Synonymous codon usage and its bias in the bacterial proteomes primarily offset guanine and cytosine content variation to maintain optimal amino acid compositions

Genshiro Esumi
University of Occupational and Environmental Health, Kitakyushu, Japan

Codon usage bias is the preferential or non-random synonymous codon usage among species. A recent review concluded that their biases are a complex phenomenon influenced by numerous factors, including genome composition, guanine and cytosine (GC) content, expression level, gene length, and recombination rates. In this paper, I present a new plot chart and show a more straightforward explanation of the primary function of synonymous codon usage and its bias.

First, I calculated each protein's amino acid compositions and its gene's nucleotide compositions from the publicly available proteome coding sequence dataset of 23 different bacteria. Next, I calculated the maximum and minimum GC contents of the possible gene variations of the amino acid composition of each protein. Finally, they were plotted together by their actual GC content on a scatter plot (scatter diagram).

The plot showed a clear tendency. Proteins with lower actual GC content genes are coded for by genes closer to the minimum possible GC content. On the other hand, proteins with higher actual GC content genes are coded for by genes closer to the maximum possible GC content. This tendency indicates that synonymous codon usage bias uniformly works toward offsetting the variation in GC content. Meanwhile, all plots of the maximum and minimum values were aligned in a row within a narrow band for each. Therefore, I considered that the optimal range of amino acid composition of the proteome is relatively limited, and that organisms use this GC offset function to meet the range conditions.

Synonymous codons are part of the genetic code table. Therefore, if synonymous codons and their usage bias have a GC offset function to maintain the optimal amino acid composition, it must be considered a fundamental function of the genetic code table assignment.

Keywords: synonymous codon, codon usage bias, amino acid composition, GC content

E-mail: esumi@clnc.uoeh-u.ac.jp

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Background

Codon usage bias is the preferential or non-random synonymous codon usage among species. A recent review concluded that their biases are a complex phenomenon influenced by numerous factors, including genome composition, guanine and cytosine (GC) content, expression level, gene length, and recombination rates [1]. In this paper, I present a new plot chart and show a more straightforward explanation of the primary function of synonymous codon usage and its bias.

Materials and methods

First, I calculated each protein's amino acid compositions and its gene's nucleotide compositions from the publicly available proteome coding sequence (CDS) dataset of 23 different bacteria [2–24]. Next, I calculated the maximum and minimum GC contents of the possible gene variations of the amino acid composition of each protein. Finally, they were plotted together by their actual GC content on a scatter plot. Eventually, 81,237 proteins from 23 different bacteria species were plotted.

I selected the 23 bacteria species by referring to the list of reference proteomes for the "Quest for Orthologs" project on the EMBL-EBI website to avoid the influence of selection bias [25]. Since this list does not include genetic information, the datasets of each bacteria species were downloaded from the NCBI website before use [2–24].

I used Microsoft® Excel for Mac v16.62 (Microsoft Corporation, Redmond, WA, USA) for composition calculations and JMP® 16.2.0 (SAS Institute Inc., Chicago, IL, USA) for creating the scatter plot.

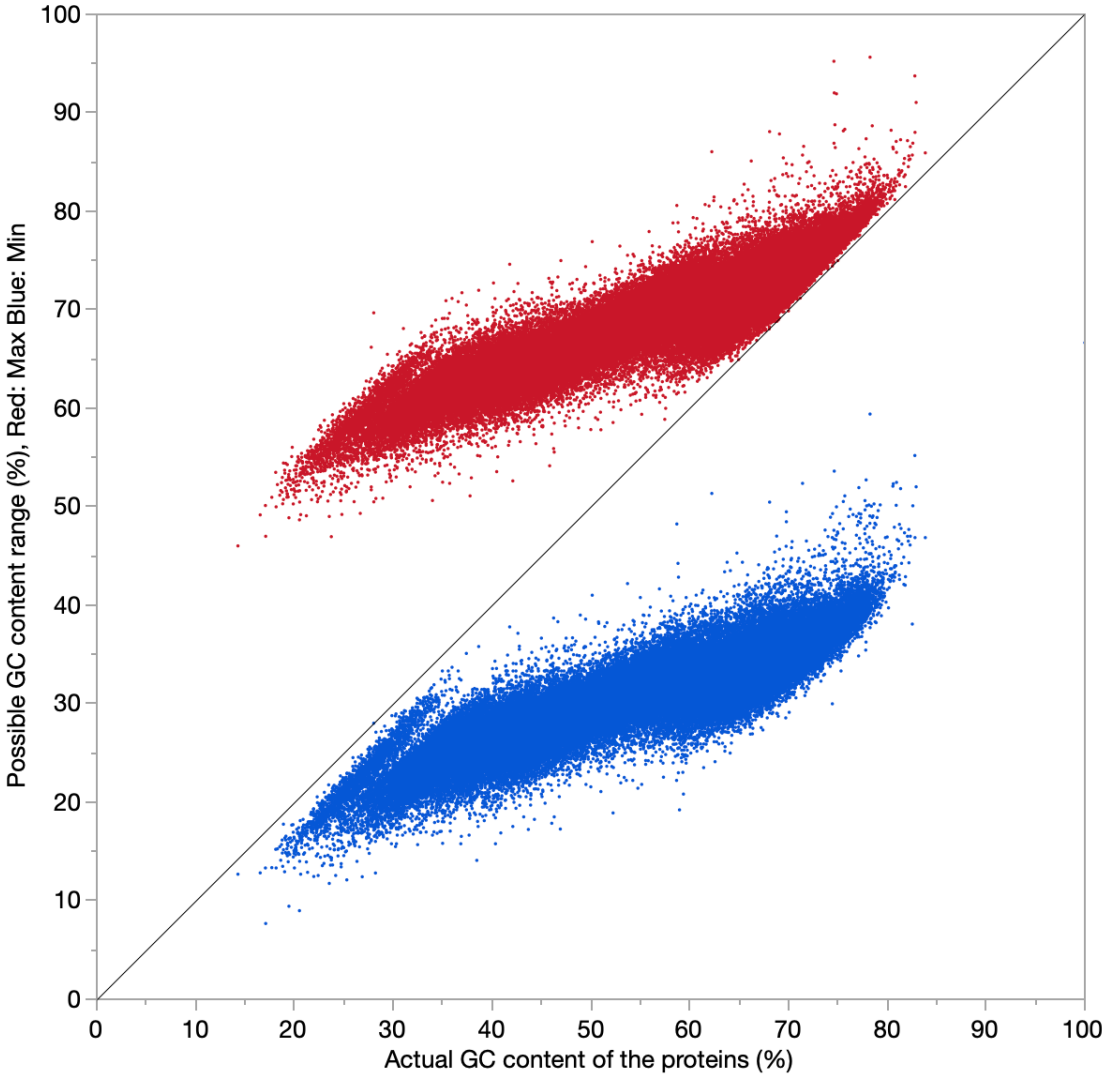
Results

The scatter plot of the possible GC range (maximum and minimum) and the actual GC content of the gene are shown in Figure 1.

The plot shows a clear tendency. Proteins with lower actual GC content genes are coded for by genes closer to the minimum possible GC content. On the other hand, proteins with higher actual GC content genes are coded for by genes closer to the maximum possible GC content.

Figure 1

Scatter plot of the possible GC range (max and min) and the actual GC content of the gene



Scatter plot of the range of possible GC content of each protein gene (y-axis) and its actual GC content (x-axis). The upper (red) dots indicate the maximum GC content, and the lower (blue) dots indicate the minimum values. The slashed line on the chart represents the actual GC content, which lies between the maximum and minimum values. There is a clear tendency for proteins with lower actual GC content to lie closer to the minimum, and proteins with higher actual GC content to lie closer to the maximum.

Discussion

The plot showed a clear tendency. Describing this tendency in another way, “genes with higher GC content dominantly use higher GC content codons among the synonymous codons,” and “genes with lower GC content dominantly use lower GC content codons among the synonymous ones.” (Figure 1). Therefore, I considered that the tendency of synonymous codon usage bias uniformly works toward offsetting the variation in GC content.

Meanwhile, all maximum and minimum values plots are aligned on each narrow band. Hence, I considered that the optimal amino acid composition range for the proteome is relatively limited, and organisms use this GC offset function to meet the range conditions.

On examining the CDS dataset, I also found that the variations in GC content are relatively small in some bacteria species. If the primary purpose of codon usage bias is to offset GC content variation, organisms with such a small GC content variation would have less necessity to adjust their codon usage biases for the GC content variations. Moreover, it might be possible for these organisms to save intracellular energy and physical resources by concentrating on using a particular synonymous codon and suppressing others. Therefore, through this discussion, I speculated that this cost reduction with these synonymous codon selections might be the origin of the bacterial codon usage bias.

In this study, I made a new explanation of codon usage bias with a unique chart. However, what is unique in my research? I explain this as follows. Previous studies have examined how organisms choose a codon among several synonymous codons [1, 26]. However, codon usage bias is a part of the translation function of the genetic code table. Therefore, in this study, I investigated the translation function itself; in other words, the relationship between input nucleic acids and output amino acids.

For this investigation, there are two possible approaches. One is to examine all the possible output amino acid compositions from a given nucleic acid composition and to compare them with their actual output composition. Another is to examine all the possible input nucleic acid compositions from a given output amino acid composition and compare them with their actual input composition. The calculated amount of the former approach would exponentially increase according to the increased amino acid residue numbers. On the other hand, I could easily calculate the latter approach when only examining the maximum and minimum possible GC content values. This is how I took this new approach and reached this finding.

Conclusion

In this paper, I showed that synonymous codon usage and its bias in bacterial proteomes primarily offset GC content variation to maintain optimal amino acid compositions. Synonymous codons are part of the genetic code table. Therefore, if synonymous codons and their usage bias have a GC offset function to maintain the optimal amino acid composition, it must be considered a fundamental function of the genetic code table assignment.

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