DOI: 10.26717/BJSTR.2017.01.000324

Jean-claude Perez. Biomed J Sci & Tech Res

ISSN: 2574-1241

Research Article Open Access

CRISPR Technology Challenge Facing the Numerical Integrity of Whole Human Genome DNA

Jean-claude Perez*

Department of Maths and Computer Science, Retired interdisciplinary researcher (IBM), France

Received: August 05, 2017; **Published:** September 01, 2017

***Corresponding author :** Jean-claude Perez, Maths and Computer Science Retired interdisciplinary researcher (IBM), 7 avenue de terre-rouge F33127 Martignas, Bordeaux metropole, France, Tel: 33 0781181112; Email: jeanclaudeperez2@gmail.com

Abstract

Background: Global analysis of 3 human genomes of increasing levels of evolution (Neanderthal /Sapiens Build34 / Sapiens hg38) reveals 2 levels of numerical constraints controlling, structuring and optimizing these genome's DNA sequences. A global constraint - called "HGO" for "Human Genome Optimum" - optimizes the genome at its global scale. The same operator applied to each of the 24 individual chromosomes reveals a hierarchical structure of these 24 chromosomes.

Results: Then analysing the single strand DNA CG / TA proportions at whole chromosomes and genome scale reveals strong fine-tuned numerical ratios evidencing the "closure" nature (Varela's autopoiesis theory) of whole human genome.

Keywords: Human genome; CRISPR; Biomathematics; Evolution; Autopoiesis

Introduction

Thanks to the CRISPR (Clustered regularly interspaced short palindromic repeats) technology, it is now possible to locally modify the genomes, and particularly the human genome [1]. Almost simultaneously, the fractal and global structures of the human genome were demonstrated [2]. In such a context, apart from ethical questions, can a local technology as powerful as CRISPR be applied, ignoring its possible effect on the possible global and long-range equilibrium and balancing at the chromosome scale or even the entire genome scale? For more than 25 years, we have been looking for possible global, even numerical, structures that would organize DNA, genes, chromosomes and even whole genomes [3-6].

We have already demonstrated a numerical structure at the scale of each human chromosome as well as on the whole genome [7-15]. In [10] we have already highlighted this numerical value of 0.6909830056, the HGO in this article: it controls the population of triplets codons analysing single stranded DNA sequence from the whole human genome.

Materials and Methods

Analyzed whole human genomes

We analyzed completely and systematically each of the 24 chromosomes of each of the following three reference genomes:

A. Neanderthal genome

B. Sapiens Build34

C. Sapiens hg38

Computing the HGOs

Let us now distinguish the two types of HGO that will be discussed:

A. Theoretical HGO (tHGO)

tHGO = (3-Phi)÷2 = 0.6909830056, where Phi is the Golden Ratio Phi = 1.618033989

B. Reference female HGO (rwHGO) : rwHGO = 0.6913477936

error (tHGO – rwHGO) = 0.6909830056 - 0.6913477936 = ¯0.0003647879784 and

C. Reference male HGO (rmHGO) : rmHGO = 0.6922864236

error (tHGO – rmHGO) = 0.6909830056 - 0.6922864236 = ¯0.001303417973

HGOwoman (LOH chr n) = [(sum C+G single strand 1 to 22 chromosomes except chrn) + (sum C+G chrn) + (sum C+G chrX) + (sum C+G single strand 1 to 22 chromosomes except chrn) + (sum C+G chr LOH n) + (sum C+G chrX)] / [(sum T+A single strand 1 to 22 chromosomes except chrn) + (sum T+A chrn) + (sum T+A chrX) + (sum T+A single strand 1 to 22 chromosomes except chrn) + (sum T+A chr LOH n) + (sum T+A chrX)]

HGOman (LOH chr n) = [(sum C+G single strand 1 to 22

chromosomes except chrn) + (sum C+G chrn) + (sum C+G chrX) + (sum C+G single strand 1 to 22 chromosomes except chrn) + (sum C+G chr LOH n) + (sum C+G chrY)] / [(sum T+A single strand 1 to 22 chromosomes except chrn) + (sum T+A chrn) + (sum T+A chrX) + (sum T+A single strand 1 to 22 chromosomes except chrn) + (sum T+A chr LOH n) + (sum T+A chrY)]

Results and Discussion

In all that follows, the general methodology will be as follows: we calculate, for the 46 chromosomes constituting each genome studied, only the single-stranded DNA sequences. In these sequences, we count the relative populations of bases T + A on the one hand, and C + G on the other hand.

Genome Unity

HGO of the 3 whole genomes : Neanderthal, Sapiens Build34 and Sapiens HG38: The three genomes we compare here are differentiated on the one hand by their respective evolution levels, on the other hand by the sample of individual genomes of which they form the syntheses, and finally by the precision of the sequencing of DNA.

The detailed analysis related to the 3 whole genomes shows the various distances and errors between real computed HGOs for each genome and theoretical HGO optimum value = 0.6909830055. Particularly, it is found that the 3 HGOs calculated for the respective 3 genomes of Neanderthal, Sapiens (2003 Build34 and 2013 hg38 Sapiens) are very close to the ideal theoretical optimal HGO = 0.6909830056 (99.67% for the least optimal genome) [16-29]. It is also observed that female genomes (XX) are more optimal than male genomes (XY). On the other hand, the genomes of Neanderthal and Sapiens (Build34 of 2003) have very close optimization levels. We believe this results from the fact that the precisions of their respective DNA sequencing are similar.

On the contrary, the hg38 genomes of 2013 show the most optimal levels, this is most certainly due to the deeper quality of their DNA sequencing (Figure 1). A summarizes HGO results for these 3 human genomes of varying levels of evolution.

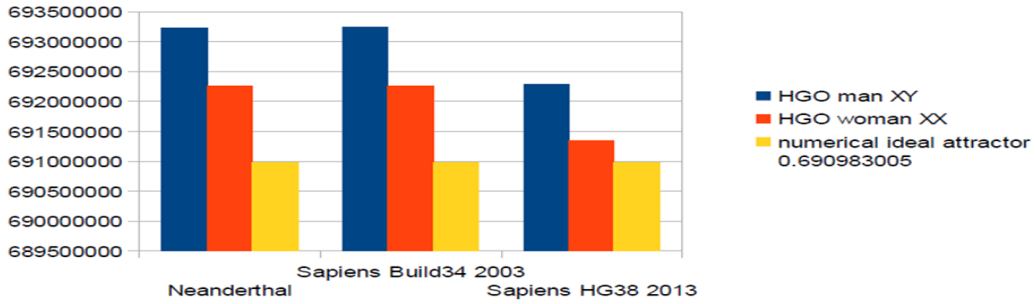

Figure 1: The respective HGOs of 3 human genomes of varying levels of evolution are shown here.

Considerations on this theoretical Human Genetic Optimum (HGO) of (3 – Phi) / 2: This formula is particularly simple. We can even make it more "beautiful", indeed: Since 1 + Phi = Phi * 2, we can write:

(3 – Phi) / 2 = C+G / T+A = (4 – (1+Phi)) / 2 = (4 – (Phi*2)) / 2 = (2*2 – Phi*2) / 2 = C+G / T+A

This new equivalent formula contains only the numbers "2" and "Phi".

A second track to be studied could consist in replacing this writing by:

(3 – Phi) / 2 = (3 – Phi) / (5 - 3) = C+G / T+A

By this artifice of writing, we thus make the "3" appear in the numerator and the denominator (!)

The formula then becomes:

A. (3-Phi) x (T+A) = 2 x (C+G) = (5-3) x (C+G)

B. 3(T+A) + 3 (C+G) = 5(C+G) + Phi(T+A)

C. 3(T+A+C+G) = 5(C+G) + Phi(T+A)

Therefore, if we consider that the single copy (single strand DNA) of the 24 chromosomes whole genomes XX or XY all lead to the same attractor HGO = (3-Phi) / 2, to write:

Considering the cumulative population of 24 chromosomes of the single human genome (single strand DNA),

We check the following Perfect Balance: "Three times the whole genome (T + A + C + G) = FIVE times (C + G) PLUS Phi times (T + A)"

A. Neanderthal

B. Sapiens Build34 2003

C. Sapiens HG38 2013

D. 689500000

E. 690000000

F. 690500000

G. 691000000

H. 691500000

I. 692000000

J. 692500000

K. 693000000

L. 693500000

Comparing HGO (Human Genome Optimum) for 3 Human Genomes: HGO man XY; HGO woman XX. numerical ideal attractor: 0.690983005.

Verification on 24 hg38 chromosomes single strand DNA:

A. CG = 1200551672

B. TA = 1737087441

C. 3×(CG+TA) = 8812917339

D. (5×CG)+(PHI×TA) = 8813424881

E. 8812917339÷8813424881 = 0.9999424126

F. 8812917339-8813424881 = ¯507542

Finally, it is remarkable that this formula is based on integers 3 or 5. In fact, these numbers are very small integers and they are Fibonacci numbers. It will therefore be interesting to postpone the error calculations on

the accuracy of these two integers 3 and 5:

(5×CG)+(Phi×TA) = 8813424881 / (CG+TA) = 2937639113 8813424881 / 2937639113 = 3.000172772 and

3×(CG+TA) = 8812917339 - (Phi×TA) = 2810666521 8812917339 -2810666521 = 6002250818 CG = 1200551672 6002250818÷CG = 4.999577243

The exact formula can then be written:

3.000172772 (T+A+C+G) = 5(C+G) + Phi(T+A) or 3(T+A+C+G) = 4.999577243 (C+G) + Phi(T+A)

Chromosomes Hierarchy

HGO spectral hierarchy of the 24 Human chromosomes: The following 2 figures (Figure 2) (Figure 3) illustrate the hierarchical spectrum of the individual HGOs of each of the 24 chromosomes for each of the three genomes analyzed. It should be noted that the upstream / downstream tipping point lies between chromosomes 14 and 21, which is closely related to the probable mechanisms explaining trisomy21 (whose disorders involve precisely these two chromosomes). Finally, we note that it is the downstream region (Figure 3) that contributes the most to the superiority of optimality of sapiens hg38 compared to sapiens Build34. We have sorted the 24 chromosomes by increasing values of CG/TA ratios in the 3 cases of compared genomes [29-35].

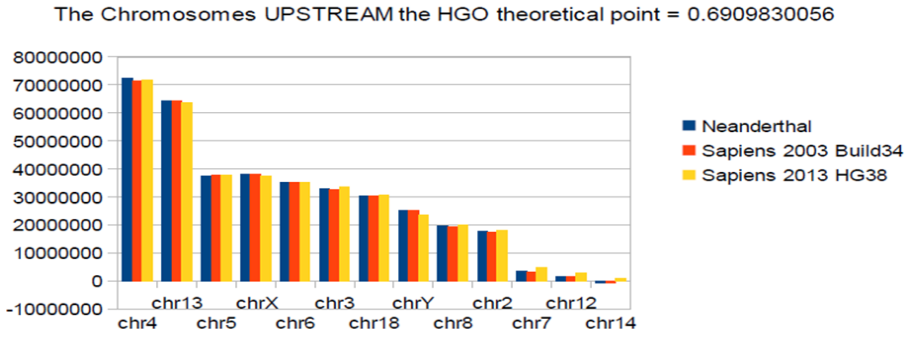

Figure 2: Chromosomes : HGO diversity of human chromosomes UPSTREAM of the numerical attractor HGO = 0.6909830056.

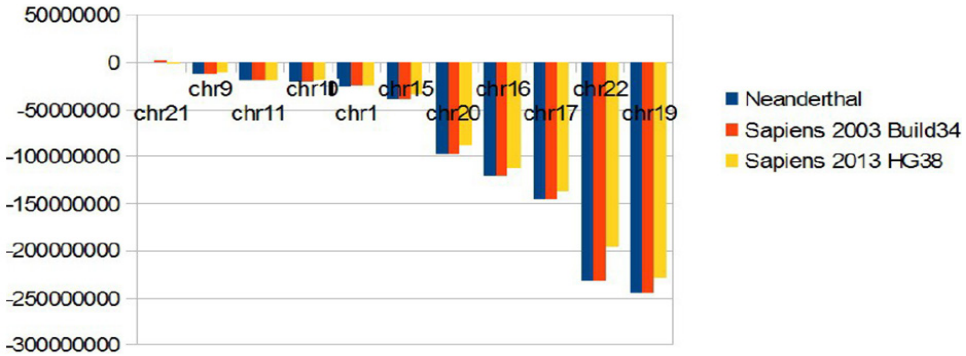

Figure 3: Chromosomes : Diversity of HGOs of human chromosomes DOWNSTREAM of the numerical attractor HGO = 0.6909830056.

It then reveals a hierarchical classification scale of 24 chromosomes ranging from 1 / Phi (chromosome4) to 3/2 Phi (chromosome 19) (Table 1).

Table 1: The respective populations and ratios of each of the 24 chromosomes of the genome HG38.

chr	C+G	T+A	CG/TA
UP			
4	72568001	117184666	0.6192619178
13			

	37772797	60210328	0.627347471
5			
	71611274	109654104	0.6530651511
0	61221521	93671508	0.6535767632
6	67360020	102718502	0.6557729979
3	78577742	119522393	0.6574311309
18	31856106	48233499	0.6604560453
0	10572683	15842360	0.66736793
8	58133960	86634176	0.6710280248
2	96769083	143779145	0.6730397722
7	64696843	94273288	0.686269084
12	54275482	78862334	0.6882307338
14	36982791	53585358	0.6901659778
DOWN			
21	16411625	23676994	0.693146478
9	50270473	71520077	0.70288617
11	55885058	78648684	0.7105657102
10	55359481	77903481	0.7106162689
1	96166571	134314441	0.7159808751
15	35578844	49062481	0.7251741713
20	28010605	35933652	0.7795089962
16	36472718	45333225	0.8045471726
17	37575444	45344760	0.8286612169
22	22 18406838 20752939 0.8869509037	22 18406838 20752939 0.8869509037	22 18406838 20752939 0.8869509037
19	28015712	30425046	0.9208108346

Cohesion Chromosomes / Genome

About the hierarchical classification of 24 single stranded chromosomes

A. chr4 -10000000

B. chr13 0

C. chr5 10000000

D. chrX 20000000

E. chr3 30000000

F. chr18 40000000

G. chr Y 50000000

H. chr8 60000000

I. chr 2 70000000

J. chr7 80000000

Diversity of Chromosomes from 3 Human Genomes The Chromosomes UPSTREAM the HGO theoretical point = 0.6909830056; Neanderthal, Sapiens 2003 Build34, Sapiens 2013 HG38 In the following, we demonstrate a real interaction, a kind of "dialogue" with feedback between the equilibrium of the whole genome and the part of each of the individual chromosomes. We must now regulate this high level of remarkable numerical constraints which seem to "frame" the CG and TA populations of each of the 24 human chromosomes on the one hand and of the entire genome on the other hand. This will be verified Diversity of Chromosomes from 3 Human Genomes. The Chromosomes UPSTREAM the HGO theoretical point = 0.6909830056; Neanderthal, Sapiens 2003 Build34, Sapiens 2013 HG38 (Table 2).

Table 2: Evidence of strong numerical constraints surrounding the relative populations C+G / T+A constituting the hierarchical metastructure of the 24 chromosomes in humans and large primates.

Genome	Extremum Top CG/TA Chr4			Extremum Down CG/TA chr19		Spectral Limits (CG/TA chr19) - (CG/TA Chr4)
	Value	Error CG/TA Chr4 vs 1/Phi	Value	Error CG/TA chr19 vs 3/2 Phi	Value	Error (3/2 Phi) – Spectral Limits

Sapiens HG38	0.6192619178	¯0.0012279291	0.9208108346	0.0062401484	0.3015489168	0.0074680776
Sapiens BUILD34	0.6193778165	-0.0013438278	0.9364951603	-0.0094441773	0.3171173438	-0.0081003495
Neanderthal	0.6185900969	0.0005561082	0.9366477274	0.0090406362	0.0095967444	0.3180576305
chimp	0.6152388655	0.0027951232	0.9279395824	0.0008885994	0.3127007169	0.0036837226
Orangutang	0.6143645844	0.0036694043	0.9252214497	0.0018295333	0.3108568653 -	0.001839871
Gorilla	0.6177456029	0.0002883858	0.9299418695	0.0028908865	0.3121962666	0.0031792723
macaque	0.6536608193	0.0356268306	0.929993709	0.002942726	0.2763328897	0.0326841046

In the following, we demonstrate a real interaction, a kind of "dialogue" with feedback between the equilibrium of the whole genome and the part of each of the individual chromosomes. We must now regulate this high level of remarkable numerical constraints which seem to "frame" the CG and TA populations of each of the 24 human chromosomes on the one hand and of the entire genome on the other hand. This will be verified.

References

1. Jun Wu (2016) In vivo genome editing via CRISPR/Cas9 mediated homology-independent targeted integration. Nature 540: 144-149.
2. Lieberman-Aiden (2009) Comprehensive mapping of long-range interactions reveals folding principles of the human genome. Science 326(5950): 289-293.
3. Perez JC (1991) Chaos DNA and neuro-computers: a golden link. Speculations in Science and Technology 14: 336-346.
4. Marcer PJ (1992) Order and chaos in DNA – the Denis Guichard Prizewinner: Jean-Claude Perez. Kybernetes 21: 60-61.
5. Perez JC (1997) L'adn Décrypté. Resurgence publisher Liege, Belgium.
6. Perez JC (2009) Codex Biogenesis. Resurgence, Liege Belgium.
7. Perez JC (2010) Codon Populations in Single-Stranded Whole Human Genome DNA Are Fractal and Fine-Tuned by the Golden Ratio 1.618. Interdisciplinary Sciences: Computational Life Sciences 2: 1-13.
8. Perez JC (2011) Caminos Interdisciplinaios. Seminario CLAVE_INTER, Espacio Interdisciplinario, Universidad de la Republica Montevideo, Uruguay.
9. Perez JC (2011) Decoding Non-Coding DNA Codes: Human Genome Meta-Chromosomes Architecture. BIT Life.
10. Sciences' 3rd Annual World Vaccine Congress, Beijing, China.
11. Perez JC (2013) The "3 Genomic Numbers" Discovery: How Our Genome Single-Stranded DNA Sequence Is "Self-Designed" as a Numerical Whole. Applied Mathematics 4: 37-53.
12. Perez J (2015) Deciphering Hidden DNA Meta-Codes -The Great Unification & Master Code of Biology. J Glycomics Lipidomics 5:131.
13. Perez JC (2017) Fractal Self-similarity, Scale Invariance and Stationary waves Codes Architecture Human Chromosomes DNA sequences.
14. Neanderthal genome (2014) The complete genome sequence of a Neanderthal from the Altai Mountains. Nature 505: 43-49.
15. Sapiens Build (2003) Finishing the euchromatic sequence of the human genome. Nature 431: 931-945.
16. Sapiens HG38 (2013) Human genome Overview.
17. Friedman R, Cross M (2013) The Golden Ratio & Fibonacci Sequence: Golden Keys to Your Genius, Health, Wealth & Excellence. 1st edn, Hoshin Media, USA.
18. Pellionisz AJ, Graham R, Pellionisz PA, Perez JC (2012) Recursive Genome Function of the Cerebellum: Geometric Unification of Neuroscience and Genomics. In: Manto M, DL, et al . (Eds) Handbook of the Cerebellum and Cerebellar Disorders. 1st edn., Springer, USA.
19. Dokukin ME, Guz NV, Woodworth CD, Sokolov I (2015) Emergence of fractal geometry on the surface of human cervical epithelial cells during progression towards cancer. New J Phys 17(3).
20. Petoukhov S (2011) Mathematics of Bioinformatics: Theory, Methods and Applications. 1st edn., John Wiley & Sons, USA.
21. Rapoport DL (2015) Möbius strip and Klein Bottle Genomic Topologies, Self reference, Harmonics and Evolution, Life.
22. Montagnier L (2017) Water Bridging Dynamics of Polymerase Chain Reaction in the Gauge Theory Paradigm of Quantum Fields. Water 9(5): 339.
23. Persaud, Dharam, O'Leary, James P (2015) Fibonacci Series, Golden Proportions, and the Human Biology. HWCOM Faculty Publications. Paper 27.
24. Hengwu Li, Daming Zhu, Caiming Zhang, Huijian Han, Keith A Crandall (2014) Characteristics and Prediction of RNA structure. BioMed Research International 8.
25. Vaezi A, Barkeshli M (2014) Fibonacci Anyons From Abelian Bilayer Quantum Hall States. Physical Review Letters 113.
26. Marshall P (2015) Evolution 2.0. Benbella Books, USA. (ISBN 1940363802).
27. Roman V Yampolskiy (2017) On the origin of synthetic life: attribution of output to a particular algorithm. The Royal Swedish Academy of Sciences, Phys. Scr.
28. Cristian Tomasetti (2017) Stem cell divisions, somatic mutations, cancer etiology, and cancer prevention. Science 1330-1334.
29. Perez JC (2017) Sapiens Mitochondrial DNA Genome Circular Long Range Numerical Meta Structures are Highly Correlated with Cancers and Genetic Diseases mDNA Mutations. J Cancer Sci Ther 9:512-527.
30. Perez (2017) DUF1220 Homo Sapiens and Neanderthal fractal periods architectures breakthrough SDRP. Journal of Cellular and Molecular Physiology 1(1).
31. Perez JC, (2017) Humans and Primates Chromosomes4 Fractal CODES: periodic stationnary waveforms charaterizing and differentiating Neanderthal and Sapiens whole chromosomes DNA sequences.
32. Perez JC (2017) Global and long range fractal differences between sapiens and neanderthal genomes.
33. Perez JC (2017) Decyphering "the MASTER CODE ®" Structure and Discovery of a Periodic Invariant Unifying 160 HIV1/HIV2/SIV Isolates Genomes. Biomed J Sci & Tech Res 1(2)-2017.
34. Varela FJ (1981) Autonomy and autopoiesis. In: Roth G & Schwegler H (Eds.) Self-organizing systems: An interdiciplinary approach. Campus Verlag, Frankfurt/New York: 14–24.
35. Kellie A, Schaefer (2017) Unexpected mutations after CRISPR-Cas9 editing in vivo, Nature. Nature Methods 14(6): 547-548.