

Energy as a constraint on the coding and processing of sensory information

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Neurons use significant amounts of energy to generate signals. Recent studies of retina and brain connect this energy usage to the ability to transmit information. The identification of energy-efficient neural circuits and codes suggests new ways of understanding the function, design and evolution of nervous systems.

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Abbreviation

SNR signal-to-noise ratio

Introduction

The analysis of constraints — the physical, chemical and biological factors that limit performance — is central to our understanding of physiological systems. For example, detailed studies of the biophysical, biochemical and biomechanical constraints on gas exchange, blood supply and limb movement have revealed both purpose and design in lungs, vascular systems, muscles and limbs [1,2].

In retina, the ability to code pictorial detail is constrained by optical blur, photon catch, neural noise, and the amplitude and speed of neural responses. Neural responses have been shown to fit optimisation models that maximise the uptake of pictorial information within these constraints [3,4]. Thus, the analysis of constraints proves that the retina is designed and engineered precisely for a well-defined purpose: that is, the efficient uptake of information from natural scenes over the daily range of light levels [5–8].

The supply of metabolic energy constrains the growth and function of many organs, including sensory organs and the brain. For example, the human brain takes 20% of the resting metabolic rate [9], and comparative studies suggest that the amount of energy used by the mammalian brain has limited its size [10,11]. In addition, the reduction of eye size in bats and subterranean animals indicates that vision makes significant demands upon resources, including energy [12].

Here, we review recent developments in our understanding of the relationship between neural energy consumption and neural processing. Analyses of synapses, action potentials and other signalling mechanisms confirm that nervous systems use much of their energy to generate and propagate neural signals. Biophysical studies show that the energy used for signalling constrains the flow of information within

and between cells. Consequently, theory and experiment are identifying energy-efficient neural codes and circuits. Thus, a better understanding of energy usage offers considerable insight into the design and evolution of sense organs and brains.

The impact of energy demands on supply

Although data are limited, brains and retinas can have a large impact on energy supply. At just 2% of body mass, the human brain consumes 20% of resting metabolic energy [9], and the brain of an electric fish may consume 60% [13]. Blowfly photoreceptors take 8% of resting oxygen consumption [14], and their specific metabolic rate (rate per gram) exceeds that of most striated muscles [15].

The rabbit retina's specific metabolic rate is higher than that of its brain, because the large currents generated in rods and cones give them a specific metabolic rate that is equal to muscle. Mammalian retina operates at and beyond the limit of its oxygen supply [16,17*], suggesting that the retinal vasculature is reduced to preserve the clarity of the retinal image.

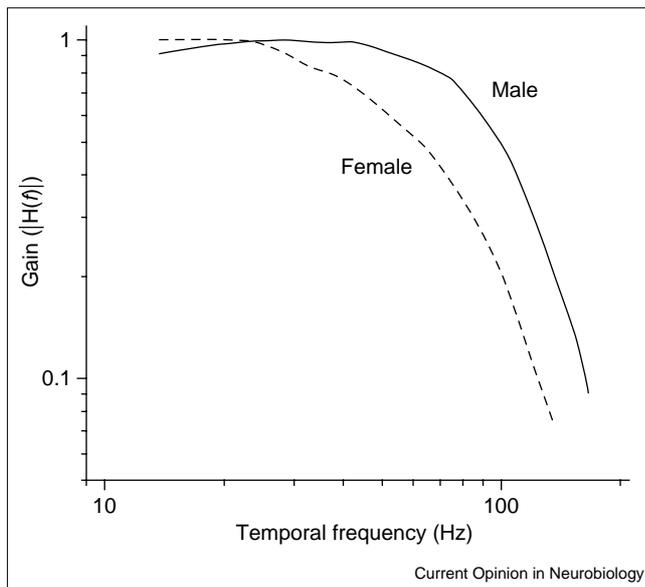
Energy usage and neural function

The high metabolic rate of brain and retina is the product of neural activity. Every signalling event uses energy, and neurons are constantly active and densely packed. Experimental data on the distribution of energy consumption among known cellular mechanisms, and their contributions to total usage, are incomplete, but the following conclusions can be drawn [9,17*].

For mammalian brain, 50% of the total energy consumption is associated with signalling, and recent studies in NMR spectroscopy, which associate energy usage with neural function by following the turnover of identified metabolites and neurotransmitters, suggest that signalling accounts for 80% of the total consumption in cortex [18,19]. This signalling cost is dominated by the activity of the Na^+/K^+ pumps, which, like mitochondria, are concentrated in axons and at synapses [20,21]. The signalling cost of recycling second messengers and neurotransmitters is less than 10%.

After subtracting 50–80% of total consumption for signalling, the remainder is the fixed cost of manufacturing and maintaining the brain. Maintaining resting potentials and counteracting leakage from organelles accounts for less than 15% of the total consumption, and the turnover of macromolecules is approximately 5% of the total. Mitochondrial proton leak [22] and axoplasmic transport could be significant but are not accounted for. Rabbit

Figure 1



Regulating bandwidth to suit functional requirements. The photoreceptors of male houseflies have a higher bandwidth (a better response at high frequencies) than those of female flies. Gain, a measure of the amplitude of the response to a sinusoidally flickering light, is plotted against the frequency of flicker. The male photoreceptor's superior response to high frequencies enables him to track faster-moving targets. This ability will improve his chances of intercepting females during the aerobic courtship pursuit [30*].

retina exhibits a similar pattern of signalling and fixed costs, with a higher energy usage for second messengers involved in phototransduction [16].

A new indirect method, which constructs 'bottom-up' energy budgets, gives a comprehensive breakdown of the signalling costs [15]. Taking biophysical and biochemical measurements of membrane conductance and transmitter release, one calculates the numbers of ions and molecules that are used to generate signals in known components such as synapses, dendrites and axons. These numbers define energy usage in terms of the ATP that must be hydrolysed to maintain ionic concentration gradients and recycle signalling molecules.

Multiplying usage in each component by the numbers of components involved (known from quantitative anatomy) gives the total energy consumption. This total is checked against measured values to validate the budget. The budget for blowfly retina [15] confirms that the reversal of ion fluxes by the Na^+/K^+ pump dominates signalling costs. Note that ion channels are often the last stage of an amplification process, such as in sensory transduction, axonal transmission and synaptic transmission.

A 'bottom-up' budget has been made for cortical grey matter (D Attwell, SB Laughlin, unpublished results). The high signalling cost in cortex is dominated by two

processes: action potential propagation along axon collaterals and postsynaptic current (SB Laughlin, D Attwell, abstract in *J Physiol* 2000, 525P:61P). Resting potentials account for less than 15% of the total energy consumption, whereas the cost of transmitter recycling is less than 5%. With the cortex devoting most of its energy consumption to sending signals across numerous and wide-ranging connections, the economical wiring patterns that reduce brain volume [23,24] must make a significant contribution to energy efficiency.

Energy consumption, signal quality and information

Energy usage is tightly coupled to neural performance. Basic biophysics links energy usage to two fundamental measures of signal quality: signal-to-noise ratio (SNR) and bandwidth (a measure of speed of response) [25,26]. Extra energy is required to improve the SNR because reliability increases as the square root of the number of stochastic events that are used to generate signals. Each stochastic signalling event, such as opening an ion channel or releasing a synaptic vesicle, requires extra energy. Raising the bandwidth also requires extra energy. The membrane time constant must be reduced by increasing conductance and this increases the flow of ionic current.

Sarpeshkar [26] made the first important step in understanding the design of energy-efficient neural circuits by extrapolating the fundamental relationships between noise, bandwidth and cost in electronic chips to cortical neurons. More recently, White *et al.* [27*] showed that the noise generated by ion channels severely degrades the performance of neural circuits. Any set of neural operations requires an adequate (and often large) number of channels and hence a certain amount of energy.

Economising on SNR and bandwidth

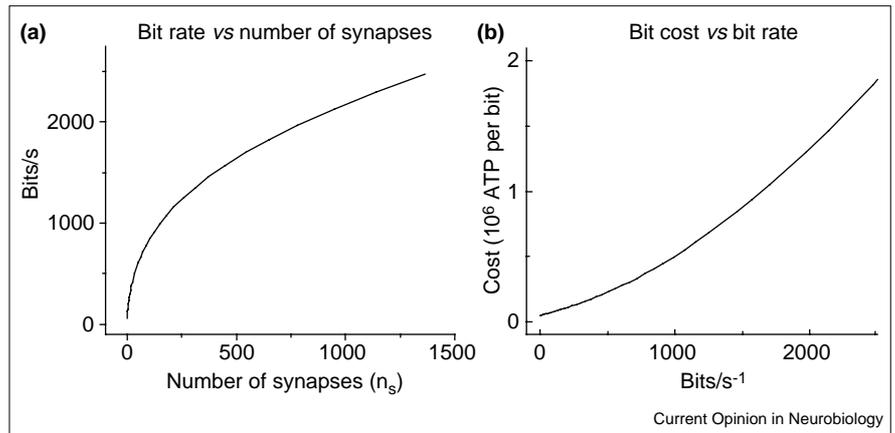
Minimising the SNR and bandwidth will save energy. There is growing evidence that sensory receptors and neurons economise by restricting the SNR and bandwidth to the minimum required to get the job "done just right-enough" [28]. In blowfly retina, colour-coding interneurons use fewer synapses than their neighbouring contrast-coding cells. This is efficient because colour signals have a poorer SNR [29].

In different species of Diptera, photoreceptor bandwidth is adjusted to fulfil behavioural requirements for better temporal resolution [25]. This adjustment has been observed recently in a single class of photoreceptor in one species. In houseflies, the contrast-coding R1-6 photoreceptors of the male have a 60% higher bandwidth and conductance than those of the female (Figure 1). The faster response helps males to track and intercept small and rapidly moving targets — that is, females [30*].

In male blowfly, the bandwidth and conductance of R1-6 photoreceptors decreases by 20% from the front to back of

Figure 2

Increasing the number of synapses that code a signal increases both the rate at which information is transmitted, the 'bit rate', and the metabolic cost of a bit, given as the number of ATP molecules hydrolysed. The curves are calculated for blowfly photoreceptors transferring a naturalistic signal to an identified interneuron via different numbers of output synapses (the blowfly uses roughly 1300). The calculations of bit rate are based on measurements of synaptic signal transfer and noise [31]. A single synapse transmits at a low rate – 55 bits/s – because its signal is badly contaminated by synaptic noise, probably from vesicle release. Transmitting the same signal across many parallel synapses improves the SNR, leading to higher bit rates. As expected from information theory, the rate does not increase linearly with the number of synapses because, with many synapses transmitting identical signals, the system is highly redundant. Redundancy greatly increases the cost per bit. The cost of synaptic transmission is calculated in a 'bottom-up' energy budget [15].



the retina (BG Burton, B Tatler, SB Laughlin, abstract in *J Physiol* 2000, 527P:95P). Apparently, the need to economise on energy usage is sufficiently strong to fine-tune bandwidth within a population R1-6 cells.

SNR, redundancy and the cost of information

Signal-to-noise and bandwidth determine the rate at which information is transmitted [31]. Increasing the SNR raises both the bit rate and the energy cost per bit, as demonstrated (Figure 2) by modelling the analogue transmission through identified and well-characterised synapses [15]. Bit rate climbs more slowly than the number of synapses, giving rise to the increase in cost per bit (Figure 2). The slow climb of the rate is symptomatic of a fundamental inefficiency in information transmission — that is, 'redundancy' (Figure 2).

Modelling shows that redundancy has a similar effect on the relationship between the number of synapses driving a spike train and the information that is encoded [32]. Thus, whenever synapses are added to boost bit rate, one expects an increase in cost per bit. This relationship penalises excessively high bit rates, especially in single neurons. It is more economical to transmit at high rates by dividing information into separate components, each transmitted by a lower rate neuron [15].

Energy, information, spikes and efficient codes

Bit cost tends to increase with bit rate when single axons transmit information in spike trains, because the number of bits per action potential falls as the frequency of action potentials increases [32,33]. Spike coding is costly. Over short distances, spike transmission is, bit for bit, as expensive as analogue transmission [15]. Furthermore, the generation of spikes changes the relationship between

energy and information. New sets of ionic currents generate new forms of code. Spike coding can threshold out the synaptic noise that accumulates in networks, so reducing a major constraint on computation [26,28].

A theoretical cost–benefit analysis of the competing constraints of energy, noise and bandwidth in electronic devices has demonstrated an optimum mix of analogue and spike signals that resembles the integration of analogue inputs by spiking cortical neurons [26]. Analysing the competing constraints of energy and noise in cell signalling and neural transmission is a promising approach [34,35] that can be extended to consider spatial constraints and the need for computation.

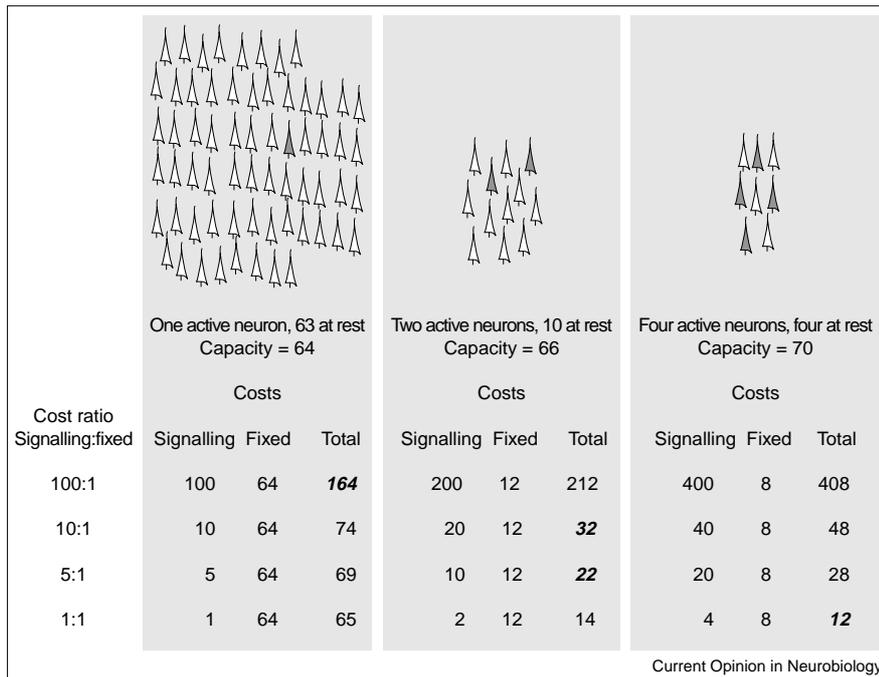
Optimisation models derive energy-efficient codes

Energy-efficient neural codes increase the ratio between the information coded by neurons and the energy involved [36]. The ability to represent information depends on the number of recognisably different patterns of spikes that can be generated in a useful time interval. This number — the 'representational capacity' — is a fundamental measure of neural performance. It defines the number of situations and actions that neurons can specify, and is closely related to the number of bits coded [36].

For a train of spikes in a single neuron, the optimum energy-efficient code minimises the number of spikes used to code a given quantity of information, or maximises the information coded by a given number of spikes.

The Boltzmann distribution, which maximises the entropy at a given mean energy, fulfils this condition and

Figure 3



Energy-efficient coding. The representational capacity of a group of neurons depends on the total number of neurons in the group and the number of neurons in the group that are active. For a simple binary scheme in which a neuron is either ON (active) or OFF (at rest) the representational capacity is the number of ways of arranging A active neurons in a group of N cells, given by $M/[A!(N - A)!]$. In these three populations of neurons N and A have been set to give similar capacities. In each case the cost of coding is given by N (fixed cost) + A (signalling cost). For simplicity, the fixed cost is set to 1, and the signalling is expressed as a multiple of the fixed cost. For the unrealistically high ratio of signalling to fixed cost of 100:1, the large group with a single active neuron (a grandmother cell) is cheapest. As one moves towards more realistic ratios of signalling to fixed cost, the size of the most economical group decreases and the number of active neurons increases. Thus, the sparseness of an energy-efficient code depends on the balance between signalling and fixed costs [36]. Figure based on unpublished results (D Attwell, SB Laughlin).

predicts an exponential distribution of spike rate, as observed in some cortical neurons responding to natural stimuli [37,38*]. Adding that ever-present constraint, noise, the optimum code depresses the use of low rates because they are less reliable. This noise-limited optimum distribution is recorded in retinal ganglion cells and in some cortical neurons [38*]; and G Garcia de Polavieja, personal communication).

Sparse coding, in which information is represented by the activity of a small proportion of neurons in a population [39], greatly increases energy efficiency [36]. The optimum distribution of activity depends on the ratio between the signalling cost of making a spike and the fixed cost of maintaining a neuron in readiness to spike. When spikes are expensive and the fixed cost is negligible, a 'grandmother neuron' code [39] is cheapest. This code associates each unique event with a single active neuron (Figure 3, left panel).

Tipping the balance from signalling costs towards fixed costs makes inactive neurons increasingly wasteful. An energy-efficient system reduces the number of neurons involved and maintains representational capacity by increasing the number of active cells (Figure 3). Consequently, the sparseness of the optimum energy-efficient code depends on the ratio of signalling to fixed costs [36]. When fixed costs are high and spikes are effectively free, the number of neurons must be minimised and representational capacity is maintained by maximising the information coded per neuron [36].

Conclusions

Brains and sense organs use significant quantities of metabolic energy to process information. This usage constrains function and penalises excessive synaptic connections, excessive lengths of connection, and the use of excessive numbers of ion channels (S Schreiber, CK Machens, AVM Herz, SB Laughlin, unpublished results).

A 'bottom-up' budget suggests that spike propagation in the cortex is particularly demanding. How much do mechanisms that reduce both the numbers of spikes used and the distances they travel — such as transient responses, opponent receptive fields [40,41] and economical wiring patterns — contribute to energy efficiency? Energy usage is tightly coupled to SNR and bandwidth. This linkage penalises over-investment, which leads to regional differences in receptor performance. With energy-demanding specialisations for time resolution [42], and higher than average specific metabolic rates [9], are auditory pathways designed to use energy efficiently?

Theoretical studies are making strong predictions about energy efficient circuit designs and spike codes. In particular, action potentials can improve efficiency by reducing noise in complicated networks, and appropriate distributions of action potentials in spike trains and in sparse representations give energy efficient codes. These predictions broadly resemble properties of cortical circuits and codes but more experiments are required to test these strong theories. Finally, can many of the adaptations of form to function found in sensory systems be explained by weighing the

energetic costs of gathering information against the contributions to fitness made by sensory information?

Update

Vijay Balasubramanian and Michael J Berry (personal communication) have recently recorded from ganglion cells in salamander retina. They find that the distribution of spike rate follows the theoretical prediction for a metabolically efficient code [38*] remarkably well. This important study provides the strongest evidence to date that spike codes have evolved to be metabolically efficient. It also supports the proposition that the number of retinal ganglion cells is limited by metabolic and vascular constraints.

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