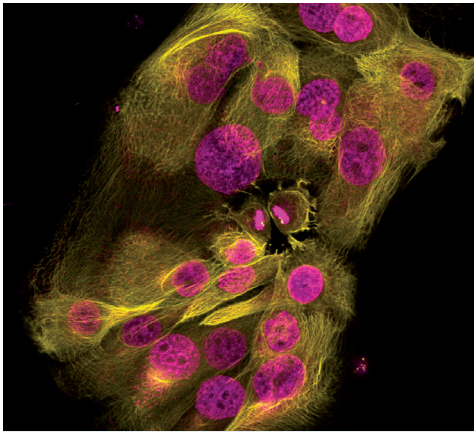


# Accurate flow control for cancer research



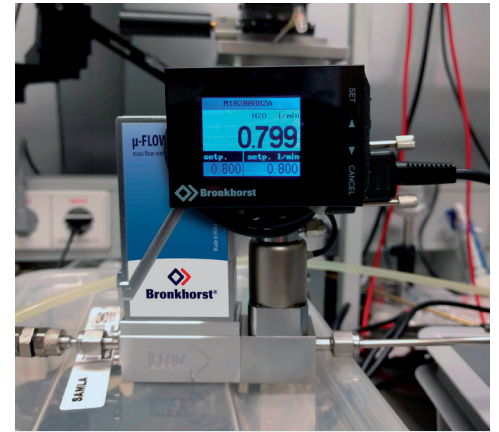
Application note A082-ME09-1017A



Living cells under the microscope. In yellow, the cytoskeleton is labeled with Yellow Fluorescent Protein; in cyan, the DNA is visualized. Note the dividing cell in the middle right of the image.  
(Photo Jalink Group / NKI, Amsterdam)

In basic cancer research, a main aim is to unravel differences between normal cells and cancer cells in order to exploit these differences in the hunt for specific cancer vulnerabilities, so that ways can be found to attack cancer cells while leaving normal cells unaffected.

Since living cells reveal much more information than dead ones, at the Netherlands Cancer Institute (NKI) advanced microscopy techniques are used to extract information about proteins and their interactions in single living cancer cells. To investigate these living cells in their 'natural habitat', Bronkhorst was asked to deliver devices for supplying water vapour and gases such as nitrogen, oxygen and carbon dioxide to mimic the conditions in our body.



Living cell microscopy setup with Bronkhorst devices incorporated

## Application requirements

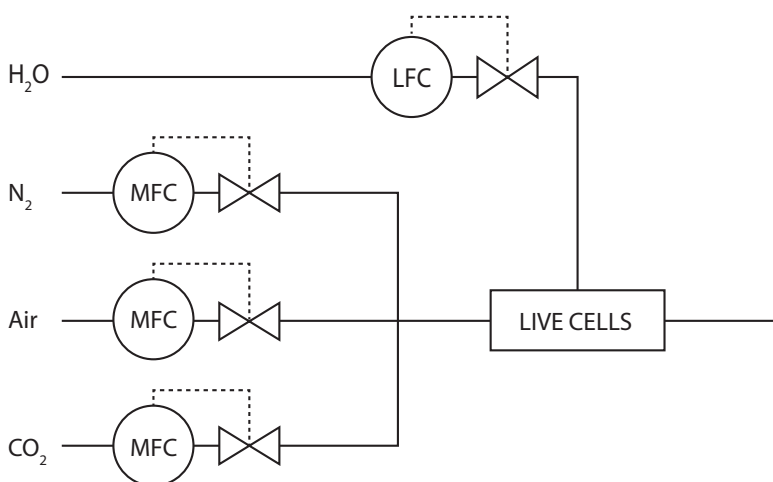
A dedicated incubator needs to be established that houses the living cells and that 'keeps them alive' under conditions that resemble the various oxygen tensions and other conditions encountered in the human body, while being able to be observed by the microscope.

To this end, the moisturised atmosphere in the incubator needs to be controlled accurately at a temperature of 37 °C and should contain at least 5% CO<sub>2</sub>. The oxygen content must be adjusted between 2% and 20%.

### Important topics

- ◆ Accurate gas flow control for O<sub>2</sub>, N<sub>2</sub> and CO<sub>2</sub>
- ◆ Accurate water vapour control
- ◆ Low on maintenance

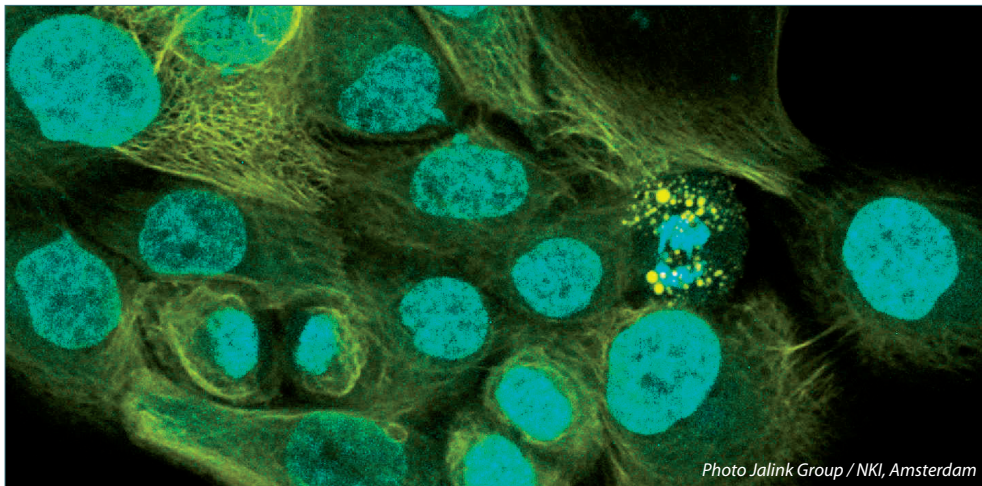
## Process solution



Flow scheme

Bronkhorst delivered three EL-FLOW Select mass flow controllers with read-out units for the controlled supply of air, nitrogen and carbon dioxide gases. By adjusting the relative flows of these gases, an atmosphere was created that contained 2-19 % O<sub>2</sub>, 0-20 % CO<sub>2</sub> and 80-100% N<sub>2</sub>. This range of gases was used in the incubator to investigate the behaviour of cancer cells, for example to investigate how cancer cells migrate during metastasis or to explore how cells use chemical signals to communicate with each other. Investigations at low oxygen content are especially relevant, as solid tumours are well known to be hypoxic - i.e. they contain less than a few % of oxygen - and this completely alters the physiology of the cells, as well as their response to anti-cancer drugs. All experiments conducted under these controlled conditions showed consistent results. An artefact of the relatively high operational temperature of 37 °C was that the DMEM medium, a salt solution used for supporting the growth of the living cells, evaporated rather fast. To replenish the evaporated water from the medium, a Bronkhorst μ-FLOW mass flow controller for liquids was used to supply a very stable flow of deionised water. Combined with a local BRIGHT controller with PiPS (Plug-in Power Supply), the μ-FLOW device supplied a controlled water flow ....

... between 0.5 and 9.6 microliter per minute. Empirically, the Netherlands Cancer Institute found that a value of 1.3  $\mu\text{l}/\text{min}$  completely compensated for evaporation. Since then, they have been capable of keeping cells alive for weeks while observing them by microscopy. Using this configuration, the relative humidity was kept below 60%, which was necessary to avoid condensation that might damage the sensitive electronics in the setup. ■



## Recommended Products



### EL-FLOW Select

EL-FLOW Select Series Mass Flow Meters/Controllers are thermal mass flow meters of modular construction with a 'laboratory style' pc-board housing. Control valves can either be integrally or separately mounted, to measure and control gas flows from lowest range 0,014...0,7 mln/min up to highest range 8...1670 ln/min.

- ◆ High accuracy (standard 0,5% Rd plus 0,1% FS)
- ◆ Rangeability in digital mode up to 1:187,5
- ◆ Fast response (down to 500 msec), excellent repeatability
- ◆ Optional Multi-Gas / Multi-Range functionality: freely programmable ranges and gas types
- ◆ Pressure ratings 64 / 100 bar (Multi-Gas / Multi-Range functionality up to 10 bar)
- ◆ Compact, modular construction



### µ-FLOW

Liquid Mass Flow Meters (LFM's) and Liquid Flow Controllers (LFC's) based on the thermal measuring principle for ultra-low flow ranges. With analog and digital output. Laboratory style housing and metal sealed sensor construction; control valves elastomer sealed. Flow ranges from 0-100 mg/h up to 0-2 g/h water-equivalent.

- ◆ No moving parts
- ◆ Thru-flow measurement
- ◆ Attitude insensitive
- ◆ Negligible dead-volume (sensor: 1,5...33  $\mu\text{l}$ )
- ◆ Fast and accurate measurement
- ◆ Stainless steel sensor
- ◆ Analog or digital: RS232, PROFIBUS DP, DeviceNet™, Modbus or FLOW-BUS



### E-8000

Bronkhorst offers Power Supply / Readout and Control Modules for use with digital Mass Flow Meters / Controllers, Pressure Meters/ Controllers and other transmitters and transducers with RS-232 communication. The E-8000 Series have one or two colour TFT displays per module for indication of measured/totalised values and a push button menu.

- ◆ Bright, wide angle, 1.8" display (TFT technology)
- ◆ User friendly operation
- ◆ Programmable alarm functions
- ◆ Fluid selection (up to 8 fluids/curves)
- ◆ Indication/operation/configuration of measured value, setpoint, totalised flow, fluid/tag number, control characteristics, fieldbus settings



- ◆ Bright, wide-angle, 1.8" display
- ◆ User friendly operation with 4 push buttons
- ◆ Programmable alarm functions
- ◆ Fluid selection (up to 8 fluids/curves)
- ◆ Multi-Gas / Multi-Range functionality
- ◆ Pressure ratings 64 / 100 bar
- ◆ Analog I/O-signals, RS232-connection; optional on-board fieldbus interface)

## Contact information



Accurate flow control  
for cancer research

A082-ME09-1017A

ME: Medical  
09: Other Medical Applications

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