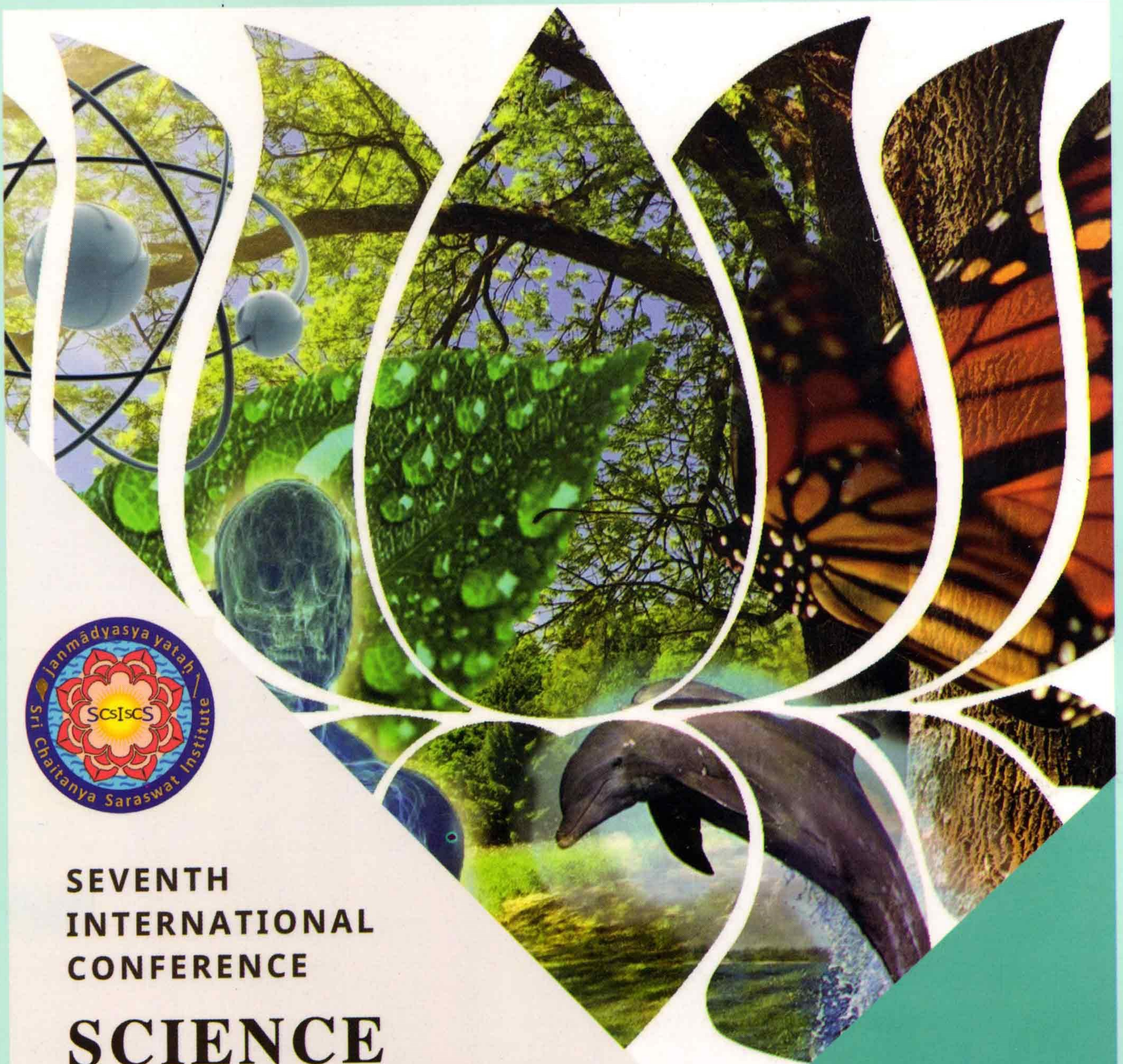

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SEVENTH INTERNATIONAL CONFERENCE

SCIENCE AND SCIENTIST 2019

UNDERSTANDING THE SOURCE AND NATURE OF CONSCIOUSNESS AND LIFE

The Scientist can explain Science, but can Science explain the Scientist?

Rutgers University

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JUNE 15-16, 2019

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CONTENTS

Talk 3:

Physics Transcended: Cell Intelligence and the Nurture of Healing

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INTRODUCTION

Imperatives derived from Cartesian reductionism underpin contemporary interpretations of multicellular organisms and the manifestation of life in protists. Our failure to elucidate the mechanisms underpinning the phenomenology of response in the living cell is seen as a failure to interpret the physics of metabolic and sensory processes; however, life transcends physics. The responsive behavior of living cells and its ability to solve novel problems has not been resolved and our standard model physics is itself not up to the task. It is here posited that living organisms survive and proliferate through complex mechanisms inimical to conventional scientific analysis. Brain function is customarily considered to result from activity at the synapses, whereas analysis of time-referenced recordings from neurons *in vitro* reveal modulations of output that result from intraneuronal data-processing. Considering brain function from the viewpoint of the neuron, farther than the network, provides revelatory insights into thought processes, and into the nature of death. More remarkably, frame-by frame analysis of phase-contrast videomicrographs substantiates that single cells of the Rhodophyte alga *Antithamnion* manifest sensory, interpretative and remedial processes that are comparable with those of more specialized phyla, for these cells can be shown to manifest intelligence and altruism. The proclivities of more highly evolved organisms are rich in resonances of the way single cells behave and this vitalism cannot be elucidated by current scientific methodologies.

A MECHANISTIC IMPERATIVE

Our era of Cartesian reductionism belies the true nature of life. Standard model physics and its satellite sciences have been dignified as a Theory of Everything (1), more recently also known as the Final Theory, Master Theory, or Ultimate Theory. A recent article assures readers that 'Physicists are on the hunt for a "theory of life" that explains why life can exist' (2) and which reprises principles previously expounded in 2010 (3) which was revisited the following year (4). The physical propensities of matter are regularly cited as underpinning living systems (5) to such an extent that physics is construed as accounting for the meaning of life (6) and the behaviour of people is dismissed as a flow system that is essentially the same as that of a river, the principle of a Constructional Law (7). This is expressed by the author in the following terms: "For a finite-size system to persist in time (to live), it must evolve in such a way that it provides easier access to the imposed currents that flow through it" (8).

For over a decade we have been informed by the repeated insistence that computers will equate to the human brain (9) though the organic functionality of the living neuron has nothing in common with the digital precision of a computer driven by algorithms. These current concepts seem to have an internal self-referential validity, but they concern trite and superficial manifestations of living systems and fail to comprehend its complexity.

THE DELUSION OF PHYSICS

To me as a biologist, the outstanding conundrums of life are not those that seek to reconcile our understanding of entropy with metabolism, or to construe a digital model that regulates evolutionary adaptation; they are how organisms behave, and interact, and resolve problems. The unimpeded drive towards the equivalence life with digital models was launched by Hungarian physicist and polymath Neumann János Lajos, later known as John von Neumann (1903-1958), who first claimed that the human brain, essentially, functioned as a digital computer (10) and from this developed the idea that, at an hypothetical juncture nick-named 'the singularity', computers would equate to, and thereafter supersede, human abilities (11). These ideas stemmed from early work on robotics which had often been regarded as approaching real life (12). As early as 1949 the American-born inventor W. Grey Walter manufactured autonomous robot-like battery-powered machines that used reflective signals detected by photoelectric cells to avoid obstacles which he claimed were as intelligent as a two-celled microorganism. He gave them a binomial name as if they were a life-form: *Machina spectulatrix* (13) and he wrote of his little models as if they were close to life and in some ways superior:

> 'The machines are fitted with a small flash-lamp bulb in the head which is turned off automatically whenever the photo-cell receives an adequate light signal. When a mirror or white surface is encountered the reflected light from the head-lamp is sufficient to operate the circuit controlling the robot's response to light, so that the machine makes for its own reflection; but as it does so, the light is extinguished, which means that the stimulus is cut off — but removal of the stimulus restores the light, which is again seen as a stimulus, and so on. The creature therefore lingers before a mirror, flickering, twittering, and jigging like a clumsy Narcissus. The behaviour of a creature thus engaged with its own reflection is quite specific, and on a purely empirical basis, if it were observed in an animal, might be accepted as evidence of some degree of self-awareness. In this way the machine is superior to many quite 'high' animals who usually treat their reflection as if it were another animal, if they accept it at all.' (14)

Fig 1: W. Grey Walter and his wife in Bristol, England, demonstrate *Machina spectulatrix,* a photocell-oriented battery-powered automaton which he claimed had the capacity of a two-celled organism. Such hubris has marked out the failure to comprehend the complexity of living organisms since the time of Descartes.

This grossly over-stated interpretation of the response of a simply designed photoreceptor-induced automaton reinforced the notion that humans were no more than machines. In a pre-electronic era the notion of life as a mechanical contrivance had been cultivated for centuries, and is rich in resonances of the teachings of Descartes, the seventeenth-century philosopher who had written of animals as organic automata incapable of thought (15). His view popularized the *bête machine* which, with the dogma of *cogito ergo sum*, set philosophers thinking instinctually of life as a mechanical process. Surprisingly, perhaps, neither of these suppositions were posited first by Descartes. The notion of animals as primarily mechanical has its roots in antiquity, with the concept of the influences of the four humors, and the dawn of medical materialism lay, not just with Descartes, but with the lesser-known French philosopher de La Mettrie who first coined the term *l'homme machine* (16). Descartes' most familiar coinage is widely expressed as *cogito ergo sum,* though (in order to make it more assimilable to his readers) Descartes had published the phrase as: *je pense, donc je suis*. The coinage of that concept lay not with Descartes but with Pereira, a Spanish physician and philosopher (17) who, in arguing for the introduction of empiricism into medical practice, proposed the phrase: it was copied 83 years later by Descartes and ever since attributed to him, "Cogito ergo sum."

PIONEERING MICROSCOPISTS AND THE BEHAVIOR OF THE CELL

For almost four centuries our thinking has derived from this mechanistic interpretation of life. During the Victoria era, microscopists were diverted by the study of the living cell, and cell behaviour became a popular topic for scholarly investigation. Most of the unprecedented, revelatory observations in the seventeenth century of Leeuwenhoek were founded on the study in real time of living cells, and his precise descriptions of the cells' behaviour are meticulously observed, from his detailed study of spermatozoa:

> 'I had seen such a multitude of live animalcules more than a million, having the size of a grain of sand and moving in a space. They ... were equipped with a tail with five to six times the body length. They progressed in a snake-like motion helped by their tail.' (18)

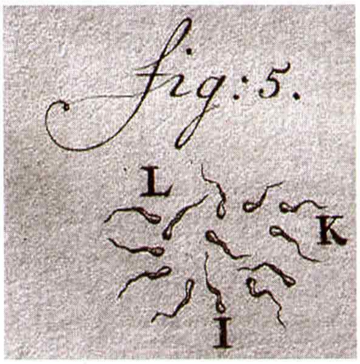

Fig 2: Antony van Leeuwenhoek's painstaking observations of spermatozoa gave an insight into fertilization. The drawings he instructed his limner to obtain give an accurate representation of the microscopical appearance of these highly motile cells. The drawing was sent in a missive to Herman Boerhaave on August 26, 1717.

His meticulous descriptions of the behaviour single cells allow us now to identify precisely what he was describing. Similarly, his remarks on discovering motile cells of *Giardia* are precise and accurate:

> 'I have sometimes also seen tiny creatures moving very prettily; some of them a bit bigger, others a bit less, than a blood-globule but all of one and the same make. Their bodies were somewhat longer than broad, and their belly, which was flattish, furnished with sundry little paws, wherewith they made such a stir in the clear medium and among

the globules, that you might even fancy you saw a woodlouse running up against a wall; and albeit they made a quick motion with their paws, yet for all that they made but slow progress.' (19)

During the Victorian era, observations of single living cells continued to preoccupy microscopists and the groundwork for our understanding of the nature of life was established. It is little known that Joseph Leidy (1823-1891) who was eminent as an American paleontologist specializing in dinosaurs, also produced some of the most vivid and accurate accounts of the behavior of amebae. On his fiftieth birthday, he was given a Hartnack microscope by his good friend Clarence S. Bement and he abandoned his ongoing research in paleontology to devote himself to the microscope, publishing detailed and painstaking accounts for the editor of the *U.S. Geological Survey*, the report in which he had previously published his dinosaur discoveries. His accounts of the behavior of these organisms was vivid:

'I have collected it from early spring to late autumn, and have retained it alive in sphagnum, in a glass case, through the winter. During the Christmas holidays, I have repeatedly exhibited it, in the living condition, to the admiration of friends. From its delicacy and transparency, its bright colors and form, as it moves among the leaves of sphagnum, desmids, and diatoms, I have associated it with the idea of a butterfly hovering among flowers. I observed many individuals of the same singular animal above indicated, but now, understanding its nature, I described it as *Difflugia (Hyalosphenia) papilio*' (20).

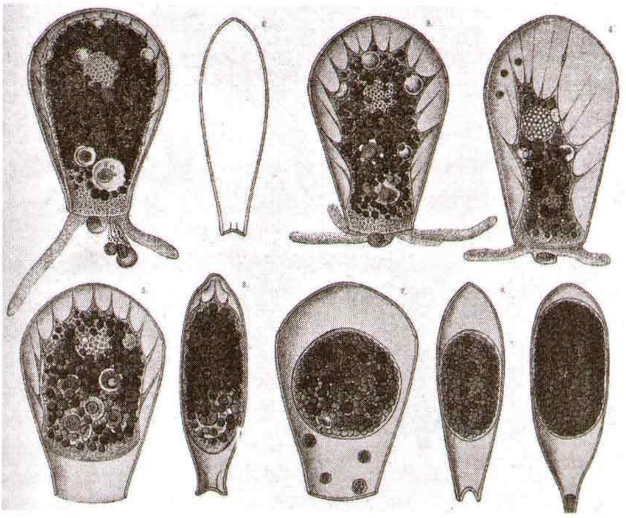

Fig 3: Although best known for his dinosaur discoveries, the American paleontologist Joseph Leidy (at the age of fifty) embarked on a period of extensive microscopical research and his detailed observations of the fluttering exploratory movements of a testate ameba he named *Hyalosphenia papilio* led him to give it an apposite specific epithet.

Meanwhile in Europe, two German microscopists, Oskar Hertwig (1849-1922) and his brother Richard (1850-1937), were using the microscope to investigate the embryology of the cecum. Oskar demonstrated the fertilization of ova by sperm, observed that a mitotic cell divides along its long axis (later known as Hertwig's Rule) and wrote that nucleic acid, now identified as DNA, is crucial for inheritance, and further concluded that all the nuclei in an embryo derive from the zygotic nucleus (21). The discovery of DNA had been made when Miescher precipitated what he subsequently called "nuclein" from isolated cell nuclei with a 1:100,000 solution of Na_2CO_3 and observed its dissolution when the pH was subsequently lowered (22). Hertwig was quick to concur that this was the substance that transmitted hereditable characteristics from one generation to the next. So we have here the basis for cell biology that was to re-emerge in the latter half of the twentieth century; successfully laid down by investigators painstakingly observing living cells.

LIVE CELL IMAGING

No longer do cell biologists painstakingly observe the behavior of cells. Current research on the microscopy of the living cell does not concern itself with the way cells behave and interact, as individuals, but as mechanistic components of a system. Indeed, the term Live Cell Imaging is defined as: "the study of living cells using time-lapse microscopy" (23) and present-day research centres on the movement and location of fluorescent proteins and synthetic fluorophores in flickering high-speed images that do not allow us to observe the methodical behavior and considered movements of a single cell. Similarly, research on brain function has focused on the neurons as a physical network of cells that communicate via the synapses through action potentials and chemical neurotransmitters.

A neuron at rest generates a resting membrane potential of −50 mV between the interior and the exterior of the cell. When stimulated, an action potential can be generated at a synapse causing the neuron to release a neurotransmitter that can either excite or inhibit its neighboring neuron from firing an action potential of its own. It is popularly said that "neurons are essentially electrical devices" (24) but this is misleading. An electrical signal in an electronic device occurs as electrons travel through a wire, whereas the electrical signals we detect from neurons are created as ions travel across the neuronal membrane. This "electrical" interpretation fails to grasp the reality: shifts in ionic balance are the consequence of chemical changes within the neuron, and these result from the activities of the cell. We can measure electrical signals within striated muscle, but it would be stretch a point to insist that an athlete runs because electrical devices within the legs caused them so to do. The race was run because of the desire to partake and the lure of competitiveness; the electrical signals are the downstream manifestation of invoking consciously controlled muscle contraction so, although we may detect electrical signals from the athlete's working musculature, that does not imply that the legs of active athletes are electrical devices. W. Gray Walter attempted to harness such an analogy; he was wrong. This mechanistic approach stems from the insistence that living organisms are machines and this pervasive attitude diverts our attention from the realities of life.

THE BRAIN IS NO COMPUTER

Action potentials emitted by neurons as electrical signals of +30 mV and frequency of ≈40 Hz which can be played back as audio. The result is an irregular buzzing sound that is irritating to the ear. Each peak in the trace corresponds to the discharge of a single action potential. Of particular interest is not the entire trace, as conventionally recorded, but the modulations within each neuron spike. These could be identified after adjusting the playback frequency to allow the perturbations within the high-amplitude region of the trace to emerge. Playing these recordings back at greatly reduced speed reveals a distinct alteration between each of the spike signals: we can experience the language of neurons, rather than the mere cacophony (25). It is clear that intraneuronal data-processing and decision-making are the key to comprehending the functioning of the brain: the simple findings of what happens at the synapses is remote from the processes that each neuron is conducting within itself. It is not merely the brain that thinks; each neuron thinks for itself.

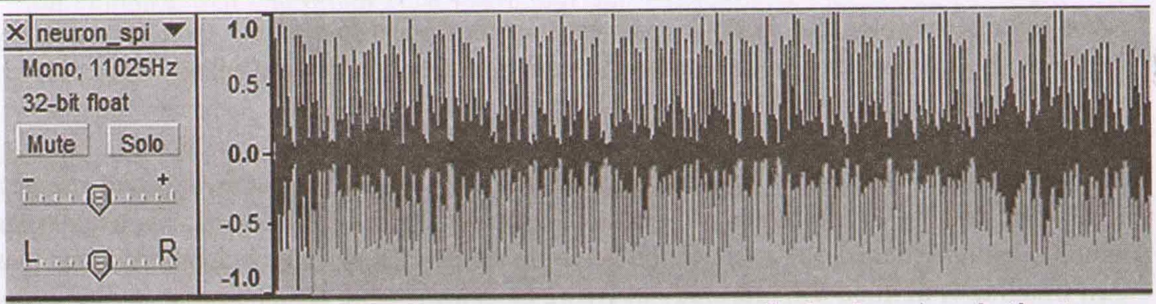

Fig 4a: Recordings made from SH-SY5Y neuroblastoma cells *in vitro* reveals the trace of the 'neuron spike' recordings that may be detected at ≈40 Hz as the action potential increases the charge across the cell membrane from -50 mV to +30 mV. Played as an audio file, the impression is similar to a buzzing sound approximating to mains frequency.

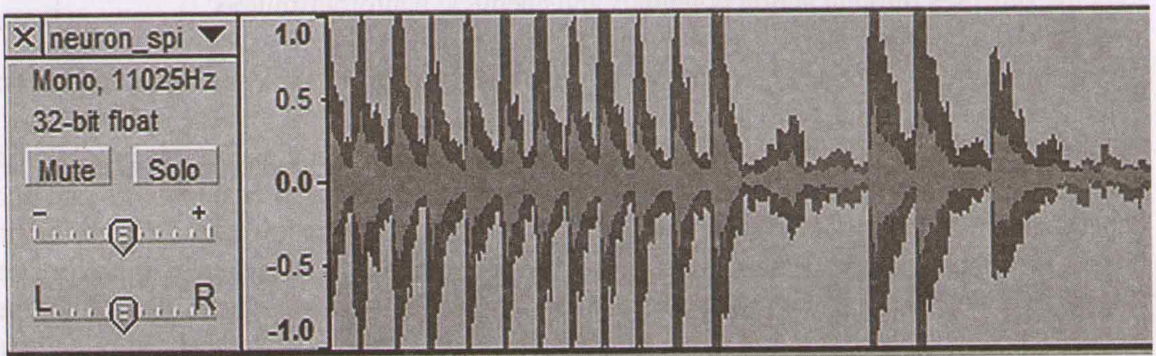

Fig 4b: Increasing the temporal separation within each discrete spike reveals subtle modulations between each emission. As an audio file, the effect is reminiscent of sea-birds roosting on a cliff. The neurons are communicating no mere 'go-' or no-go' binary impulse, but create some of the basic subtleties of a language.

We may gain an understanding of the uncomprehend complexity of each cell's behavior through a consideration of the testate amebae that so preoccupied Leidy (*q.v.*). These single-celled organisms select species-specific building materials and cement them together to produce a protective shell. They were known in the 1830s and were described in meticulous detail by Ehrenberg in a revolutionary book that emphasized the resonances between component cells and the multicellular organisms they comprise (26). Other creatures do this. The caddis-flies of the Trichoptera similarly construct protective cases in which they live, and are celebrated for their ingenuity in so doing (27) though the purpose remains unproven (28).

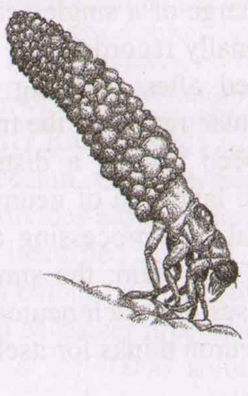

Fig 5a: The elaborate nature of a caddis-fly case is clearly exemplified in this artwork created for the Hitchcock Center for the Environment at Amherst, MA. These trichopterans are regarded as exhibiting remarkable manipulative abilities in performing this task, which clearly demonstrates ingenuity of some sophistication.

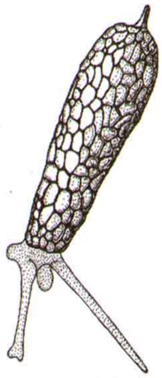

Fig 5b: Testate amebae, such as this *Difflugia,* construct similar protecting cases utilizing species-specific raw materials (in this case grains of silica sand). Unlike the trichopteran larvae, we know of no relevant organelles or sensory systems in these organisms, yet they obtain results comparable to those of highly-developed insect larvae.

Yet consider: the trichopteran larva is well equipped with a brain and eyes, appendages with manipulative claws, a muscular body with cement-secreting glands; it has evolved the functional infrastructure it needs to perform its task. The ameba, by contrast, is a formless cell without any such refinements, yet it manages to perform the same task as its arthropod descendant. The amoeba's home is more refined, for – unlike the caddis-fly – is selects specific components from a confused substrate and often assembles them with greater precision. The task performed by the single cell is superior in complexity to that undertaken by the insect larva. This fact is little known, and – if we celebrate the caddis-fly as a "stonemason" – we should sensibly appreciate the greater achievement of the lowly ameba (29). Certainly, if a testate ameba can select specific building materials and cement them together to produce an exquisitely-shaped vase, it cannot be logically argued that the highly refined human neuron merely fires (or does not fire) an ionic signal in the go- or no-go manner of a transistor. The ineffable complexity of the testate amebae was captured by the German microscopist Adolf Paul Schulze (1840-1891). Studies of the fine pseudopodia of these amebae, in which fine inclusions of bacterial dimensions travel ceaselessly up and down each cytoplasmic strand, seemingly with the intention of traffic on a distant highway and rapidly responding to microenvironmental contingency, emphasize the complexity and organizational refinement of organisms customarily regarded as "simple". In truth, they are unfathomably complex. Schulze's images were widely reproduced thereafter (30).

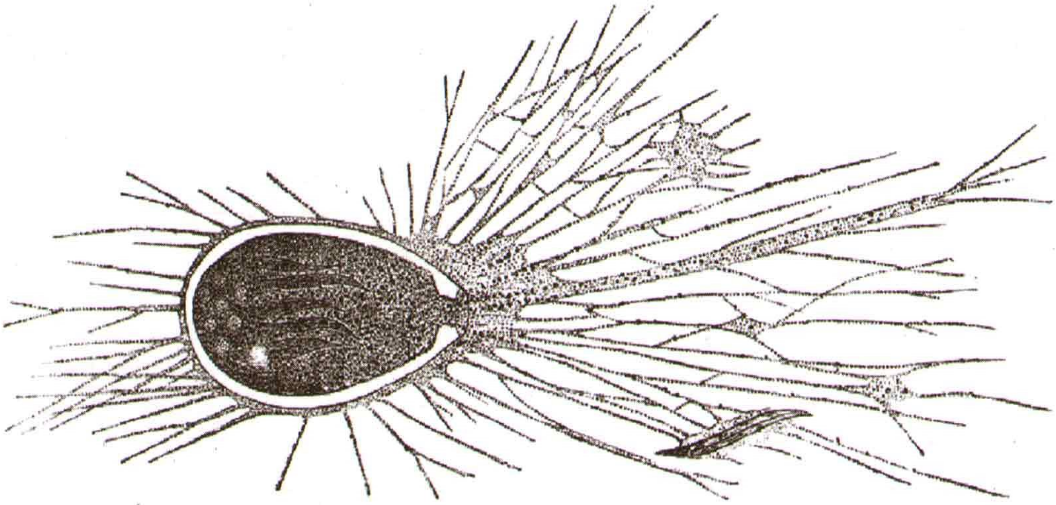

Fig 6: The German microscopist Adolf Schulze (1840-1891) produced detailed studies of testate protists, and this vivid portrayal of *Gromia oviformis* emphasizes the organizational complexity and the refinement of response exhibited by these single-celled organisms. The notion that the highly specialized neuron is merely "a transistor" cannot be substantiated.

The marine rhodophyte alga *Antithamnion* provides us with a yet more revealing insight into the complexity of single cells (31). In this instance we can truly connote intelligence with the behavior of the cell. Self-repair of damaged *Antithamnion* filaments is known, and the healing response has been documented. It seems that a hormone-like glycoprotein with α-D-mannosyl residues acts as a signaling protein (32). However, this says nothing about how *Antithamion* views the healing process. It is no more revealing than saying that the siren of a police car is frequently followed by the incarceration of a suspect. What matters (for the alga as well as the alleged miscreant) is what goes on inside the cell.

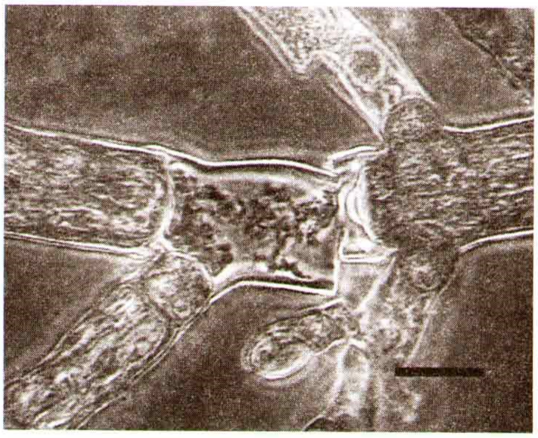

Fig 7a: Single frame of an *Antithamnion* filament from a 16 mm cinephotomicrograph filmed by Pickett-Heaps under phase-contrast illumination. The central cell has been disrupted by passing a steel needle through the cell, rupturing the cell wall and causing the cytplasamic and nuclear contents to diffuse into the surrounding medium.

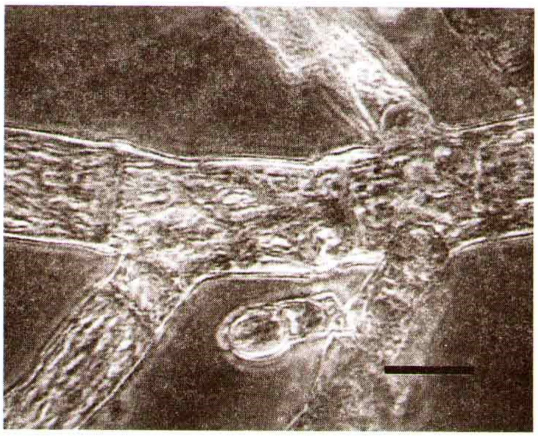

Fig 7b: After 12 hours, intercalary cells from the left have made modest progress into the evacuated cell, while the right-hand cell now occupies most of the evacuated cell wall. During this phase, some realignment of the fractured cell wall has been accomplished. The bar scale in each image represents 50 μm.

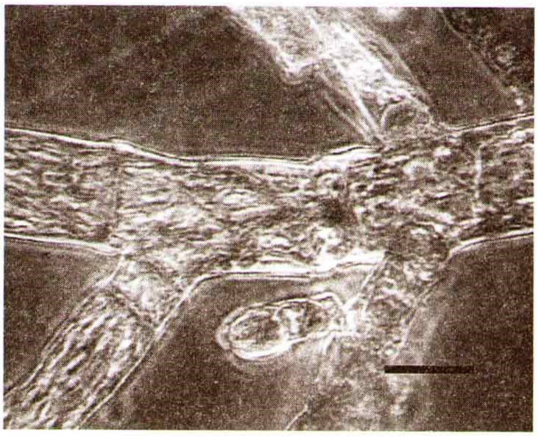

Fig 7c: When 24 hours have elapsed, freshly secreted cellulose is sealing the wound between the broken halves of the ruptured cell wall. We have no knowledge of the mechanisms that could underpin such a process. The cytoplasmic contents of the depleted cell have been reinstated and normal metabolism has been restored.

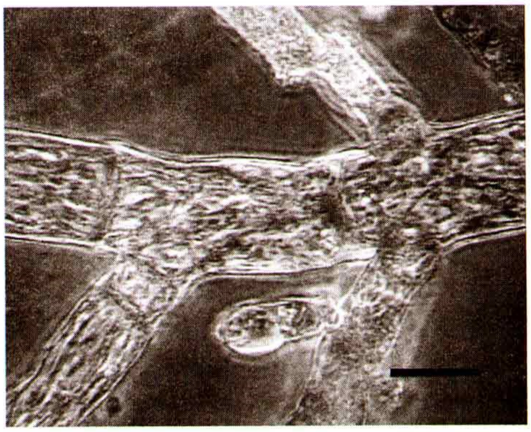

Fig 7d: After 30 hours, the experimentally severed filament has reverted close to its original state. The recognition of damage by a neighboring cell, and the institution of carefully choreographed procedures to restore the damaged cell to full functionality, reveals sensory and decision-making propensities of a high order.

The response of *Antithamnion* to the destruction of a cell within the filament is astonishing. In these uniseriate ceramiacean rhodophytes, intercalary cells grow in a filamentous form through the formation of new cells in transverse bands, a mode of asexual reproduction defined as "band growth". Under real-world conditions, the breakage of a cell of a filament would result in the continued growth of both newly-separated components into discrete colonies. The only situation in which the filamentous cells freshly separated from their neighbor can remain in apposition is on the microscopist's glass slide; were the filament to be broken by an onrush of water or being stepped upon by a passing prowler, the severed ends would inevitably become widely separated. When they are prevented from separation solely because they are constrained on the microscopist's slide, they now respond in a manner for which evolutionary adaptation cannot have prepared them. When an intercalary cell is cut across with a steel needle, the cell wall is divided, and the contents of the disrupted cell lyse out into the surrounding medium. The neighboring cells respond by recognizing the damage, and rectifying it, so that the empty cell wall is restored to full function. Within hours, the adjacent undamaged cells respond to their destroyed neighbor by cytoplasmic enlargement followed by mitosis and expansion into the now empty cell wall. This completes over 24 hours. By the time 36 hours have elapsed, the previously damaged call has been restored to full function and, even more remarkably, the ruptured cell wall has been realigned and restored to full functionality. This phenomenon has been captured on 16 mm film by Pickett-Heaps and examination of the film frames has shown conclusively that the repair and reinstatement can only be completed through the benefits of unmistakable cell intelligence (33). The response one of intelligence – constructively rectifying an unforeseeable event; the adjacent cells have to recognize the problem (through senses of which we are unaware), decide upon a course of remedial action (using cell intelligence that few would comprehend), initiate topographical realignment (without any template of which we know), expand through mitotic divisions to produce fresh cell contents (utilizing systems analysis, the nature of which we can only guess), to re-create new cell wall material (secreted by organelles that have yet to be identified), and repair – in some incomprehensible manner – the cell structures damaged in the laboratory.

Since our school days we have been instructed to regard an ameba as a lowly organism, formless and without structure. Yet they can adjust their rate of reproduction to available food supply, hunt and retrieve the food they need, and many (when their hospitable environment disappears) can survive in diminished form until conditions improve. Amebae were a topic of philosophical enquiry for pioneering microscopists and the ineffable complexity of these seemingly simple cells, competently observed, can teach us much (34). Although it is frequently asserted that a computer can closely approximate the capacity of the human brain, I here emphasize that single cells have capacities that no digital calculating device could ever hope to model, let along replicate. For a computer to show equivalence to a living cell like that of an *Antithamnion* colony I would propose the following test: Three computers on a local area network are situated side-by-side on the floor of the laboratory. On a Friday afternoon, the computer in the middle is cut apart with a blow-torch and the contents scattered nearby. The laboratory is then locked shut for the entire weekend. On the Monday morning, if the damaged computer has been restored and is now functioning perfectly, then these computers are primively modeling some aspects of a single living cell. If (as one suspects) they are unchanged since their appearance prior to the weekend lock-down, then the equivalence to a living cell has not been attained. Even if the experiment were induced to work, it would still not show mastery over the cell; living cells construct themselves by metabolic processes, using raw materials encountered through browsing, and fueling their activities through what they consume. Our computers need an elaborate factory staffed by humans for their manufacture, and they rely on an external source of electricity for their energy supply. Our arrogance in assuming that even the most advanced digital systems can bear homologous comparison to primitive living cells is discomfiting and absurd. Likewise, the notion of artificial intelligence (AI) is fanciful. It is certainly artificial, though cannot be considered as intelligence (12). The lowly algal cell can teach us much about the areas of ignorance that surround us still.

CONCLUSIONS

Life, physicists claim, is physics; current scientific thinking tends fancifully to equate the propensities of living organisms with the facility of digital computing. A consideration of single cells reveals levels of ingenuity that transcend our understanding and greatly surpass any foreseeable scientific comprehension. In some instances, unambiguous signs of intelligence can be seen in the manner in which living cells recognize a serious situation and devise remedial responses that will heal the damage. Only a consideration of the interaction and regulated autonomy of the living cell can give us a true understanding of the healing of our wounded bodies, when cells undertake to repair the microscopic plumbing of the peripheral vascular system and the reconstruction of healed skin. We praise the surgeon for intervention during an operation that leaves little scarring, heedless of the unseen labors that allow the cells to recreate what the doctor's knife as crudely cut aside. Similarly, the growth on the host of a parasitic plant like the dodder *Cuscuta* or the mistletoe *Viscum* involves precise sensory awareness, followed by the judicious alignment of replicating cells, the dissolution of the host xylem vessels and phloem tissue, enabling fusion of the vascular systems of the two genera. This is all micromanipulation and biochemistry in a choreographed sequence that is, in any given case, unique to that situation. Futhermore, once we envision the neuron as a living cell, rather than the unitary component of a grander organ, we can see that somatic death cannot be instantly invoked even through decapitation. Most of the cerebral neurons remain unaware that anything has happened, until – in time – they run short of nutriment and oxygen and become inactivated through the accumulation of carbon dioxide and other metabolites (35). The recent experiments involving the detection of neural activity of porcine brains has created an international sensation, with numerous published claims that this "revolutionizes our understanding" after the announcement in *Nature* (36). Though these experiments created worldwide interest in academia and elsewhere, a vitalistic understanding of the single, living cell would account for the phenomenon. At the moment of our idea of death, all the cells of the body are in reality alive and brain cells can certainly survive for hours. Twenty years ago, Anna Bågenholm, a Norwegian medical student, fell and was trapped under the water of a freezing stream. After intensive treatment for almost four hours (during which time she was clinically dead) faint cardiac activity was detected and she later recovered. The idea of a computer-like organ surviving for so long is difficult to comprehend – whereas the concept of individual neurons living on under conditions of metabolic stress is easier to grasp. When the body seems to die, its component cells remain viable. There is always life after death.

Our fascination with abstruse mathematical modeling and the current preoccupation with physics beguiles us into a belief that we are close to embracing a "theory of everything" when, in reality, there are incomprehensibly large tracts of understanding that few are troubling to embrace. The single cell of a lowly rhodophyte alga reveals principles that are not amenable to solution through physics, just as the single neuron will account for the survival of the brain long after the "death" or the organism. There is clearly a need to embrace a concept of vitalism that can reveal more about our ignorance than the trivial achievements of the most sophisticated digital computer software. Living cells perform acts of unimaginable intricacy and we can evince ingenuity in so many simple microorganisms. We need to study what they do and the sheer vitalism of how they live their complex lives. Cell intelligence will provide a revolution in understanding how the brain might function, and shows us much of the unfathomable realms of biology with which we have yet to engage.

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