Holographic bound and protein linguistics

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The holographic bound in physics constrains the complexity of life. The finite storage capability of information in the observable universe requires the protein linguistics in the evolution of life. We find that the evolution of genetic code determines the variance of amino acid frequencies and genomic GC content among species. The elegant linguistic mechanism is confirmed by the experimental observations based on all known entire proteomes.

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The phenomenon of life is governed by the general principles in physics, so the progress in understanding the physical world may provide new insight into the origin and evolution of life. The analogy between biology and linguistics at the level of sequences hints that the biological information is processed by underlying linguistic rules. Several attempts have been made to combine linguistic theory with biology \(\cite{1}\). But the existence of linguistics in the biomacromolecular sequences needs a physical explanation. The holographic bound, intimately related to the holographic principle, came from the deep insights of Bekenstein and Hawking in 70’s \(\cite{2,3}\). Its validity is insured by the second law of thermodynamics. Interestingly, the problem on the existence of linguistics in the biomacromolecular sequences can be explained by the holographic bound. In the past decades, the biology has been changed greatly. Wada advocated “... to determine the ‘first principles’ of bio-sciences and link them with the first principles of non-bio-sciences in order to understand the complex systems.” and Gilbert also emphasized the importance of the theoretical methods in biology \(\cite{4}\). Nowadays, the intimacy between biology and physics is unprecedented. Considering the significant role of information either in physics or in biology \(\cite{5,6}\), the gap between physics and biology may be bridged from the viewpoint of information.

In the post-genomic era, the number of entire proteomes increases rapidly. We can take all known entire proteomes as samples to study the global properties of life on our planet. The variance of GC content \(\cite{7}\) is a global property, which varies greatly among species. We also found another global property of the evolution of amino acid frequencies though they vary slightly. The mechanism of the variance of genomic GC content and amino acid frequencies was a long-standing and far-reaching problem \(\cite{8}\). The genetic code evolved in the context of four-letter alphabet when the 20 amino acids joined protein sequences chronologically \(\cite{9}\). The nature of prime biased AT/GC pressure and the reason for the correlation of GC content between total genomic DNA and the 1st, 2nd and 3rd codon positions were unknown. The profound mechanism behind the variance of amino acid frequencies has not been studied; it is worse that the amino acid frequencies are routinely assumed to be constant. All of these basic problems in biology are solved in our theoretical framework based on the formal linguistics and the evolution of genetic code.

In this paper, firstly we explain the existence of protein linguistics and the limited complexity of life in the universe in terms of the holographic bound. Secondly, a linguistic model is proposed to reveal the mechanism of the evolution of amino acid frequencies and genomic GC content as well as the protein length distribution. The excellent fit between our simulations and the experimental observations strongly supports the linguistic mechanism, where the experimental observations are based on the data of 106 entire proteomes (85 eubacteria, 12 archaeabacteria, 7 eukaryotes and 2 viruses) in database PEP \(\cite{10}\) and the data of GC content in database Genome Properties system \(\cite{11}\). The “information” is the thread of the paper, which connects traditionally irreleative problems in physics and biology with each other.

According to the holographic bound, which states that the information storage capacity of a spatially finite system is limited by a quarter of its boundary area measured in Plank area unless the second law of thermodynamics is untrue, the entropy \(S\) in a volume of radius \(R\) satisfies

\[ S \leq S_{\text{max}} \approx \left(\frac{R}{l_p}\right)^2, \tag{1} \]

where \(l_p\) is the Plank length. There is much astronomical evidence that our universe may be headed for an infinite deSitter space. The holographic bound can be applied to the observable universe with finite event horizon. Therefore we can estimate the upper limit of the information storage capability of the observable universe as \(I_{\text{univ}} \approx 10^{122}\) bits \(\cite{3}\). In the point of view in physics, the entropy in our universe is given primarily by the number of black body cosmic background photons, \(\sim 10^{90}\), which is definitely less than \(I_{\text{univ}}\).

However, the upper limit of information \(I_{\text{univ}}\) is not so large when considering the information of a system of life. Firstly, let us give a reasonable definition of a “living” system from the viewpoint of information. Many restless functional proteins, composed of 20 amino acids (a.a.), distinguish the life from the lifeless matter. Thus,
a general living system \( L(n) \) is defined as a set of all possible proteins with length no more than \( n \) a.a., each of which is in either the folded state or the unfolded state. The maximum length \( n \) indicates the complexity of the system. Then, let’s calculate the information of the system. The number of states of \( L(n) \) is \( \Omega(n) = \sum_{k=2}^{n} 2^{20^k} \), hence its information is

\[
I(n) = \log_2 \Omega(n) \approx 20^n \text{ bits.} 
\]

The exquisite single-chain structure of proteins can provide much more information storage capacity than lifeless matter. The upper limit of information \( I_{\text{univ}} \) forbids \( L(n) \), \( n > n_0 \) to exist in our universe, where \( n_0 = 94 \) a.a. such that \( I(n_0) \sim I_{\text{univ}} \). Interestingly, the most frequent protein length for the life on our planet is about \( n_0 \).

The actual system of life on the planet is not one of \( L(n) \), because the average protein length for different species, ranging from 250 a.a. to 500 a.a., are greater than \( n_0 \). Let the actual living system \( L_{\text{earth}} \) be the set of all possible proteins on the planet, and suppose \( n^* (> n_0) \) be the maximum protein length. \( L_{\text{earth}} \) must be a proper subset of \( L(n^*) \) because the information of \( L_{\text{earth}} \) is bounded by \( I_{\text{univ}} \). According to the linguistic theory, \( L_{\text{earth}} \) is a language over the alphabet of 20 amino acids. So we have demonstrated the existence of protein linguistics in terms of the holographic bound that can be derived from the second law of thermodynamics.

In early evolution when delivering the genetic information from the RNA world to the DNA-protein world, the holographic bound required the grammars to allow a very small part of protein sequences and to forbid all the others. There is a easy way to implement the forbiddance: the observable universe can not accommodate all the proteins in \( L(n^*) \). In fact, our conclusion is based on the general principle, freedom of the subtleties of the hierarchy.

If \( L(n) \) have an additional property, e.g., chirality, \( L^{'}(n) \) \( (L^{'}(n)) \) become the set of proteins composed of right-handed (left-handed) amino acids. Let \( C(n) \) be the set of all possible chiral \( L(n) \). Only up to \( n = 2 \) a.a., the information of \( C(2) \), i.e., \( I^C(2) = \Omega(2) \approx 10^{120} \text{ bits} \) is near \( I_{\text{univ}} \). Chirality might have brought too much redundant information; broken symmetry was the solution. So entropy bound is a strong law which constrains the forms of possible life in general. Let us imagine the most complex creature with the same height of us be the one whose genetic information is stored in Plank scale. The information stored in its body can be estimated as \( 1/10^3 \approx 10^{105} \text{ bits} \), which violates the holographic bound. So such complex creature can not exist.

So far, we are aware that the linguistics must play a significant role in generating proteins in the primordial time. In the following, a linguistic model is proposed to simulate the variance of the amino acid frequencies and the genomic GC contents as well as the protein length distributions.

The model consists of three parts: (i) generate protein sequence by tree adjoining grammar \([2]\); (ii) set amino acid for the leaves of grammars in (i) according to the tree of genetic code multiplicity (can be obtained from symmetry analysis, see \([3]\)) with consideration of the amino acid chronology \([4]\); and (iii) translate the protein sequences to the DNA sequences according to genetic code chronology \([5]\). The evolution of genetic code is the core of the model. There is a variant \( t \) in the model, which represents the time in evolution. A proteome for a species is defined as many a protein generated by the model with fixed \( t \), so \( t \) also identifies species in the model. Thus, the amino acid frequencies and the average protein length for a species can be calculated. The evolutionary trends of the amino acid frequencies can be determined when proteomes are generated at different time \( t \). We can also simulate the evolution of genomic GC content after translating the protein sequences to DNA sequences.

The evolution of amino acid frequencies can be explained by the model. According to the consensus chronology of amino acids to recruit into the genetic code from the earliest to the latest \([3]\): G, A, D, V, P, S, E, L, T, R, Q, I, N, H, K, C, F, Y, M, W, we sort the 106 species by the ratio \( R_{10/10} \) of average frequency for 10 later amino acids to average frequency for 10 earlier amino acids. Then we obtain the evolutionary trends of amino acid frequencies: the frequencies of G, A, D, V, P, T, R, H, W decrease, while the frequencies of S, E, I, N, K, F, Y increase and the frequencies of L, Q, C, M do not vary obviously (Fig. 1a). The variance of amino
The simulation of our linguistic model [Fig. 1b] agrees with the data of 106 species [Fig. 1a] not only in the evolutionary trends but also in the variance magnitudes for most of the amino acids. Note that no parameter is added on purpose in the model to alter the trend for a certain amino acid. The evolution of amino acid frequency is sensitive to the amino acid multiplicities [13], any disobedience of which would spoil the results. Therefore, it is the evolution of genetic code that determines the evolution of amino acid frequencies. An important property of the model is that the parameters of amino acid frequencies are constant, which indicates that the variance of amino acid frequencies developed during a short period. It agrees that the genetic code had accomplished quickly. Recently, Jordan et al observed the contemporary amino acid gain and loss, about which there were different explanations [10]. We believe that the evolution of genetic code drives the amino acid gain and loss.

The genomic GC content decreases linearly with $R_{10/10}$ for the species in database PEP. The simulation of our model agrees qualitatively with this experimental observation [see fig. 5 in [17], fig. 2 in [7] and fig. 9-1 in [5]).

And the simulation of the correlation of GC content between total genomic DNA and the first, second, and third codon positions [Fig. 2b] also agrees with the results based on the data of completed genomes [7][5][17], where the correlation slope of the third codon position is much greater than that of the first and the second positions. There is a characteristic convex in the middle of the line of the simulated GC content for the first codon position, which agrees dramatically with the experimental observations [7][5][17]. In the table of codon chronology [15], G and C (A and U) occupy all the third positions of earliest (latest) codons for 20 amino acids, while the bases appear about equally for the first and second positions. Therefore, the correlation slope for the first and second positions vary slightly while the slope for the third position varies greatly. And the lower limit $l \sim 0.3$ and upper limit $u \sim 0.7$ of the GC content among species can be explained similarly; $l + u = 1$ is required in theory.

The linguistic mechanism can also be supported by the distribution of protein length. When observing the distribution of species in the space of average protein length and the highest frequency of discrete fourier transformation of protein length distribution (the cutoff is 3000) for each of the 106 species. The distribution of the species from three domains like 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.
In conclusion, the holographic bound improves our understanding of life, which supervises the maximum complexity of life. Linguistics is necessary in storage of information in the protein/DNA sequences. We show that the particular variance of amino acid frequencies and GC content for the contemporary species are the products of certain genetic code multiplicity and amino acid chronology evolved in primordial time. The linguistic model succeeds not only in the simulations of respective aspects (amino acid frequencies [Fig. 1], GC content [Fig. 2b], protein length distribution [Fig. 3]) but also in their relationships (amino acid frequencies and GC content [Fig. 2a], amino acid frequencies and protein length distribution [Fig. 4]). So the thorough and detailed fit between simulations and experimental observations confirms the validity of the linguistic framework, which is grounded in general principles in physics.

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FIG. 4: The evolutionary flow. Relationship between average protein lengths and $R_{HQW/GV}$ for the 106 species. The species of three domains (Archaebacteria: blue square, Eubacteria: dot, Eukaryotes: red circle) gather together in respective regions and all the species form an evolutionary flow. The proteome size is represented proportionally by the tail perspective regions and all the species form an evolutionary flow. (Embedded) Simulation of the evolutionary flow, whose (upward) bending direction agrees with the direction of the experimental observation.

*We have been simulated by the linguistic model, which should be intrinsic properties related to underlying grammars [18].

We also find the relationship between the average protein length and the ratio of amino acid frequencies. The species of three domains gather in different regions in the space of the average protein length and the ratio $R_{HQW/GV}$ of average frequency for several later amino acids (H, Q, W) to average frequency for several earlier ones (G, V) [Fig. 4]. The points of all species form a bending line [Fig. 4], which can be explained as an evolutionary flow in that (i) the species with large (small) genome locate in the midstream (margin) of the flow [Fig. 4] and (ii) the (rightward) evolutionary direction parallels the directions of decreasing correlations of protein length distributions among groups of the closely related species. The evolutionary flow can be simulated by our model [Fig. 4, Embedded]. The evolutionary direction and the bending direction in the simulation agree with the evolutionary flow of the 106 species.

In conclusion, the holographic bound improves our understanding of life, which supervises the maximum complexity of life. Linguistics is necessary in storage of information in the protein/DNA sequences. We show that...