Research Article

The Ladder of Cognition: Abstract Operations, Molecular Biology, Systems Science

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Abstract

Bioinformatics of transition from signal to knowledge, experience and wisdom appears opaque. This transition has been described through four hierarchically nested specific operations to structurize the ladder of cognition. Cells could be classified according to their level in the cognitive ladder. The specific substrate proteins as required for desirable level of cellular cognition show a remarkable similar pattern in dynamical hierarchical structure in concurrence with ontological ladders in informatics, mathematics, logic and linguistics. Within the cell, several factors together make the cognitive and decision-making system labyrinthine, where molecules respond to their intangible operators as the strings respond to the fingers of a sitar player. There emerges the broad outline of organization in the design of unified systems science. The outcomes have promises for pathology and molecular medicine, cell biology and synthetic biology, psychology and psychiatry, artificial intelligence and bio-robotics.

HIGHLIGHTS

- The ladder of cognition is dynamically structurized with four hierarchically nested operations.

- A remarkable similarity is observed between the ladder of cognition and the ontological ladder in informatics, mathematics, logic, linguistics and the ladder in nature's currency.

- Proteins, which are likely to offer substrate support for cognition also show similar pattern.

- The broad outline of organization in the design of a unified systems science has emerged.

ABBREVIATIONS

CFPS: Cell Free Protein Synthesis; CREB: cAMP Response Element Binding; CTL: Cytotoxic T-Lymphocyte; DNA: Deoxyribo Nucleic Acid; ETA: Event Tree Analysis; Exp_c: Experience; HSP: Heat Shock Protein; Inf_n: Information; Knl_g: Knowledge; LPS: LipoPolySaccharide mRNA: Messenger RNA; NCC: Neural Correlates / Correspondence of Consciousness NETosis: Neutrophil Extracellular Traps-osis; NK Cell: Natural Killer Cell; NLRP: Nucleotide-binding domain, Leucine-rich Repeat-containing Protein; NMDA: N-methyl-D-aspartate; NSC: Neural Substrate of Consciousness; PPI: Protein-Protein Interaction; RBC: Red Blood Cell; RNA: Ribo Nucleic Acid; Sig_l: Signal; tRNA: Transport RNA; Wsd_m:Wisdom

INTRODUCTION

Cognition is generally thought to be a function of the nervous system. Even an ant with only 250,000 neurons rescue their wounded from battles [1]. Cellular cognition, on the other hand, is a developing discipline. "Bacteria are small but not stupid" [2]. Like human beings connected through facebook, the bacteria have phagebook for social networking [3]. Even the phages are seen to make group decision [4]. Like an individual, a single cell is wise, experienced and intelligent, has knowledge and can build up information from the signal originating out of ligand-receptor interaction. Are cells 'clouds' and 'continuum' and the function to be described as 'unfolding' and 'dynamics'? Are we describing cell 'state' or cell 'type'? Are there really laws of biology? Craig Mak raises these issues in the recent editorial of Cell Systems [5]! Molecular signal networking keeps every organelle of a cell informed about its wisdom, experience and knowledge. As a result, the language of response of a cell becomes ideology-neutral, solution-centric and holistic. The mechanism for this kind of cellular response and the behavioral repertoire as required, are based on informatics, which is still opaque. The discipline of informatics has been shuttling between signal and information. Digital computer works on the basis of binary arithmetic and Boolean algebra. Geometry and Symmetry are yet to be used in informatics. Neuroscience speaks of sensation, perception and conscious experience. Only the disciplines of linguistics and philosophy cover the whole spectrum from signal to wisdom, although without any scientific basis. Is it possible to address the mechanism by which the signal is converted into information, information transits to knowledge, knowledge transforms into experience, and the experience sublimes as wisdom? In reverse, in the downstream, are there operations, which can explain

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how the wisdom is distributed homogenously within the cell reflecting the experience and knowledge throughout? Could any known physicochemical process explain such processes or do we need new framework for such coherent understanding where, as Heisenberg puts it, "physics and chemistry belong as limiting case"? "Electrical and biological circuits are not directly parallel". Therefore, we are to go beyond physical circuitry [6]. If we say that entire cell-signaling network works automatically, then the process of enquiry ceases. A cognitive dead end is reached. By trusting solely on self-organization we skirt the real issue, the emerging patterns in the biological complexity [7] and ignore the difference between self-organizing and life-organizing systems. Could the existing frail linguistic ladder of cognition be used for explaining cellular and molecular cognition? Could different cells be classified on the basis of their behavioral skill that in turn depends on their power of cognition? The objectives of this scientific narrative are to define different milestones on the path from signal to experience, understand the possible operational process from one milestone to the next, and to develop a framework of cognitive ladder supported by existing evidence in science and which is further verifiable by experiments. The larger goal is to unfold the design of organization for a unified systems science.

METHODS

Having accepted the linguistic ladder of cognition and its in-built hierarchy as our initial substrates, the milestones within the spectrum of the ladder is defined and so also the pathway. Following this, operations from one milestone to the next have been designated and thereafter described in detail.

Defining the Milestones

Cognition starts with attending a signal, the first milestone in the path. The last milestone is the point of wisdom. Information, knowledge and experience are three more milestones in between. The milestones could be abbreviated as $Sig_l. \rightarrow Inf_n. \rightarrow Knl_g. \rightarrow Exp_c. \rightarrow Wsd_m.$ The milestones could be described as follows.

1. The signal: Signal in science is designated by an energy frequency i.e., as energy in space per unit of time. Information's space-time construct is signal. Signal works in physical, measurable, sensible plane. Signal has no meaning of its own. It is non-intentional. In terms of knowledge, signal, like data, represents merely factual knowledge.

2. Information: Information is the unit of communication between two conscious systems. It carries the 'meaning' extracted from the signal in a specific context. Information is transphysical, not totally within the physical plane of matter energy, space and time. Information, as known today, is digital. It is 'Shannonian' information that reduces mathematical uncertainty. Information in terms of knowledge is informative knowledge.

3. Knowledge: By knowledge, it is generally meant formative or the 'textbook' knowledge. Several interrelated information acquire a specific architectural invariance and irreducibility in knowledge. Therefore, knowledge can be used by the systems without further deliberation on it. Knowledge carries the meaning of information in the context of the systems as a whole.

4. Experience: Experience is dynamically piled-up interactive knowledge of several spheres that within the systems have survived the challenges of symmetry-breaking processes in life. Experience is environment-seasoned with socio-cultural bias, but systems-confined. Experience is transformative knowledge. It is like hard currency for use in long-term survival and growth of the systems.

5. Wisdom: Wisdom, the sublime knowledge, is the final essence of a large number of similar experiences of not merely one system but of several systems and is therefore, useful globally. In terms of information, wisdom is crystal information at a point. With the highest degree of accuracy and limited by error in given action, wisdom is in sync with the world, carrying always a worldview.

Defining the Pathway

The process of transition of signal to wisdom could be looked as progressive refinement of 'meaning'. Knowledge is the 'meaning' in the context of the whole system. Experience is the 'meaning' of knowledge in the context of the environment the systems live in. Wisdom carries the final meaning in sync with world transition of tangible physical to sub-physical intangible begins when signal transits to information. By sub-physical it is meant for which there is not yet a tool to measure any activity. The whole process covers a gradual transition from measurable quantity to acquisition of quality, from progressive integration to a state of becoming integral within the systems. The process is a movement from the laws of cause and effect, linear and circular causality, to the 'categorical imperative' of Immanuel Kant, a movement from epistemology to ontology! The upstream movement, in philosophical language, is gradual transcendentalization of nature while the downstream is progressive naturalization of the transcendental. This is the transition from signal processing Boolean logic to concept processing fuzzy logic to knowledge processing formal logic followed by inferential logic in experience and hermeneutics of conscious system, which includes non-verbal communication activities as well. In the language of mathematics this is a movement from arithmetic/algebraic expression to geometric representation to symmetry acquisition and then to have symmetry-manifold (?super-symmetry) that finally culminates in 'pointification (dynamically in 'moment'ification). The transition is conducted by hierarchically nested four specific operations.

Designation of the Operations

The operation between Sig_l and Inf_n is designated as operation I, between Inf_n and Knl_g as operation II, between Knl_g and Exp_c as operation III and between Exp_c and Wsd_m as operation IV.

Operations in Detail

Operations are described individually one by one.

Operation I: Simply stated it looks like conversion of signal into information, conversion of space-time construct of information into Shannonian information. Signal is represented by energy frequency. Frequency is expressed as space per unit time. Space and time together constitute "form". By an outside-in maneuver, this "form" from the physical plane goes inside

information. As a result (Figure 1), we get a process-structure together, as information, where 'action' indicates etymologically, a process [8].

Further detail

Operation I is on the phase transition of signal into information where a meaning, a concept is developed from the percept. This conversion of percept into a concept concurs with transition of arithmetic into geometry. Arithmetic number has no place in the conceptual realm while the geometric figures have [9]! There is contextualization of the content and establishment of multilevel connections with operations II and III while retaining connection with physical plane. Information has a measurable aspect, content aspect and intent aspect, a trifoliate leaf-like structure (Figure 2)

with petiole rooted in operation III. Intentionality of information is derived from its connection with operation II. Content of information is handled by operation I, which also builds up the context, while its measurable folium is based on the physical plane where it is digital and reduces mathematical uncertainty. This description completes what is meant by Shannonian information. Operation I is responsible for bringing out all of the changes mentioned above. Operational kinetic is such that a large number of information can be generated from one single signal.

Not all signals can become information because not all signals can withstand such operative maneuvering.

In the reverse, operation I delivers space, time and energy when information transits to signal.
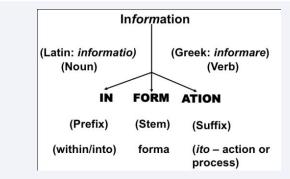

Figure 1 Information has a 'form' inside. This 'form' from the physical plane is put inside information by the Operation I. Information, etymologically, is which puts 'form' into process.
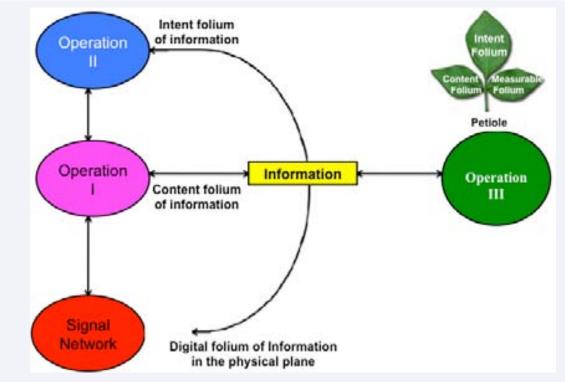

Figure 2 Shannonian information has a trifoliate leaf-like structure with its intent folium is in connection with operation II, content folium is in connection with operation I and measurable folium is in connection with the physical plane. The petiole of the leaf is clogged with operation III. Both signal and digital folium of information are in the physical plane.

Operation II

Operation II is formatting of several interrelated information, their structurization into a specific pattern (multifold symmetry) in the context of the whole system. The operative maneuver, although difficult to articulate in language of space-time dimension, consists of (i) 360^0 rotation, (ii) rotation in all dimensions followed by (iii) homogenous global distribution of the formative knowledge. Multifold symmetry [10] or an invariant reflection, rotational and radial symmetry are acquired in the 'sphere' of knowledge. In terms of information, operation II could be described as Shannonian to Gödelian transformation of information.

Further detail

Keeping information's base (physical plane), root (connection with operation III), content and intent unaltered, a specific multifold/spherical symmetry is delivered from several interrelated information by operation II during formation of knowledge. Symmetry is an invariant under any known circumstance [11].The operation bestows knowledge' the ability to act as sensor. Shannonian information, although intentional, has no such sensor property.

Not all information can become knowledge because not all information can withstand this operative maneuver as described.

In the reverse downstream movement, information is hatched out from the sphere of knowledge.

Operation III: In operation III, the 'symmetry' in knowledge is confronted with symmetry-breaking and symmetry-making processes. In three-dimensional language, the maneuver is for (i) symmetry alteration by 180^0 rotation (anti-symmetry) (ii) symmetry loss (a-symmetry) and (iii) symmetry reversal by inside-out and outside-in phenomena.

New knowledge with different content and intent develops with new symmetry following survival after repeated confrontations. In contrast to operation II that results in one single symmetry / pattern, operation III results in multiple 'sphere' of symmetries, which are stacked as manifold. The unified dynamism of these multiple invariant symmetries is expressed as experience, 'vast' and 'layered'.

Further detail

The outcome of operation III is experience. Experience is that which concurs with the reality. Inside's 'experience' is outside's 'reality' and vice versa. Since inside-becoming-out and outside-becoming-in phenomena are involved, both inside and outside of the global contents of the systems are identical in experiencing. For non-intuitive sphere eversion (there are You Tube video available on this), the mathematics of inside of a sphere becoming out, see "Immersion of manifolds" [12] and related articles on homotopy and differential topology.

Not all knowledge symmetries can get into the information-manifold and become part of interactively unified experience since all symmetries cannot withstand inside-out phenomenon. Besides, there is censoring activity of operation III.

From experience to knowledge there would be first isolation of the sphere from the manifold followed by outside-in phenomenon.

Operation IV: Of all four operations, this is the subtlest and is most difficult to articulate. The operation leads to pointification of interactive spheres with different content and intent in the symmetry-manifold stacked up in experience. Simply stated, it could be a kind of sublimation. From other perspectives, the operation looks like micro crystallization, or forming pearl, gems or diamond out of a vast information manifold. Or, it might be a kind of super-condensation of all interacting spheres of different contents and intents to occupy minimum possible 'space 'in one single point. Dynamically expressed, it is the 'moment' in Time.

Further detail

Operation IV repairs the great chasm between intentionality of information and will of the system, which in the language of Max Planck is, "inadmissible logical disjunction between causality and free will". The chasm is found in many natural systems lacking self-evolution. Through operation IV, the product wisdom gain access to and accommodate a large number of similar experiences of several systems, remains in sync with the probability waves of the world and carries a dynamic worldview.

Since only spherical symmetry could be reduced (reduction) to a point, all experiences do not sublime to wisdom.

In reverse, from single point of wisdom emerge (emergence) multiple spheres of knowledge of different size and hue.

RESULTS OF OPERATIONS

Four hierarchically organized specific operations with successive delivery of products have been shown in Figure (3), which is modified and improved from author's earlier publication on emerging patterns in the complexity[7].

The result of each operation and the distinction of their products are described below.

Information generates from signal in operation I. Their differences are shown in Table (1).

As a result of operation I, information acquires connection with operation II and III and achieves its trifoliate leaf-like structure. Information serves as a 'via media' of geometry derived from the dimensions of physical world to the symmetry of knowledge world.

Information is focal, local yet not global for the systems. Operation II precisely takes care of this by making the perceived meaning explicit in the global context within the systems. As a result there is hand-ready currency of an invariant symmetry, which can be used without further deliberation. By this operation, interactive information becomes non-digital and irreducible. While acquiring interactivity of invariant symmetries, there are developments of logic modules, which are linear and track-based having feedback loops. The knowledge can act as global sensor within the systems. The differences between Shannonian information and knowledge are shown in Table (2).

Operation III results in three more important developments: (i) Development of reversibility of the processes. (ii) Generation
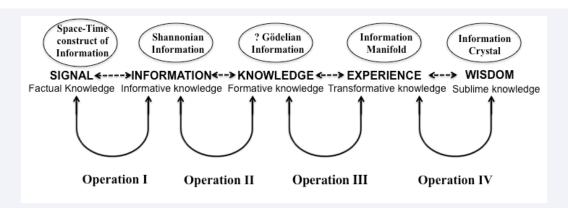
Figure 3 Structurization of successive operational processes involved in transition of signal into wisdom and vice versa. Four successive operations have been shown between five milestones, from the point of signal to the point of wisdom. Operation I is for the transit of signal into information and vice versa, operation II for information into knowledge and vice versa, operation III is for knowledge into experience and vice versa, and operation IV for experience into wisdom and vice versa. The alternate names of the milestones also have been shown in the figure.

Table 1: Difference between Signal and Information.

Parameters	Signal	Information
1.Working Plane	Works in physical, sensory plane	Works in both physical and sub-physical planes
2.Relation with space, time	Signal is space time construct of energy	Space and time are inside, with in the 'form' of information.
3. Intentionality	Non-intentional	Intentional
4.Mathematical representation	Arithmetical representation	Geometric representation
5. Dimensionality and level	Three or four-dimensional. Could be multidimensional	Multi-level. Information is a 'via media' from dimension to symmetry
6. Related to	Perception	Concept formation
7.Possibility of getting automated	Can be automated	Cannot be automated. Informational system requires constant supervision

Table 2: Difference between Shannonian information and Knowledge.

Parameters	Shannonian Information	Knowledge
1.Based on the measure of	Disorder within the system	Order within the organized system
2. Location	Focal within the systems	Global within the systems
3. Symmetry	No definite symmetry	Spherical/Multifold symmetry as invariant.
4. Ability to act as Sensor	Absent	Present.
5. Irreducibility	Can be digitized. Reducible	Irreducible.

of multiple logic modules,(iii) some of which work as inferential logic with feed forward in addition to feedback loop. Experience, thus formed, consists of multiple invariant symmetries of different spheres stacked up in several layers logically interacting with each other to make the purpose of knowledge explicit in the context of survival and growth of the systems. The differences between knowledge and experience are shown in Table (3).

While experience is intrinsically static for the world and is of limited theory value, wisdom intrinsically carries the dynamicity of a worldview. Wisdom's openness to the world offers the systems the ability to redefine itself and evolve. The difference between experience and wisdom are shown in Table (4).

Delivery of hierarchical new property is observed in these operational activities. Operation I confers intentionality to information. Operation II confers sensor property to knowledge. Operation III confers censoring property to experience. Operation

IV confers the final product synchronization with the world, multisystem dynamism and the ability to govern.

The outcomes as mentioned above are for linear hierarchical systems of operations as shown in Figure (3). With labyrinthine systems of hierarchy (see discussion below), there are additional outcomes.

DISCUSSION

The cognitive ladder, supported by four operations as described above, has five rungs. The fifth one at the top is actually not a rung but the helm, the point of origin of nested dynamicity of the ladder. The point at the helm governs all regulators and acts as a sensor for experience. It can censure as well as direct the experience. Experience is the sensor as well as censor for architectural symmetry of knowledge. Knowledge is the sensor for multileveled intentional information, which in turn is in connection with multidimensional signal.

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Table 3: Difference between Knowledge and Experience.

Parameters	Knowledge	Experience
1. Symmetry	Single multifold/spherical symmetry	Stacked up several multifold/spherical symmetries. ?Super-symmetry
2. Layers	Not layered	Layered
3. Logic	Works with only formal logic	Works with both formal and inferential logic
4. What does it define?	Defines the context of information globally within the systems	Defines the purpose of survival and growth of the systems
5. Capability	Possesses hypothesis-building capability	Possesses theory-building capability

Table 4: Difference between Experience and Wisdom.

Parameters	Experience (Information manifold)	Wisdom (Information Crystal)
1. Specific property	Censuring property	Governing property
2. Access sphere	Experience is the dynamic bridge between knowledge and wisdom	Wisdom has access to similar experience and knowledge of several systems
3. Confinement	Dynamicity is confined to the system	In sync with probability wave of the world
4. Value	Is of limited theory value	Always moves with a 'Worldview'
5. Limitation	Mere experience cannot help the system to redefine itself	Being in sync with the world, the system can redefine itself

The central rung of the ladder, the knowledge, is important because its apparently invariant symmetry has to face challenges top-down from 'life' and from the 'freedom' at the helm. Bottom up, the symmetry is constantly challenged by multidimensional intentional informational inputs. Therefore, in the dynamical cell systems and in an individual the invariance of the architectural symmetry of knowledge and super symmetry of experience are always a matter of the present.

It is stated earlier that information serves as a 'via media' from dimension in physical domain to the symmetry in knowledge domain. Information and symmetry "adumbrate at the abstract core of complex systems" [13]. Two could be complementary or supplementary to each other in different context. "Information provides diversity metrics and communicative openness, while symmetry provides regular constructive compression and ordering of processes."

If knowledge is to be articulated as a kind of information, then the closest it comes to is Gödel's concept of information (as shown in Figures 2, 3), which is non-digital, irreducible and not within Turing's limit (see in this context[14]). Another such possible candidate is Bohmian information, which is conceptualized in the context of the whole. So also is Planckian information [11]. The issue, although, is not of immediate concern of this paper, might pave the mathematical expressway from signal to wisdom.

Ladder of cognition requires substrate support. Symmetry manifolds within the systems work as the substrate for the wisdom. Symmetry, in turn, is the substrate for symmetry-manifold. Information is the substrate for knowledge symmetry. Space, time and energy are substrates for information. The freedom at the helm of the systems supports John Muir's famous statement of 1911, "When we try to pick out anything by itself, we find it hitched to everything else in the universe."

Also, there are several occasions of "information loss". In upward transition, all factual knowledge does not become informative knowledge, not all informative knowledge becomes formative knowledge, not all formative knowledge becomes transformative knowledge and not all transformative knowledge becomes part of wisdom. Wisdom is nearest to the Truth. The technique of Event Tree Analysis (ETA), which is a "forward, bottom up, logical modeling technique for both success and failure that explores responses through a single initiating event and lays a path for assessing probabilities of the outcomes and overall system analysis"[15], might be applied to assess such information loss. Perhaps following the glimpse of this whole spectrum, the Nobel poet Rabindranath Tagore wrote, "All that happen are not Truth!"

The results raise several relevant issues; possible presence of operators, nature of operational hierarchy, non-hierarchical interactions between operations, existence of any evidence from cell biology and where does all lead to? All of these merit in-depth discussion.

Possible Operator for the Operation

Is there any known operator for the operations described? Possibly yes. Affirmation comes from insights available from evidence in cell biology and neuroscience. Inside a cell, although it is difficult to pinpoint the operators except for a sense of having operation III, in human cognitive systems the apparently intangible operators can be speculated as under.

Is it contextually correct that the operator for operation I is what probably being conventionally labeled as the Mind, and the articulated nomenclature has grown in linguistics with general public consensus? Similarly, is the operator for operation II probably being conventionally called the Self? In the same vein operation III has been called "Life", life-processes, or the "processes of life" or even in sublime language as "life-principle", while the operator, which carries out operation IV has been labeled as consciousness!

At present there is no consensus on any equipment, device

or technique, which can extract meaning from signal/data except the human mind. Similarly, we do not find any technique, device or machine, which can make knowledge out of information except the "self" in presence of "life". It appears true that there is no known equipment, device, system or technology, which can generate experience from knowledge except the "life". There is no known mechanical system or technique available, which can manufacture wisdom from experience or knowledge without involving the operation of consciousness. Consciousness is that what takes care of what all happens in life, self and mind in the context of information management. Consciousness could be investigated as an operation which manages all operations of transition of signal into information, information into knowledge, knowledge into experience and experience into wisdom, also the vice versa. Our mind is sensitive to signal/information. Self is sensitive to phenomenon. Life is sensitive to change in symmetry while consciousness is sensitive to none of the above, but only to the process of submission of properties. It can reduce everything to a point (and dynamically to a moment). In this context consciousness is the greatest reductionist. Needless to say, that the designated operation does not say anything about other functions of the operator mentioned. Also, how such operators have been operating the way as mentioned makes another issue.

What has been stated would be clear when we analyze the characteristics of signal-organized systems (mechanical robots), information-organized systems (bacteria), self-organized systems (in inanimate world, a fractal, and in living world cells like antigen-recognizing dendritic cells), life-organized systems (memory lymphocyte, having information manifold as experience), and consciousness-organized systems (cerebral cortical neurons in tripartite synapse with astrocytes). The systems are arranged in a nested hierarchical manner that will be deliberated further during discussion. In bacteria, operation I is evident while other operations are hardly recognizable. In self-organizing systems, operation II is more explicit. Operation III could be better understood in life-organized systems. The self-organizing system can generate one single pattern, may be a pattern within pattern ad infinitum as seen in a fractal, but the life-organized systems has the capability to generate multiple symmetries/patterns, which are stacked as information manifold. Experience in the present scheme is not the integrated information of several unitary concepts! Multiple symmetries in the manifold becoming integral of the systems generate experience. Experience generation includes but transcends arithmetic, geometry and symmetry (see below). Consciousness operated cell (say, cortical neuron) can sublime this experience into wisdom!

With the four operators as named above and the four operations as depicted in the Figure 3, it is possible to redraw another figure as shown below (Figure 4). Perhaps in the context of human brain and mind, it describes the cognitive ladder of sensation, perception, concept formation, hypothesis generation,
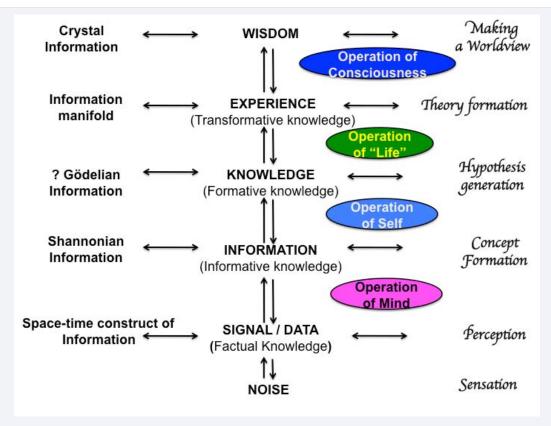

Figure 4 Cognitive ladder and the ladder of informatics are in concurrence with the ladder in linguistics at the centre. In between five rungs of the ladder, there are four operations. Operations are numerically stated as operation I, II, III and IV in Figure 3. The operators for the same operations have been projected in this figure as mind, self, life and consciousness respectively. The ladders have several lateral interceptions with each other.

theorization and generating systems' own worldview (right side of Figure 4) in consistence with the ontological ladder in informatics (left side of Figure 4). Four specific operations are in between five rungs in each of the ladders. The ladders have several lateral interceptions with each other.

In the mathematical language, the stairs or rungs would be as follows. Perception is arithmetic/algebraic. Concept formation is geometrization leading to a structure, which is still reducible. Knowledge is formation of an invariant and irreducible architectural symmetry. Experience is supported by information-manifold or symmetry-manifold. Wisdom is the ultimate cognitive point of the systems.

Nature of Hierarchy of the Operations and the Products

Nature of hierarchy as described so far is linear in a pyramidal system with large number of signals and information at the base and the Point of wisdom at the top. What matters is packaging [16] of product from a large number of substrates as shown in Figure (5).

Even in the pyramidal linear hierarchical systems, as shown in Figures (3,4), there are several problems to resolve. First, whether the downstream operation(s) can continue independent of the upstream operations? Second, whether the individual operation is bidirectional? Exactly when, how and what makes the process bidirectional? Third, whether there is any consumption or release of energy in any form, conventional or unconventional, during such phase transition? Finally, are the operations always in tandem or in otherwise?

We are describing the operations in the living systems and not in a robot. Downstream cogs can operate only to a limited extent in absence of upstream operators. Therefore, the operational systems, as described above, are required to be studied as a whole, as we do it in unit of life, within a cell. In a mechanical robot, the operation is far limited and thereby there is effort to include biochips (i.e., "life") in DNA-robotics and DNA computer.

All operations within the living systems are bidirectional. In absence of "life", as it is in a mechanical expert system and even in self-organizing system, the far-limited operations II and I are unidirectional. It is the presence of "life" which makes the operations bidirectional.

Whether such operations consume or release any conventional energy is not known. Most likely, they do. Possibility is also there for consumption/release of energy in some unconventional form, such as "dark energy". Utilization of dark energy by living entity is a possibility, which can explain their spontaneity and uncoupled action and reactions. "In search for unseen matter, physicists turn to dark sector" [17].

The operations are not exactly sequential or linear as projected in Figures (3,4). The passage is truly labyrinthine (see Figure 6), as to why so is described below.

Labyrinthine Hierarchy

The hierarchical system as described is seemingly not linear. Why? There are (i) non-hierarchical interactions between operations, (ii) bidirectional signal-less interactive loops between operations, (iii) lateral entry in the vertical hierarchy (such as mind can directly access information, self phenomenon and life symmetry) and (iv) lateral interactions between different ladders at points of correspondence/interaction. What binds
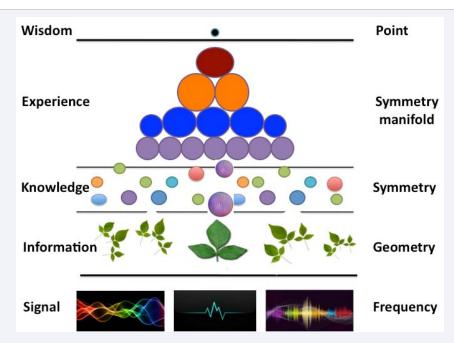

Figure 5 Packaging matters. A large number of interrelated information of trifoliate geometry shape are packed into a possible small sphere of knowledge. A large number of such spheres of different size and hue (field of knowledge) are packaged as manifold in experience. All spheres are reduced to a common point, the point of wisdom at the top. The boundary between signal and information and that between manifold and wisdom are tough. Boundary between information and knowledge and between knowledge and experience are thin and porous.
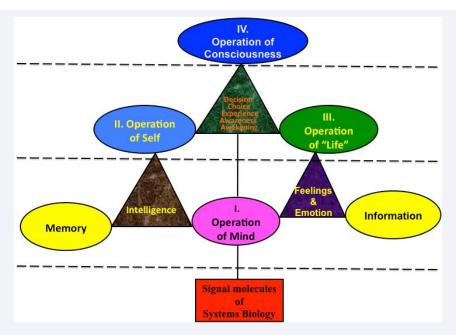
Figure 6 The cognitive labyrinth. Operation I (of mind) is immediately next to physical nest having molecular signal networks. In the same sub-physical nest of mind, information, memory, intelligence and emotion work, where information is connected (not shown in the figure) with back-up memory. The stations of operation II (of self) and III (of life) are in deeper sub-physical nest. Consciousness operates (operation IV) from the deepest nest. Only operation I (of mind) has connection with physical nest. Operation II, III and IV connect with physical nest through operation I which remains the final common pathway to the physical nest. Information, bottom-up, has no direct access to operation IV. Connections of information to operation I, II (not seen in the figure) and III are direct. Operation IV accesses information through operation II, III and I. Non-hierarchical interaction between the operations also shows a definite pattern and generates new outcomes. Operation III and I, along with information, generate emotion. Operation II and I, along with memory, generate intelligence. Awakening, awareness, experience, choice and decision are outcomes of joint operation II, III and IV. Note also the hotline connection between consciousness and mind.

this complex system at one single point at the top or at the center has been named variously as the Point, the helm, wisdom, consciousness or the operator of operation IV. All these, in dynamical live systems, make a labyrinthine hierarchy with one opening at the physical world and the other at the consciousness world. Labyrinthine hierarchy results in additional outcomes from interacting operations.

Figure (6) is a modified version of a figure in author's earlier publication on Systems Cell [18]. It shows the operations in a hierarchically stratified, nested and labyrinthine way.

In this figure we fix the operations at their respective places, but does not fix the operators. Operators cannot be localized, although their operations could be! The designated working places are their 'office room' within a defined system. While operation I (of mind) is more close to physical nest/plane, operation II (of self) and operation III (of life) are more close to operation IV (of consciousness). The additional outcomes like, feelings/emotion (result of interaction between mind information and life) and intelligence (result of interaction between self, mind and memory) are in superficial plane/nest like mind. Additional outcomes such as awakening, awareness, experience, choice and decision (result of interaction between consciousness self and life) are in the working plane/nest of self and life.

On examination of the lateral symmetry of the Figure 5, emotion and feelings are seen on the right side, representing mostly the right brain activity while the assertion by self and intelligence are on the left side representing mostly the left brain activity. Awakening awareness, experience, choice and decision are central, holistic bi-hemispheric brain activity.

Whether wakefulness and awareness are demonstrable in microscopic cell is not presently known. Whether the resting phase of a cell could be described as sleep is not yet decided. However, photosynthetic cyanobacteria and plant cells follow the pattern of circadian rhythm in their activity [19]. Circadian clock has been reported to gate cell division [20]. Awakening in such cells is heralded by conformational change in the receptivity of cell membrane. When the brain sleeps, its certain number of neurons must be in a specific resting phase. In the context of human being as a whole, it looks simple to understand that we cannot wake up without operation of our self with consciousness while we are alive. If "life" ceases to operate while one has been sleeping, one no longer wakes up. We cannot be aware of neural correlates of consciousness or wave function of quantum mechanics, all examples of extraordinary content of our consciousness, without the conjoint operation of self, consciousness and life. Unlike a robot, we can choose outside algorithmic pre-specifications because we are alive and conscious and we have a self. Therefore, Figure 5 represents the model for the cognitive organ of any living systems with four operations embedded within it.

Supportive Evidence

From Cell Biology: We look for neural correspondence/correlates/substrates of consciousness (NCC/NSC) inside the brain. Could we look inside the cell for the molecular correspondence/correlates/substrates of such cognitive

operations and operators? Inside the brain, we see networking and synapses. Inside a cell we recognize signal networks and "molecular talk" between groups of molecules in important decisions. This is the work ahead for cell biologists [18,21,22]. The major channel for information flow inside the cell is from nucleus, through cytoskeleton or cytosol, to the cell membrane and vice versa. The known repository of information manifold inside the cell is DNA and chromatin proteins.

The possible molecules for mind operation are in the cell membrane. Mind works as organ of communication between two conscious systems. So, does the cell membrane. Bruce Lipton draws a similarity of substance between cell membrane and silicon chips [23]. While silicon chips are crystal semiconductor with gates and channels so the cell membrane is liquid crystal semiconductor with gates and channels. Calcium ion channels in cells and calcium waves in astrocyte have been proposed to be molecular representatives of mind [18,22]. Every cell has an uncanny sense of self. The whole immune system works on the difference between self and non-self. Molecular representation of self is in MHC I molecules. So also the proton pumps which maintain the ionic specificity of 'self' of a cell. The self guides the informed molecules through cytosolic sea to reach respective organelle. Pressure-gated (cytoskeleton-gated) ion channels appear to be strong molecular candidate for life, since detachment of cytoskeleton from the cell membrane is the first step for either cell division or apoptosis. Recent evidence suggests that octopus and squid can rewrite their RNA [24]. The terms like coding, editing presupposes presence of intelligence, which never comes from non-intelligent molecular randomness but is the outcome of interaction between self, mind and memory and their ordered molecular representatives. In this context, molecules respond to their operators as the strings respond to the fingers of a sitar player.

That cell has emotion is evident from the phenomenon of frustrated phagocytosis [25]! That cell feels stress (genotoxic stress, metabolic stress, oxidative stress, endoplasmic reticulum stress and apoptotic stress) is evident from its stress-adaptive mechanisms like slowing of cell cycle, down regulation of housekeeping functions, activation of protective pathway e.g., through heat shock proteins and as shown in stress-triggered phase separation within a cell to 'gel or die'[26]. The possible molecules carrying feelings and emotion could be cytoskeleton. Molecular representation of cognition is in NMDA receptor, kinase activator, phosphatase regulator and CREB etc. The author suggests that nearby molecular footprint for awakening in a cell could be mutated prion protein [27], as seen in Familial Fatal Insomnia. The volition / 'will' of a cell is expressed best during apoptosis through Fas receptor, PD receptor for ligand 1 and 2, or during prolongation of 'life' through telomerase activity. Emotion, feelings, cognition, volition, awakening, and decision-making are found in consciousness-organized systems. Programmed cell death is a conscious decision of the cell, particularly so when it is executed as defense against infection. Extraordinary signal coordination between apoptosis, necroptosis (programmed necrosis), pyroptosis (programmed pore-induced intracellular traps formation), NETosis and Efferocytosis (phagocytosis of dead cells) to check infection [28, 29]indicates superb vigilantism and execution from conscious level. Another conscious decision

in a cell is membrane fusion, whether it is during fertilization or in autophagy. Kerr et al has reviewed causative association between impaired mitophagy and cognitive disorder like AD [30]. Since autophagy is a conscious decision, there are occasions when autophagy could be used as a benefit to the cell [31]. It has an expanded role in genome maintenance [32]. Other example of conscious decision of a cell is to enter M-phase of cell cycle for mitosis.

The molecules, which are outside the conventional protein-DNA-RNA-protein circularity is the "DNA-driver" in nuclear chromatin [33,34]. Histone is multimer of spherical proteins involved in 'regulating the regulators'. As mind has hotline connection with consciousness (Figure 6), so also the membrane lipids speak to histones [35]. The final common pathway for expression of the cellular language is RNA concentration wave [11].

To find out the molecular correspondence of operations and operators is a heavy job. It requires to be split into several tasks. Since the ladder of cognition is not uniformly developed over the cell populations in a multicellular organism with different systems, the first task is to segregate the cells on the basis of their skill, whether they work mainly on the basis of signals, information, knowledge or experience. Table (5) has been made on the basis of this new cellular taxonomy.

The activity of platelets and RBCs in the blood and neurons involved in several reflexes are signal-based. Metabolomics including endocrine activities are information-based. Antigen recognition is a knowledge-based activity. All memory cells are experienced cells. So also are the regulators of pacemaker cells of the heart and pacemaker neurons in the brain stem. Mark the functional distinction between neutrophil, monocyte and NK cells. All are professional killers having respective skill. However, NETosis by 'informed' neutrophil is often non-specific and might injure own cells. Because of having Toll-like receptors with symmetrized structure, monocyte knows the specific indications for killing. CTL or NK cell is an experienced killer, which in spite of intelligence input of IL-18, knows when better not to join the encounter! Therefore its perforin-dependent killing rarely fails. Perforin and apoptosome are having multimeric quaternary structure. The example of wise cell could be found in some of the stem cells. The whole wisdom is supposed to be within the totipotent stem cell. The Oocyte is a wise cell, which chooses finally one from several high-energy candidates out of millions in the run. The third column of the table on the nervous system is very preliminary. Its tentativeness leaves enough scope for further improvement.

Next task, a far easier one, is to shift focus from cellular cognition to molecular cognition, to look into the structure of protein molecules. The specific substrate proteins as required for desirable level of cellular cognition show a remarkable similar pattern in dynamical hierarchical structure in concurrence with ontological ladders in informatics, mathematics, logic and linguistics. Sequencing of amino acids is arithmetic that makes the primary structure of protein. Geometric secondary structure of protein is achieved by chain folding. The cell gets informative protein. The symmetry, the conformity in the context of the whole, is gained in protein's tertiary structure. The

outcome is 'knowledgeable' protein. Quaternary structure, may be called (?) super-symmetry, is seen in protein representing experience. Common signal proteins are polypeptides. Common informative proteins are membrane receptors, all folded proteins. Knowledgeable proteins are tertiary structured proteins such as toll-like receptors, enzymes, which all work on the basis of symmetry and conformity. Feed forward activation of enzyme by substrate is observed in phospho-fructokinase and pyruvatekinse. Caspase 11 acts as a sensor for cytoplasmic LPS [36]. The protein of inflammosome such as NLRP3 is sensor for pyroptic and necroptic pores [37], NLRP6 is also a multifaceted innate immune sensor [38]. As there are infinite variety of knowledge and experience, so there are similar number of symmetry and super-symmetry in protein structure. Small HSPs have multimeric crystal structure [39], which with other heat shock protein sensors misfolded proteins. Hemoglobin, a quaternary protein, is equipped to carry and deliver oxygen to all cells and is one of the lifeline molecules of the body. Perforin and apoptosome have quaternary structure. The sphere is a design where reflection symmetry, axial symmetry, and rotational symmetry are absolute invariant. Sphere occupies minimum space for the given volume. Sphere can be reduced to a point and a point can be enlarged to sphere. That is probably the reason why the wisdom proteins are spherical in shape as one sees histone to be multimeric spheres. The approach opens up a new way of organizing data (on the basis this new taxonomy of protein) already available from proteomics and from protein-protein interactions (PPIs) with interface water molecules and such organization is likely to throw light on interactomics of the organism, and sub-system proteostasis and thereby to complex adaptive systems theory on organelle interconnectivity [40].

DNA transcription has been mechanized in thermocycler. Translating mRNA to primary structure of protein is difficult to be mechanized since this requires application of mind (operation I) in a self-organized (operation II) system in presence of 'life' (operation III) to decode the information in a codon (a trinucleotide) in the mRNA attached to ribosome on endoplasmic reticulum floating in cytosol. With the support of operation IV, operation I, II and III have been automated inside the cell. In the context of protein synthesis, cytosol represents distributed consciousness, endoplasmic reticulum distributed mind, ribosome distributed self, mRNA distributed life, and tRNA distributed information. The ideas narrated here might be of value in cell free system (such as rabbit reticulocyte, E. coli, Wheat germ) for cell free protein synthesis (CFPS) in synthetic biology [41].

In cell signaling systems we are almost always lost amidst molecular cross talk. Another task, therefore, is to sort out the signal pathways. Sorting out begins inside the cell membrane itself (Figure 7). One group of signals is transmitted fast through microtubules of cytoskeleton. They are transmitted as vibration, on the 'emotional highway', for distribution to all other cell organelles. Signals for phagocytosis, cell cycling, cell division and apoptosis, for examples, are transmitted this way. One can envisage quantum tunneling in this communication. The other group travels relatively slowly through the 'sea' of cytosol as informed molecules, on 'intellectual pathway' carrying discrete message to respective cell organelle. Signals for metabolomics, hormones, autophagy and transcription, for examples, are transmitted this way. This sea route has little scope for quantum tunneling. However, the cargo has interfacial water and physiological nano particles with it. Eventually those, which reach nuclear membrane, go through a chiasmatic divide. Most of the microtubular/emotional/vibrational signals reach the non-DNA chromatin for epigenetic activities and most of the intellectual/informed molecules reach the DNA of the nucleus. Genome and epigenome are dynamically connected by chromatin remodelers controlling histone turnover [42]. The cells, which regularly proliferate and regenerate, use mostly cytosolic sea route. The cells, which have stable microtubules (neuron, cardiac muscle), mostly use this vibrational route. There also exists such divide of signal transmission from genome/chromatin protein to phenome.

Evidence from Neuroscience: There are neuropsychiatric disorders with disconnect at several levels such as between

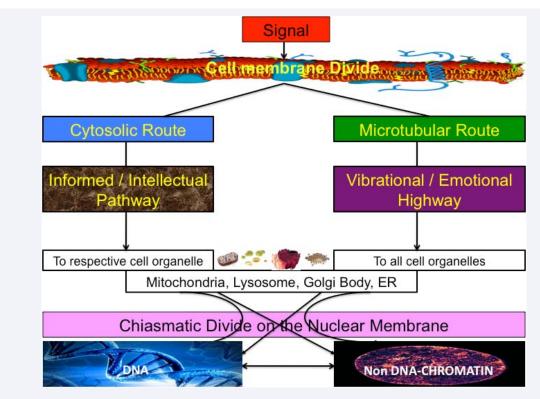| **Table 5:** Level of cognitionis different for different cells ina multicellular organism.			
Ladder of Cognition	**Cells in the body**	**Cells in the Nervous system**	**Cells in the peripheral blood**
1. Cells working mainly with signals	Skeletal muscle cell	Neurons in the peripheral ganglion and counter neurons in CNS involved in reflex activity	RBCs, Platelets
2. Informed Cell	Hepatocyte, Adipocyte. Endocrine glands Osteoblast	Retinal receptors. Cochlear Neurons. Thalamic and strialneurons	Neutrophil
3. Cells which work on input of intelligence	Tissue histiocyte, Mast cell, Osteoclast	Oligodendroglia Microglia	Eosinophil, Basophil
4. Cells which works on the basis of knowledge	Antigen-recognizing cell	Mirror neurons of cortex. Neurons of Amygdala, Septal nuclei. Neurons in hypothalamic nuclei. Cortical astrocytes	Monocyte
5. Cells which work on the basis of experience	Regulator of cardiac pacemaker cells	Regulator of pacemakers neurons in the Medulla oblongata (neurons of resp. centre, card. center, vasomotor center)	Memory T/B Cells. NK Cell
6. Cells which work on the basis of wisdom	Oocyte. Basal stem cells in intestinal and respiratory epithelium and in skin (decide on many functions of microbiota).	Cerebral cortical motor neurons (? Pyramidal neuron)with apical dendrites having a lot of dendritic spines and contributing generously to form dendritic mat, which are in sync with the probability waves outside and on the cortex.	T-Regulatory cell.

Figure 7 A signal from cell membrane to nucleus can traverse in two ways, creating the cell-membrane divide. The solid-phase route through microtubules of cytoskeleton is faster, vibrational, rhythmic and is distributed to all other organelles of the cell. Its rhythm and distribution to all other organelles make the transmission 'feminine', 'emotional', 'life-organized'. The slow pathway through 'sea-route' of cytosol is discrete and is distributed selectively to different organelle. Discreteness and selectivity make this route to be described as self-organized, 'intellectual' and 'masculine'. Both routes' end point is nucleus. On the nuclear membrane there is chiasmatic divisions of arriving signals. Vibrational signals mostly land up in the non-DNA chromatin for epigenetic influences whereas cytosolic signals mostly end at the DNA of nucleus.
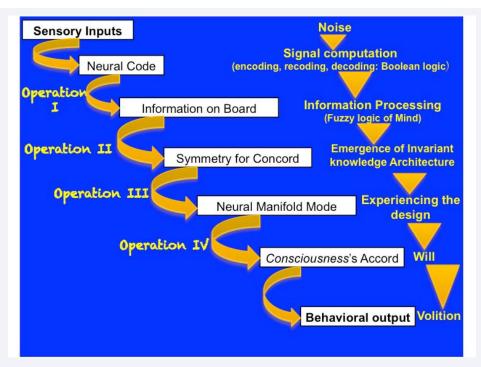

Figure 8 The layers between neural signaling and the behavior, the cascade of processes from signal to volition in the nervous system. The steps are from the signal code to on-board information, to symmetry concord, and neural multifold mode. Finally consciousness's accord results in behavioral output.

will and intention, awakening and recall of contents, between experience and choice, emotion and intelligence and so on. In constructional apraxia, there is difficulty in copying simple diagram, a defect in concept realization.

Dissociation of function of mind and consciousness is seen in several unconscious patients who although unconscious still retains the sphincter control, supposed to be a function of mind and self. There are subjects who are fully conscious but cannot recognize space time because of dysfunctional mind as in inebriated state. In the case of hemi neglect (in right hemispheric convexity infarction) there is ownership loss, a kind of disconnect with 'self'. In case of phantom limb, it is the other way round. The ownership and so the symmetry, are retained in spite of physical absence of the limb. In the vegetative state, there is total loss of function of mind (operation I) while self (operation II) and life (operation III) are intact. Consciousness in this situation has been pushed with its back on the wall. In locked-in-state subjects, while other functions of consciousness are remaining intact here is absence of volition/will.

In the light of this ladder of cognition, the layers between the physical signaling in the brain and conscious behavior could be described. Neural code (signal) is to be on board to behave as information. Concurrence is of the architectural symmetries for developing a concord. In neuroscience, neural manifold has been described as "neural modes". Therefore, it can be said that neural code (signal) on board (by operation I) develops (by operation II) concord in (operation III) neural mode (manifold) to generate experience (Figure 8). Up to the level of generation of experience, consciousness actively supports all three operations. However, volition (behavior) requires a profound top-down activity where consciousness has to intervene for the accord; consciousness has to 'will' for the volition for expression of behavior to change the rhythm of the brain and spinal cord as a whole. This operation IV is under total command of consciousness.

EMERGING LARGER WORLDVIEW

The ladder of cognition thus described relates the discipline of cell biology systematically with the discipline of neuroscience, mathematics, logic, informatics and linguistics (Table 6).

The ladders, as said, are not straight individually and are not parallel to each other. Four operators are common to all, separating five rungs in each of the ladder (Figure 9).

The ladders are intertwined having interactive points. While all ladders have a common Point (Pointillism) at the top or at the center, the whole complex appears labyrinthine in a dynamical situation with vibration and rotation. More unfolding of the knowledge of their interaction is likely to throw knowledge on the nature of the operators and vice versa. From this discussion emerges a big picture, the design for a unified systems science for signal-organized, mind-organized, self-organized, life-organized and consciousness-organized systems, with the help of nature's currency as kinetic energy, potential energy, fields, manifolds and a ground, which is not inert but participating.

CONCLUDING REMARKS AND PERSPECTIVES

Wisdom, experience and knowledge are far more complex than information and signal. We have offered the possible informatics of how the physical signal transits to trans-physical information, sub-physical knowledge and experience and non-physical wisdom through four hierarchically nested specific operations, which are constituents of cell's cognitive organ. Probably in a non-reductive way the paper has cracked the "hard problem" of consciousness and dissolved the 'myth of mind'. The penetrative narrative raises more number of questions than it addresses to, and opens up multiple new doors for science. Language, "viewed as a device for sharing thoughts and experiences rather than as a vehicle for those mental contents themselves" [43] has an important role in addressing this kind of issue. The language of good administration (decision of the cell) and the language of good science are similar. We have followed a characteristic linguistic where agencies can be replaced by operations. This certainly empowers science with a framework of cognitive ladder in consistence with the ladders in linguistics, informatics and mathematics for starting multidisciplinary experimental work on the operational labyrinth of cellular cognition. The stated view has future in artificial intelligence, expert systems, bio-robotics

Table 6: Different ladders for designing a unified systems Science.

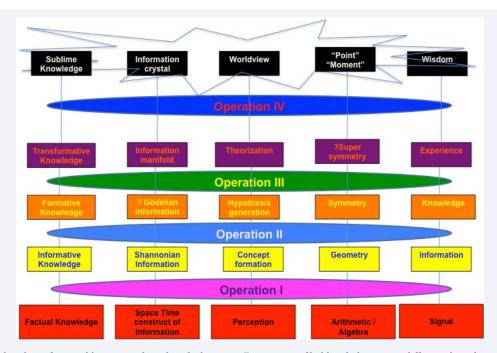| Ladder in Linguistics	Knowledge Ladder	Ladder in Informatics	Cognitive Ladder	Ladder in Mathematics	Ladder in Logic	Ladder of Systems science	Ladder of 'Currency' in nature
Wisdom	Sublime knowledge	'Crystal' Information	Worldview	Point Moment	Hermeneutic	Consciousness-organized systems	Participating active ground. Consciousness
Experience	Transformative knowledge	Information manifold	Theory	Symmetry manifold? Super-symmetry	Inferential logic	Life-organized systems	Manifolds. ? Dark energy
Knowledge	Formative knowledge	?Gödelian Information	Hypothesis	Symmetry	Formal logic	Self-organized systems	Fields. (e.g., classical or quantum fields)
Information	Informative knowledge	Shannonian Information	Concept	Geometry	Fuzzy logic	Mind-organized systems	Potential Energy. (e.g., Quantum potential)
Data/ Signal	Factual knowledge	Space-time construct of information	Percept	Arithmetic / Algebra	Boolean logic	Signal-organized systems	Energy

Figure 9 The broad outline of a possible systems-based unified science. Five strings of ladders belonging to different disciplines of science are seen to have merged at the top, on the sublime knowledge, 'information crystal', worldview, 'point'/'moment' and wisdom. Every string of ladder has five rungs and four operations in between. The strings in the figure, from the left to the right are the knowledge ladder, ladder in informatics, ladder of cognition, ladder in mathematics and the ladder in linguistics. The figure has been kept simple without showing any directionality of the process, or without showing any interaction between strings.

and even in artificial life. Now we can investigate how and when consciousness intervenes in case of conflict of autonomy between operations and how these operations are called upon when automated signaling system fails? When the governing mechanism can no longer sustain signaling network within a cell and the 'event horizon' slips into malfunction sink, how the cell in such situation becomes a victim of pathological processes and being unable to repair the fault embraces 'death horizon'? The propositions are verifiable easier in a cell-model than in the context of the brain, which might be considered an incredible co-operative cell-colony of hundred billion neurons and 2-10 times of that glial cell. Possible molecular correlate/correspondence/substrate of four operations remain to be established. Sergiu Pasca has made mini brain available on petri dish to study neuronal cells in group. We might end up with the 'laws of biology'. This emerging order is likely to have enduring influence on systems psychology [22], pathology and personalized medicine. The contents of the paper bear the potential to achieve the larger goal in science, to unfold the design of the organization for a unified systems science.

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