



## Review Article

## Nanotechnology at the Molecular Level

Gulboy Abdolmajeed Nasir<sup>1\*</sup> , Iman Abbas Khudhair<sup>2</sup> , Mohammed Ayyed Najm<sup>3</sup> ,Huda Musleh Mahmood<sup>4</sup> 

<sup>1</sup> University of Baghdad, College of Agricultural Engineering Sciences, Baghdad, Iraq; <sup>2</sup> University of Anbar, College of Science, Department of Biology, Al-Ramadi, Iraq; <sup>3</sup> Department of Pharmaceutics, Faculty of Pharmacy, Al-Rafidain University College, Baghdad, Iraq; <sup>4</sup> University of Anbar, College of Science, Department of Biotechnology, Al-Ramadi, Iraq

Received: 16 October 2022; Revised: 14 November 2022; Accepted: 19 November 2022

## Abstract

Materials with external dimensions of one or more nanometers are referred to as nanomaterials. These structures result from a number of manufacturing processes. They are used in many industries, including pharmaceuticals, which is the most significant one. Numerous variables, including size, shape, surface morphology, crystallinity, solubility, etc., affect physical properties. While new physical and chemical processes are being created constantly, the biological method is the ideal strategy for synthesizing nanoparticles since it is straightforward, safe, and economical. Different kinds of nanoparticles can be metabolically synthesized by a wide variety of biological sources, including plants, bacteria, fungi, and yeast. There are many biomolecules, including proteins and coenzymes, that can change the metal salts into the necessary nanoparticles. There were numerous techniques for creating RNA nanoparticles. The first tactic makes use of the natural RNA nanoparticles' collection process. The second strategy entails extending the widely used DNA nanotechnology approach to the field of RNA; the third strategy uses computational methods to produce RNA nanoparticles; and the fourth strategy uses preexisting RNA structures or those with known properties as fundamental building blocks in the synthesis of RNA nanoparticles. The purpose of this paper is to give an overview of the significance of RNA nanotechnology, a novel idea in the field of nanotechnology.

**Keywords:** Nanotechnology, Molecular level, Nanoparticles, Biotechnology

## تكنولوجيا النانو على المستوى الجزيئي

## الخلاصة

يشار إلى المواد ذات الأبعاد الخارجية لنانومتر واحد أو أكثر باسم المواد النانوية. تنتج هذه الهياكل عن عدد من عمليات التصنيع. يتم استخدامها في العديد من الصناعات، بما في ذلك المستحضرات الصيدلانية التي هي الأكثر أهمية. تؤثر العديد من المتغيرات، بما في ذلك الحجم والشكل ومورفولوجيا السطح والتبلور والذوبان وما إلى ذلك، على الخصائص الفيزيائية. يتم إنشاء عمليات فيزيائية وكيميائية جديدة باستمرار، والطريقة البيولوجية هي الاستراتيجية المثالية لتوليف الجسيمات النانوية لأنها مباشرة وأمنة واقتصادية. يمكن تصنيع أنواع مختلفة من الجسيمات النانوية استقلابياً بواسطة مجموعة واسعة من المصادر البيولوجية، بما في ذلك النباتات والبكتيريا والفطريات والخميرة. هناك العديد من الجزيئات الحيوية، بما في ذلك البروتينات والإنزيمات المساعدة، التي يمكنها تغيير أملاح المعادن إلى الجسيمات النانوية الضرورية. كانت هناك العديد من التقنيات لإنشاء جسيمات الحمض النووي الريبي النانوية. يستخدم التكتيك الأول عملية جمع الجسيمات النانوية الطبيعية للحمض النووي الريبي. وتنطوي الاستراتيجية الثانية على توسيع نطاق نهج تكنولوجيا الحمض النووي النانوية المستخدم على نطاق واسع ليشمل مجال الحمض النووي الريبي؛ تستخدم الاستراتيجية الثالثة الطرق الحسابية لإنتاج جسيمات الحمض النووي الريبي النانوية. وتستخدم الاستراتيجية الرابعة هياكل الحمض النووي الريبي الموجودة مسبقاً أو تلك التي لها خصائص معروفة ككامل بناء أساسية في تخليق الجسيمات النانوية للحمض النووي الريبي. الغرض من هذه الدراسة هو إعطاء لمحة عامة عن أهمية تقنية النانو RNA، وهي فكرة جديدة في مجال تكنولوجيا النانو.

\* Corresponding author: Mohammed A. Najm, Department of Pharmaceutics, Faculty of Pharmacy, Al-Rafidain University College, Baghdad, Iraq; Email: [mohammed.ayyed@ruc.edu.iq](mailto:mohammed.ayyed@ruc.edu.iq)

**Article citation:** Nasir GA, et al. Nanotechnology at the molecular level. *Al-Rafidain J Med Sci.* 2022;3:71-74. doi: 10.54133/ajms.v3i.88.

## INTRODUCTION

All of the instruments that people have developed to improve productivity, make life simpler, and alter the way we learn are collectively referred to as "technology." It also contains all the data that is related to these technologies [1]. The same material can be produced in a variety of ways and have varied quality, and additional heating activities can change the material's properties. Particles mirror the atomic dimensions on the micro scale and have an impact on all mechanical, physical, and chemical properties [2]. It has been possible to do more in-depth research on the properties of both inorganic and organic substances by fusing engineering technologies with various biological sciences [3]. Significant improvements in a variety of fields, particularly in the fields of medicine and closely linked sciences, have been made as a result of the development of production and analytical technologies. Materials with external dimensions of one or more nanometers are referred to as nanomaterials. The last material dimension before the atom is the nanoscale [4]. The fundamental cause of the observed difference between the particular criteria of the same material at two distinct scales is an increase in the surface area to volume ratio when the size of these materials decreases [5,6].

### Nano Structures and Properties

Nanostructures, which are created via a variety of manufacturing processes, are used in a wide range of industries, including medicine and the production of everyday goods [7]. Size, shape, solubility, and other physical characteristics are examples. Chemical characteristics include things like hydrophobicity, photocatalytic activities, and molecular structure [8].

### Synthesis of Nanoparticles

On a daily basis, novel physical and chemical techniques are being investigated to produce nanoparticles. Due to its simplicity of usage, biocompatibility, and low cost, the biological method is the best method for synthesizing nanoparticles [9]. Use of dangerous and extremely poisonous materials is common in the chemical and physical processes of synthesizing nanoparticles [10].

#### *Leading-edge synthesis*

The method used in this procedure is destructive; the larger molecules in the bulk material are divided into smaller ones, which are then converted into nanoparticles [11].

#### *Pyrolysis*

Heating causes a chemical breakdown process, which is what happens. The entire molecular bonding is destroyed by the high temperature [12]. Metal breaks down at a specific temperature, producing nanoparticles [13].

#### *Ball-milling*

It is a useful technique for producing vast numbers of nanoparticles. The simplest mechanical operation is the

ball mill. Numerous forms of nanoparticles are created during the ball milling process [14].

#### *Lithographic methods*

The bulk of micron-sized features can be produced via lithographic methods, but they are energy-intensive and expensive [15].

#### *Laser cutting*

With the use of the laser irradiation synthesis in solution method, producing nanoparticles is a simple and straightforward process [16].

#### *Sputtering*

This method involves ejecting particles to deposit nanoparticles [17].

#### *Bottom-up approach*

This approach is occasionally referred to as a "constructive methodology." It goes against the cutting-edge strategy. This process turns a relatively simple substance into nanoparticles [18].

#### *Chemical vapor deposition (CVD)*

In this method, the substrate is covered with a thin layer of a gaseous reactant [19].

#### *Sol-gel technique*

A sol is a colloid made up of particles suspended in a liquid stream. A solid macromolecule that has been dissolved in a liquid is called a gel. This technology is the preferred bottom-up strategy for nanoparticle synthesis since it is simple to utilize [20].

#### *Spinning*

Nanoparticles are generated through spinning. A spinning disc reactor (SDR), which aids in temperature control, is used to create the nanoparticles [21].

#### *Biological synthesis*

It entails the production of nanoparticles using a variety of living cells, including bacteria, fungi, and plant extracts (Phytonanotechnology). The manufacturing of nanoparticles in a safe and environmentally acceptable manner has been made possible by phytonanotechnology. Phytonanotechnology uses water as a reducing agent to produce materials that are biocompatible. Microorganisms are nanofactories that have a great deal of promise as economical tools, are acceptable to the environment, avoid toxic and harsh chemicals, as well as the energy requirements for producing nanoparticles [22, 23]. Microorganisms are able to accumulate and detoxify heavy metals due to the presence of many reductase enzymes [24]. These reductase enzymes are necessary for the synthesis of nanoparticles from metal salts [25]. In recent years, yeast, fungus, and bacteria have significantly contributed to the production of nanoparticles as reducing and

capping agents [26]. Different kinds of nanoparticles can be metabolically synthesized by a wide variety of biological sources, including plants, bacteria, fungi, and yeast. Proteins and coenzymes, among other biomolecules, are able to transform the metal salts into the necessary nanoparticles [27]. The plant's leaves, stems, roots, and fruits all contain these biomolecules. In addition, a variety of naturally occurring nanoparticles are produced by proteins, vitamins, and secondary metabolites [28]. Bacteria are used to create nanoparticles because of their capacity to reduce metal ions. The biological catalysts for the creation of nanoparticles are fungi. Unicellular microorganisms like yeast, which are present in about 1500 species, are also capable of producing nanoparticles [29–31].

### RNA Nanotechnology's Importance and Distinctiveness

Although RNA and DNA nanotechnologies are related fields of science, the distinctive qualities of RNA that distinguish them from DNA features may call for the creation of a new field [32,33]. Adenine, cytosine, guanine, and uridine make up RNA. Furthermore, non-canonical base pairing in RNA promotes folding into stiff structural motifs that are distinct from the structure of single-stranded DNA [34]. The non-canonical characteristic allows for interactions between loop-receptors and the production of ribozymes. Now it is possible to create an RNA with eighty nucleotides that can display up to 10 different structures [35]. In terms of thermodynamic stability, RNA nanoparticles are superior to their DNA counterparts; 4-6 RNA nucleotides are all that are needed to produce stable RNA helices in solution. In some cases, RNA can form complexes with only two nucleotides [36,37].

### Defining Features of RNA in the Body

After *in vivo* treatment, the escape of cell endosomes is a key concern. Cell surface receptors first identify therapeutic particles before allowing them to enter the endosome [38]. Purine bases in DNA undergo depurination when protonated in an acidic environment, which makes the resulting apurinic DNA brittle. This improved stability of RNA in acidic environments is particularly significant in therapy because RNA travels throughout the cell after endocytosis and remains in the endosome after cell entrance [39-42]. Another remarkable property of RNA is its ability to form nanoparticles in living cells.

### Techniques for Constructing RNA Nanoparticle

When making nanoparticles, controlled building blocks must be used. The self-assembly of RNA building blocks in a defined manner to produce bigger structures is an essential bottom-up strategy for successfully integrating biological processes and biomacromolecules with nanotechnology. During a functionalized assembly process, RNAs interact with one another. Another method for putting smaller pieces together to build a larger structure without the aid of outside forces is non-template assembly. [32,43]. There were numerous

techniques for creating RNA nanoparticles. The first method makes use of the assembly of natural RNA nanoparticles, which are capable of creating distinctive and intriguing multimers *in vivo*. To produce dimers and hexamers, the pRNA of the bacteriophage phi29 DNA packing motor interacts with two right-and-left interlocking loops [44]. It was discovered twelve years ago that it is possible to create RNA nanoparticles *in vitro* that resemble their natural counterparts [7]. The second approach is based on DNA nanotechnology, which makes use of DNA's complementarity to create nanomaterials by interacting between molecules of different DNA strands. [45-47]. The third tactic is to create RNA nanoparticles by the use of computational methods [46]. The fourth strategy entails starting with an existing RNA structure or one with a known function in order to make RNA nanoparticles. Long-term studies have focused on the structure of RNA motifs and the mechanisms underlying RNA folding [48].

### Conclusion

Similar to DNA, ribonucleic acid (RNA) can be created and controlled. Additionally, although RNA and DNA nanotechnologies are related fields of study, the distinctive qualities of RNA that distinguish them from DNA features may call for the formation of a new discipline.

### Conflict of interests

The author declares no conflict of interests.

### Source of fund

No specific fund received.

### Data sharing statement

N/A

### REFERENCES

1. Jeevanandam J, Barhoum A, Chan YS, Dufresne A, Danquah MK. Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. *Beilstein J Nanotechnol.* 2018;9:1050-1074. doi: 10.3762/bjnano.9.98.
2. Ghasem Zadeh Khorasani M, Silbernagl D, Platz D, Sturm H. Insights into nano-scale physical and mechanical properties of epoxy/boehmite nanocomposite using different AFM modes. *Polymers (Basel).* 2019;11(2):235. doi: 10.3390/polym11020235.
3. Bettencourt Luis MA, Kaiser DI, Kaur J. Scientific discovery and topological transitions in collaboration networks. *J Informetrics.* 2009;3(3):210-221. <http://hdl.handle.net/1721.1/50230>
4. Rumble J, Freiman S, Teague C. Towards a uniform description system for materials on the nanoscale. *Chemistry Int.* 2015;37(4): 3-7. doi: 10.1515/ci-2015-0402.
5. Ren J, Wang Y, Yao Y, Wang Y, Fei X, Qi P, et al. Biological material interfaces as inspiration for mechanical and optical material designs. *Chem Rev.* 2019;119(24):12279-12336. doi: 10.1021/acs.chemrev.9b00416.
6. Mandrikas A, Michailidi E, Stavrou D. Teaching nanotechnology in primary education. *Res Sci Technol Edu.* 2020;38:4:377-395. doi: 10.1080/02635143.2019.1631783.
7. Asif AKM, Hasan MZ. Application of nanotechnology in modern textiles: A review. *Int J Curr Engineer Technol.* 2018;8(2):227-231. doi: 10.14741/ijcet/v.8.2.5.
8. Gattoo MA, Naseem S, Arfat MY, Mahmood Dar A, Qasim K, Zubair S. Physicochemical properties of nanomaterials: implication in associated toxic manifestations. *BioMed Res Int.* 2014;2014:498420. doi: 10.1155/2014/498420.

9. Ijaz I, Gilani E, Nazir A, Bukhari A. Detail review on chemical, physical and green synthesis, classification, characterizations and applications of nanoparticles. *Green Chem Lett Rev.* 2020;13:3, 223-245. doi: 10.1080/17518253.2020.1802517.
10. Ahmed S, Saifullah Ahmad M, Swami BL, Ikram S. Green synthesis of silver nanoparticles using *Azadirachta indica* aqueous leaf extract. *J Rad Res Appl Sci.* 2016;9(1):1-7. doi: 10.1016/j.jrras.2015.06.006.
11. Khan I, Saeed K, Khan I. Nanoparticles: Properties, applications and toxicities. *Arabian J Chem.* 2019;(7):908-931. doi: 10.1016/j.arabjc.2017.05.011.
12. Sakkas K, Pnias D, Nomikos P, Sofianos A. Comparison of fire resistant geopolymers for passive fire protection of concrete tunnel linings. *Open Access Library J.* 2017;4:1-15. doi: 10.4236/oalib.1103327.
13. Ealia SAM, Saravanakumar MP. A review on the classification, characterization, synthesis of nanoparticles and their application. *Materials Sci Engineer.* 2017;263(3):032019. doi: 10.1088/1757-899X/263/3/032019.
14. Protesescu L, Yakunin S, Nazarenko O, Dirin DN, Kovalenko MV. Low-cost synthesis of highly luminescent colloidal lead halide perovskite nanocrystals by wet ball milling. *ACS Appl Nanomaterials.* 2018;1(3):1300-1308. doi: 10.1021/acsanm.8b00038.
15. Fu X, Cai J, Zhang X, Li WD, Ge H, Hu Y. Top-down fabrication of shape-controlled, monodisperse nanoparticles for biomedical applications. *Adv Drug Deliv Rev.* 2018;132:169-187. doi: 10.1016/j.addr.2018.07.006.
16. Davari SA, Gottfried JL, Liu C, Ribeiro EL, Duscher G, Mukherjee D. Graphitic coated Al nanoparticles manufactured as superior energetic materials via laser ablation synthesis in organic solvents. *Appl Surface Sci.* 2019;473:156-163. doi: 10.1016/j.apsusc.2018.11.238.
17. Wender H, Migowski P, Feil AF, Teixeira SR, Dupont J. Sputtering deposition of nanoparticles onto liquid substrates: Recent advances and future trends. *Coordination Chem Rev.* 2013;257(17-18):2468-2483. doi: 10.1016/j.ccr.2013.01.013.
18. Abid N, Khan AM, Shujait S, Chaudhary K, Ikram M, Imran M, et al. Synthesis of nanomaterials using various top-down and bottom-up approaches, influencing factors, advantages, and disadvantages: A review. *Adv Colloid Interface Sci.* 2022;300:102597. doi: 10.1016/j.cis.2021.102597.
19. Igumenov IK, Semyannikov PP, Trubin SV, Morozova NB, Gelfond NV, Mischenko AV, et al. Approach to control deposition of ultra-thin films from metal organic precursors: Ru deposition. *Surface Coat Technol.* 2007;201(22-23):9003-9008. doi: 10.1016/j.surfcoat.2007.04.129.
20. Bokov D, Jalil AT, Chupradit S, Suksatan W, Ansari MJ, Shewael IH, et al. Nanomaterial by sol-gel method: Synthesis and application. *Adv Material Sci Engineer.* 2021;2021: ID 5102014. doi: 10.1155/2021/5102014.
21. Begum SJP, Pratihba S, Rawat JM, Venugopal D, Sahu P, Gowda A, et al. Recent advances in green synthesis, characterization, and applications of bioactive metallic nanoparticles. *Pharmaceuticals.* 2022;15:455. doi: 10.3390/ph15040455.
22. Ahmed S, Annu, Chaudhry SA, Ikram S. A review on biogenic synthesis of ZnO nanoparticles using plant extracts and microbes: A prospect towards green chemistry. *J Photochem Photobiol B.* 2017;166:272-284. doi: 10.1016/j.jphotobiol.2016.12.011.
23. Salem SS, Fouda A. Green synthesis of metallic nanoparticles and their prospective biotechnological applications: an overview. *Biol Trace Elem Res.* 2021;199(1):344-370. doi: 10.1007/s12011-020-02138-3.
24. Singh JS, Abhilash PC, Singh HB, Singh RP, Singh DP. Genetically engineered bacteria: an emerging tool for environmental remediation and future research perspectives. *Gene.* 2011;480(1-2):1-9. doi: 10.1016/j.gene.2011.03.001.
25. Hulkoti NI, Taranath TC. Biosynthesis of nanoparticles using microbes- a review. *Colloids Surf B Biointerfaces.* 2014;121:474-83. doi: 10.1016/j.colsurfb.2014.05.027.
26. Ovais M, Khalil AT, Ayaz M, Ahmad I, Nethi SK, Mukherjee S. Biosynthesis of metal nanoparticles via microbial enzymes: A mechanistic approach. *Int J Mol Sci.* 2018;19(12):4100. doi: 10.3390/ijms19124100.
27. Madkour LH. Biogenic-biosynthesis metallic nanoparticles (MNPs) for pharmacological, biomedical and environmental nanobiotechnological applications. *Chronicles Pharm Sci.* 2018;2(1):384-444.
28. Prasad SR, Teli SB, Ghosh J, Prasad NR, Shaikh VS, Nazeruddin GM, et al. A review on bio-inspired synthesis of silver nanoparticles: their antimicrobial efficacy and toxicity. *Engineered Sci.* 2021;16:90-128. doi: 10.30919/es8d479.
29. Jeevanandam J, Chan YS, Danquah MK. Biosynthesis of metal and metal oxide nanoparticles. *ChemBioEng Rev.* 2016;3(2):55-67. doi: 10.1002/cben.201500018.
30. Narayanan KB, Sakthivel N. Biological synthesis of metal nanoparticles by microbes. *Adv Colloid Interface Sci.* 2010;156(1-2):1-13. doi: 10.1016/j.cis.2010.02.001.
31. Mukherjee A, Verma JP, Gaurav AK, Chouhan GK, Patel JS, Hesham AE. Yeast a potential bio-agent: future for plant growth and postharvest disease management for sustainable agriculture. *Appl Microbiol Biotechnol.* 2020;104(4):1497-1510. doi: 10.1007/s00253-019-10321-3.
32. Guo P. The emerging field of RNA nanotechnology. *Nat Nanotechnol.* 2010;5(12):833-42. doi: 10.1038/nnano.2010.231.
33. Yao J, Yang M, Duan Y. Chemistry, biology, and medicine of fluorescent nanomaterials and related systems: new insights into biosensing, bioimaging, genomics, diagnostics, and therapy. *Chem Rev.* 2014;114(12):6130-6178. doi: 10.1021/cr200359p.
34. Fialho DM, Roche TP, Hud NV. Prebiotic syntheses of noncanonical nucleosides and nucleotides. *Chem Rev.* 2020;120(11):4806-4830. doi: 10.1021/acs.chemrev.0c00069.
35. Afonin KA, Lindsay B, Shapiro BA. Engineered RNA nanodesigns for applications in RNA nanotechnology. *DNA RNA Nanotechnol.* 2015;1(1):1-15. doi: 10.2478/man-2013-0001.
36. Haque F, Pi F, Zhao Z, Gu S, Hu H, Yu H, et al. RNA versatility, flexibility, and thermostability for practice in RNA nanotechnology and biomedical applications. *Wiley Interdiscip Rev RNA.* 2018;9(1):10.1002/wrna.1452. doi: 10.1002/wrna.1452.
37. Vogel J, Luisi BF. Hfq and its constellation of RNA. *Nat Rev Microbiol.* 2011;9(8):578-589. doi: 10.1038/nrmicro2615.
38. Rennick JJ, Johnston APR, Parton RG. Key principles and methods for studying the endocytosis of biological and nanoparticle therapeutics. *Nat Nanotechnol.* 2021;16(3):266-276. doi: 10.1038/s41565-021-00858-8.
39. Guo P, Haque F. (Eds.). (2014). *RNA nanotechnology and therapeutics* (pp. 39-45). Boca Raton, FL, USA: CRC press.
40. Ashley CE, Carnes EC, Epler KE, Padilla DP, Phillips GK, Castillo RE, et al. Delivery of small interfering RNA by peptide-targeted mesoporous silica nanoparticle-supported lipid bilayers. *ACS Nano.* 2012;6(3):2174-2188. doi: 10.1021/nn204102q.
41. Jasinski D, Haque F, Binzel DW, Guo P. Advancement of the emerging field of RNA nanotechnology. *ACS Nano.* 2017;11(2):1142-1164. doi: 10.1021/acsnano.6b05737.
42. Shu Y, Pi F, Sharma A, Rajabi M, Haque F, Shu D, et al. Stable RNA nanoparticles as potential new generation drugs for cancer therapy. *Adv Drug Deliv Rev.* 2014;66:74-89. doi: 10.1016/j.addr.2013.11.006.
43. Guo P. RNA nanotechnology: engineering, assembly and applications in detection, gene delivery and therapy. *J Nanosci Nanotechnol.* 2005;5(12):1964-1982. doi: 10.1166/jnn.2005.446.
44. Guo S, Huang F, Guo P. Construction of folate-conjugated pRNA of bacteriophage phi29 DNA packaging motor for delivery of chimeric siRNA to nasopharyngeal carcinoma cells. *Gene Ther.* 2006;13(10):814-820. doi: 10.1038/sj.gt.3302716.
45. Aldaye FA, Palmer AL, Sleiman HF. Assembling materials with DNA as the guide. *Science.* 2008;321(5897):1795-1799. doi: 10.1126/science.1154533.
46. Guo P. The emerging field of RNA nanotechnology. *Nat Nanotechnol.* 2010;5(12):833-842. doi: 10.1038/nnano.2010.231.
47. Afonin KA, Grabow WW, Walker FM, Bindewald E, Dobrovolskaia MA, Shapiro BA, et al. Design and self-assembly of siRNA-functionalized RNA nanoparticles for use in automated nanomedicine. *Nat Protoc.* 2011;6(12):2022-2034. doi: 10.1038/nprot.2011.418.
48. Butcher SE, Pyle AM. The molecular interactions that stabilize RNA tertiary structure: RNA motifs, patterns, and networks. *Acc Chem Res.* 2011;44(12):1302-1311. doi: 10.1021/ar200098t.