The neuroscientist's guide to entropy: The observer's role and the myth of disorder

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Abstract

Entropy is a term that is frequently used in neuroscience to characterise time series and to make inferences about brain states. The purpose of this note is to support these studies by providing an overview of entropy in the context of neural systems and to address some common misconceptions — the most popular of which is that entropy is a measure of disorder. It is more accurate to say that entropy quantifies the information that is hidden from an observer — a point that we expand upon using toy models. We discuss the limitations of calculating entropy via neural time series and also suggest ways in which entropy could be used by future studies to infer the information capacity of neural systems.

Introduction

The mathematical form of entropy was first derived by Boltzmann in 1872 in his seminal work on statistical mechanics [2] and later re-derived independently by Shannon in 1942 in the context of information theory [3]. Entropy has been adopted by the neuroscience community as a measure of the information storage and processing capacity of the brain [4-11]. These measures have been used as a way of quantifying the repertoire of states that brain regions can express [12-16], as well as of the effect of disease states [17-28]. More recently, entropic measures have been popularized as a quantification of the effects of psychedelics [29-33].

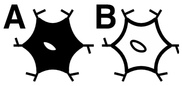
The purpose of this note is to provide support to this growing community of scientists that employ entropy as a tool in their research. Particularly, we would like to clarify some misconceptions that have made their way into the neuroscience literature — for instance that entropy is a measure of 'disorder', or that the second law of thermodynamics has something to do with a tendency toward 'chaos' or 'randomness'. In reality, entropy has little to do with concepts such as randomness or disorder, as we will expand upon in detail.

Our goal is to employ toy models in order to build a picture of what entropy actually represents in the context of neural systems. To this end, we will appeal to statistical mechanics in explicitly defining the role played by the observer and thus highlighting the often overlooked subjective nature of entropy. It is our hope that these clarifications will lead to a more useful and informative approach towards using entropy in the classification of e.g., neural timeseries and neuroimaging modalities. Furthermore, we will suggest ways in which future experiments could be designed for the specific purpose of quantifying the information storage and transmission capacity of neural systems.

Entropy is a measure of the information that is hidden from an observer

Let us imagine zooming into a neural region such that we are able to observe an individual neuron. This neuron can be in one of two states (see Box 1) — 'on' when it is firing (Fig. 1A) and 'off' when it is not firing (Fig 1B).

Figure 1: ***A)*** *a neuron in the 'on' state;* ***B)*** *a neuron in the 'off' state.*



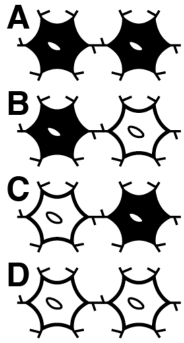
> ***<u>Box 1</u>: System states***
>
> *A state is a distinguishing feature of a system that can change with time. For instance, if the system is a die, then we could find it in six possible states at different points in time. In the case of the binary neuron in Fig. 1, the system can be either in an 'on' or an 'off' state, depending on whether the neuron is firing or not when we make the observation.*

Note that, although we refer to this simplified binary neuron for instructive purposes, the same arguments apply to any other perspectives, such as signals from local field potentials (LFPs), or from functional magnetic resonance imaging (fMRI).

Let us now zoom out slightly from the system in Fig. 1, such that we are able to observe two connected neurons. This two-neuron system can display a total of four states: 'on-on' (Fig. 2A), 'on-off' (Fig. 2B), 'off-on' (Fig. 2C), and 'off-off' (Fig. 2D).

Figure 2: *Two connected neurons in which:*

A) *both are 'on';*
B) *one is 'on' (left), and the other is 'off';*
C) *one is off (left), and one is 'on';*
D) *both are 'off'.*



The entropy is defined as the logarithm of the number of indistinguishable system states that are all compatible with an observer's measurement. To understand what this definition has to do with hidden information, consider the following three observers that are all taking measurements of the same system in Fig. 2.

> ***Box 2**: Laws of motion and initial conditions*
>
> *A law of motion is a rule that tells us what the next state of a system will be, given that we know its current state.*
>
> *For instance, a system may be able to display three different colours: red, blue, and green — these are the system's possible states. We may design this system to display these colours in the following sequence:*
>
> *blue → red → green → blue*
>
> *i.e., if the system is in the 'blue' state, then it will next be in the 'red' state etc. — this is the system's law of motion.*
>
> *An initial condition is a known starting point for the system. For the example above, the initial condition is 'blue'. If we know both the law of motion and the initial condition, we can predict the states of the system infinitely into the future.*

Observer I: This first observer knows nothing about the system in Fig. 2. This means that they do not have any information regarding laws of motion or initial conditions (see Box 2). This observer must therefore assume that they could observe any of the four total states. The entropy for this observer is therefore the logarithm of 4, or equivalently 2 bits. See Box 3 for an explanation of the relationship between logarithms and bits.

Observer II: This second observer is less ignorant than the first regarding the system in Fig. 2. Specifically, they are privy to the information that the coupling strength between the two neurons is sufficiently strong to ensure co-activation. This means that whenever one neuron in Fig. 2 activates, then so does its neighbour and therefore Observer II knows that they will never see the situation in which just one neuron fires (Fig. 2 B & C). As such, this observer must only anticipate two possible states: the one in which both neurons are 'on' (Fig. 2A) and the one in which both neurons are 'off' (Fig. 2D). The associated entropy is therefore the logarithm of 2, or 1 bit.

Observer III: This third observer knows everything there is to know about the system in Fig. 2. This is because, in addition to knowing the coupling strength (as known by Observer II), this third observer also knows that there is insufficient excitation in the system for any neurons to fire in the first place. Therefore, this third observer knows that there is actually only one state that they will ever have to reckon with — the one in which both neurons are 'off' (Fig. 2D). The corresponding entropy is therefore the logarithm of 1, or 0 bits.

We now note the following crucial point: in moving between the three observers above, the entropy changed from 2 to 1 to 0 bits *without anything having changed about the system itself*. The only thing that reduced the entropy was that the system was viewed by different observers that knew progressively more about the system in Fig. 2. In other words, the 'true' system was always one in which co-activation was ensured and in which there was insufficient excitation for any activity to occur in the first place. The point is that this information was either fully or partially hidden from the first two observers:

***Box 3:** Logarithms*

The logarithm of a number in the form of an exponent such as a^c is equivalent to the product of the exponent c and the logarithm of a, such that $log_b a^c = c log_b a$, where b is an arbitrary base that we omit in the main text.

Furthermore, we can convert to a logarithm with a different base d via: $log_d a = \frac{log_b a}{log_b d}$ where a base 2 yields units of bits.

Observer I: $log_2 4 = log_2 2^2 = 2 log_2 2 = 2$ *bits*

Observer II: $log_2 2 = log_2 2^1 = log_2 2 = 1$ *bit*

Observer III: $log_2 1 = log_2 2^0 = log_2 1 = 0$ *bits*

Entropy quantifies the amount of information about a system that is hidden from an observer.

Spatial connections

Let us now imagine that there are still two neurons as in Fig. 2, but now only one of them can be seen (Fig. 3). If the visible neuron fires, what guess would we make as to the state of the obscured neuron? The answer would depend on how much we know about the strength of the connection between the two neurons, as illustrated with the three observers below:

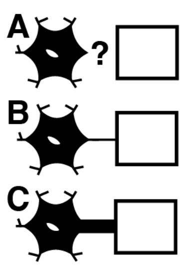


Figure 3: *Two connected neurons in which the left is in the 'on' state and the right is obscured from view (indicated by the blank square).*
A) *Observer IV does not know if the two neurons are connected.*
B) *Observer V knows that the neurons are connected, but does not know how strongly.*
C) *Observer VI knows that the two neurons are sufficiently strongly connected to ensure co-activation.*

Observer IV (Fig. 3A): The fourth observer does not know anything about the connection strength between the two neurons, or even whether they are connected at all. This means that this observer is maximally ignorant and will therefore have to assign a $50/50$ chance to the obscured neuron being either on or off. This is equivalent to saying that the entropy is at its maximum.

Observer V (Fig. 3B): The fifth observer knows a little more than the fourth, in that they know that the two neurons are in fact connected. However, they do not know precisely how strong this connection is. This means that this observer will assign higher odds to the obscured neuron being ‘on’ rather than ‘off’.

Observer VI (Fig. 3C): The sixth observer knows that the connection strength between the two neurons is sufficiently strong to ensure co-activation and therefore assigns 100% odds to the obscured neuron being ‘on’. This is equivalent to saying that the entropy is at its minimum.

Conditional entropy and mutual information

Observers IV, V, and VI illustrate the concept of conditional entropy [34-36], in which we quantify the ignorance of one part of a system, given that we know something about an entirely different part of the system.

The conditional entropy in Fig. 3	$equals$	*How ignorant we are about the state of the obscured neuron*	$given$	*What we know about the connection strength*

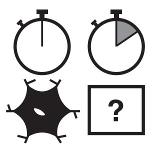
Mutual information [37-41] is a quantity that is related to conditional entropy and it tells us how much an observer’s ignorance of one part of the system is reduced by knowing something about an entirely different part of the system.

The mutual information in Fig. 3	$equals$	*Our ignorance about the obscured neuron*	$minus$	*The conditional entropy in Fig. 3*

Temporal connections

In Fig. 3 we considered the influence that one neuron exerts upon another across space via their connection. However, we can also consider influence across time. For example, if we observe a single neuron firing, we may want to guess that same neuron’s future state (Fig. 4).

Figure 4: *A neuron fires (bottom left). Time passes (stopwatch, top row), after which we make a guess as to the same neuron’s state (question mark, bottom right).*



Consider the following two observers:

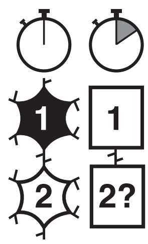
<u>Observer VII:</u> The seventh observer knows nothing about the behaviour of neurons, and as such must assign a $50/50$ chance to the future state of the neuron being on or off. This corresponds to maximum entropy.

<u>Observer VIII:</u> The eighth observer knows the refractory period of the neuron. Therefore, if the amount of time that elapses between observations is shorter than the refractory period, this observer would be certain that the future state will be 'off'. This corresponds to minimum entropy.

Transfer entropy

We will now consider a more complicated situation, in which we track two spatially connected neurons in time. Specifically, we are faced with the following situation: neuron 1 fires and we are asked to guess what the state of neuron 2 is at a future point in time (Fig. 5).

Figure 5: *A connected two-neuron system (left column, middle & bottom rows). Neuron 1 fires (left column, middle row, black). Time passes (stopwatch, top row), after which we make a guess as to the state of neuron 2 (question mark, right column, bottom row).*



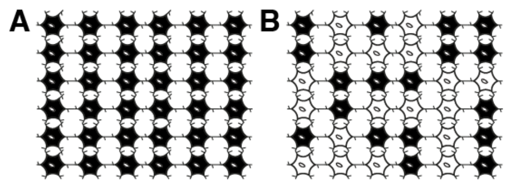
In this case, we would like to know how ignorant we are about the future of neuron 2, given that we know something about both neurons 1 and 2. The probability that we assign to neuron 2 being 'on' at a future point in time depends on what an observer knows about both the spatial properties of the system (e.g., the connection strengths), as well as its temporal properties (e.g., the refractory period). Transfer entropy [42-46] is a measure of how much the present state of one system affects the future state of a different system:

The transfer entropy between neurons 1 and 2 in Fig. 5	$equals$	*Our ignorance of the future state of neuron 2, given knowledge of the present state of neuron 2*	$minus$	*Our ignorance of the future state of neuron 2, given knowledge of the present states of **both** neurons 1 and 2*

Entropy has nothing to do with disorder

Let us zoom out to the point where we can see a network of 6×6 connected neurons. We then imagine taking snapshots of the system at two moments in time: one in which we would say that, from a visual standpoint, the system at first seems ordered (Fig. 6A) and then disordered (Fig. 6B).

Figure 6: *A connected network in which neurons have activated in a seemingly:*
A) *ordered; and*
B) *disordered manner.*



Let us now consider an observer that can only take two possible measurements:

a) All 36 neurons are active;
b) Fewer than 36 neurons are active.

Therefore, the observer only measures case a) for the single system state shown in Fig. 6A. However, the observer measures case b) for every other possible state*. The entropy associated with the ordered configuration in Fig. 6A is therefore lower. However, the order is not the *cause* of the lower entropy — the true cause is the combination of this specific system and observer, which were chosen for illustrative purposes to align with our intuition about visual order. It is perhaps with this type of non-representative example that the myth of entropy as disorder came about.

We can appreciate the fact that entropy has nothing to do with disorder by switching perspective to a different (but equally valid) observer with the ability to distinguish between all 2^{36} possible states for the system in Fig. 6. In this case, there would be no difference in entropy between those states that looked ordered and those that looked disordered — a point that leads us to the distinction between fine and coarse grained entropy.

Fine vs. coarse grained entropy and the second law of thermodynamics

The fact that entropy is a property not just of the system, but of the system *and* the observer, is more clearly highlighted for a continuous system than for the discrete systems we have been dealing with thus far (see Box 4 for the distinction between discrete and continuous systems). Let us therefore consider a phase-space* representation of a neural system, in which neighbouring states are so close to one another that they form a continuous shape [47-55] (Fig. 7A).

<u>Box 4:</u> Discrete vs. continuous states

A discrete state is one that can only take certain fixed values — e.g., the neurons in Figs. 1 through 6 can only be 'on' or 'off', but they cannot be anything in between.

A continuous state, on the other hand, is one that varies smoothly between its possible values — as opposed to the sharp jumps of the discrete states. For instance, if we assign a value of 1 to a neural region that is fully active and 0 to one that is completely inactive, then a continuous state system would allow us to take a measurement with a readout anywhere between 0 and 1.

* 2^{36} (all possible configurations) minus 1 (Fig. 6A)

* Phase space refers to a depiction in which every point represents a possible state of a system — e.g., position and momentum in classical physics fully define the state of a particle.

If we now allow some time to pass, the system's states may evolve such that, instead of the circular region as in Fig. 7A, the states have now been stretched out to the shape shown in Fig. 7B. Previously, in dealing with discrete systems, we defined entropy as the logarithm of the number of possible states that a system can adopt. However, in the case of a continuous system, the definition of entropy is now stated as follows:

The entropy is the logarithm of the volume in phase space

We note that, as the system evolves between the circular (Fig. 7A) and snake-like (Fig. 7B) regions, the total volume in phase space does not change (Liouville's theorem [56]). Therefore, the associated 'fine grained' entropy remains constant, but importantly only for an observer with the theoretical ability to track system states with infinite precision [57] — i.e., one that can resolve every point in the phase space.

We may then wonder how the entropy can remain constant as time evolves between Figs. 7A and 7B, when we know that the second law of thermodynamics states that entropy tends to increase. The solution to this apparent paradox is that in practice there is no such thing as an infinitely precise observer. Regardless of how accurate we are, there will always be some uncertainty due to limitations in resolution, which we can represent by coarse graining the region of interest in phase space (Fig. 7C). It is only then that the volume in phase space (Fig. 7D) and hence the associated 'coarse grained' entropy, increase in time as the observer gradually loses track of the system's states [58-60].

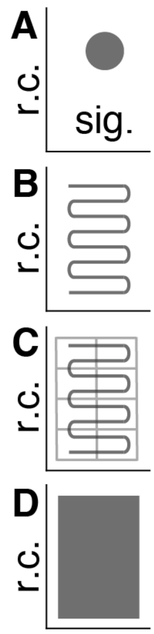


Figure 7: *A neural phase space, in which every point represents the state of a neural region in terms of its signal strength (sig., x-axis) vs. the rate of change of its signal strength (r.c., y-axis), where the signal strength could be measured in e.g., millivolts.*
A) *Every point within the circular region represents a possible state.*
B) *At a later point in time, the allowable states have evolved into the snake-like shape with an area that is equal to that of the circular region in A).*
C) *No matter how well an observer can follow the states, they will never be able to distinguish between points in the phase space that are infinitely close together. Instead, they view the space through a coarse grained 'lens', as shown by the squares — i.e., they cannot resolve two points that lie within one of the squares.*
D) *Following the coarse graining in C), all we can say is that the system states are somewhere within the rectangle, which now has a larger area than the circular region in A).*

In summary, the second law of thermodynamics states that coarse grained entropy increases due to errors compounding for an imperfect observer, not due to a tendency toward 'disorder' or 'randomness' in the system itself.

Why entropy is logarithmic

Having introduced what entropy is (and is not), we may then wonder what is special about the logarithm in quantifying the ignorance of an observer. To understand this, let us outline the three criteria that the entropy must satisfy:

<u>Criterion I</u>: The entropy must be zero when there is only one observable state.

When there is only one observable state then we do not have any doubt as to what the system is doing — i.e., our ignorance is zero. We then note that when the logarithm function has an input of one, it returns an output of zero:

logarithm of 1 observable state = 0 entropy

Therefore, the logarithm satisfies the first criterion, as a single observable state yields an entropy of zero, as required.

<u>Criterion II</u>: The entropy must be maximised when the number of states are also at their maximum.

When the number of states that we can observe is as large as the total number of states that the system can express, then our knowledge is as limited as it can be. To understand why, imagine that we look at the system at some random point in time and that we have no way of guessing what the state will be. In this case, we could observe any of the states in the system's repertoire. It then stands to reason that, if we are maximally ignorant about the system, the entropy will be bounded by the number of states that the system can theoretically adopt.

As long as the input to the logarithm increases, then its output will also increase — this property is known in mathematics as 'monotonicity' [61]. This means that when the number of observable states is at a maximum, then the logarithm of the number of states is also at a maximum:

logarithm of maximum states = maximum entropy

Therefore, the logarithm satisfies the second criterion, in that a maximum number of observable states yields maximum entropy.

<u>Criterion III</u>: The entropy must be 'extensive'.

There are two types of quantities: those that are intensive and those that are extensive.

Intensive quantities do not grow with the size of the system. An example is temperature — combining two systems that are each at a temperature of 1°C does not give a larger system that is at 2°C, rather it gives a larger system that also has a temperature of 1°C.

Extensive quantities on the other hand grow with the size of the system. An example is mass — combining two systems that each have a mass of 1kg gives a larger system that has a mass of 1 kg.

The observer's ignorance is of the extensive type. This is because the more neurons there are, the more potential there is for the observer to lose track of the states. This means that we need the entropy to grow in proportion to the number of neurons in the system being observed.

We know that when there are two neurons then the system can express a maximum of $2^2 = 4$ states (Fig. 2). Similarly, if there are three neurons, then the maximum number of states increases to $2^3 = 8$. In general, we can say that:

$$number\ of\ states = 2^{number\ of\ neurons}$$

The power rule for logarithms (see Box 3) means that:

$$\begin{aligned} log(number\ of\ states) &= log\left(2^{number\ of\ neurons}\right) \\ &= number\ of\ neurons\ \times\ log(2) \end{aligned}$$

Therefore, the logarithm satisfies the third criterion, as the entropy increases proportionally to the size of the system (number of neurons) and hence qualifies as an extensive quantity.

***Box 5**: Entropy from probability distributions*

The entropy S is defined as the negative average of all log probabilities p:

$$S = -\langle logp \rangle$$

where the angled brackets denote an average. Given the definition of the average of a variable $\langle x \rangle = \sum_i p_i x_i$, where p_i is the probability of observing the value x_i, the entropy can also be written as:

$$S = -\sum_i p_i logp_i$$

where p_i is the probability of observing the system in its i^{th} state. In the case of N equally likely states, the probability of observing any individual state is $\frac{1}{N}$. We can therefore write the entropy as:

$$\begin{aligned} S &= -\sum_{i=1}^{N} \frac{1}{N} log\frac{1}{N} = -N\frac{1}{N} log\frac{1}{N} \\ &= -log\frac{1}{N} = logN. \end{aligned}$$

Therefore, the entropy in the case of maximum ignorance is equivalent to the logarithm of the number of states.

Entropy from probability distributions

Let us go back to Fig. 2 and imagine once more that we know nothing about the two-neuron system, other than that it is in principle able to display four states. Given this maximal level of ignorance, all we can say is that there is a 25% chance of observing any one of these four states. This leads us to the following point:

Maximum entropy (ignorance) implies equal probabilities for each possible state.

This is essentially another way of stating Occam's razor [62] — given that we are maximally ignorant about a system, we assume as little as possible [63, 64]. But what happens if we are not maximally ignorant? In this case we can assign different probabilities to the system's states, based on what we know about their relative occurrence. Mathematically, we can express the entropy in terms of the average logarithms of all state probabilities (see Box 5).

Entropy in a neuroimaging experiment

We will now consider a system composed of three neurons (Fig. 8A), the total voltage of which can be measured by a neuroimaging device (Fig. 8B), which in turn displays the measured voltage in the form of a time course (Fig. 8C), which has an associated probability distribution (Fig. 8D).

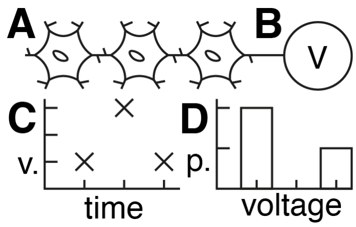


Figure 8: ***A)*** *Three connected neurons* ***B)*** *A voltmeter connected across the three neurons in A) that can determine the total voltage and thus distinguish between 0,1,2, or 3 neurons being on.* ***C)*** *The voltage (v.) measured by the voltmeter in B) (y-axis) for three time points (x-axis).* ***D)*** *The probability (p.) distribution for the time course in C), showing that voltages corresponding to one and three active neurons appear with probabilities $\frac{2}{3}$ and $\frac{1}{3}$, respectively.*

We will now consider the setup in Fig. 8 from the perspective of four different observers and consider the implications and limitations associated with what the associated entropy in each case is telling us.

<u>Observer IX: the theoretically perfect observer viewing the neural system.</u> If we imagine ourselves as an observer with unlimited resolution and access to the laws of motion (see Box 2) of the three neurons in Fig. 8A, then we would always know with certainty in which of the $2^3 = 8$ possible states the system is.

This is just a hypothetical scenario because, as previously noted, there is no such thing as a perfect observer. No matter how careful we are, there will always be some limit to our ability to track the system's states. The only thing of practical value that we can say about the theoretical perfect observer is that 'nature itself' does not lose track — i.e., the distinction between system states is never lost. This is a principle known as the conservation of information [65] and it is perhaps the most basic underlying assumption in all of classical and statistical mechanics.

The entropy for observer IX is 0

<u>Observer X: the neuroimaging device viewing the neural system.</u> The neuroimaging device (Fig. 8B) measures the total voltage across the three neurons (Fig. 8A), such that it can distinguish between the following four cases: a) zero; b) one; c) two; or d) three active neurons. If, for example, the device registers case b), then there are three possible ways in which this could have occurred (Fig. 9).

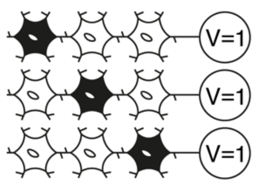


Figure 9: *The three different configurations in which the device in Fig. 8B could register one active neuron in the system shown in Fig. 8A.*

Assuming the three states in Fig. 9 are all equally probable, the entropy of the device in this case is log3, which corresponds to approximately 1.6 bits (see Box 3) — this captures a limitation in the device's resolving power.

The entropy for observer X is 1.6 bits

<u>Box 6</u>: Entropy and re-arrangements

The number of ways W of re-arranging N time points, such that n_1 have a value of '1', n_2 have a value of '2', etc. is given by:

$$W = \frac{N!}{n_1!\,n_2!\,n_3!\,...} = \frac{N!}{\prod_i n_i!}$$

where n_i is known as the occupation number of the i^{th} state. It is then convenient to deal with $logW$:

$$logW = log\left(\frac{N!}{\prod_i n_i!}\right) = logN! - log\left(\prod_i n_i!\right)$$
$$= logN! - \sum_i logn_i!$$

When the time course is long and the occupation numbers n_i are large, we can use Stirling's approximation [1]: $logx! \approx xlogx - x$, such that:

$$logW = NlogN - N - \sum_i n_i logn_i + \sum_i n_i$$

where $\sum_i n_i = N$, which means that:

$$logW = NlogN - \sum_i n_i logn_i$$

We can express the occupation number n_i in terms of the probability p_i of observing a single time point in the i^{th} state according to: $n_i = Np_i$, such that:

$$logW = NlogN - \sum_i Np_i log(Np_i)$$
$$= NlogN - NlogN\sum_i p_i - N\sum_i p_i logp_i$$

where $\sum_i p_i = 1$, and so:

$$logW = -N\sum_i p_i logp_i$$

i.e., $logW$ is the entropy associated with a single time point $-\sum_i p_i logp_i$ multiplied by the total number of time points N, therefore yielding the entropy of the total time course.

<u>Observer XI: the human experimenter viewing the time course.</u> Let us consider the time course (Fig. 8C) created by the neuroimaging device (Fig 8B). We see that the probability of one neuron firing is $\frac{2}{3}$ and the probability of three neurons firing is $\frac{1}{3}$. Recalling Boxes 3 and 5, we see that the entropy associated with this time course is $\left(-\frac{2}{3}log\frac{2}{3} - \frac{1}{3}log\frac{1}{3}\right)$ or approximately 0.9 bits. We then note that this value of entropy arises due to there being three possible ways in which to re-arrange the data points in Fig. 8C such that they form the same probability distribution in Fig. 8D, i.e., three neurons activate once and one neuron activates twice (Fig. 10).

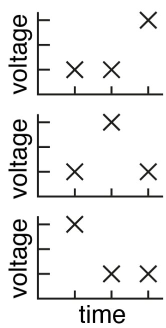


Figure 10: *The three possible ways of re-arranging the time course in Fig. 9A, such that it remains consistent with the probability distribution in* Fig. *9B. In all three cases the* probability of one neuron firing is $\frac{2}{3}$ and the probability of three neurons firing is $\frac{1}{3}$.

See Box 6 for a proof of the equivalence between re-arrangements and entropy.

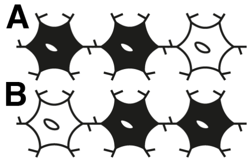
As human experimenters we are subject to a 0.9 bit level of ignorance due to an ambiguity from which we cannot divorce ourselves: there are three equally valid time courses (Fig. 10) that can all account for the same probability distribution (Fig. 8D). As the associated entropy therefore only quantifies the number of ways of re-arranging the data points, we must be cautious when making inferences about the underlying neural system.

The entropy for observer XI is 0.9 bits

Observer XII: the neural system observing itself

Finally, let us consider the entropy from the perspective of the middle neuron in Fig. 8A — i.e., this middle neuron is now the observer of the rest of the system, which consists of its two neighbours to the left and right . Specifically, we will suppose that this middle neuron only fires in response to activity from either its left (Fig. 11A), or its right neighbour (Fig. 11B).

Figure 11: *The middle neuron only fires in response to activity from either **A)** the left neuron; or **B)** the right neuron.*



Assuming that the two configurations in Fig. 11A and B are both equally likely, the entropy according to the middle neuron is log2 or 1 bit. This entropy quantifies how much information about the global system (the left and right neurons in Fig. 8A) is hidden from a local region within the same system (the middle neuron in Fig. 8A). Equivalently, we can think of this entropy as a measure of how accurately the middle neuron in Fig. 8A is able to create an internal model of its immediate environment.

It is here, from the perspective of observer XII, that we finally arrive at a measure of entropy that can in principle be used to quantify the information storage capacity of a neural region. For instance, *in vitro* electrophysiological methods [66-68] may be ideally suited for the task of counting the number of firing patterns in one (transmitting) group of neurons that all trigger the same firing pattern in a different (receiving) group. The logarithm of this number of indistinguishable firing patterns from the transmitting neurons would account for the entropy of the receiving neurons.

The entropy for observer XII is 1 bit

Note that the entropy varies from 0 bits (observer IX), to 1.6 bits (observer X), to 0.9 bits (observer XI), to 1 bit (observer XII), depending purely on the choice of perspective — i.e., with the underlying system itself having remaining unchanged.

Concluding remarks

We have discussed the role of entropy as a representation of the information that is hidden from an observer in the context of neural systems. In our last example, we saw that four different observers can measure four different values of entropy — despite the system itself remaining unchanged. These changes in entropy were brought about purely by shifting perspectives from observer IX (the theoretically perfect observer), to observer X (the neuroimaging device), to observer XI (the human experimenter), and to observer XII (the neural system itself). The purpose of this example was to stress the importance of carefully defining the role and limitations of the observer in question when using entropy in the context of neuroimaging studies.

The line of reasoning that we employed could be applied to a multitude of scenarios within neuroscience, each with a different system-observer relationship. The specific examples analysed here were chosen for being particularly simple to allow for ease of explanation and interpretation. However, in every possible scenario the point would remain the same: entropy measures the information that an observer loses when modelling a system.

We hope that our presented work will serve to help clarify concepts surrounding information theory as used in neuroscience in an accessible way. In addition to illustrating the role of the observer, our intention was to address some common misconceptions that have entered the neuroscience literature — the most prevalent of which is that entropy has something to do with disorder or randomness. Our concern with these misconceptions go beyond the need to be technically correct or to use established semantics. It is our view that being rigorous with definitions of entropy and the precise role of the observer could lead to more informative interpretations of data with richer descriptions of neural systems and less ambiguity in results. It is also possible that a more unified approach to using entropy in neuroscience could lead to theoretical advances in applying new measures of ignorance specifically to the study of the brain.

Boltzmann derived entropy to describe systems that are at thermodynamic equilibrium with their environment. It is therefore possible that, even if the above-mentioned misconceptions are dispelled, the Boltzmann form of entropy may still not be ideally suited to the study of the brain and its substructures. Furthermore, Boltzmann entropy accounts for the ambiguity that arises from multiple indistinguishable rearrangements within a single system (see Box 6). However, when describing the propagation of neural signals, it may be more informative to capture the ambiguity associated with multiple indistinguishable transmissions *between* systems. Going forward, the creation of a formal framework that can capture this type of 'transmission entropy' would create a tailored mathematical foundation of neural information transmission.

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