Fields of Dreams:

Modeling and Analysis of Large Scale Activity in the Brain

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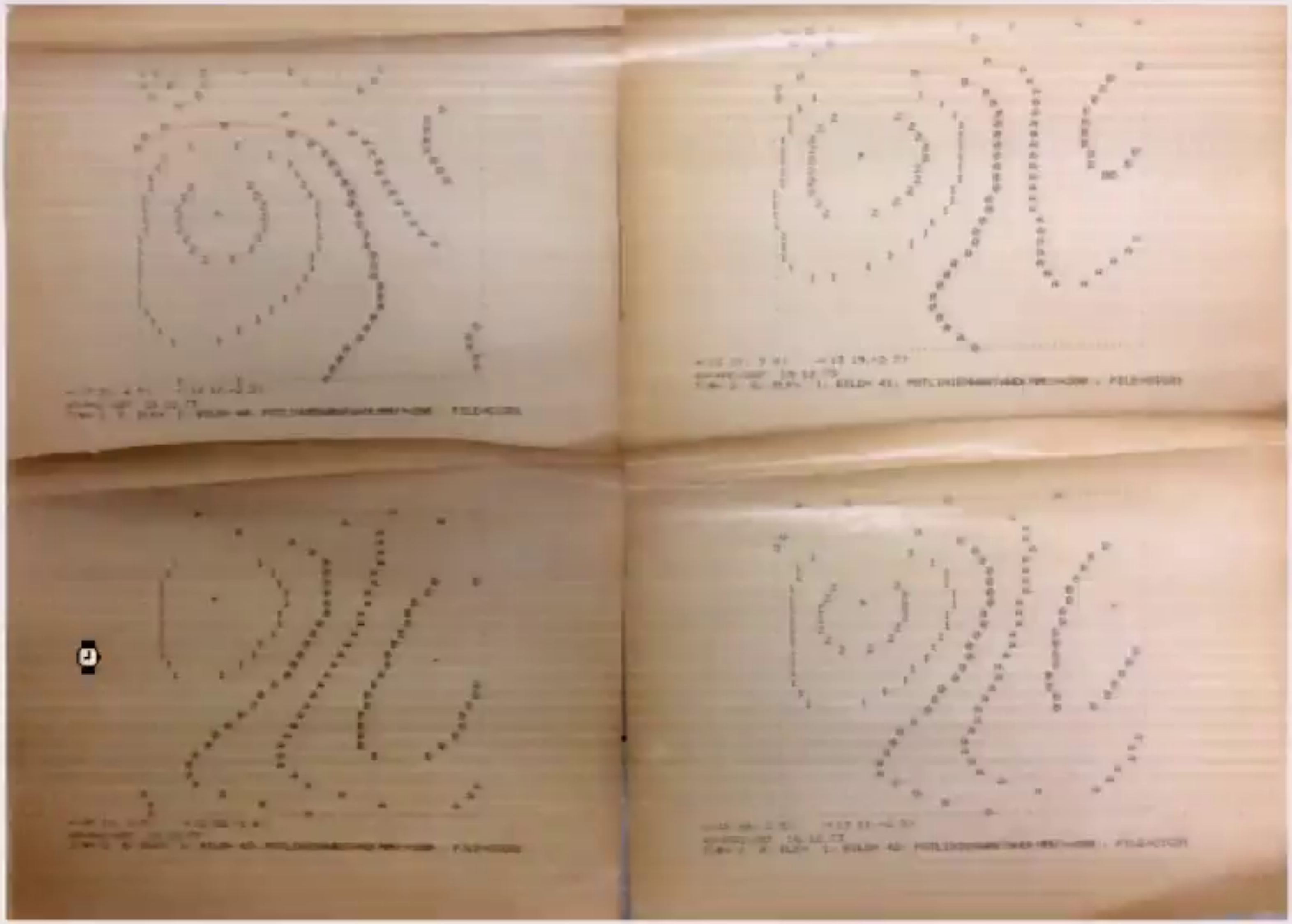
OUTLINE

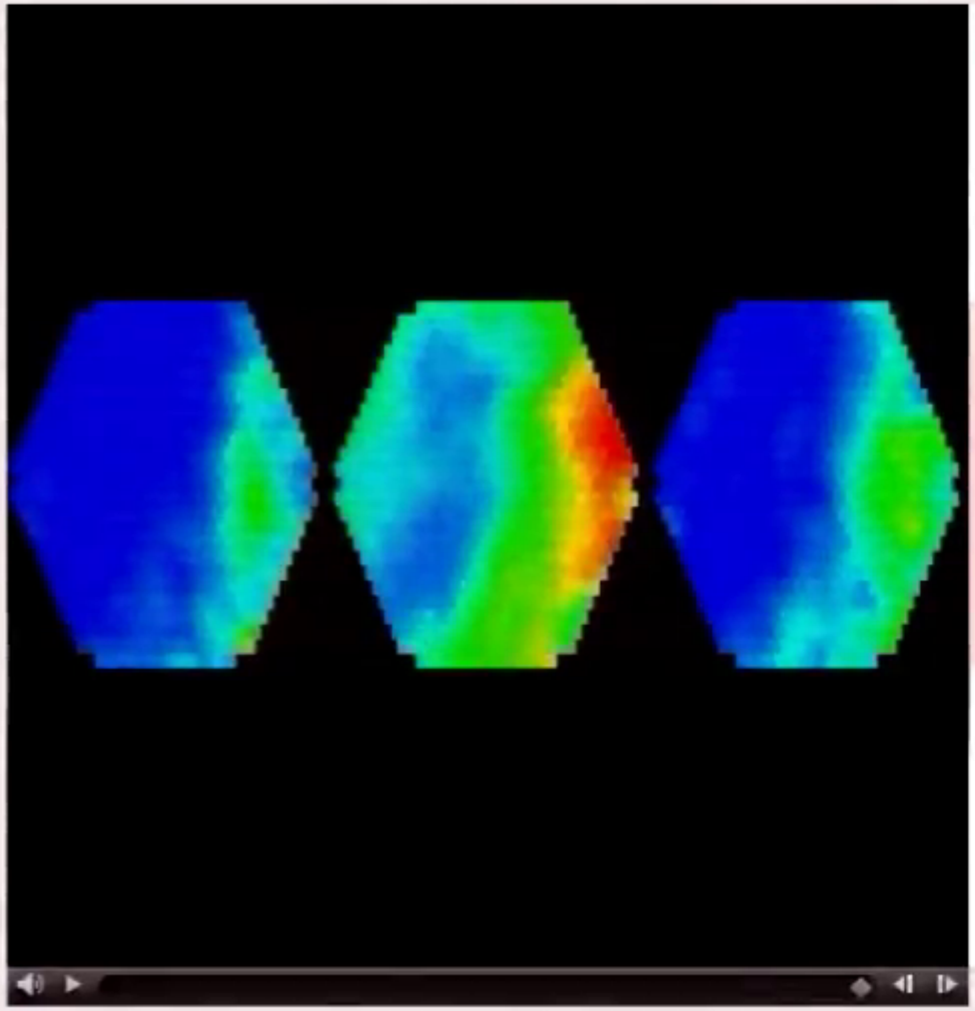
- Examples and methods of recording spatio-temporal activity
- Data analysis and challenges
- Meaning of the activity
- Approaches to modeling
- Mathematical challenges

Petsche & Rappelsberger, 1973



Spatio-temporal neural patterns

- Reflected waves (Wu lab)



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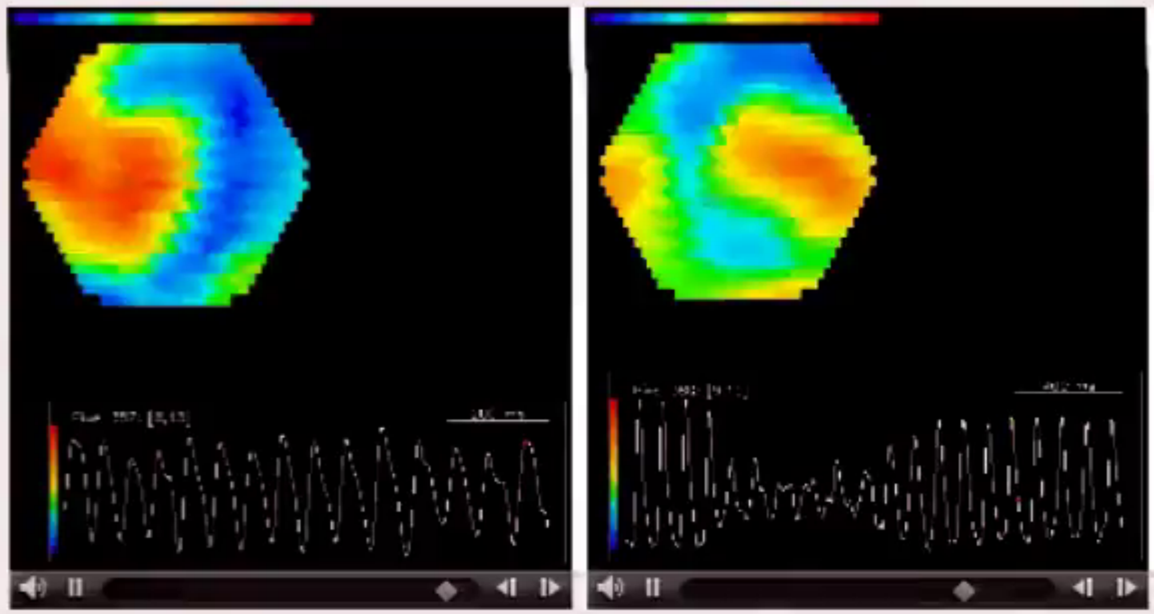

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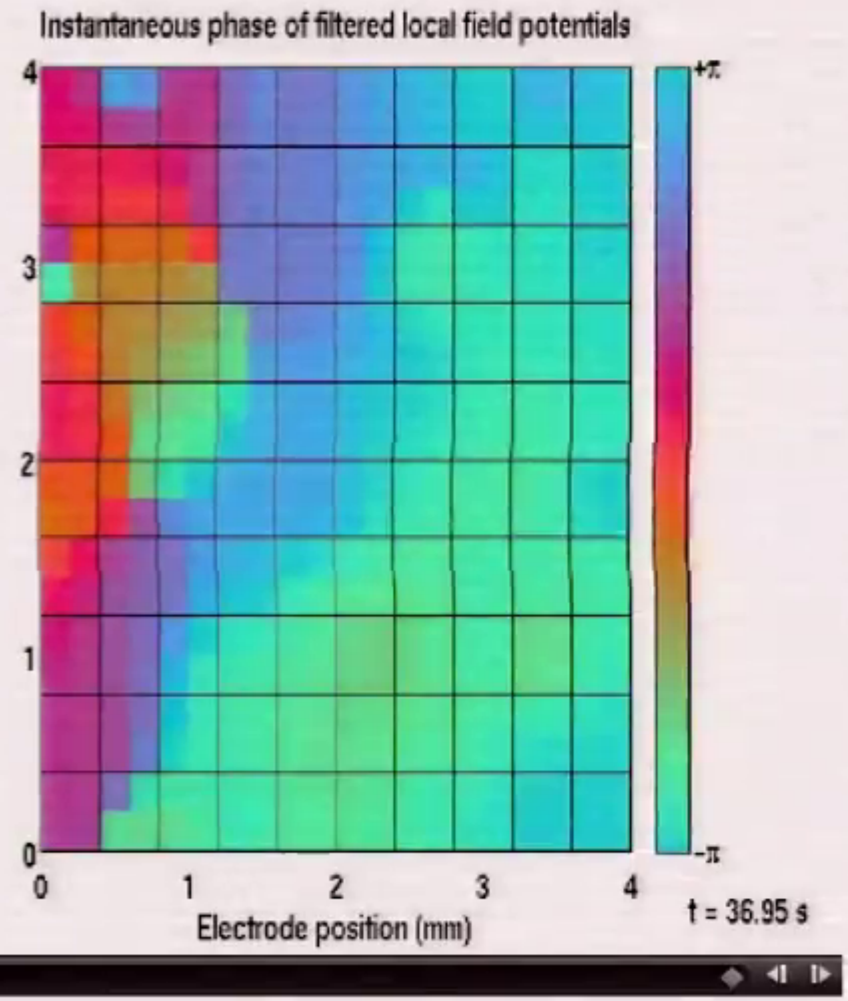

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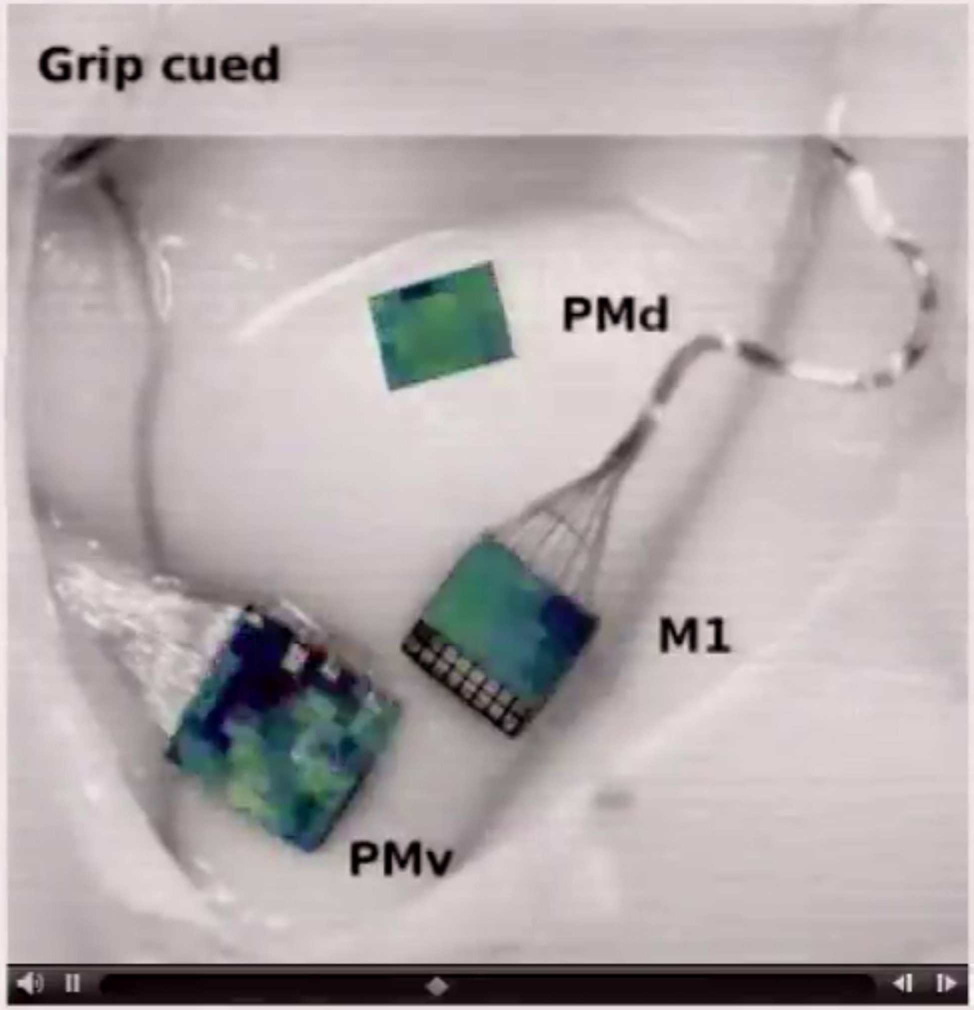

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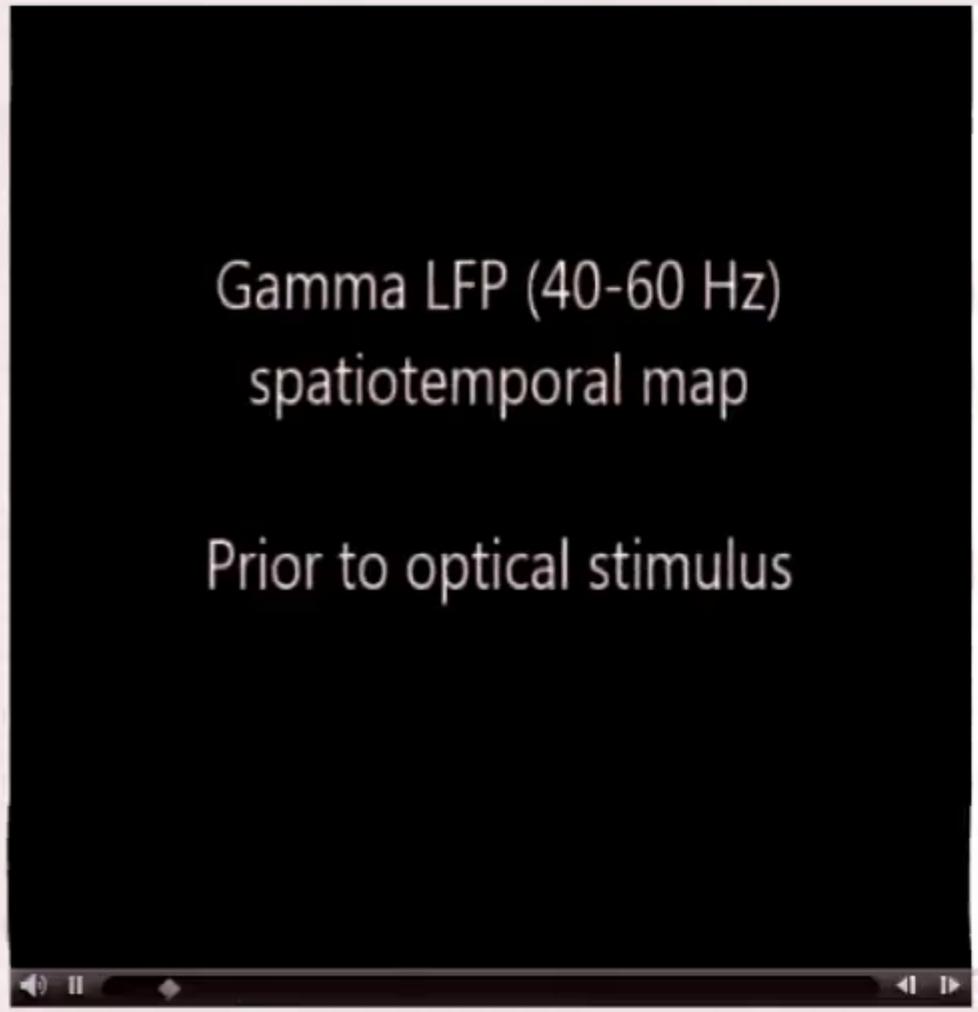

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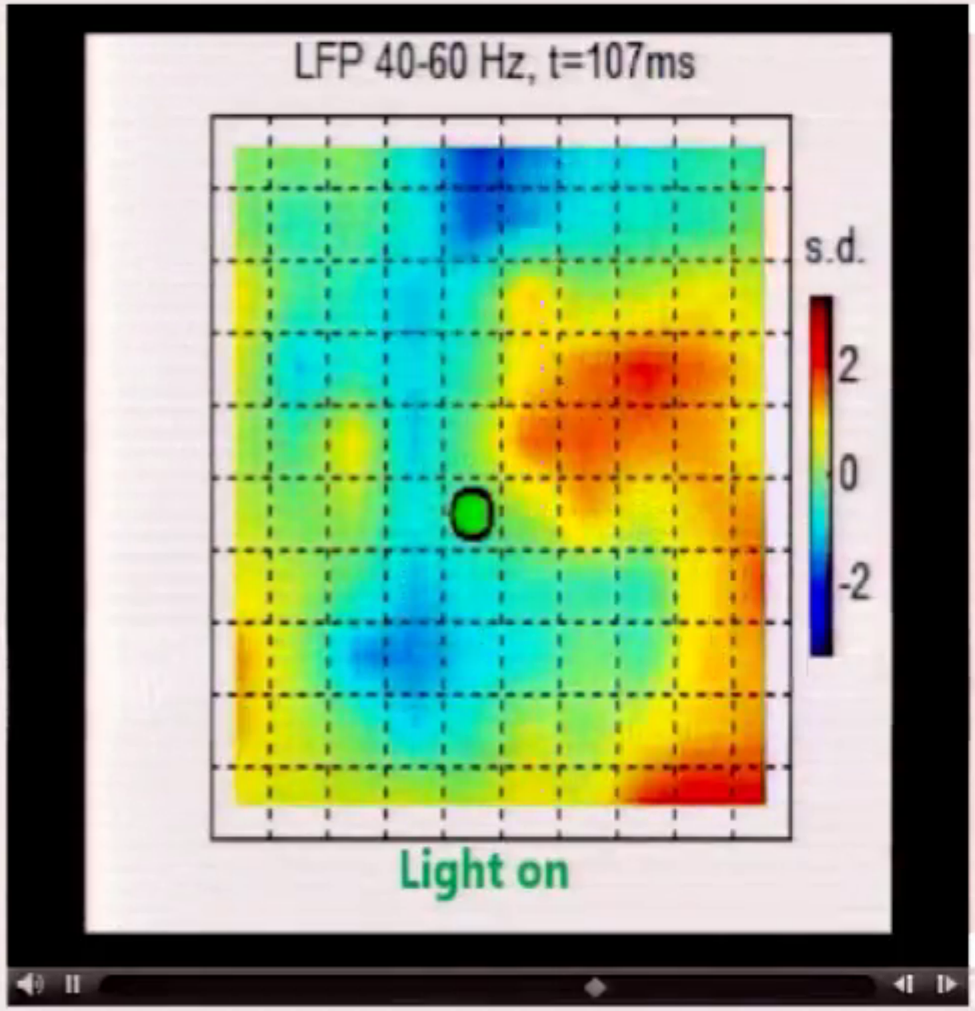
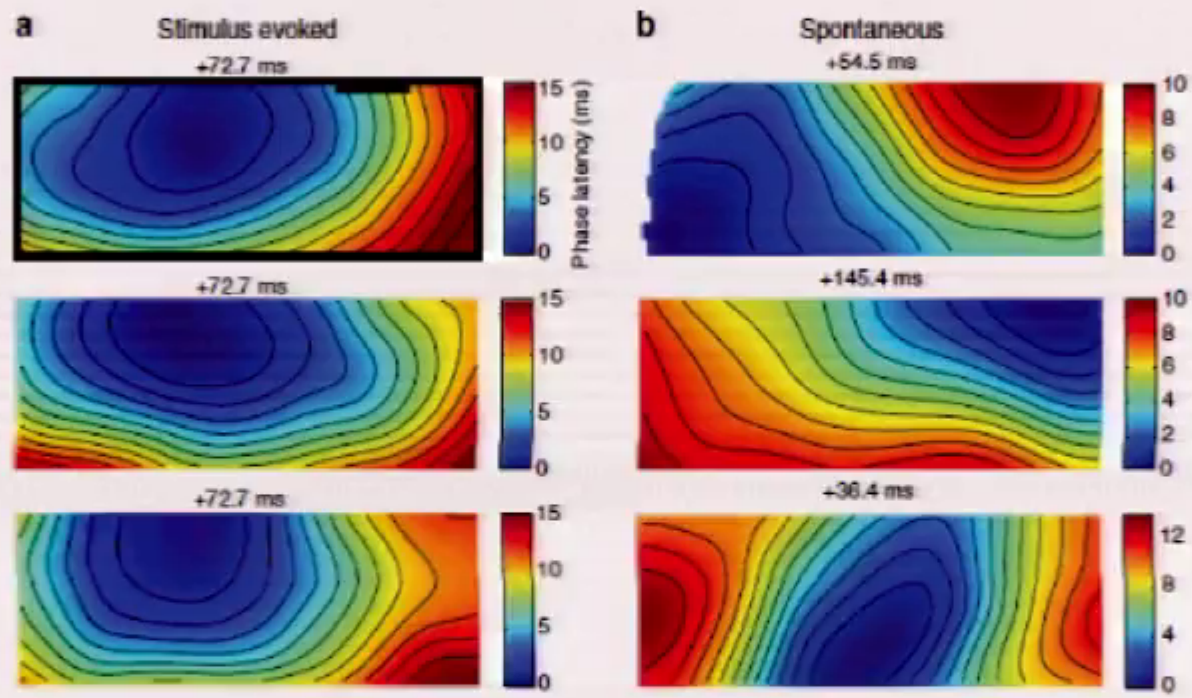


ANALYSIS/VISUALIZATION OF SPATIO-TEMPORAL DATA

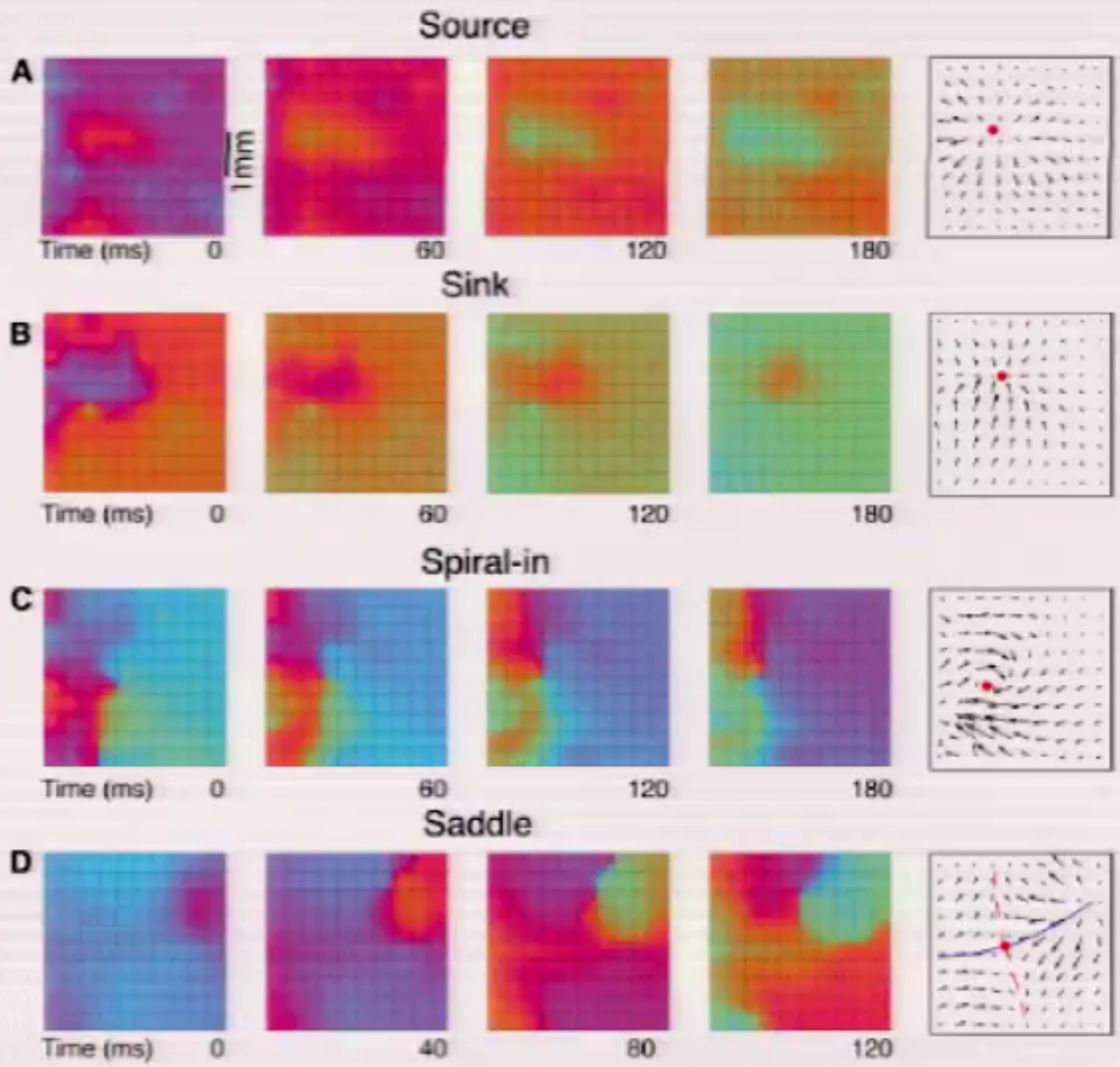
- Filter at different frequency bands
- Conversion to phase using Hilbert transform
- Extract something from this (?)
  - Fit to plane-waves or rotating waves
  - Phase latency extraction (Muller et al, 2014)
  - Gong et al use methods from fluid dynamics

PHASE-LATENCY



Complex waves in MT of marmoset

Townsend et al. • Complex Cortical Waves J. Neurosci., March 18, 2015 • 35(11):4657–4662 • 4659

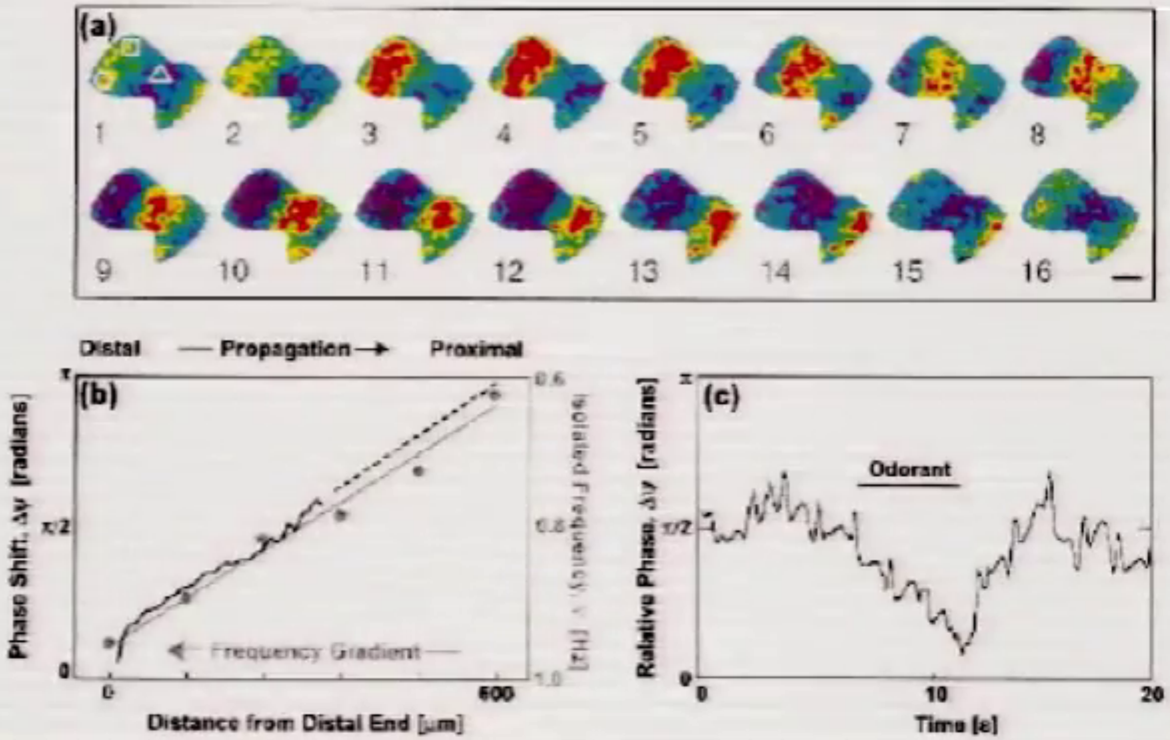


Computational role

- Do these patterns have a computational role or are they "the exhaust fumes of computation?"
- Several theories of the "meaning" of waves
- Can reflect evoked activity
- May set biases – providing a mechanistic view of Bayesian computations
- Could also be the basis for the actual computation (as in WM)

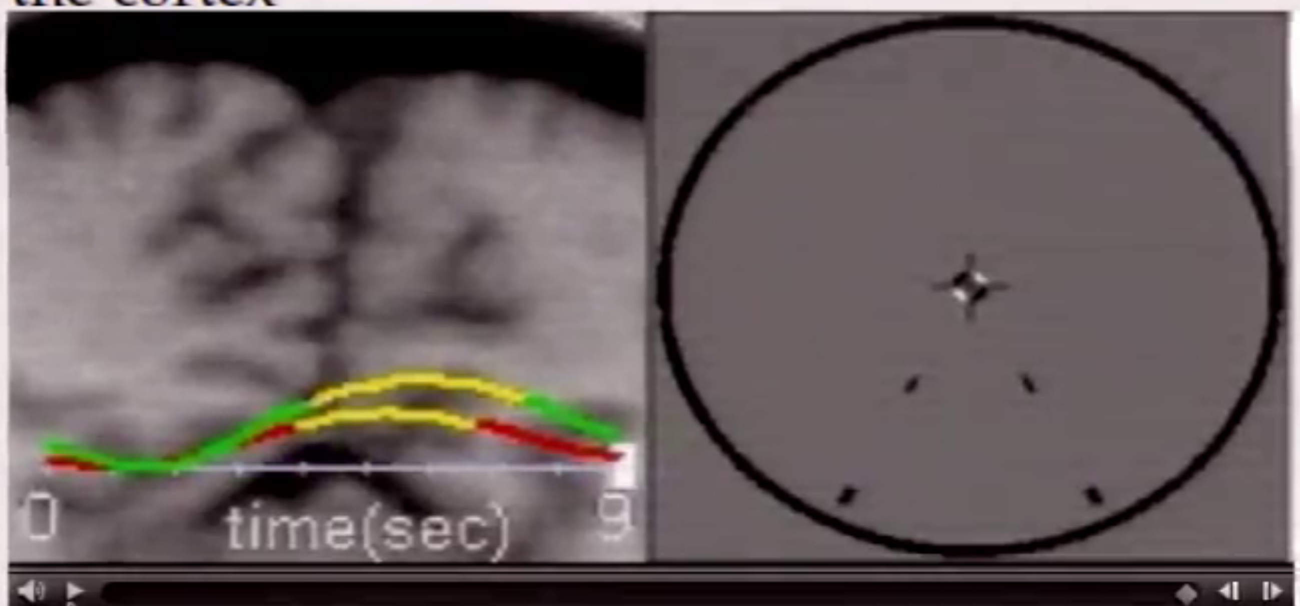
WAVES & MEMORY

David Kleinfeld & I suggested that they could set up a position code in the *Limax* olfactory lobe



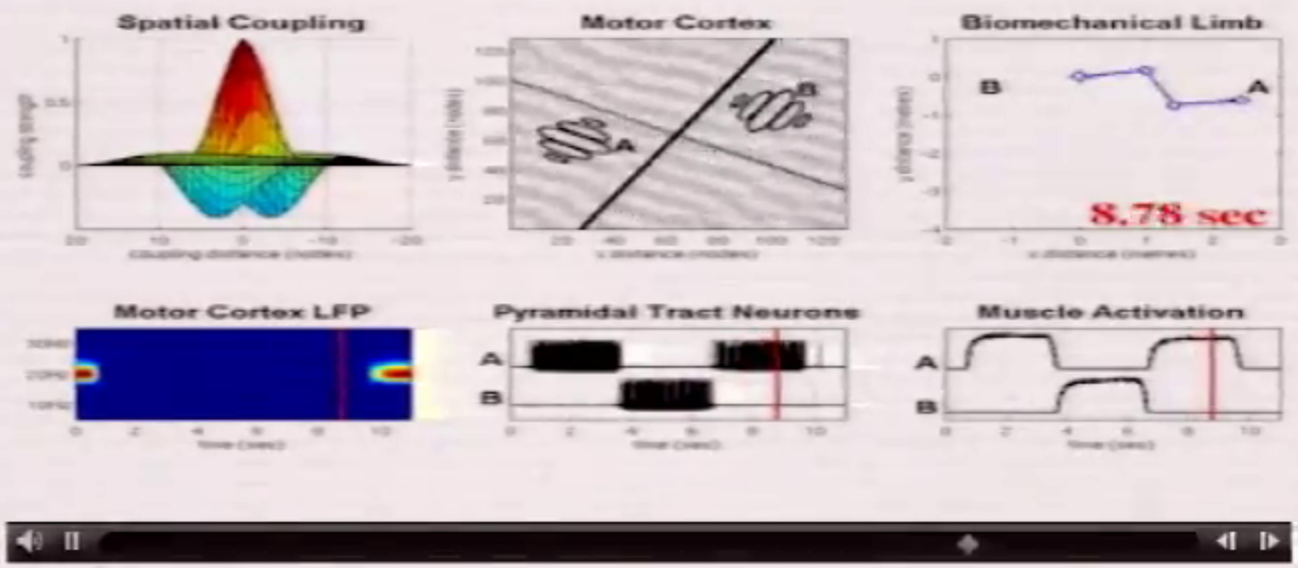
Waves & Rivalry

When the visual system receives two conflicting images, it picks a winner, but switches back and forth between the two (*Binocular rivalry*). In certain versions of this illusion, a wave is perceived. Heeger et al show that the perception is a wave across the cortex



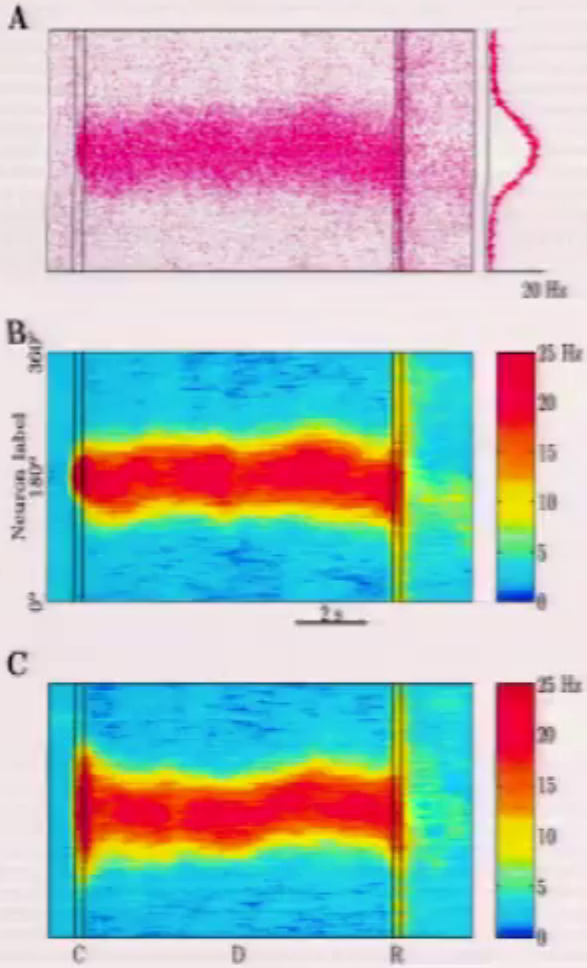
CONTROL OF LIMBS

Heitmann et al have shown that by using anisotropic dendritic fields, they can control a limb with spatio-temporal motor cortex patterns

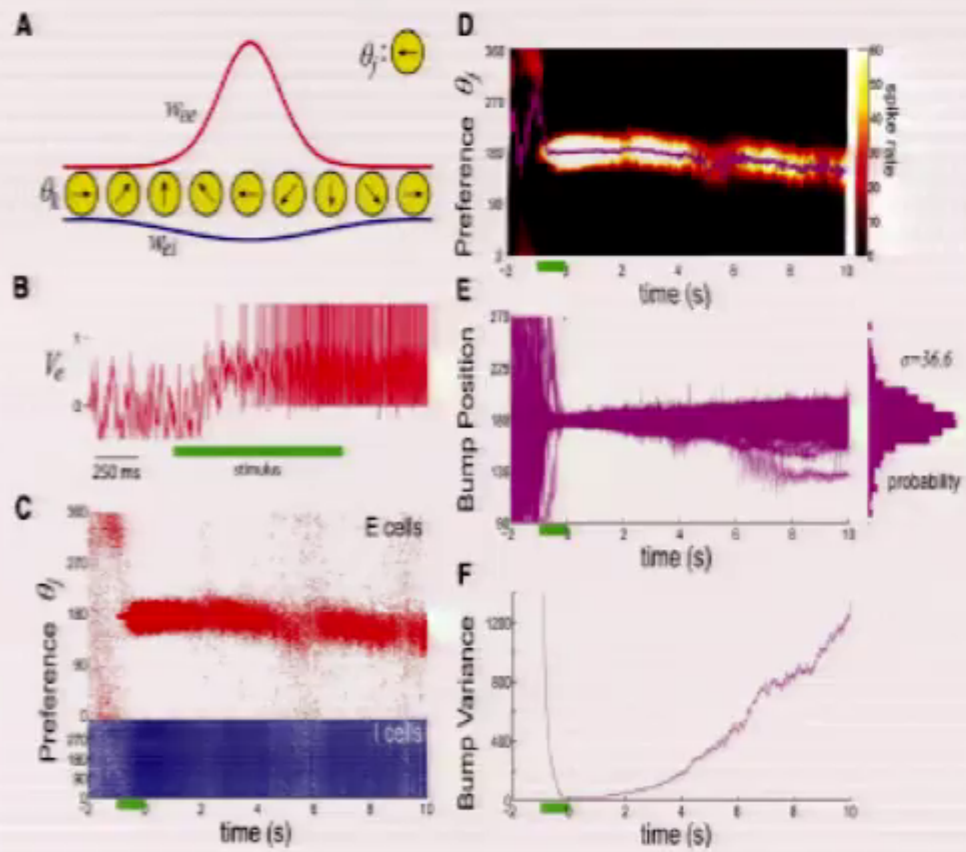


LOCAL PATTERNS - WORKING MEMORY

Compte et al [2000] (and many others - 1977 on) suggest that working memory is encoded as a spatio-temporal attractor



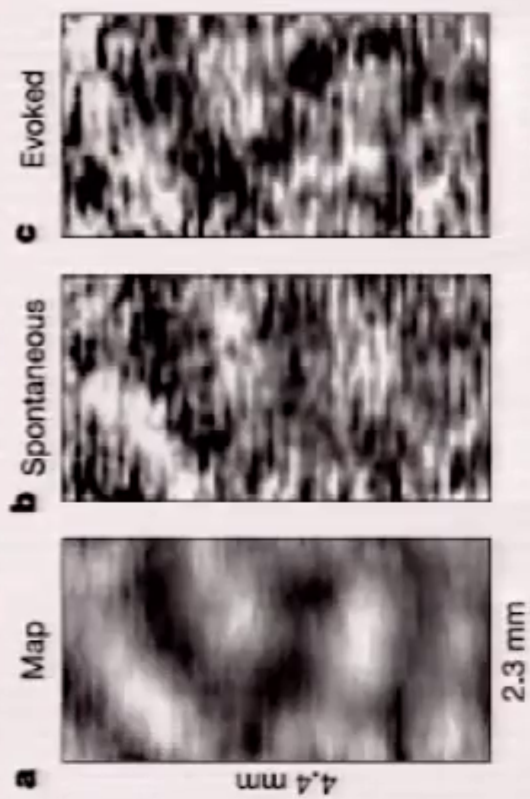
compte et al 2000 CC



Kilpatrick et al 2014 JNeurosci

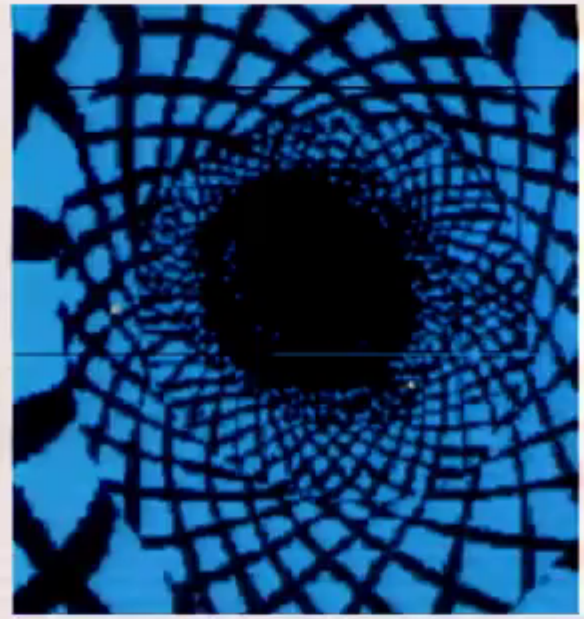
Reflecting evoked activity

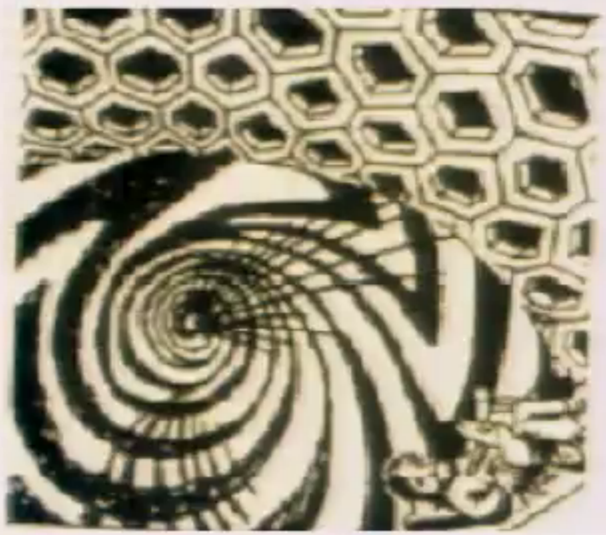
Tsodyks lab (Kenet et al, 2003) showed the ongoing activity in visual cortex was similar to that evoked by oriented bars



VISUAL HALLUCINATIONS

BE, & Cowan (1979) suggested simple visual hallucinations were a consequence of instability in the early areas of visual processing

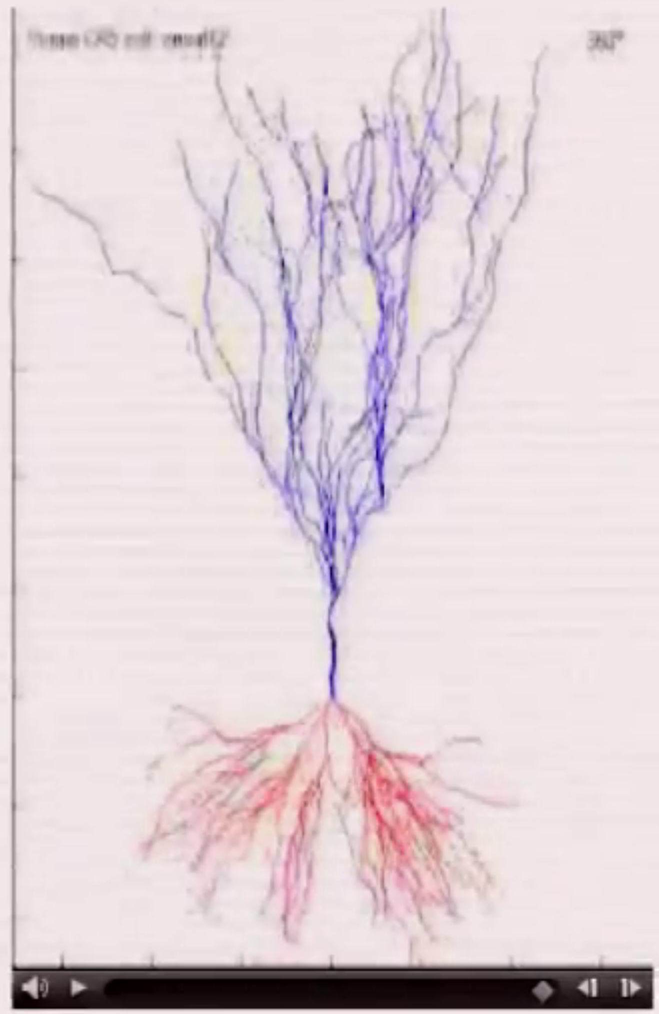




Levels of Modeling

Single neuron level

- Include all the dendrites & axons
- Ionic channels
- Imagine thousands of them in a network



NETWORKS OF SIMPLER MODELS

- Instead of full blown compartments & channels, each neuron is modeled as a one-dimensional (discontinuous) ODE

$$\frac{dV}{dt} = f(V, I)$$

- Networks become:

$$\begin{aligned}
\frac{dV_i}{dt} &= f_i(V_i, I_i) \\
I_i &= I_i^{stim}(t) + \sum_j g_{ij} s_{ij}(t) \\
\tau_{ij} \frac{ds_{ij}}{dt} &= -s_{ij} + \delta(t - t_i^{spike})
\end{aligned}$$

- Still hard to analyze, especially in spatial networks

CERTAIN REDUCTIONS ARE POSSIBLE

- It is possible to make a principle reduction of "spiking models" to a *mean field* (see Brunel, et al) but this only works in steady state
- Averaging methods (slow synapses) can be used, especially for the 1-d simpler models (slow scale is synapse)
- Weak coupling and near bifurcations (BE, Izhikevich, etc)
- Equation-free modeling
- **Can also develop heuristic neural fields models.**

Quick example of averaging - gotta be an ϵ

- Fast system depends on slow synapses

$$C\frac{dv_i}{dt} = I_{ion}(v_i, w_i) + \sum_j [g_{ij}s_j](V_R - V_i)$$

- Say, for fixed $\{s_j\}$ oscillation with frequency $F_i(\{s_j\})$
- *Slow* synapse obeys

$$\frac{ds_i}{dt} = \epsilon(-s_i + \delta(v_i - V_T))$$

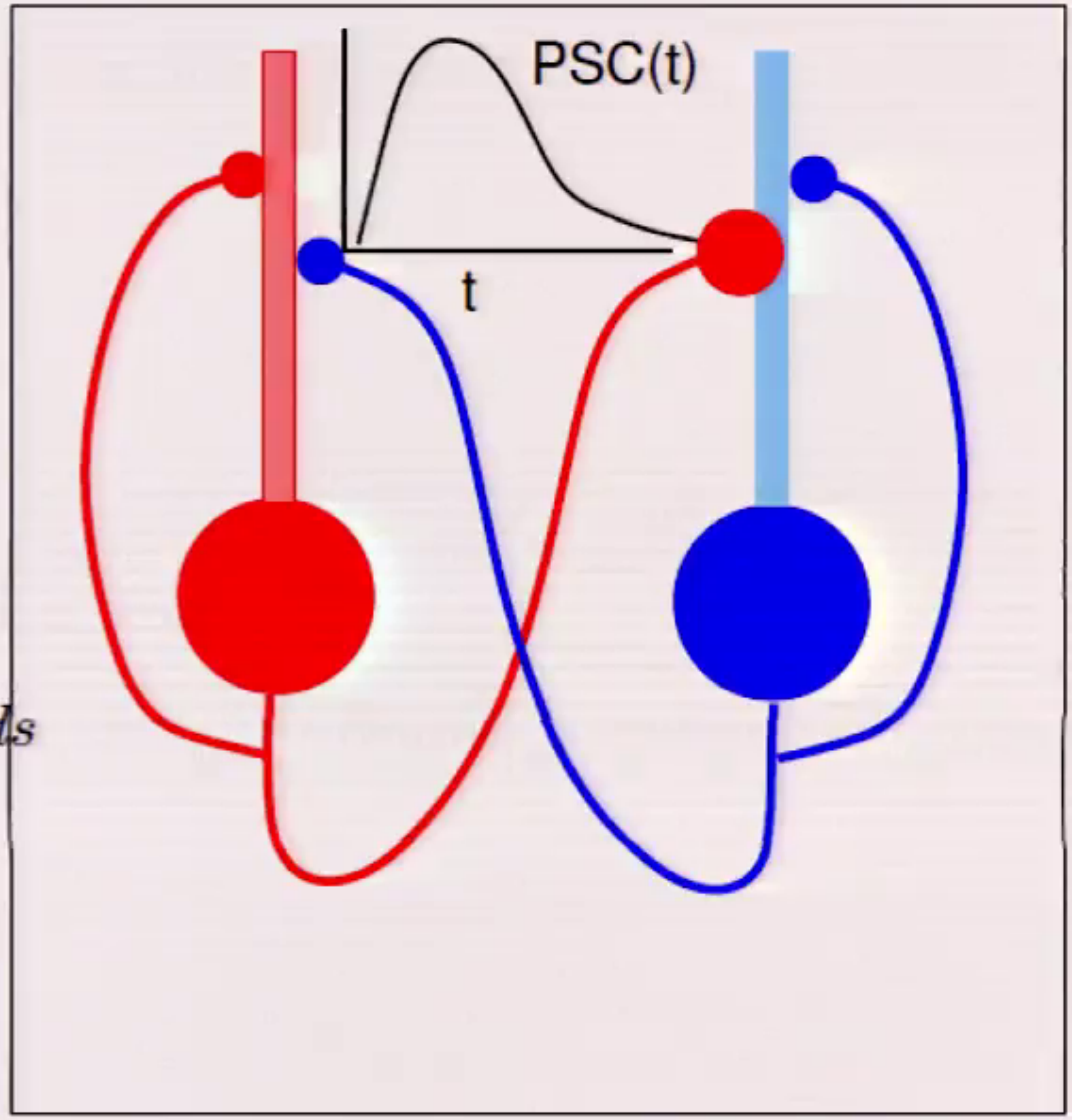
- Apply averaging to reduce to

$$\frac{ds_i}{dt} = \epsilon[-s_i + F_i(\{s_j\})]$$

Firing rate models

inducing transmitter release an a post-synaptic current (PSC)

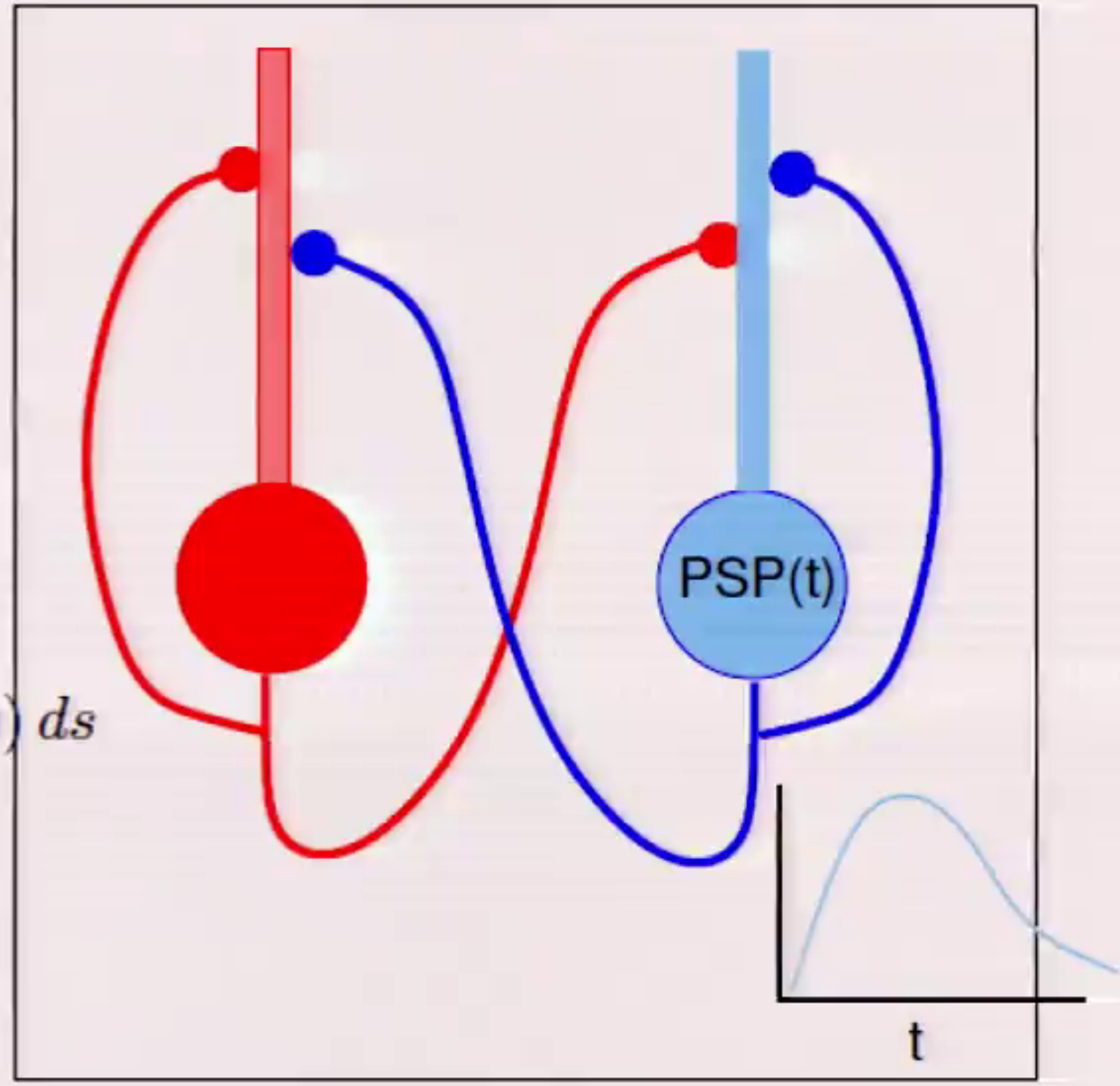
$$PSC(t) = \int^t k_s(t-s) f_e(s)\, ds$$



FIRING RATE MODELS

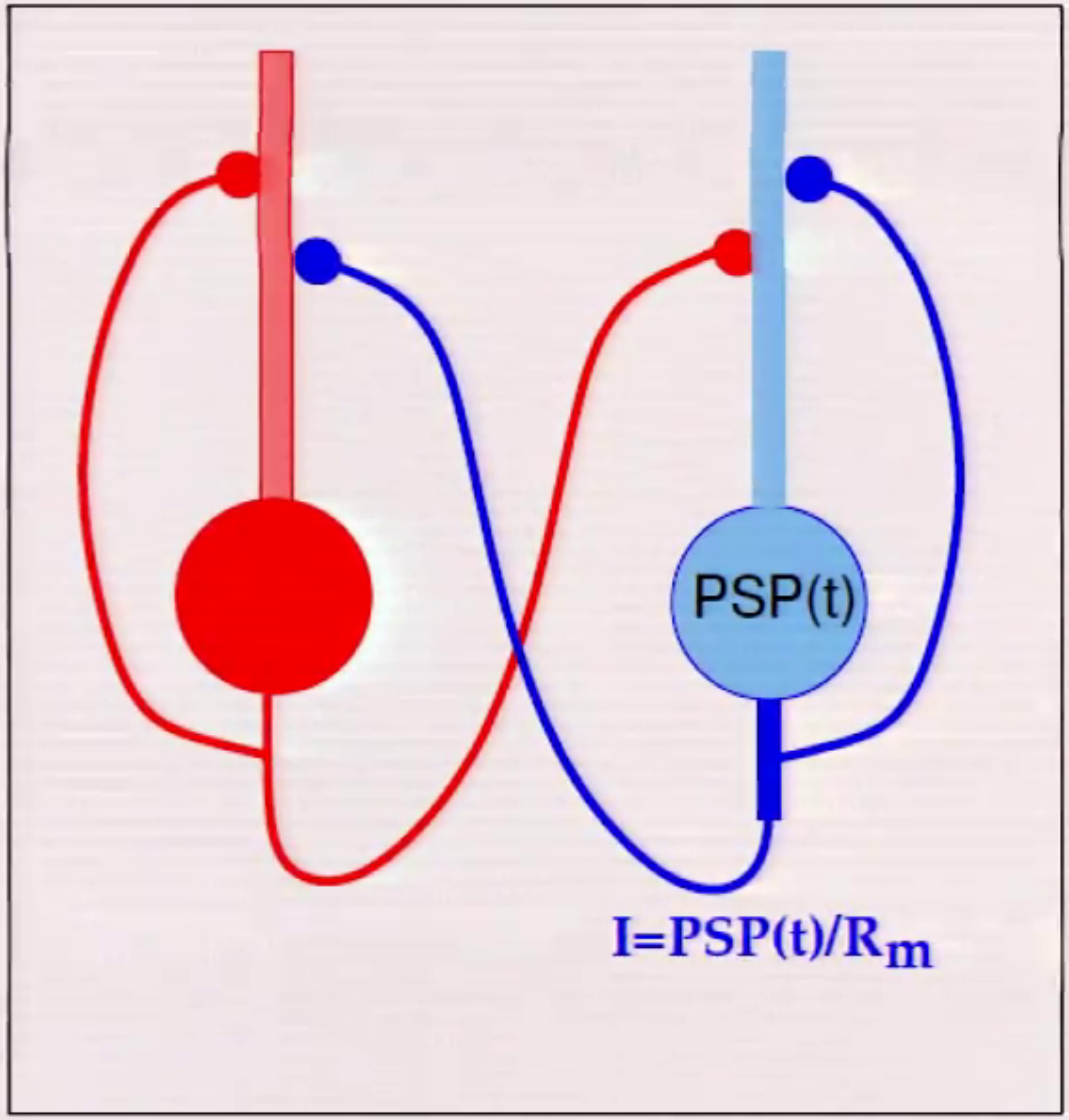
This is filtered through the dendrites for a post synaptic potential (PSP)

$$\mathrm{PSP}(t) = \int^t k_d(t-s)\mathrm{PSC}(s)\, ds$$



FIRING RATE MODELS

and becomes the current at the hillock, closing the system



SPACE CLAMPED MODELS

$$f_i(t) = F_i[I_i(t) + g_{ij} \sum_j k_d^i(t) \otimes k_s^j(t) \otimes f_j(t)]$$

- $F_i[\cdot]$ is the firing rate
- $I_i(t)$ is input currents
- g_{ij} is strength and sign of coupling

- $a(t) \otimes b(t)$ is temporal convolution
- $k_s^j(t)$ is synaptic profile
- $k_d^i(t)$ is dendritic filter
- Nonlinear Volterra equation!

Two simplifications

- Instant dendritic response and exponential synapses. Temporal response profile depends on the sender

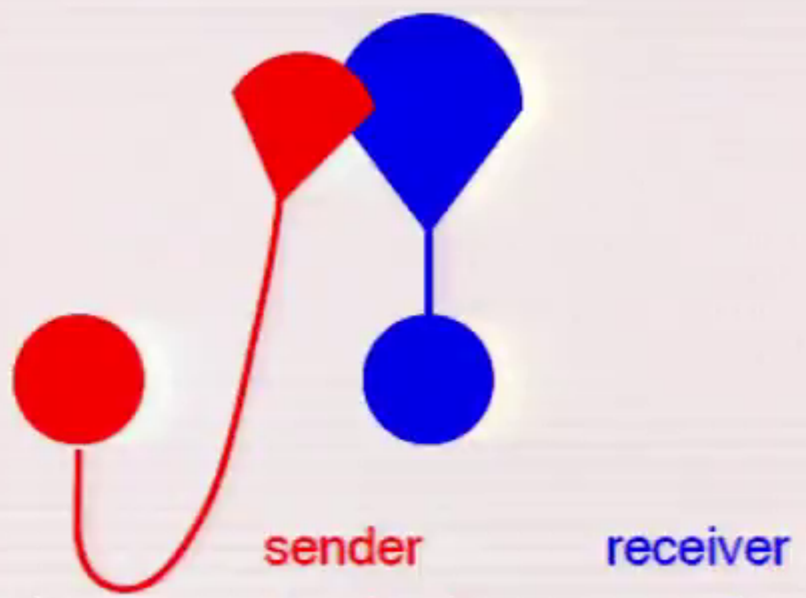
$$\tau_{s,i}\frac{du_i}{dt} = -u_i + F_i[I_i + \sum_j g_{ij}u_j]$$

- Instant synapses and exponential dendrites. Temporal response profile depends on the receiver

$$\tau_{m,i}\frac{dV_i}{dt} = -V_i + I_i(t) + \sum_j g_{ij}F_j(V_j)$$

WHAT ABOUT SPACE?

Spatial interactions depend on the combined interactions between the sender (axonal) spread and the receiver (dendritic) spread



$$W(x) = J_a(x) \star J_d(x)$$

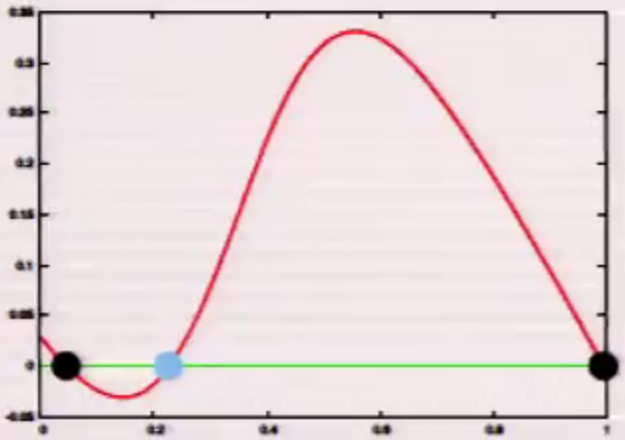
THE FINAL MODEL (FOR NOW)

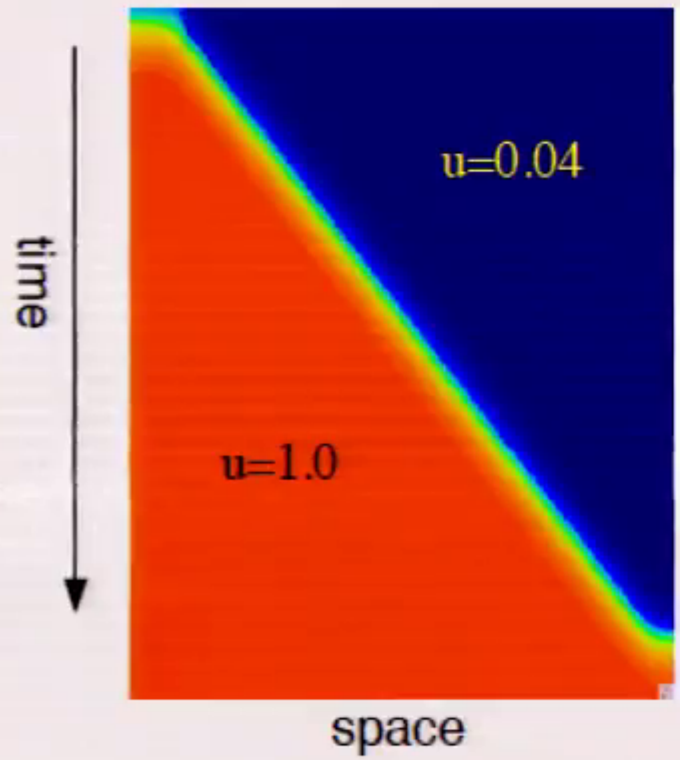
For consistency, we assume the interaction depends only on the sender(axon)

$$\begin{aligned}
\tau_e \frac{\partial u}{\partial t} &= -u + F_e[g_{ee} W_e(x) \star u - g_{ei} W_i(x) \star v + I_e] \\
\tau_i \frac{\partial v}{\partial t} &= -v + F_i[g_{ie} W_e(x) \star u - g_{ii} W_i(x) \star v + I_i]
\end{aligned}$$

The $\star$ is convolution in space (1- or 2-D)

THE SIMPLEST – THE SCALAR WAVE FRONT





$$\tau_e \frac{\partial u}{\partial t} = -u + F[J_{ee}(x) \star u]$$

Existence strategy (BE & B. McLeod)

- Traveling wave:

$$c\tau_e u' = -u + F[J_{ee} \star u]$$

- Nonlocal equation needs to be localized
- If $J_{ee}(x) = g_{ee}e^{-|x|}/2$ then invertible

$$\begin{aligned} c\tau_e u' &= -u + F[g_{ee}z] \\ z'' &= z - u \end{aligned}$$

- Use homotopy to go from restricted model (shooting!) to true model

A CLASS OF SOLVABLE MODELS

- If we replace $F(x)$ with heav$(x-\theta)$, the step function, then we can construct solutions
- E.g for the exponential,

$$c = \frac{1}{\tau_e}\frac{1-2\theta}{2\theta}$$

- Formal stability can also be determined
- Many other solvable problems

TRAVELING PULSES

- Fronts are fairly unusual (except see below); what is more common are pulses

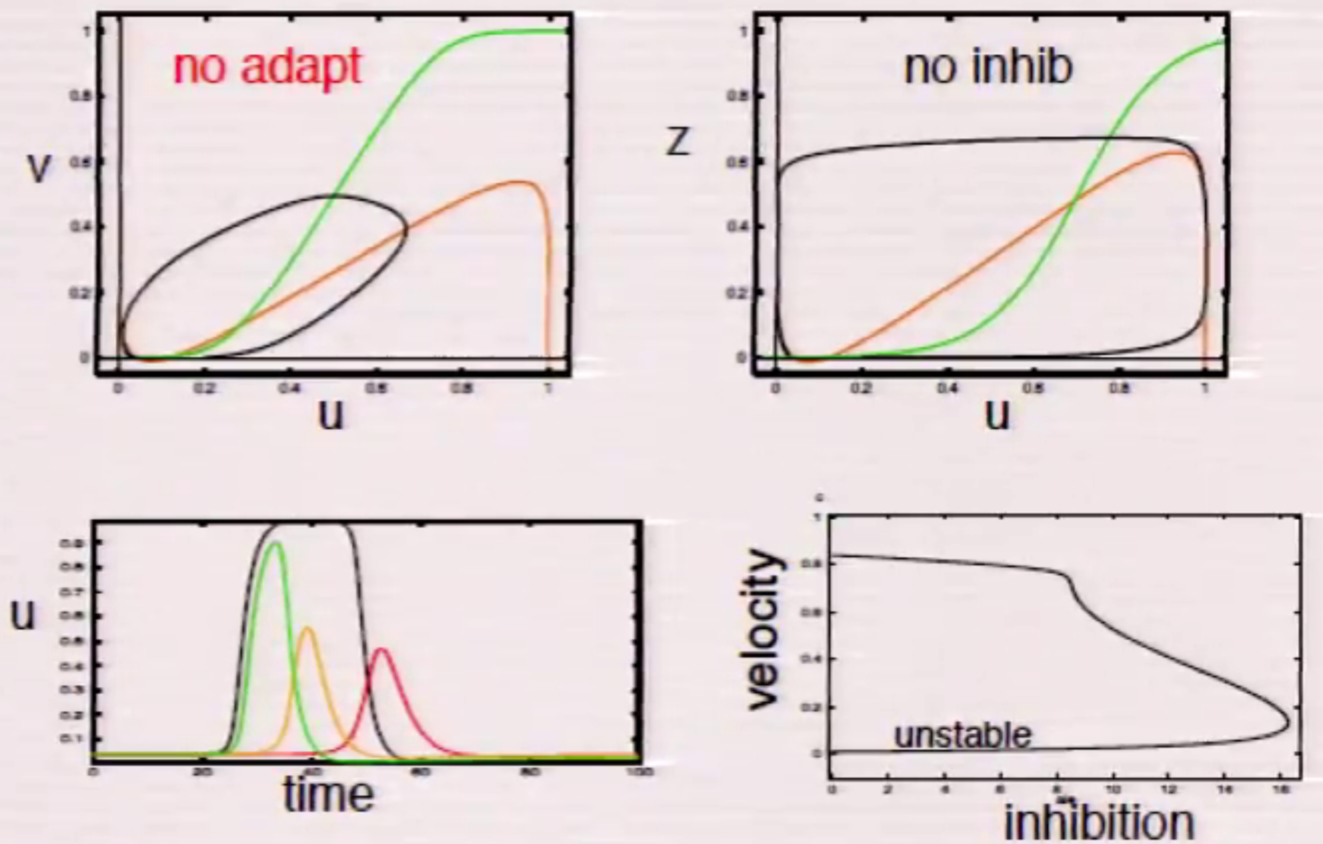
Traveling Pulses

- Fronts are fairly unusual (except see below); what is more common are pulses
- Many experiments going back to the 80's on *disinhibited slice*
  - Golomb-Amitai model conductance based adds *adaptation* that brings activity back down
  - Pinto-Ermentrout model constructs pulses using existence of fronts and singular perturbation

$$\begin{aligned} V_t &= -V + J_e(x) \star F[V] - Z \\ Z_t &= \epsilon[-Z + \alpha V] \end{aligned}$$

  - Hastings recently has some existence results for nonlinear adaptation
- What about intact inhibition?

ADAPTATION PLUS INHIBITION

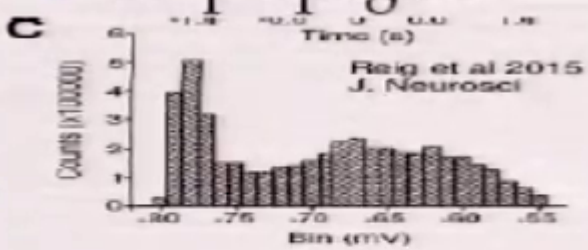


$$\tau_e u' = -u + f_e(\ldots - a_{ez} z)$$
$$\tau_z z' = -z + f(a_{ze} u - \theta_z)$$
$$\tau_i v' = -v + f_i(a_{ie} u - \ldots)$$

UP / DOWN STATES

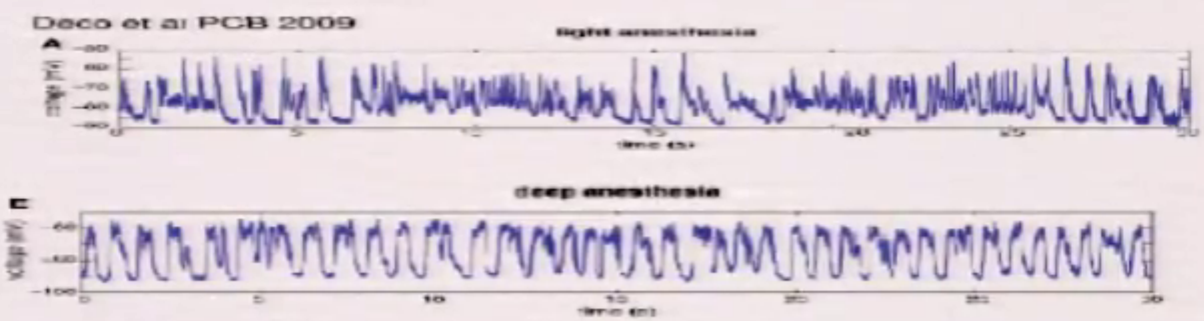
- Switch down to up and vice versa with same stimulus
- UP propagates

- Strong stimuli only transiently UP
- Larger variance in UP

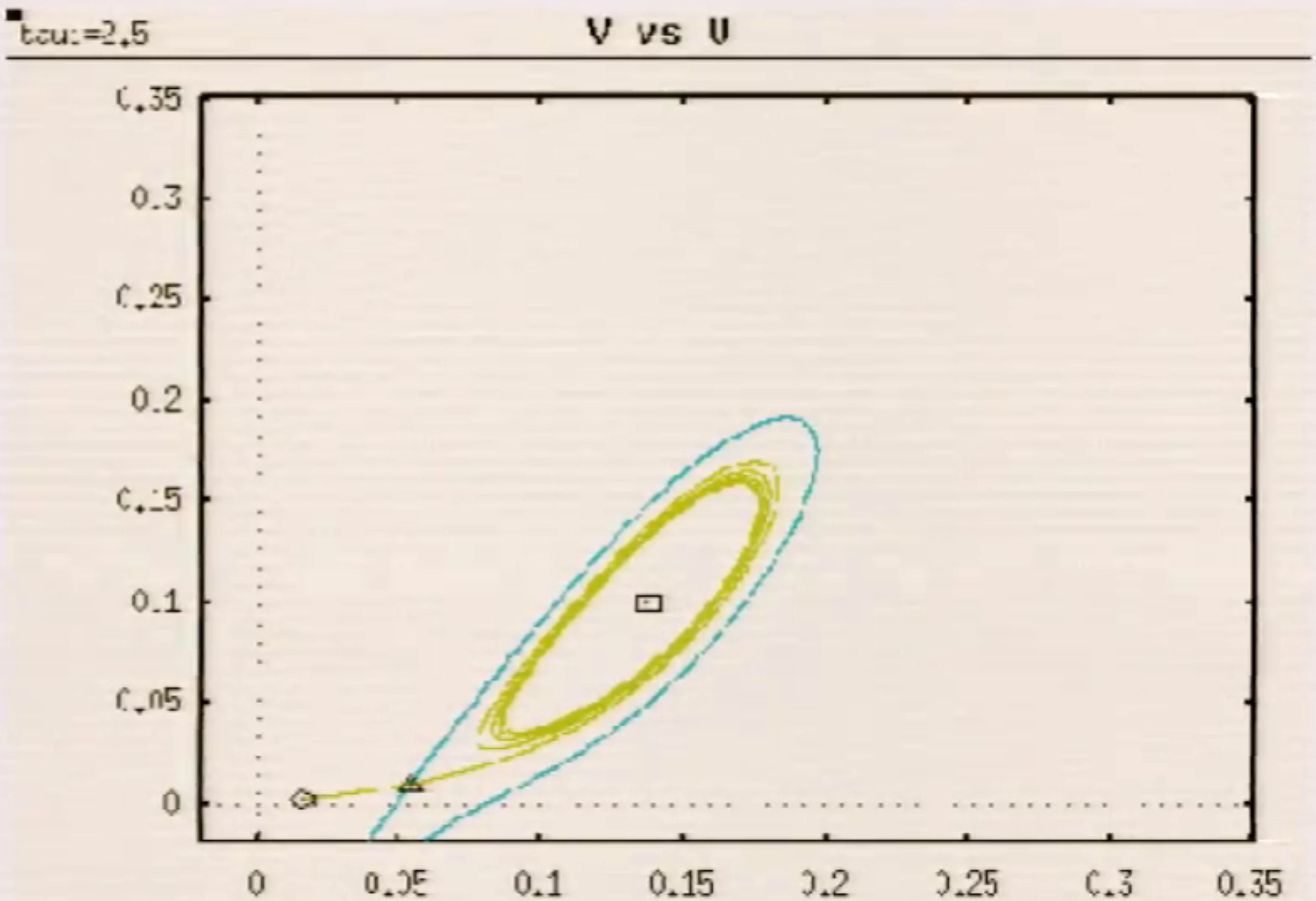


Variance UP > Variance DN

Less Rhythmic during light anesthesia



SUGGESTING A PHASE-PLANE

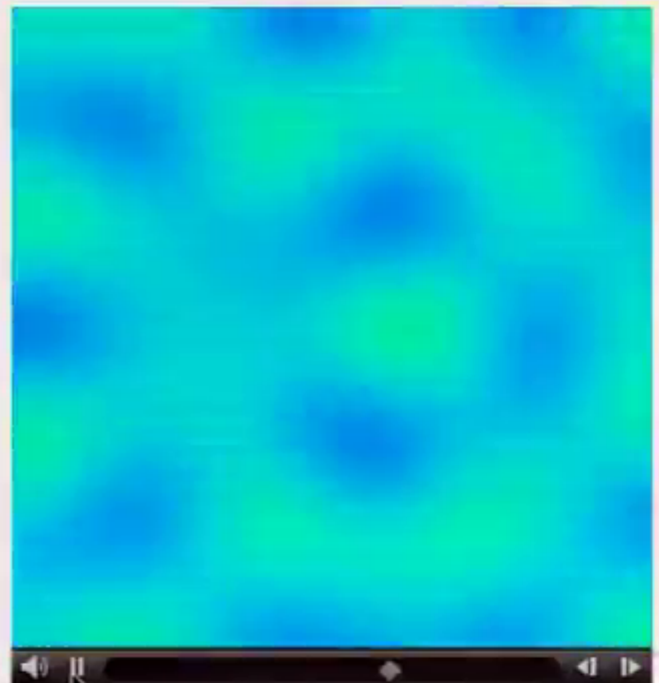


ADVERTISEMENT

- For small τ_i can get waves from DOWN to UP
- As τ_i increases, lose the UP attractor and revert to excitable
- When $f_{e,i}$ are step functions, very cool Filippov system with sliding, grazing, etc
- See MS 87 tomorrow!

Patterns with no Mexican hat

- Aghajanian has shown that 5HT (related to effects of LSD) puts neurons to up state
- If the up state is near a homoclinic LC, then can detabilize homogenize state *even when spread of E exceeds spread of I*

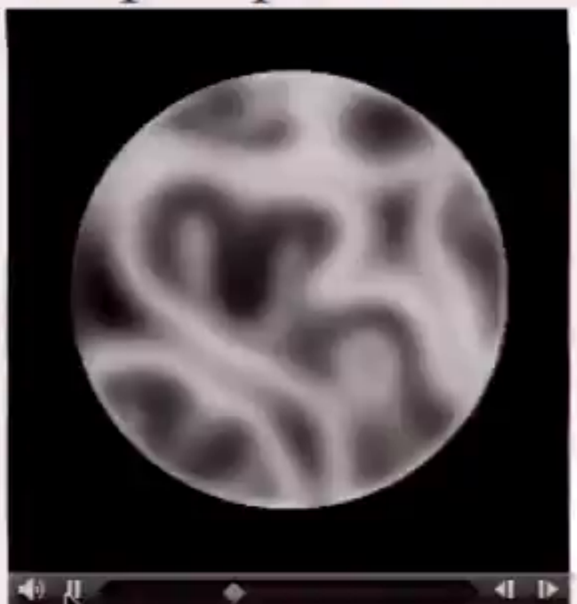


Rotating/spiral waves

- The local dynamics is either excitable or oscillatory
- Such as in the previous model for traveling waves in one-dimension
- With the right heterogeneities or initial data, spatial coupling can lead to rotating waves

Rotating waves

Class I (SNIC) excitability gives complex patterns

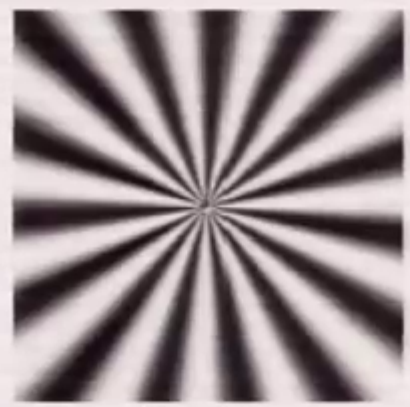


Class II (Hopf) excitability gives nice rotating waves

Ongoing activity plus stimuli equals fun

- Visual illusions can be regarded as exploiting the internal dynamics of the cortex (e.g. priors, on going activity, etc)
- Certain classes of spatially or temporally periodic stimuli can lead to complex percepts
- In pathological cases, can lead to seizures, migraines, etc (think Pokemon)
- Using the simple EI neural fields, we can provide a possible explanation

FLICKER PHOSPHENES



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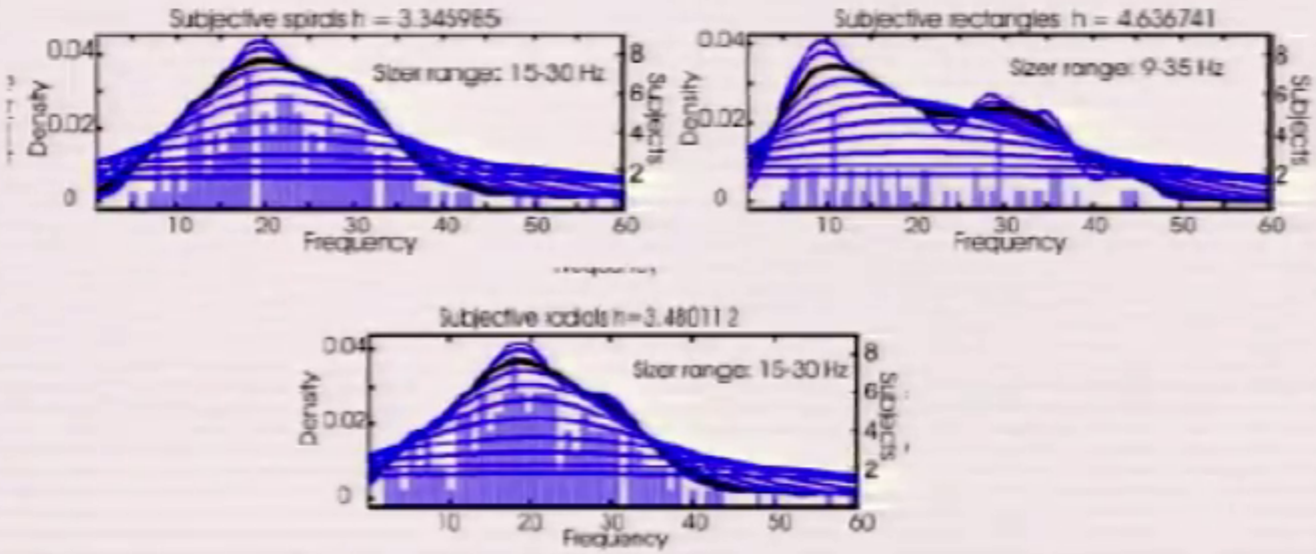
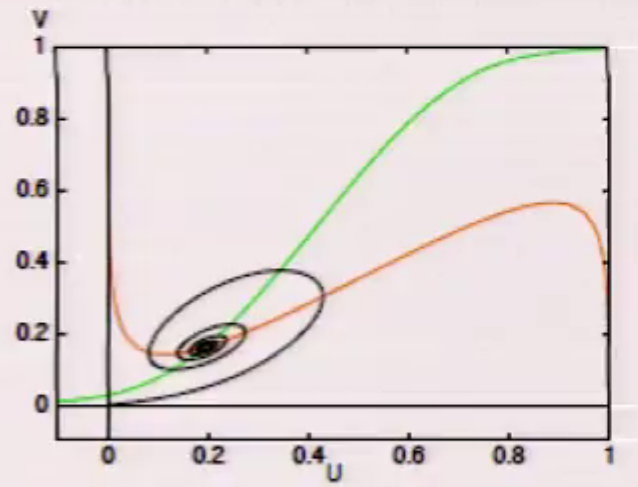


C. Becker, M.A. Elliott / Consciousness and Cognition 15 (2006) 175–196

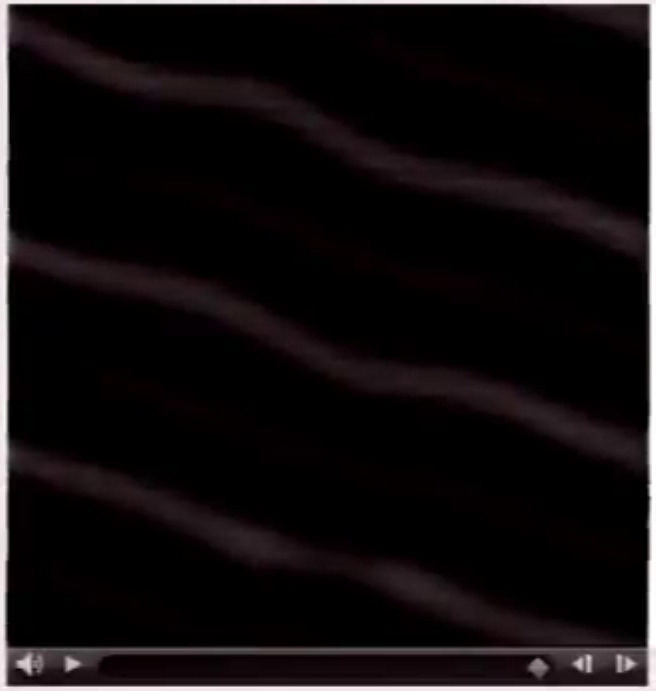
- Most prominent at 5-25 Hz uniform flicker (best binocularly)
- At low frequencies, tend to get checks/hexagons
- At high frequencies stripes

FLICKER PHOSPHENES



- Basic idea is to have a stable midle branch equilibrium point that has complex eigenvalues
- Oscillation timescale is related to the flicker frequency sensitivity
- Combine with spatial *lateral inhibition*

SIMULATIONS



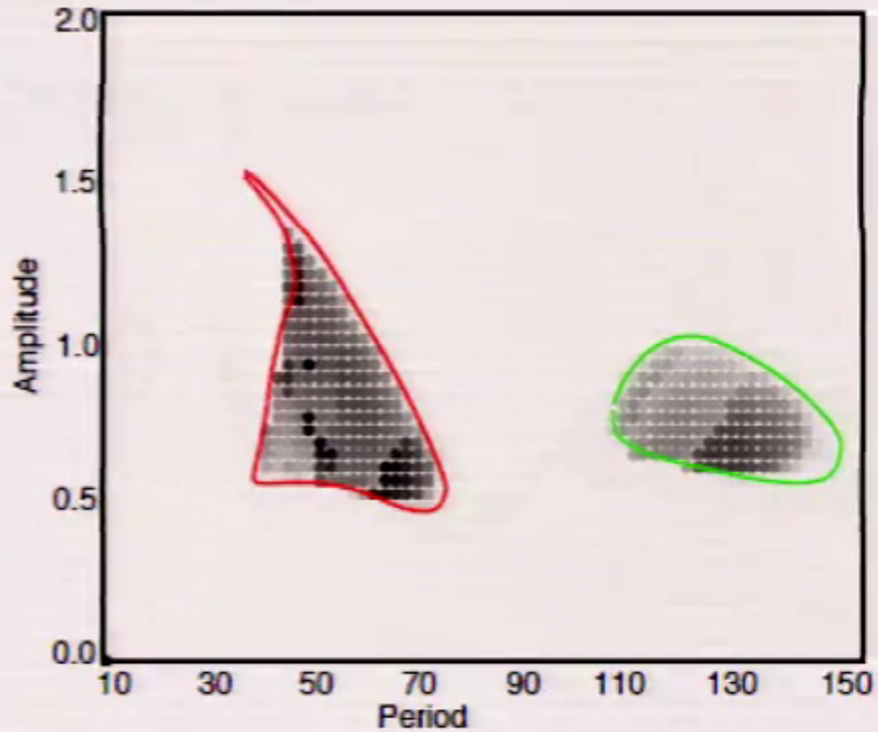
- At 16 Hz get stripes
- Due to period doubling symmetries
- -1 multiplier

- At 8 Hz get hexagons
- Can explain with symmetric bifurcation and Floquet theory
- +1 multiplier

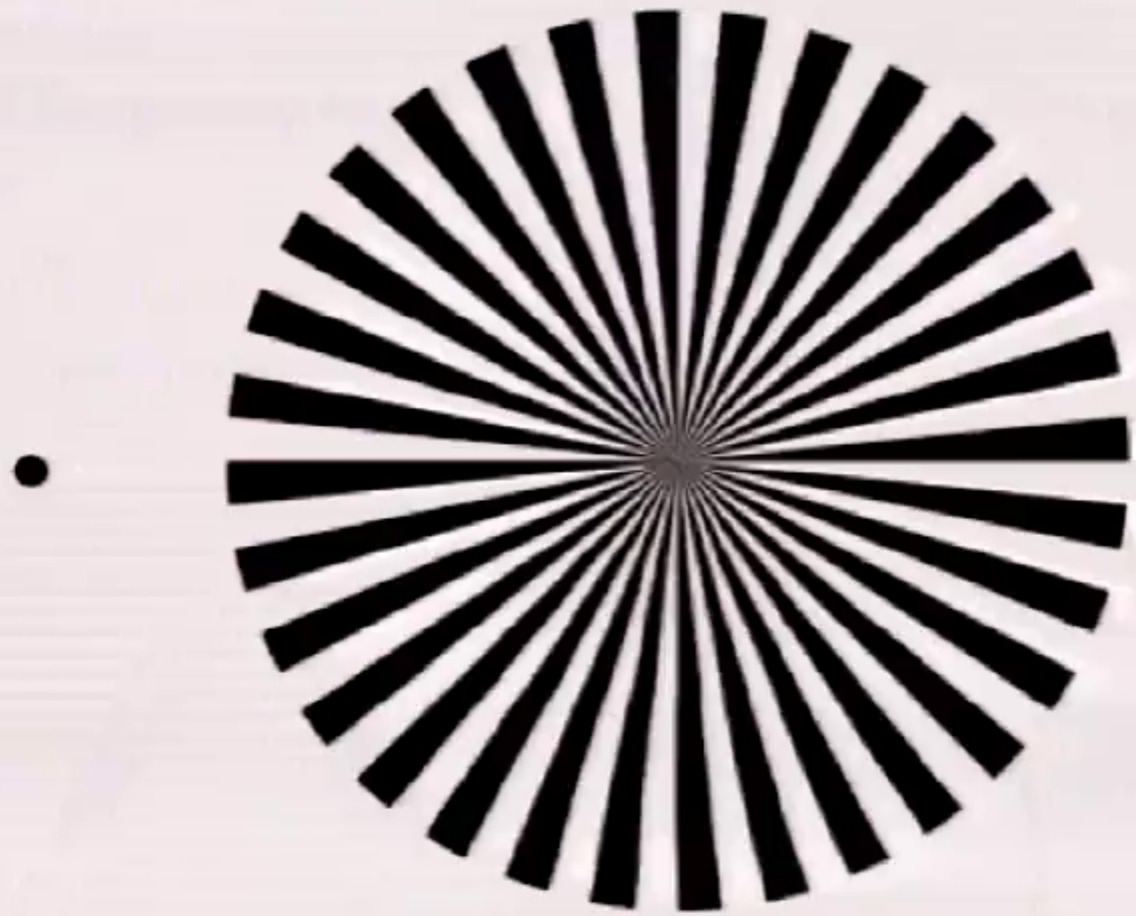
ANALYSIS

- Solve for the spatially uniform oscillation
- Linearize and take the spatial Fourier transform
- Compute Floquet multipliers
- Use this to track the stability

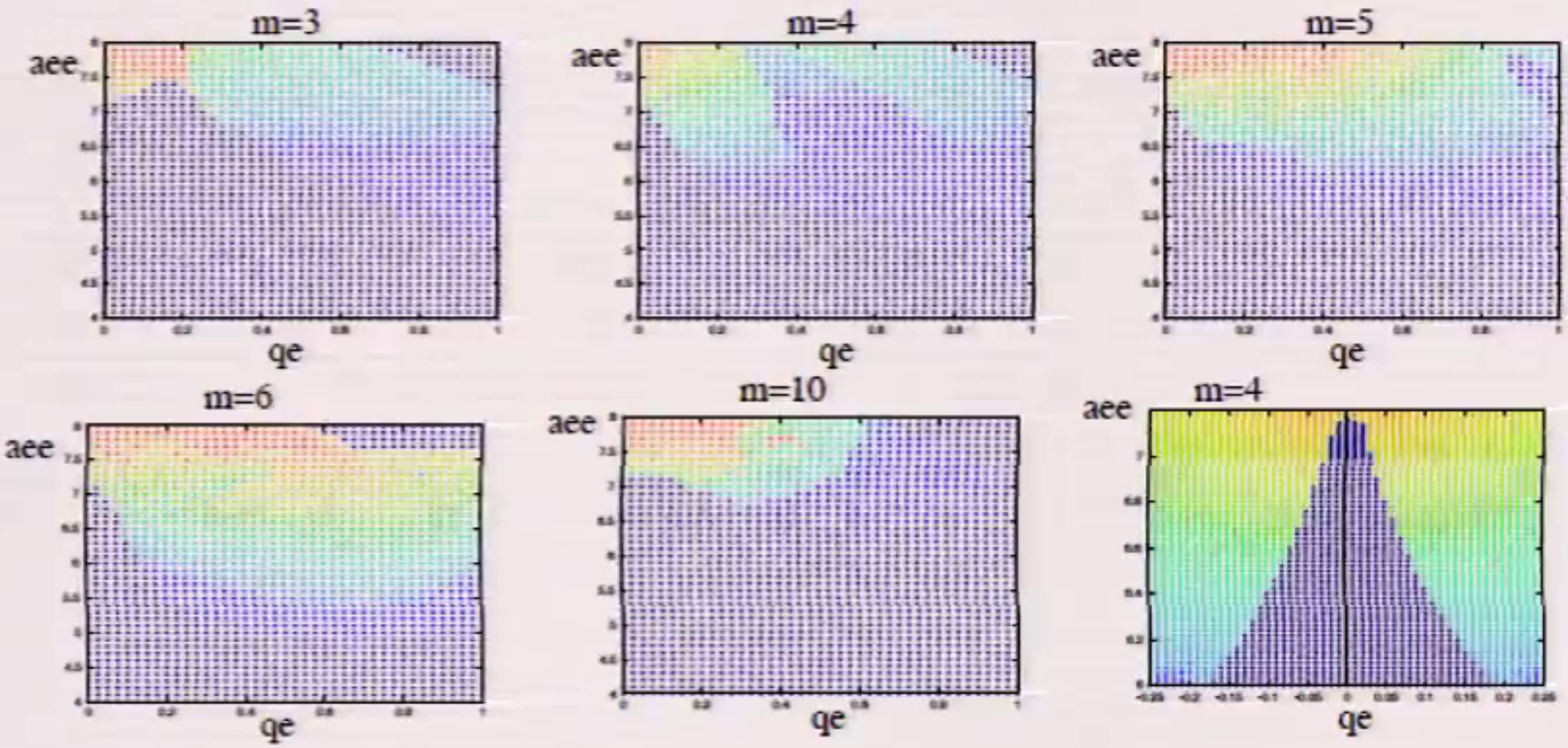
Results



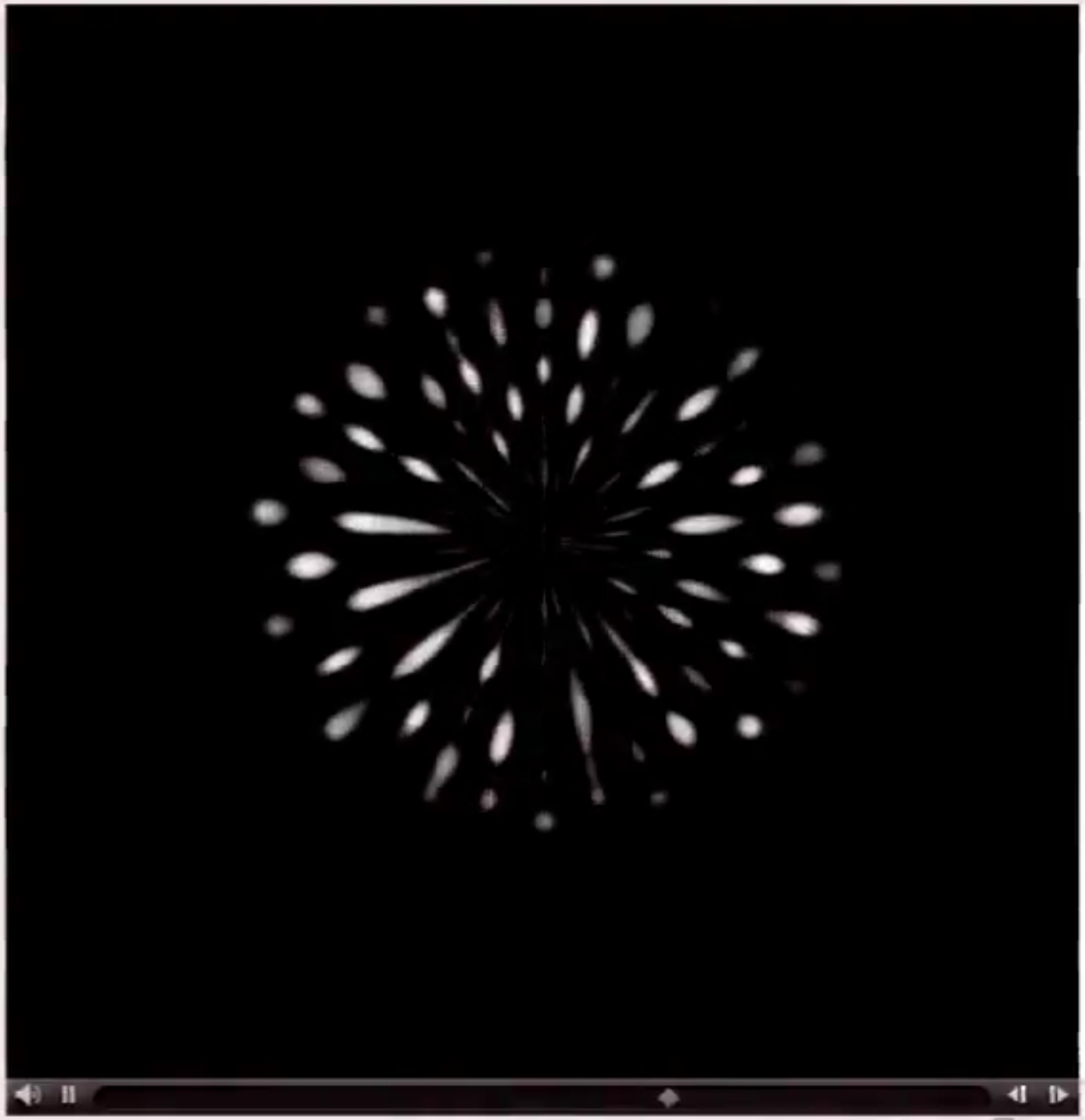
FLICKERING PINWHEEL



SAME MODEL - DIFFERENT STIMULUS



AND THE PINWHEEL



Conclusions

- With the ability of experimentalists to record at high temporal and spatial resolution, we can finally start to model and understand the role of spatio-temporal activity in cortical networks
- There are mathematical challenges related to the nonlocal interactions; stability existence, and for me, good perturbation methods
- Computational challenges related to the nonlocal interactions
  - FFT methods or inverse operator techniques
  - CUDA (GPU) computing - the B&W sims today were all done on a laptop!

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