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Research Article

The Ontological Status of Western Science and Medicine: Ten-Year Follow-up with particular Reference to Ayurveda

Alex Hankey*

Department of Biology, MIT-WPU, India

***Corresponding Author:** Alex Hankey, Department of Biology, MIT-WPU, India.

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Abstract

Background: This invited article follows up a previous paper on the same topic. It builds on the insight that, in its system of Tridosha, Ayurveda introduces principal functions of open systems applying to all levels of organism function, cell, tissue, organ, organ system, and whole organism. The delicate function of Acetyl-CoA linking lipids, Kapha, and metabolism, Pitta, confirms this insight. The holistic nature of systems functions confirms Ayurveda's insight that organism function is holistic. Here, we update previous results by adding four further levels of reasoning from an epigenetic perspective.

Methods: The epigenetics build on fundamental insights into how interrelationships between epigenetic activation of loops of genes bring cells integrated, holistic, structures of regulation.

First, Stuart Kauffman's original work in the field; second, the 'Sandwich Model' of biology; third, self-organized criticality, and its optimization of response functions to external stimuli; and fourth, development of mutual coherence between related cells.

Results: These four additions to today's molecular picture of biology show respectively that:

- Integrated structures of epigenetic regulation define all cell types in all organisms;
- Such structures endow organisms with levels of adaptability required to live in real environments;
- Self-organized criticality optimizes response functions, maximizing competitiveness of the organism in its ecological niche, and helping it to thrive and survive;
- Mutual coherence between similar cells enables them to function as integrated units, i.e. holistically.

Discussion: These four developments all concern integration of functioning, progressively increasing levels of wholeness, at which cells, tissues, and organisms function. Organism functioning can now be seen to possess extraordinarily high levels of integration, making organism function holistic.

Keywords: Ayurveda; Ontology; Integrated Regulation; Coherence; Holistic Function

Introduction

The present situation in medicine, with most life-threatening illnesses in developed countries being non-communicable diseases (NCDs) [1], makes Ayurveda uniquely positioned to offer a fundamental contribution to the future of global health care [2]. Its unique approach to regulation of physiologic function in terms of the three fundamental systems functions [3], forms the basis of an equally unique approach to the etiological stages of the onset of disease; four stages before disease becomes overtly manifest, and then irreversibly damaging [4]. These fundamental insights, which can be roughly translated into terms familiar to modern biology [5], mean that Ayurveda's inclusion in all medical education in India [6] promises to radically improve national trends in disease outcomes [7], and might eventually make India a leader in world heath care. Ayurveda's underlying philosophy, particularly its holistic ontology [8], thus has wide significance. It can also be used to establish Ayurveda's approach to preventative medicine, as well as to therapy.

A previous article with a similar title, Ontology of Western Science and Medicine[8], started from the premise that Ayurveda's three doshas, Vata, Pitta, and Kapha constitute the three principal functions of open systems, Input/Output, Thruput, and Storage [3,9]. These apply to all levels of systems function: cells, tissues, organs, organ systems, and the whole organism. Another article [10] pointed out that the delicately poised function of Acetyl Coenzyme A, with its universal applicability to all bacteria and the higher kingdoms of life, seems to confirm these insights.

The systems functions Input/Output, Turnover, and Storage are well connected (Figure 1), integrating the functions of the three doshas with each other. Such functioning is necessarily holistic. Since the three doshas apply to all organisms on the tree of life, they have evolved richly as organisms evolved in complexity, from single cells, to those with differentiated layers of cells, to various tissues, organs and organ systems. As that happened, earlier modes of dosha function continued to apply to later organisms that inherited them. The three doshas can thus be seen to apply to all levels of organisms and their identifiable subsystems: cells, tissues, organs, organ systems, and whole organism. Even complex organelles with their own DNA and bounding membranes like mitochondria and chloroplasts possess them. At every level, the three systems functions apply, and can be identified as Doshas acting at that level. In the case of organ systems, Ayurveda names 15 'subdoshas', five for each dosha. Grouped in sets of three, one set for the nervous system, one for the cardiovascular system, two for the digestive system, and one for the skin and joints, the triplets form Doshas for organ systems [9].

Since the three doshas (Tridosha) function holistically, Ayurveda insights point to organism function being holistic. That is opposite to the 'Molecular Biology' model of life [11] taught as standard in schools and colleges today, which regards molecules rather than

Figure 1

system functions as fundamental, and is therefore reductive. The disastrous effects of this deficiency are acutely felt in both the field of medicine and its associated biotechnology of drug discovery [12].

Without any scientific indication of how organisms can heal themselves, modern medicine assumes that it alone has to do all the work, and then prescribes medications based on its deficient, reductive picture of organism function. Instead of resulting in cure, most chemical drugs produce unwanted side-effects [13,14], slowly weakening the patient's overall resistance to further pathogenesis, or directly causing pathology [15]. The ongoing epidemic of chronic diseases [16-19] can be entirely attributed to these deficiencies in modern medicine's understanding of organism physiology, but some recognise traditional systems of medicine such as Ayurveda as efficacious [20].

As an invited follow-up to the previous article [8], this paper starts from the above insights into Ayurveda's [2] holistic, Tridosha, picture of organism function, and uses four kinds of discovery, some original, from recently developed fields of modern biology to build on them. Each of the four yields a further level of reasoning described in the methods section below. They build progressively deeper understanding of how organisms are structured to function holistically, gaining additional advantages from each level of functional integration.

In contrast to Ayurveda [2], modern medicine fails to cure many, if not most, NCDs [1]. That is why they are considered incurable and called chronic diseases. The source of the dysfunctions involved in chronic disease is usually failure to maintain ideal regulation of specific systems [12]. Ayurveda's systems-based, approach to understanding the physiology and its regulation [3,5] provides a different perspective on how to counter regulatory failure [21]. Its ability to treat NCDs follows from its understanding of physiological regulation [2]. This article extends that wisdom in terms of overall holistic structure of biology. The difference between Ayurveda's ontological status and that of molecular biology[11] thus assumes a position of central importance in generating a new understanding of the whole field, in which organisms are seen to function in an integrated, holistic way.

While the holistic ontology of Ayurveda was originally understood in terms of its Tridosha systems functions, which are holistic in nature, the methods outlined in the next section aim to build up further insights into organisms' holistic functioning in four stages by considering recent scientific developments, two from epigenetics; and two from complexity biology. While these developments are well known to scientists in those fields, they are not well understood by scientists or students outside those fields. Their central importance to biology as a subject area does not seem to have been appreciated – to amplify this point, their theoretical implications for the structure of organisms do not seem to have been discussed, nor their philosophical implications for the nature of life, i.e. the nature of biology itself, the primary concern of this article.

It is therefore important to be able to understand the Methods utilized to obtain the results derived in the Results section. To this end, let us consider relevant aspects of the foundations of epigenetics and complexity biology.

First, Epigenetics: The first work of relevance to our use of it was by Stuart Kauffman [22-25].

Kauffman's computer models identified a simple rule by which a genome's various loops of genes must interact, for them to function with both stability and adaptability: each loop must switch on or switch off an average of exactly two other loops of genes [24,25]. If the average is less than two, the various loops keep switching on and off like flickering electric lights; if it is more than two, the system becomes stuck and unresponsive – it is over regulated. In the first case, stability is lost; in the second, adaptability is lacking [23].

Second, the new 'Sandwich Model of Biology' [33]: This model adds to the molecular biology model [11], depicted in Figure 2a, by building epigenetic regulation of enzyme processes on top of biochemical pathways, as shown in Figure 2b. Molecular biology, which provides the wellknown genetic explanation for a cell's biochemical reactions, is seen as an open sandwich: the nucleic acid bread, buttered, as it were, by the action of Ribosomes, which create the polypeptide chains used in enzyme proteins by translating messenger ribonucleic acid (mRNA) transcribed from the cell's deoxyribonucleic acid (DNA) [11] – Figure 2a.

The Sandwich Model of Biology
(Sees Cell processes as a Sandwich)
On the Top: Processes of Epigenetic Regulation
In the Middle: The Biochemical Pathways
On the Bottom: Gene-Based Molecular Biology

Figure 2

The Molecular Biology Model of Biology
(Sees Cell processes as an Open Sandwich)
On Top: The Biochemical Pathways of the Cell
Enzymes: Catalyze the Biochemical Reactions
Polypeptide Chains constitute Enzyme Proteins
mRNA directs Ribosomes to make Polypeptides DNA in Cell
Nucleus directs synthesis of mRNA

Figure 2a

The Sandwich Model of Biology
(Sees Cell processes as a Closed Sandwich)
On Top: Epigenetic Regulatory Processes
Optimized by Self-Organized Criticality
Giving Cells Adaptability & Competitiveness
In the Middle: The Cell's Biochemical Pathways
Catalyzed by Enzyme Proteins
(Polypeptide Chains made in Ribosomes)
Directed by mRNA synthesized from DNA

Figure 2b

A vitally important aspect of the Sandwich Model is the little-known phenomenon of hormesis. Hormesis [26,27] is the reaction of a cell to nanoscopic quantities of a toxin being added to its environment; for example, for experimental cultures of cells, the medium in which they are growing. When a toxin decreases the level of products of the reaction catalysed by the enzyme that it poisons, more of the enzyme is produced [26]. Sometimes the stimulation to produce more enzyme is so strong that product levels increase [27]. Clearly, hormesis is an aspect of epigenetics in the upper layer of the Sandwich model. For reasons given in the discussion, it is universal.

Third, Complexity Biology [28]: Experiments in the field of Fractal Physiology [29] have been shown to imply that all epigenetic regulation must satisfy 'self-organized criticality' [30] (SoC). SoC means that a critical instability, like those identified in the field of phase transitions and critical phenomena [31], is present at a key location in epigenetic processes of up and down regulation of gene expression. Such locations are known as 'loci of control' [32].

Methods

The four approaches named below result in major differences between the present picture of cell function falsely assumed to be true by conventional molecular biology [11] and presented in scientific and medical education, and that which the Results section shows to be the case.

First, Stuart Kauffman's findings about interactions of loops of genes [22-25], which, as we shall see, have deep implications for our philosophical understanding of life [33,34].

Second, the 'Sandwich Model of Biology' [35] incorporating hormesis [26,27]. The reactions on a cell's biochemical pathways no longer function independently of each other.

Third, Complexity Biology [28], and its field of Fractal Physiology [29], which via SoC [30] endow epigenetic regulatory processes with properties found in critical phenomena [31], see point 4.

Fourth, Mutual Critical Coherence: internal coherence in a system reduces independence of functioning between its various components.

Results

Kauffman's work [22-25] showed that loops of genes are switched on and off in a completely integrated way, involving signals across the entire transcriptome – those sections of genome that are transcribed. Involving the whole transcriptome means that all the possible switching patterns are achieved holistically.

Each kind of cell in an organism depends on its activated genes to provide specific abilities, thus defining the cell type [11]. The overall integration of On/Off switching of loops of genes means that all cell types in all organisms [22,25] arise from integrated structures of epigenetic regulation. Integrated structures of regulation are hallmarks of holistic functioning: the way that different cell types are epigenetically constructed, endows them with an holistic quality.

The Sandwich Model of cell function [35], with its lower half based in molecular biology, and its upper half in epigenetics (Figures 2a and 2b), makes an integrated structure of regulation available to control all up- and down-regulation of activated genes generating cell enzymes in point 1. Such integrated structures mean that a change stimulated in one part of the system induces changes in other, possibly large, parts of the system, even the whole system. Processes integrated in this way may well span the entire system. This integration therefore results in a style of functioning that should be called holistic.

It is worth comparing these two points 1 and 2: In point 1, the relationship is between different loops of genes; in point 2 the integration is between genes controlling enzymes catalysing adjacent or nearby reactions on the same biochemical pathway. The holistic property in points 1 and 2 is thus rather different, being achieved in different ways.

Self-organized criticality [30], derived from Fractal Physiology [29], means that the system is held at a critical instability [31]. Instabilities possess the property of high internal coherence [31], which extends over a region of space, organising the system in a completely new way. This spatial extension gives the unstable system the property of 'wholeness', making it holistic (Figure).

This internal coherence (from critical instability) opens further possibilities. Two nearby systems possessing the same critical coherence, can become mutually coherent. For similar cells, mutual coherence enables them to function as integrated units, i.e. even more holistically.

Discussion

The four kinds of result given above may be recapitulated and further explained as follows.

Kauffman's integrated structures of epigenetic regulation [22-25] mean that the genes in each cell are activated to function as a whole. The patterns of gene activation can be further refined by migration of genes around the genome [36] making the organism more efficient. The integrated wholeness of cells in one generation thus possesses a certain flexibility, which can be adapted over generations to the needs of an organism in a specific environment that may also change.

The Sandwich Model of Biology [35] is far richer than the introduction's simple description might lead one to suspect. Its property of hormesis [26,27] enables a cell's epigenome to adapt to all environmental changes including increases and decreases in temperature, pH and oxidation reduction potential. Without these abilities, a cell's metabolic and biochemical pathways would be constantly driven out of balance by excessive build-up or depletion of particular intermediaries. Instead of functioning acceptably, the cell's system would fail.

To put this another way: all cells must keep their biochemical pathways functioning in balance, to prevent increases or decreases in specific biochemicals causing wastages or inefficiencies in function. Cells and organisms that become inefficient will be less able to compete with other organisms in their environment. This observation leads to the conclusion that all organisms, whether single cells or multicellular, must maximize their efficiency of function. Then they will naturally become as successful as they can be, coming to the fore in their ecological niche.

Increased integration of function improves an organism's overall functional efficiency. The greater degree of stability of concentrations of biochemicals on its biochemical pathways, and increased adaptability to changes in its environment raises its ability to thrive and survive [35].

Points (1) and (2) together mean that: Several levels of epigenetic regulation may be required to adequately improve coordination of various regulatory processes, particularly when needed simultaneously. As discussed below, this increases the richness of the critical point instabilities involved in self-organised criticality.

Self-organized Criticality (SoC) [30] implies the presence of critical instabilities at key locations in the epigenetic up and down regulation of gene expression known as 'loci of control' [32]. A key property of any system at an instability are critical point fluctuations, which make one or more properties of the system fluctuate wildly[31]. Such fluctuations are randomized internal motions of the system, which, being unstable, has no state of stable equilibrium to return to. Critical point fluctuations are the Sine Qua Non of critical instability; in that sense, they constitute its signature [31].

Analysis of response functions involved in epigenetic adaptation [35] leads to identification of a new reason for the universal presence of self-organised criticality, and thus for the existence of complexity biology. Critical instability occurs when the graph describing a thermodynamic process has a point of inflection parallel to the axis of one variable [35]. Graphs of response functions plot the stimulus variable on the x-axis against the response variable on the y-axis, from 0% gene activation to 100% gene activation. A vertical point of inflection (Figure) then provides the most sensitive and most efficient response [35].

Maximizing sensitivity of response makes an organism maximally competitive, and maximizes its prevalence in its ecological niche. That will in turn maximize its ability to thrive and survive. This shows that self-organised criticality [30] will, over time, inevitably emerge as a universal property of organisms [35], as is found to be the case. It provides a promising explanation for the existence of fractal physiology [29], and thus of complexity biology [28].

When biochemical pathways branch, or have loops as in the citric acid cycle [37], or as noted by Nurse [38], then additional levels of epigenetic regulation control will be required. This will increase the 'order' [39] of the critical points involved in SoC, so that the upper half of the Sandwich in the Sandwich Model [35] will typically contain critical points of higher order [39] with correspondingly richer properties [40].

To summarise: SoC [30] optimizes sensitivity of gene expression, i.e. epigenetic regulation [35]. It therefore falls in the upper half of the Sandwich Model of Biology. It maximizes efficiency of an organism's function within its environment, consequently maximizing competitiveness and enabling it to thrive and survive [35]. SoC enables organisms to increase their prevalence within their ecological niche to a maximum value. For this reason, it is found universally in analysis of organisms' physiological responses – a proposal that seems new to the biology literature.

Second: An Instability has high values of internal coherence [31], which organises a regulatory system in a previously unseen fashion. Internal coherence endows the unstable system with 'wholeness', thus making the regulatory system holistic. All regulatory systems in the upper half of the Sandwich Model may be expected to possess this property [35].

Mutual coherence results from the internal coherence of regulatory systems under SoC. By coordinating different cells' responses, overall efficiency of groups of cells, i.e. of tissues, will improve. Most tissues in most organisms may be expected to possess this property.

This represents a significant outcome of the involvement of critical instabilities in regulation of organism function. It results from the high levels of internal critical point coherence[31] that accompany critical instabilities. Mutual coherence can then develop when critical coherence within related cells has similar properties.

Further comments: The importance of understanding complexity, and by implication, fractal physiology, was emphasized by Past President of the Royal Society, Sir Paul Nurse [41], who stated in a perspectives piece in 'Cell' that science "… has to get to grips with complexity". Interestingly, an earlier, 2008 article that he published in Nature [38], pointed out the ubiquitous existence of loops in control pathways. Many molecular biologists recognize that loops are universal in such pathways, but no one seems to know what purpose they serve. Might they assist in maintaining SoC in the regulatory functions concerned?

Each of the four results, 1 to 4, makes an organism function increasingly holistically; as shown above, by treating the additions one at a time. Importantly, all four are valid: a group of researchers involving Kauffman has demonstrated both the role of criticality in gene expression [42], and optimized function of information processing [43].

Conclusions

Integrated structures of regulation endow organisms with levels of adaptability required to live in real environments; all organisms function in a highly integrated and holistic manner, because such functioning optimizes regulation and efficiency, and maximizes prevalence.

Non-reductive 'wholeness' is a property at odds with modern biology's reductive picture of cells and organisms. The molecular biology-based picture[11] only sees localized properties of individual molecules as responsible for organism function. It does not and cannot explain the additional requirements for organism survival in real environments brought out above. It should now be regarded as outmoded and incomplete.

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