THE GENETIC CODE: A CASE OF RESIDUE NUMBER SYSTEM (RNS)

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ABSTRACT

Cracking the code of life marked an interesting and significant beginning of life science. The genetic code maps the 20 amino acids to all 64 possible arrangements of the four (4) nitrogenous bases. Since its deciphering, various designs in varied fields have been proposed. This work presents a Residue Number System (RNS)-based genetic code using the concept of number tree. In conformity with Gamow’s postulation, \(4^3 = 4 \times 4 \times 4 = 64\) we present a three moduli set RNS model of the genetic code. The design sorts the codes into their “family box” or “four-codon box”. The application of RNS in bioinformatics is not new - notably its application to Smith-Waterman Algorithm. RNS has been used to successfully generate the genetic code and this advances the cause of representing the genetic code in a quaternary number system.

KEYWORDS

Residue Number System, RNS-genetic Code, Genetic Code, Number Tree, Amino-acids.

1. INTRODUCTION

The genetic code drives its relevance from the saying that “A code without translation makes sense but translation without a code does not make sense”. Francis Crick proposed the existence of a "genetic code," which is the set of all codons that specify the 20 amino acids.[1]. The concept of “pseudo-wild” led him to provide the first experimental evidence in support that the codons of the genetic code are organized in triplets [2]. George Gamow [1954] offered the first mathematical architecture of the genetic code \(4^3 = 4 \times 4 \times 4 = 64\)[3]. The first of the 64 triplet codons to be deciphered was UUU – Phenylalanine and by 1966 [4] all the 64-codons of the genetic code were cracked [4][5]. Cracking the code of life paved the way for modern molecular biological research [3]. The most prevalent representation of the canonical genetic code, found in[6][7], is a three-dimensional matrix, where each dimension corresponds to one of the three positions in the triplet code [4]. Some researchers have related various concepts of some fields of study to understanding the features of the genetic code [8][9][10][11][12]. The attempts to offer mathematical or computational approach to the genetic code have been the assignment of either binary [13]or quaternary number system[9]. Binary number system is used because is the conventional number system used in modern digital computations and quaternary system because the number of known nitrogenous bases are four (4).The genetic code representations have been extensively researched into to take advantage of digital signal processing techniques. An
innovative approach that is mathematically structured to suite implementation of computational algorithms will therefore aid modern molecular biology. It is also evident that the use of computers and mathematics is revolutionizing the field of molecular biology. And therefore an enhanced digital representation of the genetic code has the potential of transforming molecular biological processes and analysis. This approach uses Residue Number System (RNS) to generate the code of life using the concept of number trees. The triplets of bases in an amino acid in the genetic code are represented with each digit of a three (3) moduli set residue number system. In agreement with Gamow for the use of \(4 \times 4 \times 4 = 4^3 = 64\), we thus used three moduli sets, \(m_1\), \(m_2\) and \(m_3\), requiring the truncation of higher moduli sets values (\(\geq 4\)) in the three moduli set selected. Just as codon families have unique characteristics like being hydrophobic, polar or non-polar, so do the decimal values generated in each block of code. They have unique sequential numbering based on the moduli sets chosen and the order of these moduli sets. The nature of the tree of residue digits can enhance further analysis on the genetic codes. The capability of RNS to generate the genetic code signals a buoyant relationship between molecular biology and RNS. The application of RNS in the field of bioinformatics is not new [14]–[16]. This design can improve speed, offer smaller digital footprint, and lower cost of some bioinformatics or molecular biological designs, modeling and analysis. Simply, it has the potential of taking advantage of the benefits RNS offers contemporary digital applications [17].

1.1. Nucleic Acids (DNA And RNA)

The information required to produce life is all contained in the molecule DNA (deoxyribonucleic acid), which is likely the most significant molecule for life. [18, p. 255]. Nucleotide polymers make up DNA and RNA (ribonucleic acid), with the former controlling the creation of RNA through a process known as transcription [19, pp. 3–4][20]. DNA differs from RNA in that, deoxyribose sugars are used instead of ribose sugar therefore[21, p. 75 and 83]; the hydroxyl (OH) group in ribose sugar is replaced with hydrogen (H) in deoxyribose sugar at position 2’ of the ribose sugar [22]. DNA stores information as codes made up of four chemical bases, which are grouped as purines and pyrimidines. Adenine (A) and Guanine (G) are the two pyrimidine bases of DNA, while Cytosine (C) and Thymine are the two purine bases (T). The RNA has similar purines but differ in their pyrimidines – Thymine (T) is replaced with Uracil (U). The basic tenet of genetics or gene expression is that bases are the essential building blocks of amino acids and subsequently proteins. The well-known Chargaff's rule is used to pair the bases; A pairs with T and C pairs with G. The amino acids in a tabular form constitute the genetic code [23]. The genetic code can be represented in DNA and RNA form since they have nearly similar bases except for the replacement of thymine in DNA with uracil in RNA.

1.2. The Genetic Code

The genetic code is a set of rules that determine how a nucleotide sequence is converted into the amino acid sequence of proteins [24][25]. The genetic code is made of some characteristics that define its nature. It is made of triplets of codons that is non-overlapping, commaless and non-ambiguous. It is also degenerate, has polarity and is universal [26]. There are \(4^3 = 4 \times 4 \times 4 = 64\) codon combinations from four bases and each codon codes for one type of amino acid. The blocks on the table are separated by the same bases in the first two positions. The genetic code was first thought of as universal, but the mitochondria genome has different genetic codes. George Gamow [1954] unsuccessfully represented the genetic code in his “diamond code”[5][27] – Figure 3. The most prevalent representation of the canonical genetic code has a three-dimensional matrix with each dimension corresponding to one of the three locations in the triplet code [28] – Figure 4.
This work considers the standard or otherwise canonical genetic code [7]. Mathematically, the $4^3$ explains the number of bases as four (4) and the number three (3), as that which constitute a codon and its evaluation, as the number of codons in the entire genetic code. The expanded form of $4^4$ further expresses how these codes are arranged in tabular form, where each of the 4’s represents the first, second and third bases in the codon table. Table 1 presents how an RNS-genetic code is developed from a three (3) moduli set RNS system.

Table 1: An RNS – Amino acid Representation

<table>
<thead>
<tr>
<th>First Ternary Symbol</th>
<th>Base Position</th>
<th>Amino Acid</th>
<th>Base Position</th>
<th>Amino Acid</th>
<th>Base Position</th>
<th>Amino Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 0 0 0</td>
<td>TTT</td>
<td>0 0 0 0</td>
<td>TTT</td>
<td>0 0 0 0</td>
<td>TTT</td>
<td>0 0 0 0</td>
</tr>
<tr>
<td>1 1 1 1</td>
<td>CCC</td>
<td>1 1 1 1</td>
<td>CCC</td>
<td>1 1 1 1</td>
<td>CCC</td>
<td>1 1 1 1</td>
</tr>
<tr>
<td>2 2 2 2</td>
<td>...</td>
<td>2 2 2 2</td>
<td>...</td>
<td>2 2 2 2</td>
<td>...</td>
<td>2 2 2 2</td>
</tr>
<tr>
<td>4 4 4 4</td>
<td>GGC</td>
<td>4 4 4 4</td>
<td>GGC</td>
<td>4 4 4 4</td>
<td>GGC</td>
<td>4 4 4 4</td>
</tr>
</tbody>
</table>

2. Number System

A method for representing numbers in the architecture of a computer system is known as a number system [29]. The performance of computer arithmetic is frequently constrained by the carry chain of the traditional binary number system [14]. Digital electronics is achieved as voltage transitions and these are understood as either HIGH or LOW – the main idea behind binary numbers as the ideal notation for representing digital electronic circuits. Some of the major
constraints in the application of binary number system in digital electronics had been sign representation and the carrying and borrowing in digital arithmetic. As the demand for high speed data processing and transmission and also smaller digital footprints of digital designs in various fields of digital computing has become necessary, Residue Number System (RNS) has been re-invented[30]. This is as a result of the benefit it provides in overcoming some difficulties that prevent binary data representation from being a viable option for some fast computing applications.

2.1. RNS and RRNS

The greatest common divisor of the set of k pairwise relative co-prime positive integers that make up the residue number system (RNS) is 1, \((m_i, m_j) = 1\) with \(i \neq j\) and \(m_1, m_2, ..., m_{k-1}, m_k\), called moduli[17]. The interval \([0, M]\), also known as the valid range or dynamic range, which determines the practical computational range of the number system, is represented by the product \((m_1 \times m_2 \times \ldots \times m_{k-1} \times m_k)\) that is,

\[
M = \prod_{i=1}^{k} m_i
\]  

(1)

There is a distinct K-tuple representation for each integer in the residue class \(Z_m\) which is given by

\[X \rightarrow (r_1, r_2, \ldots, r_k)\] \(where\ \ r_i \equiv |X|m_i\ \ or\ \ (X \mod m_i)\)

RNS can represent signed numbers; for all scenarios of even and odd number dynamic range, the range of representable integers is divided into two equal intervals.

\[
\left[ -\frac{(M-1)}{2}, \frac{M-1}{2} \right] \quad \text{If } M \text{ is odd, and}
\]

\[
\left[ -\frac{M}{2}, \frac{(M^2 - 1)}{2} \right] \quad \text{If } M \text{ is even.}
\]

2.2. Moduli Set

The choice of moduli sets plays a significant role in designing an RNS system. The form and quantity of the chosen moduli play a significant role on the speed and complexity of internal RNS arithmetic circuits as well as the forward and reverse conversion[17, p. 8]. The moduli set selection also affect the dynamic range, the speed, as well as the VLSI implementation of RNS systems [31]. The powers of two related moduli can simplify the required arithmetic operations and this result in efficient hardware implementation of the RNS systems by using usual binary hardware [32]. For RNS implementations, a variety of moduli sets, including the two, three, four, etc., have been proposed. The three moduli sets have received some considerable research attention and the moduli set; \(2^n - 1, 2^n, 2^n + 1\) is the most projected because of its simplicity and balance moduli [33]. The RNS-Genetic code proposed requires a three moduli set, for each of the bases in a triplet of codon, and each modulus must be greater than or equal to four (4), to adequately represent the four (4) bases in each position of the codon. The dynamic range must be greater than or equal to 64 to make up for all codons in the codon table. Customarily if the first two conditions are met then the third condition will suffice. For many important operations, including forward and reverse hardware converters, some unique sets of moduli result in hardware simplifications and a decrease in latency. The approach considered for this work would work with any set of relatively prime moduli sets considered hence a more open approach to the selection of moduli sets for hardware implementation.
2.3. Converters: Forward and Reverse Converters

The forward conversion is considered as the algorithms that transform any conventional weighted number system to RNS and reverse conversion is any algorithm which transforms RNS to the weighted number system [30, pp. 49&213]. The residue-to-binary conversion is a crucial step for any successful RNS application. The traditional technique of this conversion is based on the Chinese Remainder Theorem (CRT). The reverse conversion from residue to the weighted number has some performance bottlenecks whereas the forward conversion process is relatively easier[34]. In recent years, the Chinese Remainder Theorem (CRT) or Mixed-Radix Conversion has served as the foundation for reverse conversion algorithms. In contrast to MRC, which is a sequential operation that frequently necessitates the use of numerous lookup tables, CRT frequently entails the use of a huge modulo adder, which is the product of all moduli. The new CRT I and II proposed, have simpler algorithms, improved speed and reduced hardware complexity. The research work on converters is actively on-going and the proposed RNS-Geneic code would comply with any improved converter design.

3. The Number Tree (Forest)

A tree is a discrete structure that represents hierarchical relationship between individual elements or nodes [35]. Typically, the root is the "starting" node; it has no parents, and every edge either directly or indirectly emanates from it. The predecessor node is the parent and the successor nodes are the children. Nodes without children are leaves[36] and Figure 5, shows an illustration of the nature of number trees.

![Figure 5: Nature of tree of numbers][35]

![Figure 6: Tree (forest) of Residue digits][37]

The binary tree, in which each node has two (mod 2) offspring or less, is a specific case of a number tree. The concept of number trees has been used in developing algorithms like the binary search tree, its also employed in[37]to knit a Fibonacci tree. This work has constructed an RNS-Tree (forest)—Figure 6, and used it to generate the genetic code. The RNS based tree (forest) model has the number of nodes at each level determined by the moduli set at that level – m1, m2 or m3. The number of “levels” is determined by the number of moduli sets chosen, thus 2 moduli sets give two levels, three moduli sets, three levels and so on. In an RNS based genetic code, a three moduli set is chosen since we require three levels where each level represents a particular base in a triplet of codons.
4. METHODOLOGY

When considering the design of the RNS-genetic code, we proceeded with the rudimentary conventions that there are only 4 nucleotides and 20 encoded amino acids and that each codon is a triplet of nucleotides [7]. RNS can be designed as a tree and combination of trees constitute a forest of residue numbers. The classical RNS can be generated in tabular form, given the moduli set chosen, as shown in Table 1. The concept here is to design a forest of residue numbers from the generated residue numbers with appropriate roots, nodes (internal nodes) and leaves. This design uniquely categorizes the residue numbers into blocks of data. These blocks display certain unique characteristics that have been exploited to generate the genetic code. If the moduli set of RNS are chosen such that there are at least three (3) moduli sets - m1, m2 and m3 and their dynamic range greater than or equal to 64 thus m1 x m2 x m3 ≥ 64 and each of m1, m2 and m3 greater than or equal to four (4). A tree (forest) of residue numbers can be constructed such that with appropriate truncation and digit-base assignment, the genetic code or amino acid table can be constructed from the block (tree) of residue numbers. The genetic code representationally has four (4) bases for each row, four (4) bases for each column and four (4) other bases within each block - thus a 4 x 4 x 4 or 4^3 = 64 codons. The moduli sets are chosen such that each codon in the genetic code is uniquely represented by each of the three moduli sets; m1, m2 and m3. The moduli set m1 is the root nodes of each tree (forest) and represent the first letter of each codon, the second moduli set, m2, is the child node and represents the second letter of each codon, the third moduli set, m3, is the leaves nodes of each tree and represents the third base of each codon. Thus, a collection of root, child and leaf; or a concatenation of each digit of the three chosen moduli sets constitutes a codon of the genetic code.

The number of roots of the tree (forest) is determined by the first moduli set m1, the number of nodes is represented by the second moduli set, m2, and the third moduli set m3, which is the leaf node concludes the three (3) moduli set representation of the genetic code. Since there are four (4) bases, each moduli set is truncated to four (4) residue digits, thus 0, 1, 2 and 3. The RNS-Genetic code table is completed with residue digits assigned appropriate nitrogenous bases. Thus, Thymine (T) is assigned residue digit zero (0), Cytosine (C) is assigned residue digit one (1), Adenine (A) is assigned residue digit two (2) and Guanine (G) is consigned residue digit three (3). In the case of an RNA-Genetic code Thymine (T) is replaced with Uracil (U) and assigned residue digit zero (0). The algorithm for generation of the RNS-Genetic code can be seen in section 4.1. The genetic code has some properties and therefore any model that seeks to generate it must reflect these properties. Every codon block (quartet) has the same initial two nucleotides, and they are more crucial for the specific codon-anticodon identification. This is illustrated in figure-6, where the RNS sorted into a tree, orders the first two digits of each codon block (quartet) as the same digits. The third digit changes incrementally within each block – and this explains the wobble hypothesis[38].

4.1. Design Flow – Algorithm

An algorithm is a procedure or formula for solving a problem or systematic method for producing a specified result. The five (5) key properties of algorithms are answered in the quest to generate the RNS-genetic code. The inputs are the RNS moduli sets selected (defined) and the output is the genetic code produced as results. The definite nature of the algorithm is specified by the sequence of operations defined for turning the inputs into output. It is deemed effective since it’s doable and finally stops offering the output set out to be achieved, RNS-Genetic Code. This is very relevant since it offers a codified, platform independent for arriving at our solution. Below is the algorithm required to generate the RNS-Genetic Code.
RNS Genetic Code Table($m_1, m_2, m_3$)

Input: Three relatively prime numbers $m_1, m_2, m_3$
Output: RNS Genetic code Reference Table

1. $M \leftarrow m_1 * m_2 * m_3$
2. $N \leftarrow 64$  // number of codons
3. Array GeneticCode[$N, 6$]
4. count $\leftarrow 0$
5. for $i \leftarrow 0$ to $M - 1$
6. if (($x < 4$) && ($y < 4$) && ($z < 4$))
   - GeneticCode[count, 0] $\leftarrow x$
   - GeneticCode[count, 1] $\leftarrow y$
   - GeneticCode[count, 2] $\leftarrow z$
   - GeneticCode[count, 3] $\leftarrow$ AminoAcid($x,y,z$)
   - GeneticCode[count, 4] $\leftarrow$ CodonName($x,y,z$)
   - GeneticCode[count, 5] $\leftarrow i$
   - count $\leftarrow count + 1$
7. $x \leftarrow x + 1$
8. $y \leftarrow y + 1$
9. $z \leftarrow z + 1$
10. if ($x = m_1$)
11.    $x \leftarrow 0$
12. if ($y = m_2$)
13.    $y \leftarrow 0$
14. if ($z = m_3$)
15.    $z \leftarrow 0$
16. return GeneticCode

5. RESULTS AND DISCUSSION OF MODEL

This is a novel approach of representing the Genetic code. The results of this findings, RNS-Genetic code with moduli sets 4, 5, and 7 are shown below. This work further draws the relationship of the findings to the canonical genetic code. There are two nucleic acids (DNA and RNA) and generally, the genetic code can be generated in either form. As discussed earlier the two have nearly similar nitrogenous bases except for the replacement of Thymine (T) with Uracil for the case of RNA. The RNS-Genetic code can therefore be generated as a table of DNA or a table of RNA as shown in the simulation results of Figure – 7and 8 (RNS-DNA Genetic code) and (RNS-RNA Genetic code) respectively. The choice of moduli selection plays a major role in the selection of RNS for any digital implementation. In the design, three moduli set RNS is considered since we required three residue digit concatenations for each of the 64 degenerate amino acids on the genetic code table. The design accepts any three (3) relatively prime moduli set implementation of the RNS-genetic code. The use of the number tree (forest) , suggests that the genetic code would not be affected by any change in the three (3) relatively prime moduli sets selected for implementation. As such the design can take advantage of any effectively implemented three (3) moduli sets – since the research on moduli selection and converters is ongoing. With the use of residue number trees, each of the digits that make up a particular block of code will always be in the same block irrespective of the moduli sets selected. The major difference noticed in any change of moduli sets is a change in decimal values of each of the concatenated residue digits that make up each amino acid. In Figure 7, the moduli set chosen are 4, 5 and 7 and as such the decimal digits for the first block of codons are seen as 0, 120, 100 and 80. When these moduli sets were reversed, thus 7, 5 and 4, the decimal digits for the first block of codons are 0, 105, 70 and 15 – Figure 8.
6. CONCLUSION

Our model provides the method for producing the genetic code, which has been the subject of numerous attempts to create an easier method. We successfully constructed a genetic code using the concepts of residue number system (RNS). This is the first and advances the cause of representing the genetic code in a quaternary number system. RNS promises to offer some benefits over the conventional number system (binary) in some application specific digital applications. With the fast-evolving field of bioinformatics, it is our firm belief that the RNS-Generic code model proposed would help revolutionize the field of molecular biological research and applications.

7. RECOMMENDATIONS AND FUTURE WORKS

There is the need to perform a digital (hardware) implementation of the RNS-Generic code model developed and compare its speed and area with existing models. The number of digital components required to implement the RNS based genetic table could also be assessed. This work could be further extended to consider DNA/RNA sequence (string) comparison and the concept of mutation, as viewed as biological errors. There are many similarities in the way biological and digital errors manifest; thus, the causes of errors - environmental or internal and the nature of the errors - single digit (a base), and burst (chromosomes).
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