The holographic principle and the language of genes

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We show that the holographic principle in quantum gravity imposes a strong constraint on life. The degrees of freedom of an organism can be estimated according to the theory of Boolean networks, which is constrained by the entropy bound. Hence we can explain the languages in protein sequences or in DNA sequences. The overall evolution of biological complexity can be illustrated. And some general properties of protein length distributions can be explained by a linguistic mechanism.

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INTRODUCTION

The general principles in non-living systems play significant roles in living systems. How do the principles in gravity theory or in quantum mechanism impact on our understanding of life? An organism can not keep active without the supply of energy due to the first law in thermodynamics. And it can not live long without the supply of minus entropy due to the second law in thermodynamics. But it seems that there are no direct effects of the relativity principle or the uncertainty principle on life. We found that the holographic principle, which is likely only one of several independent conceptual advances needed for progress in quantum gravity [1][2][3][4][5], profoundly constraints the forms of life and substantially impacts on the evolution of life.

The holographic principle states that there is a precise, general and surprisingly strong limit on the information content of spacetime regions. The number of quantum states in a spatial region is bounded from above by the surface of the region measured in the unit of four-fold Planck areas. This entropy bound is a strong constraint on any theory about our universe. If this principle is true, the degrees of freedom in a living system will also be constrained. From this point of view, the principles in relativity or in quantum theory constrain life in an alternative way. The holographic principle indicates that there is a strict relationship between the information storage capacity of the space and the complexity of any organism wherein. Such a basic idea can be illustrated by a simple example. Whatever a living system with n degrees of freedom is, we can conclude that it can never exist in a universe with a horizon area less than 4nl_p^2, where l_p is the Planck length.

In this paper, we estimated the immense degrees of freedom for living systems according to the theory of gene regulatory networks and Boolean networks [6][7]. We found a contradiction between the possible degrees of freedom of living systems and the maximum information storage capacity in the observed universe. Then we reconciled this contradiction in terms of the causality between the possible sequences of macromolecules for the actual living systems, which is equivalent to the existence of language of genes. We propose evidences of language of genes and we can explain the outline of protein length distributions by a linguistic mechanism of generation of protein sequences. We can also explain the leaps in the evolution of biological complexity according to the entropy bound.

IMMENSE DEGREES OF FREEDOM IN LIVING SYSTEMS

Information properly bridges biology and physics [8][9][10], which gives deep insights into the nature of life. With the development of genetics, we know that the gene regulatory networks play significant roles in development and evolution of life [11]. Based on the theory of self-organization, Kauffman proposed a general theory of Boolean networks to describe the gene regulatory networks, where the interactions between genes can represented by Boolean operations between the nodes of the network [12]. Thus, the degrees of freedom of a living system can be estimated by the number of states of the corresponding Boolean network. Proteins are the elementary units in the activities of life. So a living organism can be represented by a dynamical system of all the proteins in its body. We denote the set P as all possible protein sequences with a cutoff of protein length l. Proteins are chains concatenated by 20 amino acids. So there are m = \Sigma_{k=1}^{20^k} elements in the set P. We define a Boolean network N as the Boolean network whose nodes are elements of P (Fig. 1a). According to the definition of Boolean networks, there are two states for each node of a Boolean network: “on” or “off” [13]. A state of N represent that some nodes are “on” while the others are “off”. So a proteome can be represented by a state of N, where only the nodes corresponding to protein sequences in the proteome are “on”. The state space S consists of
all possible states of \( \mathcal{N} \) whose number is
\[
n_0' = 2^m. \tag{1}
\]
An actual species can be represented by a point in \( \mathcal{S} \). The evolution of a species can be illustrated by a trajectory in \( \mathcal{S} \) (Fig. 2b). As a preliminary consideration, the degrees of freedom of a living system can be estimated by the logarithm of number of states
\[
d' \sim \ln n_0' \sim 20^l \ln 2, \tag{2}
\]
which we will reconsider later on.

According to the holographic principle, we can calculate that the information in the observed universe is about \([11]\)
\[
I_{\text{univ}} = 10^{122} \text{ bits}. \tag{3}
\]
This value is too large for non-living systems. For example, the information of black body cosmic background photons is about \(10^{90} \) bits, which may be the largest degrees of freedom for possible non-living systems. But it is still much less than \( I_{\text{univ}} \). The remaining information storage capacity in our universe has not been wasted however for there being living systems. The degrees of freedom for living systems are so immense that may exceed the maximum information storage capacity in the observed universe.

The structure of chains of genetic macromolecules essentially provides immense degrees of freedom for living systems, because the number of possible protein sequences can be as large as \( 20^l \). For a living system, the degrees of freedom may be equivalent to that of the observed universe if the protein length is about \( n^* = 94 \) amino acids. Interestingly, the most frequent protein length for the life on our planet is about \( n^* \). The immense degrees of freedom of living systems originate from the great number of possible sequences in \( \mathcal{N} \). Most of the degrees of freedom come from the states of \( \mathcal{N} \) in which about half the nodes are “on”. On the other hand, the degrees of freedom can also come from the states in which only a minority of nodes are “on”. Our living systems belong to the latter case, where there are only thousands of proteins in actual proteomes.

**ENTROPY BOUND AND THE CAUSALITY OF SEQUENCES**

The estimate of immense degrees of freedom of a living system in the above, however, seriously contradicts the holographic principle if we consider the actual life around us. The average protein length in a proteome ranges about from 250 amino acids to 550 amino acids, and a certain number of proteins are longer than thousands of amino acids. According to the preliminary estimate, the degrees of freedoms for the actual living systems on our planet will be much larger than the maximum degrees of freedoms in the observed universe \( I_{\text{univ}} \). We have to reconcile the contradiction between the preliminary estimate of degrees of freedom of living systems and the conclusion of the holographic principle. If the holographic principle is not invalid, we must find ways to shrink the preliminary estimate of the degrees of freedom of living systems.

We introduce the causality between the states of \( \mathcal{N} \) to reveal the additional constraint on the degrees of freedom by the entropy bound. At the beginning of the evolution on the planet, the first living system may be denoted as an inertial state \( s_0 \). When the degrees of freedom of \( \mathcal{N} \) is greater than \( I_{\text{univ}} \), not all the states of \( \mathcal{N} \) can have causal relationship with \( s_0 \) unless the holographic principle is untrue. We define the set \( \mathcal{U} \) as all the states that have causal relationship with \( s_0 \), which has \( n_{s} \) states and is only a proper subset of \( \mathcal{S} \) (Fig. 1b). The nodes of \( \mathcal{U} \) constitute \( \mathcal{L} \), which is a subset of \( \mathcal{P} \). An actual living system at present corresponds to a dynamic system evolving only in the state space \( \mathcal{U} \) and a meaningful protein sequence in biology must belong to \( \mathcal{L} \). The degrees of freedom of a living system, therefore, can be defined...
entropy bounds, there is no difference for the requirement determined by some grammars. Although there are various alphabet of the language of genes consists of 4 bases. The protein language consists of 20 amino acids, and the alphabet 

Thus we obtain a language consisting of 2 words: \( aa \) and \( ba \) (ba) (aa). We can choose a subset \( aa \) and \( ab \) as the nodes of an available Boolean network, which corresponds to an actual living system in this universe. Thus we obtain a language consisting of 2 words: \( aa \) and \( ab \).

by the number of states in \( U \):

\[ d = \ln n_s, \]

where \( n_s \) is much less than \( n'_s \) and \( d \) can be rightly less than \( I_{\text{univ}} \).

THE LANGUAGE REQUIRED BY THE HOLOGRAPHIC PRINCIPLE

The causality provides a physical explanation to distinguish a part of sequences \( L \) from all possible sequences \( P \). Not all the amino acid chains or base chains are meaningful in biology. According to the theory of formal language, a language is defined by a subset of all the sequences concatenated by letters in a given alphabet \([12]\). The choice of a subset \( L \) from \( P \) is a natural way to define a formal language (Fig. 2). The protein or DNA languages originate in the constraint on the degrees of freedom of life by the entropy bound. The alphabet of protein language consists of 20 amino acids, and the alphabet of the language of genes consists of 4 bases. The arrangement of the letters in the sequences should be determined by some grammars. Although there are various entropy bounds, there is no difference for the requirement of finite degrees of freedom in life and the requirement of the language of genes for all the theories. To some extent, the language of genes is a consequence of the principles in quantum gravity. The phenomenon of life is constrained strictly by the entropy bound. The requirement of the order of sequences by the grammars cannot be explained in the context of classical physics because the degrees of freedom of life can be infinite.

The ability of speaking for human beings is determined by genes. That we can communicate with each other instinctively can be attributed to our common genes. The human language can be viewed as a transformation of cell language \([13]\). The information storage capacity of a natural language can also be estimated by the similar calculation in the above. For instance, we estimated that there are up to \( I_{\text{human}} = 26^l \) bits of information can be written in a language with 26 letters and the length of words in the language is \( l \sim 10 \), which is much less than the protein length. In this sense, the natural language is simpler than the language of genes. The value \( I_{\text{human}} \) is much less than the information in the observed universe \( I_{\text{univ}} \). So the description of the universe by natural language is always a simplified version of the actually complex world. Interestingly, there were not rare cases to reach the same goal by different routes in the history of natural sciences, such as, Riemannian Geometry and general relativity, or the theory of bundles and gauge theories. Such encounters may come from that all the descriptions in different subjects have a common ultimate theory of all the information in the universe, although we can not understand all the details of the world by only one subject.

THE LANGUAGE OF GENES AND UNDERLYING ORDER IN SEQUENCES

Several attempts have been made over the past three decades to combine linguistic theory with biology \([14][15]\). The distribution of the number of occurrences of protein domains in a genome can be a good fit of the power-law distribution known as Zipf’s law in linguistics, and we can distinguish between the protein linguistics and the language of genes according to the theory of formal language \([15]\). So the experimental observations support the existence of languages in the sequences of macromolecules. On one hand, they are required by the holographic principle. On the other hand, they are consequences of the evolution of life at the molecular level \([16][17][18][19]\). The alphabets of amino acids or bases formed at the beginning of life. And genetic code developed and fixed in the early stage of evolution. All these factors can determine whether a sequence is permitted in a life, which is equivalent to the role of grammars at the molecular level.

We found a strong evidence of the underlying mecha-
tributions are stochastic. The periodic-like fluctuations in the protein length distributions, which can never achieve if the protein length distributions are intrinsic properties of certain species. W e found that there is a close relationship between the frequency of the highest peak of the discrete fourier transformation of protein length distribution. The distribution of the species from three domains likes a rainbow. Even for the group of closely related species such as mycoplasmas (belonging to eubacteria), their distribution also form an "arch" of the rainbow. This is a strong evidence for the underlying mechanism of the protein length distributions.

\[
\mathbf{D} = (D(1), D(2), ..., D(g), ...D(c)),
\]

(5)

where there are \(D(g)\) proteins with length \(g\) in the complete proteome of a species and \(c = 3000\) is the cutoff of protein length. Our data of the protein length distributions are obtained from the data of 106 complete proteomes in the database Predictions for Entire Proteomes \[20\]. The discrete fourier transformation of the protein length distribution is:

\[
\tilde{D}(f) = \frac{1}{\sqrt{c}} \sum_{g=1}^{c} D(g) e^{2\pi i (g - 1)(f - 1)/c}
\]

(6)

Let \(f_m\) denotes the frequency of the highest peak \(\tilde{D}(f_m)\) in the discrete fourier transformation of the protein length distribution for a species. We found that there is an interesting relationship between the frequency \(f_m\) and the average protein length \(\bar{l}\) of species. The distribution of species in \(\bar{l} - f_m\) plane shows a regular pattern: the species in the three domains (Archaebacteria, Eubacteria and Eukaryotes) gathered in three rainbow-like arches respectively (Fig. 3). This pattern strongly indicates the intrinsic correlation among the protein length distributions, which can never achieve if the protein length distributions are stochastic. The periodic-like fluctuations in the protein length distribution \[21\] may also originate in the underlying mechanism of generation of protein sequences.

### EXPLANATION OF THE ORDER IN PROTEIN SEQUENCES

We propose a model to reveal the underlying mechanism in the protein sequences according to tree adjoining grammar \[22\]. In the model, protein sequences can be generated by tree adjoining operations, i.e., substituting the initial tree or auxiliary trees into each other by identifying the inner nodes (Fig. 4a) \[22\]. There is only one variant \(t\) in the model, which is the probability of substitutions in the adjoining operations and denotes different species. A certain number of proteins can be generated when \(t\) is fixed, hence we obtain a protein length distribution by the model (Fig. 4b). The properties of protein length distributions can be explained by the simulation. The outline and the fluctuations of the simulated protein length distribution agree with the actual protein length distributions in principle.

We show that there is a close relationship between the protein length distributions and grammar rules. The fluctuations in the distributions are determined by the grammar rules. The same grammar rule corresponds to the same distribution. If changing grammar rules, we obtain different outlines and fluctuations of distribution. This result suggests that the fluctuations in actual protein length distributions are intrinsic properties of certain species and may infer the underlying mechanism on the order of protein sequences.

### THE MACROEVOLUTION OF BIOLOGICAL COMPLEXITY

The evolution of complexity of life is not a linear course of increment \[23\][24\]. The entropy bound can also explain the leaps in the evolution of biological complexity. Consequently we can outline the macroevolution of life. The gene regulatory networks are accelerating networks \[25\][26\]. According to this theory, the evolution of complexity of any accelerating networks has to be slowed down and will stop at an upper limit of complexity. Hence there must be upper limits of complexity in both of the evolution of biological complexity for prokaryotes and eukaryotes, where the entropy bound is a natural upper limit. The whole evolution of biological complexity can be, therefore, divided into three steps: the evolution of unicellular life, the evolution of multicellular life and the evolution of society of human beings. The Cambrian explosion divided the first two steps. And we found that the evolution of multicellular life has reached its upper limit because the maximum non-coding DNA content is near to 1 at present. The civilization of human beings
FIG. 4: Simulation of protein length distributions by a linguistic model. a, The tree adjoining grammar. There are one initial tree and two auxiliary trees, where S and T are inner nodes and x or x x are leaves which represent the amino acids. b, The simulation of protein length distribution by the tree adjoining grammar. The properties of protein length distributions such as the outline and fluctuations can be simulated by the linguistic model.

appeared, which can be taken as an alternative form of biological complexity. The entire evolution of biological complexity should be governed by a universal mechanism of evolution. The universal language of genes in species may harmonize the evolution of life in the biosphere.

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