A complexity measure for symbolic sequences and applications to DNA

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Abstract

We introduce a complexity measure for symbolic sequences. Starting from a segmentation procedure of the sequence, we define its complexity as the entropy of the distribution of lengths of the domains of relatively uniform composition in which the sequence is decomposed. We show that this quantity verifies the properties usually required for a “good” complexity measure. In particular it satisfies the one hump property, is super-additive and has the important property of being dependent of the level of detail in which the sequence is analyzed. Finally we apply it to the evaluation of the complexity profile of some genetic sequences.

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In the last few years the term complexity has become frequent in scientific literature \[1, 2, 3\]. This has conveyed the introduction of diverse complexity measures in different areas of science. Kolgomorov’s algorithmic complexity \[4\], Lempel & Ziv’s measure \[5\], Bennet’s thermodynamic depth \[1, 6\], physical complexity \[7\] or Lopez-Ruiz, Mancini & Calvet’s complexity measure \[8\], are some of the examples that have caught most attention. In fact, this list does not reflect all the proposed complexity measures.

In spite of these efforts, and reflecting such diversity, consensus is to be reached about a precise definition of the complexity concept that would allow its quantification. It is possible that one of the main difficulties to reach that consensus is the lack of a language that is common to all the different areas of science in which the concept is meant to be introduced. As an example, the notion of information and its quantifier, the entropy, is usually present in measures proposed to evaluate the complexity of a system or of a process. At the same time, entropy, in physics is a measure of the disorder of the system, which grows as the disorder grows. However, intuitively, a complex system may simultaneously involve order as well as disorder. Two extreme cases are to be considered when, in physics, a complexity measure is searched. Firstly, a perfect crystal (a completely ordered system) and on the other hand the ideal gas (a completely disordered system). Clearly both systems have no complexity (or an extremely low complexity). In general, a properly defined complexity measure should reach its maximum at some intermediate level between the order of the completely regular and the disorder of the absolutely random. This desirable characteristic for all complexity measures is known as the one hump property.

Very often, a complex system is described as one formed by many non-linear elements that interact with each other \[9\]. These interactions give the system the capacity to auto-organize \[10\]. Given the fact that complexity comes from the interactions of the single units, these interactions must be taken into account when defining a measure that quantifies the complexity of a system. When the different parts of a system, e.g., the molecules of an ideal gas in equilibrium, do not interact, their behavior can be understood as the sum of its separated components. But, when interdependencies occur, this is not valid anymore and to quantify the complexity we need a measure that takes those bonds into consideration \[3\].

An adequate complexity measure should be super-additive, meaning that the two systems’
juxtaposition gives as a result a system in which complexity equals or exceeds the addition of the considered systems. This means that the (extensive) complexity of the whole is equal or larger than the sum of the (extensive) complexities of the parts. Here we are devoted to investigate a complexity measure for symbolic sequences. In this case, the super-additive property reads as follows: if $C_{S_1}$ and $C_{S_2}$ denote the complexities of two symbolic sequences $S_1$ and $S_2$, with corresponding lengths $L_1$ and $L_2$, then

\[(L_1 + L_2) C_{S_1 S_2} \geq L_1 C_{S_1} + L_2 C_{S_2}\]  

(1)

where $C_{S_1 S_2}$ denotes the complexity of the juxtaposition of $S_1$ and $S_2$.

The complexity measure we introduce in the present work takes into account the lengths of the segments of relatively uniform content in which a symbolic sequence is divided. To establish the segmentation we must look for compositionally homogeneous segments. Then, two extreme cases may occur after the segmentation process:

- all the resulting segments have the same length (periodic sequence),
- the sequence has not been segmented (random sequence).

These two cases correspond with the perfect crystal and the ideal gas mentioned earlier, and as we will see, they have a null complexity, according to our definition. Now the next step is to characterize what we will take as the most complex sequence, that is, we must fix a third point over the complexity plot. In order to do that, we go along the following line of reasoning: when the probability, of measuring a particular value of a certain quantity, varies inversely as a power of that value, it is said that the quantity follows a power law. The importance of the distributions following a power law in physics and related areas has been pointed out by the ubiquity of such laws in a wide range of phenomena. This type of laws rules as much the frequency of the use of words in any human language as the number of moon craters of a particular size \[11\]. In general it is accepted that a power law dependence is an indication of hierarchical organization. More interestingly, this kind of behavior also appears in brain dynamics studies. In fact, it is known that the brain constantly makes complex functional nets corresponding to the traffic between regions. In this case it is found that the probability for $k$ regions to be temporarily correlated with a given region satisfies a rule $k^{-\mu}$ where $\mu \approx 2 \[12\]$. To us, this example proves to be highly significant because brain
dynamics is a milestone case of auto-organization and undoubtedly of what we can consider as a complex system. At its time, auto-organization is seen as the modelling mechanism to a great amount of systems in Nature.

According to these precedents, we consider reasonable to take as a high complexity sequence, one that has a lengths distribution of patches of relatively uniform composition following a power law, i.e. the probability \( P(l) \) of finding a patch of relatively homogeneous composition with length \( l \), is given by:

\[
P(l) \sim \frac{1}{l^\mu}.
\]

We suppose further that the most complex sequence is the one in which the interdependence between subsegments is maximum. To quantify that interdependence, we use the autocorrelation function, \( C(l) \) \[13\]. Interdependence is maximum when the autocorrelation function is flat. There exists an interesting relationship between the exponent \( \mu \) in \( 2 \), and the behavior of the autocorrelation function \[13\]. In fact, for a length distribution law given by \[2\] it has been shown that the standard deviation in the symbol content of the sequence, \( F(l) \), has a behavior of the form

\[
F(l) \sim l^\alpha
\]

and the autocorrelation function follows a power law

\[
C(l) \sim \frac{1}{l^\gamma}
\]

with \( \gamma = 2 - 2\alpha \). For an exponent \( \mu \leq 2 \) corresponds an exponent \( \alpha = 1 \) and therefore \( \gamma = 0 \), that is, a flat autocorrelation function \[13\]. Thus, for extremely long sequences a flat autocorrelation is associated to a segments lengths distribution that complies with a power law in which \( \mu \leq 2 \). It should be emphasized that every exponent \( \mu \leq 2 \) leads to a flat autocorrelation function. However the exponent \( \mu = 1 \) corresponds to a statistically self similar distribution of patches along the sequence \[14\]. These facts suggest us to take as the most complex sequence the one with a lengths distribution of patches of relatively uniform composition is given by the law \( 2 \) with \( \mu = 1 \).

This work is organized as follows: In Section II we describe the sequence segmentation method implemented; in Section III we introduce a complexity measure and study its basic properties; in Section IV we apply the introduced measure to real genomic sequences; finally we present some conclusions.
In this section we describe the segmentation algorithm applied to the study of the sequence structure. The method is based on the Jensen-Shannon entropic divergence (JSD) and it was successfully applied to the study of DNA sequences [15]. DNA sequences are formed by patches or domains of different nucleotide composition; given the huge spatial heterogeneity of most genomes, the identification of compositional patches or domains in a sequence is a critical step in understanding large-scale genome structure [16].

The JSD is a measure of distance between probability distributions. Although it was initially defined as a distance between two probability distributions, Lin has proposed a generalization to several probability distributions [17]. Let $P^{(k)} = \{p_i^{(k)}, i = 1..N\}, k = 1..M$, a set of $M$ probability distributions ($\sum_i p_i^{(k)} = 1, k = 1..M$), for a discrete variable $X$ with $N$ possible values $X_i$; $p_i^{(k)}$ denotes the probability of occurrence of the value $X_i$ according to the distribution $P^{(k)}$. The JSD for these probabilities distributions is defined by:

\[
JS[P^{(1)}, .., P^{(M)}] = H[\sum_k \pi^{(k)} P^{(k)}] - \sum_k \pi^{(k)} H[P^{(k)}] \tag{3}
\]

where $H[P] = -\sum_j p_j \log_2 p_j$ is the Shannon’s entropy and the numbers $\pi^{(k)}, k = 1..M, \sum_k \pi^k = 1$ are weights properly chosen.

The JSD is non negative, bounded and can be interpreted in the frame of information theory [22]. Incidentally we mention that the JSD has been proposed as a complexity measure for genomic sequences [16].

In the context of symbolic sequences analysis, the probabilities $p_i$ are approximated by the frequency of occurrence of each symbol throughout the sequence. For a DNA sequence, the symbols are the nucleotides $\{A;C;T;G\}$. If we want to compare the compositional content of two symbolic sequences, let us say $S_1$ and $S_2$, of lengths $L_1$ and $L_2$, we can use the expression (3), where the weights are taken equal to $\pi^{(k)} = L_k/L, k = 1,2$, with $L = L_1 + L_2$. In this case the probability distributions $P^{(1)}$ and $P^{(2)}$ are approximated by the frequency of occurrence of the different symbols throughout each sequence.

The segmentation procedure allows to decompose the sequence into domains or subsequences with a different base composition in comparison to the two adjacent subsequences, at a given level of statistical significance or threshold, $D_u$. This threshold is associated with the level of details in which the sequence is analyzed [22].
In order to make this paper self-contained we will describe the basic steps in the segmentation procedure. For a more detailed description we refer the reader to reference [15]. Let us suppose that we define a moving cursor along the complete sequence. For each position of the cursor, it results two subsequences, one to the left and other to the right of the cursor. For each subsequence we can evaluate the occurrence frequency of each symbol and then calculate the JSD for each position of the cursor. The position that corresponds to a maximum of the JSD above the threshold elected, $D_u$, is taken as a cut point. Clearly these points corresponds to the maximum of the discrepancy between the compositional content of each subsequences. The procedure is repeated for each resulting subsequence until the JSD be greater than the threshold value.

When segmenting symbolic sequences with simple domain structures, homogeneous domains can be consistently found (if purely random fluctuations are excluded). However, when the method is applied to long-range correlated sequences, such homogeneity vanishes: by relaxing the threshold value, we find new domains within other domains, previously taken as homogeneous under a higher threshold value. This domains-within-domains phenomenon points to complex compositional heterogeneity in DNA sequences, which is consistent with the hierarchical nature of biological complexity [16]. We will back to this point at the end of the present work.

### III. DEFINITION OF THE COMPLEXITY

Let us consider a symbolic sequence $S$ of length $L$ (i.e., $L$ is the number of symbols in the sequence). Let us assume that by segmenting the sequence according to procedure described in the preceding section, we can decompose the sequence in $N_s$ patches or domains of different compositional content (up to a significance level $D_u$) [22]. Let us denote by $l_i, i = 1...N_s$, the lengths of each one of these segments. Obviously

$$\sum_{i=1}^{N_s} l_i = L \quad (4)$$

In general these lengths are not all different. Let us denote by $\Omega$ the subset of lengths $l_i$ such that $l_i \neq l_j$ if $i \neq j$:

$$\Omega = \{(l_{\alpha_1}, ..., l_{\alpha_\kappa}), l_{\alpha_i} \neq l_{\alpha_j} \text{ if } i \neq j, \kappa \leq N_s\}$$
Let $N_{\alpha_i}$ be the number of segments of length $l_{\alpha_i}$. Then $\sum_{i=1}^{\kappa} N_{\alpha_i} = N_s$. Let us consider now an arbitrary partition $A = \{A_j\}_{j=1}^{\nu}$, of the interval $[1, L]$ with $\nu - 1$ (the number of subintervals), in principle, arbitrary:

$$1 = A_1 < A_2 < ... < A_{\nu-1} < A_\nu = L$$

(5)

We name the quantity $\Delta_j = A_j - A_{j-1}$ $j = 2, ..., \nu$ as the amplitude of the corresponding subinterval.

Let us denote by $\tilde{N}_j$ the number of patches in the segmented sequence with length belonging to the interval $[A_{j-1}, A_j)$. The condition $\sum_{j=2}^{\nu} \tilde{N}_j = N_s$ is satisfied. Finally let us denote by $f_j$ the occurrence frequency of segments whose length belongs to the interval $[A_{j-1}, A_j)$ (with the convention that the interval corresponding to $j = \nu$ includes the extreme value $L$):

$$f_j = \frac{\tilde{N}_j}{N_s}; \quad \sum_{j=2}^{\nu} f_j = 1$$

(6)

From the knowledge of the frequencies $F = \{f_j\}$ we can evaluate the Shannon’s entropy

$$H_S(F; A, D_u) \equiv H[F] = -\sum_{j=2}^{\nu} f_j \log_2 f_j$$

(7)

Clearly this quantity depends on the partition $A$, and on the significance level $D_u$ at what the segmentation was done, that is, it depends on the level of detail at what the sequence was analyzed. Therefore we have included explicitly the partition $A$ and the significance value $D_u$ as arguments in $H_S$.

There are two cases in which the entropy (7) does not depend on the particular partition chosen:

1. a idealized periodic sequence and

2. a idealized random sequence.

Here what is meant by idealized is that the respective character is detected to every significant level of detail of the analysis. In the first case, there exists only one value (the period) for the length of the segments. Therefore $f_J = 1$ for some value $2 \leq J \leq \nu$ and $f_j = 0$ for all other $j$. Thus, for a periodic sequence $H_S = 0$ for any partition of the interval $[1, L]$. Analogously, due to the fact that a random sequence is not segmented at any significant
level of detail (by the proper meaning of significant), only one of the \( f_j \) is different of zero: 
\( f_\nu = 1 \). Thus we also have \( H_S = 0 \) is this case. These two extreme cases are the corresponding ones with the crystal and the isolated ideal gas, in the physical context. In that sense, 
\( H_S(F; \mathcal{A}, D_u) \) is a good candidate as a complexity measure. It should be emphasized that
\( H_S \) has information about the segmentation of the sequence. The fact that \( H_S \) vanishes for a periodic and a random sequence, suggests to investigate it as a measure of complexity. However, it should be also indicated that, in order to be a true characteristic of the sequence under study, a complexity measure must be independent of any arbitrary parameter. For it, a particular partition is adopted by refining the complexity measure.

Now we proceed to characterize, in a formal way, what we will take as the most complex sequence. Let us assume that after the segmentation procedure, at a given level of detail, the sequence \( \mathcal{S} \) is decomposed in \( N_s \) segments of uniform compositional content, and let us suppose that we are able to identify a power law for the distribution of the segments length:
\[
N_l = \frac{N_s}{Z(\mu, \lambda^*)} l^{-\mu}
\]  
(8)
where \( Z(\mu, \lambda^*) = \sum_{l=1}^{\lambda^*} l^{-\mu} \), \( \lambda^* \) is a cutoff length and \( \mu \geq 1 \). As we indicated in the introduction and for the reasons there expressed we chose \( \mu = 1 \). The cutoff \( \lambda^* \) have to do with the finite size of the sequence \( \mathcal{S} \). Its value can be deduced from the condition
\[
N_s \frac{Z(\mu - 1, \lambda^*)}{Z(\mu, \lambda^*)} = L
\]  
(9)
From the distribution law (8), and for a given partition \( \mathcal{A} \), we can evaluate the frequencies
\[
f_j = \frac{1}{N_s} \sum_{l \in [A_j, A_{j+1} - 1]} N_l,
\]  
(10)
and from these one, the entropy (7).

At this point we look for the partition \( \mathcal{A} \) that makes the entropy (7) to reach a maximum value when the frequencies (10) are replaced. Due to a fundamental property of the entropy, the maximum value of \( H_S(F; \mathcal{A}, D_u) \) is reached for a partition \( \mathcal{A} \) such that all the frequencies \( f_j \) are equal for all \( j \), that is, the number of segments belonging to the interval \([A_{j-1}, A_j)\) is the same for all \( j \). Due to the cutoff, there exists a value \( j^* \) such that \( f_j = 0 \) for \( j > j^* \). Hence, the maximum of the entropy corresponds to the biggest \( j^* \) consistent with the uniformity condition for the \( f_j \). The entropy \( H_S(F; \mathcal{A}, D_u) \) will be, in this case, \( \log_2 j^* \).
To satisfy the above two conditions, that is, the uniformity of $f_j$ for $j \leq j^*$ and the biggest value for $j^*$, we must find a partition $\mathcal{A}$ of the interval $[1, L]$ such that the number of segments in each interval is constant and equal to one. These requirements can be expressed as a set of equations to be satisfied by the extremes of each one of the intervals of the partition $\mathcal{A}$:

$$
1 + \frac{1}{2^\mu} + \ldots + \frac{1}{(A_2 - 1)^\mu} = \frac{1}{A_2^\mu} + \ldots + \frac{1}{(A_3 - 1)^\mu} \\
\frac{1}{A_3^\mu} + \ldots + \frac{1}{(A_4 - 1)^\mu} = \frac{1}{A_4^\mu} + \ldots + \frac{1}{(A_5 - 1)^\mu} \\
\vdots \\
\frac{1}{A_{j^*-2}^\mu} + \ldots + \frac{1}{(A_{j^*-1} - 1)^\mu} = \frac{1}{A_{j^*-1}^\mu} + \ldots + \frac{1}{(\lambda^*)^\mu}
$$

(11)

with $\mu = 1$.

As we are looking for the maximum $j^*$ it is obvious from the previous set of equations that we must take $A_2 = 2$. The rest of the amplitudes $\Delta_j = A_j - A_{j-1}$ can be obtained from the set of equations (11).

Now we are in position to introduce our complexity measure for an arbitrary symbolic sequence $\mathcal{S}$ of length $L$. We define it as:

$$
C_{\mathcal{S}} = H[\mathcal{F}_L],
$$

(12)

where $H[\mathcal{F}_L]$ is the entropy of the distribution of lengths of the domains in which the sequence has been decomposed, evaluated according to the partition of the interval $[1, L]$ given by the relations (11) with $\mu = 1$.

The evaluation of complexity (12) for an arbitrary sequence $\mathcal{S}$ of length $L$ requires:

1. To calculate the partition $\mathcal{A}$ corresponding to the length $L$ according to (11) for $\mu = 1$;

2. by using the segmentation procedure described in section II, at certain significance value $D_u$, evaluate the set of length $\Omega$ and from it the frequencies $f_j$ given by (6) for the partition $\mathcal{A}$;

3. finally, evaluate the entropy $H_{\mathcal{S}}$ given by (7).

Incidentally it is worth to mention that for a greater value of $\mu$ compatible with the flat autocorrelation condition ($\mu \leq 2$), the entropy $H[\mathcal{F}_L]$ evaluated following the previously
described steps, takes values extremely slow. Therefore, besides the conceptual motives that led to the election of $\mu = 1$, there are practical ones as well.

IV. APPLICATIONS AND RESULTS

In this section we apply the proposed measure to the evaluation of the complexity for some DNA sequences. In all examples the quaternary alphabet $\{A, T, C, G\}$ is used. These evaluations allow us, on one side, to study the main properties of the measure, such as the dependence with the level of detail in the analysis of the sequence and the super-additivity property; on the other we can investigate our measure as an adequate tool for unravelling certain structural features within the DNA, for instance, the content of introns and exons, and its relation with evolutionary aspect of the genome.

As it was already claimed, an appropriate complexity measure should take into account the level of detail at what the system under study is analyzed [19]. To check this dependence we apply the measure (12) to real DNA sequences with different correlation structure and to a computer generated random sequence. Figure 1 shows the complexity $C_S$ as a function of the threshold level, $D_u$, for the genomic sequences HUMTCRADCV, the ECO110k and the random one (this kind of plots are known as complexity profile). The first one is a human DNA sequence with long range correlations [20]. The second one is an uncorrelated bacterial sequence. A first remarkable aspect of $C_S$ is that there exists a range for the significance value $D_u$, $20 \leq D_u \leq 50$, for which it gets the null value when evaluated for the random sequence. This random sequence has been built with identical composition that those of the ECO110k. For $D_u$ belonging to this interval, the values of the complexity for the human sequence are greater than those for the bacterial one. This fact is consistent with taking as range of interest for the threshold the interval previously indicated. One noticeable characteristic of the complexity profiles for the natural sequences, is that, unlike those obtained for the complexity measure introduced in [16], do not go to zero as the threshold $D_u$ increases.

Another investigated aspect of $C_S$ has to do with the super-additivity property, eq. (11). In figure 2 we show the complexity profiles for the complete DNA sequences ECO110k and the human beta-globulin HUMHBB, and the weighted sum of the complexity profiles for two arbitrary subsequences of these two sequences. Clearly the equation (11) is verified. It
is obvious from the definition of $C_S$ that the complexity of any self concatenation of an arbitrary sequence is equal to complexity of the original sequence whenever the fusion point coincides with a cut point resulting from the segmentation procedure. If this is not the case, the resulting value for the complexity of the concatenated sequence might be, for very long sequences, slightly different to the complexity of the original sequence.

It is known that only a small portion of the genome of higher organisms encodes information for amino acid sequences of proteins [21]. The role of introns (continuous noncoding regions in DNA) and intergenicomic sequences (noncoding DNA fragments intertwined between coding regions) remain still unknown. The study of the statistical properties of the noncoding regions has shown the existence of long range correlations which indicate the presence of an underlying structural order in the intron and intergenicomic segments. This structural order is made apparent in the complexity profiles shown in figure 3, where we have plotted the complexity values for the coding and noncoding regions of the human chromosome 22.

Genomic sequences are a valuable source of information about the evolutionary history of species [23]. In particular it has been possible to relate some statistical characteristics observed along genomic sequences to the influences of a variety of ongoing processes including evolution [24]. In this context we conclude this work evaluating the complexity $C_S$ for homologous DNA sequences of different species; in particular for the myosin heavy-chain. In general it can be observed that there exists a concordance between the biological complexity of the species and the values of $C_S$. It should be emphasized that there exists a relationship between the percentage of introns and the long-range correlations in the sequence. This fact is clearly manifested by the complexity $C_S$ as can be observed in figure 4.

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[1] C.H. Bennett, in *Complexity, Entropy, and Physics of Information*, SFI Studies in the Sciences of Complexity, W. Zurek (Ed.), Addison-Wesley Press (1990).

[2] S. A. Kauffman. *The Origins of Order: Self-Organization and Selection in Evolution*. Oxford University Press (1993).

[3] R. Solé & B. Goodwin. *Signs of Life: How Complexity pervades Biology*. Basic Books (2000).

[4] A. N. Kolmogorov 1965. Prob. Info. Trans., 1:1-7.

[5] A. Lempel & J. Ziv 1976. IEEE Transaction on Information Theory, 22(1):75-81.

[6] S. Lloyd & H. Pagels Ann. Phys. 188:186-213 (1988).

[7] C. Adami, BioEssays 24:1085-1094 (2002).

[8] R. Lopez-Ruiz, H. Mancini & X. Calbet, Phys. Lett. A 209:321-326 (1995).

[9] D.R. Chialvo, Physica A 340:756-765 (2004).

[10] P. Bak, C. Tang & K. Wiesenfeld, Phys. Rev. Lett. 59:381-384 (1987).

[11] M. Newman, arXiv:cond-mat/0412004v2 (2005).

[12] V.M. Eguluz, D.R. Chialvo, G.A. Cecchi, M. Baliki and A. Vania Apkarian, Phys. Rev. Lett, 94, 018102 (2005).

[13] H.E. Stanley, S.V. Buldyrev, A.L. Goldberger, Z.D. Goldberger, S. Havlin, R.N. Mantegna, S.M. Ossadnik, C.-K.Peng & M. Simons, Physica A, 205: 214-253 (1994).

[14] P. Bernaola-Galván, P. Carpena, R. Román-Roldán & J., Gene 300:105-115 (2002).

[15] P. Bernaola-Galván, J. Oliver, R. Román-Roldán, Phys. Rev. Lett. 83:3336-3339 (1999).

[16] R. Román-Roldán, P. Bernaola-Galván & J. Oliver, Phys. Rev. Lett. 80:1344-1347 (1998).

[17] J. Lin, IEEE Trans. Inf. Theory 37:145-151 (1991).

[18] I. Grosse, P. Bernaola-Galvan, P. Carpena, R. Roman Roldan, J. Oliver & H.E. Stanley, Phys. Rev. E, 65:041905-16 (2002).

[19] W. Li, Complexity 3(2):33-37 (1997).

[20] C-K. Peng, S.V. Buldyrev, A.L. Goldberger, S. Havlin, F. Sciortino, M. Simons and H.E. Stanley, Nature 356, 168-170 (1992).

[21] *Genes VI*, Oxford University Press, Oxford (1997).

[22] I. Grosse, H. Herzel, S. Buldyrev and H.E. Stanley, Phys. Rev. E 61:5624-5628 (2000).
[23] M.A. Huynen and P. Bork, Proc. Natl. Acad. Sci. USA 95 5849-5856 (1998)

[24] S. V. Buldyrev, A. L. Goldberger, S. Havlin, C.-K. Peng, H. E. Stanley and M. Simons, Biophys. J. 65: 2675-2681 (1993).
FIG. 1: Complexity profiles of two natural sequences and a computer generated random sequence.

In this last case, the sequence has the same compositional content that the ECO110k.
FIG. 2: Complexity profiles for the sequences ECO110k ($L_{ECO} = 111408$ bp) and HUMHBB ($L_{HUM} = 73308$ bp). The filled symbols correspond to the complexity for the whole sequences, and the empty ones correspond to the (weighted) sum of the complexities for two arbitrary subsequences of each sequence. The subsequences were taken in such a way that their juxtaposition were equal to the complete sequence ($L_{E1} = 57120$ bp and $L_{E2} = 54288$ bp; $L_{H1} = 42720$ bp and $L_{H2} = 30588$ bp).
FIG. 3: Differences in $C_S$ between coding and noncoding regions of the sequence corresponding to human chromosome 22.
FIG. 4: Complexity profiles of myosin heavy-chain genes in different species (total length, percentage of introns): Human (28438bp, 74%), Rat (25759bp, 77%), Chicken (31111bp, 74%), Drosophila (22663bp, 66%), Brugia (11766bp, 32%), Acathamoeba (5894bp, 10%), Caenorhabditis (10780bp, 14%), Yeast (6108bp, 0%)