Deriving the Neural Code from Single Neuron Dynamics

Michael Famulare
University of Washington
Department of Physics

June 24, 2010

famulare@uw.edu

Acknowledgements

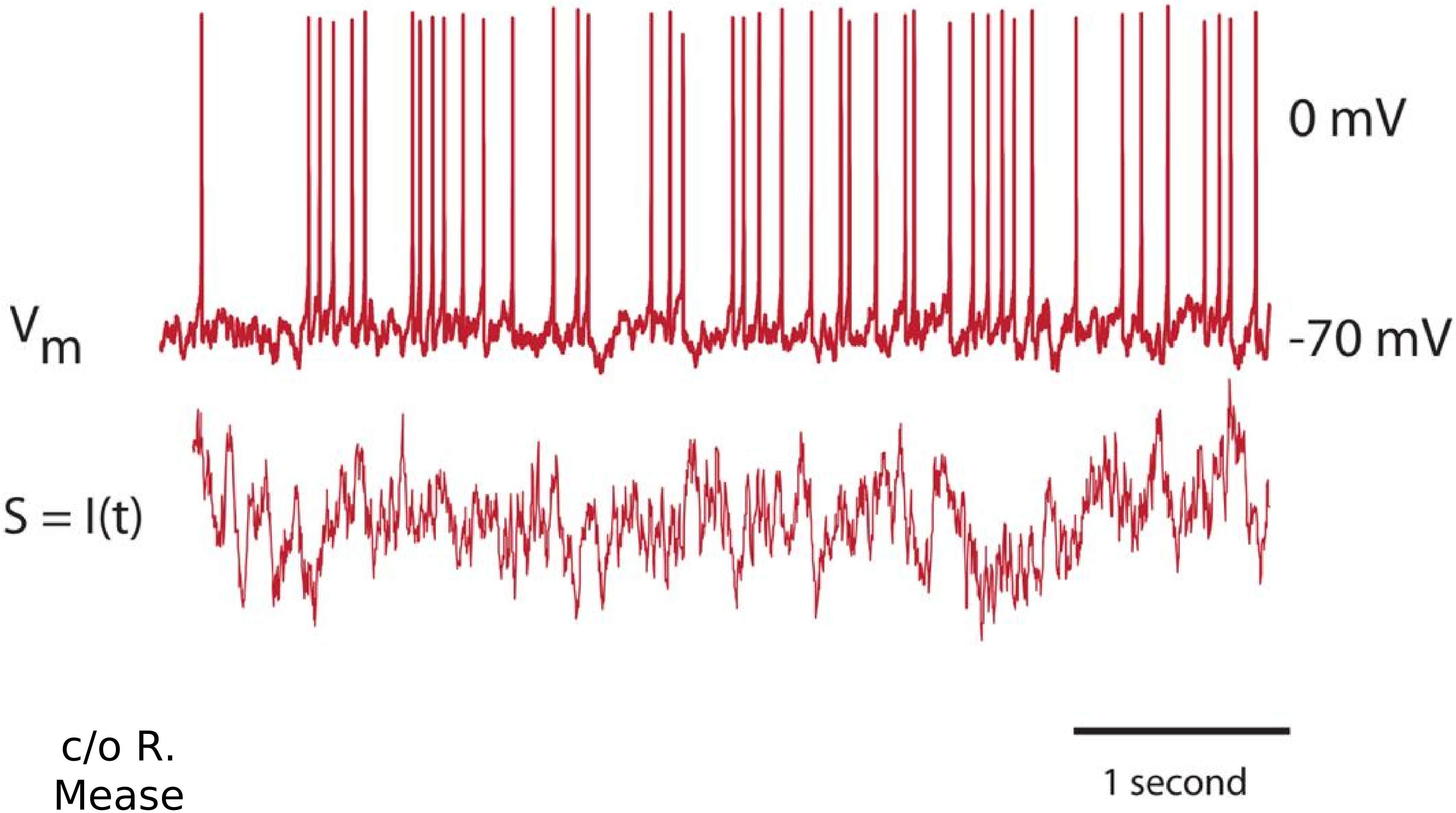
Adrienne Fairhall

Rebecca Mease

NSF

McKnight Foundation

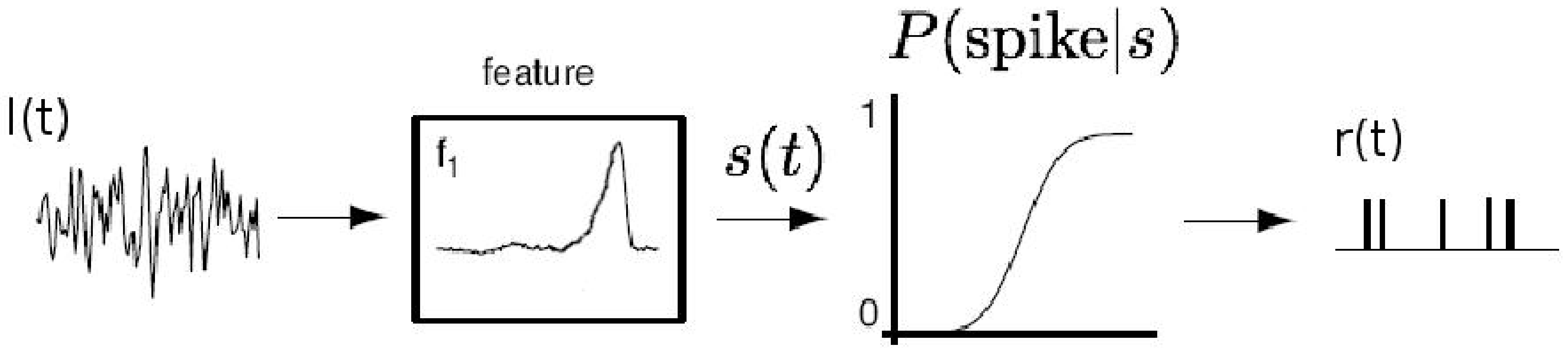
What does a spike represent?



c/o R. Mease

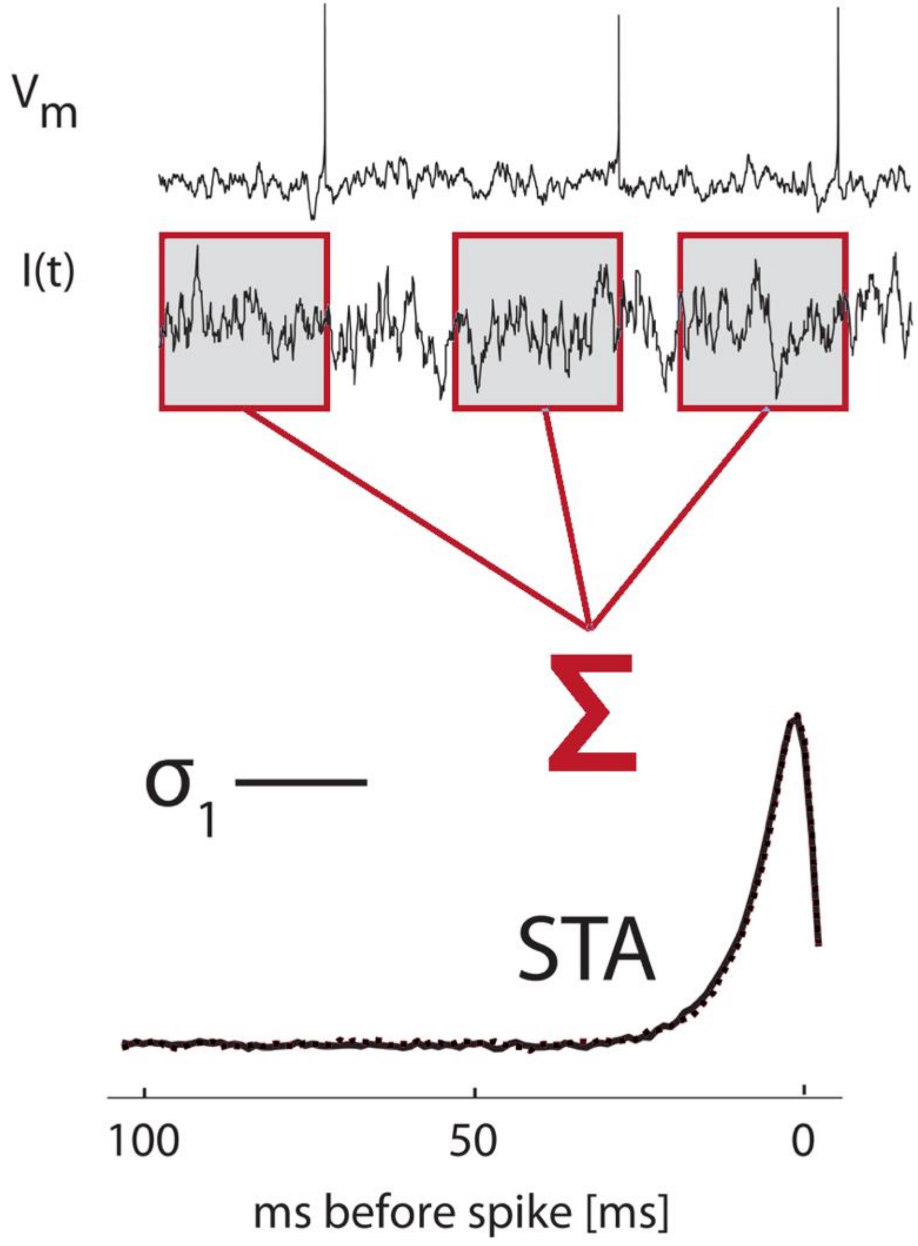
What does a spike represent?

Feature Selection: LN Model

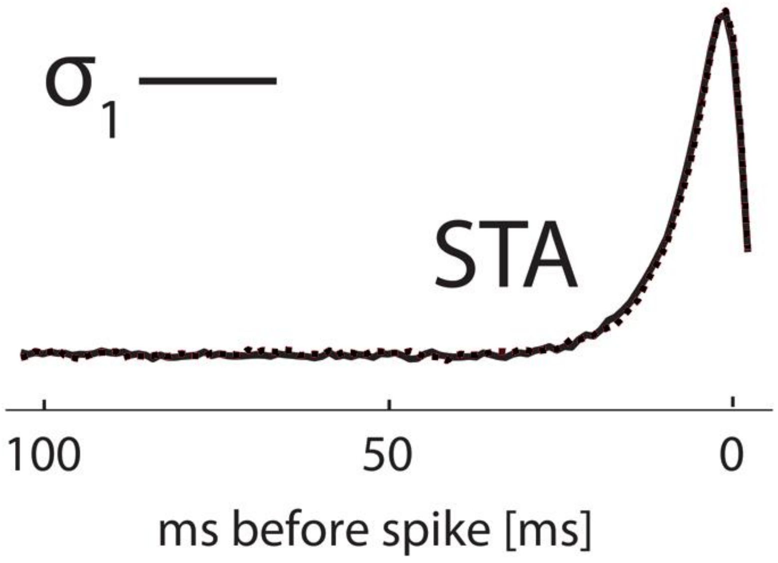


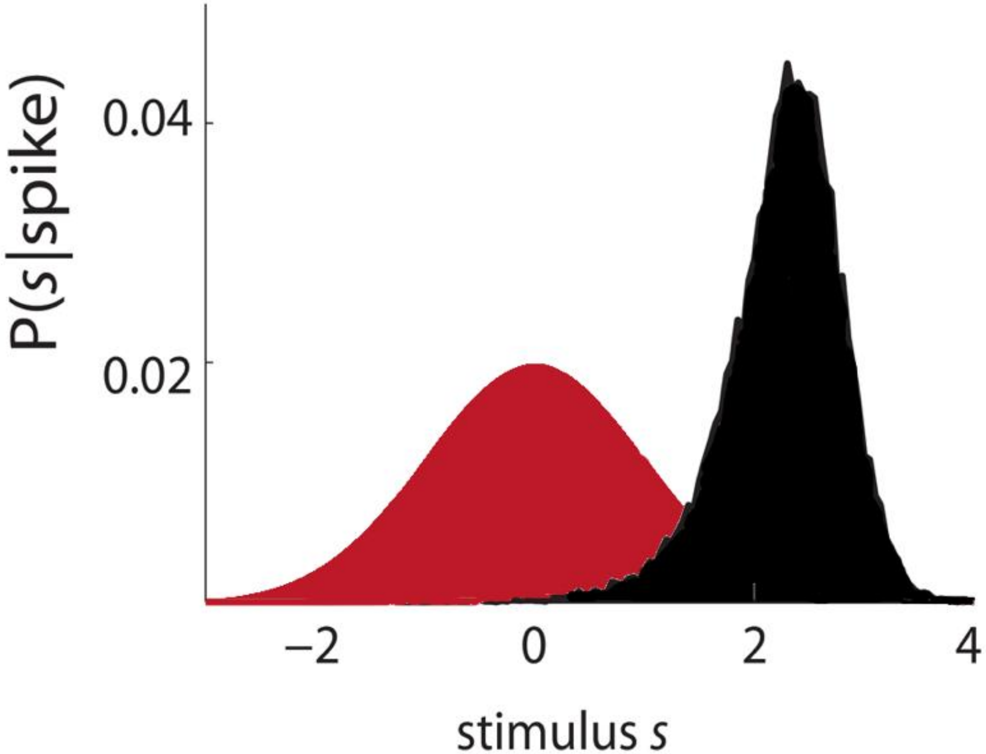
How do system dynamics determine the feature and the nonlinearity?

What does a spike represent?



What does a spike represent?





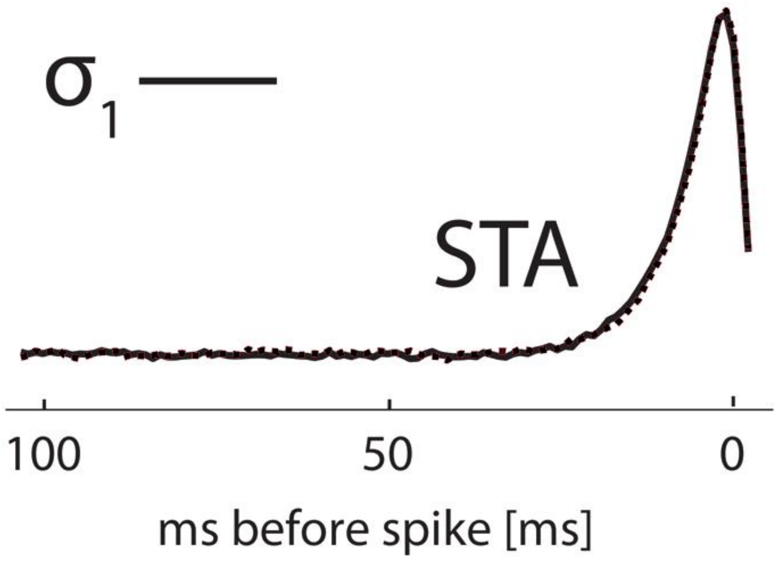
<u>Filtered stimulus</u>

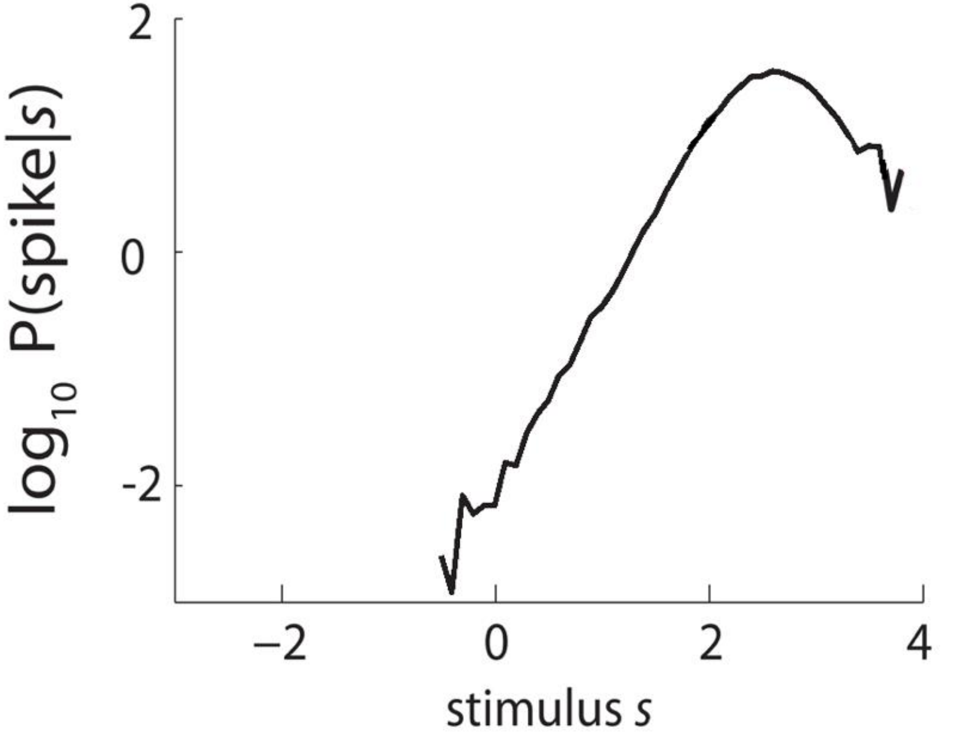
$$s(t) \equiv \mathrm{STA}(t) * I(t-\tau)$$

<u>Decision Function</u>

$$P(\mathrm{spike}|s) = \frac{p(s|\mathrm{sp})P(\mathrm{sp})}{p(s)}$$

What does a spike represent?





Filtered stimulus

$$s(t) \equiv \mathrm{STA}(t) * I(t-\tau)$$

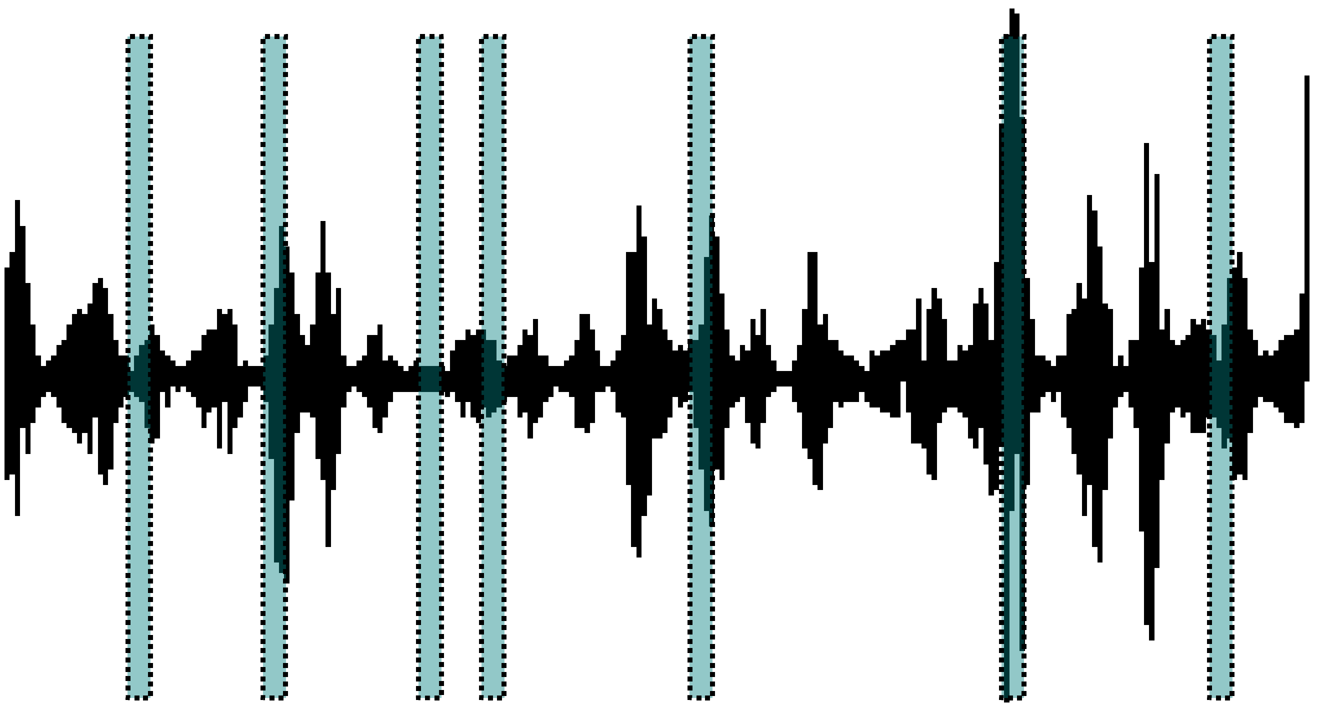
Decision Function

$$P(\mathrm{spike}|s) = \frac{p(s|\mathrm{sp})P(\mathrm{sp})}{p(s)}$$

Adaptive coding

Consider inputs with different standard deviations (different “contrast” relative to the mean)

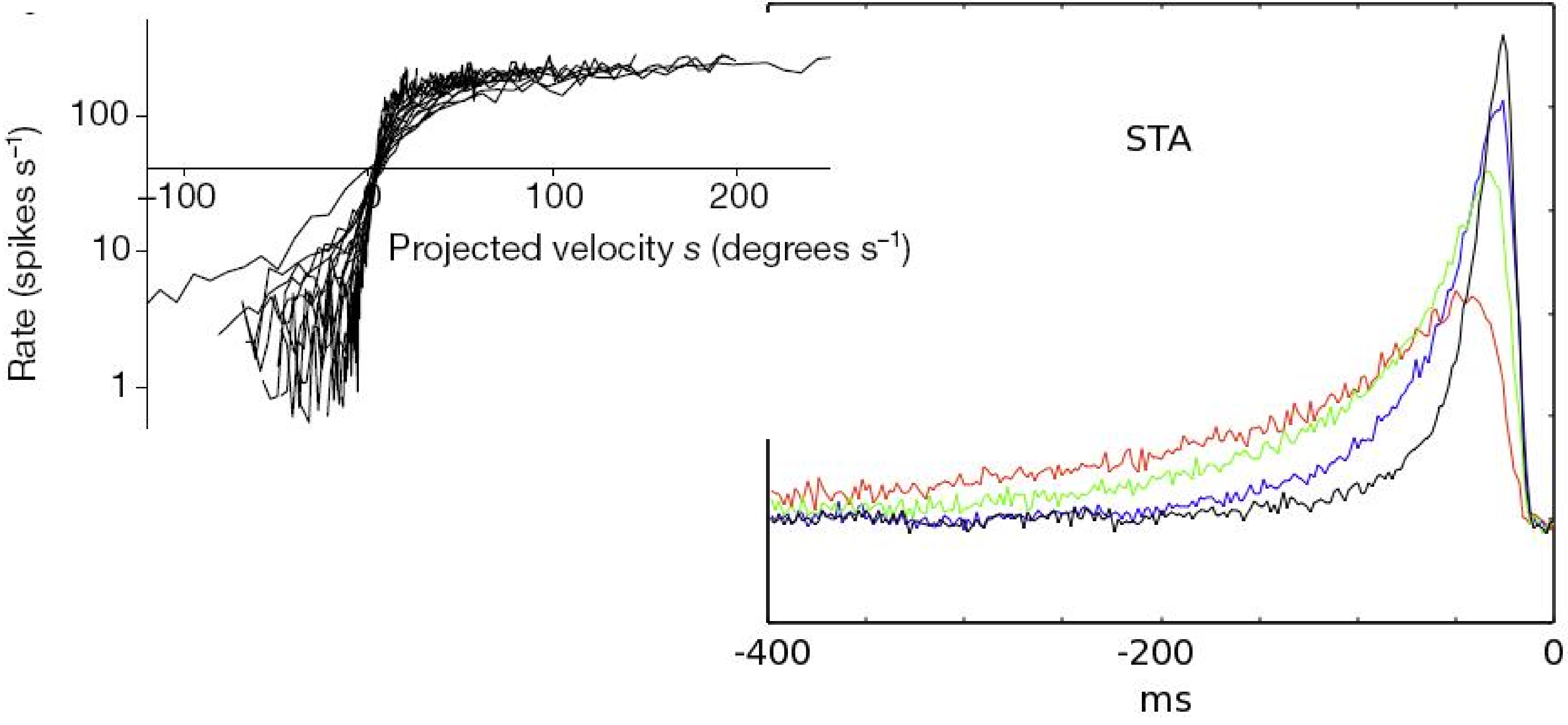
c/o A. Fairhall



How does the code change as stimulus context varies?

Adaptive coding

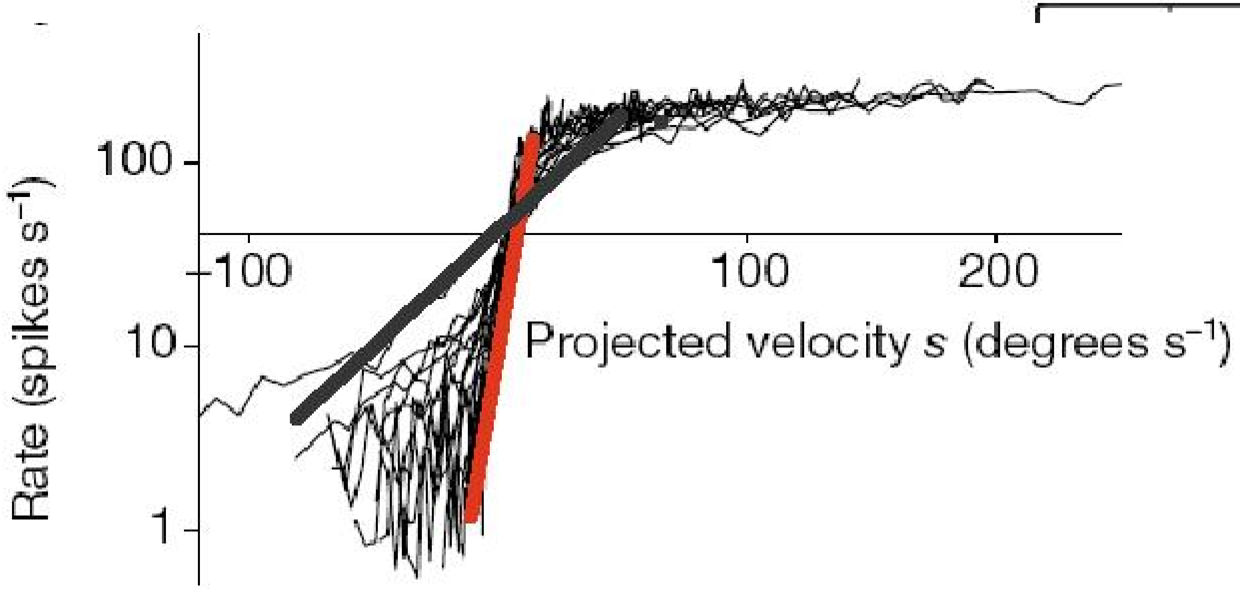
For fly neuron H1, determine the LN models locally in time throughout the stimulus presentation.

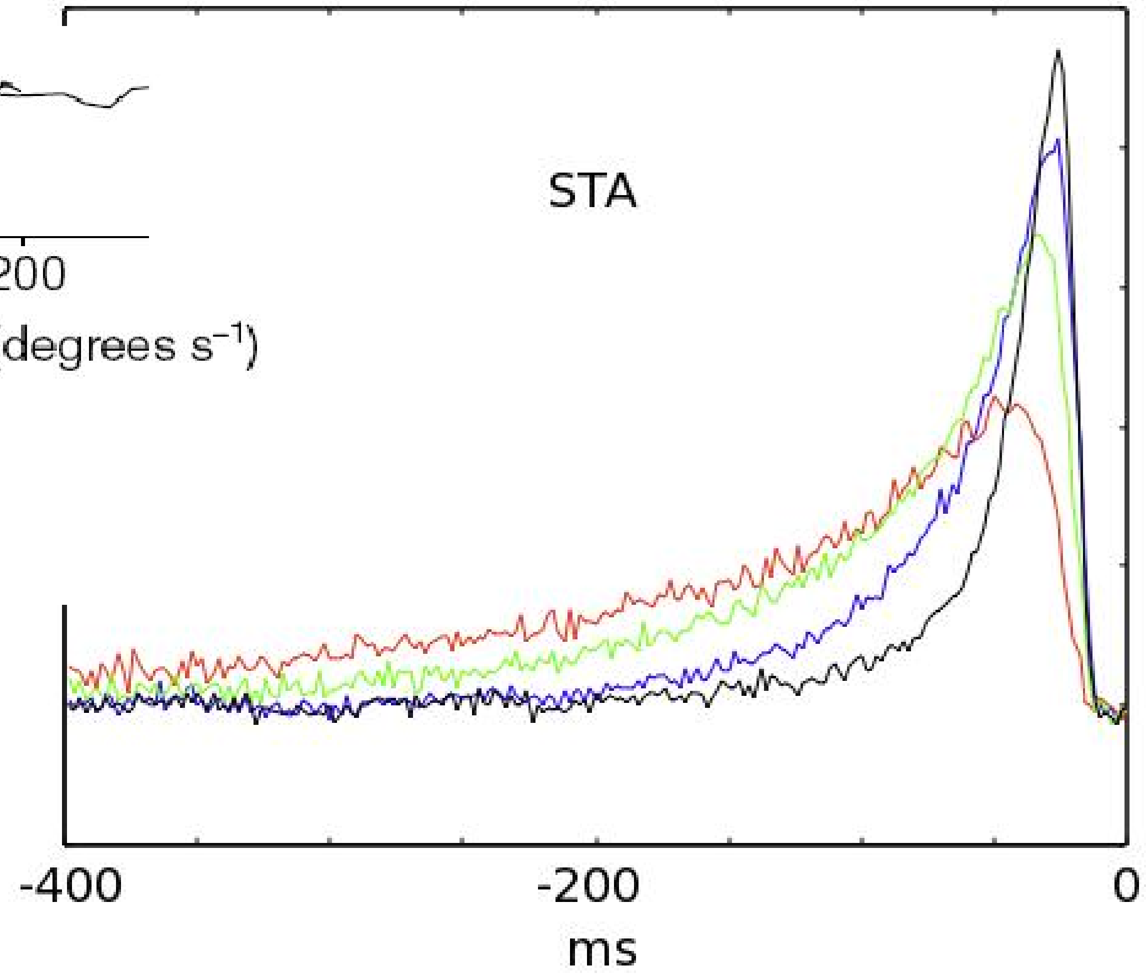


A. Fairhall, G. Lewen, R. R. de Ruyter and W. Bialek (2001)

Adaptive coding

For fly neuron H1, determine the LN models locally in time throughout the stimulus presentation.

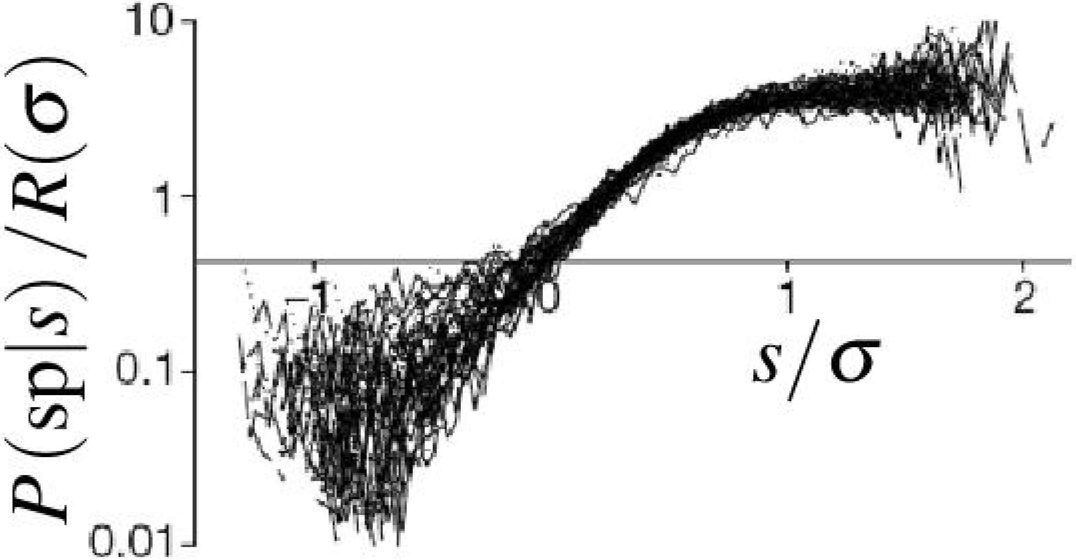


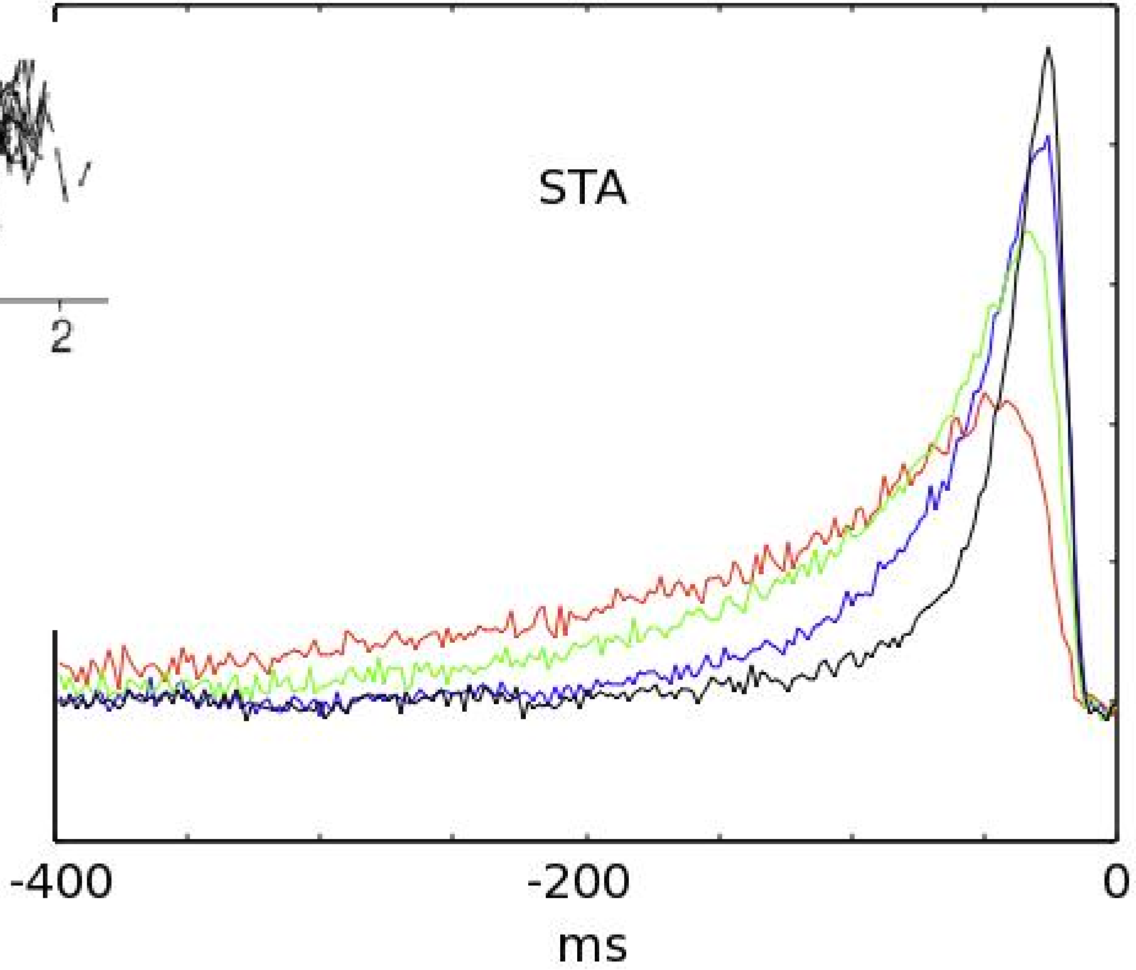


A. Fairhall, G. Lewen, R. R. de Ruyter and W. Bialek (2001)

Adaptive coding

For fly neuron H1, determine the LN models locally in time throughout the stimulus presentation.





Contrast Gain Control

$$P(\mathrm{sp}|s) = R(\sigma)P(\mathrm{sp}|s/\sigma)$$

A. Fairhall, G. Lewen, R. R. de Ruyter and W. Bialek (2001)

Dynamical origins of the code

$$P(\mathrm{sp}|I(t' \leq t)) = \int ds\, P(\mathrm{sp}|s)\, p(s|I(t' \leq t))$$

$$P(\mathrm{sp}|I(t' \leq t)) = \int \mathscr{D}\vec{v}\, \mathscr{D}\vec{w}\, \mathscr{D}\vec{x}\, P(\mathrm{sp}|\vec{v})\, p(\vec{v}|\vec{w},\vec{x},I)\, p(\vec{w},\vec{x}|I(t' \leq t))$$

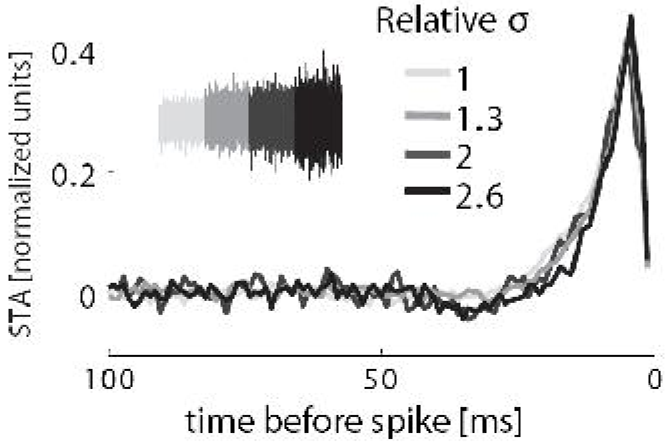
$$\text{family of inputs } \{I_{\mu,\sigma}\} \rightarrow \text{family of codes } \{P(\mathrm{sp}|I_{\mu,\sigma}(t' \leq t))\}$$

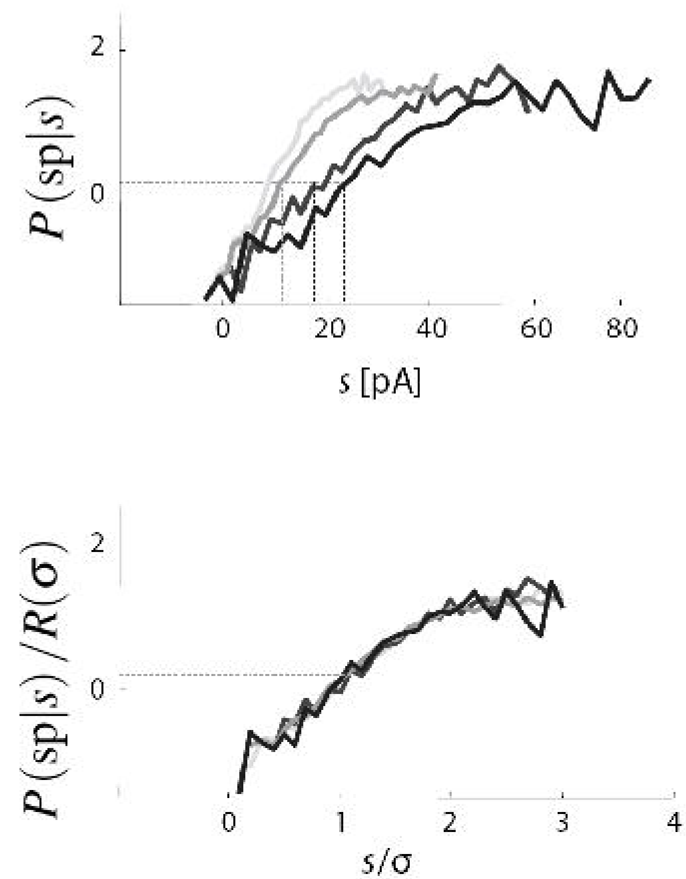
Big question for dynamics and coding:

How do you design the dynamics—the phase space and stimulus-driven flow in that space—to produce desired codes?

Contrast gain control in single neurons

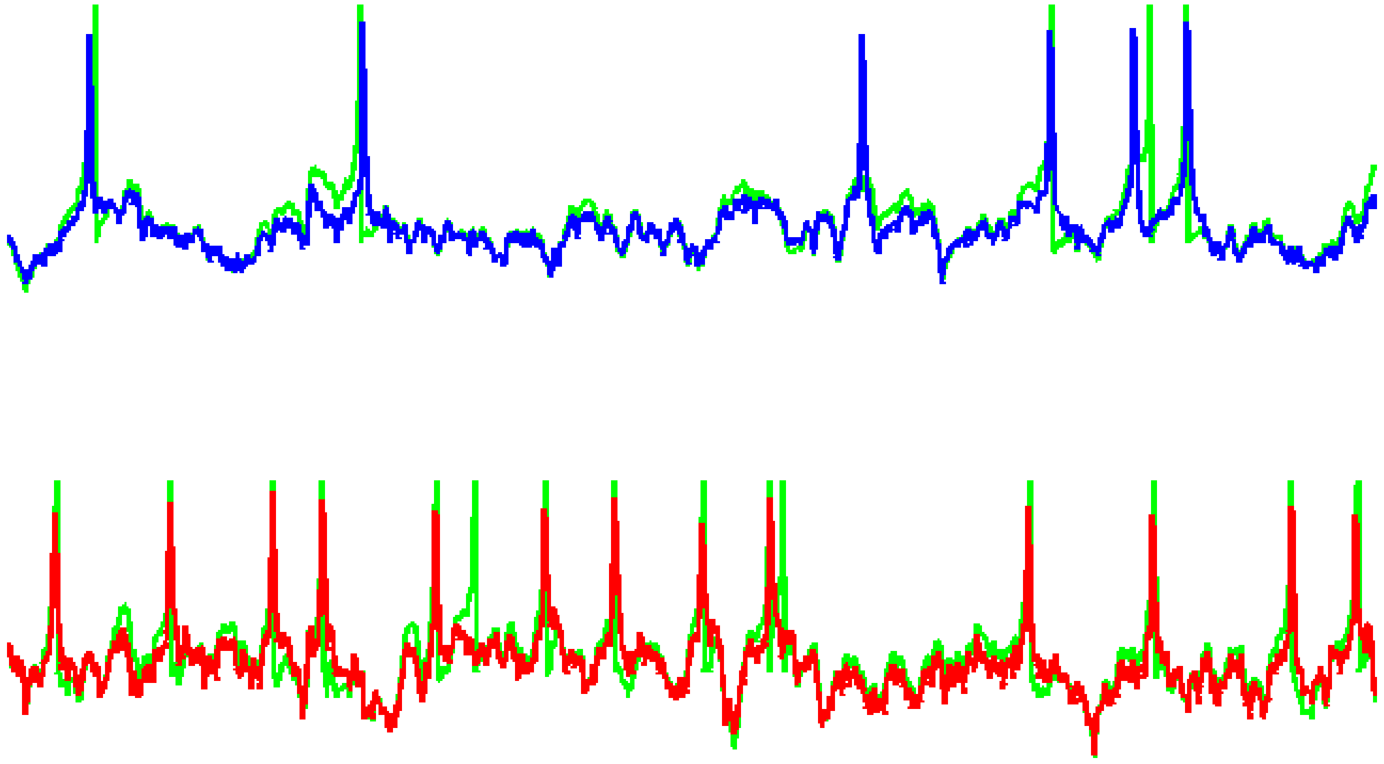
Mouse cortex (Mease, Moody, & Fairhall, submitted)



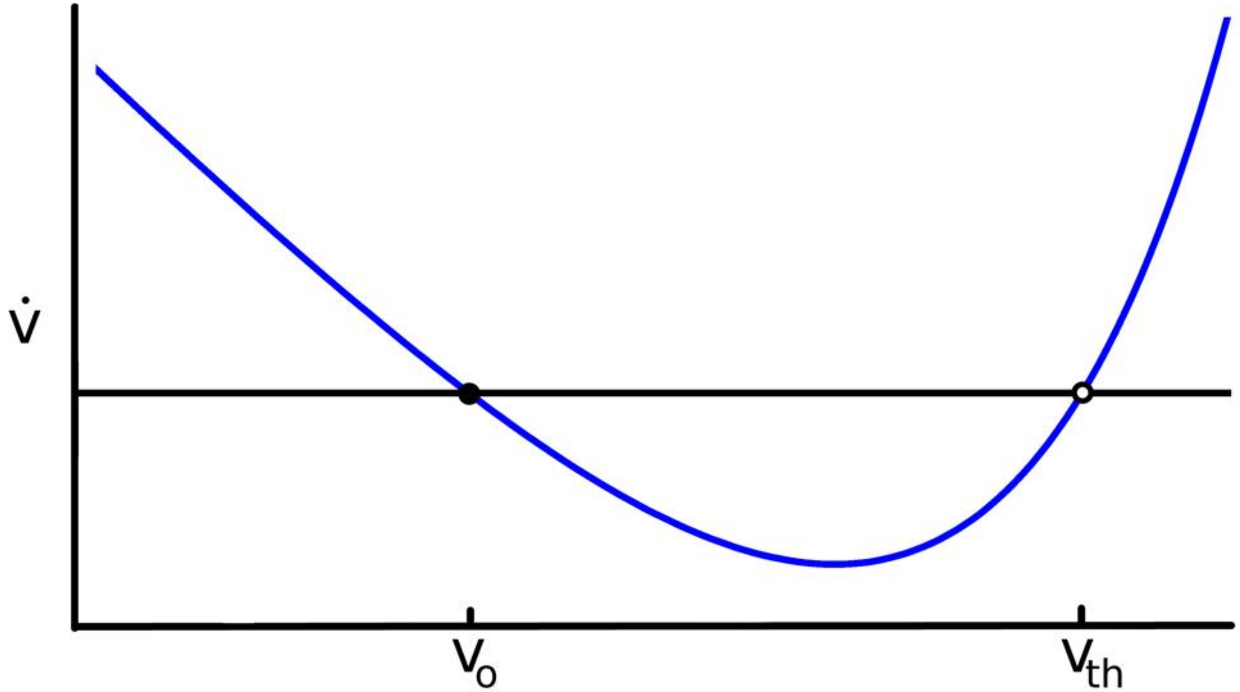


Fast adaptation experiments are fit by an exponential IF model

Optimize fit to steady-state voltage distribution, STA, and coincidence factor



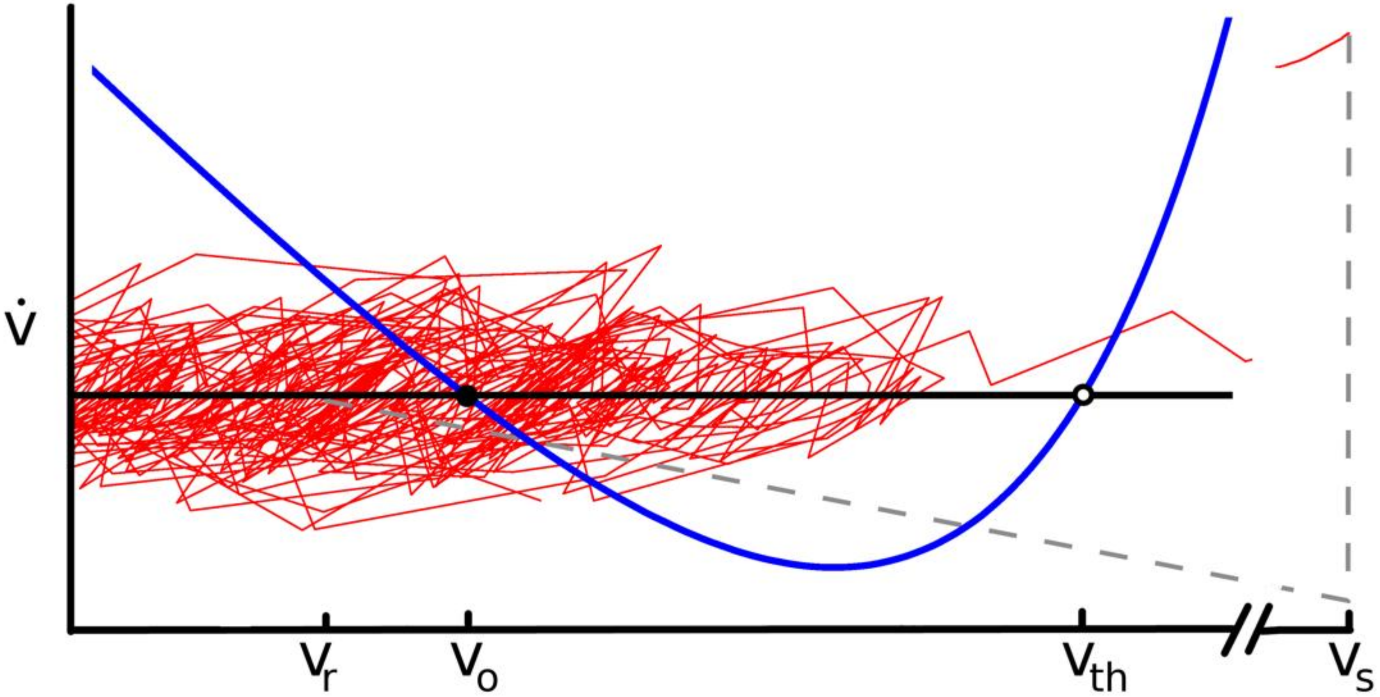
Exponential integrate-&-fire model



$$\tau\dot{v} = -(v - v_o) + f(v) + rI(t) + (v_r - v_s)\delta\,(v - v_s)\,\tau\dot{v}\mathrm{H}(\dot{v})$$

$$f(v) = (v_{th} - v_o)e^{\frac{v - v_{th}}{\Delta}}$$

Exponential integrate-&-fire model



$$\tau\dot{v} = -(v - v_o) + f(v) + rI(t) + (v_r - v_s)\delta(v - v_s)\,\tau\dot{v}\mathrm{H}(\dot{v})$$

$$f(v) = (v_{th} - v_o)e^{\frac{v - v_{th}}{\Delta}}$$

LN model code from the EIF

$$P\left(\mathrm{sp}|I(t' \leq t)\right) = \int \mathscr{D}v\, P(\mathrm{sp}|v)\, p(v|I(t' \leq t))$$

LN Model:

$$P\left(\mathrm{sp}|I(t' \leq t)\right) = \int ds\, P(\mathrm{sp}|s)\, p(s|I(t' \leq t))$$

$$p(s(t)|I(t' \leq t)) = \delta(s - \mathrm{STA} * I)$$

Dynamics in LN model form:

$$P\left(\mathrm{sp}|I(t' \leq t)\right) = \int ds \int \mathscr{D}v\, P(\mathrm{sp}|v)\, p(v|s)\, p(s|I(t' \leq t))$$

LN model code from the EIF

Decision function from dynamics:

$$P(\mathrm{sp}|s) = \int \mathscr{D}v\, P(\mathrm{sp}|v)\, p(v|s)$$

$$P(\mathrm{sp}|s) = \int dv_{(t-h)} \int dv_{(t)} P\left(\mathrm{sp}|v_{(t-h)}, v_{(t)}\right) p\left(v_{(t-h)}, v_{(t)}|s_{(t)}\right)$$

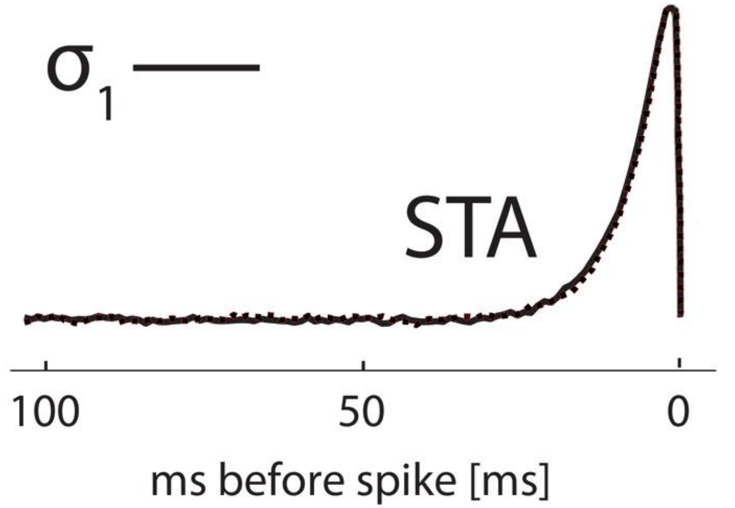
Defining spike times

$$P\left(\mathrm{sp}|v_{(t-h)}, v_{(t)}\right) = \mathrm{H}\left(v_{th} - v_{(t-h)}\right) \mathrm{H}\left(v_{(t)} - v_{th}\right)$$

Voltage estimation problem

$$p\left(v_{(t-h)}, v_{(t)}|s_{(t)}\right) = p\left(v_{(t-h)}|v_{(t)}, s_{(t)}\right) p\left(v_{(t)}|s_{(t)}\right)$$

Modeling the filtered stimulus



For everything we talk about today, the STA is monotonic and approximately exponential

$$s(t) \equiv \mathrm{STA}(t) * I(t-\tau)$$

$$\tau \dot{s} = -ks + I(t)$$

Voltage from filtered stimulus?

fer voltage from filtered stimulus

nge input variable from white noise $I(t)$ to colo

$s(t)$

$$G(v) = f(v) + (v_r - v_s)\delta(v - v_s)\tau\dot{v}\mathrm{H}(\dot{v})$$

$$\tau\dot{v} = -(v - v_o) + G(v) + I(t)$$

$$\tau\dot{s} = -ks + I(t)$$

Voltage from filtered stimulus?

fer voltage from filtered stimulus

nge input variable from white noise $I(t)$ to colo $s(t)$

$$G(v) \;=\; f(v) + (v_r - v_s)\delta(v - v_s)\tau\dot{v}\mathrm{H}(\dot{v})$$

$$\tau(\dot{v} - \dot{s}) = -(v - s) + v_o + (k-1)s + G(v)$$

$$v(t) \approx v_o + s(t) + \int_0^t \frac{dt'}{\tau} e^{\frac{t'-t}{\tau}} (k-1)s(t')$$
$$+ \int_0^t \frac{dt'}{\tau} e^{\frac{t'-t}{\tau}} G\left(v_o + s(t') + \int \frac{dt''}{\tau} e^{\frac{t''-t'}{\tau}} ((k-1)s(t''))\right)$$

Best linear estimator

$$v(t) = v_o + s(t) + \mathrm{Mess}[s(t' \leq t)]$$

$$v(t) \sim v_o + s(t) - s_o$$

We want to find a statistically optimal linear approximation to the voltage dynamics below threshold

$$p(s) = \sqrt{\frac{k}{\pi\sigma^2}} \exp\left[\frac{-k}{\sigma^2}(s - s_o)^2\right]$$

$$p(v) \propto \exp\left(\frac{-(v - v_o)^2 + 2\int f(v)}{\sigma^2}\right) \int_{max(v,v_r)}^{v_s} dv' \exp\left(\frac{(v' - v_o)^2 - 2\int f(v')}{\sigma^2}\right)$$

Minimizing the KL-divergence

$$D_{KL}(v||s) = \int dv\, p(v) \ln \frac{p(v)}{p(s)}$$

Measures the "distance" between two distributions.

We are only interested in getting below-threshold statistics correct.

$$\tilde{D} = \int_{-\infty}^{v_{th}} dv\, p(v|v \leq v_{th}) \ln \frac{p(v|v \leq_{th})}{p(s)}$$

$$k = \frac{\sigma^2/2}{\mathrm{Var}\left[v|v \leq v_{th}\right]}$$

$$s_o = \mathrm{E}\left[v|v \leq v_{th}\right]$$

Optimal Filter Intuition

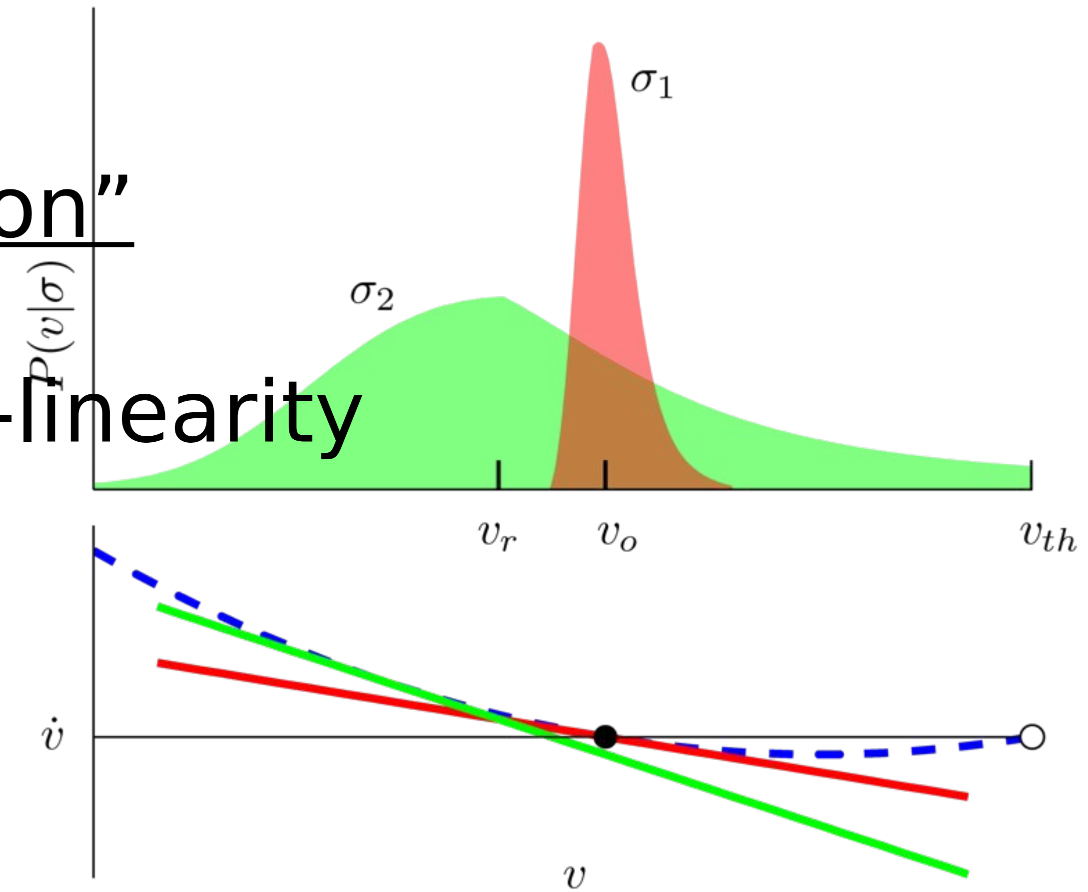
s should be a good linear estimator of the voltage

$$k = \frac{\sigma^2/2}{\mathrm{Var}\left[v | v \leq v_{th}\right]}$$

Two sources of "adaptation"

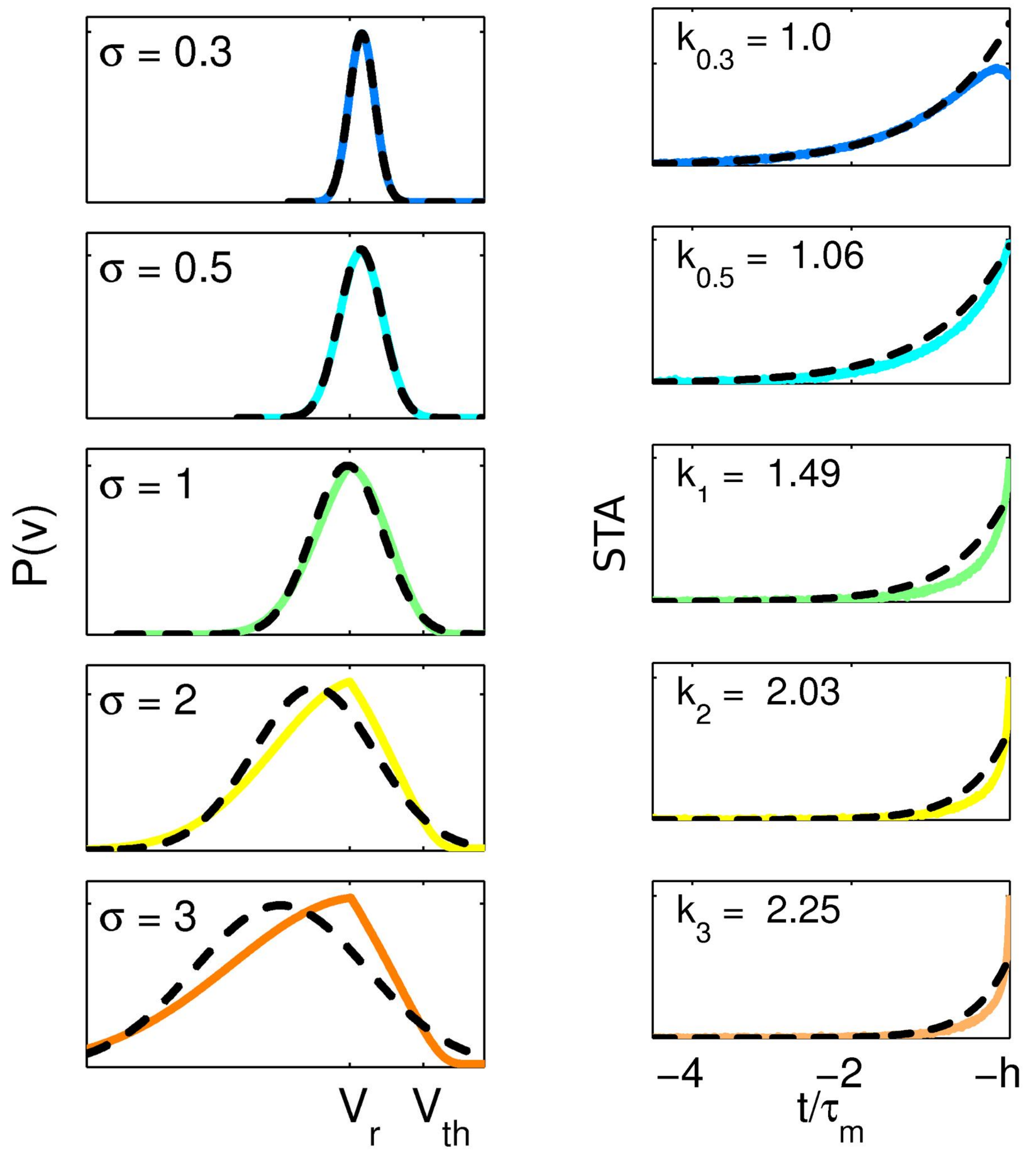
ing of sub-threshold non-linearity
us- & spike-driven

tting" due to spiking



Stochastic Linearization Results

$$k = \frac{\sigma^2/2}{\mathrm{Var}\left[v \middle| v \le v_{th}\right]}$$



Famulare & Fairhall, 2010

Voltage given filtered stimulus

We just saw how the filter time constant *k* is roughly determined by the subthreshold voltage statistics.

Given the filter, to derive the LN coding model, we need to understand $p(v_{(t)}|s_{(t)})$.

We have $v\left[s(t' \leq t)\right]$

We can study $p(v_{(t)}|s_{(t)})$ via its moments.

First Moment

We have: $v\left[s(t' \leq t)\right]$

We want: $\langle v(t)|s(t)\rangle = \langle v[s(t' \leq t)]\rangle_{\{s(t'<t)|s(t)\}}$

s is an OU-process, so everything about its moments are known.

Expand, average, and re-sum

$$\langle v(t)|s(t)\rangle = v_o + \frac{2k}{k+1}s(t) + f(v_o)\left(\frac{\Delta(k+1)}{2ks(t)}\right)\left(e^{\left(\frac{2ks(t)}{\Delta(k+1)}\right)} - 1\right)$$

$$- (v_s - v_r)\int_0^t dt' e^{\frac{t'-t}{\tau}} R(t'|s(t)) \quad + \quad \mathcal{O}(\sigma^2)$$

Deriving contrast gain control

Recall the definition of the decision function:

$$P(\mathrm{sp}|s) = \int \mathscr{D}v\, P(\mathrm{sp}|v)\, p(v|s)$$

By definition, a neuron that exhibits perfect contrast gain control obeys:

$$P\left(\mathrm{sp}|s\right) = R(\sigma) P(\mathrm{sp}|s/\sigma)$$

This implies that all moments of the voltage given the filtered stimulus must be of the form:

$$\langle (v_{th} - v(t))^n | s(t) \rangle = \sigma^n \mu_n(s/\sigma)$$

Intuition for contrast gain control

To the Board!

Constraints for gain control

$$\langle v(t)|s(t)\rangle = v_o + \frac{2k}{k+1}s(t) + f(v_o)\left(\frac{\Delta(k+1)}{2ks(t)}\right)\left(e^{\left(\frac{2ks(t)}{\Delta(k+1)}\right)} - 1\right) - (v_s - v_r)\int_0^t dt' e^{\frac{t'-t}{\tau}} R(t'|s(t)) \quad + \quad \mathscr{O}(\sigma^2)$$

For gain control, the EIF model must be tuned such that:

$$\langle (v_{th} - v(t))|s(t)\rangle = \sigma\mu_1(s/\sigma)$$

Can’t ever be strictly true!
Approximately?

Constraints for gain control

On average, to approximate perfect contrast gain control, the neuron must exhibit

$$
\begin{aligned}
1 &\gg f(v) \text{ below threshold} \\
\bar{R} &= \frac{c\sigma - (v_{th} - v_o)}{\tau(v_s - v_r)}
\end{aligned}
$$

<u>Intuition</u>:

sub-threshold dynamics should minimize distortion of the input distribution

rate feedback tunes typical distance to threshold to scale with standard deviation

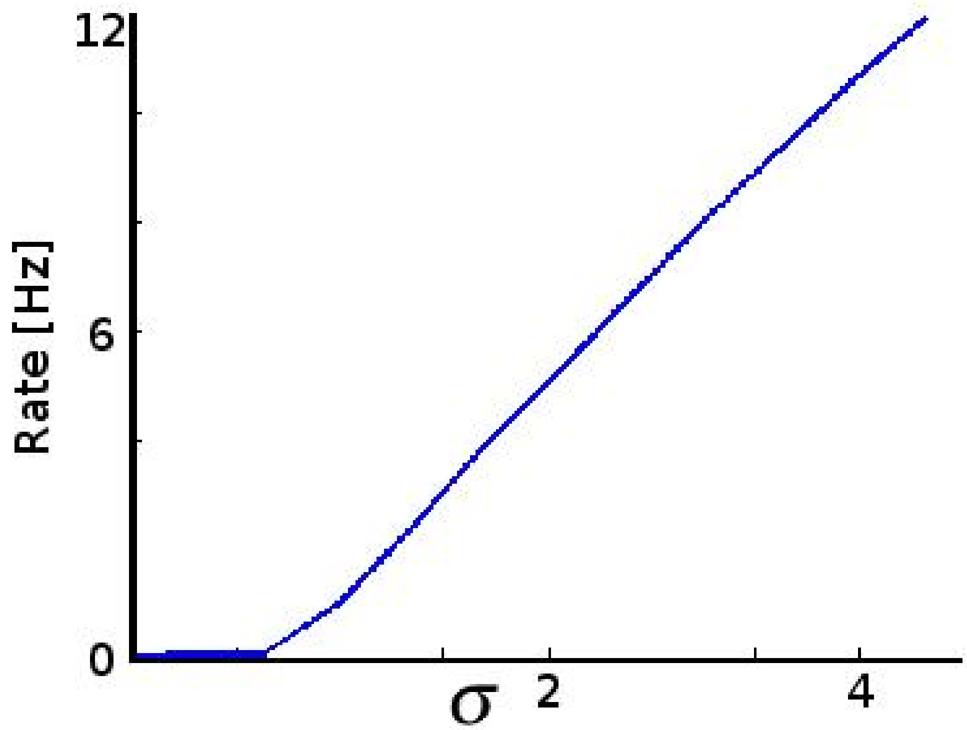
$$v_{th} - \langle V | V \leq v_{th} \rangle \propto \sigma$$

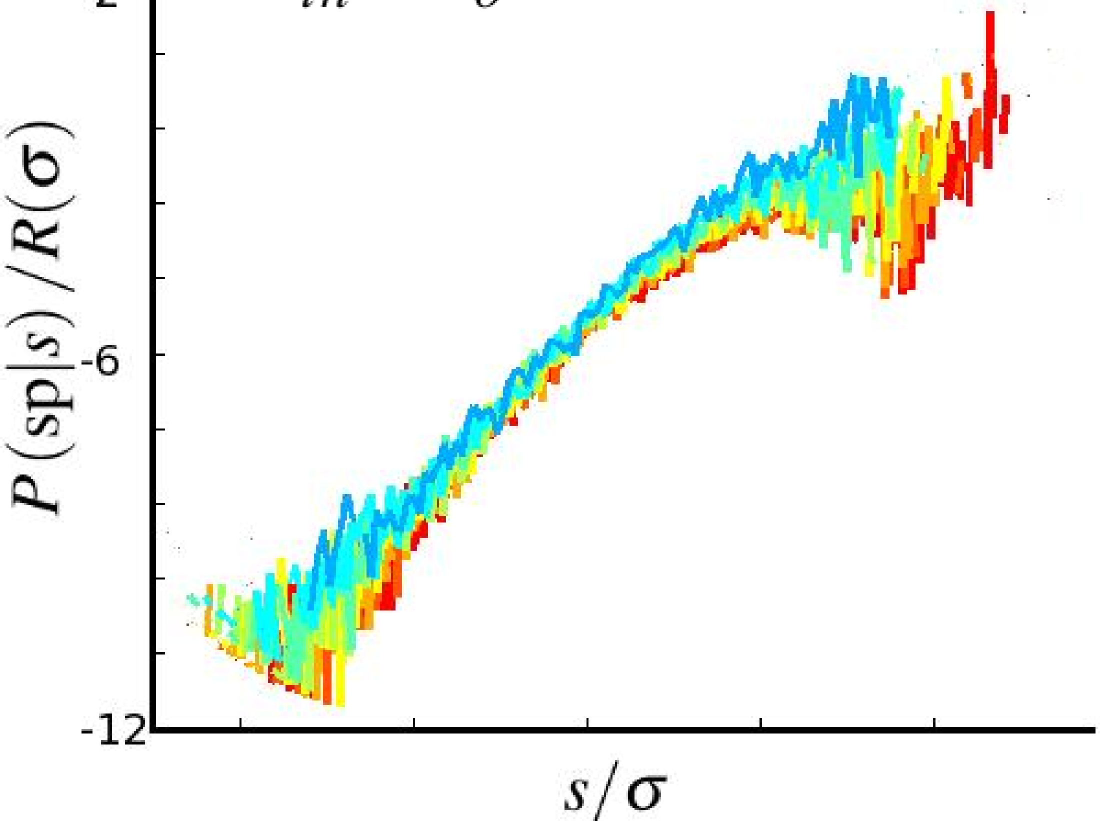
EIF simulation results

EIF has 7 parameters, 5 of which are determined by choosing units.

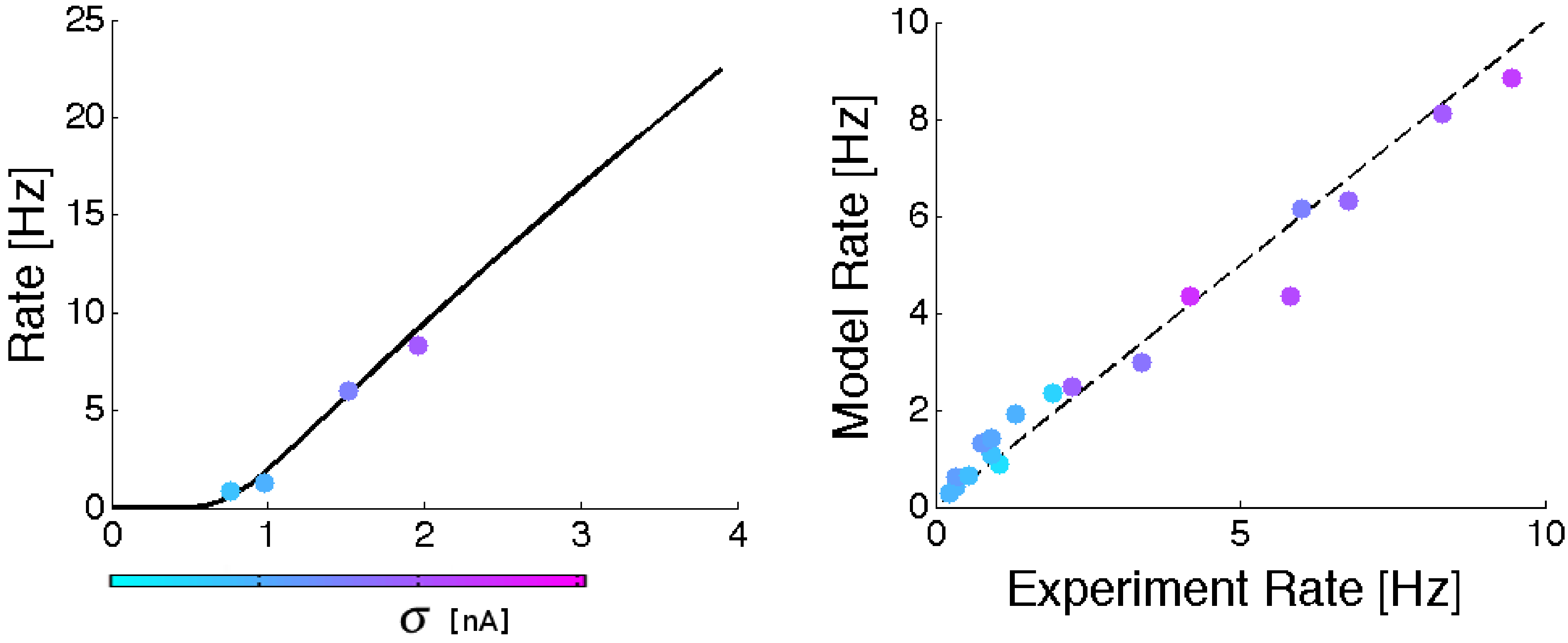
To optimize linearity of firing rate:

$$\frac{v_{th} - v_o}{\Delta} \approx 2.7 \qquad \frac{v_o - v_r}{v_{th} - v_o} \approx 0.2$$

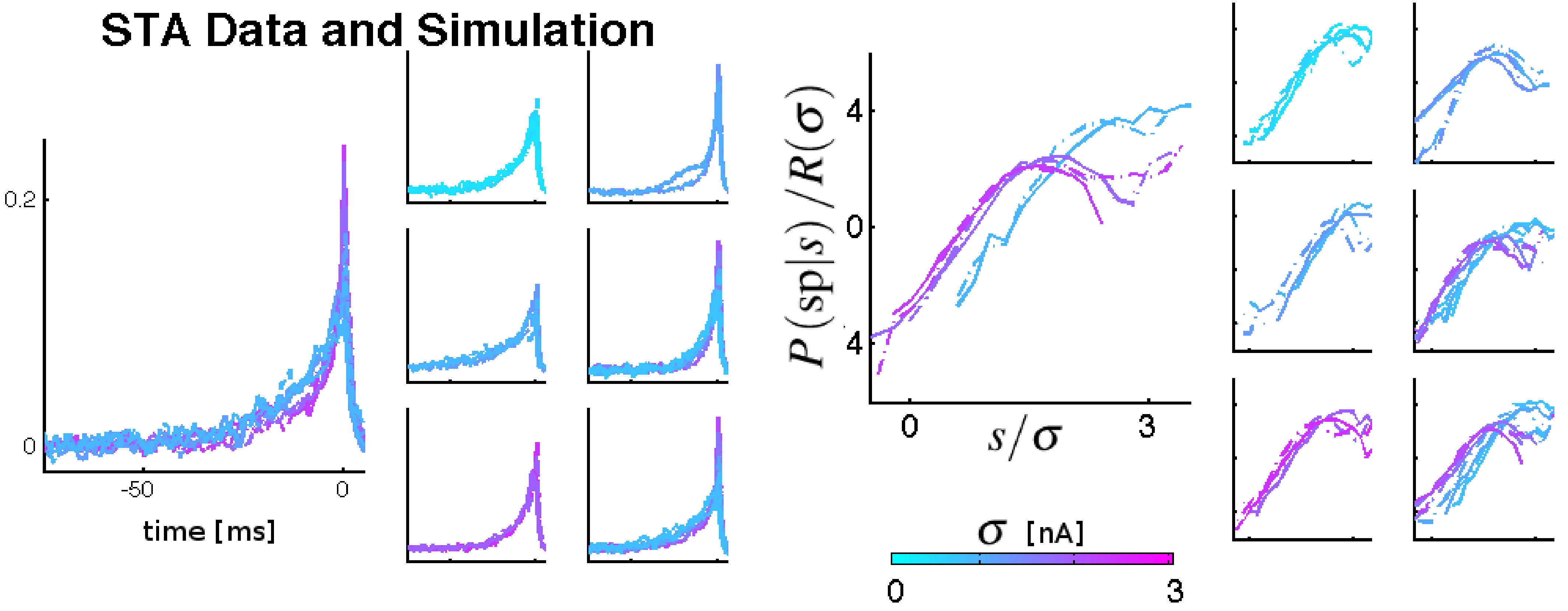




Rate and LN model comparison

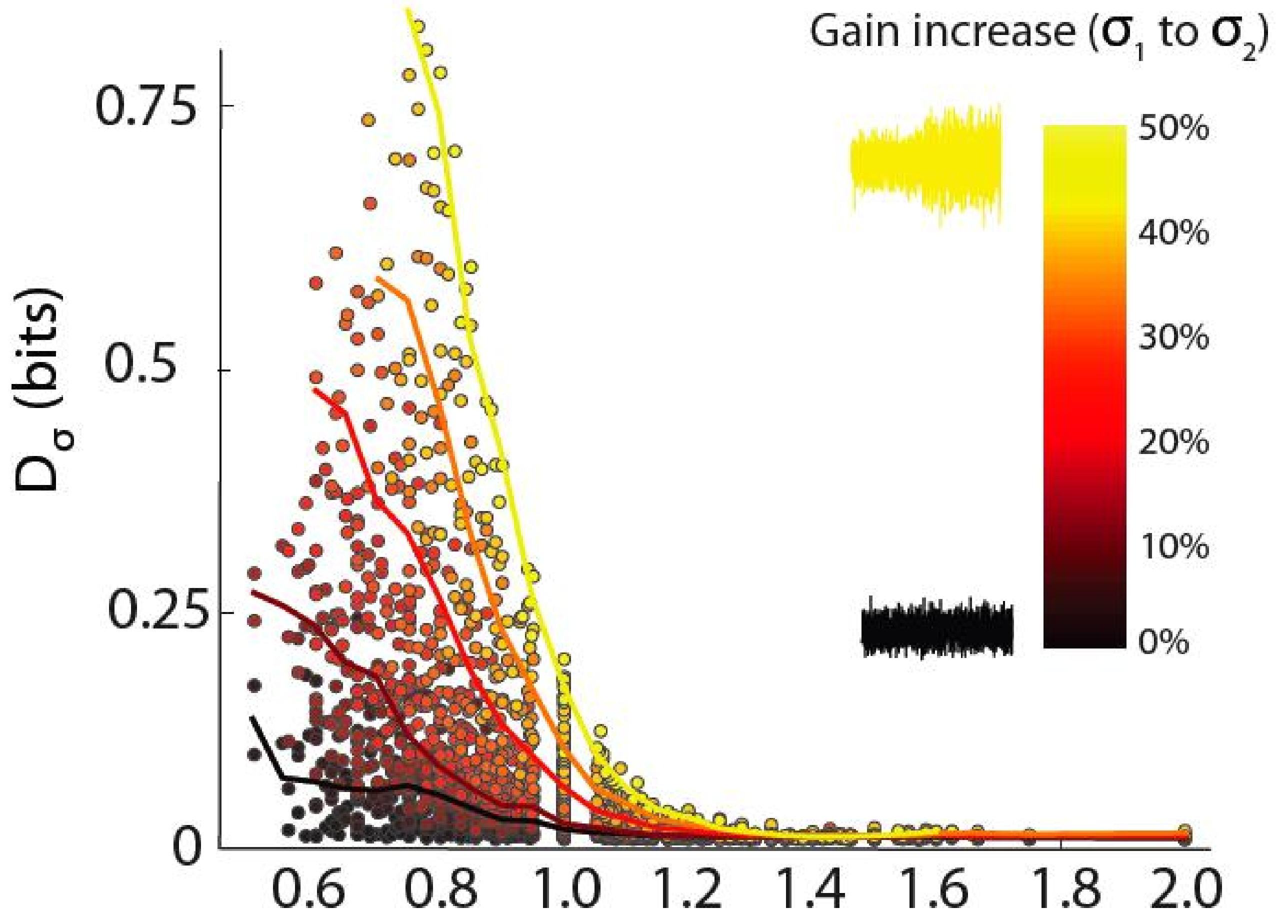


Rate and LN model comparison



Back to biophysics

Experiment and biophysical modeling finds contrast adaptation is modulated by relative amounts of sodium and potassium conc



Mease *et al*

Relating EIF to HH-style models

Minimize presence of active subthreshold channels $1 \gg f(v)$ below threshold

Relating EIF parameters to channel properties

$$\frac{v_{th} - v_o}{\Delta} \approx 2.7 \qquad \frac{v_o - v_r}{v_{th} - v_o} \approx 0.2$$

$$\frac{\bar{g}_{Na}}{\bar{g}_K} \sim \left(\frac{v_{th} - v_o}{v_o - v_r}\right) e^{\frac{v_{th} - v_o}{\Delta}} \left(\frac{v_o - E_k}{E_{Na} - v_o}\right) \left(\frac{\langle n(t)\rangle T_{ref}}{h(v_o)\tau}\right) e^{\frac{v_o - V_{1/2}}{\Delta}}$$

Relating EIF to HH-style models

Minimize presence of active subthreshold channels $1 \gg f(v)$ below threshold

Relating EIF parameters to channel properties

$$\frac{v_{th} - v_o}{\Delta} \approx 2.7 \qquad \frac{v_o - v_r}{v_{th} - v_o} \approx 0.2$$

$$\frac{\bar{g}_{Na}}{\bar{g}_K} \sim 3 \left(\frac{v_o - E_k}{E_{Na} - v_o} \right) \left(\frac{\langle n(t) \rangle T_{ref}}{h(v_o)\tau} \right) e^{\frac{v_o - V_{1/2}}{k_m/3}}$$

$$\frac{\bar{g}_{Na}}{\bar{g}_K} \sim 1$$

Summary

We introduced a general mathematical framework for thinking about how neural codes arise from dynamics

We derive and explain LN model properties for the exponential integrate-&-fire model

Specific neural coding properties strongly constrain dynamics

- perfect contrast adaptation requires only properly-tuned spike-generating currents

Strong predictions in simple models can lead to quantitative biophysical predictions