

Predictive Diagnostics on pH Reduces the Instances of Lost Process Runs

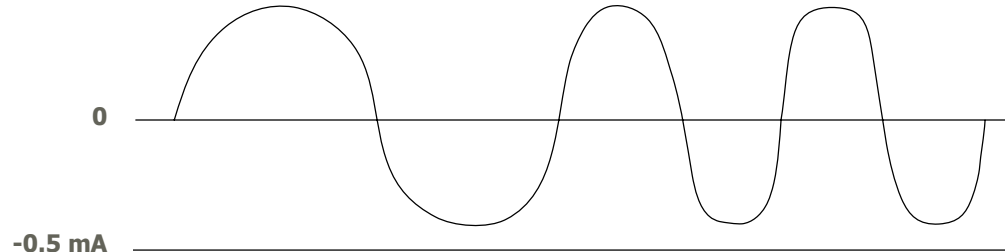
The role of the gel filled pH electrode in today's bioprocess applications is one of utmost importance. To reinforce this point consider that in both research and process development there is at least one pH electrode in-situ to the process regardless of the platform (spinner flask, glass bioreactor, disposable bioreactor, etc.) as well as an off-line chemical analyzer. And as the bioreactors increase in size so does the number of pH electrodes. To the point that a mid-size bioreactor will often have two in-situ pH electrodes, supported by an off-line chemical analyzer and governed by an SOP that makes it absolutely clear that these pH electrodes cannot see more than one steam in place (SIP) cycle. This all might seem a bit "excessive" but consider that a recent study by an industry leading end user found that 65% of all lost process runs could be attributed to in-situ sensors (pH, Dissolved Oxygen, etc.) and excessive can suddenly appear conservative.

Based on the information above it is no wonder that many end users in our industry have made it a point to investigate the potential of technologies such as neural networks and its promise of virtual sensors. However, the real solution may lay with a technology that has been in existence for twenty years and demonstrated time and time again its ability to improve both the accuracy as well as reliability of in-situ process sensors such as pH. That technology is the digital bus platform known as HART and it along with its not too distant cousins Foundation fieldbus, DeviceNet and Profibus are providing our industry with the tools needed to introduce predictive sensor diagnostics on devices as diverse as pH sensors, pressure sensors, thermal mass flow meters and more.

The Highway Addressable Remote Transducer (HART) technology first introduced some twenty years ago is the most cost effective of the digital bus platforms. This platform enables the measurement of up to four process variables; the primary variable and three secondary variables. A unique element of the HART platform is the fact that these process variables (including Temperature if desired) exist on a single 4-20mA output signal from a HART enabled transmitter. This results in up to four measurements on a single two-wire output (Fig 1 below).

HART

+0.5 mA



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As a result of the ability of HART to transmit over an existing single two-wire output it can be easily introduced as a replacement to existing analog pH transmitters.

In bioprocess pH applications the role of HART is especially critical when you consider that the pH range of the industries most common processes is between 6.8 and 7.2. This is particularly significant when you consider that the indicated process measurement of a pH electrode that has experienced a catastrophic pH failure (cracked glass) is a valid process measurement of 7.0. However, with a HART enabled pH transmitter, regardless of whether your sensor is from Mettler-Toledo, Broadley-James or Finesse, you will know if a value of 7.0 is a sensor measurement or a sensor failure.

A HART enabled pH transmitter provides the primary variable (0-14 pH) as well as the secondary variables of Glass Impedance and Reference Impedance (Fig 2 below).

Real Time Predictive Diagnostics

Measurement	Primary Variable	Secondary Variable 1	Secondary Variable 2
pH	0-14	Glass Impedance	Reference Impedance

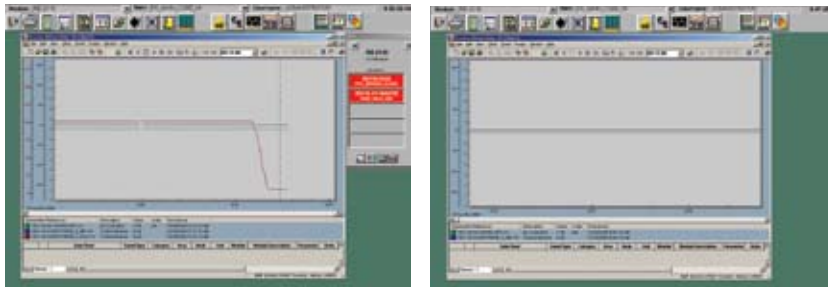
The critical role of these secondary variables in predicting in real time the performance of a pH electrode is as follows:

Glass impedance is measured real time in megohms mohm and changes as the probe ages. The most common gel filled glass pH electrodes have a glass impedance of 25-400 megohms at 25degrees C when new. In bioprocess applications the most significant ageing of the pH electrode occurs not in the process but in the cleaning and sterilization. The practice of autoclaving or steaming a pH electrode at 121 degrees c to 131 degrees C for up to 60 minutes has the effect of doubling the electrodes impedance. The resulting increased glass impedance indicates that a pH measurement is becoming sluggish and thus unable to respond effectively to changing pH environments. At some point the glass impedance will suddenly drop below 4 megohms which indicates a cracked pH electrode. This catastrophic failure will be displayed as a pH value of 7.0 and 0 millivolts, well within the biological pH range of 6.8-7.2.

Reference impedance is measured real time in kohms kohm and changes as the reference becomes fouled by either coating or contamination of the reference junction. This fouling of the reference, indicated by an increasing impedance value, causes pH drift The most common gel filled glass pH electrodes with either a teflon or ceramic reference junction will have a reference impedance of 2-20 kilohms when new.

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These secondary variables can be trended individually and assigned user defined alarms so as to provide both real time indication as well as notification of an event (Fig 3 below)

**TruBio™ OS****Others**

A catastrophic pH electrode failure is indicated by a trend of 7.0 (0 mV). Without HART technology this failure will go unreported and the process run will be lost.

Two additional tools for predictive sensor diagnostics are Slope and Offset. However, these values are not considered real time as they are calculated only after completing a two or three point calibration. It should be noted though that technology has been introduced to enable the implementation of user defined alarms on the slope as well as the offset.

Today digital bus platforms are being used extensively in other heavily regulated industries including but not limited to Petrochemical, Semiconductor and Specialty Chemical. The ability of these digital bus platforms to provide unprecedented insight into the health of critical process sensors such as pH, dissolved oxygen, pressure, temperature and more can provide implementers with significant advantages including but not limited to a dramatic reduction in the instances of lost process runs, improved product quality, increased product yields, improved technology transfer and reduced material costs.

As for their role in our industry, consider this information. The top five pharmaceuticals as well as the top three biotech's have active programs well underway to introduce these technologies into both their development and manufacturing processes.