

Neurobiology as Information Physics

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8 **Abstract**

9 This article reviews thermodynamic relationships in the brain in an attempt to consolidate current
10 research in systems neuroscience. The present synthesis supports proposals that thermodynamic
11 information in the brain can be quantified to an appreciable degree of objectivity, that many
12 qualitative properties of information in systems of the brain can be inferred by observing changes in
13 thermodynamic quantities, and that many features of the brain's anatomy and architecture illustrate
14 relatively simple information-energy relationships. The brain may provide a unique window into the
15 relationship between energy and information.

16 **Introduction**

17 That information is physical has been suggested by evidence since the founding of classical
18 thermodynamics (J Gleick 2011; S Lloyd 2006). In recent years, Landauer's principle (CH Bennett
19 2003; R Landauer 1996), which relates information-theoretic entropy to thermodynamic information,
20 has been confirmed (JMR Parrondo et al. 2015), and the experimental demonstration of a form of
21 information-energy equivalence (A Alfonso-Faus 2013) has verified that Maxwell's demon cannot
22 violate any known laws of thermodynamics (K Maruyama et al. 2009). The theoretical finding that
23 entropy is conserved as event horizon area is leading to the resolution of the black hole information
24 paradox (P Davies 2010; C Moskowitiz 2015), and there is a fundamental relationship between
25 information and the geometry of spacetime itself (R Bousso 2002; C Eling et al. 2006). Current
26 formulations of quantum theory are revealing properties of physical information (Č Brukner and A
27 Zeilinger 2003; S Lloyd 2006; V Vedral 2010; J Wheeler 1986), and information-interpretive
28 attempts to show that gravity is quantized (JW Lee et al. 2013; L Smolin 2001) could even lead to the
29 unification of quantum mechanics and the theories of relativity. Although similar approaches are
30 increasingly influential in biology (JL England 2013; JC Flack 2014; ED Schneider and D Sagan
31 2005), "a formalization of the relationship between information and energy is currently lacking in
32 neuroscience" (G Collell and J Fauquet 2015). The purpose of this article is to explore a few different
33 sides of this relationship and, along the way, to suggest that many hypotheses and theories in
34 neuroscience can be unified by the physics of information.

35 **Information bounds**

36 “How can the events in space and time which take place within the spatial boundary of a living
37 organism be accounted for by physics and chemistry?” – (E Schrödinger 1944, from KJ Friston
38 2013)

39 As a fundamental physical entity (S Lloyd 2015), information is not fully understood, and there is
40 currently a significant amount of disagreement over different definitions of information and entropy
41 in the literature (A Ben-Naim 2015; B Poirier 2014). In thermodynamics, however, information can
42 be defined as a negation of thermodynamic entropy (C Beck 2009):

43
$$I \equiv -S$$

44 A bit of thermodynamic entropy represents the distinction between two alternative states in a
45 physical system (JV Stone 2015). As a result, the total thermodynamic entropy of a system is
46 proportional to the total number of distinguishable states contained in the system (JD Bekenstein
47 2001; JD Bekenstein 2007). Because thermodynamic entropy is potential information relative to an
48 observer (S Lloyd 2006), and an observer in a physical system is a component of the system itself,
49 the total thermodynamic entropy of a system includes the portion of entropy that is accessible to the
50 observer as relative thermodynamic information (G Collell and J Fauquet 2015; J Wheeler 1989):

51
$$I_{relative} = S_{total} - S_{relative}$$

52 Since entropy in any physical system is finite (S Lloyd 2006; C Rovelli 2015), the total
53 thermodynamic entropy of any system of the brain can be quantified by applying the traditional form
54 of the universal (JD Bekenstein 1981, 1984, 2001, 2004, 2007) information-entropy bound:

55
$$S_{sys} = \zeta \frac{AEk}{\hbar c}$$

56 where A is area, E is energy including matter, \hbar is the reduced Planck constant, c is the speed of light, k is
57 Boltzmann’s constant, and ζ is a factor such that $0 \leq \zeta \leq 1$

58 Setting this factor to 1 in order to quantify the total thermodynamic entropy of a system at a certain
59 level of structure now allows us to quantify thermodynamic information by partitioning the factor
60 into a relative information component ($\zeta_I = 1 - \zeta_S$) and a relative entropy component ($\zeta_S = 1 - \zeta_I$),

61
$$I_{sys} = \zeta_I \frac{AEk}{\hbar c} = (1 - \zeta_S) \frac{AEk}{\hbar c}$$

62 Because a maximal level of energy corresponds to a maximal level of thermodynamic information,
63 and a minimal level of energy corresponds to a minimal level of thermodynamic information (TL
64 Duncan and JS Semura 2004), any transitions between energy levels occur as transitions between
65 informational extrema. So, in the event that information enters a system of the brain,

66
$$\Delta I_{sys} = \frac{\Delta E_{sys}}{kT} = \Delta \zeta_I$$

67 where T is temperature

68 and, in the event that information exits a system,

69
$$-\Delta I_{sys} = \frac{\Delta E_{surr}}{kT} = \Delta \zeta_S$$

70 Various forms of these relationships, including information-entropy bounds, have been applied in
71 neuroscience (G Collell and J Fauquet 2015; B Sengupta et al. 2013; B Sengupta and KJ Friston
72 2015; P Sterling and S Laughlin 2015). The contribution of this review is simply to show that these
73 relationships can be united into a common theoretical framework.

74 **Neurobiology**

75 “... classical thermodynamics... is the only physical theory of universal content which I am
76 convinced, that within the framework of applicability of its basic concepts, will never be
77 overthrown.” – (A Einstein 1949, from JD Bekenstein 2001)

78 This section reviews thermodynamic relationships in systems neuroscience with a focus on
79 information and energy. Beginning with neurons, moving to neural networks, and concluding at the
80 level of the brain as a whole, I discuss the energetics of processes such as learning and memory,
81 excitation and inhibition, and the production of noise in neurobiological systems.

82 The central role of energy in determining the activity of neurons exposes the close connection
83 between information and thermodynamics at the level of the cell. For instance, the process of
84 depolarization, which occurs as a transition to E_{max} from a resting state E_{min} , clearly shows that
85 cellular information content is correlated with energy levels. In this respect, the resemblance between
86 ion concentration gradients in neurons and temperature gradients in thermodynamic demons (i.e.,
87 agents that use information from their surroundings to decrease their thermodynamic entropy) is not a
88 coincidence – in order to acquire information, neurons must expend energy to establish proper
89 membrane potentials. Recall that Landauer’s principle (JMR Parrondo et al. 2015; MB Plenio and V
90 Vitelli 2001) places a lower bound on the quantity of energy released into the surroundings with the
91 removal of information from a system. Thus, reestablishing membrane potentials after depolarization
92 – the neuronal equivalent of resetting a demon’s memory – dissipates energy. Because Landauer’s
93 principle applies to all levels of structure, and cells process large quantities of information, neurons
94 use energy efficiently despite operating at several orders of magnitude above the nominal limit.
95 Parameters including membrane area, spiking frequency, and axon length have all been optimized
96 over the course of evolution to allow neurons to process information efficiently (P Sterling and S
97 Laughlin 2015). Examining the energetics of information processing in neurons reinforces the notion
98 that, while it is often convenient to imagine the neuron to be a simple binary element, these cells are
99 intricate computational structures that process more than one bit of information.

100 Relationships between information and energy can also be seen at the level of neural
101 networks. Attractor networks naturally stabilize by seeking energy minima, and the relative positions
102 of basins of attraction define the geometry of an energy landscape (DJ Amit 1992). As a result, the
103 transition into an active attractor state occurs as a transition into an information-energy maximum.
104 These transitions correspond to the generation of informational entities such as memories, decisions,
105 and perceptual events (ET Rolls 2012). In this way, the energy basins of attractor networks may be
106 analogous to lower-level cellular and molecular energy gradients; a transition between any number of
107 distinguishable energy levels follows the passage of a finite quantity of information. Since processing
108 information requires the expenditure of energy, competitive network features also underscore the
109 need to minimize unnecessary information processing. Lateral inhibition at this level may optimize
110 thermodynamic efficiency by reducing metabolic expenses associated with networks responding less
111 robustly to entering signals. Another interesting thermodynamic property of networks concerns
112 macrostates: the functional states of large-scale neural networks rest emergently on the states of
113 neuronal assemblies (R Yuste 2015). As a result, new computational properties may arise with the

114 addition of new layers of network structure. Finally, the energetic cost of information has influenced
115 network connectivity by imposing selective pressures to save energy by minimizing path length
116 between network nodes (E Bullmore and O Sporns 2009).

117 Again, in accordance with Landauer's principle, the displacement of information from any
118 system releases energy into the surroundings (MB Plenio and V Vitelli 2001; TL Duncan and JS
119 Semura 2004). This principle can be understood by imagining an idealized memory device, such as
120 the brain of a thermodynamic demon. Since information is conserved (L Susskind and G Hrabovsky
121 2014), and clearing a memory erases information, the thermodynamic entropy of the surroundings
122 must increase when a demon refreshes its memory to update information. This fundamental
123 connection between information, entropy, and energy appears in many areas of the neurobiology of
124 learning. For example, adjusting a firing threshold in order to change the probability that a system
125 will respond to a conditioned stimulus (Y Choe 2015; T Takeuchi et al. 2014) optimizes engram
126 fitness by minimizing the quantity of energy needed for its activation (S Still et al. 2012). Recurrent
127 collateral connections further increase engram efficiency by enabling a minimal nodal stimulus to
128 elicit its full energetic activation (ET Rolls 2012). Experimental evidence also shows that restricting
129 synaptic energy supply impairs the formation of stable engrams (JJ Harris et al. 2012). Because the
130 formation and disassembly of engrams during learning and forgetting optimizes the growth and
131 pruning of networks in response to external conditions, the process of learning is itself a mechanism
132 for minimizing entropy in the brain (KJ Friston 2003).

133 As another example of a multiscale process integrated across many levels by
134 thermodynamics, consider the active balance between excitation and inhibition in neurobiological
135 systems. Maintaining proper membrane potentials and adequate concentrations of signaling
136 molecules requires the expenditure of energy, so it is advantageous for systems of the brain to
137 minimize the processing of unnecessary information – to “send only what is needed” (P Sterling and
138 S Laughlin 2015). Balancing excitation and inhibition is therefore a crucial mechanism for saving
139 energy. Theoretical evidence that this balancing maximizes the thermodynamic efficiency of
140 processing Shannon information (B Sengupta et al. 2013) is consistent with experimental findings in
141 several areas of research on inhibition. For instance, constant inhibitory modulation is needed to
142 stabilize internal states, and hyperexcitation (e.g., in epilepsy, intoxication syndromes, or trauma) can
143 decrease relative information by reducing levels of consciousness (B Haider et al. 2006; K Lehmann
144 et al. 2012). Likewise, selective attention is mediated by the activation of inhibitory interneurons (G
145 Houghton and SP Tipper 1996), and sensory inhibition appears to sharpen internal perceptual states
146 (JS Isaacson and M Scanziani 2011). The need to balance excitation and inhibition at all levels of
147 structure highlights the energetic cost of information.

148 A final example worth discussing is the relationship between thermodynamics and the
149 production of noise in neurobiological systems. Noise is present in every system of the brain, and
150 influences all aspects of the organ's function (AA Faisal et al. 2008; ET Rolls and G Deco 2010; A
151 Destexhe and M Rudolph-Lilith 2012). Even in the absence of any potential forms of classical
152 stochastic resonance, the noise-driven exploration of different states may optimize thermodynamic
153 efficiency by allowing a system to randomly sample different accessible configurations. Theoretical
154 arguments suggest indeed that noise enables neural networks to respond more quickly to detected
155 signals (ET Rolls 2012), and empirical evidence implicates noise as a beneficial means of optimizing
156 the performance of diverse neurobiological processes (MD McDonnell and LM Ward 2011). For
157 example, noise in the form of neuronal DNA breaking (JU Guo et al. 2011; K Herrup et al. 2013; P
158 Tognini et al. 2015) could enhance plasticity, since any stochastically optimized configuration would
159 be more likely to survive over time as, in this case, a strengthened connection in a modifiable
160 network. Because noise is a form of relative entropy, optimizing the signal-to-noise ratio in any
161 neurobiological system promotes the efficient use of energy.

162 At the level of the brain as a whole, the connection between information and thermodynamics

163 is readily apparent in the organ's functional reliance on energy (PJ Magistretti and I Allaman 2015),
164 its seemingly disproportionate consumption of oxygen and energy substrates (e.g., ATP, glucose,
165 ketones, etc.) (S Herculano-Houzel 2011; ME Raichle and DA Gusnard 2002), its vulnerability to
166 hypoxic-ischemic damage (JP Dreier et al. 2013; PL Lutz et al. 2003) and in the reduction of
167 consciousness often conferred by the onset of energy restrictions (RG Shulman et al. 2009; J Stender
168 et al. 2016). All fMRI, PET, and EEG interpretation rests on the foundational assumption that
169 changes in the information content of neurobiological systems can be inferred by observing energy
170 changes (D Attwell and C Iadecola 2002; G Collell and J Fauquet 2015), and it is well known that the
171 information processing capacities of neurobiological systems are limited by energy supply (C
172 Howarth et al. 2012). Overall, these relationships are consistent with the form of information-energy
173 equivalence predicted by Landauer's principle and information-entropy bounds. The living brain
174 appears to maintain a state of thermodynamic optimization.

175 **Consciousness and free will**

176 *"... science appears completely to lose from sight the large and general questions; but all the more*
177 *splendid is the success when, groping in the thicket of special questions, we suddenly find a small*
178 *opening that allows a hitherto undreamt of outlook on the whole."* – (L Boltzmann 1886, from HC
179 Von Baeyer 1999)

180 Although neuroscience has yet to explain consciousness or free will at any satisfactory level of detail,
181 relationships between information and energy seem to be recognizable even at this level of analysis.
182 This section reviews attempts to conceptualize major properties of consciousness (unity, continuity,
183 complexity, and self-awareness) as features of information processing in the brain, and concludes
184 with a discussion of free will.

185 At any given moment, awareness is experienced as a unified whole. Physical information is
186 the substrate of consciousness (A Annala 2016), and the law of conservation of information requires
187 any minimal unit of information to be transferred into a thermodynamic system as a temporally
188 unitary quantity. As a result, it is possible that the passage of perceptual time itself occurs secondarily
189 to the transfer of information, and that the information present in any integrated system of the brain at
190 any observed time is necessarily cohesive and temporally unified. In this framework, the passage of
191 time would vary in proportion to a system's rate of energy dissipation. Although it is possible that
192 physical systems in general exchange information in temporally unitary quantities, it is likely that
193 many of the familiar features of the perceptual unity of consciousness require the structure and
194 activity of neural networks in the brain. The biological basis of this unity may be the active temporal
195 consolidation of observed events by integrated higher-order networks (S Dehaene and JP Changeux
196 2011; SA Greenfield and TFT Collins 2005; A Revonsuo 1999; F Varela et al. 2001). An
197 informational structure generated by the claustrum has been speculated to contribute to this
198 experiential unity (FC Crick and C Koch 2005, MZ Koubeissi et al. 2014), but it has also been
199 reported that complete unilateral resection of the system performed in patients with neoplastic lesions
200 of the region produces no externally observable changes in subjective awareness (H Duffau et al.
201 2007). Overall, it appears unlikely that the presence of information in any isolated or
202 compartmentalized network of the brain is responsible for generating the unified nature of conscious
203 experience.

204 While perceptual time is likely the product of a collection of related informational processes
205 rather than a single, globalized function mediated by any one specific system of the brain, some of
206 the perceptual continuity of consciousness may result from the effectively continuous flow of
207 thermodynamic information into and out of integrated systems of the brain. In this framework, the
208 quantum (M Prokopenko et al. 2014) of perceptual time would be the minimal acquisition of

209 information, and the entrance of information into neurobiological systems would occur alongside the
210 entrance of energy. This relationship is implicit in the simple observation that the transition of a
211 large-scale attractor network is progressively less discrete and smoother in time than the activation of
212 a small-scale engram, the propagation of a cellular potential, the docking of a vesicle, the release of
213 an ion, and so forth. Likewise, electroencephalography shows that the summation of a large number
214 of discrete cellular potentials can accumulate into an effectively continuous wave as a network field
215 potential (PL Nunez and R Srinivasan 2006), disruptions of which are often correlated with decreases
216 in levels of consciousness (H Blumenfeld and J Taylor 2003). It is also well known that higher
217 frequency network oscillations tend to indicate states of wakefulness and active awareness, while
218 lower frequency oscillations tend to be associated with internal states of lesser passage of perceptual
219 time, such as dreamless sleep or unconsciousness. The possibility that the experiential arrow of time
220 and the thermodynamic arrow of time share a common origin in the flow of information is supported
221 both by general models of time in neuroscience and the physical interpretation of time as an entropy
222 gradient (L Mlodinow and TA Brun 2014; OC Stoica 2008).

223 The subjective complexity of consciousness may show that extensive network integration is
224 needed for maximizing the mutual thermodynamic information and internal energy content of
225 systems of the brain (JS Torday and WB Miller Jr 2016). An exemplary structure enabling such
226 experience, likely one of many that together account for the subjective complexity of consciousness,
227 is the thalamocortical complex (Y Hannawi et al. 2015; RS Calabrò et al. 2015). The functional
228 architecture of such a network may show that, at any given moment in the internal model of a living
229 brain, a wide range of integrated systems are sharing mutual sources of thermodynamic information.
230 This pattern of structure may reveal that the perceptual depth and complexity of conscious experience
231 is a direct product of recognizable features of the physical brain. However, it also seems that
232 extensive local cortical processing of information is necessary for producing a refined and coherent
233 sensorium within a system, and that both the thalamocortical complex and the brain stem are
234 involved in generating the subjective complexity of consciousness (GM Edelman et al. 2011; LM
235 Ward 2011). The dynamics of attractor networks at higher levels of network structure may show that
236 quantities of complex internal information can be observed as changes in cortical energy landscapes
237 (ET Rolls 2012), with a transition between attractor states following the transfer of information. The
238 degree of subjective complexity of information enclosed by such a transition would be proportional
239 to the degree of structural integration of underlying networks.

240 Self-awareness likely arose as a survival necessity rather than as an accident of evolution (F
241 Fabbro et al. 2015), and rudimentary forms of self-awareness likely began to appear early in the
242 course of brain evolution as various forms of perceptual self-environment separation. As a simple
243 example, consider the tickle response (DJ Linden 2007), which requires the ability to differentiate
244 self-produced tactile sensations from those produced by external systems. The early need to
245 distinguish between self-produced tactile states and those produced by more threatening non-self
246 sources may be reflected by the observation that this recognition process is mediated to a great extent
247 by the cerebellum (SJ Blakemore et al. 2000). While it is possible that other similar developments
248 began occurring very early on, the evolutionary acquisition of the refined syntactical and conceptual
249 self present in the modern brain likely required the merging of pre-existing self networks with
250 higher-level cortical systems. The eventual integration of language and self-awareness would have
251 been advantageous for coordinating social groups (MS Graziano 2013), since experiencing self-
252 referential thought as inner speech facilitates verbal communication. Likewise, the coupling of self-
253 awareness to internal sensory, cognitive, and motor states (T Metzinger 2004; G Northoff et al. 2006)
254 may be advantageous for maximizing information between systems within an individual brain.
255 Neuropsychological conditions involving different forms of agnosia, neglect, and self-awareness
256 deficits do show that a reduced awareness of self-ownership of motor skills, body parts, or perceptual
257 states can result in significant disability (F Fabbro et al. 2015; S Chokron et al. 2016; MD Orfei et al.

258 2007; M Overgaard 2011; A Parton et al. 2004; M Tsakiris 2010; A Morin 2006; GP Prigatano
259 2009). Since experiencing self-awareness optimizes levels of mutual information between the
260 external world and the brain's internal model (MA Apps and M Tsakiris 2014), and this activity
261 decreases thermodynamic entropy (JS Torday and WB Miller Jr 2016), self-awareness may be a
262 mechanism for optimizing the brain's consumption of energy.

263 Thermodynamic information is also interesting to consider in the context of free will. The
264 brain is predictable within reason, and the performance of an action can be predicted before a
265 decision is reported to have been made (P Haggard 2008). Entities such as ideas, feelings, and beliefs
266 seem to exist as effectively deterministic evaluations of information processed in the brain. Whether
267 or not the flow of information is subject to the brain's volitional alteration, neuroscience also shows
268 that information can be internally real to a system of the brain, even if this information is inconsistent
269 with an external reality. That the brain can generate an externally inconsistent internal reality is
270 demonstrated by phenomena such as confabulation, agnosia, blindsight, neglect, commissurotomy
271 and hemispherectomy effects, placebo and nocebo effects, reality monitoring deficits, hallucinations,
272 prediction errors, the suspension of disbelief during dreaming, the function of communication in
273 minimizing divergence between internal realities, the quality of many kinds of realistic drug-induced
274 experiences, and the effects of many neuropsychological conditions. The apparent fact that subjective
275 reality is an active construction of the physical brain has even led to the proposal of model-dependent
276 realism (SW Hawking and L Mlodinow 2011) as a philosophical paradigm in the search for a unified
277 theory of physics. In any case, it is likely that beliefs, including those in free will, exist as
278 information, and that their internal reality is a restatement of its frequently observer-dependent
279 nature.

280 **Empirical outlook**

281 Before concluding, it is worth reviewing a few notable experiments in greater detail. While
282 considerable advances have been made in discovering how neurobiological systems operate
283 according to principles of thermodynamic efficiency (S Laughlin and P Sterling 2015), relationships
284 between information and energy in the brain are only beginning to be understood. The following
285 studies are examples of elegant and insightful experiments that should inspire future research.

286 Several recent brain imaging studies support the proposal (A Annala 2016) that
287 thermodynamics is able to explain a number of mysteries involving consciousness. For example, J
288 Stender et al. 2016 used PET to measure global resting state energy consumption in 131 brain injury
289 patients with impairments of consciousness as defined by the revised Coma Recovery Scale (CRS-
290 R). The preservation of consciousness was found to require a minimal global metabolic rate of $\approx 40\%$
291 of the average rate of controls; global energy consumption above this level was reported to predict
292 the presence or recovery of consciousness with over 90% sensitivity. These results must be replicated
293 and studied in closer detail before their specific theoretical implications are clear, but it is now
294 established that levels of consciousness are correlated with energetic metrics of brain activity. To
295 what extent there exists a well-defined "minimal energetic requirement for the presence of conscious
296 awareness" (J Stender et al. 2016) remains an open question. However, the empirical confirmation of
297 a connection between consciousness and thermodynamics introduces the possibility of developing
298 new experimental methods in consciousness research.

299 Neurobiological systems, and biological systems in general (HC Von Baeyer 1999; ED
300 Schneider and D Sagan 2005), can be considered thermodynamic demons in the sense that they are
301 agents using information to decrease their thermodynamic entropy. Landauer's principle requires
302 that, in order not to violate any known laws of thermodynamics, such agents dissipate heat when
303 erasing information from their memory storage devices. In an experimental test of this principle,
304 reviewed along with similar experiments in JMR Parrondo et al. 2015, A Bérut et al. 2012 studied

305 heat dissipation in a simple memory device created by placing a glass bead in an optical double-well
306 potential. Intuitively, this memory stored a bit of information by retaining the bead on one side of the
307 potential rather than on the alternative. By manipulating the height of the optical barrier between
308 wells, researchers moved the bead to one side of the memory without determining its previous
309 location in the potential. This process was therefore logically irreversible, requiring the erasure of
310 prior information from the memory device. Landauer's principle predicts that, since information is
311 conserved, the entropy of the memory's surroundings must increase when this occurs. A Bérut et al.
312 2012 have verified that energy is emitted when a memory is cleared. As noted by the authors, "this
313 limit is independent of the actual device, circuit or material used to implement the irreversible
314 operation." It would be interesting to study the erasure principle in the context of neuroscience.

315 Experimental applications of information theory in cell biology have already led to the
316 discovery of general principles of brain organization related to thermodynamics (S Laughlin and P
317 Sterling 2015). In one particularly interesting study, JE Niven et al. 2007 measured the energetic
318 efficiency of information coding in retinal neurons. Intracellular recordings of membrane potential
319 and input resistance were used to calculate rates of ATP consumption in response to different
320 background light intensities. These rates of energy consumption were then compared with rates of
321 Shannon information transmission in order to determine metabolic performance. It was found that
322 metabolic demands increase nonlinearly with respect to increases in information processing rate:
323 thermodynamics appears to impose a "law of diminishing returns" on systems of the brain. The
324 authors interpret these results as evidence that nature has selected for neurons that minimize
325 unnecessary information processing. Studying how thermodynamics has influenced cellular
326 parameters over the course of evolution is likely to raise many new empirically addressable
327 questions.

328 **Conclusion**

329 This article has reviewed information-energy relationships in the hope that they may eventually
330 provide a general framework for uniting theory and experiment in neuroscience. The physical nature
331 of information and its status as a finite, measurable resource are emphasized to connect neurobiology
332 and thermodynamics. As a scientific paradigm, the information movement currently underway in
333 physics promises profound advances in our understanding of the relationship between energy,
334 information, and the physical brain.

335 **Conflict of Interest**

336 *The author confirms that this research was conducted in the absence of any commercial or financial*
337 *relationships that could be construed as a potential conflict of interest.*

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346 **References**

- 347 Alfonso-Faus, A. (2013). Fundamental Principle of Information-to-Energy Conversion. *Proceedings*
348 *of the 7th European Computing Conference*. WSEAS Press.
- 349 Amit, DJ. (1992). *Modeling Brain Function*. Cambridge: Cambridge University Press.
- 350 Annala, A. (2016). On the character of consciousness. *Frontiers in Systems Neuroscience*, 10. doi:
351 10.3389/fnsys.2016.00027.
- 352 Apps, M. A., and Tsakiris, M. (2014). The free-energy self: a predictive coding account of self-
353 recognition. *Neuroscience & Biobehavioral Reviews*, 41, 85-97. doi:
354 10.1016/j.neubiorev.2013.01.029.
- 355 Attwell, D., and Iadecola, C. (2002). The neural basis of functional brain imaging signals. *Trends in*
356 *Neurosciences*, 25(12), 621-625. doi:10.1016/S0166-2236(02)02264-6
- 357 Beck, C. (2009). Generalised information and entropy measures in physics. *Contemporary Physics*,
358 50(4), 495-510. doi: 10.1080/00107510902823517
- 359 Bekenstein, J. D. (1981). Universal upper bound on the entropy-to-energy ratio for bounded systems.
360 *Physical Review D*, 23(2), 287. doi:10.1103/PhysRevD.23.287
- 361 Bekenstein, J. D. (1984). Entropy content and information flow in systems with limited energy.
362 *Physical Review D*, 30(8), 1669. doi:10.1103/PhysRevD.30.1669
- 363 Bekenstein, J. D. (2001). The limits of information. *Studies In History and Philosophy of Science*
364 *Part B: Studies In History and Philosophy of Modern Physics*, 32(4), 511-524. doi: 10.1016/S1355-
365 2198(01)00020-X
- 366 Bekenstein, J. D. (2004). Black holes and information theory. *Contemporary Physics*, 45(1). PACS:
367 89.70.+c,03.67.-a,04.70.-s,04.70.Dy,65.40.Gr
- 368 Bekenstein, J. D. (2007). Information in the holographic universe. *Scientific American*, 17, 66-73.
- 369 Ben-Naim, A. (2015). *Information, Entropy, Life and the Universe*. Singapore: World Scientific. 4-5.
- 370 Bennett, C. H. (2003). Notes on Landauer's principle, reversible computation, and Maxwell's Demon.
371 *Studies In History and Philosophy of Science Part B: Studies In History and Philosophy of Modern*
372 *Physics*, 34(3), 501-510. doi:10.1016/S1355-2198(03)00039-X
- 373 Bérut, A., Arakelyan, A., Petrosyan, A., Ciliberto, S., Dillenschneider, R., and Lutz, E. (2012).
374 Experimental verification of Landauer's principle linking information and thermodynamics. *Nature*,
375 483(7388), 187-189. doi: 10.1038/nature10872
- 376 Blakemore, S. J., Wolpert, D., and Frith, C. (2000). Why can't you tickle yourself? *Neuroreport*,
377 11(11), R11-R16. doi: 10.1097/00001756-200008030-00002
- 378 Blumenfeld, H., and Taylor, J. (2003). Why do seizures cause loss of consciousness? *The*
379 *Neuroscientist*, 9(5), 301-310. doi: 10.1177/1073858403255624
- 380 Bousso, R. (2002). The holographic principle. *Reviews of Modern Physics*, 74(3), 825. doi:
381 10.1103/RevModPhys.74.825

- 382 Brukner, Č., and Zeilinger, A. (2003). Information and fundamental elements of the structure of
383 quantum theory. In *Time, Quantum and Information*, ed. L. Castell and O. Ischebeck. Heidelberg:
384 Springer. 323-354.
- 385 Bullmore, E., and Sporns, O. (2009). Complex brain networks: graph theoretical analysis of
386 structural and functional systems. *Nature Reviews Neuroscience*, 10(3), 186-198. doi:
387 10.1038/nrn2575
- 388 Calabrò, R. S., Cacciola, A., Bramanti, P., and Milardi, D. (2015). Neural correlates of
389 consciousness: what we know and what we have to learn! *Neurological Sciences*, 36(4), 505-513.
390 doi: 10.1007/s10072-015-2072-x
- 391 Choe, Y. (2015). Hebbian Learning. In *Encyclopedia of Computational Neuroscience*, ed. D Jaeger
392 and R Jung. New York: Springer. 1305-1309. doi: 10.1007/978-1-4614-7320-6_672-1
- 393 Chokron, S., Perez, C., and Peyrin, C. (2016). Behavioral Consequences and Cortical Reorganization
394 in Homonymous Hemianopia. *Frontiers in Systems Neuroscience*, 10. doi: 10.3389/fnsys.2016.00057
- 395 Collell, G., and Fauquet, J. (2015). Brain activity and cognition: a connection from thermodynamics
396 and information theory. *Frontiers in Psychology*, 6. doi: 10.3389/fpsyg.2015.00818
- 397 Crick, F. C., and Koch, C. (2005). What is the function of the claustrum? *Philosophical Transactions
398 of the Royal Society B: Biological Sciences*, 360(1458), 1271-1279. doi: 10.1098/rstb.2005.1661
- 399 Davies, P. (2010). Universe from bit. In *Information and the Nature of Reality*, ed. P Davies and N.
400 H. Gregersen. Cambridge: Cambridge University Press. 83-117.
- 401 Dehaene, S., and Changeux, J. P. (2011). Experimental and theoretical approaches to conscious
402 processing. *Neuron*, 70(2), 200-227. doi: 10.1016/j.neuron.2011.03.018
- 403 Destexhe, A., and Rudolph-Lilith, M. (2012). *Neuronal Noise*. New York: Springer.
- 404 Dreier, J. P., Isele, T., Reiffurth, C., Offenhauser, N., Kirov, S. A., Dahlem, M. A., and Herreras, O.
405 (2013). Is spreading depolarization characterized by an abrupt, massive release of Gibbs free energy
406 from the human brain cortex? *The Neuroscientist*, 19(1), 25-42. doi: 10.1177/1073858412453340.
- 407 Duffau, H., Mandonnet, E., Gatignol, P., and Capelle, L. (2007). Functional compensation of the
408 claustrum: lessons from low-grade glioma surgery. *Journal of Neuro-oncology*, 81(3), 327-329. doi:
409 10.1007/s11060-006-9236-8
- 410 Duncan, T. L., and Semura, J. S. (2004). The deep physics behind the second law: information and
411 energy as independent forms of bookkeeping. *Entropy*, 6(1), 21-29. doi:10.3390/e6010021
- 412 Edelman, G. M., Gally, J. A., and Baars, B. J. (2011). Biology of consciousness. *Frontiers in
413 Psychology*, 2, 4.
- 414 Eling, C., Guedens, R., and Jacobson, T. (2006). Nonequilibrium thermodynamics of spacetime.
415 *Physical Review Letters*, 96(12), 121301. doi: 10.1103/PhysRevLett.96.121301.
- 416 England, J. L. (2013). Statistical physics of self-replication. *The Journal of Chemical Physics*,
417 139(12), 121923. doi: 10.1063/1.4818538

- 418 Fabbro, F., Aglioti, S. M., Bergamasco, M., Clarici, A., and Panksepp, J. (2015). Evolutionary
419 aspects of self-and world consciousness in vertebrates. *Frontiers in Human Neuroscience*, 9, 157.
420 doi: 10.3389/fnhum.2015.00157
- 421 Faisal, A. A., Selen, L. P., and Wolpert, D. M. (2008). Noise in the nervous system. *Nature Reviews*
422 *Neuroscience*, 9(4), 292-303. doi: doi:10.1038/nrn2258
- 423 Flack, J. C. (2014). Life's information hierarchy. *Santa Fe Institute Bulletin*, 28, 13-24.
- 424 Fox, D. (2015). The limits of intelligence. *Scientific American*, 305(1), 36-43.
- 425 Friston, K. J. (2003). Learning and inference in the brain. *Neural Networks*, 16(9), 1325-1352.
426 doi:10.1016/j.neunet.2003.06.005
- 427 Friston, K. J. (2010). The free-energy principle: a unified brain theory? *Nature Reviews*
428 *Neuroscience*, 11(2), 127-138. doi: 10.1038/nrn2787
- 429 Friston, K. J. (2013). Life as we know it. *Journal of The Royal Society Interface*, 10(86), 20130475.
430 doi: 10.1098/rsif.2013.0475
- 431 Gleick, J., (2011). *The Information*. New York: Random House. 269-270; 355-372.
- 432 Graziano, M. S. (2013). *Consciousness and the Social Brain*. Oxford: Oxford University Press.
- 433 Greenfield, S. A., and Collins, T. F. T. (2005). A neuroscientific approach to consciousness. *Progress*
434 *in Brain Research*, 150, 11-23. doi:10.1016/S0079-6123(05)50002-5
- 435 Guo, J. U., Ma, D. K., Mo, H., Ball, M. P., Jang, M. H., Bonaguidi, M. A., et al. (2011). Neuronal
436 activity modifies the DNA methylation landscape in the adult brain. *Nature Neuroscience*, 14(10),
437 1345-1351. doi: 10.1038/nn.2900
- 438 Haggard, P. (2008). Human volition: towards a neuroscience of will. *Nature Reviews Neuroscience*,
439 9(12), 934-946. doi:10.1038/nrn2497
- 440 Haider, B., Duque, A., Hasenstaub, A. R., and McCormick, D. A. (2006). Neocortical network
441 activity in vivo is generated through a dynamic balance of excitation and inhibition. *The Journal of*
442 *Neuroscience*, 26(17), 4535-4545. doi: 10.1523/JNEUROSCI.5297-05.2006
- 443 Hannawi, Y., Lindquist, M. A., Caffo, B. S., Sair, H. I., and Stevens, R. D. (2015). Resting brain
444 activity in disorders of consciousness. *Neurology*, 84(12), 1272-1280. doi:
445 10.1212/WNL.0000000000001404
- 446 Harris, J. J., Jolivet, R., and Attwell, D. (2012). Synaptic energy use and supply. *Neuron*, 75(5), 762-
447 777. doi: 10.1016/j.neuron.2012.08.019
- 448 Hawking, S. W. and Mlodinow, L. (2011). *The Grand Design*. New York: Random House. 7, 46.
- 449 Herculano-Houzel, S. (2011). Scaling of brain metabolism with a fixed energy budget per neuron:
450 implications for neuronal activity, plasticity and evolution. *PLoS One*, 6(3), e17514. doi:
451 10.1371/journal.pone.0017514

- 452 Herrup, K., Chen, J., and Li, J. (2013). Breaking news: thinking may be bad for DNA. *Nature*
453 *Neuroscience*, 16(5), 518-519. doi: 10.1038/nn.3384
- 454 Houghton, G., and Tipper, S. P. (1996). Inhibitory mechanisms of neural and cognitive control:
455 Applications to selective attention and sequential action. *Brain and Cognition*, 30(1), 20-43. doi:
456 10.1006/brcg.1996.0003
- 457 Howarth, C., Gleeson, P., and Attwell, D. (2012). Updated energy budgets for neural computation in
458 the neocortex and cerebellum. *Journal of Cerebral Blood Flow and Metabolism*, 32(7), 1222-1232.
459 doi: 10.1038/jcbfm.2012.35
- 460 Isaacson, J. S., and Scanziani, M. (2011). How inhibition shapes cortical activity. *Neuron*, 72(2),
461 231-243. doi: 10.1016/j.neuron.2011.09.027
- 462 Koubeissi, M. Z., Bartolomei, F., Beltagy, A., and Picard, F. (2014). Electrical stimulation of a small
463 brain area reversibly disrupts consciousness. *Epilepsy & Behavior*, 37, 32-35. doi:
464 10.1016/j.yebeh.2014.05.027
- 465 Landauer, R. (1996). The physical nature of information. *Physics Letters A*, 217(4), 188-193. doi:
466 10.1016/0375-9601(96)00453-7
- 467 Lee, J. W., Kim, H. C., and Lee, J. (2013). Gravity from quantum information. *Journal of the Korean*
468 *Physical Society*, 63(5), 1094-1098. doi: 10.3938/jkps.63.1094
- 469 Lehmann, K., Steinecke, A., and Bolz, J. (2012). GABA through the ages: regulation of cortical
470 function and plasticity by inhibitory interneurons. *Neural Plasticity*, 892784. doi:
471 10.1155/2012/892784
- 472 Linden, D. J. (2007). *The Accidental Mind*. Cambridge: Harvard University Press. 9-12.
- 473 Liu, K. C., Oztaskin, M., and Burchiel, K. J. (2012). Basics of neurosurgical techniques and
474 procedures. In *Essentials of Neurosurgical Anesthesia and Critical Care*. New York: Springer. 145.
475 doi: 10.1007/978-0-387-09562-2_14
- 476 Lloyd, S. (2006). *Programming the Universe*. New York: Random House.
- 477 Lloyd, S. (2015). Interview in *Closer to Truth: Is Information Fundamental?* Retrieved from
478 <https://www.closetotruth.com/series/information-fundamental#video-2621>
- 479 Lutz, P. L., Nilsson, G. E., and Prentice, H. M. (2003). *The Brain Without Oxygen*. New York:
480 Kluwer.
- 481 Magistretti, P. J., and Allaman, I. (2015). A cellular perspective on brain energy metabolism and
482 functional imaging. *Neuron*, 86(4), 883-901. doi: 10.1016/j.neuron.2015.03.035
- 483 Maruyama, K., Nori, F., and Vedral, V. (2009). Colloquium: The physics of Maxwell's demon and
484 information. *Reviews of Modern Physics*, 81(1), 1. doi: 10.1103/RevModPhys.81.1
- 485 McDonnell, M. D., and Ward, L. M. (2011). The benefits of noise in neural systems: bridging theory
486 and experiment. *Nature Reviews Neuroscience*, 12(7), 415-426. doi: 10.1038/nrn3061

- 487 Metzinger, T. (2004). *Being No One*. Cambridge: MIT Press.
- 488 Mlodinow, L., and Brun, T. A. (2014). Relation between the psychological and thermodynamic
489 arrows of time. *Physical Review E*, 89(5), 052102. doi: 10.1103/PhysRevE.89.052102
- 490 Morin, A. (2006). Levels of consciousness and self-awareness: A comparison and integration of
491 various neurocognitive views. *Consciousness and Cognition*, 15(2), 358-371. doi:
492 10.1016/j.concog.2005.09.006
- 493 Moskowitz, C. (2015). Stephen Hawking Hasn't Solved the Black Hole Paradox Just Yet. *Scientific
494 American*, 27.
- 495 Niven, J. E., Anderson, J. C., and Laughlin, S. B. (2007). Fly photoreceptors demonstrate energy-
496 information trade-offs in neural coding. *PLoS Biology*, 5(4), e116. doi: 10.1371/journal.pbio.0050116
- 497 Northoff, G., Heinzl, A., De Greck, M., Bermpohl, F., Dobrowolny, H., and Panksepp, J. (2006).
498 Self-referential processing in our brain—a meta-analysis of imaging studies on the self. *Neuroimage*,
499 31(1), 440-457. doi: 10.1016/j.neuroimage.2005.12.002
- 500 Nunez, P. L., and Srinivasan, R. (2006). *Electric Fields of the Brain*. New York: Oxford University
501 Press.
- 502 Orfei, M. D., Robinson, R. G., Prigatano, G. P., Starkstein, S., Rüsç, N., Bria, P., et al. (2007).
503 Anosognosia for hemiplegia after stroke is a multifaceted phenomenon: a systematic review of the
504 literature. *Brain*, 130(12), 3075-3090. doi: 10.1093/brain/awm106
- 505 Overgaard, M. (2011). Visual experience and blindsight: a methodological review. *Experimental
506 Brain Research*, 209(4), 473-479. doi: 10.1007/s00221-011-2578-2
- 507 Parrondo, J. M. R., Horowitz, J. M., and Sagawa, T. (2015). Thermodynamics of information. *Nature
508 Physics*, 11(2), 131-139. doi: 10.1038/nphys3230
- 509 Parton, A., Malhotra, P., and Husain, M. (2004). Hemispatial neglect. *Journal of Neurology,
510 Neurosurgery & Psychiatry*, 75(1), 13-21.
- 511 Plenio, M. B., and Vitelli, V. (2001). The physics of forgetting: Landauer's erasure principle and
512 information theory. *Contemporary Physics*, 42(1), 25-60. doi: 10.1080/00107510010018916
- 513 Poirier, B. (2014). *A Conceptual Guide to Thermodynamics*. Chichester: Wiley. 77-78.
- 514 Prigatano, G. P. (2009). Anosognosia: clinical and ethical considerations. *Current Opinion in
515 Neurology*, 22(6), 606-611. doi: 10.1097/WCO.0b013e328332a1e7
- 516 Prokopenko, M., and Lizier, J. T. (2014). Transfer entropy and transient limits of computation.
517 *Scientific Reports*, 4. doi: 10.1038/srep05394
- 518 Raichle, M. E., and Gusnard, D. A. (2002). Appraising the brain's energy budget. *Proceedings of the
519 National Academy of Sciences*, 99(16), 10237-10239. doi: 10.1073/pnas.172399499
- 520 Revonsuo, A. (1999). Binding and the phenomenal unity of consciousness. *Consciousness and
521 Cognition*, 8(2), 173-185. doi: 10.1006/ccog.1999.0384

- 522 Rolls, E. T. (2012). *Neuroculture*. Oxford: Oxford University Press.
- 523 Rolls, E. T., and Deco, G. (2010). *The Noisy Brain*. Oxford: Oxford University Press.
- 524 Rovelli, C. (2015). Relative information at the foundation of physics. In *It From Bit or Bit From It?*
525 ed. A Aguirre, B. Foster, and Z. Merali. Cham: Springer. doi: 10.1007/978-3-319-12946-4_7
- 526 Schneider, E. D., and Sagan, D. (2005). *Into the Cool*. Chicago: University of Chicago Press.
- 527 Sengupta, B., and Friston, K. J. Personal communication, October 7th, 2015.
- 528 Sengupta, B., Faisal, A. A., Laughlin, S. B., and Niven, J. E. (2013). The effect of cell size and
529 channel density on neuronal information encoding and energy efficiency. *Journal of Cerebral Blood*
530 *Flow & Metabolism*, 33(9), 1465-1473. doi: 10.1038/jcbfm.2013.103
- 531 Sengupta, B., Laughlin, S. B., and Niven, J. E. (2013). Balanced excitatory and inhibitory synaptic
532 currents promote efficient coding and metabolic efficiency. *PLoS Comput Biology*, 9(10), e1003263.
533 doi: 10.1371/journal.pcbi.1003263
- 534 Sengupta, B., Stemmler, M. B., and Friston, K. J. (2013). Information and efficiency in the nervous
535 system—a synthesis. *PLoS Computational Biology*, 9(7), e1003157. doi:
536 10.1371/journal.pcbi.1003157
- 537 Sengupta, B., Tozzi, A., Cooray, G. K., Douglas, P. K., and Friston, K. J. (2016). Towards a neuronal
538 gauge theory. *PLoS Biology*, 14(3), e1002400. doi: 10.1371/journal.pbio.1002400
- 539 Shulman, R. G., Hyder, F., and Rothman, D. L. (2009). Baseline brain energy supports the state of
540 consciousness. *Proceedings of the National Academy of Sciences*, 106(27), 11096-11101. doi:
541 10.1073/pnas.0903941106
- 542 Smolin, L. (2002). *Three Roads to Quantum Gravity*. New York: Basic Books. 103, 169-178.
- 543 Stender, J., Mortensen, K. N., Thibaut, A., Darkner, S., Laureys, S., Gjedde, A., and Kupers, R.
544 (2016). The minimal energetic requirement of sustained awareness after brain injury. *Current*
545 *Biology*, 26(11), 1494-1499. doi: 10.1016/j.cub.2016.04.024
- 546 Sterling, P., and Laughlin, S. (2015). *Principles of Neural Design*. Cambridge: MIT Press.
- 547 Still, S., Sivak, D. A., Bell, A. J., and Crooks, G. E. (2012). Thermodynamics of prediction. *Physical*
548 *Review Letters*, 109(12), 120604. doi: 10.1103/PhysRevLett.109.120604
- 549 Stoica, O. C. (2008). “Flowing with a frozen river.” FQXi, *The Nature of Time* essay contest.
- 550 Stone, J. V. (2015). *Information Theory*. Sheffield: Sebtel Press. 171.
- 551 Susskind, L., and G Hrabovsky (2014). *The Theoretical Minimum*. New York: Basic Books. 9; 170.
- 552 Takeuchi, T., Duszkiwicz, A. J., and Morris, R. G. (2014). The synaptic plasticity and memory
553 hypothesis: encoding, storage and persistence. *Philosophical Transactions of the Royal Society B*,
554 369(1633), 20130288. doi: 10.1098/rstb.2013.0288

- 555 Tognini, P., et al. (2015). Dynamic DNA methylation in the brain: a new epigenetic mark for
556 experience-dependent plasticity. *Frontiers in Cellular Neuroscience*, 9. doi:
557 10.3389/fncel.2015.00331
- 558 Torday, J. S., and Miller Jr, W. B. (2016). On the evolution of the mammalian brain. *Frontiers in*
559 *Systems Neuroscience*, 10. doi: 10.3389/fnsys.2016.00031
- 560 Tsakiris, M. (2010). My body in the brain: a neurocognitive model of body-ownership.
561 *Neuropsychologia*, 48(3), 703-712. doi: 10.1016/j.neuropsychologia.2009.09.034
- 562 Varela, F., Lachaux, J. P., Rodriguez, E., and Martinerie, J. (2001). The brainweb: phase
563 synchronization and large-scale integration. *Nature Reviews Neuroscience*, 2(4), 229-239.
564 doi:10.1038/35067550
- 565 Vedral, V. (2010). *Decoding Reality*. Oxford: Oxford University Press.
- 566 Von Baeyer, H. C. (1999). *Maxwell's Demon*. New York: Random House. 100-101; 165.
- 567 Ward, L. M. (2011). The thalamic dynamic core theory of conscious experience. *Consciousness and*
568 *Cognition*, 20(2), 464-486. doi: 10.1016/j.concog.2011.01.007
- 569 Wheeler, J. (1986). In *The Ghost in the Atom*, ed. P Davies and J Brown. Cambridge: Cambridge
570 University Press. 62.
- 571 Wheeler, J. A. (1989). Information, physics, quantum: the search for links. *Proceedings of the Third*
572 *International Symposium on Foundations of Quantum Mechanics*, Tokyo, 354-368.
- 573 Yuste, R. (2015). From the neuron doctrine to neural networks. *Nature Reviews Neuroscience*, 16(8),
574 487-497. doi: 10.1038/nrn3962