Statistical inference in nonlinear stochastic neurones

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How can we use rich new data to build models efficiently?

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simultaneous multisite recordings of transmembrane voltage

noisy

Djurisic et al. 2004
IO function $O = f(I)$

- $f$: cable equation – compartmental model
  - nonlinear dynamics
- Output?
  - rate, individual spikes, bursts, spike patterns?
  - stochastic formulation gives metric
- Input?
- Noise?
A stochastic neurone

\[ C_x \frac{dV_x(t)}{dt} = I_{\text{ch}} + I_{\text{int}} + I_{\text{syn}} + \sigma_x dN_{x,t} \]

\[ I_{\text{channels}} = \bar{g}_c g_c(t)(E_c - V(t)) \]

\[ I_{\text{synaptic}} = \sum_{\tau} w_{\tau} u_{\tau}^s(t)(E_s - V(t)) \]

\[ I_{\text{intercompartmental}} = f_{x,y}(V_y(t) - V_x(t)) \]
Outline

- Assume known kinetics and noiseless observations
- Relax
  - noisy observations
    - model-based smoothing
    - parameter inference
  - unknown kinetics
Known kinetics

\[ C_x \frac{dV_x(t)}{dt} = I_{\text{ch}} + I_{\text{int}} + I_{\text{syn}} + \sigma_x dN_{x,t} \]

\[ I_{\text{channels}} = g_c g_c(t)(E_c - V(t)) \]

\[
\frac{dx}{dt} = (1 - x)\alpha(V(t)) - x_t\beta(V(t)) \\
x_{t+1} = x_t + dt \left[ (1 - x_t)\alpha(V_t) - x_t\beta(V_t) \right]
\]

\[ I_{\text{synaptic}} = \sum_{\tau} w_{\tau} u_{\tau}^s(t)(E_s - V(t)) \]

\[ I_{\text{intercompartmental}} = f_{x,y}(V_y(t) - V_x(t)) \]
A big cell – 1000 compartments
Channel density distribution

A

\[ \text{est } g_{Na} \text{ vs true } g_{Na} \]

B

\[ \text{est } g_{K} \text{ vs true } g_{K} \]

C

\[ \text{est } g_{L} \text{ vs true } g_{L} \]

D

\[ \text{est } g_{\text{intercomp}} \text{ vs true } g_{\text{intercomp}} \]

E

Voltage [mV] vs Time [ms]

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Inference in stochastic neurones
Synaptic input

\[ I_{\text{synaptic}} = \sum_{\tau} w_\tau u_\tau^s(t)(E_s - V(t)) \]
Djurisic et al. 2004

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Inference in stochastic neurones
Outline

• Assume known kinetics and noiseless observations
• Relax
  – noisy observations
    • model-based smoothing (E)
    • parameter inference (M)
  – unknown kinetics
Hidden dynamical system

\[ C_x \frac{dV_x(t)}{dt} = I_{ch} + I_{int} + I_{syn} + \sigma_x dN_{x,t} \]
Hidden dynamical system

\[ p(V_{t+1} | V_t, o_t, \bar{g}) \]

\begin{align*}
V(t-2) & \quad \rightarrow \quad V(t-1) & \quad \rightarrow \quad V(t) & \quad \rightarrow \quad V(t+1) & \quad \rightarrow \quad V(t+2) \\
O(t-2) & \quad \downarrow \quad & \quad O(t) & \quad \downarrow \quad & \quad O(t+2) \end{align*}

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Inference in stochastic neurones
Hidden dynamical system

\[ p(V_{t+1} | V_t, o_t, \bar{g}) \]

\[ p(M_t | V_t) = \mathcal{N}(V_t, \sigma_O) \]

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Hidden dynamical system

\[ p(V_{t+1} | V_t, o_t, \bar{g}) \]

\[ p(M_t | V_t) = \mathcal{N}(V_t, \sigma_O) \]

\[ p(V_{1:T} | M_{1:t}) \]
Model-based smoothing – know densities

If true densities (and kinetics) are known, can do model-based smoothing.

Know lots, get lots.
Smoothing and upsampling

Temporal subsampling

Observation noise

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Inference in stochastic neurons
Voltage from [Ca]
[Ca] from voltage
EM for channel densities

**E step:** infer some expected statistics given channel densities

\[
\hat{w}_t^i = \hat{w}_t^i \left( \sum_j \frac{w_{t+1}^j p(V_{t+1}^j | V_t^i)}{\sum_k \hat{w}_t^k p(V_{t+1}^j | V_t^k)} \right)
\]

**M step:** update densities given expected sufficient statistics

\[
\langle J_{ct} J_{c't} \rangle \quad \langle J_{ct} V_t \rangle \quad \langle J_{ct} V_{t+1} \rangle
\]
EM: Unknown densities

![Graph showing voltage, gates, and current over time.](image)

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Inference in stochastic neurones
Assume known kinetics and noiseless observations
  - Channel density distributions in large compartmental models
  - Synaptic input time and strength
Noisy observations
  - EM with particle smoothing
  - model-based smoothing (E)
  - parameter inference (M)
BUT: still assume known kinetics
Spatial subsampling

A. $g_{Na}$ [mS/cm$^2$] vs. Dendrite #

B. $g_k$ [mS/cm$^2$] vs. Dendrite #

C. $g_L$ [mS/cm$^2$] vs. Dendrite #

D. $E_{[f.]} +/\!/- 1$ STD vs. Subsampling factor
E step: Particle smoothing

\[
< V_{1:T} > = \int dV_{1:T} p(V_{1:T} | M_{1:t}) V_{1:T}
= \int dV_{1:T} q(V_{1:T}) \frac{p(V_{1:T} | M_{1:t})}{q(V_{1:T})} V_{1:T}
\approx \sum_i V_{1:T}^i w_i \quad \text{(importance sampling)}
\]

- Use exact distribution
  \[q(V_t) = p(V_t | V_{1:t-1}, M_{1:t})\]
  \[\propto p(V_t | V_{t-1}) p(V_{t-1} | V_{1:t-2}, M_{1:t-2})\]

- Filter weights
  \[w_{t|i}^* = w_{t-1}^i p(M_t | V_t^i)\]
  \[\tilde{w}_t^i = w_{t|t}^i / (\sum_j w_{t|t}^j)\]

- Smoothing weights
  \[w_t^i = \tilde{w}_t^i \left( \sum_j \frac{w_{t+1}^j p(V_{t+1}^j | V_t^i)}{\sum_k \tilde{w}_t^k p(V_{t+1}^k | V_t^i)} \right)\]
Synaptic input

Synaptic conductances

Channel conductances

A

B

C

Inh spikes | Voltage [mV] | Exc spikes

Time [ms]

max conductance [mS/cm²]

HHNa, HHK, Leak, MNa, MK, SNa, SKA, SKDR

Inferred (MAP) spikes

Inferred (ML) channel densities

True parameters

Data (voltage trace)