



A novel approach to encode melodies in DNA

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ABSTRACT

DNA data storage has gained more attention last decades. DNA molecules can be used for encoding of non-biological information and as promising carriers due to greater data capacity, higher duration of the storage, and better technical failures stability. Here we propose a new method for encoding of notes and music in DNA. The encoding technique takes into account the duration and tonality of each note, enabling to encode all seven octaves by assigning a nucleotide sequence to each key. A certain set of short sequences is suggested to define the duration of note sound. The proposed method allows to encode more complicated melodies compared to the approach based on Huffman algorithm.

1. Introduction

To date, humanity has accumulated a huge amount of information (>20 zettabytes) that requires a new type of carriers for its long-term storage. It is predicted that by 2040 the amount of information will exceed three yottabytes, which will require the production of >10⁹ kg of high-purity silicon (Zhirmov et al., 2016). However, most likely, only 10⁷–10⁸ kg of such silicon will be produced by 2040. This demand causes the search for new ways for data storage including using other data carriers, among which DNA molecules are of considerable interest. Natural DNAs are long polymeric molecules consisting of two complementary polynucleotide chains. One of the advantages of DNA molecules as a data carrier is the ability to store a lot of information in a minimal physical volume. It is considered that 1 g of DNA can keep of about 500 exabytes (5*10²⁰) of information, which is equivalent to 100 billion DVDs (Church et al., 2012). A huge number of nucleotide combinations (namely, 4ⁿ, where n is the length of the sequence) makes it possible to encode all the current data accumulated.

Since the 1980s different methods for data encoding in nucleotide sequences have been proposed (Sakhabutdinova et al., 2019). However, the most optimal way is the data conversion into a binary code and, then, into nucleotides. Simple texts including hidden messages have been successfully encoded in DNA (Hodgson, 1990; Clelland et al., 1999). The ways for encoding of images and any graphic information

were proposed as well. The first one was the rune translated into DNA sequence as a part of the Microvenus project (Davis, 1996). The binary code consists of 7 lines with 5 characters visually represents of the Microvenus image (See Fig. 1). For nucleotide encoding, nucleotides were ranked by size and assigned Arabic numerals - C = 1; T = 2; A = 3; G = 4. After transformation the encoding system looks like C = X; T = XX; A = XXX; G = XXXX, where X is the presence of the corresponding nucleotide depending on the number of actual rows of such X in the binary sequence. By using a digitizing phase-change code method the nucleotide sequence was synthesized. Later, as oligonucleotide synthesis improved, full texts, audio and video files, and computer programs were encoded in DNA (Goldman et al., 2013a; Blawat et al., 2016a; Erlich and Zielinski, 2017; Organick et al., 2018a; Antkowiak et al., 2020).

The storage of music as nucleotide sequences is of particular interest. It should be noted that mathematical principles are widely used for melodies creation (e.g., for choosing a particular rhythm or adding an accent to a specific note) (Hart; Yamuna et al., 2013). Some composers tried to translate various functions and numbers into melodies. However, it is impossible to determine the exact mathematical component of hearing a sound. Nonetheless, the regularity of a rhythm can be digitized. In a computer, melodies are converted into a binary format. An analog-to-digital converter (ADC) samples the sound wave at regular intervals and assigns a binary code to the wave amplitude. The obtained binary record is stored in a computer, and a digital-to-analog converter

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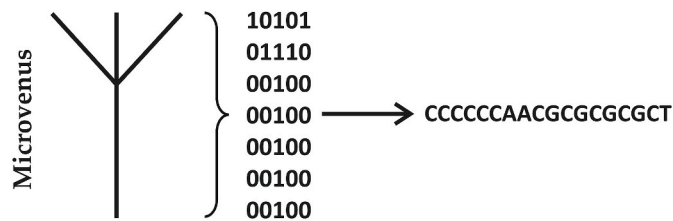


Fig. 1. The encoded rune (Microvenus project) (Davis, 1996).

(DAC) can convert it back to a sound wave. It is important how many bits are used to store a sound for better encoding quality. For 8 bits, the maximum number is available (11111111 = 255). Thus, 256 binary values from 0 to 255 can be assigned to the amplitude ([Binary Code and Storing Music](#)).

In 2013 the encoding of five files was reported upon: all 154 sonnets of W. Shakespeare (ASCII format), Watson-Crick's article about DNA structure ([Watson and Crick, 1953](#)) (PDF format), 26-s fragment of Martin Luther King's speech « I have a dream » (MP3 format), color photo of the European Bioinformatics Institute (JPG format), and description of the Huffman algorithm (ASCII format) ([Goldman et al., 2013b](#)). To encode this information, 153335 oligonucleotides with the length of 117 nt each, were synthesized. The 22 MB video was stored in DNA as well ([Blawat et al., 2016b](#)). For this, 900000 oligonucleotides consisting of two parts (190 nt encoding part and two 20 nt flanks) were obtained using the microarray method. Two-bit encoding was used as follows: 00 corresponds to A, 01 – to C, 10 – to G, and 11 – to T. Considerable attention was paid to errors elimination during oligonucleotides synthesis and DNA sequencing. More than 200 MB of information in 35 files of different types (TXT, PDF, MP3, MP4, and JPG), was stored in DNA ([Organick et al., 2018b](#)). In 2017 Twist Bioscience and Microsoft Corporation reported on storage of two audio records (songs “Smoke on the Water” by Deep Purple and “Tutu” by Miles Davis) followed by its retrieval with 100% accuracy ([DNA-Based Digital Storage](#)). These DNA-saved files were added to UNESCO's Memory of the World Archive ([Service, 2017](#)).

2. Keyboards of modern keyboard instruments. Some definitions

Modern pianos contain 88 keys grouped by octaves (Fig. 2). Other keyboard musical instruments, e.g., electronic synthesizers, may have more or fewer keys.

White keys represent the basic notes. Black keys indicate semitones (major and minor). A major tone raises the sound of a note by half of a tone, a minor tone lowers it, respectively. Duration of a note varies from the whole note to its parts, as it is shown on [Fig. 3](#). It is possible to divide note duration infinitely. However, the substantial division of notes is not common, since melodies with virtuoso speed of sound are rare, and few musicians are able to play at a high speed.

All melodies are recorded on the musical staff, consisting of five main lines. The notes locate both on the lines and between them. The notes may have certain notations showing the tempo and the volume of the melody parts (Fig. 4).

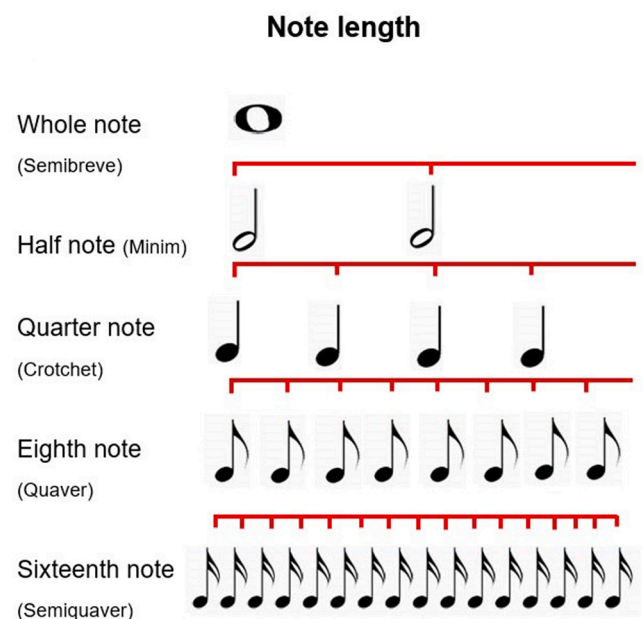


Fig. 3. Duration of notes.

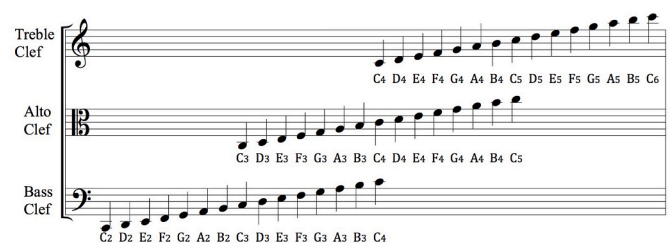


Fig. 4. The arrangement of the notes on the stave and clefs.

3. Huffman encoding

In 2009 an approach for melody conversion into a nucleotide sequence based on the modified Huffman algorithm was proposed (Ailenberg and Rotstein, 2009). According to the approach, the number of dG and dC nucleotides was reduced to decrease the formation of undesirable secondary structures. It was suggested to use three-column Huffmanns coding to denote a larger number of notes. Table 1 indicates the designation of the notes for one octave. The principle was demonstrated on the children's song "Mary Had a Little Lamb" encoded in one DNA molecule. A 844 bp DNA fragment was obtained and cloned in a plasmid vector. In order to recover the melody two amplification products with the sizes 500 and 344 bp were obtained, followed by amplicons sequencing. The melody of the song "Mary Had a Little Lamb" is shown in Fig. 5. Encoding of the song part in nucleotide sequences is shown in Table 2.

The abovementioned method is quite convenient and provides a compact record, since each note corresponds to a short nucleotide

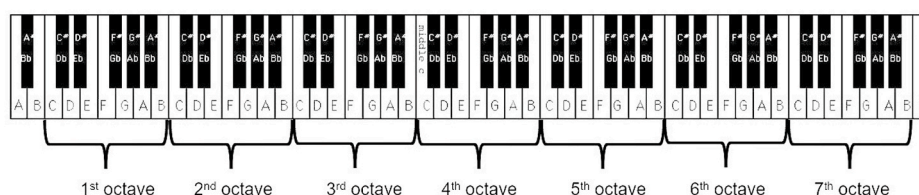


Fig. 2. Octaves of piano keyboard.

Table 1
Encoding of notes and musical symbols with nucleotides according to the Huffman algorithm.

Music code	DNA codon
Quarter note (1/4)	G
Half note (1/2)	TT
Whole note (1)	TA
Eighth note (1/8)	AT
Sixteenth note (1/16)	CT
Dot (.)	TC
A	TG
B	AC
C	AG
D	CG
E	AAT
F	AAC
G	AAG
2/4 (meter)	CAT
3/4 (meter)	CAA
4/4 (meter)	CAC
((repeat)	CAG
((repeat)	CCA
X (repeat)	CCT
2 (repeat)	CCG
3 (repeat)	CCC
4 (repeat)	AAAT



Fig. 5. Notes of the song “Mary Had a Little Lamb” (Smith et al., 2003).

sequence. However, for more complicated melodies, it is necessary to convert a larger range of notes into nucleotide sequences. Also, the method does not take into account the halftones and note combinations.

4. The new encoding method

We propose a new method for encoding of melodies, considering duration and the tone of the notes. Each note is encoded by 8 nucleotides. The first three nucleotides determine the duration of the notes and consist of G and C as follows:

- ACG – whole note.
- AGC – Half note.
- ACC – Quarter note.
- AGG – Eighth note.
- CAG – Sixteenth note.

The next five nucleotides encode the tone of the notes. In this case all keys including semitones can be encoded. We have accepted the number 88 as the total number of keys. For a smaller number of octaves the corresponding keys will not be used for encoding. Sequences were selected to retain 50% GC composition in the resulting octanucleotides. All possible pentanucleotide sequences were generated using Python 3.6 (Scripts for encoding). We have selected those ones containing two C/G nucleotides and no homopolymer fragments or repeats to exclude self-complementarity (Table 3).

The proposed approach is consistent with a method for symbol encoding described earlier (Smith et al., 2003). However, it is convenient to use DNA from oligotheca representing the set of NYRN-oligonucleotides with 8 nt coding part (Garafutdinov et al., 2022). In this case each NYRN-oligonucleotide contains 1 byte of information, wherein nucleotide C is encoded as “00”, T - “11”, A and G (purines, R) - “0” and “1”, respectively (so-called R/CT encoding). This principle can be used to translate a nucleotide sequence that stores information about a melody into a binary format. Decoding such a binary record a single “0” and “1” occurring within one byte are converted into purines A and G. Combinations “00” and “11” are converted into pyrimidines C and T respectively. The first binary symbol and the following one must be analyzed to follow the abovementioned schema. If symbols are the same they are treated as a pair and correspond to C for “00” and T for “11”. If symbols differ the first one is considered as an independent and is taken as A (“0”) or G (“1”). Then processing of a binary record continues. This approach slightly reduces the coding capacity and eliminates the problems associated with the presence of long homopolymer motifs. For instance, the encoding method proposed for Microvenus project (Davis, 1996) does not take into account biological and chemical properties of polynucleotide sequences. Hence, the capacity for R/CT encoding is 1.5 bits per nucleotide.

Service homopolymer sequences have been used to encode the start (AAATA) and the end (TTATT) of a chord. These homopolymer motifs differ from the nucleotide sequences that encode notes. Although homopolymer motifs increase the length of the coding sequence, they make it possible to encode all note combinations. It is proposed to use the AATAA pentanucleotide to encode a pause when none of the keys sounds. The pause also has a duration which is similar to the whole note duration.

To demonstrate the applicability of the approach, the well-known “Flohwalzer” (Flohwalzer) (dog’s waltz) was converted into DNA sequence. The most popular and the simplest version of the dog’s waltz is shown on Fig. 6.

“Flohwalzer” is played with the keys from 28 to 56. The melody can be represented as shown in Table 4. The first column shows the numbers of the keys (the keys played together are in brackets), and the second one shows the duration of each note.

“Flohwalzer” converted into nucleotide sequence is presented in Table 5.

The entire nucleotide sequence is as follows:
AGGAAACGAGGAACGAACCAGCAAAAATAACCGAACAACCCAA-

Table 2
Conversion of the part of the song “Mary Had a Little Lamb” into nucleotides according to Huffman algorithm.

					Ma-	ry	had	a	lit-	tle	lamb	lit-	tle	lamb	lit-	tle
m	u	*	4/4	(B1/4	A1/4	G1/4	A1/4	B1/4	B1/4	B1/2	A1/4	A1/4	A1/2	B1/4	D1/4
taac	tact	tacca	cac	Cag	ACG	TGG	AAGG	TGG	ACG	ACG	ACTT	TGG	TGG	TGTT	ACG	CGG
lamb	Ma-	ry	had	A	lit-	tle	lamb	its	fleece	was	white	as	snow			
D1/2	B1/4	A1/4	G1/4	A1/4	B1/4	B1/4	B1/4	A1/4	A1/4	B1/4	A1/4	G1)	×	2	
CGTT	ACG	TGG	AAGG	TGG	ACG	ACG	ACG	ACG	TGG	TGG	ACG	TGG	AAGTA	cca	cct	cgg

Table 3
Encoding of keys using pentanucleotide sequences.

Key number	Nucleotide sequence	Key number	Nucleotide sequence	Key number	Nucleotide sequence	Key number	Nucleotide sequence
1	A ACCA	23	G GAAAG	45	F CAGAA	67	D [#] CCAAT
2	A [#] ACCAA	24	G [#] AGAGA	46	F [#] CAAGA	68	E CACAT
3	B AAACC	25	A TAGGA	47	G CAAAG	69	F AACCT
4	C CCAAA	26	A [#] TGGAA	48	G [#] ACAGA	70	F [#] ACACT
5	C [#] CACAA	27	B TAAGG	49	A TAGCA	71	G ACCAT
6	D CAACA	28	C GGTA	50	A [#] TACGA	72	G [#] ACCTA
7	D [#] CAAAC	29	C [#] GAGTA	51	B TAAGC	73	A ACAGT
8	E ACACA	30	D GTAGT	52	C GCATA	74	A [#] ACGAT
9	F TACCA	31	D [#] TGAGA	53	C [#] GACTA	75	B CGAAT
10	F [#] TCCAA	32	E TGAAG	54	D GAAC	76	C CAGAT
11	G TAACC	33	F AAGCA	55	D [#] GTAAC	77	C [#] ACAGT
12	G [#] CCTAA	34	F [#] AGCAA	56	E TGACA	78	D ATCAG
13	A CTCAA	35	G AAAGC	57	F TACGA	79	D [#] ACGAT
14	A [#] CTAAC	36	G [#] GCAAA	58	F [#] TCAAG	80	E CGATA
15	B TCACA	37	A GACAA	59	G TAACG	81	F AGACT
16	C TCAAC	38	A [#] GAACA	60	G [#] CGTAA	82	F [#] AGCAT
17	C [#] AAGGA	39	B GAAAC	61	A CAGTA	83	G GACAT
18	D AGGAA	40	C AGACA	62	A [#] CAAGT	84	G [#] AATGC
19	D [#] AAAGG	41	C [#] AACGA	63	B CTAAG	85	A AAGTC
20	E GGAAA	42	D ACGAA	64	C TCAGA	86	A [#] AGACT
21	F GAGAA	43	D [#] AAACG	65	C [#] ACACT	87	B AGCAT
22	F [#] GAAGA	44	E CGAAA	66	D ACCAT	88	C ATAGC



Fig. 6. “Flohwalzer” melody.

GATTATTAAATAACCGAACACCCAA-
GATTATTAGGAAACGAGGAACGAAACGAAAAATAACCGAA-
CAACCCAAGATTATTAAATAACCGAACACCCAA-
GATTATTAGGAAACGAGGAACGAAACGAAAAATAACCGAA-
CAACCCAAGATTATTACCTGAGAAAAATAACCGAACACCCAA-
GATTATTACCGAGTAAATAACCGAACACCCAGAATTATTA-
TAACCGAAACACCCA-
GAATTATTAGGAAACGAGGAACGAAACGAGTAAATAACCGAAA-
CACCCAGAATTATTAAATAACCGAAACACCCA-

Table 4
Representation of the “Flohwalzer” as the numbers of the keys and the duration of the notes.

	Note sequence	Note duration
1	43-41-34- (38, 46) - (38, 46)	1/8-1/8 -1/4-1/4 - 1/4
2	43 - 41-34 - (38, 46) - (38, 46)	1/8-1/8 -1/4-1/4 - 1/4
3	43 - 41-34 - (38, 46) - 31 - (38, 46) - 29 - (39, 45) - (39, 45)	1/8-1/8 -1/4-1/4 - 1/4-1/4 -1/4-1/4 - 1/4
4	43 - 41-29 - (39, 45) - (39, 45)	1/8-1/8 -1/4-1/4 - 1/4
5	43 - 41-29 - (39, 45) - (39, 45)	1/8-1/8 -1/4-1/4 - 1/4
6	43 - 41-29 - (39, 45) - 31 - (39, 45) - 29 - (38, 46) - (38, 46)	1/8-1/8 -1/4-1/4 - 1/4-1/4 -1/4-1/4 - 1/4
7	48 - (38, 46) - 50 - (38, 46) - 53 - (39, 45) - (39, 45)	1/4-1/4 - 1/4-1/4 -1/4-1/4 - 1/4
8	53 - (39, 45) -50 - (39, 45) - 48 - (38, 46) - (38, 46)	1/4-1/4 - 1/4-1/4 -1/4-1/4 - 1/4
9	34 - (38, 46) - 31 - (38, 46) - 29 - (39, 45) - (39, 45)	1/4-1/4 - 1/4-1/4 -1/4-1/4 - 1/4
10	29 - (39, 45) - 31 - (39, 45) - 34 - (38, 46) - (38, 46)	1/4-1/4 - 1/4-1/4 -1/4-1/4 - 1/4
11	34 - (38, 46) - 31 - (38, 46) - 29 - (39, 45) - (39, 45)	1/4-1/4 - 1/4-1/4 -1/4-1/4 - 1/4
12	29 - (39, 45) - 31 - (39, 45) - 34 - (38, 46) - (38, 46)	1/4-1/4 - 1/4-1/4 -1/4-1/4 - 1/4

GAATTATTAGGAAACGAGGAACGAAACCGAGTAAATAACCGAAA-
CACCCAGAATTATTAAATAACCGAAACACCCA-
GAATTATTAGGAAACGAGGAACGAAACCGAGTAAATAACCGAAA-
CACCCAGAATTATTACCGAGTAAATAACCGAAACACCCA-
GAATTATTACACAGAAAAATAACCGAACACCCAA-
GATTATTACCTACGAAAAATAACCGAACACCCAA-
GATTATTACCGACTAAATAACCGAACACCCAGAATTATTA-

Encoding of the “Flohwalzer” as octanucleotide sequences. Nucleotides in bold are responsible for the sound duration.

- 1 AGGAAACG AGGAACGA ACCAGCAA AAATA ACCGAACA ACCCAAGA TTATT
AAATA ACCGAACA ACCCAAGA TTATT
- 2 AGGAAACG AGGAACGA ACCAGCAA AAATA ACCGAACA ACCCAAGA TTATT
AAATA ACCGAACA ACCCAAGA TTATT
- 3 AGGAAACG AGGAACGA ACCAGCAA AAATA ACCGAACA ACCCAAGA TTATT
ACCTGAGA AAATA ACCGAACA ACCCAAGA TTATT ACCGAGTA AAATA
ACCGAAAC ACCCAGAA TTATT AAATA ACCGAAAC ACCCAGAA TTATT
- 4 AGGAAACG AGGAACGA ACCGAGTA AAATA ACCGAAAC ACCCAGAA TTATT
AAATA ACCGAAAC ACCCAGAA TTATT
- 5 AGGAAACG AGGAACGA ACCGAGTA AAATA ACCGAAAC ACCCAGAA TTATT
AAATA ACCGAAAC ACCCAGAA TTATT
- 6 AGGAAACG AGGAACGA ACCGAGTA AAATA ACCGAAAC ACCCAGAA TTATT
ACCGAGTA AAATA ACCGAAAC ACCCAGAA TTATT
- 7 ACCACAGA AAATAACCGAACA ACCCAAGA TTATT ACCTACGA
AAATAACCGAACA ACCCAAGA TTATT ACCGACTA AAATA ACCGAAAC
ACCCAGAA TTATT AAATA ACCGAAAC ACCCAGAA TTATT
- 8 ACCGACTA AAATA ACCGAAAC ACCCAGAA TTATT ACCTACGA AAATA
ACCGAAAC ACCCAGAA TTATT ACCACAGA AAATAACCGAACA ACCCAAGA
TTATT AAATAACCGAACA ACCCAAGA TTATT
- 9 ACCAGCAA AAATAACCGAACA ACCCAAGA TTATT ACCTGAGA
AAATAACCGAACA ACCCAAGA TTATT ACCGAGTA AAATA ACCGAAAC
ACCCAGAA TTATT AAATA ACCGAAAC ACCCAGAA TTATT
- 10 ACCGAGTA AAATA ACCGAAAC ACCCAGAA TTATT ACCTGAGA AAATA
ACCGAAAC ACCCAGAA TTATT ACCGAGTA AAATAACCGAACA ACCCAAGA
TTATT AAATAACCGAACA ACCCAAGA TTATT
- 11 ACCAGCAA AAATAACCGAACA ACCCAAGA TTATT ACCTGAGA
AAATAACCGAACA ACCCAAGA TTATT ACCGAGTA AAATA ACCGAAAC
ACCCAGAA TTATT AAATA ACCGAAAC ACCCAGAA TTATT
- 12 ACCGAGTA AAATA ACCGAAAC ACCCAGAA TTATT ACCTGAGA AAATA
ACCGAAAC ACCCAGAA TTATT ACCGAGTA AAATAACCGAACA ACCCAAGA
TTATT AAATAACCGAACA ACCCAAGA TTATT

01100000	10110000	10000000	10000000	11000000	10000000
00000001	01111011	11000110	00000100	00000000	00001011
11011110	11000001	01100001	00000001	00000001	10000001
00000000	00000010	11110111	10001100	00001000	00000000
00010111	10111101	10000010	11000010	00000010	00000011
00000010	00000000	00000101	11101111	00000111	01000011
00000010	00000000	00000101	11101111	00000101	11000011
00000010	00000000	00001001	11101111	00011000	00010000
00000000	01001111	01111011	00000101	10000100	00001011
10000110	00000100	00000000	00010011	11011110	00110000
00100000	00000000	10011110	11110110	00001011	00001000
00010111	00001100	00001000	00000000	00100111	10111100
01100000	01000000	00000001	00111101	11011100	00010110
00010000	00101110	00011000	00010000	00000000	01001111
01111000	00101110	00011000	00010000	00000000	01001111
01111000	00000010	00011000	00010000	00000000	00101111
01111000	00110001	00001100	00001000	00000000	00010111
10111100	00010001	10000110	00000100	00000000	00010011

ACCGAAACACCGAACAAACCGACAACCGAACAAACCGAAA-
CACCGBAACAGCGAAACACCGAACAAACCGAACAAAGCGAA-
CAACCGAAACACCAACGAAGCAACGAACCGAAACACCGAACAAACCGA-
CAAACCGAACAAACCGAAAACACCGAAAACACCGAAAACACCGAAA-
CACCGBAACAAACCGAACAAACCGAAAACACCGAACAAACCGGA-
CAAAACCGAAAACACCGAACAAACCGACAACCGAACAAACCGAAA-
CACCGBAACAGCGAACCAACCGAACAAACCGAACAAACGCGAA-
CAACCGAAACACCAACGAAGCAACGAACCGAAACACCGAACAAACCGA-
CAAACCGAACAAACCGAAAACACCGAAAACACCGAAAACACCGAAA-
CACCGBAACAAACCGAACAAACCGAAAACACCGAACAAAGCGA-
CAAACCAACGAACCGAAAACACCGAACAAACCGACAAACCGGAA-
CAACCGAAACACCGAAAACAGCGAAAACACCGAACAAACCGAA-
CAAGCGAACAAACCGAAA-
CACCAACGAACCAACGAACCAACGAACCGAAACACCGAACAAACCGA-
CAAACCGAACAAACCGAAAACACCGAAAACAGCGAAAACACCGAA-
CAACCGAACAAAGCGAACAAACCGAAA-
CACCAACGAAGCAACGAACCGAAAACACCGAACAAACCGACAAACCGAA-
CAACCGAAAACACCGAAAACACCGAAAACACCGAAAACACCGAA-
CAACCGAACAAACCGAAAACACCGAACAAACGCGA-
CAAACCAACGAACCGAAAACACCGAACAAACCGACAAACCGGAA-
CAACCGAAAACACCGAAAACACCGAAAACACCGAAAACACCGAA-
CAACCGAACAAACCGAAAACACCGAACAAACCGGACAA.

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administration, Validation. **Alexey V. Chemeris:** Methodology, Project administration, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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