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汉邦科技
Hanbon Sci.&Tech.

BIO-PHARMACEUTICAL DOWNSTREAM PROCESS EQUIPMENT

PRODUCT MANUAL

▲Bio-TFF Automatic Tangential Flow Filtration System

▲ ACC 2000 × 600 Automatic Chromatography Column

Cooperative clients:

江苏汉邦科技有限公司
JIANGSU HANBON SCIENCE&TECHNOLOGY CO.,LTD.

Contents

About Us

Established in 1998, Jiangsu Hanbon Science &Technology Co., Ltd. is a national key high-tech enterprise integrating R & D, production and trade, with chromatography products as the core. The main products are: lab-scale high performance liquid chromatography system, industrial preparative liquid chromatography system, simulated moving bed chromatography system, continuous separation chromatography system,supercritical fluid chromatography system, protein purification system, and providing integrated solutions and services with chromatography products as the core.

There are more than 400 employees in the company, including more than 40 doctors and masters, and 80% of the employees have college academic credentials or higher. "Jiangsu Enterprise Academician workstation", "Jiangsu Biochemical Process Engineering Technology Research Center", "Jiangsu Industrial Preparative Chromatography Engineering Center", "Jiangsu Enterprise Graduate Workstation" and "Jiangsu Postdoctoral Innovation & Practice base" have been established successively. A full-time R & D team with more than 60 people in purification process, separation materials, mechanical design, software design and other disciplines has been established, and a powerful "Industry, University, Research and Utilization" platform has been built, and a group of experts and scholars have been gathered to improve the turnkey project from product customization to process development, engineering design, final assembly debugging and system verification.

The company owns more than 200 intellectual property achievements and has hosted more than 20 national and provincial projects successively. has established a traceability system of production process quality department, and strictly controls every link from raw material procurement, processing and manufacturing, quality inspection and installation and after-sales, so as to ensure that the products meet the requirements of GMP, cGMP and FDA. It has passed ISO9001 quality system certification, ISO14001 environmental system certification, OHSAS18001 occupational health system certification, EU CE certification and ATEX explosion-proof certification.

Wuxi APPTec, Legend and Sequoia Capital successively invested in Hanbon.

450+

More than 400 employees

40+

More than 40 doctors and masters

3+2

3 enterprise workstations and 2 research centers

100000

2 plants, covering an area of 100000 square meters

16000 square meters for macromolecular equipment plant construction

200+

More than 200 intellectual property achievements

Bio-Lab Laboratory Chromatography System

Bio-Lab®

Bio-Lab laboratory chromatography system is an efficient, fast and reliable automatic equipment independently developed by the company. It can be used for the rapid purification of protein, peptide and nucleic acid and other biological molecules from the level of microgram to gram. The system adopts modular design and intelligent software, combined with different specifications of chromatography column, which can meet the purification requirements of various biological macromolecules in the laboratory.

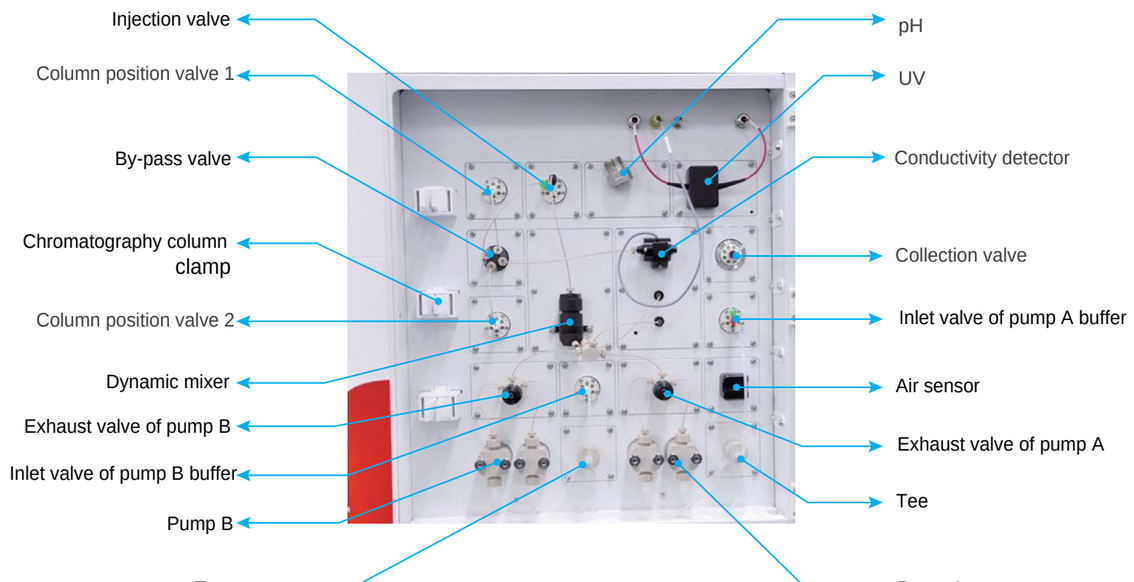
Product Features

- High performance system pump, detector, mixer and all kinds of control valves ensure high accuracy and repeatability as well as achieving purification results more quickly.
- Modular design is very convenient for system maintenance and can also realize the flexible configuration updating along with system software, which can meet different accounts login.
- Stacked design of tubes can minimize dead volume and all the wetted tubes and parts have good biological compatibility, which will protect protein in all the processes.
- The software conforms to GLP/GMP and FDA 21CFR Part11 requirements.
- Good user operation experience, satisfactory multi-level user permissions and complete audit tracking requirements.
- The comprehensive validation documentation system (DQ/IQ/OQ/PQ) supports your GMP/FDA audit.

Bio-Lab Provides Three Types of Models

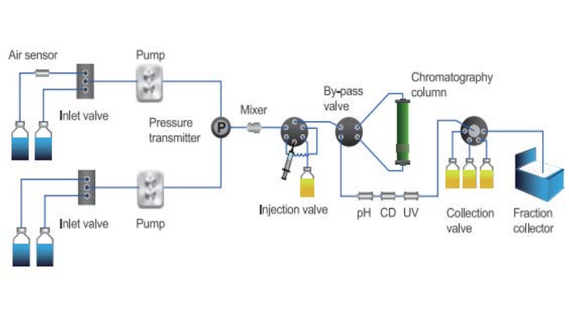
- Bio-Lab30 is applied to the purification of biomolecules from microgram to milligram, compatible with various pre-packed columns or small chromatography columns to facilitate small amount of protein fast purification in labs.
- Bio-Lab 100 is applied for the purification of biomole-cules from milligram to gram, which can meet purification demand of lab research and multi-user.
- Bio-Lab 300 is applied to protein purification at small scale.

Bio-Lab Chromatography System Configuration Drawing

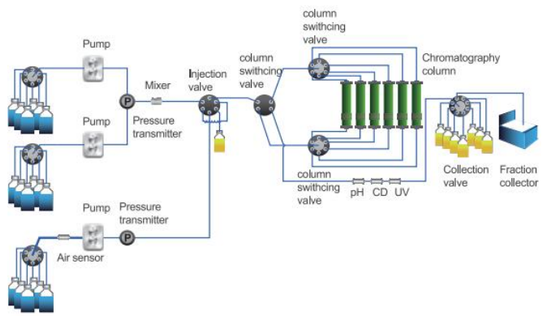


As shown above, all modules of the system are installed on the same plane, which can reduce the dead volume and is convenient for the experimenter to operate.

Bio-Lab chromatography system flow path in lab



Drawing 1 shows the basic configuration for simple and convenient protein purification



Drawing 2 shows the configuration for high-level automated protein purification

—Function Introduction of the main components in Bio-Lab® chromatography system

System pump

Material is optional: PEEK, titanium alloy or 316L stainless steel. All of them have a good compatibility with biological samples. Pump head has a self -washing function, which can stop salt and something else from being separated out at the head, and then avoid the damage or pollution to instrument. Besides, the pump adopts an electronic pressure pulsation compensation design for the gradient accuracy and repeatability to get the reproducibility.

Inlet valve

The inlet valve provides two buffer entry options: 2*2 and 2*6, to select different buffers and elution online automatically. So it can also ensure that the cleaning buffer is always online. So the column and system can get cleaned automatically with it.

Injection valve

Various injection modes can match with the valve without changing the way of pipeline connection, such as loop injection, injection pump, system pump injection.

Column position valve

We have the single column position valve and multi-position valve. The former is applied to controlling the buffer flow direction, and the by-pass function is integrated to clean the system with the column on. The multi-position valve can connect the maximum 6 chromatograph columns simultaneously, and the flow path can be automatically switched between different columns to avoid the risk of bubbles into the system during the columns switching, which is also convenient for packing material selection.

Detector

A UV-Vis detector has dual channels or four channels and wavelength is adjustable, range: 200-400 or 190nm to 700nm; The light source is deuterium lamp or tungsten lamp. Both of them have high sensitivity, reliability, durability and automatic correction, no need to preheat when starting up. Multi-channels can help detect contaminants, such as nucleic acid in proteins, or special tagged proteins, and target protein molecules that have no absorption value at 280nm. pH/ conductivity detectors are internationally famous brands. Especially the conductivity detector is matched with a temperature sensor for temperature compensation and online calibration.

Outlet valve

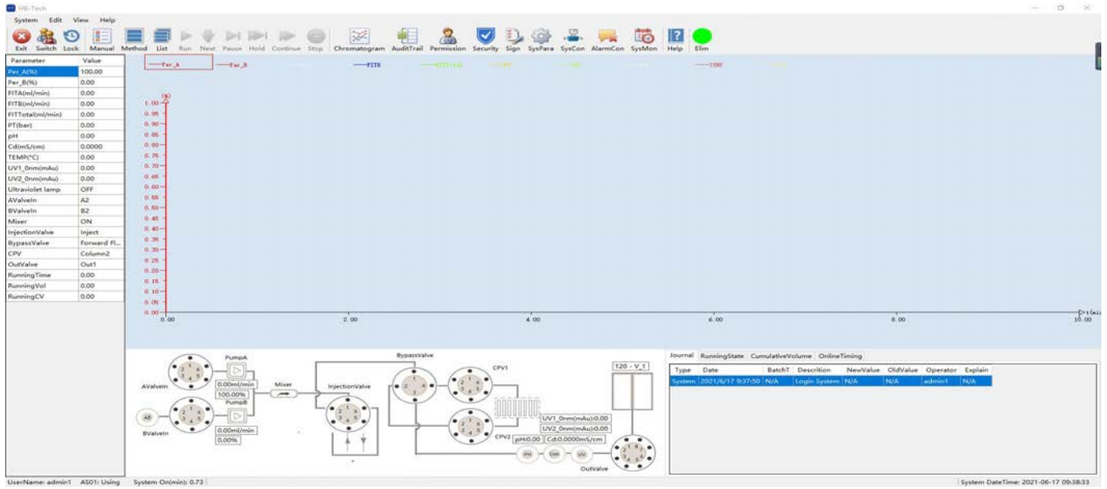
The outlet valve can automatically control the liquid to the fraction collector, waste or other outlet, such as large volume collection port.

Fraction collector

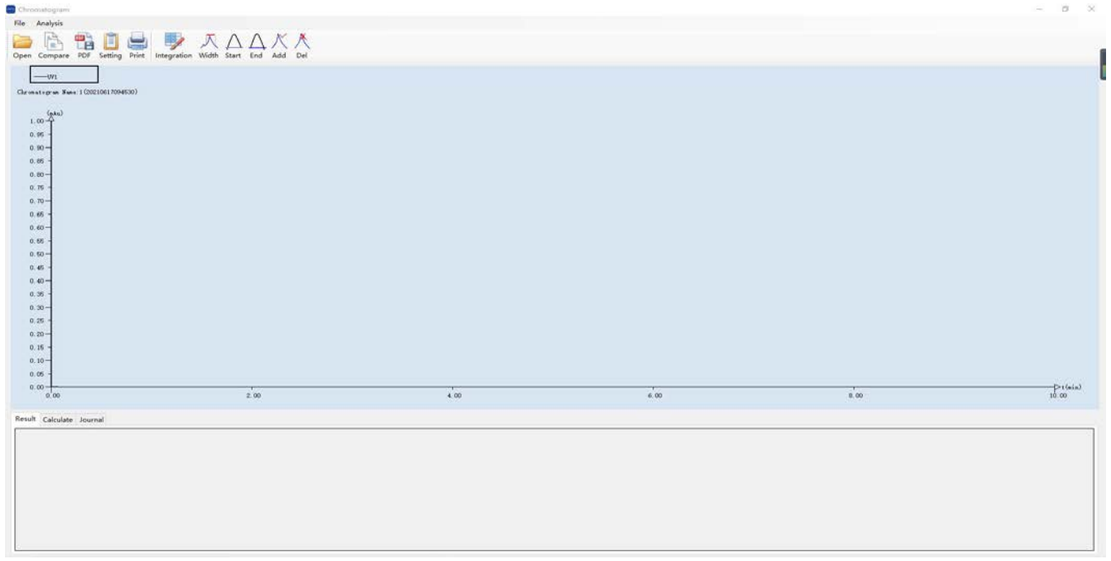
Controlled by Bio-Lab software, it can collect components according to time, volume or automatic peak recognition, stable and reliable performance, simple operation, wide application scope, small volume and light weight. What's more, the fraction collector is flexible, adopting an original motion principle: linear motion combined with rotary motion. The collection pipe can get to any collection location rapidly to have more collection ways. The precise minimum pipeline design reduces dead volume and the collection inaccuracy caused by samples spreading after the flow cell. It can broaden the function of temperature control to keep sample stable.

—Bio-lab® workstation software

Bio-Lab® chromatography workstation specially developed for low pressure chromatography by Hanbon with patents, conforming to the GLP, GMP and 21 CFR Part11 requirements. It has built-in method editing, manual or automatic control, data molecules and other modules, easy to learn, highly intelligent.



Bio-Lab® chromatography workstation adopts modular design, visual interface in both Chinese and English, so users can easily and quickly complete every operation and operation. Multi-user login, operation record tracking, digital signature to ensure the reliability and security of data.



Bio - Lab has simple and convenient method edit module and data processing module. It can quickly calculate the integration, compare the batch process of curve and evaluate the column effect, convenient for the best process development.

Laboratory Chromatography System

Bio-Lab® Standard Configuration Parameter

Model	Bio-Lab 30	Bio-Lab 100	Bio-Lab 300
System Pump	Binary piston pump, PEEK, titanium alloy or 316 L stainless steel, good biological compatibility; pump head self-washing function prevents pollution and salting out, and electronic pressure fluctuation compensation measures provide excellent gradient accuracy and repeatability for lab chromatography system to ensure the reproducibility		
Flow Rate Range	0.001~29.999ml/min	0.01~99.99ml/min	0.01~299.99ml/min
Pump-max pressure	≤30MPa	≤20MPa	≤15MPa
System-max pressure	1.3 MPa		
Flow Rate Accuracy	±0.5%		
Gradient Model	Linear, isocratic, and stepwise elution gradients which modify the gradient ratio online		
UV Detector	Two channel UV detector, deuterium lamp (standard), tungsten lamp (optional)		
Wavelength Range	190-700nm		
Absorbance Range	-5~5Au		
Wavelength Accuracy	±1		
Optical Path Data	2mm		
Conductivity Detection Range	1~999 ms/cm		
pH Detection Range	0~14		
Mixer	0.6、2、5、10ml		
Valve	Basic Configuration: injection valve, single column position valve, outlet valve. Advantages: minimum dead volume design; Modular design of valve head and the drive part; tight joint to fix tubes; easy to maintain. The sample injection valve can choose manual or automatic mode, with a loop of 100ul, 500ul, 1ml, 5ml, 10ml , 50ml or150ml.		
Fraction collector (optional)	1) 120 test tubes (height 90 ~ 180mm, diameter 13 ~ 15mm) 2) 80 test tubes (height 90 ~ 180mm, diameter 18mm) 3) Funnel plate and the collection quantity is not limited		
Software Workstation	The modular design is easy to operate. User rights establishment, audit trail and data records all comply with GMP/GLP requirements. Powerful method editing and data processing function.		
Power (kw)	1	1	1
Dimensions (cm)	600*600*620	600*600*620	590*690*670
Joint specification	1/16",1/8"	1/16",1/8"	1/8",1/4",3/16"

Bio-Lab® Optional Configuration Parameter

Detector	
UV Detector	Four-channel detector, 200-800nm
Differential Refractive Detector	RI-501、RI-502、RI-504
Valve	Electromagnetic/ rotor valve
Outlet Valve	4- channel outlet valve or 8- channel is optional
Multi Column Position Switching Valve	two 6-channel valves is optional,to connect 6 columns.
Sample Pump	High accuracy piston pump
Flow Rate Range	0.01-29.99/0.01-99.99/0.01-299.99ml/min
Pressure Range	0~20MPa
Chromatography Column Holder	Applied to 1ml, 5ml pre-packed column and 6.6-50mm diameter chromatography

LCC series chromatography columns in lab

- Applied to lab-scale biopharmaceutical R & D
- Easy operation with good biocompatibility
- Self-adjustable column volume
- A temperature jacket is included

Configuration parameter

Model	ID (mm)	Tube height (mm)	Max pressure (bar)	Column packing height (mm)	Column packing volume (mL)	Filter aperture
LCC16/20	16	200	5	20-170	4-34	Standard 5μm
LCC16/40	16	400	5	220-370	44-76	
LCC16/70	16	700	5	520-670	104-134	
LCC16/100	16	1000	5	820-970	164-194	
LCC26/20	26	200	5	20-170	10-90	
LCC26/40	26	400	5	220-370	117-193	
LCC26/70	26	700	5	520-670	276-355	
LCC26/100	26	1000	5	820-970	435-514	
LCC50/30	50	300	5	120-270	235-529	
LCC50/70	50	700	5	520-670	1020-1314	
LCC50/100	50	1000	5	820-970	1607-1901	
16 column packer	16	/	5	/	/	
26 column packer	26	/	5	/	/	
50 column packer	50	/	5	/	/	
16 adapter	/	/	5	/	/	
26 adapter	/	/	5	/	/	
50 adapter	/	/	5	/	/	

Bio-Pro Pilot & Process Chromatography System

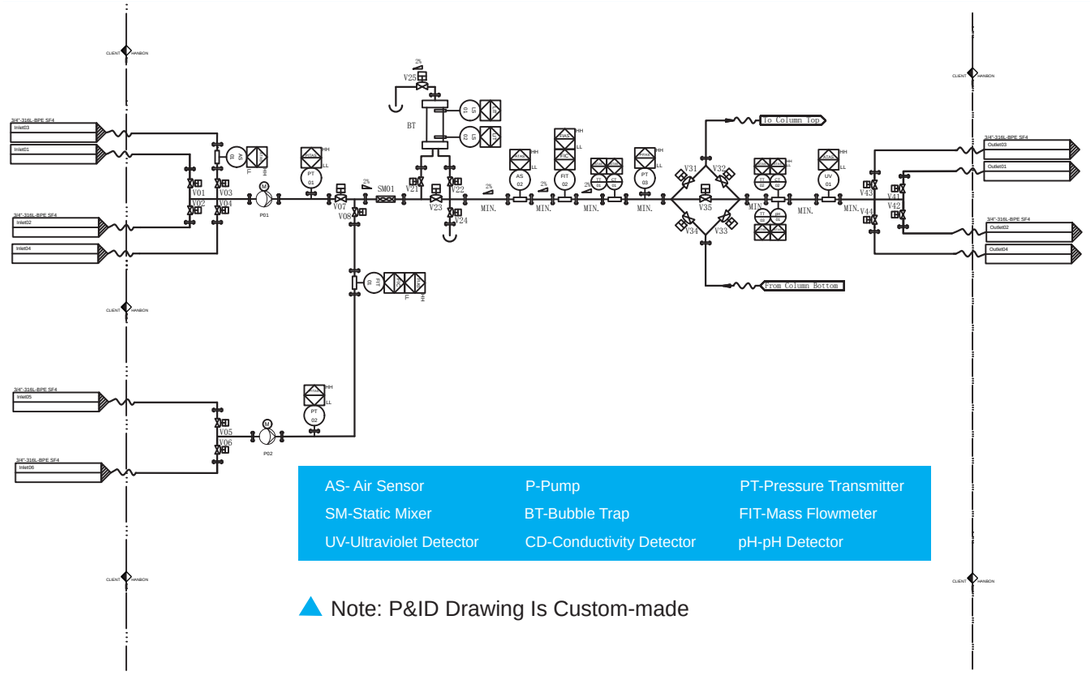
——*Pilot and Industrial Production Scale*

Bio-Pro automatic chromatography system is applied to the pilot and industrial production of bio-pharmaceutical purification process. Based on the requirements of ASME BPE and GMP, the system adopts an integrated module design which can realize multi configurations according to the specific requirements of customers. In this system, many processes can be manually or automatically carried out, stable and reliable, such as conditioning, injection, flush, elution, auto-collection, CIP, etc. Besides, we can provide you with complete verification documents which are consistent with GMP.

Product Features

- Key parts are from imported top brands, stable and reliable
- ASME BPE pipeline design; the inner wall electric throwing(Ra≤0.4um); automatic welding
- Wetted material meets USP Class VI and FDA standards.
- The system control software is developed on C# platform, which meets the requirements of FDA 21 CFR Part 11
- Complete GMP verification documents and service
- Database to store data,and mature data remote backup storage strategy

Standard Gradient System P&ID Drawing

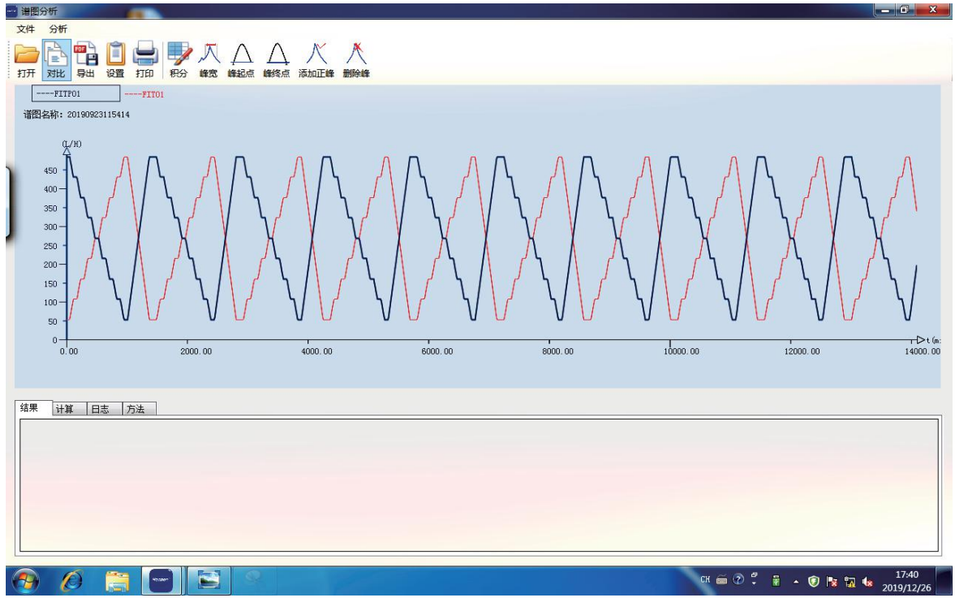


AS- Air Sensor	P-Pump	PT-Pressure Transmitter
SM-Static Mixer	BT-Bubble Trap	FIT-Mass Flowmeter
UV-Ultraviolet Detector	CD-Conductivity Detector	pH-pH Detector

▲ Note: P&ID Drawing Is Custom-made

High Precision Flow Control

Accurate control of flow and gradient can be achieved by precise PID feedback loop adjustment.



▲ Long Time (1-4000min) Stable Operation Chromatogram

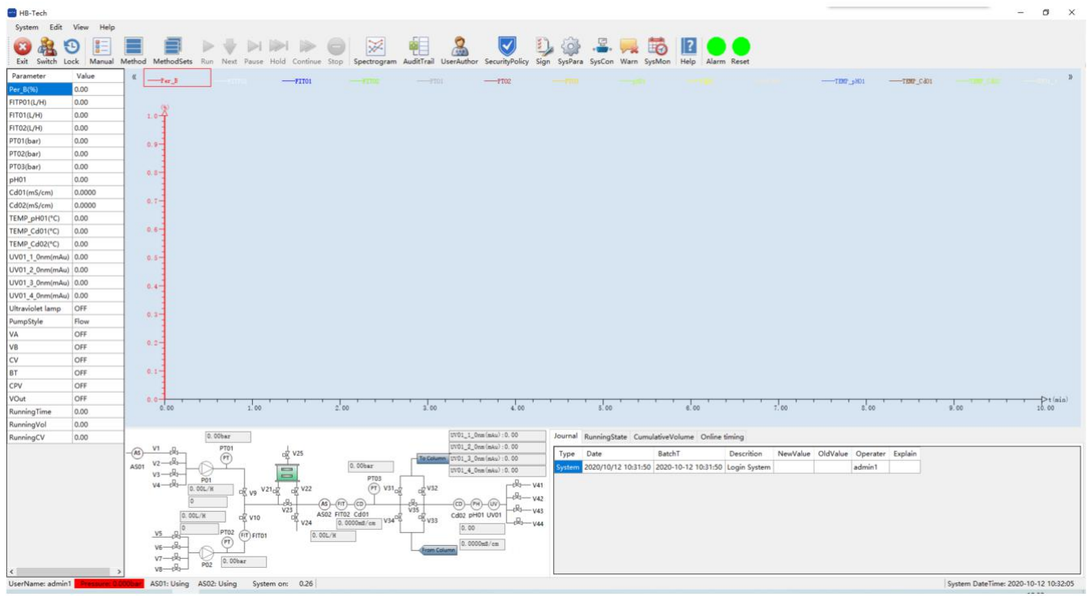
Bio-pro System Software

The system software can track production process and set parameters, including flow rate, valve switching, injection time, elution time, collection conditions, etc. It can run automatically according to the preprogram or can run manual mode with user-defined process and parameters. Designed according to the requirements of GMP and FDA 21 CFR Part11, the software has audit trail, electronic record, electronic signature, multi-level password management and other functions.

Product Features

- Monitor all running parameters; set 4 levels alarm, such as pressure, flow rate, etc.
- Good operation interface to achieve various functions
- Multi-mode operation: debug mode, manual mode, automatic mode
- Multi-level authorization administration
- Multi-task hyper-threading data processing; fast response and processing
- Complete audit trail function and data operation log
- In accordance with GAMP 5, FDA 21 CFR Part11, electronic signature and electronic records

Bio-pro System Software Interface



▲ Gradient Operation Chromatogram

Single-use Chromatography System

We can also provide single-use chromatography system, including system pump head, valve, pipeline, pressure sensor, flow meter,pH, conductivity, UV, etc., all of which are single-use replaceable components. All components are designed with aseptic pre packaging in advance, which can be directly disassembled and packaged before use and installed Exempt CIP verification. It is especially suitable for the application of multiple CDMO or multiple products on the same line.

Software Features

- All wetted parts can be directly replaced, fast and convenient;
- FDA and USP VI certificates are provided for non stainless steel wetted materials;
- The software with the same origin as non single-use system is quick to learn and convenient to use;

Single-use Chromatography Physical Picture

System Parameter Table

Mode	Bio-Pro 60	Bio-Pro 180	Bio-Pro 600	Bio-Pro 1200	Bio-Pro 1800	Bio-Pro 4400
Infusion pump	High-accuracy constant-flow pump	Sanitary quaternary diaphragm pump				
Flow range(L/h)	1~60	1~180	6~600	10~1200	45~1800	150~5000
Flow accuracy(L/h)	1% / 5ml/min	1% / 0.5L/h	1% / 1.5L/h	1% / 3L/h	1% / 5L/h	1% / 10L/h
Tubing	1/4"TC (OD6.35 X ID4.57)	3/8"TC (OD9.53 X ID7.75)	1/2"TC (OD12.7 X ID9.4)	3/4"TC (OD19.05 X ID15.75) 1"TC (OD 25.4 X ID 22.1)	1"TC (OD 25.4 X ID 22.1)	1½" TC (OD38.1 X ID34.8)
Tubing material	SS 316L(ASME BPE)，Electro polishing Ra≤0.4um					
System pressure(bar)	6					
UV-Vis Detector	Fixed wavelength 280nm / adjustable wavelength with 4 channels 200-400/200-800nm					
Conductivity range	0.1uS/cm~300mS/cm（ Explosion proof model 0.1uS / cm~500mS / cm ）					
pH range	0~14					
Power supply	220VAC 50Hz				380VAC 50Hz	
Power(KW)	1		1.5		5	
Working temperature	4~40 °C					
Compression air(bar)	5~7					
Size(mm)	1400x750x1300	1370x700x1200	1470x750x1350	1470x750x1350	1800x1200x1800	1800x1200x1800
Weight(kg)	265	230	280	295	630	700

MCC® Manual Chromatography Column

MCC adopts the compression way by manual screw to load packing materials, with the advantages of concise configuration , easy for cleaning and manual operation, applied to the switching among diversified products. The chromatography column has compact structure, convenient operation and stable performance. It can meet the requirements of most chromatography packing materials, and has good column packing effect and high column performance from the pilot to the large-scale production in demand.

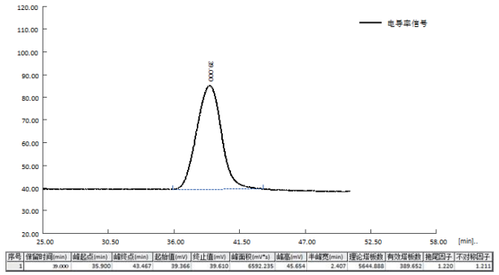
MCC includes 2 designs ----MCC-B(manual sealing) and MCC-Q(automatic sealing, pneumatic deblocking), for the various requirements from different users.

Product Features

- Imported Schott finishing glass tube with high strength, easy to seal
- Column head sideslip design, no need for manual handling
- The frit can be replaced directly at the bottom without the need to disassemble the cylinder.
- Original and highly reliable column head sealing---- manual or automatic
- Convenient, reliable and safe operation
- No dead zone in flow path, excellent cleaning performance
- Imported wetted material, according with USP Class VI and FDA.
- GMP validation files and best services

Structural Innovation

Column Performance Testing Diagram



序号	保留时间[min]	峰起点[min]	峰终点[min]	起始值[mV]	终止值[mV]	峰面积[mV*s]	峰高[mV]	半峰宽[min]	理论塔板数	有效塔板数	拖尾因子	不对称因子
1	39.000	35.900	43.467	39.366	39.610	6592.235	45.654	2.407	5644.888	389.652	1.220	1.211

Packing material: Sepharose 4 Fast Flow
Chromatography column: MCC100
Test system: Bio-lab 60 chromatography system
Balance: 0.4 mol/L NaCl
Sample: 2mol/L NaCl
Elution: 0.4 mol/L NaCl

Configuration Parameter

Item	MCC-70	MCC-100	MCC-140	MCC-200	MCC-300	MCC-400	MCC450
Column Tube ID(mm)	70	100	140	200	296	400	450
Column Height(mm)	500/ 750/ 950						
Packing Height(mm)	0~450	50~450					
	200~700	300~700					
	400~900	500~900					
Max Work Pressure(bar)	6				3		
Mesh Size(um)	10/ 23(PP) 或10/20（SS316L）				10/ 20(SS316L)		
Working Temperature	4~40						
Operation Mode	Mannual						
Inlet & Outlet Diameter (mm)	1/4" TC (OD6.35× ID4.57)		3/8" TC (OD9.53× ID7.75)			1/2" TC (OD12.7× ID9.4)	
Weight (kg)	28/30/32	34/37/40	42/47/52	57/64/71	146/156/166	191/206/221	259/271/280
Transport height (mm)	1070 1320 1520	1190 1440 1640	1190 1440 1640	1190 1440 1640	1310 1560 1760	1360 1610 1810	1360 1610 1810
Maximum height (mm)	1550 1800 2000	1670 1920 2120	1670 1920 2120	1670 1920 2120	1840 2090 2290	1890 2140 2340	1890 2140 2340
Length×width (mm)	500x500	650x650	700x700	700x700	800x800	950x950	1000x1000

Notes: 1. Imported acrylic column tubes are used for MCC400 and MCC450 chromatography columns;
2. Chromatography columns with height and air pressure requirements can be customized;
3. The recommended column height is half of the available maximum height.

ACC®Automatic Axial Compression Chromatography Column

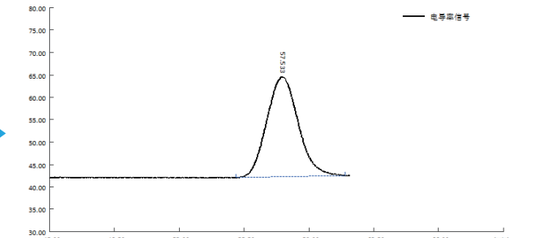
ACC series automatic axial compression column is specially designed for bio-pharmaceutical purification. The smart packing method can ensure each packing effect is consistent and chromatography results are repeatable, which can reduce the risk caused by the large difference in packing effect of each batch during production and can avoid the dependence on operators. ACC series is applied to most types of chromatography packing material and the corresponding packing methods in the bio-pharmaceutical industry to meet the production requirements of diversified products.

Product Features

- Equipped with automatic workstation for packing, unpacking and cleaning, easy to maintain
- Key components are international top brand.
- The upper and lower position of the column are protected by software, photoelectric sensor and machine for the equipment reliability and personnel safety.
- Patented piston seal design, better sealing performance.
- Patented piston exhaust structure design, convenient and quick
- Scientific distributor structure design to ensure the average distribution of liquid.
- High precision servo motor drive with high operation accuracy to ensure the piston position error is as low as 0.1mm.
- Sanitary design, no dead angle; Wetted material: consistent with the USP VI or FDA and other pharmaceutical regulations requirements.
- The column tube is made of imported acrylic or stainless steel column, and the cylinder can be rotated to facilitate the removal and cleaning of the frit.
- The software of column mounting workstation meets the require-ments of FDA Part 11, and meets the requirements of remote data backup and storage.

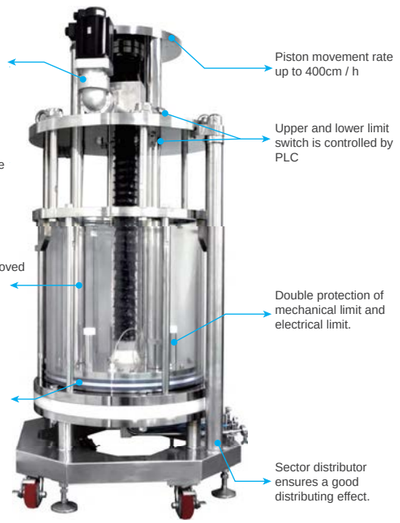
Column Effect Test Drawing

Packing material：Sepharose 4 Fast Flow
Chromatography column：ACC 450
Test system：Bio-pro 180 chromatography system
Balance：0.4 mol/L NaCl
Sample：2mol/L NaCl
Elution：0.4 mol/L NaCl

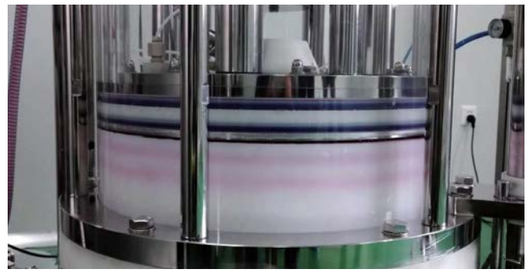


序号	保留时间[min]	峰起点[min]	峰终点[min]	起始值[mV]	终止值[mV]	峰面积[mV*s]	峰高[mV]	半峰宽[min]	理论塔板数	有效塔板数	拖尾因子	不对称因子
1	57.533	55.050	60.950	42.050	42.527	2629.157	22.278	1.947	5008.940	2058.664	1.188	1.107

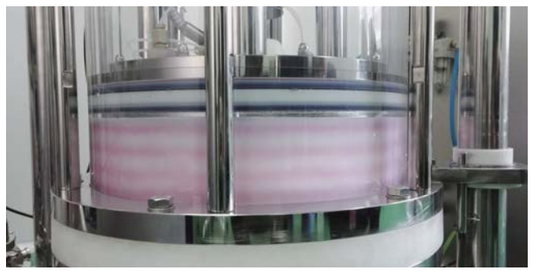
Structural innovation



Distribution test



▲ VB12 Injection Twice



▲ VB12 Injection for 4 times

Configuration Parameter

Model	ACC300	ACC400	ACC450	ACC600	ACC800	ACC1000	ACC1200	ACC1400	ACC1600	ACC200
ID （mm）	300	400	450	600	800	1000	1200	1400	1600	2000
Tube height（mm ）	600									
Recommended packing height（mm）	50-300									
Recommended packing volume （ L）	3~20	6~37	8~47	14~84	25~150	39~235	56~339	77~461	100-603	157~942
Max working pressure（bar）	4									
Frit pore size（μm）	10、20(SS316L)									
Working temperature	4~40									
Axial compression method	Automatic - electric motor axial compression									
Inlet and outlet diameter (mm)	3/8" TC (OD:9.5 ID:7.75)	1/2" TC (OD:12.7 ID:9.4)		3/4" TC (OD19.1 ID:15.8)	1" TC (OD:25.4 ID:22.1)		1.5" TC (OD:38.1 ID:34.8)		2.0" TC (OD:50.8 ID:47.5)	
Compressed air（bar ）	5~7									
Weight （ kg）	305	415	555	880	1985	3675	5615	6715	9500	16500
Power （ KW）	2.5	2.5	2.5	5	7	7	7	9	9	10
External dimension （cm）	70x70	72x72	73x73	90x90	145x115	162x128	186x150	206x170	222x195	280x249
Max maintenance height （cm）	230	235	248	248	274	279	313	330	330	330
Transport height （cm）	160	172	181	182	209	209	260	280	280	280

Notes: 1. Schott glass tube can be used for ACC 300 / 400 column tube.

2. Chromatography columns with diameter, height and air pressure requirements can be customized.

SCC® Automatic Spraying Chromatography Column

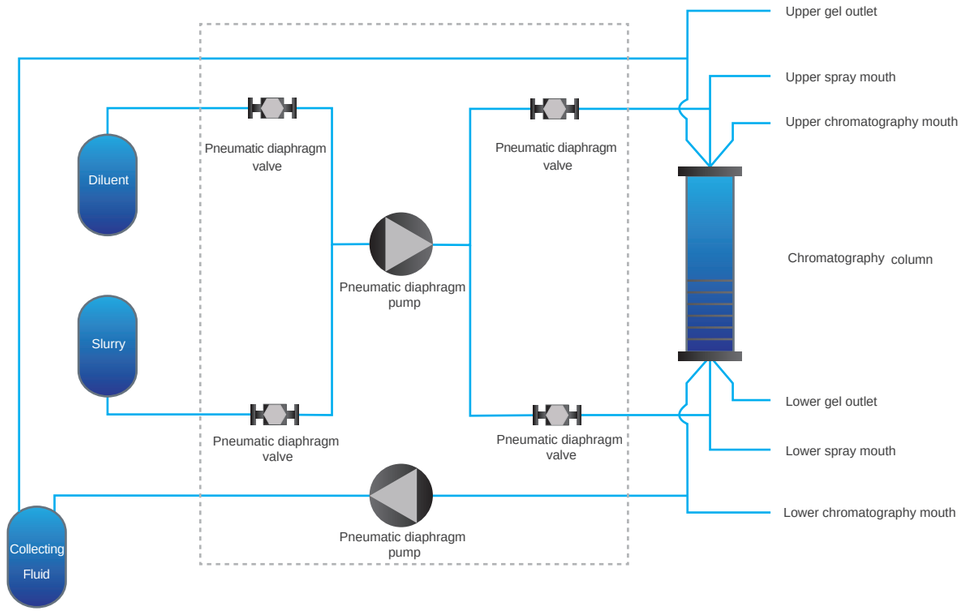
SCC series automatic chromatography column uses upper and lower spray design to realize packing, unpacking and cleaning functions. The unique spray structure design ensures the average distribution of packing material, high column effect and no stratification.

SCC series automatic chromatography column is applied to most types of chromatography packing material and the corresponding packing methods in the bio-pharmaceutical industry to meet the production requirements of diversified products.

Product Features

- Matched column packing workstation; You can choose automatic mode or manual mode for column packing, unpacking and cleaning; simple and convenient to maintain.
- Key components are international top brands.
- Patented piston seal design ensures better sealing performance.
- Scientific distributor structure design ensures the average distribution of the liquid.
- The sanitary design can guarantee a complete cleaning, with no corner missed, and the wetted materials comply with the USP VI or FDA pharmaceutical regulations.
- Column tube materials are imported acrylic or stainless steel tube (antiseptic treatment is optional).

Automatic Spray Chromatography Column P&ID Diagram



Configuration

Item	SCC-600	SCC-800	SCC-1000	SCC-1200	SCC-1600
Column ID (mm)	600	800	1000	1200	1600
Column height (mm)	600/500				
Recommend packing height (mm)	140-350				
Recommend packing volumn (L)	40-100	70-175	110-275	160-400	280-700
Maximum pressure (bar)	3				
Inlet and outlet diameter	1"TC (OD 25.4 X ID 22.1)			1½" TC (OD38.1 X ID34.8)	
Frit pore size (μm)	10,20, etc. (SS316L)				
Weight (KG)	375	610	930	1215	1815
External dimension (cm)	80x80x156	100x100x157	120x120x157	140x140x160	180x180x160

Note: Column of other diameter, height and pressure can be customized.

Automatic Slurry Tanks

Automatic slurry tank of Hanbon is used for rapid mixing of homogenate, replacement of new packing material with ethanol, adjustment of homogenate ratio, and collection of packing material during column removal. It is equipped with a specially designed low shear force agitator for mixing solid-liquid mixture, which can realize rapid mixing without damaging the packing material, and is a powerful auxiliary for realizing high column efficiency packing of chromatography column. We recommend that all automatic chromatography columns should be homogenized by automatic slurry tank.

Product Features

- In accordance with GMP requirements, manufactured according to ASME BPE standard
- All wetted materials are made from SUS316L, Ra ≤ 4um, electro-polished, the material not in contact with the liquid is SUS304, Ra ≤ 0.8um
- Low shear force agitator can not cause damage to the packing material, and compressed air can be used for stirring.
- The replacement function of homogenate buffer can be used, such as replacement from preservation solution (20% ethanol, NaOH solution) to column packing buffer solution (such as WFI), or vice versa
- It can adjust the proportion of homogenate
- With weighing module, spray ball, over-pressure protection
- Two or three frits are designed at the bottom and side to accelerate the liquid change rate of slurry tank
- Caster is added at the bottom of the equipment, which is convenient to move
- The volume of slurry tank can be customized

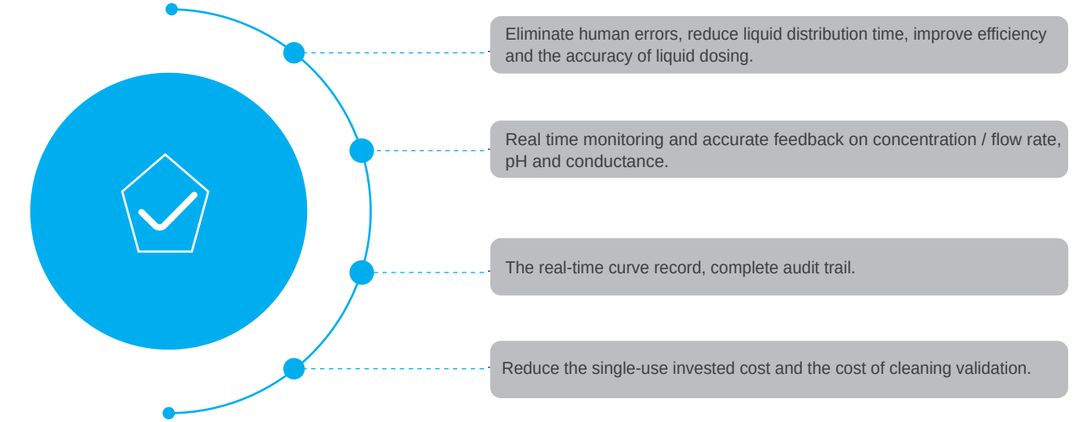
Configuration Parameter

Model	STK-200	STK-300	STK-600	STK-800	STK-1000	STK-1600
Usable volume（L）	200	300	600	800	1000	1600
Minimum mixing volume（L）	10	15	30	40	50	80
Size （WxDxH cm）	130x90x195	130x100x220	150x110x220	150x110x220	170x140x220	190x170x220
Operating pressure	-1~3bar					
Operating temperature	4~40℃					
Industrial compressed air	5~7bar，100L/min					
Clean compressed air	2~3bar，300L/min					
Material of tank body and pipeline	SS 316L(ASME BPE), electropolished Ra≤0.4um					
Seal ring material	EPDM, Provide FDA compliance certificate					
Number of inlets	3 or customized					
Number of outlets	2 or customized, 1 for slurry tank outlet, 1 for displacement solution (such as ethanol) outlet					
Spray ball	2, rotary spray ball					
Weighing Module	3					
Stirring paddle	2 or 3 layers, low shear force impeller for solid-liquid mixing					
Breathing ball	2 sets					
Frit	2 or 3 sets, BOPP frits, used for homogenate solution replacement and air stirring					
Castor	4					
Power Supply	220VAC or 380VAC,50~60Hz					

Bio-Con Inline Buffer Dilution System

Bio-con inline buffer dilution system solves the demand for the accuracy and repeatability of the complex buffer soluiton in the biopharmaceutical process. In addition, it can reduce the quantity of the liquid / storage tank, save the manpower and materials, and thus reduce the production cost.

Technical Advantage



The new building

- Reduce 60% area of liquid dosing and storage
- Reduce 90% volume of the dosing and the storage tank
- Reduce 60% staff
- Reduce the 70% cost of dosing time.

The built factory

- Reduce the cost of cleaning and verification of liquid dosing and storage tank
- Increase the accuracy of the liquid dispensing and reduce the labor cost
- Increase the scale of liquid dosing and 3 times of the productive power

Technical Principle

The basic principle of Bio-Con inline buffer dilution system is to mix a variety of concentrated buffers, including acid, alkali, salt and so on, with the injection water to make the buffer solution needed. According to the specific use conditions, different concentration can be accurately controlled.

And in this system, the stability of the control parameters can be reached within 1min.

▲ *System entrance*

▲ *Bio-Con*

▲ *System exit*
Chromatography
Ultra filtration

The Bio-Con inline buffer dilution system can also be integrated into a Bio-Pro chromatography system or the Bio-TFF tangential flow filter system, which can continuously complete the process of liquid dispensing + chromatography or liquid dispensing + tangential flow, and the overall control and data record will increase the convenience for the customer purification process.

Liquid Dosing Experiment

We have done the experiment for many times on the buffer system used in common bio- pharmaceutical purification, such as phosphate system, acetate, citrate system, Tris-HCl system and so on, which achieved excellent online dilution effect. The steady time ≤1min ,pH ±0.05, conductivity±0.05 or 1% (take large value) solution with high accuracy in the actual experiment.

Configuration Parameter

Model	Bio-Con180	Bio-Con600	Bio-Con1200	Bio-Con5000	Bio-Con9000
Flow range	1-180 L/h	6-600 L/h	10-1200 L/h	150-5000 L/h	300-9000 L/h
Flow accuracy①	±1%/0.5L/h	±1%/1.5L/h	±1%/3L/h	±1%/10L/h	±1%/20L/h
Dilution multiple of main buffe②	5-20times				
Liquid dispensing accuracy	Maximum PH accuracy ≤0.05, conductance accuracy≤0.05ms/cm or ≤±1%(take large value)				
UV detector	Single wavelength, double wavelength, or four wavelengths 200-400nm or 190-700nm				
Valve switch	Compressed air drive				
Tubing material	316LSS (ASME BPE) ,Ra≤0.4μm				
System pressure resistance	6 bar				
Power Supply	220VAC			380VAC	
Power	1.5KW	2KW	2KW	5KW	5KW
Public facilities	Compressed air 5-7bar				

Remarks:

① The flow accuracy 1%/0.5L/h takes the larger value as the criterion and takes the average value.

② Refers to the dilution multiple of phosphate, Tris and other main buffers, and the dilution ratio of buffer for PH adjustment or conductance can reach 200 times or higher.

Bio-TFF Automatic Tangential Flow Filtration System

Bio TFF system is an easy-to-use automatic ultrafiltration UF / DF system, which is suitable for biomedical process development, pilot research and small-scale production. Bio TFF system adopts innovative and intelligent design, which can not only improve process performance, but also achieve extremely low minimum operating volume, maximum ultrafiltration concentration multiple and optimal product recovery function.

We have done the experiment for many times on the buffer system used in common bio- pharmaceutical purification, such as phosphate system, acetate, citrate system, Tris-HCl system and so on, which achieved excellent online dilution effect. The steady time ≤1min ,pH ±0.05, conductivity±0.05 or 1% (take large value) solution with high accuracy in the actual experiment.

We can provide ultrafiltration / microfiltration system for clamp for Millipore / Pall / Sartorius membrane or hollow GE/ Pall / Repligen hollow fiber column.

Product Features

- Sanitary design, conforming to GMP and ASME BPE requirements.
- Quattroflow quaternary diaphragm pump, low shear force, low pulse.
- Automatic TMP control, automatic concentration, equal volumn filtration, etc.
- Comply with FDA 21 CFR Part11 requirements.
- Custom-made.
- GMP validation files and services.
- Either membrane package /hollow cored iber is optional

Application Area

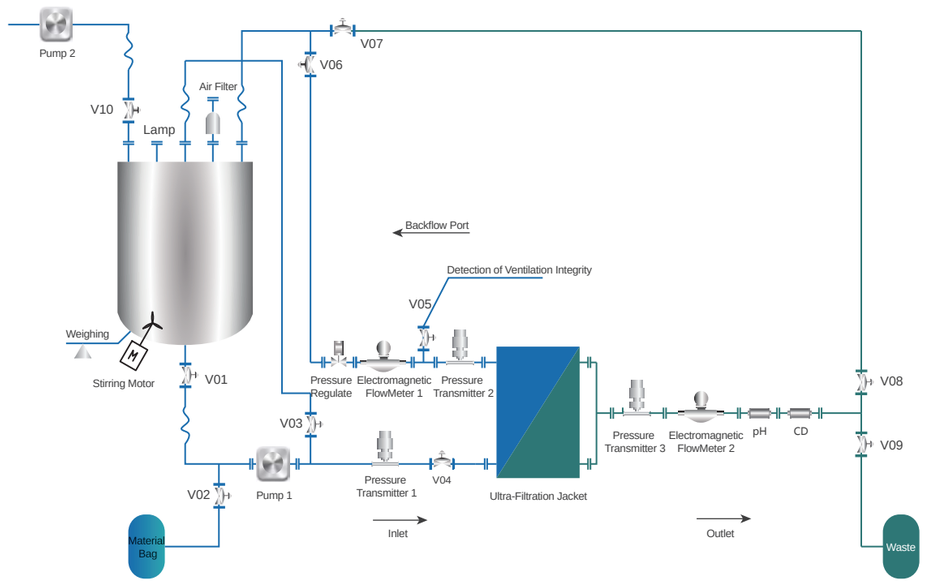
- Blood products: dealcohol, concentration and metal ion removal of albumin, globulin and other blood products
- Vaccine: clarification of cell culture medium, concentration and filtration of virus solution, removal of heat source of buffer solution
- Genetic engineering products: protein concentration, buffer replacement, cell collection
- Antibiotics: clarification of fermentation broth, removal of heat source and removal of macromolecular impurities
- Biochemical products: protein concentration, washing and filtration, separation of small and large molecules
- Biochemical products: protein concentration, washing and filtration, separation of small and large moleculesÿ
- Water for injection system: heat source removal of water system, bacteria removal and clarification

Physical Picture of Automatic Ultrafiltration System

Ultrafiltration system with fixture for membrane

Hollow fiber ultrafiltration system

P&ID Drawing of Automatic Ultrafiltration System

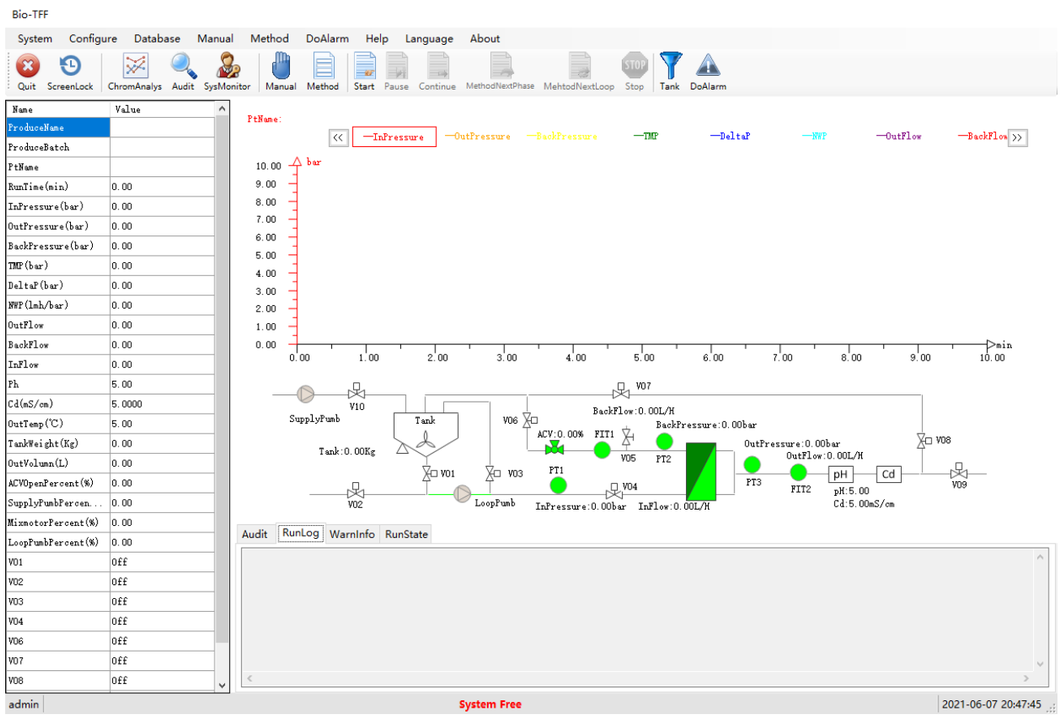


Software Instruction

The software meets the requirements of GAMP5 and FDA 21 CFR Part 11. According to the process, operation parameters can be prepared, including the liquid volume, system flow, inlet\ backflow\ outlet pressure, TMP control, △P, liquid weight inside the tank, etc. Each parameter in the process of the equipment has a special file record, and the chromatogram is drawn in real time for reference of the operator.

- Monitor all running parameters, set level 4 alarm, such as pressure, conductivity, etc.
- Good operation interface, convenient to realize various functions.
- Multi-mode operation---- debugging mode, manual mode and automatic mode.
- Comply with GAMP5 and FDA 21 CFR Part 11, conform to electronic signature record.
- The system is divided into four levels of operation authority to avoid arbitrary change of process parameters by operators.
- The system can edit the method to realize automatic CIP, concentration, filtration and other functions.
- Complete audit trail function, perfect data operation log.

Software Interface



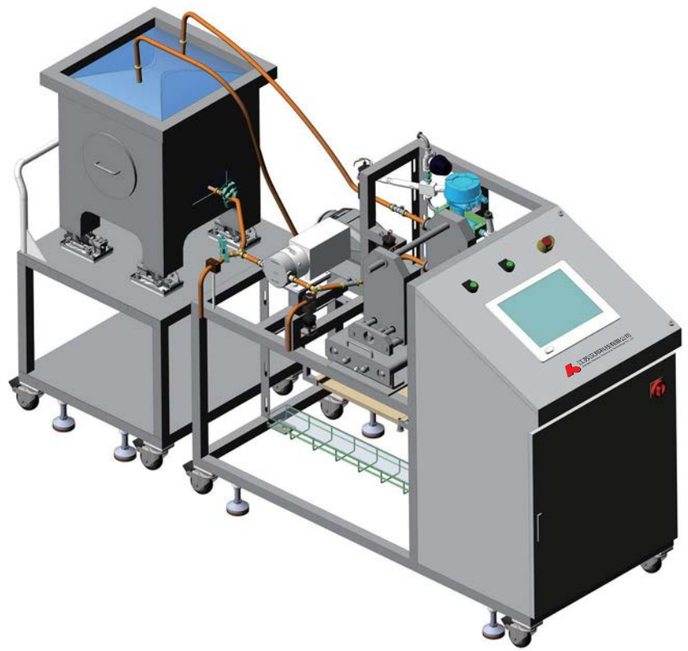
Single-use Ultrafiltration System

We can also provide single-use ultrafiltration system, including system pump head, pipeline, pressure sensor, flowmeter, pH, conductivity, UV, etc., all of which are single-use replaceable components. All components are designed with aseptic pre packaging in advance, which can be directly disassembled and packaged before use and installed after CIP verification. It is especially suitable for the application of multiple CDMO or multiple products on the same line.

Product Features

- All wetted parts can be directly replaced, fast and convenient
- FDA and USP VI certificates for non-stainless steel wetted parts
- Compact design, minimum recyclable volume and higher concentration multiple

Physical Drawing of Single-use Ultrafiltration System



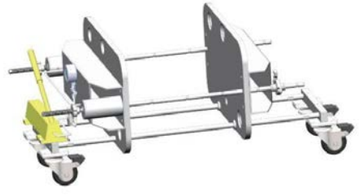
Ultra-filtration Assembly- jacket

- Adaptive for mainstream brands membrane such as Millipore /PALL/Sartorius.
- Special flow inlet and outlet design ensures the system to be cleaned thoroughly.
- Standard 316L material, standard Tri-Clamp connection.
- Various configuration can realize customized processing from research and development to pilot production scale.

Membrane Area

▲ Adaptation:0.1-0.5

▲ Adaptation:0.5-3



▲ Adaptation: Deep filteration fixture

Configuration Parameters

Item	Bio-TFF180	Bio-TFF800	Bio-TFF1200	Bio-TFF4400	Bio-TFF9000	Bio-TFF20000
Circulating pump	Sanitary quaternary diaphragm pump				Sanitary rotor pump	
Pump rate (L/H)	1~180	6~800	10~1200	150~5000	300~9000	600~20000
Filtration area (m^2)	0.1~0.5	0.1~2.5	0.5~2.5	0.5~10	1~20	2~40
pH range	0~14					
CD range (ms/cm)	0.1uS/cm~300mS/cm					
Tubing material	SS316L(ASME BPE), Ra≦0.4μm					
Solvent mixing tank (L)	Optional (20/30/50/100 and others)					
Fluid infusion pump	Optional					
System pressure (bar)	≤6					
Power	220VAC 50Hz			380VAC 50Hz		
Compressed air (bar)	5~7					

Note: Hanbon can also provide the ultrafiltration system Bio-HF with the hollow fiber column.
This configuration parameter table is also applied to the hollow fiber ultrafiltration system.
Larger specifications of ultrafiltration system can be customized.