The 31st International Symposium, Exhibit & Workshops on Preparative and Process Chromatography was held in Baltimore, MD, on July 8-11, 2018 at the Hyatt Regency Inner Harbor. The meeting was characterized by great energy and the participants were highly engaged in all phases of the Symposium from the Exhibit, to the Poster Sessions, to the Workshops and Tutorials, to the Oral Presentations, to the many social and networking functions. The symposium was attended by more than 320 people from 20 different countries (67% US; 83% industry). More than 100 pharmaceutical, biotechnology, and fine chemical companies, chromatography media, equipment and technology suppliers were represented. The PREP2018 sponsors were:

**Corporate Sponsors**
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The Symposium and Exhibit were managed by Janet Cunningham, Barr Enterprises.

Two half-day pre-conference Training Workshops, led by teams of experts in the field, were offered and attracted record numbers of attendees: (1) Fundamentals of Preparative Chromatography for Biomolecule Purification by Batch and Continuous Processes presented by G. Carta (Univ. Virginia), A. Jungbauer (BOKU, Vienna) and M. Morbidelli (ETH, Zurich); and (2) Fundamentals of Preparative Chromatography for Purification of Small and Intermediate Size APIs by Batch Chromatography, SMB, and SFC presented by G. Cox (PIC Solution and O. Dapremont (Ampac Fine Chemicals).

Two morning tutorials provided instruction in more practical aspects of preparative chromatography: Tips, Tricks, and Troubleshooting Analytical and Overloaded Prep Chromatography, taught by C. Mazza (AkzoNobel) and T. Yan (Pfizer), and Practical Concepts on Process Characterization and Validation of Biopharmaceuticals based on QbD Principles taught by G. Ferreira (MedImmune).

The Exhibit program featured 24 equipment, media, and technology suppliers, including many new, first time PREP exhibitors:

**Agilent Technologies**
- AkzoNobel/Kromasil
- Bio-Rad Laboratories
- Bio-Works

**CryoBioPhysica**
- DAIISO Fine Chem USA
- Essential Life Solutions
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- Thermo Fisher Scientific
- Wyatt Technology
- YMC America, Inc.

The exhibit provided ample opportunities to get acquainted with the very latest in stationary phases, systems, modeling software, and equipment for small, medium, and large-scale prep chromatography. Seven Vendor Workshops were also presented sponsored by Agilent Technologies, AkzoNobel/Kromasil, Bio-Rad Laboratories, GE Healthcare Life Sciences, Purolite Life Sciences, Thermo Fisher Scientific, and Wyatt Technology.

The Scientific Program included 70 oral papers divided in 5 keynote sessions, 3 plenaries, and 8 parallel sessions, as well as 90 posters.
Following tradition, the opening keynote session Industrial Case Studies in Protein Chromatography, organized and chaired by A. Hunter and T. Pabst (MedImmune), included five talks that provided opportunities to hear about some of the latest developments in the industrial purification of biopharmaceuticals. Y. Song (BMS) highlighted the process used to identify the mechanisms of antibody fragmentation and strategies to mitigate LMW species. J. Gavin (Merck & Co., Inc.) described the efforts by Merck and other companies in the ACS Biopharma Focus Group to assess and minimize the environmental impact of biologics operations as a part of an overall effort aimed at “greening healthcare”. C. Williams (Genentech) highlighted the impact of the digital transformation of process development on biopharmaceutical purification via the development and calibration of mechanistic models to predict bioprocess chromatography. C. Gerberich (GlaxoSmithKline) provided a detailed analysis of existing and new methods to determine internal and external porosities in bio-chromatography columns providing a useful summary of recommended best practices. In the concluding talk, H. Luo (MedImmune) reported on a detailed study that identified Cathepsin L as one of the major culprits affecting product quality during antibody production as well as strategies to control this enzyme using chromatographic resins.

The second keynote session, also a mainstay of the PREP Symposium, organized and chaired by T. Yan (Pfizer), focused on Preparative Chromatography in Drug Discovery, Development, and Manufacture, addressed the purification of small and medium size APIs by prep HPLC. F. Gritti (Waters) reported on a project joint with Pfizer aimed at developing recycling chromatography as a tool to obtain ultra-high resolution by prep LC. T. Kazarian (Amgen) highlighted efforts to address challenging separations of sugar-based compounds by LC and SFC using HILIC and nanoparticle-based stationary phases providing novel multimodal functionalities for these complex analytes.

J. Preston (Phenomenex) provided an extensive comparison of challenges encountered in the separation of small molecules vs. those encountered with peptides as well as the benefits and pitfalls of models used to predict separation based on the peptide sequence. T. Fornstedt (Karlstad U.) discussed modeling SFC separations, the transition from volume to mass controlled systems, and the benefits of using gradients in SFC. The final paper in the session, presented by T. Yan (Pfizer), discussed two interesting case studies addressing the challenging problem of isolating low-level impurities (present in APIs at levels of 0.05 to 0.1%) for profiling and structure evaluations using prep HPLC and SFC.

The third and fourth keynote sessions addressed Continuous and Integrated Processes for Biomolecules and Continuous and Integrated Processes for Small Molecules. Although the goal for both was to improve preparative chromatography by implementing multicolumn schemes that provide greater productivity and reduced mobile phase consumption, each session also addressed aspects that are unique to biomolecules and to small molecules purification. In the first of these keynote sessions, chaired by S. Kandula (Merck & Co., Inc.), M. Morbidelli (ETH Zurich) explained in detail the greatly improved tradeoff of productivity and capacity utilization afforded by the two-column Capture SMB and PCC processes as well as the improved tradeoff of yield and purity afforded by the MCSGP process. According to the presenter, large gains in product quality and productivity are attained when perfusion culture, Capture SMB, continuous virus inactivation, and MCSGP are implemented in a highly integrated and controlled process.
together with sophisticated automation and control systems. As noted by the presenter, such technologies can reduce the burden of cleaning and re-use validation studies as well as increase step productivity. K. Gillette (Pall Life Sciences) presented strategies for rapid process development focused on critical process parameters that are optimized to establish effective three-step continuous chromatography processes for clinical and commercial level mAb production. The next paper by A. Chibeirio (from the Mota group of at LAQV-REQIMTE NOVA, Lisbon) provided a change of gears by focusing on single column systems that can "mimic" the performance of multicolumn, continuous chromatography processes. According to the presenter, their single-column system shares the benefits of SMB but with reduced equipment complexity with potential applications to the purification of monoclonal antibodies, biosimilars, and viral vectors.

The second of the two sessions on continuous and integrated processes, chaired by O. Dapremont (Ampac Fine Chemicals), shifted the focus to small molecules. The opening paper presented by H. Johl (LEWA) addressed the integration of supercritical fluid extraction (SFE) and supercritical fluid chromatography (SFC) for the production-scale recovery and purification of natural products including chamomile, rosemary, lavender, Omega-3 fatty acids from fish oil and algae, and THC and CBD from hemp oil with processes operating at scales of 10,000 L/h. In the next paper, L. Grozdev (T.U. Munich) discussed another application to natural products using multicolumn chromatography to purify bioactive terpenes. Various process options were discussed with the conclusion that polystyrene-based resins with a multicolumn chromatography scheme yielded the best performance with >90% recovery and >98% purity and a 25% increase of productivity compared to batch chromatography. J.W. Lee (Max Planck Institute, Magdeburg) followed up with the development and experimental validation of a model predictive control strategy of a 4-zone simulated moving bed process for the separation of bicalutamide enantiomers. The experimental validation at pilot scale with four 2.5 cm ID x 15 cm long HPLC columns demonstrated stable production with 99% purity and yield. J.S. Hur (Novasep) discussed strategies and best practices to synthesize and purify APIs in a cost effective manner by implementing advanced chromatographic technologies. In the final paper, R. Woods (Ampac Fine Chemicals) addressed the issue of solvent contamination in SMB processes where >99% or even >99.9% of the solvent is recycled. The case studies presented highlighted how solvent contamination issues could throw a "wrench " into an otherwise "perfect" process and how contamination problems were identified and solved.

The last of the keynote sessions dedicated to Monoliths, Membrane Chromatography, and Column Characterization was chaired by C. Heldt (Michigan Tech). M. Rito-Palomares (Technol. de Monterrey) opened the session with a talk highlighting the application of monoliths for the purification of high-value biomolecules including the separation of PEGylated proteins using hydrophobic monoliths, the use of monoliths for in-situ ATPS, the purification of laccase with Q-type monoliths, as well as the potential for affinity monoliths using immobilized anti-

In the final paper of the session, S. Yamamoto (Yamaguchi U.) provided an overview of methods to calculate the productivity of continuous and cyclic chromatographic processes highlighting advantages and disadvantages of SMB in comparison to batch chromatography with stacked injections or repeated cyclic operation (ROC). According to the presenter, the ROC productivity can in some cases be higher than that of SMB suggesting that a careful analysis is needed in order to decide on the optimum process choice.
PEG antibodies and immunoaffinity monoliths for stem cell separations.

Next, A. Ley (Georg-August U. Goettingen) introduced the use of advanced optical microscopy techniques to visualize the structure of membranes containing a grafted 3D hydrogel for membrane chromatography as well as the kinetics of protein binding and elution in real time. The presenter suggested that the membrane can be visualized by CLSM at depths up to 7-8 μm using a specially-designed flow cell. In the next paper, D. Stein (Sartorius Stedim Biotech) described an experimental strategy using a high-throughput screening set up to determine the binding capacity and displacement effects during aggregate removal in membrane chromatography operated in flow-through mode. In a change of gears, the next two papers in the session focused on characterization of column packing. A. Martinez (T.U. Munich) described recent developments in the use of micro X-ray tomography to characterize the structure of chromatographic columns packed with agarose and methacrylic polymer based beads. The main problems associated with the low density and low X-ray absorption of these stationary phases was overcome by filling the particles with an aqueous buffer containing a radiocontrast agent and filling the extraparticle voids with an immiscible hydrophobic phase. The method allowed the 3D reconstruction of packed column structures with a 2 μm resolution and unprecedented clarity. In the final paper, S. Schweiger (BOKU, Vienna, currently with Shire) provided the results of a very extensive study comparing the packing quality, protein gradient elution, and protein breakthrough behavior of pre-packed chromatography columns ranging in size from 1 mL to 57 L. After properly accounting for extracolumn dispersion factors the presenter demonstrated the possibility of seamless scale up over 57,000 fold.

The three plenary sessions were dedicated to Mechanistic Understanding of Chromatographic Processes (chaired by L. Beaver, LAB Enterprises), Using Knowledge and Process Modeling for Design and Optimization (chaired by A. Lenhoff, U. Delaware), and to Applications to Virus, VLPs, and Vaccine Purification (chaired by M. Rito-Palomares, Technol. de Monterrey). In the first of these sessions, B. Beyer (from the Jungbauer group BOKU, Vienna) reported novel measurements of antibodies conformational changes upon adsorption onto HIC surfaces using differential scanning calorimetry (DSC). The in-situ technique showed that shifts in conformational stability occurred upon binding, but that the protein returned to its original conformation upon elution. C. Bilodeau (from the Cramer group at RPI) introduced the use of molecular dynamics simulation to examine the conformation of multimodal CEX ligands immobilized on surfaces. The results showed distinctive surface patterns with patches of hydrophobicity resulting from ligand-ligand interactions for certain ligands but not for others. The presenter indicated that future work will address how these patterns influence interactions with proteins and selectivity. The next paper by V. Kumar (from the Lenhoff group at U. Delaware) focused on the impact of resin architecture on modeling protein elution in ion exchange chromatography using a colloidal model to describe the single and multicomponent competitive interaction with the resin ligands.

C. Moore-Kelly from the Thomas group at U. Birmingham) addressed the real-time monitoring of the conformation of antibodies eluting from protein A columns. In this work, a combination of CD/fluorescence measurements, implemented with a specially designed fiber-optic cell, were used to monitor the effects of various elution conditions and buffer additives on the conformation of the eluted antibody. The last paper in the session was an industrial contribution by Y. Tao (Eli Lilly). In this study the product-HCP association observed during mAb production was extensively characterized using LC-MS to determine the distribution profiles of individual HCP species carried through difference processing steps. The data-guided approach was shown useful for developing processes that can achieve effective HCP removal.
In the session on using knowledge and process modeling, R. Khalaf (Novartis) described a comprehensive strategy based on knowledge and mechanistic modeling that allows de novo process predictions. Currently focused on ion exchange of biological molecules, the model is developed and tuned in just six working days and can be used to define optimum process sequences and conditions. In the next paper, E. Prade (Boehringer Ingelheim) introduced a standardized procedure to ensure rapid development of an effective process that allows for effective HCP, DNA, and virus removal.

According to the presenter, critical to this strategy is the choice of buffer systems that minimize the conductivity leading to improved HCP clearance.

A. Trapp (Rentschler Biopharma) presented a different strategy based on new, single-use technologies and process intensification for downstream processing. Three technologies were demonstrated, including “space-time optimization” of Protein A capture, resulting in high productivity at low residence times with minimal loss of DBC, batch chromatography in overload mode replacing traditional column processing, and adsorptive filtration for virus removal. C. Mueschen (Fraunhofer IME) illustrated modeling strategies to design and optimize processes of purifying proteins from plants including plastocyanin, aldolase, and RuBisCO. The approach uses a QSAR model to predict SMA model parameters, which are then used to predict protein separation on anion exchange resins. The last paper in the session by N. Warmeling (TU Braunschweig) focused on using chromatography to recover amino acids from the mother liquor during crystallization resulting in an integrated process that improves recovery while maintaining purity. A complete flowsheeting model was used to compare the recycling process with standard batch operation.

In the final plenary session, C. Heldt (Michigan Tech) introduced effective strategies to characterize the surface of virus particles using chemical force microscopy (CFM). CFM measures the interaction force between a virus particle and a ligand attached to an AFM tip. The method was demonstrated using both an enveloped virus (BVDV) and a non-enveloped virus (PPV) to determine the virus pl and surface charge as a function of pH as well as the virus topography. The presenter suggested that these measurements are critical to developing and understanding virus purification processes. In the next paper, P. Pereira Aguilar (from the Jungbauer group at BOKU, Vienna) presented a study on the adsorptive behavior of virus-like particles on polymer grafted ion exchangers. VLP binding was insensitive to salt concentration but, based on both CLSM imaging and transmission electron microscopy, was confined to a fairly thin layer near the chromatography bead surface. Despite this limitation, the resin was able to achieve purification with direct loading of cell culture supernatant and subsequent elution with a salt gradient. R. Silva (IBET, Portugal) presented the development of a continuous multi-column chromatographic process for the purification of extracellular vesicles (EVs). According to the presenter, continuous chromatography of these naturally occurring nanoparticles has the potential to improve not only purification efficiency and economics but also product quality.

A. Van’t Oever (Intravac) discussed the use of intensified processes to improve the yield of inactivated polio vaccine candidates that are aggregation prone. As a part of a WHO program for the global eradication of polio, Intravac is developing new vaccines based on attenuated Sabin poliovirus strains which are produced through a DSP that includes concentration, size exclusion chromatography, and anion exchange chromatography followed by inactivation. Yield improvement guided by batch-mode HTS studies, focused on minimizing aggregation and was achieved using a tandem column set-up with direct transfer of the virus between columns. M. Knight
(CC Biotech LLC) concluded the session by discussing a broad range of applications of centrifugal precipitation chromatography (CPC) including the fractionation of large proteins and virus-like particles. In one example, CPC was able separate AV9GFP with a salt gradient. According to the presenter, purity was a little less than using ultra-centrifugation but the results were nonetheless encouraging for a one-step process.

The 8 Parallel Sessions covered a broad range of topics in prep chromatography: Protein A - Fundamentals; Protein A - Resins; Stationary Phases I, II, and III; Fundamentals and Modeling of Chromatography; Alternative Chromatographic Processes; and Processes and Applied Process Modeling.

The Poster Program sponsored by Bristol-Myers Squibb and co-chaired by D. Antos (Rzeszow U., Poland) and I. Quinones-Garcia (Mersana Therapeutics) comprised a total of 90 posters presented in alternate days and covering a very broad range of chromatography problems and solutions for fine chemicals, APIs, and biomolecules. Details on the parallel and poster sessions can be found in the PREP2018 Final Program at www.PREPsymposium.org.

**Best Poster Competition Award Winners**

**First place winner – presenter from Industry:** David Nellis, Joseph Brewer, Erik Read, “Commercial-scale Chromatography Column Sanitization Enhancement through Practical Outgassing Prevention Strategies”, AstraZeneca, Frederick, MD, USA.

**First place winner – presenter from Academia:** Camille Bilodeau, Ed Lau, Shekhar Garde, Steve Cramer, “The Effect of Multimodal Ligand Chemistry and Architecture on Ligand Conformation and Presentation in Chromatographic Systems”, Rensselaer Polytechnic Institute, Troy, NY, USA, Lawrence Livermore National Laboratory, Livermore, CA, USA.

As PREP2018 Chair, I want to thank all of the sponsors, the exhibitors, the participants, the contributors, and the members of the Organizing, Scientific, and Industrial Advisory Committees for making this Symposium a success. I am delighted to announce that PREP2019 will be held again in Baltimore, MD, USA on July 7-10, 2019 at the Hyatt Regency Inner Harbor. As in past years, PREP2019 will be held in conjunction with ISPPP2019, the 39th International Symposium on the Purification of Proteins, Peptides and Polynucleotides, held on July 10-12 at the same venue. One-day overlap between the two conferences will provide PREP2019 attendees with expanded coverage of bioanalytical techniques and further advances in biopurification.

Follow program updates on the PREP Symposium website www.PREPsymposium.org, on LinkedIn, and by receiving our PREP Symposium newsletters. Contact Janet Cunningham at janet@barrenterprises.com to be added to the mailing list.

We look forward to seeing you in Baltimore in 2019 for another exciting symposium, exhibit, and educational workshop program.

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**Photo of David Nellis (left) with judging committee member C. Frech and Symposium Chair G. Carta**

**Photo of Camille Bilodeau (left) with judging committee member C. Frech and Symposium Chair G. Carta**

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*Full list of award recipients will be posted at <www.PREPsymposium.org>.*