Outline of Stimulus Identification Project

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1 Introduction

Neuroscientists have developed an extensive theory of how simple phenomena (e.g. wind direction, arm reaching angle) are encoded by single neurons, and presumably decoded by higher cognitive functions. However, much remains to be understood about how complex phenomena (e.g. visual stimuli) are encoded or decoded.

In particular, how much information about the stimulus is captured by the various subsystems of the brain, or discarded? Taking vision as an example, we know that information from the retina is passed up successive layers of visual subsystems (V1, V2, ...), and presumably information is lost as each layer successively filters the signal recieved from the previous layer.

One might also ask about the redundancy of the information encoded by different neurons. Presumably each and every neuron is not unique, but can be grouped with similar, nearby neurons, so that the entire group can be understood as a homogenous population of neurons. In that case, one would expect that the information contained by a subsample of neurons tends to plateau as one includes more and more 'redundant' neurons in the subsample.

These two questions can both be posed in the framework of information theory. In principle, we have the tools to answer these kinds of questions. We can infer the connective structure of neural circuits in living brains, and infer their patterns of neuron activation using a variety of imaging modalities, including EEG, MEG, fMRI, and calcium imaging.

However, even after the data has been collected, there exists an inferential barrier between the data and the information theoretic conclusions we might wish to make. First of all, in order to quantify the information content of a neural system, we would ideally know the encoding scheme. However, usually

the encoding scheme has to be hypothesized, and then fit to the data. And even if we had the correct encoding scheme, we still can only estimate the information content due randomness inherent in our experimental design, measurement devices, and the neuronal dynamics themselves.

This inferential barrier has classically been ignored in classical studies of encoding and decoding, for good reason. When the stimulus is relatively simple, such as wind direction, we can often discover the correct model based on intuition, and estimate its parameters in data to a high reliability. Therefore our error in estimating the information in a population of neurons might be fairly accurate.

However, the limitations of this naive approach have been recognized for more complex, multivariate phenomena. As noted by Quiroga and Panzeri,

> ... decoding algorithms may fail to decode stimuli owing to a high-dimensional response space... In such circumstances it may therefore be dangerous to rule out a candidate neuronal code only because it gives a near-chance performance with a given decoding algorithm.

To give a concrete example of why it might be difficult to estimate an encoding scheme from data, we introduce our motivating example of natural image identification (Kay 2008). Here the stimulus s is a grayscale image with 128×128 pixels. Suppose for the sake of illustration that one was able to measure neural activations directly. Then, one might suppose that the firing rate of the ith neuron as a function of the stimulus is some linear function of the pixels,

$$r_i(s) = \langle a_i, s \rangle$$

One might further assume that a_i belongs to a family of Gabor filters, parameterized by a location x_i, orientation θ_i, frequency f_i, and scale τ_i. Given that each neuron only has five parameters, this might be realtively easy. However, in fact we do not have the means to measure individual neurons, but rather voxels v_i which are some time-and-space average version of the neural activity. Hence we might model each voxel as

$$v_i(s) = \langle b_i, s \rangle$$

where now b_i is a mixture of many Gabor filters. The complexity of each voxel limits the accuracy to which we can recover its encoding parameters, even supposing we have an accurate model of encoding.

As statisticians, we can develop methodology which account for the uncertainty in estimation. Such methodology can be used for the purpose of evaluating candidate encoding schemes, and inferring the information content of neuronal populations. Depending on the quality of the measurements and the sample size, the uncertainty may be too great to draw any conclusions. In that case, statistics is at the very least informative of the difficulty of the problem, or the need to acquire more data or use different modalities.

In the next sections, we narrow our scope to a specific hypothetical model of stimulus encoding, which motivates our statistical approach for inferring the information content of a population of neurons. Section 2 introduces the measure of information we employ, Section 3 discusses methods to estimate the encoding and decoding schemes, and Section 4 proposes methodology for inferring information content given a candidate encoding scheme, which accounts for statistical uncertainty.

2 Quantifying Information

2.1 Parameterization Issues

The information content of a neural system has traditionally been understood as the mutual information between the population of neural responses, X, and the stimulus, S: that is, the information encoded by X is

$$I(S; X) = H(S) - H(S|X)$$

where H is entropy.

A signficant source of difficulty in developing a theory for encoding complex phenomena (such as visual stimuli) is that unlike in the case of simple stimuli, an obvious parameterization of the stimuli in Euclidean space may not exist. It is clear how to encode arm direction in three-dimensional space; on the other hand, it is not clear if it even makes sense to ask what is the "dimensionality" of a natural scene. One might restrict the scope to pixelized images, but this is a rather artificial and unsatisfactory solution. Without such an *a priori* parameterization, the most suitable mathemtical framework for a given stimulus space $\mathcal{S}$ is to posit distinct stimuli s as elements of a σ-algebra.

Since the dimensionality of $\mathcal{S}$ is ill-defined, the entropy $H(S)$ is undefined so the classical concepts of information theory cannot be directly applied.

An obvious idea might be to replace the external stimulus s with the most low-level neuronal representation available: e.g., in the case of vision, to replace s with the vector of firing rates of the retinal neurons, $\vec{r}^{(0)}$. While $\vec{r}^{(0)}$ can indeed be finitely parameterized, and may even have a nice mapping from the source space, there are two serious drawbacks to this approach. Firstly, the low-level mapping differs between subjects; whereas we think of the stimulus s as external to the subjects and common between experiments. Secondly, the entropy of $\vec{r}^{(0)}$ would include both signal specific to s and noise terms. In order to distinguish between signal and noise, we have to incorporate the stimulus s after all.

A next approach might be to think of $\mathcal{S}$ as a function space with some smoothness conditions, and to represent $\mathcal{S}$ in some suitable basis. An infinite basis would be needed, but the coefficients for any particular stimulus would decay in the higher dimensions, so there is some hope of being able to measure the information of the stimulus distribution. This is not an unreasonable approach, but requires many technicalities which are more or less tangential to the scientific problem.

An intuitively simpler (if mathematically less elegant) approach is to base the measure of information on *the ability to discriminate between distinct stimuli*. That is, in order to measure the information content of some neuronal system $\vec{r}$, we need to specify some *discrimination test*, and supply a *discriminator* which uses information in $\vec{r}$ to answer the discrimination test. Examples of discrimination tests are:

- I obtain $\vec{r}_1$ from s_1 and $\vec{r}_2$ from s_2. Are s_1 and s_2 the same stimulus? *(Hypothesis testing)*

- I obtain $\vec{r}$ from one of $\{s_1, \ldots, s_k\}$. Which stimulus did I chose? *(Classification)*

An individual discrimination test provides little information about the information capacity of a system $\vec{r}$. However, a large collection of such tests might be more informative; and, indeed, in the discrete setting an exact correspondence can be made between the mutual information of $\vec{r}$ and some measure of its average performance over a collection of tests.

In general, though, there are infinitely many possible measures of information based on different kinds of discrimination tests. As a start, we might look for a measure of information which does not involve a procedure that is

too complicated or arbitrary, in terms of choosing discrimination tests. To give some good and bad examples:

- Fixing some *particular* stimuli $s_1, \ldots, s_K$ and defining the information content in terms of classification performance on that set. Too arbitrary: why did you choose those stimuli in particular?

- (Packing) Choosing a probability ϵ, and declaring a set $s_1, \ldots, s_k$ as *separable* if given any s_i, s_j in the set, one can distinguish between s_i and s_j with probability $1 - \epsilon$ or better. Then defining the information content as the log of the largest k for which there exists a separable set of that size. Too complicated: given that the actual value of K might be millions or billions, there is no way to actually validate this measure experiementally.

- (Random classification) Defining some probability distribution π over stimuli, and then defining the information content in terms of *average* classification performance on a set $s_1, \ldots, s_k$ drawn randomly from π. Better: the main source of subjectivity is how to define π, but it might be acceptable to simply take some image database as representative of a "natural" distribution π. Then there is also a choice of k: more on this later!

To narrow down what we might consider an ideal measure of information, we can turn to the properties of Shannon information as a guideline. Shannon information has nice properties for describing the information content of a combined system in terms of the information of its subsystems. Given that many of our motivating scientific questions involve understanding the redundancy of neuronal subsystems, these are highly desirable properties for our application. These properties are:

1. Given a random vector $\vec{r}^{(1)}$ and an independent random vector $\vec{r}^{(2)}$, the joint entropy is the sum of the individual entropies,

$$H(r^{(1)}, r^{(2)}) = H(r^{(1)}) + H(r^{(2)})$$

2. Given non-independent random vectors, the joint entropy is the sum of individual entropies minus the mutual information,

$$H(r^{(1)}, r^{(2)}) = H(r^{(1)}) + H(r^{(2)}) - I(r^{(1)}, r^{(2)})$$

The measure of information, H, has a desirable additive property, while the mutual information I provides a measure of redundancy.

In fact, the *packing* definition of information comes close to satisfying property 1, other than the fact that the probability threshold ϵ has to be adjusted. That is,

$$P_{\epsilon'}(r^{(1)}, r^{(2)}) = P_\epsilon(r^{(1)}) + P_\epsilon(r^{(2)})$$

where ϵ' might be different from ϵ. To intuitively see why this is, the packing number P is the log number of balls which can be 'packed' into the response space R. If e^{P_1} response balls can be packed in R_1, and e^{P_2} balls can be packed into R_2, then by taking products of balls in R_1 and R_2, $e^{P_1 + P_2}$ balls can be packed into $R_1 \times R_2$. This is exact if we happened to be talking about lattices of hypercubes, but it is approximately correct for general metrics.

Since the packing definition of information is impractical to measure, requiring some estimate of all k choose 2 discrimination tests, we might hope that this nice property of packing could be obtained by using random classification. In fact, we can recover this property if we consider a range of test sizes k, which is quite feasible to do in practice. But if we are willing to make some distributional assumptions on $\vec{r}$, we can go even further and eliminate the arbitrary choice of ϵ. This is the subject of the next subsection.

2.2   Summarizing performance in random classification

Consider a large set of neurons, $r_1, \ldots, r_m$. Each neuron $r_i(s)$ is the sum of a signal term $h_i(s)$ and a noise term, ϵ_i. Let us assume that for random stimuli S drawn from distribution $S \sim \pi$, we have

$$(h_1(S), \ldots, h_m(S)) \sim N(0, \Sigma_H)$$

and

$$(\epsilon_1, \ldots, \epsilon_m) \sim N(0, \Sigma_\epsilon).$$

hence $\vec{r} \sim N(0, \Sigma_H + \Sigma_\epsilon)$.

GOAL: Find a summary statistic I for the entire curve of classification error vs number of classes, with the additivity type property.

3 Estimating Encoding Parameters

3.1 Previous Work

Consider a parametric model

$$Y \sim F_\theta(X)$$

Such a *forward model* gives the distribution of the response conditional on the stimuli features.

The *maximum likelihood* (ML) principle can be invoked to identify the stimuli $i \in S$ "most likely" to have produced y^*. Let $x_i : i \in S$ denote features of the test stimuli, and identify y^*

$$i^* = \text{argmax}_i \ell_\theta(y^*|x_i)$$

Example. We take the following as a representative approach, combining features of [1] and [2]:

- Assume the normal mutivariate linear model

$$Y \sim N(XB, \Sigma_E), \text{ where } B \in \mathbb{R}^{q \times p}$$

- Estimate B using elastic net [4]

- Estimate Σ_E using off-diagonal shrinkage of sample covariance matrix of residuals

- The ML rule takes the form

$$i^* = \text{argmin}_i (x_i^T \hat{B} - y^*)^T \hat{\Sigma}_E^{-1} (x_i^T \hat{B} - y^*) \tag{1}$$

3.2 Emprirical Bayes Approach

- *Idea*: Unlike ML, the Bayes rule surely optimizes the "correct" objective function. Can we approximate the Bayes rule?

- *Empirical Bayes*: use the data to estimate the covariances Σ_B and Σ_E, then compute posterior distribution of B

- Assume coefficients of B independent; diagonals of Σ_B can be estimated using any estimate of signal strength, e.g. *Eigenprism* [3].

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- Decision rule similiar to (1) but with "added noise" due to uncertainty of B.

$$\min(x_i^T B - y^*)^T (\text{Cov}(x_i^T B) + \hat{\Sigma}_E)^{-1}(x_i^T B - y^*)$$

- Analogous to LDA vs QDA

3.3 Covariance Estimation

Both ML approach and EB approach depend on estimates of the covariance of Y. We might assume a "Kronecker" model where $\text{Cov}(Y) = \Sigma_v \times \Sigma_t$ where Σ_v is the covariance of voxels (for a fixed time point) and Σ_t is the autocovariance of a given voxel.

New approaches to estimating covariance Σ_v might incorporate spatial information about voxel location, or functional information.

3.4 Computation

Suppose we have a $n \times p_Y$ response matrix Y and a $n \times p_X$ covariate matrix X. We have the model

$$Y = XB + E$$

where B is a $p_X \times p_Y$ coefficient matrix and E is a matrix of noise. Write

$$E = \begin{pmatrix} e_1^T \\ e_2^T \\ ... \\ e_n^T \end{pmatrix}$$

Assume the rows of E are independent, and each row is distributed

$$e_i \sim N(0, \Sigma_e)$$

Let us assume a prior distribution on the coefficients,

$$B_{ij} \sim N(0, \sigma_{B,j}^2)$$

and where B_{ij} are independent. Note that each column $j = 1, ..., p_Y$ has a different prior coviarance $\sigma_{B,j}^2$. This reflects our prior knowledge that some column of Y may have more signal than other columns.

Bayes' rule gives us the posterior mean and covariance of the coefficients B_{ij}. First, we introduce the vectorized notation $\vec{B}$ to denote the $p_X p_Y \times 1$

vector obtained by stacking the columns of B, and similarly $\vec{Y}$ to denote the $p_Y n \times 1$ vector obtained by stacking the columns of Y. Also recall the definition of Kronecker product,

$$A \otimes B = \begin{pmatrix} a_{11}B & a_{12}B & ... \\ a_{21}B & a_{22}B & ... \\ ... & ... & ... \end{pmatrix}$$

Also define

$$\Omega_e = \Sigma_e^{-1}$$

$$\Omega_b = \text{diag}\left(\frac{1}{\sigma_{b,1}^2}, ..., \frac{1}{\sigma_{b,p_Y}^2}\right)$$

The posterior mean and covariance are given as follows.

$$\text{E}[\vec{B}|Y] = (\Omega_e \otimes X^T X + \Omega_b \otimes I_{p_X})^{-1}((I \otimes X)^T(\Omega_e \otimes I)\vec{y})$$

$$\text{Cov}(\vec{B}|Y) == (\Omega_e \otimes X^T X + \Omega_b \otimes I_{p_X})^{-1}$$

Given a new observation $y_* = B^T x_* + e_*$, where y_* and x_* are column vectors, the posterior predictive distribution is

$$\text{E}[y_*|Y] = (I_{p_Y} \otimes x_*^T)\text{E}[\vec{B}|Y]$$

$$\text{Cov}[y_*|Y] = (I_{p_Y} \otimes x_*^T)\text{Cov}(\vec{B}|Y)(I_{p_Y} \otimes x_*) + \Sigma_e$$

In the following, we assume that $p_X > n$.

Naively, computing the posterior covariance takes $O(p_X^3 p_Y^3)$ operations and computing the posterior mean takes $O(p_X^2 p_Y^2)$ operations.

However, by diagonalizing the covariance matrix and taking advantage of the properties of Kronecker products, we can make the computation much more efficient.

Using simultaneous diagonalization, find V_e, D_e such that

$$\Omega_e = V_e D_e V_e^T$$

and

$$\Omega_b = V_e V_e^T$$

Note that V_e is not orthogonal. The procedure for finding V_e, D_e is well-known and also given in the code.

Furthermore, define

$$\tilde{X} = \begin{pmatrix} X \\ 0 \end{pmatrix}$$

so that $\tilde{X}$ is an $p_X \times p_X$ matrix. Then take the SVD

$$\tilde{X} = U_X D_X V_X^T$$

so that D_X and V_X are both $p_X \times p_X$. We have

$$V_X V_X^T = V_X V_X^T = I_{p_X}$$

and

$$V_X D_X^2 V_X^T = X^T X.$$

Now we can rewrite the expression

$$\mathrm{Cov}(\vec{B}|Y) == (\Omega_e \otimes X^T X + \Omega_b \otimes I_{p_X})^{-1}$$

$$= ((V_e D_e V_e^T) \otimes (V_X D_X^2 V_X^T) + (V_e V_e^T) \otimes (V_X V_X^T))^{-1}$$

$$= [(V_e \otimes V_X)(D_e \otimes D_X^2 + I_{p_X p_Y})(V_e^T \otimes V_X^T)]^{-1}$$

$$= (V_e^{-1} \otimes V_X^T)^T (D_e \otimes D_X^2 + I_{p_X p_Y})^{-1}(V_e^{-1} \otimes V_X^T)$$

In this form the expression is much each to compute since

- Only a diagonal matrix needs be inverted, and yields a diagonal matrix

- Multiplying the tranpose of a Kronecker product with a diagonal with itself is easy to compute.

To see the second point, consider computing the product

$$C = (A \otimes B)^T D (A \otimes B)$$

where A is $a_1 \times a_2$, B is $b_1 \times b_2$, and D is diagonal with

$$D = \begin{pmatrix} D_1 & 0 & 0 & 0 & \dots \\ 0 & D_2 & 0 & 0 & \dots \\ 0 & 0 & D_3 & 0 & \dots \\ \dots & \dots & \dots & \dots & \dots \end{pmatrix}$$

such that each $D_1, ..., D_{a_1}$ is $b_1 \times b_1$.

For $i, j = 1..., a_2$, let $C_{[ij]}$ denote $b_2 \times b_2$ blocks such that

$$C = \begin{pmatrix} C_{[11]} & C_{[12]} & ... \\ C_{[21]} & C_{[22]} & ... \\ ... & ... & ... \end{pmatrix}$$

Now we can write

$$C_{[ij]} = \sum_{k=1}^{a_1} a_{ki} a_{kj} B^T D_k B = \left(\sum_{k=1}^{a_1} a_{ki} a_{kj} B^T D_k B \right) = B^T \left(\sum_{k=1}^{a_1} a_{ki} a_{kj} D_k \right) B.$$

The second-to-last and last equality present two alternative methods to compute $C_{[ij]}$.

- Using the second-to-last equality, one precomputes each of the matrices $B^T D_i B$, which takes $O(b_2^2 b_1 a_1)$ operations. To compute each block, it takes $O(b_2^2 a_1)$ operations. Hence, to compute C takes $O(a_1 a_2^2 b_2^2)$.

- Using the last equality, for each block one takes $O(a_1 b_1)$ operations to compute the weighted sum of $D_1, ..., D_{a_1}$, and then $O(b_2^1 b_1)$ to multiply on the left with B^T and on the right with B.

Therefore, we see that it takes $O(a_2^2 b_2^2 b_1)$ operations to compute C.

Choosing the best of the two methods, the cost to compute C is $O(a_2^2 b_2^2 \min(a_1, b_1))$. Applying to our problem, we see that the cost to evaluate the posterior covariance using this method is $O(p_Y^2 p_X^2 \min(p_X, p_Y))$, which is a saves a factor of $\max(p_Y, p_X)$ compared to the naive approach.

4 Inferring Information Content

4.1 Finite Sample Effect

4.2 Learning Curves