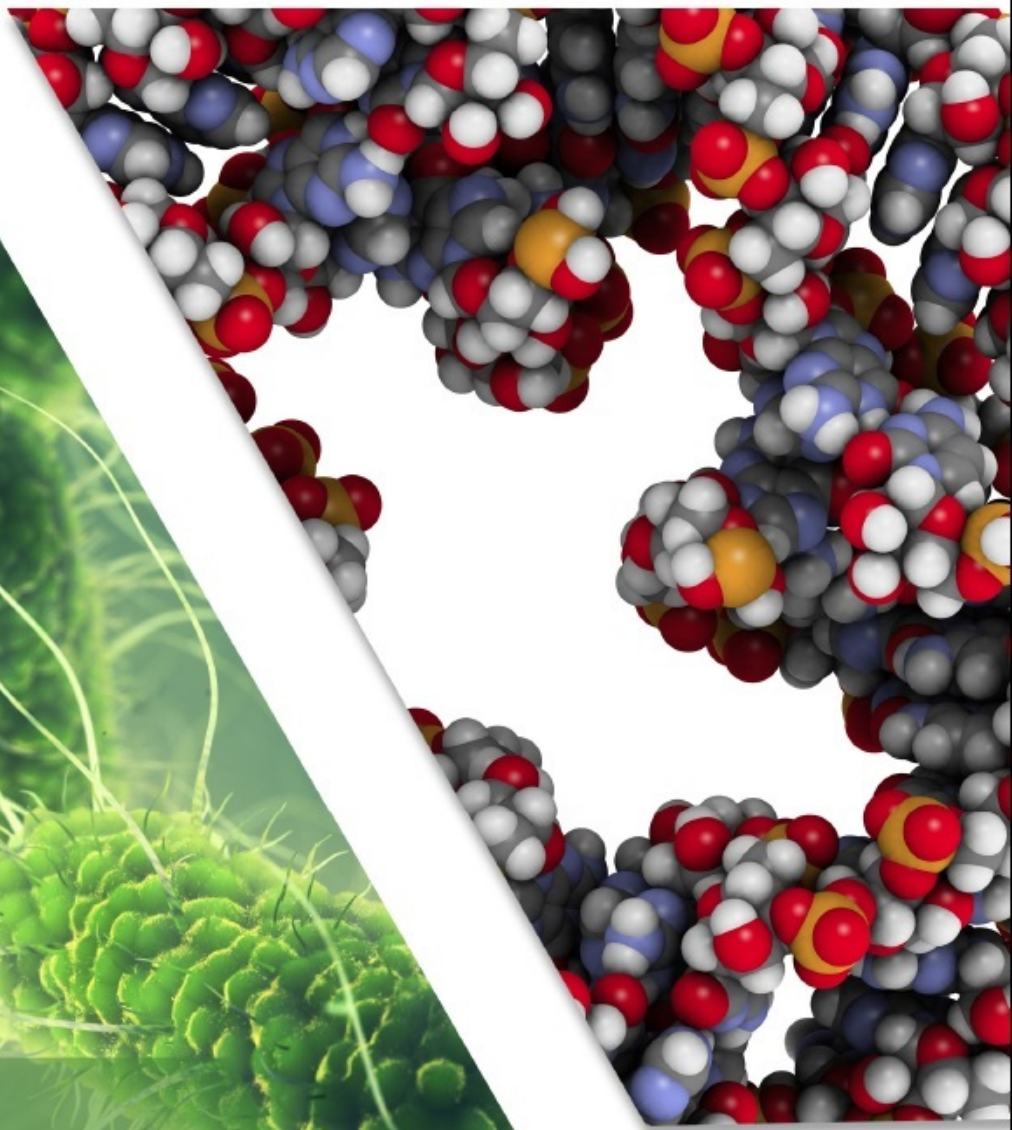


# NANOMATERIALS AND THEIR INTERACTIVE BEHAVIOR WITH BIOMOLECULES, CELLS AND TISSUES



**Yogendrakumar H. Lahir**  
**Pramod Avti**

**Bentham Books**

# **Nanomaterials and their Interactive Behavior with Biomolecules, Cells and Tissues**

**Authored by**

**Yogendrakumar H. Lahir**

*Department of Biophysics,  
University of Mumbai,  
Mumbai 400098  
India*

**&**

**Pramod Avti**

*Department of Biophysics, Research 'B' block,  
Postgraduate Institute of Medical Education and Research,  
Chandigarh 160012  
India*

## **Nanomaterials and their Interactive Behavior with Biomolecules, Cells and Tissues**

Authors: Yogendrakumar H. Lahir & Pramod Avti

ISBN (Online): 978-981-14-6178-1

ISBN (Print): 978-981-14-6176-7

ISBN (Paperback): 978-981-14-6177-4

© 2020, Bentham Books imprint.

Published by Bentham Science Publishers Pte. Ltd. Singapore. All Rights Reserved.

## **BENTHAM SCIENCE PUBLISHERS LTD.**

### **End User License Agreement (for non-institutional, personal use)**

This is an agreement between you and Bentham Science Publishers Ltd. Please read this License Agreement carefully before using the book/echapter/ejournal (“**Work**”). Your use of the Work constitutes your agreement to the terms and conditions set forth in this License Agreement. If you do not agree to these terms and conditions then you should not use the Work.

Bentham Science Publishers agrees to grant you a non-exclusive, non-transferable limited license to use the Work subject to and in accordance with the following terms and conditions. This License Agreement is for non-library, personal use only. For a library / institutional / multi user license in respect of the Work, please contact: [permission@benthamscience.net](mailto:permission@benthamscience.net).

### **Usage Rules:**

1. All rights reserved: The Work is the subject of copyright and Bentham Science Publishers either owns the Work (and the copyright in it) or is licensed to distribute the Work. You shall not copy, reproduce, modify, remove, delete, augment, add to, publish, transmit, sell, resell, create derivative works from, or in any way exploit the Work or make the Work available for others to do any of the same, in any form or by any means, in whole or in part, in each case without the prior written permission of Bentham Science Publishers, unless stated otherwise in this License Agreement.
2. You may download a copy of the Work on one occasion to one personal computer (including tablet, laptop, desktop, or other such devices). You may make one back-up copy of the Work to avoid losing it.
3. The unauthorised use or distribution of copyrighted or other proprietary content is illegal and could subject you to liability for substantial money damages. You will be liable for any damage resulting from your misuse of the Work or any violation of this License Agreement, including any infringement by you of copyrights or proprietary rights.

### ***Disclaimer:***

Bentham Science Publishers does not guarantee that the information in the Work is error-free, or warrant that it will meet your requirements or that access to the Work will be uninterrupted or error-free. The Work is provided "as is" without warranty of any kind, either express or implied or statutory, including, without limitation, implied warranties of merchantability and fitness for a particular purpose. The entire risk as to the results and performance of the Work is assumed by you. No responsibility is assumed by Bentham Science Publishers, its staff, editors and/or authors for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products instruction, advertisements or ideas contained in the Work.

### ***Limitation of Liability:***

In no event will Bentham Science Publishers, its staff, editors and/or authors, be liable for any damages, including, without limitation, special, incidental and/or consequential damages and/or damages for lost data and/or profits arising out of (whether directly or indirectly) the use or inability to use the Work. The entire liability of Bentham Science Publishers shall be limited to the amount actually paid by you for the Work.

### **General:**

1. Any dispute or claim arising out of or in connection with this License Agreement or the Work (including non-contractual disputes or claims) will be governed by and construed in accordance with the laws of Singapore. Each party agrees that the courts of the state of Singapore shall have exclusive jurisdiction to settle any dispute or claim arising out of or in connection with this License Agreement or the Work (including non-contractual disputes or claims).
2. Your rights under this License Agreement will automatically terminate without notice and without the

need for a court order if at any point you breach any terms of this License Agreement. In no event will any delay or failure by Bentham Science Publishers in enforcing your compliance with this License Agreement constitute a waiver of any of its rights.

3. You acknowledge that you have read this License Agreement, and agree to be bound by its terms and conditions. To the extent that any other terms and conditions presented on any website of Bentham Science Publishers conflict with, or are inconsistent with, the terms and conditions set out in this License Agreement, you acknowledge that the terms and conditions set out in this License Agreement shall prevail.

**Bentham Science Publishers Pte. Ltd.**

80 Robinson Road #02-00

Singapore 068898

Singapore

Email: [subscriptions@benthamscience.net](mailto:subscriptions@benthamscience.net)



## CONTENTS

FOREWORD .....	i
PREFACE .....	iii
CONFLICT OF INTEREST .....	v
CONSENT FOR PUBLICATION .....	v
ACKNOWLEDGMENT .....	vi
DEDICATION .....	vii
<b>CHAPTER 1 NANOSCIENCE, NANOTECHNOLOGY, NANOMATERIALS AND BIOLOGICAL SCIENCES</b> .....	1
OVERVIEW: NANOSCIENCE, NANOTECHNOLOGY, AND NANOMATERIALS .....	1
HISTORICAL ASPECTS OF NANOSCIENCE AND NANOTECHNOLOGY .....	3
CURRENT SCENARIO OF NANOSCIENCE, NANOTECHNOLOGY, AND NANOMATERIALS .....	5
VISUALIZATION OF BIOLOGICAL SCIENCES AT NANOSCALE .....	6
CAN NANOTECHNOLOGY BE CONSIDERED AS COMPLEMENTATION OF MICRO-TECHNOLOGY? .....	7
CONCLUSION .....	14
REFERENCES .....	14
<b>CHAPTER 2 NANOMATERIALS AND THEIR BEHAVIORAL ASPECTS</b> .....	21
INTRODUCTION AND OVERVIEW .....	21
DEFINING NANOMATERIALS .....	22
USES OF NANOMATERIALS .....	23
METAL AND METAL OXIDE NANOPARTICLES AND THEIR PHYSICOCHEMICAL FEATURES THAT IMPACT THEIR INTERACTION OR BEHAVIOR .....	27
SURFACE ENERGY .....	27
PLASMONIC NANOPARTICLES .....	28
PHENOMENON OF LIGHT SCATTERING BY NANOMATERIALS .....	31
Elastic and Thermal Scattering .....	34
PHENOMENON OF SCATTERING OF ELECTROMAGNETIC WAVES BY NANOMATERIALS .....	34
Rayleigh Scattering .....	35
MIE Scattering .....	36
Raman Scattering .....	36
Compton Scattering .....	37
X-Ray Scattering .....	37
Brillouin Scattering .....	39
PHENOMENON OF ABSORPTION OF RADIANT ENERGY BY NANOMATERIALS .....	39
IMPACT OF MEDIA ON OPTICAL BEHAVIOR OF NANOPARTICLES .....	40
SCATTERING OF RADIATIONS BY IRREGULARLY SHAPED NANOPARTICLES .....	41
APPLICATIONS OF SCATTERING, EXCITATION AND ABSORPTION PHENOMENA .....	41
The Raman Microscopy .....	44
<i>Applications of Coherent Antistokes Raman Scattering (CARS)</i> .....	46
APPLICATION OF INFRARED MICROSCOPIC AND SPECTROSCOPIC TECHNIQUES IN UNDERSTANDING THE BEHAVIOR OF NANOMATERIALS .....	48
Features That Influence the Behavior of Quantum Dots .....	49
Features that Influence the Behavior of Carbon Nanomaterials-Carbon Nanotubes, Fullerene, and Graphene .....	51
Features that Influence the Behavior of Dendrimers .....	57

CONCLUSION .....	61
REFERENCES .....	61
<b>CHAPTER 3 BIOCOMPATIBILITY AND BIOAVAILABILITY OF NANOMATERIALS</b>	
<b>OUTLINE .....</b>	<b>71</b>
<b>BIOCOMPATIBILITY, BIODISTRIBUTION, AND BIOAVAILABILITY OF</b>	
<b>NANOMATERIALS IN BIOSYSTEM: AN OVERVIEW .....</b>	<b>71</b>
<b>STRATEGIES THAT AFFECT BIOCOMPATIBILITY OF NANOMATERIALS .....</b>	<b>74</b>
<b>FUNCTIONALIZATION OF NANOMATERIALS .....</b>	<b>75</b>
<b>STABILIZATION AGAINST AGGREGATION OR AGGLOMERATION OF</b>	
<b>NANOPARTICLES .....</b>	<b>76</b>
<b>USE AND EXCHANGE OF LIGAND AND NANOMATERIALS .....</b>	<b>76</b>
<b>ROLE OF PHASE TRANSFER PROCESS DURING THE BEHAVIOR OF</b>	
<b>NANOMATERIALS .....</b>	<b>78</b>
<b>SILANIZATION .....</b>	<b>79</b>
<b>NANOMATERIALS AS AGENTS TO DEVELOP MULTIFUNCTIONAL HYBRID</b>	
<b>COATING FOR SCRATCH AND CORROSION RESISTANT SURFACES: .....</b>	<b>80</b>
<b>ROLE OF AEROGELS IN NANOMATERIALS AND NANOTECHNOLOGY .....</b>	<b>81</b>
<b>OPSONIZATION .....</b>	<b>82</b>
<b>SOME EXAMPLES OF NANOMATERIALS EXHIBITING BIOCOMPATIBILITY,</b>	
<b>BIODISTRIBUTION, AND BIOAVAILABILITY IN BIOSYSTEM .....</b>	<b>83</b>
<b>CONCLUSION .....</b>	<b>87</b>
<b>REFERENCES .....</b>	<b>88</b>
<b>CHAPTER 4 PHYSICOCHEMICAL ASPECTS THAT INFLUENCE THE INTERACTIVE</b>	
<b>BEHAVIOR OF NANOMATERIALS .....</b>	<b>94</b>
<b>INTRODUCTION AND OVERVIEW .....</b>	<b>94</b>
<b>NATURAL AND ENGINEERED NANOMATERIALS .....</b>	<b>95</b>
<b>SOME FUNDAMENTALS RELATED TO PHYSICS THAT AFFECT THE BEHAVIOR</b>	
<b>OF NANOMATERIALS .....</b>	<b>96</b>
Quantum Mechanics .....	96
Tunneling Effect .....	97
<b>SOME FUNDAMENTALS OF CHEMISTRY THAT INFLUENCE THE BEHAVIOR OF</b>	
<b>NANOMATERIALS .....</b>	<b>98</b>
Inter and Intramolecular Bonding .....	98
Large Surface Area .....	99
Hydrophobicity .....	99
<b>FACTORS AFFECTING INTERACTIONS OF NANOMATERIALS .....</b>	<b>100</b>
Ability of Nanomaterials To Get Distributed and Dispersed in Media .....	100
Application of Equilibrium Equation .....	101
Net Charge on Nanomaterials .....	101
<b>FORCES AFFECTING THE BEHAVIOR OF NANOMATERIALS IN BIOSYSTEM .....</b>	<b>102</b>
Role of Electrostatic Forces [Coulomb Forces (Fs)] During The Behavior of Nanomaterials	104
Keesom Forces, Debye Forces, and London Dispersion Forces are Under Van Der Waals	
Forces .....	107
Dispersibility and Solubility of Nanomaterials .....	108
Influence of Size of Nanomaterials During their Interactions .....	109
Influence of Shape of Nanomaterials on their Interactive Behavior .....	113
Influence of Surface Properties of Nanomaterials During the interactive behavior .....	116
Influence of the Surface Charge on Nanomaterials During their Interactive Behavior .....	116
Influence of Composition of Nanomaterials on their Behavior and Interaction .....	118
Influence of Optical Properties of Nanomaterials on their Interactive Behavior .....	119

Influence of Magnetic Properties of Nanomaterials During their Interactive Behavior .....	120
<b>CONCLUSION</b> .....	124
<b>REFERENCES</b> .....	124
<b>CHAPTER 5 INTERACTION BETWEEN NANOMATERIALS AND GLYCOCALYX, CELL MEMBRANE, CYTOSKELETON, CELL ORGANELLES AND TISSUES</b> .....	131
<b>OVERVIEW – NANOMATERIALS AND BIOSYSTEMS</b> .....	132
<b>SOME SPECIAL MODES THAT FACILITATE INTERACTIONS BETWEEN NANOPARTICLES AND CELL MEMBRANE</b> .....	136
Cell Fusogenic Proteins (CFPs) .....	136
Cell Penetrating Peptides (CPP) .....	138
Proton Sponge Hypothesis and Nanomaterials .....	139
<b>BEHAVIOR OF NANOMATERIALS</b> .....	142
<b>ROLE OF MASS TRANSPORT OF NANOMATERIALS IN BIOSYSTEM</b> .....	144
<b>SIGNIFICANCE OF DEGRADABILITY OF NANOMATERIALS IN BIOSYSTEM</b> .....	146
<b>INFLUENCE OF BIOPHYSICAL ASPECTS ON INTERACTION BETWEEN NANOMATERIALS AND THE COMPONENTS OF BIOSYSTEM</b> .....	147
<b>IMPORTANCE OF CHARACTERISTIC MEMBRANE WETTABILITY</b> .....	148
<b>INFLUENCE OF BIOCOMPATIBILITY AND BIODISTRIBUTION OF NANOMATERIALS IN BIOSYSTEMS</b> .....	148
<b>PATHWAYS RELATED TO INTERACTION OF NANOMATERIALS AND TISSUES –CLASSICAL PATHWAY; C-REACTIVE PROTEINS; LECTIN PATHWAY; ALTERNATIVE PATHWAY</b> .....	149
<b>ENDOCYTOTIC MECHANISM OF UPTAKE OF NANOPARTICLES</b> .....	151
Phagocytosis .....	151
Caveolae-mediated Endocytosis .....	153
Clathrin-mediated Endocytosis (CME) .....	153
Other Mechanisms of Cellular Uptake .....	154
<b>THE BIOCHEMICAL, BIOPHYSICAL AND FUNCTIONAL ASPECTS OF GLYCOCALYX AND ITS INFLUENCE ON NANOMATERIALS</b> .....	156
Interactions Between Nanomaterials and Glycocalyx .....	158
<b>CELL MEMBRANE: OVERVIEW</b> .....	160
Interaction Between Nanomaterials and Cell Membrane .....	163
<b>CYTOSKELETON</b> .....	165
The Interactions of Nanomaterials with Cytoskeleton .....	167
<b>CONCLUSION</b> .....	170
<b>REFERENCES</b> .....	171
<b>CHAPTER 6 INTERACTIONS BETWEEN PROTEINS AND NANOMATERIALS</b> .....	180
<b>OVERVIEW OF STRUCTURAL ASPECTS OF PROTEINS</b> .....	180
<b>THE STRUCTURAL ASPECTS OF PROTEIN</b> .....	181
The Primary Structure .....	181
Secondary Structure of Protein .....	182
Tertiary Structure of Protein .....	183
Quaternary Structure of Protein .....	183
<b>PROTEIN STABILITY</b> .....	184
<b>ZETA POTENTIAL (Z-POTENTIAL)</b> .....	184
<b>OPSONIZATION</b> .....	185
<b>OPSONINS</b> .....	186
Pentraxins .....	186
Collectins .....	186
Ficolins .....	187



<b>PROTEIN CORONA</b> .....	187
Impact of Size of Nanoparticle on Protein Corona .....	188
Impact of Morphological Aspects of Nanoparticles on Protein Corona .....	189
Impact of Surface Charge Present on Nanomaterials During the Formation of Protein Corona .....	189
Influence of Hydrophobicity on Protein Corona .....	189
Patterns of Protein Corona .....	190
Influence of Composition of Medium on the Formation of Protein Corona .....	190
Influence of Protein Conformation on Protein Corona Formation .....	192
Influence of Protein Concentration in Interacting Medium on Protein Corona .....	192
Influence of Exposure Duration on Protein Corona Formation .....	192
Role of Static and Dynamic States of Body Fluids on Protein Corona .....	193
Role of Static and Dynamic States of Body Fluids on Protein Corona .....	193
Influence of Temperature on Protein Corona Formation .....	194
Impact of pH on Protein Corona Formation .....	195
Impact of Colloidal Stability on Protein Corona Formation .....	196
Applications and Significance of Protein Corona .....	197
<b>SIGNIFICANCE OF INTERFACE DURING INTERACTIONS BETWEEN NANOMATERIALS AND PROTEINS</b> .....	201
<b>INTERACTIONS BETWEEN NANOMATERIALS AND PROTEINS</b> .....	203
<b>THE INFLUENCE OF THE INTERACTIONS BETWEEN NANOMATERIALS AND PROTEINS ON THEIR BIODISTRIBUTION</b> .....	207
<b>PROTEIN CHIP OR PROTEIN MICROARRAY AND NANOMATERIALS</b> .....	208
<b>CONCLUSION</b> .....	210
<b>REFERENCES</b> .....	211

**CHAPTER 7 INTERACTIONS BETWEEN NANOMATERIALS AND GENETIC MATERIAL (DNA AND RNA)** .....

<b>INTRODUCTION</b> .....	220
<b>AN OVERVIEW OF BIOCHEMICAL AND BIOPHYSICAL ASPECTS OF DNA</b> .....	222
<b>PHYSICOCHEMICAL FEATURES OF DNA IMPACT OF TEMPERATURE</b> .....	222
<b>OPTICAL PROPERTIES OF DNA DURING RADIATION ABSORPTION</b> .....	223
<b>RELATIONSHIP BETWEEN DENSITY AND DNA</b> .....	224
<b>INFLUENCE OF HYDROPHOBICITY AND HYDROPHILICITY CONCERNING DNA AND NANOMATERIALS</b> .....	225
<b>THE IMPACT OF pH ON DNA MOLECULE</b> .....	225
<b>IMPACT OF IONIC STRENGTH</b> .....	225
A-DNA, B-DNA, and Z-DNA .....	225
<i>Biological Significance of A-DNA</i> .....	226
<i>Biological Significance of B-DNA</i> .....	227
<i>Biological Significance of Z-DNA</i> .....	228
<b>BASE PAIR GEOMETRY IN DNA</b> .....	229
<b>MAJOR AND MINOR GROOVES OF DNA</b> .....	230
<b>DNA AND ITS HELIX OR HELICAL STRUCTURE</b> .....	230
<b>PROTEIN AND DNA BINDING INTERACTIONS</b> .....	231
<b>EFFECTS OF ENTROPY ON DNA</b> .....	232
<b>ELASTICITY OF DNA</b> .....	233
<b>OVERVIEW OF THE HARMFUL IMPACTS OF NANOMATERIALS CONCERNING DNA</b> .....	234
<b>INTERACTIONS BETWEEN NANOMATERIALS AND DNA</b> .....	235

<b>INTERACTION BETWEEN CARBON NANOPARTICLES AND GENETIC MATERIALS</b> .....	238
<b>INTERACTION BETWEEN QUANTUM DOTS AND GENETIC MATERIALS</b> .....	242
<b>INTERACTION BETWEEN DENDRIMERS AND GENETIC MATERIALS</b> .....	243
<b>INTERACTION BETWEEN HISTONE PROTEINS AND NANOMATERIALS</b> .....	244
<b>THE RNA EXHIBITS THE PHYSICOCHEMICAL AND BIOPHYSICAL FEATURES</b> ....	245
<b>ROLE OF RNA AS POLYMER</b> .....	245
<b>RNA IS A THERMODYNAMICALLY STABLE BIOMOLECULE</b> .....	246
<b>STABILITY OF RNA CONCERNING ENZYMES</b> .....	246
<b>THE RNA EXHIBITS ADAPTABILITY AND PLASTICITY</b> .....	247
<b>INTERACTIONS BETWEEN NANOMATERIALS AND RNA</b> .....	248
<b>EFFECTIVE ROLE OF RNA IN THE DEVELOPMENT OF THREE DIMENSIONAL FORMULATIONS OF NANOSCALE MATERIALS</b> .....	250
<b>STABILITY OF RNA CONCERNING CHEMICAL AND BIOCHEMICAL ASPECTS</b> .....	251
<b>CONCLUSION</b> .....	252
<b>REFERENCES</b> .....	253
<b>CHAPTER 8 INTERACTIONS BETWEEN ENZYMES AND NANOMATERIALS</b> .....	261
<b>BIOCATALYSIS</b> .....	261
<b>SUBSTRATE</b> .....	267
<b>IMMOBILIZATION OF ENZYME</b> .....	268
The Functional Roles of Nanomaterials in the Process of Immobilization of Enzyme .....	270
Nanomaterials and the Process of Immobilization of Enzymes .....	275
<b>APPLICATIONS OF IMMOBILIZED ENZYME</b> .....	277
Applications of Immobilized Enzymes in Biomedical Field .....	277
Application in Textile Technology and Industry .....	277
Application of Immobilization in Food Technology .....	278
Application of Immobilization of Enzyme in Biofuel Technology .....	278
<b>INTERACTIONS BETWEEN NANOMATERIALS AND ENZYMES</b> .....	279
<b>THE DEROGATIVE IMPACTS OF NANOMATERIALS ON ENZYMES AND THEIR ACTIVITY</b> .....	286
<b>IS THERE ANY CORRELATION BETWEEN NANOMATERIALS, ENZYMATIC ACTIVITIES, AND BIOMIMETICS?</b> .....	287
<b>CONCLUSION</b> .....	288
<b>REFERENCES</b> .....	289
<b>CHAPTER 9 NANOMATERIALS AND IMMUNE SYSTEM: INTERACTIONS</b> .....	298
<b>INTRODUCTION: OVERVIEW-IMMUNE SYSTEM IN HUMANS, NANOTECHNOLOGY, NANOSCIENCE, AND NANOMATERIALS</b> .....	298
<b>POTENTIAL ADVANTAGES OF NANOMATERIAL BASED DELIVERY SYSTEM</b> .....	302
<b>PROBABLE FLAWS OR UNDESIRABLE INTERACTIONS THAT APPEAR DURING THE APPLICATIONS OF NANOMATERIAL BASED DELIVERY SYSTEMS</b> .....	302
<b>IMMUNOMODULATION</b> .....	303
<b>NANOMATERIALS ARE COMPETENT AGENTS TO INFLUENCE THE IMMUNE SYSTEM</b> .....	304
<b>INFLUENCE OF NANOMATERIALS ON IMMUNOSTIMULATION, IMMUNOSUPPRESSION</b> .....	304
<b>INTERACTIONS BETWEEN METAL, METAL OXIDE NANOPARTICLES, AND IMMUNE SYSTEM</b> .....	308
<b>INTERACTIONS BETWEEN CARBON NANOMATERIALS AND IMMUNE SYSTEM</b> .....	312
<b>INTERACTIONS BETWEEN DENDRIMERS AND IMMUNE SYSTEM</b> .....	316
<b>INTERACTIONS BETWEEN QUANTUM DOTS AND IMMUNE SYSTEM</b> .....	318

<b>INTERACTIVE BEHAVIOR OF MESOPOROUS NANOMATERIALS AND IMMUNE SYSTEM</b> .....	320
<b>SOME OF THE ENGINEERED NANOMATERIALS INVOLVED WITH IMMUNE SYSTEM</b> .....	321
<b>POLYMERIC NANOPARTICLES</b> .....	321
<b>NANOLIPOSOMES</b> .....	322
<b>NANOEMULSIONS</b> .....	322
<b>SOLID-LIPID-NANOMATERIALS</b> .....	323
<b>CONCLUSION</b> .....	323
<b>REFERENCES</b> .....	324
<b>CHAPTER 10 BROAD SPECTRA OF APPLICATIONS BASED INTERACTIONS OF NANOMATERIALS</b> .....	331
<b>OVERVIEW</b> .....	331
<b>VARIOUS APPLICATIONS OF NANOMATERIALS</b> .....	333
Nanomaterials for Drug Delivery and Biomedical Applications .....	333
Nanomaterials as Antifungal Agents .....	337
Nanomaterials as Antiviral Agents .....	339
Nanomaterials as Antibacterial Agents .....	341
<i>Overview of the Mechanism Involved During Antimicrobial Activity of Metal and Metal Oxide Nanomaterials</i> .....	344
<i>The Carbon-Based Nanomaterials and Antibacterial Activity and The Mechanism Involved</i> .....	345
<b>NANOCOMPOSITES-A PRODUCTS OF NANOTECHNOLOGY AND THEIR BIOCOMPATIBILITY</b> .....	348
Applications of Synthetic Biopolymer Composites for Tissue Engineering Scaffolds .....	349
Applications of Bacterial Cellulose-Collagen Nanocomposite for Bone Tissue Engineering .....	349
Applications of Nanomaterials as Biosensors .....	350
Applications of Nanomaterials for Implants, Prosthesis and Tissue Engineering .....	354
Applications of Nanomaterials for Bone and Dental Implants .....	355
Applications of Nanomaterials as Cartilage Implants .....	356
Applications of Nanomaterials as Oesophageal, Tracheal and Bladder Implants .....	356
Applications of Nanomaterials as Vascular Implants and Stents .....	357
Applications of Nanomaterials as Neural Implants .....	357
Role of Nanomaterials in the Varied Aspects of Defense .....	358
Nanovaccines and Nanomaterials .....	359
<b>CONCLUSION</b> .....	361
<b>REFERENCES</b> .....	361
<b>SUBJECT INDEX</b> .....	372

## Foreword

This book comprises ten chapters; each chapter elucidates specific aspects of nanotechnology, nanoscience, and the basic concepts involved during their multifaceted interactions with and within biological systems and biomolecules.

This presentation elaborates on the introductory remarks on nanotechnology and nanoscience. There is a brief discussion on the definition of nanomaterials, scope, and applications in different fields with emphasis on biological sciences and materials sciences. The interactive behavior of nanomaterials relates to their types and nature. The successful applications of nanomaterials enormously depend on their degree of biocompatibility and bioavailability in the biosystem and at the site of the interface. The physicochemical parameters like inter and intramolecular bonding, hydrophobicity, interactive forces, surface charge, and composition of nanomaterials are well illustrated with suitable examples and supported by the references. When nanomaterials encounter a biosystem, the cellular components like glycocalyx, cell membrane, cytoskeleton, act as the first site of the interface. These components influence the interplay and uptake of the nanomaterials. These entrants form conjugates with ligands, proteins, and cause their effects, and interfere with cellular functioning. Nanomaterials undergo internalization involving phagocytosis, endocytosis. These materials show exclusive interactive behavior with proteins and this depends on the structure of protein, zeta-potential, and nature of binding. This behavior intervenes in cellular physiology and the structure. Protein microchip technology is very useful for analyzing different analytes. The internalized nanomaterials interact with the genetic materials (DNA and RNA) in a biosystem and cause changes in their geometry, physiology, stability, and biophysical aspects. Nanomaterials interact with enzymes *in vitro* and *in vivo*. This feature is used in enzyme technology, enzyme immobilization, biomimetics, and industrial enzymology. The defense mechanism of the biosystem is prone to the impacts of nanomaterials causing immunosuppression or immunostimulation. The nanomaterials intermeddle structurally and functionally with the components of the immune system transforming their roles. Lastly, all these interactive aspects congregate into the wide spectrum of the applications of nanomaterials as detection tools, imaging agents, synthesis, medical implants, and various roles in industries.

A good number of books and reviews report on the specific and selective aspects of nanoscience and nanotechnology. However, there is a need for comprehensive essays that give a consolidated overview of the physical, chemical, biological, biophysical, and molecular aspects of the interactions between nanomaterials and biomolecules, cells, and tissues. This book fulfills this need and offers an incriminated description of the incorporation of basic structural, functional, and physicochemical concepts during the interplays between nanomaterials and biomolecules. The lucid explanation in this book eases the mathematical aspects of the concerned concepts involved. This effort aims to infuse the interest in students, researchers, and foster collaboration through the multidisciplinary approach of nanoscience and nanotechnology in the recent frontiers of biological sciences and nanotechnology.

Each chapter starts with the outline of the chapter, introduction, text, and conclusion; these provide a take-home message of the information contained therein. Throughout the book, suitable examples are presented that support the concepts and are an amalgamation of past and recent research. Lastly, this presentation gives glimpses of the multidisciplinary approach and room to maneuver the various concepts from physical, chemical, applied sciences and technologies, for the betterment of their future applications.

*ii*

I feel the book will provide a handy but complete reference and review of the nanoworld to students and researchers in this field.

**Dr. A.V. Chitre**  
Former Reader & Head, Department of Chemistry  
Professor Emeritus, Sophia College, Mumbai  
Adjunct/Visiting Faculty in Biophysics  
Department of Biophysics, University of Mumbai  
Vidyanagari  
Santa Cruz (E), Mumbai 400 098  
India

## PREFACE

Nanoscience and nanotechnology both have been utilized by a man during the early days of scientific developments under various civilizations, like ancient India, ancient Mesopotamia, ancient Egypt, ancient China, Japan, *etc.* During these eras, there have been scientific developments and materials in nanofoms that might be in use as it is evident from the monuments and the products found during the excavation. Possibly a common man might not be aware of the terms like nanoparticles, nanomaterials, nano synthesis, *etc.*, except the specialized craftspersons. These specialized craftspersons might be using different terminology concerning the particular concept of dimension, size, and other properties of the materials in these eras. Nanomaterials are useful in almost all fields of present-day life. These materials have at least one dimension within 1 to 100 nm ranges.

The physicochemical features of nanomaterials, mode of their synthesis, duration of exposure, and amount of nanomaterials, *etc.*, influence their impacts on the biosystem. Most of the nanomaterials, natural and engineered, both get dispersed in all media and move across almost all types of biological barriers. This ability of nanomaterials exhibits a higher degree of derogative or beneficial interactions. These are of investigatory interest concerning biotic and abiotic components of the environment. These features make them potential agents for their varied applications in industrial, domestic, food-technology, medical, cosmetics, pharmaceutical, and other biomedical fields. Most of the administered nanomaterials get readily disbursed in the biosystem and exhibit a higher degree of metabolic interaction. Such interactions depend on the dose, physicochemical properties of nanomaterials, and cause, either conjugation or dissociation in the interactive biomolecules. The interacting nanomaterials induce changes in the biomolecular conformation, the reactive groups, molecular cross-linkage, hydrophobicity and hydrophilicity, and structural damage, and interrupt cellular functions. The harmful impacts involve micro, macromolecules, cell membrane, cell membrane receptors, cell-organelles, and metabolic pathways. The administered nanomaterials come in contact with the contents of body fluids. The adhesion of nanomaterials onto the cell membrane, even if the biomolecular corona is absent on nanomaterial. The adsorption of proteins on the surface of nanomaterials sharply reduces the adhesion in comparison to the conditions when the nanomaterials are without biological corona. The cellular uptake of the nanomaterials involves two steps: i- initial adherence of nanomaterial to the cell membrane, and ii- internalization of nanomaterial by the cell comprising the energy-dependent pathway.

In most cases, the biomolecules such as proteins, lipids, carbohydrates, *etc.*, are present in body fluids of the biosystem. These body fluids include blood, hemolymph, lymph, or any other form of fluid present in the biosystem. The interactions between nanomaterials and biomolecules relate to the specificity of binding ability of biomolecules, the composition of nanomaterial, and their surface physical-chemistry. The effect of the nanomaterial-biomolecular complex formed; generally, the compound formed is with proteins or conjugated proteins that influence the responses of the biosystem. The nanomaterial-protein complex built plays a more significant role in their biodistribution in the biosystem because the protein-nanomaterial-complex formed becomes the identity of the nanomaterials involved within the biological system. Interaction between nanomaterial and biomolecules is a dynamic process. Since proteins are relatively in abundance, they dominate these types of interplay, resulting in the formation of complexes depending on the charge on the surface of protein molecules and nanomaterials. The conformation of the protein at the interface influences the cellular uptake of the nanomaterial. Therefore the interactions between nanomaterial and protein are of great significance in biotechnology and molecular biology.

Adsorption of the proteins on the surface of nanomaterial is a complex process. It is primarily related to (i) - dielectric properties and pH of the medium, (ii)-surface morphology, and surface heterogeneity of nanomaterials and (iii) -the quaternary structure of the protein involved. This phenomenon indicates the existence of the different types of interactions between more significant multimeric proteins, nanomaterial, and small oligomeric proteins.

There is dissociation or binding of proteins present in lower concentrations, but have a higher affinity, influence the separation of conjugated proteins, and this aspect slows the kinetics. Thus the nanomaterials coated with protein can undergo enhanced cellular uptake specifically by macrophages. In most cases, opsonins are present in blood and body fluids. It enhances the ability of macrophages to recognize the surface of the particles entered the biosystem (opsonization). Opsonins like albumin, immunoglobulins, fibrinogen, and compounds of complementary system and apolipoprotein are present in body fluids. They play an active role in the clearance or elimination process in the biosystem. Apolipoproteins are the proteins that bind to lipid.

Lipids are oil-soluble substances like fat and cholesterol and form lipoproteins. These apolipoproteins transport the lipid through the lymphatic circulatory system in vertebrates and hemolymph in the case of invertebrates. The apolipoprotein and phospholipids exhibit amphipathic features having both hydrophilic and hydrophobic components, hydrophilic head and a hydrophobic tail. The apolipoprotein and phospholipids are water-soluble surround lipids and lipoproteins. These interact with enzyme cofactors, exhibit ligand-surface receptors, and low-density lipoproteins (LDL). The distribution of nanomaterials is explicit in cases, like oriented targets, like cancer cells, diseased cells, DNA, RNA, gene, *etc.* Surface-bound molecules like proteins can promote cell-specific uptake of nanomaterials. There are chances that nanomaterials can activate the intracellular signaling pathways. Their dispersibility in air, aquatic, and solid media depend on their nature and specificity.

Any material natural or engineered having nano dimensions and intend to interact with the biological system to evaluate, treat, augment, replace tissue and organ, and have specific functionality. The biocompatibility of such nanomaterials is the first and for most priority for their successful application. The biocompatibility of such materials is the ability to perform appropriate host-response in a specific application. The biocompatibility of nanomaterials depends on the molecular adsorption, mechanical, biophysical, and chemical cellular pathways during their cellular internalization. These interactions are either defensive, interfering oriented targets. Biocompatibility may concern long term or short term specifically for the implanted devices and tissue-engineered devices and conceptually, concerns with cytotoxicity, sensitization, irritation, genotoxicity, implantation, hemocompatibility, carcinogenicity, and biodegradability, *etc.* When biomaterials and hosts come in contact during surgical implants, infusion, injection, extracorporeal circuits, or *in vivo* bioreactor, *etc.*, initiate the response.

The processes like material degradation, cell adhesion, mechanical forces generated as a result of the administration as the host response progress with many possibilities like inadequate resolution, clinically relevant effects, either tolerable or non-tolerable, inflammation, hyperplasia, thrombosis, calcification, resolution of the reactions, clinically acceptable results also play a significant role the responses due to these interplays. Biomaterial components like metal ions, polymers, additives, contaminants of nanomaterials on cellular internalization involving specific mechanism, phagocytosis, endocytosis, pinocytosis, *etc.*, affect the ambient intracellular environment; this can include material degradation, generation of free radicals like ROS/RNS, cellular damage, alterations in the functionality of cell organelles, interference with apoptotic and necrotic pathways, the passage into nucleus affecting gene expression or

gene damage. This process involves material mediators for interactions, chemical structure, elasticity, shape, volume, topology, *etc.*

This presentation is an effort to understand the mechanisms and the involvement of probable parameters along with different concepts, theories, laws, and applied principles of chemistry, physics, biological sciences, and computational simulation. There is a dedicated effort to present the matter precisely, even for those who may not have a mathematical background.

### **CONFLICT OF INTEREST**

The authors confirm that there is no conflict of interest.

### **CONSENT FOR PUBLICATION**

Declared none.

**Yogendrakumar H. Lahir**  
Department of Biophysics  
University of Mumbai  
Mumbai 400098  
India

&

**Pramod Avti**  
Department of Biophysics, Research 'B' block  
Postgraduate Institute of Medical Education and Research  
Chandigarh 160012  
India



## ACKNOWLEDGMENT

Authors gratefully express their gratitude to their parents who played pivotal and primary roles in their lives. We are thankful to the research workers, writers, reviewers, whose books, review articles, and research papers have enriched and enhanced our understanding of the subject and have been referred to in this presentation. Further, we are solely thankful to these writers, researchers because their published works have inspired us to undertake this adventure. We also appreciate our students who participated in the discussion during lectures, presentations, seminars and conferences resulting in better clarity from the student point of view about the intricacies of the subject, modes of expression of the subject matter.

YKL extends his gratitude to his teachers namely Mr. H J Lahir (Late), Dr. K P Dhage (Late), Dr. A V Chitre from Sophia College, Mumbai, and Dr (Mrs.) P V Kagwade from C.M.F.R.I., Mumbai Center. The encouragement and departmental support provided by Prof, Dr. P M Dongre, and Head of the Biophysics Department are acknowledged. Dr. A V Chitre and Dr. Sivakami S from the Department of Biophysics, the University of Mumbai are also acknowledged for their critical and encouraging comments and the suggestions on various chapters of this presentation. YKL is also grateful to Mrs. Charu Lata Lahir, Jian, Panchali, Ribhu, and Hemank, for their tolerance, analytical suggestions, encouragement and inspiration during the completion of this adventure. [ MN'cuq'vj cpnhwm{ 'crr tgekvgu'vj g'] gr " qh'ikwg'o cuvtu'Mctep'Dcrk'cpf 'Uwtcl'K gt0

PA extends heartfelt gratitude to his Professors namely Professor KL Khanduja, Emeritus Professor, and Professor CM Pathak, Department of Biophysics, PGIMER, Chandigarh for their constant encouragement and support. PA is grateful to his parents and young and supportive minds of Mr. Praveen Avti and Ms. Veena for successfully bringing about the book.

## **DEDICATION**

*This work is dedicated to*

***Lahir Family***

***&***

***Avti Family.***

# Nanoscience, Nanotechnology, Nanomaterials and Biological Sciences

**Abstract:** Nanoscience and nanotechnology help manipulate or maneuver atoms and molecules to enable them to function at the nanoscale. Nanoscaled materials are the products of nanotechnology, and these are synthesized or fabricated based on specific guidelines. Nanomaterials can interact with most of the biomolecules, cell organelles, and cells, and can move across most of the biological barriers. These materials can readily be functionalized and modified as per the required targets. The modified nanomaterials become convenient tools in several fields of biotechnology, enzyme technology, tissue engineering, *etc.* In these fields, modified nanomaterials act as a vehicle for biomolecules, imaging agents, sensors, probes as diagnostic tools, devices, *etc.* The matters in the bulk form and at the nanoscale level show variable physicochemical properties, thereby, showing multifaceted abilities. These features are responsible for their variety of applications in day to day life as well as in specialized fields.

**Keywords:** Antifungal Agent, Antimicrobial Agent, Nanomaterials, Nanoscience, Nanotechnology, Sensors, Wootz Steel.

## OVERVIEW: NANOSCIENCE, NANOTECHNOLOGY, AND NANOMATERIALS

Nanoscience and nanotechnology are multifaceted aspects of science that provide information about the manipulation or maneuvering of atoms and molecules and enable them to function at the nanoscale. Such products readily interact with cell organelles, cells, and most of the biomolecules. Nanoscience guides to design and formulate nanostructures that ensure their feasible applications in various fields such as biomedicine, biomolecules, biochemical, pharmaceuticals, *etc.* In these fields, nanomaterials are applicable as a cargo vehicle (drugs, biomolecules, gene, *etc.*), imaging agents, sensors, diagnostic devices, *etc.* The industrial applications include electronics, energy storage devices, enzyme technology, tissue engineering, *etc.*

Nanoscience is a science of formation and interactions of nanomaterials. Materials that have at least one dimension within the range of 1nm to 100 nm (nm=one-billionth of a meter) are regarded as nanomaterials. The materials at the nanoscale

have different electrical, optical, thermal, and mechanical properties in comparison to their bulk forms. These properties relate atoms and molecules assembly, and interaction at the nanoscale. Nanoscience is a multidisciplinary aspect of science involving principles of material science, physics, chemistry, biological sciences, biotechnology, electronics, quantum mechanism, *etc* [1, 2]. Nano is a prefix used in metrics (metric system), and it represents anything that is one-billionth of some matter in size. It expresses a specific unit that measures mass and time. Materials at this dimension have different properties and behaviors, and both are different in comparison to the respective materials with larger sizes.

The field of nanotechnology has enormous impacts on human life. Nanoscale structures help to store information on 20 nm thick magnetic strips, dirt-resistant and scratch-resistant surfaces, materials that are suitable for tissue regeneration, *etc*. Researchers all over the world are making untiring efforts to explore advanced applications of such materials using basic and applied principles of physics, chemistry, biology, materials science, *etc*. As a result, there has been an enormous development in the field of nanodevices, microscopic development systems, structural and engineering systems, storage of information, computational investigations, biomedical devices, *etc*. The prime focus of nanoscience is on the properties of materials at the nanoscale, and the methodology involved in the synthesis, fabrication, and, assembly of these nanostructures. This science also facilitates the characterization, applications, and functionality of the nanomaterial, nanodevices, *etc*. The observations and study of these wonder materials need very specialized instruments and methodologies that should have the ability to either magnify or detect the products of chemical interactions that produce such nanomaterials in nature or otherwise.

Some of the fine aspects of nanoscience and nanotechnology include bioengineered materials and bionanoscience, quantum confined nanoscale materials, novel tools for nanoscale device patterning, imaging, and characterization, molecular nanoscience and electronic materials, *etc* [3]. James Tour and his coworkers made a nanoscale car, consisting of phenylene ethynylene (oligo), alkynyl axles, and four spherical fullerenes (C<sub>60</sub>) in 1906. This car moves on the gold surface as the temperature increases, and above 300°C, it moves very fast. (This nanoparticle has the chemical formula C<sub>430</sub>H<sub>274</sub>O<sub>12</sub> and molar mass 5632.769). In 1908, the National Nanotechnology Initiative (nano.gov) published a strategy related to nanotechnology. This document is a general guideline that governs the varied aspects involved in this technology.

Generally, nanostructures are the materials in the form of structural elements (particles), clusters, crystallites, or molecules. These products are in high demand

as they have significant academic and industrial applications. There have been tremendous efforts to study their properties and changes concerning their infinitely extended solid form to particle size consisting of countable numbers of atoms. The functions of the nanomaterials depend on their size and physicochemical properties. These parameters are of prime concern during their synthesis and investigations. At the nanoscale, the properties and functionalities of matter, such as electrical, optical and magnetic, *etc.*, change. These features are related and exhibit variations about the changes in their infinitely extended solid form to an excellent particle state. At this state of materials, their atoms are countable. This condition also exists even in the confinement of nanoscaled semiconductors or metal clusters or colloids. The nonmetallic elements, like carbon-based nanomaterials such as fullerene, nanotubes, *etc.*, also exhibit similar behavior. These features make them suitable for their pervasive applications not only in nanoscience but also in other biomedical fields [4].

## **HISTORICAL ASPECTS OF NANOSCIENCE AND NANOTECHNOLOGY**

One of the earlier established applications of nanoscience and nanotechnology has been reported during 600 BC in India. Indian blacksmiths produced wootz steel, mixing specific ingredients like wood from *Cassia auriculata* and leaves of *Calotropis gigantea*, and, other ores from the particular Indian mines. These ingredients were used during the forging process in steel industries resulting in the formation of petite cakes. These tiny cakes are called wootz steel, and, the steel formed from these was wootz steel. During this process, and, related ones, like thermal cycling and cyclic forging, catalytic segregation of elements into a different array was induced [5]. Carbon nanotubes and cementite nanowires were noticed in the microstructures of wootz steel. In ancient India, a sophisticated thermomechanical treatment related to forging and annealing had been in practice. This technique has been applied to refine steel with specific qualities. For this purpose, wootz steel cakes were used. This technique was developed and spread globally. The medieval bladesmiths could use a mineral called cohenite to reduce the brittleness of cementite (having carbon contents of 1-2% wt). Mechanical processing makes microstructure of steel to be fine-grained and superplastic at an appropriate high temperature. The addition of tiny amounts of vanadium, chromium, manganese, cobalt, nickel and other, resulted in specific bonding of cementite during thermo-cycling at temperature lowers than the formation of cementite (around 800°C). Actually, during this treatment, the formation of cementite nanowires takes place at the microstructure level [6, 7]. History of nanoscience and nanotechnology is traced at a much earlier stage. Famous glass, Lycurgus Cup; a product of the 4<sup>th</sup> century, is known for its dichroic behavior because of the presence of colloidal gold and silver particles in the glass. These

## Nanomaterials and their Behavioral Aspects

**Abstract:** Nanomaterials exhibit some extraordinary features. These features are the bases for their applications in different fields such as biomedical, pharmaceuticals, communication, warfare, clothing, sports industries, automobiles, *etc.* Reports reflect on their interactions with abiotic and biotic components of the environment. It is very imperative to understand their interactions with biomolecules or related materials. These investigations elaborate on their benefits and, damaging effects; these ascertain their appropriate applications. The concerned reactants may be natural, organic, or inorganic. Nanomaterials interact with components of an environment in a medium like air or water, on the bases of their specific structure and functional groups. During such interactions, the physiological and ecological parameters of the environment also play a significant role. The physicochemical properties of nanomaterials and surface functionalities are due to the specific modifications of the nanomaterials. The hydrophobicity or hydrophilicity of nanomaterials influences their interactions between them and the biological and ecological systems. This chapter deals with the behavior of nanomaterials, parameters, and conditions related to their interaction in a biosystem.

**Keywords:** Absorption, Applications, Drug delivery Systems, Nanomaterials, Physicochemical Properties, Plasmonic Nanoparticles, Scattering, Surface Energy, Tissues Engineering.

### INTRODUCTION AND OVERVIEW

Nanomaterials are present in the environment and influence its abiotic and biotic components. Although the world nano is relatively recent, the term, minimal particulate matter, as earlier conceived, has left its impact on animals, fungi, microbes, and plants. These particles are the products of human and natural activities or processes such as combustion, volcanic eruptions, forest fire, dust storms, tornado, domestic dust, and anthropogenic activities, *etc.* Many misconceptions or miss apprehensions, like bad air, bad/evil spirits, phobia, *etc.*, are associated with the nanomaterials. Research about nanomaterials reveals their link with respiratory, cancerous, cardiovascular diseases and mortality, *etc* [1]. During this period, these particles have not been precisely defined, characterized, or classified. Their impacts are also not technically analyzed or understood. Such particles differentiate as coarse, ultra-fine, and very fine-textured particles, (bhasm). These are used in different medical branches like Ayurveda, Homeo-

pathy, or Unani Medicine for the treatments. The inception of the nanoscale is helpful in the characterization of nanomaterials, and the related investigations enhance the understanding of mechanisms concerning their interactions with biotic and abiotic components of the environment [1].

Studies related to nanomaterials involve size, shape, and, physical features, and, characterization under the guidance of the principle of materials science and metrology (the science of measuring). Such investigations reflect on the term nanoscale (material with at least one dimension in the range  $10^{-9}$  m or 1-100 nm). Studies related to the structural and functional aspects of nanomaterials elaborate on the unique physicochemical, optical, electronic, electrical, and thermal conduction and mechanical properties, *etc.* These understandings lead to the successful micro and macro fabrications and strengthen the concept of nanotechnology, its commercialization, and commoditization [2 - 4].

## **DEFINING NANOMATERIALS**

Usually, a state or a phase of matter is defined to ease its detailed description and for identification or nomenclature. This process is solemnized based on the specific features or properties or the impacts of that matter or state. Defining nanomaterials is relatively an area of active scientific and policy-related debate [5]. Maynard (2011) expressed his view against characterizing the manufactured nanomaterials. Related definitions are helpful in identification, description (at least to some extent) of the mater under consideration to assign them a specific nature or impact as benign or hazardous. Understandably, matter at nanoscale exhibits different specific properties as compared to their corresponding bulk forms. Defining the nanomaterials helps to know about their safety, impacts, and concern precautions against their derogative effects. This topic is subjected to legitimate public concern, adaptation, and political acceptance or response and overall industrial applications. Hence, an appropriate definition is a need, even though nanomaterials show heterogeneous nature. Their category defines nanomaterials, impact on human health, and environmental risk. There are chances that technical definitions based on parameters like size, maybe deficient or insufficient but may be helpful to evaluate the risks involved in their commercial production, investment, and marketing aspects [6 - 8].

The following are the definitions approved by some of the global regulatory authorities.

1-”Nanomaterials are insoluble or biopersistent. These materials are either intentionally manufactured or fabricated with one or more external dimensions or an internal structure with the scale from 1 to 100 nm”. This definition is

regulatory and is proposed by the European Commission on cosmetics Directives. Nanomaterials include under the cosmetic category [9].

2-”The products under FDA regulation are useful in engineered nanomaterials. The prime parameters include dimension and that should be within 1nm to 100 nm range or the physical and chemical properties or biological effects that change the dimension of the nanomaterial”. This definition is a piece of advice, but this agency suggests no formal description. Cosmetics, pharmaceuticals, food, and food packaging materials come under these guidelines [10].

3-”There are mostly only outlines that are advisory definitions related to the nanomaterials that are involved in products. Such materials should be solid at 25°C and atmospheric pressure with particle size within 1nm to 100 nm at least one dimension. The materials should show unique and novel properties because of the size, the engineered particles or the aggregates and agglomerates should be within the range but not greater than 10% by weight and dimension less than 100 nm”. These are advisory definitions and applicable to all products excluding cosmetics, pharmaceuticals, food, and food packaging materials [11 - 13].

4-”Nanomaterials means a natural or manufactured active or non-active substances containing such particles, in an unbound or as an aggregate or as an agglomerate and where for 50% or more of the particles in the number, size distribution, one or more external dimensions having the size range 1nm- 100nm. The particles of fullerene, graphene flakes, and single-walled carbon nanotubes and that have one or more external dimensions below 1nm are grouped as nanomaterials” [14].

5-”Substances produced in the nanoparticulate state define as substances containing unbound particles or aggregates or agglomerate of those particles where 50% or more of the particles in number, size distribution have one or more external dimensions within the size range of 1nm -100 nm. The definition excludes natural, non-chemically modified substances and those for which the fraction in the 1nm-100nm range is a by-product of human activity”. These are the regulatory definitions based on a complex set of exemptions [15].

## **USES OF NANOMATERIALS**

Nanomaterials are of multi-utilities and are in use in varieties of industries. The silver, silicon dioxide, potassium, calcium, iron, zinc, phosphorous, boron, zinc oxide, and molybdenum nanomaterials are applicable in the field of agriculture. Tungsten, disulfide silicon dioxide, boron, clay, titanium dioxide, diamond, copper, cobalt oxide, zinc oxide, boron nitride, zirconium dioxide,  $\gamma$ -aluminum oxide, palladium, platinum, cerium-IV oxide, carnauba, aluminum oxide, silver, calcium carbonate, and calcium sulfonate are useful in the automotive/automobile industries. Silver, titanium dioxide, gold, carbon, zinc oxide, silicon dioxide, clay, sodium silicate, kojic acid, hydroxy acid, *etc.*, are used in the cosmetics either



## Biocompatibility and Bioavailability of Nanomaterials Outline

**Abstract:** Biocompatibility, biodistribution, and bioavailability are essential aspects of those nanomaterials that are used in the field of biological, biomedical, and biotechnological sciences. These are applicable like agents for the drug delivery system, biomolecules, biomedical applicants, biosensors, theranostics, *etc.* These aspects are intricately interdependent and play prime roles in successful applications of nanomaterials. The physicochemical features of cell, biosystem, and nanomaterials play a significant part in these processes. The nanomaterials can be modified or functionalized by various techniques or by conjugating with a variety of molecules that have specific functional groups or phase transfer of the nanomaterials. The highest degree of biocompatibility of the nanomaterials is attained by minimizing the cytotoxic, genotoxic, and other derogative impacts of nanomaterials with respect to the physiology of a biosystem. Bionanomaterials should be hemocompatible, histocompatible, and cytocompatible for their successful performance. Nanomaterials are functionalized or modified suitably to achieve the selected performances. This aspect needs to alter the physicochemical properties, the surface topography of the nanomaterials that permit the smooth functioning of fabricated nanomaterials. In this chapter, the biocompatibility of nanomaterials, strategies involved, probable pathways along with some examples have been reviewed. This will provide an overview of these significant aspects related to the interaction between nanomaterials and the biosystem.

**Keywords:** Bioavailability, Biocompatibility, Biodistribution, Biodispersibility, Functionalization of nanomaterials Hydrophilicity, Hydrophobicity, Wettability.

### BIOCOMPATIBILITY, BIODISTRIBUTION, AND BIOAVAILABILITY OF NANOMATERIALS IN BIOSYSTEM: AN OVERVIEW

Biocompatibility is the ability of any material to accomplish specific functions safely within a biosystem [1]. Biocompatible materials are considered to exhibit non-interfering behavior towards the biological system. The non-interfering response is related to non-thrombogenicity, non-allergenicity, non-carcinogenicity, and non-toxicity [2]. Biocompatibility is either long term or short term, explicitly concerning tissue-engineered and biomedical devices. The biomedical devices are used to evaluate, treat, augment, and replace tissue/organ and to either rectify or support the functional aspects of the organ or tissue. The

surfaces of the bionanomaterials act as an interface when these interact with biomolecules, like proteins, and cell, and cell organelles. Under these conditions, biocompatibility relates to the contextual concepts like cytotoxicity, sensitization, irritation, and genotoxicity, the success of implants, hemocompatibility, carcinogenicity, tissue engineering, biodegradability, and biodistribution. Williams suggested that there is nothing like biocompatibility, but it is the response of the biosystem towards the structure and functional components of administered nanobiomaterials [3].

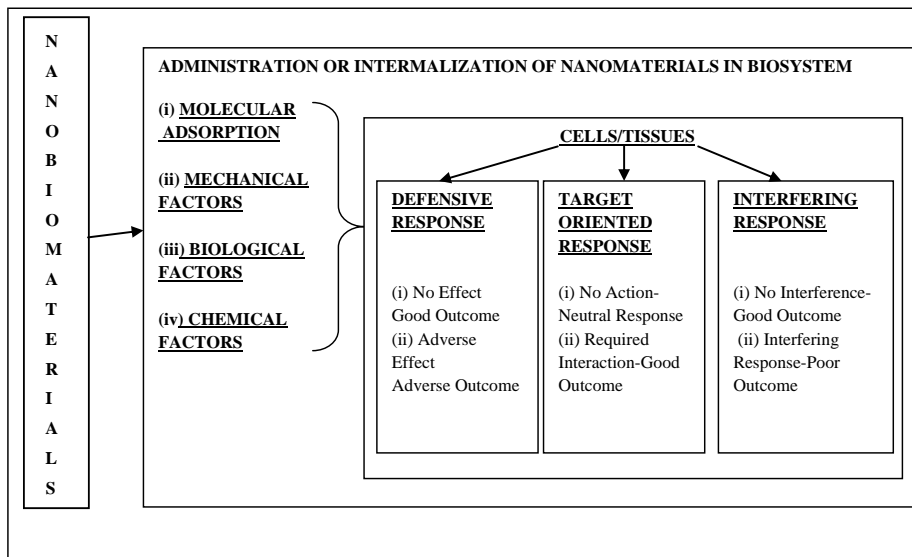
Properties like hydrophilicity and hydrophobicity depend on the nature of the surface of the nanomaterials and the medium. The surface topography or presences of adsorbed, crystalline, or amorphous molecules also play significant roles in biocompatibility, biodistribution, and bioavailability of nanomaterials in a biosystem. Hydrophilic molecules containing groups like  $\text{COO}^-$ ,  $\text{OH}^-$ ,  $\text{NH}^2$  or  $\text{SO}_3\text{H}^-$ , influence the hydrophilic nature of nanomaterial, while groups like  $\text{CH}^3$ ,  $\text{CH}_2\text{-CH}^2$ , chains, and rings of hydrocarbons, elevate the degree of hydrophobicity of nanomaterials [4].

Biological membranes exhibit attractive and repulsive responses towards water molecules. The compositional material of the layer and the corresponding surface chemistry plays a significant role during the interaction with water. One aspect of this interaction is wettability. Wettability of a material is related to a particular surface property that yields a unique value for that material. The value of the surface tension of a substance is an essential factor when wettability is under consideration. Wettability of a given substance in the specific liquid helps to measure the contact angle between a solid surface and a droplet on that surface. The surface tension is a product of internal forces that exist between two different materials. When two materials, say liquid droplet and solid surfaces, come in contact with each other and form an interface or a boundary. The force of surface tension is due to the tendency of all materials to reduce their surface area in response to the unbalanced state among the intermolecular forces. These forces are active at the point of contact between the two materials. The significant fundamental comparison of surface tension helps to understand the principle of wettability. Generally, liquids having lower values of surface tension readily spread on materials (liquids/solids). Liquids having higher amounts of surface tension do not show this tendency. This feature of a material affects its hydrophilic and hydrophobic behavior. When the multi-component solution is under consideration, its expression relates to the surface tension that depends on solubility complications of the said solution [5, 6].

The nature of a membrane and the wettability of any materials play a significant role in the degree of biocompatibility, biodistribution, and bioavailability of

nanomaterials in a biosystem. Particles that foul in the aqueous medium tend to be hydrophobic in behavior. Colloids, starch, metal colloids, complex-ion aggregates, groups of molecules, liquid-solid; and liquid-liquid suspensions or environment exhibit hydrophobic behavior. Proteins have positive and negative charges but also have a hydrophobic region and behave like hydrophobic materials. Other hydrophobic materials include clays, silicates, alumina, ferric hydroxide, oil particles, paraffin, surfactants, and greases, *etc* [5, 6].

Particles that foul in the aqueous medium tend to be hydrophobic in behavior. Colloids, starch, metal colloids, complex-ion aggregates, groups of molecules, liquid-solid; and liquid-liquid suspensions or environment exhibit hydrophobic behavior. Proteins have positive and negative charges but also have a hydrophobic region and behave like hydrophobic materials. Other hydrophobic materials include clays, silicates, alumina, ferric hydroxide, oil particles, paraffin, surfactants, and greases, *etc* [5, 6]. Generally, hydrophobic particles tend to cluster or group. This behavior lowers the interfacial free energy, *i.e.*, surface tension. There is a formation of bigger spherical particles because the spherical shape has the minimum surface area, and its exposure is limited to the hydrophilic environment. Utilizing modified surface chemistry that functions like the hydrophilic component is a useful technique to regulate the process of fouling of membrane [7, 8]. The probable pathways of intracellular biocompatibility of nanomaterials are shown in Fig. (1).



**Fig. (1).** The probable pathways of intracellular biocompatibility of nanomaterials.

## Physicochemical Aspects that Influence the Interactive Behavior of Nanomaterials

**Abstract:** Nanomaterials have occupied ubiquitous status in present-day life. Nanotechnology has become the backbone for technical aspects of energy-storing, communication industries, domestic, health, and safety, *etc.* Interactions and behavior of nanomaterials are the primary concern among the related research fraternity. The main focus is on the mechanisms involved in the interactions and the responses of nanomaterials concerning abiotic and biotic components of the environment during the pertinent research. The interactions and behavior of nanomaterials follow the basic principles of physics, chemistry, material science, biological sciences, *etc.* Nanomaterials abridge the atomic and molecular state of the matter and the respective bulk forms. In such interactions, the quantum mechanics and tunneling effect, parameters like, inter and intramolecular binding forces, hydrophobicity, and hydrophilicity, net charges, *etc.*, have functional significance. Nanomaterials exhibit the ability to get precisely designed as per the assigned functions. As a result, such nanomaterials act as preferred options in different fields like vehicles for cargo and diagnostic tools, *etc.* In this chapter, the functional roles of the physicochemical parameters and related forces are reviewed regarding the behavior of nanomaterials in the biosystem.

**Keywords:** Coulomb Forces, Electrostatic Forces, Hydrophilicity, Hydrophobicity, Intermolecular Bonding, Magnetic Properties of Nanomaterials: Quantum Mechanism, Optical Properties of Nanomaterials, Tunneling Effect.

### INTRODUCTION AND OVERVIEW

Currently, nanomaterials and nanotechnology act as the backbone in current industrial, biomedical, and academic research scenarios because nanomaterials are in use for most of the day to day life products. The behavior of nanomaterials in the biosystem is ambiguous and needs investigation concerning mechanisms involved in nanomaterials, and biomolecules, and cellular components. Nanomaterials have the advantage of being designed as per the required assigned functions to enhance avidity for interactions with a specific target such as biomolecules and cellular components. These materials interact in a derogative or helpful manner within a biological system based on their unique reactivity. The probable derogative impacts are on biomolecules, cells and tissues, and potential

interferences during these interactions. Natural and engineered nanomaterials pose challenges regarding the uncertainty about their health-hazardous potential and approvals from various regulatory authorities at different levels, *etc.*

Nanotechnology ensures appropriate designing, fabrication, and synthesis of nanomaterials with maximum precision so that engineered nanomaterials perform the designated functions. The features of engineered nanomaterials, such as surface properties, charge modifications, size, and shape, enable them to interact with the target moieties. The half-life of nanomaterials is affected while they are in circulation within a biosystem. This parameter implies that such nanoparticles and adducts formed during their interaction require prolonged duration for clearance from the biosystem.

The mechanism and severity of the interactions and behavior of nanomaterials are unpredictable, thereby making it essential to understand the mechanism involved. The current detailed investigations are concerning size, shape, chemical functionality, surface charge, composition, and biomolecular signaling, kinetics, transportation, and toxicity in cell culture and experimental animal models [1]. Properties like chemical composition or surface modification, hydrophobicity, hydrophilicity, and presence of lipophilic groups, *etc.*, of nanomaterials, play a significant role in their interactions and behavior. The ability of nanomaterials to move across most of the biological barriers and to bind with biomolecules specifically, factors or components that inhibit enzyme activity and immune system are the main points that need attention. The presence of metallic group and toxic compounds induces their respective effects during such interactions [2]. Features, like dimensions, shape, the tendency to agglomerate, crystallinity, surface coating, *etc.*, of the nanomaterials, have relatively more cytological capabilities. In a given biological system, nanomaterials having a spherical, tubular, rod, and needle-like shapes, *etc.*, exhibit kinetics of deposition and adsorption [3].

## **NATURAL AND ENGINEERED NANOMATERIALS**

Some of the common examples of natural nanomaterials are present in nature. Nanostructures present in the wings of a butterfly (morph) and peacock modify the interaction between the light waves, and the result is a brilliant blue and green hue. Soap bubbles exhibit iridescence causing varied coloration because the wall of a soap bubble is within the range of nano dimensions. Lotus plants possess some water-resistant nanostructures, *i.e.*, hydrophobic, and water molecules do not adhere to the parts of this plant. An invisible spray of water at the waterfalls or oceanic waves has the nano dimensions. Fine products of the combustion of fuel (soot) are examples of natural nanomaterials. Natural nanomaterials are produced

in nature by natural processes like combustion, volcanic eruption, mining activities, forest fires, anthropogenic physical processes, *etc.* The ambiguous behavior of nanomaterials raises doubts about the validity of their use. Engineered nanomaterials are appropriately designed, fabricated as per the requirements; this reduces the real enigma. Aspects related to derogative or beneficial effects, appropriate utility, half-life, and the clearance from biosystem, *etc.*, and the approvals from a competent authority, are primarily considered during their applications and research. These parameters should get administrative support while designing and fabricating nanomaterials for the set targeted tissue, moiety, or functions. Nanomaterials exhibit unique and intermediate dimensions between atoms and molecules, and the corresponding bulk materials. This feature has a significant role during the behavior of nanomaterials and their applications in various fields like biological, biomedical, theranostics, and other industrial applications [4].

### **SOME FUNDAMENTALS RELATED TO PHYSICS THAT AFFECT THE BEHAVIOR OF NANOMATERIALS**

The behavior of nanomaterials follows some of the fundamentals of physics. Thus, it is appropriate to enumerate some of the prime fundamentals.

#### **Quantum Mechanics**

This mechanism comes quite handy in explaining or understanding the behavior of nanomaterials because the principles involved are relatively strictly applicable to atoms and molecules. Surface to volume ratio gets enhanced at the nanoscale. The quantum mechanism is related to the motion and energy of atom along with the electrons. Since nanomaterials are low dimensional materials, their mass becomes extremely less, and as a result, the gravitational force comes to a negligible level. Under this condition, electromagnetic force becomes the regulatory parameter in controlling the behavior of atoms, molecules, and nanomaterials. Nanomaterials are elementary particles with nano size or elementary particles, and negligible mass exhibits the wave-particle duality concept. Under these conditions, such particles exhibit a wave-like nature, and it may be relatively in a distinct manner. Electrons show wave behavior, and their wave function shows their probable position. Nanomaterials exhibit quantum mechanism and manifest quantum confinement, *i.e.*, nanoparticles of specific metal have electrons restricted within the particular space. This condition of electrons does not exist in the corresponding bulk metal form. Furthermore, electrons exist at a discrete energy level; this is evident in the case of quantum dots where the impact of quantization of energy is displayed [5, 6].

## Interaction Between Nanomaterials and Glycocalyx, Cell Membrane, Cytoskeleton, Cell Organelles and Tissues

**Abstract:** Biosystems are responsive to almost all types of stimuli. These stimuli are in the form of fluctuations in their internal and external environments. Abiota, biota, and nanomaterials are interactive components of the environment. These units exhibit a wide range of reactivity because of their respective physicochemical, biomolecular, biochemical, and biophysical features. Biosystem is a complex unit of biota and these are acellular, cellular, unicellular and multicellular structurally and functionally in nature. Cell being the structural and functional unit of the biosystem, is a well-organized structure exhibiting wide variety, nature, and functions that bring about the sustenance of the biosystem. Nanomaterials are some of the most desired novel materials to be used as agents to carry drugs, as a component of biomedical aids, diagnostic tools, biomedical imaging, *etc.* Inter-actions between nanomaterials and the biosystem are very ubiquitous and at the same time ambiguous. Most of the physicochemical properties of nanomaterials play significant roles and cause impacts on interacting materials. These materials are inorganic, organic, or living. Cellular uptake of nanoparticles is a common phenomenon and has a wide range of applications in the field of nanomedicine from cell tracking, cellular to molecular imaging, disease targeting, drug/gene delivery, diagnosis, and therapy. Nanoparticle-based diagnostic or therapeutic applications are mainly attributed to the various methods of functionalization and localization in the cellular and subcellular compartments. The pre-requisite for the nanoparticle-based therapeutic applications mainly involves the mechanisms of the uptake of the nanoparticles which also determines the fate of these nanoparticles for effective efficacy. Applications of nanomaterials are dependent on the regulated interaction between biota and abiota of the environment. The wide range of functionality of nanoparticles is because of their physicochemical properties, ability to get modified or formulated readily, as per the need, and the greatest flexibility among the adaptability of biota. The potential use of nanomaterials may be the cause of their derogative impacts on abiota and biota. It is one of the prime concerns during development, formulation, and applications in varied fields to provide insight into the interactions between nanomaterials and the biosystem. One must understand the intricacies of their interactions within biosystems.

**Keywords:** Biocompatibility, Cellular-uptake, Cell membrane, Cytoskeleton, Cellular-uptake, Caveolae-mediated endocytosis, Clathrin-mediated endocytosis, Enhanced permeable and retention effect, Glycocalyx, Internationalization of nanoparticles, Phagocytosis, Proton sponge effect.

## OVERVIEW – NANOMATERIALS AND BIOSYSTEMS

Interaction between nanomaterials and biosystems is very unique. Most of the physicochemical properties of nanomaterials have their impacts on interacting material may it be inorganic, organic, or living beings. Applications of nanomaterials are dependent on the regulated interaction between biota and abiota of the environment. Biosystems are basically very responsive to the external as well as internal stimulations and the fluctuations. Let us label abiota, biota, and the nanomaterials as the reactive components of the environment. Biological reactive components and the nanomaterials exhibit a wide range of reactivity because of their physicochemical, biomolecular, biochemical, and biophysical features. This overall complex phenomenon needs a thorough understanding to make the best of the situation. In the last few decades, nanoscience and nanotechnology have made enormous progress and made nanomaterials as most suitable options for almost all aspects of industries, food technology, agriculture, pharmaceuticals, cosmetics, clothing/garment, military ware fare, chemical technology, *etc.*, the list seems to be endless. This range of functionality of nanoparticles is dedicated to their physicochemical properties, ability to get formulated and modified as per the need, and the highest degree of adaptability of biota. Increasing concern about the potential use of nanomaterials may be the cause of their derogative impacts on abiota and biota. To provide insight into the interactions between nanomaterials and biosystems, one must understand the intricacies of their interactions with biosystems.

Biosystem itself is a complex unit of biota. This unit is acellular, cellular, unicellular and multicellular structurally and functionally in nature. The cell is the structural and functional unit of the biosystem is a well-organized structure exhibiting wide variety, nature, and functions that bring about the sustenance of the biosystem. The cell is bounded by a cell membrane that is enveloped by glycocalyx externally and strengthened by the cytoskeleton internally. The component of the cell membrane is in communication with external as well as internal environment. Within the cell, cell-organelles are organized depending on the type of the cell involving endoplasmic reticulum, cytosol, cytoskeleton, and the ambient physiological fluid in and around each cell organelles and the cell itself. The interaction between nanomaterials and cells, tissue seems to be very crucial in nature.

Nanomaterials are some of the most desired novel materials to be used as agents



to carry drugs, as a component of biomedical aids, diagnostic tools, biomedical imaging, *etc.* This reflects on the probable biocompatibility of varied nanomaterials to the biosystem. Thus nanomaterials should be biocompatible and should exhibit fairly good biodistribution. These aspects play major roles during designing and formulation of natural nanomaterials and also the engineered nanomaterials to accomplish the set target, may it be a cancerous cell, diseased tissue, and should not harm the normal or nontargeted tissues. Currently, there are many types of nanoparticles that are synthesized and being used for a variety of biological and biomedical applications. Among them to name a few are the iron oxide nanoparticles, gold and silver nanoparticles, quantum dots, polymeric nanoparticles, lipid-based nanoparticles, carbon-based nanoparticles, *etc.* Most of these nanoparticles are prepared either by a bottom-up approach or a top-down approach. The most important aspect of the synthesized nanoparticles is that they are immiscible in water and have very less water solubility due to which they cannot be used directly for the biological applications due to a variety of changing physiochemical properties such as their aggregation in the solution or at physiological pH which leads to toxicity, or aggregation based macromolecular formation losing their inherent properties for which they are synthesized. This ultimately leads to non-biocompatibility and cause toxicity when used for any biological applications. Therefore, the nascent synthesized nanoparticles cannot be directly used for the biological applications unless they are surface modified to make them more biocompatible. The surface of nanomaterials, polymer, and bulk materials are different. In the dry state, there is minimal surface energy. There is a shift of groups referred to as the group mobility. The non-polar groups move to the phase boundary formed with air while under aqueous conditions, the polar groups move to the phase of the boundary, *i.e.*, at the periphery. The surface modifications approaches include either covalent modification or non-covalent modification. In case of covalent modification either the small molecule carbohydrates, surfactants, proteins, DNA, RNA, lipids or any synthesized molecule is linked covalently to enhance their water solubility at the physiological conditions.

Compounds having low molecular weight move towards the phase boundary or away from it. As a result, there is a change in the properties of the materials under consideration. On administration of synthetic and engineered nanomaterials may face some of the conditions in the biosystem. The first component of the biosystem that comes in contact with the administered nanomaterials is its body fluids. The biochemical components like proteins, lipids, and related molecules present in these body fluids interact with biomaterials either physically or chemically. In blood, the interaction between nanobiomaterials and protein involves adsorption leading to the formation of a layer. This reflects on the hemocompatibility. But this interaction depends on the nature of the protein and

## Interactions Between Proteins and Nanomaterials

**Abstract:** Proteins are among the significant biomolecular constituents in a biosystem. The structure of proteins and the nanomaterials, intracellular interactions, type of the cell, cell organelles, cell signaling and sensation, *etc.*, affect the interactions between proteins and the nanomaterials. The interface formed between proteins and nanomaterials is the original site of contact and the interplay. The behavior of the interacting components reflects on the regulatory aspects, assembly of biomolecules, and various applications in the normal functioning of a biosystem. The fundamentals related to the tendency of biomolecules and nanomaterials help to retain their stable physicochemical conformations. The interactions involving proteins and nanomaterials bring changes in both. It is essential and beneficial to understand the mechanism of these interactions and their impacts on each other. This chapter deals with the nature, structure, and behavior of protein in general and nanomaterials, their stability, the significance of zeta potential, opsonins and their role, protein corona, and the factors influencing their dynamics.

**Keywords:** Biodistribution, Bionanointerface, Nanomaterials, Opsonization, Protein Structure, Protein Corona, Protein Chip, Zeta Potential.

### OVERVIEW OF STRUCTURAL ASPECTS OF PROTEINS

In a biosystem, the prime share of the biomolecules is proteins and protein-related molecules. The internalized nanomaterials encounter proteins and interact with them within a biosystem. These interactions involve the molecular assembly of specific proteins, inter and intracellular communication, and sensation related to the cell and cell organelles. The physicochemical features of nanomaterials, proteins, and adducts formed, affect the beneficial or derogative interplay [1]. A protein molecule is a polymer made up of a specific monomer called amino acids. Generally, a protein molecule is a peptide having a minimum of 40 amino acid residues arranged in an unpredictable linear pattern. A molecule of an amino acid is basic and acidic because it has a primary group  $-NH_2$  at one end and acidic group  $-COOH$  at the other end. Thus, each amino acid exhibits a double function, *i.e.*, bifunctionality. This feature of amino acids tends to link linearly forming peptide bonds involving an amine group of one amino acid and the carboxyl group of another amino acid. The structural, physical, chemical, bio-

chemical properties are related to the substituent present on the side chain of the amino acid. Further, the side-chain substituent plays a vital role in the functionality of the amino acids as acidic, basic, and neutral molecules. This feature also ensures the functions of amino acids as essential amino acids, and these are essential for an individual [2].

A protein may not be a polypeptide as it is a structurally very long polypeptide. Generally, there can be about 40 or 100 amino acid residues to 10,000 amino acids in various proteins. Monomeric and the multimeric proteins are the two categories of protein molecules. Monomeric proteins and multimeric protein classes depend on the type of nature and the number of peptides present in it. A protein molecule having one peptide chain is monomeric protein, while protein molecules having more than one peptide chain is multimeric protein. The peptide chains of multimeric protein are the protein subunits. These sub-units are either identical to each other or different. Insulin is a multimeric protein and consists of two sub-units. Of the two sub-units, one consists of 21 amino acid residues, and the second sub-unit consists of 30 amino acid residues [3, 4].

Proteins are also grouped based on their chemical composition. Simple proteins consist of only amino acid residues and can have more than one sub-unit. All these sub-units are amino acids. The conjugated proteins have one or more non-amino acid entities as their structural components. These components may be either inorganic or organic. These components act as additional fundamental aspects of the protein. Such parts are the prosthetic groups. Proteins are also classified based on the types of prosthetic groups present in their molecules. If a prosthetic group present in a protein molecule is a lipid, the protein is called lipoprotein; when a prosthetic group present in protein is a carbohydrate, the protein is a glycoprotein. Some of the proteins have metal-ion; such proteins are the metalloproteins. Prosthetic groups are a very significant component of a conjugated protein [4].

## **THE STRUCTURAL ASPECTS OF PROTEIN**

The structural aspects of proteins include primary, secondary, tertiary, and quaternary structural components.

### **The Primary Structure**

The primary structure of protein consists of amino acids organized in a linear sequence and constitutes peptide or protein. This sequential arrangement starts with amino-terminal N- and ends at the C-carboxyl terminal of amino acid. There are two terminals on an amino acid residue, one terminal residue shows a free amino group, while the other terminal amino acid has a free carboxyl group.

According to the peptide theory, there are three types of peptides. These are open peptides, cyclic peptides, and branched peptides [5]. The open peptide includes amino acids linked by a peptide bond to form a polypeptide chain. Each amino acid as a unit is residue. A polypeptide chain formed by the same sub-units is an open peptide. Cyclic peptides are composed of mixtures of amino acids containing L and D oliguria residues and glycine. The backbone is composed of H-bonds. These are also cyclic compounds having a peptide bond along with primarily L-amino acids and non-protein amino acids. The cyclic peptides also referred to as cyclotides, are disulfide-rich sub-macro cyclic proteins having around 28 to 37 amino acids. It contains an amide head, and the tail is cyclized peptide as a backbone having cyclic cystine knot. Structurally these sub-macromolecules are chains of polypeptides containing a circular sequence of bonds, *e.g.* cyclosporine [6, 7]. The branched peptides represent a non-continuous chain of carbon bonds and compulsorily have a carbon atom; the carbon atoms show a linear pattern, and it acts as a branching point or branching site. All branches have one or more aspects of the non-continuous link. Such cases are most common in plants [8].

### **Secondary Structure of Protein**

The secondary structure of the protein includes  $\alpha$ -helix and  $\beta$ -sheet ( $\beta$ -pleated sheets). These two components interact with each other, involving a hydrogen atom of an amino group and oxygen atom of the carboxyl group resulting in the formation of peptide linkage. This type of linkage ensures a strong structural and functional backbone of the protein. Alpha ( $\alpha$ ) helix, a component of the secondary structure of protein adopts a coiled spring-like shape; it has an established coiled structure based on hydrogen bonds. Hydrogen bonds are present between the =N-H of amide group and =O of the carboxyl group. This helix is right-handed spirally coiled clockwise. The hydrogen bonds formed are oriented parallel to the axis of the helix formed. One turn of this coiled structure or spiral consists of 3.6 amino acid residues. The H-bond is present between the carboxyl group of one amino acid and the amino group of other amino acid oriented with four amino acid residues. In a given spiral of the helix group, R- is always on the outer side, not within the spiral [4, 9].

The ( $\beta$ ) beta-pleated sheets constitute the second component of the secondary aspect of protein. Two  $\beta$ -pleated sheets are either the same or different in a protein molecule. The two  $\beta$ -pleated sheets are bonded with each other by H-bonds. The H-bonds in peptide linkage and atoms involved are of different regions of a single chain that folds or bends on itself, forming an intrachain bond or comprise atoms that belong to different peptides chain in a given protein molecule. Proteins have more than one intra-chain. A single protein molecule containing a  $\beta$ -sheet should

## Interactions Between Nanomaterials and Genetic Material (DNA and RNA)

**Abstract:** Genetic material is a stable biomolecule in an organism. The intact and integrated transfer of genetic information from the parental generation to the offspring (daughter cells) is essential. This transfer acts as a basis and ensures the conveyance of somatic and sex-linked traits from generation to generation. The DNA contains genetic information and is present in eukaryotes and prokaryotes, while viruses have genetic information either in DNA or RNA. The genetic information plays a prime role in maintaining structural, physiological originality and modifications by retaining the specific pattern of transcription, translation, and replication of genetic material during cell proliferation, cell cycle, cell differentiation, *etc.* Cellular behavior reflects on the structural, functional, and genetic health of a cell, tissues, and an organism. The formulations of nanomaterials are in concern with the targeted moieties. The nanomaterials have spread their tentacles in most of the fields following the functional and procedural aspects of the biological and non-biological sciences. Different types of nanomaterials are produced in order to meet the demands of various domains like biotechnology, biomedical sciences, industrial, material sciences, *etc.* Nanomaterials cause either beneficial or harmful effects in a biosystem and the environment. The disoriented biochemical, biophysical, and biomolecular impacts are due to the adverse effects of nanomaterials on genetic contents. This condition brings disorganized functionality of the genetic information and the cell. The evaluation of their implications on biomolecules like DNA and RNA is essential to understand the mechanism involved. This chapter deals with the overall biochemical, physiological, and biophysical aspects of genetic contents, along with the impacts of various types of nanomaterials

**Keywords:** Annealing, Bionanointerface, Carbon Nanomaterials, Dendrimers, DNA, Histone- Proteins, Hydrophobicity And Hydrophilicity, Quantum Dots.

### INTRODUCTION

Genetic integrity is the foundation of morphological, physiological, and genetic functionality of all the organisms. This genetic information also maintains the phylogenetic status of a species. Studies related to genetics help in understanding the number of malfunctioning in a life form. Genetic integrity appears to be a significant aspect related to the synthesis of proteins that are needed from time to time in the life of a creature. The genetic materials play a prime role in maint-

aining the structural, physiological originality during the transcription, translation, and replication of genetic elements, and the normal cellular functions like cell proliferation, cell cycle, and cell differentiation [1]. There are natural processes like repairing DNA damages; this process retains and restores the originality of genetic materials in species. The rate of repair or restoration of genetic information varies in different cells, tissues, and organisms. Parameters like age, physiological, and pathological status of a species are also related to genetic integrity. A biological cell with damaged genetic material is likely to undergo irreparable dormancy state, senescence, apoptosis, and uncontrolled defective cell division, *etc* [1].

Nanotechnology and nanoscience have made exceptional advancements, and their products have found suitable applications in most of the fields. The nanomaterials are useful and beneficial because of their specific features like small size, the higher surface to volume ratio, ease of modifications of surface chemistry, and their ability to conjugate with multivalent ligands. These physicochemical features enhance the degree of avidity of the fabricated nanomaterials for targets like biological tissues, cells, biomolecules, and cell organelles [2]. DNA forms several alternative structures like non-B forms of DNA. These forms are more in numbers and detected in a genome. These non-B forms of DNA play an active role in the varied cellular processes and cause instability in the genetic information of an organism. These non-B Forms of DNA influence gene functions, regulation of immune response, telomere maintenance, and recombination in a cell. The antigen variations in human concerning pathogens and developmental conditions result in the diversity in the genome of a biosystem. These non-B forms of DNA are concerned with transcription and translation also [3].

The polymorphic form-DNA exhibits different assemblies and conformational forms like right-handed A form, left-handed Z form, triplex, G-quadruplex forms, i-motif forms under different physiological conditions [4]. Sathees and Leiber mentioned the existence of cruciform-DNA, Z- DNA, sticky DNA, slipped DNA structure (RNA–DNA hybrid), E DNA (e-motif) [5]. Different conformational and assembled forms of DNA are potential agents for human diseases. The cruciform (hairpin) form of DNA concerns with genetic instability, male infertility, recurrent abortions, Emanuel syndrome, and polycystic kidney disease. The triplet form causes hereditary neurological disorders, follicular lymphoma, and other types of cancers [5].

## **AN OVERVIEW OF BIOCHEMICAL AND BIOPHYSICAL ASPECTS OF DNA**

A genetic material, *i.e.*, DNA, is bestowed with storing information related to the originality of the cells, species, and also for the functionality of specific cells in an organism. Generally, the genetic material in a life form is stable and intact and is essential for the DNA to maintain its structural, functional, and phylogenetic integrity and identity. This fundamental and technical originality of the genetic information in totality is an essential aspect during normal processes, such as transcription, translation, replication, even during the hereditary transfer from one generation to another. This feature is functionally significant to avoid erroneous genetic configuration. DNA is among one of the macro biomolecules correctly attributed to genetic aspects of an organism and protein synthesis. DNA is a double-stranded bipolar helical structure. The two strands are polymer composed of monomer units referred to as the nucleotide. The monomer unit consists of one of the nitrogen nucleobases among cytosine, adenine, guanine, thymine, pentose sugar (deoxyribose and ribose), and phosphate groups. Phosphate groups and sugar are bounded, and nitrogen nucleobases involving covalent bond and hydrogen bonds. These nitrogen bases are pyrimidines (thymine and cytosine) and purines (adenine and guanine).

The backbone of DNA resists cleavage. Each strand is anti-parallel and coiled around the same axis having pitch 34 Å (3.4 nm) and radius 10 Å (1.0 nm). Mendelkerm and co-workers reported the width of DNA between 22 to 26 Å (2.2 to 2.6 nm) and the size of one monomer unit 3.3Å (0.33nm) [6 - 8]. Primarily two forces maintain the stability of the DNA molecule. The hydrogen bonds are present between nucleotides, and base stacking interactions involving aromatic nucleobases are also responsible. Nucleotide bases align at a right angle to the axis of the DNA, forming  $\pi$ -bonds, thereby reducing the interactions between them [9].

## **PHYSICOCHEMICAL FEATURES OF DNA IMPACT OF TEMPERATURE**

Melting temperature is an essential parameter during its interaction with nanomaterials [10]. DNA is prone to fluctuations in temperature. DNA gets denatured when its double-stranded structure is disturbed or the double-stranded changes into two single-stranded conformations. The denatured DNA elevates the degree of absorption of UV radiation. It is a potential parameter to denature DNA molecules. As temperature increases, the frequency of breaking of Hydrogen bonds between the two strands also increases. A temperature at which 50% of DNA gets denatured, *i.e.*, the double-stranded DNA sample becomes 50% single-

## Interactions Between Enzymes and Nanomaterials

**Abstract:** Enzymes are proteins, but all proteins are not enzymes. Enzyme interactions concern with the biochemical and physiological transformations encompassing most of the life activities. Understanding such events will help to predict particular biochemical, biocatalytic, and enzyme reactions involved. These investigations also help to predict clinical and remedial aspects of dysfunctionalities of physiological processes. Chemical enzymes have their impediments that pose difficulties during their industrial applications. Biological enzymes also referred to as biocatalysts, are chemospecific, and applicable conveniently to carry out varied biological activities. This feature is related to the identification and selection of a particular functional group, among others. This selection is physical or chemical but depends on parameters like the nature of the solvent, atomic orbitals, concentration, pH, temperature, *etc.* Their industrial and biological applications increase using the enzyme immobilization technique. Nanomaterials have occupied significant status in the present day scenario. These materials are better options for this technique because these materials offer features like high specific surface area, improved dispersibility, low mass transfer resistance, *etc.* The mechanism of enzyme activity is quite complicated. The necessary steps incriminated are binding of the enzyme with the specific substrate. The complementary shape, size, charge, hydrophobicity, and hydrophilicity, *etc.*, of a substrate, play a significant role in its binding with an enzyme. Nanomaterials are potential components that act as a matrix during the process of enzyme immobilization. These nanostructures elevate the efficacy of biocatalyst, specific surface area, mass transfer resistance, and loading of the capable enzyme, *etc.* The unique physicochemical features like size, surface properties, ease of modulation of nanomaterials, *etc.*, ensure better performance of enzymes and improve their applications in different fields likes biomedical, pharmaceuticals, biomolecular, food, and packaging technology, agricultural practice, and biochemical investigations *in vitro* as well as *in vivo*. Some of the fundamental properties of enzymes can be modified to suit the functionality concerning the set targets. This chapter deals with the structure, nature, and regulatory dynamics of the enzyme. The enzyme immobilization technique, its advantages, and interactions with different nanomaterials along with biomimicking agents are also discussed.

**Keywords:** Active Energy, Biocatalysis, Biomimicking, Enzymes-Action, Enzyme-Immobilization, Free Energy, Nanomaterials, Toxic-Impacts.

### BIOCATALYSIS

It is a challenge to know about biological activities. Most of the biological activ-



ities are related to or involve proteins, and organic enzymes are proteins. The interactions involving proteins form a considerable umbrella and encompass most of the biological activities and interactions. The catalysts comprise the biocatalysts and regulate such interplays. The biocatalytic events help to predict a particular biochemical, biomolecular reaction that takes place during physiological functionalities. These interactions take place involving either change at the bond level or the reaction center level or similarity at the reaction center. The studies concerning biocatalysts help to understand their potential applications and biomolecular transformations. These transformations assign functions to an enzyme in a sequential biological, biochemical, and chemical reaction [1]. This feature is related to the identification and selection of a particular functional group, among others present on the substrate and enzyme molecule. The choice is physical or chemical but is dependent on parameters like the nature of the solvent, atomic orbitals, concentration, pH, temperature, *etc.* Prediction of such selectivity is quite tricky [2]. The biological catalytic interactions are generally harmless in the sense that they do not form any unwanted by-products. These interactions are occurring in a specific direction; *i.e.*, these prefer to either make or break a chemical bond in one direction. These interactions take place because of the three-dimensional conformation of the reactants. The enzyme and biocatalysts can differentiate between the varied groups present in different zones of the molecule of a substrate. Sometimes two or more compounds have non-identical structural aspects but are not mirror images of each other and exhibit two different conformations [3]. The biocatalysis concerns the enhancement of the rate of the interaction or transformation of biomolecules, organic compounds within the biosystem. The ability of microorganisms to produce enzymes is useful in food technology, beverage, fermentation technology to get the desired commercial products, and to maintain a specific state of the food and other merchandise of economic importance, *etc.* There is a need to produce fine chemicals and other chemicals that are useful in pharmaceutical and related industries, and these based on biocatalytic and enzymatic interactions [1].

There are two types of enzymes namely, endoenzymes and exoenzymes. The secretory cells are the site of the production and location of actions for biocatalyst. Most of the biocatalysts are considered to be endoenzymes. Sometimes an endoenzyme (single molecule) acts as an exoenzyme also. The endoamylase splits larger amylose molecules into smaller chains of dextrin, while exoenzymes operate on the subunits of a polymer at one end of the polymer [4]. The prokaryotic and eukaryotic cells produce exoenzyme. These biological molecules are the product of cells, but these function outside the cell. Exoenzymes are secreted in the cell but act outside the cell. Most of these enzymes break down macromolecules, add a specific group, conjugate

temporarily. These act as participants in a multiplex reaction or associated with two or more subunits of a complex molecule or biological macromolecule. Exoenzymes break down the macromolecules and help in the movements of the smaller micromolecules across the membrane. The subunit molecules conveniently move across the cell membrane or biological membrane. Generally, digestive enzymes come under this group [5 - 9]. The flowchart representing the cellular release of protein enzyme is shown in Fig. (1).

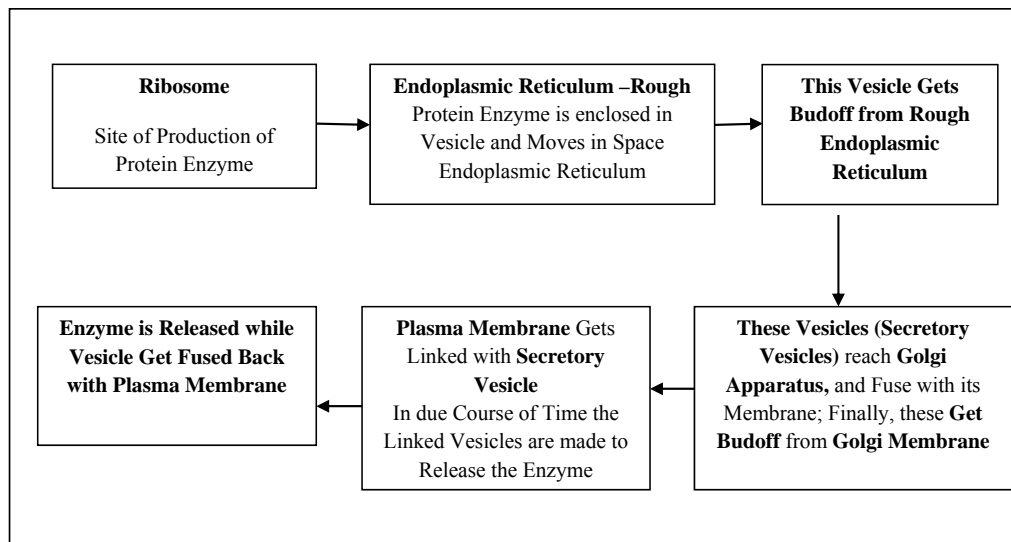


Fig. (1). The flowchart representing the cellular release of protein enzyme.

The biological enzymes are either anabolic or catabolic in action. The anabolic biocatalysts regulate the building up processes leading to the formation of a complex biomolecule from the respective simpler subunits. The resultant complex has a higher molecular weight than the subunits. The photosynthesis, synthesis of proteins, and other macro biomolecules are the products of anabolic enzyme activities. The formation of glucose is one such example. Other examples include synthesis of proteins, nucleic acids, biomolecules, or organic and inorganic molecules having very high molecular weight, complex conformations. During this process, molecular energy in the form of ATP is used up. Catabolic enzymes break the complex molecule with high molecular weight and complex conformation into its sub-units. Such processes release molecular energy in the form of ATP.

The enzymes are macromolecules and regulate specific chemical, biochemical, and biomolecular interactions. These macromolecules act on particular chemicals

## **Nanomaterials and Immune System: Interactions**

**Abstract:** Drug delivery systems, vaccination, and diagnostic imaging are the main aspects that enhance the effectiveness of human health and safety. This system protects an organism against microbes, viruses, parasites, and allergens. The immune system represents the level of the ontogenic and phylogenetic development of a biosystem. The degree of efficiency to protect against infection varies in different organisms. Overall, the functional mechanism of the immune system is complicated. Any molecule, or a pathogen entering the human body or a biosystem, has to face various components of the immune system. It is imperative to understand the concept of the interactions between nanomaterials and the components of the immune system. This understanding will improve, improvise, and elevate the degree of clinical translation of nanomedicine in the field of human health and safety. There seems to be an enormous scope of studies related to the intricacies of interaction occurring at the bio-nano-interface. These efforts will guide to design the rational nanomaterials that are either fabricated or synthesized with specific targets. The study of the modes or the patterns involved during the interactions between nanomaterials and the immune system can maintain the appropriate defense system of the individual against infections, xenobiotics, and any foreign molecule. This chapter deals with the applications of nanomaterials in the delivery system, competence of nanomaterials concerning the immune system, immunomodulation, immunosuppression, immunostimulation, and interactions between various nanomaterials and the components of the immune system.

**Keywords:** Immunomodulation, Immunosuppression, Immunostimulation, Immunological Memory, Nanomaterials.

### **INTRODUCTION: OVERVIEW-IMMUNE SYSTEM IN HUMANS, NANOTECHNOLOGY, NANOSCIENCE, AND NANOMATERIALS**

All organisms have some defense system and specialized mechanism dedicated to the protection against the derogative impacts of microbes, viruses, and parasites, and any agent (xenobiotics) that causes sickness or any form of infection. This protective system exhibits the ontogenic and phylogenic development in different organisms. The mechanism and functionality of the immune system are complicated. Despite enormous research in the field of immunology, still, there exist some lacunae concerning the mechanism involved during the interactions between nanomaterials and components of the immune system. Further, this mechanism becomes more ambiguous because of the wide variety of nanomate-

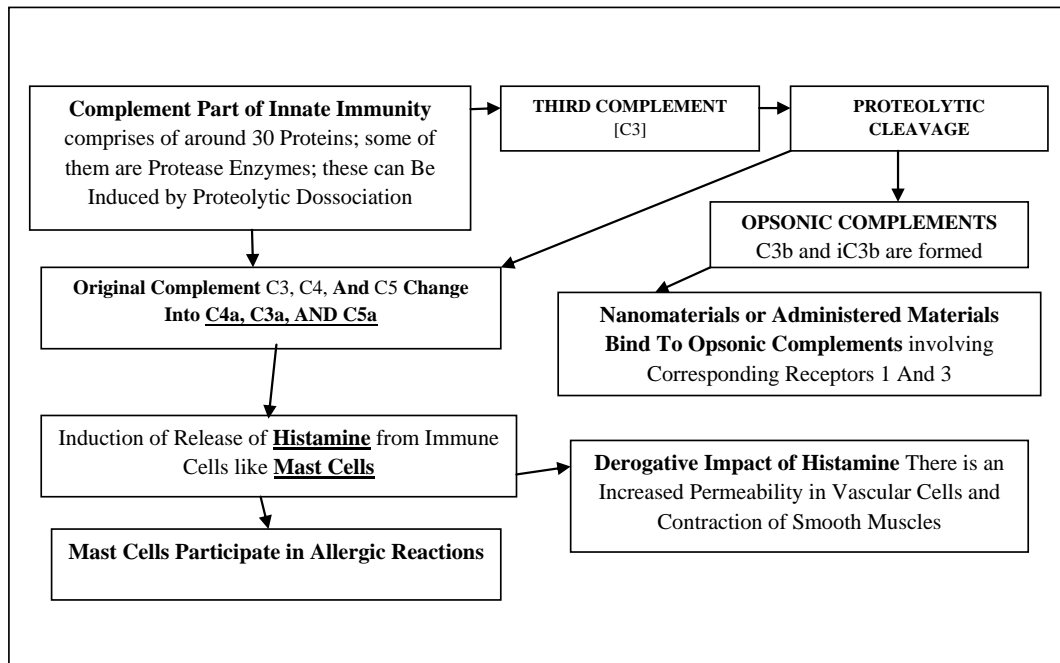
rials. Nanomaterials are the products of nanoscience either fabricated or formulated, as per the targeted applications in pharmaceutical, imaging, biomedical implants, and other related applications.

The blood cells like monocytes, platelets, leukocytes, and dendritic cells in tissues, and macrophages in the lungs, tend to engulf the internalized nanoparticles involving phagocytosis among humans and the vertebrates. The fluid components, like plasma proteins, opsonins, and related complements, also get involved in the interactions between nanomaterials, immune cells, and proteins. These interactions can influence the uptake, biodistribution, and the clearance of the internalized nanomaterials. This response can cause a disturbance in the distribution of nanomaterials and divert them from the target tissue and organ [1]. The immune system has two sub-components, namely, innate and adaptive resistant components. The main features of the innate component (network) are non-specificity and cell-mediated responses. Its humeral parts are present in body fluids. An appropriate exposure causes immediate remedial reactions that may not have immunological memory. The features of adaptive immune system concern with the pathogen and are antigen-specific in function. There is a lag time between exposure and duration of maximal response. The exposure leads to immunological memory. There is a complex conglomerating functionality between protein and the cells that regulate the short term and long term efficacies of the immune system. The innate immunity stands for fast and broad response spectrum affectivity. It utilizes proteins present in the blood, body fluids, and tissues.

Cells, such as macrophages, dendritic cells, neutrophils, mast cells, and natural killer cells participate in innate immunity [2, 3]. Innate immunity is the first line of defense among human beings and is non-specific. Its function depends on the Pattern Recognition Receptors (PRPs) that identifies a broad and conserved molecular pattern of the target. This innate immune system recognizes the foreign bodies that enter in a biosystem. It is also responsible for proinflammatory responses [2]. The adaptive immunity has a high degree of specificity, but slow functionality and antibodies identify the antigen. The cells like B-cells and T-cells play their role in antigen-antibody interaction [2, 3].

Nanomaterials activate the complement system-a component of the innate immune system, significantly. It is a complex system comprising of about thirty proteins; some of these are functionally protease enzymes, and the proteolytic dissociation induces these proteins. These all have a functional role that involves binding interaction with the surfaces of the foreign body. During the process of activation of complement, the third complement protein referred to as (C3), undergoes proteolytic cleavage, resulting in the formation of two opsonic

complements called (C3b) and (iC3b)]. Macrophages identify nanoparticles or administered materials. The distributed materials in the human body bind with this opsonic complement [C3b] and [iC3b], involving corresponding complement receptors 1 and 3 present in the recipient. Nanoparticles follow three primary pathways, namely classical, lectin, and alternative pathways during their cellular internalization. As the activation of complement system progresses, anaphylatoxins (also referred to as biologically active complement peptides namely, C4a, C3a, C5a), are the action of the product of proteolytic enzyme causing cleavage of the original molecules (C3, C4, and C5). These anaphylatoxins induce the release of histamine from immune cells, like mast cells. These immune cells also participate in allergic reactions. The histamine increases the permeability of vascular cells and even during the contraction of smooth muscle. Anaphylatoxins promote some of the physiological conditions, like distressed breathing, acute changes in blood pressure, chest pain, declined output from heat and cardiac arrest, *etc.*, (Fig. 1) [4 - 6].



**Fig. (1).** The flow chart representing the probable process of activation of complement peptides (also called biological active complement peptides).

## Broad Spectra of Applications Based Interactions of Nanomaterials

**Abstract:** Advancements in the nanoscience, nanotechnology and material science involve the principles of fundamental physical, chemical, and biological sciences. These scientific advancements have opened a vast horizon for understanding the mechanisms of the physiology of life and the environment. This progress has also provided suitable materials and appropriate methodology concerning the developments. Nanomaterials are the bridge between the atomic and molecular and bulk form of matter. These nanoscaled materials are modified, fabricated, and reach most of the biological targets in life forms. As a result, these become useful materials for applications in medical sciences, industrial processes, health care, and home security. The biological components, such as cells and tissues in the biosystem and nanomaterials, interact amicably with restrictions concerning their physicochemical features. Nanomaterials exhibit biocompatibility and bioavailability within the physiological environment. This ability is the primary basis of their applications in almost every sphere of investigation, diagnosis, and treatment of ailments. Enzyme technology, DNA and RNA technology, tissue engineering, military, and communications, energy, and many industrial processes are the fields where different nanomaterials are useful and provide beneficial and desired results. In this chapter, various potential application based interactions related to medical sciences, biomolecular investigations, biotechnology, genetic engineering, tissue engineering, environmental aspects, military, *etc.*, have been envisaged.

**Keywords:** Antibacterial nanomaterials, Antifungal nanomaterials, Antiviral nanomaterials, Bladder and cartilage implants, Drug delivery, Nanomaterials and defense, Nanomaterials as biocomposites, nanomaterials as neural, nanotechnology, Nanomaterials for tissue culture, Vascular tracheal implants,.

### OVERVIEW

The nanoscience, nanotechnology, and materials sciences are the basis for the ever-increasing pace of development. These developments meet the challenges related to industrial, health, agricultural, natural, manufacturing, energy, digital expression and communication, neuronal, and cognitive fields. These make provisions for long-lasting technologies that take care of the problems related to these fields and also digital currencies, hydrogen energy storage, brain to brain in-

terface and robotics, *etc.* These fields reflect on many interdependent technologies that influence the society, economy, and the environment. The advancements in the area of nanoscience, nanotechnology, and materials science are the fast-paced changes in materials science. The materials science perceives the matter to be recognizable as functional materials, next-generation materials, and self-assembling materials. The substances that function on the borrowed principles from biological aspects and adopt a new behavior pattern accordingly are considered to be functional materials. Super light and active materials get affected or react in accordance to the environmental changes and generally culminate as smart materials. These original materials come under next-generation substances; can stimulate the components of the environment, the central users. Materials that exhibit self-assembly behavior constitute a large scale, very precise, able to improve their properties concerning strength, tear resistance, conductivity, *etc.*, and are included in next-generation substances [1].

Matters get organized in different types and this organizing concerns with the current advancements in materials science. Smart materials are the material with one or more specifically modified properties. The external changes or stimuli like stress, electric or magnetic field, temperature, pH, moisture, *etc.*, help in such modifications during the designing of these materials. Thermo bimetal self-regulate and consume energy for a more extended period. Furthermore, these bimetal are activated thermally and can make glass to shade after being exposed to sunlight. Superomniphobic materials can float on aqueous fluid and repel oil. These behave like water bugs on the surface of the water pond. Auxetic contents change their thickness under force. These become thicker in the perpendicular direction to the direction of force applied. These materials either have hinge-like structures, or some of their parts act like a hinge, which gets flexed under stretch. Such auxetic materials are suitable for packaging, pads for knee and elbow, robust shock absorbing material, sponge materials for mops, and materials for body armor, *etc.* Aerogels are ultra-light porous materials, and they are modifications from the gel after replacing the liquid present by air or gas. Aerogels have extremely low density, conductivity, and give polystyrene (Styrofoam) feel when touched. These materials are useful to improve thermal insulation, as chemical absorbents to clean the spills, these are suitable materials for electrochemical supercapacitors, and shock absorbers. Biomaterials are derived from natural sources or synthesized in the laboratory. These materials are appropriate to replace or increase the inherent functionality of the organ or body part. These are the potential materials to improve the drug delivery system and degree of acceptance of graft among transplants. Graphene consists of only carbon elements. The arrangement of the carbon atoms in a typical hexagonal pattern, forming a single sheet with thickness, equals the thickness of one atom. These materials are very light but strong and similar to graphite [2]. These nanomaterials

are suitable for the use of low-cost solar cells and display screens in inexpensive mobile devices. These are suitable to store hydrogen for cars powered by the fuel cell, like biomedical and chemical sensors, ultracapacitors and faster-charging batteries, *etc.* Graphene nanomaterials are advantageous for use in integrated transistors. These form the functional components of actuators, nanoelectromechanical systems (the devices that integrate electrical and mechanical systems functionally). These systems also include pumps or motors and good options for physical, chemical, and biological sensors.

Nano-factories are the devices that act as nanomachines. These interact with reactive molecules involving mechanosynthesis and form correct assembled structures of organic products. These products follow a specific arrangement of the macroscopic sized pattern with atomic precision. A material product with large scale assembly exhibit specific behavior, *i.e.*, in an organized system, the components form an organized structure with its local parts in a particular sequence. Thus, the bottom-up approach results in the formation of 3D sequenced structures like DNA, RNA, and protein that come in this category. Substances under metamaterial have specifically and precisely arranged geometrical shaped materials and influence light and sound unconventionally. Such materials are useful in aerospace devices, devices to monitor fractures, and to manage smart solar power devices. Self-healing materials are referred to as intelligent materials work as a biological system, and incorporate a repair mechanism helping the healing of damaged tissues. These materials include polymers, ceramics, and can rectify intrinsic damage caused due to the devices. These materials also reduce the impact of degradation, enhance life span, and are cost-effective [1, 3]

## **VARIOUS APPLICATIONS OF NANOMATERIALS**

Tremendous advancement has taken place in all spheres of life due to the innovative technologies in recent times. Improvements in the fields of nanotechnology and materials science have played significant roles in these advancements. These two disciplines provide methodologies and suitable materials for specific applications for such developments. Nanomaterials are aptly modified or fabricated those help involvements in different investigations and brought successful and useful applications in industries, health care, and home security in addition to the cosmetics and pharmaceutical advancements.

### **Nanomaterials for Drug Delivery and Biomedical Applications**

Drug delivery is the fundamental aspect of health care and safety; it delivers genes, biomolecules, and drugs to a specific site in a biosystem. Parameters like an increased area of the reactants that offers a more significant number of atoms and molecules that interact, bind, adsorb, and facilitate the delivery process.



**SUBJECT INDEX****A**

- Absorbance 29, 223, 238  
 hypochromic 238
- Acids 23, 25, 77, 78, 79, 82, 117, 122, 141, 153, 154, 156, 157, 162, 195, 196, 201, 202, 208, 225, 265, 277, 279, 283, 286, 307, 349, 352, 357, 358, 337
- 6-amino penicillanic 277
- 16-mercapto-hexadecanoic 358
- arginyl glycocylate aspartic 156
- ascorbic 77, 352
- cellular retinoic 279
- complex molecule N-acetyl neuraminic 162
- folic 154, 265
- humic 195, 196, 202
- hyaluronic 157
- kojic 23
- lactic 307
- malolactic 265
- mercaptoundecanoic 79
- polyglycolic 349
- polyinosinic 208
- polylactic 82, 307, 337, 349, 357
- polylactic acid-co-glycolic 349
- silicone phosphoric 122
- sulphonic 78
- tannic 141
- uric 352
- Acquired immunodeficiency syndrome 359
- Actin 152, 156, 166, 167, 168, 169  
 assembly 152  
 network acts 169  
 polymerization of 169
- Action 73, 82, 115, 140, 154, 249, 287, 289, 344  
 concentration-dependent toxic 115  
 enzymatic 154, 249  
 homeostatic 82  
 intense antimicrobial 344  
 neutral response 73  
 proton pumping 140  
 synergistic 287, 289
- Acute phase proteins (APPs) 186
- Adaptive resistant components 299
- Adenocarcinoma 112
- Adhesion 10, 11, 106, 116, 157, 159, 160, 163, 166, 167, 304, 311, 345, 349, 355, 356  
 cellular 157, 160, 345, 349, 355, 356  
 mucosal 304  
 physical 106
- ADP-ribose polymerase 168
- Affinity capillary electrophoresis techniques 204
- Albumin 145, 153, 192  
 -bound nanoparticles 145  
 receptors 153, 192
- Alkaline phosphatase activities 280, 283
- Alzheimer's disorder 335, 336, 337
- Ampere's law 33
- Analytical 30, 31, 209  
 microchip 209  
 techniques 30, 31
- Antigens 137, 149, 185, 186, 187, 299, 303, 305, 313, 316, 321, 322, 323, 360  
 classical pathway 149  
 encapsulated 321  
 encapsulating 321  
 function-associated 137  
 vaccine 360
- Anti-HIV-agents 339
- Anti-immune diseases prevention 302
- Antimicrobial activity 345, 346, 347  
 concentration-dependent 347  
 restricted 347
- Apolipoproteins 83, 204, 336
- Apoptosis 74, 109, 110, 145, 168, 187, 221, 312, 315, 319, 338  
 mitochondrial 168
- Application of immobilization 278  
 in food technology 278  
 of enzyme in biofuel technology 278
- Applications and significance of protein corona 197
- Apurinic DNA hydrolyzes 225
- Arterial natriuretic peptides secretion 158

- Artificial chaperons 11, 206  
Aspartate 280, 284, 285  
  aminotransferase 280  
  transaminase 284, 285  
Atomic force microscopy (AFM) 106, 232, 341  
Autoimmune diseases 301, 304, 306, 308  
Auxetic contents change 332  
Auxiliary H-bond donor 236  
Azido purine horseradish peroxidase enzyme 147
- B**
- Bacillus subtilis* 347  
Bacterial 195, 320, 349  
  activation activity 320  
  cellulose-collagen nanocomposite 349  
  exo-polysaccharides 195  
Binding 76, 138, 157, 160, 188, 193, 196, 203, 205, 232, 236, 239  
  affinity 188, 193, 196, 236, 239  
  capacity 76, 239  
  efficiency 157  
  entropy 232  
  interactions, receptor-ligand 203  
  of immunoglobulins 160, 205  
  protein 138  
Binding energy 37, 54, 163, 237, 239, 240, 241, 242, 243, 249  
  order, restricted 237  
Binding process 242, 266, 279, 314  
  direct protein 314  
Bioactive textiles 359  
Bioavailability of nanomaterials 9, 71, 72  
Biocatalysts 13, 261, 262, 263, 264, 265, 270, 274, 288, 350  
  anabolic 263  
  exquisite 265  
Biocatalytic 12, 261, 262  
  pharmacy-based industries practice 12  
Biochemical 97, 358  
  redox interactions 97  
  sensors 358  
Biomolecules 1, 8, 9, 83, 85, 94, 123, 124, 141, 142, 180, 197, 200, 203, 208, 209, 210, 228, 243, 246, 250, 251, 263, 273, 301, 305, 313, 335, 351, 353, 354  
  complex 263  
  endogenous 305  
  flexible 246  
  influences proteins 142  
  left-handed double-helical 228  
  mobilizing 209  
  multifunctional 246  
  polycationic 243  
  polymer 246  
  prime 251  
  single-stranded functional 250  
  transfer 141  
Biosensors 71, 75, 272, 277, 279, 285, 350, 351, 352, 353, 354  
  developing nano 352  
  field-effect 354  
Bladder cells 356  
  cancerous 356  
  smooth 356  
Blood 84, 88, 112, 145, 152, 208, 311  
  circulatory system 145  
  coagulation 88  
  intoxication 311  
  macrophages 112  
  proteins 84, 152, 208  
Blood flow 143, 145, 157, 193, 357  
  abnormal 145  
  average rate of 193  
Blood vessels 144, 145, 156, 158, 193, 194, 204, 357  
  clogging 204  
Body fluids 10, 11, 83, 84, 86, 137, 159, 191, 192, 193, 194, 195, 203, 299, 310, 323, 324  
  components of 323, 324  
  human 137  
  influence 159  
Boltzmann equation 101  
Boltzmann's constant 101, 234  
Bone marrow 112, 115, 302, 316, 320  
  formation 115  
  suppression 302  
Bone tissue 349, 356  
  engineering 349  
Bovine serum albumin (BSA) 79, 202, 204, 205, 208, 244, 305  
Bragg's Law 38  
Brain 336, 337, 358  
  cancer 337  
  neurotransmitter 336  
  rain stimulation 358  
BSA 205, 208

- fetuin proteins 208
  - gold nanoparticles interact 205
- C**
- Cancer 98, 111, 153, 221, 303, 304, 306, 308, 322, 335, 350
    - breast 111
    - colorectal 322
    - prostate 322
  - Cancer cells 87, 139, 143, 153, 154, 210, 361
    - cervical 139, 154
    - lung 361
  - Candida albicans* 338
  - Candida rugosa* 275
  - Carbohydrate recognizing domain (CRD) 186
  - Carbon-based nanomaterials 3, 11, 88, 115, 167, 238, 313, 314, 335, 345, 346
    - single-layered 346
  - Carbon nanomaterials 51, 53, 87, 241, 272, 281, 282, 312, 313, 338, 341, 346, 353
    - masked 313
    - natural 241
  - Catalase enzyme 74, 277, 286, 287
    - action 74, 287
    - natural 74
    - technique 74
  - Catalase phosphoryl transferability 267
  - Catalysis, acid-base 246
  - Catalysts 24, 78, 123, 249, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 276, 277, 278, 287, 288
    - adsorbed 269
    - alkaline 123
    - based biological 267
    - biological 278
    - chemical 24, 264, 278
    - co-localized 274
    - heterogeneous 273
    - homogeneous 249, 273
    - immobilized 270
    - phase transfer 78
    - thermolabile 265
  - Cathepsin- $\beta$ -mediated mechanism 112
  - Cell fusogenic proteins (CFPs) 136, 137
  - Cell membrane 9, 10, 112, 132, 137, 148, 156, 160, 161, 162, 163, 164, 165, 167, 170, 191, 338, 343, 344, 345, 346, 360, 361
    - bacterial 343, 346
    - cancer 360
    - coated bacterial 361
    - integrity of 164, 345
    - microbial 344
    - natural 164
    - transduce 137
  - Cell Penetrating Peptides (CPP) 138, 140
  - Cellular 341, 352
    - heparine sulfate 341
    - totipotency 352
  - Cellular internalization 113, 114, 136, 300, 312, 314, 319
    - convenient 113
  - Cellular signaling 110, 153
    - processes 110
  - Chemical vapor deposition technique 80
  - Chitosan 13, 82, 206, 270, 307, 334, 337, 349
    - and Halloysite nanotubes 349
    - deacetylation functionalize 82
    - polyvinyl pyrrolidone blend 82
  - Cholinesterase 311
  - Chromosomal 134, 170, 237, 238
    - breaks 238
    - defects 237
    - fragmentation 134, 170
  - Chronic autoimmune syndrome 360
  - Chronotropic 158
    - effects 158
    - impact 158
  - Chymotrypsin 265, 279, 280, 281, 284
    - denatured 280
  - Circular dichroism technique 202
  - Circulating 186, 197
    - biomarkers 186
    - proteins 186, 197
  - Clathrin-mediated endocytosis (CME) 10, 132, 153, 154
  - Cleavage 150, 168, 222, 246, 299, 300, 351
    - hydrolytic 351
    - proteolytic 299, 300
  - Clusters 2, 29, 30, 32, 33, 73, 122, 148, 161, 319, 339
    - ferrite nanoparticle 122
    - magnetic nanoparticle 122
  - Collision theory 273
  - Colorimetric enzyme techniques 350
  - Complementation of micro-technology 7
  - Complement cascade 149, 186
    - activation 149
  - Copolymers 197, 348
    - multiblock 197

Corona 146, 188, 189, 190, 191, 193, 198, 199  
  distal 188  
  fuzzy 190  
Cosmetology 287  
Co-structure directing agent (CSDA) 87  
Cytokinesis 170  
Cytomegalovirus infection 339  
Cytotoxic 114, 306, 315, 345  
  allotropic form, common 345  
  -antibody 306  
  effects 315  
  interaction, mediated 114

## D

Damage 85, 110, 115, 118, 157, 221, 235,  
  238, 338, 341, 343, 344, 346, 348, 358  
  chromosomes 238  
  irreversible chromosomal 338  
  mechanical 346  
  numerical chromosomal 235  
  repairing DNA 221  
Dendrimers 57, 58, 59, 60, 61, 141, 146, 169,  
  243, 244, 284, 285, 305, 316, 317, 334,  
  347, 354  
  amino-terminated 59  
  anionic 61  
  carbosilane 285  
  carbosilane-phosphorous 285  
  charged 244  
  generation polypropylene imine 60  
  phosphorous 284  
  polyamidoamine 317, 347  
  polypropylene imine 305  
  properties of 57, 59  
  respective 243  
Dendrimer synthesis 58, 59  
Derjaguin-landauverway overbeek (DLVO)  
  103, 196  
Deserno's model 112  
Detergent technology 276  
Dialysis amyloidosis 201  
Diffraction analysis 38  
Diffused reflection of light 31  
Dihydrofolate reductase-thymidylate synthase  
  268  
Directed evolution technique 267  
Diseases 21, 131, 135, 137, 153, 206, 221,  
  306, 336, 343, 344, 355, 358, 359  
  cardiovascular 21

  complex immune 306  
  degenerative 355, 358  
  infectious 343  
  neurodegenerative 206, 336  
  polycystic kidney 221  
Disorders 157, 168, 206, 221, 277, 301, 302,  
  335, 336  
  autoimmune 301, 302  
  curing neurodegenerative 206  
  diagnose muscle 277  
  major neurodegenerative 335  
  nervous 336  
  neurological 221, 336  
  renal 157  
DNA 5, 6, 135, 141, 207, 224, 230, 231, 233,  
  234, 235, 236, 240, 241, 242, 243, 319,  
  331, 338, 360  
  and dendrimer 243  
  and enzyme technology 5  
  and RNA technology 135, 331  
  binding plasmid 141  
  chip technology 6  
  chromosomal 224  
  damage 207, 234, 236, 319, 338  
  detecting multi-allele 242  
  elasticity of 233, 234  
  helix for initiation of transcription 230  
  molecules influence 235  
  nitrogen bases 230  
  polymerase activity 241  
  protein interactions 231  
  quantum dots conjugates 242  
  satellite 224  
  single molecule of 233, 242  
  single-strand 240  
  vaccines 360  
DNA molecules 26, 222, 223, 224, 225, 229,  
  230, 241  
  denature 222  
  docked 241

## E

Electrocatalysis 82  
Electromagnetic 8, 9, 29, 30, 33, 34, 36, 38,  
  39, 96, 119, 120  
  force 9, 96  
  radiations 34, 35, 39, 119, 120  
  waves 8, 29, 30, 33, 34, 36, 38, 39  
Electromagnetic field 40

- transmitting 40
  - Electrophoresis 204, 239, 242
    - affinity capillary 204
  - Emanuel syndrome 221
  - Embryogenesis 115
  - Emission 31, 41, 42, 43, 47, 49, 55, 87, 119, 146, 209, 210, 318
    - anti-Stokes 47
    - fluorescent 209, 210
    - size-dependent fluorescence 87
  - Endocytosis 10, 132, 138, 139, 140, 141, 142, 151, 153, 156, 160, 162, 164, 166, 169, 205
    - clathrin-mediated 10, 132, 153
    - micro-pinocytosis-fluid phase 156
    - of nanomaterial 140
    - receptor-mediated 205
  - Endocytotic mechanism of uptake of nanoparticles 151
  - Endothelium 157, 158, 160
    - experimental purposes 158
    - derived vasoconstrictors 158
  - Energy 28, 33, 35, 36, 39, 40, 48, 104, 105, 106, 116, 241
    - deposited 48
    - electronic 36
    - entropic 241
    - potential 104, 105, 106, 116
    - thermal 28, 35, 39, 40
    - transporting 33
  - Energy levels 34, 39, 45, 46, 50, 96
    - discrete 45, 96
    - distinct 50
  - Enzymatic activities 13, 99, 159, 233, 274, 275, 281, 282, 284, 286, 287, 347
    - elevated coupled 274
    - loss of 99, 284
  - Enzymatic interactions 12, 147, 262, 264
    - oxidative 147
  - Enzyme activity 9, 13, 159, 207, 261, 263, 264, 265, 271, 272, 275, 280, 281, 282, 285, 286
    - anabolic 263
    - cyclooxygenase-2 207
    - increased heparanase 159
    - non-competitive restricted 13
    - restricted 286
  - Enzymes 10, 241, 247, 265, 273, 277, 283, 284, 285, 287, 299, 300, 307, 345
    - cyclooxygenase 307
    - cytosolic 285
    - dehydrogenase 283
    - deoxyribonuclease restriction 241
    - ferroxidase 287
    - glucose oxygenase 284
    - glycopeptide transpeptidase 265
    - heparanase 10
    - immobilization technology 277
    - lactate dehydrogenase 273
    - leucine-aminopeptidase 287
    - nuclease 247
    - protease 299, 300
    - superoxide dismutase 345
  - EPR process 143
  - Escherichia coli* 346
  - Esterification 276, 278
  - Exocytosis 11, 156, 162, 166
  - Exoenzymes break 263
  - Exoribonucleases 247
- ## F
- Fatty acids 153, 334, 278
    - free 278
  - Fatty acid synthase enzyme 265
  - Fc-Rc receptors of antibody 312
  - Fetuin proteins 208
  - Fibrosis 207, 234, 237
  - Flavo adenine dinucleotide (FAD) 284
  - Fluorescence microscopy 46, 170
  - Fluorescence quenching 240
    - technique 204
  - Fluorescence technique 110, 235, 240
    - green 110
  - Fluorescent 32, 79, 170
    - dendritic nanoprobe 170
    - lamps 32
    - nanoclusters 79
  - Forces 9, 34, 46, 47, 72, 94, 96, 102, 103, 104, 105, 106, 107, 108, 109, 112, 185, 233, 234, 239, 240, 247, 332
    - atomic 239, 240, 247
    - electrostatic 94, 104, 112, 185
    - frictional 46
    - gravitational 9, 96
    - hydrophobic 112
    - restoring 46
  - Formulation 108, 115, 118, 131, 133, 134, 136, 145, 152, 207, 303, 305, 306, 334, 337, 340

anticancer doxorubicinliposomal 152  
colloidal 207  
core-shell micelle 145  
Fullerene 4, 51, 55, 56, 235, 238, 241, 242,  
282, 283, 315, 316, 345, 347  
nanomaterials-Buckminster 4  
Fullerene derivatives 283, 305, 307, 316  
water-soluble 307  
Fusion proteins 136  
Fusogenic peptide 137, 138

## G

Gauss's law 33  
Gel 12, 81, 164, 269, 270, 332, 348  
calcium phosphate 12, 269  
polyacrylamide 270  
Gene 85, 134, 135, 229, 246, 250, 305, 312,  
315  
delivery systems 85  
expression 134, 135, 246, 250, 305, 312,  
315  
transcription 229  
Gene regulation 352, 244  
epigenetic 352  
Genetic 83, 234  
materials delivery 83  
regulations 234  
Genetic materials 11, 12, 220, 221, 222, 224,  
235, 236, 237, 238, 240, 241, 242, 243,  
252  
damaged 221  
nature of 12, 235  
Genotoxicity 72, 234  
carbon nanotubes cause 234  
Glucose 170, 210, 263, 270, 271, 278, 284,  
288, 335, 353  
isomerase 270  
oxidase 170, 271, 284, 288  
Glycopeptide dendrimers 160  
Glycopolymers 160  
Glycoproteins 10, 156, 157, 158, 160, 161,  
181, 210, 306, 339, 360  
rabies virus 306  
Glycosphingolipids 161  
Glycosylated nanomaterials 160  
Gold 3, 23, 24, 28, 119, 120, 205, 206, 279,  
280, 281, 286, 287, 345  
colloidal 3

Gold nanoparticles 4, 29, 30, 79, 109, 111,  
113, 114, 164, 168, 202, 204, 205, 236,  
339, 358  
capped 168, 236  
carboxyl 164  
cation ammonium 164  
protected 168  
synthesized 79  
Guanine-nucleotide exchange factors 166

## H

Hallow vault protein 360  
Health care 135, 235, 331, 333, 350  
human 235  
industry 350  
Hearing abilities 32  
Helicases 247, 283  
Hemoglobin 147, 191, 207  
free 191  
Hemolysis 85, 193, 243, 311, 315  
anionic moieties cause 315  
dendrimers cause 243  
Heparan sulfate technique 159  
Hepatic 110, 205  
lesions 110  
sinusoids 205  
Hepatocellular carcinomas 153  
Hepatotoxicity 252  
High-resolution transmission electron  
microscopy (HRTEM) 115  
Human 109, 111, 112, 117, 118, 305, 311  
acute monocytic leukemia 311  
epithelial colorectal adenocarcinoma cells  
111, 112  
leukemic cells 109  
leukocytes antigens molecules 305  
micro endothelial cells (HMEC) 117, 118  
Human colon 112, 114, 311  
adenocarcinoma cells 112, 114  
carcinoma cells 311  
Hybrid coating technique 9  
Hydrolases 146, 351  
lysosomal 146  
Hypersensitive reactions 302

## I

Immobilization 264, 269, 270, 271, 272, 274, 275, 276, 277, 278, 279, 281, 320  
microwave-assisted 270

Immunity 13, 299, 300, 302, 303, 316, 320, 360, 361  
acquired 316  
adaptive 299, 303, 360  
antibacterial 361  
cell-mediated 320  
innate 13, 299, 300, 316

Immunosuppression phenotype M-2 159

Immunosuppressive 306, 307  
agents 14, 306, 307  
interactions 14

Inflammatory responses 187, 234, 309, 313, 314, 315, 319

Inhibitors 106, 191, 208, 264, 265, 283, 284, 287, 336  
acetylcholinesterase 336  
allosteric 265  
artificial 284  
cholinesterase 336  
competitive 265  
electron secretase 336  
feedback 265  
inter- $\alpha$ -trypsin 191  
non-peptides 106

Integrated circuit technology 7

**K**

Keesom 107  
forces 107  
interactions 107

**L**

Lab-on-a-chip technique 7

Lactoperoxidase 147

Levansucrase 342

Ligand 76, 77, 84, 196, 273, 340, 350  
binding 350  
conjugation 84  
density 340  
exchange 76, 77, 196  
-modified nanoparticles 273

Ligand molecules 76  
amphiphilic 77, 76  
attached 77

charged 76

Light 39, 44, 49  
microscopy 49  
radiation 39, 44

Light scattering 8, 12, 31, 32, 33, 34, 36, 40, 111, 117, 235  
dynamic 12, 235  
electrophoretic 117  
phenomenon of 31, 34  
static 111

Lipase enzyme 275, 276, 278  
immobilized 275, 276, 278

London dispersion force (LDF) 107, 108

Low-density lipoproteins (LDL) 154

## M

Macropinocytosis 154, 155

Magnetic field 33, 34, 120, 121, 122, 124, 209, 233, 332  
external 121, 122  
low 233  
non-uniform 121  
uniform 121

Magnetic force 7, 357  
microscope 7

Magnetic immunoassay technique 209

Magnetic nanoparticles 28, 74, 122, 123, 147, 168, 274, 353, 357  
iron oxide 123  
uncoated 168

Mannan-binding-lectin (MBL) 149, 150  
pathway 149

Maxwell's equations 33, 34

Maxwell's hypothesis 33

Mechanisms of cellular uptake 154

Mechanosynthesis 333

Mediated inflammatory carcinogenic response 238

Mediators 151, 250  
proinflammatory 151

Medical pathologies 277

Membrane 61, 149, 152, 153, 154, 161, 167, 203, 343, 345  
internalization process 154  
lipids 343, 345  
proteins 61, 149, 153, 161, 167  
receptors binding 152  
stabilization 153  
tension 153

- wrapping resistive 203
  - Membrane-bound 136, 140
    - ATPase proton pumps 140
    - compartments 136
  - Membrane fusion 136, 137
    - proteins 136
  - Mercapto-hexadecanoic acid (MHA) 358
  - Metabolites 74, 159, 264, 277, 344, 352
    - cellular 264
    - toxic 344
  - Metal 31, 352
    - nanoparticles system 31
    - organic framework (MOF) 352
  - Microbes 186, 187, 298, 341, 342, 344, 345, 346, 347, 351, 352, 353
    - multidrug-resistant 344
    - probiotic 346
  - Microbial 323, 342, 344, 346, 347
    - colonization, sustaining 342
    - metabolism 346
    - spectrum 344, 347
  - Micromanipulation technique 6
  - Microscopy 6, 49, 97, 111, 164, 165, 240, 341
    - confocal 111
    - infrared 49
    - scanning electron 97, 341
    - scanning probe 164
    - transmission electron 341
  - Mie's theory 33, 41
  - Mobility 11, 76, 166, 167, 231, 240, 243, 271, 272, 273, 285, 348, 358
    - electrophoretic 76, 243
    - highest intrinsic 240
    - polymer chain 348
  - Modifications 57, 133, 252, 279, 349, 317
    - 5-biotinylated 252
    - collagen 349
    - covalent 57, 133, 317
    - enzymatic 279
  - Modified dot blot technique 244
  - Molecular optics laser examiners (MOLE) 44
  - Monomeric proteins 181
  - Mononuclear phagocyte system (MPS) 58, 86, 145, 205, 309
  - Moor's Law 4
  - Multistep enzyme catalytic cycle 268
  - Multivalent ions influence interaction 202
  - Murine 152, 319
    - macrophage cells 319
    - macrophages 152
  - Muscles, intestinal smooth 158
  - Mutations 98, 206, 234, 241
    - dominant-negative 206
    - spontaneous DNA 98
  - Myeloid-derived suppression cells 147
  - Myeloperoxidase 147
- ## N
- Nanobiomaterials 72, 73, 133, 134
    - administered 72
  - Nano-drug 143, 144, 163, 195
    - carriers 143, 144, 163, 195
    - internalization of 143, 144
  - Nanomaterial based delivery systems 302
  - Nanoparticle-protein-corona 11, 206
  - Nanoporous materials 26
  - Nanosized glycomaterials 160
  - Nanovaccines 359, 360
    - lipid-antigenic 360
  - Natural 82, 186, 1995, 207, 210, 299, 305, 317
    - killer cells 82, 186, 207, 210, 299, 305, 317
    - organic matters (NOM) 195
  - Natural photonic crystals 25
  - Necrosis 109, 234, 301, 319
    - diameter cause 109
  - Neurogenesis 357
  - Non-protein amino acids 182
  - Nucleic acids 141, 144, 145, 150, 223, 227, 242, 245, 249, 252, 253, 347, 351
    - double-stranded 150
  - Nucleosomes 231, 244
  - Nucleotide oligomerization 312
- ## O
- Oscillation 29, 35, 39
  - Oscillator, harmonic 46, 47
  - Oxidase 74, 147, 288
    - lactate 288
    - xanthine 147
  - Oxidase enzyme 74
    - cytochrome 74
    - terminal 74
  - Oxidation 11, 80, 82, 123, 183, 184, 236, 345
    - cellular 345
    - liquid-phase 80
    - wet air 80



- Oxidative 114, 115, 134, 147, 234, 235, 238, 311  
  damage 115, 234  
  dependant DNA breakage 235  
  DNA adduct 134  
  DNA damage 114, 238  
  enzymes 147  
  explosion 311
- Oxidative stress 74, 234, 238, 286, 287, 309, 319, 323, 338, 342, 345, 346  
  cellular 74  
  inducing 234
- P**
- Parkinson's disorder (PD) 335, 336
- Pathways 10, 100, 140, 145, 149, 150, 158, 164, 207, 268, 347  
  endocytic 140, 164  
  endogenous 145  
  lectin 10, 149  
  mannan-binding-lectin 150  
  mannan/mannose-binding-lectin 150  
  metabolic 100, 268  
  phagocytic 207  
  photochemical transfer 347  
  secretory 158
- Peptide motifs 10, 156  
  fusogenic 10
- Peptides 136, 137, 138, 139, 144, 145, 180, 181, 182, 302, 304, 318, 320, 334  
  cell fusogenic 137  
  cell-fusogenic 137  
  cell-penetrating 138, 139
- Peroxidase 146, 147, 271, 281, 282, 286, 288  
  enzymes 286  
  horseradish 147, 281  
  soya bean 271, 282
- Phagocytes 86, 113, 185, 186, 197, 198, 205, 207, 208, 210, 313, 314, 317  
  mononuclear 113, 317  
  resident 207, 210
- Phagocytic cells 302, 310  
  mononuclear 310
- Phagocytic system 187  
  mononuclear 187
- Phagocytosis 10, 11, 13, 113, 114, 151, 152, 155, 185, 187, 197, 305, 309  
  of nanoparticles 114, 152  
  processes 185
- Phospholipases 278
- Phospholipids 83, 162, 166, 278, 313  
  amphipathic 162
- Photocatalytic 4, 55, 56  
  activity 55, 56  
  nature 4
- Plank's 35  
  constant 35  
  equation 35
- Plasma 29, 30, 81, 119, 120, 150, 159, 191, 192  
  organic 81
- Plasma proteins 13, 149, 159, 190, 191, 205, 299, 310, 311, 324  
  absorbed 159  
  haptoglobin 191  
  human 191
- Plasmon excitation 27
- Polyethylene glycol 76, 82, 83, 118, 151, 187, 203, 284, 303, 310, 313, 314  
  charged 118  
  neutral 83  
  varied amine 284
- Polyethylene terephthalate 24
- Polyfunctional reagents 270
- Poly(lactic-co-glycolic-acid) 356
- Polymerase 223, 235, 247, 283  
  chain reaction (PCR) 223  
  nuclease 247  
  poly-ADP-ribose 235
- Polymer chain ordering 348
- Polymers 139, 140, 141, 145, 152, 196, 202, 233, 234, 245, 246, 247, 248, 262, 269, 280, 284, 303, 321, 333, 334, 357  
  biochemical 245  
  biodegradable 145, 321, 357  
  cationic 139  
  complicated 233  
  electrospun 357  
  hydrophilic 196, 280  
  multifunctional 284  
  self-avoiding 233  
  surfactant 202
- Polypeptide 181, 182, 192, 266  
  multifunctional 266
- Pressure 23, 27, 32, 55, 80, 83, 141, 143, 229, 231  
  atmospheric 23  
  interstitial fluid 143  
  osmotic 141

- transmembrane 55
  - vapor 27
  - Progressive degenerative process 335
  - Properties 2, 3, 22, 23, 27, 28, 29, 31, 40, 53, 57, 59, 76, 77, 81, 101, 116, 121, 133, 164, 233, 235, 242, 246, 248, 267, 274, 285, 307, 320, 322, 348
  - amphiphilic 76
  - anti-corrosion 81
  - dynamic 164
  - electrical 31, 77
  - electro-hydrodynamic 242
  - hydrophilic 322
  - immunosuppressive 307
  - ionic 274
  - novel 23
  - paramagnetic 121
  - physical 27, 40, 101, 116
  - redox 285
  - rheological 59
  - thermal 53
  - Proteases 150, 265, 278, 281
  - Protein binding 14, 191, 200, 205, 207, 230, 232, 247, 310, 318
    - nanomaterials influencing 200
  - Protein corona 11, 180, 187, 188, 189, 190, 191, 192, 193, 194, 197, 198, 199, 208, 309, 310
    - applications of 11, 198
    - composition of 188, 199
    - functional 199
    - pattern of 190, 193, 194
  - Protein enzyme 209, 263
    - cellular release of 263
  - Protein fibrillation 198
  - Protein kinase 235
  - Protein microarray technique 209
  - Protein nanomaterials interaction 11
  - Protein-protein process 106
  - Proteins 11, 180, 181, 183, 184, 188, 190, 191, 192, 198, 201, 202, 203, 204, 205, 206, 209, 210, 231, 310
    - adsorption of 150, 188, 189, 190, 191, 192, 193, 194, 199, 204, 205
    - amyloidogenic 201
    - aqueous phase 79
    - cavin 153
    - cell-fusogenic 10
    - cell-penetrating 138
    - cell surface 314
    - cellular tumor 110
    - chimeric 136
    - classical Acute Phase 186
    - clusterin 188
    - complementary 199
    - complex aggregate 184
    - conformational changes in 11, 189, 206
    - conjugated 161, 181
    - cyclic 182
    - cytological 206
    - denaturation 99
    - fusogenic 138
    - globular 265
    - heterodimer 184
    - histone 231, 244, 352
    - homodimer 184
    - immobilized 209
    - intracellular 360
    - iron repressor 249
    - macrophage inhibitory 317
    - membrane scission 154
    - mucin domain 137
    - multi-enzymatic 266
    - multimeric 181
    - native 11
    - non-histone 252
    - nucleating 169
    - synaptosomal-associated 153
    - tertiary structure of 183
    - transmembrane 156, 160, 161, 162
    - transmembrane lipid transporter 162
    - vaccine 321
    - vesicle-associated membrane 153
    - zombie 267
  - Proton(s) 10, 55, 97, 98, 132, 139, 140, 141, 142, 280
    - defy difficulties 98
    - sponge effect 132, 142
    - sponge hypothesis 10, 139, 141
    - translocate 140
    - tunneling process 98
- ## Q
- Quantum 2, 29, 33, 43, 46, 47, 48, 50, 107, 120, 240, 318
    - confinement effect 120
    - confinement impact 50
    - high fluorescent 318

Quantum dots (QD) 4, 5, 24, 49, 50, 113, 114, 118, 169, 210, 242, 244, 273, 318, 319, 347  
and DNA interact and result 242  
coated 118  
conjugated 347  
electrophoretic mobility assay 242  
nanomaterials 210  
photoluminescence of 210  
semiconducting 4  
zinc oxide 5  
Quantum electrodynamics 34

## R

Raman scattering technique 46  
Reaction 6, 57, 76, 78, 101, 105, 116, 147, 198, 223, 228, 241, 244, 249, 262, 265, 267, 268, 270, 288, 300, 301, 302, 306, 317, 245, 359  
agglomerative 105  
allergic 300, 301, 302, 306  
biochemical 265, 317  
chemical 57, 116, 241, 262, 267  
consecutive 268  
dynamic time-course-chemical 101  
hypersensitivity 301  
immune 228  
multiphase 249  
organic 345  
particular membrane 270  
polymerase chain 223  
Reactive oxygen species (ROS) 55, 109, 115, 118, 167, 286, 338, 345, 347  
Receptors 83, 137, 152, 154, 159, 161, 166, 168, 186, 187, 197, 199, 200, 300, 303, 311, 312, 313, 319, 351, 352  
carbohydrates 312  
cellular 137  
chemokine 311  
complex 161  
endothelial stabilizing 159  
glucose 152  
immune 312  
ligand cell 83  
oligomerization-domain 319  
target epidermal 137  
toll likes 313  
transmembrane 161  
Resonance 30, 31, 56, 286

active plasmon 30  
electron spin 286  
particular plasmon 30  
plasmonic 31  
Retention effect 10, 113, 132, 144  
Rheo-fluid system 359  
Rheokinase 155  
Rheumatoid arthritis 360  
RNA 12, 135, 246, 248, 247, 248, 249, 250, 251, 252, 253, 306, 308, 331  
backbone of 246, 247  
biochemical stability of 252  
double-stranded 247  
folding of 250  
interfering 137, 247, 250, 306  
nucleobases 250  
oligonucleotides 246  
plastic nature of 248  
polygon 248, 308  
scaffoldings 252  
technology 12, 135, 249, 251, 252, 253, 331  
RNase 246, 247  
enzyme 246, 247  
enzymes modulate 247  
RNS formation 234  
Robotic process automation program 283

## S

Scaffold 244, 274, 279, 349, 356, 357  
electrospun polystyrene 356  
salt bridge 244  
vascular 357  
Semiconductor nanomaterials 78, 273  
luminescent 273  
Semiconductor nature 53, 54, 354  
noncrystalline 354  
Sensors 1, 5, 7, 13, 28, 29, 210, 309, 313, 318, 333, 350, 353, 354, 358, 359  
accelerative 358  
biological 333  
chemical 333, 350, 353  
electrochemical 210  
health monitoring 358  
immune 354  
intracellular 318  
Serine proteases 150, 284  
well-characterized 284  
Serum 114, 186, 190, 197, 207  
fetal bovine 114, 207

- Serum albumin 79, 194, 204, 205, 207, 208, 244, 305  
  bovine 79, 204, 205, 244, 305  
  human 194, 207, 208
- Serum proteins, bovine 244
- Shear stress 188, 193, 194  
  dynamic 188
- Signaling 100, 152, 160, 167, 235, 267, 287, 312, 315  
  activities 267  
  cascade 152, 160  
  cassette 315  
  interruption 235  
  ligand-dependent receptor 167  
  proteins 312  
  redox 287  
  system 100
- Signaling pathways 85, 166, 167, 168, 198, 235, 315, 319  
  inducing 198
- Signals 13, 30, 46, 48, 110, 161, 203, 303, 307, 309, 316, 321, 335, 350, 351, 352, 353, 358  
  co-stimulatory 321  
  electrical 350  
  emitting bright 335  
  essential cellular 110  
  false-positive 203  
  inhibitory 13  
  processing autonomy 358  
  stimulatory 316  
  transductions 161
- Silica nanoparticles 110, 115, 141, 188, 191, 192, 196, 199, 207, 208, 280, 281, 310, 320  
  amorphous 115, 207, 208  
  mesoporous 110, 141, 320
- Silicon dioxide 23, 24  
  disulfide 23
- Silicon nanowires 280, 282, 353  
  field-effect transistor 353
- Silver nanoparticles 5, 24, 77, 79, 110, 115, 287, 309, 310, 339, 340, 344  
  antibacterial 115  
  sized 309
- Single carbon nanotube 54
- Small-angle X-ray scattering technique 38
- Species, reactive oxygen 55, 118, 338, 347
- Spectrophotometry 223
- Spectroscopic 48, 204  
  techniques 48  
  titrations 204
- Spectroscopy 45, 49, 240  
  fluorescent 240  
  infrared 45
- Spectrum 34, 43, 48, 340  
  antiviral 340  
  electromagnetic 34, 48
- Stabilizing siRNA 247
- Staphylococcus aureus* 347
- Static light scattering (SLS) 111
- Steel 3, 51, 52, 357  
  high carbon 52  
  industries 3  
  stainless 357
- Stem cells 114, 147, 349  
  human adipose-derived 114  
  mesenchymal 349
- Stokes 42, 43, 44, 273  
  -Einstein equation 273
- Stone-Wales defects 53
- Stress 39, 51, 52, 74, 110, 111, 157, 198, 233, 234, 286, 312, 332, 352, 355  
  cellular 74  
  genotoxic 110  
  physical 39, 355  
  titanium dioxide nanoparticles cause 286  
  xenobiotic 312
- Structural 2, 136, 239, 244, 245, 340, 352  
  -activity-relationship 136  
  deformations 239, 244, 245  
  elements 2  
  flexibility 340  
  tunability 352
- Substances 23, 72, 83, 108, 121, 147, 165, 187, 270, 323, 332, 333, 334, 335, 352, 357  
  apoptotic 187  
  lipids-oil-soluble 83  
  nanoscaled 165  
  nanosized 334  
  superparamagnetic 121
- Substantia nigra 335
- Substrate channeling technique 268
- Sugar 144, 222, 225, 230, 250, 278  
  H-bonds 250  
  molecules 144  
  pentose 222  
  stacking interactions 250
- Superparamagnetic 151, 199, 353

- nano worms 151
  - Suppress cell death 118
  - Surface active agents (SAA) 87
  - Surface charge 9, 11, 13, 31, 83, 85, 117, 163, 164, 189, 195, 196, 197, 204, 284, 286
    - and electron transport 31
    - isoelectric point 195
  - Surface energy 133, 202
    - free 202
    - minimal 133
  - Surface glycoprotein 339
  - Surface plasmon 28, 30, 31
    - polariton (SPPs) 30, 31
    - resonance 28, 30
  - Surface topography 71, 72
  - Synthesis 2, 3, 57, 58, 59, 76, 77, 78, 80, 100, 104, 136, 283, 284, 287
    - controllable targeting 136
    - controlled 57
    - facile 58
  - Synthetic 349
    - biopolymer composites for tissue engineering scaffolds 349
    - polymer nanocomposites 349
- T**
- Taq DNA polymerase 280, 282
    - enzymes 280
  - Target 108, 117, 137, 199, 240, 242, 299, 336, 351, 354
    - analytes 354
    - DNA 240, 242
    - non-nucleic acid 351
    - protein 137
    - receptor 199
    - systemic cellular 117
    - tissues 108, 299, 336
  - Taxonomical inter-relationship 224
  - T-cells 13, 137, 299, 303, 304, 305, 306, 307, 311, 315, 316, 320, 339, 360
    - immunoglobulin domain 137
    - in bone marrow 320
    - proliferation 311
    - receptor 303, 360
    - cytotoxic 360
    - functions of 303, 307
    - helper 316
    - killer 360
    - Technique 3, 6, 7, 38, 41, 46, 48, 75, 80, 81, 111, 117, 122, 123, 143, 164, 169, 224, 227, 236, 240, 242, 244, 277, 289, 349, 350, 351, 356
      - annealing 122
      - biomimetics 289
      - biophysical 236
      - dipsticks 350
      - electroporation 277
      - electrospun 356
      - fluorescent 143, 169
      - freeze-drying 349
      - industrial 277
      - microscopic 240
      - recombinant 351
  - Technology 31, 49, 50, 78, 261, 262, 270, 248, 278, 332, 351
    - analytical 351
    - click chemistry 270
    - dairy 278
    - fermentation 262
    - green synthesis 78
    - interdependent 332
    - lithographic pattern 31
    - packaging 261
    - semiconductor 49, 50
  - Therapy 87, 88, 131, 304, 306, 318, 335
    - anti-glioma 306
    - diabetic 335
    - medical 88
    - photodynamic 318
    - photothermal 87
  - Thermal conductivity 53, 81, 348
    - low 81
  - Thin films 4, 30, 40
    - sensing 30
  - Thrombocytes 193
  - Thrombogenicity 311
  - Tissue 2, 135, 349
    - engineering scaffolds 349
    - reconstructions 135
    - regeneration 2
  - Toll-like receptors (TLRs) 304, 309, 312, 315, 319
  - Toxic effects 286
  - Toxicity 59, 61, 109, 133, 134, 135, 136, 164, 165, 170, 195, 198, 207, 303, 307, 346
    - cellular 109, 346
    - clinical 134, 170
    - reduced 87

systemic 135, 136  
Transcription 156, 220, 221, 222, 228, 230,  
231, 243, 245, 250, 319  
  process of 228, 245  
  regulating 231  
Transcriptional promoter 226  
Transcriptomics 209, 210  
Transcytosis 153, 155  
Transesterification 278  
Transferases 351  
Transformation 9, 41, 83, 85, 97, 226, 261,  
262, 268, 277, 344, 352  
  chemical 9, 97  
  enzymatic 85  
  genetic 344  
  interconversions of energy and chemical 9,  
  97  
  physiological 261  
Transport proteins 343  
Tumor(s) 14, 110, 111, 117, 135, 140, 141,  
143, 144, 153, 288, 319, 335  
  detecting multiple 335  
  environmental 141  
  neuroendocrine 117  
  spheroid 111  
  suppressor 110  
Tumor tissue 142, 143  
  disrupts 143

## U

UV-VIS spectrometry 235

## V

Vaccination 298  
Vaccines 75, 301, 305, 313, 320, 322, 336,  
359, 360  
  anticancer 360  
  efficient malaria 360  
  hepatitis 322  
  intranasal 322  
  seasonal influenza 322  
  silicon-based nano 320  
  therapeutic 322  
  traditional 360  
Van der Waal interactional forces 239  
Vascular 142, 354  
  endothelial factors 142

  graft, synthetic 354  
Vascularization 144  
  non-uniform 144  
Velocity 33, 34, 35, 47, 78, 103, 101, 114,  
158, 193, 194  
  angular 33  
  high Brownian's 103  
Versatile technique 38  
Vibrational 37, 42, 43, 44, 45, 46, 47, 119  
  coordination 45  
  eigenstate 47  
  energy states 44  
  relaxation 42, 43  
  resonance 46  
  state 37, 42, 44, 45  
  transition 46  
Vibrations 32, 43, 46, 48, 49, 120  
  molecular 46  
  quantized microscopic 120  
Viral 339, 360  
  infection treatment 339  
  -like proteins (VLPs) 360  
Viricides 341  
  fabricated 341  
Virtual 44, 47  
  energy states 44  
  state acts 47  
Virus 137, 227, 322, 339, 341  
  cell-associated 339  
  cell-free 339  
  disease-causing 339  
  herpes 339  
  influenza 137

## W

Waves 26, 31, 32, 34, 38, 39, 40, 47, 48, 50,  
95, 119  
  acoustic pressure 32  
  crystalline lattice 39  
  electronic 50  
  neutron 38  
  oceanic 26, 95  
  optic 47  
  radio 34  
Wide-angle X-rays scattering technique 39

## X

Xanthoxidase 147

X-ray diffraction techniques 349

## **Z**

Z-DNA 228, 242

    biological significance of 228

    biomolecule 228

    form 242

Zinc oxide 23, 24, 206, 281

    disulfide 24

Zinc oxide nanoparticles 237, 312, 345