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Review Article

Humanities and Spirit in Cell Science. A Cell Could Be Considered a Universe for Learning Behavior

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Abstract

This is an era of science when there is a remarkable mismatch between the amount of data on hand and the lack of related concepts and ideas in the mind. In such a period of time, this review article is penned down based on the career-long experience of the author on the observable behavior of the biological cell system in normal and pathological states. The article points out an emerging direction opposite to the present trend in cell science studded with machine metaphor, AI, and synthetic life. Observation of humanities and spirit (consciousness) in cell science resurrects the reality of a cell as an embodiment of life. Molecules, although, form the basis of behavior, the cell operates with non-observable human faculties such as information, mind, self, and 'life', and the operational attributes of consciousness such as will, cognition, and emotion/feelings. Hints to the solutions to several complex big issues that humanity has been facing such as violence, free will, dark energy, and the parallel universe, could be obtained from the intelligent behavior of a cell. The protoplasm of a cell, psychoplasm of the psyche, and 'plasm' of multiple universe(s) are brought into focus and suggested to operate in continuity.

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The cell is the unit of biological reality, an observable holograph of the universe, an embodied, embedded, enacted, and extended unit of consciousness-Mother Nature in action. Our body is made of approximately 37 trillion cells, which form tissues, organs, and systems. Since Robert Hooke in the early 1600s discovered the dead cell and Anton van Leeuwenhoek the living cell in the late 1600s the credit goes to the cell biologists who have unraveled the mystery of cells and offered us evidence-based data to learn the behavior of biological cells. This paper aims to look at the science of cells from the perspectives of the humanities and the spirit (consciousness).

The cell is one of the conscientious systems. It has a remarkable aesthetic sense. It follows its own ethics. Examined carefully, the cell could be found to have uphold some specific values, which the cell is so comfortable with. The rulebook of a cell follows its underlying conscience, ethics, aesthetics, and values. The attitude is considered here as the outcome of the combined interaction of the above four underpinning the system (Figure 1). Attitude and behavior are the two sides of the same coin. The cell thus could be our silent behavioral preceptor from which we can acquire knowledge for dealing with difficult complex situations and handling issues in life.

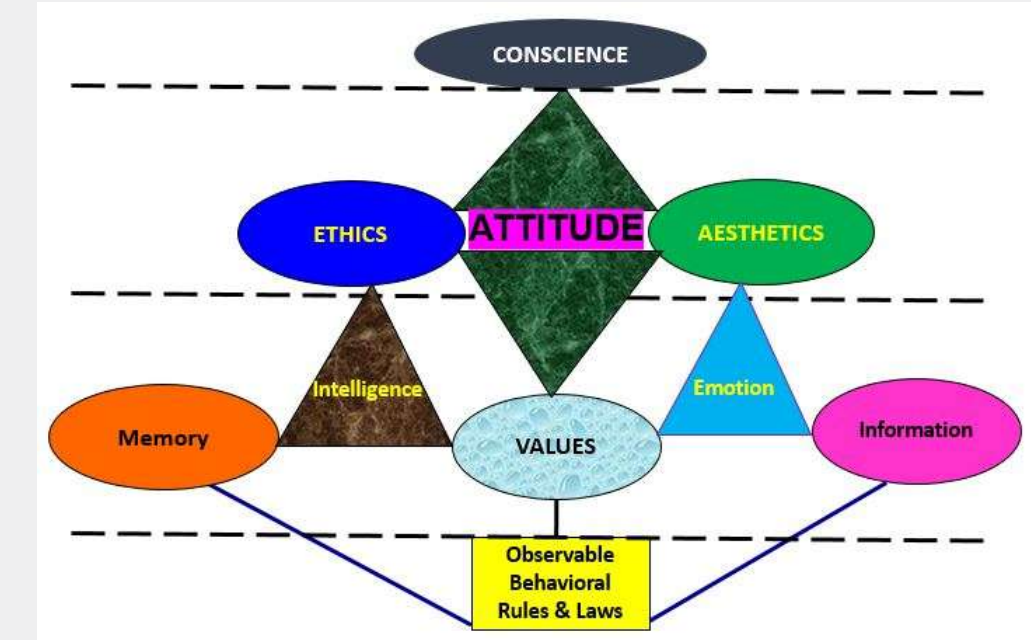

Figure 1: *The interrelationship between conscience, ethics, aesthetics, and values is shown to build up attitude. Attitude is reflected as observable behavioral rules and laws. Intelligence is a reflection of informational inputs from memory on the background of ethics, and values. Emotion reflects the information in real time of 'life' on the background of aesthetics and values. Note that ethics and aesthetics operate from a plane deeper than the plane of intelligence and emotion, which in turn operate from a plane deeper than the plane of the observable behavioral rules and laws.*

As a consequence of the three characteristics in behavior, the cell is steady and slow, avoids unnecessary confrontation and follows the path of least resistance. The system cell is not deaf and dumb as it appears, but opportunistic! All these qualities equip a cell as a perfect candidate for evolution.

Automation, Autonomy, and Autocracy in a Cell

One can learn the difference and relationship between automation, autonomy, and autocracy from the systems made of cells. There are several functions of a cell that are "automated". The term automated has been used as the machine metaphor. There are molecular robots [2,3] operating within a cell according to the timing set by the cell's molecular clock [4]. They are coupled, one with the other. Several signaling systems of a cell are automated and integrated within the signalosome. Even many of our summative behaviors such as gait, locomotion, and the way of communication exhibit patterns, and are automated through extrapyramidal systems of the nervous system. Physical automation is a programmed activity. There is no scope for asymmetry and uncertainty management by an automated machine. Biological automation is supervened by its autonomy! A cell can manage uncertainty and asymmetry, although on a smaller scale. In machine automation, the feedback negative control system is dominant. The feedback positive control system is conspicuous by its absence in a machine. The feedback positive control system is also infrequent in a living cell. The reason is, such control system might be used as a part of the vicious cycle to lead a downhill course for the breakdown of the systems. Unlike in a machine, there are feed-forward positive controls within a living system, as exhibited by the muscular system coupled with nervous system activity, an example of as if informing the boss that the task has begun, the boss can modify it!

A cell also exhibits autonomous behavior. This autonomy is consciously conferred to a unit of a complex system when the concerned system has achieved the desired degree of perfection, which in the language of education means competencies. Until and unless the desirable competencies are achieved, the license to practice as a physician is not offered to medical graduates. The competency-based education system revolves around this key concept! In our multi-system body, the heart has been given autonomy, the lungs have been given autonomy, and the kidney, liver, and intestine have been conferred autonomy. But the limbs and the genital organs are not, although genital organs work under the executive control of the autonomic nervous system.

Autonomy does not, however, mean whatever one wishes to do can do so! This autonomy is conferred within the holonomy of the whole system where one autonomous body respects the boundary of autonomy of the others. Besides, there is the scope for regionalism in cell systems without compromising holism. Multicellular aggregate could be regionalized by different intercellular gap junctions and the cell system bioelectricity [5]. Despite unpredictable perturbations, the behavior of a single cell could be coordinated and reprogrammed for large-scale anatomical effects during embryogenesis and regeneration activity [6].

When one autonomous entity fails to respect other autonomous entities within the system, or encroaches on other's autonomy, the behavior is designated as autocratic! "My way, or no way!" An example of such behavior is that of a virulent microbe. In a disease state, the cell showing such autocratic behavior is termed malignant!

Autonomy to Autocracy; Overcoming several Checkpoints

Uncoupled spontaneity is a characteristic of any living entity. This is absent in the non-living entity. This spontaneity is the source of behavioral autonomy. A single cell is an autonomous body; autonomous metabolically, reproductively, and in making choices. However, in a multi-cellular organism, this autonomy is adjusted within the holonomy of the systems. Pathological autonomy, not desirable by the systems, is exhibited by malignant cells. A malignant cell develops a special kind of metabolic autonomy (Warburg Effect), senescence-overcoming autonomy, apoptosis-circumventing autonomy, cell cycle autonomy, and genotoxicity-overcoming autonomy to bypass mitotic catastrophe. It achieves the state of almost 'immortality' [7]. This kind of uncontrolled behavioral autonomy is acquired in a cascading manner through a defined pathological process morphologically manifested as dysplasia, graded as mild, moderate, and severe, which enters the pathway of multi-step carcinogenesis.

There are multistep checkpoints by genes for curbing such autonomy at the level of signal transduction, at the level of DNA repairing, and at the level of control of cell cycle, respectively called the Gatekeeper gene, Guardian gene, and the Governor gene, exemplified by the APC gene, P53 gene, and RB (retinoblastoma) gene respectively. If behavioral autonomy is uncontrollable at the signal transduction level, the cell is asked by its Guardian gene to introspect at its DNA, and cell cycling is temporarily withheld, while the Guardian gene tries to repair the damaged DNA. If DNA seems not repairable, its cycling is permanently stopped, and the cell is dumped for immature senescence and apoptosis. When all checkpoints are overcome, the malignant autonomy induces secretion of immunosuppressive factors e.g., TGF-beta which paralyzes CTLs and NK cells, and immunosuppressive cell-surface ligands such as PD-L1, which prevents the mechanism of cell killing by CTLs.

Two Broad Groups of Intracellular Communication Systems

A cell has an excellent communication system (Figure 2) within. This communication could be divided into two categories [8]. When any message has to be sent to all organelles simultaneously and instantaneously, communication happens through the information highway constituted by its cytoskeleton. In this way, all organelles are instantaneously alerted for a common purpose! This communication is a critical component used for maintaining holism. Mostly non-discrete and emotion-laden messages regarding cell cycling, cell division, apoptosis, phagocytosis, etc., are sent this way. In the second set of communication, when the individual organelle, one or several, has to be informed discretely and specifically with different information, the cytosolic sea route is preferred, a slow, discrete, and specific communication. Examples are metabolic signals, autophagy signals, genetic messages to the DNA for transcription, etc.

There are two 'divides' of the signals on the way. The first, signals hitting the cell membrane are sorted out for mechano-vibrational transmission through the cytoskeleton. or for passage through the cytoplasmic sea route. The second divide is on the nuclear membrane where signals undergo a chiasmatic sorting out and division. Signals coming through the informational highway mostly choose the epigenetic pathway to histone inside the nucleus, while signals reaching the nuclear membrane through sea-route preferably hit on the DNA. A few signals show chiasmatic crossover. There is a cross-talk between histone and DNA. Cell

biology experts say that the wisdom of the nucleus stays with the Histone rather than DNA [9].

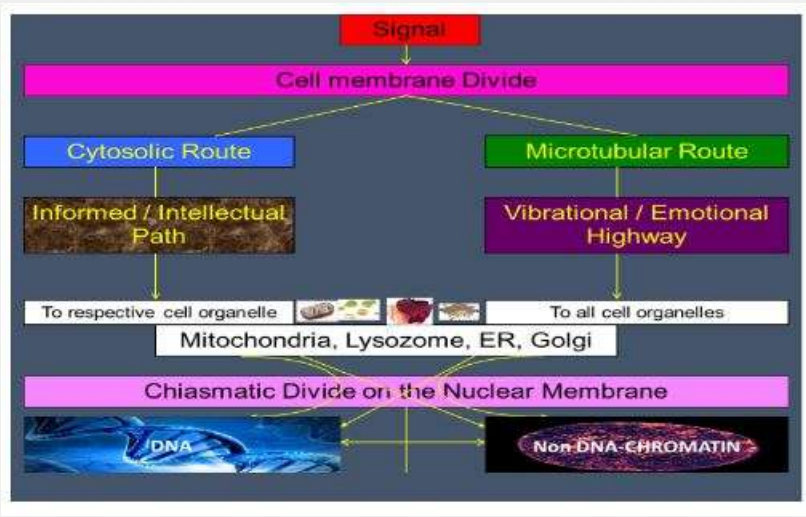

Figure 2: *Signals which hit on the cell membrane are sorted out into two broad groups. There is a cytosolic route taken up by the discrete intelligent information which is also specific for individual organelle. The microtubular route is chosen by information that is to be distributed to all organelle almost instantaneously. On the nuclear membrane, there is a chiasmatic divide of the inputs. Inputs from the cytosolic route mostly reach the nucleotides and a few cross over to the histone. The inputs from the microtubular system mostly reach the histone and a few crosses to DNAs. The images of cell orgenelles have been taken from Google image.*

The first set of communication through cytoskeleton crumbles in the neurons of a dementia patient. Formation of neurofibrillary tangles inside the neurons is the hallmark of Alzheimer's disease! Another hallmark of the same disease is the extracellular deposition of amyloid plaque originating from endoplasmic reticular stress due to misfolded proteins, which are converted into amyloid and thrown out of the cell!

Like the cytoskeleton within the system, there is a communication system in the body in a wider sense. Integrin-mediated cell adhesions provide dynamic, bidirectional crosstalk links between the extracellular matrix and the cytoskeleton [10]. Bioconductive connectional system (BCS), as suggested by Franco Bistolfi, establishes an amazing connection of histomorphology, chemistry, biophysical structure, solid state physics and finally shifts the paradigm of "cell-as chemistry" to the "life in the electromagnetic pool". Intercellular matrix, integrin receptor, intercellular junction, and cytoskeleton are four components of BCS. The BCS is also a target for non-ionizing radiation therapy [11]. Bjorn Nordenstrom has long proposed [12] another communication system through biologically closed electrical circuits (BCEC), the electrical circuits generated by ions around blood cells, and vascular interstitial closed circuits (VICC), generated by ion movements in the interstitial space.

Communication in the Cellular Systems; A Learning Hub for Synthetic Biology

From physiology we are familiar with two communication systems; the faster one by the nervous system and the slower one by the endocrine system.

At the biochemical level, we know of the communication of molecular robots. In between cells, there are cell adhesion molecules (CAMs), cell junctional molecules (CJMs), and substrate adhesion molecules (SAMs), many of which are involved in cell-matrix communication. These molecules could be traced from invertebrates to vertebrates and are important in topobiology [13] where the spatial location of cells determines their structural organization and functional differentiation. Besides these individual molecules of communication there is another unique way of communication between cells, usually within an organ, by extracellular vehicles (EV), which is surrounded by a lipid bilayer membrane and contains specific proteins, lipids, or even DNAs and RNAs, miRNAs [14, 15]. These EVs are often found to circulate in plasma.

At the biophysical level we have mentioned two emerging communication networks; closed circuit communication by cellular ionic charge (BCEC and VICC), and bioconducting connectional system (BCS). BCS, CJM, and microtubular communication from an extensive communication system.

At a still deeper level, the communication through the morphic field, as suggested by Rupert Sheldrake, merits further investigation. According to him [16], the genes and gene products are not enough for understanding the development of plants, and their morphogenesis. Morphogenesis also depends on organizing fields. Similar arguments apply to the development of animals.

In this network of communication systems, there is a transition from the material to the nonmaterial plane and vice versa. When and how are in the research hypothesis phase [17]. In the cellular systems, we could observe informed communication between a receptor and its ligand, knowledgeable communication between the enzyme and its substrate, experienced communication between DNA-repairing enzyme and the DNA, or between the protein perforin and the cell membrane of a microbe or a parasite, and finally the wise communication between the histone and the DNAs. Although these insightful statements appear metaphorical at first glance counter the cell-as-a-machine metaphor prevalent at the present time and could be the new research hypotheses for practicing evidence-based cell science.

Mutual Cellular Cooperation: The Needy and the Rich, Cost-Benefit trade-off, and its Failure:

A thinking unit consumes relatively greater visible energy compared to its metabolic need. Astrocytes in the brain produce 20 times more ATPs than neurons and transfer those ATPs freely to associated neurons busy in the thinking process. We do not have another example of a cell passing its hard cash, the ATPs, so profusely and easily to another cell. There is no requirement for such astrocytes where neurons do not handle information and transmits only signals, as in a ganglion in the peripheral nervous system, and in a nucleus within the central nervous system! Between the astrocytes and the neurons, there are lactate shuttle and glutamate shuttle! In a simple version, this is an example of mutual cooperation between the needy and the

rich, with a cost-benefit trade-off within a plural system! In a complex situation demanding an economic choice between a creative and repetitive boring activity, glutamate is cleared from the surroundings of neurons quickly by the glial cells during the neuron's creative activity. Failing so, the glutamate accumulation leads to, as has been suggested in the lateral prefrontal cortex, development of mental fatigue [18].

If required, even the mitochondria could be transferred between metabolically rich and metabolically compromised cells. Such intercellular mitochondria transfer is one of the mechanisms of immunometabolic crosstalk, that is impaired in obesity [19]. Exercise, which is prescribed as a lifestyle-changing method for several metabolic diseases, might lead to mitochondrial impaired function when becomes 'excessive' [20]. Another new terrain of mutual cooperation between cells is cell senescence with extracellular vehicles (EV) exchange. "EVs secreted from senescent cells can promote senescence of other cells and EVs secreted from nonsenescent cells can rejuvenate senescent cells" [21]. In some viral infections of mice, intercellular transfer of telomeres from the antigen-presenting cell (APC) to T cells increases T cell longevity with the promotion of long-term immunological memory [22]. The gift of telomeres from APC to T cell is to keep T cell young!

In machine metaphor, the mainstream literatures describe molecular talk, or cross-talk between cells, as signal-based. The talk between two live entities is always information-based. Any meaningful talk between two live entities demands intelligence. Cellular intelligence is not signal-based but information-based. Extraction of the meaning from a signal requires mind operation. The mind is a human attribute.

Nonviolence, Self-Défense and Violence in Cell Behavior

Human behavior could be considered a very complex collective behavior of the cells the being constituted of. This has a genetic basis, environmental conditioning that begins in the stressful growth in the mother's womb under uncertainty, stressful moulding of the head (brain) during birth, and neuronal conditioning by the environmental visuals and learning experiences throughout life. In spite of the existence of all such factors, the individual cell of the body retains the core lesson of distinguishing violence, nonviolence, and self-defense. to guide us and help taking decisions in difficult situations. In our body, there are more microbes than the number of body cells! Our intestine has commensal microbes 10 times more than the total number of cells in our body! There is no issue of violence, nonviolence, and self-defense in such cohabitation. Once in a while, a microbe changes its position from a commensal to a virulent one. Or, some extraneous microbe may attack the cell. The cell responds, unfurling all its resources and supply, wilfully changing its receptors, transduction of signals, and gearing up the killing mechanisms for its self-defense. When found it is beyond its capacity to control the violence within, the cell might send a signal to the immune system; NK cell, cytotoxic T lymphocyte, even B lymphocyte, again all are mindfully applied in self-defense. When the cell or the body system fails to contain such uncalled-for violence, the doctors inject antibiotics of choice adopting a more violent means to stop the invader's violence, taking, however, maximum care to prevent collateral damage. Besides, there are occasions when a cell takes a load of all viruses and kills itself through the apoptotic pathway.

When a nonviolent cell indulges in violence it is a disease state. Hemophagocytic syndrome of autonomously activated macrophages is fatal!

The Cell, a Mini Universe within the Systems of a Mini Multiverse

In present science, there is an issue on the largest scale, whether there is one universe or multiple or parallel universe(s)! A single live cell is an exact replica of our live universe. Our body, an ensemble of several universe(s), represents the multiverse!

Max Tegmark has mathematically constructed the existence of four types of multiverse [23]. A multiverse mathematically could be an infinitely extended universe, which is often called Megaverse (Tegmark's Type I Multiverse). The second kind of multiverse is a hyperdimensional universe with outpouching from or evagination of one universe (Tegmark's Type II Multiverse)! In popular language, this is described as the metaverse. If our cell is a holographic representation of the universe, our body obviously does not represent either type I or type II.

One thing to note is that on the cosmic scale, 'life' is impossible in the hyperdimensional Metaverse. Only deadly and powerful viruses occupy such a space. However, some of the body cells can have hyperdimensional space within, where viruses could hide and take shelter. To kill such a virus hidden in the hyperdimensional space within the cell, it needs exposure of the cell to nascent/Mother nature which can fight such a demon with ten-dimensional weaponry (Figure 3). Kaluza-Klein's proposed theory speaks of 10-dimensional space.

Figure 3: *Durga-Puja festival in Kolkata, West Bengal, India has been included on UNESCO's list of 'Intangible Cultural Heritage of Humanity' in December 2021. The figure shown here is one of the thousands of models of the Idol of Goddess Durga under preparation, where one of the forms of Mother Nature, Goddess Durga, is shown to kill the demon of Corona-19 virus with her ten hands (c.f., ten dimensions of space; Kaluza and Klein).*

Physiologically our body cells do not also belong to different types of the universe(s), superposed one upon another (Tegmark's Type III Multiverse) with different laws so that the Schrodinger's cat could be alive in one, and considered dead in another! Our body is comparable to the systems of Multiverse, Tegmark's Type IV, where every cell belongs to its own universe, yet the source is common to all cells. The rules and laws are broadly similar in all universe(s), all cells, with only contingent modifications as necessary for an organized complex system, where autonomy is conferred to the perfected ones within the holonomy!

Every cell individually functions peacefully since it is in communion beyond the spell of zero-point energy (ZPE) states, i.e., with the Source of multiple universe(s). As a constituent of the organizing systems of the body, all cells are in communion with this ultimate source through the cortical neurons of the nervous system! The cortical neurons are connected with the source supracortically, through the porous boundary of the nervous systems. This interaction, communication, and dialogue between inside and outside our brain, between the neurons and the perineuronal voids have become an important research frontier for neuroscience!

Probably the underlying imagined background 'ether' of material science and the real protoplasm of cell biology are not traceable beyond ZPE. The inactive "ether" of physical science could be replaced in the science of consciousness by a ground that is willfully intentional, live, sentient, and event-making, but having no background. Carl Jung in 1935, rightly stated psychology as "the science of consciousness." LaViolette [24] had been very close to psychology when he put forward the properties of the three basic substrates in etheron, also called the transmuting ether! In the science of consciousness, this etheron is the ground consciousness. What are then these three transmuting substrates? The substrate with sentient property in etheron is the self of cognitive psychology! Feed forward loop (retrocausality from material perspective) is characteristic of the presence of 'life', the second substrate, which has the ability to run homeostasis through such loops! The event-making substrate could be what in cognitive psychology has been called the mind! Three substrates of etheron, therefore, in the terminology of cognitive science are self, life, and mind respectively! Like the protoplasm of material science, one could look for "psychoplasm" in the context of the psyche. Psychoplasm is defined as "a primordial substance held to supply the basis of the psychical as well as of the physical" [25], which we find is nothing but the ground consciousness on which self, life, and mind operate! The most rarefied of this plasm could be the multiversal 'plasm', the plasm (the Essence) of multiple universes. The protoplasm of a cell, the psychoplam of the systems psyche, and the multiversal 'plasm' probably operate in continuity.

The Multiverse, conceptually, acknowledges pluralism without any major compromise with individualism, and rewards individualism within the systems of pluralism. In this sense, our body is a multiverse constituted by trillions of universe(s) of cells. That cell biology is immersive in multiversal cosmology becomes evident when the science documents [26] a fascinating faculty of the slime moulds and unicellular ciliate creating patterns similar to what is seen in space and hyperspace, and integrating spatial information for adapting behavior.

Interestingly, the female birth canal is constructed in the image of the universe with three voids and two intervening tunnels [27]. The interstellar space is represented by vaginal space. The uterine cavity represents the intergalactic void. The ampulla in the Fallopian tube is the void three, for fertilization. The cervical canal is the first tunnel (the tunnel between interstellar and intergalactic space) and the isthmus of the uterine

tube is the second tunnel (the tunnel between intergalactic space and the border of the universe)!

The universe might run on autopilot, but each of the trillions of life-forms riding on this pilot vehicle is an autonomous entity. Should the universe, like the individual cell, be alive, then the source of this emerging new cellular perspective is identical to the source of the Multiverse!

Cell-Virus Interaction; A Unique Area of Emerging Behavior

The cell runs its machinery according to the rules set by the cell itself. However, the cell may not be always aware of its laid down rules. On the other hand, a virus knows the rules of a cell in detail and also knows the loopholes of such rules. The virus does not attack the rules of the cell! A virus takes advantage of the loopholes of the rules of the cells to its own advantage for self-proliferation within the cell.

A virus is an entity with "doubtful integrity". What do we mean by such terms? An entity with "doubtful integrity" regularly applies the 'rules' to rule others, but uses the loopholes of the rules for its own proliferation!

A cell can clear the virus load within, only when the cell regains its self-esteem, and actively plugs the loopholes. In terms of molecular medicine, we are yet to identify such molecules of self-esteem.

Free Will of a Cell

Does the cell have free will? Yes. Free will is another issue in philosophy and neuroscience. A singular cell, say a paramecium, has free will (and free won't) and so it can freely decide to do or not to do accordingly. The cells are the constituents of us and therefore, we too have free will (and free won't). The cell can break its established pattern, and make a new pattern, and therefore, we too can do so! One might go into the genetic roots of this attitude within some basic nucleotide base pairs which are evolutionary conserved and even nurtured! What I mean to say is that Free will is not a property of evolutionary emergence! It had been there in a single cell, and it is still there in multicellular complex organisms like us! A single cell operates with limited infrastructure and capacity. The cells in our organized body are more restricted in freedom due to systems effect!

In this context attention is drawn to a few recently published papers. Physarum polycephalum can find the shortest path through a maze, construct networks like humans, solve computationally difficult puzzles, make multi-objective foraging decisions, balance nutrient intake, and even often behave irrationally [28]. A bacteria or protists, free-living single-celled organisms can cope with varying environments, locate prey and potential mates, and escape from predators similar to any free-living animal [29]. Unicellular Stentor roeseli exhibits the hierarchy of complex avoidance behavior [30]. We have already mentioned the ability of slime moulds and ciliates to integrate complex spatial information, of ATP transfer between astrocytes and neurons, mitochondria transfer between macrophage and adipocytes, transfer of EV from nonsenescent cells to rejuvenate senescent cells, and telomere transfer by APC cell to T cell. Are these all mindless, thoughtless, trickless, automated unconscious processes? Is it possible by merely robotic intelligence? According to mainstream science, it is yes! And, this is followed by attempts to produce a computational model of

multilevel development of cognitive abilities in an artificial neural network [31], although since 1980s it has been reported that habituation and sensitization do not require a cell with neuron character. This is observed in a non-neural cells as well [32,33].

According to the author, there exists an alternate approach to this issue where it is assumed that the faculties of the human psyche such as mind, information, self, life, and consciousness are already present in a single cell, and each of them has molecular correlates. We accept the existence of cell psychology [34] for an explanation of cellular cognitive activities.

Cell Psyche

The cell is a thinking live entity, and has its own intelligence. The basis of communication in robotic intelligence is signal-based. It is automated and can be expressed by an algorithm. Communication in cellular intelligence is information based. Information is autonomous and its exchange demands not an algorithm but an organogram. There are experimental evidence that double stranded DNA helices can recognise mutual sequence homology without any physical contact in a protein-free medium. This necessitates invocation of information mechanics in the process [35]. What converts a signal into a piece of information is what in colloquial language has been called the mind.

The cell has a mind of its own which it asserts through the manipulation of its ion channels. Biochemical representation of such mind action is reflected in the Na+-K+ ion channel in the stimulus-excitation coupling, and the Ca++ ion channel in excitation-contraction coupling. Deterioration of the mind function in clinically unconscious patients is identified by the loss of sphincter control. The appearance of the mind in a growing kid is identified by the development of control over this sphincter.

A cell is a self-organizing system with reversal of the second law of thermodynamics. The underlying logic and the ethics a cell follows in behavior supposedly originate from this self-sense. Its ion pumps maintain the cell's ionic self-identity! Molecular representative of the 'self' sense of a cell (I, me, and mine) are HLA molecules. The immune system works mostly on the basis of the distinction between self and non-self, and on the difference between the pattern familiar to cell and the pattern not-so-familiar to cell. The pattern might be exogenous, Pathogen Associated Molecular Pattern (PAMP), or endogenous, Damage Associated Molecular Pattern (DAMP).

The cell is an embodiment of 'life'. The sign of 'life' is homeostasis. Any entity that can maintain uncertainty-certainty homeostasis, symmetry-breaking and symmetry-making homeostasis, and homeostasis in consumption of non-observable (dark) and visible energy is considered alive. Cells could withstand uncertainty created by oxidative, metabolic, and endoplasmic reticular stress. A cell is capable of retaining symmetry in apoptotic crises and during mitotic catastrophes. Protein-synthesis apparatus is the lifeline of cells, active in information channeling to its different organelles through different signal networks, some of which are made automated following achievement of the desired degree of perfection. Cytoskeleton-gated ion channels are the final biochemical representations of the 'life'-line of a cell. The cytoskeleton integrates all vital organelles of the cell with the cell membrane mechanically, spatiotemporally, and informationally.

Detachment of cytoskeleton from the cell membrane disturbs the 'life' of a cell that occurs regularly in two distinct situations; prior to mitosis for spindle formation, and prior to apoptosis. Emotion is another characteristic of 'life' (see below). The subtlety of conversion of visible energy into non-observable energy plays role in protein structurization. The brain constitutes 2% of body weight but consumes nearly 20% of cardiac output. Where is this visible energy consumed? In the thinking process! A neuron consumes more observable energy than a non-thinking cell like an astrocyte that produces ATPs for neurons.

Information, mind, self, and life are the human attributes in cell science. Cellular consciousness is required in their coordination. Three operational attributes of human consciousness namely, cognition, will, and feeling/emotion, are also observed in the behavior of a cell. We have cited a number of evidence in this direction. Cells have a will. On the basis of 4E (embodied, embedded, enacted, and extended) cognition, the cell makes decisions in favor or against of its various behavioral activities such as cell division, apoptosis, necroptosis, pyroptosis and autophagy. There is a death receptor on the cell membrane, and there is a corresponding ligand cytokine, Tumor Necrosis Factor (TNF) in the plasma. However, all cells are not on a death row. Suicide is a conscious decision following which the death ligand activates the death receptor! Besides making decisions, cells learn. Cell expresses emotion (see section below).

Because of possessing this systems psyche, a cell can turn its immediate focus into a broader perspective as happens when the cell becomes aware of its genetic machinery being misused for the proliferation of an invaded virus. The virus-loaded cell prefers death (either by suicide, apoptosis, or being killed by an NK cell or a cytotoxic T lymphocyte) and to save others! Because of consciousness, the cell also can change its attention into broader awareness, as happens when virulent bacteria enters it. Cell's awareness of PAMP sends awareness signals to the cells of the immune system.

Our research hypothesis, therefore, is as follows. Consciousness, self, 'life', mind and information constitute the systems psyche. They are the constituents of the organogram of the decision-making labyrinth of a living entity. Consciousness is identified by its ability to learn, make a will, feel and express it emotionally. Life in its subtlest form is identified by its ability to control homeostasis; uncertainty-certainty homeostasis, asymmetry-symmetry homeostasis, and dark energy-visible energy homeostasis. Self is the CEO of the cell systems and is categorically identical to consciousness. The self takes care of the logic and ethics of the system. The mind as an organ of communication between two conscious systems is identified by its operation of transforming a signal into a piece of information at the level of zero-point energy state, and vice versa. There are molecular correlates for all family members of consciousness which constitute the psyche. The psychoplasm is inseparable from the protoplasm and makes cognition possible in 4E model. The mind is responsible for embodied cognition, while the self for the embedded. Life adds enacted cognition while consciousness coordinates the system with extended cognition (Figure 4).

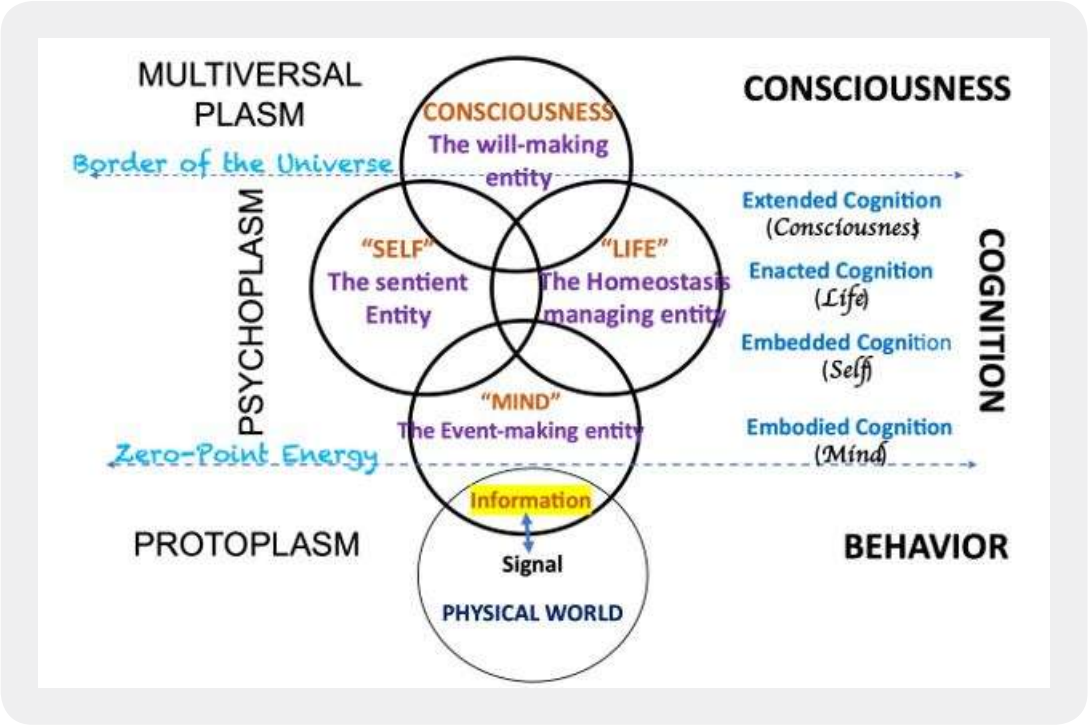

Figure 4: *In the Worldview with axiology of Consciousness, Cognition, and Behavior (shown on the right of the figure), and The Multiversal Plasm, Psychoplasm, and Protoplasm (shown on the left of the figure), the Faculties of the systems psyche have been operative as phases in the psychoplasm (middle of the figure), as a will-making entity (consciousness), the sentient entity (self), the homeostasis-managing entity (life), and the event-making entity (mind), which are responsible for extended cognition, enacted cognition, embedded cognition, and embodied cognition respectively. Behavior is observed in the physical world following the conversion of information into signals by the faculty of mind. For a cell, the protoplasm as a whole participates in behavior.*

A Specialty of the Brain and Neurons

"Both neuroscience and the humanities seek to understand the nature of representation and simulation, yet seldom in dialogue or collaboration. Neuroscience tries to assign metrics of brain activity to specific representations of the outer world. ……The humanities encompass what ancient Greeks named mimesis, a complex field ranging from representations of internal and external worlds in arts and literature, to social synergies and "contagion," to the aesthetic gestält of cultures" [36]. Neuromimesis is supposed to connect neuroscience and humanities [37].

In the human being, the organ brain occupies the topmost position in biological and cognitive evolution, fully equipped to operate in the continuum of the multiversal plasm, psychoplasm, and protoplasm. The brain has 10^{11} neurons. Interestingly, there are approximately 10^{11} stars in a galaxy and approximately 10^{11} galaxies in a universe! Dark energy and dark matter prevail in both cosmology and neuroscience. The signal-making operation of the protoplasm of neurons operates in continuity with the operation of intention and information in the psychoplasm, and up above the hill with the operation of the 'will' of consciousness

in the multiversal plasm. The brain is thus an open system, open informationally and intentionally to help the manifestation of the 'will' generated by consciousness. The neuronal cell membrane is polarised for this task, and for this purpose its genes are kept 'serene' in absence of mitois, without much disturbance of its microtubular systems! Such immersive neuroscience in three plasms holds the key to human transformation.

Elementary Phenomena and Motivation

The origin of motivation is not in the mind, nor in 'life'. Motivation arises from the private facets of self. To understand this private facet of 'self', we are to examine the very basic and elementary phenomena, which participated during the holographic separation of self as the system's executive from the unconditional consciousness. The phenomenon of separation begins with a "desire" for new creation, the expression of "Sex", followed by the birth of something new as a separate system with the expression of "Life". Informational conditioning of the existence of the new born system results in its "Ego". Besides, there is always a tendency in the living system for sharing its property with others, an expression of "Love". The system separation process is accompanied by the "Death" of the homogeneity of the unformatted nature. The phenomena mentioned are absolutely elementary in nature. Any live system having a 'self' cannot avoid, bypass or skip its influence. The elementary phenomenology is sandwiched between the surface phenomenology of the material (classical and quantum) world and the depth phenomenology of the self and life. Each of the major five organelles of a cell represents one of the five elementary phenomena; cell membrane Love, DNA-replication machinery Sex, DNA-transcription apparatus Life, lysosome, the Ego, and Mitochondria the Death! The author designates this as the Pentagon (Figure 5) of cell psychology [38].

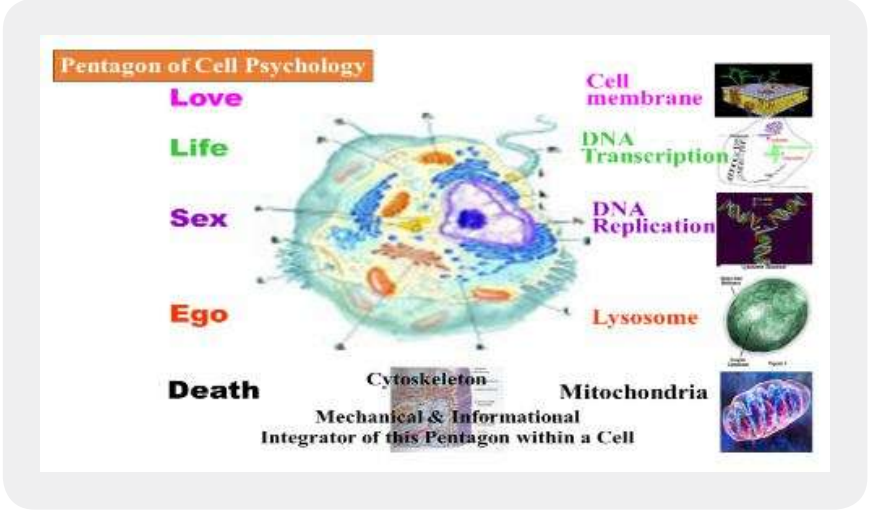

Figure 5: *Cell membrane, DNA-transcription apparatus, DNA-replication Apparatus, Lysosome, and Mitochondria are five important organelles, constructing the 'Pentagon" of cell psychology. They biologically represent five phenomena at the elementary level namely Love, Life, Sex, Ego, and Death respectively. All motivational roots of a cell could be traced back to this Pentagon of cell Psychology. The cytoskeleton is a Spatio-temporal, mechanical and informational integrator of the five important organelles within the cell. The images of cell and subcellular organelles have been taken from Google Images*

Apoptosis, the programmed cell death, has evolved only following the evolution of sex by cell fusion. "The certainty of death was absent at the origin of life", argues Lynn Margulis in Scientific American [39]. "Unlike humans and other mammals, many organisms do not age and die." "The process of programmed, inevitable death evolved only after our symbiotic microbial ancestor, some two billion years ago, became sexual individual". "Cannibalistic fusion and its thwarting by programmed death became inextricably linked to seasonal survival and to individuality." The behavior of the organelle of a cell in a complex motivational situation could help us to learn the attitude and behavior as required when a human being is tossed between either life or death situations!

Love is a dominant motivational factor. The author has an interesting view on this [40]. Love is a cortical manifestation of supracortical consciousness. Love also has a genetic basis. One cannot love music or a flower unless one possesses genes for it. Most of our non-housekeeping genes are in "inactive" phase unless they are turned on. Love does this miracle at the molecular level. Love "turns on" the genes. An affair of love is an expression of the desire of the genes to bloom. In hatred, one wants to keep that particular set of genes "buried". Biochemical changes in love run parallel to the biochemical machinery of gene expression. In other words, if genes are there, in a stimulating environment love will automatically manifest from genomics to proteomics and metabolomics.

Ego is another determinant factor in motivation. However, from a misdirected motivation of ego, there happens lysosomal injury of the endothelium, accentuated arteriosclerosis, and hypertension. The ego of a person is managed with buttering by a manipulator! All lipid-coated bacteria (mycobacteria) are seen to survive very well within lysosomes! Research may be initiated on why the egoistic personalities are more prone to develop tuberculosis (and may be leprosy) when exposed to an infective environment, why sudden onset of vitiligo (a disorder of melanocytes of skin) in an otherwise normal adult happens with psychosocial disorder of ego!

If one comes with a research hypothesis that the psychosomatic contribution to the immunopathogenesis of systemic lupus erythematosus (SLE), is a severe unresolved conflict between sex, love, and ego (S, L, E) in a young lady, the author cannot reject the hypothesis outright. Many SLE patients give past history of incest! The person who is supposed to protect is attacking, an example of autoimmune destruction at the system level. In SLE, there is an anti-DNA antibody, interfered cell membrane functions, and lysosomal injury too!

Stress and Emotion of a Cell

Cells suffer from stress and overcome it as well. The stress could be oxidative stress in handling free radicals, metabolic stress in malnutrition, endoplasmic stress of protein misfolding, genotoxic stress to meet the demand of number in the game, and also apoptotic stress in controlling the population. In most situations, the cell remains calm. How? Most likely by getting back to a zero-point energy state! Because of the cell's access to a zero-point energy state, the cell could remain calm and steady, could follow the path of least resistance, and become proactive for evolution in opportune moments. One can learn behavior from how the cell handles and go beyond such stressful situations!

Cells also have emotions. The cell's emotional behavior is observed occasionally in a phenomenon labeled "frustrated phagocytosis"[41], when the cells fail to phagocytose the desired object and throw out the destructive enzymes outside (Figure 6).

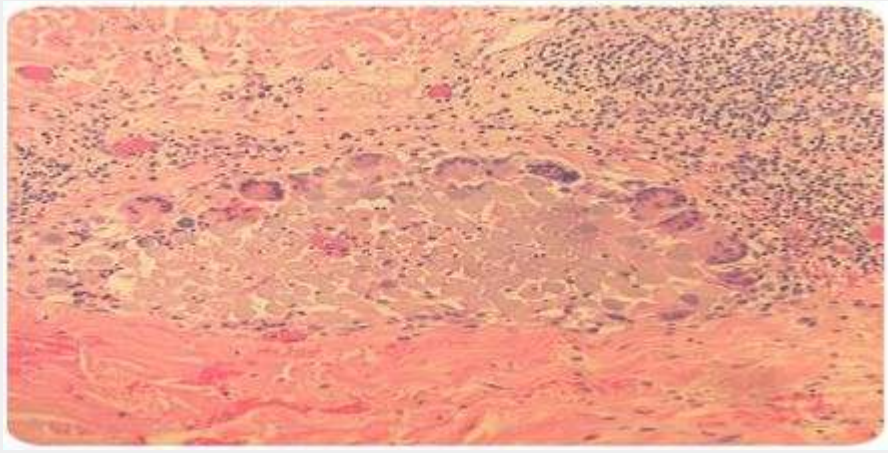

Figure 6: *A large number of phagocytes appear to engulf the suture materials but fail, and pour destructive enzymes around that lead to inflammation and fibrosis (The source of this figure in Goggle Image is acknowledged).*

This kind of release of destructive chemicals initiates inflammation and fibrosis. Frustrated phagocytosis is one of the mechanisms of fibrosis in occupational lung disease, especially in asbestosis. A lively cell is emotionally nonviolent but may become violent in a disease state such as hemophagocytic syndrome. In our body system, we have happiness hormones such as dopamine, endorphin, oxytocin, serotonin, etc. Cancer patients suffer not only physically but also emotionally. In the human beings, emotion internalized offer internal strength to grow. Any outburst of emotion leads to self-suffering, frustration, autodigestion, and even leads to suicide or homicide with collateral damage.

Emotion is a double-edged weapon for any of us, and I will cite one very similar situation inside a cell. The cell has a critical enzyme called cytochrome C. It resides, rather is treasured, between the two membranes of a multifaceted mitochondrion. When inside, within this membrane-bound space of mitochondria, cytochrome C participates in the electron transport and helps the generation of ATPs from Kreb's tricarboxylic acid cycle. The powerhouse of energy, the mitochondrion, tries to retain this enzyme always within. Once there is a leakage of cytochrome C from the mitochondria inside the cytosol, there is activation of the enzyme, caspase 9, through activation of the Apoptotic induction factor (AIF). Oh lo, the cell moves toward suicide! There are 10 genes whose products regulate and decide whether cytochrome C would reside within the mitochondrial membrane or leak into the cytosol. Three of the gene products are anti-apoptotic (BCL-2, BCL-X, MCL1), two of them are pro-apoptotic (BAX, BAK), and five (BAD, BIM, BID, Puma, Noxa) are 'sensors' which sense the situation both inside and outside the mitochondria and stimulate either pro-apoptotic or anti-apoptotic factors accordingly. Therefore, at the emotional cross, one can always look at

his/her cell for inspiration! The research question here is, is cytochrome C a molecular representative of emotion inside the cell in the same way the sense of self (I, me, mine) is represented at the molecular level by HLA gene products or ion pumps through the cell membrane?

Error in Perception of the Immune Lymphocytes Leads to Disease

Like all live entities having a psyche, the cell perceives. However, the perception is not always error-free! When the immune lymphocytes perceive a friend as the enemy and do not apply the brake, they commit a mistake. The result is autoimmunity! The same lymphocytes commit a blunder when they perceive the enemy as a friend, and fail to press the defense accelerator! The result is a checkless malignancy (Figure 7).

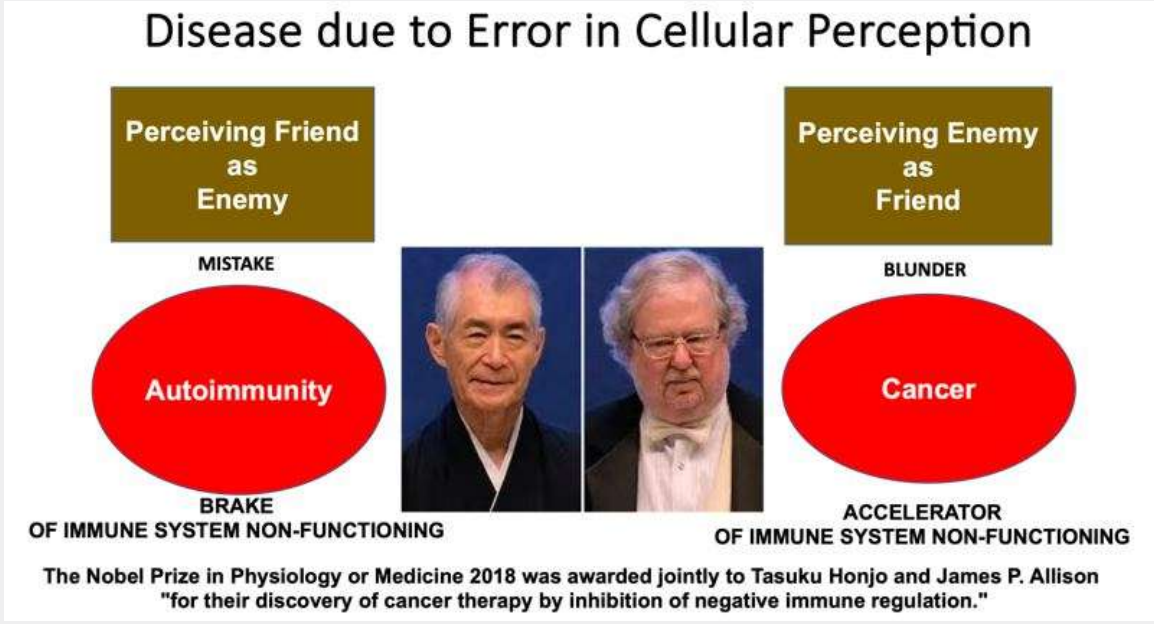

Figure 7: *Fig. 7. Cellular Perception sometimes can go wrong. On one occasion, it's a mistake. On the other occasion, it is a blunder! Where the immune cell is supposed to apply the brake but fails to do so it is surely a mistake and results in autoimmune disease. On another occasion, it does not press the accelerator perceiving the enemy as a friend and helps malignant autonomy to flourish. This is a blunder in cellular perception!*

The Dark Energy and Visible Energy within a Cell

Science has a complex issue of dark energy and visible energy! Our universe consists of approximately 70% of dark energy, 25% of dark matter, 4% of invisible matter, and only 1% of the visible matter!

A living cell participates in the ecosystem of dark and visible energy homeostasis in this universe. While human cells constitute only 0.01% of the total biomass of the earth, microbes contribute to approximately 17% of the biomass of the planet. Imagine the biomass in the entire universe and its relation to energy ecology!

There exist several explanatory gaps in the energy economy of our cells, between cardiac output consumption, ATP production, and the expenditure in metabolism, and for other works. The brain constitutes 2% of body weight but consumes nearly 20% of cardiac output. The adult heart weighs 250-300 gm, about 0.3% of the body weight, but consumes 4-5% of cardiac output. In the brain, perhaps this high consumption of visible energy could be explained in terms of information generation, thought formation, knowledge development, and storage of experience as information manifold, supported logistically by concomitant protein folding within neurons and glial cells.

Our research hypothesis is as follows. A thinking entity consumes more amount of visible energy compared to its expenditure on metabolism and other functions. Additional visible energy is consumed and converted into invisible dark energy during the process of thinking, which converts the signal into a piece of information, develops a symmetry of knowledge from several related information, generates experiences with information manifold, and often crystallizes information into wisdom. In the reverse process, when the wise decision, as will, manifests in the behavioral signal, invisible dark energy is released as visible energy.

The hypothetical phenomenon could be correlated with the cascading operation of the mind, self, life, and consciousness within the psyche and to protein undergoing primary, secondary, tertiary, quaternary, and spherical structure formation, or in the reverse [42, 43].

Connections of the Four Ladders

From this cellular behavior, new multidisciplinary science can take birth should we be able to connect the following four ladders.

1. The ladder of cognition: Signal, Non-digitized information, Non-digitized and non-factorizable information (what we call Knowledge), Information manifold (the Experience), and the Information crystal (commonly known as Wisdom).

2. The ladder of Cellular Protein structure: Unfolded polypeptide as signal protein, folded protein of secondary structure (Informed protein, e.g., receptor protein), folded protein of tertiary structure (Knowledgeable protein, e.g., enzymes), folded protein of quaternary structure (Experienced protein, e.g., perforin, or DNA-repairing enzyme), and Spherical protein (Wisdom protein, e.g., histone).

3. The ladder of Energy Source in Cosmology: Visible Energy. Dark Energy, Dark matter, Dark matter Manifold, and the Source of the Multiverse (the Essence of the Multiversity).

4. The ladder of Operations of the constituents of the Psyche: Operation I by Mind converts the signal into a piece of information, Operation II by Self processes information into Knowledge, Operation III is executed by Life to develop Experience from knowledge, and Operation IV is conducted by Consciousness to transform experience into Wisdom.

Figure 8 consolidates this idea of the connections between protein chemistry, information science, operations of the psyche, and the resources of energy for further workup.

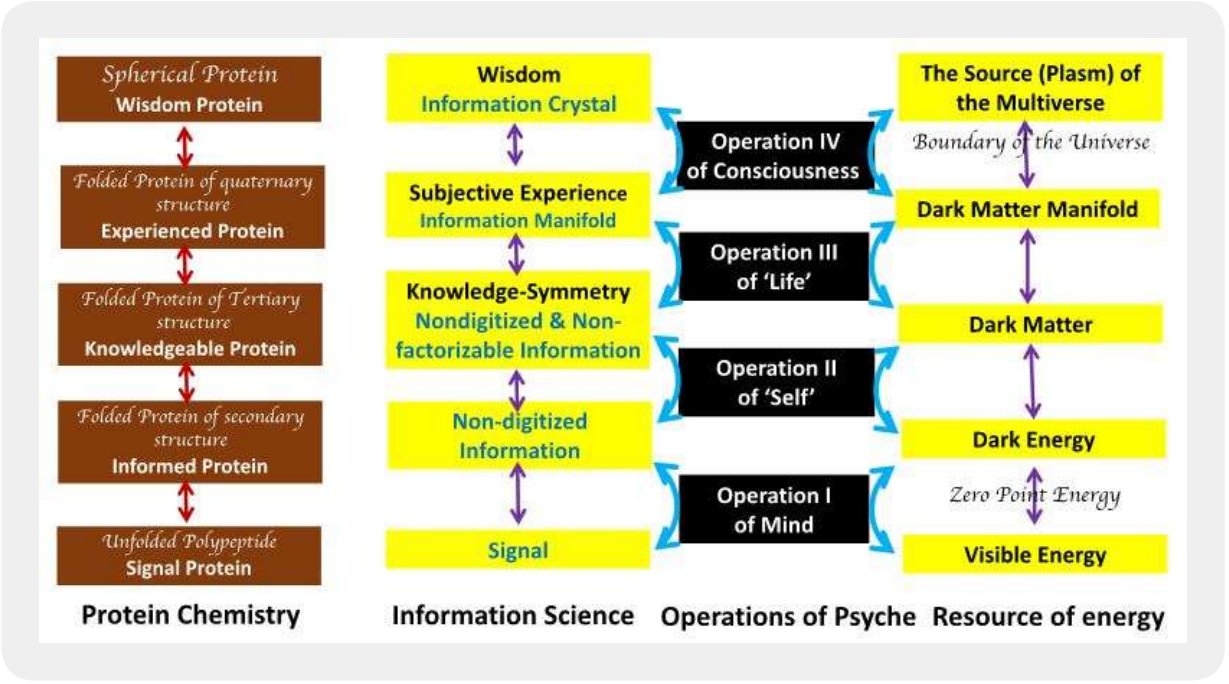

Figure 8: *The figure concretizes the idea of the connection between cell biology, information science, operations of the psyche, and the cosmological resources of energy. On the extreme left side, the proteins, based on their structure, are placed on a ladder as signal protein, informed protein, knowledgeable protein, experienced protein, and wisdom protein. Next to it is shown the ladder constituted by signal, non-digitized information, non-digitized and non-factorizable information, information manifold, and the information crystal. On the extreme right side, shown is the ladder of visible energy, dark energy, dark matter, dark matter-manifold, and the Essence (Plasm) of the Multiversity, which is considered the OR (Objective Reality) in Science of Consciousness. Note that the transition of dark energy and visible energy happens across the ZPE, while the transition of the dark world to the world of enlightenment is across the boundary of the universe. Four operations of the faculty of Psyche within the psychoplasm are suggested to execute the transitions.*

Conclusions and Perspective

Murray Gell-Mann, the Nobel Laureate in Physics, 1994 said, "…we need to overcome the idea, so prevalent in both academic and bureaucratic circles, that the only work worth taking seriously is highly detailed research in a specialty. We need to celebrate the equally vital contribution of those who dare to take what I call "a crude look at the whole". Unlike philosophy, science speaks in a common universal language that too in a third person's perspective, and never claims infallibility. "The fundamental strength of science is that it compels its practitioners to confront their own fallibility… Science is not always right – very far from it. What marks it out from other fields of human endeavor is that, because of its formalized humility, it's always ready to correct itself when it makes a mistake" (Mike Taylor). The statements are applicable to this article as well.

There is no need to expand the article further. There is a need to examine the article both from its essence and from its detail. The cell could be a wonderful teacher for learning behavior in many complex situations. We fumble, but the cell shows the way! This is possible because the cell is not inert, and is not merely a material robot. The molecular robots within a cell carry out their perfected mechanical behavior under the guidance of proactive elements of 'life', mind, self, and consciousness. Rather than focusing on one or a few molecular signals, this paper creates a 360º view of cell behavior and suggests the existence of molecular correlates of the constituents of the psyche.

In the wave-particle duality of quantum physics, preferring the particle over the wave gives birth to material science while focussing on the wave teaches us to encompass humanity and leads us to the spirit. In cell science, however, it is impossible to advance without striking a balance between the 'protoplasm' and the molecules. Within the Worldview of the Multiversal plasm, Psychoplasm, and the Protoplasm, or of Consciousness, Cognition, and Behavior the article creates the perspective where the manifested behavior is at the bottom, the cognitive molecules are at the center and the psychic operators are at the top. There are molecular correlates of the faculty of the human/cell psyche. A single cell is proactively immersed in an open multiversal cosmology, interacts with visible and dark energy, maintaining its free will and autonomy, rules over several molecular robots and automated signaling system, and handles different kinds of stress and emotion. The cell is a minuscule universe indeed! The neuroplasm is the best 'home' for the constituents of the psyche and holds the key to multiversal plasm-guided human transformation.

Another perspective emerging from this paper asserts that the discipline of pathology is not merely the science of the morbid, or of broken down autopilot cells! Pathology is the life story of the cells, tissue, organs, and systems. We are on the doorstep of a new frontier in pathology, which might be named psychopathology, and on a new dimension of psychomolecular laboratory medicine.

Technology is a powerful and valuable partner in the science of life, and biology. Looking at such behavioral expressions of cells, several Indian Institutes of Technology have started a four-year Bachelor of Technology curriculum on Biologically-Inspired Systems Science (BISS). Already there are biologically inspired life-saving devices such as Artificial kidneys and Heart-lung machines. Neural networks and Artificial intelligence (AI) are also biologically inspired human-made devices. Science is craving for a new technology that could tap the inexhaustible resources of dark energy for routine use. Since only 'life' can harness dark energy, a question is whether it is possible to fabricate a dark energy harnessing technology from synthetic biology or using the apparently 'immortal' malignant cell!

We conclude this article with the humility of a cell that sounds in silence, "Conduct yourself. The kingdom of your constitution is made of millions of units like us."

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