Controlling Neurons

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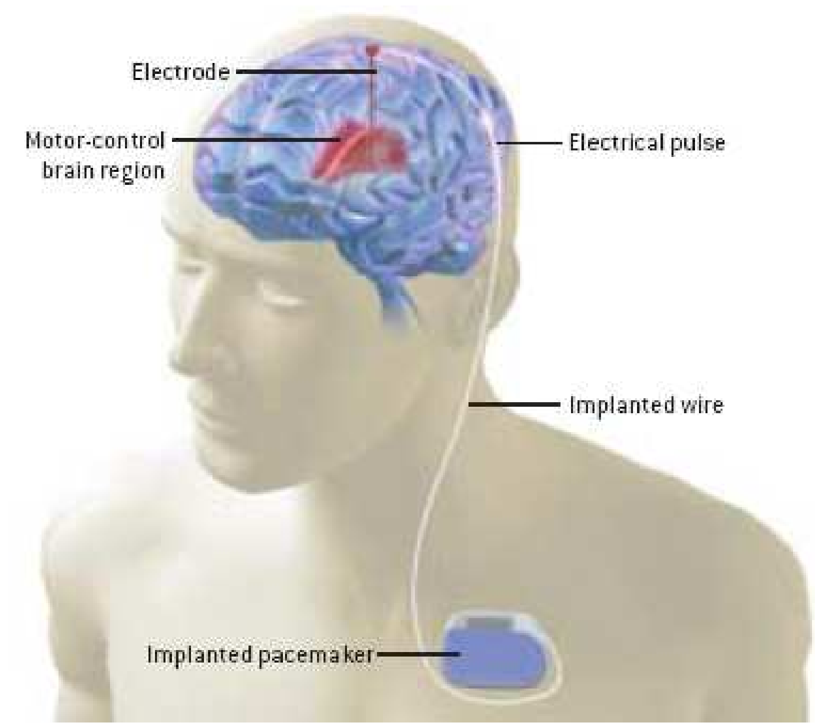
Motivation: Deep Brain Stimulation

- approved by US FDA for treatment of Parkinson's disease



- What is the best type of stimulation to get desired results?

Outline

This talk: more modest goal

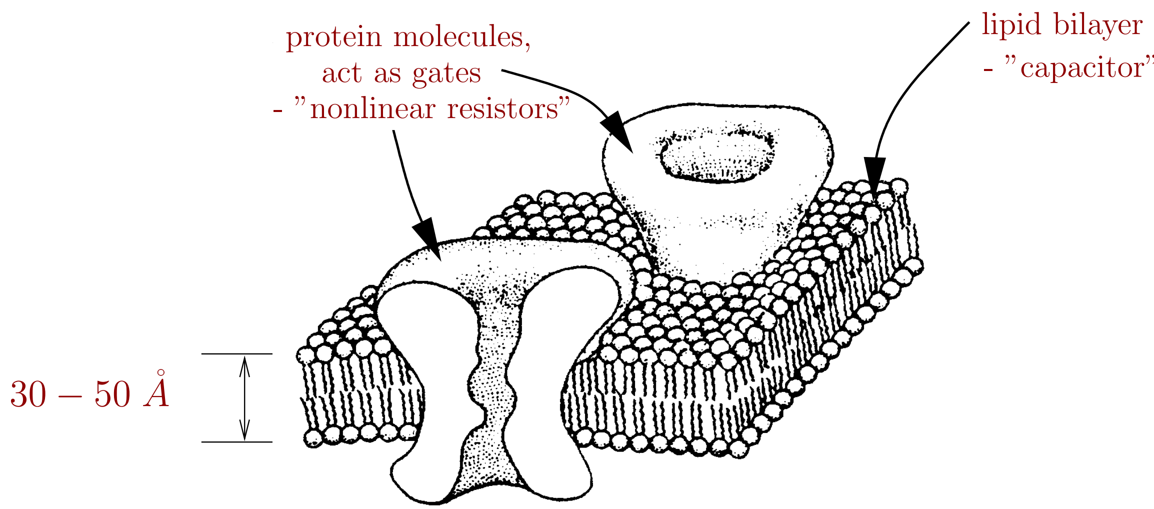
Suppose want *single* neuron to fire at certain time.

What current stimulus will make this happen?

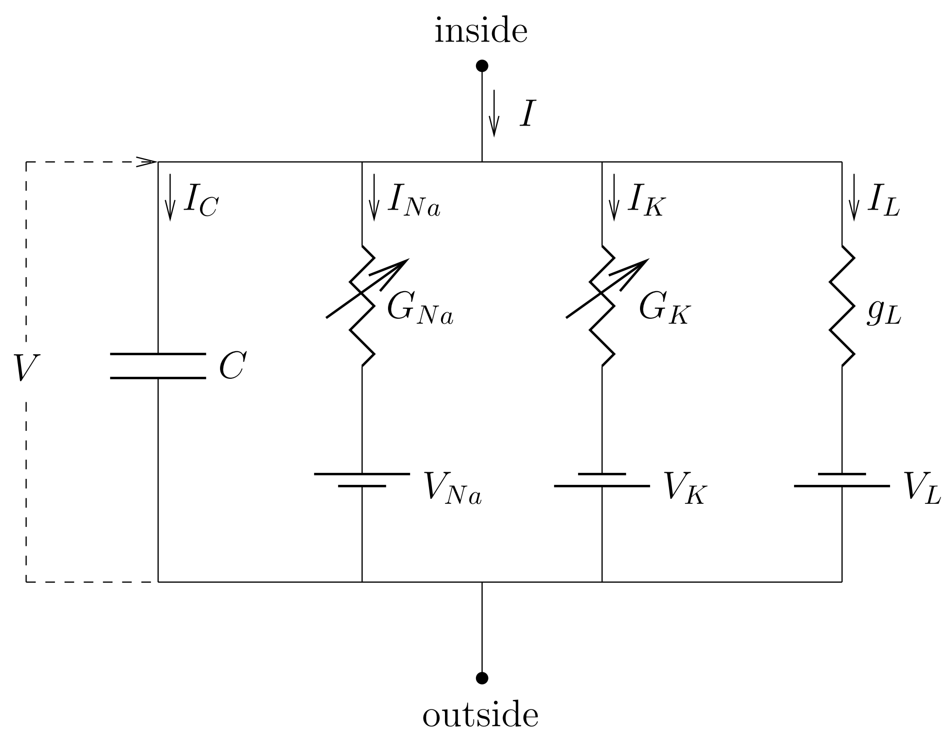
- **Neural modeling/phase response curves**
- **Optimal $I(t)$: general results and examples**
- **Feedback control**
- **Conclusions**

Neural Modeling

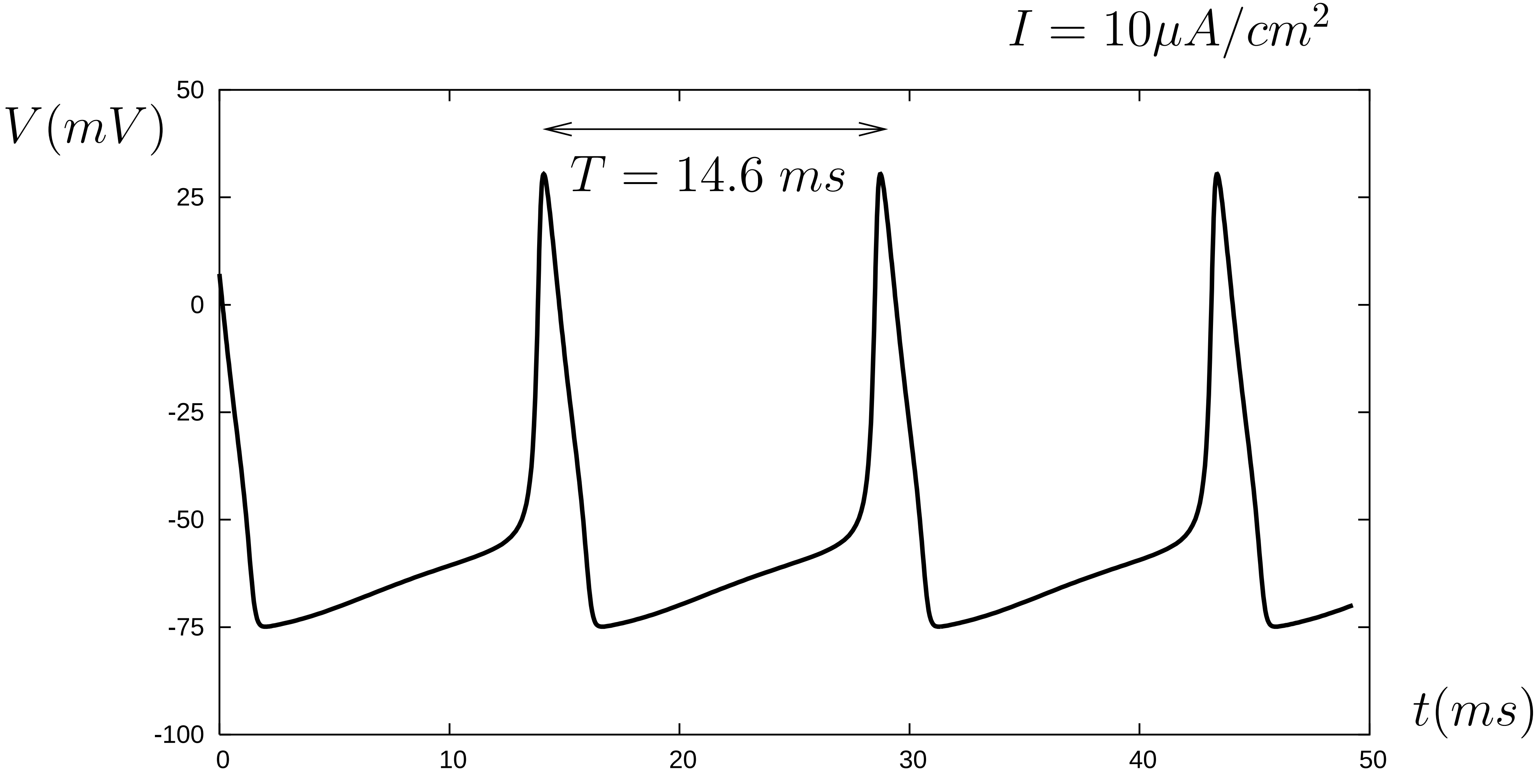
neuronal membrane



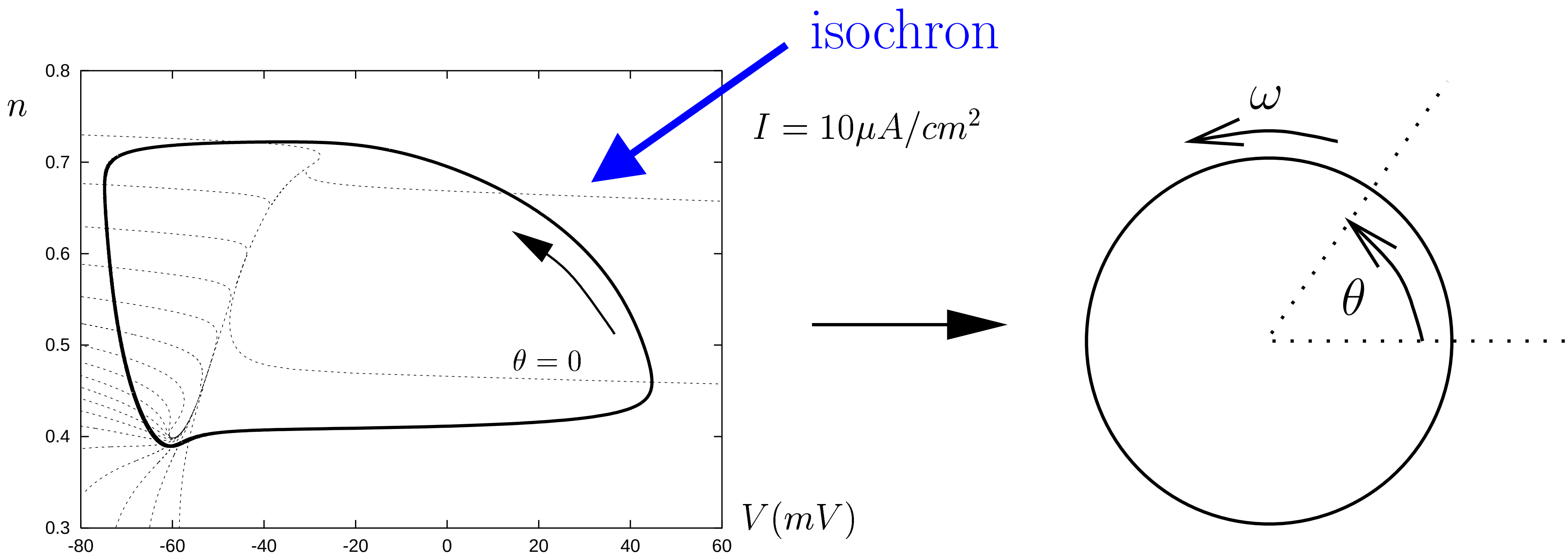
Hodgkin−Huxley model



Neural Modeling



Neural Modeling



$$\frac{d\mathbf{X}}{dt} = \mathbf{F}(\mathbf{X}) \longrightarrow \frac{d\theta}{dt} = \omega$$

Neural Modeling

$$\frac{d\mathbf{X}}{dt} = \mathbf{F}(\mathbf{X}) + \underbrace{\epsilon\mathbf{G}(\mathbf{X}, t)}_{\text{perturbation}}$$

$$\frac{d\theta}{dt} = \frac{\partial\theta}{\partial\mathbf{X}} \cdot \frac{d\mathbf{X}}{dt} = \frac{\partial\theta}{\partial\mathbf{X}} \cdot (\mathbf{F}(\mathbf{X}) + \epsilon\mathbf{G}(\mathbf{X}, t)) = \omega + \epsilon\frac{\partial\theta}{\partial\mathbf{X}} \cdot \mathbf{G}(\mathbf{X}, t)$$

Evaluate on limit cycle $\mathbf{X}_0$ for unperturbed system:

$$\frac{d\theta}{dt} = \omega + \epsilon\, \mathbf{Z}(\theta) \cdot \mathbf{G}(\mathbf{X}_0, t), \qquad \mathbf{Z}(\theta) = \left.\frac{\partial\theta}{\partial\mathbf{X}}\right|_{\mathbf{X}_0(\theta)}.$$

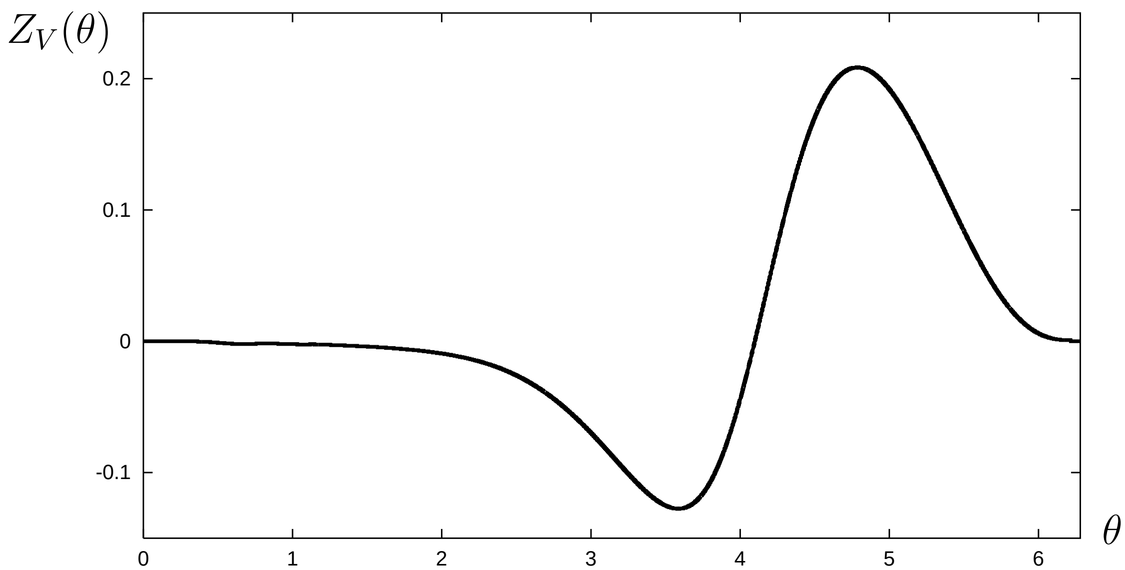
Suppose $\epsilon\mathbf{G} = \epsilon\mathbf{G}(t) = (I(t), 0)$, $I(t)$ = current stimulus

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

Phase Response Curves (PRCs)

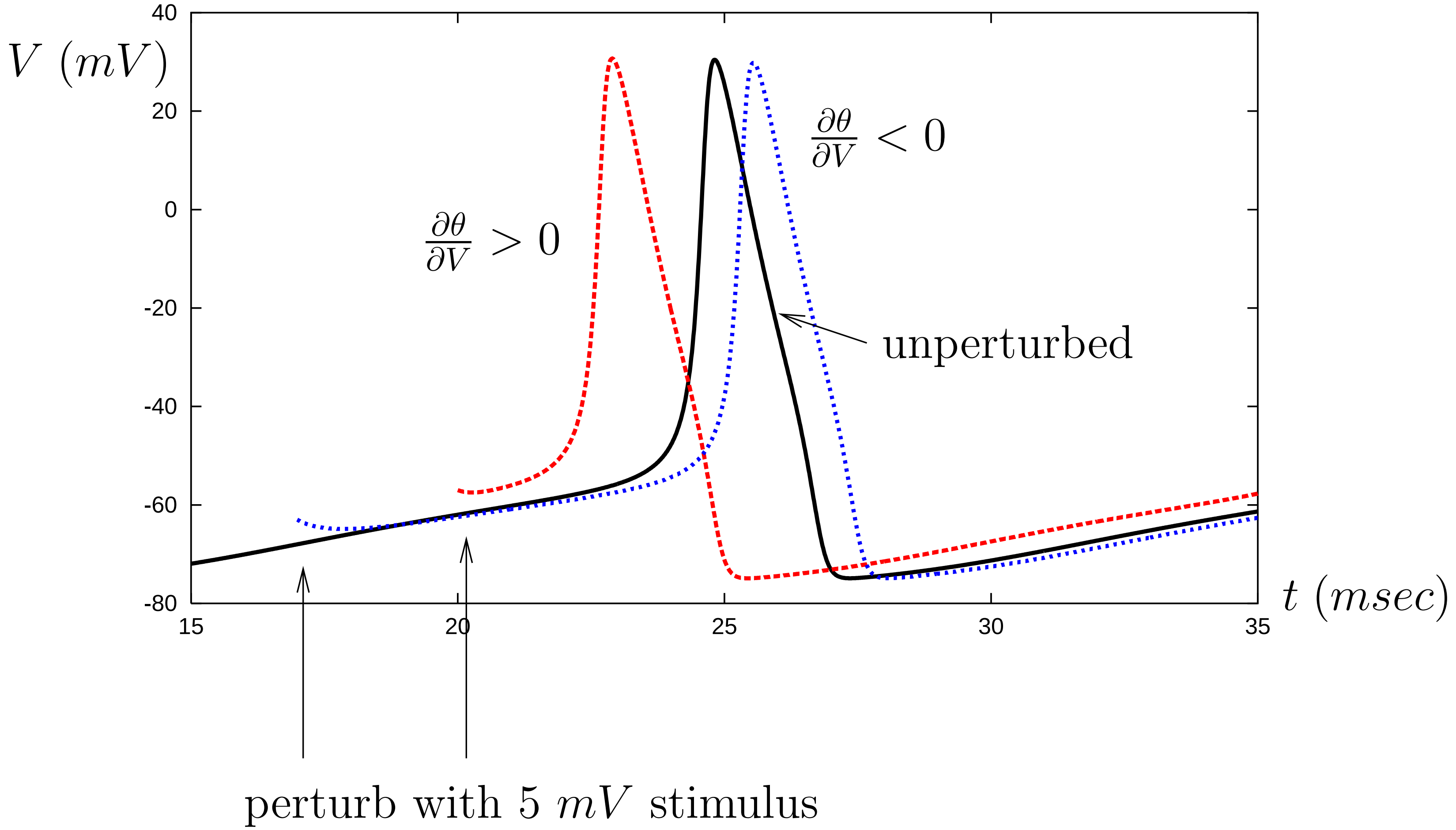
$$Z_V(\theta) = \frac{\partial \theta}{\partial V} = \lim_{\Delta V \to 0} \frac{\Delta \theta}{\Delta V}$$

captures effect of impulsive perturbations in the voltage



phase response curve for Hodgkin-Huxley equations

Phase Response Curves (PRCs)



Phase Response Curves and Bifurcations

- **SNIPER bifurcation** **(HR)**

$$Z_V(\theta) \sim 1 - \cos(\theta)$$

- **saddle-node bifurcation of periodic orbits** **(HH)**

$$Z_V(\theta) \sim \sin(\theta - \theta_0)$$

- **supercritical Hopf bifurcation** **(FN)**

$$Z_V(\theta) \sim \sin(\theta - \theta_0)$$

- **homoclinic bifurcation** **(ML)**

$$Z_V(\theta) \sim e^{-\lambda\theta}$$

different bifurcation $\longrightarrow$ different PRC
$\longrightarrow$ different response

Optimal $I(t)$ for Specified Time of Firing

Consider

$$\frac{d\theta}{dt} = f(\theta) + Z(\theta)I(t)$$

$f(\theta)$ **gives neuron's baseline dynamics**
$Z(\theta)$ **is neuron's phase sensitivity function**
$I(t)$ **is a current stimulus**

$\theta \in [0, 2\pi)$, $\theta = 0$ **corresponds to neuron firing**

Suppose for specified time t_1, **want to find input** $I(t)$ **which evolves from** $\theta(0) = 0$ **to** $\theta(t_1) = 2\pi$ **and minimizes**

$$G[I(t)] = \int_0^{t_1} [I(t)]^2 dt$$

Optimal $I(t)$ for Specified Time of Firing

Apply calculus of variations to minimize

$$C[I(t)] = \int_0^{t_1} \underbrace{\left\{ [I(t)]^2 + \lambda \left(\frac{d\theta}{dt} - f(\theta) - Z(\theta) I(t) \right) \right\}}_{P[I(t)]} dt.$$

Euler-Lagrange equations:

$$\frac{\partial P}{\partial \theta} = \frac{d}{dt}\left(\frac{\partial P}{\partial \dot{\theta}}\right), \qquad \frac{\partial P}{\partial \lambda} = \frac{d}{dt}\left(\frac{\partial P}{\partial \dot{\lambda}}\right), \qquad \frac{\partial P}{\partial I} = \frac{d}{dt}\left(\frac{\partial P}{\partial \dot{I}}\right)$$

$$\Rightarrow \frac{d\theta}{dt} = f(\theta) + \frac{\lambda [Z(\theta)]^2}{2}, \qquad \frac{d\lambda}{dt} = -\lambda f'(\theta) - \frac{\lambda^2 Z(\theta) Z'(\theta)}{2},$$

$$I(t) = \frac{\lambda(t) Z(\theta(t))}{2}.$$

Need to find $\lambda(0) = \lambda_0$ so that $\theta(0) = 0, \theta(t_1) = 2\pi$.

Some Useful Results

- **The Hamiltonian function**

$$H(\theta, \lambda) = \lambda f(\theta) + \frac{1}{4}\lambda^2[Z(\theta)]^2$$

  conserved on trajectories for Euler-Lagrange eqns

- **Theorem: Suppose $f(0) > 0$ and $Z(0) = 0$, as is commonly the case for neurons. Then for any $t_1 > 0$, an optimal $I(t)$ exists and is unique.**

Some Useful Results

definition: An *intrinsically oscillatory neuron* **is one which fires periodically in the absence of input $I(t)$.**

phase reduction $\Rightarrow f(\theta) = \omega > 0$, **period** $T = 2\pi/\omega$.

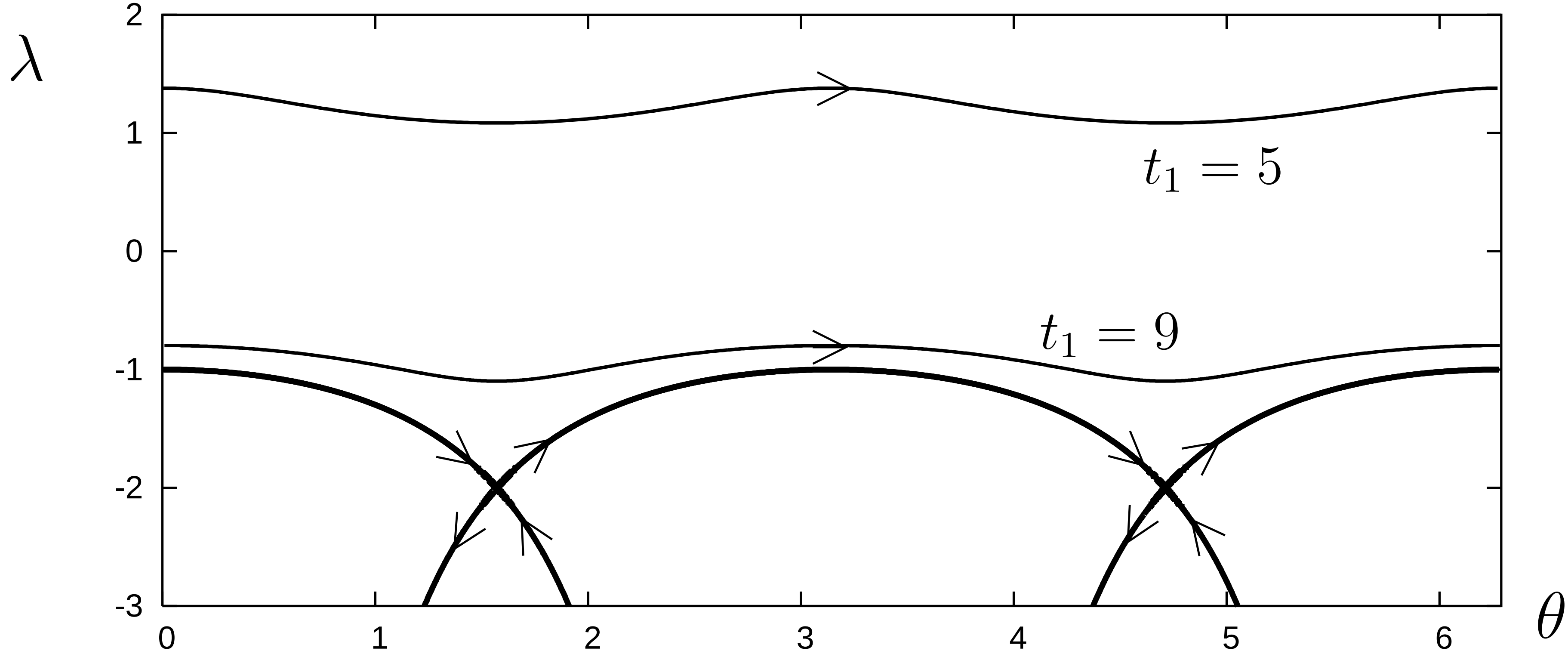
- **For intrinsically oscillatory neurons**

$$I(t) = -\frac{(t_1 - T)\omega^2 Z(\omega t - 2\pi t(t_1 - T)/(t_1 T))}{\int_0^{2\pi} [Z(\theta)]^2 d\theta} + \mathcal{O}((t_1 - T)^2).$$

That is, for small $|t_1 - T|$ **the optimal current** $I(t)$ **is proportional to** $Z(\cdot)$.

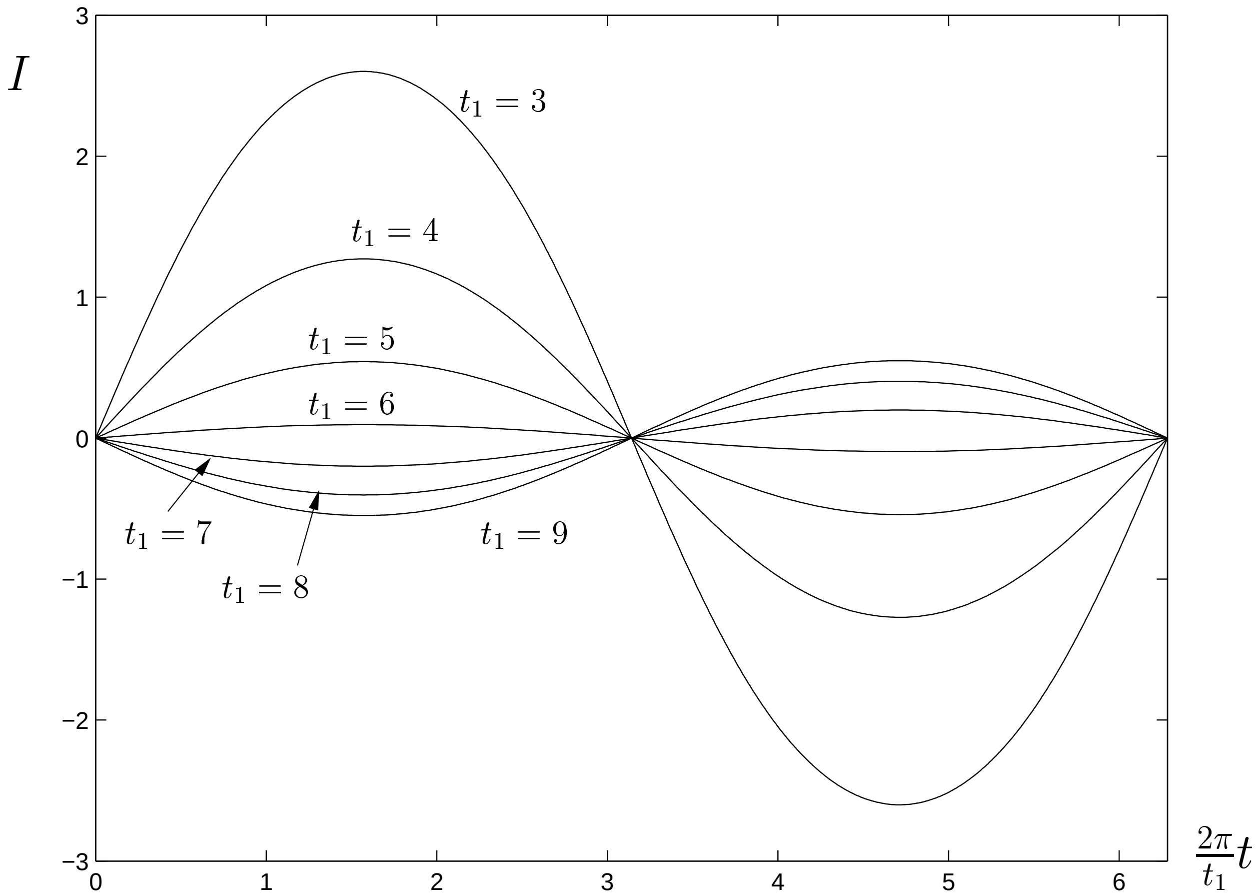
Example 1: $f(\theta) = \omega, Z(\theta) = Z_d \sin\theta$

For $\omega = Z_d = 1$, phase space for Euler-Lagrange eqns:



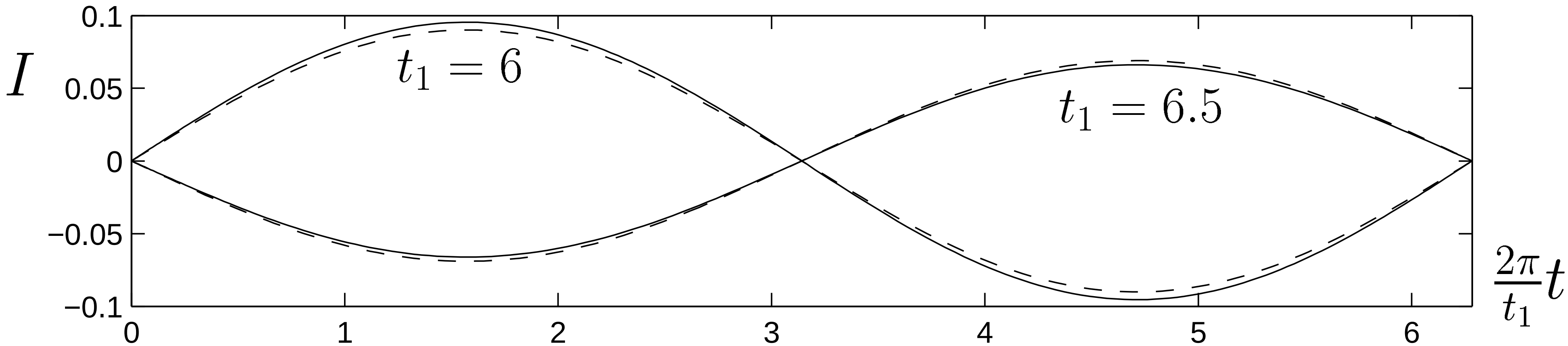
Example 1: $f(\theta) = \omega, Z(\theta) = Z_d \sin\theta$

Optimal $I(t)$ for different values of t_1



Example 1: $f(\theta) = \omega, Z(\theta) = Z_d \sin\theta$

Small $|t_1 - T|$ approximation

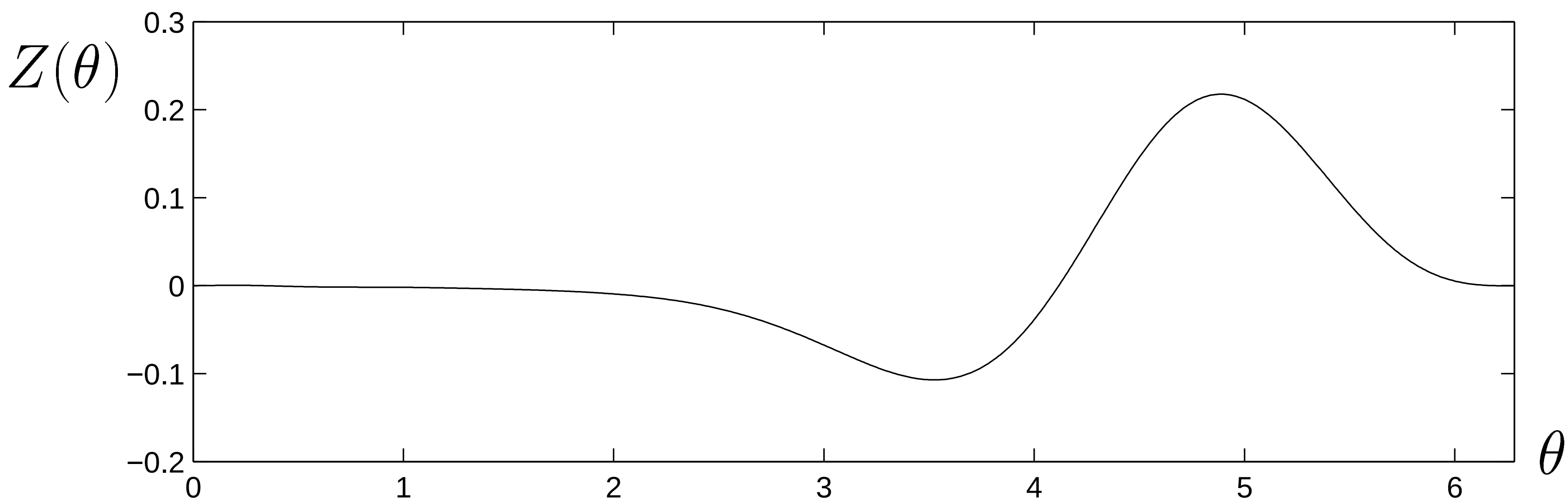


solid: from shooting method
dashed: approximation

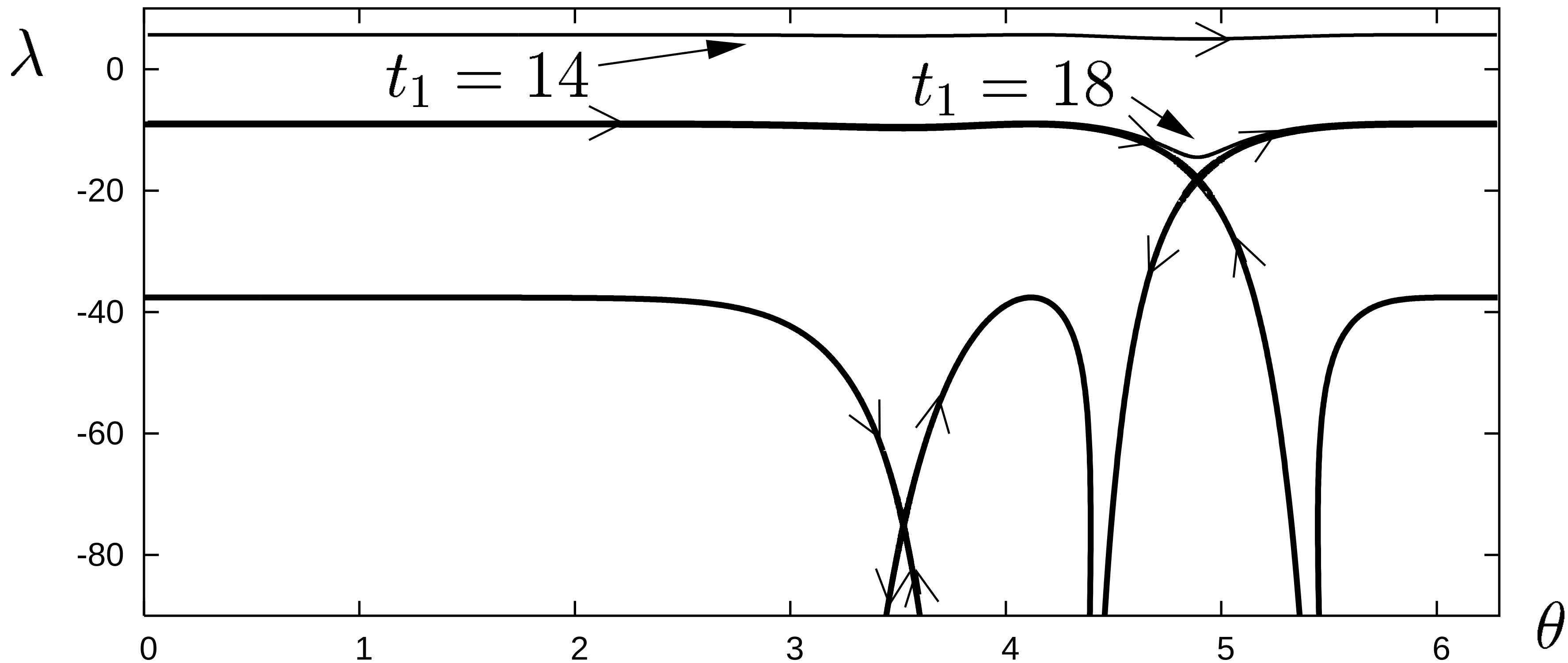
Example 2: Hodgkin-Huxley equations

model for generation of action potentials for squid giant axon, based on dynamical interplay between ionic conductances and electrical activity

for injected baseline current $I_b = 10$, fires periodically with $T = 14.63$ ms

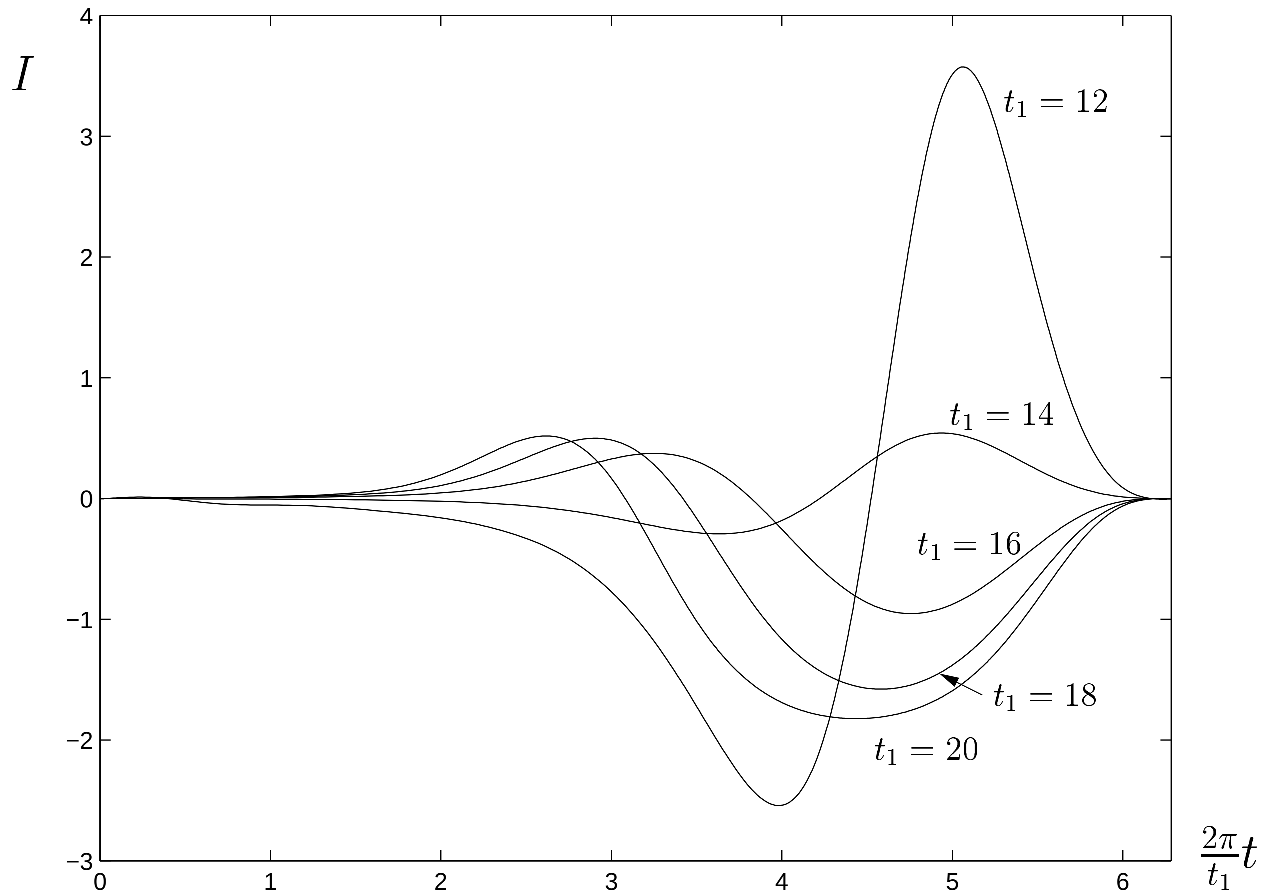


Example 2: Hodgkin-Huxley equations



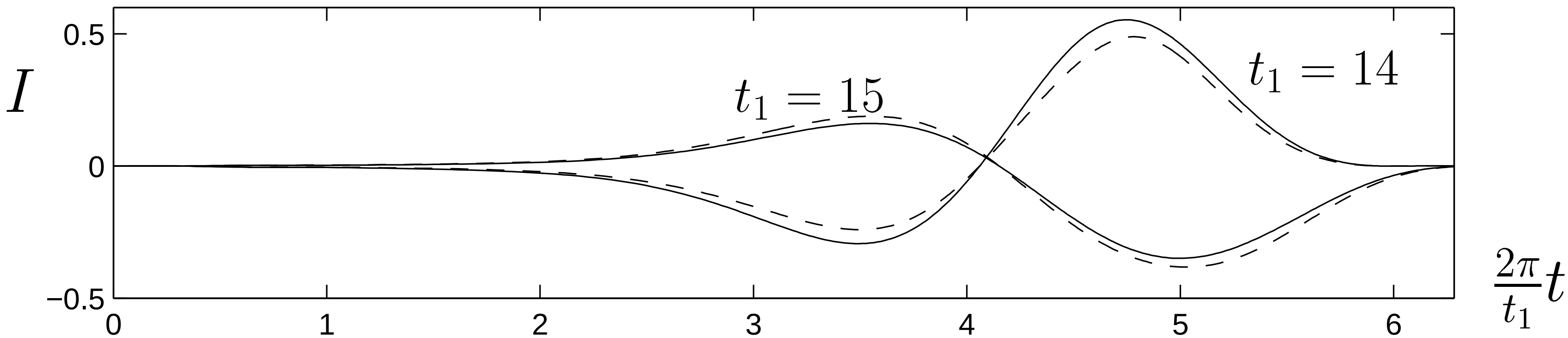
Example 2: Hodgkin-Huxley equations

Optimal $I(t)$ for different values of t_1



Example 2: Hodgkin-Huxley equations

Small $|t_1 - T|$ approximation



solid: from shooting method
dashed: approximation

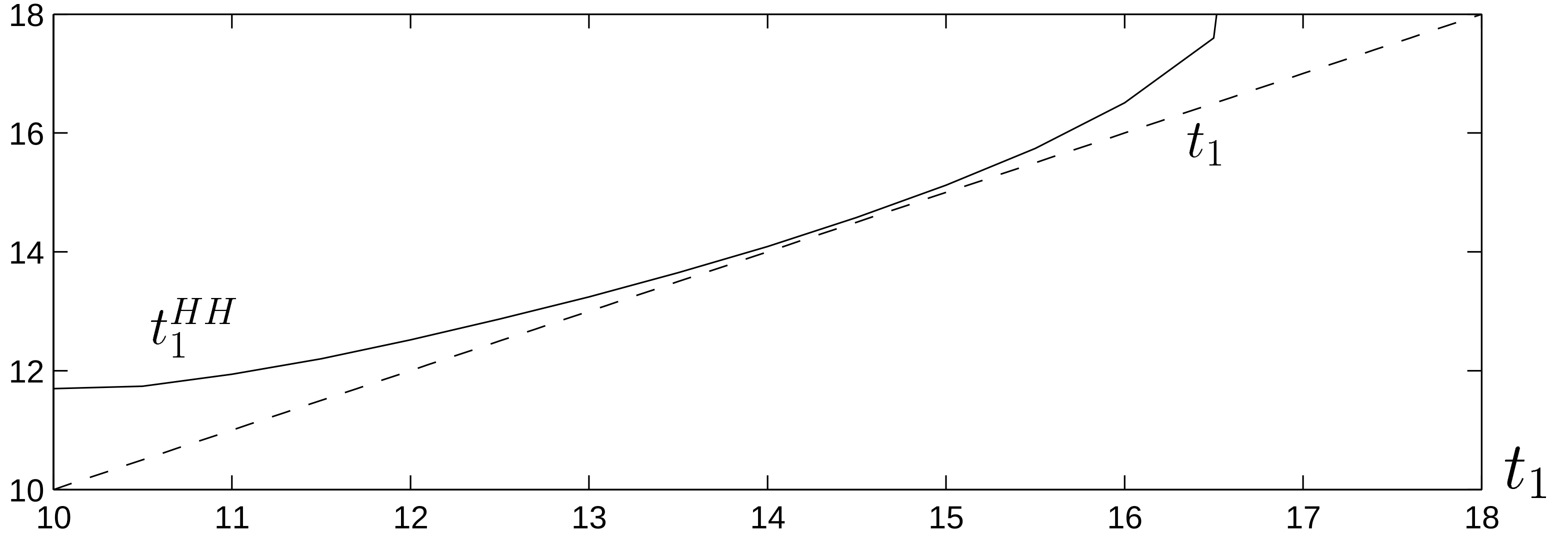
Example 2: Hodgkin-Huxley equations

Comparison to full Hodgkin-Huxley equations:

- **Choose** t_1
- **Inject optimal** $I(t)$ **found from phase model into full equations up to time** t_1
- $I(t) = 0$ **for** $t > t_1$
- **Compare time neuron fires to** t_1

Example 2: Hodgkin-Huxley equations

Using $I(t)$ from phase model works well for full Hodgkin-Huxley equations for $t_1 \approx T$



Optimal $I(t)$ for Minimizing Time of Firing

Suppose want to get neuron to fire as soon as possible, subject to constraint

$$|I(t)| \leq \bar{I} \;\; \forall \;\; t$$

In time dt, phase advances by

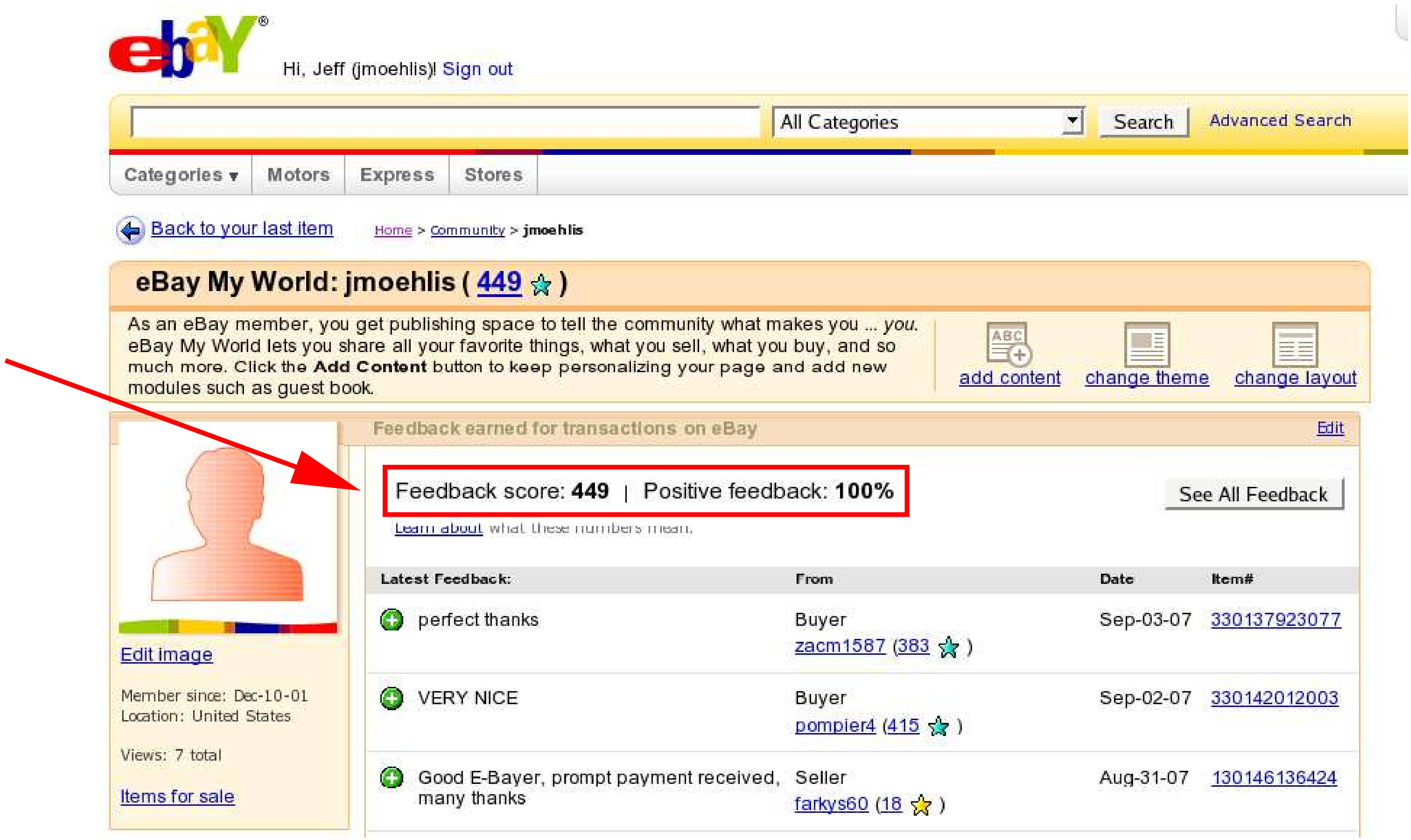
$$d\theta = [f(\theta) + Z(\theta)I(t)]dt.$$

To maximize $d\theta$ at each time step, take

$$I(t) = I^{bb}(\theta(t)) = \begin{cases} \bar{I} & \text{for} \;\; Z(\theta(t)) > 0 \\ -\bar{I} & \text{for} \;\; Z(\theta(t)) < 0 \end{cases}.$$

"bang-bang control"

Feedback



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Latest Feedback:
From
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Item#
perfect thanks
Buyer zacm1587 (383)
Sep-03-07
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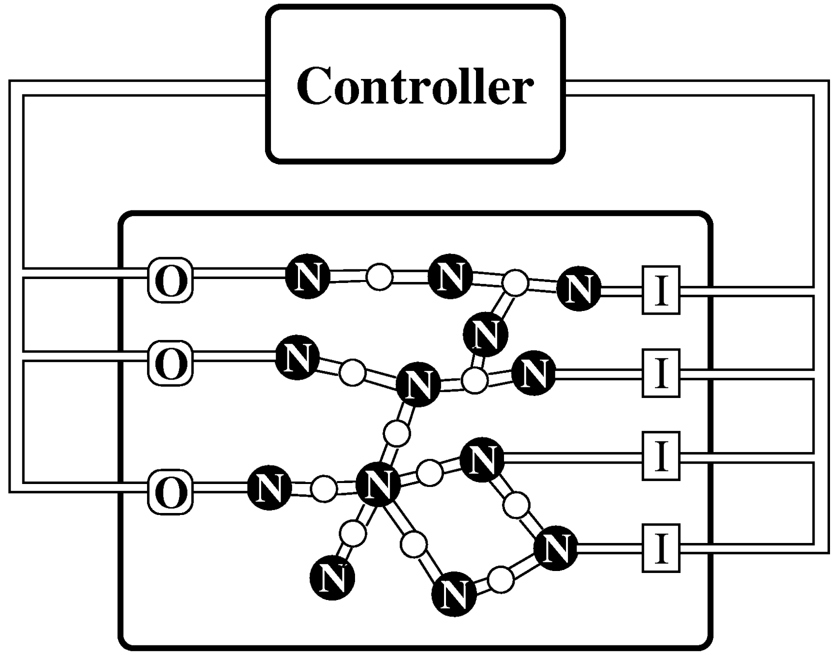
Feedback Control



Neural Network

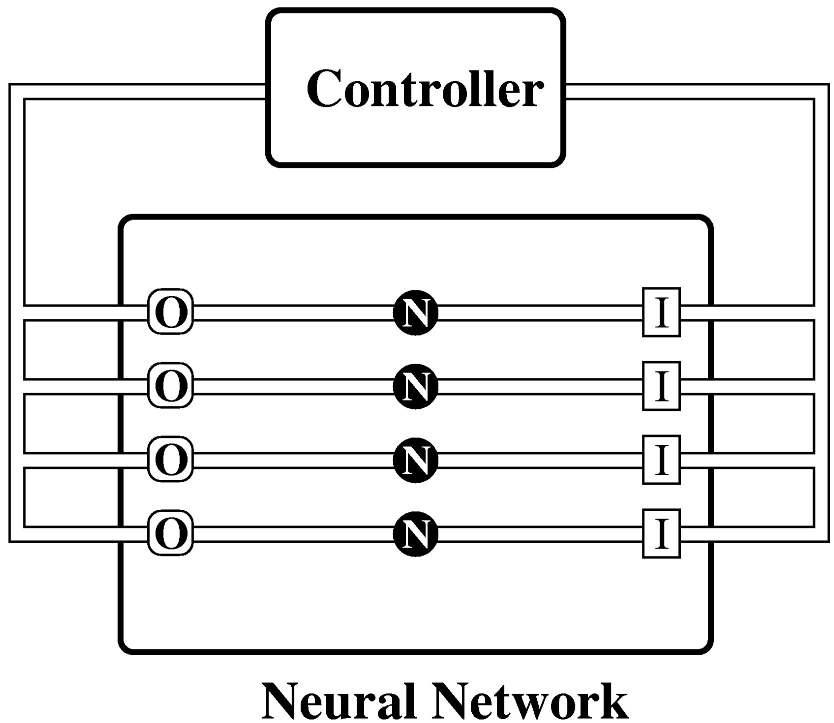
Challenges:

- all we can measure is voltage
- unknown network topology
- non-identical neurons, non-identical coupling

Feedback Control

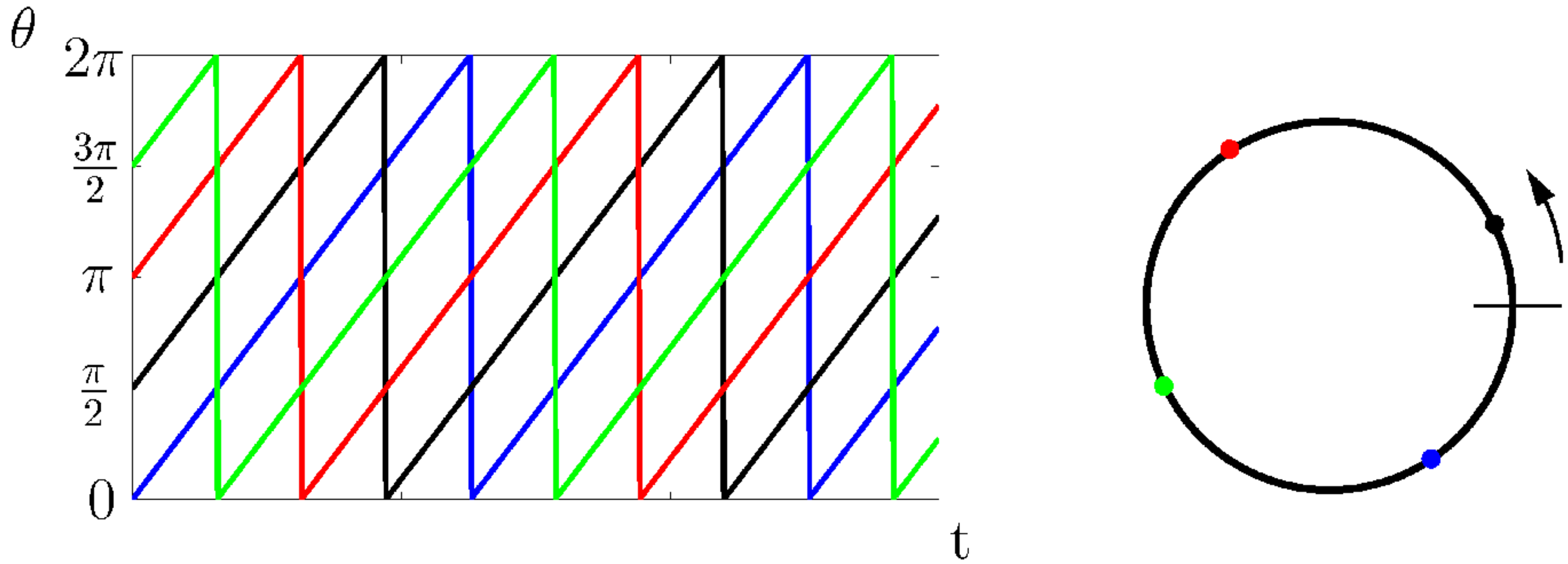
A Simplified Problem:

- identical uncoupled phase oscillators, each with input/output



Feedback Control

Desynchronize population by controlling groups of neurons to have "equally staggered" reference trajectories



cf. Tass et al

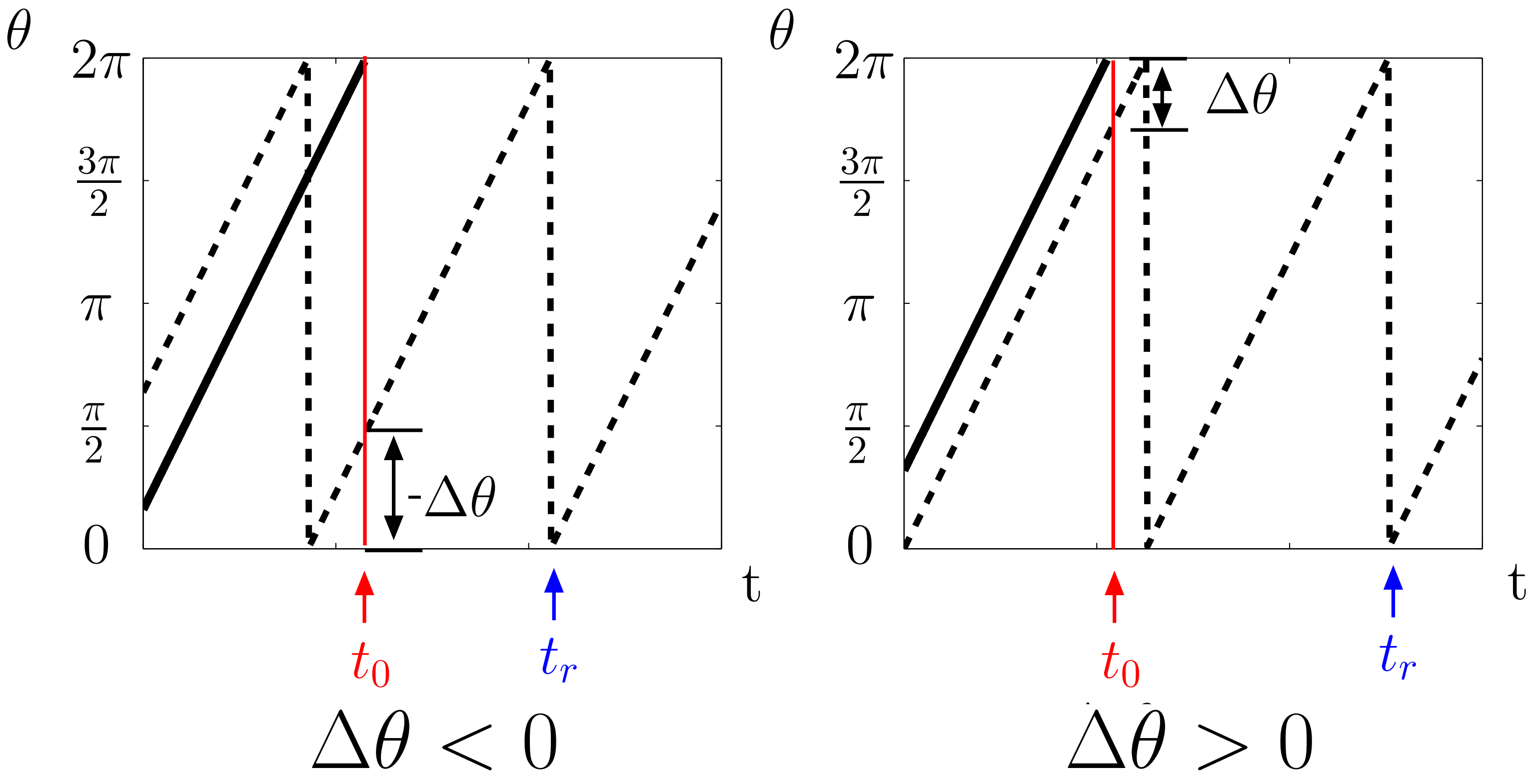
$\Rightarrow$ Control of single neurons

Feedback Control

- **suppose PRC for neuron is known**
- **event-based control: only detect when neuron fires**
- **charge balance constraint:**

$$\int_{\theta=0}^{\theta=2\pi} u(t)\, dt = 0 \qquad I(t) \to u(t)$$

Reference Trajectories and Errors



$$\Delta\theta = \begin{cases} \theta - \theta_r \,, & \text{for} \quad |\theta - \theta_r| \le \pi \\ \theta - \theta_r - \mathrm{sgn}(\theta - \theta_r)2\pi \,, & \text{for} \quad |\theta - \theta_r| > \pi \end{cases}$$

$$-\pi < \Delta\theta \le \pi$$

Intuitive Idea

$$\frac{d\theta}{dt} = \omega + Z(\theta)u(t)$$

If $\Delta\theta < 0$, want to speed up neuron

- **take** $u(t) \leq 0$ **when** $Z(\theta) < 0$
- **take** $u(t) \geq 0$ **when** $Z(\theta) > 0$

If $\Delta\theta > 0$, want to slow down neuron

- **take** $u(t) > 0$ **when** $Z(\theta) < 0$
- **take** $u(t) < 0$ **when** $Z(\theta) > 0$

Theorem

For $\theta(0) = 0$,

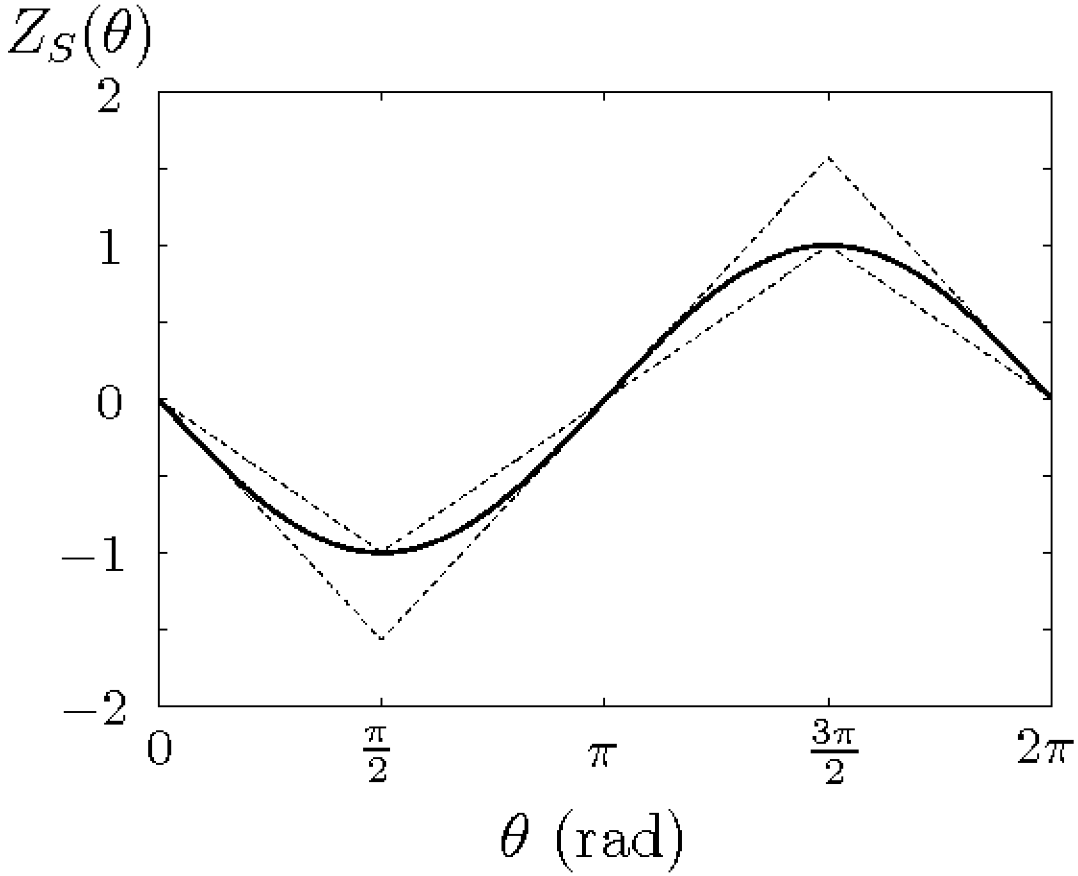
$$Z(\theta) = -\sin(\theta)$$

$$u(t) = \begin{cases} c\Delta\theta \quad , & \text{for} \quad 0 \le t < t_s/2 \\ -c\Delta\theta \, , & \text{for} \quad t_s/2 \le t < t_s \\ 0 \quad , & \text{otherwise}, \end{cases}$$

$$t_s = \frac{2\pi - |\Delta\theta|/2}{\omega},$$

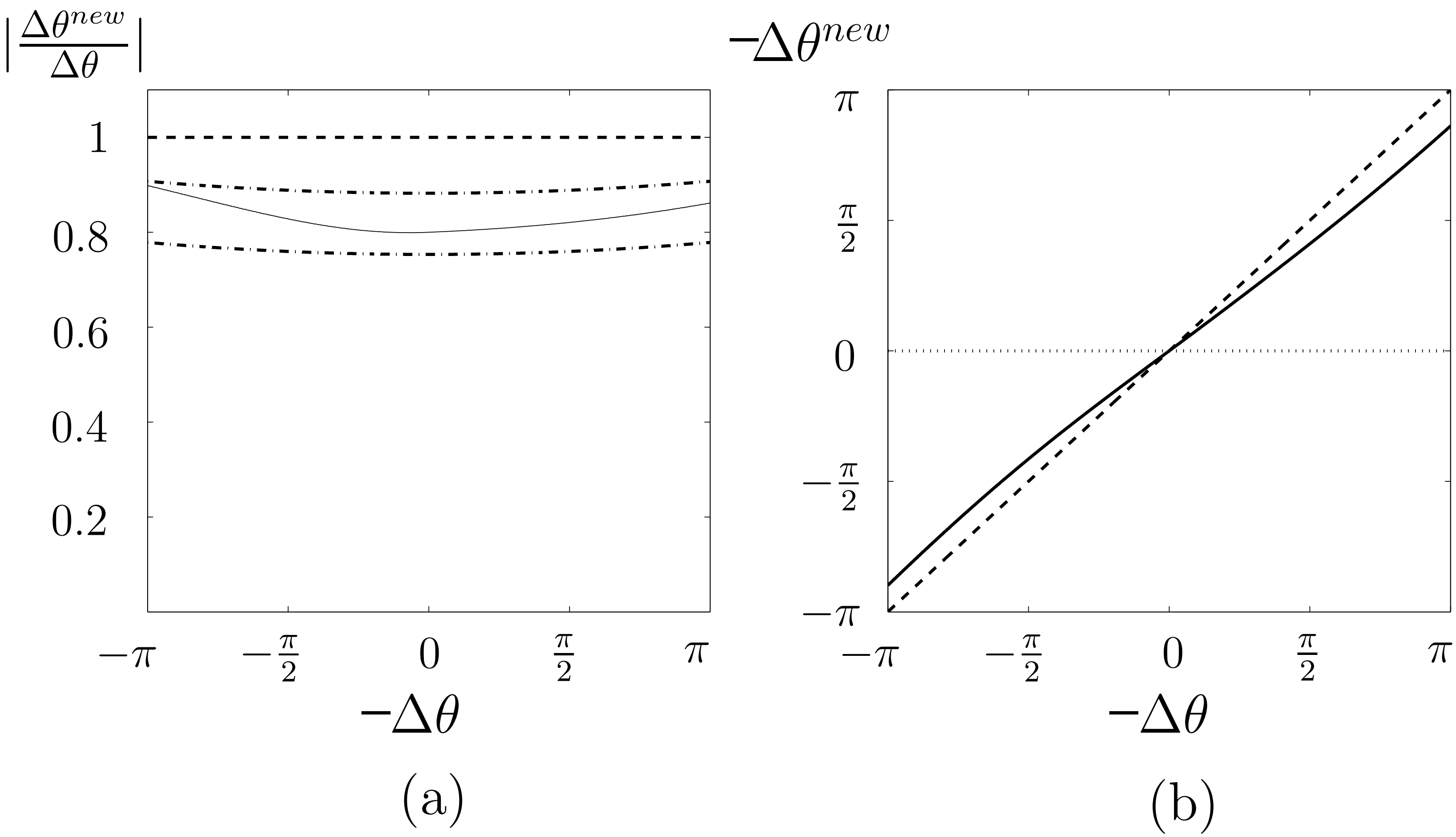
the phase error of the oscillator will be a contraction in the limit of small, positive c.

Proof



Use PRC bounds, Gronwall's Lemma to bound the solution.
Show contraction for all $\Delta\theta \in (-\pi, \pi]$.

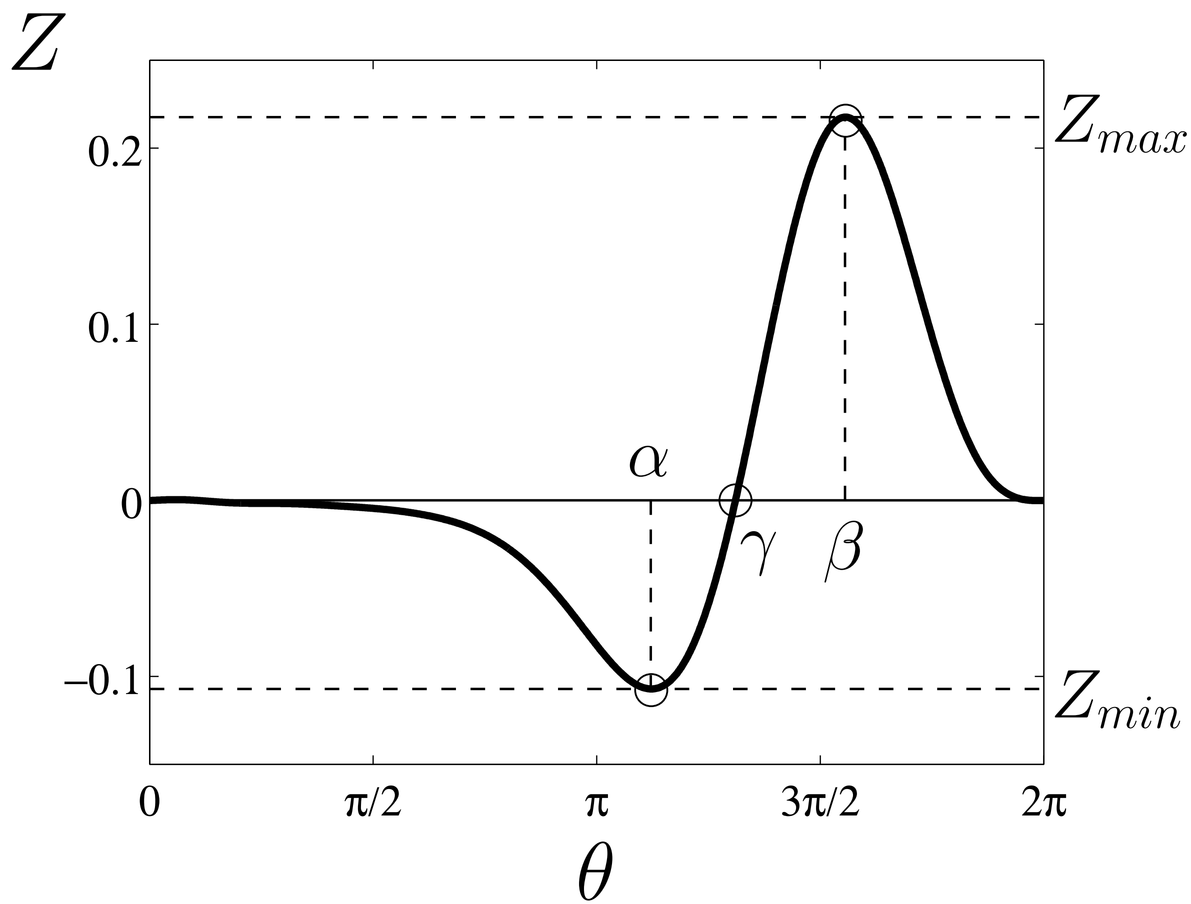
An Example



$$\omega = 1, \qquad c = 0.05$$

Impulsive Control Law

Definitions



Impulsive Control Law

Two appropriately timed δ-function inputs:

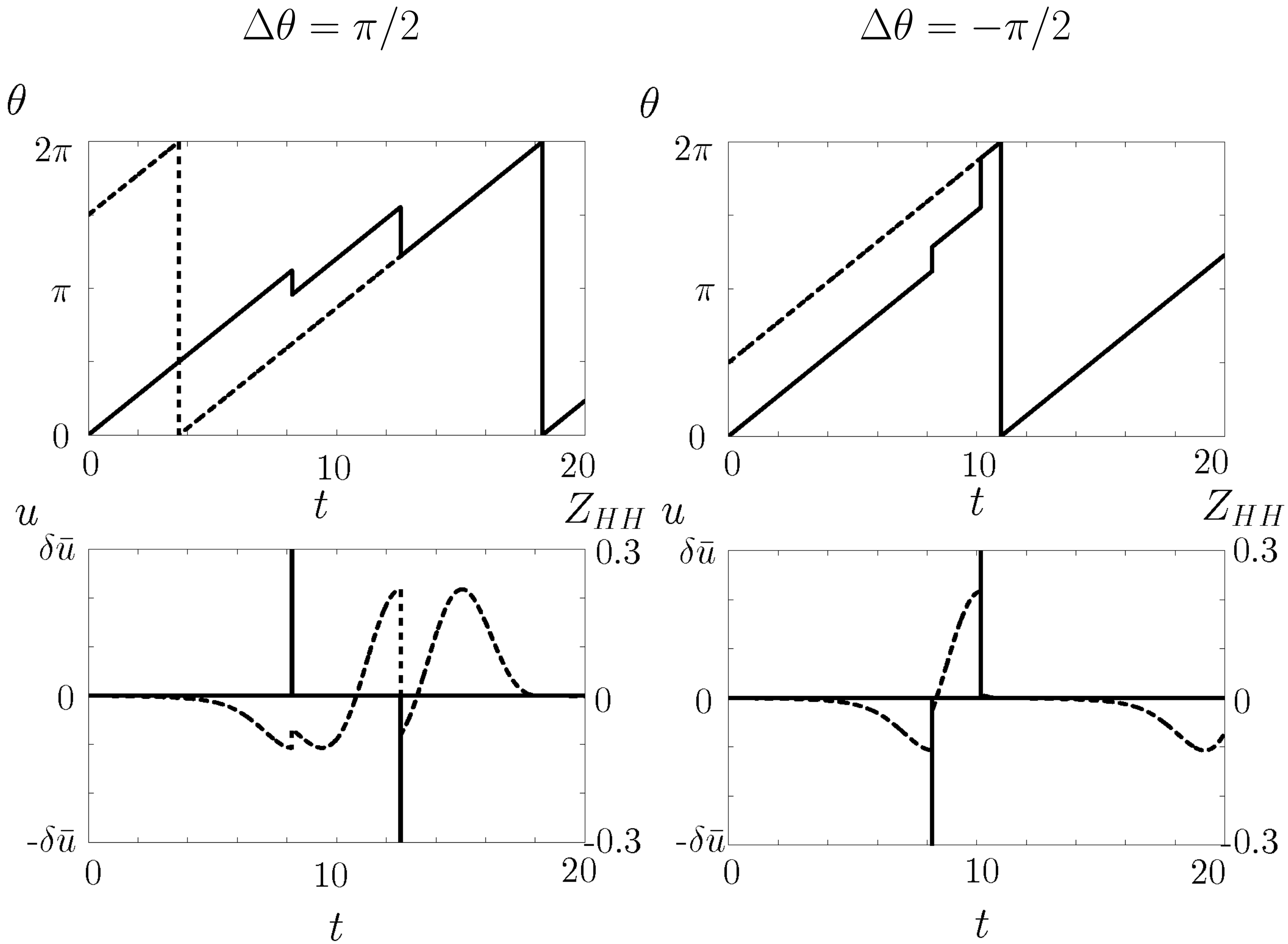
$$u(t) = \bar{u}(-\delta(t - t_1) + \delta(t - t_2))$$

where

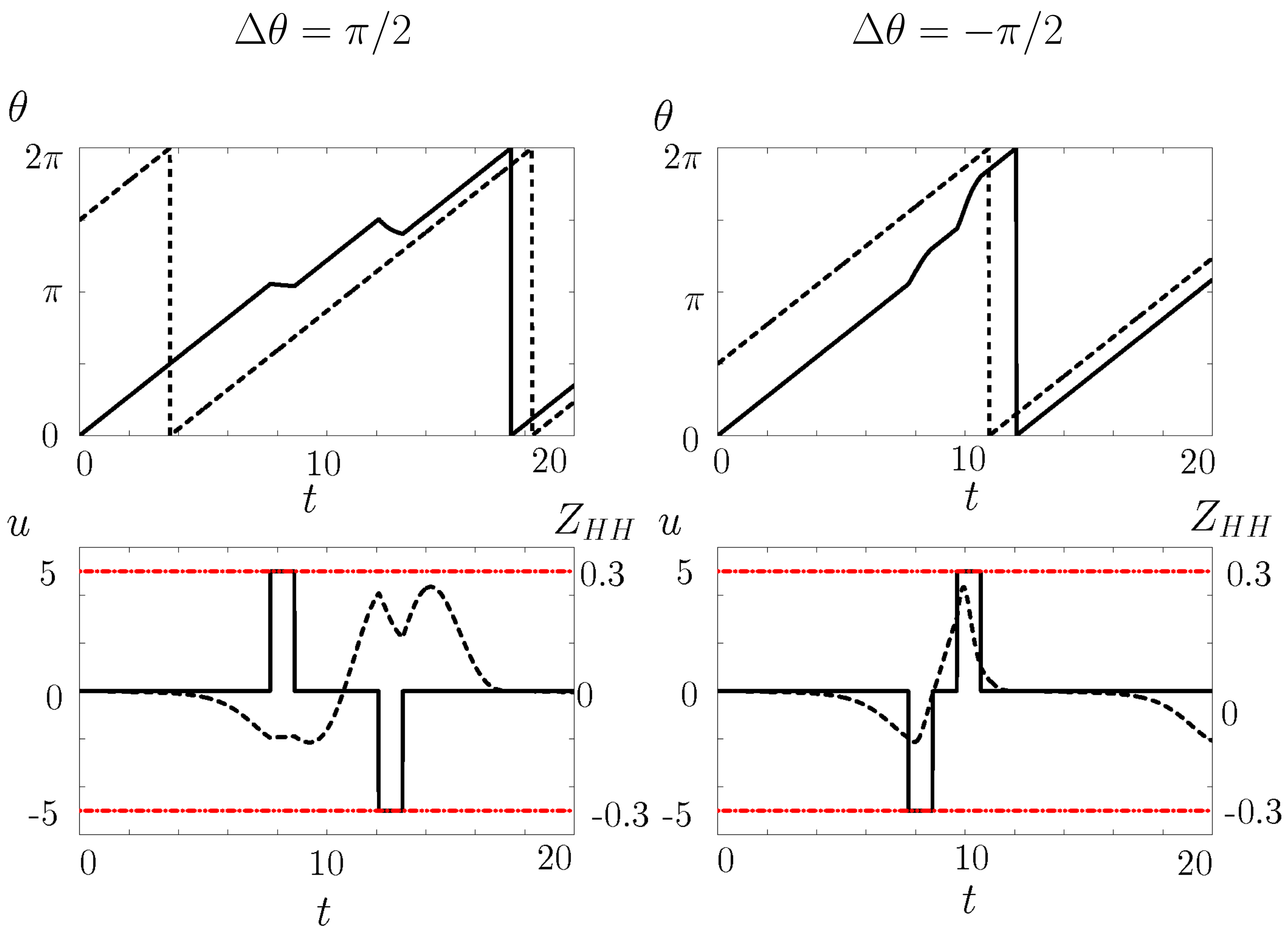
$$t_1 = \frac{\alpha}{\omega}, \qquad t_2 = \frac{1}{\omega}(\beta - Z_{min}\bar{u}), \qquad \bar{u} = \frac{\Delta\theta}{Z_{max} - Z_{min}}$$

- **reduces phase error to zero**
- **problem: control input may be too large**

Impulsive Control Law

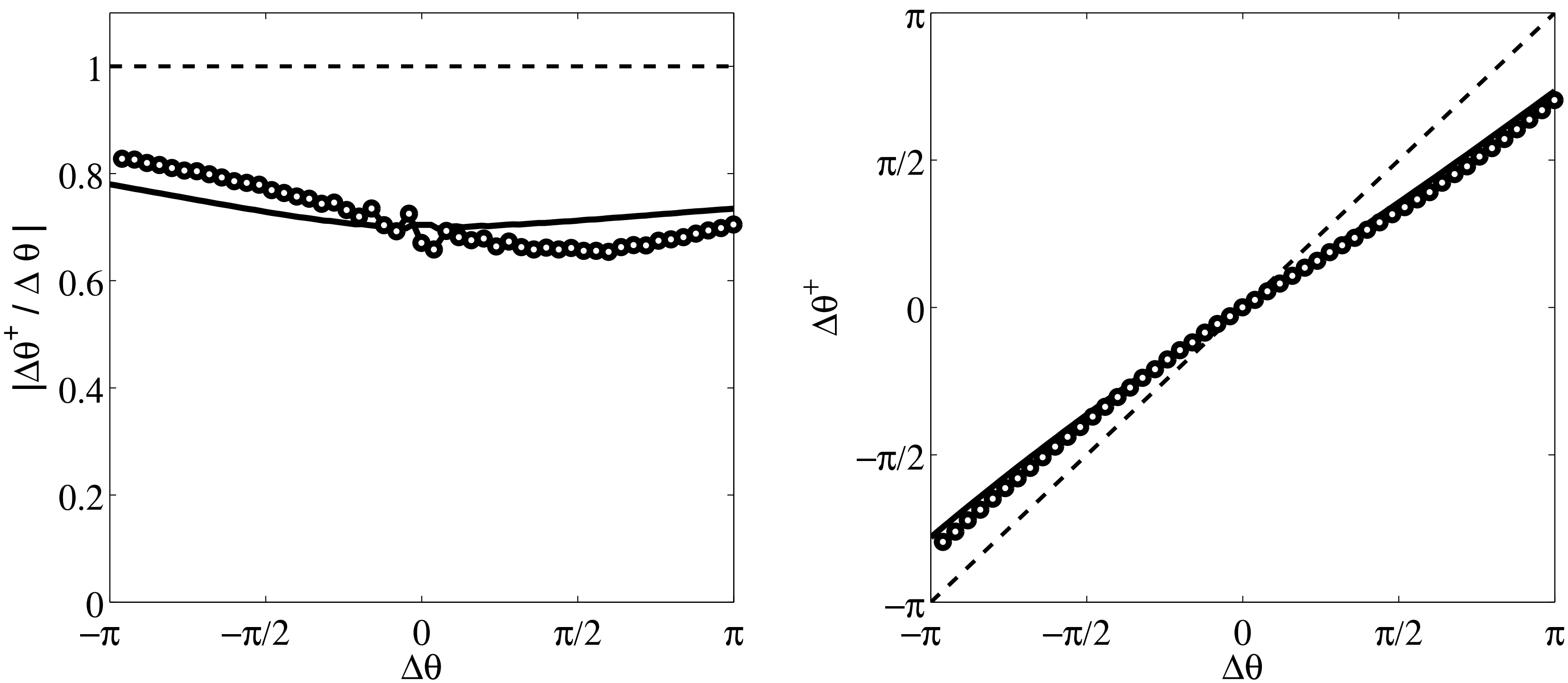


Quasi-Impulsive Control



Quasi-Impulsive Control

Theorem: For a range of control parameters, the phase error map will be a contraction.



Conclusions

Optimal $I(t)$ for specified time of firing t_1

- **for typical neuron models, exists and is unique**
- **for intrinsically oscillatory neurons and t_1 approximately equal to natural period, $I(t)$ proportional to phase response curve $Z(\theta)$**

Event-based feedback control

- **impulsive, quasi-impulsive, $\cdots$**

Future Work :

- **control of real neurons, collaboration with Tay Netoff (Minnesota)**
- **networks**

Collaborators

- **Eric Shea-Brown, professor, Univ. Washington**
- **Herschel Rabitz, professor, Princeton University**

JM, E. Shea-Brown, H. Rabitz, *ASME J. Comp. Nonlin. Dyn.* **1, 358-367, 2006.**

- **Per Danzl, graduate student, UCSB**

P. Danzl, JM, CDC07

P. Danzl, JM, ACC08

Postdoc Positions at UCSB

- **Postdoc #1, joint with Francesco Bullo**
  - **collective decision-making strategies**
  - **multi-agent stochastic search algorithms**
- **Postdoc #2**
  - **dynamics of individual and coupled oscillators, including neuroscience applications**

Existence and Uniqueness of Optimal $I(t)$

Theorem

Suppose $f(0) > 0$, $Z(0) = 0$, so that $H_0 = f(0)\lambda_0$. Then for any $t_1 > 0$, an optimal $I(t)$ exists and is unique.

Proof

$$t_1 = \int_0^{t_1} dt = \int_0^{2\pi} \frac{d\theta}{f(\theta) + \frac{\lambda[Z(\theta)]^2}{2}} = \int_0^{2\pi} \frac{d\theta}{\sqrt{[f(\theta)]^2 + [Z(\theta)]^2 H_0}}$$

$$H_0 \to \infty \Rightarrow t_1 \to 0, \quad H_0 \to \max\left(-[f(\theta)]^2/[Z(\theta)]^2\right) \Rightarrow t_1 \to \infty$$

Differentiating, we have

$$\frac{\partial t_1}{\partial H_0} = -\frac{1}{2}\int_0^{2\pi} \frac{[Z(\theta)]^2 d\theta}{([f(\theta)]^2 + [Z(\theta)]^2 H_0)^{3/2}} < 0 \quad \Rightarrow \quad \frac{\partial t_1}{\partial \lambda_0} < 0$$

Example 2: Theta Neuron Model

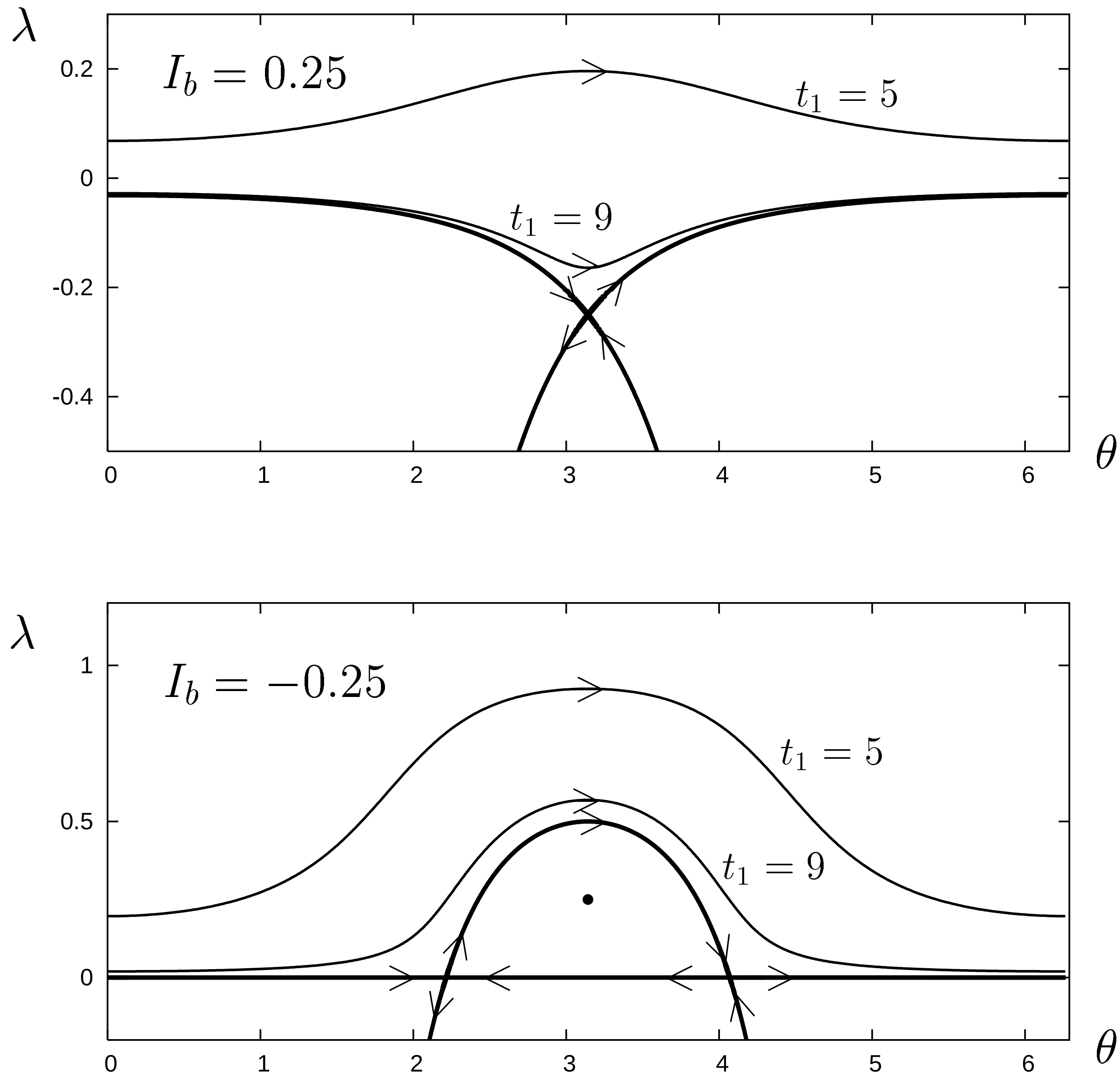
$$\frac{d\theta}{dt} = 1 + \cos\theta + (1 - \cos\theta)\left(I(t) + I_b\right),$$

$I_b > 0$: **superthreshold Type I neuron;**
fires periodically with period $\pi/\sqrt{I_b}$ **when** $I(t) = 0$

$I_b < 0$: **subthreshold Type I neuron;**
does not fire without $I(t)$

$$\begin{aligned} f(\theta) &= 1 + \cos\theta + I_b(1 - \cos\theta) \\ Z(\theta) &= 1 - \cos\theta \end{aligned}$$

Example 2: Theta Neuron Model



Example 2: Theta Neuron Model

Optimal $I(t)$ **for** $I_b = -0.25, t_1 = 30$