

Improve Production Efficiencies and Yields Using Automated On-Line Sampling Systems for Fermentors and Bioreactors



Improving production quality, efficiency, and yield is the objective of every commercial biotechnology process. A key to improving production bioprocesses is found in improved and frequent process monitoring — which means, practically, automation of assay tasks now routinely performed manually. The FDA supports and encourages this activity with the formation and development of the PAT (process analytical technology) initiative within the FDA regulatory structure. The features and benefits of the on-line series of automated reactor sampling (ARS) systems supplied by Groton Biosystems are detailed here.

ON-LINE AUTOMATIC ASSAYS

Today the most vital late-stage and production assay measurements, with the exception of basic temperature, dissolved gases, and pH, continue to be performed using off-line, manually operated laboratory instruments. For example, amino acid analysis, cell viability, and nutrient monitoring are typically performed using traditional off-line instruments. This leads to inevitable delays and potential for human errors in sample handling. The historical nature of these data would be difficult to incorporate in a real-time control loop for the associated system. Real-time sampling and monitoring of the state of the reactor for all vital parameters of the process is necessary to practically achieve the goal to improve production efficiency. The ARS series of automatic on-line sample systems for bioreactors (cell culture and fermentation) has been introduced by Groton Biosystems to fill the need for a programmable, universal sampling interface between the process vessel and all analytical instruments and assay systems associated with and required for control of the bioprocess.

UNIVERSAL INTERFACE

The ARS system is designed to permit programmed, sterile sampling of a bioreactor or fermentor with direct, automatic delivery of the acquired sample to associated analytical instruments or assay devices. These instruments are connected to and are controlled by the ARS. This permits the facility's process monitoring to be performed through continued use of familiar, robust, and validated laboratory instruments while enjoying the productivity benefits of a completely automated

sample interface and instrument control structure. The ARS has been used successfully to monitor both cell culture and fermentation processes. In addition, the ARS system is available in models that scale up from development to production reactors and fermentors. The ARS series is compatible with the standard sample ports found on such vessels. It has been successfully coupled to standard nutrient monitors, HPLC systems (for amino acid analysis), ion-chromatography systems, and fraction collectors. Interfaces for cell viability counters and other analytical instruments are in development. Multiplexed input reactor ports and output instrument ports permit the ARS to connect a suite of laboratory analytical instruments to a number of reactors to enjoy the advantages of sampling automation throughout the entire installation. Groton supplies complete fluidic, mechanical, and software interfaces for all supported instruments.

STERILE

The benefits, features, and advantages of the ARS would be of little value if reactor and fermentor sterility was not protected during operation. The design of the ARS incorporates a clean-in-place (CIP) module and either chemical sanitation or steam-in-place sterilization or both, depending on the size of the supported reactor and the type of connected analytical instrument(s). The ARS automatically performs a CIP process on all components in contact with the sample after each sample acquisition. In addition the mechanical design of the ARS incorporates a unique reactor isolation module (RVI) comprising a series of automatic, sanitary diaphragm valves to isolate the reactor from the external environment when idle. The RVI is cleaned and sanitized as part of the inter-sample CIP process of the ARS. Results recorded from mammalian and microbial installations using development to pilot plant scale reactors and fermentors at customer sites confirm that the ARS with RVI reactor isolation systems do maintain reactor and/or fermentor sterility while simultaneously permitting completely automatic sample collection and unattended assay instrument operation.

The ARS is an efficient, user friendly, and reliable system to automate bioprocess assay instruments. Reactor sterility is maintained by the ARS CIP system.

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