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Sentience and Consciousness in Single Cells: How the First Minds Emerged in Unicellular Species

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A reductionistic, bottom-up, cellular-based concept of the origins of sentience and consciousness has been put forward. Because all life is based on cells, any evolutionary theory of the emergence of sentience and consciousness must be grounded in mechanisms that take place in prokaryotes, the simplest unicellular species. It has been posited that subjective awareness is a fundamental property of cellular life. It emerges as an inherent feature of, and contemporaneously with, the very first life-forms. All other varieties of mentation are the result of evolutionary mechanisms based on this singular event. Therefore, all forms of sentience and consciousness evolve from this original instantiation in prokaryotes. It has also been identified that three cellular structures and mechanisms that likely play critical roles here are excitable membranes, oscillating cytoskeletal polymers, and structurally flexible proteins. Finally, basic biophysical principles are proposed to guide those processes that underly the emergence of supracellular sentience from cellular sentience in multicellular organisms.

Motto: *Nothing in biology makes sense except in the light of cells.*

1. Introduction

There is a growing suspicion among biologists, ethologists, and geneticists that mental states, awareness, consciousness or, to use a more general term, sentience, is an inherent feature of life. This proposition, of course, is not new but it has never been part of the standard model. Over a century ago anatomist Charles Minot (1902) maintained that "A frank unbiased study of consciousness must convince every biologist that it is one of the fundamental phenomena of at least all animal life if not, as is quite possible, of all life."[1,2] Since then several prominent biologists and life scientists have expressed similar sentiments. George Gaylord Simpson noted that "All the essential problems of living organisms are already solved in the one-celled ... protozoan and these are only elaborated in man or the other multicellular animals."[3] In her Nobel speech geneticist Barbara McClintock referred to the "... knowledge the cell has of itself and how it utilizes this knowledge in a 'thoughtful' manner."[4,5] Evolutionary biologist Lynn Margulis, in a paper provocatively titled "The conscious cell," maintainted that "... consciousness, awareness of the surrounding environment, starts with the beginning of life itself."[6,7] We concur. One of us (Baluška) has expressed similar sentiments[8,9] and the other (Reber) recently wrote a book on the topic noting that the proposal that life and consciousness are co-terminous also has important implications for the neurocognitive sciences and the philosophy of mind.[10,11]

Two critical elements, however, have been largely absent from these proposals and, perhaps, kept this perspective from becoming part of mainstream evolutionary biology. The first is acknowledging the fact that sentience is a necessity for an adaptive life. Within standard approaches to evolutionary biology, sentience/consciousness is viewed as a feature that emerged at some time in some species and is not regarded as essential for all life. We will present arguments supporting the contention that this position is wrong – that, in fact, all adaptive and functioning organisms, from the earliest on, must be sentient, conscious, and have an ontological self-awareness. A non-sentient organism, we maintain, would be an evolutionary dead-end. As philosopher Thomas Nagel might put it, "there is something that it is like to be a Paramecium."

The second missing element is identifying one or more coherent mechanisms through which the non-sentient, prebiotic slurry of molecules became the epistemic foundation of a sentient agent – in short, how "the material creates the mental," or what philosopher David Chalmers famously called the "hard problem" of consciousness. There have been a few efforts here but the issue has been largely neglected by cell biologists.

2. Biological Basis of Consciousness and Sentience Remain Elusive

Before we get into the details of our model, let us be clear about what we mean by sentience or consciousness as it is manifested

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in unicellular species. We are referring to feelings, subjective states, a primitive awareness of events, including an awareness of internal states. We are using these terms in what is generally referred to as a "folk psychology" fashion. It is likely that these forms of sentience are experienced along a valenced "good-bad" continuum and that the internal representational form is determinative of actions. A prokayote encountering a nutrient rich environment and detecting these life-enhancing molecules experiences, in our framework, a feeling, an internal state of satisfaction and decisions about suspending locomotion are engaged. One moving into an environment with an uncomfortably high salt content has a negative subjective state that elicits movement back toward a remembered earlier, less aversive environment. In these and scores of similar experiences, all of which are well-known in cell biology, prokaryotes, we maintain, experience valence-marked, subjective, internal, representational states. We are calling all these forms of subjective awareness, either of environmental events or of organismal internal states, sentience, consciousness.

A fundamental axiom of our model is that these internal, subjective forms of sentience are an essential component of all life forms. They emerged with the first appearance of life and all more complex, varied forms of mental life are the result of evolutionary mechanisms. Just as all life forms extant and extinct are the descendants of a singular event some 3.5 billion years ago, so all the varied forms of mental life, of sentience, are derived directly from those initial ancient prokaryotic species. In short, life and sentience are co-terminous. We find it interesting that evolutionary biologists, psychologists, philosophers are all comfortable with the notion that the bio-physical elements of life appeared just once but, somehow, are uncomfortable with the notion that mental elements accompanied them.

There are reasons why there has been relatively little research into this topic and it can be traced to the tendency to begin (and often end) with the focus on human consciousness, the human mind. In 2005 the American Association for the Advancement of Science ranked the question "What is the biological basis of consciousness?" as the second most important and challenging unsolved scientific problem (the first was "What is the universe made of?").[12] Implicit in the asking was the assumption that it was human consciousness that the editors were concerned with. As we (and others) have noted,[8–11] this tendency to approach the issue of consciousness from a *Homo sapiens*-centered perspective has been problematical.

It invited two lines of research that yielded fascinating insights into the cognitive functions of a variety of species but have had little impact on the core issue. One approach attempted to identify the neural correlates in humans responsible for consciousness and examine the evolutionary tree for evidence of those structures or homologues of them. The other sought to identify the cognitive and/or behavioural functions that were deemed diagnostic of consciousness and then look for the point(s) in the evolutionary scheme of things where species with the appropriate behaviors first appeared. We have no problems with either branch of research, but it is unlikely in the extreme that either strategy is going to get at the underlying issues: the co-terminous nature of life endowed with sentience and a theory of the initial emergence of consciousness on this planet. As one of us (Reber 2018) outlined,[11] the field is awash with squabbles over which species have the right biological structures to support consciousness, which behavioral functions are diagnostic of awareness, where in the great panoply of life an unambiguous sentience emerged – and little progress has been made.

What is far more likely is that when life first originated, sentience "came along for the ride" and what is needed is a cellular-based and evolutionarily bottom-up theory of sentience and consciousness.[8–11,13–16] Our point, in a twist on Theodosius Dobzhansky's famous statement,[17] is "Nothing in biology makes sense except in the light of cells." One of us recently put forward a novel model of the origins of mental life, dubbed the Cellular Basis of Consciouness (CBC), based on the assumption that the cellular nature of life is inherently linked with consciousness.[11] Here, we elaborate further on this theory. We also review a number of molecular processes that appear to be viable candidates for the biological mechanism through which a mental, phenomenal element comes to accompany the emergence of life. We are agnostic as to which is more or less likely to be correct and, in fact, suspect that the final answer(s) here will look rather different. But we will not know until we begin the actual, laboratory-based explorations.

3. Consciousness Is an Inherent Property of Cellular Organisms

From the CBC perspective, awareness of self and the capacity to detect, interpret, and experience the valenced characteristics of the environment is essential for survival and evolution.[10,11,18–23] Environments are in constant flux. The concentration of the nutrients in the surrounding medium shifts; temperature gradients change; there is an unrelenting assault from viruses, toxins, predators – and, furthermore, these conditions are continuously changing. Without an internal, subjective awareness of these changes, without being able to make decisions about where to move, how to modify gene-expression adaptively for shifts in nutrient levels, how to match the ambient temperature with a memory of what it was in a previous location for adaptive movement, a prokaryote would be a Darwinian dead-end. Moreover, all cellular life, starting with unicellular organisms, is sensitive to anesthetics[24] and, importantly in this respect, plants and several unicellular organisms generate endogenous anesthetics when they are wounded or stressed.[20,25,26] In the classic model, a nonsentient agent, one lacking sensations and awareness of its environment should not be responsive to anesthetics. If an organism has no affective experiences why would it be sensitive to anesthetics or produce its own?

There are arguments against our overall proposition but they suffer from various problems. For example, take the one put forward by prominent philosopher Daniel Dennett (2017) who argues that behaviors such as learning or communicating, when observed in unicellular or simpler multicellular species, are nothing but the blind actions of genetic programs that spin themselves out without awareness or other internal subjective states.[27] In his terms they have "competence" but lack "comprehension" of what they are doing. This proposition is not wrong in any fundamental way. It is true, as he notes, that termites build nests without any mental plan whereas humans build cathedrals with well-constructed blueprints. The deeper question that concerns us is whether that more primitive state, the one where competence is displayed, is one that has a subjective, sentient component. Dennett demurs on this point. He grants the proposition that prokayotes are subjectively self-aware a non-zero probability of being true. We agree but argue that that probability is, in fact, 1.0.[27]

Prokaryotes[28] such as bacteria are extremely adept organisms. They have elaborate sensory systems, learn to navigate their environments, anticipate regular shifts in events about them, lay down surprisingly resilient memories, communicate with each other, display a primal form of altruistic behavior, detect and evaluate in a contextual manner diverse aspects of their environment including temperature gradients and nutrient levels, determine the valence of objects they encounter, and use this information to make adaptive decisions (see Reber, 2018; Chapter 4 for details).[11] Biophysicist Jané Kondev was so taken with the range of behaviors of *Escherichia coli* that he expressed the opinion that they seemed to simply have "free will."[29]

In order for an insentient organism to carry out such an array of behaviors, each of these highly adaptive functions would have to have specific sequences of DNA that guided behavior independent of any subjective sense of what was being felt, perceived, reacted to, learned, and recalled. This is, from a basic evolutionary biological point of view, far less likely than simply having a singular sentience co-occur with the emergence of life. In short, Daniel Dennett's "competence without comprehension" proposal provides us with no additional explanatory power. We simply end up with a list of things that we know prokaryotes can do. It also suffers from the "emergentist's dilemma." That is, if these ancient species are not sentient, then somewhere along the panoply of life an organism evolved a mental life, consciousness. Where and how did this happen? What forms or structures are needed? Which species can be included under the umbrella of sentience? As noted above, when these kinds of issues are introduced they have invariably led to squabbles, not progress (see Reber 2018 for details).[11]

Our proposal cuts through this hypothetical cluster of insentient functions. It does not avoid the problem of emergentism, but it puts it in a far more tractable framework and tells us where to look. It is also eminently falsifiable, fits comfortably within existing models of cell biology, and critically, is one with considerable explanatory power. What we are arguing is that the maximally adaptive process would be for the first unicellular organisms to have sentience encoded in its DNA and, in virture of such a subjective capacity to monitor its metabolic and behavioral functions, be able to react adaptively to each of the valenced objects and events it encountered. This, we maintain, is where the first minds appeared and the mental states and functions of all subsequent species are derived from this ur-consciousness. It happened only once on this planet and, like the underlying biomechanical processes that gave rise to life, every other species carries these essential pieces of genetic material that code for sentience.

4. Excitable Membranes, Cytoskeletal Polymers, and Structurally Flexible Proteins as Cellular Components Critical for Generation of Sentience and Consciousness

However, concluding that sentience and life are co-terminous is an in-principle argument. What is needed, of course, is indentifying the candidate biomechanism(s) that could give rise to sentience. We know of only one other effort at solving this problem. It was laid out in an unusual forum, a letter written by a group of prominent neurocognitive researchers (see ref. [30]) to Christoph Koch and published in *Scientific American* – Koch was on the board of advisers of Scientific American Mind. The letter was a follow-up on arguments made in a 2014 paper by Cook, Carvalho, and Damasio and focused on irritability, a hyper-sensitivity that is characteristic of all cells.[31] They maintained that:

> [The] sudden onslaught of positively-charged ions (cations) into the alkaline cytoplasm – the very definition of membrane excitability– is the key phenomenon involved in a cell's 'awareness' of its environment ('sentience'). . . . [The] problems of sentience, awareness, and ultimately primate self-consciousness begin with the response of excitable cells to external stimuli that threaten to disturb cellular homeostasis.

We are in agreement with this position, with one caveat. In the earlier paper Cook et al.[31] maintain that this mechanism is not operative in plants. Below we identify relevant cellular functions that are present in flora. As noted above, while we are largely restricting our current explorations to individual prokaryotic cells, we do so with the understanding that whatever mechanisms operate at the level of prokaryotes will carry on their functions in eukaryotes and multicellular organisms. A basic principle of evolutionary biology is that adaptive forms and functions, once established, are rarely jettisoned – and when they are (e.g., the spine in the hagfish, limbs in snakes), the traits lost can re-assert themselves should the context change. The cavefish that lost its eyes would recover them rapidly (in evolutionary time scales) under appropriate circumstances. The genes for the jettisoned traits remain embedded in the genome.

There are at least three possible subcellular sources for the emergence of sentience and consciousness at the cellular and subcellular levels that would seem to be candidates here. First are the excitable membranes, ones equipped with critical proteins enriched especially in highly ordered lipid rafts.[32–36] Second are the excitable and vibrating microtubules and actin filaments in cells.[37–39] The third are biological quasicrystals with fivefold symmetry.[40,41] A closer look at each will indicate why these structures and processes are likely candidates for the biomechanisms responsible for sentience in unicellular organisms.

4.1. Excitable Membranes

The critical property of the cellular plasma membrane is its excitability linked inherently to environmental cues and signals.[30,42] A second important feature of cellular membranes, particularly relevant for the cellular basis of sentience, is that their lipid bilayers have quasi-crystalline properties.[43,44] These structural characteristics of cells are general and ubiquitous and emerging as the most likely sources of cellular awareness. Their relevance is emphasized by noting that diverse anesthetics, ones that produce loss of consciousness in humans, also cause loss of responsiveness in all animals and plants.[25,45–47] Excitable membranes appeared early in the biological evolution of cells[48–51] and are present not only in eukaryotes but also in prokaryotic species as well as in eukaryotic organelles of endosymbiotic origin.[19,52–54] A recent study revealed that the sensitivity of plant movements and behavioral responses to local and general anesthetics is linked to excitable membranes, action potentials, and to endocytic vesicle recycling.[25] In contrast to views that plants lack excitable membranes,[30,32] plants display their own plant-specific action potentials based on their excitable membranes.[25,42,48] In both plants and animals, excitability of membranes is linked to awareness of their environment and anesthetics compromise this function, making them unresponsive to environmental cues.

4.2. Vibrating and Excitable Cytoskeletal Polymers

A second possible source of sentience and consciousness at the cellular level is the dynamic cytoskeleton. Microtubules are regarded as important in this respect,[29–31,38,40,41,54,55] and terahertz oscillations in tubulin have also been found to be affected by exposure to anesthetics.[40] Besides microtubules, the actin filaments behave as an excitable medium that, in addition to transporting vesicles and organelles, also transports ionic waves.[39,56–58] Dynamic actin cytoskeleton also supports lipid rafts, which are highly ordered domains of excitable membranes that are particularly sensitive to diverse anesthetics.[33–36] These ordered domains of biological membranes are crucial for signal transduction and often undergo endocytic vesicle recycling.[59] Moreover, electrostatic interactions at endocytic and plasma membranes control endomembrane-based signaling.[60]

4.3. Biological Quasicrystals with Fivefold Symmetry

Finally, there are indications that special proteins, in particular those having fivefold symmetries and quasicrystal properties, are relevant for the cellular and subcellular levels of sentience.[42,43] In this respect, it is important to recognize that the three-dimensional structure of proteins is not dictated solely by the sequence of amino acids; proteins dynamically select one of several possible conformations according to physico-chemical conditions.[61] This flexible behavior of proteins suggests that proteins also contribute to subjectivity within single cells.[61–65] Ladislav Kováč[63] proposed that such proteins exhibit features of molecular sentience. Albert Szent Györgyi[66] opined that structurally flexible proteins can act as bioelectronic devices due to their electrons moving within their dynamic domains. Relevant here are trans-membrane proteins that underlie the bio-electric excitability of membranes controlling cell growth, development, movement, and morphogenesis in both unicellular and multicellular organisms.[67,68] Many of these proteins are discussed as so-called Maxwell's demons, acting as thermodynamic ratchets, or imaginary gatekeepers, to support ordered life processes inside cells.[69–72] These metaphoric demons could, in principle, use survival-relevant information and knowledge accumulated over the whole of biological evolution[61,69] to support living systems by resisting (though not violating) the second law of thermodynamics.

5. Synaptic and Ephaptic Principles Guide Generation of Supra-Cellular Sentience and Consciousness

A unique feature of cells based on limiting membranes is that the lipid bilayer-based membranes enclose spherically shaped compartments, a property that allows them to generate highly specific micro-niches, ones that generate and maintain mechanisms typical for living systems on the basis of energy fluxes accomplished at the plasma membrane. This outside–inside dichotomy seems likely to play a central role in generating internal (subjective) awareness of the outside world, hence representing the basis for cellular sentience.[30,31,73,74]

How could individual cellular consciousness generate larger-order supracellular consciousness of multicellular organisms? In fact, this crucial question is relevant already at the level of the eukaryotic cell, which is, in fact, a consortium of several prokaryotic cells transformed into the cytoplasm, mitochondria, plastids and perhaps also nuclei.[75–81] These organelles of eukaryotic cells lived originally independent lives and are also enclosed via membranes equipped with critical proteins endowing sentience and an internal awareness of features of the external world. Eukaryotic cells are – evolutionarily speaking – multi-cellular assemblies based on three (animals) or four (plants) originally independent organisms/cells.[75,77–81] In contrast to simpler prokaryotic cells, which are strictly unicellular organisms, complex eukaryotic cells are multi-cellular organisms (cells within cells).[74–76] In order to integrate the eukaryotic cells into a single coherent supracellular unit, individual partner cells use their synaptic cell–cell adhesion domains to negotiate the structural and functional unity seen in present supracellular eukaryotic cells.[76] In this sense, the pre-eukaryotic cell emerged from the union of two different cells[77–81] and the actin-based host cell transformed into the cytoplasm enclosed by the plasma membrane, and the tubulin-based guest cell transformed into the eukaryotic nucleus with associated microtubular cytoskeleton.[75,77–80]

Later, during evolution of such multi-cellular eukaryotic cells, bacteria were internalized and transformed into the energy power-houses of eukaryotic cells: mitochondria and plastids. These new bacterial organelles allowed evolution of higher cellular complexity and embarking on the true multicellular evolutionary pathway leading to complex fungi, animals, and plants.[81] It might be speculated that the synaptic-like nature of the eukaryotic cell[76] is the central feature allowing evolution of true multicellularity, which was never attained by in the prokaryote domains. Finally, the multi-cellular nature of the eukaryotic cell has profound implications for the sentience of such a multi-cellular cell. There are up to four cells within a cell (three in animal and four in plant cells) underlying generation of fundamentally higher levels of cellular sentience and consciousness in eukaryotic cells.[74] Ecologist Tom Fenchel[82] stated that the eukaryotic cell can be viewed as a cellular consortium acting as a self-contained ecosystem. It is relevant in this respect that all living systems require biocommunication to solve problems during their evolution.[83–85]

Besides synaptic principles, another possible mechanism might be provided via ephaptic phenomena when the adjacent cells do not need to be in direct structural contacts but interact via extracellular electric and electromagnetic fields.[86–89] Such ephaptic coupling is found in tissues organized by other excitable cells, such as cardiac muscle cells,[90–92] and it can be expected to be active in any tissue composed of excitable cells assembling into such oscillating units. In plants, the best candidate for such an ephaptic unit is the oscillating zone of the root apex.[42,93]

Anesthetics provide an ideal experimental tool to test our concept that cellular sentience and consciousness are based on excitable membranes and cytoskeletal polymers. One recent study revealed that membranes of plant cells, as well as their dynamic cytoskeleton supporting endocytic vesicle recycling, are sensitive to anesthetics.[25,47] Moreover, unicellar protozoa such as Paramecium are known to be sensitive to anesthetics.[94] Plants, such as model plant *Arabidopsis thaliana*, can act as ideal models for future studies that seek to unravel the roles of cells and their cellular organization in generating cellular and supracellular levels of sentience and consciousness.

6. Conclusions

In this essay we have made two coherent sets of arguments, both of which have solid foundations in evolutionary biology and the biophysics of cellular function. In the first, we argued that sentience, awareness/consciousness appeared with the first emergence of life. A unicellular organism that feels and has a sensitivity to its surrounds, that can subjectively evaluate the beneficial or injurious nature of objects it encounters, perceive nutrient gradients, recall the properties of previously encountered environments, and communicate with other organisms is going to be highly adaptive and functional. The advantage of being sentient is significant, particularly when having to navigate an environment in constant flux – a situation that would have been impossible to survive without some form of awareness of self and surround. Hence, it is virtually certain that sentience accompanied life from the earliest life-forms on this planet. All subsequent instantiations of mental life, all more complex cognitive organisms, up to and including human consciousness, evolved from this singular event; just as all forms and all aspects of life followed the same evolutionary path.

The other task we took on is the more difficult one, to identify the biomolecular and biophysical mechanisms that could have been present as the first life-forms emerged from the prebiotic slurry. Here, admittedly, we are speculating – but it is an educated speculation based on known properties of cellular biology. We have identified three potential structures/processes: a) excitable membranes with critical proteins enriched in highly ordered lipid rafts; b) excitable, vibrating microtubules and actin filaments; and c) structurally flexible proteins and biological quasicrystals with fivefold symmetry. Whether one or all of these can be shown to be operative in generation of cellular sentience and consciousness is an empirical question. We anxiously await the future research.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords

cell, consciousness, cytoskeleton, Evolution, Membrane Excitability, Mind, Sentience

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