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?
Spontaneous Activity Is Similar In Different Parts Of The Developing Nervous System

Chick Spinal Cord (E11)

Rat Hippocampus (Garaschuk et al., 1998)

Ferret Retina (Penn et al., 1998)
Interneurons Retrogradely Labeled By Calcium Dyes Injected Into The Ventrolateral Funiculus (VLF) Are Rhythmically Active (A.Ritter, P.Wenner, S.Ho)
At The Beginning Of A Spontaneous Episode Fluorescent Activity Begins Ventro-laterally And Then Spreads Dorso-medially (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, \( n \)

\[
\tau_a \, a' = a_\infty(\text{input}) - a
\]

\[
\tau_a \, a' = a_\infty(n.a) - a
\]
Spontaneous Rhythmic Episodes Can Be Modeled By An Excitatory Network With ‘Fast’ And ‘Slow’ Depression

Network behavior is modeled by three variables

Network Activity
Activity-dependent Fast depression
Activity-dependent Slow depression

\[
\begin{align*}
\tau_a a' &= a_{\infty}(s.d.a) - a \\
\tau_d d' &= d_{\infty}(a) - d \\
\tau_s s' &= s_{\infty}(a) - s
\end{align*}
\]

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

OSC: “cycles”
SS: silent phase
syn’s depressing

Full system:
s, slow depression

syn’s recovering
Fast/Slow Dissection -- $a-s$ “phase plane”

“Kick” out of Silent Phase => shorter Active Phase.
THEORY

![Diagram showing theoretical model with activity states and thresholds.]

EXPERIMENT

![Graphs showing experimental data with episode duration and interval.]

Reduction Of Connectivity Mimics The Recovery Of Activity During Excitatory Blockade

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

**Experiment**
- Time (mins): 15 30 45 60 75 90 120
- Interval (mins): 5 10 15 20 25

**Model**
- Time: 500 1000 1500 2000 2500 3000 3500
- Interval: 5 10 15 20 25
Phase space interpretation for effect of reduced connectivity

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

n, effective connectivity
A Mechanism for Depression of Synaptic Current.

A cell’s current balance eqn:

\[ C_m \ V'_i = -[I_{\text{spike}}(V_i, w_i) + I_{\text{syn}} + I_{\text{pump}}] \]

where

\[ I_{\text{syn}} = g_{\text{syn}}(V_i - V_{\text{syn}}) \sum_j q_{j,i}(t) \]

and for GABA_A-mediated synaptic current:

\[ V_{\text{syn}} = (RT/F) \log\left(\frac{[Cl^-]_{\text{int}}}{[Cl^-]_{\text{ext}}}\right). \]

\[ V_i < V_{\text{syn}} \implies [Cl^-]_{\text{int}} \downarrow \implies V_{\text{syn}} \downarrow \]

during activity

0 \quad V_{\text{syn}} \quad V_{\text{Th}} \quad V_{\text{rest}} \quad V
Changes in $[\text{Cl}]\text{_{int}}$ and $E_{\text{GABA}}$ are responsible, in part, for the postepisode depression of evoked currents (Chub & O'Donovan)

**Diagram:**
- Intracellular current
- Isoguvacine puffs
- Chloride Flux
- Chloride concentration (mM)
- GABA equilibrium Potential
- 2 min
- 500 µA
Changes In Intracellular Chloride Concentration And $E_{\text{GABA}}$ Depend On The Membrane Potential During The Episode (N.Chub)
Minimal Model for Episodic Rhythm, with \([\text{Cl}^-]_{\text{int}}\) as Slow Variable

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

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

\[
C\ell' = \left[I_{\text{pump}} + I_{\text{syn}}\right]/\tau_{C}\ell
\]

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

\[I_{\text{syn}} = g_{\text{syn}} \ d \ f(V) \ (V - V_{\text{Cl}})\]

with

\[V_{\text{Cl}} = \frac{RT}{F} \log(C\ell/[\text{Cl}^-]_{\text{ext}}),\]

\(f(V)\), the firing frequency at \(V\), is sigmoid increasing. \(I_{\text{pump}}, I_{\text{syn}} > 0\) correspond to inward \text{Cl}^- flux.
All-to-all excitatory coupling. Non-identical cells: \( I_{\text{min}} < I_j < I_{\text{max}} \)

If \( I_{\text{max}} > 1 \) some cells fire spontaneously. Slow depression, no cycles.

\[
v'_j = -v_j + I_j - g_{\text{syn}}(v_j - v_{\text{syn}}) \sum_k q_k s_k
\]

\[
  i f \quad v_j(t_f) = 1, v_j(t_f^+) = 0.
\]

\[
q'_j = \alpha_q P_q(t - t_f)(1 - q_j) - \beta_q q_j
\]

\[
s'_j = \alpha_s(1 - s_j) - \beta_s P_s(t - t_f)s_j
\]

\(q_j(t)\) - 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; I_{\text{min}}=0; I_{\text{max}}=1.1
\( \gamma \), 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:

$$s_j' = \alpha_s (1 - s_j) - \beta_{s,j}^S s_j$$

where $\beta_{s,j}^S$ depends on $g_{syn}$ and $j$

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

Consider simplification, $s_j$ are uniform, $= S$

No indication of bistability, although system shows episodic rhythms.
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
Increased heterogeneity leads to larger dynamic range.
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.