Electronics Case Study Article
Exclusive to *Sensors* Magazine

Supplying Space to Grow: Advanced Flow Sensor Takes Off in Bioreactor

Since the launch of the space program it has been found that biological cell functions can be altered by long-term exposure to a zero gravity environment. Because this has important implications for biotechnological research, the European Space Agency (ESA) has conducted a series of microgravity experiments to study the ups and downs of life in space.

In order to cultivate yeast cells for study, a miniature bioreactor was developed for the second international microgravity laboratory (IML-2) mission in July 1994. This particular project was intended to evaluate the effects of mixing and stirring on cell biology. The research was carried out aboard Spacelab, a pressurized laboratory designed to be transported in the cargo bay of U.S. National Aeronautics and Space Administration (NASA) Space Shuttles.

The bioreactor, which consists of a cultivation chamber, a regulation unit and fluid reservoirs, provides a stable and controlled environment to permit a continuous supply of fresh cells for experiments. It was designed to perform complex fluid control operations, yet it was required to fit in a container measuring only 63 x 63 x 87 millimeters, according to bioreactor designer Mecanex SA in Nyon, Switzerland.

Mecanex SA managed the bioreactor development in conjunction with Space Biology Group at the Swiss Institute of Technology in Zurich, responsible for functional and biological testing. The system concept was devised by the Institute of Microtechnology (IMT) at the University of Neuchatel, Switzerland, designer of the microfabricated components and electronics.

During the nine-day trip through space, the bioreactor supplied fresh nutrient solution to cells in the 3-milliliter cultivation chamber at an adjustable rate between 0.2 and 1.5 milliliters per hour, using a silicon piezoelectric micropump developed by IMT. The device also was equipped with electrodes to regulate the pH of the yeast culture. Measurements of the temperature, pH and redox potential of the culture were taken by a sensor and transmitted via on-line data transfer to ground control.

Once the technical feasibility of the bioreactor design had been proven it was further improved and launched a second time in the Shuttle-to-Mir mission S/MM-03, which was conducted aboard the Space Shuttle Atlantis in March 1996.

A Fluid Delivery

Although the bioreactor was relatively successful during its first flight, delivery of the nutrient solution was affected by the presence of air bubbles and variations in the chamber pressure. To ensure smooth operation during the reflight, a pump filter and controlled flow systems were added to the design. The flow system, made up of a sensor and accompanying electronics, measures the pressure difference from one end of a flow restriction channel to the other. In this way the exact fluid volume is determined, thereby allowing greater control of the micropump flow rate.

Production of the device began with two silicon piezoresistive pressure sensors produced by Micronas in Bevaix, Switzerland. To form the flow sensor, the sensor dice were mounted on a ceramic substrate with a flow restriction channel integrated between them. Holes were then laser-drilled in the substrate to allow fluid connections to the channel. This sensor was designed jointly by Micronas; IMT; and Microflow Engineering SA, an engineering company located in Neuchatel.

According to Marc Boillat, a scientific staff member for IMT, the output volume is a linear function of the difference in pressure from one end of the flow channel to the other, which is dependent on channel geometry and viscosity of the liquid. Because viscosity is largely determined by temperature, the piezoresistors of the pressure sensors also operate as temperature sensors, allowing on-chip measurement of the fluid temperature. This allows the systems to adjust flow rates in order to compensate for changes in viscosity, maintaining precise delivery despite temperature variations.

"The excellent stability and low drift of the pressure sensors allows a direct calculation of the two pressure outputs to obtain the flow signal," notes Boillat. He adds that there is little risk of sensor degradation because only the underside of the sensors is exposed to the nutrient solution.

Mission Accomplished

Evaluation of the cultivation experiment has shown that mixing of the culture does indeed influence the growth of yeast cells in microgravity. Technically, the bioreactor performed very well and the controlled flow system improved the instrument's reliability, according to project leader Space Biology Group.

The short response time of the sensor -- less than 2 milliseconds -- provides minute dosing capabilities with a resolution of 0.1 microliters. In addition to this project, the accuracy, stability and speed demonstrated by this flow sensor design make it suitable for use in various chemical analysis and medical applications.

With the completion of this miniature bioreactor project, it is apparent that such advanced electronic systems play an important role in biotechnological research, both on Earth and beyond. And thanks to the support of agencies such as NASA and ESA'S PRODEX program, similar research and development programs will continue to fly.

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