The Response Dynamics of Neural Oscillator Populations

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Outline

I. The Locus Coeruleus (LC) and a Visual Discrimination Task

II. Mathematical Models for Neurons, including Phase Reduction

III. Predictions for Peri-Stimulus Time Histograms (PSTHs) for Individual Neurons

IV. Extension to Coupled Neurons

V. Conclusions and Work in Progress

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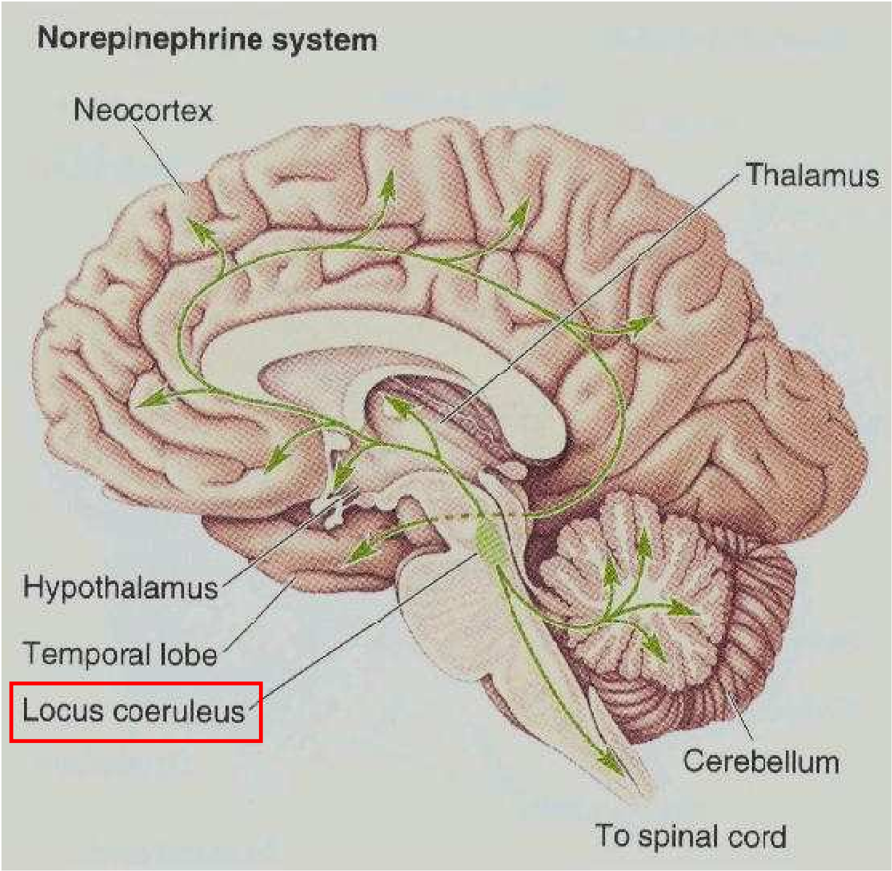
pattern $\sim$ synchronous firing of neurons

nice PDE application

The Locus Coeruleus (LC)



from *Neuroscience: Exploring the Brain* **by M.F. Bear, B.W. Connors, and M.A. Paradiso, 2001**

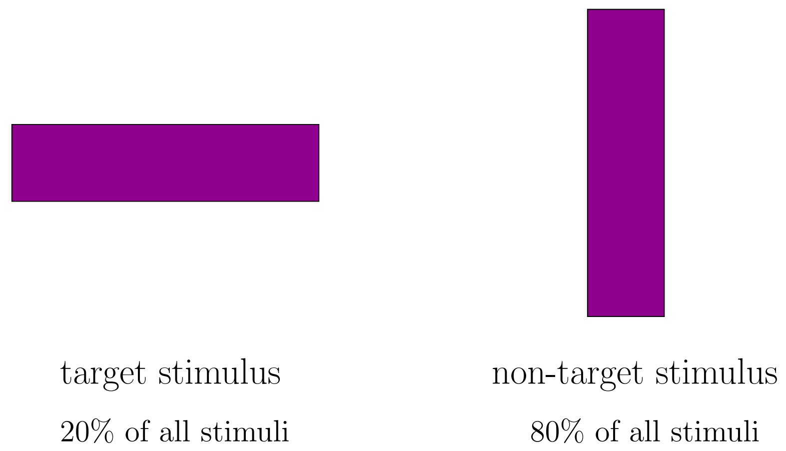
The Locus Coeruleus (LC)

- **The LC is a nucleus in the brain consisting of approximately 15,000 neurons for monkeys (one nucleus in each hemisphere)**
- **Each LC neuron can make more than 250,000 synapses**
- **LC neurons release the neurotransmitter** *norepinephrine*, **which regulates arousal, sleep-wake cycles, memory, learning, stress, ...**

A Visual Discrimination Task

Aston-Jones et al, *J. Neuroscience* **14:4467, 1994**

Monkey presented with a sequence of visual stimuli:

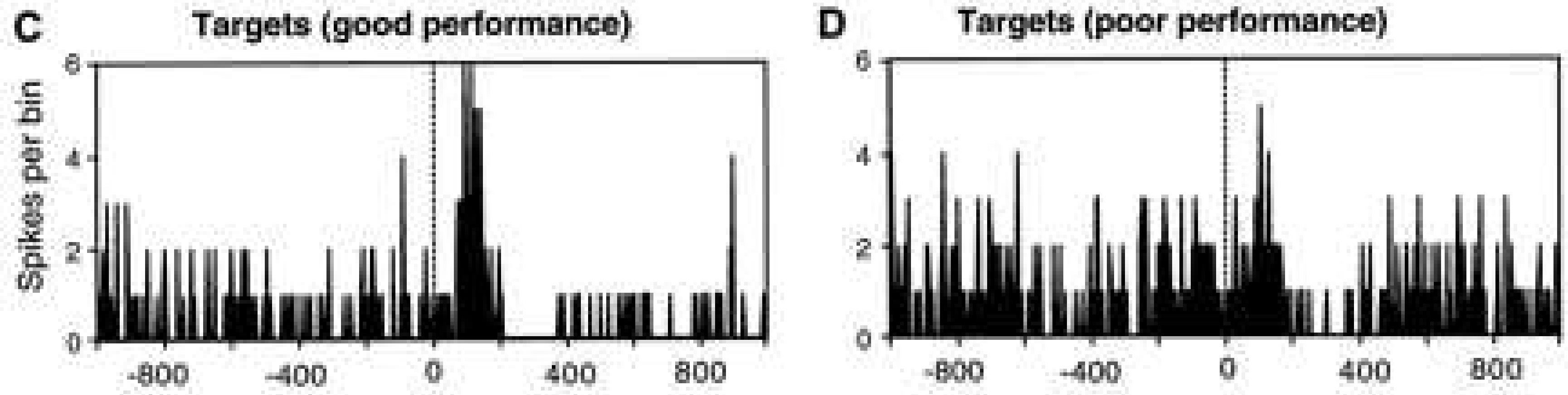


Monkey trained to respond to target stimuli by releasing a lever, measure response of LC neurons

- **correct response: gets juice**
- **incorrect response: time out period**

A Visual Discrimination Task

Phasic State | Tonic State



$t\ (ms)$ | $t\ (ms)$

Peri-Stimulus Time Histograms (PSTHs) for an LC neuron, from Usher et al, *Science* 283:549, 1999

Phasic State

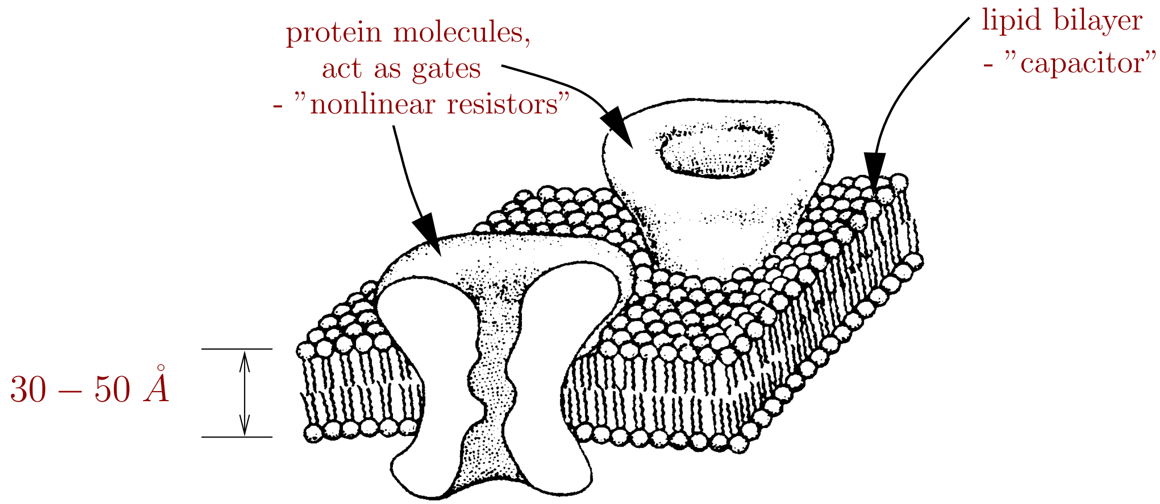
- good performance
- slower (2 spikes/second)
- larger response to stimulus
- more synchrony

Tonic State

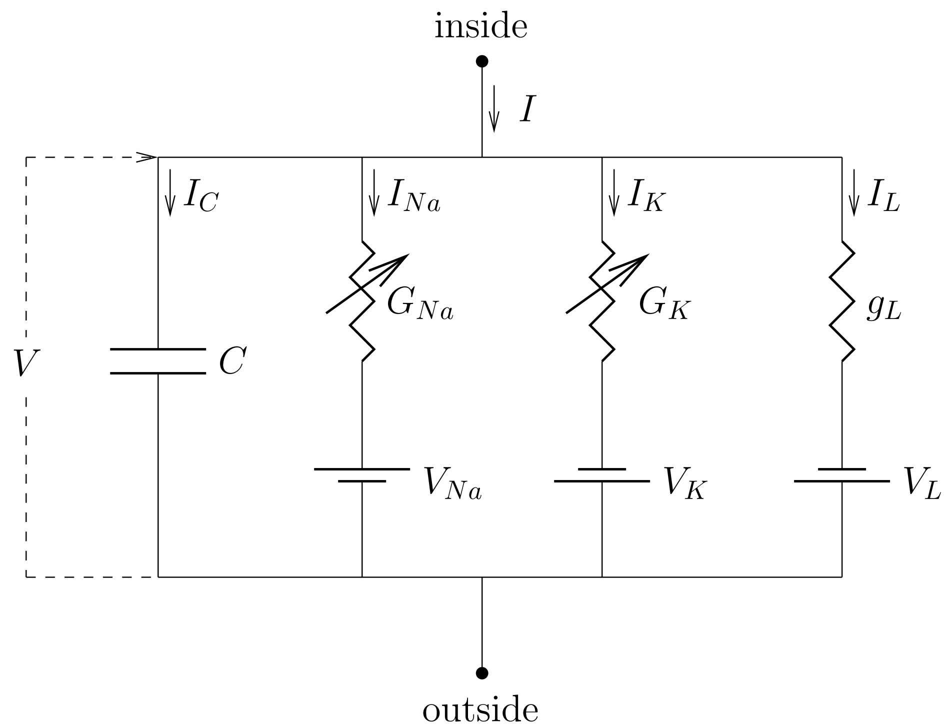
- poor performance
- faster (3 spikes/second)
- smaller response to stimulus
- less synchrony

Neural Modeling: Phase Reduction

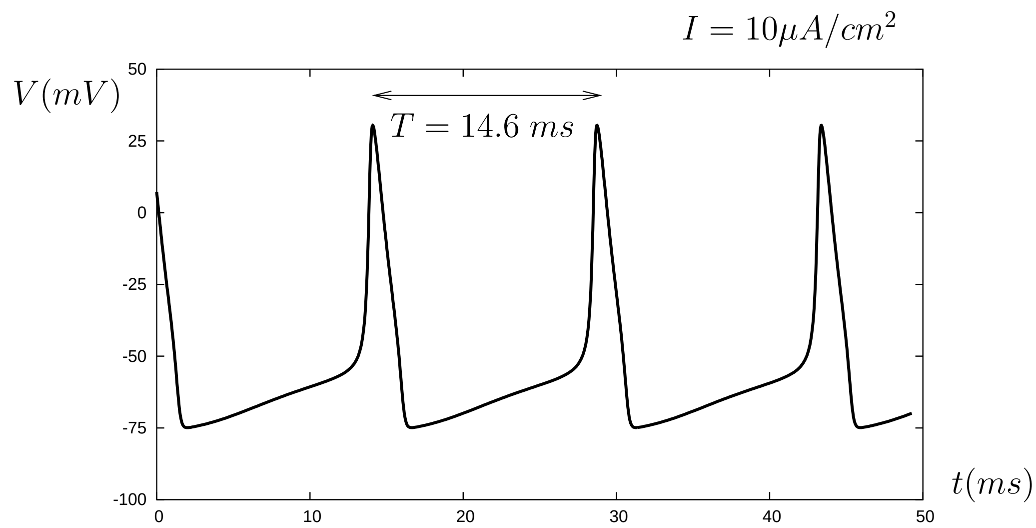
neuronal membrane

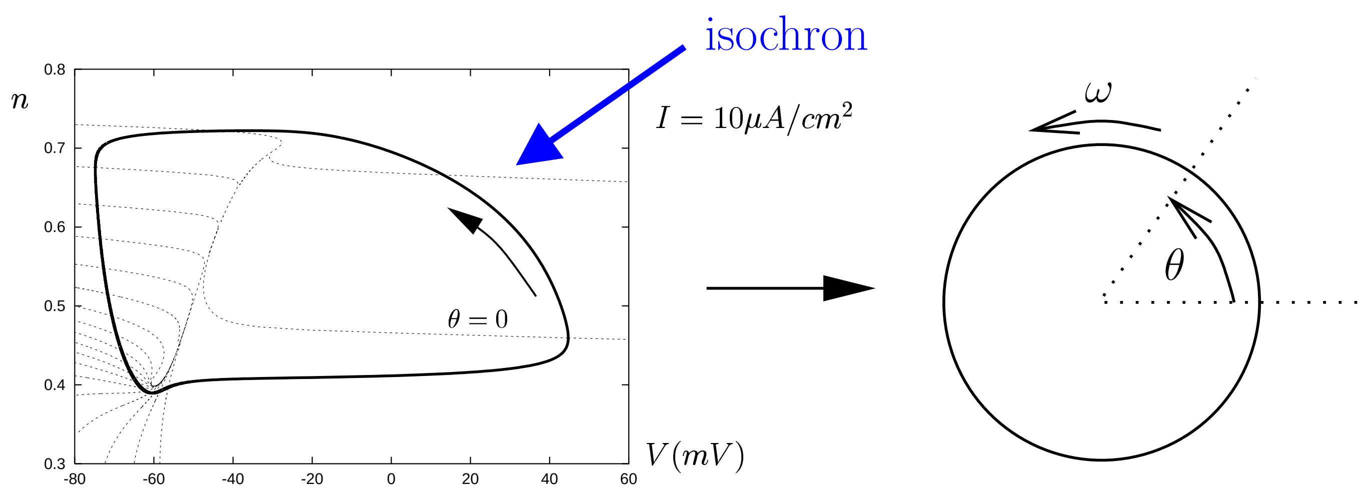


Hodgkin−Huxley model



Neural Modeling: Phase Reduction



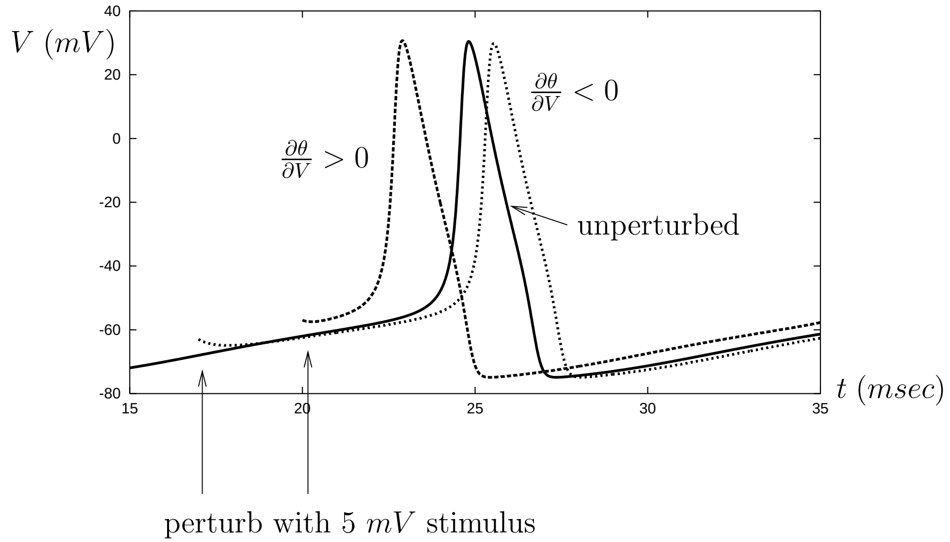


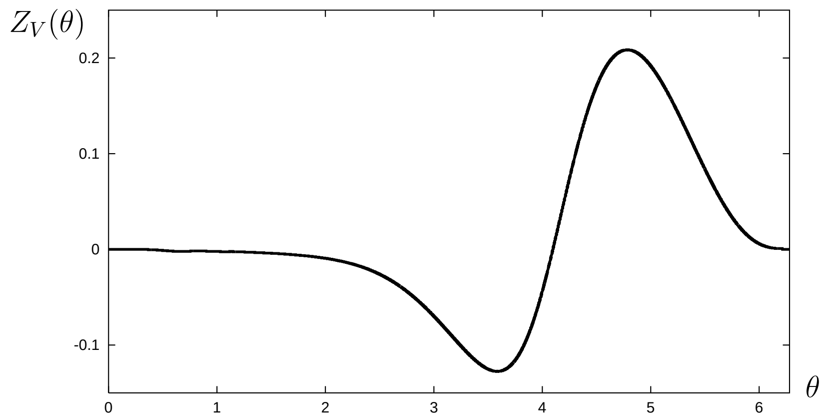
$$\frac{d\theta}{dt} = \omega + Z_V(\theta)I(t)$$

Phase Response Curves (PRCs)

$$Z_V(\theta) = \frac{\partial \theta}{\partial V} = \lim_{\Delta V \to 0} \frac{\Delta \theta}{\Delta V}$$

captures effect of impulsive perturbations in the voltage



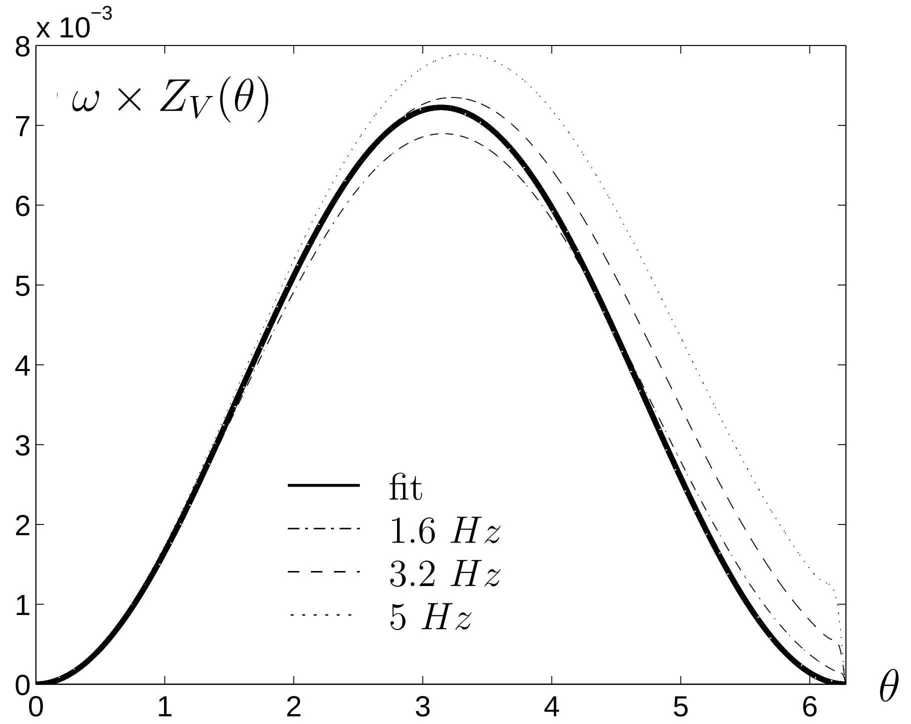


Phase Response Curves (PRCs)

other types of neurons
have different PRCs

Hindmarsh-Rose:

$$Z_V(\theta) = \frac{c}{\omega}(1 - \cos\theta)$$



- **Form of PRC can be understood in terms of what bifurcation gives rise to periodic firing**

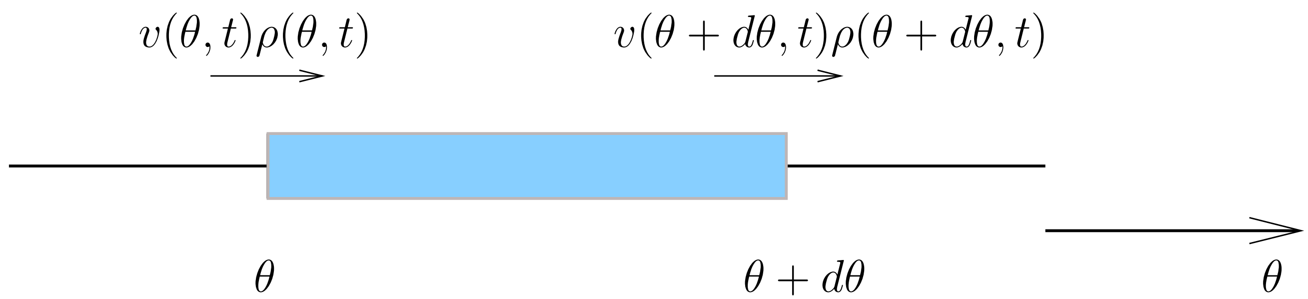
E. Brown, JM, and P. Holmes, to appear *Neural Computation*

Show movies!

Predictions for PSTHs

$$\frac{d\theta}{dt} = \omega + Z_V(\theta) I(t) \equiv v(\theta, t)$$

$\rho(\theta, t)d\theta \equiv$ **prob. neuron has phase in** $[\theta, \theta + d\theta)$ **at time** t



$$\underbrace{\frac{\partial}{\partial t}[\rho(\theta, t)d\theta]}_{\text{rate of change of probability}} = \underbrace{v(\theta, t)\rho(\theta, t)}_{\text{flux in}} - \underbrace{v(\theta + d\theta, t)\rho(\theta + d\theta, t)}_{\text{flux out}}$$

$$\Rightarrow \quad \boxed{\frac{\partial \rho}{\partial t} = -\frac{\partial}{\partial \theta}[v\rho] = -\frac{\partial}{\partial \theta}[(\omega + Z_V(\theta)I(t))\rho]}$$

Predictions for PSTHs

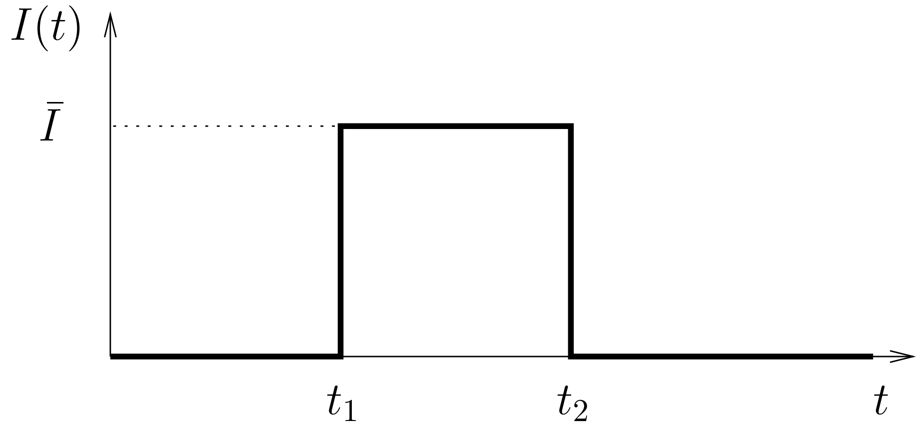
ICS: stimuli come at random times

$$\Rightarrow \rho(\theta, 0) = \frac{1}{2\pi}$$

$$\begin{aligned} \text{Note} : FL(t) &\equiv v(0,t)\rho(0,t) \\ &= \text{flux at spike point } \theta = \theta_s = 0 \\ &= \text{probability/unit time that neuron fires} \end{aligned}$$

$FL(t)$ **gives prediction for suitably normalized PSTH**

Solution for Step Function Stimulus

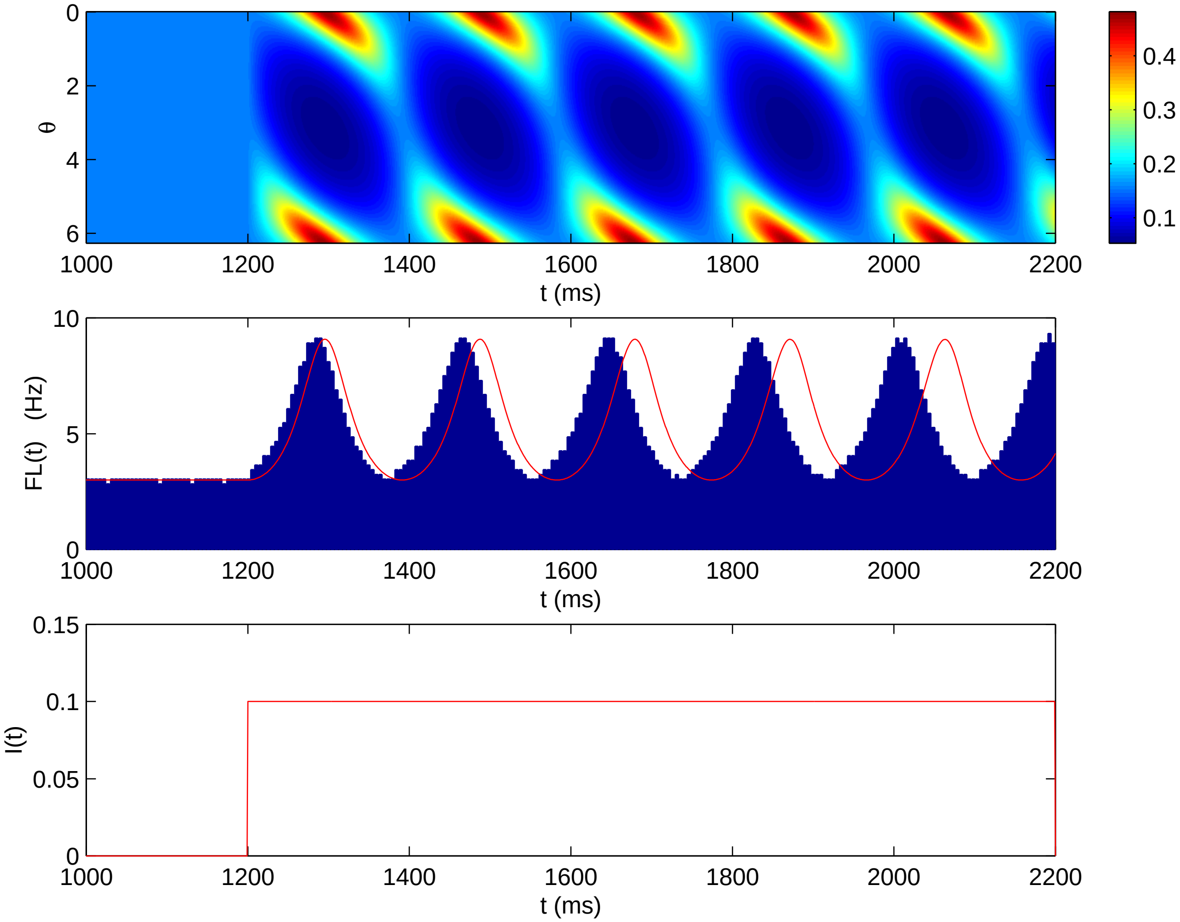


Can solve for $\rho(\theta, t)$ using method of characteristics.

exact formulas → detailed understanding

Solution for Step Function Stimulus

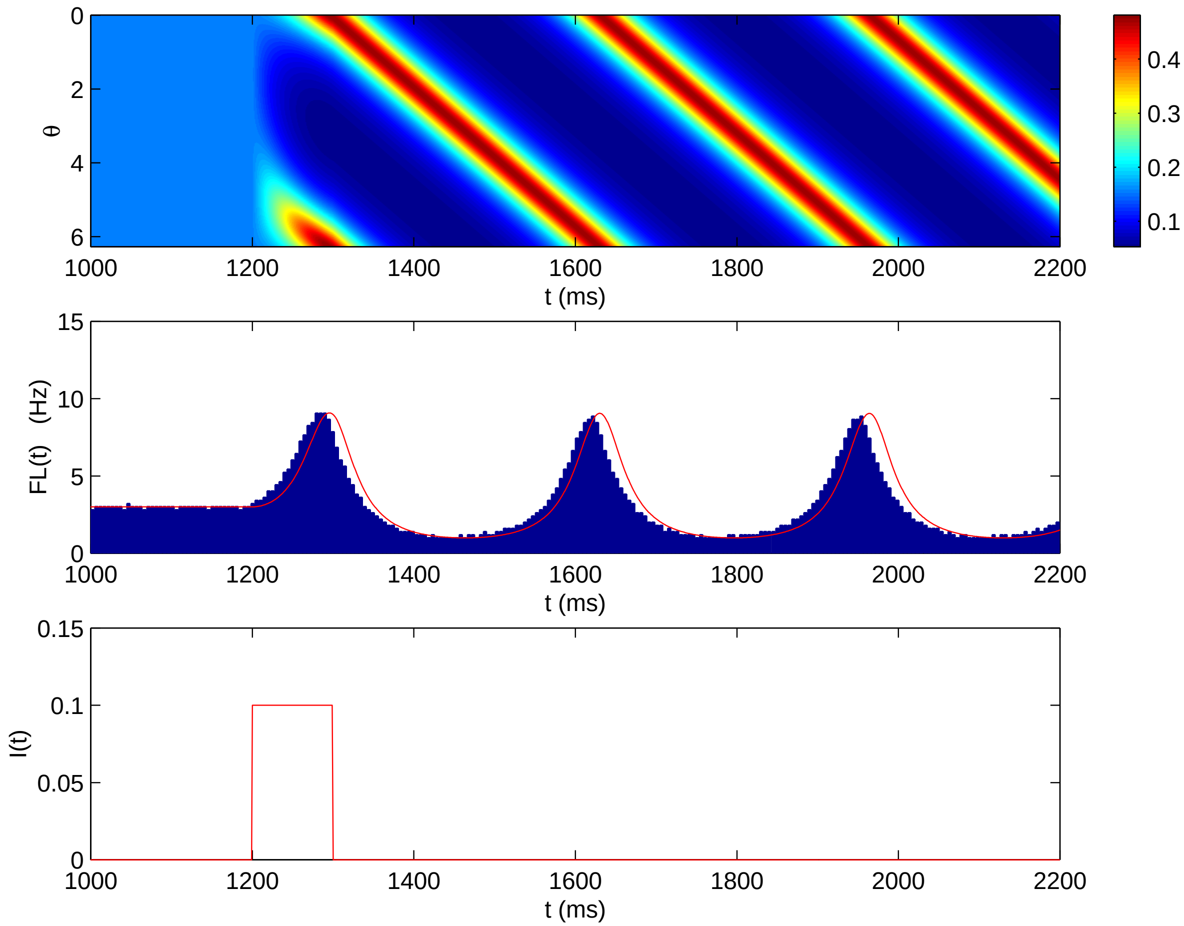
While stimulus is on, $\rho(\theta, t)$ is periodic with period $P = \int_0^{2\pi} \frac{d\theta}{\omega + \bar{I} Z_V(\theta)}$



$t_1 = 1200, \quad t_2 = \infty, \quad \bar{I} = 0.1, \quad \sigma = 0, \quad f = 3Hz$

Solution for Step Function Stimulus

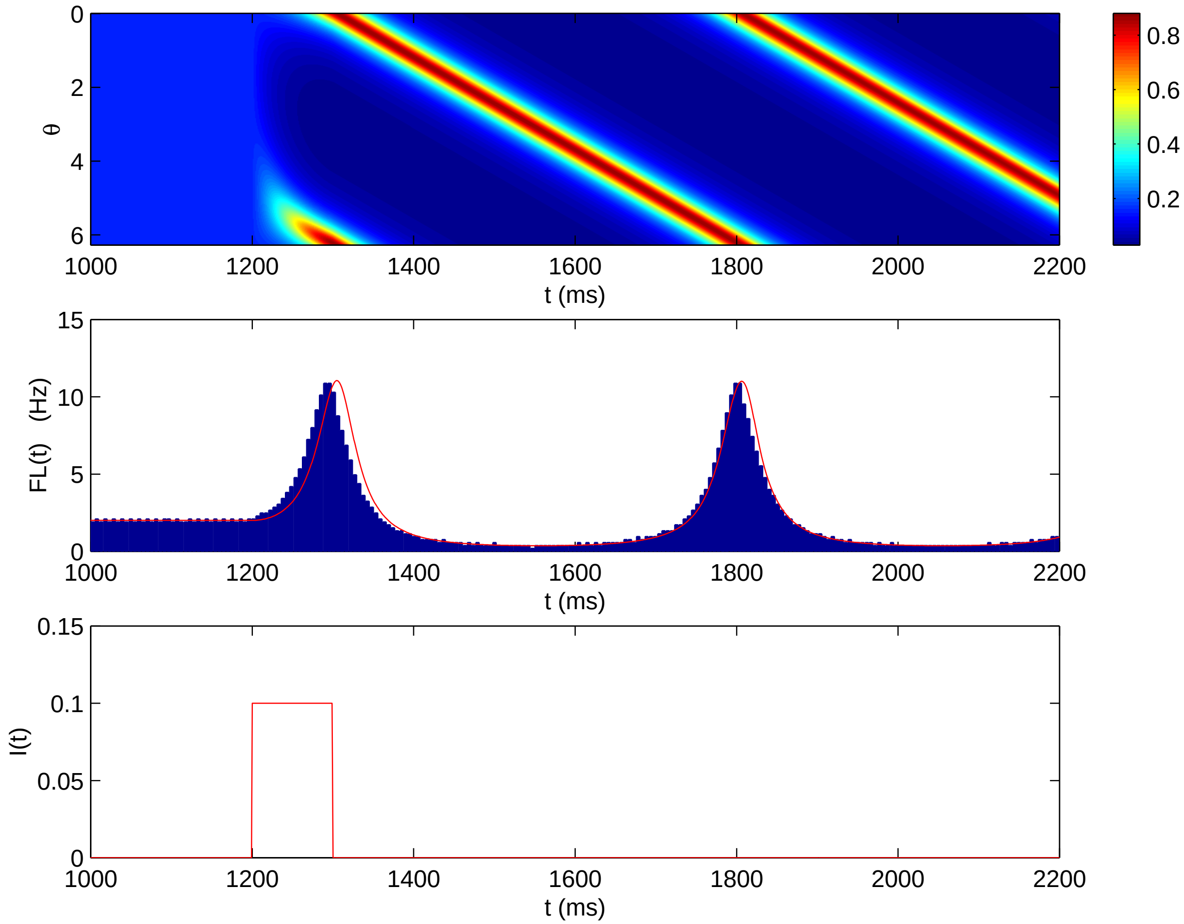
For $t > t_2$, $\rho(\theta, t)$ is traveling wave rotating with frequency ω, determined by $\rho(\theta, t_2)$



$t_1 = 1200, \quad t_2 = 1300, \quad \bar{I} = 0.1, \quad \sigma = 0, \quad f = 3Hz$

Solution for Step Function Stimulus

The response is larger for neurons with lower baseline firing frequencies.



$t_1 = 1200, \quad t_2 = 1300, \quad \bar{I} = 0.1, \quad \sigma = 0, \quad f = 2Hz$

Solution for Step Function Stimulus

The response is larger for neurons with lower baseline firing frequencies.

$$\textbf{Can show that } FL_{peak} - FL_{base} \sim \frac{1}{\omega}$$

Effect of Noisy Current

Suppose that in addition to the "deterministic" $I(t)$, the input current also contains a noisy component:

$$I(t) + \sigma\eta(t)$$

where $\eta(t)$ is a real Gaussian white noise random process with

$$\langle\eta(t)\rangle = 0, \qquad \langle\eta(t)\eta(t')\rangle = \delta(t - t').$$

Here σ represents the r.m.s. noise strength.

Effect of Noisy Current

We then obtain the following stochastic differential equation:

$$\frac{d\theta}{dt} = \underbrace{\omega + Z_V(\theta)I(t)}_{v(\theta,t)} + \sigma Z_V(\theta)\eta(t)$$

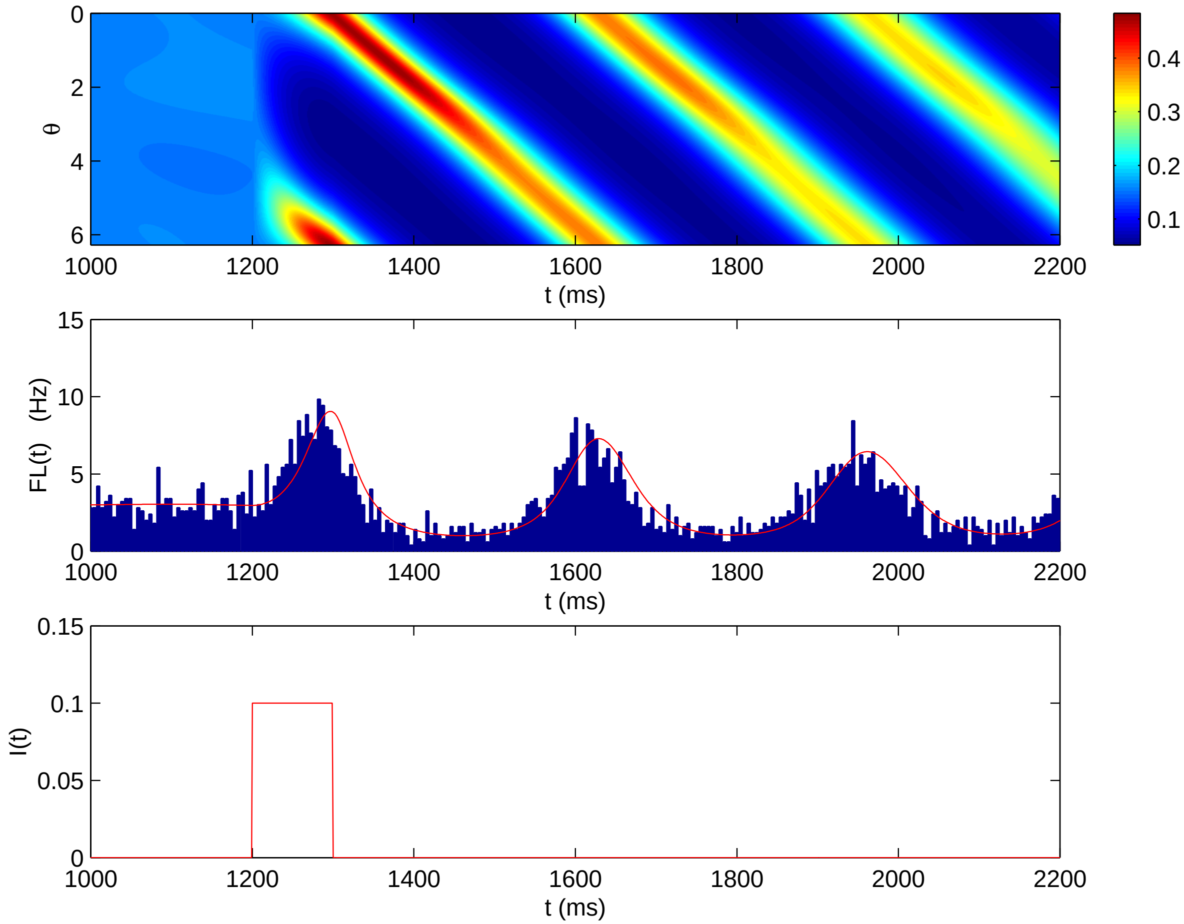
In the probabilistic formulation, we obtain the Fokker-Planck equation

$$\frac{\partial\rho(\theta,t)}{\partial t} = -\frac{\partial}{\partial\theta}[v(\theta,t)\rho(\theta,t)] + \frac{\sigma^2}{2}\frac{\partial^2[Z_V^2(\theta)\rho(\theta,t)]}{\partial\theta^2}$$

This PDE is solved numerically using the Crank-Nicholson method.

Effect of Noisy Current

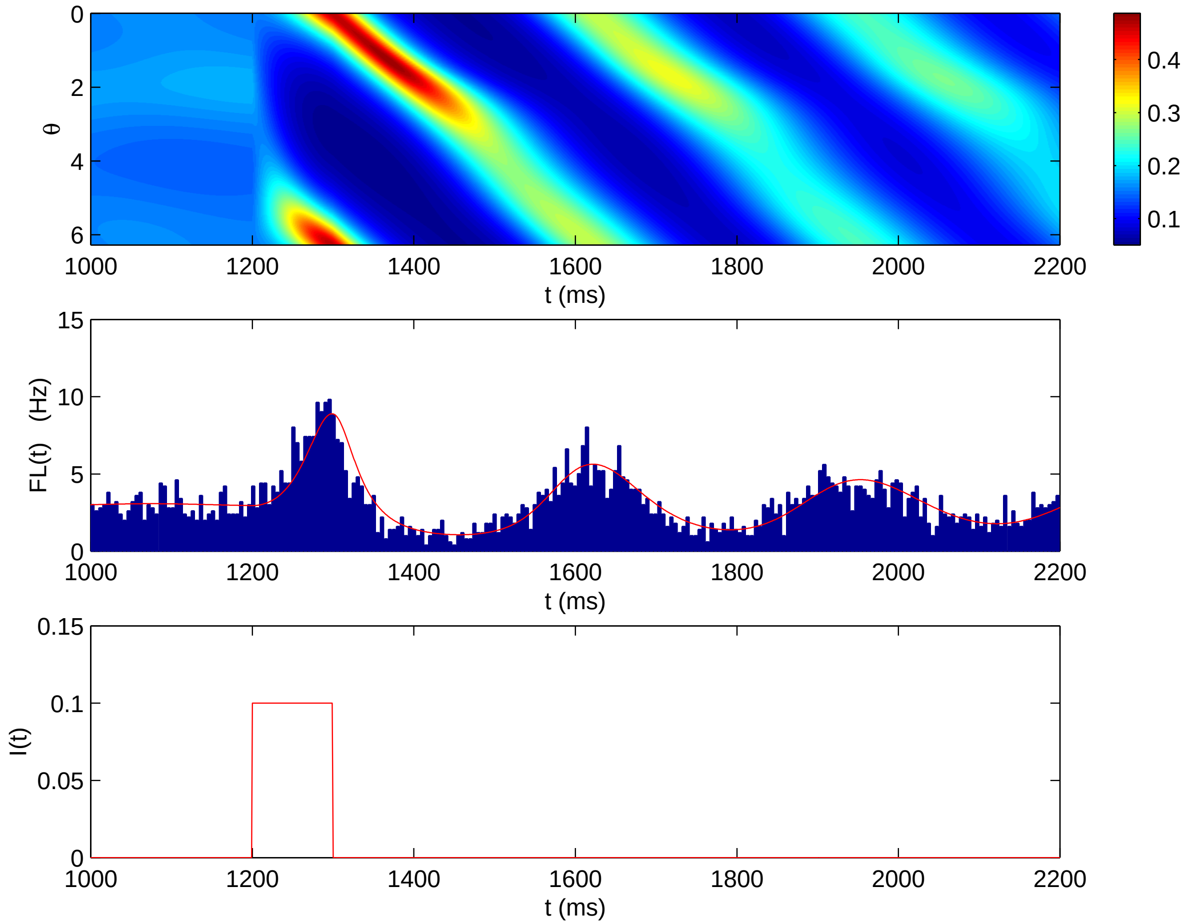
Noise leads to a decay in the ringing in the PSTHs.



$t_1 = 1200, \qquad t_2 = 1300, \qquad \bar{I} = 0.1, \qquad \sigma = 0.1, \qquad f = 3Hz$

Effect of Noisy Current

Larger σ gives quicker decay in the ringing.



$t_1 = 1200,\quad t_2 = 1300,\quad \bar{I} = 0.1,\quad \sigma = 0.2,\quad f = 3Hz$

Effect of Noisy Current

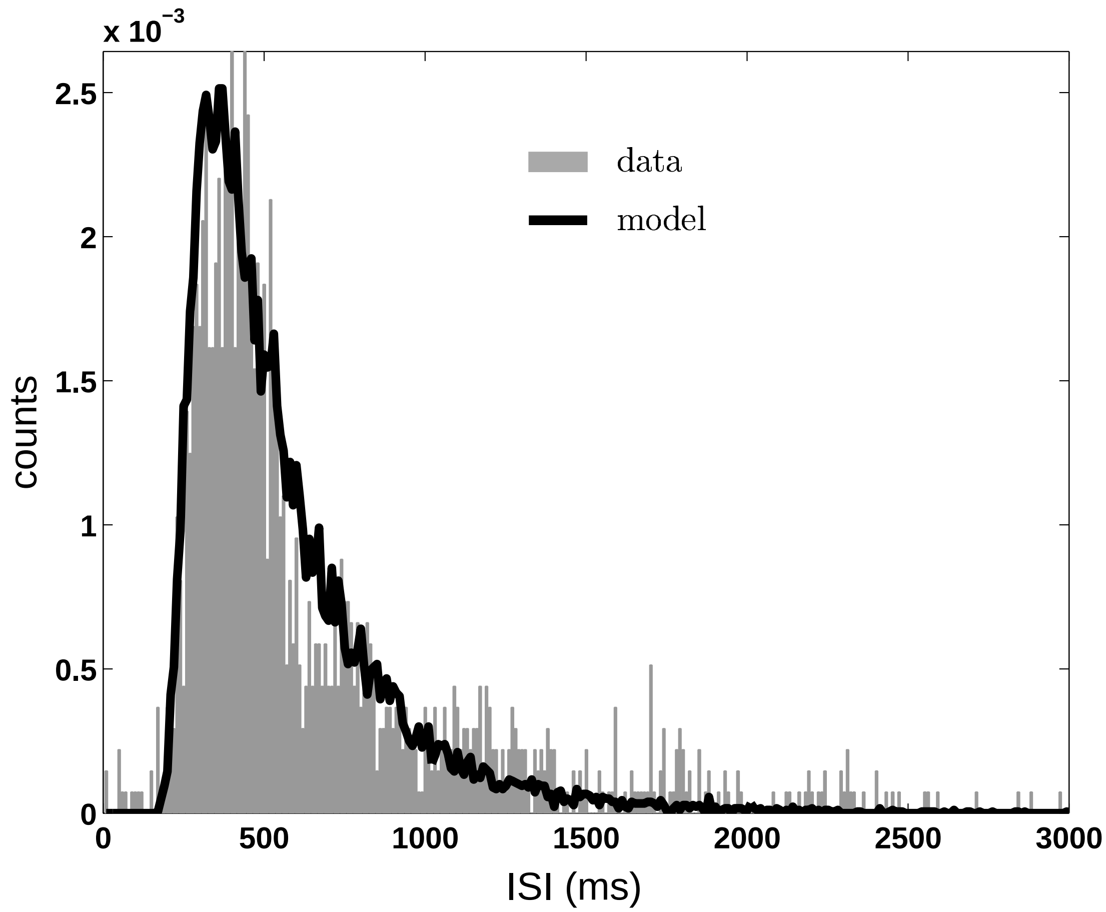
Larger σ gives quicker decay in the ringing.

Note: Can show that

$$\textbf{Flux Envelope} \sim \exp\left(-\frac{\sigma^2 \hat{Z_V}^2 (t-t_2)}{2}\right), \qquad t > t_2$$

$$\hat{Z_V} = \frac{1}{2\pi}\int_0^{2\pi} [Z_V(\theta)]^2 d\theta$$

Noise and Freq Dist Important



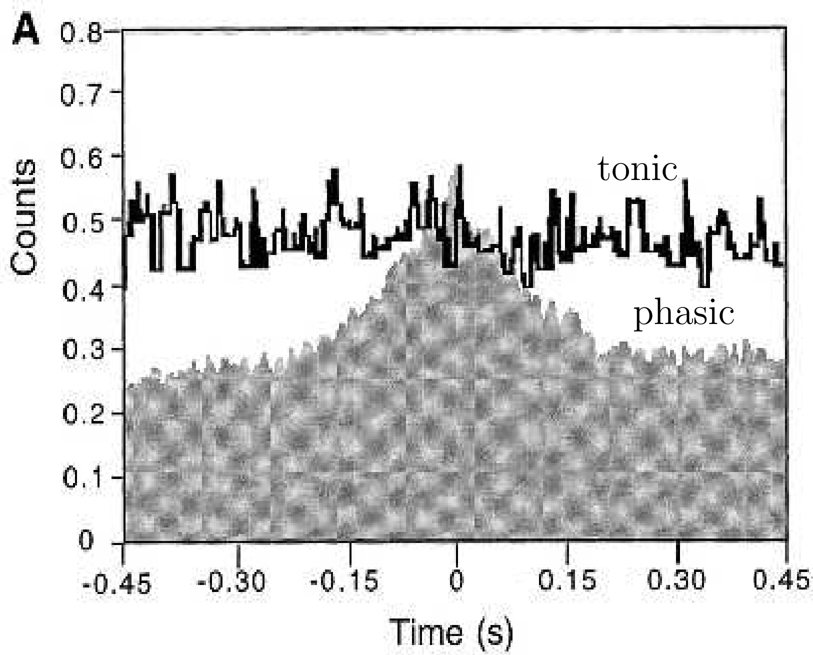
Noise: $\sigma = 0.45$

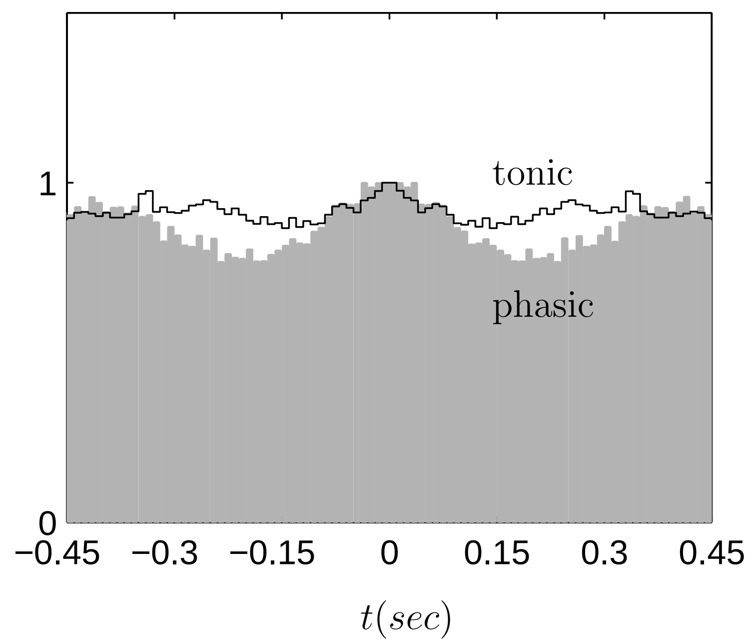
Frequency Distribution:

phasic 2 ± 0.3 **Hz**
tonic 3 ± 0.45 **Hz**

Weak Coupling Captures...

...Cross Correlograms

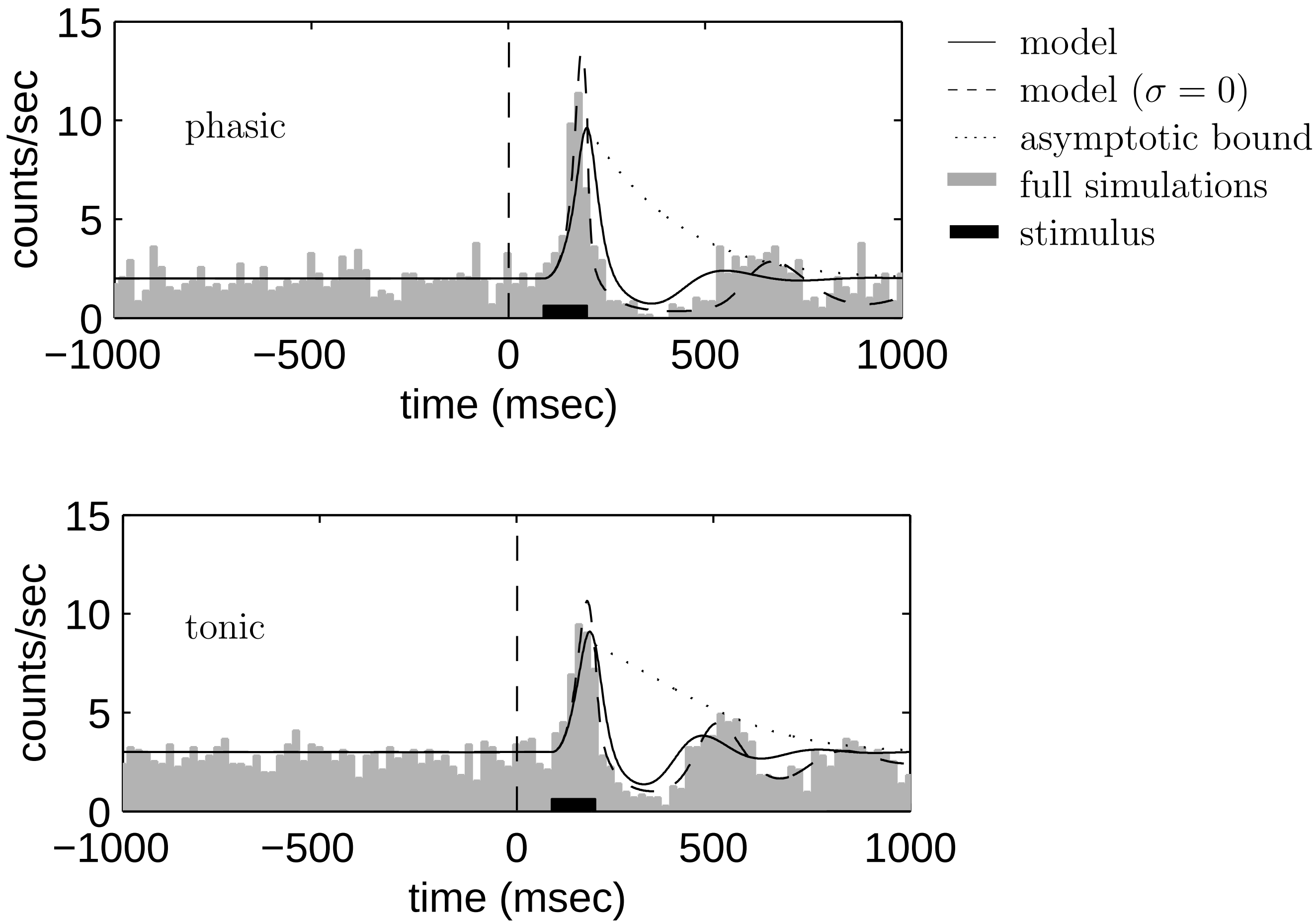




$\alpha_e = 0.05$
$\alpha_s = 0.01$
$\sigma = 0.45$
$N = 100$

Weak Coupling Captures...

...and Response to Stimuli



Conclusions

I. The LC and a Visual Discrimination Task

II. Model LC neurons as Hindmarsh-Rose neurons, reduce to phase model in presence of external stimulus

III. Predictions for PSTHs: Fokker-Planck Equation

- lower baseline activity $\Rightarrow$ larger response
- noise $\Rightarrow$ decay of ringing

IV. To explain experimental results: noise, frequency distribution, weak coupling

V. Other Applications

- matching experimental data for Eriksen task
- similar analysis for other neuron types

Collaborators

- **Eric Brown, graduate student, Princeton University**
- **Phil Holmes, professor, Princeton University**
- **Ed Clayton, postdoc, University of Pennsylvania**
- **Janusz Rajkowski, staff scientist, University of Pennsylvania**
- **Gary Aston-Jones, professor, University of Pennsylvania**
- **Jonathan Cohen, professor, Princeton University**

E. Brown, JM, and P. Holmes, to appear *Neural Computation*.

E. Brown, JM, P. Holmes, E. Clayton, J. Rajkowski, G. Aston-Jones, submitted to *Journal of Computational Neuroscience*

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Similar Analysis for Other Neuron Types

- **SNIPER bifurcation** **(HR)**
- **saddle-node bifurcation of periodic orbits** **(HH)**
- **supercritical Hopf bifurcation** **(FN)**
- **homoclinic bifurcation** **(ML)**
- **integrate-and-fire neurons**

$$\text{different bifurcation} \rightarrow \text{different PRC}$$
$$\rightarrow \text{different response}$$

Eriksen Task

Stimulus	Response
>>>>>	R
<<<<<	L
>><>>	L
<<><<	R