

# METTLER TOLEDO APPLICATION NOTE

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## pH Control In Fermentation Plants

### BACKGROUND

A typical batch fermentation process starts with sterilization to destroy completely all micro-organisms found in the mash and reactor. The mash is heated in the fermenter or a special cooking vessel by injecting live steam or by means of steam coils set in the vessel. Holding the temperature at 121 °C (250 °F) for 30 minutes is usually adequate to destroy all living organisms in the mash. As shown in Figure 1, a heating/cooling jacket maintains the temperature of the fermenter.

A fermentation cycle can be divided into two phases: the growth phase and the production phase. Initially during the growth phase, cells grow very slowly while adapting to the reactor environment. After the adaptation period, the cell culture grows exponentially, releasing enzymes as a byproduct of the metabolic process. During the production phase, the molecular products are formed through a series of chemical reactions catalyzed by the enzymes. For many fermentation processes, these two phases are concurrent.

### THE PROCESS

pH is one of the most important measurements used to indicate the course of the fermentation process. It detects the presence of specific chemical factors that influence growth, metabolism, and final product.

For example, the pH of commercial mash of *P. chrysogenum* (penicillin production) must be closely monitored and controlled in both the growing phase and the production phase. Early in the growth phase, the pH of the mash is carefully maintained between 4.5 and 5.5, depending on the mash formulation. The range is set to ensure the most favorable condition for growth. The metabolism of glucose and rapid consumption of ammonia during this phase adversely affect the medium by lowering the pH. If the medium is not adjusted, growth may be inhibited and the fermentation may take a long time to reach the optimal range required for penicillin production.

In the production phase, the organism starts to metabolize other sugars (lactose) and amino compounds because of the depletion of glucose. The liberation and accumulation of ammonia from the metabolism of amino compounds will cause the pH to rise slowly. The pH is allowed to rise to about 7 and is controlled at this point until the end of production. Depending on the culture and several other factors, it has been found that the optimum pH range for penicillin production lies between 6.8 and 7.8. The pH is carefully monitored and controlled in this range by the addition of sulfonic acid. Finally, at the end of the fermentation, the pH rises and production stops. Figure 1 depicts the pH control loop implemented on a standard fermenter.

### INSTRUMENTATION

The Mettler Toledo Model 2100 pH/ORP analyzer is well suited for fermentation applications by virtue of its ease of use. In addition, the Model 2100 has SensoCheck<sup>®</sup> for descriptive diagnostic capabilities. Temperature compensation is often not required because many applications operate near pH 7, the isopotential point. In applications where there is a significant change in the measured pH with temperature change, a separate RTD (Pt 1000) can be used to provide a temperature-compensated pH measurement. The pH sensor of choice for fermentation applications is the InPro<sup>®</sup> 3200, which is designed to withstand repeated sterilizations to 130 °C (266 °F) and can be mounted in the InFit<sup>®</sup> 761-25CIP fully sterilizable housing, certified by an independent international institute to meet the highest hygienic standards.

## PRODUCTS

### 2100 pH Analyzer

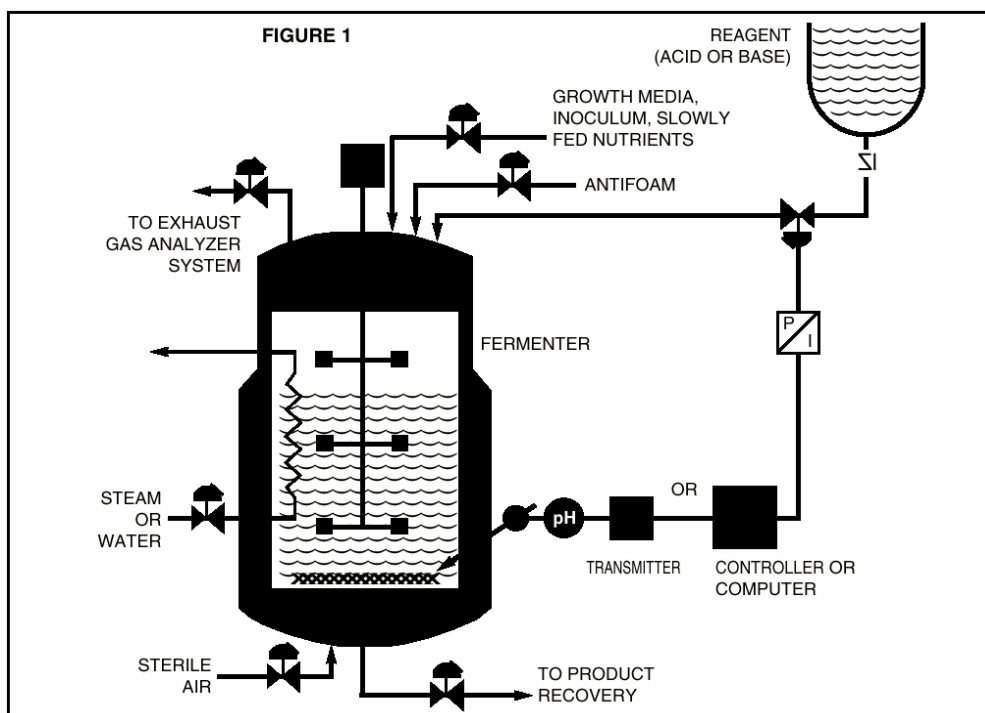
- Detachable front panel and plug-in terminals for ease of installation
- All functions accessible through the keypad for increased ease of use
- Continuous sensor and transmitter diagnostics to monitor performance
- FM certification for Class I, Div 1 & 2 Environments and CSA General Purpose Approval
- 3 year warranty

### InPro® 3200

- Gel electrolyte eliminates fill requirements to reduce maintenance
- Steam-sterilizable & autoclavable for hygienic and CIP/SIP applications
- Meets 3A guidelines and EHEDG Certification to ensure maximum cleanability
- High pressure resistance
- Silver ion trap to minimize electrode contamination
- Integral RTD for higher measurement accuracy
- Rugged IP67 rated quick connect VaioPin connector

### InFit® 761-25CIP Housing

- Steam-sterilizable & autoclavable for hygienic and CIP/SIP applications
- Meets 3-A guidelines and EHEDG Certification to ensure maximum cleanability
- Exclusive o-ring positioning guarantees perfect sealing, permitting full CIP procedures to be performed without any compromise of sterility
- Specially designed smooth surfaces of the housing and o-rings prevent the adherence of microorganisms
- Recommended for use with Mettler-Toledo safety weld-in sockets to provide the highest level of protection for personnel, equipment and the environment



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