<https://helda.helsinki.fi>

DNA Nanotechnology

Yaradoddi, Jayachandra

Springer Nature Switzerland
2019

Yaradoddi , J , Kontro , M H , Ganachari , S V , Sulochana , M B , Agsar , D , Tapaskar , R & Shettar , A 2019 , DNA Nanotechnology . in L Martinez , O Kharissova & B Kharisov (eds) , Handbook of Ecomaterials : DNA Nanotechnology . vol. 2019 , Springer Nature Switzerland , Switzerland , pp. 3561-3572 . https://doi.org/10.1007/978-3-319-68255-6_191

<http://hdl.handle.net/10138/326417>

https://doi.org/10.1007/978-3-319-68255-6_191

unspecified

acceptedVersion

Downloaded from Helda, University of Helsinki institutional repository.

This is an electronic reprint of the original article.

This reprint may differ from the original in pagination and typographic detail.

Please cite the original version.

DNA NANOTECHNOLOGY

Jayachandra S. Yaradoddi^{1,2,6*}, Merja Kontro², Sharanabasava V. Ganachari^{1*}, Sulochana M. B.³
Dayanand Agsar⁴, Rakesh Tapaskar⁵ and Ashok S. Shettar¹

¹ Centre for Material Science, Advanced research in Nanoscience & Nanotechnology, School of Mechanical Engineering, KLE Technological University, Hubballi-580031, Karnataka, India

² Department of Environmental Sciences, University of Helsinki, Niemenkatu 73, Lahti 15140, Finland

³ Department of PG Studies and Research in Biotechnology, Gulbarga University, Kalaburagi-585106, INDIA

⁴ Department of PG Studies and Research in Microbiology, Gulbarga University, Kalaburagi-585106, INDIA

⁵ Energy Cluster, Centre for research in Renewable & Energy Systems, School of Mechanical Engineering, KLE Technological University, Hubballi-580031, Karnataka, India.

⁶ Extremz Biosciences Private Limited (Govt. of Karnataka Funded Start-up), CTIE start up street, KLE Technology University campus, Hubballi-580031, Karnataka, India.

ABSTRACT

Since from the past few decades DNA appeared as an excellent molecular building block for the synthesis of nanostructures because of its probable encoded and confirmation intra- and intermolecular base pairing. Various ease strategies and consistent assembly techniques have been established to manipulate DNA nanostructures to at higher complexity. The capability to develop DNA construction with precise special control has permitted scientists to discover novel applications in many ways, such as scaffolds development, sensing applications, nano devices, computational applications, nano robotics, nano electronics, biomolecular catalysis, disease diagnosis, drug delivery. The present report emphasis to brief the opportunities, challenges and future prospective on DNA nanotechnology and its advancements.

1. Introduction:

DNA Nanotechnology is the manipulation of DNA at the nanoscale to take advantage of its unique properties. This is often employed to produce individual molecules that includes DNA or RNA or protein. Hence, in traditionalist's prospective DNA nanotechnology is a biomolecular engineering. This arena has intended to produce molecular assemblies and devices in which the entire application is to use DNA as a manipulation material.

Fig 1: The cellular and genomic organization of typical animal cells.

Highly distinguished properties of DNA base pairing provide a controlled mechanism for DNA interactions; thus, the sequence assemblages enable a distinct, balanced design of the DNA structures in sizes ranging from nanometers (Fig. 2) to millimeter, and molecular signaling pathways passes the information. Unfortunately, no other such molecular manipulation technology exists, that would design the complete biosynthesis of complex biomolecules from simple precursor molecules and varied traditional biomolecular systems [1].

Fig. 2) Depicting structure and measurement of deoxyribose nucleic acid (DNA) molecule.

The main accomplishment of DNA nanotechnology is likely to be achieved via 3 key mechanisms: 1) Quantitative understanding of DNA thermodynamics, especially in predicting DNA molecular folding using single stranded DNA, and how they forms networks with each other [2], 2) Quick fall of cost and improvement in the quality of DNA synthesis [3]. 3) Cell-free DNA synthesis that has led to the purity of DNA by avoiding the interference of nucleases enzymes and additional characteristic features associated within the cells. In the past, DNA nanotechnology has been extensively thought to establish drug producing systems, i.e. ‘smart therapeutics’, and tools and devices for molecular biological science, and other strategies that can function well inside existing cells [4-7].

The well characterized DNA base pairing regulates the complex DNA interactions, and the highly preserved duplication of genetic codon has permitted the standard strategy for precisely distinct DNA assemblies of varied sizes measured in terms of nanometers to millimeters. The molecular machineries of the cell can precisely process the information. No alternative

molecular manipulation technology occurs, that empowers the fully *de novo* pathway of a correspondingly multifaceted and varied set of molecular organizations [1].

The field of nucleic acid nanotechnology has contributed well versed techniques to shape nano and micron sized structures [8, 9]. These structures are very helpful in determination of growth of other materials. Both nucleic acids DNA and RNA can construct structures like scaffolds, which are reasonably accurately with predictable characteristics. RNA assemblages of hundreds nanometers in size have been possible to construct in vitro as well as in vivo [10]. Potential applications of the DNA nanotechnology involves the following:

1.1 Cell-free technology

To function in complex, great variety of different environments, humans have developed molecular sensors, motors and devices to compile information about the environment, and to adjust the optimal environment. The sensor information then used to further regulate the controlling circuits of the built motors and devices to alter activity. Similarly, the cell free DNA nanotechnology has progressed in of constructing the unique functional mechanisms, assemblies and self-motivated devices, which are needed to produce molecular machines that could compete with several behavioral complexity observed in biology [1].

1.2 In lysates and stable cells

The complex intracellular circumstances are completely different from the cell free molecular units. Within the cell DNase and RNases could hinder and damage the constructed unique manmade functional systems. The organized intracellular compartments prevent the free diffusion and dispersion of nucleic acid carried inside the cell. Instead of using living cells, the optimal, controlled conditions for gene devices can be created using solution such as serum, cell lysates, cell fixation. The augmentation of gene devices to such conditions offer part of intricacy properties of living organisms, and simultaneously they lack adverse properties that can block the proper function of man-made molecular nanodevices.

1.3 DNA nanotechnology in permanent cells.

Fixed or permanent cells have retained significant quantity of structural composition inside cell and in organelles, where the special distribution of molecules like proteins and mRNA have been preserved. The subcellular distribution of proteins and mRNA inside fixed cells can be visualized using fluorescent in situ hybridization (FISH) and immunostaining methods. Increased sensitivity and specificity of such imaging methods are very much essential, and can be achieved to a greater extent by using DNA nanotechnology. For example, molecular probes

used in the hybridization chain reaction (HCR) (Dirks and Pierce, 2004) have empowered the concurrent mapping of as much as five target mRNA in vertebrate embryos [12, 13].

Hybridization as a conservative connector strand aims at mRNA sequences, were able to undergo controlled catalysis of polymerization reaction carried out with two kinds of fluorescent tagged hairpin like monomers; resulted in signal associated with a specific amplified mRNA could be mapped through fluorescent microscope.

1.4 Interaction with the cell surface markers

The complex compartments and structures contained by the mammalian cells turn distinct vessels featured for various biological reactions. Lipid bilayer coated cell surface molecules include many surface protein molecules repeatedly segregate one cell type to another. Current chapter demonstrated the DNA nanotechnology could be premeditated interaction with cell surface markers; aptamers, antibodies [14]. For example, potential DNA-based therapeutics target cells in the bloodstream and cell surface markers and usually don't necessitate the reception of nanostructure.

2. DNA nanostructures as drug-delivery vehicles

Reports till today described probability of functioning nano devices and assemblies in cell culture, cell lysate also demonstrated how the nano systems interaction occurs with cell surface proteins. Following sections designates about the challenges that are associated by the delivery of nano devices inside mammalian cells, further deliberates their usage as vehicles for drug delivery.

2.1 Cellular uptake of DNA nanostructures.

Through the manipulation of folate associated DNA nanotubes aims at folate receptors that are excessive expression of a genes on many tumor cells. Mao et al., 2008 [7] have effectively demonstrated even huge DNA nanostructures can goes into the cells. Further altered as nanotubes by means of fluorescent label to nanotube fragments and nanotubes were affected upon receptor binding [7].

2.2 Dynamic DNA nanodevices inside living cells

The dynamic DNA devices that operates inside the cells that retort to specific environmental signals; the devices comprise those sense comprehensive environmental change in the pH as a chemical variable, latest development in direction of detecting specific biomolecular information transporters can allow variation of levels of gene expression and this chapter

foremost stage in order construct sense circuits in identification to analyze complex molecular markers.

2.3 Molecular computation.

In dynamic DNA nanotechnology understanding multiple layers biomolecular circuits and multi input are the major accomplishments. Yet, the foremost advantages of DNA nanotechnology can be realized through the 'bio computers', especially when they are compared with other technologies mainly based on artificial gene controlling networks. Firstly, nucleic acid circuits rely upon the constituents robotically simple, reasonably premeditated at micro molecular level, and assures higher grade of regulating pathways. Secondly, component could be designated by altering the sequence, which modulates informal increase of system size in cohesive fashion. Thirdly, at many nucleic acid dynamic devices have a comparatively small DNA footprint in comparison with the system assembled via genetically encoded proteins.

2.4 Genetically programmed structures and devices

Long lasting embedded regulation of gene expression is very much needed for the application of gene therapy in metabolic engineering. The RNA scaffolds and regulatory elements programmed, copied within the viable cells that are perhaps suitable for medical applications compared to synthetic DNA systems. Manipulation of DNA must hold compatibility with transcription that needs pervasive adaptation towards the investigational method and molecular design. Even though this may appear similar and considerable contest, so because broad work has already been made by many researchers.

3 Advancements in DNA nanotechnology:

The effective design and assemblages of the DNA nanotechnology as described above will leads to many research avenues and advancements. With lots of information on properties of nanostructure self-assemblages will open new frontiers in various applications such as computers, electronics, scaffolds preparations, sensors development etc. To fabricate and compute nanoelectronics and nano photonic devices, to regulate the macromolecular especially protein interactions of both intracellular and extracellular means, for the fabrication of scaffold's exclusively in nanomedicine and profitable applications especially in therapeutic drug industry, they may also contain innovative drug transport systems, nano sensors in-vivo sensing of DNA inside living cells. Though, the applications of DNA nanotechnology is not limited these areas, which is also plays key role in super supramolecules used to create 3D DNA structures with synthetic molecules as key components.

3.1 Scaffolds for Nanoelectronics or Nanophotonics

One of the main application of DNA nanotechnology is its ease assembly with other, less controllable materials. There are hardly we can see the materials which are meant to design nanoelectronics (Fig. 3), nanophotonics devices, example DNA nanoassemblages can be used in nanophotonic and nanoelectronic devices, where beginning of a hierarchy or process upwards of DNA-centered assembly is coherence by stepwise design, lithographical techniques of micro as well as macro level scale patterning. Current progress of superficially enabled self-assembly, distinct mechanisms of biochemical properties can allow more accurate alignment of the nanoelectronic and nanophotonics components to reliable, scale-up designs that could be assembled with visualization systems.

Fig. 3: Nanoelectronic or electrochemical DNA nano biosensors

3.2 Enzyme Cascade Scaffolds

The deoxyribose nucleic acid (DNA) centric assemblage intricate protein arrangements or arrays is other field of progression to look forward near future. Protein complexes intern play

an important role in metabolic activities and breeding in existing organisms [15]. The requisite locations for cofactors and substrates are structurally similar, the activation site can be stereoselective and extremely susceptible towards vindictive dislocation. In inspiration from the nature scientist now have found diverse approaches in regulation and controlling of catalytic activities of the enzymes, and to realize the mechanism of enzyme function and pathways [16-20]. In comparison with the recent conventional methods, DNA nanotechnology is very efficient and well-regulated approach to establish organizational and rearrangement by using cogent model and structure [21]. Assembling cofactors and enzymes on DNA nanostructure scaffolds have paved the way for scientist to investigate the important constraints for controlling catalytic activity, detachment between each molecules and relative contiguous position [22-26].

The main contest in assembling several proteins in DNA nanostructures is purely depends on the virtual angle and site. In a group of consistent broad techniques for location defined interfuse of the proteins with oligonucleotides recognized appropriately accumulation of diversified proteins of attention. A model organization, singular protein with numerous linking positions can be conjoin distinct deoxyribose nucleic acid sequences to allow complete alignment regulation of protein connected with the DNA nanoassemblages.

3.3 Nano Sensors

Extensive area of DNA nanotechnology towards improvisation of keen biomolecular technologies accomplishing the activities of sense-compute and triggering actions constructed on essential data rich deoxyribose nucleic acid fragments and assemblies. Instance, progress of “smart molecular doctors” is been transformed the area of modified medication. The SMD has the similar tasks as actual doctors, comprising analytic and therapeutic roles, nevertheless it functions completely at molecular and cell level. Precise treatment to the specific unhealthy cells to remedy them on the individual cells provides impressive drug effectiveness and relative slight reaction because of lesser quantity of drug dosages needed in comparison with the conventional treatments. (Figure 3

DNA Nano Biosensors

Fig. 4: Showing a typical DNA nanobiosensor device

3.4 From Nano to Angstrom Technology

Alive cells contain ample of data, advanced technologies will demonstrate structural organization and precision of these cells at biomolecular level. The DNA nanostructure are attractively controlled, then they have gifted to control the biomolecules coarse stage in comparison to the nature. Humans require surplus regulation, we need to work on the boundaries nanoscale fabrication which is up to angstrom level. All the characteristics features have gained importance in past decades. For instance, several conventional methods deliberated in RNA nanostructure construction [36, 37).

Nowadays there are several manipulation or engineering approaches in progress [38, 39). Advancements in the characterization techniques mainly X-ray diffraction, NMR and cryo-electron microscopy have backs the development of angstrom technology. Especially, cryo-electron microscopy permits crystal unrestricted organizational elucidation in increased classified proteins very much similar to X-RAY crystallography techniques [40, 41]. Use of DNA origami frames together organizational hosts, complex DNA structures and RNA

requisite proteins could be analyzed up to 10^{-10} (angstrom) level through the use of freezing electron microscope [42].

Thus, the advancement will fetch scientists and researchers to access atomic as well as molecular level of structure information (this many times happens in combination of different advanced techniques) DNA nanotechnology definitely heightens the present technology to the next level. Over the past few decades, DNA nanotechnology and DNA nanostructures are transforming from infancy to fully-fledged growth. Hopefully, the current technology will overcome all the limitations of biology, chemistry, physics and engineering and which is evolved to take up the new challenges associated with the public. In upcoming stage of structural DNA nanotechnology, unusual complex intramolecular interactions between DNA, RNA and proteins with aid of angstrom technology, which demonstrates the foremost problems and opportunities in especially molecular insights of design, assembly and computational approaches.

DNA Nano Biosensors

Fig 5: General DNA nanosensors

4. Future Prospectus:

The major physical and chemical challenges involved in transformation of DNA nanostructures are: price of artificial DNA, less vintage of multifaceted 3-dimensional structures, susceptibility of DNA towards temperature, ionic strength and DNases activity. Scientists started working on the critical parameters through improving origami technology hinging tactics in order to enhance the assemblage yields [31] and cut down the assembly time and through developing appropriate purification methodologies for industrial scale synthesis [32]. Utmost significant factor in development of DNA nanostructures is its biocompatibility conditions for efficient folding, rather by thermal annealing under higher magnesium concentrations [33,34].

Certainly, many severe problems must be addressed before being the use of DNA nanorobots use in especially drug transport systems within the cell. Scientists have to discover technique to preserve DNA nanoassemblies from the activities of enzymes. Condensed DNA nanostructures broadly exhibit comparative stability upon nuclease enzyme for a shorter time [28, 29].

Upcoming investigation are to be made in the direction of tolerance towards the degradation process through the biochemical cross connecting of designated DNA constituents or labeled DNA supportive variations. Recognizing molecular mechanism through these DNA nanoassemblies arrive into the cells before they get damaged by endosomal actions [30]. Another main problem includes tissue distribution and immunity have to be elucidated.

References:

- [1] Yuan-Jyue Chen, Benjamin Groves, Richard A. Muscat and Georg Seelig (2015). DNA nanotechnology from the test tube to the cell, DOI: 10.1038/NNANO.2015.195.
- [2] Bloomfield, V. A., Crothers, D. M. & Ignacio Tinoco, J. (2000). Nucleic Acids: Structures, Properties and Functions (University Science Books).
- [3] Carlson, R (2009). The changing economics of DNA synthesis. *Nature Biotechnol.* 27, 1091–1094
- [4] Dittmer, W. U., Reuter, A. & Simmel, F. C. A (2004). DNA-based machine that can cyclically bind and release thrombin. *Angew. Chem. Int. Ed.* 43, 3550–3553

- [5] Yurke, B., Mills, A. P. Jr & Cheng, S. L. (1999). DNA implementation of addition in which the input strands are separate from the operator strands. *BioSystems* 52, 165–174
- [6] Benenson, Y., Gil, B., Ben-Dor, U., Adar, R. & Shapiro, E (2004). An autonomous molecular computer for logical control of gene expression. *Nature* 429, 423–429.
- [7] Ko, S., Liu, H., Chen, Y. & Mao, C (2008). DNA nanotubes as combinatorial vehicles for cellular delivery. *Biomacromolecules* 9, 3039–3043.
- [8] Zhang F., Nangreave J., Liu Y., Yan H (2014). Structural DNA nanotechnology: state of the art and future perspective. *Journal of the American Chemical Society*, 136, 11198–11211.
- [9] Grabow W.W., Jaeger L. (2014). RNA self-assembly and RNA nanotechnology. *Accounts of Chemical Research*, 47, 1871–1880.
- [10] Delebecque C.J., Lindner A.B., Silver P.A., Aldaye F.A. (2011).
- [11] Organization of intracellular reactions with rationally designed RNA assemblies. *Science*, 333, 470–474.
- [12] Dirks, R. M. & Pierce, N. A. (2004). Triggered amplification by hybridization chain reaction. *Proc. Natl Acad. Sci. USA* 101, 15275–15278.
- [13] Choi, H. M. T. et al. (2010). Programmable in situ amplification for multiplexed imaging of mRNA expression. *Nature Biotechnol.* 28, 1208–1212.
- [14] Choi, H. M. T., Beck, V. A. & Pierce, N. A. (2014). Next-generation in situ hybridization chain reaction: higher gain, lower cost, greater durability. *ACS Nano* 8, 4284–4294.
- [15] Keefe, A., Pai, S. & Ellington, A. (2010). Aptamers as therapeutics.
- [16] *Nature Rev. Drug Discov.* 9, 537–550
- [17] Bairoch, A. *Nucleic Acids Res.* (2000). 28, 304–305.
- [18] Hammes, G. G.; Wu, C. W. *Science* (1971). 172, 1205–1211.
- [19] Drews, J. *Science* (2000). 287, 1960–1964.
- [20] Khosla, C.; Harbury, P. B. (2001). *Nature*, 409, 247–252.
- [21] Ostermeier, M. (2009). *Curr. Opin. Struct. Biol.*, 19, 442–448.
- [22] Fu, Y.; Zeng, D.; Chao, J.; Jin, Y.; Zhang, Z.; Liu, H.; Li, D.; Ma, H.; Huang, Q.; Gothelf, K. V.; Fan, C. (2013). *J. Am. Chem. Soc.*, 135, 696–702.
- [23] Fei Zhang, Jeanette Nangreave, Yan Liu and Hao Yan. (2014). *J. Am. Chem. Soc.*, 136, 11198–11211.

- [24] Wilner, O. I.; Weizmann, Y.; Gill, R.; Lioubashevski, O.; Freeman, R.; Willner, I (2009). *Nat. Nanotechnol.*, 4, 249–254.
- [25] Fu, J. L.; Liu, M. H.; Liu, Y.; Woodbury, N. W.; Yan, H (2012). *J. Am. Chem. Soc.*, 134, 5516–5519.
- [26] Fu, J.; Yang, Y.; Buck, A. J.; Liu, M.; Liu, Y.; Walter, N. G., Woodbury, N. W.; Yan, H. (2014). *Nat. Nanotechnol.*, 9, 531–536.
- [27] Saghatelian, A.; Guckian, K. M.; Thayer, D. A.; Ghadiri, M. R.J. (2003), *Am. Chem. Soc.* 125, 344–345.
- [28] Simon, P.; Dueymes, C.; Fontecave, M.; Decout, J. L. *Angew. (2005) Chem., Int. Ed.*, 44, 2764–2767.
- [29] Fu, Y. M.; Zeng, D. D.; Chao, J.; Jin, Y. Q.; Zhang, Z.; Liu, H. J.; Li, D.; Ma, H. W.; Huang, Q.; Gothelf, K. V.; Fan, C. H. (2013). *J. Am. Chem. Soc.*, 135, 696–702.
- [30] Mei, Q. A.; Wei, X. X.; Su, F. Y.; Liu, Y.; Youngbull, C.; Johnson, R.; Lindsay, S.; Yan, H.; Meldrum, D. (2011). *Nano Lett.*, 11, 1477–1482.
- [31] Castro, C. E.; Kilchherr, F.; Kim, D. N.; Shiao, E. L.; Wauer, T.; Wortmann, P.; Bathe, M.; Dietz, H. (2011). *Nat. Methods*, 8, 221–229.
- [32] Modi, S.; Nizak, C.; Surana, S.; Halder, S.; Krishnan, Y. (2013). *Nat. Nanotechnol.*, 8, 459–467.
- [33] Ke, Y. G.; Bellot, G.; Voigt, N. V.; Fradkov, E.; Shih, W. M. (2012) *Chem. Sci.*, 3, 2587–2597.
- [34] Lin, C. X.; Perrault, S. D.; Kwak, M.; Graf, F.; Shih, W. M. (2013) *Nucleic Acids Res.*
- [35] Martin, T. G.; Dietz, H. (2012). *Nat. Commun.*, 3, 1103.
- [36] Myhrvold, C.; Dai, M. J.; Silver, P. A.; Yin, P. (2013). *Nano Lett.*, 13, 4242–4248.
- [37] Ariga, Katsuhiko; Hill, Jonathan P; Lee, Michael V; Vinu, Ajayan; Charvet, Richard; Acharya, Somobrata (2008). "Challenges and breakthroughs in recent research on self-assembly". *Science and Technology of Advanced Materials*. 9 (1): 014109.
- [38] Guo, P. X. (2010). *Nat. Nanotechnol*, 5, 833–842.
- [39] Shukla, G. C.; Haque, F.; Tor, Y.; Wilhelmsson, L. M.; Toulmé, J.-J.; Isambert, H.; Guo, P.; Rossi, J. J.; Tenenbaum, S. A.; Shapiro, B.A. (2011) *ACS Nano*, 5, 3405–3418.
- [40]

- [41] 38) Lai, Y. T.; Cascio, D.; Yeates, T. O. (2012). *Science*, 336, 1129–1129.
- [42] 39) King, N. P.; Sheffler, W.; Sawaya, M. R.; Vollmar, B. S.; Sumida, J. P.; Andre, I.; Gonen, T.; Yeates, T. O.; Baker, D. (2012). *Science*, 336, 1171–1174.
- [43] 40) Li, X. M.; Mooney, P.; Zheng, S.; Booth, C. R.; Braunfeld, M.
- [44] B.; Gubbens, S.; Agard, D. A.; Cheng, Y. F. (2013). *Nat. Methods*, 10, 584–590.
- [45] 41) Liao, M.; Cao, E.; Julius, D.; Cheng, Y. (2013). *Nature*, 504, 107–112.
- [46] 42) Scheres, S. (2014). *Foundations of Nanoscience: Self-Assembled Architectures and Devices*; Foresight Institute: Palo Alto, CA,; p 55.

Keywords: DNA nanotechnology, enzyme cascade scaffolds, nano devices, computational applications, nano robotics, nano electronics, biomolecular catalysis