Hierarchical generalized linear models of dendritic integration and somatic membrane potential

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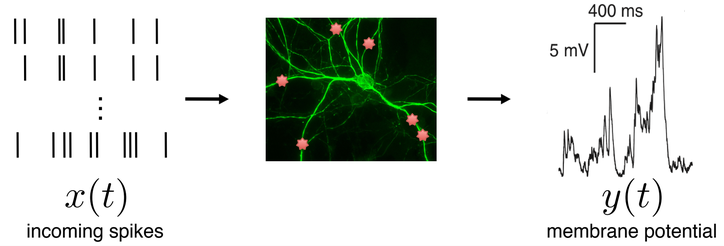
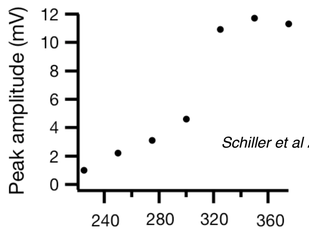
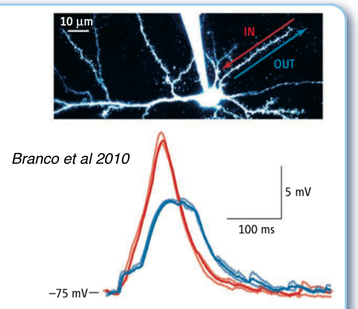
The problem



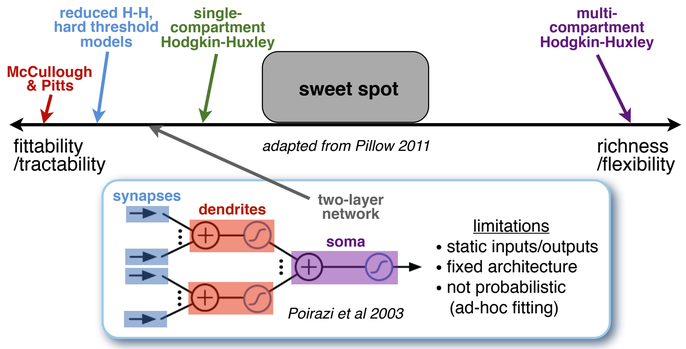
Peak somatic membrane potential is a nonlinear function of dendritic stimulation...



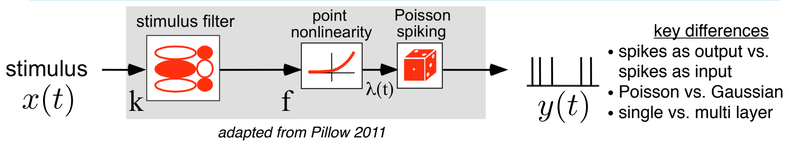


...and sensitive to temporal order of inputs.

Existing models



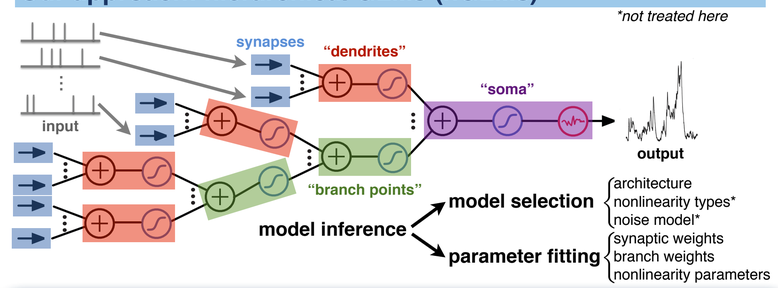
GLMs in Neuroscience 101

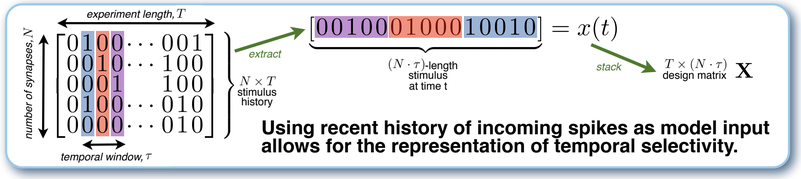


GLMs offer a battle-tested set of tools for building statistical models in neuroscience.

Whiteboard

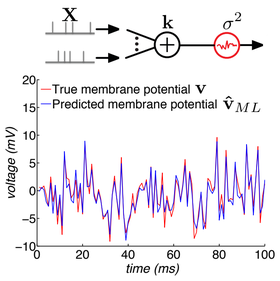
Our approach: hierarchical GLMs (hGLMs)





Using recent history of incoming spikes as model input allows for the representation of temporal selectivity.

Warm-up: single linear dendrite

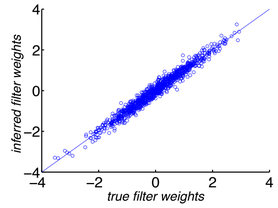


likelihood: $P(\mathbf{v} \mid \mathbf{k},\, \mathbf{X}) = \left(\frac{1}{\sqrt{2\pi\sigma^2}}\right)^T \exp\left[-\frac{\|\mathbf{v} - \mathbf{X}\mathbf{k}\|^2}{2\sigma^2}\right]$

ML estimate: $\mathbf{k}_{ML} = \left(\mathbf{X}^T\mathbf{X}\right)^{-1}\mathbf{X}^T\mathbf{v}$

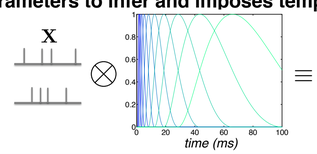
generation parameters

$\sigma^2 = 1$
$T = 4000 \quad \mathbf{k} \sim N(0,1)$
$N = 10 \quad \mathbf{X} \sim 1\%\,\text{spikes}$
$\tau = 100$



✓ *concave log likelihood*
✓ *closed form ML solution*
✓ *vanilla linear regression*

Basis expansion of linear filter reduces number of parameters to infer and imposes temporal smoothness.



number of basis functions

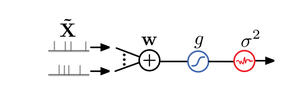
linear stage: $\mathbf{X}\mathbf{k} \rightarrow \tilde{\mathbf{X}}\mathbf{w}$

number of weights: $N \cdot T \rightarrow N \cdot M$

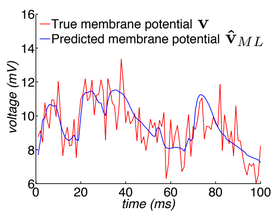
$b_j(\tau) = \begin{cases} \frac{1}{2}\cos\left(a\log[\tau + c] - \phi_j\right) + \frac{1}{2} & \tau \text{ s.t. } a\log[\tau + c] \in [\phi_j - \pi, \phi_j + \pi] \\ 0 & \text{else} \end{cases}$

Pillow et al 2008

Single nonlinear dendrite



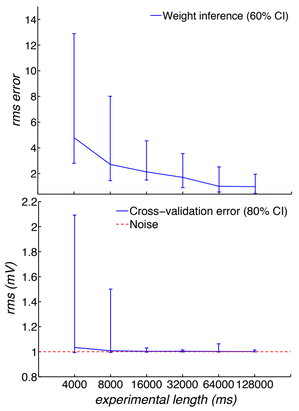
likelihood: $P(\mathbf{v} \mid \mathbf{w},\, \tilde{\mathbf{X}}) = \left(\frac{1}{\sqrt{2\pi\sigma^2}}\right)^T \exp\left[-\frac{\left\|\mathbf{v} - g\left(\tilde{\mathbf{X}}\mathbf{w}\right)\right\|^2}{2\sigma^2}\right]$



generation parameters

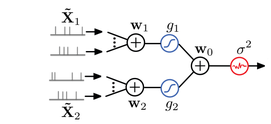
$g(x) \equiv \frac{\alpha}{1 + e^{-x}}$

$\sigma^2 = 1 \quad \alpha \sim u(1,10)$
$N = 10 \quad \mathbf{X} \sim 1\%\,\text{spikes}$
$\tau = 100 \quad \mathbf{w} \sim \text{lognormal}(1,1)$



✗ *non-concave log likelihood*
✗ *nontrivial ML problem*
✓ *solvable anyways*

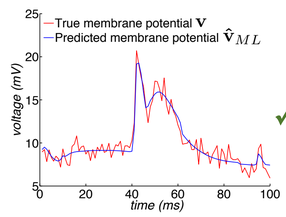
Two-layer network: "partial" inference (known architecture)

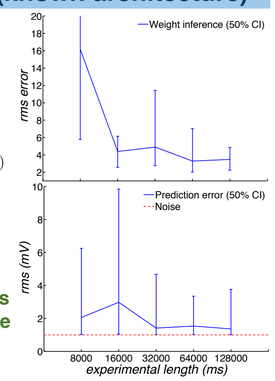


generation parameters

$g_i(x) \equiv \frac{\alpha_i}{1 + e^{-x}}$

$\sigma^2 = 1 \quad \alpha_i \sim u(1,10)$
$N = 10 \quad \mathbf{X}_i \sim 1\%\,\text{spikes}$
$\tau = 100 \quad \mathbf{w}_i \sim \text{lognormal}(.35,1)$

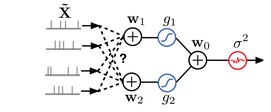




✓ **inference in two-layer networks possible using only input spikes and *somatic* membrane potential**

likelihood: $P(\mathbf{v} \mid \{\mathbf{w}_i\}, \left\{\tilde{\mathbf{X}}_i\right\}) = \left(\frac{1}{\sqrt{2\pi\sigma^2}}\right)^T \exp\left[-\frac{\left\|\mathbf{v} - \sum_{i=1}^2 w_0^{(i)} g_i\left(\tilde{\mathbf{X}}_i\mathbf{w}_i\right)\right\|^2}{2\sigma^2}\right]$

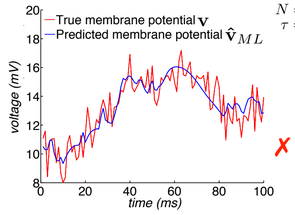
Two-layer network: "full" inference (unknown architecture)

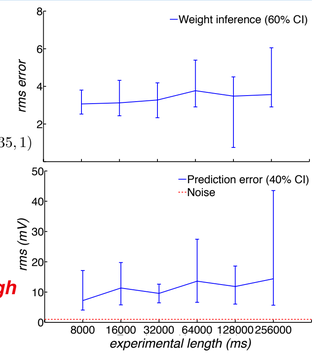


generation parameters

$g_i(x) \equiv \frac{\alpha_i}{1 + e^{-x}}$

$\sigma^2 = 1 \quad \alpha_i \sim u(1,10)$
$N = 10 \quad \mathbf{X} \sim 1\%\,\text{spikes}$
$\tau = 100 \quad \mathbf{w}_i \sim \text{lognormal}(.35,1)$
+ random assignment of synapses to dendrites





✗ *naive Laplacian prior is not enough to reliably learn structure*

posterior: $P(\{\mathbf{w}_i\} \mid \mathbf{v}, \left\{\tilde{\mathbf{X}}_i\right\}) \propto \overbrace{\left(\frac{1}{\sqrt{2\pi\sigma^2}}\right)^T \exp\left[-\frac{\left\|\mathbf{v} - \sum_{i=1}^2 w_0^{(i)} g_i\left(\tilde{\mathbf{X}}\mathbf{w}_i\right)\right\|^2}{2\sigma^2}\right]}^{\text{Gaussian likelihood}} \overbrace{\frac{1}{Z(\lambda)} \exp\left[-\lambda \sum_{i=1}^2 |\mathbf{w}_i|\right]}^{\text{Laplacian prior (to encourage pruning of extraneous connections)}}$

Future work

- smarter structure learning (synapse-wise Laplacian prior)
- smart initialization (Bussgang)
- more efficient optimization (EM)
- extension to hidden state space models
- fitting model to data from compartmental models and glutamate uncaging experiments
- comparing functional architecture (inferred by the model) to anatomical morphology
- studying how functional architecture may depend on input statistics, neuromodulators

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Acknowledgements

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