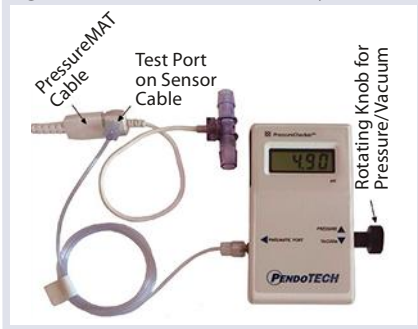


Figure 5: PressureChecker assembly



conversions. The PressureMAT system serves as a voltage source and processes the output signal from the sensor into a pressure reading. It is therefore required as an intermediate device to integrate the sensors into a control system for building a feedback control loop. Once the sensors are inserted into a flow path, data will be transmitted to the PressureMAT system at intervals as frequent as 1 data point per second. Pressure data can be viewed on the PressureMAT monitor display. Outputs (4–20 mA) from the PressureMAT transmitter can be brought into a data handling system, which facilitates data recording and processing.

A CASE STUDY

We clarified cell culture harvest from a 1,000-L bioreactor using an LAPX404 disc-stack centrifuge from Alfa Laval (www.alfalaval.com), followed by depth filtration using Pod A1HC filters and 0.2- μ m filtration with Express SHC filters, both from Millipore Corporation (www.millipore.com). The cell culture in defined media was harvested after 14 days, showing a viable cell density of 2.96 cells/mL and cell viability of 68%. This process was continuous, with no break tanks in between the steps (Figure 1). Flow rate throughout the clarification train remained constant at 5 L/min. We collected filtrate in 200-L collection containers, each with a 0.2- μ m filter attached. As each collection bag was replaced during culture clarification, the 0.2- μ m filter was also replaced to reduce the number of interruptions in the overall process and reduce potential bioburden or endotoxin contamination of the final filtrate.

Comparing Figures 2 and 4, it's clear that the combined PendoTECH pressure sensor and PressureMAT system are **SUPERIOR** to the analog stainless steel pressure gauges alone. This new approach offers frequent, accurate, and automatic pressure readings that provide a complete picture of depth filter performance. The information assists in process monitoring, process improvement, and trouble-shooting.

Before obtaining the sensors, we set up stainless steel pressure gauges in front of both filters (Figure 2). We recorded pressure readings manually and calculated the pressure differential as the difference between readings from those two gauges. The stability of the pressure differential at a constant flow rate indicates almost no change on the depth filter's performance throughout the process.

To test the pressure sensors and PressureMAT system, we installed half-inch sensors into the flexible tubing directly upstream of both the depth filter and the 0.2- μ m filter without tee connectors. Cell culture was clarified from a 1,000-L bioreactor using the same process train described above. A similar (but not identical) feed stream was used in this particular case study.

Cell culture in defined media was harvested after 16 days, showing a viable cell density of 3.56 cells/mL and viability of 63%. Pressure data were collected using the PendoTECH single-use pressure sensors and PressureMAT system (Figure 3). We took pressure readings (Figure 4),

every 30 seconds during processing. The “valleys” in those pressure readings (about every 50 minutes) represent replacement of a 0.2- μ m filter and a 200-L filtrate collection bag. Small pressure decreases seen at ~7-minute intervals are due to the discharge of solids from the centrifuge bowl. Each time the centrifuge enters a discharge period, the feed flow is stopped until that discharge period ends, so the pressure differential dropped to zero at those times.

Because the pressure differential remained unchanged, we attributed the increase in pressure readings from both filters during the filling of each individual bag to increased fouling of the 0.2- μ m filter. The pressure differential remained constant at ~5 psi for the first 120 minutes of processing, at which point 600 L of cell culture harvest were filtered. At the end, the pressure differential reached 8 psi. Regardless of that minor increase, the pressure differential did not approach the maximum allowable value for this depth filter (20 psi).

A spike in pressure at ~85 minutes was due to a piece of kinked tubing. The PressureMAT monitor's audible alarm, which can be triggered by a predetermined high or low pressure value, alerted the operator to the flow-path obstruction. Without that alarm, it could have gone unnoticed. The alarm set point can also trigger an internal relay that can be easily wired to automate process control by shutting off a pump or opening a valve.

Comparing Figures 3 and 5, it's clear that the combined PendoTECH pressure sensor and PressureMAT system are superior to the analog stainless steel pressure gauges alone. This new approach offers frequent, accurate, and automatic pressure readings that provide a complete picture of depth filter performance. The information assists in process monitoring, process improvement, and trouble-shooting. In addition, the automated pressure monitoring and recording function can free up operators for other tasks, reducing the labor demand of these operations.