The INDIA Mutations and B.1.617 Variant:
Is there a global "strategy" for mutations and evolution of variants of the SARS-CoV2 genome?

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ABSTRACT.

In this paper, we run for all INDIA mutations and variants a biomathematical numerical method for analysing mRNA nucleotides sequences based on UA/CG Fibonacci numbers proportions (Perez, 2021). In this study, we limit ourselves to the analysis of whole genomes, all coming from the mutations and variants of SARS-CoV2 sequenced in India in 2020 and 2021. We then demonstrate - both on actual genomes of patients and on variants combining the most frequent mutations to the SARS-CoV2 Wuhan genomes and then to the B.1.617 variant - that the numerical Fibonacci AU / CG metastructures increase considerably in all cases analyzed in ratios of up to 8 times. We can affirm that this property contributes to a greater stability and lifespan of messenger RNAs, therefore, possibly also to a greater INFECTUOSITY of these variant genomes.

I - INTRODUCTION.

After various papers related SARS-CoV2 origins and evolution (Perez, 2020) and (Perez§Montagnier, 2020), in (Perez, 2021), we presented a biomathematical method based on mRNA genomes and spikes UA/CG Fibonacci nucleotides proportions. Particularly we demonstrated a real correlation between variants evolution (UK, South Africa, California, Brazil) and the amount of long range Fibonacci metastructures.

In order to test this hypothesis, we are interested in the 2 countries in which the effect of variants seems uncontrollable: Brazil and India.
We chose India because the sequencing of genomes is more systematic and reliable there than in Brazil.
For this we proceed in 2 steps:
- Analyzing the first variants of 2020. For this we rely on this publication:
(Muttineri et al, 2021),
https://www.google.com/url?sa=t&source=web&rct=j&url=https://journals.plos.org/plospathogens/article/file%3Fid%3D10.1371/journal.pone.0246173%26type=printable&ved=2ahUKEwj3zdnnZnorwAhUQKBoKHUxnDBEQFjABeqQICBAC&usg=AOvVaw1A79ux6UbetOpoRx_jT-M

2/ Then we study the most recent changes of 2021. For that we rely on this systematic approach:
(Srivastava Surabhi et al, 2021), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7895735/
And more particularly on this Indian GEAR19 database:
https://data.ccmb.res.in/gear19/variants

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 13 5 8 13 21 34 55 89 144 233 377 610 \textbf{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 \url{https://www.ncbi.nlm.nih.gov/nuccore/NC_045512}

\textbf{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 1 1 1 1 0 1 0 1 1 0 1 1 0 1...
U A A U U A A U A U 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 1 0 1 0 1 0 0 1 0...
G G G G G G G G G 987 bases CG

The SPIKE analyzes 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 and if we consider the mRNA sequence in its linear form, as will be the case throughout this study.

\section*{2.2 - Analyzes of reference variants :}

\subsection*{2.21/ Analyzing the first variants of 2020 :}

- Analyzing the first variants of 2020. For this we rely on this publication:

(Muttineri et al, 2021),
\url{https://www.google.com/url?sa=t&source=web&rct=j&url=https://journals.plos.org/plospathogens/article/file%3Fid%3D10.1371/journal.pone.0246173%26type%3Dprintable&ved=2ahUKEwj3zdnZnorwAhUQKBoKHUxnD_EQFjABegQICBAC&usg=AOvVaw1A79ux6UbetoPoRx_iT-Mk}

The full-genome viral sequences were deposited in the dataset of GISAID (EPI\_ISL\_431101, EPI\_ISL\_431102, EPI\_ISL\_431103, EPI\_ISL\_431117, EPI\_ISL\_438139, EPI\_ISL\_437626, EPI\_ISL\_438138) and NCBI GenBank (MT415320, MT415321, MT415322, MT415323, MT477885, MT457402, MT457403).

Now we analyse:

GenBank (MT415320, MT415321, MT415322, MT415323, MT477885, MT457402, MT457403)

Main data source for mutations : \url{https://covariants.org/}
2.22/ Analyzing 28 INDIAN mutations applied to SARS-CoV2 Wuhan reference genome:

Then we study the most recent changes of 2021. For that we rely on this systematic approach:
(Srivastava Surabhi et al, 2021), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7895735/

And more particularly on this Indian GEAR19 database:
https://data.ccmb.res.in/gear19/variants

We test 2 possible variant scenarios:
If separate mutations are INDIABn,
INDIACn, progressive descent by accumulating mutations by decreasing probabilities.
Example
INDIAC1 = INDIAB1
INDIAC2 = INDIAC1 + INDIAB2
INDIAC3 + INDIAC2 + INDIAB3 ...
.../...
INDIAC28 = INDIAC27 + INDIAB28

Then we study the most recent changes of 2021. For that we rely on this systematic approach:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7895735/
And more particularly on this Indian GEAR19 database:
https://data.ccmb.res.in/gear19/variants

link Table 5%

https://mail.google.com/mail/u/0/#inbox/KtbxLzGLmpFSTVtcKRqRlmnxKrplVzgNnq?projector=1&messagePartId=0.1

2.23/ Analyzing 28 INDIAN mutations applied to B.1.617 India variant genome:

We run the same 28 genomes simulations starting from the India variant B.1.617.

2.24/ simulations of possible future mutations of the variant B.1.617.

In (Pragya Yadav et al, 2021), the authors provide a list of the 33 main mutations characterizing the genomes of the Indian variant B.1.617.
On the other hand, we have just studied the impact of the 28 most frequent mutations in India, those which represent more than 5% of contaminations).
It is clear that these 2 sets of mutations partially overlap. However it would be interesting to simulate the effect of some of the 28 mutations when they are absent in B.1.617. Indeed, their high frequency makes it possible to suggest their possible future addition to B.1.617. This is what we will simulate in the last paragraph 3.3.

III - RESULTS and DISCUSSION.

3.1 - Analyzing the first variants of 2020:
Now we analyse from (Muttineri et al, 2021):

**GenBank** (MT415320, MT415321, MT415322, MT415323, MT477885, MT457402, MT457403)

INDIAA1 MT415320
https://www.ncbi.nlm.nih.gov/nuccore/MT415320

INDIAA2 MT415321
https://www.ncbi.nlm.nih.gov/nuccore/MT415321

INDIAA3 MT415322
https://www.ncbi.nlm.nih.gov/nuccore/MT415322

INDIAA4 MT415323
https://www.ncbi.nlm.nih.gov/nuccore/MT415323

INDIAA5 MT457402
https://www.ncbi.nlm.nih.gov/nuccore/MT457402

INDIAA6 MT457403
https://www.ncbi.nlm.nih.gov/nuccore/MT457403

INDIAA7 MT477885
https://www.ncbi.nlm.nih.gov/nuccore/MT477885

Table 1 - Mutations Table from paper https://journals.plos.org/plosone/article/figure?id=10.1371/journal.pone.0246173.t003

| Reference | Alias number line in Table1 | GENBANK Identification | Date       | Number of 17711 UA/CG metastructures |
|-----------|-----------------------------|-------------------------|------------|-------------------------------------|
| SARS-CoV2 |                             | NC_045512.2             | 18-JUL-2020| 8                                   |
| Wuhan     |                             |                         |            |                                     |
| INDIAA1   | MT415320.1                  | MT415320.1              | 30-APR-2020| 23                                  |
| INDIAA1   |                             | MT415321.1              | 30-APR-2020| 8                                   |
| INDIAA3   | MT415322.1                  | MT415322.1              | 30-APR-2020| 33                                  |
| INDIAA4   | MT415323.1                  | MT415323.1              | 30-APR-2020| 45                                  |
| INDIAA5   | MT457402.1                  | MT457402.1              | 12-MAY-2020| 45                                  |
Genomes lengths:

| Sequence  | Length |
|-----------|--------|
| VSARSCOV2REF | 29903  |
| VINDIAA1   | 29900  |
| **VINDIAA2** | **29903** |
| VINDIAA3   | 29888  |
| VINDIAA4   | 29890  |
| VINDIAA5   | 29890  |
| VINDIAA6   | 29890  |
| VINDIAA7   | 29899  |

6 of the 7 cases have deletions. Only VINDIAA2 has the same length as SARS-CoV2 Wuhan reference.

Only 4 difference bases: it is precisely the only one that has not increased the number of metastructures.

Number of different bases: $+/\text{VSARSCOV2REF} - \text{VINDIAA2} = 4$

Locations: $(\text{VSARSCOV2REF} - \text{VINDIAA2})/\text{VINDIAA2}$

| Location |
|----------|
| 241 3037 14408 23403 |

Nucleotides values in SARS-CoV2 ref: $(\text{VSARSCOV2REF} - \text{VINDIAA2})/\text{VSARSCOV2REF}$

| Nucleotide |
|-----------|
| CCCA      |

Nucleotides values in VINDIAA2: $(\text{VSARSCOV2REF} - \text{VINDIAA2})/\text{VINDIAA2}$

| Nucleotide |
|-----------|
| TTTG      |

i.e. 3 out of 4 CG mutations ==> UA

From the results below I deduce that the deletions of 5 cases out of 6 studied cases contributed to considerably increase the UA / CG metastructures of 17711 bases.
Figure 1 – Recall SARS-CoV2 Wuhan genome metastructures.

Figure 2 – INDIAA1 genome metastructures.
Figure 3 - INDIAA2 genome metastructures.

Figure 4 - INDIAA3 genome metastructures.
Figure 5 - INDIAA4 genome metastructures.

Figure 6 - INDIAA5 genome metastructures.
3.2 - INDIAN VARIANTS SIMULATIONS with mutations on SARS-CoV2 Wuhan:

We work now from these published data:
We test 2 possible variant scenarios: (Srivastava Surabhi et al, 2021), and more particularly on this Indian GEAR19 database: https://data.ccmb.res.in/gear19/variants

If separate mutations are INDIABn,

INDIACn, progressive descent by accumulating mutations by decreasing probabilities.
Example
INDIAC1 = INDIAB1
INDIAC2 = INDIAC1 + INDIAB2
Then we study the most recent changes of 2021. For that we rely on this systematic approach:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7895735/
And more particularly on this Indian GEAR19 database:
https://data.ccmb.res.in/gear19/variants

On the table of 28 Indian mutations > 5% of cases, The progressive study of the 29 genomes by integrating mutations step by step according to their frequency should give very interesting Fibonacci on the scale of the whole genome.

**INDIAC**

INDIACn, progressive descent by accumulating mutations by decreasing probabilities.
Example INDIAC2 = INDIAC1 + INDIAB2

APL Language session mutations...

```
VINDIAC1, VSARSCOV2REF
VINDIAC1[23403], 'G'
VINDIAC2, VINDIAC1
VINDIAC2[3037], 'T'
VINDIAC3, VINDIAC2
VINDIAC3[241], 'T'
VINDIAC4, VINDIAC3
VINDIAC4[14408], 'T'
VINDIAC5, VINDIAC4
VINDIAC5[28881], 'A'
VINDIAC6, VINDIAC5
VINDIAC6[28883], 'C'
VINDIAC7, VINDIAC6
VINDIAC7[28882], 'A'
VINDIAC8, VINDIAC7
VINDIAC8[25563], 'T'
VINDIAC9, VINDIAC8
VINDIAC9[18877], 'T'
VINDIAC10, VINDIAC9
VINDIAC10[26735], 'T'

VINDIAC11, VINDIAC10
VINDIAC11[28854], 'T'
VINDIAC12, VINDIAC11
VINDIAC12[22444], 'T'
VINDIAC13, VINDIAC12
VINDIAC13[313], 'T'
VINDIAC14, VINDIAC13
VINDIAC14[5700], 'A'
VINDIAC15, VINDIAC14
VINDIAC15[11083], 'T'
VINDIAC16, VINDIAC15
VINDIAC16[13730], 'T'
```
Table 3 – Summary on the 28 most frequent India country mutations applied to SARS-CoV2 Wuhan genome.

| position | Genome location | ref | alt | gene | Amino Acids mutations | Percent | Number of 17711 UA/CG metastructures |
|----------|-----------------|-----|-----|------|------------------------|---------|--------------------------------------|
| SARS-CoV2 Wuhan | 23403 | A | G | "S:614" | "D614G" | 85 | 8 |
| INDIAC1 | 3037 | C | T | "ORF1a:924" | "F924F" | 84 | 8 |
| INDIAC3 | 241 | C | T | "5'UTR" | "NA" | 84 | 8 |
| INDIAC4 | 14408 | C | T | "ORF1b:314" | "P314L" | 84 | 8 |
| INDIAC5 | 28881 | G | A | "N:203" | "R203K" | 42 | 31 |
| INDIAC6 | 28883 | G | C | "N:204" | "G204R" | 41 | 31 |
| INDIAC7 | 28882 | G | A | "N:203" | "R203K" | 40 | 46 |
| INDIAC8 | 25563 | G | T | "ORF3a:57" | "Q57H" | 25 | 35 |
| INDIAC9 | 18877 | C | T | "ORF1b:1804" | "L1804L" | 25 | 25 |
| INDIAC10 | 26735 | C | T | "M:71" | "Y71Y" | 25 | 10 |
| INDIAC11 | 28854 | C | T | "N:194" | "S194L" | 23 | 10 |
| INDIAC12 | 22444 | C | T | "S:294" | "D294D" | 22 | 8 |
| INDIAC13 | 313 | C | T | "ORF1a:16" | "L16L" | 21 | 8 |
| INDIAC14 | 5700 | C | A | "ORF1a:1812" | "A1812D" | 20 | 8 |
|   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|
| INDIAC15 | 11083 | G | T | "ORF1a:3606" | "L3606F" | 14 | 8 |
| INDIAC16 | 13730 | C | T | "ORF1b:88" | "A88V" | 11 | 29 |
| INDIAC17 | 28311 | C | T | "N:13" | "P13L" | 10 | 29 |
| INDIAC18 | 23929 | C | T | "S:789" | "Y789Y" | 10 | 41 |
| INDIAC19 | 6312 | C | A | "ORF1a:2016" | "T2016K" | 10 | 41 |
| INDIAC20 | 8917 | C | T | "ORF1a:2884" | "F2884F" | 10 | 41 |
| INDIAC21 | 1947 | T | C | "ORF1a:561" | "V561A" | 7 | 41 |
| INDIAC22 | 9389 | G | A | "ORF1a:3042" | "D3042N" | 6 | 41 |
| INDIAC23 | 6573 | C | T | "ORF1a:2103" | "S2103F" | 6 | 41 |
| INDIAC24 | 4354 | G | A | "ORF1a:1363" | "E1363E" | 6 | 41 |
| INDIAC25 | 25528 | C | T | "ORF3a:46" | "L46F" | 6 | 48 |
| INDIAC26 | 15324 | C | T | "ORF1b:619" | "N619N" | 6 | 36 |
| INDIAC27 | 3267 | C | T | "ORF1a:1001" | "T1001I" | 6 | 36 |
| INDIAC28 | 3634 | C | T | "ORF1a:1123" | "N1123N" | 6 | 36 |

**Average** | | | | | | **26.25%** | **26.89**

Table 4 – Recall summary main results from Table3.
| Genome       | percent | Number of 1 |
|--------------|---------|-------------|
| SARS-CoV2 Wuhan | 8       | 8           |
| INDIAC1      | 85      | 8           |
| INDIAC2      | 84      | 8           |
| INDIAC3      | 84      | 8           |
| INDIAC4      | 84      | 8           |
| INDIAC5      | 42      | 31          |
| INDIAC6      | 41      | 31          |
| INDIAC7      | 40      | 46          |
| INDIAC8      | 25      | 35          |
| INDIAC9      | 25      | 25          |
| INDIAC10     | 25      | 10          |
| INDIAC11     | 23      | 10          |
| INDIAC12     | 22      | 8           |
| INDIAC13     | 21      | 8           |
| INDIAC14     | 20      | 8           |
| INDIAC15     | 14      | 8           |
| INDIAC16     | 11      | 29          |
| INDIAC17     | 10      | 29          |
| INDIAC18     | 10      | 41          |
| INDIAC19     | 10      | 41          |
| INDIAC20     | 10      | 41          |
| INDIAC21     | 7       | 41          |
| INDIAC22     | 6       | 41          |
| INDIAC23     | 6       | 41          |
| INDIAC24     | 6       | 41          |
| INDIAC25     | 6       | 48          |
| INDIAC26     | 6       | 36          |
| INDIAC27     | 6       | 36          |
| INDIAC28     | 6       | 36          |
Figure 9 – Increase of 17711 UA/CG metastructures with whole INDIAN variant genomes with cumulated mutations vs percent frequencies (vs SARS-CoV2 Wuhan).

From this analysis, we can draw 3 conclusions:

a / this is a simulation of genomes made from SARS-CoV2 and the most frequently encountered mutations in India. So, if it is certain that the first genomes exist in some patients, some others, towards the end of the list of 28 genomes, may not exist but could potentially emerge.

b / it is noted that none of the 28 cases found UA / CG metastructures of 177122 bases in quantity LESS than 8, a value which characterizes SARS-CoV2 Wuhan. So, if there was no correlation between these Fibonacci metastructures and the evolution of variants, we should find cases less than 8.

c / out of the 28 cases of genomes studied, 20 of them saw an increase in the number of metastructures of 17,712 bases, or more than 2/3 of the genomes studied. The average of the 28 cases is 26.89, ie 3.36 times more than the SARS-CoV2 Wuhan and D614G reference genomes.

3.2 - INDIAN VARIANTS SIMULATIONS with mutations on B.1.617 variant:

The strain of the variant B.1.617 has grown exponentially in India since the beginning of 2021. We are going to redo the 28 previous analyzes no longer from the SARS-CoV2 Wuhan genome but by inserting the SINDIAFULL spike already analyzed in (Perez, 2021).
This therefore amounts to applying the successive mutations to a type B 1.617 genome, at least at the level of its Spike sequence.

Indeed,

B.1.617 lineage

This strain, also known as the “double mutant virus”, has spread rapidly through India. The strain has been dubbed the “double mutant virus” due to two of the concerning mutations it carries.

These two key mutations are:

- E484Q
- L452R

Further studies on the strain are needed to determine its transmissibility, although it is suspected to do so due to its spike protein mutations which are thought to increase immune evasion and receptor binding. Whether vaccine efficacy is affected also needs further research.

SINDIAFULL is the Spike B.1.617 from (Perez-2021).

Recall Spike location

\[
\text{gene}="S"
\]

\[
\text{ATGTTGTT}
\]

\[
\frac{1}{2} V_{\text{SINDIAFULL}}
\]

\[
\text{ATGTTGTT}
\]

\[
\frac{1}{2} V_{\text{VB1617}}
\]

SINDIAFULL is the Spike B.1.617 from (Perez-2021).

Recall Spike location

\[
\text{gene}="S"
\]

\[
\text{ATGTTGTT}
\]

\[
\frac{1}{2} V_{\text{SINDIAFULL}}
\]

\[
\text{ATGTTGTT}
\]

\[
\frac{1}{2} V_{\text{VB1617}}
\]

R,,GFIBOZOOMS VB1617

VINDIAC1,,VB1617
VINDIAC1[23403],,G'
VINDIAC2,,VINDIAC1
VINDIAC2[3037],,T
VINDIAC3,,VINDIAC2
VINDIAC3[241],,T
VINDIAC4,,VINDIAC3
VINDIAC4[14408],,T
VINDIAC5,,VINDIAC4
VINDIAC5[28881],,A'

\[
\text{GAGGTGAA}
\]

\[
\text{TCTTGATG}
\]
Table 5 - Summary on the 28 most frequent India country mutations applied to B.1.617 genome.

| position | Genome location | ref | alt | gene | Amino Acids mutations | Percent | Number of 17711 UA/CG metastructures |
|----------|-----------------|-----|-----|------|-----------------------|---------|-------------------------------------|
| SARS-CoV2 Wuhan | | | | | | 8 |
| B1617 | 23403 | A | G | "S:614" | "D614G" | 85 | 31 |
| INDIAC1 | 3037 | C | T | "ORF1a:924" | "F924F" | 84 | 31 |
| INDIAC3 | 241 | C | T | "5'UTR" | "NA" | 84 | 31 |
| INDIAC4 | 14408 | C | T | "ORF1b:314" | "P314L" | 84 | 46 |
| INDIAC5 | 28881 | G | A | "N:203" | "R203K" | 42 | 35 |
| INDIAC6 | 28883 | G | C | "N:204" | "G204R" | 41 | 35 |
| INDIAC7 | 28882 | G | A | "N:203" | "R203K" | 40 | 25 |
| INDIAC8 | 25563 | G | T | "ORF3a:57" | "Q57H" | 25 | 10 |
| INDIAC9 | 18877 | C | T | "ORF1b:1804" | "L1804I" | 25 | 10 |
| INDIAC10 | 26735 | C | T | "M:71" | "Y71Y" | 25 | 8 |
| INDIAC11 | 28854 | C | T | "N:194" | "S194L" | 23 | 29 |
| INDIA C12 | INDIA C13 | INDIA C14 | INDIA C15 | INDIA C16 | INDIA C17 | INDIA C18 | INDIA C19 | INDIA C20 | INDIA C21 | INDIA C22 | INDIA C23 | INDIA C24 | INDIA C25 | INDIA C26 | INDIA C27 | INDIA C28 |
|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 22444 | 313 | 5700 | 11083 | 13730 | 28311 | 23929 | 6312 | 8917 | 1947 | 9389 | 6573 | 4354 | 25528 | 15324 | 3267 | 3634 |
| C | T | C | T | C | T | C | T | C | T | C | T | C | T | C | T | C |
| "S:294" | "ORF1a:16" | "ORF1a:1812" | "ORF1a:3606" | "ORF1b:88" | "N:13" | "S:789" | "ORF1a:2016" | "ORF1a:2884" | "ORF1a:561" | "ORF1a:3042" | "ORF1a:2103" | "ORF1a:1363" | "ORF3a:46" | "ORF1b:619" | "ORF1a:1001" | "ORF1a:1123" |
| "D294D" | "L16L" | "A1812D" | "L3606F" | "A88V" | "P13L" | "Y789Y" | "T2016K" | "F2884F" | "V561A" | "D3042N" | "S2103F" | "E1363E" | "L46F" | "N619N" | "T1001F" | "N1123N" |
| 22 | 21 | 20 | 14 | 11 | 10 | 10 | 10 | 10 | 7 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| 29 | 29 | 29 | 29 | 41 | 48 | 36 | 36 | 36 | 36 | 36 | 36 | 36 | 36 | 62 | 62 | 62 |

Table 6 - Recall summary main results from Table5.
| Genome     | percent | Number of 1 |
|------------|---------|-------------|
| SARS-CoV2 Wuhan |         | 8           |
| B.1.617     |         | 31          |
| INDIAC1     | 85      | 31          |
| INDIAC2     | 84      | 31          |
| INDIAC3     | 84      | 31          |
| INDIAC4     | 84      | 46          |
| INDIAC5     | 42      | 35          |
| INDIAC6     | 41      | 35          |
| INDIAC7     | 40      | 25          |
| INDIAC8     | 25      | 10          |
| INDIAC9     | 25      | 10          |
| INDIAC10    | 25      | 8           |
| INDIAC11    | 23      | 29          |
| INDIAC12    | 22      | 29          |
| INDIAC13    | 21      | 29          |
| INDIAC14    | 20      | 29          |
| INDIAC15    | 14      | 29          |
| INDIAC16    | 11      | 41          |
| INDIAC17    | 10      | 48          |
| INDIAC18    | 10      | 36          |
| INDIAC19    | 10      | 36          |
| INDIAC20    | 10      | 36          |
| INDIAC21    | 7       | 36          |
| INDIAC22    | 6       | 36          |
| INDIAC23    | 6       | 36          |
| INDIAC24    | 6       | 36          |
| INDIAC25    | 6       | 34          |
| INDIAC26    | 6       | 62          |
| INDIAC27    | 6       | 62          |
| INDIAC28    | 6       | 62          |
The most remarkable result is the fact that the very simple combination of the 4 most frequent mutations (85% of cases) and the variant B.1.617 is sufficient to multiply by 4 to 6 (31 to 46 against 8 for SARS-CoV2 Wuhan (the number of Fibonacci metastructures of 17,712 AU / CG bases. We also note that out of the 28 genomes studied, only one of them possesses the 8 characteristic metastructures of SARS-COV2 Wuhan. The average of the other 27 is 34.57, i.e. 4.32 times more and some cases are 8 times more INDIA26-28 : 62).
Figure 11 – Comparing long range 17711 UA/CG Fibonacci metastructures between SARS-CoV2 Wuhan and India variant B.1.617 with the 28 most frequent India country mutations.
3.3 - simulations of possible future mutations of the variant B.1.617.

In (Pragya Yadav et al., 2021), the authors provide a list of the 33 main mutations characterizing the genomes of the Indian variant B.1.617. On the other hand, we have just studied the impact of the 28 most frequent mutations in India, those which represent more than 5% of contaminations. It is clear that these 2 sets of mutations partially overlap. However, it would be interesting to simulate the effect of some of the 28 mutations when they are absent in B.1.617. Indeed, their high frequency makes it possible to suggest their possible future addition to B.1.617. This is what we will simulate in this last paragraph.

Table 7 – The 33 main mutations from India variant B.1.617 from (Pragya Yadav et al., 2021). From Figure 1:nCharacteristics and neutralization of VUI B.1.617 variant: A)nThe common nucleotide changes observed in majority of the isolates and clinical sequences. We identify 22 other frequent mutations in India (frequency greater than 5% of contaminations) but absent in the Indian variant B.1.617.

| Genome location | Reference SARS-CoV2 | Mutation B.1.617 | Percent | 17711 UA/CG Fibonacci metastructures |
|-----------------|---------------------|------------------|---------|--------------------------------------|
| B1.1617         | All 32 following mutations | 53              |         |                                      |
| 210 GT          | G                   | T                |         |                                      |
| 3457 CT         | C                   | T                |         |                                      |
| 11201 CT        | C                   | T                |         |                                      |
| 16134 CT        | C                   | T                |         |                                      |
| 20396 CT        | C                   | T                |         |                                      |
| 21895 GA        | G                   | A                |         |                                      |
| 22917 AG        | A                   | G                |         |                                      |
| 23604 CT        | C                   | T                |         |                                      |
| 26767 GA        | G                   | A                |         |                                      |
| 27520 CT        | C                   | T                |         |                                      |
| 29402 GT        | G                   | T                |         |                                      |
| 241 GT INDIAC3  | G                   | T                |         |                                      |
| 4965 AG         | A                   | G                |         |                                      |
| 14408 TG INDIAC4 | T                  | G                |         |                                      |
| 16852 CT        | C                   | T                |         |                                      |
| 20401 TC        | T                   | C                |         |                                      |
| 21987 GA        | G                   | A                |         |                                      |
| 23012 GA        | G                   | A                |         |                                      |
| 24775 TG        | T                   | G                |         |                                      |
| 27382 GC        | G                   | C                |         |                                      |
|        |        |        |        |        |        |
|--------|--------|--------|--------|--------|--------|
| 27638  | AG     | A      | G      |        |        |
| 29742  | CG     | C      | G      |        |        |
| 3037   | AT     | A      | T      |        |        |
| 8491   | CT     | C      | T      |        |        |
| 14772  | TG     | T      | G      |        |        |
| 17523  | GC     | G      | C      |        |        |
| 21846  | TC     | T      | C      |        |        |
| 22022  | AT     | A      | T      |        |        |
| 23403  | TC     | T      | C      |        |        |
| 25469  | GT     | G      | T      |        |        |
| 27385  | GT     | G      | T      |        |        |
| 28881  | GT     | G      | T      |        |        |
|        |        |        |        |        |        |
| Other mutations common in India but absent in the Indian variant B.1.617 |
|        |        |        |        |        |        |
| 28883  | SINDIAC6 | G    | C    | 41   | 53   |
| 28882  | SINDIAC7 | G    | A    | 40   | 32   |
| 25563  | SINDIAC8 | G    | T    | 25   | 21   |
| 26735  | SINDIAC10 | C   | T    | 25   | 14   |
| 28854  | SINDIAC11 | C   | T    | 23   | 8    |
| 22444  | SINDIAC12 | C   | T    | 22   | 31   |
| 313    | SINDIAC13 | C   | T    | 21   | 31   |
| 5700   | SINDIAC14 | C   | A    | 20   | 31   |
| 11083  | SINDIAC15 | G   | T    | 14   | 31   |
| 13730  | SINDIAC16 | C   | T    | 11   | 28   |
| 28311  | SINDIAC17 | C   | T    | 10   | 40   |
| 23929  | SINDIAC18 | C   | T    | 10   | 48   |
| 6312   | SINDIAC19 | C   | A    | 10   | 48   |
| 8917   | SINDIAC20 | C   | T    | 10   | 48   |
| 1947   | SINDIAC21 | T   | C    | 7    | 48   |
| 9389   | SINDIAC22 | G   | A    | 6    | 48   |
| 6573   | SINDIAC23 | C   | T    | 6    | 48   |
| 4354   | SINDIAC24 | G   | A    | 6    | 48   |
| 25528  | SINDIAC25 | C   | T    | 6    | 38   |
| 15324  | SINDIAC26 | C   | T    | 6    | 45   |
| 3267   | SINDIAC27 | C   | T    | 6    | 45   |
| 3634   | SINDIAC28 | C   | T    | 6    | 45   |
| **Average** |   |   |   | **15.05%** | **37.68** |

Nota : We rename these successive mutants SINDIA6 for B.1.617 consensus + INDIA6 etc ...
Analysing the 32 mutations consensus India variant B.617:

We run here the 32 mutations applied to SARS-CoV2 reference Wuhan genome:

B1617REF = VSARSCOV2REF
B1617REF[210] C
B1617REF[210] T
B1617REF[241] C
B1617REF[241] T
B1617REF[3037] C
B1617REF[3037] T
B1617REF[3457] C
B1617REF[3457] T
B1617REF[4965] C
B1617REF[4965] T
B1617REF[8491] G
B1617REF[8491] A
B1617REF[11201] A
B1617REF[11201] G
B1617REF[14408] C
B1617REF[14408] T
B1617REF[14772] G
B1617REF[14772] A
B1617REF[16134] C
B1617REF[16134] T
B1617REF[16852] G
B1617REF[16852] T
B1617REF[17523] G
B1617REF[17523] T
B1617REF[20396] A
B1617REF[20396] G
B1617REF[20401] T
B1617REF[20401] G
B1617REF[21846] C
B1617REF[21846] T
B1617REF[21895] T
B1617REF[21895] C
B1617REF[21987] G
B1617REF[21987] A
B1617REF[22022] G
B1617REF[22022] A
B1617REF[22917] T
B1617REF[22917] G
B1617REF[23012] G
B1617REF[23012] C
B1617REF[23403] A
Figure 12 – Comparing long range 17711 UA.CG Fibonacci metastructures between SARS-CoV2 Wuhan and India variant B.1.617 Reference Consensus (Pragya Yadav et al, 2021) including 32 mutations.

Now we will apply to this strain B.1.617 consensus the progressive accumulation of the 22 other frequent mutations in India (frequency greater than 5% of contaminations) but absent in the Indian variant B.1.617.
For this purpose, as we did in the previous §, we will apply to B.1.617 consensus each of the 22 mutations, accumulating them one by one and respecting the order of their frequency of contamination in India (here in the order INDIAC6, then INDIAC6 + INDIAC7, then INDIAC6 + INDIAC7 + INDIAC8 ... as these mutations appear in Table 7.

Nota : We rename these successive mutants SINDIA6 for B.1.617 consensus + INDIA6 etc...

SINDIAC6, B1617REF
SINDIAC6[28883]
G
SINDIAC6[28883], 'C'
SINDIAC7, SINDIAC6
SINDIAC7[28882]
G
SINDIAC7[28882], 'A'
SINDIAC8, SINDIAC7
SINDIAC8[25563]
G
SINDIAC8[25563], 'T'
SINDIAC10, SINDIAC8
SINDIAC10[26735]
C
SINDIAC10[26735], 'T'
SINDIAC11, SINDIAC10
SINDIAC11[28854]
SINDIAC11[28854], 'T'
SINDIAC12, SINDIAC11
SINDIAC12[22444]
C
SINDIAC12[22444], 'T'
SINDIAC13, SINDIAC12
SINDIAC13[313]
C
SINDIAC13[313], 'T'
SINDIAC14, SINDIAC13
SINDIAC14[5700]
C
SINDIAC14[5700], 'A'
SINDIAC15, SINDIAC14
SINDIAC15[11083]
G
SINDIAC15[11083], 'T'
SINDIAC16, SINDIAC15
SINDIAC16[13730]
C
SINDIAC16[13730], 'T'
SINDIAC17, SINDIAC16
SINDIAC17[23929]
C
SINDIAC17[23929], 'T'
SINDIAC18, SINDIAC17
SINDIAC18[23929]
C
SINDIAC18[23929], 'T'
SINDIAC19, SINDIAC18
SINDIAC19[6312]
C
SINDIAC19[6312], 'A'
SINDIAC20, SINDIAC19
| C          | SINDIAC20[8917] |
|------------|----------------|
| T          | SINDIAC21[1947] |
| G          | SINDIAC22[9389] |
| G          | SINDIAC23[6573] |
| C          | SINDIAC24[4354] |
| G          | SINDIAC25[25528] |
| C          | SINDIAC26[15324] |
| C          | SINDIAC27[3267] |
| C          | SINDIAC28[3634] |
| T          | SINDIAC29[3458] |

Table 8 - Evolution of 17711 UA/CG metastructures with whole INDIAN variant genomes with cumulated mutations vs percent frequencies (vs. B.1.617 REF variant).
Here, unlike the 2 previous simulations where most of the mutations INCREASED the number of long AU / CG metastructures, here almost all of the mutations DECREASE the number of these long metastructures. It is true that the level of these metastructures of 17711 AU / CG bases is very IMPORTANT in the reference genome B.1.617 Ref.

The level of the B.1.617 consensus reference variant genome is however more than 6.6 times higher than that of the Wuhan SARS-CoV2 reference genome.

The average level of these 22 nested mutations applied to the variant genome consensus reference B.1.617 is however more than 4.7 times higher than that of the reference genome SARS-CoV2 Wuhan.
CONCLUSIONS.

In this study, we limit ourselves to the analysis of whole genomes, all coming from the mutations and variants of SARS-CoV2 sequenced in India in 2020 and 2021. We then demonstrate - both on actual genomes of patients and on variants combining the most frequent mutations to the SARS-CoV2 Wuhan genomes and then to the B.1.617 variant - that the numerical Fibonacci AU / CG metastructures increase considerably in all cases analyzed in ratios of up to 8 times. We can affirm that this property contributes to a greater stability and lifespan of messenger RNAs, therefore, possibly also to a greater INFECTUOSITY of these variant genomes.
In this study, we looked for the presence and number of UA / CG Fibonacci metastructures. We are interested in the longest of 17,711 bases, for genomes of 29,000 bases. These genomes concerned, for some, real patients, and, for others, the 28 mutations and variants most frequent in India, those which represent more than 5% of the cases of infections of the country.

**Out of a total of 87 genomes analyzed:**
- None ("NONE") of them contained a number of metastructures LOWER than those of the reference SARS-CoV2 Wuhan genome.
- Eleven (11) among them contained the same number of metastructures as the reference genome.
- 76 of them contained a GREATER number of metastructures than the reference genome, i.e. 87% of cases. The average increase in the number of metastructures for the 76 cases studied is 4.11 times the number of SARS-CoV2 UA/CG 17711 Fibonacci metastructures. (4.11 = 32.86 / 8).

Note the impact of the new B.1.617 variant which, combined with the 4 most frequent mutations (85% of contaminations in the country), multiplies by 4 ("four") the number of metastructures of 17,711 bases compared to the reference genome SARS-CoV2 (8 ==> 31). It is therefore clear that the evolutionary pressure of mutations and variants operates on the mRNAs of viruses a sort of adaptation and even OPTIMIZATION of the AU / CG ratios of the entire genome. Only the virus "knows" this STRATEGY, and we think we have unveiled a corner of the veil here …

**When we run the most frequent mutations in India whole country, on the reference consensus B.1.617 India Variant, the level of the B.1.617 consensus reference**
variant genome is more than 6.6 times higher than that of the Wuhan SARS-CoV2 reference genome.

"We can add that the evolution of the virus towards the" Fibonacci "variants was favored by the anti-spike protein antibodies of the original SARS-CoV2 virus from Wuhan. Nature or God will not facilitate the reaction of vaccinators to end to this pandemic ". Luc Montagnier.

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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), Patricia 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 physical 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

(Muttineri et al, 2021), Muttineni R, Kammili N, Bingi TC, Rao M. R, Putty K, Dholaniya PS, et al. (2021) Clinical and whole genome characterization of SARS-CoV-2 in India. PLoS ONE 16 (2): e0246173. doi: 10.1371/journal.pone.0246173 https://www.google.com/url?sa=t&source=web&rct=j&url=https://journals.plos.org/plospathogens/article/file%3Fid%3D10.1371/journal.pone.0246173%26type%3Dprintable&ved=2ahUKEwj3zdnZnorwAhUQKBoKHUXnD_EQFjABegQICBAC&usg=A0vVaw1A79ux6UbetoPoRxFkJT-Mk

(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_Technologymol_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, 2021) Perez, J. SARS-CoV2 Variants and Vaccines mRNA Spikes Fibonacci Numerical UA/CG Metastructures. Preprints 2021, 2021040034 (doi: 10.20944/preprints202104.0034.v5). Perez, J. SARS-CoV2 Variants and Vaccines mRNA Spikes Fibonacci Numerical UA/CG Metastructures. Preprints 2021, 2021040034 (doi: 10.20944/preprints202104.0034.v5).
https://www.preprints.org/manuscript/202104.0034/v5

(Pragya Yadav et al., 2021), Pragya Yadav, et al., Neutralization of variant under investigation B.1.617 with sera of BBV152 vaccinees bioRxiv 2021.04.23.441101; doi: https://doi.org/10.1101/2021.04.23.441101

(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

(Srivastava Surabhi et al, 2021), SARS-CoV-2 genomics: An Indian perspective on sequencing viral variants, J Biosci. 2021; 46(1): 22. Published online 2021 Feb 20. doi: 10.1007/s12038-021-00145-7, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7895735/

(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