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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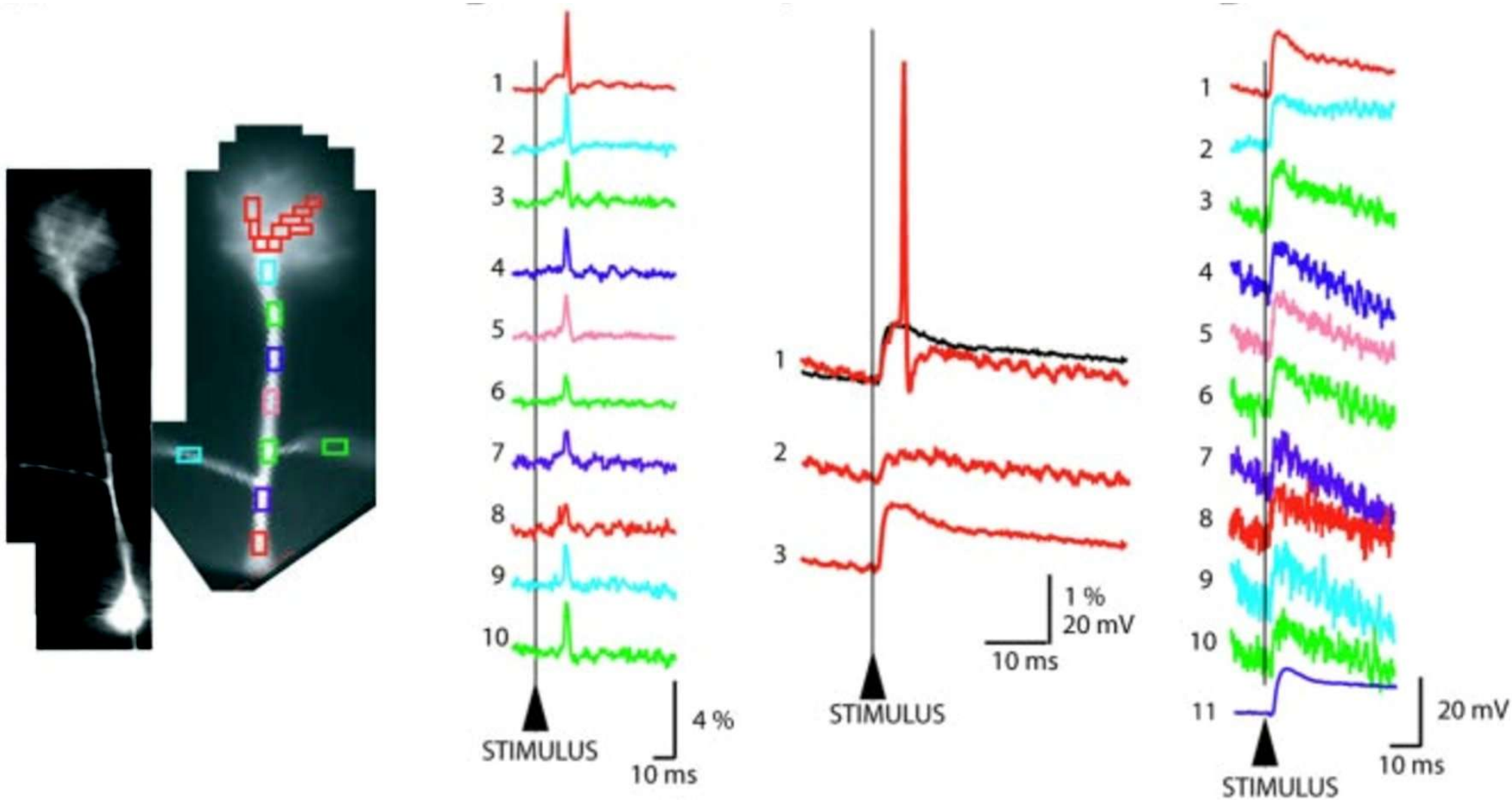


simultaneous multisite recordings of transmembrane voltage noisy

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?

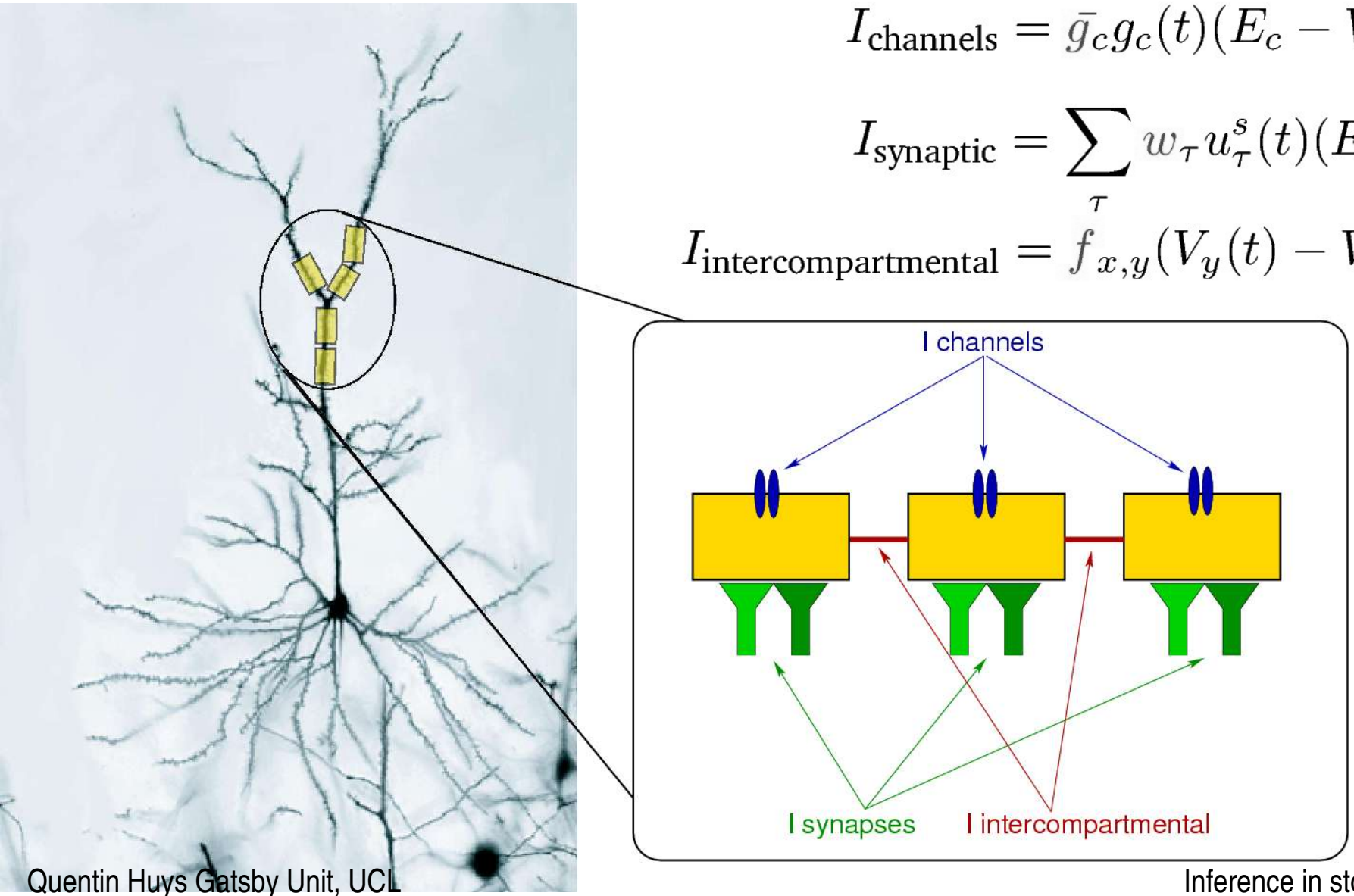
A stochastic neurone

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

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

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

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



Outline

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

Known kinetics

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

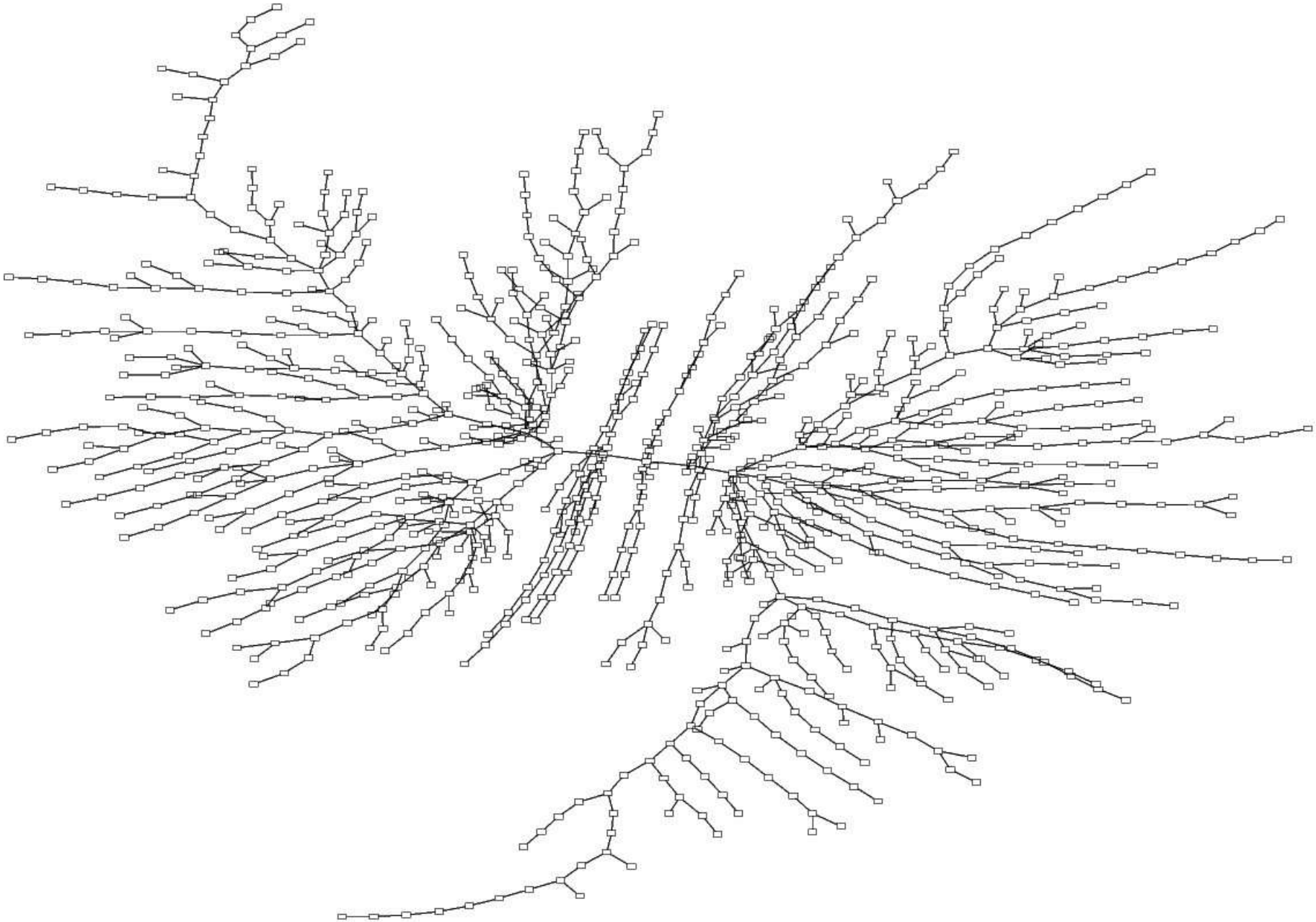
$$I_{\text{channels}} = \bar{g}_c g_c(t)(E_c - V(t))$$

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

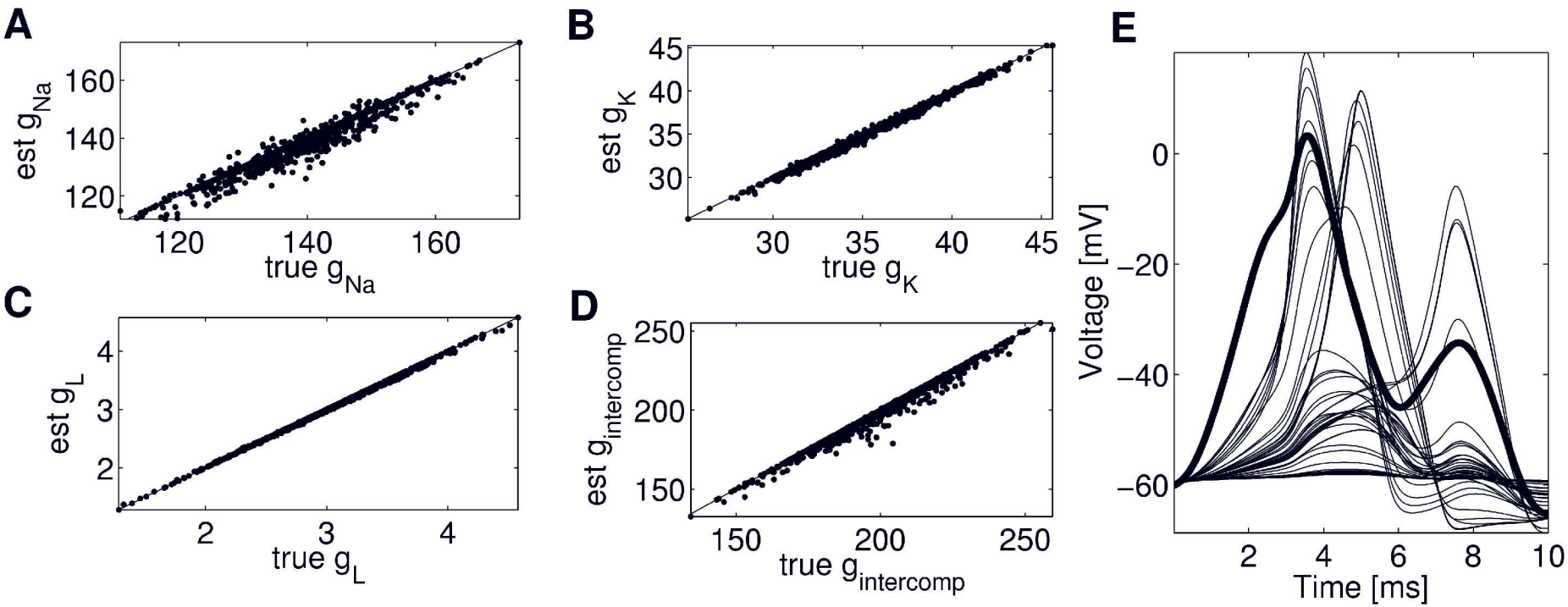
$$I_{\text{synaptic}} = \sum_{\tau} w_\tau u_\tau^s(t)(E_s - V(t))$$

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

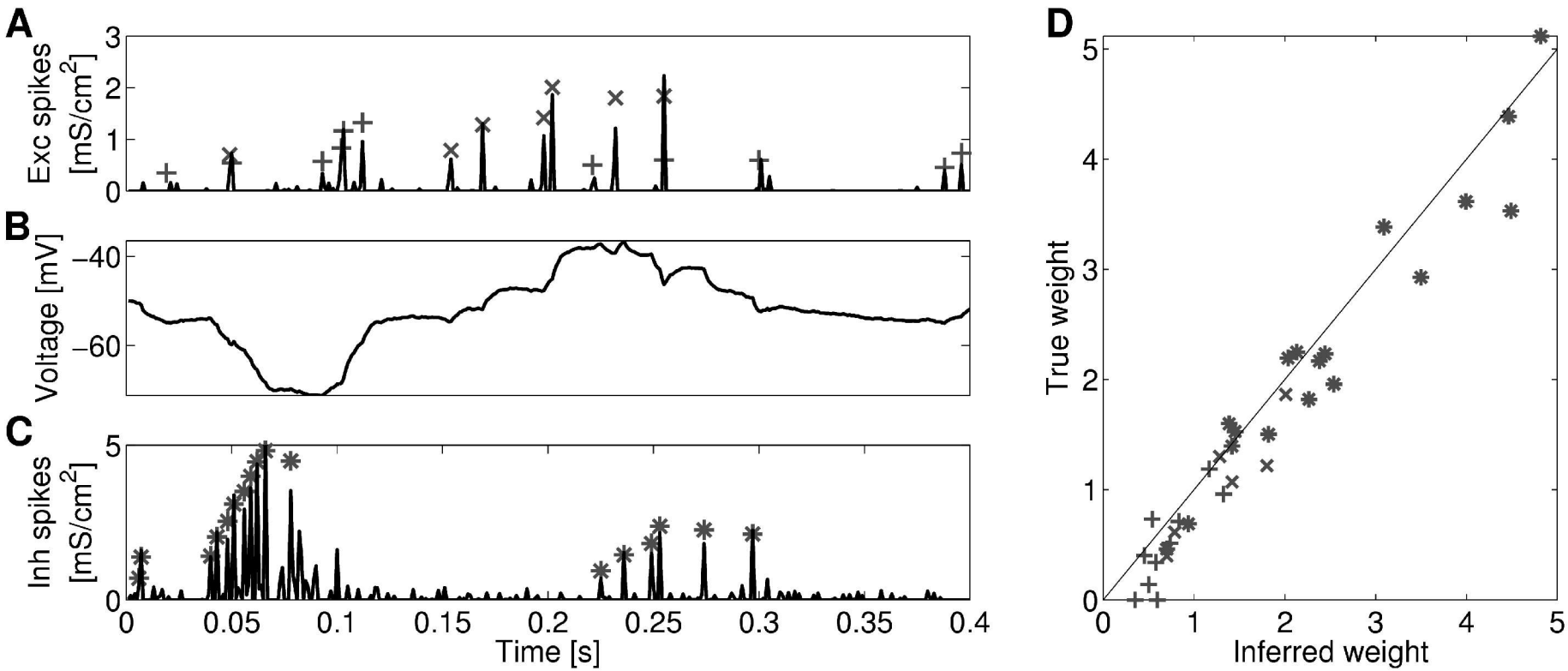
A big cell – 1000 compartments



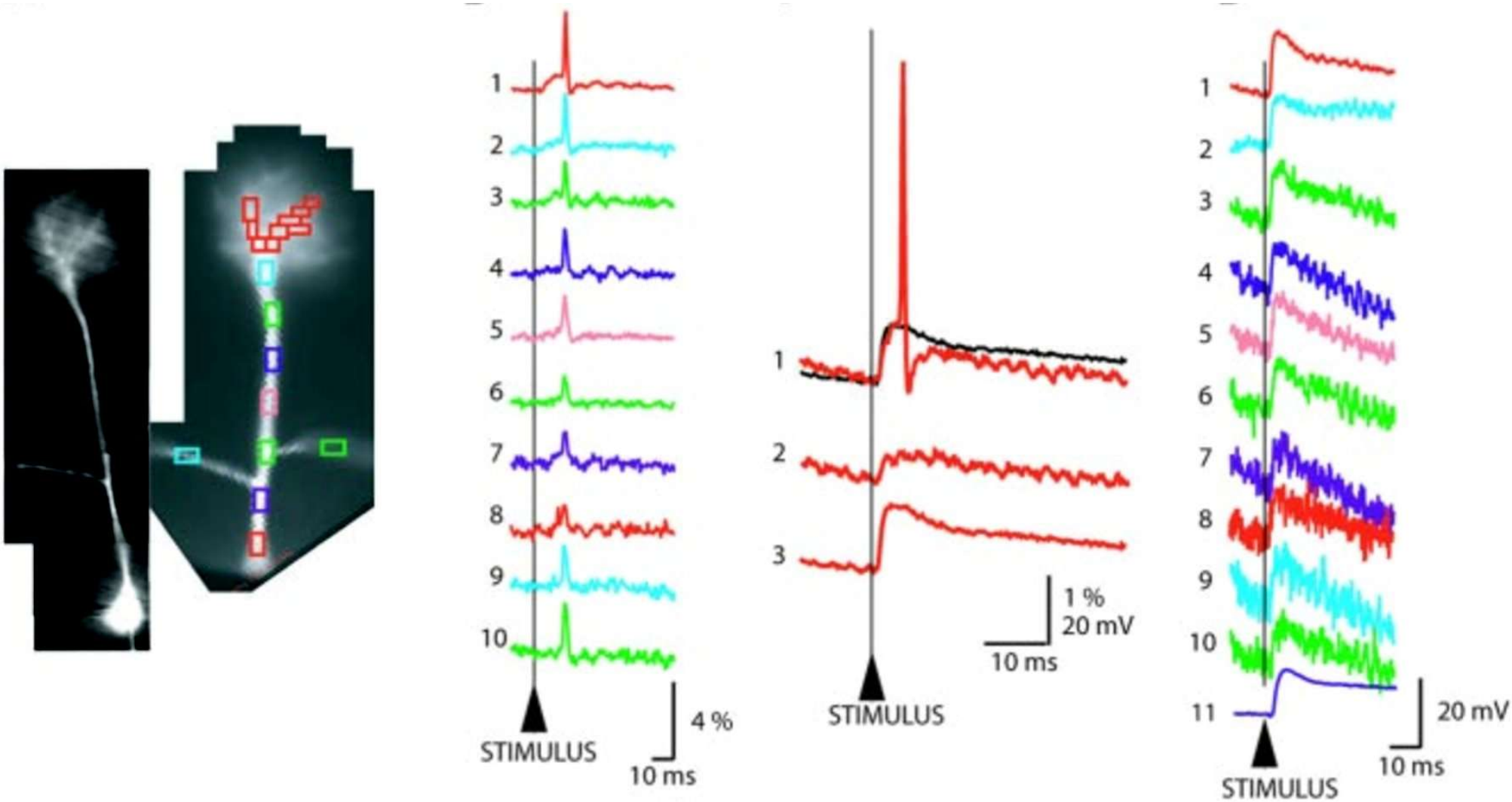
Channel density distribution



Synaptic input



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



simultaneous multisite recordings of transmembrane voltage

noisy

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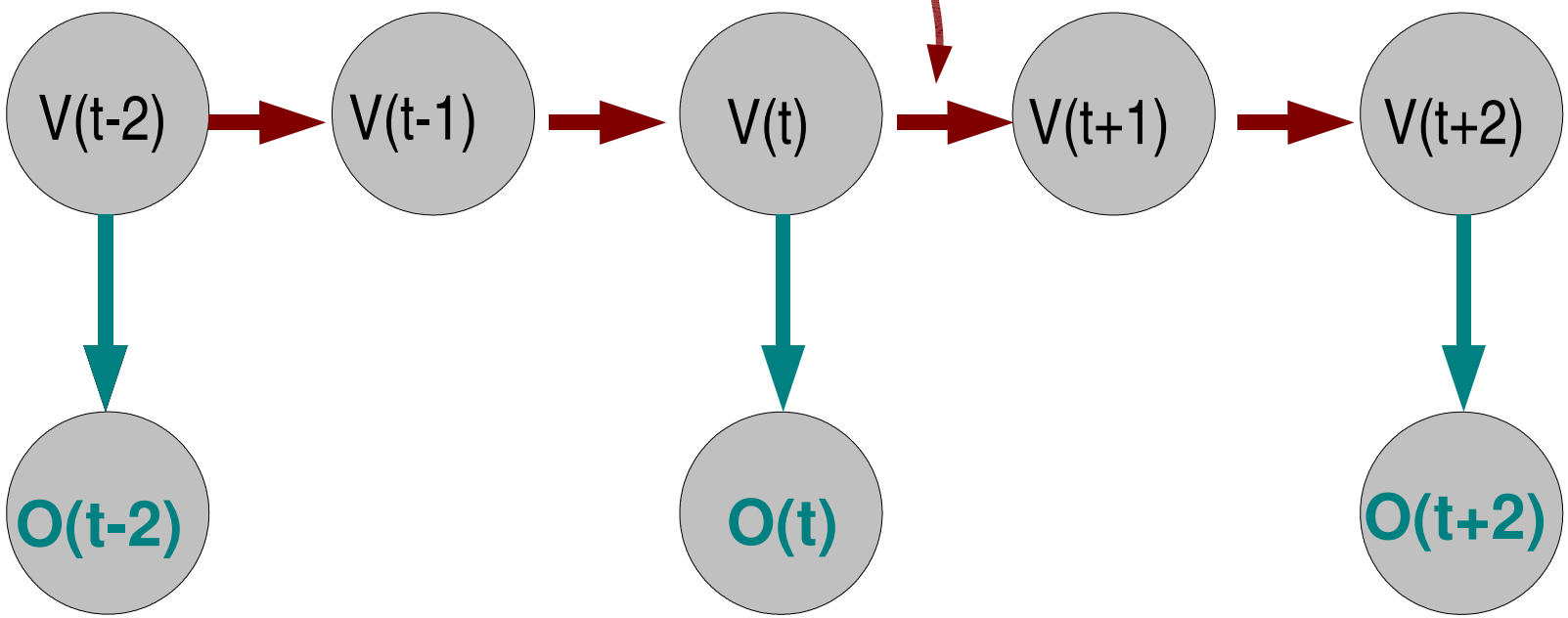
Outline

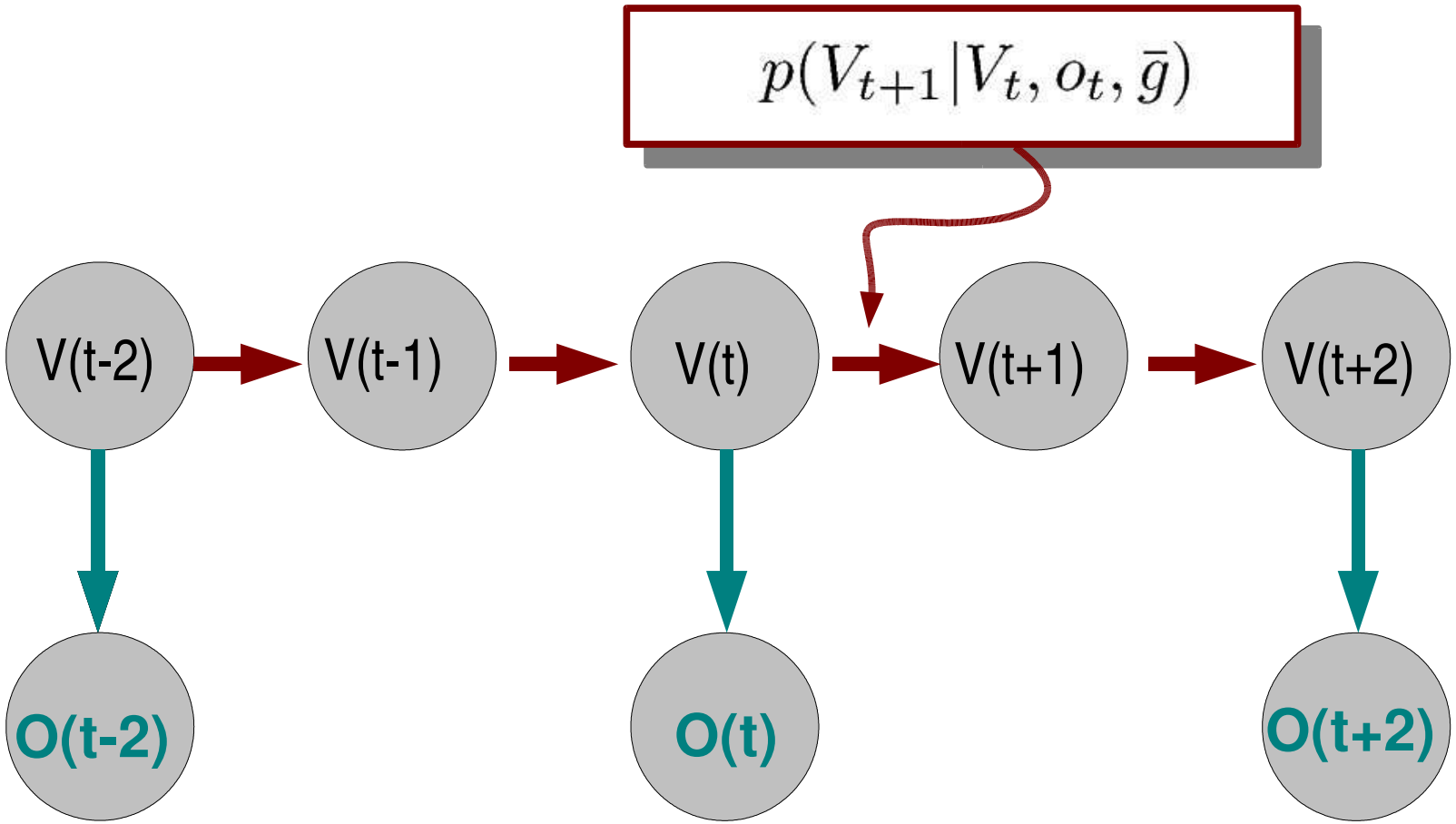
- Assume known kinetics and noiseless observations
- Relax
  - noisy observations
    - model-based smoothing (E)
    - parameter inference (M)
  - unknown kinetics

Hidden dynamical system

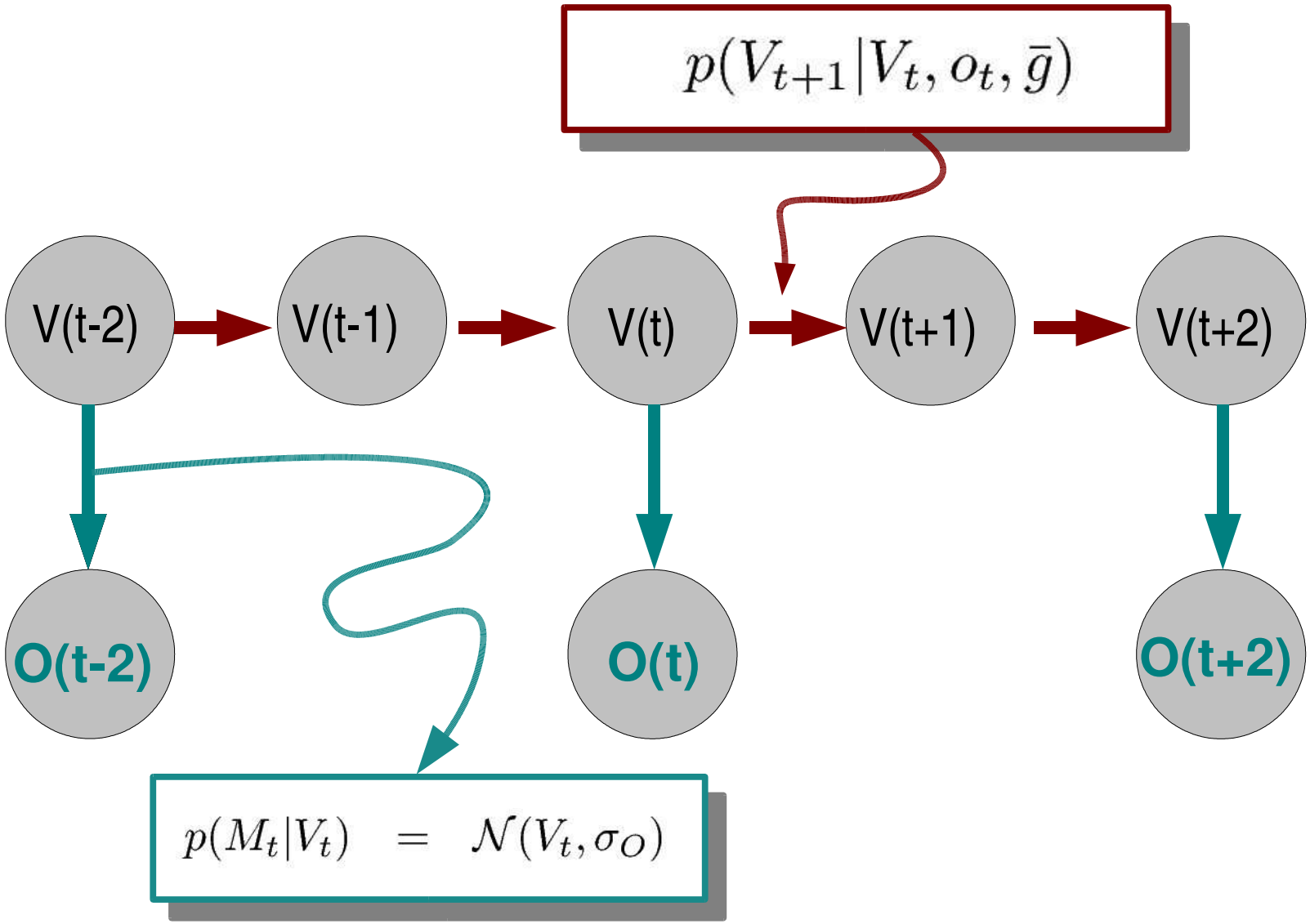
$$C_x \frac{dV_x(t)}{dt} = I_{\text{ch}} + I_{\text{int}} + I_{\text{syn}} + \sigma_x dN_{x,t}$$



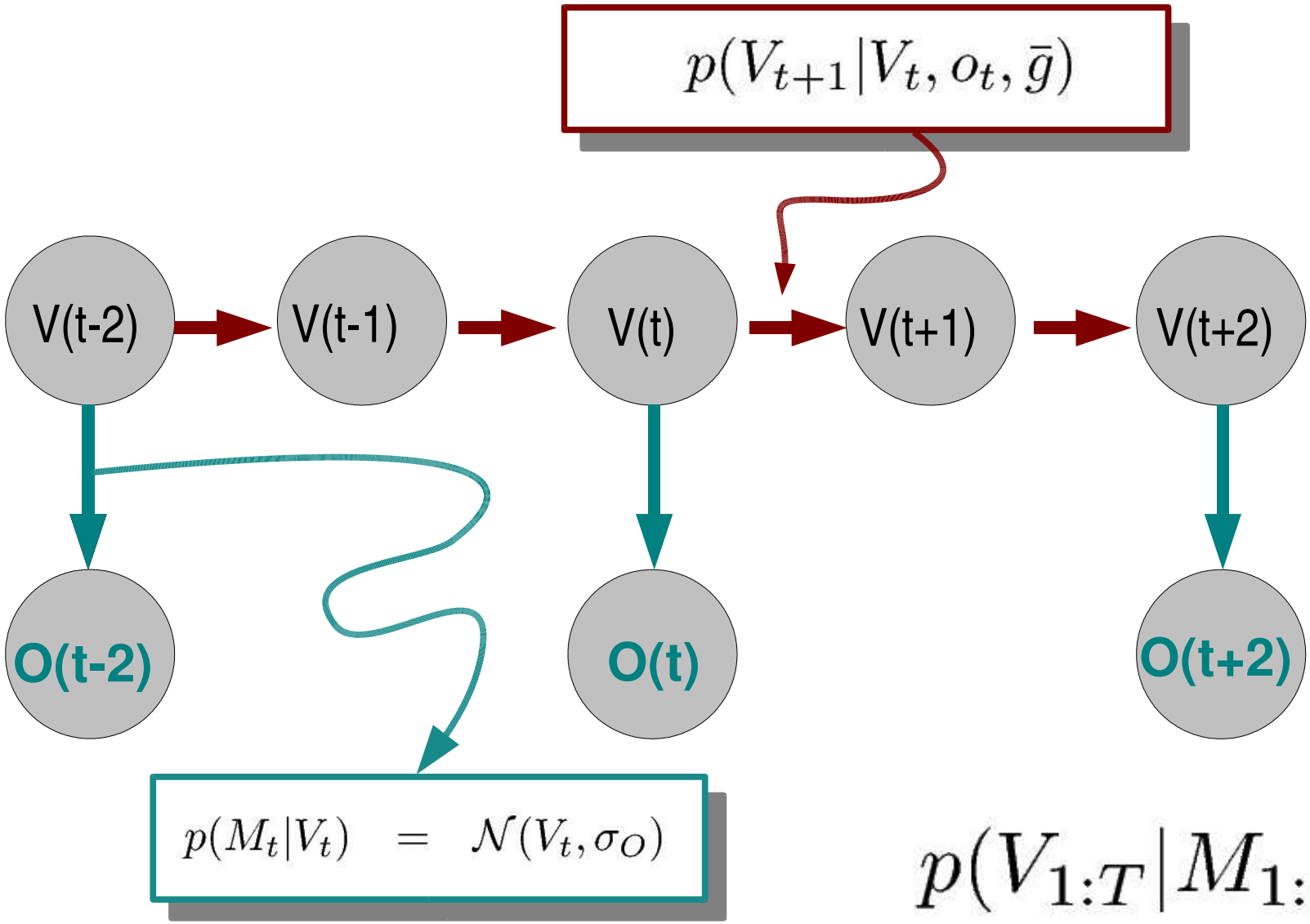
Hidden dynamical system



Hidden dynamical system



Hidden dynamical system

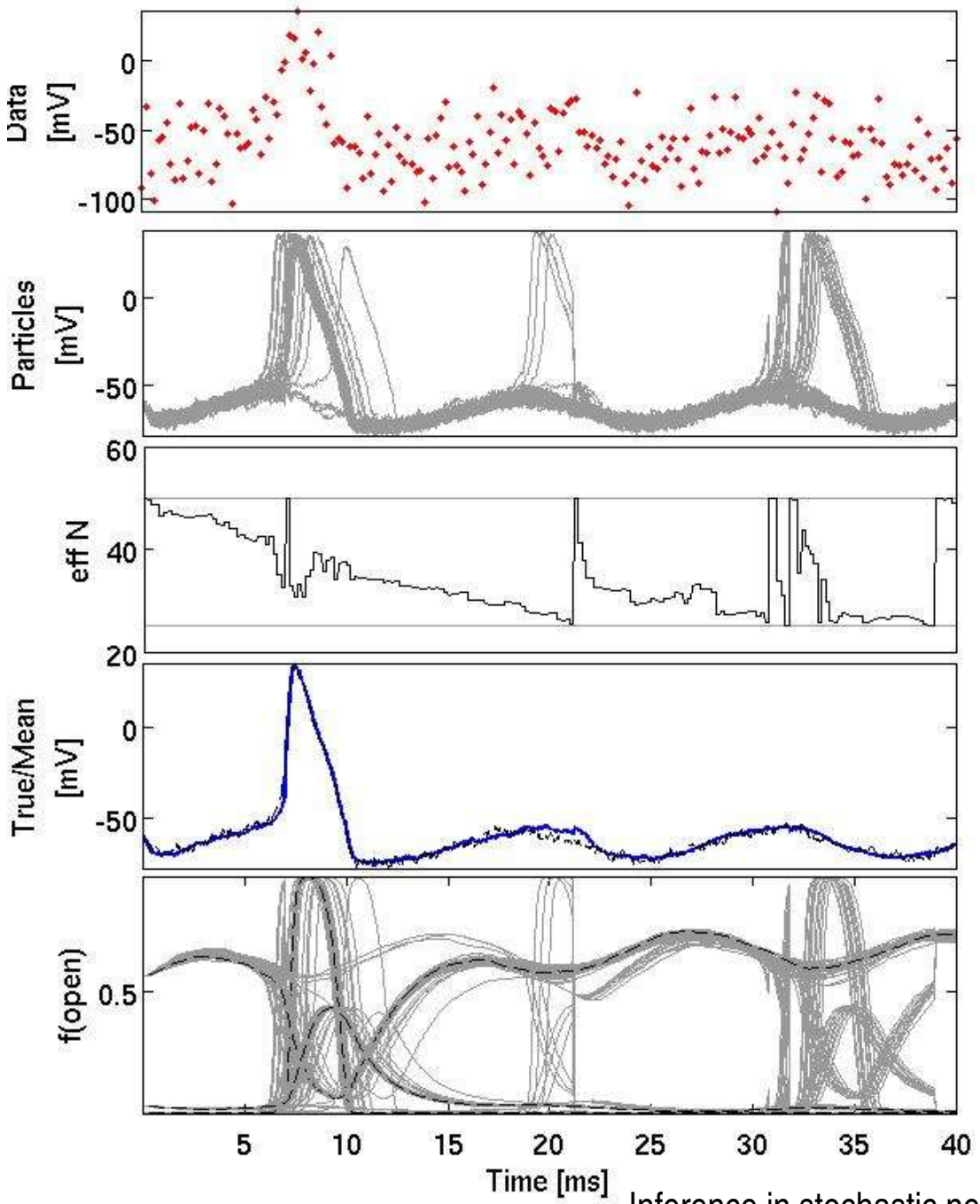


$$p(V_{1:T}|M_{1:t})$$

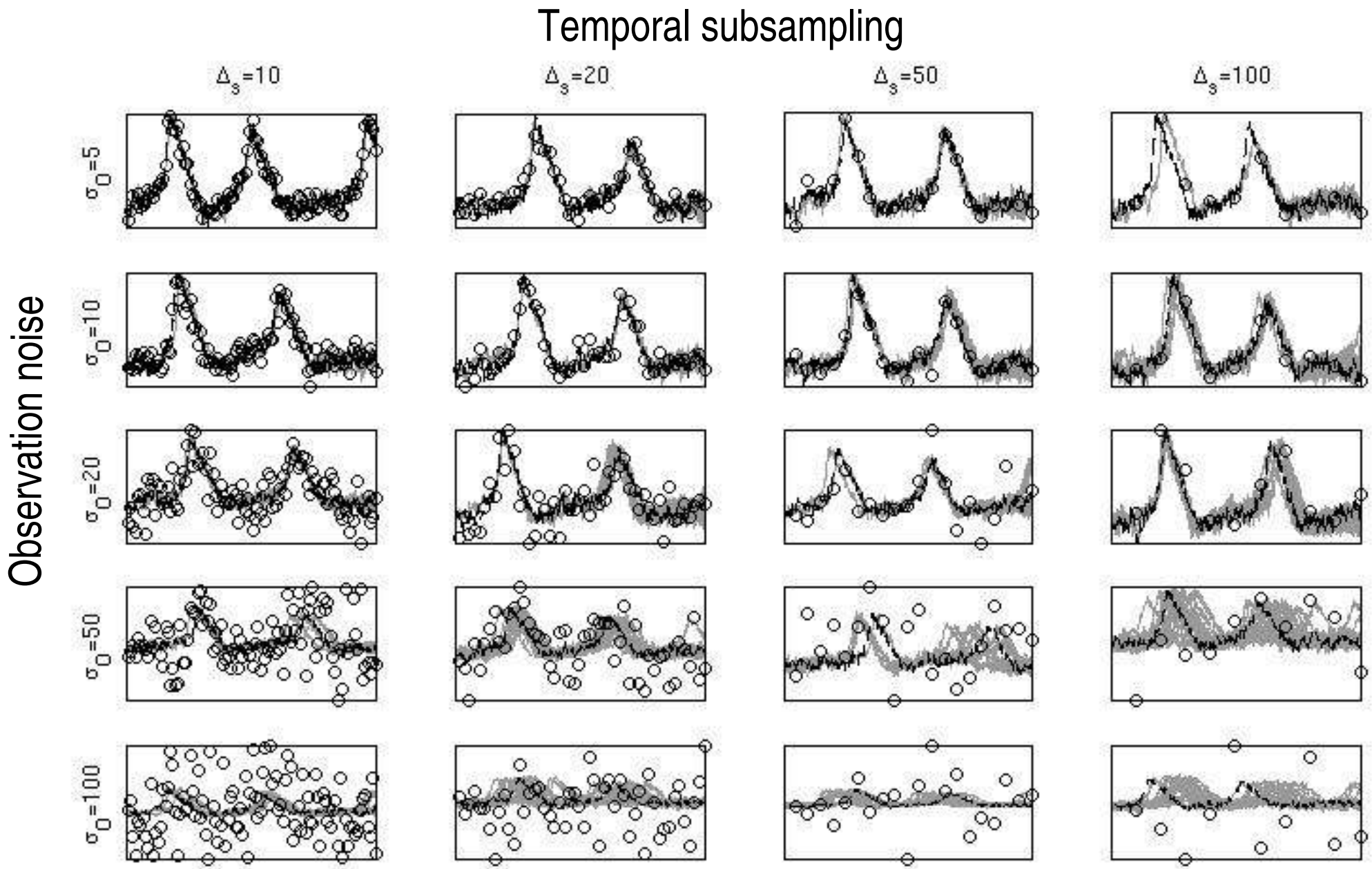
Model-based smoothing – know densities

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

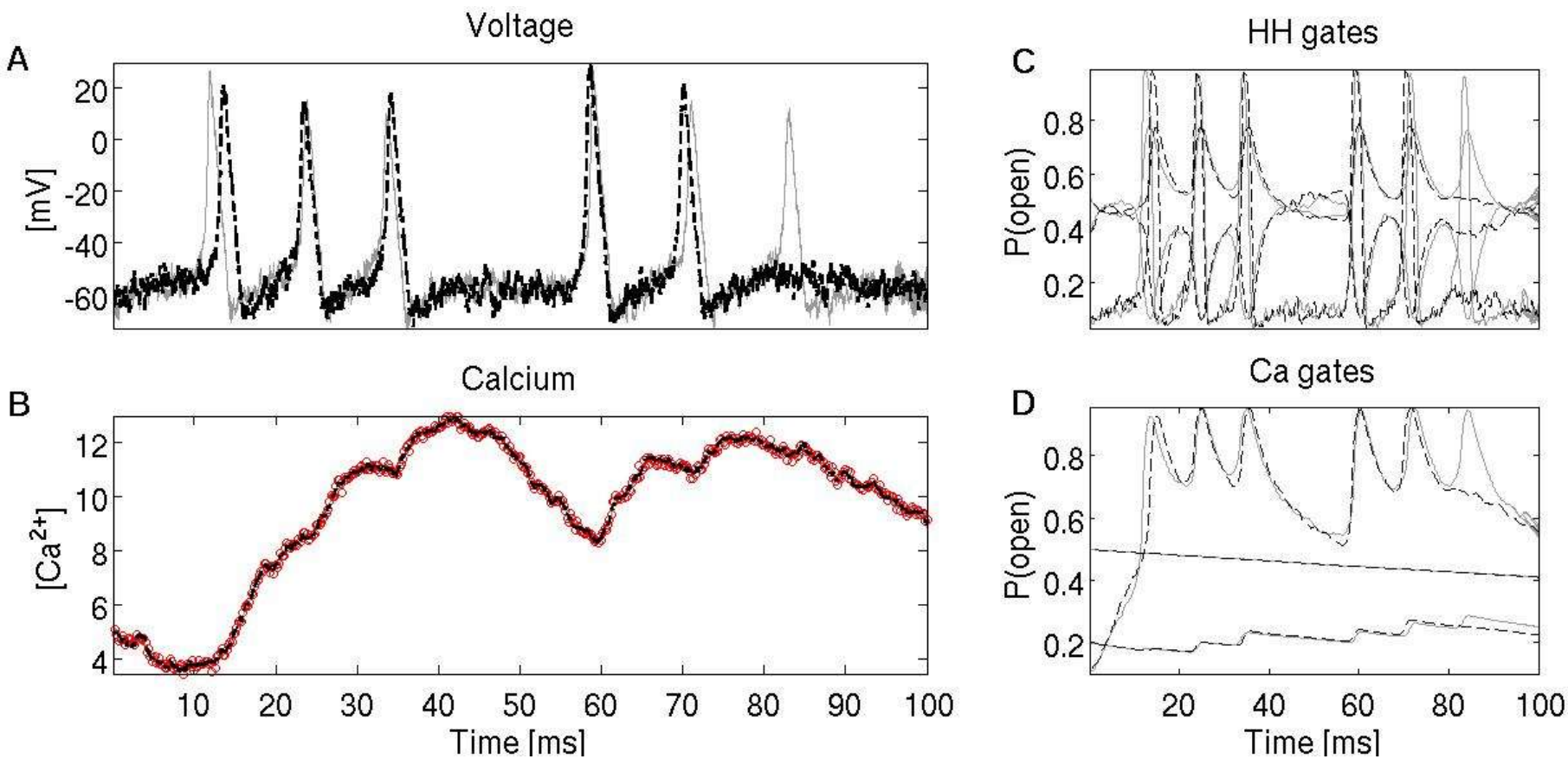
Know lots, get lots.



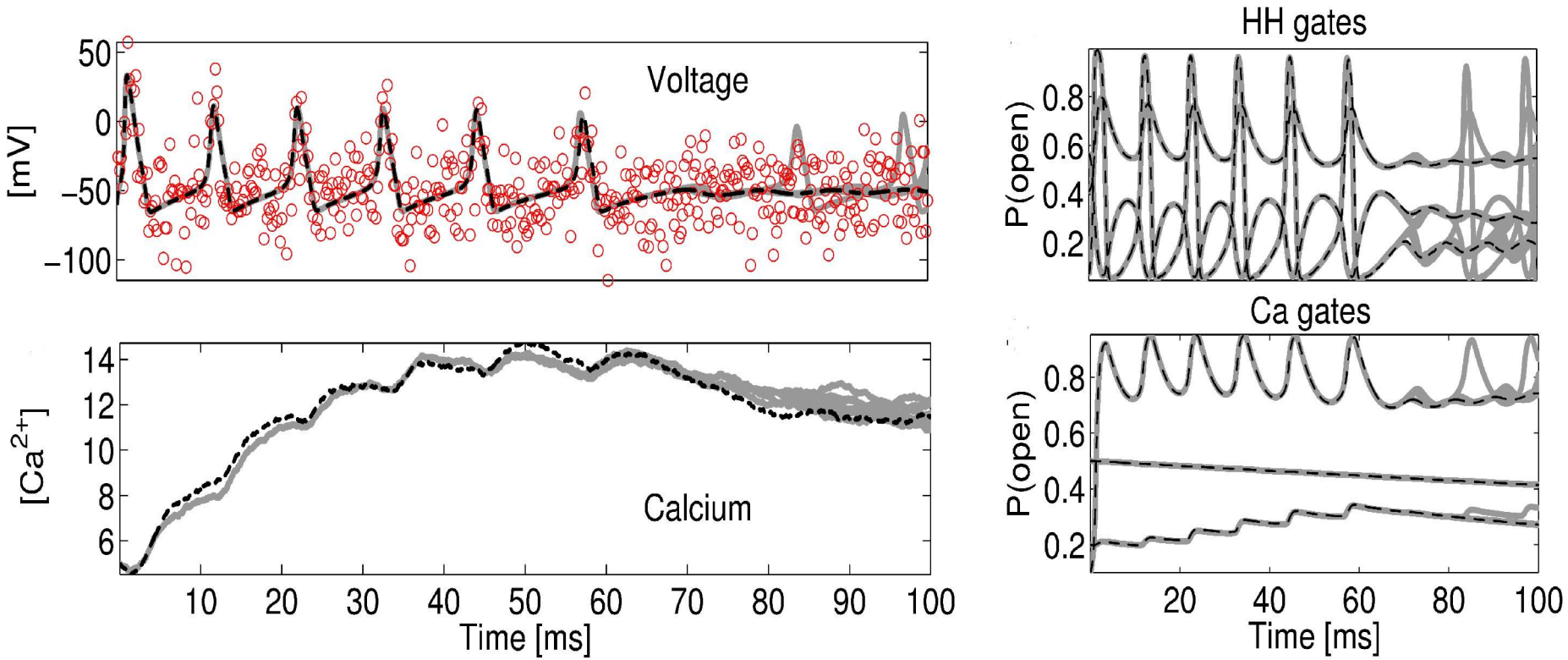
Smoothing and upsampling



Voltage from [Ca]



[Ca] from voltage



EM for channel densities

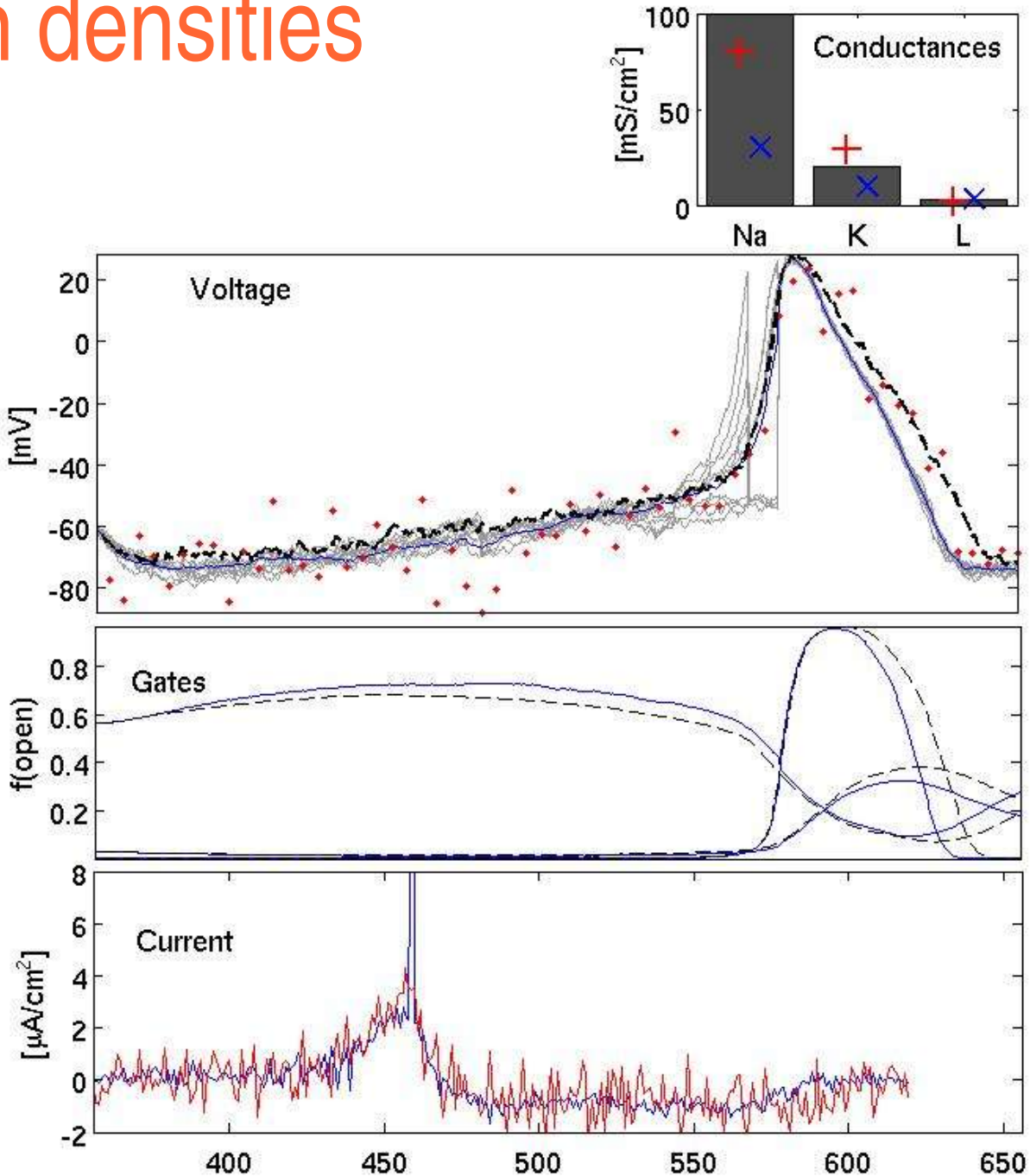
E step: infer some expected statistics given channel densities

particle smoother: $$w_t^i = \tilde{w}_t^i \left(\sum_j \frac{w_{t+1}^j p(V_{t+1}^j | V_t^i)}{\sum_k \tilde{w}_t^k p(V_{t+1}^j | V_t^k)} \right)$$

M step: update densities given expected sufficient statistics

$$\langle J_{ct} J_{c't} \rangle \quad \langle J_{ct} V_t \rangle \quad \langle J_{ct} V_{t+1} \rangle$$

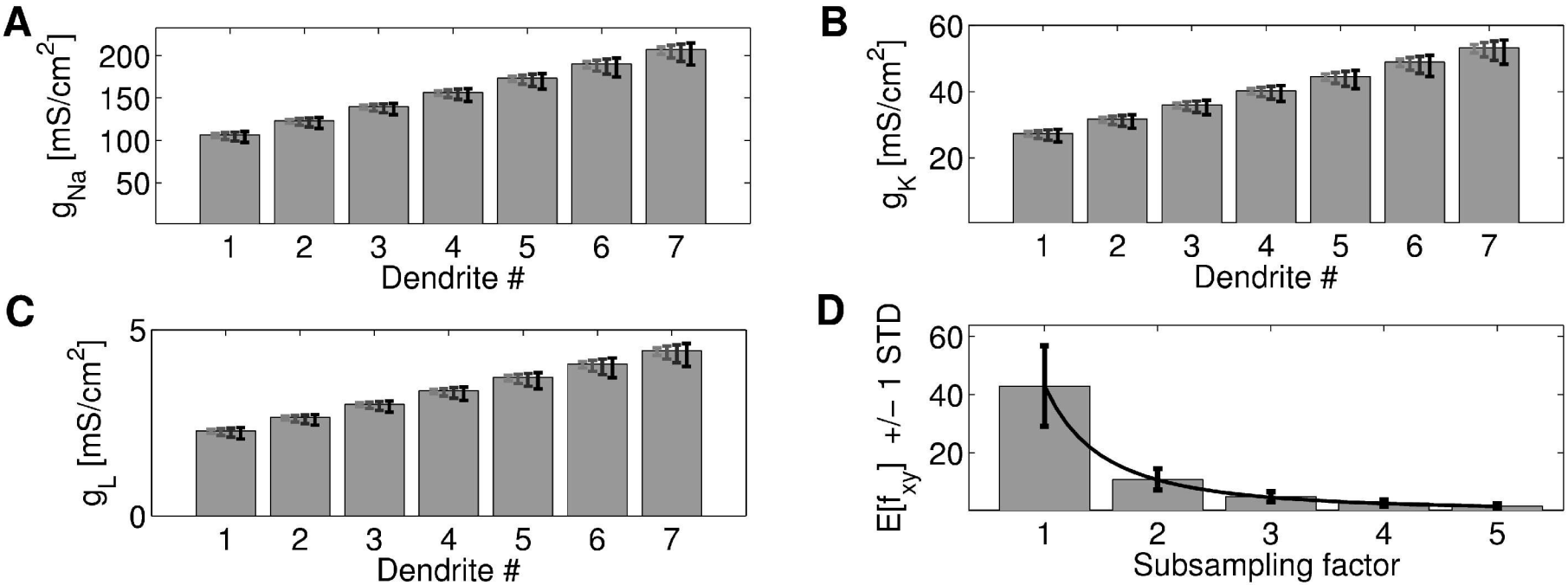
EM: Unknown densities



Discussion

- 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



E step: Particle smoothing

$$
\begin{aligned}
< V_{1:T} > &= \int dV_{1:T} p(V_{1:T}|M_{1:t}) V_{1:T} \\
&= \int dV_{1:T} q(V_{1:T}) \underbrace{\frac{p(V_{1:T}|M_{1:t})}{q(V_{1:T})}}_{w} V_{1:T} \\
&\approx \sum_i V_{1:T}^i w_i
\end{aligned}
$$

(importance sampling)

$$\boxed{V_{1:T}^i \sim q(V_{1:T})}$$

use exact distribution

$$
\begin{aligned}
q(V_t) &= p(V_t|V_{1:t-1}, M_{1:t}) \\
&\propto p(V_t|V_{t-1}) p(V_{t-1}|V_{1:t-2}, M_{1:t-2})
\end{aligned}
$$

filter weights

$$w_t^{*i} = w_{t-1}^i p(M_t|V_t^i) \quad \tilde{w}_t^i = w_t^{*i} / (\textstyle\sum_j w_t^{*j})$$

smoothing weights

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

Synaptic input