

# **Entropy Change in Biological Thermodynamics**

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**Abstract:** Based on the new research of possible entropy decrease in isolated system under existence of internal interactions, the biological systems possess many internal interactions, in which entropy decrease is possible. Further, we propose the universal formula on entropy change in any systems for outside and inside. Systems biology and evolution are discussed. Life always changes from every individual to total system for various levels and different times. This not only input energy, and more is determined by tissues, structures and interactions inside system. Inside and outside combination determines the growth and evolution of life system. From this health is researched. It is not possible that self-assembly, self-organization, self-production, self-fabrication, self-maintaining, etc., all are always entropy increase. The biological membrane is already a natural existent Maxwell demon. Thermodynamics as science must be developed, from this will accelerate the next great advance.

Keywords: Biology, Entropy, System, Internal Interaction, Evolution.

## **1. INTRODUCTION**

Thermodynamics in biology (biothermodynamics) is an important problem. Edsall and Gutfreund (1983) discussed generally biothermodynamics. It corresponds to the metabolism of living matter (Kane, et al. 1978) and a spontaneous process (Hames, et al. 2000). Hill (1977) discussed free energy transduction in biology. Westerhoff and van Dam (1987) studied thermodynamics and control of biological free energy transduction. Kennedy (2001) researched biothermodynamics for sustainability of action in ecosystems. Von Stockar (2010) reviewed biothermodynamics of live cells as a tool for biotechnology and biochemical engineering.

Prigogine proposed the theory of dissipative structure, in which entropy can decrease for an open system, and derived a well known formula:

$$dS = d_i S + d_e S , \qquad (1)$$

So far the challenge for life science is that for foreseeable future it will still have an incomplete knowledge of all of the components and interactions that make up biological systems (NRC 2009). In this paper we research entropy change in biological systems, in which entropy decrease is possible due to complex internal structures and interactions.

## 2. NEW RESEARCH ON BIOLOGICAL THERMODYNAMICS AND SYSTEMS BIOLOGY

It is known that thermodynamics is based on statistics. But, in the statistics a basic principle is statistical independence: It shows that various interactions among these subsystems should not be considered (Landau, et al. 1980). If various internal complex mechanism and interactions cannot be neglected, a state with smaller entropy (for example, self-organized structure) will be able to appear under some conditions. In this case, the statistics and the second law of thermodynamics (entropy increase always in isolated system) should be different (Chang, 1997, 2005, 2012, 2013a).

We proposed that when various internal complex interactions exist, entropy decrease in an isolated system is possible (Chang 1997, 2005), which includes physics (Chang 2012, 2013b, 2015), chemistry (Chang 2013c), astronomy (Chang 2013d) and social sciences (Chang 2013e), etc. In biology the neuroscience, the permeable membrane, the molecular motor, etc., are all some internal interactions, so entropy decrease is possible in some isolated biological systems (Chang 2013a). Further, we proposed a universal formula for any isolated system (Chang 2005):

$$dS = dS^a + dS^i. (2)$$

Here  $dS^a$  is an additive part of entropy and is always positive, and  $dS^i$  is an interacting part of entropy and can be positive or negative. It is symmetry with Eq. (1). From this we derived a complete symmetrical structure on change of entropy:

$$Entropy \rightarrow \begin{cases} increase.\\ dS = d_i S + d_e S.\\ dS = dS^a + dS^i. \end{cases}$$
(3)

Entropy decrease may be the dissipative structure for an open system, or be the internal interactions for an isolated system (Chang 2015).

Moreover, some new statistics are already researched, for example, nonextensive statistics, generalized statistics, and anomalous statistical dynamics, fractional statistical equations, etc. From these cases the second law of thermodynamics should be developed.

The basic principles of biology include that cell is the smallest independent unit of life; cells can be organized into complex and multicellular organisms; all organisms function within interdependent communities and so on. The biosphere has many levels, and various complex interactions exist in a single level and among different levels. The biological complexity is across various levels, from cell-to-cell communication related with behavior to the impact of genetic regulatory pathways on the health of organisms.

In biology various internal interactions can be found everywhere. Photosynthesis use energy from the sun to make complex carbon-containing molecules like sugars and starches. The genetic variation, cells differentiation and spontaneous mutations of other biological components all are these typical internal interactions. Further, new kinds of gene regulation continue to be discovered, including epigenetic mechanisms, for which change gene expression without changing the underlying gene sequence (NRC 2009). Moreover, restoration of damaged ecosystems, and minimize harmful impacts of human activities determines mainly some internal interactions in the bigger ecosystems.

Systems biology is origin of living functions produced from interactions among their various components. It explores the region between individual components and the system, and may combine molecular biology and system, and may be various systems of different levels (Westerhoff et al. 2004; Alberghina et al. 2005; O'Malley et al. 2005).

Systems biology seeks a deep quantitative understanding of complex biological processes through dynamic interactions of components that may include multiple molecular, cellular, organismal, population, community, and ecosystem functions. It has expanded to molecular components involved in intrinsic cellular processes including gene expression, metabolism, structure and force generation, etc. It attempts to establish predictive models at all levels of biological organization, from the molecular, through the organism, population, ecosystem, and finally, the global scales (NRC 2009).

We propose the universal formula on entropy change in any systems for outside and inside:

$$Systems \rightarrow \begin{cases} outside : dS = d_i S + d_e S.\\ inside : dS = dS^a + dS^i. \end{cases}$$
(4)

Systems biology defines difference between a living organism and any nonliving object is that an organism is a system of material components that are organized in such a way that the system can autonomously and continuously fabricate itself, meaning it can live longer than the lifetimes of all its individual components. It is essentially relational and views everything that happens inside a living cell in the context of a functional organization that makes self-fabrication possible. In systems biology there have many rich internal interactions, and entropy decrease should be possible. For much biological systems and heath, environment and various ecosystems there have all both outside and inside. Cellular systems can be represented in "wiring diagrams", in which the components are proteins, nucleic acids and other biologically active molecules, while the wires are interactions among those components (NRC 2009).

Networks of proteins interact at a biochemical level to form complex metabolic machines that produce distinct cellular products. Circuits of nerve cells are the most complex networks that act in a

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coordinated fashion to produce learning, memory, movement and cognition, etc. Woese and Fox (1977) said: "The time has come for biology to enter the nonlinear world". General nonlinearity obeys not an addable of entropy increase law. Entropy decrease in isolated system often is related with nonlinearity (Chang, 1997). Biological systems are very complex nonlinear dynamical systems. Interactions among molecular components derive cell and various tissues as basis of life.

Systems biology is one on function and mechanism. It explains the emergence of systemic functional properties of the living cell as a result of the interactions of its components (Hofmeyr 2007), whose important theorem is related with systems dynamics and cell functions (Wolkenhauer et al. 2005). Different components in cell interact and produce certain structures and corresponding functions. Various cells interact to develop and maintain more structures and tissues with functions. Further, usual proteins interact with one another, often forming large edifices that act as complex molecular machines.

In fact in system theory internal interactions must exist inside any systems. A bigger system is isolated, but in which some smaller subsystem may be open. It is also a global viewpoint. In cybernetics the feedback is namely typical internal interaction.

## 3. BIOLOGICAL EVOLUTION AND ENTROPY DECREASE

Evolutionary biology studies the evolutionary processes that produced the diversity of life on Earth, starting from a single common ancestor. These processes include natural selection, common descent, and speciation.

So far the general evolution theory includes mainly: 1. Darwinian evolutionism by natural selection, in which environment determines evolution. It is often an isolated system, for example, Galapagos Islands. 2. Kropotkin's theory of mutual aid as a factor of evolution. 3. Based on the self-organization theory and study of complexity, Lovelock and Margulis (1974) proposed the Gaia hypothesis, which describes the biosphere of total earth as a control system, in which the homeostasis of self-organization, self-control, self-production maintain the world we live in (Sagan et al. 1987). And Margulis (1976) proposed again the symbiosis and endosymbiosis theory in evolution (Margulis et al. 1985, 1991). Earth is a single self-adjust system, and is determined together by environment and life. Its main equation is:

$$CH_4 + 2O_2 \Leftrightarrow CO_2 + 2H_2O.$$
 (5)

Theory of mutual aid, Gaia hypothesis, and the symbiosis and endosymbiosis theory in evolution all must have interactions inside systems. They are the nonlinear whole ecology and evolutionism, in which environment and life transform each other, and determine evolution and derive living complexity.

The evolution lacks to choose some structures with maximum entropy (Schrödinger, 1944), or maximum free energy (Nicolis & Prigogine, 1977), or maximum efficiency of thermodynamics (Westerhoff & van Dam, 1987). The physical and chemical systems at far-equilibrium tend probably to metastable state, which may form the isolated system with better order and power of self-assembly (SA) (Back et al. 1997; Frauenfelder et al. 2001).

Dobzhansky (1973) proposed a well known viewpoint: "Nothing in biology makes sense except in the light of evolution". Hofmeyr (2007) think the meaning of organism is only associated each other.

Rashevsky (1954) considered that organism may be only explained by relations. It contacts with the relational theory of biology. Rosen (1958, 1959, 1962, 1971, 1991) proposed relational biology, self-reproducing automaton, and the replicative metabolism-repair or (M,R) systems, in which theory of organisms has within itself an ineluctable ontological component. It is a science of fabrication as essential part, in which organisms are themselves fabricators; they build new things, they make new things, they deploy new things (Rosen, 1958a,b, 1959b, 1972, 1991; Letelier *et al.* 2006).

Maturana and Varela (1980) proposed the autopoiesis theory. Letelier, et al., (2003, 2006) contacted (M,R)-systems, the autopoietic system and metabolized network, and analyzed terms of (M,R) systems for organization invariance and metabolic closure.

Von Neumann (1966) proposed the self-reproducing automaton based on the general and logical theory of automata. Hofmeyr (2007) discussed the metabolism-construction-assembly system, which is the system self-fabricating. The purpose of an organism is to fabricate itself, i.e., self-fabrication.

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In biology origins of order are spontaneously due to self-assembly (SA) and self- organization (SO) (Kauffman 1993; Hofmeyr 2007). SA and SO are universal phenomena. SO is base of any organizations, and may form self-production (SP) and self-maintaining (SM), and must be a nontrivial form of self-maintaining (NTSM), whose structure is a core of metabolism. SA, SO and SM must possess both conditions on inside and outside. The base of SM is autocatalysis, which products bigger self-reaction and self-maintain network (Kauffman 1993; Steel 2000). This is necessarily internal interaction. Hofmeyr (2007) proposed the self-fabricating metabolism-construction-assembly system, i.e., (M,C,A) organisation of living cells, and the isolated self-assembly constructs finally the self-replication process.

Organism is a machine with self-production, whose existence passes through circulated whole network maintained. Complex components determine total system. System can maintain due to more self-organization than exterior circumstance, so system is self-sustaining, and is an autopoietic system (AS). Membrane is key factor of maintaining biological energy of systems (Pereto 2005).

Self-sustain products circulated network (Moreto et al. 2005). The evolutionary self-sustain is a precondition for existence of evolutionary system. Szathmary, et al., (1997) proposed that life depends on replicators that can exist in an unlimited heredity, which is internal interaction. Ruiz-Mirazo, et al., (2004) applied the hereditary autonomous systems (HAS) in the synthesis of life, which is also internal interaction.

Hordijk and Steel (2004) detected autocatalyctic, self-sustaining sets in chemical reaction systems. For evolution the adjustability of life is a process through different generations produced spontaneously, for example, the autocatalysis cycle (Ganti 2003). Cycle proves an explained method for growth and reproduction. Much biological systems possess cycles, which include multifarious biochemical metabolized cycles, cellular cycles, propagated cycles and a big cycle of whole ecosphere, etc (Smil 1997). A key is cycles in life systems, which and internal interactions form tissues. Various cycles are not related to surroundings, which all are internal interactions in isolated systems.

In biological systems various evolutions are not only open and absorbed energy, and must be the cooperative self-interactions each other. Because of the conversation of total energy in isolated system, all in the systems must be evolution and absorbed energy, so it forms the Darwin evolutionism with competition. But, this should be more universal evolutionism with competition and cooperation. In particular, the cooperation is more important in an ecosystem and in the same population, for example, the cooperation is indispensable in human evolution.

Hofmeyr (2007) pointed out: "The essence of life must lie somewhere between molecule and autonomously living, unicellular organism." Every organism is all a system that may be self-production, and is composed of various substances, and is independent. Modern biology explains life from an evolutionary viewpoint, with reproduction (of cells) and replication (of DNA).

Organisms possess self-regulation and self-steering, and achieve self-formation and self-generation. Bak, et al., (1987, 1993, 1995) proposed the evolutionary dynamics model with self-organized criticality, which only passes through self internal dynamics to form a critical state. New characters may obtain new forms of interactions.

In a word, internal interactions may form tissues, and produce functions, and obtain further self-formation and self-generation, etc.

## 4. BIOLOGICAL GROWTH AND CHANGE

Every biological body is an isolated system at least certain time. If entropy always increases, it will be unable to growth and development.

The first law of thermodynamics points out that the internal energy U of an isolated system is constant, and U=K(kinetic energy)+V(potential energy). It is known that entropy is a measure of the molecular disorder in a system. Usual molecular kinetic energy increases, then disorder and entropy increase. But, when internal interaction in an isolated system exists, i.e., the kinetic energy is transformed to the potential energy, then the order increases, the kinetic energy and entropy decrease (Chang 2014a).

Based on the entropy viewpoint, the metabolism is that food passes through internal organization and interaction to transform into order and entropy decrease.

Life always changes from every individual to total system for various levels and different times. Biological growth and evolution are their common basic character. It includes dormancy, which may pass through adjustment and decrease to smaller entropy in isolated system. These not only induct energy and negative entropy, and more determine tissues, structures and interactions inside biological systems. Inside and outside combination determines the evolution of life system. It holds for various levels and times from life to death (Fig.1). But, the main difference of life for before and after moments consists in physiological tissues and internal interactions.



Fig1. Relation of Life and Growth

Growth and change of life, one hand, must input food and energy with certain heat quantity, which is outside input dietetics. On the other hand, they determine internal transition power, for example, enzyme and passage, etc. It is similar with the efficiency of heat machine. Improved efficiency is related with medicine, in particular, healing treatment. Caducity is namely income falling short of expenditure.

Edelman (1987) proposed Neural Darwinism, in which the selection is also Maxwell demon. In conscious process brain self acts each other (Edelman 1989, 2006), which is also internal interaction.

Simple mathematical models may show very complicated dynamics (May 1976; Abraham et al. 1972). Schaffner (1993) researched discovery and explanation in biology and medicine, in which general reduction-replace model constructs relations of theories and models between different levels.

# 5. NEW BIOLOGY, HEALTH AND THERAPEUTICS

New biology studies the laws of physics play out in the crowded and decidedly non-equilibrium environment of the cell, and derives new equations to describe the complex network interactions that characterize living systems (NRC 2007).

Modern biology discovers many diseases result typically from small defects in many genes, rather than catastrophic defects in a few genes (Altshuler et al. 2008). The viral infection is outside causation of disease, but later system entered virus unstill becomes an isolated one. Therefore, it is crucial that understanding how genes work together and interactions in regulatory networks.

We proposed an entropy index of health on human body: dS/dt should be least, even at period of time, man (woman) can regulate breath, body and ideology, and reach to dS/dt<0. We assume that entropy decrease as an index of health and therapeutics in biophysics may be applied to investigate cure of disease. It is often propitious to prolong of life for many animals and human practices, and Qigong and various practices are often related to these order states with entropy decrease (Chang 2013a). I think life should lie in a combination between motion and rest, and in a balance between chaos and order.

Everyone health is determined by the interactions between human complex structural and metabolic networks, which include many internal interactions inside this system.

Lipton (2005) proposed new biology, whose center is membrane and energy field. Membrane and surroundings influence each other and product function of actions, so it becomes the real brain in cell. Membrane is necessarily internal interaction, and is already Maxwell demon with selective direction, in which IMPs is namely on-off of demon.

Combined Eq.(1) and Eq.(2), we proposed quantitatively a universal entropy theory on evolution of any natural and social systems (Chang 2014b, 2015). The total formula of entropy change is:

$$dS = dS^{a} + dS^{i}_{+} - dS^{i}_{-} + dS_{i} + dS^{+}_{e} - dS^{-}_{e}.$$
 (6)

When

$$dS^{a} + dS^{i}_{+} + dS_{i} + dS^{+}_{e} > dS^{i}_{-} + dS^{-}_{e},$$
(7)

entropy increase dS>0, the system tends to disorder. When

$$dS^{a} + dS^{i}_{+} + dS_{i} + dS^{+}_{e} < dS^{i}_{-} + dS^{-}_{e},$$
(8)

entropy decrease dS<0, the system tends to order. Both differences are determined by the input negative entropy flow in open system and the internal interactions in isolated system  $dS_e^- + dS_-^i$ . It may provide some directive predictions for new technologies as the tissue engineering.

#### 6. CONCLUSION

In a word, thermodynamics is science. It should be developed, and must be developed. Law on entropy increase cannot become a belief, and even more cannot be infinite extension. Otherwise, this will derive various fallacies (Chang 2012, 2018).

For much robust and precise complex biological systems constructed from noisy and imperfect parts in nature, various internal interactions exist widely. We cannot think that all these beautiful processes, and self-assembly, self-organization, self-production, self-fabrication, self-maintaining, etc., all are always entropy increase. In fact, the biological membrane is already a natural existent Maxwell demon. We no other than develop thermodynamics, and investigate completely change of entropy, then may more understand the essence of life, and develop the theoretical biology, systems biology, evolutionary biology and synthetic biology, etc., and then accelerate the next great advance.

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