Models of visual neuron function

Quantitative Biology Course Lecture
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What is the “neural code”? 

Electrical activity: nerve impulses
How does neural activity relate to brain function?

Use visual system:

- Lateral Geniculate Nucleus (LGN)
- Well characterized
- Intuitive function
- Population input to the cortex
Starting point: recordings in the LGN

1. Still relatively simple non-linear transforms on stimulus
2. Population input to the visual cortex

Retina
Lateral Geniculate Nucleus (LGN)
The Visual Cortex
Extracellular recordings (Jose-Manuel Alonso Lab)
Visual stimulus

“Cat-cam” movies from Peter Koenig’s Lab

(Kayser et al, 2004)
LGN neuron responses

500 ms
Understanding and Decoding Neural Signals
Outline

1. Introduction to “receptive fields”

2. Building a visual neuron model
   
   The LN (Linear-Non-linear) model

3. The problem of temporal precision and the need for new statistical methods
   
   Maximum-likelihood modeling

4. Research: Application of maximum-likelihood modeling to explain precise timing of neuronal responses
Coding like the muscle

Muscle picture with motoneuron

Little contraction

Lots of contraction
The receptive field

LGN responses related to how much the stimulus matches the receptive field

Linear comparison:

\[ R = \sum_{\vec{x}} K_{sp}(\vec{x}) \cdot S(\vec{x}) \]
The receptive field

LGN responses related to how much the stimulus matches the receptive field

Linear comparison:

\[ R = \sum_{\vec{x}} K_{sp}(\vec{x}) S(\vec{x}) \]
The receptive field

Spatial features of image matter in relation to RF

Neuron is tuned for a given stimulus over a certain range.
Circuitry of the retina

pigment epithelium
rods
cones
outer limiting membrane
Müller cells
horizontal cells
bipolar cells
amacrine cells
ganglion cells
nerve fiber layer
inner limiting membrane
...but vision involves motion

Motion in the visual scene/self motion

Eye movements
- saccades, microsac.
- ocular drift
LGN response during movie

Raster plot

PSTH: peri-stimulus time histogram
What does neural activity look like during a time-varying stimulus?
Visual neuron function: the spatiotemporal receptive field

What stimuli are represented by a neuron's response?

Spike-Triggered Average (STA) stimulus: “receptive field”
Visual neuron function: the spatiotemporal receptive field

What stimuli are represented by a neuron's response?

Spike-Triggered Average (STA) stimulus: “receptive field”
Implicit Problems with Modeling

> Too many parameters
The “temporal receptive field”

Spatiotemporal Stimuli

Full-field stimuli
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The “temporal receptive field”

Full-field stimuli
How measure the receptive field?
The spike-triggered average

Stimulus-response cross-correlation

$$k(\tau) \propto \int dt \ r(t) \ s(t - \tau)$$
Linear model predictions

Temporal Stimulus (full-field) $\times$

Temporal Receptive Field $=$

Filtered stimulus

$r_{est}(t) = r_0 + \int d\tau \ k(\tau) \ s(t - \tau)$
Mathematical result
(take functional derivative of MSE)

Layman’s summary:
In the presence of Gaussian noise (uncorrelated) stimuli, the best linear model for the neuron is proportional to the spike triggered average.

\[ r_{est}(t) = r_0 + \int d\tau \ k(\tau) \ s(t - \tau) \]

Mean Squared Error (MSE)
\[ \text{MSE} = \sum_t [r(t) - r_{est}(t)]^2 \]

Stimulus-response cross-correlation
\[ k(\tau) \propto \int dt \ r(t) \ s(t - \tau) \]
Temporal Stimulus (full-field)

\[ x \]

Temporal Receptive Field

= Filtered stimulus

Linear model predictions

Firing Rate

Observed firing rate
How map linear function to firing rate?

“LN” (Linear-Non-Linear) model of encoding

\[ \text{Observed firing rate} \]

\[ \lambda(t) = \nu(g) \circ K(\tau) \circ s(t) \]

Firing Rate

0 100 150 200 250 ms

Hz

0 500

Stimulus \( s(t) \)
Linear Kernel \( K(\tau) \)
Non-linearity \( \nu(g) \)
Firing Rate \( \lambda(t) \)

Observed firing rate
Measuring reliability of RF “model”: the non-linearity
Measuring reliability of RF “model”: the non-linearity

LN Model of Encoding

\[ \text{Pr}\{\text{spike}|g\} \]

Firing Rate (Hz)

Generating Function \( g \)
Bussgang’s Theorem

Layman’s summary:
In the context of simple non-linearities, the “optimal” receptive field is STIL given by the spike-triggered average in the context of Gaussian white noise ***
Receptive field predictions

Temporal Stimulus (full-field)

\[ \times \]

Temporal Receptive Field = Filtered stimulus

\[ x \]

Firing Rate

LN Model

Observed firing rate
How quantify quality of model fit?

Matlab Interlude
Problems with visual neuron modeling

1. Looking at higher time resolution reveals that the LN model is insufficient

2. Non-linearities “force” the use of Bussgang’s theorem -> only use STA, and need noise stimuli

3. r2 is not the best measure for evaluating a non-linear system

(also, it requires multiple repeats to estimate a good firing rate)
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Maximum Likelihood Approach

Stimulus

Linear Kernel

Non-linearity

Poisson process

Response (Spike Train)

Likelihood: probability that model explains data

Find the “maximum likelihood”:

The probability that the spikes were generated by a model with a certain choice of parameters

\[ LL = \sum_{t_{spk}} \log Pr\{spk|t_{spk}\} - \sum_{t} Pr\{spk|t\} \]

Firing rate when there is an observed spike

Firing rate when there is no observed spike
Problem: complicated function to maximize!

The maximum likelihood:

\[
LL = \sum_{t_{spk}} \log Pr\{spk|t_{spk}\} - \sum_t Pr\{spk|t\}
\]

Paninski (2004):

No local minima in likelihood surface given certain forms of non-linearity (f)

Matlab can solve for optimal parameters in very little time!

[e.g., 2 minutes of data, 0.5 ms resolution ~ 20 seconds]
LN model is fit “optimally” using maximum likelihood

Quick Matlab Interlude
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Receptive field predictions

Temporal Stimulus (full-field)

\[ \text{Temporal Receptive Field} = \text{Filtered stimulus} \]

Neuron’s Firing Rate

“LN Model”

Actual
Receptive field predictions

Neuron's Response

Spike Rasters

"Function-based" Prediction

Neuron's Firing Rate

“LN Model”

Actual

0 Hz

500 Hz

Firing Rate

0 Hz

500 Hz

Actual
Neuron is “tuned” to the stimulus

Need to “suppress” neuron’s response during periods of stimulus that matches RF

Refractoriness and Neural Precision

e.g., Berry and Meister, 1998
Brillinger, 1992
Keat et al., 2001
Paninski, 2004
Pillow et al., 2005
...
Generalized Linear Model (GLM)

Stimulus

Linear Kernel

Non-linearity

Poisson process

Response (Spike Train)

Paninski (2004):
Optimal solution for model parameters (no matter how many parameters!)

But, spike history term does not explain the temporal resolution of the data.
GLM model does not explain LGN temporal precision

**Data** (60 reps x-validated)

- **LN**
- **GLM**

**Despite matching ISI distributions**

![Graphical representation of data and model comparisons](image)
What about “network” suppression?

Refractoriness and precision model

Network suppression model

“Tuned” Stimulus

LGN neuron spikes

Suppression after spikes

Others neurons in network active
What about “network” suppression?

Refractoriness and precision model

Network suppression model
Directly fit *multiple* receptive fields

Stimulus

RF

1

Spike generation

RF

2

(Rectified)

Suppression

-- Alternative to spike-triggered covariance

-- Simplest way to incorporate two RFs

Response

(Spike Train)

-- Application to neurons that process stimuli non-linearly (e.g., on-off cells in mouse retina)
“Precision” explained by suppression

Data (60 reps x-validated)

LN
GLM
Suppression
2 minutes of FF stimulation

30 sec unique sequence repeated 60 times

Significant improvement across all recorded neurons
Precision computation

Linear Filter
Suppressive filter **

Stimulus

RF

Spike generation

(Rectified)
Suppression

Suppression

Linear Filter

firing rate

- sup

linear

0 20 40 60 80 100 120 140 160
-100 -80 -60 -40 -20 0
General role of local inhibition?

- **Retina**
  - Exc: bipolar cell
  - Inh: spiking amacrine
  - Local inhibitory interneuron

- **LGN**
  - Exc: RGC input
  - Inh: interneurons

- **V1**
  - Exc: LGN input
  - Inh: interneurons

Long-range excitatory projection
Circuitry of the retina

ROLE IN SPATIAL PROCESSING

ROLE IN TEMPORAL PROCESSING
1. Visual neuron modeling
   - Don’t forget the LN model -- it is everywhere
   - Basis for sensory models in neuroscience (“minimal model”)

2. Neuroscience has been (but no longer is?) stuck with standard statistics
   - Brought field to where it is (VERY USEFUL) but ... could not go much further
   - Neuroscience-statisticians are having large impact on basic science
     (Emory Brown, Liam Paninski, Rob Kass, Valerie Ventura, Han Amarsingham, ... )

3. Maximum likelihood modeling
   - System of models that have smooth likelihood surface
   - Ability to solve higher-order models with limited data