

NANO – Today's Fascinating Phenomenon

Nanoparticles, nanostructures
and nanotechnology:
ingenious forms of matter

From the phenomenon's discovery
to its biomedical applications

*The enigmatic reality of NANO
Ingenious forms of matter opening up vast spaces
to revolutionary scientific and new technology developments*

Anton Fojtík

Milan Kálal

Tasilo Prnka

Karel Šperlink

Miroslav Mašlání

Radek Zbořil

Vladimír Bencko

Milan Šiňor

The publication "NANO – Today's Fascinating Phenomenon" is published under the LE 15013 project "Professional Contact Organization for New Materials and Technologies" implemented in the framework of the EUPRO II program coordinated by the Ministry of Education, Youth and Sports of the Czech Republic in order to support the integration of Czech research and development into the European research center network. COMTES FHT a.s. is the coordinator of the project.

The book is an English version of the publication "NANO – fascinující fenomén současnosti" which was published by The Czech Society for New Materials and Technologies (CSNMT) in the year 2013. In our opinion, this book can serve as a high-quality textbook for students in this scientific field focused on the application of nanotechnologies in biology and medicine.

We dedicate this book to the memory of our dear colleague Ing. Tasilo Prnka, DrSc.. Taso was a leader of founding the Nanosection at CSNMT, an excellent promotor of the nano research in the Czech Republic, the initiator of the "Nanotechnology for Society" program, the "METAL" and "NANOCON" conferences and he also represented the CSNMT in the management committee of the "Federation of European Materials Societies".

Associate Professor Ing. Karel Šperlink, CSc.
President of CSNMT

Ing. Libor Kraus
Chairman of the Board, COMTES FHT

FOREWORD

This publication is dedicated to nanostructures, nanoparticles and nanotechnology. After presenting an explanation of the basic terms and principles of this modern branch of science, the book then focuses its attention primarily on nanotechnology's possible uses in biomedicine, where its potential applications literally know no bounds. Since research in these areas is continuously on the rise, the accreditation of new fields of study dedicated to preparing specialists needed in "nano" is currently taking place. For this reason every publication dealing with these issues is greatly welcome, in particular if it can also be used in student instruction. In my opinion this book certainly meets this condition.

In this publication, the authors have successfully not only created a highly readable description of the interesting history of the discovery of nanoparticles themselves, but they have also illustrated the latest state of knowledge in this scientific discipline, including the use of the unique qualities of the described nanostructures in research and practical applications (particularly in medicine).

A brief glance at this book quickly shows that it will appeal both to absolute beginners, who are just considering learning more about this topic (for these readers the first chapters will be particularly useful), as well as to more experienced researchers, who already work in this scientific discipline. The many pictures, tables and illustrations will make it easier for readers to digest the large quantity of information. The book's colourfulness also makes it attractive, and I believe it will increase the publication's appeal.

Readers will further find in *Appendix I* an easy to understand basic aspects of quantum mechanics. Studying this Appendix is not necessary for working with this book and it can be skipped without fear. It is included here, however, for those readers who desire not only "to know" about nanotechnology but also "to understand" and "make sense" of it. Readers can make the move to this higher level of knowledge at any time they want to. Naturally, achievement of this goal requires a certain level of knowledge of mathematics and physics, which it is necessary to acquire first for this purpose.

Until today, Czech market has lacked a book of this kind. For that reason, I am certain that it will soon find many readers and will become an indispensable "textbook" in the libraries of everyone who has decided to study this incredibly interesting, fast-developing field. I also believe that this book has the potential to become a useful "handbook" for scientists working with nanoparticles, nanostructures and nanotechnologies, as well as for applied science teams. Such people will enjoy using this book in their work. At the same time it can help expand their spectrum of knowledge in certain areas of their research.

In conclusion, I would also like to thank the team of authors for completing this task. It was not easy, but they have been dedicated and successful in it. I sincerely wish the book many satisfied readers.

Prof. MUDr. Jozef Rosina, PhD.
Dean of the Faculty of Biomedical Engineering, CTU in Prague

CONTENTS

1	INTRODUCTION.....	13
2	HISTORY.....	17
2.1	First experiments.....	17
2.2	The period of inception.....	19
3	NANOTECHNOLOGY TODAY.....	21
4	NANOSTRUCTURES AND NANOPARTICLES.....	23
5	THE PHYSICAL NATURE OF NANOSTRUCTURES.....	27
5.1	The quantum well.....	28
5.2	The quantum dot.....	31
5.3	Summary of the spatial restriction phenomenon.....	33
6	FABRICATION OF QUANTUM NANOSTRUCTURES.....	34
6.1	Top-down.....	34
6.2	Bottom-Up.....	34
7	MAJOR METHODS FOR THE FABRICATION AND STUDY OF NANOSTRUCTURES.....	35
7.1	Chemical methods.....	35
7.2	Chemical use of micellar systems.....	35
7.3	Chemical etching.....	36
7.4	Pulsed laser method.....	36
7.5	Shadow (or “molecular”) lithography.....	36
8	SOME METHODS FOR NANOSTRUCTURE DETECTION.....	39
8.1	Electron microscopy.....	39
8.2	Scanning tunneling microscopy.....	39
8.3	Atomic force microscopy.....	41
8.4	Liquid chromatography.....	42
9	TOWARDS QUANTUM NANOSTRUCTURES.....	43
9.1	The dimensional effect in semiconductor nanoparticles.....	43
9.2	Exciton.....	43
9.3	Localized particles.....	44
9.3.1	Excitons.....	44
9.4	Absorption spectra of semiconductors.....	45
9.5	Exciton absorption.....	45
9.6	Absorption spectra of nanoparticles.....	46
9.7	The structure of nanoparticle spectra.....	47
9.8	Q – the magic agglomeration number.....	48
9.9	The size effect of Q – particles.....	48
9.10	Photo – oxidation of particles – optical mill.....	51
9.11	The influence of the environment on surface properties.....	51
9.12	Confirmation of higher excited states of nanoparticles.....	52
10	SURFACE PROPERTIES.....	54
10.1	Surface-modified nanoparticles.....	55
10.2	Charge carriers in semiconductor nanoparticles.....	56
11	MULTI-LAYER “SANDWICH” STRUCTURES.....	58
11.1	Charge separation – the mechanism of sensitization.....	59
11.2	Charge separation – photovoltaic materials.....	63
11.3	Photoelectron emission from quantum nanostructures.....	63
11.4	Interaction between charge carriers ($e^- + h^+$).....	66

12 SILICON NANOPARTICLES	69
13 METHODS OF SYNTHESIS OF IRON NANOPARTICLES AND IRON OXIDES	73
13.1 Chemical methods (precipitation, crystallization)	73
13.1.1 Synthesis of Fe_3O_4 nanoparticles by oxidative hydrolysis of FeS	73
13.1.2 Synthesis of Fe_3O_4 nanoparticles by alkaline hydrolysis of Fe^{2+} and Fe^{3+} ...	74
13.1.3 Synthesis of $\beta\text{-Fe}_2\text{O}_3$ by solid-state reaction.....	74
13.2 Thermal decomposition (pyrolysis).....	75
13.2.1 Synthesis of iron nanoparticles by decomposition of ferrihydrite	75
13.2.2 Synthesis of $\text{Fe}(0)$ nanoparticles by reduction of iron oxides	76
13.2.3 Synthesis of $\gamma\text{-Fe}_2\text{O}_3$ nanoparticles from ferrous acetate.....	76
13.3 Other methods.....	77
13.3.1 Sonochemical methods	77
13.3.2 Spark erosion	77
13.3.3 Synthesis in microwave discharge	78
13.3.4 Laser pyrolysis	78
13.3.5 Synthesis of Fe_3O_4 magnetosomes using magnetotactic bacteria	80
14 APPLICATIONS OF IRON AND IRON OXIDE NANOPARTICLES	81
14.1 The use of Fe_3O_4 and $\gamma\text{-Fe}_2\text{O}_3$ nanoparticles in medicine and bioapplications	81
14.1.1 Contrast agents in magnetic resonance imaging (MRI)	81
14.1.2 Biomagnetic separation	81
14.1.3 Magnetic carriers of cytotoxic agents	82
14.1.4 Nanoparticles in hyperthermia therapy	82
14.2 Nanoparticles as catalysts.....	82
14.3 Iron nanoparticles and groundwater purification.....	83
REFERENCES (CHAPTERS 1-14)	85
15 APPENDIX A – THE BASICS OF QUANTUM MECHANICS.....	88
15.1 Wave properties of particles.....	88
15.2 The Schrödinger equation.....	88
15.3 Selected simple quantum systems.....	92
15.3.1 A particle in an infinite potential well	92
15.3.2 Particles in a finite potential well	95
15.3.3 Passage of a particle through a potential barrier (tunnel effect)	97
15.3.4 The harmonic oscillator	99
16 APPENDIX B – IRON AND IRON OXIDES	102
16.1 Iron.....	102
16.2 Iron oxides.....	103
16.2.1 Ferric oxide – Fe_2O_3	103
16.2.2 Ferrous-ferric oxide – Fe_3O_4 (magnetite)	107
16.2.3 FeO – wüstite	107
17 BIOTECHNOLOGY	108
17.1 Lessons from nature – molecular biology.....	108
17.2 Biological structural particles.....	109
17.2.1 Nucleic acids (DNA, RNA)	112
17.2.2 Proteins and peptides	117
17.2.3 Lipids	122
17.2.4 Polysaccharides	123
18 BIOLOGICAL NANOSTRUCTURES AND MICROSTRUCTURES.....	126
18.1 Strategies for creating structures at the molecular level.....	126
18.1.1 Biomolecular self-assembly	127

18.1.2	Bio-molecular self-organization	128
18.2	The biological environment at the nanoscale.....	129
18.2.1	Gravity and inertia	129
18.2.2	Thermal motion.....	129
18.2.3	Water environment	130
18.3	Hierarchical structures.....	130
18.4	Biomineralization.....	133
18.4.1	Snail – Abalone	136
18.4.2	Magnetotactic bacteria.....	137
18.5	Biological membranes.....	137
18.6	Molecular channels and pumps.....	139
18.7	Molecular motors.....	139
18.8	A molecular factory – the cell.....	143
18.8.1	The nucleus.....	144
18.8.2	Protein synthesis.....	145
18.9	Application of biomolecules and biosystems – biotechnology.....	147
18.9.1	Protein engineering	148
18.9.2	DNA in biotechnology	148
18.9.3	RNA biotechnologies	158
18.9.4	Peptides and proteins in biotechnology	160
18.9.5	The use of lipids in bio(nano)technologies	167
18.9.6	Other biological objects	168
18.9.7	Conclusions.....	169
19	NANO IN BIOTECHNOLOGIES	170
19.1	Bionanotechnology.....	171
19.2	Biotechnology, biopharmaceutics and medicine.....	173
20	IMAGING AND ANALYTICAL METHODS, DEVICES FOR NANOTECHNOLOGIES	175
20.1	Modern imaging and analytical methods and devices.....	175
20.1.1	Optical imaging and analysis.....	177
20.1.2	Electron microscopy and analysis	189
20.1.3	Scanning probe microscopy.....	193
20.1.4	X-ray diagnostics and nuclear imaging	196
20.1.5	Medical ultrasound	201
20.1.6	Selected molecular biological analytical techniques	201
20.2	Nanoscale biosensors.....	212
20.2.1	Cantilever array sensors	212
20.2.2	Nanotube sensors	214
20.2.3	Nanowire-based sensors.....	216
20.2.4	Bio-bar code assay.....	217
21	NANOMATERIALS IN NANO-BIOAPPLICATIONS.....	219
21.1	Nanoparticles for biomolecular diagnosis.....	219
21.1.1	Gold nanoparticles	220
21.1.2	Use in electrochemical detection	222
21.1.3	Quantum dots	222
21.2	SiO ₂ nanoparticles.....	226
21.2.1	Use in optical detection.....	226
21.2.2	More examples of the use of silica nanoparticles.....	227
21.3	Magnetic nanoparticles.....	228
21.3.1	Applications in magnetic resonance imaging.....	228

21.3.2	Applications in magnetic labelling	229
21.4	Other nanoparticles.....	229
21.5	Carbon nanomaterials.....	230
21.5.1	C ₆₀ – fullerenes	230
21.5.2	Fullerene synthesis	231
21.5.3	Properties and applications.....	232
21.6	Carbon nanotubes.....	232
21.6.1	Structure	234
21.6.2	Synthesis	234
21.6.3	Doped carbon nanotubes	235
21.6.4	Endohedral carbon nanotubes	236
21.6.5	Functionalized carbon nanotubes	236
21.6.6	Properties and applications.....	236
21.6.7	Potential applications in biotechnology and nanomedicine	237
21.7	Hydroxyapatite nanoparticles (NanoHAP).....	239
21.8	Silver nanoparticles.....	239
21.9	Dendrimers.....	241
21.10	Ormosils.....	242
21.11	Polymeric nanofibers.....	243
21.12	Nanoporous materials.....	244
21.13	PEG (polyethylene glycol).....	245
22	BIOTECHNOLOGY, PHARMACY AND NANOTECHNOLOGY.....	246
22.1	The contribution of biotechnologies to pharmacology and pharmacy.....	248
22.1.1	Human genome research	248
22.1.2	Diagnostics.....	249
22.1.3	Therapeutics	249
22.1.4	Pharmacogenetics	250
22.1.5	Vaccines and antibodies	250
22.1.6	The current drug discovery procedure	251
22.1.7	A brief description of the new drug discovery process.....	253
22.1.8	Compound synthesis	253
22.1.9	Biological compound libraries.....	254
22.1.10	Receptor (target) identification.....	255
22.1.11	Target screening.....	256
22.2	Prospects of micro- and nanotechnology applications.....	257
22.2.1	Applying modern imaging and analytical methods.....	259
22.3	Targeted drug delivery.....	259
22.3.1	Modes of drug delivery	260
22.4	New systems of targeted drug delivery – contribution of nanotechnology....	262
22.4.1	Drug carriers	263
23	NANO IN MEDICINE.....	269
23.1	Overview of the field of nanomedicine.....	269
23.2	Imaging and diagnostic methods and equipment.....	270
23.2.1	In vitro diagnostics.....	270
23.2.2	In vivo nano-imaging	272
23.3	Tissue engineering.....	274
23.3.1	Materials and the types of synthesis of tissue support structures	276
23.3.2	Selected techniques for scaffold synthesis	276
23.4	Tissue regeneration – the benefits of nanotechnology.....	277

23.4.1	Intelligent biomaterials and smart implants	277
23.4.2	Bioactive signalling molecules	278
23.4.3	Cell based therapies.....	279
23.4.4	Basis for a strategic research agenda.....	279
23.5	The contribution of nanotechnology to cancer therapy.....	280
23.5.1	Czech Republic's National Cancer Control Programme (NCCP).....	281
23.5.2	Support for cancer research in the Czech Republic	282
23.5.3	The Cancer Nanotechnology Plan	285
23.5.4	The present benefits of nanotechnology in cancer treatment	286
23.5.5	Opportunities from the fundamental understanding of cancer processes	287
24	MOLECULAR BIOTECHNOLOGY	291
24.1	Bioproduction.....	292
24.2	Monoclonal antibodies.....	292
24.3	Cell cultures.....	292
24.3.1	Plant cell cultures	293
24.3.2	Insect cell cultures.....	293
24.3.3	Mammalian cell cultures	293
24.4	DNA recombination technology.....	293
24.5	Cloning.....	294
24.5.1	Molecular cloning	294
24.5.2	Cell cloning.....	294
24.5.3	Animal cloning.....	295
24.6	Protein engineering.....	295
24.7	Biosensors.....	295
24.8	DNA profiling (fingerprinting).....	296
25	NANO-BIO OUTLOOKS	297