BioProcess™ Resin Mixer

CHROMATOGRAPHY RESIN HANDLING

BioProcess™ Resin Mixer is an automated tank for chromatography resin handling, designed for large-scale biopharmaceutical manufacturing (Fig 1). The mixer allows convenient, automated mixing of large resin volumes that would be cumbersome and time-consuming to prepare by manual mixing.

BioProcess™ Resin Mixer helps to generate and transfer a homogenous slurry, which plays a critical role in ensuring a well-packed column and a robust and efficient purification process when resin volumes increase.

Seamless handling of chromatography resins from column packing to unpacking:

- Automated capability to support column packing and cleaning-in-place (CIP).
- Controlled and gentle mixing of resin slurry.
- Compatible with AxiChrom™ chromatography columns.

Supporting the column packing workflow

Bulk chromatography resins are supplied in 20% ethanol or another suitable solution when transported and stored. Before a column is packed, the resin is often transferred to a packing solution and prepared as a homogenous slurry, which is essential for optimal column packing and effective protein purification. BioProcess™ Resin Mixer is a vessel designed to support the preparation and storage of chromatography resins in large-scale manufacturing operations (Fig 2).

The system is available in three standard sizes; 500, 1250, and 2000 L to cover a broad range of chromatography column sizes (Fig 3). All BioProcess™ Resin Mixer sizes have the same minimal working volume, expanding the use across column sizes.

Fig 1. BioProcess™ Resin Mixer is an automated mixer system for production of large-scale volumes of resin slurries for packing in downstream chromatography columns.

- Transfer of slurry to/from resin container
- Precise control of slurry quantity
- In-tank slurry concentration adjustment—concentration or dilution
- Buffer exchange before and after use
- Loosening sedimented slurry by air blow and gentle stirring
- Agitating slurry during temporary storage and prior to column packing
- Transfer of slurry to/from chromatography column

Fig 2. Typical steps in the preparation and storage of chromatography resin slurries prior to column packing and/or storage of the resin.

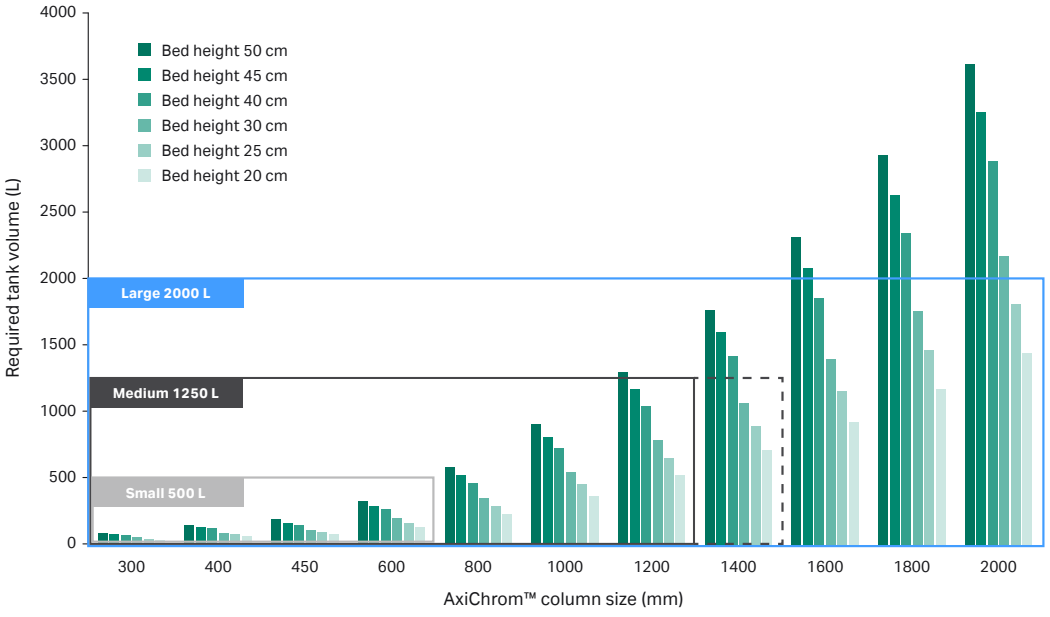

Fig 3. BioProcess™ Resin Mixer is available in 500, 1250, and 2000 L sizes to accommodate mixing of resin for most chromatography column sizes. The medium sized tank can be used with larger columns when the bed height is lower (30, 25, and 20 cm).

Reducing manual handling through automation

BioProcess™ Resin Mixer is operated through a Rockwell™ programmable logic controller (PLC). A dedicated screen ensures easy interaction and the software includes a library of premade Unit operations and Equipment phases (Fig 4), which enables automation of typical workflows. The BioProcess™ Resin Mixer bottom valve can be remotely controlled from the AxiChrom™ Master during packing and unpacking of an AxiChrom™ chromatography column.

The PLC follows the ANSI/ISA-88 standard. Using ANSI/ISA-88-based functionality, protocols and processes are developed independently of process equipment.

BioProcess™ Resin Mixer can also be controlled using control systems such as DeltaV™ or manufacturing execution system (MES) via Ethernet IP or PROFIBUS™ DP for control from systems such as SCADA or DCS. This facilitates integration with other downstream equipment for efficient column packing solutions.

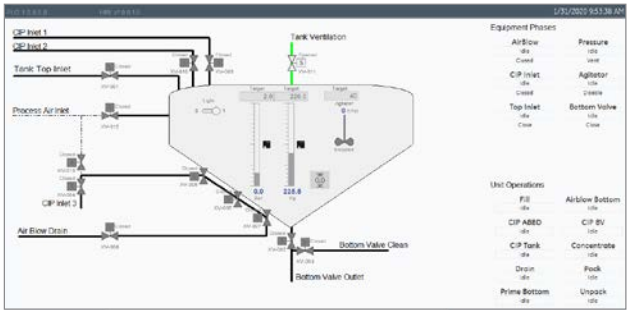

Fig 4. The user-friendly interface of BioProcess™ Resin Mixer PLC software. The software includes a library of premade unit operations covering typical operations to enable automation of typical workflows.

Equipment phases

- Airblow: dissolves sedimented resin by injecting compressed air through the bottom nets.
- Agitator: starts/stops the agitator at a set speed.
- CIP inlet: manual control of the spray balls and automatic operation with a timed cycle.
- Inlet resin: opens/closes the resin inlet valve.
- Outlet resin: opens/closes the resin bottom valve. Opens/closes of the bottom valve prime/clean valve port and operates the bottom valve from AxiChrom™ Master.
- Tank pressure: pressurizes the tank at a set pressure and open vent filter.

Unit operations

- Fill: starts the agitator with a set speed and fills the tank through the resin inlet until the weight setpoint is reached.
- Airblow bottom: injects compressed air through the bottom nets with the vent valve open. The agitator will start automatically at the set speed. It is also possible to set the speed to 0 to keep it still.
- CIP ABBV (airblow bottom valve): cleaning-in-place (CIP) hoses connecting the airblow filter valves.
- CIP BV (bottom valve): CIP of the tank bottom valve through the CIP port.
- CIP tank: cycled operating of the CIP spray balls with a set time.
- Concentrate (Fig 5): starts the agitator with a set speed and pressurizes the tank. The buffer is drained/decanted out through the bottom filters until the set weight is achieved.
- Drain: the tank is pressurized and drained out thought the bottom valve. Airblow filters are injected with compressed air.
- Pack: used for transfer of the resin slurry to the column.
- Prime bottom: priming of the tank bottom valve and hoses connected to the column.
- Unpack: used when transferring the resin back to the tank from the column.

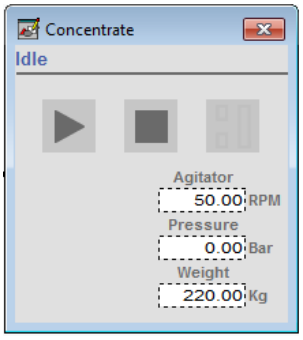

Fig 5. The Concentrate interface.

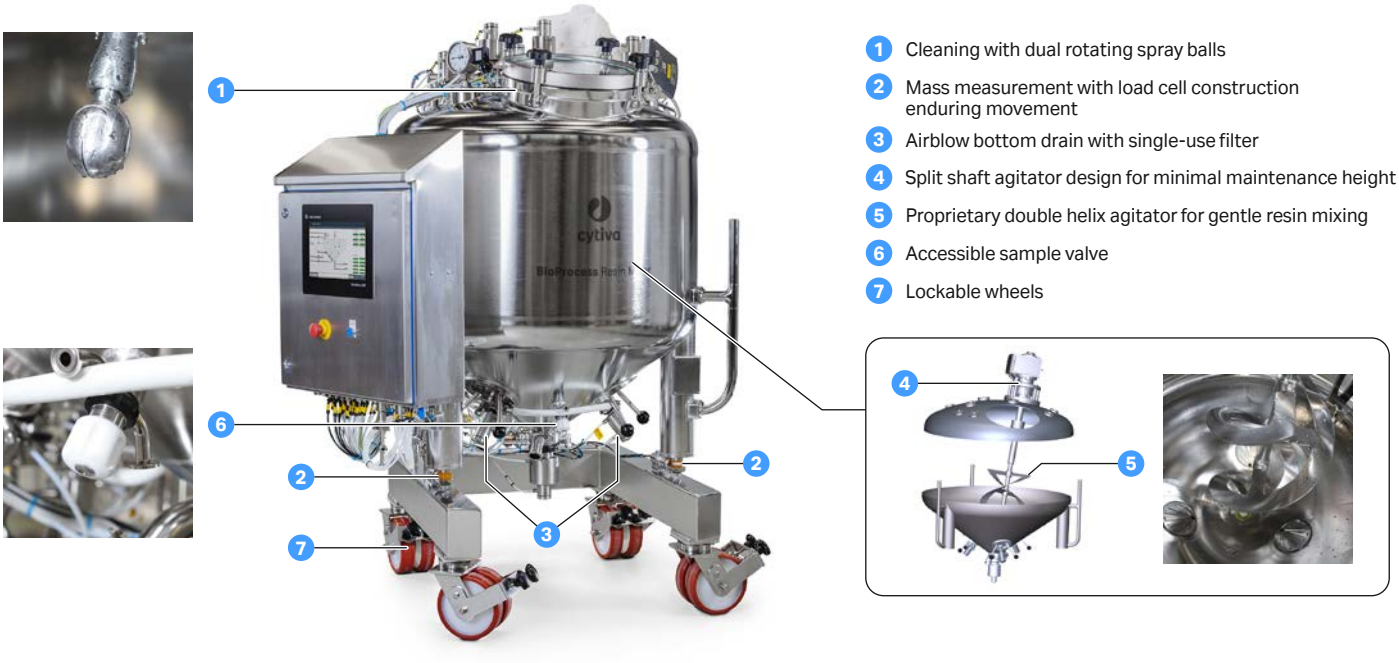

Fig 6. Components and features of BioProcess™ Resin Mixer.

Intuitive design ensures gentle handling of resin from start to finish

Gentle handling of resin is important to maximize resin lifetime and quality. BioProcess™ Resin Mixer supports all packing methodologies, including pressure packing of brittle resins. The proprietary double helix agitator of the BioProcess™ Resin Mixer creates an even particle size distribution throughout the slurry, generating a homogenous slurry (Fig 6). It also prevents excessive shear forces that can otherwise lead to resin degradation, clogged nets, and increased back pressure. The airblow function is used to gently loosen sedimented resin by blowing air through the bottom filters before the agitator is started.

To obtain the correct amount of chromatography resin for packing to target bed height or compression, it is important to measure the slurry concentration correctly. For example, when packing a 50% slurry to a target bed height of 20 cm at a Packing Factor (PF) of 1.15, an inaccuracy of ± 2% in the slurry concentration can cause the final packed bed height to vary between 19.2 and 20.8 cm. A critical parameter to obtain the correct slurry concentration is to take a representative sample of the homogenous slurry for the concentration determination.

The double helix agitator ensures a continuous and robust mixing of the slurry even at the minimal working volume. A sample valve allows for sampling for offline slurry concentration determination. In addition, to support slurry concentration adjustment, accurate mass measurement is achieved by the mass load cells and the possibility to set the target weight during filling of resin or buffer into the tank. The load cells are mounted on the frame under the tank legs to reduce footprint. The load cells are mechanically locked during movement.

Single-use elements reduce changeover time

The airblow buffer drain valve has a disposable filter which is easily assembled and disassembled using a bayonet assembly with 140 mm PE sinters (Fig 7). This reduces cleaning and validation requirements and supports a fast and efficient changeover between resins. In addition, a gasket is avoided within the tank. The same disposable and proven filter design is used for AxiChrom™ 140 mm. The airblow buffer drain valve is based on a flush design making it more drainable and is used for buffer change and slurry concentration by filtering the supernatant through the bottom filters with the tank pressurized with a set pressure from the PLC.

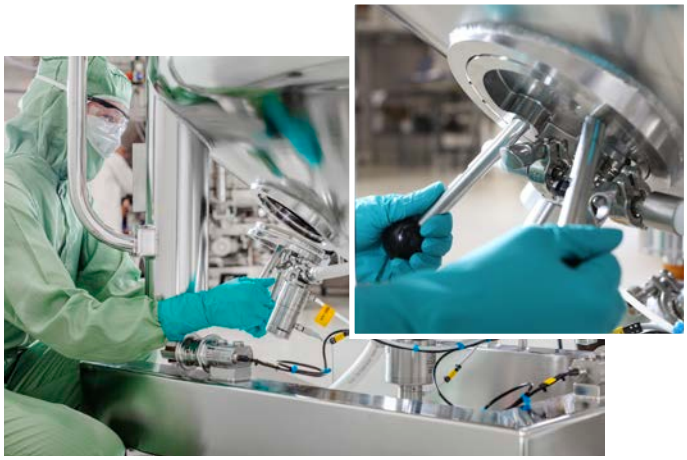

Fig 7. The airblow buffer drain valve for buffer change and slurry concentration.

Minimizing resin loss

BioProcess™ Resin Mixer is designed to support minimal resin loss. Before transferring the resin to the column, the bottom valve can be primed to avoid air bubbles and to optimize resin use. During the end of the column packing operation, spray balls (see Fig 6) can be manually pulsed with buffer to flush out the last amount of resin left in the tank. Furthermore, the BioProcess™ Resin Mixer can be directly connected to AxiChrom™ Master and AxiChrom™ chromatography columns for automated column packing. The intelligent design of AxiChrom™ chromatography columns further supports reduced/minimized resin loss.

Suitable for GMP manufacturing

BioProcess™ Resin Mixer is designed and constructed to enable cleaning and sanitary handling, and the wetted parts are compliant with USP Class VI, EMA/410/01 and FDA CFR 21§177. Two high efficiency rotating spray balls ensure fast and efficient CIP. Cleaning cycle timing can be controlled and preprogrammed from the PLC to allow for both automated and manual cleaning. The maintenance height is low due to a split-shaft agitator design.

BioProcess™ Resin Mixer follows both the Pressure Equipment Directive (PED) 2014/68/EU, ASME Section VIII Div 1 or China TSG 21 for the design and fabrication of pressure equipment.

The system is delivered with comprehensive operating instructions and extensive system documentation including assembly drawings, PID, and system specifications. Installation and operation qualification (IQ/OQ) protocols are available. IQ/OQ can be performed either by the user or by a certified specialist.

Other tools to support the column packing workflow

Slurry can be prepared manually, mechanically, or by using our Media Wand™ and Media Handling Unit slurry mixing and transfer tool. Shaking gives good results but is often not practical for larger volumes. For stirring, a soft stirrer without sharp edges is preferred. Connected to the Media Handling Unit, Media Wand™ (Fig 8) can be used to remove the transport solution and resuspend the resin in packing solution directly in the container. The resin is transferred to the slurry tank in one operation, which makes Media Wand™ suitable for large-scale packing (Fig 9).

Fig 8. Media Wand™ connected to the Media Handling Unit.

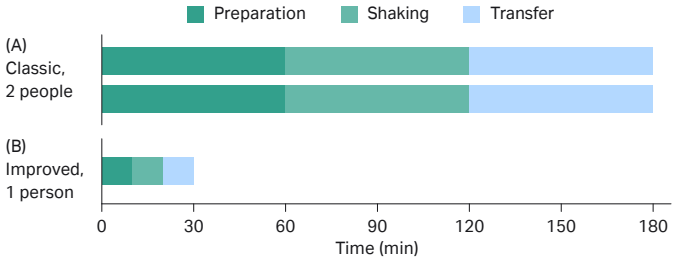

Fig 9. Compared with (A) a classic approach, the use of (B) Media Wand™ and Media Handling Unit offers a simplified workflow for time-savings to be achieved in slurry preparation for packing of larger columns. Time estimates are for slurry preparation from large-scale resin volumes of typically more than 50 L.

BioProcess™ Resin Mixer specifications

Basic characteristics

Operating pressure	0–2.5 bar g (0–0.25 MPa, 0–36.3 psi)
Process air consumption	200 NL/min
Instrument air consumption	50 NL/min
Pressure requirement, process air/instrument air	2.5–10/6–10 bar g (0.25–1.0 MPa, 36.3–145 psi/ 0.6–1.0 MPa, 87–145 psi)
Number of inlets	6
Number of outlets	4
Tank bottom valve	1
Spray balls	2
Protection class	IP55
Tank, piping material	316L
Process wetted gaskets and elastomers	EPDM, FFKM, PTFE
Design temperature range	4°C to 80°C
Power supply	3 × 400 VAC, 50Hz (CE)/ 3 × 480 VAC, 60 Hz (UL)
Design code	PED/ASME/TSG

Mixer size and volume characteristics

	Tank size		
	500 L	**1250 L**	**2000 L**
Dimensions (W × H × D) (mm)	1575 × 1999 × 1433	1837 × 2317 × 1734	2007 × 2576 × 1881
Dry weight (kg)	550	850	1125
Minimum operating volume (L)	30	30	30
Maximum operating volume (L)	500	1250	2000

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