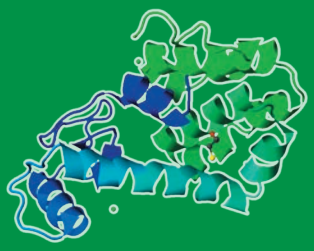
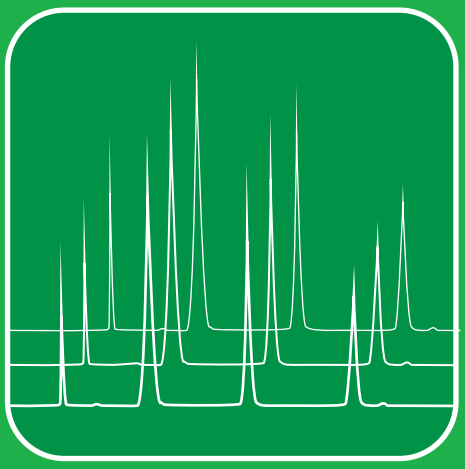
YMC
EUROPE GMBH
The Selectivity Company

BioPro
IEX Resins





Antibodies

Oligonucleotides

Proteins / Peptides

www.ymc.de

BioPro IEX:

Designed for bioseparations

Contents

Ion exchange chromatography

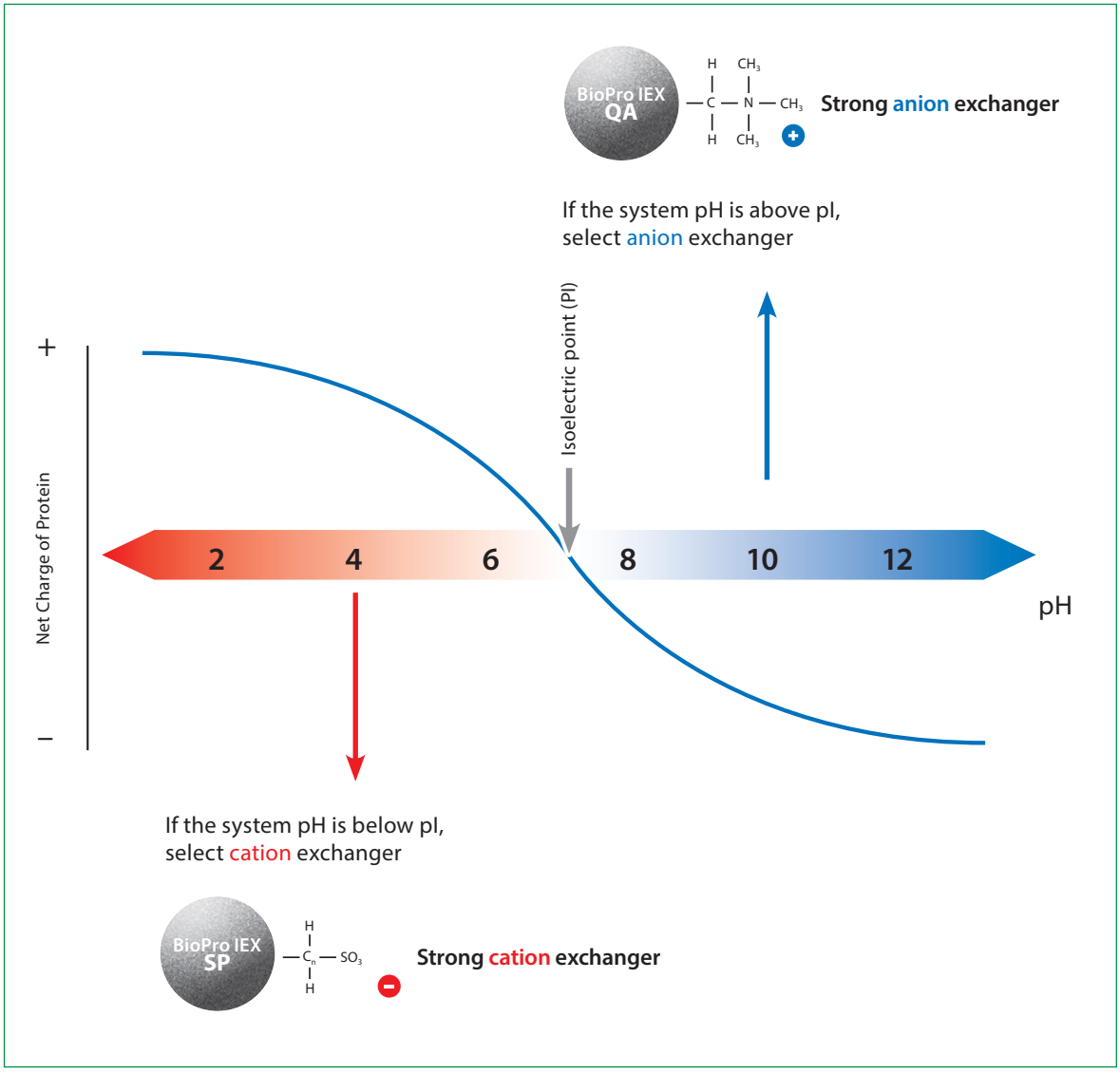
Ion-exchange (IEX) chromatography separates biomolecules according to differences in their overall surface charges. The resin contains charged groups that form reversible interactions with the charged amino acid side chains on a biomolecule's surface. These are then eluted from the column using gradients, either salt concentration or pH.

Salt ions compete with biomolecules for the charged groups on the resins. This means that as the salt concentration in the mobile phase increases, the biomolecules will start to be released from the resin and elute from the column.

The proteins with the lowest net charge will be eluted first, and those with the highest net charge will come off last.

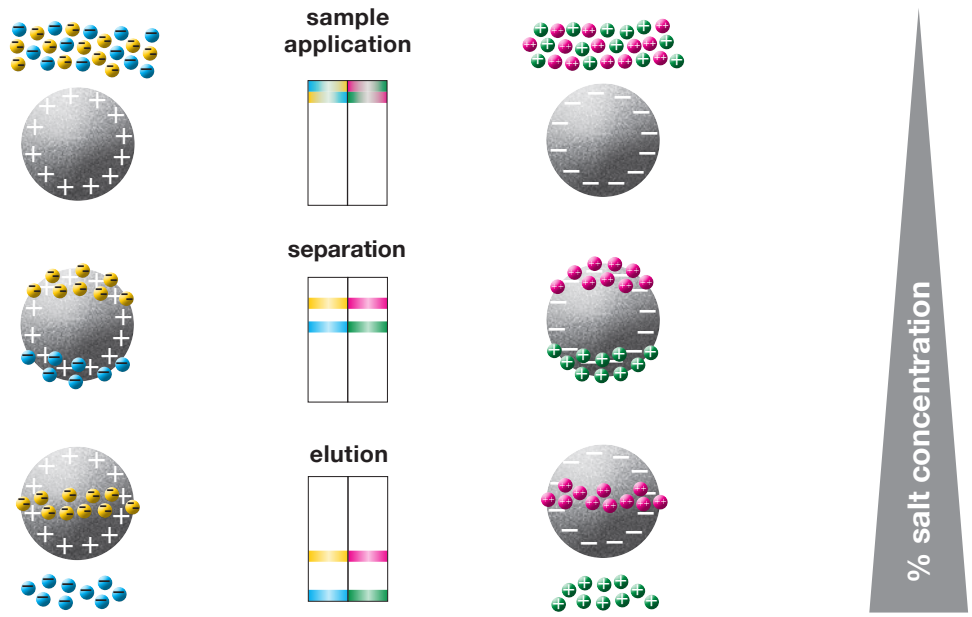
With a pH gradient, the order of elution depends on the isoelectric points (pI) of the biomolecules being separated. The isoelectric point is the pH at which the charged groups on a biomolecule cancel one another out, making the overall charge for that biomolecule zero.

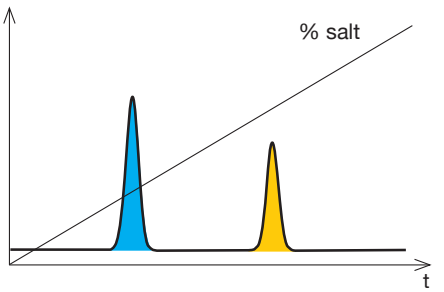
With cationic resins, for example, while the pH of the mobile phase is below the isoelectric point of a biomolecule, its overall charge will be positive and it will bind to the resin. When the pH of the mobile phase rises above the isoelectric point, the overall surface charge of the biomolecule will become negative and it will be released from the resin and will elute from the column.

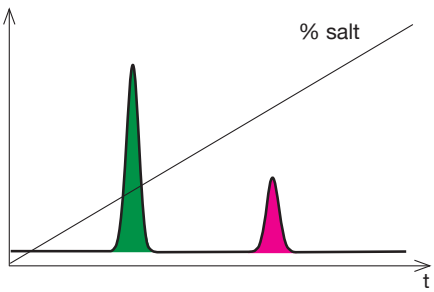


Anion exchange

Cation exchange







Ion exchange

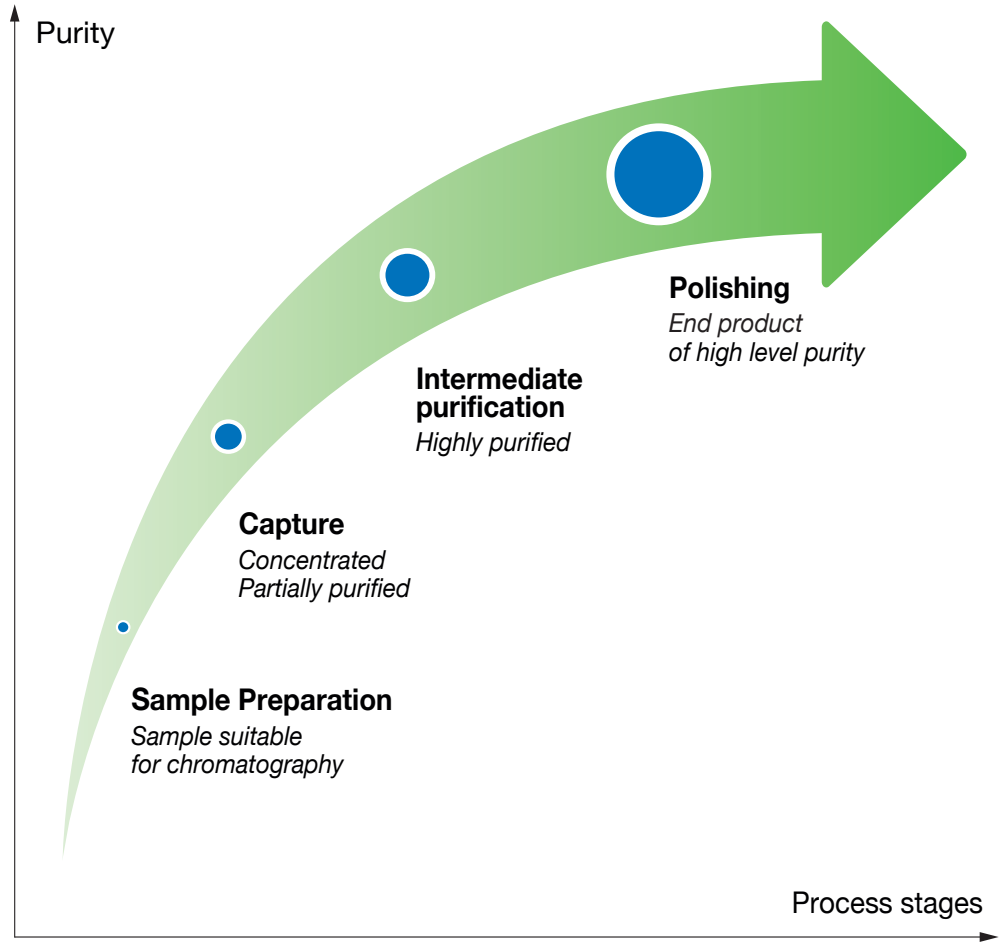
Stationary Phase: Charged surface
positive: anion exchange
negative: cation exchange

Mobile Phase: Buffers for elution with increasing salt concentration.
Alternatively, the pH of the mobile phase can be changed for elution.

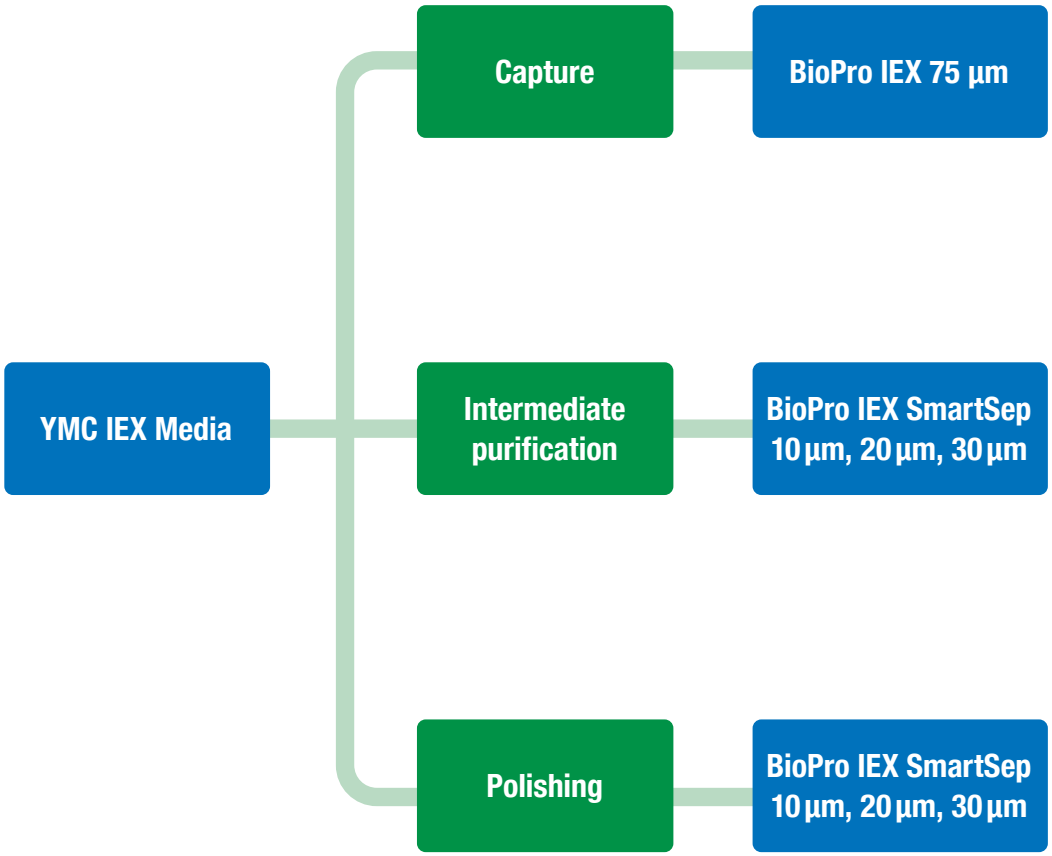
Elution order: First compounds which have the same charge as the surface, last compounds which are oppositely charged to the surface.

A purification strategy usually includes three parts:

- initial product capture
- intermediate purification stages
- the final polishing step



The capture step aims at isolating and concentrating the targets. It requires that the media has a high binding capacity even at high flow rates and easy scale-up steps. The intermediate purification is for removing the bulk impurities. The polishing step is used for removing all traces of impurities. The corresponding media should exhibit high resolution and low non-specific adsorption. YMC´s IEX resins can be used for all stages during the whole process from the capture to the final polishing.



YMC resins can be used in:

- Bind/elute-mode
- Flow-through-mode

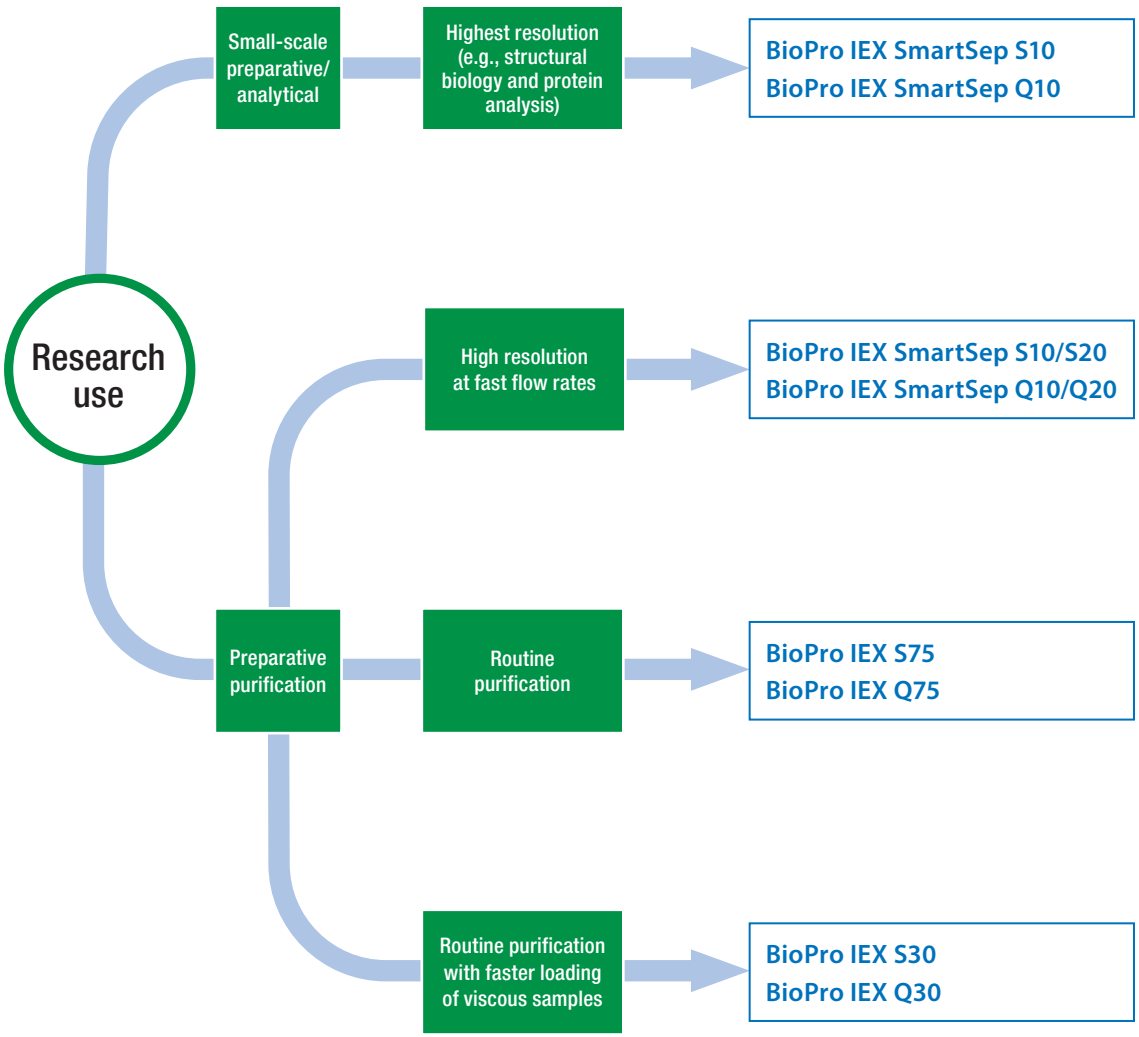
YMC resins are used in various applications:

- Antibodies
- Proteins
- Peptides
- Oligonucleotides

Flow-through-mode for the removal of impurities such as:

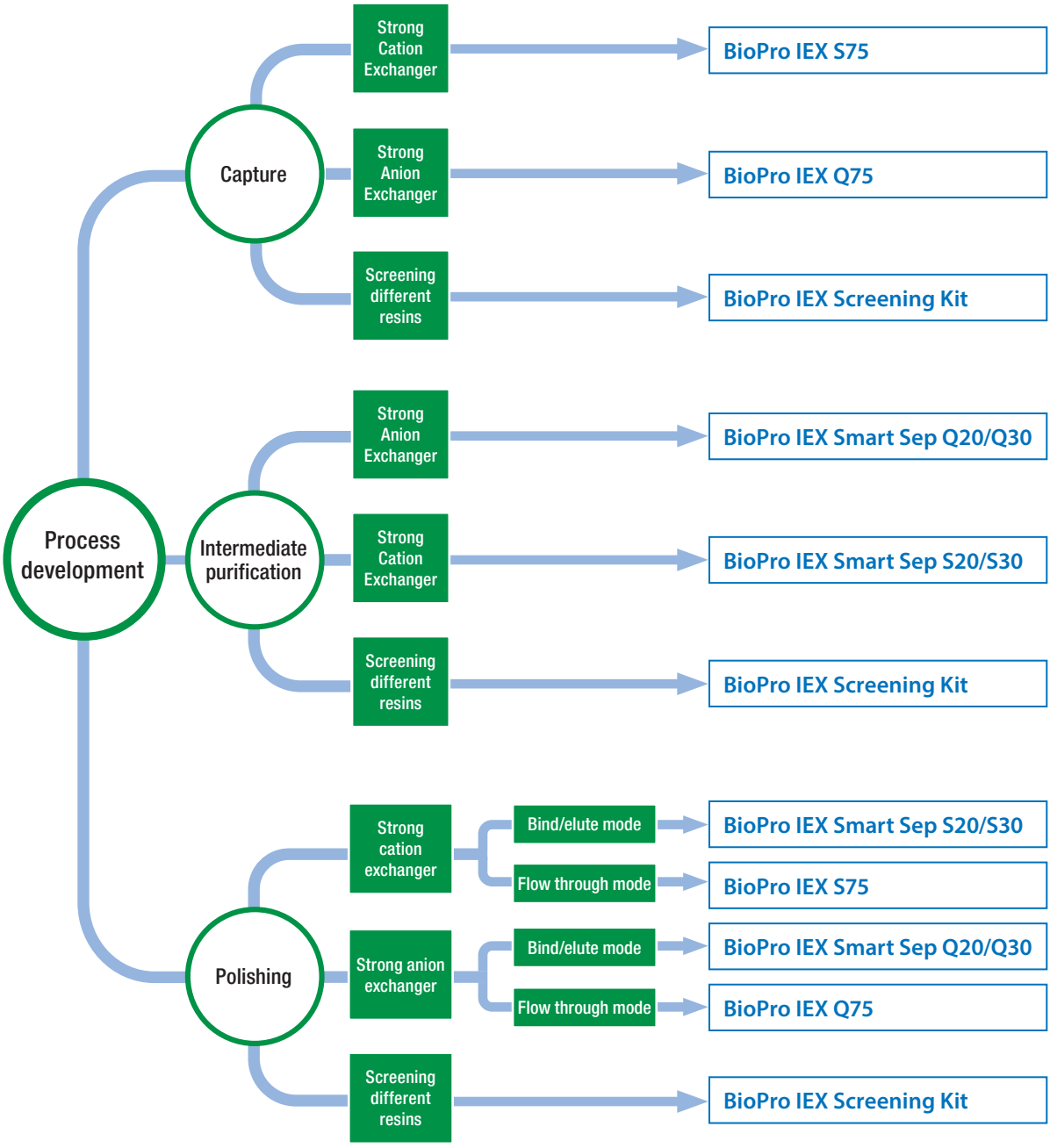
- DNA
- Viruses
- Host cell proteins
- Aggregates

Guide to IEX media selection



Screening Guide

Robocolumn®	Bulk pack	BioPro Screening Kit	Minichrom™	Packed anal. Columns
Miniaturized prepacked columns (50 µL, 200 µm and 600 µL) High-throughput process development	Chromatography resins for self-packing	Prepacked columns (1 mL and 5 mL)	Prepacked columns with different dimensions and volumes	Prepacked PEEK columns 50 x 4.6 mm ID 100 x 4.6 mm ID



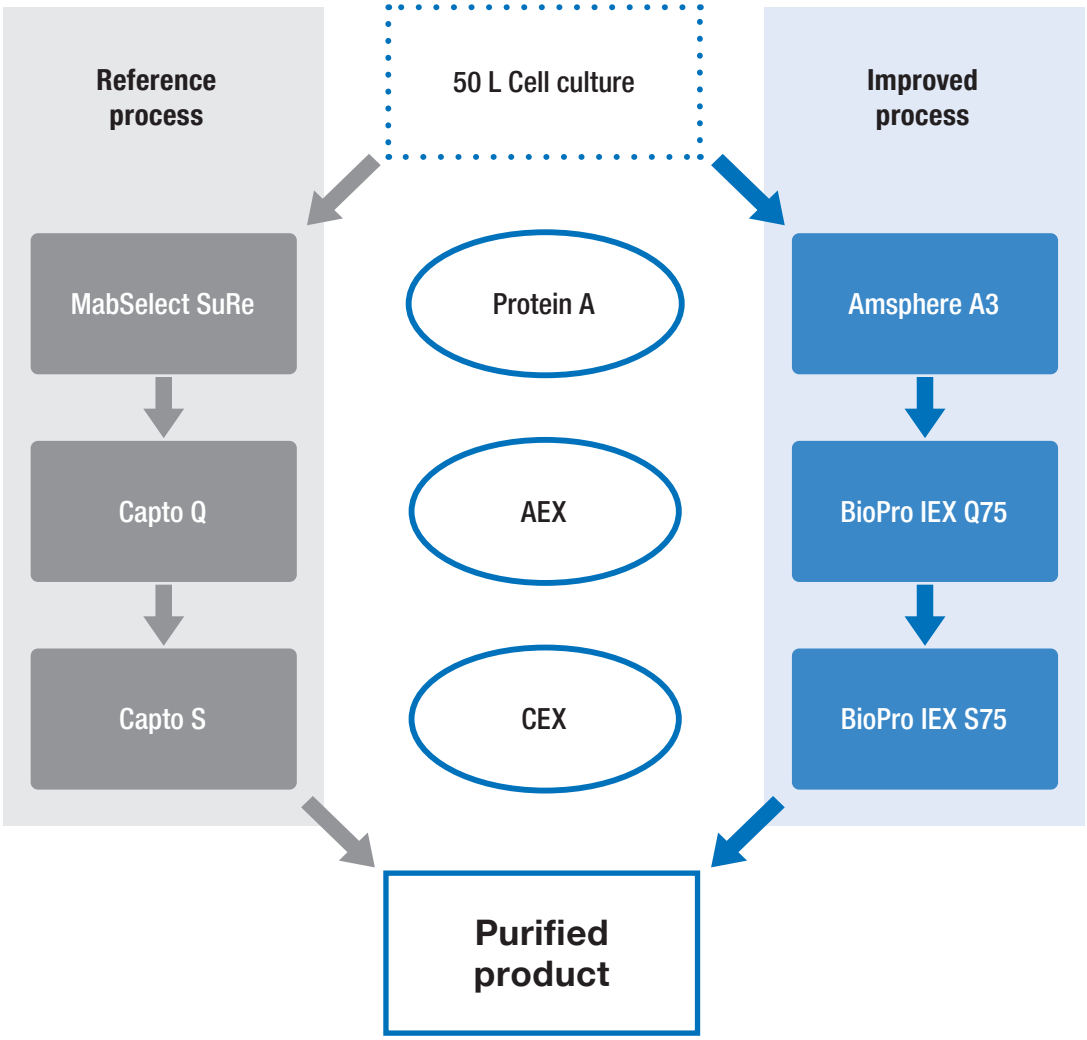
BioPro IEX Resins
Screening Kits

Various types of screening kits available

Please contact your YMC representative

Purification of monoclonal antibodies

The purification of a mAb from a 50 L CHO cell culture was studied under GMP conditions using BioPro IEX S75 and BioPro IEX Q75 ion exchange resins. The final three-step process succeeded in producing mAbs with high purity and efficiency. The results were directly compared with those achieved using competitive IEX resins under identical conditions.



Process flow sheet

This shows the resins used for the three-step reference and the improved process

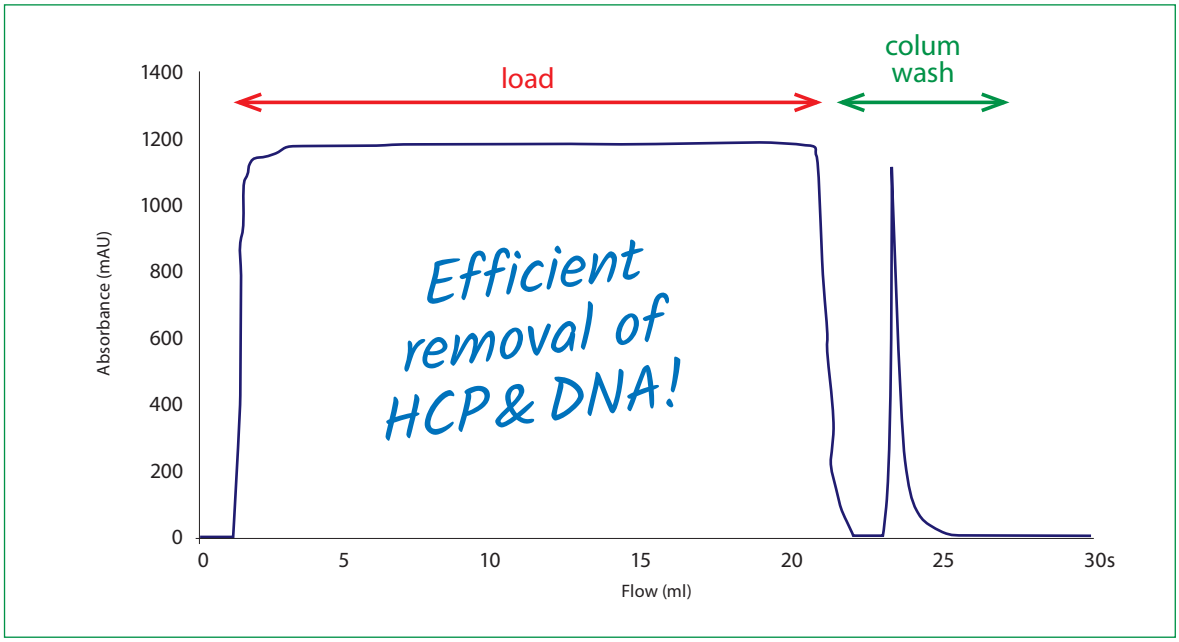
- Step 1: Affinity chromatography using Amsphere A3 resin from JSR Life Sciences for a first clean-up of the cell culture
- Step 2: Anion exchange chromatography using YMC´s BioPro IEX Q75 resin after dilution with 25 mM Tris-HCl buffer
- Step 3: Cation exchange chromatography using YMC´s BioPro IEX S75 as the final polishing step

Use of an identical process sequence and identical experimental conditions ensured full comparability of the results

Anion exchange process conditions

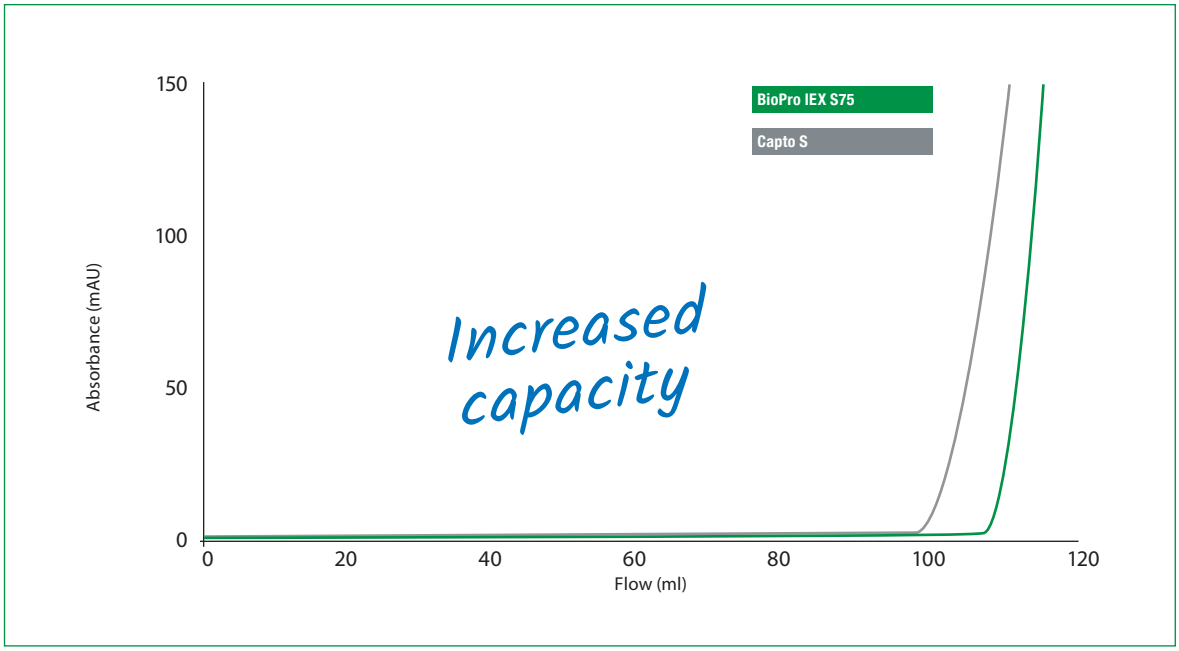
- The highly efficient removal of host cell protein (HCP) and DNA was achieved using YMC's BioPro IEX Q75.
- An optimisation study was carried out to evaluate the influence of pH on this step. Product yield and residual HCP concentration were constant between pH 8.0 and 9.0.

➜ robust & flexible process!



Cation exchange process conditions

- Comparison of the DBC breakthrough curves for BioPro IEX S75 and a competitive resin
- An increased capacity is clearly visible and this improves the efficiency of the overall process with a larger amount of product purified with each chromatographic cycle.



An improved purification process was successfully developed. The results shown in the table below clearly indicate the potential for process optimisation achievable using YMC resins. By addressing this potential, purities and yields can be improved to increase the overall productivity and the cost-efficiency of the related processes.

Results for improved three-step process for the purification of IgG compared to the reference process

Process step	HCP (ng / mg IgG)		DNA (pg / mg IgG)		mAb Monomer (%)	
Cell culture fluid (Ref.)	127,000		66,900,000			
	Ref.	YMC / JSR	Ref.	YMC / JSR	Ref.	YMC / JSR
Protein A capture	194	145	26,200	18,000	–	98.6
AEX	4.57	**0.64**	1.12	**< 0.44**	92.2	**98.5**
CEX	3.04	**0.46**	1.98	**< 0.12**	93.9	**98.6**

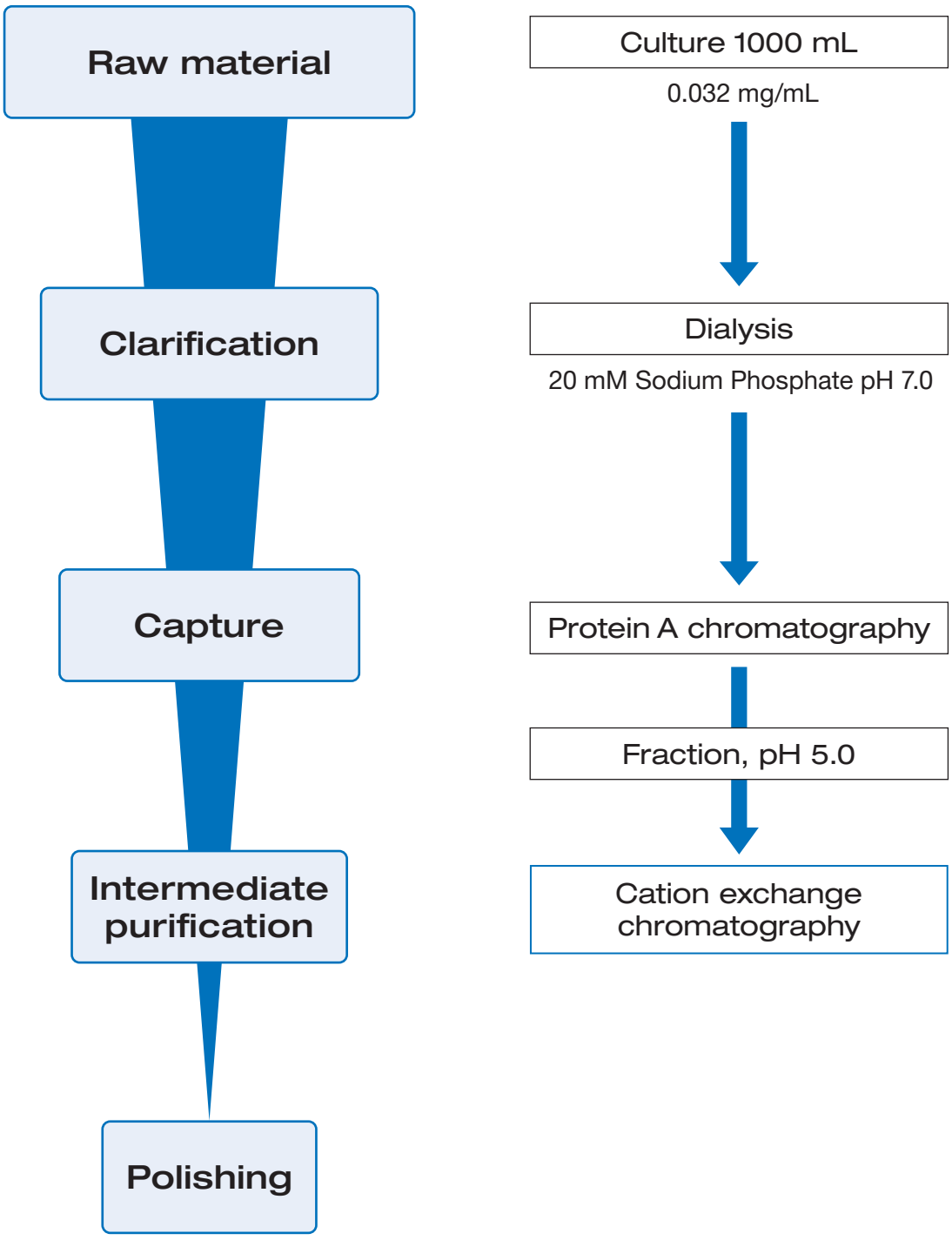
More efficient removal of HCP and DNA

Result summary

- **The highly effective purification of the developed process is apparent**
- **YMC´s BioPro IEX resins are the ideal choice for efficient purification of mAb**
- **The AEX step was particularly effective in reducing residual impurities**
- **The CEX step was successful as the last step for polishing, removing the remaining trace contaminants**
- **With 98.6 % yield the process had a very high recovery of purified mAbs**

Purification Scheme for Adalimumab

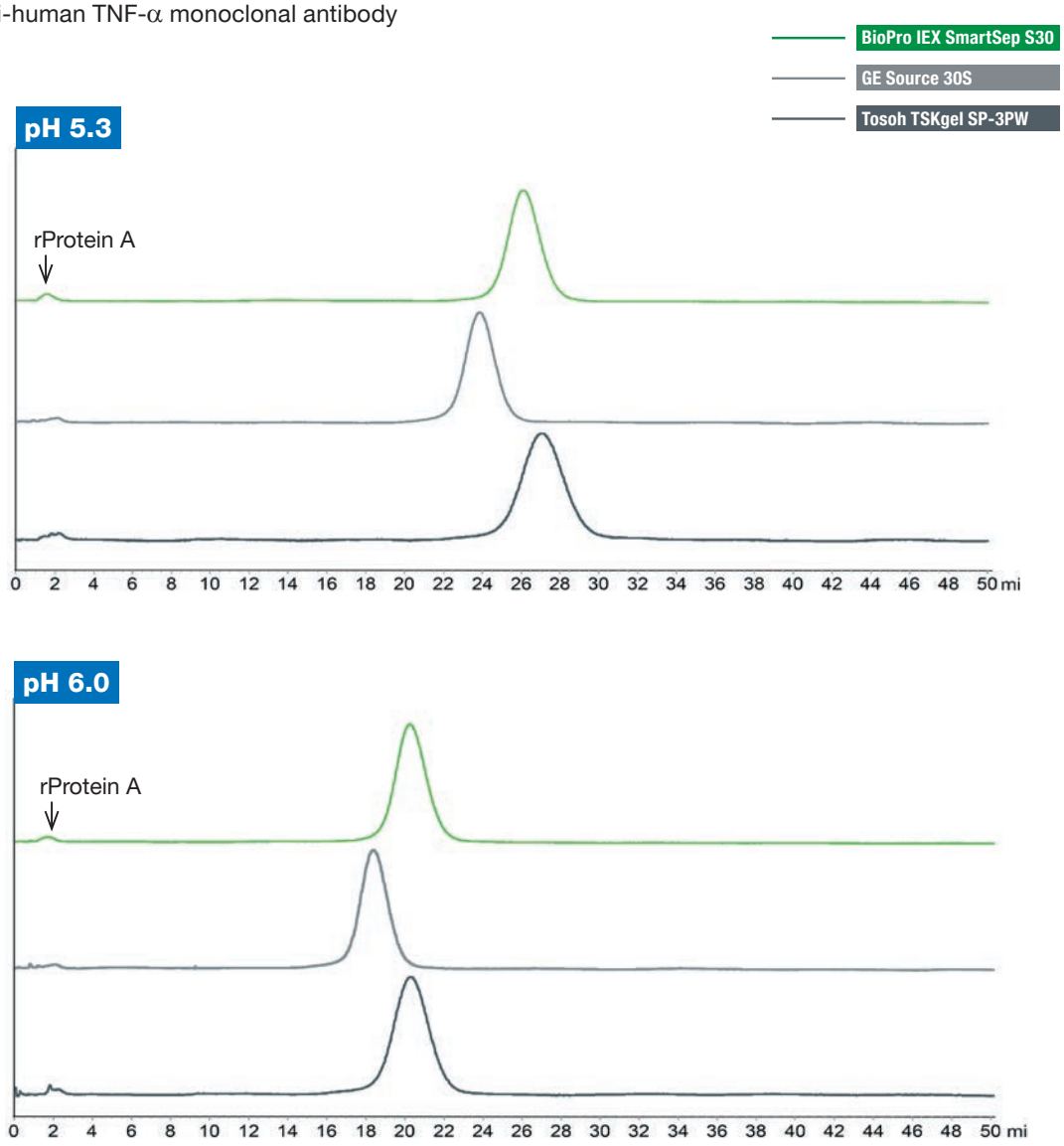
For the purification of monoclonal antibodies high demands are required from the resin used. Factors influencing the binding characteristics of IgG are pH, linear velocity and/or salt concentration (conductivity) at the time the sample is loaded onto the column. Therefore, a resin with highly stable performance is required with regard to all those factors. In order to demonstrate the performance of BioPro IEX resins, several studies have been performed.



Purification of anti-human TNF-a monoclonal antibody was performed using BioPro IEX Smart-Sep and the influence of factors such as pH, linear velocity and salt concentration were studied. The BioPro IEX SmartSep material shows good performance in all the tests.

Comparison of the Performance of BioPro IEX SmartSep and Competitors´ Products for the Purification of anti-human TNF-α monoclonal antibody

Anti-human TNF-α monoclonal antibody



Column:	50 x 5.0 mm ID
Eluent:	A) 20 mM citric acid-NaOH (pH 5.3) B) Eluent A containing 0.5 M NaCl
Gradient:	0–100% B (0-30 CV)
Flow rate:	180 cm/hr (0.59 mL/min)
Temperature:	ambient
Detection:	UV at 280 nm
Sample:	Anti-human TNF-α monoclonal antibody (after affinity chromatography)
IgG Load:	0.1 mg
Injection:	0.25 mL

Influence of pH, linear velocity and salt concentration on the purification of IgG using BioPro IEX SmartSep

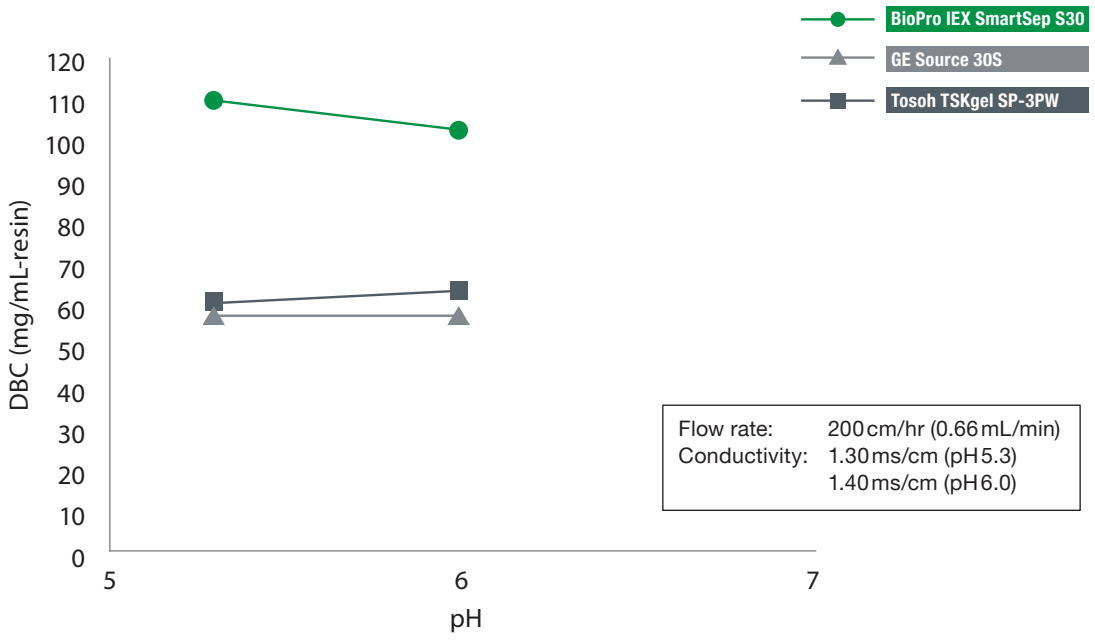
Experimental conditions

pH: 6.0 vs. 5.3
Linear velocity: 200–800 cm/hr
Salt concentration: 0–50 mM NaCl

Column:	50 x 5.0 mm ID	Temperature:	ambient (25 °C)
Eluent:	A) 20 mM citric acid-NaOH buffer (pH 5.3 or 6.0) B) Eluent A containing 0.5 M NaCl	Detection:	UV at 280nm
		Sample:	1.5 mg/mL human polyclonal IgG in equilibration buffer
Flow rate:	200–800 cm/hr (0.66-2.62 mL/min)		

Influence of pH

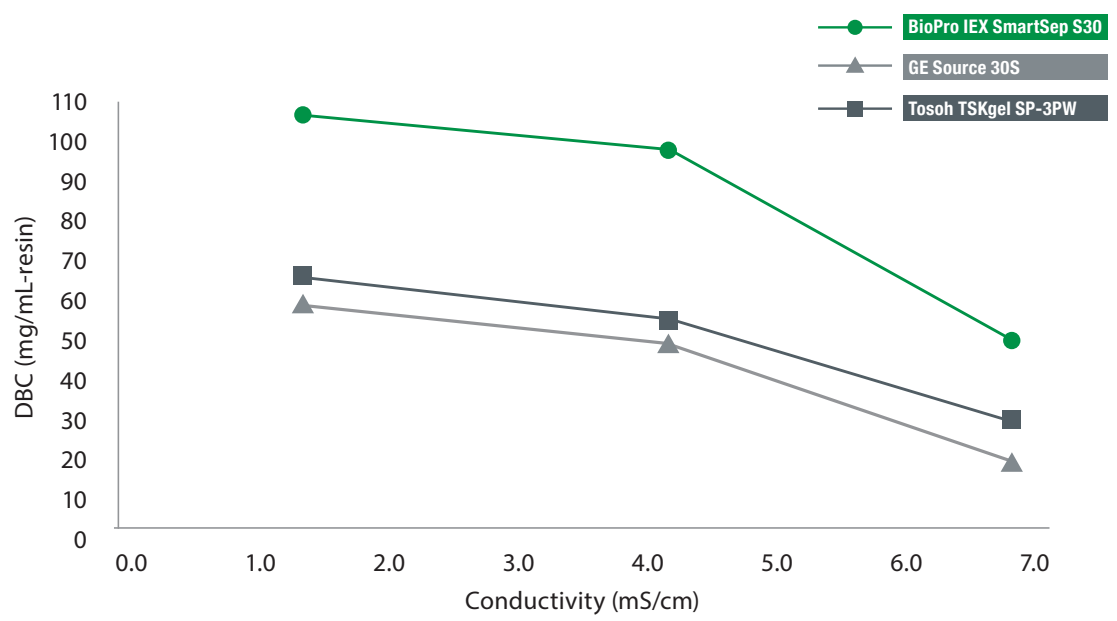
pH	DBC (mg/mL-resin, 10% breakthrough)	
	pH 5.3	pH 6.0
BioPro IEX SmartSep S30	**110**	**103**
Tosoh TSKgel SP-3PW (30 µm)	61	64
GE Source 30S (30 µm)	58	58



High binding capacities are achieved regardless of the pH of elution. Therefore, milder eluting conditions for IgG can be selected to protect the product purity.

Influence of salt concentration

	DBC (mg/mL-resin, 10% breakthrough)		
pH	**5.3**		
NaCl concentration	**0 mM**	**25 mM**	**50 mM**
Conductivity	**1.36 mS/cm**	**4.14 mS/cm**	**6.8 mS/cm**
BioPro IEX SmartSep S30	**107**	**97**	**50**
Tosoh TSKgel SP-3PW (30 µm)	64	55	27
GE Source 30S (30 µm)	58	49	19



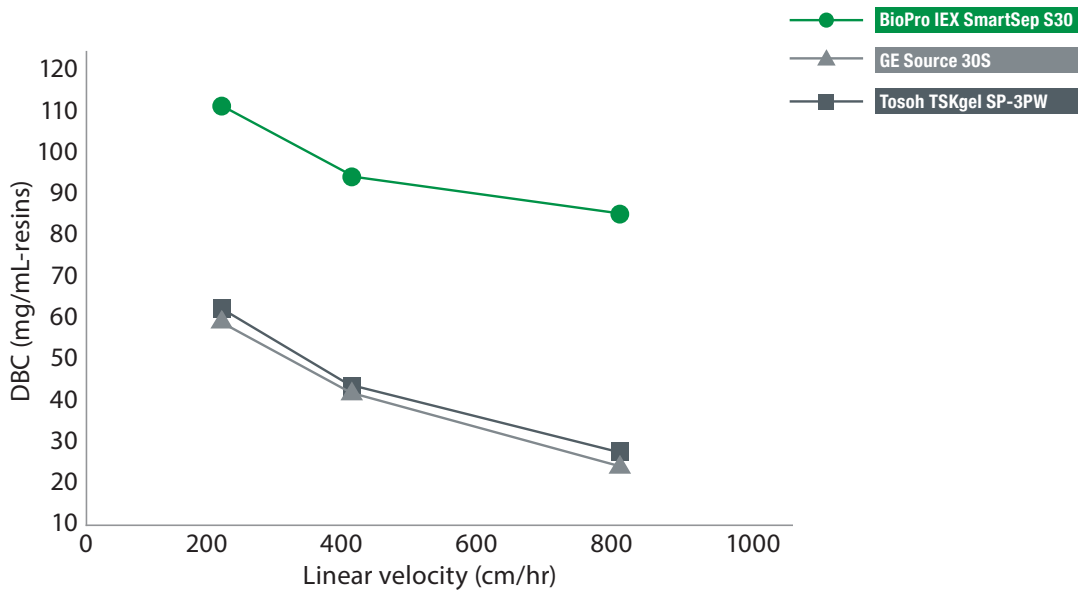
Flow rate: 200 cm/hr (0.66 mL/min)
Sample: 1.5 mg/mL human polyclonal IgG in equilibration buffer containing 0.25, 50 mM NaCl

BioPro IEX SmartSep S30 has a higher tolerance to salt concentration. This simplifies the desalting process after Protein A chromatography and will help to shorten the production process.

Purification of monoclonal antibodies

Influence of linear velocity

Linear velocity	DBC (mg/mL-resin, 10% breakthrough)		
	200 cm/hr	400 cm/hr	800 cm/hr
BioPro IEX SmartSep S30	**110**	**93**	**84**
Tosoh TSKgel SP-3PW (30 µm)	61	42	26
GE Source 30S (30 µm)	58	41	23

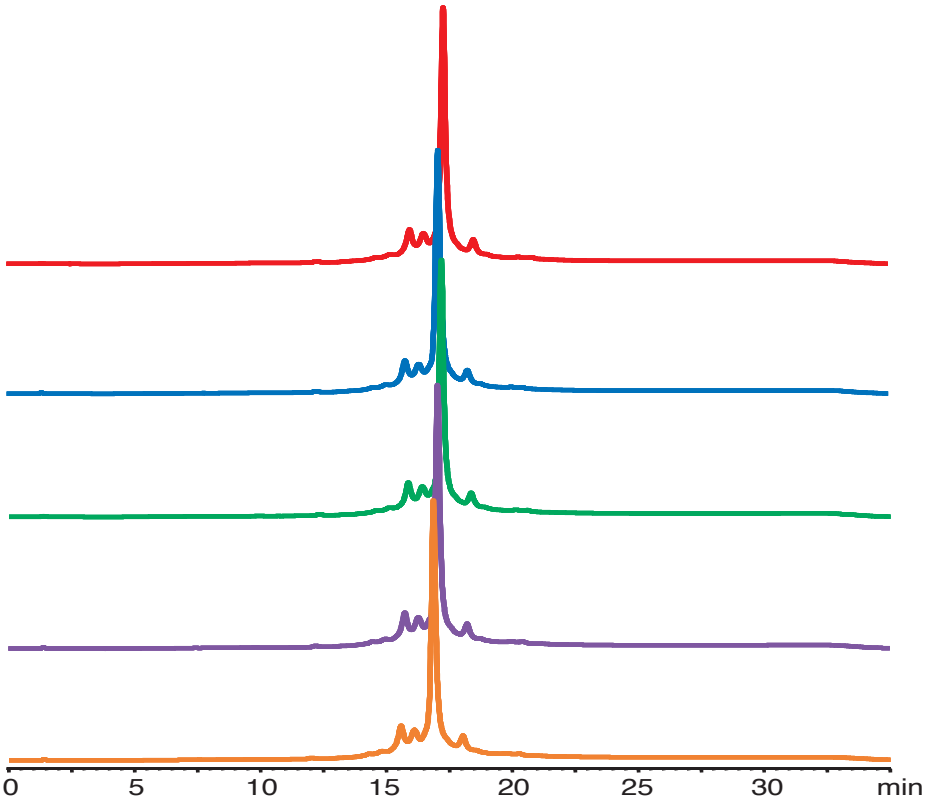


BioPro IEX SmartSep S30 maintains higher binding capacity values over a wider range of linear velocities. This will increase the product throughput for the purification process.

Conclusions

BioPro IEX SmartSep resins meet the highest demands for the purification of monoclonal antibodies. High binding capacity is achieved regardless of elution of pH, linear velocity or salt concentration. This allows purification processes to be carried out more efficiently.

- **Higher throughput with no loss of efficiency**
- **Simplification of desalting processes**
- **Reduced processing costs**
- **Short delivery time for industrial-scale quantities**
- **Full compliance with GMP regulations**



Purified monoclonal antibody IgG1

Purification of oligonucleotides

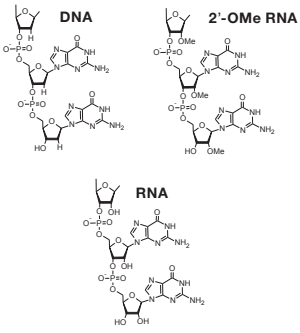
Examples of analysis under the optimised conditions

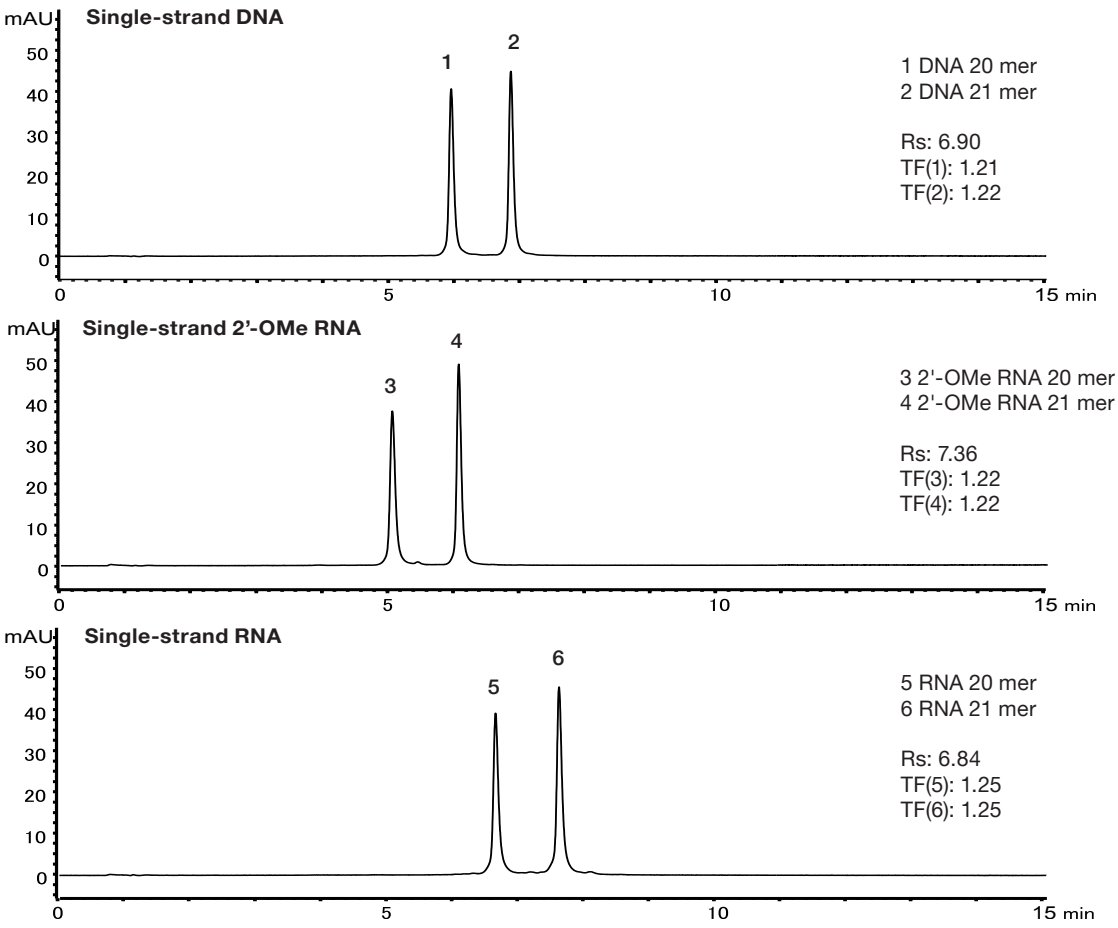
Nucleic acids such as antisense RNA (asRNA), small interfering RNA (siRNA) and aptamers are expected to be the next generation of biopharmaceuticals. In order to provide these drugs, purification and analytical separations that can recognize slight structural differences after synthesis are important issues.

Samples

1	Single-strand DNA	5'-TCATCACACTGAATACCAAT-3' (DNA 20 mer)
2		5'-GTCATCACACTGAATACCAAT-3' (DNA 21 mer)
3	Single-strand RNA	5'-U(M)C(M)A(M)U(M)C(M)A(M)C(M)A(M)C(M)U(M)G(M)A(M)A(M)U(M)A(M)C(M)C(M)A(M)A(M)U(M)-3' (2'-OMe RNA 20 mer)
4		5'-G(M)U(M)C(M)A(M)U(M)C(M)A(M)C(M)A(M)C(M)U(M)G(M)A(M)A(M)U(M)A(M)C(M)C(M)A(M)A(M)U(M)-3' (2'-OMe RNA 21 mer)
5		s5'-UCAUCACACUGAAUACCAAU-3' (RNA 20 mer)
6		5'-GUCAUCACACUGAAUACCAAU-3' (RNA 21 mer)

N(M)=2'-OMe RNA





Column:	BioPro IEX QF (5 µm) 100 x 4.6 mm ID	Flow rate:	1.0 mL/min
Part No.:	QF00S05-1046WP	Temperature:	25 °C
Eluent:	A) 10 mM NaOH	Detection:	UV at 260 nm
	B) 10 mM NaOH containing 1.0 M $NaClO_4$	Injection:	4 mL (5 nmol/mL each)
	25-55%B (0–15 min), 100%B (15–20 min)		

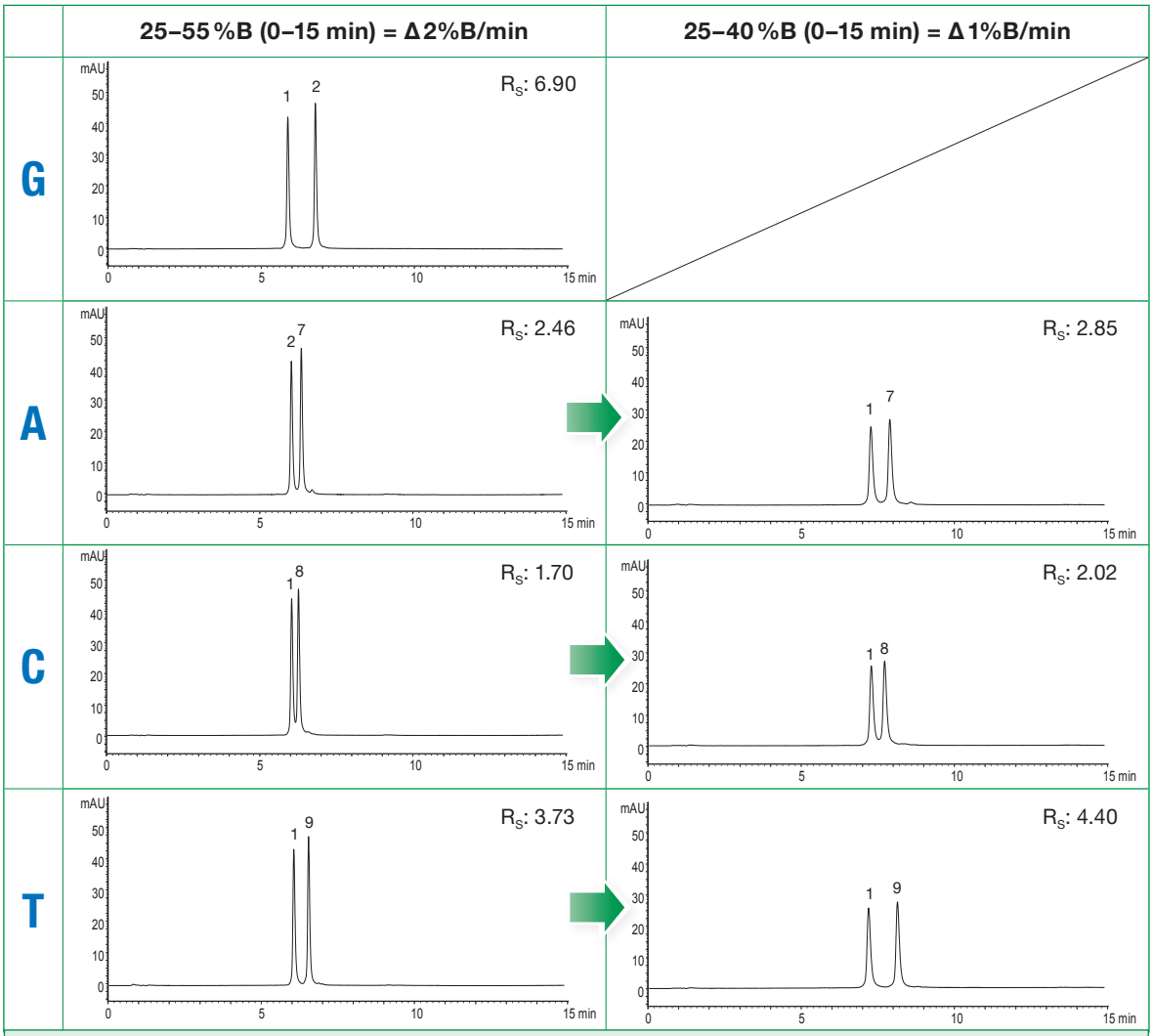
Good separation without carry over or peak tailing of oligonucleotides was achieved by optimisation of the buffer/counter ion in the mobile phase and gradient profile, and by using the non porous anion exchange column BioPro IEX QF.

Separation of ssDNAs with single-base differences

Samples

1	Single-stranded DNA	5'-TCATCACACTGAATACCAAT-3' (DNA 20 mer)
2		5'-**G**TCATCACACTGAATACCAAT-3' (DNA 21 mer)
7		5'-**A**TCATCACACTGAATACCAAT-3' (DNA 21 mer)
8		5'-**C**TCATCACACTGAATACCAAT-3' (DNA 21 mer)
9		5'-**T**TCATCACACTGAATACCAAT-3' (DNA 21 mer)

When ssDNAs (single-stranded DNAs) with single-base differences (differing in the type of base of 5' end of DNA 21mer) are analysed under the conditions described, all of the peak separations got worse. By using a shallower gradient, improved separations could be achieved.

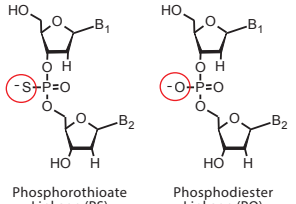


Column:	BioPro IEX QF 5 mm, 100 x 4.6 mm ID
Eluent:	A) 10 mM NaOH B) 10 mM NaOH containing 1.0 M $NaClO_4$
Flow rate:	1.0 ml/min
Temperature:	25 °C
Detection:	UV at 260 nm
Injection:	4 ml (each 5 nmol/ml)

Samples

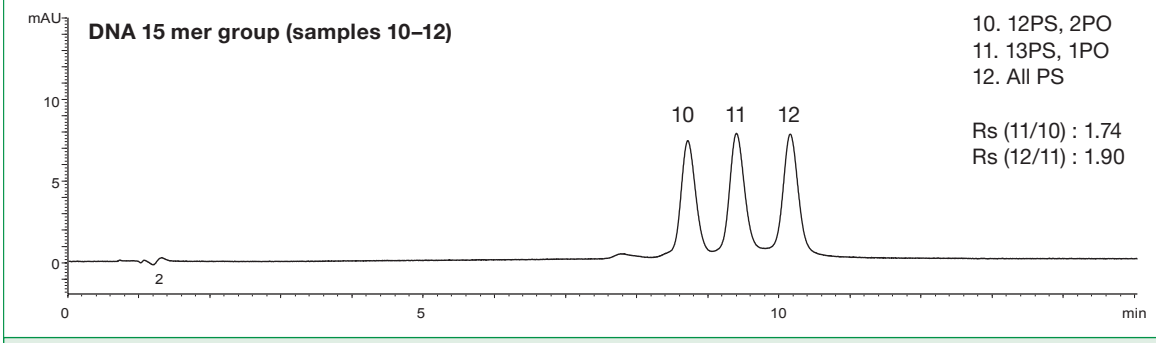
10	Single-stranded DNA	5'-T^T^T^T^T^T^T^T^T^T^T^T^T^TTT-3' (DNA 15 mer 12PS, 2PO)
11		5'-T^T^T^T^T^T^T^T^T^T^T^T^T^TT-3' (DNA 15 mer 13PS, 1PO)
12		5'-T^T^T^T^T^T^T^T^T^T^T^T^T^T-3' (DNA 15 mer All PS)
13	Single-stranded RNA	5'-U^C^A^U^C^A^C^A^C^U^G^A^A^U^A^C^C^A^A^U-3' (RNA 20 mer All PS)
14		5'-G^U^C^A^U^C^A^C^A^C^U^G^A^A^U^A^C^C^A^A^U-3' (RNA 21 mer All PS)

^=Phosphorothioated



Using the optimised conditions described, [all PS], [13PS, 1PO] and [12PS, 2PO] of DNA 15mer (samples 10–12) were clearly separated by ion exchange chromatography.

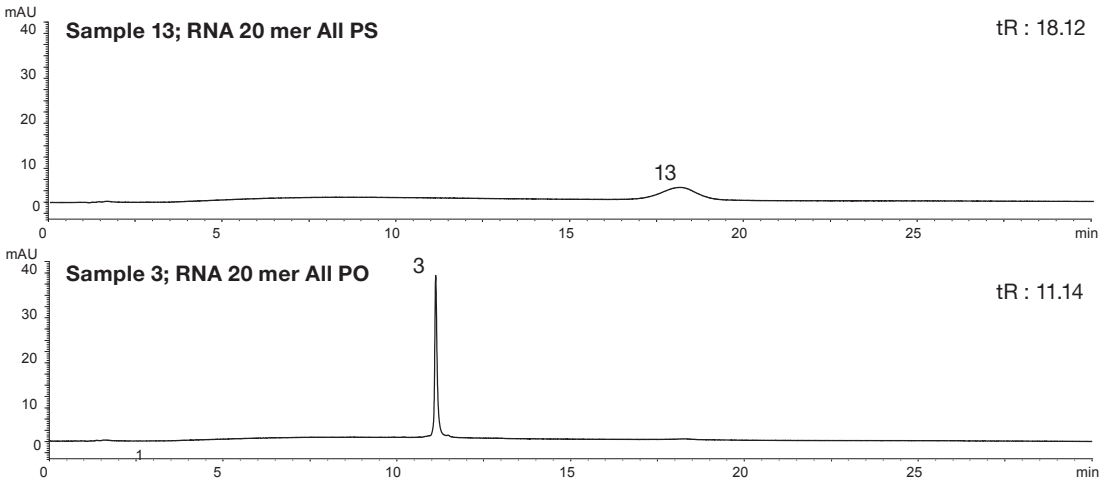
Resolution of phosphorothioate oligonucleotides with different degrees of thiolation



Column:	BioPro IEX QF 5 mm, 100 x 4.6 mm ID	Flow rate:	1.0 ml/min
Eluent:	A) 10 mM NaOH	Temperature:	25 °C
	B) 10 mM NaOH containing 1.0 M $NaClO_4$	Detection:	UV at 260 nm
Gradient:	40–70%B (0–15 min), 100%B (15–20 min)	Injection:	6 ml (each 3.3 nmol/ml)

The separation of RNA 20mer all PS (sample 13) is compared with RNA 20mer all PO (sample 3) under the same conditions. Since acidity of all PS is much higher than that of all PO, a higher salt concentration is required for elution. The peak of all PS is much broader because it is thought that all PS contains as many as 219 (524, 288) stereoisomers.

Difference in required salt concentrations for eluting modified RNA (All PS) and normal RNA (All PO)



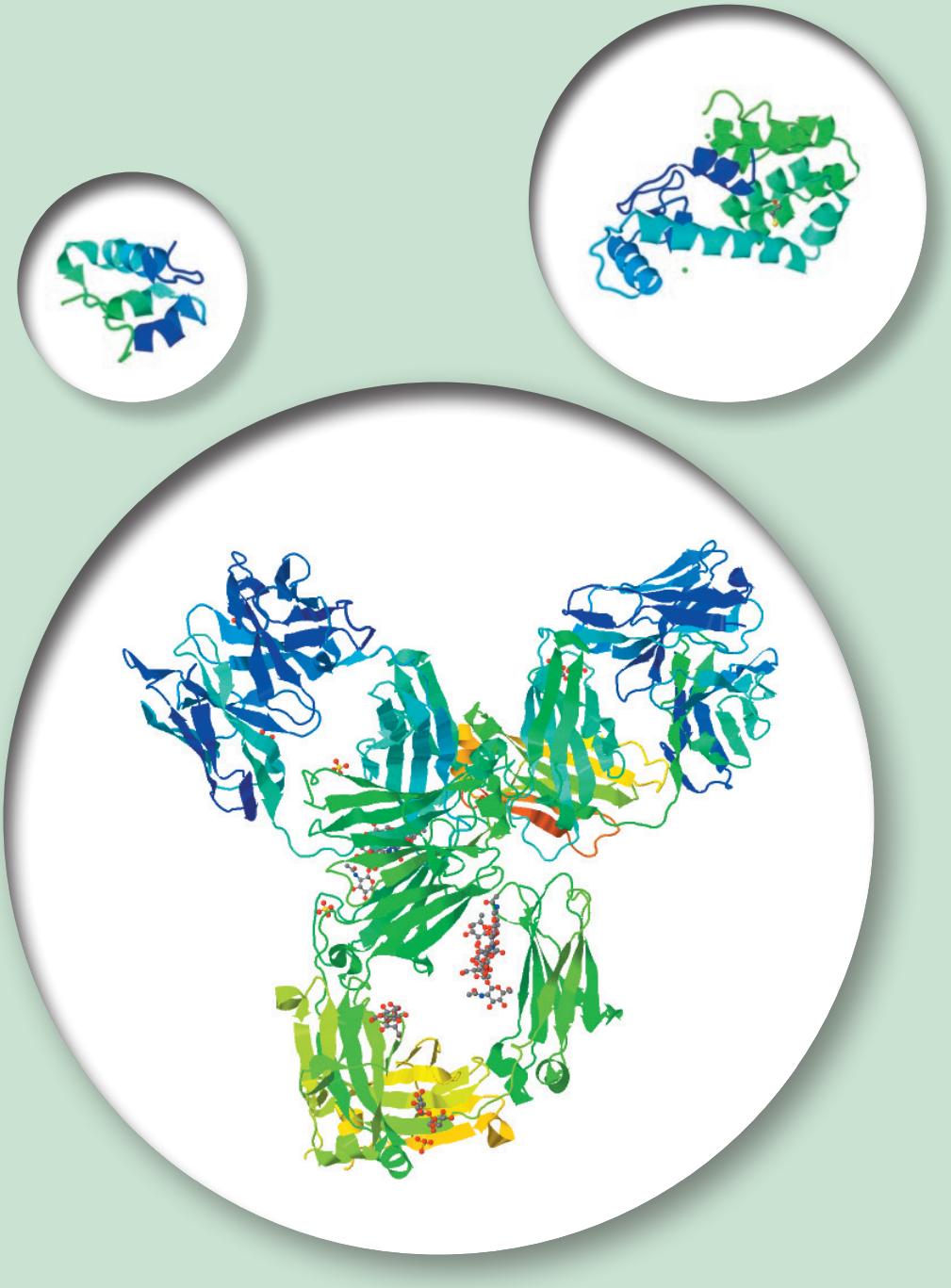
Column:	BioPro IEX QF 5 mm, 100 x 4.6 mm ID	Flow rate:	1.0 ml/min
Eluent:	A) 10 mM NaOH	Temperature:	25 °C
	B) 10 mM NaOH containing 1.0 M $NaClO_4$	Detection:	UV at 260 nm
Gradient:	10–100%B (0-30 min)	Injection:	2 ml (10 nmol/ml)

Conclusions

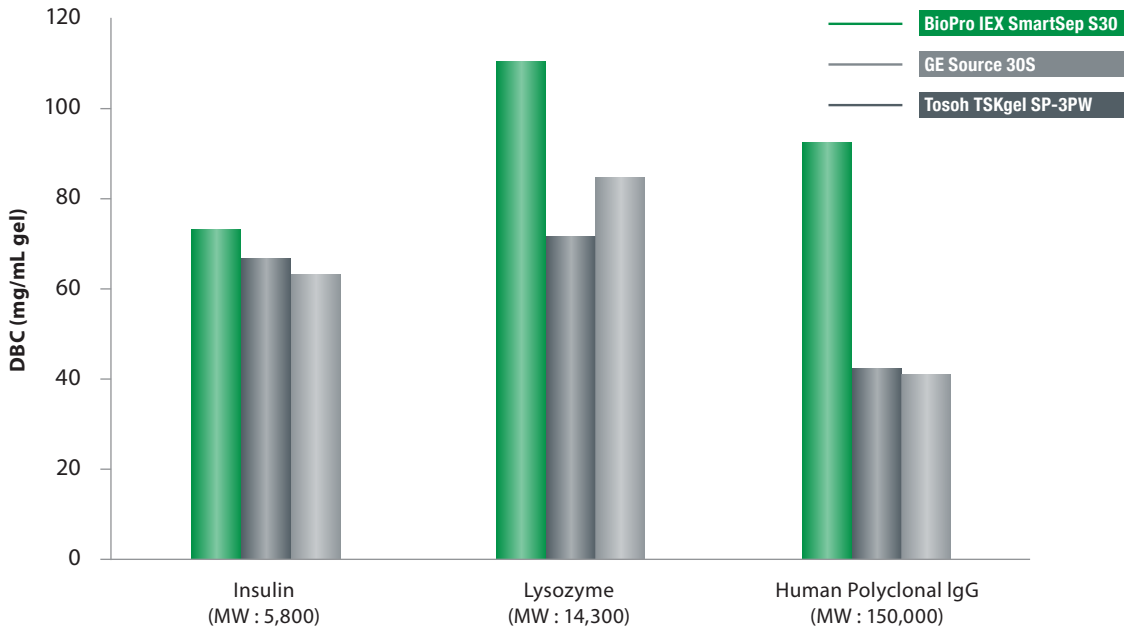
By using BioPro IEX :

- **Each ssDNA, ssRNA and 2'-OMe ssRNA with single-base differences in length can be successfully separated.**
- **[All PS], [13PS, 1PO] and [12PS, 2PO], which consist of 15-mer ssDNA, can also be separated under the optimised conditions.**
- **Higher salt concentration is required to elute All PS compared to eluting All PO.**
- **All PS with single-base differences in length can be separated to a limited extent and for further optimisation is required.**

Purification of proteins and peptides

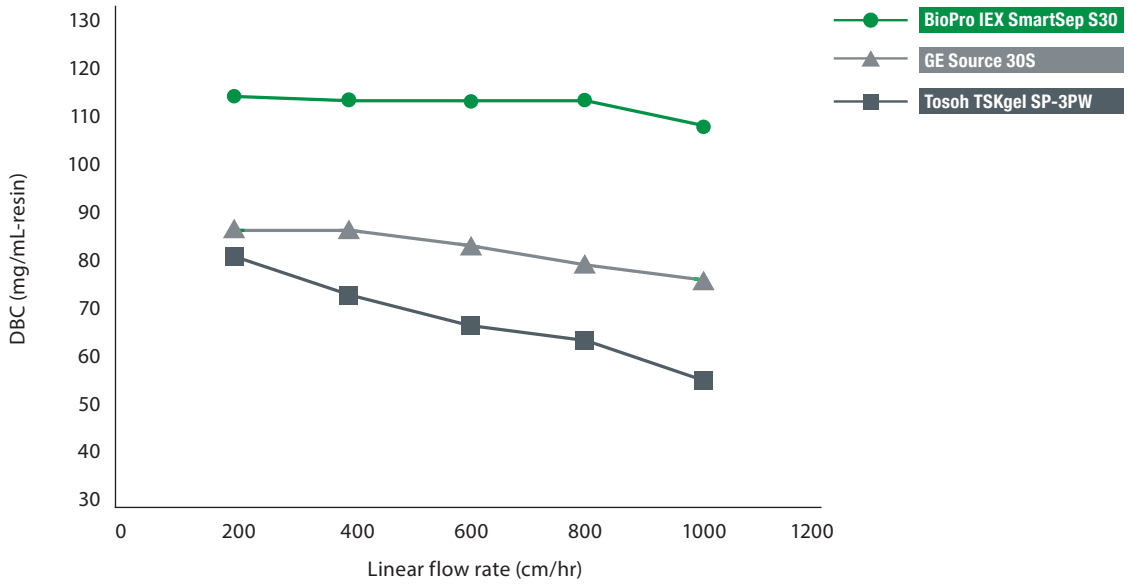


Comparison of the Performance of BioPro IEX SmartSep and Competitors´ Products in the Purification of Lysozyme , Insulin and Polyclonal IgG



Column:	50 x 5.0 mm ID
Flow rate:	400 cm/hr (1.32 mL/min)
Temperature:	25 °C

BioPro IEX SmartSep shows higher dynamic binding capacity for both small peptides and large proteins.



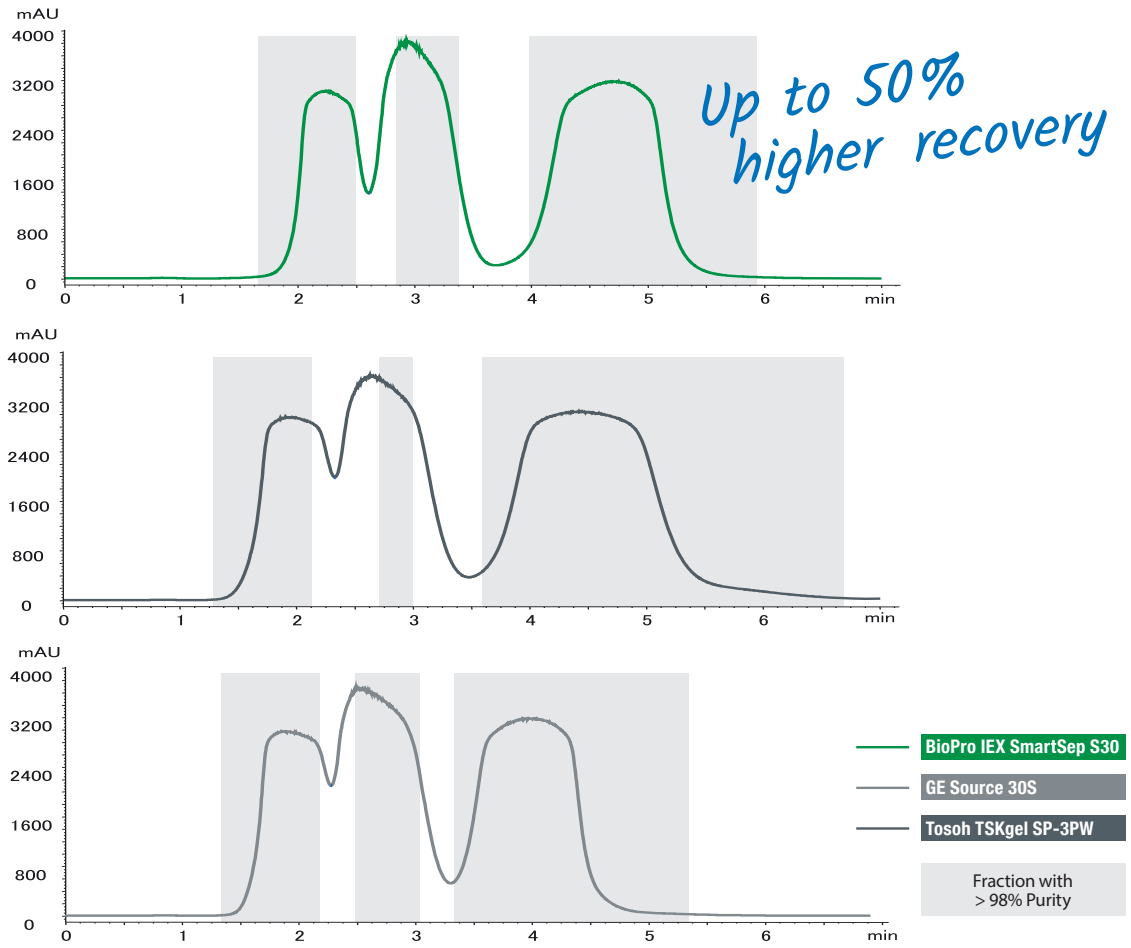
Column:	50 x 5.0 mm ID
Equilibration buffer:	20 mM Glycine-NaOH (pH 9.0)
Linear velocitiy:	200-1,000 cm/hr (0.66 mL/min-3.27 mL/min)

YMC's BioPro IEX resins show higher dynamic binding capacities over the full range of applicable flow rates.

Purification of proteins and peptides

BioPro IEX SmartSep resins offer the perfect solution for challenging separations. With the high binding capacity and recovery, the resins allow high-throughput purifications and increased productivity. Easy elution of target compounds improves the whole process.

Comparison of resolution with competitors' materials



Column:	50 x 5.0 mm ID
Eluent:	A) 20 mM NaH_2PO_4-Na_2HPO_4 (pH 6.8) B) 20 mM NaH_2PO_4-Na_2HPO_4 (pH 6.8) containing 0.5 M NaCl
Gradient:	0-100% B, 30 column volumes
Flow rate:	1600 cm/hr (5.23 mL/min)
Temperature:	25 °C
Detection:	UV at 220 nm
Injection:	20 mL (30 mg Proteins)
Sample:	1. Ribonuclease A (0.5 mg/mL) 2. Cytochrome c (0.5 mg/mL) 3. Lysozyme (0.5 mg/mL)

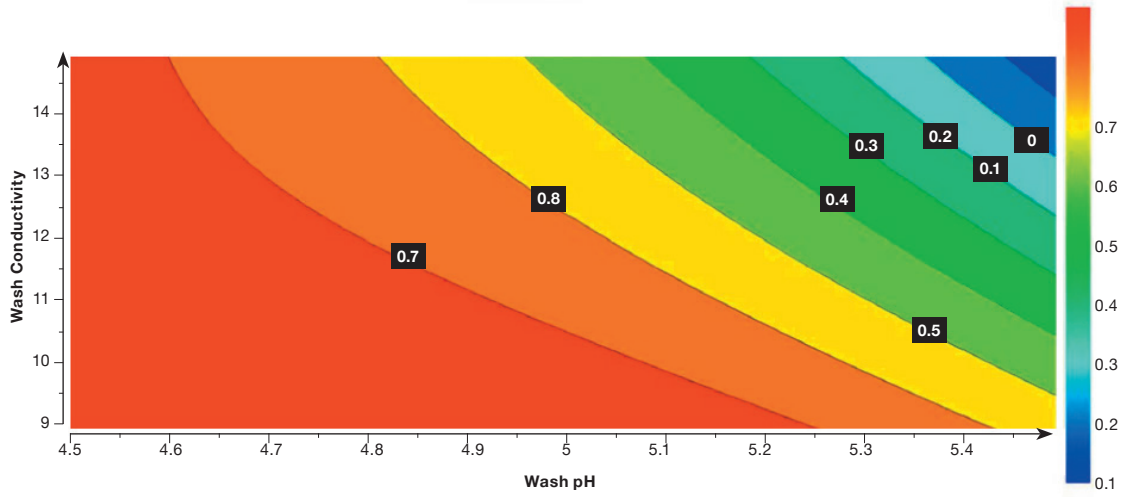
	Recovery (> 98% Purity)			
	Ribonuclease A	Cytochrome c	Lysozyme	**Total**
BioPro IEX SmartSep S30	**90.5 %**	**81.5 %**	**99.3 %**	**90.7 %**
TSKgel SP-3PW	74.2 %	54.4 %	99.5 %	76.9 %
GE Source 30S	87.2 %	76.0 %	99.5 %	87.8 %

BioPro IEX SmartSep S30 maintains its high resolution and high sample loading ability even at 1600 cm/hr and under high loading condition (30 mg/mL). It allows up to 50% higher recovery for specific target compounds compared to the competitor's materials. These features of the BioPro IEX SmartSep material indicate the possibility of cost savings for your purification.

The monoclonal antibody IgG (PI = 8.9) was purified in a two-step process out of cultured medium. The two combined separation modes are affinity and ion exchange chromatography.
For the second step, the strong cation exchanger BioPro S75 is used in bind-and-elute mode. In order to evaluate the optimum purification conditions, the influence of salt concentration and pH during the washing phase were analysed in a DoE (design of experiments) process.

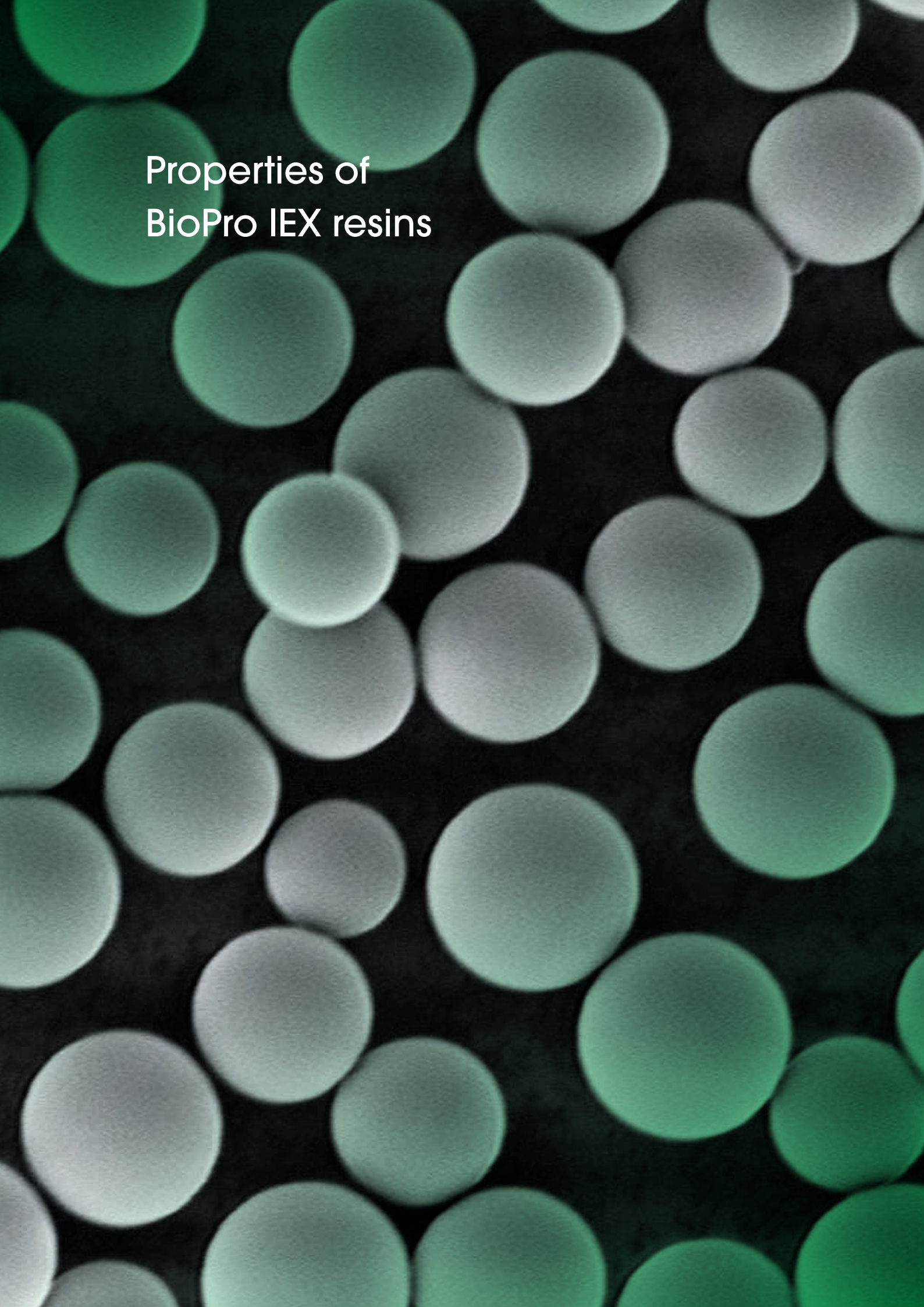
Recovery (%) at various salt concentrations and pH

Conductivity \ pH	4.5	5.0	5.5
15 mS/cm	72.2	40.1	0.0
12 mS/cm	73.4	68.2	10.1
9 mS/cm	73.1	69.5	64.0



Response surface plot (Recovery Area out/Area in)

These results show that the recovery is higher if the washing step is performed under acidic conditions. As the target mAb should not be denatured, pH 5 was chosen for the purification. A conductivity of 10 mS/cm was selected for the washing step.


Properties of
BioPro IEX resins

Scale up and availability of BioPro IEX

- Predictable scale-up process
- Preparative grade resins with particle sizes from 10 µm to 75 µm up to several thousand litres
- Full compliance with GMP requirements
- Short delivery for industrial-scale quantities
- High capacity with low operating pressures even at high flow rates
- Reduced processing costs
- Prepacked columns with 5 µm porous resins
- Non-porous resins for fast analysis

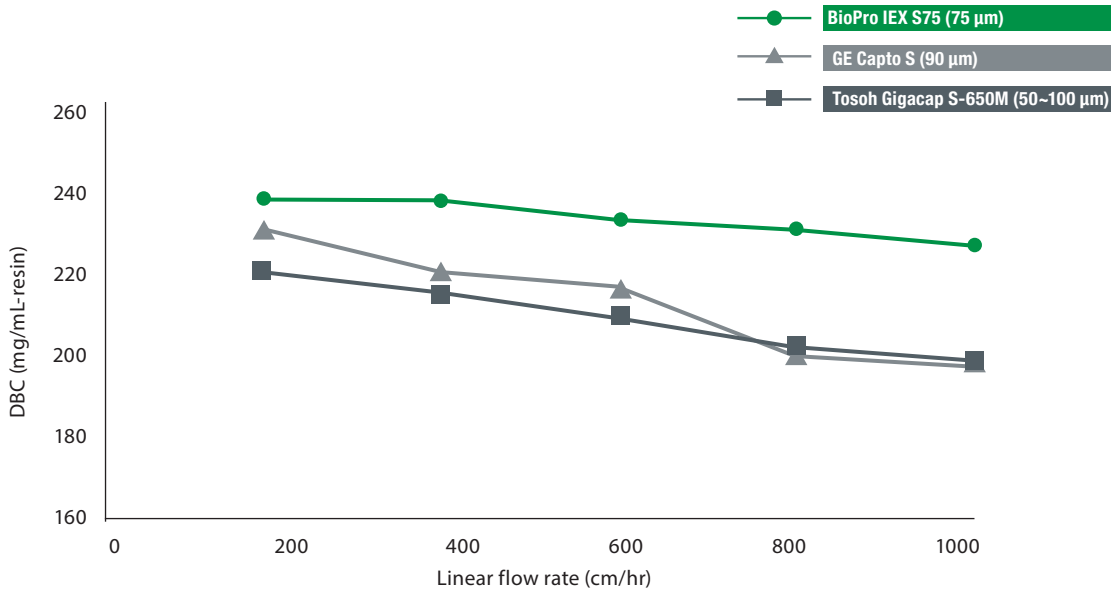
Mission Statement

YMC will never knowingly change any product that is being used in a validated production process or validated analytical method.

High dynamic binding capacity

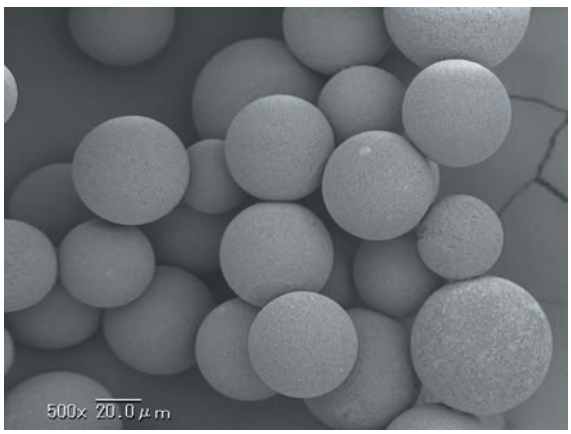
High binding capacity and high recovery

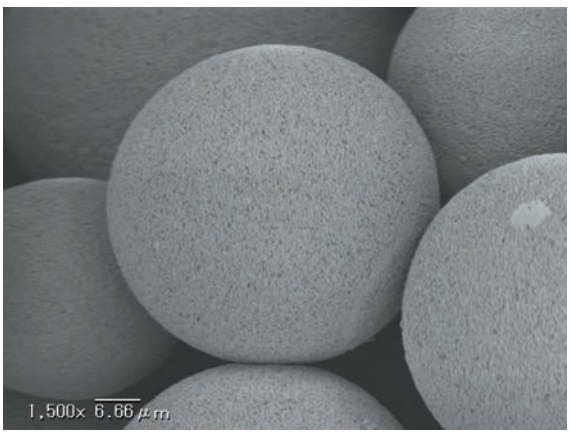
The porous versions of BioPro IEX show high dynamic binding capacity (DBC) and excellent recovery, making them useful for preparative separations of proteins and antibodies.



Column:	BioPro IEX S75, 50 x 5.0 mm ID
Sample:	1.0 mg/ml Lysozyme in equilibration buffer
Eluent:	A) 20 mM Glycine-NaOH (pH 9.0)
	B) 20 mM Glycine-NaOH (pH 9.0) containing 0.5 M NaCl
Detection:	UV at 300 nm

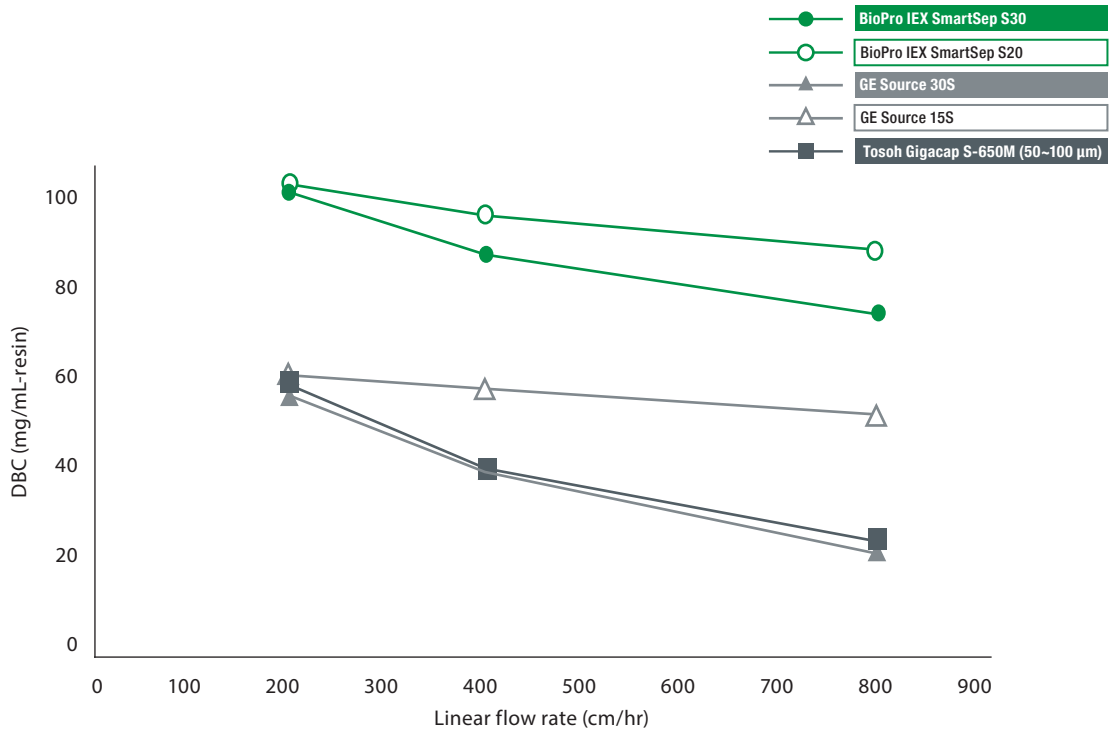
The sample loading at high flow rates is determined by the dynamic binding capacity of an ion exchange resin.
The dynamic binding capacity of BioPro IEX is excellent even at high flow rates. When compared to similar competitor products it consistently exhibits a higher dynamic binding capacity. This results in higher sample loading in a preparative processes.





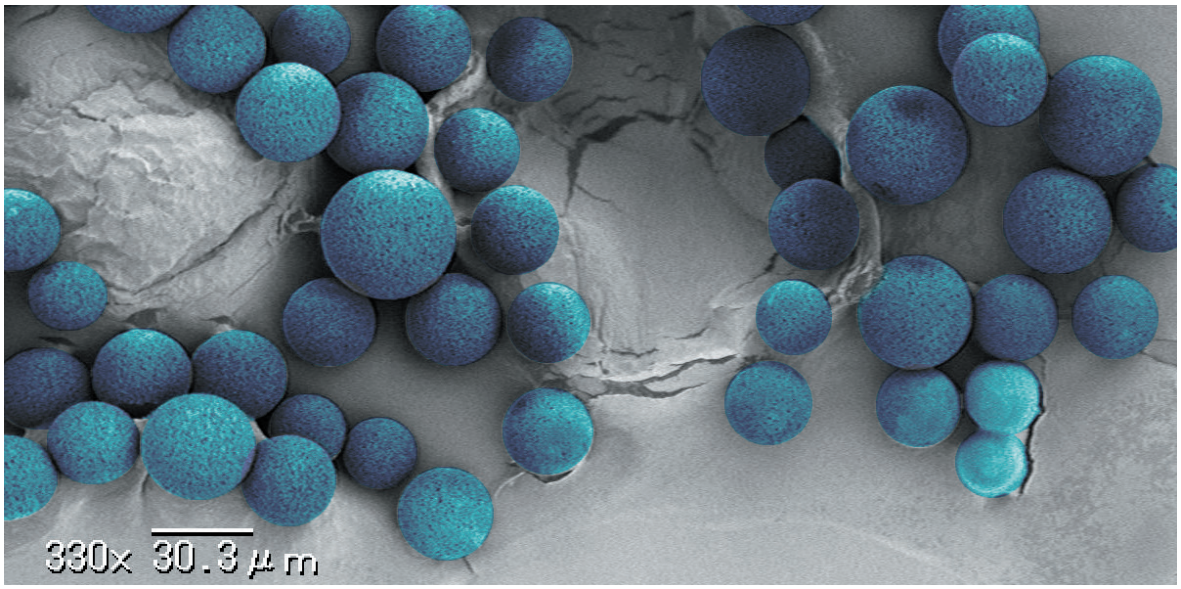
BioPro IEX S75 Particles

Comparison of the DBC for human polyclonal IgG at different flow rates for BioPro IEX SmartSep S30 and competitors' products.



Column:	50 x 5.0 mm ID
Equilibration buffer:	20 mM Glycine-NaOH (pH 9.0)
Linear velocitiy:	200-1,000 cm/hr (0.66 mL/min-3.27 mL/min)

BioPro IEX SmartSep shows considerably higher DBC across a wide range of linear velocity. A high DBC at flow rates of up to 1,000 cm/hr can reduce process time and significantly increase productivity.



BioPro IEX S30 Particles

Excellent alkaline CIP stability

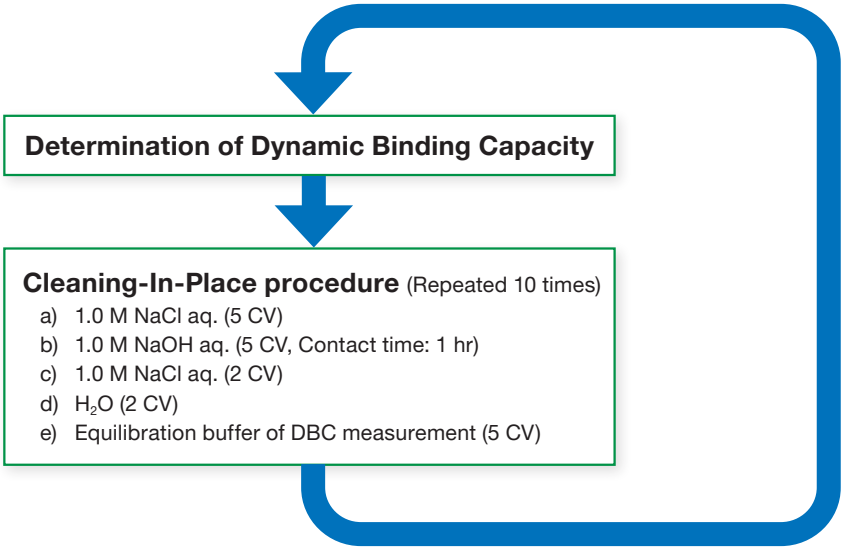
Cleaning-in-place (CIP) is essential for the economic use of packed chromatography columns. Efficient cleaning procedures increase the lifetime of the separation process and thereby contribute to the overall cost effectiveness. In addition, powerful CIP procedures strongly increase the safety and productivity of every downstream process.

Sodium hydroxide (NaOH) solutions are well established for the removal of precipitated proteins, hydrophobic proteins, nucleic acids, endotoxins and viruses and have become the first choice for cleaning and sanitising of chromatography resins. In order to optimise process development time and costs, there is an increasing demand for efficient cleaning procedures and compatible chromatography resins.

IEX resins from YMC are fully compatible with typical CIP procedures.

As an example, CIP studies have been performed using NaOH solutions with BioPro IEX S75/Q75 as well as with BioPro IEX SmartSep S30/Q30.

All YMC IEX resins maintain their performance values even after 100 CIP cycles.



DBC (IgG) (BioPro IEX SmartSep S30, BioPro IEX S75)

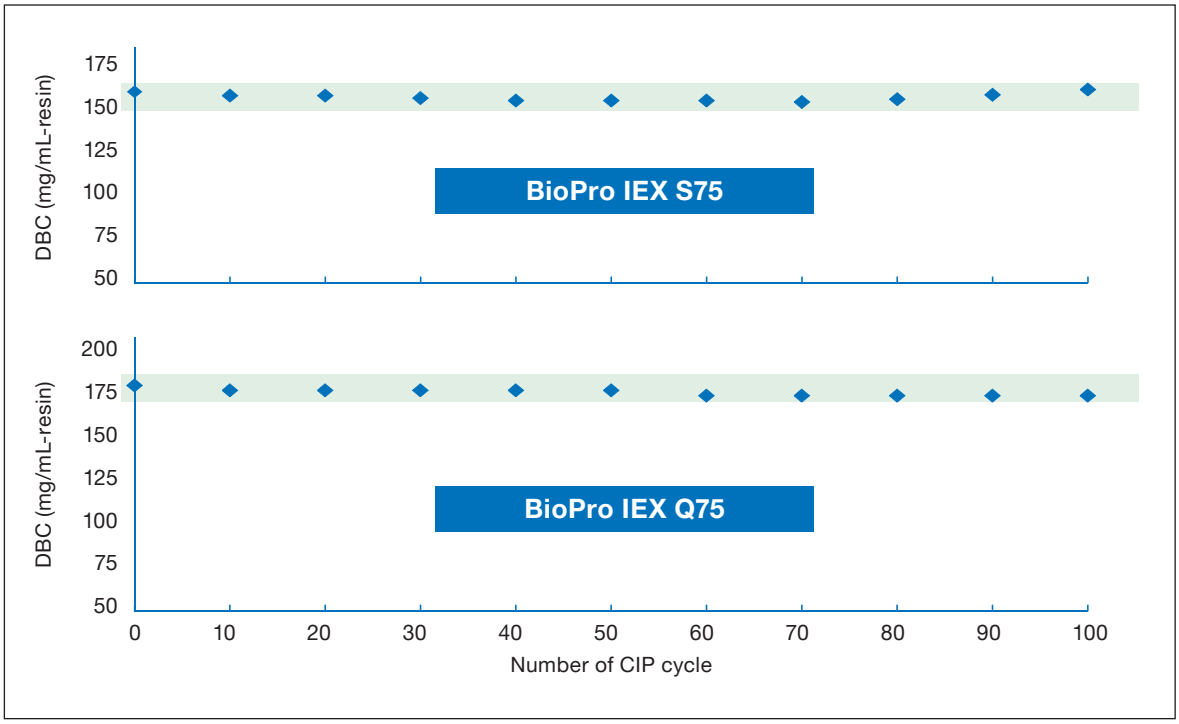
Column:	50 × 5.0 mm ID	Temperature:	25 °C
Equilibration buffer:	20 mM citric acid-NaOH (pH 5.3)	Detection:	UV at 280 nm
Elution buffer:	Equilibration buffer containing 0.5 M NaCl	Sample:	1.5 mg/mL human polyclonal IgG in equilibration buffer
Flow rate:	200 cm/hr (0.66 mL/min)		

DBC (BSA) (BioPro IEX SmartSep Q30, BioPro IEX Q75)

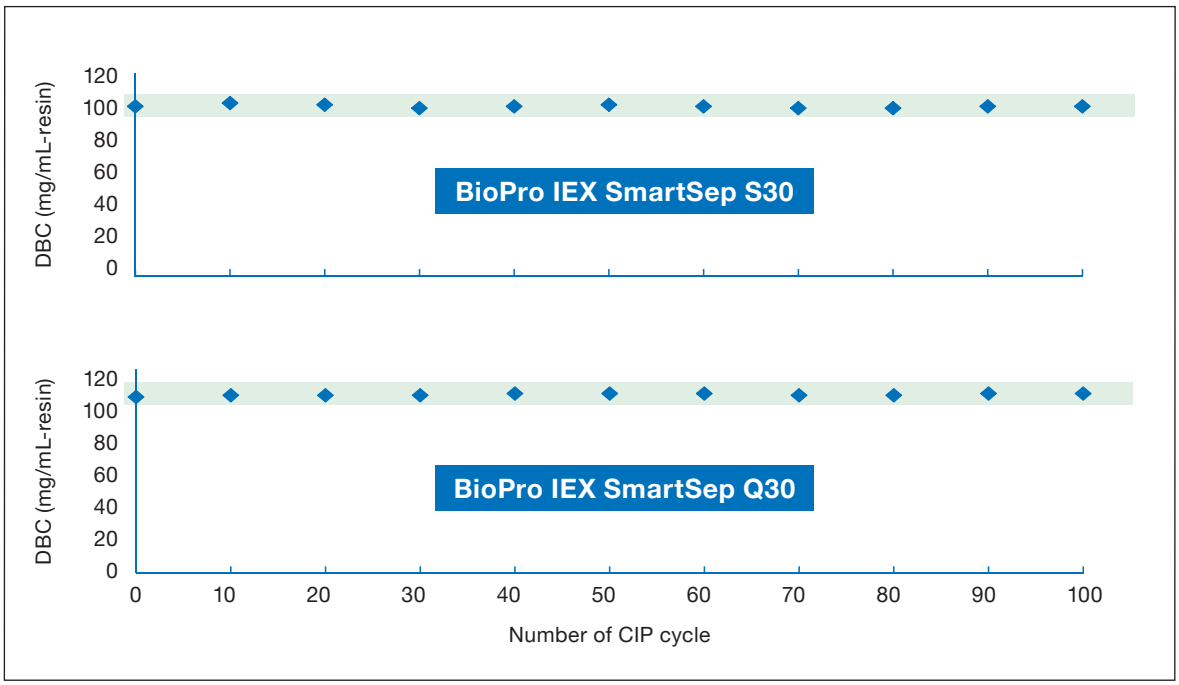
Column:	50 × 5.0 mm ID	Temperature:	25 °C
Equilibration buffer:	20 mM Tris-HCl (pH 8.6)	Detection:	UV at 280 nm
Elution buffer:	Equilibration buffer containing 0.5 M NaCl	Sample:	1.5 mg/mL BSA in equilibration buffer
Flow rate:	200 cm/hr (0.66 mL/min)		

CIP cycle

Column:	50 × 5.0 mm ID
Flow rates:	200 cm/hr (1.0 M NaCl, H_2O, Buffer)
	30 cm/hr (1.0 M NaOH)
Temperature:	25 °C

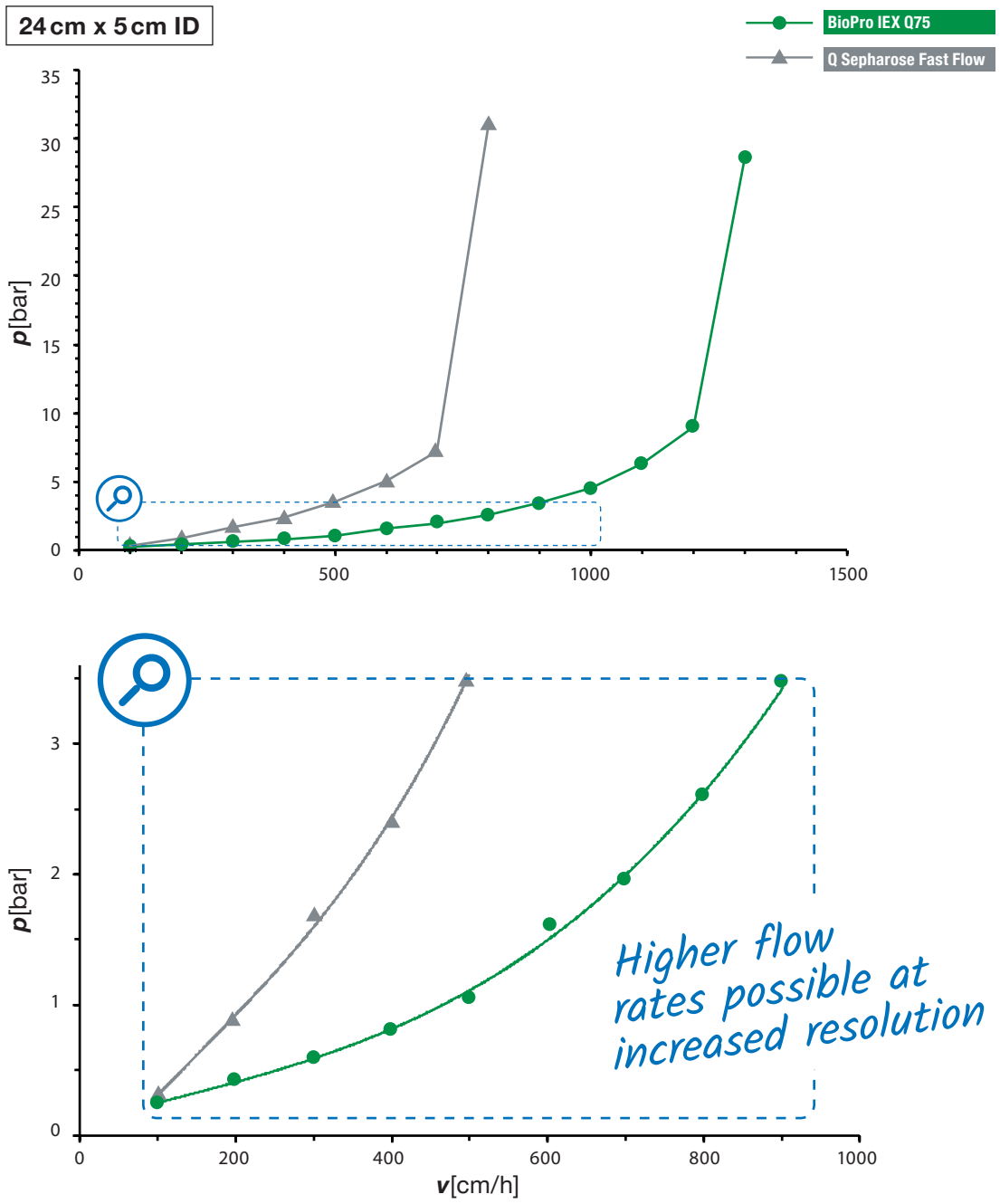


BioPro IEX S75 and Q75 maintain their binding capacity even after 100 CIP cycles.
BioPro IEX resins show excellent alkaline CIP stability.



BioPro IEX SmartSep S30 and Q30 maintain their binding capacity even after 100 CIP cycles.
BioPro IEX SmartSep resins show excellent alkaline CIP stability.

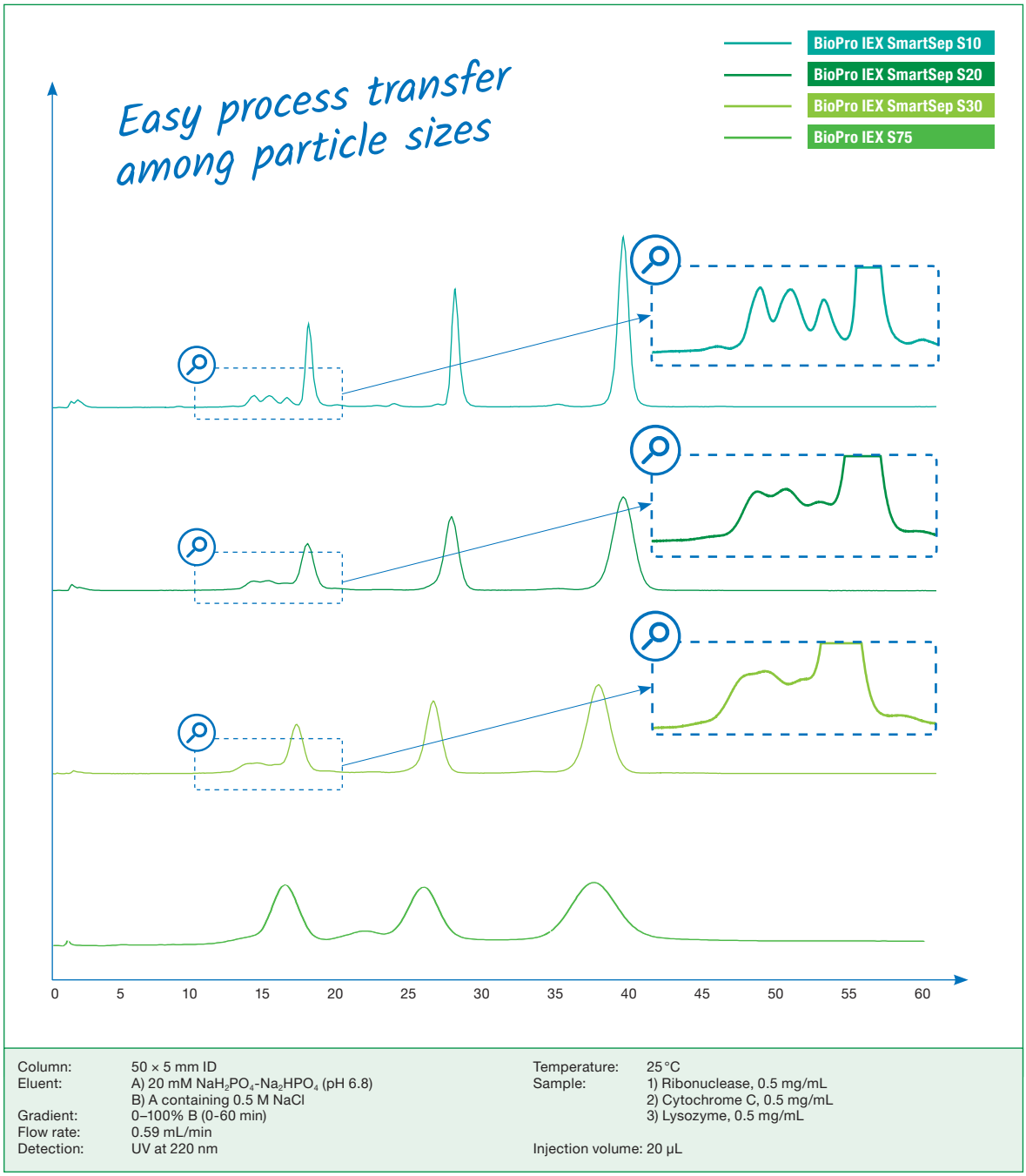
Pressure-flow characteristics



Column:	ECO^{PLUS}, 50 mm ID, max. bed length 250 mm, AB version
Resin amount (gravity settled in 1 M NaCl):	470 mL
Slurry concentration:	40 %
Consolidation flow velocity:	60 cm/h
Consolidated bed height:	24 cm
Mobile phase:	1 M NaCl solution

The pressure-flow curve of BioPro IEX Q75 suggests reversible compression behaviour over a wide range of linear flow velocity. Despite using smaller particles (75 µm) compared to the 90 µm particle size of the competitor's resin, BioPro IEX Q75 shows much better pressure flow characteristics. Higher flow rates can be applied to increase the throughput.

- **Improved resolution**
- **Higher flow rates possible**
- **Increased productivity**



Column:	50 × 5 mm ID	Temperature:	25 °C
Eluent:	A) 20 mM NaH_2PO_4-Na_2HPO_4 (pH 6.8)	Sample:	1) Ribonuclease, 0.5 mg/mL
	B) A containing 0.5 M NaCl		2) Cytochrome C, 0.5 mg/mL
Gradient:	0–100% B (0-60 min)		3) Lysozyme, 0.5 mg/mL
Flow rate:	0.59 mL/min		
Detection:	UV at 220 nm	Injection volume: 20 µL	

One of the advantages of YMC's BioPro IEX resins is its full scalability. This property provides an identical chromatographic behaviour across all particle sizes. This is beneficial, as separation and fractionation can be optimised on the analytical scale. Depending on the required resolution the optimal bead size can be selected. Then, the process can be reliably transferred to the production scale. This enables highly flexible implementation of BioPro IEX resins, resulting in a perfectly tailored solution.

An illustrated example is depicted below for the three enzymes ribonuclease, cytochrome c and lysozyme. This shows that the separation of the main peaks remains stable across the four different particle sizes. If the highest resolution is required, 10 µm particles are the optimum choice. 10 µm particles allow the isolation of trace impurities.

During a capturing process the 75 µm material demonstrates adequate separation. The three main peaks are well separated.

Specifications and Ordering information

BioPro IEX for Capture

BioPro IEX Series	BioPro IEX Q75	BioPro IEX S75
Ion exchange type	strong anion exchanger	strong cation exchanger
Charged group	$-R-N^{+}(CH_3)_3$	$-R-SO_3^-$
Matrix	Hydrophilic polymer beads	
Pore size	Porous	
pH Range	2–12	
Compression factor	1.05–1.15	
Particle size	75 µm	
Pressure resistance	0.3 MPa	
Typical flow rate	200–1000 cm/hr Max. 2000 cm/hr	
Ion-exchange capacity	min. 0.10 meq/ml-resin	
Dynamic binding capacity	min. 160 mg/ml-resin (BSA)	min. 160 mg/ml-resin (lysozyme)

Regulatory support file available under non-disclosure agreement.
Used in validated cGMP-manufacturing processes.

Customised material available on request.
DMF registered with FDA.

BioPro IEX SmartSep for intermediate purification and polishing

BioPro IEX Series	BioPro IEX SmartSep Q10	BioPro IEX SmartSep Q20	BioPro IEX SmartSep Q30	BioPro IEX SmartSep S10	BioPro IEX SmartSep S20	BioPro IEX SmartSep S30
Ion exchange type	strong anion exchanger			strong cation exchanger		
Charged group	$-R-N^{+}(CH_3)_3$			$-R-SO_3^-$		
Matrix	Hydrophilic polymer beads					
Pore size	Porous					
pH Range	2–12					
Compression factor	1.05–1.15					
Particle size	10 µm	20 µm	30 µm	10 µm	20 µm	30 µm
Pressure resistance	Regular use: 3 MPa Max.: 4 MPa	Regular use: 2 MPa Max.: 3 MPa		Regular use: 3 MPa Max.: 4 MPa	Regular use: 2 MPa Max.: 3 MPa	
Typical flow rate	200–1000 cm/hr Max. 2000 cm/hr					
Ion-exchange capacity	min. 0.08 meq/ml-resin					
Dynamic binding capacity	min. 100 mg/ml-resin (BSA)			min. 100 mg/ml-resin (lysozyme)		

Screening kits and bulk samples for media selection and method development

YMC offers a number of ion exchange screening kits based on 1 mL or 5 mL columns and also bulk resin samples for testing. This provides a significant advantage and efficiency in resin screening and purification method development.

1 ml Type (26 x 7.0 mm ID)

- Resin screening
- Purification method development

5 ml Type (26 x 15.6 mm ID)

- Purification method development
- Loadability studies

Please contact us to order your free bulk resin samples for testing.

YMC Europe GmbH · Schöttmannshof 19 · 46539 Dinslaken · Phone +49 (0)2064 427-0 · Fax +49 (0) 2064 427-222 · Email: info@ymc.de · www.ymc.de

Availability

- Large production capacity for YMC's IEX resins
- Lot sizes up to 400 L available
- Short delivery time even for large quantities
- Full compliance with GMP requirements

Strong anion exchanger: BioPro IEX Q

Product	Particle Size	Code	Pack Sizes*					
			50 ml	250 ml	1 L	5 L	10 L	20 L
BioPro IEX SmartSep Q10	10 µm	QSA0S10	✔	✔	✔	✔	✔	✔
BioPro IEX SmartSep Q20	20 µm	QSA0S20	✔	✔	✔	✔	✔	✔
BioPro IEX SmartSep Q30	30 µm	QSA0S30	✔	✔	✔	✔	✔	✔
BioPro IEX Q75	75 µm	QAA0S75	✔	✔	✔	✔	✔	✔

* Larger or customised pack sizes are available on request.

Strong cation exchanger: BioPro IEX S

Product	Particle Size	Code	Pack Sizes*					
			50 ml	250 ml	1 L	5 L	10 L	20 L
BioPro IEX SmartSep S10	10 µm	SSA0S10	✔	✔	✔	✔	✔	✔
BioPro IEX SmartSep S20	20 µm	SSA0S20	✔	✔	✔	✔	✔	✔
BioPro IEX SmartSep S30	30 µm	SSA0S30	✔	✔	✔	✔	✔	✔
BioPro IEX S75	75 µm	SPA0S75	✔	✔	✔	✔	✔	✔

* Larger or customised pack sizes are available on request.

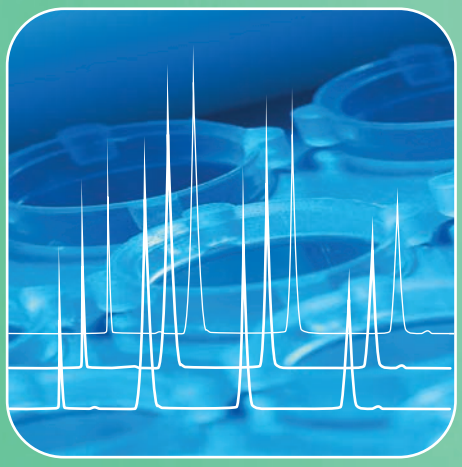
Regulatory support file available under non-disclosure agreement. Used in validated cGMP-manufacturing processes. Customised material available on request. DMF registered with FDA.

Preparative screening kits

Product name*	Particle Size	Pack size	Column volume	Product code
BioPro IEX Q75	75 µm	5 / pack	1 mL	BPQAA0S75-01PK
			5 mL	BPQAA0S75-05PK
BioPro IEX SmartSep Q30	30 µm	5 / pack	1 mL	BPQSA0S30-01PK
			5 mL	BPQSA0S30-05PK
BioPro IEX SmartSep Q20	20 µm	5 / pack	1 mL	BPQSA0S20-01PK
			5 mL	BPQSA0S20-05PK
BioPro IEX S75	75 µm	5 / pack	1 mL	BPSPA0S75-01PK
			5 mL	BPSPA0S75-05PK
BioPro IEX SmartSep S30	30 µm	5 / pack	1 mL	BPSSA0S30-01PK
			5 mL	BPSSA0S30-05PK
BioPro IEX SmartSep S20	20 µm	5 / pack	1 mL	BPSSA0S20-01PK
			5 mL	BPSSA0S20-05PK
IEX Selection Kit Q75/S75/Q30/S30	30 µm, 75 µm	4 / pack 1 per resin	1 mL	BPSIA0S99-01PK
			5 mL	BPSIA0S99-05PK

* Other screening kits are available on request

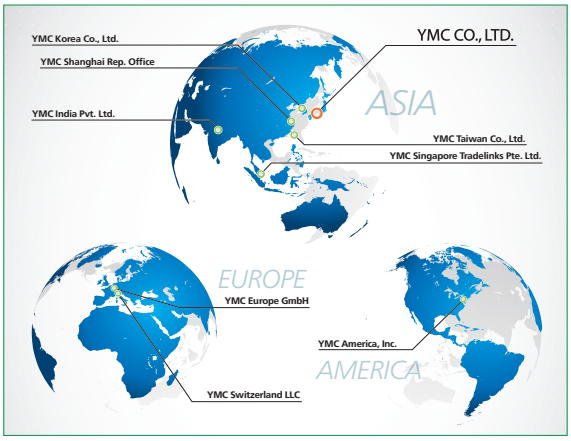
More about YMC



Fully Integrated Manufacturing

YMC operates a fully integrated manufacturing process for the BioPro IEX resins. This process includes the manufacture of the base beads and the modification for the IEX functionality.

This gives YMC complete traceability and control over the entire manufacturing process. YMC can guarantee reliable product supplies for today and in the future.



Global Supplies

BioPro IEX resins are available worldwide through a dedicated support network headed by YMC operations in Japan, the US and in Europe to ensure easy, reliable method transfer between research and production sites across the world. Batch sizes up to 400 L are available, in many different packaging formats. Individual supply agreements are common for validated processes.

Quality Control

The rigorous quality control procedures set by YMC start with the manufacturing of the base material. Every batch is evaluated for compliant reproducibility to ensure consistent performance. The YMC facilities are certified according to ISO 9001. Quality agreements are common for validated processes. The manufacturing site is regularly audited successfully by numerous pharmaceutical companies all around the globe.

Regulatory Support

Since all YMC processes and working procedures are thoroughly monitored and documented, YMC always has been in perfect condition to prove full compliance with the requirements. The BioPro IEX resins are supplied with the full technical documentation to show compliance with all applicable regulations. The resins are registered for Drug Master Files and are in use for GMP production of biotherapeutics.

Ideally suited for use with BioPro IEX stationary phases:
Glass columns made by YMC for biochromatography

ECO columns

Glass columns for low and medium pressure applications

Inner diameter: 10–80 mm
Column volumes: 0–5 L

- Easy piston adjustment
- Heating/cooling jacket for temperature sensitive applications
- 1 m long glass bodies for SEC applications

ECO^{PLUS} columns

Glass columns for medium and high pressure applications

Inner diameter: 5–50 mm
Column volumes: 0–1 L

- Easy assembly with Quick-Lock system
- Faster runs due to increased pressure limits
- Improved reproducibility due to calibrated glass body

YMC Pilot^{PLUS}

Glass columns for pilot scale BioLC applications

Inner diameter: 0–200 mm
Column volumes: 0–25 L

- Bubble-free column packing due to unique drain function
- Easy unpacking with removable column body
- 100% biocompatibility

Prepacked Glass Columns

Save time and purchase a prepacked glass column

You may choose from services which include packing of

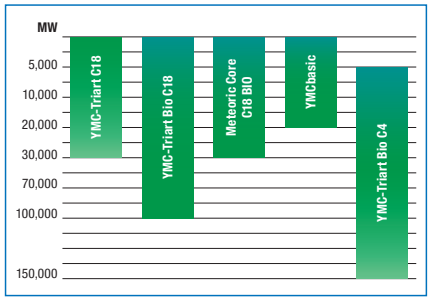
- New ECO and ECO^{PLUS} columns in standard and custom dimensions
- Your used ECO or ECO^{PLUS} columns
- BioPro IEX resins and other stationary phases

Did you know that you can also...
... contact us for on-site packing support?
... learn how to pack a column for yourselves in a YMC seminar?

For further information please contact YMC:
Phone: +49 (0)2064 427-0
Email: info@ymc.de

Proteins / Peptides

HIC	IEX	SEC	RP
BioPro HIC HT	BioPro IEX QA	YMC-Pack Diol-60	YMC-Triart C18
BioPro HIC BF	BioPro IEX QF	YMC-Pack Diol-120	YMC-Triart Bio C18
	BioPro IEX SP	YMC-Pack Diol-200	Meteoric Core C18 BIO
	BioPro IEX SF	YMC-Pack Diol-300	YMCbasic
		YMC-SEC MAB	YMC-Triart Bio C4



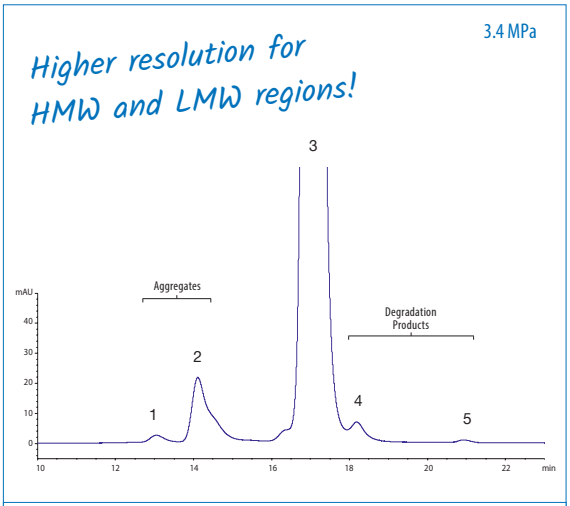
(Monoclonal) Antibodies

HIC	IEX	SEC	RP
BioPro HIC HT	BioPro IEX QA	YMC-Pack Diol-200	YMC-Triart Bio C4
BioPro HIC BF	BioPro IEX QF	YMC-Pack Diol-300	
	BioPro IEX SP	YMC-SEC MAB	
	BioPro IEX SF		

Oligonucleotides / Nucleic Acids

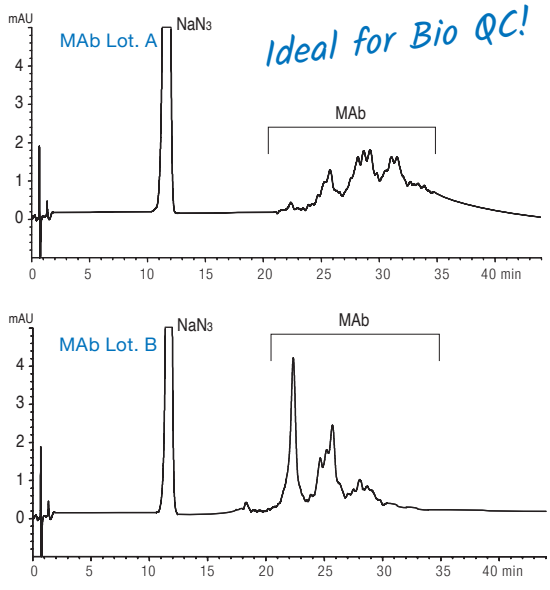
IEX	RP
BioPro IEX QA	YMC-Triart C18
BioPro IEX QF	YMC-Triart Bio C18
	YMC-Triart C8
	Hydrosphere C18

YMC-SEC MAB – Simultaneous analysis of antibodies, fragments and aggregates



Column:	YMC-SEC MAB (3 µm, 25 nm) 300 x 4.6 mm ID
Part No.:	DLM25S03-3046WT
Eluent:	0.1 M phosphate buffer (pH=7) containing 0.2 M NaCl
Flow rate:	0.165 mL/min
Temperature:	25 °C
Detection:	UV at 280 nm
Cell path:	10 mm
Injection:	10 µL (5 mg/mL)
Sample:	Avastin

BioPro IEX Columns - Outstanding resolution and excellent reproducibility



Column:	BioPro IEX QF (5 µm) 100 x 4.6 mm ID
Part No.:	QF00S05-1046WP
Eluent:	A) 20 mM Tris-HCl (pH 8.1) B) 20 mM Tris-HCl (pH 8.1) containing 0.5 M NaCl
Gradient:	10–25%B (0-60 min)
Flow rate:	1.0 mL/min (360 cm/hr)
Temperature:	25 °C
Detection:	UV at 220 nm
Injection:	14 µL (0.1 mg/mL)
Sample:	Mouse monoclonal IgG1 anti-human IgG4 (Purified by DEAE chromatography, containing NaN_3)

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