Nonlinear Dynamics of Cellular and Network Excitability and Oscillations

John Rinzel

Computational Modeling of Neuronal Systems
Fall 2007

- Wilson-Cowan ('72) – rate model for excitatory/inhibitory popul'ns.
- Firing rate model for binocular rivalry – competing inhibitory popul'ns + adaptation.
- Rhythms in developing spinal cord -- "excitatory" popul'n, + synaptic depression.

See review chapters: JR w/ B Ermentrout, 1998
Borisyuk w/ JR, 2005

Firing rate model (Amari-Wilson-Cowan) for dynamics of excitatory-inhibitory populations.

$$\tau_e \, dr_e/dt = -r_e + S_e(a_{ee} \, r_e - a_{ei} \, r_i + I_e)$$

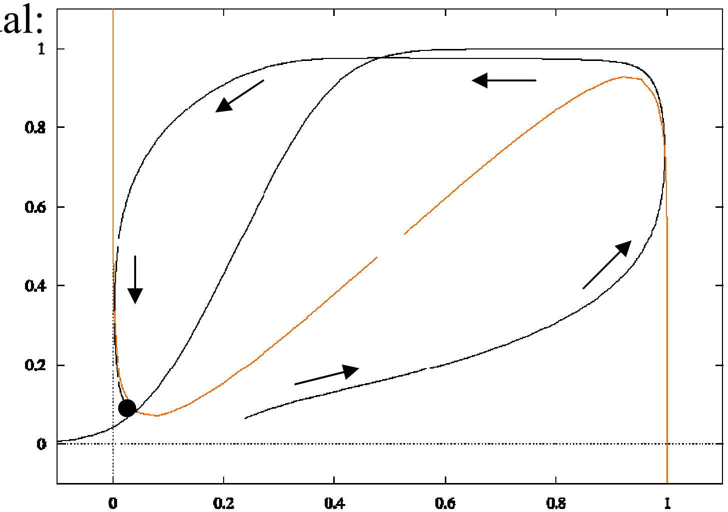
$$\tau_i \, dr_i/dt = -r_i + S_i(a_{ie} \, r_e - a_{ii} \, r_i + I_i)$$

Wilson HR, JD Cowan. Excitatory and inhibitory interactions in localized populations of model neurons. Biophys J 12:1-22, 1972.

$r_i(t)$, $r_e(t)$ -- average firing rate (across population and "over spikes")

τ_e , τ_i -- "recruitment" time scale

S_e(input) , S_i(input) – input/output relations – typically sigmoidal:
$S(x)=1/[1+\exp((\theta-x)/k)]$ where
θ – "threshold"; k -- steepness (steeper for smaller k).

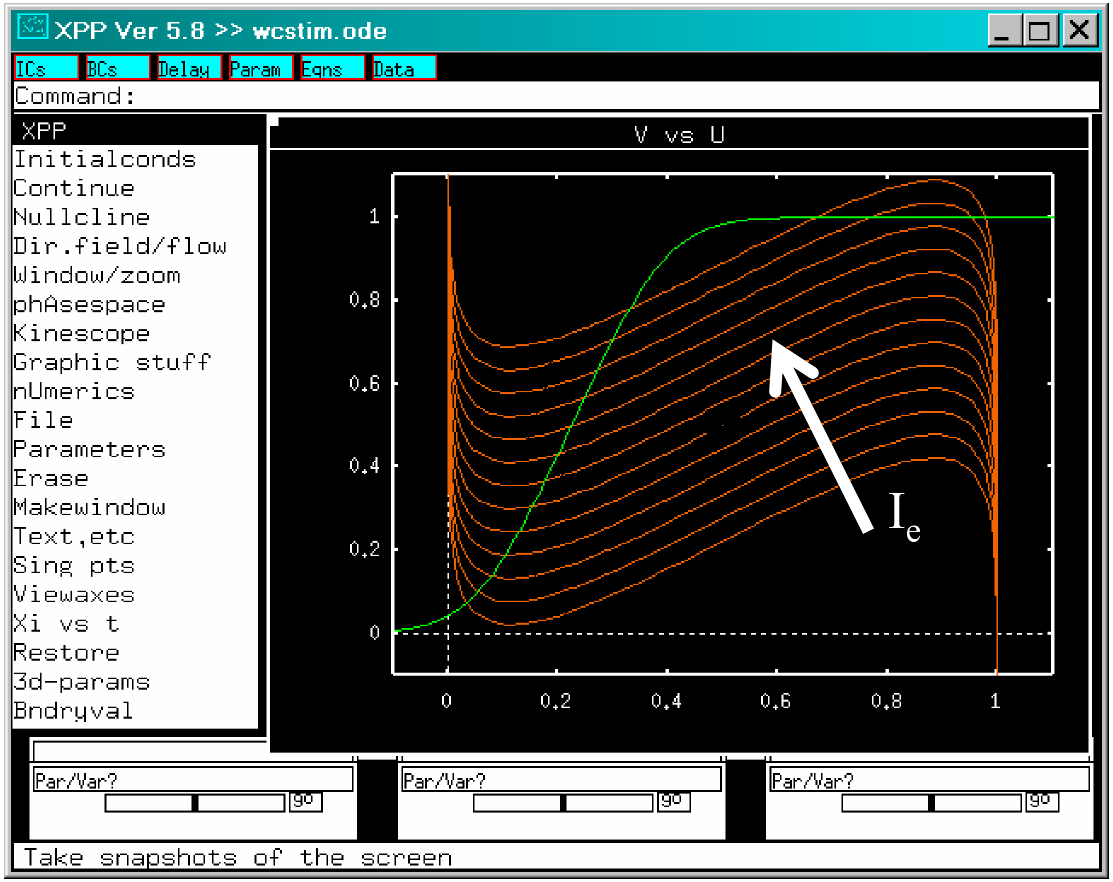


a_{ee} etc – "synaptic weights"

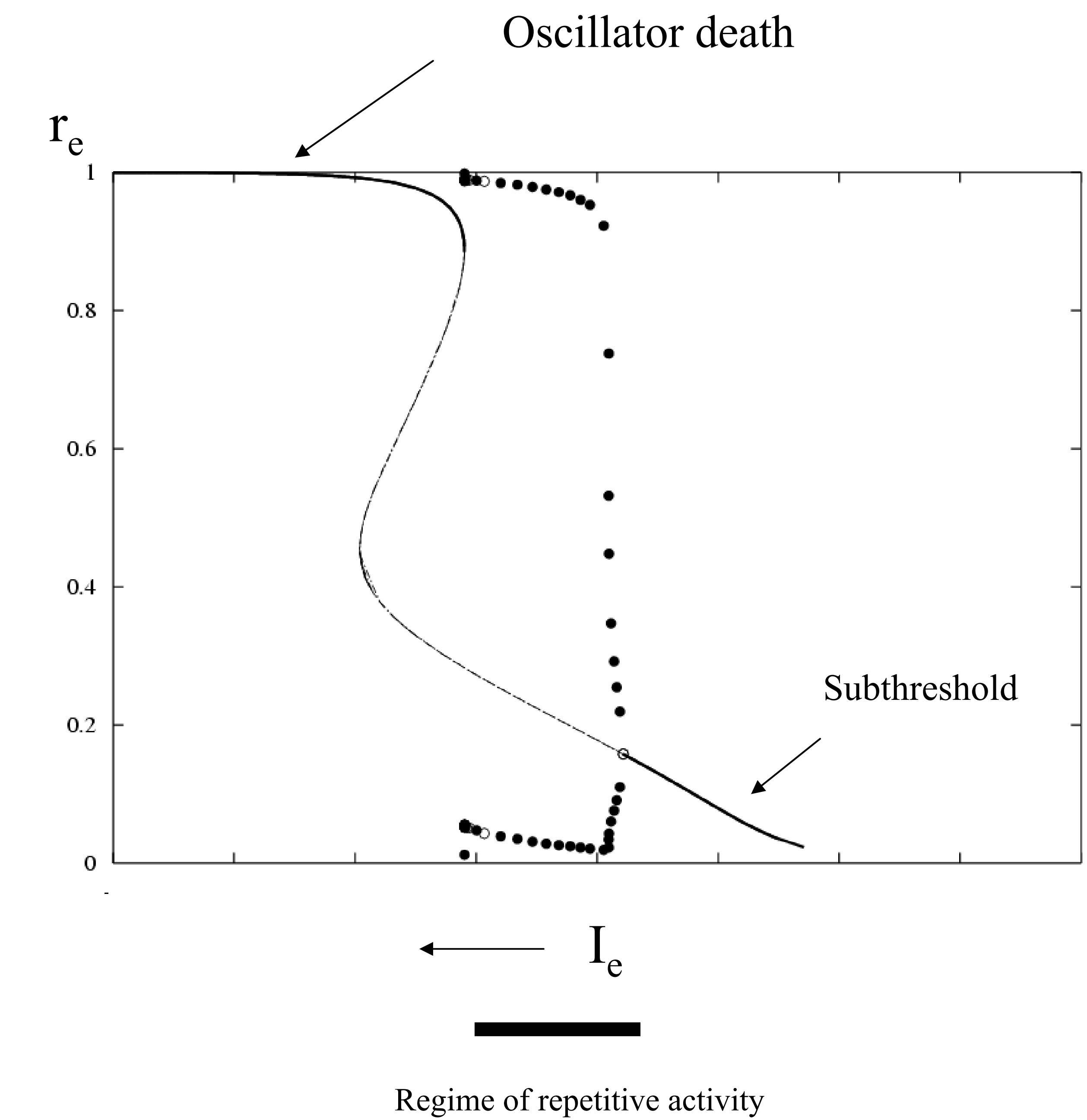
Network has no spatial structure;
cells are random and sparsely connected.

What are τ_e and τ_i?
JR: recruitment time constants for the network.

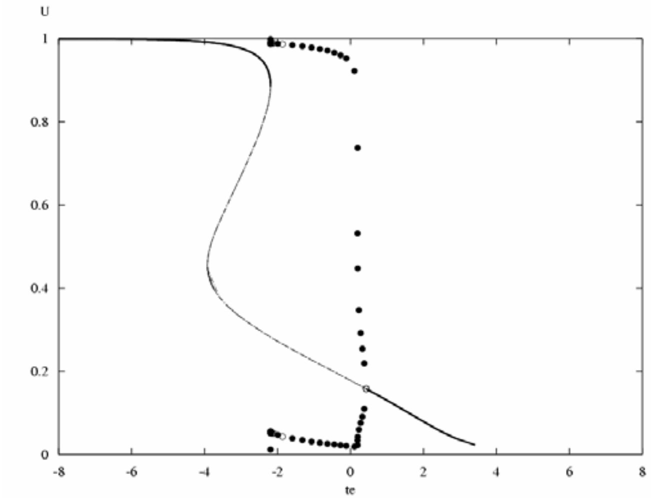
Wilson-Cowan Model
dynamics in the phase plane.



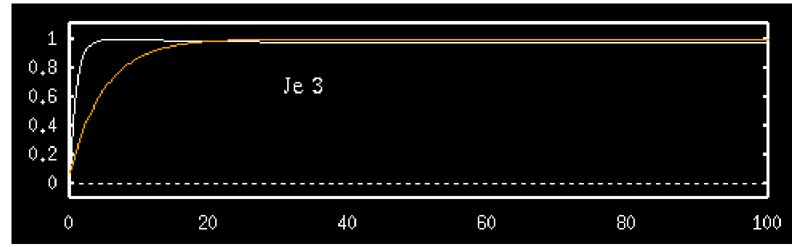
Phase plane, nullclines for range of J_e.

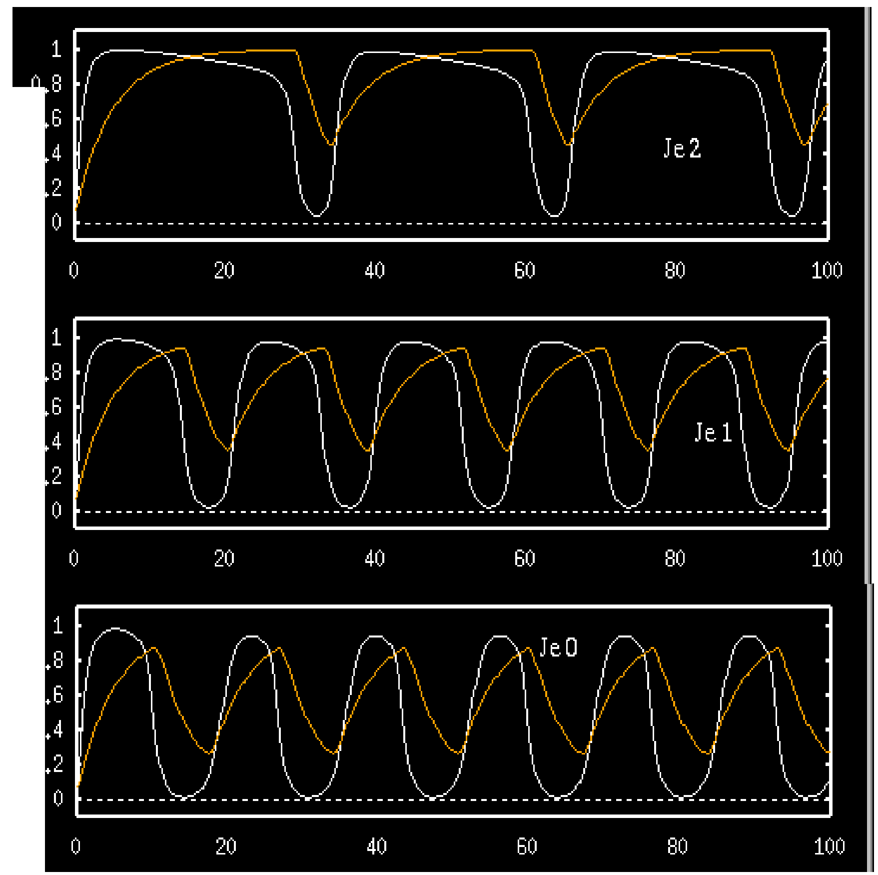


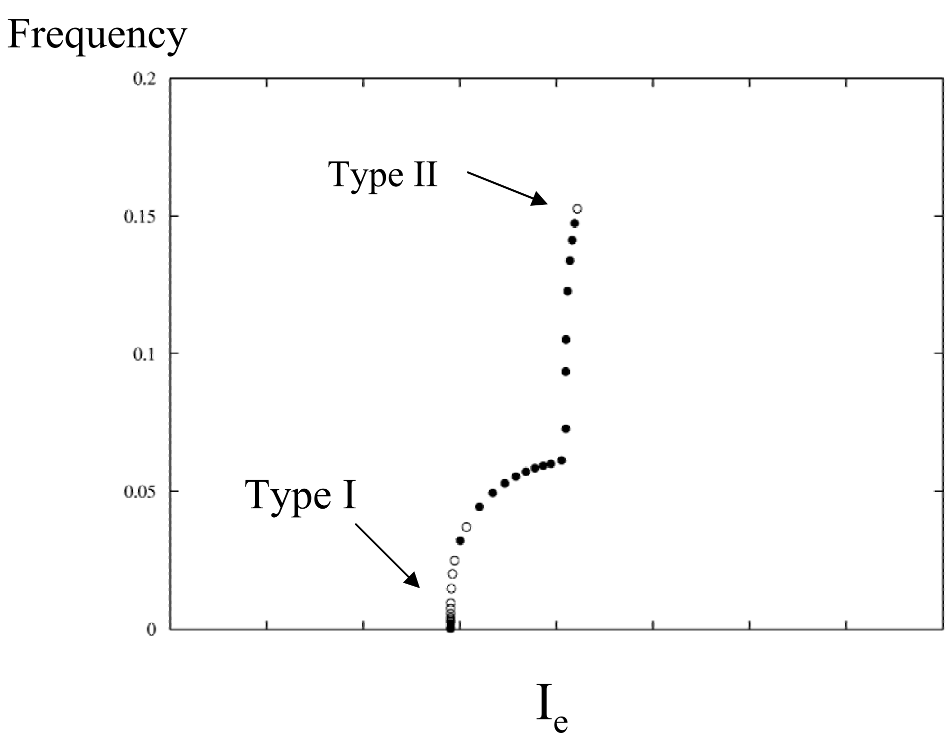
Oscillator death
r_e
1
0.8
0.6
0.4
0.2
0
Subthreshold
I_e
Regime of repetitive activity



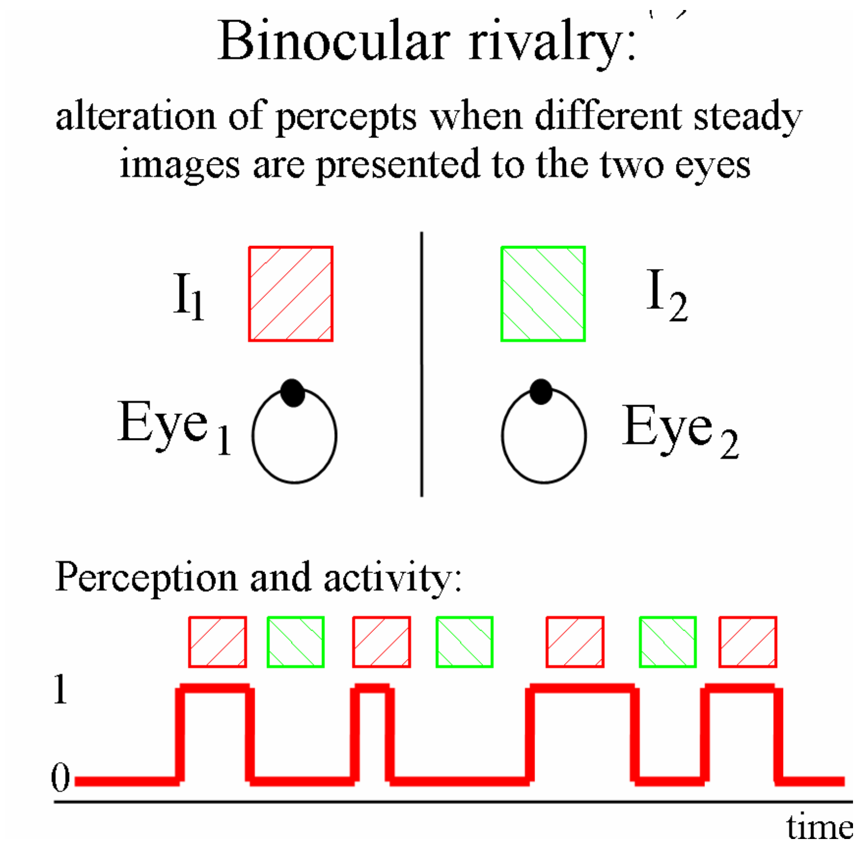
"Oscillator Death" but cells are firing



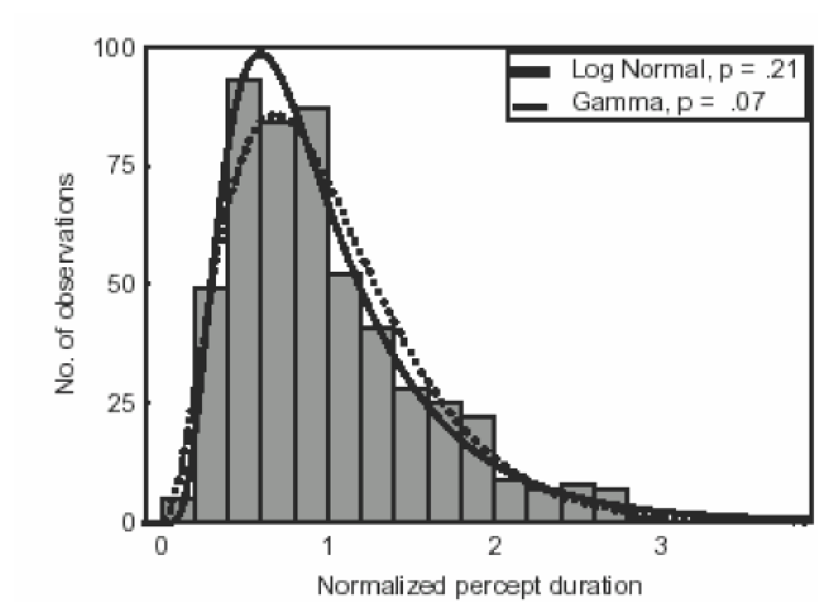




Dynamics of Perceptual Bistability



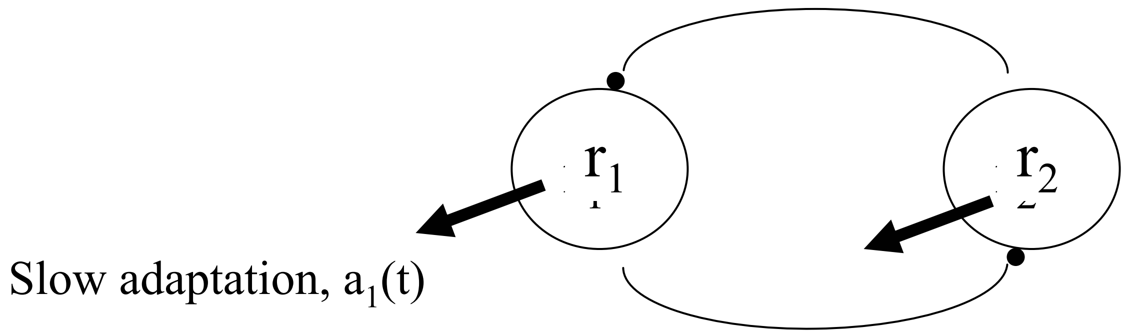
Mutual inhibition with slow adaptation ➔ alternating dominance and suppression



w/ N Rubin, A Shpiro, R Curtu, R Moreno

Idealized Models for Binocular Rivalry

Two mutually inhibitory populations, corresponding to each percept.
Firing rate model: $r_1(t)$, $r_2(t)$
Slow negative feedback: adaptation or synaptic depression.



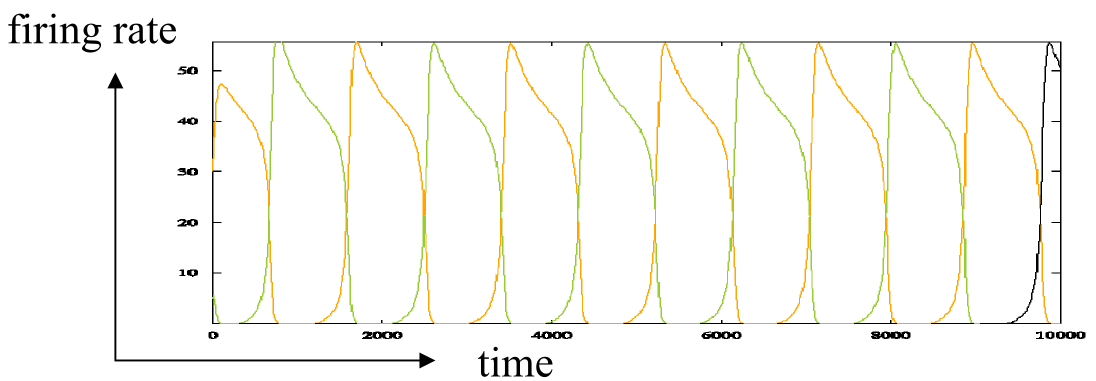
Wilson; Laing and Chow

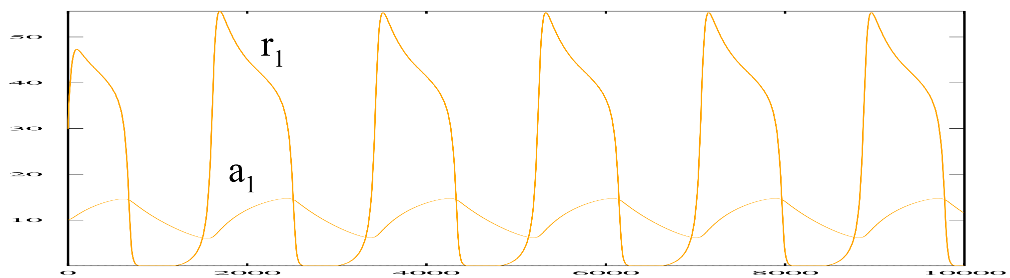
$$\tau\, dr_1/dt = -r_1 + f(-\beta r_2 - \varphi\, a_1 + I_1)$$
$$\tau_a\, da_1/dt = -a_1 + f_a(r_1)$$

$$\tau\, dr_2/dt = -r_2 + f(-\beta r_1 - \varphi\, a_2 + I_2)$$
$$\tau_a\, da_2/dt = -a_2 + f_a(r_2)$$

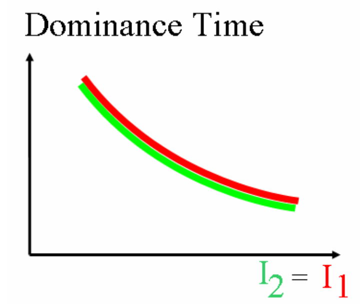
$$\tau_a >> \tau\,, \quad f(u)=1/(1+\exp[(\theta-u)/k])$$

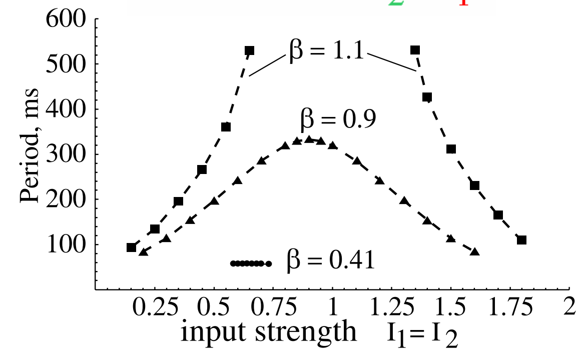
w/ N Rubin, A Shpiro, R Curtu, R Moreno





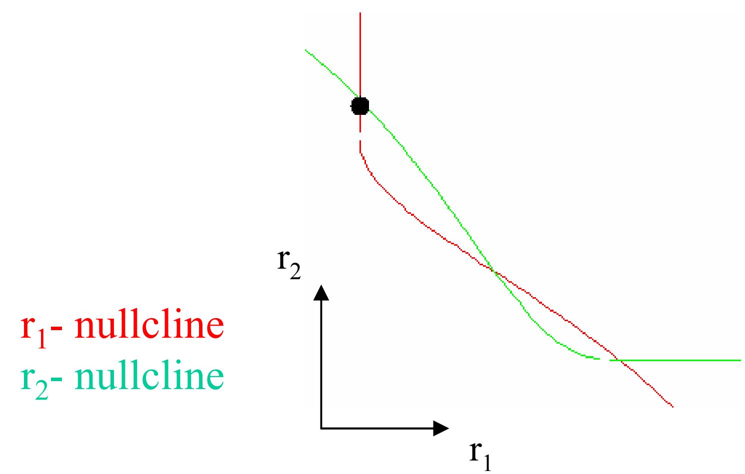
Levelt's Proposition I:





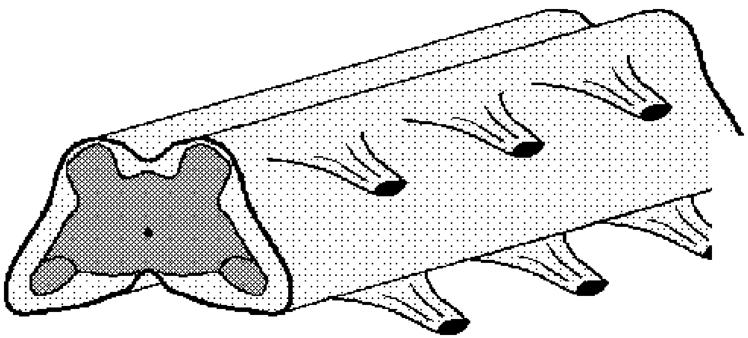
Fast variables: r_1 , r_2

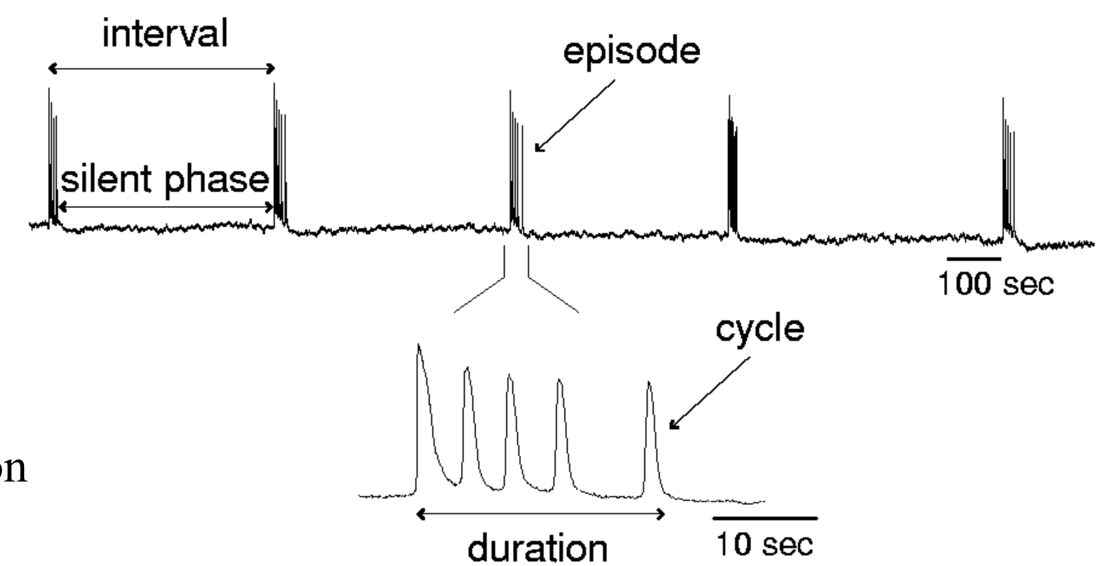
phase plane changes slowly, τ_a



Modeling the rhythmic dynamics of developing spinal cord

J Rinzel, NYU

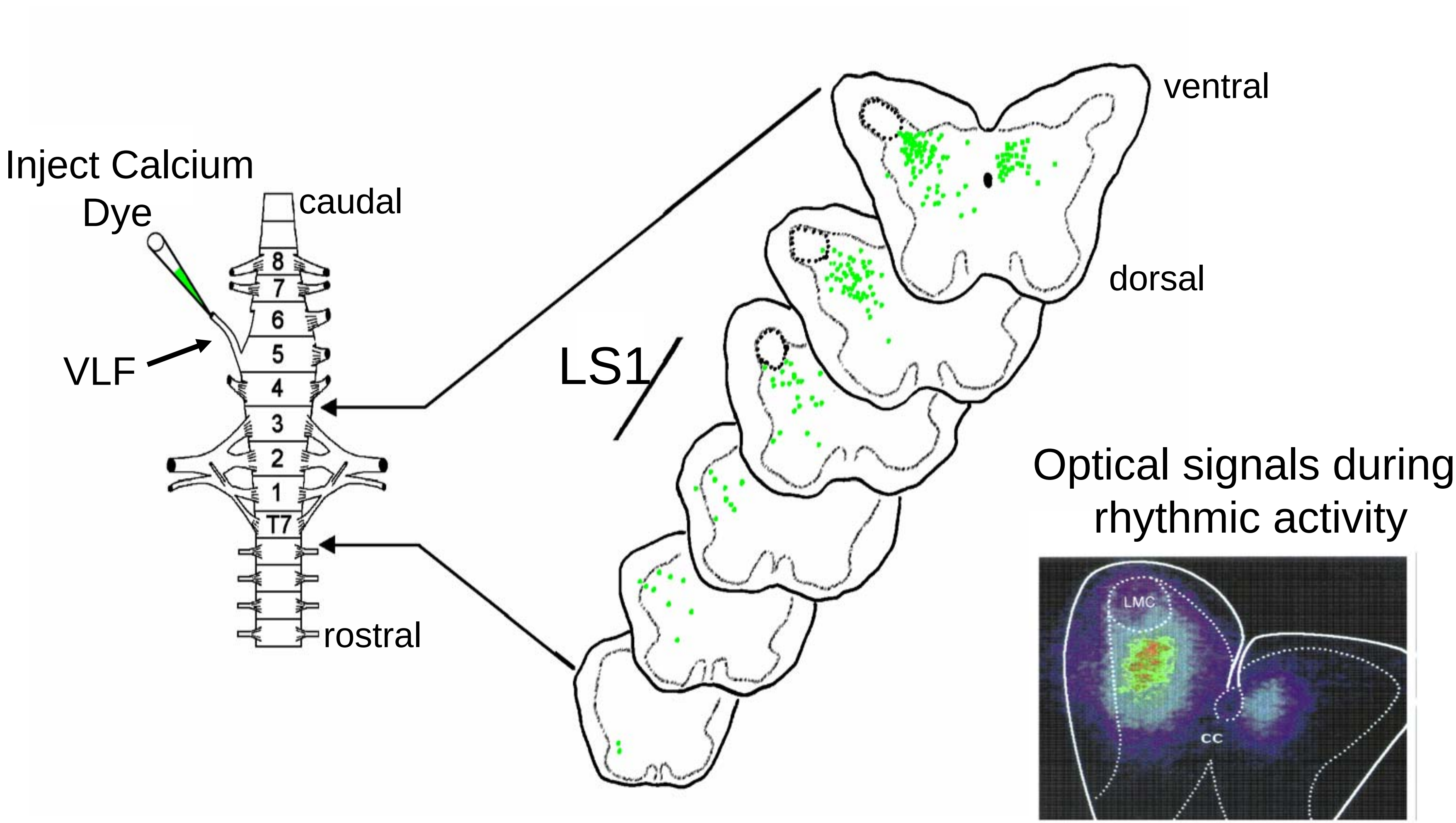




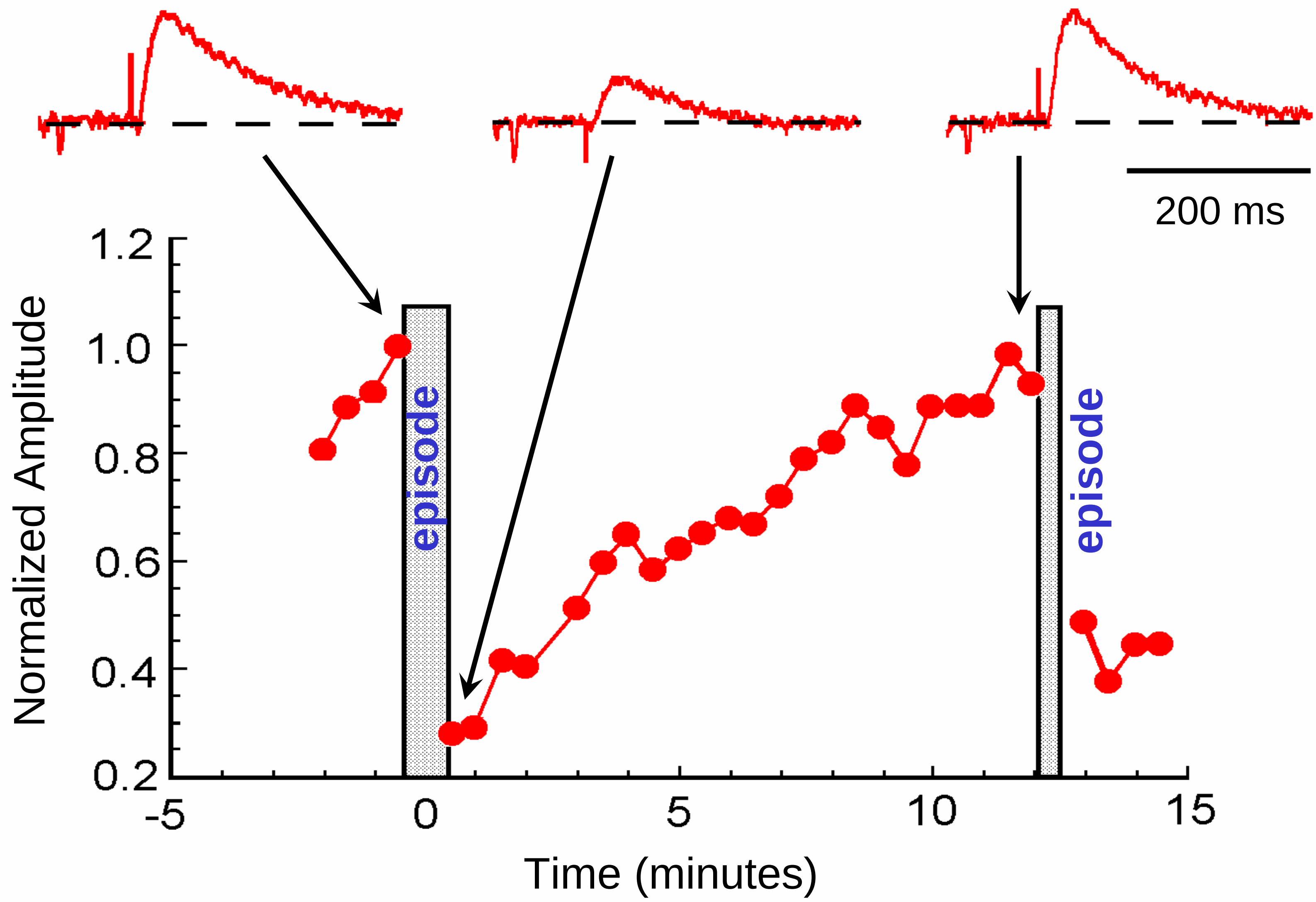
Background - network depression
An *ad hoc* firing rate model
Predictions/confirmations
A specific mechanism for depression
A minimal cell-based network model
Mean field model?

J Tabak, M O'Donovan, C Marchetti, B Vladimirski

Interneurons Retrogradely Labeled By Calcium Dyes Injected Into The Ventrolateral Funiculus (VLF) Are Rhythmically Active (A.Ritter, P.Wenner, S.Ho)



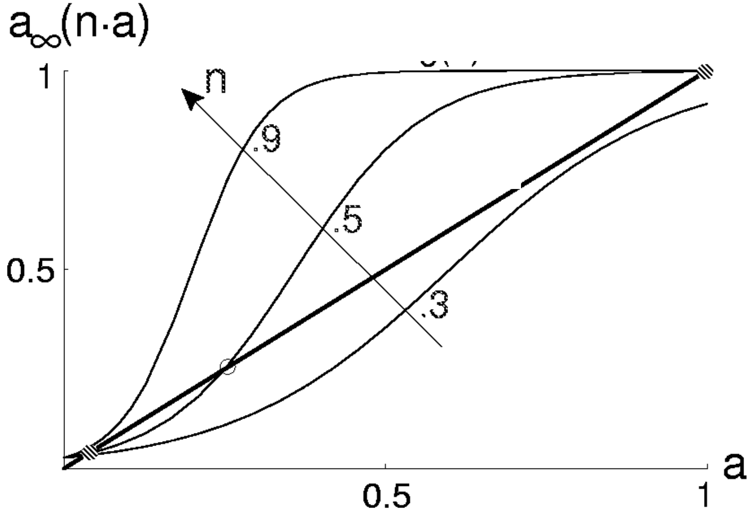
Synaptic Potentials Are Transiently Depressed After An Episode Of Spontaneous Activity

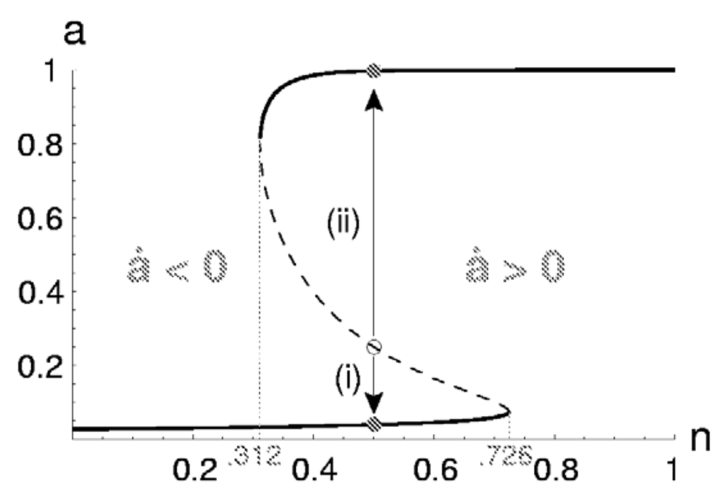


Basic Model: mutual excitatory network.
Activity level, ***a(t)*** ; availability of synaptic input, ***n***

$$\tau_a \; a' = a_\infty(input)-a$$

$$\tau_a \; a' = a_\infty(n.a)-a$$





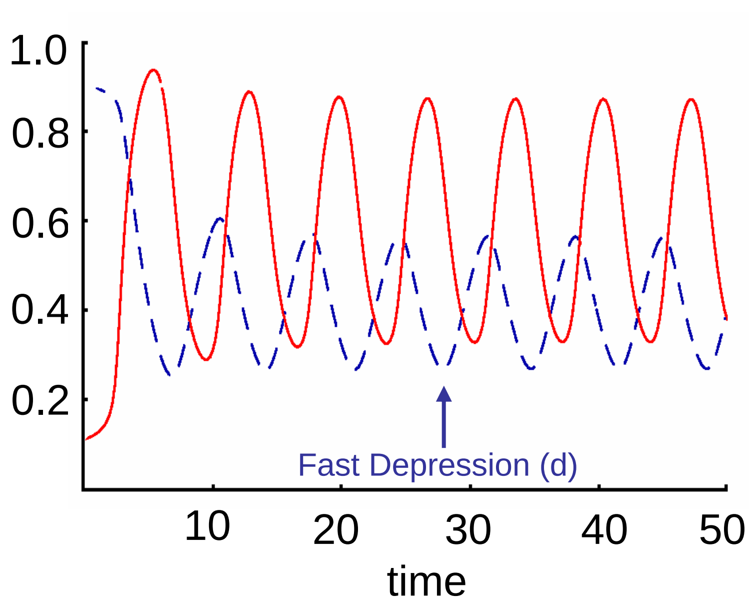
Spontaneous Rhythmic Episodes Can Be Modeled By An Excitatory Network With ‘Fast’ And ‘Slow’ Depression

J Neuroscience, 2000.

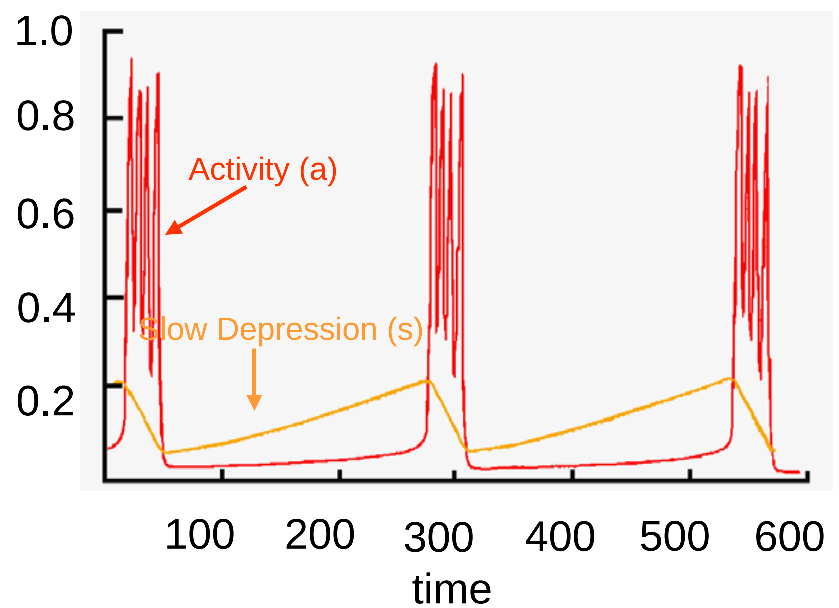
Network behavior is modeled by three variables

Network Activity	$\tau_a a' = a_\infty(s.d.a)-a$
Activity-dependent Fast depression	$\tau_d d' = d_\infty(a)-d$
Activity-dependent Slow depression	$\tau_s s' = s_\infty(a)-s$

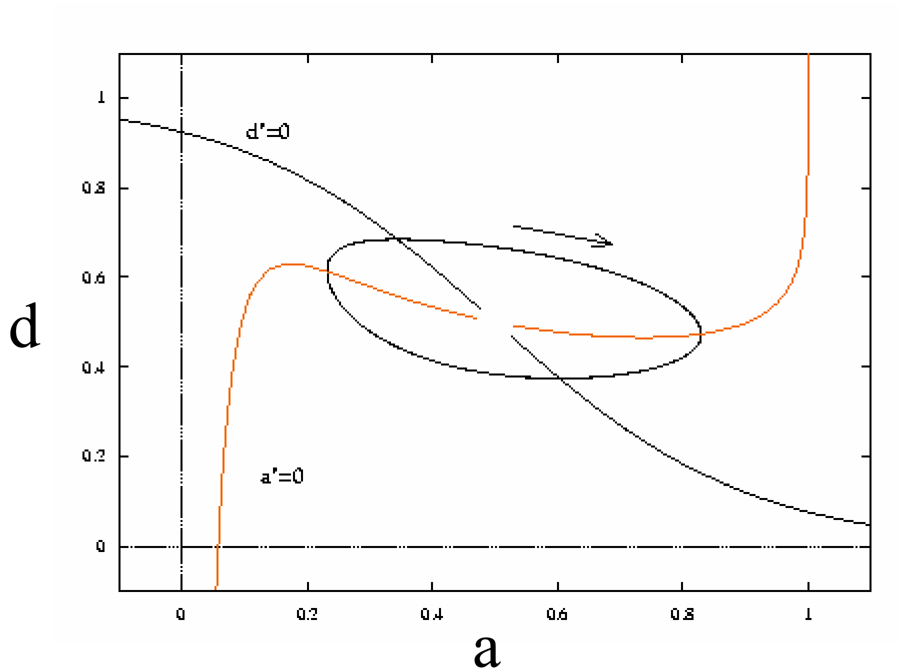
Delayed Fast Depression Leads to Oscillations

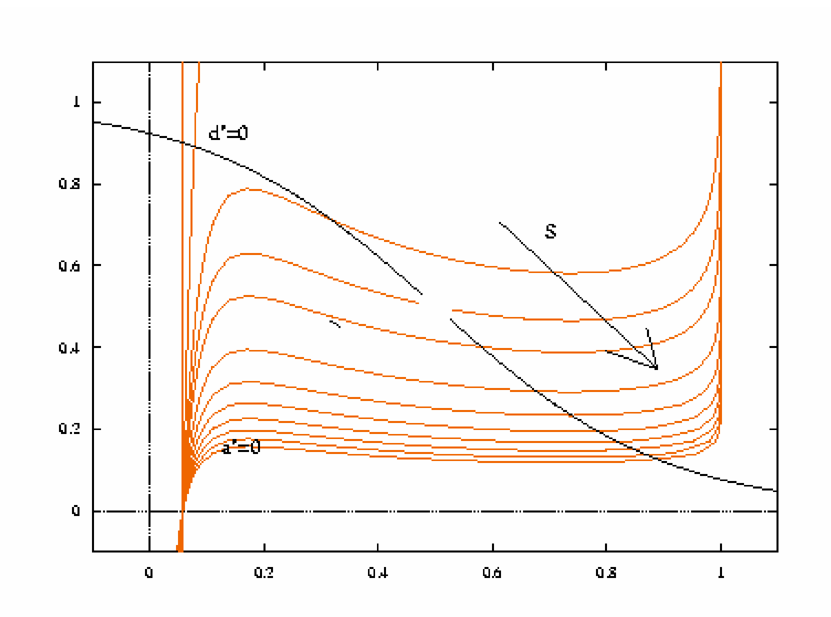


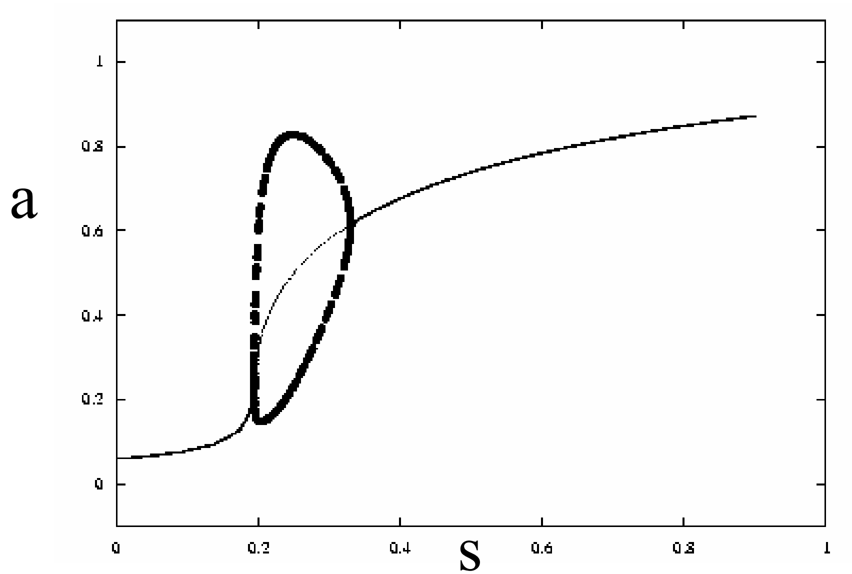
Fast and Slow Depression Produces Episodic Oscillations



Cycling dynamics: a-d phase plane, s-fixed.



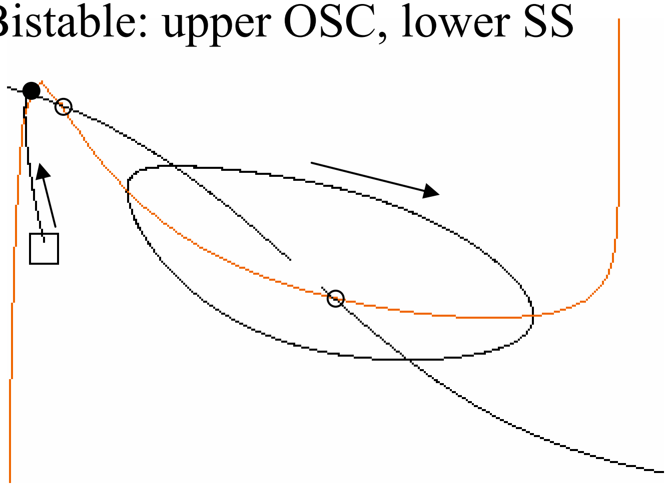


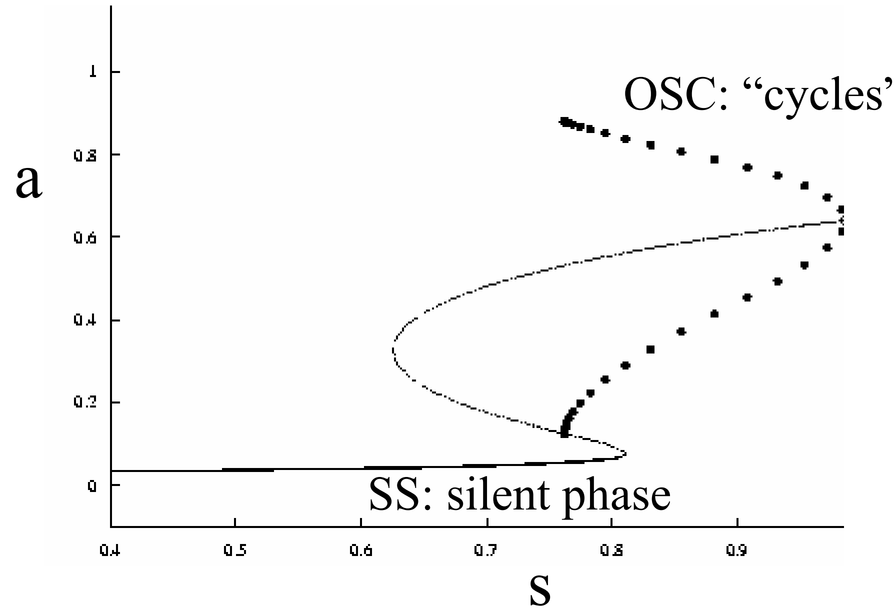


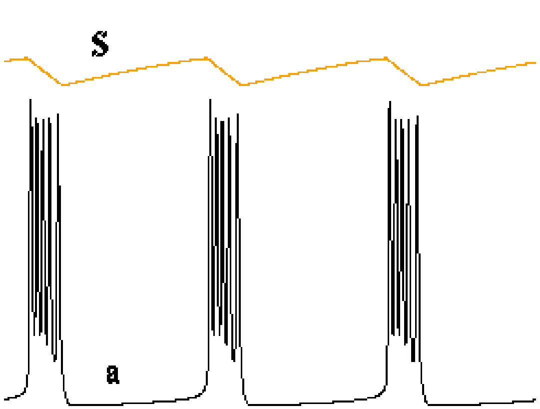
Prescribed slow back-and-forth s(t) “looks like” episodes, but it’s not autonomous.

FAST/SLOW Analysis

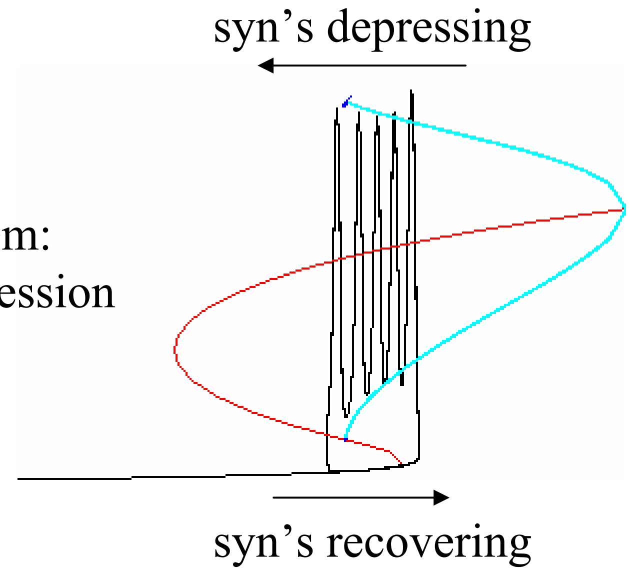
a-d phase plane, s fixed.
Bistable: upper OSC, lower SS



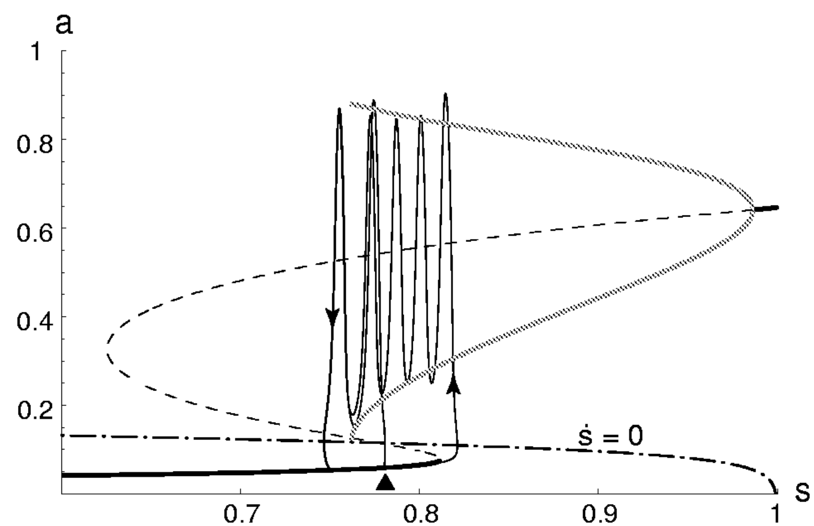




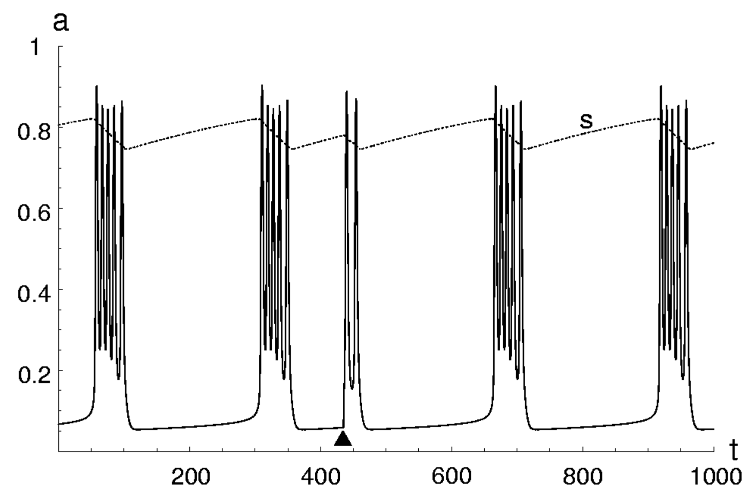
Full system:
s, slow depression



Fast/Slow Dissection -- ***a-s*** "phase plane"



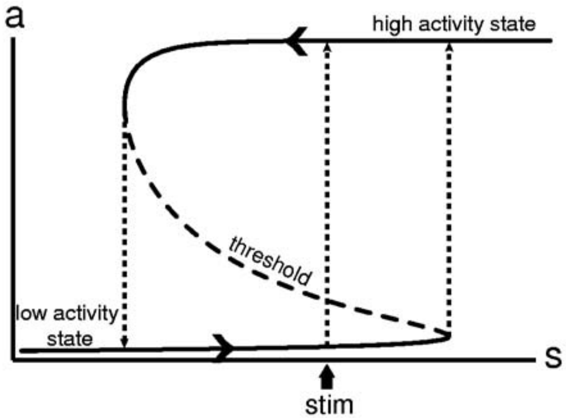
"Kick" out of Silent Phase => shorter Active Phase.

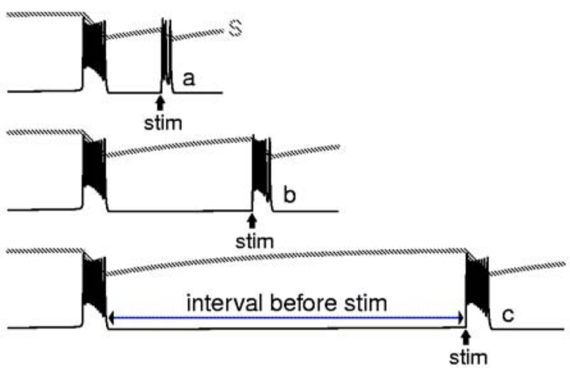


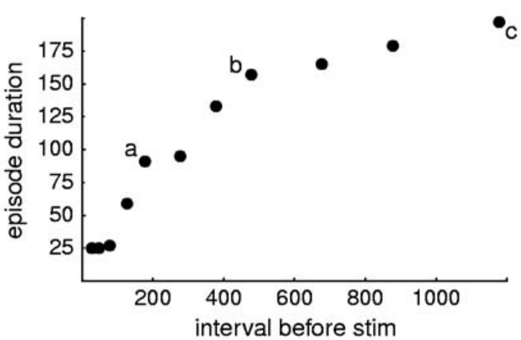
J Neuroscience, 2001.

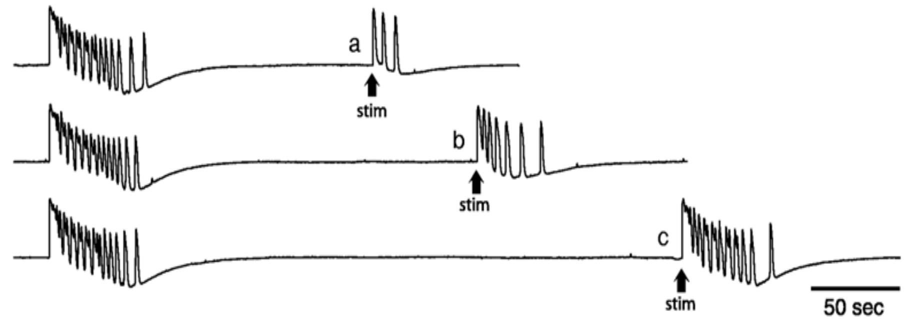
THEORY

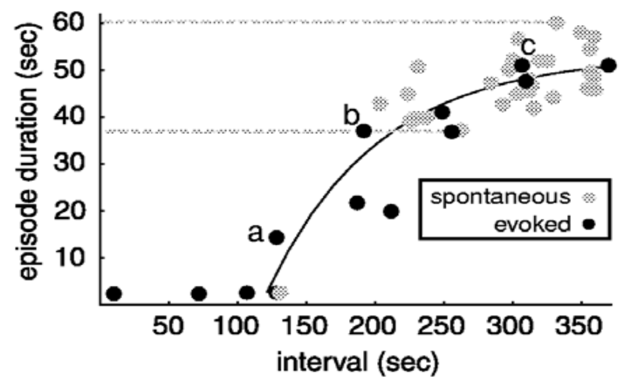
EXPERIMENT

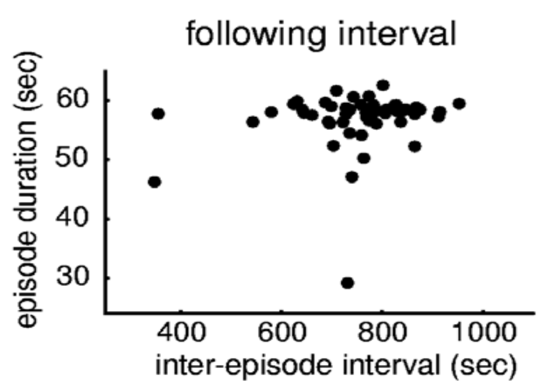










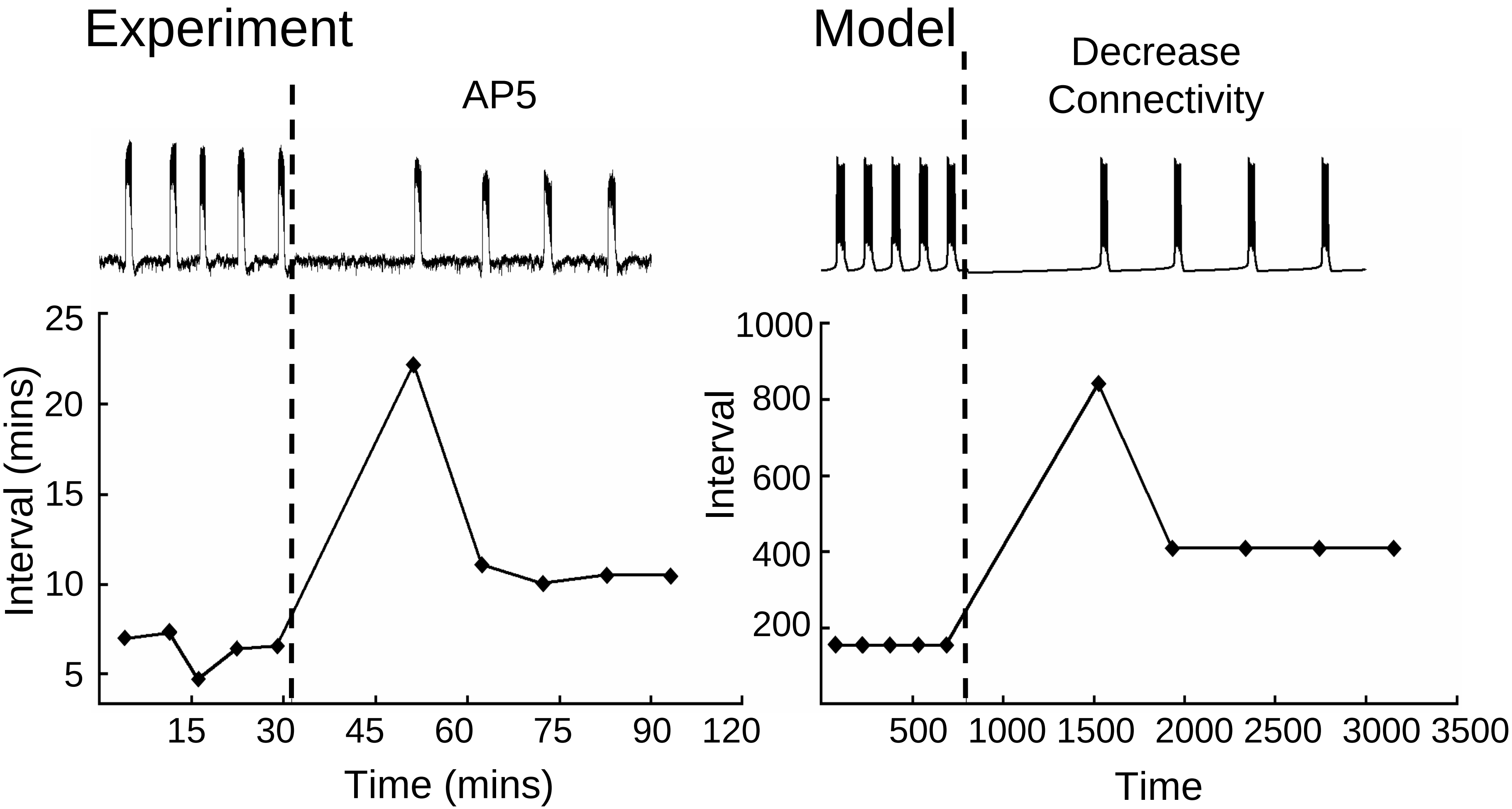


MORE….?

NMDA blocker…

Reduction Of Connectivity Mimics The Recovery Of Activity During Excitatory Blockade

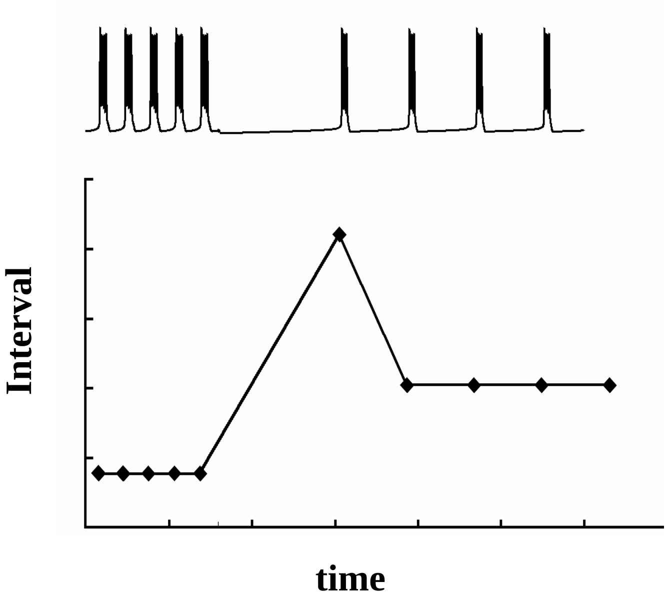
$$\tau_a a' = a_\infty(n.s.d.a)-a$$

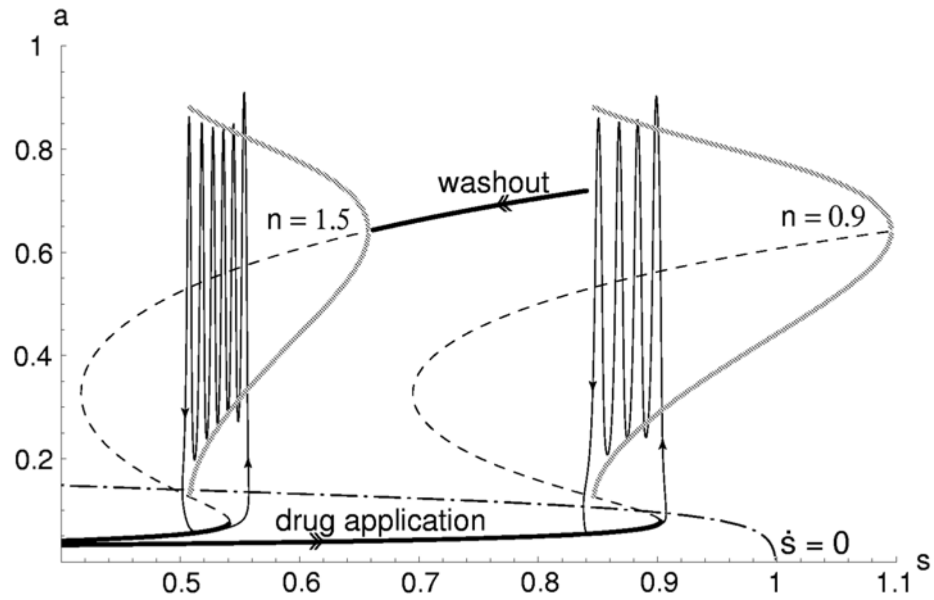


Phase space interpretation for effect of reduced connectivity

$$\tau_a \, a' = a_{\infty}(n.s.d.a) - a$$

n, effective connectivity





MORE….?

LIF cell-based network

N-cell I&F network.
w/ J Tabak, B Vladimirski

All-to-all excitatory coupling. Non-identical cells: $I_{min} < I_j < I_{max}$

If $I_{max} > 1$ some cells fire spontaneously. Slow depression, no cycles.

$$v_j' = -v_j + I_j - g_{syn}(v_j - v_{syn}) \sum_k q_k s_k$$

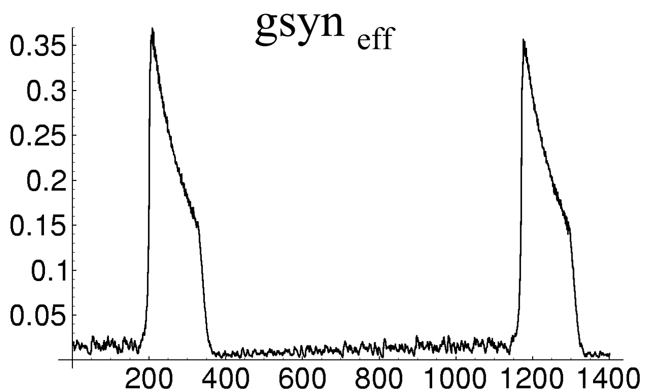
$$if \quad v_j(t_f) = 1, v_j(t_f^+) = 0.$$

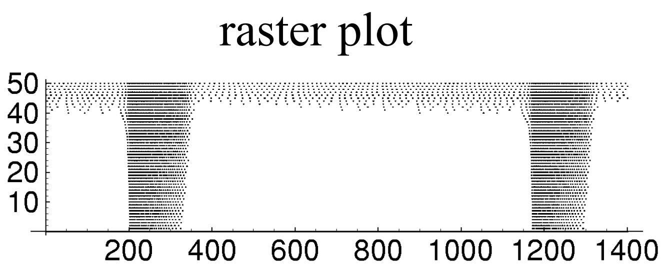
$$q_j' = \alpha_q P_q(t - t_f)(1 - q_j) - \beta_q q_j$$

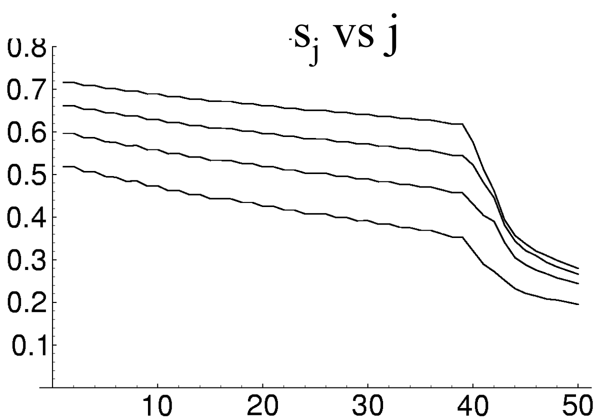
$$s_j' = \alpha_s(1 - s_j) - \beta_s P_s(t - t_f) s_j$$

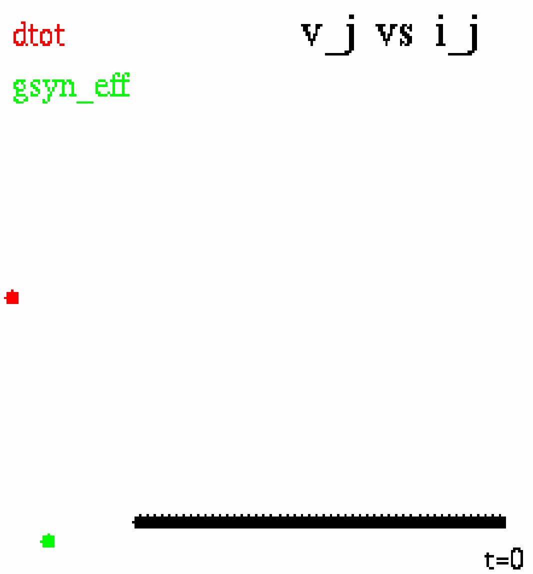
$q_j(t)$ - fast unitary postsynaptic conductance,
$s_j(t)$ - slow depression,
$P_{q,s}$ - square pulse of duration $\tau_{q,s}$.

N-cell I&F network; N=50; Imin=0; Imax=1.1

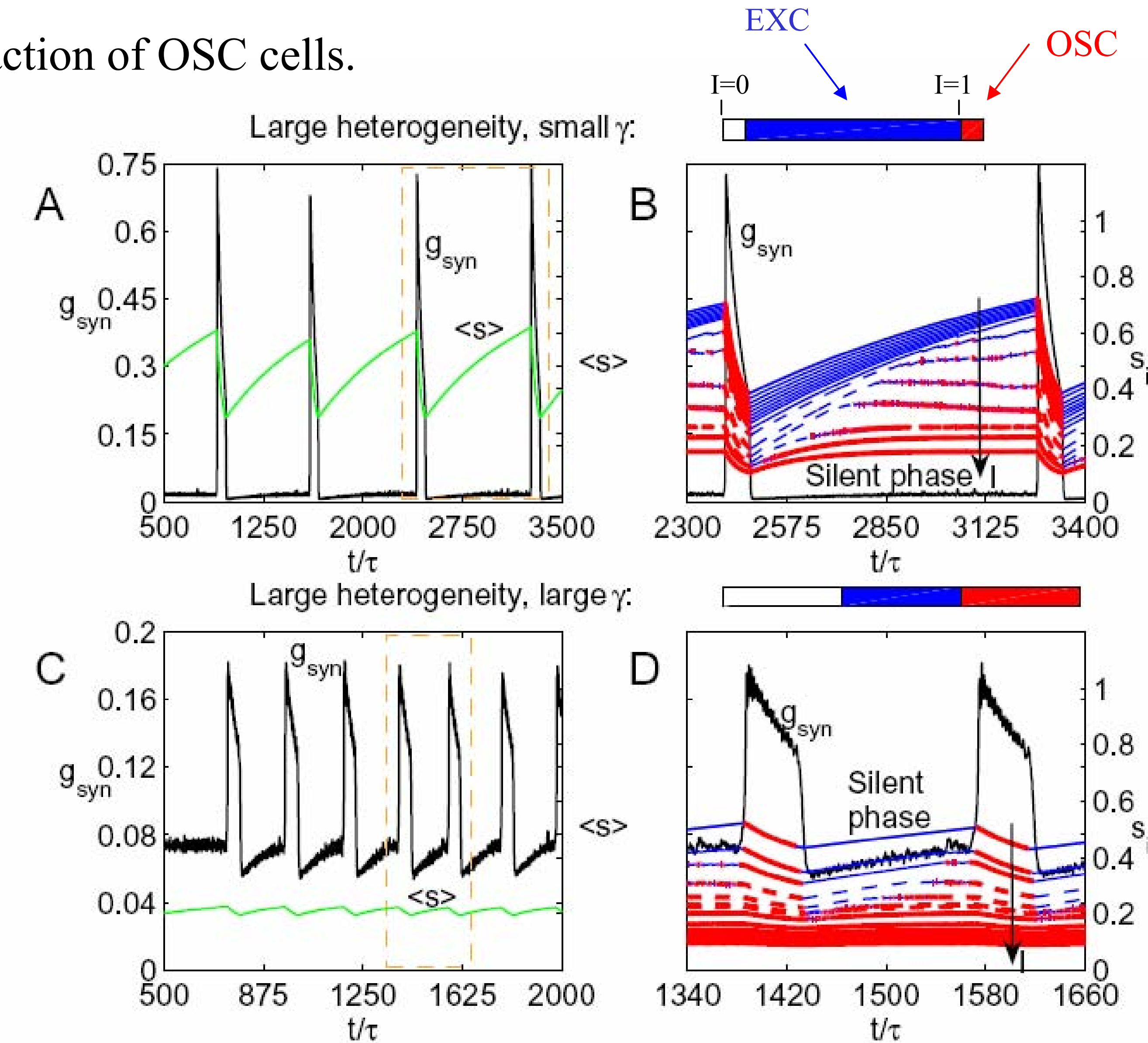








γ, fraction of OSC cells.



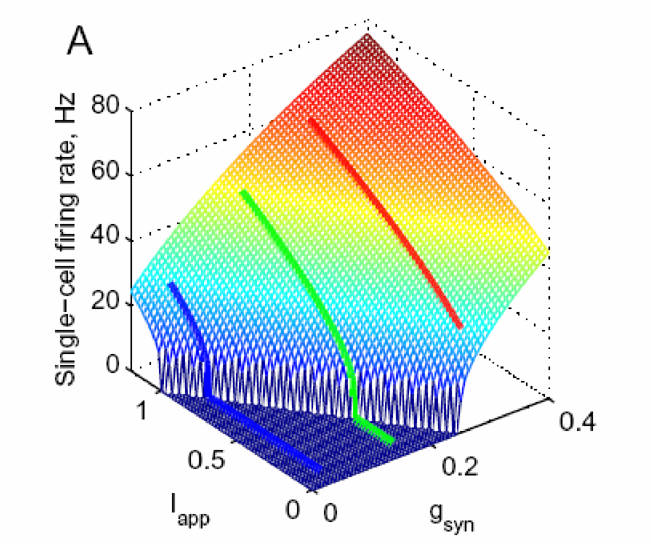
Fast/slow analysis.   Fast spiking dynamics, slow depression.

- asynchronous spiking
- total synaptic conductance is constant for fast dynamics, s_j frozen
- cells are firing periodically, frequency $r_j=r(g_{syn},I_j)$
- $g_j(t)$ replaced by temporal average

Self-consistency eqn replaces fast dynamics:

$$g_{syn} = \overline{g}_{syn} N^{-1} \sum_{i=1}^{N} s_i(t)\hat{q}(g_{syn},\ I_i)$$

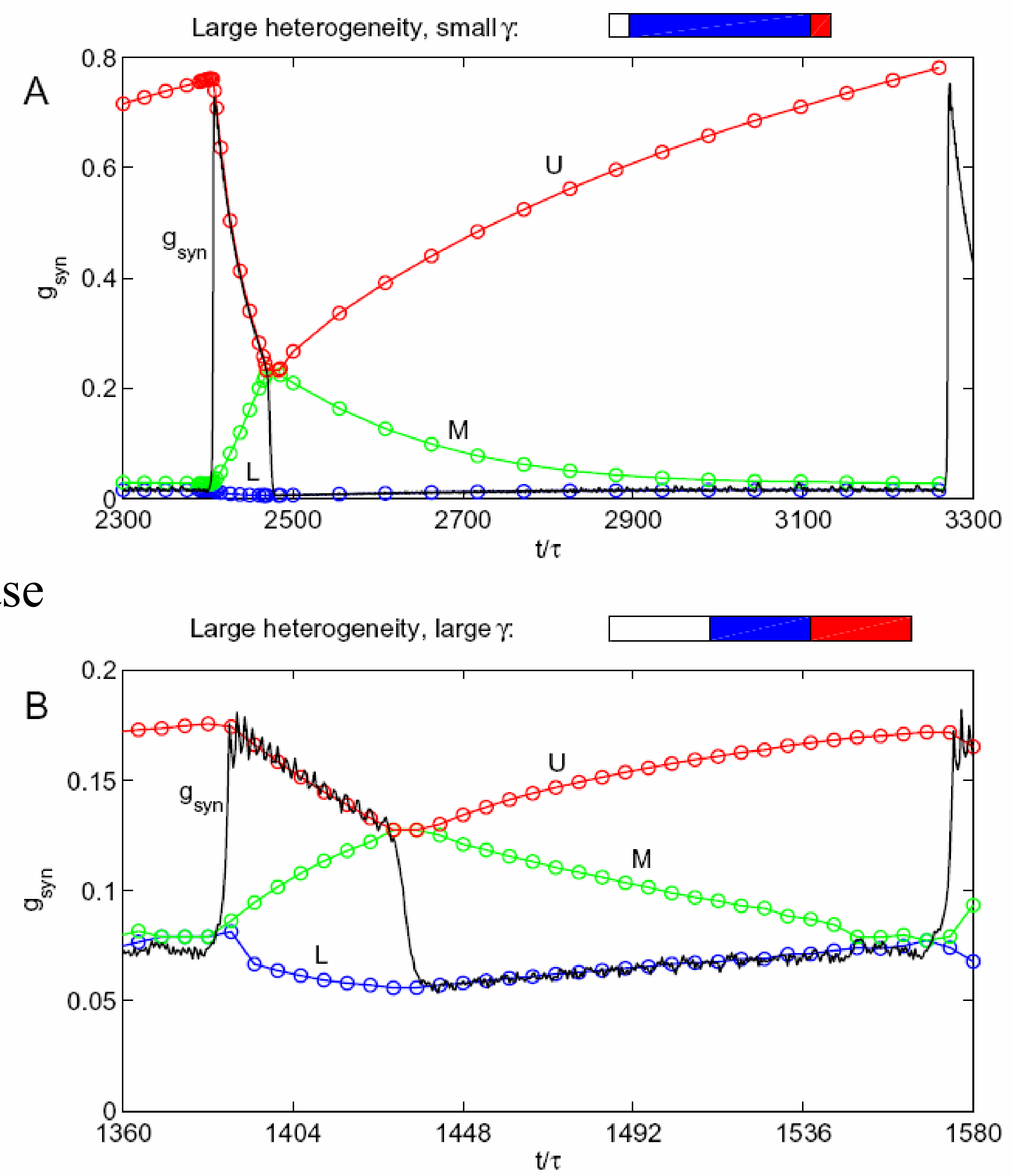
Slow dynamics: $s_j' = \alpha_s (1-s_j) - \langle\beta_{s,j}\rangle s_j$ where $\langle\beta_{s,j}\rangle$ depends on g_{syn} and j



Does self-consistency eqn lead to multi-branched surface, given $\{s_j\}$?

Demonstration of bistability:

Use self-consistency at each t, with current values of $\{s_j\}$ – find 3 states: L, M, U…
U-M coalesce at end of Silent Phase
L-M at end of Active Phase



MORE….?

$GABA_A$-V_{syn} : cloride dynamics

w/ C Marchetti, J Tabak, M O'Donovan
J Neurosci 2005

A Mechanism for Depression of Synaptic Current.

A cell's current balance eqn:

$$C_m \; V_i' = -[I_{spike}(V_i, w_i) + I_{syn} + I_{pump}]$$

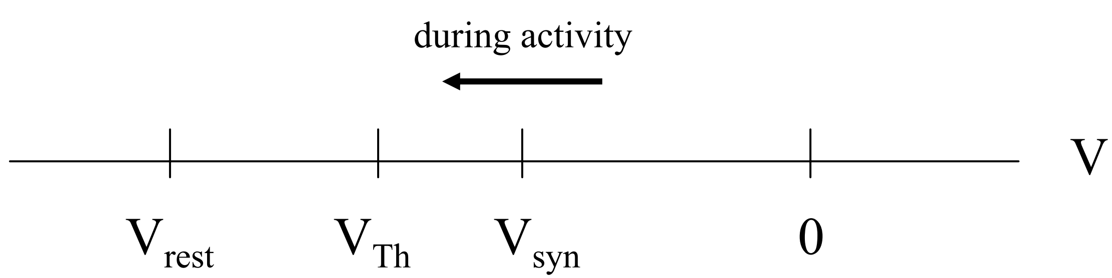
where

$$I_{syn} = g_{syn}(V_i - V_{syn}) \;\; \sum_j q_{j,i}(t)$$

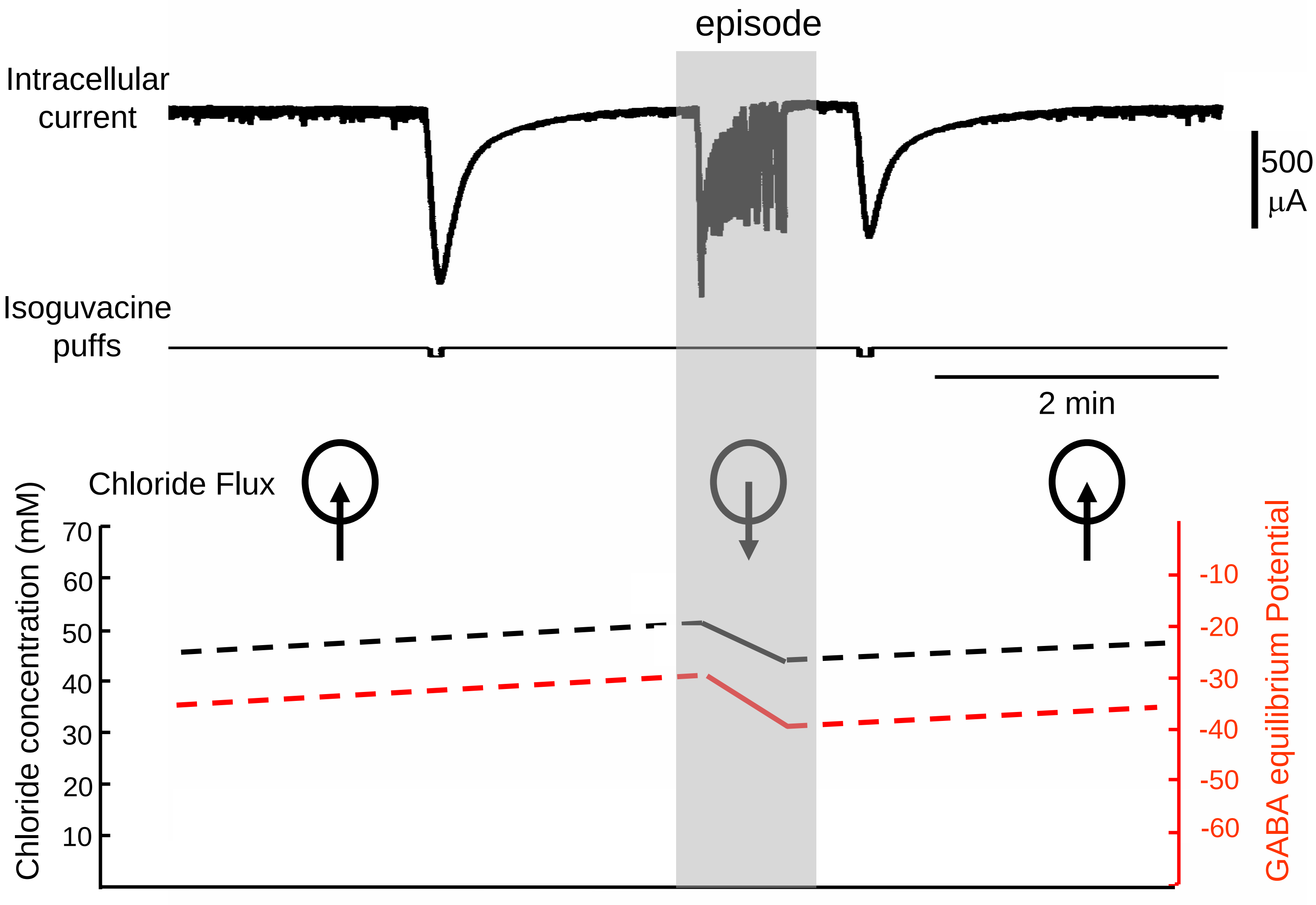
and for GABA$_A$-mediated synaptic current:

$$V_{syn} = (RT/F)log([Cl^-]_{int}/[Cl^-]_{ext}).$$

$V_i < V_{syn}$ ==> $[Cl^-]_{int} \downarrow$ ==> $V_{syn} \downarrow$



Changes in $[Cl^-]_{int}$ and E_{GABAA} are responsible, in part, for the postepisode depression of evoked currents (Chub & O'Donovan)



Minimal Model for Episodic Rhythm, with $[\mathrm{Cl}^-]_{int}$ as Slow Variable

$$V' = -[(V - V_{rest}) + I_{syn}]/\tau_m$$

$$d' = [d_\infty(V) - d]/\tau_d$$

$$Cl' = [I_{pump} + I_{syn}]/\tau_{Cl}$$

.

$V(t)$ is t-averaged membrane potential, $d(t)$ is the fast depression factor, $Cl(t)$ =$[\mathrm{Cl}^-]_{int}$

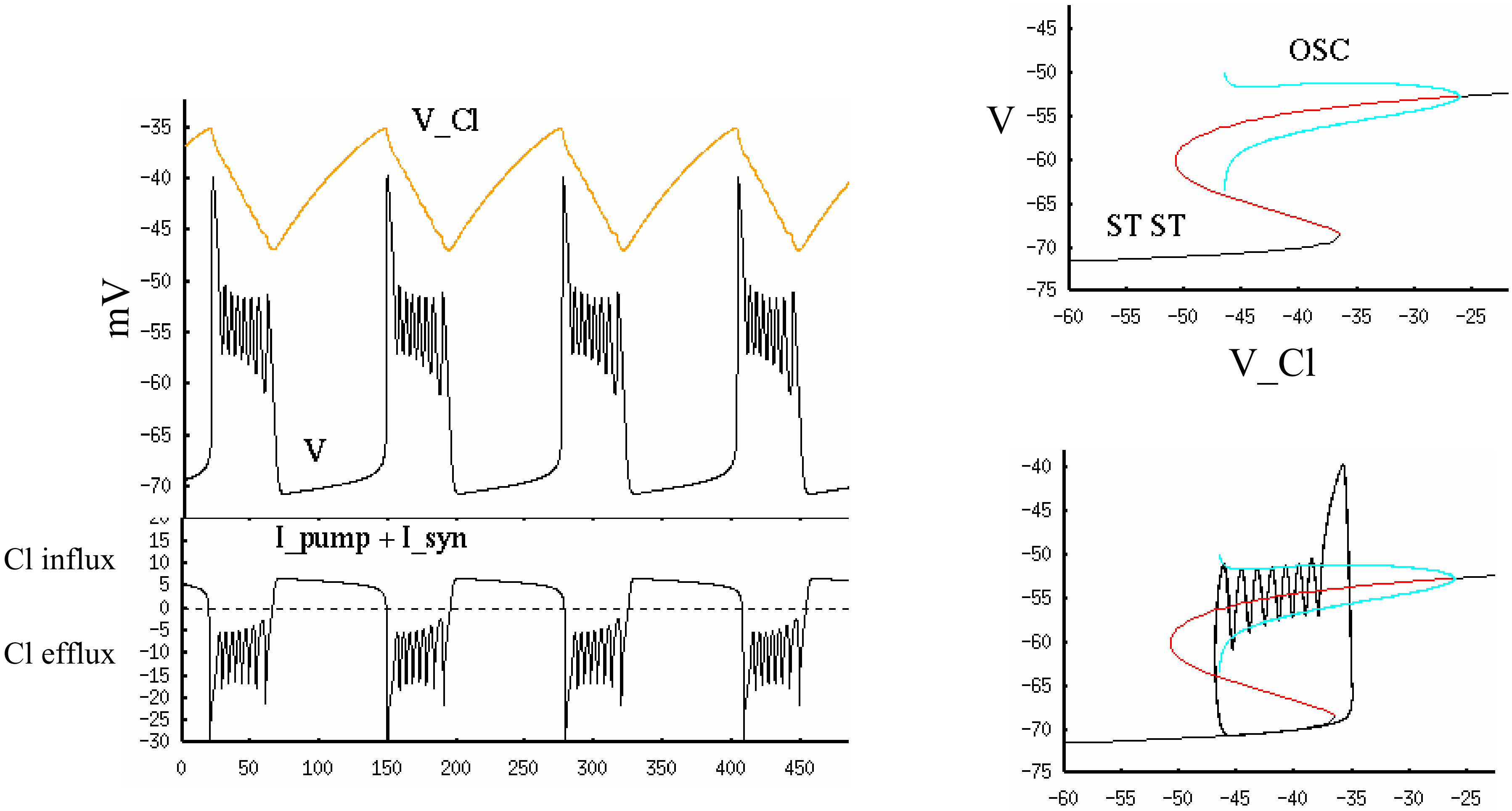
$$I_{syn} = g_{syn}\ d\ f(V)\ (V - V_{Cl})$$

with

$$V_{Cl} = (RT/F) log(Cl/[Cl^-]_{ext}).$$

$f(V)$, the firing frequency at V, is sigmoid increasing. $I_{pump}, I_{syn} > 0$ correspond to inward Cl^- flux.

FAST/SLOW Analysis



SUMMARY

***Ad hoc* Mean Field model:**

Episodic rhythms - generated from mutual excitation with slow synaptic depression;
- fast depression yields cycling during episodes.

Bistability of fast subsystem leads to predictions for correlations between SP duration and next AP duration.

Prediction/test for effect of reduced connectivity.

$GABA_A$ synapses are "functionally" excitatory, ie $V < V_{Cl}$; V_{Cl} is depolarized and it oscillates together with episodes; minimal model shows it.

N-cell network model:

Cycling during AP? Stochastic synapses for initiating next AP?

Dynamics of heterogeneous network.