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Principles and Applications of Deoxyribonucleic Acid Computing: A Brief Review

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ABSTRACT

Deoxyribonucleic acid (DNA) computing is a rapidly evolving field that uses DNA molecules as fundamental components of computer devices and performs computational processes, creating molecular scale autonomous programmable computers that provide data inputs and outcomes in molecular form. It incorporates ideas and information from a variety of disciplines, including molecular biology, computer science, chemistry, mathematics, and physics. DNA computing is employed to address various combinatorial issues that arise due to its high parallelism and density storage. Recently, this technology has drawn and received a lot of interest for its potential applications in many fields such as nanotechnology, bioengineering, and medicine. It holds great potential in addressing key challenges in these fields, but significant efforts are needed to overcome current limitations and fully realize its potentiality. This review paper aims to provide a brief overview about the principles of DNA computing and its applications. The paper also discusses the DNA computing benefits, challenges and limitations and suggests future directions for research.

Keywords: DNA Computing, Security, Biosensor, Disease Diagnosis, Drug Delivery.

1. INTRODUCTION

Growing interest in the idea of using DNA molecules to perform computations has been observed in the past few years, especially since there is always an urgency to find a method for continuously boosting computing performance without any miniaturization limits. DNA computing is a fast developing field in which DNA molecules are used as a medium for computational processes [1]. It stands as an interdisciplinary field, combing computer science, chemistry, mathematics, and molecular biology, to develop computational processes using DNA molecules[2]. What makes DNA an attractive candidate for building new computational systems, is that DNA is a one-of-a-kind and versatile material that can store and process data in a highly parallel and dense manner [1,3]. Unlike conventional electronic computing, DNA computers operate without electronic components, relying solely on biochemical reactions in a test tube, where DNA strands serve as software and enzymes as hardware [4]. It has the appearance of a transparent water solution in a test tube, which is tiny enough that a drop of water may contain more than a trillion pieces of information subjected to parallel operation [5]. In essence, DNA computing provides numerous advantages, including parallel computing, enormous storage capacity, low power consumption, and molecular processing [6].

The inception of DNA computing research was inspired by the intrinsic similarities between the workings of DNA and Charles Bennett's Turing machine [7]. Turing machines process information and store it as a series or set of symbols, operating very similarly to biological machinery [8]. The first practical demonstration of employing DNA molecules as a computational medium was championed by Leonard Adleman [2]. While his initial goal was to demonstrate the viability of biomolecular computation, his study also revealed that the advent of this new computational paradigm may give an advantage over standard electrical computing approaches [5]. Since then, numerous research

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teams have put forth designs for DNA computers. This rapidly evolving field has opened up new possibilities for solving difficult and challenging problems in diverse areas, including bioengineering, and medicine [6]. Yet, despite these promising prospects, DNA computing confronts several obstacles that warrant consideration, particularly concerning the reliability and scalability of DNA-based systems. In this review paper, our focus is on elucidating the essential facets of DNA's role in computing, providing an overview of its applications, delineating its benefits and challenges, and charting the future directions of this burgeoning field.

The paper is organized into the following sections: Section 2 presents the structure and bases of DNA. Section 3 expounds upon the motivation, history, and principles underpinning DNA computing. Section 4 explains the methods employed for implementing DNA computing. In Section 5, we explore the diverse applications of DNA computing. Section 6 introduces the challenges and future directions within the domain of DNA computing. Finally, Section 7 offers the concluding remarks.

2. DNA STRUCTURE AND BASES

The DNA molecules are a double-stranded helix structure in the shape of a twisted ladder that contains the genetic information of living organisms [9]. DNA is usually compared to a code or a blueprints collection as it carries the blueprints and instructions necessary to build other cells components, such as protein molecules. As shown in fig. 1, DNA is made up of two lengthy polymers of nucleotides, which are little, fundamental components. Each nucleotide is made up of (deoxyribose) a sugar with a phosphate group attached to one of four different types of bases. Adenine (A), Cytosine (C), Guanine (G) and Thymine (T), are the four types of nucleotide bases [9,10]. These nucleotide components join together through the linkage of phosphates and sugars to form lengthy polymer chains. The bases are put in a certain order that codifies the genetic information. This fundamental structure of DNA, elucidated through X-ray diffraction evidence by Rosalind Franklin and Maurice Wilkins [11], was first proposed by James Watson and Francis Crick's in 1953 [12].

The binding of DNA nucleotides base-to-base follows a strict rule: Adenine (A) pairs exclusively with Thymine (T), and Cytosine (C) pairs solely with Guanine (G), and vice versa. For instance, if sequence N is ATTCGTG, its complement, N', is TAAGCAC. Double stranded DNA will be created when N and N' combine (or hybridize). Consequently, each DNA sequence has a natural complement as depicted in Fig. 1. Hydrogen bonds hold the two strands of DNA's complementary base pairs together. The two integral strands are joined in an anti-parallel (polarity-reversed) way to form the double helix. The 3’ end and the 5’ end are two different endpoints on each DNA strand that distinguish its polarity [10]. The elucidation of the DNA structure revolutionized the field of molecular biology and paved the way for new technologies, like DNA computing.

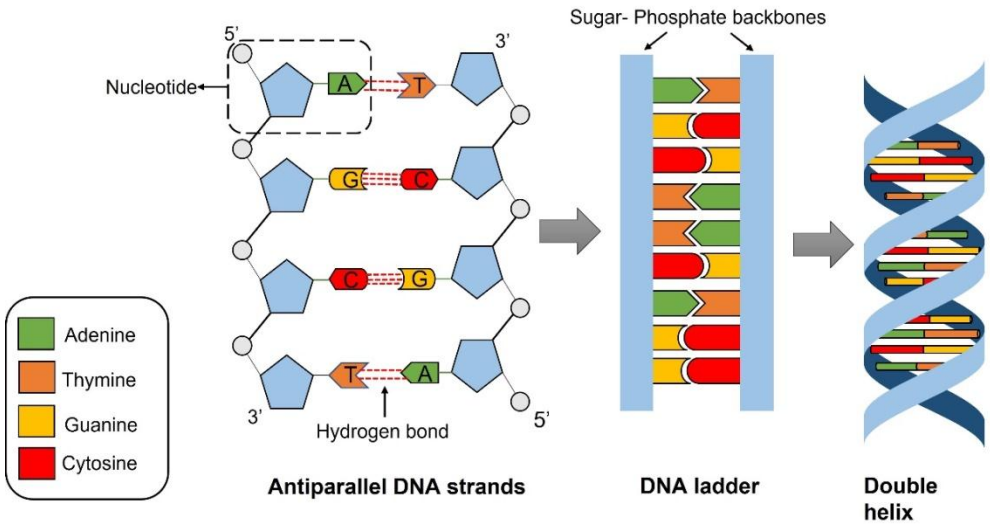

Figure 1: A DNA Molecule illustration

3. DNA COMPUTING MOTIVATION, HISTORY, AND PRINCIPLE

As mentioned the field of DNA computing has recently arisen a transformative force in various scientific domains [8]. The main reason why researchers are interested in this new field is to overcome the limitation and boundaries of the current computational models. Despite the huge advance and miniaturization in the silicon technology still there are some limitations we face with the current technology such as: power consumption, circuit integration dimensions, and clock frequency [13]. Moreover, DNA exhibits unique capabilities that hold the promise of revolutionizing biological electronics and optical instrumentation, encompassing biosensors and probes. The DNA computing field of study has the ability to alter our comprehension of computing theory and practice. The foundation of DNA computing lies in the premise that DNA strands can represent data and execute logical operations. A large portion of DNA computing is based on creating algorithms that decode information stored in the nucleotides sequence that form the DNA double helix, then break and build new connections between them to reach an answer.

The concept of DNA computing traces its origins to the visionary ideas of American physicist Richard Feynman in 1959, wherein he introduced his theories on nanotechnology, which included the notion that individual molecules or perhaps atoms may be employed for computation [14]. However, DNA computing was physically first proposed by Leonard Adleman an American computer scientist form the Southern California University in 1994, who demonstrated that DNA can be utilized to resolve a computational problem known as the "Hamiltonian path problem" utilizing regular laboratory techniques. [2]. The problem is a variation of the "traveling salesman problem". The problem state that given X cities, design a path that visits each city only once while beginning and terminating at the given location [1] as illustrated in fig. 2. There is (X-1)! /2 potential paths for X cities. When cities grow in number, so does the number of feasible path possibilities. For instance, there are around 180,000 possible paths for 9 cities, and 200 trillion paths for 17 cities. The fastest supercomputer would be swiftly overwhelmed by crude force attempts to compute all ways to solve the issue for more cities. However, this approach becomes practical if DNA computing is possible. DNA enables us to approach a computing problem from a different angle due to its distinctive data structure and capacity for several parallel operations [1,15]. While traditional silicon-based computers predominantly execute operations sequentially, DNA computers, classified as Non-von Neumann stochastic machines, adopt a different approach, emphasizing parallelism [15]. Regarding the DNA remarkable data density, the four bases of DNA, A, C, T and G, are used to encode a strand of DNA. This is like how ones and zeros are used to encode a string of binary data in electronic computers. The size of a half-inch sugar cube, about one gram of dried DNA has the capacity to store as much data as a trillion compact discs. [13]. The fact that DNA has complementary double stranded is another important property, which may be used in different ways. One illustration is error correction. DNA mistakes can be caused by a variety of things. For example DNA enzymes make mistakes, cutting in the wrong places or inserting a T instead of G. Environmental factors like UV rays from the sun and thermal energy can also harm DNA. The correct DNA sequence can be restored by repair enzymes using the complement strand as a reference if one of the double-stranded DNA's strands is affected by the error [1,15]. This repertoire of operations, combined with synthetic chemistry, forms the basis for DNA computing. DNA contains many different operations that enable it to carry out even the most sophisticated computations, including synthesizing, mixing, annealing, melting, amplifying (copying), cutting, pasting, and more, similar to how a CPU has a fundamental set of operations like logical operators and addition [1,13]. Moreover, enzymes do not operate sequentially in the test tube, addressing one DNA molecule at a time. Instead, multiple copies of enzymes can act concurrently on multiple DNA molecules. This capacity for massive parallelism underscores the strength and power of DNA computing.

4. METHODS OF IMPLEMENTATION

We will briefly overview the fundamental operations that were adapted from biochemical processes for use as computational tools. As mentioned, DNA computing replaces existing computational techniques with a number of biochemical activities. Adleman asserted that we would have to use the resources and tools we already had in order to construct a DNA computer [2]. These tools basically consisted of the following: Watson-crick pairing, ligases,

nucleases, polymerase, gel electrophoresis, and DNA synthesis. By employing these tools, Adleman conducted experiments to address the "Hamiltonian path problem".

First, he utilized DNA strands to symbolize cities with the letters A, C, T, and G. Each city was represented by a different sequence of these four letters. For instance, Atlanta may have the code ACTTGCAG. Subsequently, these molecules were combined in a test tube, with certain DNA strands binding together. As demonstrated in Table 1, if two cities are connected, the linking genetic sequence is given the first four letters of one city and the last four letters of the other. A conceivable solution is represented by a chain of these strands. All conceivable DNA strand combinations, which stand in for the answers, are quickly generated in the test tube within a few seconds. Adleman uses chemical processes to eliminate the incorrect molecules, leaving just the flight pathways that link all cities. He used PCR with two 'start' and 'end' DNA pieces as primers and gel electrophoresis to identify only those pieces of the right length. Applying the example demonstrated in fig. 2 and Table 1, the DNA sequence represents the specific path of the solution, will be GCAGTCGGACTGGGCTATGTCCGA.

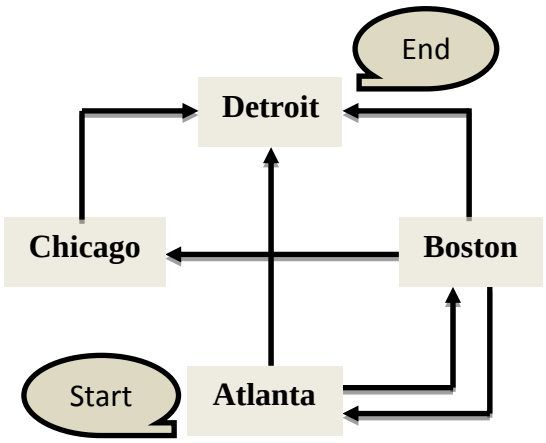

Figure 2: simple graph for the Hamiltonian path problem with four cities

Table 1: represent the DNA name given for each city and the genetic sequence between the connected cities.

CITY	DNA NAME	COMPLEMENT
Atlanta (A)	ACTTGCAG	TGAACGTC
Boston (B)	TCGGACTG	AGCCTGAC
Chicago (C)	GGCTATGT	CCGATACA
Detroit (D)	CCGAGCAA	GGCTCGTT

FLIGHT	DNA FLIGHT NUMBER
A➔B	GCAGTCGG
A➔D	GCAGCCGA
B➔C	ACTGGGCT
B➔D	ACTGCCGA
B➔A	ACTGACTT
C➔D	ATGTCCGA

5. APPLICATIONS OF DNA COMPUTING

DNA computing holds the potential to catalyze revolutionary advancements across diverse disciplines. Originally, many applications centered on the resolution of mathematical conundrums, engineering complexities, and computational quandaries, such as Boolean circuits, chained integer arithmetic, as well as addition and subtraction operations [8]. In recent years, the application spectrum of DNA computing has notably expanded to encompass problem-solving paradigms, security enhancement, biosensing innovations, and targeted drug delivery mechanisms. Building upon the multifaceted applications of DNA computing, this paper turns its attention to two pivotal domains where DNA technology has demonstrated profound impact: security and biosensing. Delving into the realm of security, we explore how DNA computing has transcended conventional boundaries to offer innovative solutions. Subsequently, our focus narrows to the realm of biosensors, where DNA-based systems exhibit remarkable potential to revolutionize detection mechanisms. This exploration unveils the transformative potential of DNA technology across diverse spheres of science and technology.

A. Cryptography based on DNA computing

Information security and confidentiality are important issues, particularly in light of the internet's explosive expansion and pervasive use it is essential to safeguard the data from unauthorized access. Unauthorized access has the potential to compromise users' important

information or compromise the confidentiality and integrity of their data. As modern encryption methods become more vulnerable, the task of information security is actively seeking novel approaches to fortify its transmitted data. A promising avenue to rejuvenate the domain of cryptography and steganography emerges through the integration of DNA computing, presenting new horizons for robust algorithms.

Cryptography is the science of securing the content of messages and communications. After Adleman's study, DNA cryptography was formed. It is the study of how to use DNA as an information carrier. It is a revolutionary method that aims to solve a gap in current security and cryptography systems [16]. Information is carried through the DNA nucleotides in DNA cryptography where A stands for binary value 00 (decimal value 0), C for binary value 01 (decimal value 1), G for binary value 10 (decimal value 2), and T for binary value 11 (decimal value 3) as illustrated in Table 2. Table 3 contrasts DNA-based encryption with conventional cryptography [16]. Many researchers have been conducted on DNA cryptography. For example A notable stride in this direction has been taken by Ashish Gehani, Thomas LaBean, and John Reif of Duke University, who propose an innovative intrusion detection model employing DNA in cryptographic applications [17]. They advocate for DNA cryptography centered on one-time pads, leveraging DNA computing's immense data storage and computational prowess. They assert that while practical applications of cryptographic systems using one-time pads are presently confined to conventional electronic media, the potential for substantial one-time pad capacity arises from DNA's capability to store a staggering 108 terabytes of data per gram [17]. In [16] P.Surendra and co-author introduced a novel DNA encryption technique grounded in mathematical matrix manipulation, accompanied by a secure key generation algorithm to facilitate the encryption process. Within this approach, the text message undergoes conversion into ASCII code, subsequently occupying a 4x4 matrix. Employing mathematical manipulations and cyclic scrambling operations on this matrix, each cycle involves an XOR operation with the initial key. This iterative process effectively scrambles the data, rendering the message unreadable. Furthermore, the encryption system integrates a robust key generation scheme. By XORing the outcome of matrix manipulations with the generated key, a compact cipher is produced. The efficacy of this methodology stems from its ability to generate distinct cipher texts for identical message texts and even for the same key. Consequently, it obviates any indications or insights facilitating educated guesses regarding the plaintext. N. UbaidurRahman and co-authors [18] describe an innovative, dynamic and scure encryption, and decryption algorithm based on DNA to overcome some of the methods used in DNA Cryptography drawbacks. Such as the fact that some of their phases still include modular arithmetic cryptography or that they are based on biological laboratory experiments, which are inappropriate for usage in the digital computing environment. To address this gap, they present an innovative DNA cryptography that employs the Central Dogma of Molecular Biology (CDMB). A. Belazi and co-authors [19] Introduced a novel encryption scheme for medical images is proposed, integrating chaos and DNA computing across two encryption rounds. This approach is underpinned by a key generation layer and follows a permutation-substitution-diffusion structure. To generate secret keys for chaotic systems, the SHA-256 hash function and initial secret keys are employed. The algorithm consists of six steps for each encryption round: block-based permutation, pixel-based substitution, DNA encoding, bit-level substitution (i.e., DNA complementing), DNA decoding, and bit-level diffusion. Remarkably, this scheme combines pixel-based and bit-level substitution in a cascading manner for image encryption, a unique feature identified through comprehensive literature exploration. The key-streams in the bit-level substitution leverage the logistic-Chebyshev map, while the sine-Chebyshev map is instrumental in producing key-streams for bit-level diffusion. This process is iterated once more using fresh secret keys to derive the final encrypted image. Thorough security analyses and computer simulations validate the scheme's robustness against various forms of attacks. Notably, the scheme's low complexity underscores its potential for real-time image applications that require both security and speed. G. Qaid and co-author [20] Introduced a novel lightweight encryption method called “DNA-based lightweight cryptography (LWCD)” to address the encryption needs of Internet of Things (IoT) devices. LWCD uses DNA sequences as keys for encryption rounds, accommodating the limited resources of IoT devices. The encryption process involves substitution and transposition, designed to be efficient for resource-constrained devices thereby

facilitating secure and streamlined communications among them. Leveraging the inherent randomness of DNA sequences, a robust secret key is derived, fortified against potential attacks. The method presents an amalgamation of efficiency and potency.

Table 2: coding DNA bases.

DNA base	Code
A	00
C	01
G	10
T	11

Table 3: Comparison between Traditional Cryptography and DNA Cryptography methods

Items	Traditional Cryptography	DNA Cryptography
Ideal System	Silicon chip based	DNA chip based
Information Storage	Silicon computer chips	DNA strands
Processing Time	Slow	Fast
Storage Capacity	1 gm silicon chip contains 16 Mega-bytes	1 gm DNA chip contains 108 terabytes
Performance Dependency	Implementation and system configuration	Environmental conditions

B. DNA-based biosensors

Biosensors serve as analytical tools that convert biological or chemical reactions into electrical signals. Biosensors can be categorized into two main groups: traditional (such as enzyme and thermal biosensors, among others) and novel biosensors (such as DNA-based biosensor). Despite the utilization of traditional biosensors across various domains over the last decade, these conventional approaches have been marred by several challenges and limitations [21]. For instant the two most important characteristics of a perfect biosensor are speed and sensitivity. Traditional biosensors often rely on experimental techniques, which may be time and money consuming as illustrated in Table 4. Most significantly, these biosensors' findings accuracy is not entirely dependable and has to be verified numerous times. In contrast, DNA biosensors, can deliver accurate data quickly and affordably. It has larger range of detection targets, and a longer lifetime [22]. As a result, they are becoming into effective monitoring tools across several industries [23].

A biosensor system comprises of five key components that work in harmony to identify and provide information about a specific analyte of interest as shown in Figure 3 [24]. Analyte: An analyte is a substance of particular interest that requires identification or detection. Bioreceptor: The bioreceptor is a molecule with the specific function of recognizing and interacting with the analyte. Transducer: The transducer serves as a crucial element in the biosensor system by converting one form of energy into another. Its primary role is to transform the biological recognition event into a measurable signal. Electronics: Electronics play a vital role in the process by handling and conditioning the signal generated by the transducer. They prepare this signal for further analysis. Display: Typically, a computer or similar device is used as the display component in a biosensor system. It presents the results in an understandable format, often as a graphical curve or numerical value [24]. In DNA acid-based biosensors, the sensing elements consist of oligonucleotides, which are comprised of a defined sequence of bases. These oligonucleotides can be either a segment of DNA or RNA. Nucleic acid biosensors function in two main ways: they either rely on the precise and selective binding (hybridization) of complementary DNA/RNA strands or act as exceptionally specific receptors for various biochemical or chemical substances [25]. The application of DNA and its structural assembly is well-recognized for the detection of specific targets, which can encompass nucleic acids, proteins, metal ions, and small biological molecules. Advancements in DNA nanotechnology have enabled the utilization of dynamic networks formed through DNA hybridization to enhance the signal amplification in biosensors. Furthermore, DNA serves as a versatile material for constructing intricate three-dimensional nanostructures and orchestrating various other functional components [22]. These significant strides in the field of DNA-based biosensors have facilitated their remarkable application in diverse areas such as clinical diagnosis, environmental pollution monitoring, food analysis, drug development, and biomedical research [21]. Various types of DNA biosensors have been established, encompassing DNA hybridization-based biosensors, functional DNA strand-based biosensors, and DNA template-based biosensors [22]. Researchs have been carriedout across these distinct types with the objective of enhancing their performance characteristics and expanding their applications. For example, M.S. Bacchu and

coauthors [26] developed an electrochemical DNA biosensor to detect Salmonella enterica serovar Typhi (S. Typhi), which is crucial for early-stage typhoid diagnosis and outbreak prevention. The biosensor exhibited a wide detection range, from 1 × 10^−6 to 1 × 10^−22 mol/L for S. Typhi complementary linear target and from 1.8 × 10^5 to 1.8 CFU/mL for real S. Typhi samples. It demonstrated excellent specificity, even against bases mismatched and different bacterial cultures. Notably, the biosensor had a low limit of detection and could be reused over 6 to 7 times. Practicality was confirmed by detecting S. Typhi in various samples, including blood, poultry feces, egg, and milk, with recoveries ranging from 96.54% to 103.47%. This biosensor holds promise as a diagnostic tool for monitoring S. Typhi in clinical and food samples. In different study Atchara Lomae and co authours [27] introduced a paper-based electrochemical DNA sensor for COVID-19 diagnosis. The biosensor was focusing on detecting the specific SARS-CoV-2 (N gene) sequence. This sensor was integrated with a portable Sensitsmart electrochemical potentiostat and a smartphone app, enabling rapid testing within 42 minutes. The sensing platform exhibited a broad linear range from 0.1 nM to 200 nM and a low detection limit of 1 pM, indicating its high sensitivity for SARS-CoV-2 DNA detection. Importantly, it displayed remarkable specificity for detecting the SARS-CoV-2 N gene in comparison to other DNA sequences, highlighting the effectiveness of the acpcPNA probe.

In the evolution of DNA nanotechnology, the field has seen the emergence of DNA-based nanodevices for the creation of DNA-based biosensors. When coupled with the process of DNA amplification, DNA nanostructures have demonstrated their ability to significantly enhance the detection efficiency in the construction of DNA-based biosensors [28]. An illustrative example of this is the DNA walker. For instated, Yunwei Zhao and co-authors [29] developed a highly sensitive aptasensor for detecting pesticides with zero background fluorescence. This aptasensor utilizes copper nanoparticles (CuNPs) stabilized by poly(T) as a fluorescent signal and a three-dimensional (3-D) DNA walker to amplify the signal. This zero-background aptasensor offers a straightforward method for detecting pesticides, with potential applications in food safety and environmental monitoring.

6. BENEFITS, CHALLENGES AND FUTURE DIRECTIONS

Despite the fact that DNA computing technology is still a long way from supplanting the silicon chip, and much of the research done so far has been theoretical, yet there have been

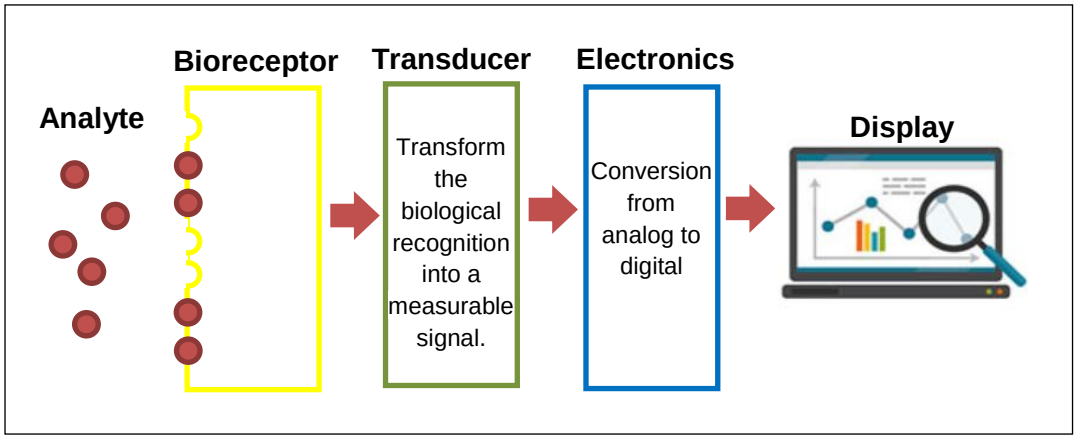

Figure 3: An illustration of biosensors system components

Table 4: Comparison between Traditional biosensor and DNA-based biosensors

Characteristics	Traditional Biosensors	DNA-based Biosensors
Recognition element	Typically uses antibodies, enzymes, or chemical receptors as recognition elements.	Utilizes DNA sequences as recognition elements, which can be selected for their complementary base-pairing properties with specific target sequences.
Sensitivity and	It can be influenced by the affinity	DNA sequences exhibit high specificity due to

Selectivity	of the chosen recognition element for the target molecule. Cross-reactivity with similar molecules is a common challenge.	the complementary base-pairing interactions. This enables the detection of specific DNA sequences, RNA, proteins, or other biomolecules with minimal cross-reactivity. This high specificity is particularly valuable in molecular diagnostics and genetic analysis
Speed	Low	Higher
Biocompatibility	Less	Better to be accepted by the biosystem [28].
Stability	The response of transducers and electronics can be temperature-sensitive, which may influence the stability of a biosensor [24].	It can retain its initial structure even in moderately acidic or alkaline environments and has the capability to recuperate from a denaturation process at temperatures as high as 95°C once it has been cooled down [28].

several references to its potential applications. It also appears to be the first actual example of nanotechnology, bridging the gap between biological and computational sciences. The sophisticated capabilities of DNA are one of the most significant factors in making DNA computers the most successful bimolecular computers in the development of intelligent biomolecular computing devices, for disease diagnosis and drug delivery. They have the potential to revolutionize disease diagnosis by enabling rapid and accurate detection of disease biomarkers [13]. The concept of cancer diagnosis and therapy based on the inhibition of a cancer gene expression is an effective example of the application of biomolecular computers [23]. Shapiro Lab is well-known for developing and programming tiny biomolecular computer devices which made entirely of DNA and other biological molecules where a trillion of them can fit into a drop of water to identify signs of particular cancers in a test tube [23]. It was made of a restriction enzyme as hardware and double strand DNA as software. It could only be in one of two states "yes" or "no", if the biomolecular computer identifies or found the cancer genes it switches to "yes" and release the drug capable to stop can genes from being expressed in response otherwise it remains in "no" states. Though cancer-detecting computers are still in their infancy and can only work in test tubes for the time being, however, Shapiro and his research team foresee future where, it will be possible to diagnose and treat cancer by injecting biomolecular devices directly into living human beings [4]. The breakthroughs in DNA computing have led to the creation of new tools and technologies for building and manipulating DNA-based nanostructures, such as DNA origami [30,31]. These structures can be programmed to self-assemble into intricate shapes and patterns, making them ideal templates for building nanoscale devices and circuits [31]. In addition, DNA can be utilized as a chemical tool for controlling the behaviour of other molecules, such as enzymes, by designing DNA sequences that bind to specific target molecules and trigger a specific response [32]. Furthermore, targeted medication delivery is another application of DNA-based nanostructures. In this application, pharmaceuticals are encased in DNA-based nanostructures that can release the drugs only in reaction to particular environmental cues or stimuli [33].

DNA computing's advantage lies in its potential to interface with various physiological environments. The capability to directly interact with physiological conditions enables responses to biological signals within living cells, potentially facilitating intelligent diagnostics and treatments. However, before this technology can be extensively used, there are a number of issues that must be resolved.

- Cost: One of the major challenges is the high cost and complexity of DNA synthesis and sequencing, which limit the DNA computing scalability [5].
- Complexity of computing: as computing complexity increases, the required number of DNA molecules in the algorithm grows exponentially. This heightened quantity of DNA molecules within the system can result in a correspondingly elevated error rate due to processes like synthesis and purification [31].
- In parallel operations, individual DNA computer operations are fairly slow; each stage may takes hours or days to complete with the need of significant human or mechanical interaction between steps [1, 34].

- Accuracy: DNA biochemical reactions are sensitive to reaction conditions. Enhancing the efficiency of these reactions, which significantly influences computing accuracy, is a pressing issue in DNA computational models [31].
- Duration: DNA has short shelf life, about 6 months, and it can only be used once, as reuse can contaminate reaction vessels and lead to less accurate results [1, 35]. Additionally, even for relatively simple straightforward problems, generating solution sets may necessitate impractically vast amounts of memory.
- Universality: The absence of a universal computing system limits the broad adoption of DNA computing since most DNA computing models are specialized for particular types of problems. this lack of standardization in DNA computing protocols, typically offer problem-dependent solutions possibly involving new 'hardware' fabrication for each problem which makes it challenging to compare results between different studies[31,34]. In the contrast classical, electronic computers have already a built-in hardware, which means that no significant pre-computing activities are required. Furthermore, most electronic computers use pre-loaded algorithms, which help to solve most computational problems with less effort.

To overcome these challenges, significant research and development efforts are needed in this area. New DNA sequencing and synthesis methods need to be developed that are faster, cheaper and more accurate [22]. The processes of building alternative DNA structures are experience-based, which restricts the extensive DNA application in many sectors. As a result, strategies for simplifying the DNA design process must be presented. A proposed option is to create more automated DNA design tools to assist researchers in simplifying the DNA structure design process [22]. Standardization of DNA computing protocols is also essential to ensure reproducibility and comparability of results. Efforts are needed to develop DNA computing standardized protocols that can be widely adopted by researchers and industry [22, 34]. In addition to addressing these challenges, there are several future directions for DNA computing. One area of active research is the development of DNA-based nano-robots for targeted drug delivery. Another area of interest is to utilize DNA computing in personalized medicine, where genetic information can be used to tailor medical treatments to individual patients.

7. CONCLUSION

The potential applications of DNA computing are tremendous. It has evolved into a promising data analysis technique, as well as demonstrating the capacity and capability to convey information in nanotechnology and other fascinating applications. However, significant challenges need to be overcome to realize its full potentiality. Research efforts are needed to develop new DNA sequencing and synthesis methods, standardize DNA computing protocols, and explore the new applications of this technology. DNA computing will presumably overcome its current obstacles with further research and development, opening the door for efficient and effective computing applications in many different fields.

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- Conflict of Interest: Authors declare they have no conflict of interest.

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