Universitatea Politehnica Timișoara

Politehnica University of Timisoara

Awarding the Honorary Degree of

DOCTOR HONORIS CAUSA

to

Prof. dr. ing.
Traian V. CHIRILĂ

Timișoara
The 1st of October 2015

Universitatea Politehnica Timișoara

Decernarea Titlului Academic de

DOCTOR HONORIS CAUSA

domnului

Profesor dr. ing. TRAIAN V. CHIRILĂ

Timișoara
1 Octombrie 2015

Professor Traian V. CHIRILĂ, PhD

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adresat domnului

Prof. dr. ing. Traian V. CHIRILĂ

din partea

Senatului Universităţii Politehnica Timişoara

addressed to

Professor Traian V. CHIRILĂ, PhD

by

the Senate of Politehnica University Timisoara

RO

Laudatio

Distinşi oaspeţi şi colegi,
Onorată asistenţă,
Doamnelor şi domnilor,

Senatul Universității Politehnica Timișoara s-a reunit astăzi în ședință festivă pentru a acorda titlul academic de DOCTOR HONORIS CAUSA domnului Profesor Dr. Ing. TRAIAN V. CHIRILĂ, Director Științific la Queensland Eye Institute din Brisbane, în Australia, Profesor la Queensland University of Technology, University of Queensland (Australian Institute for Bioengineering and Nanotechnology) și University of Queensland (Faculty of Medicine and Biomedical Sciences). Este o bucurie deosebită pentru noi ca un cercetător științific remarcabil, cu largă recunoaștere și apreciere internațională, absolvent al Facultății de Chimie Industrială din cadrul Universității Politehnica Timișoara, să îmbogățească, de astăzi, galeria personalităților excepționale cărora universitatea noastră le-a acordat acest titlu meritoriu. Titlul de DOCTOR HONORIS CAUSA, cea mai înaltă distincție pe care o poate acorda Senatul Universității, reprezintă, totodată, o recunoaștere a meritelor științifice și inginerești ale laureatului și, nu în ultimul rând, este expresia atașamentului și dragostei statornice a laureatului față de orașul tinereții – Timișoara şi îndeosebi față de Universitatea Politehnica Timișoara.

Domnul Profesor dr. ing. TRAIAN V. CHIRILĂ s-a născut la data de 14 februarie 1948 la Arad. Copilăria și-a petrecut-o la Chișineu Criș, județul Arad, acolo unde a absolvit și liceul în anul 1966. În 1972 obține diploma de inginer chimist al Facultății de Chimie Industriala din Timișoara, specializarea Tehnologia Compușilor Macromoleculari, iar în 1981 devine doctor în Chimie la aceeași facultate. După depunerea tezei de doctorat, a acceptat să fie trimis ca specialist în prelucrarea polimerilor într-o țară din nordul Africii, în Libia. În decembrie 1982 ajunge în Austria unde s-a prezentat la un lagăr de refugiați și a cerut azil politic, Profesorul Chirilă a stat aici șapte luni până când Australia l-a acceptat ca refugiat politic și l-a repartizat la Perth, Western Australia, unde va rămâne pentru următorii 22 de ani.

Onorată asistență,

În 1984 Profesorul Chirilă a devenit Research Fellow la School of Applied Chemistry de la Curtin University of Technology din Perth, unde episodic a fost implicat în geochimia organică. În 1986 este angajat la Lions Eye Institute din Perth ca Senior Scientist, unde a înființat un departament de cercetare și dezvoltare a biomaterialelor polimerice pentru aplicații în oftalmologie, primul de acest fel în lume. Între 1989 și 1994, a fost Director Adjunct pentru cercetare.

Profesorul Chirilă a devenit membru (fellow) al Royal Australian Chemical Institute (RACI) în 1992, primind Medalia RACI Polymer Division Citation în 1993 și Medalia RACI Applied Research în 1999. I se confera profesorate la University of Western Australia (1992 - 2005), precum și la Curtin University of Technology (1999 - 2006).

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Laudatio

Distinguished guests and colleagues,
Honourable audience,
Ladies and Gentlemen,

The Senate of Politehnica University of Timisoara has gathered today in a ceremonial meeting to confer the academic title of DOCTOR HONORIS CAUSA on Professor TRAIAN V. CHIRILA, BEng, PhD, the Chief Scientist of the Queensland Eye Institute in Brisbane, Australia, and Honorary Professor at Queensland University of Technology, the University of Queensland (at the Australian Institute for Bioengineering and Nanotechnology), and the University of Queensland (at the Faculty of Medicine and Biomedical Sciences). It is a great pleasure for us to see that a remarkable scientist, internationally acknowledged and respected, a graduate of the Faculty of Industrial Chemistry of the University Politehnica Timisoara, joins today the gallery of exceptional personalities on whom our university has conferred this praiseworthy title. The title of DOCTOR HONORIS CAUSA, the highest distinction that can be awarded by the Senate of the University represents at the same time a recognition of the laureate's scientific and engineering abilities and, not at the least, is an expression of the laureate's lasting attachment and love for the city of his youth – Timisoara, and especially for the Politehnica University of Timisoara.

Professor TRAIAN V. CHIRILA was born on 14th of February in Arad, Romania. He spent his childhood in Chisineu Cris, Arad County, where he also graduated from high school in 1966. In 1972 he graduates as Bachelor of Chemical Engineering from the Faculty of Industrial Chemistry in Timisoara, in the specialty Technology of Macromolecular Compounds, and in 1981 he is awarded a PhD in chemical sciences by the same faculty. After obtaining his PhD degree, he accepted to go as a specialist in polymers processing to a country in North Africa, Libya. In December 1982 he reaches Austria where he asks for political asylum, and then he waited for seven months until Australia accepted him as a political refugee and relocated him to Perth, Western Australia, where he spend the next 22 years.

Honourable audience,

In 1984, Professor Chirila became a Research Fellow in the School of Applied Chemistry at Curtin University of Technology in Perth, where episodically he was involved in organic geochemistry. In 1986 he moves to the Lions Eye Institute in Perth as a Senior Scientist, where he established a department of research and development of polymeric biomaterials for applications in ophthalmology, the first of its kind in the world. Between 1989 and 1994, he was the Assistant Director for research.

Professor Chirila became a fellow of the Royal Australian Institute of Chemistry (RACI) in 1992, and he was awarded the RACI Polymer Division Citation in 1993 and the RACI Applied Research Medal in 1999. He accepted honorary professorial appointments at the University of Western Australia (1992-2005) and also at Curtin University of Technology (1999-2006).

În 2005, Profesorul Chirilă este încadrat la nou-înființatul Queensland Eye Institute (QEI) din Brisbane, unde i s-a oferit postul de Senior Scientist pentru a continua cercetările sale, dar și pentru a fonda un departament de biomateriale oftalmice și inginerie tisulară oftalmică. În prezent este Directorul Științific al Institutului, fiind în același timp și profesor onorific la două universități: Queensland University of Technology și University of Queensland (atât la Australian Institute for Bioengineering and Nanotechnology, cât și la Faculty of Medicine and Biomedical Sciences). De asemenea, este cercetător onorific la University of Western Australia.

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Domnul Profesor dr. ing. Traian V. Chirilă este inventatorul corneei artificiale AlphaCorTM (cunoscută inițial ca și „Chirila keratoprosthesis") și al implantului orbital AlphaSphere™, în prezent amândouă fiind aplicate clinic. Împreună cu colegii din colectivul de cercetare de la Queensland Eye Institute a investigat și raportat pentru prima data utilizarea proteinelor din mătase (silk proteins) ca biomateriale în ingineria tisulară oftalmică.

Onorat auditoriu,

Activitatea științifică a domnului profesor Chirilă este recunoscută pe plan internațional, domnia sa fiind membru al Australasian Society for Biomaterials and Tissue Engineering, New York Academy of Sciences si American Chemical Society. Totodată, este membru în colectivele de redacție a 11 reviste de specialitate. În anul 2002, profesorului Chirilă i s-a decernat Diploma de Excelență de către Euro-Asia Promotion & Cultural Foundation, iar în 2014 a primit Premiul de Excelență al Societății Române de Biomateriale. De asemenea, a devenit Membru Emerit al Fundației Politehnica Timișoara.

Rezultatele obținute de profesorul Chirilă sunt în diverse domenii de cercetare, care includ știința polimerilor, hidrogeluri, biomateriale oftalmice, ingineria tisulară oftalmică și medicina oftalmică regenerativă, polimeri supramoleculari, administrarea controlată a agenților bioactivi și istoria științei. Contribuțiile sale la știința biomaterialelor sunt recunoscute de toți cei care lucrează în acest domeniu, iar numele său este legat indisolubil de activitatea și rezultatele sale în domeniul oftalmologiei și prevenirii orbirii. Activitatea lui științifică nu se rezumă numai la aplicațiile polimerilor în oftalmologie. Profesorul Chirilă a studiat interacțiunea dintre radiația laser de înaltă energie și polimeri; a inventat și dezvoltat hidrogeluri sintetice conținând melanină, care sunt capabile să absoarbă radiația UV și regiunea albastră a spectrului vizibil; a investigat mecanismul și prevenirea calcifierii spontane a hidrogelurilor sintetice și a demonstrat că formarea forțată a rețelelor polimerice interpenetrante (IPN) reduce depunerea de calciu; a dezvoltat un nou concept pentru crearea unui endoteliu corneal artificial; precum și alte proiecte de cercetare. Majoritatea proiectelor sunt menite în ultima instanță să contribuie la eforturile mondiale pentru eradicarea orbirii. Rezultatele muncii sale au fost prezentate în circa 180 de articole de specialitate, cărți și capitole de carte, peste 180 de conferințe la manifestări științifice și 13 patente. A fost invitat să prezinte conferințe în China, Statele Unite, Japonia, România, Italia, Franța, Elveția, Coreea, Germania și Olanda. Demn de remarcat este faptul că, începând din anul 1987, a obținut fonduri de cercetare de peste 13 milioane de AU$.

Activitatea științifică a profesorului Chirilă este strâns legată de cea de pregătire a viitorilor cercetători. Elocventă în acest sens este îndrumarea, până în prezent, a unui număr de 14 studenți în vederea obținerii titlului de doctor.

In 2005, Professor Chirila is offered a position at the newly-established Queensland Eye Institute, to continue his research as a Senior Scientist and also to establish a department of ophthalmic biomaterials and ophthalmic tissue engineering. Currently, he is the Chief Scientist of the institute, and also holds honorary professorships at two universities: Queensland University of Technology and the University of Queensland (at both the Australian Institute for Bioengineering and Nanotechnology and the Faculty of Medicine and Biomedical Sciences). He is also a Honorary Research Fellow at the University of Western Australia.

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Professor Traian V. Chirila is the inventor of the AlphaCor™ artificial cornea (initially known as the "Chirila keratoprosthesis") and of the AlphaSphere™ orbital implant, both currently in clinical practice. He and his colleagues at Queensland Eye Institute were the first to investigate and report the use of silk proteins as biomaterials in ophthalmic tissue engineering.

Ladies and Gentlemen,

Professor Chirila's scientific activity has been widely recognized internationally. He is a member of Australasian Society for Biomaterials and Tissue Engineering, New York Academy of Sciences and American Chemical Society. Also, he is a member of the editorial boards of 11 scientific journals. In 2002, he was awarded Diploma of Excellence of the Euro-Asia Promotion & Cultural Foundation, and in 2014 he received the SRB Excellence Award from the Romanian Society for Biomaterials. He also became an Emeritus Member of the Politehnica Foundation.

The results obtained by Professor Chirila are in diverse research fields including polymer science, hydrogels, ophthalmic biomaterials, ophthalmic tissue engineering and regenerative medicine, supramolecular polymers, controlled release of bioactive agents, and history of science. His contributions to the science of biomaterials are recognized by all those working in this field and his name is forever linked to his contributions to ophthalmology and prevention of blindness. His scientific activity is not limited to the applications of polymers in ophthalmology. Professor Chirila has investigated the interaction between high-energy laser radiation and polymers; he invented and developed melanin-containing synthetic hydrogels, which are able to absorb UV and blue radiation; he has investigated the mechanism and prevention of spontaneous calcification of synthetic hydrogels and he demonstrated that the enforced formation of polymer interpenetrating networks (IPNs) can reduce calcium deposition; he developed a new concept for an artificial corneal endothelium; and other research projects. Most of the projects are intended to ultimately contribute to the worldwide efforts to eradicate blindness. The results of his work are presented in about 180 articles and book chapters, over 180 presentations at scientific gatherings, and 13 patents. He was invited to present lectures in China, USA, Japan, Romania, Italy, France, Switzerland, Korea, Germany and the Netherlands. It is also to be noted that, starting with 1987, he obtained research funds exceeding AU$13 million.

Professor Chirila's scientific activity is closely associated with the education of future scientists. In this respect, he supervised to date 14 doctoral theses.

Stimați colegi,

Senatul Universității Politehnica Timișoara acordă astăzi onorantul titlu de DOCTOR HONORIS CAUSA unei personalități proeminente a lumii academice şi ştiinţifice contemporane, Domnului Profesor Doctor Inginer TRAIAN V. CHIRILĂ de la Queensland Eye Institute din Brisbane, pentru activitatea şi rezultatele obținute în domeniile chimiei, științei polimerilor și oftalmologiei regenerative, dar şi pentru ataşamentul și devotamentul pentru țara natală – România.

Vă mulțumesc,

Timişoara, 01.10.2015

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Dear Colleagues,

The Senate of the University Politehnica Timisoara granted today the honorary title of DOCTOR HONORIS CAUSA to a prominent personality of the contemporary academic and scientific world, Professor TRAIAN V. CHIRILA, BEng, PhD of the Queensland Eye Institute in Brisbane, Australia, for the activity and results obtained in the research fields of chemistry, polymer science and regenerative ophthalmology, and also for his attachment and devotion to his motherland – Romania.

Thank you,

Timisoara, 01.10.2015

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Experiența în Educație şi Cercetare

Experience in Education and Research

Professor TRAIAN V. CHIRILĂ, PhD
Chief Scientist at Queensland Eye Institute

Experience in Education and Research

Biographical Background

Traian V. Chirila was born and educated in Romania, where he obtained a BEng in polymer technology and a PhD in organic chemistry (1981). He is a graduate of the Politehnica University of Timisoara. After ten years of doing research in polymers and organic chemistry, he left the country and relocated in 1983 to Australia as a political refugee. During 1984 he was a Research Fellow at the School of Applied Chemistry of Curtin University of Technology in Perth. In 1986 he joined Lions Eye Institute in Perth as a Senior Scientist where he established a department for research and development of polymeric biomaterials for ophthalmology.

Scientific Qualification

Professor Chirila was made a Fellow of Royal Australian Chemical Institute (RACI) in 1992, and received the RACI Polymer Division Citation in 1993 and the RACI Applied Research Medal in 1999. He held adjunct professorships at University of Western Australia (1992 to 2005) and at Curtin University of Technology (1999 to 2006). In 2005, Professor Chirila joined the newly founded Queensland Eye Institute (QEI) in Brisbane, where he was offered a position of Senior Scientist to continue his research and to establish a department of ophthalmic biomaterials and tissue engineering. Currently, he is the Chief Scientist of the institute, holds three Honorary Professorships at the Queensland University of Technology, the University of Queensland (in the Australian Institute for Bioengineering and Nanotechnology), and University of Queensland (in the Faculty of Medicine and Biomedical Sciences), as well as a Honorary Research Fellowship at the University of Western Australia. He is a member of Australasian Society for Biomaterials and Tissue Engineering, New York Academy of Sciences, and American Chemical Society, and on the editorial boards of 10 journals. Professor Chirila was awarded in 2002 the Diploma of Excellence by the Euro-Asia Promotion & Cultural Foundation. In 2014 he was awarded the SRB Excellence Award by the Romanian Society for Biomaterials, and also became an Emeritus Member of Politehnica Foundation, in Timisoara, Romania.

Professor Chirila's main research interests include polymer science, hydrogels, ophthalmic biomaterials, ophthalmic tissue engineering, regenerative ophthalmic medicine, supramolecular polymers, sustained drug release, history of science. He is the inventor of the AlphaCor™ artificial cornea, and the AlphaSphere™ orbital implant, both in current clinical practice. He and his colleagues at QEI have been the first to investigate and use silk proteins as biomaterials in ophthalmic tissue engineering. Professor Chirila's activity has resulted to date in about 180 journal articles and book chapters, the same number of conference presentations, and 13 patents; he is currently editing his third book on ophthalmic biomaterials. He was invited to present lectures in China, USA, Japan, Romania, Italy, France, Switzerland, Korea, Germany and The Netherlands. He obtained since 1987 over AU$ 13 million as research funding. Professor Chirila supervised to date 14 doctoral students.

Curriculum Vitae

Professor TRAIAN V. CHIRILĂ, PhD
Chief Scientist at Queensland Eye Institute

CURRICULUM VITAE

1. **Family name:** CHIRILĂ
2. **Given names:** Traian
3. **Date of birth:** 14 February 1948
4. **Place of birth:** Arad, Romania
5. **Citizenship:** Australian
6. **Education:**

Institution	Degree(s) or Diploma(s) obtained:
Politehnica University of Timisoara (1972) Faculty of Chemical Engineering	Diploma in chemical engineering, specialized in Polymer Technology **(B Eng)**
Politehnica University of Timisoara (1981) Faculty of Chemical Engineering	**PhD** in Organic Chemistry ("Alcohol, ester and ether derivatives of 1,3-dioxolane and 1,3-dioxane")
Royal Australian Chemical Institute (1983)	**C Chem**
Council on Overseas Professional Qualifications (1984) Canberra, Australia	**PhD Assessment**

7. **Employment history**

1972 - 1974	Research Engineer, Politehnica University of Timisoara, Faculty of Chemical Engineering, Romania. Research on solvents for polymer coatings.
1974 - 1982	Research Scientist, Central Institute for Chemical Research, Laboratory of Timisoara, Romania. Research on: synthesis of additives for polymers; solvation and plasticization; polyurethane chemistry; stereochemistry of cyclic compounds. Supervising pilot-scale and industrial processes for production of solvents and plasticizers.
March - Dec. 1982	Laboratory Manager, Klöckner-Humboldt-Deutz GmbH, on location at the Chemical Complex of Abu-Quammash, Lybia. Supervision of quality control testing of poly(vinyl chloride). Development of special testing techniques
1983- 1984	Research Fellow, Curtin University of Technology, School of Applied Chemistry, Perth, Western Australia. Research in organic geochemistry: correlation between maturation of sedimentary organic matter and distribution of aromatic compounds; new maturity indicators; kinetics of maturation.
1985 - 1986	Chemist, Macdonald Hamilton and Co., Environmental Services, Perth, Western Australia, 1985; Australian Assay Laboratories, Perth, Western Australia, 1985 to 1986. Routine analytical work on ore minerals and environmental contaminants.
1986 - 2005	Senior Scientist, Lions Eye Institute (LEI), Perth, Western Australia - Department of Biomaterials and Polymer Research.

2005 - 2010 Senior Scientist, Queensland Eye Institute (QEI), Brisbane, Queensland. In charge of research in ophthalmic biomaterials and bioengineering.

since 2010 Chief Scientist, Queensland Eye Institute (QEI), Brisbane, Queensland.Australia.

8. Positions in Academic and Professional Associations

Academic affiliations

1992 - 2004 Adjunct Associate Professor, Faculty of Medicine and Dentistry, University of Western Australia, Perth;

1994 - 1999 Adjunct Senior Research Fellow, School of Applied Chemistry, Curtin University of Technology, Perth, Western Australia.

1999 - 2002 Adjunct Professor, School of Applied Chemistry, Curtin University of Technology, Perth, Western Australia.

2003 - 2006 Adjunct Research Professor, School of Applied Chemistry, Curtin University of Technology, Perth, Western Australia.

since 2005 Adjunct Professor, Science and Engineering Faculty, Queensland University of Technology, Brisbane;

2005 - 2014 Adjunct Professor, Australian Institute for Bioengineering and Nanotechnology, University of Queensland, Brisbane;

since 2006 Adjunct Professor, Faculty of Medicine and Biomedical Sciences, University of Queensland, Brisbane;

since 2013 Honorary Research Fellow, Faculty of Science, University of Western Australia, Perth; 2013

since 2015 Honorary Professor, Australian Institute for Bioengineering and Nanotechnology, University of Queensland, Brisbane;

Membership to Professional Associations

1983 - 1992 Member of Royal Australian Chemical Institute, and Fellow since 1992.

1984 - 1987 The Institution of Engineers, Australia.

1986 - 2008 Association of Professional Engineers, Scientists and Managers, Australia.

1991 - 1998 Australian and New Zealand Association for the Advancement of Science.

since 1992 Australasian Society for Biomaterials and Tissue Engineering, Inc.

1992 - 1994 Inventors Association of Western Australia, Inc.

1992 - 1998 Interdisciplinary Club for Biomaterials in Ophthalmology.

1992 - 2004 Society for Biomaterials, USA.

since 1992 KPro Study Group.

since 1994 The New York Academy of Sciences.

1995 - 1997 International Society for Ocular Trauma.

2001 - 2002 Swiss Society for Biomaterials .

since 2003 The American Branch of Romanian Academy of Scientists.

since 2003 The Romanian Academy of Scientists (corresponding member).

2003 - 2005 International Society of Dacryology and Dry Eye.

since 2006 American Chemical Society.

Other appointments and membership

- *Member*, the Site Laboratory Safety Committee for the Queen Elizabeth II Medical Centre, Perth, Western Australia.
- *Assessor* for National Health and Medical Research Council (Australia) grant proposals.
- *Assessor* for Australian Research Council grant and fellowship proposals.
- *Reviewer* for the Ophthalmic Research Institute of Australia (ORIA) grant applications.
- *Reviewer* for Health Research Council of New Zealand grant applications.
- *Reviewer* for the Natural Sciences and Engineering Research Council (NSERC/CRSNG) of Canada grant applications.
- *Reviewer* for the Wellcome Trust grant applications.
- *Reviewer* for National Research Foundation of Singapore grants applications.
- Western Australia Polymer Group of the Royal Australian Chemical Institute, *Secretary* (1988 to 1990); *Chairman* (1991 to 1995).
- The Royal Australian Chemical Institute Polymer Division Standing Committee, *Member* (1991 to 1998).
- *President,* The Romanian Community of Western Australia, Inc. (1991 to 1994).

9. International invited lectureship and visiting scholarship

People's Republic of China, 19 Sep–8 Oct 1993

• Visiting Professorship (scholarship from the National Nature Science Foundation of China). Lecture "*Polymers as ophthalmic biomaterials: past, present, future"* presented at Peking University, Tsinghua University (both in Beijing), and Tianjin University (Tianjin). Also, visited as a guest scientist Academia Sinica (Beijing); Tong Ren Hospital (Beijing); National Research Institute for Family Planning (Beijing); Institute of Biomedical Engineering (Tianjin); and Zhejiang University (Hangzhou).

United States of America, 7–10 October 1995

Invited lecture "*Artificial cornea based on interpenetrating polymer networks"* presented at the Intersociety Polymer Conference on Creation, Utilization, and Recycling of Multiphase Polymer Systems. Organized by the American Chemical Society, the American Physical Society and Macro Group (UK), and held in Baltimore, Maryland.

Japan, 13-19 March 1996

AIST Guest Researcher at the Osaka National Research Institute, Osaka. Also, visited as a guest scientist the Research Center for Biomedical Engineering at Kyoto University (Kyoto); Bionic Design Research Group at the National Institute for Advanced Interdisciplinary Research (Tsukuba); Functional Molecules Laboratory at the National Institute of Materials and Chemical Research (Tsukuba). Lecture "*Artificial cornea based on interpenetrating polymer networks"* presented in Osaka and Kyoto.

Romania, 28 August-12 September 1996

Guest lecturer at the Politehnica University of Timisoara. Lecture *"Advances in artificial cornea: the use of synthetic polymers"* presented at the Faculty of Industrial Chemistry and Environmental Engineering. Visiting Professor at the Ophthalmologic Clinic of Timisoara.

People's Republic of China, 6-25 May 1997

Visiting Professorship (scholarship from the National Nature Science Foundation of China) at Tianjin University and Nankai University (Tianjin), Tsinghua University (Beijing) and Wuhan University (Wuhan). Lectures "*Advances in biomaterials for eye surgery"* presented at Tianjin University and "Artificial substitutes for cornea and vitreous body: are they possible by the use of polymers?" at Wuhan University.

Invited plenary speaker at the International Conference on Biorelated Polymers, Controlled Release Drugs and Reactive Polymers, Xi'An, 8-11 May 1997. Lecture presented: "*Advances towards a functional artificial cornea".*

Italy, 8-12 September 1997

Visiting Professor at Universitá degli Studi di Napoli "Federico II", the Department of Materials and Production Engineering in Naples. Lecture presented: *"The use of hydrogels as artificial cornea and artificial vitreous".*

France, 20-25 September 1997

Guest lecturer at Hôtel-Dieu Hospital, the Department of Ophthalmology, in Paris. Lecture presented: "*Hydrogel core-and-skirt keratoprosthesis".*

Switzerland, 25-28 September 1997

Visiting Professor at the Universitäts-Augenklinik, in Basel. Lecture presented: "*The use of hydrogels as artificial cornea and artificial vitreous".*

United States of America, 17-18 March 2000

Invited lecture "*A hydrogel artificial cornea: from conception to clinical trials"* presented at the Symposium on Biomedical Polymers for the 21st Century – Overview and Ophthalmic Applications. Organized by the Schepens Eye Research Institute, Harvard Medical School, held in Boston, Massachusetts.

Japan, 31 October-19 November 2001

Visiting Professor at Tokushima University, Tokushima. Lecture "*Development of a hydrogel artificial cornea with porous skirt, and clinical trials"* presented at the Department of Ophthalmology, 31 October 2001.

Guest speaker at the Menicon 50th Anniversary International Symposium in Nagoya, Nagoya Congress Center. Lecture *"Research on artificial cornea – development of a hydrogel keratoprosthesis from conception to clinical trials*" presented on 18 November 2001. Guest scientist at the Menicon Central R&D Laboratory, Kasugai.

Japan, 17-19 February 2005

Invited speaker at the Artificial Cornea Symposium, within the joint 29th Japan Cornea Conference and 21st Annual Meeting of Keratoplasty Society of Japan, held in Tokushima. Lecture *"History of artificial cornea in Japan"* presented on 19 February 2005.

Korea, 5-9 November 2007

Invited speaker at the Sixth Pacific Rim International Conference on Advanced Materials, held at Jeju Island. Lecture *"Silk as substratum for cell attachment and proliferation"* presented on 7 November 2007.

Germany, 25 May 2011

Invited lecture *"Artificial corneal endothelium. A novel concept based on electroosmosis through pores created by ion track-etching"* presented at the GSI Helmholtzzentrum für Schwerionenforschung GmbH in Darmstadt.

The Netherlands, 28 August 2014

Invited lecture "*Ophthalmic regenerative medicine: the use of silk proteins as template for growing corneal and retinal cells"* presented at University of Twente in Enschede.

Romania, 17-20 September 2014

Keynote speaker at the 6th International Conference on Biomaterials, Tissue Engineering & Medical Devices, held in Constanta. Lecture "*Ophthalmic regenerative medicine: the use of silk proteins as template for growing corneal and retinal cells"* presented on 18 September 2014.

10. Corporate experience

1993 - 2001	*Managing Director*, Medical Biomaterials Pty Ltd (ACN 009 166 509),
1995 - 1998	*Project Manager,* The Lions Eye Joint Venture, Syndicated R&D Project (Artificial Cornea),
2001- 2003	Court-appointed *Consultant and Polymer Expert* to Bausch & Lomb Pty Ltd in the patent litigation vs. Novartis AG,
2001 - 2004	Chief Scientific Officer, Argus Biomedical Pty Ltd (ABN 82 009 166 509),
2004 - 2005	Chief Scientific Officer, CooperVision Surgical (ABN 12 060 200 553),
2005 - 2006	Scientific Advisor, CooperVision Surgical (ABN 12 060 200 553).

11. Editorial Activities

Member in Editorial Board:

- Journal of Biomaterials Applications (Reviews Editor to 2015)
- Biomaterials
- Recent Patents on Materials Science
- The Open Materials Science Journal (Associate Editor)
- The Open Macromolecules Journal
- International Journal of Biomaterials
- Progress in Biomaterials
- Advances in Biomaterials
- The Open Biomaterials Journal
- The Open Conference Proceedings Journal

Guest Editor

- *Progress in Polymer Science*, Special issue "Polymer Science and the Eye", vol. 23, issue #3 (1998).
- *Journal of Functional Biomaterials*, Special issue "Advances in Ophthalmic Biomaterials", vol. 4 (2013).

Editor

- *Biomaterials and Regenerative Medicine in Ophthalmology*, Woodhead Publishing Ltd, Cambridge, U.K. and CRC Press, Boca Raton, U.S.A., 2010. ISBN: 978-1-84569-443-2.

Reviewer for:

- Acta Biomaterialia
- Advanced Healthcare Materials
- Advances in Materials Science and Engineering
- American Journal of Drug Delivery
- American Journal of Polymer Science
- Australian Journal of Chemistry
- Biomacromolecules / Biomaterials
- Biomedical Materials
- BioMed Research International
- Biosensors and Bioelectronics
- Biotechnology Progress
- British Journal of Ophthalmology
- Cells and Materials
- Clinical and Translational Science
- Clinical Ophthalmology
- Cornea
- Current Drug Delivery
- European Journal of Pharmaceutics and Biopharmaceutic
- Expert Review of Medical Devices
- Indian Journal of Medical Research
- International Journal of Biomaterials
- International Journal of Pharmaceutics
- Investigative Ophthalmology & Visual Science
- Journal of Biomaterials Applications
- Journal of Biomaterials Science-Polymer Edition
- Journal of Biomedical Materials Research
- Journal of Controlled Release
- Journal of Biomaterials Science-Polymer Edition
- Journal of Biomedical Materials Research
- Journal of Controlled Release
- Journal of Functional Biomaterials
- Journal of Materials Research
- Engineering and Physics
- Medical Practice and Reviews
- PLOS One
- Polymer Chemistry
- Polymer Degradation and Stability
- Polymer International
- Polymer Review
- Polymers
- Progress in Biomaterials
- Progress in Polymer Science
- Recent Patents on Materials Science
- Recent Patents on Nanomedicine
- Regenerative Medicine
- Science
- Soft Matter
- The Open Macromolecules Journal
- The Open Materials Science Journal
- Trends in Polymer Science

12. Membership to conference organizing committees

1989 International Symposium "Advances in Biomedical Polymers", Perth, Australia, February 1989.
1992 The 19th Australian Polymer Symposium, Perth, Australia, February 1992.
1993 The 3rd Pacific Polymer Conference, Gold Coast, Australia, December 1993.
1996 The 21st Australian Polymer Symposium, Wollongong, Australia, February 1996.
1996 Chair and organizer, "Conference on Medicine", a Science & Technology Seminar sponsored by the Embassy of Italy, Perth, Australia, 17 April 1996.
1998 IUPAC World Polymer Congress (37th International Symposium on Macromolecules, MACRO-98), Gold Coast, Australia, July 1998.
1998 98 Workshop on Tissue Engineering, Tianjin, P. R. China, October 1998.
2002 The 25th Australasian Polymer Symposium, Armidale, Australia, February 2002.
2003 First International Conference on Medical Implants, Bethesda, MD, USA, July 2003 (Program Committee and International Advisory Board).
2009 The 11th Pacific Polymer Conference, Cairns, Australia, December 2009.
2010 Tissue Engineering & Regenerative Medicine International Society (TERMIS) 2010 Asia-Pacific Meeting and Annual Conference, Sydney, Australia, September 2010 (International Scientific Committee).
2010 BIT's 3rd Annual World Congress of Regenerative Medicine & Stem Cells 2010, Shanghai, China, December 2010 (Advisory Board).

13. Awards and Honours

The Polymer Division Citation 1993.

Awarded by the Polymer Division of the Royal Australian Chemical Institute for "outstanding research in polymeric biomaterials as well as the promotion of polymer science in Western Australia."

1999 Applied Research Award and Don Rivett Medal.

Awarded by the Royal Australian Chemical Institute for significant contribution "towards the development of, or innovation through, applied research" over the preceding ten years.

The Diploma of Excellence for 2002

Awarded by the Euro-Asia Promotion & Cultural Foundation (Romanian Branch) at the 2nd Forum for the New Europe (24 October 2002, Brasov, Romania) for "the invention of an artificial cornea".

Corresponding Member of the Romanian Academy of Scientists

Elected by secret ballot at the meeting of the Academy's National Scientific Council held on 30 May 2003.

SRB Excellence Award

Awarded by the Romanian Society for Biomaterials at the 6th International Conference on Biomaterials, Tissue Engineering & Medical Devices (17-20 September 2014, Constanta, Romania) for "the scientific contribution in the field of biomaterials".

Emeritus Member of Politehnica Foundation

Awarded on 26 September 2014 by the Board of Politehnica Foundation from Timisoara, Romania, for "contributions in several areas of biomaterials and polymer science".

Listed in

- *"Who's Who in Engineering - Australia and New Zealand"*
- *"The Australian Directory of Academics"*
- *"Who's Who and Who's What in Western Australia"*

14. Research Topics

- Novel biomaterials for ocular implants
- Artificial intraocular lenses, new concepts and designs
- Tissue-material interactions
- Calcification of implants
- Phototoxicity and protection
- Ultraviolet-absorbing polymers
- Artificial cornea
- Artificial vitreous substitutes
- Interaction of laser radiation with polymers
- Controlled release of bioactive agents
- Photoresponsive polymers
- Characterization of polymers
- Delivery of therapeutic oligodeoxyribonucleotides
- Synthesis and modification of oligodeoxyribonucleotides
- Development of polymer substrates for cell growth
- Biodegradable hydrogels
- Interpenetrating polymers networks
- Artificial vitreous substitutes
- Self-healing hydrogels
- Tissue engineering
- Ocular surface reconstruction
- Controlled release of bioactive agents
- Artificial corneal endothelium
- Retinal cells transplantation
- Interaction of laser radiation with polymers
- Crosslinking of collagen
- Calcification of hydrogels

15. Patents

1	"Method for preparation of 2-isopropyl-1,3- dioxolane"	**Romanian Patent 62685**	24 Feb. 1976
2	"Method for the preparation of a cyclic acetal mixture obtainable in a one-pot procedure, used for pains and varnishes".	**Romanian Patent 63233**	26 Oct. 1976
3	"Polychloroprene and polyurethane adhesive compositions".	**Romanian Patent 65389**	21 June 1977
4	"Method for the preparation of an additive for foundry bonded moulding mixtures".	**Romanian Patent 74298**	31 March 1980
5	"Method for the preparation of 2-ethylhexyl acetate".	**Romanian Patent 74314**	31 March 1980
6	"Method of making photoprotective hydrophilic polymers and ocular devices thereof".	**U. S. Patent 5,252,628**	12 Oct. 1993
7	"Keratoprosthesis and method of producing the same".	**Australian Patent 650156**	10 Feb.1994
8	"Keratoprosthesis"	**U. S. Patent 5,300,116**	5 Apr. 1994
9	"Method of producing a keratoprosthesis".	**U. S. Patent 5,458,819**	17 Oct. 1995
10	"Cross-linking of collagen in situ and uses thereof in wound healing".	**Australian Patent 719661**	10 June 1998
11	"Ocular socket prosthesis".	**Australian Patent 726152**	2 Nov. 2000
12	"Ocular socket prosthesis".	**U. S. Patent 6,346,121 B1**	12 Feb. 2002
13	"Method of insertion of keratoprostheses".	**U. S. Patent 6,423,093 B1**	23 July 2002

16. Research Grants Awarded

(1) University of Western Australia, Faculty of Medicine Research and Scholarships Committee (1987): "Chemical effects in the eye of the flexible polymeric biomaterials as intraocular implants". **A$3,886.**

(2) Industry Research and Development Board of the Commonwealth Department of Industry, Technology and Commerce of Australia, Generic Technology Grant No. 15001 (1987–1990): "New biomaterials for surgical implantation", co-awarded with I.J. Constable. **A$504,300.**

(3) National Health and Medical Research Council (Australia), Project Grant No. 880049 (1988–1990): "Critical evaluation and further development of ocular biomaterials", co-awarded with I.J. Constable and L.N. Walker. **A$103,354.**

(4) Alcon Laboratories, Inc., U.S.A. (1989–1994): "New concepts and novel materials for soft intraocular lenses", co-awarded with G.D. Barrett and I.J. Constable. **US$300,000.**

(5) National Health and Medical Research Council (Australia), Project Grant No. 910167 (1991–1993): "Application of biomaterials chemistry for the development of a functional keratoprosthesis", co-awarded with I.J. Constable and G.J. Crawford. **A$321,394.**

(6) Clive and Vera Ramaciotti Foundations, Project Grant No. A722 (1992): "Biomaterials for artificial intraocular lens duplicating radiation-absorbing properties of the natural lens", co-awarded with I.J. Constable. **A$20,950.**

(7) Australian Research Council, Project Grant (1992): "Studies of the relationship between polymerization parameters and polymer microstructure", as an associate investigator with D.J.T. Hill, P.J. Pomery and A.K. Whittaker (University of Queensland).

(8) Raine Medical Research Foundation, Project Grant (1992–1995): "Controlled release of angiogenic agents in vivo", co-awarded with M.D. Grounds, C.A. Mitchell, M.A.L. Maley, D.J. Wood and A.R. Harvey. **A$177,404.**

(9) National Health and Medical Research Council (Australia), Project Grant No. 940707 (1994–1996): "Biomaterials for permanent vitreous substitution", co-awarded with I.J. Constable. **A$137,835.**

(10) The Lions Clubs International Foundation, Oak Brook, IL, U.S.A. (1994): Equipment grant. **US$50,000.**

(11) The Ophthalmic Research Institute of Australia and the OPSM Research and Charitable Foundation (1995): "Further development and in vivo assessment of a new type of keratoprosthesis", co-awarded with G.J. Crawford and I.J. Constable. **A$17,000.**

(12) Research and Development Syndicate (1995–1998): "Development of an artificial cornea", co-awarded with I.J. Constable and G.J. Crawford. **A$2,800,000.**

(13) Australian Retinitis Pigmentosa Association Grant (1996): "Antisense mediated treatment of retinitis pigmentosa", co-awarded with P. E. Rakoczy and I. J. Constable. **A$18,000.**

(14) Raine Medical Research Foundation, Project Grant (1996–1997): "Strategies for the treatment of autosomal dominant diseases. Retinitis pigmentosa", co-awarded with P.E. Rakoczy and C.M. Lai. **A$156,258.**

(15) The Ophthalmic Research Institute of Australia and Royal Australian College of Ophthalmologists Grant (1997): "Development of a new orbital implant from poly(2-hydroxyethyl methacrylate)", co-awarded with G.J. Crawford, C.R. Hicks, S. Vijayasekaran, A.B. Clayton, J.H. Fitton and I.J. Constable. **A$5,000.**

(16) Australian Retinitis Pigmentosa Association Grant (1998): "Antisense mediated treatment of retinitis pigmentosa", co-awarded with P. E. Rakoczy and K. Bos. **A$20,000.**

(17) National Health and Medical Research Council (Australia), Project Grant No. 990430 (1999–2000): "Clinical trial of a poly(HEMA) keratoprosthesis", co-awarded with C. R. Hicks, G. J. Crawford and I. J. Constable. **A$111,895.**

(18) The Ophthalmic Research Institute of Australia Grant (2000): "Development and evaluation of a non-viral delivery system for therapeutic antisense oligodeoxynucleotides in the treatment of subretinal neovascu larisation", co-awarded with P. E. Rakoczy and X. Lou. **A$21,000.**

(19) National Health and Medical Research Council (Australia), Competing Clinical Trials/Large Scale Grant No.139066 (2001–2003): "Multi-centred clinical evaluation of a novel keratoprosthesis", co-awarded with I. J. Constable, C. R. Hicks and G. J. Crawford. **A$ 510,000.**

(20) AusIndustry (Australia), R&D START Grant No. GRA02059 (2001–2003): "Development of the Kera-Clear artificial cornea", with Argus Biomedical Pty Ltd. **A$472,520.**

(21) Australian Research Council, Discovery-Project DP0208223 (2002–2004): "Calcification of acrylic hydro gels in abiotic media: mechanism and control",co-awarded with J. M. Webb, A. K. Whittaker and D. J. T. Hill. **A$305,000.**

(22) National Health and Medical Research Council (Australia), Development Grant No. 254717 (2003): "A new device for ophthalmic drug delivery", co-awarded with C. R. Hicks, X. Lou and I. J. Constable. **A$118,000.**

(23) Department of Health, Government of Western Australia, Medical and Health Infrastructure Fund Grant Ref. 03-04009, Round 7 (2004). **A$34,317.**

(24) Department of Health, Government of Western Australia, Medical and Health Infrastructure Fund Grant Ref. 04-02689, Round 8 (2005). **A$53,196.**

(25) Australian Research Council, Discovery-Project DP0663037 (2006–2008): "Biodegradable porous HEMA-based polymers: innovative strategies for the design and tuneable single-step production of a novel class of scaffolds for tissue engineering", co-awarded with M. V. Baker, A. K. Whittaker and H.-B. Kraatz. **A$560,000.**

(26) Smart State Innovation Projects Fund (Queensland), National and International Research Alliances Program (2006–2009): "The International Biomaterials Research Alliance", co-awarded with teams from University of Queensland, Royal Brisbane Hospital, University of California at Santa Barbara, Washington University at St. Louis, University of Warwick, and Queen Mary College University of London). **A$4,000,000.**

(27) Goldman Sachs JBWere Foundation, Annual Grants Program (2007). **A$10,000.**

(28) Australian Research Council, Discovery-Project DP0878615 (2008–2010): "Generation of peptidomimetic surfaces for biomaterials applications", co-awarded with I. Blakey, D. J. T. Hill and C. J. Hawker. **A$560,000.**

(29) National Health and Medical Research Council (Australia), Project Grant No. 553038 (2009–2011): "Development of a novel bioengineered tissue construct for repairing the eye", co-awarded with D. Harkin, D. Hutmacher and I. Schwab. **A$323,125.**

(30) The Ophthalmic Research Institute of Australia (ORIA)/Vision Australia Inc. Grant (2009): "Development of an artificial silk membrane for retinal pigment epithelial cell growth', co-awarded with A. Kwan and D. Harkin. **A$25,000.**

(31) The IHBI Collaborative Research Development Scheme 2012 Grant (2012–2013): "An innovative biomimetic model for studying the pathomechanisms of ageing and age-related macular degeneration in the eye", co-awarded with B. Feigl, D. Harkin, D. Hutmacher, A. Weiss and P. Dalton. **A$30,000.**

(32) The Ophthalmic Research Institute of Australia (ORIA)/RANZCO Eye Foundation Grant (2013): "Preparation of human endothelial silk fibroin constructs for transplantation", co–awarded with P.W. Madden, P.S. Beckingsale and D.G. Harkin. **A$43,550.**

(33) National Health and Medical Research Council (Australia), Project Grant No. 1049050 (2013–2015): "A novel mesenchymal stromal cell and biomaterial for corneal reconstruction", co-awarded with D. Harkin, L. Hirst, D. Hutmacher and K. Atkinson. **A$489,980.**

(34) Macular Disease Foundation Australia, Research Grant 2014-2016: A novel tissue substitute for repairing the outer retina in patients with AMD", co-awarded with D. Harkin, A. Shadforth, T. Kwan and N. Barnett. **A$200,000.**

(35) National Health and Medical Research Council (Australia), Project Grant No. 1080302 (2015–2017): "A fibroin-based prosthetic Bruch's membrane for the treatment of age-related macular degeneration", co-awarded with D. Harkin, F. Chen, and N. Barnett. **A$519,154.**

Lista completă a publicațiilor

Complete list of publications

Professor TRAIAN V. CHIRILĂ, PhD
Chief Scientist at Queensland Eye Institute

ARTICLES

1974

(1) Blaga A., Vladea R. and **Chirila T.**
On the synthesis of 2-isopropyl-1,3-dioxolane. ***Bul. Stiint. Teh. Inst. Politeh. Timisoara Ser. Chim.***, **19(1**): 139-145, 1974. {***Chem. Abstr.* 83** *(1975): 79121k}.*

1977

(2) **Chirila T.**
Penta and hexaatomic cycloacetal esters. Synthesis and characterization of some 2-carbalkoxymethyl-1,3-dioxolanes (dioxanes). [Rom.] ***Rev. Chim.*** (Bucharest), **28(8**): *7*30-733, 1977. {***Chem. Abstr.* 88 (1978):** *22780y}.*

(3) **Chirila T.** and Pape R.
Comparative study of the methods for direct synthesis of five and six-membered cyclic ketals of acetone. Preparation of 2,2-dimethyl-4-hydroxymethyl-1,3-dioxolane. [Rom.] ***Rev. Chim. (Bucharest),* 28(9):** 827-830, 1977. *{Chem. Abstr.* **88 (***1978): 22719k}.*

(4) Blaga A. I., Pape R. F. and **Chirila T.**
Acid-catalysed acetalisation. I. The influence of kind and concentration of acid catalysts in synthesis of bis-1,1-(2',2'-ethylhexyloxy)-2-methylpropane. ***Rev. Roum. Chim.,* 23(4):** 581-586, 1977. *{Chem. Abstr. 89 (1978): 163005g}.*

1979

(5) **Chirila T.** and Prosteanu N.
Comments on the structural analysis by infrared spectrometry of cyclic acetals and ketals. The analysis of some 1,3-dioxolanes in the specific spectral region. [Rom.] ***Anal. Univ. Timisoara Ser. St. Fiz-Chim.,* 17(1)**: 53-63, 1979. {***Chem. Abstr.* 95** *(1981): 5942e}.*

(6) **Chirila T.**
The advantages of using dimethyl sulfoxide as a solvent in the synthesis of nitriles of higher fatty acids. [Rom.] ***Rev. Chim. (Bucharest),* 30(8):** 738-739, 1979. *{Chem. Abstr.* **92 (***1980): 41277p}.*

(7) Lőcsei V., **Chirila T.** and Csunderlik C.
Structural investigations by 1H-NMR spectrometry on new derivatives of 1,3-dioxanic type. ***Bul. Stiint. Teh. Inst. Politeh. Timisoara Ser. Chim.,* 24(1)***:*** 102-108, 1979. *{Chem. Abstr.* **95** *(1981): 150553h}.*

(8) **Chirila T.,** Csunderlik C. and Demian B.
Acid catalysed acetalisation. III. Investigations on the diastereoisomerism of 2-methyl-2-ethyl-4-hydroxymethyl-1,3-dioxolane. ***Bul. Stiint. Teh. Inst. Politeh. Timisoara Ser. Chim.,* 24(2):** 87-93, 1979.

1980

(9) **Chirila T**. and Prosteanu N.
Investigating the intramolecular hydrogen bonds in 2-hydroxymethyl-1,4-dioxaspiro[4.5]decane. [Rom.] ***Rev. Chim. (Bucharest),* 31(2)**: 135-139, 1980. {***Chem. Abstr.* 93** *(1980): 94656p}.*

(10) Lőcsei V., **Chirila T.**, Lucaciu N. and Pape R. F.
Polyurethane analysis. I. Considerations on NMR analysis. Applications in investigating the structure of prepolymers for microcellular elastomers. [Rom.] ***Mater. Plast. (Bucharest),* 17(2):** 89-92, 1980. *{Chem. Abstr.* **93** *(1980): 187513e}.*

(11) Csunderlik C. and **Chirila T.**
1H-NMR Investigations of the conformation of the spirodioxolanes derived from vicinal diols. I. The ketal of cyclohexanone and racemic 2,3-butanediol. ***Bul. Stiint. Teh. Inst. Politeh. Timisoara Ser. Chim.*, 25(1)**: 87-93, 1980.

1981

(12) Munteanu D., Tincul I. and **Chirila T.**
Stabilization of polyolefins by grafting. [Rom.] ***Mater. Plast. (Bucharest)*, 18(3)**: 147-154, 1981. *{Chem. Abstr.* **96** *(1982): 52698k}.*

(13) Facsko O. and **Chirila T.**
The use of high performance liquid chromatography for the analysis of fatty acids mixtures obtained by the oxidation of n-paraffins. [Rom.] ***Rev. Chim. (Bucharest),* 32(11):** 1111-1115, 1981. *{Chem. Abstr.* **96** *(1982): 228231u}.*

1982

(14) Csunderlik C., **Chirila T.** and Bacaloglu R.
1H-NMR investigations on the conformation of the spirodioxolanes derived from vicinal diols. II. The ketal of cyclohexanone and racemic 1,2-propanediol. ***Org. Magn. Reson.,* 18(3):** 153-156, 1982.

(15) **Chirila T.**
4-Acyloxymethyl-1,3-dioxolanes. Synthetic methods; structural analysis by vibration-rotation spectrometry. [Rom.] ***Rev. Chim. (Bucharest),* 33(3)***: 217-222, 1982. {Chem. Abstr.* 97 (1982):** *38869f}.*

(16) Lőcsei V., Facsko O. and **Chirila T.**
The aminolysis of carbamates. I. The kinetics of the aminolysis of benzyl N-phenylcarbamate with ethanolamine. ***J.Prakt. Chem.,* 324(5):** 816-826, 1982.

(17) **Chirila T.**
Studies on structure and conformational analysis of 5,5-disubstituted 1,3-dioxanes. I. Synthesis and characterization of some 5-ethyl-5-hydroxymethyl-1,3-dioxanes. [Rom.] ***Rev. Chim. (Bucharest),* 33(9):** 820-825, 1982. *{Chem. Abstr.* **98 (***1983): 71382k}.*

(18) Csunderlik C. and **Chirila T.**
Studies on structure and conformational analysis of 5,5-disubstituted 1,3-dioxanes. II. Investigations by proton magnetic resonance spectrometry of the conformation of 5-ethyl-5-hydroxymethyl-1,3-dioxanes. [Rom.] ***Rev. Chim. (Bucharest)*, 33(11)**: 1001-1008, 1982. *{Chem. Abstr.* **99** *(1983): 4829u}.*

1983

(19) Lőcsei V., Facsko O. and **Chirila T.**
The aminolysis of carbamates. II. The kinetics and mechanism of the aminolysis of benzyl N-phenylcarbamate with ethanolamine in aprotic solvents. ***J. Prakt. Chem.,* 325(1):** 49-54, 1983.

1985

(20) Alexander R., Kagi R. I., Rowland S. J., Shepard P. N. and **Chirila T.V.**
The effects of thermal maturity on distributions of dimethylnaphthalenes and trimethylnaphthalenes in some Ancient sediments and petroleum***s. Geochim. Cosmochim. Acta.,* 49(2):** 385-395, 1985.

1989

(21) **Chirila T.V.,** Constable I. J., Russo A. V. and Linton R. G.:
Ridley intraocular lens revisited: chemical analysis of residuals in the original lens material. ***J. Cataract Refract. Surg.,* 15(3):** 283-288, 1989.

(22) **Chirila T.V.,** Russo A.V. and Constable I.J.
Chemical investigations of ultraviolet-absorbing hydrogel material for soft intraocular lenses. ***J. Cataract Refract. Surg.,* 15(5):** 504-509, 1989.

1990

(23) **Chirila T.V.,** Constable I.J., van Saarloos P.P. and Barrett G.D.:
Laser-induced damage to transparent polymers: chemical effect of short-pulsed (Q-switched) Nd:YAG laser radiation on ophthalmic acrylic biomaterials. I. A review. ***Biomaterials,* 11(5):** 305-312, 1990.

(24) **Chirila T.V.,** Barrett G.D., Russo A.V., Constable I.J., van Saarloos P.P. and Russo C.I.
Laser-induced damage to transparent polymers: chemical effect of short-pulsed (Q-switched) Nd:YAG laser radiation on ophthalmic acrylic biomaterials. II. Study of monomer release from artificial intraocular lenses. ***Biomaterials,* 11(5):** 313-320, 1990.

1991

(25) **Chirila T.V.,** Walker L.N., Constable I.J., Thompson D.E. and Barrett G.D.
Cytotoxic effects of residual chemicals from polymeric biomaterials for artificial soft intraocular lenses. ***J. Cataract Refract. Surg.,*** **17(2)**: 154-162, 1991.

(26) **Chirila T.V.,** Barrett G.D., Fletcher W.A., Russo A.V. and Constable I.J.
Further studies on ultraviolet-absorbing hydrogels for intraocular lenses: Relationship between concentration of a polymerizable benzophenone, absorption, and extractability. ***J. Cataract Refract. Surg.***, **17(5):** 596-603, 1991.

(27) **Chirila T.V.,** Cooper R.L., Constable I.J., Richardson G.W. and Vijayasekaran S.
"Black prosthesis" revisited: A study of epinephrine-induced pigment deposits on poly(methyl methacrylate). ***Graefe's Arch. Clin. Exp. Ophthalmol.***, **229(6)**: 578-582, 1991.

1992

(28) **Chirila T. V.**:
Polymeric materials in ophthalmology: recent advances in Western Australia. ***Chem. Aust.***, **59(2):** 52-55, 1992.

(29) **Chirila T.V., C**ooper R.L., Constable I.J. and Horne R.
Radiation-absorbing hydrogel-melanin blends for ocular devices. ***J. Appl. Polym. Sci.***, **44(4):** 593-604, 1992.

(30) **Chirila T.V.** and van Saarloos P.P.
Ablation of poly(2-hydroxyethyl methacrylate) by 193-nm excimer laser radiation. ***J. Appl. Polym. Sci.***, **44(8):** 1355-1363, 1992.

(31) Vernon C.F., Klauber C., van Saarloos P.P. and **Chirila T.V**.
Interaction between acrylic polymers and high energy excimer laser radiation. ***Polym. Int.,*** **27(3):** 243-248, 1992.

(32) Chleboun J.O., Martin R.N., Mitchell C.A. and **Chirila T.V.**
bFGF enhances the development of the collateral circulation after acute arterial occlusion. ***Biochem. Biophys. Res. Commun.***, **185(2):** 510-516, 1992.

(33) **Chirila T.V.**, Thompson D.E. and Constable I.J.
In vitro cytotoxicity of melanized poly(2-hydroxyethyl methacrylate) hydrogels, a novel class of ocular biomaterials. ***J. Biomater. Sci. Polym. Edn,*** **3(6):** 481-498, 1992.

1993

(34) **Chirila T.V.**, Constable I.J., Crawford G.J., Vijayasekaran S., Thompson D.E., Chen Y.C., Fletcher W.A. and Griffin B.J.
Poly(2-hydroxyethyl methacrylate) sponges as implant materials: In vivo and in vitro evaluation of cellular invasion. ***Biomaterials***, **14(1):** 26-38, 1993.

(35) Crawford G.J., Constable I.J., **Chirila T.V**., Vijayasekaran S. and Thompson D.E.
Tissue interaction with hydrogel sponges implanted in the rabbit cornea. ***Cornea***, **12(4)**: 348-357, 1993.

(36) **Chirila T.V.,** Chen Y.C., Griffin B.J. and Constable I.J.
Hydrophilic sponges based on 2-hydroxyethyl methacrylate. I. Effect of monomer mixture composition on the pore size. ***Polym. Int***., **32(3)**: 221-232, 1993.

(37) Chen Y.C., **Chirila T.V.** and Russo A.V.
Hydrophilic sponges based on 2-hydroxyethyl methacrylate. II. Effect of monomer mixture composition on the equilibrium water content and swelling behaviour. ***Mater. Forum***, **17(1)**: 57-65, 1993.

(38) **Chirila T.V**.
Melanized poly(HEMA) hydrogels: basic research and potential use. ***J. Biomater. Appl.***, **8(2**): 106-145, 1993.

1994

(39) **Chirila T.V**., Vijayasekaran S., Horne R., Chen Y.C., Dalton P.D., Constable I.J. and Crawford G.J.
Interpenetrating polymer network (IPN) as a permanent joint between the elements of a new type of artificial cornea. ***J. Biomed. Mater. Res***., **28(6):** 745-753, 1994.

(40) **Chirila T.V.,** Tahija S., Hong Y., Vijayasekaran S. and Constable I.J.
Synthetic polymers as materials for artificial vitreous body: Review and recent advances. ***J. Biomater. Appl***., **9(2):** 121-137, 1994.

(41) van Saarloos P.P., Vernon C.F., **Chirila T.V.** and Klauber C.:
An X-ray photoelectron spectroscopy study of poly(methyl methacrylate) surface modified by 193-nm laser radiation. ***Polym. Bull.***, **33(3)**: 331-338, 1994.

(42) **Chirila T.V.**
Modern artificial corneas: the use of porous polymers. ***Trends Polym. Sci.***, **2(9):** 296-300, 1994. [cover page article].

(43) **Chirila T.V.**
Potential risks of endocapsular polymerization [Letter]. ***J. Cataract Refract. Surg***., **20(6)**: 675, 1994.

1995

(44) Plant G.W., Harvey A.R. and **Chirila T.V.**
Axonal growth within poly(2-hydroxyethyl methacrylate) sponges infiltrated with Schwann cells and implanted into the lesioned rat optic tract. ***Brain Res.***, **671(1):** 119-130, 1995.

(45) **Chirila T.V.**, Constable I.J., Vijayasekaran S. and Ben-nun J.
Melanin-containing hydrogel intraocular lenses: A histopathological study in animal eyes. ***J. Biomater. Appl.***, **9(3):** 262-274, 1995.

(46) **Chirila T.V.**, Constable I.J., Hong Y., Vijayasekaran S., Humphrey M.F., Dalton P.D., Tahija S.G., Maley M.A.L., Cuypers M.J.H., Sharp C., Moore S.R., Davies M.J.
Synthetic hydrogel as an artificial vitreous body. A one-year animal study of its effects on the retina. ***Cells Mater.,*** **5(1):** 83-96, 1995.

(47) **Chirila T.V.,** Yu D.Y., Chen Y.C. and Crawford G.J.
Enhancement of mechanical strength of poly(2-hydroxyethyl methacrylate) sponges. J*. Biomed. Mater. Res*., **29(8)**: 1029-1032, 1995.

(48) Dalton P.D., Jefferson A., Hong Y., **Chirila T.V.**, Vijayasekaran S. and Tahija S.G.
The use of Fourier transform infrared spectrometry for monitoring the retention of polymers in the vitreous humour. *Bio-Med. Mater. Eng.,* **5(3):** 185-193, 1995.

(49) Dalton P.D., **Chirila T.V**., Hong Y. and Jefferson A.
Oscillatory shear experiments as criteria for potential vitreous substitutes. *Polym. Gels Netw.*, **3(4):** 429-444, 1995.

1996

(50) Mitchell C.A., Davies M.J., Grounds M.D., McGeachie J.K., Crawford G.J., Hong Y. and **Chirila T.V**.
Enhancement of neovascularization in regenerating skeletal muscle by the sustained release of erucamide from a polymer matrix. *J. Biomater. Appl*., **10(3**): 230-249, 1996.

(51) Hong Y., **Chirila T.V.**, Vijayasekaran S., Davies M.J. and Maley M.A.L.
In vitro cytotoxicity assay of synthetic hydrogels as potential vitreous substitutes. *In Vitro Toxicol*., **9(1):** 73-82, 1996.

(52) Vijayasekaran S., **Chirila T.V.**, Hong Y., Tahija S.G., Dalton P.D., Constable I.J. and McAllister I.L.
Poly(1-vinyl-2-pyrrolidinone) hydrogels as vitreous substitutes: Histopathological evaluation in the animal eye. *J. Biomater. Sci. Polym. Edn*, **7(8)**: 685-696, 1996.

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SUBMITTED MANUSCRIPTS

(1) **Chirila T.V.** and Suzuki S.
The intraocular lens. Chapter in ***Handbook of Biomaterial Properties,*** 2nd edition, W. Murphy, J. Black and G. Hastings, editors. Springer Science+Business Media LLC, New York. Submitted 20-FEB-2014.

(2) **Chirila T.V.** and Hong Y.
The vitreous humor. Chapter in ***Handbook of Biomaterial Properties***, 2nd edition, W. Murphy, J. Black and G. Hastings, editors. Springer Science+Business Media LLC, New York. Submitted 20-FEB-2014.

(3) **Chirila T.V.** and Suzuki S.
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(4) **Chirila T.V.**, Suzuki S., Hirst L.W. and Harkin D.G.
Reconstruction of the ocular surface using biomaterial templates. Chapter in ***Biomaterials and Regenerative Medicine in Ophthalmology***, 2nd edition, T.V. Chirila and D.G. Harkin, editors. Elsevier, Oxford. Submitted 13-SEP-2014.

(5) Shadforth A.M.A., **Chirila T.V**., Harkin D.G., Kwan A.S.L. and Chen F.K.
Biomaterial templates for the culture and transplantation of retinal pigment epithelial cells: a critical review. Chapter in ***Biomaterials and Regenerative Medicine in Ophthalmology***, 2nd edition, T.V. Chirila and D.G. Harkin, editors. Elsevier, Oxford. Submitted 29-OCT-2014.

(6) **Chirila T.V.** and Harkin D.G.
An introduction to ophthalmic biomaterials and their role in tissue engineering and regenerative medicine. Chapter in ***Biomaterials and Regenerative Medicine in Ophthalmology***, 2nd edition, T.V. Chirila and D.G. Harkin, editors. Elsevier, Oxford. Submitted 15-JAN-2015.

(7) Shadforth A.M.A., Suzuki S., Theodoropoulos C., Richardson N.A., **Chirila T.V.** and Harkin D.G.
A prosthetic Bruch's membrane fabricated from silk fibroin supports RPE cell function. ***J. Tissue Eng. Regen. Med.***, submitted 28-APR-2015.

(8) Suzuki S., Dawson R.A., **Chirila T.V.**, Shadforth A.M.A., Hogerheyde T.A., Edwards G.A. and Harkin D.G.
Treatment of silk fibroin with poly(ethylene glycol) for the enhancement of corneal epithelial cell growth. ***J. Funct. Biomater.,*** submitted 23-APR-2015.

CONFERENCE PRESENTATIONS

(1) "Influence of thermal maturation on trimethylnaphthalenes" (poster with R. Alexander), Gordon Research Conferences, Organic Geochemistry Section, Plymouth, New Hampshire, USA, August 1984.

(2) "Chemistry of ocular biomaterials", America's Cup Ophthalmology Congress, Perth, Australia, February 1987.

(3) "Ocular biomaterials and the chemist's involvement in ophthalmology", Royal Australian Chemical Institute Seminars, University of Western Australia, Perth, Australia, October 1987**.** ***Invited lecture.***

(4) "Further development of flexible biomaterials for intraocular lenses", The 19th Annual Scientific Congress of the Royal Australian College of Ophthalmologists, Perth, Australia, October 1987.

(5) "The scope for development of ophthalmic surgical biomaterials" (with I.J. Constable and R.C. Austen), Materials' Technology and Profit Conference, Melbourne, Australia, November 1988.

(6) "Polymers as implantable ophthalmic biomaterials which protect the retina against photic damage" (with I.J. Constable), The 17th Australian Polymer Symposium, RACI-DITAC Polymer Materials Workshop, Brisbane, Australia, February 1989.

(7) "Light toxicity and chemical absorbers for intraocular lenses", The 26th International Congress of Ophthalmology, Singapore, March 1990.

(8) "Interaction between acrylic polymers and high energy excimer laser radiation" (with P.P. van Saarloos, C.F. Vernon and C. Klauber), POLYMER 91-IUPAC International Symposium, Melbourne, Australia, February 1991.

(9) "Synthetic polymers as biomaterials for ophthalmic surgery", The 19th Australian Polymer Symposium, Perth, Australia, February 1992. ***Invited lecture.***

(10) "HEMA-Based hydrogel sponges" (with Y.C. Chen, I.J. Constable and G.J. Crawford), The 19th Australian Polymer Symposium, Perth, Australia, February 1992.

(11) "The characterisation of radiation-modified polymer surface using XPS" (with C.F. Vernon, C. Klauber and P.P. van Saarloos), The 19th Australian Polymer Symposium, Perth, Australia, February 1992.

(12) "Melanized acrylic hydrogels - novel biomaterials for photoprotective intraocular lenses" (with I.J. Constable and P.P. van Saarloos), Fourth World Biomaterials Congress, Berlin, Germany, April 1992.

(13) "A new approach to the development of a functional keratoprosthesis" (with G.J. Crawford and I.J. Constable), The Tenth Afro-Asian Congress of Ophthalmology, Jakarta, Indonesia, July 1992.

(14) "A new approach to the development of a functional keratoprosthesis" (with G.J. Crawford and I.J. Constable), The 24th Annual Scientific Congress of the Royal Australian College of Ophthalmologists, Sydney, Australia, November 1992. ***The Kabi Pharmacia R.A.C.O. Award for the best scientific paper and original research.***

(15) "Erucamide enhances neovascularization in regenerating skeletal muscle" (poster with C.A. Mitchell, J.K. McGeachie, G.J. Crawford and M.D. Grounds), Advances in Delivery of Therapeutic and Diagnostic Agents '92 Conference, Sydney, Australia, December 1992.

(16) "Polymers as ophthalmic biomaterials: a survey of basic research and some achievements", University of Queensland, Brisbane, Australia, March 1993. ***Invited lecture (by The University of Queensland Chemical Society and Department of Chemistry, University of Queensland).***

(17) "Polymers as ocular biomaterials", Royal Australian Chemical Institute Seminars, Curtin University of Technology, Perth, Australia, April 1993.

(18) "Composite artificial cornea based on interpenetrating networks, a novel concept of keratoprosthesis: manufacture, testing, and results in animal models" (with G.J. Crawford and I.J. Constable), International Conference on Materials for Biomedical Applications, Isola di Capri, Italy, June 1993.

(19) "A new approach to the development of a functional keratoprosthesis" (with G.J. Crawford and I.J. Constable), First International Symposium of Ophthalmology, Bordeaux, France, September 1993.

(20) "Continued development and evaluation of a composite keratoprosthesis" (with G.J. Crawford and I.J. Constable), The 25th Annual Scientific Congress of the Royal Australian College of Ophthalmologists, Hobart, Australia, November 1993.

(21) "Experimental vitreous substitution with amidoglycolates" (with I.J. Constable, S. Tahija and I.L. McAllister), The 25th Annual Scientific Congress of the Royal Australian College of Ophthalmologists, Hobart, Australia, November 1993.

(22) "Homo-IPN at the interface between elements of a novel artificial cornea" (with I.J. Constable and G.J. Crawford), Third Pacific Polymer Conference (PPC-3), Gold Coast, Australia, December 1993.

(23) "Molecular motion in solid and hydrated poly(2-hydroxyethyl methacrylate) as revealed by variable temperature 13C CPMAS NMR" (with D.J.T. Hill, A.K. Whittaker and M.R. Whittaker), Third Pacific Polymer Conference (PPC-3), Gold Coast, Australia, December 1993.

(24) "High water content hydrogels as potential substitutes of human vitreous" (poster with Y. Hong and I.J. Constable), Third Pacific Polymer Conference (PPC-3), Gold Coast, Australia, December 1993.

(25) "Quantitative microscopic study of porous characteristics of PHEMA sponges" (poster with Y.C. Chen, I.J. Constable, B.J. Griffin and J. Kuo), Third Pacific Polymer Conference (PPC-3), Gold Coast, Australia, December 1993.

(26) "A novel concept of artificial cornea based on porous polymers and interpenetrating polymer networks" (with P.D. Dalton, I.J. Constable and G.J. Crawford), Fourth Annual Conference of Australian Society for Biomaterials, Sydney, Australia, January/February 1994.

(27) "A new approach to the development of a functional keratoprosthesis" (with G.J. Crawford and I.J. Constable), The 27th International Congress of Ophthalmology, Toronto, Canada, June 1994.

(28) "Clinical imperatives for polymeric biomaterials in ophthalmology" (with I.J. Constable), Conference on Engineering and the Physical Sciences in Medicine (EPSM'94), Perth, Australia, September 1994.

(29) "Artificial cornea: a novel core-and-skirt design" (with P.D.Dalton, G.J. Crawford and I.J. Constable), Conference on Engineering and the Physical Sciences in Medicine (EPSM'94), Perth, Australia, September 1994.

(30) "Neocollagen synthesis within hydrogel sponges implanted into the rabbit cornea" (with S. Vijayasekaran, G.J. Crawford, D.E. Thompson-Wallis and I.J. Constable), The ORIA National Ophthalmic and Visual Science Meeting, Geelong, Australia, December 1994.

(31) "Poly(2-hydroxyethyl methacrylate) sponge as tissue-equivalent matrix in an artificial cornea" (with D.E. Thompson-Wallis, G.J. Crawford, S. Vijayasekaran and I.J. Constable), Fifth Annual Conference of Australian Society for Biomaterials, Melbourne, Australia, January/February 1995.

(32) "Crosslinked PVP hydrogel as a vitreous substitute" (poster with Y. Hong, S. Vijayasekaran and P.D. Dalton), Fifth Annual Conference of Australian Society for Biomaterials, Melbourne, Australia, January/February 1995.

(33) "Poly(N-vinyl-2-pyrrolidinone) as a vitreous substitute" (with P.D. Dalton, Y. Hong, A. Jefferson and S. Tahija), The 20th Australian Polymer Symposium, Adelaide, Australia, February 1995.

(34) "Molecular motion in solid poly(hydroxyethyl methacrylate) as revealed by variable temperature 13C CPMAS NMR" (with D.J.T. Hill, A.K. Whittaker and M.R. Whittaker), The 20th Australian Polymer Symposium, Adelaide, Australia, February 1995.

(35) "Preliminary evaluation of a hydrogel composite keratoprosthesis in the rabbit cornea" (with G.J. Crawford and S. Vijayasekaran), Second KPro Study Group Meeting, Rome, Italy, June 1995.

(36) "Core-and-skirt keratoprostheses: a review and recent advances" (with G.J. Crawford and I.J. Constable), Second KPro Study Group Meeting, Rome, Italy, June 1995.

(37) "Artificial cornea based on interpenetrating polymer networks", ACS Intersociety Polymer Conference, Baltimore, USA, October 1995. ***Invited lecture.***

(38) "Preliminary evaluation of a hydrogel core-and-skirt keratoprosthesis in the rabbit cornea" (with G.J. Crawford and I.J. Constable), The 27th Annual Scientific Congress of the Royal Australian College of Ophthalmologists, Melbourne, Australia, November 1995.

(39) "Conjunctival coverage of a hydrogel keratoprosthesis: an animal study" (poster with C.R. Hicks, G.J. Crawford and I.J. Constable), The 27th Annual Scientific Congress of the Royal Australian College of Ophthalmologists, Melbourne, Australia, November 1995.

(40) "Oscillatory shear studies of potential vitreous substitutes" (with P.D. Dalton, Y. Hong, A. Jefferson and I.J. Constable), The ORIA National Ophthalmic and Visual Science Meeting, Geelong, Australia, December 1995.

(41) "Assessment of corneal collagenase production in response to hydrogel polymers" (with B.W. Ziegelaar, C.R. Hicks and J.H. Fitton), The ORIA National Ophthalmic and Visual Science Meeting, Geelong, Australia, December 1995.

(42) "Poly(N-vinyl-2-pyrrolidinone) as a vitreous substitute" (with P.D. Dalton, A. Jefferson and Y. Hong), The Fourth Pacific Polymer Conference (PPC-4), Kauai, Hawaii, USA, December 1995.

(43) "Enhancement of mechanical strength of poly(2-hydroxyethyl methacrylate) sponges" (with A.B. Clayton, P.D. Dalton and X. Lou), The 21st Australian Polymer Symposium, Wollongong, Australia, February 1996.

(44) "Molecular dynamics of poly(hydroxyethyl methacrylate) in the solid-state probed by variable temperature 2D NMR" (with D.J.T. Hill, A.K. Whittaker and M.R. Whittaker), The 21st Australian Polymer Symposium, Wollongong, Australia, February 1996.

(45) "Rheological evaluation of potential vitreous substitutes" (with P.D. Dalton, Y. Hong, A. Jefferson and I.J. Constable), The 21st Australian Polymer Symposium, Wollongong, Australia, February 1996.

(46) "Hydrogel core-and-skirt keratoprostheses in pigs" (poster with C.R. Hicks, G.J. Crawford, I.J. Constable and P.D. Dalton), The 4th World Congress on the Cornea, Orlando, USA, April 1996.

(47) "Tissue melting in relation to a hydrogel keratoprosthesis: the role of anticollagenolytics" (poster with G.J. Crawford, C.R. Hicks, J.H. Fitton, B.W. Ziegelaar, A.B. Clayton and I.J. Constable), The Association for Research in Vision and Ophthalmology, Annual Meeting, Fort Lauderdale, USA, April 1996; I***nvest. Ophthalmol. Vis. Sci.,* 37(Suppl.), abstract 1453 (1996).**

(48) "Development of an artificial corneal button for penetrating keratoplasty: design, biocompatibility and results in animals" (poster with C.R. Hicks, P.D. Dalton, A.B. Clayton, J.H. Fitton, B.W. Ziegelaar, S. Vijayasekaran, G.J. Crawford and I.J. Constable), The Association for Research in Vision and Ophthalmology, Annual Meeting, Fort Lauderdale, USA, April 1996; ***Invest. Ophthalmol. Vis. Sci.*, 37(Suppl.), abstract 2524 (1996).**

(49) "Current projects on ocular biomaterials at the Lions Eye Institute: a brief overview", Conference on Medicine, Science and Technology Seminars 1996 — Biomaterials, Sponsored by the Embassy of Italy, Perth, Australia, 17 April 1996.

(50) "Hydrophilic sponges based on 2-hydroxyethyl methacrylate" (with A.B. Clayton, P.D. Dalton and X. Lou), Fifth World Biomaterials Congress, Toronto, Canada, May/June 1996.

(51) "Increasing the biocompatibility of keratoprosthesis materials" (with J.H. Fitton, A.B. Clayton, C.R. Hicks, B.W. Ziegelaar, S. Vijayasekaran, P.D. Dalton, Y. Hong, G.J. Crawford and I.J. Constable), Fifth World Biomaterials Congress, Toronto, Canada, May/June 1996.

(52) "Reduction of collagenase activity associated with keratoprosthesis materials" (poster with J.H. Fitton, C.R. Hicks, B.W. Ziegelaar, A.B. Clayton, P.D. Dalton and I.J. Constable), Fifth World Biomaterials Congress, Toronto, Canada, May/June 1996.

(53) "Rheological assessment of potential vitreous substitutes" (poster with P.D. Dalton and A. Jefferson), Fifth World Biomaterials Congress, Toronto, Canada, May/June 1996.

(54) "Surgical approaches to reducing keratoprosthesis extrusion in an animal model" (poster with C.R. Hicks, P.D. Dalton, A.B. Clayton, S. Vijayasekaran, J.H. Fitton, B.W. Ziegelaar, G.J. Crawford and I.J. Constable), Fifth World Biomaterials Congress, Toronto, Canada, May/June 1996.

(55) "Characterization of PVP hydrogels as potential vitreous substitutes" (poster with Y. Hong, S. Vijayasekaran, J.H. Fitton, P.D. Dalton, B.W. Ziegelaar and I.J. Constable), Fifth World Biomaterials Congress, Toronto, Canada, May/June 1996.

(56) "Histopathology of PVP hydrogels as vitreous substitutes" (poster with S. Vijayasekaran, Y. Hong, S.G. Tahija, P.D. Dalton, I.J. Constable and I.L. McAllister), Fifth World Biomaterials Congress, Toronto, Canada, May/June 1996.

(57) "Artificial cornea: a design based on interpenetrating polymer networks", Advances in Polymers III: Designer Polymers, Victorian Polymer Group Symposium, Melbourne, Australia, 27 September 1996. ***Invited speake***r.

(58) "Evaluation of a hydrogel core-and-skirt keratoprosthesis in the rabbit cornea" (with G.J. Crawford, C.R. Hicks and I.J. Constable), The 12th International Congress of Eye Research, Yokohama, Japan, September/October 1996.

(59) "The Chirila keratoprosthesis in animals: clinical results" (with C.R. Hicks, A.B. Clayton, S. Platten, G.J. Crawford, S. Vijayasekaran and I.J. Constable), The 28th Annual Scientific Congress of the Royal Australian College of Ophthalmologists, Perth, Australia, November 1996.

(60) "Reduction of the initial collagenase response after implantation of a hydrogel KPro material in the rabbit cornea" (with J.H. Fitton, B.W. Ziegelaar, C.R. Hicks, G.J. Crawford and I.J. Constable), The 28th Annual Scientific Congress of the Royal Australian College of Ophthalmologists, Perth, Australia, November 1996.

(61) "Keratoprosthesis: clinical results in animals" (with C. Hicks, A. Clayton, S. Platten and H. Fitton), The ORIA National Ophthalmic and Visual Science Meeting, Canberra, Australia, November/December 1996.

(62) "Cell interactions with hydrogel sponge material of a keratoprosthesis" (with S. Vijayasekaran, J.H. Fitton, C.R. Hicks, B.W. Ziegelaar, S. Platten, G.J. Crawford and I.J. Constable), The ORIA National Ophthalmic and Visual Science Meeting, Canberra, Australia, November/December 1996.

(63) "Enzyme responses to keratoprosthesis material" (with B. Ziegelaar, J.H. Fitton, T. Clayton, C.R. Hicks, S. Vijayasekaran, S. Platten, G.J. Crawford and I.J. Constable), The ORIA National Ophthalmic and Visual Science Meeting, Canberra, Australia, November/December 1996.

(64) "Mechanical properties of macroporous PHEMA sponges" (with A.B. Clayton and X. Lou), Seventh Annual Conference of Australian Society for Biomaterials, Nelson Bay, Port Stephens, Australia, March 1997.

(65) "Physically crosslinked PVA: the next generation of hydrogels?" (with P. Dalton and K. Rowe), Seventh Annual Conference of Australian Society for Biomaterials, Nelson Bay, Port Stephens, Australia, March 1997.

(66) "Cell interactions with hydrogel sponge material of a keratoprosthesis" (with S. Vijayasekaran, J.H. Fitton, C.R. Hicks, B.W. Ziegelaar and T. Clayton), Seventh Annual Conference of Australian Society for Biomaterials, Nelson Bay, Port Stephens, Australia, March 1997.

(67) "The enzymatic response to keratoprosthesis materials" (with B.W. Ziegelaar, H. Fitton and A.B. Clayton), Seventh Annual Conference of Australian Society for Biomaterials, Nelson Bay, Port Stephens, Australia, March 1997.

(68) "Advances towards a functional artificial cornea", International Conference on Biorelated Polymers, Controlled Release Drugs and Reactive Polymers, Xi'An, People's Republic of China, May 1997. ***Plenary lecture.***

(69) "Hydrophilic sponges based on 2-hydroxyethyl methacrylate: synthesis of hydroxyl-containing crosslinking agents and their effects on mechanical strength" (with X. Lou and A.B. Clayton), International Conference on Biorelated Polymers, Controlled Release Drugs and Reactive Polymers, Xi'An, People's Republic of China, May 1997.

(70) "Evaluation of biodegradation in vitro and retention in vivo of a PVP hydrogel as a vitreous substitute" (poster with Y. Hong, S. Vijayasekaran and V.A. Alder), The Association for Research in Vision and Ophthalmology, Annual Meeting, Fort Lauderdale, USA, May 1997; ***Invest. Ophthalmol. Vis. Sci.***, **38(Suppl.), abstract 423 (1997).**

(71) "Keratoprostheses for implantation into diseased eyes" (poster with C.R. Hicks, X. Lou, J.H. Fitton, B.W. Ziegelaar, S. Platten, G.J. Crawford and I.J. Constable), The Association for Research in Vision and Ophthalmology, Annual Meeting, Fort Lauderdale, USA, May 1997; ***Invest. Ophthalmol. Vis. Sci.***, **38(Suppl.), abstract 2340 (1997).**

(72) "Cellular interactions with hydrogels of the Chirila Keratoprosthesis" (poster with J.H. Fitton, S. Vijayasekaran, B.W. Ziegelaar, C.R. Hicks, A.B. Clayton, G.J. Crawford and I.J. Constable), The Association for Research in Vision and Ophthalmology, Annual Meeting, Fort Lauderdale, USA, May 1997; ***Invest. Ophthalmol. Vis. Sci.,*** 3**8(Suppl.), abstract 2341 (1997).**

(73) "The development of an orbital implant allowing direct muscle attachment" (with C.R. Hicks, G.J. Crawford, A.B. Clayton, S. Vijayasekaran, J.H. Fitton and I.J. Constable), The XI-th Congress of the European Society of Ophthalmology, Budapest, Hungary, June 1997.

(74) "Biodegradation in vitro and retention in the rabbit eye of crosslinked PVP hydrogel as a vitreous substitute" (poster with Y. Hong and S. Vijayasekaran), The 13th European Conference on Biomaterials, Göteborg, Sweden, September 1997.

(75) "Keratoprosthesis based on interpenetrating polymer network", World Congress on Medical Physics and Biomedical Engineering, Nice, France, September 1997.

(76) "High water content hydrogel as vitreous substitutes: a study of retention in animal eyes" (with Y. Hong, S. Vijayasekaran and P.D. Dalton), World Congress on Medical Physics and Biomedical Engineering, Nice, France, September 1997.

(77) "An orbital implant allowing direct muscle attachment" (with C.R. Hicks, I.T. Morris, J. McAllister, S. Vijayasekaran, A.B. Clayton, G.J. Crawford and I.J. Constable), The 29th Annual Scientific Congress of the Royal Australian College of Ophthalmologists, Sydney, Australia, November 1997.

(78) "The modulation of cellular responses to poly(HEMA) hydrogel surface: phosphorylated surfaces decrease collagenase production in vitro" (with B.W. Ziegelaar, J.H. Fitton, A.B. Clayton and S.T. Platten), Eighth Annual Conference of Australian Society for Biomaterials, Marysville, Australia, March 1998.

(79) "Extracellular matrix production by corneal cells in response to poly(HEMA) hydrogels: effects of polymer formulation and surface morphology" (with M.A.L. Maley, J.H. Fitton and X. Lou), Eighth Annual Conference of Australian Society for Biomaterials, Marysville, Australia, March 1998.

(80) "Approaches to improving the success rate of keratoprosthesis implantation" (poster with C.R. Hicks, J.H. Fitton, S. Vijayasekaran, S. Platten, G.J. Crawford and I.J. Constable), The Tenth Anniversary Congress of the Royal College of Ophthalmologists (UK), Glasgow, Scotland, April 1998.

(81) "Keratoprosthesis implantation in a rabbit model" (video with C.R. Hicks, P.D. Dalton, X. Lou, S. Platten, G.J. Crawford and I.J. Constable), The Tenth Anniversary Congress of the Royal College of Ophthalmologists (UK), Glasgow, Scotland, April 1998.

(82) "Implantation of a novel orbital implant in a rabbit model" (video with C.R. Hicks, A.B. Clayton, S. Vijayasekaran, B. Ziegelaar, G.J. Crawford and I.J. Constable), The Tenth Anniversary Congress of the Royal College of Ophthalmologists (UK), Glasgow, Scotland, April 1998.

(83) "High water content PVP hydrogels as potential vitreous substitutes: physical and biological performance" (with Y. Hong), IUPAC World Polymer Congress, 37th International Symposium on Macromolecules, Gold Coast, Australia, July 1998.

(84) "Modulation of PHEMA sponge characteristics by changes in reactivity and hydrophilicity of crosslinking agents" (with X. Lou and P.D. Dalton), IUPAC World Polymer Congress, 37th International Symposium on Macromolecules, Gold Coast, Australia, July 1998.

(85) "Biodegradation ***in vitro*** and retention in the rabbit eye of crosslinked PVP hydrogel as a vitreous substitute" (with Y. Hong and S. Vijayasekaran), IUPAC World Polymer Congress, 37th International Symposium on Macromolecules, Gold Coast, Australia, July 1998.

(86) "Polymeric biomaterials and their applications in eye surgery", Royal Australian Chemical Institute, Women in Chemistry Group and Health, Safety & Environmental Group, Chemistry Centre of Western Australia, Perth, Australia, July 1998**. *Invited address.***

(87) "Cellular response to copolymer hydrogels: fibronectin deposition, focal adhesions and collagenase production" (with M.A.L. Maley, B.W. Ziegelaar, X. Lou and C.J. Pudney), 22nd Annual Scientific Conference of the Matrix Biology Society of Australia and New Zealand, Hahndorf, Australia, September 1998.

(88) "Nonbiodegradable scaffolding for tissue ingrowth in a novel artificial cornea", 98 Workshop on Tissue Engineering, Tianjin, People's Republic of China, October 1998.

(89) "Surface modification of poly(2-hydroxyethyl methacrylate) hydrogels with poly(ethylene oxides) by the solvent-controlled generation of physical interpenetrating polymer networks" (with Y. Hong, X. Lou, K. Yao and F. Shen), 98 Workshop on Tissue Engineering, Tianjnin, People's Republic of China, October 1998.

(90) "Preparation and evaluation of chemically linked oligonucleotides to a PVP hydrogel: a preliminary study on sustained release of antisense oligonucleotides" (with X. Lou, K.L. Garrett and P.E. Rakoczy), Ninth Annual Conference of Australian Society for Biomaterials, Canberra, Australia, March 1999.

(91) "A new type of PHEMA sponge: formation and characterization" (with X. Lou, S. Vijayasekaran, M.A.L. Maley, C. Hicks and B. Higgins), Ninth Annual Conference of Australian Society for Biomaterials, Canberra, Australia, March 1999.

(92) "Calcification of poly(2-hydroxyethyl methacrylate) hydrogel sponges implanted in the rabbit cornea" (with S. Vijayasekaran, T. Robertson, X. Lou, C.R. Hicks and J.H. Fitton), Ninth Annual Conference of Australian Society for Biomaterials, Canberra, Australia, March 1999.

(93) "Pilot study of the Chirila keratoprosthesis in human patients" (with C.R. Hicks, G. J. Crawford, X. Lou, S. Platten, S. Vijayasekaran and I.J. Constable), Third KPro Study Group Meeting, Birmingham, UK, June 1999.

(94) "Polymer research and applications in ophthalmology", RACI ***Applied Research Award and Don Rivett Medal Presentation Address***, National Chemistry Week Dinner, Fremantle, Australia, 24 July 1999.

(95) "Synthetic hydrogels as biomaterials in ophthalmic surgery", Special Research Centre for Advanced Minerals and Materials Processing Seminars, University of Western Australia, Perth, Australia, 14 October 1999. ***Invited lecture.***

(96) "Keratoprosthesis: clinical trial" (with C.R. Hicks, X. Lou, G.J. Crawford, S. Vijayasekaran, M. Maley and I.J. Constable), Australian Ophthalmic and Visual Science Meeting, Australian National University, Canberra, Australia, December 1999.

(97) "Preparation of and cellular invasion in sequential homo-IPN sponges based on PHEMA" (with X. Lou, S. Vijayasekaran, M.A.L. Maley, C.R. Hicks and I.J. Constable), Australian Ophthalmic and Visual Science Meeting, Australian National University, Canberra, Australia, December 1999.

(98) "Hydrogels as a drug carrier for therapeutic oligonucleotides: a preliminary study" (with X. Lou, K. Garrett, P. Rakoczy and I.J. Constable), Australian Ophthalmic and Visual Science Meeting, Australian National University, Canberra, Australia, December 1999.

(99) "A hydrogel artificial cornea: from conception to clinical trials", Symposium on Biomedical Polymers for the 21st Century, Overview and Ophthalmic Applications, Harvard Medical School, The Schepens Eye Research Institute, Boston, USA, March 2000. ***Invited lecture.***

(100) "Chirila keratoprosthesis: clinical trial" (with C. R. Hicks, G. J. Crawford, X. Lou, S. Vijayasekaran and I. J. Constable), EVER 2000 – European Association for Vision and Eye Research Conference, Palma de Mallorca, Spain, October 2000; ***Ophthalmic Res.*, 32 (Suppl.2), abstract 3142 (2000).**

(101) "Artificial cornea with porous skirt: an example of tissue engineering?", Frontiers in Tissue Engineering: West Australian Symposium, Tissue Engineering Research Centre (TERC) Workshop, University of Western Australia, Perth, Australia, October 2000. ***Invited lecture.***

(102) "The evaluation of the Chirila keratoprosthesis in humans" (with G. J. Crawford, C. Hicks, X. Lou and I. J. Constable), The 104th Annual Meeting of the American Academy of Ophthalmology, Dallas, USA, October 2000.

(103) "Chirila KPro I: an overview" (with G. J. Crawford, C. R. Hicks, X. Lou, I. J. Constable, S. Vijayasekaran, D. Tan and B. Mulholland), The 4th KPro Study Group and the 6th International Ocular Surface Society Joint Meeting, Fort Lauderdale, USA, May 2001.

(104) "Chirila KPro II: case histories" (with D. Tan, G. J. Crawford, C. R. Hicks, X. Lou, S. Vijayasekaran and I. J. Constable), The 4th KPro Study Group and the 6th International Ocular Surface Society Joint Meeting, Fort Lauderdale, USA, May 2001.

(105) "Chirila KPro III: keratoprosthesis or not?" (with C. R. Hicks, G. J. Crawford, D. Tan and I. J. Constable), The 4th KPro Study Group and the 6th International Ocular Surface Society Joint Meeting, Fort Lauderdale, USA, May 2001.

(106) "The outcomes of keratoprosthesis surgery" (with G. Crawford, C. Hicks, X. Lou, D. Tan and I. Constable), The 19th Congress of the European Society of Cataract and Refractive Surgeons, Amsterdam, The Netherlands, September 2001.

(107) "Synthetic penetrating keratoplasty using a hydrogel keratoprosthesis, the Chirila KPro: surgical technique, case histories and outcomes" (with G. J. Crawford, C. R. Hicks, X. Lou, D. T. Tan, G. R. Snibson and I. J. Constable), The 27th Annual Meeting of the Castroviejo Cornea Society, New Orleans, USA, November 2001.

(108) "Research on artificial cornea – development of a hydrogel keratoprosthesis form conception to clinical trials", Menicon 50th Anniversary International Symposium, Nagoya, Japan, November 2001. ***Invited lecture.***

(109) "A successful application of acrylic hydrogels: AlphaCor™ artificial cornea and its clinical evaluation", Polymers in Dentistry, Medicine and Surgery (PDMS 2002) Symposium, RACI Polymer Division, Brisbane, Australia, February 2002. ***Plenary lecture.***

(110) "Overview of polymeric biomaterials for synthetic corneas", The 29th International Congress of Ophthalmology, Sydney, Australia, April 2002**. *Invited lecture.***

(111) "Outcomes and risk factors for synthetic penetrating keratoplasty with AlphaCor" (with C. R. Hicks, G. J. Crawford, X. Lou, D. Tan, G. R. Snibson, G. Sutton, N. Downie, I. J. Constable), The Association for Research in Vision and Ophthalmology, Annual Meeting, Fort Lauderdale, USA, May 2002. (Abstract# 2991).

(112) "AlphaCor: device, technique and outcomes" (with G. J. Crawford, C. R. Hicks, D. T. Tan, G. R. Snibson, G. Sutton, X. Lou and I. J. Constable), EVER 2002 – European Association for Vision and Eye Research Conference, Alicante, Spain, October 2002.

(113) "Non-biodegradable polymer scaffolds for tissue engineering", The 2nd Cottesloe Beach Symposium: Stem Cells and Tissue Engineering, Perth, Australia, November 2002. ***Invited lecture.***

(114) "Biointegration of non-biodegradable matrix: the artificial cornea story", Bioscience Frontiers for the Real World 2002 Conference: Frontiers in Tissue Engineering, Brisbane, Australia, November 2002. ***Invited lecture.***

(115) "Deposits in artificial corneas: risk factors and prevention" (with C. Hicks, G. Crawford, L. Werner, D. Apple and I. Constable), The Australasian Ophthalmic and Visual Sciences Meeting, Sydney, Australia, December 2002.

(116) "Diffusion of calcium ions in poly(2-hydroxyethyl methacrylate) hydrogels" (with D.J.T. Hill, Zainuddin and A.K. Whittaker), The 26th Australian Polymer Symposium, Noosa, Australia, July 2003.

(117) "Clinical outcomes of artificial cornea (AlphaCor) implantations" (with H. Eguchi, H. Shiota, C. R. Hicks, G. J. Crawford, D.T. Tan, G.R. Sutton and G. Snibson), The 57th Congress of Clinical Ophthalmology of Japan, Nagoya, Japan, October/November 2003.

(118) "Artificial corneas", Ophthalmology Study Day 2004, Fremantle Hospital and Health Services, Corporate Staff Development, Fremantle, Australia, 5 August 2004. ***Invited lecture.***

(119) "Diffusion of calcium ions and formation of calcium phosphate deposits in radiation crosslinked PVA/PVP hydrogels" (with Zainuddin, D. J. T. Hill, A. K. Whittaker and K. Strounina), The 228th American Chemical Society National Meeting, Division of Polymer Chemistry, Philadelphia, USA, August 2004.

(120) "AlphaCor: current outcome data" (with C. R. Hicks, X. Lou, G. J. Crawford and I. J. Constable), The 16th International Congress of Eye Research, Sydney, Australia, August/September 2004.

(121) "In vitro study of the calcification of PHEMA hydrogels in simulated body fluid" (with Zainuddin, D. J. T. Hill and A. K. Whittaker), Polymers in Medicine and Surgery, Cambridge, UK, September 2004.

(122) "Tissue engineering in the eye: a biointegrable artificial cornea", The Australian Institute for Bioengineering and Nanotechnology Seminars, University of Queensland, Brisbane, Australia, 17 November 2004. ***Invited seminar presentation.***

(123) "The role of phosphate and carboxylic groups on the reduction of calcification of hydrogel implants" (with Zainuddin, D. J. T. Hill and A. K. Whittaker), The 27th Australian Polymer Symposium, Adelaide, Australia, November 2004.

(124) "History of artificial cornea in Japan", The Joint 29th Japan Cornea Conference and 21st Annual Meeting of Keratoplasty Society of Japan, Tokushima, Japan, February 2005. ***Invited symposium speaker.***

(125) "Introducing the Queensland Eye Institute and a brief presentation of its polymer-related research program", The Polymer Group Meetings, Queensland University of Technology, Brisbane, Australia, 19 September 2005. I***nvited seminar presentation.***

(126) "Introducing the Queensland Eye Institute and its polymer-related research", The Polymer Chemistry Group Research Seminars, University of Queensland, Brisbane, Australia, 20 October 2005. I***nvited seminar presentation.***

(127) "Drug-induced spoliation of the hydrogel in an artificial cornea (AlphaCor™)" (with D. A. Morrison, Z. Gridneva and C. R. Hicks), The 28th Australasian Polymer Symposium & Australasian Society for Biomaterials 16th Conference, Rotorua, New Zealand, February 2006.

(128) "Bioactive hydrogels for tissue engineering: a study of calcium phosphates deposition in radiation-formed PVA/PVP hydrogels" (with Zainuddin, D. J. T. Hill and A. K. Whittaker), AINSE Radiation 2006 Conference, Sydney, Australia, April 2006.

(129) "Biodegradability of linear poly(2-hydroxyethyl methacrylate)" (with I. Keen and A. K. Whittaker), The 29th Australasian Polymer Symposium, Hobart, Australia, February 2007.

(130) "Bombyx mori silk fibroin as a biomatrix substrate for ex vivo expansion of human and rabbit corneal epithelial cells" (poster with C. Kim, L.A. Oliveira, Zainuddin, I.R. Schwab and M.I. Rosenblatt), The Association for Research in Vision and Ophthalmology (ARVO), Annual Meeting, Fort Lauderdale, USA, May 2007**. Abstract 1884/B955.**

(131) "Bombyx mori silk fibroin as a biomatrix substrate for ex vivo expansion of human and rabbit corneal epithelial cells" (poster with I. R. Schwab, L. A. Oliveira, C. Kim, Zainuddin, T. Blankenship and M. I. Rosenblatt), The 5th Annual Meeting of the International Society for Stem Cell Research (ISSCR), Cairns, Australia, June 2007.

(132) "Preparation and characterization of the degradation behavior of PHEMA-peptide conjugate sponges by photoinitiated phase-separation polymerization" (poster with M. V. Baker, D. H. Brown, Y. Casadio and H.-B. Kraatz), International Conference on Materials for Advanced Technologies 2007 (ICMAT 2007), Singapore, July 2007. Poster A-5-P025. **Award winning presentation.**

(133) "Preparation and characterization of the degradation behavior of PHEMA-peptide conjugate sponges by photoinitiated phase-separation polymerization" (poster with M. V. Baker, D. H. Brown, Y. S. Casadio and H.-B. Kraatz), The ARC Australian Research Network for Advanced Materials (ARNAM) 2007 Annual Workshop, Canberra, Australia, July 2007. Presentation 14-2 (Conference Booklet, p. 94). **Award winning presentation.**

(134) "Silk as substratum for cell attachment and proliferation" (with Z. Barnard, Zainuddin and D. Harkin), The Sixth Pacific Rim International Conference on Advanced Materials and Processing (PRICM-6), Jeju Island, Korea, November 2007. ***Invited presentation.***

(135) "Cytotoxicity of linear poly(2-hydroxyethyl methacrylate) made by control radical polymerization techniques" (with I. Keen, Z. Barnard, Zainuddin and A. Whittaker), International Congress on Biohydrogels, Viareggio, Lucca, Italy, November 2007.

(136) "Development of retinal pigment epithelial cell culture on Bombyx mori silk fibroin (BMSF) membrane for retinal transplantation" (with A. Kwan, S. Cheng, Z. Barnard, Zainuddin and D. Harkin), The 39th Annual Scientific Congress of The Royal Australian and New Zealand College of Ophthalmologists, Perth, Australia, November 2007.

(137) "Retinal pigment epithelial cell culture on silk substrate for retinal tissue transplantation" (with S. Cheng, A. Kwan, Z. Barnard, Zainuddin and D. Harkin), The Australasian Ophthalmic and Visual Sciences Meeting - 2007, Canberra, Australia, December 2007.

(138) "Bombyx mori silk fibroin membranes as potential substrata for epithelial constructs used in the management of ocular surface disorders" (poster with Z. Barnard, Zainuddin, D.G. Harkin, I.R. Schwab and L.W. Hirst), The Australasian Ophthalmic and Visual Sciences Meeting - 2007, Canberra, Australia, December 2007.

(139) "Bombyx mori silk fibroin membranes as potential substrata for epithelial constructs used in the management of ocular surface disorders" (with Z. Barnard, Zainuddin, D.G. Harkin, I.R. Schwab and L.W. Hirst), CSIRO Conference "Fibrous Proteins: transforming structural knowledge into new materials", Mount Eliza, Melbourne, Australia, 31 March – 3 April 2008.

(140) "Synthesis and characterisation of hydrogels with biodegradable crosslinks via one pot RAFT polymerisation" (with I. Keen and A. Whittaker), The 30th Australasian Polymer Symposium, Melbourne, Australia, 30 Nov. – 4 Dec. 2008.

(141) "Development of supramolecular hydrogels as injectable artificial vitreous substitutes" (poster with H. H. Lee, A. Whittaker, F. Rasoul, C. Hawker and B. Dargaville), The 30th Australasian Polymer Symposium, Melbourne, Australia, 30 Nov.- 4 Dec. 2008.

(142) "Supramolecular hydrogels as injectable artificial vitreous substitutes" (poster PC1-91 with B. Dargaville, C. Hawker, H. H. Lee-Wang, F. Rasoul and A. Whittaker), The European Polymer Congress (EPF'09), Graz, Austria, 12-17 July 2009.

(143) "Green routes to porous polymer materials for tissue engineering" (with M. V. Baker, D. H. Brown, Y. Casadio, I. Keen, S. Paterson and A. Whittaker), International Conference on Green and Sustainable Chemistry (ICGSC 2009), Singapore, 3-5 Aug. 2009.

(144) "Evaluation of fibroin-based scaffolds for ocular tissue reconstruction" (with L. J. Sinfield, K. A. George, D. W. Hutmacher and D. G. Harkin), Institute of Health & Biomedical Innovation (IHBI) Inspires Postgraduate Conference, Brisbane, Australia, Nov. 2009.

(145) "A method for the diversity oriented surface modification of PHEMA" (with Z. Merikan, Q. H. Lee and I. Blakey), The 11th Pacific Polymer Conference (PPC-11), Cairns, Australia, 6-10 Dec. 2009.

(146) "Use of mineral-coated polysaccharide capsules as 3-D biomimetic environments for transfection of human skeletal cell population" (with D. Green, K. Partridge, J. Babister, S. Mann and R. O. C. Oreffo), The 11th Pacific Polymer Conference (PPC-11), Cairns, Australia, 6-10 Dec. 2009.

(147) "Novel supramolecular hydrogels as artificial vitreous substitutes" (with H. H. Lee-Wang, I. Blakey, B. Dargaville, C. Hawker, H. Peng, F. Rasoul and A. Whittaker), The 11th Pacific Polymer Conference (PPC-11), Cairns, Australia, 6-10 Dec. 2009.

(148) "ARGET ATRP of 2-hydroxyetrhyl methacrylate using ascorbic acid as a reducing agent" (poster with S. Paterson, M. Baker, I. Keen, D. Brown and A. Whittaker), The 11th Pacific Polymer Conference (PPC-11), Cairns, Australia, 6-10 Dec. 2009.

(149) "Laser radiation modification of PHEMA hydrogels and the effect on the attachment of human corneal epithelial cells" (poster with Zainuddin, Z. Barnard, G. Watson and A. K. Whittaker), The 11th Pacific Polymer Conference (PPC-11), Cairns, Australia, 6-10 Dec. 2009.

(150) "Novel hydrogelators for the creation of supramolecular self-healing hydrogels as artificial vitreous. First generation: linear polymers" (poster with H. H. Lee-Wang, I. Blakey, H. Peng, F. Rasoul, A. Whittaker and B. Dargaville), The 20th Annual Australasian Society for Biomaterials and Tissue Engineering (ASBTE) Conference, Brisbane, Australia, 10-12 Feb. 2010.

(151) "Composite fibroin scaffolds for corneal tissue engineering" (poster with K. A. George, S. P. Kale, L. J. Sinfield, S. C. Kundu, P. D. Dalton, D. W. Hutmacher, I. R. Schwab and D. G. Harkin), The 20th Annual Australasian Society for Biomaterials and Tissue Engineering (ASBTE) Conference, Brisbane, Australia, 10-12 Feb. 2010.

(152) "Synthesis and degradation of PLLA-co-succinic anhydride networks" (with K. A. George and E. Wentrup-Byrne), The 20th Annual Australasian Society for Biomaterials and Tissue Engineering (ASBTE) Conference, Brisbane, Australia, 10-12 Feb. 2010.

(153) "Novel supramolecular hydrogels as artificial vitreous substitutes" (with H.H. Lee, I. Blakey, F. Rasoul, A.K. Whittaker and B.L. Dargaville), The 239th Conference of the American Chemical Society (ACS), San Francisco, USA, March 2010.

(154) "Development of ultra-thin fibroin membrane for RPE cell transplantation" (poster with D.G. Harkin, K.A. George, A.M.A. Shadforth, S. Cheng and A. S. Kwan), The Association for Research in Vision and Ophthalmology (ARVO), Annual Meeting, Fort Lauderdale, USA, May 2010; **abstract 5248/A67.**

(155) "Fibroin-based materials support cultivation of limbal stromal cells" (poster with L. J. Sinfield, K. George, Zainuddin, D. Hutmacher, I.R. Schwab and D.G. Harkin), The Association for Research in Vision and Ophthalmology (ARVO), Annual Meeting, Fort Lauderdale, USA, May 2010; **abstract 6211/D776.**

(156) "Development of an ultra-thin fibroin membrane for RPE cell transplantation" (poster with A. Shadforth, K.A. George, S. Cheng, A.S. Kwan and D.G. Harkin), Tissue Engineering & Regenerative Medicine International Society (TERMIS) 2010 Asia-Pacific Meeting, Sydney, Australia, 15-17 Sep. 2010; **abstract 372.**

(157) "Fibroin-based materials support co-cultivation of limbal epithelial and stromal cells" (poster with L. Sinfield, K.A. George, Zainuddin, D.W. Hutmacher and D.G. Harkin), Tissue Engineering & Regenerative Medicine International Society (TERMIS) 2010 Asia-Pacific Meeting, Sydney, Australia, 15-17 Sep. 2010; **abstract 376.**

(158) "Tissue engineered fibroin scaffolds for ocular tissue reconstruction" (with L. J. Sinfield, K. A. George, S. L. Ainscough, D. W. Hutmacher and D. G. Harkin), Institute of Health & Biomedical Innovation (IHBI) Inspires Postgraduate Conference, Brisbane, Australia, Nov. 2010.

(159) "PLLA-based networks for biomedical applications" (with K.A. George, F. Schue and E. Wentrup-Byrne), 2010 International Chemical Congress of Pacific Basin Societies (PACIFICHEM 2010), Honolulu, Hawaii, USA, 15-20 December 2010; **abstract MACR 261.**

(160) "Controlled porosity of fibroin thin films synthesized from ternary fibroin-PEO-water solutions for corneal regeneration" (with K.A. George, L. Sinfield and D.G. Harkin), 2010 International Chemical Congress of Pacific Basin Societies (PACIFICHEM 2010), Honolulu, Hawaii, USA, 15-20 December 2010; **abstract HEAL 255.**

(161) "Novel hydrogelators for the creation of supramolecular self-healing hydrogels as artificial vitreous substitutes: Second generation" (with I. Blakey, B. Dargaville, F. Rasoul, A. Whittaker and H.H. Lee), The 32th Australasian Polymer Symposium, Coffs Harbour, Australia, 13-16 February 2011; **abstract W 1.12.**

(162) "HEMA-based copolymer hydrogels enhance the growth of HLE cells" (poster with Zainuddin, Z. Barnard and A.K. Whittaker), The 32th Australasian Polymer Symposium, Coffs Harbour, Australia, 13-16 February 2011; **abstract P 42.**

(163) "Investigating the hydrogen bonding back-fold behaviour of poly(propylene glycol) and poly(ethylene glycol) to 2-ureido-4[1H]-pyrimidinone (UPy)" (poster with I. Blakey, B. Dargaville, T.F.A. De Greef, E.W. Meijer, M.M.L. Nieuwenhuizen, F. Rasoul, A. Whittaker and H.H. Lee), The 32th Australasian Polymer Symposium, Coffs Harbour, Australia, 13-16 February 2011; **abstract P 64.**

(164) "Surface modification and topology profiling of PHEMA for biomaterial applications" (with Z. Merican, D.W. Green and I. Blakey), The 32th Australasian Polymer Symposium, Coffs Harbour, Australia, 13-16 February 2011; **abstract W 3.3.**

(165) "Synthesis and enzymatic degradation of PHEMA and P[HEMA-co-PEGMA] hydrogel sponges and gels" (with S.M. Paterson, D.H. Brown and M.V. Baker), Second International Conference on Multifunctional, Hybrid and Nanomaterials (Hybrid Materials 2011), Strasbourg, France, 6-10 March 2011.

(166) "Tissue engineered fibroin scaffolds for ocular tissue reconstruction" (with L. J. Bray, K. A. George, S. L. Ainscough, D. W. Hutmacher and D. G. Harkin), Australian Society for Medical Research (ASMR) Postgraduate Conference, Brisbane, Australia, May 2011.

(167) "Use of silk fibroin as a substratum for human corneal endothelium transplantation" (with P.W. Madden, K.A. George, J.N.X. Lai, G. Rodriguez and D.G. Harkin), Tissue Engineering & Regenerative Medicine International Society (TERMIS) European Chapter 2011 Annual Meeting, Granada, Spain, 7-10 June 2011.

(168) "Fibroin-based materials support co-cultivation of limbal epithelial and stromal cells" (with L.J. Bray, K.A. George, D.W. Hutmacher and D.G. Harkin), Tissue Engineering & Regenerative Medicine International Society (TERMIS) European Chapter 2011 Annual Meeting, Granada, Spain, 7-10 June 2011.

(169) "Tissue-engineered fibroin scaffolds for ocular tissue reconstruction" (poster with L. J. Bray, K. A. George, D. W.Hutmacher and D. G. Harkin), Institute of Health & Biomedical Innovation (IHBI) Inspires Postgraduate Conference, Brisbane, Australia, Nov. 2011.

(170) "Laser scanning confocal microscopy vs scanning electron microscopy for characterization of polymer morphology: Sample preparation drastically distorts morphologies of poly(2-hydroxyethyl methacrylate)-based hydrogels" (with S.M. Paterson, Y.S. Casadio, D.H. Brown and M.V. Baker), The 10th Asia-Pacific Microscopy Conference (APMC 10); The 2012 International Conference on Nanoscience & Nanotechnology (ICONN 2012); and The 22nd Australian Conference on Microscopy & Microanalysis (ACMM 22), Perth, Australia, 5-9 Feb. 2012.

(171) "Silk fibroin as substratum for corneal and retinal cells", The 16th NSW Stem Cell Network Workshop: Stem Cell Treatment for Eye Diseases, Sydney, Australia, 16 April 2012. ***Invited keynote speaker.***

(172) "Tissue-engineered fibroin scaffolds for ocular tissue reconstruction" (poster with L. J. Bray, K. A. George, D. W. Hutmacher and D. G. Harkin), The 16th NSW Stem Cell Network Workshop: Stem Cell Treatment for Eye Diseases, Sydney, Australia, 16 April 2012. ***Award winning poster.***

(173) "Catalytic routes to biodegradable porous polymer materials for tissue engineering" (with M.V. Baker, D.H. Brown, S. Paterson and J.A. Shaw), The 2nd International Conference on Molecular and Functional Catalysis (ICMFC-2), Biopolis, Singapore, 30 July-1 August 2012.

(174) "Silk fibroin as substratum in ocular tissue engineering" (poster), The 3rd TERMIS World Congress, Vienna, Austria, 5-8 Sep. 2012; **abstract 21.P19.**

(175) "Tissue-engineered fibroin scaffolds for ocular tissue reconstruction" (poster with L.J. Bray, K.A. George, D.W. Hutmacher and D.G. Harkin), The 3rd TERMIS World Congress, Vienna, Austria, 5-8 Sep. 2012; **abstract 28.P15.**

(176) "An in vitro 3-D cell culture model for studying pathomechanisms of AMD" (poster with A.M.A. Shadforth, D.G. Harkin, A. Weiss, D.W. Hutmacher and B.K. Feigl), The Association for Research in Vision and Ophthalmology (ARVO), Annual Meeting, Seattle, USA, 4-9 May 2013; **abstract 314/D0350.**

(177) "Ophthalmic regenerative medicine: the use of silk proteins as template for growing corneal and retinal cells", University of Twente, Enschede, The Netherlands, 28 August 2014. ***Invited lecture.***

(178) "Ophthalmic regenerative medicine: the use of silk proteins as template for growing corneal and retinal cells", The 6th International Conference on Biomaterials, Tissue Engineering & Medical Devices, Constanta, Romania, 17-20 September 2014. ***Invited keynote speaker.***

(179) "Ultrathin silk fibroin membranes as prosthetic Bruch's membrane", (poster with A.M.A. Shadforth, S. Suzuki, C. Theodoropoulos, N.A. Richardson and D.G. Harkin), Asia ARVO Meeting, Yokohama, Japan,16-19 February 2015; **abstract 348-P58-18.**

(180) "Ophthalmic regenerative medicine: the use of silk proteins as a template for corneal cells", Molecular Basis of Disease seminar series, Menzies Health Institute Queensland, School of Medical Science, Griffith University, Gold Coast, 2 April 2015. ***Invited seminar presentation.***

(181) "Modifications of silk fibroin membranes to enhance human corneal limbal epithelial cell growth for ocular surface regeneration" (with S. Suzuki, R.A. Dawson, A.M. Shadforth, L.J. Bray, and D.G. Harkin), The 24th Annual Conference of the Australasian Society for Biomaterials and Tissue Engineering (ASBTE), 7-10 April 2015, Sydney, Australia.

Teze de doctorat conduse

Supervised PHD Theses

Professor TRAIAN V. CHIRILĂ, PhD
Chief Scientist at Queensland Eye Institute

List of Supervised PhD Theses

1. **Yi-Chi Chen (1994)**
   Synthesis and evaluation of porous hydrogels for biomedical purposes.

2. **Ye Hong (1997)**
   Hydrogels with high water content for use in vitreoretinal surgery.

3. **Paul D. Dalton (1998)**
   Semi-crystalline PVA hydrogels prepared from DMSO/H2O solutions as potential vitreous substitutes.

4. **Sarojini Vijayasekaran (1999)**
   Development of an artificial cornea: A histopathological study.

5. **Karina George (2007)**
   Synthesis, characterization and in vitro evaluation of PLLA-co-succinic anhydride networks.

6. **Ylenia Casadio (2009)**
   Biodegradable PHEMA-based biomaterials.

7. **Stefan Paterson (2012)**
   The synthesis of PHEMA-based materials for tissue engineering.

8. **Hui Hui Lee (2012)**
   Novel hydrogelators for the creation of supramolecular self-healing hydrogels as artificial vitreous substitutes.

9. **Laura Bray (2012)**
   Evaluation of fibroin-based scaffolds for ocular tissue reconstruction.

10. **Miriem Santander Borrego (2014)**
    Investigations of the influence of the topography and surface chemistry of poly(2-hydroxyethyl methacrylate) based hydrogels on surface properties and cell adhesion.

11. **Chien-Yu Sharon Lin (2015)**
    Production and in vitro evaluation of macroporous alginate hydrogel fibres for nerve tissue engineering.

12. **Peter Gillies (current)**
    Microvascular endothelial cells of the human corneal limbus: Isolation, characterization and control within a limbal tissue substitute.

13. **Audra Shadforth (current)**
Development of a cultured tissue substitute to repair the ageing retina.

14. **Natalie McKirdy (current)**
Can a silk extract be neuroprotective in the retina? An investigation of Bombyx mori silk sericin and non-peptide components.

Disertație

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Universitatea Politehnica Timişoara

SILK PROTEINS IN OPHTHALMIC REGENERATIVE MEDICINE: RECONSTRUCTION OF THE OCULAR SURFACE

Universitatea Politehnica Timișoara

Traian V. CHIRILĂ

Abstract

This dissertation presents an account of the research work carried out by the author and his colleagues on the topic of the reconstruction of ocular surface by using proteins isolated from silk as templates for growing cells, including progenitor/stem cells, to generate new tissue. It is demonstrated here that silk fibroin and sericin can function as suitable substrata for the corneal epithelial cells of the human eye, and therefore these materials will play an important role in the prevention of blindness caused by ocular surface disorders.

Introduction

There are many definitions of the concept of 'biomaterial', all conveying essentially the same meaning [Williams, 1999; Williams, 2014; Ratner ***et al.***, 2004]. Basically, a biomaterial is any material, either natural or artificial, intended to interface with certain biological systems in the human body in order to direct the course of a therapeutic strategy. In other words, we call biomaterials those materials that are implanted into our body with the aim of evaluating or treating damage or disease, and of augmenting or replacing tissues, organs or functions.

Although our eye **(Figure 1)** is an organ of great complexity, it is more accessible to medical observation and surgical manipulation than most of the other organs. This probably explains why the eye was the organ in which the first transplantation of donor tissue was successfully performed in humans [Zirm, 1906].

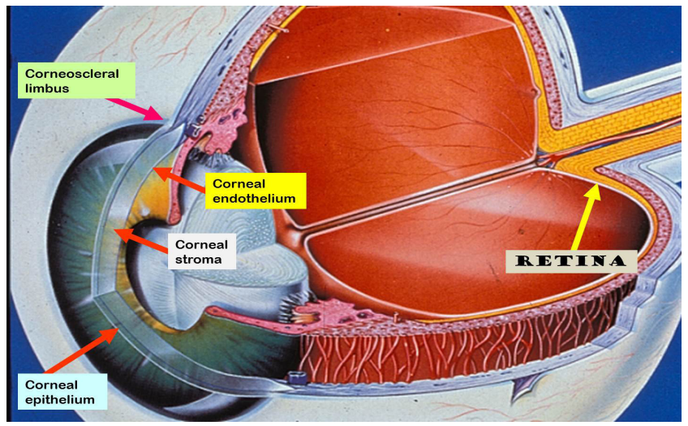

Fig. 1: A picture of the human eye structure, emphasizing the details of the anterior segment.

However, prior to this episode, the eye was also the organ where foreign materials were implanted for the first time with the purpose of fulfilling, in today's terms, a role as biomaterials. In this respect, we should mention the proposition and (probable) use of glass as an artificial cornea by G. Pellier de Quengsy in 1789 [Amalric, 1996/1997; Remky, 1996/1997; Chirila ***et al.***, 1998; Chirila and Hicks, 1999]; the use by Onofrio Abbate in 1862 [Forster, 1923] of gutta-percha and casein for the same purpose; Lang's artificial globes made of celluloid [Lang, 1887]; or the artificial corneas developed also from celluloid [Dimmer, 1891]. The modern era of ophthalmic biomaterials has been triggered by the use of fully synthetic polymers, at the time when poly(vinyl alcohol) gels were inserted as socket implants [Thiel, 1939], to be followed by the first artificial corneas made of poly(methyl methacrylate) (PMMA) [Wünsche, 1947; Franceschetti, 1949; Kuwahara, 1950; Györffy, 1951], a landmark not exempted from some controversy regarding priority [Chirila and Crawford, 1996], and culminating with the much better known and undisputed development of Ridley's PMMA intraocular lens (IOL) [Ridley, 1951; Ridley, 1952]. A few years later, poly(1-vinyl-2-pyrrolidinone) became the first synthetic polymer to be implanted in the vitreous cavity as a vitreous substitute [Scuderi, 1954]. In parallel developments, the synthetic polymers also aroused the interest of the contact lens manufacturers, and currently they dominate this market.

The field of ophthalmic biomaterials has now become firmly established as an integral and essential part of the ocular tissue engineering and regenerative ophthalmology. Implantable replacements made of biomaterials include artificial intraocular lenses, artificial corneas (keratoprostheses) and corneal reconstructs, refractive intracorneal inserts, vitreous substitutes, tubular devices and canaliculi for glaucoma and lacrimal surgery, carriers for sustained release of ocular drugs, surgical adhesives, viscoelastics for ocular surgery etc. Currently, going beyond prosthetic replacements and devices, novel types of ophthalmic biomaterials are being developed by manipulating chemically or biochemically both the bulk structure and the surface of materials, leading to complex systems able to play a role in the stimulation of target cells with an aim to heal and regenerate damaged tissues in the eye. Such biomaterials serve for the creation of tissue-engineered constructs to be used in new regenerative strategies that are promoted and advanced in ophthalmology. The essential task of tissue engineering is to develop substitutes for restoring, maintaining, or improving tissue function [Skalak *et al.*, 1988]. It is a multidisciplinary field that should be regarded as the next step in the development of biomaterials. Going further, tissue engineering should be regarded as a part of regenerative medicine [Atala, 2007], for which there is too a range of available definitions [Daar and Greenwood, 2007]. An abbreviated definition [Mason and Dunnill, 2008] would be that the regenerative medicine "replaces or regenerates human cells, tissue or organs, to restore or establish normal function". This discipline is more sophisticated and complex than tissue engineering, as it makes use of a combination of advanced biological and technological approaches to achieve a proper self-healing process.

Over the past decade, I and my colleagues at Queensland Eye Institute in Brisbane, Australia, have been developing biomaterial substrata and templates for the attachment, growth and proliferation of a variety of eye cells, aiming at therapeutic strategies to treat or prevent blinding conditions through strategies specific to both tissue engineering and regenerative medicine. These substrata/templates are fabricated from silk proteins, which we isolate and purify from the cocoons produced by the larvae ("silkworms") of domesticated or wild silk moths.

Brief introduction to the science of silks

Silks belong to the group of fibrous proteins, alternatively known as 'fibrilar' or 'structural' proteins, where also collagens, elastin, keratins and myosins belong. In nature, the silks are produced only by species of the phylum ***Arthropoda***, more specifically by organisms in classes ***Arachnida*** and ***Insecta***, and subphylum ***Myriapoda***. Silks are polypeptidic composites that contain in their primary structure highly repetitive sequences of amino acids. A silk is stored in the organism as a liquid, which is converted into fibres when sheared (spun) upon its extrusion from the organism in order to generate a certain external structural pattern (web, cocoon, etc.). Such patterns have to fulfil specific evolutionary tasks, including protection, reproduction, physical support, or foraging.

The most investigated silk is that produced by the domesticated silkworm, the larva of *Bombyx mori* silk moth **(Figure 2)**. The cocoons, generated by silkworms as part of the reproductive cycle of this species, are made of silk threads. The hierarchical organization of a silk thread commences with the macromolecules of a protein called FIBROIN, and progresses to nanofibrils, then to microfibrils, further to brins, and ultimately to the silk threads where the fibroin monofilaments are glued together in pairs and coated by another protein called SERICIN. As macromolecular compounds, the silk proteins are naturally designed block copolymers. As proteins, fibroin and sericin are more specifically defined through their primary structures. B. mori fibroin (henceforth, BMSF) consists of a heavy-chain fibroin with a molecular weight (MW) of about 360 kDa, linked covalently through disulphide bonds to a light-chain fibroin (MW~25 kDa), to which a glycoprotein (known as protein P25, or 'fibrohexamerin') is associated non-covalently. The predominant amino acids in BMSF include glycine, serine and alanine. In insect BMSF, disulphide bond connects 6 molecules of heavy fibroin to 6 molecules of light fibroin, and a single molecule of P25 is attached physically to this unit [Inoue et al., 2000; Sehnal and Žurovec, 2004]. The secondary structure of insect fibroin involves a mixture of conformations including α-helix, antiparallel β-sheets, random coil and other [Craig, 1997]. The distribution of such conformations dictates the evolutionary value of the silk for the organism that generated it.

Fig.2: Photographs of the Bombyx mori silk moth and the cocoons produced by its larvae. The cocoons for research were supplied by Tajima Shoji Co. Ltd., Yokohama, Japan.

The predominant amino acids in *B. mori* sericin (henceforth, BMSS) include glycine, serine and aspartate. Unlike BMSF, however, the number and molar mass of the polypeptidic units in BMSS are disputed. According to some investigators, there can be as many as 15 or even more polypeptides in BMSS [Sprague, 1975]. It was also suggested [Rutherford and Harris, 1940] that this large number of fractions is caused by the hydrolytic degradation during processing, and that BMSS may be actually a homogeneous material. The genomic analysis showed the presence of 6 genes that encode for sericin [Gamo, 1982; Michaille *et al.*, 1989; Julien *et al.*, 2005], and therefore at least 6 major polypeptides are expected in BMSS. A review [Chirila *et al.,* 2013] has disclosed a range between 20 and 400 kDa for the values reported in literature for the MWs of the polypeptidic units in BMSS.

The silk proteins may also possess a tertiary structure that is the result of a combination of extensive hydrogen bonding, high crystallinity and hydrophobic interactions.

Silk proteins as biomaterials

The medical use of *B. mori* silk threads dates back to the beginning of Common Era, when Galen of Pergamon proposed them as surgical sutures [Muffly *et al.*, 2011]. In ophthalmic surgery, silk sutures came much later, after Williams used them for the first time in cataract operations [Williams, 1866], and Kuhnt in corneoscleral surgery [Kuhnt, 1883]. However, the medical applications of *B. mori* silk have not stopped with the sutures. Over the past decades, with the advancements in understanding the structure of silk proteins and with the progress in the methodology to isolate silk's polypeptidic components, new applications emerged for the two main constitutive proteins, fibroin and sericin [Minoura *et al.,* 1990; 1995a; 1995b]. Due to an array of desirable properties (i. e., they can be processed into various forms; do not elicit toxic or traumatic effects to living tissues; elicit low immune response; are permeable for oxygen, fluids and biomolecules; degrade protractedly in physiologic media and the resulting products do not accumulate in the body; and fibroin, in particular, also displays suitable mechanical strength), the silk proteins have been extensively investigated as biomaterials for tissue engineering, regenerative medicine and sustained drug delivery [Altman *et al.*, 2003; Vepari and Kaplan, 2007; Hakimi *et al.*, 2007; Murphy and Kaplan, 2009; Wenk *et al.*, 2011; Harkin *et al.*, 2011; Kasoju and Bora, 2012; Harkin and Chirila, 2012; Kundu *et al.*, 2013; Chirila *et al.*, 2013; Pereira *et al.*, 2014].

The feasibility of utilizing silk proteins as biomaterials for reconstructing tissue of clinical significance in the human eye was first reported by our group, when we demonstrated that primary human corneal limbal epithelial cells could attach and proliferate on membranes of BMSF at levels comparable to those observed on tissue culture plastic (TCP) substrata, both in serum-supplemented and serum-free media [Chirila *et al.*, 2007; 2008]. Subsequent work has established BMSF as a functional substratum of significant potential in ocular tissue engineering [Chirila *et al.*, 2010; Kwan *et al.*, 2010; Harkin *et al.,* 2011; Harkin and Chirila, 2012]. Our investigations extended also to BMSS [Chirila *et al.*, 2013], to the fibroin produced by a wild species of silk moth, ***Antheraea pernyi*** [Bray *et al.*, 2013a; Hogerheyde *et al.*, 2014], and to modified BMSF [Suzuki *et al.*, 2015]. We have reported extensively on the evaluation of silk proteins as substrata for corneal cells (epithelial, limbal epithelial, limbal mesenchymal stromal, endothelial) [Chirila *et al.*, 2007; 2008; 2010; 2013; 2015; Bray *et al.*, 2011; 2012; 2013a; 2013b; Hogerheyde *et al.*, 2014; Madden *et al.*, 2011], and retinal pigment epithelial cells [Kwan *et al.,* 2010; Shadforth *et al.*, 2012]. We have investigated the effect of various sterilization procedures on the quality of BMSF membranes [George *et al.*, 2013].

We have established methods (see an example in **Figure 3) t**o make various types of templates like those depicted in **Figure 4**. Membrane thicknesses as low as 2-3 μm can be achieved in our laboratory.

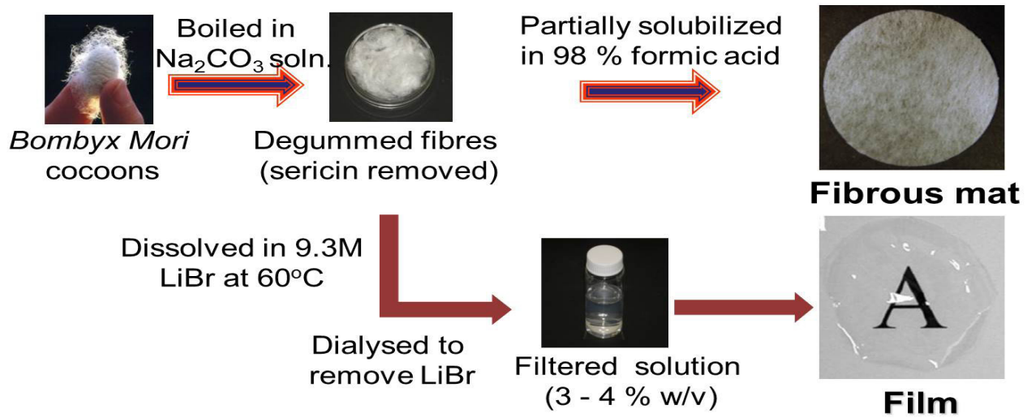

Fig. 3: An example of a protocol for the preparation of films and fibrous membranes from B. mori silk fibroin (BMSF).

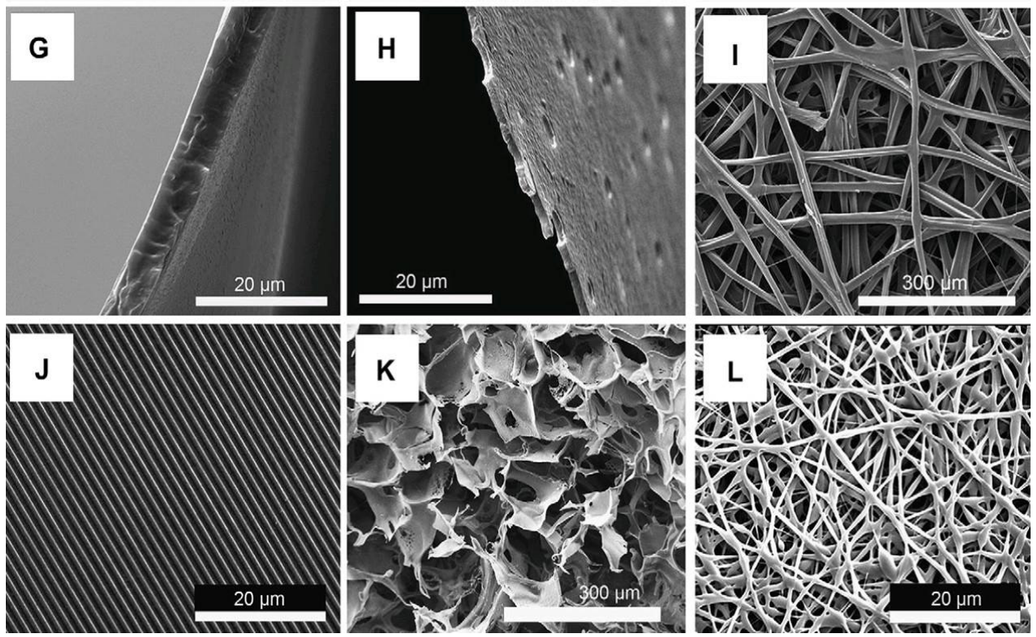

Fig. 4: Templates made from BMSF. G: thin film; H: ultrathin porous film; I: fibrous mat; J: patterned film; K: porous sponge (by freeze-drying); L: fibrous meshwork (by electrospinning). [Adapted from Harkin *et al.*, 2011].

This dissertation presents an account of our research involving silk proteins. The work described here was aimed at the repair or regeneration of damaged or diseased ocular surface.

The ocular surface and its disorders

The ocular surface (henceforth, OS) can be defined a complex entity that conceptually results from the functional integration of its anatomical components (conjunctival epithelium, corneoscleral limbal epithelium, corneal epithelium, glandular epithelia, tear film) with the adjacent structures (eyelid, eyelashes, lacrimal glands, meibomian glands, nasolacrimal duct). Strictly speaking, the cornea as a whole is not a part of this entity: only its associated epithelia belong formally to OS **(Figure 5).**

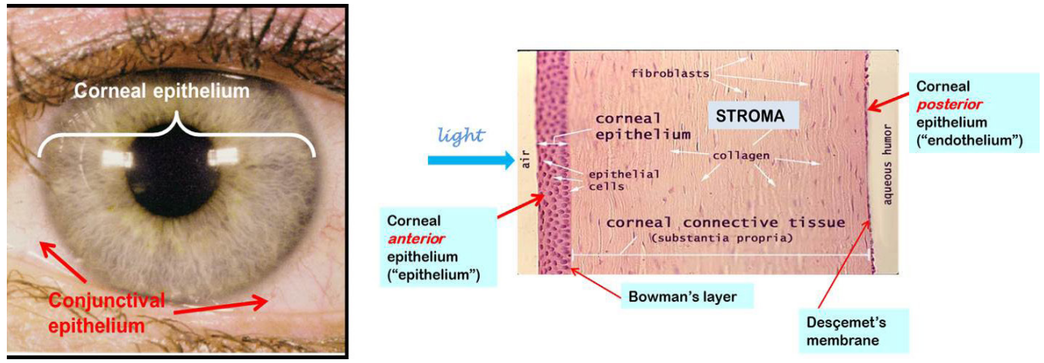

Fig. 5: The main epithelia defining the ocular surface (left), and a section through the whole cornea (right). Only the corneal epithelium is common to both regions.

The quality of our vision is determined to a significant degree by the quality of our OS. Clear vision requires a healthy, wet, smooth and continuous OS. The roles of OS include: (a) maintenance of corneal transparency; (b) protection against external injury and infection; (c) contribution to the visual optics; (d) comfort. While OS is specialized to cope with these tasks, there are many acute, chronic or cicatrizing pathological conditions that can lead to massive tissue destruction or can trigger aggressive inflammatory response from the OS. The result is irreversible scarring of the conjunctiva and opacification of the cornea, which translates into blindness. The spectrum of what is commonly covered by the term 'ocular surface disorders' (or 'diseases') is extensive, ranging from minor dry eye syndrome to potentially blinding conditions such as chemical burns or consequences of multiple surgeries. In an effort to classify the ocular surface disorders [Kruse, 2002], ten categories have been proposed, comprising of more than 60 different pathological conditions, in addition to chemical, thermal, irradiation and mechanical injuries.

Of particular severity is a condition known as 'limbal stem cell deficiency' (henceforth, LSCD), which can be either a component or a consequence of most of the pathologies or injuries. Corneal epithelial progenitor/stem cells reside in the corneoscleral limbal region of the eye [Davanger and Evensen, 1971; Schermer *et al.*, 1986], as indicated in **Figure 6.** The more limbal epithelium is damaged, the more capacity of OS to heal is reduced, which therefore suggests that depletion of progenitor/stem cells in the eye can be associated with conditions leading to partial or total loss of vision. When the damage to OS is less severe, LSCD is partial.

Advanced LSCD is associated with congenital, immunological or infectious diseases, or can be caused by chemical or thermal burns, by chronic use of topical drugs, by repeated surgeries and by contact lens wear, and – if not managed – leads to irreversible blindness.

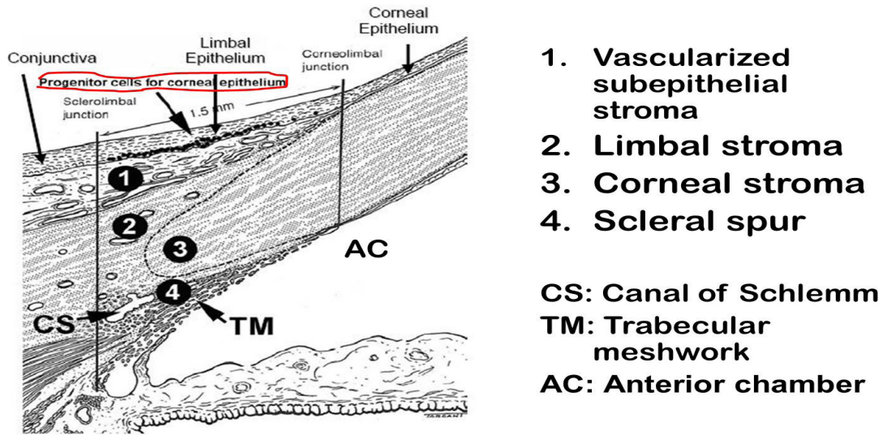

Fig. 6: Schematic drawing of the corneoscleral limbal region in the human eye, including the localization of progenitor/stem cells. *[Modified from Hogan et al., 1971].*

The treatment of the OS disorders in general and of LSCD in particular is complicated and – by necessity – based mainly on surgical approaches. While minor or moderate LSCD can be managed by medication and observation, or by debridement of unwanted invading conjunctival tissue, the severe LSCD cases require both surgical replacement of abnormal tissue and restoration of the corneal epithelial progenitor/stem cells. Both stages are essential: removal of abnormal/diseased tissue and its subsequent replacement have almost no chance of clinical success if significant LSCD remains. The anatomical localization of corneal progenitor/stem cells and the advances in stem cell biology opened the era of 'cellular surgery' [Kinoshita and Nakamura, 2005] as a therapeutic strategy against severe OS disorders. In principle, epithelial cells from the OS, including cells from the limbal region, are harvested from the healthy contralateral eye of the patient, and then expanded by growing them onto a template (membrane, scaffold etc.) until a confluent a healthy cellular layer is achieved. The resulting cell/template autograft is then implanted at the site of damage in the OS of the diseased contralateral eye of the same patient. When the cells are harvested from a living relative of the patient or from cadaveric eyes (allografts), serious immunological and biosafety issues can be involved. An important issue in this strategy is the choice of a template suitable for the attachment of cells and their subsequent growth into a layer or into a 3-D pattern in order to generate a biocompatible implantable cell/template construct. Human amniotic membrane (henceforth, AM) has been so far the most successful substratum used in the reconstruction of OS, but other naturally-derived biomaterials and synthetic biomaterials (polymers) have been also proposed and investigated in vitro or in vivo (animals), and even trialled in human patients [for reviews see Chirila *et al.,* 2010; 2015].

As the clinical success has been variable, the quest for an ideal biomaterial template able to promote and support the growth of corneal epithelial cells is still very much alive. On this background, we have proposed and investigated extensively the silk proteins as a candidate. An overview of the results achieved in our experiments is presented in next section of this dissertation.

Isolation of fibroin and sericin

We established detailed protocols [Chirila *et al.*, 2008; 2013; Bray *et al.*, 2012; 2013a; 2013b] to isolate and purify the fibroins produced by the silkworms *B. mori* (BMSF) and ***A. pernyi*** (APSF), as well as the sericin produced by the former (BMSS). In principle, the silk fibroin solutions were prepared by the removal of sericin from the cocoons in hot aqueous solutions of sodium carbonate, dissolution of raw fibroin in concentrated solutions of lithium bromide or in neat calcium nitrate tetrahydrate, and dialysis against pure water. The raw, or so-called 'degummed fibroin' fibres, have also been evaluated as scaffolds for corneal cells [Bray *et al.,* 2012; 2013b]. Sericin (BMSS) was isolated from cocoons by autoclaving, filtration and dialysis. The membranes or scaffolds (porous, fibrous) from BMSF, APSF and BMSS were then prepared by the evaporation of water from the respective solutions at room temperature, followed by stabilization through water annealing in a vacuum enclosure at room temperature, or through treatment with polar solvents such as alcohols.

Growth of corneal epithelial cells on BMSF templates

In our first experiments involving BMSF as a substratum, primary human corneal limbal epithelial cells (henceforth, HCLECs) were cultivated in serum-supplemented media in the presence of feeder cells (γ-irradiated murine 3T3 cells) [Chirila *et al.,* 2007]. The results **(Figure 7)** strongly suggested that BMSF could perform satisfactorily as a substratum.

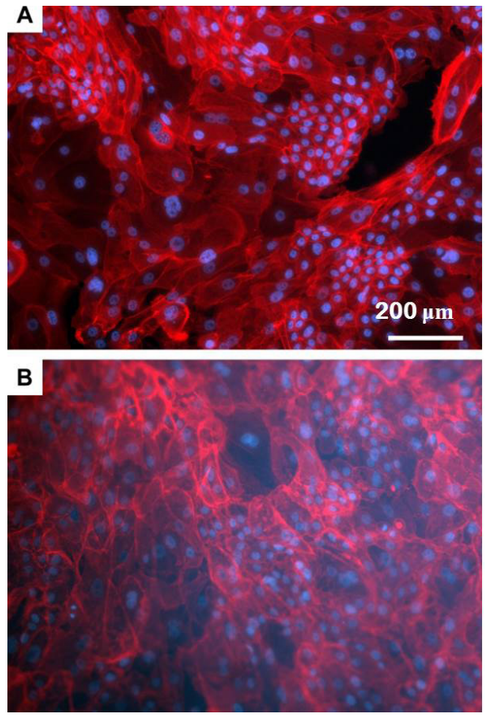

Fig. 7: Primary human corneal limbal epithelial cell culture grown in the Green's medium on BMSF compared to that grown on tissue culture plastic (TCP). The culture medium includes foetal bovine serum (FBS). A: The culture on TPC displaying DAPI-stained nuclei (blue) and phalloidin-stained cytoskeletal actin (red); B: Culture of the same cell type on BMSF stained identically to that on TCP. The hazy background is caused by the inherent faint fluorescence of the BMSF under UV light. The scale bar is valid for both panels and represents 200 µm. *[Adapted from Chirila et al., 2007].*

These results were confirmed in a subsequent experimental study [Chirila *et al.,* 2008], when the same cells were cultivated in a serum-free medium. The performance of BMSF as a suitable substratum for corneal epithelial cells was further investigated using a commercially available line (HCE-T) of SV40-immortalized corneal epithelium cells, which does not include populations of stem cells. In this study [Harkin *et al.,* 2011], a comparison between BMSF and AM, the latter being the "gold standard" in surgical reconstruction of OS, has been reported for the first time with respect to their ability of supporting cell growth. The BMSF membranes performed similarly to the AMs, including the deposition patterns of glycoproteins associated with the formation of basement membrane. The influence of serum proteins as components of the culture medium was also investigated, and we concluded that the presence of serum favoured cell growth. **Figure 8** summarizes these results.

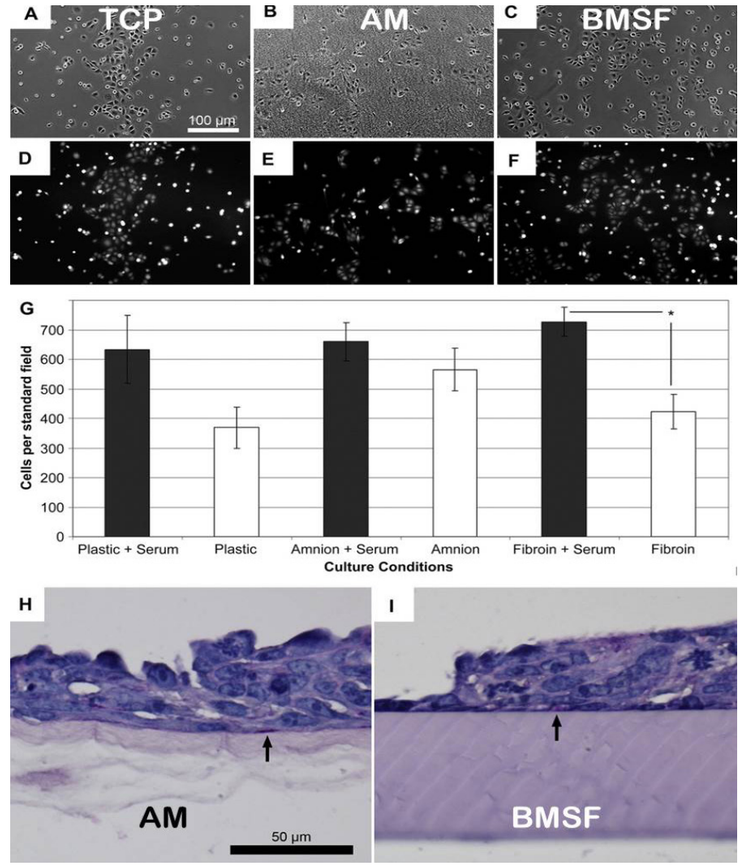

Fig. 8: Comparison of the growth of human corneal epithelial cell line HCE-T on either TCP (A & D), human donor amniotic membrane (B & E), or BMSF membrane (C & F). Cells were cultivated in the presence of 10% FBS for 4 hours staining with fluorescein diacetate. A, B, C: Phase contrast micrographs; D, E, F: Corresponding fluorescence images captured using a fluorescein filter. G: Quantitative comparison of cell attachment to TCP, amniotic membrane and BMSF, when seeded with or without FBS. The bars represent mean values ± s.e.m. for the total number of viable cells. The asterisk indicates statistically significant difference. H: Histological section of a confluent culture after 2 weeks of growth on amniotic membrane at the air-liquid interface. Staining with Schiff's reagent following oxidation with periodic acid (PAS method) indicates evidence of glycoprotein deposition (arrow). I: Histological section of a culture on BMSF, processed identically.
[Adapted from Harkin et al., 2011].

Comparison between BMSF and AM was further investigated [Bray *et al.,* 2011] by growing HCLECs on these membranes. In addition, histologic cell culture sections were compared against histologic sections of the central and limbal regions of human corneal tissue **(Figure 9).** The cells were less densely distributed on both AM and BMSF when compared to the native tissues. Within the limited duration of the experiment, more layers of cells formed and more basement membrane glycoproteins were deposited on AM than on BMSF. However, the deposition on AM appeared disorganized.

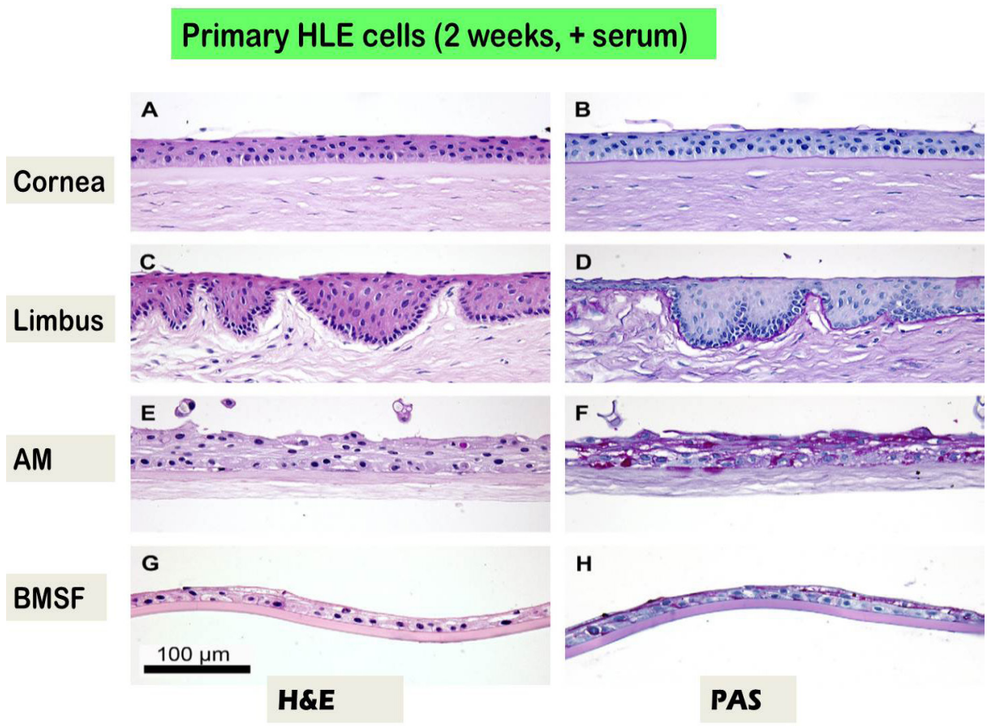

Fig. 9: Comparative histology: Human central cornea (A & B); human corneal limbal region (C & D); primary human corneal limbal epithelial cells grown on amniotic membrane (E & F); the same cells grown on BMSF membrane (G & H). The sections in A, C, E & G were stained with haematoxylin/eosin and those in B, D, F & H by PAS method. The cells were cultivated in serum-supplemented medium for 2 weeks prior to fixation in formaldehyde. *[Adapted from Bray et al., 2011].*

The results suggested that a regenerative process would likely take longer on BMSF than on AM, but in longer term the latter would perform at a similar level as the former. We have also investigated the issue of the cells' phenotype. Research carried out on the repair of OS over the last decade clearly suggested that the efficacy of the implantable HCLEC/template constructs is ultimately determined by the phenotype of the attached cells. ***If*** the cells do not display 'stemness' after having been expanded in culture, and ***if*** the epithelial phenotype is not maintained, then the implant will not be able to fulfil the very demanding task of participating efficaciously in a regenerative process, and there will be eventually little or no chance of clinical success. Our immunohistochemical analysis [Bray *et al.,* 2011] **(Figure 10)** demonstrated unequivocally the presence in cultures on each substratum of the progenitor cell marker ***ΔNp63***, which is a truncated isoform of the transcription factor ***p63*** and is specific to the immature cells of the progenitor cell population [Pellegrini *et al.,* 2001].

The cells also stained positively for the expression of the cytokeratins K3 and K12, a cytoskeletal marker of maturation of cells into epithelial cells. Our findings strongly suggested that the implantation of a HCLEC/BMSF construct would be effective as a strategy to reconstruct the ocular surface.

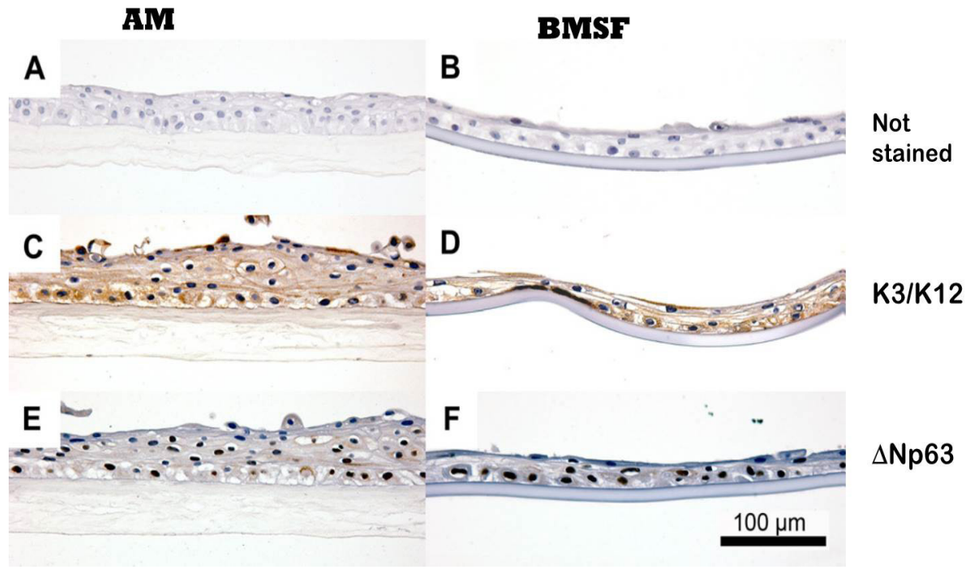

Fig. 10: Immunophenotyping for the constructs of the primary human corneal limbal epithelial cells grown on amniotic membrane (A, C & E) and on BMSF membrane (B, D & F). The negative controls (A & B) were obtained by omitting the step of primary antibody incubation. C & D: Positive immunostaining for cytokeratins K3 and K12; E & F: Positive immunostaining for the transcription factor ΔNp63. *[Adapted from Bray et al., 2011].*

Effect of porosity, permeability and surface topography

Aiming at creating 3-D templates from BMSF, we induced porosity by adding poly(ethylene glycol) (PEG) of high MW, in this case 900 kDa, to the processing solutions. As shown in **Figure 4(H),** well defined pores could be generated in the BMSF membranes. It was expected that the presence of pores would be beneficial for the cell growth due to increased diffusional transport of oxygen, nutrients and cellular waste products, and to improved intercellular communication. However, our preliminary experiments showed no increase in the number of attached cells and no improvement of their proliferation. On the contrary, the non-porous membranes performed better as substrata for HCLECs [Bray *et al.,* 2012]. Based on a study form another research group [Higa *et al.,* 2010], we have subsequently used a PEG with a much lower MW (0.3 kDa) [Suzuki *et al.,* 2015]. The pores could not be visualized microscopically, but both permeability of the BMSF membranes to relatively large biomolecules, and the roughness of its surface increased. However, no significant improvement of mechanical properties of the PEG-treated membranes could be noticed, and the attachment and growth of human corneal epithelial cell line HCE-T remained inferior to that on TCP **(Figure 11)**, which we also confirmed using HCLECs **(Figure 12).** So far, we can only conclude that by treating BMSF membranes with low-molecular-weight PEGs there are only minor gains in their performance as substrata for corneal epithelial cells. Neither the porous structure, which otherwise may contribute actually to the improvement of the intercellular communication, nor the surface roughness seems to promote specific interactions leading to the enhancement of cell attachment.

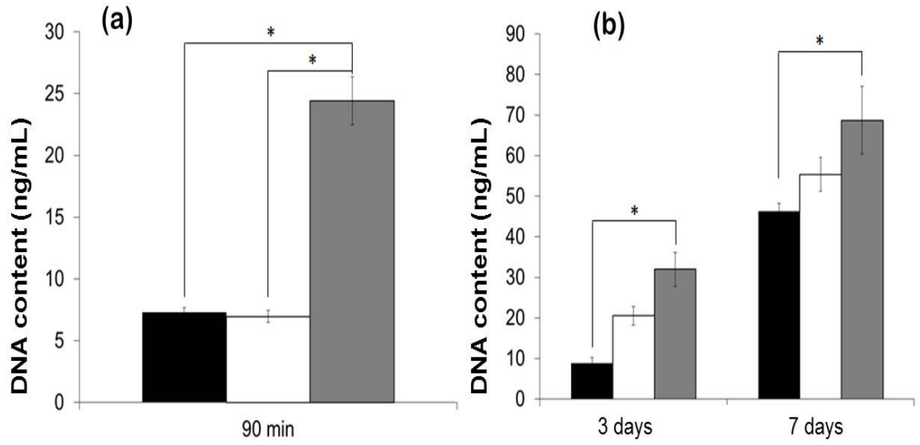

Fig. 11: Attachment and proliferation of HCE-T cell line on BMSF membranes. Details are provided in the insert. The bars represent mean values ± s.e.m. for the total DNA content, which is related directly to the number of cells. The asterisks indicate statistically significant differences. *[Adapted from Suzuki et al., 2015]*

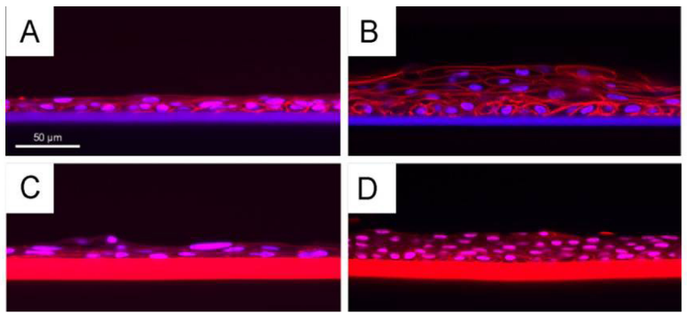

Fig. 12: Cultures of primary human corneal limbal epithelial cells grown on various BMSF substrata, as detailed in the insert. γ-Irradiated 3T3 murine fibroblasts were used as feeder cells. Intense auto-fluorescence of the crosslinked fibroin can be noticed in panels C and D. *[Adapted from Suzuki et al., 2015]*

Evaluation of BMSS as a template for cell growth

For decades, the second major polypeptidic unit in the B. mori silk thread – the sericin (BMSS) – has been regarded as responsible for the allergic reactions seen in people handling silk, and for the inflammatory tissue response induced by silk sutures. After a thorough examination of the existing literature, I concluded that the qualification of BMSS as a sensitizing agent was rather speculative and that, in many instances, the reports were either misinterpreted or misquoted. Furthermore, some recent results [Aramwit *et al.,* 2009; Hakimi *et al.,* 2010] seem to invalidate such qualification. Our own investigation on the ability of BMSS to function as a template for the attachment and proliferation of HCLECs led to surprising results [Chirila *et al.,* 2013]. Not only that we did not find evidence for any cytopathologic effect, but the ability of BMSS to enhance the attachment of HCLECs was superior to that displayed by either BMSF or BMSF-BMSS blends (with low content of BMSS), or even by TCP **(Figure 13)**.

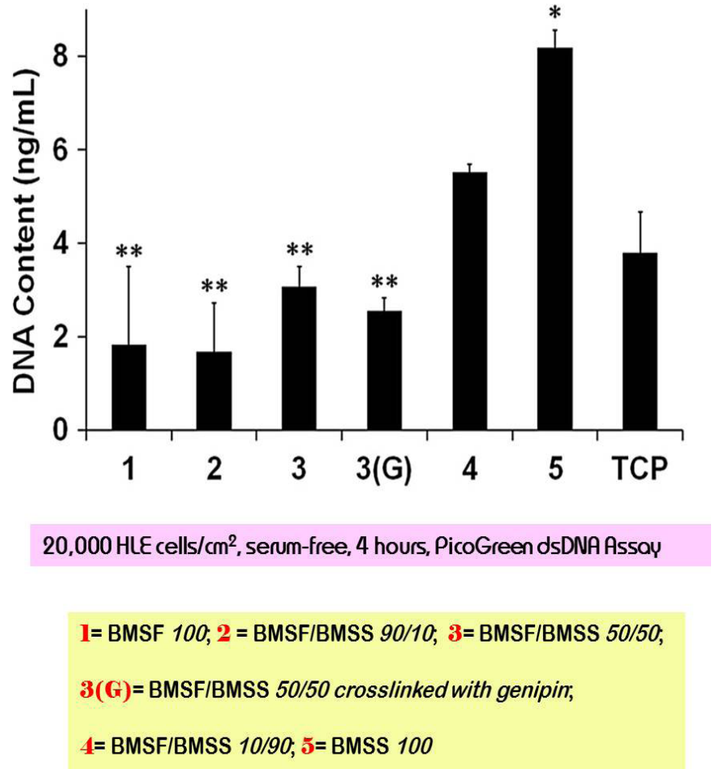

Fig. 13: Comparison of the attachment of primary human corneal limbal epithelial cells to membranes of fibroin (BMSF), sericin (BMSS), their blends, and tissue culture plastic (TCP). The numbers on the abscissa are explained in the insert. The bars represent mean values ± s.e.m. for the total DNA content, which is related directly to the number of cells. The differences between the samples marked with a single asterisk and each of those marked with double asterisk are statistically significant. Except for sample 3(G), all other samples were processed by water-annealing. *[Adapted from Chirila et al., 2013].*

Unfortunately, there is a drawback to using BMSS membranes: they proved to be mechanically weak **(Figure 14).** Even after chemical crosslinking, the membranes were inferior in strength to BMSF. Currently, we are investigating whether the enzyme-catalyzed self-crosslinking of sericin or inter-linking with fibroin could have an effect on mechanical strength [Chirila and Suzuki, unpublished results].

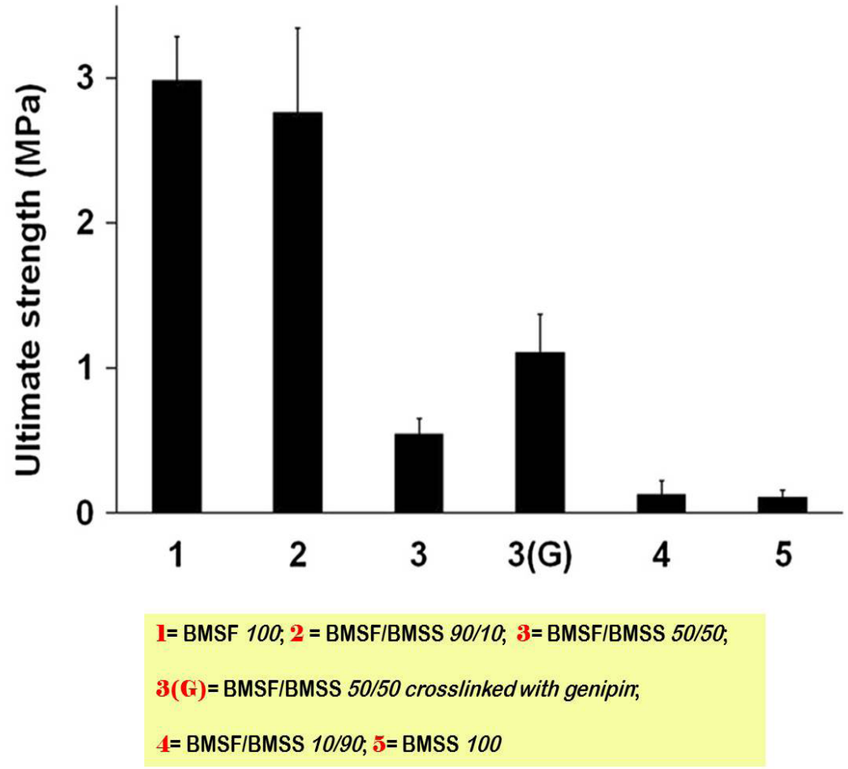

Fig. 14: Comparison of the mechanical strength of 10-µm membranes made of BMSF, BMSS and their blends. The numbers on the abscissa are explained in the insert. The bars represent mean values ± s.e.m. for the ultimate strength of samples measured in an Instron 5848 microtester, calculated from 6 measurements carried out for each specimen at the physiologic temperature (37°C). *[Adapted from Chirila et al., 2013].*

The problem of cell attachment to silk proteins

When we consider the essential role played in cell adhesion process by the integrin binding sites located on the cell surface, the mechanism of cell attachment to silk fibroins appears debatable, and therefore worth to investigate. It is known that the integrin receptors interact specifically with certain peptide domains (ligands) present in the extracellular matrix components, and that these integrin-binding domains are ultimately responsible for the adhesion and survival of anchorage-dependent cells. A typical ligand peptide motif is the arginine-glycine-aspartic acid (Arg-Gly-Asp or RGD) sequence found in fibronectin. When such motifs are present on a substratum, and are also sterically accessible, they can promote the attachment of cells, followed by spreading, proliferation and differentiation. However, neither BMSF nor BMSS contain RGD or any other peptide motif that would act as a ligand to integrins [Lotz and Collona-Cesari, 1979; Minoura *et al.,* 1995a; Zhou *et al.*, 2000].

On the other hand, the fibroins isolated from the silk produced by the larvae of wild silk moths in the family ***Saturniidae***, genus ***Antheraea***, such as ***A. pernyi, A. mylitta*** and ***A. yamama***i, which do not feed on mulberry leaves, contain RGD domains in their structure [Minoura *et al.*, 1995a; Yukuhiro *et al.*, 1997; Sezutsu and Yukuhiro, 2000], and thus are perceived to be more suitable as substrata for cells. The absence in BMSF of adhesion peptide domains makes it rather difficult to explain its cell-adhesive properties, which have been indeed proved to be suitable for growing a large variety of cells. It was suggested [Minoura *et al.,* 1995a] that the large proportion of arginine present in BMSF may contribute to this process, or that the cell adhesion is the result electrostatic interactions. More recently, two peptides have been isolated from BMSF, which were assumed to be unknown adhesion ligands [Yamada *et al.,* 2004]. There has been no confirmation so far of this assumption. We can only surmise that the cell-adhesive properties of BMSF may be a result of a favourable combination of non-specific interactions based on surface characteristics (charge, wettability and topography).

We attempted to increase the attachment of HCLECs to BMSF by blending it with APSF [Bray *et al.,* 2013a]. A comparison of the cell attachment, however, revealed no significant differences between the blended fibroins, including also the pure components **(Figure 15).**

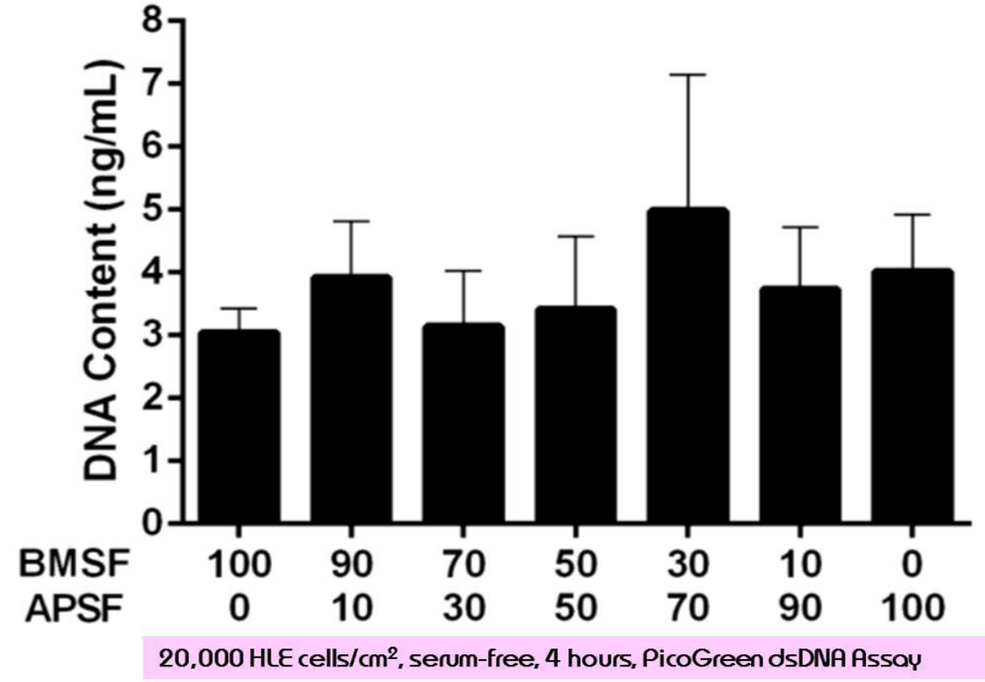

Fig. 15: Comparison of the attachment of primary human corneal limbal epithelial cells to membranes of ***B. mori*** silk fibroin (BMSF), A. pernyi silk fibroin (APSF), and their blends. Details are given in the insert. The bars represent mean values ± s.e.m. for the total DNA content, which is related directly to the number of cells. *[Adapted from Bray et al., 2013a].*

Another strategy that we attempted was the incorporation of the RGD ligand peptide motif by chemical functionalization of the BMSF surface (**Figure 16)**. Although a dose-dependent increase in the amount of attached cells was evident **(Figure 17)**, the differences were not statistically significant [Bray *et al.*, 2013a]. Our findings suggest that the adhesion through RGD ligands may have a complex mechanism, and unless the factors contributing to this mechanism are elucidated, any strategic attempt appears of a limited value.

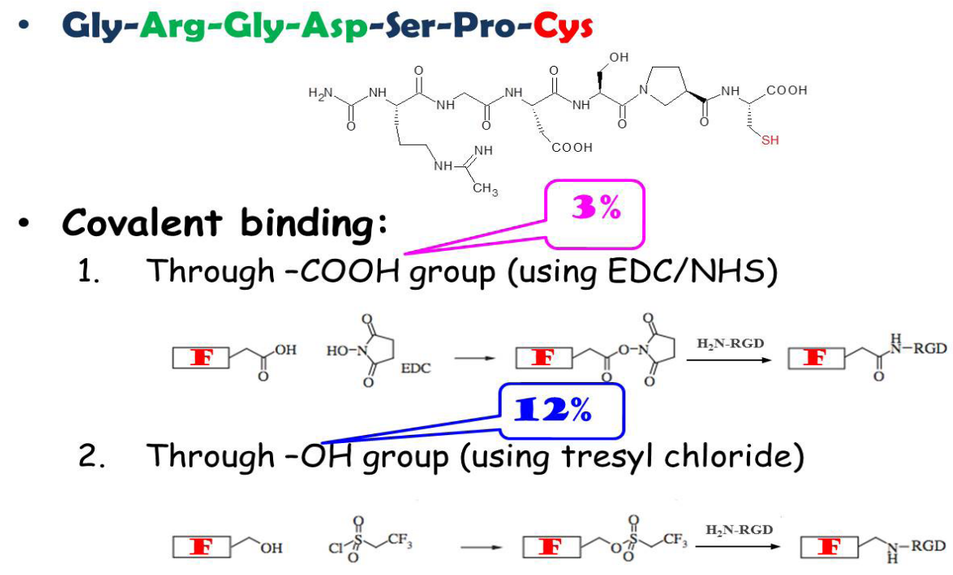

Fig. 16: Chemistry of the surface functionalization of BMSF membranes with the Arg-Gly-Asp (RGD) peptide sequence, with an aim of enhancing cell attachment.

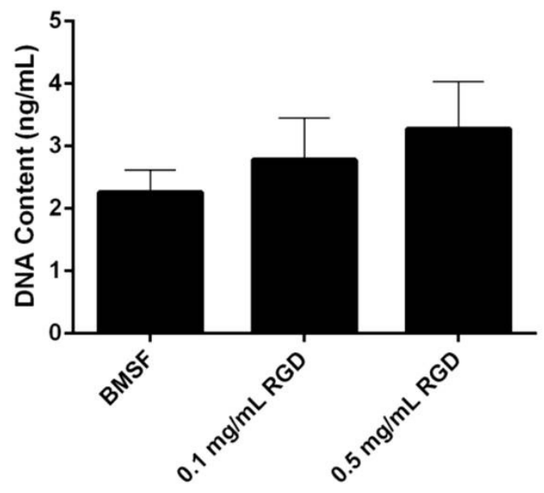

Fig. 17: Comparison of the attachment of primary human corneal limbal epithelial cells to BMSF membranes as such, and to membranes that were modified by the covalent functionalization with an RGD-containing peptide (as shown in Figure 16). *[Adapted from Bray et al., 2013a].*

Conclusion

The research programme described in this dissertation proves that the silk proteins have an established role in the tissue engineering and regenerative medicine of the eye. Both fibroin and sericin can function successfully as templates for cell attachment and growth. In addition, these materials display a series of important properties that make them specifically useful as templates. A number of questions still remain to be addressed, especially in relation to the enhancement of cell adhesion and mechanical strength, and research is in progress in our laboratories and elsewhere.

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NOTE: The marked references (†) present research published by the author and his colleagues.

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Domnului Prof. dr. ing. TRAIAN V. CHIRILĂ

who recommended awarding the Honorary Degree of

DOCTOR HONORIS CAUSA
to Professor TRAIAN V. CHIRILĂ, PhD

Chief Scientist at Queensland Eye Institute

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Doctor Honoris Causa

Domnului Profesor dr. ing.

Traian Chirilă

de la QUEENSLAND EYE INSTITUTE SOUTH BRISBANE
AUSTRALIA

pentru valoroase contribuții în domeniul învățământului și cercetării științifice.

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