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Templated DNA Technology: The Future is Waiting

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Abstract: DNA, a principle biomolecule of the genome has important applications in biological fields such as genetics, cancer research, medicine and biotechnology. Besides, its application in various biological fields, DNA has currently gained demand in the field of nanotechnology because of its structural stability, sequence programmability, natural ability to self-assemble and to interact with wide range of molecules. The current review, develops a basic understanding of DNA nanotechnology and elucidates the history and applications of DNA Nanotechnology in different areas. The article also reviews some case studies on DNA Nanotechnology, Molecular machine systems and medical Nano robots that allows the diagnosis of pathogens and individual cell therapy along with

***Keywords**: DNA Nanotechnology, Nanostructure, Structural DNA Nanotechnology, Dynamic DNA Nanotechnology, Nanomedicine and Biosensors.*

INTRODUCTION

Nucleic acids have been the core foundation for encoding the genome in all living organisms on earth. The DNA, a principle biomolecule of our genetic makeup has predominant applications in the field of medicine, agriculture, forensics, disease diagnosis and treatment etc. In the recent times, DNA has an important application in the field of Nanotechnology [1]
Nanotechnology is a branch of engineering science that deals with construction, design, manipulation and application of atoms or molecules less than 100 nanometres. It is an interdisciplinary field. It has several applications in the biological field and is used in the drug delivery system, new therapies, earlier diagnosis and effective treatment of many diseases without damaging the healthy cells present in the surrounding [2]
DNA is used as structural nanomaterial in the field of Nanotechnology. The utilization of non-biological, artificial nucleic acids for technological purpose is called as DNA Nanotechnology [3]. It is an emerging field of nanotechnology that involves DNA, a promising building block for the construction of nanostructures. Because of the properties like the ability of self-assembly high compatibility, and low cytotoxicity of DNA makes it suitable for nanotechnologists to produce nanostructure out of it [4]
DNA Nanotechnology provides the multidisciplinary research areas, designing of biological nanostructures and helping the medical sciences as well. It opened up a vast opportunity for many students pursuing their course in different fields of biology [5]

HISTORY OF DNA NANOTECHNOLOGY

With the advancements of the nanotechnology, biologists have popped up with brilliant ideas of bringing DNA into the "Nano-World". It all began in early 1980s by Nadrian Seeman, who was motivated to create a three-dimensional DNA lattice for orienting large molecules, to remove the difficulty process of obtaining pure crystal.

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Seeman and his colleagues first described a process to create a self-assembling nanostructure. They create tiles made up of DNA with sticky ends which were allowed to hybridize to form a cubic structure [6]. This method made it futurable to form a variety of nanostructures based on differences in sequences, instead of being dependent on the environmental surrounding (pH, salt and temperature) of DNA [7]

The first DNA nano-machine was demonstrated in 1999 and later improved by Bernard Yurke in the following year. New abilities continued the designing of DNA structures throughout 2000s. In 2006, Paul Rothemond first discovered DNA origami which consist of a long strand where folding is associated by several short strands. Thus, the field of DNA Nanotechnology had grown from 2001. This increased the scientific advances during that decade.

FUNDAMENTAL CONCEPTS OF DNA NANOTECHNOLOGY

DNA nanotechnology is used as a process to create a self-assembling nanostructure, in which molecular components autonomously organize into stable structures. The component materials are strands of nucleic acids such as DNA. The nucleic acid molecule is a long chain polymer (polynucleotide) composed of monomeric units called nucleotides. DNA is well fitted in this nano-world or nano-scale as there exists base pairing rules which form specific nano-scale structure of nucleic acid double helix. This kind of property is absent in other materials, which lack the capability of self-assembling.

In DNA, although Adenine is equal to Thymine and Guanine is equal to Cytosine, there is no restriction on the ratio (A+T)/ (G+C); nor is there any restriction on sequence of bases in an individual polynucleotide chain. Thus, there an advantage of being easily assembled into predictable nanoscale structures by hydrogen bonding. This kind of programmability makes DNA suitable for designing and fabricating nanostructures [8]

Many of the researchers have approached with the innovative ideas to construct dynamic structures. This has led to the development of several macroscopic structures with nano-size feature. In DNA nanotechnology, the base sequences of the strands are rationally constructed or designed by researchers so that the base pairing interactions can cause the strands to assemble themselves into desired conformations [9]

WHY DNA IN NANOWORLD?

DNA is well suited in in the nanoworld because of the binding between two nucleic acid strands depends on simple base pairing rules and form the desired nanoscale structure of the nucleic acid double helix. More reasons are mentioned below:

- DNA’s ladder like structure provides the key frame to work on the combined form of DNA and Nanotechnology.
- The length of DNA is about 500 angstroms.
- The shape of the DNA nanostructures can be controllable to work on it.
- The synthesis of single stranded DNA is less expensive.
- The self-assembly property of DNA makes it easy to construct variety of structures. [10]

CONSTRUCTION OF DNA NANOSTRUCTURE

A Molecular engineer uses distinct properties of DNA such as structural stability and programmability of sequences, predictable self-assembly for the formation of DNA Nanostructure. DNA Nanostructures are made up of DNA which acts both as structural and functional element. These structures are designed with preciously engineered, controllable shape, size, surface chemistry, function and energy. [11]

There is different designing software which is used to facilitate the design of DNA Nanostructures such as Tiomot, DAE DALUS (DNA origami sequence design algorithm for user-defined structures) and Con.DO (Computer aided engineering of DNA origami) has been developed for designing DNA Nanostructures. [12]

The construction of DNA Nanostructures is done by using following motifs-

- Stem Loop (Hair Pin) Structure- Unpaired region occur in ssDNA or RNA. The structure is also hairpin or hair pin loop.
- Sticky ends- An overlap is a stretch of unpaired nucleotides in the of DNA molecules. These overhangs are mostly palindromic. These are used to combine two DNA Nanostructures together via hybridization of their complementary ssDNA.
- Holliday Junction- Two parallel DNA helices form a junction with one strand of each DNA helix crossing over to the other DNA helix forming double stranded DNA Nanostructures. [13]

These DNA Nanostructures are present in different forms such as Structural DNA Nanotechnology and Dynamic DNA Nanotechnology.

STRUCTURAL DNA NANOTECHNOLOGY

Structural DNA Nanotechnology generally derived from the Seeman's revolutionary idea that DNA could be used as a physical material for self-assembling nanoscale structures. DNA being a molecule storing and transmitting genetic information is an excellent nanoscale building block because of its specific three-dimensional conformation.

In 2009 Seeman's group was first to assemble 3D DNA crystals from designed sticky-end connections rather than simple, non-specific base stacking. This work represents a milestone to Seeman's vision hosts to organize guest protein molecules facilitate protein crystallography. [14]

DNA nanotubes with increase in its complexity and functionality have been designed by a number of approaches, including DNA TILE assembly, DNA origami and wireframe nanotubes [15]

The inorganic nanomaterials of Structural DNA Nanotechnology are used in solar cells, laser diodes, phototransistor etc. of their unique optical and electronic properties.

DYNAMIC DNA NANOTECHNOLOGY

Dynamic DNA Nanotechnology involves the creation of nanoscale devices made of DNA whose primary function arises from their ability to undergo controlled motion or reconfiguration. [16]

The ability to design response to environment is a foundation for designing nanomaterials, devices, and machinery that can sense the local environment, energy and forces at molecular scale. The accessible mechanical properties of DNA-based design can be expanded by using single stranded DNA, which behaves like a flexible polymer or bundles of many dsDNA helices that exhibits bending stiffness. It can be controlled to design anisotropic mechanical behavior.

Mechanical design of DNA like DNA motors led to expanded function of dynamic nanodevices to construct joints for angular motion, sliding joints that can achieve translation or rotors for continuous rotation. Dynamic DNA Nanotechnology also used in sensing, drug delivery, computation and nanorobotics. [17]

APPLICATION OF DNA NANOTECHNOLOGY

Dr. Dan Luo and his group at Cornell University have engineered DNA with myriad of DNA manipulating enzymes and created various DNA-based nanostructures including

DNA-dendrimers (DNA-trees), DNA nano-barcodes and hydrogel DNA. Among which, the DNA dendrimers and DNA nano-barcodes have been employed to detect multiple pathogens (including Ebola, Anthrax, HIV etc.) and DNA hydrogel is used for the treatment of diabetes [18,19]

DNA Computing was first proposed by Adleman in 1994, in order to solve complex problems. DNA computer have DNA strands which hold so much in memory and multiple operations at once thus solving decomposable problems much faster [20]. DNA chips based on the microarrays and fluorescently labelled probes have been employed in the detection of HPV DNA [21]. Nanoelectronics had been highly dependent on the complementary symmetry metal-oxide semi-conductor (CMOS) technology which has a vital role in the analogue circuits such as image sensors, data converters, digital logic circuits, micro controllers and microprocessors [22]

In 1996, a new technology called the 'Sticker DNA' model was introduced by Roweis and his colleagues which applies Random Access Memory (RAM) and does not require any enzyme and has capability of becoming the universal method for DNA computing [23]. DNA Nanotechnology provides a brand-new perspective both in the field of medicine and pharmacology. The development of nanomedicine by the use of liposome-based nanoparticles to carry minute number of chemotherapeutic agents to affected cancer sites. The albumin-bound nanostructures are used to enhance the permeability of the endoplasmic reticulum for cancer therapy [24].

Biosensors are efficient as they have a high ratio surface area to volume as well as adjustable properties like electronic, magnetic and optical. Due to these properties it works as drug delivery vehicles, contrast agents and diagnostic devices [25]. Dendriworms made of dendrimer units of magnetic nanoworms used for intracellular delivery of small interfering RNA (siRNA). This RNA is responsible for both activation and silencing of mammalian genes [26].

CONCLUSION

The DNA out of many engineering materials is most useful in the field of nanotechnology. The increase in the modifications of DNA in the field of Nanotechnology is the major step for forward researchers.

The ability of DNA for self-assembly and making of programmable nanostructures can create compatible devices, which is beneficial in many fields of science, especially in the medicines, therapy treatments and electronic devices. Various DNA Nanostructures have been used for protein characterization, enzyme, assembly, biosensing and drug delivery.

Today researchers are developing different molecular devices which will soon be used in cancer treatment and to reduce the toxic effect of the chemotherapy. Researchers also developed the DNA walkers (walking bipedal nano robots and the walkers moves on a DNA track) and Nano-mosquitoes (used in militaries and also determine the protein structure). Nanomedicine researchers are developing different nanoparticles such as graphene, gold and silver for the treatment of different diseases and injuries. Some ethical problems will arise on the developing DNA Nanostructures. The technologies being new can have an effect on humanity as it can behave as we might not expect from their macro and micro-siblings.

Scientists are still uncovering the difficulties of having nanostructures in our life and the field might get amplified in future, beyond the scope of this review.

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ABBREVIATIONS

DNA-Deoxyribonucleic acid; HIV-Human Immunodeficiency Virus; TILE-Task Individual Load and Environmental; 3D-3 Dimensional; LASER-Light Amplification by Stimulated Emission of Radiation; ssDNA-Single Stranded Deoxyribonucleic acid; dsDNA-Double Stranded Deoxyribonucleic acid; siRNA-Small Interfering Ribonucleic acid

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