Neural Encoding

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From stimulus to behaviour

Sensory input → Brain → Motor output
The brain as a computer

- Information processing to extract features and generate outputs
- Statistical inference
- Physical implementation irrelevant, possible to replicate *in silico*?
The neural code

- **Encoding**: Prediction of neural response to a given stimulus: $P(R|S)$
- **Decoding**:
  - Given response, what was the stimulus: $P(S|R)$
  - Prosthetics: given firing pattern, what will be the motor output: $P(M|R)$
Understanding the *neural code* is like building a dictionary.

- Translate from outside world (sensory stimulus or motor action) to internal neural representation
- Translate from neural representation to outside world
- Like in real dictionaries, there are both one-to-many and many-to-one entries in the dictionary
Encoding: Stimulus-response relation

Predict response \( R \) to stimulus \( S \). Black box approach. This is a supervised learning problem, but:

- Stimulus \( S \) can be synaptic input or sensory stimulus.
- Responses are noisy and unreliable: Use probabilities.
- Typically many input (and sometimes output) dimensions
- Responses are non-linear
  - Assume non-linearity is weak. Make series expansion?
  - Or, impose a parametric non-linear model with few parameters
- Need to assume causality and stationarity (system remains the same). This excludes adaptation!

\[ r(\alpha s_1 + \beta s_2) = \alpha r(s_1) + \beta r(s_2) \text{ for all } \alpha, \beta. \]

\(^1\)Linear means: \( r(\alpha s_1 + \beta s_2) = \alpha r(s_1) + \beta r(s_2) \) for all \( \alpha, \beta \).
Response: Spikes and rates

Response consists of spikes. Spikes are (largely) stochastic. Compute rates by trial-to-trial average and hope that system is stationary and noise is really noise.

Often, we try to predict $R$, rather than predict the spikes.
Paradigm: Early Visual Pathways

[Figure: Dayan and Abbott, 2001, after Nicholls et al, 1992]
Retinal/LGN cell response types

On-centre off-surround

Off-centre on-surround
Mach bands
V1 cell response types (Hubel & Wiesel)

Odd
- Simple cells, modelled by Gabor functions
- Also complex cells, and spatio-temporal receptive fields
- Higher areas
- Other pathways (e.g. auditory)

Even
Not all cells are so simple...

Intermediate sensory areas (eg. IT) have face selective neurons. In the limbic system, neurons appear even more specialised [Quiroga et al., 2005].
In higher areas the receptive field (RF) is not purely sensory. Example: pre-frontal cells that are task dependent [Wallis et al., 2001]
To study neural encoding, we need a model. There is an inevitable trade-off between realism and complexity.

Simple models: normative theories
Detailed models: how implemented in the brain
From stimulus to response

What is the correct \( P(R|S, \theta) \), where \( \theta \) is a model parameter?
Strategy: Maximise the likelihood \( P(R|S, \theta) \)
We assume a Poisson model. For N trials, we write the likelihood

\[ P(R|S, \theta) = \prod_{i=1}^{N} P(r_i|s_i, \theta) = \prod_{i=1}^{N} \frac{1}{r_i!} (\theta s_i)^{r_i} e^{-\theta s_i} \]
Model likelihood

\[
P(R|S, \theta) = \prod_{i=1}^{N} P(r_i|s_i, \theta)
\]

\[
= \prod_{i=1}^{N} \frac{1}{r_i!} (\theta s_i)^{r_i} e^{-\theta s_i}
\]

has a maximum close to 2.
In practice, we use the logarithm

$$
\log P(R|S, \theta) = \log \prod_{i=1}^{N} P(r_i|s_i, \theta)
$$

$$
= \sum_{i}^{N} r_i \log \theta - \theta s_i + C
$$

Terms in $C$ does not depend on $\theta$, so can be ignored.
To find the maximum, differentiate:

\[
\frac{\partial}{\partial \theta} \log P(R|S, \theta)
\]
Find the maximum:

\[
\log P(R|S, \theta) = \sum_{i} r_i \log \theta - \theta s_i + C
\]

\[
\frac{\partial \log P(R|S, \theta)}{\partial \theta} = \sum_{i} \frac{r_i}{\theta} - \sum_{i} s_i
\]
Find the maximum:

\[
\frac{\partial \log P(R|S, \theta)}{\partial \theta} = \sum_i \frac{r_i}{\theta} - \sum_i s_i
\]

\[
\hat{\theta} = \frac{\sum r_i}{\sum s_i}
\]

In this example I obtain \(\hat{\theta} = 1.92\), close to the true value \(\theta = 2\).
The predicted rate can be $<0$.

In biology, unlike physics, there is no obvious small parameter that justifies neglecting higher orders. Rectification requires infinite orders, for instance. Check the accuracy of the approximation post hoc.

Averaging and ergodicity

$\langle r \rangle$ formally means an average over many realizations over the random variables of the system (both stimuli and internal state). This definition is good to remember when conceptual problems occur.

An ergodic system visits all realizations if one waits long enough. That means one can measure from a system long enough, true averages can be obtained.

This however requires stationarity, internal states are not allowed to change.
A more realistic response

Response \( r \) (spikes/s) vs. Stimulus \( s \)
A more realistic response

This requires a non-linear transformation $r(s) \sim \text{Poisson}(f(\theta s))$. 
Neural responses depend on the stimulus history

Introducing a linear temporal kernel $k(t)$ with

$$r(t) = \text{Poisson}(f(\int dt' s(t')k(t - t'))).$$
$r(t) = \text{Poisson}(f(\int dt's(t')k(t-t')))$

- Linear: spatial and temporal filter kernel $k$
- Non-linear function giving output spike probability: rectification, saturation
- Poisson spikes $p_{\text{spike}}(t) = \lambda(t)$ (noisy)
Fitting a linear model

\[ r(t) = \text{Gaussian}(\int dt' s(t')k(t - t')) \]

This has closed form MLE: \( \hat{k} = (S^T S)^{-1} S^T R \)

Data comes from model with exponential nonlinearity. The model recovers the kernel well, but cannot predict the rates.
Spike triggered average (STA)

Spike times \( t_i \), \( r(t) = \sum \delta(t - t_i) \)

\[ g_1(\tau) = \frac{1}{\sigma^2} \langle r(t) s(t - \tau) \rangle = \frac{1}{\sigma^2} \sum t_i s(t_i - \tau) \]
Linear models for spiking neurons

Application on H1 neuron [Rieke et al., 1996]. Prediction (solid), and actual firing rate (dashed). Prediction captures the slow modulations, but not faster structure. This is often the case.
Poisson GLM log-likelihood has no closed form MLE:

$$\log P(R|S, \theta) = \sum_i r_i \log f(k \ast s_i) - \sum_i f(k \ast s_i)$$

Use numerical minimisation of the neg. log-likelihood (scipy.optimize.fmin or fminsearch in Matlab) This recovers the kernel and rates correctly.
Fitting non-linear models

Poisson GLM log-likelihood:

$$\log P(R|S, \theta) = \sum_{i} r_i \log f(k \ast s_i) - \sum_{i} f(k \ast s_i)$$

Bernoulli GLM log-likelihood:

$$\log P(R|S, \theta) = \sum_{i} r_i \log f(k \ast s_i) + \sum_{i} (1 - r_i) \log(1 - f(k \ast s_i))$$

For \( f(x) = 1/(1 + \exp(-x)) \), this is logistic regression.

When \( f \) is convex (log(f) is concave) in parameters, e.g. \( f(x) = [x]_+ \), or \( f(x) = \exp(x) \), then log \( \mathcal{L} \) is concave, hence a global maximum exists.
Figure: Over-fitting: Left: The stars are the data points. Although the dashed line might fit the data better, it is over-fitted. It is likely to perform worse on new data. Instead the solid line appears a more reasonable model. Right: When you over-fit, the error on the training data decreases, but the error on new data increases. Ideally both errors are minimal.
Fits with many parameters/short data typically require regularization to prevent over-fitting.

Regularization: punish fluctuations (smooth prior, ridge regression)

\[ \hat{k} = (S^T S + \lambda I)^{-1} S^T r \]

Regulariser \( \lambda \) has to be set by hand.
Poisson GLM results

[Chichilnisky, 2001]
Colors are the kernels for the different RGB channels
Kernel can also be in spatio-temporal domain.

This V1 kernel does not respond to static stimulus, but will respond to a moving grating ([Dayan and Abbott, 2002]§2.4 for more motion detectors)
Integrate and fire model

Parameters are the $k$ and $h$ kernels

- $h$ can include reset and refractoriness

For standard I&F: $h(t) = \frac{1}{R} (V_T - V_{reset}) \delta(t)$
Figure 2. Parameters obtained from fits to RGC data for the IF model (a–c) and the LNP model (d, e). a, Filters $\tilde{k}$ and spike–response currents $\tilde{h}$ obtained for five ON cells in one retina. b, Corresponding filters for four OFF cells. c, Histograms of model scalar parameters and for all 24 cells in three retinas. d, Comparison of linear filters for the IF model (gray) and LNP model (black) for one ON cell (top) and one OFF cell (bottom). e, Measured LNP point nonlinearities for converting filter output to instantaneous spike rate.

[Pillow et al., 2005] Fig 2
Figure 3: Responses of an ON cell to a repeated stimulus. a. Recorded responses to repeated stimulus (top), simulated LNP.

- RGC
- LNP
- IF

b. Rate (sp/s)

C. Variance (sp²/bin)
Poisson GLM with spike feedback

[Weber and Pillow, 2017]
Spike feedback allows modelling neuron types

[Weber and Pillow, 2017]
Even more complicated models

A retina + ganglion cell model with multiple adaptation stages [van Hateren et al., 2002]

But how to fit the parameters?
Generalization to networks.

- Unlikely to have data from all neurons
- Predict of cross-neuron spike patterns and correlations
- Correlations are important for decoding (coming lectures)
- Estimate 'functional coupling', $O(N \times N)$ parameters
- Uses small set of basis functions for kernels

[Image: Coupled spiking model diagram]

[Pillow et al., 2008]
Network models

Note uncoupled case still correlations due to RF overlap, but less sharp. [Pillow et al., 2008]
Unclear however if the IF model would perform better here than the Poisson GLM.
Summary

Predicting neural responses
In order of decreasing generality

- Linear models: simple, exact inference, but miss essential aspects of neural physiology
  - Note higher orders may be captured by Wiener kernels, see Dayan & Abbott, chapter 2. Require more data to fit.

- Poisson GLM model: fewer parameters, spiking output, but lacks precise spike timing

- More neurally inspired models (I&F, GLM with spike feedback): good spike timing, but hard to fit, require careful regularization

- Biophysical models: in principle very precise, but in practice unwieldy
A simple white noise analysis of neuronal light responses.

*Theoretical Neuroscience*.
MIT press, Cambridge, MA.

Prediction and Decoding of Retinal Ganglion Cell Responses with a Probabilistic Spiking Model.

Spatio-temporal correlations and visual signalling in a complete neuronal population.

Invariant visual representation by single neurons in the human brain.

*Spikes: Exploring the neural code*.

Processing of Natural Temporal Stimuli by Macaque Retinal Ganglion Cells.
Single neurons in prefrontal cortex encode abstract rules. 

Capturing the dynamical repertoire of single neurons with generalized linear models. 