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Principles of Biology in Service of Technology: DNA Computing

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ABSTRACT/RESUME

Abstract: *As commonly known that living beings cannot survive without natural sources available on earth, technology is no exception; it cannot develop without the inspiring help given by the same nature.*
The field of biology has extensively participated in the computing field through the "code of life" DNA (Deoxyribo Nucleic Acid) since it was discovered by Adelman in the past century. This combination gave birth to DNA Computing, which is a very interesting new aspect of biochemistry. It works massively parallel with high energy efficiency, and requiring almost no space.
The field of molecular computing is still new and as the field progresses from concepts to engineering, researchers will address these important issues.
By the use of encoding data into DNA strands, many NP-complete problems have been solved and many new efficient techniques have been proposed in cryptography field.
The aim of this paper is to give an overview of bio-inspired system and to summarize the great role of DNA molecule in servicing of the technology field.

I. Introduction

Steve Jobs, co-founder of Apple Inc., said, "I think the biggest innovations of the 21st century will be at the intersection of biology and technology. A new era is beginning."
Biology is a great reference to be used to solve millions of problems in computer science or any other field. This intermingling of biology and technology leads to emerge a new field called "BIO-TECHNOLOGY" that is still new until today. Biotechnology can be applied in several areas as it is illustrated in Fig.1.

Figure 1. *Areas of Bio-technlogy*

From the field of biology we can find an attractive branch which is DNA molecule (Deoxyribo Nucleic Acid).
Deoxyribonucleic acid (more commonly known as DNA) is a complex molecule that contains all of the information necessary to build and maintain an organism. It is the hereditary material in humans and almost all other organisms (more detail is given in section III).

This little miraculous molecule is very active and its presence proved to solve many problems in wide and different fields of science.

DNA fingerprinting is one of the great discoveries in the past century. DNA analysis can help to convict criminals, exonerate the wrongly accused, and identify victims of crime, disasters, and war.

Services of DNA can appear clearly in nanotechnology leading to create a new field called DNA Nanotechnology which is the design and manufacture of artificial nucleic acid structures for technological uses. In this field, nucleic acids are used as non-biological engineering materials for nanotechnology rather than as the carriers of genetic information in living cells.

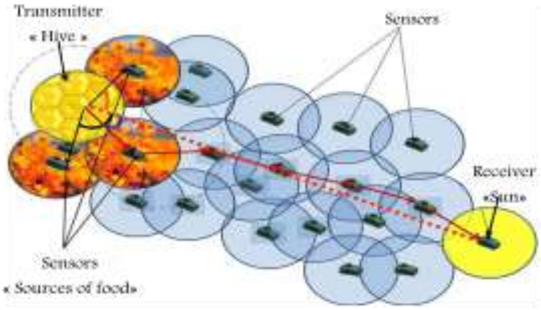
This famous DNA molecule can be also used for computation creating a field known as Bio-Computing, molecular computing or DNA Computing. In this field, information is represented using the four genetic alphabet characters (A, G, C, and T) rather than the binary alphabet (1 and 0) used by current computers. This revolutionary DNA computing is used to solve many NP-complete problems with great success.

The success of this little DNA molecule in computation allows the appearance of the DNA Cryptography and DNA steganography that can be defined as a hiding data in terms of DNA Sequence.

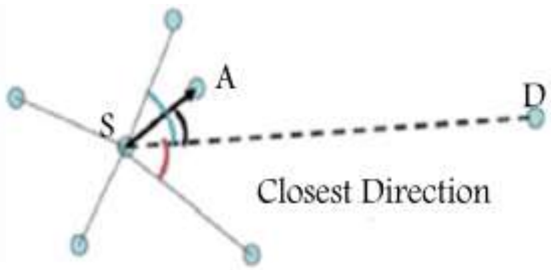
We have chosen to present this paper as follows: first, we have given an overview of bio-inspired systems and bio-inspired algorithms. Then, we have given a snapshot about the DNA molecule, its components and its chemical structure, followed by a concise presentation of DNA Nanotechnology. Afterward, we have mentioned one of the fields of computing called 'DNA computing' by giving its purposes, mentioning also some biological operations used for computing, and finally given some of its advantages. Finally and briefly, we have present DNA cryptography and steganography.

II. Biologically inspired system

We can find good and efficient solutions for many difficult and hard problems, but afterwards we discovered that these solutions existed in nature from millions of years before. Aksa et.al [1] prove that the idea of geographic routing protocols proposed to solve the problem of routing in ad hoc and sensor network already exists in nature exactly with the same principle (see Fig.2).
The authors have made a comparison between geometric field and bio-inspired system through two proposed algorithms DIR [2] (compass routing protocol) and BeeRP (Bee Routing Protocol) [1] which is inspired from bees' communication. They confirm that both algorithms are similar having the same intrinsic principle based on direction towards the destination in routing, whereas their tools differ.



(a)



(b)

Figure 2. *(a) BeeRP, (b) DIR [1]*

The vital conclusion is: "If nature possesses these ceaseless accurate treasures for centuries since their existence, why not to exploit them now?"

Accordingly, Artificial Intelligence (AI) has been known as reproducing the abilities of human brains; nowadays a wide range of biological structures are used for imitation (imitating their models (see Fig.3)), or valorizing their knowledge or changing the paradigm of just extracting by learning from nature, or by doing the things in the way that nature does.

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Figure 3. *Imitation*

The word biology is derived from the Greek words: bios (meaning life) and logos (meaning study) and is defined as the science of life and living organisms.
In this field, biologists study the structure, function, growth, origin, evolution and distribution of living organisms.

The inspiration from biological systems, called bio-inspired systems, can be seen in many applications including aerodynamics of vehicles, structures, multifunctional materials, drugs, robots …etc.
Recently, bio-inspired systems witness an amazing evolution in several scientific environments with the collaboration of several scientists such as engineers, chemists, physicians, biologists that look for copying the biological processes and apply them in different areas of technology and science.

Likewise, bio-inspired algorithms (BIA) witness a wide fame in computer science since they solved many complicated problems by referring to nature (see Fig. 4).

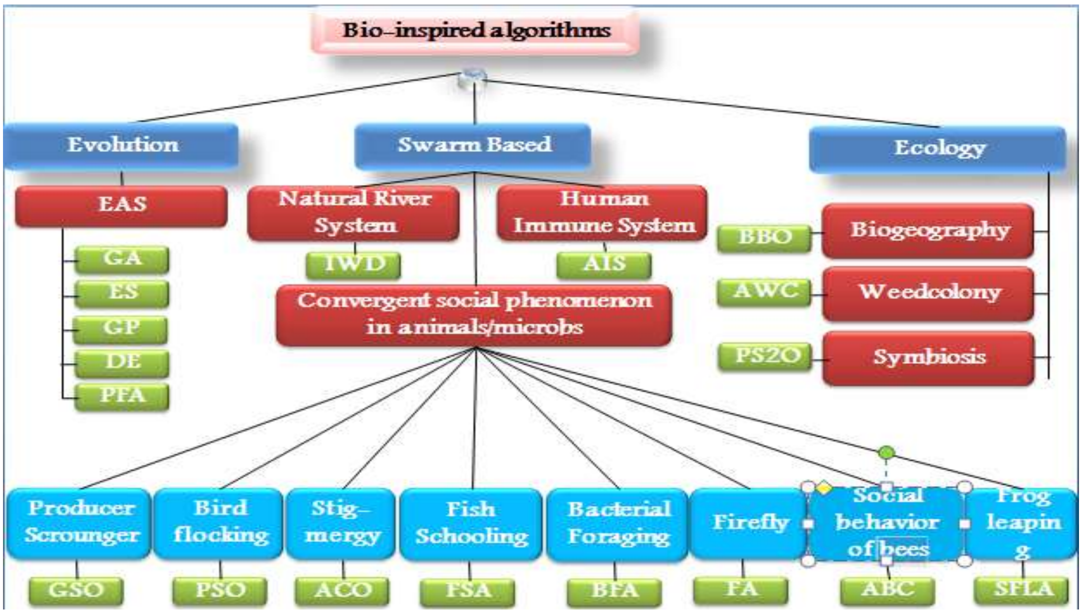

Figure 4. *Taxonomy of Bio-inspired algorithms [3]*

Many bio-inspired technics are used to solve different problems linked to computer networks as it is shown in Table I. This relationship between computer networks and biology was named Bio-inspired Networking.

Bio-inspired networking is defined as a class of strategies for efficient and scalable networking under uncertain conditions [4].

Table 1. *Categorization of biological phenomena and networking algorithms mimicking these concepts [4].*

Biological principle	**Application fields in networking**
Swarm Intelligence and Social Insects	Distributed search and optimization; routing in computer networks, especially in MANETs, WSNs, and overlay networks; task and resource allocation
Firefly Synchronization	Robust and fully distributed clock synchronization
Activator-Inhibitor Systems	(self-) organization of autonomous system; distributed coordination; continuous adaptation of system parameters in highly dynamic environments
Artificial Immune System	Network security; anomaly and misbehavior detection
Epidemic Spreading	Content distribution in computer network (e.g. in

	DTNs); overlay networks; analysis of worm and virus spreading in the Internet
Cellular Signaling Networks	Coordination and control in massively distributed system; programming of network-centric operating sensor and actor networks

With the cooperation of bio-inspired methods, computer science, computational mathematics and communication networks (see Fig. 5), the forthcoming networks are expected to be autonomous, scalable and adaptive. During millions of years of evolution, nature has developed a number of different systems that present many characteristics required for the future generation networks.

The research is not only copying from nature for modeling and simulation, but also visualization and measurement which are essential methodologies to understand difficult and complex mechanisms and regulations in living bodies (see Fig.6).

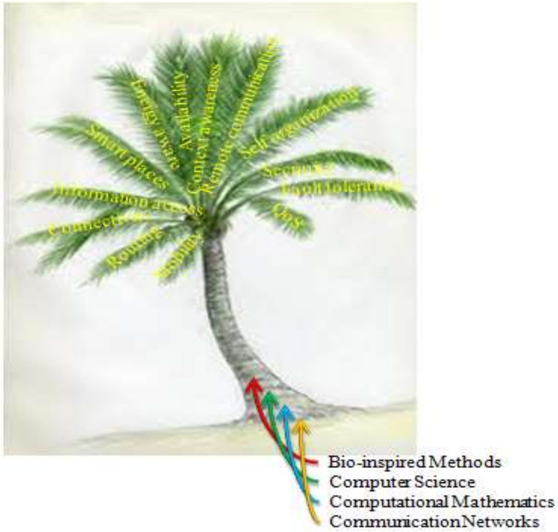

Figure 5.*Bio-inspired Networks and Systems*

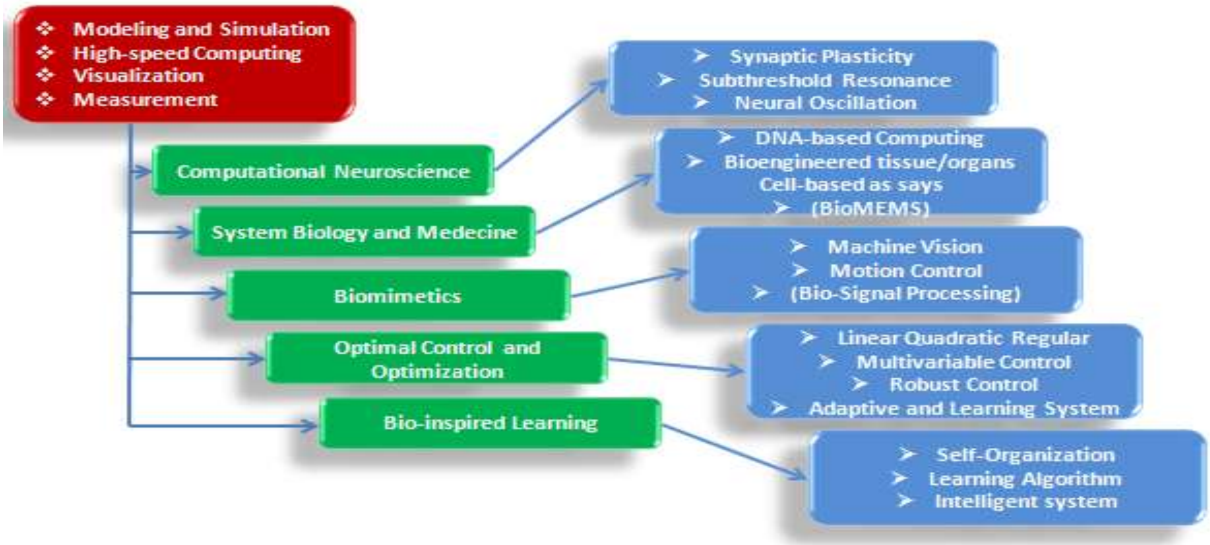

Figure 6. *Research discipline of Bio-inspired system and Technology.*

In general, we shared the same point of view with several researchers who summarize it in one expression: "biology is an oldest technology".

The following section will give a snapshot of one of the most miraculous sides of biology which is DNA molecule.

III. DNA biologically

DNA (Deoxyribo Nucleic Acid) is the hereditary material in humans and almost all other organisms. It is a long molecule that contains our unique genetic code. The main role of DNA in the cell is the long-term storage of information.

DNA is a double stranded sequence of four nucleotides: Adenine (A), Guanine (G), Cytosine (C), and Thymine (T) (see Fig. 7). The chemical structure of the famous double- helix DNA was discovered by James Watson and Francis Crick in 1953. It consists of a particular bond of two linear sequences of bases. This bond follows a property of complementarity: Adenine bonds with Thymine (A-T) and vice versa (T-A), Cytosine bonds with Guanine (CG) and vice versa (G-C). This is known as Watson-Crick complementarity. Each DNA strand has two different ends that determine its

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polarity: the 3.'end, and the 5.'end. The double helix is an anti-parallel (two strands of opposite polarity) bonding of two complementary strands [5].

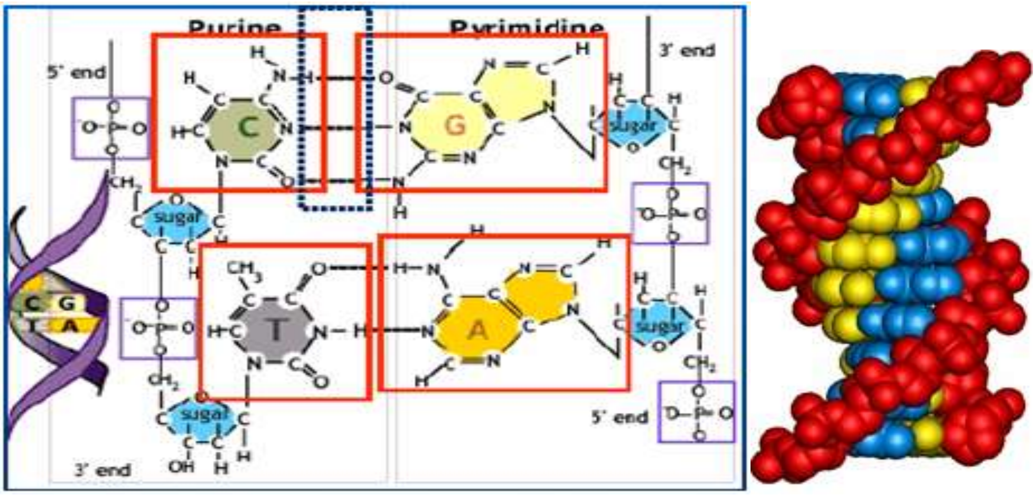

Figure 7. *DNA molecule*

IV. DNA Nanotechnology

In Nanoscience, we use structures smaller than a length characteristic of a phenomenon exhibit new chemistry and physics. And in Nanotechnology we can working with these structures, one by one, or cluster by cluster to design and develop stronger materials, faster acting switches, drugs and cosmetics, more storage.

In fact, Nanotechnology is the art and science of manipulating matter at nanoscale. Many applications of this hot field are cited in Fig.8

Figure 8. *Application of Nanotechnology*

DNA nanotechnology (also known as Nucleic Acid Nanotechnology) is a branch of nanotechnology concerned with the design, study and application of synthetic structures based on DNA.

Briefly, DNA nanotechnology takes advantage of the physical and chemical properties of DNA rather than the genetic information it carries. It can enable the realization of high-sensitivity, multiplexed bioanalytical assays for many different applications as it is illustrated in Fig. 9.

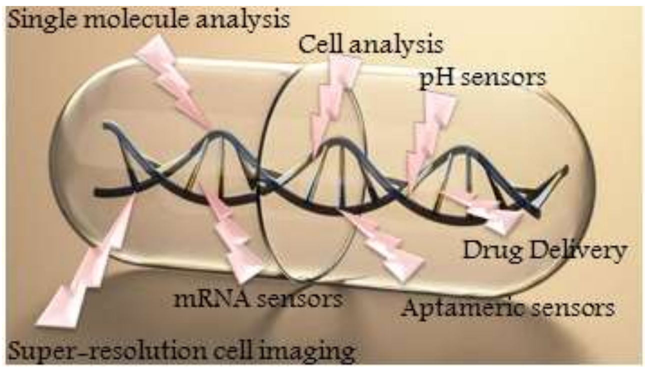

Figure 9*. Applications of DNA Nanotechnology*

Obviously, DNA nanotechnology has various applications, but mostly used in DNA computing or bio-molecular computing as it will be presented in the following section.

V. DNA computing

Until now, the word ''computer'' has become synonymous with an electronic computing machine. But, the limitation of this traditional silicon based computer drives to discover a new invention called

"DNA Computing". This latter is a brand new research area which receives more and more attentions from both biologists and computer scientists.

DNA computing was introduced by Leonard Adleman of the University of Southern California, in 1994 [6] who showed how to use tools of molecular biology to solve difficult computational problems.

The goal of DNA computing focuses on the use of strands of DNA to encode a problem, and to manipulate them using techniques commonly available in any molecular laboratory, in order to simulate operations which can generate solution [7].

The name of DNA computing should not be confused with bio-computing [7]. Usually, bio-computing refers to everything that the computer scientists can do, to help the biologists in the study of genes. For instance, algorithms and data structures have been developed to investigate the properties of the sequences of nucleotides in DNA or RNA (Ribonucleic Acid). In DNA computing, instead, molecular biology is suggested to solve the problems that computer scientists face. On the other hand, DNA computing is not similar to Genetic Algorithm (GA) [7]. GA simulates the rules of the nature of evolution in computation. In this way, GA searches for the optimal solution of a problem [7].

The models of DNA computing are based on different combinations of the following biological operations on DNA strands [8]:

- Melting/annealing: break apart/bond together two single DNA strands.
- Synthesis of a desired DNA strand of polynomial length.
- Separation of the strands by length.
- Merging: pour two (or more) test tubes into one.
- Extraction: extract the strands that contain a given pattern as a substring.
- Amplifying: make copies of DNA strands by using the Polymerase Chain Reaction (PCR).
- Polymerization: transform a single strand that has a portion of double-stranded subsequence into an entire double-stranded molecule.
- Cutting: cut DNA strands by using restriction enzymes.
- Ligation: paste DNA strands with complementary sticky ends by using ligases.
- Substitution: substitute, insert, or delete DNA sequences by using PCR site-specific oligonucleotide mutagenesis.
- Marking single strands by hybridization.
- Destroying the marked strands.
- Detection: given a tube, check if it contains at least one DNA strand.

These operations are used to write “molecular programs”, whose input is a tube with DNA strands or molecules and output is “yes”, “no” or (set of) tube(s) [7].

There are several advantages to using DNA instead of silicon:

- Based on parallel data processing
- DNA Computer has Big Data storage capacity
- DNA computers are many times smaller than today's computers.
- Unlike the toxic materials used to make traditional microprocessors, DNA biochips can be made cleanly.
- The large supply of DNA makes it a cheap resource.
- As long as there are cellular organisms, there will always be a supply of DNA.
- Low power consumption

The power of DNA computing lies in its high speed, energy efficiency, and economical information storing. For example, at the moment when Adleman carried out his experiment, DNA computing was approximately 1 200 000 times faster than the fastest supercomputers [7]. A DNA computer could permit information storing 10^{12} times more effectively and take 10^{10} times less energy than the existing computers [8].

VI. DNA for NP-Complete problem

L. Adleman, the founder of DNA computing, set up a problem and showed how DNA could be used to solve it (table 2 summarizes the Adleman Approach). The problem that he set up was a Hamiltonian path problem. The well-known travelling salesman problem is a related problem where a salesman is given a list of cities, that he must visit, and the connections between those cities, and the goal is to find the shortest route to visit every city exactly once. With 100 cities, for example, there exists an algorithm to solve the problem in 10^{147} operations which would take much longer than the age of the universe to solve by all the computers in the world. Adleman demonstrated, using only 50 Pico moles of DNA, how DNA could be used to solve a Hamiltonian path problem with 7 cities and 14 connections (see

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Fig.10). With DNA, the initial state is created by synthesizing DNA molecules with a certain sequence and after some reactions, a new molecule is produced with the answer. It took one second for the DNA to come up with answers, but it took him a week to dig out the answer from the DNA soup. The Hamiltonian path problem is one of a class of problems called NP-complete. NP problems are problems that can be solved by a non-deterministic Turing machine in polynomial time, which means that a conventional computer must guess a solution (non-deterministic) and then check the solution in polynomial time. The process of "guessing" though makes the entire process unachievable in polynomial time which makes the problem difficult in the sense that it can take an extremely long time to get a solution as the problem gets bigger. An NP-complete problem is essentially the hardest of all NP problems, since all NP problems can be reduced to it. Therefore, theoretically, any NP problem can be solved using Adleman's method. Other NP-complete search problems have been successfully solved using DNA and recombinant DNA technology.

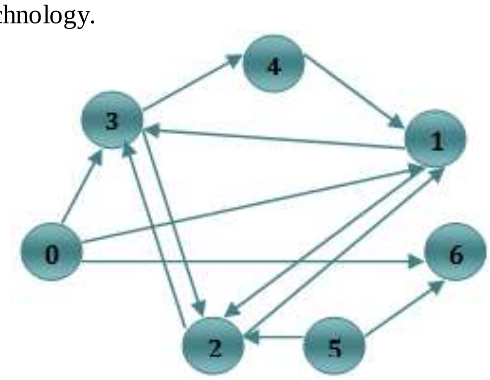

***Figure 10**. Directed graph, used in Adleman experience, with node 0 as source and node 6 as destination.*

***Table2.** Adleman's algorithm for solving TSP problem*

Step	**Realization**
Generate random paths through the graph	Mix together all edges and all nodes except v_{in} and v_{out}. The ligation reaction generates (all!?) possible paths in the network
Keep only those paths which begin with v_{in} and end with v_{out}.	Use PCR with primers for v_{in} and v_{out}. Thus just molecules which begin at v_{in} and end at v_{out} are amplified
If the graph has n nodes, then keep only those paths which exactly enter n nodes	Run the above product through an agarose gel and separate the (n-1) k-sequences. For purification you can start at 2 again.
Keep all paths which enter each node at least once.	Extract all sequences containing v_i with a magnetic bead system for all different i
If any paths remain, say ''Yes'', otherwise ''No''_.	Amplify the above product by PCR and run it through a gel.

Richard Lipton in December 1994 published an important paper allowing the development of molecular computers to move forward [9]. He described how DNA base pairs can be translated into 0s and 1s and how Boolean algebra can be done with molecules. For example, "and" is done by separating DNA strands by their sequence, while "or" is performed by mixing two DNA solutions together. Theoretically, that is all that is necessary for DNA to simulate any normal desktop computer. The unrestricted DNA model described by Lipton includes the following operations that can be done with DNA:

- Synthesis of a desired strand,
- separation of DNA strands,
- merging of DNA strands,
- extracting a strand with a given pattern,
- annealing single stranded complementary DNA into double stranded DNA,
- amplification with PCR,
- cutting of DNA with restriction enzymes,
- ligation of DNA strands,
- and finally, detecting the presence of certain DNA.

Table 3 summarizes the biological operations and table 4 summarizes the Boolean operations used by Lipton. With these primitive operations, it is possible to write a molecular program that does something useful. In fact, a lot of these programs look like programs in common languages. The DNA operations can be viewed as subroutine calls that are made when needed.

***Table3.** Approach of Lipton using bio-operations*

Step	**biological operation**

Get a large number of copies of any short single strand	PCR
Generate a double strand of DNA from complementary single strands.	Put them together and let them anneal
Extract sequences which contain a chosen pattern of a particular length	Use a magnetic bead system. You can just get about 90% of the wanted strands, so you have to run an amplification step, perhaps.
Detect if there is a strand in a test tube.	PCR

Table 4. *Approach of Lipton using Boolean operations*

Step	Boolean operation
Get all strands where x_i = 1 or x_i = 0 respectively	Extract operation for either x_i or $\overline{x_i}$
Get all strands fulfilling $F_1 \wedge F_2$	Get all strands fulfilling F_1, then use this result and get all strands fulfilling F_2.
Get all strands fulfilling $F_1 \vee F_2$	Get all strands fulfilling F_1 and call this T_1. Use the rest and extract all strands Fulfilling F_2, call this T_2. Mix T_1 and T_2 together

Since the original experience of Adleman, inundations of ideas were proposed by researchers. There are researchers who are succeeded in solving some hard problems [11] and others have developed several different models for solving other problems of computation using DNA computing [12].

In Table5, we mentioned some first NP-Complete problems solved by biological operations.

Table 5. *First DNA algorithms for NP-Complete problems*

NP-Complete problem	Reference
Hamiltonian Path Problem (HPP)	[6], [13]
Boolean satisfiability	[9]
3-colouring	[14]
Quantified Boolean formulae	[15]
Independent set	[16]
Knapsack	[17]
Subgraph isomorphism	[18]
Maximum clique	[19]
Circuit satisfiability	[20]
(3_2)-system	[21]
Shortest common superstring	[22]
Bounded Post correspondence	[23]
MAX-CNF satisfiability	[24]
K-SAT problem	[25]

VII. DNA cryptography and Steganography

VII.1. DNA cryptography

Cryptography has long history beginning by the Egyptian's hieroglyphic writing; known as symbolic and image writing used before 4000 years ago. Passing through Mesopotamian languages with their contradictory and controversial aspects (Summerian language was of the upper class, whereas the Akkadian was of the lower one), to the twentieth century, where it switched its role from social communication to world war and politics.

The function of cryptography is to transmit a message between a sender and receiver using a secret key where no spy is can understand it (see Fig.11). Plaintext is a sequence of drawn from a finite alphabet, such as that of a natural language. Encryption is the process of scrambling the plaintext, which is a set of characters (numbers, letters…), using a specified algorithm and a secret key. The output is a sequence of characters known as the ciphertext. Using this key, the encrypted message can be transformed to its original form, this reverse process called Decryption.

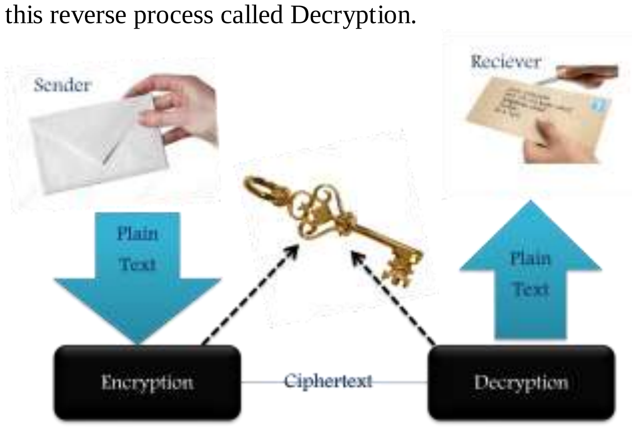

***Figure 11**. Cryptography*

Because secrets and sensitive information must be protected against any unauthorized access, many

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researchers have looked for new cryptographic techniques such as the biotechnological methods.
DNA Cryptography is a new emerging field from speedily growing bio-molecular computation (see Fig.12). As technology is growing much faster, data protection is getting more important and it is necessary to design the unbreakable encryption technology to protect the sensitive information.

One of the DNA-based cryptography schemes can be generally expressed below [26]:

- **Encryption**:
  - ✓ Take one or more input DNA strands (considered to be the plaintext message).
  - ✓ Append to them one or more randomly constructed “secret key” strands.
  - ✓ Resulting “tagged plaintext” DNA strands are hidden by mixing them within many other additional “distracter” DNA strands which might also be constructed by random assembly.
- **Decryption**:
  - ✓ Given knowledge of the “secret key” strands. ·
  - ✓ Resolution of DNA strands can be decrypted by a number of possible known recombinant DNA separation methods: Plaintext message strands may be separated out by hybridization with the complements of the “secret key” strands might be placed in solid support on magnetic beads or on a prepared surface.

These separation steps may be combined with amplification steps and/or PCR [27].

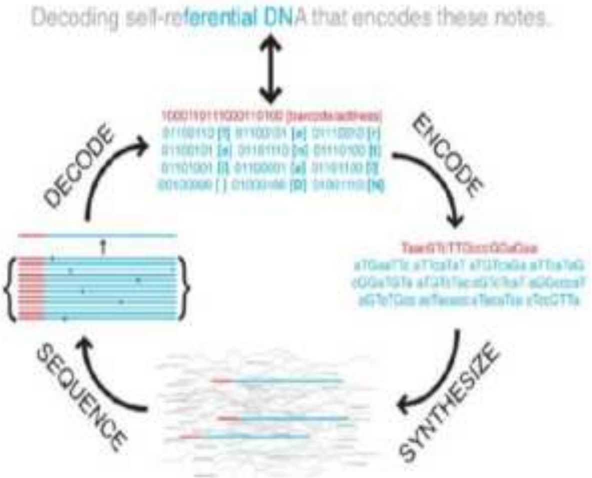

Figure 11. *DNA Encryption and Decryption Mechanism [27]*

During the 2nd World War, Clelland et al. [28] used artificial DNA strands, which contained secret messages. Each character is encoded by a triplet nucleotide (see Table 6) using the following encoding and decoding functions [29]:

- *Encoding function:*
  $E : X \rightarrow Y$
  $X \in \{A, B, C,..., Z, 0, 1,..., 9, ".", ",", ":", "\sqcup"\}$
  $Y \in \{xyz : x, y, z \in \{A, C, G, T\}\}$
- *Decoding function*:
  $D : Y \rightarrow X$.

Table 6. *Clelland code table. Modified from Clelland et al.[28].*

Character	DNA Code	Character	DNA Code
A	**CGA**	**U**	**CTG**
B	**CCA**	**V**	**CCT**
C	**GTT**	**W**	**CCG**
D	**TTG**	**X**	**CTA**
E	**GGC**	**Y**	**AAA**
F	**GGT**	**Z**	**CTT**
G	**TTT**	**0**	**ACT**
H	**CGC**	**1**	**ACC**
I	**ATG**	**2**	**TAG**
J	**AGT**	**3**	**GCA**
K	**AAG**	**4**	**GAG**
L	**TGC**	**5**	**AGA**
M	**TCC**	**6**	**TTA**
N	**TCT**	**7**	**ACA**
O	**GGA**	**8**	**AGG**
P	**GTG**	**9**	**GCG**
Q	**AAC**	**⊔**	**ATA**
R	**TCA**	**,**	**TCG**
S	**ACG**	**.**	**GAT**
T	**TTC**	**:**	**GCT**

Table 7 resumes a comparison of traditional and DNA cryptography.

Table 7. *Comparison of traditional and DNA cryptography [30]*

Characteristics	**Traditional Cryptography**	**DNA cryptography**
Security	Less	More
Time	Minutes to hours	Hours to days
Storage capacity	In Mb	In TB
Dependency	On Implementation environment	On environmental conditions

Adleman proposed the hypothetical model of DNA computing for any bio-molecular computational problem which provides vast parallel computing. As his background stemmed from computer encryption, he particularly envisioned DNA computing in helping to create encryption and decryption algorithms in the area of cryptography.

Many scientists have projected a various DNA-based encryption algorithms (see Table 8), but it is too early to decide the perfect complete model for some cryptographic functions, such as DNA authentication methods, digital signature and secure data storage as these cryptographic models are still in the initial phase.

Table 8. *Some DNA algorithms*

DNA Algorithm	reference
Proposed the original idea of hiding data in DNA and RNA	[30]
Inspired Pseudo Biotic DNA Based Cryptographic Mechanism Against Adaptive Cryptographic Attacks	[31]
DWT based coding DNA watermarking for DNA copyright protection	[32]
Proposed an improved algorithm named the Table Lookup Substitution Method (TLSM)	[33]
Decrease the usage of asymmetric cryptography	[34]
Increased security	[35]
Analyzed the different approaches on DNA based Cryptography, DNA binary strands support feasibility and applicability of DNA-based Cryptography	[36]
Efficient DNA-Based Cryptographic Mechanism to Defend and Detect Black hole Attack in MANETs	[37]

All These techniques can be used for authentication or to store data for long time.

Some algorithms that are available in DNA Cryptography have limitations for they still use modular arithmetic cryptography at some of their steps or they are biological laboratory experiment based which is not suitable in the digital computing environment.

VII.2. DNA Steganography

The roots of steganography can be traced back to ancient Greece. This word “steganography” is composed of two words “steganos” and “graphie”. The first word means “covered or protected”, and the second means “writing”. Hence, “steganography” means “concealed writing”. It is the art of hiding specific information inside a great excess of similar-appearing information.

DNA steganography is very unique from traditional steganographic techniques in a sense that it is hard to break by adversaries because of the complex computations and covert nature of DNA. It also offers large storage density as compared to the traditional storage devices. Making DNA as a medium to hide the data for secrecy is a novel method. Its advantages and a few disadvantages are listed below [38].

Advantages of DNA steganography

- Novel Covert medium.
- Large amount of data hiding space available.
- Publicly available database of DNA sequences.
- Flexible encoding scheme.
- Using suitable techniques of data compression large amount of data can be embedded in small DNA sequence whereas a similar technique using Image or other media as cover will embed lesser data.

Disadvantages of DNA steganography

- If data is stored in a digital DNA sequence its prone to computer based attacks
- DNA sequence if suspected by an attacker may somewhat make the data being transferred vulnerable to attacks as its cover will be lost
- Large amount of computations required for encoding procedures making it slower compared to traditional cryptographic methods.

In the recent years, much of the research work has been carried out in DNA based data-hiding techniques Table 9 mentions some of them.

Table 9. *DNA based data-hiding techniques*

Technique	Reference
A novel data hiding method based on deoxyribonucleic acid coding	**[39]**
Steganography: A Review of Information Security Research and Development in Muslim World	**[40]**
DNA Based Cryptographies techniques : A Review	**[41]**
An information security based literature survey and classification framework of data storage in DNA	**[42]**
DNA sequence watermarking based on random circular angle	**[43]**

VIII. Conclusion

DNA is one of the most powerful bio-sources used to solve difficult problems in different scientific fields. Today, various techniques are used to carry out DNA computation. Researchers use these techniques to perform the operations on informative DNA molecules.
DNA computing is a branch of computing which uses DNA, biochemistry, and molecular biology to solve complex mathematical problems.

Cryptography is the art of converting the original message into human unreadable code, which cannot be reversed to the original message. DNA Cryptography is a new active and promising field in information security. It is one of the fastest technologies which works on concepts of DNA computing. It combines classical solutions in cryptography with the strength of the genetic material.
In the future, the power of this tiny miraculous molecule imposes its presence in many scientific fields to solve many recurring, old or new problems.

Conflict of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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