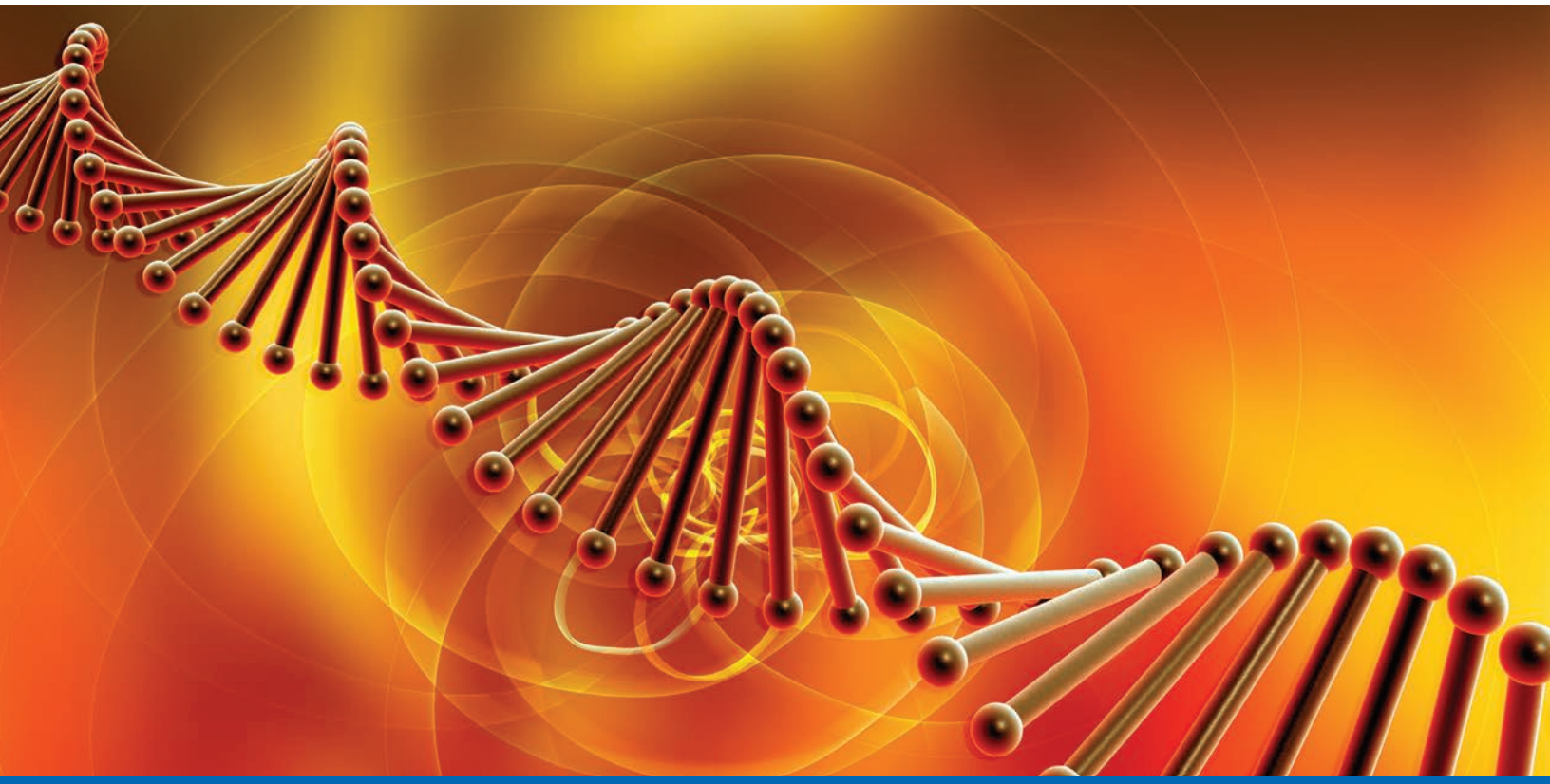
Biopharmaceutical Process and Quality Consortium

4th Biopharmaceutical Summit 2015



MAY 18-22, 2015

May 18-19, 2015: Workshop on "Raw Material Variability and its Process Control in Biotherapeutics Production"

May 20-22, 2015: Advanced Training on PAT and QbD Principles in Biopharmaceuticals

Hosted by: *Biopharmaceutical Process and Quality Consortium (BPQC), University of Massachusetts Lowell, Massachusetts BioManufacturing Center (MBMC)*

Summit Chair: *Rajesh G. Beri, Ph.D., Lonza Biologics Inc. / Co-Chair: Seongkyu Yoon, Ph.D., UML*

Inn & Conference Center, Lowell MA
University of Massachusetts Lowell

UMASS LOWELL
Learning with Purpose

University of Massachusetts Lowell

May 18, 2015

Dear Biopharmaceutical Summit Attendees,

On behalf of the Engineering faculty and staff at the University of Massachusetts Lowell, welcome to our campus. We are pleased to host the Fourth Annual Biopharmaceutical Summit.

Approximately one in every four drugs introduced to the market is a biopharmaceutical. The industry is booming and the U.S. biopharmaceutical industry has tremendous economic impact. However, there are tremendous technological challenges that affect production and purification of this highly specialized and complex process. The specialized nature of these pharmaceuticals and complexities involved in their production are major drivers of increasing healthcare costs.

Over the next five days, you'll join scientists, engineers and industry representatives in discussing "Raw material variability and its process control," one of the most pressing and industrially relevant biopharmaceutical challenges of our time. There will be workshops, in-depth training and keynote speeches by industry and academic leaders. And there will be plenty of opportunities for networking with professionals from major biopharmaceutical manufacturers and technology providers such as Biogen, Genzyme, Pfizer, Johnson & Johnson, Waters and GE.

This Summit is truly a collaboration between academia and industry. We are confident that by the end of your time at UMass Lowell, you will have collectively taken significant steps in providing a roadmap for the next-generation biopharmaceutical industry.

With your active participation, the University of Massachusetts, Lowell, in collaboration with a number of academic and industry partners, will form an industry-specific consortium to promote development of advanced biomanufacturing science and technology and to upgrade existing technology. The consortium will strive to share resources and promote innovation throughout the industry.

Thank you for joining us.

Sincerely,

Joseph Hartman, Ph.D., P.E.
Dean, Francis College of Engineering
University of Massachusetts, Lowell

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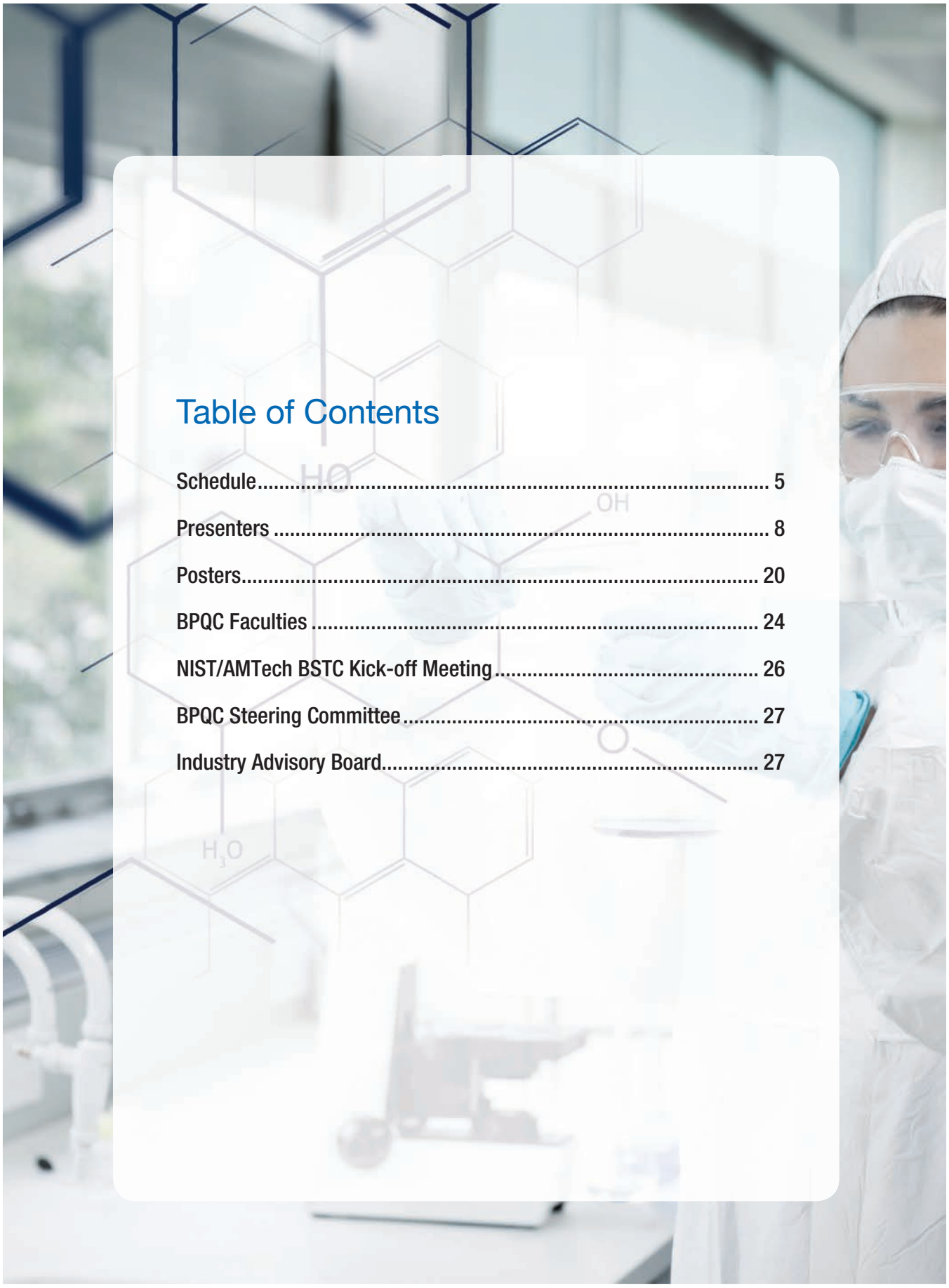

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SCHEDULE

PART I. WORKSHOP May 18 (Monday): 8:00 AM – 5:00 PM

8:00 AM	**REGISTRATION**
8:30 AM	**WELCOME AND INTRODUCTION (Joseph Hartman, Ph.D., P.E., Dean of Engineering, UML)**
8:40 AM	**Session I: Regulatory and Industrial Challenges** (8:40 – 8:50 AM) Session Chair: Thomas Ryll, Ph.D., Sr. Director of Cell-Culture Development, Biogen **PLENARY PRESENTATION: "Control of Glycosylation During Biopharmaceutical Production"** (8:50-9:30) Michael Butler, Ph.D., Distinguished Professor, Univ. of Manitoba, Canada **T1: "Control of Antibody Glycosylation: A Case Study."** (9:30-10:00) Rajesh G. Beri, Valerie Canning, Brian Hadley, Jim Heimbach, and Joe Kauten, MSAT, Lonza Biologics, Inc., and Robert Gerber, GSK
10:00 AM	**BREAK**
10:20 AM	**T2: "Product Quality Pitfalls - Variable and Complex Materials in Biologics Manufacturing"** Mark D. Leney, Ph.D., Deputy Director, Quality & Regulatory Affairs, Mass Biologics Lab – UMass Medical School (10:20-10:50) **T3: "A case study in technical risk assessment strategy for upstream bioprocess raw materials"** Terrence Dobrowsky, Ph.D., Scientist, Biogen (10:50-11:20) **PANEL DISCUSSION** (11:20 -12:00 PM) Panelists: Session Chair and Speakers
12:00 PM	**NETWORKING LUNCH**
1:30 PM	**Session II: Practices** Session Chair: Jack Prior, Ph.D., Sr. Director of Manufacturing Technology, Genzyme **T4: "Controlling Raw Material Variability in Biomanufacturing: A CMO Perspective on Industrial Challenges"** Seshu Tummala, Ph.D., Scientist, Mammalian Manufacturing R&D, Lonza Biologics (1:30-2:00) **T5: "Monitor and control raw material variability through supplier collaborations"** Ting Wang, Ph.D., Sr. Engineer, Process Development, Amgen (2:00-2:30) **T6: "Raw Material Control Strategies"** Dave Kolwyck, Dir. of Global Manufacturing Sciences, Biogen (2:30-3:00)
3:00 PM	**BREAK**
3:10 PM	**T7: "Managing Raw Material Variation in Vaccines Production"** Jeff Doyle, Manager, Process Analytical Sciences Group, Pfizer (3:10-3:40) **T8: "Data Analytics: MVA Approaches to Identify the Impact of Raw Materials on Product and Process Variation in Biologics Manufacturing"** Steven Mehrman, Ph.D., Principal Scientist, Janssen Pharmaceuticals (3:40-4:10) **PANEL DISCUSSION** (4:10 – 5:00 PM) Panelists: Session Chair and Speakers
5:00 PM	**RECEPTION AND NETWORKING POSTER SESSION** 20-30 posters will be presented

SCHEDULE

PART I. WORKSHOP May 19 (Tuesday): 8:00 AM – 5:00 PM

8:00 AM	**REGISTRATION**
8:20 AM	**Session III: Emerging Technologies** (8:20-8:30) Session Chair: Rashmi Kshirsagar, Ph.D., Director of Cell Culture Development, Biogen
	T9: "Downstream Platform Process Optimization for mAbs with New and Emerging Technologies" Kumar Dhanasekharan, Ph.D., Director of Process Development, Cook Pharmica LLC (8:30-9:00)
	T10: "Monitoring Multiple Attributes of Biopharmaceuticals in Development, Production, and Quality Control of Biopharmaceuticals with Mass Detection" Sean M. McCarthy, Ph.D., Principal Scientist, Waters (9:00-9:30)
	T11: "X-ray Fluorescence Method Development for Monitoring Inorganics in Raw Materials: Challenges, Strategies and Case Studies" Jessica Mondia, Ph.D., Scientist, Biogen (9:30-10:00)
	T12: "Predicting Cell Culture Robustness through Poloxamer Characterization" Amr S. Ali, Scientist, Biogen (10:00-10:30)
10:30 AM	**BREAK**
10:40 AM	**Session IV: Biopharmaceutical Consortium Session – Driving for Future** Session Chair: Kevin Bittorf, Ph.D., Pharmaceutical Executive in Residence, Chair of Advisory Board (10:40 – 10:50)
	"Advanced Biomanufacturing Consortium" Seongkyu Yoon, Ph.D., Assistant Professor, Univ. of Massachusetts Lowell (10:50-11:10)
	"Continuous Biomanufacturing" Mark-Henry Kamga, Ph.D. Candidate, Univ. of Massachusetts Lowell (11:10-11:30)
	"Glycosylation Modeling and Control" Sha Sha, Ph.D. Candidate, Univ. of Massachusetts Lowell (11:30-11:50)
12:00 PM	**NETWORKING LUNCH**
1:30 PM	**Session V: Path-forward** Session Chair: Sadettin Ozturk, Ph.D., Associate Deputy Director, Process Development, Mass Biologics Lab
	T13: "How to Integrate Raw Material Variability in QbD Risk Assessment Sun Koo Kim, Ph.D., Sr. Scientist, Bayer, CA (1:30-2:00)
	T14: "Mitigation of Chromatography Adsorbent Lot Variability through a Molecule Specific Binding Strength Test and an Adaptive Control Strategy" Carson Tran, Engineer I, Biogen (2:00-2:30)
	T15: "Dynamic Control Strategies: A current view of "What goes in, What goes on, and What comes out" Brian Fahie, Ph.D., Director of Technical Development, Biogen (2:30-3:00)
	T16: "Application of the CHO Genome to CHO HCP Studies" Kelvin Lee, Ph.D., Professor, Department of Chemical Engineering, University of Delaware (3:00-3:30)
	PANEL DISCUSSION (3:30 – 4:00 PM) Panelists: Session Chair and Session V Speakers
4:00 PM	**CLOSING REMARKS** (Carl Lawton, Ph.D., Associate Professor and Director of Mass Biomanufacturing Center, UML)

PART II. BPQC BUSINESS MEETING AND RECEPTIION May 20, 2015 (Wednesday), 9:00 AM - 4:00 PM

9:00 AM (Location TBD)	**Business meeting with consortium member companies** For appointment, RSVP (bpqc@uml.edu or seongkyu_yoon@uml.edu, 978-934-4741)

SCHEDULE

PART III. ADVANCED TRAINING ON PAT/QBD IN BIOPHARMACEUTICALS

May 20-22, 2015 (Wednesday through Friday), 8:00AM - 5:00PM/ Falmouth 300, North Campus, UML

Module #	Description	Type	Instructor
Day 1	**Multivariate Data Analysis**		
M1, 8AM	Principal Component Analysis, Review	Lecture	NS
M2, 9AM	Tutorial on Principal Component Analysis	Tutorial	NS/SY
M3, 10AM	Partial Least Squares, Review	Tutorial	NS
M4, 11AM	Tutorial on Partial Least Squares	Tutorial	NS/SY
12 PM	**Lunch**		
M5, 1PM	Batch Evolution Modeling I (Modeling)	Lecture	NS
M6, 2PM	Batch Evolution Modeling II (Validation)	Lecture	SY
M7, 3PM	Case Study Demonstration	Tutorial	NS/SY
M8, 4PM	Tutorial on Batch Evolution Modeling	Tutorial	NS/SY
Day 2	**Batch Modeling & DOE**		
M9, 8AM	Batch Level Modeling I	Lecture	NS
M10, 9AM	Tutorial on Raw Material and CC Impact on CQA	Tutorial	NS/SY
M11, 10AM	Batch Level Modeling II	Lecture	SY
M12, 11AM	Tutorial on CQA Prediction	Tutorial	NS/SY
12PM	**Lunch**		
M13, 1PM	DOE Concepts	Lecture	SY
M14, 2PM	Modeling, Optimization and Validation	Lecture	NS
M15, 3PM	Tutorial on Modeling Building with Media/CQA	Tutorial	NS/SY
M16, 4PM	Tutorial on Robustness and Design Space	Tutorial	NS/SY
Day 3	**QbD and Design Space Assessment**		
M17, 8AM	Design Space	Lecture	SY
M18, 9AM	Tutorial on Design Space Building	Tutorial	NS/SY
M19, 10AM	CQA Specification	Lecture	NS
M20, 11AM	Tutorial on CQA Specification	Tutorial	NS/SY

For questions: bpqc@uml.edu, or Seongkyu Yoon (Seongkyu_yoon@uml.edu; 978-934-4741),
Nirav Shah (nirav.shah@umetrics.com, 978-738-3513)

PRESENTERS

Michael Butler

Scientific Director, MabNet
Distinguished Professor, Department of Microbiology, University of Manitoba, Winnipeg

Michael Butler is a Distinguished Professor of Animal Cell Technology at the University of Manitoba, Canada. His previous appointments include Associate Dean of Scientific Research at Manitoba and Principal Lecturer in Biotechnology at Manchester Metropolitan University. He has also been a Visiting Scientist at MIT (USA), Animal Virus Institue (Pirbright, UK) and the Universities of Oxford and Rio de Janeiro. He holds degrees in Chemistry and Biochemistry from the Universities of Birmingham, London (UK) and Waterloo (Canada). His research work and teaching 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. He has always collaborated closely with industry and is a past recipient of the Canadian national Synergy Award for University-Industry innovation. He is presently director of MabNet, a Canadian network for Mab production and founder of Biogro Technologies Inc., a spin-off company dedicated to serum-free media development.
Hobbies: Tennis, Music (piano, guitar and voice}

Title: The control of glycosylation during biopharmaceutical production
Abstract: The glycoform profile of a monoclonal antibody (Mab) determines many functional properties that affect therapeutic efficacy. Common variations of the conserved Fc glycan include galactosylation, fucosylation and sialylation. The observed glycan profile of the final product can depend upon the producer cell line, the growth media, the culture conditions as well as the Mab protein structure. The presentation will review the parameters that can be controlled in order to minimize batch to batch variation of Mab glycosylation. Strategies will also be discussed to produce Mabs with pre-defined glycan structures.

Rajesh Beri

Head, Mammalian Research & Technology (CMO)
LCMB – Portsmouth, NH

Rajesh Beri is currently the Head of Research & Technology for Lonza's Mammalian Manufacturing Business Unit. His responsibilities include research, development and implementation of innovative technologies. In his previous role as Director, Manufacturing Sciences and Technology at Lonza Biologics, Portsmouth, NH, he managed a group of 45 scientists and engineers responsible for process transfer and scale up, process characterization, manufacturing and regulatory support. During his tenure as Director MSAT, Rajesh and his team successfully transferred 20 processes, performed process characterization of 10 processes and received approval for 3 products.

Rajesh received his Bachelors of Technology in Chemical Engineering from the Indian Institute of Technology, Mumbai, India and his Masters and Doctorate degrees in Chemical Engineering from Worcester Polytechnic Institute, Worcester, MA. He has over 20 years' experience working in the Biotech Industry in Process Development, Process Scale up, Manufacturing Sciences, Facility & Equipment design and has worked on 40 biologics derived from either Mammalian or Microbial cultures. He has previously worked at BioChem Pharma, Dow Chemicals, GlaxoSmithKline and Amgen. His hobbies include hiking, biking and coaching youth sports.

Title: Control of Antibody Glycosylation: A Case Study

Mark D Leney

Deputy Director, MassBiologics (Quality and Regulatory Affairs)
Assistant Professor, Department of Medicine, UMass Medical School

Mark D. Leney, PhD, is current Deputy Director at MassBiologics (Quality) and an assistant professor of at the University of Massachusetts Medical School. Dr. Leney is responsible for the oversight of licensed and IND product manufacturing, in house and CMO business, covering both legacy vaccine as well as modern recombinant biologics. Dr. Leney is an active member of the Parenteral Drug Association and has served (or continues to serve) on task forces drafting PDA technical documents concerning the quality of extemporaneously compounded investigational drugs, phase appropriate application of cGMPs, the quality of pharmaceutical glass containers and quality considerations in advanced therapy medicinal products (cell, gene and tissue based therapies).

Prior to working at MassBiologics, Dr Leney served as a forensic investigator for the US Department of Defense. Dr Leney holds a B.Sc, in Biological Sciences from the University of Edinburgh, and a Ph.D. from the University of Cambridge where his research combined mathematical and evolutionary biology and biological anthropology. Dr Leney was a postdoctoral Cox Fellow at New College, Oxford, a departmental lecturer at the Institute of Biological Anthropology, Oxford and a member of the faculties of archaeology, biology, and anthropology at the University of Oxford, also holding post-doctoral fellowships from the European Union and the Oak Ridge Institute for Science and Education.

Title: Product Quality Pitfalls - Variable and Complex Materials in Biologics Manufacturing

Abstract: The presentation will address some practical challenges in managing raw materials utilized in the manufacture of GMP biologics. A series of examples will be used to illustrate a) issues arising from complex and or exotic materials – including undefined components in 'chemically defined' media and polymorphic raw materials, b) problems resulting from undetected failures by raw material supplier/ manufactures - including the upstream management of the manufacturer's own raw materials and the manufacturer's own quality system and c) questions concerning adventitious agent and TSE risks in biologics manufacturing. Risk mitigation and risk avoidance strategies are proposed and discussed with a focus on distinguishing defined/bounded risks (which are typically mitigated) from hypothetical/unbounded risk (which are typically avoided or simply accepted) in practical strategies to translate biologic candidate molecules through development and into GMP manufacturing.

Terrence Doborowsky

Scientist, Cell Culture Development, Biogen

errence Dobrowsky received his BS in Chemical Engineering from the University of Notre Dame in 2005 and his PhD in Chemical and Biomolecular Engineering from Johns Hopkins University in 2010. Since joining Biogen's Cell Culture Development Department in 2010 he has contributed to both early and late stage clinical programs serving as upstream process development lead for multiple products. Terrence's initial work focused on platform process development and application but has recently begun to support Cell Culture Development's initiatives to increase process robustness through increased understanding of raw material variation and associated risk.

Title: A case study in technical risk assessment strategy for upstream bioprocess raw materials

Abstract: Variability in upstream bioprocess raw materials have been linked to significant biopharmaceutical production deviations even resulting in the rejection of entire supply campaigns. Advances in process control capabilities are under development to compensate or remove this variability, however limited resources dictate that only a fraction of the incoming material variation can be compensated for. Determining what variability and in which materials will pose the greatest risk to the overall process or product is not straightforward. Here, we describe a case study in risk assessment strategy wherein technical observations and analysis drive the semi-quantitative ranking of raw materials by increasing risk. Initial observations are made via paper exercise considering item specifications, certificates of analysis, manufacturing methods and the final intended medium formulation. Analytical resources are devoted to those materials of highest risk to assess unidentified impurities followed by a subsequent re-ranking of risk. These assessments will then drive new sourcing or technical control strategies to mitigate risk.

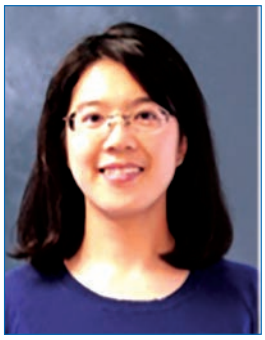
Seshu Tummala

Principal Scientist, Research and Technology, Lonza Biologics, Inc.

Seshu Tummala, PhD is currently a Principal Scientist in the Research and Technology group at Lonza Biologics, where his main responsibilities are implementation of Process Analytical Technology (PAT) initiatives and Raw Material Characterization strategies for large-scale upstream bioprocessing operations. He gained his expertise with cell culture manufacturing via various roles in process development and manufacturing sciences at institutions including Abbott Laboratories, Percivia, Sanofi Pasteur, Alnylam, as well as Lonza Biologics. He received his BS in Chemical Engineering from Johns Hopkins University and MS and PhD in Chemical Engineering from Northwestern University. He has published in journals related to bioprocessing including Biotechnology & Bioengineering and Biotechnology Progress and has presented at numerous venues on various topics related to cell culture process development. Dr. Tummala is also a member of the Biophorum Operations Group (BPOG) Raw Material Variability workstream.

Title: Controlling Raw Material Variability in Biomanufacturing: A CMO Perspective on Industrial Challenges

Abstract: Based on regulatory guidances and advanced quality risk management practices, the biopharamaceutical industry is greatly focused on enhancing process robustness to ensure product quality. Development of an effective raw material characterization strategy is vital to acheiving this objective. Through definition and examples, the approach currently being developed by Lonza Biologics for minimizing raw material variability for improvement of large-scale upstream operations will be discussed.



Ting Wang

Senior Engineer in Process Development, Amgen

Ting Wang is a Senior Engineer in Process Development at Amgen. She is responsible for implementing an internal raw material information system to enable automated suppliers' data capture as part of knowledge management system for Amgen products' life cycle management. Collaborating with cross-functional teams, she provides scientific and technical inputs in the area of multivariate analysis and predictive modeling towards understanding and mitigating raw material variations and risk. Ting's background is in Pharmaceutical Sciences, and she earned her PhD degree from University of Maryland at Baltimore. Her PhD research in Pharmaceutical Excipients variability has been recognized through several awards and projects, including US Pharmacopeia (USP) fellowships (2011, 2012), Outstanding Contributed Paper Award (Regulatory Science, AAPS, 2010), International Pharmaceutical Excipient Council (IPEC) foundation awards (2012), etc. Ting is member of International Society for Pharmaceutical Engineering (ISPE) and American association of Pharmaceutical Scientists (AAPS).

Title: Monitor and Control Raw Material Variability through Supplier Collaborations

Abstract: Raw material variation poses risk to process and product in Biopharmaceutical manufacturing. To minimize and control the risk from raw material, it is critical to understand and manage the supply chain. We are utilizing Identify, Track and Control Variation (ITCV) with multivariate analysis to understand and reduce raw material variation and therefore increase control. Collaborating with suppliers, we have developed a database to automatically capture and host suppliers' data with flexibility and scalability built into the system. Suppliers' data is analyzed to understand lot-to-lot variability and also combined with our internal data for process monitoring and control purposes. Other approaches to enrich raw material data for understanding and controlling will also be presented.

David Kolwyck

Director, Manufacturing Science - Raw Materials, Biogen

David Kolwyck has participated in the biopharmaceutical industry as both a supplier and end user for 12+ yrs in the areas of upstream raw materials, single use systems and specialty chemicals. He has extensive experience in manufacturing and supply chain scale-up and has supported the launch of numerous commercial products by creating integrated raw material delivery solutions both as a supplier and end user. In support of leveraging supply chain data for process monitoring he has facilitated the development of digital data integration solutions between suppliers and producers to increase supply chain transparency. His interests outside of the office include road biking and fishing.

Title: "Raw Material Control Strategies"

Abstract: This presentation will be an overview of the development of raw material control strategies and data monitoring systems which are both application and clinical stage specific. This presentation will review the stages of raw material controls and how those controls are defined based on process development characterization data and data available from the raw material supply chain. By using a risk based and clinical stage specific approach the risk of impact from raw material variability on the clinical process can be monitored to avoid unnecessary delays in clinical manufacturing.

Jeffrey Doyle

Manager, PAT Projects, Pfizer

Supporting the delivery of value driven Process Analytical Technology for the US based Pfizer Specialty Biotech sites, Jeff leads multiple cross-functional PAT project teams. Before joining the Process Analytical Sciences Group (PASG), Jeff led advanced data analysis and manufacturing process monitoring. Achievements within PASG include successful PAT implementations in the manufacture of both mAbs and vaccines. He holds a B.S. in Chemical Engineering from Clarkson University.

Title : Managing Raw Material Variation in Vaccines Production

Abstract: All raw material and process intermediate manufacturing processes have variation and it is expected the product of any variable process will also vary. Pfizer manages the anticipated raw material variation through a system of characterization, risk assessment, intake testing, and process monitoring. For process intermediates, especially for vaccine chemistry, classical small molecule techniques have been deployed to manage the variation through analytics and Process Analytical Technologies.

Steven Mehrman

Principal Scientist, Janssen Pharmaceuticals

Steve Mehrman is a Principal Scientist at Janssen Pharmaceuticals and is currently working in the Cell Technologies group supporting development of biologics through application of process modeling and feedback control strategies. He is in his 16th year with Johnson & Johnson and has previously worked in small molecule API development focused on crystallization and polymorphism control using Raman and Particle size analyzers to scale and technical transfer processes. Steve has also worked in solids drug product development focused on process modeling of fluid bed granulation utilizing PAT (NIR and Lasentec) as part of clinical supply and tech transfer.

Steve earned a B.S. in chemistry from Minnesota State University followed by a PhD in Organic Chemistry from the University of Nebraska working with Prof. James M. Tackas; Thesis: Transition metal Mediated Organo-Metalic Catalysis. Upon graduation he joined Johnson & Johnson as a Post-Doc working with Ahmed Abdel-Magid in chemical development.

Steve has received a number of accolades while at Johnson & Johnson related to data analytics and process understanding including the Standard of Leadership and SPARK innovation awards. He is also a principal investigator on over 45 published patents while at Johnson and Johnson.

Current work has been focused on building infrastructure and application for global deployment of chemometric and process models to be used for development, control and monitoring of processes across Janssen. As part of this effort standard approaches to understand impact of raw materials on product and process as to minimize assumptions made by project teams.

Data Analytics: MVA Approaches to Identify the Impact of Raw Materials on Product and Process Variation in Biologics Manufacturing

Abstract: Production of biologicals is inherently multivariate in nature, a complex endeavor by itself. The complicated cell machinery and its associated process controls become increasingly difficult to optimize while maintaining Critical Quality Attributes (CQA's) when variations in Raw Materials are introduced to the system. Multivariate analysis (MVA) can be applied to processing data to help identify correlations between raw materials and their effect on non-desirable product quality attributes. This presentation will overview approaches used to help decouple the complicated relationship of raw material impact on process and product quality attributes using standard statistical processes (PCA, PLS) and their application to biological product development and life cycle management.

Kumar Dhanshekharan

Director, Process Development, Cook Pharmica LLC

Dr. Dhanasekharan is Director of Process Development at Cook Pharmica in Bloomington, Indiana and is responsible for cell culture, purification, analytical, and formulation development including lab operations and scale-up to meet client drug substance and drug product needs. Cook Pharmica is an integrated contract development and manufacturing organization providing the pharmaceutical and biopharmaceutical industries with biologics drug substance and parenteral manufacturing in vials and prefilled syringes. Prior to his current role, Kumar worked for 5.5 years at Genzyme in various roles including process development, process engineering and most recently served as the Associate Director of Process Sciences and Technology at Genzyme in Framingham, Massachusetts. He was responsible for manufacturing process development for both cell culture and protein purification for enzyme replacement therapies in driving a science and risk-based strategy for continuous process improvements including improved control strategies, cell culture productivity and downstream recovery improvements. In a previous role, he led the implementation of Quality by Design (QbD) principles in development and successfully led a QbD based Lyophilization scale-up and tech. transfer project for approval. He also led efforts in viral risk mitigation which resulted in an invention and patent on a UV-C based viral inactivation device. He also provided technical leadership for several projects related to Consent Decree remediation. Prior to joining Genzyme, Kumar led small-molecule process development focused on API crystallization at Bend Research Inc., Bend, OR. Prior to that he was group leader for consulting services at Fluent Inc. (Now ANSYS) with focus on both small-molecule and biologics development and manufacturing challenges across upstream, downstream, and Fill/ Finish operations. Kumar has a Ph.D. in Food Science from Rutgers University and a Bachelor's in Chemical Engineering from Indian Institute of Technology, Chennai, India. He has over 50 conference presentations and over 10 peer-reviewed publications.

Downstream Platform Process Optimization for mAbs with New and Emerging Technologies

Abstract: High titers, particularly for monoclonal antibodies, continue to push the challenges to downstream processing. This talk will examine solutions that are becoming available in the marketplace with respect to new harvest clarification technologies, high capacity resins, and membrane technologies. Although continuous manufacturing has taken center stage for emerging trends, there are multiple ways to create streamlined downstream process with appropriate use of single-use and semi-continuous approaches. Actual process data with a model antibody will be presented for the evaluated technologies.

Sean M. McCarthy

Principal Scientist and Senior Manager, Waters Corporation

Sean M. McCarthy, Ph.D. joined Waters Corporation as a Senior Scientist in 2008. Since that time he has held positions as a Principal Scientist and Senior Manager. He has led scientific groups in a variety of application areas including protein and peptide chromatography, oligonucleotide analysis, medicinal chemistry, and method development.

Sean received his Ph.D. in inorganic chemistry from the University of Vermont in 2005 completing his thesis titled “Semi-Combinatorial Development of Iron and Manganese Based Oxidatively Robust, Environmentally Benign, Oxidation Catalysts”. Following completion of his Ph.D., he was an NIH postdoctoral trainee at the University of Vermont in the Pathology department working under Albert van der Vliet. His work focused on oxidative stress related to airway diseases and environmental oxidants using a variety of biochemical and mass spectrometric techniques.

Title: Monitoring Multiple Attributes of Biopharmaceuticals in Development, Production, and Quality Control of Biopharmaceuticals with Mass Detection

Abstract: During development, formulation, and process optimization for biotherapeutics it is necessary to monitor those properties of the therapeutic molecule and excipients that are critical quality attributes (CQAs). Often these types of analyses are conducted using optical detection. Recently there has been a trend in the biopharmaceutical industry to incorporate mass spectrometry for routine assays. In particular the industry is seeking to monitor post-translational modifications (PTMs), glycosylation profiles, excipients with UV and mass data by implementing Multi Attribute Methods (MAMs) which incorporate mass data. These assays are targeted towards downstream processes including in process and QC assays. Incorporating MAMs into downstream assays require availability of instrumentation which is easily deployed in GMP environments and require limited training.. Historically, mass spectrometry has required highly trained personnel and valuable laboratory space to implement but recently this landscape has started to change.

In this presentation we will discuss the use of a cost effective, compact, and easy to use mass detector for routine monitoring of biotherapeutics which enables the implementation of MAMs. We will discuss a variety of assays which benefit from the addition of mass data to deliver specificity and sensitivity not possible with optical only detection. Our discussion will include examples of analyses of peptides, proteins, released N-Glycans labeled with a novel labeling reagent, and detergents commonly used in biopharmaceutical formulations. We will compare results to those generated using orthogonal detectors and high end mass spectrometers.

Jessica Mondia

Scientist, Cell Culture Development, Biogen

Jessica Mondia received her PhD in physics from the University of Toronto in 2005. She held two post-doctoral positions: one in Germany at the Max Planck Research Group, Institute for Optics, Information and Photonics studying the optical properties of nanoparticles; and another in the Biomedical Engineering and Physics Departments at Tufts University studying silk-based biophotonic devices and laser ablation of biomaterials. In 2012 Jessica joined Biogen Idec, where she has been developing analytical methods to characterize cell culture raw material and working on biopharmaceutical forensic investigations.

Title: X-ray Fluorescence Method Development For Monitoring Inorganics In Raw Materials: Challenges, Strategies and Case Studies

Abstract: Numerous studies have demonstrated the impact of metals on cell growth and therapeutic protein quality. Monitoring and controlling both nutrient-relevant metals and impurities is key to process consistency. One strategy to mitigate inconsistencies is to measure inorganics in the raw materials used for cell culture. However, routine investigations of raw materials have been hindered due to the time and labor demands of traditional metal analysis techniques such as inductively coupled plasma mass spectrometry and atomic absorption spectroscopy. A promising tool for (bio-) pharmaceutical multi-elemental analytics is energy-dispersive x-ray fluorescence (EDXRF), which offers a cheaper, easier (click-of-a-button) and faster (minimal sample preparation) alternative. Since EDXRF is relatively new to the biopharmaceutical industry, this presentation will cover the challenges, strategies and long-term robustness of EDXRF for use in monitoring inorganics in raw materials.

Amr S. Ali

Scientist, Cell Culture Development, Biogen

I am currently researching methods of characterizing all cell culture raw materials used in the upstream process in order to increase process robustness. Previously, I worked in the Analytical Development group in Biogen researching methods of correlating nuclear magnetic resonance (NMR) and near infrared spectroscopy (NIR) and applying this method in the NIR wavelength selection process. I hold a Master of Science degree in bioinformatics and Bachelor of Science degree in Biomedical Engineering, both from Boston University. I am currently pursuing my Ph.D. in analytical biochemistry in the department of chemistry and chemical biology at Northeastern University.

Title: Predicting Cell Culture Robustness through Poloxamer Characterization

Abstract: Poloxamer 188 is routinely used in cell culture to protect cells from shear forces and detaches them from bubbles in sparged bioreactors. Recent trends show that certain poloxamer 188 lots have a significant negative effect on cell culture viability and can cause massive loss in viable cell density. Furthermore, this would negatively affect Biogen's manufacturing efficiency. Previously, size exclusion chromatography (SEC) with refractive index detection was used to differentiate types of poloxamers but was never used to investigate differences within one type. This work demonstrates that SEC can detect various species within a specific poloxamer type and with additional characterization of poloxamer's hydrophobicity profile through reverse phase chromatography, can predict the cell culture viability before a poloxamer lot is used in manufacturing.

PRESENTERS

Sun Koo Kim

Founder of QBD Works/Senior Manager, Bayer Healthcare

Dr. Sun K. Kim is a Quality-by-Design Evangelist - transforming how Product Development is executed in the Biologics, Pharmaceutical and Medical Devices industry. In addition, he teaches at Keio University and Stanford University. His current focus of research is Quality-by-Design, Agile Development of Drugs and Therapeutics.

He received his MS and PHD in Mechanical Engineering at Stanford University. Sun was recently a Professor at Keio University in Japan. Prior to Silicon Valley days, he served in the Korean Army and worked at BMW in Munich, Germany.

Title: How to Integrate Raw Material Variability in QbD Risk Assessment

Abstract: Raw material variability is just as important as process parameter variability.
How can development teams integrate both into their design space studies in a Quality by Design workflow?
QbD Risk Assessment provides the answer.

Carson Tran

Engineer, Process Development Engineer, Biogen

Carson Tran received his Bachelor of Science in Chemical Engineering from the University of Notre Dame in 2009 and his Master of Science in Chemical Engineering from Northeastern University in 2014. Over the last four years, he has been working at Biogen Inc., where his focus is on developing and optimizing challenging protein/oligonucleotide chromatography processes. He has also worked on developing ultrafiltration, viral filtration, and depth filtration unit operations.

Title: Mitigation of Chromatography Adsorbent Lot Variability through a Molecule Specific Binding Strength Test and an Adaptive Control Strategy

Abstract: Lot-to-lot variability in chromatographic adsorbent lots is of particular concern for purification processes where sensitive separations of product-related impurities (aggregates, misfolded or clipped species) are carried out, and can often result in negative impact to one or more critical quality attributes (CQAs) of the target product. Since the impact of adsorbent lot variability tends to be specific to the product being purified, vendors of chromatographic adsorbents may not be able to achieve the required level of control in adsorbent lot variability to ensure your target product quality profile is achieved. At times, biologics manufacturers have designed control strategies aimed at screening and selecting specific adsorbent lots that achieve the target CQA profile, while rejecting adsorbent lots that fail, when using a fixed manufacturing process. However, sourcing the ideal adsorbent lots may be challenging, since the specific adsorbent property that is impacting process performance may not be known.

This case study will focus on the best strategy for removing undesirable product-related isoforms, for a hydrophobic interaction chromatography (HIC) step. The process performance for this unit operation was highly sensitive to small changes in column loading as well as to changes in the HIC adsorbent lot. Adjusting the wash step volume based on molecule-specific small scale use test for a particular lot or blend of adsorbent lots allowed for consistent product recovery and product quality to be achieved.

Brian Fahie

Director, Technical Development, Biogen

Brian Fahie, Ph.D. is currently a Director within Technical Development at Biogen. Dr. Fahie's career path has included technical and management leadership roles with global responsibility for both large and small molecule development. Dr. Fahie is well respected for building world class organizations by effectively defining and differentiating between strategic capabilities and needed capacity.

Title: Dynamic Control Strategies: A current view of "What goes in, What goes on, and What comes out".

Abstract: Our understanding of structure and activity relationships is continually evolving allowing for an ever more refined approach to the development of biologic therapies. This in turn necessitates a better understanding of both the raw materials and the process parameters used to manufacture both drug substances and drug product. In fact, the state of "current understanding" can dramatically change over the commercial lifecycle of a product challenging the current view of a static control strategy. Subtle changes in raw material attributes can cause unexpected product quality variance necessitating an ongoing evaluation of critical material attributes of the raw materials. In this presentation we will explore the interconnectivity of "What goes in, What goes on and What comes out" and how we may need to add flexibility to "What goes on", when acceptance of a change in "What goes in" is necessitated in an environment of "What comes out" not changing.

Kelvin Lee

Professor, Chemical and Biomolecular Engineering, University of Delaware

Kelvin H. Lee is Gore Professor of Chemical and Biomolecular Engineering at the University of Delaware and is Director of the Delaware Biotechnology Institute. He received a BSE in Chemical Engineering from Princeton and PhD in Chemical Engineering from Caltech. He spent several years in the Biotechnology Institute at the ETH in Zurich, Switzerland and also completed a postdoc in Caltech's Biology Division. He is a Fellow of the American Institute for Medical and Biological Engineering and a Fellow of the American Association for the Advancement of Science.

Title: Application of the CHO Genome to CHO HCP Studies

Abstract: This presentation will discuss an application of genomics and proteomics related to CHO host cell proteins (HCPs). In particular, proteomics was used to identify difficult to remove HCPs using a series of studies to identify HCPs that change significantly in expression level as a function of cell age. Other difficult to remove HCPs are those that are product associated or that coelute on polishing resins. We identified a difficult to remove HCP that appears to have an impact on product formulations. In particular, the HCP appears to have an impact on degradation of polysorbates.

Application of Multivariate Analysis on Downstream Process Materials for Biologics Manufacturing

Marta C. Abad (Mass Biologics)

Abstract: Production of biologicals is inherently multivariate in nature, a complex endeavor by itself. The complicated cell machinery and its associated process controls become increasingly difficult to optimize while maintaining Critical Quality Attributes (CQA's) when variations in raw materials are introduced to the system. Multivariate analysis (MVA) can be applied to processing data to help identify correlations between raw materials and their effect on non-desirable product quality attributes. This presentation will overview approaches used to help decouple the complicated relationship of raw material impact on process and product quality attributes using standard statistical processes and their application to biological product development and life cycle management.

Flux balance analysis under different amino acid addition strategy in mammalian cell culture

Zhuangrong Huang, Kurt Brorson, Cyrus Agarabi, Scott Lute, Seongkyu Yoon (FDA, UML)

Abstract: One of the ultimate goals of systems biology research is to obtain a comprehensive understanding of the control mechanisms of complex cellular metabolisms. Flux Balance Analysis (FBA) is an important method for the quantitative estimation of intracellular metabolic flows through complex metabolic pathways and the elucidation of cellular physiology. Amino acid and glucose consumption, cell growth, antibody production and N-glycosylation patterns are always a key consideration during upstream process optimization, especially media optimization. Gaining knowledge on their interrelations and the relevant cellular physiology could provide good insight for higher and more consistent antibody production. The depletion of some amino acids other than the key nutrients such as glucose and glutamine also will affect the cell growth and product productivity and quality. Using a metabolic model, we will perform flux balance analysis FBA to investigate the metabolic changes and elucidate the cell behavior under different amino acid addition strategy. This analysis could facilitate the bioprocess optimization to some extent.

Multiplexed Hydrogel Microparticle Suspension Arrays for Facile Ribosomal RNA Integrity Assays

Yader Duenas, JaeHun Lee, Sukwon Jung, Hyunmin Yi (Tufts Univ.)*

Abstract: Rapid and reliable RNA integrity assay is important for a wide range of applications in genomics, diagnostics and biopharmaceutical processes, yet the existing technologies have certain limitations such as large amount of sample required, high cost of equipment and/or long turnaround times. We address this issue by developing a simple assay method to analyze bacterial ribosomal RNA (rRNA) from complex total RNA samples utilizing shape-encoded and single-stranded DNA-conjugated hydrogel microparticle suspension arrays with no need for target amplification and under standard fluorescence imaging conditions. Specifically, we demonstrate that our simple microparticle-based sensing scheme is reliable, sequence-specific and presents a responsive binding behavior to target total RNA concentrations. Moreover, the higher relative stability of 16S rRNA over 23S rRNA is proved by using a simple shape encoding-based multiplexed format assay. Combined, these findings represent a significant step toward cheap, fast, simple, and reliable assays for the analysis of RNA integrity and general analytical assays in bioprocesses.

Rapid and selective biomolecule conjugation via EDC/NHS reaction onto acrylic acid-co-acrylamide-co-bisacrylamide microspheres

Eric Liu, Sukwon Jung, Hyunmin Yi (Tufts Univ.)*

Abstract: Rapid, reliable, and cost-efficient analytical monitoring of products affected by raw materials variability is a critical component in biopharmaceutical process control, however current technologies do not allow for adequate control of the raw materials. For example, detecting changes in glycosylation profile of products upon modifying raw materials is important in determining product efficacy and raw materials control, but conventional liquid chromatography-mass spectrometry (LC-MS) techniques are inadequate in glycosylation profiling. There is therefore a need for facile biosensing platforms to overcome this critical bottleneck. Here, we demonstrate robust poly(acrylic acid-co-acrylamide-co-bisacrylamide) (pAMB) microsphere biosensing platforms for the rapid, selective and facile conjugation of model biomolecules via 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) / N-hydroxysuccinimide (NHS) chemistry. Tunable, uniform and porous hydrogel pAMB microspheres with abundant carboxylic acid functional groups are fabricated via surface tension-induced droplet formation in patterned PDMS molds and photoinduced radical polymerization. These microparticles are subsequently reacted with amine-functional fluorescent dyes and proteins via EDC/NHS chemistry. Fluorescence imaging demonstrates uniform and selective incorporation of target biomolecules in pAMB microspheres. Furthermore, kinetics results show rapid biomolecular conjugation under optimized conditions. These results illustrate the potential of our simple, powerful, and general fabrication-conjugation scheme for rapid and reliable analytical monitoring of biopharmaceutical products for process control.

Multi-variate data analysis for Protein A chromatography column

Ketki Behere, Seongkyu Yoon (UML)

Abstract: The objective of this project was to build a regression model which could explain the variability in the batch column chromatography dataset and provide some predictability to the user. The first step was to build a Batch Evolution Model (BEM) which could explain each chromatography step in detail and provide predictability power to the loading and elution step. The eventual goal of this project was to give a direct comparison between the different batches which had different resin.
It was also required to identify the important response variables out of the given seven (Column height, column diameter, Asymmetry, HETP, resin capacity, loading and elution concentration) which provided significant contribution to the given dataset and thus can be extrapolated to batch chromatography in general. A validation of the BLM model was required to prove the efficiency of the model.
The BEM model gave considerable predictability to the loading and elution steps and confirmed that those process steps were most important in the entire batch run. The BLM model gave definite segregation between the batches with different resin. Three response variables were identified to show significant contribution to the dataset. Those were the column height, HETP and elution concentration.

A genomics approach towards development of cell culture media formulation

Hemlata Bhatia, Seongkyu Yoon (UML)

Abstract: Biosimiliar drugs are emerging very fast as the patents of innovator's drugs are expiring. Media formulation development has to be carried out for each biosimiliar, which takes up a significant amount of time and generally, a random approach is taken to improve the product titer. A more targeted approach i.e. genomics study of host cell as a function of media composition can provide useful information to explain the product titer variability. A 2-step mechanistic model correlating product titer with media composition taking gene expression as connecting link can have a potential application in targeted media formulation development.

Core Research Facilities

Hamelin Therasa (UML)

Abstract: Core Research Facilities at the University of Massachusetts Lowell have a mission to provide world-class instrumentation and facilities to our faculty researchers and to prepare our students as the next generation of researchers. Our Core Research Facilities are managed by professional staff.

We share our scientific expertise and capabilities with the research community to attain our universal goal to provide access to expertise and facilities to conduct scientific research for the public good. Since purposeful education is a cynosure of our mission, our resource offerings are collectives of our experts, students, methods and instrumentation.

We offer hundreds of instruments and resources in a variety of areas including: bio and materials sciences and characterization, photolithography, mega materials, nanofabrication, gamma, reactor and neutron facilities and robotic testing.

Impacts of Multidrug Efflux Pumps on The Antimicrobial Effectiveness in Pseudomonas aeruginosa

Xiyu Li, Duy Lam, Guixin (Susan) He (UML)

Abstract: Pseudomonas aeruginosa is a gram-negative opportunistic pathogen that has been found to have increased resistance to multiple antimicrobials. The major resistance mechanisms in P. aeruginosa are the multidrug efflux pumps. The purpose of this study was to evaluate the effects of multidrug Effllux Pumps on the antimicrobial effectiveness. The efflux pumps that we evaluated are MexCD-OprJ and MexB. The wild type P. aeruginosa K767 was used to compare with two other strains K1523 (K767 ΔMexB) and K1521 (K767 ΔMexCD-OprJ). The antibiotics and (nanomaterials) were used in this study include gentamycin, tobramycin, erythromycin, tetracycline, oxacillin. The antimicrobial effectiveness tests were carried out by using Clinical and Laboratory Standards Institute (CLSI) standard method. The antimicrobial effectiveness of tetracycline, tobramycin, and gentamicin was significantly increased on the strain K1521 (K767 ΔMexCD-OprJ); the antimicrobial effectiveness of oxacillin and erythromycin were also significantly increased on the strain K1523 (K767 ΔMexB).

Hybridoma Bioreactor Processes: Dynamic Flux Balance Analysis

Thomas Reimonn, Seongkyu Yoon (UML)

Abstract: Dynamic flux balance analysis (DFBA) is a powerful technique to characterize intracellular reaction fluxes during microbial fermentation processes. DFBA consists in optimizing the biomass production rate subject to the constraints of linear stoichiometry system and extracellular media uptake/excretion rates. The benefit of DFBA is that it can calculate intracellular reaction fluxes as they change during fermentation processes.

A series of informed amino acid supplementation experiments were performed by the FDA and the data made public for further analysis. In order to understand the effects of media changes in the Mus musculus cell line, a dynamic flux balance analysis was performed on the 12 fermentation experiments using a genome-scale mouse metabolic model during the growth phase. The calculated reaction fluxes were examined using principal component analysis (PCA) and partial least squares regression (PLS). The results indicate that amino acid supplementation has little effect on the metabolic state of the cell culture during growth, and increases product yield by preventing depletion of critical nutrients towards the end of the culture. Additionally, the DFBA shows that metabolic state varies more at the beginning of the culture but less by the middle of the growth phase.

Feed on Demandtm – a Novel Technique to Monitor, Control, Manage, and Automate Upstream Mammalian and Microbial Feeding Protocols

Greg Emmerson, Sam Watts, George Barringer (Stratophase)

Abstract: A novel system, the Ranger™, and method for in-situ, real time monitoring and control of nutrient feeding in upstream bioreactors and fermentors is described. MRI (Metabolic Rate Index) is a Process Variable generated in real time by the Ranger that describes the overall state of the metabolic environment of the process under observation and is highly sensitive to any molecular level perturbation in the process media, such as occurs when a biological process is fed nutrients and carbon sources. MRI data in the Ranger system is used to construct an automatic feeding protocol – Feed on Demand – that responds at a cellular level to changes in nutrient concentration in media as a result of metabolic activity and automates feeding to maintain a proscribed optimum nutrient concentration to produce high quality, high yield product. The system is applicable to all scales of operation from process development to commercial production and is compatible with SUBs. This technology is applicable in microbial, fungal, and mammalian cultures.

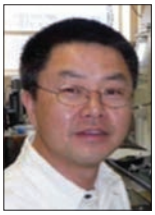
BPQC FACULTIES

Dr. Seongkyu Yoon is director of the Massachusetts BioManufacturing Center (MBMC), process system engineering and an assistant professor in the department of Chemical Engineering of the University of Massachusetts Lowell. His research area is Life Sciences Systems Engineering. Research covers Process Analytical Technology (PAT) and Quality by Design (QbD), Application of Design of Experiment (DoE) and MultiVariate Data Analysis (MVDA), supply chain management in biologics, and chemometrics in life sciences. Research aims at developing innovative systems technology with which one can improve drug development efficiency and manufacturing productivity, and developing innovative diagnostic systems and tools for selected diseases with chemometrics framework. He is currently developing system tools using a genomics and metabolic flux analysis approach to explain variability to productivity and quality of CHO (Chinese Hamster Ovary) mammalian cell-culture product. Integration of medical devices with multivariate statistical method is also being explored to develop practical diagnostic tools.

Dr. Yoon completed his Ph. D. in Chemical Engineering from McMaster University (Hamilton, Canada) under Prof. John F. MacGregor's supervision. Afterwards, he worked at Umetrics (Kinnelon, NJ) with Dr. Svante Wold and Nouna Kettaneh. He provided consulting and teaching on multivariate data analysis, experimental design, and batch analysis in various industries, pharmaceutical, biologics, semi-conductor, petrochemical, and financial. Before joining UMass Lowell, Dr. Yoon worked at Biogen Idec Biopharmaceutical Inc. as process analytics group leader of manufacturing sciences. He implemented MSPC (Multivariate Statistical Process Control) to all unit operations of both commercial and clinical manufacturing. This pioneering work significantly improved manufacturing robustness and clarity. The MSPC system is now considered as an industry standard which most biopharmaceutical manufacturers adapted as common manufacturing system. He also worked at Hyundai Petrochemical (now LG Chemistry) as a process engineer and implemented Advanced Process Control and Real-time Optimizer to ethylene manufacturing process in early 1990.

Dr. Hyunmin Yi is currently an Assistant Professor at the Department of Chemical and Biological Engineering of Tufts University. He received his B.S. in Chemical Technology and M.S. in Biochemical Engineering from Seoul National University, and Ph.D. in Chemical Engineering from the University of Maryland at College Park. He has published over 30 research articles in peer-reviewed journals such as Analytical Chemistry, Journal of Materials Chemistry, Langmuir, Nano Letters, Biotechnology and Bioengineering, and Lab-on-a-Chip.

He has extensive service activities for the biochemical engineering community as a panelist at many NSF grant proposal review panels, reviewer for over 20 journals, and has been chair for several sessions at ACS and AIChE National Meetings. He is currently the lead-PI on two NSF research grants. Professor Hyunmin Yi's broad research interests are viral nanobiotechnology and biosensors. In the first area, his group utilizes genetically modified tobacco mosaic viruses (TMV) for readily controlled metal nanoparticle synthesis toward applications in environmental catalysis, organic synthesis and energy. In the second area, soft-lithographic techniques are enlisted for robust fabrication of polymeric hydrogel microparticles toward rapid and reliable in-situ bioprocess monitoring. The overarching theme in both of these areas is to understand and exploit the selective and programmable properties of biological and biochemical materials and interactions in facile fabrication and assembly of multifunctional materials.



Dr. Jin Xu is director of the Massachusetts BioManufacturing Center (MBMC) Protein Analysis and Characterization Laboratory and an associate professor in the UMass Lowell Chemistry Department. He currently oversees and actively participates in protein structural/functional studies, protein product characterization and analytical development at MBMC. With his expertise in protein chemistry and biophysics, Dr. Xu also designs and conducts studies on the relationship between protein folding and protein productivity/quality.

Before joining UMass Lowell, Dr. Xu received his Ph.D in Biochemistry from the University of North Texas. Afterwards, he worked as Senior Research Scientist and Principal Scientist at Wyeth Pharmaceuticals for over five years, before most recently establishing and leading the protein chemistry group at Percivia, LLC.

BPQC FACULTIES

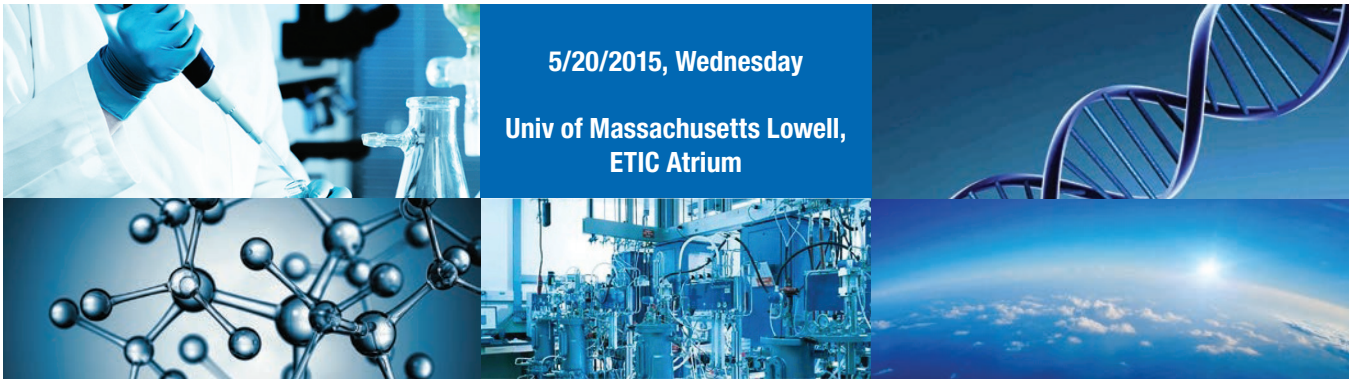
Dr. Carl W. Lawton is director of the Massachusetts BioManufacturing Center (MBMC) and Associate Professor in the Department of Chemical Engineering at UMass Lowell. As director of the MBMC, Dr. Lawton is responsible for overseeing the coordination and completion of process development client services including expression development, fermentation and cell culture development, downstream processing, process optimization and characterization. He works closely with companies on the verge of biopharmaceutical production to give them the opportunity to utilize the Center's services to economically address staffing needs and learning curve constraints and to optimize time to market.

Dr. Lawton creates and teaches customized training programs for biopharmaceutical manufacturing workforce as well as advising and teaching undergraduate and graduate students in the fields of chemical and biochemical engineering and others. He also is responsible for developing and maintaining an applied research program which focuses on technological advances to improve the quality, cost and productivity of large-scale biomanufacturing production. Before joining UMass Lowell and creating the MBMC, Dr. Lawton was a bioengineering process consultant to companies on both the east and west US coasts and in Canada.

Dr. Sanjeev Manohar is a Professor at the Department of Chemical Engineering at the University of Massachusetts Lowell and associate dean of the college of engineering. He holds Master's degrees in Chemistry from the University of Madras and in Organic Chemistry from Southern Illinois University and a Ph.D. in Organic/Polymer Chemistry from the University of Pennsylvania. His research is based on the synthesis and characterization of nanostructured materials for energy storage and medical applications; optically transparent, conducting films of carbon nanotubes on flexible substrates with performance that can rival commercial indium-tin-oxide conducting coatings; chemical warfare agent sensing using carbon nanotube coatings on flexible substrates; photocapacitors and batteries from dye-sensitized solar cells using a completely new design strategy involving plant extracts, and nanocarbons; green chemistry approaches to polymer/metal catalysts for fuel cells; synthesis and characterization of conducting polymer nanotubes/fibers and composites with noble metals; and controlled and targeted drug delivery across the blood-brain-barrier for treatment of Alzheimer's disease using nanoparticulate drug carriers.

Dr. Sadettin Ozturk is currently the Head of Process and Analytical Development, MassBiologics and Assistant Professor of Medicine, University of Massachusetts, Medical School. He has had a long career in cell culture process development, technology transfer, product licensing, and commercial manufacturing. His early contributions to the field focused on applying chemical engineering principles and process control strategies to the optimization and scale-up of cell culture processes. The scope of his work has expanded over the years, but it has always been focused on advancing cell technology. He was responsible for the development of numerous cell culture based processes and novel technologies that helped not only the companies that he worked for (Verax, Bayer, GlaxoSmithKline, and Johnson & Johnson), but contributed to the rest of the field through his numerous presentations and publications. Sadettin led process development activities and played a key role in the licensing and commercialization of two monoclonal antibodies, Stelera, and Simponi. In addition, he transferred and supported the commercial manufacturing of Kogenate and BeneFix. Sadettin has published numerous research articles, given presentations, delivered keynote lectures, and edited books. He is a member of several societies including ESACT, American Association for the Advancement of Science, New York Academy of Sciences, American Chemical Society, and American Institute of Chemical Engineering. Sadettin is involved in these scientific organizations and other community activities by serving on their Scientific Advisory Boards and organizing meetings and sessions. He has served Biochemical Technology (BIOT) division of American Chemical Society as the Division Chair, and then as a Councilor. He co-authored a well-respected book in the field entitled Cell Culture Technology for Pharmaceutical and Cellular Therapies. Sadettin also serves on Editorial and Review Boards for several journals and other publications.

NIST/AMTECH BIOMANUFACTURING SCIENCE AND TECHNOLOGY CONSORTIUM (BSTC) KICK OFF MEETING



AGENDA May 20 (Wednesday): 8:00 AM – 5:00 PM

8:00 AM	**REGISTRATION AND NETWORKING**
8:30 AM	**Welcome and Introduction/ Update** Seongkyu Yoon/Coordinator, Joe Hartman/Dean of Engineetring
9:30 AM	**Advanced Biomanufacturing – Broad Perspective (Facilitator: TBD)** - Industry perspective 1 (Biopharm Company) - Industry perspective 2 (Biopharm Company) - Research upstream perspective (Prof Kelvin Lee, UD) - Research downstream perspective (TBD) - Regulatory perspective (FDA or regulatory specialist) - Government perspective (Mike Tarlov, NIST) - Innovator perspective (Supplier, TBD) - Educators perspective (TBD) - Non-biomanufacturing perspective (Mel Koch, UW/CPAC)
10:30 AM	**BREAK**
10:45 AM	**Brainstorming (Facilitator: TBD) - 3 breakout sessions** - Advanced biomanufacturing – future statement - Biomanufacturing research – research challenges - Industry expectation on Advanced Biomanufacturing Consortium (BSTC)
12:00 PM	**LUNCH AND BRAINSTORNING SHARING**
1:00 PM	**CONCLUDING REMARKS**

ATTENDEES

Biopharmaceutical Core-faculty and Advisory Board Members: Rajesh Beri (Lonza), Thomas Ryll (Biogen), Jack Prior (Genzyme), Sadettin Ozturk, Neil Schauer, Tom Porter(Pfizer), William Thomas, Jin Xu, Carl Lawton

Academic co-directors: Weishou Hu (UMN), Hyunmin Yi (Tufts), Mel Koch (UW), Naz Karim (TAMU), Kelvin Lee (UD), William Bentley (UMD)

Industrial contributors: Chris Hwang (Genzyme), Anurag Khetan (BI), Daniel Bauer (GE), David Beattie/Vin Donovan (EMD Millipore), Brandon Downey/David Lyon/Jeff Breit (Bend Research), John Cadwell (Fibercell Systems), Maurizio Cattaneo (Biovolutions), Dharmesh Bhanushall (GSK), Brian Lee (PBS Biotech), Brad Pindzola (TIAX), Bert Frohlich (Shire), Jason Starkey (Pfizer), Kathleen Mihlbachler (Lewa), Sun Koo Kim (Bayer), Jean-Francois Hamel (MIT), Ann D'Ambruoso (ApplikonBio), David Strachan (Kaiser), Terry Hudson (Genentech), Melissa Calcagni (RDC), John Smelko (Biogen)

Education/Training Contributors: Bruce Van Dyke (QCC)

PI & Co-PI: Seongkyu Yoon (UML), Eric Masse (UML), Carl Lawton (UML), Kevin Bittorf (UML)

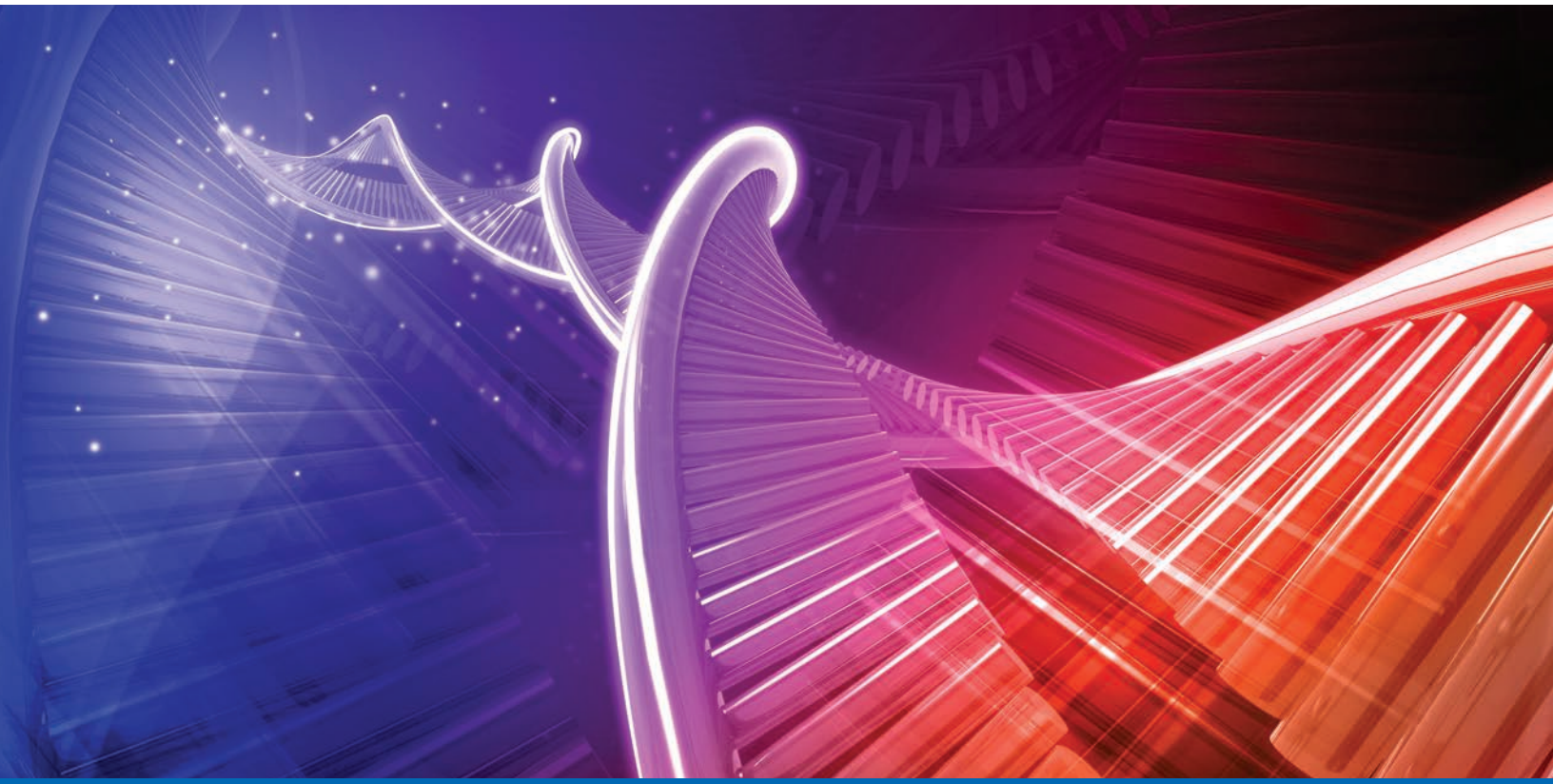
State Institute: Beth Nicklas/Susan Windham-Bannister/Pamela Norton (MLSC) **Advisors**: Mike Tarlov(NIST), Kurt Brorson(FDA)

BPQC STEERING COMMITTEE

Seongkyu Yoon, Assistant Professor of Chemical Engineering, Univ. of Massachusetts Lowell
Carl Lawton, Associate Professor of Chemical Engineering, Univ. of Massachusetts Lowell
Jin Xu, Associate Professor of Chemistry, Univ. of Massachusetts Lowell
Hyunmin Yi, Associate Professor of Chemical and Biological Engineering, Tufts University
Sanjeev Manohar, Professor of Chemical Engineering, Univ. of Massachusetts Lowell
Sadettin Ozturk, PhD, Mass Biologics, UMass Medical School, Head of Development and Analytical Technology

BPQC ADVISORY BOARD

(For question about the industry advisory board, please contact BPQC, bpqc@uml.edu)
Kevin Bittorf, Pharmaceutical Executive in Residence, University of Massachusetts Lowell
Neil Schauer, VP of Technical Operations, Avaxia Biologics Inc.
Thomas Ryll, Sr. Director of Cell-Culture Development, Biogen
Jack Prior, Sr. Director of Bioprocess Engineering, Genzyme
William Thomas, VP of Process Development, Mass Biologics
Tom Porter, Sr. Director of Analytical Research & Development, Global Biologics, Pfizer



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