Madhulika Pradhan · Krishna Yadav ·
Nagendra Singh Chauhan *Editors*

Biomaterial-Inspired Nanomedicines for Targeted Therapies

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First, we thank Almighty God for giving us this opportunity to serve the scientific fraternity through the book Biomaterial-Inspired Nanomedicines for Targeted Therapies. The book is dedicated with heartfelt appreciation to the pillars of our journey—our families, friends, teachers, and all the well-wishers who have illuminated our path with unwavering support and encouragement.

To our families, whose love and understanding have been a constant source of strength, we express our deepest gratitude. Your enduring support has fueled our aspirations and provided the foundation upon which our academic pursuits rest.

To our teachers and mentors, whose guidance has shaped our intellect and fueled our passion for discovery, we extend our sincerest appreciation.

To our friends, whose camaraderie has been a source of joy and inspiration, thank you for sharing this intellectual voyage with us.

To all our well-wishers, whose positive energy and encouragement have been a *driving force, we are profoundly grateful. Your belief in our endeavors has been a constant motivation and a reminder of the broader community that stands behind us.*

Preface

In the relentless pursuit of advancing medical and pharmaceutical science, the fusion of biomaterials and nanotechnology has paved the way for groundbreaking innovations in the field of targeted therapies. This book, titled *Biomaterial-Inspired Nanomedicines for Targeted Therapies* embarks on a journey through the intricate landscapes of biomaterial-inspired nanomedicines, unraveling the transformative potential of this dynamic intersection.

Over the last decade, the convergence of biomaterials and nanotechnology has emerged as a beacon of hope in the realm of medicine. This volume serves as a comprehensive guide, capturing the essence of the most recent developments in the design and application of nanomedicines for precise and targeted therapeutic interventions.

The focus of this book extends across a spectrum of diseases and health conditions, ranging from neurological disorders and autoimmune skin diseases to cancer, cardiovascular disorders, and beyond. It serves as a testament to the diverse and promising applications of biomaterial-inspired nanomedicines in the quest for effective and personalized treatments.

Readers will find within these pages a wealth of information on the challenges and triumphs encountered in the development of targeted therapies. The book not only explores the intricacies of nano-biomaterial systems but also sheds light on cellular uptake mechanisms, in vitro and in vivo behaviors, and the controlled release of therapeutic entities within target cells. Moreover, safety, toxicity concerns, and regulatory considerations associated with these innovative therapies are thoughtfully examined.

This compilation is tailored to cater to a wide audience, including students, researchers, scientists, and academicians immersed in the multidisciplinary field of biomaterial-inspired nanomedicines. The aim is to provide a resource that not only informs but also inspires further exploration and advancement in this rapidly evolving field.

As the title suggests, the book stands as a testament to the transformative potential of biomaterial-inspired nanomedicines in achieving targeted therapies. It is our sincere hope that this collection of insights, challenges, and breakthroughs will contribute significantly to the collective understanding of this burgeoning field, propelling the journey toward more effective and personalized treatments for a multitude of ailments.

Abhanpur, Chhattisgarh, India	Madhulika Pradhan
Bhilai, Chhattisgarh, India	Krishna Yadav
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As we present *Biomaterial-Inspired Nanomedicines for Targeted Therapies*, we extend our heartfelt gratitude to the individuals and institutions whose support and contributions have been instrumental in bringing this collaborative endeavor to fruition.

We would like to express our sincere appreciation to the esteemed authors whose expertise and dedication have enriched the content of this book. Your commitment to advancing knowledge in the fields of biomaterial-based nanomedicines is truly commendable.

Our sincere thanks go to the reviewers whose insightful feedback and constructive criticisms have played a crucial role in refining the quality and depth of the chapters. Your commitment to scholarly excellence has been invaluable.

We extend our gratitude to the editorial and production teams for their meticulous efforts in shaping and polishing the manuscript. Your dedication to ensuring the clarity, coherence, and overall quality of this work is highly appreciated.

Special thanks to the contributing institutions and universities that have provided a nurturing environment for our authors, fostering an atmosphere of research and innovation in the realms of pharmacy, medicine, and technology.

To our colleagues, mentors, and peers who have provided support, encouragement, and valuable discussions, we are deeply grateful for your intellectual contributions that have enriched the content of this book.

Last but not least, we extend our appreciation to our families and friends for their unwavering support and understanding during the demanding phases of book development. Your encouragement has been a source of strength, and we are grateful for the patience and encouragement you have shown.

This book stands as a testament to the collective efforts of a dedicated community committed to advancing knowledge and pushing the boundaries of innovation. Thank you all for being integral parts of this journey.

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About the Editors

Madhulika Pradhan holds the position of Professor and researcher at Gracious College of Pharmacy in Abhanpur, Chhattisgarh, India, accumulating a total of 16 years of academic and research experience. She obtained her Ph.D. in Pharmaceutical Technology in 2016 from Pt. Ravishankar Shukla University, Raipur, India. Dr. Pradhan has an extensive publication record, contributing numerous articles, including research, reviews, and book chapters, to nationally and internationally recognized publishing houses like Elsevier, Springer Nature, Taylor & Francis, among others. Notably, she holds two international patents for her work and currently boasts an H-index of 20 and an I-10 index of 32. Her primary research focus revolves around the development of novel drug delivery systems for dermal disorders, particularly psoriasis and other autoimmune skin disorders, utilizing modern statistical and computational tools. Dr. Pradhan is an active member of professional societies such as the Association of Pharmaceutical Teachers of India and the Indian Pharmacy Graduates Association. She has presented research papers at various international (Malaysia, Singapore, Denmark, South Korea, and the USA), national, and state-level conferences, earning awards for scientific excellence in several instances.

Krishna Yadav presently serves as an Assistant Professor and active researcher at the Rungta College of Pharmaceutical Sciences and Research, Kohka-Kurud Road, Bhilai 490024, Chhattisgarh, India. With a cumulative experience of 8 years in academia and research, he earned his Ph.D. in Pharmaceutical Technology in 2022 from Pt. Ravishankar Shukla University, Raipur, India. Dr. Yadav boasts an H-index of 16 and an I-10 index of 26. His extensive publication record includes research articles, reviews, and chapters in nationally and internationally recognized publications such as Elsevier and Springer Nature. Notably, he holds an Australian Patent among his other achievements. Dr. Yadav has been honored with various international (Malaysia and South Korea), national, and state-level awards for excellence in research at different conferences. His primary research focus lies in developing innovative formulations and drug delivery techniques for treating various diseases including psoriasis, breast cancer, and bone disorders. Actively involved in exploring experimental designs, pharmacometrics modeling and employing modern statistical and computational approaches, Dr. Yadav aims to maximize treatment efficacy while minimizing adverse effects.

Nagendra Singh Chauhan earned his M. Pharm. and Ph.D. from the Department of Pharmaceutical Sciences, Dr. H.S. Gour University, Sagar, in 2006 and 2011, respectively. With approximately 16 years of research experience, he currently serves as a Senior Scientific Officer Grade-I and Government Analyst at Drugs Testing Laboratory Avam Anusandhan Kendra, Raipur, Chhattisgarh, India. Dr. Chauhan specializes in Natural Product Isolation and phytopharmacology. He has authored over 80 articles published in national and international journals, contributed to 40 book chapters, and edited 10 books for publishers such as Academic Press, CRC, and Wiley. Notably, he recently edited books titled *Advances and Avenues in the Development of Novel Carriers for Bioactives and Biological Agents* and *Natural Products in Vector Borne Disease Management*, published by Academic Press. Dr. Chauhan has received over 3700 citations with an h-index of 31 and an i10 index of 53 on Google Scholar, and a Scopus h-index of 24 with

1700 citations. He is an active member of various professional and academic organizations, including the Society of Pharmacognosy, India, International Natural Product Sciences Taskforce (INPST) society, SILAE: Società Italo-Latinoamericana di Etnomedicina (The Scientific Network on Ethnomedicine, Italy), Institutional Human Ethical Committee, Association of Pharmaceutical Teachers of India (APTI), and Indian Pharmacy Graduates' Association.

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Introduction to Biomaterial-Inspired Nanomedicines

1

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Abstract

Nanobiomaterials combine nanotechnology methods with biomaterials to create customized structures for enhanced biomedical applications at the boundary between nanotechnology and biology. This chapter focuses on the basic principles and current advancements related to the development, production, analysis, interactions with host organisms, and medicinal uses of nanostructured biomaterials. It includes the basic comprehension of inorganic nanoparticles (NPs), organic nanocomposites, surface biofunctionalization, imaging agents, drug delivery platforms, regenerative scaffolds, theranostics, and translational problems. The integration of NPs and biomaterials into bioresponsive interfaces is a groundbreaking development that enhances diagnostics, therapeutics, and personalized nanomedicine.

Keywords

Nanobiomaterials · Nanomaterials · Biomaterials · Therapeutic · Drug delivery

1.1 Introduction

The phrase “nanobiomaterials” refers to the merging of two scientific fields, nanomaterials, and biomaterials, creating a new paradigm where the extremely small and the biological perfectly combine. Nanomaterials, which are characterized by functional entities smaller than 100 nm, combine with biomaterials to create materials that are specifically engineered to interact with biological entities [1]. This synthesis occurs at the nanoscale, encompassing several domains using the transformational capabilities of nanotechnology. Nanostructured biomaterials, which include NPs, nanofibers, nanosurfaces, nanowires, and nanocomposites, play a crucial role in driving progress in biomedical fields such as drug delivery, tissue regeneration, cancer treatment, medical imaging, and theranostics [1, 2].

The core component of nanobiomaterials is the NP, which is a complex molecular structure composed of polymers or inorganic materials. NPs can take on various shapes, including spheres, needles, crystals, and polygons [3]. The achievement of optimal performance in design and synthesis relies on characteristics such as size, shape, and customized interactions with cell membranes. Nanobiomaterials, unlike larger materials, utilize their small size to improve characteristics, resulting in a significant change from materials that are not reactive with biological systems to materials that are reactive with biological systems [3].

The advancement in illness treatment demonstrates a movement from the larger scale to the molecular level, with nanobiomaterials leading this transformative change. Their aptitude to traverse the intricate structure of cells, tissues, and organs signifies the advent of a novel era in regenerative medicine and the replication of physiological processes [4]. Surface modification plays a crucial role in enabling specific applications in several medical disciplines.

However, when nanobiomaterials are introduced into the complex environment of the human body, they interact with the immune system, which in turn affects how well the materials work [5]. Parameters like as size, shape, and surface chemistry play a crucial role in determining the safety and effectiveness of a product [3]. The constant concerns about the harmful effects of NPs and their ability to remain in biological systems require a careful reevaluation of design standards to enable the seamless integration of nanobiomaterials into living organisms.

Above all, the field of nanobiomaterials is continuously growing, and the development of non-toxic, multifunctional designs for bioresponsive and biosensing capabilities is becoming an important area of focus. The need to tackle obstacles in the process of using nanobiomaterials in nanomedicine is crucial to achieving significant advancements in this field [3]. The rise of nanomaterial application is substantiated by the subsequent survey conducted using data from Scopus for published publications pertaining to nanomaterial design. The study has revealed a significant increase in the proportion of articles focused on the utilization of nanotechnology, particularly in the domains of biomedical and biological engineering (Fig. 1.1), in comparison to other disciplines. This chapter explores the introductory information regarding the structure, composition, nature, type, production, application, and regulatory concerns regarding the emergence of nanobiomaterials. Besides, the detailed application of these nanobiomaterials in various diseased conditions has been mentioned in their respective chapters.

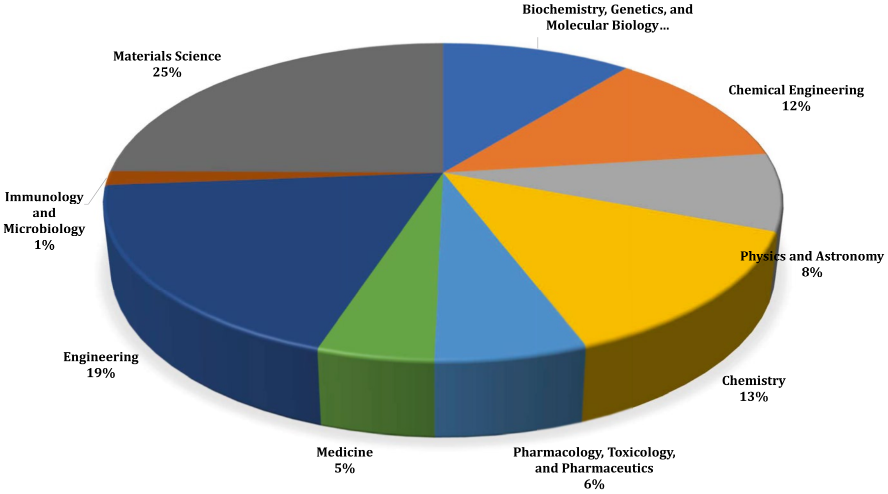

Fig. 1.1 A survey of the published articles in Scopus uses the term "nanomaterials" for "biomedical and other applications," including "materials science and engineering." (Survey, December 2023)

1.2 Ideal Property of Nanomaterials

Nanomaterials possess a diverse range of distinctive and customizable characteristics, rendering them highly relevant in a multitude of domains, particularly in biological applications. These features are frequently unique and desirable compared to their bulk counterparts due to their extremely small size and quantum phenomena. Here are some key properties that distinguish nanomaterials for biological applications [6, 7]:

- **High Surface Area**: NPs have an extremely large surface area relative to their volume, allowing more active sites for reactions. This enhances their overall reactivity and interactions.
- **Customizable Size and Geometry**: The size and shape of nanomaterials can be precisely controlled during fabrication, enabling custom-tailored properties. Altering dimensions leads to different optical, electronic, and other effects.
- **Special Optical Capabilities**: Light scattering and absorption phenomena unique to the nanoscale let NPs manipulate light in useful ways. This leads to applications in solar harvesting, light emission, and sensing.
- **Tunable Electronic Properties**: Quantum effects become dominant at small size scales, significantly changing nanomaterials' electronic properties compared to bulk. This tunability is highly valuable.
- **Improved Mechanical Properties**: Nanoscale materials often demonstrate better strength, hardness, and durability than bulk forms. The large surface area and low defect density reinforce the material's mechanical performance.
- **Enhanced Thermal Properties**: Properties including thermal conductivity and expansion can be superior to bulk equivalents. This helps with insulation, heating, cooling, and more.
- **Biomedical Compatibility**: Proper surface conditioning enables biocompatible nanomaterials to safely interact with biological systems for imaging, sensory, and therapeutic roles.

These distinguishing features of NPs make them particularly versatile for a variety of biological applications, providing exclusivity for [6, 7]:

- **Biosensors**: NPs' sensitivity to minute biochemical stimuli aids precise diagnostic and analytical applications.
- **Catalysts**: High surface area and tunable electronics help nanomaterials catalyze reactions with precision and efficiency.
- **Contrast Agents**: As imaging contrast improvement agents, NPs enhance the clarity of MRI, CT scan, and other visualizations.
- **Cosmetics**: Nanomaterial inclusion in skincare/cosmetics enhances absorption and effectiveness.
- **Drug Delivery**: NP transport within the body minimizes drug waste and side effects through targeted delivery.

- **Electronics and Solar Cells**: Nanoscale photovoltaic materials, transistors, and diodes offer performance improvements like efficiency.
- **Filtration and Remediation**: Environmental cleanup of water sources and soil benefits from NPs' reactivity and separation capabilities.

1.3 Nanostructured Biomaterials

Nanobiomaterials referred to as nanostructured biomaterials, have gained popularity in the dynamic field of biomaterial sciences. This category includes a wide variety of components, such as NPs, nanofibers, nanosurfaces, and nanocomposites [8]. These components are crucial in several applications, such as repairing and regenerating human tissue, delivering drugs and genes, treating cancer, and conducting medical imaging [9]. The incorporation of these intricately designed nanobiomaterials, sourced from polymers, metals, ceramics, and composites, in nanoscale or nanostructured formats has expanded the boundaries of biomedical research and innovation [6].

The NP is a crucial component of nanobiomaterials, possessing adaptability and distinctive properties. NPs may be produced in several shapes, such as spherical, cylindrical, star-shaped, and other configurations. The NPs may have a core composed of many layers, each with specific functionalities [10]. An example of this is the combination of magnetic and luminous layers, which enables the identification and manipulation of particles. Usually, the core is surrounded by thin layers of inert materials, such as silica, that have either absorbed or chemically attached organic molecules, enriching the NPs with extra functionalities [10].

Additionally, the NP frequently undergoes further modification by adding a layer of linker molecules. These molecules have a vital function in enabling further modifications, displaying reactive groups at both ends [11, 12]. The linker is attached to one end of the NP surface and can be combined with substances such as antibodies, biocompatible compounds, or other functional entities. The utilization of many layers enables the precise adjustment and personalization of nanobiomaterials to fulfill particular criteria in diverse biological uses [13].

The investigation of nanostructured biomaterials is a groundbreaking endeavor in the field of biomedical research, with the potential to completely change the healthcare and medical technology sectors. The complex and versatile nature of nanobiomaterials highlights their potential to tackle complicated difficulties and facilitate novel solutions in the quest for improved human health and well-being [1, 2].

1.4 Host-Nanobiomaterial Interactions

The integration of nanomaterials into biological systems necessitates the harmonization of contrasting domains, where results emerge through intricate communication between biomaterials and tissues, directing the behaviors of cells and proteins.

To understand these dynamic exchanges, it is necessary to use an interdisciplinary approach that covers surface physicochemistry, tissue biomechanics, and cellular signaling cascades to develop biocompatible platforms [14].

After being introduced into the body, proteins that are adsorbed onto a material-tissue interface have a role in modifying the initial adhesion characteristics and macrophage polarization, leading to the development of a temporary orientation in the physiological space [15]. The innate responses alternate between isolating foreign substances by forming a fibrous capsule and integrating into the body's tissues through controlled resolution of inflammation and restructuring of cells and scaffolds [14].

The phenotypes are controlled by reciprocal cues present in the nano- and micro-scale features of the material. These signals trigger mechanotransductive, electrostatic, and receptor-mediated pathways. Excessive hydrophobicity or surface roughness triggers the generation of pro-inflammatory cytokines and hinders phagocytosis. Therefore, materials science and engineering tools should focus on creating scaffolds that imitate and balance important characteristics like stiffness, ligand patterning, degradation kinetics, and nanotopography [14, 16].

In general, biocompatibility encompasses a complex framework designed for specific regeneration situations. This framework includes several factors such as timed immunomodulation to promote natural healing, targeted prevention of fouling, and tactics to attract cells for implantation. To better understand how material surfaces actively influence local cell phenotypes, it is necessary to continue studying and clarifying the mechanisms behind bioresponsive, pro-integrative designs that promote innervation, vascular perfusion, and selective biofilm development [16].

By integrating ideas from immunology, bioengineering, and materials science, the future of bionanomaterial devices, probiotics, and synthetic tissues holds the potential for remarkable mimicry of biological systems and enhanced functioning. This will be achieved through carefully designed and manufactured structures [16, 17].

1.5 Classification of Nanomaterials

A fundamental classification delineates engineered versus non-engineered nanomaterials. The former entails intentional creation for defined purposes leveraging the novel electromagnetic, optical, and chemical qualities manifesting at reduced nanoscales [11, 18]. These custom syntheses allow strict parameterization yielding particles with capabilities matching intended uses spanning biomedicine, energy storage, catalysis, sensing, and more.

Conversely, non-engineered nanomaterials occur naturally or incidentally as by-products of processes like combustion or mineral weathering. Such particles demonstrate more heterogeneous traits and primarily raise toxicology considerations rather than prospects for directed applications. However, increasing research elucidates how natural NP transport and impacts across environmental systems could inform safer engineering approaches [18, 19].

1.5.1 Based on Dimension

Among engineered particles, categorization by dimensional restrictions on electron mobility provides further insight into the origins of distinct nanomaterial properties. Quantum dots (QDs) exemplify zero-dimensional structures where electrons remain confined in all axes, enabling precise tuning of optical attributes for bioimaging and sensing applications [20]. Based on the dimension, nanomaterials can be classified into four categories: 0-,1-,2-, and 3-dimension (Fig. 1.2). One-dimensional nanotubes and nanowires facilitate electron propagation along their axial direction only, creating anisotropic metamaterials with enhanced conductivity, aspect ratios, and tensile strength. Two-dimensional nanoflakes and plates exhibit planar electron mobility with retained vertical restrictions that augment surface area and Beer-Lambert absorption behavior beneficial in catalytic and energy storage roles. Finally, three-dimensional particles like nanospheres approach bulk-scale electron freedom and thus fail to confer advantages over macroscale materials without added surface modifications or compositional novelty [20]. Overall, parsing nanomaterials based on the intentionality of design and degrees of dimensional freedom grants frameworks for rationalizing the immense diversity of nanostructures against the performance of the specific application made accessible at these reduced scales. It further enables grouping to guide safety evaluations and regulatory considerations

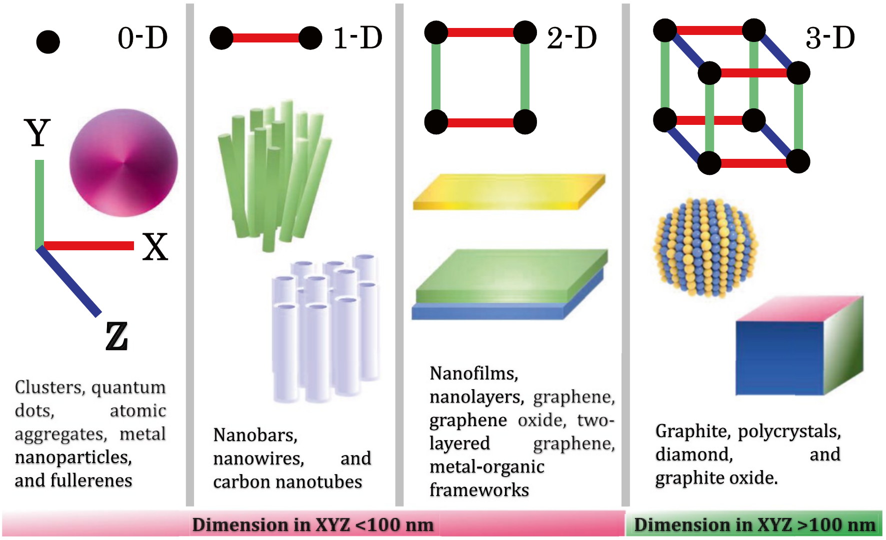

Fig. 1.2 Classification of nanomaterials based on dimension

for both engineered and incidental NPs as nanotechnology integrates more extensively across commercial and environmental areas [11, 20].

1.5.2 Based on Nanostructures

Engineering materials at the nanoscale enable meticulous control over structural attributes to confer customized properties meeting specialized needs across applications. The capacity to restrict dimensions under nanometers gives rise to quantum mechanical, enhanced optical, and heightened reactive effects [20]. Strategically designing features like shape or structure facilitate multifunctional NPs for targeted diagnostics and therapeutics within biological contexts. Figure 1.3 exhibits an array of structures acquired by the nanomaterials.

For instance, nanospheres with tunable membranes and aqueous cores allow controlled encapsulation and timed release of medications to optimize drug delivery while minimizing off-target bioavailability. Elongated nanorods exhibit directionally amplified plasmonic photothermal properties that heighten ablation capacities for malignancies. Star-shaped and core-shell NP geometries offer expanded surface area-to-volume ratios that improve sensing resolvability by concentrating local electromagnetic fields and light absorption [21, 22].

Likewise, functionalizing carbon nanotubes or QDs with hydrophilic coatings boost solubility for enhanced transportation within intracellular environments while their elongated and electron-confining configurations heighten thermal imaging contrasts and charge-dependent emissions ideal for biosensing applications [21]. Stimuli-responsive platforms add another dimension through transformations triggered by biological microenvironments, external signals, or internal state changes to enable precision therapeutic activation only upon reaching target pathologies.

Further, specialized nanofabrication techniques grant extensive diversification of NP designs to balance geometries against requisite surface properties and integrated

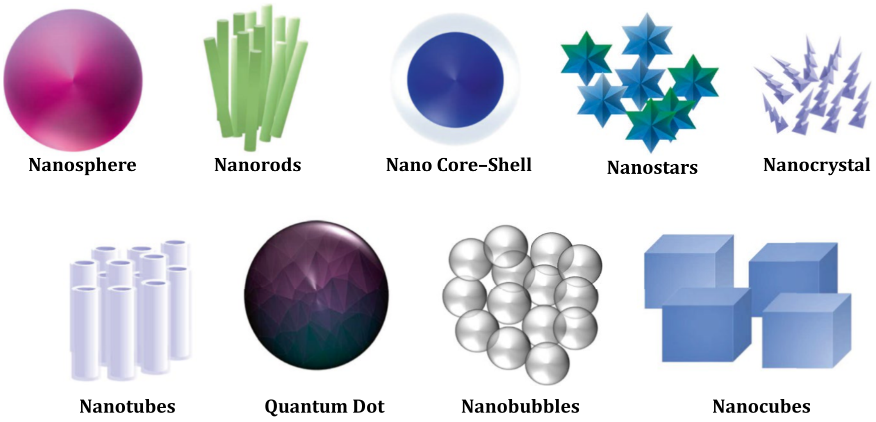

Fig. 1.3 Classification of nanomaterials based on structure

cargo that empower multifaceted solutions matching intended contexts. The capacity to restrict and configure matter on scales matching proteins, membranes, and DNA provides avenues for custom-engineering tools seamlessly interfacing with biological systems in ways previously impossible [23]. However, realizing the full promise requires ongoing assessment of potentially hazardous persisting consequences [21, 24].

1.5.3 Based on Composition

Nanomaterials derive extensive utility from their composition alongside geometrical attributes, necessitating classification frameworks encompassing both facets. Delineation by organic versus inorganic origins provides insight into inherent chemical properties and compatibilities guiding biological applications (Fig. 1.4). Meanwhile, characterization by fabrication methodology reveals processing-structure-function interrelationships across scales that inform efforts toward precision nanometer-regime engineering [21]. As nanostructures bridge the atomic and bulk scales, nuanced distinctions arise between organic and inorganic species in their formation pathways, available compositions, and resultant properties.

Inorganic nanomaterials encompass structures formed via precipitation of atomic or molecular precursor units and their subsequent growth into crystalline or

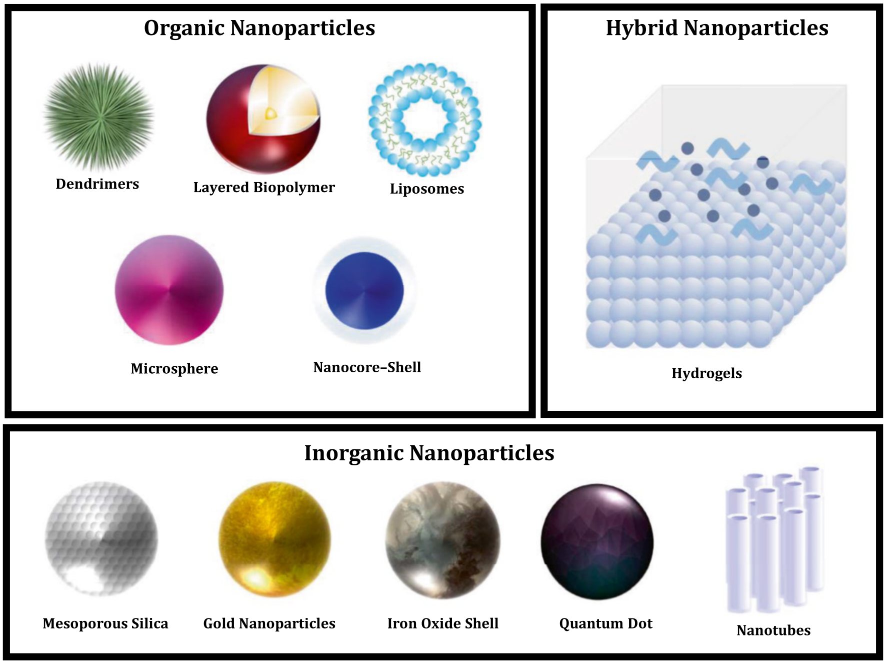

Fig. 1.4 Classification of nanomaterials based on composition

amorphous solids [25]. Common foundation units range from metals like iron, gold, or zinc to nonmetals including carbon, sulfur, and silicates. Joining frequently involves covalent, ionic, or metallic bonding into extended but confined geometries. Exemplars include inorganic nanocrystals like QDs, metal oxide frameworks, and nanoporous gold particles. Their precisely defined, stereospecific atomic lattices confer enhanced electrical, optical, and magnetic qualities but demand high-energy or high-pressure processing approaches [21, 26].

By contrast, organic nanomaterials incorporate self-assembled structures formed from the entanglement and ordering of synthetic or natural macromolecules like polymers, lipids, peptides, or carbohydrates [27–29]. Alignment stems from non-covalent interactions, π-π stacking, hydrophobic interactions, and hydrogen bonding between adjacent molecules and nanostructural components [30]. Illustrative cases encompass polymeric micelles, nucleic acid origami, lipid vesicles, and virus capsid assemblies [31]. While lacking long-range order, such soft nanostructures gain versatility—easily incorporating disparate functional elements from drug payloads to imaging agents within their interiors or membranes. Their near-ambient assembly conditions and monomer sequence programmability empower extensive morphological control [30].

Identifying optimal processes for intended functionality demands evaluating these manufacturing tradeoffs. Moreover, the universe of available nanomaterials spanning carbonaceous, metallic, ceramic, polymeric, and hybrid materials provides immense choice [30]. However, material selection hinges on application demands—biocompatibility and eco-safety for in vivo usage, high signal sensitivity for sensing, and stable surface functionalization for drug conjugation [32]. Determining ideal candidates requires filtering through composition-morphology-property relationships across classes against performance objectives and safety risk thresholds.

1.6 Synthesis of Nanomaterials

In the field of nanotechnology, the synthesis of nanomaterials is a crucial area that opens up several possibilities for applications in various fields, including electronics and medicinal sciences. Table 1.1 provides a succinct summary of several methodologies utilized in the synthesis approach, classified as either top-down or bottom-up techniques [33].

1.7 Characteristics of Nanomaterials

To understand biocompatible nano-enabled platforms, it is essential to adopt an interdisciplinary strategy that encompasses surface chemistry, tissue biomechanics, and signaling pathway research. This approach allows for the characterization of the complex and dynamic interactions involved [34].

Table 1.1 Techniques for synthesis of different nanomaterials [26]

S. no.	Name of technique	Principle	Merits	Demerits	Application in the production of nanomaterials
Top-down approaches					
1	Mechanical milling	Reducing the size of bulk materials by ball milling	Large-scale production possible	Difficult to control particle size distribution	Producing nanoscale powders of metals, alloys, etc.
2	Mechanochemical processing	Inducing chemical reactions during milling by generation of shear bands and subgrains	Fast processing speed to nanoscale	Difficult to achieve specific chemical reactions	Facilitating reactions requiring high temperature
3	Electroexplosion	Passing high-density electric pulse through metal wire causing extremely high temperature and explosion	Unique properties difficult to obtain otherwise	Equipment-intensive, low yield	Generating aerosols of Au, Ag, Cu, etc. NPs
4	Sputtering	Bombarding the sample surface with energetic ions leads to the ejection of atoms/clusters	High-purity product with low toxicity	Poor control over particle size and shape	Depositing thin films of NPs
5	Laser ablation	Interaction of high-power laser pulse with sample surface causing localized heating and material ejection	Better control by tuning laser parameters	Complex process, limited scalability	Generating NP-seeded plasma
6	Lithography	Using masks, molds, or focused energy beams to create nanopatterns	High-resolution nanopatterning	Multiple complex steps	Fabricating integrated circuits, sensors, etc.
7	Aerosol methods	Generating NPs in a gaseous environment	High purity products	Slow production rate	Producing metal/metal oxide NPs

(continued)