

The physical basis of memory[☆]

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ABSTRACT

Neuroscientists are searching for the engram within the conceptual framework established by John Locke's theory of mind. This framework was elaborated before the development of information theory, before the development of information processing machines and the science of computation, before the discovery that molecules carry hereditary information, before the discovery of the codon code and the molecular machinery for editing the messages written in this code and translating it into transcription factors that mark abstract features of organic structure such as anterior and distal. The search for the engram needs to abandon Locke's conceptual framework and work within a framework informed by these developments. The engram is the medium by which information extracted from past experience is transmitted to the computations that inform future behavior. The information-conveying symbols in the engram are rapidly generated in the course of computations, which implies that they are molecules.

The most obvious thing about memory is that it is full of facts acquired from experience. That's because its basic function is to transmit acquired information forward in time so that it may inform future behaviors. It follows that, when thinking about what the material basis of memory might be, the first question to ask is, How does the memory mechanism transmit information? For more than a century, neuroscientists have refused to ask that question. By not asking it, we have brought the neurobiology of learning and memory to a conceptual impasse, a conceptual hole from which we must emerge in order to move forward. In this essay, I attempt to explain how we got into this hole and what has to be done to get out of it.

John Locke would feel intellectually at home with the theory of memory embraced almost universally by contemporary neuroscientists. It is his theory of the mind translated into a theory of how the brain works. In broad outlines, Locke's theory of the mind went like this: The senses deliver a variety of different sensations in response to the different stimuli that impinge upon them. These sensations are the primitive facts of experience. Locke called them the primitive *ideas* that the world conveys to the mind. When two primitive sensations co-occurred repeatedly either in time or in space an association formed between them. Concepts were clusters of associated primitive sensations. One might think of them as mental dust balls where the sensations (primitive ideas) are the particles in the dust ball and the hairs linking the particles are the associations. Locke believed that associations could form between clusters as well as between primitive sensations.

In contemporary neurobiology, neurons selectively tuned to various aspects of experience take the place of primitive sensations, plastic synapses (aka Hebbian synapses) take the place of associations and cell assemblies take the place of Locke's concepts.

Locke's associations were conductive links; they conducted activation from one sensation or cluster of sensations to the sensations/clusters with which it/they had become associated. The activation-conducting faculty of the associative connection explained our trains of thought—why one thought led to another.

Associations are not themselves facts; nothing we would want to call a fact about the world outside the mind follows from the fact that two otherwise unspecified entities have become associated in a mind. I know from my interactions with other neuroscientists that it is not clear to many of them that associations are not empirical facts out there in the world. I explain why they are not, by reference to what one prominent neuroscientist gave me as an example of an association that was an empirical fact stored in the brain:

Suppose I tell someone who pays no attention to popular culture that there is an association in the minds of some people between JA and BP. The existence of this association has been electrophysiologically confirmed in the brain of a patient (Rodrigo Quian Quiroga, 2019; Quiroga, Reddy, Kreiman, Koch, & Fried, 2005). If this association in the brain is taken to reflect a fact out there in the world, what can a brain infer from knowledge of it? That the town JA is close to the town BP? That JA weather often follows BP weather? That JA gave birth to BP?

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That JA rotates around the BP? That JA is a solvent for BP. That JA is the father of BP? That JA and BP were once married? That JA and BP are co-owners of a carwash? I submit that the answer is, None of the Above. Imputing an association between two otherwise unspecified entities tells you nothing about those entities nor about the nature of a relation between them. This becomes obvious when that information-less assertion is contrasted with the assertion that JA is the former wife of BP. That's a fact in the world out there. From it many inferences may be made, such as that JA is neither a solvent nor a town nor a weather pattern. A general property of facts is that knowledge of them enables inferences. That JA is associated with BP is not a fact, because no inferences may be made from it.

The unbreakable embrace of Locke's theory by neuroscientists explains why we have still not discovered the physical basis of memory, despite more than a century of efforts by many leading figures. Researchers searching for the physical basis of memory are looking for the wrong thing (the associative bond) in the wrong place (the synaptic junction), guided by an erroneous conception of what memory is and the role it plays in computation. That is the hole we have dug for ourselves. I turn now to what has to be done to scramble up out of it.

Most cognitive scientists have embraced an information processing view of the mind, also called the computational theory of mind. This conception of mind rests on three mathematical/scientific/engineering developments undreamed of in Locke's day: 1) The emergence of a science of physically realized computation. 2) The development of a mathematical theory that made information a measurable physical quantity. 3) The incorporation of this theory into the foundations of physics and into the engineering of computing machines and modern communication technology.

Locke was a dualist. For a dualist, computation went on in minds, not in machines. It was not until a century after Locke's death that Babbage began to think about how computation could be realized in a machine (Halacy, 1970). It was more than a century after that before i) Turing (1936) laid the conceptual foundations on which the theory of computation rests; ii) The first computing machines honoring Turing's conception were constructed (Copeland, 2010; Zuse, 2010). iii) Shannon (1948) made information a measurable physical quantity.

The emergence of computing and communication technology in the middle of the previous century led to a radically new, non-associative theory of mind, the computational theory of mind (Chomsky, 1956; Marr, 1982; Newell, Shaw, & Simon, 1958; Newell & Simon, 1975; Turing, 1950; von Neumann, 1958). Researchers operating within this framework take it for granted that brains remember facts—many hundreds of thousands of them.

That memories contain learned facts about the world may seem so obvious as to need no documentation. However, it was explicitly denied in the behaviorist tradition that dominated psychology prior to the rise of cognitive psychology (Hull, 1930; Skinner, 1950). Moreover, the behaviorist view of memory as a collection of conditioned reflexes has been given a more modern sounding formulation in the connectionist literature, which treats brains as sub-symbolic (Miiikkulainen, 1993; Smolensky, 1986). And finally, the role of memory as the transmission medium for the acquired facts that guide future behavior goes unmentioned in neurobiological reviews of the search for the engram (Poo et al., 2016; Tomonori, Duszkiwicz, & Morris, 2013). These reviews focus entirely on the Hebbian synapse. Given this history, I must spend some time reminding the reader that the cognitive science literature, in which I include the insect navigation literature, documents beyond reasonable argument that brains contain facts, lots of them.

The average native speaker of English has a vocabulary of about 40,000 words (Brysaert, Stevens, Mandera, & Keuleers, 2016). Some of us even know a few more than that. The cognitive science literature shows that we can remember thousands of drawings of objects and thousands of boring vacation slides and the even more boring target and distractor items in visual search experiments—objects and scenes and drawn objects that we have seen or felt or smelled only once for a few

seconds or less (Brady, Konkle, Alvarez, & Oliva, 2008; Hutmacher & Kuhbandner, 2018; Konkle, Brady, Alvarez, & Oliva, 2010; McGann, 2017; Shepard, 1967; Standing, 1973).

Remembering scenes, locations and smells is not unique to humans. Ants and bees remember numerous terrain snapshots together with their location and compass orientation when their visual system took the snapshot and stored it in memory (Ardin, Peng, Mangan, Lagogiannis, & Webb, 2016; Beyaert, Greggers, & Menzel, 2012; Degen et al., 2016; Freas & Cheng, 2018; Jin, Landgraf, Klein, & Menzel, 2014; R. Menzel & Greggers, 2015; Stone, Mangan, Wystrach, & Webb, 2018). They also remember observed azimuthal positions of the sun and the phase of their circadian clock (the time of day) at which the sun was observed to have that position above the profile of the local horizon (Gallistel, 1998). Bees and ants also remember the compass direction of local food sources. They compute the difference between the current azimuth of the sun and the compass direction of a food source to determine the angle that they should fly relative to the sun in order to go to that food source (Gallistel, 1998; Menzel & Eckoldt, 2016). Bees remember the range and bearing of food sources communicated to them by the dances of returning foragers. They rely on their memory of the dance-communicated information to guide their flights to the dance-indicated locations (Menzel & Eckoldt, 2016). These flights may occur days after the dance was observed (Menzel et al., 2011).

We, like rodents and bees, remember innumerable abstract quantitative facts: distances, directions, durations, numerosities, rates and probabilities. Like the rodents and the bees, we make computational use of these remembered quantitative facts throughout each day. Consider, for example, what happens when a spouse asks whether we can stop to pick up the cleaning on our way from work to pick up our preschool children. We estimate the earliest we can leave work given the number of tasks to be completed before we do so and the remembered times required to complete each task. We compute the extra distance to be driven, using our cognitive map. We estimate the distribution of expected driving times, given the distance to be driven and our remembered experiences with traffic in that part of town at that time of day. We recall the distribution on how long it takes to find a parking spot near the cleaners, the distribution on how long a visit to the cleaners lasts, the probability of our arriving at the preschool before the grace period expires, and the magnitude of the penalty for arriving after it expires. We recall all these quantitative facts and add it all up in the few seconds before we answer our spouse. Most of this computation goes on subconsciously.

Computations on quantitative facts stored in memory—including distributional facts about numerosities, durations, rates and probabilities—are not confined to humans; primates and rodents do them, too (Berkey, Cavdaroglu, & Balci, 2016; Breton, Conover, & Shizgal, 2014; Cheeseman et al., 2014; Drugowitsch, Mendonça, Mainen, & Pouget, 2019; Freestone, Balci, Simen, & Church, 2015; Li & Dudman, 2013; Tosun, Gür, & Balci, 2016; Yang & Shadlen, 2007).

Memories of the abstract quantitative facts gleaned from experience play no role in the contemporary search for the engram. Neuroscientists' embrace of Locke's theory explains this absence: these remembered facts are not the traces of past sensations. Sensations produced by physically measurable stimuli acting on sensory receptors were the source of Locke's primitive ideas. They were also the triggers for Hull's conditioned reflexes and for Skinner's operants. They are also the inputs to the bottom layer of a neural net. Distances, durations, and numerosities are not inputs to neural nets, because the radical empiricism that motivates these models requires sensory inputs, just as did Locke's theory. Durations, distances, numerosities, rates and probabilities neither vibrate, nor reflect, nor emit energy of any kind. A fortiori, there are no sensory receptors specialized for converting these aspects of our experience to neural signals. These aspects of our experience have no qualia. Also, there is no omniscient supervisor that teaches either us or insects to recognize durations, distances, directions. Nonetheless, our behavior—and the behavior of ants and bees—is continually informed by

these abstract quantitative facts gleaned from previous experience and communicated to contemporary computation by the engram.

Numerous neurons in the brains of diverse species fire selectively to numerosities, distances, directions and durations (Alexander et al., 2020; Ditz & Nieder, 2016; Eichenbaum, 2014; Haimerl et al., 2019; Jacob, Vallentin, & Nieder, 2012; Kutter et al., 2018; Ledergerber & Moser, 2017; Lever, Burton, Ali Jeewajee, O’Keefe, & Burgess, 2009; Tudusciuc & Nieder, 2007). However, the mechanisms underlying the firing of these neurons (e.g., place neurons, boundary vector neurons, head-direction neurons, elapsed-time-in-task neurons) remain as mysterious as the mechanisms underlying the behaviors based on those same remembered facts, because the firing of these neurons depends on facts about environmental geometry and task durations committed to memory hours, days, months and years earlier (Sheintuch et al., 2020).

A prime example of the computational manipulation of quantitative information (current location) is dead reckoning in the desert ant (Fig. 1). Dead reckoning, also known as path integration, is the integration of the velocity vector with respect to time (how fast one is going in what direction) to obtain the position vector with respect to time (where one now is). There is consensus in the animal navigation literature that this computation is foundational in the navigation of ants and bees, as it is in traditional human navigation. Path integration requires combining on a moment to moment basis the signal from a neural compass and a signal from a neural odometer. The ant’s odometer counts its steps, just as the odometer on a car counts wheel turns. The ant keeps track of where it is by adding up its step by step displacements—how far each step moved it in which direction (Wittlinger, Wehner, & Wolf, 2006).

Displacement is signaled by a 2-element polar vector—a string of two signals for quantities. One element, the compass element, represents the direction of the displacement relative to the sun’s azimuth (its position above the horizon). The other represents the length of a step (just as the Romans measured distance by a pace). The compass signal depends on the learned solar ephemeris, the position of the sun above the local horizon as a function of the time of day, as determined by the phase of the ant’s circadian clock. The ephemeris function is committed to memory during exploratory outings made prior to the first foraging trips.

For mathematical reasons, the 2-element polar displacement vector is probably converted to a 2-element Cartesian vector, one element specifying change in longitude and the other change in latitude (Gallistel, 1990; Vickerstaff & Cheung, 2010). Thus, the ant’s current estimate of its position is the sum of successive Cartesian displacement vectors over the course of its journey. This vector is the symbol in memory that carries the information about the ant’s current location. Several of the journeys in Fig. 1A lasted more than an hour and covered more than 1200 m. To keep in memory the running vector sum that

represents its current location, the brain of the ant must have a mechanism that sums without leakage the values of two different time-varying quantities (the two elements of its cumulative displacement vector). In more technical language, it must have a thermodynamically stable integrator, an integrator that does not leak. An integrator that does not leak is another way of describing a memory mechanism that endures indefinitely, to which one can add new values as experience delivers them.

In the course of its journey, the ant makes snapshots of landmarks (Cheng & Cody, 2015; Freas & Cheng, 2018; Freas, Whyte, & Cheng, 2017; Wystrach, Buehlmann, Schwarz, Cheng, & Graham, 2020). It stores them in memory, making them available to aid its navigation the next time it goes that way. When the foraging ant finds food, it stores the location of the food, that is, it copies into another memory location the current dead-reckoning vector, the vector that represents its current location; hence the location of the food it has found. It also stores the odor of the food (Buehlmann, Graham, Hansson, & Knaden, 2014). It then inverts its location vector to obtain the vector for its nest given its current location. It converts that Cartesian vector to the range (distance) and bearing (compass direction) of its nest (a polar vector), and sets its course for home accordingly (Fig. 1).

In thinking about the properties of the engram, we must consider the physical implications of these well-established behavioral facts: We must look for a physical system capable of storing diverse facts, such as distances, directions, durations, probabilities, locations, compass bearings, snapshots and odors—in a form that enables them to rapidly enter into computations conducted in the indefinite future. The genesis of current behavior generally depends on diverse facts entered into memory at various times in the past in widely varying contexts. The circumstances under which these diverse facts might enter into future computations cannot be foreseen at the times when they are committed to memory. (Who knew a spouse would someday ask us to stop at the cleaners on the way to pick up the children?) Thus, the engram carries a large amount of diverse information acquired at diverse times under diverse circumstances over indefinite time spans. Physical efficiency must be an important consideration in this information-transmission function, as it is in all practical communication channels. Vast amounts of information must be carried in a medium that requires little or no energy for its preservation (i.e., its transmission forward in time) and takes up a minimal amount of physical space.

In order to pass into and through a channel of communication, a message must be encoded (Shannon, 1948). Therefore, those of us pursuing the material basis of memory must ponder what the code might be and how it could be physically realized (Gallistel, 2017a, 2017b) This question about the memory code makes neuroscientists deeply uncomfortable, for which reason, it is never posed in the vast literature on the neurobiology of memory. Answering it requires one to specify the

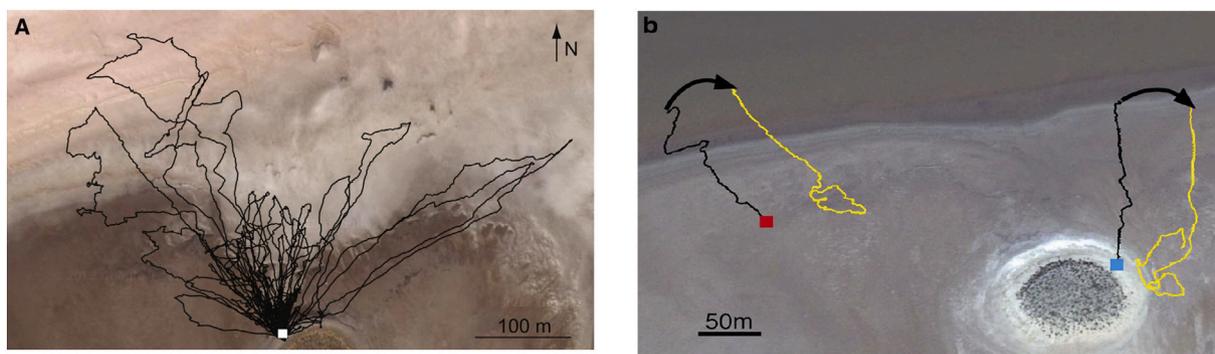


Fig. 1. A. Tracks of *Cataglyphis* ants foraging on a salt pan in Tunisia. Note the scale bar. (Buehlmann et al., 2014 used by permission of authors and publisher). B. Tracks of two ants displaced from a food source at the beginning of the homeward leg. Black traces are the outward journeys; yellow, the homeward journeys. The red and blue squares mark the nest entrance. The arrows indicate the displacement (Huber & Knaden, 2015, used by permission of the authors and publisher). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

principles that govern the mapping from the quantitative facts in question to the physically realized structure in the brain that encodes a given fact, just as one learns in a first course in molecular biology the principles that govern the mapping from codon sequences in DNA to the protein structures for which those sequences code and the mapping from homeobox genes to the abstract aspects of organic structure for which the proteins produced by homeobox genes code (e.g. anterior, dorsal, distal, see [Carroll, 2005](#)).

The neuroscientific literature abounds in assertions of the form: the activity of this neuron, or more commonly, this pattern of firing across this neuronal ensemble, encodes this experiential fact. There are three problems with these assertions. First, there is no code book, nothing that would enable one to deduce in advance the pattern of firing that would encode a given fact ([Gallistel, 2017c](#)). Second, the evidence is purely correlational—these neurons fire in this situation. Further experiment often reveals that the same firing occurs in response to other facts, often many and diverse other facts ([Bhattarai, Lee, & Jung, 2020](#); [Schuette et al., 2020](#); [Sheintuch et al., 2020](#)). This destroys the essence of a code, namely that it be an invertible mapping: From reading the pattern of firing, the reading device can know what that bit of code communicates (cf [Reilly, Cros, Varol, Yemini, & Hobert, 2020](#)). Finally, and most importantly, the firing of a neuron or a neuronal ensemble is an *expression* of a memory, not the memory itself. Treating firing patterns as memories is analogous to confusing the activity of the LEDs in the screen of a mobile phone with the phone's memory. The phone's memory does not reside in LEDs, much less in the light they emit; the light emitted by the screen's LEDs communicates to us—the users of the information—the consequences of the computations performed by the phone's CPU on the contents of its memory. Similarly, the firing of a head-direction or a place cell gives other parts of the brain access to geometric information stored somewhere else; it reveals the existence of a memory for the geometry of the environment. The firing of that cell is not the physical realization of the memory that makes the geometry-based firing possible ([Keinath, Julian, Epstein, & Muzzio, 2017](#)). The firing of neurons communicates information through space, that is, to other neurons; the engram communicates information through time.

Claims about neural encodings seldom pay attention to the principles that govern efficient codes. Efficient codes transmit information using minimal physical resources, such as energy and mass. Such codes have a basis set of elements out of which meaningful, that is, fact preserving, messages are constituted in accord with a set of combinatorial principles. The alphabet is one example. Its basis set is the set of 26 letters. Most letters are sub-semantic; they have no free-standing interpretation. Morse code is another example. It piggy backs on the alphabet, using a smaller basis set—a set of three inter-click intervals, all of them integer multiples of the interclick interval for the dot—to build element strings (sequences of inter-click intervals) with alphabetic and punctuational meanings.

The genetic code is another example. Its basis set consists of 4 nucleotides. They are sub-semantic. The words in this code—the minimum strings of nucleotides that have meaning—are nucleotide triplets called codons. Most codons code for amino acids; a few code for punctuation. Amino acids are the building blocks of proteins.

Proteins are the building blocks of organic structures. However, many proteins are not the bricks in any structure, they are the addresses of other genes (transcription factors). Combinations of these transcription factors define the body axes (anterior and dorsal), the distal points of appendages and neuronal types ([Reilly et al., 2020](#)). The similarity of multi-level molecular-biological codes to multi-level written language codes is striking: Letters code for phonemes; phonemes are the building blocks of words; words are the building blocks of sentences. At each level, different combinatorial principles come into play—both in the molecular biology and in human language.

Morse was engaged in an engineering task when he constructed his system. That made him sensitive to considerations of physical efficiency. He could, for example, have used a unary code for the letters instead of a

combinatorial code. In a unary code, 1 click would code for 'A', 2 clicks for 'B', ... 26 clicks for 'Z' and 36 clicks for '9'. Telegraphic transmission would be orders of magnitude slower had Morse adopted a unary code. Therefore, the energy consumed and the time taken in generating and transmitting the signals that carry the messages would be much greater per message transmitted. Morse crudely anticipated Shannon in making the lengths of the strings for different letters approximately inverse to the frequency with which the different letters appear in English communications. In doing so, he further increased the rate at which information could be transmitted using his code and further minimized the energetic and temporal costs of transmitting it.

Labeled-line codes or labeled neuronal assembly codes are often postulated by neuroscientists (This neuron encodes threeness. This cell assembly encodes the rat's fear of the box in which it has been shocked.) These would appear to be unary codes, like the hashmark code for number ([Gallistel, 2017c](#)). Their proponents do not specify the elements of these codes nor any combinatorial principles. Unary codes are grossly inefficient.

The above examples of the basic principles underlying otherwise wildly diverse efficient codes suggest that the basis set for the engram code must consist of a small set of code elements, probably sub-semantic, from which the elements of a secondary code are constructed. This secondary code must be like the alphabet and the gene: principled orderings of its elements must be capable of encoding any encodable fact, whether abstract, like number, distance, duration and probability, or concrete, like odor, light intensity patterns, and vibrational patterns.

What might the elements of this secondary code be? I suggest that the numbers are the word elements in a universal engram code, the code used by neural tissue to transmit facts into the indefinite future regardless of the type of fact and the species of animal. On this suggestion, the minimal arrangement of code elements with free-standing meaning are those that encode quantities that can be represented with individual rational numbers, quantities such as distances, durations and probabilities. [Gelman and Gallistel \(1978\)](#) called these neurobiological numerals *numérons*.

Strings of numerons that encode concrete facts, like colors, odors and faces, are vectors in the brain ([Chang, Bao, & Tsao, 2017](#); [Chang & Tsao, 2017](#); [Stevens, 2015](#); [Stevens, 2016, 2018](#)). Vectors—strings of numbers—are capable of encoding anything that we know how to encode—colors, odors, faces, snapshots, maps, whatever. We know this, because everything we currently know how to encode is currently encoded by strings of bits in computer memory.

Regardless of what they represent, down deep bit strings are numbers, because the combinatorial operations in a computer are logico-mathematical operations on numbers. Encryption algorithms depend on the arithmetic operations on these bit strings. Thus, in the memory channel, where our store of experientially acquired facts resides, it's numbers all the way down.

In thinking about what the physical realization of numerons might be, the single most consequential consideration is that they must be *generable*—rapidly, in very large numbers, at little energetic cost ([Gallistel, 2017a, 2017b](#)). Consider again dead reckoning. Some of the trips in [Fig. 1A](#) cover approximately a kilometer. A kilometer measured in the ant's 1 mm paces is 1,000,000 paces. That means the net displacement vector that represents the ant's current location must have been incremented roughly 1,000,000 times. Each increment must have produced a physical entity that differed from the entity that represented the ant's immediately preceding location. The computational machinery adding up the successive displacements must be capable of distinguishing each preceding location vector from all of the succeeding location vectors. The numerons composing the location vector must be capable of representing a vector quantity that varies over 6 orders of magnitude in the course of an hour. These considerations imply the generation of 2,000,000 distinguishably different numerons in the brain of the ant in less than an hour, just to keep track of where it is.

That 2,000,000 number does not count the snapshots the ant takes along the way. At its most basic, a snapshot is a record of photon catches. There are roughly 100 ommatidia in each ant eye and 7 receptors in each ommatidium, thus about 1400 photon-catching elements. It may well be that not every receptor in every ommatidium contributes its photon catch to a snapshot. Also, there is redundancy in the photon catches from ommatidium to ommatidium. This redundancy, which is traceable to the statistics of the visual environment, makes it likely that a bandwidth-reducing coding scheme is applied to the signals generated by the photon captures before the transient visual signals are converted to a snapshot in memory. Nonetheless, it seems likely that a snapshot must consist of something like 100 pixels, with 3–8 bits required to store the contrast at each pixel. That implies the generation of 100 3–8 bit snapshot-encoding numerons in a fraction of a second. To this must be added the bits required to record the location and heading of the ant when the snapshot was taken.

The engram must consist of information-bearing physical structures. The generatability question is, where do the information-bearing structures (e.g., the numerons) come from? Do they pre-exist, like neurons and synapses and the bit registers in a computer? In other words, have they been formed long before acquired information is inscribed in their structure? Or, are they generated at the moment they are required, like the bit patterns at the output of a CPU and the DNA in a replicating organism or a cell undergoing division?

The generatability question raises the further question, How big and complex are the information-bearing structures that constitute the engram? Are they small and simple like polynucleotides (strings of nucleotides, base pairs in DNA and RNA)? In that case, they will be easy to generate rapidly in large numbers with little energy consumption. If they are big and complex like neurons and synapses, their generation will take much longer and require much more energy. Also, the resulting cellular- and circuit-level structures will occupy orders of magnitude larger volumes than the volumes occupied by information bearing molecules, like the polynucleotides. Moreover, because they will have to be generated well in advance of the time when acquired information is inscribed in their structure, cellular level structures will be like the bit registers in a computer; they will take up space even when they carry no information. By contrast, information-bearing molecules like RNA can be produced at the moment the acquired information needs to be stored, and destroyed when it is no longer needed.

Polynucleotides are synthesized at rates ranging from 10 to 100 nucleotides/s (Milo & Phillips, 2016). Because there are 4 nucleotides, each successive location in a string of nucleotides can carry 2 bits of information. Thus, an n -bit polynucleotide numeron could be generated in roughly n centi-seconds. A 21-bit polynucleotide can encode slightly more than 2,000,000 biochemically distinguishable numerons. It can be synthesized step by step as the ant runs. Moreover, only one ATP has to be hydrolyzed in order to add a nucleotide to the string. Thus, the total energetic cost of storing the current location vector in two polynucleotide strings over the course of an hour's run covering a kilometer would be less than 100 ATPs. By way of comparison, transmitting a single spike (nerve impulse) in an unmyelinated fiber, releasing the transmitter substance and taking it back up consumes approximately 100,000,000 ATPs (Gallistel, 2017b).

These elementary considerations about the speed and physical efficiency of communicating stored facts by means of the only biological structures that are known to function as transmitters of information (polynucleotides) suggests that the time is long past when neurobiologists should have stopped thinking about memory within the conceptual framework provided by 17th and 18th century empiricist philosophers. They should have long ago begun thinking about it within the conceptual framework provided by contemporary information sciences and by molecular biology. Memory is a medium that transmits encoded information gleaned from past experience to the computations that inform future behavior. Within this conceptual framework, the concept of an efficient code is foundational. Some elementary calculations within that

conceptual framework imply that the material realization of the engram is probably not to be found in the synapse, much less in multi-neuron cell assemblies (the neural equivalent of Locke's dust-ball concepts); it is to be found in information-bearing molecules inside neurons, operated on by molecular level computational machinery (Akhlaghpour, 2020).

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