



TOSOH THE CUSTOMER MAGAZINE

NO. #01
2018

APPLICATIONS/ALPS/AQUARIUMS



TOSOH BIOSCIENCE

02 EDITORIAL DEAR READER

Welcome to the spring issue of the Tosoh Bioscience customer magazine. From April 10 to 13, analytica 2018 will open doors in Munich. We invite you to visit our booth (A2.412) to discuss your separation needs with our specialists and check out the news from Tosoh.

You are working in downstream processing and would like to enjoy a thorough update on latest trends? Just check out page 8 and save the date for the next HIC/DSP (former HIC/ RPC) Conference, which will take place in February 2019 in Interlaken, in the Swiss Alps.

In this issue we continue our series of portraits of Tosoh colleagues: We would like to introduce Patrick Stahlberg to you, a colleague who recently joined our Sales team.

ENJOY READING AND STAY INFORMED.

REGINA ROEMLING | SENIOR MARKETING MANAGER
TOSOH BIOSCIENCE GMBH

THE SUPER-T - COMIC #8



JUST CHECK IT HERE: HIC-DSP.ORG

➤ CONTENT

- | | | |
|------------------|---------------------------|-----------------------|
| ➤ PAGE [02 - 03] | ➤ EDITORIAL | ➤ SCHOLARSHIP |
| ➤ PAGE [04 - 05] | ➤ APPLICATION DSP | ➤ APPLICATION GPC |
| ➤ PAGE [06 - 07] | ➤ TOSOH HISTORY | ➤ PEOPLE BEHIND TOSOH |
| ➤ PAGE [08] | ➤ HIC/DSP CONFERENCE 2019 | ➤ NEWS & EVENTS |

➤ IMPRESSUM

- TOSOH BIOSCIENCE GMBH
➤ IM LEUSCHNERPARK 4 | 64347 GRIESHEIM | T: +49 [0] 6155 70437-00 | F: +49 [0] 6155 8357900 | INFO.TBG@TOSOH.COM

03 WHAT'S NEW SCHOLARSHIP

TOSOH BIOSCIENCE WELCOMES SCHOLARSHIP RECIPIENT IN THE EUROPEAN HEADQUARTERS

SIMON HÄNLE, MASTER STUDENT IN PHARMACEUTICAL BIOTECHNOLOGY AT THE BIBERACH UNIVERSITY OF APPLIED SCIENCES IN GERMANY, RECEIVED A SCHOLARSHIP, THE DEUTSCHLANDSTIPENDIUM, PARTLY SPONSORED BY TOSOH BIOSCIENCE GMBH. THE SUPPORT FROM TOSOH BIOSCIENCE IS NOT ONLY FINANCIAL. SIMON WILL RECEIVE SCIENTIFIC AND TECHNICAL SUPPORT FROM OUR EXPERTS IN THE PURSUIT OF HIS STUDY AND CAREER. WE INVITED HIM TO OUR EUROPEAN HEADQUARTERS TO DISCUSS ABOUT HIS MASTER'S THESIS AND ABOUT HIS FUTURE.

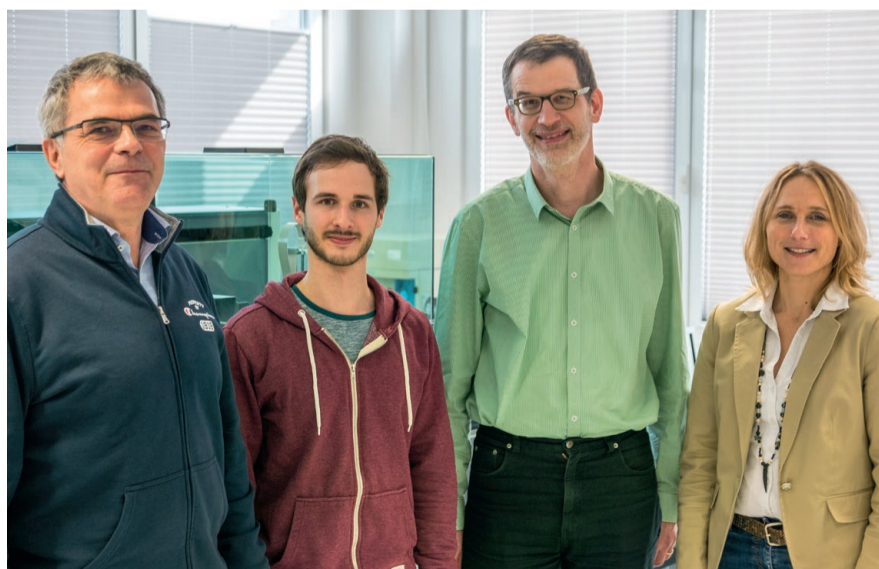
Over the course of his university studies, Simon has worked very ambitiously to achieve excellent results and has voluntarily participated in research projects at the Institutes of the University. The Biberach University of Applied Sciences awarded a scholarship to him, the Deutschlandstipendium. This scholarship follows the principle of public-private partnership. Businesses or foundations, in this case Tosoh Bioscience GmbH, sponsor fifty percent; the Federal Government of Germany matches this amount.

Simon already heard about Tosoh products when working in laboratories using TSKgel columns. His first direct contact with Tosoh Bioscience occurred during the Scholarship Ceremony. Regina Römling our Senior Marketing Manager awarded the scholarship personally. She invited Simon to visit Griesheim to get to know Tosoh Bioscience better. He came to our office in February and met colleagues from Technical Support and Marketing.

Simon, delighted that Tosoh Bioscience provides students insights into the work of a manufacturer of chromatography columns, stated: "I hope to develop good cooperation with my scholarship provider. For a student, contacts in companies such as Tosoh Bioscience are important starting points for networking. With a scholarship, vice versa, companies naturally also try to establish contact with students or educational institutions to attract the attention of future specialists or to participate in teaching."

At the end of the visit, Simon shared some impressions he gathered in our headquarters: "I was pleasantly surprised to see how much time everyone took to introduce the company and talk to each other. Above all, I was impressed by the intensive cooperation with customers on a very personal level, despite the large and increasing number of projects."

However, Simon's interest is more in research and development. He is currently working on his master's thesis at Boehringer Ingelheim in Biberach and plans to continue his career with a Ph.D. thesis in natural sciences. He is looking for suitable institutes and research institutions that are primarily concerned with disease mechanisms and tumor genesis. On a longer term, he would like to stay in the pharmaceutical industry and be involved in the development of new therapeutic approaches and their implementation.



➤ SIMON HAD THE OPPORTUNITY TO DISCOVER THE TOSOH BIOSCIENCE APPLICATION LAB.

FROM LEFT TO RIGHT: DR. EGBERT MÜLLER, TECHNICAL DIRECTOR, SIMON HÄNLE, SCHOLAR, ACHIM SPRAUER, SENIOR TECHNICAL SPECIALIST PROCESS, AND HEIKE ROSENFELD, MARKETING PROJECT SPECIALIST

04 APPLICATION DOWNSTREAM PROCESSING

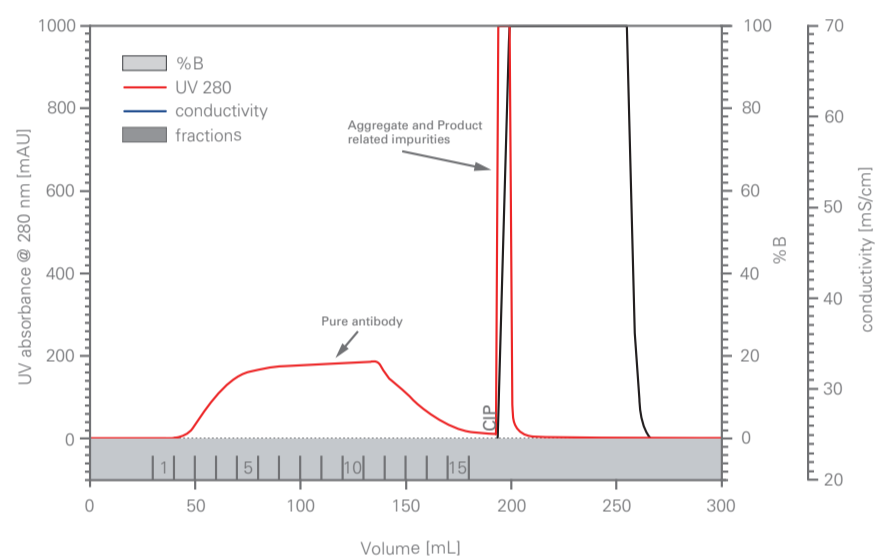
TWO-STEP PURIFICATION OF MONOCLONAL ANTIBODIES

BIOPHARMACEUTICALS ARE EXPECTED TO GENERATE MORE THAN HALF OF GLOBAL PHARMACEUTICAL REVENUE BY 2020 [1]. IN THIS DRUG CLASS, ANTIBODIES ARE THE PREDOMINANT MOLECULES WITH OVER 400 CANDIDATES IN THE CLINICAL PIPELINE. HOWEVER, DRIVEN BY CURRENT CHALLENGES ON COSTS AND TIME, THERE IS A NEED FOR MORE EFFICIENT ANTIBODY PURIFICATION METHODS. THE HIGH CAPACITIES AND UNIQUE SELECTIVITIES OF TOYOPEARL AF-rPROTEIN A HC AND TOYOPEARL NH2-750F ENABLE THE DESIGN OF A TWO-STEP ANTIBODY PURIFICATION PROCESS.

Standard downstream processing (DSP) for antibodies usually involves three chromatographic steps. These three subsequent steps remove product-related impurities such as antibody aggregates and fragments, host-cell proteins (HCP), endotoxins, viruses, and DNA [1]. The first step - capturing on protein A resin - leads to purities > 95%. An intermediate purification step and a polishing step using any combination of cation-exchanger (CEX) or anion-exchanger (AEX), hydrophobic interaction chromatography, or mixed-mode chromatography remove the remaining impurities.

We developed a new two-step DSP method. Capturing is performed on a high-capacity Protein A resin - TOYOPEARL AF-rProtein A HC-650F [2]. Intermediate and polishing are achieved in a single step on a salt-tolerant anion exchanger - TOYOPEARL NH2-750F. This latter resin is not only removing viruses and DNA, as expected. It is also eliminating aggregates and the other product-related impurities [3]. The figure on the right is depicting the purification profile of a post-Protein A aggregated mAb in flow-through mode.

The use of the cost-optimized TOYOPEARL AF-rProtein A HC leads to a significant productivity increase at the capturing step [4]. Moreover, halving the number of subsequent chromatography steps not only reduces the costs of the overall process and the production time. It is even increasing productivity further through decreasing development costs and duration, while total yield increases.



PURIFICATION PROFILE OF THE ANION EXCHANGE FLOW THROUGH STEP

REFERENCES:

- [1] BIOENGINEERING 2014, 1, 188-212; DOI:10.3390/BIOENGINEERING1040188
- [2] TOSOH APPLICATION NOTE A17P05: HOW TO...IMPROVE PERFORMANCE OF THE PROTEIN A CAPTURING STEP
- [3] TOSOH APPLICATION NOTE A15P80: MAB AGGREGATE REMOVAL IEC IN BIND/ELUTE AND FLOW THROUGH MODE
- [4] TOSOH APPLICATION NOTE A16P04: A HIGH CAPACITY PROTEIN A RESIN DESIGNED TO REDUCE PRODUCTION COSTS

05 APPLICATION GPC

EcoSEC: A TOOL TO DETERMINE THE PROCESS PROPERTY RELATIONS IN POLYMERS

THE EXCELLENT REPRODUCIBILITY OF GPC ANALYSES ON THE EcoSEC AMBIENT TEMPERATURE GPC SYSTEM TOGETHER WITH THE DEDICATED CALCULATION WORKSTATION ACCOUNT FOR THE PRECISE DETERMINATION OF THE MOLAR MASS OF A POLYMER. BOTH FEATURES ALLOW ESTABLISHING DIRECT RELATIONS BETWEEN THE DEGREE OF POLYMERIZATION AND THE MOLAR MASS, LEADING TO THE CHARACTERIZATION OF PROCESS PROPERTIES.

Polyvinyl chloride (PVC) is a thermoplastic polymer that has the property of softening under temperature and hardening when cooled. The average molecular weight and the molar mass distribution (MMD) of PVC extensively influence its properties. The number of monomer units in a polymer chain is referred to as the degree of polymerization (DP). The DP of a polymer can provide indications on the molecular weight of a polymer. Synthetic polymers always comprise a set of macromolecules of varying DP and respectively varying molecular weight. Polymers with identical composition but different molecular weights may exhibit different physical properties. In general, increasing DP values correlate with higher melting temperature and higher mechanical strength. Here, we show the variation in MMD with increasing the DP of PVC samples.

The molar mass averages and molar mass distributions of two PVC samples, PVC 6 (DP = 620-660) and PVC 13 (DP = 1270-1370), were determined via a dual flow RI detector using the EcoSEC GPC System and semi-micro TSKgel GPC columns in THF. Figure 1 shows the GPC chromatograms of the two PVC samples. The MMD of PVC 6 is shifted to the lower molar mass region compared to that of PVC 13. This result shows that the DP is directly related to the molar mass of PVC.

The EcoSEC workstation software was used to calculate a calibration curve and determine the MMD and the average molecular weights. Each sample was injected three times to determine the coefficient of variation. The reproducibility of the measurements is excellent. Figure 2 depicts the differential and cumulative distributions of molar masses.

Even though the amount of crystalline regions of PVC is meager, many researchers study the crystallization behavior. The crystallinity of PVC is inversely proportional to the molar mass. In this study, PVC 6 showed a low molar mass from which we can conclude a higher crystallinity. With an increase of crystallinity, the polymer tends to show higher tensile strength. These reasons make PVC 6 attractive for applications such as the production of rigid plates, extruded sheets, draw films, blow bottles, and injection molding.

However, the tensile strength decreases with increasing molar mass, but due to longer polymer chains, the tensile strain or the elongation of the polymer increases. Due to these reasons, PVC 13 can be used for agricultural films, general flexible films, sheets, artificial leathers, wires and cables, food films, and tape.

To summarize, the GPC analysis shows that PVC 13 has a higher MMD compared to PVC 6. GPC analysis reveals the direct relationship between the degree of polymerization (DP) and the molar mass of PVC. GPC is a great tool to investigate the process property relations in polymers.

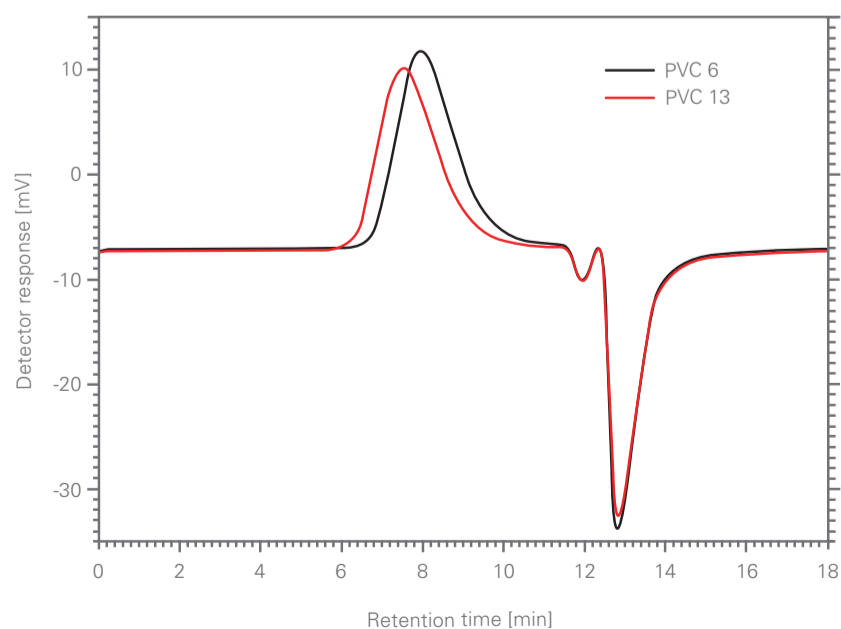


FIGURE 1: ELUGRAMS OF THE TWO PVC SAMPLES

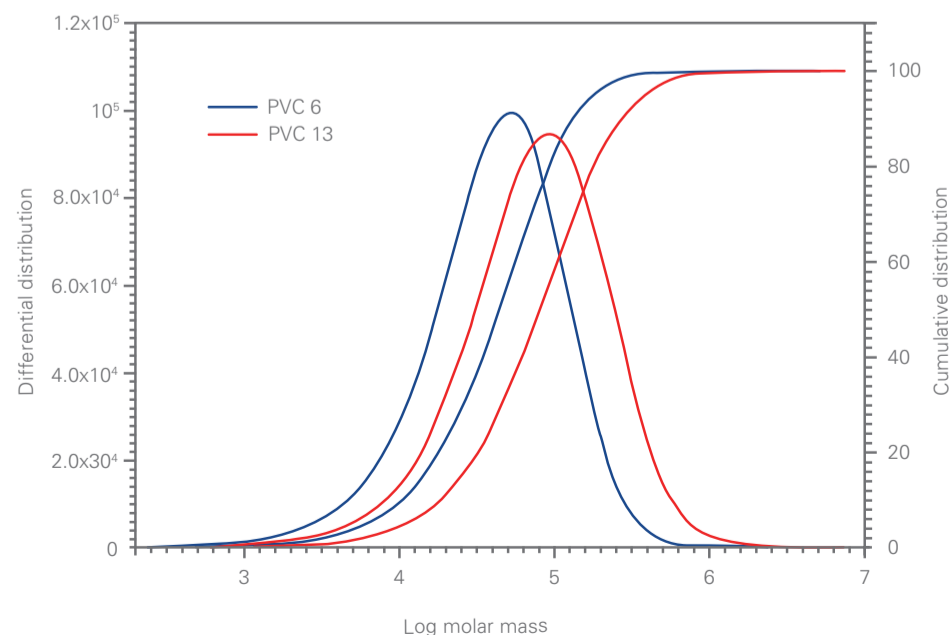


FIGURE 2: MOLAR MASS DISTRIBUTIONS

06 HISTORY TOSOH CORPORATION

A BRIEF HISTORY OF TOSOH'S BIRTH

AS TOSOH CELEBRATED ITS DAY OF FOUNDATION ON FEBRUARY 11, LET'S TAKE A LOOK AT TOSOH'S PAST - AND AT THE HISTORY OF THE NANYO COMPLEX, WHERE MOST OF THE CHROMATOGRAPHY PRODUCTS OF TOSOH BIOSCIENCE ARE PRODUCED.

The Industrial Revolution of the 18th century's saw soda (sodium carbonate) become an industrially mass-produced product and is raw material for soaps, glasses, and ceramics. In Japan, Tokusaburo Iwase, who was working as an engineering director for the chemical manufacturer Nippon Soda, envisioned and planned the construction of an ideal modern chemical plant that will utilize the ammonia-soda process for the mass production of soda.

Iwase decided to leave Nippon Soda along with 33 other colleagues who firmly believed in and supported his vision. They independently established Toyo Soda Manufacturing in Yamaguchi Prefecture on February 11, 1935. Serving as the first president of Toyo Soda Manufacturing, Iwase worked to build the company's foundations over a span of nine years before stepping down in 1944. He was later considered to be one of the leading pioneers of Japan's soda manufacturing industry.

The chemical plant expanded its operations later to include cement, petrochemicals, and other specialty businesses, and further diversified its products to become a supplier of a wide range of industrial chemicals, functional and advanced materials to many companies over the world.

In 1987, Toyo Soda Manufacturing was renamed and came to be known as Tosoh Corporation. Since then, Tosoh's leaders adopted a two-fold focus on large-volume commodities with high value-added specialties. By doing so, the company has been able to stay resilient against the inevitable ups and downs of the business environment in commodities while participating in highly technology-intensive industries with its specialties operations – the division Tosoh Bioscience belongs to. This strategy has proved to be a successful one as Tosoh continues to surge ahead in the global business market and to launch top-of-the-class products year after year.

What started out as a small soda-making factory developed into a comprehensive chemical enterprise. The expansion of TOYOPEARL manufacturing capacity and corporate R&D capabilities will further strengthen this continuous development.



➤ NANYO COMPLEX: PRE-CONSTRUCTION SITE 1935



➤ THE NANYO COMPLEX TODAY – AERIAL PHOTO 2017

07 PEOPLE BEHIND TOSOH

PATRICK STAHLBERG – TOSOH BIOSCIENCE GMBH, GRIESHEIM, GERMANY

PATRICK STAHLBERG IS THE NEWEST MEMBER OF THE TOSOH BIOSCIENCE'S SALES TEAM. PATRICK WORKS AS TECHNICAL SALES SPECIALIST IN THE TEAM OF DR. ELKE PROHASKA. WE ASKED PATRICK TO GIVE SOME INSIGHTS ABOUT HIM AND HIS ON-BOARDING TIME AT TOSOH BIOSCIENCE.

Tosoh Bioscience (TB): Patrick, you joined Tosoh Bioscience some months ago. How did you get to know about Tosoh?

Patrick Stahlberg (PS): During my education and my studies in biotechnology, I often worked in the field of biochromatography. However, I never met Tosoh products in the laboratory during this time. When I registered my master's thesis, I saw a flyer about an internship in the Business Development Department of Tosoh Bioscience on the black board. Since I have been interested in working in the field of business development/sales for a long time, I applied for this internship. The first impressions from both sides were quite positive, and instead of an internship, I got a real job!

TB: Could you please tell our readers a little bit about yourself and what you do for Tosoh?

PS: As a technical sales specialist at Tosoh Bioscience, I have the responsibility for customer support in the western part of Germany, Switzerland, Spain, and Portugal. As an employee in the Business Development team, I am the direct contact person for customers who already work with our process resins and lab scale columns or plan to work with them in the future. I provide immediate assistance, support, and information to address all the questions and needs of our customers regarding purification and analysis of biomolecules.

TB: What motivated you to switch from a technical position to a Business Development role?

PS: During the last years when working in various laboratories, I felt more and more, that interacting with people outside the laboratory would also be a lot of fun. Working in the field has a unique appeal to me. I enjoy being able to combine my experience in the laboratory with the work in sales. By participating in international congresses, conferences and through customer visits, this role offers a high degree of variety and offers something new every day.

TB: What part of the work do you like most?

PS: I particularly like the responsible handling of the customer's concerns. From my time in the laboratory and as a customer, I have often gained negative experience with sellers, who were solely interested in increasing sales. A proper consultation often took place only on the sidelines. From this, I was able to learn a lot and know what matters when it comes to giving the customers good care. I now work in a well organized international team, and through the exchange with my experienced colleagues, I learn something new at each meeting. Of course, I also like traveling and having interesting conversations with customers or at congresses.

TB: What were the highlights during your first months at Tosoh?

PS: I learned a lot about myself and how I deal with new challenging situations. In the first few months, I already handled demanding orders, which required well-planned cooperation and consultation with our facilities in the United States and Japan. With the help of our sales team, I was able to process these orders successfully.

TB: What are your interests besides Chromatography?

PS: In my spare time or after a day at the office I like running or lifting weights at the gym. As long as the weather is good and time permits, I also go to the tennis court with friends. After a long journey, it may also be a good computer game or a movie. My great passion, however, are seawater aquariums. Simulating a complex ecosystem, such as that of a coral reef, in your living room always poses new challenges. It is like a small bioreactor in which it is about maintaining the right conditions for healthy growth of the corals. If I correctly tackle these challenges, I am rewarded by the indescribable colorful splendor of the living creatures. I could sit in front of my aquarium for hours and observe the reef inhabitants in their fascinating ways of life.



➤ PATRICK AT WORK...



➤ ... AND HIS REWARD AFTER A SUCCESSFUL DAY AT WORK.

08

WHAT'S HAPPENING HIC/DSP CONFERENCE 2019



11TH HIC/DSP IN INTERLAKEN, FEBRUARY 18-21, 2019 TACKLING FUTURE CHALLENGES IN BIOSEPARATION

THE BIOSEPARATION WORLD UNDERWENT SIGNIFICANT EVOLUTIONS IN THE LAST DECADES, SO WILL THE HIC/RPC CONFERENCE. IN 2019, WE WILL COME BACK WITH A DIFFERENT FACE... WELCOME TO THE HIC/DSP CONFERENCE!



The HIC/DSP conference is providing a platform for a better understanding of the chromatographic isolation and purification of biological targets. The scientific program will still have a focus on molecular interactions and hydrophobic separations. However, the conference will broaden its scope through dedicated sessions on the chromatographic purification of specific biomolecules using all kinds of separation modes.

From basic theory to industrial scale purification, recognized professionals will share their expertise and experiences on all aspects of chromatographic separation and process design for biomolecules. Discussions about novel approaches and theories will balance the practical elements of chromatographic development and implementation.

➤ CHECK OUT WWW.HIC-DSP.ORG TO SUBMIT YOUR ABSTRACT TODAY

NEWS & EVENTS | MEET TOSOH BIOSCIENCE



MEET TOSOH AT TRADESHOWS AND CONFERENCES

UPCOMING EVENTS

- APRIL 10 - 13 | 2018 ➤ ANALYTICA 2018 | MUNICH [GERMANY]
- MAY 23 - 24 | 2018 ➤ BIOFORUM | LODZ [POLAND]
- SEP. 9 - 12 | 2018 ➤ ESBES | LISBON [PORTUGAL]
- OCT. 3 - 4 | 2018 ➤ ILMAC LAUSANNE | LAUSANNE [SWITZERLAND]

TRAININGS | WORKSHOPS

- JUNE 12 - 14 | 2018 ➤ CHROMATOGRAPHY IN PROCESS DEVELOPMENT & PRODUCTION | BASIC COURSE IN GERMAN | STUTTGART [GERMANY]
- JUNE 19 - 21 | 2018 ➤ CHROMATOGRAPHY IN PROCESS DEVELOPMENT & PRODUCTION | BASIC COURSE IN GERMAN | STUTTGART | [GERMANY]

➤ FIND THE LATEST UPDATES ON WWW.SEPARATIONS.EU.TOSOHBIOSCIENCE.COM/NEWS-EVENTS/EVENTS