Brief Report

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Comparisons of Distribution of CpG Islands through the Sex-Chromosomes between Rat (*Rattus norvegicus*) and Swine (*Sus scrofa*)

Shilpa Tewari

College of Animal Biotechnology, Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana 141004 Punjab, India; shilpatewari781@gmail.com

Abstract: CpG islands typically occur at or near the transcription start site of genes, particularly housekeeping genes, invertebrates. Normally a C (cytosine) base followed immediately by a G (guanine) base (a CpG) is rare in vertebrate DNA because the cytosines in such an arrangement tend to be methylated. Described DNA methylation mediated gene silencing occurs by direct inhibition of transcription factor binding to their relative sites and by recruitment of methyl binding domain proteins. The present study aims at predicting the CpG islands using Perl and R environment codes. The results indicated that the average length of the CpG islands in the X-chromosomes is comparable, however, the number of CpG islands is three times in swine (13539), as compared to that of rats (4465). The average CpG percent and the Average Guanine+Cytosine percent are also similar in the X-Chromosomes of both species. Similar results were evident for Y-Chromosome. The results obtained need validation through wet-lab experimentation.

Keywords: CpG island; in silico prediction; X-chromosome; Y-chromosome

Introduction

CpG islands are the developed key genomic features in epigenetic research. The role of DNA methylation can be discovered by characterizing their methylation state. By mapping of DNA methylation in various cell types, it was clear the lack of methylation in the majority of CpG islands, but numerous cases were found of differentially methylated, or even constitutively methylated regions that are well defined as CpG islands based on their sequence content (Dindot et al., 2009). Antequera and Bird (1993) suggested that mammalian promoters belong to two different categories in terms of base composition and DNA methylation. The region is devoid of methylation that has a higher G+C content than the genome average, while the rest have a methylation pattern and base composition indistinguishable from bulk DNA. Regulatory regions are made up of a variable number of short modules to which activators and repressors bind in such a way that their integrated contributions result in the correct expression of the gene. Despite the sequence diversity among promoters, genes transcribed by RNA polymerase II can be classified in two different and mutually exclusive groups according to the distribution of CpG dinucleotides across their 5′ ends. The frequency of CpGs is the same as the genome average, which is roughly one of every 100 nucleotides. Genes belonging to the other group are surrounded by a region ~ 1 kb long where the frequency of CpGs is approximately 10 times higher than the genome average. CpG involves transcriptional regulation and their potential use as markers to localize genes in genome sequences. The contrast between the island and non-island DNA is so sharp because CpGs occur at the expected frequency at CpG islands based on their G+C content, whereas CpGs in bulk DNA is 20% of their expected frequency, due to the spontaneous deamination (Suzuki and Bird (2008), Illingworth et al. (2008), Futscher (2002)).

Materials and Methods

The present study aims to identify CpG islands using a comparative biocomputational approach**.** The sequence of in X Chr and Y Chr *Rattus norvegicus* and *Sus scrofa* will be downloaded from NCBI Genome (https://www.ncbi.nlm.nih.gov/genome). The downloaded chromosome sequences were subjected to notepad++ for further modification. Then the sequences were subjected to Perl code for predicting the statistical data. The statistical data were subjected to an R programming environment for further cleaning and getting the predicted data.

Results and Discussion

The average island length of *Rattus norvegicus* in the X-chromosome is 596.19 and *Sus scrofa* has an average island length of 580.44 it means *Rattus norvegicus* has a greater average island length as compared to *Sus scrofa* as shown in the table. Variation in island length is more in both species. The standard error of the CpG island of the X-chromosome of *Rattus norvegicus* is 3.68 and in *Sus scrofa* the value is2.02. It means *Rattus norvegicus* has a greater variation in their genome. Island number varies in both species. X-chromosome of *Rattus norvegicus* island number is 4465 and in *Sus scrofa* the value is 13539. It means *Sus scrofa* has more island number as compared to *Rattus norvegicus*. Average G+C concentration is close to each other in both species. In the X-chromosome of *Sus scrofa*, the value is54.5 and the case of the *Rattus norvegicus* value is 53.03. The average CpG concentration is close to each other as shown in Table 1. The value of average CpG concentration in *Rattus norvegicus* is 4.94 and in the case of *Sus scrofa* it is 5.13. It means there is a small difference in the value of both species. The average ratio (Observed CpG/Expected CpG) is 0.73 in *Rattus norvegicus* in the case of *Sus scrofa* 0.7. It means the value of the average ratio of *Rattus norvegicus* is greater than the value of *Sus scrofa*. We have got the minimum island length which is the same in both species. Both species have a similar value that is 500. The maximum island length value of *Sus scrofa* is 5639 and in the case of *Rattus norvegicus* that is 4484. It means *Sus scrofa* has a maximum island length as compared to *Rattus norvegicus*.

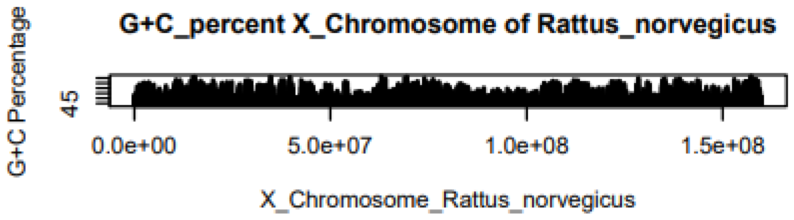
Table 1. Final parameters of CpG island in in X-chromosome of Rattus norvegicus and *Sus scrofa.*

Features	**Rat**	**Swine**
Average Island Length	596.19	580.44
Standard error (Island Length)	3.68	2.02
Island Number	4465	13539
Average G+ C percent	53.03	54.5
Standard error G+ C percent	0.07	0.05
Average CpG percent	4.94	5.13
Standard error CpG percent	0.01	0.01
Average Ratio	0.73	0.70
Standard error Ratio	0	0
Minimum Island length	500	500
Maximum Island length	4484	5639

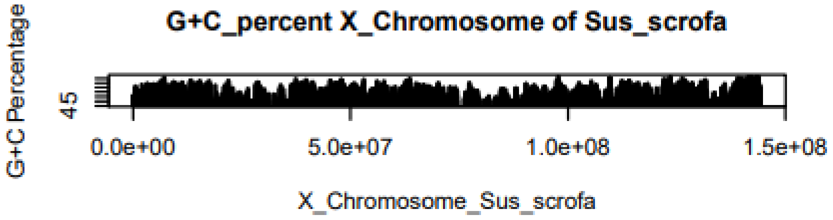
The average island length of *Rattus norvegicus* in Y-chromosome is 560.46 and *Sus scrofa* has an average island length of 567.28 it means *Sus scrofa* has a greater average island length as compared to *Rattus norvegicus* as shown in the table. Variation in island length is more in both species. The standard error of the CpG island of Y-chromosome of *Rattus norvegicus* is 12.67 and in *Sus scrofa* the value is 4.55. It means *Rattus norvegicus* has a greater variation in their genome. Island number varies in both species. Y-chromosome of *Rattus norvegicus* island number is 110 and in *Sus scrofa* the value is 1820. It means *Sus scrofa* has more island number as compared to *Rattus norvegicus*. Average G+C concentration is close to each other in both species. In the Y-chromosome of *Sus scrofa* the value is 53.86 and in the case of the *Rattus norvegicus* value is 52.7. The average CpG concentration is close to each other as shown in Table 2. The value of average CpG concentration in *Rattus norvegicus* is 4.73 and in the case of *Sus scrofa,* it is 4.96. It means there is a small difference in the value of both species. The average ratio (Observed CpG/Expected CpG) is 0.7 in *Rattus norvegicus* in the case of *Sus scrofa* 0.7. We have got the minimum island length which is the same in both species. Both species have a similar value that is 500. The maximum island length value of *Sus scrofa* is 2650 and in the case of *Rattus norvegicus*, that is 1059. It means *Sus scrofa* has a maximum island length as compared to *Rattus norvegicus*.

Table 2. Final parameters of CpG island in in Y-chromosome of Rattus norvegicus and *Sus scrofa.*

Features	**Rat**	**Swine**
Average Island Length	560.46	567.28
Standard error Island Length	12.67	4.55
Island Number	110	1820
Average G+ C percent	52.7	53.86
Standard error G+ C percent	0.37	0.11
Average CpG percent	4.73	4.96
Standard error CpG percent	0.06	0.02
Average Ratio	0.7	0.7
Standard error Ratio	0.01	0
Minimum Island length	500	500
Maximum Island length	1059	2650

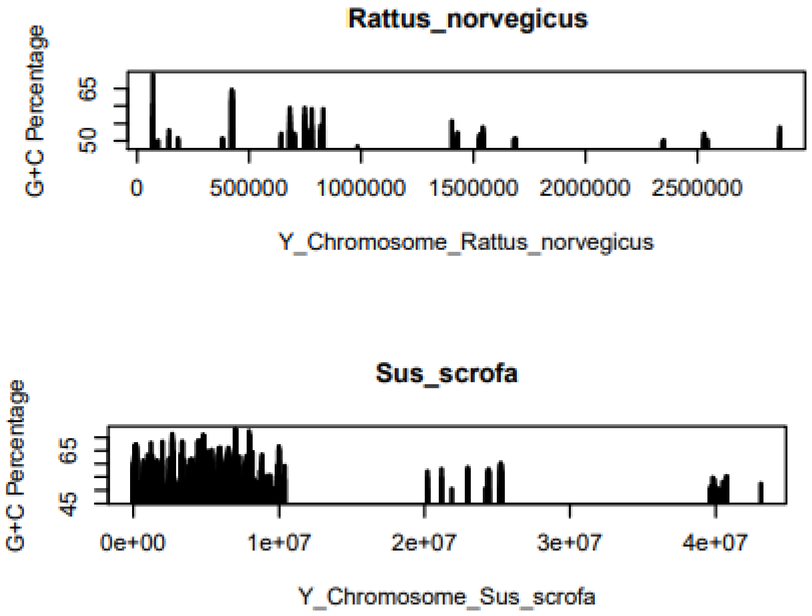


(A)



(B)

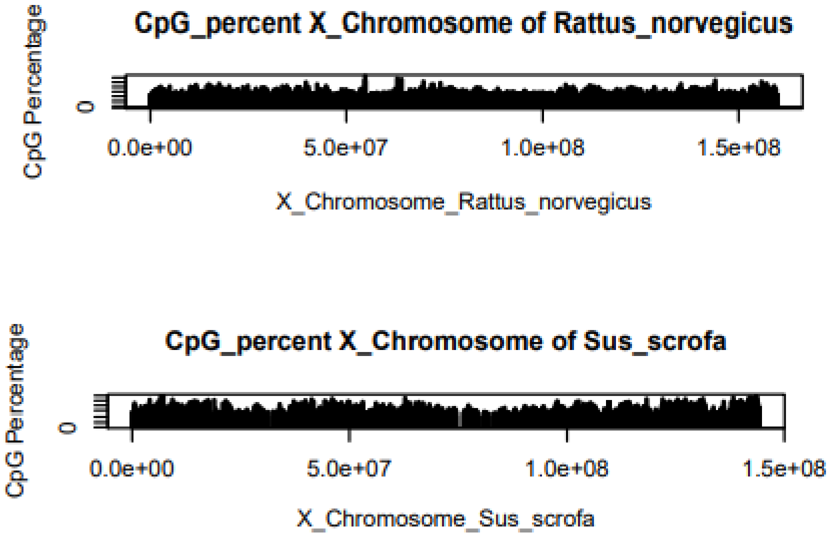
Figure 1. G+C% of *Rattus norvegicus* in X-chromosome, (B) G+C% of *Sus scrofa* in X-chromosome. The X-axis of the graph describes the length of the chromosome. Where e is the exponential constant, for example, 5.0e+07 can be written as 5*107. On the Y-axis, the graph shows the G+C%. At some positions, we have obtained the higher G+C% whereas at some positions we have obtained the lower G+C%.



(A)

(B)

Figure 2. (A) G+C% of *Rattus norvegicus* in Y-chromosome, (B) G+C% of *Sus scrofa* in Y-chromosome. The X-axis of the graph describes the length of the chromosome. Where e is the exponential constant, for example, 5.0e+07 can be written as 5*107. On the Y-axis, the graph shows the G+C%. At some positions, we have obtained the higher G+C% whereas at some positions we have obtained the lower G+C%.



(A)

(B)

Figure 3. (A) CpG Percentage of *Rattus norvegicus* in X-chromosome, (B) CpG Percentage of *Sus scrofa* in X-chromosome. The X-axis of the graph describes the length of the chromosome. Where e is the exponential constant, for example, 5.0e+07 can be written as 5*107. On the Y-axis, the graph shows the CpG Percentage.

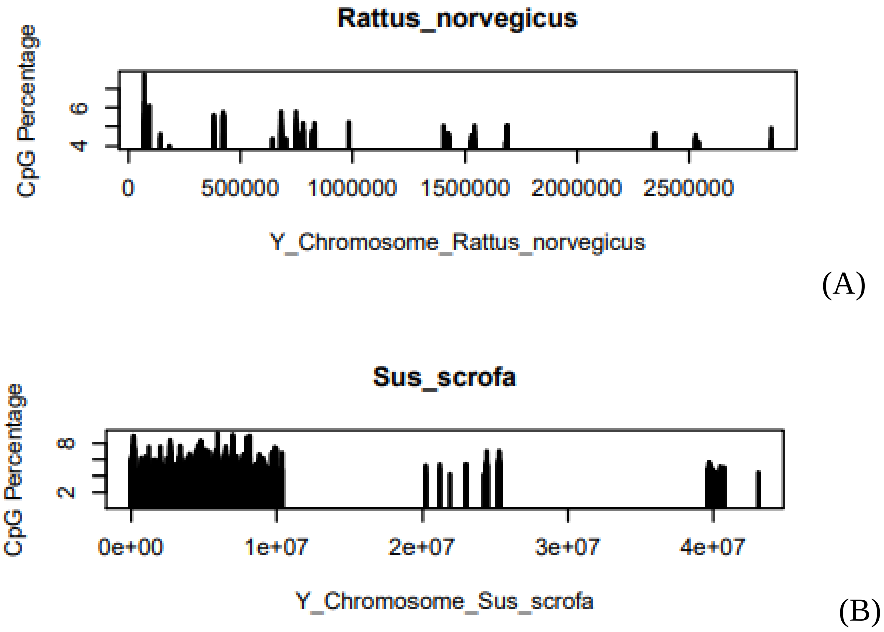


Figure 4. (A) CpG Percentage of *Rattus norvegicus* in Y-chromosome, (B) CpG Percentage of *Sus scrofa* in Y-chromosome. The X-axis of the graph describes the length of the chromosome. Where e is the exponential constant, for example, 5.0e+07 can be written as 5*107. On the Y-axis, the graph shows the CpG Percentage.

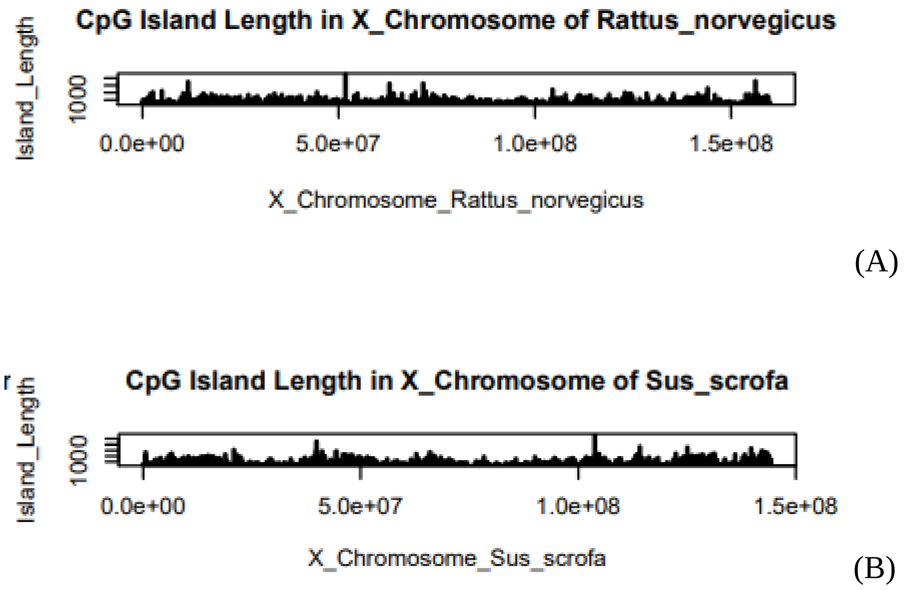


Figure 5. (A) Island Length of *Rattus norvegicus* in X-chromosome, (B) Island Length of *Sus scrofa* in X-chromosome. The X-axis of the graph describes the length of the chromosome. Where e is the exponential constant, for example, 5.0e+07 can be written as 5*107. On the Y-axis, the graph shows the Island Length.

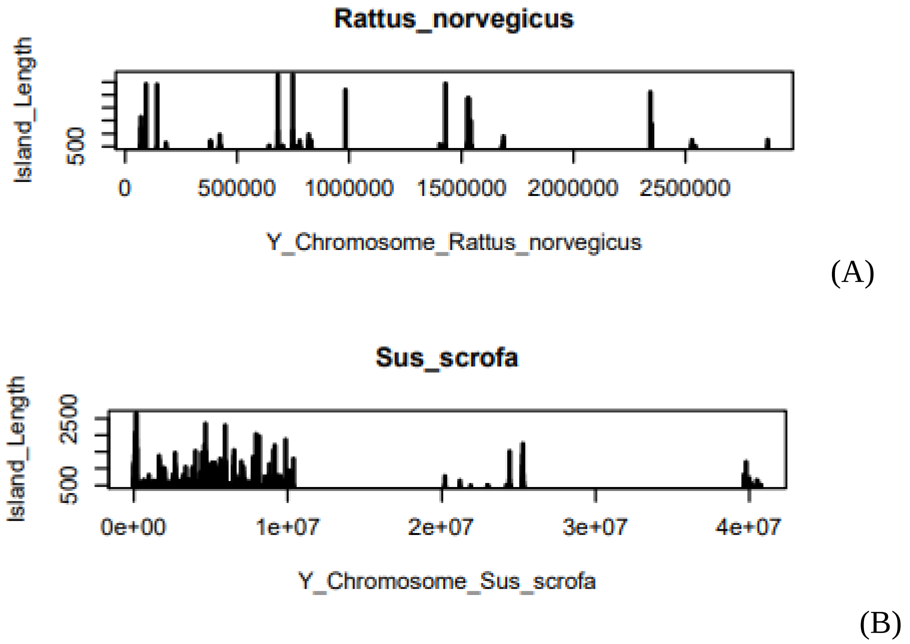


Figure 6. (A) Island Length of *Rattus norvegicus* in the Y-chromosome, (B) Island Length of *Sus scrofa* in the Y-chromosome. The x-axis of the graph describes the length of the chromosome. Where e is the exponential constant, for example, 5.0e+07 can be written as 5*107. On the Y-axis, the graph shows the Island Length.

In prokaryotes it is associated with restriction-modification systems, targeting short palindromic or nearly palindromic sites. DNA methylation is used as a signal for the regulation of a particular DNA protein interaction. Methylation systems typically comprise of a DNA methylase and one or more DNA binding proteins which will overlap the target methylation site on DNA, subsequently blocking methylation of that site.The laboratory rat (*Rattus norvegicus*) have incalculable benefits to human health it is mostly used in experimental medicine and drug production. The diploid number chromosome is 42 in *Rattus norvegicus* and has an autosomal complement consisting of seven pairs of metacentrics, three pairs of submetacentric, and 10 pairs of acrocentrics. The X-chromosome is an acrocentric of medium size and the Y is the smallest acrocentric of the complement (Duncan and Van Peenen 1971). Rattus norvegicus, has multiple copies of Sry Y-chromosome while the maximum mammals have only a single copy (Turner *et al.* 2007). Pigs (*Sus scrofa*) have been domesticated in the old world since antiquity. Pig provides valuable products to humans; including fertilizer, leather, pork, and a variety of medicines an indigenous pig has a diploid number of chromosomes (2n) of 38, which includes 18 pairs of autosomes and one pair of allosomes or sex-chromosomes. First, 5 pairs of autosomes are submetacentric, the next 2 pairs are subtelocentric, a subsequent 5 pairs are metacentrics, the remaining six pairs are telocentric and sex-chromosomes are metacentrics in nature. The first chromosome was the longest pair and a thirteenth pair was the second largest, while a Y-chromosome was the smallest in the karyotype of the pig (Vishnu *et al.* 2015).

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