

Prediction, information, and inference: with application to neuroimaging

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Abstract

Neuroscientists have a variety of tools for quantifying multivariate dependence: mutual information, linear correlation-based statistics, Fisher information, and more recently, measures of performance on supervised learning tasks such as classification. We argue that both mutual information and classification accuracy capture intuitive properties of an “information coefficient” for a channel, and we proceed to develop a general axiomatic characterization of information coefficients for channels consisting of a pair of input and output random variables. Arguably, the key properties of an information coefficient are that (i) it is a scalar measure of multivariate dependence, and (ii) that it satisfies a *stochastic data-processing inequality*: any coefficient with such properties can be used for model selection. We show how prediction tasks can be used to define a general class of information coefficients which includes mutual information, as well as a novel information coefficient, *average Bayes accuracy*, which can be considered an “idealization” of classification accuracy. Furthermore, we consider the possibility of developing a general theory of statistical inference for this class of information coefficients. Concretely, we derive a lower confidence bound for average Bayes accuracy as well as a novel lower confidence bound for mutual information.

1 Introduction

Historically, neuroscience has largely taken a reductionist approach to understanding the nervous system, proceeding by defining elements and subele-

ments of the nervous system (e.g. neurons), and investigating relationship between two different elements, or the response of an element to external stimulation: say, the response of a neuron’s average firing rate to skin temperature. At one level of abstraction, neuroscientists might seek to characterize the functional relationship between elements, but at a higher level of abstraction, it may be sufficient to report scalar measures of dependence. Since neural dynamics are generally both stochastic and nonlinear, it was a natural choice for early neuroscientists to adopt Shannon’s *mutual information* as a quantitative measure of dependence. But as new technologies enabled the recording of neural data at larger scales and resolution, the traditional reductionist goals of neuroscience were supplemented by increasingly ambitious attempts within neuroscience to understand the dynamics of neural ensembles, and by efforts originating within psychology and medicine to link the structure and function of the entire human brain to behavior or disease. The larger scope of the data and the questions being asked of the data created an increasing demand for multivariate statistical methods for analyzing neural data of increasingly high dimension. Due to the complexity, variety, and practical difficulties of multivariate statistical analysis of the brain, alternative measures of multivariate dependence such as linear-based correlational statistics, or Fisher information, started to gain traction. For the most part, alternative measures of dependence sacrifice flexibility for a gain in practical convenience: linear-based statistics such as canonical correlation or correlation coefficients fail to capture nonlinear dependencies, and Fisher information requires strong parametric assumptions. Therefore, it was of considerable interest when Haxby (2001) introduced the usage of *supervised learning* (classification tasks) for the purpose of quantifying stimulus information in task fMRI scans. Since then, an entire subfield of neuroimaging, multivariate pattern analysis (MVPA) has been established dedicated to quantifying multivariate information in the brain, and both mutual information and classification accuracy are used by practitioners within the field. Judging from the language used by the practitioners themselves, it is intuitively clear to them how classification accuracies can be used to quantify information in brain scans. However, a more thorough examination of the practice raises many questions with regards to the use of classification accuracy as a coefficient of information: this is one motivation for the current work. But taking a step back, it would seem valuable at this historical juncture to examine the intuitive properties of “information” as a measure of multivariate dependence, and not only consider whether classification ac-

curacy can be considered or used to derive a new information coefficient, but whether other such coefficients might also exist, and whether a unified theory can be developed to account for all of them. This is the larger purpose of the current work, and towards that end we not only propose a general class of information coefficients which unifies both information-theoretic and supervised-learning-based approaches, but with an eye toward practical applications, we also examine the question of inferring these quantities from data. An initial result in this direction is the derivation of nonparametric lower confidence bounds for average Bayes accuracy (a novel information coefficient closely related to classification accuracy,) and an inequality between average Bayes accuracy and mutual information, which, combined with the preceding result, yields a novel lower confidence bound for mutual information.

1.1 Organization

The rest of the paper is organized as follows. Section 2 plays the role of a “background” section that gives the basics of mutual information and supervised learning as they are used in neuroscience, as well as practical issues related to estimation. In section 3, we present an axiomatic characterization of information coefficients, and introduce a general class of information coefficients which satisfies our axioms. We define a new information coefficient belonging to this class, average Bayes accuracy, and we also show how mutual information can be considered an “extended member” of the class. In section 4 we develop the basic theory of what kinds of inferences about our information coefficients are possible discuss the kinds of experimental designs and supervised learning pipelines which are needed to enable such inference. Concretely, we develop a lower confidence bound for average Bayes accuracy. In section 5 we outline a comparative theory for different coefficients within our framework: how are the different information coefficients related? We discuss the calculus of variations as a possible general technique for establishing inequalities between different information coefficients, and in particular we derive a “randomized Fano’s inequality”: a lower bound for mutual information as a function of average Bayes accuracy. Combined with our lower confidence bound for average Bayes accuracy, this yields a novel lower confidence bound for mutual information. We provide a practical data analysis example in section 6. A discussion section includes future directions and loose ends are treated, and most of the technical proofs and lemmas are

found in the appendix.

2 Background

2.1 Mutual information and its usage

While Shannon’s theory of information was motivated by the problem of designing communications system, the applicability of mutual information was quickly recognized by neuroscientists. Only four years after Shannon’s seminal paper in information theory (1948), McKay and McCullough (1952) inaugurated the application of mutual information to neuroscience. If \mathbf{X} and \mathbf{Y} have joint density $p(\mathbf{x}, \mathbf{y})$ with respect to the product measure $\mu_x \times \mu_y$, then the mutual information is defined as

$$I(\mathbf{X}; \mathbf{Y}) = \int p(\mathbf{x}, \mathbf{y}) \log \frac{p(\mathbf{x}, \mathbf{y})}{p(\mathbf{x})p(\mathbf{y})} d\mu(\mathbf{x})d\mu(\mathbf{y}).$$

where $p(\mathbf{x})$ and $p(\mathbf{y})$ are the marginal densities with respect to μ_x and μ_y ¹. Since then, mutual information has enjoyed a celebrated position in both experimental and theoretical neuroscience. Experimentally, mutual information has been used to detect strong dependencies between stimulus features and features derived from neural recordings, which can be used to draw conclusions about the kinds of stimuli that a neural subsystem is designed to detect, or to distinguish between signal and noise in the neural output. Theoretically, the assumption that neural systems maximize mutual information between salient features of the stimulus and neural output has allowed scientists to predict neural codes from signal processing models: for instance, the center-surround structure of human retinal neurons matches theoretical constructions for the optimal filter based on correlations found in natural images [cite].

The mutual information measures the information “capacity” of a channel consisting of an input \mathbf{X} and an output \mathbf{Y} , and satisfies a number of important properties.

1. The channel input \mathbf{X} and output \mathbf{Y} can be random vectors of arbitrary dimension, and the mutual information remains a scalar functional of the joint distribution $p(\mathbf{X}, \mathbf{Y})$.

¹Note that the mutual information is invariant with respect to change-of-measure.

2. When \mathbf{X} and \mathbf{Y} are independent, $I(\mathbf{X}; \mathbf{Y}) = 0$; otherwise, $I(\mathbf{X}; \mathbf{Y}) > 0$.

3. The data-processing inequality: for any vector-valued function \vec{f} of the output space,

$$I(\mathbf{X}; \vec{f}(\mathbf{Y})) \leq I(\mathbf{X}; \mathbf{Y}).$$

4. Symmetry: $I(\mathbf{X}; \mathbf{Y}) = I(\mathbf{Y}; \mathbf{X})$.

5. Independent additivity: if $(\mathbf{X}_1, \mathbf{Y}_1)$ is independent of $(\mathbf{X}_2, \mathbf{Y}_2)$, then

$$I((\mathbf{X}_1, \mathbf{Y}_1); (\mathbf{X}_2, \mathbf{Y}_2)) = I(\mathbf{X}_1; \mathbf{Y}_1) + I(\mathbf{X}_2; \mathbf{Y}_2).$$

Three additional consequences result from the data-processing inequality:

- *Stochastic data-processing inequality* If \vec{f} is a stochastic function independent of both \mathbf{X} and \mathbf{Y} , then

$$I(\mathbf{X}; \vec{f}(\mathbf{Y})) \leq I(\mathbf{X}; \mathbf{Y}).$$

This can be shown as follows: any stochastic function $\vec{f}(\mathbf{Y})$ can be expressed as a deterministic function $\vec{g}(\mathbf{Y}, W)$, where W is a random variable independent of \mathbf{X} and \mathbf{Y} . By independent additivity,

$$I(\mathbf{X}; \mathbf{Y}) = I(\mathbf{X}; (\mathbf{Y}, W)).$$

Then, by the data-processing inequality,

$$I(\mathbf{X}; \mathbf{Y}) = I(\mathbf{X}; (\mathbf{Y}, W)) \geq I(\mathbf{X}; \vec{g}(\mathbf{Y}, W)) = I(\mathbf{X}; \vec{f}(\mathbf{Y})).$$

- *Invariance under bijections.* If \vec{f} has an inverse \vec{f}^{-1} , then

$$I(\mathbf{X}; \vec{f}(\mathbf{Y})) \leq I(\mathbf{X}; \mathbf{Y}) = I(\mathbf{X}; \vec{f}^{-1}(\vec{f}(\mathbf{Y}))) \leq I(\mathbf{X}; \vec{f}(\mathbf{Y})),$$

therefore, $I(\mathbf{X}; \vec{f}(\mathbf{Y})) = I(\mathbf{X}; \mathbf{Y})$.

- *Monotonicity with respect to inclusion of outputs.* Suppose we have an output ensemble $(\mathbf{Y}_1, \mathbf{Y}_2)$. Then the individual component \mathbf{Y}_1 can be obtained as a projection of the ensemble. By the data-processing inequality, we therefore have

$$I(\mathbf{X}; \mathbf{Y}_1) \leq I(\mathbf{X}; (\mathbf{Y}_1, \mathbf{Y}_2)).$$

Intuitively, if we observe both \mathbf{Y}_1 and \mathbf{Y}_2 , this can only *increase* the information we have about \mathbf{X} compared to the case where we only observe \mathbf{Y}_1 by itself.

And it is the property of *invariance under bijections*, inclusive of non-linear bijections, which qualifies mutual information as a *non-linear measure of dependence*. Linear measures, such as Pearson correlation, are not invariant under bijections.

Besides the formal definition, there are a number of well-known alternative characterizations of mutual information in terms of other information-theoretic quantities: the *entropy* H :

$$H_\mu(\mathbf{X}) = - \int p(\mathbf{X}) \log p(\mathbf{X}) d\mu(\mathbf{X}),$$

and the *conditional entropy*:

$$H_\mu(\mathbf{X}|\mathbf{Y}) = - \int p(\mathbf{Y}) d\mu_y(\mathbf{Y}) \int p(\mathbf{X}|\mathbf{Y}) \log p(\mathbf{X}|\mathbf{Y}) d\mu_x(\mathbf{X}).$$

Some care needs to be taken with entropy and conditional entropy since they are not invariant with respect to change-of-measure: hence the use of the subscript in the notation H_μ . In particular, there is a difference between *discrete entropy* (for counting measure) and *differential entropy* (for Lebesgue measure.) Intuitively, entropy measures an observer's uncertainty of the random variable \mathbf{X} , supposing the observer has no prior information other than the distribution of \mathbf{X} . Conditional entropy measures the *expected uncertainty* of \mathbf{X} supposing the observer observes \mathbf{Y} .

However, regardless of the base measure, the following identities hold:

$$I(\mathbf{X}; \mathbf{Y}) = H_{\mu_x \times \mu_y}((\mathbf{X}, \mathbf{Y})) - H_{\mu_x}(\mathbf{X}) - H_{\mu_y}(\mathbf{Y}).$$

$$I(\mathbf{X}; \mathbf{Y}) = H_\mu(\mathbf{Y}) - H_\mu(\mathbf{Y}|\mathbf{X}). \quad (1)$$

The second identity (1) is noteworthy as being practically important for estimation of mutual information. Since the entropies in question only depend on the marginal and conditional distributions of \mathbf{Y} , the problem of estimating $I(\mathbf{X}; \mathbf{Y})$ can be reduced from a $\dim(\mathbf{X}) + \dim(\mathbf{Y})$ -dimensional nonparametric estimation problem to a $\dim(\mathbf{Y})$ -dimensional problem: hence this identity is a basis of several methods of estimation used in neuroscience, such as Gastpar (2014).

However, by symmetry, we also have the flipped identity

$$I(\mathbf{X}; \mathbf{Y}) = H_\mu(\mathbf{X}) - H_\mu(\mathbf{X}|\mathbf{Y}). \quad (2)$$

In neuroscience studies, where \mathbf{X} is the controlled stimulus, and \mathbf{Y} is the neural activity, the two mirror pairs (1) and (2) have different interpretations. Rather than providing a basis for practical estimation, (2) provides an *interpretation* of the mutual information. Loosely speaking, $H_\mu(\mathbf{X})$ is the uncertainty of \mathbf{X} before having observed \mathbf{Y} , and $H_\mu(\mathbf{X}|\mathbf{Y})$ is the uncertainty of \mathbf{X} after having observed \mathbf{Y} , hence $H_\mu(\mathbf{X}) - H_\mu(\mathbf{X}|\mathbf{Y})$ is how much the observation of \mathbf{Y} has *reduced* the uncertainty of \mathbf{X} . Stated in words,

$$I(\mathbf{X}; \mathbf{Y}) = \text{average reduction of uncertainty about } \mathbf{X} \text{ upon observing } \mathbf{Y}.$$

We list these properties of mutual information in preparation for section 3.1, where we prepare a “minimal” set of properties for an information coefficient, and consider how much of the functionality of the mutual information would be preserved by an alternative information coefficient satisfying only those minimal properties.

But what, exactly, is the functionality of mutual information in neuroscience? How it is used in practice? A nice summary of the applications of mutual information is provided in the introduction of Gastpar (2014). Taking their list as a starting point, we briefly overview the main use-cases of mutual information, and illustrate each with a representative example.

- Example: Comparison of decoders in Nelken. Property (i) is important to enable model comparison. Property (iii) is needed because relationships may be nonlinear.
- Example: Redundancy in population code of retina. Property (i)-(iii) and (v) are needed to obtain a meaningful measure of redundancy.
- In general, symmetry not important, but additivity is desirable for measures of redundancy. Property (ii) can usually be enforced since any measure needs to have a unique “minimum” value for the case of independence.

2.2 Supervised learning

- Supervised learning task is defined using a prediction task.
- 1. A predictive model is learned using training data

- 2. The performance of the model on the prediction task is estimated using independent test data
- Classical examples of prediction tasks: regression and classification
- Third example: identification
- Definition of Bayes prediction model
- General definition of supervised learning task
- SL performance can be a scalar
- SL can be used to test for independence
- Bayes performance satisfies data-processing inequality
- How SL is interpreted in MVPA as information
- Section 3, we'll see how Bayes performance can be legitimately considered a measure of information

2.3 Connections

- Information theory and decoding. Fano's inequality
- Quiroga's method
- MVPA people use them interchangeably

3 Information, uncertainty and prediction

In the previous section, we examined how mutual information and supervised learning are used in neuroscience. By analyzing the use-cases of each method side-by-side, and by reviewing the known connections between the two methods, we hoped to suggest the notion that both mutual information and supervised learning are being employed as means of quantifying the same underlying concept. In this section, we propose a reification of this underlying concept of “information”, and propose the *minimal* properties needed for a functional to be considered an *information coefficient*. We argue that these minimal properties are sufficient to support many of the existing use-cases of mutual information and supervised learning in neuroscience.

3.1 Axiomatic characterization of information

We claim that neuroscientists use both mutual information and supervised learning to quantifying a common concept of “information.” Furthermore, we claim that neuroscientists largely share a set of common intuitions about information.

- *Intuition 1: Information is a measure of dependence.* If \mathbf{X} and \mathbf{Y} are statistically independent, then \mathbf{X} gives no information about \mathbf{Y} , and vice-versa.

This intuition is employed when researchers test the null hypothesis of chance accuracy for classification. If the null is accepted, the researcher concludes that there is no information in the predictors about the response.

- *Intuition 2a: Monotonicity with respect to inclusion of outputs.* If \mathbf{Y}_1 and \mathbf{Y}_2 are ensembles of neurons (or individual neurons), then the combined ensemble $(\mathbf{Y}_1, \mathbf{Y}_2)$ has equal or more information about \mathbf{X} than either component by itself.
- *Intuition 2b: Noise adds no information.* If, in the previous example, \mathbf{Y}_2 is independent of \mathbf{X} , then \mathbf{Y}_2 adds no information to the ensemble.

The non-informativity of noise is vital for the purpose of *localizing* information within fMRI voxels (as is done in searchlight analysis.) Since noise voxels fail to improve classification performance (and indeed, sometimes harm empirical performance,) the optimal searchlight radius will concentrate on clusters of signal voxels, and minimize the inclusion of noise voxels.

- *Intuition 3: Information can be used as a basis of model selection.* Among multiple encoding/decoding models, a more accurate model should tend to have greater information relative to less accurate models.

Compared to the first two, this third intuition is somewhat less obvious, but nevertheless appears as an important use-case for mutual information, as seen in the application of mutual information to choose encoding models.

Given the first two intuitions, we find that an essential property of information is that it can be said to ‘increase’—i.e., there exists at least a partial ordering on information. Furthermore, there should exist a minimal element

in this ordering, which is the information between independent variables—that is, ‘no information.’ However, this is fully consonant with either information being quantified as a scalar quantity, or as a positive-definite matrix. Indeed, Fisher information could be taken as an example of a matrix-valued information coefficient. However, the problem with matrix-valued coefficients is that channels may be incomparable within the partial ordering. Thus, if we consider the third intuition an important property of an information coefficient, then it should be scalar to enable model comparison.

We find that all of the preceding intuitions follow from the following axioms.

Axioms of information

Let $\mathcal{I}(\mathbf{X}; \mathbf{Y})$ denote an *information coefficient*. Then,

1. $\mathcal{I}(\mathbf{X}; \mathbf{Y})$ is a scalar functional of the joint distribution $p(\mathbf{X}, \mathbf{Y})$.
2. When \mathbf{X} and \mathbf{Y} are independent, $\mathcal{I}(\mathbf{X}; \mathbf{Y}) = 0$; otherwise, $\mathcal{I}(\mathbf{X}; \mathbf{Y}) \geq 0$.
3. The stochastic data-processing inequality. If \vec{f} is stochastic vector-valued function of the output space independent of (\mathbf{X}, \mathbf{Y}) , then

$$\mathcal{I}(\mathbf{X}; \vec{f}(\mathbf{Y})) \leq \mathcal{I}(\mathbf{X}; \mathbf{Y}).$$

Since this minimal list of properties is a subset of the properties of mutual information, it is clear that mutual information satisfies the axioms. However, classification accuracy does not satisfy the axioms—we will see in section how to define a proper information coefficient based on supervised learning.

Now let us check that any information coefficient $\mathcal{I}(\mathbf{X}; \mathbf{Y})$ necessarily satisfies the intuitions. Intuition 1 is satisfied by property (ii). We gave a general argument in ?? how Intuition 2a follows from the data-processing inequality. Intuition 2b follows from the stochastic data-processing inequality, taking $\vec{f}(\mathbf{Y}_1) = (\mathbf{Y}_1, \mathbf{Y}_2)$.

Now, in order to justify intuition 3, we need to formalize the notion of “model selection.” A complete discussion of model selection falls outside the scope of the paper, so we limit the discussions to the important special case of selecting an encoding model.

Let \mathbf{X} be some environmental stimulus, and

$$\mathbf{Y} = \vec{f}(g(\mathbf{X}))$$

where \vec{f} is a stochastic function independent of \mathbf{X} , and g is an *encoding function*, which is known to lie in some class of functions \mathcal{G} . The goal of model selection is estimate g .

Given multiple competing models $(\hat{S}_1, \hat{g}_1), \dots, (\hat{S}_k, \hat{g}_k)$, we obtain a lower confidence bound on the maximum score,

$$M = \max_{i=1}^k \mathcal{I}(\mathbf{Y}; \hat{g}_i(\mathbf{X})).$$

We can then test each individual model for the hypothesis $H_i : \mathcal{I}(\mathbf{Y}; \hat{g}_i(\mathbf{X})) < M$. All of the models which are rejected are considered ‘candidate models.’ While a common next step is to select a single model from the set of candidates (e.g. using a measure of complexity), this is not essential to our discussion. For now, we are only concerned that the model selection procedure should at the very least, *not reject* the *correct* model g in the circumstance that g is included in the initial set of candidate models. A necessary condition for this criterion is that the correct model g maximizes the information:

$$\mathcal{I}(\mathbf{Y}; g(\mathbf{X})) = \sup_{g \in \mathcal{G}} \mathcal{I}(\mathbf{Y}; g(\mathbf{X})). \quad (3)$$

Indeed, the criterion (3) follows directly from the stochastic data-processing inequality. After all, given any alternative encoding model g' , we have

$$\mathcal{I}(\mathbf{Y}; g(\mathbf{X})) = \mathcal{I}(\vec{f}(g(\mathbf{X})); g(\mathbf{X}))$$

3.2 Axiomatic characterization of supervised learning

3.3 A general class of information coefficients

The general idea is to look at reduction of uncertainty.

- Prediction loss is a measure of uncertainty. Mean-square loss corresponds to variance.
- Consider two prediction problems: in one case you are given no side information, and in the second case you are given \mathbf{Y} . The difference in risk between the two problems gives a measure of uncertainty reduction.
- In regression, this gives “variance explained” as a measure of information.

- In classification, we get a normalized form of Bayes accuracy.
- In randomized classification, we get (normalized) average Bayes accuracy.
- We can prove that any prediction task yields an information measure i.e. satisfying the three axioms.
- If the no-information risk is known in advance, we say the information measure is estimable.
- Mutual information can be characterized this way, but it is not estimable.
- Mutual information can be derived as a limit of linear combinations of normalized ABA, due to channel coding theorem. Still not estimable due to limit property.

4 Statistical inference

- Only lower bounds are possible, because...

5 Connections

6 Applications

7 Discussion