Introduction to Computational Neuroscience

Biol 698
Math 635

Biol 498
Math 430

Neuronal Networks

Reference:

• *Mathematical Foundations of Neuroscience*, by G. B. Ermentrout & D. H. Terman - Springer (2010), 1st edition. ISBN 978-0-387-87707-5

• Phase plane analysis of neural nets. B Ermentrout. InThe Handbook of Brain Theory and Neural Networks. MIT Press (2007)

Overview

- ☑ Firing rate models - Single cells
- ☑ Firing rate model - Population of neurons
- ☑ The Wilson-Cowan equations
- ☑ Populations of excitatory neurons
- ☑ Populations of inhibitory neurons
- ☑ Up-down states

POPULATION MODELS

Firing rate models / population models:

☑ Hodgkin-Huxley-type models track the spiking of every neuron

☑ Firing rate models track the averaged behavior of the spike rates of groups of neurons within the circuit

Rate models are the underlying “biology” in the theory of neural networks

Connectionist and back-propagation models are connected through rate models

HEURISTIC DERIVATION

☑ $u_i(t)$: observable output

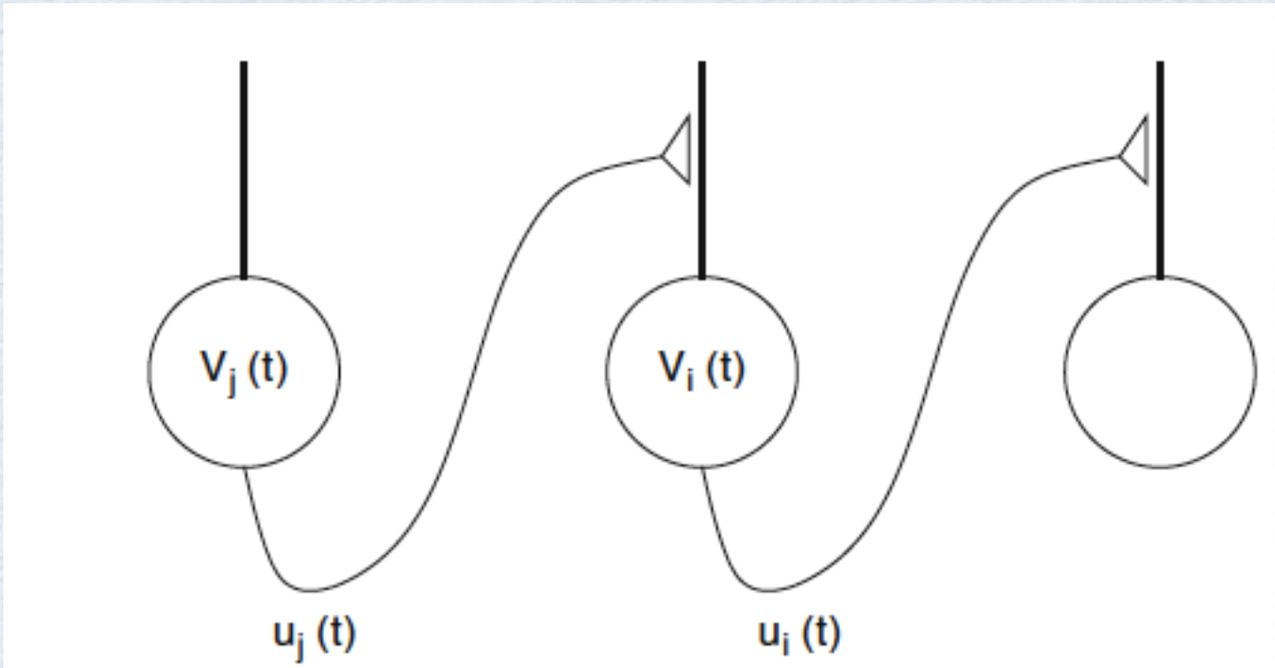
☑ $V_i(t)$: somatic potential

☑ $u_i(t)$ and $V_i(t)$ depend in a nonlinear way

$$u_i(t) = F_i(V_i(t))$$

☑ $u_i(t)$ determines the instantaneous number of spikes that a neuron fires in an infinitesimal time interval

☑ $u_i(t)dt$: probability of a spike occurring in the time interval (t,t+dt)

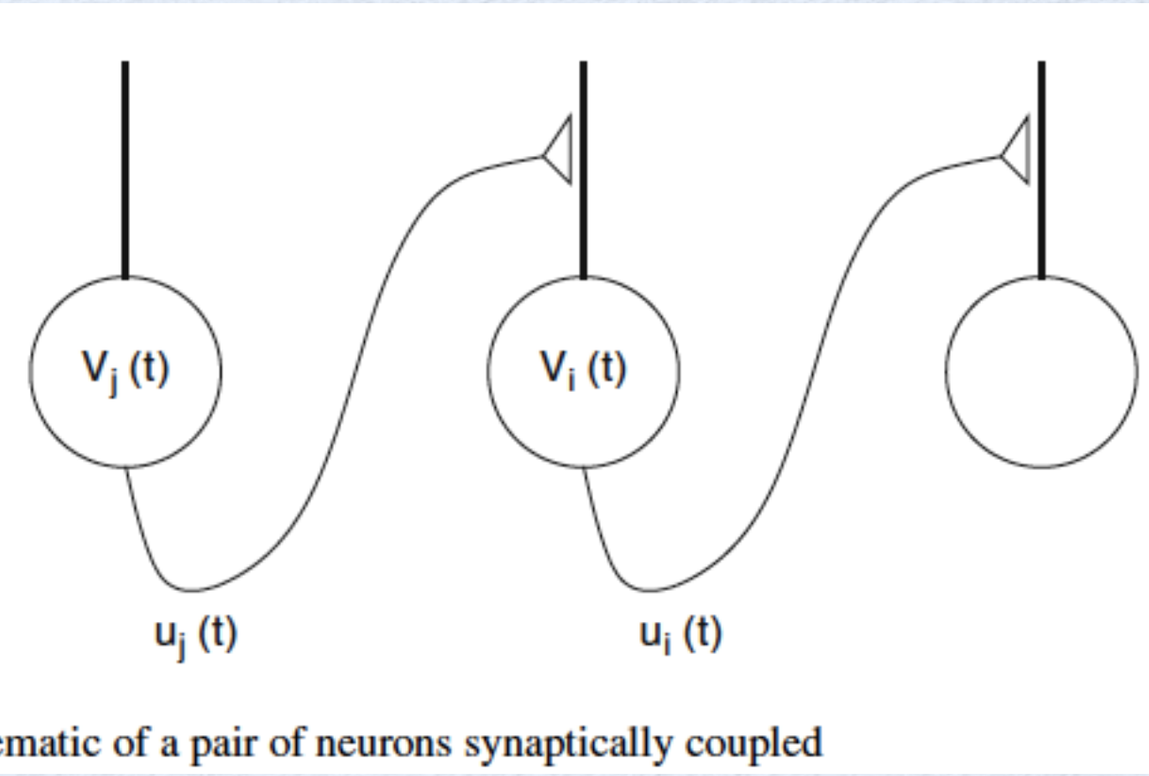


Schematic of a pair of neurons synaptically coupled

HEURISTIC DERIVATION

☑ Φ_{ij}: postsynaptic potential appearing on postsynaptic cell i due to a single spike from presynaptic cell j

☑ $t_1, t_2, \ldots, t_m$: firing time of the presynaptic cell



Schematic of a pair of neurons synaptically coupled

☑ $G_{ij}(t)$: total potential received at the soma

$$G_{ij}(t) = \sum_{l} \Phi_{ij}(t - t_l)$$

☑ τ_{ij}: axonal delay in the spike arising at cell j arriving at cell i

$$G_{ij}(t) = \int_{t_0}^{t} \Phi_{ij}(t - s) u_j(s - \tau_{ij}) \mathrm{d}s$$

HEURISTIC DERIVATION

Assumption: linear summation

$$u_i(t) = F_i(V_i(t))$$

$$G_{ij}(t) = \int_{t_0}^{t} \Phi_{ij}(t-s)u_j(s-\tau_{ij})\mathrm{d}s$$

$$V_i(t) = \sum_j G_{ij}(t) = \sum_j \int_{t_0}^{t} \Phi_{ij}(t-s)F_j(V_j(s-\tau_{ij}))\mathrm{d}s$$

$$u_i(t) = F_i\left(\sum_j \int_{t_0}^{t} \Phi_{ij}(t-s)u_j(s-\tau_{ij})\mathrm{d}s\right)$$

HEURISTIC DERIVATION

- ☑ R_M: membrane resistance
- ☑ τ_m: time constant
- ☑ I: presynaptic current

$$\tau_m \frac{d\Phi}{dt} + \Phi = R_M I(t)$$

Assumption:

$$I(t) = \exp(-t/\tau_d) - \exp(-t/\tau_r)$$

- ☑ τ_r: rise time
- ☑ τ_d: decay time

$$\Phi(t) = \frac{\tau_d}{\tau_d - \tau_m}\left(e^{-t/\tau_d} - e^{-t/\tau_m}\right) - \frac{\tau_r}{\tau_r - \tau_m}\left(e^{-t/\tau_r} - e^{-t/\tau_m}\right)$$

HEURISTIC DERIVATION

☑ If Φ is a sum of exponentials, the integral equation can be broken into a set of differential equations

$$x(t) = \int_{t_0}^{t} \mathrm{e}^{-(t-s)/\tau} y(s-r)\mathrm{d}s$$

$$\frac{\mathrm{d}x}{\mathrm{d}t} = y(t-r) - \frac{1}{\tau}\int_{t_0}^{t} \mathrm{e}^{-(t-s)/\tau} y(s-r)\mathrm{d}s = y(t-r) - x(t)/\tau.$$

$$\frac{\mathrm{d}x}{\mathrm{d}t} + x/\tau = y(t-r)$$

HEURISTIC DERIVATION

- Homogeneous populations of neurons: $\Phi_{ij} = w_{ij}\ \Phi$
- w_{ij}: magnitude of the connections

$$V_i(t) = \sum_j G_{ij}(t) = \sum_j \int_{t_0}^{t} \Phi_{ij}(t-s) F_j(V_j(s-\tau_{ij}))\mathrm{d}s$$

$$(LV_i)(t) = \sum_j w_{ij} F_j(V_j(t-r))$$

- L: linear homogeneous differential operator

HEURISTIC DERIVATION

- ☑ Homogeneous populations of neurons: $\Phi_{ij} = w_{ij}\,\Phi$
- ☑ w_{ij}: magnitude of the connections
- ☑ z_{ij}: synaptic drive

$$u_i(t) = F_i\left(\sum_j \int_{t_0}^{t} \Phi_{ij}(t-s)u_j(s-\tau_{ij})\mathrm{d}s\right)$$

$$z_i(t) = \int_{t_0}^{t} \Phi(t-s)u_i(s-r)\mathrm{d}s$$

$$(Lz_i)(t) = u_i(t-r) = F_i\left(\sum_j w_{ij} z_j(t-r)\right)$$

HEURISTIC DERIVATION

- ☑ Less restrictive assumption: $\Phi_{ij} = w_{ij}\ \Phi_i$
- ☑ w_{ij}: magnitude of the connections
- ☑ z_{ij}: synaptic drive

$$(L_i V_i)(t) = \sum_j w_{ij} F_j(V_j(t-r))$$

- ☑ Less restrictive assumption: $\Phi_{ij} = w_{ij}\ \Phi_j$

$$(L_i z_i)(t) = F_i\left(\sum_j w_{ij} z_j(t-r)\right)$$

HEURISTIC DERIVATION

What's the meaning of these assumptions?

☑ $\Phi_{ij} = w_{ij}\,\Phi_i$: the response of neuron i to any inputs depends (up to a scalar constant which could be negative or positive) only on the properties of the postsynaptic cell

☑ Valid assumption if the shape and temporal properties of the presynaptic currents are the same no matter what type the presynaptic cell is (NMDA is slower than AMPA; AMPA is faster than GABA)

☑ $\tau_m \gg \{\tau_d,\tau_r\} \rightarrow \Phi(t) \approx \exp(-t/\tau_m)/\tau_m$

$$\tau_{m,i}\frac{dV_i(t)}{dt} + V_i(t) = \sum_j w_{ij}\,F_j(V_j(t-r))$$

HEURISTIC DERIVATION

What's the meaning of these assumptions?

☑ $\Phi_{ij} = w_{ij}\,\Phi_j$: the shape of the postsynaptic potential depends only on the presynaptic cell

☑ We can distinguish different types of synapses (and it allows incorporation of synaptic depression and facilitation

☑ $\tau_d \gg \{\tau_m, \tau_r\} \rightarrow \Phi_j(t) \approx \exp(-t/\tau_d)/\tau_d$

$$\tau_d \frac{dz_i(t)}{dt} + z_i(t) = F_i\left(\sum_j w_{ij} z_j(t-r)\right)$$

DERIVATION FROM AVERAGING

☑ Conductance-based network model

$$C\frac{\mathrm{d}V_i}{\mathrm{d}t} + I_i(V_i, \ldots) = -\sum_j g_{ij} s_j (V_i - V_{\mathrm{syn},j}),$$

$$\tau_{\mathrm{syn}}\frac{\mathrm{d}s_i}{\mathrm{d}t} + s_i = R_i(V_i, s_i).$$

☑ I_i: all nonlinear conductances which lead to action potentials

☑ Assumption: a synapse from cell j produces the same conductance change regardless of the postsynaptic target

☑ Assumption: $\tau_m \gg 1$ (slow synapses) $\rightarrow$ $s_i = \mathrm{const}$

☑ Assumption: $V_{syn,j} = V_e$ (all neurons are excitatory)

DERIVATION FROM AVERAGING

- Conductance-based network model

$$C\frac{dV_i}{dt} + I_i(V_i, \ldots) = -\sum_j g_{ij} s_j (V_i - V_{\text{syn},j}),$$

$$\tau_{\text{syn}}\frac{ds_i}{dt} + s_i = R_i(V_i, s_i).$$

$$G_i = \sum_j g_{ij} s_j$$

- Bifurcation diagram: $V_i(t) = \bar{V}_i(t; G_i)$

- Two types of behavior: stable fixed-points and limit cycles with period $T_i(G_i)$

DERIVATION FROM AVERAGING

- ☑ Conductance-based network model

$$C\frac{\mathrm{d}V_i}{\mathrm{d}t} + I_i(V_i, \ldots) = -\sum_j g_{ij} s_j (V_i - V_{\mathrm{syn},j}),$$

$$\tau_{\mathrm{syn}}\frac{\mathrm{d}s_i}{\mathrm{d}t} + s_i = R_i(V_i, s_i).$$

$G_i = \sum_j g_{ij} s_j$

$V_i(t) = \bar{V}_i(t; G_i)$

$$\frac{\mathrm{d}s_i}{\mathrm{d}t} = \frac{1}{\tau_{\mathrm{syn}}}(-s_i + R_i(\bar{V}_i(t; G_i), s_i)).$$

- ☑ Fixed-point case: straightforward
- ☑ Limit cycle case: averaging

DERIVATION FROM AVERAGING

☑ Averaging

$$\frac{\mathrm{d}s_i}{\mathrm{d}t} = \frac{1}{\tau_{\mathrm{syn}}}(-s_i + \langle R_i(\bar{V}_i(t;G_i), s_i)\rangle)$$

$$\langle R_i(\bar{V}_i(t;G_i), s_i)\rangle = \frac{1}{T_i(G_i)}\int_0^{T_i(G_i)} R_i(\bar{V}_i(t;G_i), s_i)\mathrm{d}t \equiv Q_i(G_i, s_i)$$

$$\tau_{\mathrm{syn}}\frac{\mathrm{d}s_i}{\mathrm{d}t} + s_i = Q_i\left(\sum_j g_{ij}s_j, s_i\right)$$

DERIVATION FROM AVERAGING

☑ Q(G,s):

$$\frac{ds}{dt} = \alpha(V)(1-s) - \beta s$$

$\beta = 1/\tau_{syn}$

$R(V,s) = \alpha(V)\tau_{syn}(1-s)$

☑ α(V) is zero except when the neuron spikes

☑ Assumption: the width of a spike is independent of the firing rage of the neuron

DERIVATION FROM AVERAGING

☑ Q(G,s):

$$\int_0^T \alpha(\bar{V}(t))\tau_{\text{syn}}\mathrm{d}t = \mu$$

☑ μ is a constant independent of T

☑ F(G): firing rate of the conductance-based model given the synaptic conductance G

$$F(G) \equiv \frac{1}{T(G)}$$

$$Q_i(G_i, s_i) \equiv \frac{1}{T_i(G_i)} \int_0^{T_i(G_i)} R_i(\bar{V}_i(t; G_i), s_i)\mathrm{d}t = \mu_i F_i(G_i)(1 - s_i)$$

DERIVATION FROM AVERAGING

$$\tau_{\text{syn}} \frac{\mathrm{d}s_i}{\mathrm{d}t} + s_i = Q_i \left(\sum_j g_{ij} s_j, s_i \right)$$

$$Q_i(G_i, s_i) \equiv \frac{1}{T_i(G_i)} \int_0^{T_i(G_i)} R_i(\bar{V}_i(t; G_i), s_i) \mathrm{d}t = \mu_i F_i(G_i)(1 - s_i)$$

$$\tau_i \frac{\mathrm{d}s_i}{\mathrm{d}t} = \mu_i F_i \left(\sum_j g_{ij} s_j \right) (1 - s_i) - s_i$$

POPULATION OF NEURONS

☑ The main role of firing rate models is to examine large numbers of neurons in some "average" fashion

☑ Spiking events are probabilistic
☑ Post-stimulus time histogram (PSTH): repetition of the same stimulus over many trials
☑ PSTH is effectively a firing rate (number of spikes per unit of time)
☑ PSTH assumes that recording simultaneously from N nearby locations and from one location N times give the same result
☑ Assumption: neurons fire independently of each other
☑ Then, the firing rate of the population and a single neuron are exactly the same: Population firing rate.

☑ Is the independence assumption reasonable?

THE WILSON-COWAN EQUATIONS

$$\tau_e \frac{dE}{dt} = -E + (1 - r_e E) F_e(\alpha_{ee} E - \alpha_{ie} I + T_e(t)),$$
$$\tau_i \frac{dI}{dt} = -I + (1 - r_i I) F_i(\alpha_{ei} E - \alpha_{ii} I + T_i(t)),$$

☑ T_e, T_i: input from the thalamus

☑ r_e, r_i: refractory fraction of the neurons available to fire

☑ $(1\text{-}r_e E)$, $(1 - r_i I)$: fraction of neurons available to fire given they have an absolute refractory period of r_e and r_i respectively

☑ F(u): gain functions

$$F(u) = 1/(1 + \exp(-\beta(u - u_T)))$$

F(u): probability of firing (rather than an actual firing rate)

THE WILSON-COWAN EQUATIONS

- Scalar recurrent model:

$$\frac{\mathrm{d}u}{\mathrm{d}t} = -u + F(\alpha u + \beta)$$

- α: strength of the connections
- β: input

THE WILSON-COWAN EQUATIONS

☑ Scalar recurrent model:

$$\frac{du}{dt} = -u + F(\alpha u + \beta)$$

☑ Fixed-point: $-u + F(\alpha u + \beta) = 0$

☑ Control parameter: β

☑ Saddle-node bifurcation: $-1 + \alpha F'(\alpha u + \beta) = 0$

THE WILSON-COWAN EQUATIONS

☑ Two-population networks

$$\tau_1 u_1' = -u_1 + F_1(w_{11}u_1 + w_{12}u_2),$$
$$\tau_2 u_2' = -u_2 + F_2(w_{21}u_1 + w_{22}u_2).$$

Theorem. *Consider the planar system*

$$x' = f(x, y),$$
$$y' = g(x, y),$$

such that $f_y g_x > 0$ *for all* (x, y). *Then there are no limit cycles.*

If $F_i'(u) > 0$ and $w_{12}w_{21} > 0$, then there are no limit cycles and there are just fixed points

THE WILSON-COWAN EQUATIONS

- Two-population networks

$$\tau_1 x_1' = -x_1 + f(w_{11}x_1 + w_{12}x_2 + s_1)$$
$$\tau_2 x'_2 = -x_2 + f(w_{21}x_1 + w_{22}x_2 + s_2)$$

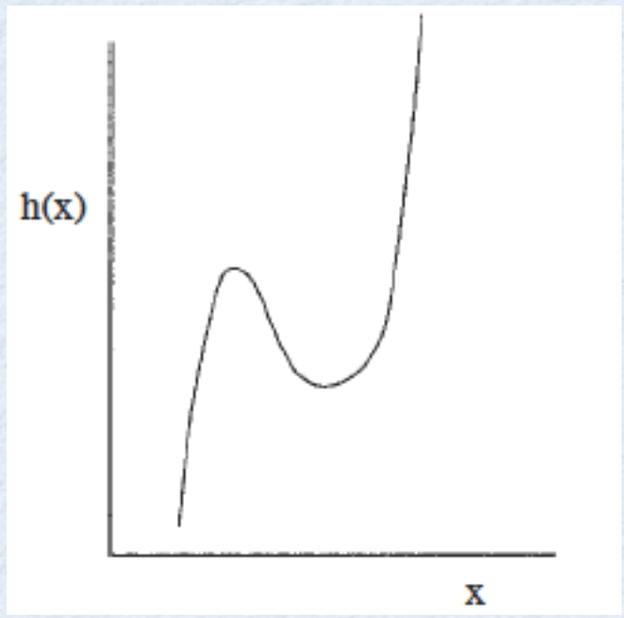
- x_1-nullcline

$$x_2 = (-w_{11}x_1 - s_1 + f^{-1}(x_1))/w_{12}$$

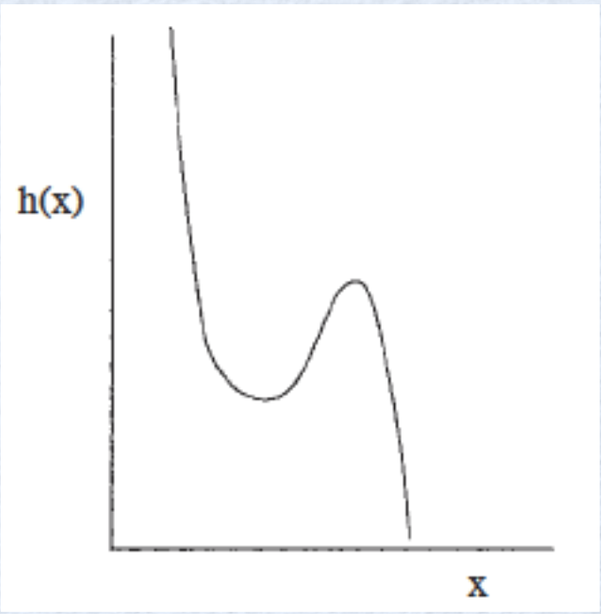
- x_2-nullcline

$$x_1 = (-w_{22}x_2 - s_2 + f^{-1}(x_2))/w_{21}$$

- $h(x) = (-w_s\, x - s\, f^{-1}(x))/w_c$
- $f(x) = 1 / (1 + \exp(-x))$
- h(x) is monotone if
  - w_s is positive
  - small and negative
- h is cubic
  - w_s is large
  - wc determines the properties of h



- $w_c > 0$ (mutual excitation)



- $w_c < 0$ (mutual inhibition)

THE WILSON-COWAN EQUATIONS

- Two-population networks

$$\tau_1 u_1' = -u_1 + F_1(w_{11}u_1 + w_{12}u_2),$$
$$\tau_2 u_2' = -u_2 + F_2(w_{21}u_1 + w_{22}u_2).$$

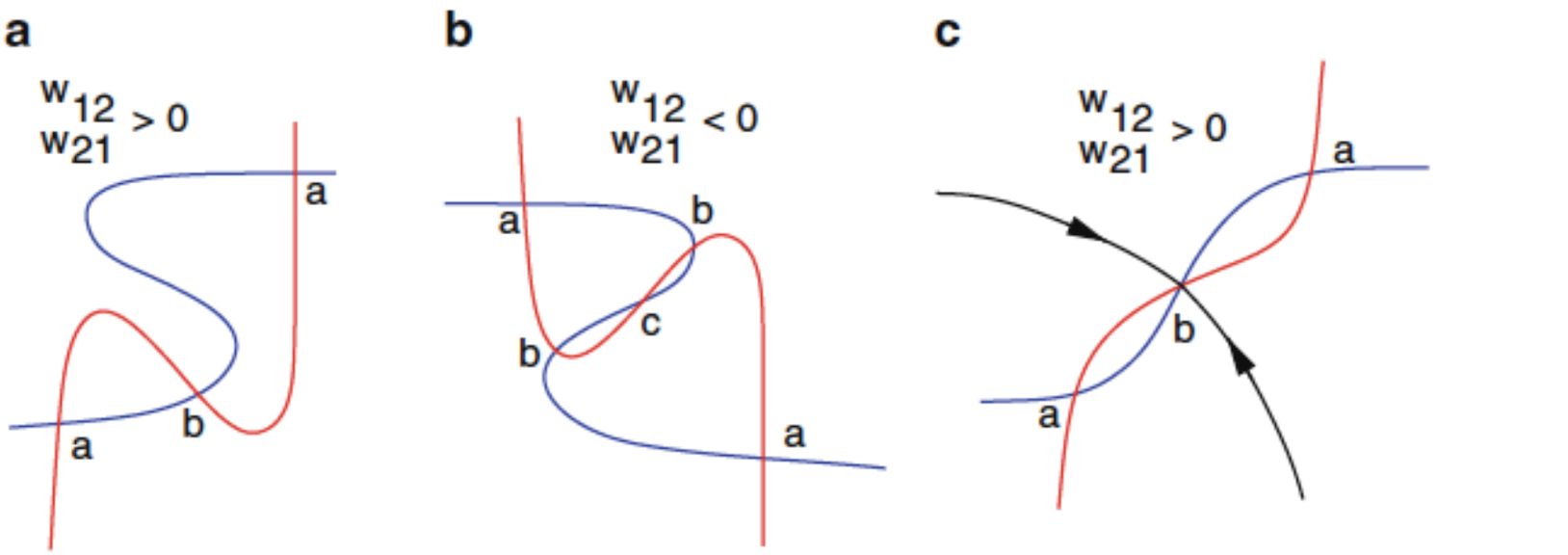
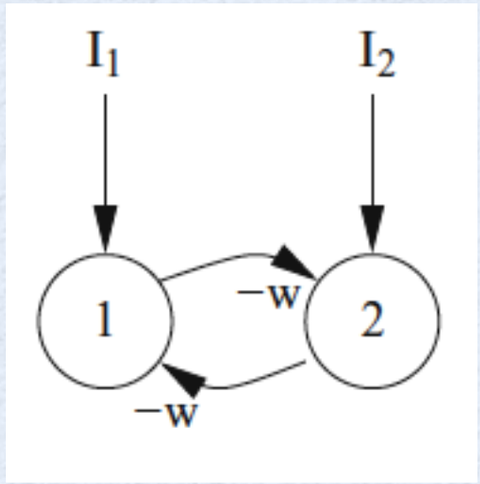


Fig. 11.2 Nullcline configurations for mutually excitatory–inhibitory networks: (a) mutual excitation, (b) mutual inhibition, (c) mutual excitation with weak self-connections

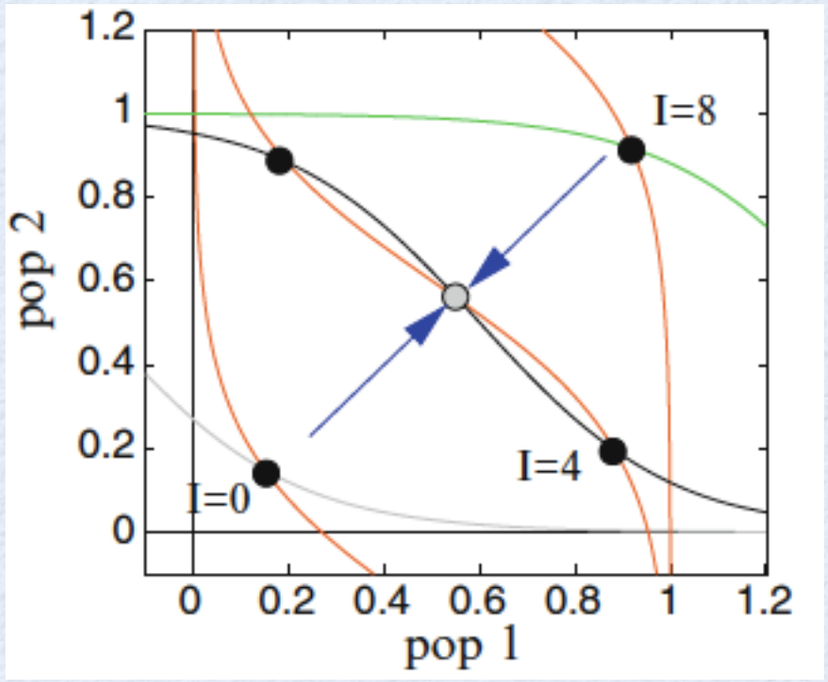
- Any fixed-points which occur on the intersection of two outer branches: stable node
- Any fixed-points which occur on the intersection of two inner branches: unstable node
- Any other fixed-point: saddle

THE WILSON-COWAN EQUATIONS

☑ Choice between two or more competing sensory inputs



$$\tau_1 u_1' = -u_1 + F_1(w_{11}u_1 + w_{12}u_2),$$
$$\tau_2 u_2' = -u_2 + F_2(w_{21}u_1 + w_{22}u_2).$$

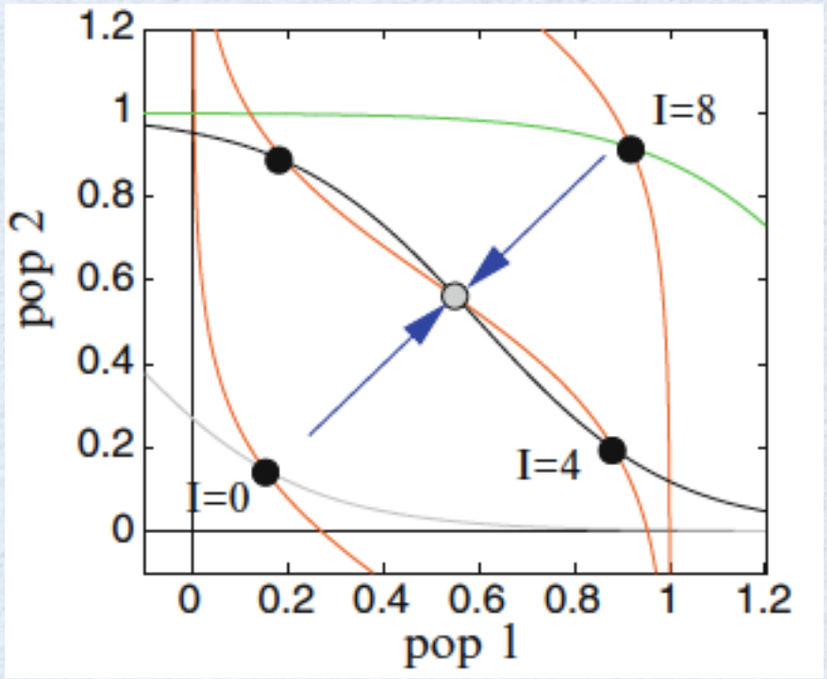


☑ Competition between two neural pools or populations

$$F(u) = 1/(1 + \exp(-(u - 1))) \qquad w = 5$$

THE WILSON-COWAN EQUATIONS

- Competition between two neural pools or populations



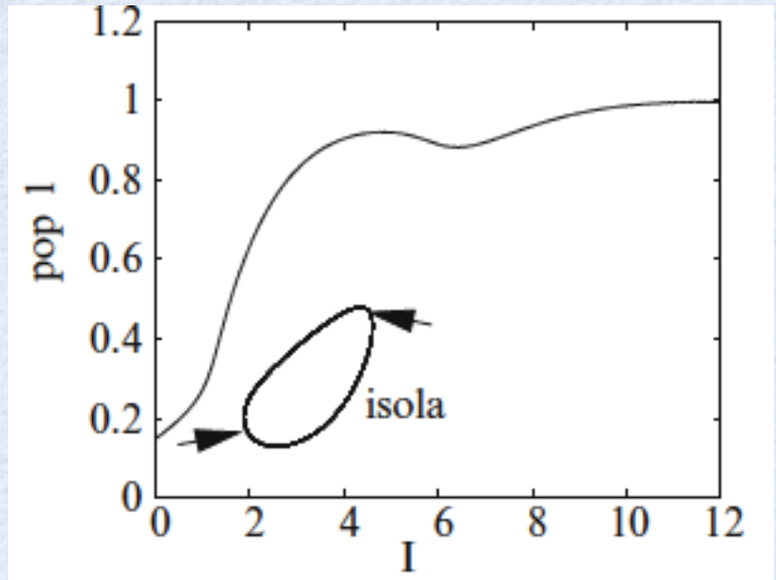
- Low inputs values: both units fire equally at the same (low) value
- Intermediate input values:
  - Homogeneous fixed-point is unstable
  - Two stable fixed-points: “winning” units
  - Separatrix (blue arrows): stable manifold of the saddle.
- High input values: both units fire equally at the same (high) value

THE WILSON-COWAN EQUATIONS

☑ Competition between two neural pools or populations

☑ If there is a slight bias in the inputs, then as the input increases, the favored population will always win

☑ With a strong enough perturbation it is possible to switch to the less favored population (for a limited range of inputs)



☑ Isola:

- ☑ small island of solutions
- ☑ fold bifurcations (arrows)
- ☑ As the bias disappears, the isola grows and merges with the main branch of solutions
- ☑ As the bias increases, the isola shrinks to a point and disappears
- ☑ Symmetry-breaking instabilities, bifurcations and pattern formation: the symmetric solution loses stability owing to the negative interactions and results in new solutions which are no longer symmetric

THE WILSON-COWAN EQUATIONS

- Excitatory-inhibitory pairs

$$\tau_1 u_1' = -u_1 + F(w_{11}u_1 - w_{12}u_2 + I_1),$$
$$\tau_2 u_2' = -u_2 + F(w_{21}u_1 - w_{22}u_2 + I_2).$$

- u_1: excitatory population
- u_2: inhibitory population

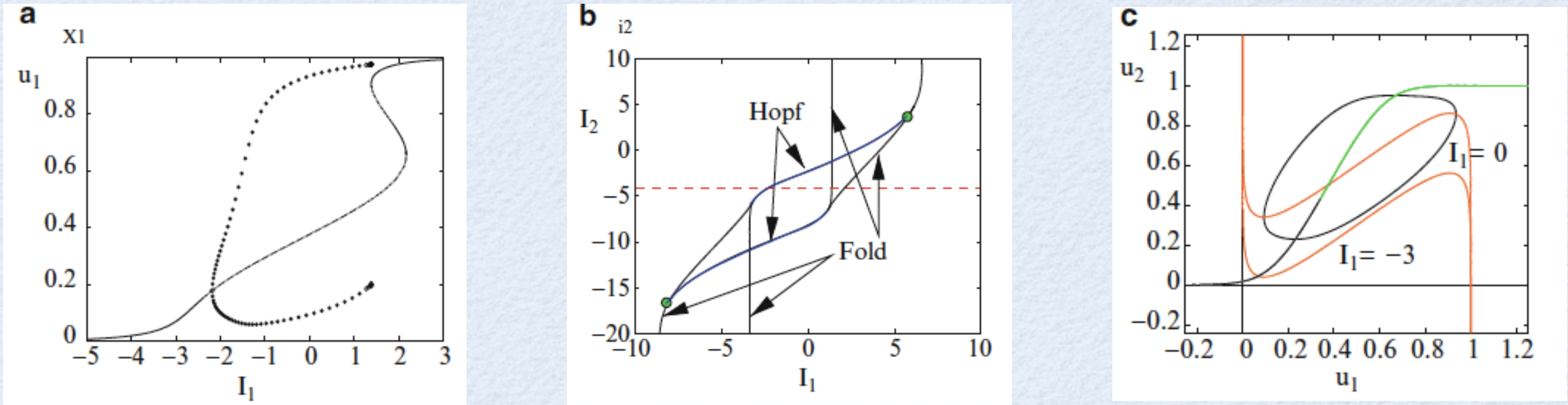


Fig. 11.4 Sample bifurcation diagram for an excitatory and inhibitory population. The parameters are $w_{11} = 12$, $w_{12} = 10$, $w_{21} = 16$, $w_{22} = 4$, and $\tau = 2$. (**a**) Behavior of u_1 as I_1 increases, $I_2 = -4$. (**b**) Two-parameter diagram as a function of the inputs, I_1, I_2. *Green circles* indicate Takens–Bogdanov points. (**c**) Phase plane for $I_2 = -4$, $I_1 = 0$

THE WILSON-COWAN EQUATIONS

- Up-down states

  - In prefrontal cortical slices, local recurrent networks of excitatory and inhibitory neurons are able to produce epochs of sustained firing both spontaneously and through stimulation

  - Two states: firing and quiescent

  - Observed in extracellular and intracellular recordings of neurons

THE WILSON-COWAN EQUATIONS

- ☑ Up-down states

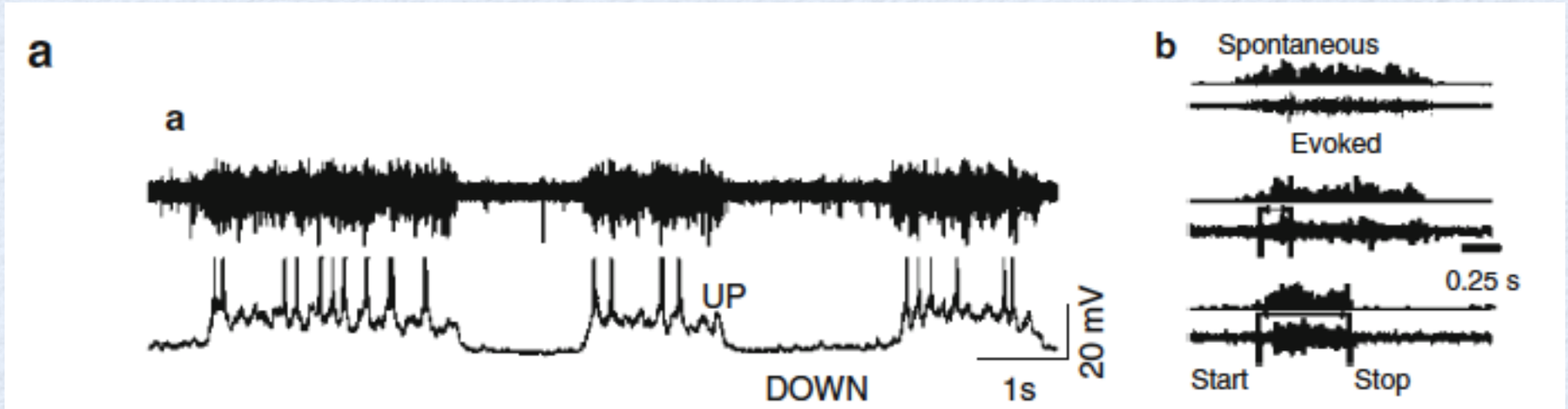
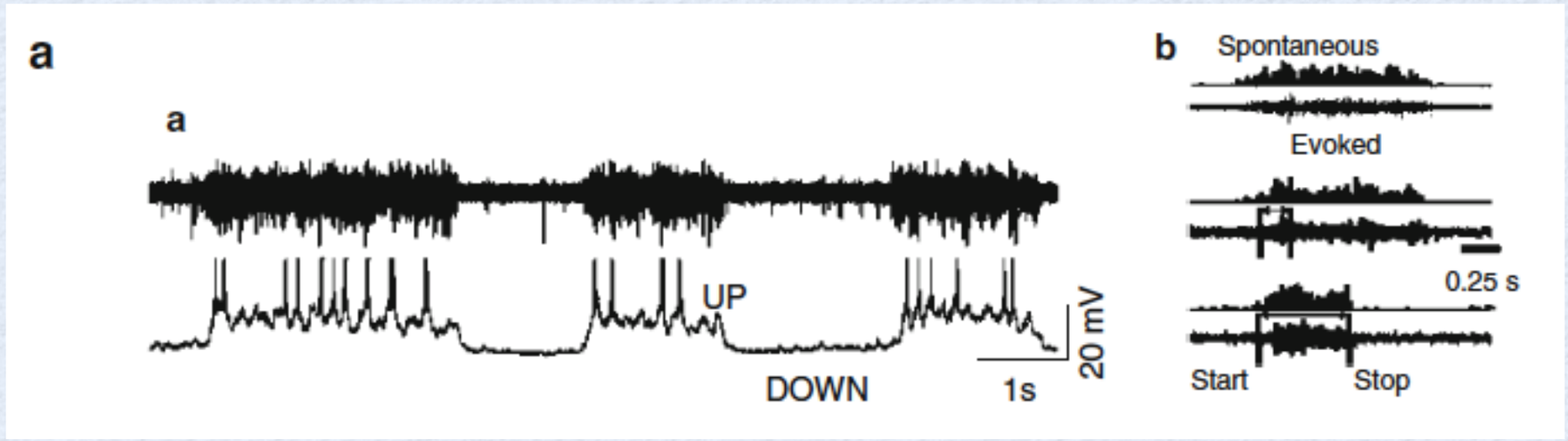


Fig. 11.5 Modeling up and down states in cortex. (**a**) Experimental data from Shu et al. [247] showing (*a*) extracellular (*upper curve*) and intracellular (*lower curve*) recordings over about 10 s, and (*b*) evoked states via external stimuli. (**b**) Simulation of up–down states in a noisy Wilson–Cowan model showing spontaneous switching. (**c**) Phase-plane explanation of the balanced bistable state. The parameters are $\tau_1 = 5$, $\tau_2 = 3$, $w_{11} = 16$, $w_{21} = 24$, $w_{12} = 10$, $w_{22} = 6$, $I_1 = -3.7$, and $I_2 = -6.7$. Colored noise is added to the inputs. *SM* stable manifold

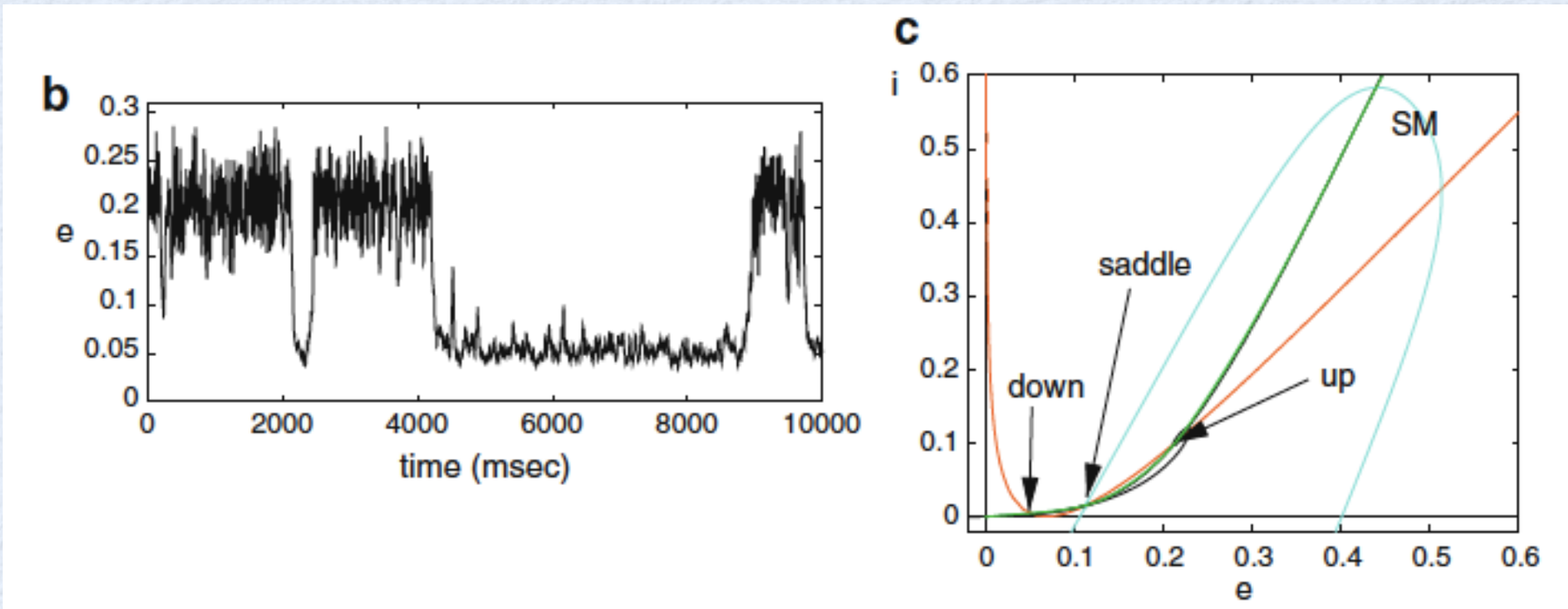
THE WILSON-COWAN EQUATIONS

- ☑ Up-down states
  - ☑ The network undergoes bouts of sustained activity lasting up to 4s followed by quiescence
  - ☑ During bouts of activity, the membrane potential is depolarized (``up state'') compared with that during the quiescent period (``down state'')
  - ☑ Stimuli allow one to switch from the down to the up state and vice-versa
  - ☑ Depolarizing stimuli can switch the network from the up to the down state (!)
  - ☑ When the network is in the down state, very strong stimuli cause a brief bout of activity immediately followed by a return to the down state.



THE WILSON-COWAN EQUATIONS

☑ Up-down states



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THE WILSON-COWAN EQUATIONS

☑ Up-down states - phase plane

☑ Two stable fixed-points: up and down states (bistable system)

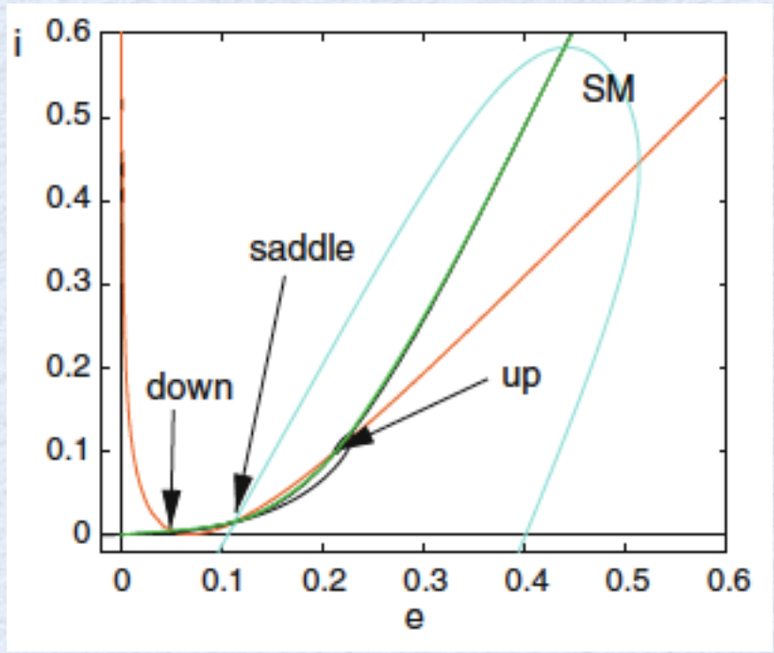
☑ Saddle point separating these states. Its stable manifold acts as a threshold

☑ Modest stimuli will take the system from the down to the up state and vice-versa

☑ If a stimulus takes the excitatory population beyond about 0.4, then there will be an immediate return to the down state

☑ Curved stable manifold allows switches from up to down due to strong depolarization

☑ A depolarizing shock in the up state can take the system to the down state



THE WILSON-COWAN EQUATIONS

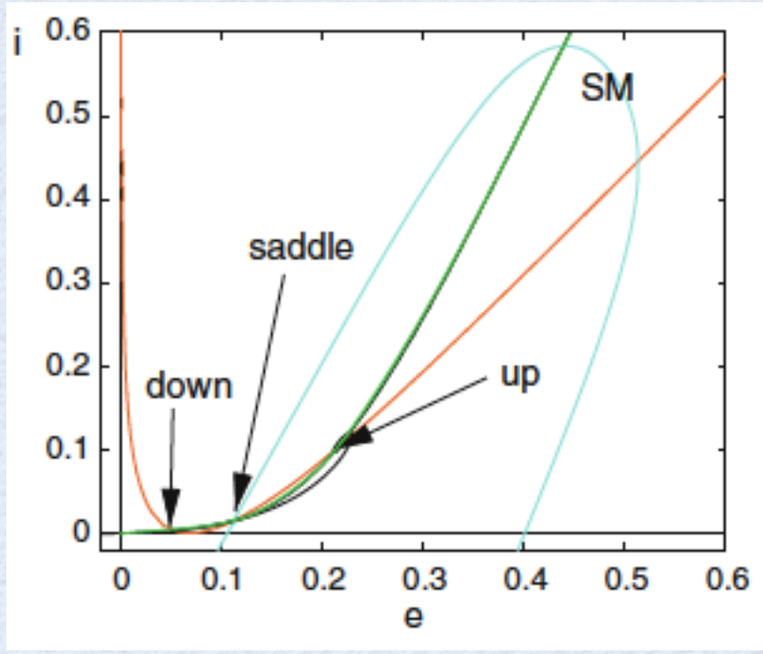
☑ Up-down states - phase plane

☑ Delay before going on the down state which is dependent on the amplitude of the stimulus (stimulus close to the stable manifold but slightly beyond the right-hand branch will take much longer to go the the down state than will a stronger stimulus)

☑ Strong stimuli during the down state can induce a brief period of activation followed by a return to the down state as well

☑ Adding small amounts of noise to the model equations can cause spontaneous transitions between up and down states

☑ Upper state is closer to instability and hass complex eigenvalues. This could explain the fact that the upper state is much noisier than the lower state



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