Retinal origin of orientation maps in visual cortex

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The orientation map is a hallmark of primary visual cortex in higher mammals. It is not yet known how orientation maps develop, what function they have in visual processing and why some species lack them. Here we advance the notion that quasi-periodic orientation maps are established by moiré interference of regularly spaced ON- and OFF-center retinal ganglion cell mosaics. A key prediction of the theory is that the centers of iso-orientation domains must be arranged in a hexagonal lattice on the cortical surface. Here we show that such a pattern is observed in individuals of four different species: monkeys, cats, tree shrews and ferrets. The proposed mechanism explains how orientation maps can develop without requiring precise patterns of spontaneous activity or molecular guidance. Further, it offers a possible account for the emergence of orientation tuning in single neurons despite the absence of orderly orientation maps in rodents species.

It has long been known that the primary visual cortex of higher mammals is organized into functional maps. One of the most studied is the orientation map, which captures the preferred orientation of neurons across the cortical surface. Optical imaging methods have revealed that preferred orientation on the cortex changes continuously in a quasi-periodic fashion, except at intermittent point discontinuities (pinwheels) and line discontinuities (fractures), where orientation preference seems to jump. Although much effort has been devoted to the study of cortical maps, we still lack a full account of how they develop and what part they play in normal visual processing.

The quasi-periodicity of cortical maps has been postulated to establish sensory modules that serve to process signals from a single location on the visual field by a heterogeneous set of receptive fields. However, it is now recognized that some species lack orientation maps despite having simple cells that show normal receptive field structure and orientation selectivity. Similarly, the expression of ocular dominance columns varies widely across individual members of a species and is entirely absent in some species that, nevertheless, show normal evoked potentials to stereoscopic stimuli. Such findings raise doubts about the functional significance of cortical maps in visual processing.

Important clues regarding the wiring of orientation maps and receptive fields of neurons are found in early development. In kittens, orientation-tuned responses can be measured as soon as the kittens open their eyes about a week after birth. Orientation columns (the clustering of cells with similar preferences) and maps are also present at this early stage. This organization can be established without exposure to normal visual experience, which is otherwise needed for receptive fields and maps to reach full maturation.

The development of the spatial structure of cortical receptive fields also offers important hints. A key observation is that simple-cell receptive fields seem to develop without an intermediate phase of segregation between ON and OFF subregions (as assumed by dominant developmental models). This is surprising because the classical view holds that numerous geniculate afferents, with overlapping ON- and OFF-center receptive fields, must be sorted out by cortical neurons to generate simple cells with segregated ON and OFF subregions. However, this segregation process has never been observed experimentally. Instead, the available data in cats indicate that the ratio of simple cells (which have one or more segregated subregions) to complex cells (which have overlapping ON and OFF responses) remains approximately constant during development. This suggests that cortical cells have a normal receptive field organization as soon as it is possible to record visually driven responses from them.

How can receptive fields and maps be wired so early in development? Our study builds upon the statistical connectivity hypothesis, which provides some initial answers to this question. The basic idea is that receptive fields and orientation maps in the cortex are constrained by the spatial distribution of ON- and OFF-center receptive fields in retinal mosaics, a notion that goes back to pioneering work in the 1980s. These constraints seed the structure of receptive fields and maps in the cortex upon which other developmental processes, such as activity-dependent refinement and maintenance, act during the critical period.

The present work advances the theory by answering an important question: how does the model generate periodic orientation maps? Here we show that the periodicity of the map can arise from the moiré interference pattern of retina ganglion cell (RGC) mosaics, which is mirrored in the lateral geniculate nucleus (LGN) and generates a quasi-periodic input into the cortex. As we will see, this insight provides a simple explanation for the generation of simple-cell receptive fields and orientation maps, making new predictions about their organization.

A central prediction of the model is that iso-orientation domains should lie on a hexagonal lattice on the cortical surface. Here we show that this arrangement is observed in all four different species examined so far—monkeys, cats, ferrets and tree shrews—providing...
experimental support for the model. Moreover, our analyses demonstrate that the model admits regimes in which orientation tuning in individual cells can arise without the emergence of an orderly orientation map, potentially extending the theory to incorporate rodent species.

RESULTS

Orientation maps as moiré interference of RGC mosaics

We propose that the cortical orientation map is seeded by moiré interference\(^\text{30}\) between ON- and OFF-center receptive fields of one class of ganglion cell in the retina (Fig. 1). We introduce our model by considering an ideal case where the locations of ON- and OFF-center receptive fields lie at the vertices of perfect hexagonal lattices. This is a sensible starting point because it is known that their local structure is a noisy hexagonal lattice\(^\text{28} \), as inferred from the fact that the angle formed by a cell body with its neighbors of the same sign has modes at multiples of 60 degrees (see Supplementary Fig. 1 for another demonstration). The ON and OFF lattices are also known to be independent from each other in the sense that knowledge of the location of a cell from one sign does not provide information as to the location of cells of the other\(^\text{31,32} \). When two hexagonal lattices are superimposed in such a way, the result is a periodic interference pattern (Fig. 1a). An important property of the resulting pattern is that the nearest neighbor of an ON-center cell is an OFF-center cell (and vice versa) (Fig. 1b), a feature that is also observed in the statistics of RGC mosaics reconstructed experimentally\(^\text{28,33} \). We call such a pair of opposite-sign, nearest neighbors a dipole and assign to it an orientation that is perpendicular to the line joining the centers of the constituent receptive fields (Fig. 1b).

The statistical wiring model posits that pooling inputs of nearby RGC receptive fields (relayed by cells in the LGN\(^\text{34} \)) using an isotropic weighting function is sufficient to generate orientation tuning and simple-cell receptive field structure\(^\text{26,27} \). If the input to a cortical cell is dominated by a single RGC dipole, the resulting receptive field will be a structure similar to that of a simple cell, with side-by-side sub-regions of opposite sign, and its preferred orientation will match that of the dipole (Fig. 1b). The receptive fields generated by the model are not always dominated by single dipoles\(^\text{26} \), but those satisfying this condition tend to be the ones that are most sharply tuned for orientation (Fig. 1d). Thus, the orientation of RGC dipoles provides a good approximation to the structure of the orientation map seeded by the model. This simplification allows us to derive and understand many important properties of the cortical map predicted by the theory in a simple and intuitive manner.

Periodicity of the orientation map

From the preceding discussion it is clear that the period of the orientation map is determined by the period of the moiré pattern itself, \(d_M\) (Fig. 1a), which is given by\(^\text{35} \)

\[
d_M = \frac{1 + \alpha}{\sqrt{\alpha^2 + 2(1 - \cos \theta)(1 + \alpha)}} d = S \times d
\]

Here \(d\) represents the spacing of the first lattice, \((1 + \alpha)d\) is the spacing of the second lattice and \(\theta \) their relative orientation. We define the scaling factor as the ratio between the period of the interference pattern and that of the lattice, \(S = d_M / d \) (Fig. 1c). This ratio is
Figure 2 Moiré scaling factor and orientation map periodicity. Each column depicts examples of different scaling factors. The operating regimes illustrated are the ones shown by a, b and c in Figure 1c. (a) Examples of the resulting moiré interference patterns. (b) The preferred orientations of well tuned cells (left) and filtered orientation maps (right). Format as in Figure 1d. (c) Autocorrelations of orientation maps show hexagonal structure, indicating that iso-orientation domains lie on a hexagonal lattice (see also Fig. 1d). (d) Enlarged area from the maps in b showing the predicted micro-architecture of orientation preference. Preferred orientation changes gradually in the left and middle panels. In the right panel, orientations are distributed as a salt-and-pepper-like pattern. (e) Histogram of the orientation differences between pairs of nearby cells (<100 µm) on the cortical surface. Similar orientations cluster in the left and middle panels. In the right panel, preferred orientations at nearby locations are uncorrelated. The uniform distribution of angular differences in the right histogram is a signature of salt-and-pepper organization. Scale bar in a, 1 mm on the retinal surface. Scale bars in b–d, 1 mm of cortical space.

important because it determines how many RGC receptive fields are involved in the construction of one cortical hypercolumn.

The parameters α and θ determine the scaling factor and the operating regime of the model. Operating regimes that yield small values of the scaling factor (less than ~3) generate a salt-and-pepper-like organization, in which neighboring cells have orientations that independent of each other, because the period of the interference pattern becomes comparable to the distance between the centers of the receptive fields of nearest neighbors in the mosaics (Fig. 2). Operating regimes with scaling factors between 4 and 16 generate interference patterns that, after the cortical magnification factor is taken into account (see the calculation in Supplementary Discussion), can match the periodicity of experimentally measured maps in primates (Fig. 2). Regimes near the origin (α,θ) = (0,0) generate large scaling factors, and, as a consequence, preferred orientation changes very slowly across cortical space (Fig. 2).

Orientation maps have hexagonal symmetry

One surprising prediction can be derived from the ideal model by examining the structure of the moiré interference patterns. Each pattern is periodic: all possible orientations appear within one cycle and change smoothly across cortical space (Fig. 1a,d). The hexagonal symmetry of the interference pattern predicts that (assuming an isotropic magnification factor) locations with the same orientation preference should be arranged in a hexagonal lattice pattern on the cortical surface as well (Figs. 1d and 2c).

We tested this prediction using published orientation maps from different species. In each case, we begin by representing each map as a two-dimensional image θ(x,y) and compute a two-dimensional (circular) autocorrelation as follows:

\[ r(\Delta x, \Delta y) = \frac{1}{N} \sum_{x,y} \left[ \exp(2i\theta(x,y)) + \exp(2i\theta(x+\Delta x, y+\Delta y)) - 1 \right] \]

In other words, two copies of the same map are shifted relative to each other by (Δx,Δy) and the agreement between the orientations in the shifted maps is assessed in the region of overlap by an averaged vector resultant (the region of overlap having N pixels). If all the values between two maps in overlapped areas match closely, we obtain a value r = 1. If the orientations at each location between two maps are orthogonal, r = −1.

The autocorrelation functions, evaluated in two individuals of four different species, showed a pattern of discrete, secondary peaks around the origin that resemble a hexagon (Fig. 3a) (see also...
Supplementary Fig. 2). In each case, the autocorrelation functions are scaled and rotated to map the local peak with the largest magnitude onto the point (0,1) in the plane. The statistical significance of the local peaks is assessed by generating control maps with an isotropic amplitude spectrum matching that of experimental maps and computing the distribution of amplitudes of secondary peaks from such a family of control maps (calculation detailed in Supplementary Fig. 3). All the secondary peaks shown in Figure 3a as black dots attain a significance level of P < 0.002. In other words, the local peaks are very unlikely to have been generated by chance, assuming the null hypothesis that orientation maps are isotropic.

Next, we computed the average autocorrelation function across individuals and species (Fig. 3b). The result shows local peaks that very closely match the hexagonal prediction. The distribution of local maxima in the individual cases, superimposed on top of the mean autocorrelation function, cluster around the vertices of the hexagon. This observation can be validated by the distribution of the angular location of the peaks relative to the reference point at (0,1), which is clearly bimodal (Fig. 3c). When we fit the angular distribution with a mixture of von Mises components, we find the data are best explained by a mixture of two components (Fig. 3c; model selection by Bayesian information criterion). The modes of the components match very well their predicted locations at 60 and 120 degrees. Thus, the angular distribution of local maxima is consistent with that of a hexagonal lattice. When the same analysis is repeated on the control maps, the magnitudes of all of these local maxima are statistically significant (bootstrap analysis, P < 0.002). The scale bar equals the orientation map period. (c) Angular location of local peaks in the autocorrelation function in panel b relative to the reference peak. The distribution is bimodal with modes near 60 and 120 degrees, as predicted by the model. Bimodality was established by a mixture of von Mises distributions using the Bayes information criterion to select the order of the model. The red solid line shows the probability distribution of the best fit. (d) The same analysis performed on control maps. Here the distribution of local peaks is much more isotropic. (e) One component (red line) is sufficient to account for the control data. In a–d local peaks were considered only if their distances to the origin were within ±33% of the map period.
is almost uniform, with a depletion of points near the reference point that results from the alignment procedure (Fig. 3d,e). Finally, for comparison, we performed the same analysis on orientation maps generated by an activity-dependent model. We found that this model does not generate autocorrelations with any secondary peaks of statistically significant magnitude ($P > 0.05$; data not shown).

### Effects of RGC lattice noise on map periodicity

Of course, RGC mosaics are not perfect hexagonal lattices. This raises the question of whether the proposed mechanism is capable of seeding an orientation map after the addition of realistic amounts of noise in the positions of the RGC receptive fields. We tested this by perturbing the vertices of the hexagonal lattices with independent two-dimensional Gaussian noise to match the nearest-neighbor statistics in experimentally measured mosaics. A ratio between the standard deviation and the average of the lattice spacing of $\sigma/d = 0.12$ provides a very good match to the distributions of nearest-neighbor receptive fields in the experimental data (Fig. 4a). We find that even with this realistic degree of noise, the interference pattern remains strong enough to generate a periodic orientation map (Fig. 4b,c). The periodicity of the map can be evaluated by measuring the amplitude and location of the secondary peaks in the autocorrelation of the simulated orientation map as a function of noise (Fig. 4b). The normalized period of the map (relative to the ideal case) remains stable (Fig. 4b, right) and the magnitude of the secondary peak is positive and substantially larger than zero (Fig. 4b, middle), indicating a robust periodic structure.

Insight into the robustness of the seeded map is gained by calculating the number of original dipoles in the interference pattern that are lost as positional noise increases (Fig. 4c) and, of those that remain, how much their orientation is perturbed relative to that of their original configuration (Fig. 4d). A dipole is defined by two cells of opposite sign that are nearest neighbors of each other. As the positional noise increases the conditions defining a given dipole may cease to hold, in which case we say the dipole is ‘lost’. Simulations show a roughly linear increase in the fraction of dipoles lost with increasing noise, reaching a value of 27% for realistic values (Fig 4c). Thus, about 73% of the dipoles of the original pattern survive. Of those dipoles remaining, their orientation is close to that of their original configuration (Fig. 4d). These analyses clarify the reasons behind the robustness of the seeded map to positional noise. An example of an interference pattern with realistic noise and the resulting orientation map is provided in Supplementary Figure 4.

### Robustness of receptive field structure to positional noise

What is the spatial structure of simple-cell receptive fields generated by the model, and how are they affected by the presence of positional noise? To answer this question, we fitted a two-dimensional Gabor function to the simulated simple-cell receptive fields at randomly chosen cortical sites. The Gabor function was defined by:

$$h(x', y') = A \exp \left( - \left( \frac{x'^2}{2\sigma_x^2} + \frac{y'^2}{2\sigma_y^2} \right) \right) \cos(2\pi f x' + \phi)$$

where the coordinate system $(x', y')$ is obtained by translating the original by $(x_0, y_0)$ and rotating it by $\gamma$:

$$x' = (x - x_0) \cos \gamma + (y - y_0) \sin \gamma$$

$$y' = -(x - x_0) \sin \gamma + (y - y_0) \cos \gamma$$

In the $(x', y')$ plane, the modulation of the sinusoidal function is along the $x'$ axis, and $\sigma_x$ and $\sigma_y$ represent the width of the Gaussian envelope along each axis respectively, $f$ represents spatial frequency and $\phi$ is the spatial phase. Even-symmetric profiles are obtained for $\phi = 0$ and odd-symmetric profiles are obtained for $\phi = \pi/2$.

We analyzed the data by looking at the distribution of $n_e = \sigma_x f$ and $n_o = \sigma_y f$, as previously done in the experimental study of primate data. These numbers can be thought as a measure of the width of the Gaussian envelope along each axis in units of the period of the underlying sinusoidal grating.

We found that the distribution of $n_e$ and $n_o$ remains largely unaffected by changes in scaling factor and amount of RGC lattice noise (Fig. 5). The reason for this is that the local structure of receptive fields is solely dependent on the statistics of nearest-neighbor distributions (Fig. 4a). So long as there is a high probability that the nearest neighbor of one receptive field is another of the opposite sign, the model will generate dipoles that can induce similar families of simple-cell receptive fields. The theory thus admits a regime in which single neurons can be well tuned for orientation despite the absence of a smooth orientation map, as is observed in rodents (Fig. 2, right column).

The distribution of spatial phases of the predicted receptive fields is also of interest (Fig. 5). The simulations indicate that odd-symmetric receptive fields tend to be well tuned for orientation. This is due to the fact that inputs to a cell dominated by a single dipole will generate a well tuned, odd-symmetric receptive field. Even-symmetric receptive fields can be either broadly tuned (with one effective subregion) or sharply tuned (with three effective subregions of alternating signs). The tendency for well tuned cells in the model to shift their spatial phase toward odd symmetry is consistent with experimental observation.

### DISCUSSION

Where do orientation maps come from? Here we put forward the notion that periodic orientation maps arise from the moiré interference pattern of quasi-regular retinal mosaics (Fig. 1). A central prediction...
of the model is that iso-orientation domains should be arranged approximately in a hexagonal lattice on the cortical surface. Indeed, we found this property in all four different species tested: ferrets, tree shrews, cats and monkeys. Such a universal property of maps provides support for a single mechanism at work in different species and one that is consistent with the model’s prediction. A recently published geometric analysis of orientation columns provides further evidence of their hexagonal structure18.

Several puzzling findings of visual development are parsimoniously explained by the model. Moiré interference explains how cortical receptive fields and maps may arise even in the absence of precisely structured activity in the developing thalamus22,36,39. This is because RGC mosaics themselves can develop without the need for visual experience40. The theory solves the dilemma of how simple cells can arise in early development without an intermediate phase of segregation between ON- and OFF-center inputs19,20. It further accounts for a segregation of ON- and OFF-center afferents into cortical domains41. Both results are a consequence of the limited overlap between nearest neighbors in retinal mosaics.

The emergence of orientation columns is also explained by the model, as in this scheme cortical neurons in a column receive inputs from the same set of RGCs and thus their receptive fields are constrained in the same way. If the input partly determines the preferred orientation of the cortical column, the emergence of orientation columns is easily understood. Experimental support for this idea is provided by the recent finding that the distribution of ON- and OFF-center receptive fields in the LGN predicts the orientation preference of its target cortical column42. This result is noteworthy because it, if holds across all cortical positions, implies that the orientation map is already coded in the LGN. Competing theories based on activity-dependent wiring do not account for the orientation bias present in the LGN input and how it can successfully predict the preferred orientation of their cortical targets.

During development, a diverse set of receptive fields is observed in the thalamus, some of which show ON and OFF subregions and orientation tuning43. Such an intermediate stage is consistent with our model in that, before the pruning of retino-geniculate inputs, thalamic cells may pool from receptive fields of both signs, resulting in receptive fields similar to those generated by the model. Reference 43 postulated that this intermediate stage, along with activity-dependent learning, could generate orientation-tuned cells in the cortex. We note that unless one also incorporates the key constraints established by the retinal input, such a mechanism alone fails to account for the emergence of orientation columns.

The simultaneous mapping of simple-cell receptive fields in a population of nearby cortical cells can also serve to test our hypothesis that receptive fields are constructed from a limited number of inputs. For example, a recent two-photon imaging of mouse visual cortex reveals that nearby simple-cell receptive fields often share common subregions with the same location and shape44, consistent with the notion that they are all constructed from a limited input26.

The model admits a regime in which single cells are well tuned despite the absence of an orientation map. This was demonstrated by the invariance of the receptive field structure (documented by the distribution of \((n_r, n_s)\) values) with changes in the scaling factor and positional noise (Fig. 5). The theory thus offers a potential explanation for how the properties of simple-cell receptive fields could be similar in mice, cats and monkeys27,45. We must exercise caution as a small scaling factor is only one possible explanation of this phenomenon. In general, if the emergence of the moiré interference pattern is disrupted for any reason, it will lead to a failure in the creation of orientation maps. To some extent this situation may already arise at the fovea, where dedicated one-to-one lines for ON- and OFF-center receptive fields increase their overlap compared to those in parafovea. Indeed, near the fovea the orientation map appears disrupted in double-label 2-deoxyglucose studies46, which is also consistent with the fact that orientation-tuned neurons near the fovea are fewer and more broadly tuned than those in the parafovea47.

The present scope of the model is limited to explaining how the inputs from the contralateral eye, which invade the cortex ahead of those from the ipsilateral eye, could establish an initial blueprint for receptive fields and maps. The orientation map is expected to change as input from the ipsilateral eye is accommodated and both orientation maps come into register, but not so much as to erase all vestiges of the initial map organization15. Even during this process, the geniculate inputs will continue to constrain the range of preferred orientations attainable at any cortical site from any given eye. In other words, these constraints ought to be taken into account in models that study activity-dependent matching of the orientation maps of the two eyes.

Finally, the theory predicts the existence of what could be called orientation scotomas: at some locations, the cortex cannot represent every orientation equally well. This results from the fact that limited retinal resources at some locations prohibit the implementation of receptive fields with a complete set of preferred orientations (Fig. 1d). We are now testing this prediction by mapping human orientation discrimination thresholds of very small stimuli in the far periphery. A confirmation of orientation scotomas would provide further support for the theory and challenge the present view of the cortex as analyzing the local image by a homogeneous set of filters tuned to different orientations. Although the preceding hypothesis is controversial, we note that a previous study48 found that pairs of cells in the cortex must have their receptive field centers one receptive field diameter apart to ensure their orientation preferences are, on average, orthogonal to one another, a finding consistent with the notion of orientation scotomas.

To summarize, moiré interference offers a mechanism for the initial seeding of a periodic orientation map and simple-cell receptive fields that does not require specific patterns of spontaneous thalamic activity, the presence of molecular markers or cortical scaffolding. The simplicity of the model, the parsimonious explanations it offers to several key findings, and the recent confirmation of several of its predictions are all encouraging. The hexagonal structure in the autocorrelations of orientation maps of various species now provides additional support for our hypothesis, which awaits its ultimate test—an experiment that can reveal a correlation between the structure of the RGC mosaics and the orientation maps measured in the same individuals.

**METHODS**

Methods and any associated references are available in the online version of the paper at http://www.nature.com/natureneuroscience/.

**Note:** Supplementary information is available on the Nature Neuroscience website.

**ACKNOWLEDGMENTS**

We are grateful to A. Benucci and M. Carandini (University College London) for sharing their imaging data of cat primary visual cortex, supported by research grant EY017396 to M. Carandini. We also thank D. Fitzpatrick (Max Planck Florida Institute), L. White (Duke University), W. Bosking (University Texas at Austin) and Y. Li (UC Berkeley) for sharing existing ferret and tree shrew maps. We thank M. Carandini, D. Fitzpatrick, R. Shapley, J.-M. Alonso and E. Callaway for providing comments on earlier versions of this manuscript. This work was supported by research grant EY018322 (D.L.R.).
AUTHOR CONTRIBUTIONS
Both S.-B.P. and D.L.R. were responsible for the theoretical concepts, computer simulations and writing.

COMPETING FINANCIAL INTERESTS
The authors declare no competing financial interests.

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ONLINE METHODS

The simulations were performed using the statistical wiring model published earlier. We briefly summarize the algorithm here and refer the reader for justification of the parameters selected to our earlier work26-27.

Structure of retinal ganglion cell mosaics. Simulated RGC mosaics were generated by adding various amount of random displacement to each vertex of a hexagonal lattice that represents the position of ON- and OFF-center receptive fields26. The centers of RGC receptive field position vectors are defined by

\[
\mathbf{r}_{ij}\text{OFF} = d L_{ij} + \mathbf{n}_{ij},
\]

\[
\mathbf{r}_{ij}\text{ON} = \left(1 + \alpha \right)d R_{ij} L_{ij} + \mathbf{n}_{ij} + \mathbf{n}_0.
\]

Here \(d\) represents the grid spacing for the OFF mosaic, \((1 + \alpha)d\) represents the grid spacing for the ON mosaic, the matrix

\[
R_{ij} = \begin{bmatrix}
\cos \theta & \sin \theta \\
-\sin \theta & \cos \theta
\end{bmatrix}
\]

represents the relative rotation between the ON and OFF mosaics, \(\mathbf{n}_{ij}\) represents two-dimensional, Gaussian (independent and identically distributed) noise with a standard deviation \(\sigma\), and \(L_{ij}\) are the vertices of a hexagonal grid

\[
L_{ij} = \frac{1}{2} \begin{bmatrix}
1 & 1 \\
\sqrt{3} & -\sqrt{3}
\end{bmatrix} i, j = 0, \pm 1, \pm 2, \ldots
\]

The standard deviation of the noise, \(\sigma\), is conveniently expressed as a fraction of the grid spacing, \(d\). The noise-free ideal model corresponds to \(\sigma = 0\). A random relative spatial shift between the two mosaics \(\mathbf{n}_{ij}\) can be added. However, except for the particular case where \(\alpha = 0\), this has no consequence for the results because a rotation and translation can be written as a rotation around a different center.

To calculate nearest-neighbor statistics in experimental mosaics, we used digitized maps of receptive field reconstructions from the macaque monkey retina, published in ref. 33, modeling the center of the receptive fields as a two-dimensional Gaussian with a standard deviation of 60 \(\mu\)m in retinal space.

Statistical connectivity and receptive field computation. The statistical wiring model includes a stochastic component that allows cells in the same cortical column to develop slightly different receptive fields, because both the probability of connection and its strength are random variables26. In this work, we did not simulate the whole model but only computed the mean receptive field at each location. We have previously shown the mean receptive field can be computed as a weighted sum of the afferent LGN input:

\[
\Psi = \sum_i \exp\left(-d_i^2/2\sigma^2\right) \Psi_i^{\text{LGN}}
\]

where

\[
\sigma = \sqrt{\sigma_{\text{conn}}^2 + \sigma_{\text{syn}}^2}
\]

and where \(\Psi_i^{\text{LGN}}\) is the receptive field of the \(i\)th LGN neuron and \(d_i\) is the distance between the locations of the LGN afferent and the cortical site where we are calculating the mean receptive field. The values of \(\sigma_{\text{conn}}\) and \(\sigma_{\text{syn}}\) were set as 25 \(\mu\)m of cortical space, and they represent the rates of the spatial falloff of the probabilities of connectivity and synaptic strength, respectively, which are assumed to be Gaussian. (See ref. 27 for a detailed description of these parameters and derivations.)

Cortical map measurements. After the mean receptive field was calculated at each cortical position, we estimated its preferred orientation and selectivity from its Fourier transform \(\Psi(\omega)\) as follows. The preferred orientation is defined as

\[
\theta_{\text{pref}} = \arg(\mu)/2,
\]

Orientation selectivity index (OSI) was defined as

\[
\text{OSI} = \frac{\int |\Psi(\omega_{\text{pref}} + \theta)| \exp(2i \theta) d\theta}{\int |\Psi(\omega)| d\theta}
\]

where \(\omega_{\text{pref}} = |\theta|\) is the preferred spatial frequency of the receptive field filter.

Selectivity-weighted orientation map. The predicted OSI varies across the cortex and is maximal at locations where cortical sites receive input dominated from a single dipole. These strongly tuned sites contribute largely to the orientation tuning in the cortex, thus seeding the orientation map. To identify the location and preferred orientation angles of such signals, we sampled the cortical locations with an OSI higher than a specified threshold OSI > 0.25 (Figs. 1d and 2d and Supplementary Fig. 4). For visualization, a smooth continuous version of the map is obtained by diffusion of orientations with a Gaussian window of 140 \(\mu\)m in cortical space. These smooth maps are shown in the right panels of Figures 1d and 2b and Supplementary Figure 4.

Analysis of experimental orientation maps. Regions of interest (ROI) in the experimental maps were selected by avoiding areas that were too close to the V1/V2 boundary and having moderate size (~3 x 3 orientation periods). For each individual we chose between two and four non-overlapping ROIs. Selecting ROIs of intermediate size is important because locally the maps have hexagonal structure, but over a long range the orientation of the structure can drift. In such a case, computing the autocorrelation of over a very large area can obliterate the secondary peaks observed in the autocorrelation function using smaller ROIs. Conversely, the smaller the ROI, the more likely we are to obtain peaks in the autocorrelation by mere chance. Thus, we adopted a strategy where we averaged the autocorrelation functions of non-overlapping ROIs for each individual after appropriate normalization (see Supplementary Fig. 2).

To compute the statistical significance of secondary peaks in the autocorrelation function, we calculated the probability that they could have resulted by chance from control orientation maps. These control maps were generated by enforcing their Fourier amplitude spectrum to be isotropic and having the same marginal, radial amplitude spectrum as the map under consideration (a detailed description of the method is provided in the Supplementary Discussion and Supplementary Fig. 3).

Orientation maps in cat are from ref. 49, and tree shrew and ferret data were provided by D. Fitzpatrick (Max Planck Florida Institute), with L. White, W. Bosking and Y. Li (personal communication). Orientation maps from monkey primary visual cortex were obtained from reference 50.

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Supplementary Discussion

Auto-correlation of retinal ganglion cell mosaics shows hexagonal structure

Wässle and colleagues first observed that the local structure of cell mosaics was approximately hexagonal\(^1\), as the histogram of the angular difference of all neighbors to a reference cell within some distance showed a mode at 60\(^\circ\). Their analysis was based on the location of the cell bodies (not the receptive fields). However, the same conclusion holds true if one uses the actual centers of the receptive field themselves, obtained by simultaneously mapping them by means of electrode arrays\(^2\).

Supplementary Fig 1 shows a (smoothed) auto-correlation of a sample mosaic of receptive field centers shown on the left. These data are from one of the reconstructed mosaics in Gauthier et al (2009). The center peak at the origin was removed to ease visualization. It can be seen the structure of the secondary peaks is clearly hexagonal. Further, one can also detect the presence of additional peaks beyond the secondary peaks, indicating the spatial scale over which the RGC mosaic is hexagonal extends farther than its immediate neighborhood. The spatial scale over which such hexagonal structure is present is now a matter of additional research.

Auto-correlation function in individual maps

As already mentioned in the text, regions of interest (ROI) in the experimental maps were selected by avoiding areas that were too close to the V1/V2 boundary and having an intermediate size. For each individual we choose between 2 to 4 non-overlapping ROIs (this choice was limited by the field of view of the camera and the size of the ROI). After calculating the auto-correlation for each individual ROI (three sample calculations are shown in Supplementary Fig 2), the result is scaled and rotated so that the dominant secondary peak mapped to the (1,0) point in the plane. The transformed images were then averaged to yield the
average auto-correlation for that individual animal (Supplementary Fig 2, right panel). These are the images, along with their local maxima, that are presented in Fig 3a.

**Statistical significance of secondary peaks in the auto-correlation function**

To verify if the secondary peaks in our calculations are statistically significant, we calculated the probability they could have resulted by chance from control maps the power spectrum of which were isotropic (see Supplementary Figure 3 for a flow chart of this calculation). This was done by first generating an isotropic Fourier spectrum that matched the marginal radial spectrum from the measured map. We then assigned random phases to each coefficient and iterated a number of times the following steps:

1. Perform an inverse Fourier transform, resulting in a complex image
2. Normalize each pixel value (a complex number) to have a magnitude of one
3. Take a 2D FFT of the result
4. Enforce amplitude spectrum to equal that of the isotropic control.

After a number of iterations (=1000), the algorithm produces an orientation map where the spectrum satisfies the constrained imposed by the isotropic spectrum and where every pixel in the complex image has a magnitude of one. The phase of this image represents a control orientation map. We generated a family of $N=500$ such control images.

Next, we calculated a set ($M=500$) of average auto-correlation images by randomly sampling (without replacement) $K$ of them, where $K$ was the actual number of ROIs used in each case (2 to 4), and averaging them after alignment with the dominant peak. From this set of auto-correlation control images we can calculate the probability that each of the local maxima observed in the average auto-correlation could have resulted by chance under the null hypothesis that the map was isotropic. This is done by looking at the values attained at the same location of the peak in the family of control average auto-correlations. Then we ask how many of the control values exceed the one actually measured and divide it by the their total number to obtain the $p$-value.
Example of mosaic and map with realistic levels of noise

An example of an interference pattern and the resulting orientation map with realistic levels of noise is shown in Supplementary Fig 4. Under this conditions it is difficult under visual inspection to observe a clear interference pattern, but the robustness of the structured input becomes evident in clustering of dipoles with similar orientation in the orientation map.

Relationship between mosaic parameters and the period of orientation columns

What scaling factors are necessary to match the period of the map observed in the retina to the observed periodicity in the cortex?

The following estimates are based on the published reconstructions of RGC receptive fields of M. fascicularis 3. By computing the mean and standard deviation of nearest neighbor distances for each class of cells (Fig 4), and by assuming the mosaics arise from a noisy hexagonal lattice, one can estimate the magnitude of the positional noise and the grid spacing of the lattice.

Using the magnocellular mosaic in Figure 2 of Gauthier et al. (2009), we obtain $d_{ON} = 156\mu m$, $d_{OFF} = 142\mu m$. In both cases, independent estimates of the noise expressed as a fraction of the grid spacing was $\sigma = 0.12 \times d$. Thus, in terms of the parameters used in Figure 1 this implies that $\alpha = 0.105$ and $d = 142\mu m$.

In the primate eye, the nonlinear relationships between retinal eccentricity (in mmr) and visual angle (in deg) is given by, $A = 0.1 + 4.21E + 0.038E^2$ (we will adopt mmr to mean "millimetres on the retina" while mmc will denote "millimetres on the cortex"). The reconstruction of this particular mosaic originates from a 9 mmr eccentric location,
corresponding to 41° of visual angle. At this eccentricity, the cortical magnification factor is approximately 0.146 mmc/deg.\textsuperscript{5} From the above formula, we also obtain 
\[ \frac{dA}{dE} = 4.21 + 0.076E \text{ (deg/mmr)} \]
which evaluated at 9mmr gives 4.9 deg/mmr. This means that at this retinal eccentricity we obtain a factor of
\[ 4.9 \text{deg/mmr} \times 0.146 \text{mmc/deg} = 0.715 \text{mmc/mmr}. \]

The period of the orientation map in \textit{M. fascicularis} is approximately 0.750mmc\textsuperscript{6-7}, which translates to a period on the retina of 1.05mmr. We conclude that if the orientation map were to be set up by the mosaics of magnocellular RGCs we would need a scale factor of 
\[ S = \frac{1.05 \text{mmr}}{0.142 \text{mmr}} = 7.4 \]
Finally, having \[ S = 7.4 \] and \[ \alpha = 0.1 \], we estimate the relative rotation between the arrays to be \[ \theta = 6 \text{deg} \] (from the equation provided in the main text).

Similar estimates can be performed for the parvocellular mosaics. Our estimates here result in \[ d_{ON} = 106\mu m, \quad d_{OFF} = 101\mu m \] and \[ \sigma = 0.13 \times d \] for both mosaics. This generates values of \[ \alpha = 0.05 \] and \[ d = 101\mu m \]. Thus, the estimated scaling factor would be 
\[ S = \frac{1.05 \text{mmr}}{0.101 \text{mmr}} = 10.4 \]
from which we estimate a relative rotation of \[ \theta = 5 \text{deg} \].

These analyses predict that there RGC mosaics for ON- and OFF-center cells should not be statistically independent. We should be able to measure a consistent angular difference between the two. One way to do this is to compute the auto-correlations for both ON- and OFF-center mosaics as shown in \textbf{Supplementary Figure 1} and see if the hexagonal structures have different angles. Such studies are currently under way.
Supplementary Figure Legends

Supplementary Fig 1. Autocorrelation of the receptive field locations mapped by multi-electrode array show clear hexagonal structure (red hues correspond to higher correlation values). Thus the hexagonal structure of RGC mosaics is reflected both in the cell body locations as well as in the receptive field locations.

Supplementary Fig 2. Calculation of auto-correlation function in a single individual. A number of non-overlapping ROIs (three exemplified in this case) are obtained from the orientation map. Their auto-correlations are then computed and the largest local maxima identified (solid dots). Each auto-correlation image is then rotated and scaled so as to bring the dominant peak to the point (0,1). The average of these normalized functions results in the average auto-correlation shown on the right. Scale bars represents the map period in each case.

Supplementary Fig 3. Statistical significance of local peaks in auto-correlation functions. Orientation control maps are generated by a procedure that ensures they have the same radial Fourier amplitude spectrum as the measured ones. Their auto-correlation functions serve as a family that represent control samples for the maps in the ROIs. We then calculate what would be the family of auto-correlations we can expect given $K$ ROIs, where $K$ is the actual number of ROIs we used to calculate the auto-correlation function in each case. From this family we can obtain the distribution of amplitudes at any location in the map and use their values to estimate the probability that the magnitude of the local peak we measure could have resulted by chance. As the number of functions we generated was $M=500$ we can only assess significance down to a level of $p<0.002$, which was attained in all cases. Thus, the magnitude of the local peaks seen in the data are very unlikely to have resulted by chance.
Supplementary Fig 4. Example of mosaics and orientation map perturbed by a realistic level of noise. Scale bar 1mm of cortical space. Format is the same as Fig 1d.
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Sample OFF-center RGC mosaic

Auto-correlation with center peak suppressed
Data
Orientation map
Amplitude spectrum
Isotropic spectrum
Control map #1
Control map #N
Control auto-correlation #1
Control auto-correlation #N
Control average auto-correlation #1
Control average auto-correlation #M
Measured auto-correlation
and assessment of statistical significance
