汉邦科技
Hanbon Sci.& Tech.

CONTINUOUS CHROMATOGRAPHY SEPARATION SYSTEM

2018-2019

PRODUCT MANUAL



No.1-9 Jixian Road, Economic development zone,
Huai'an, Jiangsu, China 223005

0086-0517-83706931

0086-0517-83706903

qczhu@hanbon.com.cn

www.jshanbon.com/en/

HANBON SCI. & TECH.

CONTENTS

CONTINUOUS CHROMATOGRAPHY
SEPARATION SYSTEM

01

Simulated Moving Bed Separation / 01

Separation Principle
Product Features
Technical Advantages
Configuration Parameter
Application Fields
Case Study

02

Continuous Ion Exchange Technology / 10

Continuous Ion Exchange Advantages
Characteristics of A ContinuousIon Exchange System
Software and Control System
Configuration Parameter
Application Fields
Application Case Reference
Online Fast Detection/Monitoring System
Automatic Desolved System

03

Appendix / 20

Attached list 1 Sugar degree- density comparison table
Attached list 2 Industrial preparative column packing material capacity
Attached list 3 Mesh number、Inch、μm conversion table

01 *Simulated Moving Bed Separation*



▲ ***Simulated Moving Bed (SMB)***

The simulated moving bed is a kind of mass transfer equipment that uses the adsorption principle to conduct liquid separation operation. By means of countercurrent continuous operation, the position of material inlet and outlet of the fixed bed adsorption module can be changed to produce the effect of continuous adverse movement of adsorbent and continuous forward movement of materials.



The production capacity and separation efficiency of SMB are higher than those of the fixed adsorption bed, and SMB can avoid the problems of the moving bed adsorbent wear, dust blocking equipment or pipelines, etc. Therefore, this technology has been widely concerned and applied in recent years.

Separation Principle

Principle of two - column continuous chromatography

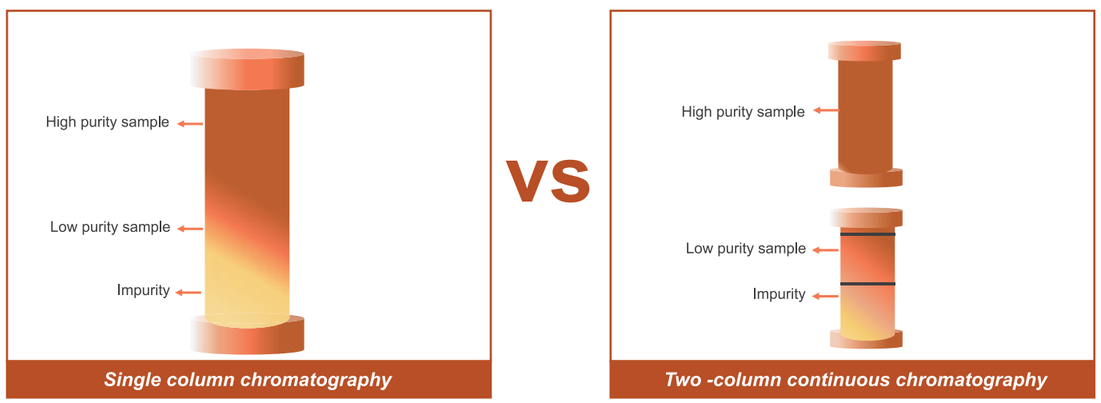


Figure1-1

Figure1

Figure1-2

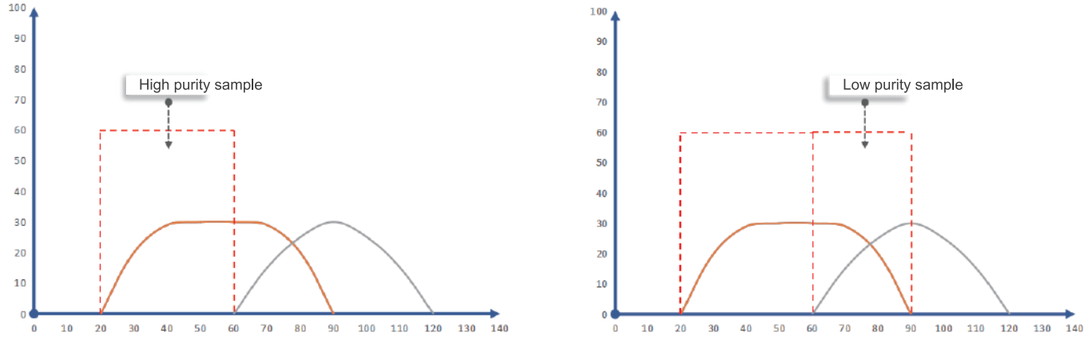


Figure2-1

Figure2-2

Figure2

Retention time 20-60min | Single column recovery is low

As shown above (2-1), in single-column chromatography, only samples with a retention time of 20-60min can be collected due to the limitation of sample purity. Samples with a retention time of 60-90min have to be discarded. So the single column recovery is low.

Retention time 20-60min | The recovery of the two-column was significantly increased

As shown above (2-2), low purity samples discarded by a single column with a retention time of 60-90min flowed into the second column in the two-column continuous chromatography for continuous separation, and the recovery rate was significantly increased.

Separation Principle

Two-component SMB separation principle

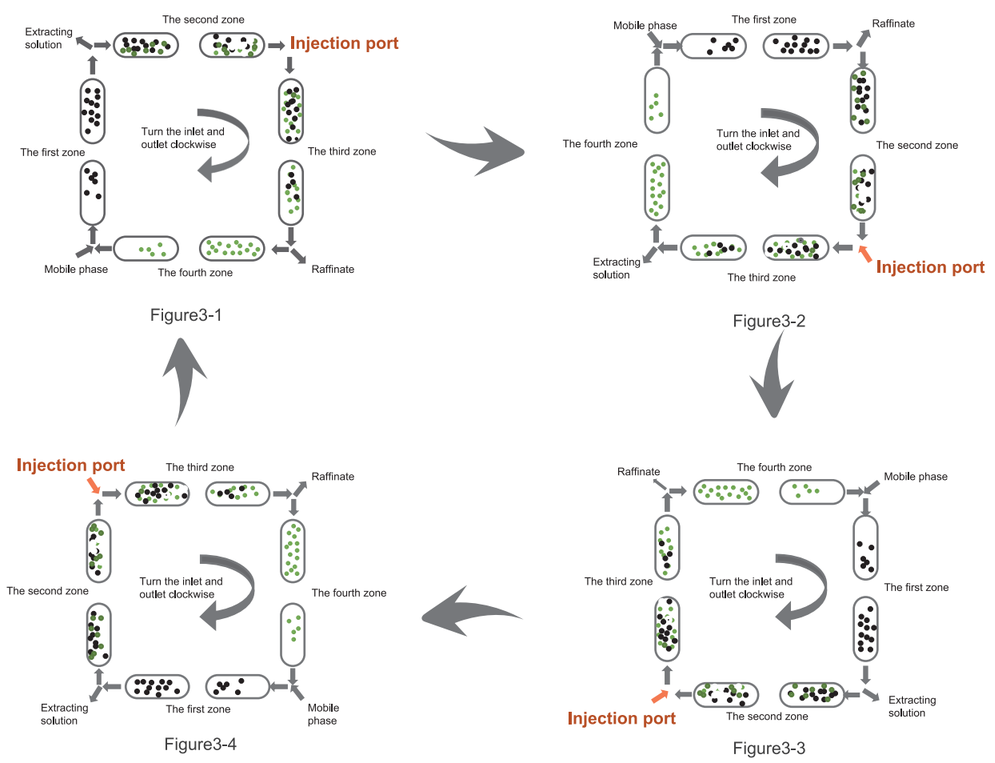


Figure3

Taking the running process of pneumatic valve type SMB as an example, 8 chromatographic columns, 2 columns in a group, are divided into four zones by four inlet and outlet (injection port, raffinate, mobile phase and extracting solution). The second zone and the third zone are used to separate samples. The first zone and the fourth zone are used to collect qualified products while regenerating stationary phase and mobile phase.

After a time, raw materials move clockwise with mobile phase and input/output through valve switch. Feedstock and collection are done in the new input/output.
The above operation is repeated until the inlet and outlet position returns to the origin (figure 3-1), which forms a cycle. In this cycle, the effect of adverse movement of adsorbents and raw materials is simulated to realize continuous feeding and continuous collection of products.

Separation Principle

Three-component SMB separation principle

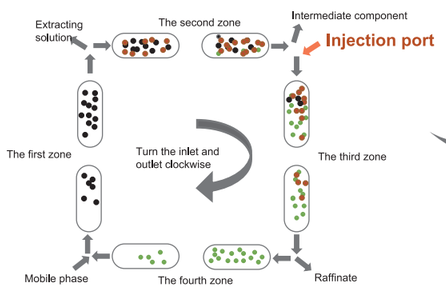


Figure4-1

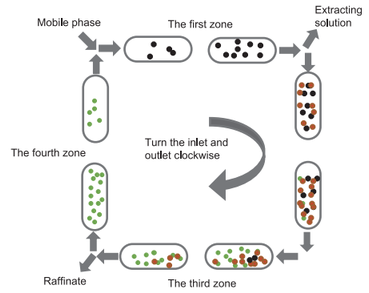


Figure4-2

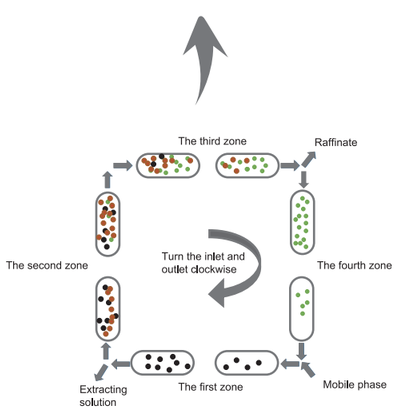


Figure4-4

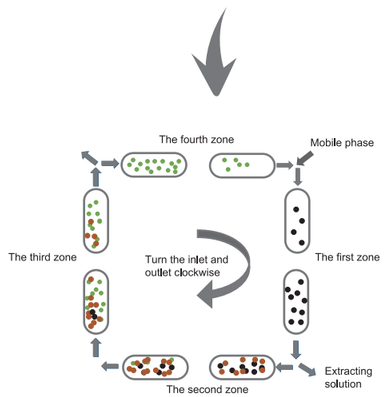


Figure4-3

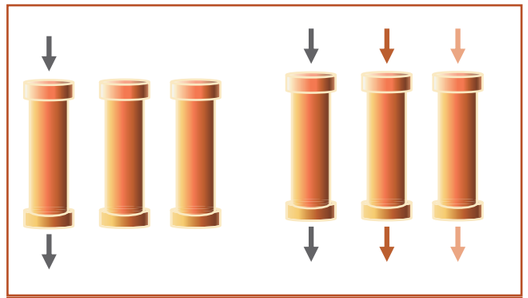
Figure4

Taking the running process of pneumatic valve type SMB as an example, Figure 4 shows a cycle process of three-component separation.

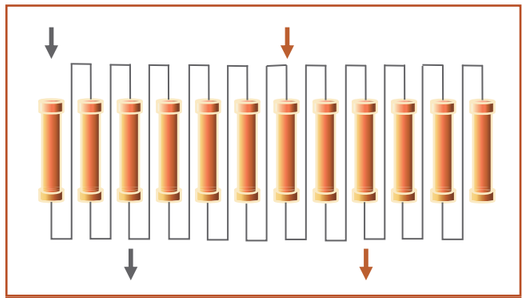
Compared with the two-component separation, the sampling model of the three-component separation is different. Only one high-dose sampling is performed in one cycle, and the extracting solution and the raffinate are collected first, and the intermediate components are finally collected.

Product Features

- Complete a variety of separation modes within the range of 1-12 columns: single column separation, batch type separation, SMB separation, SSMB separation.

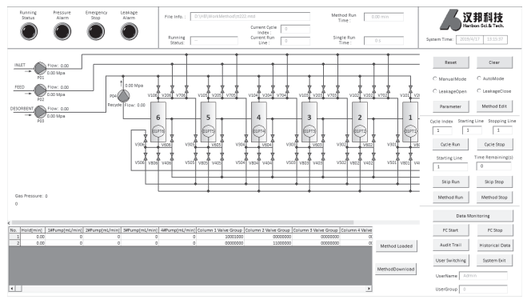


Single column separation ***Batch type separation***



SMB/SSMB separation

- Increase production efficiency by 2-3 times and reduce medium and mobile phase by 30%-50%.
- The valve group design realizes the minimum pipeline fixed volume
- Key components are of first-line well-known brands, stable and reliable.
- Complete DQ/IQ/OQ/PQ verification file system ensures the product quality.
- The control software is based on GE or SIEMENS configuration software mode, and conforms to requirements of FDA 21CFR Part 11.



▲ SMB Control interface diagram



▲ SMB Simulation software interface diagram

- Optional English and Chinese interface, visual flow control chart, easy to operate
- Simulation software, simulating craft process, looking for the conversion process of a single column into continuous chromatography
- Built-in manual or automatic control, method editing, data recording and analysis, alarm emergency stop and other modules
- Multi-level users permission setting,audit tracking and electronic signature ensure the reliability and security of data

Technical Advantages

Process comparison of single column separation and continuous chromatography separation (separation of xylitol)

Single column separation	Continuous chromatographic separation
Percent yield<70%	Percent yield>90%
High solvent consumption	The general dosage is about 50% of the single column
Low packing efficiency	The general dosage is about 50% of the single column
Low concentration of the product and high consumption of post-processing	High concentration of the product and simple post-processing
High environmental pressure	Low environmental pressure
Gradient elution	Isocratic elution (Typical)
High running cost	Low running cost
Suitable for complex component separation	Suitable for two-component, pseudo-two-component or simple three-component separation

Process comparison of membrance separation and continuous chromatography separation (separation of Inulin)

Barrier separation process	Continuous chromatographic separation process
Low purity	High purity (the purity >99% according to the resin properties)
High solvent consumption	The general dosage is about 30% of the barrier process
Low concentration of the product and high consumption of post-processing	High concentration of the product and simple post-processing
Large amount of sewage treatment	Small amount of sewage treatment
Short life of filter element	Long life of resin
High running cost	Low running cost
Suitable for separation of two-components with very different molecular weights	The separation was not affected by the molecular weight difference

Configuration Parameter



Low pressure SMB series

Model	NS9001S	NS9001M	NS9001L
Resin content(m^3)	0.004-0.01	0.5-2	≥2
Pressure rang (MPa)	＜1	＜0.6	＜0.6
Handling capacity (per day)	Kilogram class	hundreds kilogram class	tonner
Running mode	Group valve (Pneumatic valve/solenoid valve)	Pneumatic valve type	Pneumatic valve type
Quantity of chromatographic column	2-12		
Range of application	Sugar, amino acids, citric acid, vitamins		

High pressure SMB series

Model	NS9002S	NS9002M	NS9002L
Packing quantity (g)	30-100	1000-3000	≥3000
Pressure limit (MPa)	1-20	1-15	1-15
Handling capacity (per day)	Gram class	Hundreds gram class	Kilogram class
Running mode	Pneumatic valve type/Multi-position valve type	Pneumatic valve type	Pneumatic valve type
Quantity of chromatographic column	2-12		
Range of application	Chiral drugs, Isomeric drugs, natural products		

Application Fields



Application Case Reference

CASE1-HFCS (high fructose corn syrup) separation

Material Composition	Physical Characteristics	Unit Capacity (g /h* per liter resin)	Resin Loading Level (L)
Miscellaneous sugar:3% Fructose:42% Glucose:55%	Feed temperature (℃) :60-70 Feed concentration (brix) :50-60 Feed conductance (μS/cm) : < 20	70	60

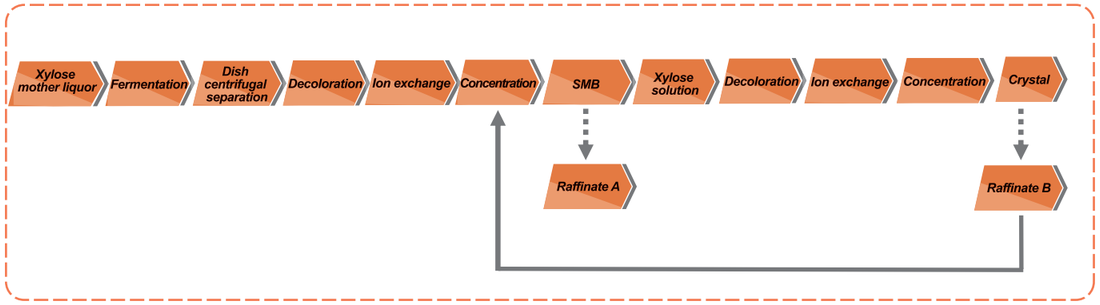
Material Composition	Fructose Purity	Fructose concentration	Fructose yield	Glucose Purity	Glucose Concentration	Ratio of Material to Water
Separation results	97%	33%	＞92%	88%	＞20%	＜1.0

CASE2- Fluoxetine separation

No.	Items	DAC50 separation	SMB separation
1	Handling Capacity (g/h)	5	10
2	Solvent Consumption (L/h)	4.8	2.7
3	Purity (%)	98.73	99.2
4	Yield (%)	78	92
5	Cost Comparison (%)	100	70

Application Case Reference

CASE3- Annual processing of 4000 tons of xylose mother liquor



The market price of Xylose mother liquor (concentration 70%, xylose content 35%) is 1200 yuan/ton, and the annual income is 4.8 million yuan.

After the SMB separation and purification, the yield of xylose is calculated as 95%, and the annual production content was 70% xylose liquor: about: 4000 tons *35%*70%*95%/(70%*70%)=1900 tons;
Output of the residual liquid A：4000-1900=2100 tons

The crystallization yield is calculated at 55% after SMB purification, annual production of crystal xylose with the content of 98.5% and above: 1900 tons *70%*70%*55%/98.5%=519.8 tons；
Second xylose mother liquor（residual liquid B）is about：(1900 tons*70%-519.8)/70%=1157.4 tons

Schedule of Gains

Items	Twice xylose mother liquor (Raffinate B)	Raffinate A	Crystallization of Xylose	Earnings
Output (ton)	1157. 4	2100	519.8	
Unit price (yuan/ton)	1200	1200	14500	
Total (ten thousand yuan)	138.9	252	753.7	1144. 6

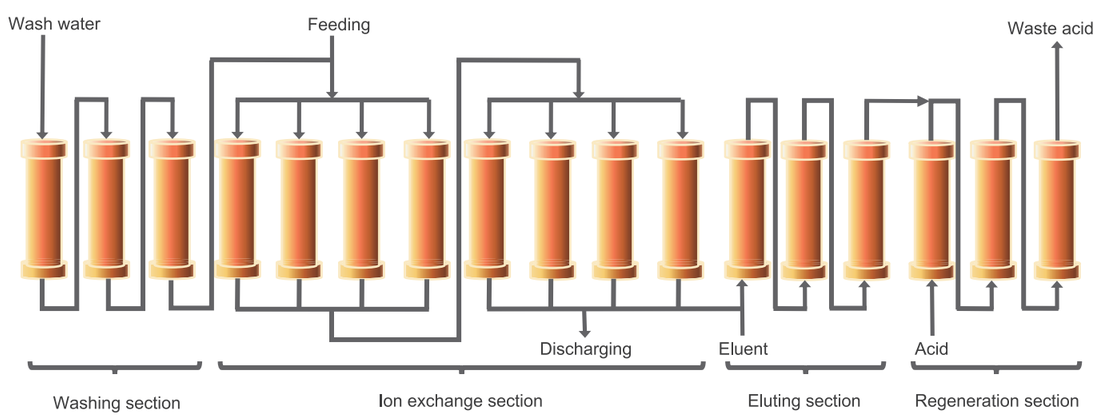
The running cost of xylose mother liquor is about $100 USD perton.
Compared with the direct sale of xylose mother liquor, after SMB separation, the new revenue per year is:
11.446-4.8-3.2=3.446 million RMB

02 Continuous Ion Exchange Technology



▲ *Continuous ion exchange chromatography system*

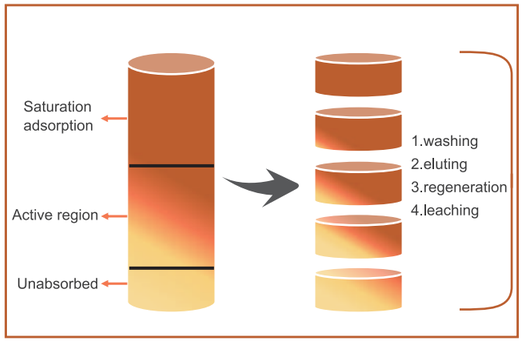
Continuous ion exchange technology is developed by combining the traditional fixed resin bed technology with the continuous counter-current system. This technology concentrates each process of the traditional resin chromatography in one system and operates the multi-stage separation steps at the same time, so as to reduce the discharge of sewage and waste liquid, reduce the usage amount of solvent and improve the utilization rate of the resin. At present, it is mainly used for purification of effective components such as sugars, antibiotics, amino acids and natural products.

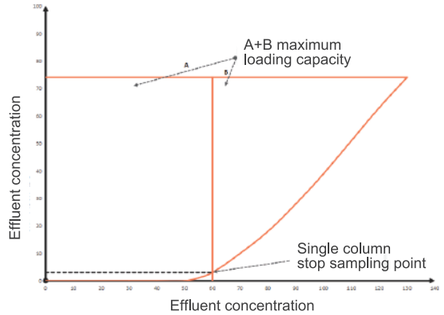


Continuous Ion Exchange Advantages

01 *Improve the utilization of ion exchange column*

In the fixed bed, the columnar bed has a large volume and serious gully flow. When the sample flows through, the sample loading must be stopped for further operation. At this time, the resin utilization rate is only about 60%. The continuous ion exchange technology abstractly divides the chromatographic column into several small units. After saturated loading of each small unit, washing, elution regeneration, washing balance and other operations were carried out successively. The treated blank resin unit is returned to the bottom of the column for recycling, which greatly improves the utilization the resin.





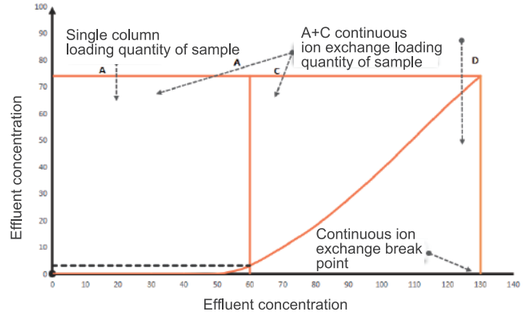


Figure 5

A: Single column maximum loading quantity of sample
B: Loading quantity of sample after flowing through
A+B: Maximum loading capacity of resin column
A+C: Continuous ion exchange loading quantity of sample
D: Unabsorbed sample (flowing into the second column)

In the single column ion exchange mode, the operator should stop sampling when the sample passes through the end of the column, and the utilization rate of resin column is about 60%.
In the continuous ion exchange mode, feeding is continuous after a column of sample flowing through. The resin utilization rate of one column can reach 100% (A+C). The sample after flowing through (D) enters the second column.

02 Increase the product concentration

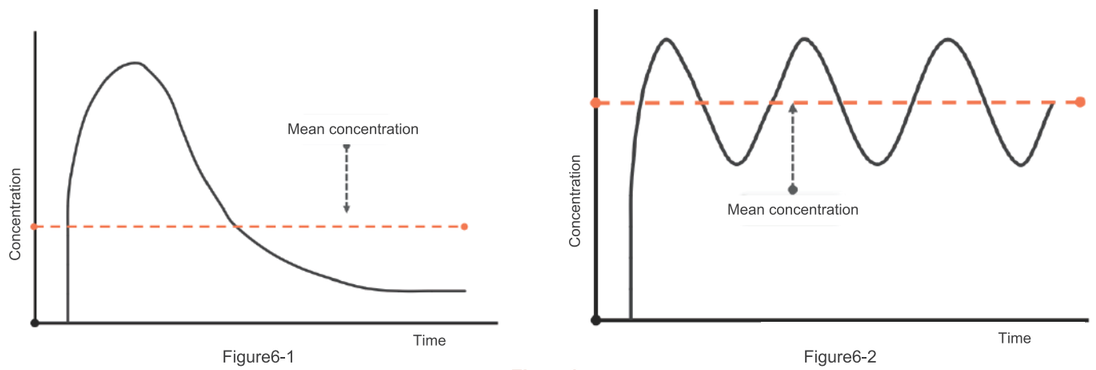


Figure6-1 Figure6-2

Figure6

The concentration of single column elution was changed as shown in figure 6-1. First, the eluent topped the water, then the product flowed out and the concentration rapidly increased. After reaching the peak, the concentration slowly decreased. Elution was stopped when the concentration decreased to a certain value.

Concentration changes about continuous ion exchange elution are shown in figure 6-2. The initial concentration change is the same as that of the single column. When the concentration drops to a certain value, the concentration rises again when the next saturated resin column is connected in series. Each time the concentration drops, the next saturated resin column is connected in series to ensure that the concentration is always at a high level, so as to reduce the energy consumption in the post-treatment process.

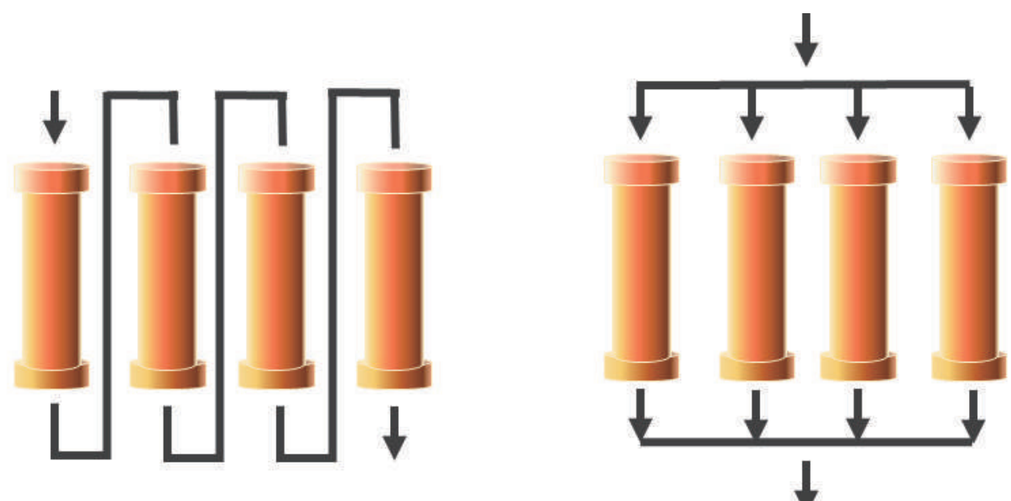
03 Reduce the consumption of mobile phase and output of waste solvent

In the processes of elution, leaching and regeneration, Resin will produce a large number of solutions, which can be divided into low concentration, medium concentration and high concentration solutions according to the content of impurities. The high-concentration impurity solution is discharged as wastewater, while the low-concentration and medium-concentration impurity solution can be used in the next resin column to realize the cyclic utilization of water and solvent. Therefore, continuous ion exchange technology can effectively reduce the usage of water and solvent, quantity of wastewater effluent, the volume of solvent recovery and energy consumption.

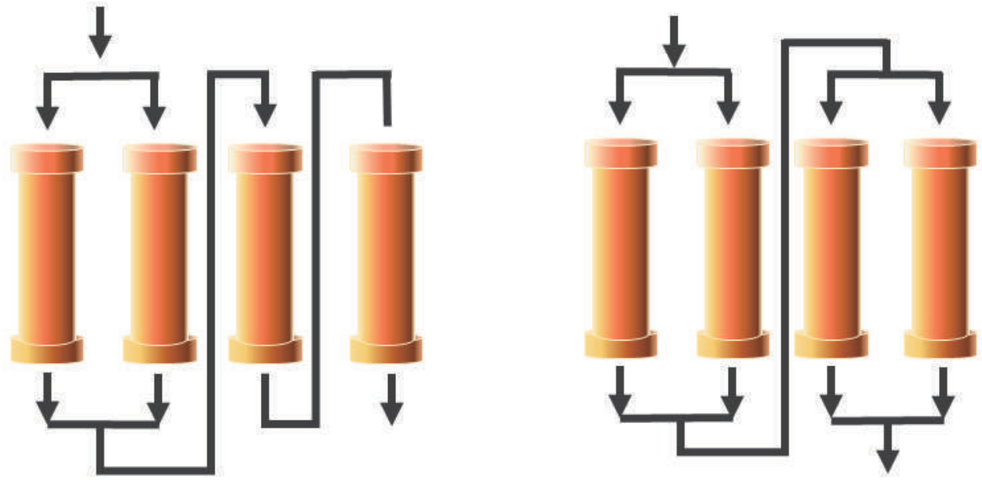
04 Prolong the working life of resin

Continuous ion exchange process can prolong the service life of resins. This is because on the one hand, compared with the single-column process, the raw material is always in a high-speed flow, so as to avoid long-term contact between the resin and the component of the material that is injurious to the resin. On the other hand, in continuous ion exchange process, the change of concentration in the whole process is relatively moderate, and the change of resin shrinkage is slow, which can reduce the proportion of resin breakage caused by resin shrinkage.

05 The flexible system configurations meet different separation process needs



Series flow *Parallel flow*

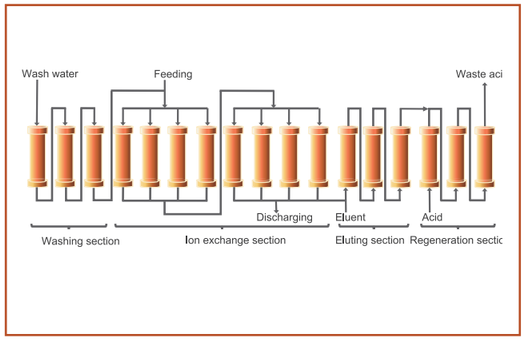


Series-parallel connection flow I *Series-parallel connection flow II*

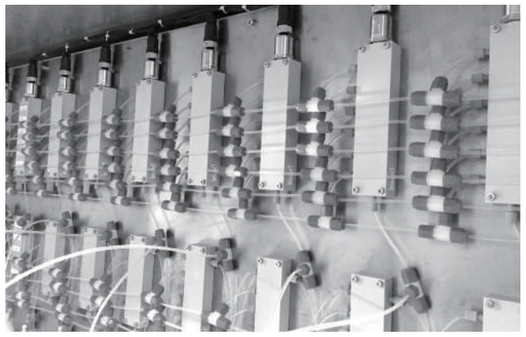
Figure7

Characteristics of a continuous ion exchange system

- Complete a variety of separation modes within the range of 1-12 columns, which can be applied to the purification process development and verification of many varieties.



- The design of valve group type realizes smaller dead space of the pipeline.

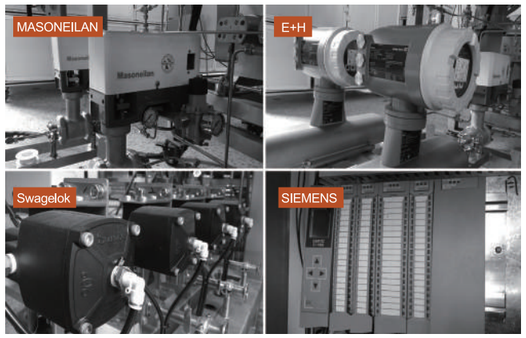


- UV, pH, RID detectors and other detectors are optional to monitor the parameter changes in the process of chromatography.



UV/RID Detectors

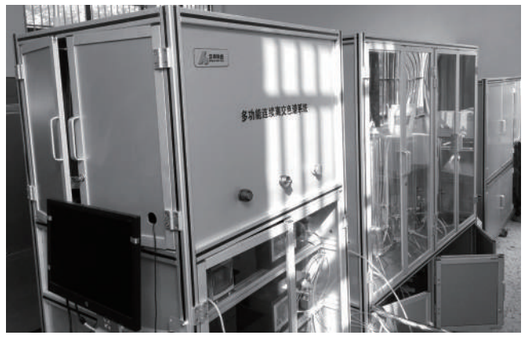
- Key parts are from Siemens, E+H and other well-known brands to improve the reliability and stability of equipment in the production process.



- Complete DQ/IQ/OQ/PQ verification file system ensures product quality.

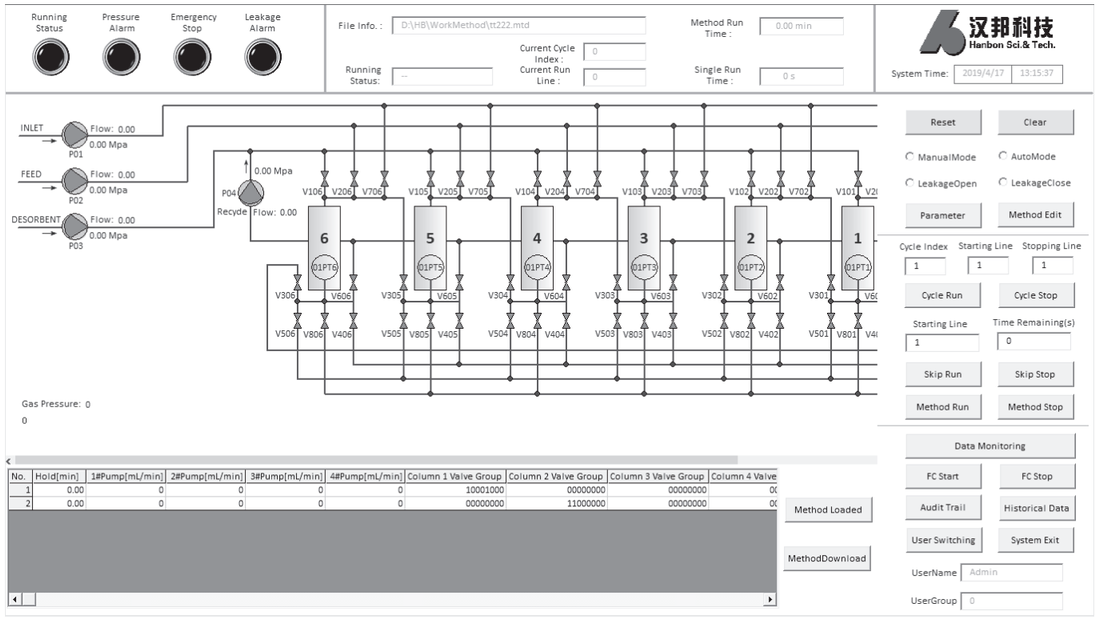


- The professional technology platform can realize one-stop service from method development to production amplification.



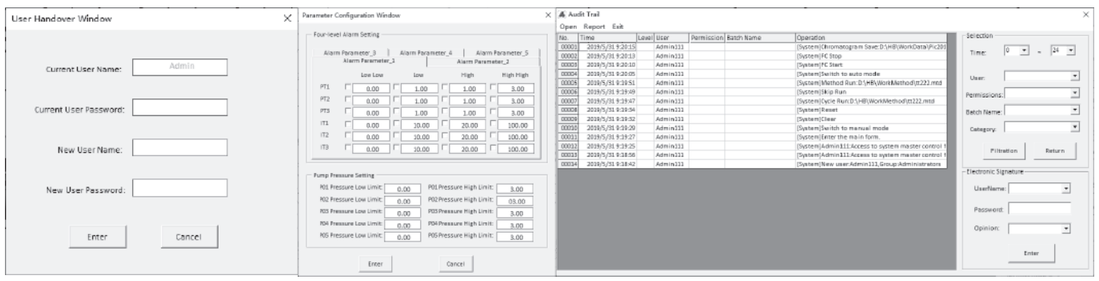
Software and Control System

- Continuous ion exchange device control software twice developed on the basis of GE's iFix software or Siemens platform, following the requirements of GAMP 5 and FDA 21 CFR Part 11.



- Visual flow control diagram, optional Chinese or English interface, easy to operate

- There are built-in manual or automatic control, method editing, data recording and analysis, alarm emergency stop and other modules. At the same time multi-level user permission settings, audit tracking and electronic signature are used to ensure the reliability and security of data.



Configuration Parameter



Continuous Ion Exchange System

Type	NS9003S	NS9003M	NS9003L
Resin content (m^3)	0.005-0.02	0.5-2	≥2
Pressure range (MPa)	＜0.6	＜0.5	＜0.5
Handling capacity (per day)	Kilogram class	hundreds kilogram class	tonner
Running mode	Solenoid valve package/carousel type	Pneumatic valve type	Pneumatic valve type
Quantity of chromatographic column	12-30		
Range of application	Sugar, amino acids, antibiotics, vitamins, plant extracts, proteins (affinity chromatography)		

Application Fields

Food　Drugs　Natural products　Petrochemical engineering

Application Case Reference

CASE 1——Continuous ion exchange process of an antibiotic

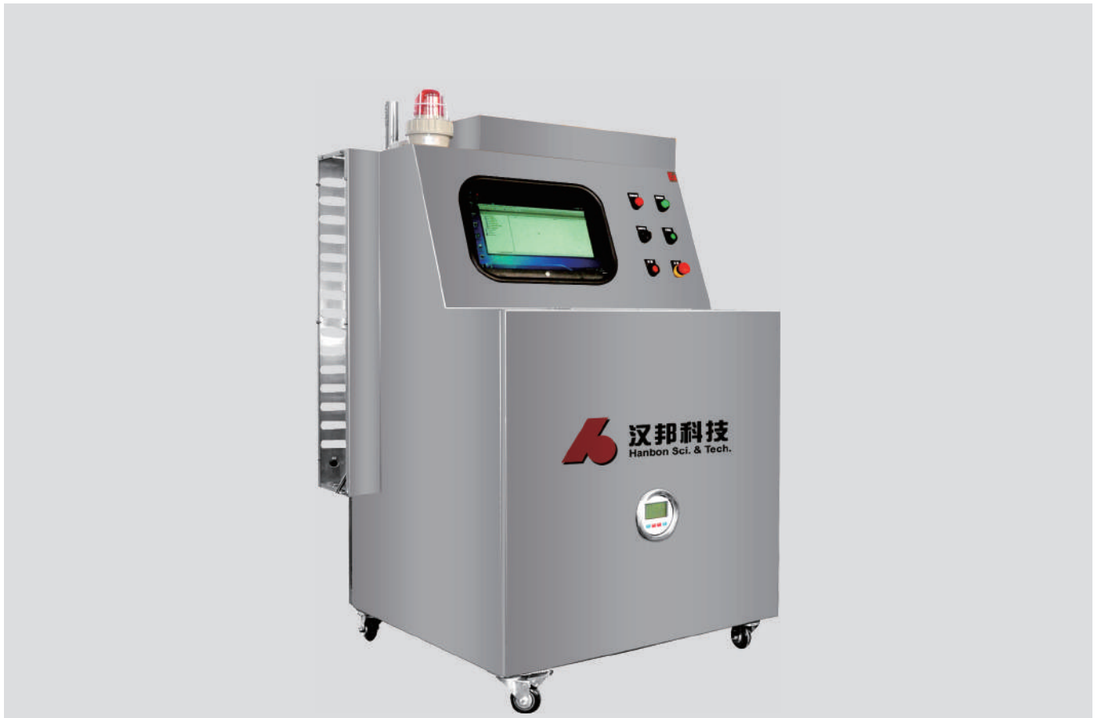
	Name	Single column	Continuous chromatographic	Increasing rate（%）
To produce 1kg of a certain antibiotic	Time (hours/cycle)	26	16	-38.5%
	Resin yield per unit (kg/m * cycle)	85.4	120.3	+40.9%
	Capacity per unit time (kg/m * hours)	3.3	7.5	+127%
	Sewage quantity (L)	130	33	-74.6%
	Continuous production or not	No	Yes	
	Product purity	＜99	＞99	
	Degree of automation	Low	High	
	Production people required for each shift (person)	5-8	1	
	Water, electricity and gas (yuan /kg)	1.5	0.9	-40%
	Depreciation of equipment (10 years) (yuan /kg)	---	---	---
	Total(yuan/kg)	26.5	13.7	-48.3%

CASE 2——Functional sugar ion exchange de-ashing process

In the process of functional sugar production, ion exchange method is usually used to remove inorganic ion impurities and organic impurities in crude products. Compared with continuous ion exchange technology, resin consumption, device size, water consumption, acid and Alkali consumption are needed much more in the traditional single column ion exchange. Taking 2000 tons of FOS as an example, the economic indexes of single column process and continuous ion exchange process were compared.

Process parameter	Single column process	Continuous ion exchange process
Capacity (tons/year)	2000	2000
Annual operation time/hour	7200	7200
Resin consumption (tons/year)	26	5.2
Resin cost (ten thousand yuan/year)	66	1.3
Hydrochloric acid consumption (tons/year)	162	39
Hydrochloric acid cost (ten thousand yuan/year)	10.53	2.53
Alkali consumption (tons/year)	222	64.5
Alkali cost (ten thousand yuan/year)	16.87	4.92
Water consumption (tons/year)	30000	10800
Water cost (ten thousand yuan/year)	6.00	2.16
Wastewater quantity (ton/year)	22000	10000
Wastewater treatment cost (ten thousand yuan/year)	6.60	3.00
Total cost (ten thousand yuan)	105.00	25.62
Cost saving (ten thousand yuan)		79.38

Online Fast Detection/Monitoring System



Product profile

On-line rapid detection or process monitoring and analysis are realized in the traditional chromatographic column through this system to avoid manual sampling and sample sending. According to the self-defined parameters, the system can control the elution pump, elution valve and collection valve in real time, so the system can be extended to the automatic system.
Multiple chromatographic columns can be simultaneously monitored by a set of on-line fast detection/monitoring system.

Product features

- Online sampling, online dilution, injection, detection and analysis are fully automated
- Avoid manual sampling, point plate, inspection, reinspection, etc., to save labor costs
- The test results can control tank switching automatically to avoid personal errors
- Save tanks and save space
- It can be customized according to user requirements and extended to automatic control system
- The software meets the requirements of FDA 21 CFR Part 11

Automatic Desolved System



Product profile

Automatic desolved system is a new solvent dispensing technology. It can monitor the concentration of solvent online, realize the automatic desolved and detection of online solvent through mass flow meter, flow regulating valve, online mixer, etc., and ensure the precision and stability of the solvents through advanced closed-loop control technology.

Product features

- With stable ratio and good reproducibility
- Online closed loop intelligent control can improve the dispensing precision
- Be safe and reliable, with high degree of automation
- Save workshop space and lower investment on tanks to reduce production cost

Attached list 1 Sugar degree- density comparison table

Sugar degree	Density	Sugar degree	Density	Sugar degree	Density	Sugar degree	Density
1.03	1.004	19.04	1.079	37.17	1.165	55.02	1.261
2.05	1.008	20.16	1.084	38.16	1.170	56.06	1.267
3.06	1.012	21.05	1.088	39.14	1.175	57.10	1.273
4.07	1.016	22.16	1.093	40.12	1.180	58.13	1.279
5.07	1.020	23.04	1.097	41.08	1.185	59.17	1.285
6.06	1.024	24.13	1.102	42.04	1.190	60.01	1.290
7.05	1.028	25.21	1.107	43.18	1.196	61.02	1.296
8.02	1.032	26.07	1.111	44.13	1.201	62.02	1.302
9.00	1.036	27.13	1.116	45.07	1.206	63.02	1.308
10.20	1.041	28.19	1.121	46.00	1.211	64.02	1.314
11.16	1.045	29.03	1.125	47.11	1.217	65.00	1.320
12.11	1.049	30.08	1.130	48.03	1.222	66.15	1.327
13.05	1.053	31.12	1.135	49.13	1.228	67.12	1.333
14.22	1.058	32.14	1.140	50.03	1.233	68.02	1.339
15.16	1.062	33.17	1.145	51.12	1.239	69.05	1.345
16.08	1.066	34.18	1.150	52.01	1.244	70.01	1.351
17.00	1.070	35.19	1.155	53.08	1.250	71.12	1.358
18.13	1.075	36.19	1.160	54.14	1.256	72.00	1.360

Attached list 2 Industrial preparative column packing material capacity

Type	DAC 50	DAC 80	DAC 100	DAC 150	DAC 200	DAC 300	DAC 450	DAC 500	DAC 600	DAC 800	DAC 1000	DAC 1200
Column spec. (mm)	50*250	80*250	80*250	150*250	200*250	300*250	450*250	500*250	600*250	800*250	1000*250	1200*250
10μm packing material dosage (kg)	0.35	0.9	1.4	3.2	5.6	13	28	35	50	90	140	202

Attached list 3 Mesh number、Inch、μm conversion table

No.	Mesh number	Inch	μm
1	10	0.0661	1880
2	12	0.0555	1410
3	14	0.0469	1190
4	18	0.0394	1000
5	20	0.0331	841
6	25	0.0280	707
7	30	0.0232	595
8	35	0.0197	500
9	40	0.0105	420
10	45	0.0138	354
11	50	0.0107	297
12	60	0.0098	250
13	70	0.0083	210
14	80	0.0070	177
15	100	0.0059	149
16	120	0.0049	125
17	140	0.0041	105
18	170	0.0035	88
19	200	0.0029	74
20	230	0.0024	63
21	270	0.0021	53
22	325	0.0017	44
23	400	0.0015	37
24	550	0.0009	25
25	800	0.0006	15
26	1250	0.0004	10
27	3000	0.0002	5
28	15000	0.00004	1