Single-Use Technologies V: Building The Future Proceedings

3-21-2022

Measuring the liquid volume in a flexible bioprocess container with Single Use Pressure Sensors

Nick Troise

James Furey

Measuring the Liquid Volume in a Flexible Bioprocess Container with Single Use Pressure Sensors

Nick Troise
R&D Engineer II
March, 2022

Phone: +1.609.799.2299
Email: nick.troise@PendoTECH.com

PENDOTECH®
Adding Value To Your Process

Agenda

- Introduction
- Highlight Technology
- Application Overview
- Background on Pascal's Principle and Hydrostatic Pressure
- Review Validation Experiment
- Analyze Results
- Discuss Key Takeaways
- Areas of Improvement
- Conclusion and Next Steps

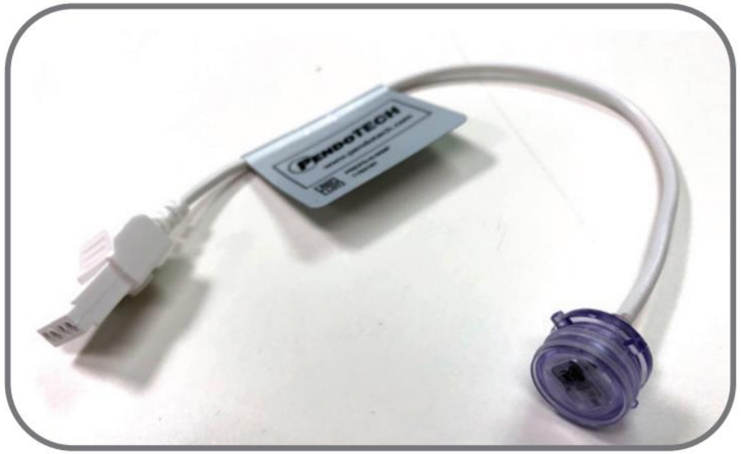
Nick Troise

R&D Engineer II

- Graduated from Rowan University in Biomedical Engineering with a dual minor in Math and Computer Science
- Started working with PendoTECH in 2017 as an intern and started full time in 2019
- Responsibilities are focused on new product design/development, and product validation
- Represent PendoTECH on the Bioprocess System's Alliance (BPSA) X-ray Irradiation Committee
- Fun Facts:
  - Avid fan of both Chess and MMA
  - Lost about 70 lbs (32 kg) in last 10 months

Single Use Port Plate Pressure Sensor

- Designed for integration with flexible bioprocess containers (BPC)
  - Buffer/media storage bags, mixing bags, bioreactors, etc.
  - Interfaces with port welded onto BPC



- Single Use Pressure Sensor
  - Liquid or gas applications
  - No calibration required (plug and play)
  - Low cost and can be disposed with rest of assembly

- Key Features
  - Same MEMS-HAP sensing technology as inline pressure sensors
  - Qualified for use up to 15 psig/1.03bar (equivalent to a 34ft/10m tall bag)
  - Fluid contact materials all USP Class VI and ADCF
  - Validated by customers to weld to various bag materials
  - Gamma Irradiation Compatible

Key Applications

- Safety-
  - Preventing over-pressurization of a flexible BPC
- Performance
  - Monitoring pressure in a SU Bioreactor
- Leak Testing
  - Pre-use integrity test via pressure decay
- **Volume Measurement by hydrostatic pressure**

Application Overview

- Measuring volume of a flexible BPC
  - Important for monitoring levels of a buffer or media storage
  - Alert operators when bags are running low or need to be switched

- Current Solutions:
  - Load Cells
    - Very Accurate and high resolution
    - Expensive, can be difficult to integrate, and requires calibration
  - Level Sensors
    - Several different styles: Conductive, ultrasonic, capacitance, etc.
    - Affordable and accurate, but can be affected by factors in the e
    - Generally pretty invasive

Using Pascal's Principle to measure liquid volume

- Define mathematical equation for hydrostatic pressure

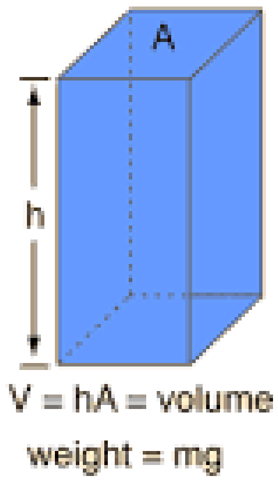
$$\Delta P = \rho g(\Delta h)$$

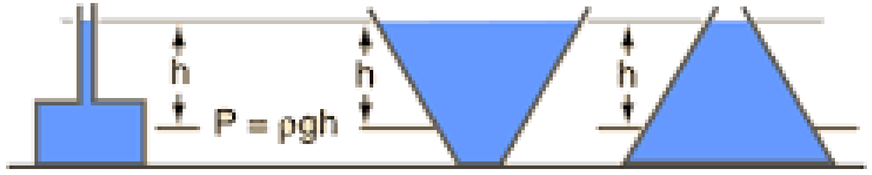
ΔP = hydrostatic pressure
ρ =fluid density
g = acceleration due to gravity,
Δh = height of the liquid.

- *In a static environment, the depth of a liquid generates a force that is directly proportional to the height of the liquid*
  - Independent of the volume, shape, total mass, or area of fluid

- Given a known pressure and fluid density, can solve for Δh

- With Δh and cross section area (A) can determine the volume of liquid



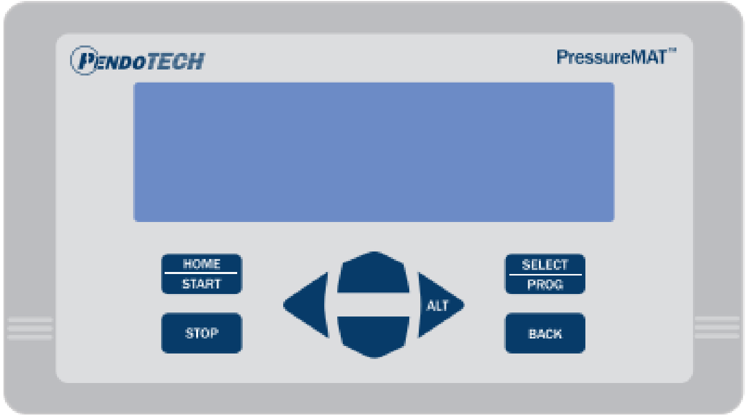


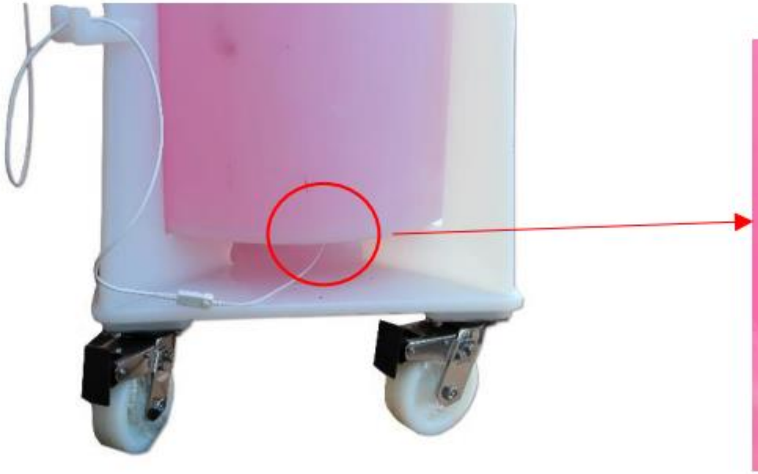
Important Requirements

- No external or head pressure in the system
  - Or at least must be quantified so it can be offset before calculating Δh
- Locational Accuracy of the Sensor
  - Precise location must be known, ideally directly on bottom of bag
  - Otherwise the pressure will not correlate to the true liquid level
- High Resolution Pressure Reading
  - Water column of 1 in (in Aq) = 0.036 psi (2.5 mbar)
  - Must be able to detect very small changes in pressure for accurate level measurements

Validation Experiment

- PendoTECH Port Plate installed on the bottom of a 200L 2D BPC
- Supported by custom 200L tote with cut-out for port plate sensor
- Monitor: PMAT2HR
  - Specializes in low pressure applications
  - Zero offset stability = ± 0.003psi (0.21mbar)





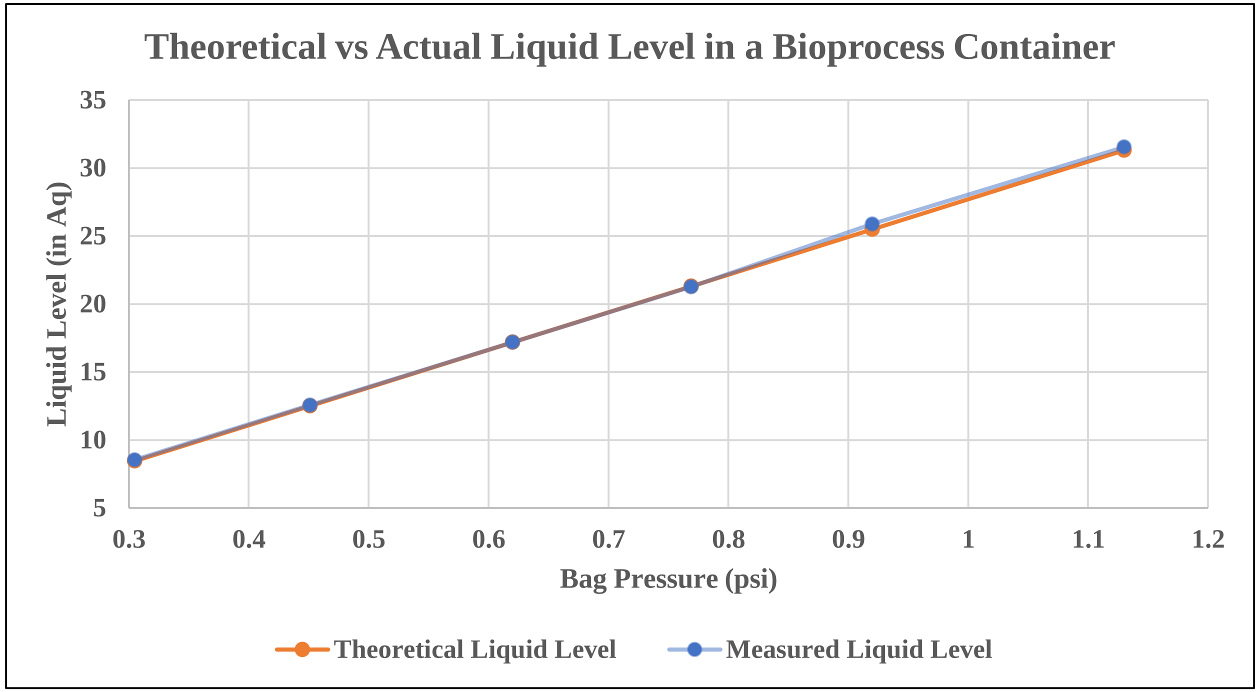
Validation Experiment (cont.)

- Filled container dyed water to make physical measurements of liquid level with caliper
  - Slits cut into side to easily identify meniscus of liquid level
  - Measured every 0.20psi or 14mbar (4-6 in Aq) until BPC was full

- Calculated volume using equation for volume of a cylinder: $V=\pi r^2 h$
  - No direct volume reference
  - Graduation marks on tote used as a sanity/reasonableness check

Results Analysis

Bag Pressure Measured (psi)	Theoretical Liquid Level (in Aq)*	Measured Liquid Level (in Aq)*	Percent Error	Calculated Volume (L)
0.305	8.45	8.54	1.07%	53.2
0.451	12.50	12.56	0.48%	78.2
0.620	17.18	17.19	0.06%	107.1
0.769	21.31	21.27	0.19%	132.5
0.920	25.49	25.88	1.53%	161.2
1.13	31.31	31.54	0.73%	196.5

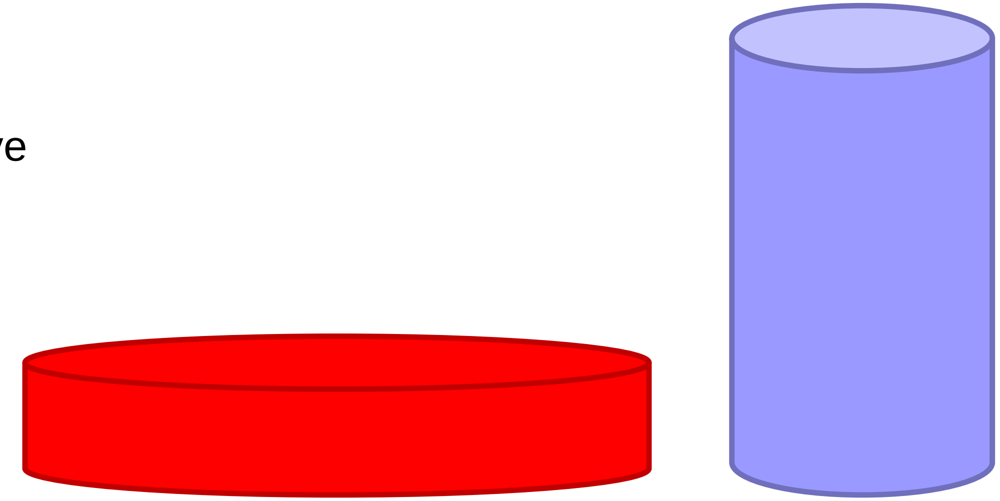


- Theoretical and measured liquid levels extremely similar
  - Differed by an average <1%
- Greatest error was 1.53% at 0.920 psi
  - Within sensor's accuracy spec of ±2% of reading
- Relationship between liquid level and bag pressure was perfectly linear as expected
- Qualitative comparison of volume using graduation marks on tote
  - Bag filled to 160L mark, calculated volume was 166L, ≈4% error

Key Observations

- Hydrostatic pressure can be used to measure liquid level very accurately under the right conditions
  - Sensor location precisely determined
  - High resolution pressure reading

- Correlation to total liquid volume is highly dependent on bag geometry
  - Calculation typically assumes an ideal or perfect shape
  - Folds/creases caused by deployment can significantly impact volume calculation
  - Cross Sectional Area key contributor to volume accuracy
    - Greater ratio of area to height, increases potential inaccuracy
  - Even with poor deployment/bag geometry, can still be used for relative volume measurements
    - E.g. Gas Gauge
  - Under ideal settings, can measure volume very accurately
    - Comparable performance to load cell and other technologies



Potential Improvements

- Use a 3D BPC with multiple sensor ports
  - Larger sample size = more data for repeatability/consistency
  - Easier to work with/deploy for volume calculations

- Reliable reference for volume measurement
  - Measuring liquid level is good step, but volume accuracy is the ultimate goal
  - Requires an accurate control to evaluate
  - Calibrated scale below BPC, or flow meter on fill line to measure actual volume

Conclusion and Next Steps

- Following Pascal's Principle, a single use port plate pressure sensor can accurately measure the liquid level in a flexible bioprocess container
  - With correct setup this can be used to accurately measure the volume in a BPC in a cost-effective, simple, and minimally invasive manner
- Complete a re-vamped application validation experiment
  - Implement improvements previously discussed to quantitatively assess volume accuracy
  - Can perform with a gamma irradiated sensor to further challenge gamma compatibility in setting that reflects actual customer usage
- Partner with end-users for additional data and feedback

Thank you