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Title: Predictive neuronal adaptation as a basis for consciousness.

Authors: Artur Luczak, Yoshimasa Kubo

Correspondence: Luczak@uleth.ca

Affiliation:

Canadian Center for Behavioural Neuroscience; University of Lethbridge, AB, Canada.

Abstract

Being able to correctly predict the future and to adjust own actions accordingly, offers great survival advantage. In fact, this could be the main reason for organisms to evolve their brains. The most mysterious feature of brain activity: consciousness, also seems to be related to predicting the future and detecting surprise: a mismatch between actual and predicted situation. Even at the single neuron level, predicting future activity and adapting synaptic inputs accordingly, is the best strategy to maximize metabolic energy for a neuron. Following on those ideas, here we examine if surprise minimization by single neurons could be a basis for consciousness. First, we show in simulations that as a neural network learns a task, then the surprise within neurons, defined as: difference between actual and expected activity, changes similarly as consciousness of a learned skill in humans. Moreover, implementing adaptation of neuronal activity to minimize surprise at fast time scales (tens of ms), resulted in improved network performance. This improvement is likely due to the fact that adapting activity based on the internal predictive model, allows each neuron for a more “educated” response to stimuli. Based on those results, we propose that: neuronal predictive adaptation to minimize surprise could be a basic building block of conscious processing. This is because, adapting activity toward a predicted level, allows neurons to exchange not only information about stimulus but also about its internal model predictions and thus, to build more complex predictive models. To be precise, we provide an equation to quantify consciousness as the amount of surprise minus the size of the adaptation error. Since neuronal adaptation can be studied experimentally, this allows for directly testing our hypothesis. Specifically, we postulate that any substance affecting neuronal adaptation will also affect consciousness. Interestingly, our predictive adaptation hypothesis is consistent with multiple ideas presented previously in diverse theories of consciousness, such as global workspace theory, integrated information, attention schema theory, and predictive processing framework. In summary, we present a theoretical, computational and experimental support for the hypothesis that neuronal adaptation is a possible biological mechanism of conscious processing, and we discuss how this could provide a step toward a unified theory of consciousness.

Keywords: biological learning algorithms, brain-inspired artificial neuronal networks, neuronal adaptation, theory of consciousness.

1. Introduction

“How does the brain work? Gather enough philosophers, psychologists, and neuroscientists together (ideally with a few mathematicians and clinicians added to the mix) and I guarantee that a group will rapidly form to advocate for one answer in particular: that the brain is a prediction machine” (Seth, 2020). Predictive processing was also suggested to be one of the most promising approaches to understand consciousness (Yufik and Friston, 2016; Hohwy and Seth, 2020). Nevertheless, it is still not clear how predictive processing could be implemented in the brain (Lillicrap et al., 2020), as most of proposed algorithms require a precise network configuration (Rao and Ballard, 2005; Bastos et al., 2012; Whittington and Bogacz, 2017), which could be difficult to achieve, considering variability in neuronal circuits (y Cajal, 1911).

To address this problem, we proposed that single neurons can internally calculate predictions, which eliminates requirement of precise neuronal circuits (Luczak et al., 2020). Biological neurons have a variety of intracellular processes suitable for implementing predictions (Gutfreund et al., 1995; Stuart and Sakmann, 1995; Koch et al., 1996; Larkum et al., 1999; Ha and Cheong, 2017). The most likely candidate for realizing predictive neuronal mechanism appears to be calcium signaling (Bittner et al., 2017). For instance, when a neuron is activated, it leads to higher level of somatic calcium lasting for tens of ms (Ali and Kwan, 2019). As neuron activity is correlated with its past activity within tens of ms (Harris et al., 2003), thus lasting increase in calcium concentration may serve as a simple predictive signal that a higher level of follow up activity is expected. Note that many basic properties of neurons are highly conserved throughout evolution (Kandel et al., 2000; Gomez et al., 2001; Roberts and Glanzman, 2003), therefore a single neuron with predictive mechanism could provide an elementary unit to build predictive brains for diverse groups of animals.

This idea is further supported by a theoretical derivation showing that the predictive learning rule provides an optimal strategy for maximizing metabolic energy of a neuron. The details of derivation are described in (Luczak et al., 2020) and a summary is depicted in Fig. 1. Shortly, E_b represents energy received from blood vessels in form of glucose and oxygen, which is a non-linear function of local neuronal population activity, including the considered neuron j activity (x_j) (Devor et al., 2003; Sokoloff, 2008). E_{ele} represents the energy consumed by a neuron for electrical activity, which is mostly a function of the presynaptic activity (x_i) and respective synaptic weights (w_{ij}) (Harris et al., 2012). A neuron also consumes energy on housekeeping functions, which could be represented by a constant E_h . As described in (Luczak et al., 2020), this formulation shows that to maximize energy balance, a neuron has to minimize its electrical activity (be active as little as possible), but at the same time, it should maximize its impact on other neurons’ activities to increase blood supply (be active as much as possible). Thus, weights have to be adjusted to strike a balance between two opposing demands: maximizing the neuron’s downstream impact and minimizing its own activity (cost). This energy objective of a cell could be paraphrased as the “*lazy neuron principle*”: *maximum impact with minimum activity*. We can calculate such required changes in synaptic weights Δw that will maximize neuron’s energy E_j by using gradient ascent method. As a result, we found that maximizing future energy balance by a neuron leads to a predictive learning rule, where a neuron adjusts its synaptic weights to *minimize surprise*: i.e. the difference between actual (x_j) and predicted activity ($\tilde{x}_j$) (Luczak et al., 2020).

To maximize energy, neuron needs to maximize local blood supply
by activating other neurons, while minimizing own activity:

Maximum impact with minimum cost (lazy neuron principle)

Energy balance of neuron j : $E_j = E_b - E_{ele} - E_h$

energy from local blood flow
controlled by neuronal population activity
energy consumed
on electrical activity
energy consumed
on housekeeping

Predictive learning rule: $\Delta w_{ij} = \frac{\partial E_j}{\partial w_{ij}} \approx x_i (x_j - \tilde{x}_j)$

pre-synaptic
activity
post-synaptic
activity
predicted
activity

Figure 1. Synaptic learning rule derivation by maximizing neuron metabolic energy balance (see main text for details; adopted from (Luczak et al., 2020).

Interestingly, this derived learning rule was shown to be a generalization of Hebbian based rules and other biologically inspired learning algorithms, such like predictive coding and temporal difference learning (Luczak et al., 2020). Thus, this predictive learning rule may provide a theoretical connection between multiple brain-inspired algorithms, and may offer a step toward development of a unified theory of neuronal learning.

The goal of this paper is to show that properties ascribed to consciousness could be explained in terms of predictive learning within single neurons. For that, first we will implement a predictive learning rule in an artificial neural network, and then we will use those simulation results together with biological evidence to propose a predictive neuronal adaptation theory of consciousness.

2. Methods

Implementation of a predictive learning rule in a neural network

To study how properties of predictive learning rule may relate to consciousness processes, we created a recurrent neural network. It had 420 input units, 50 hidden units, and 10 output units as illustrated in Fig. 2A. The network was trained on a hand-written digit recognition task MNIST (LeCun et al., 1998), with 21x20 pixels from center of each image given as input to the network. The details of network training are described in (Luczak et al., 2020). Shortly, first, network is presented with only input signal and activity starts propagating throughout the network till it converges to a steady-state and neurons activity stop changing as

depicted in Fig. 2B. This is repeated for 1600 randomly chosen stimuli. During this phase, we also trained a linear model to predict the steady-state activity. Specifically, for each neuron separately, the activity during twelve initial time steps of the $(x_{(1)}, \dots, x_{(12)})$ was used to predict its steady-state activity at time step 120: $x_{(120)}$ such that: $x_{(120)} \approx \tilde{x} = \lambda_{(1)} * x_{(1)} + \dots + \lambda_{(12)} * x_{(12)} + b$, where $\tilde{x}$ denote predicted activity, λ and b correspond to coefficients and offset terms of the least-squares model, and terms in brackets correspond to time steps (Fig. 1B). Next, a new set of 400 stimuli was used where from step 13 the network output was clamped at values corresponding to image class. For example, if the image of number 5 was presented, then the value of the 5th output neuron was set to '1', and values of the other 9 output neurons was set to '0', and network was allowed to settle to the steady-state. That steady-state was then compared with predicted steady-state activity, which was calculated using the above least-squares model. Then for each neuron, the weights were updated based on the difference between the actual (x_j) and its predicted activity ($\tilde{x}_j$) in proportion to each input contribution (x_i), as prescribed by the predictive learning rule in Fig. 1.

Figure 2. (A) Simplified schematic of our recurrent network architecture. For visualization, only a small subset of neurons is shown. (B) Sample neuron activity in response to a stimulus. Initially the network receives only input signal (bottom blue trace), but after 12 steps the output signal is also presented (a.k.a. clamped phase; bottom black trace). The red dot represents steady-state activity predicted from initial activity (in shaded region). The dashed line shows activity the same neuron in response to the same stimulus if the output would not be clamped (x_F ; a.k.a. free phase), which neuron ‘wants’ to predict. Green insert: synaptic weights (w) are adjusted in proportion ($\propto$) to the difference between steady-state activity in clamped phase (x) and predicted activity ($\tilde{x}$) (adopted from (Luczak et al., 2020)).

3. Results

Neuronal surprise reproduces stages of skill consciousness

The network using predictive learning rule showed a typical learning curve, with rapid improvement in performance in the first few training epochs, and with plateauing performance during later training epochs (Fig. 3A). Notably, this shape of learning curve is also typical for skill learning in humans, where initially at the novice level there are fast improvements, and it takes exponentially more time to improve skills at e.g. elite athlete level (Newell and Rosenbloom, 1981). However, what is new and interesting here, is how surprise: i.e. the difference between actual and predicted activity, evolved during network training (Fig. 3B) and how it compares to the stages of ‘skill consciousness’, as explained below.

It was observed that learning involves the four stages of "conscious competence" (Broadwell, 1969; Das and Biswas, 2018) (Fig. 3C): (1) Unconscious incompetence – where individual does not know what he/she doesn’t know, and thus that individual is not aware of own knowledge deficiencies (e.g. foreigner may not know about certain local traffic regulations). (2) Conscious incompetence – where the individual recognizes own lack of knowledge or skills, but does not have those skills (e.g. a car passenger who does not know how to drive). (3) Conscious competence – where the individual develops skills but using it requires conscious effort (e.g. beginner car driver). (4) Unconscious competence - where due to extensive practice, the individual can perform learned tasks on “autopilot” (e.g. driving car on the same route every day).

Here we illustrate how the above stages of conscious competence could be recapitulated by the network with our predictive learning rule. We used the neuronal surprise as a proxy measure of consciousness, which is motivated by previous theoretical (Friston, 2018; Waade et al., 2020) and experimental work (Babiloni et al., 2006; Del Cul et al., 2007), which will be discussed in later sections. We calculated the surprise for each neuron j as: $\langle |x_j - \tilde{x}_j| \rangle$, where $|\dots|$ denotes absolute value, and $\langle \dots \rangle$ denotes averaged across all 400 images presented in a single training epoch. The neuronal surprise was defined as mean surprise across all of neurons. To better illustrate the network behavior, we plotted accuracy (a.k.a. competence) vs surprise (a proxy of consciousness) (Fig. 3D). Initially, when the network was presented with an input image, the neurons in the hidden layer could almost perfectly predict what will be the steady-state activity after the output units are clamped (Fig. 3B, first few epochs). This is because the network starts with random connections and the signal coming from 10 output units is relatively weak in comparison to the signal coming to the hidden layer from a much larger number of input units: 420. Thus, the steady-state activity which neurons learn to predict when only the input image is presented, it is not much different from the steady-state activity when input image is presented together with clamped outputs. This is similar to the “unconscious incompetence” stage as the network is almost completely “not aware” of the teaching (clamped) signal (Fig. 3D, blue line). However, as the activity of the output neurons is most correlated with any discrepancy

between the actual and the predicted activity in hidden layer neurons, thus the synaptic weights from output neurons are most strongly modified. Consequently, as the learning progresses, the hidden neurons are more and more affected by the output units, and their surprise: discrepancy between actual and predicted activity increases. This is analogous to the “conscious incompetence” where the network becomes “aware” of the clamped teaching signal, but the network did not learn yet how to classify images correctly (Fig. 3D, light blue). In result, as magnitude of surprise $|x_j - \tilde{x}_j|$ increases, then other synaptic weights start also changing more, as follows from the predictive learning rule in Fig. 1. Those synaptic updates make the activity driven by the input image, closer to the desired activity represented by the clamped output units. This could be characterized as “conscious competence”, where the surprise signal allows the network to learn and to become more competent on that task (Fig. 3D, yellow line). Finally, as network learns to predict the image class with high accuracy, then surprise: the difference between predicted and clamped teaching signal is diminishing, which is analogous to an expert who achieved “unconscious competence” (Fig. 3D, green line). This, that the neuronal surprise recapitulates the stages of conscious competence, by first increasing and then decreasing during learning, was a general phenomenon across different datasets and across diverse network architectures (Suppl. Fig. 1).

Figure 3. Neuronal surprise in network with predictive learning rule. (A) Learning curve showing accuracy of the network across learning epochs. (B) Change in neuronal surprise ($|actual - predicted activity|$) averaged over all neurons (see main text for details). (C) Diagram of the four stages of "conscious competence" during skill learning. (D) Neuronal surprise (proxy of skill consci.) vs accuracy (a.k.a. competence) during network learning. This is replotting data from panel A vs panel B, where each point corresponds to a single time epoch. Colors indicate conceivable extent of corresponding stages of "conscious competence" from panel C.

Surprise reduction by neuronal adaptation

Derivation of the predictive learning rule in Fig. 1 shows that the best strategy for a cell to maximize metabolic energy is by adjusting its synaptic weights to minimize surprise: $|x - \tilde{x}|$. However, this change in surprise does not need to take minutes or hours as typically required for structural synaptic modification to occur (Xu et al., 2009). Neurons have adaptation mechanisms, which could serve to reduce surprise at much faster time scale of tens of ms (Whitmire and Stanley, 2016).

Neural adaptation is a ubiquitous phenomenon that can be observed in neurons in the periphery as well as in the central nervous system, in vertebrates as well as in invertebrates (Whitmire and Stanley, 2016; Benda, 2021). Neuronal adaptation can be defined as the change in activity in response to the same stimulus. The stimulus can be a current injection into a single neuron or a sensory input like sound, light, or whisker stimulation. Usually, neuron activity adapts in exponential-like fashion, with rapid adaptation at the beginning and then later plateauing at a steady-state value (Fig. 4A). Typically, neuronal adaptation is shown as the decrease in activity in response to excitatory stimuli. However, neurons can also adapt by increasing its spiking ability when inhibitory stimulus is presented, like e.g. injection of constant hyperpolarizing current (Aizenman and Linden, 1999). Thus, adaptation could be seen as change in neurons activity toward a typical or ‘expected’ level.

To investigate effect of adaptation on neuronal processing, we implemented a brain-inspired adaptation mechanism in the units in our network. For that, during the clamped phase at time step 120, the activity of each neuron was nudged toward predicted state (Fig. 4B). Specifically, activity of neuron j at time step t was calculated as: $x_{j,t} = a * \tilde{x} + (1 - a) * \sum_i (w_{i,j} * x_{i,t-1})$, where $0 \leq a \leq 1$ is a parameter denoting strength of adaptation. For example, for $a=0$ the adaptation is equal to zero and network activity is the same as in original network described in Fig. 2. To update synaptic weights, we used the same learning rule as in Fig. 1: $\Delta w_{i,j} = x_i(x_j - \tilde{x}_j)$, but here we used x_j at time step 140 after activity with adaptation converged to a steady-state (x_A). Interestingly, across variety of network architectures and across different datasets, networks with implemented adaptation achieved better accuracy than the same networks without adaptation (Suppl. Table 1). This could be due to fact that if activity in clamped phase is much different from expected activity (without clamp) then learning may deteriorate as those two network states could be in different modes of the energy function (Scellier and Bengio, 2017). Adaptation may reduce this problem by bringing clamped state closer to expected. To give an analogy, if part of a car is occluded by a tree, then purely on sensory information we cannot say what is behind that tree. However, based on our internal model of the world we know what shape has a car, and thus we can assume that the rest of the car is likely behind the tree. Similarly, neuronal adaptation may allow a neuron to integrate the input information with predictions based on its internal model and adjust its activity based on this combined information leading to a more appropriate response.

Figure 4. Adaptation in neurons and in our model. (A) Cartoon illustration of typical neuronal adaptation in response to constant stimuli. Note that after initial increase, neuronal activity moves closer toward activity level without stimulus. (B) Similarly in our model, adaptation shifts neuronal activity toward activity level without clamp (predicted activity). Insert: We propose to define single neuron correlate of consciousness (sNCC) as neuronal adaptation. Arrows denote that activity adapts toward predicted activity, which approximates activity without clamp.

4. Hypothesis and Theory

Predictive adaptation as signature of consciousness

It is largely accepted that consciousness is a gradual phenomenon (Francken et al., 2021). It was also suggested that even a single cell may have a minimum level of consciousness, based on the complexity of behavior and information processing within each cell (Reber, 2016; Baluška and Reber, 2019). For example, each single cell contains a large network of biochemical interactions allowing it for highly adaptive behavior (Suppl. Fig.2)(Yang et al., 2020). This includes sensing and navigating toward food, avoiding variety of hazards and cope with varying environments (Kaiser, 2013; Boisseau et al., 2016). For instance, single-cell organisms were shown to be able to ‘solve’ mazes (Tero et al., 2010), to ‘memorize’ the geometry of its swimming area (Kunita et al., 2016), and to learn to ignore irritating stimulus if cell’s response to it was ineffective (Tang and Marshall, 2018). Those adaptive behaviors likely require organism to build some sort of internal predictive model of its own place in environment, which could be considered as a basic requirement for consciousness.

The results presented in Fig. 3 suggest that level of consciousness could be related to amount of surprise. This is also supported by results from human EEG studies, where neuronal signature of surprise: P300, closely reflects conscious perception (Del Cul et al., 2007; Dehaene and Changeux, 2011). Here, we propose that in a neuron, adaptation could be seen similarly to P300, as a measure of surprise and thus it could provide estimate of level of “conscious cellular

perception". Specifically, as described above, surprise could be defined as a difference between actual (x) and predicted activity ($\tilde{x}$). Because adaptation changes neurons activity toward a predicted activity level, thus size of adaptation ($|x - x_A|$) is directly related to size of surprise: ($|x - \tilde{x}|$). Thus, we propose to define single neuron correlate of consciousness (sNCC) as magnitude of neuronal adaptation $sNCC = |x - x_A|$, (Fig 4B). Based on this, we hypothesize that single-cell predictive adaptation is a minimal and sufficient mechanism for conscious experience.

Generalized definition of consciousness as process of surprise minimization

First, we will explain the main ideas using a simplified example and later we will present how it can be generalized. Let's have a two-dimensional environment, where at each location P there is certain amount of food. There is also an organism who wants to go to location with the highest amount of food. That organism has only limited information, thus it does not know exactly how much food is at any given location, but based on past experience, the organism has an internal model of the environment to help with predictions. For instance, let's assume that the strongest smell of food comes from the East direction, indicating that most food is at point: P_s , where s stands for sensory evidence (Fig. 5). However, concentration of food in the past was highest in North direction. The internal model combines this information and predicts the highest probability of food in NorthEast direction at point P_p , where p stands for predicted. Based on this, the organism adapts and moves towards P_p to location P_A , where A stands for adaptation. When organism arrives to P_A location, then it can compare actual amount of food at that location with predicted one, and update internal model accordingly if there was a discrepancy. For this example, let's assume that the maximum (m) concentration of food was actually in North-NorthEast direction, at point P_m , which is more to the North than the predicted location (Fig. 5). Thus, by combining sensory information and internal model predictions, our organism was able to appropriately adapt its behavior.

In the above-described case, we could say that our organism was quite conscious of its environment as it made close to optimal decision. We can quantify it by measuring how close to optimal location organism moved: $d(P_A, P_m)$, as compared if it would move in reflex-like fashion to location determined purely by sensory stimulus: $d(P_s, P_m)$, where $d(., .)$ denotes a distance between 2 points. Specifically, we can define organism consciousness of environment as $C_e = d(P_s, P_m) - d(P_A, P_m)$, (Fig. 5, insert). Note, that if an organism has a good model of external environment to correctly predict location with maximum food, then: $P_p \approx P_m$, and thus the first term in C_e : $d(P_s, P_m) \approx d(P_s, P_p)$, where this distance $d(P_s, P_p)$ between sensory evidence (P_s) and model prediction (P_p) is a description of surprise. The second term in C_e : $-d(P_A, P_m)$, describes how far organism is after adaptation (P_A) from location with maximum food/energy (P_m). This could be seen as an error term, which could arise if predictive model is incorrect or if organism is unable to move exactly to predicted location. Thus, according to the above definition of C_e , consciousness is equivalent to surprise, if error term is 0, which would be the case for organism able to perfectly adapt.

Figure 5. Insert: Consciousness (C_e) is defined here as a surprise: distance between obtained sensory information (P_s) and expected information. However, if system can not appropriately adapt that information, then conscious perception is reduced (error term). Expected information is denoted by P_p and it is calculated by internal predictive model, which based on partially available data tries to approximate actual state of the environment (P_m). Thus, term $d(P_s, P_m)$ reflects perfect surprise, when prediction P_p would be exact ($P_p = P_m$). Schematic on the left illustrates concept of C_e for sample organism living in 2D environment (see main text for details).

Although here we used a two-dimensional environment as an example, this can be generalized to high-dimensional sensory space. Let's consider a simple organism which can sense concentration of 10 substances in deep ocean. As organism swims it changes its position in 3D space, but more importantly, concentration of substances indicating location of food and predators also changes with each movement. Thus, 3D space translates to 10D sensory space, which is more relevant to that organism behavior. Therefore, distances d in $C_e = d(P_s, P_m) - d(P_A, P_m)$, may be more appropriately calculated in sensory space of that organism, instead of standard 3D spatial coordinates. For example, this is what we did in case of neurons in Fig. 3 & 4. Neuron senses its local environment through variety of channels located especially in synapses. Activity of a neuron affects other neurons, which through feedback loops change synaptic inputs to that neuron, and thus its sensory environment. Because neuron gets energy from blood vessels which dilation is controlled by coordinated activity of local neurons, thus neuron may 'want' to move in sensory space corresponding to activity patterns resulting in most local blood flow. Therefore, change in neuron activity is equivalent to a movement in chemical sensory space, where different locations in that space correspond to different amount of energy obtained by a neuron. Note that word "environment" in C_e refers to this high dimensional sensory space rather than to typical 3D space.

This generalization to sensory space also allows to see notions introduced earlier in Figs. 3 and 4 as special cases of environmental consciousness C_e . For example, when organism has perfect model of external environment, then it can correctly predict location with maximum food, thus $P_p = P_m$, as we explained before. However, if that organism can also move exactly to predicted location such that: $P_A = P_p$, then also $P_A = P_m$. In such case error term $d(P_A, P_m)$ becomes 0, and thus $C_e = d(P_s, P_m)$. Considering the above case that $P_m = P_A$, C_e can be also

expressed as $C_e = d(P_s, P_A)$, which is a distance by how much organism moved or adapted. Thus, in case of neuron described in Fig. 4, $C_e = d(P_s, P_A) \approx d(x, x_A) = |x - x_A| = sNCC$. Similarly, as mentioned earlier, C_e becomes equivalent to surprise if organism perfectly adapts ($P_A = P_p = P_m$). In such case we can write $C_e = d(P_s, P_p) \approx |x - \tilde{x}|$, which is distance between stimulus evoked activity and model prediction, which we used to quantify skill consciousness in Fig. 3. Thus, C_e is function of surprise and ability of organism to adapt to minimize that surprise.

Hypothesis validation

A hypothesis, by definition, should generate testable predictions. Our main hypothesis is that *neuronal adaptation is a neuronal correlate of consciousness*. This implies that neurons, and thus brains, without adaptation cannot be conscious. Therefore, our hypothesis predicts that any mechanism which affects neuronal adaptation will also affect consciousness.

This prediction was shown to be correct for diverse group of neurochemicals involved in sleep and anesthesia, which also alter neuronal adaptation. For instance, levels of multiple neuromodulators in the brain such as serotonin, noradrenaline and acetylcholine are significantly different between waking and sleep in REM and non-REM stages (España and Scammell, 2011). Whole-cell voltage clamp recordings in vitro in pyramidal neurons demonstrated that all those neuromodulators also affect neuronal adaptation (Satake et al., 2008). Similar results were obtained when testing various substances used for anesthesia, such as urethane (Sceniak and MacIver, 2006), pentobarbital (Wehr and Zador, 2005) and ketamine (Rennaker et al., 2007). Moreover, it was shown that large variety of anesthetics, including butanol, ethanol, ketamine, lidocaine, and methohexital are blocking calcium-activated potassium channels, which mediate neuronal adaptation (Dreixler et al., 2000). Interestingly, considering a broad spectrum of molecular and cellular mechanisms affected by different anesthetic compounds, there remains significant uncertainty what is the single mechanism underlying anesthesia (Armstrong et al., 2018). Our theory suggests that what all anesthetics could have in common it is the ability to disturb neuronal adaptation. Thus, our theory provides clearly testable predictions, which could be (in)validated using pharmacological and electrophysiological methods.

Predictive adaptation as a step toward unified theory of consciousness

Important consequence of a neuron adapting its activity toward a predicted level is that it allows neurons to exchange information about its predictions. Thus, neuron output activity is not exclusively driven by its synaptic inputs, but it is also function of its internal predictive model.

* Connection to optical illusions.

This may explain multiple phenomena linked to conscious perception, such like optical illusions. For example, let's consider a neuron tuned to detect horizontal lines. Such neuron may learn that even when feed-forward inputs are not exactly consistent with a line (e.g. due to partial occlusion), then usually it receives later top down signal indicating detection of a line due to

combining information from other parts of the image by higher cortical areas. Thus, in case of image with illusory contours, this neuron may receive less activation from feed-forward inputs, as parts of line are missing. However, based on experience with occluded objects, that neuron may predict that it will receive soon top-down signals indicating a line, thus in expectation it will increase its activity toward predicted levels. As a consequence, other neurons receiving this predictive information will be even more likely to interpret it as a line, resulting in positive feedback loops and coherent perception of a line.

Similar explanation could also apply in case of ambiguous images like the Rubin vase (face) optical illusion. If a set of neurons in association cortex receive inputs suggesting image of a face, then they will increase their activity according toward that “believe”, triggering a global activity pattern giving a single perception of a face.

* Connection to global neuronal workspace theory.

Described above a large scale neuronal convergence to a single “believe” is very similar to a theory of global neuronal workspace (GNW)(Baars, 2002; Dehaene and Changeux, 2011). Briefly, GNW states that organism is conscious of something, only when many different parts of the brain have access to that information. And if that information is contained only in the specific sensory or motor area, then organism is unconscious of that something. In our theory, consciousness is on a continuous scale. However, if activity is different from expected across many parts of the brain, then our measure of C_e will be also larger as compared to a single brain area, and because the brain is a highly non-linear system, C_e could be orders of magnitude larger when the difference between expected and predicted signal is exchanged in feedback loops across entire brain. Thus, if brain during waking has close to maximum C_e , and low C_e during e.g. sleep, with intermediate values of C_e existing only shortly during transition between those states, then this could reconcile apparent difference between both theories. Note also that according to the GNW theory, a key signature of information accessing consciousness is the P300 component, which as mentioned earlier reflects surprise (Donchin, 1981; Mars et al., 2008). This is similar to our theory where C_e is defined in terms of surprise (Fig. 5). Therefore, taken all together, GNW may be seen as a special case in our theory, with C_e discretized to have only two values.

* Connection to integrated information theory.

Our theory is also consistent with main ideas of integrated information theory (IIT). The IIT quantifies consciousness as the amount of information generated by an integrated complex of elements above and beyond the information generated by its individual parts, which is denoted as Φ (Tononi, 2015; Tononi and Koch, 2015). Similarly, in our case, if two cells can communicate then this will allow each of them to make better predictions and thus to increase combined C_e , by reducing error term: $d(P_A, P_m)$. For instance, if cell #1, just by chance, has more receptors to detect substance $s1$, and cell #2, has instead slightly more receptors for substance $s2$, then by communicating predictions to each other, both cells will be able to better detect food which secretes $s1$ and $s2$ (i.e. the wisdom of crowds (Friedman et al., 2001). This simplified example can be directly extended to neurons, where each has unique pattern of connections, thus providing partly novel information to other neurons. However, there is one important difference

between Φ and C_e . While Φ can be computed purely based on connectivity pattern, C_e depends also on stimulus. If stimulus is unexpected then surprise term $d(P_s, P_m)$ will increase, and thus even without any change in network architecture, organism will be more conscious of that stimuli. However, on average, elements with more complex connectivity patterns, which have higher integrated information Φ will also have higher C_e , as more information sources will be available for each element to improve predictions, thus reducing error term in C_e .

* Connection to attention schema theory.

It was also proposed that consciousness requires building an internal model of incoming information. For example, the brain constructs a simplified model of the body to help monitor and control movements of the body, and similarly it may construct at more abstract level an internal model of attention, which could form basis for consciousness (Graziano and Kastner, 2011; Graziano and Webb, 2015). In our theory, an internal model is likewise a crucial part of defining consciousness. Although our predictive model is at the single-cell level, communication between neurons could allow to form more complex models at the network level. Note that due to neuronal adaptation toward predicted activity, each neuron sends to others information reflecting its internal model predictions. Thus, neurons in higher areas build its internal models based on combining information from other neuron models. This suggest that higher order models like model of attention proposed by Graziano could be a direct consequence of building brain from elements with internal models as described by our theory.

* Connection to predictive processing.

Our theory is most closely related to predictive processing framework. This theoretical framework posits that the brain's overall function is to minimize long-term average prediction error (Hohwy and Seth, 2020). It also proposes that to accomplish it, the brain needs to have a generative model of its internal and external environment and continually update this model based on prediction error (Friston, 2005, 2010; Friston et al., 2017). Our theory is fully consistent with this description. However, our work provides three novel and important contributions to that framework:

(1) We derived mathematically that predictive processing maximizes metabolic energy of a neuron (Fig. 1), which provides biologically-bound theoretical basis for predictive processing framework.

(2) Based on the above theoretical considerations and based on computational simulations, we showed in that a single neuron could be the basic element for building diverse predictive networks (Figs. 2 & 3). This offers solution how predictive processing could be implemented in the brain without need for precisely designed neuronal circuits.

(3) Most importantly, we showed that neuronal adaptation could be the mechanism for conscious processing (Fig. 4), and based on this we proposed quantitative definition of consciousness (Fig.5).

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507

508 **Author contributions**

509 AL conceived the project, analyzed data, performed computer simulations and wrote the
510 manuscript; YK performed computer simulations and contributed to writing manuscript.

511

512 **Competing interests**

513 The authors declare no competing interests.

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References

- Aizenman CD, Linden DJ (1999) Regulation of the rebound depolarization and spontaneous firing patterns of deep nuclear neurons in slices of rat cerebellum. *Journal of neurophysiology* 82:1697-1709.
- Ali F, Kwan AC (2019) Interpreting in vivo calcium signals from neuronal cell bodies, axons, and dendrites: a review. *Neurophotonics* 7:011402.
- Armstrong R, Riaz S, Hasan S, Iqbal F, Rice T, Syed N (2018) Mechanisms of anesthetic action and neurotoxicity: lessons from molluscs. *Frontiers in physiology* 8:1138.
- Baars BJ (2002) The conscious access hypothesis: origins and recent evidence. *Trends in cognitive sciences* 6:47-52.
- Babiloni C, Vecchio F, Miriello M, Romani GL, Rossini PM (2006) Visuo-spatial consciousness and parieto-occipital areas: a high-resolution EEG study. *Cerebral Cortex* 16:37-46.
- Baluška F, Reber A (2019) Sentience and consciousness in single cells: how the first minds emerged in unicellular species. *BioEssays* 41:1800229.
- Bastos AM, Usrey WM, Adams RA, Mangun GR, Fries P, Friston KJ (2012) Canonical microcircuits for predictive coding. *Neuron* 76:695-711.
- Benda J (2021) Neural adaptation. *Current Biology* 31:R110-R116.
- Bittner KC, Milstein AD, Grienberger C, Romani S, Magee JC (2017) Behavioral time scale synaptic plasticity underlies CA1 place fields. *Science* 357:1033-1036.
- Boisseau RP, Vogel D, Dussutour A (2016) Habituation in non-neural organisms: evidence from slime moulds. *Proceedings of the Royal Society B: Biological Sciences* 283:20160446.
- Broadwell MM (1969) Teaching for learning (XVI). *The Gospel Guardian* 20:1-3.
- Das MS, Biswas D (2018) Competence Learning Model. *International Journal of Management, Technology And Engineering*.
- Dehaene S, Changeux J-P (2011) Experimental and theoretical approaches to conscious processing. *Neuron* 70:200-227.
- Del Cul A, Baillet S, Dehaene S (2007) Brain dynamics underlying the nonlinear threshold for access to consciousness. *PLoS biology* 5:e260.
- Devor A, Dunn AK, Andermann ML, Ulbert I, Boas DA, Dale AM (2003) Coupling of total hemoglobin concentration, oxygenation, and neural activity in rat somatosensory cortex. *Neuron* 39:353-359.
- Donchin E (1981) Surprise!... surprise? *Psychophysiology* 18:493-513.
- Dreixler JC, Jenkins A, Cao Y-J, Roizen JD, Houamed KM (2000) Patch-clamp analysis of anesthetic interactions with recombinant SK2 subtype neuronal calcium-activated potassium channels. *Anesthesia & Analgesia* 90:727-732.
- España RA, Scammell TE (2011) Sleep neurobiology from a clinical perspective. *Sleep* 34:845-858.
- Francken J, Beerendonk L, Molenaar D, Fahrenfort J, Kiverstein J, Seth A, van Gaal S (2021) An academic survey on theoretical foundations, common assumptions and the current state of the field of consciousness science.
- Friedman J, Hastie T, Tibshirani R (2001) *The elements of statistical learning: Springer series in statistics* New York.
- Friston K (2005) A theory of cortical responses. *Philosophical Transactions of the Royal Society B: Biological Sciences* 360:815-836.

Friston K (2010) The free-energy principle: a unified brain theory? *Nature Reviews Neuroscience* 11:127-138.

Friston K (2018) Am I self-conscious?(Or does self-organization entail self-consciousness?). *Frontiers in psychology* 9:579.

Friston KJ, Parr T, de Vries B (2017) The graphical brain: belief propagation and active inference. *Network Neuroscience* 1:381-414.

Gomez M, De Castro E, Guarin E, Sasakura H, Kuhara A, Mori I, Bartfai T, Bargmann CI, Nef P (2001) Ca²⁺ signaling via the neuronal calcium sensor-1 regulates associative learning and memory in *C. elegans*. *Neuron* 30:241-248.

Graziano MS, Kastner S (2011) Human consciousness and its relationship to social neuroscience: a novel hypothesis. *Cognitive neuroscience* 2:98-113.

Graziano MS, Webb TW (2015) The attention schema theory: a mechanistic account of subjective awareness. *Frontiers in psychology* 6:500.

Gutfreund Y, Yarom Y, Segev I (1995) Subthreshold Oscillations and Resonant-Frequency in Guinea-Pig Cortical-Neurons - Physiology and Modeling. *J Physiol-London* 483:621-640.

Ha GE, Cheong E (2017) Spike Frequency Adaptation in Neurons of the Central Nervous System. *Exp Neurobiol* 26:179-185.

Harris JJ, Jolivet R, Attwell D (2012) Synaptic energy use and supply. *Neuron* 75:762-777.

Harris KD, Csicsvari J, Hirase H, Dragoi G, Buzsáki G (2003) Organization of cell assemblies in the hippocampus. *Nature* 424:552-556.

Hohwy J, Seth A (2020) Predictive processing as a systematic basis for identifying the neural correlates of consciousness. *Philosophy and the Mind Sciences* 1.

Kaiser AD (2013) Are myxobacteria intelligent? *Frontiers in microbiology* 4:335.

Kandel ER, Schwartz JH, Jessell TM (2000) *Principles of neural science*: McGraw-Hill New York.

Koch C, Rapp M, Segev I (1996) A brief history of time (constants). *Cerebral Cortex* 6:93-101.

Krizhevsky A, Hinton G (2009) Learning multiple layers of features from tiny images.

Kunita I, Yamaguchi T, Tero A, Akiyama M, Kuroda S, Nakagaki T (2016) A ciliate memorizes the geometry of a swimming arena. *Journal of The Royal Society Interface* 13:20160155.

Larkum ME, Zhu JJ, Sakmann B (1999) A new cellular mechanism for coupling inputs arriving at different cortical layers. *Nature* 398:338-341.

LeCun Y, Bottou L, Bengio Y, Haffner P (1998) Gradient-based learning applied to document recognition. *Proceedings of the IEEE* 86:2278-2324.

Lillicrap TP, Santoro A, Marris L, Akerman CJ, Hinton G (2020) Backpropagation and the brain. *Nature Reviews Neuroscience*:1-12.

Luczak A, McNaughton BL, Kubo Y (2020) Neurons learn by predicting future activity. *Nature Machine Intelligence* (in revision), bioRxiv <https://www.biorxiv.org/content/10.1101/2020.09.25.314211v3>.

Mars RB, Debener S, Gladwin TE, Harrison LM, Haggard P, Rothwell JC, Bestmann S (2008) Trial-by-trial fluctuations in the event-related electroencephalogram reflect dynamic changes in the degree of surprise. *Journal of Neuroscience* 28:12539-12545.

Newell A, Rosenbloom PS (1981) Mechanisms of skill acquisition and the law of practice. *Cognitive skills and their acquisition* 1:1-55.

Rao RP, Ballard DH (2005) Probabilistic models of attention based on iconic representations and predictive coding. In: *Neurobiology of attention*, pp 553-561: Elsevier.

- Reber AS (2016) Caterpillars, consciousness and the origins of mind. *Animal Sentience* 1:1.
- Rennaker R, Carey H, Anderson S, Sloan A, Kilgard M (2007) Anesthesia suppresses nonsynchronous responses to repetitive broadband stimuli. *Neuroscience* 145:357-369.
- Roberts AC, Gланzman DL (2003) Learning in *Aplysia*: looking at synaptic plasticity from both sides. *Trends in neurosciences* 26:662-670.
- Satake T, Mitani H, Nakagome K, Kaneko K (2008) Individual and additive effects of neuromodulators on the slow components of afterhyperpolarization currents in layer V pyramidal cells of the rat medial prefrontal cortex. *Brain research* 1229:47-60.
- Scellier B, Bengio Y (2017) Equilibrium propagation: Bridging the gap between energy-based models and backpropagation. *Frontiers in computational neuroscience* 11:24.
- Sceniak MP, MacIver MB (2006) Cellular actions of urethane on rat visual cortical neurons in vitro. *Journal of neurophysiology* 95:3865-3874.
- Seth A (2020) Preface: The Brain as a Prediction Machine. In Mendonça D, Curado M, Gouveia SS, editors *The Philosophy and Science of Predictive Processing*.
- Sokoloff L (2008) The physiological and biochemical bases of functional brain imaging. In: *Advances in Cognitive Neurodynamics ICCN 2007*, pp 327-334: Springer.
- Stuart G, Sakmann B (1995) Amplification of EPSPs by axosomatic sodium channels in neocortical pyramidal neurons. *Neuron* 15:1065-1076.
- Tang SK, Marshall WF (2018) Cell learning. *Current Biology* 28:R1180-R1184.
- Tero A, Takagi S, Saigusa T, Ito K, Bebber DP, Fricker MD, Yumiki K, Kobayashi R, Nakagaki T (2010) Rules for biologically inspired adaptive network design. *Science* 327:439-442.
- Tononi G (2015) Integrated information theory. *Scholarpedia* 10:4164.
- Tononi G, Koch C (2015) Consciousness: here, there and everywhere? *Philosophical Transactions of the Royal Society B: Biological Sciences* 370:20140167.
- Waade PT, Olesen CL, Ito MM, Mathys C (2020) Consciousness fluctuates with surprise: an empirical pre-study for the synthesis of the free energy principle and integrated information theory.
- Wehr M, Zador AM (2005) Synaptic mechanisms of forward suppression in rat auditory cortex. *Neuron* 47:437-445.
- Whitmire CJ, Stanley GB (2016) Rapid sensory adaptation redux: a circuit perspective. *Neuron* 92:298-315.
- Whittington JC, Bogacz R (2017) An approximation of the error backpropagation algorithm in a predictive coding network with local hebbian synaptic plasticity. *Neural computation* 29:1229-1262.
- Xu T, Yu X, Perlik AJ, Tobin WF, Zweig JA, Tennant K, Jones T, Zuo Y (2009) Rapid formation and selective stabilization of synapses for enduring motor memories. *Nature* 462:915-919.
- y Cajal SR (1911) *Histologie du système nerveux de l'homme & des vertébrés: Cervelet, cerveau moyen, rétine, couche optique, corps strié, écorce cérébrale générale & régionale, grand sympathique: A. Maloine.*
- Yang D, Park SY, Park YS, Eun H, Lee SY (2020) Metabolic engineering of *Escherichia coli* for natural product biosynthesis. *Trends in biotechnology* 38:745-765.
- Yufik YM, Friston K (2016) Life and understanding: the origins of “understanding” in self-organizing nervous systems. *Frontiers in systems neuroscience* 10:98.

Supplemental materials

Suppl. Figure 1. Neuronal surprise for convolutional network trained with predictive learning rule on CIFAR-10 dataset. Plot convention is the same as in Fig. 3 in main text. (A) Learning curve. (B) Change in neuronal surprise averaged over all neurons. (C) Neuronal surprise (proxy of skill consci.) vs accuracy (a.k.a. competence). Those results show that convolutional network with predictive learning rule also shows behavior similar to stages of conscious competence.

The details of this convolutional network were described in (Luczak et al., 2020), and code is available at: <https://github.com/ykubo82/bioCHL/tree/master/conv>. Shortly: the network had an input layer of size: 32x32x3, corresponding to the size of a single image with 3 color channels in CIFAR-10 dataset (this dataset consists of 5000 training and 1000 test images for each of 10 classes (Krizhevsky and Hinton, 2009)). The network had two convolutional and pooling layers followed by one fully connected output layer. The filter size for all the convolutional layers is 3x3 with stride 1, and the number of filters is 256 and 512 for first and second convolutional layers, respectively. This network with predictive learning rule achieved test accuracy of 79.97% (chance level: 10%), which is comparable accuracy to training the same network with backpropagation through time algorithm (79.12%) (Luczak et al., 2020).

Network architecture (number of neurons in each layer)	Dataset	Accuracy without adaptation	Accuracy with adaptation
ConvNet: 1024-32-64-2, kernels: 3x3 in 2nd & 3rd layer	CIFAR (2)	92.36%	94.17%
784-1000-10	MNIST	98.02%	98.31%
784-50-10	MNIST	95.03%	96.26%
784-50-10; lateral connections in hidden layer	MNIST	95.08%	96.02%
784-50-10; lateral connections in hidden and output layer	MNIST	94.51%	95.88%

Suppl. Table 1. Comparison of neural network performance with and without neuronal adaptation. To better evaluate difference in performance, we used networks with relatively small number of neurons. This made more difficult for the networks to solve presented tasks, which resulted in easier to see differences in accuracy. To reduce training time needed for convolutional network (ConvNet), we only used 2 classes from CIFAR-10 dataset. To speedup computations we also set $\tilde{x} = x_F$, which is justified by our previous results showing that correlation between $\tilde{x}$ and x_F was $R=1 \pm 0.0001$ SD (Luczak et al., 2020). For all MNIST networks we used adaptation strength $a = 0.1$ and for ConvNet $a = 0.2$. Across different network architectures and datasets, implementing neuronal adaptation improved network performance (best accuracy marked in bold).

Suppl. Figure 2. Sample biosynthetic pathways in *Escherichia coli* [from: (Yang et al., 2020)]. It illustrates complexity of information processing within a single cell.