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Development of a dissolved CO2 sensor in true single-use format

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Development of a Dissolved CO_2 Sensor in True Single-Use Format

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Abstract

Currently, it is mainly reusable dissolved CO_2 sensors that are used for measurements in single-use (SU) bioreactors for clinical production and GMP-sized processes. For sterilization purposes, reusable sensors are autoclaved within SU probe sleeve adapters prior to their aseptic installation into a gamma irradiation-sterilized SU bioreactor. Alternatively, reusable sensors are mounted on bag-integrated, gamma-sterilized SU adapter wells equipped with a gas permeable membrane that separates the non-sterile sensing elements from the cell culture.

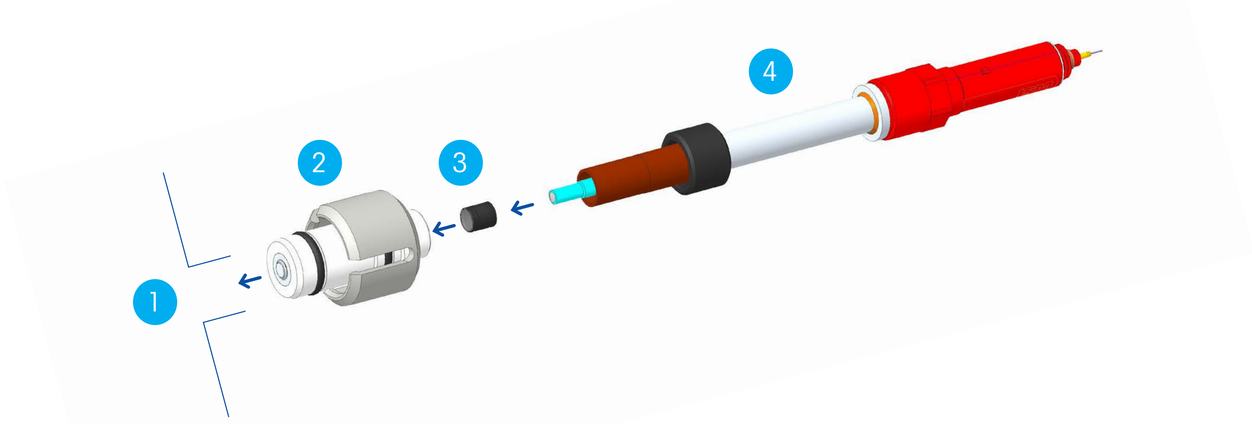
Although these reusable sensors are based on the industry accepted Severinghaus principle [1], they do not offer the full advantages of sensors in true SU format that users appreciate. For example, when operating SU pH or dissolved oxygen (DO) sensors fully integrated in SU bioreactors, additional autoclaving steps are not needed, and sensing elements are directly exposed to the cell culture media for reliable and consistent measurement performance without the need of an additional barrier membrane that adds to sensor response time.

Objectives

Our objective was to develop a sensor with the same advantages as offered by SU pH and DO sensors. The SU dissolved CO_2 sensor shall have:

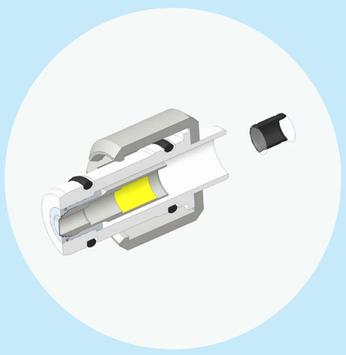
- A form factor that leads to its safe integration into SU bioreactor bags.
- A dry storage life of 36 months.
- A post-gamma irradiation measurement performance similar to reusable dissolved CO_2 sensors based on the Severinghaus principle.
- High-cost sensor head components in a detachable, reusable format.
- USP <87> biocompatibility post-gamma and post-X-ray irradiation.
- A user-friendly gel electrolyte handling concept [2].

The design concept:



1 Bag port
2 InSUS 507 SU sensor
3 Gel electrolyte capsule
4 Reusable sensor head InSUS H50i with internal pH sensor

Final Design – Sensor and SU Bioreactor Integration



InSUS 507 SU sensor with CO_2-permeable membrane (sterile barrier) in direct contact with media

Sensor installation in SU bag film via an 1" Eldon James weld-in port

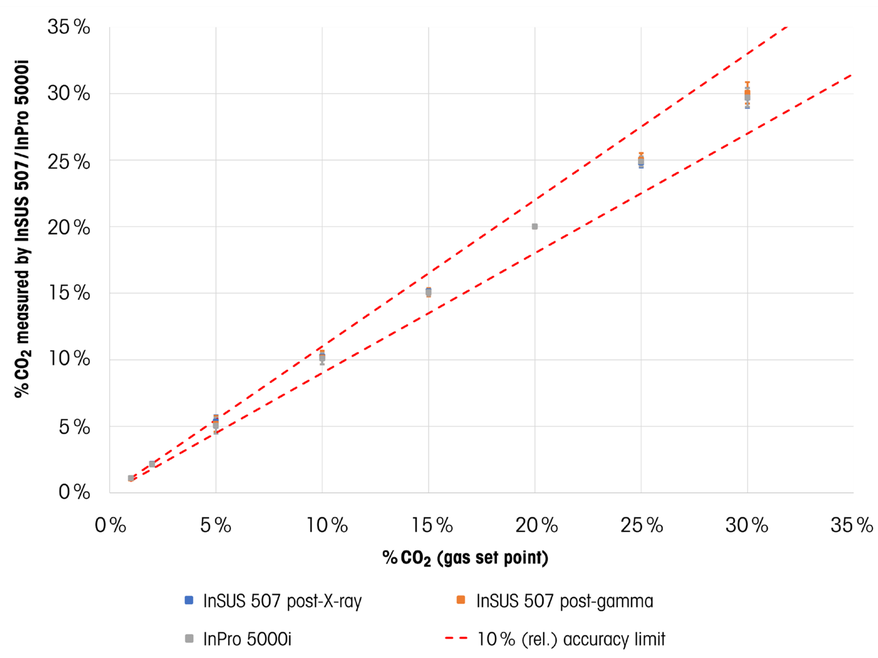
Methods – Post-gamma Sensor Characterization

Sensors were gamma irradiated at 45–55 kGy to ensure a minimum irradiation dose of 45 kGy. After irradiation, accelerated aging was performed. The scope of the accelerated aging process was to simulate the 36-month shelf life of the sensors. For the sensor characterization, the following performance criteria were checked:

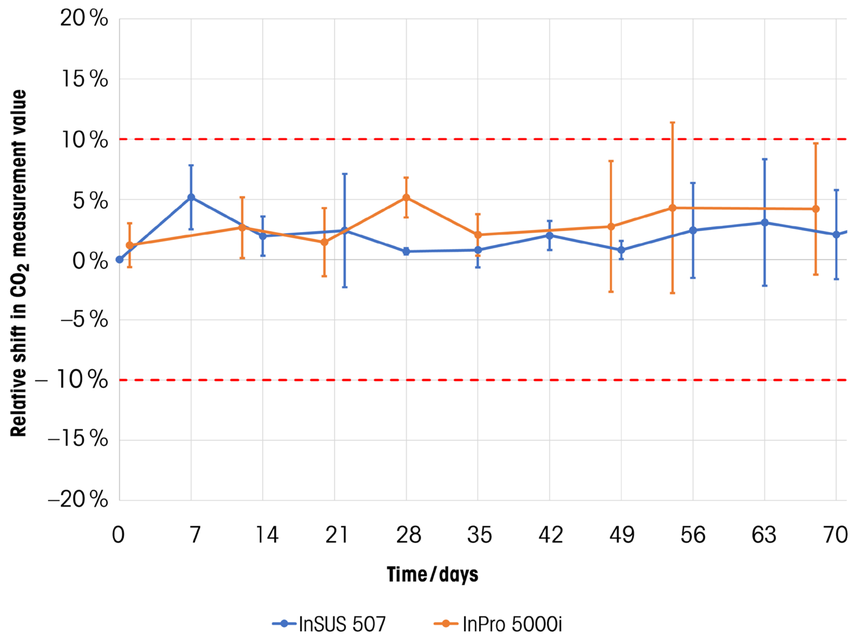
- Accuracy at different CO_2 gas mixtures.
- Long-term measurement stability in liquid media at 37 °C at 10 % CO_2.
- The results were compared to analogous data from standard reusable METTLER TOLEDO InPro 5000i CO_2 sensors.

Results

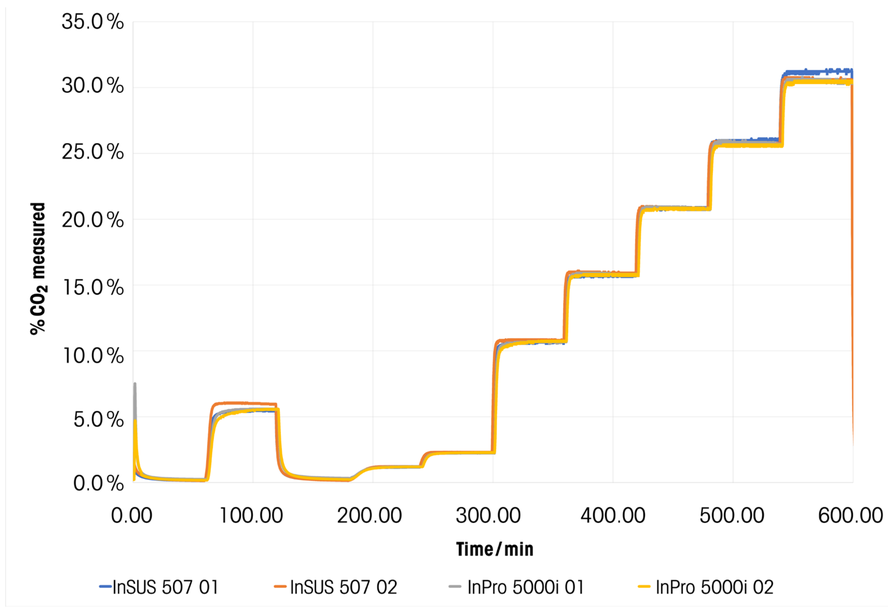
Accuracy: Comparable performance to reusable InPro 5000i sensor, within accuracy specification of ± 10 % (rel.) of reading after process calibration at 20 % CO_2. (Mean values with 2σ error bars)



Long term measurement stability in liquid media at 37 °C at 10 % CO_2: Comparable performance as reusable InPro 5000i sensor for 70 days



Response time comparison with reusable InPro 5000i sensor



Conclusion

The design of the InSUS 507 single-use dissolved CO_2 sensor meets the targets for convenient and safe deployment in SU bioreactor bags. Its measurement performance allows for reliable in-line monitoring and control of dissolved CO_2 in cell culture processes in SU format.

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References

1) Severinghaus, John W.; Bradley, A. Freeman (1958). "Electrodes for Blood pO2 and pCO_2 Determination". Journal of Applied Physiology. American Physiological Society. 13 (3): 515–520

2) Aratori, Davide; Schmidt, Sebastian, "Sensor and a Device for a Sensor Containing Gel Electrolyte", EP4170336A2, 2023.

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