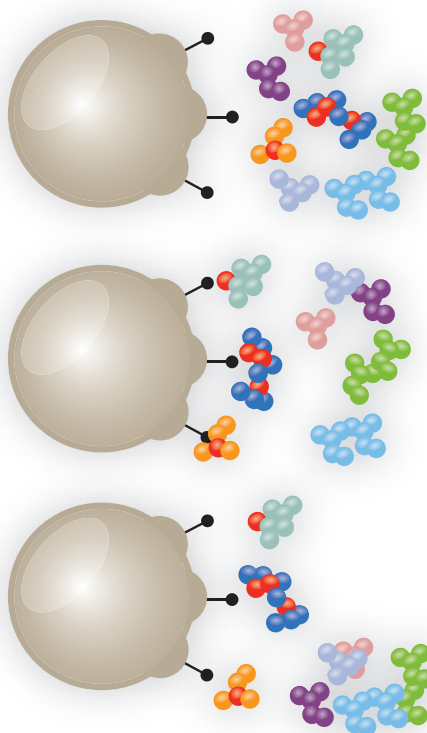


Hydrophobic Interaction Chromatography (HIC)

Selection Guide



Principles of HIC

Proteins in aqueous solution have various surface residues exposed to solvent to different degrees, dependent on protein structure. These residues can be hydrophilic, for example they may carry charges, or they can be hydrophobic, such as those in the amino acids phenyl alanine, tyrosine and tryptophan. Hydrophobic groups will prefer to bury themselves internally in the protein 3D structure but some will be exposed. Salts can be used to precipitate or crystallize proteins out of solution – to cause the proteins to self-associate. Scientists have been aware, since Hofmeister, that different salts play a significant role in self-association or the association with hydrophobic surfaces. Figure 1 shows a small selection of salts used in chromatography that modulate hydrophobic interactions. The salts are ordered from right to left in order of increasing “salting out” effect. These phenomena form the basis for hydrophobic interaction chromatography (HIC). A chromatographic matrix containing hydrophobic groups, binds proteins from aqueous solutions to different extents depending on the protein structures and a range of controllable factors including concentrations of salts, pH, temperature and organic solvents (Fig 2).

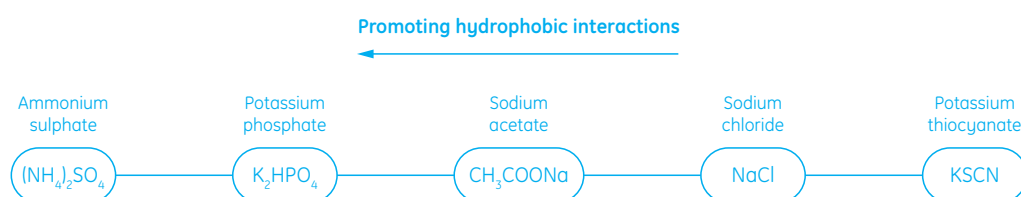


Fig 1. In general, salts that increase surface tension in aqueous solutions also promote hydrophobic interactions.

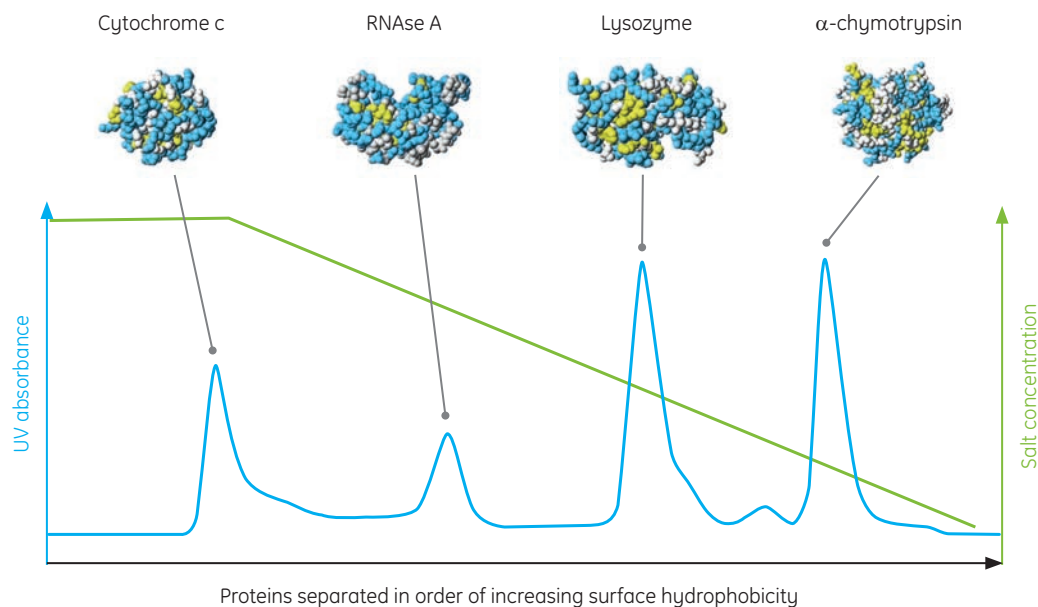


Fig 2. An illustration of the elution of 4 model proteins with their different 3D structures from a HIC column, using a descending salt concentration gradient. Yellow colors indicate hydrophobic residues.

HIC suits all stages of a purification process. Application examples include high-yield capture, polishing monoclonal antibodies, removing truncated species from full-length forms, separating active from inactive forms, and clearing of viruses. HIC is frequently used to remove impurities with the product recovered in the flow-through, as well as in the more conventional bind-elute mode. HIC forms one of the orthogonal techniques in a classic approach to purifying biomolecules by charge, hydrophobicity and size in a 3-step protocol. It complements adjacent purification steps in that the mobile phases used to bind or elute proteins are similar to those coming from preceding or leading to subsequent techniques. Since proteins are loaded at high and eluted at low salt concentrations, HIC is ideal to use after ion exchange or salt precipitation of a product or impurities, as shown in Figure 3.

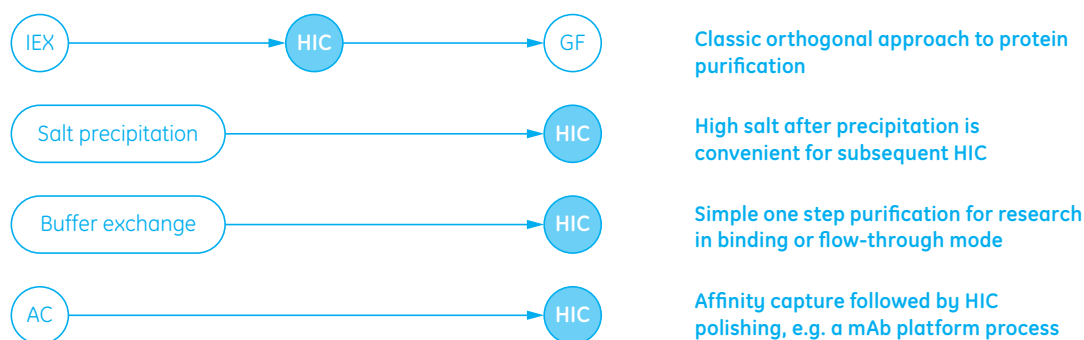


Fig 3. Illustrates various typical positions for HIC steps in purification schemes.

Typically, sample is applied in high salt and eluted with a gradient down to buffered low salt. Additives such as ethanol, ethylene glycol or amino acids may be tested to improve performance in various ways. In a capture unit operation, where the primary aim is to isolate and concentrate target molecule, a step gradient is often preferred for elution rather than a linear gradient. Using the PreDicator™ 96-well filter plate approach to medium selection (see Fig 4) simplifies choosing the best medium and operating conditions regardless of the application.

HIC is widely used in industrial processes. Early capture steps with crude feed may require the use of larger-particle media and, conversely, polishing applications may require small particle media and shallow gradients. For a regularly-used production process, considerations around robustness and economy demand optimization and method characterization before scale-up.

Challenges

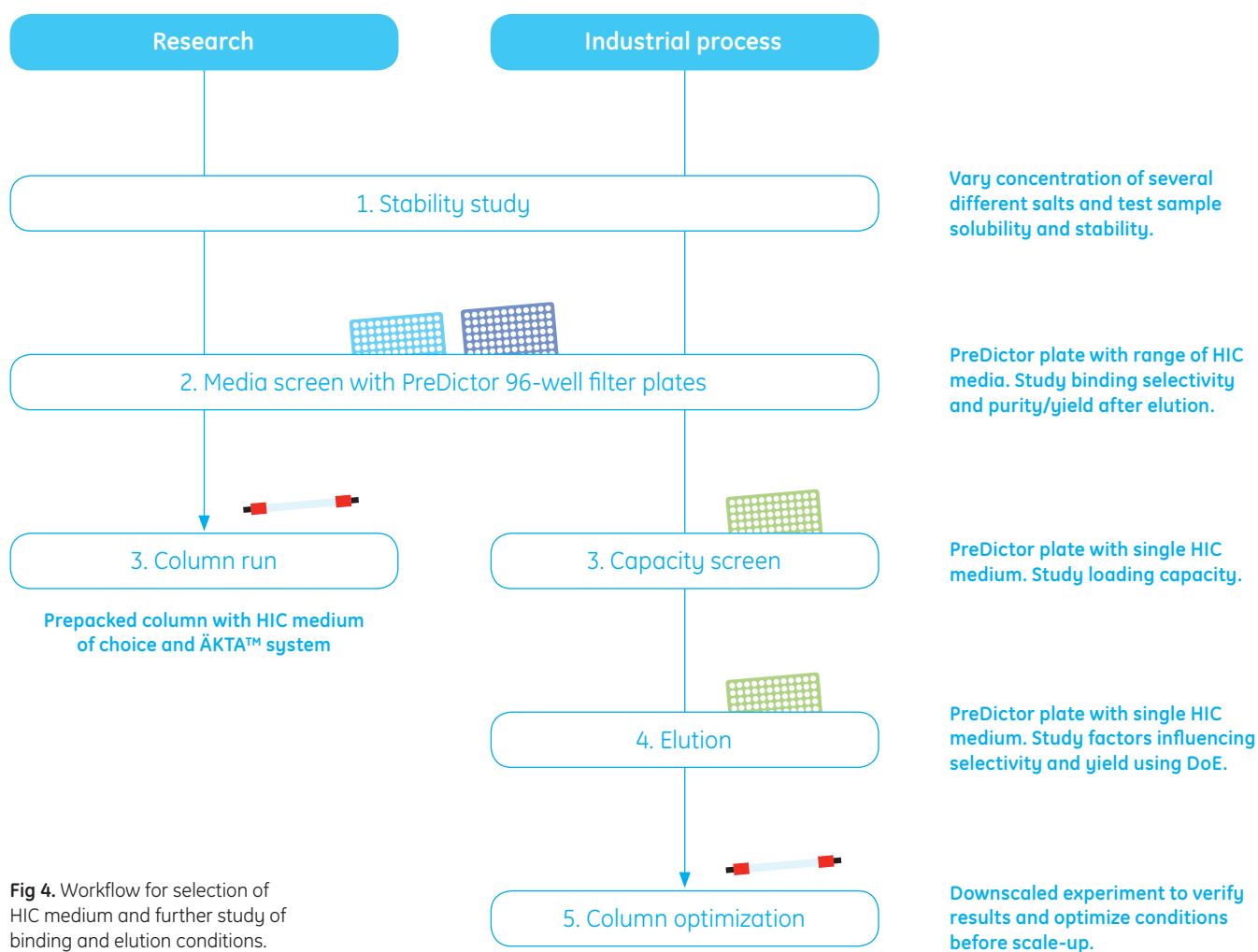
Although HIC is a powerful purification technique, successful choice of HIC media and conditions for their use can be challenging. Whereas separations in gel filtration and ion exchange are relatively simple to predict and modulate, making first choices easy, HIC is more complex. Experience shows that binding is hard to forecast and optimal elution conditions can depend on many factors. Sometimes yields are unexpectedly low due to unfavorable solvent conditions, or denaturation of target protein on the hydrophobic surface. The range of additives that can be used to enhance performance also complicates choices. Today, GE Healthcare offers a wide range of HIC media, covering strong to weak hydrophobic interactions, on various matrices and with a range of bead sizes to fit most applications and scales. The exciting news is that through application of PreDicator plates prefilled with HIC media, a more systematic approach to choosing the appropriate HIC media and run conditions can be applied. This translates into a greater probability of achieving success at the lab bench and a speedier way to optimize and characterize a method for scale up in process development.

Media selection routes

The preferred workflow depends on the application; primarily, whether or not the purification will be scaled up in an industrial process.

For many applications in research, media selection is dictated simply by the purity required. The successful choice of medium depends on finding the right binding selectivity with good product recovery, whilst the need for method optimization and characterization is generally less than for a process that will be scaled up and used for regular industrial production.

The workflow begins in the same way for both types of applications, as illustrated in Figure 4.



1. Stability study

Some proteins are more stable than others. One reason why a particular HIC medium or salt concentration or pH may be better than another for a specific protein is if it does not cause precipitation or denaturation, which otherwise can reveal itself as low yield, peak broadening or even multiple peaks in chromatography. Varying the type of salt and salt concentration in a study to make sure the intended mobile phase does not cause precipitation or denaturation allows subsequent purification within a stability window. Ammonium sulfate, sodium chloride and other salt solutions are tested over a range of

concentrations and pH's. A simple approach uses a 96-well microtiter plate and light scattering at A_{350} nm to detect precipitation. Figure 5 shows a stability study of a protein using light scattering*. In some cases mobile phases may include additives, such as amino acids or sugars, which stabilize protein structure. For the subsequent HIC media screening, maximum salt concentrations 10% to 15% below the point of precipitation should be used.

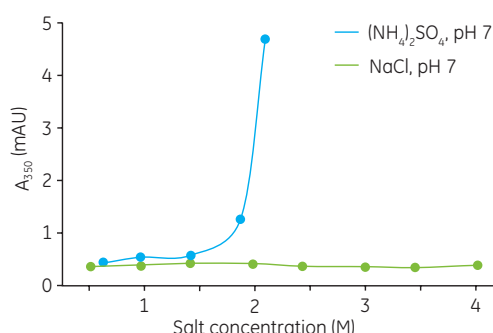
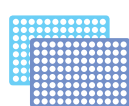


Fig 5. Solubility of a protein in different salts.

*For further details, see Application note: High throughput screening of HIC media in Predictor plates for capturing recombinant Green Fluorescent Protein from *E. coli*, code number 28-9964-49



2. Media screen with PreDicator 96-well filter plates

The first step to select the appropriate HIC medium follows naturally after the stability study. Choose the medium with the best binding selectivity that gives good product recovery after elution. PreDicator plates are available covering eight HIC media. One plate type has four relatively low hydrophobicity media, the other has four relatively high hydrophobicity media (Fig 6), see also description of the range of hydrophobic media on page 8. Each plate type is also available with either 6 or 50 μ L of medium in every well. For initial screening, especially where sample is in short supply, choose the 6 μ L plates. In some cases it will be desirable to screen all of the media using both high and low hydrophobicity plates.

The recommended first experiment with the PreDicator plate examines binding conditions in order to determine the selectivity of the different media for the product relative to impurities. Using a range of salt concentrations which keep the sample stable in solution (from the stability study) analysis of both the target protein and total protein in the flow-through indicates the medium with best binding selectivity. Wash and recover bound material, using uniform elution conditions over the plate (for example a step down to low salt), to study the yield as well as purity of the product. Yields above 60% in this format are considered indicative of good performance.

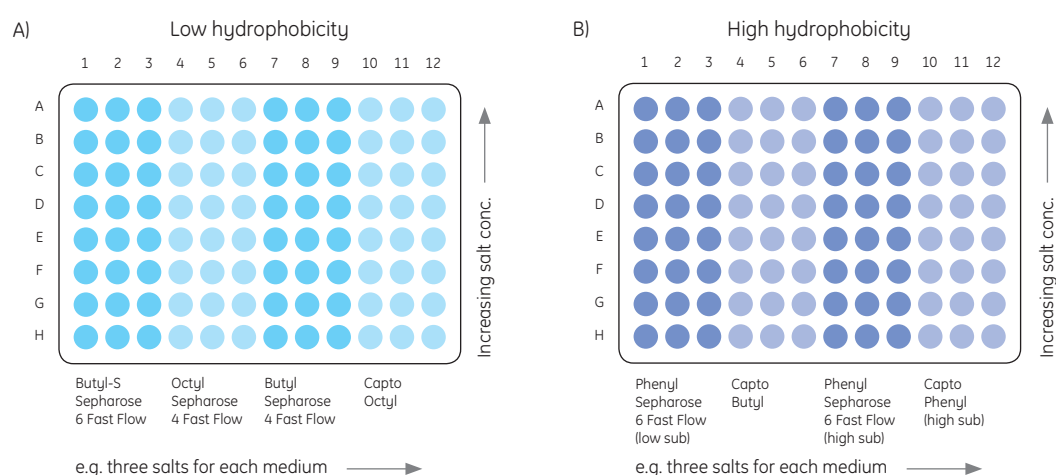


Fig 6. Illustration of the PreDicator plates covering low (A) and high (B) hydrophobicity media. Each plate type is available with 6 or 50 μ L of medium per well. This example shows how media can be screened for binding product in three different salts over a range of salt concentrations.



3. Research – Column run

For research applications whose purpose is to quickly develop a single step purification, the HIC medium and conditions that give best results from the media screen can be transferred to a suitable scale of column directly. Most convenient is to use a prepacked column selected from the the HiTrap™ or HiScreen™ ranges. Alternatively bulk media can be packed in an empty column that matches the performance of the medium, for example from the HiScale™ range.



3. Industrial process – Capacity screen

In the industrial workflow, there is considerable interest in determining the loading capacity. This is frequently done with the 6 µL PreDicator plates to limit the amount of sample required. Excess sample is applied throughout a plate containing a single HIC medium to determine the loading capacity under different conditions.

Further details of this and other kinds of related experiments can be found in the Handbook: High-throughput Process Development with PreDicator Plates. Principles and Methods, code number 28-9403-58.



4. Industrial process – Elution

Following investigation of capacity, study elution conditions in more detail to find those which offer the best selectivity and yield. Using a 50 µL PreDicator plate with a single HIC medium, several factors that influence elution, such as salt concentration, pH and perhaps the addition of an organic solvent can be tested using Design of Experiments (DoE) to derive a statistical model describing the impact of these factors on yield and purity. Such work results in the characterization of a design space that describes performance in relation to key operating parameters, and is in accordance with modern Quality by Design (QbD) principles.



5. Industrial process – Column optimization

Following PreDicator plate experiments the next step in industrial process development is to verify performance in column format. Prepacked columns are quick and reliable and the PreDicator RoboColumn™ is one option designed for parallel experiments with a robotic system. HiTrap and HiScreen prepacked columns are widely used for initial verification and further optimization using a chromatography system. A recommended experimental approach is to use a scaled-down model of the envisaged full-scale unit operation with the same relative sample load, flow velocity, bed height, and other operating conditions. HiScreen prepacked columns have bed heights of 10 cm, and for 20 cm bed heights that are frequent in large-scale applications, two columns can be connected in series. Alternatively, the chosen HIC medium can be self-packed in a HiScale column of suitable dimensions.

QbD, HTPD, and DoE

In industrial development, it is recommended to follow a screening, optimization, characterization workflow to create a robust downstream process that will assure product quality with best possible yield and economy. Today this approach has been well described in the context of QbD in the regulatory guidelines from ICH; Q8, Q9, Q10 and Q11.

There are usually many factors that can be studied and high-throughput process development (HTPD) methods using DoE are recommended.

For further details see the Handbook: High-throughput Process Development with PreDicator Plates. Principles and Methods, code number 28-9403-58.

Generally, the outcome of downstream process development will use a capture to polishing schedule to take a product from the crude source to pure bulk substance. Each unit operation will achieve defined goals when operated within a defined range of controlled conditions. Only media appropriate for use at scale to achieve these goals should be tested. A HIC step will be integrated with other steps such as affinity chromatography and ion exchange, as well as filtration of various kinds and possibly centrifugation and other techniques.

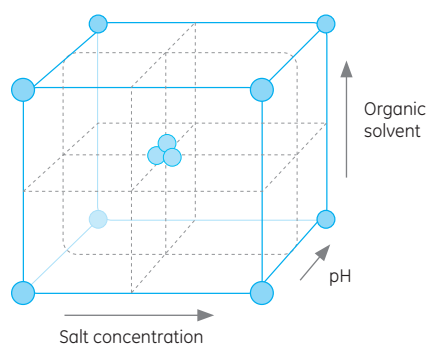


Fig 7. DoE. An illustration of a full factorial design with triplicate center points to study responses to three factors: Salt concentration, pH and organic solvent concentration.

Products

GE Healthcare introduced the first commercial HIC media in 1977 and now offers one of the broadest ranges of HIC media on the market, covering most common laboratory and industrial applications. In addition to the range of HIC products, hydrophobic interaction frequently plays a role in the use of multimodal chromatography media. These media are often described as salt-tolerant ion exchangers, or ion exchangers offering unique selectivity. GE Healthcare offers Capto™ MMC and Capto adhere in this class*.

Our BioProcess™ media family is developed and supported for the large-scale manufacture of biopharmaceuticals. This support includes validated manufacturing methods, secure long-term media supply, safe and easy handling, and Regulatory Support Files (RSF) to assist process validation and submissions to regulatory authorities. In addition, Fast Trak Training & Education provide high-level, hands-on training for all key aspects of bioprocess development and manufacturing.

*Further descriptions can be found in Data files: Capto MMC, code number 11-0035-45 and Capto adhere, code number 28-9078-88.

Capto media

Capto media are based on a highly-rigid agarose matrix that gives significantly improved pressure/flow properties with maintained control over pore structure. The rigid matrix enables a larger operating space than earlier media with possibilities to use higher bed heights and higher flow rates during purification of samples.

Custom Designed Media (CDM)

In addition to our standard BioProcess media GE Healthcare also offers custom designed media (CDM) where standard media do not give optimal performance. By tailoring a chromatography medium for a specific problem a CDM project aims to give a more robust process and improved economy. These projects can go from start to validated production in as little as six months. CDM media are produced with the same high quality as other GE Healthcare BioProcess media and with security of supply.

Wide range covering capture to polishing

To achieve the full separation potential of HIC in a range of applications demands a wide range of media with different hydrophobicities and operational properties. This is achieved by varying the base matrices and the chemical nature of the ligands. Especially for industrial downstream processes, different bead sizes may be demanded by the application, in particular for capture or polishing. Bead-size choice considers both the resolving power needed and the pressure drop over the bed – impacted by sample viscosity and often limited by equipment specifications in large-scale applications. Finally, the range covers media with more open bead structures suitable for very large proteins: Octyl Sepharose™ 4 Fast Flow and Butyl Sepharose 4 Fast Flow. Figures 8 and 9 show results from a study based on 100 experiments where six model proteins of varying size, hydrophobicity and charge were eluted in the same ammonium sulfate gradient.

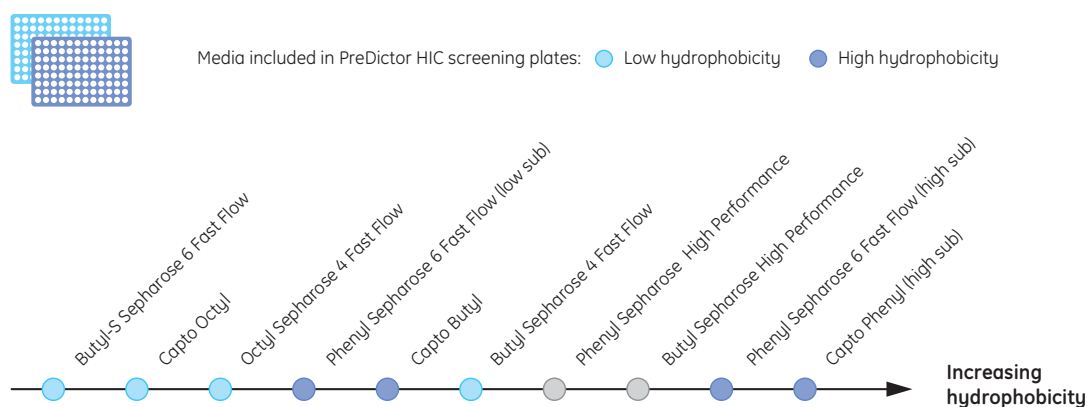


Fig 8. Hydrophobicity map of HIC media. Based on elution studies of the six model proteins: ovalbumin, α -chymotrypsinogen, ribonuclease, lactoferrin, lysozyme, α -amylase.

Figure 9 shows the results from the elution study of the six model proteins in a two-dimensional matrix. The average retention volume (expressed as column volumes, CV) was calculated as a measure of the relative hydrophobicity of each medium (X-axis). To display resolving power, pairwise resolution was averaged (Y-axis). The average resolution naturally follows the particle size to a large extent, but differences in selectivity for the specific proteins also play a part. Especially note the improved performance of the latest generation Capto media.

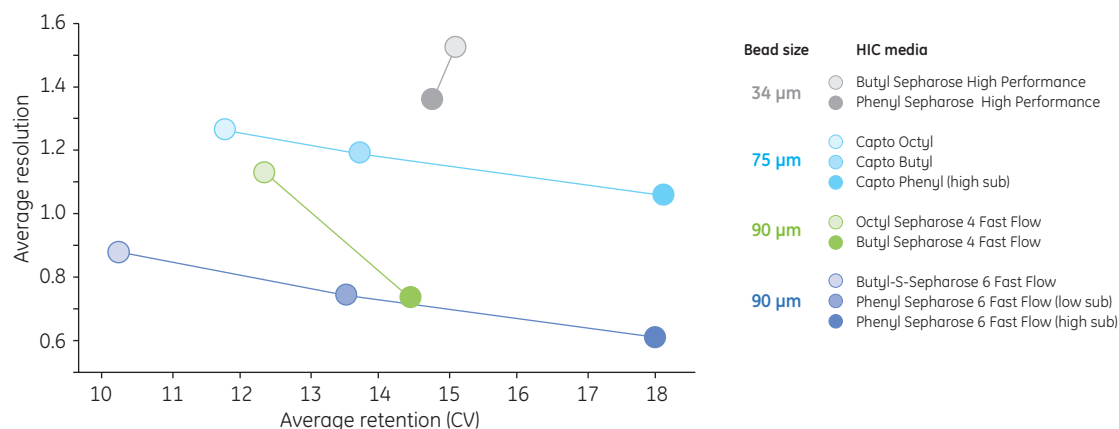


Fig 9. Illustrating the broad range of HIC media from GE Healthcare expressed in terms of resolving power and hydrophobicity. Based on elution studies of the six model proteins: ovalbumin, α -chymotrypsinogen, ribonuclease, lactoferrin, lysozyme, α -amylase.

Formats

- **PreDicator 96-well filter plates** have 6 or 50 μL volumes of medium in each well. Two types of plate are designed for media screening, and contain four low and four high hydrophobicity media respectively. Other plates with single media are listed in ordering information.

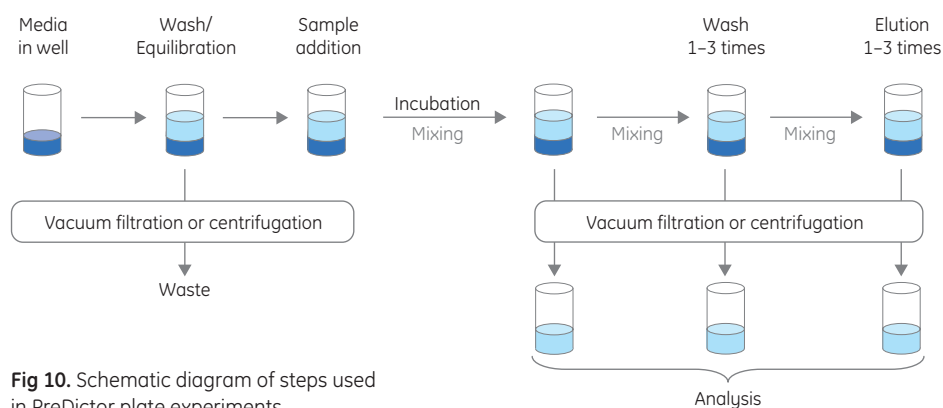


Fig 10. Schematic diagram of steps used in PreDicator plate experiments.

- **PreDicator RoboColumn** units are miniaturized chromatography columns prepacked with BioProcess media including HIC media. Each unit contains eight identical columns and three different volumes are available: 50, 200, and 600 μL .
- **HiTrap** prepacked columns, in 1 or 5 mL sizes, are ideal for many research applications.
- **HiScreen** prepacked columns are designed for column verification, scouting and optimization experiments. They are packed with 4.7 mL of medium and have a bed height of 10 cm to limit the amount of sample required whilst giving adequate plate numbers to indicate the scalability of a separation.
- **HiScale** is a family of pressure-stable, empty lab-scale columns designed for packing bulk media for process development and preparative chromatography. Diameters are 16, 26, or 50 mm with a choice of three tube lengths to cover bed heights up to 40 cm.
- **ReadyToProcess™** prepacked, prequalified and presanitized large-scale columns are designed for purification of biopharmaceuticals. They are available with a range of BioProcess media, including HIC media, in four different sizes: 1, 2.5, 10, and 20 L, all with 20 cm bed heights.

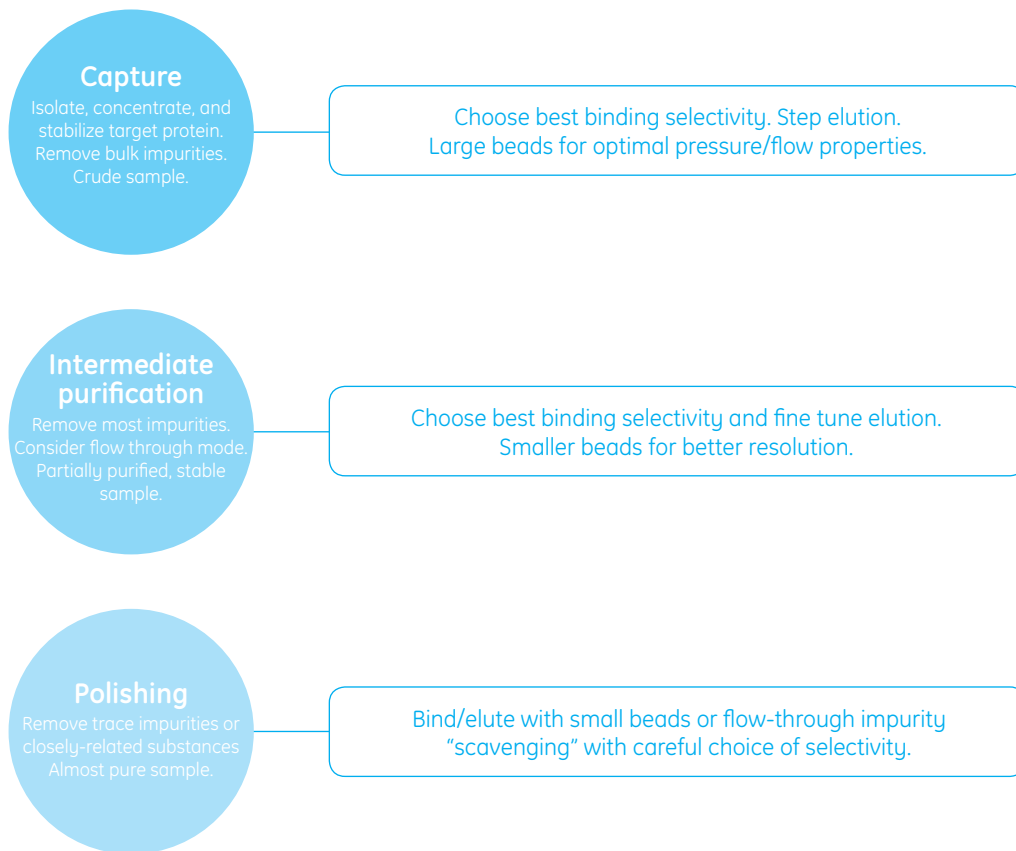
Software

Assist™ software for PreDicator plates supports HTPD using parallel screening of chromatographic conditions in a 96-well plate format. The software allows fast and efficient evaluation of parameters for binding/wash/elution conditions as well as media screening. Assist software is used throughout the workflow from planning and experimental design through to data evaluation.

Other equipment

PreDicator plates can be operated manually using multi-channel pipettes. Removal of liquid can be by centrifugation or vacuum. Both PreDicator plates and PreDicator RoboColumn units can be operated in automated workflows using robotic systems. PreDicator formats prefilled with BioProcess media are fully tested for parallel screening on Tecan® Freedom EVO® workstation. The combination of Tecan's robotic integration and liquid handling expertise together with the versatile PreDicator platform gives the user a fully automated system for HTPD.

Capture to polishing



Select the appropriate media

Protein purification can be divided into capture, intermediate purification and polishing, depending upon the goals and nature of the challenges. HIC can be used at any of these stages and Capto media offer a wide range of operating conditions. Choosing the right medium depends very much on getting the binding selectivity right, as described throughout this guide.

- 1 In general, use Capto media for optimal productivity in capture or intermediate steps. Average bead size 75 μm .
- 2 Use Sepharose Fast Flow media for capture at flows up to 300 cm/h and when Capto media do not offer required binding selectivity. Average bead size 90 μm .
- 3 Finally, the challenges associated with polishing might require small beads to achieve high resolution, as offered by Sepharose High Performance media. Average bead size 34 μm .

Ordering information

Product	Code number	
1 Capto media		
Capto Octyl	25 mL	17-5465-01
	100 mL	17-5465-02
HiTrap Capto Octyl, 5 × 1 mL		17-5465-08
PreDicator Capto Octyl, 6 µL, 4 × 96-well filter plates		17-5465-16
PreDicator Capto Octyl, 50 µL, 4 × 96-well filter plates		17-5465-17
Capto Butyl	25 mL	17-5459-01
	100 mL	17-5459-02
	1 L	17-5459-03
	5 L	17-5459-04
HiScreen Capto Butyl, 1 × 4.7 mL (0.77 × 10 cm)		28-9924-73
HiTrap Capto Butyl, 5 × 1 mL		17-5459-08
HiTrap Capto Butyl, 5 × 5 mL		17-5459-09
PreDicator Capto Butyl, 6 µL, 4 × 96-well filter plates		17-5459-16
PreDicator Capto Butyl, 50 µL, 4 × 96-well filter plates		17-5459-17
PreDicator RoboColumn Capto Butyl, 200 µL		28-9860-97
PreDicator RoboColumn Capto Butyl, 600 µL		28-9861-83
Capto Phenyl (high sub)	25 mL	17-5451-01
	100 mL	17-5451-02
	1 L	17-5451-03
	5 L	17-5451-04
HiScreen Capto Phenyl (high sub), 1 × 4.7 mL (0.77 × 10 cm)		28-9924-72
HiTrap Capto Phenyl (high sub), 5 × 1 mL		17-5451-08
HiTrap Capto Phenyl (high sub), 5 × 5 mL		17-5451-09
PreDicator Capto Phenyl (high sub), 6 µL, 4 × 96-well filter plates		17-5451-16
PreDicator Capto Phenyl (high sub), 50 µL, 4 × 96-well filter plates		17-5451-17
PreDicator RoboColumn Capto Phenyl (high sub), 200 µL		28-9860-88
PreDicator RoboColumn Capto Phenyl (high sub), 600 µL		28-9861-82

2 Sepharose Fast Flow media		
Octyl Sepharose 4 Fast Flow	25 mL	17-0946-10
	200 mL	17-0946-02
	1 L	17-0946-03
	5 L	17-0946-04
HiScreen Octyl FF, 1 × 4.7 mL (0.77 × 10 cm)		28-9269-86
HiTrap Octyl FF, 5 × 1 mL		17-1359-01
HiTrap Octyl FF, 5 × 5 mL		17-5196-01
PreDicator Octyl Sepharose 4 Fast Flow, 6 µL, 4 × 96-well filter plates		17-0946-16
PreDicator Octyl Sepharose 4 Fast Flow, 50 µL, 4 × 96-well filter plates		17-0946-17
PreDicator RoboColumn Octyl Sepharose 4FF, 200 µL		28-9861-02
PreDicator RoboColumn Octyl Sepharose 4FF, 600 µL		28-9861-91
Butyl Sepharose 4 Fast Flow	25 mL	17-0980-10
	200 mL	17-0980-01
	500 mL	17-0980-02
	5 L	17-0980-03
	10 L	17-0980-04
HiScreen Butyl FF, 1 × 4.7 mL (0.77 × 10 cm)		28-9269-84
HiTrap Butyl FF, 5 × 1 mL		17-1357-01
HiTrap Butyl FF, 5 × 5 mL		17-5197-01
PreDicator Butyl Sepharose 4 Fast Flow, 6 µL, 4 × 96-well filter plates		17-0980-16
PreDicator Butyl Sepharose 4 Fast Flow, 50 µL, 4 × 96-well filter plates		17-0980-17
PreDicator RoboColumn Butyl Sepharose 4FF, 200 µL		28-9861-00
PreDicator RoboColumn Butyl Sepharose 4FF, 600 µL		28-9861-89

Note: Other pack sizes available on request for all HIC media.
 ReadyToProcess single use columns available on request for all HIC media.
 Contact your local sales representative.

Product	Code number	
Sephacose Fast Flow media, continued		
Butyl-S Sepharose 6 Fast Flow	25 mL	17-0978-10
	200 mL	17-0978-02
	1 L	17-0978-03
	5 L	17-0978-04
HiScreen Butyl-S FF, 1 × 4.7 mL (0.77 × 10 cm)		28-9269-85
HiTrap Butyl-S FF, 5 × 1 mL		17-0978-13
HiTrap Butyl-S FF, 5 × 5 mL		17-0978-14
PreDicator Butyl-S Sepharose 6 Fast Flow, 6 µL, 4 × 96-well filter plates		17-0978-16
PreDicator Butyl-S Sepharose 6 Fast Flow, 50 µL, 4 × 96-well filter plates		17-0978-17
PreDicator RoboColumn Butyl-S Sepharose 6FF, 200 µL		28-9861-01
PreDicator RoboColumn Butyl-S Sepharose 6FF, 600 µL		28-9861-90
Phenyl Sepharose 6 Fast Flow (low sub)	25 mL	17-0965-10
	200 mL	17-0965-05
	1 L	17-0965-03
	5 L	17-0965-04
HiScreen Phenyl FF (low sub), 1 × 4.7 mL (0.77 × 10 cm)		28-9269-89
HiTrap Phenyl FF (low sub), 5 × 1 mL		17-1353-01
HiTrap Phenyl FF (low sub), 5 × 5 mL		17-5194-01
PreDicator Phenyl Sepharose 6 Fast Flow (low sub), 6 µL, 4 × 96-well filter plates		17-0965-16
PreDicator Phenyl Sepharose 6 Fast Flow (low sub), 50 µL, 4 × 96-well filter plates		17-0965-17
PreDicator RoboColumn Phenyl Sepharose 6FF (low sub), 200 µL		28-9860-99
PreDicator RoboColumn Phenyl Sepharose 6FF (low sub), 600 µL		28-9861-88
Phenyl Sepharose 6 Fast Flow (high sub)	25 mL	17-0973-10
	200 mL	17-0973-05
	1 L	17-0973-03
	5 L	17-0973-04
	10 L	17-0973-06
	60 L	17-0973-60
HiScreen Phenyl FF (high sub), 1 × 4.7 mL (0.77 × 10 cm)		28-9269-88
HiTrap Phenyl FF (high sub), 5 × 1 mL		17-1355-01
HiTrap Phenyl FF (high sub), 5 × 5 mL		17-5193-01
PreDicator Phenyl Sepharose 6 Fast Flow (high sub), 6 µL, 4 × 96-well filter plates		17-0973-16
PreDicator Phenyl Sepharose 6 Fast Flow (high sub), 50 µL, 4 × 96-well filter plates		17-0973-17
PreDicator RoboColumn Phenyl Sepharose 6FF (high sub), 200 µL		28-9860-98
PreDicator RoboColumn Phenyl Sepharose 6FF (high sub), 600 µL		28-9861-84

3 Sepharose High Performance media		
Butyl Sepharose High Performance	25 mL	17-5432-01
	200 mL	17-5432-02
	1 L	17-5432-03
	5 L	17-5432-04
HiScreen Butyl HP, 1 × 4.7 mL (0.77 × 10 cm)		28-9782-42
HiTrap Butyl HP, 5 × 1 mL		28-4110-01
HiTrap Butyl HP, 5 × 5 mL		28-4110-05
PreDicator RoboColumn Butyl Sepharose HP, 200 µL		28-9861-73
PreDicator RoboColumn Butyl Sepharose HP, 600 µL		28-9861-95
Phenyl Sepharose High Performance	75 mL	17-1082-01
	1 L	17-1082-03
	5 L	17-1082-04
HiScreen Phenyl HP, 1 × 4.7 mL (0.77 × 10 cm)		28-9505-16
HiTrap Phenyl HP, 5 × 1 mL		17-1351-01
HiTrap Phenyl HP, 5 × 5 mL		17-5195-01
PreDicator RoboColumn Phenyl Sepharose HP, 200 µL		28-9861-05
PreDicator RoboColumn Phenyl Sepharose HP, 600 µL		28-9861-94

Product	Code number	Related literature	Code number
Screening plates/Selection kit		Data files	
PreDictor HIC Screening high hydrophobicity, 6 µL, 4 × 96-well filter plates	28-9923-92	PreDictor 96 well filter plates and Assist software	28-9258-39
PreDictor HIC Screening high hydrophobicity, 50 µL, 4 × 96-well filter plates	28-9923-97	PreDictor Robocolumn	28-9886-34
PreDictor HIC Screening low hydrophobicity, 6 µL, 4 × 96-well filter plates	28-9923-95	HiScreen preppacked columns	28-9305-81
PreDictor HIC Screening low hydrophobicity, 50 µL, 4 × 96-well filter plates	28-9923-98	HiTrap Selection kit	18-1143-21
HiTrap HIC Selection Kit, 7 × 1 mL	28-4110-07	HiScale columns	28-9755-23
		ReadyToProcess columns	28-9159-87
		Capto Phenyl, Capto Butyl and Capto Octyl	28-9558-57
		Butyl Sepharose HP and Phenyl Sepharose HP	18-1172-87
		Butyl Sepharose 4 FF	18-1020-70
		Phenyl Sepharose 6 FF	18-1020-53
		Butyl-S Sepharose 6 FF	11-0026-34
		Capto Adhere	28-9078-88
		Capto MMC	11-0035-45
		Brochures	
		Plug&Play. ReadyToProcess. Ready to use technologies for greater speed and agility in bioprocessing	28-9790-83
		When nothing else works-Custom Designed Media	28-9279-40
		Application note	
		High throughput screening of HIC media in Predictor plates for capturing recombinant Green Fluorescent Protein from <i>E. coli</i>	28-9964-49
		Handbooks	
		High throughput Process Development with Predictor Plates. Principles and Methods	28-9403-58
		Hydrophobic Interaction Chromatography & Reversed Phase Chromatography: Principles and Methods	11-0012-69
		Protein Purification. Principles, high resolution methods and applications. Third edition. Edited by J-C Jansson, 2011. Publ. John Wiley & Sons. ISBN 978-0-471-74661-4.	28-9953-26

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