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SARS-CoV2 Variants and Vaccines mRNA Spikes Fibonacci Numerical UA/CG Metastructures

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ABSTRACT.

In this paper, we suggest a biomathematical numerical method analysing mRNA nucleotides sequences based on UA/CG Fibonacci numbers proportions.
This method is used to evaluate then compare the spike genes related to the main SARS-CoV2 VARIANTS circulating presently within the world.
The 9 main results proposed to be reproduced by peers are:

1/ SARS-CoV2 genome and spike evolution in one year 2020-2021.
2/ SARS-CoV2 Origins.
3/ Comparing 11 reference variants spikes.
4/ analysing 32 CAL.20C california variant patients spikes.
5/ Toward a meta mRNA Fibonacci gene end message code.
6/ analysing S501 UK, S484 South Afrika and « 2 mutations » IINDIA variants.
7/ Suggesting a possible variants spike mRNA palindrome symmetry metastructure improving mRNA stability then infectuosity.
8/ Analysing Fibonacci Metastructures in the mRNA coding for the vaccines PFIZER and MODERNA.
9/ Does the CG-rich modification of the synonymous codons of the spikes of the 2 mRNA vaccines affect the expression and quantity of SARS-CoV2 antibodies?

Particularly, we suggest the following conjecture at mRNA folding level :
CONJECTURE of SARS-CoV2 VARIANTS:
The growth of long Fibonacci structures in the shape of "podiums" for almost all of the variants studied (UK, California, South Afrika, India, etc.) suggests the probable folding of the Spike mRNA in the form of a "hairpin", which can strengthen the cohesion and the lifespan of this mRNA.

Finally, we show that this kind of Fibonacci matastructures disapears TOTALLY analysing the published mRNA sequences of PFIZER and MODERNA vaccines. One fact is certain, the 2 mRNAs of the Moderna and Pfizer vaccines will result in a low functionality of the spike vaccine because by doping these sequences in CG rich, their designers, in search of greater STABILITY of these RNAs will have built, according to us , sequences which, as soon as they are inserted into the human host, will seek to mutate, like SARS-CoV2 variants, towards CG ==> UA forms in order to improve, paradoxically, their STABILITY and probably also their LIFETIME.. Particularly, using new biomathematics theoretical methods (Master code and numerical standing waves), and comparing the Spikes of the 2 vaccines Moderna and Phizer, we conclude a very probable difference in stability and shelf life of the 2 respective mRNAs of these 2 vaccines. However, the *"State of the Art"* will tell you that their 2 protein sequences are strictly identical. However, by having modified their synonymous codons using different strategies, no one can guarantee that the quantity of antibodies generated will be identical in the 2 cases.

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I- INTRODUCTION.

30 years ago, after pioneering in A.I (Perez, 1988, 1991), we published in a paper entitled "chaos, dna, and neuro computers: the golden link" (Perez, 1991), a numerical method based on Fibonacci numbers to analyse dna sequences available at this time. In 2017 (Perez, 1997, 2017, 2019), we revisited this method to démonstrate application of this method in mtDNA mutations involved on Human cancers.
58 years ago, (Montagnier L. § Kingsley Sanders F., 1963) Luc Montagnier had described the isolation of an infectious double helix RNA in cells infected with a picornavirus. It is perhaps likely that there is an analogous form in the coronavirus, specifically on VARIANTS mRNA spikes. This structure is very stable, resistant to RNase, and can therefore retain the genetic information of the virus for a long time. The palindromic structures detected here could constitute a "hairpin" double stranded RNA form.

II- METHODS and DATA SOURCES.

2.1 - Computing FIBONACCI metastructures:

Consider the sequence of Fibonacci numbers

0 1 1 2 3 5 8 13 21 34 55 89 144 233 377 610 **987 1597 2584** 4181 6765 10946 17711 28657 46368 75025 121393 196418 317811 514229 832040 1346269 2178309 3524578 5702887...

Example of the SPIKE from WUHAN reference genome, this mRNA SPIKE is 3822 bases UCAG in length.
Recall WUHAN reference https://www.ncbi.nlm.nih.gov/nuccore/NC_045512
Severe acute respiratory syndrome coronavirus 2 isolate Wuhan-Hu-1, complete genome NCBI Reference Sequence: NC_045512.2

the longest Fibonacci structures would therefore measure 2584 bases.
When looking for such structures, the first one found is in 1200 location:
therefore, the bases located between 1201 and 3784 (1200 + 2584):
These 2584 bases are broken down respectively into:
1597 bases UA
et 987 bases CG

Here are the first 20 basics that the reader can easily check:
SPIKREF[1200+¼20]
G U A A UU A G A G G U G A U G A A G U
0 1 11 1 11 0 1 0 0 1 0 1 1 0 1 1 0 1.../...
U AA U U A A U A AA U 1597 bases UA

G U A A UU A G A G G U G A U G A A G U
1 0 0 0 0 0 0 1 0 1 1 0 1 0 0 1 0 0 1 0.../...
G G GG G G G 987 bases CG

The SPIKE analysis of this Wuhan-Hu-1 reference genome reports 63 metastructures of this type if we close the sequence on itself (as in mtDNA or bacteria) and 7 metastructures if we consider the mRNA sequence in its linear form, as will be the case throughout this study.

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2.2 - **Analysis of reference variants :**

We analysed 5 tracks of variants:
UK variant N501Y
South Afrika variant E484K
Brazil variant N501Y + E484K
California variant L452R
India variant E484Q + L452R

Main data source : https://covariants.org/

==> VARIANT South Afrika MUTATIONS :

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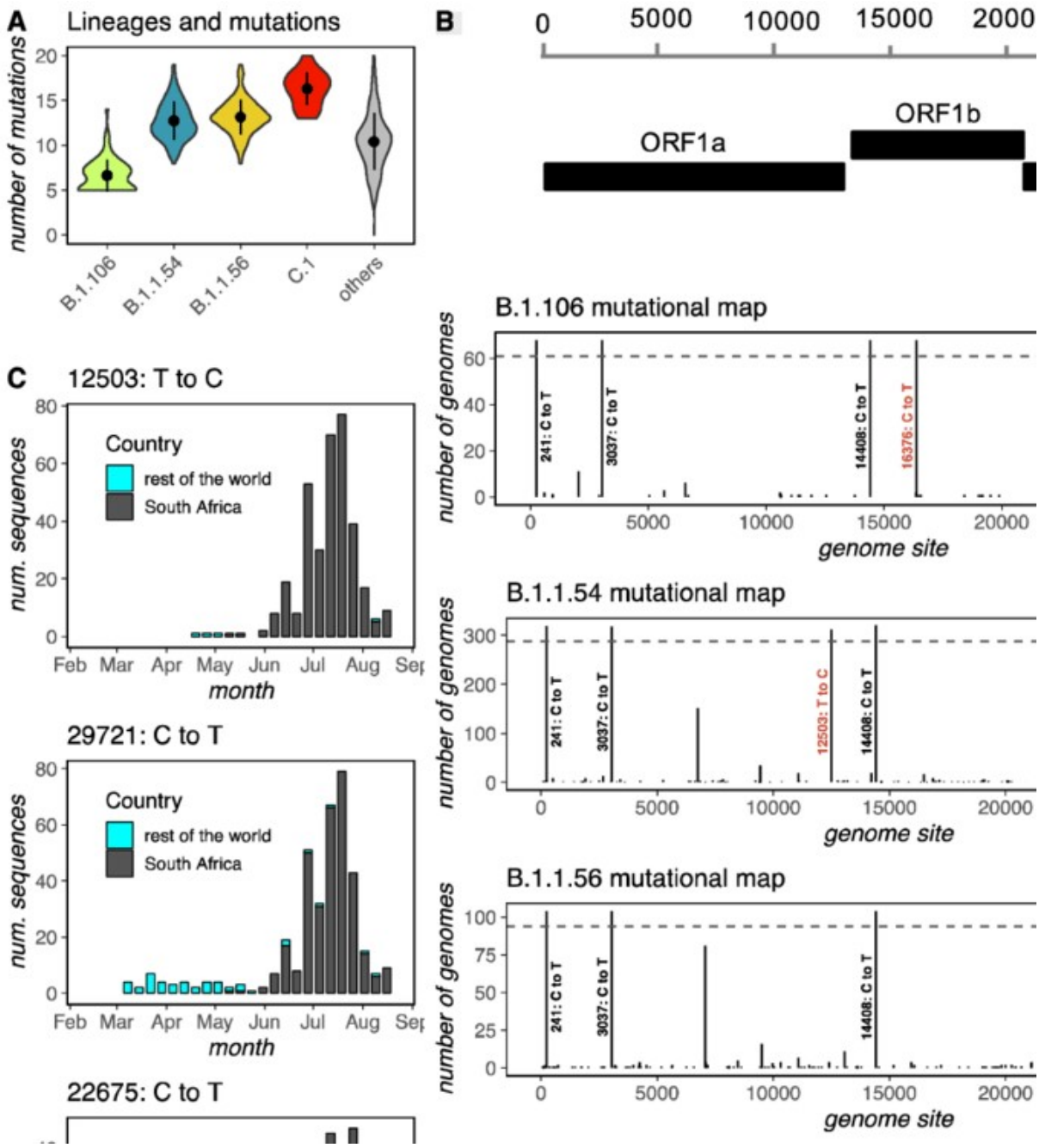

Figure 1- Mutations of the 4 reference variants from South Africa.

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==> VARIANT U.K. MUTATIONS :

Source (Da Silva Filipe et al, 2020), https://www.nature.com/articles/s41564-020-00838-z

Table 1 - Mutations in U.K. variant.

gene	nucleotide	amino acid
ORF1ab	C3267T	T1001I
	C5388A	A1708D
	T6954C	I2230T
	11288-11296 deletion	SGF 3675-3677 deletion
spike	21765-21770 deletion	HV 69-70 deletion
	21991-21993 deletion	Y144 deletion
	A23063T	N501Y
	C23271A	A570D
	C23604A	P681H
	C23709T	T716I
	T24506G	S982A
	G24914C	D1118H
Orf8	C27972T	Q27stop
	G28048T	R52I
	A28111G	Y73C
N	28280 GAT->CTA	D3L
	C28977T	S235F

==> VARIANT BRAZIL MUTATIONS :

Sources

First reference :

VARIANTS BRAZIL JAPAN (Naveca F et al, 2021)

https://virological.org/t/phylogenetic-relationship-of-sars-cov-2-sequences-from-amazonas-with-emerging-brazilian-variants-harboring-mutations-e484k-and-n501y-in-the-spike-protein/585

Phylogenetic relationship of SARS-CoV-2 sequences from Amazonas with emerging Brazilian variants harboring mutations E484K and N501Y in the Spike protein

second reference : (Gröhs Ferrareze P. A. , et al, 2021),

E484K as an innovative phylogenetic event for viral evolution: Genomic analysis of the E484K spike mutation in SARS-CoV-2 lineages from Brazil.https://www.biorxiv.org/content/10.1101/2021.01.27.426895v1

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Genomic Region	Nucleotide / Amino acid		
	B.1.1.28-AM-II	B.1.1.28(K417T/E484K/N501Y)	B.1.1.28(E484K)
ORF1a		T733C C2749T C3828T / ORF1a:S1188L A5648C / ORF1a:K1795Q	C100T
	A6319G A6613G	A6319G A6613G	
		C12778T	T10667G / ORF1a:L3468V C11824T C12053T / ORF1a:L3930F
ORF1b		C13860T G17259T / ORF1b:E1264D	
Spike		C21614T / S:L18F C21621A / S:T20N C21638T / S:P26S G21974T / S:D138Y G22132T / S:R190S A22812C / S:K417T G23012A / S:E484K A23063T / S:N501Y C23525T / S:H655Y C24642T / S:T1027I	G23012A / S:E484K
	G25088T / S:V1176F	G25088T / S:V1176F	G25088T / S:V1176F
ORF3a	T26149C / ORF3a:S253P	T26149C / ORF3a:S253P G28167A / ORF8:E92K	C28253T
N/ORF9b		C28512G / N:P80R, ORF9b:Q77E A28877T / N:R203K G28878C / N:R203K	G28628T / N:A119S

Figure 2. Mutations of 3 Brazil variants.

==> VARIANT CAL.20C from California Mutations (L452) :

It is possible that S13I increases the efficiency of cleavage on the 12 amino-peptide terminal, which may increase the volume of S-protein on the host cell

CAL.20C has three unique amino acid substitutions in its spike protein. The spike protein is the part of the virus that interacts and locks into proteins from the human host cell, essentially the key to open the host to the virus. Among these are S13I and W152C in the N-terminal domain, and L452R in the receptor-binding domain.

Reference (Wenjuan Zhang et al, 2021)

https://www.medrxiv.org/content/10.1101/2021.01.18.21249786v1.full.pdf+html

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ANALYSIS W152C Mutation :

Among these are S13I and W152C in the N-terminal domain, and L452R in the receptor-binding domain.

Other general source :
https://www.forbes.com/sites/williamhaseltine/2021/02/03/concerns-grow-over-the-newly-discovered-southern-california-covid-19-variant/

32 CALIFORNIAS patients genomes from GenBank :

CA1ID: MW433772.1 California 5 January

CA3ID: **MW433769.1** California 5 January 2021

CA5ID: **MW433764.1** California 5 January 2021

CA6ID: **MW433763.1** California 5 January 2021

CA8ID: **MW433758.1** California 5 January 2021

CA10ID: **MW433752.1** California 5 January 2021

CA11ID: **MW505197.1** California 2 February 2021

CA17ID: **MW505189.1** California 22 January 2021

CA19ID: **MW505187.1** California 2February 2021

CA20ID: **MW505186.1** California 2February 2021

CA25ID: **MW505149.1** California 22 January 2021

CA27ID: **MW505147.1** California 22 January 2021

CA51ID: **LR883179.1** netherland 25 January 2021

CA52ID: **MW525111.1** California 26 January 2021

CA53ID: **MW525040.1** USA MO 26 January 2021

CA54ID: **MW525020.1** USA FL 26 January 2021

CA55ID: **MW524999.1** USA NY 26 January 2021

CA56ID: **MW524976.1** USA CA 26 January 2021

CA57ID: **MW524942.1** USA CA 26 January 2021

CA58ID: **MW523875.1** USA CA 26 January 2021

CA59ID: **MW523873.1** USA CA 26 January 2021

CA60ID: **MW523867.1** USA TX 26 January 2021

CA61ID: **MW523795.1** USA CA 26 January 2021

CA62ID: **MW523792.1** USA CA 26 January 2021

CA63ID: **MW519791.1** USA NV 25 January 2021

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CA64ID: **MW519755.1** USA AZ 25 January 2021

CA65ID: **MW519751.1** USA AZ 25 January 2021

CA66ID: **MW519739.1** USA CA 25 January 2021

CA67ID: **MW519738.1** USA CA 25 January 2021

CA68ID: **MW519725.1** USA CA 25 January 2021

CA69ID: **MW519715.1** USA CA 25 January 2021

CA70ID: **MW519708.1** USA CA 25 January 2021

==> Indian « 2 mutations » variant :

samples with the E484Q and L452R, soient South Afrika + california variants

Sources :
https://www.bbc.com/news/world-asia-india-56507988
and
https://pib.gov.in/PressReleaseIframePage.aspx?PRID=1707177

We must note that variant is E484K while Indian variant is E484Q.

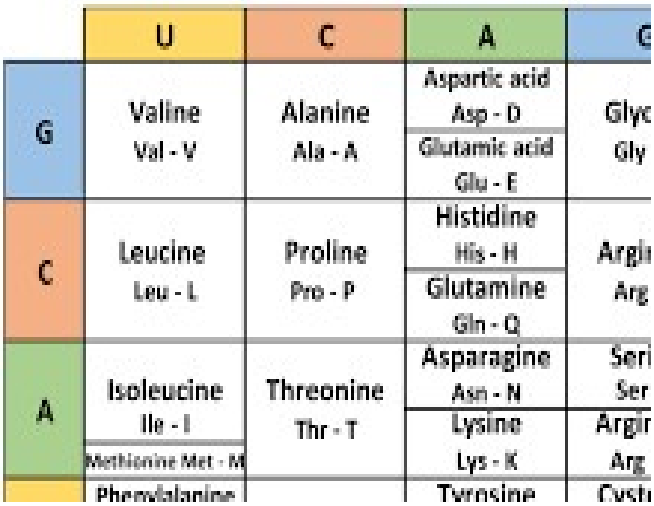

Figure 3- Recall Universal Genetic Code Table.

III- RESULTS and DISCUSSION.

3.1- SARS-CoV2 genome and spike evolution in one year 2020-2021.

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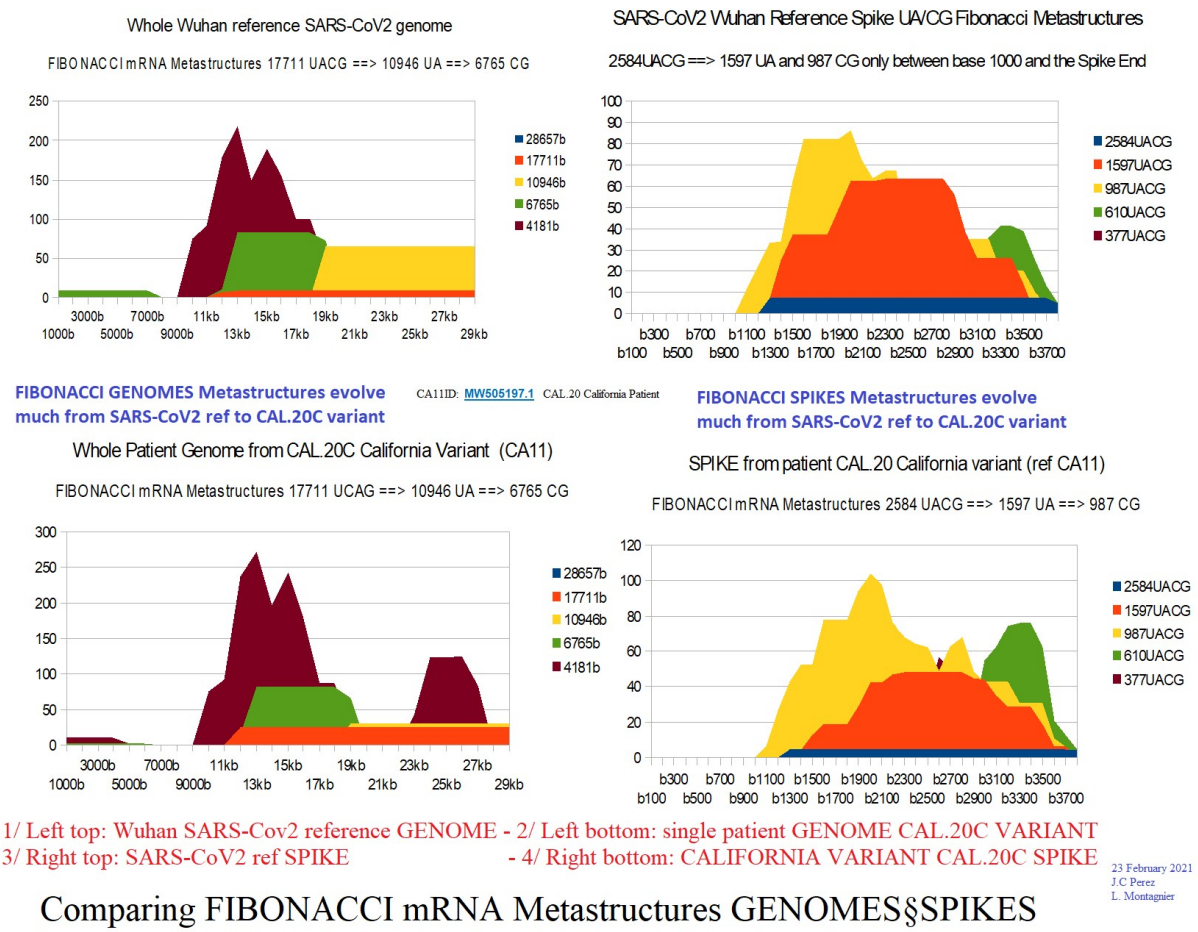

Figure 4 - comparing SARS-CoV2 genome and spike evolution between wuhan strain (january 2020) and CAL.20C variant (january 2021).

At the level of the genomes, the very long Fibonacci metastructures (17711nt) increase a lot, which means a reinforcement of the overall mRNA structure of the genome.
On the contrary, the overall metastructure of the spike seems to be reduced, although this variant has evolved at the level of amino acid mutations (mutations in CAL.20C california L452R, S13I, W152C).

3.2- SARS-CoV2 ORIGINS.

Fibonacci metastructures "shed a radically new light on" the relationships already recognized or suspected "between the 4 Sars-CoV2 Wuhan (1/2020), SARS-covZC45 (2017), SARS-covZXC21 (2015) and bat RATG13 genomes (2013). To this evidence of manipulation of CODONS synonymous with Spike of one or the other between SARS-CoV2 and beats RATG13, to the question "which of the 2 was manipulated?" (Perez, 2020), (Perez§Montagnier, 2020), (Castro-Chavez, 2020). We can assert that it is the SARS-Cov2 spike that has been manipulated to modify synonymous CODONS while retaining the functionality of the same amino acids. We believe that this manipulation will most certainly have attenuated the virulence and pathogenicity of SARS-) CoV2 opposite bat RATG13 * (blue regions of the 2 images of their Spikes).

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Moreover, if at the level of the 4 respective genomes, the strong neighborhoods between SARS-CoV2 and bat RATG13 on the one hand, and ZC45 and ZXC21 on the other hand are confirmed by these Fibonacci metastructures (vertical analogies in the image), a less expected bi-duality is highlighted at the level of their 4 respective spikes: on the one hand, this obvious neighborhood between ZXC21 and bat RATG13, and, on the other hand, although less obvious, this other neighborh

==> ZXc21

https://www.google.com/url?sa=t&source=web&rct=j&url=https://www.ncbi.nlm.nih.gov/nuccore/MG772934&ved=2ahUKEwi63MmXkIfvAhVPrxoKHc7rBkAQFjAAegQIBBAD&usg=AOvVaw2DaPGodhGxK_sv2JPdNU29

Bat SARS-like coronavirus isolate bat-SL-CoVZXC21, complete genome
GenBank: MG772934.1

/collection_date="Jul-2015"
21483..25220
/note="S"
/codon_start=1
/product="spike

==> Bat Ratg13

https://www.google.com/url?sa=t&source=web&rct=j&url=https://www.ncbi.nlm.nih.gov/nuccore/MN996532&ved=2ahUKEwjO1KKqkIfvAhVlx4UKHYypB4oQFjABegQIARAC&usg=AOvVaw1NImUic0dN6Ke140Hf408t

Bat coronavirus RaTG13, complete genome
GenBank: MN996532.2

Go to:
LOCUS MN996532 29855 bp RNA linear VRL 24-NOV-2020
COMMENT On Oct 13, 2020 this sequence version replaced MN996532.1.
/isolation_source="fecal swab"

/collection_date="24-Jul-2013"

/gene="S"

CDS 21560..25369
/gene="S"

==> ZC45

https://www.google.com/url?sa=t&source=web&rct=j&url=https://www.ncbi.nlm.nih.gov/nuccore/MG772933&ved=2ahUKEwig_s_0j4fvAhUPKBoKHe_oD44QFjAAegQIBBAD&usg=AOvVaw0IPCwtlOcZJxs4SzfZhzPu

Bat SARS-like coronavirus isolate bat-SL-CoVZC45, complete genome
GenBank: MG772933.1

/collection_date="Feb-2017"

SPIKE
CDS 21549..25289
/note="S"
/codon_start=1

The following SARS-CoV2 "quadrille", bat RATG13, ZC45 and ZXC21 is remarkable for its enigmatic nature over the actual origins of SARS-CoV2. Indeed, when the first 2 are

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supposed to be of natural origin, we have the certainty and the proofs that the last 2 were read to the point - and published - by military laboratories.
Fibonacci analysis of these 4 genomes and their Spike genes will reveal links, subfamilies and correlations 2 to 2 between these 4 key genomes in the history and genesis of the COVID-19 pandemic.

Genomes scale analysis :

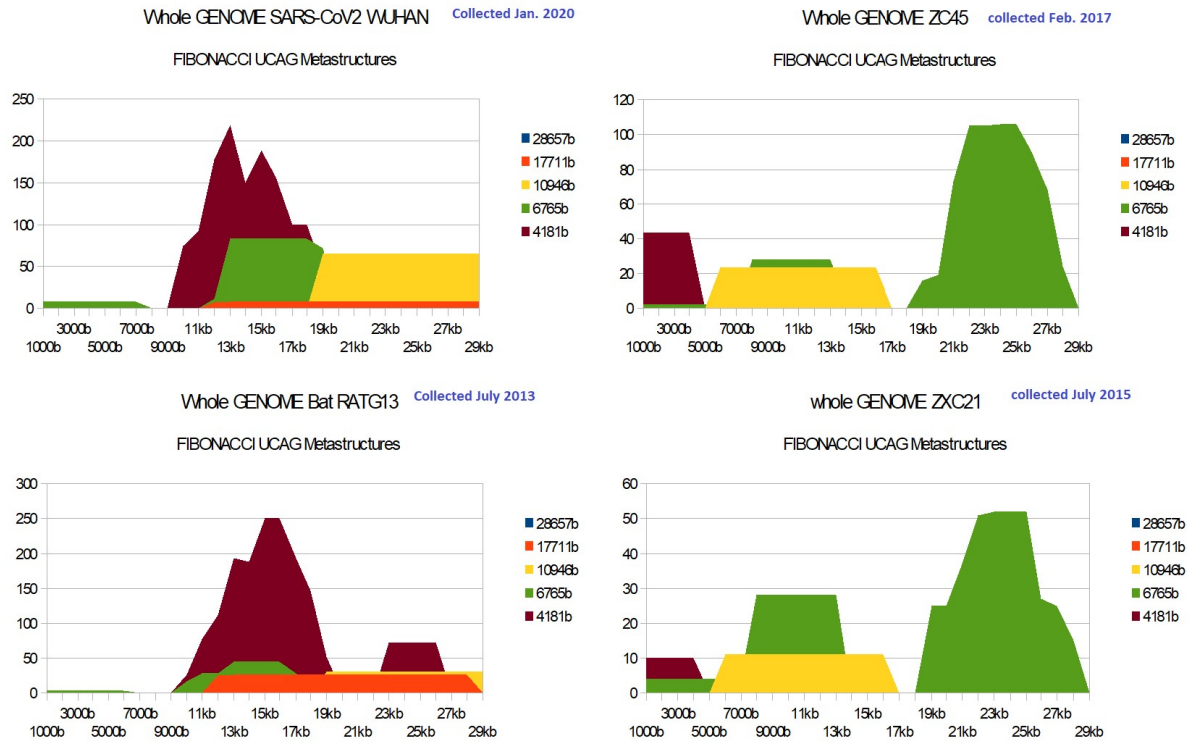

Figure 5 - remarkable vertical analogies (SARS-CoV2 vs bat RaTG13).

Spikes scale analysis :

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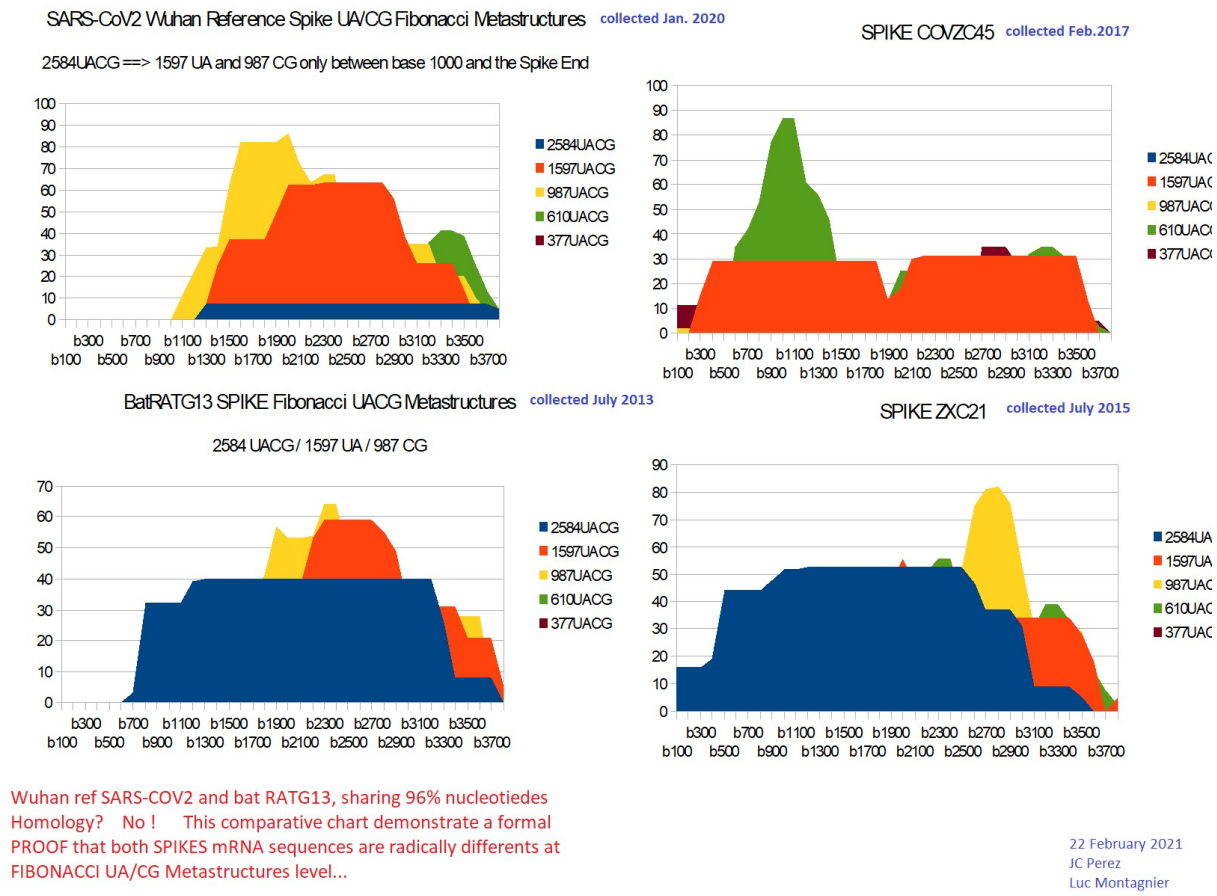

Figure 6 – remarkable horizontal analogies (Bat RATG13 vs ZXC21).

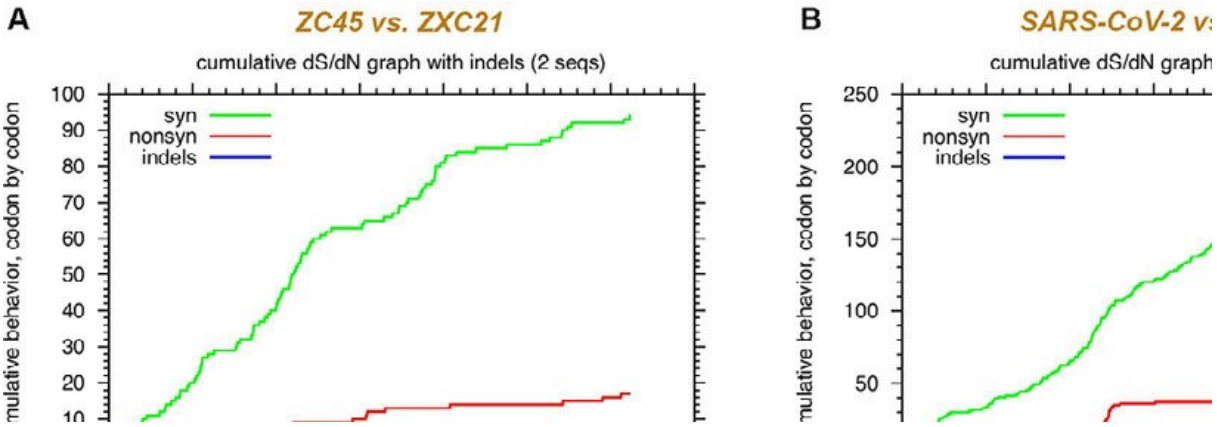

Figure 7 – Evidence of patterns analogies at Synonimes/non synonimes codons.

FIG. 7 concerning the abnormal number of synonymous codons between SARS-CoV2 and bat RATG13 on the one hand and ZXC21 and ZC45 on the other hand confirms and reinforces the dichotomy which has just been revealed here by the Fibonacci analyzes. Particularly, both bat RATG13 and ZXC21 Spikes provide a high level of Fibonacci long range UA/CG resonances (blue coloured in Fig7). For us, that is the proof of natural evolutionary contraints contrarly the 2 remaining spikes SARS-CoV2 and ZC45.

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Let us summarize the respective results of figures 5, 6 and 7: figure 5 (genomes) confirms the above dichotomy natural versus laboratory. indeed, a double vertical analogy clearly classifies these 4 genomes into 2 + 2 by the clear graphic correlation of their Fibonacci images.

On the contrary (figure 6 spikes), the comparative analysis of the 4 spikes clearly shows a horizontal dichotomy between SARS-CoV2 and ZC45 on the one hand and bat RATG13 and ZCX21 on the other hand. Does this mean that ZC45 would have served as a "model" for SARS-CoV2 while ZXC21 would have "inspired" bat RATG13, or rather the reverse if we take into account the respective dates: bat RATG13 (2013/2020) ZXC21 (2015) ZC45 (2017) SARS-CoV2 (2019/2020).

SARS-Cov2 is directly linked to RaTG13 as ZC45 is linked to ZXC21 and the reduction or even disappearance of the 2584 UACG metastructures in SARS-Cov2 and ZC45 shows that practically ZC45 is “made from” ZXC21 like SARS-Cov2 from RaTG13.

3.3- Comparing 11 reference variants spikes.

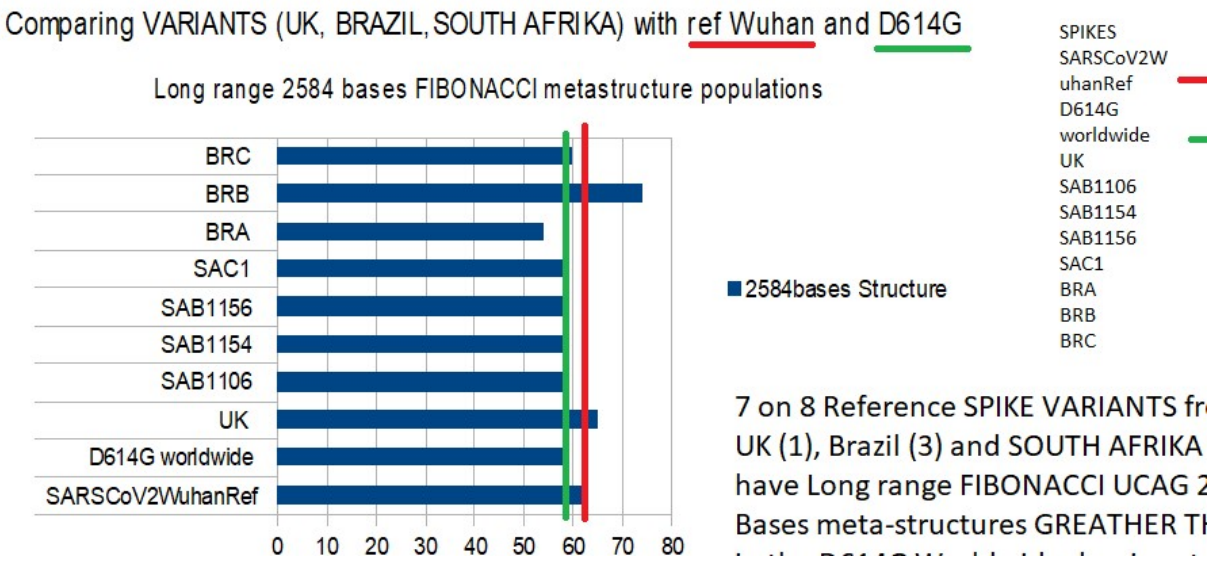

Figure 8- Comparing CIRCULAR Fibonacci metastructures between reference variants and Wuhan and D614G worldwide spikes.

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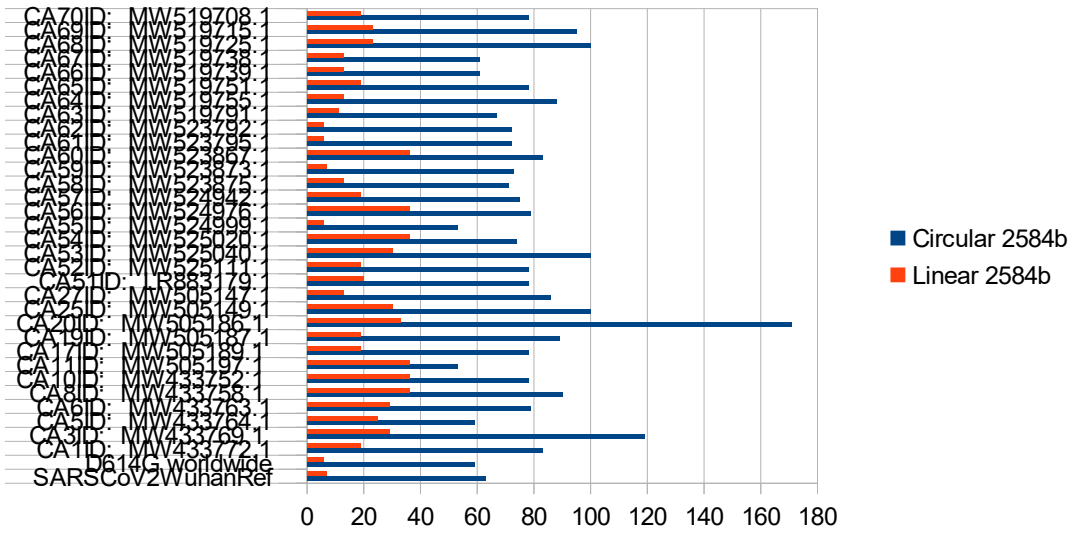

Figure 9- Comparing CIRCULAR and LINEAR Fibonacci metastructures between 32 CAL.20C Sample patients spikes variants and Wuhan and D614G worldwide spikes.

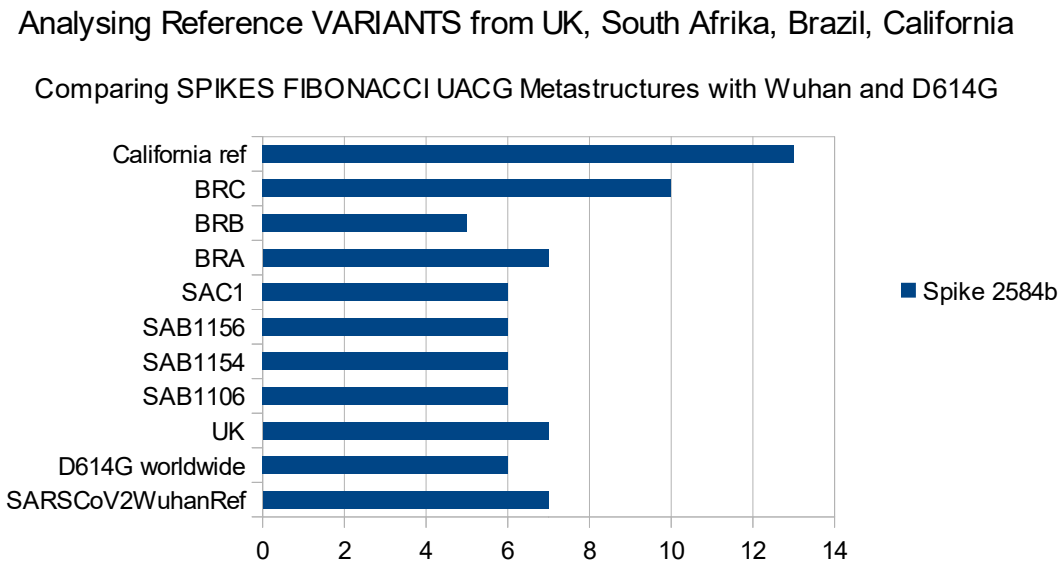

Figure 10- Comparing LINEAR Fibonacci metastructures between reference variants and Wuhan and D614G worldwide spikes.

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Table 2 - Comparing LINEAR Fibonacci metastructures between reference variants and Wuhan and D614G worldwide spikes.

SPIKES	Spike 2584b
SARSCoV2W	7
D614G worldw	6
UK	7
SAB1106	6
SAB1154	6
SAB1156	6
SAC1	6
BRA	7
BRB	5
BRC	10
California ref	13

In this & 3, we try to answer the question: "Do the variants strengthen or reduce the level of Fibonacci metastructures of the Spikes vis-à-vis the original Wuhan and worldwife D614G strains?".

We carry out 2 types of additional analyzes: on the one hand by considering the mRNA spike looped back on itself (ring like: figures 8 and 9), which is inaccurate here but nevertheless provides information which makes sense, which corresponds to the situation actual (figure 10 and table 2).

Globally, it appears a significant increase in Fibonacci structures for the variants, but these variants being only theoretical sequences, we will see in the following & that this increase in metastructure of the variant spikes is much more pronounced in the case of patients (see study of CAL.20C variant patients).

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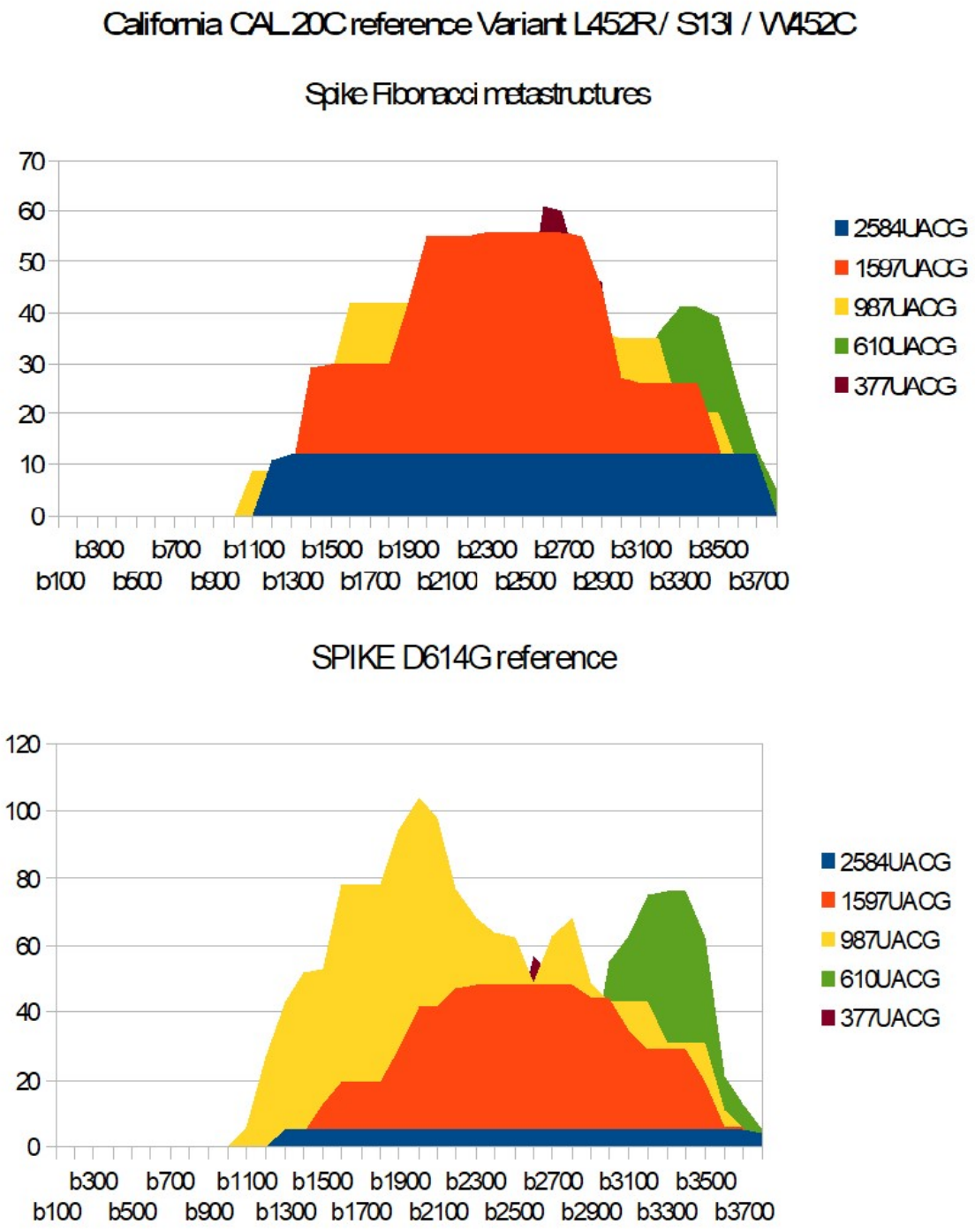

Figure 11 – Comparing reference variant CAL.20C Fibonacci metastructures with worldwide spike D614G.

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3.4- analysing 32 CAL.20C california variant patients spikes.

This section analyzes the genomes and spikes of 32 patients with the California variant CAL.20C. Figure 11 and tables 4 to 6 summarize 2 major results:
- the very great diversity of the results.
- the very clear trend of an increase in the number of Fibonacci structures compared to the reference genome D614G.
But the new most remarkable is the one which will be the subject of the next & 5 ...

Data sources : GenBank.

Table 3 – Variant California CAL.20C : 32 individual patients spikes.

32 L452 R variants	S13I California variant mutation			W152C California variant mutation			2584 UCAG FIBONACCI circular matastructures population D614G spike: 59	2584 UCAG FIBONACCI linear matastructures population D614G spike: 5	*"mRNA checksum natural law" SPIKE*	17711 UCAG FIBONACCI linear matastructures population D614G genome : 8
	AGU regular (S13)	AUU variant (I13I)	Other (deletions)	UGG regular (W152)	UGU variant (152C)	Other (deletions)				
CA1		AUU			UGU		83	19	1597 1597	5
CA3		AUU				GCA	119	29	1597 1595	21
CA5			UAA			UGA	59	25	1597 1598	11
CA6			UAC			ACU	79	29	1597 1595	31
CA8		AUU				AUG	90	36	1597 1596	8
CA10			UAC			ACA	78	36	1597 1594	9
CA11		**AUU**				**GGU**	**53 <==**	**36**	**1597 1594**	**25**
CA17		AUU			UGU		78	19	1597 1597	9
CA19		AUU			UGU		89	19	1597 1597	39
CA20			UAG			CUU	171	33	1597 1597	39
CA25		AUU			UGU		100	30	1597 1596	28
CA27		AUU			UGU		86	27	1597 1598	28
CA51			UCA			UAU	78	20	1597 1598	47
CA52		AUU			UGU		78	19	1597 1597	8
CA53		AUU			UGU		100	30	1597 1596	29
CA54		AUU				AUU	74	36	1597 1592	9

CA55	**AGU**			**UGG**			**53 <==**	**6**	**1597 1599**	**12**
CA56			CUA			ACC	79	36	1597 1595	35
CA57		AUU			UGU		75	19	1597 1597	33
CA58	AGU			UGG			71	13	1597 1598	43
CA59			UCA			GAU	73	7	1597 1601	43
CA60			GCA			GAA	83	36	1597 1589	39
CA61		AUU			UGU		72	6	1597 1599	39
CA62		AUU			UGU		72	6	1597 1599	13
CA63		AUU			UGU		67	11	1597 1597	33
CA64		AUU			UGU		88	12	1597 1598	26
CA65		AUU			UGU		78	19	1597 1597	28
CA66		AUU			UGU		61	12	1597 1598	33
CA67		AUU			UGU		61	12	1597 1598	40
CA68		AUU				GAA	100	22	1597 1597	12
CA69		AUU				GAA	95	22	1597 1597	33
CA70		AUU			UGU		78	19	1597 1597	3

Table 4 - VARIANT L452R and variability S13I california CAL.20C vs HIV/SIV « EIE » (July 2020: Perez, J. C., & Montagnier, L. (2020). COVID-19, SARS AND BATS CORONAVIRUSES GENOMES PECULIAR HOMOLOGOUS RNA SEQUENCES. *International Journal of Research -GRANTHAALAYAH*, *8*(7), 217-263. https://zenodo.org/record/3975589).

CALIFORNIA VARIANT S13I	AGU regular (S13)	AUU variant(I13I)	Other (deletions)	Total (L452R)
Number of strains	2	22	8	32
% of strains	6,00%	69,00%	25,00%	100,00%
Nota		94% mutations or deletions where HIV/SIV « EIE » Perez§Montagnier article are involved		

Nota :For information, a first mutation is located in the HIV zone (S13I). 3 bases after kenya (1 in chart) and 8 bases before the second Hiv (2 in chart). See Perez§Montagnier 2020.

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We analyzed here (table 3) the genomes and spikes of 32 patients with the California variant CAL.20C. The result is very interesting:

for the circular structures analysis of the spike, 30 out of 32 cases increase the metastructures 2584 AU / CG vis-à-vis the reference D614G (column 8).

For the linear structures analysis of the spike (column 9), the integrity of the 32 cases increases these same metastructures 2584 AU / CG.

At the level of whole genomes, the 17711 UA / CG metastructures (column 11) increase in 30 out of 32 cases with respect to the reference genome D614G.

We can only conclude that the reference variants are only textbook cases, much less rich in synonymous mutations than the genomes of real patients. We conclude that a large number of synonymous mutations specific to each patient reinforce the overall structure of genomes and spikes, it suffices to observe the diversity of the results for each of the 32 patients.

Another remark, if all 32 patient cases have the L452R, for the 2 remaining mutations characterizing CAL.20C, there is a large diversity of individual cases for mutations S13I and W152C: someones have one or other or none between these mutations. There are also cases with deletions overlaping these S13I or W152C crucial mutations. Finally, we must conclude that the key of variants evolution and pathogenicity knowledge provides more from individual patients sequences full analysis that from theoretical reference variants description.

Table 5 - VARIANT L452R and variability W152C california CAL.20C vs HIV/SIV « EIE » (July 2020: Perez, J. C., & Montagnier, L. (2020). COVID-19, SARS AND BATS CORONAVIRUSES GENOMES PECULIAR HOMOLOGOUS RNA SEQUENCES. *International Journal of Research -GRANTHAALAYAH*, *8*(7), 217-263. https://zenodo.org/record/3975589).

W152C California variant mutation	UGG regular (W152)	UGU variant (152C)	Other (deletions)	Total (L452R)
Number of strains	2	16	14	32
% of strains	6,00%	50,00%	44,00%	100,00%
Nota		94% mutations or deletions just after where HIV/SIV « EIE » Perez§Montagnier article are involved		

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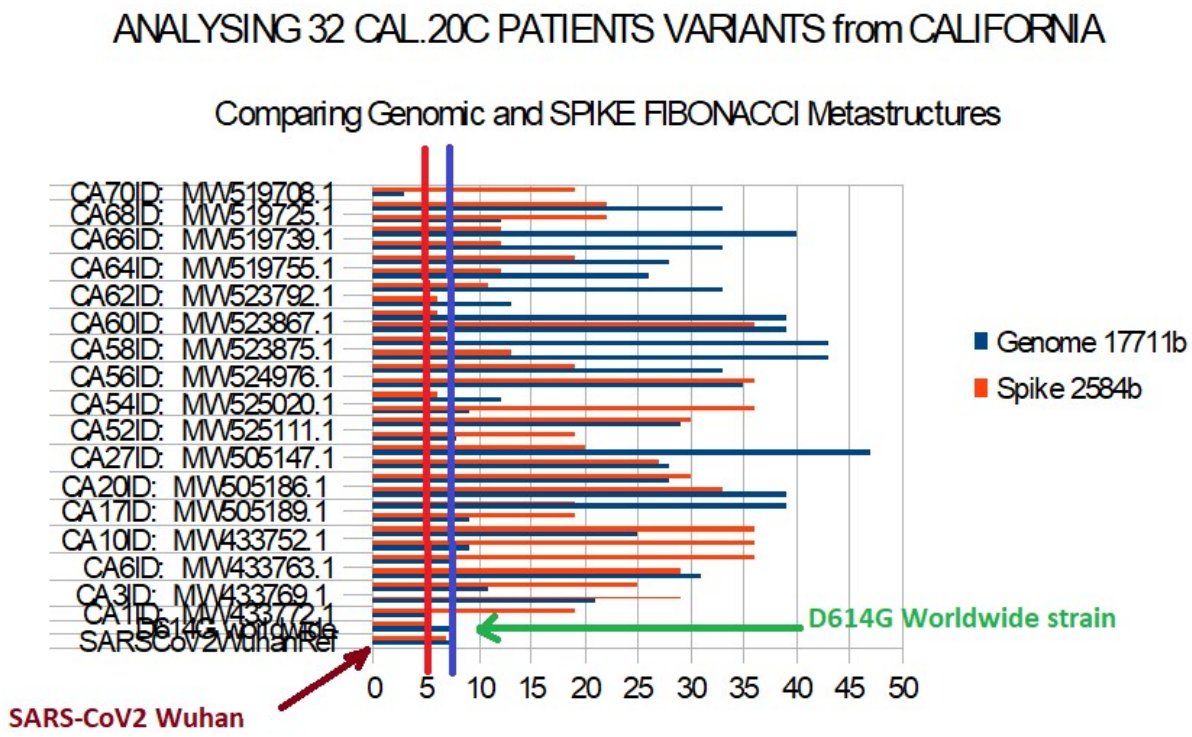

Figure 12 – Comparing genome and spike between 32 CAL.20C patients and ref Wuhan and D614G worldwide reference.

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Table 6 - Comparing genome and spike between 32 CAL.20C patients and ref Wuhan and D614G worldwide reference.

SPIKES	Genome 1771	Spike 2584b
SARSCoV2WuhanRef	8	7
D614G worldwide	8	5
CA1ID: MW433772.1	5	19
CA3ID: MW433769.1	21	29
CA5ID: MW433764.1	11	25
CA6ID: MW433763.1	31	29
CA8ID: MW433758.1	8	36
CA10ID: MW433752.1	9	36
CA11ID: MW505197.1	25	36
CA17ID: MW505189.1	9	19
CA19ID: MW505187.1	39	19
CA20ID: MW505186.1	39	33
CA25ID: MW505149.1	28	30
CA27ID: MW505147.1	28	27
CA51ID: LR883179.1	47	20
CA52ID: MW525111.1	8	19
CA53ID: MW525040.1	29	30
CA54ID: MW525020.1	9	36
CA55ID: MW524999.1	12	6
CA56ID: MW524976.1	35	36
CA57ID: MW524942.1	33	19
CA58ID: MW523875.1	43	13
CA59ID: MW523873.1	43	7
CA60ID: MW523867.1	39	36
CA61ID: MW523795.1	39	6
CA62ID: MW523792.1	13	6
CA63ID: MW519791.1	33	11
CA64ID: MW519755.1	26	12
CA65ID: MW519751.1	28	19
CA66ID: MW519739.1	33	12
CA67ID: MW519738.1	40	12
CA68ID: MW519725.1	12	22
CA69ID: MW519715.1	33	22
CA70ID: MW519708.1	3	19

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3.5- Toward a meta mRNA Fibonacci gene end message code.

This point is at a level of fundamental research of mechanisms unknown to biology. Indeed, we demonstrate how, beyond and above the STOP codon which commands the protein manufacturing machinery to end the process, there would exist a sort of "end of gene message", which would be addressed to, on the scale of messenger RNA, this "code" would be digital in nature, carried by the ultimate UA / CG metastructure of Fibonacci. We observe that this message would be of Nature GIGOGNE, constituted like the Russian dolls of a nesting of proportions all ending on one of the 3 bases of the STOP codon. This discovery is validated in this article on 43 Spikes from UK, South Afrika, BRAZIL and CALIFORNIA variants. Of these Spikes, 32 were from real patients.

In each box of the penultimate column of table 3, there are 2 very close numbers: the first number 1597 is the optimal number of UA bases with a final resonance of 2584 UACG which would end in the immediate vicinity of the codon stop UAA of the Spike. The second number (ie. 1598) is the real number of UA bases contained among these last 2584 bases of the spike. Remember that 2584 bases cover 2/3 of the spike which has about 3800 bases. It is therefore a strong meta-structure which would control the relative proportions of nucleotides in the spike.

Table 7 – Distributin of cases around the 3 bases of the UAA stop codon of the spike.

1597 UA base:	Number cases
1594	2
1595	3
1596	3
1597 A	11
1598 A	8
1599 T	8
1600	3
1601	2
1602	1
others	2

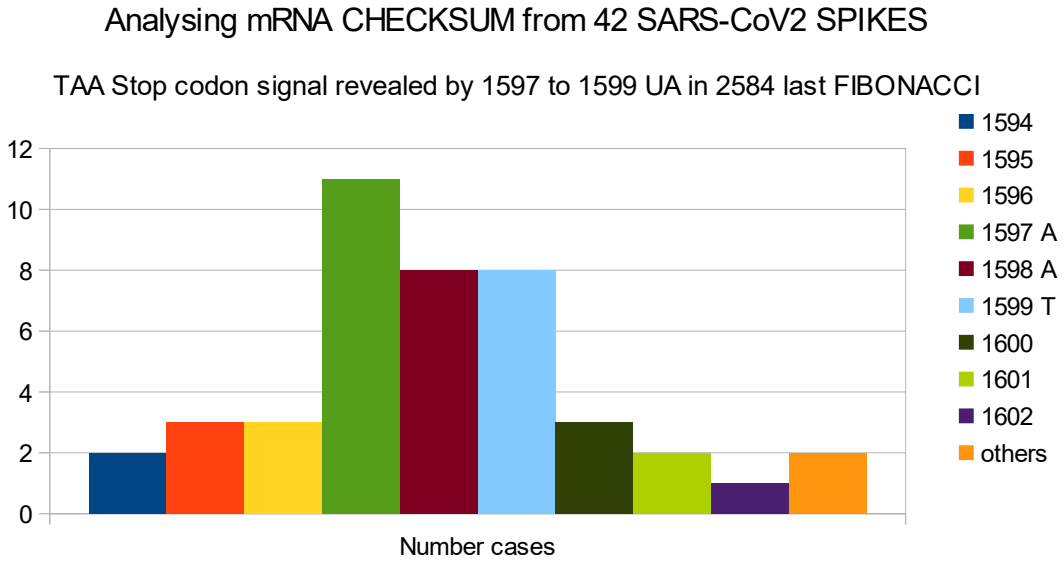

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Figure 13 - histogram perfectly illustrating the "bell" concentration of cases around the 3 bases of the UAA stop codon of the spike.

Table 7 and the histogram of FIG. 13 illustrate this remarkable phenomenon of "end-of-gene meta-structure" generalized to the 32 spike strains of CAL.20C patients plus 11 spikes of reference variants, for a total of 43 cases. The histogram perfectly illustrates the "bell" concentration of cases around the 3 bases of the UAA stop codon of the spike.

3.6- analysing S501 UK, S484 South Afrika, and last "2 mutations" Indian variants.

N501 UK VARIANTS

Mutation Information

- S:N501 has appeared multiple times independently: each can be associated with different accompanying mutations
- Amino-acid changes are S:N501Y (nucleotide mutation A23063T), S:N501T (nucleotide mutation A23064C), and S:N501S (nucleotide mutation A23064G)

½SN501Y„SN501T„SN501S„SPIKD614G
3822
SN501Y[1500+ 1 2 3]
AAT
SN501Y[1500+ 1 2 3] ='TAT'
SN501T[1500+ 1 2 3] ='ACT'
SN501S[1500+ 1 2 3] ='AGT'

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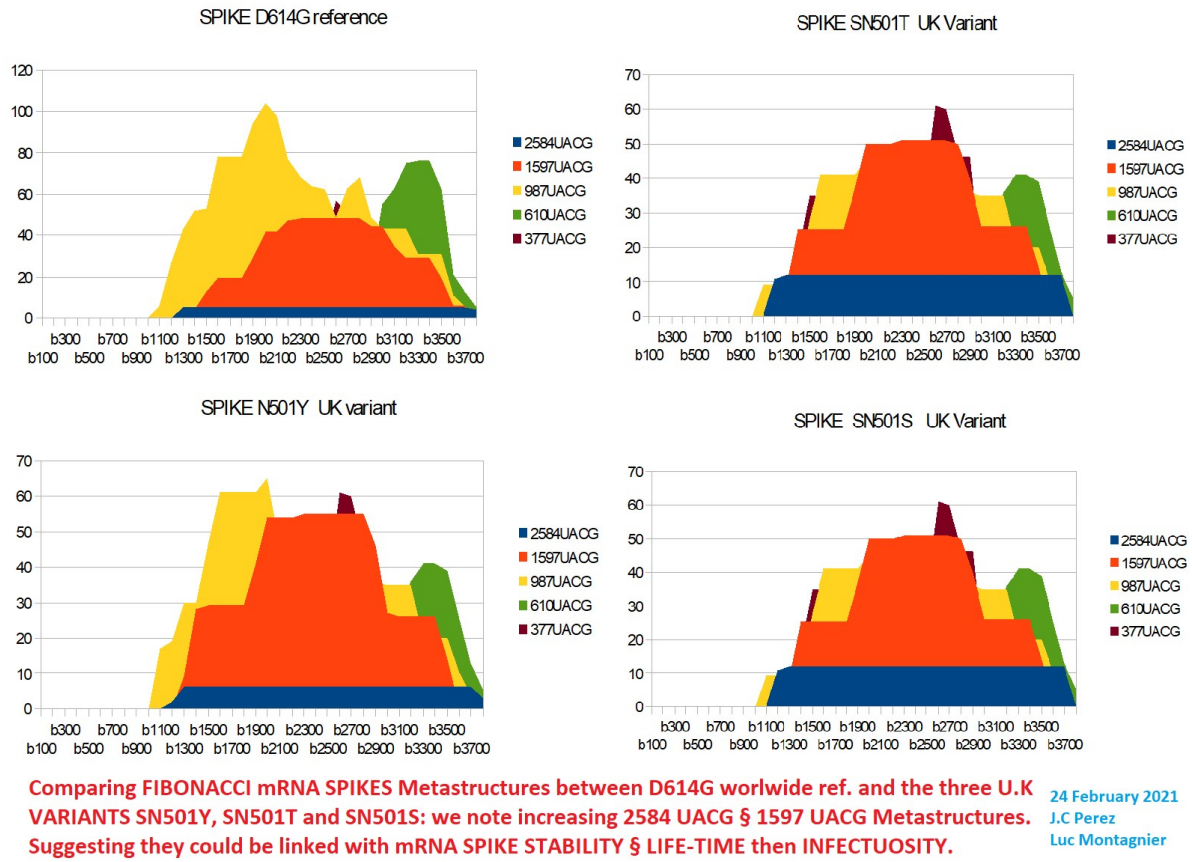

Figure 14 - Comparing 3 UK variants Spike codon 501 mutations with reference D614G spike.

For the English variant (Figure 14), we see that at least 2 of the 3 mutations significantly increase the long metastructures of 2584 UACG bases (blue regions in Figure 14). This can generate better stability and life of the mRNA of the spine of these variants, and therefore correspond to the increase in infectivity and pathogenicity observed in patients who are victims of this English variant.

South Afrika VARIANT

20H/501Y.V2

Also known as B.1.351

Announced in December 2020, 501Y.V2 originated and/or initially expanded in South Africa (Tegally et al., medRxiv).

501Y.V2 is associated with multiple mutations in Spike, including: S:N501Y (see S:N501 page), S:E484K, S:K417N, and S:D80A. Additionally, there is a deletion at 242-245. There is also a mutation in Nucleocapsid: N:T205I and a deletion in ORF1a(Nsp6) at positions 3675-3677 (also seen in 501Y.V1 and 501Y.V3).

GAA ==> AAA E484K
AAG ==> AAU K417N
GAU ==> GCU D80A

SE484K[237+1 2 3] = 'GCT' SE484K[1248+1 2 3] = 'AAT' SE484K[1449+1 2 3] = 'AAA'

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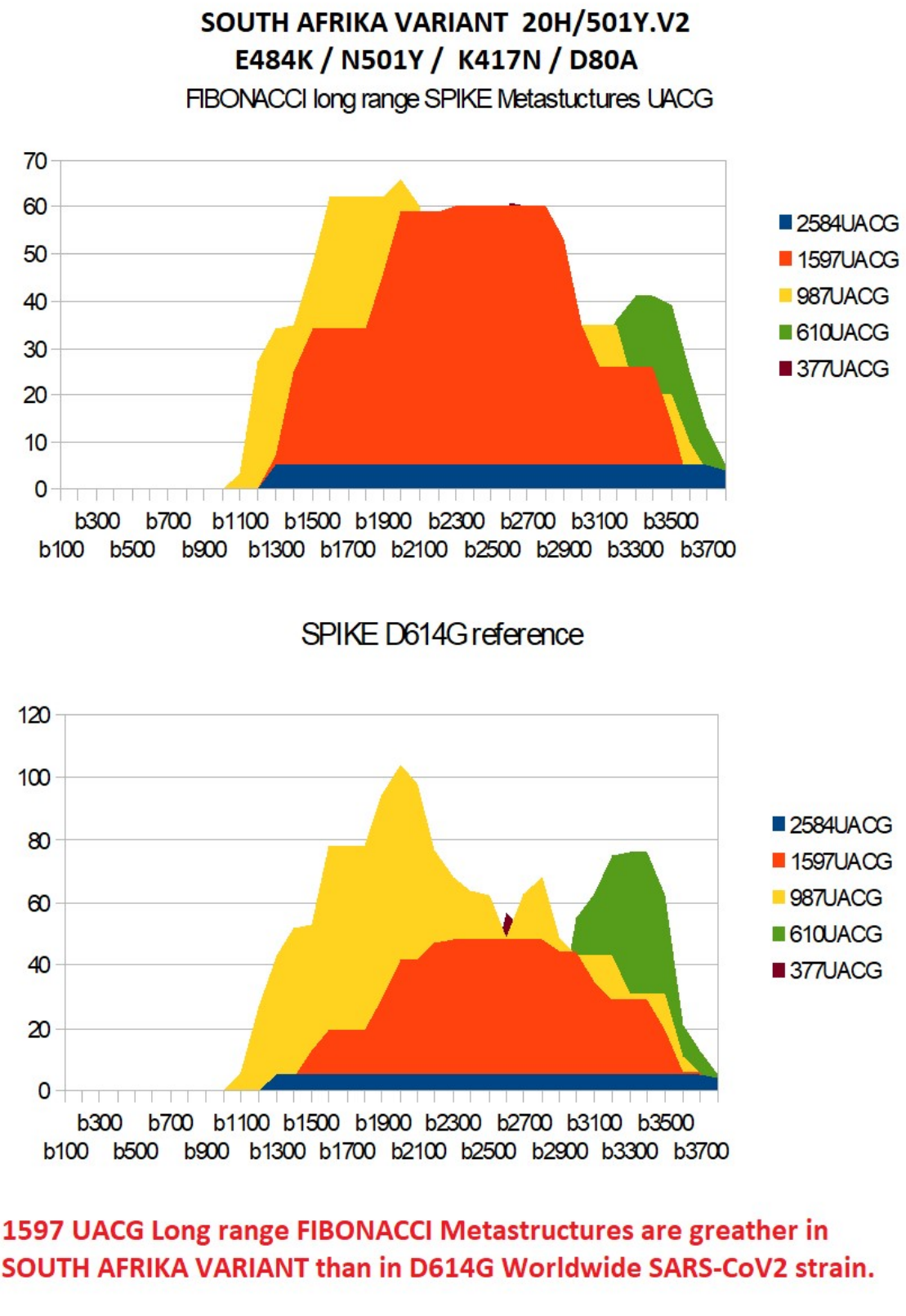

Figure 15- Comparing South Afrika variant spike with reference D614G spike.

For this South African variant (figure 15), we see above all a strong increase in metastructures 1597 UACG (orange in figure 15).

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On the other hand, the "podium" shape, already observed for the English variant, becomes very clear here. This enigmatic form will be the subject of the next and last paragraph & 7 ...

Indian « 2 mutations » variant :

We analyse here 2 cases :
Basic variant

Full variant

In BASIC VARIANT, we modify spike D614G only with these 2 mutations:E484Q and L452R.

In FULL VARIANT, we manage the fusion between South Afrika variant, California variant and the small change vs. South Afrika variant doing E484Q.

SINDIABASIC

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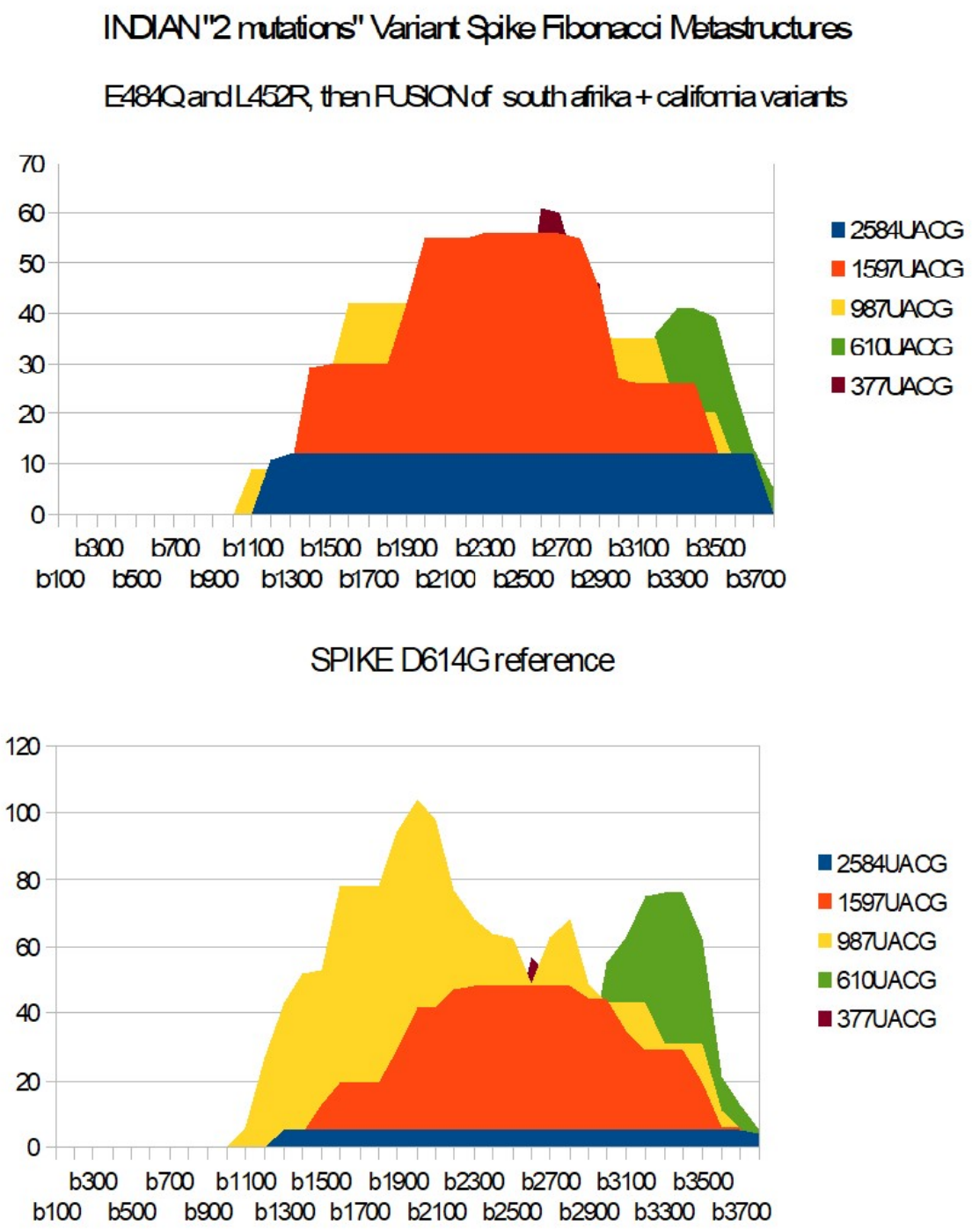

Figure 16 – Analysing INDIAN variant Basic (only with 2 mutations E484Q and L452R

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SINDIAFULL :

We run following process :

SINDIAFULL = SPIKD614G

Dim SE484K 3822 bases

Dim S614CALREF 3822 bases

Locations of differences in nucleotides between SINDIAFULL and S614CALREF :

38 456 1355

Values of mutations to do in SINDIAFULL :

TTG

SINDIAFULL[38 456 1355] = 'TTG'

Locations of differences in nucleotides between SE484K South Afrika and S614CALREF :

239 1251 1450 1501

Values of mutations to do in SINDIAFULL :

CTAT

SINDIAFULL[239 1251 1450 1501] = 'CTAT'

Manage difference E484K to E484Q :

SINDIAFULL[1355] = 'G'

Control :

cumulate SINDIAFULL different SPIKD614G

7

cumulate SINDIAFULL different INDIABASIC

6

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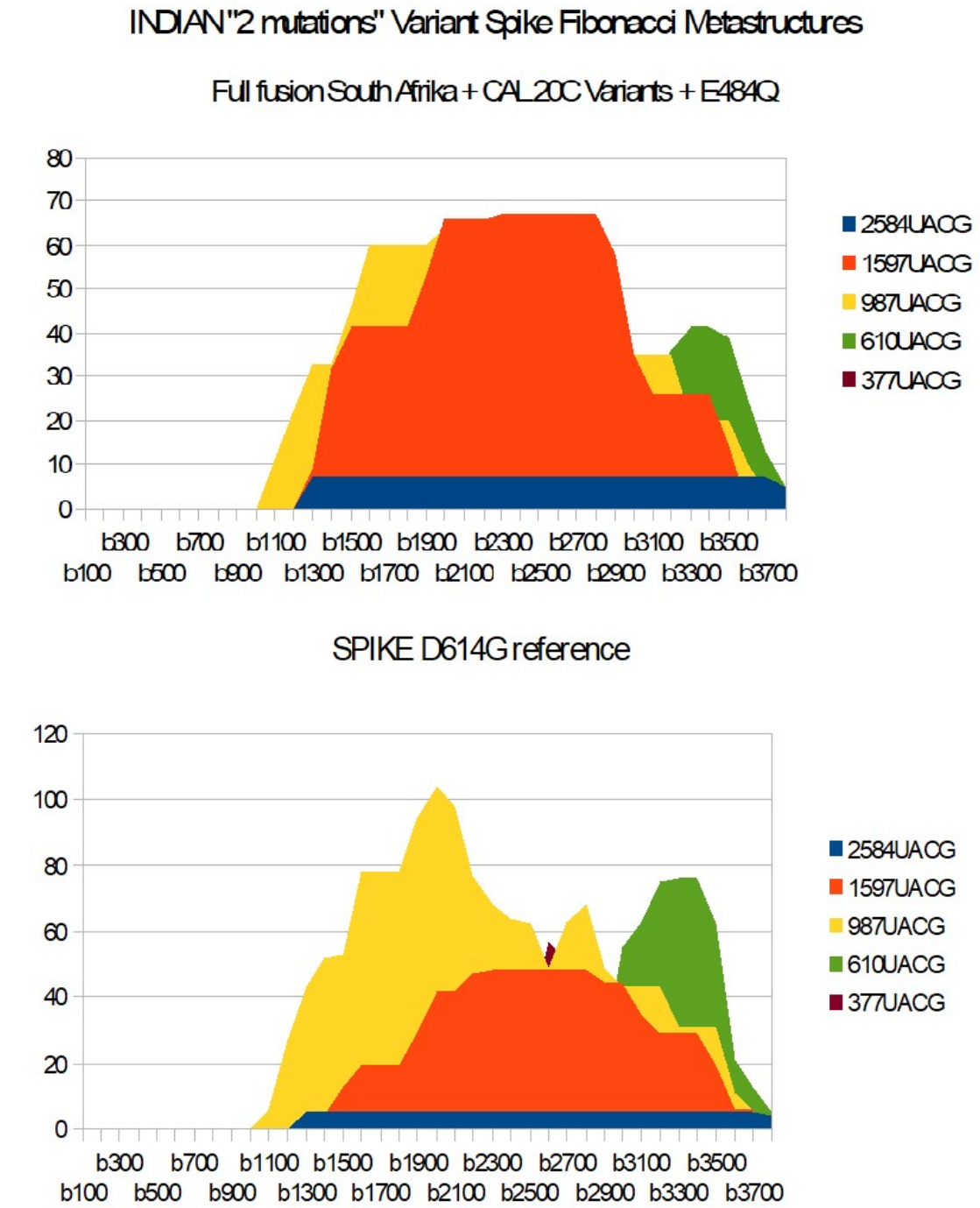

Figure 17 – Analysing INDIAN variant Full (fusion CAL.20C and South Afrika + difference with South Afrika E484Q)

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Samples with the E484Q and L452R, then South Afrika + california variants

https://www.bbc.com/news/world-asia-india-56507988

https://pib.gov.in/PressReleaseIframePage.aspx?PRID=1707177

3.7- Suggesting a possible variants spike mRNA palindrome symmetry metastructure improving mRNA stability then infectuosity.

Here, we have gathered several pieces of evidence showing that, as they evolve, the variants would constitute and reinforce a kind of Palindrome-type symmetry based on "Russian doll" interlocking of their MRNA, which could lead to a double strand. of the "hairpin" type, thus reinforcing the stability and the lifespan of the Spike MRNA, thus certainly the increasing contagiousness of the variant virus.

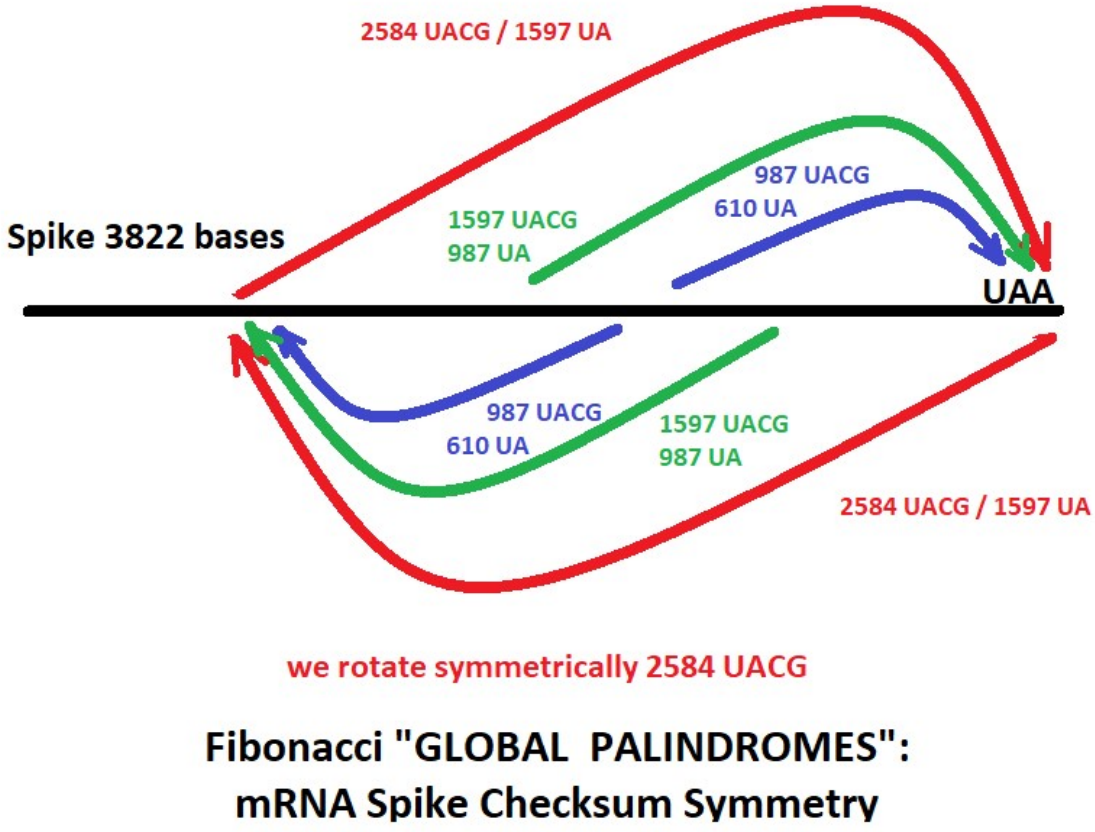

Figure 18 – « Fibonacci GLOBAL PALINDROMES » scenario test.

Clearly more pronounced "PODIUM-like" structures appear in these UK, South Afrika, India, California (figures 14 to 17) variants than in the strain D614G Spike.

The structures in orange 1597UACG form a curious "PODIUM" ...

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Is this the sign of a PALINDROME TYPE SYMMETRY BETWEEN 2 STRUCTURES FIBONACCI 1597 UACG?

FIBONACCI PALINDROMES EFFECT?

It would seem that in these UK variants, (especially Figure 14, the 2 on the right, particularly right, bottom : Spike UK SN501S variant), a kind of phenomenon FIBONACCI PALINDROMES (Symmetry) as presented and schematized in handwritten graph (part in orange STRUCTURES 1597 UACG)

Addresses first and last STRUCTURES of 1597UACG :

First : 1111+1597 = 2708 end of the first 1597 structure.

Last : 1973+1597 = 3570 end of the last 1597 structure.
Then, we considere now area between 1973 and 2708.

The first structure : V1 = SN501S[1111 on 1597]

The last structure: V2 = SN501S[1973 on 1597]

Building the symmetrical palindrome of V2 : V2 = rotate V2

Now, we test « hypothetical global palindrome nature » matching on various dimensions :

Comparing matching between the 100 first bases of V1 and the 100 first bases of V2.

In fact, this is similar with comparing the 100 first bases of the first 1597 structure with the 100 last bases of the last 1507 structure...

100 bases test :

V1[on 100] = 'UA' ==> 66 bases

V2[on 100] = 'UA' ==> 61 bases

Then, we continue :

200 bases test :

V1[on 200] = 'UA' ==> 129 bases

V2[on 200] = 'UA' ==> 129 bases

Then, we continue :

300 bases test :

V1[on 300] = 'UA' ==> 198 bases

V2[on 300] = 'UA' ==> 192 bases

Then, we continue :

400 bases test :

V1[on 400] = 'UA' ==> 258 bases

V2[on 400] = 'UA' ==> 249 bases

Then, we continue :

500 bases test :

V1[on 500] = 'UA' ==> 324 bases

V2[on 500] = 'UA' ==> 308 bases

Then, we continue :

…/...

800 bases test :

V1[on 800] = 'UA' ==> 501 bases

V2[on 800] = 'UA' ==> 495 bases

Then, we continue :

1000 bases test :

V1[on 1000] = 'UA' ==> 613 bases

V2[on 1000] = 'UA' ==> 615 bases

Then, we continue :

1200 bases test :

V1[on 1200] = 'UA' ==> 743 bases

V2[on 1200] = 'UA' ==> 742 bases

Then, we continue :

…/...

1400 bases test :

V1[on 1400] = 'UA' ==> 877 bases

V2[on 1400] = 'UA' ==> 872 bases

Then, we continue :

1500 bases test :

V1[on 1500] = 'UA' ==> 934 bases

V2[on 1500] = 'UA' ==> 936 bases

Then, we continue :

FULL 1597 bases test :

V1[on 1597] = 'UA' ==> 987 bases

V2[on 1597] = 'UA' ==> 987 bases

Then 987 UA and 610 CG

Globally, the palindrome like mRNA folding is good...

Palindrome symmetry test on the first 80 bases of the first 1597 UACG and the first 80 bases of the symmetrical of the last 1597 UACG. They are superimposed face to face like Palindrome.

It does appear C <==> G relations on the hypothetical double strand of mRNA.

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ON 80 BASES...

```
CC C  C    CC C            C CC  C       C C  C   C    C   C
 G            G G   GG G G          G     G      G    G
```

IDEM ON 100 BASES...

```
CC C  C    CC C            C CC  C       C C  C   C    C   C       C
 G            G G   GG G G          G     G      G    G   G       G    G GG
```

Nota : « » is a U or A nucleotide (space).

Paticularly, we suggest the following conjecture at mRNA folding level (Mengwen et al, 2006):

CONJECTURE of SARS-CoV2 VARIANTS:
The growth of long Fibonacci structures in the shape of "podiums" for almost all of the variants studied (UK, California, South Afrika, India, etc.) suggests the probable folding of the Spike mRNA in the form of a "hairpin", which can strengthen the cohesion and the lifespan of this mRNA.

3.8 – Analysing Fibonacci Metastructures in the mRNA coding for the vaccines PFIZER and MODERNA :

Stanford University team published and provide experimental sequence information for the RNA components of the initial Moderna (https://pubmed.ncbi.nlm.nih.gov/32756549/) and Pfizer/BioNTech (https://pubmed.ncbi.nlm.nih.gov/33301246/) COVID-19 vaccines (Dae Eun Jeong et al, 2021).

Then we analysed using the same method the hypothetic metastructure of this mRNA vaccine...

Here are the results :

Dim VACCINPFIZER = 4175 bases.
Dim VACCINMODERNA = 4004 bases.

Figure 1: Spike-encoding contig assembled from BioNTech/Pfizer BNT-162b2 vaccine.

GAGAATAAACTAGTATTCTTCTGGTCCCCACAGACTCAGAGAGAACCCGCCACC***ATGTTCGTGTTCCTGGTGCTGCTGCCTCTGGTGT***
CCA GCCAGTGTGTGAACCTGACCACCAGAACACAGCTGCCTCCAGCCTACACCAACAGCTTTACCAGAGGCGTGTACTACCCCGACAAGGTGTT
CAGATCCAGCGTGCTGCACTCTACCCAGGACCTGTTCCTGCCTTTCTTCAGCAACGTGACCTGGTTCCACGCCATCCACGTGTCCGGCACC
AATGGCACCAAGAGATTCGACAACCCCGTGCTGCCCTTCAACGACGGGGTGTACTTTGCCAGCACCGAGAAGTCCAACATCATCAGAGGCT
GGATCTTCGGCACCACACTGGACAGCAAGACCCAGAGCCTGCTGATCGTGAACAACGCCACCAACGTGGTCATCAAAGTGTGCGAGTTCCA
GTTCTGCAACGACCCCTTCCTGGGCGTCTACTACCACAAGAACAACAAGAGCTGGATGGAAAGCGAGTTCCGGGTGTACAGCAGCGCCAAC
AACTGCACCTTCGAGTACGTGTCCCAGCCTTTCCTGATGGACCTGGAAGGCAAGCAGGGCAACTTCAAGAACCTGCGCGAGTTCGTGTTTA
AGAACATCGACGGCTACTTCAAGATCTACAGCAAGCACACCCCTATCAACCTCGTGCGGGATCTGCCTCAGGGCTTCTCTGCTCTGGAACC
CCTGGTGGATCTGCCCATCGGCATCAACATCACCCGGTTTCAGACACTGCTGGCCCTGCACAGAAGCTACCTGACACCTGGCGATAGCAGC
AGCGGATGGACAGCTGGTGCCGCCGCTTACTATGTGGGCTACCTGCAGCCTAGAACCTTCCTGCTGAAGTACAACGAGAACGGCACCATCA
CCGACGCCGTGGATTGTGCTCTGGATCCTCTGAGCGAGACAAAGTGCACCCTGAAGTCCTTCACCGTGGAAAAGGGCATCTACCAGACCAG
CAACTTCCGGGTGCAGCCCACCGAATCCATCGTGCGGTTCCCCAATATCACCAATCTGTGCCCCTTCGGCGAGGTGTTCAATGCCACCAGA
TTCGCCTCTGTGTACGCCTGGAACCGGAAGCGGATCAGCAATTGCGTGGCCGACTACTCCGTGCTGTACAACTCCGCCAGCTTCAGCACCT
TCAAGTGCTACGGCGTGTCCCCTACCAAGCTGAACGACCTGTGCTTCACAAACGTGTACGCCGACAGCTTCGTGATCCGGGGAGATGAAGT
GCGGCAGATTGCCCCTGGACAGACAGGCAAGATCGCCGACTACAACTACAAGCTGCCCGACGACTTCACCGGCTGTGTGATTGCCTGGAAC
AGCAACAACCTGGACTCCAAAGTCGGCGGCAACTACAATTACCTGTACCGGCTGTTCCGGAAGTCCAATCTGAAGCCCTTCGAGCGGGACA
TCTCCACCGAGATCTATCAGGCCGGCAGCACCCCTTGTAACGGCGTGGAAGGCTTCAACTGCTACTTCCCACTGCAGTCCTACGGCTTTCA
GCCCACAAATGGCGTGGGCTATCAGCCCTACAGAGTGGTGGTGCTGAGCTTCGAACTGCTGCATGCCCCTGCCACAGTGTGCGGCCCTAAG
AAAAGCACCAATCTCGTGAAGAACAAATGCGTGAACTTCAACTTCAACGGCCTGACCGGCACCGGCGTGCTGACAGAGAGCAACAAGAAGT
TCCTGCCATTCCAGCAGTTTGGCCGGGATATCGCCGATACCACAGACGCCGTTAGAGATCCCCAGACACTGGAAATCCTGGACATCACCCC
TTGCAGCTTCGGCGGAGTGTCTGTGATCACCCCTGGCACCAACACCAGCAATCAGGTGGCAGTGCTGTACCAGGACGTGAACTGTACCGAA
GTGCCCGTGGCCATTCACGCCGATCAGCTGACACCTACATGGCGGGTGTACTCCACCGGCAGCAATGTGTTTCAGACCAGAGCCGGCTGTC
TGATCGGAGCCGAGCACGTGAACAATAGCTACGAGTGCGACATCCCCATCGGCGCTGGAATCTGCGCCAGCTACCAGACACAGACAAACAG
CCCTCGGAGAGCCAGAAGCGTGGCCAGCCAGAGCATCATTGCCTACACAATGTCTCTGGGCGCCGAGAACAGCGTGGCCTACTCCAACAAC
TCTATCGCTATCCCCACCAACTTCACCATCAGCGTGACCACAGAGATCCTGCCTGTGTCCATGACCAAGACCAGCGTGGACTGCACCATGT

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ACATCTGCGGCGATTCCACCGAGTGCTCCAACCTGCTGCTGCAGTACGGCAGCTTCTGCACCCAGCTGAATAGAGCCCTGACAGGGATCGC
CGTGGAACAGGACAAGAACACCCAAGAGGTGTTCGCCCAAGTGAAGCAGATCTACAAGACCCCTCCTATCAAGGACTTCGGCGGCTTCAAT
TTCAGCCAGATTCTGCCCGATCCTAGCAAGCCCAGCAAGCGGAGCTTCATCGAGGACCTGCTGTTCAACAAAGTGACACTGGCCGACGCCG
GCTTCATCAAGCAGTATGGCGATTGTCTGGGCGACATTGCCGCCAGGGATCTGATTTGCGCCCAGAAGTTTAACGGACTGACAGTGCTGCC
TCCTCTGCTGACCGATGAGATGATCGCCCAGTACACATCTGCCCTGCTGGCCGGCACAATCACAAGCGGCTGGACATTTGGAGCAGGCGCC
GCTCTGCAGATCCCCTTTGCTATGCAGATGGCCTACCGGTTCAACGGCATCGGAGTGACCCAGAATGTGCTGTACGAGAACCAGAAGCTGA
TCGCCAACCAGTTCAACAGCGCCATCGGCAAGATCCAGGACAGCCTGAGCAGCACAGCAAGCGCCCTGGGAAAGCTGCAGGACGTGGTCAA
CCAGAATGCCCAGGCACTGAACACCCTGGTCAAGCAGCTGTCCTCCAACTTCGGCGCCATCAGCTCTGTGCTGAACGATATCCTGAGCAGA
CTGGACCCTCCTGAGGCCGAGGTGCAGATCGACAGACTGATCACAGGCAGACTGCAGAGCCTCCAGACATACGTGACCCAGCAGCTGATCA
GAGCCGCCGAGATTAGAGCCTCTGCCAATCTGGCCGCCACCAAGATGTCTGAGTGTGTGCTGGGCCAGAGCAAGAGAGTGGACTTTTGCGG
CAAGGGCTACCACCTGATGAGCTTCCCTCAGTCTGCCCCTCACGGCGTGGTGTTTCTGCACGTGACATATGTGCCCGCTCAAGAGAAGAAT
TTCACCACCGCTCCAGCCATCTGCCACGACGGCAAAGCCCACTTTCCTAGAGAAGGCGTGTTCGTGTCCAACGGCACCCATTGGTTCGTGA
CACAGCGGAACTTCTACGAGCCCCAGATCATCACCACCGACAACACCTTCGTGTCTGGCAACTGCGACGTCGTGATCGGCATTGTGAACAA
TACCGTGTACGACCCTCTGCAGCCCGAGCTGGACAGCTTCAAAGAGGAACTGGACAAGTACTTTAAGAACCACACAAGCCCCGACGTGGAC
CTGGGCGATATCAGCGGAATCAATGCCAGCGTCGTGAACATCCAGAAAGAGATCGACCGGCTGAACGAGGTGGCCAAGAATCTGAACGAGA
GCCTGATCGACCTGCAAGAACTGGGGAAGTACGAGCAGTACATCAAGTGGCCCTGGTACATCTGGCTGGGCTTTATCGCCGGACTGATTGC
CATCGTGATGGTCACAATCATGCTGTGTTGCATGACCAGCTGCTGTAGCTGCCTGAAGGGCTGTTGTAGCTGTGGCAGCTGCTGCAAGTTC

GACGAGGACGATTCTGAGCCCGTGCTGAAGGGCGTGAAACTGCACTACACA**TGATGA**CTCGAGCTGGTACTGCATGCACGCAATGCTAGCT
GCCCCTTTCCCGTCCTGGGTACCCCGAGTCTCCCCCGACCTCGGGTCCCAGGTATGCTCCCACCTCCACCTGCCCCACTCACCACCTCTGC
TAGTTCCAGACACCTCCCAAGCACGCAGCAATGCAGCTCAAAACGCTTAGCCTAGCCACACCCCCACGGGAAACAGCAGTGATTAACCTTT
AGCAATAAACGAAAGTTTAACTAAGCTATACTAACCCCAGGGTTGGTCAATTTCGTGCCAGCCACACCCTGGAGCTAGCA

Cyan: Putative 5' UTR Green: Start Codon Yellow: Signal Peptide Orange: Spike encoding region Red: Stop codon(s) Purple: 3' UTR Blue: Start of polyA region (incomplete)

Figure 19: Spike-encoding contig assembled from BioNTech/Pfizer BNT-162b2 vaccine.

Figure 2: Spike-encoding contig assembled from Moderna mRNA-1273 vaccine.

GGGAAATAAGAGAGAAAAGAAGAGTAAGAAGAAATATAAGACCCCGGCGCCGCCACC***ATGTTCGTGTTCCTGGTGCTGCTGCCCCTGG***
TGAGCAGCCAGTGCGTGAACCTGACCACCCGGACCCAGCTGCCACCAGCCTACACCAACAGCTTCACCCGGGGCGTCTACTACCCCGACAAGG
T GTTCCGGAGCAGCGTCCTGCACAGCACCCAGGACCTGTTCCTGCCCTTCTTCAGCAACGTGACCTGGTTCCACGCCATCCACGTGAGCGGC
ACCAACGGCACCAAGCGGTTCGACAACCCCGTGCTGCCCTTCAACGACGGCGTGTACTTCGCCAGCACCGAGAAGAGCAACATCATCCGGG
GCTGGATCTTCGGCACCACCCTGGACAGCAAGACCCAGAGCCTGCTGATCGTGAATAACGCCACCAACGTGGTGATCAAGGTGTGCGAGTT
CCAGTTCTGCAACGACCCCTTCCTGGGCGTGTACTACCACAAGAACAACAAGAGCTGGATGGAGAGCGAGTTCCGGGTGTACAGCAGCGCC
AACAACTGCACCTTCGAGTACGTGAGCCAGCCCTTCCTGATGGACCTGGAGGGCAAGCAGGGCAACTTCAAGAACCTGCGGGAGTTCGTGT
TCAAGAACATCGACGGCTACTTCAAGATCTACAGCAAGCACACCCCAATCAACCTGGTGCGGGATCTGCCCCAGGGCTTCTCAGCCCTGGA
GCCCCTGGTGGACCTGCCCATCGGCATCAACATCACCCGGTTCCAGACCCTGCTGGCCCTGCACCGGAGCTACCTGACCCCAGGCGACAGC
AGCAGCGGGTGGACAGCAGGCGCGGCTGCTTACTACGTGGGCTACCTGCAGCCCCGGACCTTCCTGCTGAAGTACAACGAGAACGGCACCA
TCACCGACGCCGTGGACTGCGCCCTGGACCCTCTGAGCGAGACCAAGTGCACCCTGAAGAGCTTCACCGTGGAGAAGGGCATCTACCAGAC
CAGCAACTTCCGGGTGCAGCCCACCGAGAGCATCGTGCGGTTCCCCAACATCACCAACCTGTGCCCCTTCGGCGAGGTGTTCAACGCCACC
CGGTTCGCCAGCGTGTACGCCTGGAACCGGAAGCGGATCAGCAACTGCGTGGCCGACTACAGCGTGCTGTACAACAGCGCCAGCTTCAGCA
CCTTCAAGTGCTACGGCGTGAGCCCCACCAAGCTGAACGACCTGTGCTTCACCAACGTGTACGCCGACAGCTTCGTGATCCGTGGCGACGA
GGTGCGGCAGATCGCACCCGGCCAGACAGGCAAGATCGCCGACTACAACTACAAGCTGCCCGACGACTTCACCGGCTGCGTGATCGCCTGG
AACAGCAACAACCTCGACAGCAAGGTGGGCGGCAACTACAACTACCTGTACCGGCTGTTCCGGAAGAGCAACCTGAAGCCCTTCGAGCGGG
ACATCAGCACCGAGATCTACCAAGCCGGCTCCACCCCTTGCAACGGCGTGGAGGGCTTCAACTGCTACTTCCCTCTGCAGAGCTACGGCTT
CCAGCCCACCAACGGCGTGGGCTACCAGCCCTACCGGGTGGTGGTGCTGAGCTTCGAGCTGCTGCACGCCCCAGCCACCGTGTGTGGCCCC
AAGAAGAGCACCAACCTGGTGAAGAACAAGTGCGTGAACTTCAACTTCAACGGCCTTACCGGCACCGGCGTGCTGACCGAGAGCAACAAGA
AATTCCTGCCCTTTCAGCAGTTCGGCCGGGACATCGCCGACACCACCGACGCTGTGCGGGATCCCCAGACCCTGGAGATCCTGGACATCAC
CCCTTGCAGCTTCGGCGGCGTGAGCGTGATCACCCCAGGCACCAACACCAGCAACCAGGTGGCCGTGCTGTACCAGGACGTGAACTGCACC
GAGGTGCCCGTGGCCATCCACGCCGACCAGCTGACACCCACCTGGCGGGTCTACAGCACCGGCAGCAACGTGTTCCAGACCCGGGCCGGTT
GCCTGATCGGCGCCGAGCACGTGAACAACAGCTACGAGTGCGACATCCCCATCGGCGCCGGCATCTGTGCCAGCTACCAGACCCAGACCAA
TTCACCCCGGAGGGCAAGGAGCGTGGCCAGCCAGAGCATCATCGCCTACACCATGAGCCTGGGCGCCGAGAACAGCGTGGCCTACAGCAAC
AACAGCATCGCCATCCCCACCAACTTCACCATCAGCGTGACCACCGAGATTCTGCCCGTGAGCATGACCAAGACCAGCGTGGACTGCACCA
TGTACATCTGCGGCGACAGCACCGAGTGCAGCAACCTGCTGCTGCAGTACGGCAGCTTCTGCACCCAGCTGAACCGGGCCCTGACCGGCAT
CGCCGTGGAGCAGGACAAGAACACCCAGGAGGTGTTCGCCCAGGTGAAGCAGATCTACAAGACCCCTCCCATCAAGGACTTCGGCGGCTTC
AACTTCAGCCAGATCCTGCCCGACCCCAGCAAGCCCAGCAAGCGGAGCTTCATCGAGGACCTGCTGTTCAACAAGGTGACCCTAGCCGACG
CCGGCTTCATCAAGCAGTACGGCGACTGCCTCGGCGACATAGCCGCCCGGGACCTGATCTGCGCCCAGAAGTTCAACGGCCTGACCGTGCT
GCCTCCCCTGCTGACCGACGAGATGATCGCCCAGTACACCAGCGCCCTGTTAGCCGGAACCATCACCAGCGGCTGGACTTTCGGCGCTGGA
GCCGCTCTGCAGATCCCCTTCGCCATGCAGATGGCCTACCGGTTCAACGGCATCGGCGTGACCCAGAACGTGCTGTACGAGAACCAGAAGC
TGATCGCCAACCAGTTCAACAGCGCCATCGGCAAGATCCAGGACAGCCTGAGCAGCACCGCTAGCGCCCTGGGCAAGCTGCAGGACGTGGT
GAACCAGAACGCCCAGGCCCTGAACACCCTGGTGAAGCAGCTGAGCAGCAACTTCGGCGCCATCAGCAGCGTGCTGAACGACATCCTGAGC
CGGCTGGACCCTCCCGAGGCCGAGGTGCAGATCGACCGGCTGATCACTGGCCGGCTGCAGAGCCTGCAGACCTACGTGACCCAGCAGCTGA
TCCGGGCCGCCGAGATTCGGGCCAGCGCCAACCTGGCCGCCACCAAGATGAGCGAGTGCGTGCTGGGCCAGAGCAAGCGGGTGGACTTCTG
CGGCAAGGGCTACCACCTGATGAGCTTCCCCAGAGCGCACCCCACGGAGTGGTGTTCCTGCACGTGACCTACGTGCCCGCCCAGGAGAAG
AACTTCACCACCGCCCCAGCCATCTGCCACGACGGCAAGGCCCACTTTCCCCGGGAGGGCGTGTTCGTGAGCAACGGCACCCACTGGTTCG
TGACCCAGCGGAACTTCTACGAGCCCCAGATCATCACCACCGACAACACCTTCGTGAGCGGCAACTGCGACGTGGTGATCGGCATCGTGAA
CAACACCGTGTACGATCCCCTGCAGCCCGAGCTGGACAGCTTCAAGGAGGAGCTGGACAAGTACTTCAAGAATCACACCAGCCCCGACGTG
GACCTGGGCGACATCAGCGGCATCAACGCCAGCGTGGTGAACATCCAGAAGGAGATCGATCGGCTGAACGAGGTGGCCAAGAACCTGAACG
AGAGCCTGATCGACCTGCAGGAGCTGGGCAAGTACGAGCAGTACATCAAGTGGCCCTGGTACATCTGGCTGGGCTTCATCGCCGGCCTGAT
CGCCATCGTGATGGTGACCATCATGCTGTGCTGCATGACCAGCTGCTGCAGCTGCCTGAAGGGCTGTTGCAGCTGCGGCAGCTGCTGCAAG

TTCGACGAGGACGACAGCGAGCCCGTGCTGAAGGGCGTGAAGCTGCACTACACC**TGATAATAG**GCTGGAGCCTCGGTGGCCTAGCTTCTTG
CCCCTTGGGCCTCCCCCCAGCCCCTCCTCCCCTTCCTGCACCCGTACCCCCGTGGTCTTTGAATAAAGTCTGAGTGGGCGGCAAAAAAAAA

Cyan: Putative 5' UTR Green: Start Codon Yellow: Signal Peptide Orange: Spike encoding region Red: Stop codon(s) Purple: 3' UTR Blue: Start of polyA region (incomplete)

Figure 20: Spike-encoding contig assembled from Moderna mRNA-1273 vaccine.

It is interesting to note that the starting region of the Spike was modified in both vaccines. We show

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i (Perez§Montagnier 2020) that this crucial region contains « EIE » HIV like inserts, particularly HIV1 Kenya.

Recall the 100 first bases of SARS-CoV2 Spike :
ATGTTTGTTTTTCTTGTTTTATTGCCACTAGTCTCTAGTCAGTGTGTTAATCTTACAACCA
GAACTCAATTACCCCCTGCATACACTAATTCTTTCACAC

It is interesting comparing this region with the same areas in both vaccines (***bold***).

What should we conclude about this total absence of Fibonacci metastructures in the mRNAs of these 2 vaccines?
This means that, although functional, these mRNAs will have a short lifespan and their overall physical structure will be very weak. These mRNAs will be able to split rather quickly into separate fragments which will risk combining with other mRNAs present in their environment.

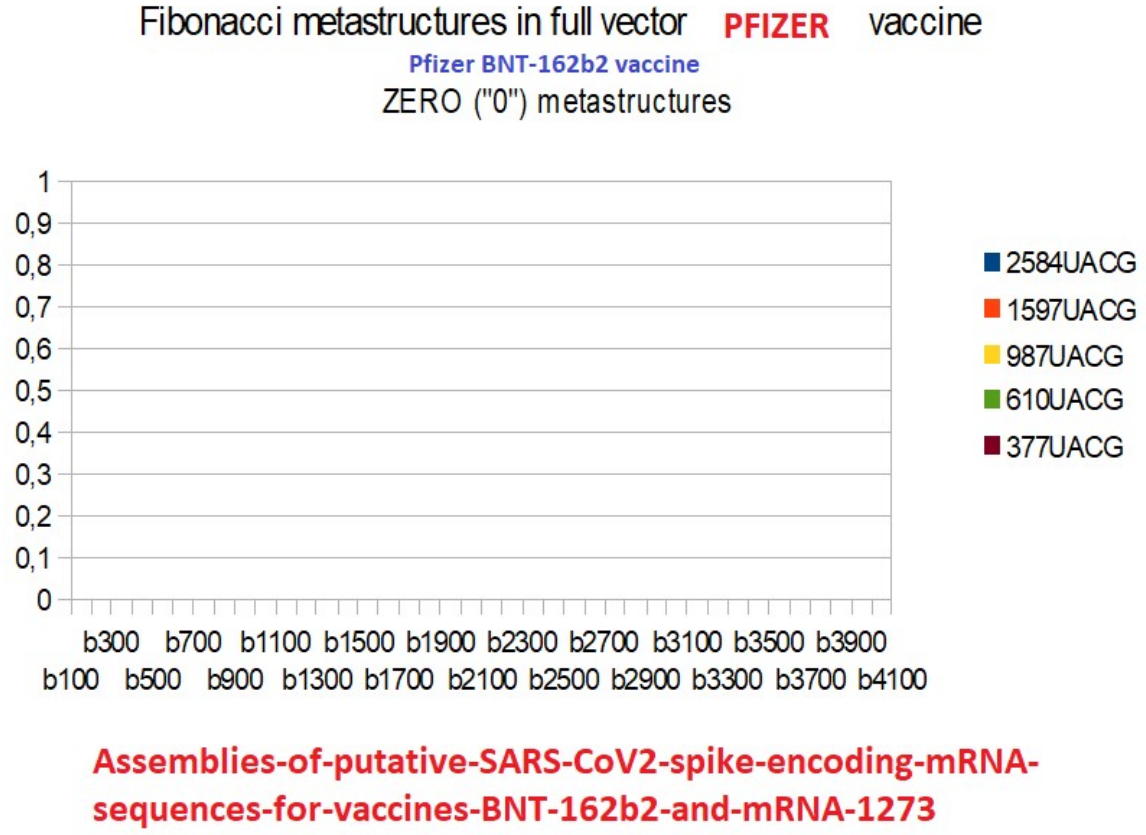

Figure 21 – Flat response for Fibonacci Metastructures from **BioNTech/Pfizer BNT-162b2 vaccine.**

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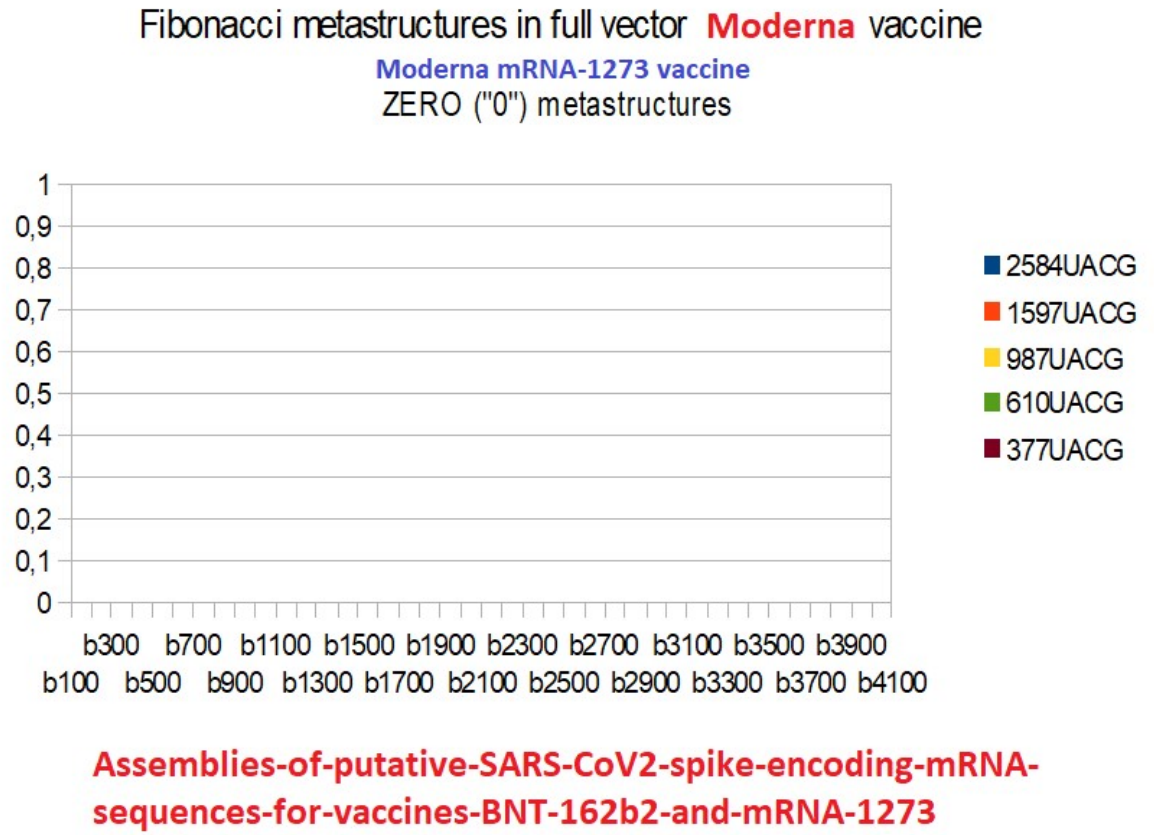

Figure 22 – Flat response for Fibonacci Metastructures from **Moderna mRNA-1273 vaccine.**

We will now explain the technological reasons which, in the design of these 2 vaccines, led to such differences between the Fibonacci structures of real sarscov2, their variants and these 2 mRNA vaccines.
A necessary but not sufficient condition for the possible emergence of Fibonacci UA / CG metastructures is that the ratio between the total number of UA and CG bases of the analyzed sequence is> 1 and, ideally, close to the optimum Phi = 1.618, the "Golden ratio". Let us calculate these ratios for certain sarscov2 genomes and spikes various variants, then for the 2 mRNAs of the Moderna and Pfizer vaccines.

Table 8 below demonstrates how the entire genomes as well as the spikes as well as the different variants all have an AU / CG ratio very close to 1.618. The maximum error is less than 4%. On the contrary, the 2 mRNAs of the Pfizer and Moderna vaccines have radically INVERTED ratios such as CG> UA.

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Table 8 – Comparing various UA/CG ratios from 20 SARS-CoV2, variants, and mRNA vaccines.

MRNA sequence	Ratio UA/CG	**Error 1.618 – ratio UA/CG**
Whole Genomes		
SARS-CoV2 ref	1.633465434	**-0.01543144473**
SARSCOV2 D614G	1.633233533	**-0.01519954393**
Bat RATG13	1.629006692	**-0.0109727035**
CoVZC45	1.570467483	**0.04756650582**
CoVZXC21	1.575760201	**0.04227378801**
VCA19 (patient California variant ref Table4)	1.633710647	**-0.01567665833**
Spikes		
Spike SARS-CoV2 ref	1.680224404	**-0.06219041493**
D614G	1.678346181	**-0.0603121918**
Bat RaTG13	1.661774983	**-0.04374099353**
CoVZC45	1.600834492	**0.01719949665**
CoVZXC21	1.627988748	**-0.009954759242**
SCA19 (patient California variant ref Table4)	1.682105263	**-0.06407127416**
Variant UK SN501Y	1.678346181	**-0.0603121918**
Variant UK SN501T	1.676470588	**-0.05843659924**
Variant UK SN501S	1.676470588	**-0.05843659924**
Variant South Afrika SE484K	1.680224404	**-0.06219041493**
Variant INDIABASIC (ref §3.6)	1.676470588	**-0.05843659924**
Variant INDIAFULL (ref §3.6)	1.682105263	**-0.06407127416**
MRNA vaccines		
Pfizer	0.7593763169	**0.8586576721**
Moderna	0.6132151491	**1.00481884**

Faced with such a distortion between the real and "humanized" SARS-CoV2 strains and its variants on the one hand, and the mRNAs of the 2 vaccines on the other hand, we will now try to answer 2 essential questions:
1 / Is there a mutation "strategy" governing the adaptation of the virus and its variants to its host? This strategy, if it exists, will ALSO constitute a strong mutation constraint for the 2 mRNAs of the Moderna and Pfizer vaccines? Table 10 below will answer this key question.
2 / For what technological reasons did the designers of the 2 mRNA vaccines decide to "dope" the sequences constituting their vaccines in CG bases?

Does this predominance of AU / CG ratios located around Phi = 1.618 extend to other SARS-CoV2 genes?

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In Table 9, we demonstrate this generalization. Only 2 sequences, very short, have a UA / CG ratio <1. We find that the entire genome, the large ORF1ab gene, the spike gene, as well as the average of all genes finely obey this law. The average cumulative error over all genes is .03. (1.85%)

Particularly, the gene ORF1ab17 with a ratio <1 is a very short quasi palindrome mRNA sequence:

Coronavirus frameshifting stimulation element

stem-loop 1"
Semi palindrome

cggtg taag tgcagcccgt cttaca
13501 ccg

The second region with UA/CG < 1

```
stem_loop    29728..29768
                     /inference="COORDINATES:
                     profile:Rfam-release-14.1:RF00164,Infernal:1.1.2"
                     /note="basepair exception: alignment to the Rfam model
                     implies coordinates 29740:29758 form a noncanonical C:T
                     basepair, but the homologous positions form a highly
                     conserved C:G basepair in other viruses, including SARS
                     (NC_004718.3)"
                     /function="Coronavirus 3' stem-loop II-like motif (s2m)"
```

VSARSCOV2REF[29727+¼(29768-29727)]
TTCACCGAGGCCACGCGGAGTACGATCGAGTGTACAGTGAA

This sequence is also very short.

Recall SARS-CoV2 Wuhan references
https://www.ncbi.nlm.nih.gov/nuccore/NC_045512

Table 9 – Computing UA/CG ratio for all SARS-CoV2 Wwuhan reference genes.

MRNA sequence	Ratio UA/CG	**Error 1.618 – ratio UA/CG**
Whole Genomes		
SARS-CoV2 ref	1.633465434	**¯0.01543144473**
Genes		
5 UTR	1.245762712	**0.3722712771**
ORF 1AB	1.669927264	**¯0.05189327461**
ORF1 ab1	1.061068702	**0.5569652867**
ORF1 ab2	1.508519004	**0.1095149851**
ORF1 ab3	1.785202864	**¯0.167168875**
ORF1 ab4	1.742230347	**¯0.1241963583**

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ORF1 ab5	1.742230347	**¯0.1241963583**
ORF1 ab6	1.740112994	**¯0.1220790054**
ORF1 ab7	1.621052632	**¯0.003018642579**
ORF1 ab8	1.605263158	**0.01277083111**
ORF1 ab9	1.492647059	**0.1253869302**
ORF1 ab10	1.355932203	**0.2621017856**
ORF1 ab11	1.682341651	**¯0.06430766167**
ORF1 ab12	1.620639535	**¯0.002605545884**
ORF1 ab13	1.61322314	**0.004810848504**
ORF1 ab14	1.940509915	**¯0.322475926**
ORF1 ab15	1.820189274	**¯0.2021552854**
ORF1 ab16	1.650491277	**¯0.03245728832**
ORF1 ab17 §	0.6470588235	**0.9709751655**
ORF1 ab18	+1.750000000	**¯0.131966011**
SPIKE	1.680224404	**¯0.06219041493**
ORF3a	1.532110092	**0.08592389726**
Gene E (ref Yan Li Meng)	1.620689655	**¯0.002655666172**
Gene M	1.347368421	**0.2706655679**
ORF6	1.347368421	**0.2706655679**
ORF7a	1.614285714	**0.003748274714**
ORF7b	2.219512195	**¯0.6014782061**
ORF8	1.79389313	**¯0.1758591408**
Gene N	1.117647059	**0.5003869302**
ORF10a	+1.925000000	**¯0.306966011**
ORF10b	1.769230769	**¯0.1511967802**
ORF10c	2.222222222	**¯0.6041882332**
3UTR	1.726190476	**¯0.1081564872**
coordinates	0.7826086957	**0.8354252933**
AVERAGE	**1.588022181**	**0.03001180791 (1.85%)**
MRNA vaccines		
Pfizer	0.7593763169	**0.8586576721**
Moderna	0.6132151491	**1.00481884**

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Table 10 – Comparing UA ==> CG and CG ==> UA mutations in 15 worldwide SARS-CoV2 variants (source https://covariants.org/).

Variant reference	**UA ==> CG**	**CG ==> UA**
20E(EU1) https://covariants.org/variants/20A.EU1	1	1
20A.EU2 https://covariants.org/variants/20A.EU2	1	3
20I/501Y.V1 https://covariants.org/variants/S.501Y.V1	1	6
20H/501Y.V2 https://covariants.org/variants/S.501Y.V2	0	4
20J/501Y.V3 https://covariants.org/variants/S.501Y.V3	3	5
20C/S:452R https://covariants.org/variants/S.L452R	2	2
20C/S:484K https://covariants.org/variants/20C.S.484K	1	2
20A/S:484K https://covariants.org/variants/20A.S.484K	4	8
20A/S:439K https://covariants.org/variants/20A.S.484K	0	1
S:677H.Robin1 https://covariants.org/variants/S.Q677H.Robin1	1	4
S:677P.Pelican https://covariants.org/variants/S.Q677P.Pelican	1	3
20A/S:98F https://covariants.org/variants/S.S98F	0	1
20C/S:80Y **https://covariants.org/variants/S.D80Y**	**0**	**8**
20B/S:626S https://covariants.org/variants/S.A626S	0	0
20B/S:1122L https://covariants.org/variants/S.V1122L	0	0
Total	**15**	**48**

Let out of the 15 variants referenced > 3 times more CG ==> UA than UA ==> CG.
A very marginal residual number consists of U / A or C / G.
Morality: variants, by synonymous mutations most often seek to optimize (ie. "NATURALIZE")
the mRNA of the genome by privileging the UA, and probably the ratio UA / CG Close to phi 1.618, this is what the
fibonacci show on the variants by our curves.

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As for the MODERNA and PFIZER mRNAs, they are MAJORITY in CG, therefore Fibonaccis UA / CG NULS.

Now, what about this second question :

« For what technological reasons did the designers of the 2 mRNA vaccines decide to "dope" the sequences constituting their vaccines in CG bases? »

In (Jackson et al, 2020), we could read : *«Last, codon optimization and modification of nucleotides have contributed to translation efficiency. For example, optimization of guanine and cytosine (GC) content can have a significant impact (Kudla et al, 2016) and has been well established with DNA vaccines ».*

(Kudla et al, 2016) detailed this « CG rich manufacturing technology » : *« Mammalian genes are highly heterogeneous with respect to their nucleotide composition, but the functional consequences of this heterogeneity are not clear. In the previous studies, weak positive or negative correlations have been found between the silent-site guanine and cytosine (GC) content and expression of mammalian genes. However, previous studies disregarded differences in the genomic context of genes, which could potentially obscure any correlation between GC content and expression. In the present work, we directly … »*

Then a new question :
“Can we distinguish between natural variants and variants triggered by vaccines?”

This D80Y spike variant would be a good candidate for this variant from vaccine question

because it has a high number of syn C ==> U mutations.
We recall here this detailed variant :

Dedicated 20C/S:80Y Nextstrain build

Defining mutations

Nonsynonymous:

- **S:**D80Y
- **N:**S186Y
- **N:**D377Y
- **ORF1a:**T945I
- **ORF1a:**T1567I
- **ORF1a:**Q3346K
- **ORF1a:**V3475F
- **ORF1a:**M3862I
- **ORF1b:**P255T

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- ORF7a:R80I

Synonymous:

- G4960T
- C6070T
- C7303T
- C7564T
- C10279T
- C10525T
- C10582T
- C27804T

Of full list of 18 nucleotide mutations, 15 are mutations to T (possibly related to APOBEC-like editing within host, see (Simmonds, 2020).
This variant is found in at least 10 countries across Europe.
S:D80Y

S:D80Y is the opposite end of the loop 'tucked in' by the 69/70 deletion (hypothetical association). See MutationS:H69- for more detail on the impact of 69/70 deletion.

This strain is present everywhere in Europe.
Quite rightly, Professor Luc Montagnier asks me:
"I put my question again in another form: all the variants that you have studied have in the sequence of their Spyke proteins a Fibonacci YES series? Why? because it is a rule of harmonization of Nature followed by the variants during their passage through their successive hosts. The m-RNA sequences of vaccines were chosen by technologists ignoring these laws, which only had the aim of increasing the stability of their messages."
This is why I researched and found what technological reasons led them to make mRNA CG rich.

But another more speculative question then arises:
Between these 2 disjoint universes that are mRNA and proteins, would having a HYPER STRUCTURED mRNA be able to transmit "a certain dynamic energy during the passage into amino acids" to the future protein, which would make it more stable? , more functional?
If so, our Fibonacci are used for that.One fact is certain, the 2 mRNAs of the Moderna and Pfizer vaccines will result in a low functionality of the spike vaccine because by doping these sequences in CG rich, their designers, in search of greater STABILITY of these RNAs will have built, according to us , sequences which, as soon as they are inserted into the human host, will seek to mutate, like SARS-CoV2 variants, towards CG ==> UA forms in order to improve, paradoxically, their STABILITY and probably also their LIFETIME.

3.9 - Does the CG-rich modification of the synonymous codons of the spikes of the 2 mRNA vaccines affect the expression and quantity of SARS-CoV2 antibodies?

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Analyzing Master Code fractal structure and stationary waveforms differences between Moderna and Phizer Spikes mRNA.

In (Perez, 2015 and Perez, 2018), we present a unifying theoretical method, from the atomic masses of their bioatoms C O N H S P, the 3 biological universes of RNA, DNA and proteins. We published various articles involving applications based on this basic research (Perez, 2017b, Perez, 2017c).

The Master Code of the sequence can be applied indistinctly to all DNA or RNA sequences irrespective of the fact that they are coding proteins or not, and to all protein sequences. To every nucleotide triplet (codon), or amino acid (AA), can be associated a cypher comprised between -3 and +7. These cyphers were established in relation with the atomic masses of the chemical elements C,N,O,H,S,P constituting the nitrogen bases (purines and pyrimidines) and the amino acids. They allow a simple numerical translation of the 64 codons and 20 amino acids. Exposing here the concepts leading to this code goes beyond the scope of this article and we refer the budding mathematicians to the article (Perez, 2018) *"Six Fractal Codes of Biological Life: perspectives in Exobiology and Artificial Intelligence Biomimetism Decisions Making, 2018"*. One could oppose the criticism that this representation reduces too drastically the physico-chemical reality of the translated sequences. However, it allows their underlying geometrical reality to be measured. This mathematical conversion has the advantage to reduce the complexity of the problem. We can cite here the great mathematician and physicist Von Neumann who used to say with humor *"There's no sense in being precise when you don't even know what you're talking about".*

Although the amino acid sequences of the spikes of the 2 mRNA vaccines are identical, it is interesting to analyze with these biomathematic methods their nucleotide sequences which are very different. Indeed (& 3.8), we have seen that these 2 sequences were doped with CG rich nucleotides at the level of the synonymous codons coding for the same amino acid, therefore without affecting the sequence of the spike protein.

In Figure 23 below, we see that, while the 2 Moderna and Phizer protein sequences (blue proteomics curves) are identical, their respective Genomics curves (red curves) are very different. We observe in particular a completely chaotic fractal roughness in the case of Phizer spike. In fact, in the case of the 2 spikes of these vaccines, a large number of synonymous codons were modified in order to dope these sequences in CG bases without altering the amino acid sequence. We believe that this exceptional fractal roughness could affect the stability and the lifespan of the RNA, whereas the corn sought by the designers of Pfizer-Biontech was, precisely, to increase the stability of these RNAs. One advantage will be that these RNAs will be quickly destroyed (around ten days). On the other hand, the fragility of these RNAs could lead to "breaks" of the RNA strand, with the risk of erratic combinations (HERV retrovirus for example, naturally present in the cell).

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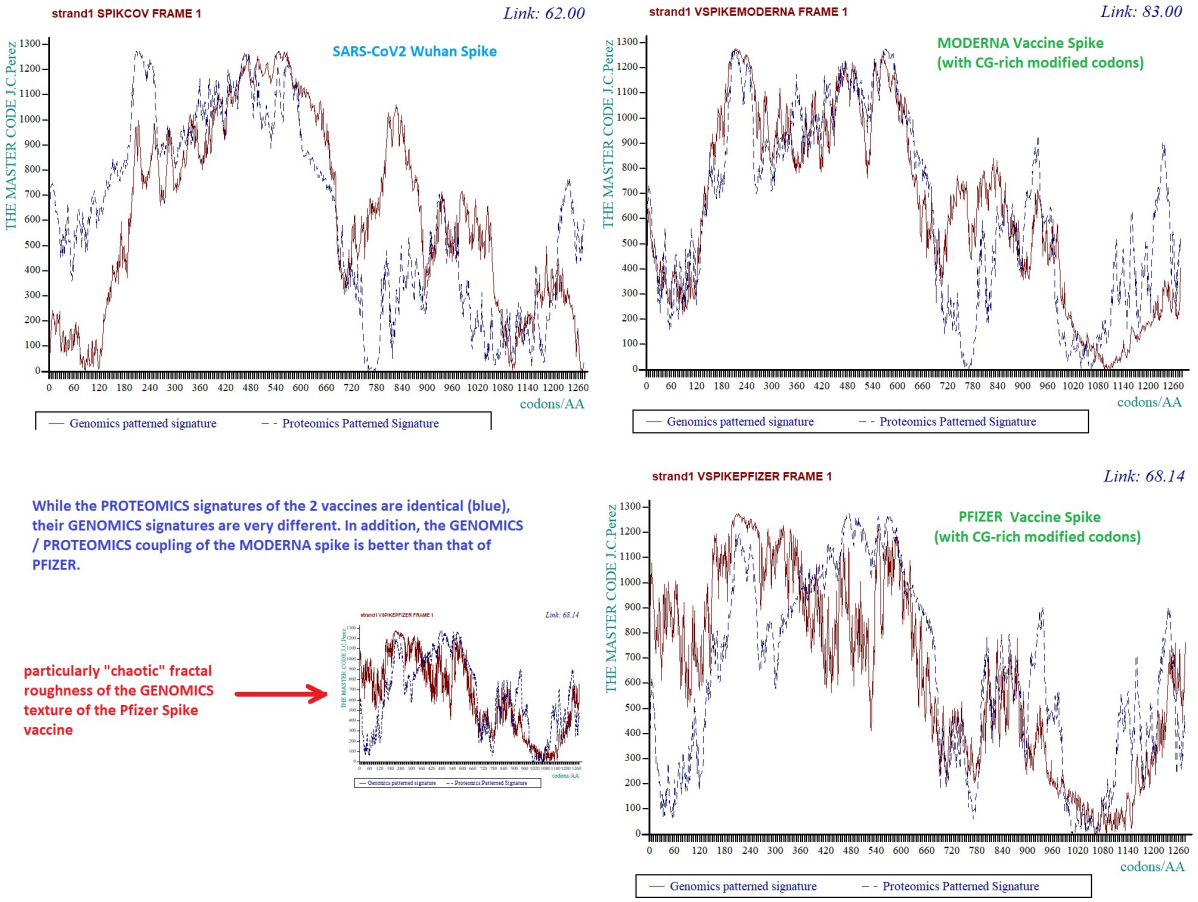

Figure 23 – Comparing Master Code Genomics/Proteomics between SARS-CoV2 Wuhan, Moderna and Phizer spikes.

Computing Standing waves :

In (Perez,2018), we describe this biomathematical method associating with any Genomics sequence periodic waves (numerical where period is a number of nucleotides).

The Genomics master code is generalized to meta-codons that no longer have 3 nucleotides as a codon, but 4, 5, … 100 nucleotides. Then we analyze the textures by the undulatory code. It then appears dissonances and resonances that will reveal periods of discrete waves, resonances, and standing waves.

This method provides a global analysis of the roughness or fractal texture of the DNA sequences at the whole sequence scale. To do this, we generalize the method of numerical analysis of the "Master Code". Thus, we restructure the sequence into different generic sequences based on "meta codons", no longer triplets of 3 nucleotides, but values ranging from 1 to 100 nucleotides. This method of analysis will then reveal, in most cases, discrete waves or interferences, most often dissonances resulting from Genomics Master code texture analysis. However, sometimes there will emerge kinds of resonances where all scales of analysis appear to be in symbiosis.

The following Figure 24 shows this kind of waveforms in the 3 cases of Spike sequences providing from SARS-CoV2 Wuhan reference, Moderna vaccine and Phizer vaccine.

Figure 24 below illustrates and confirms, as before, standing waves of 8 nucleotides quite similar for SARS-CoV2 and Moderna spikes. On the contrary, the Spike Phizer is characterized by a different frequency: period of 7 nucleotides.

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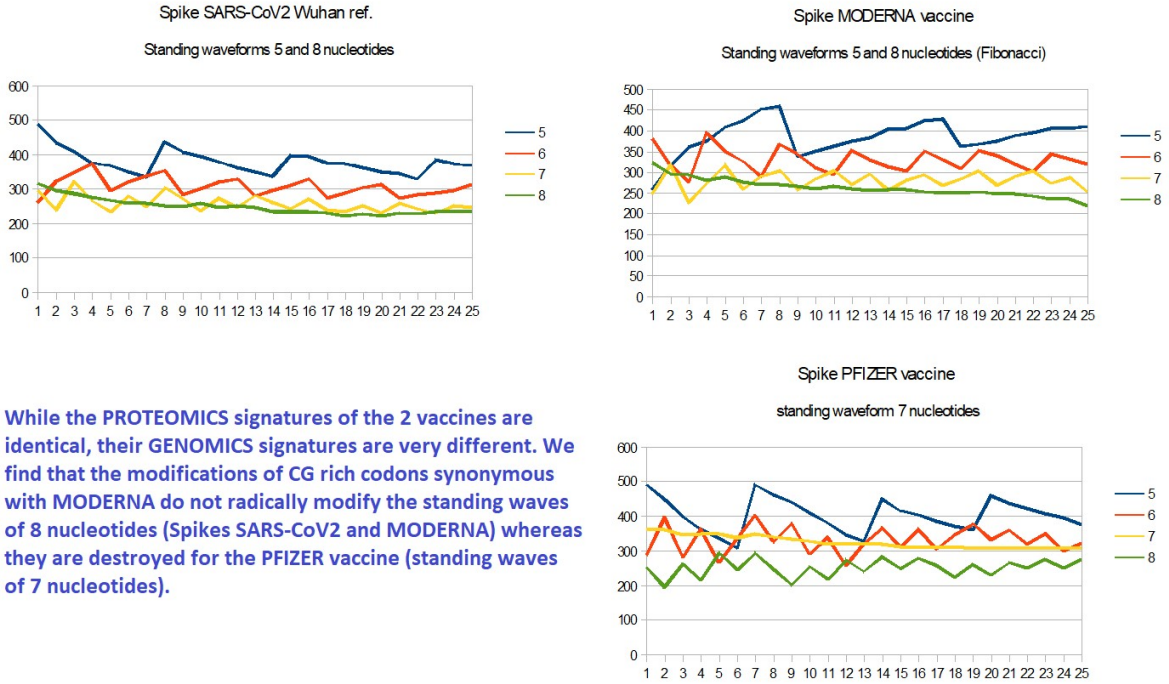

Figure 24 – Comparing numerical « Standing waves » between SARS-CoV2 Wuhan, Moderna and Phizer spikes.

From this comparison of the Spikes of the 2 vaccines Moderna and Phizer, we conclude a very probable difference in stability and shelf life of the 2 respective mRNAs of these 2 vaccines. However, the *"State of the Art"* will tell you that their 2 protein sequences are strictly identical. However, by having modified their synonymous codons using different strategies, no one can guarantee that the quantity of antibodies generated will be identical in the 2 cases.
No one can affirm that this difference in the 2 mRNAs will not have contributed to the dynamic formation of the spike protein. This is all the more complex since these mRNAs contain certain modified U / T bases. Professor Roland Baker (Molecular Genetics, U.C. Berkeley) said me *" T is for thymine used in DNA. U is for uracil used instead of T for mRNA. The mRNA vaccines made by Moderna and Pfizer use neither. Instead they use 1-methyl-3'-pseudouridylyl which is either shows a m1Ψ or simply Ψ. 1-methyl-3'-pseudouridylyl is used to increase the half-life of the mRNA. Otherwise it degrades too quickly. "*

One might wonder why such a period of 8 nucleotides is important? We observe that the spikes of SARS-CoV2 (and all its variants), as well as the Moderna spike, retain this period 8, unlike the Phizer spike.
8 is a Fibonacci number, and Figure 25 below illustrates how these Fibonacci periods (8 13 21 34 55 89 ...) are conserved at the scale of whole genomes SARS-CoV2 wuhan, but also in this variant CAL 21C collected from a Californian patient (Table3, CA51). It even appears that these Fibonacci standing wave periods at the scale of the entire genome would be "reinforced" in the case of the Californian variant (Figure 25).

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Although these 2 genomes are significantly different (29903nt for SARS-CoV2 and 29754nt for CA51).
CA51 contains one deletion encompassing S13I and another deletion encompassing W152C (see Table3), 2 of the 3 characteristic mutations of the California variant CAL.20C. However, despite this high level of deletions of the CAL.20C genome, the level of Fibonacci standing waves is preserved and even here reinforced. At the same time, the number of Fibonacci UA / CG metastructures (Table3) is also reinforced with respect to the reference genome.

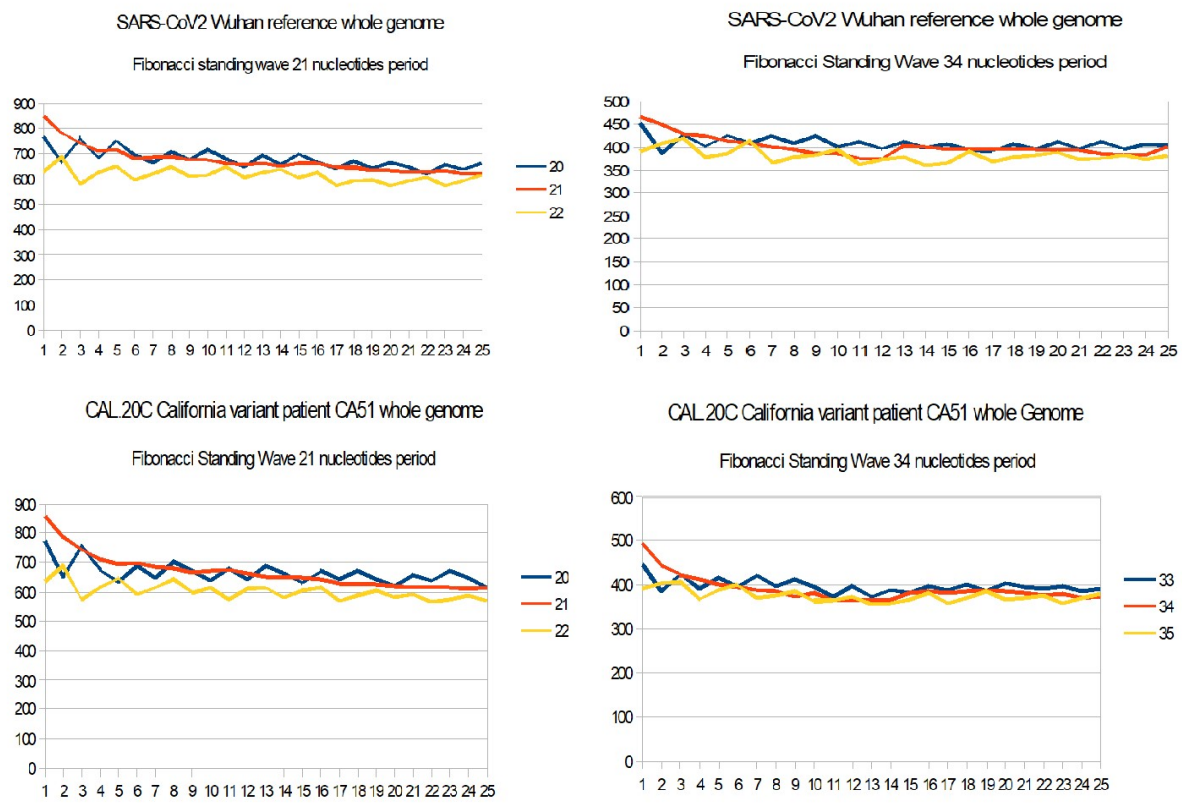

Figure 25 – Comparing Fibonacci Standing Waves between SARS-CoV2 Wuhan and CAL.20C single patient whole genomes.

IV- CONCLUSIONS.

First, this study of Spikes by Fibonacci metastructures highlights 4 first conclusions:

- It presents a clarification by the image of links already suspected by multiple researchers between the spikes of bat RATG13, ZXC21, ZC45 and SARS-CoV2.

- As we had predicted and already verified (WA state USA) in (Perez & Montagnier 2020), some variants deleted as a priority our predicted « EIE » HIV-like fragments

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from the dense HIV region at the start of the spike. This is the case with the English variant but also with several patients of the California variant CAL.20C.

- Overall, the reference spikes of all the variants studied here have a reinforcement of the most significant Fibonacci structures (2584 bases). But this phenomenon is amplified and confirmed when we analyze the spikes of patients (32 CAL.20C patients).

- We note the total absence of Fibonacci metastructures in the mRNAs of both mRNA vaccines PFIZER and MODERNA. This means that, although functional, these mRNAs will have a short lifespan and their overall physical structure will be very weak. These mRNAs will be able to split rather quickly into separate fragments which will risk combining with other mRNAs present in their environment.

We will also conclude the tendency of the variant spikes to strengthen their overall structure, which may be correlated with their greater cohesion and lifespan of their mRNA spike, and probably the greater infectivity and pathogenicity of the variants.

Of the 7 clusters of results presented here, 3 will deserve to be revisited, reproduced and extended more deeply:

1 / point -II-
Fibonacci metastructures "shed a radically new light on" the relationships already recognized or suspected "between the 4 Sars-CoV2 Wuhan (1/2020), SARS-covZC44 (2017), SARS-covPZXC2P1 (2015) and bat RATG13 genomes (2013). To this evidence of manipulation of CODONS synonymous with Spike of one or the other between SARS-CoV2 and beats RATG13, to the question "which of the 2 was manipulated?". We can assert that it is the SARS-Cov2 spike that has been manipulated to modify synonymous CODONS while retaining the functionality of the same amino acids. We believe that this manipulation will most certainly have attenuated the virulence and pathogenicity of SARS-) CoV2 opposite bat RATG13 * (blue regions of the 2 images of their Spikes).
Moreover, if at the level of the 4 respective genomes, the strong neighborhoods between SARS-CoV2 and bat RATG13 on the one hand, and ZC45 and ZXC21 on the other hand are confirmed by these Fibonacci metastructures (vertical analogies in the image), a less expected bi-duality is highlighted at the level of their 4 respective spikes: on the one hand, this obvious neighborhood between ZXC21 and bat RATG13, and, on the other hand, although less obvious, this other neighborhood between ZC45 and SARS -CoV2 (horizontal analogies in the image).

2 / the point -V-
This point is at a level of fundamental research of mechanisms unknown to biology. Indeed, we demonstrate how, beyond and above the STOP codon which commands the protein manufacturing machinery to end the process, there would exist a sort of "end of gene message", which would be addressed to, on the scale of messenger RNA, this "code" would be digital in nature, carried by the ultimate UA / CG metastructure of Fibonacci. We observe that this message would be of Nature GIGOGNE, constituted like the Russian dolls of a nesting of proportions all ending on one of the 3 bases of the STOP codon. This discovery is validated in this article on 43 Spikes from UK, South Afrika, BRAZIL and CALIFORNIA variants. Of these Spikes, 32 were from real patients.

3 / point -VII-

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Here, we have gathered several pieces of evidence showing that, as they evolve, the variants would constitute and reinforce a kind of Palindrome-type symmetry based on "Russian doll" interlocking of their MRNA, which could lead to a double strand. of the "hairpin" type, thus reinforcing the stability and the lifespan of the Spike MRNA, thus certainly the increasing contagiousness of the variant virus.

In (Demongeot § Henrion-Caude, 2020), Alexandra Henrion-Caude and Jacques Demongeot proposed in 2020 a possible universel starting RNA 22 nucleotides sequence which could be a candidate bootstrap at origins of Life in a RNA primitive world.

Professor Luc Montagnier observes that these authors attribute an essential role in the origin of life to a circular RNA of 22 nucleotides. This is the length of our “EIE” (Exogenous Insertion Elements) in SARS-CoV2 genome published in https://zenodo.org/record/3975578

Particularly, this hyper constrainst circular 22nt sequence codes for the 20 amino acids + codon stop + only one redondant amino acid (MET). We found this archaic mRNA sequence using BLASTn long (14nt) contiguous sequences in HIV mRNA genomes... and also in SARS-CoV2 Wuhan reference mRNA genome !

But consider the circular character of this primitive RNA 22 nucleotides long UCAG. So, here is our original result on its multiple and SYSTEMATIC Fibonacci proportions as soon as it is a CIRCULAR RNA sequence ...

5' AUGGUACUGCCAUUCAAGAUGA 3'
AUGGUACUGCCAUUCAAGAU G ==> A 13AU 8CG
AUGGUACUGCCAUUCAA G ==> AUGA 13AU 8CG
AUGGUACUGCCAUU C ==> AAGAUGA 13AU 8CG
AUGGUACUGC C ==> AUUCAAGAUGA 13AU 8CG
AUGGUACUG C ==> CAUUCAAGAUGA 13AU 8CG
AUGGUACU G ==> CCAUUCAAGAUGA 13AU 8CG
AUGGUA C ==> UGCCAUUCAAGAUGA 13AU 8CG
AUG G ==> UACUGCCAUUCAAGAUGA 13AU 8CG
AU G ==> GUACUGCCAUUCAAGAUGA 13AU 8CG

Seen from the point of view of the *autopoiesis* Francisco Varela theory (ref Varela), autonomy of Indoor vs. Outdoor systems) these results could be interpreted as the rest of the loop of 21 UACG (outdoor) "seen" from a base C or G (indoor). So the perceived signal is a kind of Fibonacci resonance ... By virtue of Francisco Varela's theory of *autopoiesis* (Varela § Maturana, 1980) that we applied to Artificial Intelligence in the 1980s by creating the *“fractal chaos”* artificial neural network (Perez 1988). Thus, the Fibonacci numbers, therefore the optimal proportion of the golden ratio would perhaps have already been present from the first moments of life on earth, a life for which they would have served as a "matrix" …

*"If I followed correctly, the circular RNA sequence obeys the Fibonacci rule. If we extrapolate, we can think that Life was formed (or was created, according to our religion) from this RNA according to a mathematical principle? "*LM?

Actually, the RNA sequence proposed by the article by Alexandra Henrion-Caude, which seems to “spring” from nowhere can only intrigue the reader. Indeed, what is certain with this sequence is that God, or panspermia, or self-organization are indeed Mathematicians ...

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Indeed : They already know how to count 4 + 5 + 6 + 7 = 22.
I meant 4C, 5G, 6U, 7A
Let C + G = 9
U + A = 13
We are already very close to the 13/8 = Phi ratio, the same one that we can verify in all SARSCOV2 genomes. But also, pyrimidine purines:

4C+6U=10UC
5G+7A=12AG
10=2x5
12=2x6

5 and 6 these 2 key numbers associated with the harmonious but unstable shape of the Pentagon (5) and the harmonious but stable form of the Hexagon (6).

It is no coincidence that Nature (flowers) or religions - also - have invented stars with 5 or 6 branches ....

And the structure of RNA and DNA are built around Pentagons and Hexagons ...And "Pollack's Water Fourth state" structure of WATER (https://www.pollacklab.org/), also built around the hexagon ...

So EVERYTHING seems to be potentially written in these 22 nucleotides ...

We also note 2x6 = 12 bases in primers of palindromes or mirror series:

AUGGUA mirror and UCAAGA quasi palindrome.

Finally, we will note cs 5 triplets of consecutive nucleotides:

GAA UGG GCC AUU CAA

Symetries purines pyrimidines on 4 of the 5 TRIPLETS

UGG CAA

GCC AUU

Finally, we must recall this open question :
CONJECTURE of SARS-CoV2 VARIANTS:
The growth of long Fibonacci structures in the shape of "podiums" for almost all of the variants studied (UK, California, South Afrika, India, etc.) suggests the probable folding of the Spike mRNA in the form of a "hairpin", which can strengthen the cohesion and the lifespan of this mRNA.

Three final conclusions :

One fact is certain, the 2 mRNAs of the Moderna and Pfizer vaccines will result in a low functionality of the spike vaccine because by doping these sequences in CG rich, their designers, in search of greater STABILITY of these RNAs will have built, according to us, sequences which, as soon as they are inserted into the human host, will seek to mutate, like SARS-CoV2 variants, towards CG ==> UA forms in order to improve, paradoxically, their STABILITY and probably also their LIFETIME...

Secondly, using new biomathematics theoretical methods (Master code and numerical standing waves), and comparing the Spikes of the 2 vaccines Moderna and Phizer, we conclude a very probable difference in stability and shelf life of the 2 respective mRNAs of these 2 vaccines. However, the *"State of the Art"* will tell you that their 2 protein sequences are strictly identical. However, by having modified

their synonymous codons using different strategies, no one can guarantee that the quantity of antibodies generated and sensitivity to variants will be identical in the 2 cases (Kustin et al, 2021).

Despite the immense progress of Biology, the RNA universe remains today still full of unexplained mysteries. However, it is said, as we will see, that it would have constituted the first crucible of life. This is why we will have to exercise the greatest caution, on the one hand in the face of an mRNA virus such as SARS-CoV2, but even more in the face of the unpredictable evolution of new vaccines, themselves based on RNA.

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VI- REFERENCES.

(Castro-Chavez, 2020), F. Castro-Chavez, (June 2020), Anticovidian v.2: COVID-19: Hypothesis of the Lab Origin versus a Zoonotic Event Which Can Also be of a Lab Origin, GJSFR, August 2020, https://zenodo.org/record/3988139#.YGMMaq8zaM8

(Dae Eun Jeong et al, 2021), Dae Eun Jeong et al, Assemblies-of-putative-SARS-CoV2-spike-encoding-mRNA-sequences-for-vaccines-BNT-162b2-and-mRNA-1273, GitHub, March 2021, https://github.com/NAalytics/Assemblies-of-putative-SARS-CoV2-spike-encoding-mRNA-sequences-for-vaccines-BNT-162b2-and-mRNA-1273

(Da Silva Filipe, 2020), da Silva Filipe, A., Shepherd, J.G., Williams, T. *et al.* Genomic epidemiology reveals multiple introductions of SARS-CoV-2 from mainland Europe into Scotland. *Nat Microbiol* **6,** 112–122 (2021). https://doi.org/10.1038/s41564-020-00838-z

.

(Demongeot§Henrion-Caude, 2020), Demongeot J. § Henrion-Caude A. , Footprints of a Singular 22-Nucleotide RNA Ring at the Origin of Life, Biology 2020, 9(5), 88; **https://doi.org/10.3390/biology9050088**

(Gröhs Ferrareze P. A. , et al, 2021), Patrícia Aline Gröhs Ferrareze, et al, E484K as an innovative phylogenetic event for viral evolution: Genomic analysis of the E484K spike mutation in SARS-CoV-2 lineages from Brazil
bioRxiv 2021.01.27.426895; doi: https://doi.org/10.1101/2021.01.27.426895

(Jackson et al, 2020), Jackson, N.A.C., Kester, K.E., Casimiro, D. *et al.* The promise of mRNA vaccines: a biotech and industrial perspective. *npj Vaccines* **5,** 11 (2020). https://doi.org/10.1038/s41541-020-0159-8

(Kudla et al, 2016), Kudla, G., Lipinski, L., Caffin, F., Helwak, A. & Zylicz, M. High guanine and cytosine content increases mRNA levels in mammalian cells. *Plos Biol.* **4**, e180 (2016). High guanine and cytosine content increases mRNA levels in mammalian cells

(Kustin T. et al, 2021), Evidence for increased breakthrough rates of SARS-CoV-2 variants of concern in BNT162b2 mRNA vaccinated individuals, Talia Kustin et al, medRxiv Preprints, **Doi:** https://doi.org/10.1101/2021.04.06.21254882

(Mengwen et al, 2006), Mengwen Jia, Liaofu Luo, The relation between mRNA folding and protein structure,Biochemical and iophysical Research Communications, Volume 343, Issue 1,2006,Pages 177-182,ISSN 0006-291X, https://doi.org/10.1016/j.bbrc.2006.02.135. (https://www.sciencedirect.com/science/article/pii/S0006291X06004451)

(Montagnier L. § Kingsley Sanders F., 1963), Luc Montagnier and F. Kingsley Sanders « Replicative Form of Encephalomyocarditis virus RNA », Nature 199. 664-667. 1963

(Naveca Felipe et al, 2021), Phylogenetic relationship of SARS-CoV-2 sequences from Amazonas with emerging Brazilian variants harboring mutations E484K and N501Y in the Spike protein, Virological.org, 2021, **https://virological.org/t/phylogenetic-relationship-of-sars-cov-2-sequences-from-amazonas-with-emerging-brazilian-variants-harboring-mutations-e484k-and-n501y-in-the-spike-protein/585**

(Perez, 1988), Perez J.C., De nouvelles voies vers l'Intelligence Artificielle, 1988, Ed. MASSON ELSEVIER, EAN 978-2225818158 ISBN 2225818150, https://livre.fnac.com/a223887/Jean-Claude-Perez-De-Nouvelles-voies-vers-l-intelligence-artificielle

(Perez, 1991), J.C. Perez (1991), "Chaos DNA and Neuro-computers: A Golden Link", in Speculations in Science and Technologyvol. 14 no. 4, ISSN 0155-7785, January 1991
Speculations in Science and Cell Motility 14(4):155-7785
https://www.researchgate.net/publication/258439719_JC_Perez_1991_Chaos_DNA_and_Neuro-computers_A_Golden_Link_in_Speculations_in_Science_and_Technologyvol_14_no_4_ISSN_0155-7785

(Perez, 1997), Perez J.C, L'ADN décrypté, Ed. Marco Pietteur, ISBN : 2-87211-017-8
●EAN : 9782872110179, https://www.editionsmarcopietteur.com/resurgence/91-adn-decrypte-9782872110179.html

(Perez, 2009), Perez J.C, Codex biogenesis – Les 13 codes de l'ADN (French Edition) [Jean - Claude ... 2009);

Language: French; ISBN -10: 2874340448; ISBN -13: 978-2874340444
https://www.amazon.fr/Codex-Biogenesis-13-codes-lADN/dp/2874340448

(Perez, 2015), Deciphering Hidden DNA Meta-Codes -The Great Unification & Master Code of Biology, journal of Glycémies abd Lipidomics, https://www.longdom.org/abstract/deciphering-hidden-dna-metacodes-the-great-unification-amp-master-code-of-biology-11590.html , ISSN: 2153-0637, **DOI:** 10.4172/2153-0637.1000131

(Perez, 2017), J.C Perez, 2017, Sapiens Mitochondrial DNA Genome Circular Long Range Numerical Meta Structures are Highly Correlated with Cancers and Genetic Diseases mtDNA Mutations
January 2017 Journal of Cancer Science and Therapy 09(06) DOI: 10.4172/1948-5956.1000469

(Perez , 2017b), Jean Claude Perez, "**The Master Code of Biology: Self-assembly of two identical Peptides beta A4 1-43 Amyloid In Alzheimerâ€™s Diseases**," Biomedical Journal of Scientific & Technical Research, Biomedical Research Network+, LLC, vol. 1(4), pages 1191-1195, September.
Handle: *RePEc:abf:journl:v:1:y:2017:i:4:p:1191-1195*
DOI: 10.26717/BJSTR.2017.01.000394

(Perez, 2017c), Perez JC (2017) The "Master Code of DNA": Towards the Discovery of the SNPs Function (Single-Nucleotide Polymorphism). J Clin Epigenet. 3:26. doi: 10.21767/2472-1158.100060 , https://clinical-epigenetics.imedpub.com/the-master-code-of-dna-towards-the-discovery-of-the-snps-function-singlenucleotide-polymorphism.pdf

(Perez, 2018), Perez, J.C. Six Fractal Codes of Biological Life:perspectives in Exobiology, Cancers Basic Research and Artificial Intelligence Biomimetism Decisions Making. Preprints **2018**, 2018090139 (doi: 10.20944/preprints201809.0139.v1). Perez, J.C. Six Fractal Codes of Biological Life:perspectives in Exobiology, Cancers Basic Research and Artificial Intelligence Biomimetism Decisions Making. Preprints 2018, 2018090139 (doi: 10.20944/preprints201809.0139.v1).
https://www.preprints.org/manuscript/201809.0139/v1

(Perez, 2019) , Perez, J. Epigenetics Theoretical Limits of Synthetic Genomes: The Cases of Artificials *Caulobacter (C. eth-2.0), Mycoplasma Mycoides (JCVI-Syn 1.0, JCVI-Syn 3.0 and JCVI_3A), E-coli and YEAST chr XII. Preprints* **2019**, 2019070120 (doi: 10.20944/preprints201907.0120.v1).
https://www.preprints.org/manuscript/201907.0120/v1

Perez J.C, (2020). "WUHAN COVID-19 SYNTHETIC ORIGINS AND EVOLUTION."International Journal of Research - Granthaalayah, 8(2), 285-324.
https://doi.org/10.5281/zenodo.3724003

(Perez§Montagnier, 2020a), Perez, j.c, & Montagnier, L. (2020, April 25). COVID-19, SARS and Bats Coronaviruses Genomes unexpected Exogeneous RNA Sequences.
https://doi.org/10.31219/osf.io/d9e5g

(Perez%Montagnier, 2020b), Jean claude Perez, & Luc Montagnier. (2020). COVID-19, SARS AND BATS CORONAVIRUSES GENOMES PECULIAR HOMOLOGOUS RNA SEQUENCES. International Journal of Research -GRANTHAALAYAH ISSN (print): 2394-3629 July 2020, Vol 8(07), 217 – 263 DOI: Https://doi.org/10.29121/granthaalayah.v8.i7.2020.678, Vol 8(07), 217 – 263(Vol 8(07), 217 – 263), Vol 8(07), 217–Vol 8(07), 263. http://doi.org/10.5281/zenodo.3975578

(Rapoport § Perez, 2018),

Rapoport D. § Perez J.C, Golden ratio and Klein bottle Logophysics: the Keys of the Codes of Life and Cognition.
Quantum Biosystems. 9(2) 8-76. ; Vol. 9 – n.2 – 2018

(Simmonds P, 2020), P. Simmonds, Rampant C->U hypermutation in the genomes of SARS-CoV-2 and other coronaviruses – causes and consequences for their short and long evolutionary trajectories. bioRxiv 2020.05.01.072330; doi: https://doi.org/10.1101/2020.05.01.072330

(Varela § Maturana, 1980), Maturana H. & Varela F.J. (1980). Autopoiesis and cognition : the realization of the living. Reidel, Boston.

(Wenjuan Zhang et al, 2021), Emergence of a novel SARS-CoV-2 strain in Southern California, USA, medRxiv 2021.01.18.21249786; doi: https://doi.org/10.1101/2021.01.18.21249786