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Three-dimensional visual feature representation in the primary visual cortex

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Abstract

In the cat primary visual cortex, it is accepted that neurons optimally responding to similar stimulus orientations are clustered in a column extending from the superficial to deep layers. The cerebral cortex is, however, folded inside a skull, which makes gyri and fundi. The primary visual area of cats, area 17, is located on the fold of the cortex called the lateral gyrus. These facts raise the question of how to reconcile the tangential arrangement of the orientation columns with the curvature of the gyrus. In the present study, we show a possible configuration of feature representation in the visual cortex using a three-dimensional (3D) self-organization model. We took into account preferred orientation, preferred direction, ocular dominance and retinotopy, assuming isotropic interaction. We performed computer simulation only in the middle layer at the beginning and expanded the range of simulation gradually to other layers, which was found to be a unique method in the present model for obtaining orientation columns spanning all the layers in the flat cortex. Vertical columns of preferred orientations were found in the flat parts of the model cortex. On the other hand, in the curved parts, preferred orientations were represented in wedge-like columns rather than straight columns, and preferred directions were frequently reversed in the deeper layers. Singularities associated with orientation representation appeared as warped lines in the 3D model cortex. Direction reversal appeared on the sheets that were delimited by orientation-singularity lines. These structures emerged from the balance between periodic arrangements of preferred orientations and vertical alignment of same orientations. Our theoretical predictions about orientation representation were confirmed by multi-slice, high-resolution functional MRI in the cat visual cortex. We obtained a close agreement between theoretical predictions and experimental observations. The present study throws a doubt about the conventional columnar view of orientation representation, although more experimental data are needed.

Keywords

Orientation columns; visual cortex; cat; singularity

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1. INTRODUCTION

Since Hubel and Wiesel proposed a revolutionary concept of functional architecture in the mammalian primary visual cortex, it has been thought that neurons optimally responding to specific orientations of local contours and vision through the left- or right-eye pathway are arranged in columns penetrating from the pia to white matter (Hubel & Wiesel, 1962). This concept indicates that a two-dimensional (2D) tangential layout of preferred orientations along the cortical surface, “orientation map” (Erwin et al., 1995), is sufficient for understanding the three-dimensional (3D) representation of preferred orientations in the visual cortex. There have been experimental reports on the 2D functional maps using optical imaging of intrinsic signals (Bonhoeffer Grinvald, 1991; Crair et al., 1997), and to reproduce the maps theoretically using computer simulation based on self-organization models (Swindale, 1982; Linsker, 1986; Miyashita & Tanaka, 1992; Miller, 1992, 1994; Swindale, 1996).

However, because the cerebral cortex, with a finite thickness, folds in a complex manner, and anatomical minicolumns are arranged radially around the crown of the gyri, functional columns may also be highly deformed. This in turn raises the question of how visual features are represented in the curved cortex. Despite a great success to reveal various functional columnar structures, optical imaging is limited to exposed cortical regions, and has an inability to resolve depth-dependent optical signals. Alternatively, functional magnetic resonance imaging (fMRI) techniques which have been widely used in humans can be used to image columnar structures. Various fMRI approaches including conventional blood oxygenation-level dependent contrast have been utilized for high-resolution mapping in animals (Kim et al., *Nature Neuroscience*, 2000; Duong et al., *PNAS*, 2001; Zhao et al., *NeuroImage*, 2005; Fukuda et al., *JNS*, 2006; Moon et al., *JNS*, 2007). Among currently available approaches, cerebral blood volume (CBV)-weighted fMRI with exogenous contrast agents provides the highest sensitivity, and high specificity to neuronal active sites (Zhao et al., *NeuroImage*, 2005). Furthermore, columnar maps obtained with CBV-weighted fMRI were validated by intrinsic optical imaging in the same animals (Fukuda et al., *JNS*, 2006). Thus, in the present paper, we propose to use this CBV-weighted fMRI for mapping 3D orientation columns.

In the present study, we attempted to examine the 3D representation of preferred orientations and directions on the basis of the standard Hebbian learning rule. We assumed a five-layer structure of the model visual cortex: 2 superficial (layers 2 and 3), 1 middle (layer 4) and 2 deep (layers 5 and 6) layers. In computer simulation, based on a biologically plausible assumption that visual feature representation starts to develop from layer 4 that receives geniculocortical inputs (Albus & Wolf, 1984), we gradually expanded the range of the self-organization of visual features from the middle layer to superficial and deep layers. Simulations reproduced the columnar organization of preferred orientations in a flat part of the model visual cortex, and orientation singularities formed vertical lines. The preferred direction also tended to be organized in a columnar fashion, although it was sometimes reversed abruptly along the depth direction. In contrast, in a curved part of the model cortex, simulations showed a wedge-like structure representing a single orientation, penetrating from the cortical surface to deeper layers. Orientation singularities appeared as warped lines like hairpins, which terminated at pinwheel centers on the cortical surface. The reversal of preferred directions occurred more frequently in the deeper layers than in the flat part of the model cortex. These simulated results indicate that functional columns are not rigid but flexibly deformed to reconcile with the global curvature of the visual cortex. The wedge-like orientation columns and the warped orientation line singularities predicted by the model were confirmed by multi-slice high-resolution fMRI of the cat visual cortex.

2. METHODS

2.1 Mathematical Modeling

We extended the previously reported model (Nakagama & Tanaka, 2004) to describe the formation of orientation, direction, ocular dominance and retinotopic representation in the 3D primary visual cortex. For simplicity, among 6 layers of the visual cortex, we omitted layer 1, because there are massive fibers running tangentially within the layer and neurons exist sparsely. In the other 5 layers, we assumed that neurons represent *a priori* primitive visual features such as ocular dominance, orientation preference, direction-of-motion preference and the center of the receptive field for simplicity. The cortical arrangement of the visual features was modified by local intracortical interaction among neurons, which change an initial random arrangement of visual features to form an orderly arrangement over the 3D primary visual cortex.

2.1.1 3D global structure of the model visual cortex—One of the purposes of this study is to investigate the effect of the global curvature of the visual cortex on visual feature representation. Therefore, we assumed a “stadium-shape” of the model cortex with a finite thickness, which is embedded inside a box composed of $128 \times 128 \times 72$ voxels. Each voxel represents a cortical neuron. The outer and inner surfaces, respectively, correspond to the cortical surface and the boundary between the grey and white matter. The model cortical depth was set at 30 voxels with a 6-voxel thickness of each layer from layer 2 to layer 6. We assumed the thickness of the model cortex to be 2mm, meaning one voxel is $66\mu\text{m}$. The periodic boundary condition was adopted to minimize a small-size effect.

2.1.2 Visual feature space—The feature space (FS) is given by the direct product of the space of the visual field (VF), the circular symmetric space of the preferred direction (PD) and the space of ocular dominance (OD): $\text{FS} = \text{VF} \times \text{PD} \times \text{OD}$. Space VF is the 2D visual field (26×54 grids), in which the position of a receptive field center of a cortical neuron is defined. The periodic boundary condition was imposed on space VF so as to be consistent with the periodic boundary condition imposed on the model visual cortex. The preferred orientation is an axis at right angles with the preferred direction of motion. The space OD is subdivided into five groups, in which groups 1 and 5 are driven exclusively by one of the two eyes, group 3 is driven by the two eyes equally, and groups 2 and 4 receive imbalanced inputs from the two eyes.

2.1.2 Energy function—We assume that a cortical neuron located at j in the model visual cortex represents a set of visual features (k, θ, μ) , where k , θ and μ indicate the position of the receptive field, preferred direction and ocular dominance, respectively. The ocular dominance μ takes a value of $\{-1, -1/2, 0, 1/2, +1\}$: $\mu = 1$ represents exclusively the left eye dominance and $\mu = -1$ exclusively the right eye dominance. The preferred direction θ takes one of 16 values out of $0, \pi/8, 2\pi/8, \dots, 15\pi/8$. The preferred orientation was assumed to be orthogonal to the preferred direction and invariant under rotational transformation of π . When a cortical neuron j represents $(k, \theta, \mu)\sigma_{j,k,\theta,\mu}$ takes 1, and otherwise, 0. An equation of

$\sum_{k,\theta,\mu} \sigma_{j,k,\theta,\mu} = 1$ is valid because any cortical neuron is supposed to represent only one set of features.

The state of the visual feature arrangements is characterized by the energy function:

$$H = - \sum_{j,j'} \sum_{k,\theta,\mu,k',\theta',\mu'} V_{j,j'} \Gamma_{k,\theta,\mu;k',\theta',\mu'} \sigma_{j,k,\theta,\mu} \sigma_{j',k',\theta',\mu'} + c \sum_{l=2}^6 \sum_{k,\theta,\mu} \left(\sum_{j \in \text{layer } l} \sigma_{j,k,\theta,\mu} \right)^2. \quad (1)$$

Here, $V_{j,j'}$ represents the 3D cortical interaction between a pair of visual features represented by neurons j and j' . This interaction is determined by the convolution of the dendritic arbor function with the axonal arbor function. It is known that in the adult cortex, there are long-range tangential and inter-layer connections. However, we assume that the axonal arbor of nearby cortical neurons mainly works for column formation in the early developmental stage, and we omit the long-range c. This assumption indicates that the interaction does not depend on the global morphology of the cortex and is identical for any positions either in the superficial layers or deep layers of the curved cortex. Therefore, we identify the cortical interaction as the dendritic integration, which is simply given by the Gaussian function:

$$V_{j,j'} = \frac{1}{2\pi\lambda_v^2} \exp\left(-\frac{d_{j,j'}^2}{2\lambda_v^2}\right), \quad (2)$$

where λ_v is the excitatory interaction length in the cortex ($\lambda_v = 2.0$ corresponding to 132 μm), and $d_{j,j'}$ indicates the distance between cortical neurons j and j' within the cortex. $\Gamma_{k,\theta,\mu;k',\theta',\mu'}$ represents the correlation function of input signals. The second term represents a constraint on the representation of the visual features to avoid imbalanced representation and results in each layer covering all the feature space as uniformly as possible. The constraint was imposed layer by layer. $j \in l\text{th} - \text{layer}$ indicates a neuron j located within the l -th layer of the model cortex except layer 1. The value of the coefficient of constraint c was set at 0.008.

Let us derive the correlation function of input signals. Signal input to a cortical neuron, $\eta_{k,\theta,\mu}^{\text{in}}$, optimally responding to visual feature (k, θ, μ) , is derived from its receptive field $R_{k,\theta;l,\phi}$ and local visual images $\xi_{l,\phi,\mu}^{\text{image}}$, is given by

$$\eta_{k,\theta,\mu}^{\text{in}} = \sum_{l,\phi,\mu} R_{k,\theta;l,\phi} \xi_{l,\phi,\mu}^{\text{image}}. \quad (3)$$

Here, l, μ and ϕ indicate a position in the visual field, eye dominance and direction of movement of a visual image. The correlation function $\Gamma_{k,\theta,\mu;k',\theta',\mu'}$ between $\eta_{k,\theta,\mu}^{\text{in}}$ and $\eta_{k',\theta',\mu'}^{\text{in}}$ is given by

$$\Gamma_{k,\theta,\mu;k',\theta',\mu'} = \left\langle \eta_{k,\theta,\mu}^{\text{in}} \eta_{k',\theta',\mu'}^{\text{in}} \right\rangle, \quad (4)$$

where the brackets denote the ensemble average over all presented visual images. We simply assume that the local components of images obey white noise regarding the position and direction of motion with a strength of correlation between the two eyes r :

$$\left\langle \xi_{l,\phi,\mu}^{\text{image}} \xi_{l',\phi',\mu'}^{\text{image}} \right\rangle = \gamma \delta_{l,l'} \delta_{\phi,\phi'} \left[(1+r)/2 + (1-r)\mu\mu'/2 \right]. \quad (5)$$

Thereby, the correlation function $\Gamma_{k,\theta,\mu;k',\theta',\mu'}$ is given by

$$\Gamma_{k,\theta,\mu;k',\theta',\mu'} = \gamma \sum_{l,\phi} R_{k,\theta;l,\phi} R_{k',\theta';l,\phi} [(1+r)+(1-r)\mu\mu'/2]. \quad (6)$$

If we suppose the input signal receptive field $R_{k,\theta;l,\phi}$ to be given by the product of the positional component and directional component, it is expressed by

$$R_{k,\theta;l,\phi} = \exp\left(-\frac{d_{k,l}^2}{2\lambda_{rf}^2}\right) [\cos^{2n}(\theta - \phi) + b\cos(\theta - \phi) + b]. \quad (7)$$

Here, $d_{k,l}$ and λ_{rf} represent the distance between the positions k and l in the visual field, and the spatial extent of the input signal receptive field. The directional component of the input signal receptive field is given by the sum of the orientation-bias component and direction-bias component. A positive integer n as the exponent determines the sharpness of orientation tuning. The larger n , the sharper the orientation tuning becomes. Taken together, the correlation function $\Gamma_{k,\theta,\mu;k',\theta',\mu'}$ is given by the direct product of correlation functions of the components of visual features:

$$\Gamma_{k,\theta,\mu;k',\theta',\mu'} = S_{k,k'} \Psi_{\theta,\theta'} O_{\mu,\mu'}, \quad (8)$$

where $S_{k,k'}$, $\Psi_{\theta,\theta'}$ and $O_{\mu,\mu'}$ represent component correlation functions regarding the position of receptive field centers in the visual field, direction of motion and ocular dominance, respectively. These component correlation functions are given by

$$S_{k,k'} = \exp\left(-\frac{d_{k,k'}^2}{2\lambda_{corr}^2}\right), \quad (9)$$

$$\Psi_{\theta,\theta'} = 2a_0^2 + \sum_{m=1}^{\infty} a_m^2 \cos m(\theta - \theta'), \quad (10)$$

$$O_{\mu,\mu'} = \frac{(1+r)+(1-r)\mu\mu'}{2}. \quad (11)$$

Here, λ_{corr} is the positional correlation length equal to $\sqrt{2}\lambda_{rf}$, which is set at 1.0. The directional component of the correlation function is given as a Fourier cosine series. The order of $m=1$ represents the correlation between a pair of directions of stimulus motion, whereas the order of $m=2$ represents the correlation between a pair of axes of motion, which are orthogonal to the preferred orientations. Parameters $\{a_m\}_{m=0}^{2n}$ are determined by the values of n and b .

2.1.3 Computer simulation—At the beginning of the simulation, we randomize visual features in the model cortex. In the middle layer of the cortex, neurons receive random inputs from either eye ($\mu = +1$ or -1), because the layer is geniculocortical input layer. In the

other layers, neurons receive random inputs with ocular dominance of either of +1, +1/2, 0, -1/2, or -1, and preferred direction of either of 0, $\pi/8$, $2\pi/8$, $\dots$, or $15\pi/8$. The RF center position is also randomized retaining rough retinotopy according to the probability:

$$A_{k,j} = \exp\left(-\frac{d_{J_k,j}^2}{2\lambda_{\text{Ret}}^2}\right), \quad (12)$$

where $d_{J_k,j}$ represents the distance between cortical position j and position J_k that retinotopically corresponds to the position k in the visual field, where λ_{Ret} represents the roughness of retinotopy ($\lambda_{\text{Ret}} = 3.5$). For each trial of updating visual features in the simulation, a new candidate for a set of visual features is selected according to the same probability distribution as in the initial randomization, and then the old set of features is replaced with the new one according to the probability determined by the energy difference between the states before and after the trial of replacement:

$$\Pr(\text{before} \rightarrow \text{after}) = \frac{1}{1 + \exp[\beta(H^{\text{after}} - H^{\text{before}})]}. \quad (13)$$

Here, H^{before} and H^{after} represent the energy before and after the trial of replacement, respectively. The parameter β , which determines the steepness of the logistic function of the right-hand side of Eq. (13) in the transition region, was set at $\beta = \infty$. Thereby, the probability takes 1 when H^{after} is smaller than H^{before} , otherwise 0. The repetition of the update procedure likely decreases the energy of the system and realizes an equilibrium cortical arrangement of visual features when the change in energy becomes negligibly small.

In the present model, in which the cortical interaction function is isotropic, clustering of similar visual features occurs but columnar organization cannot be formed even in flat parts of the model visual cortex when the simulation is carried out to update features sampled randomly from the entire model cortex. So, we carried out the simulation according to the following schedule of spatial simulated annealing that we call hereafter, which assists the formation of iso-orientation domains continuously extending from layer 2 to layer 6. For simulation step t in the interval of $1 \leq t < T_1$, simulation was performed only in the middle layer whose upper and lower boundaries were located at 13 and 18 voxels from the bottom of the model cortex. For $T_1 \leq t \leq T_2$, the inner boundary z^{inner} and the outer boundary z^{outer} of the simulation range in the depth direction was gradually changed as

$z^{\text{inner}} = 13 - \lceil 12 \times \frac{t - T_1}{T_2 - T_1} \rceil$, and $z^{\text{outer}} = 18 + \lceil 12 \times \frac{t - T_1}{T_2 - T_1} \rceil$. For $T_2 < t$, simulation was carried out in all model visual cortex. Here, one simulation step is defined as the trial numbers of updating features by the total number of voxels within which simulation is conducted. That is, for 1 simulation step, each voxel is tried to be updated, on average, once. Parameters T_1 and T_2 were set at 100 and 350 simulation steps. The simulation of the present model without the anisotropic cortical interaction likely reproduced columnar structures of visual features owing to the spatial simulated annealing.

2.1.4 Analyses of cortical feature representations—An output response of neuron j to the presentation of visual images through either eye is given by the integration of evoked activities at nearby neurons through the dendrite. Therefore, the output neuronal response is expressed by

$$\eta_{j;k,\theta,\mu}^{out} = \sum_{j',l,\phi} V_{j;j'} \sigma_{j';l,\phi,\mu} R_{l,\phi;k,\theta}. \quad (14)$$

Here we suppose that a global stimulus like an oriented grating stimulus moving in the direction θ is presented to both eyes. The direction tuning curve of model cortical neuron j is defined by

$$\zeta_j^{dir}(\theta) = \sum_{k,\mu} \eta_{j;k,\theta,\mu}^{out}. \quad (15)$$

The preferred direction of the neuron j is determined when $\zeta_j^{dir}(\theta)$ takes the maximum at $\theta = \theta_j^{pref}$. The orientation tuning curve of model cortical neuron j is defined by the sum of responses to opposite directions orthogonal to the stimulus orientation φ as follows:

$$\zeta_j^{ori}(\varphi) = \frac{1}{2} \sum_{k,\mu} (\eta_{j;k,\varphi-\pi/2,\mu}^{out} + \eta_{j;k,\varphi+\pi/2,\mu}^{out}). \quad (16)$$

The preferred orientation of this neuron is determined when the orientation tuning curve $\zeta_j^{ori}(\varphi)$ takes the maximum at $\varphi = \varphi_j^{pref}$. The ocular dominance of neuronal responses is defined by the contrast form of responses to the left-eye and right-eye stimuli as follows:

$$O_j = \frac{\sum_{k,\theta,\mu} \mu \eta_{j;k,\theta,\mu}^{out}}{\sum_{k,\theta,\mu} \eta_{j;k,\theta,\mu}^{out}}. \quad (17)$$

To analyze orientation and direction singularities, we calculated the gradient vectors of the preferred direction and orientation, $\vec{\nabla} \theta_j^{pref}$ and $\vec{\nabla} \varphi_j^{pref}$, where the position vector in the model cortex is given by (x_j, y_j, z_j) as follows:

$$\vec{\nabla} \psi_j = \left(\frac{\psi(x_j+h, y_j, z_j) - \psi(x_j-h, y_j, z_j)}{2h}, \frac{\psi(x_j, y_j+h, z_j) - \psi(x_j, y_j-h, z_j)}{2h}, \frac{\psi(x_j, y_j, z_j+h) - \psi(x_j, y_j, z_j-h)}{2h} \right) \quad (18)$$

where ψ denotes the preferred direction θ^{pref} or the preferred orientation φ^{pref} , and h indicates the distance between nearest neighbor model neurons that is the size of the voxel corresponding 66 μm . When we illustrated orientation-singularity lines or direction-discontinuity sheets, for absolute value of the gradient vector larger than 0.01 rad/ μm for orientation and 0.02 rad/ μm for direction, we plotted the grey spot at that position in the model cortex.

The positions of orientation pinwheel centers along the model cortical surface are determined automatically as the points around which the circular integration of the orientation difference amounts to just $\pm\pi$, where the circular integration is taken in the counterclockwise direction. The counterclockwise or clockwise pinwheel centers are defined by the sign of the integral. Thus-defined pinwheel centers coincided with the position of

high-gradient of preferred orientations along the cortical surface. The relative number of pinwheel centers within ocular dominance subregions is analyzed according to the previously introduced method (Hübener et al. 1997). Namely, the left- or right-eye specific subregions are defined as the domains in which model neurons are classified into the top 20% of total number of neurons. The border subregions of ocular dominance are defined as the domains in which neurons exhibit binocularity within 20%.

2.2 Experimental Methods

2.2.1 Multi-slice fMRI imaging—With approval of the Institutional Animal Care and Use Committee at the University of Pittsburgh, we used a cat in an fMRI experiment. Orientation column-resolution fMRI was performed on cat visual cortex at 9.4 T. The cat was anesthetized with isoflurane (0.8 – 1.0%) and immobilized with pancuronium bromide ($0.2 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{hr}^{-1}$, i.v.). The imaging positions were selected in the region of dorsal surface and smaller surface veins, based on high-resolution 3D anatomical images. fMRI data were acquired using the multi-slice 2D gradient-echo EPI sequence with the following parameters: TR = 2.0 s, TE = 10 ms, matrix = 96×96 , and FOV = $2 \times 2 \text{ cm}^2$, after an intravascular bolus injection of a dextran-coated monocrystalline iron oxide nanoparticles (MION) contrast agent (20 mg Fe kg^{-1} body weight). Slice thickness of $500 \mu\text{m}$ was chosen to achieve sufficient sensitivity, and an inter-slice distance of $375 \mu\text{m}$ was used to improve nominal resolution along a slice direction. Visual stimulation was given binocularly. Eight different orientations with high-contrast square-wave full-field moving gratings (0.15 cpd , 2 Hz , movement direction reversal per 0.5 s) were presented sequentially (22.5° angle increments, 10 s per angle) during the one cycle of 80 s . One stimulation cycle was repeated ten times continuously (i.e., total 800 s per run). Twenty runs were performed for signal averaging.

2.2.2 Reconstruction of 3D orientation representation—First, we obtained single-condition maps for the 8 stimulus orientations at 8 slices according to Kalatsky and Stryker's method (Kalatsky & Stryker, 2003). We embedded each single-condition map into a rectangular solid region of $192 \times 192 \times 25$ voxels, each of which was the size of $104 \times 104 \times 125 \mu\text{m}^3$. The detail of this embedding method is schematically shown in Supporting Figure 1. Then we applied the 2D Gaussian filtering with the standard deviation of $193 \mu\text{m}$ to the single-condition maps for 8 stimulus orientations at each slice. Then we applied the same filtering to these single condition maps in the depth direction. The preferred orientation at each voxel was determined by the vector-sum method (Bonhoeffer & Grinvald, 1991). Next, we calculated the orientation gradient at each voxel using Eq. (18) to show the region of orientation singularities. When we visualized high-orientation-gradient regions, we used the same threshold value in the model.

3. RESULTS

3.1 Representation of preferred orientation and direction

We used a model visual cortex that consisted of two rectangular blocks sandwiched by two curved blocks in order to mimic the flat and curved parts of the visual cortex, respectively (Fig. 1a, b). The depth of the model cortex was 30 voxels in computer simulation. When we assume the depth to be 2 mm , one voxel size corresponds to $66 \mu\text{m}$. The rectangular blocks simulate flat parts between the lateral sulcus and the crown of the lateral gyrus, whereas the curved blocks simulate the crown of the lateral gyrus. To minimize the size effect, we imposed a periodic boundary condition on the model visual cortex. In the computer simulation, we assumed the standard deviation of the dendritic arbor of cortical neurons to be 2 voxels, which corresponds to $132 \mu\text{m}$. This implies a diameter of $264 \mu\text{m}$, which falls in a plausible range for the tangential diameter of stellate cell dendritic arborization and

pyramidal cell basal dendritic arborization in the visual cortex (290 ± 88 (SD) μm , $n = 12$; estimated from the data shown in Sholl, 1953).

The computer simulation formed a 3D structure of orderly arrangements of preferred orientations (shown by different colors in Fig. 1a). Along the model cortical surface, either in the flat or curved parts, the preferred orientation changed continuously except at singularity points called pinwheel centers (white dots), around which the preferred orientation changes in a circular fashion (Bonhoeffer & Grinvald, 1991). The preferred orientation did not change much in the depth direction of the flat parts of the model cortex, which can be seen in the sidewall of the model cortex (Fig. 1a). This indicates that preferred orientations are arranged in a columnar fashion in the flat cortical parts. On the other hand, in the curved parts of the model cortex, preferred orientations were arranged in a wedge-like structure, where the width of orientation columns became narrower from the superficial to deeper layers. It should be noted that tips of some wedge-like columns did not reach the bottom of the model visual cortex, which corresponds to the boundary between the grey and white matter.

Preferred directions were also arranged almost continuously along the cortical surface, except along discontinuity lines across which the preferred direction changed by 180° (Fig. 1b). Such direction-discontinuity lines (Kim et al., 1999) or direction fractures (Kisvarday et al. 2001; Swindale et al. 2003) are indicated by white lines. They were terminated or branched at pinwheel centers shown as black dots in Fig. 1b, which is consistent with a previous experimental finding (Weliky et al. 1996; Kim et al., 1999) and a theoretical prediction (Tanaka, 1995, 1997). Like iso-orientation domains, iso-direction domains tended to extend vertically in the flat part of the model cortex. However, there were occasions in which the preferred direction was reversed somewhere along the cortical depth.

To more clearly visualize orientation representation particularly along the cortical depth, we illustrated iso-orientation lines (Fig. 1c). In the flat part of the cortex, iso-orientation lines tended to penetrate throughout the cortical depth. In contrast, in the curved part, some iso-orientation lines exhibited V-shape, although some connected the cortical surface with the bottom of the cortex, forming wedge-like orientation columns (Fig. 1c).

The present model also demonstrates the emergence of ocular dominance patches and an orderly retinotopic arrangement of the receptive field center. A sharp segregation of ocular dominance was observed around the middle layer of the model visual cortex (Fig. S2a). Based on the comparison of the ocular dominance map with the orientation map on the same section in the middle layer (Fig. S2b), the distribution of the number of pinwheel centers against ocular dominance (Fig. S2c) reveals that more pinwheel centers tended to exist in the monocular regions than in the binocular regions. This geometric relationship agrees with experimental observations (Crair et al., 1997; Hübener et al. 1997). We also found that the present model forms a regular retinotopic representation in the 3D model visual cortex (Fig. S3a, b): Positions of receptive field (RF) centers were represented in a wedge-like structure in a curved part of the cortex, whereas they were represented in a vertical column in the flat part (Fig. S3c). The simulated retinotopic arrangement seemed quite regular and continuous within the resolution of the model cortex, in contrast to the presence of singularities in orientation and direction representations.

3.2 3D structures of orientation and direction singularities

We calculated the gradient of the preferred orientation and direction according to Eq. (18) (Methods), and illustrated the regions in which the gradient was higher than $0.01 \text{ rad}/\mu\text{m}$ for orientation and $0.02 \text{ rad}/\mu\text{m}$ for direction. The high-orientation-gradient regions appeared as thin rods (Fig. 2a, b). Note that these rods passed through pinwheel centers at any given

layer. In the flat part of the cortex, 82 % of high-orientation-gradient rods tended to stand straight, and the other small percent (18 %) were V-shaped lines or hairpins. From visual inspection, all rods that reached the cortical surface intersected perpendicularly to the cortical surface (Fig. 2a). In contrast, in the curved part of the cortex, 34 % of high-orientation-gradient rods appeared to be hairpins whose ends were located on the cortical surface, whereas the other percent of rods (66 %) were almost straight lines connecting the cortical surface with the bottom of the cortex (Fig. 2b). The appearance of the V-shaped orientation singularity lines is due to the fact that clockwise and counterclockwise orientation pinwheel centers in a plane parallel to the cortical surface get closer and finally they are merged to vanish, as the plane moves down from the surface to deeper layers.

On the other hand, high-direction-gradient regions appeared as thin, curved and distorted sheets (Fig. 2c, d). Figure 2c (the top view in Fig. 2a) shows the high-direction-gradient sheets in the flat part of the model visual cortex, whereas Fig. 2d illustrates the side view in Fig. 2b, showing the high-direction-gradient sheets in the curved part. From visual inspection, the high-direction-gradient sheets seemed to intersect with the cortical surface or the bottom of the cortex at right angles. The intersections formed the direction-discontinuity lines on the cortical surface, which are indicated by blue lines in Figs. 2c and d (corresponding to the white lines in Fig. 1b). The high-direction-gradient sheets were delineated by the high-orientation-gradient rods (red rods) or the upper and lower cortical surfaces. This 3D relationship is a natural extension of the 2D relationship between pinwheel centers and direction-discontinuity lines (Fig. 1a, b). Hereafter, we refer to high-orientation-gradient rods as pinwheel lines and high-direction-gradient sheets as direction-discontinuity sheets. As seen in Fig. 2d, when we move radially from the cortical surface to the bottom of the cortex, the direction-discontinuity sheets became crowded. Even in the flat part (Fig. 2c), direction-discontinuity sheets covered a non-negligible area of the cortex when we see the cortex from the top. Such patterns indicate that when an electrode penetrates vertically into the visual cortex for electrophysiological recording, the preferred direction along the electrode track can reverse somewhere in the middle of the cortical depth.

To examine how the preferred orientation and direction changed in the flat and curved parts of the model cortex, we sampled 40 traces of preferred orientations (Fig. 3a) and preferred directions (Fig. 3b) along the cortical depth from the surface to the bottom of the cortex perpendicularly to the cortical surface. Here we sampled the traces every other pixel along the cortical surface. Figure 3a shows changes in the preferred orientation in 20 traces for the curved (left) and flat parts (right). To clarify the changes of preferred orientations along the cortical depth, we showed preferred orientations relative to the orientations at the cortical surface at which the artificial electrode touched down. Most traces in either the curved or flat parts showed gradual changes in the preferred orientation deviating from the orientations at the cortical surface. Some traces showed large changes of preferred orientations in the middle of the cortical depth in the curved part. The mean amplitudes of changes in the preferred orientation along the depth were 35.1° and 30.5° , and the standard deviations of the amplitudes of changes in the preferred orientation were 35.0° and 16.0° , in the flat and curved parts, respectively. These values indicate that in the curved cortex, the preferred orientation changes drastically in some traces but it is rather constant in the other traces, whereas in the flat cortex, the preferred orientation changes moderately in all traces.

Changes in the preferred direction along the cortical depth are shown in Fig. 3b. Most traces tended to show similar changes in the preferred orientation (Fig. 3a) either in the curved or flat part. Some of them, however, showed abrupt changes by 180° , as marked by solid lines, in the middle of the cortical depth. More reversals of preferred directions were found in the deeper layers in the curved part in these samplings. Figure 3c represents the depth-

dependent probabilities to hit direction reversals in the flat (blue) and curved parts (red) of the cortex, by sampling 14336 traces in the flat part and 14476 traces in the curved part, discarding the other traces in the transition regions between the flat and curved parts. If the direction-discontinuity sheets are flat plane and intersect the cortical surface with right angles, the probability to hit direction reversals is independent of the depth and Fig. 3c show uniform distribution in the flat part. However, direction reversals tended to occur more frequently midway through the cortical depth than near the cortical surface or the bottom of the cortex. This tendency reflects that direction-discontinuity sheets were wavy. The small probability to hit direction reversals near the cortical surface and the bottom of the cortex indicates that the direction-discontinuity sheets tended to intersect the cortical surface and the bottom of the cortex at right angles. In contrast, in the curved part, the preferred direction reversed more frequently in deeper layers than in superficial layers. The direction reversal in deeper layers appeared twice to three times more frequently in the curved part than in the flat part.

3.3 Orientation representation reconstructed by high-resolution fMRI

To compare simulated results with the feature representation in the cat visual cortex, we performed measurement of orientation representation in the cat visual cortex using high-resolution fMRI with continuous cyclic 8-orientation stimulation (Fukuda et al. 2006; Moon et al., 2007). fMRI data were acquired using the multi-slice 2D gradient echo planar imaging (EPI) sequence in $2 \times 2 \text{ cm}^2$ around the lateral gyrus including areas 17 and 18 (Fig. 4a), following an intravascular bolus injection of iron oxide contrast agent (MION). Eight 0.5-mm-thick slices were obtained from a 3.125-mm-thick slab (center-to-center distance of neighboring slices = 0.375 mm) (Fig. 4b). Eight single-condition maps responding to binocular full-field gratings were obtained for each slice. Then, 8 orientation polar maps (Fig. 4c) were calculated for different depths in the rectangular region, where color and brightness indicate the preferred orientation and orientation selectivity, respectively. Each map shows the characteristic spatial clustering of preferred orientations.

For 3D reconstruction of orientation representation, we applied Gaussian low-pass filtering to 64 single-condition maps with a standard deviation of $193 \mu\text{m}$. Thus, we successfully reconstructed the 3D representation of preferred orientations as a 3D orientation angle map around the cat lateral gyrus and associated orientation singularities in the left hemisphere. Figure 5 shows the dorso-antero-lateral view of the 3D orientation representation. The columnar organization of preferred orientations appeared on the right wall of the 3D map, indicating that preferred orientations are arranged in a columnar fashion in the flat cortical region, as expected. The dorsal view exhibits a conventional orientation map with pinwheel-like arrangements of preferred orientations. The small white regions indicating high orientation gradient coincided with the location of the pinwheel centers. The cave in the antero-lateral part indicates the location of the white matter.

The orientation representations and orientation-singularity lines in the $125\text{-}\mu\text{m}$ -thick slices show the tendency of orientation columns to terminate at the bottom of the grey matter at right angles with the boundary between the grey and white matter (Fig. 6a, lateral view). The regions of high orientation gradient appeared as nearly straight rods (Fig. 6b), which terminated at pinwheel centers on the cortical surface (Fig. 5). Figure 6c shows the lateral view of orientation representation in the section more medial to the section shown in Fig. 6a, which does not contain the white matter. Around the horizontal dotted line in this section, which corresponds to the bottom of the curved cortex in the medial region of recording, iso-orientation domains are not aligned vertically, different from those in Fig. 6a. Orientation-singularity lines are fractioned around there (Fig. 6d). These features imply that iso-orientation domains and singularity lines tend to run along the radial axes of the gyrus. In the coronal sections around the gyrus, preferred orientations are arranged in wedge-like

columns rather than straight columns (Fig. 6e, g, posterial view), whereas iso-orientation domains run orthogonal to the white matter closer to the flat parts of the cortex (white arrow heads in Fig. 6e). Tips of some wedges representing single orientations (black arrow heads in Fig. 6e, g) did not reach the white matter, which indicates that orientation preferences can differ between the superficial and deep layers along the radial axes of the gyrus. Related to this feature, the orientation-singularity lines appeared as hair-pins (Fig. 6f, h).

To visualize the orientation columns around the curved and flat cortices, we illustrated iso-orientation lines, where an orientation interval between adjacent lines was 15° , in 3 slices of the coronal section and in 1 slice of the sagittal section in Fig. 7. In the curved cortex, although some iso-orientation lines tended to reach the white matter, many lines were hairpins or converged to some points in the grey matter, and hence did not connect the cortical surface with the white matter (Figs. 7a–c). These characteristic features agree with the simulated results in the curved part of the model cortex (Fig. 1c), although the simulated iso-orientation lines were more regularly arranged. On the other hand, iso-orientation lines tended to connect the cortical surface and the white matter straightly in the flat cortex as shown in the dotted square of Fig. 7d. Interestingly, even in the flat cortex, some iso-orientation lines were hairpins or converged to points in the grey matter. This indicates that all orientation columns in the flat cortex are not necessarily straight columns.

Since the low-pass filtering does not produce artificial structure more complex than the structure reconstructed from raw data, which is advantageous for the columnar hypothesis in the flat cortex. However, it cannot be denied that even if fine columnar organization exists in the curved cortex, the filtering smears out fine structure in the deep layers and produces hairpin singularity lines by annihilating pairs of orientation singularities of opposite signs running parallel in the depth direction. Such annihilation can occur for two singularity lines located closer than the width of the Gaussian filtering due to the fact that the filtering tends to eliminate smaller iso-orientation domains by expanding larger iso-orientation domains. Nevertheless, if ideal wedge-like orientation columns are formed, the column widths uniformly decrease from the cortical surface to white matter, keeping the ratio of widths between nearby columns equal at any cortical depth. The application of the low-pass filtering does not merge orientation-singularity lines to vanish. Therefore, the emergence of hairpin singularity lines are regarded as evidence against the idea of wedge-like orientation columns continuously penetrating the gray matter.

When the planes of the slice sections are not parallel to the straight columns that penetrate throughout the grey matter, they may appear to terminate in the middle of the cortical depth. Also, when orientation columns are wavy, even if penetrating throughout the grey matter, they may appear to terminate in the middle of the cortical depth. To examine quantitatively whether orientation columns continuously extend throughout the cortical depth at least within the imaged region, we defined the penetration index: It takes 1 when we can find a continuous path from the surface down to the white matter, keeping the same orientation within the range of 22.5° , and otherwise 0. The penetration indices were averaged in flat or curved parts both for the experimental and theoretical results. To estimate average penetration indices, we used 14336 traces ($=56 \times 128 \times 2$ pixels) in the up- and downside of the flat parts and 14336 traces ($\cong [72 \times \pi/4] \times 128 \times 2$ pixels) in the most lateral curved parts in the simulated result, and 636 and 830 traces in the flat and curved parts, respectively, in the experimental result. The average penetration index estimated from the fMRI data was 0.87 for the flat cortex, and 0.78 for the curved cortex. These values indicate that not all orientation columns continue from the cortical surface to the white matter. However, some orientation columns reach the white matter, even if they may be wavy. The fact that the average penetration index is smaller in the curved part than in the flat part indicates that orientation columns more often terminate somewhere in the cortical depth in the curved

cortex, consistent with visual inspection of Figs 6 and 7. On the other hand, in the simulated results, the average penetration index was 0.99 in the flat part of the cortex, and 0.89 in the curved part. It is quite likely that these values are larger than those obtained from the experiment, because detailed connectivity among different neurons and its complexity were omitted in the model. However, these two values again indicate orientation columns in the curved cortex more frequently terminate somewhere in the cortical depth than do those in flat cortex. Taken together, the experiment and theory show that the cortical curvature partially deforms columnar organization and disrupts some columns in the middle of the cortical depth.

4. DISCUSSION

4.1 Topological properties of singularities

According to topology theory, the space spanned by the preferred orientation, which is a parameter invariant under the 180° rotational transformation, is isomorphic to S^1 . Since the fundamental group of S^1 , $\pi_1(S^1)$, is equivalent to the set of integers that correspond to the winding number: $\{0, \pm 1, \pm 2, \dots\}$ (Tanaka, 1995, 1997) (about topology theory, for example, see Bredon, 1993), a possible singularity of orientation representation should be a point in the 2D visual cortex, that is, a pinwheel center. When we extend the model visual cortex from 2D space to 3D space, it appears as a line, which is often observed as a defect called the disclination line in the nematic liquid crystal (Mermin, 1979). For example, in the flat cortex, in which preferred orientations are ideally arranged in a straight columns (Fig. 8a), orientation singularity appears as straight lines penetrating from the cortical surface to the bottom of the cortex (Fig. 8b). Our simulated 3D orientation representation showed that some orientation singularity lines were wavy even in the flat part of the cortex (Fig. 2a), as schematically shown in Fig. 8c. On the other hand, the space spanned by the preferred direction, which is invariant under 360° rotational transformation, is also isomorphic to S^1 . However, the cortical layout of direction preferences is constrained by the orientation preference layout, as originally explained by Swindale et al with their experimental observations (1987). Because the preferred orientation is continuously represented in the visual cortex except at pinwheel centers, the preferred direction that is orthogonal to the preferred orientation cannot be represented continuously around the pinwheel centers. Namely, when one traces an arbitrary small circle that contains only one pinwheel center in its inside, the preferred direction should change by 180° . This indicates that one round trip along the fictitious cortical circle always results in the reversal of the preferred direction. Generally, there can be the odd number of points where the preferred direction abruptly changes by 180° along the circle. When one shrinks the arbitrary circle into the pinwheel center, the trajectory of the direction reversal points form lines, i.e., direction-discontinuity lines or direction fractures, and should be terminated at the pinwheel center. This supports the idea that direction-discontinuity lines are terminated or branched at pinwheel centers in the 2D representation. This topological feature was found in the simulated result (Fig. 1b), which is schematically illustrated in the 2D space on the cortical surface and the bottom of the cortex in Fig. 8c. In the 3D visual cortex, we can generalize this concept: the direction-discontinuity appears as 2D sheets, and a direction-discontinuity sheet is delimited by orientation-singularity lines, as schematically shown in Fig. 8c. Although an odd number of direction-discontinuity sheets are allowed to meet along one orientation-singularity line, we did not find such a case in the simulation results (Fig. 2c, d). This may be due to strong tension induced by the feature representation where direction-discontinuity sheets are positioned close together.

4.2 Curvature effects

The cerebral cortex is packed into the skull and folded in a complex manner. Accordingly, most parts of the cerebral cortex are curved. It would be expected that sensory feature representation is constrained by the curvature of the cortex. Schematic pictures of columnar organization for feature representation shown in many textbooks (see Kandel et al., for example) may be too simple, particularly in the curved part of the gyrus. As Hubel and Wiesel suggested (Hubel & Wiesel, 1962), wedge-like columns appear in the apical segment of the post-lateral gyrus because the columns are parallel to the radial fiber bundles and perpendicular to cortical layers. The present simulation and fMRI data demonstrated that orientation columns were likely to appear as wedge-like columns rather than straight columns in curved parts of the cortex, as schematically shown in Fig. 8d.

More interestingly, the columns do not necessarily extend from the cortical surface to the white matter. Related to this property, the present studies showed that orientation singularities were not necessarily straight lines penetrating from the cortical surface to the white matter. Some of them appear as hairpins (Fig. 8e), as shown in the simulation (Figs. 2a and b) and in the fMRI data from cat visual cortex (Figs. 6f and h). Since the topological constraint on the preferred orientation and direction should be valid in the bulk of the cortex either flat or curved, a likely configuration of the direction-discontinuity sheets and orientation-singularity lines is as shown in Fig. 8d. The original view of the configuration of orientation columns as the stacked-slab arrangement (Hubel et al., 1977) has been revised as a view of a pinwheel arrangement of preferred orientations (Bonhoeffer & Grinvald, 1991), retaining the concept of organization of straight columns. The present study suggests that columnar organization may be more complex than expected from the conventional hypercolumn picture: orientation columns are distorted to reconcile with the global curvature of the visual cortex. The wedge-like shape of an orientation column and the interruption of columns in the deeper layers can release the tension induced by the columnar organization in curved grey matter. Our model indicates that such a structure emerges from the competition between the tendencies of periodic arrangement and radial alignment of orientation representation in a curved cortex. Because a large part of area 17 is located near the crown of the gyrus, anatomical minicolumns arranged along the radial fiber bundle may functionally represent different orientations in superficial layers and deep layers in area 17. Moreover, the present model predicts that the preferred direction can more frequently reverse in the deeper layers around the gyrus than in the flat cortex (Fig. 3c). To date, it is thought that the cortical information representation obeys a columnar organization rule. The present study suggests that careful examination of functional architecture is needed, because different pieces of information can be represented in an identical anatomical minicolumn at different layers, particularly around the crowns of gyri and perhaps at fundi.

4.3 Comparisons with previous experiments

Originally, Mountcastle demonstrated the possibility of columnar representation of response properties to peripheral stimuli in the somatosensory cortex (Mountcastle, 1957). Hubel and Wiesel confirmed the similar columnar structure in the primary visual cortex in cats (Hubel & Wiesel, 1962, 1963) and monkeys (Hubel & Wiesel, 1974). Subsequently, it has been reported that preferred orientations and directions are not necessarily represented in a columnar fashion in the cat visual cortex (Bauer, 1982; Bauer et al., 1985; Berman et al., 1987). Bauer reported that the preferred orientations jump by 90° along the vertical track of the electrode penetration in the cat visual cortex (Bauer, 1982). The present simulation and fMRI data show that the tips of some wedge-like columns do not touch the white matter, and orientation-singularity lines pass through along the tips of the wedge-like columns. This suggests that preferred orientation can change in the vertical penetration of electrodes along the radial fiber bundles. On this point, our simulated results partially support Bauer's

experimental finding (Fig. 3a). However, in the simulated tracks, the preferred orientation changed gradually. We did encounter some rare abrupt changes larger than 60° , because the probability that an electrode hits an orientation-singularity line is extremely low. The simulation results rather seem to support the observation of little variation of preferred orientations between the superficial and deep layers reported by Murphy and Sillito (Murphy & Sillito, 1986). Bauer has also reported that the receptive field position shifted in the electrode penetration along the radial fiber bundles (Bauer, 1983). We did not, however, find in the simulated results shift of the receptive field position as large as Bauer reported (Fig. S2).

For the discontinuity of preferred directions, Berman et al. reported that direction reversals occurred more frequently in infragranular layers than in supragranular layers (Berman et al. 1987). Because this tendency was common between area 18, which occupies a relatively flat part of the cortex, and area 17 located on the crown of the lateral gyrus, they suggested that direction reversal is caused by a short periodicity of the preferred direction compared with the periodicity of the preferred orientation. They denied the possibility that the higher proportion of direction reversals in infragranular layers than in supragranular layers is caused by the relative crowding of columns in infragranular layers at the crown of the lateral gyrus. The present simulation also showed the preferred direction was frequently reversed even in a flat part of the model cortex, indicating that direction reversal likely occurs not only as a result of cortical curvature (blue histogram in Fig. 3c). Indeed, preferred directions were represented in the model cortex with a shorter periodicity than preferred orientations, as Berman et al. suggested. It is thought, however, that the order of maturation of feature representation may be related to the existence of direction reversals in deep layers in area 18. In the present simulation, we assumed that orientation and direction preferences first mature in the middle layer (layer 4), followed by maturation in the other layers. This seems to increase the number of direction reversals in the middle layer (Fig. 3c). On the other hand, it is known that layer 6 of the cat visual cortex receives geniculocortical inputs. The maturation of visual feature representation may occur in layer 6 as early as it does in layer 4, because at P7 in kittens, highly branched terminals are restricted primarily to layer 4, and some axons also have branches within layer 6 (Ghosh & Shatz, 1992). If it is the case, the mismatch of representation in layers 4 and 6 likely occurs. Although the delayed maturation of the representation in layer 5 may tend to eliminate this mismatch, there is a possibility that some mismatches may remain, resulting in more direction reversals in deep layers, as found experimentally. There is another possibility that detailed intra- and inter-lamina connections, which we omitted in the model, may contribute to the creation of direction reversals in deep layers. Even far from the gyrus crown, the visual cortex is not completely flat, and more or less curved. Weak curvature may also produce more direction reversals in the deeper layers. Therefore, the simulated difference in the probability of the occurrence of direction reversals in the superficial and deep layers in a curved part of the model cortex can be attributed to the curvature of the cortex, and we can say that the more steeply curved the cortex is, the more often the direction reversal occurs.

Very recently, some of the present authors observed that the intravascular MION injection can improve the spatial specificity of fMRI signals to microvessels because of the reduction of macrovessel contributions, and also increase the signal sensitivity with the use of high magnetic fields (Fukuda et al., 2006; Moon et al., 2007). Blood-volume-weighted fMRI with MION injection obtained at 9.4T was successfully used for functional columns in the cat visual cortex, and iso-orientation domains reconstructed from fMRI were almost identical to those of intrinsic signal optical imaging in a flat part of the visual cortex (Fukuda et al., 2006). Looking closely at the iso-orientation domains in the curved part shown in Fig. 9 of Fukuda et al., 2006, we can see the iso-orientation domains did not necessarily penetrate from the pia to white matter, although they tended to be arranged perpendicularly to the

cortical surface. In addition, the width of the iso-orientation domains systematically decreased from the superficial to deep layers in the gradually curved cortex. This is a piece of evidence that supports the presence of wedge-like orientation columns. The fMRI measurement in the present study was performed using the same techniques as those used in ref. 19, but with 8 slices along the cortical depth, and we succeeded in reconstructing 3D orientation representation for the first time. The overall structure of the representation agreed qualitatively with that obtained from our simulation. However, if cortical depth-dependent fMRI can merely reflect changes in intracortical penetrating or emerging vessels, which run almost parallel to column directions and orthogonal to the cortical surface, then our 3D maps obtained from fMRI may not provide true functional columns. Careful evaluation between vessel patterns and fMRI maps indicated that there was no obvious correlation between the two, and microvessels including intracortical capillaries and small pre-capillary arterioles appeared to be responsible for column-specific functional signals (Fukuda et al., 2006). Thus, microvessel-weighted fMRI can detect 3D functional columns. In our studies, 500- μm thick slices with an inter-slice distance of 375 μm were limited for obtaining precise 3D functional architecture, and slice-direction resolution can be improved by obtaining thinner slices with extensive signal averaging. Further technical progress is expected to elucidate detailed structures about not only orientation preference but also direction preferences in the future.

4.4 Limitation of the model

In the present model, we attempted to reproduce the cortical representation of visual features in a simplified version of self-organization models. We assumed an identical short-range interaction function irrespective of the locations, which tended to produce a similar periodicity of feature representation anywhere. If the long-range inter-layer connections work for the dominant interaction for the formation of feature representation in the early stage of development, orientation columns are more likely to penetrate continuously through the gray matter.

For the formation of wedge-like columns in the curved cortex, each of which penetrates the gray matter, it can be explained by another model in which cortical interaction also changes depending on the cortical depth. In this model, however, we need to assume the interaction range to be infinitesimally short at the bottom of the cortex to reproduce crowded fine columns near the white matter. Therefore, we discarded such a model, although it is needed to examine experimentally to what extent the interaction range depends on the cortical depth.

Moreover, in the present model, response properties of model cortical neurons are characterized by a set of *a priori* visual features (Nakagama & Tanaka, 2004). That is, we did not consider the formation of receptive fields of neurons from layer 4 to other layers, which are regarded to be achieved by selective inter-layer afferent connections. Instead, the self-organization of visual feature representation gradually evolves from the middle layer to the other layers as a result of applying the spatial simulated annealing, which was found to be a unique method in the present model for obtaining vertical columns spanning all the layers in the flat parts of the model cortex. Whereas in the conventional simulated annealing temperature is gradually decreased with simulation time so as to eliminate defects from the system, spatial simulated annealing gradually expands the spatial range of inter-layer cortical interactions so as to increase the tendency of feature domains to be orthogonal to the cortical surface. Therefore, the key factor is the thickness of the middle layer. If we choose the thickness of the middle layer larger than one period of preferred orientation arrangements, the orthogonal arrangements of preferred orientations are not achieved. Accordingly, preferred orientations are not aligned in columns spanning all the layers even applying the spatial simulated annealing. In our simulations, the thickness of the middle

layer was set at 6 pixels, which corresponds to 396 μm . The assumption of such a thin middle layer enabled to form visual feature columns.

It might be possible, in principle, to take into account inter-layer interactions by extending the model drastically. However, the inter-layer connectivity that has been reported so far is too complex and even dependent on cell types (Wiesel & Gilbert, 1983). In addition, these connections change to mature during the development of visual feature representation (Albus & Wolf, 1984). If we try to consider such complicated and modifiable connection patterns, we will need many control parameters and it would be practically hopeless to evaluate the effects of all these parameters on the resulting orientation representation. Namely, the complexity of the model increase dramatically. On the other hand, generally, it is trivial that a model containing more parameters can better reproduce natural phenomena. Considering a reasonable balance between the reproducibility of experimental observations and the model complexity, we built a model as simple as possible. One of such simple models can be the present model that highlights the curvature effects of the visual cortex on the formation of 3D feature representation as a boundary condition. In this sense, we called our model *minimal model*. Despite the simplicity of the model, we found wedge-like orientation columns and highly warped orientation-singularity lines. These theoretical predictions and the consistent fMRI experimental findings suggest that local structure of orientation representation is affected by the cortical global curvature. The anisotropy of orientation representation in the tangential and vertical directions originated from the way of simulation, but not the anisotropy of interaction or neural connectivity. We expect that some other map formation models such as the self-organizing feature map (Obermayer et al. 1990) and elastic net model (Goodhill and Cimonieriu, 2000) can reproduce similar 3D orientation representation when one extends the models to work in the 3D space, and applies the spatial simulated annealing as we used. Therefore, we think that the present results are not specifically dependent on the model. This suggests that the observed 3D feature representation is a general structure resulted from the boundary condition, where the boundary shape is determined by the global morphology of the visual cortex.

Grossberg and Seitz (2003) have proposed another model that account for the formation of functional columns assuming that ocular dominance and orientation maps are formed in the subplate which appears transiently during development and that it provides instruction to all other layers in an activity-dependent manner. They did not argued how the functional columns can be deformed in the curved cortex. It may be, however, possible that their model also explains the deviation from straight columns in the curved cortex by assuming that transient radial connections from the subplate to other cortical layers. It is because instruction from the orientation map early established in the subplate results in more iso-orientation domains in the superficial layers than in the deep layers, which disrupts orientation columns extending from superficial to deep layers. Such an extension of the model is another interesting subject of a future study.

The present model has an evident limitation in reproducing physiological properties of neurons in the 3D visual cortex, since it does not incorporate realistic inter-layer interaction. The extension of the present model to a more realistic model by taking into account inter- and intra-laminar connections as well as geniculocortical inputs depends on the future progress of computers of higher performance and information on details of anatomical inter- and intra-laminar connectivity and strengths of the connections. Farther studies will be required to investigate the hierarchical formation of receptive fields of neurons as well as feature representation in each cortical layer.

5. Conclusion

We wish to have a simpler model of the cerebral cortex, which seems to be highly complex from the microscopic scales to macroscopic structure. Hubel and Wiesel's hypercolumn view is one of the successful examples of such modeling. However, the present simulation of visual feature representation together with the high-resolution fMRI experiment on the cat throw a doubt about the idea of columns extending from pia to white matter especially in regions where the cortex is curved, although more extensive experiments are needed to confirm our observations. We also found that singularities associated with visual feature representation increased their dimensionalities than those in the conventional model by one in the 3D cortex.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Three-dimensional self-organized orientation and direction representation. a: Representation of preferred orientations in the 3D model visual cortex is shown in color. The color code of preferred orientations is shown to the right of the figure. The white dots indicate pinwheel centers. b: Representation of preferred directions of motion in the 3D model cortex is shown in color. The color code of preferred directions is shown to the right of the figure. The white lines and black dots indicate the direction-discontinuity lines and pinwheel centers, respectively. c: Iso-orientation lines are shown on the visible surface of the model cortex, where orientation interval between adjacent lines is 15° . To make it easier to compare the simulated orientation representation with an fMRI-reconstructed orientation representation shown later, fictitious cortical coordinates are shown. The curved parts of the model cortex in the opposite sides both can correspond to a gyrus near the medial part of the visual cortex, whereas the flat part corresponds to the lateral part of the visual cortex. The inner surface of the model cortex corresponds to the bottom of the cortex. Abbreviations: A – Anterior, P – Posterior, M – Medial, and L – Lateral.

Figure 2.

Orientation-singularity lines and direction-discontinuity sheets in the model cortex. The grey rods show orientation-singularity lines around flat (a) and curved (b) parts of the model cortex. The grey sheets indicate direction-discontinuity sheets around the flat (c) and curved (d) parts of the cortex. The red lines in c and d indicate orientation-singularity lines, and the blue lines indicate direction-discontinuity lines that appear as intersections between the direction-discontinuity sheets and the model cortical surface.

Figure 3.

Changes of preferred orientation and direction along vertical tracks. a: Changes in the preferred orientation relative to the orientation at the cortical surface are plotted along vertical tracks from the cortical surface to the bottom of the cortex in a curved part (left) and a flat part (right) of the model visual cortex. b: Changes in the preferred direction relative to the direction at the cortical surface are plotted along vertical tracks in a curved part (left) and a flat part (right) of the model cortex. c: The probability to hit direction reversals is plotted in the flat (blue) and the curved (red) parts of the model cortex. Model cortical layers are shown along the abscissa.

Figure 4. Multi-slice high-resolution fMRI of cat visual cortex. Top view (a) and coronal view (b) reconstructed from a 3D venogram, respectively. Venous vessels were enhanced in the dark intensity dots and lines from tissues. The disk region of a 1.5-cm diameter with a 3.125-mm thickness (red circle in a, and red rectangle in b) was selected for subsequent imaging of 8 slices. (c) Orientation polar maps reconstructed in 8 imaging slices, where preferred orientations and orientation selectivity are indicated by color shown to the right and brightness (not shown). The slice number is assigned from the bottom to the top in the imaging rectangular parallelepiped. The white scale bar placed at the bottom of slice #0 indicates 1mm. Abbreviations: A – Anterior, P – Posterior, L – Left, and R – Right.

Figure 5.

Three-dimensional orientation representation in the left hemisphere reconstructed from the fMRI. Preferred orientations are given by the color code placed to the right. High orientation gradients are shown as small light grey regions, which correspond to the locations of pinwheel centers. The cave in the antero-lateral part indicates the location of the white matter. The cortical coordinate system is placed to the right and the black scale bar below the figure indicates 1 mm. Abbreviations: A – Anterior, P – Posterior, M – Medial, L – Lateral, D – Dorsal and V – Ventral.

Figure 6.

Orientation representations and high orientation gradients in typical sections. a, c, e and g: Orientation representations in 4 typical sections shown in color in the same convention as in Fig. 5. b, d, f and h: High-orientation-gradient regions in the corresponding sections shown in grey. a and b are taken from a nearly sagittal section which contains the white matter. c and d are taken from the section medial to the section of a and b. e and f, and g and h are taken from different coronal sections. The horizontal dotted line in c indicates the bottom of the curved cortex in the medial bank. The white arrow heads in e indicate the locations where nearly straight orientation columns reach the boundary between the grey and white matter, whereas the black arrow heads in e and g indicate the locations where wedge-like orientation columns terminate in the middle of the cortical depth. The cortical coordinates are common for a, b, c and d, and for e, f, g and h, respectively, which are shown to the right. Abbreviations: A – Anterior, P – Posterior, M – Medial, L – Lateral, D – Dorsal and V – Ventral. Black scale bars indicate 1 mm.

Figure 7.

Iso-orientation line maps in 4 typical sections. The orientation interval between adjacent iso-orientation lines are 15° . a, b and c are taken from 3 different coronal sections, and d is taken from a nearly sagittal section. The square in d indicates a section of a flat part of the cortex. The cortical coordinates (common for a, b and c) are shown to the right. Abbreviations: A – Anterior, P – Posterior, M – Medial, L – Lateral, D – Dorsal and V – Ventral. Black scale bars indicate 1mm.

Figure 8. Schematic diagrams of orientation singularities and direction discontinuities. a and d: Orientation representations in the flat and curved parts, respectively. b and e: Orientation-singularity lines (solid lines) in the flat and curved parts, respectively. c and f: 3D configurations of orientation singularities and direction discontinuities in the flat and curved parts. A direction-discontinuity sheet is delimited by orientation-singularity lines (solid lines) and direction-discontinuity lines on the cortical surface (dotted lines). In the curved part of the visual cortex, the direction-discontinuity sheets tend to be folded more frequently than in the flat cortex. The short black (closer to the direction-discontinuity sheets) and grey (behind the sheets) arrows indicate preferred directions arranged near the direction-discontinuity lines, whereas the thin line segments indicate preferred orientations.