

# **Engineered for maximum yield**

Biopharmaceutical active ingredients are proteins that have to be isolated from the fermentation broth in which they are produced. These purification processes always involve several process steps and each of these time-consuming and cost-intensive steps leads to losses of the target protein. Overall, this results in huge losses of the valuable component. The ANDRITZ rotor stator high-gradient magnetic separator MES-RS was developed to overcome these losses and extract more from less.

# SINGLE-STAGE PROTEIN PURIFICATION

The "all-in-one" approach of the ANDRITZ MES-RS simplifies the conventional cascade of process steps, resulting in a single unit for the entire process. An impressive example of the efficiency of this technology is the purification process for equine chorionic gonadotropin (eCG). The standard purification process achieves an overall yield of 28%. When using the MES-RS, the protein harvesting step results in a yield of 97%, which means an overall process yield of 75%. Starting from the same batch size of fermentation broth, this means the final product output is three times higher. The magnetic separator enables the extraction of a single protein fraction directly from the non-purified complex feedstock, thus setting new standards in efficiency and yield intensification.

The MES-RS concept for protein purification, which utilizes high-gradient magnetic separation (HGMS) technology, allows ANDRITZ Separation to offer a novel downstream process for biopharmaceuticals. The state-of-the-art technology for protein purification is liquid chromatography, which requires multistage pretreatment to be able to process a complex feedstock. The MES-RS therefore reduces the effort for downstream processing while substantially increasing the yield.



Lab-scale MES-RS in operation, © KIT, Karlsruhe

### **MAIN APPLICATIONS**

- · Monoclonal antibodies (mAb)
- Hormones
- Enzymes
- Vaccines
- · Biopharmaceutical proteins
- · Feedstocks with extremely low titer
- · Feedstocks with high downstream effort
- Magnetic particles

# YOUR BENEFITS

- Avoids multi-stage pretreatment steps in downstream processing
- Single unit for prepurification, including first liquid chromatography step
- Target protein yield of up to 95%
- Purity of up to 97% after single-stage process
- Reduction of processing time to just several minutes
- Purification of broths that previously could not be purified
- Processing in accordance with GMP and ATEX requirements
- Fully automatic operation

# PROCESSING PARAMETERS

Separator type	MES-RS 25	MES-RS 100	MES-RS 1000				
Process chamber volume [I]	0.25	1					
Loaded particle capacity [g]	25–100	50-500	500-5,000				
Flow rate [I/min]	0.5	3	30				
Fermenter batch size [I]	0.5-10	2-500	50-5,000				
Operating principle	0 ,	Highly selective binding of proteins to functionalized bead surface					
Separation principle	· ·	Magnetic capture of magnetized, functionalized particles					
Operating temperature	5-40°C	5-40°C					
Operating mode	Batch	Batch					
Operating hours	24/7, fully a	utomatic					
Construction material	Stainless st	Stainless steel					
Optional feature	Adjustable	Adjustable magnetic flux density					





The ANDRITZ MES-RS process: Minimized losses in single-stage isolation process

# Highly efficient extraction and purification of proteins through magnetic separation

# **OPERATING PRINCIPLE**

In contrast to filtration or sedimentation techniques, the MES-RS separates only magnetizable components from the fermentation broth, and neither density nor particle size have any influence on the separation efficiency. The principle of magnetic separation, which is described in the following four steps, provides a highly selective method of extracting and purifying proteins.

Magnetic beads coated with a highly selective, functionalized surface (magnetic particles) are used to adsorb a specific protein fraction (step 1).

The process chamber of the MES-RS, which separates the magnetic particles, consists of an arrangement of multiple separation discs. The magnetic field magnetizes the particles and the separation discs, which causes the two components to attract (step 2). By applying a magnetic field to the magnetic particles, it is possible to extract both the magnetic particles and the adsorbed proteins.

Since an electromagnet is used, the separation forces can be switched on and off. In addition, it is possible to rotate every second separation disc (rotor stator principle), which allows the captured magnetic particles to be reconverted into a slurry (step 3).

Both features of the MES – the electromagnet and the rotor stator design – make it possible to carry out several process steps within one process chamber. The concentrated and purified target protein can be discharged directly out of the MES-RS process chamber (step 4).

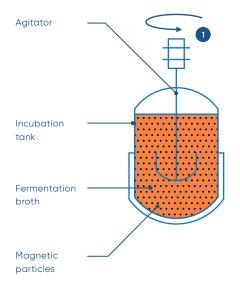
# STEP 1: BINDING OF TARGET PROTEIN

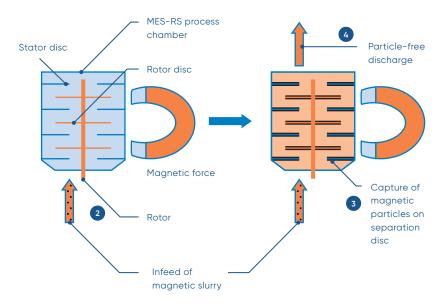
 Mixing of magnetic particles and fermentation broth, binding of target protein to highly functionalized magnetic particle surface

# STEP 2:

# **SEPARATION OF MAGNETIC PARTICLES**

- 2 Feeding of magnetic slurry into the process chamber
- 3 Separation of particles on separation discs by magnetization
- 4 Discharging of particle–free waste slurry until the feed tank is empty

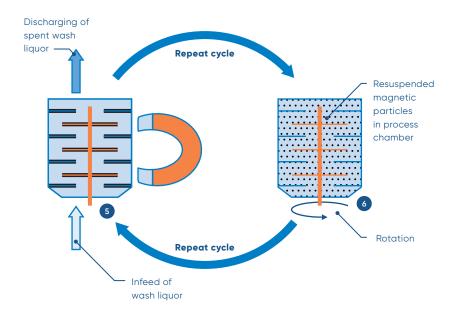




### STEP 3:

### **WASHING OF PARTICLES**

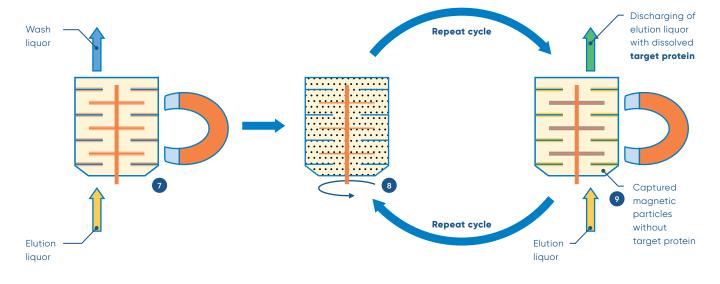
- 5 Capture of particles and displacement of mother liquor by wash liquor
- Reconversion of particle cake into slurry to remove impurities from the particle cake
- 5 6 Repetition as often as necessary



### STEP 4:

# **ELUTION OF TARGET PROTEIN**

- Capture of particles and displacement of wash liquor by elution liquor until the process chamber is filled with 100% elution liquor
- 8 Reconversion of particle cake into slurry to elute target proteins from magnetic particles
- Capture of particles and displacement of protein-enriched elution liquor
- 8 9 Repetition as often as necessary



"The ANDRITZ magnetic separator is the next step in chromatographic process intensification and therefore has the potential to revolutionize product purification processes in biotechnology."

PROFESSOR DR. ING. MATTHIAS FRANZREB

Inventor and expert in biopurification

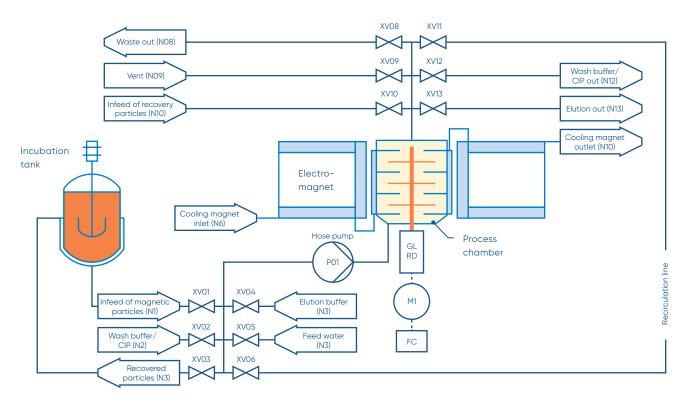


# **Technical data**

Separator type	Process chamber volume [1]	Magnetic field strength [T]	Depth [mm]	Width [mm]	Height	Weight [kg]	Drive [kW]	Power
MES-RS 100	1	0.2	750	1,400	1,800	750	1	3.6
MES-RS 1000	10	0.2	1,000	1,800	1,800	1,500	3	15

All technical data are approximate and subject to change without notice.

# Piping and instrumentation



The piping and instrumentation diagram (P&ID) shows the setup of the MES-RS process skid. Depending on the process, the built-in actuators are used to carry out the process steps necessary for the purification process.

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