Theoretical analysis indicates ‘the principle of fluctuations’ fundamentally control life phenomena. : What is life?

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Abstract

The proposition of the existence of fundamental systems which control or manage life phenomena has not given the solution. The profiles of gene expression or the pathways for the protein interactions have been elucidated. However, those are the results of the gene expression patterns and the pathways only under steady states and have not been elucidated the fundamental systems or principles of complex life phenomena. Hence, do really the systems or principles exist which fundamentally control or manage the complex life phenomena? I logically proved that 'the principle of fluctuations' control or manage the fundamental life phenomena. In other words, life phenomena exist on the basis of 'the principle of fluctuations'. Hence, living bodies can cope with the change of diverse conditions. Replication of DNA, DNA mismatch repair, gene expression, translation into amino acids, production of proteins, the process of energy productions and the process of signal transductions are not be firmly operated in 100%. Notwithstanding, living bodies operate life phenomena without hindrance. This means the existence of 'fluctuations' fundamentally. Life phenomena are operated harmoniously. Since living bodies are constructed by molecules, living bodies must be accepted the uncertainty principle in the field of physics. It is impossible to make mathematical formulas, because life phenomena are too complex and too flexible to

make such formulas. Living bodies are not machines. Therefore, I suppose that life is the states of operation of life phenomena on the basis of ‘fluctuations’, because the boundary line between living conditions and dead conditions is not be able to be defined.

Introduction

Since physicist Dr.Schrödinger published the book ‘What is life?’ in 1944, the proposition “what is life?” has been one of the most important propositions in the field of life science[1]. But still now, the solution of the proposition has not been elucidated. The fields of systems biology and bioinformatics emerged to solve to the proposition which the systems control or manage life phenomena. However, these fields have not been given the solution to the existence of the fundamental systems which control or manage life phenomena so far. I think that the way of trials to elucidate life phenomena in terms of systems biology or bioinformatics are correct. However, even if gene expression profiles by microarrays and protein interaction pathways were elucidated, or analysis of biological information were performed, those trials have not been given the solution to the proposition of the existence of the systems which control or manage fundamental life phenomena. Living bodies maintain homeostasis under the steady state, but if once those conditions are damaged by some kinds of stresses, the homeostasis brake and other life phenomena set in motion[2, 3]. Do really replication of DNA, gene expression, translation into amino acids, protein production, pathways of energy production of glycolysis or TCA cycle and pathways of signal transductions which are essential for life, support life phenomena all together harmoniously? The solution to this proposition is NO! Many systems and pathways have been elucidated, but even one of them has not been the fundamental systems which control or manage life phenomena. In the fields of systems biology and bioinformatics, the concept of robustness advocated and those scientists emphasize that systems cope with diverse life phenomena by the existence of robustness[4, 5]. And in the fields of chemical biology, biophysics, physical biology, those scientists emphasized the existence of the system on the assumption of mechanism or physicalism[6-20]. Trials to elucidate life phenomena have also been performed by complex system and self-organization, these trials have not been successful so far [21-25]. Are life phenomena systematic such as machines which can be designed by mathematical formulas? When living bodies fall into danger and certain systems do not operate fully, living bodies operate the other systems to compensate for the danger to survive. It is redundancy. Hence, how does make an interpretation of the existence of redundancy? How is the uncertain principle of physics adapted for life phenomena[26, 27]? It is very significant to elucidate life phenomena. Hence, the propositions which theoretical biologists try to elucidate, are ‘what is the fundamental principle to control and manage life phenomena?’ and “What is life?” I emphasize that the system does not exist to control or manage life phenomena fundamentally, but ‘fluctuations’ exist on the basis of life phenomena. The uncertainty principle of physics is the basis of the existence of ‘fluctuations’. Because living bodies are constructed by molecules, life phenomena are operated by the uncertainty principle of physics. Finally, the solution of the proposition “What is life?” is supposed to be the condition which life phenomena are controlled or managed by ‘fluctuations’.

The definition of words and phrases.

Before the discussion, the definition of words or phrases is significantly important. Because scientists must use appropriate words or phrases. In the fields of systems biology and bioinformatics, the word “robustness” is used to express flexible strength of the systems of life phenomena. But the real meaning of robustness is to withstand or overcome adverse conditions by dictionaries[28-38]. If life phenomena are not based on the systems, flexibilities, randomness and vagueness, ‘fluctuations’ is thought to be appropriate to express the principle of control the system of life phenomena.

Systematic or nonsystematic?

Are life phenomena systematic or nonsystematic? There must be only two choices. In the fields of systems biology and bioinformatics, scientists emphasize that life phenomena are the aggregation of individual systems, and life phenomena are smoothly controlled or managed by robustness on the basis of the aggregation of those systems. Forthermore, some scientists in those fields try to make mathematical formulas on the basis of mechanism or physicalism. On the contrary, I emphasize that systems are controlled or managed by 'the principle of fluctuations' which are constructed which is existed on the basis of unstable life phenomena. Because of the existence of 'the principle of fluctuations', the values of blood examinations from one healthy human have the unevenness (Table 1). However, human beings can act life phenomena harmoniously. This means that life phenomena are controlled or managed fundamentally on the basis of 'fluctuations'. In other words, life phenomena are controlled or managed on the basis of 'the principle of fluctuations' fundamentally. Endosymbioses have dramatically altered eukaryotic life, but were thought to have negligibly affected prokaryotic evolution. By analyzing the flows of protein families, the evidence that the double-membrane, Gram-negative prokaryotes were formed as the result of a symbiosis between an ancient actinobacterium and an ancient clostridium. The resulting taxon had been extraordinarily successful, and had profoundly altered the evolution of life by providing endosymbionts necessary for the emergence of eukaryotes and by generating Earth's oxygen atmosphere. Their double-membrane architecture and the observed genome flows into them suggest a common evolutionary mechanism for their origin: an endosymbiosis between a clostridium and actinobacterium[39]. Why sex evolved and persists is a problem for evolutionary biology, because sex disrupts favorable gene combinations and requires an expenditure of time and energy. Further, in organisms with unequal-sized gametes, the female transmits her genes at only half the rate of an asexual equivalent. Many modern theories that provide an explanation for the advantage of sex incorporate an idea originally proposed by Weismann more than 100 years ago: sex allows natural selection to proceed more effectively because it increases genetic variation. Dr. Goggard and colleagues tested this hypothesis, which still lacked robust empirical support, with the use of experiments on yeast populations. Capitalizing on recent advances in the molecular biology of recombination in yeast, they produced by genetic manipulation strains that differed only in their capacity for sexual reproduction. They show that, as predicted by the theory, sex increases the rate of adaptation to a new harsh environment but has no measurable effect on fitness in a new benign environment where there is little selection[40]. If the systems are robust in human cells, tissues and organs, life phenomena may not cope with flexibly the dangerous conditions which menace the homeostasis. Further, if systems exist on the basis of life phenomena, living bodies could not acquire these flexibilities, in other word, ‘the principle of fluctuations’. Hence, any living bodies such as bacteria, yeast, human beings may be disturbed evolution. In that case, the systems must not have the space to acquire other systems, because the systems must be constructed completely. I deductively and logically proved that life phenomena do not exist on the basis of systems. It is very difficult to prove logically that life phenomena are not fundamentally controlled or managed by the systems. Even if only 5000 molecules control or manage all biological activities in a certain living body, the systems maintain homeostasis. If the systems are damaged, the living body copes with redundancy. But if the systems were not able to maintain homeostasis, the living body will die. Is it possible to predict which and how the pathways or the systems cope with those crises? It depends on the size and type of crises. Therefore, as a result, it is impossible to predict how to cope with those crises. Because, life phenomena are controlled or managed by the principle of uncertainty in the field of physics. In other words, I deductively and logically proved life phenomena are unstably fluctuated under those crises. If ‘fluctuations’ do not exist under the crises for life, living bodies may be accepted the crises and stop biological activities. Notwithstanding, living bodies manage to survive. This is for the sake of existence of ‘fluctuations’. But it is impossible to predict how to manage to survive. I proved by abduction as stated an above-mentioned. If the systems exist fundamentally control or manage life phenomena, life phenomena may be controlled or managed by the gene products of house-keeping genes. However, these genes products must be classified into the several essential pathways such as DNA replication, DNA mismatch repair, gene expression, translation into amino acids, production of proteins, the process of energy productions, and the process of signal transductions and so on. And the existence of upper systems or the link to totally control or manage to these pathways is not identified still now. In addition, it is undeniable to predict how much amount or genes and proteins must be different from individual living bodies, and how to respond.

Mechanism, physicalism, probability theory and the uncertainty principle

Systems biology, bioinformatics, chemical biology, biophysics and physiological biology ultimately exist on the basis of mechanism or physicalism. But because of the uncertainty principle in the field of physics, life phenomena are not able to be predictable. In case of DNA replication or DNA mismatch repair, there exist mistakes in certain probabilities. And the timing of gene expression and gene expression pattern are also considered by probability theory. The timing of working, permutation, combination and the efficiency of working of proteins are also considered by probability theory. Hence, how much amount of proteins is secreted? How fast are the proteins degraded?

Do pathways of energy productions usually produce the same amount of energy? How are those pathways exact and fast under stress? How fast does the concentration in blood of antibiotics increase, in case of giving antibiotics? It is impossible to solute these propositions. Because life phenomena are exceedingly complex and unpredictable. It is further more impossible to design mathematical formulas. Because all of life phenomena must be considered by probability theory. There manifestly exist the differences of biological activities among individual living bodies from the results of research and treatment. This is the way Heisenberg stated the uncertainty principle originally: If the measurements on any objects are made, and the x-component of its momentum with an uncertainty Δp can be determined at the same time, it is impossible to know its x-position more accurately than $\Delta x = h/\Delta p$, where h is a definite fixed number given by nature. It is called "Plank's constant". Hence, it means that life phenomena have the uncertainty and are not predictable even in an instant future. This means that the positions and momentums of molecules are not predictable.

Living bodies are not machines.

The academic discipline which I advocate theoretical molecular biology, is a science to elucidate life phenomena logically and theoretically. Life phenomena must be considered by probability theory, and exist on the basis of 'the principle of fluctuations'.

According to ‘fluctuations’, life phenomena which are not machinelike, flexibly cope with the changes of environments and crises of homeostasis. I inductively proved as a stated above. I will elucidate the proposition which living bodies are machines. Firstly, if living bodies were machines, living bodies could not accomplish evolution. Furthermore, DNA replication, DNA mismatch repair, gene expression, translation into amino acids and productions of proteins might have mistakes. If living bodies were machines, living bodies must not accomplish evolution and not make mistakes in case of DNA replication, DNA mismatch repair, gene expression, translation into amino acids, productions of proteins and so on, because living bodies must be created in 100% machinelike. Hence, the solution is that living bodies are not machines. Firstly, if there do not exist ‘fluctuations’, individual cells cope with crises of homeostasis in 100% uniformly. And tissues or organs which are the aggregate of cells also cope with in 100% uniformly. But living bodies operate biological activities harmoniously without hindrance and cope with crises of homeostasis. To sum up, life is on the basis of ‘fluctuations’. Blood examinations were performed from only one male (Table 1). The results show that there were certain different measured values of two blood samples which were took at interval of only one hour. Even at the same time, the measured values of two blood samples have difference. These were measurement errors. However, instead of the existence of unevenness of blood examinations, human beings can perform life phenomena without any obstructions. This means that life phenomena fundamentally have unevenness. Hence, life phenomena are based on the uncertainty principle in the field of physics, and the measured values of blood examinations must not be able to predictable only in one hour. Because, the systems which control or manage life phenomena are based on 'fluctuations'. I proved the existence of 'fluctuations' inductively. Secondly, I will prove life phenomena are controlled or managed by the uncertainty principle. Can we predict our life phenomena or body conditions in one hour, one week or one year? This is impossible. We will be able to interpret the events such as life phenomena or body conditions by the analysis of gene expression profiles or the pathways of protein interactions. Hence, life phenomena must not be predictable according to the uncertainty principle in the field of physics. This means that there exist uncertainties of life phenomena on the basis of 'fluctuations'. I proved an above-mentioned deductively. Thirdly, why living bodies can perform evolution? If the systems which control or manage are robust, evolution might not be performed. Hence, the systems which control or manage life phenomena must have flexibilities to acquire new characters or traits. This means that there do not exist the robust systems, but must namely exist flexible 'fluctuations'. I proved an above-mentioned deductively.

It is impossible to make mathematical formulas.

It is also impossible to make mathematical formulas. That is not why analytical capabilities of the present time computers are not sufficient to analyze more than billions of interactions of molecules in living bodies. If it will be possible to analyze more than billions of interactions of molecules in living bodies, will it be possible to make mathematical formulas in the future? And if all systems of life phenomena were elucidated in the future, will it be declared to elucidate life phenomena completely? The solution of these prepositions is NO! It is impossible to make mathematical formulas to elucidate the systems or the principles of life phenomena, because life phenomena are too complex, and biology is different from mathematics or physics. And many systems operate together and are connected with other systems on the same time in life phenomena. Hence, it is impossible to make mathematical formulas and elucidate the systems or the principles of life phenomena fundamentally. I inductively proved that the systems do not exist on the basis of life phenomena. Some theoretical biologists try to make mathematical formulas, but living bodies do not live and cope with crises of homeostasis in 100% uniformly. That is why that it is impossible to make mathematical formulas.

What is life?

Can the boundary line between living conditions and dead conditions be defined in terms of biological and philosophical point of views? Is it possible to define when living bodies die? The solutions for these propositions may be that living conditions and dead conditions are continuous sequentially. Because living bodies are not machines, it will not be impossible to define the boundary line between living conditions and dead conditions. The important fact is that life phenomena are not predictable, not be able to make mathematical formulas to elucidate the systems, and exist on the basis of 'fluctuations'. That is why living bodies are able to operate diverse biological activities and cope with crises of homeostasis harmoniously.

Conclusion

Here, I logically and theoretically proved that the solutions for the propositions of the systems or principles which control and manage life phenomena fundamentally are 'the principle of fluctuations'. I name this thought as Itoh's 'the principle of fluctuations'. And the proposition of "What is life?" may be supposed to operate or perform biological activities on the basis of 'fluctuations'.

Methods summary

Blood examinations were performed from only one male at interval of only one hour. And blood examinations were performed from the same person on the same time as a negative control.

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Table 1 Blood examinations	positive data								negative control			
	10:00 27/8 2010	11:00 27/8 2010	10:00 8/9 2010	11:00 8/9 2010	10:00 3/12 2010	11:00 3/12 2010	10:00 27/12 2010	11:00 27/12 2010	10:00 15/10 2010	10:00 15/10 2010	10:00 5/1 2011	10:00 5/1 2011
Red Blood Cell (RBC) (X10000μL)	474	487	466	468	479	473	490	496	475	471	464	463
Hemoglobin (Hb) (g/dL)	14.5	14.6	14.3	14.2	14.4	14.4	15.1	15.3	14.5	14.7	14.1	14.2
Hematcrit (Ht) (%)	44.8	46.6	45	45.2	45	45.5	46.2	46.5	45.8	45.6	43	42.7
White Blood Cell (WBC) (/μL)	7010	7560	6540	6980	8940	9170	7160	7220	7440	7510	7820	7970
Platelet (Plt) (X10000μL)	22.6	24.7	23.5	22.5	23.1	23.8	24.3	24.7	25.6	24.3	25.5	25.5
Aspartate Amino Transferase (AST) (U/L)	71	77	62	58	39	39	44	45	42	44	50	48
Alanine Amino Transferase (ALT) (U/L)	141	146	113	116	70	67	97	99	65	65	103	102
Alkaline Phosphatase (ALP) (U/L)	251	248	333	309	268	247	264	273	237	237	246	246
Lactate Dehydrogenase (LDH) (U/L)	195	246	238	210	194	200	174	171	230	246	180	165
γ-Glutamyl Transpeptidase (γ-GTP) (U/L)	185	192	159	160	184	179	209	214	141	144	182	176
Leucine Amino Peptidase (LAP) (U/L)	75	79	72	72	76	73	78	81	69	70	76	76
Blood Urea Nitrogen (BUN) (mg/dL)	13.5	13	17.8	16	8.8	8.5	9.3	9.4	7.3	7.6	13.6	13.6
Creatinine (Cre) (mg/dL)	0.77	0.81	0.75	0.79	0.78	0.73	0.74	0.75	0.71	0.73	0.72	0.71