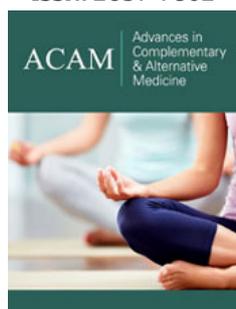


Theoretical Approaches of Entropic Systems Biology in The Integration of The Alternative Medicine and Conventional Medicine

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Abstract

It is known that the traditional medicines have been overtaken and led by the conventional medicine for decades partially because of the failure of the advanced biological theory. In fact, there might be two categories of the systems biologies, that is, the conventional systems biology which is based on the DNA-RNA-protein central dogma with the shorts of full thermodynamic mechanism especially the information, and the alternative systems biology or entropic systems biology which is absolutely based on the thermodynamic mechanism. The deep relation between the two categories of the systems biology could be considered as the scientific basis of the alternation and integration between the conventional medicine and complementary or alternative medicine. Previously, we promoted the concept of entropic systems biology in which biological structure, energy and information are simultaneously encoded in the biological processes. we also showed that the conventional medicine and traditional Chinese medicine might target different variables of the entropic system in clinical practises. In this article, we will describe the scientific basis of entropic systems biology as a promising platform, in which the conventional medicine and alternative medicine or complementary medicine might be theoretically integrated into an integrated medicine.

Keywords: Complementary or alternative medicine; Integrative medicine; Conventional medicine or biomedicine; Thermodynamic mechanism; Complex systems; Conventional systems biology; Alternative systems biology; Entropic systems biology; Theoretical platform for the integrated medicine

Introduction

Living organism works as a super system, in which the phenotypic emergence is usually completed together by the parts inside the body, sometimes triggered by the factors around the environment. After decade's molecular anatomy of the cell, a branch of biology called systems biology now provides biologists a platform to study networks of a group of function-related genes and/or proteins through computational and mathematical approaches. Meanwhile, the conventional medicine, also known as Western medicine or biomedicine, is continuously improved along the progresses of the systems biology. By following the concept of systems biology, the clinical practise of the conventional medicine is complemented or alternated by traditional medicines (TMs) originated from Europe, China, India and Africa. For this reason, TMs are referred to as complementary or alternative medicines (CAMs), together with the conventional medicine as a systemically integrated medicine [1].

Traditional medicines include traditional Chinese medicine (TCM), which is a medical science gradually formed and developed through long-term medical practice under the guidance of ancient philosophy. The concepts of Yin Yang and Qi might be originated from the symmetry and free energy, probably entropic forces generated from the entropy of symmetry breaking in the universe. The dynamic rearrangement of Five Phases, such as Fire (火), Water (水), Wood (木), Metal or Gold (金), and Earth or Soil (土) driven by Qi generates a wide array of phenomena in the nature and human body. TCM is born with the characteristic features of

systems and syndrome-oriented diagnosis and treatment. Although the diagnosis and treatment of TCM are lacking solid current scientific evidence and biological mechanism, it is indeed a systems science far from “fraught with pseudoscience” [2]. In addition, the diagnosis and treatment of the conventional medicine are also not entirely based on the scientific evidence with known biological mechanism. For instance, there are still not enough scientific evidence and mechanism in many aspects of the conventional medicine such as psychotropic medication. For this reason, many hospitals including Mayo Clinic initiated integrative medicine care decades ago to help patients through the approaches of meditation, massage therapy, acupuncture, dietary supplements and more.

As partially open thermodynamic systems, living organisms including human body are essentially the entropic systems [2]. Based on this principle, the numerous phenomena of the living organisms are interpreted by the fundamental laws of thermodynamics. In 1944, a pioneer in life science Erwin Schrödinger promoted a hypothesis that living organisms feed on “negative entropy” [3]. Therefore, there are parallelly two categories of biology: conventional biology and alternative biology in the life science for decades. Indeed, the conventional biology is essentially based on the biological central dogma focusing the cell proliferation, cell differentiation, cell survival and/or cell death etc. through the approaches of studying DNA replication, RNA transcription, protein translation and so on. However, the alternative biology is mainly based on the thermodynamic mechanism to explore the systemic processes such as the information processing in neural networks and organism aging in lifespan, as well as essential roles in gene expression, molecular folding and various of biological processes [4-28]. In short, the thermodynamic mechanism of the biological processes is more tightly related to the body's information processing which is highly involved in the alternative therapeutical approaches such as meditation, massage therapy and acupuncture. It might be the reason why the conventional systems biology is necessary to be complemented or alternated by the alternative systems biology. In parallel, the conventional medicine is required to be supplemented and integrated with alternative medicine. Previously, we promoted the concept of entropic systems biology in which biological structure, energy and information are simultaneously encoded in the biological processes. we also showed that the conventional medicine and traditional Chinese medicine might target different variables of the entropic system in clinical practises [2]. In this article, we will describe the possibility of entropic systems biology as a theoretical platform to promote the integration of the complementary or alternative medicine and conventional medicine.

Characteristic Features of Complex Systems

In dictionary, system means a group of related parts that move or work together, e.g., a body of a person, in which matter, energy and information are three of essential elements [29]. There are various types of systems including closed system, open or partially open system, dissipative system [30], autopoietic system [31], energy system and information system [32,33]. To

study a complex system, the series of interdisciplinary approaches have been created in past decades, such as systems and network theory [34,35], cybernetics [36], self-organization [37], chaos and fractals [38,39], information geometry [40], complexity theory and systems theory [41,42]. In a super system or systems, lower level of systems functions as a subsystem to be a set of components of a larger system, in which multiscale of subsystems hierarchically interact one other in multiple dimensions and multiple ways by following systemic rules. The linear and nonlinear complex systems mathematically and physically possess the fundamental differences of the characteristic features, especially the multiscale emergences of the strong phenotypes at much higher randomness. In natural systems, the movement of matter is driven by energy under the guidance of information. It is known that living organism belongs to partially open nonlinear thermodynamic system far from equilibrium. According to this point of view, the system of organism must be a partially open thermodynamic system including the parts of matter (biomolecules), energy and information with the characteristic features of chaos and fractals, self-organization and complexities of network systems. Theoretically, all the types of systems especially thermodynamic systems are the putative entropic systems bearing the specific variables of the parts moving or working together via entropic forces, in which matter, energy and information dynamically convert one to another by following certain mathematical equations (Figure 1) [2,43,44].

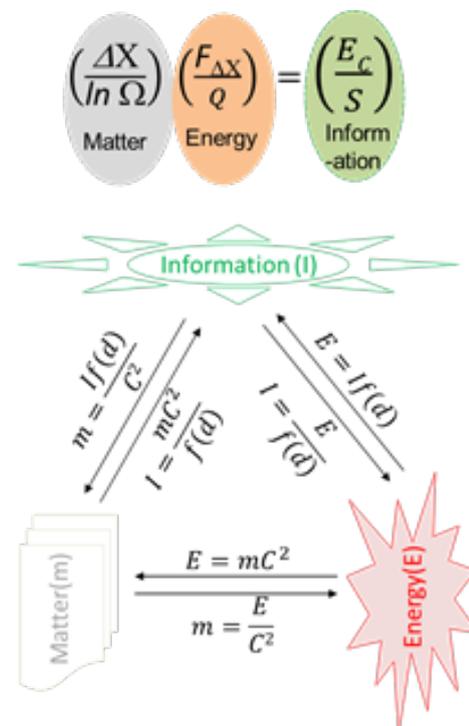


Figure 1: The mathematical equations involved in the conversions of matter, energy, and information in the thermodynamic entropic system. In the figure, the variables are represented as: microstate (Ω), macrostate (ΔX), heat energy (Q), entropic force ($F_{\Delta X}$), entropy (S), matter (m), energy (E), information (I), light speed (C), function (f) and Maxwell's Demon Constant (d).

Conventional Systems Biology and Alternative Systems Biology

The modern biology and/or systems biology could be divided into two categories: conventional biology and/or systems biology which highly focuses on DNA-RNA-protein biological central dogma, and alternative biology and/or systems biology which mainly focuses on thermodynamic mechanism. While conventional systems biology is the main melody of current biology, alternative systems biology is not the gene-centrism but more physically thermodynamic and mathematically quantitative. It is likely that conventional systems biology might pay more attention on the life phenomena of the biological processes, but alternative systems biology could be more related to the essences of life.

In the post-genomic era, the bioinformatics of computational and mathematical approaches allows larger amounts of data to be analyzed and consequently put back together as an artificial system called systems biology [45]. It is no doubt that systems biology will bring a promise to biologists and conventional medical doctors to understand a body of a cell as a partially open system, in which subsystems hierarchically interact each other at multiscale to accomplish DNA replication, RNA transcription, protein translation, cell proliferation and differentiation, cell survival and death. Notably, systems biology mainly relies on the gene-centrism in which individual cell or organism are a network complex of signalosome or Reactome constructed by pieces of the products of genes. Frankly speaking, this type of conventional systems biology is far from the super system in which the gene-products work together driven by the systemic force and guided by the systemic information. This pitfall of the conventional systems biology might be a sole reason why low reproducibility in experimental researches and high failure rate in clinical translational biomedicine.

Therefore, it is reasonable that the conventional systems biology needs to be complemented and integrated with alternative or complementary systems biology which bears thermodynamic mechanism. It is well known that entropy plays a central role in all of the thermodynamic processes through the entropic forces, which are the emergent forces resulting from the entire system. As mentioned above, there is an ample amount of evidences that both entropy and entropic force are essential for all the biological processes including gene expression, protein folding and assembly, molecular recognition, and conscious processing [21-26]. Following this rationale, we previously promoted the concept of aquamoleculomics since from a single aquamoleculosome to a single cell, even an individual body, all of which belong to the entropic systems consisting of microstate (Ω), macrostate (ΔX), heat energy (Q), entropic force ($F\Delta X$) and entropy (S) [46]. To be integrated with the alternative systems biology, the concepts and biological data in the conventional systems biology have to be converted into that in entropic system. In the entropic system, there are no nucleotides and amino acids, DNAs and proteins, even omics and signalosomes, just microstate, macrostate, entropy and so on. The law of entropic

system is based on a mathematic equation integrated from the entropic equations of thermodynamics and statistical mechanics, in which the thermodynamics between the biological structure, energy and information could be simultaneously quantitated [47]. Distinguished from the conventional systems biology of the gene-centrism, the alternative systems biology are fundamentally based on thermodynamic mechanism, in which the gene expression, the assembly and disassembly of gene-products and cell cycle progression are driven by the entropic force and guided by entropic information. Apparently, the main disadvantage of the conventional systems biology is the formation of the signalosome network without specific working force and information.

Theoretical Modernization of The Complementary or Alternative Medicine

Traditional medicines include traditional European medicine, traditional Chinese medicine and other Asian or African traditional medicines. In many Asian or African countries, traditional medicines still provide the primary health care to more than 80% of the population. In western developed countries, traditional medicines such as acupuncture, herbs, tai chi and yoga, message and meditation etc. are currently used as the complementary or alternative medicines.

As a complementary or alternative medicine, traditional medicines especially in China have been suffered to be modernized for decades so that to satisfy the conventional medicine and to increase the acceptance in western countries. Because of philosophical style, TCM was created with the concept of systems bearing the characteristic features of thermodynamic pattern such as matter structure (形), energy force (气) and informational spirit (神) of the human body [2]. Therefore, it is very difficult to harmonize the format of TCM into conventional medicine theoretically and experimentally even via the approaches of the current systems biology. In previous article, we promoted entropic systems biology which might be an alternative approach to theoretically scientize TCM in future [2]. In this novel theoretical model, "five phases" of Wuxing could be specifically designed to the five variables of entropic system, in which water was ordered to be microstate, earth was ordered to be macrostate, fire was ordered to be energy, metal was ordered to be entropic force, and tree was ordered to be entropy respectively [2]. In the entropic system, the macrostates of meridians and acupuncture points could be dynamically rearranged along the temporo-spatial related entropy and entropic forces. Indeed, as a complementary or alternative medicine, the theoretic system of TCM is closer to the alternative systems biology. After the modernization through this approach, TCM should become an alternative medicine which might be compatible to the integrated medicine with the solid scientific basis (Figure 2). In short, it is difficulty, but might be unnecessary to modernize TCM with the approaches of the conventional systems biology in which the different variables are focused on.

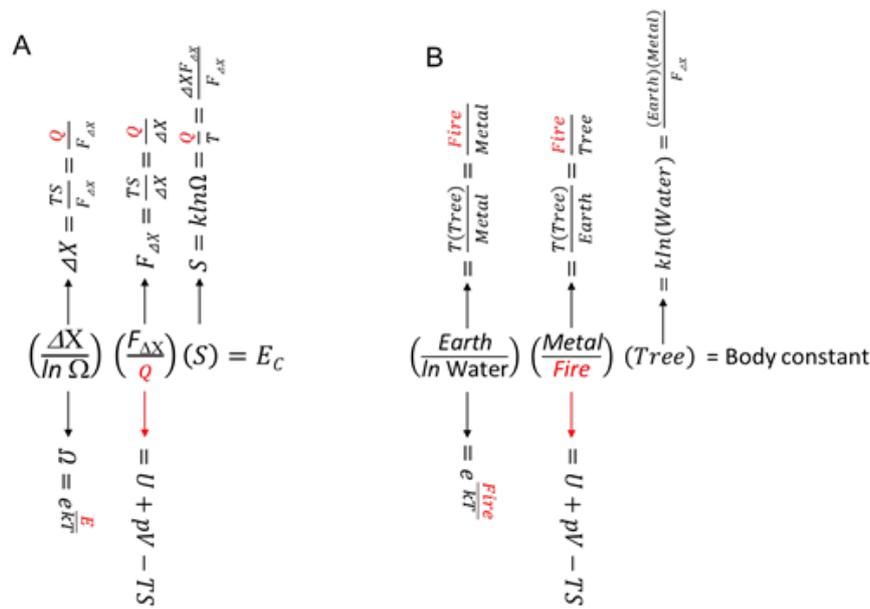


Figure 2: The mathematical equations involved in the conversions of matter, energy, information and entropic variables in the thermodynamic entropic system and Wuxing of traditional Chinese medicine. In the figure, the variables are represented as: microstate (Ω), macrostate (ΔX), heat energy (Q), temperature (T), entropic force ($F\Delta X$) and entropy (S), Boltzmann constant (k), matter (m), energy (E), internal energy (U), pressure (p), volume (V), information (I).

Entropic Systems Biology: A Theoretical Platform of The Integrated Medicine

As a super thermodynamic system, human body maintains homeostasis through a thermodynamic mechanism coordinating with the environment via the communications of matter, energy and information. In the conventional systems biology or medicine, human body consists of eleven subsystems which are nervous, cardiovascular, endocrine, lymphatic, respiratory, digestive, urinary, reproductive, skeletal, muscular and integumentary systems respectively. All these subsystems are well defined through the approaches of cell biology, immune biology and molecular biology, but all of which are based on the specific biological molecules such as DNAs/RNAs, proteins and signalosomes. To fully understand the mechanisms of biological processes, the conventional systems biology must be complemented with alternative systems biology through the approaches of thermodynamic mechanism, especially to interpret how DNAs/RNAs, proteins and signalosomes create human consciousness and minds.

In the entropic systems biology, the subsystems interact each other to form a unified larger system of organism completely obeying to a set of laws in thermodynamic systems. In the integrated systems biology, there are no more specific biological molecules such as DNAs/RNAs, proteins and signalosomes, just the different entropic variables such as microstate (Ω), macrostate (ΔX), heat energy (Q), entropic force ($F\Delta X$) and entropy (S). In TCM, the concepts of the body and disease including diagnosis and treatment are thought to be entropic manners. For example, there

are yet no defined scientific evidences of biological structures for qi, meridians, and acupuncture points. Fortunately, the philosophical contexts of Yin Yang and five phases in TCM exactly fit the concepts of the positive and opposite symmetry, and five variables of entropic system respectively [2]. After modernized with entropic systems biology or the alternative systems biology, TCM could be completely integrated with the conventional systems biology. The biological properties of Qi, meridians, and acupuncture points could also be scientifically interpreted according to the integrated entropic systems biology.

It is believed that self-organization is a critical process for the creation, evolution and multiplication of life. Up to date, there is still not an accurate model theoretically interpret the biological mechanism of the self-organization in living system. The entropic system model might be a qualified candidate to carry out the task to describe the processes and mechanisms of the self-organizations. In a dissipative entropic system, the rearrangement of macrostates could be hypothetically triggered by self-organization triggering factor (SOTF) when the system carrying the self-organized criticality (SOC) state [47,48]. Biochemical oscillation and physical convection are believed to be essential processes in living organisms. Thus, the dissipative structures could be generated in Rayleigh-Bénard convection and B-Z chemical reaction oscillation, which probably share the common mechanism in the thermodynamic equilibrium processes of biological processes [2]. It also could be the scientific mechanism of TCM's diagnosis and treatment via the two major syndrome differentiations of the pulse patterns (thermodynamic convection) and the tongue coatings (chemical reaction oscillation).

According to Schrödinger’s theory of “negative entropy”, we might also hypothesize that there are two thermodynamic entropic systems, positive entropic system and negentropic system. If true, the two entropic systems might coordinatively drive the

biological processes of molecular synthesis and hydrolysis even cell proliferation and differentiation, just likely playing tai chi inside cell and/or in human body through the biochemical oscillation and physical convention (Figure 3).

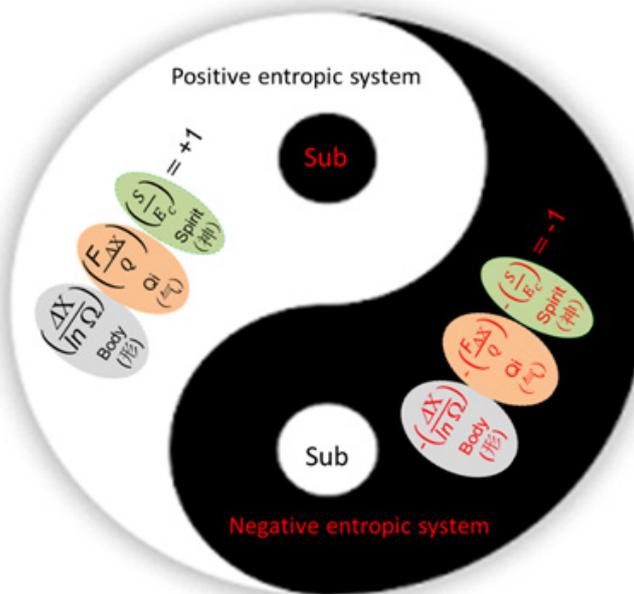


Figure 3: The schematic depiction for the thermodynamical integrated model of the positive and negative entropic systems in human body.

In future, there might be only one integrated biology or medicine eventually. In this unified system, all biological and psychological phenomena will be properly interpreted, and all diseases will be

precisely diagnosed and treated based on the mathematically, physically and biologically matured entropic systems biology or entropic systems medicine (Figure 4).

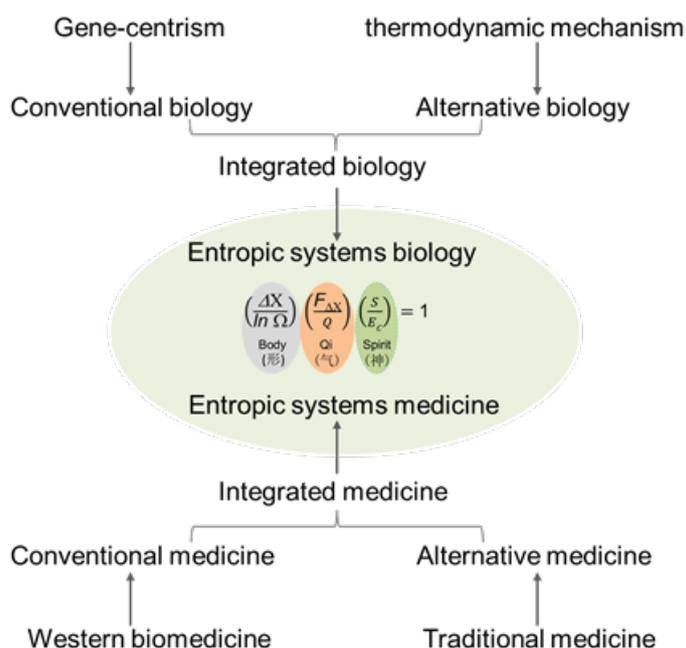


Figure 4: A theoretical platform of entropic systems biology or medicine for the integration of conventional biology or medicine and systems biology or medicine.

Discussion

The current systems biology or conventional systems biology might be short of full thermodynamic mechanism which is believed to be the essence of the life. Therefore, the conventional systems biology is highly necessary to be complemented with the alternative systems biology or entropic systems biology, which is absolutely based on the thermodynamic mechanism. In addition, the theoretical modernization of traditional medicines might be the key step for the good complementariness, alternation and integration. It might be a long way to convince the conventional biologists and/or medical doctors that the scientific basis of the alternative systems biology probably includes the symmetry, thermodynamic and complex systems. Nonetheless, science only depends on the human being, but nature goes its own way without lie.

In summary, to promote the integration of the complementary or alternative medicine with the conventional medicine, it is important for us to understand why they could alternate and to know how they could complement each other, even they could be integrated into a unified medicine. Notably, the modern systems biology could be divided into two categories: conventional systems biology of gene-centrism and alternative systems biology or alternative systems biology of thermodynamic mechanism. Predictably, the two categories could be mathematically, physically and biologically united together as the integrated systems biology in future. Indeed, the successful theoretical integration can help the integration of the modernized traditional medicines with the conventional medicine in clinical practises. It is believable that the entropic systems biology or medicine could provide us a scientific platform to realize the ideal. Presently, the uncountable impasses in front are how to define the variables of entropic system in cells and organs, even our body so that the emergent phenomena could be algorithmically measurable at multiscale complexities in both TMs and the conventional medicine. There might be a possibility, but extremely difficult, to establish entropic systems biology with the concept of "aquamoleculomics" since both the current conventional and alternative biology ignore H₂O molecules which are supposed as mother of life [46]. Moreover, it could be "aquamoleculosome", but not cell, might be the essential unit of the structure, energy and information in the living organisms. To modernize TMs, the advanced information technology especially in silico approaches such as cloud computing will be a candidate path to the mission. Once it came to true, all mysteries of life including conscious mind would be finally unveiled. If so, biologists, mathematicians and physicists, even intelligent robots, all of them could also become competent medical doctors in the entropic systems medicine.

It is true that the alternative medicine or traditional medicine has been overtaken and led by the conventional medicine for several decades. It is also believed that the failure of the theoretical theory is one of the reasons why it happened. Thus, the development of the current theory in the alternative medicine is obviously an emergent requirement to advance the integration with the conventional

medicine. In 1928, the great British scientist Arthur Eddington wrote in *The Nature of the Physical World*: "The law that entropy always increases holds, I think, the supreme position among the laws of Nature". In the biological thermodynamic mechanism, a given macrostate contains corresponded groups of compatible microstates which are dynamically regulated by free energy to create temporo-spatial entropic information guiding the behaviors of the system. Therefore, the integrated entropic systems medicine could be placed at the supreme position among the different types or levels of medicines in future. Currently, the concept of the alternative systems biology or entropic systems biology is just at the beginning for the modernization of TMs and the initiations of the integration between the conventional medicine and alternative medicine. There is no doubt that it could be a long march to reach the destination through the development of the experimental and clinical approaches in the novel medical care system.

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