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A thermodynamical model of non-deterministic computation in cortical neural networks

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Abstract

Neuronal populations in the cerebral cortex engage in probabilistic coding, effectively encoding the state of the surrounding environment with high accuracy and extraordinary energy efficiency. A new approach models the inherently probabilistic nature of cortical neuron signaling outcomes as a thermodynamic process of non-deterministic computation. A mean field approach is used, with the trial Hamiltonian maximizing available free energy and minimizing the net quantity of entropy, compared with a reference Hamiltonian. Thermodynamic quantities are always conserved during the computation; free energy must be expended to produce information, and free energy is released during information compression, as correlations are identified between the encoding system and its surrounding environment. Due to the relationship between the Gibbs free energy equation and the Nernst equation, any increase in free energy is paired with a local decrease in membrane potential. As a result, this process of thermodynamic computation adjusts the likelihood of each neuron firing an action potential. This model shows that non-deterministic signaling outcomes can be achieved by noisy cortical neurons, through an energy-efficient computational process that involves optimally redistributing a Hamiltonian over some time evolution. Calculations demonstrate that the energy efficiency of the human brain is consistent with this model of non-deterministic computation, with net entropy production far too low to retain the assumptions of a classical system.

1. Introduction

To compute the most likely state of the surrounding environment, a cortical neural network must select an optimal system state in the present context from a large probability distribution. Researchers have previously modeled this inherently probabilistic computation with Bayesian statistics [1], random-connection models [2], or Fano factor analysis of spike variance over time [3]. For individual neurons, the Hodgkin–Huxley equations provide a good approximation of firing patterns under steady-state conditions [4]. But channel leak and spontaneous subthreshold fluctuations in membrane potential significantly contribute to the likelihood of a given cell reaching action potential threshold [5–8]. Indeed, the relationship between membrane voltage, ion conductances, and channel activation, given by the Hodgkin–Huxley equations,

is a classical limit that emerges from intrinsically stochastic processes [9–11]. Notably, cortical neurons actively maintain a coordinated ‘up-state’, allowing electrical noise to gate signaling outcomes [12]. Yet despite extensive literature on the statistical randomness of neuronal population coding and interspike variability, the mechanistic basis for achieving inherently probabilistic signaling outcomes across a cortical neural network is not well-understood.

Mean field theory has been usefully employed to model probabilistic coding in cortical neural networks [13, 14]. This methodology allows an exploration of the solution space, leading to the selection of a system state from a probability distribution [15]. At the mean field limit, the network achieves a fixed state, where excitatory and inhibitory contributions are balanced, so that fluctuations dominate the network level dynamics [16, 17]. As a

result, the application of mean field theory has led to a better understanding of the contribution of internal membrane fluctuations to signaling outcomes [18] and how stochastic events shape network-level dynamics [19, 20].

Biological systems gradually achieve a more ordered configuration over time by identifying a more compatible state with their environment, simply by reducing predictive errors [21, 22]. This view, known as the free energy principle, asserts that learning systems strive toward ‘the minimization of surprise’, with new information continually prompting the revision of erroneous priors [23, 24]. Similarly, the concept of ‘free energy’ has been regularly employed in the machine learning field to solve optimization problems through a process of gradient descent [25, 26]. It should be noted however that ‘free energy’ is a statistical quantity, not a thermodynamic quantity, in these contexts. For the past 40 years, researchers have striven to explain computation, in both biological and artificial neural networks, in terms of ‘selecting an optimal system state from a large probability distribution’ [27, 28]. Yet a mechanistic connection between probabilistic computation and energy efficiency has remained elusive.

This report presents a thermodynamic basis for mean-field theory, with the Hamiltonian being modeled not only as a computational quantity but also as an energetic quantity. Modeling cortical information processing as an iterative process of minimizing entropy and maximizing free energy ties together the bio-energetic efficiency of the system with the computational accuracy of the system. In this model, noise drives a non-deterministic computation, with the compression of information entropy paired with a release of free energy, which directly affects signaling outcomes. The extraordinary energy efficiency of the human brain is shown to be compatible with this model.

2. Methods

2.1. A thermodynamic mean field model

A mechanistic process of thermodynamic computation is modeled with a Hamiltonian $\langle H \rangle_t$, which is the sum of all potential and kinetic energies in a non-equilibrium system. The Hamiltonian operates on a vector space, with some spectrum of eigenvalues, or possible outcomes, that can be obtained from a measurement. That measurement provides an exact solution for the Hamiltonian. This computational process resolves the amount of free energy available to the system F_t , which is the total amount of energy in the system $\langle H \rangle_t$ less the temperature-entropy generated by the system TS_t :

$$F_t = \langle H \rangle_t - TS_t. \quad (1)$$

If no time has passed, or no interactions take place, the reference Hamiltonian H_0 is the sum of all

degrees of freedom ξ_i for all probabilistic components of the system:

$$H_0 = \sum_{i=1}^N h_i(\xi_i). \quad (2)$$

If some time has passed, or interactions have taken place, the Hamiltonian H_t of the system can be modeled as the mixed sum of all pairwise interactions:

$$H_t = \sum_{(i,j) \in \mathcal{P}} V_{i,j}(\xi_i, \xi_j). \quad (3)$$

The mean field is then given by:

$$h_i^{\text{MF}}(\xi_i) = \sum_{\{j|(i,j) \in \mathcal{P}\}} V_0(\xi_i, \xi_j) Z_0(\xi_j) \quad (4)$$

where V_0 represents the trace over $V_{i,j}$ and Z_0 represents the trace over $e^{-\tilde{H}/k_B T}$. As the encoding system is perturbed, by interacting with its surrounding environment, the Hamiltonian evolves over time:

$$H_t = H_0 + \Delta H. \quad (5)$$

The Hamiltonian is dependent on an enormous number of contributing parameters. For this reason, it is computationally challenging to identify an exact solution, and variational methods in statistical physics use approximations to do so. Of course, different ‘measurements’ may yield different solutions, with different spectra of eigenvalues. To model this variational outcome, we can employ a trial Hamiltonian:

$$\tilde{H}_t = H_0 + \langle \Delta H \rangle. \quad (6)$$

The original Hamiltonian has the same spectrum of eigenvalues as the trial Hamiltonian. However, the original Hamiltonian differs from the trial Hamiltonian by some positive value, such that:

$$\langle \tilde{H}_t \rangle = \langle H_0 + \langle \Delta H \rangle \rangle = x \langle H_t \rangle. \quad (7)$$

Since:

$$\langle \tilde{H} \rangle_t = x \langle H_0 + \Delta H \rangle, \quad (8)$$

the free energy of the trial Hamiltonian must be greater than or equal to the free energy of the original Hamiltonian. This is known as the Bogoliubov inequality:

$$\tilde{F}_t = \langle \tilde{H} \rangle_t - TS_t \geq F_t = \langle H \rangle_t - TS_t. \quad (9)$$

The computation results in energy being redistributed across the system, with some trial Hamiltonian maximizing free energy availability. That trial Hamiltonian will be thermodynamically favored. Yet the full account must always be balanced—with the total amount of energy in the system, represented by the Hamiltonian, being the sum of all free energy and temperature-entropy.

2.2. The entropy of the system

For a classical thermodynamic system, the macrostate of the system is a distribution of microstates, given by the Gibbs entropy formula. Here, k_B is the Boltzmann constant, E_i is the energy of microstate i , p_i is the probability that microstate occurs, and the Gibbs entropy of the system is given by S :

$$S = -k_B \sum p_i \ln p_i. \quad (10)$$

Yet the behavior of cortical neural networks can be better described as a statistical ensemble of microstates [1, 2]. And so, in this model, the macrostate of the system is formally described as a statistical ensemble of all component pure microstates, given by the von Neumann entropy formula:

$$S(\rho) = -\text{Tr}(\rho \ln \rho). \quad (11)$$

Here, entropy is a high-dimensional volume of possible system states, represented by the trace across a density matrix ρ . ρ is the sum of all mutually-orthogonal pure states ρ_x , each occurring with some probability p_x :

$$\rho = \sum p_x \rho_x. \quad (12)$$

Each component state is described by a state vector ψ_x . For example, the state of each neuron $|\psi_x\rangle$ at time t is uncertain, described as having some probability of switching to an on-state (1) and some probability of remaining in an off-state (0). ρ_x is defined as the outer product of this finite dimensional vector space. The mixed sum of all these component pure states is therefore:

$$\rho = \sum p_x |\psi_x\rangle \langle \psi_x|. \quad (13)$$

The cortical neural network is an open non-equilibrium thermodynamic system (system A), comprised of N units, each described by a state vector ψ_{Ax} , operating within a surrounding environment (system B), comprised of M units, each with a state vector ψ_{Bx} . Each system is described by a density matrix, or a mixed sum of orthonormal pure states. The system and its surrounding environment are initially uncorrelated with each other, and the combined system is created by the tensor product of the two density matrices:

$$\rho_A \otimes \rho_B = \rho_{AB}. \quad (14)$$

Each orthonormal pure state generates a Hilbert space, and any pure states that are identical cannot physically co-exist. Identifying non-distinguishable states (or linear correlations between pure states) will therefore compress the von Neumann entropy of the combined system. Any redundancies are eliminated

during a linear transformation. And so, as the encoding thermodynamic system 'A' is perturbed, by interacting with its surrounding environment, thermodynamic system 'B', the density matrix undergoes a time evolution, from $\rho_{AB} \rightarrow \rho'_{AB}$:

$$\rho_{AB} \rightarrow \rho'_{AB} = \rho(t) = U \rho_{AB} U^\dagger. \quad (15)$$

The unitary change in basis is provided by the time shift operator U :

$$U = e^{-i\hat{H}t}. \quad (16)$$

The time interval is not defined until all component pure states are defined and the trial Hamiltonian is resolved. Only when the unitary change in basis occurs, and the state of the encoding system (the internal state) evolves to match the state of the surrounding environment (the external state), with free energy being maximized, will both the Hamiltonian operator and the time interval be numerically solved.

During this time evolution, correlations are identified between the two particle systems [29, 30]. If the systems are uncorrelated, the states are additive and the total entropy of the combined system remains unchanged. But if any component pure states between the two systems are correlated, entropy will be compressed. Here, entropy is additive in uncorrelated systems, but it is subtractive in correlated systems, as mutual redundancies in system states are recognized and reduced. This process of compression leads to the subadditivity rule:

$$\begin{aligned} S(\rho_{AB}) &= S(\rho_A) + S(\rho_B) \\ &= S(\rho'_A) + S(\rho'_B) \geq S(\rho'_{AB}). \end{aligned} \quad (17)$$

Thermodynamic system 'A' essentially solves a computationally complex problem by identifying correlations with its surrounding environment, thermodynamic system 'B'. An optimal system state in the present context is selected from a broad probability distribution, as information is compressed. The most thermodynamically favored and 'optimal' system state is the one that is both most correlated with the surrounding environment and most compatible with existing anatomical and physiological constraints.

2.3. The free energy of the system

The Helmholtz equation can be used to calculate the net change in free energy over some period of time t . In a thermodynamic system that traps heat to accomplish work, the net change in Helmholtz free energy F_t is equivalent to the enthalpy E_t , less the amount of temperature-entropy TS_t generated over that period of time:

$$F_t = E_t - TS_t. \quad (18)$$

The Helmholtz free energy equation applies in contexts where pressure is not constant, but temperature is, while the Gibbs free energy equation applies in contexts where temperature is not constant, but pressure is. If the overall temperature and pressure of the system remain constant, the change in Helmholtz free energy F_t is equivalent to the change in Gibbs free energy G_t :

$$G_t = E_t - TS_t. \quad (19)$$

The Gibbs free energy of a given neuron is related to its membrane potential:

$$G_t = -nFV_t. \quad (20)$$

Given these relationships, the neuronal membrane potential at time t is given by the trial Hamiltonian, less the temperature-entropy of the system, divided by the Faraday constant F and the quantity of electrons transferred during the computation n :

$$\tilde{V}_t = \frac{\langle \tilde{H} \rangle_t - T\tilde{S}_t}{-nF}. \quad (21)$$

2.4. The neuronal membrane potential

The Nernst equation calculates the temperature-dependent voltage shift in an electrochemical cell at thermodynamic equilibrium, based on the type and quantity of charge moving across the cellular membrane:

$$V_t - V_0 = \frac{RT}{nF} \ln(Q_r), \quad (22)$$

where:

V_t is the electrochemical potential of the cell after some time t has passed (in volts),

V_0 is the starting potential of the cell (in volts),

R is the universal gas constant ($R = 8.314\,472\,\text{J K mol}^{-1}$),

T is the temperature in degrees Kelvin ($T = 310.15\,\text{K}$ under standard conditions),

F is the Faraday constant ($F = 9.648\,53 \times 10^4\,\text{C mol}^{-1}$),

n is the number of electrons that are transferred during the reaction, and

Q_r is the reaction quotient, which defines the equilibrium potential of the reaction.

It is important to note the Nernst equation is specifically used for describing the resting potential of a neuron, not the action potential itself, which is a non-equilibrium process. This equation calculates the likelihood of a neuron firing an action potential upon some perturbation to the resting state (e.g. any event that increases the membrane potential or prompts inward sodium currents). Once the system has shifted away from equilibrium, the action potential goes to completion and the Nernst equation cannot describe

that non-equilibrium process. However, this computational process only affects the resting potential, so these time-dependent perturbations, occurring in the context of thermodynamic equilibrium, can be described by the Nernst equation.

3. Results

3.1. A thermodynamic computation maximizes free energy and drives signaling outcomes

The total entropy of system A and system B, prior to compression, is defined as:

$$S_{\text{total}} := S_0 = S(\rho_{AB}). \quad (23)$$

The net entropy of system A and system B, after compression, is defined as:

$$S_{\text{net}} := S_t = S(\rho'_{AB}). \quad (24)$$

The change in entropy during compression is equivalent to the quantity of correlations identified between system A and system B:

$$\Delta S = S_t - S_0 = S(\rho'_{AB}) - S(\rho_{AB}). \quad (25)$$

The quantity of entropy is *maximized* when the system state is completely random and all non-zero eigenvalues have equal probability p_x . The randomness of information is *minimized* if a more predictable value is identified. In general, the von Neumann entropy of the system is less than maximal when some system states are more likely than others. $S(\rho'_{AB})$ and $S(\rho_{AB})$ reach equality only if no correlations are identified at all. During the time evolution, entropy is reduced, such that:

$$\Delta S \leq 0. \quad (26)$$

The energetic account must always be balanced, with the net amount of energy acquired by the encoding system distributed toward either free energy or entropy:

$$\Delta E = \Delta G + T\Delta S. \quad (27)$$

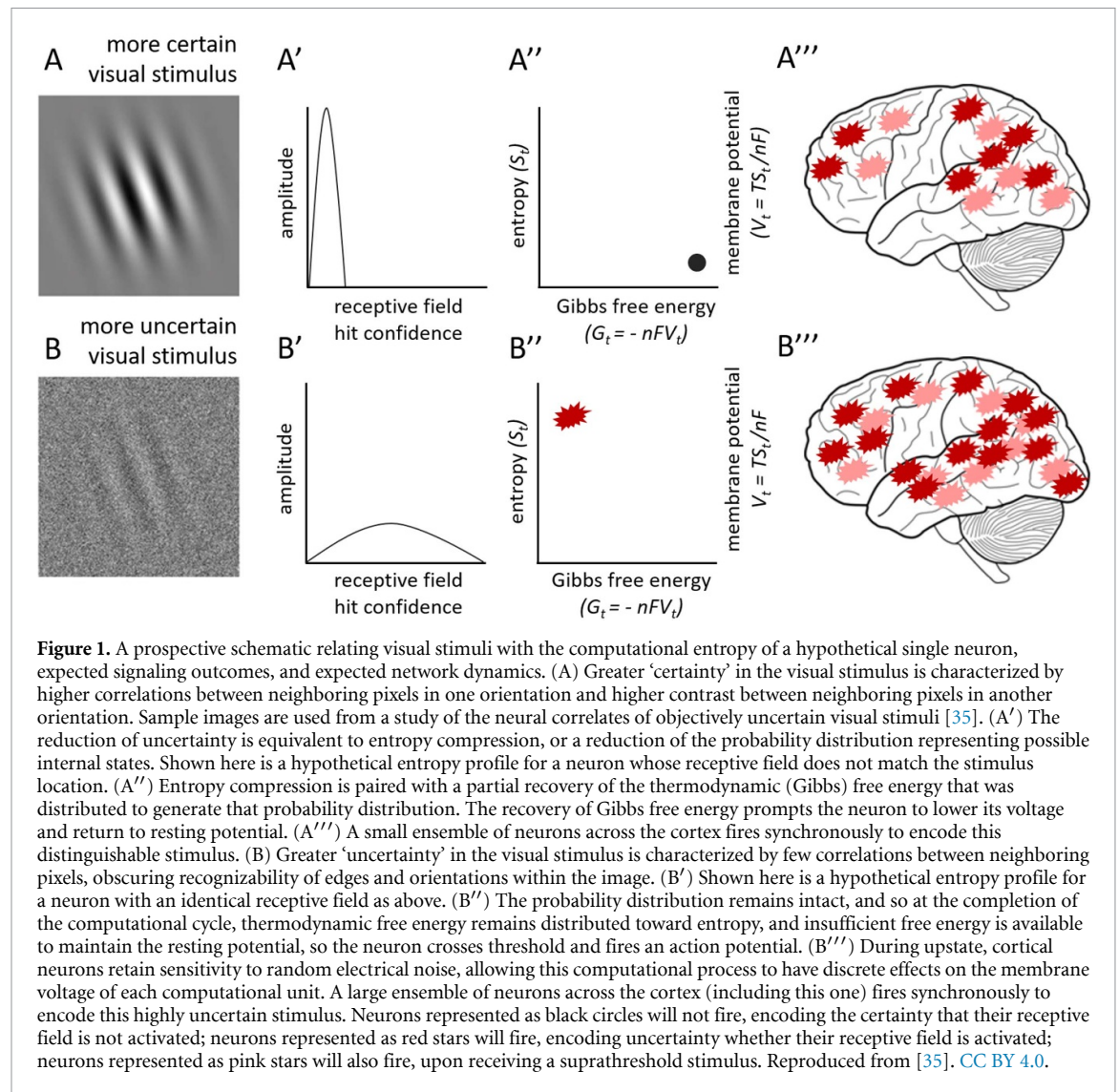
In order to balance the account, any loss of entropy during compression must be paired with a release of free energy, with $\Delta G = G_t - G_0$:

$$\Delta G \geq 0. \quad (28)$$

Since the total energy of the system does not change over the time evolution, these two values are equivalent:

$$-T\Delta S = \Delta G. \quad (29)$$

The compression of information entropy is paired with free energy release. This conservation law is known as the Landauer principle [31–34]. This free



energy is available to do *work*, allowing the system to attain a more ordered state. This *work* involves shifting the resting membrane potential to optimally encode the state of the surrounding environment. This increase in Gibbs free energy, upon information compression, is paired with an decrease in the neuronal membrane potential:

$$\Delta \tilde{V} = -\frac{\Delta \tilde{G}}{nF}, \text{ with } \tilde{V}_t \leq V_t. \quad (30)$$

Information compression locally increases free energy and locally decreases the membrane potential. Neurons which have gained *certainty* during the computation will therefore gain free energy and move further away from action potential threshold, restoring their resting potential. By contrast, neurons which have gained *uncertainty* during the computation will lose free energy and move toward action potential threshold, increasing the likelihood of firing a signal.

In this model, information compression both decreases the distribution of possible system states and increases the amount of thermodynamic free

energy which is available to encode the optimal system state, resulting in the synchronous firing of an ensemble of neurons across the cortex (figure 1). During the computation, the trial Hamiltonian is resolved, energy is redistributed, and the system physically instantiates the solution to a computational problem, by identifying the most likely state of the surrounding environment.

3.2. Estimating net entropy production in the human brain

If the system gains internal heat over time t , then this energy can be distributed toward increasing entropy or increasing the amount of free energy available to do work. Minimizing the amount of entropy therefore leaves more free energy available to do work within the system. Since energy is always conserved, the account must always be balanced, as the trial Hamiltonian is resolved. If the brain does engage in such non-deterministic computation, with a trial Hamiltonian maximizing free energy availability, then the brain should exhibit better-than-classical energy efficiency. The inefficiency of the system, or

the net entropy production, can be calculated using empirical measures. The amount of temperature-entropy $T\Delta S$ produced over time $t = \Delta$ is equal to the net change in enthalpy ΔE less the change in available free energy ΔG :

$$T\Delta S = \Delta E - \Delta G. \quad (31)$$

The enthalpy E is the total heat content of the system. If work is done *on* a system, ΔE is equal to the net change in internal energy of the system ΔU *plus* the net work done on the system ΔW . If work is done *by* the system, ΔE is given by the net change in internal energy of the system ΔU *minus* the net work done by the system ΔW . In the case of reversible changes to the quantities of either volume V or pressure p (non-electrical work), $\Delta W = -V\Delta p$. For a cortical neural network—a far-from-equilibrium thermodynamical system of electrochemical cells, which actively traps energy to accomplish work—the quantity of ΔE is given by:

$$\Delta E = \Delta U - \Delta W. \quad (32)$$

The change in the total heat content of the system ΔE is given by the net energy gained by the system ΔU subtracted by the amount of work completed by the system ΔW over some period of time t . The net energy ΔU is given by the quantity of thermal energy entering the system ΔU_{in} subtracted by the quantity of thermal energy exiting the system ΔU_{out} over time t . Combining equations (31) and (32) yields:

$$T\Delta S = \Delta U_{\text{in}} - \Delta U_{\text{out}} - \Delta W - \Delta G. \quad (33)$$

The net inefficiency of the system, given the temperature-entropy $T\Delta S$, is equal to the net change in internal energy of the system ΔU , less the work done by the system ΔW , less the change in free energy ΔG .

Now that all energy in the system is accounted for, we can calculate values for ΔU_{in} , ΔU_{out} , ΔW , ΔG , and T , to estimate the quantity of ΔS generated by the human brain. The net change in internal energy of the system ΔU is equivalent to the caloric value supplied by the bloodstream to serve the neural network (provided by the energy input ΔU_{in}) minus the amount of excess heat produced during that period of time (provided by the energy output ΔU_{out}). To make a calculation based on neuronal signaling activity only, the change in free energy ΔG can be estimated as the quantity of energy used to set up the resting potential, while the amount of work ΔW can be estimated as the quantity of adenosine triphosphate (ATP) expended on setting up the electrochemical resting potential. Since these quantities are redundant over these timescales, only the work done to accomplish these tasks, ΔW , is accounted here. The quantity of entropy ΔS produced in the human brain over time

t can then be estimated by accounting for the constant overall temperature of the system, T :

$$\Delta S = \frac{\Delta U_{\text{in}} - \Delta U_{\text{out}} - \Delta W - \Delta G}{T}. \quad (34)$$

The energy consumed by the human brain over the course of a day is approximately 20% of oxygen intake and 20% of calories consumed by the body, a value that remains relatively constant regardless of variation in mental tasks or amount of motor activity [36, 37]. In adult males, this energetic usage is approximately 400 kilocalories or 1673.6 kJ per day. This estimated rate of ΔU_{in} is equal to 19.37 J s^{-1} or 19.37 W .

At rest, the human brain has an estimated metabolic rate of $3.5 \text{ ml O}_2/100 \text{ g min}^{-1}$, with venous blood flow removing heat [38]. This rate yields a sustained jugular venous-to-arterial temperature difference of 0.3°C [39, 40]. This value corresponds to an estimated heat production of approximately $6 \text{ J kg}^{-1} \text{ min}^{-1}$ [41, 42]. The rate of ΔU_{out} is therefore estimated to be 0.14 J s^{-1} or 0.14 W .

The amount of energy expended on work ΔW can be estimated by quantifying ATP turnover in the human brain. The quantity of ATP used on signaling processes in rat neocortex has been estimated at $21 \mu\text{mol g}^{-1} \text{ min}^{-1}$ [43], with experimental measurements of total ATP use approximating $30\text{--}50 \mu\text{mol g}^{-1} \text{ min}^{-1}$ [44–47], although estimates vary in both directions [48, 49]. Limiting the estimate to signaling processes only, the ATP turnover in neocortical grey matter (GM) is $0.35 \mu\text{mol g}^{-1} \text{ s}^{-1}$.

Assuming the human brain has a similar rate of ATP turnover to other mammals, the quantity of ATP used on signaling processes in the human brain can be calculated by estimating the total amount of neocortical GM. The size of the human brain by volume is rather variable, with a measured range of $1053\text{--}1499 \text{ cm}^3$ in adult men and $975\text{--}1398 \text{ cm}^3$ in adult women [50, 51]. The quantity of GM is $49.4\%\text{--}58.5\%$ in adult men and $52.1\%\text{--}59.6\%$ in adult women, both averaging 55% [52]. Since the average adult male brain is 1.4 kg [53], the approximate quantity of GM is 770 g , and so the estimated ATP turnover rate in this energetically expensive tissue is 0.27 mmol s^{-1} . In living cells, the hydrolysis of one ATP molecule releases 57 kJ mol^{-1} of energy. Given these values, the GM of the average adult male brain expends ATP on neuronal signaling processes at a rate of 15.36 J s^{-1} or 15.36 W . This is the estimated value of ΔW .

Here, ΔU_{in} is the amount of incoming caloric energy (19.37 J s^{-1}), ΔU_{out} is the heat loss from the system (0.14 J s^{-1}), ΔW is the amount of energy used to set up the electrochemical resting potential (15.36 J s^{-1}), and ΔG is the amount of free energy stored in the neuronal membrane that is released during the action potential. [The latter quantity is negligible at these second-long timescales, because all free energy is eventually distributed toward either

entropy or work.] Each parameter is provided as a rate of energy turnover in Joules per second, or Watts. Equation (34) can be used to calculate the quantity of energy lost to entropy in the human brain every second, given by ΔS . Using the values for each parameter as described above, and a system temperature T equal to 37 °C or 310 K, the value of ΔS over the course of $t = 1$ s can be calculated by substituting values into equation (34):

$$\Delta S = \frac{19.37\text{J} - 0.14\text{J} - 15.36\text{J} - 0.00\text{J}}{310} = 0.012\text{J}. \quad (35)$$

This exercise suggests the human brain is 99.9% energy-efficient, an estimate that corresponds well with other models demonstrating the remarkable energetic efficiency of cortical neurons within the central nervous system [43–49]. The high rate of energetic turnover in these cells should contribute to significant quantities of entropy and heat production, yet this seems not to be the case. There is far too much ordered work happening here. In addition to electrochemical signaling, neurons undergo anabolic metabolism, gene transcription, protein manufacture, post-translational modification, protein transport, and membrane remodeling, all processes which require energetic expenditure. Notably, these activity-dependent tasks maintain the ordered state of the neuron and ensure the physical structure retains an optimal configuration to encode information within the neural network. These non-signaling tasks are not included in the budget for ATP turnover given here, and may further increase the energy expenditure of cortical neurons. In addition, the 45% of brain weight which is not cortical GM is not included in this estimate, contributing to 20% of the total ATP turnover of the brain, or an additional 3.8J s^{-1} . As a result, the total amount of energy expended on performing work appears to exactly match total caloric uptake—leading to the astonishing conclusion that the human brain is nearly 100% energy efficient.

And so, with excellent estimates for caloric intake, heat output, ATP turnover, and temperature—based on empirical data—the quantity of energy expended to complete *work* within the mammalian central nervous system is found to be curiously efficient. As a result of this extraordinary efficiency, the estimated quantity of *entropy* produced by the human brain is far too low to retain the assumptions of a classical system.

It seems highly unlikely that a physical system whose primary job is to process information creates no physical information entropy at all. Usefully, this model shows how a heat-trapping system might cyclically generate and compress information entropy,

recovering free energy as that thermodynamic quantity of information entropy is parsed for *consistency* or correlations with the surrounding environment.

3.3. Predictions

The theoretical model presented here results in an energy-efficient, non-deterministic, system-wide computation. As correlations are identified, and information entropy is physically compressed, the thermodynamic computing system takes on a more ordered state and becomes more compatible with its surrounding environment. This theoretical framework therefore offers a putative mechanistic link between non-deterministic computation and extraordinary energy efficiency in the mammalian brain.

This new framework for modeling non-deterministic computation in cortical neural networks makes specific predictions with regard to the wavelength of thermal free energy released upon information compression [54], and the contribution of these localized thermal fluctuations to network dynamics [55]. This approach also makes specific predictions about the expected effects of electromagnetic stimulation and pharmacological interventions on perceptual content during neural computation [56]. Some further predictions of the theory, prompted by the present model, include:

3.3.1. Cortical neurons should exhibit characteristics of a quantum system

In this new theoretical model, cortical neurons redistribute a Hamiltonian operator to minimize entropy and maximize free energy, with this computational process driving signaling outcomes. This is explicitly a model of quantum computation, with probabilistic coding cyclically generating and compressing quantum information. Certainly doubt has been cast on the hypothesis that the brain is a quantum system [57]. If this hypothesis is true, then empirical measures of Coulomb scattering profiles, decoherence timescales, ionization dynamics and dissipation rates should meet the established criteria for a quantum system. In addition, there should be a demonstrable relationship between thermodynamic quantities, evident in neurophysiological data. The reduction of uncertainty during information compression (a reduction in the distribution of component microstates) should be proportional to the quantity of free energy released. That quantity of free energy released upon information compression should prompt a shift in membrane potential. Specifically, cortical neurons which have gained uncertainty during the computation should lose free energy to entropy and fire an action potential, while

cortical neurons which have gained certainty during the computation will restore their resting potential. In short, the contribution of quantum information processing to signaling outcomes should be measurable.

3.3.2. Cortical neurons should demonstrate exceptional energy efficiency

In this new theoretical model, a cortical neural network selects an optimal system state in the present context from a large probability distribution, in a process of non-deterministic computation. This naturally leads to the compression of information entropy and the release of free energy. If cortical neurons are indeed able to recover the energy that is normally dissipated irreversibly toward the production of entropy, their net entropy production should be well below classical expectations for the amount of work being completed. If cortical neurons do undergo a physical process of non-deterministic computation, then empirical studies should confirm these cells to be significantly more energy-efficient than neurons in spinal reflex circuits, which have purely deterministic signaling outputs. This prediction can be tested by comparing ATP turnover in cells of similar size, with similar firing rates and similar levels of gene expression, protein turnover, and intracellular transport. If cortical neurons are classical computational units, obeying the null hypothesis, then these cells should exhibit purely classical energy efficiency.

3.3.3. Engineered neural networks with the physical properties of a cortical neural network should achieve spontaneous unprogrammed exploratory behavior

One challenge for both organisms and robotics is spontaneously exploring the local environment in search of predictive value, without being explicitly programmed to do so [58]. Recent advances in state-of-the-art robotics have involved introducing a library of robot action primitives, parameterized by arguments which are gradually adopted under a reinforcement learning policy [59]. Yet current robotics rely on classical computing architecture; these are not generalized intelligence systems, and they must be programmed for certain tasks. Even if these systems are programmed to continuously improve their behavior on a given task, through learning and remodeling, they are unable to spontaneously try new tasks. In these classical systems, there is simply no spontaneous acceleration from rest without programmed priors and policies. For example: a robot which has effectively learned how to navigate complex environments with careful steps will not spontaneously search inside a box without explicit prompting, nor will it observe and imitate humans or other robots who do so. There is no curiosity, no spontaneous exploration, and no novel approaches to problem solving. Such generalized intelligent abilities remain out of reach for today's robotics. By contrast, in this

model of quantum computing architecture, energy is periodically redistributed around the system, to achieve highly energy-efficient work at the molecular level in service of goals at the systems level. For this reason, far-from-equilibrium systems that trap *heat* to do *work* can spontaneously explore their environment and gain knowledge about it through this method of non-deterministic computation, by updating the internal state to match the external state. This theoretical framework predicts that computational energy efficiency is deeply tied to generalized intelligence, and one cannot exist without the other. For this reason, computational hardware with similar anatomical and physiological properties to our own brains should exhibit both exceptional energy efficiency and an ability to creatively solve problems.

3.3.4. Engineered neural networks with the physical properties of a cortical neural network should require fewer time and energy resources to solve computationally complex problems

Another challenge for both organisms and robotics is minimizing the time and energy resources utilized while solving decision problems. The system must encode the most likely state of the surrounding environment, using one or more sensory modalities impinging on a layered neural network architecture, then make a decision on the appropriate response in that context. In classical computing architecture, computationally complex problems can be solved through brute force methods [60] or cascading classifiers [61]. Alternatively a large solution space can be explored, with a minimization of energy expenditure achieved through gradient descent [25, 26]. In this model of quantum computing architecture, time and energy are uncertain until these variables are resolved into a mutually compatible state for all computational units within the system. For this reason, this theory predicts that fewer time and energy resources should be needed to solve computationally complex problems using this method of thermodynamic computation. Once again, engineered hardware with similar anatomical and physiological properties should exhibit biologically-comparable time and energy efficiency during decision problems, if the Hamiltonian can be effectively redistributed.

4. Discussion

4.1. Modeling noise in complex systems

Environmental noise and random fluctuations are fundamental components of any complex system, from the microscopic to the macroscopic scale. One of the earliest and most often studied examples is the current-biased Josephson junction, which is a metastable system activated by current fluctuations, with non-monotonic temporal dynamics and superconducting properties [62]. In Josephson junctions, a

cumulative distribution function of switching currents supplies sufficient information to extract a signal from the noise [63]. These findings may be generalizable; the speed and direction of molecular motors depend on the characteristics of noisy inputs, with any changes in the parameters prompting spontaneous flux reversals [64]. By formally extending these models into quantum theory, noise induced stability may be exploited to improve quantum computation and superconductivity at ambient temperatures [65, 66].

General formulations of noise-enhanced stability in complex systems has aided the modeling of biological systems [67] and financial markets [68]. Unsurprisingly, decades of modeling complex systems using inherently probabilistic methods have also uncovered a critical role for noise in cortical neuron dynamics. The effects of random noise contribute to the highly variable inter-spike interval observed in cortical neurons [69]. Noise not only prompts thresholding dynamics (including phase transitions) in individual computational units, but also leads to stochastic resonance, noise-induced synchronization and large-scale oscillations at the systems level [70]. Interestingly, noise-induced resonant activation and noise-enhanced stability is observed in both neural network models [71] and in memristive neural network architecture [72]. External stimuli contribute to these internal dynamics within the human brain; the regularity of spike trains recorded in the auditory system, triggered by the frequency ratio of sinusoidal input signals, correlates with the reported feeling of harmony or disharmony during sound perception [73]. Importantly, the entropy of the cortical neural network is shown to be high with discordant information and low with harmonious information, in agreement with the present model, which proposes that our brains identify correlations within a dataset to drive synchronous signaling outcomes.

Simple models discovered and researched over the past century have also proven to be highly valuable in articulating the fundamental physics underlying self-organization and spontaneous dynamics. The Ising model has been particularly informative. In these lattice structures, the magnetic dipole moment or spin state can be $+1$ or -1 , with neighboring atoms interacting to settle into the lowest entropy state. Any impurities in the ideal lattice structure will spoil this orderly behavior, but only within narrow time and temperature intervals. As dimensionality increases, or time and temperature are scaled, these phase transitions become less predictable, due to the emergence of an exponential error. Yet crucially, these exponents are transitory, permitting error correction during the computation [74].

Exact solutions can be found for Ising models in one or two dimensions. However, Ising models of three dimensions or more, with mixed component structures, are not self-averaging and are therefore

numerically unsolvable [75]. However, these models demonstrate the emergence of a dominant random fixed point, giving rise to stable attractor dynamics through stochastic resonance [76]. So, although no exact solutions can be found for Ising models in three dimensions or more, these systems can be productively described by a locally varying mean field which gives rise to these stable attractor dynamics [77]. The parallels between this literature and the present model are notable; in both, the instantiation of a low-entropy system state is paired with spontaneous rotational symmetry emerging across the system, as the Hamiltonian is resolved and eigenvalues for all component pure states are realized. Indeed, the new model asserts that the resolution of (inherently uncertain) atomic states (provided by the von Neumann entropy of the system) will be paired with the resolution of each neuronal membrane potential.

4.2. Relationship between this model and the free energy principle

While prior efforts used statistical methods to model the inherently probabilistic patterns of cortical neural network activity [1–3, 18], the present model combines the computational and thermodynamic properties of the mean field approach to provide a mechanistic basis for energy-efficient non-deterministic computation in cortical neural networks. This model of neural computation both vindicates and elaborates Friston's free energy principle [21–24], providing a thermodynamic basis for the reduction of 'surprise' during predictive processing.

The minimization of free energy is a general principle that underlies many of the techniques that are commonly used in signal processing and machine learning, particularly for the key tasks of model selection, inference, and local optimization. Similarly, the constrained maximum entropy principle provides a standard approach for the selection of a probabilistic model when the only information available on the quantity of interest consists of statistical averages. Indeed, the maximum entropy principle favors the system to select a probability distribution q which solves an optimization problem. This optimization problem involves minimizing the variational density over external states, parameterized by the distribution of internal states. The constrained maximum entropy principle is therefore equivalent to the free energy principle which posits that, as a system approaches a nonequilibrium steady-state, one can describe its dynamics as minimizing the self-information, or the von Neumann entropy, of its internal states. This model is compatible with the present report.

4.3. A comparison with empirical evidence of entropy production in the brain

A recent study usefully provided data on empirical measures of entropy in the human brain during various tasks. These data can be compared against

the present study's prediction that higher *uncertainty* is associated with greater numbers of neurons firing synchronously across the cerebral cortex [78]. Notably, the authors of this paper show that entropy increases with cognitive demand; a restful state is associated with low entropy, while gambling and motor tasks are associated with high entropy. This finding fits perfectly with the findings of the present study, which demonstrate that high levels of uncertainty should be associated with larger quantities of neurons synchronously firing across the cortex.

Importantly, the authors also demonstrate that a non-equilibrium system will still break detailed balance (thereby producing entropy $S > 0$) even if the state probabilities remain constant in time, as is the case in the Ising system. Furthermore, this study demonstrates there is no need to assume the system is Markovian, as in many neural network models. And indeed, the system under consideration—a cortical neural network engaging in probabilistic coding—is not Markovian, with a stationary transition matrix. It is a continuous stochastic process, with any state change prompted by an exponential random variable: the U-matrix. This system has a finite or countable state space, with dimensions equal to the transition matrix; it has some initial state j and it has some non-negative number of computational units N , each having some probability of transitioning from j to k . The posterior probability, at the completion of a computation, is dependent on the state of the environment, the amount of time that has passed, and the history of system states. It is *not* independent of its environment, it is *not* independent of the amount of time that has passed; and it is *not* memoryless, as in a Markovian process. In short, theory and experiment are well in agreement here.

4.4. A comparison with empirical evidence of energy efficiency in the brain

Another recent study presents valuable data on empirical measures of energy use in the human brain, which can be compared against the estimates of the present study [48]. Critically, this study supports the conclusions of the present study, by empirically demonstrating through quantitative imaging techniques that the human brain is nearly 100% energy efficient. Their conclusion is worth citing at length here: 'An enormous amount of ATP molecules (approx. 5.7 kg) is produced and utilized by the human cortical GM and WM in a single day, which is equivalent to the complete oxidative combustion of 56 g glucose per day (assuming an ATP/glucose ratio of 36); and this ATP consumption amount is almost five times of the total weight of human cortical GM and WM (approx. 1.2 kg). It is clear that the ATP turnover rate in a normal brain has to be extremely high and the majority of the energy generated in the

process is used by the cortical GM with a large population of neuronal cell bodies, dendrites and synapses and high densities of mitochondria and capillary. Such a high energy demand can be only satisfied by extremely efficient ATP production through oxidative phosphorylation in the mitochondria and rapid balance between ATP utilization and production.'

At the cellular level too, the authors' quantitative measures line up reasonably well with the present study. Zhu *et al* state: 'The energy expenditure of a single human cortical neuron was calculated to be 4.7 billion ATPs per second (i.e. 4.7×10^9 ATPs/neuron/s) after correcting the glia cell energy contribution to the total energy expenditure. This value is substantially higher than that of 3.3×10^9 ATPs/neuron/s indirectly estimated for the rat brain [45].' This amount includes all energy expenditure, not just energy expended on signaling processes, but it does not account for white matter. With 86 billion neurons in the human cortex, the authors of this previous study estimate that 0.67 mmol of ATP are used each second. This quantity is substantially higher than our present estimate of 0.27 mmol of ATP used each second (based largely on rat data from Attwell lab). Since the human brain is not expected to accomplish more work (in J) than energy entering the system (in J), these empirical data are likely to converge on a central value with additional measurements and further careful analysis. In any case, theory and experiment are again well in agreement. All published studies indicate the human brain is far more energy efficient than is possible under classical assumptions.

5. Conclusions

The extraordinary energetic efficiency of the central nervous system has been noted, particularly among theorists who query whether this competence is intrinsically linked to the production of information entropy [79, 80] or the exascale computing capacity of the brain [81, 82]. In this report, energy is indeed being expended on the production of information—but rather than being an abstract quantity, or a quantity that is irreversibly lost, this quantity is released back into the system as free energy as information is physically compressed, in accordance with the Landauer principle.

This approach models how cortical neural networks produce entropy in a thermodynamic sense, then evaluates whether information processing emerges from such a lean assumption. Indeed, all thermodynamic systems must create entropy, with that quantity related to the pressure, temperature, density, and volume of the system. If a hot, dense, non-heat-dissipating system appears to be nearly 100% energy-efficient, *and also exhibits extraordinary computational power*, the sensible logic is *not* that entropy is not being produced at all, but rather that

correlations are being extracted and entropy is being compressed, in accordance with physical laws.

This report demonstrates that information generation and compression can occur in far-from-equilibrium systems, with the system naturally encoding the likely state of its surrounding environment, as it takes on a more ordered state over time. As encoding system A interacts with its surrounding environment, system B, the trial Hamiltonian is resolved through a unitary change in basis. Entropy is additive if the systems are uncorrelated, but subtractive if the systems are correlated (that is, if the internal state matches the external state). And so, as the encoding system becomes correlated with its surrounding environment, the total entropy of the combined system is compressed. Yet some uncertainty or entropy will always remain at the completion of each thermodynamic computing cycle, respecting the second law of thermodynamics: the quantity of energy entering the system places a hard limit on the amount of entropy that can be generated, and the quantity of entropy generated places a hard limit on the amount of compression that can occur. Perfect energy efficiency would imply a perfect correlation with the surrounding environment, and so continued operation of the system within a changing environment requires continued uncertainty. However, the quantity of entropy is minimized during the computation, as signals are extracted from the noise and an optimal system state is selected from a large probability distribution.

This study shows a mechanistic connection between probabilistic coding and computational energy efficiency in cortical neural networks. Moving forward, exploring the exact relationship between energetic efficiency and non-deterministic computation may prove useful to the fields of neuroscience, machine learning, and physics.

Data availability statement

All data that support the findings of this study are included within the article (and any supplementary files).

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