CONSTRUCTIVE MATHEMATICAL ANALYSIS
7 (2024), No. SI, pp. 27-36
http://dergipark.org.tr/en/pub/cma
ISSN 2651 - 2939

Research Article

Hadamard matrices of genetic code and trigonometric functions

Dedicated to Professor Paolo Emilio Ricci, on occasion of his 80th birthday, with respect and friendship.

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ABSTRACT. Algebraic theory of coding is one of the modern fields of applications of algebra. Genetic matrices and algebraic biology have been the latest advances in further understanding of the patterns and rules of genetic code. Genetics code is encoded in combinations of the four nucleotides (A, C, G, T) found in DNA and then RNA. DNA defines the structure and function of an organism and contains complete genetic information. DNA paired bases of (A, C, G, T) form a geometric curve of double helix, define the 64 standard genetic triplets, and further degenerate 64 genetic codons into 20 amino acids. In trigonometry, four basic trigonometric functions ($\sin x, \tan x, \cos x, \cot x$) provided bases for Fourier analysis to encode signal information. In this paper, we use these 4 paired bases of trigonometric functions ($\sin x, \tan x, \cos x$, and $\cot x$) to generate 64 trigonometric triplets like 64 standard genetic code, further examine these 64 trigonometric functions and obtained 20 trigonometric triplets like 20 amino acids. This parallel shows a similarity connection between universal genetic codes and the universality of trigonometric functions. This connection may provide a bridge to further uncover patterns of genetic code. This demonstrates that matrix algebra is one of promising instruments and of adequate languages in bioinformatics and algebraic biology.

Keywords: Hadamard matrix, trigonometric functions, genetic code, algebraic biology.

2020 Mathematics Subject Classification: 15A15, 33B10, 92B05.

1. INTRODUCTION

The genetic code is encoded in combinations of the four nucleotides (A, C, G, T) found in DNA and the four nucleotides (A, C, G, U) found in RNA.The complementary pairs of the four nitrogenous bases in DNA are A-T (adenine and thymine), C-G (cytosine and guanine). The following table gives a complete list of 64 triplets (codons) with corresponding 20 amino acids with three (one) letter code and stop codons.

Table 1 shows that there are 64 triplets or codons. One can see that some amino acids are encoded by several different but related base triplets. Also three triplets (UAA, UAG, and UGA) are stop codons. No amino acids are corresponding to their code. The remaining 61 triplets represent 20 different amino acids. Petoukhov [18] showed the "Biperiodic table of genetic code" as illustrated below:

8×8 matrix table Table 2 shows a great symmetrical structure and has led to many discoveries [8, 9, 10, 11, 12]. By using three fundamental attributive mappings, the stochastic characteristic of the biperiodic table and symmetries in structure of genetic code were recently investigated in [8, 9, 10, 11, 12].

Received: 27.08.2024; Accepted: 04.10.2024; Published Online: 16.12.2024
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DOI: 10.33205/cma.1539666

TABLE 1. The universal genetic code and amino acids.

First Position	**Second Position of Codon**				**Third Position**
	U	**C**	**A**	**G**	
U	UUU Phe [F]	UCU Ser [S]	UAU Tyr [Y]	UGU Cys [C]	**U**
	UUC Phe [F]	UCC Ser [S]	UAC Tyr [Y]	UGC Cys [C]	**C**
	UUA Leu [L]	UCA Ser [S]	UAA Ter [end]	UGA Ter [end]	**A**
	UUG Leu [L]	UCG Ser [S]	UAG Ter [end]	UGG Trp [W]	**G**
C	CUU Leu [L]	CCU Pro [P]	CAU His [H]	CGU Arg [R]	**U**
	CUC Leu [L]	CCC Pro [P]	CAC His [H]	CGC Arg [R]	**C**
	CUA Leu [L]	CCA Pro [P]	CAA Gln [Q]	CGA Arg [R]	**A**
	CUG Leu [L]	CCG Pro [P]	CAG Gln [Q]	CGG Arg [R]	**G**
A	AUU Ile [I]	ACU Thr [T]	AAU Asn [N]	AGU Ser [S]	**U**
	AUC Ile [I]	ACC Thr [T]	AAC Asn [N]	AGC Ser [S]	**C**
	AUA Ile [I]	ACA Thr [T]	AAA Lys [K]	AGA Arg [R]	**A**
	AUG Met [M]	ACG Thr [T]	AAG Lys [K]	AGG Arg [R]	**G**
G	GUU Val [V]	GCU Ala [A]	GAU Asp [D]	GGU Gly [G]	**U**
	GUC Val [V]	GCC Ala [A]	GAC Asp [D]	GGC Gly [G]	**C**
	GUA Val [V]	GCA Ala [A]	GAA Glu [E]	GGA Gly [G]	**A**
	GUG Val [V]	GCG Ala [A]	GAG Glu [E]	GGG Gly [G]	**G**

TABLE 2. Biperiodic table of genetic code.

CCC	CCA	CAC	CAA	ACC	ACA	AAC	AAA
CCU	CCG	CAU	CAG	ACU	ACG	AAU	AAG
CUC	CUA	CGC	CGA	AUC	AUA	AGC	AGA
CUU	CUG	CGU	CGG	AUU	AUG	AGU	AGG
UCC	UCA	UAC	UAA	GCC	GCA	GAC	GAA
UCU	UCG	UAU	UAG	GCU	GCG	GAU	GAG
UUC	UUA	UGC	UGA	GUC	GUA	GGC	GGA
UUU	UUG	UGU	UGG	GUU	GUG	GGU	GGG

Genetic information is transferred by means of discrete elements: 4 letters of the genetic alphabet, 64 triplets, 20 amino acids, etc. General theory of signal processing utilizes the encoding of discrete signals by means of special mathematical matrices and spectral representations of signals to increase reliability and efficiency of information transfer [25, 1]. This paper considers classical trignometric functions of $\sin x, \cos x, \tan x$ and $\cot x$. These four functions form the complementary pairs $\sin x$ and $\cos x$, $\tan x$ and $\cot x$. In this paper, we use these 4 paired bases of trigonometric functions ($\sin x, \cos x, \tan x$, and $\cot x$) to generate 64 triplets similar to 64 standard genetic code, further examine these 64 trigonometric functions and obtained 20 trigonometric functions similar to 20 amino acids. This parallel shows a similarity connection between universal genetic codes and the universality of trigonometric functions. This connection may provide a bridge to further uncover patterns of genetic code. This deomnstrates that matrix algebra is one of promising instruments and of adequate languages in bioinformatics and algebraic biology.

2. HADAMARD MATRICES

By a definition a Hadamard matrix of dimension "n" is the $(n \times n)-$matrix $H(n)$ with elements "$+1$" and "-1". It satisfies the condition

$$H(n) * H(n)^T = n * I_n, \tag{2.1}$$

where $H(n)^T$ is the transposed matrix and $H(n)$ is the $(n * n)$-identity matrix. The Hadamard matrices of dimension 2^k are formed, for example, by the recursive formula $H(2^k) = H(2)^{(k)} = H(2) \otimes H(2^{k-1})$ for $2 \le k \in N$, where $\otimes$ denotes the Kronecker (or tensor) product, (k) means the Kronecker exponentiation, k and N are integers, $H(2)$ is showed in Figure 1. In this article, we will mark by black (white) color all cells in Hadamard matrices which contain the element "$+1$" (the element "-1" correspondingly).

Rows of a Hadamard matrix are mutually orthogonal. It means that every two different rows in a Hadamard matrix represent two perpendicular vectors, a scalar product of which is equal to 0. The element "-1" can be disposed in any of four positions in a Hadamard matrix $H(2)$.

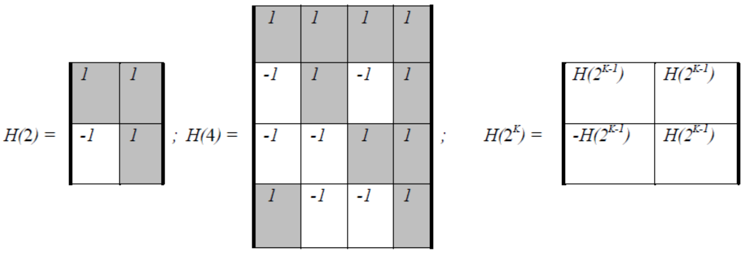

FIGURE 1. The family of Hadamard matrices $H(2^k)$ based on the Kronecker product. Matrix cells with elements "$+1$" are marked by black color.

A Kronecker product of two Hadamard matrices is a Hadamard matrix as well. A permutation of any columns or rows of a Hadamard matrix leads to a new Hadamard matrix. Hadamard matrices and their Kronecker powers are used widely in spectral methods of analysis and processing of discrete signals and in quantum computers. A transform of a vector $\bar{\mathbf{a}}$ by means of a Hadamard matrix H gives the vector $\bar{\mathbf{u}} = H * \bar{\mathbf{a}}$, which is named Hadamard spectrum. A greater analogy between Hadamard transforms and Fourier transforms exists [1]. In particular the fast Hadamard transform exists in parallel with the fast Fourier transform. The whole class of multichannel "spectrometers with Hadamard transforms" is known [27], where the principle of tape masks (or chain masks) is used, and it reminds one of the principles of a chain construction of genetic texts in DNA. Hadamard matrices are used widely in the theory of coding (for example, they are connected with Reed-Muller error correcting codes and with Hadamard codes [17]), the theory of compression of signals and images, a realization of Boolean functions by means of spectral methods, the theory of planning of multiple-factor experiments and in many other branches of mathematics.

Rows of Hadamard matrices are called Walsh functions or Hadamard functions which are used for a spectral presentation and a transfer of discrete signals [1, 3, 31]. Walsh functions can be represented in terms of product of Rademacher functions $r_n(t) = \text{sign}(\sin 2^n \pi t), n = 1, 2, 3, \ldots,$ which accept the two values "$+1$" and "-1" only (here "sign" is the function of a sign on argument). Sets of numerated Walsh functions (or Hadamard functions), when they are united in square matrices, form systems depending on features of such union. Hadamard matrices are connected with Walsh-Hadamard transforms, which are the most famous among non-sinusoidal orthogonal transforms and which can be calculated by means of mathematical operations of addition and subtraction only (see more details in [1, 28, 31]). Hereinafter we will use the simplified designations of matrix elements on illustrations of Hadamard matrices: the symbol "+" or the black color of a matrix cell means the element "$+1$"; the the symbol "$-$" or the white color of a matrix cell means the element "-1". The theory of discrete signals pays special attention to quantities of changes of signs "+" and "$-$" along each row and each column in Hadamard matrices. These quantities are connected with an important notion of "sequency" as a generalization of notion of "frequency" [1, p. 85]. Normalized Hadamard matrices are unitary operators. They serve as one of the important instruments to create quantum computers, which utilize so called Hadamard gates (as evolution of the closed quantum system is unitary) [16].

Algebraic biology knows already examples of applications of Walsh functions (alongside with other systems of basic functions) to spectral analysis of various aspects of genetic algorithms and sequences [6, 2, 5, 14, 24, 31, 32]. The book [32] contains a review of investigations made by various authors about Walsh orthogonal functions in physiological systems of supra-cellular levels as well. We investigate whether structures of the genetic code have such direct relations with Hadamard matrices which can justify systematic applications of Walsh-Hadamard functions to spectral and other analysis of many inherited biological structures of various levels. This paper proposes relevant evidences about connections of Hadamard matrices with the genetic code in its Kronecker's matrix form of presentation.

We note that standard genetic code can be constructed by Kronecker product process from a 2×2 to 4×4 and then 8×8 matrices as illustrated in Figure 2.

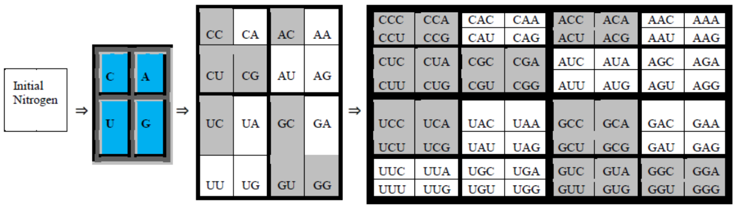

FIGURE 2. Genetic code matrices.

This 8×8 matrix represents a universal genetic code. It served as a basis for the central dogma of microbiology (DNA→RNA→Protein). The shapes of DNA motions form DNA double hélix [7]. Mathematical structure of DNA code has been viewed as the other secrets of life [26]. Four bases of trignometric functions of $\sin x, \cos x, \tan x$, and $\cot x$ may offer further insights of DNA bases of A, C, G, and T.

3. HADAMARD MATRIX OF TRIGONOMETRIC FUNCTIONS

The fundamental elements of trigonometry are $\sin x, \cos x, \tan x$, and $\cot x$. These 4 elements form the trigonometry relation base pairs $T = [\sin x, \tan x; \cos x, \cot x]$ like DNA base pairs [A, T; G, C]. This T matrix evolves from a 2×2 matrix to a 4×4 matrix and then to an 8×8 matrix as illustrated below:

TABLE 3. 2×2 matrix $T^{[1]}$.

$\sin x$	$\tan x$
$\cot x$	$\cos x$

TABLE 4. 4×4 matrix $T^{[2]}$.

$\sin x \sin x$	$\sin x \tan x$	$\tan x \sin x$	$\tan x \tan x$
$\sin x \cot x$	$\sin x \cos x$	$\tan x \cot x$	$\tan x \cos x$
$\cot x \sin x$	$\cot x \tan x$	$\cos x \sin x$	$\cos x \tan x$
$\cot x \cot x$	$\cot x \cos x$	$\cos x \cot x$	$\cos x \cos x$

TABLE 5. 8×8 matrix $T^{[3]}$.

$\sin x \sin x \sin x$	$\sin x \sin x \tan x$	$\sin x \tan x \sin x$	$\sin x \tan x \tan x$	$\tan x \sin x \sin x$	$\tan x \sin x \tan x$	$\tan x \tan x \sin x$	$\tan x \tan x \tan x$
$\sin x \sin x \cot x$	$\sin x \sin x \cos x$	$\sin x \tan x \cot x$	$\sin x \tan x \cos x$	$\tan x \sin x \cot x$	$\tan x \sin x \cos x$	$\tan x \tan x \cot x$	$\tan x \tan x \cos x$
$\sin x \cot x \sin x$	$\sin x \cot x \tan x$	$\sin x \cos x \sin x$	$\sin x \cos x \tan x$	$\tan x \cot x \sin x$	$\tan x \cot x \tan x$	$\tan x \cos x \sin x$	$\tan x \cos x \tan x$
$\sin x \cot x \cot x$	$\sin x \cot x \cos x$	$\sin x \cos x \cot x$	$\sin x \cos x \cos x$	$\tan x \cot x \cot x$	$\tan x \cot x \cos x$	$\tan x \cot x \cos x$	$\tan x \cos x \cos x$
$\cot x \sin x \sin x$	$\cot x \sin x \tan x$	$\cot x \tan x \sin x$	$\cot x \tan x \tan x$	$\cos x \sin x \sin x$	$\cos x \sin x \tan x$	$\cos x \tan x \sin x$	$\cos x \tan x \tan x$
$\cot x \sin x \cot x$	$\cot x \sin x \cos x$	$\cot x \tan x \cot x$	$\cot x \tan x \cos x$	$\cos x \sin x \cot x$	$\cos x \sin x \cos x$	$\cos x \tan x \cot x$	$\cos x \tan x \cos x$
$\cot x \cot x \sin x$	$\cot x \cot x \tan x$	$\cot x \cos x \sin x$	$\cot x \cos x \tan x$	$\cos x \cot x \sin x$	$\cos x \cot x \tan x$	$\cos x \cos x \sin x$	$\cos x \cos x \tan x$
$\cot x \cot x \cot x$	$\cot x \cot x \cos x$	$\cot x \cos x \cot x$	$\cot x \cos x \cos x$	$\cos x \cot x \cot x$	$\cos x \cot x \cos x$	$\cos x \cos x \cot x$	$\cos x \cos x \cos x$

Either addition or multiplication can be applied to each cell of these 64 triplets as illustrated below in the case of **multiplication operation**:

TABLE 6. 8×8 matrix $T^{[3]}$ with multiplication $(\times)$.

$\sin^3 x$	$\sin^2 x \tan x$	$\sin^2 x \tan x$	$\tan^2 x \sin x$	$\sin^2 x \tan x$	$\tan^2 x \sin x$	$\tan^2 x \sin x$	$\tan^3 x$
$\sin^2 x \cot x$	$\sin^2 x \cos x$	$\sin x \tan x \cot x$	$\sin x \tan x \cos x$	$\tan x \sin x \cot x$	$\tan x \sin x \cos x$	$\tan^2 x \cot x$	$\tan^2 x \cos x$
$\sin^2 x \cot x$	$\sin x \cot x \tan x$	$\sin^2 x \cos x$	$\sin x \cos x \tan x$	$\tan x \cot x \sin x$	$\tan^2 x \cot x$	$\tan x \cos x \sin x$	$\tan^2 x \cos x$
$\cot^2 x \sin x$	$\sin x \cot x \cos x$	$\sin x \cos x \cot x$	$\cos^2 x \sin x$	$\cos^2 x \tan x$	$\tan x \cot x \cos x$	$\tan x \cos x \cot x$	$\cos^2 x \tan x$
$\sin^2 x \cot x$	$\cot x \sin x \tan x$	$\cot x \tan x \sin x$	$\tan^2 x \cot x$	$\sin^2 x \cos x$	$\cos x \sin x \tan x$	$\cos x \tan x \sin x$	$\tan^2 x \cos x$
$\cot^2 x \sin x$	$\cot x \sin x \cos x$	$\cot^2 x \tan x$	$\cot x \tan x \cos x$	$\cos x \sin x \cot x$	$\cos^2 x \sin x$	$\cos x \tan x \cot x$	$\cos^2 x \tan x$
$\cot^2 x \sin x$	$\cot^2 x \tan x$	$\cot x \cos x \sin x$	$\cot x \cos x \tan x$	$\cos x \cot x \sin x$	$\cos x \cot x \tan x$	$\cos^2 x \sin x$	$\cos^2 x \tan x$
$\cot^3 x$	$\cot^2 x \cos x$	$\cot^2 x \cos x$	$\cos^2 x \cot x$	$\cot^2 x \cos x$	$\cos^2 x \cot x$	$\cos^2 x \cos x$	$\cos^3 x$

This 8×8 matrix has 64 cells. Applying addition or multiplication operation to each cell, it degenerates into 20 different cells due to the commutative nature of addition/multiplication operation like 20 amino were acids degenerated from the 64 universal genetic code. These 20 different cells and frequency distribution are illustrated below:

TABLE 7. Trigonometric functions.

Different Matrix Cell with Addition $(+)$	Different Matrix Cell with Addition $(\times)$	Frequency from 8×8 Matrix $T^{[3]}$
$3\sin x$	$\sin^3 x$	1
$3\cos x$	$\cos^3 x$	1
$3\tan x$	$\tan^3 x$	1
$3\cot x$	$\cot^3 x$	1
$2\sin x + \cos x$	$\sin^2 x \cos x$	3
$2\sin x + \tan x$	$\sin^2 x \tan x$	3
$2\sin x + \cot x$	$\sin^2 x \cot x$	3
$2\cos x + \sin x$	$\cos^2 x \sin x$	3
$2\cos x + \tan x$	$\cos^2 x \tan x$	3
$2\cos x + \cot x$	$\cos^2 x \cot x$	3
$2\tan x + \sin x$	$\tan^2 x \sin x$	3
$2\tan x + \cos x$	$\tan^2 x \cos x$	3
$2\tan x + \cot x$	$\tan^2 x \cot x$	3
$2\cot x + \sin x$	$\cot^2 x \sin x$	3
$2\cot x + \cos x$	$\cot^2 x \cos x$	3
$2\cot x + \tan x$	$\cot^2 x \tan x$	3
$\sin x + \cos x + \tan x$	$\sin x \cos x \tan x$	6
$\sin x + \cos x + \cot x$	$\sin x \cos x \cot x$	6
$\sin x + \tan x + \cot x$	$\sin x \tan x \cot x$	6
$\cos x + \tan x + \cot x$	$\cos x \tan x \cot x$	6
20	**20**	**64**

Each cell of this matrix represents an relation curve. The graphical representations of these curves (with addition/multiplication) are shown below:

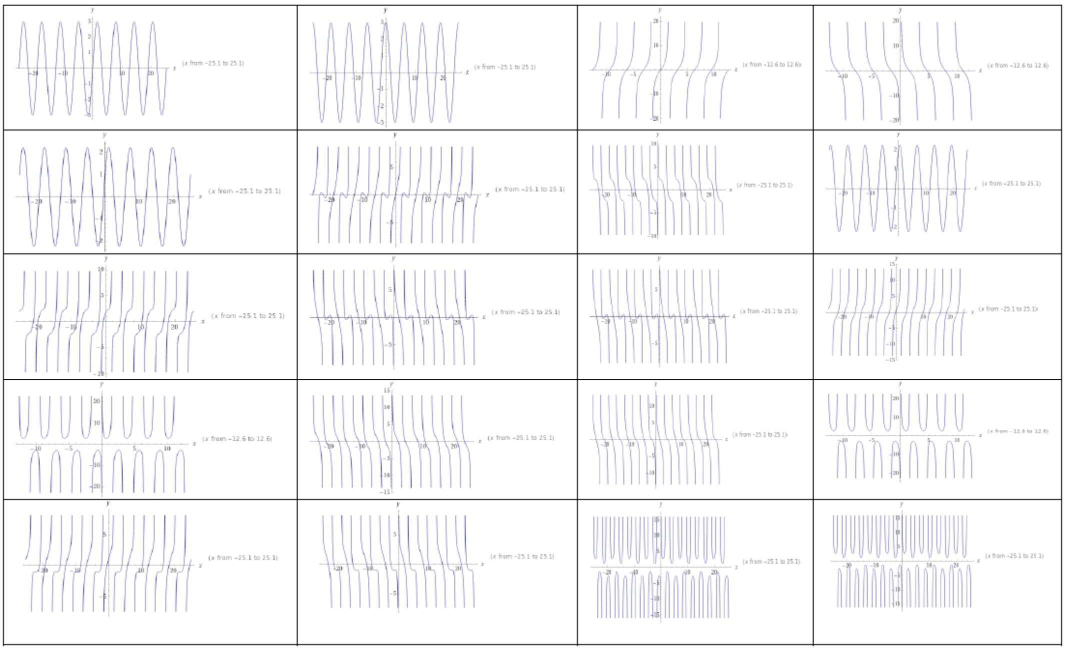

FIGURE 3. Twenty trigonometric curves with addition.

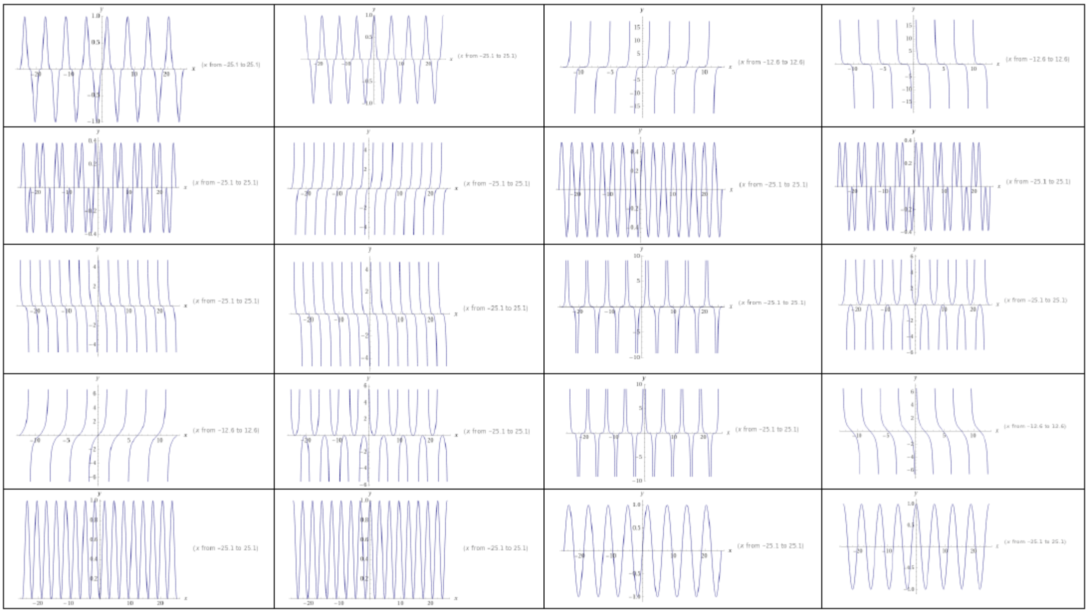

FIGURE 4. Twenty trigonometric curves with multiplication.

These curves are either bounded or unbounded. These curves may serve as basis to model the expressions of human thoughts like the 20 amino acids as the building blocks of the proteins. The orthogonal relationships of sine and cosine functions along with these building blocks of thinking frequency curves provide the basis for Fourier series that can be used to represent various thinking frequency curves. Throughout the history of humankind, trigonometry as human mind activities, has been applied in almost every area from geometry to nature [24].

4. MATRIX GENETICS AND ALGEBRAIC BIOLOGY

Matrix genetics which can be interpreted as a part of algebraic biology on the genetic systems by means of their matrix forms of presentation. One can name additionally the following main reasons for an initial choice of such form of presentation of molecular ensembles of the genetic code:

- Information is usually stored in computers in the form of matrices.
- Noise-immunity codes are constructed on the basis of matrices.
- Quantum mechanics utilizes matrix operators through the connections with matrix forms of presentation of the genetic code. The significance of matrix approach is emphasized by the fact that quantum mechanics arises in a form of matrix mechanics as formulated by W. Heisenberg.
- Complex and hypercomplex numbers, which are utilized in physics and mathematics, possess matrix forms of their presentation. The notion of number is the main notion of mathematics and mathematical natural sciences. In view of this, investigation of a possible connection of the genetic code to multi-dimensional numbers in their matrix presentations can lead to very significant results.

- Matrix analysis is one of the main investigation tools in mathematical natural sciences. The study of possible analogies between matrices, which are specific for the genetic code, and famous matrices from other branches of sciences can be heuristic and useful.
- Matrices, which are a kind of union of many components in a single whole, are subordinated to certain mathematical operations, which determine substantial connections between collectives of many components. These kinds of connections can be essential for collectives of genetic elements of different levels as well.

Matrix genetics are developed during last decade intensively [8, 9, 10, 11, 18, 19, 20, 21, 22]. Let us list some of interesting results which were obtained in these works:

- new phenomenological rules of evolution of the genetic code;
- multi-dimensional algebras for modelling and for analysing the genetic code systems;
- hidden interrelations between the golden section and parameters of genetic multiplets;
- relations between the Pythagorean musical scale and an important class of quint genetic matrices which show a molecular genetic basis with a sense of musical harmony and of aesthetics of proportions;
- cyclic algebraic principles in the structure of matrices of the genetic code;
- materials for a chronocyclic conception, which connects structures of the genetic system with chrono-medicine and a problem of an internal clock of organisms, etc.

Spectral methods of decomposition of signals on orthogonal systems of functions such as $\sin(x)$ and $\cos(x)$ have proved themselves for a long time as especially important in the theory of signals and informatics in general. Researchers of genetic informatics attempt to address to them already (see, for example, the works [13, 15] which pay attention to the importance of spectral methods in this field). But an infinite quantity of orthogonal systems of functions exists. It is difficult for researchers of molecular-genetic systems to make a choice of one of infinite number of possible orthogonal systems as an adequate one for spectral methods in the field of genetic informatics. They should make here rather a volitional choice, risking the waste of many years of work in the case of the failure of such a choice. They make this choice usually, proceeding from secondary reasons, which do not have a direct relation to genetic systems. For example, they choose the system of orthogonal harmonious functions, which is applied in the classical frequency Fourier-analysis, because this system has extensive applications in technical fields.

The results described in our article show the relation of the genetic code with the orthogonal systems of functions, which relate to Hadamard matrices, and which possess a special meaning for genetic informatics and its spectral methods. The orthogonal systems of functions connected with Hadamard matrixes are picked out by nature from the infinite set of basic systems for their deep connection with an essence of molecular-genetic coding. A consistent investigation of bioinformatics systems should be done from the viewpoint of the theory of Hadamard matrices and their applications. In particular, the comparative analysis of various genetic sequences on their Hadamard spectrums is interesting. The described results give important help in a choice of research tool from an infinite set of orthogonal systems of functions and from a set of variants of noise-immunity codes.

In the spectral analysis of genetic sequences (for example, their correlation functions), it is meaningful to spend their decomposition on orthogonal vectors-rows of Hadamard genomatrices, instead of on trigonometric functions of the frequency Fourier-analysis. Investigations of Hadamard spectrums in mathematical genetics are perspective and well-founded. Especially since some works are already known as applications of Walsh functions (alongside with other systems of basic functions) to spectral analysis of various aspects of genetic algorithms and sequences [6, 2, 5, 14, 23, 29, 30]. The book [32, p. 416] contains a review of works about applications of Walsh orthogonal functions in some other fields of physiology.

The discovery of connections of the genetic matrices with Hadamard matrices leads to many new possible investigations using methods of symmetries, of spectral analysis, etc. One can expect that those Walsh-Hadamard functions, which are related to the described genetic Hadamard matrices, will be used effectively in the spectral analysis of genetic sequences. It seems that investigations of structural and functional principles of bio-information systems from the viewpoint of quantum computers and of unitary Hadamard operators are very promising. A comparison of orthogonal systems of Walsh-Hadamard functions in molecular-genetic structures and in genetically inherited macro-physiological systems can give new understanding to an interrelation of various levels in biological organisms. Data about the genetic Hadamard matrices together with data about algebras of the genetic code can lead to new understanding of genetic code systems, to new effective algorithms of information processing and, perhaps, to new directions in the field of quantum computers.

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