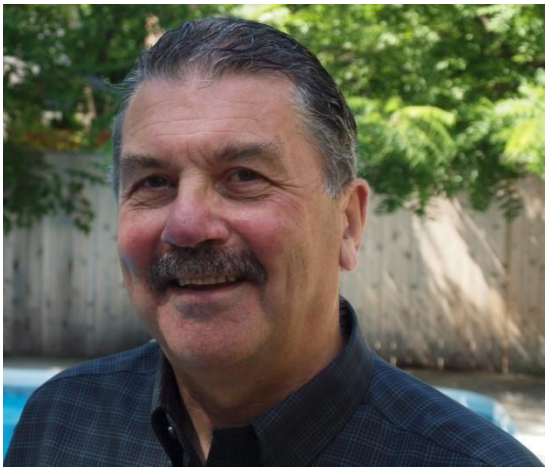
Cell Technology Group and publications

Michael Butler is the Chief Scientific Officer (CSO) of the National Institute of Bioprocessing Research & Training (NIBRT), Adjunct Full Professor in University College Dublin as well as Distinguished Professor Emeritus of the University of Manitoba, Canada. He holds degrees in Chemistry and Biochemistry from the Universities of Birmingham, London (UK) and Waterloo (Canada). After a period of several years as Principal Lecturer in Biotechnology at Manchester Metropolitan University Dr. Butler was appointed as Professor and NSERC/Apotex Industrial Research Chair in Fermentation Technology in the Department of Microbiology, University of Manitoba.



In 2008, he was named Distinguished Professor and in 2010 became Scientific Director of MabNet, an NSERC-funded national network focused on platform processes for monoclonal antibody production. His other appointments have included Associate Dean of Scientific Research at Manitoba and Visiting Scientist at MIT (USA), Animal Virus Research Institute (Pirbright, UK) and the Universities of Oxford and Rio de Janeiro.

His research work focuses on the development of bioprocesses using mammalian cells for the production of recombinant proteins, monoclonal antibodies and viral vaccines. He is particularly interested in the bioprocess conditions that can be used to control the biochemical structure of glycoproteins and hence the quality of biopharmaceuticals. He has always collaborated closely with industry and is a past recipient of the Canadian national Synergy Award for University-Industry innovation. He has been President of the International Society for *Protein Expression in Animal Cells (PEACe)* and on the editorial board of several journals and major reference works including Encyclopedia of Cell Technology, Biotechnology Advances, Biotechnology and Bioengineering and Comprehensive Biotechnology.

He is the founder of Biogro Technologies Inc., a spin-off company dedicated to serum-free media development. He has authored seven books on mammalian cell technology and over 170 scientific articles (with > 4,300 citations).

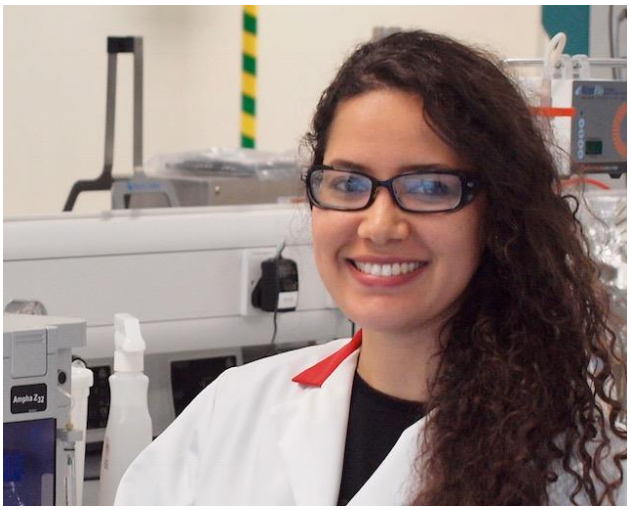
Nga Lao / Research & Lab Manager

Nga has a PhD in Molecular Biology from Maynooth University. Since then she became a senior Research Fellow in the Department of Genetics at Trinity College Dublin and Research Associate at University College Cork. This was followed by further post-doctoral appointments at the Conway Institute and School of Biology at University College Dublin. Before coming to NIBRT Nga was for several years a Research Fellow at the National Institute for Cellular Biotechnology (NICB) at Dublin City University. She has extensive experience of mammalian cell culture, protein purification and product characterization.

Adam Bergin / PhD student.

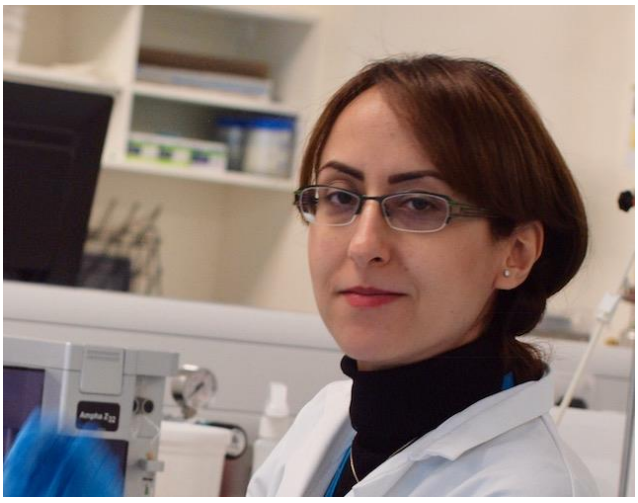
Adam was awarded a BSc in Biotechnology from NUI Maynooth, followed by an MSc in Bioprocess Engineering from Dublin City University. He worked for two years in Pfizer Grange Castle as a Technical Services Process Scientist, as part of the New Product Introduction team. His current Ph.D. research will be awarded through University College Dublin. The title of his project is "Strategies for continuous culture of mammalian cells". Projects: Strategies for Continuous Culture of mammalian cells. Proposal (a) To establish control points in metabolism of producer cells. Identifying critical process parameters that affect productivity through analysis of steady states (b) Design a scale down process for biomanufacturing using a cell separator (eg: ATF or acoustic). (c) Establish methods of control for enhanced productivity parameters that affect productivity through analysis of steady states (d) Design a scale down process for biomanufacturing using a cell separator (eg: ATF or acoustic). (e) Establish methods of control for enhanced productivity.

Leticia Martins Mota / PhD student



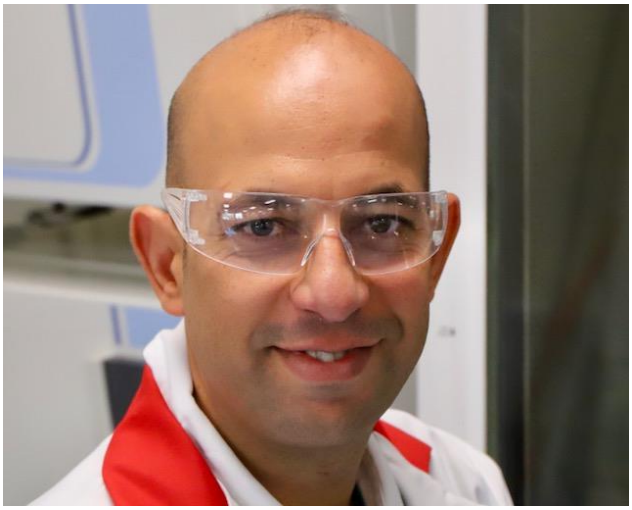
Letícia completed her chemical technician degree in 2007 followed by a degree in Pharmacy from Federal University of Alfenas, Brazil in 2014. During her undergraduate period she was selected and funded by the Brazilian federal government to study and research at University of Manitoba, Canada, for one year. She continued her education with an MBA in Cosmetology completed in 2017. From 2014 to 2017 she worked in the R&D, Regulatory Affairs and Strategic Purchasing departments at pharmaceutical companies in Brazil. In September 2017 she started her Ph.D. at UCD and joined the NIBRT Cell Technology Group as a Ph.D. researcher under the supervision of Dr Michael Butler. Her research is on Design of Single Glycoform Antibodies using Solid Phase Enzymatic Remodelling. Projects: Chemoenzymatic glycan remodelling Proposal (a) Optimize reaction conditions for targeted glycoform production by enzymatic modification (b) Determine receptor binding capacity of specific glycoforms produced. (c) Focus on defucosylation using a novel fucosidase for enzymatic remodelling or use a fucose transferase inhibitor in the bioprocess. Establish the relationship between fucosylated glycans and Fc receptor binding.

Elham Salimi / Post-doctoral researcher



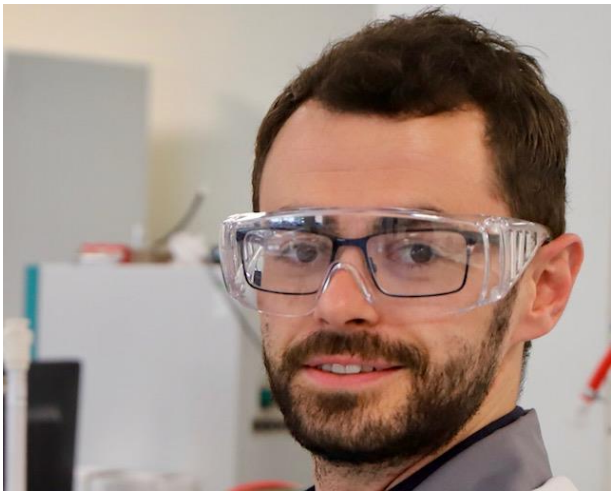
Elham gained her BSc in Electrical Engineering before her MSc and PhD in the new field of investigating the dielectric properties of biological cells. Elham has applied her knowledge of electrical engineering to understand how cells behave in electromagnetic fields. Her PhD research was entitled "Dielectrophoresis study of electroporation effects on dielectric properties of biological cells". This area is particularly important in the development of methods of monitoring and control cell growth in bioreactors used in the production of biopharmaceuticals. She has been able to model the structure and electrical profile of CHO cells that are used extensively in large-scale production. She has come to NIBRT with a post-doctoral Flaherty Scholarship to study and model the process of apoptosis using a biocapacitance probe and an impedance-based flow cytometer.

Ismael Obaidi / Post-doctoral researcher



Following a BSc in Pharmacy and MSc in Pharmacology Ismael completed his PhD at the Conway Institute of University College Dublin in a research programme involved in testing the carcinogenicity of food additives on human cell lines. This gave him extensive experience in cell culture techniques which he is now applying to the Kerry/ Enterprise Ireland project on the identification of bioactive components in plant and microbial hydrolysates.

Andrew Quigley / Post-doctoral researcher



Andrew gained a BSc in Chemistry in Maynooth University. This was followed by a PhD in Analytical Chemistry at Waterford Institute of Technology. The title of his thesis was "Development of novel microextraction methods for the analysis of selected trace compounds in bovine milk". He has also gained experience as a contract analyst for various companies. This experience now is being applied to the extraction and analysis of bioactive components from microbial and plant hydrolysates in the Kerry /Enterprise Ireland funded project.

Cell Technology Publications (last 2 years)

2018

Azita Fazelkhah , Katrin Braasch , Samaneh Afshar , Elham Salimi , Michael Butler , Greg Bridges and Douglas Thomson Quantitative Model for Ion Transport and Cytoplasm Conductivity of Chinese Hamster Ovary Cells. Scientific Reports submitted 2018

Afshar,S., Fazelkhah,A., Salimi,E., Butler,M.. Thomson, D.J., and G. E. Bridges, G.E. Dielectric Properties of Single Cells Subjected to Heat Shock Using DEP Cytometry. Transactions on Microwave theory and techniques submitted 2018

Elham Salimi , Katrin Braasch , Azita Fazelkhah , Samaneh Afshar , Bahareh Saboktakin Rizi , Kaveh Mohammad , Michael Butler, Greg E. Bridges , Douglas J. Thomson Single Cell Dielectrophoresis Study of Apoptosis Progression Induced by Controlled Starvation. Bioelectrochemistry 124: 73-79: 2018

Ting-Hsuan Chen , Wen-Chun Liu, Chia-Ying Lin , Chia-Chyi Liu, Jia-Tsrong Jan, Maureen Spearman, , M Butler and Suh-Chin Wu. Glycan-masking hemagglutinin vaccines produced in CHO cells against multi-clade/subclade H5N1 avian influenza virus infections. Biotech Bioeng accepted 2018; doi-org.uml.idm.oclc.org/10.1002/bit.26810

Michael Butler and Venkata S. Tayi. Solid phase enzymatic re-modelling to produce single glycoform antibodies. BMC Proceedings 2018, 12(Suppl 1):P-135; 33-34. DOI 10.1186/s12919-018-0097-x

Tayi,VS and Butler,M.. (2018) Solid-phase enzymatic remodeling produces high yields of single glycoform antibodies. Biotechnology Journal 13**,** e1700381 DOI: 10.1002/biot.201700381

2017

Azita Fazelkhah, Katrin Braasch, Samaneh Afshar, Gregory Bridges, Michael Butler, and Douglas Thomson. Quantitative Model for Ion Transport and Cytoplasm Conductivity of Chinese Hamster Ovary Cells. Biophysical Journal submitted 2017.

Butler M., Reichl I.U. (2017) Animal Cell Expression Systems. In: Advances in Biochemical Engineering/Biotechnology. Springer, Berlin, Heidelberg DOI: 10.1007/10_2017_31 2

Afshar S, Fazelkhah A, Salimi E, Thomson D, Bridges G and Butler M**.** Change in the dielectric response of single cells induced by nutrient deprivation over a wide frequency range. IEEE MTT-S International Microwave Symposium Digest. 872-875: 2017.

Pedram Madadkar, Rahul Sadavarte, Michael Butler, Yves Durocher and Raja Ghosh. Preparative separation of monoclonal antibody aggregates by cation-exchange laterally-fed membrane chromatography. J. Chromatography B 1055-1056: 158-164, 2017

Ali Razaghi, Carina Villacrés, Vincent Jung, Narges Mashkour, Michael Butler, Leigh Owens, Kirsten Heimann**.** Improved therapeutic efficacy of mammalian expressed-recombinant interferon gamma against ovarian cancer cells Experimental Cell Research 359: 20-29. 2017

B.Dionne, N.Mishra and M.Butler. A low redox potential affects monoclonal antibody assembly and glycosylation in cell culture. Journal of Biotechnol. 246: 71-80. 2017

Natalie Krahn, Maureen Spearman, Markus Meier, July Dorion-Thibaudeau, Matthew McDougall, Trushar R. Patel, Gregory De Crescenzo, Yves Durocher, Jörg Stetefeld and Michael Butler**.** Inhibition of glycosylation on a camelid antibody uniquely affects its FcγRI binding activity. European Journal of Pharmaceutical Sciences 96:428-439 2017

E. Salimi, K. Braasch, M. Butler, D. J. Thomson, and G. E. Bridges. Dielectrophoresis study of temporal change in internal conductivity of single CHO cells after electroporation by pulsed electric fields. Biomicrofluidics 11, 014111: 2017.

Hengameh Aghamohseni, Maureen Spearman, Kaveh Ohadi, Katrin Braasch, Murray Moo-Young, Michael Butler, Hector M. Budman. A semi empirical glycosylation model of a camelid monoclonal antibody under hypothermia cell culture conditions. Journal of Industrial Microbiology & Biotechnology 44(7) 1005-1020 2017.

Ting-Hsuan Chen , Yin-Yu Liu , Jia-Tsrong Jan , Ming-Hsi Huang , Maureen Spearman , Michael Butler and Suh-Chin Wu. Recombinant hemagglutinin proteins formulated in a novel PELC/CpG adjuvant for H7N9 subunit vaccine development. Antiviral Research 146:213-220:.2017

Kaveh Mohammad, Douglas A. Buchanan, Katrin Braasch, Michael Butler and Douglas J. Thomson. CMOS single cell dielectrophoresis cytometer. Sensors and Actuators B 249: 246–255: 2017

CONFERENCE ABSTRACTS

Michael Butler, Katrin Braasch, Elham Salimi, Samaneh Afshar , Gregory Bridges and Douglas Thomson. Dielectric monitoring of mammalian cells in a bioreactor. Cell Culture Engineering meeting, Tampa, Florida, USA May 2018

Neha Mishra, Maureen Spearman, Lynda J Donald, Helene Perreault, Michael Butler. Comparison of two glycoengineering methods aimed at reducing fucosylation of a camelid heavy-chain monoclonal antibody. Protein Expression in Animal Cells (PEACe) Valencia, Spain September 2017

Michael Butler and Venkata Tayi Solid phase enzymic re-modelling to produce single glycoform antibodies. 25th ESACT meeting, Lausanne, Switzerland May 2017

Natalie Krahn, Cal D'Eall, Rob Pon, Martin Rossotti, Greg Hussack, Maureen Spearman, Debbie Callaghan, Jörg Stetefeld, Michael Butler, Yves Durocher and Jamshid Tanha Designing a camelid/human heavy-chain antibody with enhanced antitumour activity. 25th ESACT meeting, Lausanne, Switzerland May 2017

INVITED LECTURES

On-line and Off-line monitoring of CHO cell health in a bioreactor to allow for early identification of cell death. Valerie Fitzgerald, Adam Bergin and Michael Butler. Bioproduction Congress, KNect365, Dublin October 2018

Control of antibody glycosylation during the upstream or downstream stages of a bioprocess. Bioproduction Congress, KNect365, Dublin October 2018

Opportunities for Modification of Glycan Structures at Various Stages During a Bioprocess` Simposio de Produccion y Regulacion de Biofarmacos, Instituto Biomedical UNAM, Mexico May 2018

Curso International sobre cultivo de celulas de mamifero y la produccion de biofaramacos (3 lectures) Instituto Biomedical UNAM, Mexico May 2018

Dielectric Monitoring of Mammalian cells in a Bioreactor. Instituto de Biotecnologia, UNAM, Mexico May 2018

Modification of glycosylation of antibodies during the upstream or downstream stages of a bioprocess. Cambridge Healthtech. Bioprocessing Summit Europe, Lisbon, Portugal March 2018

Introduction to Cell Culture (6 lectures). PepTalk Protein Science Cambridge Healthtech.Institute, San Diego, USA January 2018

Reducing glycoprotein heterogeneity in a mammalian cell bioprocess. Animal Cell Technology Industry Platform (ACTIP), Nantes, France November 2017

Methods for Product Quality Monitoring and Controlling Glycosylation. Cell Culture & Upstream Process Development Session of . BioProduction 2017 Knect365 Conference Dublin October 2017

Dielectric Monitoring of Mammalian cells in a Bioreactor. Protein Expression in Animal Cells (PEACe) Valencia, Spain September 2017

Strategies for the control of glycosylation during the production of a recombinant protein. Cambridge Healthtech 9th Annual Optimizing Cell Line Development. Boston August 2017

Monitoring the electrical profile of cells during a bioprocess. NICB/ Dublin City University June 2017
Dielectric Monitoring of Mammalian cells in a Bioreactor. Bioprocess International Summit, Amsterdam April 2017

Predictions of glycosylation profiles from cell engineering and bioprocess control. Cambridge Healthtech Biotherapeutics Analytical Summit, Bethesda Maryland USA March 2017

Books on Bioprocessing authored and edited by M.Butler