

Deoxyribonucleic Acid Based Nanotechnology

Author

Nguyen, NT

Published

2015

Journal Title

Micro and Nanosystems

Version

Accepted Manuscript (AM)

DOI

[10.2174/187640290702151216123523](https://doi.org/10.2174/187640290702151216123523)

Rights statement

© 2015 Bentham Science Publishers. This is the author-manuscript version of this paper. Reproduced in accordance with the copyright policy of the publisher. Please refer to the journal website for access to the definitive, published version.

Downloaded from

<http://hdl.handle.net/10072/101787>

Griffith Research Online

<https://research-repository.griffith.edu.au>

Deoxyribonucleic acid based nanotechnology

Nam-Trung Nguyen^{a*}

^aQueensland Micro- and Nanotechnology Centre, Griffith University, Brisbane, Qld 4111, Australia

Abstract: Deoxyribonucleic acid (DNA) is the coding material in living organisms. Complementary pairs of nucleobases contribute to the Watson-Crick helical shape of DNA. The nucleobases are connected through hydrogen bonding. This unique feature not only allows for genetic information to be stored but also the assembly of complex nanostructures. DNA-based nanotechnology utilizes DNA as the engineering materials. DNA nanodevices can be designed to work as a drug carrier with programmable selectivity, sensor and computer. Since DNA is a natural material, the application of DNA nanodevices in a biological environment ranging from the relatively simple cell to a complex living organism is a complex, risky but rewarding task.

Please provide
corresponding author(s)
photograph

Keywords: DNA nanotechnology, structural DNA nanotechnology, dynamic DNA nanotechnology, DNA assembly

Deoxyribonucleic acid (DNA) based nanotechnology uses exclusively DNA as an engineering material to build nanodevices. Since the concept of DNA base pairing and its thermodynamics are well understood, DNA based nanotechnology allows the precise design of both structural and dynamic devices with sizes ranging from nanometers to millimeters. Thus, DNA-based nanotechnology is a bottom-up technology that can form complex structures, which are not accessible by conventional top-down technologies such as lithography. Chen et al. recently gave a comprehensive review on this technology [1].

Biological systems have the ability of sensing information, processing information and giving back a feedback. Molecular sensors, computational circuits and actuators exist in living organisms. The first step to mimic these natural systems is to emulate these functions in a cell-free environment without the complex interaction with DNAs and ribonucleic acids (RNAs). DNA as an engineering material to form relatively large structures on the order of micrometers has been identified in the 1980s [2].

The so-called DNA origami is a folding technique of DNA to create two-dimensional (2D) [3] and three-dimensional (3D) structures [4]. The technique uses a long single strand acting as a scaffold. The desired shape is programmed with a large number of short staple strands bound to the different places on the long scaffold strand. The image of the desired shape is designed as a raster image of the scaffold DNA. The design is then fed into a computer program that calculates

the positions of the staple strands. The complementary staples are positioned at the specific places that are later connected through Watson-Crick base pairing. The precise construction of these DNA nanostructures allows them to be used as drug delivery tools. DNA nanodevices act as scaffolds for the attachment or container for the delivery of functional therapeutic groups and targeting moieties.

DNA based nanotechnology has progressed further from the structural design of static structures to dynamic DNA nanotechnology. The above folding technique through static hybridization has been extended with the dynamic, competitive hybridization, which is programmed through DNAzyme catalysis or DNA strand displacement reactions. This technique allows the design nanodevices with moving parts and dynamic behavior such as actuators [5]. Dynamic DNA technology allows the design and fabrication of molecular motors and molecular circuits and catalytic amplifiers.

Most of the above nanodevices were designed and tested in a cell-free environment. In a cellular environment, DNA nanodevices may interact with proteins that interfere with their function and performance. With the targeted applications in cell culture and living organisms, DNA-based nanodevices should be stable in media such as cell lysates and serum. Ko et al. [6] were first to demonstrate the cellular uptake of large DNA nanostructures. The uptake efficiency can be further improved with modifications such as coating the device with viral capsid proteins [7]. Sensing RNAs in a cell could reveal the identity and health of a cell. DNA nanodevices are ideal to work as probes, or molecular beacons, to detect specific RNA sequences in living cells. A relevant application of this technology is the detection of rare circulating tumor cells in blood.

* Correspondence to:

Nam-Trung Nguyen, Queensland Micro- and Nanotechnology Centre, Griffith University, Brisbane, QLD 4111, Australia. Email: nam-trung.nguyen@griffith.edu.au

A major application of dynamic DNA based nanotechnology is molecular circuitry or molecular biocomputer. For instance, Kahan-Hanum et al. [8] introduced DNA nanodevices as logic AND-gates into breast cancer cells. The fluorescent output was only activated in the presence of two input molecules. Most of the recent works on DNA nanodevices for drug delivery and sensing were performed in cell cultures. The next challenge is their applications in multicellular organisms. As mentioned above, the major hurdles here are delivery to the site of interest and the stability of the engineered DNA structure. Another emerging issue is the toxicity of DNA nanodevices in living organisms.

The recent success in using DNA nanodevices for drug delivery and sensing promises their huge potential in therapeutics and diagnostics. The ability to perform logic operation will improve the performance and specificity of DNA-based diagnostic technology. The combinatory logic operation of multiple biomarkers that can be performed in a living organism will lead to a high level of specificity. DNA

nanodevices will not only sense but also reprogram a cell and even a whole organism. DNA nanodevices that deliver DNA or RNA transcription programs can bypass the immune system and reprogram cells for tissue and organ regeneration. In terms of nanotoxicity, the next generation of DNA nanodevices should be customized for the immune responses of the host organism, thus these devices could potentially be engineered for personalized immunotherapy.

REFERENCES

- [1] Chen YJ, Groves B, Muscat RA, Seelig G, *Nature Nanotech.* 2015; 10: 748-760.
- [2] Seeman NC, *Nucleic acid junctions and lattices, J. Theor. Biol.* 1982; 99:237-247.
- [3] Rothemund PWK, *Nature* 2006, 440: 297-302.
- [4] Douglas SM et al., *Nature* 2009, 459: 414-418.
- [5] Yurke B, Turberfield AJ, Mills AP, Jr, Simmel FC, Neumann JL, *Nature* 2000, 406:605-608
- [6] Ko S, Liu H, Chen Y, Mao C, *Biomacromolecules* 2008; 9:3039-3043.
- [7] Mikkila J et al. *Nano Lett.* 2014; 14:2196-2200.
- [8] Kahan-Hanum M, Douek Y, Adar R, Shapiro E, *Sci. Rep.* 2013; 3:1535.