WHITE PAPER

Evaluation of Non-Process Contact Capacitance Point Level Measurements on the Outside of Hygienic Bubble Traps

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Summary

This white paper evaluates the effectiveness of a non-contacting capacitance level probe for measuring and controlling the point level in a hygienic bubble trap. Unlike process contact technologies, this probe is mounted to the outside of the bubble trap; as a result, it does not make physical contact with the process fluid.

This means there is no need to account for certain regulatory requirements, such as Clean in Place (CIP) and Sterilize in Place (SIP), to preserve the hygienic purification process. We have used the VEGA VEGAPOINT 21® capacitance point level probe on an LJ Star® Hygienic Bubble Trap and found it to be an effective, reliable and scalable method for controlling the point level.

This offers a convenient solution for many downstream biopharmaceutical processes, such as chromatography, that rely on the use of hygienic bubble traps to separate gas bubbles from the fluid phase for an effective operation.

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Introduction

Hygienic bubble traps are used extensively in downstream biopharmaceutical purification processes, such as chromatography, and can be applied to a range of single-use products.

Gas bubbles in process fluid and buffer solutions can affect the operation of the resin bed by impeding flow through the resin column, as well as limiting contact with the resin, meaning a decrease in separation efficiency and resolution.

Bubble traps, therefore, work to separate gas bubbles from the fluid by allowing the bubbles to rise to the top while the fluid remains at the bottom.

Figure 1 – Hygienic Bubble Trap

It is crucial to be able to accurately monitor and control the fluid level in the bubble trap to allow for the efficient separation of the gas bubbles, and this is where a level sensor comes in.

Various technologies have been used to measure the hygienic bubble trap fluid level in biotech processes, each with their own benefits and limitations, but the key difference is whether the sensor is in direct contact with the fluid or gas in the bubble trap, or whether it measures the fluid level through the glass cylinder wall.

This white paper investigates non-process contact point level measurements with electrical capacitance sensors, which are fitted to the outside of the glass cylinder and gauge the level inside the bubble trap using an electric current.

Hygienic Bubble Trap Design

The design and proper operation of bubble traps are essential to avoid bubbles being drawn into the fluid outlet rather than being separated from the process fluid.

The working volume of a bubble trap is typically 60-80% of its total volume, and the fluid should have a residence time of approximately 15 seconds in the bubble trap. This means that if the flow rate of the fluid in a biotech purification system is 4 liters per minute, for example, then the hygienic bubble trap working volume should be sized for 1 liter of fluid at 60-80% capacity.

THE IMPORTANCE OF LEVEL CONTROL

The fluid level is critical to efficiently separate gas bubbles from the fluid. If the level is too low, the buoyant force of the gas bubbles does not have the residence time necessary to rise above the fluid level before being drawn into the bubble trap fluid outlet, so gas bubbles may exit the bubble trap with the fluid.

On the other hand, if the level of the fluid is too high, fluid as well as gas bubbles may be drawn into the gas vent line and may cause issues with cleaning and sterilization (CIP and SIP). This leads to problems with bioburden control and batch to batch contamination.

It is generally not necessary to control the exact level of fluid in the hygienic bubble trap, but to control the level within the range of 60-80% of the maximum height of the bubble trap, as shown in Figure 2. In order to maintain this level, point level sensors can be used to open and close the bubble trap gas vent valve.

Once the fluid level drops below a low level probe, the gas vent valve can be opened on the bubble trap to allow gas to exit and the fluid level to increase. Once the increasing level is sensed at the high level probe, the gas vent valve can be closed.

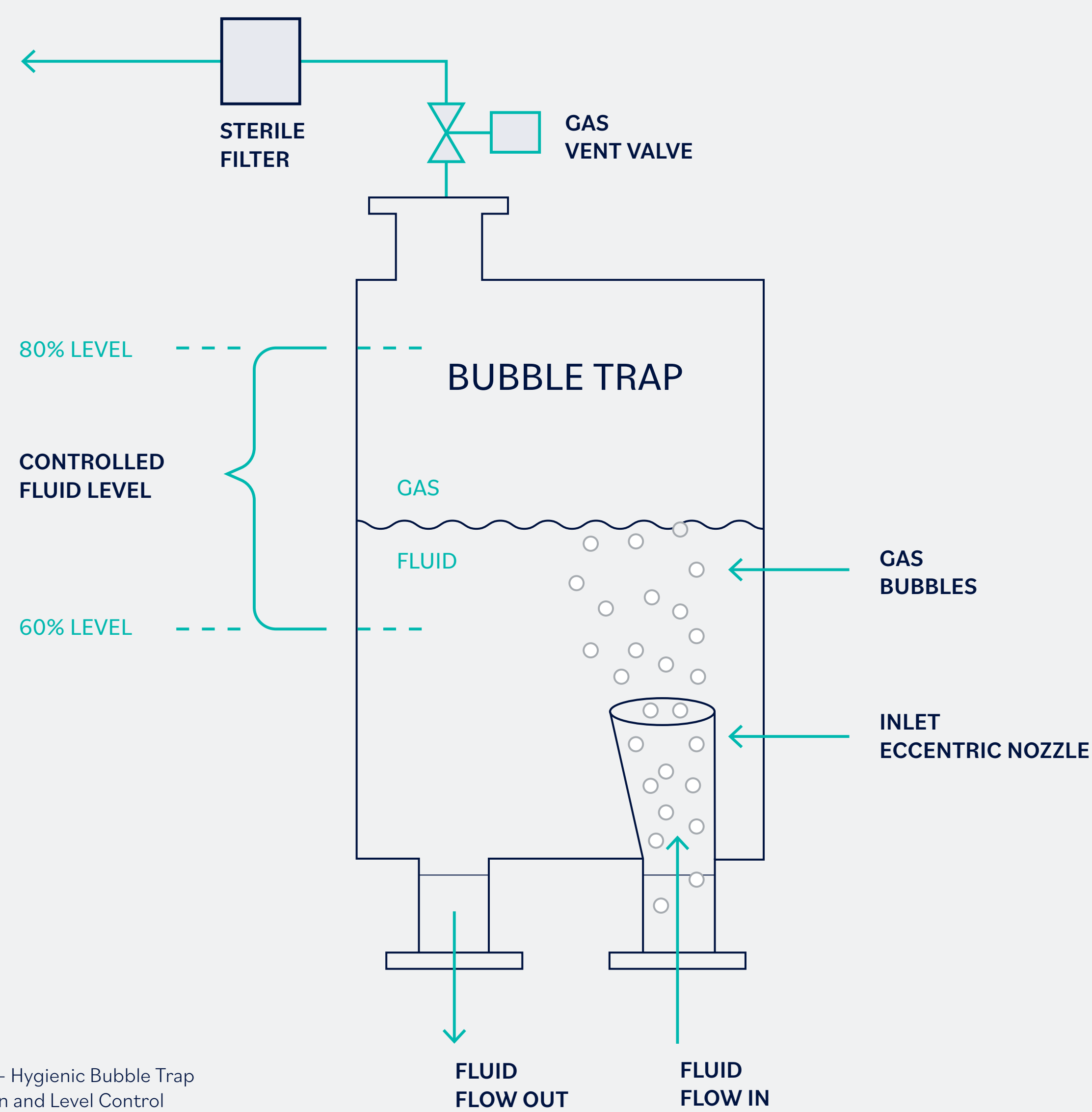


Figure 2 – Hygienic Bubble Trap Operation and Level Control

But why does the level in a hygienic bubble trap vary to begin with?

At the start of the purification process, the process tubing, purification equipment, and bubble trap may be empty. As fluid enters the hygienic bubble trap, the gas vent line valve will be closed and fluid will flow into the inlet of the hygienic bubble trap until there is an equilibrium between the pressure before the bubble trap inlet, the pressure after the bubble trap fluid outlet, and the gas pressure at the top of the bubble trap.

At that equilibrium point, the level will remain constant – fluid flow into the hygienic bubble trap equals fluid flow out. The level will only change if there is an imbalance between inlet pressure, outlet pressure, and gas headspace pressure. If the headspace pressure remains constant, fluid flow IN equals fluid flow OUT and the bubble trap level stays the same.

However, as gas bubbles are separated from the fluid, due to buoyant force, the new fluid level equilibrium point will decrease to a lower level. Fluid level in the bubble trap can then be increased by venting gas through the gas vent filter.

Technologies for Level Control

One option for level control is a continuous level probe, which may be used in a PID control algorithm to modulate the opening/closing of the gas vent control valve, thereby maintaining the level at a specific point as defined by the controller set point.

In almost all applications, though, continuous level sensing and control is overkill. The bubble trap will work properly provided that the fluid level is controlled anywhere between 60% and 80%. Continuous level sensing and control is also substantially more expensive than controlling based on point level (high level and low level operating points).

There are several different types of level sensor technologies that have been developed and utilized in the biotech industry and they can be generally categorized as Process Contact Technologies and Non-Process Contact Technologies.

PROCESS CONTACT TECHNOLOGIES

In process contact technologies, the level sensor is in direct contact with either the fluid or the gas in the bubble trap. The most commonly used process contact technologies to measure fluid level in a hygienic bubble trap have included:

- Conductivity
- Capacitance
- Differential Pressure
- RADAR (Guided Wave or Through Air)

There are advantages and disadvantages to each approach. Since there is physical contact between the sensor and the fluid in a hygienic purification process, all of these types of sensors must meet certain regulatory requirements, including:

- Cleanability
- Sterilizability
- Sensor Wetted Parts Composition
- Sensor Surface Finish
- Hold-Up Volumes
- Sensor Extractables and Leachables
- Sensor Chemical Reactivity with the Purification Process

The risk of using a direct process contact level technology in a hygienic process must be evaluated and taken into account.

NON-PROCESS CONTACT TECHNOLOGIES

Alternatively, there are several non-process contact level sensors that have been successfully used to measure hygienic bubble trap fluid levels. In this case, the sensors gauge the presence or absence of fluid at a certain level through the bubble trap glass cylinder and are, therefore, physically isolated from the hygienic process by the cylinder wall. These non-process contact sensor technologies have included:

- Optical technologies, such as transmission, refraction and reflection of light, and lasers
- Inductive sensors
- Capacitance sensors

Again, each sensor technology has its own benefits and short-comings, but they all share the advantage that they don't have to meet the same regulatory requirements and risk assessments as contact technologies because the sensors do not make physical contact with the hygienic process. This white paper investigates non-process contact point level measurements utilizing electrical capacitance sensors.

Capacitance Level Probe Theory

Capacitance level probes are available from many different instrument suppliers, including VEGA®, Endress+Hauser® and Baumer®. The operating principle is basically the same, with minor modifications made by each manufacturer to the level probe design, electronic circuitry, filtering, and configuration.
These subtle differences can improve measurement, reliability and repeatability in a bubble trap application.

CAPACITANCE LEVEL SENSORS: HOW THEY WORK

A capacitive level sensor consists of two conductive electrodes (plates) to form a sensing capacitor, with insulating (non-conductive or "dielectric") material separating the electrodes. The capacitor stores electrostatic energy in an electric field between the electrodes. As an alternating current is applied to the circuit, the capacitor's ability to store this energy (a measurement known as "capacitance") increases as the volume of fluid between the insulating electrodes increases.

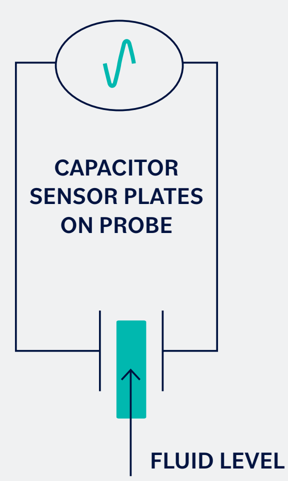


Figure 3 – Capacitance Probe

A capacitance level sensor works by gauging capacitance in reference to the dielectric constant of the material being measured and the voltage being used to complete the circuit. This method of level measurement is sometimes called RF level since Radio Frequencies are applied to the capacitor circuit. The electric circuit for basic continuous capacitance level sensors is shown in **Figure 4**.

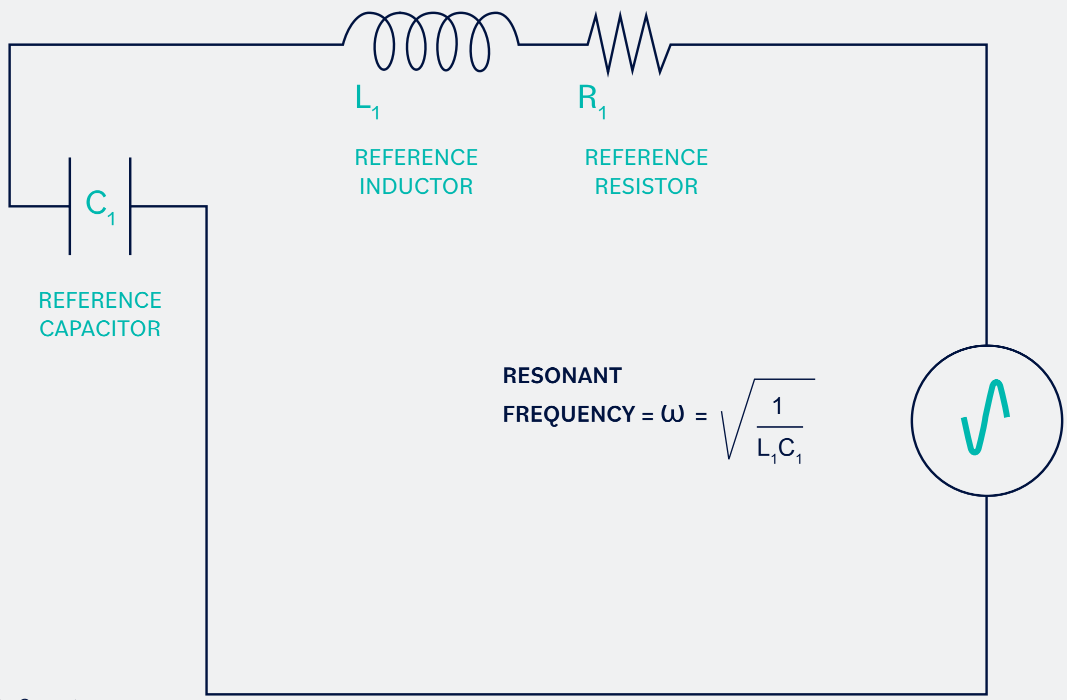


Figure 4 – Basic Capacitance Probe Electrical Circuit

These capacitance measurements can then be used to infer the fluid levels in a vessel. Higher levels of dielectric material result in greater capacitance, meaning the level can be inferred by measuring electrical capacitance.

Similarly, a change in the fluid dielectric properties will also be seen as an apparent change in level, even though the actual physical level remains unchanged. Capacitance level sensors should always be calibrated using a fluid with the approximate same dielectric constant as the process fluid. In the case of point level sensing, the capacitance charge stored between the capacitor electrodes is compared to a set target capacitance, and a switch is activated when the capacitance exceeds this target due to an increase in fluid level.

As noted, a change in the dielectric properties of the process fluid would also affect the apparent measured fluid level, and we will discuss possible ways of overcoming this effect later in this paper.

PROCESS CONTACTING CAPACITANCE LEVEL PROBES

The capacitance level probe electrical circuit was originally designed for the probe to be in contact with the actual process fluid. In hygienic applications, the point level probe is wetted by the process. The electrical circuit takes into account the effects of changing process fluid dielectric, as well as resistance. The electrical diagram of the process fluid contacting point level probe is shown in **Figure 5**.

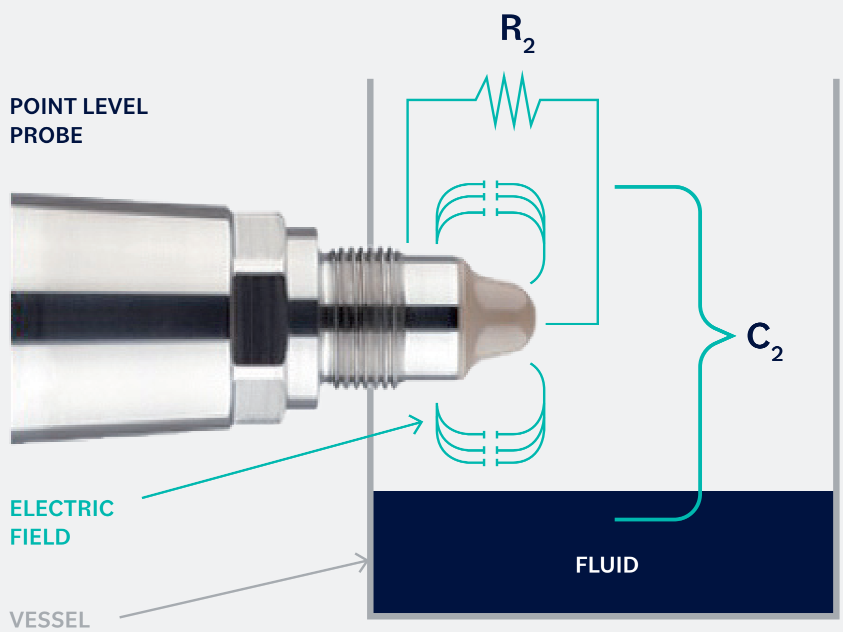


Figure 5 – CONTACTING
Capacitance Level Probe

The electrical circuit for a capacitance point level probe that is in direct contact with the process fluid is shown in **Figure 6**.

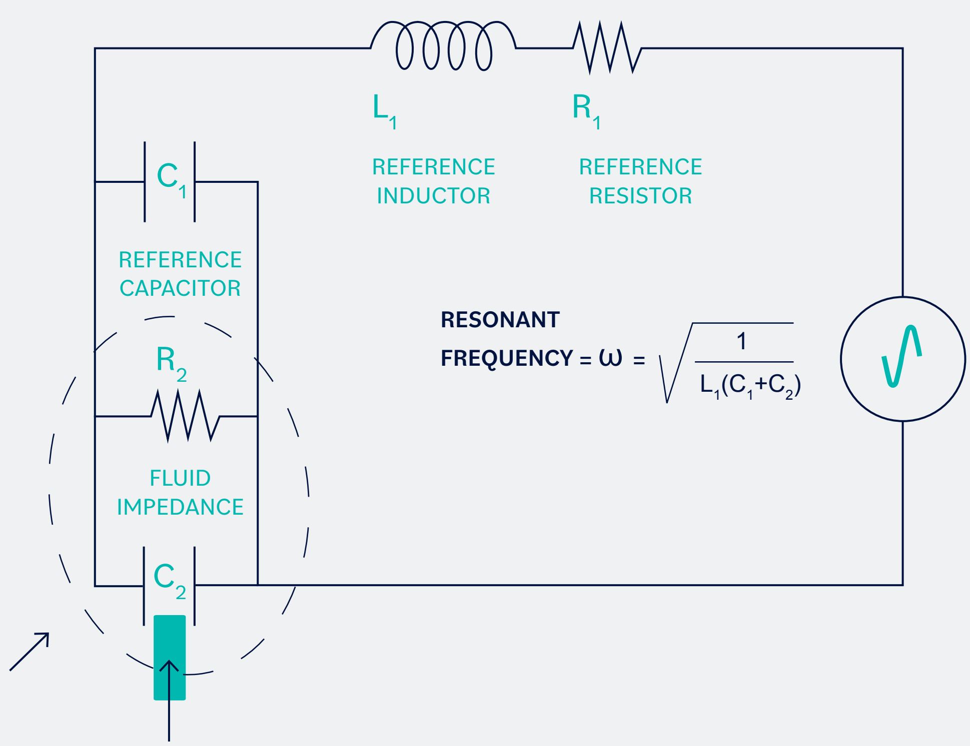


Figure 6 – CONTACTING
Capacitance Level Probe

PROCESS NON-CONTACTING CAPACITANCE LEVEL PROBE

When it comes to non-contact point level sensing, the capacitance level probe is isolated from the process fluid by the glass wall of the hygienic bubble trap so the sensor probe does not make physical contact with the process fluid. However, the electric field generated by the frequency oscillator is able to penetrate low dielectric solids, such as glass and plastics.

Glass is an insulator and has a relatively low dielectric of approximately 5, as well as a very low conductivity (high resistance).

In the hygienic bubble trap point level application, the electric RF field generated by the oscillator circuit penetrates this glass wall insulator, as shown in **Figure 7**.

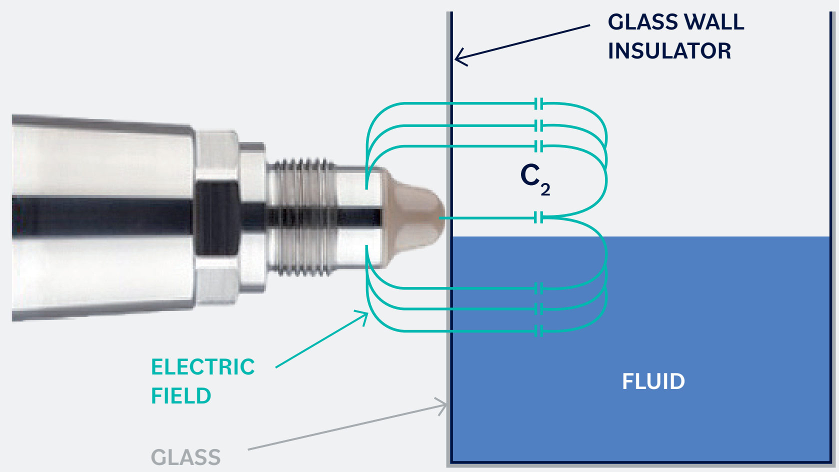


Figure 7 – NON CONTACTING Capacitance Level Probe

The electrical circuit for a non-contact capacitance level sensor is shown in **Figure 8**.

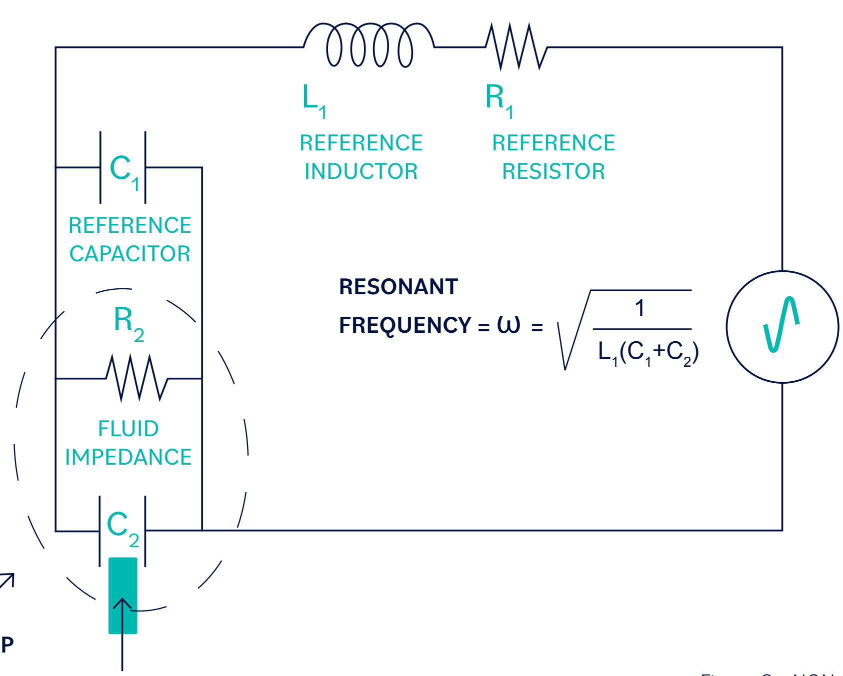


Figure 8 – NON CONTACTING Capacitance Level Probe Electrical Circuit

This electrical circuit can be simplified because the electrical resistance of the glass vessel wall is extremely high. Because of this, the resistance of $\mathbf{R_2}$ has minimal effect on the electrical circuit and can be ignored – see **Figure 9**.

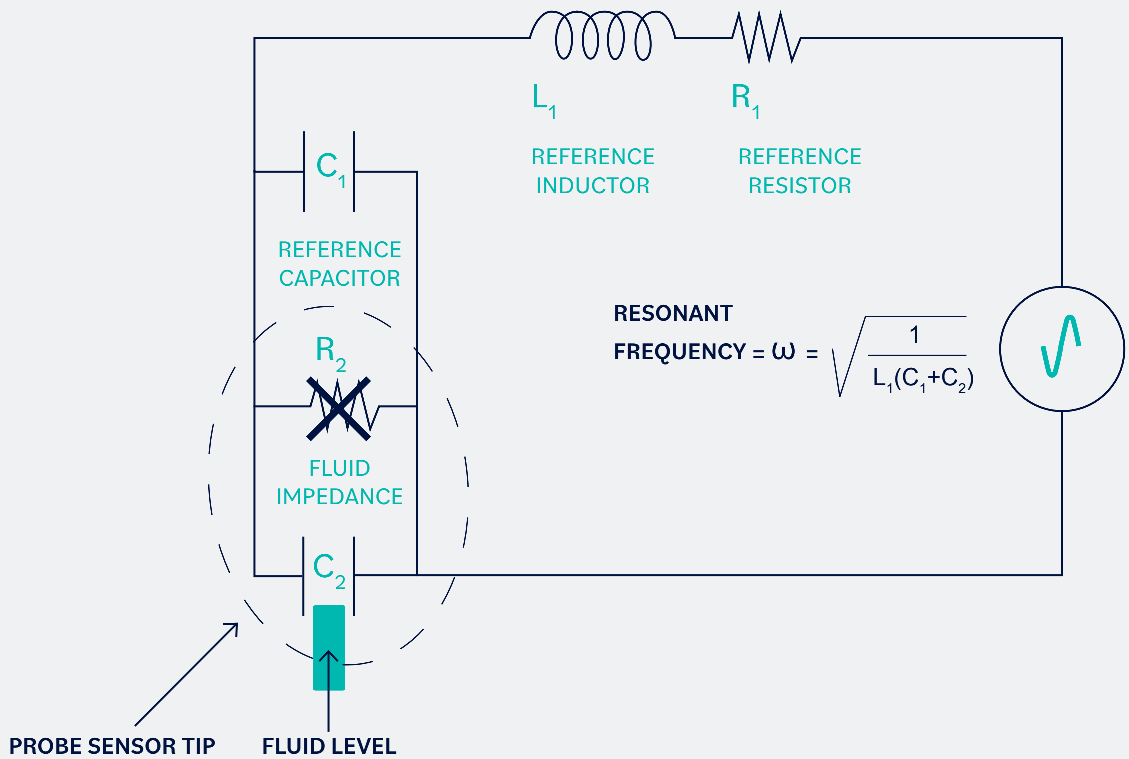


Figure 9 – NON CONTACTING
Capacitance Level Probe Electrical Circuit

Note: The resistance $\mathbf{R_2}$ is important in applications where the level sensor probe tip is in direct contact with the process fluid. Should the resistance of the process fluid be low, the resistance of $\mathbf{R_2}$ has a greater effect on the electrical circuit and the voltage drop across $\mathbf{R_1}$ will increase. $\mathbf{C_1}$ and $\mathbf{C_2}$ are in parallel so, in a non process fluid contact scenario: **Total Capacitance = C_1 + C_2**

Any change in the sensor capacitance, $\mathbf{C_2}$, will change the voltage drop across the reference resistor, $\mathbf{R_1}$.

To alarm on point level and activate the switch, the capacitance point level probe only has to compare either the change in voltage drop across $\mathbf{R_1}$ or the change in Resonant Frequency as $\mathbf{C_2}$ varies capacitance.

The Test

HARDWARE

This paper evaluates a VEGA VEGAPOINT 21® capacitance point level probe on an LJ Star® Hygienic Bubble Trap.

FIGURE 10 – VEGAPOINT 21® POINT LEVEL CAPACITANCE PROBE

FIGURE 11 – LJ STAR® BUBBLE TRAP

The study was performed with the two point level probes mounted to the outside of the hygienic bubble trap, as shown in **Figure 12**.

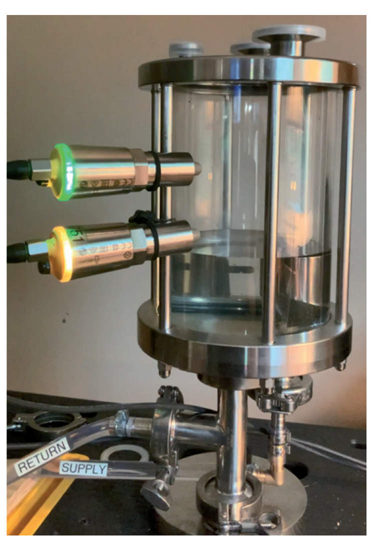


FIGURE 12 – VEGAPOINT 21® CAPACITANCE PROBE AND LJ STAR® BUBBLE TRAP

In this application, two VEGAPOINT 21® point level switches were evaluated; one as a low level sensor and the second as a high level sensor. During normal operation of the bubble trap, the fluid level should be between the low level probe and the high level probe.

In an actual hygienic purification operation, should the fluid level in a bubble trap drop below the low level sensor, the gas vent at the top of the bubble trap would open, allowing the gas to be vented through a sterile filter. As the gas is vented, the fluid level in the bubble trap will increase. Once the fluid level is sensed at the high level sensor, the gas vent valve will close.

The VEGAPOINT 21® point level switches are mounted to the hygienic bubble trap support rods and are isolated from the actual process fluid by the wall of the glass cylinder. The close proximity to the process fluid, even as sensed through the borosilicate glass wall, provides the acceptable change in sensor capacitance necessary to activate the switch output and signify fluid level at that sensor point.

A boss clamp with half coupling was fabricated in order to hold the level probe against the bubble trap glass cylinder. This mounting boss clamp is shown in **Figure 13, Figure 14 and Figure 15**.

FIGURE 13 – BOSS HEAD
MOUNTING CLAMP

FIGURE 14 – BOSS MOUNTING CLAMP
WITH VEGAPOINT 21®

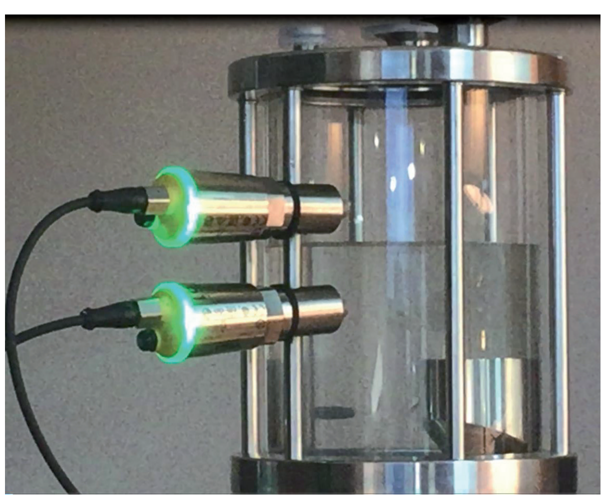


FIGURE 15 – BOSS MOUNTING CLAMP WITH
VEGAPOINT 21® MOUNTED TO HYGIENIC BUBBLE TRAP

With the VEGAPOINT 21® point level capacitance probe in direct contact with the glass wall of the bubble trap, the dielectric of the fluid caused enough change in capacitance $\mathbf{C_2}$ to be sensed.

The capacitance sensor only has to sense a change in dielectric between the glass/air compared to the dielectric of the glass/process fluid. In typical purification processes, the dielectric constant of Water for Injection (WFI) is approximately 15. Buffer solutions typically have a dielectric of over 50 and distilled water has a dielectric constant of approximately 80.

Note that the dielectric constant of borosilicate glass is approximately 5. Air, by definition, has a dielectric constant of 1. In this evaluation, distilled water was used.

CONFIGURATION

The VEGAPOINT 21® capacitance point level switch was configured using PACTware® and the VEGAPOINT 21® point level switch DTM. The VEGAPOINT 21® capacitance point level switch output status was configured for "Hysteresis Function". As explained in the VEGAPOINT 21® Operation Manual, the "Hysteresis Function" has the task of keeping the switching state of the output stable. When the Switching Point (**SP**) is reached, the output switches state and remains in this switching state. Only when the Reset Point (**RP**) is reached does the output switch back.

If the measured variable moves between switching and reset point, the state of the output does not change. The VEGAPOINT 21® capacitance point level switch used in this evaluation has two independent switch outputs with two independent Switching Points **SP**. For the bubble trap point level application, only one of the two switch points is used. The second switch point is spare and will be used in another hygienic application where it is necessary to sense and differentiate process fluid from foam and from air. In the bubble trap application, there is no reason to differentiate foam.

It is not necessary to know the dielectric constant of the fluid in the bubble trap. In the setup of the VEGAPOINT 21® configuration, there is an option for "User Defined Application", where the capacitance probe can be placed in contact with the bubble trap. If the probe is in contact with glass/water, the VEGAPOINT 21® probe is selected to be "Covered". When the process fluid level is below the VEGAPOINT 21® probe, the probe is selected to be "Uncovered".

This "learning process" allows for automatic switching of the output based on the sensed dielectric of the glass/fluid at the sensor point. The actual units of the Switching Point **SP** are dependent on the instrument manufacturer. The units for the VEGAPOINT 21® capacitance point level switch are "% Resonant Frequency", while the units for an Endress+Hauser FTW23® capacitance level switch are "% Coverage". Based on differences between the process fluid in the bubble trap (distilled water), the optimal settings for the Switching Point **SP** and Reset Point **RP** were determined to be 83.00% Resonant Frequency and 84.00% Resonant Frequency, respectively.

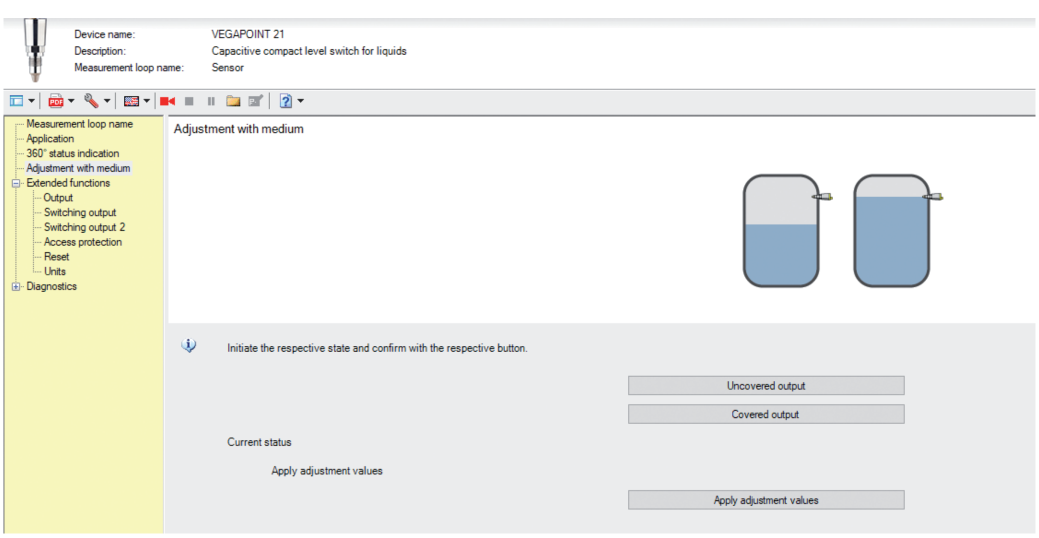
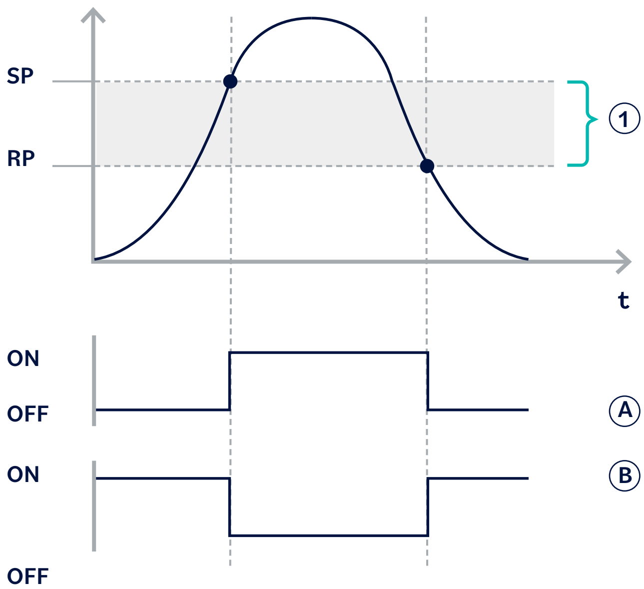


Figure 16 – VEGAPOINT 21® Configuration Software



SP Switching point

RP Reset point

A HNO (Hysterese Normally Open) = Closing contact

B HNC (Hysterese Normally Closed) = Opening contact

t Timeline

1 Hysteresis

Figure 17

OBSERVATIONS

In the actual test, the distilled water in the bubble trap had a reading of 83% Resonant Frequency, as measured with the sensor tip on the outside of the glass cylinder. The Resonant Frequency was 87% when the fluid level was below the point level probe and the level probe sensed air instead of process fluid. In other words, the % Resonant Frequency increased when the probe tip sensed a low dielectric fluid (air) and the % Resonant Frequency decreased when the probe tip sensed a high dielectric fluid, such as distilled water.

In this test, we can deduce that any Resonant Frequency below 83% is due to the point level probe sensing a fluid. If the Resonant Frequency is above 84%, we know that the point level probe is sensing air.

For this technology to be repeatable and accurate, the dielectric of the process fluid must be substantially higher than the dielectric of air and the bubble trap glass wall. This is the case in a biopharmaceutical purification process, where air, by definition, has a dielectric of 1 and the dielectric constant of borosilicate glass is approximately 5.

- Almost all process fluids have a dielectric of 10+.
- Water for Injection (WFI) is approximately 15.
- Buffer solutions are typically 50+.
- Distilled water is approximately 80.

When in doubt, the Switching Point **SP** should be set based on Water for Injection being present in the bubble trap. All other typical fluids, such as protein solutions, buffer solutions, and chromatography storage solutions have a dielectric above 15.

The hysteresis of the Window Function is 1% Resonant Frequency, since the Switching Point **SP** is 83% and the Reset Point **RP** is 84%. In the testing conducted on a bubble trap containing water, this 1% hysteresis value equates to a level hysteresis of about 1/8" (3mm). Even if we configured a much wider hysteresis by setting the Reset Point **RP** higher than 84% Resonant Frequency, the level of the fluid would still be accurately controlled. In no case should the Reset Point **RP** be set above the % Resonant Frequency of air as the switch will not change state when sensing fluid again.

Conclusions

We are able to confidently conclude that the point level capacitance probe mounted to the outside of a hygienic bubble trap is an effective and reliable method for controlling point level. The tested point level probe was shown to have a repeatability of approximately 1/8”, depending on the physical mounting position on the exterior of the bubble trap.

To achieve this repeatability of 1/8”, it was necessary to “tune” the point level probe configuration parameters to the specific installation and physical design of the bubble trap. This is easy to configure through PACTware® so the technology can be integrated into existing processes with minimal disruption.

The point level probe capacitance depends on several key factors:
1. Strength of electric field
2. Thickness and dielectric of the glass cylinder wall
3. Mounting angle of the probe against the glass cylinder
4. Dielectric of the process fluid

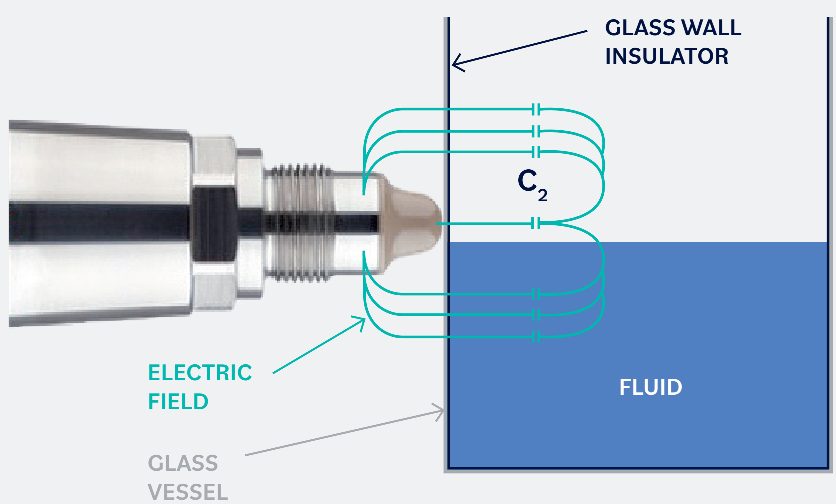


Figure 18 - NON CONTACTING
Capacitance Level Probe Electric Field

If the configuration parameters are not precisely tuned, then the repeatability was shown to increase from 1/8” to approximately 1/4”. This is not a concern, though, since the bubble trap level is typically controlled between 60% and 80% of the full height and volume, as noted earlier.

We also evaluated the functionality of the probe with some “external interference” within the electric field by placing a finger against the outside of the bubble trap wall in proximity to the point level probe. The distance from the finger to the point level probe could be as close as 1/4” without causing a measurable effect.

The mounting of the probe was found to be an important factor in terms of the repeatability of the sensed probe level. The angle of the mounted probe against the glass cylinder should be as close as possible to perpendicular. Since the probe mounting boss is attached to the head plate support rod, a spacer is added between the point level probe and the mounting head boss, as shown in **Figure 19**.

Figure 19 - Head Boss Spacer

Different sized spacers allow the probe to be mounted perpendicular to a bubble trap of any size, ensuring that the probe tip maintains physical contact with the glass cylinder wall.

This makes it a scalable solution for reliable bubble separation in a wide range of single-use products and evolving purification processes.

Unlike a contact sensor, this capacitance probe also has the benefit of not needing to undergo Clean in Place (CIP) or Sterilize in Place (SIP) because it does not come into physical contact with the process fluid.

It is easy to configure, and to integrate with existing equipment, and is an efficient and reliable way of controlling and optimizing the operation of the hygienic bubble trap as a vital element in the purification process.

Acknowledgements

Appreciation and credit is given to LJ Star and VEGA for the lending of the equipment for this paper. The following are registered trademarks of the respective companies:

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About the Author

Dan Klees is an industry expert and thought leader, and Principal Biotech Consulting Engineer at Agilitech. Dan served 14 years as the founding chairman of the ASME BPE Process Instrumentation Subcommittee and holds nine U.S. and European patents related to hygienic process measurement, single-use and disposable instrumentation, as well as instrument calibration methods. Through his extensive knowledge of biopharmaceutical operations, metrology, process instrumentation, FDA regulations, cGMP requirements and more, he is recognized as a subject matter expert on biopharmaceutical process instrumentation, process optimization, and manufacturing.

Klees is also a published author, graduate school guest lecturer and founder of consulting company, Critical Approach, LLC.

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