

Patterns and Waves in Inhomogeneous Neural Media

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- Most theoretical studies of cortical patterns and waves treat the cortex as a homogeneous medium or a random heterogeneous medium.

- There are a variety of sources of non-random inhomogeneities

- I. External inputs

- II. Long-range horizontal connections

- III. Chemical markers during development

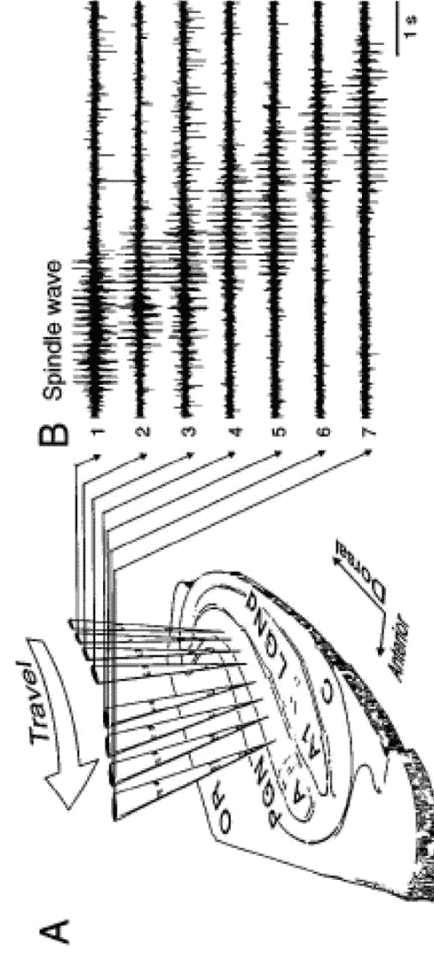
- Motivates the study of wave propagation and pattern formation in an inhomogeneous neural medium

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I. Stationary and traveling waves: inhomogeneous inputs

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Traveling wave *in vitro*



- Traveling waves observed in cortical and thalamic slices after blocking inhibition (Kim/Bal/McCormick 1995, Golomb/Amitai 1997, Wu/Guan/Tsau 1999)

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One-dimensional rate model with adaptation

- Consider the following one-dimensional rate model with adaptation:

$$\tau \frac{\partial u(x,t)}{\partial t} = -u(x,t) + \int_{-\infty}^{\infty} w(x|x')F(u(x',t))dx' - \beta v(x,t) + I(x)$$

$$\frac{1}{\varepsilon} \frac{\partial v(x,t)}{\partial t} = -v(x,t) + u(x,t)$$

$u(x,t)$ represents cortical activity and $F(u)$ is a firing rate function

$v(x,t)$ represents slow adaptation of strength β and rate μ

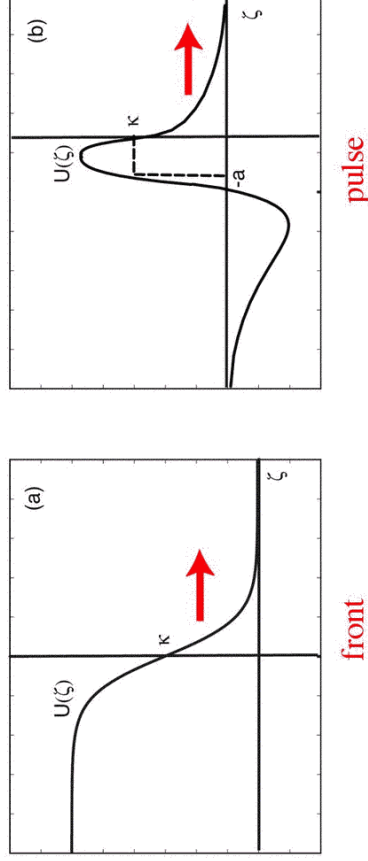
$w(x|x')$ is an excitatory synaptic weight distribution

$I(x)$ is an inhomogeneous input

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Homogeneous network

- $w(x|x') = W(x - x')$ [with $W(x)$ monotonically decreasing] and $I(x) = 0$.
- For $\beta = 0$ there exists a unique traveling front solution (Ermentrout/McLeod 1993)
- For $\beta > 0$ and sufficiently small ε there exists a fast/slow pair of traveling pulse solutions (Pinto/Ermentrout 2002)



$$u(x, t) = U(\zeta), \quad \zeta = x - ct$$

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Traveling fronts ($\beta > 0$)

- Take $F(u) = \Theta(u - \kappa)$ where κ is a threshold and Θ is a Heaviside function
- Seek a front solution of the form $u(x, t) = U(\xi)$ with $\xi = x - ct$, $c > 0$, such that $U(0) = \kappa$ and $U(\xi)$ is a monotonically decreasing function of ξ :

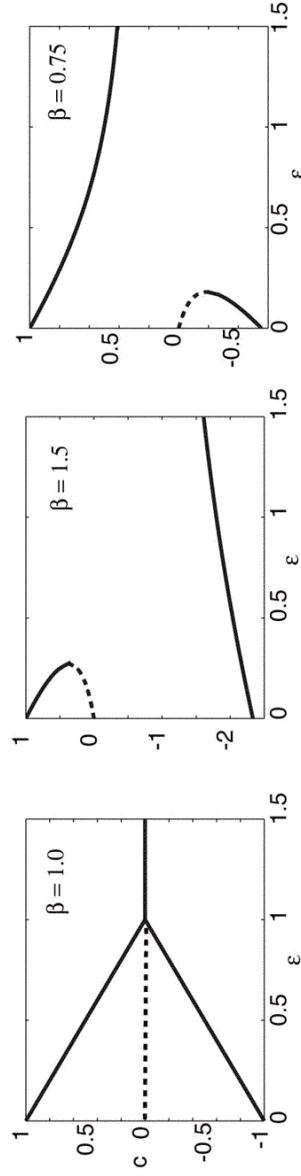
$$\begin{aligned}
 -cU'(\xi) + U(\xi) &= \int_{-\infty}^0 W(\xi - \xi') d\xi' - \beta V(\xi) \\
 -\frac{c}{\varepsilon} V'(\xi) &= -V(\xi) + U(\xi)
 \end{aligned}$$

➔ second order ODE for $U(\xi)$ with matching conditions at $\xi = 0$

- Consider an exponential weight distribution $W(x) = (2d)^{-1} \exp(-|x|/d)$

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- (i) If $2\kappa(I + \beta) = 1$ then there exists a stationary front for all ε . At a critical value of ε the front bifurcates into a left and a right moving wave.
- (ii) If $2\kappa(I + \beta) > 1$ then there is a single left-moving wave for all ε , together with a pair of right-moving waves that annihilate at a critical value of ε
- (ii) If $2\kappa(I + \beta) < 1$ then there is a single right-moving wave for all ε , together with a pair of left-moving waves that annihilate at a critical value of ε



$\kappa = 0.25$

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Front bifurcation

- Bifurcation of stationary front persists for a smooth sigmoidal nonlinearity
- $$F(u) = F_0 [1 + \tanh(\gamma(u - \kappa))]]$$
- Perform a perturbation expansion in powers of the wavespeed c . There is a supercritical pitchfork bifurcation to bidirectional waves (*Bressloff/Folias 2003*)
 - Analogous to front bifurcation (Ising-Bloch transition) in reaction diffusion systems
(*Rinzel/Terman 1982, Hagberg/Meron 1994, Bode 1997, Rubin 1999, Pratt/Li 2003*).
 - A stationary front can undergo a Hopf bifurcation to a breathing front in the presence of a weak input inhomogeneity.
 - Hopf instability can also occur away from the front bifurcation point in the high gain limit $\gamma \rightarrow \infty$

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Inhomogeneous input

- Monotonically varying input $I(x)$ can stabilize a stationary front:
- $$(1 + \beta)U(x) = \int_{-\infty}^{x_0} W(x - x') dx' + I(x), \quad V(x) = U(x)$$
- Translation symmetry is broken: center x_0 of front given by $U(x_0) = \kappa$
 - Linearize about stationary front: $u(x, t) = U(x) + p(x, t)$, $v(x, t) = U(x) + q(x, t)$

$$\frac{\partial p(x, t)}{\partial t} = -p(x, t) + \int_{-\infty}^{\infty} W(x - x') \Theta'(U(x' - \kappa)) p(x', t) dx' - \beta q(x, t)$$

$$\frac{1}{\epsilon} \frac{\partial q(x, t)}{\partial t} = -q(x, t) + p(x, t)$$

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- Setting $p(x, t) = p(x)e^{i\mu}$, $q(x, t) = q(x) e^{i\mu}$ leads to the eigenvalue equation

$$(\lambda + 1)p(x) = \frac{W(x - x_0)}{|U'(x_0)|} p(x_0) - \frac{\varepsilon\beta}{\lambda + \varepsilon} p(x)$$

- We have used the identity $\Theta'(U(x - \kappa)) = \frac{\delta(x - x_0)}{|U'(x_0)|}$

EITHER $p(x_0) = 0$ and $\lambda + 1 + \frac{\varepsilon\beta}{\lambda + \varepsilon} = 0$

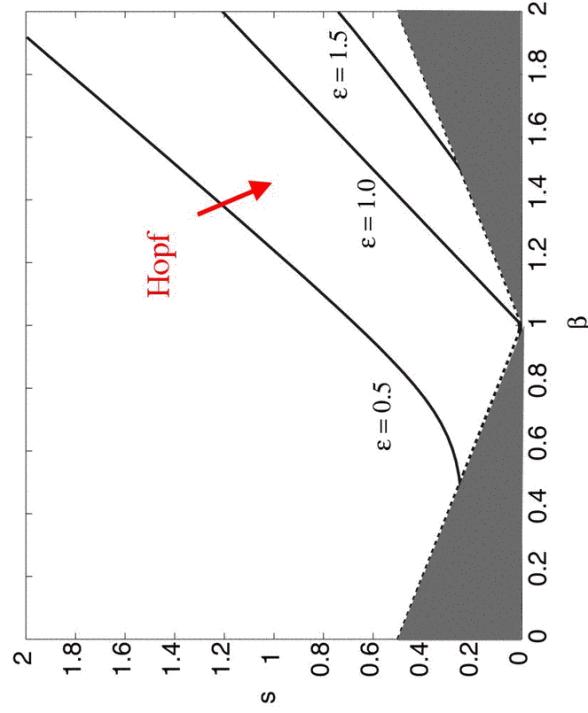
OR $p(x) = AW(x - x_0)$ and $\lambda + 1 + \frac{\varepsilon\beta}{\lambda + \varepsilon} = \frac{1}{2|U'(x_0)|}$

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- Reducing input gradient $D = |I'(x_0)|$ induces a Hopf bifurcation at

$$D_c = \frac{1}{2} \frac{\beta - \varepsilon}{1 + \varepsilon} \quad \omega_H = \sqrt{\varepsilon(\beta - \varepsilon)}$$

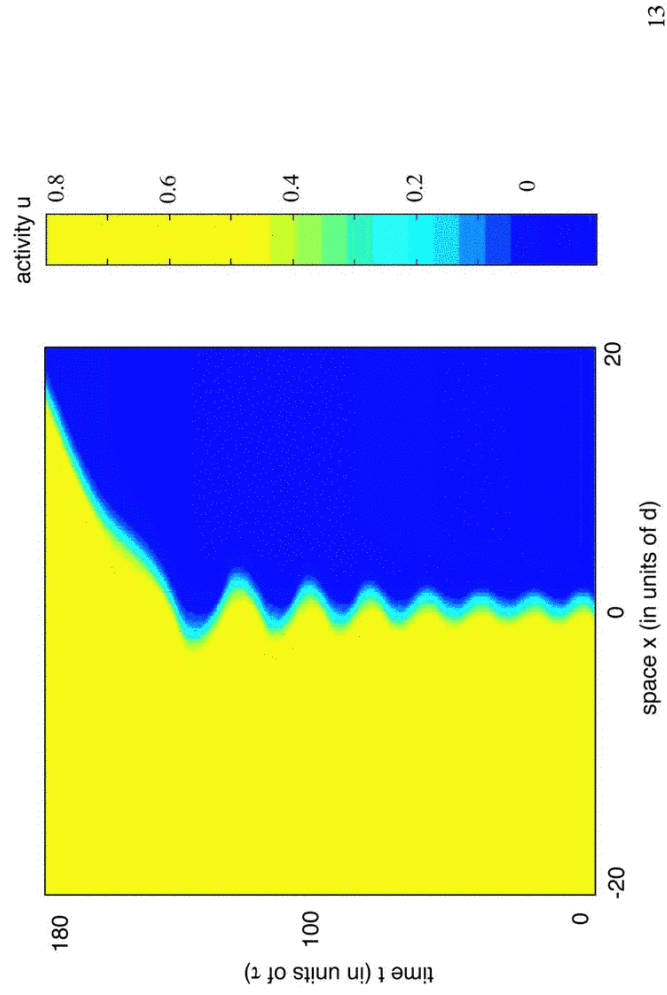
- Stability diagram for $I(x) = -s \tanh(x/2)$



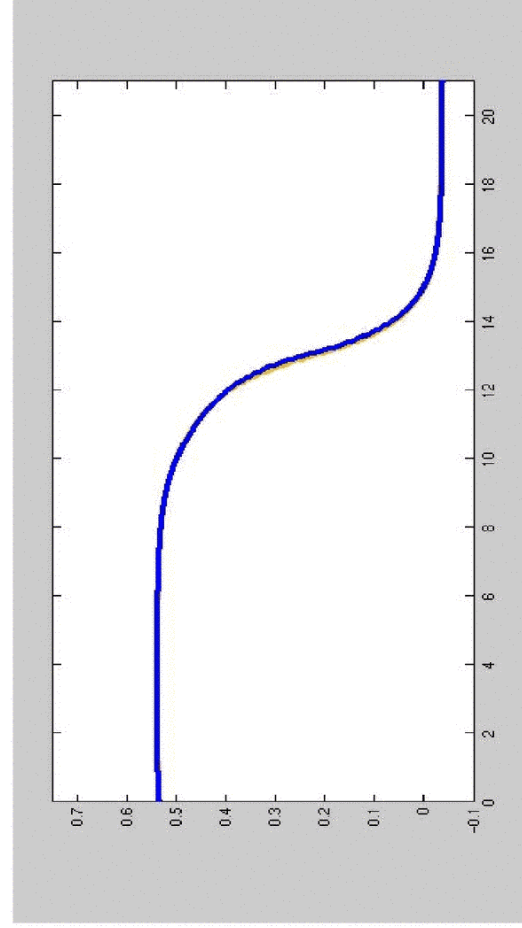
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Breathing front

- Hopf instability of the stationary front induces an oscillatory wave or breather
(Bressloff/Folias 2003)



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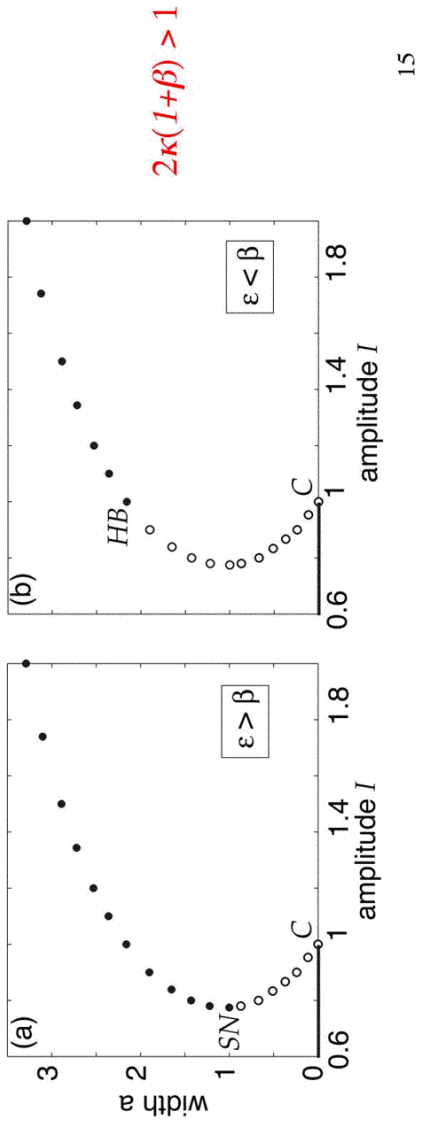
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Stationary pulse

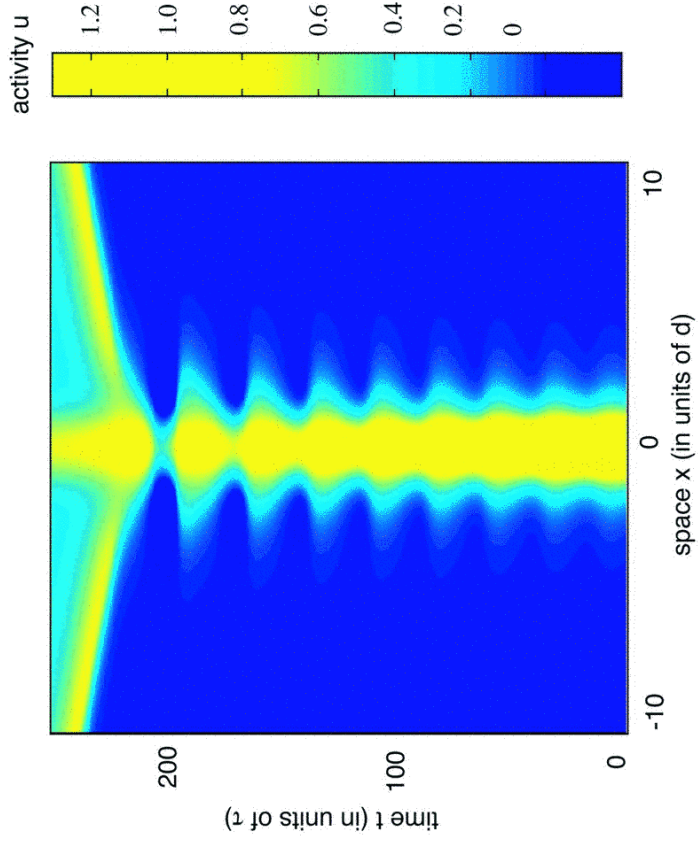
- Gaussian input $I(x) = I \exp(-x^2/2\sigma^2)$ can stabilize a stationary pulse of width a :

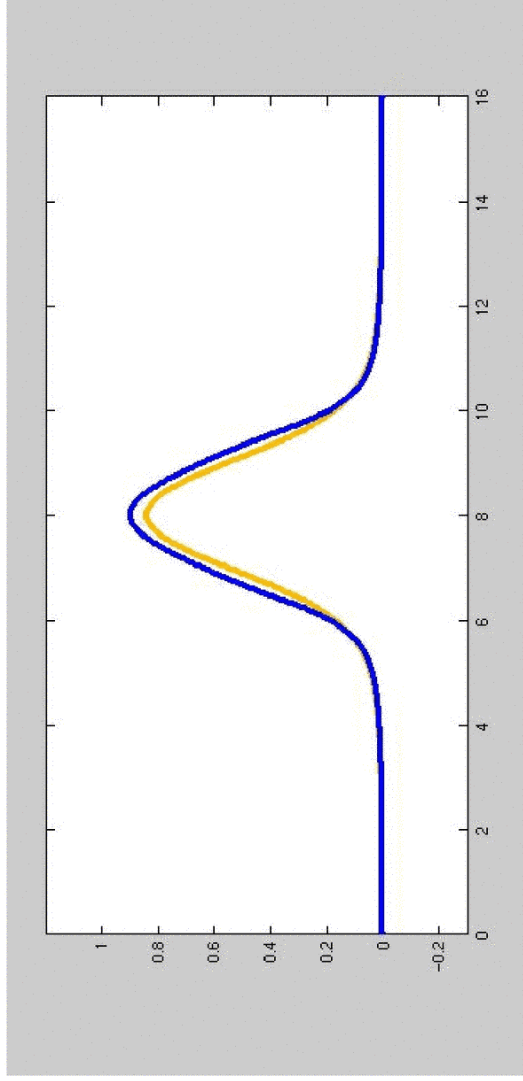
$$(1 + \beta)U(x) = \int_{-a/2}^{a/2} W(x - x') dx' + I(x), \quad V(x) = U(x)$$

- Width a determined by threshold condition $U(\pm a/2) = \kappa$



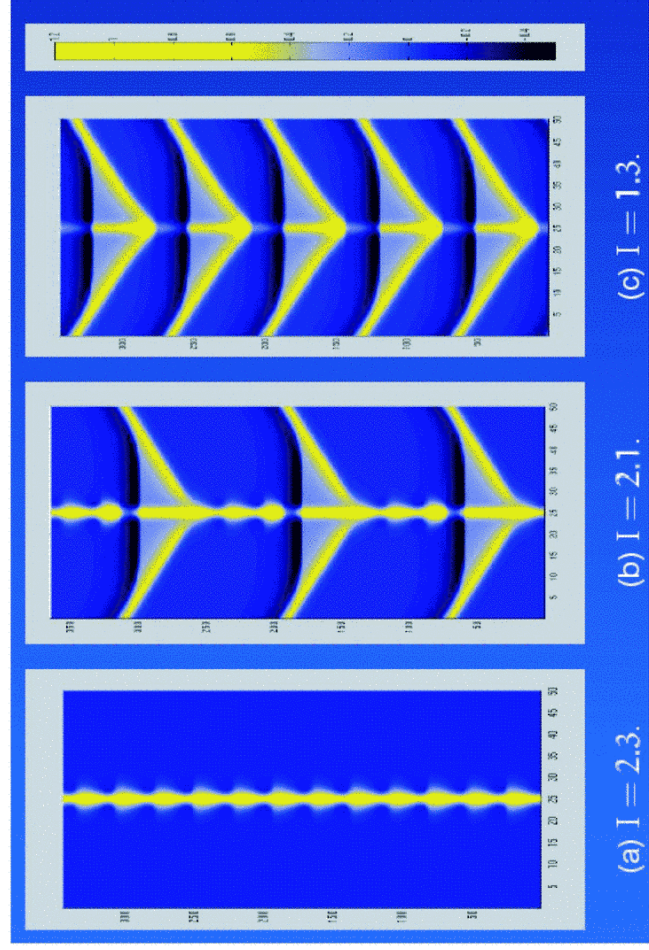
Breathing pulse





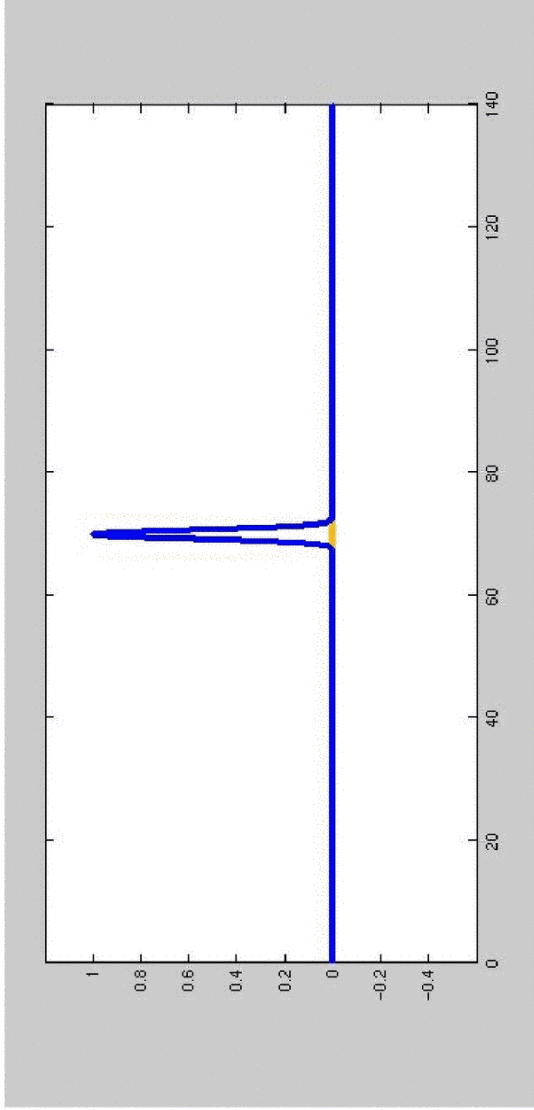
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Pulse emitter and mode-locking



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1: 1 mode-locking



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Biophysical model

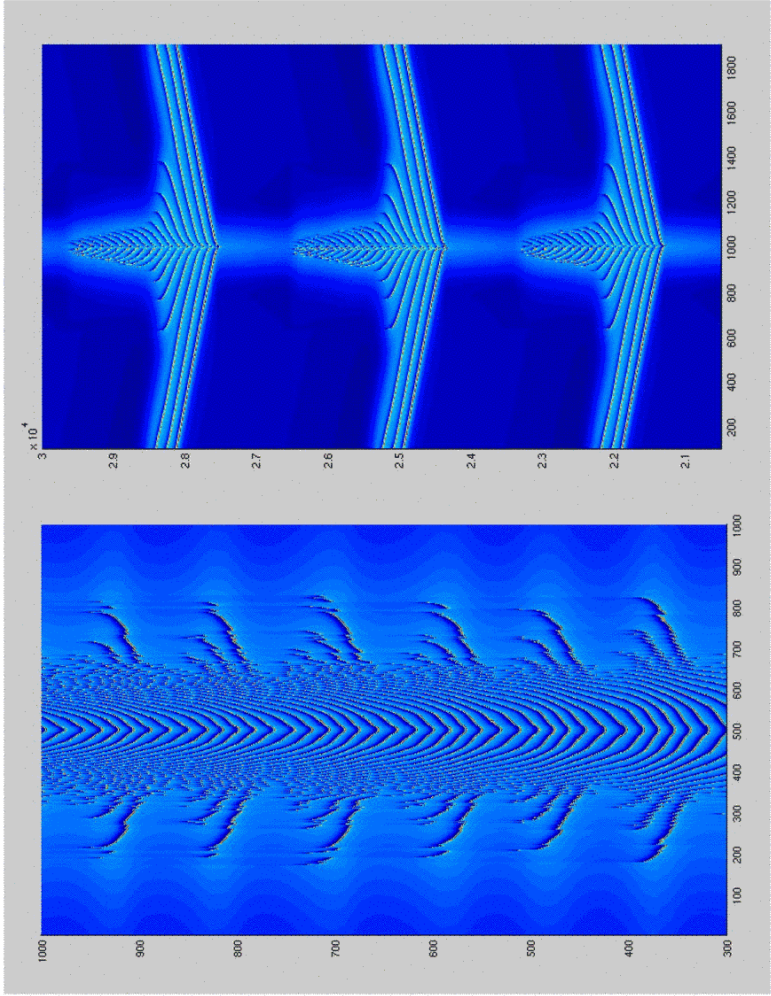
$$C \frac{dV_j}{dt} = -I_{ion}(V_j) - I_j^{syn}(t)$$

$$I_j^{syn}(t) = g_{syn} \sum_k w(j-k) s_k(t) (V - V_{syn})$$

$$\frac{ds_j}{dt} = K(V_j(t))(1-s_j) - \eta s_j, \quad K(V) = \frac{K_0}{1 + e^{-\gamma(V-V_T)}}$$

$$I_{ion}(V) = g_L(V - V_L) + g_K n^4 (V - V_K) + g_{Na} h m^3 (V - V_{Na}) + g_q q (V - V_q)$$

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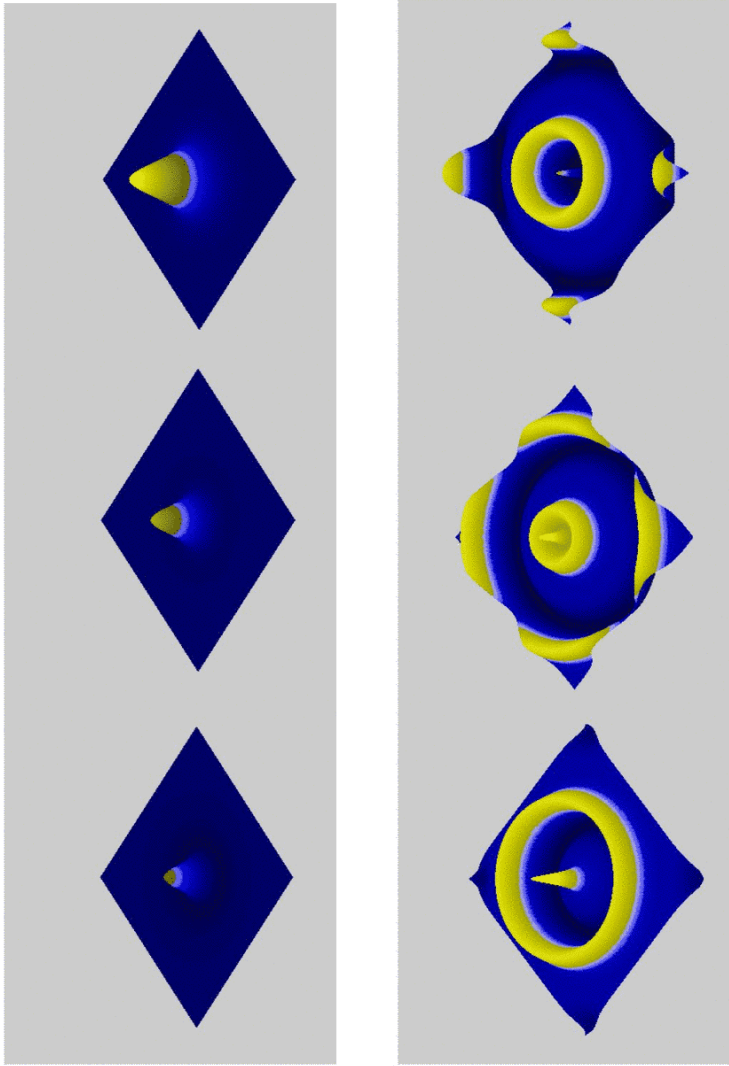


breather

pulse-emitter

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2D breathers



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II. Cortical pattern formation: inhomogeneous weights

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Continuum model of V1

- Treat primary visual cortex (V1) as a continuous 2D medium evolving according to the rate equation

$$\tau \frac{\partial a(\mathbf{r}, t)}{\partial t} = -a(\mathbf{r}, t) + \int w(\mathbf{r} | \mathbf{r}') F(a(\mathbf{r}', t)) d\mathbf{r}' + h(\mathbf{r}, t)$$

- Usually the weight distribution w is assumed to be isotropic and homogeneous:

$$w(\mathbf{r} | \mathbf{r}') = W(|\mathbf{r} - \mathbf{r}'|)$$

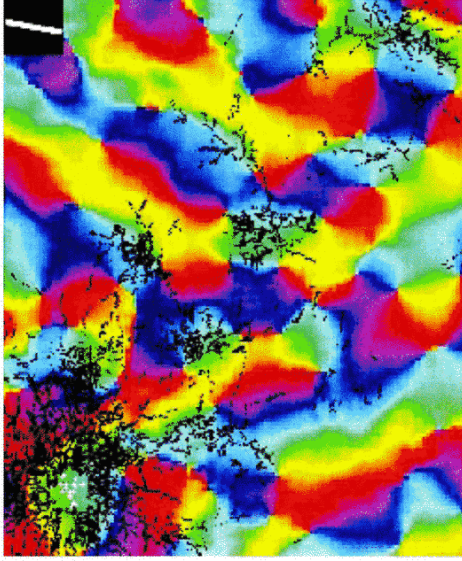
- Weight distribution w is then invariant with respect to the Euclidean group $\mathbf{E}(2)$ of rigid body motions in the plane:

$$w(\gamma\mathbf{r} | \gamma\mathbf{r}') = w(\mathbf{r} | \mathbf{r}'), \quad \gamma \in \mathbf{E}(2)$$

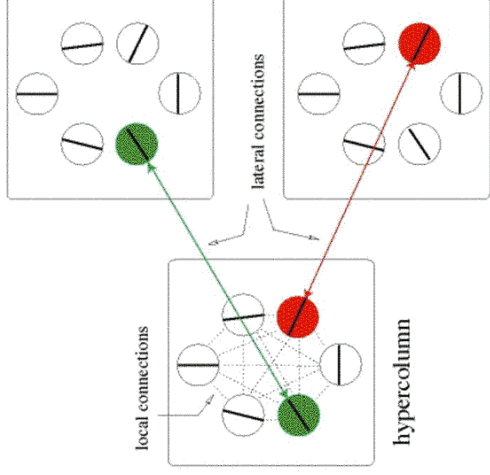
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Long-range horizontal connections

- The assumptions of isotropy and homogeneity break down when long-range horizontal connections are taken into account.
- Long-range horizontal connections (i) link cells in different hypercolumns with similar feature preferences and (ii) are anisotropic



Tree shrew (Bosking et al 1997).



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$R^2 \times S_1$ continuum model of V1

- Collapse each hypercolumn to a point (spatial coarse-graining). State of the hypercolumn at \mathbf{r} specified by $\{a(\mathbf{r}, \theta), 0 \leq \theta < \pi\}$ where θ is orientation preference

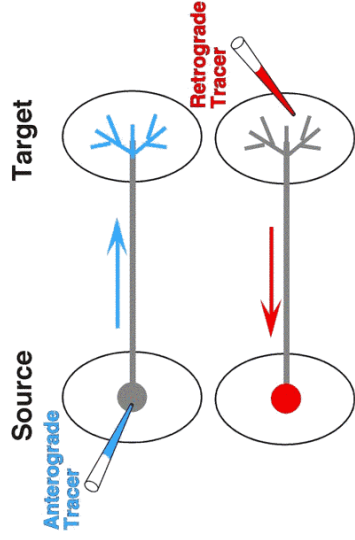
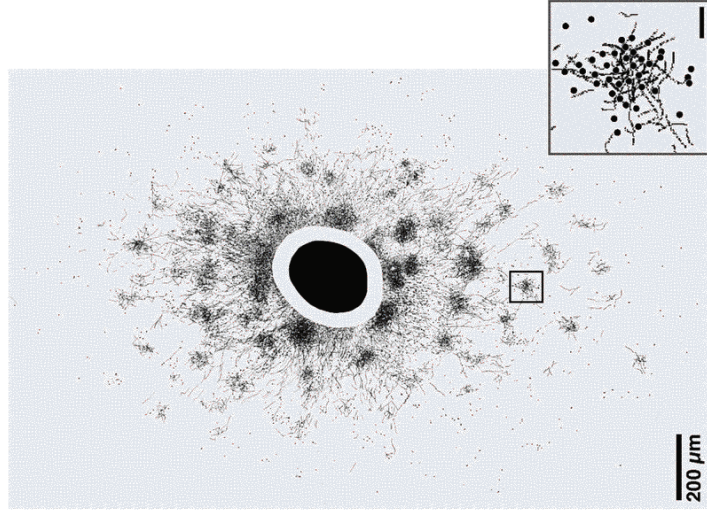
$$\tau \frac{\partial a(\mathbf{r}, \theta, t)}{\partial t} = -a(\mathbf{r}, \theta, t) + \int_0^\pi \int w(\mathbf{r}, \theta | \mathbf{r}', \theta') F(a(\mathbf{r}', \theta', t)) d\mathbf{r}' d\theta'$$

- Anisotropy implies that weight distribution w is invariant under a special shift-twist action of the Euclidean group (*Bressloff/Cowan/Golubitsky/Thomas 2001*)

$$\begin{aligned} s \circ (\mathbf{r}, \theta) &= (\mathbf{r} + \mathbf{s}, \theta), & \text{translation} \\ \xi \circ (\mathbf{r}, \theta) &= (R_\xi \mathbf{r}, \theta + \xi) & \text{rotation} \\ \kappa \circ (\mathbf{r}, \theta) &= (R_\kappa \mathbf{r}, -\theta) & \text{reflection} \end{aligned}$$

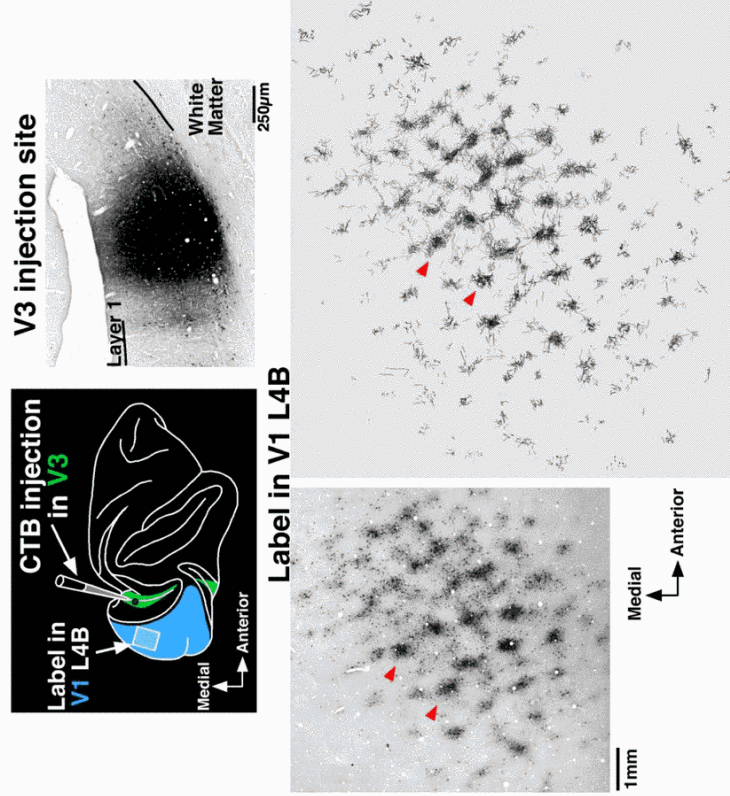
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Anisotropy in macaque?



Bi-directional CTB tracer injection in layers 2/3 of macaque reveals reciprocal patchy horizontal connections (Angelucci et al 2002)

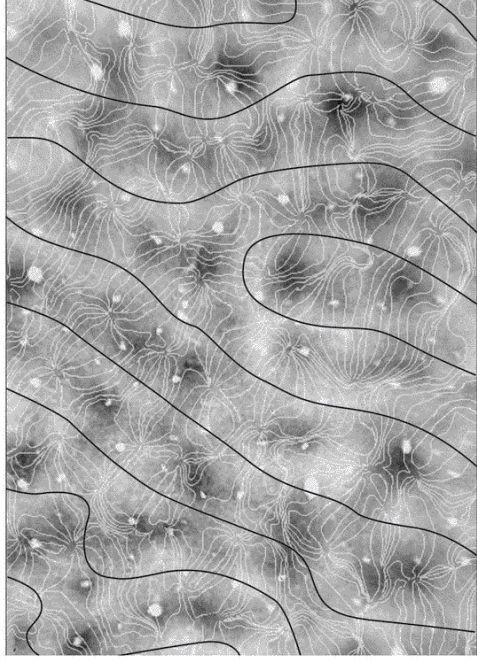
Feedback connections to V1 from extrastriate areas



Angelucci et al, J. Neurosci (2002)

Orientation singularities (pinwheels)

- Sites of rapid change in orientation preference that tend to align with centers of OD stripes
- Approximately half coincide with CO blobs, regions that are more metabolically active and stain for cytochrome oxidase

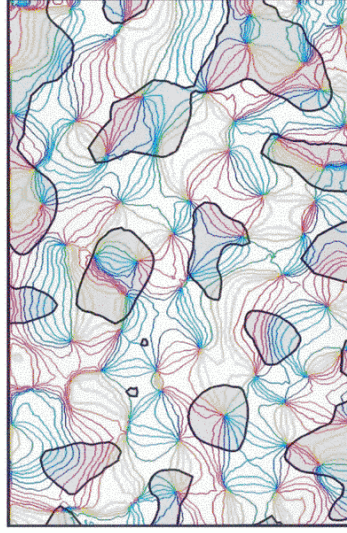


Map of iso-orientation contours and OD boundaries of macaque V1 (Blasdel 2001)

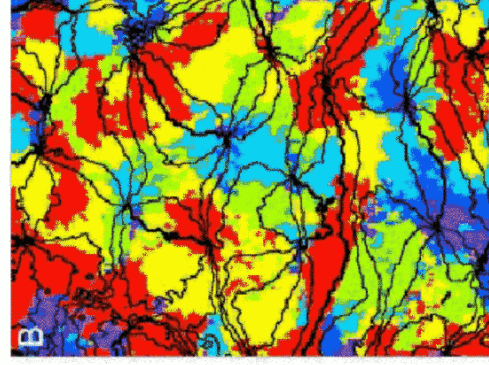
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The spatial frequency map

- High and low SF preferences located at pinwheels
- Iso-SF and iso-orientation contours approximately orthogonal around pinwheels



Iso-orientation contours and low SF preferences in cat (Bonhoffer et al 1995)



Iso-orientation contours and SF preferences in cat. Low SF, high SF (Issa et al 2000).

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Periodically modulated weights

- Horizontal connections tend to run *parallel* to the direction of the cell's orientation preference: **periodic variation in direction of anisotropy**
- Around pinwheels expect weak anisotropy due to rapid variation in orientation preference: **periodic variation in degree of anisotropy**
- Some cells outside CO blob regions do not make horizontal projections (*Yabuta and Callaway 1999*): **periodic variation in coupling strength**

Correlations between horizontal connections and periodic feature maps



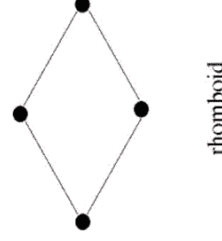
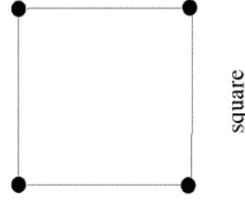
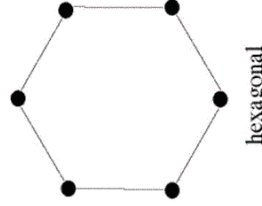
breaking of continuous translation symmetry

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- Decompose weights into local and long-range parts:

$$w(\mathbf{r} | \mathbf{r}') = W(|\mathbf{r} - \mathbf{r}'|) + \beta W^\Delta(\mathbf{F}(\mathbf{r}), \mathbf{F}(\mathbf{r}'))$$
- Assume that feature preference map \mathbf{F} is doubly periodic with respect to some regular planar lattice L , $\mathbf{F}(\mathbf{r} + \mathbf{l}) = \mathbf{F}(\mathbf{r})$ for all $\mathbf{l} \in L$

- Lattice sites could represent distribution of orientation pinwheels or CO blobs



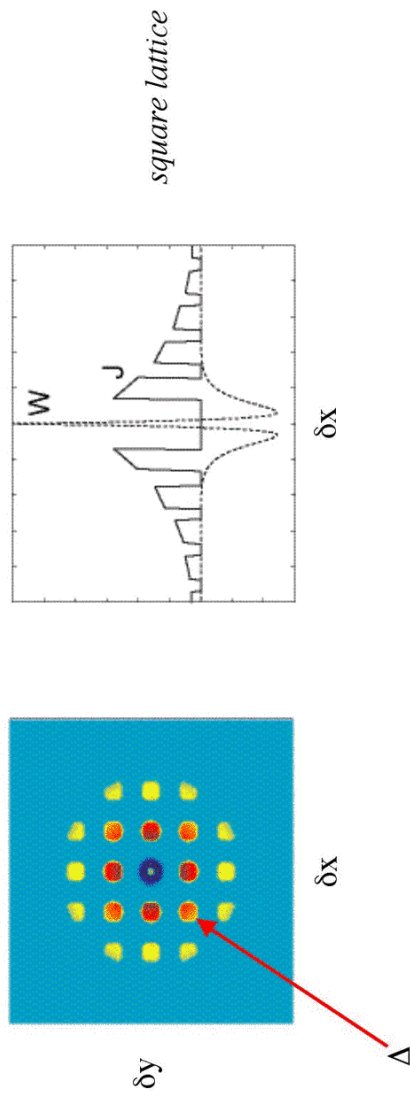
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Isotropic weights

- Let Δ denote a local patch function such that

$$W^\Delta(\mathbf{F}(\mathbf{r}), \mathbf{F}(\mathbf{r}')) = \sum_{l \in L} J_l \Delta(\mathbf{r} - \mathbf{r}' - l)$$

where J_l is a monotonically decreasing function of l for $l \neq 0$.



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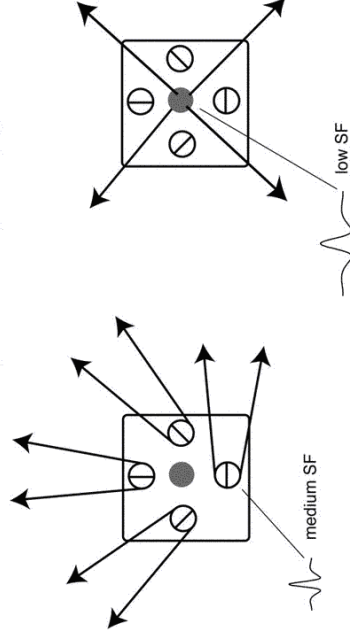
Anisotropic weights

$$W^\Delta(\mathbf{F}(\mathbf{r}), \mathbf{F}(\mathbf{r}')) = \sum_{l \in L} A_l(\mathbf{F}(\mathbf{r})) J_l \Delta(\mathbf{r} - \mathbf{r}' - l)$$

with $\mathbf{F} = (\theta, p)$ and $A_l(\mathbf{F})$ the anisotropy factor

$$A_l(\mathbf{F}) = \frac{1}{2\eta(p)} \Theta[\eta(p) - |\theta - \arg l|]$$

- Direction of anisotropy correlated with orientation preference θ and degree of anisotropy η is correlated with spatial frequency p .



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One-dimensional model

$$\frac{\partial u(x,t)}{\partial t} = -u(x,t) + \int_{-\infty}^{\infty} w(x|x')F(u(x',t))dx' + I(x')$$

with

$$w(x|x') = W(|x-x'|) + (1 + \epsilon D(x))J(x-x')$$

where $W(x)$ is a Mexican hat function, $D(x)$ is d -periodic and

$$J(x) = \sum_n J_n \Delta(x - nd_0) \quad d_0 = 2d$$

- Linearize about a uniform state u_0 by setting $u(x,t) = u_0 + e^{\lambda t} u(x)$

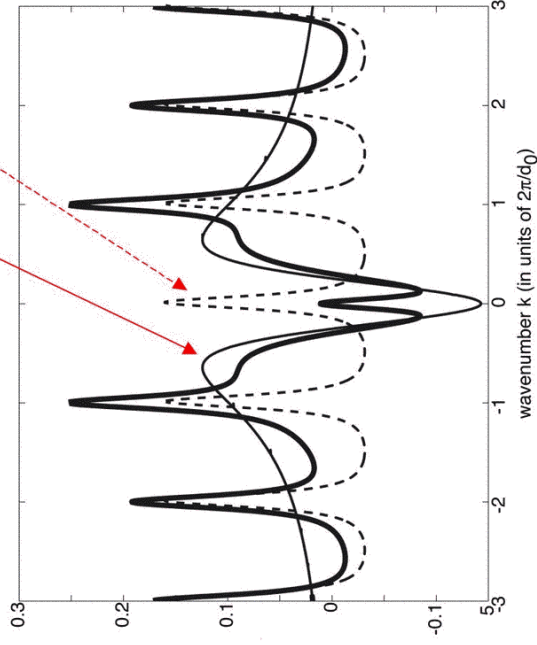
$$\lambda u(x) = -u(x) + \mu \int w(x|x')u(x')dx' \quad \mu = F'(u_0)$$

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Homogeneous weights ($\epsilon = 0$)

- Eigenmodes are of the form $u(x) = e^{ikx}$ such that $\lambda = \lambda(k)$ with

$$\lambda(k) = -1 + \mu(\tilde{W}(k) + \tilde{J}(k))$$

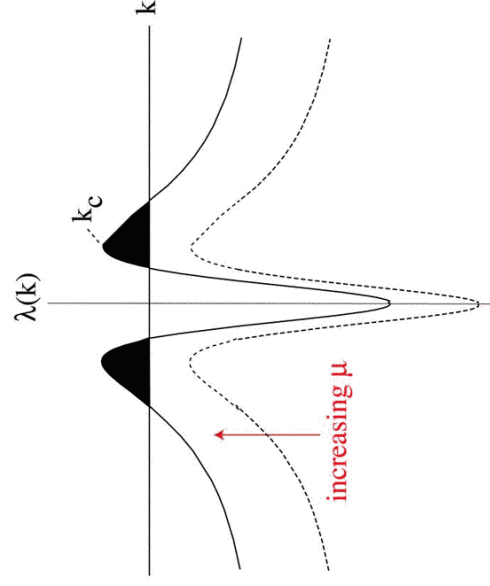


Fourier transforms

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Turing instability

- For sufficiently small μ we have $\lambda(k) < 0$ for all k and fixed point is stable
- Increasing the gain μ destabilizes the fixed point due to excitation of a band of modes around the critical wavenumber k_c with $\lambda(k_c) = \max_k \{\lambda(k)\}$
- Mexican hat + horizontal connections implies $k_c \sim 2\pi/d_0 = \pi/d$



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Inhomogeneous weights ($\varepsilon > 0$)

- Weight distribution is periodic:
- $$w(x + nd | x' + nd) = w(x | x')$$
- Eigenvalue problem for cortical pattern formation can be analyzed using Bloch wave theory: solutions of the form

$$u(x) = e^{ikx} a_k(x), \quad a_k(x + d) = a_k(x)$$

Proof: Write eigenvalue equation as $Hu(x) = \lambda u(x)$ and introduce translation operator $T_n u(x) = u(x + nd)$. Then $T_n H = H T_n$. Schur's lemma implies that T_n and H have the same eigensolutions:

$$Hu(x) = \lambda u(x), \quad T_n u(x) = C(n)u(x)$$

Since $T_n T_m = T_{n+m}$ we have $C(n) = e^{ink}$ for some k and result follows.

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- Introduce Fourier series

$$D(x) = \sum_q D_q e^{iqx}, \quad q = 2\pi m/d, \quad m \in \mathbb{Z}$$

- Eigenvalue equation becomes

$$[\lambda - \lambda_0(k)] \tilde{u}(k) = \varepsilon \sum_q \Lambda_q(k) \tilde{u}(k - q)$$

where

$$\lambda_0(k) = \tilde{W}(k) + \tilde{J}(k) - \mu, \quad \Lambda_q(k) = \tilde{J}(k - q) D_q$$

- If the inhomogeneity is weak ($\varepsilon \ll 1$) then we can use perturbation theory to determine λ .

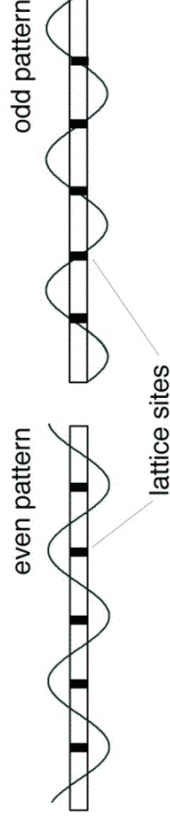
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- If $k_c \approx \pi/d$ then there are two dispersion branches $\lambda_{\pm}(k)$ arising from strong coupling between e^{ikx} and e^{-ikx}

$$\lambda_{\pm}(k) \approx \lambda_0(k) + \varepsilon [\Lambda_0(k) \pm \Lambda_Q(k)], \quad Q = 2\pi/d$$

- Corresponding pair of eigenmodes

$$u^+(x) = \cos(k_c x) \quad u^-(x) = \sin(k_c x)$$



- Explicit breaking of translation symmetry: commensurability of cortical patterns with the periodic feature maps.

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Commensurate-incommensurate transition in cortex

- Consider a pattern of the form

$$u(x, X, T) = A(X, T)e^{ik_c x} + A^*(X, T)e^{-ik_c x}$$

where $X = \varepsilon^{1/2}x$ and $T = \varepsilon t$ are slow space and time variables associated with long-wavelength spatial modulations of the amplitude.

- Assume the near resonance condition

$$\frac{\pi}{d} = k_c + \sqrt{\varepsilon}q$$

- Use perturbation methods to derive a nonlinear equation for the (complex) amplitude $A(X, T)$: cf. a periodically forced fluid convective system (Coulet 1986)

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Multiple scale analysis of nonlocal equation (Bressloff 2003)

- Introduce a multiple scale version of 1D non-local evolution equation:

$$\varepsilon \frac{\partial u(x, X, T)}{\partial T} = -u(x, X, T) + \int_{-\infty}^{\infty} w(x, X | x') f(u(x', X + \sqrt{\varepsilon}[x' - x], T)) dx'$$

- Decompose weights into local and long-range parts

$$w(x, X | x') = W(|x - x'|) + (1 + \varepsilon D(x, X))J(x - x')$$

near resonance condition $\rightarrow D(x, X) = \cos(2(k_c x + qX))$

- Perturbation series expansion in $\sqrt{\varepsilon}$

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- Can then derive a Ginzburg-Landau equation of the form

$$\frac{\partial A}{\partial T} = \omega A + \frac{\partial^2 A}{\partial X^2} - |A|^2 A + \gamma A^* e^{i2qX}$$

(after rescaling) where ω , γ are model-dependent coefficients.

- Setting $A = Re^{i\Psi}$ we obtain the pair of equations

$$\frac{\partial R}{\partial T} = \omega R - R^3 + \frac{\partial^2 R}{\partial X^2} - R \left(\frac{\partial \Psi}{\partial X} \right)^2 + \gamma R \cos(2(\Psi - qX))$$

$$R \frac{\partial \Psi}{\partial T} = R \frac{\partial^2 \Psi}{\partial X^2} + 2 \frac{\partial R}{\partial X} \frac{\partial \Psi}{\partial X} - \gamma R \sin(2(\Psi - qX))$$

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- There exist stationary solutions of the form

$$\Psi = \Psi_0(X) \equiv qX + \frac{p\pi}{2}, \quad R = R_0$$

- The odd- p solutions are unstable with respect to phase fluctuations
- The phase $\Phi = \Psi - \Psi_0$ for even- p solutions evolves according to the sine-Gordon equation

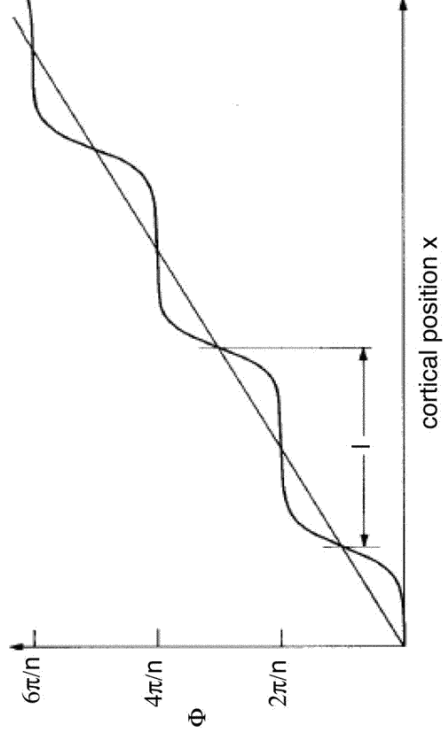
$$\frac{\partial \Phi}{\partial T} = \frac{\partial^2 \Phi}{\partial X^2} - \gamma \sin(2\Phi)$$

- There exists a critical value of mismatch q_0 such that for $q < q_0$ the pattern is pinned to the lattice with $\Phi = \pi p$ and

$$q_0^2 = \frac{8\gamma}{\pi^2}$$

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- When $q > q_0$ soliton-like solutions occur (Bak 1981)

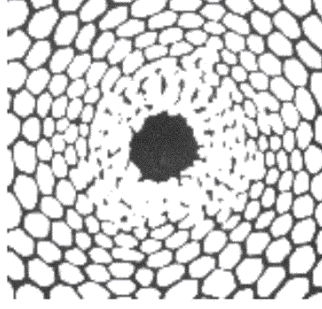
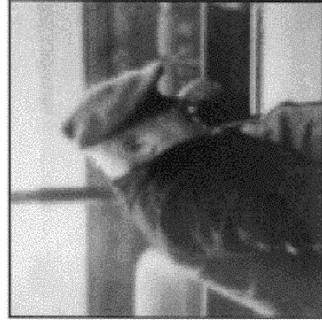


- Mechanism for generating phase defects during cortical pattern formation

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Hallucinations

- Under normal conditions the visual cortex analyzes an image by breaking it up into various local features such as edges.



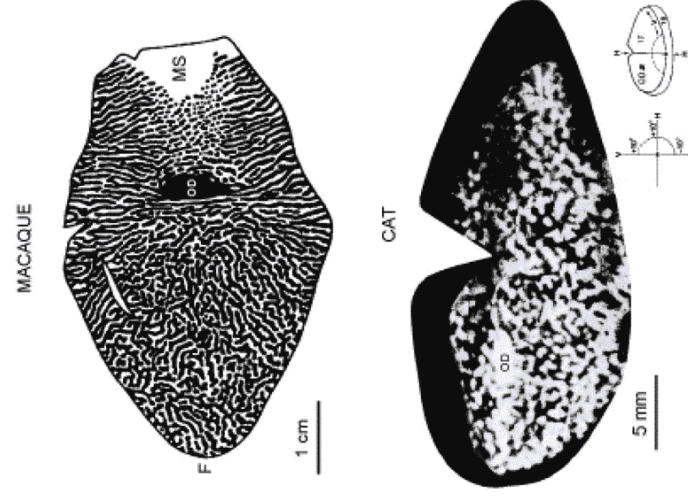
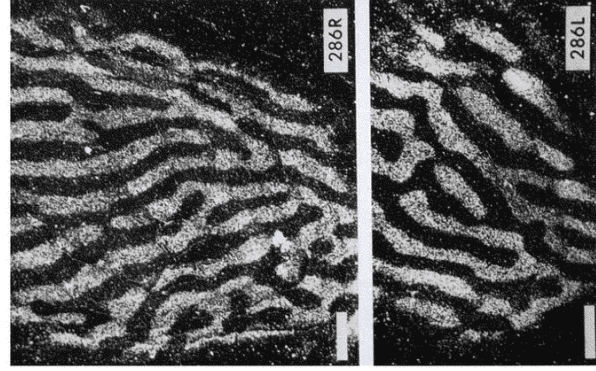
- The spontaneous formation of a cortical activity pattern that is commensurate with the underlying orientation feature map could lead to an ordered lattice of oriented edges during an hallucination.

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III. Cortical development: inhomogeneous chemical markers

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Development of ocular dominance columns

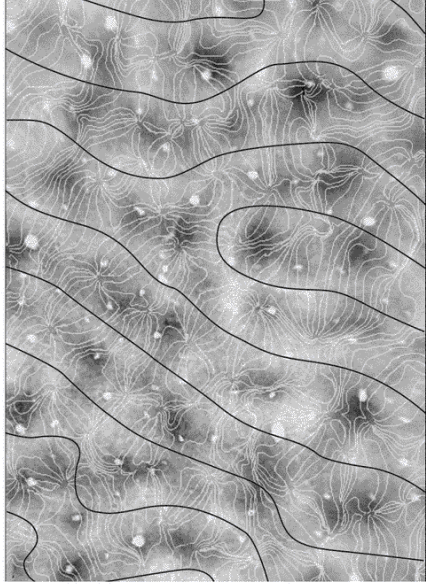


Intra-ocular injection of proline revealing ocular dominance (OD) columns in layer 4C of macaque and cat

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Alignment with CO blobs

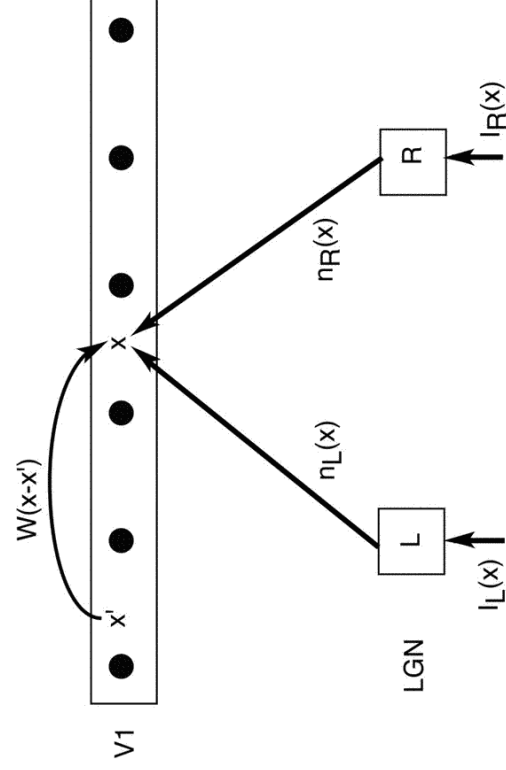
- Experimental evidence suggests that CO blobs occur early in development and are associated with intrinsic chemical markers (*Murphy et al 1998, 2001*).



- What is the mechanism for aligning OD columns with the CO blobs?

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- Activity-dependent models of cortical development typically assume that feedforward afferents evolve according to some competitive Hebbian mechanism in the presence of fixed lateral interactions.



- The CO blobs may induce a spatially periodic chemical modulation of Hebbian learning during early OD development resulting in alignment.

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Modified Swindale model (Bressloff/Oster 2003)

- Let $n_R(\mathbf{r}, t)$ and $n_L(\mathbf{r}, t)$ denote the left and right eye densities of connections from the LGN to V1.

$$\tau \frac{\partial n_L}{\partial t} = [-\mu(n_L - \gamma) + w_S * n_L - w_A * n_R + D]n_L(N - n_L)$$

$$\tau \frac{\partial n_R}{\partial t} = [-\mu(n_R - \gamma) + w_S * n_R - w_A * n_L + D]n_R(N - n_R)$$

where $w * n = \int w(\mathbf{r} | \mathbf{r}')n(\mathbf{r}')d\mathbf{r}'$ and D represents effects of chemical markers

- Set $\mathbf{n} = (n_L, n_R)$. Homogeneous fixed points at $\mathbf{n} = (N, 0)$ or $\mathbf{n} = (0, N)$ are monocular, whereas fixed points at $\mathbf{n} = (0, 0)$ or $\mathbf{n} = (N, N)$ are binocular.
- There is another homogeneous fixed point $\mathbf{n}^* = (n^*, n^*)$ such that $[\cdot] = 0$

- Reducing the parameter μ can destabilize the binocular state \mathbf{n}^* leading to the formation of OD stripes via a Turing instability
- A spatially periodic inhomogeneity D provides a mechanism for aligning the centers of the developing OD stripes with the lattice of CO blobs. Set $n(x) = n_L(x) - n_R(x)$.

