



Bioprocessing & Bioreactors

Reliability and Reproducibility in Mass Flow Control



Bronkhorst,

YOUR Partner for Bioprocessing and
Bioreactor Applications



Why Bronkhorst?

- ◆ Worldwide representation and service at factory level
- ◆ Widest product portfolio for low flows of gases and liquids
- ◆ Fulfilling bioreactor application requirements
- ◆ Stainless Steel SS316L wetted parts and FDA/USP elastomer sealing
- ◆ Highest accuracy in the market ($\pm 0,5\%$ of Reading plus $\pm 0,1\%$ of Full Scale)
- ◆ Widest range of communication interfaces available for MFMs/MFCs on the market
- ◆ Standard and customised instruments to meet customer requirements
- ◆ More than 40 years of experience in bioprocessing & bioreactor applications



We understand bioreactors

We provide well-built solutions for bioreactor gas and liquid. Bronkhorst's flow instruments are suitable for benchtop and industrial bioreactors. They are accurate, robust, reliable, and compact. As tailored manifold solutions or open frame installations, they can also be integrated into your equipment. Long-term relationships with major and innovative biotechnology equipment manufacturers have demonstrated that our mass flow controllers are well suited for the job and have strengthened our portfolio with market-specific modifications.

Bioreactors are used to produce bioethanol and other biofuels, pharmaceuticals, fine chemicals, vitamins, vaccines, colorants etc. Because accurate dosing of air, nitrogen, oxygen, and carbon dioxide into microbial and cell cultures is critical, the keywords are accuracy and reproducibility.

In this market brochure, we would like to show some of these applications and the solutions that our instruments can provide.

> Examples of applications

Bioreactor gas dosing

- ◆ Gas dosing for bacterial, yeast and mammalian cell growth
- ◆ Flow control in pharmaceutical biotechnology
- ◆ Controlled CO₂ supply for algae growth
- ◆ Gas mixing setup to calibrate oxygen sensor for monitoring beer quality

Bioreactor liquid dosing

- ◆ Nutrient dosing
- ◆ Buffer solution dosing
- ◆ Reagent dosing



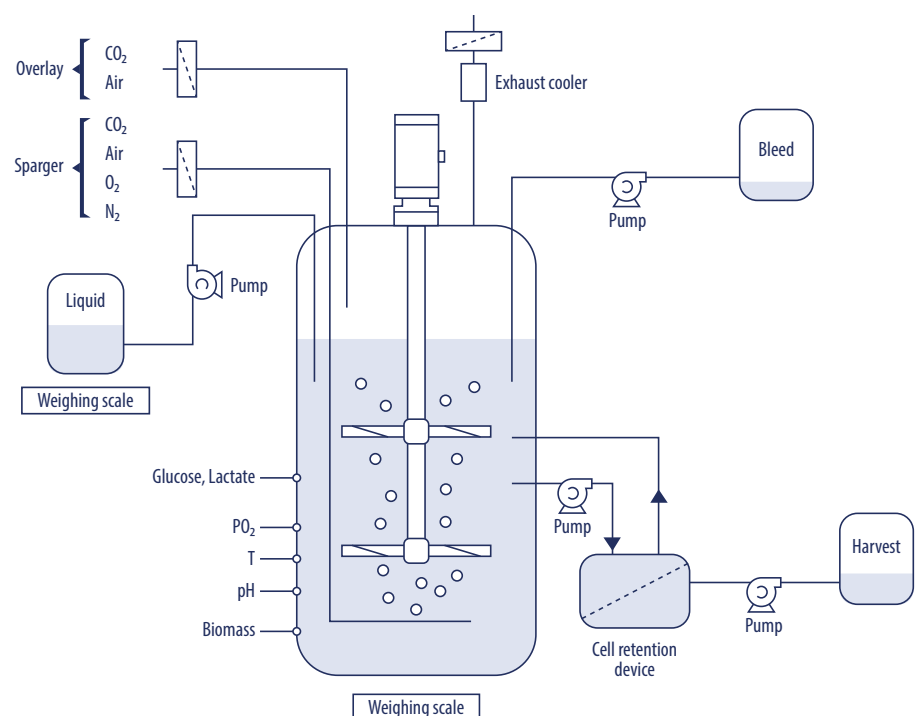


Reliable and reproducible gas control

Air, O₂, N₂, and CO₂ are the four most commonly used gases for gassing bioreactors. Bacteria and cells are grown using air and oxygen. Typically, N₂ is used to calibrate the pO₂ sensor and reduce the O₂ content. CO₂ is commonly used to control the pH value in the liquid phase.

To be able to deliver high-quality biological products over time, optimal conditions inside a bioreactor are required. These conditions can only be maintained if the corresponding process is made reliable and reproducible. Bronkhorst instruments are among the most accurate instruments in the market. The physical reliability can be expressed as a MTBF number, which is 130 years. Moreover, the digital parameters of our instruments can provide the user with diagnostic information on the status of the process and of the meters or controllers themselves.

How the gassing of a bioreactor works:





APPLICATION

Gas dosing for bioreactors

Bacteria are the workhorses of biotechnology, where they are used to create chemically, pharmaceutically, or biologically active substances such as drugs, vaccines and other complex organic molecules. Bacteria have long been used in the production of fermented foods and beverages such as yoghurt and wine. Bacterial habitats are created in bioreactors where bacteria can grow in a controlled environment by conditioning the temperature, gas and liquid concentrations, and pH value.

➤ Application requirements

Accurate and reproducible dosing of gases such as oxygen or carbon dioxide to bioreactors is essential to control bacterial growth rate. Moreover, for easy scaling-up, a full range of dosing equipment is available, and be mutually interchangeable.

A reproducible and reliable gas flow is crucial for a safe operation of bioreactors.

BIOREACTOR MASS FLOW CONTROLLER FEATURES (depending on model and flow range)	DESCRIPTION
USP CLASS VI for FDA compliance	Biocompatibility of used sealing materials
ADI-free	All sealing materials are free of Animal Derived Ingredients
Wetted parts	Stainless Steel 316L (or equivalent)
EN10204 3.1 material certificate	Inspection certificates of material laboratory analyses of all machined wetted parts
Degreased instrument	For use with Oxygen enriched media
Surface roughness	Ra 0.8 µm (micro meter)
Dynamic range	Dynamic range up to 1 : 200
Compact Flow Controller series (IP40)	IQ-FLOW, FLEXI-FLOW and MANI-FLOW for compact bioreactor applications
General purpose Flow Controller series (IP40)	EL-FLOW Select/Base and FLOW-SMS for broad range of bioreactor applications
Industrial Flow Controller series (IP65)	IN-FLOW and MASS-STREAM for industrial set-ups and open frame installations
Process connections	Compression type, Face seal, Tri-clamp DIN32676 (serie B)
Multi-Gas functionality	Up to 8 flow curves, for example Air, N ₂ , O ₂ and CO ₂
Calibration on actual gas or with conversion model	Both methods available for optimization of process and economical aspects
Calibration certificate	Documented accuracy and repeatability of the instrument
Mean Time Between Failure (MTBF)	130 years



Industrial (IP65) Thermal Mass Flow Meters for Gases



APPLICATION

Liquid flow control for optimising growth of microorganisms

Mammalian cells and microorganisms are being used more than ever before to produce pharmaceuticals and (bio)chemicals. Microorganisms in a bioreactor need liquid nutrients, buffer solutions and reagents. Precise flow control of these liquids ensures consistent growth and controllable results.

In case researchers in institutes or industry want to know what conditions cause biological cells to grow faster or slower, flow control of liquid nutrients or other additives can be used to optimise the cell growth.

➤ Application requirements

Many types of nutrients, buffer solutions and reagents are involved to create an optimal environment for microorganisms. Therefore, a wide liquid compatibility of instrumentation is needed. Also, liquid-independent measurement and control of mass or volume are necessary. Since small and large liquid doses could be needed in different situations, a large dynamic range of dosing equipment is much desired. Bronkhorst instruments mini-CORI-FLOW and ES-FLOW are dedicated to provide these requirements and offer compact alternatives for weighing scales. ES-FLOW is specifically suitable for several cleaning methods.



ES-FLOW™ ES-1031
Ultrasonic flow meter for low flow rates



MINI CORI-FLOW™ M13V141
Low Flow Coriolis Mass Flow Controller for Liquids and Gases



SMART maintenance and diagnostics for bioreactors

Bronkhorst digital Mass Flow Controllers and Meters provide a variety of parameters for enhanced measurement, control, and diagnostics functionality that is useful in bioreactors. The internal microcontroller primarily supports the device's flow measurement and control functions, as well as digital or analog communication. Additional parameters are implemented for diagnostic purposes, such as use with bioreactors. Bronkhorst instrument parameters can provide useful information for effective integration into maintenance systems, achieving optimal reliability, and minimising downtime.

➤ Smart Functions of our gas and liquid instruments:

- ◆ **Response Alarm:** together with a variably adjustable timer (max. value of 255 s), this alarm reliably indicates whether the specified setpoint is reached within the pre-set time
- ◆ **Timer:** with a variably adjustable timer (max. value of 255 s), this alarm reliably indicates whether the specified setpoint is reached within the pre-set time
- ◆ **Measure:** indicates the actual value of the flow
- ◆ **Set Point:** if the set point specified by the higher-level control was read in and accepted by the device at all
- ◆ **Valve Output:** (= coil current) allows a conclusion to be drawn about contamination
- ◆ **Power-Up Alarm Message:** can detect an unforeseen and time-critical drop in the power supply
- ◆ **Hardware alarm and error messages:** a possible malfunction of the device is signalled, which can be used on the plant side for corresponding further alarm messages or specific actions by the plant control
- ◆ **Operation Hours:** indicates the total number of hours that an MFC has been energised since it was first started up
- ◆ **Calibration Date:** is the date of the last calibration of the respective instrument



Artist impression of a customised, multi-channel flow solution

Leader in low-flow measurement and control technology

Bronkhorst High-Tech is leading in the field low flow fluidics handling technology. We offer an extensive product range of thermal, Coriolis and ultrasonic flow meters and controllers for low flow rates of gases and liquids. Our flow instruments are used for a variety of applications in laboratory, machinery, industrial and hazardous areas. By sharing our knowledge and closely cooperating with OEM customers, we develop customer specific low flow solutions, e.g. of multifunctional, pretested modules or skids for gas, liquid or vapour flow control. With our headquarters based in Ruurlo (NL), Bronkhorst is represented by 12 wholly owned subsidiaries in Europe, in the USA and in Asia and additionally by a network of distributors in more than 30 countries worldwide.

> Customer first

In addition to the extensive standard product range, Bronkhorst collaborates with customers to develop the best customized process measurement and flow control solution. Our global perspective, but with local focus, ensures that our international distributor network is able to provide on-site support and discuss the best solution to any given application. This ethos also includes product adjustments to ensure that the finer details of your application will always be met with a bespoke solution if necessary.



> Facts & figures

- ◆ More than 40 years experience in Mass Flow & Pressure
- ◆ More than 1.000.000 instruments in the field
- ◆ Approx. 600 employees at headquarters in the Netherlands
- ◆ 12 branch offices; approx. 200 employees
- ◆ Representation in >40 countries; >20 factory level service offices
- ◆ 20% of employees active in R&D and development
- ◆ Cleanroom according to ISO 14644-1 Class 6 with Class 5 flow benches
- ◆ ISO 9001 and ISO 14001 certified
- ◆ Bronkhorst Calibration Center, ISO 17025:2017

> Worldwide support

Support can be offered from many different locations around the globe. You can find our nearest distributor/service office on our web page www.bronkhorst.com/distributors

For urgent matters, our International Support Team is available 24/7 to answer your request immediately or ensure appropriate further action. Just call: +31 859 02 1866



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