Metastability in a Stochastic Neural Network Modeled as a Velocity Jump Markov Process

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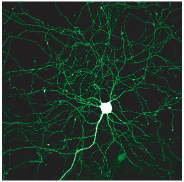
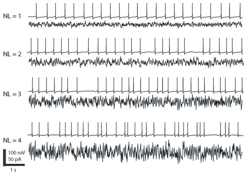
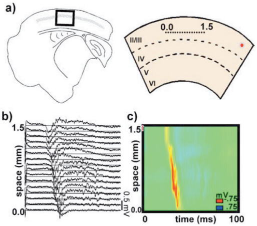
Multiscale dynamics

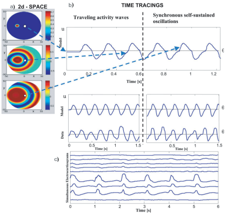
Brain dynamics is noisy at the single cell level...but often observe coherent states at the macroscopic level

noisy spike trains





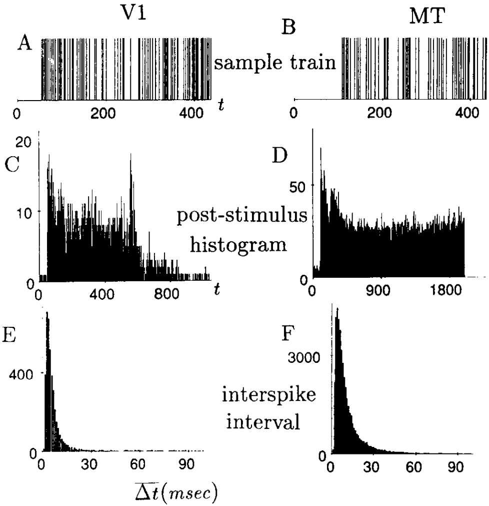




coherent waves and oscillations at network level

Single cell recordings

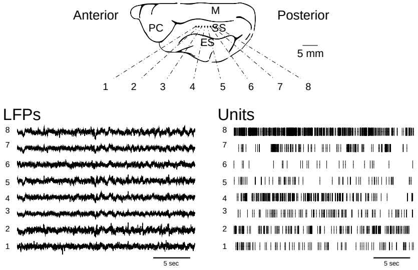
Single cell recordings *in vivo* suggest that individual cortical neurons are noisy with inter-spike intervals (ISIs) close to Poisson (Softy and Koch 1993)

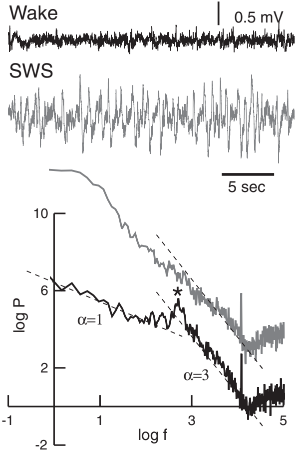


Local field potential (LFP)

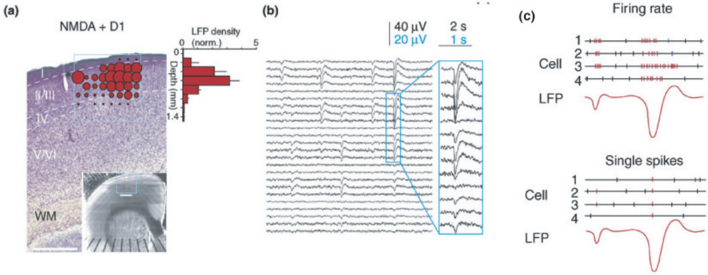
"1/f" noise in LFP recordings of parietal cortex of awake cats (Bedard et al Destexhe 2006)

Multisite bipolar LFP recordings (Destexhe et al 1999)





NEURONAL AVALANCHES (BEGGS AND PLENZ 2003, 2004)

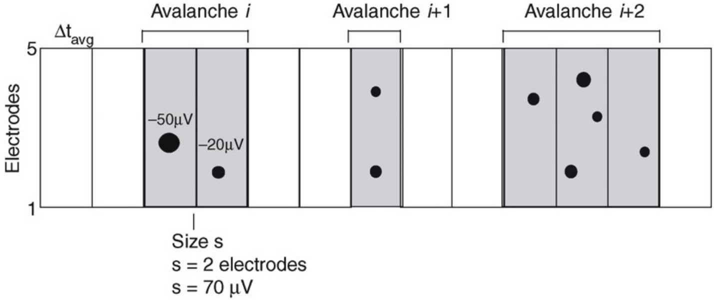


(a) Slice of rat somatosensory cortex. LFP measured at multiple sites (in superficial layers) by an 8×8 multi-electrode array with spacing 200 μm.

(b) Examples of LFP population spikes

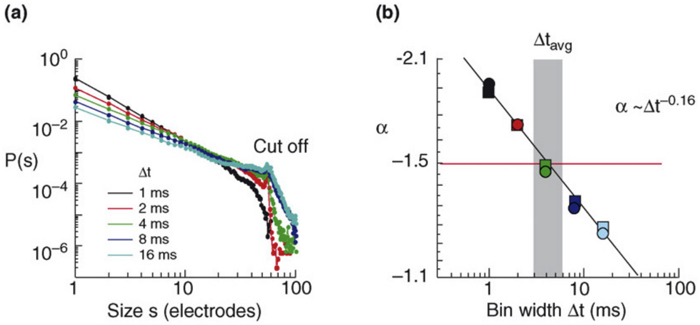
(c) Each LFP spike represents the synchronous activity of multiple neurons in a local population

Defining an avalanche



- Each point represents time of occurrence of an LFP spike. Grouped into an avalanche when peaks occur in contiguous time bins of width Δt_{avg}. Avalanche terminated when there is an empty time bin
- Size of an avalanche s is either the number of active electrodes or the sum of participating LFP spike amplitudes

Power–law behaviour



- Distribution $P(s)$ of avalanche sizes s is a heavy–tail distribution that exhibits a power law over several orders of magnitude

$$P(s) \propto s^{\alpha}$$

- Find that $\alpha = -1.5$ irrespective of value of Δt_{avg} (2-6 m sec)

Part I. Neural master equation

Master equation I [Buice, Chow and Cowan (BCC), Bressloff (PCB)]

- Consider M homogeneous networks labelled $k = 1, \ldots M$, each containing N identical neurons

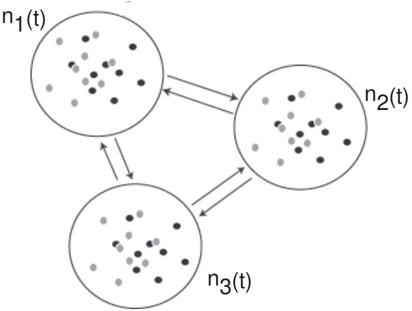
- Suppose that in the interval $[t, t + \Delta t)$, $n_k(t)$ neurons in the kth population fire an action potential or spike

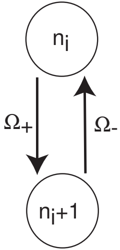
- Define population firing rate in terms of the number of neurons that spike in the interval Δt

$$a_k(t) = \frac{n_k(t)}{N \Delta t}.$$

- Treat the number of active neurons $n_k(t)$ as a stochastic variable that evolves according to a one–step jump Markov process

MASTER EQUATION II





- Rates of state transitions $n_k \to n_k \pm 1$ are chosen so that under a mean-field approximation one obtains deterministic Wilson-Cowan equations – transition rates not unique!

Master equation III

- Let $P(\mathbf{n}, t)$ with $\mathbf{n} = (n_1, \ldots, n_M)$ denote probability that $m_i(t) = n_i$ for all i

- Probability distribution evolves according to birth-death master equation

$$\frac{dP(\mathbf{n}, t)}{dt} = \sum_k \left[(\mathbb{T}_k - 1) \left(\Omega_k^-(\mathbf{n}) p(\mathbf{n}, t) \right) + (\mathbb{T}_k^{-1} - 1) \left(\Omega_k^+(\mathbf{n}) p(\mathbf{n}, \mathbf{t}) \right) \right]$$

where $\mathbb{T}_k^{\pm 1} F(\ldots, n_k, \ldots) = F(\ldots, n_k \pm 1, \ldots)$

- Transition rates are (for sigmoid function F)

$$\Omega_k^-(\mathbf{n}) = \frac{n_k}{\tau_a}, \quad \Omega_k^+(\mathbf{n}) = \frac{N\Delta t}{\tau_a} F\left(\sum_l w_{kl} n_l / N\Delta t \right)$$

Mean–field approximation

- Multiply both sides of master equation by n_k and sum over all states $\mathbf{n}$. This gives

$$\frac{d}{dt}\langle n_k\rangle = \sum_{r=\pm 1} r\langle T_{k,r}(\mathbf{n})\rangle$$

  where $\langle f(\mathbf{n})\rangle = \sum_{\mathbf{n}} P(\mathbf{n},t)f(\mathbf{n})$ for any function of state $f(\mathbf{n})$.

- Assume all statistical correlations can be neglected so that $\langle T_{k,r}(\mathbf{n})\rangle \approx T_{k,r}(\langle \mathbf{n}\rangle)$

- Setting $a_k = (N\Delta t)^{-1}\langle n_k\rangle$ leads to the mean–field equation

$$\tau_a \frac{d}{dt}a_k = -a_k + F\left(\sum_l w_{kl}a_l\right)$$

Comparison of PCB and BCC master equations

- It's all about the bin size Δt!
- Master equation keeps track of *changes* in spiking activity.
- PCB model assumes that network operates in a Gaussian-like regime close to an asynchronous state for large N. Thus changes in population activity could be slow ie can set $\Delta t = 1$.
- BCC model assumes that the network operates in a Poisson-like regime for large N. Therefore, necessary to take $\Delta t \to 0$ as $N \to \infty$ with $N\Delta t = 1$ fixed.

Effects of fluctuations

- Can adapt methods from chemical master equations in PCB model: system-size expansion in N^{-1}, Langevin approximation, WKB or path integral methods for metastable states
- No small parameter ($1/N$) in BCC model. However, one can analyze the moment hierarchy using factorial moments or a loop expansion of a path integral representation.
- Both models determine how higher order correlations couple to mean-field dynamics (see also Touboul, Ermentrout...)
- BCC model has been used to analyze power law behavior in terms of directed percolation theory

Neural Langevin equation I

- Set $\Delta t = 1$ and introduce the rescaled variables $x_k = n_k/N$ and corresponding transition rates

$$\Omega_{k,-1}(\mathbf{x}) = \frac{x_k}{\tau_a},\ \Omega_{k,1}(\mathbf{x}) = \frac{1}{\tau_a} F\left(\sum_l w_{kl} x_l\right).$$

- Carrying out a Kramers–Moyal expansion to second order in $\epsilon = N^{-1/2}$ then leads to the multivariate FP equation

$$\frac{\partial P(\mathbf{x},t)}{\partial t} = -\sum_{k=1}^{M} \frac{\partial}{\partial x_k} \left[V_k(\mathbf{x}) P(\mathbf{x},t)\right] + \frac{\epsilon^2}{2} \sum_{k=1}^{M} \frac{\partial^2}{\partial x_k^2} \left[B_k(\mathbf{x}) P(\mathbf{x},t)\right]$$

with

$$V_k(\mathbf{x}) = \Omega_{k,1}(\mathbf{x}) - \Omega_{k,-1}(\mathbf{x}), \quad B_k(\mathbf{x}) = \Omega_{k,1}(\mathbf{x}) + \Omega_{k,-1}(\mathbf{x})$$

Neural Langevin equation II

- The FP equation determines the probability density function for a corresponding stochastic process $\mathbf{X}(t) = (X_1(t), \ldots, X_M(t))$, which evolves according to the neural Langevin equation

$$dX_k = V_k(\mathbf{X})dt + \epsilon b_k(\mathbf{X})dW_k(t).$$

  with $b_k(\mathbf{x})^2 = B_k(\mathbf{x})$.

- Here $W_k(t)$ denotes an independent Wiener process such that

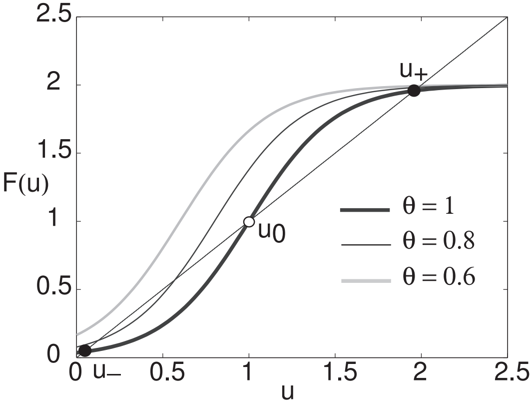
$$\langle W_k(t)\rangle = 0, \quad \langle W_k(t)W_l(s)\rangle = \delta_{k,l}\min(t,s).$$

- Langevin equation captures the relatively fast stochastic dynamics within the basin of a attraction of a stable fixed point (or limit cycle) of the corresponding deterministic rate equations

- Rigorous analysis of Langevin approximation can be carried out by extending work of Kurtz on chemical master equations (Buckwar and Riedler 2012)

Part II. WKB approximation and rare event statistics

SINGLE–POPULATION MODEL: BISTABLE NETWORK



$$\frac{du}{dt} = -u + F(wu), \quad F(u) = \frac{f_0}{1 + e^{-\gamma(u-\theta)}}.$$

BIRTH-DEATH MASTER EQUATION

$$\frac{dP(n,t)}{dt} = T_+(n-1)P(n-1,t) + T_-(n+1)P(n+1,t) - (T_+(n)+T_-(n))P(n,t)$$

- Birth and death rates

$$T_+(n) = NF(n/N), \quad T_-(n) = n,$$

- Write steady-state solution in terms of probability current $J(n)$:

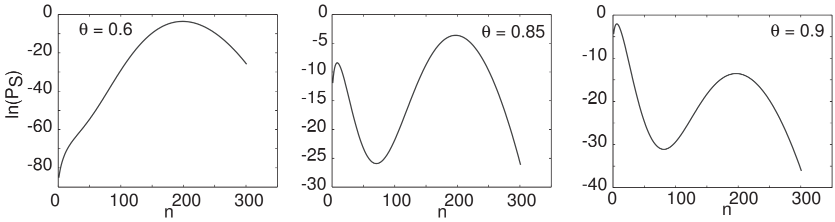
$$J(n+1) = J(n), \quad J(n) = T_-(n)P_S(n) - T_+(n-1)P_S(n-1).$$

- $J(0) = 0 \implies J(n) = 0$ for all $n \geq 0$ so steady-state solution is

$$P_S(n) = \frac{T_+(n-1)}{T_-(n)} P_S(n-1) = P_S(0) \prod_{m=1}^{n} \frac{T_+(m-1)}{T_-(m)}$$

with $P_S(0) = 1 - \sum_{m\geq 1} P_S(m)$.

STEADY-STATE DISTRIBUTION



For large N, steady-state solution of master eqn is ($x = n/N$)

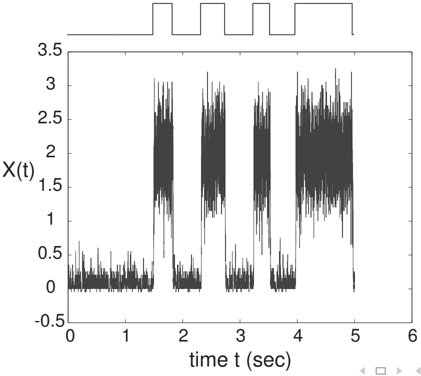
$$P_S(x) = \mathcal{A} \exp\left(N \int^x \ln \frac{\Omega_+(x')}{\Omega_-(x')} dx' \right)$$

whereas soln of FP eqn is

$$P_S(x) = \mathcal{A}' \exp\left(2N \int^x \frac{\Omega_+(x') - \Omega_-(x')}{\Omega_+(x') + \Omega_-(x')} dx' \right)$$

Noise-induced switching

- Bistable deterministic network with stable fixed points $x = x_{\pm}$ and saddle $x = x_0$.
- Noise induces switching between basins of attraction for finite N – exponentially small escape rates $r_{\pm} \sim e^{-N\tau_{\pm}}$.
- Rare transitions allow network to approach steady state PDF in limit $t \to \infty$



WKB APPROXIMATION

- Set $x = n/N$.
  Place an absorbing BC at saddle u_0. Eigenvalue expansion of PDF:

$$P(x,t) = c_0 P_0(x) \mathrm{e}^{-\lambda_0 t} + c_1 P_1(x) \mathrm{e}^{-\lambda_1 t} + \cdots .$$

- For large N, $\lambda_0 \sim \mathrm{e}^{-NE_0}$ with $E_0 = \mathcal{O}(1)$. Can identify λ_0 with MFPT to escape basin of attraction of metastable state u_-, say.

- Can approximate $P_0(x)$ by a solution to the stationary master equation with a reflecting BC at u_0– quasistationary solution

- Take $P_0(x)$ to have the WKB form

$$P_0(x) \sim K(x) \mathrm{e}^{-NW(x)}, \quad K(S) = 1, W(S) = 0,$$

- Asymptotic expression for λ_0 (large-deviation theory)

$$\log \lambda_0 \sim N[W(x_0) - W(x_-)]$$

HAMILTON–JACOBI EQUATION FOR W

- Expansion in powers of N^{-1} yields Hamilton-Jacobi eqn for W:

$$H(x,p) = \sum_{r=\pm 1} \Omega_r(x)\,[\mathrm{e}^{rp} - 1] = 0, \quad p = \frac{\partial W}{\partial x}$$

with $\Omega_+(x) = F(wx),\ \Omega_-(x) = x$

- Classical mechanical interpretation: H determines the motion of a "particle" with position x and conjugate momentum p

$$\dot{x} = \frac{\partial H}{\partial p} = -x\mathrm{e}^{-p} + F(wx)\mathrm{e}^{p}$$
$$\dot{p} = -\frac{\partial H}{\partial x} = \left[\mathrm{e}^{-p} - 1\right] + wF'(wx)\,[\mathrm{e}^{p} - 1]$$

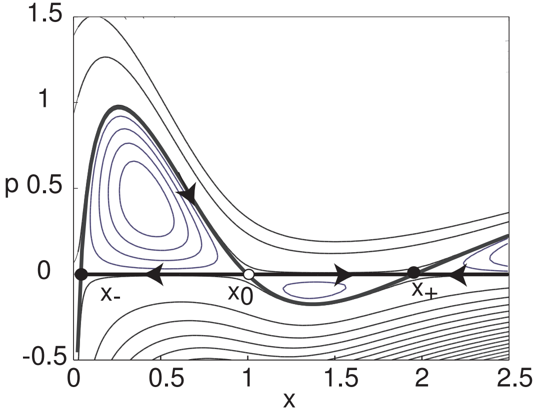
t is a parameterization of paths rather than time.

- $W(x)$ with $W(S) = 0$ determined by action along zero energy trajectories of Hamiltonian system: most probable fluctuational path from S to x (in the large–N limit)

HAMILTON–JACOBI EQUATION FOR W

Since HJ equation is a quadratic in e^p, there are two classes of zero–energy solution

$$p = 0, \quad p = p_*(x) \equiv \ln \frac{\Omega_-(x)}{\Omega_+(x)}.$$



Matched asymptotics

- Can calculate pre factor using matched asymptotics - need to match absorbing BC at u_0
- Along an activation trajectory ($p = p_*(x)$)

$$P_0(x) = \frac{A}{\sqrt{xF(wx)}} \mathrm{e}^{-NW(x)}, \qquad W(x) = \int^x \ln\left[\frac{y}{F(wy)}\right] dy$$

- Along a relaxation trajectory ($p = 0$)

$$P_0(x) = \frac{B}{F(wx) - x}$$

- Find that exit time from metastable state around x_- is

$$\lambda_0 = \frac{2\pi}{\sqrt{-1 + wF'(wx_0)}} \frac{1}{\sqrt{|-1 + wF'(wx_-)|}} \sqrt{\frac{x_0}{x}} \mathrm{e}^{N[W(x_0) - W(x_-)]}$$

Part III. Path-integral formulation of neural master equation

Path integral formulation I

- Consider the representation of the joint probability density for the fields $\mathbf{\Phi}_i = \{\Phi_i(s), 0 \leq s \leq t\}$, with $\Phi_i = Nu_i$ and u_i satisfying the deterministic rate equation.

- Rewrite as an infinite product of Dirac delta functions:

$$P[\mathbf{\Phi}] = \mathcal{N} \prod_{s \leq t} \prod_i \delta\left(\partial_t \Phi_i + \alpha \Phi_i - NF\left(\sum_j W_{ij} \Phi_j / N \right) \right),$$

- Introduce the Fourier representation of the Dirac delta function:

$$P[\mathbf{\Phi}] = \int \prod_i D\widetilde{\mathbf{\Phi}}_i e^{-S[\mathbf{\Phi}, \widetilde{\mathbf{\Phi}}]}, \qquad D\widetilde{\mathbf{\Phi}}_i \sim \mathcal{N} \prod_{s \leq t} d\widetilde{\Phi}_i(s)$$

where each $\tilde{\Phi}_i(s)$ is integrated along the imaginary axis.

Path integral formulation II

- Deterministic action is

$$S[\mathbf{\Phi}, \widetilde{\mathbf{\Phi}}] = \int dt \sum_i \widetilde{\Phi}_i(t) \left[\partial_t \Phi_i + \alpha \Phi_i - NF\left(\sum_j W_{ij} \Phi_j / N \right) \right]$$

- Path integral representation persists when fluctuations are taken into account, with modified action

$$S[\mathbf{\Phi}, \widetilde{\mathbf{\Phi}}] \quad = \quad \int dt \sum_i \widetilde{\Phi}_i \left[\partial_t \Phi_i + \alpha \Phi_i - NF\left(\sum_j W_{ij} \Psi_j / N \right) \right],$$

where $\Psi_j = \widetilde{\Phi}_j \Phi_j + \Phi_j$.

Moment equations

- Given $P[\mathbf{\Phi}]$, we can calculate mean–fields according to

$$\langle\langle \Phi_k(t_1)\rangle\rangle = \int \prod_i D\mathbf{\Phi}_i \Phi_k(t_1) P[\mathbf{\Phi}] = \int \prod_i D\mathbf{\Phi}_i \int \prod_i D\widetilde{\mathbf{\Phi}}_i \; \Phi_k(t_1) \mathrm{e}^{-S[\mathbf{\Phi},\widetilde{\mathbf{\Phi}}]}$$

- Similarly, two–point correlations are given by

$$\langle\langle \Phi_k(t_1)\Phi_l(t_2)\rangle\rangle = \int \prod_i D\mathbf{\Phi}_i \int \prod_i D\widetilde{\mathbf{\Phi}}_i \; \Phi_k(t_1)\Phi_l(t_2) \mathrm{e}^{-S[\mathbf{\Phi},\widetilde{\mathbf{\Phi}}]}$$

- In terms of the physical activity variables $m_i(t)$,

$$\langle m_k(t)\rangle \equiv \sum_{\mathbf{n}} n_k P(\mathbf{n}, t) = \langle\langle \Phi_k(t)\rangle\rangle,$$

$$\begin{aligned}&\langle m_k(t) m_l(t)\rangle - \langle m_k(t)\rangle\langle m_l(t)\rangle \\ &\quad = \langle\langle \Phi_k(t)\Phi_l(t)\rangle\rangle - \langle\langle \Phi_k(t)\rangle\rangle\langle\langle \Phi_l(t)\rangle\rangle + \langle\langle \Phi_k(t)\rangle\rangle \delta_{k,l}.\end{aligned}$$

LARGE DEVIATIONS I

- Perform rescaling $\Phi_i \to \phi_i = \Phi_i/N$ so that we have a path-integral of the form

$$P \sim \int \prod_i D\phi_i \int \prod_i D\widetilde{\phi}_i \, e^{-NS[\phi,\widetilde{\phi}]}$$

- Rescaled action is

$$S[\phi,\widetilde{\phi}] \;=\; \int dt \left[\sum_i \widetilde{\phi}_i \partial_t \phi_i + \mathcal{H}(\phi,\widetilde{\phi})\right]$$

and

$$\mathcal{H}(\phi,\widetilde{\phi}) = \sum_i \widetilde{\phi}_i \left[\alpha\phi_i - F\left(\sum_j W_{ij}\psi_j\right)\right]$$

Large deviations II

- In the limit $N \to \infty$, the path integral is dominated by the "classical" solutions $\boldsymbol{u}(t), \widetilde{\boldsymbol{u}}(t)$:

$$\left.\frac{\delta S[\phi, \widetilde{\phi}]}{\delta \phi_i(t)}\right|_{\widetilde{\phi}=\widetilde{\boldsymbol{u}}, \phi=\boldsymbol{u}} = 0, \quad \left.\frac{\delta S[\phi, \widetilde{\phi}]}{\delta \widetilde{\phi}_i(t)}\right|_{\widetilde{\phi}=\widetilde{\boldsymbol{u}}, \phi=\boldsymbol{u}} = 0.$$

- These equations reduce to

$$\frac{\partial u_i}{\partial t} = -\frac{\partial \mathcal{H}(\boldsymbol{u}, \widetilde{\boldsymbol{u}})}{\partial \widetilde{u}_i}, \quad \frac{\partial \widetilde{u}_i}{\partial t} = \frac{\partial \mathcal{H}(\boldsymbol{u}, \widetilde{\boldsymbol{u}})}{\partial u_i}.$$

- Hamiltonian dynamical system in which u_i is a "coordinate" variable, $\widetilde{u}_i$ is its "conjugate momentum"
- Equivalent to WKB Hamiltonian under a canonical transformation

Part IV. Beyond the neural master equation

Limitations of the neural master equation

- Transition rates are not uniquely determined
- What is τ_a?
- Mean-field dynamics given by an activity-based rate equation. What about a current or voltage-based equation? Unlike number of active neurons, current is not a discrete variable.
- Neglects synaptic dynamics ie assumes that time-scale τ of synaptic dynamics smaller than Δt. But $\Delta t \to 0$ in Poisson regime and could be small in Gaussian regime.

Velocity-jump Markov model I (PCB/Newby)

- $U_k(t)$ is a population averaged synaptic current evolving as

$$\tau dU_k(t) = \left[-U_k(t) + \sum_{k=1}^{M} w_{kl} A_l(t) \right] dt.$$

- The stochastic population firing rate is given by

$$A_k(t) = \frac{N_k(t)}{N\Delta t}$$

- $N_k(t)$ evolves according to a one-step jump Markov process

$$N_k(t) \to N_k(t) \pm 1$$

with transition rates

$$\Omega_+ = \frac{N\Delta t F(U_k)}{\tau_a}, \quad \Omega_- = \frac{n_k}{\tau_a}.$$

- Take limit $N \to \infty$, $\Delta t \to 0$ with $N\Delta t = 1$.

Velocity-jump Markov model II

- Example of a stochastic hybrid system
- $U_k(t)$ is a piecewise deterministic variable coupled to the discrete jump Markov processes $N_l(t)$
- The Markov processes are coupled to $U_k(t)$ via the transition rates
- Introduce the probability density

$$\Pr\{U_k(t) \in (u_k, u_k + du, N_k(t) = n_k; k = 1, \ldots, M\} = p(\mathbf{u}, \mathbf{n}, t | \mathbf{u}_0, \mathbf{n}_0, 0) d\mathbf{u}$$

with $\mathbf{u} = (u_1, \ldots, u_M)$, $\mathbf{n} = (n_1, \ldots, n_M)$.

NEURAL CHAPMAN-KOLMOGOROV EQUATION

- p evolves according to the Chapman-Kolmogorov (CK) equation

$$\frac{\partial p}{\partial t} + \frac{1}{\tau}\sum_k \frac{\partial[v_k(\mathbf{x})p(\mathbf{x},\mathbf{t})]}{\partial u_k}$$
$$= \frac{1}{\tau_a}\sum_k \left[(\mathbb{T}_k - 1)\left(\omega_-(n_k)p(\mathbf{x},t)\right) + (\mathbb{T}_k^{-1} - 1)\left(\omega_+(u_k)p(\mathbf{x},\mathbf{t})\right)\right],$$

with $\mathbf{x} = (\mathbf{u},\mathbf{n})$, and

$$\omega_+(u_k) = F(u_k), \quad \omega_-(n_k) = n_k, \quad v_k(\mathbf{x}) = -u_k + \sum_k w_{kl}n_l.$$

- In the limit $\tau \to 0$ for $\tau_a > 0$ fixed, we recover the BCC neural master equation with $\mathbf{u} = \mathbf{u}(\mathbf{n})$ such that

$$v_k(\mathbf{u}(\mathbf{n}),\mathbf{n}) = 0.$$

Limiting case $\tau_a \ll \tau$

- In the limit $\tau_a \to 0$ for $\tau > 0$ fixed we obtain the deterministic voltage or current-based equation

$$\tau \frac{du_k(t)}{dt} = \left[-u_k(t) + \sum_{k=1}^{M} w_{kl} \langle N_k(t) \rangle \right] dt.$$

where

$$\langle N_k(t) \rangle = \sum_{\mathbf{n}} n_k \rho(\mathbf{n}, \mathbf{u}(t))$$

- $\rho(\mathbf{n}, \mathbf{u}(t))$ is the steady-state density of the birth-death process and is given by M independent Poisson processes with rates $F(u_k)$:

$$\langle N_k(t) \rangle = F(u_k(t)).$$

- What about the regime $0 < \epsilon \ll 1$ with $\epsilon = \tau_a/\tau$?

Path integral

- Path-integral representation of stochastic dynamics

$$p(\mathbf{x},\tau|\mathbf{x}_0,0)=\int_{\mathbf{x}(0)=\mathbf{x}_0}^{\mathbf{x}(\tau)=\mathbf{x}}\mathcal{D}[\mathbf{p}]\mathcal{D}[\mathbf{x}]\,\exp\left(-\frac{1}{\epsilon}S[\mathbf{x},\mathbf{p}]\right)$$

with action

$$S[\mathbf{x},\mathbf{p}]=\int_0^\tau\left[\sum_{\alpha=1}^{M}p_\alpha\dot{x}_\alpha-\lambda_0(\mathbf{x},\mathbf{p})\right]dt.$$

- λ_0 is the Perron eigenvalue of the following linear operator equation

$$\sum_m A(n,m;\mathbf{x})R^{(0)}(\mathbf{x},\mathbf{p},m)=[\lambda_0(\mathbf{x},\mathbf{p})-\sum_{\alpha=1}^{M}p_\alpha v_\alpha(\mathbf{x},n)]R^{(0)}(\mathbf{x},\mathbf{p},n),$$

Perron eigenvalue I

- Use the ansatz

$$R^{(0)}(\mathbf{x},\mathbf{p},\mathbf{n}) = \prod_{\alpha=1}^{M} \frac{\Lambda_\alpha(\mathbf{x},\mathbf{p})^{n_\alpha}}{n_\alpha!}.$$

- Using the explicit expressions for $\mathbf{A}$ and v_α, we find that

$$\sum_{\alpha=1}^{M}\left(\left[\frac{F(x_\alpha)}{\Lambda_\alpha}-1\right]n_\alpha + \Lambda_\alpha - F(x_\alpha)\right) - \lambda_0$$
$$= -\sum_{\alpha=1}^{M} p_\alpha\left[-x_\alpha + \sum_\beta w_{\alpha\beta} n_\beta\right].$$

- Collecting terms in n_α for each α yields

$$\frac{F(x_\alpha)}{\Lambda_\alpha} - 1 = -\sum_{\beta=1}^{M} p_\beta w_{\beta\alpha},$$

PERRON EIGENVALUE II

- Collecting terms independent of all n_α gives

$$\lambda_0 = \sum_{\alpha=1}^{M} \left[\Lambda_\alpha - F(x_\alpha) - x_\alpha p_\alpha\right].$$

- Solving for each Λ_α in terms of $\mathbf{p}$, we have

$$\lambda_0(\mathbf{x}, \mathbf{p}) \equiv \sum_{\alpha=1}^{M} \left[\frac{F(x_\alpha)}{1 - \sum_{\beta=1}^{M} p_\beta w_{\beta\alpha}} - x_\alpha p_\alpha - F(x_\alpha)\right]$$

Gaussian approximation I

- Performing the rescaling $\mathbf{p} \to i\mathbf{p}/\epsilon$ in path-integral

$$P(x,t) = \int_{\mathbf{x}(0)=\mathbf{x}_0}^{\mathbf{x}(\tau)=\mathbf{x}} D[\mathbf{x}]D[\mathbf{p}]$$

$$\times \exp\left(- \int_0^\tau i \sum_\alpha p_\alpha \left[\dot{x}_\alpha + x_\alpha - \sum_\beta \frac{w_{\alpha\beta} F(x_\beta)}{1 - i\epsilon \sum_\gamma w_{\gamma\beta} p_\gamma} \right] dt \right)$$

- The Gaussian approximation involves Taylor expanding the Lagrangian to first order in ϵ, which yields a quadratic in p:

$$P(x,t) = \int_{\mathbf{x}(0)=\mathbf{x}_0}^{\mathbf{x}(\tau)=\mathbf{x}} D[\mathbf{x}]D[\mathbf{p}] \exp\left(\int_0^\tau \left[i \sum_\alpha p_\alpha \left(\dot{x}_\alpha + x_\alpha - \sum_\beta w_{\alpha\beta} F(x_\beta) \right) - \right.\right.$$

where $Q_{\alpha\gamma}(\mathbf{x}) = \sum_\beta w_{\alpha\beta} F(x_\beta) w_{\gamma\beta}$

Gaussian approximation II

- Performing the Gaussian integration along similar lines to the one-population model yields the multi-variate Onsager-Machlup path-integral

$$P(\mathbf{x}, t) = \int D[\mathbf{x}] \mathrm{e}^{-\mathcal{A}[\mathbf{x}]/\epsilon},$$

with action functional

$$\mathcal{A}[\mathbf{x}] = \frac{1}{4} \int_0^\tau \sum_{\alpha,\beta} \left(\dot{x}_\alpha(t) - V_\alpha(\mathbf{x}(t))\right) \mathcal{Q}^{-1}_{\alpha\beta}(\mathbf{x}) \left(\dot{x}_\beta(t) - V_\beta(\mathbf{x}(t))\right) dt,$$

where $V_\alpha(\mathbf{x}) = -x_\alpha + \sum_\beta w_{\alpha\beta} F(x_\beta)$.

- The corresponding Ito Langevin equation is

$$dX_\alpha(t) = V_\alpha(\mathbf{X})dt + \sqrt{2\epsilon} \sum_\beta w_{\alpha\beta} \sqrt{F(x_\beta)} dW_\beta(t),$$

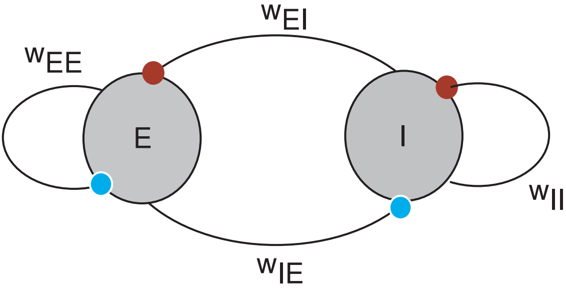
where $W_\alpha(t)$ are independent Wiener processes.

Part V. Metastability in a two population model

E-I network (PCB/Newby)

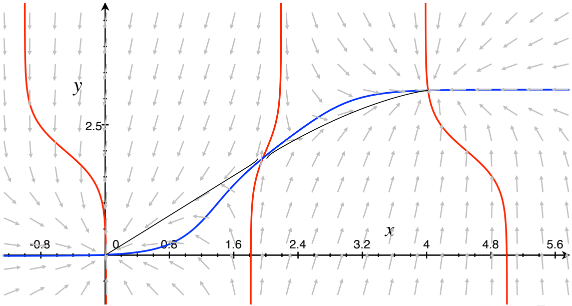
- Consider an E-I network with mean-field equations

$$\frac{dx}{dt} = -x + w_{EE}F(x) - w_{EI}F(y)$$
$$\frac{dy}{dt} = -y + w_{IE}F(x) - w_{II}F(y),$$



Phase-plane trajectories

- Red curves show the x-nullclines, and blue curve show the y-nullcline.
- The red nullcline through the saddle is its stable manifold and acts as the separatrix Σ between the two stable fixed points
- Two deterministic trajectories are shown (black curves), starting from either side of the unstable saddle and ending at a stable fixed point



Quasipotential

- The quasi-potential can be obtained by finding zero energy solutions of Hamilton's equations

$$\dot{\mathbf{x}} = \nabla_{\mathbf{p}} \mathcal{H}(\mathbf{x}, \mathbf{p}), \quad \dot{\mathbf{p}} = -\nabla_{\mathbf{x}} \mathcal{H}(\mathbf{x}, \mathbf{p}),$$

with $\mathbf{x} = (x, y), \mathbf{p} = (p_x, p_y)$ and $\mathcal{H} = \lambda_0$.

- Substituting for $\mathcal{H}$, Hamilton's equations have the explicit form

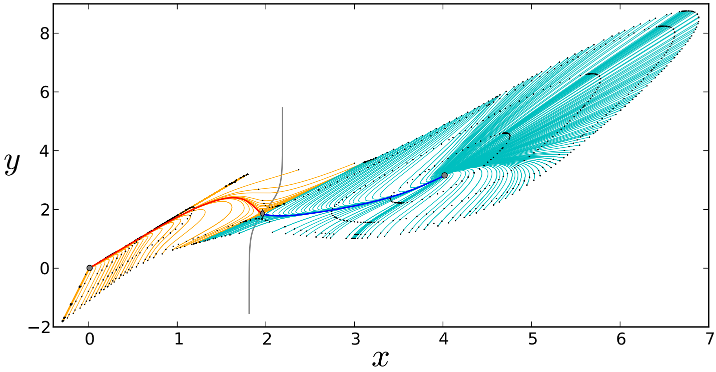
$$\begin{aligned} \frac{dx_\alpha}{dt} &= -x_\alpha + \sum_\beta \frac{w_{\alpha\beta} F(x_\alpha)}{1 - \sum_{\gamma=1}^M p_\gamma w_{\gamma\alpha}} \\ \frac{dp_\alpha}{dt} &= p_\alpha - \frac{F'(x_\alpha)}{1 - \sum_{\gamma=1}^M p_\gamma w_{\gamma\alpha}} + F'(x_\alpha) \end{aligned}$$

- The quasi-potential Φ is the action along a zero energy solution curve $\mathbf{x}(t)$:

$$\frac{d\Phi}{dt} \equiv \sum_{\alpha=1}^M \frac{\partial \Phi}{\partial x_\alpha} \frac{dx_\alpha}{dt} = \sum_{\alpha=1}^M p_\alpha \frac{dx_\alpha}{dt},$$

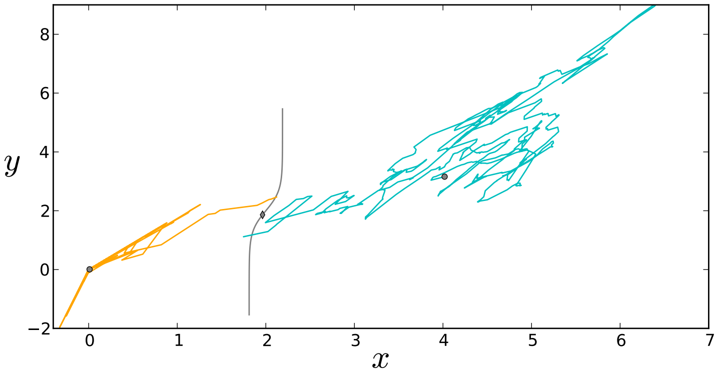
Characteristic paths of maximum likelihood

- Rays originating from the left (right) stable fixed point are shown in orange (cyan)
- The ray connecting to the saddle shown in red (blue).
- The grey curve is the separatrix Γ

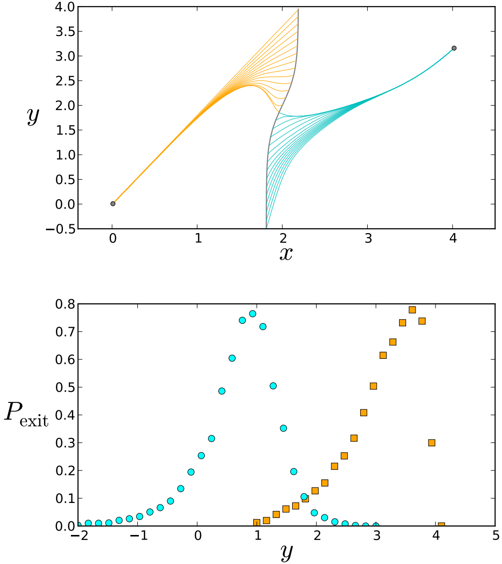


Stochastic trajectories

- Sample trajectories of the two-population model

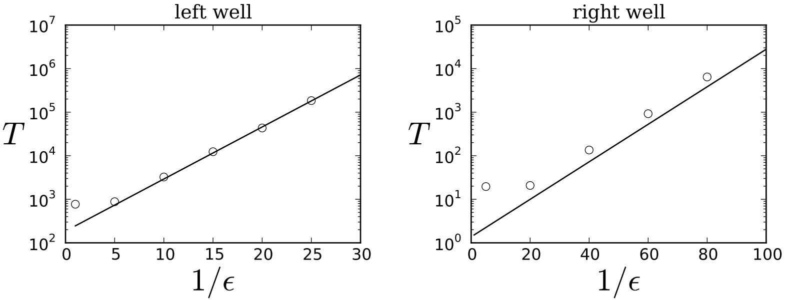


Crossing the separatrix



Mean FPT

- Good agreement between analytical results and Monte Carlo simulations



Future directions

- Apply stochastic phase reduction method to noise driven synchrony of coupled E-I networks
- Extend master equation framework to continuum neural fields (see eg. path integral methods of Buice and Cowan)
- Derivation of a master equation from first principles using multi-scale analysis
- Incorporation of other biophysical processes such as synaptic depression, channel noise etc.

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