Shannon information and self-similarity in whole genomes

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Abstract

The Shannon information (SI) in distributions of occurrence frequency of short words in whole genomes is shown to exhibit universality. For given word length, the SI in genomes of all lengths is the same as that in random sequences of a universal lengths $L_r$. For the shorter words $L_r$ is far shorter than the genome. For example, $L_r \sim 1000$ bases for three-letter words. We further show that whole genomes are highly self-similar in the sense that any segment of the genome down to a length of $\Lambda_{\text{sim}}$, about twice $L_r$, also shares the universal property. We devise a simple genome growth model in which genome-size sequences grown by maximally stochastic segmental duplication and random mutation possess the universal and self-similar properties of genomes.

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1. Introduction

Recently it was shown that frequency distributions of overlapping $k$-mers, or $k$-spectra [1], of complete genomes exhibit universality [2,3]. For a given word length $k$, the Shannon information (SI) [4], or equivalently the relative spectral width (SW) [2] is the same for all complete genomes irrespective of their lengths and base compositions, or profiles. The length of the genomes range from 0.4 to 230 Mb (million bases) and their combined probability of $(A+T)$ range from 0.25 to 0.75. In the papers cited, the SI and SW were calculated as reduced Shannon information (RSI) [2] and reduced spectral width (RSW) [3], which are quantities relative to those of a random sequence whose profile match that of the genome. These quantities are defined such that trivial dependence on base composition is to a large part eliminated and that $\text{RSI} \approx \text{RSW} \approx 1$ for any random sequence. The universality is inferred from the computed RSI [2] (and RSW [3]) being proportional to genome length (Fig. 1).
Fig. 1. RSI from 135 complete microbial genomes and 127 eukaryotes. Each symbol is the RSI value of one $k$-spectrum from one complete sequence. Left panel, RSI color-coded (gray scale) by organism; right panel, RSI color-coded by $k$. Data have been multiplied by factors of $10^{-k}$ to delineate the $k$-bands for better viewing. Data for which $4k > L$, when $RSI \approx 1$ for any sequence, have been discarded. Straight lines in the plots give $RSI \propto L$.

Fig. 2. Left panel: Average RSW of $k$-spectra, $k = 2$ to 10, of segments from the 246 Mb chromosome I of H. sapiens. Lengths of the segments are $1/2^n$ of full length, $n = 1$ to 21, and for each length eight segments are randomly selected. Data for which segment length is less than $4^k$ are not included. Right panel: Same for the and the 4.6 Mb genome of E. coli, except that lengths of the segments are $1/2^n$ of full length, $n = 1$ to 15.

The observed universality can be simply expressed in terms of equivalent random-sequence lengths (in bases), $L_r(k)$, one for each $k$, such that the universal genomic Shannon information is equal to that in a random sequence of length $L_r(k)$. The data in Fig. 1 summarized by the relation $L_r(k) = L_{r0} \exp(ak)$, $2 \leq k \leq 10$, where $a = 0.94 \pm 0.07$ and $L_{r0} = 42 \pm 17$. This relation defines a universality class of genomes. Plasmodium falciparum is the sole exception to the class [2].

2. Self-similarity

For the smaller $k$’s, $L_r(k)$ is far shorter then the genomes. For instance, $L_r(2)$ is only about 300 and $L_r(6)$ is of the order of 10,000, as compared to the canonical length of 2 Mb for microbial genomes and the length of 100 Mb for some of the eukaryotic chromosomes. This being the case, one may ask whether individual segments from a genome in a (universality) class also belong to the class. Fig. 2 shows the result of
testing this idea on two complete sequences, chromosome I of *Homo sapiens* (left panel) and the genome of *Escherichia coli* (right panel). In each case, for a given \( k \), \( k = 2 \) to 10, eight segments of length one \( 2^n \) th, \( n = 1, 2, \ldots \), of the full genome length, down to a length that is just less than \( L_r(k) \), are randomly selected from the genome and their RSW computed. With \( L_r(2) \approx 300 \) b and the lengths of the *H. sapiens* chr. I and *E. coli* being 230 and 4.6 Mb, respectively, the maximum \( n \) used for the two genomes are 21 and 15, respectively. The computed RSW for the segments together with the RSW of the full sequence are plotted against segment length \( L \). In the panels, data for the same \( k \) form clear *k-bands* suggesting a linear relation between RSW and \( L \) (lines in figure). If the data point from a segment sits on a parallel line that goes through the data point from the complete sequence, then the \( L_r \) of that segment is the same as that of the complete sequence and that segment is said to be similar to the complete sequence. Data shown in Fig. 2 suggest the *H. sapiens* chr. I and *E. coli* genomes to be self-similar down to a length not much greater than \( L_r(k) \).

Complete genome sequences used in the present study were downloaded from the genome FTP site of the (USA) National Center for Biotechnology Information. The 163 complete microbial genomes (the prokaryotes) were downloaded on October 9, 2003 from ftp://ftn.ncbi.nih.gov/genomes/Bacteria/ and the 127 chromosome sequences of ten complete eukaryotic (the eukaryotes) were downloaded on July 15, 2003 from ftp://ftp.ncbi.nih.gov/genomes/. For each complete sequence and each \( k \) we determine \( \Lambda_u \), the length above which all segments are similar to the genome, and \( \Lambda_d \), the length below which no segment is similar to the genome, by computing the RSW in sets of randomly selected segments of length \( L \), where \( L \) is taken in steps decreasing from \( 10 L_r(k) \) to \( L_r(k) \). \( \Lambda \) is said to be a self-similar length if the RSW for each segment of length \( \Lambda \) is within a factor of two of \( \Lambda/L \) times the RSW for the genome.

3. Results and discussion

Results for \( \Lambda_u \) and \( \Lambda_d \) for \( k = 5 \) are given in the Fig. 3. Results for \( \Lambda_u \) and \( \Lambda_d \), \( k = 2 \) to 8 (not shown, see http://pooh.phy.ncu.edu.tw/cdy/genome/self_sim/main.html for details and more results) have the following general property: (i) Except for \( k = 2 \), in most cases \( (\Lambda_u - \Lambda_d)/\Lambda_d \leq 1 \) and decreases with increasing \( k \). (ii) Even for \( k = 2 \) \( (\Lambda_u - \Lambda_d)/\Lambda_d \leq 2 \) for most cases. (iii) In a few cases \( \Lambda_u \) is up to an order of magnitude greater than \( \Lambda_d \). (iv) For the prokaryotes, the difference between \( \Lambda_u \) and \( \Lambda_d \) is small, both being close to the eukaryotic \( \Lambda_d \). The averages and standard deviations of \( \Lambda_u \) and \( \Lambda_d \) and given in Table 1 and Fig. 4(A). Denoting by \( \Lambda_{sim} \) the average of the prokaryotic \( \Lambda_u \) and \( \Lambda_d \) and the eukaryotic \( \Lambda_d \) we have \( \Lambda_{sim}(k) \approx \Lambda_d(0)(\alpha_k k) \), \( 2 \leq k \leq 8 \), where \( \alpha_k \approx 0.780 \) and \( \Lambda_d(0) = 166 \pm 120 \). The eukaryotic \( \Lambda_u \) is noticeably greater than \( \Lambda_{sim} \). This is a reflection of the higher textual inhomogeneity in the eukaryotic genomes. The results satisfy the inequality \( 4^k < L_r(k) < \Lambda_{sim}(k) \). In most cases \( L_r(k) \) is not much greater than \( 4^k \) and, except for \( k = 2 \), \( \Lambda_{sim}(k) \) is less than twice \( L_r(k) \). In this sense genomes are highly uniform and are very close to being maximally self-similar.

In [2], a minimal universal model for genome growth [5] in which growth is dominated by maximally stochastic segmental duplications was used to explain the rise of the universality class. With three universal parameters the model generates sequences that belong to the genomic universality class [2]. Here we compute \( \Lambda_u \) and \( \Lambda_d \) from the model sequences for the twenty-four *H. sapiens* chromosomes. The results are compared with the genomic \( \Lambda_{sim} \) in Fig. 4(B). The agreement between data and model is excellent. The relatively small standard deviations on the model results reflect the small sample size (24 sequences versus
Table 1
Average standard deviation $\Lambda_u$ and $\Lambda_d$ for complete eukaryotic and prokaryotic

<table>
<thead>
<tr>
<th>$k$</th>
<th>Eukaryotes</th>
<th></th>
<th>Prokaryotes</th>
<th></th>
<th>Model sequence (H. sapiens)</th>
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<tr>
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<td>$\Lambda_d$</td>
<td>$\Lambda_u$</td>
<td>$\Lambda_d$</td>
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<td>$\Lambda_d$</td>
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<td>2</td>
<td>4.20 ± 2.18 E2</td>
<td>1.63 ± 1.26 E3</td>
<td>5.43 ± 3.69 E2</td>
<td>1.12 ± 1.12 E3</td>
<td>6.45 ± 1.24 E2</td>
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<td>3</td>
<td>9.62 ± 4.43 E3</td>
<td>2.08 ± 1.65 E3</td>
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<td>1.07 ± 0.15 E3</td>
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<td>4</td>
<td>3.35 ± 0.92 E3</td>
<td>4.88 ± 3.89 E3</td>
<td>2.66 ± 1.55 E3</td>
<td>3.47 ± 2.61 E3</td>
<td>2.20 ± 0.28 E3</td>
</tr>
<tr>
<td>5</td>
<td>6.39 ± 2.03 E3</td>
<td>1.18 ± 0.91 E4</td>
<td>6.15 ± 3.17 E3</td>
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</tr>
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<td>1.63 ± 0.48 E4</td>
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<td>6.82 ± 5.71 E4</td>
<td>3.99 ± 1.96 E4</td>
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<td>3.16 ± 0.30 E4</td>
</tr>
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<td>8</td>
<td>9.77 ± 3.23 E4</td>
<td>1.76 ± 1.62 E5</td>
<td>1.10 ± 0.45 E5</td>
<td>1.20 ± 0.55 E5</td>
<td>9.14 ± 0.76 E3</td>
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</tbody>
</table>

Fig. 4. (A) Average and standard deviation of $L_u$ and $L_d$ ($\Lambda_u$ and $\Lambda_d$ in text) for complete prokaryotic eukaryotic genomes. (B) Genome data is the average of prokaryotic $\Lambda_u$ and $\Lambda_d$ and eukaryotic $\Lambda_d$, model data is average of $\Lambda_u$ and $\Lambda_d$ from 24 model sequences for the 24 human chromosomes.

276 sequences in the genome set) and the fact that textually sequences generated in the minimal model are significantly more homogeneous than genomes.

References


