A Universal Design Principle for Visual System Pinwheels

Charles F. Stevens

The Salk Institute, La Jolla, Calif., USA

That all mammalian brains share a common design is widely appreciated, and recent evidence indicates that axonal and dendritic arbors also conform to a single general design principle [Snider et al., 2010]. At macro- and microscales, one can argue that brains are the 'same'. Does this same 'sameness' extend to the mesoscale structure of brains? In other words, can we find structural principles that hold at the level of neural circuit design? Recently published work by Kaschube et al. [2010] argues that, indeed, pinwheels in the visual system do share a single design, an observation that raises the possibility of common brain designs from the micro-through meso- to macroscales.

What are pinwheels, and where are they found? Neurons in the primary visual cortex are tuned to specific locations in the visual world and also to the orientation of a line or edge at that location [Hubel and Wiesel, 2005]. Thus, many visual cortical neurons are capable of responding to light at a particular location, but only those cells whose preference matches the orientation of an edge or line at that point will generate spikes. The collection of neurons that look at a particular point but have individual cells tuned to all possible orientations are arranged in a structural motif called a 'pinwheel' [Blasdel and Salama, 1986; Bonhoeffer and Grinvald, 1991]. The cells in a pinwheel with a particular orientation

preference fall along spokes that radiate from a single center point. Furthermore, the preferred orientation, which runs from vertical (0° angle) through horizontal (90° angle) back to the vertical (0° which is equivalent to 180°), progresses in an orderly way as one proceeds circumferentially around the pinwheel center. A schematic pinwheel, whose borders are indicated by the dotted square, embedded in a 4 × 4 pinwheel array is represented in figure 1a, with orientations of 0°, 22.5°, 45°, 67.5°, 90°, 112.5° and 135°, and 157.5° labeling the spokes of the pinwheel where the cells are tuned to those preferred orientations. The lines in this figure represent iso-orientation contours, with the heavy lines designating 0°, 45°, 90° and 135°.

Pinwheels come in two distinct types, clockwise (+) and counterclockwise (−). The pinwheel outlined by the dotted square in figure 1a is a clockwise type whose preferred orientation increases as you progress clockwise around the center. Counterclockwise pinwheels increase the angle of their preferred orientation as you go counterclockwise around the center.

Pinwheels tend to tile the cortex in a particular way so that clockwise and counterclockwise pinwheels are, as seen in figure 1a, surrounded by nearest neighbors with the opposite sign. This sort of tiling means that neurons with a particular orientation preference form a spoke that runs

from the center of one pinwheel to the centers of its neighbors, an arrangement that minimizes the lengths of 'wires' needed to establish and make use of the response properties of the cortical cells [Durbin and Mitchison, 1990]. However, figure 1a is misleading because the actual lattice of pinwheel centers is sloppy rather than perfectly regular as shown in the illustration. Iso-orientation lines from an actual patch of visual cortex are illustrated in figure 1b, where it can be seen how different real pinwheels are from the ones shown in the idealized version in figure 1a.

Pinwheels were first discovered in the primary visual cortex (V1 or area 17) [Blasdel and Salama, 1986; Bonhoeffer and Grinvald, 1991], but they have now been demonstrated in area 18 (V2) [Swindale et al., 1987] and in the motion-sensitive visual cortical area known as MT where the spokes of the pinwheels indicate the neuron preference for the direction of an object's movement rather than for the orientation of edges [Diogo et al., 2002]. Furthermore, when information from the retina is misrouted through the auditory thalamus to the primary auditory cortex (A1), the cortical cells in A1 respond to oriented edges in the visual world and are arranged with the pinwheel motif [Sharma et al., 2000].

Because of noise in the lattice of pinwheel centers, and because pinwheels are

Fig. 1. Maps of the visual cortex with iso-orientation contours. **a** An idealized array of pinwheels with the boundaries of one pinwheel delineated by the dotted box. Heavier lines represent iso-orientation contours with orientations of 0°, 45°, 90° and 135°. The thinner lines designate iso-orientation contours with angles half-way between those of the heavier lines. The orientations associ-

ated with cells in the pinwheel (dotted box) label the spokes of that pinwheel. The (+) and (–) at the pinwheel centers designate clockwise and counterclockwise pinwheels. A hypercube is designated by lines indicating the lengths of its sides (Λ). **b** Iso-orientation contours for a region of the actual cortex defined by optical imaging.

not all just the same size, as shown in figure 1b, determining if the pinwheels from different species share a common design is a difficult problem. This is the problem attacked by Kaschube et al. [2010] who developed quantitative methods for comparing pinwheels. The first step in their approach is easy (but not as easy as it sounds): count the number of pinwheel centers in patches of the cortex to get the average density ν (ν = number of pinwheel centers per square millimeter of the cortical surface area). The reciprocal of density ν^{-1} is the average pinwheel size (square millimeter per pinwheel).

The second step is to find what is often known as the ‘hypercube’ area. Using optical imaging methods, one can find regions of the cortex where the neurons respond to, say, vertical lines. The average cortical distance from a particular orientation region to the next one with that same orientation is, as indicated in figure 1a, measured as Λ in millimeters, so that a cortical area Λ^2 is associated with the orientation repeat. Λ^2 is the hypercube area in square millimeters. Now a way to characterize pinwheel structure independently of pinwheel size variation is to use the quantity ρ , the number of pinwheels per hypercube area; you divide the area Λ^2 by the average area per pinwheel (which is the reciprocal of density, $1/\nu$) so that $\rho = \nu\Lambda^2$. For the idealized pinwheel array illustrated in figure

1a, there are 4 pinwheels per hypercube area. What makes this way of characterizing pinwheels useful is that ρ has a different value for different kinds of pinwheel arrangements from perfectly regular, as in the square lattice in figure 1a (where $\rho = 4$), to a striped arrangement which can easily have a value of $\rho = 0.3$.

Kaschube et al. [2010] studied the pinwheel patterns determined from over 100 primary visual cortices from mammals representing the orders carnivora (ferret, *Mustela putorius*), scandentia (tree shrew, *Tupaia belangeri*) and primates (galago, *Otolemur crassicaudatus*). The average hypercube and pinwheel sizes from the different cortices were found to vary considerably as illustrated in the graph in figure 2a, where the hypercube area is plotted as a function of the pinwheel area for the various cortical samples. As can be seen, these data are quite orderly and are fitted in the figure by a straight line with a slope of $\pi = 3.1416$ that gives the number of pinwheels per hypercube. The fact that these data are all fitted by a single value for pinwheels per hypercube supports the idea that they share a common structure, a conclusion confirmed by additional quantitative comparisons of pinwheel properties, such as the distribution of nearest neighbor distances [Kaschube et al., 2010].

The fact that the number of pinwheels per hypercube area has a value very close

to π is not just a numerological oddity, but rather arises from a class of theories about how the pinwheel patterns are formed. This class of theories follows from some very simple ideas (e.g. the notion that the pinwheel structure should be the same at any location over the cortex), and the result (number of pinwheels per hypercube = π) does not depend on any free parameters. The agreement between the observed properties of pinwheels from three different mammalian orders and the very general analysis [Kaschube et al., 2010] provides good evidence for mesoscale uniformity in the arrangement of components in neural circuits.

If we accept the idea that pinwheels have a common design, three questions need answering. What does the success of the theory for pinwheel formation say about the underlying mechanisms? Why do rodents and lagamorphs lack pinwheels in their visual cortex? And are there pinwheels, as yet undetected, outside the visual system? I consider these questions in turn.

The class of pattern formation theories considered by Kaschube et al. [2010] are beautiful because they are simple and general. But the very generality of the theory has the disadvantage that it constrains properties of possible mechanisms without specifying what those mechanisms are. The class of theories is equally good

Fig. 2. Quantitative properties of pinwheel areas. **a** Hypercube area plotted as a function of pinwheel area for the three species indicated. The line has a slope of 3.1416 and gives the number of pinwheels per hypercube. Data replotted from figure 2a in the study of Kaschube et al. [2010]. **b** Pinwheel area as a function of the V1 area on a double logarithmic plot for various species. Data for V1 and pinwheel areas for primates (bush baby, owl monkey,

squirrel monkey and macaque) and for cat from table 2 in the study of Xu et al. [2004]. V1 areas for the tree shrew from the same table, and for ferret from Law et al. [1988]. Pinwheel areas for tree shrew, ferret and bush baby, with the same value as given by Xu et al. [2004], are from data presented in figure 1a in the study of Kaschube et al. [2010]. The scaling law line for primates is a least squares fit with a slope of -0.15 and an intercept of -0.52 .

for activity-dependent, genetically based and mixed mechanisms.

The paper by Kaschube et al. [2010] makes the case for a universal pattern formation mechanism for pinwheel generation, but rodents and lagamorphs have been reported to lack pinwheels in their primary visual cortices [Van Hooser, 2007]. Indeed, direct simultaneous recording from virtually all neurons in the superficial half of rat V1 shows that the orientation preferences are distributed at random rather than according to a pinwheel structure [Ohki et al., 2005]. Rats are well known to have bad vision – they would be legally blind if they were humans – and perhaps this accounts for their lack of pinwheels. But gray squirrels have much better visual acuity, two or three times better than rats (but still legally blind), yet also fail to manifest pinwheels in V1 [Van Hooser et al., 2005]. Despite the lack of pinwheels, the responses of individual neurons in the rodent V1 are not different from other species: their cells have receptive fields that are tuned to position, orientation and spatial frequency in just the same ways as, say, cat or monkey V1 neurons. So why would a supposed universal mechanism for pinwheel generation fail to operate in rodents and lagamorphs?

Answering this question in a really satisfactory way obviously depends on carrying out, in a range of large rodent and lagamorph species, definitive imaging studies of the sort done in rat [Ohki et al., 2005],

and on understanding the biological mechanisms of pinwheel generation. For primates, pinwheel size decreases as the area of V1 becomes larger as illustrated in figure 2b, but this decrease is quite gradual: the pinwheel area depends on the V1 surface area to the -0.15 power (straight line in fig. 2b). Moreover, not all pinwheel areas follow this same empirical relation. As shown in figure 2b, pinwheel areas for tree shrew, ferret, bush baby and cat – a carnivore not studied by Kaschube et al. [2010] – increase with the cortical area. If a rat had pinwheels the size of those in cat, its entire V1 would have only two dozen (a 5×5 array in a V1 of about 7 mm^2), and if the rat had pinwheels that were the size of those in the tree shrew (holder of the world record for pinwheel smallness), it would have about five dozen (about an 8×8 array). The corresponding numbers of pinwheels for the gray squirrel would be about 10 times those for rats – the gray squirrel V1 is about 10 times the area of a rat V1 [Van Hooser, 2007] – a value consistent with the approximately 3-fold improvement in acuity (because acuity varies as the square root of ‘pixel’ number).

The observations above suggest a plausible reason why these rodent species (and lagamorphs studied) lack pinwheels. The possible existence of long-range interactions between pinwheels was originally proposed because the simplest pattern formation mechanisms for generating pinwheels do not give stable patterns in the

absence of long-range interactions; with only nearest neighbor interactions, pinwheels that initially form annihilate one another and disappear during the pattern generation process [Wolf and Geisel, 1998]. If the necessity for long-range interactions is believed, then even the pinwheel array for the gray squirrel may be too small for stable pinwheels to develop. The extent of binocular representation in V1 can also be important in pinwheel stabilization [Reichl et al., 2009], and this may help explain the lack of pinwheels in rodents and lagamorphs.

If the pinwheel motif is indeed general, perhaps other cortical areas use this same mesoscale structure. For example, perhaps the reason pinwheels are found in the auditory cortex of ferrets when retinotectal axons are misrouted to the auditory thalamus [Sharma et al., 2000] is that these visual inputs tap into a pinwheel motif that is already present as a result of the auditory thalamocortical projections. We know how to detect pinwheels in the visual system, but we do not know what stimuli to use to reveal them in other areas and there are too many possible combinations of stimulus parameters to search effectively for non-visual pinwheels. But if pinwheels are eventually found to exist outside of the visual cortices, the common design of mesoscale structures described by Kaschube et al. [2010] would be even more general than we currently imagine.

References

- Blasdel GG, Salama G (1986): Voltage-sensitive dyes reveal a modular organization in monkey striate cortex. *Nature* 321:579–585.
- Bonhoeffer T, Grinvald A (1991): Iso-orientation domains in cat visual cortex are arranged in pinwheel-like patterns. *Nature* 353:429–431.
- Diogo AC, Soares JG, Albright TD, Gattass R (2002): Two-dimensional map of direction selectivity in cortical visual area MT of Cebus monkey. *An Acad Bras Cienc* 74:463–476.
- Durbin R, Mitchison G (1990): A dimension reduction framework for understanding cortical maps. *Nature* 343:644–647.
- Hubel DH, Wiesel TN (2005): *Brain and Visual Perception*. New York, Oxford University Press.
- Kaschube M, Schnabel M, Loewel S, Coppola DM, White LE, Wolf F (2010): Universality in the evolution of orientation columns in the visual cortex. *Science* 330:1113–1116.
- Law MI, Zaksas KR, Stryker MP (1988): Organization of primary visual cortex (area 17) in the ferret. *J Comp Neurol* 278:157–180.
- Ohki K, Chung S, Ch'ng YH, Kara P, Reid RC (2005): Functional imaging with cellular resolution reveals precise micro-architecture in visual cortex. *Nature* 433:597–603.
- Reichl L, Loewel S, Wolf F (2009): Pinwheel stabilization by ocular dominance segregation. *Phys Rev Lett* 102:1–4.
- Sharma J, Angelucci A, Sur M (2000): Induction of visual orientation modules in auditory cortex. *Nature* 404:841–847.
- Snider J, Pillai A, Stevens CF (2010): A universal property of axonal and dendritic arbors. *Neuron* 66:45–56.
- Swindale NV, Matsubara JA, Cynader MS (1987): Surface organization of orientation and direction selectivity in cat area 18. *J Neurosci* 7:1414–1427.
- Van Hooser SD (2007): Similarity and diversity in visual cortex: is there a unifying theory of cortical computation? *Neuroscientist* 13: 639–656.
- Van Hooser SD, Heimel JA, Chung S, Nelson SB, Toth LJ (2005): Orientation selectivity without orientation maps in visual cortex of a highly visual mammal. *J Neurosci* 25:19–28.
- Wolf F, Geisel T (1998): Spontaneous pinwheel annihilation during visual development. *Nature* 395:73–78.
- Xu X, Bosking W, Sary G, Stefansic J, Shima D, Casagrande V (2004): Functional organization of visual cortex in the owl monkey. *J Neurosci* 24:6237–6247.