell network would be that selection of cell types, and their arrangement, that maximizes the amplitude of synchrony for a given limit of total metabolic supply. The consequences of these assumptions are as follows.

2. Selection for "small-world" connectivity

Our arguments are based upon properties demonstrated in simulations of cortical gamma synchrony, and travelling waves [11,12]. Closely situated cells are able to exchange synchronous pulses with smaller phase difference of afferent and efferent pulses. Therefore minimization of the total axonal lengths of their interconnections maximises synchrony magnitude (and uptake) while minimizing axonal metabolic cost.

In the dilute network of neuronal connections, the metric distance of soma separation is proportional to “degree of separation” in the topological sense. Therefore maximization of synchrony, by minimizing axonal lengths, selects a neural network with “ultra-small world” connectivity. This requires, in turn, that the average density of synaptic connectivity decline with distance as a power function [13].

A power function is the sum of exponential functions, and pre-synaptic densities of cortical neurons decline roughly exponentially [14]. Therefore small-world connectivity can be approximated from populations of neurons with differing characteristic ranges.

3. Local variability of axonal ranges in the selected population

Equal approximations to a power function can be achieved by combining different relative densities of a variety of cell types, each type characterised by axonal length. Simplifying to only two types, Figures 2 and 3 show where long/short axon length is large ($\lambda_\beta >> \lambda_\alpha$) approximation of a power curve requires the ratio of local neurons to patch neurons be large ($N_\beta >> N_\alpha$).

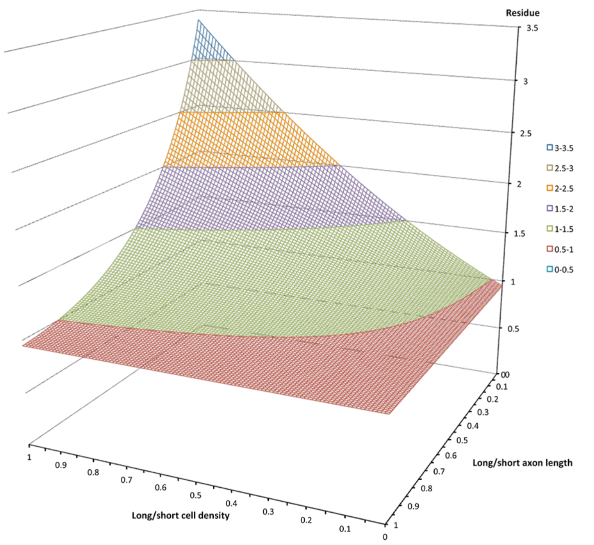

Figure 2 Equal approximations to a power function can be achieved with a variety of combinations of cell densities and axonal ranges. Colour margins show fit-residual isocontours.

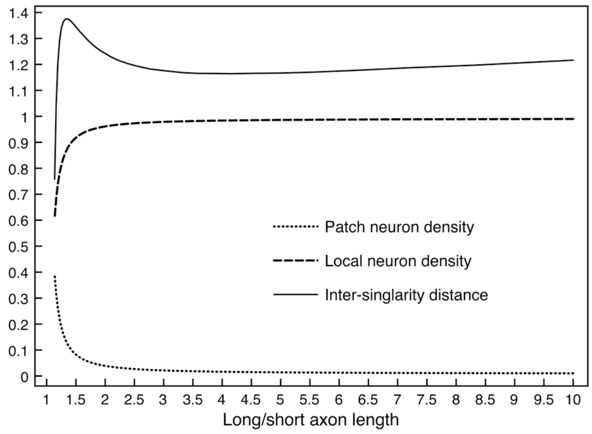

Figure 3 Cell densities and axonal ranges of local and patch neurons vary approximately inversely for equivalent fits to a power function obtained along the lowest-residual iso-contour in Figure 2. Intersingularity distance (cp Figure 4) is comparatively invariant over this range.

4. Resolution into macrocolumns

It can be shown that, where J is the magnitude of synchronous oscillation, and $\mathbf{q},\mathbf{r}$ are positions of excitatory neurons in the cortex,

$$J \propto \int_{\mathbf{q}}\int_{\mathbf{r}} (N_\alpha \lambda_\alpha e^{-\lambda_\alpha|\mathbf{q}-\mathbf{r}|} + N_\beta \lambda_\beta e^{-\lambda_\beta|\mathbf{q}-\mathbf{r}|}) d\mathbf{q} d\mathbf{r}$$

Therefore synchrony is maximized by selection of that ensemble of cells in which the cells with relatively short but dense axons are closely situated to each other. Such packing forces the cells with long-range axons to form connections at longer range, enforcing a “patchy” connection system. Arrangement in an hexagonal patchwork optimizes this synchrony-facilitating orderliness, but a clearly demarcated arrangement of this type is only possible where

$$\frac{local\ cells}{local\ cells + patch\ cells} = \frac{N_\beta}{N_\alpha + N_\beta} \geq \frac{\pi}{2\sqrt{3}}$$

This follows simply from the ratio of area of a circle to a hexagon, when local cells are enclosed within an hexagonal patch-connection frame. Therefore the absence of a clearly columnar arrangement does not imply a loss of the small world organization, nor does it deny that both short-range local connections, and longer-range functional connections are present – the distinct types are merely more entangled with each other. (See Figure 4.)

Thus, variation of the clarity of demarcation of columns in differing cortical areas, and between species, need not reflect major differences in function.

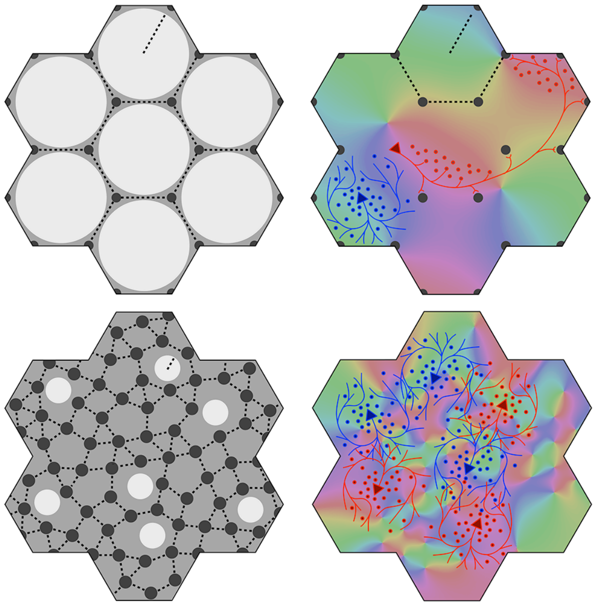

Figure 4 Variation of the structure of macrocolumns at extremes of the axonal lengths and cell numbers in Figure 3. Top: With large long/short axon length ratio, clearly resolved hexagonal organization emerges, with long (red) patch connections linking "like to like", and highly clustered short intracortical axons (blue). Bottom: near-complete loss of resolution when long/short axon ratio approaches 1.

5. A Mobius map within macrocolumns

Restated in physical terms, the maximization of J requires the populations of cells of differing axonal range be geometrically arranged so as to permit maximum resonance throughout the system. Since the amplitude of synchronous oscillation declines with distance of separation of cell bodies, then the system of patch connections and the local neurons within each macrocolumn must achieve a 1:1 connection system, promoting resonance between cells in each macrocolumn, and the surrounding patch system, and thus forming an input map of the cortical surround, projected onto each macrocolumn. If it is additionally assumed that the competition for crucial resources is not simply between individual neurons, but also between closely situated pre-synapses arising from the same cell, then "winner take all" competition between closely situated synaptic connections would develop, and at equilibrium each cell would then require high firing correlation with some of its neighbors, and low firing correlation with other neighbors – and be correspondingly strongly linked to some neighbors by "saturated" synapses, and weakly to others by "sensitive" synapses. This intra-cellular constraint, along with the requirement to form a 1:1 map of connections between each macrocolumn and its patchy-connection surround, can be met if the connections within the macrocolumn form a closed system analogous to a Mobius strip. Figure 5 (top) shows how a dynamic equilibrium of synaptic connections can thus be struck. The mapping of the patch system onto the macrocolumn can be expressed as

$$\mathbf{P}(\left|\mathbf{R}-\mathbf{C}_j\right|,\vartheta) \rightarrow \mathbf{p}^{[2]}(\left|\mathbf{r}-\mathbf{C}_j\right|,\pm\vartheta+\varphi)$$

where $\mathbf{P}$ is the plane of the patchy connections, and $\mathbf{R}$ are cortical positions with reference to these, while $\mathbf{p}$ and $\mathbf{r}$ are corresponding plane and positions within a macrocolumn. . The square brackets (*here* [2]) indicate the map's resemblance, if viewed from a third dimension, to a 2:1 map formed by squaring a complex vector. $\mathbf{C}_j$ is the origin of both $\mathbf{P}$ and $\mathbf{p}^{[2]}$ for the $j-th$ local map, and corresponds to the position of the OP singularity in that macrocolumn. ϑ is the polar angle of $\mathbf{R}$, chirality of the local map is indicated by $\pm\vartheta$, and φ is the orientation of the local map relative to the global map.

Figure 5 (bottom) shows further requirements for synchrony maximization. On the input map, radial lines on the surrounding cortex must map about a centre, analogous to an OP singularity. The Mobius strip-like folding of connections means that "OP" from 0 – 180 degrees is mapped 0 – 360 degrees about the singularity – concealing a superposition of diametrically opposite lines projected from the cortex to the macrocolumn. To further increase resonance, patch connections must link "like to like" OP in forming multiple 1:1 maps, and adjacent macrocolumns must also be so arranged as to increase resonance by linking "like to like" map positions on adjacent macrocolumns, as closely as possible within a roughly hexagonal framework. Thus, the properties of V1 sketched in Figure 1 are reproduced.

These considerations apply to the development of the cortex prior to the beginning of vision at birth.

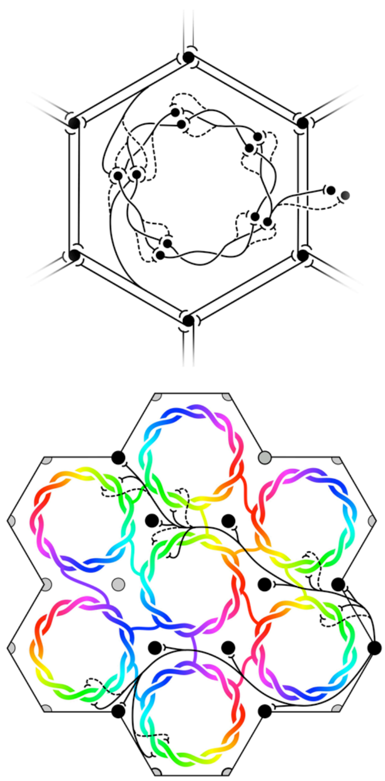

Figure 5 Maximization of synchrony with local synaptic competition leads to Mobius ordering, within macrocolumns.
Top: Equilibrium disposition of saturated (solid) and sensitive (dashed) synapses in the developing neocortex. Bottom: "Like to like" saturated patchy connections map the same part of the surrounding cortical field onto homologous cell positions on the Möbius configuration.

6. Consequences of eye-opening and development of responses to stimuli

The dynamic equilibrium of synaptic activity described above presumably gives rise to some persistence of the structure on Hebbian principles, but subsequent to birth, inputs from the direct visual pathway must produce strong perturbations from equilibrium, and overwriting of the Mobius structure by later learning.

To fire rapidly in the mature brain, individual neurons in V1 require direct visual input from their receptive fields, in summation with "contextual" signals transferred laterally by the patch system – and on firing, they give rise to further, laterally spreading, contextual signals, forming travelling waves.

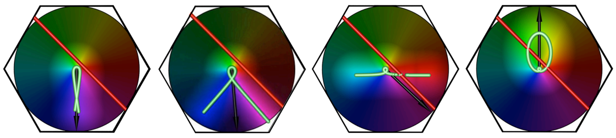

Figure 6 In V1, lateral transmission via patchy connections, plus input from direct visual pathway, summates above threshold for action potentials. Results for a line moving from left to right, and oriented at 45 degrees to the line of passage, with stimulus speed/wave speed, left to right, 0.1, 0.5, 1.0, 1.5.

The transfer of these waves from the wider cortex to each macrocolumn, considered as transfer to a Mobius-like map, is then a mapping with time lags of an image, O, given by

$$O(\mathbf{P},t) \rightarrow O\left(\mathbf{p}^{[2]}, t + \frac{|\mathbf{R}-\mathbf{r}|}{v}\right)$$

where v is the wave speed.

This permits the simulation of V1 neuron responses to visual moving lines, by calculating the corollary inputs reaching a macrocolumn at the time the direct visual input reaches the same macrocolumn, as shown in Figure 6.

The results match the experimental data of Basole et al. [15] – data considered incompatible with earlier notions of V1 neuron OP specificity.

In the case of a visual line of given length, the selective neuron responses vary not only with line orientation, but also with its inclination to the direction of travel, and speed, as shown in Figure 7. Notably, the "classic" property of elementary OP is seen only for low stimulus speeds.

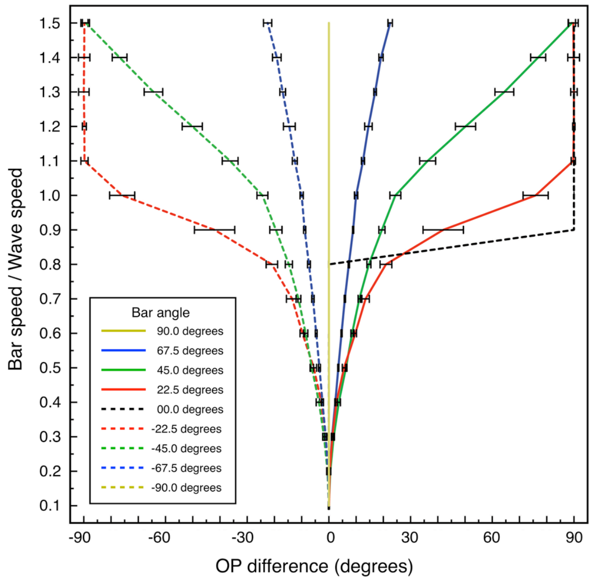

Figure 7 Simulation results: change in apparent OP, and standard error of the estimate, as a function of bar speed to wave speed, for lines at different orientations to their directions of motion. Bar length 6 macro-column diameters.

The results of Basole et al. have been otherwise explained by assuming V1 neurons show specific tuning to combinations of object orientation, spatial frequency and temporal frequency [16]. We have shown that Issa et al.'s description is equivalent to the effect of Hebbian learning upon the properties demonstrated in our simulation. Overwriting of the pre-natal Mobius maps by post-natal Hebbian learning also explains the consolidation of "like to like" patchy connections, and the continuity and completeness required by dimension-reduction models [7] of response maps.

7. Interactions between cortical areas

The same principles of self-organization should apply widely in the cortex. If so, then cortical areas self-organized into patchy connections and macrocolumns could also interact with other cortical areas via cortico-cortical fibers. Favorov and Kursun [17] have demonstrated the potential of neocortical layer 4 to permit near-linear superposition of impulses relayed via cortico-cortical fibers. Co-resonance among sets of macrocolumns at multiple scales would thus be possible. With such an ante-natal organization, after birth, signals from the environment could then produce complex contextual superpositions of waves relayed between groups of Mobius maps.

One such instance is modeled in Figure 8, showing how neuron responses to compound aspects of moving visual stimuli could arise. Similarly, return transmission from higher to lower cortical areas might mediate some aspects of attention.

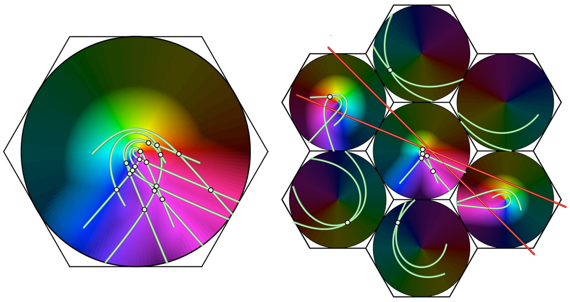

Figure 8 Inter-areal interactions. Right: a complex of macrocolumns in V1, three of which are concurrently activated by a moving visual line. Left: A column in a higher visual area, which is co-resonant at equilibrium with the lower-centre complex. Transient signals from the lower to the higher system, result in superposition of signals representing different positions on, and times of passage of, the moving line.

8. Conclusions

Our account emphasizes the importance of cooperative and competitive processes in embryonic development, in addition to genetically programmed developmental cascades. It explains diverse aspects of neural architecture and function in a unified way, including the ante-natal emergence of functional structures in V1, the origin of macrocolumns and superficial patch connections, their tendency to hexagonal periodicity, their interareal and interspecies variation, and the response properties of V1 neurons, including the post-natal abnormalities produced by visual deprivation. The model can also be combined with models utilizing Turing pattern formation, to account for the origin of OD columns. The principles may (with appropriate adjustment for local cell forms and the organization of input pathways) be applicable to other sensory modes, and even motor cortex. At the time of writing preliminary evidence has been obtained of the existence of Mobius-like organization in macrocolumns of the sensorimotor cortex.

As well as the capacity to explain empirical data, there are interesting implications for theories of neural information processing. The ultra-small-world configuration implies that the organization is near a maximum for speed and energy-efficiency of processing. Synaptic storage capacity can reach theoretical maximum entropy, under the assumption that available metabolic resources are sufficient to sustain only 50% of synapses at maximum saturation. The modular organization offers a potential for the rapid expansion of the cerebral cortex seen in its evolution.

Perhaps most importantly, the model indicates that brain function may be built upon a primary, *ab initio*, spatial organization that can act as a reference framework for sensory inputs from the environment as well as for internal dynamics of the Freeman type. Not abstract features, but superimposed spatio-temporal images, may form the kernel of cerebral information processing.

Acknowledgement
Dedicated to Adrienne Edith Wright.

References

1. Hubel, D. H., and Wiesel, T. N. (1959). Receptive fields of single neurones in the cat's striate cortex. *J. Physiol.* 148, 574–591.

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

3. Muir, D. R., Da Costa, N. M. A., Girardin, C. C., Naaman, S., Omer, D. B., Ruesch, E., et al. (2011). Embedding of cortical representations by the superficial patch system. *Cereb. Cortex* 21, 2244–2260.

4. Hubel, D. H. (1981). Acceptance Address. The Nobel Prize in Medicine.

5. Horton, C. H., and Adams, D. L. (2005). The cortical column: a structure without a function. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 360, 837–862.

6. Rakic, P. (2008). Confusing cortical columns. *PNAS* 105, 12099-12100.

7. Swindale, N. V. (1996). The development of topography in the visual cortex: a review of models. *Network* 7, 161–247.

8. Wright, J.J., and Bourke, P.D. (2013). On the dynamics of cortical development: synchrony and synaptic self-organization. *Frontiers in Computational Neuroscience*. DOI: 10.3389/fncom.2013.00004

9. Downes, J. H., Hammond, M. W., Xydas, D., Spencer, M., Becerra, V. M., Warwick, K., et al. (2012). Emergence of a small-world functional network in cultured neurons. *PLoS Comput. Biol.* 8:e1002522. doi: 10.1371/journal.pcbi.1002522

10. Heck, N., Golbs, A., Riedemann, T., Sun, J.-J., Lessmann, V., and Luhmann, H. J. (2008). Activity dependent regulation of neuronal apoptosis in neonatal mouse cerebral cortex. *Cereb. Cortex* 18, 1335–1349.

11. Wright, J. J. (2009). Generation and control of cortical gamma: find- ings from simulation at two scales. *Neural Netw.* 22, 373–384.

12. Wright, J. J. (2010). Attractor dynamics and thermodynamic analogies in the cerebral cortex: synchronous oscillation, the background EEG, and the regulation of attention. *Bull. Math. Biol.* 73, 436–457.

13. Cohen, R., and Havlin, S. (2003). Scale- free networks are ultrasmall. *Phys. Rev. Lett.* 90:058701. doi: 10.1103/PhysRevLett.90.058701

14. Braitenberg, V., and Schüz, A. (1991). *Anatomy of the Cortex: Statistics and Geometry.* Berlin, New York: Springer.

15. Basole, A., White, L. E., and Fitzpatrick, D. (2003). Mapping of multiple features in the population response of visual cortex. *Nature* 423, 986–990.

16. Issa, P., Rosenberg, A., and Husson, T. R. (2008). Models and measurements of functional maps in V1. *J. Neurophysiol.* 99, 2745–2754.

17. Favorov, O.V., and Kursun, O. (2011). Neocortical layer 4 as a pluripotent function linearizer. *J. Neurophysiol.* 105, 1342-1360. doi: 10.1152/jn.00708.2010

18. Bosking, W. H., Zhang, Y., Schofield, B., and Fitzpatrick, D. (1997). Orientation selectivity and the arrangement of horizontal connec- tions in tree shrew striate cortex. *J. Neurosci.* 17, 2112–2127.