Genetic Phase Angle Distance (GPAD)

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Abstract

It is hypothesized that a mapping of the biochemical properties of genetic nucleotides into the three dimensional $\mathbb{R}_3$ Clifford algebra will yield a novel and meaningful evolutionary distance measure. The nucleotides A,T,C,G are mapped according to three biochemical properties (amino/keto, purine/pyrimidine, weak/strong), resulting in four base-vectors. A weighted linear combination of the base-vectors as codon triplets results in a "Tetrahedral Genetic Code" (TGC), where all 64 codons map to 64 unique codon-vectors in the space. Phase distance θ is measured as the angle between sequentially neighboring codon-vectors, and a sequence of codons is measured as the total path length in radians of the vector as it traverses the TGC. Angular difference $\Delta\theta$ is computed as the absolute value of the difference in phase θ between sequences, at homologous loci. The Genetic Phase Angle Distance (GPAD) is computed as the $\Delta\theta$ mean. GPAD is computed on a sample sequence matrix for 11 different species and compared side by side to the Equal-input distance and phylogenetic tree computed on that same species matrix.

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I. Introduction

There has been a growing discontent in the fringes of the Biosciences concerning the erroneous emphasis of its methodologies upon the *discrete information* contained within the genome. There is call for a more explicit study of the different kinds of representations that can exist in biology vis-a-vis complex dynamical systems. Beyond the observables known from physics, there is a need for new observables in biology that will increase its intelligibility and facilitate the quantification of *collective* biological organization. (Bailly & Longo, 2009; Longo, Miquel, Sonnenschein, & Soto, 2012; Rocha & Hordijk; Simeonov, 2010) In this paper I will present a novel method of deriving molecular evolutionary distances via a three dimensional representation of the genetic code, and argue the validity of a unique subjective ontology which might be observed at the level of molecular biology.

Over the past decade, a number of new methods of genomic analysis have been introduced. The fractal properties of DNA (Cattani, 2010), the ability to generate linguistic statements from its codons (Lee et al., 2011), and the application of quantum algorithms to the genetic code (Patel, 2001; Rieper, Anders, & Vedral, 2010) emphasize the *interactions* between molecules, rather than treating a single base as an individual unit of information. Current evidence indicates that genomes are complex landscapes defined by physical structures and forces of extremely long range which can appropriately be considered another level of genetic coding. (Mauger, Siegfried, & Weeks, 2013; Melkikh, 2013) In particular, genomic signal processing (Chheda, 2012) involves a reconceptualization of biological information, as much as it offers new and interesting methods of accessing its content. The signal analytic genomic model and measure presented in this work are called the Tetrahedral Genetic Code (TGC) and Genetic Phase Angle Distance (GPAD), respectively.

II. An Imaginary Science

To begin, it must be acknowledged that the established methods of molecular biology, and specifically the genetic code, are practically irrefutable. Nevertheless, while the triplet genetic code is the most common lookup table used to decode genomic information, the elegance of the three letter genetic code has often focused analysis of the human genome on the *sequence* of nucleotides, neglecting the possibility of additional codes in the genome both within and outside the coding regions. (Parker & Tullius, 2011; Robins, Krasnitz, & Levine, 2008) This can be compared to the dangerously misleading ball-and-stick models of chemistry, with which we tend to assume that the actual bonding phenomenon is concentrated along those very lines. A molecule is not a hard and rigid object, but rather, a dense bundle of energy characterized by smoothness and dynamics. (Hyde, 1997) Similarly, the cell is not a computer, indifferent to the sequence data it processes. The genome is fundamentally different: its states depend upon its knowledge content. (Stern, 2000)

A simple and effective way to gain insight into the collective nature of biological information is to extend it metaphorically into more recent models of physics and the mathematics of complexity. Whereas in physics we may wonder, “can one hear the shape of a drum?” (Kac, 1966), in biology we might ask if the cell can “hear” the shape of a protein. In (Brown, 1972), we are reminded that a mathematical description of cellular activity might be compared with a practical art form like cookery, in which the taste of a cake (protein shape), although literally indescribable, can be conveyed to a reader in the form of a set of injunctions called a recipe (an amino acid sequence). In both cases, we arrive at a qualitative, rather than quantitative, description which is characteristic of systems thinking – from objects to relationships. (Capra, 1996)

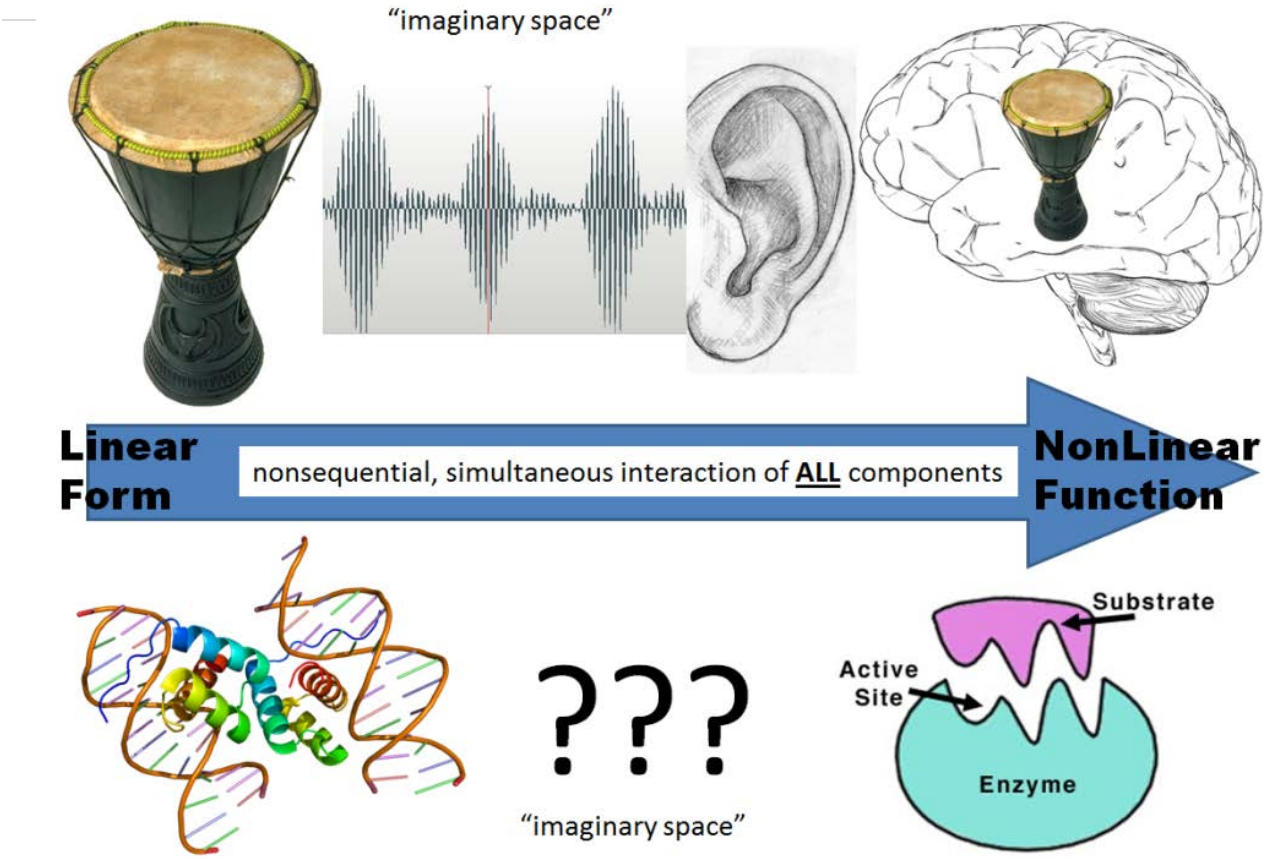


Figure 1: Biological information is mediated through the immediate ontological experience of the observer with the observed.

The drum metaphor is of particular interest as an introduction to, and justification of, the signal processing techniques used in computation of the TGC and GPAD. In Figure 1 we see a comparison of the re-creation of the form of a drum in the mind of a listener, to the generation of a functional enzyme from its discrete sequence. The physical drum is composed of many elements which can be taken apart and analyzed reductively. One can also analyze the collection of all the parts as a single unit and attempt to infer, laboriously, the role that each part contributes to the overall tonal quality of the drum. Or, as a better alternative, we may just strike the drum and take a listen. By permitting a relationship between the observer and the observed, we can at once, and with little effort, extrapolate the component parts such as the material of construction and the tautness of the head; more importantly, we can assign a sonic function to the drum, as if it were a member of an orchestra.

Considering these two methods of drum analysis, we can see immediately that an attempt to understand the function of the drum from a reductionist point of view is futile. Even if we manage, by some major effort, to model the drum as a collection (of parts), we will gain very little knowledge of its timbre. Likewise, it is common knowledge that the derivation of protein shape via amino acid sequence is nearly intractable. It is tempting to consider that there might exist some mediator of protein from form to function as a direct, subjective, sensational experience. That the cellular environment and molecular structures are capable of supporting this type of behavior through a quantum interpretation of biology is becoming increasingly supported in the literature. (Plankar, Brežan, & Jerman, 2013; Rieper et al., 2010; Rowlands, 2007) How to mold the measure of a molecular "experience" into the form of a science is the central question in the transition from bioinformatics to biosemiotics.

III. The Mathematics of Complex Signals

The mathematics of complexity is one of relationships and patterns. Complexity in the natural world is manifested through implicit and explicit order. The implicit order can be encoded in 'hidden variables' that enable semantic enfolding and unfolding in the formal world. (Bohm, 1952) Looking again at Figure 1, the physical drum is explicit, its mental recreation is implicit, and the "encoded hidden variables" are represented by the complex waveform that lies between them.

In terms of genomics, the distinguishing biochemical properties of DNA nucleotides can encode three overlapping modes of discrete computation simultaneously: each nucleotide can be described as a purine or pyrimidine, as containing an amino or keto group, and by having either two or three hydrogen bond pairings with its complimentary base. Thus the explicit order, a single structural change within a DNA strand, can be described by three different characteristics

at once. It is through the formal superposition of these variables in an abstract mathematical space called a "phase space", that we hope to find, in the experiment to follow, an implicit order of the genetic sequences. The three nucleotide characteristics are represented by independent coordinates in three dimensions of the phase space. Thus, a single point in the space describes the simultaneous state ("taste") of the entire system. (Capra, 1996) In this way, we transform the genetic sequence into a signal like unto the complex sonic waveform of the drum. From there, we may treat the waveform via a plethora of computational techniques which have already been used extensively and with significant success in bioinformatics, including such tools as hidden Markov models and neural networks, the discrete Fourier transform (DFT), FIR digital filtering, wavelets, and spectrograms. (Anastassiou, 2001) The techniques used in the computation of the TGC and GPAD are founded upon the work of (Cristea, 2005). Similar analytical methods can be found in (Brodzik & Peters, 2005), the dyadic and Hadamard genomatrices of (Petoukhov, 2010), and in (Rowlands, 2007) genetic formulation of the Dirac nilpotent algebra.

IV. Computational Framework

The tetrahedral genetic code (TGC) was computed and rendered using the *Mathematica* package 'clifford.m' which implements general operations of a Clifford algebra on the language of the computer algebra program *Mathematica,* and has been enriched with functions to draw multivectors in $\mathbb{R}_3$. (Aragon-Camarasa, Aragon-Gonzalez, Aragon, & Rodriguez-Andrade, 2008) The package 'clifford.m', a user guide, a palette with the most common predefined functions, the notebook with the calculations by (Zhang, Zhu, Peng, & Chen, 2006), as well as the explicit Mathematica code for all calculations in this experiment are available for download (see Appendix B).

A vector has a length (scalar value) and direction, which we can represent as a directed line segment in 3D; it can stem from the origin of a Euclidean coordinates system and move to a point in three dimensions. Geometric algebra has four basic computing elements in 3D physical space: scalar, vector, bivector, and trivector. Linear compositions of geometric algebra's basic computing elements are called multivectors, and are denoted by uppercase Latin letters, such as **A**, **B**, and **C**. We use the term *k*-vector to denote a *k*-dimensional subspace, which is formed from the outer product of vectors. For any *k*-vector $\mathbf{A}_k$, when $k = 0, 1, 2,$ or 3, $\mathbf{A}_k$ represents a scalar, vector, bivector, or trivector, respectively. (Zhang et al., 2006)

Nucleotide and Codon Mappings

All elements of the TGC will be represented by 1-vectors: $\mathbf{A}_1$, $\mathbf{T}_1$, $\mathbf{G}_1$, $\mathbf{C}_1$; where each symbol is the first letter of the respective genetic nucleotide Adenine, Thymine, Guanine, or Cytosine. In *Mathematica* code, we denote the j-th basis vector as e_j. Accordingly, the $\mathbb{R}_3$ geometric algebra basis vectors are e_1, e_2, and e_3. The four nucleotides are mapped as:

$$\mathbf{A}_1 = e_1 + e_2 + e_3$$
$$\mathbf{T}_1 = e_1 - e_2 - e_3$$
$$\mathbf{G}_1 = -e_1 - e_2 + e_3$$
$$\mathbf{C}_1 = -e_1 + e_2 - e_3$$

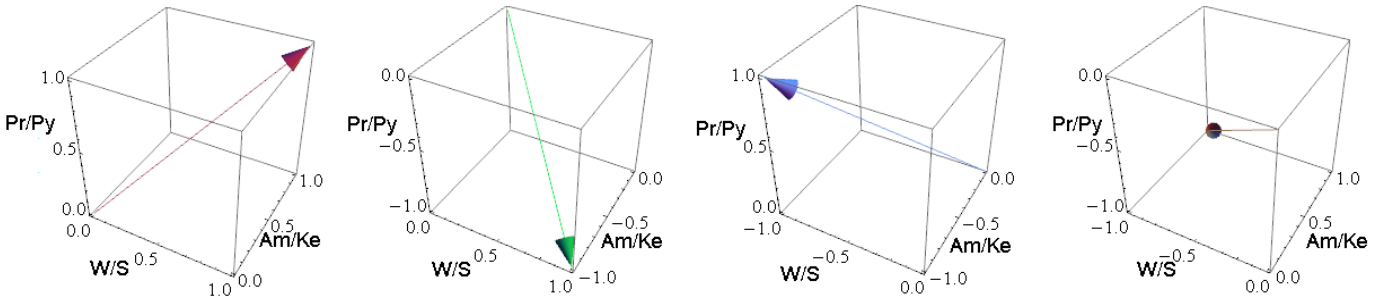


Figure 2: Nucleotides are mapped into a complex vector space, as represented in Mathematica using 'clifford.m' (Aragon, 2008).

The sign values play the important role of distinguishing the three specific biochemical characteristics (one on each axis) associated with each nucleotide. For e_1, a positive sign indicates that the base has a 'weak' 2-hydrogen bond pairing with its compliment in the opposite strand; a negative sign indicates a 'strong' 3-hydrogen bond pairing. Similarly along e_2, positive values indicate a nucleotide with an amino group and negative values give a nucleotide with a keto group. Finally, in e_3 the positive and negative signs represent the purines and pyrimidines, respectively. The nucleotide 3-D mappings are visualized in Figure 2.

The mapping of a codon from the standard genetic code into the vector space is accomplished as a weighted, linear combination of its three vector nucleotide components, resulting in a composite vector. Given a protein-coding sequence, each codon is decomposed into its first, second and third elements; the first nucleotide is denoted by α, the second by β, and the third by γ. Following, each vector is given a multiplicative weighting factor according to its relative importance (due to degeneracy) in determining the codon's resultant amino acid. Given a sequence containing N number of codon triplets, the codon-vector sequence is defined as

$$\delta_n(\{\{\alpha_n,\beta_n,\gamma_n\},\{\ldots\},\{\alpha_N,\beta_N,\gamma_N\}\}) \rightarrow \{\{4\alpha_n + 2\beta_n + \gamma_n\},\{\ldots\},\{4\alpha_N + 2\beta_N + \gamma_N\}\},$$
$$(n = 1, 2, \ldots., N;\ \alpha, \beta, \gamma \in \{\mathbf{A}_1, \mathbf{T}_1, \mathbf{G}_1, \mathbf{C}_1\})$$

An ordered mapping of all 64 genetic codons into the vector space yields 64 unique vectors, and is visualized as tetrahedral in shape. Taken all at once, the genetic code, mapped as the TGC, is shown in Figure 3. The tetrahedral representation expresses the symmetry and degeneration of the genetic code; generates mappings of nucleotide, codon and amino acid sequences into genomic signals; and translates multiple modes of biochemical properties into a single, simultaneous, signal property. Codons corresponding to the same amino acid are mapped to neighboring points within the tetrahedron, i.e., related codons are clustered. The complex

mappings cluster the multiple representations of the same amino acid in contiguous regions of the space. (Cristea, 2003)

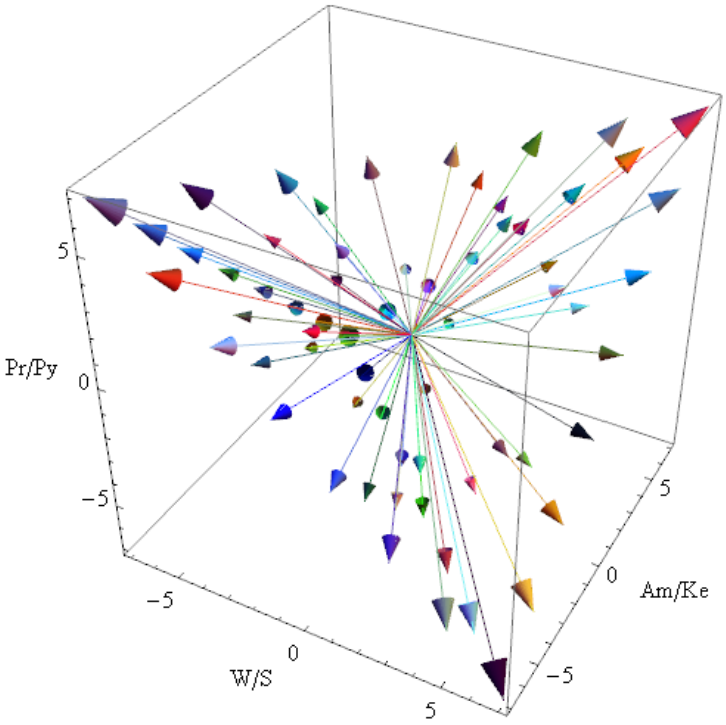


Figure 3: 64 codons map to 64 unique vector positions resulting in a tetrahedral genetic code.

Genetic Phase Angle Distance

For any two consecutive codon-vectors, $\delta_i(\{\alpha_i, \beta_i, \gamma_i\})$ and $\delta_j(\{\alpha_j, \beta_j, \gamma_j\})$, let $\theta_{(i,j)}$ be the angle between them. For N=64 unique elements of the TGC, there exist $\frac{64^2}{2}$ possible $\theta_{(i,j)}$. The two-dimensional matrix of all ordered combinations between pairs of codon-vectors is a finite field of $\theta_{(NxN)}$. If each position of the resulting matrix is assigned a color and intensity requisite to the value of its measured angle, a fractal-like pattern with interesting symmetries emerges (Figure 4).

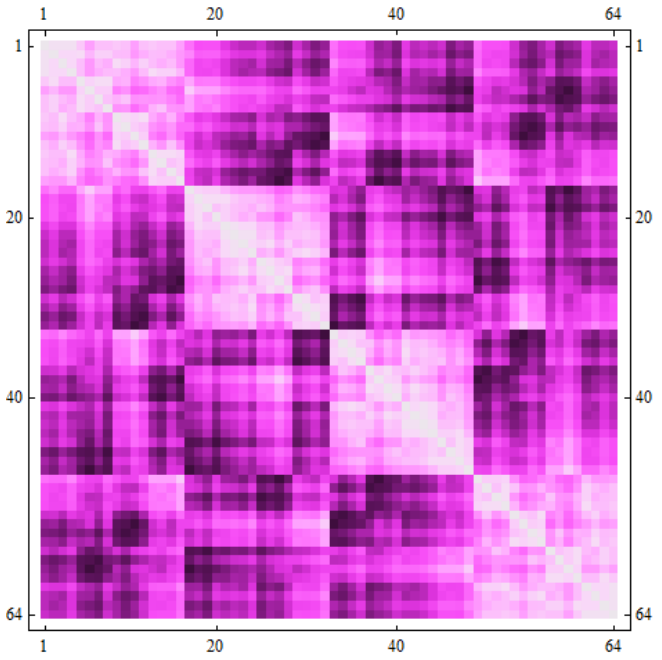


Figure 4: A matrix of all possible values of θ (small θ→light, large θ→dark).

Any given protein-coding sequence can be plotted linearly as a path within the finite $\theta_{(NxN)}$ matrix; or more simply, a genetic sequence mapped into the TGC is the smooth path on the surface of a sphere which is drawn

as a result of a vector traversing the sequential codon-vector positions. This sequential path of angles is then transferred to a Cartesian plot with phase angle (in radians) on the y-axis and time (in arbitrary units) on the x-axis. The θ sequence paths of the first exon of the β-globin gene for the two species Human and Gallus is shown in Figure 5. Also shown in the figure is the immediate precursor of the Genetic Phase Angle Distance (GPAD) measure, Δθ, defined as the absolute value of the difference between the two sequence paths. This measure will be used in the following section in an attempt to derive evolutionary distances between a number of distantly related species.

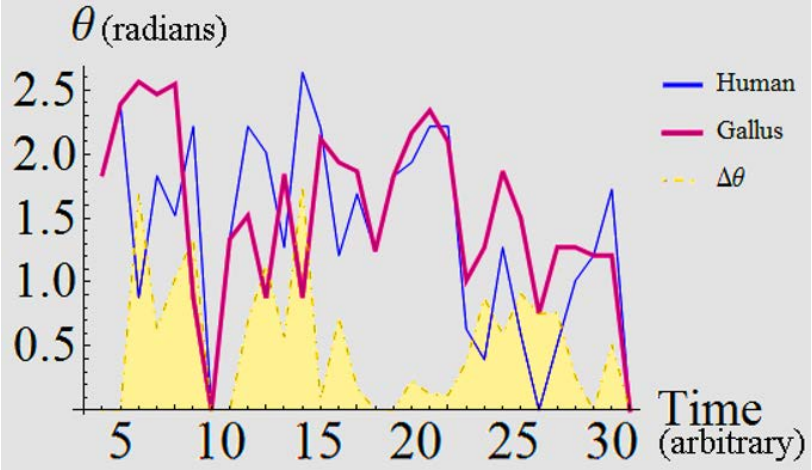


Figure 5: θ and Δθ sequence plots of the first exon of the β-globin gene for Human and Gallus.

V. Experimental Setup and Results

An initial test of the validity of the GPAD was conducted by taking the measure over a sample set of genetic sequences, and making a direct comparison to an established distance measure over that same sample set. The sequences for the β-subunit of hemoglobin for eleven different species were located using (Jafarzadeh & Iranmanesh, 2013), and confirmed by BLAST (Altschul, 1997). The curated sequences were then imported into the MEGA5 software (Tamura et al., 2011) and an alignment was performed using the MUSCLE algorithm (Edgar, 2004). It should be noted that a major drawback of the current GPAD computational framework is the inability to properly handle indel mutations. Because the framework is set up as a direct mapping from pairs of codon-vectors to their corresponding angle measure, any gap-containing

alignment (example: {A,-,G}) will not receive coordinates in the vector space. Rather, gap-containing triplets are mapped to the origin (zero). For this reason, the sequence and alignment parameters were selected with the primary goal of limiting the effect of indel mutations. Table 1 (Appendix A) gives the eleven aligned β-globin sequences under examination.

The procedure for transformation of the eleven genetic sequences into TGC θ and Δθ sequence paths was performed as outlined in the previous section, resulting in an ($i_x j_x k$) matrix where i and j represent the ordered combinations of all species in the sample set, and k is the Δθ sequence between the ith and jth species. The ($i_x j_x k$) matrix is then reduced to ($i_x j$) by taking the mean angular distance within each Δθ path, resulting in a single value at every position of the square matrix. This final procedure is formalized, and an example given, in Figure 6.

The GPAD matrix was compared to a set of sixteen standardized distance measures by taking the difference of matrices $\frac{2}{N^2}\Sigma\Sigma\left|\boldsymbol{a}_{(i,j)} - \boldsymbol{b}_{(i,j)}\right|$, resulting in a measure of variance between them. Table 2 gives the results of this similarity test, revealing a significant match between GPAD and the 'Equal-input' model (Tamura et al., 2011). The GPAD matrix for all eleven species, along with a representation of its values according to relative color and intensity, is shown in the upper section of Figure 7. For direct comparison, a second matrix was constructed with the same aligned sequences using the Equal input model, shown in the lower half of the figure.

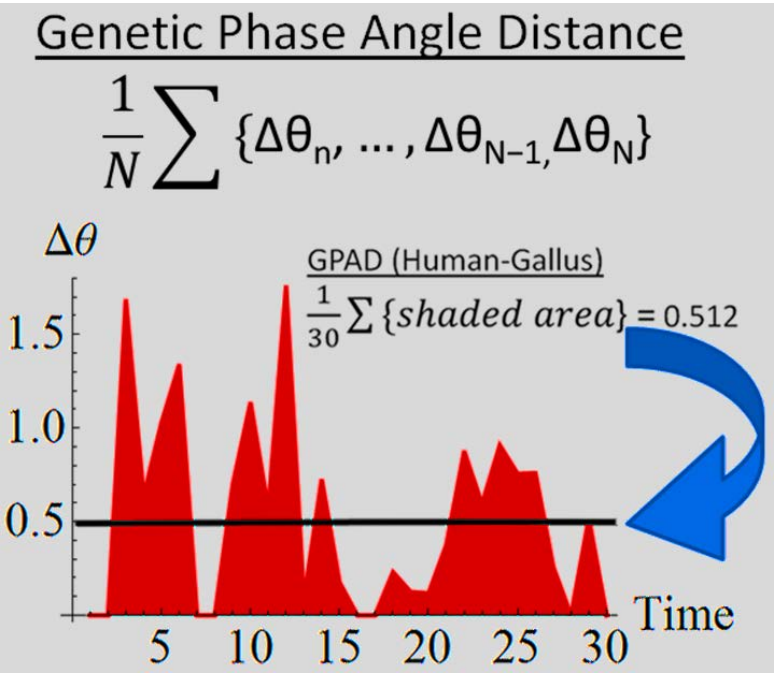
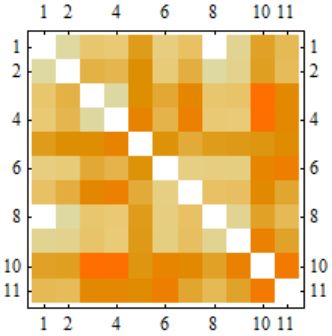


Figure 6: GPAD is calculated as the normalized mean Δθ between two homologous protein-coding sequences.

A second experiment was conducted in order to further explore the similarity between the GPAD and Equal-input models. The mean θ sequence path between all eleven species, and the Δθ and GPAD of each species sequence against that mean were computed. A phylogenetic tree, rooted to Gallus, was computed on the species matrix using the following settings: UPGMA, Equal-input model, neighbor-joining, bootstrap replications: 500, uniform rates among sites. These additional GPAD-distance-from-mean values and phylogenetic analysis are shown in Figure 8.

	Distance Model	Variance
aa sub.	Equal input	0.100
	Poisson	0.101
	JTT	0.105
	Dayhoff	0.105
	Dayhoff-G	0.106
	JTT-G	0.108
	p-distance	0.142
nucleotide sub.	LogDet	0.154
	Tajima-Nei	0.159
	Tamura-Nei	0.159
	Max Likelihood	0.159
	JC+G	0.160
	Tamura3	0.167
	kimura2	0.168
	jukes-cantor	0.169
	p-distance	0.214

Table 2: difference of matrices between GPAD and sixteen standardized distance measures.




```
{{0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
 {0.046, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
 {0.413, 0.459, 0, 0, 0, 0, 0, 0, 0, 0, 0},
 {0.402, 0.449, 0.054, 0, 0, 0, 0, 0, 0, 0, 0},
 {0.512, 0.558, 0.562, 0.616, 0, 0, 0, 0, 0, 0, 0},
 {0.344, 0.391, 0.491, 0.457, 0.55, 0, 0, 0, 0, 0, 0},
 {0.422, 0.468, 0.603, 0.627, 0.483, 0.336, 0, 0, 0, 0, 0},
 {0.000, 0.046, 0.413, 0.402, 0.512, 0.344, 0.422, 0, 0, 0, 0},
 {0.176, 0.222, 0.415, 0.395, 0.516, 0.341, 0.423, 0.176, 0, 0, 0},
 {0.500, 0.503, 0.877, 0.852, 0.526, 0.607, 0.589, 0.500, 0.624, 0, 0},
 {0.442, 0.440, 0.599, 0.601, 0.578, 0.653, 0.493, 0.442, 0.497, 0.693, 0}},
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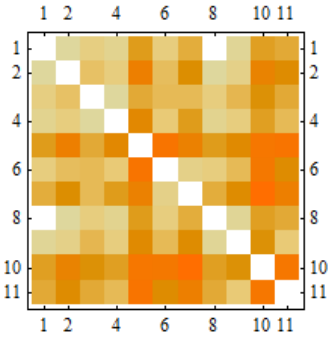


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{{0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
 {0.074, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
 {0.241, 0.336, 0, 0, 0, 0, 0, 0, 0, 0, 0},
 {0.156, 0.245, 0.074, 0, 0, 0, 0, 0, 0, 0, 0},
 {0.455, 0.581, 0.398, 0.518, 0, 0, 0, 0, 0, 0, 0},
 {0.245, 0.343, 0.344, 0.293, 0.651, 0, 0, 0, 0, 0, 0},
 {0.397, 0.515, 0.344, 0.455, 0.580, 0.199, 0, 0, 0, 0, 0},
 {0.000, 0.074, 0.245, 0.156, 0.455, 0.245, 0.397, 0, 0, 0, 0},
 {0.114, 0.199, 0.345, 0.245, 0.517, 0.344, 0.516, 0.114, 0, 0, 0},
 {0.453, 0.578, 0.514, 0.453, 0.647, 0.646, 0.721, 0.453, 0.514, 0, 0},
 {0.398, 0.516, 0.398, 0.344, 0.651, 0.516, 0.581, 0.398, 0.293, 0.647, 0}}
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Figure 7: Side by side comparison of sequences from Table XX using distance measures: GPAD (upper) and Equal input model (lower).

VI. Discussion/Conclusion

The Tetrahedral Genetic Code is a projection of multiple modes of nucleotide biochemical information into a complex phase space, represented by the $\mathbb{R}_3$ Clifford geometric algebra. A genetic sequence of triplet codons mapped into this space can be thought of as the path on the surface of a sphere correlating to the motion of angular transitions between consecutive codon-vectors. Any two homologous coding sequences can plotted as a function of angular distance (radians) in time, and the positive difference between their paths is interpreted as a distance of molecular evolution. The GPAD is the mean score of this difference.

It is difficult to quantify the accuracy and utility of the GPAD due to the small size of the experimental sample set and sequence length. Nevertheless, even a quick subjective assessment of the results leaves little doubt that GPAD is at least as effective a measure of evolutionary distance as many of the distance measures currently in regular use. The figure with the colored matrices shows quite plainly that the two data sets follow the same overall trend; and closer inspection of the numerical values reveals that in many cases, those values are in the same neighborhood. As noted in Table 2, the average variance between the two matrices in the figure is 0.1, meaning that the two measures are indeed quite similar. Also of note in that table is the segregation of amino-acid and nucleotide substitution models, with amino-acid substitution faring better in all cases. It is supposed that this is due to the fact that GPAD is also based to some degree on amino-acid substitution.

The phylogenetic analysis in Figure 8 shows the peculiar correspondence of the Equal-input lineage to the increasing order of species GPAD-distance-from-mean scores. As shown in better detail in Figure 9 (Appendix A), the mean θ path most closely resembles the most recent sequence, human, while the most distant sequence, opossum, has the widest variation from the

mean. Other than the interchange of the goat/bovine and mouse/rat branches, the two lists fall into an identical ordering. This additional information lends support to the similarity of GPAD to the Equal-input model. However, because the distance-from-mean approach is an atypical assessment of inheritance, it is unclear if the similarity in ordering is coincidental, if it is also observed in the standard models, or if it is detecting some central tendency or attraction via the mechanisms of evolution toward some 'optimal' amino-acid sequence, represented by the mean θ path. It will be interesting to see, in future study, if the GPAD-distance-from-mean continues to exhibit this unexpected property.

human	gorilla	chimpanzee	rabbit	mouse	rat	bovine	goat	lemur	gallus	opossum
0.233	0.233	0.265	0.280	0.337	0.348	0.387	0.391	0.412	0.420	0.524

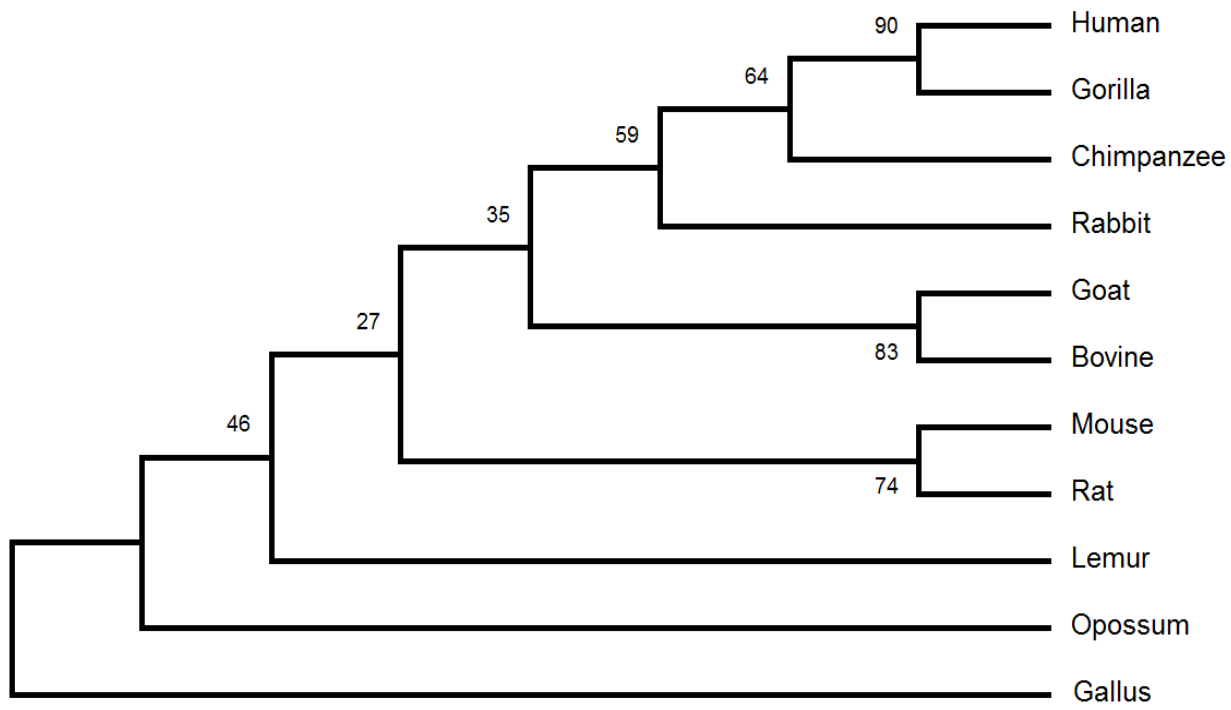

Figure 8: A table of GPAD-distance-from-mean scores, compared to phylogenetic analysis (boostrap consensus values at branch points).

What is particularly interesting about the mean θ path is that it does not represent some explicit genetic sequence, but rather, it represents a relative configuration of the *relationships between* codons. In other words, for any given path, there exist many codon sequences that will satisfy its angular distance relationships. There is no stipulation in the GPAD for origination or direction of travel through the three dimensional vector space: its only measure is angle. It is noted, however, that the vector magnitude and direction of travel are possible avenues for further study. It may also be interesting to assess the θ and $\Delta\theta$ paths in comparison to protein domains, to perhaps uncover new clues about the nature of protein folding.

Because of the ambiguous, non-directional, property of the θ path, a useful metaphor is that the path is like unto a musical melody, wherein the relative frequencies between neighboring notes is important, but not the absolute values of the frequencies of individual notes: the melody is recognized irrespective of the key in which it is reproduced. (Petoukhov, 2010) The process of "recognition" of an in-tune or out-of-tune molecular sequence or conformation is a good candidate for the emergence of the "self" in self-replication, via the coarse-graining of phase space. (England, 2012) Indeed, the Tetrahedral Genetic Code and Genetic Phase Angle Distance could be an important step in the development of a statistical method reminiscent of quantum mechanics, helping to uncover why nonsynonymous sequences can assume very similar functional shapes and domains (Parker, 2011), and why changing the nucleotides in the third position of codons in regulatory elements increases the rate of transcription of these elements many fold (Robins et al., 2008; Subramaniam, Pan, & Cluzel, 2013), among the many outstanding problems of molecular biology.

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Appendix A – Additional Figures

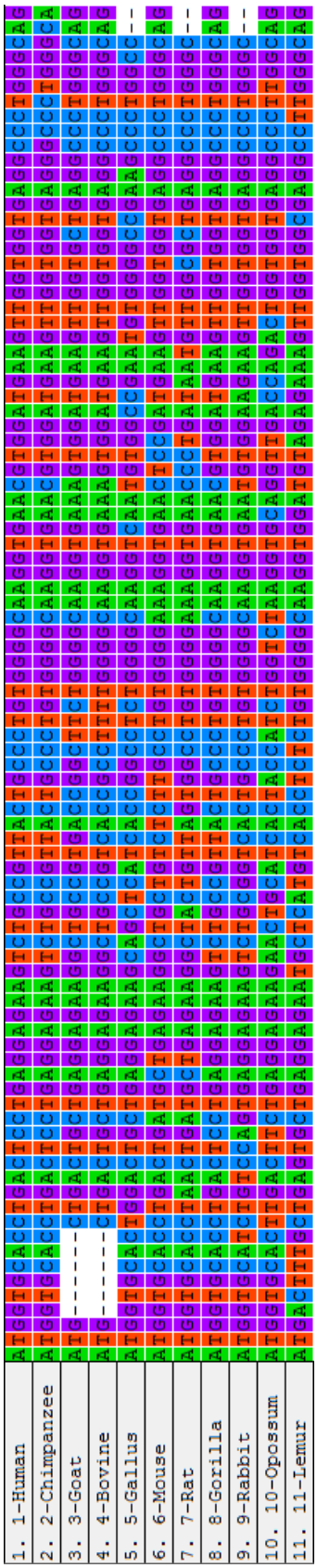

Table 1: The coding sequences of the first exon of B-globin gene in 11 different species, aligned by codon homology using MUSCLE {Edgar 2004 #133}.

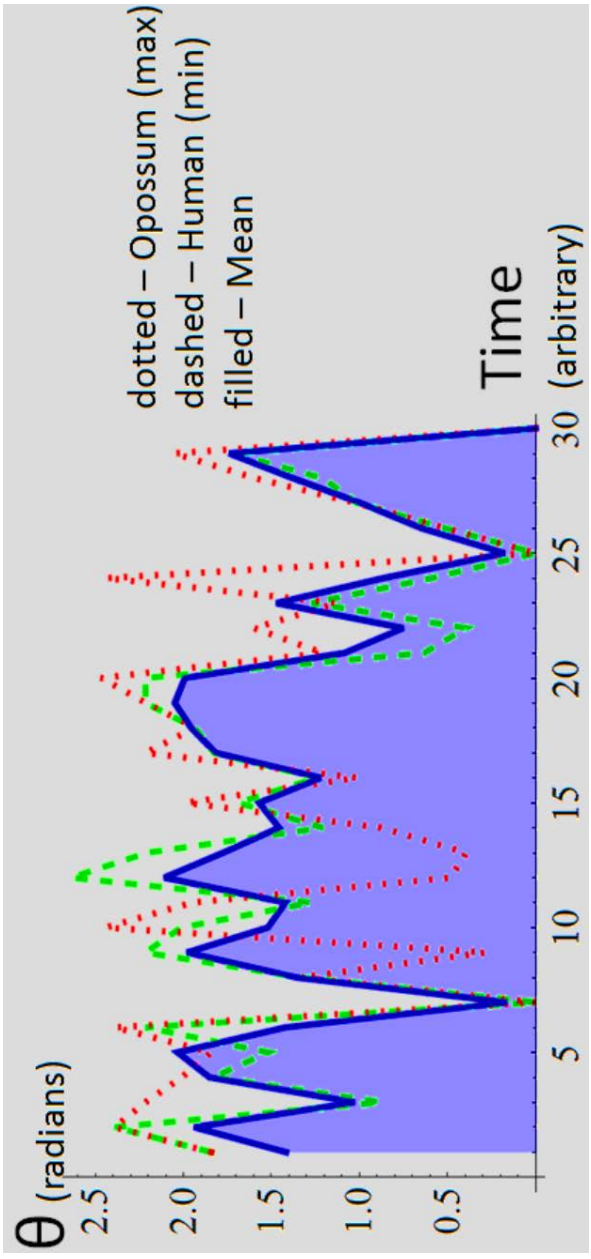

Figure 9: the θ paths of maximum and minimum variance from the mean θ path.

Appendix B – Explicit *Mathematica* computational code

This code is also available as a Mathematica notebook file in the supplemental materials located at: https://docs.google.com/file/d/0Bzgyyvz44CkRUkx1aVRqNTZxVTA/edit?usp=sharing

```
(* !!! push 'shift-enter' to execute the notebook !!! *)

(*import the clifford algebra package clifford.m; available for download
http://www.fata.unam.mx/aragon/software*)
<<clifford.m

(*computation:  map nucleotides into 3D vector space*)
{a=Distribute[e[1]+e[2]+e[3]],c=Distribute[-e[1]+e[2]-e[3]],g=Distribute[-e[1]-
e[2]+e[3]],t=Distribute[e[1]-e[2]-e[3]]};

(*graphic:  vector-codons*)
{"A",GADraw[a],"T",GADraw[t],"G",GADraw[g],"C",GADraw[c]}

(*graphic:  3D plot of Tetrahedral Genetic Code*)
{{AAA=Distribute[Simplify[4a+2a+a]],AAT=AAT=Distribute[Simplify[4a+2a]]+t,AAC=Distribute[Simplify
[4a+2a+c]],AAG=Distribute[Simplify[4a+2a+g]]},{ATA=Distribute[Simplify[4a+a]]+Distribute[2t],ATT=
Distribute[Simplify[4a+2t+t]],ATC=Distribute[Simplify[4a+2t+c]],ATG=Distribute[Simplify[4a+2t+g]]
},{ACA=Distribute[Simplify[4a+2c+a]],ACT=Distribute[Simplify[4a+2c+t]],ACC=Distribute[Simplify[4a
+2c+c]],ACG=Distribute[Simplify[4a+2c+g]]},{AGA=Distribute[Simplify[4a+2g+a]],AGT=Distribute[Simp
lify[4a+2g+t]],AGC=Distribute[Simplify[4a+2g+c]],AGG=Distribute[Simplify[4a+2g+g]]},{TAA=Distribu
te[Simplify[4t+2a+a]],TAT=Distribute[4t]+Distribute[2a]+Distribute[t],TAC=Distribute[Simplify[4t+
2a+c]],TAG=Distribute[Simplify[4t+2a+g]]},{TTA=Distribute[4t]+Distribute[2t]+Distribute[a],TTT=Di
stribute[Simplify[4t+2t+t]],TTC=Distribute[Simplify[4t+2t+c]],TTG=Distribute[Simplify[4t+2t+g]]},
{TCA=Distribute[Simplify[4t+2c+a]],TCT=Distribute[Simplify[4t+2c+t]],TCC=Distribute[Simplify[4t+2
c+c]],TCG=Distribute[Simplify[4t+2c+g]]},{TGA=Distribute[Simplify[4t+2g+a]],TGT=Distribute[Simpli
fy[4t+2g+t]],TGC=Distribute[Simplify[4t+2g+c]],TGG=Distribute[Simplify[4t+2g+g]]},{CAA=Distribute
[Simplify[4c+2a+a]],CAT=Distribute[Simplify[4c+2a+t]],CAC=Distribute[Simplify[4c+2a+c]],CAG=Distr
ibute[Simplify[4c+2a+g]]},{CTA=Distribute[Simplify[4c+2t+a]],CTT=Distribute[Simplify[4c+2t+t]],CT
C=Distribute[Simplify[4c+2t+c]],CTG=Distribute[Simplify[4c+2t+g]]},
{CCA=Distribute[Simplify[4c+2c+a]],CCT=Distribute[Simplify[4c+2c+t]],CCC=Distribute[Simplify[4c+2
c+c]],CCG=Distribute[Simplify[4c+2c+g]]},
{CGA=Distribute[Simplify[4c+2g+a]],CGT=Distribute[Simplify[4c+2g+t]],CGC=Distribute[Simplify[4c+2
g+c]],CGG=Distribute[Simplify[4c+2g+g]]},
{GAA=Distribute[Simplify[4g+2a+a]],GAT=Distribute[Simplify[4g+2a+t]],GAC=Distribute[Simplify[4g+2
a+c]],GAG=Distribute[Simplify[4g+2a+g]]},
{GTA=Distribute[Simplify[4g+2t+a]],GTT=Distribute[Simplify[4g+2t+t]],GTC=Distribute[Simplify[4g+2
t+c]],GTG=Distribute[Simplify[4g+2t+g]]},
{GCA=Distribute[Simplify[4g+2c+a]],GCT=Distribute[Simplify[4g+2c+t]],GCC=Distribute[Simplify[4g+2
c+c]],GCG=Distribute[Simplify[4g+2c+g]]},
{GGA=Distribute[Simplify[4g+2g+a]],GGT=Distribute[Simplify[4g+2g+t]],GGC=Distribute[Simplify[4g+2
g+c]],GGG=Distribute[Simplify[4g+2g+g]]},drawcode={drawcodeA={AAAd=GADraw[AAA],AATd=GADraw[AAT],A
ACd=GADraw[AAC],AAGd=GADraw[AAG],ATAd=GADraw[ATA],ATTd=GADraw[ATT],ATCd=GADraw[ATC],ATGd=GADraw[A
TG],ACAd=GADraw[ACA],ACTd=GADraw[ACT],ACCd=GADraw[ACC],ACGd=GADraw[ACG],AGAd=GADraw[AGA],AGTd=GAD
raw[AGT],AGCd=GADraw[AGC],AGGd=GADraw[AGG]},drawcodeT={TAAd=GADraw[TAA],TATd=GADraw[TAT],TACd=GAD
raw[TAC],TAGd=GADraw[TAG],TTAd=GADraw[TTA],TTTd=GADraw[TTT],TTCd=GADraw[TTC],TTGd=GADraw[TTG],TCA
d=GADraw[TCA],TCTd=GADraw[TCT],TCCd=GADraw[TCC],TCGd=GADraw[TCG],TGAd=GADraw[TGA],TGTd=GADraw[TGT
],TGCd=GADraw[TGC],TGGd=GADraw[TGG]},drawcodeC={CAAd=GADraw[CAA],CATd=GADraw[CAT],CACd=GADraw[CAC
],CAGd=GADraw[CAG],CTAd=GADraw[CTA],CTTd=GADraw[CTT],CTCd=GADraw[CTC],CTGd=GADraw[CTG],CCAd=GADra
w[CCA],CCTd=GADraw[CCT],CCCd=GADraw[CCC],CCGd=GADraw[CCG],CGAd=GADraw[CGA],CGTd=GADraw[CGT],CGCd=
GADraw[CGC],CGGd=GADraw[CGG]},drawcodeG={GAAd=GADraw[GAA],GATd=GADraw[GAT],GACd=GADraw[GAC],GAGd=
GADraw[GAG],GTAd=GADraw[GTA],GTTd=GADraw[GTT],GTCd=GADraw[GTC],GTGd=GADraw[GTG],GCAd=GADraw[GCA],
GCTd=GADraw[GCT],GCCd=GADraw[GCC],GCGd=GADraw[GCG],GGAd=GADraw[GGA],GGTd=GADraw[GGT],GGCd=GADraw[
GGC],GGGd=GADraw[GGG]}}};
Show[drawcode]

(*computation:  map codons into Tetrahedral Genetic Code*)
{AAA=ToVector[Distribute[Simplify[Simplify[4a+2a+a]]]],AAT=ToVector[Distribute[Simplify[4a+2a+t]]
],AAC=ToVector[Distribute[Simplify[4a+2a+c]]],AAG=ToVector[Distribute[Simplify[4a+2a+g]]],ATA=ToV
ector[Distribute[Simplify[Simplify[4a+2t+a]]]],ATT=ToVector[Distribute[Simplify[4a+2t+t]]],ATC=To
Vector[Distribute[Simplify[4a+2t+c]]],ATG=ToVector[Distribute[Simplify[4a+2t+g]]],ACA=ToVector[Di
stribute[Simplify[Simplify[4a+2c+a]]]],ACT=ToVector[Distribute[Simplify[4a+2c+t]]],ACC=ToVector[D
istribute[Simplify[4a+2c+c]]],ACG=ToVector[Distribute[Simplify[4a+2c+g]]],AGA=ToVector[Distribute
[Simplify[Simplify[4a+2g+a]]]],AGT=ToVector[Distribute[Simplify[4a+2g+t]]],AGC=ToVector[Distribut
e[Simplify[4a+2g+c]]],AGG=ToVector[Distribute[Simplify[4a+2g+g]]],TAA=ToVector[Distribute[Simplif
y[Simplify[4t+2a+a]]]],TAT=ToVector[Distribute[Simplify[4t+2a+t]]],TAC=ToVector[Distribute[Simpli
```

```
fy[4t+2a+c]]],TAG=ToVector[Distribute[Simplify[4t+2a+g]]],TTA=ToVector[Distribute[Simplify[Simpli
fy[4t+2t+a]]]],TTT=ToVector[Distribute[Simplify[4t+2t+t]]],TTC=ToVector[Distribute[Simplify[4t+2t
+c]]],TTG=ToVector[Distribute[Simplify[4t+2t+g]]],TCA=ToVector[Distribute[Simplify[Simplify[4t+2c
+a]]]],TCT=ToVector[Distribute[Simplify[4t+2c+t]]],TCC=ToVector[Distribute[Simplify[4t+2c+c]]],TC
G=ToVector[Distribute[Simplify[4t+2c+g]]],TGA=ToVector[Distribute[Simplify[Simplify[4t+2g+a]]]],T
GT=ToVector[Distribute[Simplify[4t+2g+t]]],TGC=ToVector[Distribute[Simplify[4t+2g+c]]],TGG=ToVect
or[Distribute[Simplify[4t+2g+g]]],CAA=ToVector[Distribute[Simplify[Simplify[4c+2a+a]]]],CAT=ToVec
tor[Distribute[Simplify[4c+2a+t]]],CAC=ToVector[Distribute[Simplify[4c+2a+c]]],CAG=ToVector[Distr
ibute[Simplify[4c+2a+g]]],CTA=ToVector[Distribute[Simplify[Simplify[4c+2t+a]]]],CTT=ToVector[Dist
ribute[Simplify[4c+2t+t]]],CTC=ToVector[Distribute[Simplify[4c+2t+c]]],CTG=ToVector[Distribute[Si
mplify[4c+2t+g]]],CCA=ToVector[Distribute[Simplify[Simplify[4c+2c+a]]]],CCT=ToVector[Distribute[S
implify[4c+2c+t]]],CCC=ToVector[Distribute[Simplify[4c+2c+c]]],CCG=ToVector[Distribute[Simplify[4
c+2c+g]]],CGA=ToVector[Distribute[Simplify[Simplify[4c+2g+a]]]],CGT=ToVector[Distribute[Simplify[
4c+2g+t]]],CGC=ToVector[Distribute[Simplify[4c+2g+c]]],CGG=ToVector[Distribute[Simplify[4c+2g+g]]
],GAA=ToVector[Distribute[Simplify[Simplify[4g+2a+a]]]],GAT=ToVector[Distribute[Simplify[4g+2a+t]
]],GAC=ToVector[Distribute[Simplify[4g+2a+c]]],GAG=ToVector[Distribute[Simplify[4g+2a+g]]],GTA=To
Vector[Distribute[Simplify[Simplify[4g+2t+a]]]],GTT=ToVector[Distribute[Simplify[4g+2t+t]]],GTC=T
oVector[Distribute[Simplify[4g+2t+c]]],GTG=ToVector[Distribute[Simplify[4g+2t+g]]],GCA=ToVector[D
istribute[Simplify[Simplify[4g+2c+a]]]],GCT=ToVector[Distribute[Simplify[4g+2c+t]]],GCC=ToVector[
Distribute[Simplify[4g+2c+c]]],GCG=ToVector[Distribute[Simplify[4g+2c+g]]],GGA=ToVector[Distribut
e[Simplify[Simplify[4g+2g+a]]]],GGT=ToVector[Distribute[Simplify[4g+2g+t]]],GGC=ToVector[Distribu
te[Simplify[4g+2g+c]]],GGG=ToVector[Distribute[Simplify[4g+2g+g]]]};

(*graphic:  colored matrix of full set of \[Theta] between neighboring vector-codons*)
{codons={AAA,AAT,AAC,AAG,ATA,ATT,ATC,ATG,ACA,ACT,ACC,ACG,AGA,AGT,AGC,AGG,TAA,TAT,TAC,TAG,TTA,TTT,
TTC,TTG,TCA,TCT,TCC,TCG,TGA,TGT,TGC,TGG,CAA,CAT,CAC,CAG,CTA,CTT,CTC,CTG,CCA,CCT,CCC,CCG,CGA,CGT,C
GC,CGG,GAA,GAT,GAC,GAG,GTA,GTT,GTC,GTG,GCA,GCT,GCC,GCG,GGA,GGT,GGC,GGG},
{c1,c2,c3,c4,c5,c6,c7,c8,c9,c10,c11,c12,c13,c14,c15,c16,c17,c18,c19,c20,c21,c22,c23,c24,c25,c26,c
27,c28,c29,c30,c31,c32,c33,c34,c35,c36,c37,c38,c39,c40,c41,c42,c43,c44,c45,c46,c47,c48,c49,c50,c5
1,c52,c53,c54,c55,c56,c57,c58,c59,c60,c61,c62,c63,c64}=Thread[ConstantArray[codons,64]],
{r1=N[MapThread[VectorAngle,{codons,c1}]],r2=N[MapThread[VectorAngle,{codons,c2}]],r3=N[MapThread
[VectorAngle,{codons,c3}]],r4=N[MapThread[VectorAngle,{codons,c4}]],r5=N[MapThread[VectorAngle,{c
odons,c5}]],r6=N[MapThread[VectorAngle,{codons,c6}]],r7=N[MapThread[VectorAngle,{codons,c7}]],r8=
N[MapThread[VectorAngle,{codons,c8}]],r9=N[MapThread[VectorAngle,{codons,c9}]],r10=N[MapThread[Ve
ctorAngle,{codons,c10}]],r11=N[MapThread[VectorAngle,{codons,c11}]],r12=N[MapThread[VectorAngle,{
codons,c12}]],r13=N[MapThread[VectorAngle,{codons,c13}]],r14=N[MapThread[VectorAngle,{codons,c14}
]],r15=N[MapThread[VectorAngle,{codons,c15}]],r16=N[MapThread[VectorAngle,{codons,c16}]],r17=N[Ma
pThread[VectorAngle,{codons,c17}]],r18=N[MapThread[VectorAngle,{codons,c18}]],r19=N[MapThread[Vec
torAngle,{codons,c19}]],r20=N[MapThread[VectorAngle,{codons,c20}]],r21=N[MapThread[VectorAngle,{c
odons,c21}]],r22=N[MapThread[VectorAngle,{codons,c22}]],r23=N[MapThread[VectorAngle,{codons,c23}]
],r24=N[MapThread[VectorAngle,{codons,c24}]],r25=N[MapThread[VectorAngle,{codons,c25}]],r26=N[Map
Thread[VectorAngle,{codons,c26}]],r27=N[MapThread[VectorAngle,{codons,c27}]],r28=N[MapThread[Vect
orAngle,{codons,c28}]],r29=N[MapThread[VectorAngle,{codons,c29}]],r30=N[MapThread[VectorAngle,{co
dons,c30}]],r31=N[MapThread[VectorAngle,{codons,c31}]],r32=N[MapThread[VectorAngle,{codons,c32}]]
,r33=N[MapThread[VectorAngle,{codons,c33}]],r34=N[MapThread[VectorAngle,{codons,c34}]],r35=N[MapT
hread[VectorAngle,{codons,c35}]],r36=N[MapThread[VectorAngle,{codons,c36}]],r37=N[MapThread[Vecto
rAngle,{codons,c37}]],r38=N[MapThread[VectorAngle,{codons,c38}]],r39=N[MapThread[VectorAngle,{cod
ons,c39}]],r40=N[MapThread[VectorAngle,{codons,c40}]],r41=N[MapThread[VectorAngle,{codons,c41}]],
r42=N[MapThread[VectorAngle,{codons,c42}]],r43=N[MapThread[VectorAngle,{codons,c43}]],r44=N[MapTh
read[VectorAngle,{codons,c44}]],r45=N[MapThread[VectorAngle,{codons,c45}]],r46=N[MapThread[Vector
Angle,{codons,c46}]],r47=N[MapThread[VectorAngle,{codons,c47}]],r48=N[MapThread[VectorAngle,{codo
ns,c48}]],r49=N[MapThread[VectorAngle,{codons,c49}]],r50=N[MapThread[VectorAngle,{codons,c50}]],r
51=N[MapThread[VectorAngle,{codons,c51}]],r52=N[MapThread[VectorAngle,{codons,c52}]],r53=N[MapThr
ead[VectorAngle,{codons,c53}]],r54=N[MapThread[VectorAngle,{codons,c54}]],r55=N[MapThread[VectorA
ngle,{codons,c55}]],r56=N[MapThread[VectorAngle,{codons,c56}]],r57=N[MapThread[VectorAngle,{codon
s,c57}]],r58=N[MapThread[VectorAngle,{codons,c58}]],r59=N[MapThread[VectorAngle,{codons,c59}]],r6
0=N[MapThread[VectorAngle,{codons,c60}]],r61=N[MapThread[VectorAngle,{codons,c61}]],r62=N[MapThre
ad[VectorAngle,{codons,c62}]],r63=N[MapThread[VectorAngle,{codons,c63}]],r64=N[MapThread[VectorAn
gle,{codons,c64}]]},codonmatrix={r1,r2,r3,r4,r5,r6,r7,r8,r9,r10,r11,r12,r13,r14,r15,r16,r17,r18,r
19,r20,r21,r22,r23,r24,r25,r26,r27,r28,r29,r30,r31,r32,r33,r34,r35,r36,r37,r38,r39,r40,r41,r42,r4
3,r44,r45,r46,r47,r48,r49,r50,r51,r52,r53,r54,r55,r56,r57,r58,r59,r60,r61,r62,r63,r64}};
MatrixPlot[codonmatrix,ColorFunction->"GreenPinkTones",ColorFunctionScaling->True]

(*computation:  the following function will be used to import and format genetic sequences *)
dnamap[x_List]:=Module[{x1=x,x2,x3,x4,bb,cc},bb=Append[Drop[x,1],A];cc=Append[Drop[bb,1],A];x2=Pa
rtition[x,3]/.{A,A,A}->AAA/.{A,A,T}->AAT/.{A,A,C}->AAC/.{A,A,G}->AAG/.{A,T,A}->ATA/.{A,T,T}-
>ATT/.{A,T,C}->ATC/.{A,T,G}->ATG/.{A,C,A}->ACA/.{A,C,T}->ACT/.{A,C,C}->ACC/.{A,C,G}-
>ACG/.{A,G,A}->AGA/.{A,G,T}->AGT/.{A,G,C}->AGC/.{A,G,G}->AGG/.{T,A,A}->TAA/.{T,A,T}-
>TAT/.{T,A,C}->TAC/.{T,A,G}->TAG/.{T,T,A}->TTA/.{T,T,T}->TTT/.{T,T,C}->TTC/.{T,T,G}-
>TTG/.{T,C,A}->TCA/.{T,C,T}->TCT/.{T,C,C}->TCC/.{T,C,G}->TCG/.{T,G,A}->TGA/.{T,G,T}-
>TGT/.{T,G,C}->TGC/.{T,G,G}->TGG/.{C,A,A}->CAA/.{C,A,T}->CAT/.{C,A,C}->CAC/.{C,A,G}-
```

```
>CAG/.{C,T,A}->CTA/.{C,T,T}->CTT/.{C,T,C}->CTC/.{C,T,G}->CTG/.{C,C,A}->CCA/.{C,C,T}-
>CCT/.{C,C,C}->CCC/.{C,C,G}->CCG/.{C,G,A}->CGA/.{C,G,T}->CGT/.{C,G,C}->CGC/.{C,G,G}-
>CGG/.{G,A,A}->GAA/.{G,A,T}->GAT/.{G,A,C}->GAC/.{G,A,G}->GAG/.{G,T,A}->GTA/.{G,T,T}-
>GTT/.{G,T,C}->GTC/.{G,T,G}->GTG/.{G,C,A}->GCA/.{G,C,T}->GCT/.{G,C,C}->GCC/.{G,C,G}-
>GCG/.{G,G,A}->GGA/.{G,G,T}->GGT/.{G,G,C}->GGC/.{G,G,G}->GGG/.A->0/.T->0/.G->0/.C->0;Return[x2]];

(*computation:  enter aligned protein-coding sequences here; sequences must be of the form:
{A,T,G,G,T,0,0,0,....}; note that indel gaps must be indicated by '0' *)
a1=Human={A,T,G,G,T,G,C,A,C,C,T,G,A,C,T,C,C,T,G,A,G,G,A,G,A,A,G,T,C,T,G,C,C,G,T,T,A,C,T,G,C,C,C,T
,G,T,G,G,G,G,C,A,A,G,G,T,G,A,A,C,G,T,G,G,A,T,G,A,A,G,T,T,G,G,T,G,G,T,G,A,G,G,C,C,C,T,G,G,G,C,A,G}
;
b1=Chimpanzee={A,T,G,G,T,G,C,A,C,C,T,G,A,C,T,C,C,T,G,A,G,G,A,G,A,A,G,T,C,T,G,C,C,G,T,T,A,C,T,G,C,
C,C,T,G,T,G,G,G,G,C,A,A,G,G,T,G,A,A,C,G,T,G,G,A,T,G,A,A,G,T,T,G,G,T,G,G,T,G,A,G,G,G,C,C,C,T,G,G,G
,C,A};
c1=Goat={A,T,G,0,0,0,0,0,0,C,T,G,A,C,T,G,C,T,G,A,G,G,A,G,A,A,G,G,C,T,G,C,C,G,T,G,A,C,C,G,G,C,T,T,
C,T,G,G,G,G,C,A,A,G,G,T,G,A,A,A,G,T,G,G,A,T,G,A,A,G,T,T,G,G,T,G,C,T,G,A,G,G,C,C,C,T,G,G,G,C,A,G};
d1=Bovine={A,T,G,0,0,0,0,0,0,C,T,G,A,C,T,G,C,T,G,A,G,G,A,G,A,A,G,G,C,T,G,C,C,G,T,C,A,C,C,G,C,C,T,
T,T,T,G,G,G,G,C,A,A,G,G,T,G,A,A,A,G,T,G,G,A,T,G,A,A,G,T,T,G,G,T,G,G,T,G,A,G,G,C,C,C,T,G,G,G,C,A,G
};
e1=Gallus={A,T,G,G,T,G,C,A,C,T,G,G,A,C,T,G,C,T,G,A,G,G,A,G,A,A,G,C,A,G,C,T,C,A,T,C,A,C,C,G,G,C,C,
T,C,T,G,G,G,G,C,A,A,G,G,T,C,A,A,T,G,T,G,G,C,C,G,A,A,T,G,T,G,G,G,G,C,C,G,A,A,G,C,C,C,T,G,G,C,C,0,0
};
f1=Mouse={A,T,G,G,T,G,C,A,C,C,T,G,A,C,T,G,A,T,G,C,T,G,A,G,G,A,A,G,G,C,T,G,C,T,G,T,C,T,C,T,T,G,C,C,T
,G,T,G,G,G,G,A,A,A,G,G,T,G,A,A,C,T,C,C,G,A,T,G,A,A,G,T,T,G,G,T,G,G,T,G,A,G,G,C,C,C,T,G,G,G,C,A,G}
;
g1=Rat={A,T,G,G,T,G,C,A,C,C,T,A,A,C,T,G,A,T,G,C,T,G,A,G,G,A,A,G,G,C,T,A,C,T,G,T,T,A,G,T,G,G,C,C,T,G
,T,G,G,G,G,A,A,A,G,G,T,G,A,A,C,C,C,T,G,A,T,A,A,T,G,T,T,G,G,C,G,C,T,G,A,G,G,C,C,C,T,G,G,G,C,0,0};
h1=
Gorilla={A,T,G,G,T,G,C,A,C,C,T,G,A,C,T,C,C,T,G,A,G,G,A,G,A,A,G,T,C,T,G,C,C,G,T,T,A,C,T,G,C,C,C,T,
G,T,G,G,G,G,C,A,A,G,G,T,G,A,A,C,G,T,G,G,A,T,G,A,A,G,T,T,G,G,T,G,G,T,G,A,G,G,C,C,C,T,G,G,G,C,A,G};
i1=
Rabbit={A,T,G,G,T,G,C,A,T,C,T,G,T,C,C,A,G,T,G,A,G,G,A,G,A,A,A,G,T,C,T,G,C,G,G,T,C,A,C,T,G,C,C,C,T,G
,T,G,G,G,G,C,A,A,G,G,T,G,A,A,T,G,T,G,G,A,A,G,A,A,A,G,T,T,G,G,T,G,G,T,G,A,G,G,C,C,C,T,G,G,G,C,0,0};
j1=
Opossum={A,T,G,G,T,G,C,A,C,T,T,G,A,C,T,T,C,T,G,A,G,G,A,G,A,A,A,G,A,A,C,T,G,C,A,T,C,A,C,T,A,C,C,A,T,
C,T,G,G,T,C,T,A,A,G,G,T,G,C,A,G,G,T,T,G,A,C,C,A,G,A,C,T,G,G,T,G,G,T,G,A,G,G,C,C,C,T,T,G,G,C,A,G};
k1=
Lemur={A,T,G,A,C,T,T,T,G,C,T,G,A,G,T,G,C,T,G,A,G,G,A,G,A,A,T,G,C,T,C,A,T,G,T,C,A,C,C,T,C,T,C,T,G,
T,G,G,G,G,C,A,A,G,G,T,G,G,A,T,G,T,A,G,A,G,A,A,A,A,G,T,T,G,G,T,G,G,C,G,A,G,G,C,C,T,T,G,G,G,C,A,G};

(*computation:  this section generates the \[Theta] path, vector angles between neighboring sets
of codon-vectors, for each of the sequences above*)
{aa1=dnamap[a1],aa2=Append[Drop[aa1,1],{0,0,0}],aa3=N[Thread[VectorAngle[aa1,aa2]]]/.Indeterminat
e->0};
{bb1=dnamap[b1],bb2=Append[Drop[bb1,1],{0,0,0}],bb3=N[Thread[VectorAngle[bb1,bb2]]]/.Indeterminat
e->0};
{cc1=dnamap[c1],cc2=Append[Drop[cc1,1],{0,0,0}],cc3=N[Thread[VectorAngle[cc1,cc2]]]/.Indeterminat
e->0};
{dd1=dnamap[d1],dd2=Append[Drop[dd1,1],{0,0,0}],dd3=N[Thread[VectorAngle[dd1,dd2]]]/.Indeterminat
e->0};
{ee1=dnamap[e1],ee2=Append[Drop[ee1,1],{0,0,0}],ee3=N[Thread[VectorAngle[ee1,ee2]]]/.Indeterminat
e->0};
{ff1=dnamap[f1],ff2=Append[Drop[ff1,1],{0,0,0}],ff3=N[Thread[VectorAngle[ff1,ff2]]]/.Indeterminat
e->0};
{gg1=dnamap[g1],gg2=Append[Drop[gg1,1],{0,0,0}],gg3=N[Thread[VectorAngle[gg1,gg2]]]/.Indeterminat
e->0};
{hh1=dnamap[h1],hh2=Append[Drop[hh1,1],{0,0,0}],hh3=N[Thread[VectorAngle[hh1,hh2]]]/.Indeterminat
e->0};
{ii1=dnamap[i1],ii2=Append[Drop[ii1,1],{0,0,0}],ii3=N[Thread[VectorAngle[ii1,ii2]]]/.Indeterminat
e->0};
{jj1=dnamap[j1],jj2=Append[Drop[jj1,1],{0,0,0}],jj3=N[Thread[VectorAngle[jj1,jj2]]]/.Indeterminat
e->0};
{kk1=dnamap[k1],kk2=Append[Drop[kk1,1],{0,0,0}],kk3=N[Thread[VectorAngle[kk1,kk2]]]/.Indeterminat
e->0};

(*computation:  build the \[Theta] paths as rows and columns in the species NxN matrix;  please
note that this process is HARD CODED for 11 species:  additional species must be added manually
according the form given*)
{row={aa3,bb3,cc3,dd3,ee3,ff3,gg3,hh3,ii3,jj3,kk3}};
{column1=ConstantArray[aa3,11],column2=ConstantArray[bb3,11],column3=ConstantArray[cc3,11],column
4=ConstantArray[dd3,11],column5=ConstantArray[ee3,11],column6=ConstantArray[ff3,11],column7=Const
```

```
antArray[gg3,11],column8=ConstantArray[hh3,11],column9=ConstantArray[ii3,11],column10=ConstantArr
ay[jj3,11],column11=ConstantArray[kk3,11]};

(*computation:  number of codons in sequence -> n *)
{n=Length[aa3]};

(*computation:  compute the \[CapitalDelta]\[Theta] from \[Theta] paths *)
{\[CapitalDelta]\[Theta]1=Abs[row-column1],\[CapitalDelta]\[Theta]2=Abs[row-
column2],\[CapitalDelta]\[Theta]3=Abs[row-column3],\[CapitalDelta]\[Theta]4=Abs[row-
column4],\[CapitalDelta]\[Theta]5=Abs[row-column5],\[CapitalDelta]\[Theta]6=Abs[row-
column6],\[CapitalDelta]\[Theta]7=Abs[row-column7],\[CapitalDelta]\[Theta]8=Abs[row-
column8],\[CapitalDelta]\[Theta]9=Abs[row-column9],\[CapitalDelta]\[Theta]10=Abs[row-
column10],\[CapitalDelta]\[Theta]11=Abs[row-column11]};

(*computation:  compute the mean score of \[CapitalDelta]\[Theta], the GPAD distance, for each
position in the matrix*)
GPAD1={Total[Part[\[CapitalDelta]\[Theta]1,1]]/n,Total[Part[\[CapitalDelta]\[Theta]1,2]]/n,Total[
Part[\[CapitalDelta]\[Theta]1,3]]/n,Total[Part[\[CapitalDelta]\[Theta]1,4]]/n,Total[Part[\[Capita
lDelta]\[Theta]1,5]]/n,Total[Part[\[CapitalDelta]\[Theta]1,6]]/n,Total[Part[\[CapitalDelta]\[Thet
a]1,7]]/n,Total[Part[\[CapitalDelta]\[Theta]1,8]]/n,Total[Part[\[CapitalDelta]\[Theta]1,9]]/n,Tot
al[Part[\[CapitalDelta]\[Theta]1,10]]/n,Total[Part[\[CapitalDelta]\[Theta]1,11]]/n};
GPAD2={Total[Part[\[CapitalDelta]\[Theta]2,1]]/n,Total[Part[\[CapitalDelta]\[Theta]2,2]]/n,Total[
Part[\[CapitalDelta]\[Theta]2,3]]/n,Total[Part[\[CapitalDelta]\[Theta]2,4]]/n,Total[Part[\[Capita
lDelta]\[Theta]2,5]]/n,Total[Part[\[CapitalDelta]\[Theta]2,6]]/n,Total[Part[\[CapitalDelta]\[Thet
a]2,7]]/n,Total[Part[\[CapitalDelta]\[Theta]2,8]]/n,Total[Part[\[CapitalDelta]\[Theta]2,9]]/n,Tot
al[Part[\[CapitalDelta]\[Theta]2,10]]/n,Total[Part[\[CapitalDelta]\[Theta]2,11]]/n};
GPAD3={Total[Part[\[CapitalDelta]\[Theta]3,1]]/n,Total[Part[\[CapitalDelta]\[Theta]3,2]]/n,Total[
Part[\[CapitalDelta]\[Theta]3,3]]/n,Total[Part[\[CapitalDelta]\[Theta]3,4]]/n,Total[Part[\[Capita
lDelta]\[Theta]3,5]]/n,Total[Part[\[CapitalDelta]\[Theta]3,6]]/n,Total[Part[\[CapitalDelta]\[Thet
a]3,7]]/n,Total[Part[\[CapitalDelta]\[Theta]3,8]]/n,Total[Part[\[CapitalDelta]\[Theta]3,9]]/n,Tot
al[Part[\[CapitalDelta]\[Theta]3,10]]/n,Total[Part[\[CapitalDelta]\[Theta]3,11]]/n};
GPAD4={Total[Part[\[CapitalDelta]\[Theta]4,1]]/n,Total[Part[\[CapitalDelta]\[Theta]4,2]]/n,Total[
Part[\[CapitalDelta]\[Theta]4,3]]/n,Total[Part[\[CapitalDelta]\[Theta]4,4]]/n,Total[Part[\[Capita
lDelta]\[Theta]4,5]]/n,Total[Part[\[CapitalDelta]\[Theta]4,6]]/n,Total[Part[\[CapitalDelta]\[Thet
a]4,7]]/n,Total[Part[\[CapitalDelta]\[Theta]4,8]]/n,Total[Part[\[CapitalDelta]\[Theta]4,9]]/n,Tot
al[Part[\[CapitalDelta]\[Theta]4,10]]/n,Total[Part[\[CapitalDelta]\[Theta]4,11]]/n};
GPAD5={Total[Part[\[CapitalDelta]\[Theta]5,1]]/n,Total[Part[\[CapitalDelta]\[Theta]5,2]]/n,Total[
Part[\[CapitalDelta]\[Theta]5,3]]/n,Total[Part[\[CapitalDelta]\[Theta]5,4]]/n,Total[Part[\[Capita
lDelta]\[Theta]5,5]]/n,Total[Part[\[CapitalDelta]\[Theta]5,6]]/n,Total[Part[\[CapitalDelta]\[Thet
a]5,7]]/n,Total[Part[\[CapitalDelta]\[Theta]5,8]]/n,Total[Part[\[CapitalDelta]\[Theta]5,9]]/n,Tot
al[Part[\[CapitalDelta]\[Theta]5,10]]/n,Total[Part[\[CapitalDelta]\[Theta]5,11]]/n};
GPAD6={Total[Part[\[CapitalDelta]\[Theta]6,1]]/n,Total[Part[\[CapitalDelta]\[Theta]6,2]]/n,Total[
Part[\[CapitalDelta]\[Theta]6,3]]/n,Total[Part[\[CapitalDelta]\[Theta]6,4]]/n,Total[Part[\[Capita
lDelta]\[Theta]6,5]]/n,Total[Part[\[CapitalDelta]\[Theta]6,6]]/n,Total[Part[\[CapitalDelta]\[Thet
a]6,7]]/n,Total[Part[\[CapitalDelta]\[Theta]6,8]]/n,Total[Part[\[CapitalDelta]\[Theta]6,9]]/n,Tot
al[Part[\[CapitalDelta]\[Theta]6,10]]/n,Total[Part[\[CapitalDelta]\[Theta]6,11]]/n};
GPAD7={Total[Part[\[CapitalDelta]\[Theta]7,1]]/n,Total[Part[\[CapitalDelta]\[Theta]7,2]]/n,Total[
Part[\[CapitalDelta]\[Theta]7,3]]/n,Total[Part[\[CapitalDelta]\[Theta]7,4]]/n,Total[Part[\[Capita
lDelta]\[Theta]7,5]]/n,Total[Part[\[CapitalDelta]\[Theta]7,6]]/n,Total[Part[\[CapitalDelta]\[Thet
a]7,7]]/n,Total[Part[\[CapitalDelta]\[Theta]7,8]]/n,Total[Part[\[CapitalDelta]\[Theta]7,9]]/n,Tot
al[Part[\[CapitalDelta]\[Theta]7,10]]/n,Total[Part[\[CapitalDelta]\[Theta]7,11]]/n};
GPAD8={Total[Part[\[CapitalDelta]\[Theta]8,1]]/n,Total[Part[\[CapitalDelta]\[Theta]8,2]]/n,Total[
Part[\[CapitalDelta]\[Theta]8,3]]/n,Total[Part[\[CapitalDelta]\[Theta]8,4]]/n,Total[Part[\[Capita
lDelta]\[Theta]8,5]]/n,Total[Part[\[CapitalDelta]\[Theta]8,6]]/n,Total[Part[\[CapitalDelta]\[Thet
a]8,7]]/n,Total[Part[\[CapitalDelta]\[Theta]8,8]]/n,Total[Part[\[CapitalDelta]\[Theta]8,9]]/n,Tot
al[Part[\[CapitalDelta]\[Theta]8,10]]/n,Total[Part[\[CapitalDelta]\[Theta]8,11]]/n};
GPAD9={Total[Part[\[CapitalDelta]\[Theta]9,1]]/n,Total[Part[\[CapitalDelta]\[Theta]9,2]]/n,Total[
Part[\[CapitalDelta]\[Theta]9,3]]/n,Total[Part[\[CapitalDelta]\[Theta]9,4]]/n,Total[Part[\[Capita
lDelta]\[Theta]9,5]]/n,Total[Part[\[CapitalDelta]\[Theta]9,6]]/n,Total[Part[\[CapitalDelta]\[Thet
a]9,7]]/n,Total[Part[\[CapitalDelta]\[Theta]9,8]]/n,Total[Part[\[CapitalDelta]\[Theta]9,9]]/n,Tot
al[Part[\[CapitalDelta]\[Theta]9,10]]/n,Total[Part[\[CapitalDelta]\[Theta]9,11]]/n};
GPAD10={Total[Part[\[CapitalDelta]\[Theta]10,1]]/n,Total[Part[\[CapitalDelta]\[Theta]10,2]]/n,Tot
al[Part[\[CapitalDelta]\[Theta]10,3]]/n,Total[Part[\[CapitalDelta]\[Theta]10,4]]/n,Total[Part[\[C
apitalDelta]\[Theta]10,5]]/n,Total[Part[\[CapitalDelta]\[Theta]10,6]]/n,Total[Part[\[CapitalDelta
]\[Theta]10,7]]/n,Total[Part[\[CapitalDelta]\[Theta]10,8]]/n,Total[Part[\[CapitalDelta]\[Theta]10
,9]]/n,Total[Part[\[CapitalDelta]\[Theta]10,10]]/n,Total[Part[\[CapitalDelta]\[Theta]10,11]]/n};
GPAD11={Total[Part[\[CapitalDelta]\[Theta]11,1]]/n,Total[Part[\[CapitalDelta]\[Theta]11,2]]/n,Tot
al[Part[\[CapitalDelta]\[Theta]11,3]]/n,Total[Part[\[CapitalDelta]\[Theta]11,4]]/n,Total[Part[\[C
apitalDelta]\[Theta]11,5]]/n,Total[Part[\[CapitalDelta]\[Theta]11,6]]/n,Total[Part[\[CapitalDelta
]\[Theta]11,7]]/n,Total[Part[\[CapitalDelta]\[Theta]11,8]]/n,Total[Part[\[CapitalDelta]\[Theta]11
,9]]/n,Total[Part[\[CapitalDelta]\[Theta]11,10]]/n,Total[Part[\[CapitalDelta]\[Theta]11,11]]/n};
```

```
(*computation:  compile the final GPAD species NxN matrix*)
{GPAD={GPAD1,GPAD2,GPAD3,GPAD4,GPAD5,GPAD6,GPAD7,GPAD8,GPAD9,GPAD10,GPAD11},G1=LowerTriangularize
[GPAD];};

(*graphic:  line plots of \[Theta] and \[CapitalDelta]\[Theta] sequences*)
ListLinePlot[{aa3,ee3,Abs[aa3-ee3]},AxesLabel->{"Time","\[Theta]"},LabelStyle-
>Directive[Large],PlotStyle->{Thin, Thick, DotDashed},PlotLegends->{"Human","Gallus",
"\[CapitalDelta]\[Theta]"}, Filling->{3->Axis}]
ListPlot[{aa3,bb3,cc3,dd3,ee3,ff3,gg3,hh3,ii3,jj3,kk3},Joined->True]

(*graphic:  colored distance matrices and numerical values*)
"GPAD distance model"
{MatrixPlot[10*GPAD],Grid[LowerTriangularize[Round[GPAD,.001]]]}
"aa Equal input model"
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.074,0,0,0,0,0,0,0,0,0,0},{0.241,0.336,0,0,0,0,0,0,0,0,0},{0.156,0
.245,0.074,0,0,0,0,0,0,0,0},{0.455,0.581,0.398,0.518,0,0,0,0,0,0,0},{0.245,0.343,0.344,0.293,0.65
1,0,0,0,0,0,0},{0.397,0.515,0.344,0.455,0.58,0.199,0,0,0,0,0},{0,0.074,0.245,0.156,0.455,0.245,0.
397,0,0,0,0},{0.114,0.199,0.345,0.245,0.517,0.344,0.516,0.114,0,0,0},{0.453,0.578,0.514,0.453,0.6
47,0.646,0.721,0.453,0.514,0,0},{0.398,0.516,0.398,0.344,0.651,0.516,0.581,0.398,0.293,0.647,0}},
ss1=Total[Total[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
{MatrixPlot[10*ss2/ss1],Grid[ss],"avg. variance from GPAD:",Total[Total[Abs[G1-
ss]]]/(Length[GPAD1]^2/2)}

(*graphic and computation:  the following are computations for variance among species
\[CapitalDelta]\[Theta] sequences*)
"mean \[CapitalDelta]\[Theta] path (blue), max variance (Gallus-red), min variance (Human-green)"
{\[Theta]lists={aa3,bb3,cc3,dd3,ee3,ff3,gg3,hh3,ii3,jj3,kk3},mean=Total[\[Theta]lists]/11};
{Q1=ListLinePlot[aa3,Joined->True, PlotStyle->{Green,Thick,Dashed},LabelStyle-
>Directive[Medium]],Q2=ListLinePlot[jj3,Joined->True,PlotStyle->{Thick,Red,Dotted},PlotRange-
>All,LabelStyle->Directive[Large]],Q3=ListLinePlot[mean,Joined->True,PlotStyle->{Thick},Filling-
>Axis,LabelStyle->Directive[Large]]};
Show[Q1,Q2,Q3]
"species \[CapitalDelta]\[Theta] sample variance"
Insert[Grid[{{human,chimpanzee,goat, bovine, gallus, mouse, rat
,gorilla,rabbit,opossum,lemur},Round[GPADdfm={Total[Abs[mean-aa3]]/n,Total[Abs[mean-
bb3]]/n,Total[Abs[mean-cc3]]/n,Total[Abs[mean-dd3]]/n,Total[Abs[mean-ee3]]/n,Total[Abs[mean-
ff3]]/n,Total[Abs[mean-gg3]]/n,Total[Abs[mean-hh3]]/n,Total[Abs[mean-ii3]]/n,Total[Abs[mean-
jj3]]/n,Total[Abs[mean-kk3]]/n},.001]},ItemStyle->Bold],{Background-
>{None,{GrayLevel[0.7`],{White}}},Dividers->{Black,{2->Black}},Frame->True,Spacings-
>{2,{2,{0.7`},2}}},2]
Insert[Grid[{{human,gorilla,chimpanzee,rabbit,mouse,rat,bovine,goat,lemur,gallus,opossum},mscore=
Round[{ma=0.23284501764755344`,mh=0.23284501764755344`,mb=0.26520825221347477`,mi=0.2801537785626
766`,mf=0.3366484379469853`,mg=0.34801275899539164`,md=0.3865115704383374`,mc=0.3907329410343434`
,mk=0.41245681795049266`,me=0.4198599439243205`,mj=0.524309630621361`},.001]},ItemStyle-
>Bold],{Background->{None,{GrayLevel[0.7`],{White}}},Dividers->{Black,{2->Black}},Frame-
>True,Spacings->{2,{2,{0.7`},2}}},2]

(*computation:  set of 16 standardized distance measures for comparison to GPAD*)
"avgerage variance from GPAD for 16 standardized distance measures:"

"aa p-distance"
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.071,0,0,0,0,0,0,0,0,0,0},{0.214,0.286,0,0,0,0,0,0,0,0,0},{0.143,0
.214,0.071,0,0,0,0,0,0,0,0},{0.357,0.429,0.321,0.393,0,0,0,0,0,0,0},{0.214,0.286,0.286,0.25,0.464
,0,0,0,0,0,0},{0.321,0.393,0.286,0.357,0.429,0.179,0,0,0,0,0},{0,0.071,0.214,0.143,0.357,0.214,0.
321,0,0,0,0},{0.107,0.179,0.286,0.214,0.393,0.286,0.393,0.107,0,0,0},{0.357,0.429,0.393,0.357,0.4
64,0.464,0.5,0.357,0.393,0,0},{0.321,0.393,0.321,0.286,0.464,0.393,0.429,0.321,0.25,0.464,0}},ss1
=Total[Total[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
{MatrixPlot[10*ss2/ss1],Grid[ss]};
Total[Total[Abs[G1-ss]]]/(Length[GPAD1]^2/2)
"aa Equal input model"
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.074,0,0,0,0,0,0,0,0,0,0},{0.241,0.336,0,0,0,0,0,0,0,0,0},{0.156,0
.245,0.074,0,0,0,0,0,0,0,0},{0.455,0.581,0.398,0.518,0,0,0,0,0,0,0},{0.245,0.343,0.344,0.293,0.65
1,0,0,0,0,0,0},{0.397,0.515,0.344,0.455,0.58,0.199,0,0,0,0,0},{0,0.074,0.245,0.156,0.455,0.245,0.
397,0,0,0,0},{0.114,0.199,0.345,0.245,0.517,0.344,0.516,0.114,0,0,0},{0.453,0.578,0.514,0.453,0.6
47,0.646,0.721,0.453,0.514,0,0},{0.398,0.516,0.398,0.344,0.651,0.516,0.581,0.398,0.293,0.647,0}},
ss1=Total[Total[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
{MatrixPlot[10*ss2/ss1],Grid[ss]};
Total[Total[Abs[G1-ss]]]/(Length[GPAD1]^2/2)
"aa Poisson model"
```

```
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.074,0,0,0,0,0,0,0,0,0,0},{0.241,0.336,0,0,0,0,0,0,0,0,0},{0.154,0
.241,0.074,0,0,0,0,0,0,0,0},{0.442,0.56,0.388,0.499,0,0,0,0,0,0,0},{0.241,0.336,0.336,0.288,0.624
,0,0,0,0,0,0},{0.388,0.499,0.336,0.442,0.56,0.197,0,0,0,0,0},{0,0.074,0.241,0.154,0.442,0.241,0.3
88,0,0,0,0},{0.113,0.197,0.336,0.241,0.499,0.336,0.499,0.113,0,0,0},{0.442,0.56,0.499,0.442,0.624
,0.624,0.693,0.442,0.499,0,0},{0.388,0.499,0.388,0.336,0.624,0.499,0.56,0.388,0.288,0.624,0}},ss1
=Total[Total[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
{MatrixPlot[10*ss2/ss1],Grid[ss]};
Total[Total[Abs[G1-ss]]]/(Length[GPAD1]^2/2)

"aa Dayhoff model"
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.073,0,0,0,0,0,0,0,0,0,0},{0.234,0.33,0,0,0,0,0,0,0,0,0},{0.15,0.2
38,0.074,0,0,0,0,0,0,0,0},{0.463,0.593,0.404,0.517,0,0,0,0,0,0,0},{0.275,0.384,0.377,0.313,0.73,0
,0,0,0,0,0},{0.419,0.541,0.354,0.46,0.628,0.211,0,0,0,0,0},{0,0.073,0.234,0.15,0.463,0.275,0.419,
0,0,0,0},{0.107,0.187,0.315,0.228,0.5,0.355,0.5,0.107,0,0,0},{0.435,0.554,0.519,0.44,0.753,0.713,
0.81,0.435,0.469,0,0},{0.386,0.5,0.405,0.353,0.62,0.534,0.56,0.386,0.287,0.602,0}},ss1=Total[Tota
l[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
{MatrixPlot[10*ss2/ss1],Grid[ss]};
Total[Total[Abs[G1-ss]]]/(Length[GPAD1]^2/2)
"aa Jones-Taylor-Thornton (JTT) model"
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.076,0,0,0,0,0,0,0,0,0,0},{0.243,0.341,0,0,0,0,0,0,0,0,0},{0.156,0
.245,0.076,0,0,0,0,0,0,0,0},{0.493,0.629,0.425,0.546,0,0,0,0,0,0,0},{0.283,0.396,0.369,0.32,0.752
,0,0,0,0,0,0},{0.458,0.587,0.381,0.496,0.699,0.211,0,0,0,0,0},{0,0.076,0.243,0.156,0.493,0.283,0.
458,0,0,0,0},{0.112,0.196,0.329,0.237,0.538,0.375,0.554,0.112,0,0,0},{0.455,0.576,0.562,0.475,0.7
44,0.762,0.886,0.455,0.498,0,0},{0.402,0.518,0.427,0.371,0.645,0.553,0.601,0.402,0.299,0.655,0}},
ss1=Total[Total[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
{MatrixPlot[10*ss2/ss1],Grid[ss]};
Total[Total[Abs[G1-ss]]]/(Length[GPAD1]^2/2)

"aa DayhoffG model"
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.074,0,0,0,0,0,0,0,0,0,0},{0.239,0.342,0,0,0,0,0,0,0,0,0},{0.152,0
.244,0.074,0,0,0,0,0,0,0,0},{0.493,0.641,0.427,0.552,0,0,0,0,0,0,0},{0.286,0.404,0.396,0.326,0.79
7,0,0,0,0,0,0},{0.437,0.57,0.367,0.48,0.675,0.218,0,0,0,0,0},{0,0.074,0.239,0.152,0.493,0.286,0.4
37,0,0,0,0},{0.108,0.191,0.322,0.231,0.531,0.366,0.518,0.108,0,0,0},{0.451,0.582,0.545,0.457,0.81
6,0.756,0.864,0.451,0.487,0,0},{0.397,0.521,0.423,0.366,0.664,0.558,0.586,0.397,0.295,0.63,0}},ss
1=Total[Total[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
{MatrixPlot[10*ss2/ss1],Grid[ss]};
Total[Total[Abs[G1-ss]]]/(Length[GPAD1]^2/2)
"aa Jones-Taylor-Thornton (JTT) G"
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.077,0,0,0,0,0,0,0,0,0,0},{0.249,0.352,0,0,0,0,0,0,0,0,0},{0.158,0
.251,0.076,0,0,0,0,0,0,0,0},{0.523,0.674,0.448,0.582,0,0,0,0,0,0,0},{0.295,0.416,0.384,0.332,0.81
5,0,0,0,0,0,0},{0.481,0.622,0.397,0.52,0.754,0.216,0,0,0,0,0},{0,0.077,0.249,0.158,0.523,0.295,0.
481,0,0,0,0},{0.113,0.199,0.336,0.24,0.569,0.387,0.578,0.113,0,0,0},{0.471,0.602,0.59,0.494,0.806
,0.806,0.947,0.471,0.515,0,0},{0.413,0.537,0.446,0.386,0.688,0.578,0.631,0.413,0.306,0.683,0}},ss
1=Total[Total[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
{MatrixPlot[10*ss2/ss1],Grid[ss]};
Total[Total[Abs[G1-ss]]]/(Length[GPAD1]^2/2)
"kimura2"
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.049,0,0,0,0,0,0,0,0,0,0},{0.116,0.174,0,0,0,0,0,0,0,0,0},{0.088,0
.144,0.049,0,0,0,0,0,0,0,0},{0.361,0.442,0.286,0.322,0,0,0,0,0,0,0},{0.189,0.253,0.22,0.204,0.508
,0,0,0,0,0,0},{0.252,0.322,0.27,0.305,0.558,0.16,0,0,0,0,0},{0,0.049,0.116,0.088,0.361,0.189,0.25
2,0,0,0,0},{0.102,0.158,0.189,0.144,0.399,0.236,0.342,0.102,0,0,0},{0.362,0.402,0.402,0.366,0.443
,0.508,0.583,0.362,0.42,0,0},{0.256,0.325,0.27,0.221,0.42,0.304,0.4,0.256,0.272,0.494,0}},ss1=Tot
al[Total[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
{MatrixPlot[10*ss2/ss1],Grid[ss]};
Total[Total[Abs[G1-ss]]]/(Length[GPAD1]^2/2)
"jukes-cantor"
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.049,0,0,0,0,0,0,0,0,0,0},{0.116,0.173,0,0,0,0,0,0,0,0,0},{0.088,0
.144,0.049,0,0,0,0,0,0,0,0},{0.36,0.441,0.286,0.322,0,0,0,0,0,0,0},{0.188,0.252,0.22,0.204,0.508,
0,0,0,0,0,0},{0.252,0.322,0.269,0.304,0.556,0.158,0,0,0,0,0},{0,0.049,0.116,0.088,0.36,0.188,0.25
2,0,0,0,0},{0.102,0.158,0.188,0.144,0.399,0.236,0.341,0.102,0,0,0},{0.36,0.399,0.399,0.36,0.441,0
.508,0.582,0.36,0.42,0,0},{0.252,0.322,0.269,0.22,0.42,0.304,0.399,0.252,0.269,0.485,0}},ss1=Tota
l[Total[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
{MatrixPlot[10*ss2/ss1],Grid[ss]};
Total[Total[Abs[G1-ss]]]/(Length[GPAD1]^2/2)
"Tamura3"
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.049,0,0,0,0,0,0,0,0,0,0},{0.116,0.174,0,0,0,0,0,0,0,0,0},{0.088,0
.144,0.049,0,0,0,0,0,0,0,0},{0.363,0.445,0.288,0.324,0,0,0,0,0,0,0},{0.189,0.254,0.22,0.204,0.511
,0,0,0,0,0,0},{0.253,0.323,0.27,0.306,0.562,0.160,0,0,0,0,0},{0,0.049,0.116,0.088,0.363,0.189,0.2
53,0,0,0,0},{0.102,0.159,0.189,0.144,0.402,0.236,0.343,0.102,0,0,0},{0.363,0.403,0.404,0.367,0.44
4,0.509,0.584,0.363,0.420,0,0},{0.256,0.326,0.27,0.222,0.421,0.305,0.4,0.256,0.273,0.495,0}},ss1=
Total[Total[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
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```
{MatrixPlot[10*ss2/ss1],Grid[ss]};
Total[Total[Abs[G1-ss]]]/(Length[GPAD1]^2/2)
"Tajima-Nei"
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.05,0,0,0,0,0,0,0,0,0,0},{0.119,0.181,0,0,0,0,0,0,0,0,0},{0.091,0.
15,0.05,0,0,0,0,0,0,0,0},{0.388,0.489,0.297,0.337,0,0,0,0,0,0,0},{0.194,0.263,0.231,0.214,0.547,0
,0,0,0,0,0},{0.257,0.333,0.281,0.32,0.603,0.163,0,0,0,0,0},{0,0.05,0.119,0.091,0.388,0.194,0.257,
0,0,0,0},{0.105,0.165,0.198,0.149,0.418,0.241,0.349,0.105,0,0,0},{0.375,0.426,0.414,0.377,0.457,0
.525,0.617,0.375,0.429,0,0},{0.27,0.351,0.282,0.228,0.433,0.325,0.435,0.27,0.28,0.528,0}},ss1=Tot
al[Total[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
{MatrixPlot[10*ss2/ss1],Grid[ss]};
Total[Total[Abs[G1-ss]]]/(Length[GPAD1]^2/2)
"Maximum Likelihood"
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.05,0,0,0,0,0,0,0,0,0,0},{0.118,0.178,0,0,0,0,0,0,0,0,0},{0.088,0.
145,0.05,0,0,0,0,0,0,0,0},{0.368,0.452,0.299,0.335,0,0,0,0,0,0,0},{0.194,0.261,0.225,0.208,0.534,
0,0,0,0,0,0},{0.269,0.345,0.281,0.317,0.589,0.162,0,0,0,0,0},{0,0.05,0.118,0.088,0.368,0.194,0.26
9,0,0,0,0},{0.102,0.16,0.195,0.147,0.425,0.249,0.367,0.102,0,0,0},{0.377,0.416,0.433,0.381,0.487,
0.549,0.632,0.377,0.458,0,0},{0.257,0.329,0.281,0.227,0.468,0.315,0.411,0.257,0.284,0.503,0}},ss1
=Total[Total[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
{MatrixPlot[10*ss2/ss1],Grid[ss]};
Total[Total[Abs[G1-ss]]]/(Length[GPAD1]^2/2)
"JC+G"
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.05,0,0,0,0,0,0,0,0,0,0},{0.117,0.177,0,0,0,0,0,0,0,0,0},{0.089,0.
147,0.05,0,0,0,0,0,0,0,0},{0.377,0.468,0.298,0.336,0,0,0,0,0,0,0},{0.193,0.261,0.226,0.21,0.544,0
,0,0,0,0,0},{0.261,0.336,0.279,0.317,0.6,0.162,0,0,0,0,0},{0,0.05,0.117,0.089,0.377,0.193,0.261,0
,0,0,0},{0.103,0.162,0.193,0.147,0.421,0.243,0.357,0.103,0,0,0},{0.377,0.421,0.421,0.377,0.468,0.
544,0.629,0.377,0.444,0,0},{0.261,0.336,0.279,0.226,0.444,0.317,0.421,0.261,0.279,0.518,0}},ss1=T
otal[Total[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
{MatrixPlot[10*ss2/ss1],Grid[ss]};
Total[Total[Abs[G1-ss]]]/(Length[GPAD1]^2/2)
"LogDet (Tamura-Kumar)"
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.047,0,0,0,0,0,0,0,0,0,0},{0.118,0.181,0,0,0,0,0,0,0,0,0},{0.095,0
.156,0.05,0,0,0,0,0,0,0,0},{0.391,0.5,0.293,0.334,0,0,0,0,0,0,0},{0.2,0.273,0.253,0.232,0.539,0,0
,0,0,0,0},{0.26,0.343,0.297,0.348,0.64,0.165,0,0,0,0,0},{0,0.047,0.118,0.095,0.391,0.2,0.26,0,0,0
,0},{0.118,0.183,0.206,0.157,0.408,0.245,0.356,0.118,0,0,0},{0.379,0.454,0.401,0.368,0.425,0.549,
0.686,0.379,0.434,0,0},{0.281,0.376,0.294,0.234,0.39,0.365,0.52,0.281,0.281,0.574,0}},ss1=Total[T
otal[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
{MatrixPlot[10*ss2/ss1],Grid[ss]};
Total[Total[Abs[G1-ss]]]/(Length[GPAD1]^2/2)
"Tamura-Nei model"
{ss={{0,0,0,0,0,0,0,0,0,0,0},{0.05,0,0,0,0,0,0,0,0,0,0},{0.118,0.179,0,0,0,0,0,0,0,0,0},{0.091,0.
151,0.05,0,0,0,0,0,0,0,0},{0.396,0.509,0.298,0.34,0,0,0,0,0,0,0},{0.194,0.263,0.23,0.213,0.561,0,
0,0,0,0,0},{0.254,0.328,0.278,0.318,0.622,0.162,0,0,0,0,0},{0,0.05,0.118,0.091,0.396,0.194,0.254,
0,0,0,0},{0.105,0.166,0.193,0.147,0.42,0.24,0.348,0.105,0,0,0},{0.374,0.425,0.409,0.374,0.448,0.5
27,0.611,0.374,0.428,0,0},{0.271,0.357,0.279,0.228,0.425,0.321,0.447,0.271,0.278,0.55,0}},ss1=Tot
al[Total[ss2=ss+Transpose[ss]]](*ss1 and ss2 are for matrix coloring purposes only*)};
{MatrixPlot[10*ss2/ss1],Grid[ss]};
Total[Total[Abs[G1-ss]]]/(Length[GPAD1]^2/2)
```