Inferring synaptic conductances from spike trains with a biophysically inspired point process model

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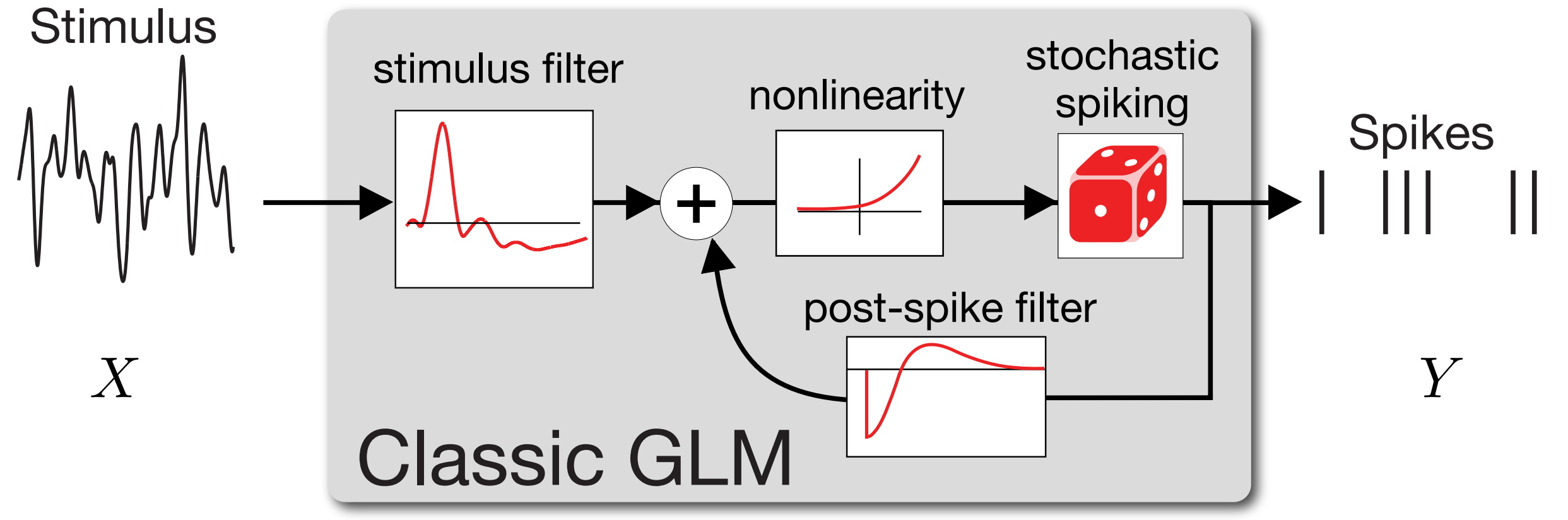
Motivation

Generalized linear models: tractable descriptive models of spike responses



Problems: 1) lack clear biophysical interpretation, accuracy
2) do not generalize well over stimulus conditions

Biophysical interpretation of the GLM

- passive membrane dynamics: $\frac{dV}{dt} = g_e(t)(E_e - V) + g_i(t)(E_i - V) + g_l(E_l - V)$
- g_e and g_i are linear functions of the stimulus:

filter

$$g_e(t) = (\mathbf{k}_e * X)(t) + b_e$$
$$g_i(t) = (\mathbf{k}_i * X)(t) + b_i$$

- total conductance ($g_e + g_i + g_l = \tau^{-1}$) constant

$\Longrightarrow$ excitation and inhibition have equal and opposite tuning: $k_e = -k_i$

Integrating $\frac{dV}{dt}$ gives $V(t) = (E_e - E_i)\int_0^T e^{-\frac{t-s}{\tau}}(\mathbf{k}_e * X)(s)ds + const$

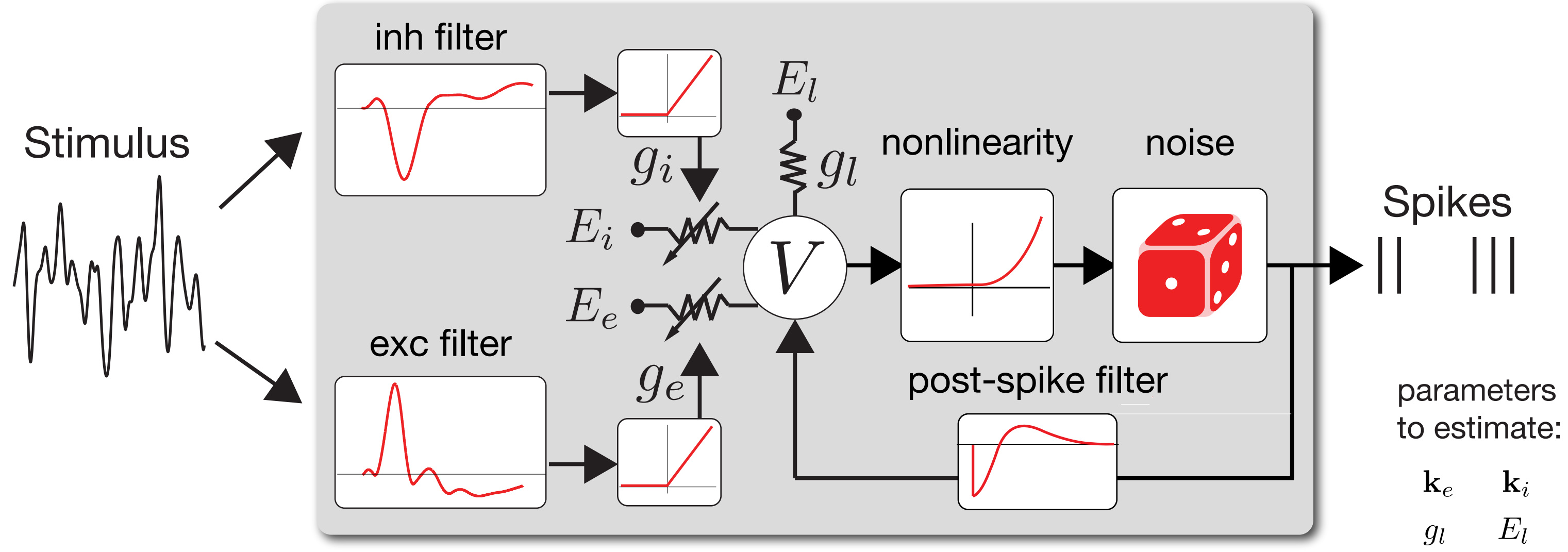
$= (E_e - E_i)(\mathbf{k}_{GLM} * X)(t) + const$ where $\mathbf{k}_{GLM} = \mathbf{k}_e * e^{-\frac{t}{\tau}}$

$\Longrightarrow$ Voltage linear in the stimulus!

Add Poisson spiking to get a GLM: $Y_t \sim \mathrm{Poisson}(f(V(t)))$

Conductance-based spiking model (CBSM)

Relax the constraints
- excitatory and inhibitory inputs are not linear in real neurons
- model conductances as independent LN models
- stimulus-dependent gain (time constant)



parameters to estimate:
$\mathbf{k}_e$ $\mathbf{k}_i$
g_l E_l
$\mathbf{h}_{spk}$

fixed values:
$E_e = 0mV$
$E_i = -80mV$
$w = 4$
$c = -70$

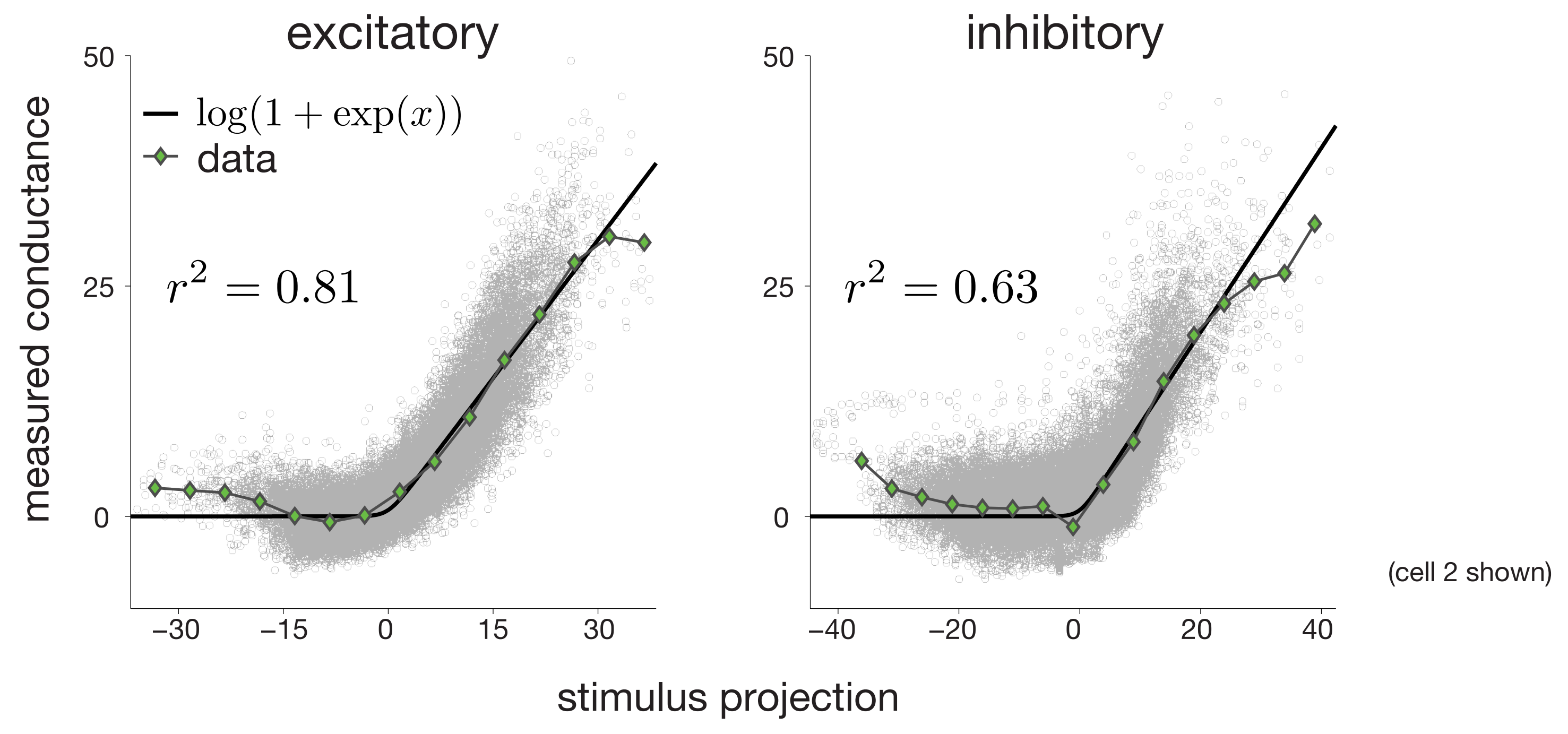
$$\frac{dV}{dt} = g_e(t)(E_e - V) + g_i(t)(E_i - V) + g_l(E_l - V)$$
$$g_e(t) = f_e((k_e * X)(t))$$
$$g_i(t) = f_i((k_i * X)(t))$$
$$Y_t \sim \mathrm{Poisson}\left(\exp\left(\frac{V_t - c}{w} + h_{spk}^\top Y_{hist}\right)\right)$$

solve on discrete lattice

(Mensi, Naud, & Gerstner, 2011)

Conductance nonlinearity

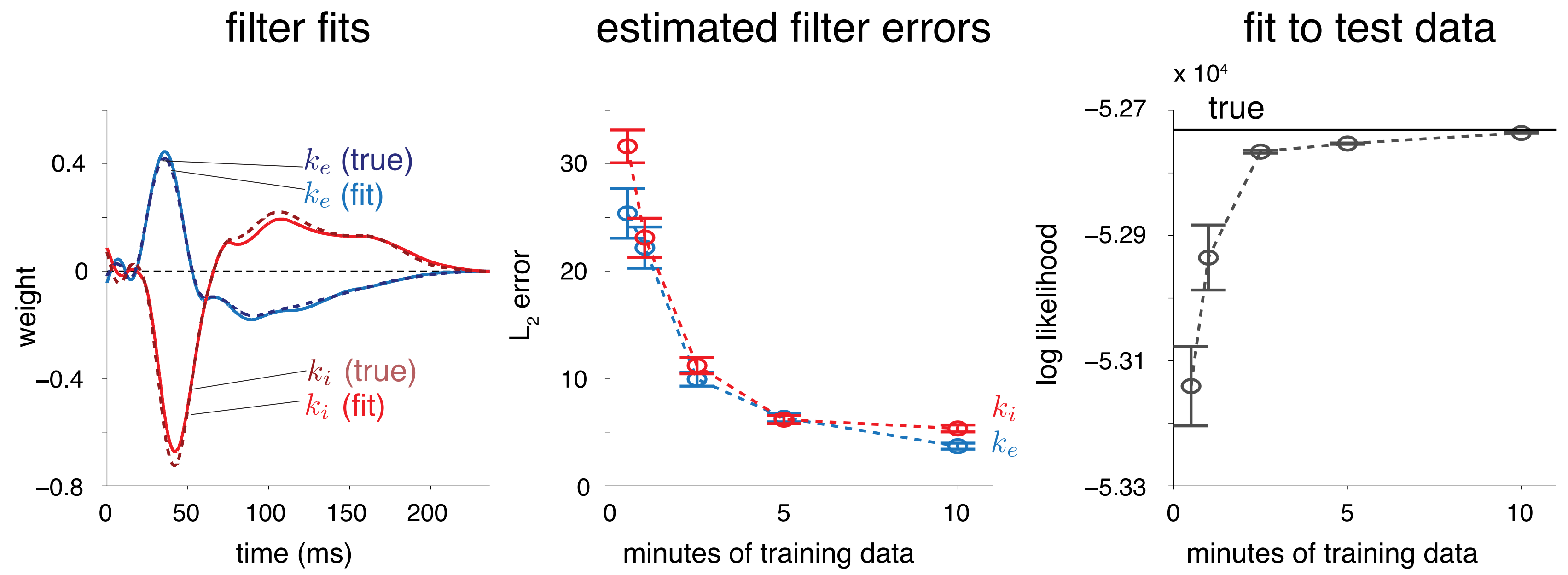
- macaque on-Parasol retinal ganglion cells (Trong & Rieke, 2008)
- full-field, single contrast white noise stimulus (0-60Hz), 6s trials
- recorded from same cell spikes, inhibitory and excitatory currents
  - cell-attached and whole-cell voltage clamp recordings (10kHz sampling)
- conductances well-described by rectified linear function of stimulus



(cell 2 shown)

Maximum likelihood fitting

- conjugate-gradient methods converge to true filters using simulated data

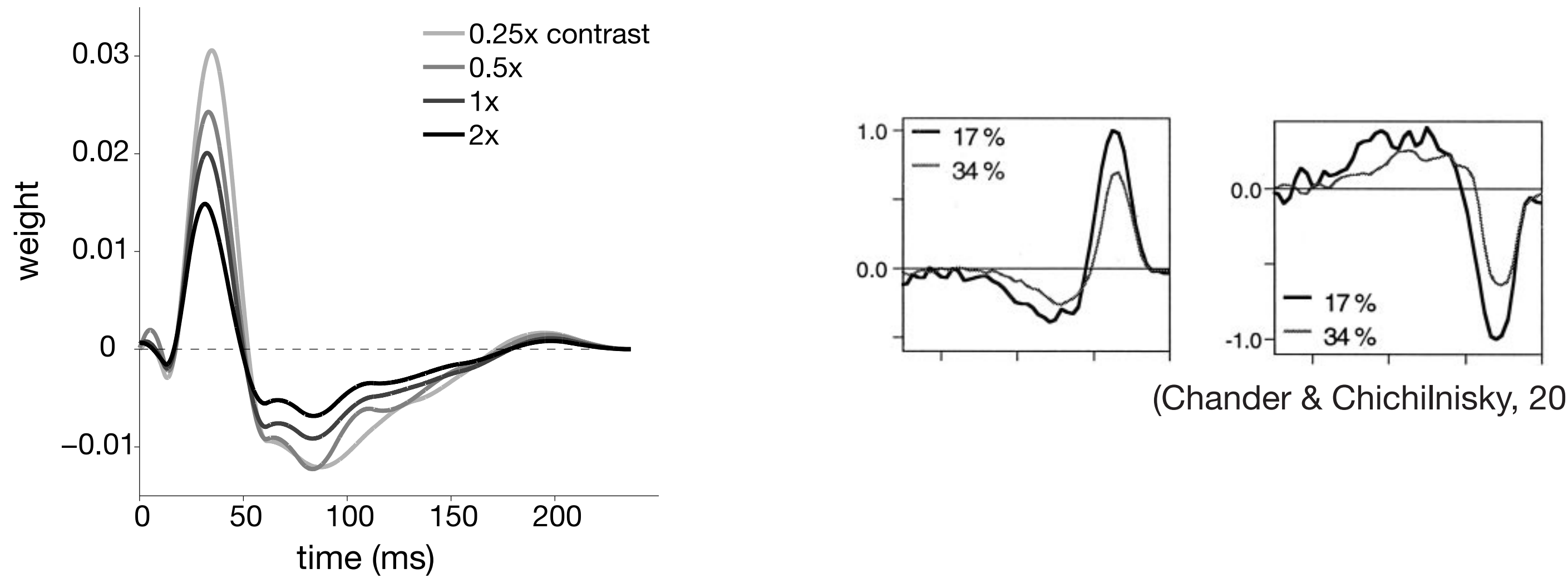

filter fits

estimated filter errors

fit to test data

Responses at multiple contrast levels

- simulated from fixed conductance model, fit linear filter with GLM

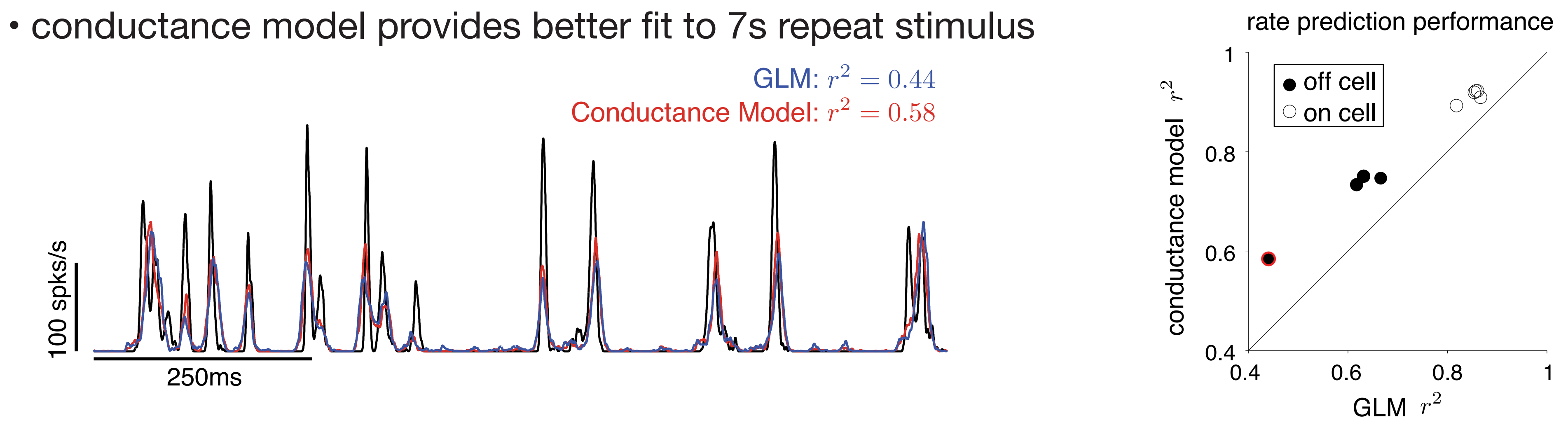

filters at different contrasts

experimental data

(Chander & Chichilnisky, 2001)

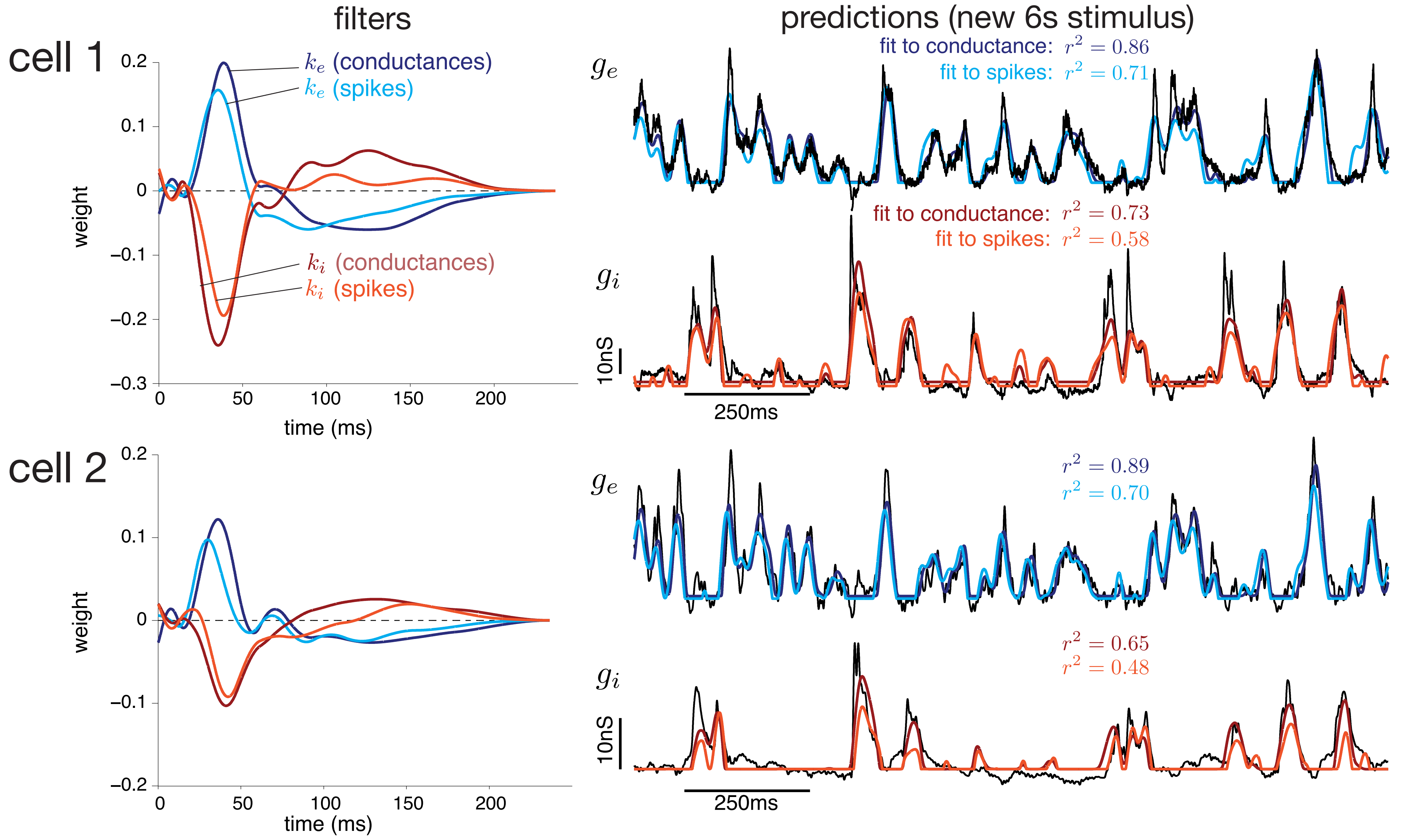
Extracellular recordings: comparison to GLM

- ML fit to 5min recording of macaque RGCs, binary noise (Pillow et al., 2005)
- conductance model provides better fit to 7s repeat stimulus



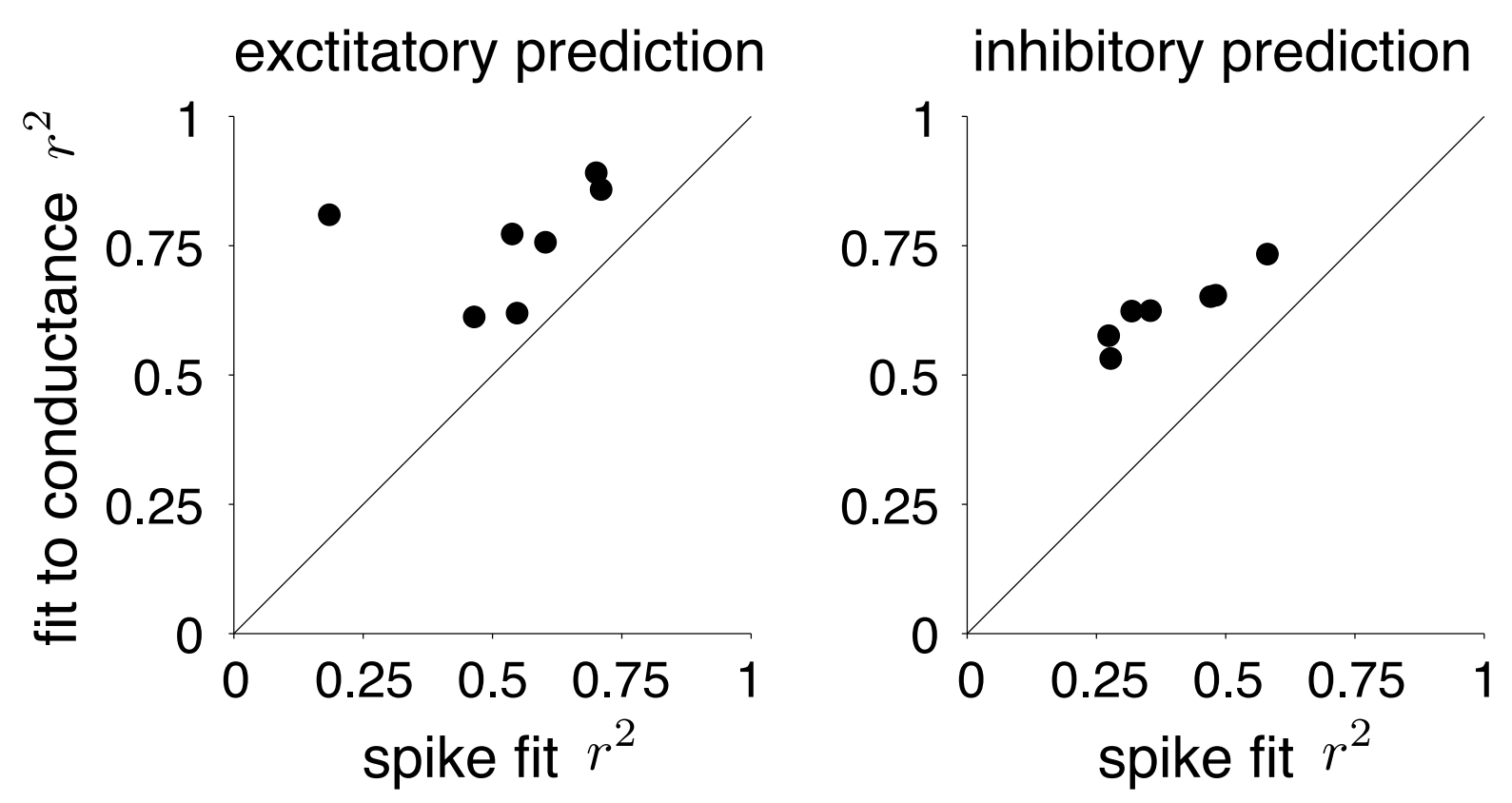
Inferring inputs in retinal ganglion cells

- model fit to spikes, compared to intracellularly recorded inputs (scaled)


filters

predictions (new 6s stimulus)

population summary
- 7 cells



Conclusions

- accurately predict excitatory and inhibitory conductance tuning from spikes
- nonlinear characterization of inputs improves prediction accuracy
- model produces adaptive behavior: stimulus-dependent time constant

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