HOW TO USE THE BIONET GAS MODULE ON AN F0/F1 OPTIMALLY FOR MY PROCESS?

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For the controlled production of microorganisms or living systems, gasification needs are always a critical part of the process regardless of its phase and its configuration can be challenging.
Versatility and reliability are essential, on the one hand to find the conditions that optimize the process and on the other hand to reproduce the conditions entered from the software interface. Bionet is aware of this, so a gas module has been developed that gives the end user the flexibility to choose the lines needed for the process (up to 5 lines), as well as the possibility to incorporate extra lines in the future, providing expandability to the equipment and the process.
For more details on the configuration possibilities, depending on whether you have Rosita 1.12 or Rosita 2.0 software a Bionet Bench-top bioreactor, we recommend that you take a look at details that matter "The new configurable and expandable gas module of our F0-baby and F1 benchtop bioreactors will unlock the potential of your bioprocess"

HOW MANY GASES DO I NEED FOR MY PROCESS?

Depending on the process type it can vary from one to multiple gases, in some basic processes with a low requirement of gases in which only air is used via sparger, to high demanding processes where multiple gases or low gas flow rates are required, as well as, the combination of sparger and overlay supply. In this case, the **Bionet gas module** allows for the supply of Air, O_2, CO_2, and N_2, and a total combination of 5 mass flow controllers.

HOW AM I GOING TO INTRODUCE THESE GASES THROUGH THE BIOREACTOR VIA SPARGER AND/OR VIA OVERLAY?

The most common way to supply gases to the bioreactor is through a sparger, that would bubble the air from the vessel bottom. For mammalian cells, overlay is commonly combined with sparger aeration as the oxygen mass transfer is not as efficient as in microbial cultures, this is due to lower agitation speed to avoid shear stress (which reduces the % of dissolved oxygen), the larger size of the cells, etc.

WHAT FLOW RATE DO I NEED FOR EACH GAS?

The flow rate of gas into the bioreactor is another important factor to consider. The flow rate affects the mixing of the culture, and the transfer of oxygen and nutrients to the microorganisms, and even the foam formation. Despite the gasses related to the O_2 consumption, there are other critical gas like the CO_2 which is used for pH control due to its acidifying effect.

The supplied flow of each gas depends mainly on the working volume, the cell type, and the bioreactor inlet (sparger or overlay).

The table 1 summarize the gas requirements of microbial and cell cultures systems. *CITATION Bri08 \l 3082* (Brian McNeil and Linda M. Harvey, 2008)

	Cell culture	Microbial culture	Cell culture	Microbial culture
Gas	Sparging		Overlay	
Air	0.1 vvm	1-2 vvm	0.1 vvm	10% of the air to sparger
0_2	10% of air	20-30% of air	NA	NA
CO_2	10-25% of air	20-30% of air	10% of the air to sparger	NA
N2	10-25% of air	20-30% of air	NA	NA

Table 1: General guide as to the gas requirements of both microbial and cell cultures

HOW CAN I AVOID CONTAMINATION AT THE GAS INLET?

The gases supplied to the bioreactor must be free of airborne microorganisms, so the lines must be supplied with sterilizable 0.22 µm filters.

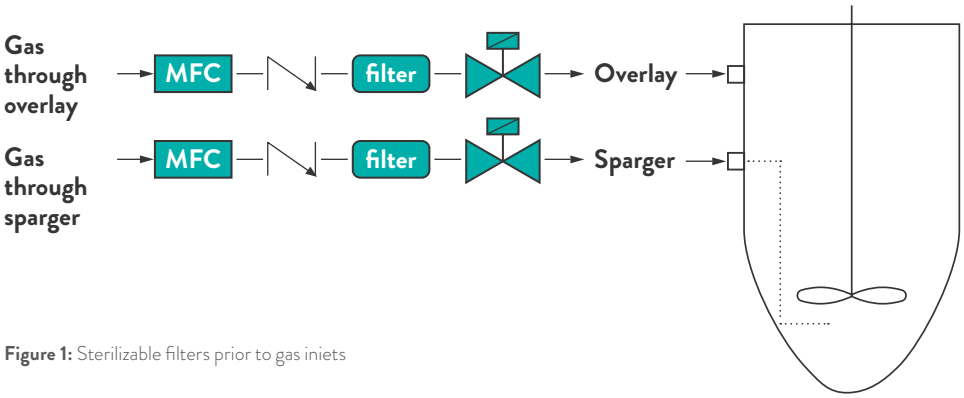

Figure 1: Sterilizable filters prior to gas iniets

SOME EXAMPLES OF THE GAS MODULE ACCORDING TO THE TYPE OF PROCESS

Aerobic processes

In aerobic processes, only air is generally used to supply oxygen, and together with agitation, oxygen saturation is maintained at optimum values. In some processes with high O_2 consumption demand, the air is enriched with pure O_2, and if the SW allows it, the O_2 enrichment mixture from the gas module is automatically regulated according to the needs of the culture. In many processes, applying this strategy will depend on economically evaluating the process and its impact on the final product specifications due to the high cost of pure O_2.

In microbial cultures the supply of gases is done by bubbling through the sparger, only in some cases or special stages of the process such as maintaining positive pressure without bubbling, requires the supply of gases through the overlay (Fig. 2).

Anaerobic processes

Processes with low oxygen consumption requirements, such as microaerophilic cultures, or strictly anaerobic processes, require the use of air and nitrogen mixtures or directly only nitrogen.

Due to the high cost of nitrogen, its consumption can be optimised by regulating its supply according to the O_2 control in cascade with the SW on the gas module, if this is allowed as in the case of ROSITA (Fig. 3). Many strictly anaerobic processes provide nitrogen to displace dissolved O_2, and then turn off the nitrogen supply once optimal conditions are reached.

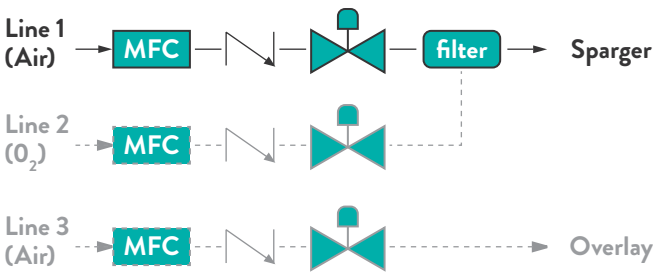

Figure 2: Common gas configuration for an aerobic microbiological process

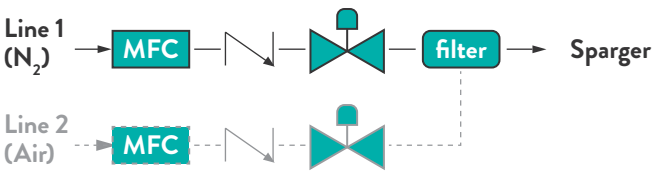

Figure 3: Common gas configuration for an anaerobic microbiological process

Mammalian Cell Processes

In mammalian cells culture, there are several special needs in terms of gasses which requires a special configuration in the gas module (Fig. 4). The oxygen transfer is not as efficient as in microbiological cultures, due to the cells need gentle agitation which decreases oxygen transfer. To improve oxygen transfer and ensure to cover the oxygen demand, a gas supply strategy is needed that involves air and oxygen inlet by sparger and/or overlay, under the O_2 enrichment strategy as previously commented.

Other difference between the requirements of a microbial culture comparing to a cell culture using mammalian cells, is the pH control in these cultures, using CO_2 for acidification instead liquid solutions.

Usually, the products obtained by cell culture are high value-added products (monoclonal antibodies, cellular tissues, etc.), so even though the gas strategy involves a higher cost, these requirements and their cost are economically justified.

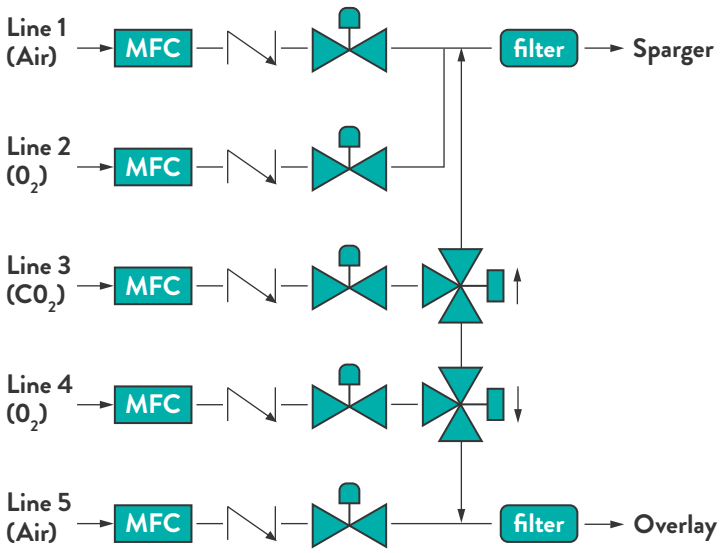

Figure 4: Common gas configuration for a cell culture process

REFERENCES

Brian McNeil and Linda M. Harvey. (2008). *Practical Fermentation Technology*. John Wiley & Sons Ltd.