Synaptic architecture and intrinsic dynamics in neuronal network activity patterns

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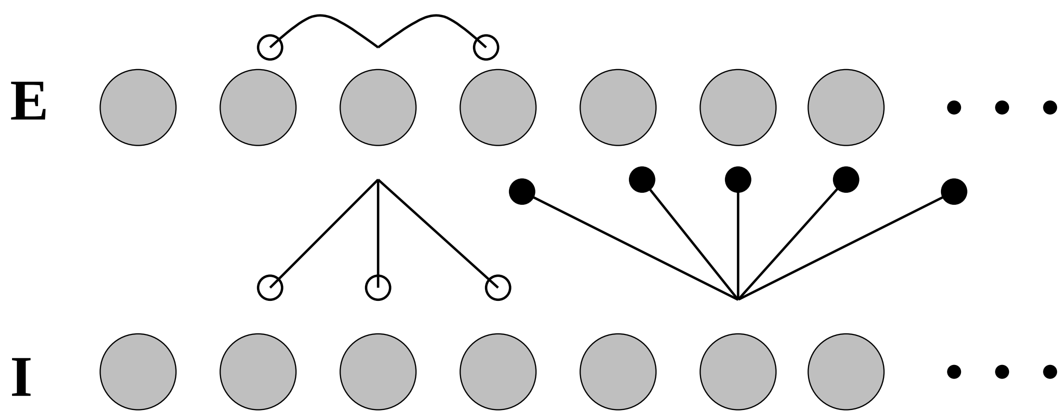
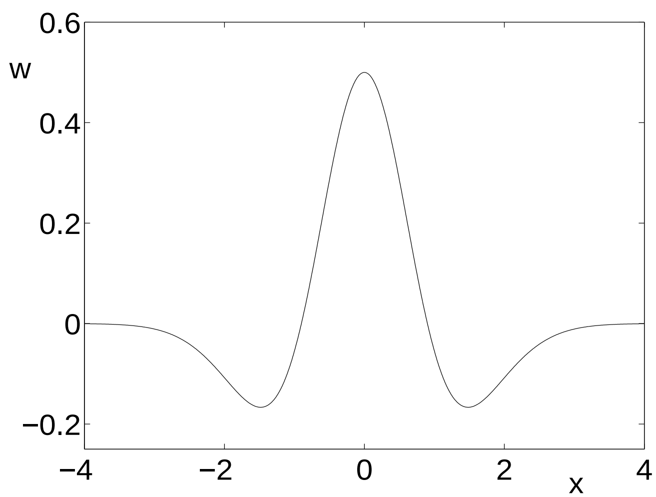
Recipe for localized, sustained activity (bumps)



e.g. Wilson/Cowan/Amari: $u_t(x,t) = h - \sigma u(x,y) + \int_{-\infty}^{\infty} w(x-y) f(u(y,t))\, dy$



$$\begin{cases} w(x) > 0 \text{ on } (-\bar{x}, \bar{x}) \\ w(-\bar{x}) = w(\bar{x}) = 0 \\ w(x) < 0 \text{ on } (-\infty, -\bar{x}) \cup (\bar{x}, \infty) \end{cases}$$

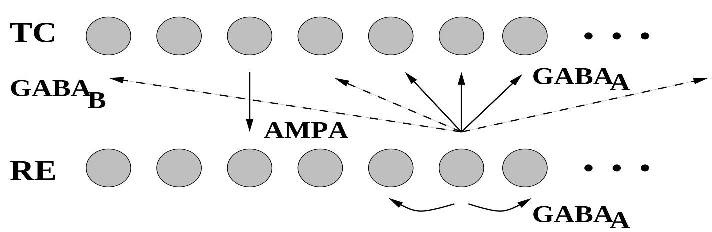
IDEA:
Bumps can also occur w/o E-E!

Bumps without E-E connections

- head direction system (mammals): anterior dorsal thalamic nuclei [Taube et al.]
- localized activity in thalamic slices from rat and mouse [Sohal, Huntsman & Huguenard, 2000]
- basal ganglia: STN = E, GPe = I
- hippocampal CA1: pyramidal cells = E, interneurons = I

Questions

1. Can an E-I network w/o E-E connections sustain localized activity on its own?



2. If so, under what conditions?
3. In general, what architectures allow sustained, localized activity?

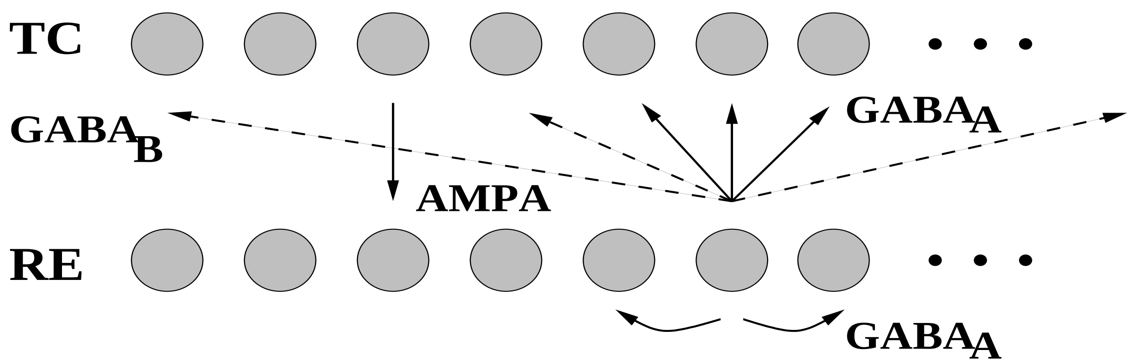
Thalamic network

TC =thalamocortical relay cells

RE =thalamic reticular cells

GABA_A = fast inhibition

GABA_B = slow tickler inhibition



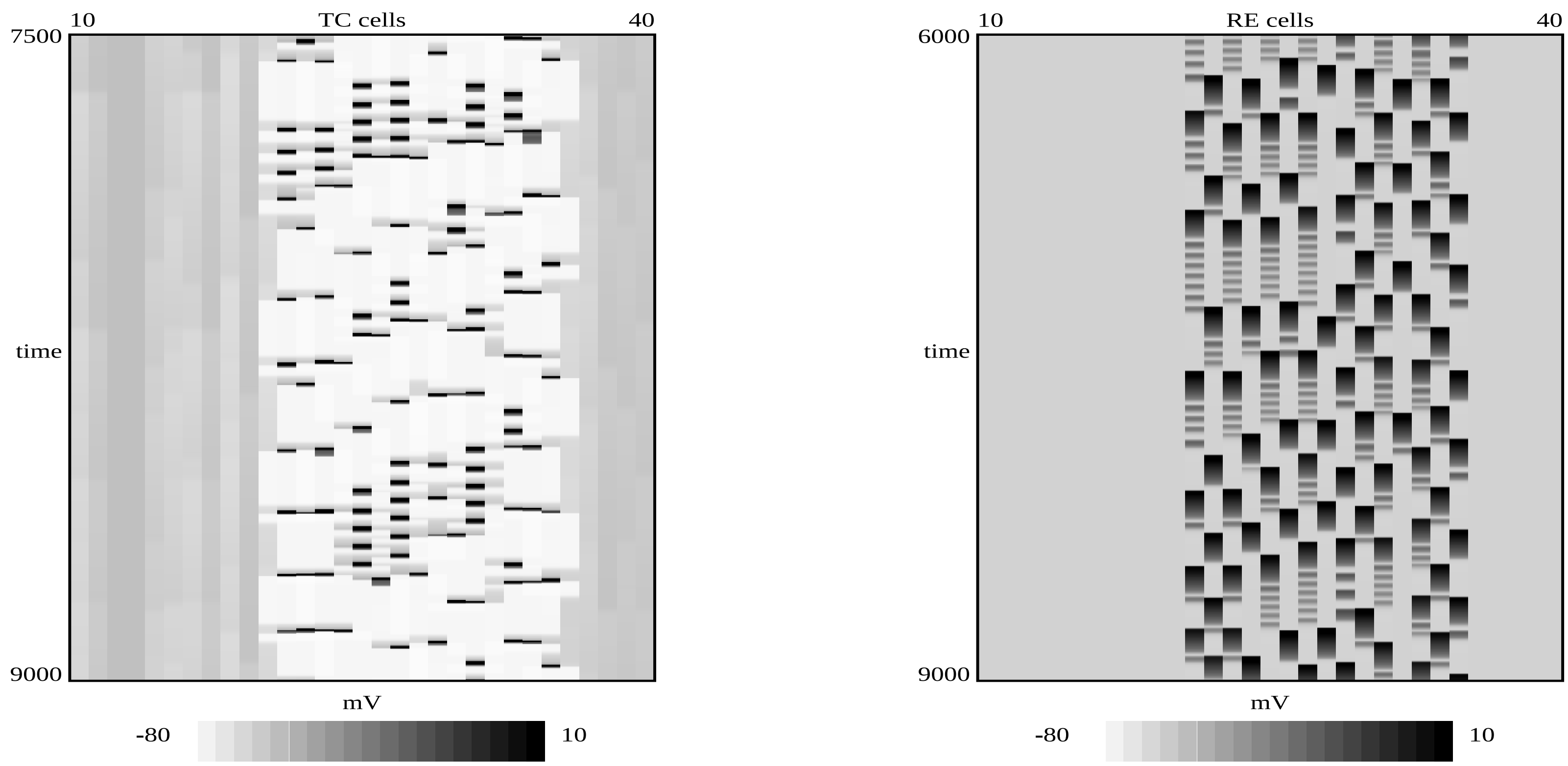
TC:

$$v' = -I_T(v,y) - I_L(v) - I_A - I_B - I_{ctx}$$
$$y' = \phi(y_\infty(v) - y)/\tau_y(v)$$

RE:

$$w' = -I_{T'}(w,z) - I_{L'}(w) - I_{A'} - I_E - I_{ctx'}$$
$$z' = \psi(z_\infty(w) - z)/\tau_z(w)$$

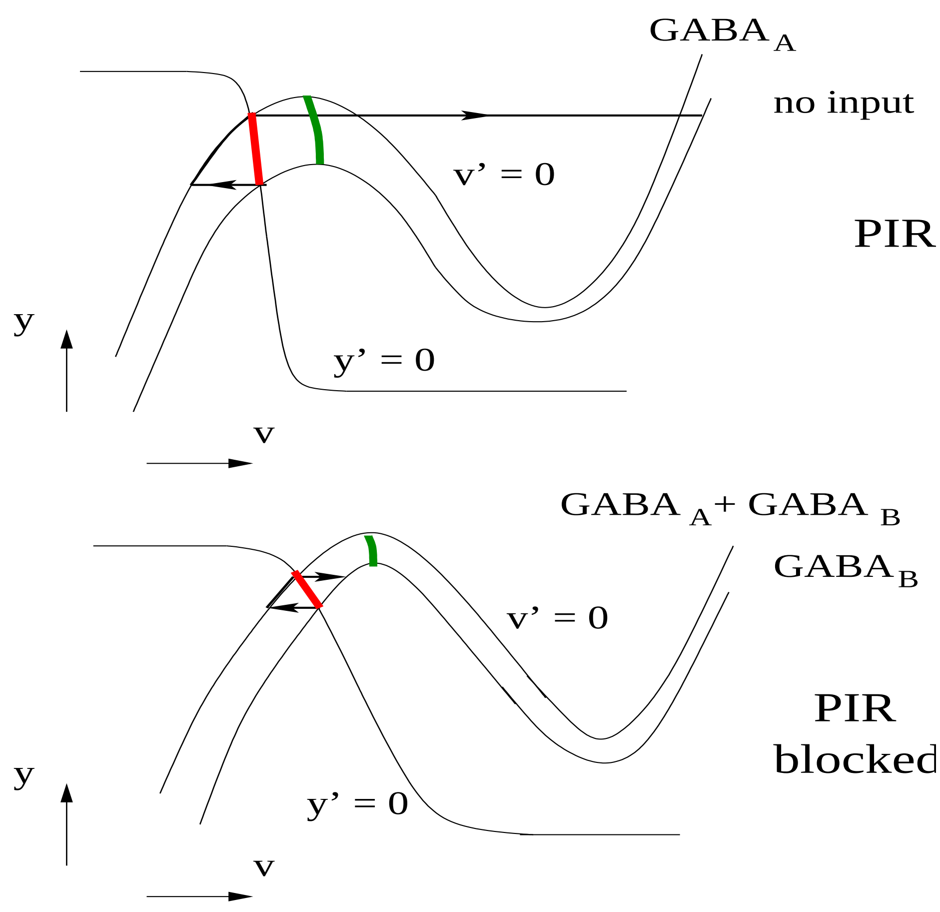
Sustained localized activity occurs [Rubin, Terman & Chow, JCNS, 2001]



Sustained Activity and Block of Propagation

◇ activity is sustained by post-inhibitory rebound (PIR)

◇ $GABA_B$ from ticklers builds up and blocks TC cell rebound



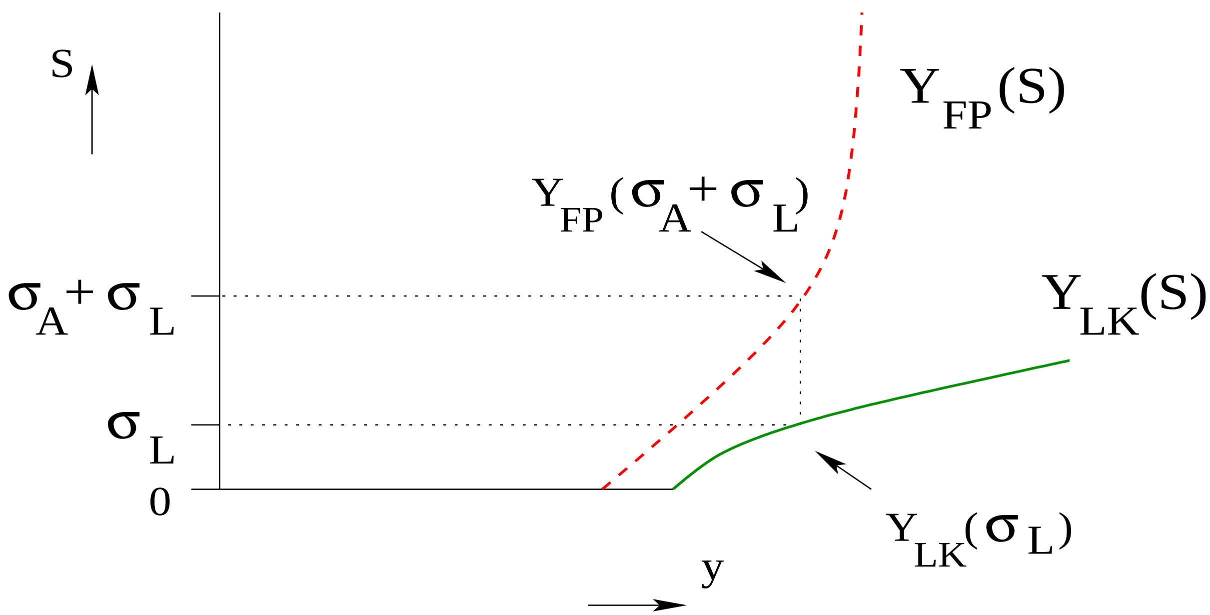
Continuum limit

Synaptic currents become

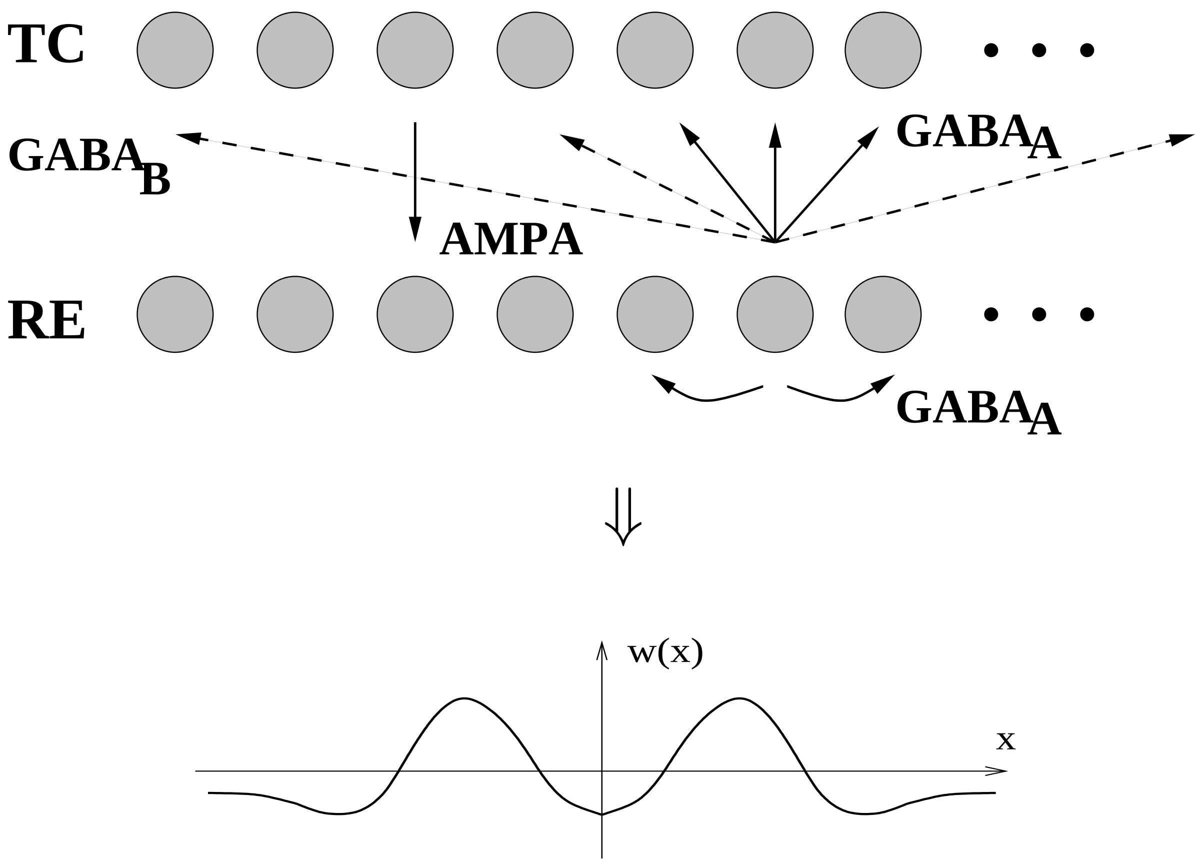
$$I_K(x,t) = g_K(v(x,t) - v_{th}) \int_{-\infty}^{\infty} w_K(x,y) s_K(y,t)\, dy$$

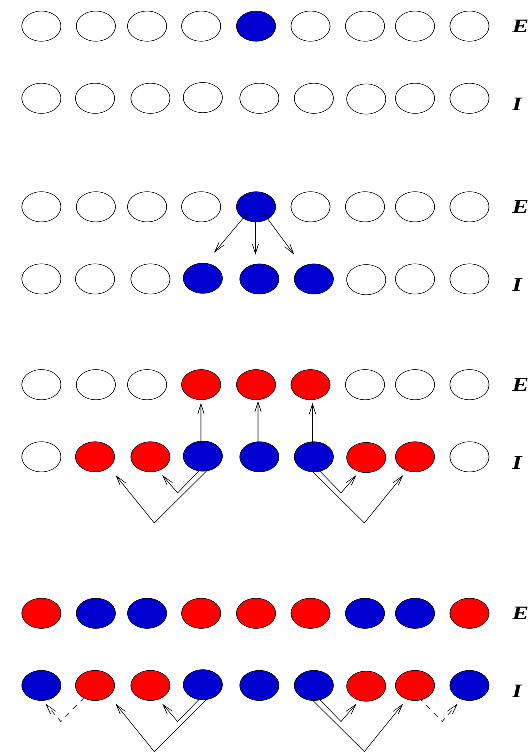
where $K = A, B, E, A'$ respectively.

Let σ_A = GABA$_A$ inhibition, σ_L = GABA$_B$ inhibition from bump of size L $\Rightarrow$ consistency condition:



E-I network without E-E connections





off-center coupling

Analysis

- consider $u_t(x,t) = -u(x,t) + \int_{-\infty}^{\infty} w(x-y) H(u(y,t))\,dy + h$
- follow Amari:

$\longrightarrow$ let $W(x) = \int_0^x w(t)\,dt$

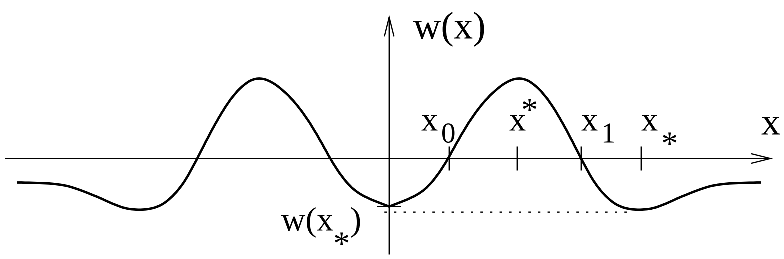
$\longrightarrow$ for a stationary bump on $(0, a)$,

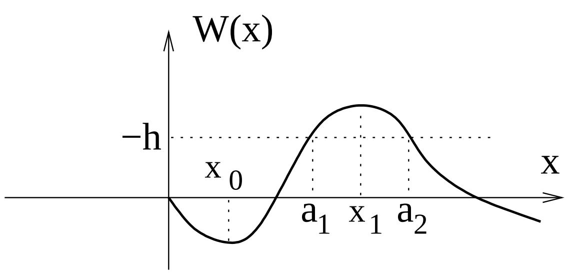
$$u(x) = \int_0^a w(x-y)\,dy + h = W(x) - W(x-a) + h$$

$\longrightarrow$ $u(0) = u(a) = 0 \;\Rightarrow\; (*)\; W(a) + h = 0$

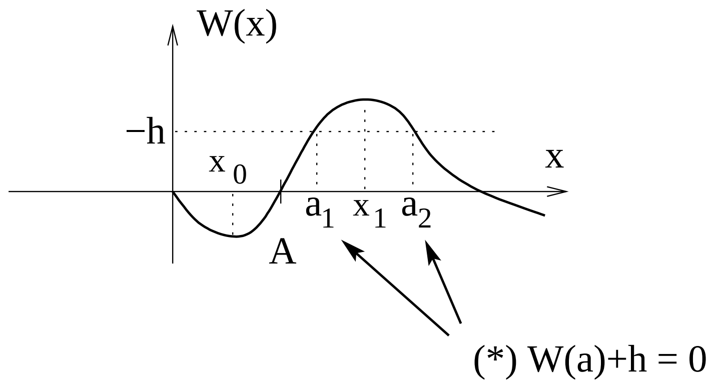
- assume

$(E1)$ $h \leq 0$, $(E2)$ $W(x) + h > 0$ for an $x \in \mathbb{R}^+$ & $\lim\limits_{x\to\infty} W(x) < -h$





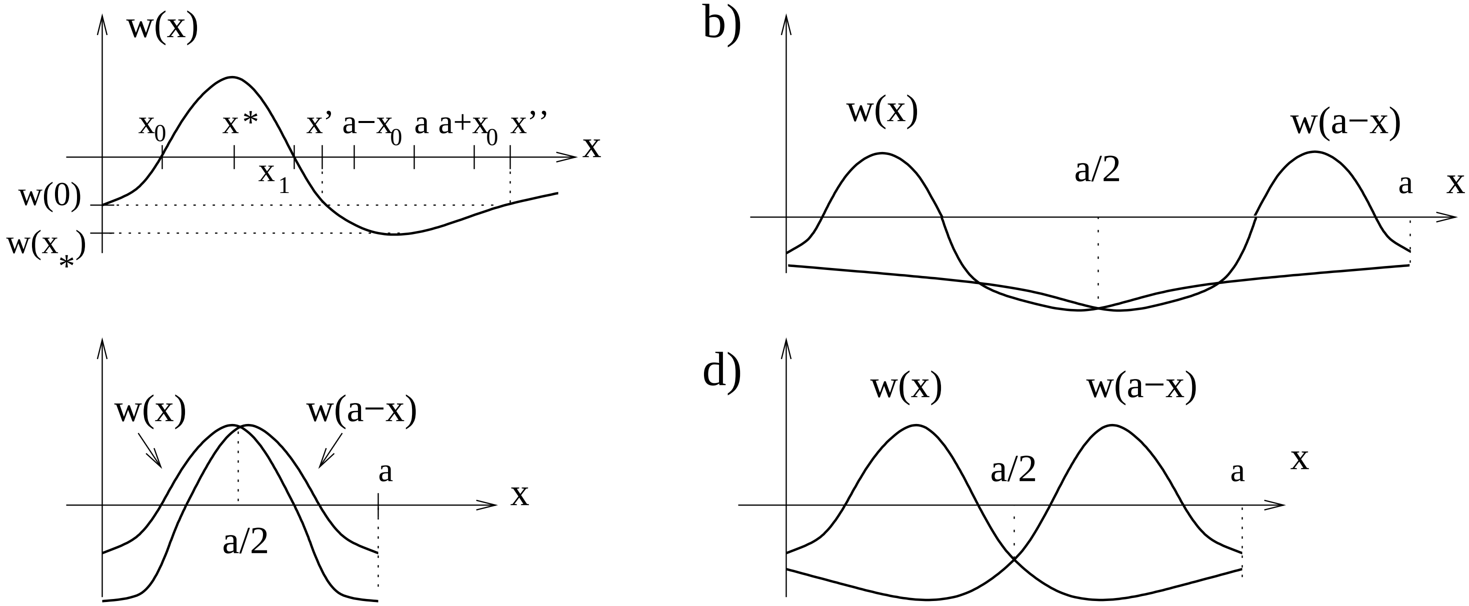
Nonexistence results



- a_1 does not give a bump (in particular $u_1'(0) < 0$)
- a_2 does not necessarily give a bump (in particular, if $0 < a_2 - a_1 < A$, then $u_2(a_1) < 0$)
- Small $|h| \Rightarrow$ large a_2. If a_2 is *too* large, then no bump.

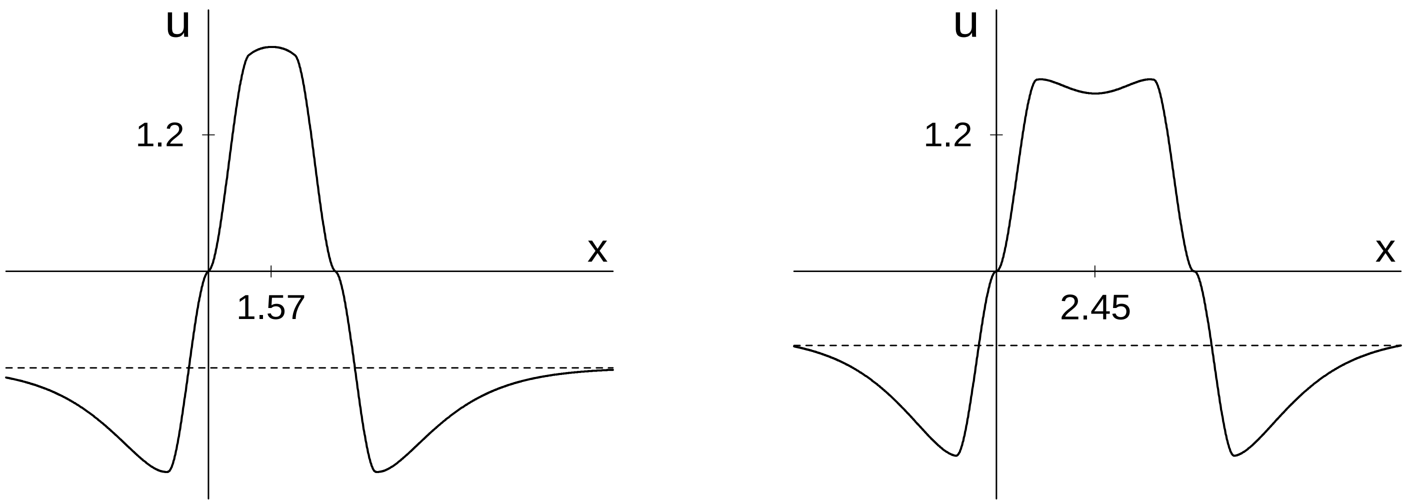
Existence results

- **Assume also: $(E3)$ $w(a_2 \pm x_0) < w(0)$; i.e., $a_2 \in$ valley of $w(x)$.**
- **Theorem: Assume $w(x)$ as above and fix h such that $(E1)-(E3)$ hold and $a_2/2 > x_1$. Then the function $u_2(x)$ defined by $(*)$ with $a = a_2$ is a bump solution, with $u_2(x) > 0$ if and only if $x \in (0, a_2)$.**
- **Theorem: If $a_2/2 \in (x_1, x_*]$, then $u_2'(x)$ has one zero on $(0, a_2)$, at a global maximum at $x = a_2/2$. If $a_2/2 > x_*$, then $u_2'(x)$ has at least three zeros on $(0, a_2)$, including a local minimum at $x = a_2/2$.**



- **Additional hyp. on w or $h \Rightarrow u_2(x)$ is a valid bump for $a_2/2 \le x_1$.**

Numerical examples: tooth



Proposition: If $a_2/2 > a_1$, $u_2(x) > 0$ on $(0, a_2)$, then $u_2(a_2/2) > -h$.

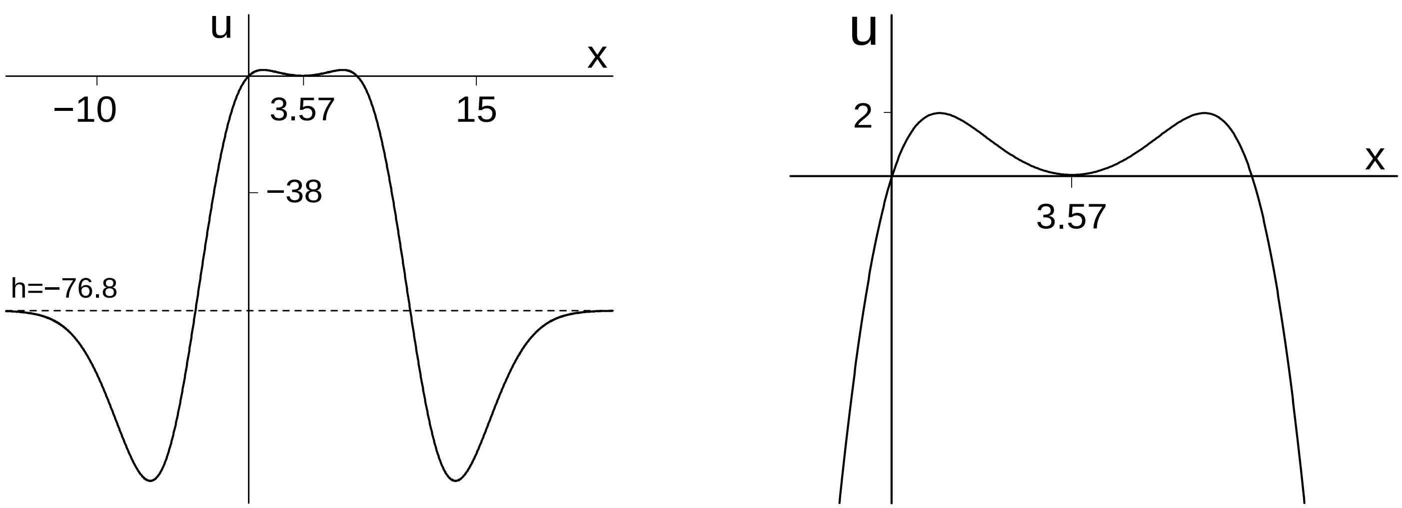
Birth and death mechanisms

- can show bumps only exist for a finite interval of a (or h) values
- no saddle-nodes; bump amplitude/width do not go to 0
- two mechanisms:

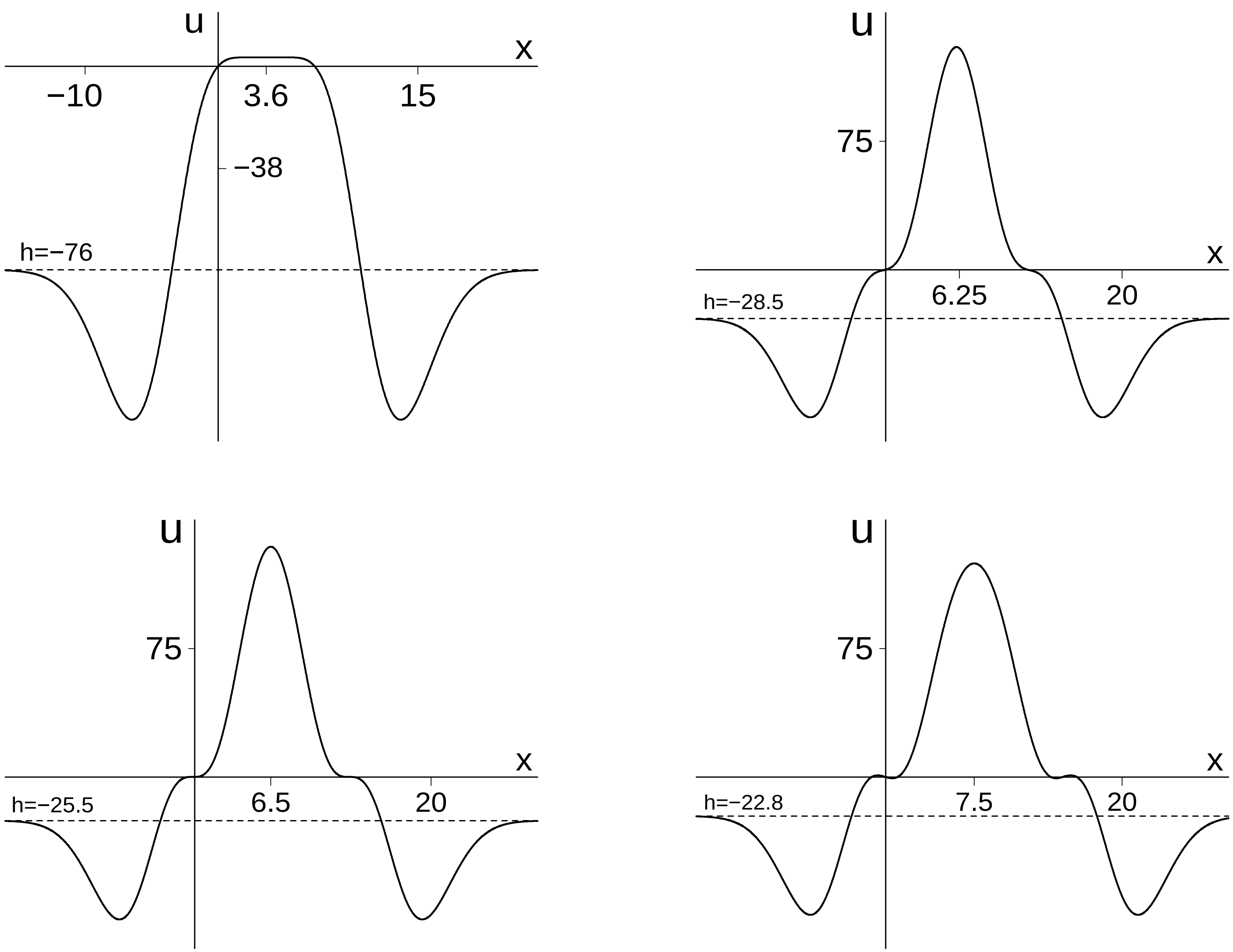
  internal tangency: $u(x) = u'(x) = 0$ at some point in $(0, a)$, else $u(x) > 0$

  boundary tangency: $u(0) = u'(0) = 0$, $u(a) = u'(a) = 0$
- as $|h| \downarrow$, birth is ***always*** internal tangency; death may be either

Numerical example: birth



Numerical example: growth and death (movie)



Spatial variation in coupling

$$\begin{cases} u_t(x,t) = -u(x,t) + \int_{-\infty}^{\infty} w(x-y)p(y)H(u(y,t))\,dy + h \\ p(x) = 1 + \epsilon(1+\cos(\rho x + \phi))\,; \text{ w.l.o.g. } \rho = 1 \end{cases}$$

First, consider bumps on $(0,a)$ with $\phi = 0$:

- $u(0) = u(a) = 0$ now gives two equations

$$0 = \int_0^a w(\eta)p(\eta)\,d\eta + h,\ 0 = \int_0^a w(a-\eta)p(\eta)\,d\eta + h$$

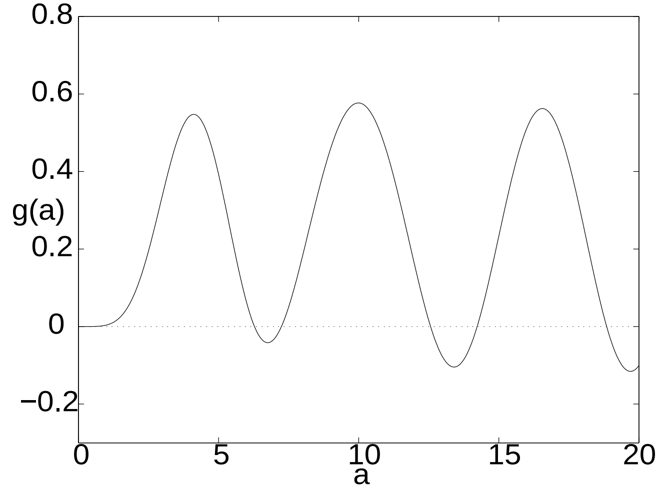
- subtract to obtain

$$g(a) := \int_0^a w(a-\eta)p(\eta)\,d\eta - \int_0^a w(\eta)p(\eta)\,d\eta$$

- look for zeros of g (e.g. $2n\pi$); then check whether these satisfy $u(a) = 0$ for $h \leq 0$ and $a = a_2$

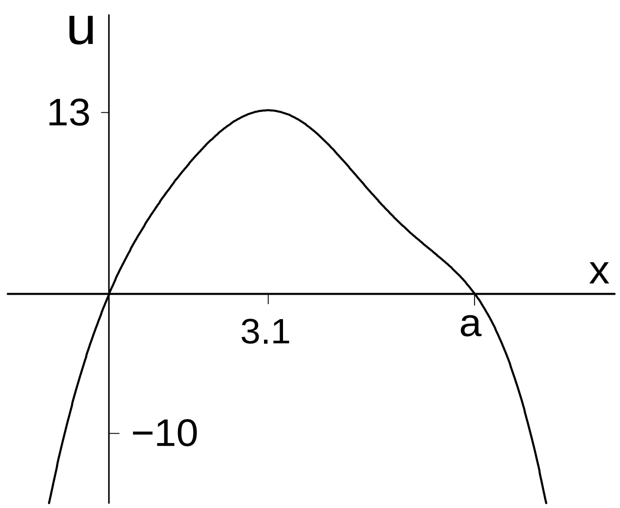
Bump pinning

- zeros of g are independent of $\epsilon > 0$:

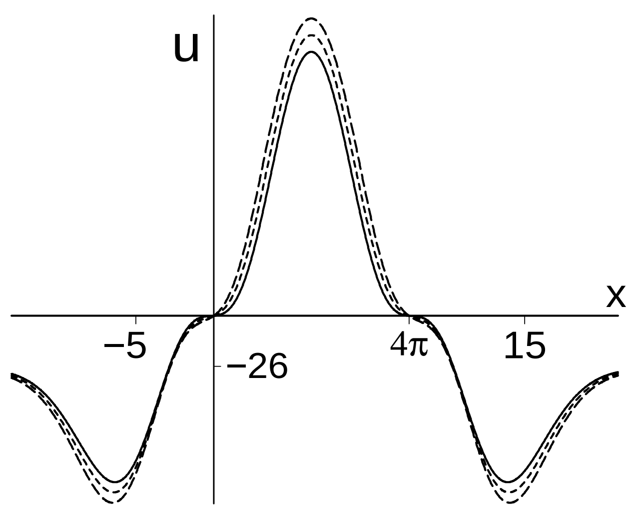


- only a subset gives valid bumps; each a in subset has corresponding $h \leq 0$

$a \approx 7.25, \epsilon = 0.1$

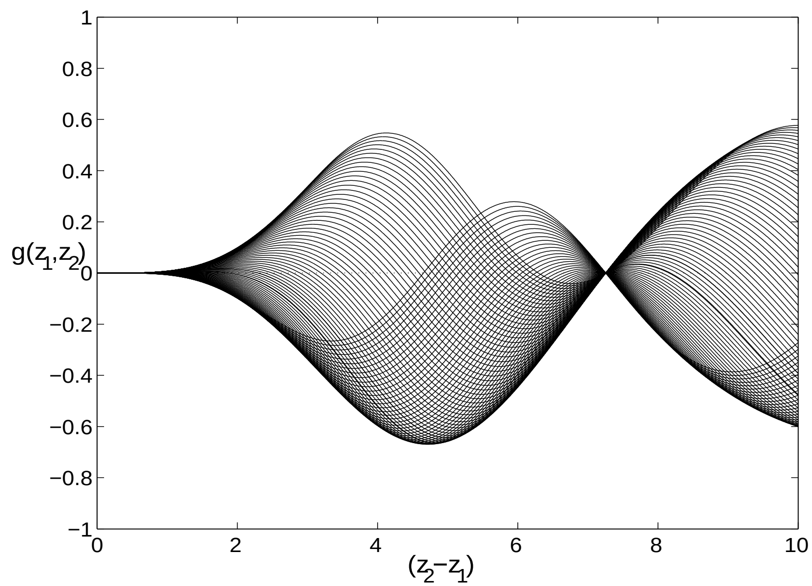


$a = 4\pi$



Bumps on (b_1, b_2) with arbitrary phase shift ϕ

- similar analysis $\Rightarrow g(b_1, b_2)$
- can show $g = g(z_1, \delta)$ where $z_1 = b_1 - \phi$ and δ = bump length
- for our choice of $p(x)$, we find numerically that for each choice of ϕ and starting position b_1,
  - a small, discrete set of bump sizes can occur, and
  - one particular size (not $2n\pi$) always belongs to this set:



Summary

- off-center coupling can yield a single linearly stable bump, if the long-range inhibition dominates the local inhibition

  open: how does this apply in more biological models? two layers?

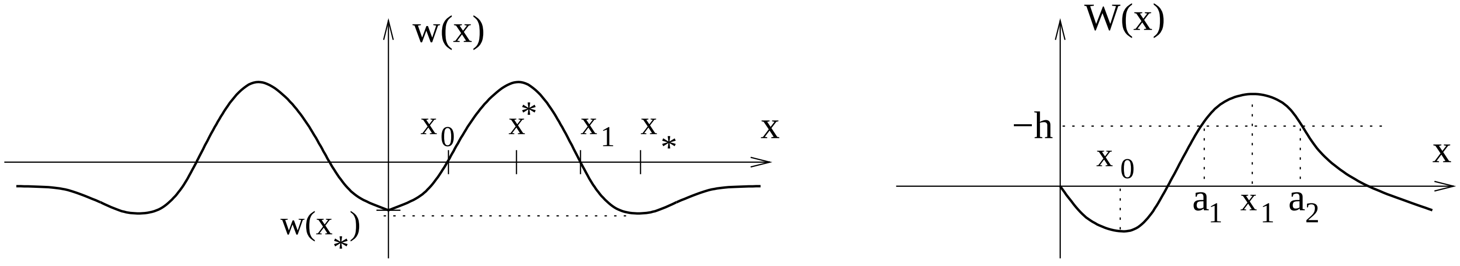
- this mechanism favors "wide" bumps, which may have interior local minima

- these bumps form/disappear via tangencies, not shrinkage

  open: multi-bumps? time-dependent solutions? interactions?

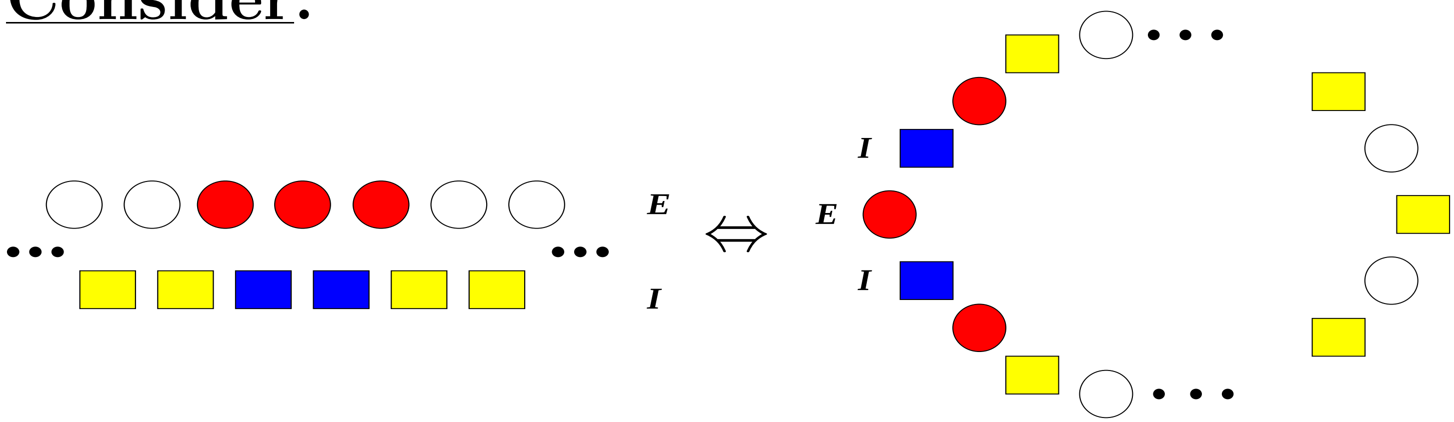
- spatial variation in coupling induces pinning, such that bumps can only exist for discrete background activity levels

  open: invariant bump length? other inhomogeneities? significance of pinning?



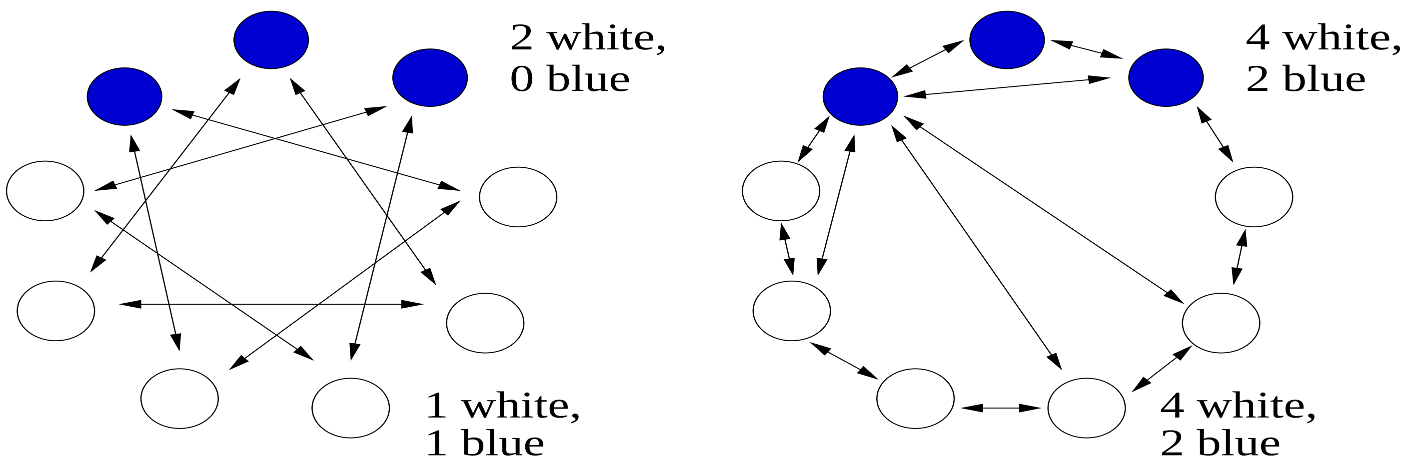
What about other architectures?

- Q: How does a pattern of synchrony restrict the possible architectures in a network? [w/Golubitsky & Josic]
- Consider:



- Golubitsky & Stewart: A clustered solution, with robust synchrony within clusters, can exist iff there is a *balanced coloring* corresponding to that solution.
- Above: # { connections from cells of A to cells of B } is a constant $c(A, B)$ for $A, B \in$ {red, blue, white, yellow}.

- Problem: For given k, l, N_E, N_I, find a nontrivial balanced coloring (with min number of connections).
- Example (one population; $N = 9, k = 3$):



- Note: Which k are selected is arbitrary – connections are homogeneous.
- Idea: abstract mathematical approach $\Rightarrow$ architectural possibilities precisely specified; activity pattern observed thus gives information about synaptic architecture

Change gears

- **Consider a network of recurrently connected excitatory cells (*E-E connections only*).**
- **Focus on details of intrinsic and synaptic dynamics.**
- **Result: A reminder that these details can strongly shape pattern formation.**

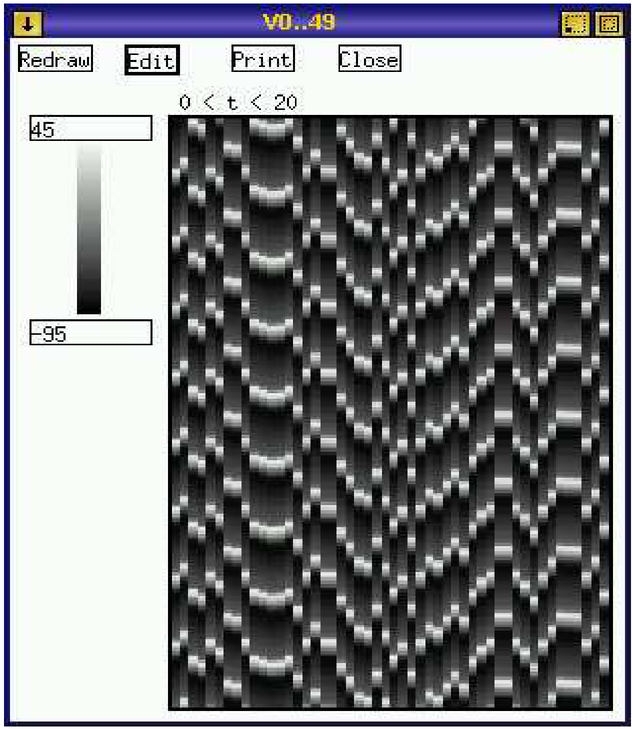
Case I: Hodgkin-Huxley neurons with all-to-all coupling [Drover, Rubin, Su, & Ermentrout]

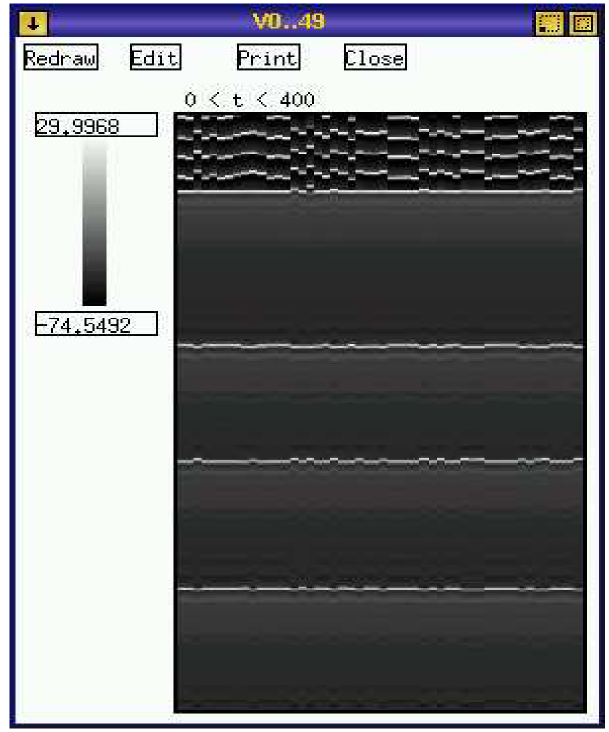
$$\begin{cases} C\frac{dV}{dt} = f(V,h) - g_{syn}s(V - V_{syn}) \\ \frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)h \\ \frac{ds}{dt} = \alpha(V)(1-s) - s/\tau_{syn} \end{cases}$$

where

$$\begin{aligned} f(V,h) = I_0 - g_{Na}h(V - V_{Na})m_\infty^3(V) \\ -g_K(V - V_K)n^4(h) - g_L(V - V_L) \end{aligned}$$

Numerics

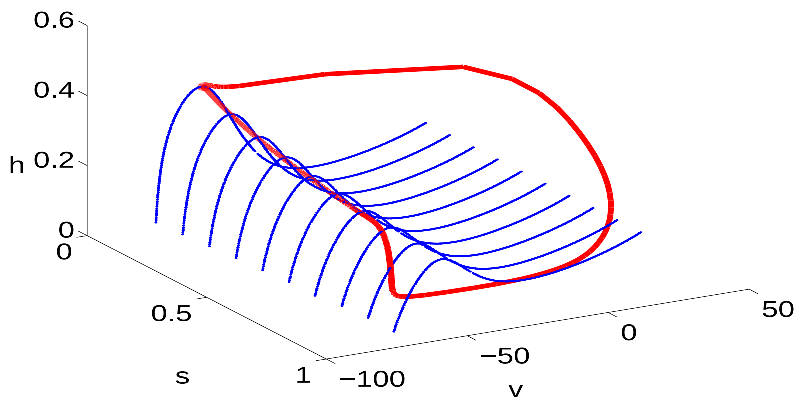


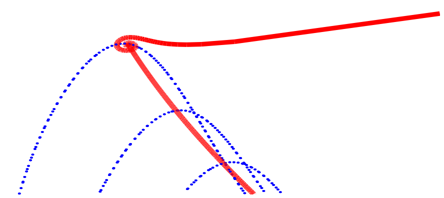


Type I: oscillations emerge with zero frequency; excitation desynchronizes (Ermentrout, 1996)

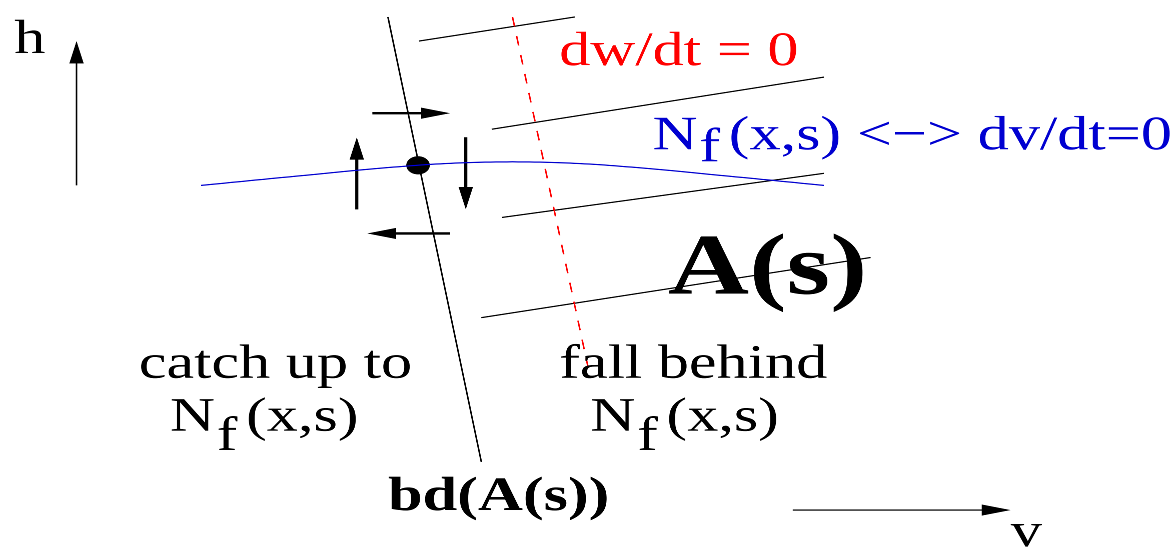
Type II: oscillations emerge with nonzero frequency; excitation synchronizes (Somers & Kopell, 1993; Hansel et al., 1995)

What causes the slowing? (movie)





fix s**:**



$$A(s) = \{(v,h) : \frac{dh}{dt}(v,h) < \frac{dN_f}{ds}(v,s)\frac{ds}{dt}\}$$

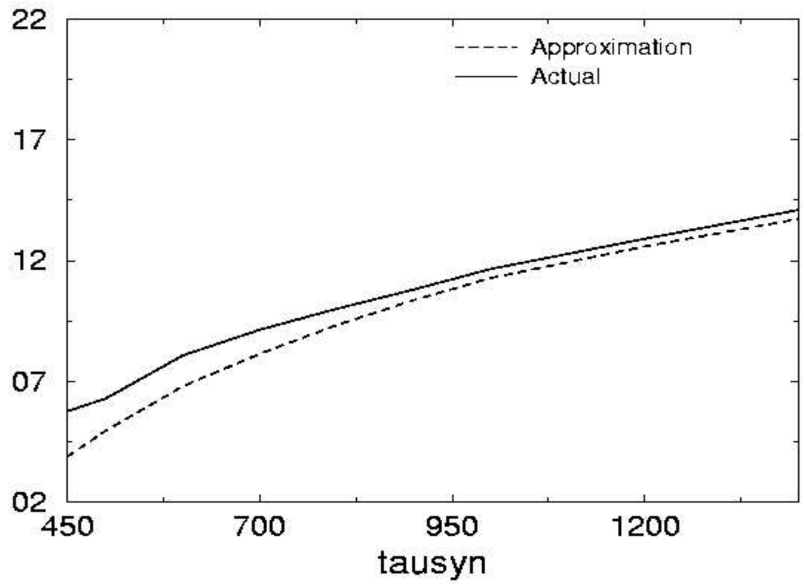
Delay estimation

$$\begin{aligned} z_1 &= v - \hat{v}(s) \\ z_2 &= w - \hat{w}(s) \end{aligned} \Rightarrow \frac{dz}{ds} = -\frac{\tau_{syn}}{s} f(z)$$

linearize about $(0, 0)$ and solve:

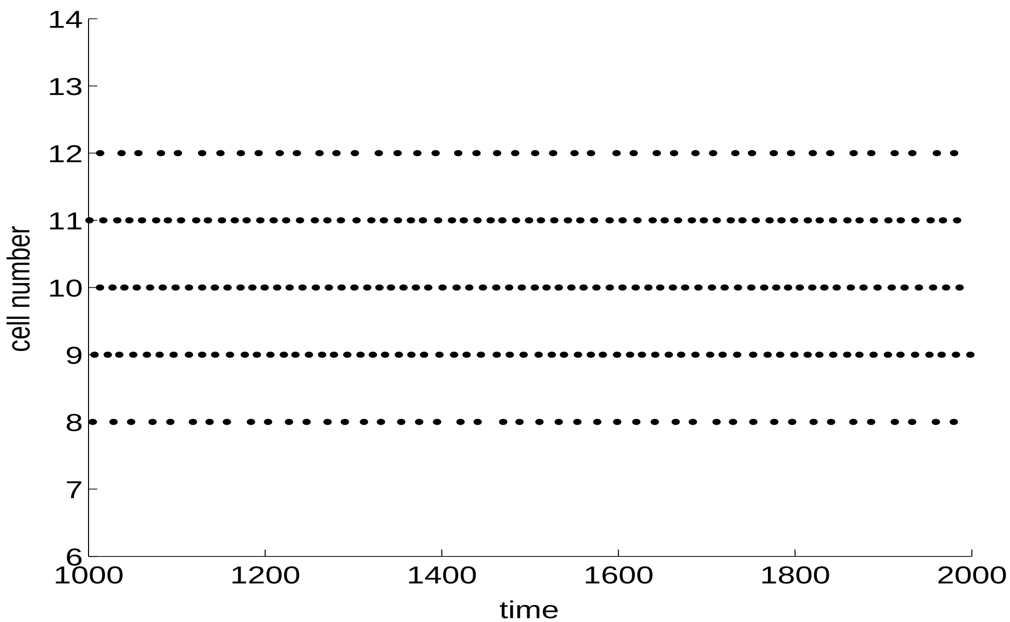
$$z(s) = z(s_0)\exp(-\tau_{syn}\int_{s_0}^{s} f_z(0,0)\,dw)$$

s



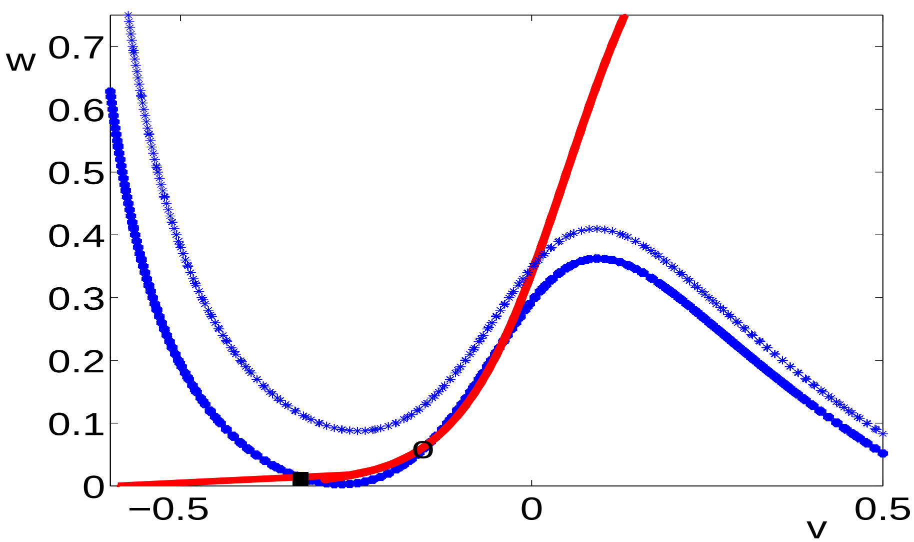
Case II: Eliminate all-to-all coupling ⇒ sustained, localized activity with E-E coupling only! [w/ A. Bose]

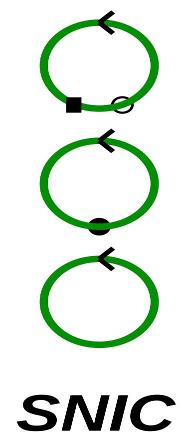
works with Type I as above (numerics in Drover and Ermentrout, SIAP, 2003) or Type II:



Equations (movie)

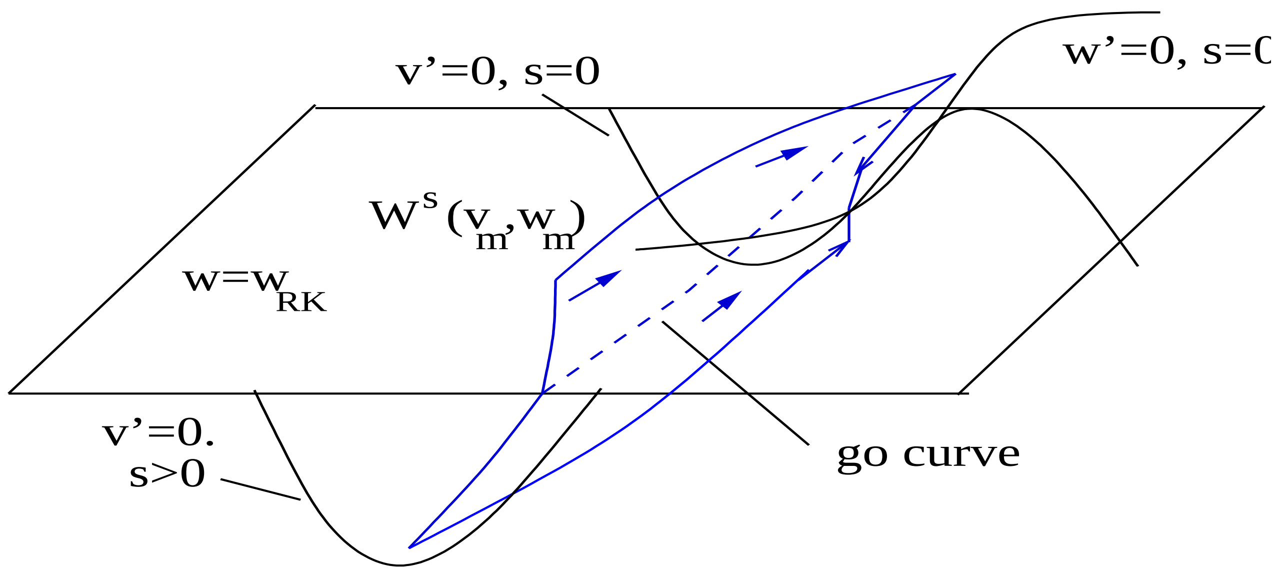
$$\begin{cases} v_i' = -I_{Ca} - I_K - I_L - \bar{g}_{syn}[v_i - E_{syn}]\left[c_O s_i + \Sigma_{j=1}^{j=3} c_j[s_{i-j} + s_{i+j}]\right] \\ w_i' = [w_\infty(v_i) - w_i]/\tau_w(v_i) \\ s_i' = \alpha[1 - s_i]H_\infty(v_i - v_\theta) - \beta s_i \ (s_i = 0 \textbf{ for } i < 1, i > N) \\ \quad = \begin{cases} -\beta s_i \textbf{ for } v_i < v_\theta \\ 0 \textbf{ for } v_i > v_\theta, \ \textbf{with } s_i = 1 \end{cases} \end{cases}$$



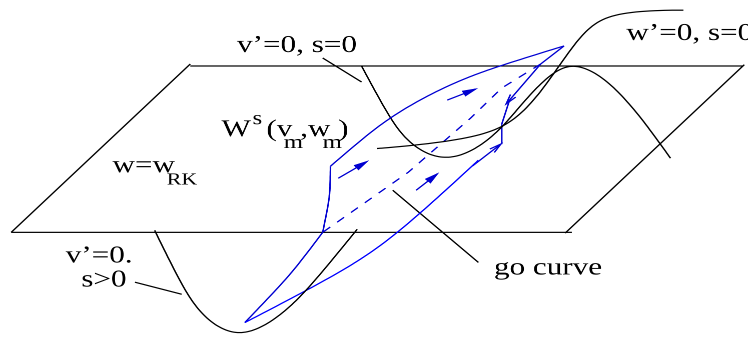


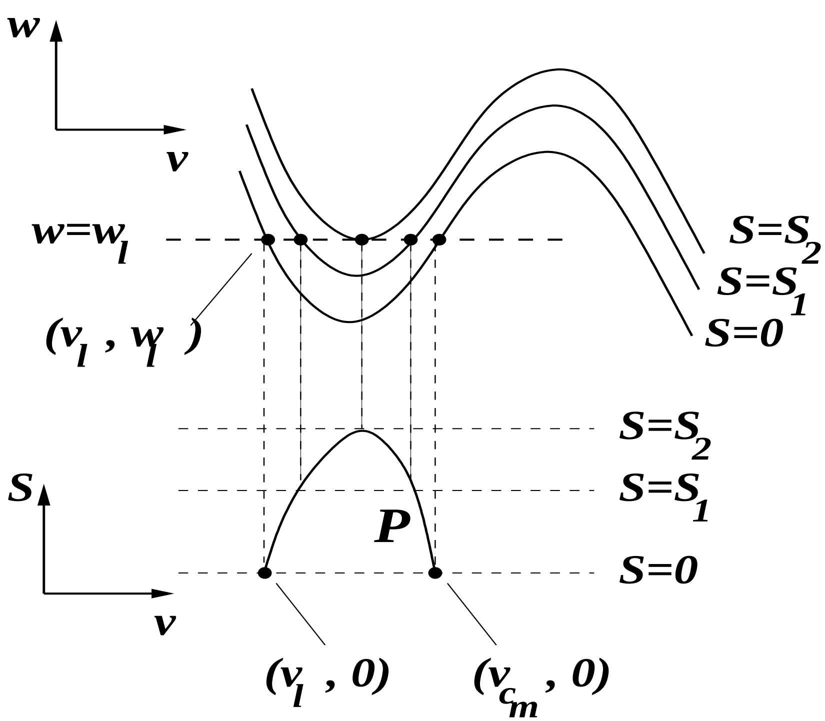
Geometry

$$\begin{cases} v_i' = f(v_i, w_i) - \bar{g}_{syn} S_i \\ w_i' = g(v_i, w_i) \\ S_i' = -\beta S_i \end{cases}$$

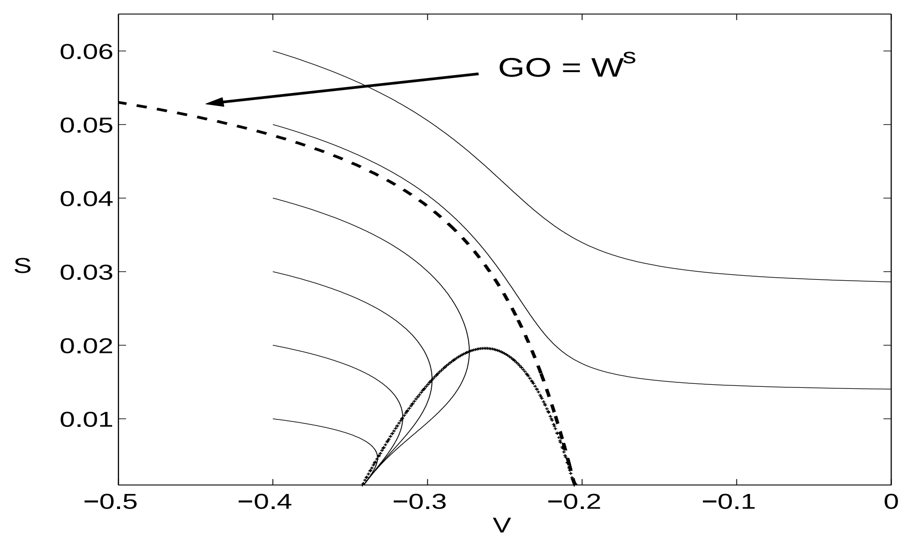


Geometry 2

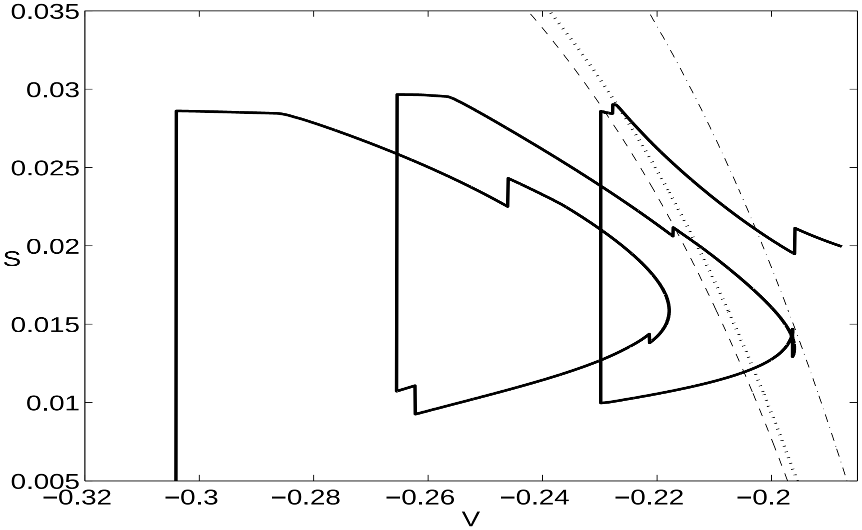


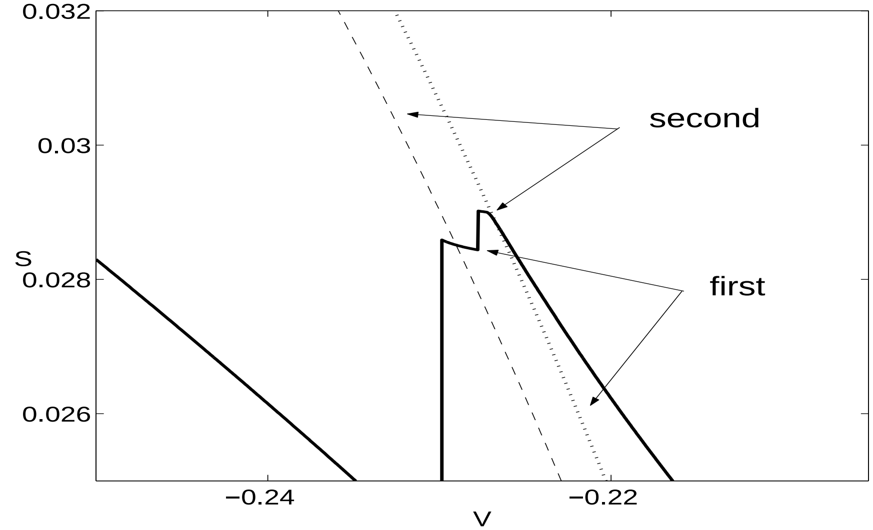


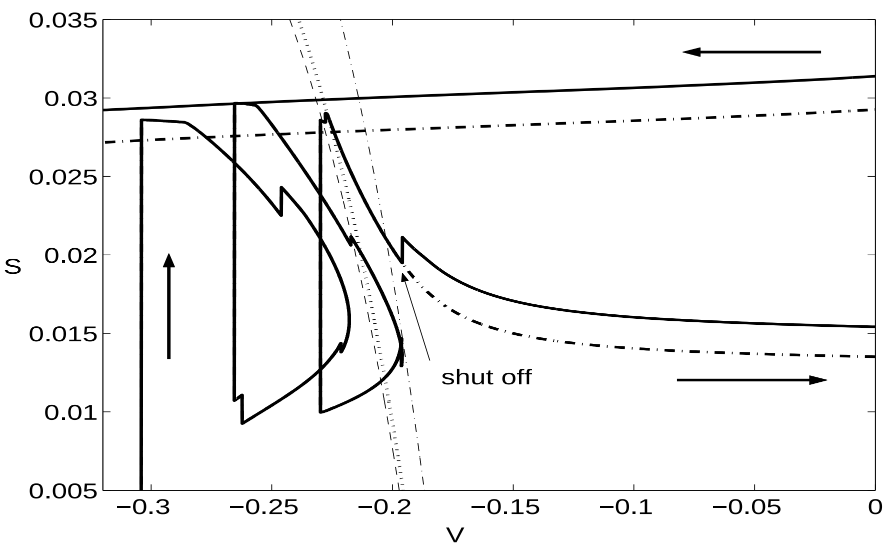
w fixed:

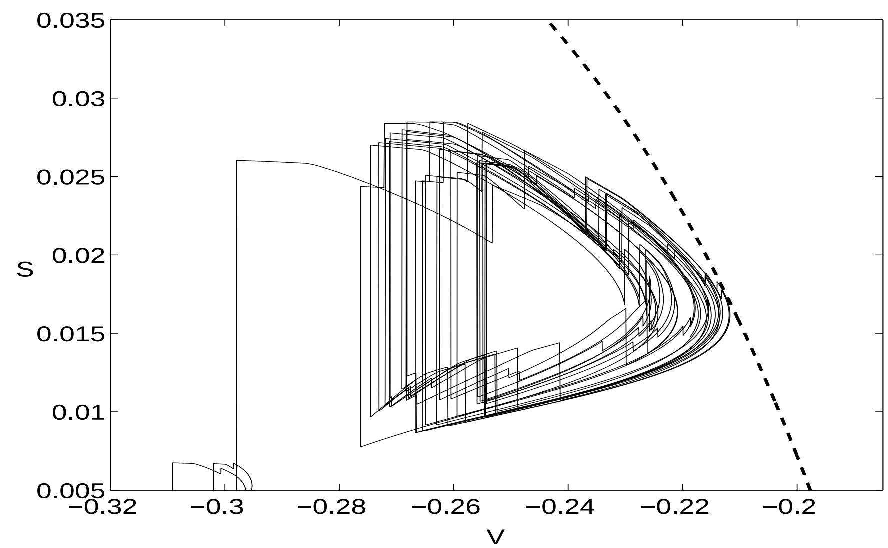


Implications



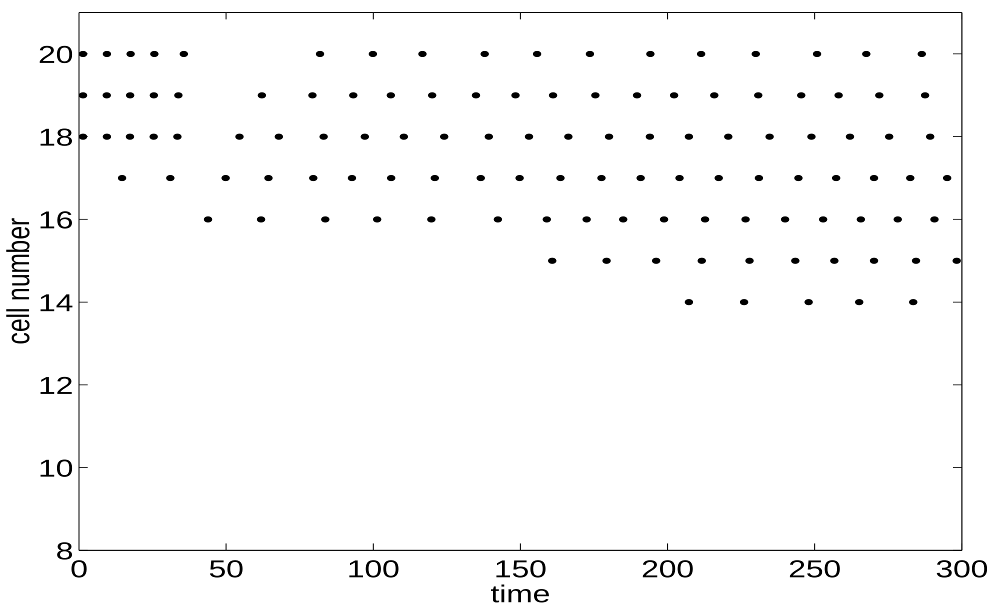






Properties of solutions

- can get bumps of any size
- size selected is sensitive to parameters of initial shock
- details of bumps are sensitive
- also get propagation with recruitment after variable delays – short delays follow long delays



SUMMARY

- **Intrinsic and synaptic dynamics can give unexpected results.**
- **Geometric viewpoint is useful for understanding observations.**
- **OPEN: Are these figments of models or do neurons operate in these regimes?**