

RSC Smart Materials

Biointerfaces

Where Material Meets Biology

Edited by Dietmar W Hutmacher and Wojciech Chrzanowski



Biointerfaces Where Material Meets Biology

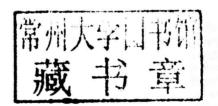
Edited by

Dietmar Hutmacher

Queensland University of Technology, Kelvin Grove, Australia Email: dietmar.hutmacher@qut.edu.au

Wojciech Chrzanowski

University of Sydney, Sydney, Australia Email: wojciech.chrzanowski@sydney.edu.au







RSC Smart Materials No. 10

Print ISBN: 978-1-84973-876-7 PDF eISBN: 978-1-78262-845-3

ISSN: 2046-0066

A catalogue record for this book is available from the British Library

© The Royal Society of Chemistry 2015

All rights reserved

Apart from fair dealing for the purposes of research for non-commercial purposes or for private study, criticism or review, as permitted under the Copyright, Designs and Patents Act 1988 and the Copyright and Related Rights Regulations 2003, this publication may not be reproduced, stored or transmitted, in any form or by any means, without the prior permission in writing of The Royal Society of Chemistry or the copyright owner, or in the case of reproduction in accordance with the terms of licences issued by the Copyright Licensing Agency in the UK, or in accordance with the terms of the licences issued by the appropriate Reproduction Rights Organization outside the UK. Enquiries concerning reproduction outside the terms stated here should be sent to The Royal Society of Chemistry at the address printed on this page.

The RSC is not responsible for individual opinions expressed in this work.

Published by The Royal Society of Chemistry, Thomas Graham House, Science Park, Milton Road, Cambridge CB4 0WF, UK

Registered Charity Number 207890

For further information see our web site at www.rsc.org

Printed and bound by CPI Group (UK) Ltd, Croydon, CRO 4YY

Biointerfaces Where Material Meets Biology

RSC Smart Materials

Series Editors:

Hans-Jörg Schneider, Saarland University, Germany Mohsen Shahinpoor, University of Maine, USA

Titles in this Series:

- 1: Janus Particle Synthesis, Self-Assembly and Applications
- 2: Smart Materials for Drug Delivery: Volume 1
- 3: Smart Materials for Drug Delivery: Volume 2
- 4: Materials Design Inspired by Nature
- 5: Responsive Photonic Nanostructures: Smart Nanoscale Optical Materials
- 6: Magnetorheology: Advances and Applications
- 7: Functional Nanometer-Sized Clusters of Transition Metals: Synthesis, Properties and Applications
- 8: Mechanochromic Fluorescent Materials: Phenomena, Materials and Applications
- 9: Cell Surface Engineering: Fabrication of Functional Nanoshells
- 10: Biointerfaces: Where Material Meets Biology

How to obtain future titles on publication:

A standing order plan is available for this series. A standing order will bring delivery of each new volume immediately on publication.

For further information please contact:

Book Sales Department, Royal Society of Chemistry, Thomas Graham House, Science Park, Milton Road, Cambridge, CB4 0WF, UK Telephone: +44 (0)1223 420066, Fax: +44 (0)1223 420247

Email: booksales@rsc.org

Visit our website at www.rsc.org/books

Preface

Biointerfaces: Surfaces that Guide Biology!

This book brings together scientists and engineers that work in diverse fields of physics, chemistry, biology, biotechnology, materials science, diagnostics, and medicine, with a broad focus on biointerface science. The engineered biomolecular interfaces described and discussed in the book are designed to recapitulate the functions of their natural counterparts. By uniting physical science and the engineering of surfaces with biology, fresh prospects are opened up and bridge the gap between fundamental research and development of application-oriented technologies and products.

The rapidly ageing population, maintaining high levels of activity well into retirement, together with the rising incidence of obesity- and diabetes-related dysfunction of the musculoskeletal system, results in an increasing number of surgeries that require implantable devices. There are now millions of cases each year requiring implantable fixation devices (over 6 million fractures in the USA alone; 11 fractures every minute). Regeneration of tissues can be aided with new classes of materials, *e.g.*, bioceramics, hydrogels or composites, which are emerging as the most promising approaches in many clinical applications. Despite many advances in materials synthesis and device design, the implantation of biomaterials almost universally leads to the device being enveloped in avascular fibrotic tissue that walls off the device from the body. This can be detrimental to the function of the implant/device, reducing its lifetime, and often necessitates repeated surgery and device replacement.

The implantation of a material/device into body is followed by the immediate interactions of body fluids, cells and tissues with the surface. These interactions are critical for obtaining the desired functionality of the material/device and, subsequently, they determine the success of the specific medical procedure. The communication between biological structures

RSC Smart Materials No. 10 Biointerfaces: Where Material Meets Biology Edited by Dietmar Hutmacher and Wojciech Chrzanowski © The Royal Society of Chemistry 2015 Published by the Royal Society of Chemistry, www.rsc.org vi Preface

(i.e., cells and tissues) and implanted physical objects (i.e., device or material) occurs at the interface (termed the biointerface), and the surface of the implanted material is a key element that determines the outcomes of this communication. Surface properties are of special significance when biological and microbiological interactions are considered.

There are several, surface-related cues presented to biological milieu, which includes surface texture (also topography), mechanical properties, chemical composition, surface charge and stability of the surface (degradability). These cues can be presented to cell and tissues as two- and threedimensional structures. It is well established that each of the surface parameters can modulate first interactions with the body fluids, and then cellular responses such as cell attachment, migration and differentiation. Although each of the individual parameters has been shown to be effective in controlling some of the biological functions, it is well known that there is a complex interplay between these parameters that may strengthen (cumulative effects) or weaken specific design modalities. Therefore, by tailoring the mechanical properties of materials, chemical composition, topography, and charge it is possible to design functional surfaces, which effectively control biological and microbiological responses. For example, osseointegration is often a key aim, which can be achieved by nanopatterning of the surface or attaching signalling molecules such as peptides.

This book describes the most recent advances in the manufacture and characterisation of biointerfaces that aim to provide the desired and predicted biological responses. It covers a wide range of materials and techniques used in the investigations of biomaterials, with a focus on musculoskeletal applications. Importantly, the book includes several examples of translational research and contains many 'how to do' or 'walk the talk' sections, which makes it suitable for student readers to gain a new knowledge how to design, fabricate and characterise a new generation of technologies and products based on biointerface science.

D. W. HutmacherW. Chrzanowski

Contents

Section A Biomolecular Interfaces for Cell Modulations

Chapter 1	Diff Jorg	rentiation	erfaces to Control Stem Cell s Paredes, Alessandro Polini and	3
	1.1	Modification of	Biomaterial Surfaces with Proteins	3
		1.1.1 Introduc	etion	4
		1.1.2 Influenc Adhesion	e of Modified Surfaces on Cell n	5
		1.1.3 Influenc	e of Modified Surfaces on Cell	
		Prolifera	tion and Differentiation	9
	1.2	Methods of Pro	tein Immobilization	11
		1.2.1 Surface	Functionalization	11
		1.2.2 Determi	nation of Successful	
		Function	nalization of Proteins, Growth	
			or Peptides	16
	A		ocols for the Visualization and	
		Immobilization		17
			or the Visualization of Protein on a	
			sing Atomic Force Microscopy	17
			to Determine the Degree of	
			lization of Growth Factors and Small	
			n Naturally Derived Type I Collagen	
		Hydrogels		20
			to Immobilize Growth Factors and	
			tides by 'Classic' Physicorption	21

RSC Smart Materials No. 10

Biointerfaces: Where Material Meets Biology

Edited by Dietmar Hutmacher and Wojciech Chrzanowski

© The Royal Society of Chemistry 2015

Published by the Royal Society of Chemistry, www.rsc.org

			A Protocol to Immobilize Growth Factors and		
			Small Peptides by Polydopamine		
			Coating-based Physisorption	22	
			Protocol to Immobilize Growth Factors and		
			Small Peptides by Silanization-based	22	
	D . C		Physisorption	23	
	Refe	rences		23	
Chapter 2	Add	itive M	anufacturing and Surface Modification		
			rials using Self-assembled		
		olayer		30	
			Vaithilingam, Ruth D. Goodridge,		
			C. Christie, Steve Edmondson and		
			M. Hague		
	2.1	Testone	reference in more and additional contributions.	20	
	2.1		luction	30	
		2.1.1		31	
	2.2	2.1.2		33	
	2.2		ive Manufacturing	34	
			Selective Laser Melting	35	
	2.3		ce Modification	40	
		2.3.1	Issues with Current Surface Modification	10	
		2 2 2	Techniques	40	
		2.3.2	Surface Modification Using Self-assembled Monolayers	11	
		222		41	
		2.3.3	Functionalisation of Self-assembled Monolayers	44	
	2.4	Case		46	
	2.4	2.4.1	Functionalisation of Selective Laser	40	
		2.4.1	Melted Parts with Ciprofloxacin using		
			Self-assembled Monolayers	46	
		2.4.2		40	
		2.4.2	Surface Functionalisation using	16	
	2.5	Concl	Ciprofloxacin	46	
		erences		51	
	Reit	erences		51	
Chapter 3	Pro	bing Bi	ointerfaces: Electrokinetics	55	
	Ralj	Zimme	ermann, Jérôme F. L. Duval and		
	Carsten Werner				
	3.1	Introd	duction	55	
	3.2		amental Principles and Theory	56	
	0.2	3.2.1	Streaming Current and Streaming Potential	30	
		0.2.1	Measurements in Rectangular		
			Microchannels	56	
		3.2.2		60	

Contents	ix
----------	----

	3.3	Electrokinetic Analysis to Unravel Electrosurface	
		Phenomena at Biointerfaces	61
		3.3.1 Segment Distribution of Stimuli-responsive	
		Soft Thin Films	61
		3.3.2 Composition and Structure of Biohybrid	
		Hydrogels	64
		3.3.3 Fluidity Modulation in Phospholipid Bilayers	
		by Electrolyte Ions	66
	3.4	Summary	69
	A	Appendix: Methods	70
		A.1 Measurement of Streaming Current/Potential	70
		A.2 Simulations of the Electro-Hydrodynamics at	
		Diffuse Soft Interfaces	70
		A.3 Thin Polymer Films for Streaming	
		Current/Potential Measurements	71
	Refe	erences	71
Chapter 4	Gro	wth Factor Delivery Systems for the Treatment	
Chapter 1		Cardiovascular Diseases	74
		alia Zapata, Elisa Garbayo, Maria J. Blanco-Prieto and	, .
		pe Prosper	
	ren	ot 170spei	
	4.1	Introduction	74
	4.2	Drug Delivery Systems for Growth Factors	77
	1.2	4.2.1 Growth Factors	78
		4.2.2 Biomaterials	79
	4.3	Growth Factor Drug Delivery Systems for Cardiac	, ,
	110	Applications	86
		4.3.1 Angiogenesis	86
		4.3.2 Direct Effect on Cardiac Cell Proliferation,	00
		Remodeling, Tissue Protection and	
		Differentiation	88
		4.3.3 Other Proteins	90
		4.3.4 Combined Therapies	91
	4.4	Growth Factor Delivery Systems and Cell Therapy	93
	4.5	Conclusions	94
		nowledgements	95
		erences	95
	1010		50
		Section B Structural Biointerfaces	
Chapter 5	Tito	nium Phosphate Glass Microspheres as Microcarriers	
Chapter 5		In Vitro Bone Cell Tissue Engineering	105
		ty J. Lakhkar, Carlotta Peticone, David De Silva-Thompson,	103
	ivar	n B. Wall, Vehid Salih and Jonathan C. Knowles	
	F 4	Introduction	× 0 =
	5.1	INTRODUCTION	105

X

	5.2	Produ	ction of Titanium Phosphate Glass	
		Micros	spheres by Flame Spheroidisation	107
			Materials	109
		5.2.2	Equipment	109
		5.2.3		110
		5.2.4		111
		5.2.5		112
		5.2.6	Preparation of Glass Microspheres	113
		5.2.7	Expected Outcomes and Other	
			Considerations	114
	5.3	Visual	isation and Quantification of Microsphere	
		Degrae	dation by Time-lapse Imaging	115
		5.3.1	Materials	116
		5.3.2	Equipment	116
		5.3.3	Setting Up a Time-lapse Experiment	117
		5.3.4	Expected Outcomes and Other	
			Considerations	120
	5.4	Cell C	ulture of Microspheres with Bone Cells	121
		5.4.1	Materials and Reagents	123
		5.4.2		123
		5.4.3	0	124
		5.4.4	Sample Preparation for Scanning Electron	
			Microscopy	126
		5.4.5		127
	5.5		ary: On-going Work and Future Directions	128
	Refe	erences		129
Chapter 6	Bioi	nterfac	es Between Cells and Substrates in Three	
	Din	ension	s	133
	Ada	m S. Ha	yward, Neil R. Cameron and Stefan A. Przyborski	
	6.1		tructural and Physiological Relevance of	
		Three-	-dimensional Biointerfaces	133
	6.2		Natural and Synthetic Materials to Create	
		Three-	-dimensional Biointerfaces	134
		6.2.1	Sandwiching Cells with Extracellular Matrix	
			Proteins	135
		6.2.2	Hydrogels	136
		6.2.3	Electrospun Polymer Fibres	136
		6.2.4	Three-dimensional Printed Scaffolds	137
		6.2.5	Porous Polymeric Scaffolds	138
		6.2.6	Emulsion Templating and Alvetex®	139
	6.3		ods to Examine Cell Behaviour in Three	
			nsions: Alvetex [®] Case Study	141
		6.3.1	Imaging of Live Cells	141

~		
('0	nto	nts

Contents		xi		
	6.3.2 Histology and Immunocytochemistry	143		
	6.3.3 Electron Microscopy	145		
	6.3.4 Metabolic Assays and Other Functional			
	Experiments	146		
	6.3.5 Genomics and Proteomics	147		
	6.3.6 Cell Retrieval	147		
	6.4 Future Direction of Biointerfaces in Three Dimensions	148		
	References	149		
	Section C Multi-functional Biointerfaces			
Chapter 7	Interfaces in Composite Materials	153		
	Ensanya A. Abou Neel, Wojciech Chrzanowski and			
	Anne M. Young			
	7.1 Introduction	153		
	7.1.1 Biomedical Applications of Composites	154		
	7.2 Composite Interfaces	155		
	7.2.1 Filler–Matrix	156		
	7.2.2 Composite-surrounding Environment	157		
	7.3 State-of-the-Art 'Talking' to Living Organisms	160		
	7.3.1 Smart Composites Based on Biomimetic			
	Matrices	161		
	7.3.2 On-demand Responsive Composites	161		
	7.3.3 Composites Based on Smart Fillers	163		
	7.3.4 Functionalized Composites	163		
	7.4 Interfaces of Clinical Importance	164		
	7.4.1 The Osteochondral Interface	164		
	7.4.2 Neuromuscular Prosthesis-Tissue Interface	168		
	7.4.3 Composite–Dentin Interface	169		
	7.5 Step-by-Step Preparation of an Example of Smart			
	Composites	171		
	7.5.1 Synthesis of Poly(lactide-co-propylene			
	glycol-co-lactide) co-oligomer	171		
	7.5.2 Methacrylation of Poly(lactide-co-propylene			
	glycol-co-lactide) co-oligomer	172		
	7.5.3 Preparation of the Composite	172		
	7.6 Advances and Challenges	172		
	References	173		
Chapter 8	Bioactive Conducting Polymers for Optimising the Neural			
	Interface	192		
	Josef Goding, Rylie Green, Penny Martens and			
	Laura Poole-Warren			
	8.1 Introduction	192		

xii	Contents

	8.2	Conducting Polymers	193
		8.2.1 Mechanism of Conduction	193
		8.2.2 Fabrication	194
		8.2.3 Characterisation	196
		8.2.4 Biomedical Applications of Conducting	
		Polymers	201
		8.2.5 Limitations of Conducting Polymers in	
		Neural Interfaces	206
	8.3	Biofunctionalisation of Conducting Polymers	206
		8.3.1 Incorporation of Bioactive Molecules	206
		8.3.2 Conducting Polymers as Bioactive Surfaces	208
		8.3.3 Conducting Polymers as Drug Delivery	
		Devices	209
		8.3.4 Limitations of Biofunctionalised Conducting	
		Polymers	210
	8.4	Modified Biofunctional Conducting Polymers	
		for Neural Interfaces	211
		8.4.1 Structured Conducting Polymers	211
		8.4.2 Conducting Polymer Composites	212
	8.5	Conclusion	215
	A	Appendix: Methodologies and Practical Advice	215
		A.1 Fabrication: Electrochemical Deposition	216
		A.2 Characterisation	216
	Refe	erences	218
Chamten 0	n.l.		
Chapter 9		caprolactone-based Scaffolds Fabricated Using Fused	
		osition Modelling or Melt Extrusion Techniques for	221
		e Tissue Engineering	221
		rina S. P. Poh, Michal Bartnikowski, Travis J. Klein,	
	Gile	s T. S. Kirby and Maria A. Woodruff	
	9.1	Introduction	221
	9.1		221
		9.1.1 Bone Tissue Engineering9.1.2 Polymers Used in Bone Tissue Engineering	221
	9.2	Scaffold Fabrication Techniques	223
	9.4	9.2.1 Principles of Additive Manufacturing: Fused	223
		Deposition Modelling and Melt Extrusion	224
	9.3	Polycapralactone Scaffolds	227
	9.0	9.3.1 Physical Characteristics of Polycaprolactone	221
		Scaffolds	227
		9.3.2 Polycaprolactone Scaffold <i>In Vitro</i> Analysis	229
	9.4	Polycaprolactone-based Composite Scaffolds	230
	2.7	9.4.1 Polycaprolactone with Hydroxyapatite	230
		9.4.2 Polycaprolactone with Tricalcium	250
		Phosphate	231
		- mospitate	201

Contents xiii

	9.5		Functionalisation of Polycaprolactone-based	
		Scaffold	ds	237
		9.5.1	Polycaprolactone with Bone Marrow Aspirate	237
		9.5.2	Polycaprolactone with Heparin	237
		9.5.3	Collagen-mimetic Peptide: The Peptide	
			Sequence GFOGER	238
			Plasma Modification and Fibronectin	
			Coating	238
			Hydroxyl Functionalisation	239
			Carbonated Hydroxyapatite–Gelatin	
			Composite	240
			Phlorotannin Conjugations	240
	9.6		prolactone-based Scaffolds as Drug Carriers	240
			Antibiotics	240
			Adeno-associated Virus Encoding Bone	
			Morphogenetic Protein-2	241
			Bone Morphogenetic Protein	242
	9.7		ed Scaffold Architecture	246
			Scaffolds with Vascular Channels	246
			Hybrid Osteochondral Scaffolds	247
	9.8		l Studies	249
	9.9	Conclu		249
	A		dix: Methods Section	250
			lixing Polycaprolactone with Bioactive Glass	
			articles by Fast Precipitation into Excess	
			00% Ethanol	250
			Tathematical Derivation of Melt Extruded	200
			caffold Microfilament Diameter from	
			ranslational Velocity	251
	Ackı	nowledge		252
		rences		252
		Section	D Chemo-structural Biointerfaces	
		Section	b chemo structurar biometraces	
Chapter 10) Hig	h Throu	ghput Techniques for the Investigation of	
	Cell	-Materia	al Interactions	259
	Laur	ren R. Cle	ements, Helmut Thissen and Nicolas H. Voelcker	
	10.1	Introd	luction	259
	10.1	10.1.1		239
		10.1.1	and Topography on Cell Behaviour	260
		10.1.2		262
		10.1.2		202
		10.1.3		265
	10.2	Gradi	Overview of High-throughput Techniques ent Surfaces	265
	10,2	10.2.1		267
		10.2.1	Topography Gradients	269

xiv	Contents

		10.2.2	Chemical Gradients	280
		10.2.3	Biological Density Gradients	292
		10.2.4		295
		10.2.5	Topography: The Chemistry of	
			Two-dimensional Gradients	296
		10.2.6	Two-dimensional Topography Gradients	299
	10.3	Conclu		300
		ences		301
	110101			001
Chapter 1	1 Graft	ing of F	unctional Monomers on Biomaterials	312
Chapter 3			lahl and Jing Zhong Luk	
	11.1	Introdu	action	312
	11.2	Method	ds for Grafting of Functional Monomers	313
		11.2.1	Simultaneous Grafting	313
		11.2.2	Peroxy/hydroxyl Grafting	318
		11.2.3	Controlled Radical Polymerisation	
			Grafting from a Surface	320
		11.2.4	Plasma Polymerisation	322
		11.2.5	Grafting of Functional Monomers to	
			Porous Substrates	325
	11.3	Charac	terisation of Grafted Materials	326
		11.3.1		328
		11.3.2	Physical Characterisation of Surfaces	332
		11.3.3		332
		11.3.4	Lateral Distribution of Grafted Chains	333
		11.3.5	Penetration Depth of Grafted Chains	335
	11.4		iding Remarks	337
		owledge		337
		ences		337
	Refer	circes		337
Chanter 1	2 Desi	on of Me	obile Supramolecular Biointerfaces for	
Chapter			f Biological Responses	343
			ad Nobuhiko Yui	0.10
	J			
	12.1	Introdu	uction	343
	12.2	Hydrat	ed Viscoelastic Factor of Polymeric	
		Biomat		346
	12.3		ing Dynamic Surface for Regulation of	
			ed Viscoelastic Factor	348
	12.4		ical Responses on the Dynamic Surfaces	350
	12.4	12.4.1	The Effect of Hydrated Viscoelastic	330
		12.4.1	Properties on Fibrinogen Adsorption	250
		12.4.2	Platelet Responses on the Dynamic	350
		12.4.2	Surfaces	254
			Surfaces	354

		12.4.3	Adsorption and Adhesion Behavior of Fibronectin and Human Umbilical Vein	
			Endothelial Cell on the Dynamic Surfaces	355
			The Effect of Hydrated Viscoelastic	
			Properties on the Adhering Morphology of	
			the Fibroblasts	358
		-	ments	359
	Refer	ences		360
	Section	E Inte	erfaces that Control Bacterial Responses	
Chapte			nesion and Interaction with Biomaterial	
	Surfa		1 -1 1 2 1 2 1 1 1 1 1	365
	Li-Ch	ong Xu a	and Christopher A. Siedlecki	
	13.1	Introdu	action	365
	13.2	Bacteri	al Adhesion and Biofilm Formation on	
		Biomat	erial Surfaces	367
		13.2.1	Adherence of Planktonic Bacterial Cells to	
			Surfaces	367
		13.2.2	Accumulation and Proliferation of	
			Bacterial Cells	368
		13.2.3		369
	13.3		Influencing Bacterial Adhesion and	
			tion with Biomaterial Surfaces	371
		13.3.1	Biomaterial Surface Properties Affect	
			Bacterial Adhesion	371
		13.3.2	Effect of Plasma Proteins on Bacterial	
			Adhesion on Biomaterial Surface	372
		13.3.3	Interaction of Bacteria and Platelets on	
	40.4	T 1. 21. 24	Biomaterial Surfaces	374
	13.4			2=0
			erial Surfaces	378
		13.4.1	C .	378
		13.4.2	Principles of the Inhibition of Bacterial	270
		13.4.3	Adhesion by Textured Surfaces Bacterial Adhesion and Biofilm Formation	379
		13.4.3	on Textured Surfaces	380
	13.5	Racteri	al Adhesion Assay Methods and	300
	13.3		ques Used in Studying Bacteria–Material	
		Interac		382
		13.5.1		383
		13.5.2		383
		13.5.3	Atomic Force Microscopy	385
	13.6	Summa		387

XVI	

	Α	Appendix: Methods	388	
		A.1 Typical Parameters for AFM Imaging of		
		Microphase Separation Structure in		
		Polyurethane Biomaterial Surfaces in Solution	388	
		A.2 Immobilization of Bacterial Cells on an AFM		
		Probe	389	
		A.3 Functionalization of an AFM Probe with		
		Antibodies	389	
	Acknowledgements			
	References			
Chapter	14 Antii	microbial Interfaces	399	
	Sabe	el P. Valappil		
	14.1	Introduction	399	
	14.2		400	
		14.2.1 Quorum Sensing	401	
		14.2.2 Production of Biofilm Matrix	402	
		14.2.3 Biofilm Dispersion	403	
	14.3	Biofilm Infection	404	
	14.4		405	
	14.5	Challenges of Antimicrobial Material Design	406	
		14.5.1 Anti-adhesive surfaces	406	
		14.5.2 Contact-active Materials	409	
		14.5.3 Controlled-drug Delivery Agents	410	
	14.6	The Interface Between Veterinary and Human		
		Antibiotic Use	411	
	14.7	Strategies to Control Antimicrobial Resistance	411	
		14.7.1 Role of Antibacterial Metal Ions	412	
	14.8	Future Directions	412	
	Acknowledgements			
	Refer	rences	416	
Cultinat	I wa cl corr		404	

Contents