Spike Timing Control of Oscillatory Neuron Models Using Impulsive and Quasi-Impulsive Charge-Balanced Inputs

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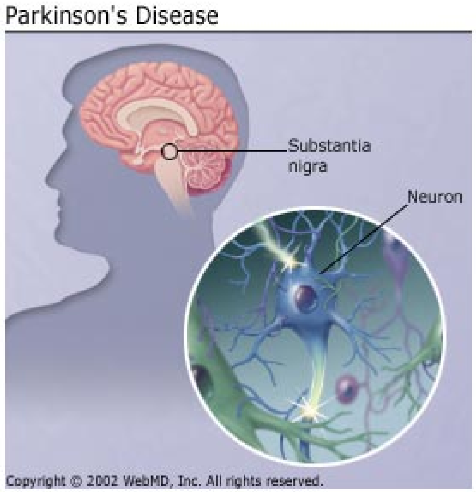
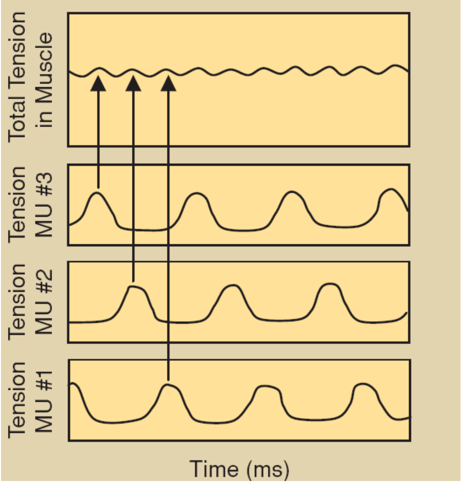
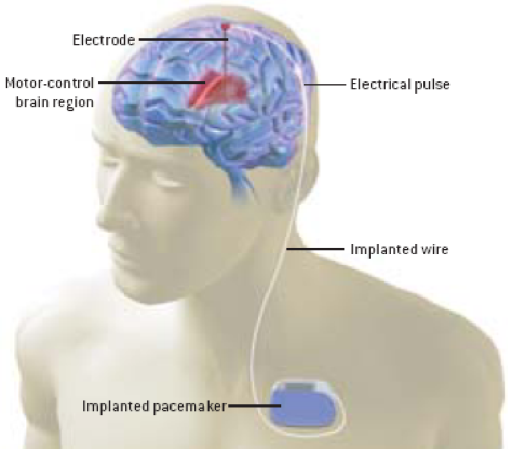
Motivation

- Pathological spiking synchrony
  - **Electrical Deep Brain Stimulation**
  - Parkinson's disease: tremors
  - Epilepsy: seizures
- Neuromuscular control
- Neural processing and computation



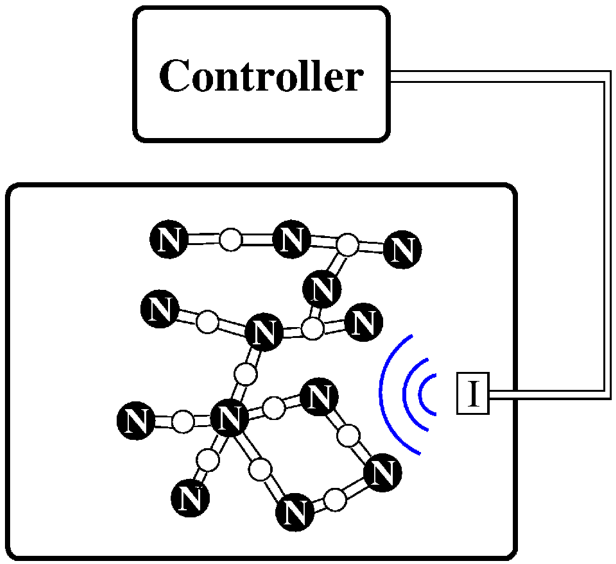




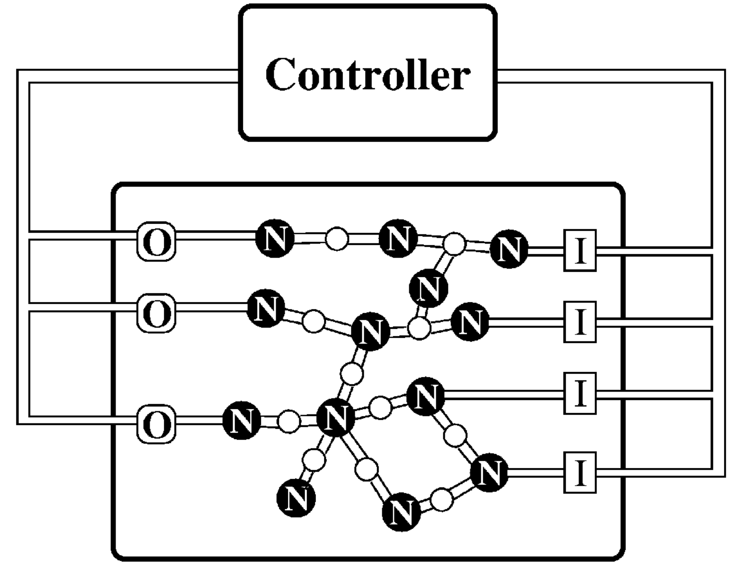
[Lynch & Popovic *CSM* '08]

[George '03]

EDBS – A Conceptual Overview



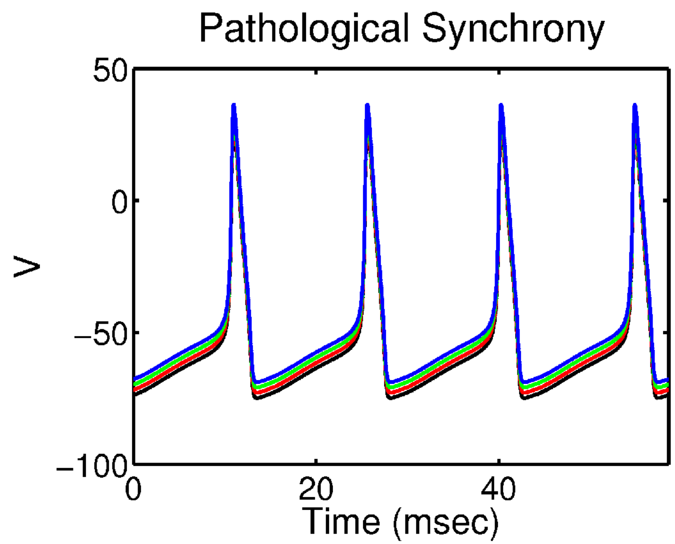
Current **open-loop** clinical implementation

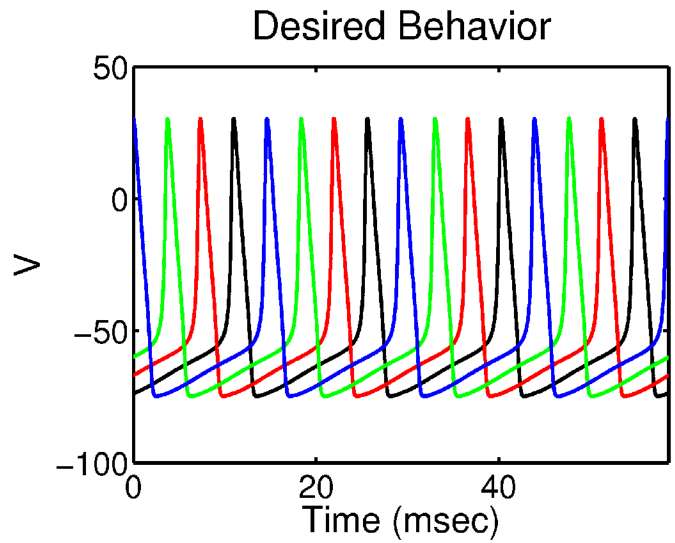


Proposed **feedback** architecture using micro-electrode arrays

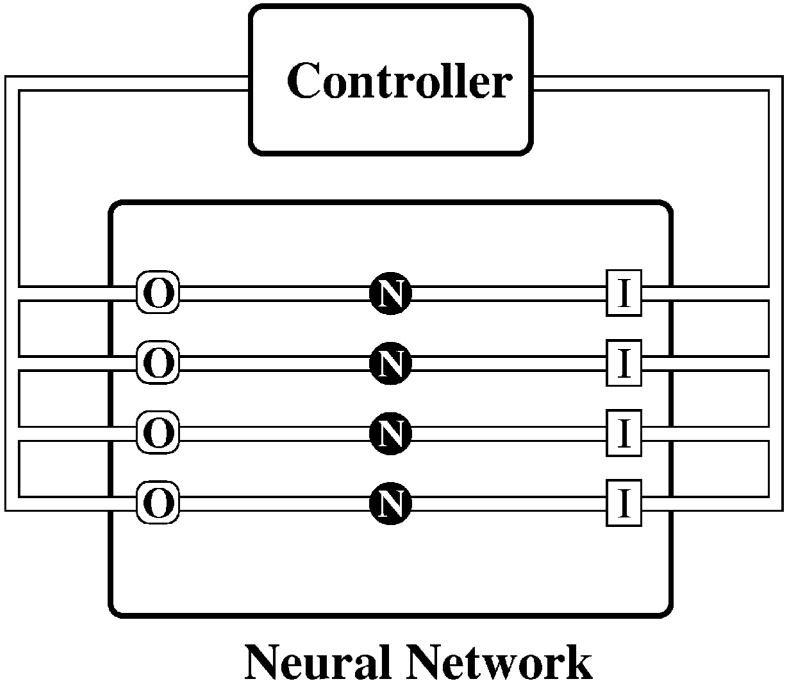
Challenges: **nonlinear** dynamics, limited **observability**, **constrained** control signals, unknown network **topology**

A Simplified Toy System





Objective – Desynchronize neural firing using minimal energy and maintaining charge balance.



Conductance-based Neuron Models

Hodgkin-Huxley: a prototypical neuron model

(Nobel prize 1963)

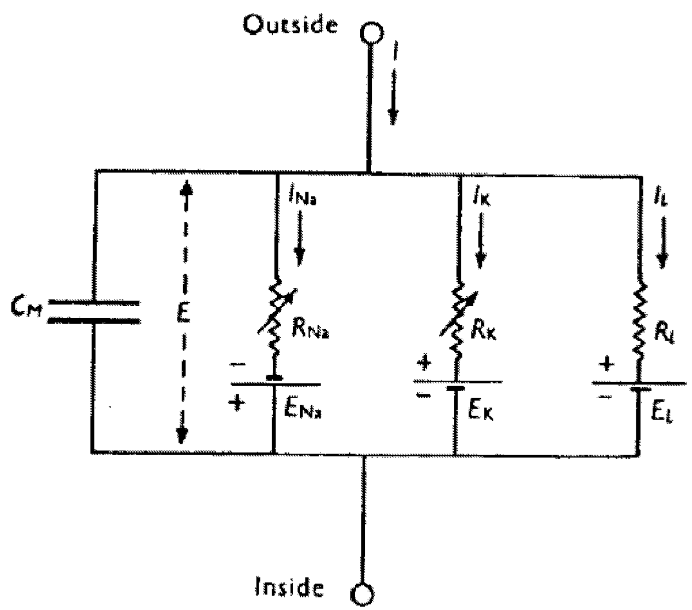
Additive control → $I(t)$

$$
\begin{aligned}
\dot{V} &= (I_b + I(t) - \bar{g}_{Na} h (V - V_{Na}) m^3 - \bar{g}_K (V - V_K) n^4 - \bar{g}_L (V - V_L))/C \\
\dot{m} &= a_m(V)(1-m) - b_m(V) m \\
\dot{h} &= a_h(V)(1-h) - b_h(V) h \\
\dot{n} &= a_n(V)(1-n) - b_n(V) n
\end{aligned}
$$

$$
\begin{aligned}
\alpha_m(V) &= 0.1(V+40)/(1-\exp(-(V+40)/10)) \\
\beta_m(V) &= 4\exp(-(V+65)/18) \\
\alpha_h(V) &= 0.07\exp(-(V+65)/20) \\
\beta_h(V) &= 1/(1+\exp(-(V+35)/10)) \\
\alpha_n(V) &= 0.01(V+55)/(1-\exp(-(V+55)/10)) \\
\beta_n(V) &= 0.125\exp(-(V+65)/80)
\end{aligned}
$$

[Adapted from Brown et al. '04]

Highly nonlinear, oscillatory when $I_b > 10\text{mA}$



[Hodgkin & Huxley '52]

State Feedback Linearization

Reference voltage: $V_r(t)$

Error: $e = V - V_r$

$$\dot{V} = I(t)/C + f_V(V, \mathbf{n})/C$$
$$\dot{\mathbf{n}} = f_{\mathbf{n}}(V, \mathbf{n})$$

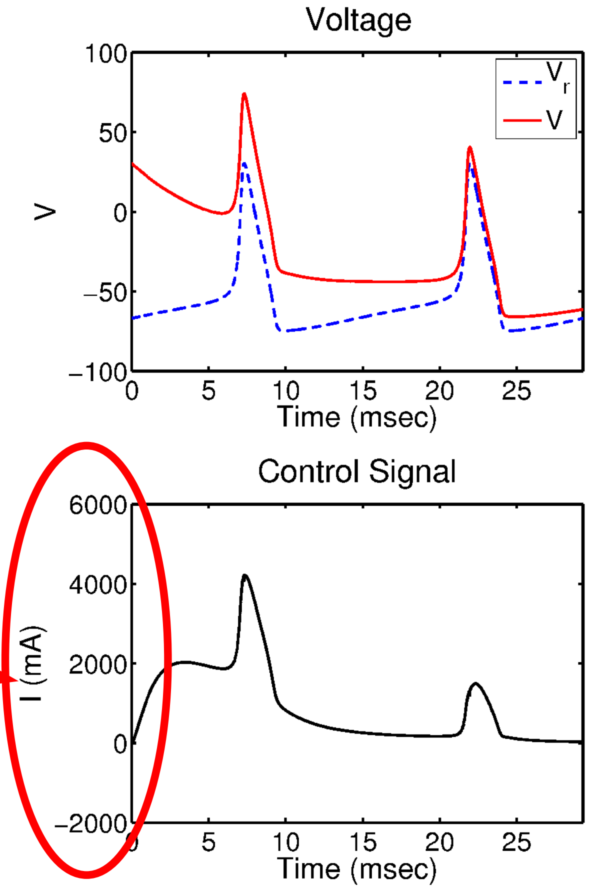
Not observable

Desired error dynamics

$\dot{e} = \gamma e$ achieved with

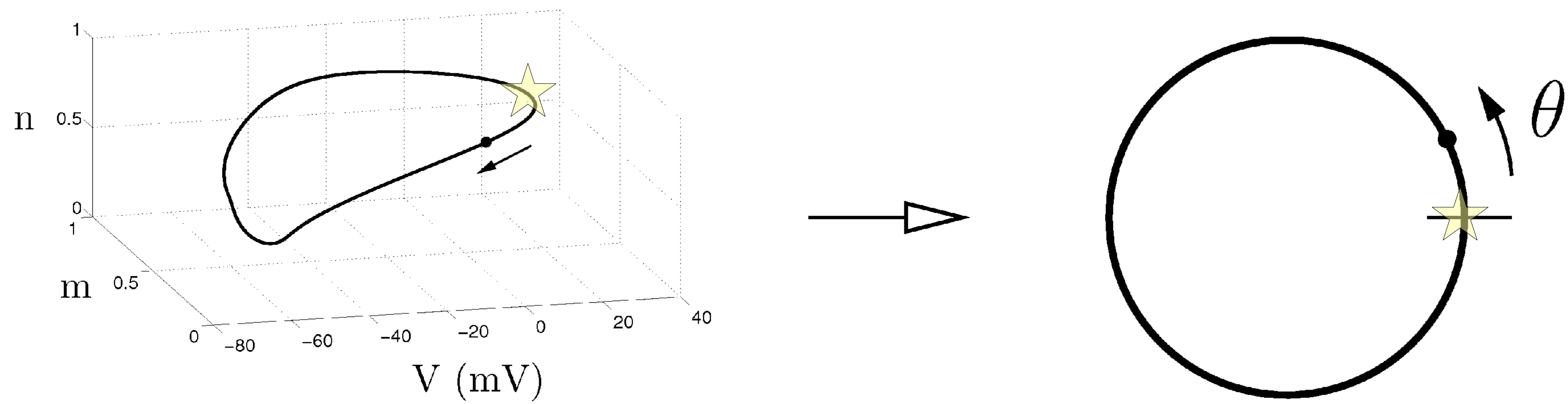
$$I(t, V, \mathbf{n}) = C(\gamma(V - V_r) + \dot{V}_r) - f_V(V, \mathbf{n})$$

Note scale!



For spiking neurons, $\dot{V}_r$ generates **very large** control signals! Can we design a **smarter** controller?

Phase reduction to 1-D per neuron



$$C\dot{V} = I_g(V, \mathbf{n}) + I_b + I(t)$$
$$\dot{\mathbf{n}} = \mathbf{G}(V, \mathbf{n})$$

$$V \in \mathbb{R}$$
$$\mathbf{n} \in [0, 1]^m$$

$$\dot{\theta} = \omega + \frac{I(t)Z(\theta)}{C}$$

$$u(t) \equiv I(t)/C$$
$$\theta \in [0, 2\pi)$$

Phase response curve

Standard form: $\dot{\theta} = \omega + Z(\theta)u(t)$

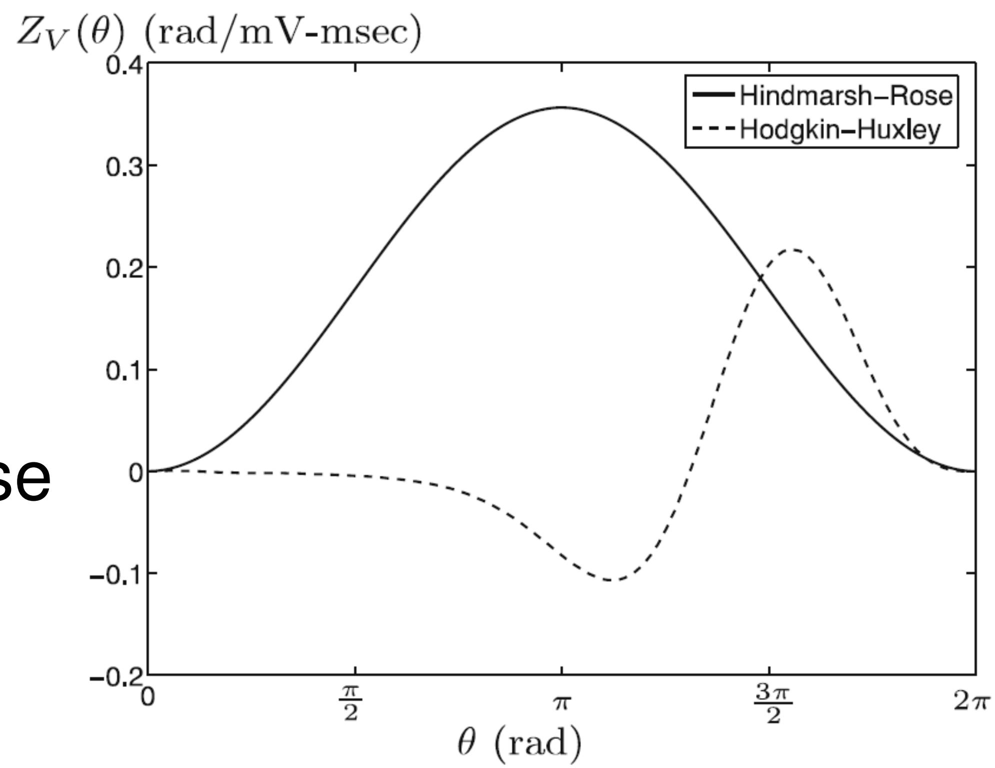
"Simple clocks" [A. Winfree, '80]

Phase Response Curves

- Computed Numerically
  - Solve adjoint equation e.g. [Ermentrout '02]
  - Response to small impulse

$$Z_V(\theta) \approx \frac{\Delta\theta}{\Delta V}$$

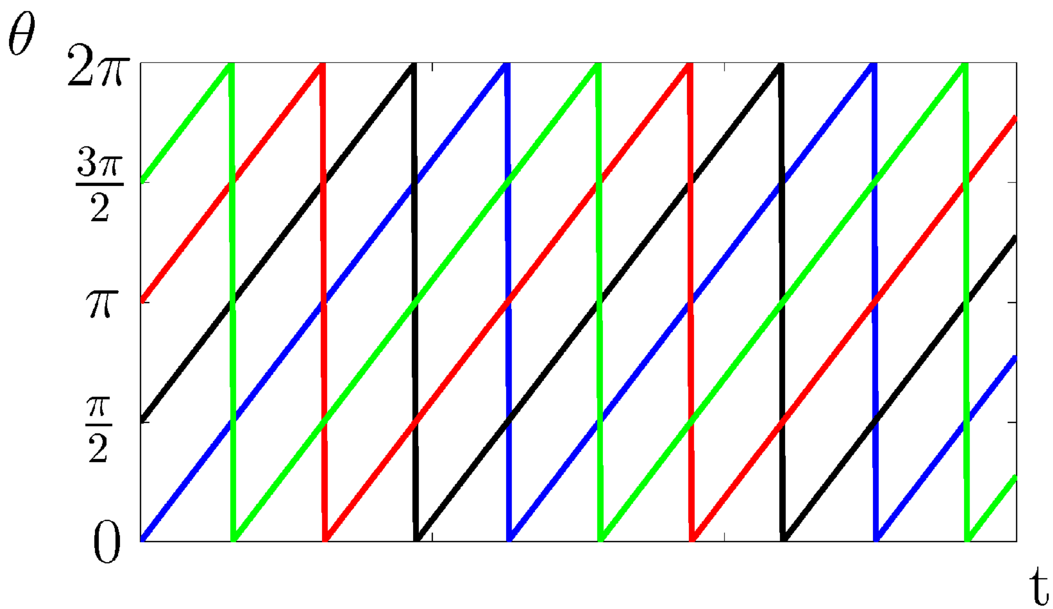
  - Type I: Hindmarsh-Rose
  - Type II: Hodgkin-Huxley

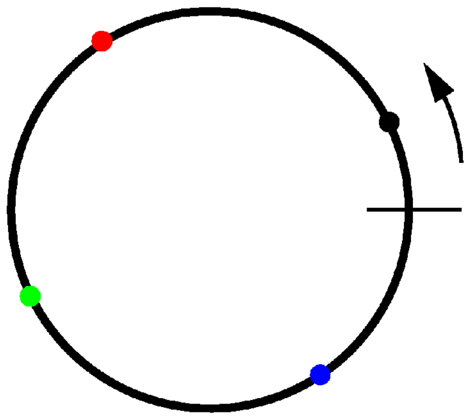


[P.D. et al. *JCNS* '08]

$$\dot{\theta} = \omega + Z_V(\theta)u(t)$$

Phase Desynchronization (Balancing)





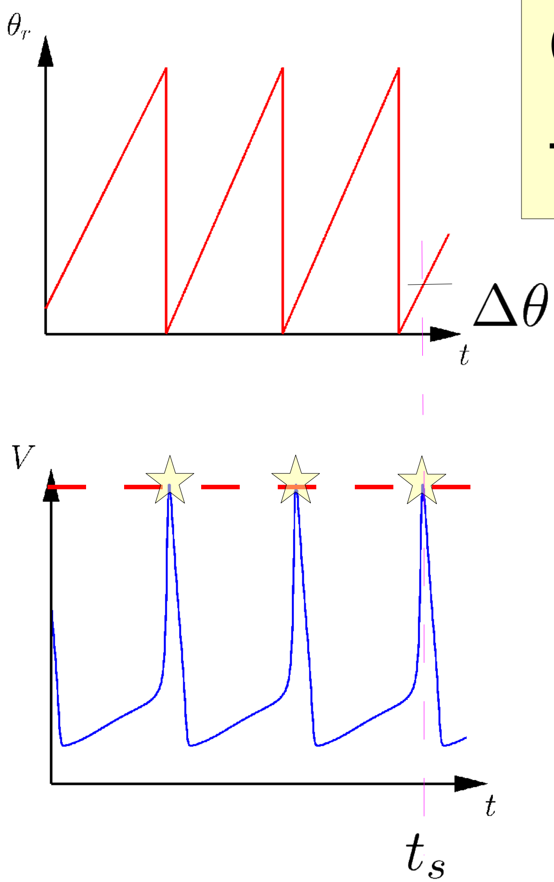
Order parameter [Kuramoto '84]: $r(t)e^{\sqrt{-1}\psi(t)} = \frac{1}{N}\sum_{i=0}^{N} e^{\sqrt{-1}\theta_i(t)}$

Control $|r(t)| \rightarrow 0$ by driving each θ_j to $\theta_{rj} = \omega t + \frac{2\pi(j-1)}{N}$

Challenge: θ_j is only observable when the neuron j spikes

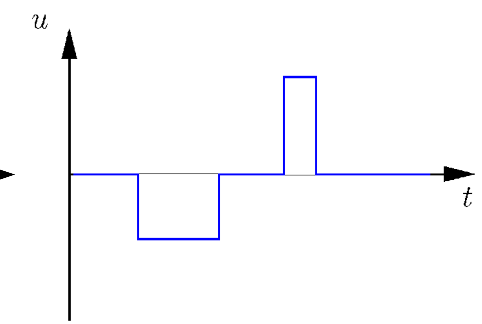
Event-Based Control

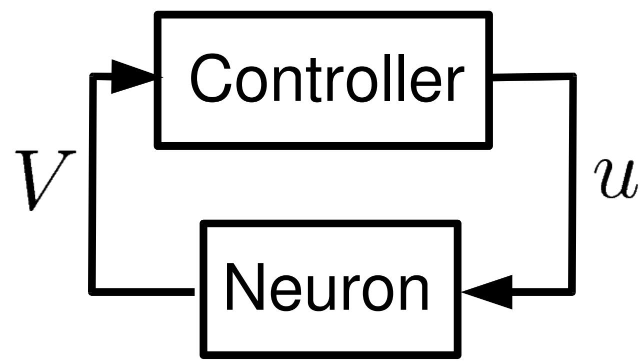
Open-loop variable waveform triggered by voltage spike



$\Delta\theta$
t_s

$$u(t) = f(\Delta\theta, t_s)$$

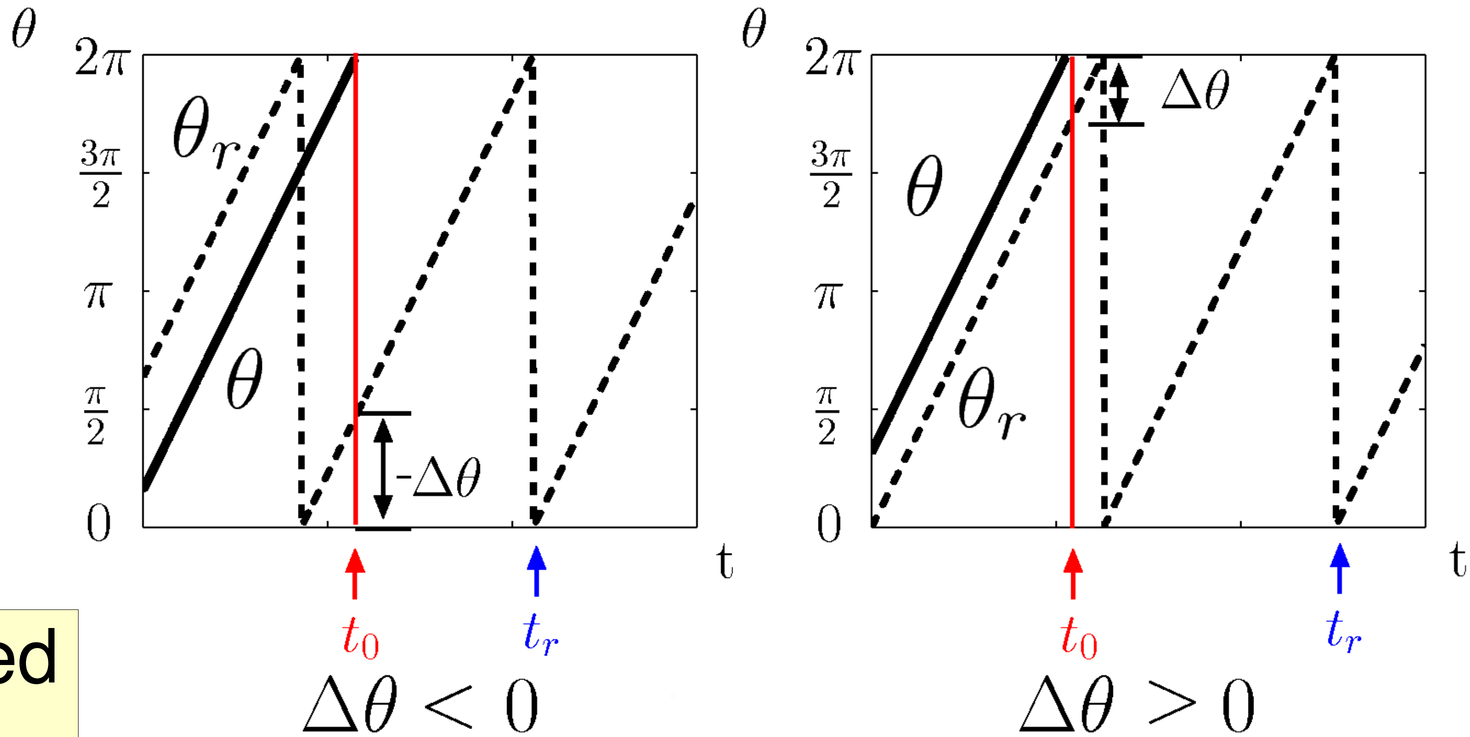




Constraint:
Charge Balance

e.g. [Åström & Bernhardsson '02]

Reference Trajectories and Errors



speed up

slow down

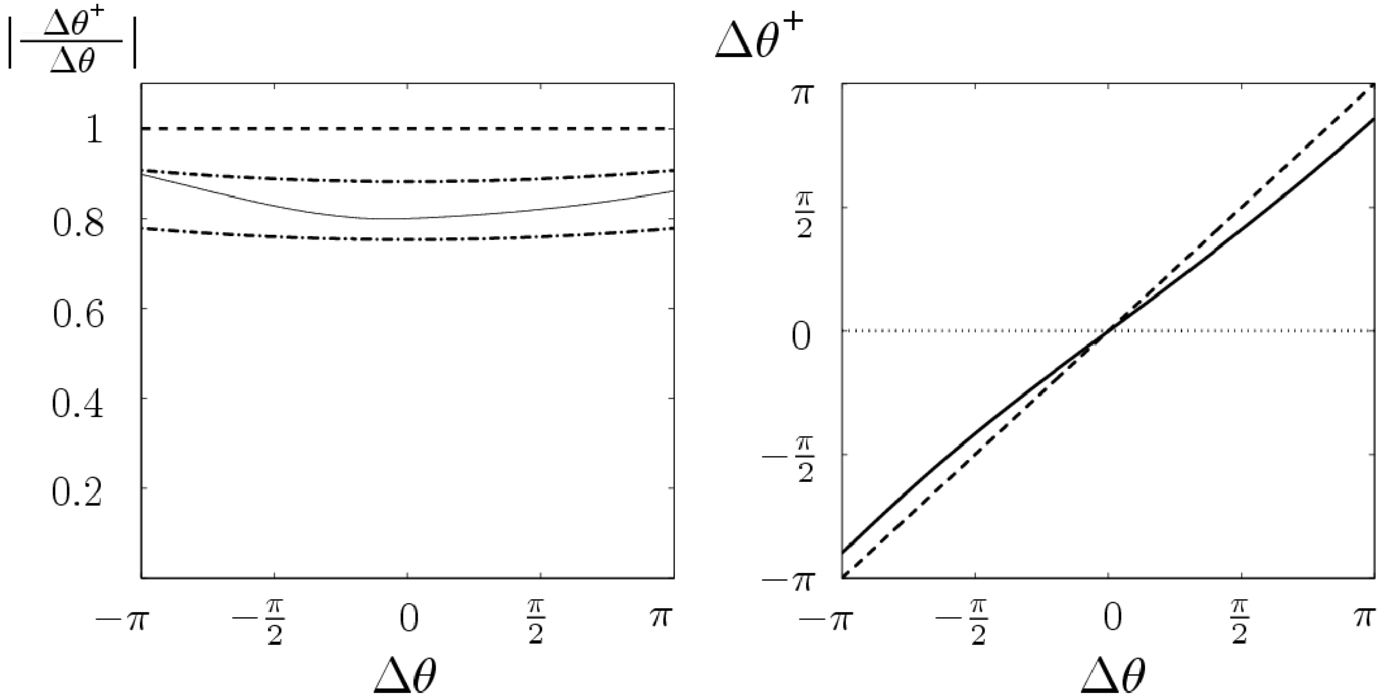
Phase wrapping function:

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

Control Objective – Reference Tracking

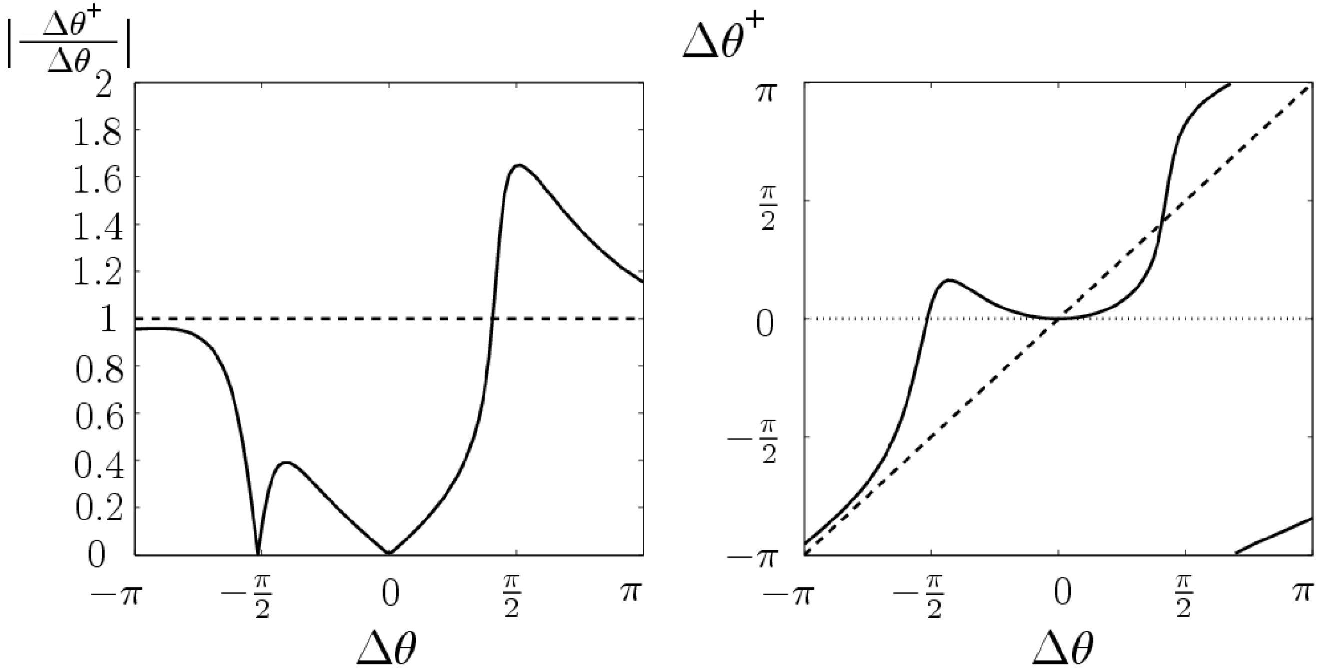
- Define discrete phase errors at concurrent event times
  - $\Delta\theta$:= the phase error at the initial spike event
  - $\Delta\theta^+$:= the phase error at the subsequent spike event
- **Global convergence** $\Leftrightarrow$ the $\Delta\theta \mapsto \Delta\theta^+$ map has a globally attracting fixed point at zero
  - globally, in the sense of **full measure** over $[-\pi, \pi)$
- **Global monotonic convergence** $\Leftrightarrow$ $\left|\frac{\Delta\theta^+}{\Delta\theta}\right| \leq 1$

Global Monotonic Convergence Example



- Oscillator simulation results from an early controller developed using asymptotics for a simplified Type II PRC [P.D. & J. Moehlis *CDC* '07]
  - Convergence is **global** and **monotonic**

Global Convergence Example



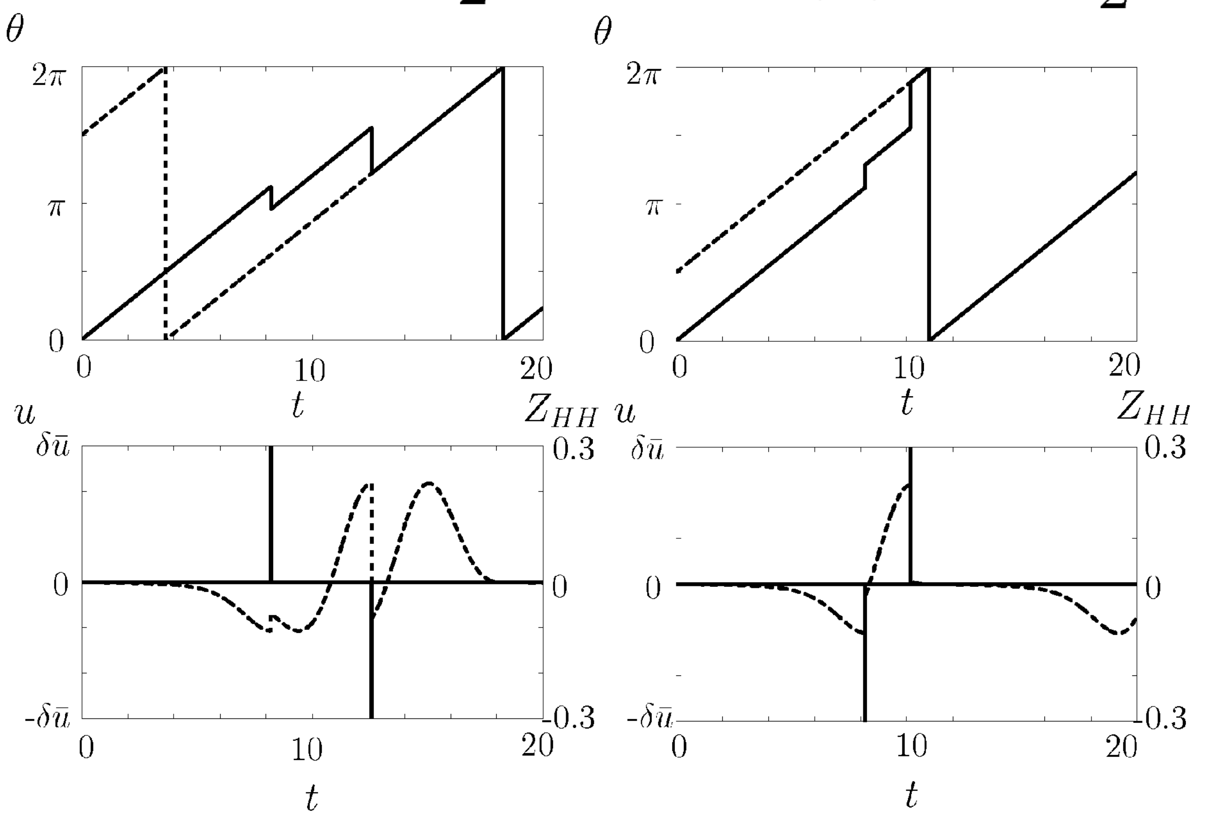
- Oscillator simulation results from an early heuristic controller for Hodgkin-Huxley [P.D. & J. Moehlis *CDC* '07]
  - Global convergence but **not** monotonic
  - No considerations of optimality: **can we do better?**

Impulsive Spike Timing Control

$$
\begin{aligned}
u(t) &= \tilde{u}(\delta(t-t_1)-\delta(t-t_2)) \\
\tilde{u} &= \frac{(1-K)\Delta\theta}{Z_{\max}-Z_{\min}} \\
t_1 &= \frac{\alpha}{\omega} \\
t_2 &= \frac{1}{\omega}(\beta + Z_{\min}\tilde{u})
\end{aligned}
$$

$$
\begin{aligned}
Z_{\min} &= \min(Z(\theta)) = Z(\alpha) \\
Z_{\max} &= \max(Z(\theta)) = Z(\beta)
\end{aligned}
$$

$\Delta\theta(0) = \frac{\pi}{2}$ $\qquad$ $\Delta\theta(0) = -\frac{\pi}{2}$



Fact: This control law reduces the phase error to zero, and is $\mathcal{L}_1$-optimal for the unconstrained case.

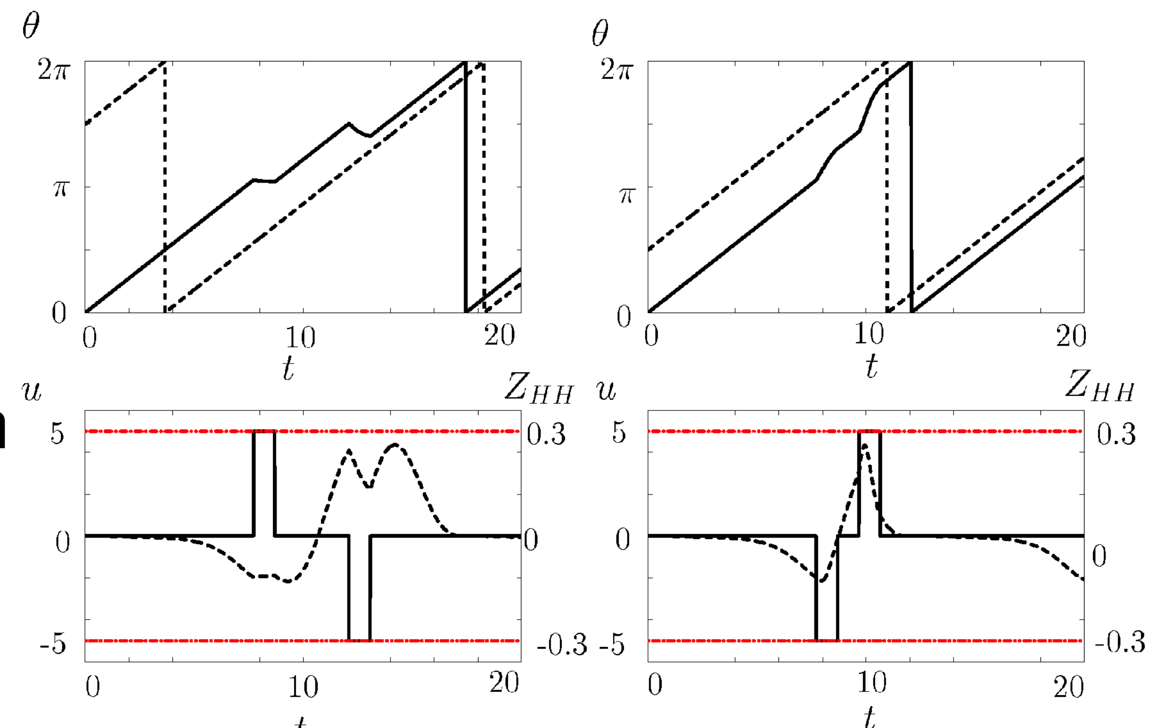
Problem: Control spikes may be much too large.

Quasi-Impulsive Control

$$u(t) = \begin{cases} 0 & , \quad \text{for} \quad 0 \le t < t_A \\ \text{sgn}(\Delta\theta)\bar{C} & , \quad \text{for} \quad t_A \le t < t_B \\ 0 & , \quad \text{for} \quad t_B \le t < t_C \\ -\text{sgn}(\Delta\theta)\bar{C} & , \quad \text{for} \quad t_C \le t < t_D \\ 0 & , \quad \text{for} \quad t_D \le t \end{cases}$$

$$\begin{aligned} t_A &= t_1 - \left|\frac{\tilde{u}}{2\bar{C}}\right| \\ t_B &= t_1 + \left|\frac{\tilde{u}}{2\bar{C}}\right| \\ t_C &= t_2 - \left|\frac{\tilde{u}}{2\bar{C}}\right| \\ t_D &= t_2 + \left|\frac{\tilde{u}}{2\bar{C}}\right| \end{aligned}$$

- In practice, we have magnitude limits
  - $|u(t)| \le \bar{C}$
  - Use non-zero-duration waveforms
  - Desired correction factor: $\Delta\theta^+ = K\Delta\theta$



$\Delta\theta(0) = \frac{\pi}{2}$ $\qquad$ $\Delta\theta(0) = -\frac{\pi}{2}$

Well-Posedness I

Condition	Minimum admissible correction factor K_{min}
$0 < \theta(t_1^+)$	$1 + \frac{\alpha(Z_{max} - Z_{min})}{\pi Z_{min}}$
$\theta(t_1^+) < \gamma$	$1 + \frac{(\gamma - \alpha)(Z_{max} - Z_{min})}{\pi Z_{min}}$
$\gamma < \theta(t_2^+)$	$1 - \frac{(\beta - \gamma)(Z_{max} - Z_{min})}{\pi Z_{max}}$
$\theta(t_2^+) < 2\pi$	$1 - \frac{(2\pi - \beta)(Z_{max} - Z_{min})}{\pi Z_{max}}$

Given a Type II phase response curve, our correction factor K must satisfy $K \geq K_{min}$, given above.

Well-Posedness II

Condition	Minimum admissible control magnitude C_{min}
$0 < t_A$	$\frac{\omega\pi(1-K)}{2\alpha(Z_{max}-Z_{min})}$
$t_B < t_C$	$\max_{\Delta\theta\in(-\pi,\pi]}\left(\frac{\omega\Delta\theta(1-K)}{(\beta-\alpha)(Z_{max}-Z_{min})-Z_{min}(1-K)\Delta\theta}\right)$
$\theta(t_B) < \gamma$	$\max_{\Delta\theta\in(-\pi,\pi]}\left(\frac{-\omega(1-K)\Delta\theta}{2[(\gamma-\alpha)(Z_{max}-Z_{min})-Z_{min}(1-K)\Delta\theta]}\right)$
$\theta(t_C) > \gamma$	$\frac{\omega\pi(1-K)}{2(\beta-\gamma)(Z_{max}-Z_{min})}$
$\theta(t_D) < 2\pi$	$\max_{\Delta\theta\in(-\pi,\pi]}\left(\frac{-\omega(1-K)\Delta\theta}{2[(2\pi-\beta)(Z_{max}-Z_{min})+Z_{max}(1-K)\Delta\theta]}\right)$

Given a desired correction factor K, it is only achievable if $\bar{C} \geq C_{min}$ given above.

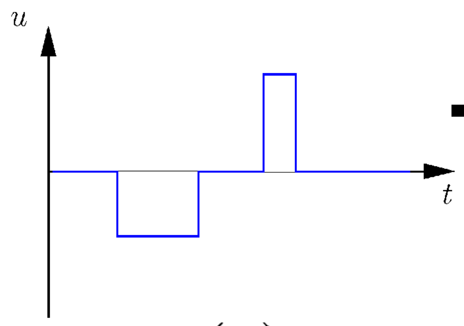
Controller Performance Validation

Impulsive control is **exact**, but the quasi-impulsive approximation must be checked:

- We have proven convergence for phase oscillators
  - But how close is its performance to the desired K ?
- Will it work for the full-dimensional Hodgkin-Huxley system?
  - How to initialize and extract phase?

We will simulate using $K = 0.7$ and $\bar{C} = 1.7\text{mA}$

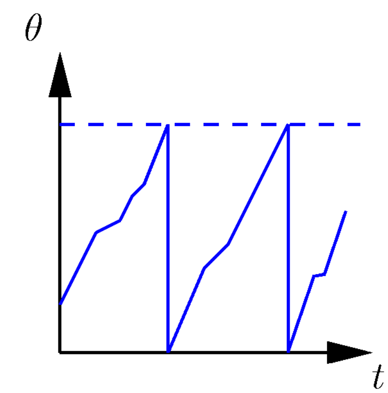
Computational Considerations:
State Vector ⇨ Phase Mapping



$I(t)$

$$(\dot{V}, \dot{n})^T = F(V, n, I(t))$$

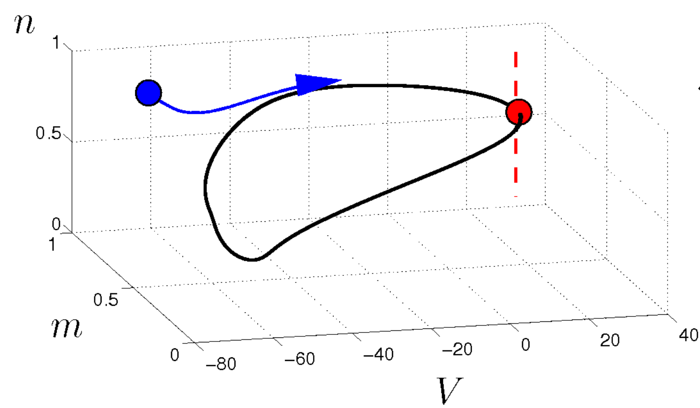
$$(V, n)^T \mapsto \theta$$



$\theta(t)$

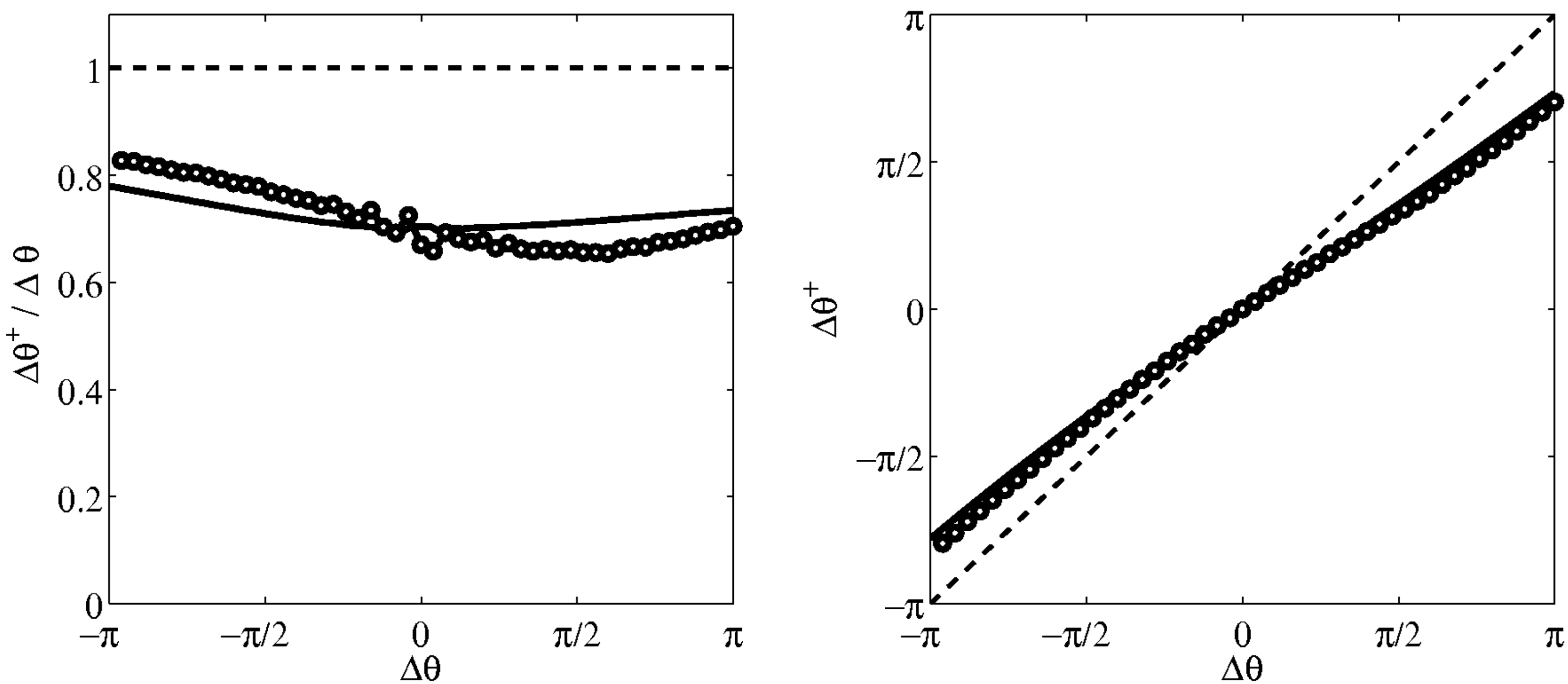
$(V, n)^T$

T_s



Details available in
[P.D. et al. *JCNS* '08]

Quasi-Impulsive Control
Global Monotonic Convergence



Solid: simulation data for phase-reduced models

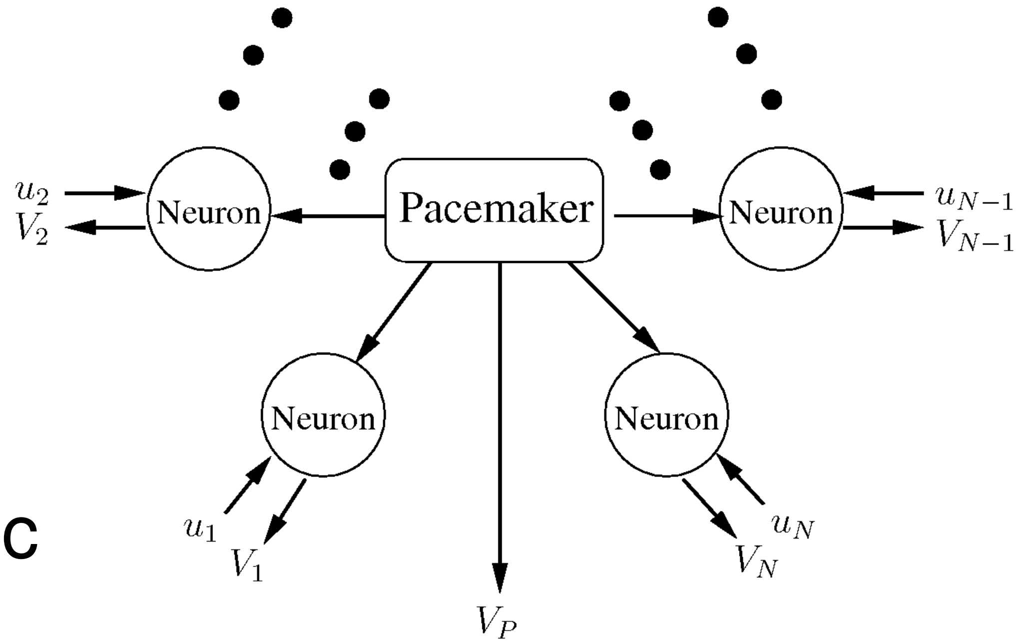
Dashed: stability limits

Circles: simulation data for conductance-based models (50 points)

Current Research:

Pacemaker-Driven Neural Population

- A natural extension of our event-based single neuron control
- All neurons are stimulated by an uncontrollable periodic pacemaker spike



  - Estimate future pacemaker spikes with an observer
  - Use 3 impulses: 2 to correct phase error, 1 to null out the pacemaker. Impose the charge-balance constraint.

Desynchronizing a Pacemaker-Driven Neural Network

- Here, we're getting closer to the real pathology
  - In absence of control we get synchrony
  - With our control we asymptotically go towards desynchronized spike times.
- Preliminary simulation results are encouraging
  - There exist parameter sets that give global asymptotic convergence
  - Is not sensitive to small noise in the pacemaker

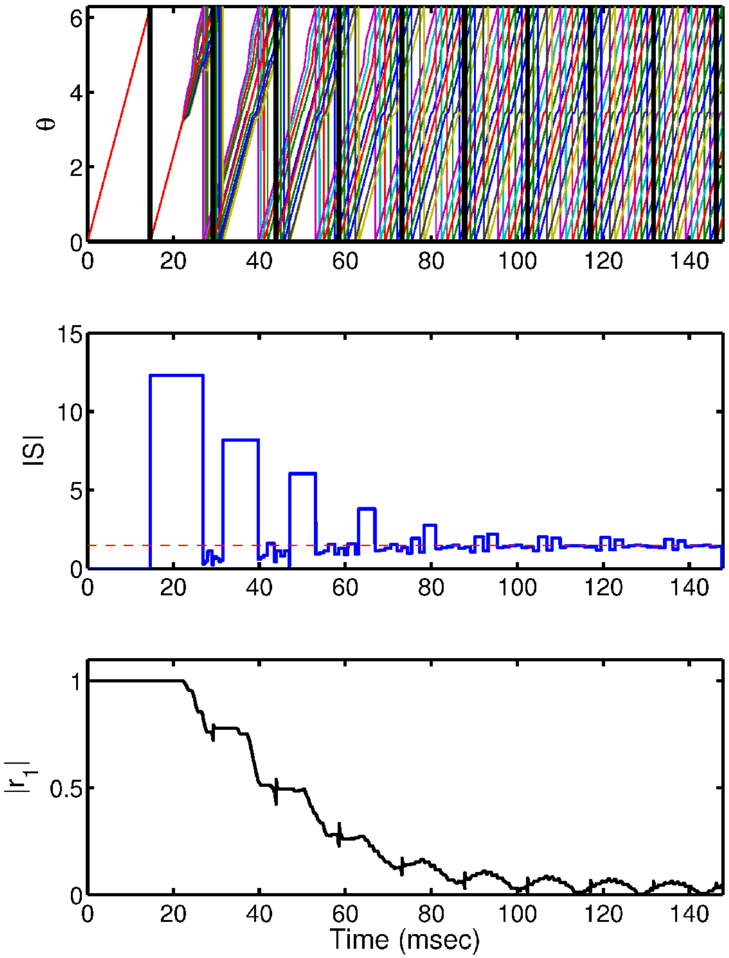
Impulsive Pacemaker Control

- Purely impulsive case gives an exact solution:
  - Now we have 3 spikes

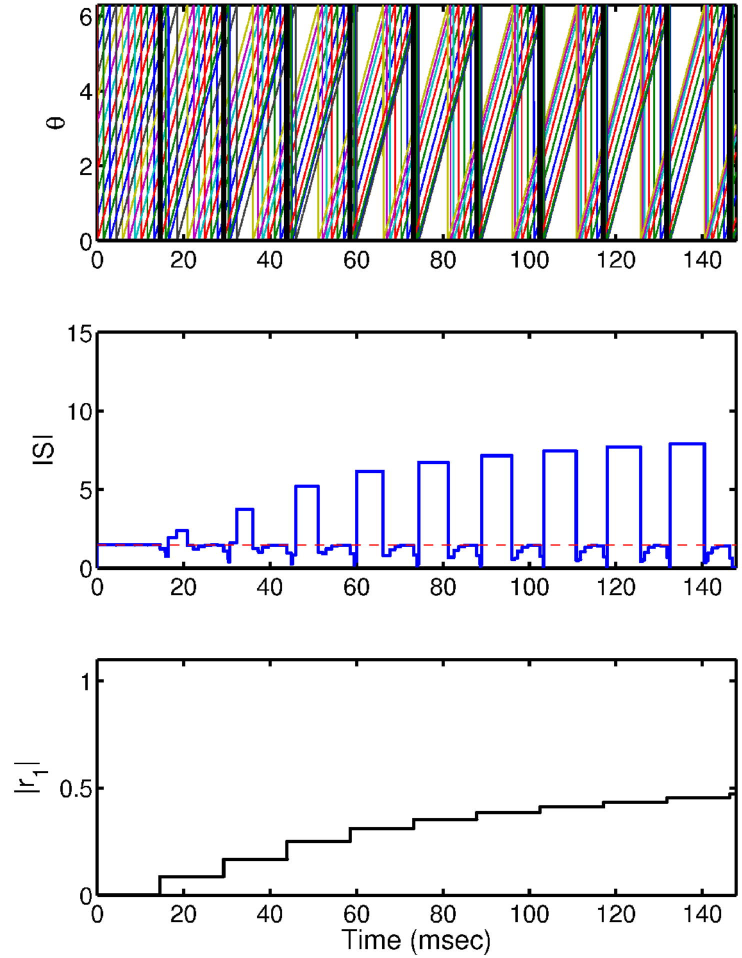
$$
\begin{aligned}
u_i(\tilde{t}_i) &= \bar{u}_{i,1}\delta(\tilde{t}_i - t_{i,1}) - K_P\delta(\tilde{t}_i - \tilde{t}_P^+) + \bar{u}_{i,2}\delta(\tilde{t}_i - t_{i,2}) \\
t_{i,1} &= \frac{\alpha}{\omega} \\
t_{i,2} &= \frac{\beta}{\omega} - \frac{Z_{min}(K_P Z_{max} + (1-K_e)\Delta\theta_i)}{\omega(Z_{max} - Z_{min})} \\
\bar{u}_{i,1} &= \frac{K_P Z_{max} + (1-K_e)\Delta\theta_i}{Z_{max} - Z_{min}} \\
\bar{u}_{i,2} &= \frac{-(\Delta(1-K_e)\theta_i + K_P Z_{min})}{Z_{max} - Z_{min}}
\end{aligned}
$$

  - $\tilde{t}_i$ time since neuron i last spiked
  - $\tilde{t}_P^+$ is the predicted time of the next pacemaker spike

Bounded Quasi-Impulsive Control: Preliminary Simulation Results

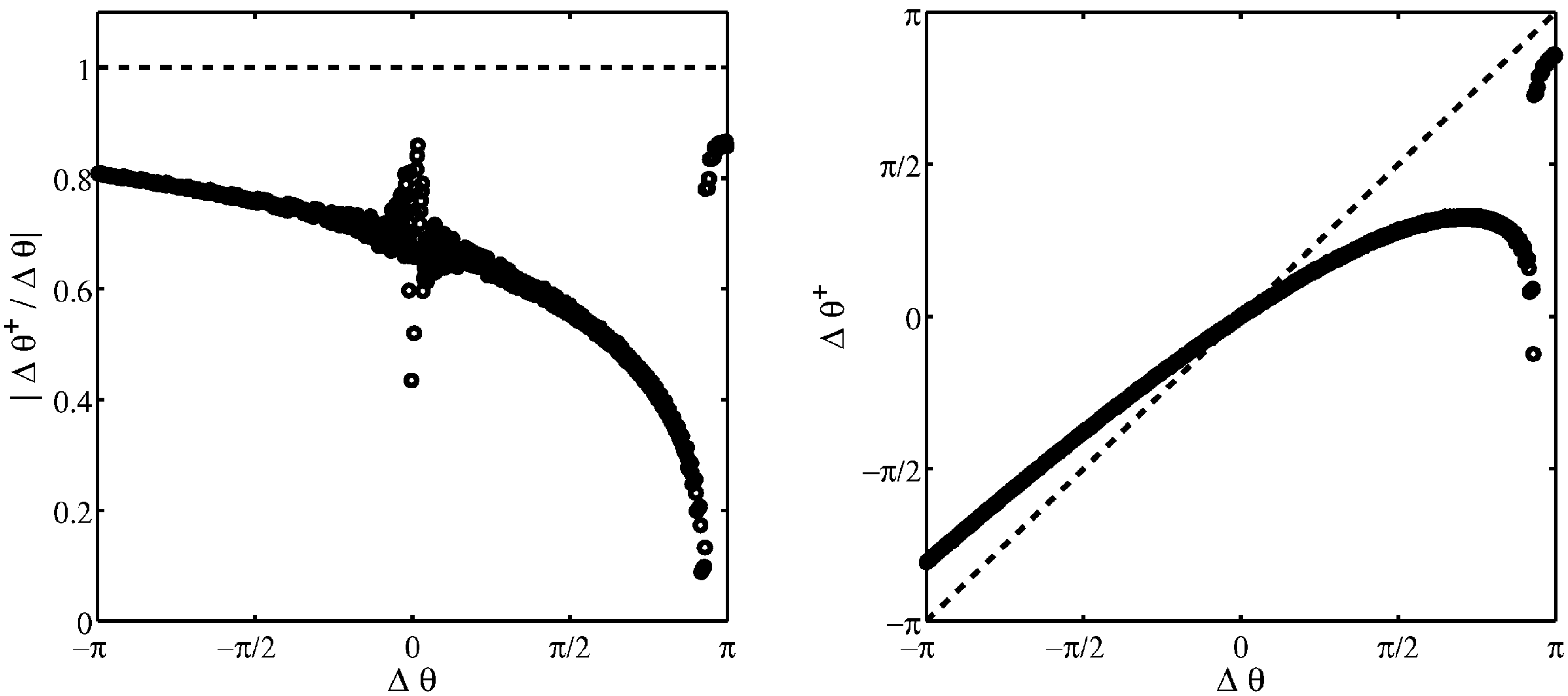


De-synchronization with control



Synchronization without control

Global Monotonic Convergence



1000 simulations on the full-dimensional neuron models with $K_e = 0.7$, $\bar{C} = 2$, and $K_P = 1$ shows global monotonic convergence

Summary

- Neurons as nonlinear oscillators
  - Phase reduction and phase response curves
- Single neuron spike timing control
  - Objective: spike periodically with given phase
  - Constraints: $|u(t)| \leq \bar{C}$ and $\int_{t^*}^{t^*+T} u(t)dt = 0$
- Future work: non-trivial network topologies
  - Pacemaker-driven populations
  - Biological architectures