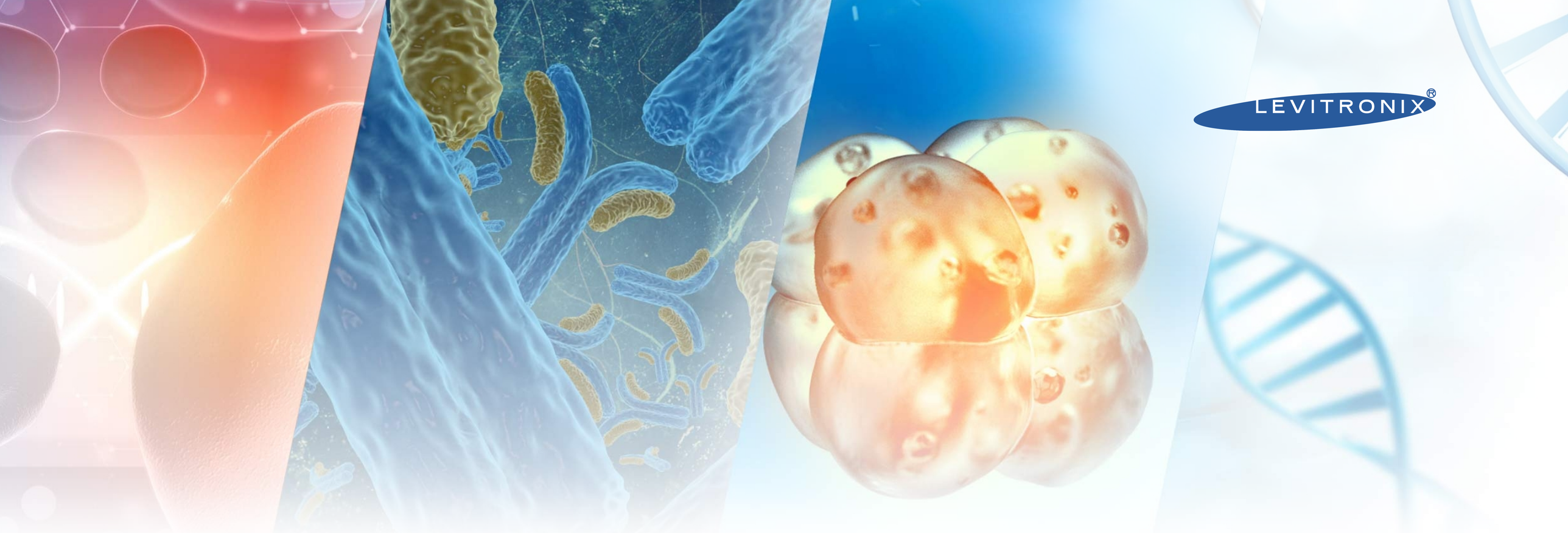


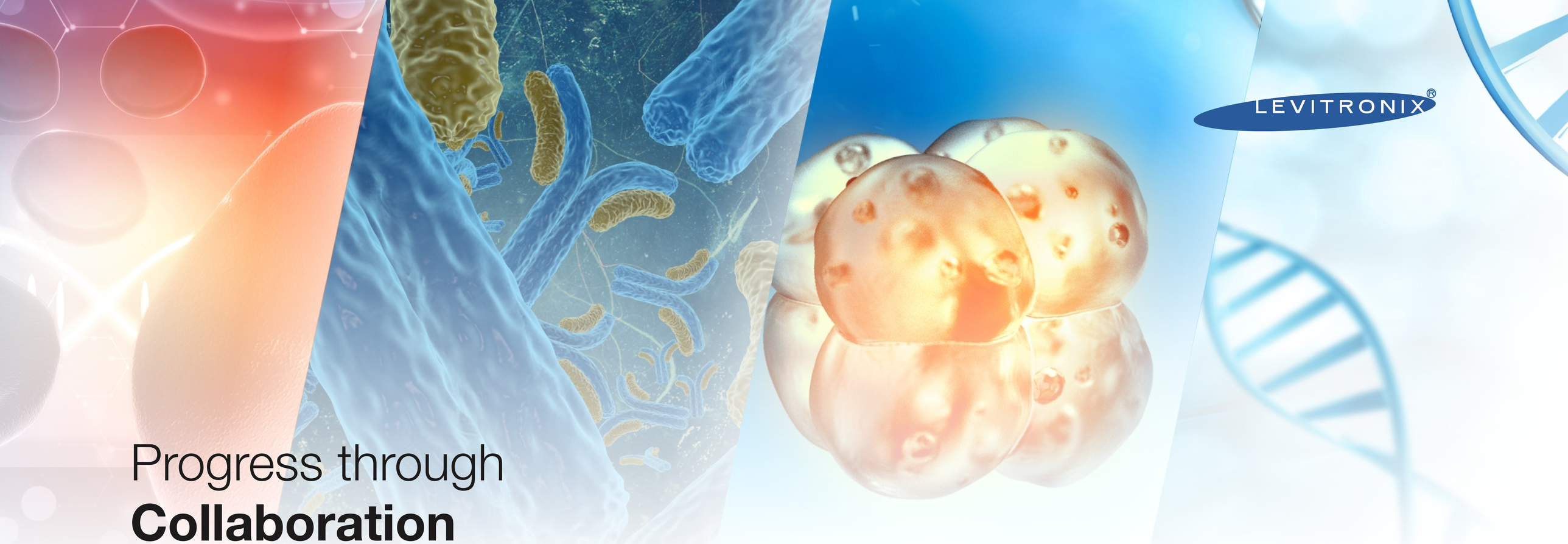
LEVITRONIX®

LEVITRONIX® BIOPROCESSING CONFERENCE 2022

June, 2

Hotel Royal Sonesta Boston
Cambridge, MA : USA

CONFERENCE BOOKLET



Progress through **Collaboration**

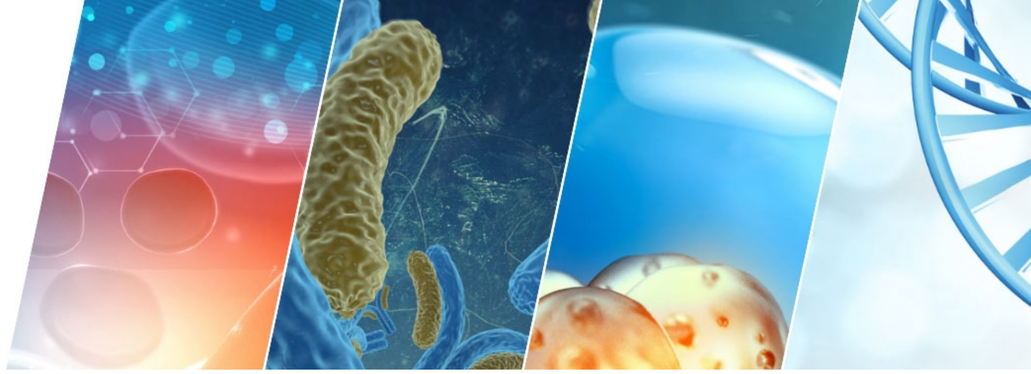
Rapid progress in biotechnology is poised to change the world in the years to come. However, the ever-increasing complexity of medicine confronts bioprocessing with significant challenges. Novel manufacturing technologies such as Single-Use or Continuous Manufacturing are still in an early stage of implementation.

We at Levitronix® believe that to build on the progress that the industry has made, end-users, system- and component suppliers must come together to reinforce what it takes to foster the trust and tight collaboration that's vital to the future success of bioprocessing.

The Levitronix® Bioprocessing Conference brings industry professionals together to make a change.

CONFERENCE AGENDA

Last update: 29 April



8:00 AM — REGISTRATION AND BREAKFAST PROVIDED BY LEVITRONIX

9:15 AM — Welcome & Introduction
Adrian Ljutic Levitronix

9:30 AM — KEYNOTE
Intensification, Integration, and Interrogation of Bioprocesses
Prof. Dr. Charles Cooney

10:00 AM — COFFEE BREAK PROVIDED BY LEVITRONIX

FOCUS BLOCK PERFUSION

10:30 AM — The Application of Levitronix® Pumps in the Scale Up of an Intensified Perfusion Process
Nikta Farsai Boehringer Ingelheim, Scientist II

11:00 AM — Contribution of Product Sieving to the Passage of High Molecular Weight Species in ATF and TFF Perfusion Cell Cultures
Magdalena Pappenreiter Bilfinger Life Science

11:30 AM — Process Intensification with Xcellerex APS
Radhika Jayakar Cytiva, New Product Introduction Leader

NOON — LUNCH BREAK PROVIDED BY LEVITRONIX

FOCUS BLOCK HARVEST

1:00 PM — Use of Modern Centrifugal Pumps in Bioprocess Design
Mark Gibson Abbott, Manager R&D Process Development

1:30 PM — New Approach for Single-Use Clarification of Biological Solutions
Bettina Ledergerber Filtrox, Global Application Engineer

2:00 PM — The Unique Development and Application of a Single-Use Disc Stack Centrifuge in Harvesting Biological Solids
Derek Ettie GEA Westfalia Separator, Director Separation Sales

2:30 PM — Integration of a Drive System Based on Magnetic Levitation Technology to Power a Stirred Bioreactor
Stefan Seidel ZHAW, Research Assistant

3:00 PM — COFFEE BREAK PROVIDED BY LEVITRONIX

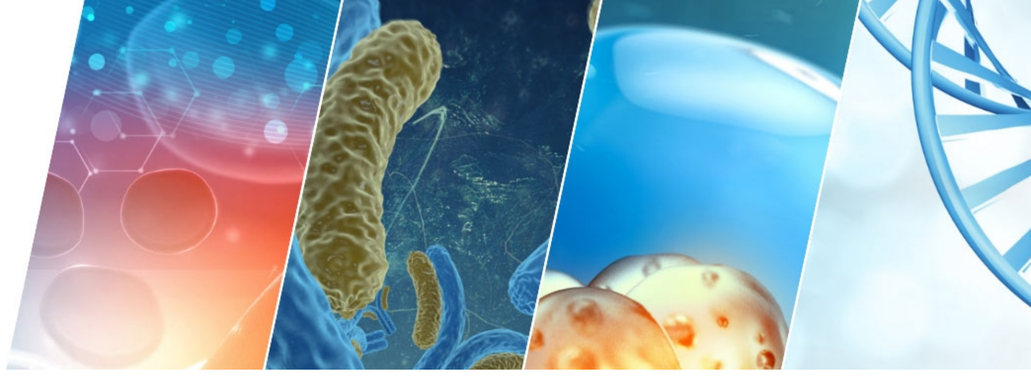
3:30 PM — Comparison of Maglev Centrifugal Pumping and Quaternary Diaphragm Pumping Effects on mRNA Encapsulated LNP
Mark McElligot bioX, Principal Process Engineer

4:00 PM — Concentration of E.Coli whole cells with a hollow fiber single use FlowAssembly
Bengt Persson Sartorius Stedim, Global Product Specialist Hollow Fiber Technology

4:30 PM — Evolution of Upstream Bioprocessing for Viral Vector Production
Maurizio Cattaneo Artemis Biosystems, Inc., Founder and CEO

6:00 PM — EVENING RECEPTION AT ROOFTOP PROVIDED BY LEVITRONIX

CONFIRMED SPEAKER



Prof. Dr. Charles Cooney

Professor Emeritus
Massachusetts Institute of Technology

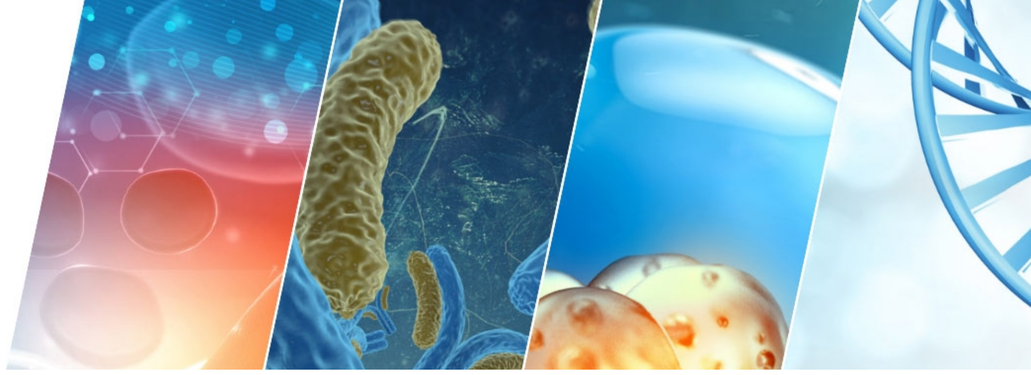
Charles L. Cooney is the Robert T. Haslam (1911) Professor of Chemical and Biochemical Engineering, Emeritus in the Department of Chemical Engineering at MIT and founding Faculty Director, Emeritus of the Deshpande Center for Technological Innovation. His academic career has focused on biotech and pharma process design, operation, economics and control; continuous processing has been a reoccurring theme throughout his research. He has been involved as founder, advisor or board member of over 25 companies and currently sits on the Boards of Directors of Codiak Bioscience, Innovent Biologics (1801.HK), Elektrofi, Iterative Scopes, Levitronix Technologies, LayerBio, Boyd Technologies and is chairman of GreenLight Bioscience. He was a member of the FDA Pharmaceutical Sciences Advisory Committee 2003-2006 and chair from 2005-2006. Prof. Cooney's research and teaching interests span a range of topics in biochemical engineering, pharmaceutical manufacturing and technological innovation. He has published over 250 research papers, over 25 patents and co-authored or edited 5 books including Development of Sustainable Bioprocesses: Modeling and Assessment, Wiley Press 2006. His teaching has focused on bioprocess development and manufacturing and technological innovation and is interested in the process of stimulating technological innovation and its translation from the university into new company creation.

Intensification, Integration and Interrogation of Bioprocesses

With increasing emphasis on biotherapeutics to meet unmet medical needs, continued scaling of global production and the introduction of new therapeutic modalities, we see a continuing need to develop bioprocesses faster and less expensively with assurance of high quality.

The strategy to achieve these goals involves three pillars: process intensification to reduce both variable and fixed costs, through high productivity, process integration to enhance speed of manufacturing and assure robust outcomes, and process interrogation to implement process control with on-line monitoring to assure consistent high product quality and minimal cost. These pillars provide a framework that provides guidance to those developing the tools and the processes supporting biotherapeutics manufacturing.

CONFIRMED SPEAKER



Nikta Farsai

Cell Culture Process Science
Boehringer Ingelheim

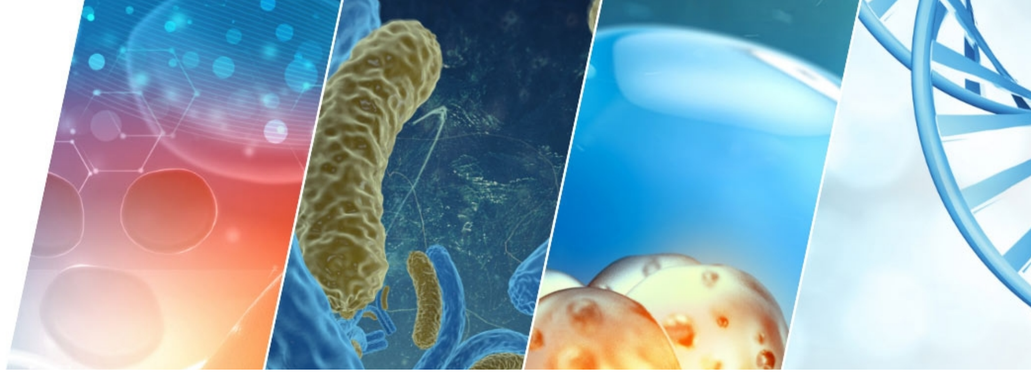
Nikta has over 7+ years of experience in pharmaceutical industry. She has been with Boehringer Ingelheim for 3 years and is a scientist II. She holds a Masters of Biostatistics from CSUEB and a Bachelor of Biotechnology from UC Davis. Previously, she worked at Genentech in commercial bulk drug substance manufacturing.

The Application of Levitronix® Pumps in the Scale Up of an Intensified Perfusion Process

As the demand for more cost-effective flexible processes is on the rise for the manufacturing of biologicals, process intensification has demonstrated to be a useful approach for this improvement. For the upstream process, perfusion cell culture has improved the yield for biological production. In our study, we used Levitronix® pumps for our perfusion process using Tangential flow filtration (TFF).

We were able to robustly scale up our intensified process from the bench to pilot scale using TFF process with disposable recirculating Levitronix® pumps. Process performance was comparable across the different scale, demonstrating no impact to the process.

CONFIRMED SPEAKER



Magdalena Pappenreiter

Junior Researcher
Bilfinger Life Science GmbH

After MSc graduation, Magdalena Pappenreiter started her career at Bilfinger Life Science GmbH as Biotechnologist in R&D with responsibilities in software development and soft-sensor implementation for advanced bioprocessing. She is currently a Junior Researcher at Bilfinger and a PhD student at the University of Natural Resources and Life Sciences (BOKU) in the field of integrated continuous bio manufacturing with emphasis on upstream processing. Her focus is on the implementation of process control models for perfusion, which are required for robust and stable process integration to subsequent downstream units.

Contribution of Product Sieving to the Passage of High Molecular Weight Species in ATF and TFF Perfusion Cell Cultures

Tangential flow filtration systems are widely used cell retention devices in perfusion cultures, but significant challenges occur with prolonged operation. A well-known and common issue includes membrane fouling, which leads to low efficiency and increased product retention. In this work, different process set ups and conditions were tested using magnetic levitation pumps for low shear TFF systems in small-scale perfusion bioreactors (200 ml). Process parameters such as cell growth, cell specific productivities and product sieving were compared with ATF systems. A novel concept based on the application of reverse flow across the hollow fiber using two magnetically levitating pumps was validated with a CHO cell line producing a recombinant monoclonal antibody (IgG). This approach makes it a valuable alternative to conventional ATF systems and can be used in various scales.

Moreover, a correlation between the passage of high molecular weight species (HMWS) to the harvest stream of the perfusion process and the mode of operation as well as the degree of product sieving was found. This results in important aspects in terms of product quality in integrated continuous bioprocesses.

CONFIRMED SPEAKER

Radhika Jayakar

New Product Introduction Leader
Cytiva

With an MBA and a Master's in Biotechnology, Radhika has been in the Consumer Products and Biopharma industry for the last 19 years. She has had a diverse career with roles in R&D, business development and product management. Her key focus over the last 3 years as New Product Introductions Leader within Cytiva has been in the Continuous Bioprocessing segment where she has led the APS NPI from product concept through to commercialization. Her strong understanding of customer needs as well as her deep knowledge on upstream continuous technologies has been key to the making of the Automated Perfusion System. Radhika is a mother to a 10-year-old and an avid traveler. Radhika welcomes you to explore the world of perfusion and possibilities through her presentation!

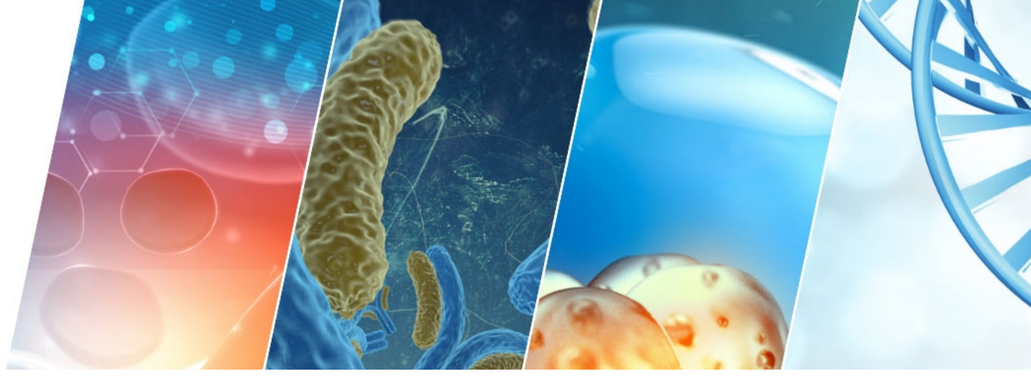
Process Intensification with Xcellerex APS

The Cytiva Xcellerex™ APS (Automated Perfusion System) enables mammalian cell culture customers to enhance existing batch seed, fed-batch production, and existing perfusion processes.

This technology has been tested using a traditional final seed stage (N-1) process controlled in perfusion mode using tangential flow filters for cell retention. This process was compared to the same process cultivated in a ReadyToProcess WAVE™ 25 bioreactor. The intensified N-1 seed perfusion process was seeded from an N-2 culture of Chinese hamster ovary (CHO) cells expanded in HyClone™ ActiPro™ medium and was fed in perfusion mode using HyClone™ Cell Boost™ Supplements 7a and 7b. The seed process achieved a final concentration of 179 million cells/mL. Seed viability and cell density growth trends were comparable to 5L and 25L N-1 perfusion seed cultures grown in a WAVE™ 25 bioreactor. All three seed cultures were expanded into a fed-batch flask process, all providing similar profiles for cell density, culture viability, protein productivity, and target protein product functional chemistry.

The fully automated control loops built into the Cytiva APS system empower customers to plug-and-play a fluid control system. This system is designed to pair with the current Xcellerex™ XDR-50, XDR-200, and XDR-500 using a standard perfusion bioreactor consumable. The APS maintains culture flow rates over and through a tangential flow filtration (TFF) ReadyToProcess™ hollow fiber filter, while monitoring for filter fouling by changes in filter pressure differentials using in situ pressure sensors. By offering automatic filter and media/permeate collection switching, the system reduces manual check-in and in-process manual manipulations to sustain a perfusion process relative to manual systems. Additional automated fluid controls ensure sustained media levels in the bioreactor and cell bleed functions via gravimetric and flow rate control. The form factor for the system allows for standardization of an operation foot-print for perfusion operations for culture volumes from 28L to 500L.

CONFIRMED SPEAKER



Mark Gibson

Manager R&D Process Development
Abbott Diagnostics

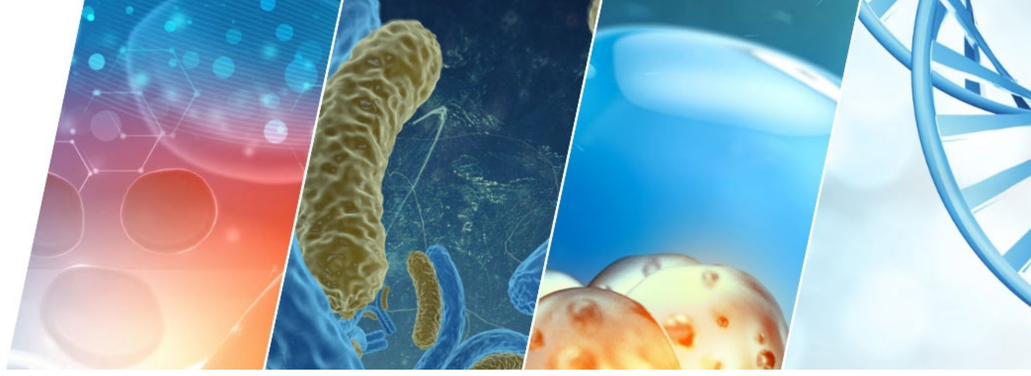
From fermentation laboratory technician to R&D Process Development Manager, leading manufacturing process teams to produce recombinant Antigens fromE. coli and Yeast fermentations.
Mark studied part-time to complete both Bachelor's and Master's Degree whilst working full-time. Progressed to Large-scale fermentation Team Leader, which involved; Technical Transfer of existing and new processes,Qualification of Facility,Utility and Equipment and development/ re-development of processes (utilizing newinnovative technologies), to increase product recovery and yields.

In his current position, Mark has a team of dedicated scientists who are deisgning and developing processes for the expression of various biologic molecules from mammalian and microbial culture systems. He's a Subject Matter Expert for Fermentation and TFF processes, with a passion for innovation and process improvement (Single Use Systems integration).

Use of Modern Centrifugal Pumps in Bioprocess Design

Bioprocessing technology is continuously evolving; higher density cultures and larger volume equipment are being employed to produce biomolecules; from monoclonal antibodies to recombinant antigens and many variants in between. At Abbott we are designing and developing state-of-the-art processes to produce different biologic molecules in both microbial and mammalian culture systems and have found that some well-known tools and technologies show limitations when used in state-of-the-art process designs. During the pandemic response we (Abbott) utilized our deep immunoassay understanding and platform process development strategies to rapidly bring to market new EUA tests for Covid-19. But we also had to expand our toolbox to enable rapid batch turnover and improve process flow between unit operations such as CHO cell culture harvesting and concentration prior to purification. Traditional culture clarification by normal flow filtration of high-density transient transfection cultures was very time consuming, utilizing large surface area filters and peristaltic pumps was inefficient, prone to fouling and expensive. Utilizing tangential flow hollow fiber filters and Levitronix controller and centrifugal pumps, we were able to simplify, reduce hands on time and improve process safety.

CONFIRMED SPEAKER



Bettina Ledergerber

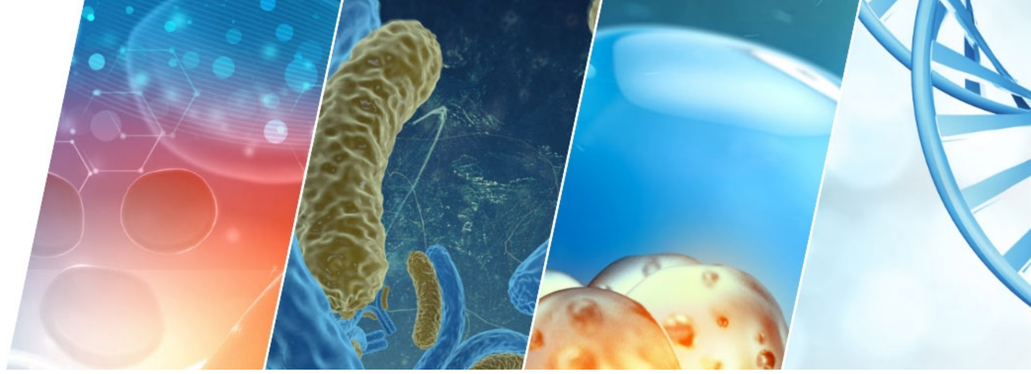
Global Application Engineer
Filtrox

Bettina Ledergerber is the global application engineer for Life Science at FILTROX. She is responsible for advising customers on filtration challenges and finding suitable solutions for new filtration tasks, especially for products produced biotechnologically by cell cultivation. Bettina brings a broad knowledge in the field of filtration with filter aids, also known as precoat or alluvial filtration. Furthermore, her experience includes supporting the sales team at trade shows and assisting in the development of new products. Due to her experience in the field of food microbiology, she is also familiar with the cultivation characterization of microorganisms.
Bettina holds a bachelor's degree in biotechnology from the Zurich University of Applied Sciences where she is currently also pursuing her master's degree in Life Sciences with the specialization in pharmaceutical biotechnology.

New Approach for Single-use Clarification of Biological Solutions

Depth filtration is one of the most efficient and economical types of filtrations and is often used in the biotechnology industry as the first step after cultivation of cells. In this process, the cells are often cultivated at high cell densities (HCD) so that they produce a specific target molecule. Depending on the cell types chosen, they may need further processing before harvest, such as lysis. Subsequently, the cells and cell fragments respectively, are to be removed using various processes so that the subsequent chromatography steps can be performed. However, these high cell densities and the different upstream process steps pose a major challenge in the subsequent downstream process. Here we show that with the help of a filter aid and the right choice of filter media, a significantly higher filter capacity can be achieved. By adding a filter aid to the unfiltered cell culture, a filter cake is formed on top of the filter layer, which leads to an increased filtration capacity. Based on the cell suspension to be filtered, different filter aids, and mixtures thereof, can be added. In addition to the maximized capacity, turbidity is also significantly reduced, so that chromatography or sterile filtration can be performed directly if necessary. This reduces the number of purification steps in the downstream process, which in turn saves time.

CONFIRMED SPEAKER



Derek Ettie

Director Separation Sales, Pharma
and Industrial Applications - North America
GEA Westfalia Separator

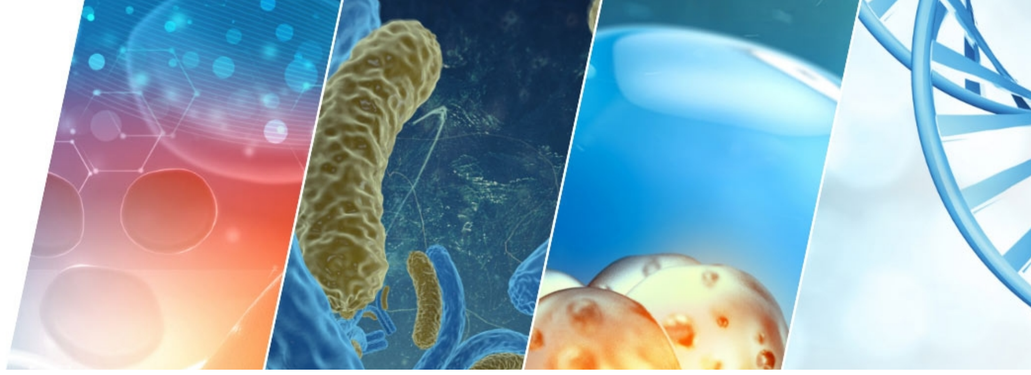
A Georgia Institute of Technology graduate with a degree in Chemical Engineering and a 38 year career in the centrifuge industry. Began at Sharples Separation as a process engineer with the responsibility of the start up and optimization of decanter and disc stack centrifuges in the pharmaceutical, chemical, food and Waste Water Treatment industries. Transitioned into the position of regional sales engineer for decanter centrifuges in the chemical and waste treatment industries at Sharples in the Chicago office. Became North American Centrifuge Market Manager of the Chemical/Pharmaceutical industry for GEA Westfalia Separator based out of Northvale, NJ. Moved into a Engineering and Sales Director position for the GEA North American Centrifuge process industries which included Dairy, Beverage, Chem/Pharma, and Renewable Fuels applications. His group responsibility included sales engineers, project engineers, electrical engineer and process engineer disciplines. Currently, Derek is Director of North American sales in the Chem/Pharma, Environmental, Marine, Energy, Oil and Gas markets.

The Unique Development and Application of a Single Use Disc Stack Centrifuge in Harvesting Biological Solids

GEA will be presenting on the new Kytero® single use disc stack centrifuge for harvesting mammalian and ecoli cells.

Initially GEA started the design based on the typical concept: stainless steel bowl, driven from the bottom by use of a spindle. We designed a single use bowl including a single use disc stack contained and supported by mechanical seals for a closed system. However, the mechanicals seals proved not to be robust/reliable and did not provide user friendly operation. Thus, GEA was looking for a new concept without a mechanical seal. GEA approached Levitronix® with our problem and due to their excellent technological knowledge, they were able to help us design a 100% bio-contained system without the use a mechanical seals. Working closely with the Levitronix® team in Switzerland, GEA tested new design concepts and created a prototype design which has since been successfully tested widely in the USA and Europe. Based on the success these tests the kytero 500 separator model was launched in Sep 2021. As a follow-on to the kytero 500, the larger model version – the kytero 2000 – which was already officially presented on the BPI West in San Diego in March 2022 will be launched this year
GEA very much appreciated the very fast and very professional working relationship with the Levitronix® team in the US, during this critical and successful product development effort.

CONFIRMED SPEAKER



Stefan Seidel

Research Assistant
ZHAW Zurich University of Applied Sciences

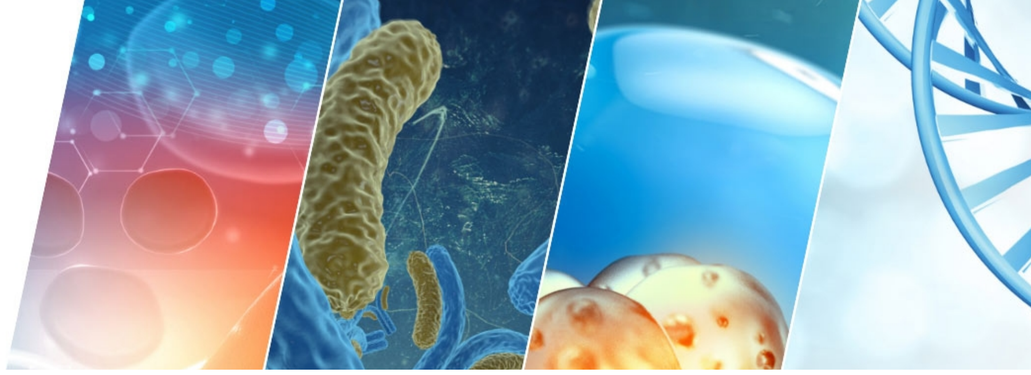
Stefan Seidel is a research assistant at the Institute of Chemistry and Biotechnology at the Zurich University of Applied Sciences. He holds a Bachelor's degree in Biotechnology and a Master's degree in Applied Computational Life Sciences and is currently a PhD candidate at TU Berlin.

In addition to teaching in the Bachelor's and Master's programs, he works on various research and development projects in the field of biochemical engineering and cell cultivation techniques. His focus is on classical process engineering characterization as well as Computational Fluid Dynamic (CFD) simulations and their validation using Shadowgraphy and Particle Image Velocimetry (PIV) measurements.

Integration of a Drive System Based on Magnetic Levitation Technology to Power a Stirred Bioreactor

Stirred bioreactors are still the most widely used bioreactors in biopharmaceutical production. Traditionally, the stirrer is driven via a shaft. However, this always carries the risk of contamination. An alternative is the stirred bioreactor developed here, which is magnetically driven by the Levitronix® BPS-i30 pump drive. This allows a contactless and magnetically driven stirrer which reduces the risk of contamination and provides an enormous rotational speed range. Typically, a distinction is made in bioreactor design between cell culture and microbial design, as different requirements are to be met by the system in each case. With the help of our developed system, it is possible to achieve similar or better cultivation results compared to commercially available benchtop bioreactors (in terms of cell density and productivity). In a first step, CFD simulations were performed for the process characterization. This resource-saving procedure allowed various setups to be investigated on the computer and suitable designs can be preselected. In particular, different stirrer designs were investigated. Selected designs were then characterized in the laboratory using standard biochemical engineering characterisation methods (mixing time, power input, oxygen transfer etc.). Following this, the system was biologically evaluated and compared with commercially available bioreactors. CHO cell lines were used on the one hand and an Escherichia Coli strain on the other.

CONFIRMED SPEAKER



Mark McElligot

Owner / Principal Process Engineer
bioX LLC

Mark McElligott has over 25 years of diversified Process Engineering experience operating as an industry subject matter expert in Single-Use Systems programming, development, design, and deployment. Mark's experience includes process development and process engineering for facilities and equipment used to support mRNA, Microbiome, mAb, ERT, GCT, HBOC, attenuated vaccine, and MDI/DPI drug manufacturing modalities. Process Development and Manufacturing Science experience inclusive of process design, product development, comparability assessments/testing, process equipment/instrumentation design, as well as relevant analytical methods development.

Mark is the owner of bioX LLC, based in Salem, NH. bioX provides a stage for the industry to conduct caparison, physical/mechanical, biological, and chemical testing across all manufacturing operations. bioX provides pilot scale manufacturing process feasibility testing, along with manufacturing operations expertise.

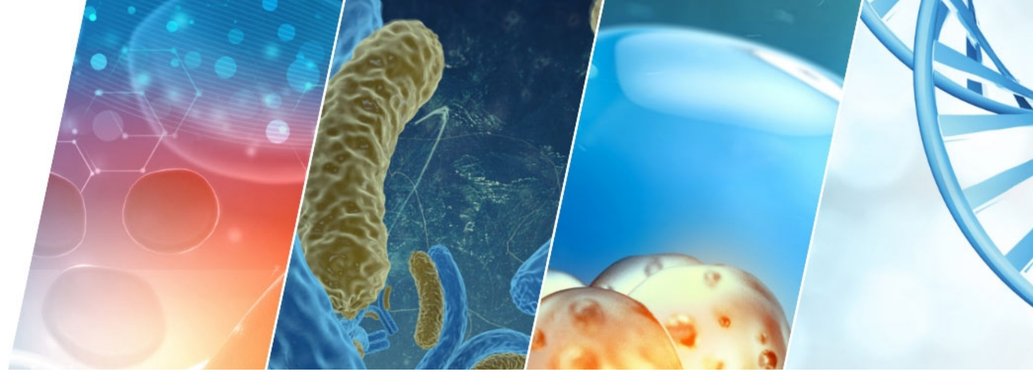
Mark holds an MS in Engineering from Purdue University where is also currently a Doctoral candidate in Engineering and Technology.

Comparison of Maglev Centrifugal Pumping and Quaternary Diaphragm Pumping Effects on mRNA encapsulated LNP

Messenger ribonucleic acid (mRNA) encapsulated in lipid nanoparticles (LNPs) is a vaccine modality that has found recent effectiveness and prominence within the biotech and pharma industries. Both the mRNA and LNP are susceptible to physical degradation and may present as fragmentation, aggregation, precipitation, fusion or leakage of mRNA from the LNP during manufacturing operations.

One proposed mechanism of physical degradation is processing of vaccine process intermediate solutions using recirculated pumping during unit operations such as tangential flow filtration (TFF). Some instances of prolonged recirculated pumping involve TFF which is a filtration unit operation used throughout the industry to concentrate and/or diafilter a product pool with a desired buffer. This study evaluates and compares a SU maglev centrifugal pump and a SU quaternary diaphragm pump and their associated physical effects on degradation of the mRNA and LNP fluid streams during typical manufacturing unit operations.

CONFIRMED SPEAKER



Bengt Persson

Global Product Specialist
Hollow Fiber Technology
Sartorius Stedim

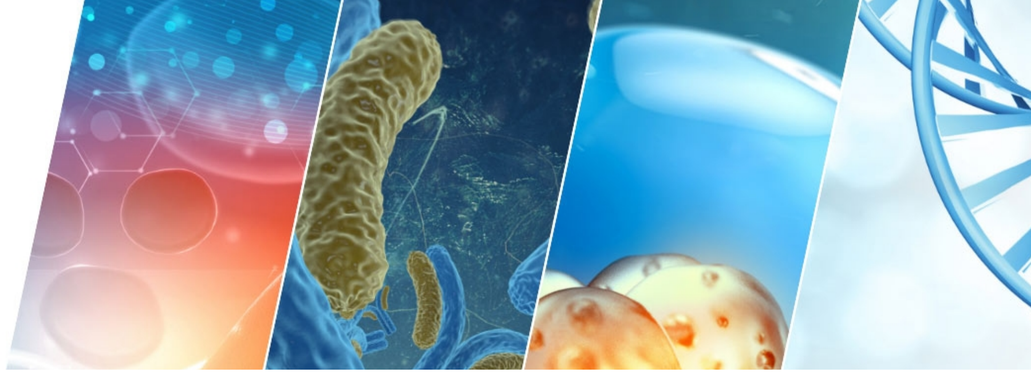
A founder at WaterSep BioSeparations, Bengt Persson has 40 years of experience in the biopharmaceutical industry; marketing and selling hollow fiber and flat sheet cassette membrane products and chromatography products to large pharmaceutical companies and life sciences organizations. He has founded and run companies in Europe and in the United States and has extensive experience in international sales and distribution, biopharmaceutical operations, as well as product marketing and business development. Bengt earned his Masters of Science in Chemical Engineering from the University of Lund in Sweden in 1976. Shortly thereafter he joined Millipore Corporation, where he held several sales and marketing positions in Europe. In 1984, Bengt signed on with Filtron Technology, as President and Founder of Filtron Scandinavia. Following Filtron's acquisition by Pall Corporation in 1995, Bengt was named Pall's Senior Vice President of Marketing for crossflow products. Subsequently, Bengt held vice president and director positions at Lonza Biologics. Amersham and GE Healthcare. In the early 2000s, Bengt founded a management consulting company in Boston, which focused on employee development and productivity enhancement, before joining WaterSep. At the acquisition of WaterSep BioSeparations by Sartorius in 2020, Bengt joined the Global Application Service Group. Bengt resides in Boston, MA.

Concentration of E.Coli whole cells with a hollow fiber single use FlowAssembly

A 10 L fermentation batch of E. Coli whole cells were concentrated 3.5 X and diafiltered with a 0.1 N PBS buffer. For concentration of the E Coli whole cells, an Investigator24 Green, 750 K MWCO hollow fiber membrane module was used, incorporated into a Single Use FlowAssembly with a PuraLev 600SU pump, a LeviFlow LFS-03SU SU flowmeter, feed, retentate and permeate pressure sensors and silicone tubing. The single use FlowAssembly was controlled by a Console LCO 600 unit.

A 3.5 X concentration was achieved with 4 DV volumes and a cell yield of >90%.

CONFIRMED SPEAKER



Maurizio Cattaneo

Founder and CEO
Artemis Biosystems, Inc.

Maurizio Cattaneo is the co-founder and CEO of Artemis Biosystems, a company specializing in process intensification for viral vectors and vaccine manufacturing. He is co-inventor of the patented VHUÒ technology which enables the rapid manufacturing of Viral Vectors for commercial production. The VHUÒ technology was validated through a NIIMBL grant together with MassBiologics for the cost-effective biomanufacturing of Lentiviral Vectors. Dr. Cattaneo directed and designed a multi-product pilot plant facility for the preclinical and clinical manufacturing of early phase clinical material.

He was also the founder and CTO of Ivrea Pharmaceuticals an early stage start-up developing a melanoma therapeutic and responsible for CMC to support Phase I/II Clinical Trials. Dr. Cattaneo is a certified pharmaceutical industry professional (CPIP) and holds a bachelor of applied science and engineering from the University of Toronto and a PhD in Chemical Engineering from McGill University.

Evolution of Upstream Bioprocessing for Viral Vector Production

Currently, cell and gene therapy commercial operations use Batch bioreactors which comprise a fixed volume and a limited number of cells and result in low vector yields and low vector stability at 37°C. Internal and published studies from commercial operations achieve total lentiviral vector yields around 2E+10 TU/L. Most recently, perfusion bioreactors have been adopted by commercial manufacturers which perfuse fresh media and remove waste materials at a controlled rate lead to higher cell densities as well as which results in increased vector production.

TFF Perfusion bioreactors using low shear recirculation pumps have been used to increase HEK293 cell densities up to 80 million cells per mL by continuously perfusing fresh media and removing waste metabolites. While standard hollow fiber filters used in ATF perfusion trap viral vectors inside the bioreactor, the tubular membrane VHU filter module together with a low shear Levitronix® pump allows the continuous transfer of unstable vectors such as Lentivirus to 2-8°C which leads to improved stability of the vector and results in higher yields and improved vector quality compared to batch processes. Total yields up to 6E+11 TU/L or 30-fold higher than batch have been achieved with stable producer cell lines.


LEVITRONIX®