Applikon BioSep: Acoustic cell retention device

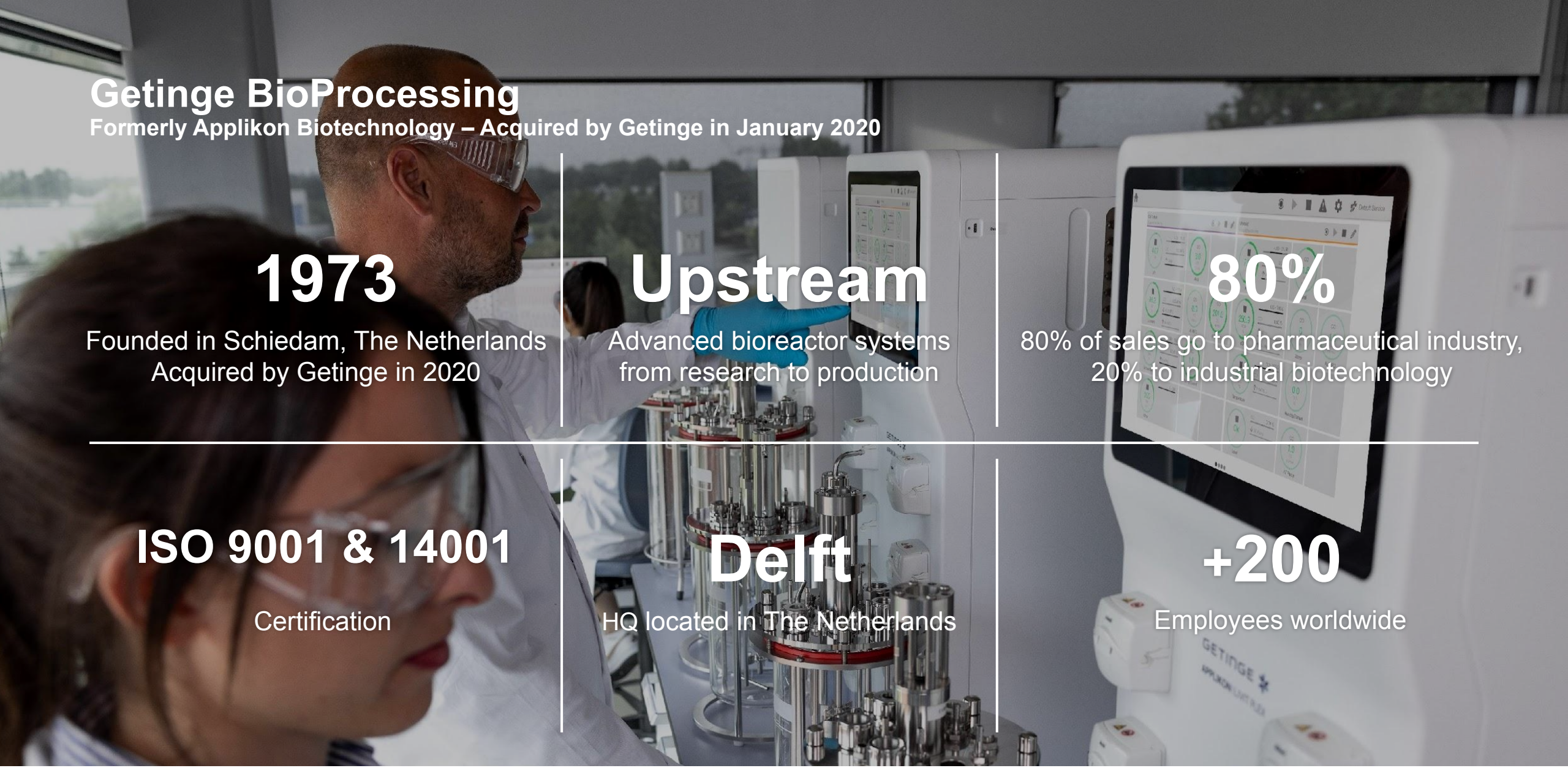
Introduction presentation

2026 V1

GETINGE

Getinge BioProcessing

Formerly Applikon Biotechnology – Acquired by Getinge in January 2020



1973

Founded in Schiedam, The Netherlands
Acquired by Getinge in 2020

Upstream

Advanced bioreactor systems
from research to production

80%

80% of sales go to pharmaceutical industry,
20% to industrial biotechnology

ISO 9001 & 14001

Certification

Delft

HQ located in The Netherlands

+200

Employees worldwide

GETINGE

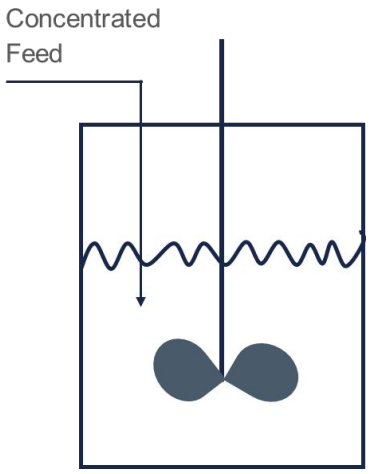
Continuous cultivation

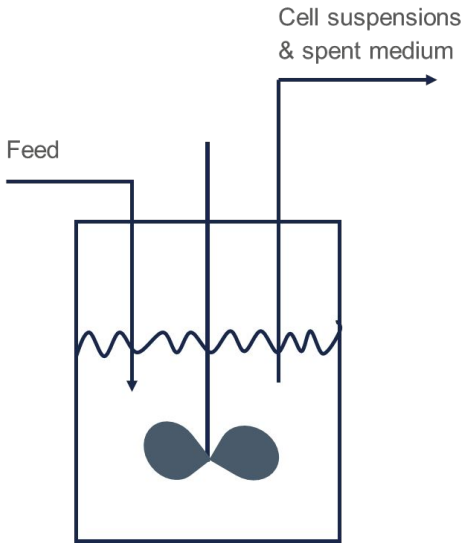
Fed-batch

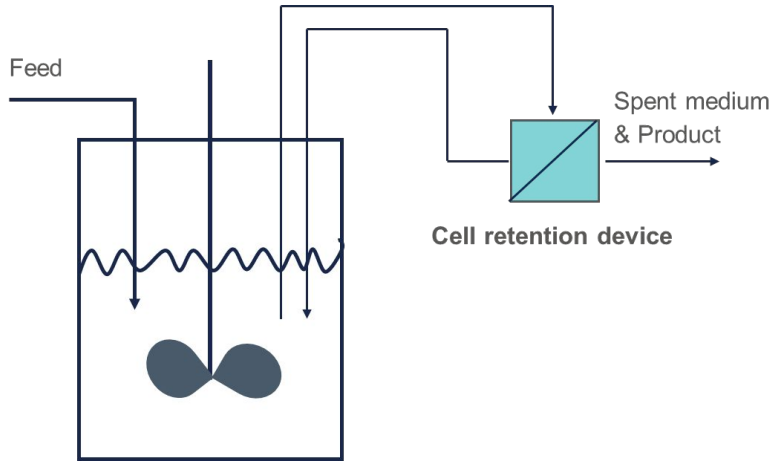
Continuous (Chemostat)

Perfusion

- Retains or recycles cells back into the bioreactor while adding fresh media continuously
- Maintains high cell densities and stable environment over long periods.
- Increased productivity and product quality







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Cell retention device

An essential to realize high-yield perfusion culture

Prerequisites of cell retention device

- Achieve high cell retention efficiency inside the bioreactor
- Support stable and long-term operations
- Cleanable, sterilizable and reusable
- Preserve high culture viability by avoiding cell damage from mechanical shear stress and not altering cell metabolism.

Cell retention techniques applying centrifugation

Technique	Principle	Disadvantage
Centrifugation	Uses centrifugal force to separate cells based on density differences	High energy consumption, potential cell damage due to shear forces
Hydrocyclones	Uses centrifugal force in a conical vessel to separate cells based on density	Lower separation efficiency, potential for cell damage due to shear forces
Gravitational Settling	Relies on gravity to settle cells out of the culture medium	Slow separation process, large area required, limited efficiency for small cells

Shear forces and slow processes found in centrifugation limit the potential of cell retention.

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Cell retention techniques applying filtration

Technique	Principle	Disadvantage
Spin-filters	Combines filtration and centrifugal forces to separate cells	Mechanical wear and tear, potential for cell damage, fouling issues
Tangential Flow Filtration (TFF)	Filters cells by flowing the medium tangentially across the filter surface	Membrane fouling, requires regular cleaning and maintenance, limited by shear sensitivity of cells.
Dynamic Filtration	Uses a rotating or vibrating filter to prevent clogging and enhance filtration efficiency	Mechanical complexity, potential for cell damage

Membrane fouling (Clogging) reduces the cell separation efficiency of filtration techniques

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BioSep - Scalable cell retention device

Product End of Life

Product successor announced in 2026

Mini BioSep (1 L/day)

Applicable for
- MiniBio 500 mL & 1000 mL
- AppliFlex ST 500 mL

Applikon BioSep Medium

Applicable for
- Applikon autoclavable 2~7 L
- AppliFlex ST 3 L

BioSep 50 L/day

Applicable for
- Applikon autoclavable 15 & 20 L
- SIP systems (60L)

BioSep 200 L/day

Applicable for
- SIP systems (130L)
- Large scale single-use system

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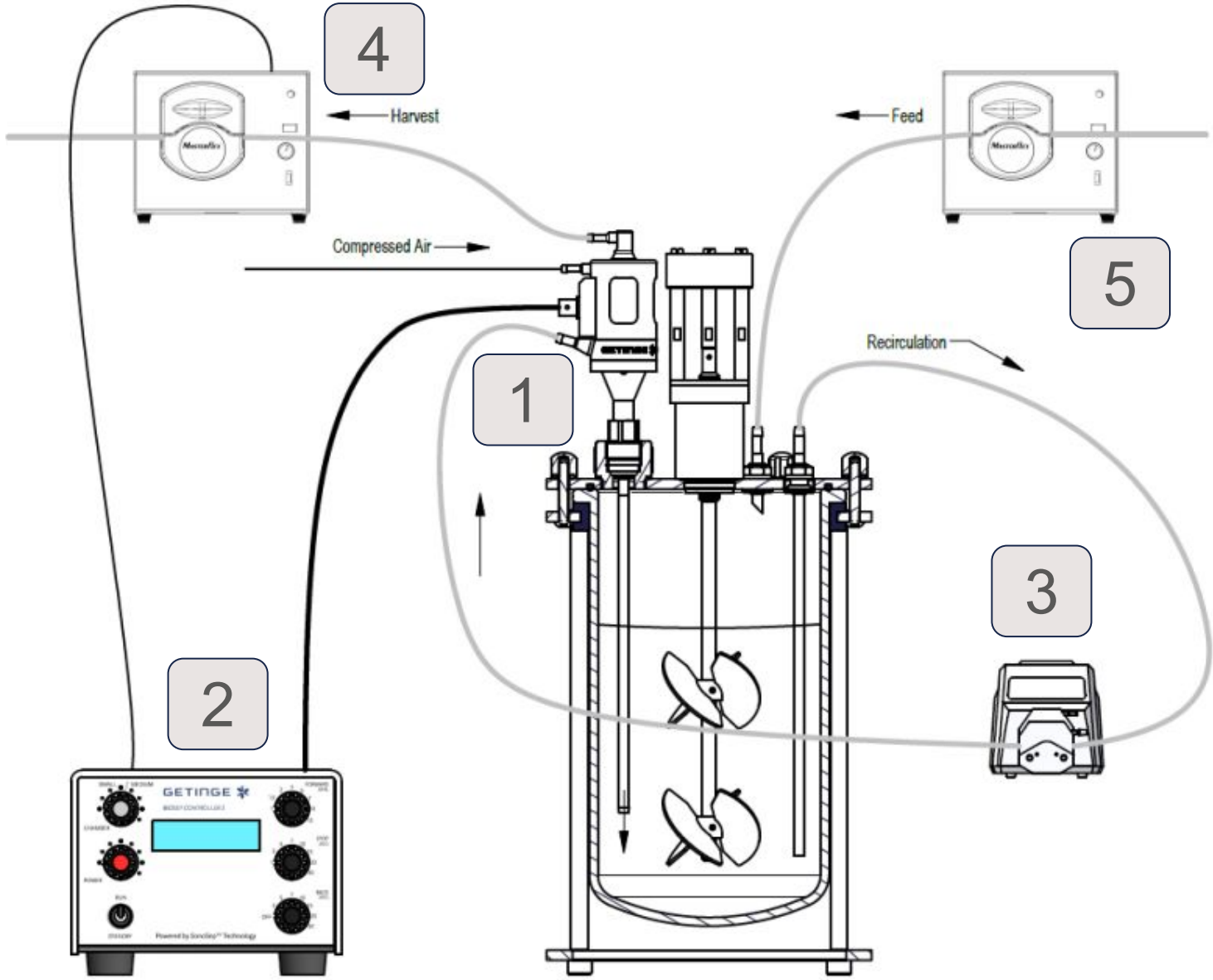
BioSep system setup

Complete acoustic perfusion system

The Applikon BioSep **Medium** Setup

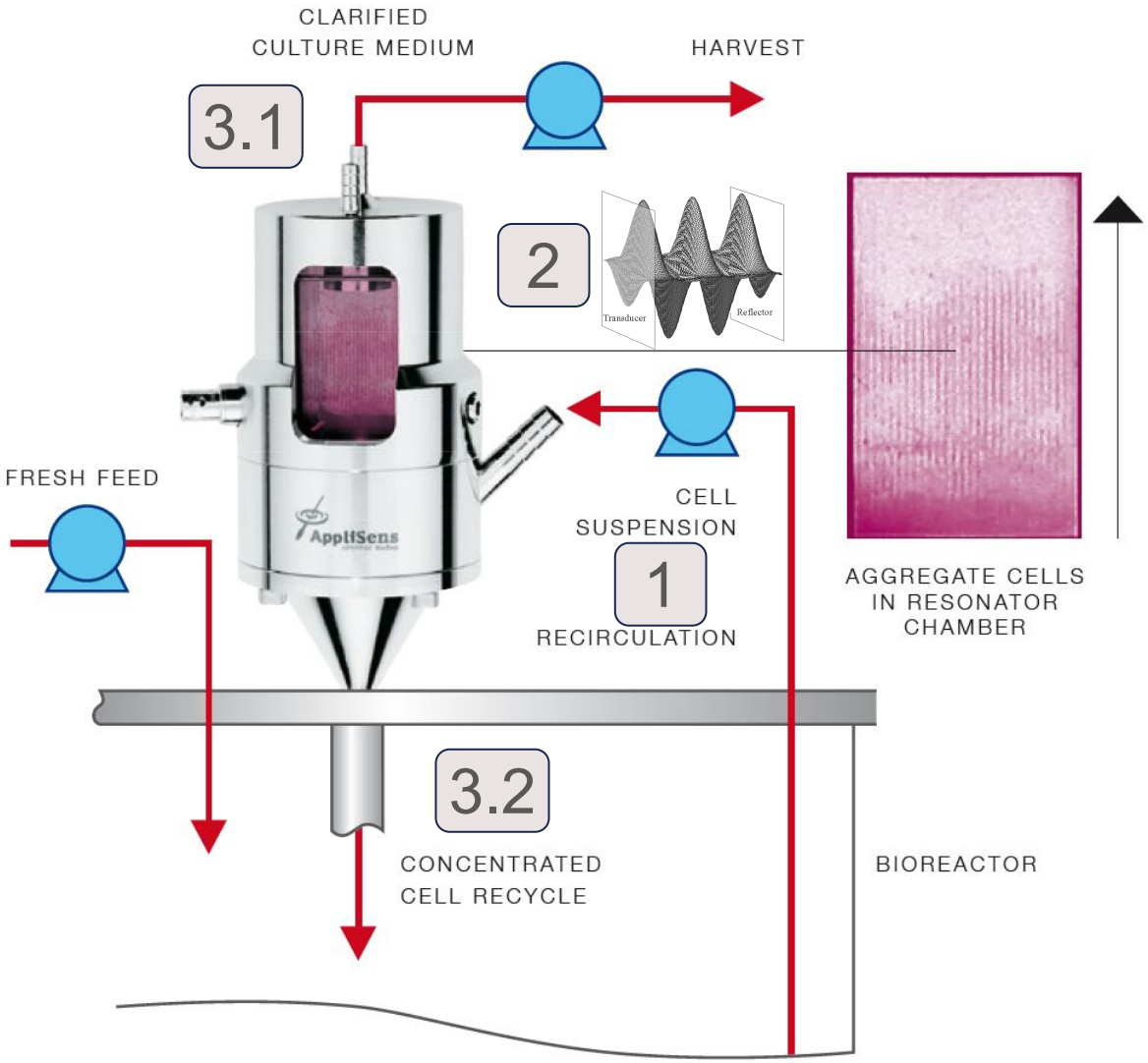
1. Applikon BioSep **Medium**
2. Applikon BioSep Control Lab
3. Recirculation pump
4. Harvest pump
5. Feed pump (in bioprocess controller)



Schematic illustration of a Applikon BioSep Medium system

BioSep operation

Techniques to retain cells in the bioreactor



(1) Cell suspensions from the bioreactor are pumped into the resonator chamber mounted on the bioreactor head plate.

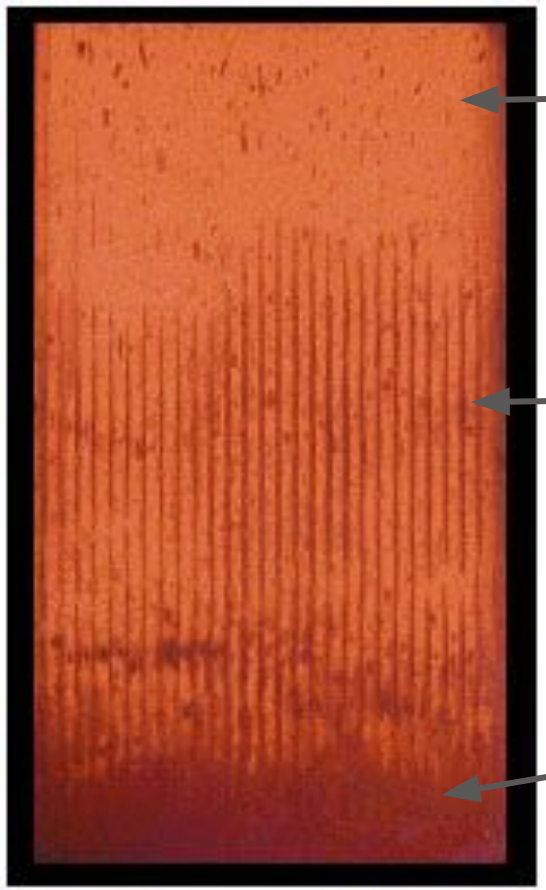
(2) The standing acoustic waves force suspension cells into planes, where they form loose aggregates.

(3.1) The clarified harvest flow passes through the acoustic field, while (3.2) the concentrated cells are returned to the bioreactor.

Inside the BioSep chamber

Zoom in how cells are retained

Flow direction



Clarified harvest

Cell “banding”

The ultrasonic forces in the resonator aggregate and hold the suspended cells stationary against the flow, thereby clarifying the harvest stream.

Concentrated cell suspensions

Rapidly recycled to the bioreactor in the return stream where they are dispersed by agitation

Benefits of using BioSep

- No problems of membrane fouling or clogging, which occurs in filtration devices
- No cell damage due to shear stress
- Scalable perfusion solution

Applikon BioSep Medium	BioSep 50 L/day	BioSep 200 L/day
Applicable for • Applikon autoclavable 2~7 L • AppliFlex ST 3 L	Applicable for • Applikon autoclavable 15 & 20 L • SIP systems (60L)	Applicable for • SIP systems (130L) • Large scale single-use system

BioSep : Acoustic cell retention device
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System performance of BioSep

Design for effective cell separation

BioSep performance which achieves cell separation efficiency between 90~99%

	Operating perfusion rate	Cell concentration in the bioreactor
BioSep Medium	1~10 L/day	Up to 100 million cells/mL*
BioSep 50 L/day	5~50 L/day	Up to 20 million cells/mL
BioSep 200 L/day	25~200 L/day	Up to 50 million cells/mL

The separation efficiency (SE) of the BioSep system depends on the cell concentration and harvest rate and is defined as:

$$SE = 100\% \times \left(1 - \frac{\text{Cell concentration in the harvest flow}}{\text{Cell concentration in the bioreactor}}\right)$$

SE is controlled by adjusting the power level to the resonator and the run/stop cycle time ratio for both the resonator and harvest pump. The maximum capacity that can be achieved depends on the properties of the cell line and medium composition.

*results obtained with technical model organism, not with cell cull culture

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Proven achievements of using BioSep

Examples of improved bioprocess performance

Benefits of using BioSep

- High productivity yield with > 90% cell separation efficiency
- Achieved long-term bioprocess (up to months)

BioSep maintenance

Easy to clean and sterilize for next bioprocess works

Cleaning

- Disassemble the BioSep assembly and clean the resonator chamber with a pipette brush/a soft brush and detergent solution

Disassembled Applikon BioSep Medium

Sterilization

BioSep Medium and 50 L/day

・Fully autoclavable

・Mount BioSep on the bioreactor head plate and autoclave together with the bioreactor

・NOT INTENDED FOR STEAM-IN-PLACE STERILIZATION

BioSep 200 L/day

・The resonator can be sterilized by in-Situ sterilization as well as off-line autoclaving

Summary

Outstanding solutions of BioSep as an acoustic cell retention device

- ☑️ Achieve high cell retention during perfusion culture
- ☑️ Preserve high culture viability by avoiding cell damage from mechanical shear stress and not altering cell metabolism
- ☑️ Support stable and long-term operations
- ☑️ Cleanable, sterilizable and reusable

BioSep becomes the perfect solution for perfusion culture.

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PASSION FOR LIFE