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Innovative Merge of Computational Approaches and Experimental Techniques
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Preface

Only 50 years after Richard Feynman’s “There’s plenty of room at the bottom” talk, nanotechnology has emerged at the forefront of science and technology developments. Engineered nanomaterials (ENMs) have found a wide range of applications, covering different areas of human life. The further development of new materials at the “nano” scale (100 nm or less) is highly profitable for modern chemistry, physics, medicine etc. There are currently over 1100 commercial products on the shells which incorporate nanomaterials and their manufacturing has become an industry worth over $1 000 000 000 000 per year. However, since at least some nanoparticles can possess a negative impact on human health and the environment, designing novel nanomaterials must be always accompanied by precaution preceded by a comprehensive risk assessment.

Unfortunately, the information available in the literature on the methods available for this purpose is fragmented. The reviews published so far refer mainly to the methodology and the results of research obtained based on the experimental work. In our opinion, there is a strong demand for a comprehensive review and discussion documenting the latest achievements not only of empirical methodologies, but also of computational techniques that might significantly support or even reduce the number of required experiments. Thus, based on our scientific experience from the last few years, we have proposed a book that for the first time brings together both points of view in one, inclusive source. We believe that really comprehensive risk assessment related to this important, fast-growing group of nanospecies is possible only when these two complementary groups of techniques are employed.

The book consists of 13 chapters. Chapter 1 briefly introduces the most important problems related to the safe use of nanomaterials and opens the volume. Since the spectrum of nanomaterials is very wide, the authors selected a
group of nanoparticles based on graphene (its synthesis method was awarded the 2010 Nobel Prize) as the case study. The three following chapters (Chapters 2–4) provide more details related to different levels and aspects of ENM toxicity assessment by using *in vitro* and *in vivo* experimental procedures. In contrast to testing conventional chemicals, the toxicity testing of nanoparticles always requires the evaluated structure to be characterized in detail by employing various microscopic techniques. This is because the investigated structures may vary along with time of the experiment (aggregate, agglomerate *etc.*). Thus, Chapter 5 presents experimental techniques for structural characterization. As mentioned, computational (chemoinformatic) methods may serve as a significant support for experimental risk assessment. In Chapter 6 the authors discuss the potential of such techniques for exploring experimental data and discovering nano–bio interaction mechanisms. The next two chapters (Chapters 7 and 8) treat in more detail the computational modeling of interactions between (carbon- and metal-based) nanoparticles and various biological systems (*i.e.*, DNA and proteins). Since nanoparticles’ toxicity and other properties are fundamentally linked to the structure, they can therefore be predicted with reliable structure–toxicity and/or structure–property relationship models. Indeed, the next three chapters present the currently developed methods for making reliable predictions by employing thermodynamic cartography and structure/property mapping techniques (Chapter 9), nano-QSAR (Chapter 10) and the structure–reactivity models (Chapter 11). Chapter 12 is devoted to exposure assessment of ENMs, which requires both experimental (analytical) work and computational modeling studies. Exposure assessment might be crucial for comprehensive assessing of risk, because even if a considered substance is toxic, the risk could be low when no one is highly exposed to this species. On the contrary, when a nanoparticle is less toxic, but the exposure level is high, the resultant risk could be relatively high. In the final chapter (Chapter 13) the authors present an example of the comprehensive risk assessment of self-decontaminating surface materials, which combines life-cycle analysis with traditional risk assessment parameters (characterization, exposure, effects *etc.*) to understand nanoparticles’ exposure and effects in different environmental settings.

The scope of the book is to discuss recent progress and challenges in the risk assessment of engineered nanomaterials, performed with the use of empirical and computational techniques. We noticed that very often the main difficulty in developing computational methods for the risk assessment of ENMs is the lack of appropriately measured empirical data to calibrate the models. On the other hand, experimentalists could probably reduce costs and time spent in their labs if they knew more about the abilities of currently developed computational methods. Both issues originate from the fact that usually the efforts of empirical and computational risk assessors are not well coordinated. We hope this book would serve as a bridge that covers the gap between specialists on the experimental and computational sides.

With great pleasure, we take this opportunity to thank all authors for devoting their time and hard work enabling us to complete the current volume.
“Towards Efficient Designing of Safe Nanomaterials”. We believe that with the excellent contributions from all authors this book will provide a common platform for both the theoretician and the experimentalist – not only those involved in research on nanomaterials, but also all others who are planning to start in this area of research, and especially graduate students. We are grateful to the editors at the Royal Society of Chemistry for their excellent cooperation and to our family and friends for their support.

Tomasz Puzyn, Gdańsk, Poland
Jerzy Leszczynski, Jackson, MS, USA
# Contents

## Chapter 1  Graphene: Properties, Biomedical Applications and Toxicity  
*T. C. Dinadayalane, D. Leszczynska and J. Leszczynski*

1.1 Introduction .................................................. 1  
1.2 Structure and Properties of Graphene ................................. 4  
  1.2.1 Biomedical Applications of Graphene ......................... 7  
  1.2.2 Toxicity of Graphene-based Nanomaterials .................... 14  
1.3 Conclusions .................................................. 23  
Acknowledgements ............................................... 23  
References ...................................................... 23

## Chapter 2  In Vitro Toxicity Assessment of Metallic Nanomaterials  
*L. K. Braydich-Stolle, N. M. Schaeublin and S. M. Hussain*

2.1 Introduction .................................................. 27  
2.2 Silver Nanomaterials ............................................ 29  
2.3 Gold Nanomaterials ............................................. 30  
2.4 Titanium Dioxide Nanomaterials .................................. 31  
2.5 Manganese Nanomaterials ....................................... 33  
2.6 Copper Nanomaterials .......................................... 34  
2.7 Iron Oxide Nanomaterials ....................................... 34  
2.8 Aluminium Nanomaterials ....................................... 34  
2.9 Biocompatibility of Nanomaterials ............................... 35  
2.10 Conclusions .................................................. 37  
References ...................................................... 37

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Chapter 3  In Vivo Testing of Nanomaterials  
S. Hirano

3.1 Administration Methods  
3.1.1 Via Airways  
3.1.2 Dermal Exposure  
3.1.3 Oral and Intravenous Routes  
3.1.4 Other Routes  
3.2 Kinetics, Dynamics and Translocation of Nanoparticles  
3.3 Toxicity Outcome of Nanomaterials  
3.3.1 Carbons  
3.3.2 Metals and Metal Oxides  
3.3.3 Ceramics and Other Materials  
3.3.4 Nanofibers  
3.4 Summary and Implications  
References

Chapter 4  Nanotoxicity: Are We Confident for Modeling? – An Experimentalist’s Point of View  
D. Berhanu and E. Valsami-Jones

4.1 Introduction  
4.2 The Complexity of Nano Compared to Bulk  
4.2.1 From One Material to Hundreds of Different Nanoparticles  
4.2.2 From Hundreds of Sample-specific Datasets to Physico-chemical Properties-based Toxicity  
4.2.3 Poorly Produced Nanoparticles vs. Well-defined Samples  
4.3 How to Design a Toxicity Experiment  
4.3.1 Comparative Nanotoxicity Studies  
4.3.2 Property-based Nanotoxicity Studies  
4.4 Remaining Challenges of Nanoparticles’ Characterisation  
4.4.1 Can a Minimum Set of Suitable Techniques be Established?  
4.4.2 The Intermediate State: Nanoparticles in Media  
4.5 Integration of Datasets in Models: How Can We Contribute?  
4.5.1 Data Assessment for Literature Data Modelling  
4.5.2 Bridging the Gaps with the Knowledge Acquired in Other Fields  
4.6 Conclusions  
Acknowledgements  
References
Chapter 5  Experimental Approach to the Structure and Properties of Nanoparticles

K. J. Kurzydlowski, M. Lewandowska and M. J. Wozniak

5.1 Introduction 69
5.2 Imaging Nanoparticles 70
  5.2.1 Electron Microscopy 70
  5.2.2 Scanning Probe Microscopy 74
5.3 Measuring the Size, Size Distribution and Shape of Nanoparticles 78
  5.3.1 X-ray Diffraction 78
  5.3.2 Laser Diffraction 81
  5.3.3 Image Analysis 82
  5.3.4 Parameters Describing the Size, Size Distribution and Shape of Nanoparticles 86
5.4 Summary 87
Further Reading 88

Chapter 6  Nanoinformatics for Safe-by-Design Engineered Nanomaterials

C. P. Roca, R. Rallo, A. Fernández and F. Giralt

6.1 Introduction 89
6.2 Nanoinformatics for ENM Data Management 90
  6.3.1 Case Study 1: Self-organizing Maps (SOM) Analysis of ENM Data Sets 94
  6.3.2 Case Study 2: System Biology Approach for the Analysis of Nano–Bio Interactions 97
6.4 Conclusions 104
Acknowledgements 104
References 105

Chapter 7  Interactions of Carbon Nanostructures and Small Gold Clusters with Nucleic Acid Bases and Watson–Crick Base Pairs and Nanocontacts Involving Mn–C60–Mn (M = Au, Ag, and Pd; n = 2–8) System: Computational Elucidation of Structures and Characteristics

M. K. Shukla, F. Hill and J. Leszczynski

7.1 Introduction 109
7.2 Interaction of C60 with Nucleic Acid Bases and Watson–Crick Base Pairs 110
Chapter 8  Theoretical Studies of Interaction in Nanomaterials and Biological Systems 148
H. Tzoupis, A. Avramopoulos, H. Reis, G. Leonis, S. Durdagi, T. Mavromoustakos, G. Megariotis and M. G. Papadopoulos

8.1 Introduction 148
8.2 Li@C60 150
8.3 Sc2@C72 155
8.4 Ti@C28 157
8.5 Analysis of the Binding Energy in Biological Systems 163
8.6 Amino Acid Fullerene Derivatives Bound to HIV-1 PR 166
8.7 MMK16 into COX-2/LOX-5 Enzymes 170
8.8 Aliskiren in Solution and Bound to Renin 172
8.9 Drug–Biosurface Interactions 174
Acknowledgements 178
References 178

Chapter 9  Thermodynamic Cartography and Structure-Property Mapping of Potential Nanohazards 186
A. S. Barnard

9.1 Introduction 186
9.1.1 Strategic Approaches to Predicting Nanohazards 189
9.1.2 Combining Theory, Simulation and Experiment 191
9.2 Thermodynamic Cartography of Nanoscale Titania 193
9.2.1 Comparison with Experiment 200
9.3 Structure-Property Mapping of Photocatalysis 203
9.3.1 Comparison with Experiment 207
Chapter 10  Nano-QSAR: Advances and Challenges  
B. Rasulev, A. Gajewicz, T. Puzyn, D. Leszczynska and J. Leszczynski

10.1 Introduction 220
10.2 What Makes a Nanoparticle Unique? 223
10.3 Modeling Nanoparticle Properties 223
10.4 QSAR Methodology and Basic Principles 224
10.5 Extending the QSAR Paradigm to Nanoparticles 225
10.6 Nano-QSAR Modeling of Physico-chemical Properties 227
  10.6.1 Solubility 228
  10.6.2 Elasticity (Young’s Modulus) 235
10.7 Nanoparticle Toxicity: Concerns and Challenges 241
10.8 Nano-QSAR and Prediction of Toxicity 241
10.9 Applications of Nano-QSAR for Biological Activities 249
10.10 Conclusions 249
Acknowledgements 250
References 250

Chapter 11  Development and Evaluation of Structure–Reactivity Models for Predicting the In Vitro Oxidative Stress of Metal Oxide Nanoparticles  
E. Burello and A. Worth

11.1 Introduction 257
11.2 Mechanism of Electron Transfer 259
11.3 Energy Band Structure Calculation of Metal Oxides 261
11.4 Comparison of Model Predictions with Literature Data 266
  11.4.1 Titania (Rutile and Anatase) 266
  11.4.2 Magnetite and Maghemite 270
  11.4.3 Zinc Oxide 273
  11.4.4 Ceria 275
  11.4.5 Copper Oxide (CuO) 277
Chapter 12  Modeling the Environmental Release and Exposure of Engineered Nanomaterials  
F. Gottschalk and B. Nowack

12.1 Introduction  
12.2 Environmental Release and Exposure in REACH  
12.3 Environmental Release and Exposure Assessment for ENMs  
12.3.1 Early Qualitative Release/Exposure Analysis  
12.3.2 Predictive Quantitative Modeling  
12.3.3 Analytical and Experimental Efforts  
12.4 Adequacy of the REACH Release Parameters for ENMs  
12.5 Outlook for Future Modeling and Experimental Work  
Acknowledgement  
References

Chapter 13  Comprehensive Environmental Assessment of Nanotechnologies: a Case Study Using Self-decontaminating Surface Materials  

13.1 Introduction  
13.1.1 Life-cycle Approach for Assessing the Risk of Nanotechnologies  
13.1.2 A Case Study for Comprehensive Environmental Assessment  
13.1.3 Comprehensive Environmental Assessment Framework  
13.2 Evaluation of Nanotechnologies  
13.2.1 Development and Production  
13.2.2 Self-decontaminating Surface Use  
13.2.3 Heating, Ventilation, and Air Conditioning (HVAC) Systems  
13.2.4 Coatings and Paints
CHAPTER 1

Graphene: Properties, Biomedical Applications and Toxicity

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1.1 Introduction

Among numerous commercial endeavors, nanotechnology is regarded as the key technology of the 21st century. It provides novel products and facilitates applications of innovative techniques in medicine, pharmacy, computer technology, and sensing. Therefore, it holds promise for potential global socio-economic benefits. In 2011, there were about 1100 commercial products that include nanomaterials. It is a common belief that nanotechnology could assist in solving many global problems that society faces. These include environmental and health concerns of the fast-growing human population, as well as access to clean water and affordable energy. The quickly growing applications of nanomaterials are due to their unique properties which offer advantages over conventional materials.

The variety of various nanomaterials is too big to cover in a single chapter. Therefore, we decided to focus on one particular class of species and discuss in
details its characteristics and applications. Since the 2010 Nobel awards validate the importance of graphene not only in basic research but also in various commercial applications, we selected this nanomaterial as the main subject of our chapter.

The demand for carbon nanostructures, particularly carbon nanotubes (CNTs) and graphene, is increasing rapidly in electrical, mechanical, and biomedical applications. This is due to their outstanding thermal, electrical, mechanical, optical and other unique properties. Although the intense interest and continuing experimental success of graphene-based devices facilitate their various applications, the reliable production of high quality samples of graphene on a large scale is very difficult. At present, great efforts have been made toward the preparation of graphene nanosheets. Among them, the chemical reduction of exfoliated graphene oxide (EGO) is the most commonly used approach due to its low cost for large-scale production. In the case of carbon nanotubes, closely related to graphene, controlling their size and diameter is still very challenging. The availability of carbon nanotubes, both in quality and quantity, has stimulated the worldwide pursuit of carbon nanotubes for technological applications. Nevertheless, carbon nanotubes (especially single-walled carbon nanotubes (SWCNTs)) are still quite expensive. To assist experimental studies, the structures, reactivities, and functionalization of defect-free and Stone–Wales defective SWCNTs have been investigated by our group, using quantum chemical calculations.

The morphology of graphene is different from that of CNTs; for example, the length of CNTs influences their toxicity but graphene and graphene oxide (GO) do not have a “length”. An important similarity between these carbon nanomaterials is that both graphene/graphene oxide and carbon nanotube structures vary according to the synthetic processes employed. Such processes can also change their physical properties, including dispersity, surface functionality, and their toxicity. In the materials science world, carbon nanostructures such as fullerenes, carbon nanotubes and graphene are famous for their small dimension and unique architecture, and several possible applications in diversified areas. In addition to these carbon nanostructures, scientists now produce a plethora of carbon-based nanoforms such as ‘bamboo’ tubes, ‘herringbone’ and ‘bell’ structures. Figure 1.1 shows a “family tree” of carbon nanoforms that were obtained by applying various transformations to graphene (details of operations are provided in the figure). Though the diagram is non-exhaustive (primarily for clarity), this chart is useful to classify the nanoforms by morphology and provides a first step towards a standardized nomenclature.

The research involving graphene has grown at a spectacular pace in the last few years. Several potential applications have been proposed for graphene. These include conductive and high-strength composites, energy storage and energy conversion devices, sensors, field emission displays and radiation sources, hydrogen storage media, and nanometre-sized semiconductor devices, probes, and interconnect (Scheme 1.1). Impressive advances have been made in
Figure 1.1 “Family tree” of primary carbon nanoforms showing the topological relationships between them. Forms which have not been identified experimentally are faded. (Reproduced from ref. 19. Copyright 2011, with permission from Elsevier Ltd.)

Scheme 1.1 Various applications of graphene including biomedical applications.