Universitat Autònoma de Barcelona

NANOTECHNOLOGY BASED ON DNA

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1. INTRODUCTION

In autumn 1980, the crystallographer Nadrian C. Seeman was in a campus pub, when he saw Escher's ***Depth***, a woodcut which represents a lattice. This picture inspired him an idea, that was a new method to obtain the structure by X-Ray diffraction without the complicated crystallization process. This new approach consisted in a 3D DNA lattice which could be used to orient hard-to-crystallize molecules.

Since this first contact with the DNA as a material until nowadays, some researchers have been working with this biomolecule and they achieved great results, for example DNA Origami or 2D lattice (used for arrays).

Figure 1. **Maurits Cornelis Escher's *Depth*.** It's the woodcut, which inspired Seeman for 3D DNA lattice.

2. NANOSTRUCTURES' DESIGN

DNA nanostructures must be rationally designed so that the individual nucleic acid strands will assemble into the desired structures. This process usually has two steps[1]:

- **Motif Design:** This step is the design of secondary structure. This step is not performed in the laboratory, it's done in the computer with specialized software, but some of them are free, for example http://cadnano.org/windows-installation. To design the secondary structrure, there are different approaches:
  - **Tile-based structures**
  - **Folding structures**
  - **Dynamic assembly**
- **Sequence design:** This step has similar goals to protein design. The sequence is designed to favor the desired target structure and to disfavor other structures. In this step is important the symmetric minimitzation inside the sequence.

3. KINDS OF DNA-BASED NANOMATERIALS

DNA is a quite mouldable biomolecule, so, there are different types of DNA nanomaterials [2]:

3.1. Structural DNA nanotechnology

Crossover Junctions:

They are the basis of structural DNA nanotechnology. They are based on the binding of DNA duplexes by their complementary sequences. In Crossover Junctions, DNA duplexes are bound by two or more positions, fixing its relative orientations and reducing its movements (*Fig. 2*). Crossover junctions can lead to a big diversity of nanostructures based on DNA. These kinds of structures are usually used for 2D arrays. The combination of these structures can generate a huge surface that can be modified.

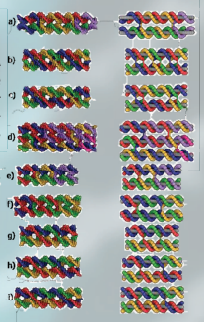

Figure 2. **Crossovers Junctions. a)** DX, **b)** PX, **c)** JX, **d)** TX, **e)** DAE, **f)** DAO, **g)** DPE, **h)** DPON and **i)** DPOW.

Holliday Junctions:

It is a crossover of 4 single DNA strands are used with nucleotide sequences which stop the mobility of the structure (*Fig. 3a*).

This junction has a sensible cationic geometry, so, in high concentration of metallic cations, the structure gets stabilized on closed conformation (*Fig 3b*).

These structures could be used to make big 2D-arrays or even 3D-arrays.

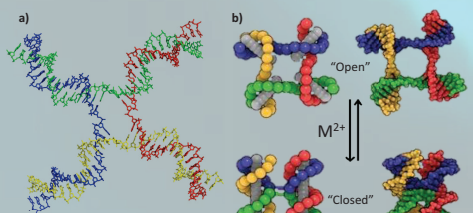

Figure 3. **Holliday Junctions. a)** Schema of Holliday Junctions' molecular structure. It shows the interactions of the four strands. **b)** It is a graphic representation of the different conformations, showing the alternation of open and closed with cations.

n-Point stars:

These structures are anti-parallel DNA duplexes made in star shape. These structures have a big structural diversity. These type of nanostructures can be divided into two groups: "Sticky" Ends, the structure can bind other structures, and "Blunt" Ends, the structure cannot bind other structures (*Fig. 4a-c*).

These structures can be used to form 2D-arrays (*Fig. 4e*), or can be used like a vertex to generate 3D structures (*Fig. 4d*).

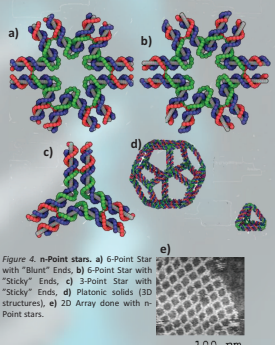

Figure 4. **n-Point stars. a)** 6-Point Star with "Blunt" Ends, **b)** 6-Point Star with "Sticky" Ends, **c)** 3-Point Star with "Sticky" Ends, **d)** Platonic solids (3D structures), **e)** 2D Array done with n-Point stars.

3D DNA nanostructures:

The combination of DNA duplex and complementary sequences to form stable bindings and thus generate a large number of three-dimensional DNA nanostrucutures (*Fig. 5a*), even DNA nanotubes (*Fig. 5b*).

These structures are the perfect candidates for molecular encapsulation, structural support for the manufacture of other nanostructures or can be nanoscale building blocks.

These structures were ideated by Seeman, to avoid the crystallization process of molecules.

Figure 5. **3D DNA nanostructures. a)** Example of 3D DNA 'nanocube, **b)** Examples of 3 different 'kinds' of DNA nanotubes, frontal (upper) and lateral plane (lower).

DNA Origami:

It was developed in 2006 by Paul Rothemund. The arrangement of a long scaffold of ssDNA is controlled by the positioning of numerous smaller staple strands (*Fig. 6a*) determined by geometric analysis of the nanostructure designed. (*Fig. 6b*)

The sequence of every staple strand is unique because if it does not happen, the nanoparticle wouldn't be well-folded [3].

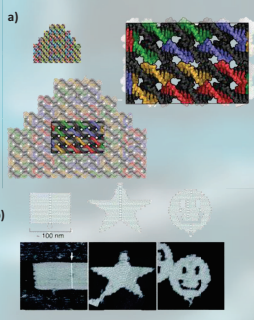

Figure 6. **DNA Origami. a)** Interactions' schema between long single DNA strand (black) and staples strands (various colours) **b)** Different structures which Rothmund obtained in his experiments.

3.2. Nanodevices based on DNA

Devices based on Structural Transitions:

These structures are made as static structures, but are designed so that dynamic reconfiguration is possible after the initial assembly. Systems could change states based on the presence of control strands or different buffer conditions. Examples:

- A device was based on the transition from B-DNA to Z-DNA. It responds to a change in buffer conditions.
- A device that could switch from a paranemic-crossover (PX) conformation to a double-junction (JX2) conformation, it is known as "molecular tweezer".
- DNA walkers are a class of nucleic acid that perform directional motion along linear track.

Sequence Dependent Devices:

The true power of using DNA is its programmability. The most effective way to construct multiple devices is to make them sequence dependent. The rate of response is limited by strand diffusion time. Examples:

- The same device which can switch from PX to JX2 if the sequence, which interacts the device, has the adequate primary structure.
- DNA walkers, because their interactions with other DNA sequences, RNA sequence or different surface are conditioned by the sequence.

3.3. Other kinds of nanoparticles based on DNA

- **Attachment or Integration of DNA onto Surfaces** → Binding of DNA, onto nanomaterials' surface.
- **DNA based organization of Metal Nanoparticles** → To use DNA to assemble metals or semiconducting nanoparticles.
- **Construction of Quantum Dots Arrays Using DNA (*Fig. 7*)** → Quantum dots are ideal fluorophores for multicolour and ultrasensitive applications in nanobiotechnology.
- **DNA-Directed Assembly of Nanowires** → DNA is used as a template for directed synthesis of silver chains.
- **DNA-Functionalized Nanotubes** → DNA molecules increase the CNT solubility in organic media.
- **DNA-Based Biosensors** → The function is the fact that two strands of DNA stick to each other by virtue of chemical attractive forces.

Figure 7. **3D representation of DNA conjugated a Quantum Dot.** In this picture, what binds DNA and QD is the green cylinder, it could be

4. DNA NANOTECHNOLOGY APPLICATIONS [4],[5]

4.1. General applications

- Seeman's three-dimensional nucleic acid lattice was designed to orient molecules inside it which are hard-to-crystallize. Allowing determination of molecule structure
- DNA can be used as template for the assembly of electronic elements, due to its ability to arrange other molecules (silver-DNA nanowires). DNA nanotechnology as programmable matter.
- DNA walkers have been used as nanoscale assembly lines to move nanoparticles and direct chemical synthesis

4.2. In nanomedicine

- To use hollow DNA box to make "smart drugs" for targeted drug delivery. There are two versions: one acting outside the cell, in extracellular media, and another acting inside the cell, and it can be until 48h in cytosol.
- Some diseases can be detected by a specific DNA sequence. This sequence must be conjugated to other nanostructured materials by detecting the response. This is a DNA biosensor to diagnosis.

4.3. DNA Origami

- A DNA nanorobot, that is filled with drug, will only open with specific "keys" which belong to targeted cells.
- A DNA origami delivery vehicle for Doxorubicin where the drug is intercalated between origami nanostructures [6].
- A multi-switchable 3D DNA box origami has a mechanism which only responds to a unique set DNA or RNA keys.
- To use DNA origami rods, replacing liquid crystals, is advatangeous in protein NMR spectroscopy because is tolerant with detergents (membrane proteins).

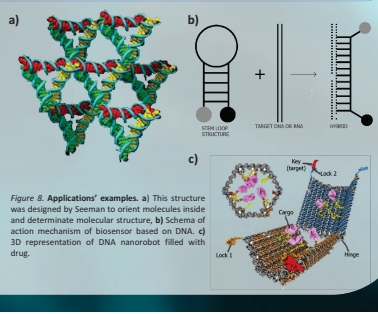

Figure 8. **Applications' examples. a)** This structure was designed by Seeman to orient molecules inside and determinate molecular structure. **b)** Schema of action mechanism of biosensor based on DNA. **c)** 3D representation of DNA nanorobot filled with drug.

5. CONCLUSIONS

Conclusions and a look to the future:

- DNA has some physicochemical properties, which can allow us to create some different structures or devices.
- Seeman's idea was 3D DNA lattice to avoid crystallization process, since this first idea, researchers have developed a new branch in nanotechnology.
- Currently, there are some structures or devices with different applications, and this is due to DNA programmability and malleability.

DNA nanotechnology present is extraordinary, but maybe the future could be better: new structures, new devices, new applications, and the most interesting , the industrialization of this science

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Figures have been taken from this articles, some Nanorex's documents and the Depth's and QD's image was searched in Google Images.