Computational analysis of the SARS-CoV-2 and other viruses based on the Kolmogorov's complexity and Shannon's information theories

J. A. Tenreiro Machado · João M. Rocha-Neves · José P. Andrade

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Abstract This paper tackles the information of 133 RNA viruses available in public databases under the light of several mathematical and computational tools. First, the formal concepts of distance metrics, Kolmogorov complexity and Shannon information are recalled. Second, the computational tools available presently for tackling and visualizing patterns embedded in datasets, such as the hierarchical clustering and the multidimensional scaling, are discussed. The synergies of the common application of the mathematical and computational resources are then used for exploring the RNA data, cross-evaluating the normalized compression distance, entropy and Jensen–

Shannon divergence, versus representations in two and three dimensions. The results of these different perspectives give extra light in what concerns the relations between the distinct RNA viruses.

Keywords COVID-19 · Kolmogorov complexity theory · Shannon information theory · Hierarchical clustering · Multidimensional scaling

1 Introduction

In December 2019, a mysterious pneumonia with unknown etiology was reported in the city of Wuhan, Province of Hubei, China [1]. The International Committee on Taxonomy of Virus (ICTV) named the virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2]. Globally, to the 30th of July 2020, according to the World Health Organization Coronavirus Disease 2019 (COVID-19) Situation Report, 10,185,374 confirmed cases of COVID-19 are reported, resulting in 503,862 deaths.

The scientific community reacted as never before, and many researchers focused on this urgent topic [3–10]. The mathematical and computer science communities are also studying this challenging problem, and we testimony the recent emergence of new models and algorithmic approaches. This common multidisciplinary research will allow the human kind

J. A. T. Machado (✉)
Department of Electrical Engineering, Institute of Engineering, Polytechnic of Porto, Rua Dr. António Bernardino de Almeida, 431, 4249-015 Porto, Portugal
e-mail: jtm@isep.ipp.pt

J. M. Rocha-Neves · J. P. Andrade
Department of Biomedicine – Unity of Anatomy, Faculty of Medicine of University of Porto, Porto, Portugal
e-mail: joaorochaneves@hotmail.com

J. P. Andrade
e-mail: jandrade@med.up.pt

J. M. Rocha-Neves
Department of Physiology and Surgery, Faculty of Medicine of University of Porto, Porto, Portugal

J. P. Andrade
Center for Health Technology and Services Research (CINTESIS), Porto, Portugal

to implement a robust and fast response to a problem that is causing a severe global socioeconomic disruption, and most probably will lead to the largest global recession since the Great Depression.

The present paper follows this trend by studying the genetic information by means of mathematical and computational tools. The starting point is the information encoded in the ribonucleic acid (RNA), a polymeric molecule essential in various biological roles.

The evolutionary origin and divergence of eucaryotes is mostly recoverable from their genetic relationships. The phylogeny of core genes, such as those for ribosomal proteins, provides a reasonable representation of many billions of years [11]. Unfortunately, the diversity of viruses prevents such a reconstruction of virus evolutionary histories as they lack any equivalent set of universally conserved genes on which to construct a phylogeny. Viral diversity is far greater than that of other organisms, with significant differences in their genetic material, RNA or deoxyribonucleic acid (DNA), and configurations (double or single stranded), as well as the orientation of their encoded gene. The smallest virus genomes [12] contain over 2,500 genes [13]. The RNA is a nucleic acid that is essential to all forms of life, and it is found in nature generally as single-stranded (ss) rather than a paired double-stranded (ds) like DNA. In DNA, there are four bases: adenine (A) complementary to thymine (T) and cytosine (C) complementary to guanine (G). In the RNA, uracil (U) is used instead of thymine.

Like DNA, RNA can carry genetic information. An RNA virus is a virus that has RNA as its genetic material encoding a number of proteins. This nucleic acid is usually single-stranded RNA (ssRNA), but there are double-stranded RNA (dsRNA) viruses. These viruses exploit the presence of RNA-dependent RNA polymerases in eucaryotes cells for replication of their genomes. Many human diseases are caused by such RNA viruses such as influenza, severe acute respiratory syndrome (SARS), COVID-19, Ebola disease virus, chikungunya, Zika virus, influenza B and Lassa virus [14].

The RNA is usually sequenced indirectly by copying it into complementary DNA (cDNA), which is often amplified and subsequently analyzed using a variety of DNA sequencing methods. Therefore, the genomic sequences of the RNA viruses are published

presenting the four bases, namely adenine (A), cytosine (C), guanine (G) and thymine (T).

This genetic information is analyzed by means of the Kolmogorov's complexity and Shannon's information theories. In the first case, the so-called normalized information distance (*NID*) is adopted. In the second, a statistical approach is considered, by constructing histograms for the relative frequency of three consecutive bases (triplets). The histograms are interpreted under the light of entropy, cumulative residual entropy and Jensen–Shannon divergence. The results obtained for each theory, that is, the values assessing the virus genetic code under the light of the Kolmogorov's complexity and the Shannon's information, are further processed by means of advanced computational representation techniques. The final visualization is obtained using the hierarchical clustering (HC) [15–20] and multidimensional scaling (MDS) techniques [21–27]. Three alternative representations, namely dendrograms, hierarchical trees and three-dimensional loci, are considered.

According to the ICTV, human coronavirus belongs to the Betacoronavirus genus, a member of the Coronaviridae family, categorized in the order Nidovirales [28]. It has been categorized into several genera, based on phylogenetic analyses and antigenic criteria, namely: (i) Alphacoronavirus, responsible for gastrointestinal disorders in humans, dogs, pigs and cats; (ii) Betacoronavirus, including the bat coronavirus, the human severe acute respiratory syndrome (SARS) virus, the Middle Eastern respiratory syndrome (MERS) virus and now the SARS-CoV-2; (iii) Gammacoronavirus, which infects avian species; and iv) Deltacoronavirus [2, 29].

Four coronaviruses broadly distributed among humans (229E, OC43, NL63 and, HKU1) frequently cause only common cold symptoms [2, 12]. The two other strains of coronaviruses are linked with deadly diseases and zoonotic in origin, i.e., the SARS-CoV and MERS-CoV [30]. In 2002–2003, there was an outbreak of SARS beginning in Guangdong Province in China and affecting 27 countries subsequently [31]. It was considered the first pandemic event of the twenty-first century, due to the SARS-CoV infecting 8098 individuals with 774 deaths [31]. In 2012, in the Middle East, MERS-CoV caused a severe respiratory disease that affected 2494 individuals and 858 deaths [2]. In both epidemics, bats were the original host of these two coronaviruses [2].

Coronaviruses contain a positive-sense, single-stranded RNA genome. The genome size for coronaviruses ranges from 26.4 to 31.7 kilobases, and it is one of the largest among RNA viruses.

The rapid spread of SARS-CoV-2 raises intriguing questions such as whether its evolution is driven by mutations, recombination or genetic variation [32]. This information is now being applied to the development of diagnostic tools, effective antiviral therapies and in the understanding of viral diseases. Although numerous studies have been done from the biological and medical perspective, to help further understand SARS-CoV-2 and trace its origin, this paper reports the use of multidimensional scale techniques for the finding of the similarities and the relationships among COVID-19 strains themselves and between other described viruses.

For that, we have collected a set of 37 complete genome sequences of SARS-CoV-2 virus obtained in several countries from patients with COVID-19. To help verify whether it is possible to trace the original or intermediate host of SARS-CoV-2, we obtained the genomic sequences of SARS-CoV-2 virus in other hosts, including bats (16 genomic sequences), pangolins (8 genomic sequences) and environment (market of Wuhan) [13]. We have also collected 23 genomic sequences of the coronavirus that cause mild symptoms related to common cold in man (229E, OC43, NL63 and, HKU1). The genomic sequences of SARS-CoV (10 genomic sequences) and a MERS-CoV (13 genomic sequences) were also gathered. For comparison and control, we also obtained sequences of other deadly pathogenic RNA viruses such as Lassa (6 genomic sequences), Ebola (6 genomic sequences), dengue (7 genomic sequences), chikungunya (1

genomic sequence) and influenza B (2 genomic sequences).

The diagram of Fig. 1 summarizes the main historical flow of coronavirus in what concerns the twenty-first-century epidemics.

To the authors' best knowledge, this paper analyzes for the first time a large number of viruses associated with the combination of several distinct mathematical and computational tools. In short, we have the cross-comparison of:

- The genomic sequences of 133 viruses.
- The data treatment by means of Kolmogorov's complexity and Shannon's information theories, using normalized compression distance, entropy, cumulative residual entropy and Jensen–Shannon divergence.
- Two clustering computational techniques, namely the hierarchical clustering and multidimensional scaling.
- The visualization of the results by means of dendrograms, trees and point loci.

The results indicate clearly the superior performance of the approaches based on the Kolmogorov's complexity measure and the MDS three-dimensional visualization. Moreover, the characteristics of the coronaviruses within the large set of tested cases are highlighted. We conclude that:

- The association between the Kolmogorov perspective and the three-dimensional MDS representation leads to be the best results.
- The clusters are easily distinguishable and we observe the relation between the new SARS-CoV-2 virus and some CoV found in bats and in the pangolin.

Fig. 1 Coronavirus related to twenty-first-century epidemics. ICST: The International Committee on Taxonomy of Virus—Coronavirus Study Group, WHO: World Health Organization

Bearing these ideas in mind, the paper is organized as follows. Section 2 introduces the mathematical and computational tools adopted in the follow-up. Section 3 analyzes the data by means of the complexity and information theories accompanied by the HC and MDS computational visualization resources. Finally, Sect. 4 summarizes the main conclusions.

2 Fundamental tools

2.1 Distance metrics

Evaluating the similarity degree between several objects, each having a number of features requires the definition of a distance. The calculation of a function d of two objects x_A and x_B can be interpreted as a distance if $d(x_A, x_B) \geq 0$ and satisfies the following axioms [33]:

$$\begin{aligned} \text{identity : } d(x_A, x_B) &= 0 \text{ if } x_A = x_B \\ \text{symmetry : } d(x_A, x_B) &= d(x_B, x_A) \\ \text{triangle inequality : } d(x_A, x_B) &\leq d(x_A, x_C) \\ &+ d(x_C, x_A). \end{aligned} \quad (1)$$

We find in the literature a variety of different functions that can tackle datasets and shed light to distinct characteristics [34]. For a set of numerical vectors $(x_1, \dots, x_N)^T \in \mathbb{R}^n$, the Minkowski norm $L_n : (\sum_{k=1}^N |x_k|^n)^{\frac{1}{n}}$, and in particular the Manhattan and Euclidean cases, L_1 and L_2 for $n = 1$ and $n = 2$, are often used [35]. In the case of DNA analysis, these norms support different algorithms [36–38] that allow the comparison of data sequences. We can also mention metrics such as the Chi-square [39], Hamming [40] and edit [41] distances. Nonetheless, the selection of the optimal distances for a specific application poses relevant challenges [42–45]. In fact, the adoption of a given metric often depends on the user experience that performs several numerical experiments before selecting one or more distances. Due to these issues, assessing the similarity of several objects is not a straightforward process and we can adopt both non-probabilistic and probabilistic information measures to obtain distinct perspectives between object similarities.

2.2 Kolmogorov complexity theory

The Kolmogorov complexity, or algorithmic entropy, addresses the information measurement without relying on probabilistic assumptions. The information measurement focuses an individual finite object described by a string and takes into consideration that ‘regular’ strings are compressible [46]. The Kolmogorov complexity of a string x , denoted as $K(x)$, can be defined as the length of the shortest binary program that, given an empty string ψ at its input, can compute x on its output in a universal computer, and then halts. Therefore, $K(x)$ can be interpreted as the length of the ultimate compressed version of x .

The information distance of two strings (or files) $\{x_A, x_B\} \in \Sigma$, where Σ denotes the space of the objects, can also be computed by means of the conditional Kolmogorov complexity $K(x_A|x_B)$ [47, 48]. This concept can be read as the length of the shortest program to obtain x_A , if x_B is provided for input. In heuristic terms, if the two strings are more/less similar, then the calculation is less/more difficult and, consequently, the size of the program is smaller/larger. Therefore, the following inequality always holds

$$K(x_A|x_B) \leq K(x_A). \quad (2)$$

Under the light of these concepts, the universal distance metric [47] denoted as normalized information distance (NID):

$$\begin{aligned} NID(x_A, x_B) &= \frac{\max\{K(x_A|x_B), K(x_B|x_A)\}}{\max\{K(x_A), K(x_B)\}}, \quad \{x_A, x_B\} \in \Sigma, \end{aligned} \quad (3)$$

was proposed.

From equation (2), we have that the NID may take values in the range $[0, 1]$. Moreover, we have $NID(x_A, x_A) \approx 0$ and $NID(x_A, \psi) \approx 1$, where ψ is an empty object that has no similarity to x_A . It is shown [47] that the NID is a distance because it satisfies the axioms defined in (1), up to some additive precision, but is non-computable [47]. In spite of this limitation, the NID gives the basis for the so-called normalized compression distance (NCD), which is a computable distance [45]. The computability comes with the cost of using a good approximation of the Kolmogorov complexity by a standard compressor

$C(\cdot)$ (interested readers for the discussion between the equivalence of the *NID* and the *NCD* can find further details in [33]).

The *NCD* is given by:

$$NCD(x_A, x_B) = \frac{C(x_A x_B) - \min\{C(x_A), C(x_B)\}}{\max\{C(x_A), C(x_B)\}}. \quad (4)$$

The *NCD* has values in the range $0 < NCD(x, y) < 1 + \epsilon$, assessing the distance between the files x_A and x_B . The parameter $\epsilon > 0$ reflects ‘imperfections’ in the compression algorithm. The values of $C(x_A)$ and $C(x_B)$ are the sizes of each of the compressed files x_A and x_B , respectively, and $C(x_A x_B)$ is the compressed size of the two concatenated files considered by the compressor as a single file.

Let us consider, for example, that $C(x_B) \geq C(x_A)$. Expression (4) says that the distance $NCD(x_A, x_B)$ assesses the improvement due to compressing x_B using data from the previously compressed x_A and compressing x_B from scratch, expressed as the ratio between their compressed sizes.

Obviously, the approximation of the *NID* by means of the *NCD* poses operational obstacles. Due to the non-computability of the Kolmogorov complexity, we cannot predict how close is the *NCD* to the real value of the *NID*, and the approximation may yield arithmetic problems, particularly in the case of small strings where numerical indeterminate forms may arise [33, 49]. Moreover, the compressor (as an approximation of the Kolmogorov complexity) must be ‘normal’ in the sense that given the object $x_A x_A$ the compressor C should produce an object with almost to an identical size to the compressed version of x_A . This is a limitation for the universality of the *NCD* since in specific applications the best performing loss-less algorithms (e.g., JBIG, JPEG2000 and JPEG-LS in image compression) do not satisfy such propriety [50]. Nevertheless, key results were already obtained using the *NCD* in image distinguishability [51], image OCR [52], malware recognition [53] and genomic analysis [54, 55].

2.3 Shannon information theory

Information theory [56] has been applied in a variety of scientific areas. The most fundamental piece of the theory is the information content I of a given event x_i having probability of occurrence $P(X = x_i)$:

$$I(X = x_i) = -\ln(P(X = x_i)), \quad (5)$$

where X is a discrete random variable.

The expected value of the information, the so-called Shannon entropy [57, 58], is given by:

$$\begin{aligned} H(X) &= E(-\ln(X)) \\ &= -\sum_i P(X = x_i) \ln(P(X = x_i)), \end{aligned} \quad (6)$$

where $E(\cdot)$ denotes the expected value operator.

Expression (6) obeys the four Khinchin axioms [59, 60]. Several generalizations of Shannon entropy have been proposed, relaxing some of those axioms, and we can mention the Rényi, Tsallis and generalized entropy [61–63], just to name a few.

A recent and interesting concept is the cumulative residual entropies ε given by [64, 65]:

$$\varepsilon(X) = -\sum_i P(X > x_i) \log(P(X > x_i)). \quad (7)$$

Within the scope of information theory, we can formulate also the concept of distance discussed in Sect. 2.1. The Kullback–Leibler divergence between the probability distributions X_1 and X_2 is defined as [34, 66–69]:

$$D_{KL}(X_1 \parallel X_2) = \sum_i P(X_1 = x_i) \ln\left(\frac{P(X_1 = x_i)}{P(X_2 = x_i)}\right). \quad (8)$$

From this, we obtain the Jensen–Shannon divergence, $JSD(X_1 \parallel X_2)$, or distance, given by:

$$\begin{aligned} JSD(X_1 \parallel X_2) \\ = \frac{1}{2} [D_{KL}(X_1 \parallel X_{12}) + D_{KL}(X_2 \parallel X_{12})], \end{aligned} \quad (9)$$

where $X_{12} = \frac{1}{2}(X_1 + X_2)$.

Alternatively, the $JSD(X_1 \parallel X_2)$ can be calculated as:

$$\begin{aligned} JSD(X_1 \parallel X_2) &= \frac{1}{2} \sum_i P(X_1 = x_i) \ln(P(X_1 = x_i)) \\ &\quad + \frac{1}{2} \sum_i P(X_2 = x_i) \ln(P(X_2 = x_i)) \\ &\quad - \sum_i P(X_{12} = x_i) \ln(P(X_{12} = x_i)). \end{aligned} \quad (10)$$

2.4 Hierarchical clustering, multidimensional scaling and visualization

The HC is a computational technique that assesses a group of N objects X_i , $i = 1, \dots, N$, in a q -dimensional space, and tries to rearrange them in a visual structure with objects Y_i highlighting the main similarities between them in the sense of some predefined metric [70].

Let us consider N objects defined in a q -dimensional real-valued space and a distance (or dissimilarity) measure δ_{ij} between pairs of objects. The first step is to calculate a $N \times N$ -dimensional matrix, $\Delta = [\delta_{ij}]$, where $\delta_{ij} \in \mathbb{R}^+$ for $i \neq j$ and $\delta_{ii} = 0$, $(i, j) = 1, \dots, N$, stands for the object to object distances [71]. The HC uses the input information in matrix Δ and produces a graphical representation consisting in a dendrogram or a hierarchical tree.

The so-called agglomerative or divisive clustering iterative techniques are usually adopted for processing the information. In the first approach, each object starts in its own cluster and the computational iterations merge the most similar items until having just one cluster. In the second, all objects start their own cluster and the computational iterations separate items, until each object has his own cluster. For both approaches, the numerical iterations follow a linkage criterion, based on the distances between pairs, for quantifying the dissimilarity between clusters. The maximum, minimum and average linkages are possible criteria. The distance $d(x_A, x_B)$ between two objects $x_A \in A$ and $x_B \in B$ can be assessed by means of several metrics such as the average linkage given by [72]:

$$d_{av}(A, B) = \frac{1}{\|A\| \|B\|} \sum_{x_A \in A, x_B \in B} d(x_A, x_B). \quad (11)$$

The clustering quality can be assessed by means of the cophenetic correlation [73]:

$$c = \frac{\sum_{i < j} (x(i, j) - \bar{x})(y(i, j) - \bar{y})}{\sqrt{\left[\sum_{i < j} (x(i, j) - \bar{x})^2 \right] \left[\sum_{i < j} (y(i, j) - \bar{y})^2 \right]}}, \quad (12)$$

where $x(i, j)$ and $y(i, j)$ stand for the distances between the pairs X_i and X_j , in the initial measurements, and Y_i

and Y_j , in the HC chart, respectively, and $\bar{x}$ denotes the average of x .

Values of c close to 1 (to 0) indicate a good (weak) cluster representation of the original data. In MATLAB, c is computed by means of the command `cophenet`.

In this paper, we adopt the agglomerative clustering and the average linkage [74, 75] for tackling the matrix of distances based on the *JSD* metric (10).

The MDS is also a computational technique for clustering and visualizing multidimensional data [76]. Similarly to what was said for the HC, the input of the MDS is the matrix $\Delta = [\delta_{ij}]$, $(i, j) = 1, \dots, N$. The MDS is to adopt points for representing the objects in a d -dimensional space, with $d < q$, that try to reproduce the original distances, δ_{ij} . The MDS performs a series of numerical iterations rearranging the points in order to optimize a given cost function called stress S . We have, for example, the residual sum of squares and the Sammon criteria:

$$S = \left[\sum_{i < j} (\phi_{ij} - \delta_{ij})^2 \right]^{\frac{1}{2}}, \quad (13a)$$

$$S = \left[\frac{\sum_{i < j} (\phi_{ij} - \delta_{ij})^2}{\sum_{i < j} \phi_{ij}^2} \right]^{\frac{1}{2}}. \quad (13b)$$

The resulting MDS points have coordinates that produce a symmetric matrix $\Phi = [\phi_{ij}]$ of distances that approximate the original one $\Delta = [\delta_{ij}]$. In MATLAB, the commands `cmdscale` and `Sammon` can be adopted for the classical MDS and the Sammon stress criterion.

The interpretation of the MDS locus is based on the patterns of points [77, 78]. Therefore, objects with strong (weak) similarities are represented by fairly close (distant) points. The MDS locus is interpreted on the relative positions of the point coordinates. So, the absolute position of the points or the shape of the clusters has usually a special meaning, and we can magnify, translate and rotate the locus for achieving a good visualization. In the same line of reasoning, the axes of the plot do not have units or physical meaning. The quality of the produced MDS locus can be evaluated using the stress plot and the Shepard diagram. The stress plot shows S versus d and decreases monotonically. Usually, low values of d are adopted, and present computational resources

allow a direct three-dimensional representation, but often some rotations and magnification are required to achieve the best visual perspective. The Shepard diagram plots ϕ_{ij} against δ_{ij} for a given value of d , and a narrow (large) scatter of points indicates a good (weak) fit between the original and the reproduced distances.

3 The dataset

The information of 133 publicly released genomic sequences was collected in the Global Initiative on Sharing Avian Influenza Data (GISAID) and the GenBank of the National Center for Biotechnology Information (NCBI) databases (<https://www.gisaid.org/>, <https://www.ncbi.nlm.nih.gov/genbank>). The information regarding the sequences and serial numbers is given in Table of “Appendix.”

The mathematical tools of Kolmogorov and Shannon theories are used to compare and extract relationships among the data and to identify viral genomic patterns. The viral genomes are analyzed from the perspective of dynamical systems using HC and MDS. Dendrograms and trees are generated by HC algorithms, and a three-dimensional visualization through MDS visualization. Several clusters with medical and epidemiological interest were visualized. The MDS loci provide a key visualization of the relation of SARS-CoV-2 with the other known coronavirus affecting humans.

The several non-coronavirus pathogenic viruses analyzed are very well delimited in several independent and easily delineated clusters (Zika, Chikungunya, Dengue, Lassa, Ebola, Influenza B).

The several types of coronaviruses that cause mild disease (common flu) are very well separated from the other coronavirus clusters. Interestingly, the types, 229E, HkU1, NL63 and OC43, form separated mini-clusters within a big well-defined cluster

There are two well-defined CoV-19 or SARS-CoV clusters. The two environmental SARS-CoV-2 were aggregated with the human SARS-CoV-2. To differentiate the human MERS-CoV, a zoom was made to isolate it forming a separate cluster. The MERS-CoV obtained from camels was included in this cluster. SARS-CoV formed another independent and well-segregated cluster. The CoV from bats and pangolin is

dispersed among these several clusters of coronavirus forming sometimes clusters of few elements. Note that the bat CoV RaTG13 is near to one of the SARS-CoV clusters. This coronavirus is the closest known relative of SARS-CoV-2 [79].

For processing the RNA information consisting of ASCII files with the four nitrogenous bases, we consider two approaches. The first one follows the Kolmogorov complexity theory described in Sect. 2.2. Therefore, we consider the compressors `zlib` and `bz2` (see <https://www.zlib.net> and <https://sourceware.org/bzip2/>) followed by the *NCD* distance (4). Nonetheless, the two algorithms give almost identical results, and therefore, only the `zlib` is considered in the follow-up.

The application of the *NCD* produces a symmetrical matrix A , 133×133 dimensional that is tackled and visualized by means of a dendrogram and a HC tree obtained by the program Phylip <http://evolution.genetics.washington.edu/phylip.html> and MDS using MATLAB <https://www.mathworks.com/products/matlab.html>. The corresponding charts are represented in Figs. 2, 3 and 4.

It is known that the three-dimensional plots require some rotation in the computer screen. Therefore, Fig. 5 shows the MDS locus in a different perspective, without point labels and the cluster of SARS-CoV-2 connected by a line.

The second approach follows the Shannon information theory described in Sect. 2.3. Therefore, we start by considering non-overlapping (codon or anticodon) triplets of bases and the histograms of relative frequency for each virus. In a second phase, after having the histogram for the complete set of virus, we process them using entropy concepts. Before continuing, we must clarify that we tested the adoption of n -tuples, with $n = 1, 2, 3, 4$, in the DNA information analysis of a large set of superior species such as mammals, where the genetic information is considerably larger and the construction of histograms for large values of n does not pose problems of statistical significance (since the number of histograms bins grows as 4^n). It was observed that $n = 3$ is a ‘good value,’ since $n = 1$ leads to poor results, $n = 2$ improves things but is still insufficient, while $n = 4$ gives almost identical results to $n = 3$.

In a first experiment, we consider the Shannon entropy H vs fractional cumulative residual entropy ε as possible descriptors of the 133 histograms. Figure 6

Fig. 2 Dendrogram for the set of 133 viruses using the *NCD* and *zlib* based on the Kolmogorov complexity theory

Fig. 3 HC tree for the set of 133 viruses using the *NCD* and *zlib* based on the Kolmogorov complexity theory

shows the resulting two-dimensional plot, that is, the Shannon entropy H vs the fractional cumulative residual entropy ε , for the set of 133 viruses. We observe some separation between virus, but we have some difficulties due to the high density of points in some areas.

We now try the other computational techniques introduced in Sect. 2. In the follow-up, we consider identical input information, that is, the *JDS* and the corresponding matrix Δ for the set of 133 viruses, and we compare the distinct computational clustering and visualization techniques.

Figures 7, 8 and 9 show the dendrogram, the HC tree and the three-dimensional MDS locus,

respectively. The dendrogram is the simplest representation and it is straightforward to interpret. However, this technique does not take full advantage of the space. The HC tree uses more efficiently the two-dimensional space, but we now have more difficulties in reading the most dense clusters. The three-dimensional MDS takes advantage of the computational representation, but requires some rotation/shift/magnification in the computer screen.

Successive magnifications can be done and are necessary to achieve a more distinct visualization. Therefore, we can say that all representations have their own pros and cons, although the three-dimensional MDS is, *a priori*, the most efficient method.

Fig. 4 MDS three-dimensional locus for the set of 133 viruses using the *NCD* and *zlib* based on the Kolmogorov complexity theory with the cluster of SARS-CoV-2 connected by a line

Since the three-dimensional plot requires some rotation in the computer screen, Fig. 10 shows the MDS locus in a different perspective, without point labels and the cluster of SARS-CoV-2 connected by a line.

The MDS 3D following the Kolmogorov method isolated the several groups of virus in several extended groups. The cluster of SARS-CoV-2 is very extended. Note that the SARS-CoV-2 virus found in the market of Wuhan is very near of the SARS-CoV-2 cluster. The CoV found in the pangolin also forms a cluster mixing with the upper part of the SARS-CoV-2 cluster. Bat CoV virus forms also a diffuse cluster lacking some contiguity. The bat CoV Yunnan

RaTG13 is very near the SARS-CoV-2 cluster. There is a big cluster formed by the different CoV that causes a mild respiratory disease (common cool).

Other pathogenic RNA virus clusters, i.e., Lassa virus, Zika, influenza B and Ebola, can be easily separated from the CoV clusters. However, with this methodology, the cluster formed by the dengue virus is not very far, in some views, from a part of the cluster formed by the CoV that causes mild respiratory disease.

The SARS CoV virus forms another independent cluster. MERS-CoV from humans forms another extended cluster and in the vicinity of the CoV virus from camel.

Fig. 5 MDS three-dimensional locus for the set of 133 viruses using the *NCD* and *zlib* based on the Kolmogorov complexity theory, without point labels and the cluster of SARS-CoV-2 connected by a line

4 Conclusions

This paper explored the information of 133 RNA viruses available in public databases. For that purpose, several mathematical and computational tools were applied. On the one hand, the concepts of distance and the theories developed by Kolmogorov and Shannon for assessing complexity and information were recalled. The first involved the normalized compression distance and the *zlib* compressor for the DNA. The second understood the use of histograms of triplets of bases and their assessment through entropy, cumulative residual entropy and Jensen–Shannon divergence. On the other hand, the advantages of hierarchical clustering and multidimensional scaling algorithmic techniques were also discussed. Representations in two and three dimensions, namely by

dendrograms and trees, and loci of points or points and lines, respectively, were compared. The results revealed their pros and cons for the specific application of the set of viruses under comparison.

The MDS 3D in the Kolmogorov perspective leads to be the best visualization method. We have not only the clusters easily distinguishable, but we find also the relation between the new SARS-CoV-2 virus and some CoV found in bats (the primary host of the virus) and in the pangolin, the likely intermediate host. The SARS-CoV-2 found in the environment, namely the Market of Wuhan where the epidemic probably started, is indistinguishable from the SARS-CoV-2 found in humans.

This type of methodology may help to study how an animal virus jumped the boundaries of species to infect humans, and pinpoint its origin, as this

Fig. 6 Shannon entropy H vs fractional cumulative residual entropy ε for the set of 133 viruses, with the cluster of SARS-CoV-2 connected by a line

knowledge can help to prevent future zoonotic events [80]. The statistical and computational techniques allow different perspectives over viral diseases that may be used to grasp the dynamics of the emerging COVID-19 disease. These methodologies [79] may

help interpreting future viral outbreaks and to provide additional information concerning these infectious agents and understand the dynamics of viral diseases.

Fig. 7 Dendrogram for the set of 133 viruses using the *JSD* based on the Shannon information theory

Fig. 8 HC tree for the set of 133 viruses using the *JSD* based on the Shannon information theory

Fig. 9 MDS three-dimensional locus for the set of 133 viruses using the *JSD* based on the Shannon information theory, with the cluster of SARS-CoV-2 connected by a line

Fig. 10 MDS three-dimensional locus for the set of 133 viruses using the *JSD* based on the Shannon information theory, without point labels and the cluster of SARS-CoV-2 connected by a line

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Appendix

i	Glyph	Bank	Serial No	Virus strain	Length
1	●	GISAID	NC_009019.1	Bat coronavirus HKU4-1, complete genome	40363
2	●	GISAID	NC_009020.1	Bat coronavirus HKU5-1, complete genome	40574
3	●	GISAID	NC_009021.1	Bat coronavirus HKU9-1, complete genome	38745
4	●	Genbank	EF065515.1	Bat coronavirus HKU9-3, complete genome	38280
5	●	Genbank	MN090332.1	Bat coronavirus Ra-TG13, complete genome	35066
6	●	Genbank	DQ022305.2	Bat SARS coronavirus HKU3-1, complete genome	38973
7	●	Genbank	GQ153539.1	Bat SARS coronavirus HKU3-4, complete genome	39129
8	●	Genbank	DQ071815.1	Bat SARS coronavirus Rps, complete genome	38954
9	●	Genbank	MG772933.1	Bat SARS-like coronavirus isolate bat-SL-CoVZC45, complete genome	39242
10	●	Genbank	MG772934.1	Bat SARS-like coronavirus isolate bat-SL-CoVZXC21, complete genome	39090
11	●	Genbank	MK211370.1	Coronavirus BtRs-BetaCoV YN2018A, complete genome	39034
12	●	Genbank	MK211370.1	Coronavirus BtRs-BetaCoV YN2018B, complete genome	39748
13	●	Genbank	MK211377.1	Coronavirus BtRs-BetaCoV YN2018C, complete genome	39024
14	●	Genbank	MK211379.1	Coronavirus BtRs-BetaCoV QX2018, complete genome	39104
15	●	Genbank	hCoV-19/bat/Yunnan/RaTG13/2013	hCoV-19 bat Yunnan RaTG13 2013	31517
16	●	Genbank	MN011518.1	Miniopterus pusillus bat coronavirus HKU8-related isolate 6610, complete genome	37726
17	●	Genbank	MN011524.1	Miniopterus schreibersii bat coronavirus I-related isolate 161454, complete genome	37175
18	●	Genbank	MN018261.1	Dengue virus 1 isolate D15121, complete genome	11602
19	●	Genbank	MN018285.1	Dengue virus 1 isolate D15446, complete genome	14623
20	●	Genbank	MN018288.1	Dengue virus 1 isolate D16001, complete genome	14622
21	●	Genbank	MK517775.1	Dengue virus 2 isolate BeAr84948, complete genome	14973
22	●	Genbank	MN018350.1	Dengue virus 2 isolate D16047, complete genome	14610
23	●	Genbank	MN018342.1	Dengue virus 2 isolate D17096, complete genome	14610
24	●	Genbank	MN018367.1	Dengue virus 3 isolate D15121, complete genome	14593
25	●	GISAID	CoV-19/Germany/NRW-15/2020	GISAID hCoV-19 Germany NRW-15 2020	31549
26	●	GISAID	CoV-19/USA/MN44-MDH44/2020	GISAID hCoV-19 USA MN44-MDH44 2020	31278
27	●	GISAID	CoV-19/Australia/NSW05/2020	hCoV-19 Australia NSW05 2020	31655
28	●	GISAID	CoV-19/Belgium/GHB-03021/2020	hCoV-19 Belgium GHB-03021 2020	31592
29	●	GISAID	CoV-19/France/BFC2709/2020	hCoV-19 France BFC2709 2020	31582
30	●	GISAID	CoV-19/France/IDF0571/2020	hCoV-19 France IDF0571 2020	31588
31	●	GISAID	CoV-19/France/IDF3218/2020	hCoV-19 France IDF3218 2020	31624
32	●	GISAID	CoV-19/Germany/Baden-Wuerttemberg-1/2020	hCoV-19 Germany Baden-Wuerttemberg-1 2020	31444
33	●	GISAID	CoV-19/Germany/BavPat1/2020	hCoV-19 Germany BavPat1 2020	31594
34	●	GISAID	CoV-19/Germany/BavPat2/2020	hCoV-19 Germany BavPat2 2020	31423
35	●	GISAID	CoV-19/Italy/CDGI/2020	hCoV-19 Italy CDGI 2020	31628
36	●	GISAID	CoV-19/Italy/FVG-ICGEB-S1/2020	hCoV-19 Italy FVG-ICGEB-S1 2020	31512
37	●	GISAID	CoV-19/Italy/INM7/2020	hCoV-19 Italy INM7 2020	31524
38	●	GISAID	CoV-19/Japan/TK-20-31-3/2020	hCoV-19 Japan TK-20-31-3 2020	31474
39	●	GISAID	CoV-19/Portugal/PT0020/2020	hCoV-19 Portugal PT0020 2020	31119
40	●	GISAID	CoV-19/Portugal/PT0036/2020	hCoV-19 Portugal PT0036 2020	31095
41	●	GISAID	CoV-19/Singapore/8/2020	hCoV-19 Singapore 8 2020	31346
42	●	GISAID	CoV-19/Spain/Madrid201709/2020	hCoV-19 Spain Madrid201709 2020	31535
43	●	GISAID	CoV-19/Spain/Madrid201738/2020	hCoV-19 Spain Madrid201738 2020	31535
44	●	GISAID	CoV-19/USA/WAS-UWS/2020	hCoV-19 USA WAS-UWS 2020	31666
45	●	GISAID	CoV-19/Vietnam/VRO3-38142/2020	hCoV-19 Vietnam VRO3-38142 2020	31685
46	●	Genbank	LC528233.1	SARS-CoV-2 Hu DP Kng 19-027 RNA	39343
47	●	Genbank	MT024521.1	Severe acute respiratory syndrome coronavirus 2 isolate 2019-nCoV USA-CSA 2020, complete genome	39469
48	●	Genbank	MT044257.1	Severe acute respiratory syndrome coronavirus 2 isolate 2019-nCoV USA-IL2 2020, complete genome	39444
49	●	Genbank	MT007544.1	Severe acute respiratory syndrome coronavirus 2 isolate Australia VIC01 2020, complete genome	39561
50	●	Genbank	MT135041.1	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2 105 human 2020 CHN, complete genome	39103
51	●	Genbank	MT135042.1	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2 231 human 2020 CHN, complete genome	39103
52	●	Genbank	MT135043.1	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2 233 human 2020 CHN, complete genome	39103
53	●	Genbank	MT135044.1	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2 235 human 2020 CHN, complete genome	39103
54	●	Genbank	MT123012.2	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2 IGTC92 human 2020 CHN, complete genome	39350
55	●	Genbank	MT126808.1	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2 SP02 human 2020 BRA, complete genome	39404
56	●	Genbank	MT093631.2	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2 WH-09 human 2020 CHN, complete genome	39413
57	●	Genbank	MT049051.1	Severe acute respiratory syndrome coronavirus 2 isolate SARS-CoV-2 Yunnan-01 human 2020 CHN, complete genome	39350
58	●	Genbank	MN966527.1	Severe acute respiratory syndrome coronavirus 2 isolate WIV02, complete genome	39652
59	●	Genbank	MN908947.3	Severe acute respiratory syndrome coronavirus 2 isolate Wuhan-Hu-1, complete genome	39684
60	●	Genbank	LC528233.1	Severe acute respiratory syndrome coronavirus 2 SARS-CoV-2 Hu DP Kng 19-027 RNA, complete genome	39343
61	●	Genbank	LC528233.1	V2 - Severe acute respiratory syndrome coronavirus 2 SARS-CoV-2 Hu DP Kng 19-027 RNA, complete genome	39343
62	●	GISAID	CoV-19/pangolin/Guangxi/P1E/2017	GISAID hCoV-19 pangolin Guangxi P1E 2017	31503
63	●	GISAID	CoV-19/pangolin/Guangxi/P4L/2017	GISAID hCoV-19 pangolin Guangxi P4L 2017	31522
64	●	GISAID	CoV-19/pangolin/Guangxi/P5L/2017	GISAID hCoV-19 pangolin Guangxi P5L 2017	31503
65	●	GISAID	CoV-19/pangolin/Guangdong/1/2019	hCoV-19 pangolin Guangdong 1 2019	31331
66	●	GISAID	CoV-19/pangolin/Guangxi/P1E/2017	hCoV-19 pangolin Guangxi P1E 2017	31503
67	●	GISAID	CoV-19/pangolin/Guangxi/P2V/2017	hCoV-19 pangolin Guangxi P2V 2017	31506
68	●	GISAID	CoV-19/pangolin/Guangxi/P5E/2017	hCoV-19 pangolin Guangxi P5E 2017	31507
69	●	GISAID	CoV-19/pangolin/Guangxi/P5L/2017	hCoV-19 pangolin Guangxi P5L 2017	31503
70	●	Genbank	JX503060.1	Human coronavirus 229E isolate 0349, complete genome	35849
71	●	Genbank	KU291448.1	Human coronavirus 229E isolate HCoV-229E BNI GER 2015, complete genome	35834
72	●	Genbank	JX503061.1	Human coronavirus 229E isolate J0304, complete genome	35811
73	●	Genbank	KT770556.1	Human coronavirus HKU1 isolate BJ01-p9, complete genome	39065
74	●	Genbank	KT770556.1	Human coronavirus HKU1 isolate BJ01-p9, complete genome	39065
75	●	Genbank	HM034837.1	Human coronavirus HKU1 isolate Caen1, complete genome	39247
76	●	Genbank	HM040245.1	Human coronavirus HKU1 isolate SH7244, complete genome	39064
77	●	Genbank	DQ445911.1	Human coronavirus NL63 isolate Amsterdam 057, complete genome	36080
78	●	Genbank	DQ445912.1	Human coronavirus NL63 isolate Amsterdam 496, complete genome	36080
79	●	Genbank	MG772808.1	Human coronavirus NL63 isolate CN0601 14, complete genome	36105
80	●	Genbank	MG772808.1	Human coronavirus NL63 isolate KHH-HH-3808-24-May-2019, complete genome	36105
81	●	Genbank	JX504050.1	Human coronavirus NL63 isolate NL63 RPTEC 2004, complete genome	36498
82	●	Genbank	KU521535.1	Human coronavirus NL63 isolate NL63 UF 2 2015, complete genome	36469
83	●	Genbank	KY142829.1	Human coronavirus OC43 isolate 2007-09, complete genome	40259
84	●	Genbank	KF923888.1	Human coronavirus OC43 isolate 2145A 2010, complete genome	40259
85	●	Genbank	KF923894.1	Human coronavirus OC43 isolate 5552 2007, complete genome	40002
86	●	Genbank	MH121431.1	Human coronavirus OC43 isolate HCoV-OC43 ACRI-0213 2016, complete genome	40143
87	●	Genbank	KX344031.1	Human coronavirus OC43 isolate LRT1-238, complete genome	40766
88	●	Genbank	MK303625.1	Human coronavirus OC43 isolate MDS16, complete genome	40521
89	●	Genbank	KX338978.1	Human coronavirus OC43 isolate MY-U1753 13, complete genome	40438
90	●	Genbank	KX338979.1	Human coronavirus OC43 isolate MY-U1753 13, complete genome	40438
91	●	Genbank	MN026164.1	Human coronavirus OC43 isolate OC43-KLFJ01-2018, complete genome	40318
92	●	Genbank	MG977452.1	Human coronavirus OC43 isolate TNP 12643, complete genome	40435
93	●	Genbank	MG812630.1	Lassa marnarenavirus isolate 80787 segment L Z protein and L protein genes, complete cds	10456
94	●	Genbank	MH215284.1	Lassa marnarenavirus isolate LF18040 segment L Z protein and L protein genes, complete cds	10635
95	●	Genbank	MH215286.1	Lassa marnarenavirus isolate LF18041 segment L Z protein and L protein genes, complete cds	10503
96	●	Genbank	MH215288.1	Lassa marnarenavirus isolate LF18042 segment L Z protein and L protein genes, complete cds	10578
97	●	Genbank	KU961072.2	Lassa marnarenavirus isolate Topo 2016 7082 segment L, complete sequence	11444
98	●	Genbank	KM822131.1	Lassa virus strain Z0948-SLE-2011 segment L Z protein (Z) and polymerase (L) genes, complete cds	11072
99	●	Genbank	AY278487.3	SARS coronavirus B202, complete genome	40147
100	●	Genbank	AY864806.1	SARS coronavirus B202, complete genome	38014
101	●	Genbank	FJ829296.1	SARS coronavirus ExoN1, complete genome	39417
102	●	Genbank	AY278489.2	SARS coronavirus GD01, complete genome	40231
103	●	Genbank	JN854286.1	SARS coronavirus HKU-39849 isolate recSARS-CoV HKU-39849, complete genome	39012
104	●	Genbank	DQ498174.1	SARS coronavirus strain CVT, complete genome	39044
105	●	Genbank	AY304488.1	SARS coronavirus SZ16, complete genome	38971
106	●	Genbank	AY338174.1	SARS coronavirus Taiwan TC1, complete genome	39157
107	●	Genbank	AY394850.2	SARS coronavirus WHU, complete genome	39504
108	●	Genbank	AY274110.3	Severe acute respiratory syndrome-related coronavirus isolate Tor2, complete genome	40174
109	●	Genbank	MK731985.1	Zaire ebolavirus isolate Ebola virus H.sapiens-wt COD 2018 BEN163-MANA12-13, complete genome	26795
110	●	Genbank	MK731986.1	Zaire ebolavirus isolate Ebola virus H.sapiens-wt COD 2018 BEN163-MANA12-16, complete genome	26937
111	●	Genbank	MK731987.1	Zaire ebolavirus isolate Ebola virus H.sapiens-wt COD 2018 BEN164-MANA1-11, complete genome	26918
112	●	Genbank	MK731988.1	Zaire ebolavirus isolate Ebola virus H.sapiens-wt COD 2018 BEN164-MANA1-13, complete genome	26803
113	●	Genbank	MK731989.1	Zaire ebolavirus isolate Ebola virus H.sapiens-wt COD 2018 BEN164-MANA1-163, complete genome	26797
114	●	Genbank	MK731990.1	Zaire ebolavirus isolate Ebola virus H.sapiens-wt COD 2018 BEN164-MANA1-17, complete genome	26973
115	●	Genbank	KX030139.1	Middle East respiratory syndrome coronavirus isolate MERS-CoV KOR KKH-17, complete genome	39991
116	●	Genbank	KX030494.1	Middle East respiratory syndrome coronavirus isolate MERS-CoV KOR Seoul 050-1-2015, complete genome	39809
117	●	Genbank	KX030496.1	Middle East respiratory syndrome coronavirus isolate MERS-CoV KOR Seoul 077-2-2015, complete genome	39777
118	●	Genbank	KX030497.1	Middle East respiratory syndrome coronavirus isolate MERS-CoV KOR Seoul 080-3-2015, complete genome	39816
119	●	Genbank	KX030498.1	Middle East respiratory syndrome coronavirus isolate MERS-CoV KOR Seoul 162-1-2015, complete genome	39804
120	●	Genbank	KX030499.1	Middle East respiratory syndrome coronavirus isolate MERS-CoV KOR Seoul 169-2015, complete genome	39805
121	●	Genbank	KX030500.1	Middle East respiratory syndrome coronavirus isolate MERS-CoV KOR Seoul 177-3-2015, complete genome	39816
122	●	Genbank	KX030495.1	Middle East respiratory syndrome coronavirus isolate MERS-CoV KOR Seoul066-2015, complete genome	39813
123	●	Genbank	KT225476.2	Middle East respiratory syndrome coronavirus isolate MERS-CoV THA CU 17.06.2015, complete genome	40317
124	●	Genbank	KF958702.1	Middle East respiratory syndrome coronavirus isolate MERS-CoV Jeddah-human-1, complete genome	39441
125	●	Genbank	KJ477102.1	Middle East respiratory syndrome coronavirus, complete genome	39468
126	●	Genbank	KU740200.1	Middle East respiratory syndrome coronavirus isolate MERS CoV camel Egypt NRCE-NC163 2014, partial genome	39882
127	●	Genbank	KF917527.1	Middle East respiratory syndrome coronavirus isolate MERS-CoV Jeddah-Camel-1, complete genome	39441
128	●	GISAID	CoV-19/Wuhan/IVDC-HB-envF13-20/2020	GISAID sea food market hCoV-19 Wuhan IVDC-HB-envF13-20 2020	31664
129	●	GISAID	CoV-19/Wuhan/IVDC-HB-envF13-21/2020	GISAID sea food market hCoV-19 Wuhan IVDC-HB-envF13-21 2020	31655
130	●	Genbank	MT048815.1	Influenza B virus (B Arizona 2019) segment 1 polymerase PB1 (PB1) gene, complete cds	5047
131	●	Genbank	MT048817.1	Influenza B virus (B California 77) segment 1 polymerase PB1 (PB1) gene, complete cds	4893
132	●	Genbank	EU037962.1	Chikungunya virus Wuerzburg 1, complete genome	16542
133	●	Genbank	KX893855.1	Zika virus strain Zika virus Homo sapiens VEN UF-2 2016 complete genome	15782

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