Open Access
Full Length Article

REVIEW ARTICLE

DNA Computing: A Review of Promises and Potential

Muhammad Sami Ullah[1], Waqar Aslam[2], Hira Nazir[3]

[1,3]Department of Computer Science & IT, University of Central Punjab, Bahawalpur Campus, Pakistan.
[2]Department of Computer Science & IT, The Islamia University of Bahawalpur, Bahawalpur, Pakistan.

ABSTRACT

Deoxyribonucleic acid (DNA) computing is prospectively an enabler to solve complex problems. It is based on a blend of computing and biology. The silicon based computers follow a set of instructions with implied meaning to achieve the goal. They are becoming smaller and faster, but the question is how long this trend can sustain. Currently each silicon chip of personal computers has 50 to 60 million transistors on a small sized integrated circuit (IC). According to quantum physics, if the silicon chip continues to decrease in size, the effective transmission of signals will be reduced. Silicon chips are made of toxic substances such as arsenic which can cause damage to nerve cells and immune system, especially in children. Silicon chips consume lots of energy and dissipate heat. To deal issues resulting from the limitations of silicon chips, DNA computing is emerging as a promising alternative. It has the potentials of parallel and distributed processing, massive storage of data, scalability, adaptability (through learning or evolution) and flexibility to minimize costs. It also promises to solve complex NP problems that are difficult to solve by current computability. The goal of this paper is to explore technical dimensions of DNA computing by identifying the new uses of nucleic acids, problems, right questions and DNA molecule potentials.

Keywords: DNA, Protein Sequence Analysis, Molecular Logic Gates, DNAzyme

Author`s Contribution
[1,2,3]Manuscript writing, Data analysis, Interpretation, Conception, Synthesis, Planning of research, Interpretation and Discussion, Data Collection

Address of Correspondence
Muhammad Sami Ullah
samiiub@gmail.com

Article info.
Received: March 19, 2018
Accepted: May 03, 2019
Published: June 30, 2019

***Cite this article**: Ullah MS, Aslam W, Nazir H. DNA Computing: A Review of Promises and Potential. J. Inf. commun. technol. robot. appl.2019; 10(1):93-101*

***Funding Source:** Nil*
***Conflict of Interest:** Nil*

INTRODUCTION

The field of DNA computing is becoming very attractive and exciting. The expectations are high: it is supposed to solve many complex problems, which the conventional silicon based computers would take several years to solve or even cannot solve. The DNA computers in the form of biochip sensors are small enough to fit in human bodies. They can identify abnormal cell structures, diseased cells, control releasing of required insulin for diabetic patients, etc. The seven point HPP (Hamiltonian Path Problem) was solved by demonstrating the DNA computation in test tubes [1]. Adleman constructed DNA representing paths through a graph that didn't repeat vertices, and used separation techniques to find the longest strand, which gave him the Hamiltonian path he was looking for. Operations performed by DNA molecules, such as creating a duplicate copy of itself, creating a new output strand from two or more input strands and separating strands according to the desired length, make

it general purpose and computationally universal just like today's digital computers [2]. A single strand of DNA is composed of four nucleotide bases in a sequence, which represents the "Genetic code": A (adenine) of one strand is hydrogen bonded to T (thiamine) of another strand, while G (guanine) of one strand is hydrogen bonded to C (cytosine) of another strand (please see Figure 1). Nucleotides within a single strand are connected with one another by phosphodiester bonds, which are stronger than hydrogen bonds. Under appropriate conditions, DNA strand, for example GTACT, produces second "Watson Crick" complementary strand composed of DNA sequence CATGA, which are hydrogen bonded to each other. By using the self-assembly (annealing) properties of DNA, we can develop a one gram DNA chip capable of storing huge amount of data equal to 1 Trillion CDs and can achieve high degree of parallelism as present in state-of-the-art super computers to solve thousands of specific problems such as finding Hamiltonian path, producing desired proteins, pattern recognition, encoding the messages and so on. Currently research on DNA computing is focused on four major problem areas:

- Designing of new basic operations in DNA computing;
- Designing DNA based algorithms;
- Encoding information in DNA molecules;
- Minimization of errors in DNA computation. [2-4].

We focus on one of these problem areas to formulate our research question:

"Which basic operations can be carried out in DNA computing?"

The motivation for selecting this problem area is due to its fundamental role in DNA computing paradigm. We consider introduction of computational operations leverage a development platform for other areas. Specifically in this paper, we present the basic computational operations that can be carried out in test tubes containing DNA strands in comparison with the basic operations performed by electronic digital devices.

Rest of the paper is structured as follows. Section 2 consists of DNA basic computational operations and their uses. Section 3 covers the DNA positive and negative aspects. In Section 4, the concept of DNA microchip is presented, while Section 5 concludes the paper.

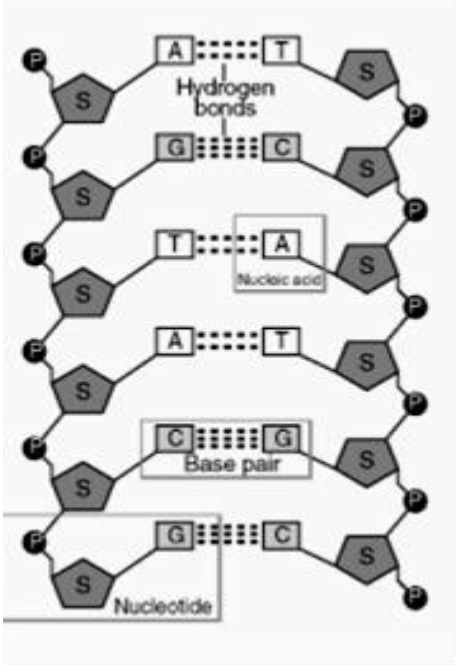

Figure 1. Hydrogen and phosphodiester bonds between complementary nucleotides and nucleotides on the same strand of DNA [5].

COMPUTATIONAL OPERATIONS ON DNA STRANDS

The basic operations in DNA computing are listed below:

1. DNA strands can be constructed that may consist of any desired string of the letters A, T, C and G;
2. Single strands can be prepared by heating double strands;
3. Single strands can be converted into double strands under appropriate conditions by using enzymes such as polymerases;
4. DNA strands can be cut into different strands by using restriction enzymes such as Nucleases;
5. Multiple copies of DNA strand can be constructed by using the PCR (polymerase chain reaction). Thus, we can generate desired sequence of DNA strand in billions in a test tube within a few days;
6. DNA strands can be separated by lengths of different sizes using the process of electrolysis, in which positively and negatively charged strands of different lengths will move towards Anode and Cathode respectively at different speeds;
7. For a present DNA, we can append to its selected

subset or to all, a given string of DNA.

DNA AND COMPUTATIONAL PROBLEMS

There are three categories of computational problems: easy, hard and incomputable [6]. Working of DNA molecules resemble with the working of Turing machines [7]. Using Turing machines, solutions to NP-complete problems remain undiscovered because computation time increases tremendously with input size. Such problems are thought to be solvable due to the massive parallelism property of DNA. Contrary to Turing machines in which the computation time increases exponentially with input size, DNA molecules have a linear relationship between the input size and computation time. We can solve NP-complete problems by generating all possible sequences of DNA strands and finding out the right sequence as an output. Algorithms based on DNA computations have been the major area of interest of many researchers. Algorithm's speed for predicting RNA secondary structure with time complexity $O(n^3)$ is very fast and has high accuracy [8].

DNA can perform computationally intensive operations efficiently. Even its applicability can be extended with same accuracy to encode and process information. Using basic computational operations, Adleman found Hamiltonian path (a long strand of DNA) representing various cities. Using similar level of efficiency, we can solve various classes of NP problems, encrypt/decrypt the messages, use the bases such as A, C, G and T to represent characters or binary information, forecast the future behaviors of DNA computers [9], human genomes, exchange rates (by analyzing the DNA sequences) and certain biochemical processes. Applicability of DNA computing extends beyond expectations. For instance, analyzing injury and automatic healing of a wound can be made possible by DNA computing. Bacteria can be programmed to make them inactive (dormant) or active under certain chemical reactions. After waking up, they will consume certain chemicals, multiply and will become dormant again. In contrast, silicon based computers face two major problems. One, computer chips are made of toxic substances such as arsenic, which can cause damage to nerve cells and immune system especially in children. Two, silicon based chips are energy inefficient, consuming lots of energy and dissipating heat [10], [11]. The promising alternative DNA computing is more energy efficient, and less toxic due to using the biological material such as amino acids instead of silicon and other inorganic materials [12]. Currently DNA computing provides at most 10^{14} operations per second (a rate of 100 Teraflops, i.e. 100 trillion floating point operations per second). Compare it with 10^{12} operations per second as provided by silicon based computers. The pairing and sequencing among nucleotide bases A, T, G and C is very useful for identification and correction of error in a cell. It can be used for flow and error control while transmitting information from one molecule to another molecule of DNA.

DNA COMPUTING: POSITIVE AND NEGATIVE ASPECTS

DNA exhibits a property that can be applied to achieve computability: reaction of complementary bases with each other. Similarly, the ability of self-healing, self-assembly and massive parallelism (sequencing of a large number of DNA molecules at once) can also be used in computation, as each molecule of DNA can act as a separate nanoprocessor. On the down side, error rates in DNA computing are still high. Minimizing error rates is still a challenging problem as are other open problems. These include but are not limited to achieving huge number of DNA based computational operations and the transmission of information in a DNA computer, from one molecule of DNA to another molecule. Research initiatives to address these problems are already taken but much work is still needed. The idea of creating a living 'brain creature' through DNA computing raises some problematic questions in our minds: should we give it the rights of a human being? Can we create life? Thinking about solutions to this end, will create a lot of problems and may turn some immature people or non-believers against the creator of this universe.

DNA AND BINARY REPRESENTATION

DNA molecules can be used to represent the binary language (0 or 1) as shown in Figure 2. For this, catalytic DNA or deoxyribozyme is used in contact with some substrate of nucleotide sequences. Deoxyribozyme was prepared in the laboratory [13]. Catalytic DNA or

deoxyribozyme is different from the normal structure of DNA as it acts as a catalyst to provoke chemical reactions. A catalyst speeds up the reaction while it remains unchanged after the chemical reaction. Various types of catalytic DNA or deoxyribozymes can be prepared in the laboratory such as s-cleaving, catalytic deoxyribozyme or deoxyribozymes that split its own strand or other strands of nucleotides.

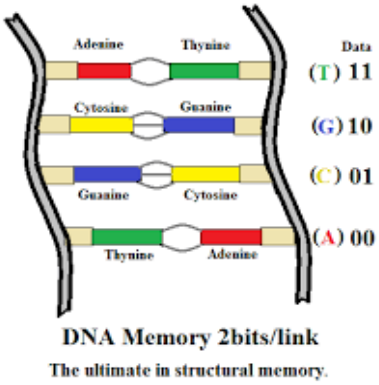

Figure 2.A depiction of two bits of data per link.

Deoxyribozymes E6 (shown in Figure 3) and E8-17 are used for binary representation. Both E6 and E8-17 have catalytic core and internal loop, but the internal loop in E8-17 is fixed while the internal loop in E6 can be substituted with the desired nucleotide sequence. Deoxyribozyme can have either of two states, active or inactive. Active state represents ON (1) while inactive state represents OFF (0). An input oligonucleotide (a short chain of nucleotide) or complementary sequence of nucleotide is mixed to a chemical solution containing catalytic DNA (deoxyribozyme), annealing to deoxyribozyme and splitting into smaller molecules, thus representing an active state. We can reset the catalytic DNA by removing the input oligonucleotide by introducing another complementary sequence of oligonucleotide, so deoxyribozyme will again become OFF or inactive. The process of breaking a molecule into smaller ones is known as cleavage. Cleavage occurs by introducing the input oligonucleotide into the chemical solution containing the deoxyribozyme. If there is a cleavage of substrate, the output is 1, while no cleavage in the solution represents 0. If there is no input oligonucleotide in the solution, catalytic DNA will remain inactive. Thus catalytic DNA can be treated as an ON, OFF switch or a logic gate. We can use a bulk of catalytic DNAs to represent any number of binary strings.

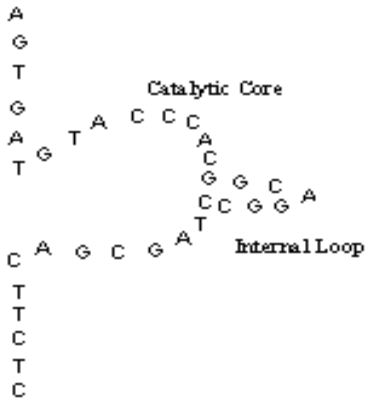

Figure 3. The structure of E6 Deoxyribozyme.

The deoxyribozyme in a solution binds with matching oligonucleotide and changes its structure or becomes active, thus becoming difficult to detect whether the reaction took place or not in the solution. In other words, we can say that computation is fast within the solution but access to solution is slow. In order to know that the solution is in active state or binary 1, fluorescence based substrate is used as it doesn't cleave. The amount of fluorescence in a solution indicates that reaction has occurred but it also takes time. MAYA-II, a successor of MAYA-I (23 logic gates) and made up of 100 logic gates (Catalytic DNA or DNAzyme), can play a tic-tac-toe game [14].

DNA BASED LOGIC GATES

Encoded strands of DNA may be used as processing units or molecular logic gates to produce certain output strands. Fork I enzyme of nuclease was used to simulate a NAND gate [15]. Researchers have simulated logic gates by using DNA but their works lack generalization. Recent models have proposed single stranded DNA (ssDNA), double stranded (dsDNA) and restriction enzyme to execute bio molecular reaction in a controlled way [16], [17]. Experiments conducted in this context considered any random sequence strand as true and its complementary strand as false. The presence of dsDNA is taken for true, otherwise false. A generalized hairpin based approach is proposed to overcome challenges such as uniformity in representing 1s and 0s, reducing

error rates and reusability of molecular logic gates but this approach needs verification in a biochemical laboratory [18].

DNA AND MICROCHIPS

Fabrication of millions of small pieces of DNA in 2D is done on a solid substrate such as silicon wafer or thin sheet of glass with fluorescent labeling and detection. Porous solid substrate is suitable for DNA microchip as it offers certain good features such as compatibility with lithography, fluorescence and micro spotting, and faster data acquisition. On the other hand, non-porous substrate provides slow data acquisition, not compatible with photolithography, fluorescence and micro spotting thus not suitable for DNA microchip. Trillions of polymeric molecules derived from DNA fragments are immobilized in each reaction cell. DNA fragments may be shorter or longer strands of complementary DNAs. Probes are the known sequences of DNA fragments, such as ATCTGC… represent a single probe. Three technologies are required to design a DNA microchip: Photolithography, Ink jetting and Mechanical micro spotting. In Ink jetting, DNA molecule is expelled from tiny nozzle assembled with piezoelectric device. In mechanical micro spotting, DNA samples are picked and deposited on predetermined locations of slide by a robotic system. In short, entire human genome can be provided on a single chip.

Any one of the above mentioned technologies can be used for the manufacturing of DNA microchip for mutation detection and gene (a sequence of nucleotides that controls the production of a biologically functional molecule) expression. Each technology has specific advantages and disadvantages in fabrication of a DNA microchip. A DNA micro array consists of millions of genes. For instance, cancerous genes may be encrypted in DNA microarray for the recognition of cancer in patients [19]. Different selection methods for the recognition of seven types of cancerous genes present on the micro array are compared [20]. For example, DNA microchip can be implanted inside or outside of the human body as a sensing device to sense the amount of glucose in the blood stream, which can transmit this vital information to silicon chip to trigger appropriate actions such as displaying glucose level on a screen or activating another DNA microchip to prepare insulin per the requirement of a diabetic patient. DNA microchip can transmit vital information regarding cellular processes, biochemical changes during sickness, genetic makeup, protein synthesis, working of individual genes, etc., from the body to silicon chip to facilitate doctors in diagnosing diseases at early stages. These days, the genetic structure of a dissected tumor is analyzed using a computer. This technique is still not accurate enough; so much work is being done in the field of bioinformatics to make it more accurate. The aim is to attach DNA microchip to record the changes in genetic makeup and cancerous strands of DNA.

DNA AND CRYPTOGRAPHY

Efficient DNA molecular structure allows parallelism and extra ordinary storage, promising bright future for cryptography. DNA and chaotic systems based cryptography is an emerging area and has gained increasing attention by researchers due to its excellent results as reflected by corresponding security analysis. This is especially true for encryption of color images and videos. Due to this combination (DNA and chaotic systems), the performance of encryption algorithms is reaching new levels of security [21-29]. The problems of studying this emerging paradigm are challenging for the researchers. There is a need to benchmark the performance of these combinations along with reference images and videos.

The DNA operations and the mapping rules for DNA encoding and decoding for converting the text or image data into DNA molecules are given in Tables 1 and 2. Although, these encryption schemes provide promising security analysis results for resistance against multiple attacks, larger key space and sensitivity to chaotic secret keys but at the cost of increased computational complexity. The issue of complexity due to inclusion of DNA can be minimized by using specialized software, visual DNA Strand Displacement (DSD) that is designed to optimize the standard DNA operations. Aligning the design of current DNA based operations to DSD seems an initial step towards realization of DNA computers.

Table 1. Eight kinds of DNA mapping rules.								
	1	**2**	**3**	**4**	5	**6**	**7**	**8**
A	00	00	11	11	01	10	01	10
G	11	11	00	00	10	01	10	01
C	10	01	10	01	00	00	11	11
T	01	10	01	10	11	11	00	00

Table 2. The three DNA operations.				
+	A	G	C	T
A	A	G	C	T
G	G	C	T	A
C	C	T	A	G
T	T	A	G	C
−	A	G	C	T
A	A	T	C	G
G	G	A	T	C
C	C	G	A	T
T	T	C	G	A
⊕	**A**	**G**	**C**	**T**
A	A	G	C	T
G	G	A	T	C
C	C	T	A	G
T	A	C	G	A

DNA STRAND DISPACEMENT

DNA strand displacement, an enzyme free method, is the process of replacing a shorter hybridization region with a longer, double-stranded hybridization region. DNA strand displacement technology is being used by different researchers for DNA computations, molecular computation, designing biological logic circuits and also solving the instability issues of logic gates. Arithmetic operations, addition, subtraction and multiplication, are tested and validated for 2-dimensional matrices using the software, visual DSD, which applies the concept of DNA strand displacement technology [30]. These operations can be extended to n-dimensional matrices. DNA strand displacement technology has been used for the fabrication of nanostructures and devices to perform biosensing and logic functions, such as AND, OR and NOT [31]. In this context, a novel Biological Information Processing System (BIPS) was constructed on a self-assembled, spatially addressable single-stranded DNA tile (SST) nanostructure. The DNA strand displacement technology has also been used to design an 8 bit adder/subtractor with domain labels of "f" and "t", where domain "f" represents binary 0 (regions of low concentration) while domain "t" represents binary 1 (regions of high concentration) [32]. BCD adder, designed in visual DSD, uses DNA strand displacement technology achieves suitable computing power, which is a good indicator for the future development of complex circuits [33]. The modular property of logic inverter gate using the concept of DNA strand displacement technology is also simulated in DSD software [34]. Similarly, a 4 bit full adder circuit using dual rail method is designed and simulated in visual DSD [35]. A very first step in designing the clock signal generator with 1/2 duty cycle based on Chemical Reaction Network (CRN) has been taken, duly verifying the design using Original Differential Equations (ODE) analysis [36]. The simplification of clock signal with $^{M}/_{N}$ duty cycle and modulation may be directed towards future work as a challenge.

RESEARCH CHALLENGES AND HINDRANCES

The chemical properties of DNA molecules restrict the massive adoption of DNA technology. These properties prevent scalability, synthesizing of molecules for DNA storage, algorithmic realization, enough reliability of security algorithms, detectability and correctability of DNA operations. Thus bottlenecks in laboratory experiments towards integrated system are introduced, making it difficult to operate DNA without specific restrictions on enzymes. Of high and fundamental importance are few research challenges:

- Can we extract any single piece of data without retrieving all the data?
- Can a random access method be devised for rewriting the encoded data?
- To what extent the PCR and other techniques such as gene editing technique (CRISPR–Cas9) can be helpful in rewriting the encoded data? Mathematical formulae in devising encoding schemes in this context may be a very helpful tool.
- What will be the role of DNA computers in big data analysis for data/pattern/process mining towards intelligent decision making for greater profit margins in corporations and companies?

- What levels of privacy and security of data, images and videos can be ensured? This is particularly relevant to the exponentially emerging domain of big data, which is not handled efficiently by the current software tools [37]. To this end, an enabler for DNA cryptography is the DNA arithmetic and corresponding biological operations [38].
- Can we replace the conventional object names in IoT with DNA support? [39]. A proposal is to manage this issue by generating unique DNA sequences for each object. In this way non-living objects will have their own DNA based identification.
- How DNA bases can be sequenced for designing large scale molecular circuits? A DNA circuit experiences unwanted DNA strand displacements that affects the desired functionality of molecular circuit. A tool or an algorithm may be proposed for preventing the unintentional bindings of strands to one other. In this regard an algorithm based on intended and unintended DNA strands has been proposed to design the base sequences that form only the intended double stranded DNAs, thus effectively preventing the unintended double stranded DNAs [40].
- How to realize reliable DNA codes? DNA code design plays a vital role in the field of DNA computing and its applications in DNA nanotechnology and bioinformatics. In order to improve the efficiency of DNA computing, reliable DNA codes has been designed by devising a new algorithm called BPSON algorithm, which combines BAT and PSO algorithms [41]. Other algorithms proposed for this purpose are random search algorithms, exhaustive methods, directed graph, template matching strategies, simulated annealing, genetic algorithms, iterative genetic search, hybrid strategy algorithms, INSGA-II, etc. [42-51]. Deep learning is not much used in designing DNA codes [52].
- How to optimize DNA scanning methods? There is a huge amount of data in the biological world, and these data contain important information. Discovering this hidden information can help speed up research in biology and its allied sciences. For this purpose, there is a need to devise efficient DNA scanning methods such as nested hash tables and set operations to identify inherent patterns and their relative positions [53]. Other DNA pattern scanning method is DNA motif finding, though it discloses the hidden information such as individual traits and disease defects [54], [55]. The tools and methods based on DNA motif finding can be optimized to prevent them from information leakage.
- How to overcome time and space complexity issues in the implementation of DNA assembly? DNA assembly is the process of finding the correct sequence of the nucleotide bases in DNA. To address this key challenge, methods like bloom filter can be optimized [56].

CONCLUSION

Various dimensions of DNA computing have been explored in this paper. By exploiting the potential of DNA, we can facilitate our life. The enormous computability provided by DNA computing can leverage the field of Computer Science towards solving complex problems in a cost effective way by managing time, energy and costs (monetary and psychic). Catalytic DNA or DNAzyme, for instance E6 and E8-17, prepared in the laboratory, are used for the representation of binary data and implementation of molecular logic gates such as AND, NAND, OR and NOT. Thus Adder Circuits, Shift Registers, etc., can also be prepared by using catalytic DNA, though further research is needed to overcome the issues of uniformity and generalization. Lastly, we have discussed the feasibility of DNA microchips, which can be implanted inside or outside the human body as a sensing device to sense biochemical changes during sickness. Such changes may be communicated wirelessly to maintain electronic health records. DNA computing is rather the beginning of a journey for the researchers, publishers and readers who are interested in this field.

Conclusively, there is a need to improve the DNA strands utilization, improve the models based on DSD, prove the correctness and validation of models based on DSD, reduce the reversible reactions and reduce the instability issues of logic gates.

REFERENCES

1. Adleman, L.M., "Molecular Computation of Solutions to Combinatorial Problems," in Science, 1994. 266: pp. 369-378.
2. Lipton, R.J., "DNA solution of hard computational problems," in Science, 1995. 268: pp. 542-545.
3. Marathe, A., Condon, A.E., and Corn, R. M., "On combinatorial DNA word design," in J. of Comput Biol., 2001. 8: pp. 201-219.
4. Roweis, S.a.W., E., "On the reduction of errors in DNA Computation," in Journal of Computational Biology, 1999. 6: pp. 65-75.
5. Kang, Z., Zhen, H.G. and Jin, X, "An algorithm of DNA computing on 0-1 planning problem," in Advances in Systems Science and Applications, 2005. 5(4): pp. 587-593.
6. Casti, J.L., "Computing the uncomputable," in Complexity, 1997. 2(3): pp. 7-12.
7. Benenson, Y., Paz-Elizur T., Adar, R., Keinan, E., Livneh, Z. and Shapiro, E., "Programmable and autonomous computing machine made of biomolecules," in Nature, 2001. 414(430-434).
8. Zhendong, L., Hengwu, L. and Daming, Z., A "Predicting Algorithm of RNA Pseudoknotted Structure Based on Stems," in Kybernetics, 2010. 39(6): pp. 1050-1057.
9. Landweber, L.F.a.B., E. B "DNA Based Computers II," in American Mathematical Society, 1999.
10. Forbes, N., "Life After Silicon: Ultrascale Computing," in The Industrial Physicist, 1997: pp. 20-23.
11. Kevin, B. "How DNA computers will work," 2000. [Online]. https://computer.howstuffworks.com/dna-computer.htm. [Accessed: 10 May 2019].
12. Garfinkel, L.S., "Biological Computing," 2000. [Online]. http://www.technologyreview.com/computin g/12087. [Accessed: 10 May 2019].
13. Breaker, R.R., Joyce, G. F., "A DNA enzyme with Mg2+ dependent RNA phophoesterase activity," in Chemistry & Biology, 1995. 2(10): pp. 655-660.
14. MacDonald, J., et al. "Medium Scale Integration of Molecular Logic Gates in an Automaton," in Nano Lett., 2006. 6(11), pp. 2598–2603.
15. Mulawka, J.J., Wasiewicz, P. and Plucienniczak, A., Another Logical Molecular NAND Gate System, in Proc. of the 7th Int. Conf. on Microelectronics for Neural Fuzzy and Bio-Inspired Systems (MicroNeuro'99). 1999. pp. 340-345.
16. Gearheart, C.M., Rouchka, E. C. and Arazi. DNA-based dynamic logic circuitry. in 53rd IEEE International Midwest Symposium on Circuits and Systems (MWSCAS). 2010. IEEE.
17. Gearheart, Christy & Rouchka, Eric & Arazi, Benjamin. "DNA-Based Active Logic Design and Its Implications," in Journal of Emerging Trends in Computing and Information Sciences, 2012. 3(5): pp. 756-766.
18. Zoraida, B.S.E., Arock, M., Ronald, B.S.M. and Ponalagusamy, R., A novel generalized model for constructing reusable and reliable logic gates using DNA, in Natural Computation, ICNC'08. Fourth International Conference. 2008, IEEE.
19. Vert, J.P., "Kernel methods in genomics and computational biology," in Signal and Image Processing, Ecole des Mines de Paris, France, pp. 22, 2007. doi:10.4018/978-1-59904-042-4. ch002.
20. Wiliński, A.a.O., S., "Gene selection for cancer classification," in COMPEL - The International Journal for Computation and Mathematics in Electrical and Electronic Engineering, 2009. 28(1): pp. 231-241.
21. Meng Ge, Ruisong Ye, "A novel image encryption scheme based on 3D bit matrix and chaotic map with Markov properties," in Egyptian Informatics Journal, 2019. 20(1): pp. 45-54.
22. A. Fatahbeygi and F. A. Tab, "A highly robust and secure image watermarking based on classification and visual cryptography," in Journal of Information Security and Applications, vol. 45, pp. 71–78, 2019.
23. C. Li, Y. Zhang, and E. Yong, "Journal of Information Security and Applications When an attacker meets a cipher-image in 2018 : A year in review," in Journal of Information Security and Applications, vol. 48, pp. 1–9, 2019.
24. X. Chai, X. Fu, Z. Gan, Y. Lu, and Y. Chen, "A color image cryptosystem based on dynamic DNA encryption and chaos," in Signal Processing, vol. 155, pp. 44–62, Feb. 2019.
25. J. A. Alzubi, O. A. Alzubi, G. Suseendran, and D. Akila, "+ A Novel Chaotic Map Encryption Methodology for Image Cryptography and Secret Communication with Steganography," in International journal of Recent Technology and Engineering (IJRTE), vol. 8, no. 1C2, May, pp. 1122–1128, 2019.
26. S. Kandar, D. Chaudhuri, A. Bhattacharjee, and B. Chandra, "Image encryption using sequence generated by cyclic group," in Journal of Information Security and Applications, vol. 44, pp. 117–129, 2019.
27. Y. Luo, X. Ouyang, J. Liu, and L. CAO, "An Image Encryption Method Based on Elliptic Curve Elgamal Encryption and Chaotic Systems," in IEEE Access, vol. 7, pp. 38507–38522, 2019.
28. A. Belazi, M. Talha, S. Kharbech, W. E. I. Xiang, and S. Member, "Novel Medical Image Encryption Scheme Based on Chaos and DNA Encoding," in IEEE Access, vol. 7, pp. 36667–36681, 2019.
29. Z. Liu, C. Wu, and J. U. N. Wang, "A Color Image Encryption Using Dynamic DNA and 4-D Memristive Hyper-Chaos," in IEEE Access, vol. 7, pp. 78367–78378, 2019.
30. L. Yang, C.Z., H. Lv and Q. Zhang, N-dimensional matrices operation based on DNA strand displacemen, in Tenth International Conference on Advanced Computational Intelligence (ICACI). 2018. pp. 490-501.
31. X. Zhang, Y.N., C. Shen et al., "Fluorescence resonance energy transfer-based photonic circuits using single-stranded tile self-assembly and DNA strand displacement,"

in Journal of Nanoscience and Nanotechnology, 2017. 17(1): pp. 1053–1060.
32. Han, W., & Zhou, C., “8-Bit Adder and Subtractor with Domain Label Based on DNA Strand Displacement,” in Molecules 2018. 23(11).
33. Shi, C.Z.a.Q.Z., Four digits BCD adder with DNA strand displacement, in 4th International Conference on Systems and Informatics (ICSAI). 2017: Hangzhou. pp. 1688-1692.
34. Singh, A.K.G.a.H., “DNA strand displacement-based logic inverter gate design,” in Micro & Nano Letters, 2017. vol. 12 (no.9): pp. 611-614.
35. D. Hu, C.Z., B. Wang and Q. Zhang, Four-bit full adder-subtracter based on DNA strand displacement, in Third International Conference on Advances in Electrical, Electronics, Information, Communication and Bio-Informatics (AEEICB). 2017: Chennai. pp. 67-74.
36. D. Wen, L.G., Y. Lu, C. Zhang and X. You, A DNA strand displacement reaction implementation-friendly clock design, in IEEE International Conference on Communications (ICC). 2017: Paris. pp. 1-6.
37. Gupta, R., “Journey from data mining to Web Mining to Big Data,”. in IJCTT, 2014. 10(1): pp. 18-20.
38. D. A. Zebari, H.H., S. R. M. Zeebaree and D. Qader Zeebaree, , Multi-Level of DNA Encryption Technique Based on DNA Arithmetic and Biological Operations doi: 10.1109/ICOASE.2018.8548824, in International Conference on Advanced Science and Engineering (ICOASE). 2018. pp. 312-317.
39. Daniele Miorandi, S.S., “Internet of things: Vision, applications and research challenges,” in Ad Hoc Networks, 2012: pp. 1497-1516.
40. Nakakuki, Y.Y.a.T., A tool for the design of DNA base sequences for molecular circuits, in 17th International Conference on Control, Automation and Systems (ICCAS) 2017. pp. 669-674.
41. K. Liu, B. Wang, H. Lv, X. Wei and Q. Zhang, "A BPSON Algorithm Applied to DNA Codes Design," in IEEE Access, vol. 7, pp. 88811-88821, 2019. doi: 10.1109/ACCESS.2019.2924708.
42. A. J. Hartemink, D. K. Gifford, J. Khodor, "Automated constraint-based nucleotide sequence selection for DNA computation", Biosystems, vol. 52, no. 1, pp. 227-235, Oct. 1999.
43. R. Penchovsky, J. Ackermann, "DNA library design for molecular computation", J. Comput. Biology., vol. 10, no. 2, pp. 215-229, Jul. 2003.
44. M. Arit, S. Kobayashi, "DNA sequence design using templates", New Gener. Comput., vol. 20, no. 3, pp. 263-277, Sep. 2002.
45. W. Liu, S. Wang, L. Gao, F. Zhang, J. Xu, "DNA sequence design based on template strategy", J. Chem. Inf. Comput. Sci., vol. 43, no. 6, pp. 2014-2018, Aug. 2003.
46. U. Feldkamp, S. Saghafi, W. Banzhaf, H. Rauhe, "DNASequenceGenerator: A Program for the construction of DNA sequences", International Workshop on DNA-Based Computers, pp. 23-32, 2001.
47. F. Tanaka, M. Nakatsugawa, M. Yamamoto, T. Shiba, A. Ohuchi, "Towards a general-purpose sequence design system in DNA computing", Proc. Congr. Evol. Comput.(CEC), vol. 1, pp. 73-78, May 2002.
48. Z. Ibrahim, N. K. Khalid, K. S. Lim, S. Buyamin, J. A. A. Mukred, "A binary vector evaluated particle swarm optimization based method for DNA sequence design problem", Proc. IEEE Student Conf. Res. Develop., pp. 160-164, Dec. 2011.
49. A. J. Ruben, S. J. Freeland, L. F. Landweber, "PUNCH: An evolutionary algorithm for optimizing bit set selection", International Workshop on DNA-Based Computers, pp. 150-160, 2001.
50. C. Xu, Q. Zhang, B. Wang, R. Zhang, "Research on the DNA sequence design based on GA/PSO algorithms", Proc. 2nd Int. Conf. Bioinf. Biomed. Eng., pp. 816-819, May 2008.
51. Y. Wang, Y. Shen, X. Zhang, G. Cui, J. Sun, "An improved non-dominated sorting genetic algorithm-II (INSGA-II) applied to the design of DNA codewords", Math. Comput. Simul., vol. 151, pp. 131-139, Sep. 2018.
52. C. Zhu, C. Zhou, B. Wang, "Development of conceptual learning model based on various stability features", IEEE Access, vol. 7, pp. 37961-37969, 2019.
53. N. Deng, X. Chen, D. Li and C. Xiong, "Frequent Patterns Mining in DNA Sequence," in IEEE Access, vol. 7, pp. 108400-108410, 2019. doi: 10.1109/ACCESS.2019.2933044.
54. X. Wu, H. Wang, M. Shi, A. Wang and K. Xia, "DNA Motif Finding Method Without Protection Can Leak User Privacy," in IEEE Access, vol. 7, pp. 152076-152087, 2019. doi: 10.1109/ACCESS.2019.2947261.
55. T. K. K. Ho and J. Gwak, "Toward Deep Learning Approaches for Learning Structure Motifs and Classifying Biological Sequences From RNA A-to-I Editing Events," in IEEE Access, vol. 7, pp. 127464-127474, 2019.
56. S. Nayak and R. Patgiri, "A Review on Role of Bloom Filter on DNA Assembly," in IEEE Access, vol. 7, pp. 66939-66954, 2019. doi: 10.1109/ACCESS.2019.2910180.