

## Contents

**Preface** XIII

**Contributors** XV

<b>1</b>	<b>An Introduction to Bio-nanohybrid Materials</b>	<b>1</b>
	<i>Eduardo Ruiz-Hitzky, Margarita Darder, Pilar Aranda</i>	
1.1	Introduction: The Assembly of Biological Species to Inorganic Solids	1
1.2	Bio-nanohybrids Based on Silica Particles and Siloxane Networks	4
1.3	Calcium Phosphates and Carbonates in Bioinspired and Biomimetic Materials	9
1.4	Clay Minerals and Organoclay Bio-nanocomposites	13
1.5	Bio-Nanohybrids Based on Metal and Metal Oxide Nanoparticles	20
1.6	Carbon-based Bio-nanohybrids	22
1.7	Bio-nanohybrids Based on Layered Transition Metal Solids	28
1.8	Trends and Perspectives	31
	References	32
<b>2</b>	<b>Biomimetic Nanohybrids Based on Organosiloxane Units</b>	<b>41</b>
	<i>Kazuko Fujii, Jonathan P. Hill, Katsuhiko Ariga</i>	
2.1	Introduction	41
2.2	Monolayer on Solid Support	45
2.3	Layered Alkylsiloxane	53
2.4	Organic–Inorganic Hybrid Vesicle “Cerasome”	59
2.5	Mesoporous Silica Prepared by the Lizard Template Method	65
2.6	Future Perspectives	69
	References	71

<b>3</b>	<b>Entrapment of Biopolymers into Sol–Gel-derived Silica Nanocomposites</b> 75
	<i>Yury A. Shchipunov</i>
3.1	Introduction 75
3.2	Sol–Gel Processes 77
3.2.1	Chemistry 77
3.2.1.1	Hydrolysis 77
3.2.1.2	Condensation 78
3.2.1.3	Sol–Gel Transition 78
3.2.2	Silica Precursors 79
3.2.2.1	Orthosilicic Acid 80
3.2.2.2	Sodium Metasilicate 80
3.2.2.3	Alkoxides 80
3.2.3	Two-Stage Approach to Biopolymer Entrapment 82
3.3	Biocompatible Approaches 84
3.3.1	Modified Sol–Gel Processing 84
3.3.1.1	Method of Gill and Ballesteros 84
3.3.1.2	Low-Molecular and Polymeric Organic Additives 85
3.3.2	Organically-modified Precursors 86
3.3.3	Biocompatible Precursors by Brennan <i>et al.</i> 87
3.4	One-Stage Approach Based on a Silica Precursor with Ethylene Glycol Residues 88
3.4.1	Precursor 88
3.4.2	Role of Biopolymers in Sol–Gel Processing 89
3.4.3	Advantages of One-Stage Processes 96
3.4.4	Hybrid Biopolymer–Silica Nanocomposite Materials 98
3.4.5	Enzyme Immobilization 99
3.5	Perspectives 102
	References 103
<b>4</b>	<b>Immobilization of Biomolecules on Mesoporous Structured Materials</b> 113
	<i>Ajayan Vinu, Narasimhan Gokulakrishnan, Toshiyuki Mori, Katsuhiko Ariga</i>
4.1	Introduction 113
4.2	Immobilization of Protein on Mesoporous Silica 116
4.3	Immobilization of Protein on Mesoporous Carbon and Related Materials 124
4.4	Immobilization of Other Biopolymers on Mesoporous Materials 133
4.5	Immobilization of Small Biomolecules on Mesoporous Materials 137
4.6	Advanced Functions of Nanohybrids of Biomolecules and Mesoporous Materials 141
4.7	Future Perspectives 149
	References 150

<b>5</b>	<b>Bio-controlled Growth of Oxides and Metallic Nanoparticles</b>	<b>159</b>
	<i>Thibaud Coradin, Roberta Brayner, Fernand Fiévet, Jacques Livage</i>	
5.1	Introduction	159
5.2	Biomimetic Approaches	160
5.3	<i>In vitro</i> Synthesis of Hybrid Nanomaterials	165
5.3.1	Polysaccharides	165
5.3.1.1	Alginates	165
5.3.1.2	Carrageenans	169
5.3.1.3	Chitosan	171
5.3.2	Proteins	174
5.3.2.1	Gelatin	174
5.3.2.2	Collagen	175
5.3.2.3	Protein Cages and Viral Capsids	177
5.3.3	Lipids	180
5.3.4	DNA Scaffolds	181
5.4	Perspectives: Towards a “Green Nanochemistry”	183
	References	184
<b>6</b>	<b>Biom mineralization of Hydrogels Based on Bioinspired Assemblies for Injectable Biomaterials</b>	<b>193</b>
	<i>Junji Watanabe, Mitsuru Akashi</i>	
6.1	Introduction	193
6.1.1	Biom minerals as Nanomaterials	193
6.1.2	Nanomaterials for Biofunctions	196
6.2	Fundamental Concept of Bioinspired Approach	197
6.2.1	Bioinspired Approach to Materials	197
6.2.2	Concrete Examples of the Bioinspired Approach	198
6.3	Alternate Soaking Process for Biom mineralization and their Bio-functions	199
6.3.1	Nanoassembly by Polyelectrolytes	199
6.3.2	Alternate Soaking Process for Biom mineralization	200
6.3.3	Biom mineralization of Hydrogels for Bio-functions	201
6.4	Electrophoresis Process for Biom mineralization	203
6.4.1	Innovative Methodology of Electrophoresis Process for Biom mineralization	203
6.4.2	Application for Injectable Materials	204
6.5	Conclusions	206
	References	206
<b>7</b>	<b>Bioinspired Porous Hybrid Materials via Layer-by-Layer Assembly</b>	<b>209</b>
	<i>Yajun Wang, Frank Caruso</i>	
7.1	Introduction	209
7.2	Porous Materials	209
7.2.1	Microporous Materials	210

7.2.2	Mesoporous Material	210
7.2.3	Macroporous Materials	211
7.3	LbL Assembly	213
7.4	LbL Assembly on MS Substrates	214
7.4.1	Encapsulation of Biomolecules in MS Particles	214
7.4.2	MS Spheres as Templates for the Preparation of Hollow Capsules	218
7.4.3	Preparation of Protein Particles via MS Sphere Templating	220
7.4.4	Template Synthesis of Nanoporous Polymeric Spheres	221
7.5	LbL Assembly on Macroporous Substrates	225
7.5.1	LbL Assembly on Tubular Substrates	226
7.5.2	LbL Assembly on 3DOM Materials	229
7.5.3	LbL Assembly on Naturally Occurring Porous Substrates	231
7.6	Summary and Outlook	232
	References	233
<b>8</b>	<b>Bio-inorganic Nanohybrids Based on Organoclay Self-assembly</b>	<b>239</b>
	<i>Avinash J. Patil, Stephen Mann</i>	
8.1	Introduction	239
8.2	Synthesis and Characterization of Organically Functionalized 2:1 Magnesium Phyllosilicates	240
8.3	Magnesium Organophyllosilicates with Higher-order Organization	243
8.4	Intercalation of Biomolecules within Organically Modified Magnesium Phyllosilicates	246
8.4.1	Protein–Organoclay Lamellar Nanocomposites	247
8.4.2	DNA–Organoclay Lamellar Nanostructures	252
8.4.3	Drug–Organoclay Layered Nanocomposites	253
8.5	Hybrid Nanostructures Based on Organoclay Wrapping of Single Biomolecules	254
8.5.1	Organoclay-wrapped Proteins and Enzymes	254
8.5.2	Organoclay-wrapped DNA	258
8.6	Functional Mesolamellar Bio-inorganic Nanocomposite Films	260
8.7	Summary	262
	References	262
<b>9</b>	<b>Biodegradable Polymer-based Nanocomposites: Nanostructure Control and Nanocomposite Foaming with the Aim of Producing Nano-cellular Plastics</b>	<b>271</b>
	<i>Masami Okamoto</i>	
9.1	Introduction	271
9.2	Nano-structure Development	272
9.2.1	Melt Intercalation	272
9.2.2	Interlayer Structure of OMLFs and Intercalation	273
9.2.2.1	Nano-fillers	273
9.2.2.2	Molecular Dimensions and Interlayer Structure	274
9.2.2.3	Correlation of Intercalant Structure and Interlayer Opening	277

9.2.2.4	Nanocomposite Structure	278
9.3	Control of Nanostructure Properties	282
9.3.1	Flocculation Control and Modulus Enhancement	282
9.3.2	Linear Viscoelastic Properties	284
9.3.3	Elongational Flow and Strain-induced Hardening	288
9.4	Physicochemical Phenomena	290
9.4.1	Biodegradability	290
9.4.2	Photodegradation	295
9.5	Foam Processing using Supercritical CO <sub>2</sub>	296
9.5.1	PLA-based Nanocomposite	296
9.5.2	Temperature Dependence of Cellular Structure	298
9.5.3	CO <sub>2</sub> Pressure Dependence	301
9.5.4	TEM Observation	305
9.5.5	Mechanical Properties of Nanocomposite Foams	307
9.6	Porous Ceramic Materials via Nanocomposites	307
9.7	Future Prospects	309
	References	310
<b>10</b>	<b>Biomimetic and Bioinspired Hybrid Membrane Nanomaterials</b>	<b>313</b>
	<i>Mihail Barboiu</i>	
10.1	Introduction	313
10.2	Molecular Recognition-based Hybrid Membranes	314
10.2.1	Multiple Molecular Recognition Principles	314
10.3	Self-organized Hybrid Membrane Materials	318
10.3.1	Ionic-conduction Pathways in Hybrid Membrane Materials	318
10.3.1.1	Ionic-conduction Pathways in Macrocyclic Hybrid Materials	319
10.3.1.2	Ionic-conduction Pathways in Peptido-mimetic Hybrid Materials	319
10.3.2	Self-organization in Hybrid Supramolecular Polymers	324
10.3.2.1	Self-organization by Base Pairing in Hybrid Supramolecular Polymers	325
10.3.2.2	Self-Organization of the Guanine Quadruplex in Hybrid Supramolecular Polymers	328
10.4	Dynamic Site Complexant Membranes	330
10.5	Conclusions	333
	References	334
<b>11</b>	<b>Design of Bioactive Nano-hybrids for Bone Tissue Regeneration</b>	<b>339</b>
	<i>Masanobu Kamitakahara, Toshiki Miyazaki, Chikara Ohtsuki</i>	
11.1	Introduction	339
11.2	Composite of Bioactive Ceramic Particles and Polymers	340
11.3	Bone-bonding Mechanism of Bioactive Materials	341
11.3.1	Interface between Bone and Bioactive Material	341
11.3.2	Simulated Body Fluid	342
11.3.3	Hydroxyapatite Formation on Bioactive Materials	343

11.4	Sol–Gel-derived Bioactive Nano-hybrids	345
11.4.1	Silicate-based Nano-hybrids	345
11.4.2	Nano-hybrids Starting from Methacryloxy Compounds	347
11.4.3	Nano-hybrids Based on Other than Silicate	349
11.4.4	Nano-hybrids Combined with Calcium Phosphates	353
11.5	Nano-hybrid Consisting of Bone-like Hydroxyapatite and Polymer	354
11.5.1	Biomimetic Process	354
11.5.2	Hydroxyapatite Deposition on Polymers Modified with Silanol Groups	356
11.5.3	Hydroxyapatite Deposition on Natural Polymers	357
11.5.4	Hydroxyapatite Deposition on Synthetic Polymers	358
11.5.5	Control of the Structure of Hydroxyapatite	359
11.6	Nano-hybrid Consisting of Hydroxyapatite and Protein	360
11.7	Conclusion	361
	References	361

## 12 Nanostructured Hybrid Materials for Bone Implants

### Fabrication 367

*María Vallet-Regí, Daniel Arcos*

12.1	Introduction	367
12.2	Bone: A Biological Hybrid Nanostructured Material	369
12.3	Biomimetic Materials for Bone Repair. The Hybrid Approach	372
12.3.1	The Hybrid Approach	374
12.4	Synthesis and Properties of Organic–Inorganic Hybrid Materials for Bone and Dental Applications	375
12.4.1	Class I Hybrid Materials	375
12.4.1.1	BG–Poly(vinyl Alcohol)	375
12.4.1.2	Silica Particles–pHEMA	378
12.4.2	Class II Hybrid Materials	378
12.4.2.1	PMMA–SiO <sub>2</sub> Ormosils	380
12.4.2.2	PEG–SiO <sub>2</sub> Ormosils	380
12.4.2.3	PDMS–CaO–SiO <sub>2</sub> –TiO <sub>2</sub> Ormosils	380
12.4.2.4	PTMO–CaO–SiO <sub>2</sub> –TiO <sub>2</sub> Hybrid Materials	383
12.4.2.5	MPS–HEMA Ormosils	383
12.4.2.6	Gelatine–SiO <sub>2</sub> Systems	384
12.4.2.7	Poly( $\epsilon$ -Caprolactone)–Silica Ormosils	385
12.4.2.8	Bioactive Star Gels	387
12.4.2.9	The Synthesis of Bioactive Star Gels	388
12.4.2.10	How to Characterize Bioactive Star Gels?	389
12.4.2.11	The Bioactivity of the Star Gels	389
12.4.2.12	The Mechanical Properties of Bioactive Star Gels	391
12.5	Conclusion	392
	References	393

<b>13</b>	<b>Bio-inorganic Conjugates for Drug and Gene Delivery</b>	<b>401</b>
	<i>Jin-Ho Choy, Jae-Min Oh, Soo-jin Choi</i>	
13.1	Introduction	401
13.2	Synthesis of Bio-inorganic Conjugates	403
13.3	Bio-inorganic Conjugate for Efficient Gene Delivery	407
13.3.1	Cellular Uptake Kinetics of LDH-FITC Into Cells	407
13.3.2	Effect of As-myc-LDH Hybrid on the Suppression of Cancer Cells	408
13.4	Bio-inorganic Conjugate for Efficient Drug Delivery	409
13.4.1	Cellular Uptake of MTX-LDH Hybrid	409
13.4.2	Effect of MTX-LDH on Cell Proliferation and Viability	409
13.4.3	Effect of MTX-LDH Hybrid on the Cell Cycle	410
13.4.4	Potential of Bio-inorganic Conjugates for Gene and Drug Delivery	411
13.5	Cellular Uptake Mechanism of LDH	412
13.5.1	Endocytosis of LDH	412
13.5.2	Endocytic Pathway of LDH	413
13.6	Conclusion	415
	References	415
<b>14</b>	<b>Halloysite Nanotubes, a Novel Substrate for the Controlled Delivery of Bioactive Molecules</b>	<b>419</b>
	<i>Yuri M. Lvov, Ronald R. Price</i>	
14.1	Halloysite Structural Characterization	419
14.2	Macromolecule Loading and Sustained Release	422
14.2.1	Nanotubule Loading Procedure	422
14.2.2	Drugs and Biocides	423
14.2.3	Globular Proteins	427
14.3	Nanoassembly on Tubules and at the Lumen Opening	428
14.4	Catalysis in a Nanoconstrained Volume of the Tubule Lumen	431
14.5	Multilayer Halloysite Assembly for Organized Nanofilms. Forming Low Density Tubule Nanoporous Materials	436
14.5.1	Tubule-Polycation Multilayer	436
14.5.2	Assembly of Tubule/Sphere Multilayer Nanocomposites	437
14.6	Applications: Current and Potential	438
	References	439
<b>15</b>	<b>Enzyme-based Bioinorganic Materials</b>	<b>443</b>
	<i>Claude Forano, Vanessa Prévot</i>	
15.1	Introduction	443
15.2	Enzymes versus Inorganic Host Properties	445
15.2.1	Enzyme Properties	445
15.2.2	Inorganic Host Structures	446
15.3	Immobilization Strategy	446
15.3.1	Adsorption Process	448
15.3.2	Encapsulation Processes	449
15.3.3	Nanostructuring of Enzyme-based Films	450

15.3.4	Covalent Grafting	452
15.4	Bioinorganic Nanohybrids	454
15.4.1	Immobilization of Enzymes in 2-D Inorganic Hosts	454
15.4.1.1	Immobilization in Clay Minerals and Related Materials	454
15.4.1.2	Immobilization in Layered Double Hydroxides	457
15.4.1.3	Immobilization in Layered Metal Oxides	460
15.4.1.4	Immobilization in Layered Zirconium Phosphate and Phosphonate	461
15.4.2	Immobilization of Enzymes in 3-D Inorganic Hosts	464
15.4.2.1	Immobilization in SiO <sub>2</sub>	464
15.4.2.2	Immobilization on Alumina	467
15.4.2.3	Immobilization in Zeolite	469
15.4.2.4	Immobilization in Hydroxyapatite and Tricalciumphosphate	471
15.5	Enzyme–Host Structure Interactions	471
	References	476

<b>Index</b>	<b>485</b>
--------------	------------