# Meeting Report: 28th International Symposium, Exhibit and Workshops on Preparative and Process Chromatography


The **28th International Symposium, Exhibit & Workshops on Preparative and Process Chromatography** was held in Philadelphia, PA, on July 26-29, 2015 at the Loews Hotel. The symposium was attended by more than 350 people from 21 different countries (68% US, 32% non-US; 17% from academia, 83% from industry). More than 45 pharmaceutical, biotechnology, and fine chemical companies were represented along with 44 chromatography media, equipment and technology suppliers.

PREP2015 sponsors were, **Ampac Fine Chemicals, Bristol-Myers Squibb**, **Elsevier/Journal of Chromatography A**, **Genentech**, **GlaxoSmithKline**, **MedImmune**, **Merck & Co., Inc.**, **Phenomenex, Pfizer**, and **Shire.**

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

Four pre-conference **Training Workshops**, led by a team of experts in the field, were offered: (1) **Preparative Chromatography for Biomolecule Purification**, (2) **Preparative Chromatography for Purification of APIs**, (3) **Continuous Chromatography for Biomolecule Purification**, and (4) **Regulatory Fundamentals and QbD for Biopharmaceuricals**.

The **Exhibit program,** included 25 equipment, and media suppliers:

Ace Glass
Agilent Technologies
AkzoNobel/Kromasil
Bio-Rad Laboratories
Biotech USA LLC
Buchi Corporation
ChromWorks
DAISO Fine Chem USA
Essential Life Solutions
Graver Technologies
KANEKA Corporation
Knauer
Labomatic USA
LEWA-Nikkiso America
Mitsubishi Chemical Corporation
NOVASEP
Phenomenex
Purolite
Semba Biosciences
Separation Methods Technologies
SP Scientific-Genevac
Thermo Fisher Scientific
Tosoh Bioscience
Waters Corporation
YMC America

The exhibit provided ample opportunities to get acquainted with the very latest in stationary phases, systems, software, and equipment for small, medium, and large-scale prep chromatography. Five **Vendor Workshops** were also presented by **AkzoNobel/Kromasil**, **LEWA-Nikkiso America**, **Mitsubishi Chemical Corporation**, **Purolite**, and **Thermo Fisher Scientific**.

The **Scientific Program** included 74 oral papers in 4 keynote sessions, 7 plenaries, and 8 parallel sessions, as well as 90 posters.

The opening keynote session, sponsored by **Elsevier/Journal of Chromatography A**, was **In Memory of Georges Guiochon (1931-2014)**. Guiochon, who started the PREP Symposium in 1985 and chaired it annually until last year, is widely considered as one of the pillars of preparative chromatography. He published well over 1,000 papers and several books, including "Fundamentals of Preparative and Nonlinear Chromatography" (Academic Press), the most authoritative treatment of the subject to date. As of July 2015, according to Web of Science™ (Thomson Reuters), Guiochon's scientific articles have been cited more than 29,000 times. The session included technical talks by the following internationally recognized leading scientists:

A. Felinger, Univ. Pecs, HUNGARY

M. Morbidelli, ETH Zurich, SWITZERLAND

A. Seidel-Morgenstern, Max Planck Inst. for Dynamics of Complex Technical Systems, Magdeburg, GERMANY

T. Fornstedt, Karlstad Univ., Uppsala, SWEDEN

F. Gritti, Univ. of Tennessee, Knoxville,TN, USA

In addition, session co-chairs K. Mihlbachler (LEWA-Nikkiso) and I. Quinones-Garcia (Shire) presented more personal perspectives about the impact Guiochon had on them as graduate students and on the chromatography community.

The next keynote session on **Industrial Case Studies in Protein Chromatography** included talks by MedImmune, Merck, Bristol-Myers Squibb, and Roche. T. Pabst (MedImmune) introduced **novel**

**protein A ligands engineered to enable elution at milder pH while retaining high mAb binding capacities.** J. Welsh (Merck) illustrated how **miniature columns can be used effectively in a high throughput-screening format to save time and materials in mAb purification process development**. G. Barker (Bristol-Myers Squibb) described a **strategy that integrates high-throughput process development (HTPD) tools with mathematical modeling to predict column behavior** from batch isotherms and batch uptake curves. T. von Hirschheydt (Roche) concluded the session by addressing the challenges encountered in the **manufacture and purification of novel antibody formats including bispecific antibodies (CrossMAbs)** both through upstream and downstream process improvement strategies.

The third keynote session was dedicated to **Preparative Chromatography in Medicinal Chemistry.** P. Searle (AbbVie) described **integrated purification solutions for medicinal chemistry and high-throughput synthesis** in pharmaceutical discovery where each product is purified immediately upon reaction to allow the accelerated production of vast libraries. H. Eastwood (Amgen) described **use of mixed mode columns for the analysis and prep purification of complex nucleotide sugar mixtures.** J. DaSilva (Merck & Co., Inc.) demonstrated a **systematic approach for impurity isolation by utilizing multiplatform chromatographic systems in parallel** resulting in a streamlined overall workflow with shorter timelines. In the last talk of the session, K. Chen (Merck & Co., Inc.) described their **automated purification workflow integrating crude analysis, purification, fraction analysis, final QC and compound registration into one central database**.

The last of the four keynote sessions, sponsored by **Phenomenex**, was dedicated to **Process Scale Purification of Peptides and Oligonucleotides**. G. Erickson (CBL Biopharma) presented several examples of **chemically synthesized complex peptides, including the commercial 36-amino acid Fuzeon® peptide, where different chromatographic purification strategies resulted in cost and purity advantages**. S. McIntyre (Almac) presented a number of case studies where **optimum chromatographic modalities and operating conditions where developed to produce peptides of appropriate quality at high recovery**. M. Biba (Merck & Co., Inc.) described the **purification of synthetic oligonucleotides**, increasingly important as part of antisense and siRNA drugs. According to the presenter, successful oligos purification methods typically include ion-pair RPLC or SAX-LC. The last paper in the session presented by R. Black (Bristol-Myers Squibb) discussed the science behind the **selection of stationary and mobile phase, and column size for the medium scale purification of peptides**.

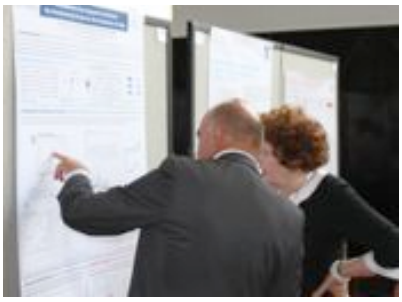
**Advances in Understanding and Modeling Biomolecular Interactions in Chromatographic Purification** was the subject of an exciting plenary. A. Lenhoff (U. Delaware) introduced a new approach to **characterize protein adsorption on chromatographic materials using small-angle neutron and X-ray scattering**. It appears that these techniques are capable of revealing aspects of protein binding with unprecedented level of molecular detail. S. Banerjee from the group of S. Cramer (RPI) presented **molecular modeling techniques to predict binding free energies of proteins to multimodal chromatographic surfaces** along with a comparison of modeling and experimental results based on single molecule force spectroscopy. A. Osberghaus from the group of J. Hubbuch (KIT) continued on the theme illustrating how **molecular dynamics (MD) simulation can be used to gain fundamental insight and a link to global process understanding**. In the final paper, D. Antos (Rzeszow U., Poland) addressed the problem of **solubility limitations encountered during protein elution from overloaded chromatographic columns.** Her model-based approach provides a way to predict conditions where supersaturation occurs during elution in order to be able to avoid undesirable precipitation within the column.


The next plenary session was devoted to **Innovative Chromatographic Materials**. O. Thomas (U. Birmingham) discussed the development of new **magnetic microparticles to streamline and improve the efficiency of processes used for protein purification**, with special emphasis on valuable veterinary proteins. A process called

"**High-Gradient Magnetic Fishing**" (HGMF) was described making efficient use of magnetic particles in bioprocessing. S. Dimartino (U. Canterbury, NZ) described advances in **manufacturing chromatographic columns via 3D printing technology** and the their use as models to characterize flow heterogeneity by deliberately building in defects. R. Khalaf from the group of M. Morbidelli (ETH, Zurich) addressed the behavior of **new stationary phases containing polyelectrolyte (PLE) brushes**. A model based on a modified Langmuir isotherm was used to describe protein binding. The final talk by R. Marcus (Clemson U.) described the **chemical modification of uniquely structured fibers (C-CP fibers) via lipid-tethered ligands** for biochromatography applications.

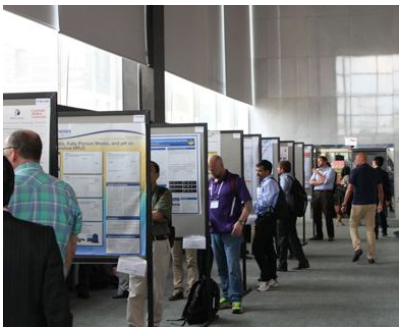
The next plenary addressed **Chromatography for Large Biomolecule Purification**. A. Jungbauer (BOKU, Vienna) discussed the preparative **high-resolution separation of variants of virus-like particles (VLPs) using polymethylmethacrylate monoliths**. The presenter demonstrated the production of at least 150 doses of a VLP-based vaccine in 2 hours with a 1 mL monolith. R. Silva (iBET, Portugal) discussed the **chromatographic purification of VLPs as a candidate hepatitis C vaccine**. A process using insect-cell based expression coupled with flow-through and bind-elute chromatographic steps was shown to form the basis for a GMP-compliant manufacturing process. P. Baumann (KIT) illustrated the use of **high-throughput screening (HTS) tools to rapidly develop efficient processes for VLP production** based on bacterial cells expression systems. In the concluding talk, A. Podgornik (FKKT, Slovenia) discussed the use of novel **mixed-mode monoliths for the chromatographic purification of plasmid DNA (pDNA)**. The presenter demonstrated a single step process removing RNA, HCP, and genomic DNA to purify 1.5 mg of pDNA per mL of monolith directly from a cell lysate.

A plenary session on **Monoliths and Membrane Chromatography** provided further examples of emerging materials and processes for biomolecule purification. J. Rasmussen (3M) presented new **anion exchange membranes based on a bioinspired ligand with high protein binding capacity and salt tolerance**. The presenter noted that capacities approaching or exceeding 200 mg/mL of membrane volume are possible. J. Buyel (RWTH Aachen U.) showed how **membrane filtration could substitute chromatographic purification steps** for plant-derived ELP-tagged biopharmacautical proteins. H. Bai (SnG, Inc., Japan) introduced **novel perfusion chromatography media based on pulverized silica monoliths** packed in chromatography columns. According to the presenter, the new media provides better resolution for peptides and proteins compared to traditional materials despite their larger particle size and lower operating pressure. In the final paper, K. Rogler (Pall Life Sciences) illustrated the **benefits of coupling single-pass tangential flow filtration (SPTFF) to multicolumn chromatography (MCC) for continuous capture of biomolecules**. The combined SPTFF-MCC process was shown to be economically advantageous for low-titer feedstock.



The final three plenaries were dedicated to **Supercritical Fluid Chromatography (SFC)**, **Centrifugal Partitioning and Countercurrent Chromatography (CPC/CCC)**, and **Manufacturability and Integration of Bioprocess Chromatography**. In the **SFC session**, J. McCauley (Waters) highlighted the use of **SFC for the separation, measurement, and isolation of trace impurities** found in APIs and other feedstocks. Fractions recovered from SFC were found to be appropriate for 1D and 2D NMR. J. Preston (Phenomenex) discussed using **SFC with polysaccharide stationary phases for chiral separation**. The presenter noted that SFC could be conveniently used for fast screening at the analytical and prep scale and then switched to LC for larger scale separations. M. Wong (Genentech) provided an overview of Genentech's purification groups supporting small molecule purification and isolation in medicinal chemistry. While the majority of compounds are separated by RP-HPLC, **compounds that are sensitive to water or that are found in acidic or basic environments are best purified by SFC**. In the final talk of the session, T. Fornstedt (Karlstadt U., Sweden) offered **theoretically based guidelines for reliable scale-up of preparative SFC**.

The **CPC/CCC session** provided updates and advances in these **support-free chromatographic separation processes**. L. Marchal (Nantes U., France) provided an overview of CPC focusing on **advanced tools to visualize and understand how hydrodynamics are affected by scale including a new dimensionless correlation that can be used to predict flow pattern transitions**. J.-H. Renault (URCA, France) discussed applications of CPC to the **purification of alkaloids from Catharanthus roseus industrial extracts** reporting productivities up to 2.5 kg/L column/day. G. Yanik (PDR-Separations.com) described advances in CCC technology based on **automated method development strategies for prep-scale purification**. D. Thornton (GlaxoSmithKline) discussed two **examples of CCC applications developed based on automated solvent screening strategies** and transferred to the one-liter scale for processing.



The last session of the symposium on **Manufacturability and Integration of Bioprocess Chromatography** featured three papers by MedImmune, Biogen Idec, and AbbVie). N. Birkett (MedImmune) described an **automated, scale-down approach to evaluate their platform purification process** for mAbs, bispecifics, and Fc-fusion proteins enabling screening 48 candidates in two days with just 16 mg of protein.

S. Siva (Biogen Idec) described their efforts to **streamline implementation of high-throughput robotics systems in bioprocess development** with new tools that simplify use by non-experts. The final talk by N. Ram (AbbVie) described the use of **single column recycle chromatography as a simpler alternative to continuous chromatography** for applications including enrichment of variants for characterization as well as biologics manufacturing.

The **8 Parallel Sessions** covered a broad range of important topics in prep chromatography: **Strategies and Processes for Biomolecule Purification**; **Stationary Phases for small molecules and for biomolecules**; **Process Modeling and Design**; **Continuous Chromatography for small molecules and for biomolecules**; **Bioprocess Chromatography**; and **Chromatographic Theory**.

The **Poster Program** comprised a total of 90 posters presented in alternate days and covering a tremendous range of prep chromatography problems and solutions for fine chemicals, APIs, and biomolecules. A complete list of the oral and poster papers can be found at www.PREPsymposium.org.

Winners of the **Best Poster Awards**, selected by an independent panel of judges, were recognized on Wednesday.

### Best Poster Award Winners*

**First place winner** - presenters from Academia – **J. Angelo**, A. Lenhoff, "Determinants of Protein Elution Rates from Preparative Ion-exchange Adsorbents", University of Delaware, Newark, DE, USA

**First place winner** - presenters from Industry – **L. Tsang**, K. Dave, J. Calzada, G. Barker, M. Borys, Z. Li., Y. Li, "Comparing Definitive Screening Design to Traditional Experimental Designs for Hydrophobic Interaction Chromatography Optimization", Bristol-Myers Squibb, USA

*Full list of award recipients is available at www.PREPsymposium.org

On behalf of the Organizing Committee and as PREP2015 Chair, I want to thank all of the sponsors, the exhibitors, the participants, the contributors, and the members of the Scientific and Industrial Advisory Committees for making this Symposium a success.

**PREP2016 will be held again at the Loews Philadelphia Hotel, in Philadelphia, PA, on July 17-20, 2016**. Program details will be posted in the near future at www.PREPsymposium.org.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