Sealed Chamber For Cmos-Mea

Tech ID: 34887 / UC Case 2026-877-0

BACKGROUND

Technical Problem

1. Evaporation and Osmolarity Shifts: In open-well culture systems and vapor permeable closed systems, media evaporation causes osmotic toxicity especially during long-term electrophysiology experiments that can last days or weeks. Even inside a highly humidified incubator significant evaporation occurs over time. This alters the osmolarity of the cell culture medium, increases salt concentrations and affects electrophysiology, which in cells are driven by ionic gradients. By creating a hermetic, non-evaporative liquid seal, this invention completely halts evaporation and maintains a stable osmotic environment.

2. Contamination and Environmental Cross-Talk: Open designs leave cultures vulnerable to airborne particulate, bacterial or fungal contamination, especially during transport or when handled outside a sterile hood for imaging or electrical recording. The sealed well insert physically isolates the biological sample, protecting it from external contaminants and preventing cross-talk between separate wells. This is important especially when combined with electrophysiology equipment which cannot fully or easily be sterilized due to complex and sensitive electronics.

3. Incompatibility of Closed-System Benefits with Legacy Hardware: Researchers looking for closed, tightly controlled fluidic environments have traditionally been forced to abandon standard commercial CMOS-MEA platforms in favor of bespoke microfluidic chips and bespoke electrode arrays. This invention solves this compatibility barrier by offering a retrofit mechanism. Clamping or gluing a base to the exterior of existing, commercially available well and adding sealing to this allows full use of sophisticated commercial equipment.

4. This insert eliminates the direct air gap above the cell culture media. Removing this interface completely prevents the water evaporation and subsequent boundary-layer shifts that typically degrade long-term cultures.

5. Traditional MEAs must sit inside bulky, expensive incubators to maintain gas and temperature stability. This invention inherits the self-contained environmental isolation of the prior patent. Because gas and fluid exchange are handled through dedicated routing within the closed well, the MEA device can function reliably on a benchtop, inside a microscope chamber or in specialized testing setups without losing

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OTHER INFORMATION

KEYWORDS

Complementary Metal-Oxide-Semiconductor, Microelectrode Array, Cell culture, Organoids, Neuro-organoids, Brain organoids

CATEGORIZED AS

- **Engineering**
  - Engineering
- **Sensors & Instrumentation**
  - Analytical
  - Biosensors

RELATED CASES

2026-877-0, 2025-959-0

environmental control.

6. Precise, Multi-Gas and pH Equilibrium: The architecture leverages the closed-system mechanics of the prior application to maintain strict carbon dioxide, oxygen and carbonic acid equilibrium. It allows researchers to introduce targeted gas-controlled fluids or direct gas feeds to regulate pH and oxygen levels precisely at the sensor surface, achieving localized environmental profiles (such as deep hypoxia) that are impossible to maintain in an open petri dish structure.

TECHNOLOGY DESCRIPTION

Method of transforming commercial CMOS-MEA wells or other petri dish-type wells into sealed fluidic chambers for incubator-free sealed cell culture

This invention is a specialized insert designed for commercial CMOS-MEA wells that adapts the closed, non-evaporative cell culture technology of patent application WO2025024652A1 to petri-dish-like well structures. The apparatus operates by securing a base to the exterior of the well via clamping or gluing, using a mechanical screw or clamp mechanism to tightly compress the well insert against the base. Using with gas-impermeable and biocompatible gaskets, this architecture establishes a completely isolated fluidic environment that prevents liquid or gas ingress and egress. Integrated ports in the lid enable precise fluid ingress, air evacuation, continuous liquid flow and the targeted introduction of compounds to modulate cellular electrical activity.

Key Components of the Device:

The device assembly consists of an external mounting collar designed to couple mechanically to the outer perimeter of the pre-existing, rigid plastic or ceramic well housing of the CMOS-MEA. By anchoring exclusively to this exterior structure, the collar establishes a mechanical load path that completely bypasses the delicate internal silicon sensor matrix. Within this collar sits the fluidic well insert manifold, which is fabricated as a rigid plug that fits precisely inside the internal well diameter. This manifold contains internal fluidic routing channels terminating in external fluidic interfaces such as tapered hose barbs or female Luer lock connectors. It may also feature an integrated, rigid mechanical stop collar engineered to establish an absolute axial displacement limit during assembly.

Axial force is applied through an axial compression mechanism, which can be configured either as an internally threaded, free-spinning outer sleeve that engages the external mounting collar or as a circumferential array of peripheral bolts. This mechanism transforms rotational force into uniform downward linear displacement without imparting torsional shear to the underlying seals. The sealing interface itself relies on a dual-concentric elastomeric gasket system situated on the lower face of the insert manifold. If gas impermeability is not needed, or a material with sufficient gas barrier function as well as biocompatibility is chosen, then only one gasket is needed.

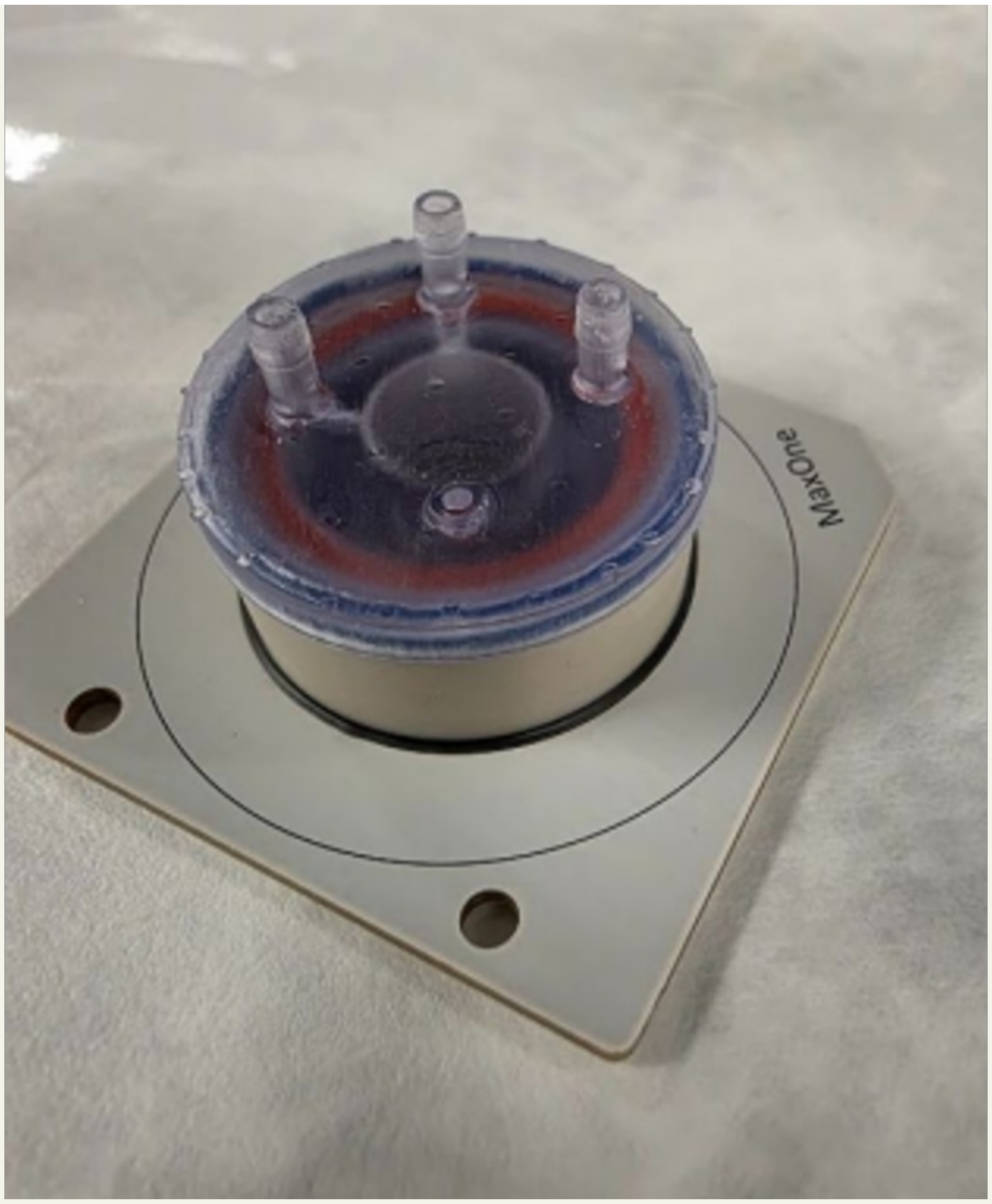
These gaskets include an inner ring and an outer ring positioned in close proximity, which work together to form a redundant hermetic barrier against the internal well wall. The operational method establishes a controlled, non-evaporative fluidic environment through a precise sequence of mechanical and hydraulic steps. First, the external mounting collar is rigidly secured to the outer perimeter of the CMOS-MEA well ring using a structural adhesive or a high-friction mechanical clamp. Once this base is secure, the fluidic well insert manifold, pre-fitted with the gasket(s), is aligned and lowered into the internal cavity of the CMOS-MEA well.

Next, the axial compression mechanism is engaged and driven downward using a torque-limiting instrument, such as a calibrated torque screwdriver or torque wrench. This instrument rotates the threaded sleeve or the peripheral bolting array until the integrated stop collar seats firmly against the mounting collar. This action achieves a precise, reproducible percentage of elastomeric deflection across both gaskets without overloading the underlying chip architecture. Finally, fluid is injected under positive pressure through the designated ingress port, forcing the gas phase out through the egress port as the liquid front rises. This process continues until the entire internal headspace is occupied by liquid, which effectively eliminates the gas-liquid interface.

By combining the external mounting base with a rigid well insert and dedicated fluidic ports, this device converts a standard open-top electrophysiology well into a completely closed microfluidic chamber. This mechanical arrangement allows the fluidic and thermodynamic principles of the parent patent to be applied directly to commercial MEA hardware. The hydraulic method of filling the well through these ports completely eliminates the gas-liquid interface right above the sensor matrix. This directly replicates the non-evaporative environment of the parent patent, stopping media evaporation and stabilizing osmolarity over long-term recordings without needing complex incubation infrastructure.

The entirely fluid filled well and gasketed sealing enables this closed-system isolation to function in a live electrophysiology context. This sealing means thqat the well remains entirely isolated from atmospheric gas fluctuations while maintaining a safe envirornment for the cells. This complete isolation also allows for precise localized control over gas concentrations and compound delivery directly at the sensor surface. Consequently, researchers can achieve the exact environmental stability and precise chemical modulation described in the previously filed patent application using existing electrophysiology well designs.

Fluidic Well Insert showing dual gaskets



APPLICATIONS

CMOS-MEA analysis of organoids - particularly brain organoids.

ADVANTAGES

Existing attempts to manage the environment in CMOS-MEA wells include commercial perfusion lids provided by equipment manufacturers or custom-built lids developed by academic laboratories. These systems typically maintain an atmospheric air gap above the cell culture media and rely on external incubator infrastructure to balance temperature and gas concentrations. The current invention differs by eliminating the gas-liquid interface entirely through a hermetic seal. By avoiding the air gap, it stops evaporation at the root and operates stably without specialized incubation enclosures.

Another approach involves using gas-permeable film lids stretched over the top of the culture wells. While these films allow gas exchange and attempt to restrict evaporation, they introduce new technical challenges. Water vapor still escapes through the film over extended periods, which gradually alters media osmolarity during long-term experiments. Furthermore, the temperature differential between the warm media and the cooler film lid causes significant condensation to form on the underside of the film. This condensation can drop back into the well, disrupting the local environment, or it can obscure optical imaging. This invention solves these issues by using a rigid well insert with gas-impermeable gaskets that completely seals the chamber. Since there is no air layer, there is no evaporation and condensation within the well.

Researchers who require strict fluidic isolation and automated drug delivery often turn to custom microfluidic or organ-on-a-chip platforms, usually fabricated from PDMS or injection-molded plastics. While these platforms achieve excellent environmental control, they are incompatible with high-density commercial CMOS-MEA hardware. Choosing these custom systems forces researchers to abandon market-standard recording consoles, losing access to high-resolution electrical stimulation and sub-cellular recording capabilities. This invention acts as a bridge by providing a retrofittable microfluidic environment that clamps directly onto existing commercial well structures, allowing users to keep their high-density sensor infrastructure while gaining the benefits of a closed fluidic circuit.

In comparison to the previously filed WO2025024652A1: The previous patent application describes a standalone closed-system cell culture vessel that eliminates the air gap using a gas-permeable, liquid-impermeable film. However, that design cannot be applied directly to commercial CMOS-MEA chips, which feature rigid plastic or ceramic well walls permanently bonded around a highly fragile silicon sensor. Attempting to press a simple film or standard lid onto these pre-existing commercial well rims leads to uneven sealing, fluid leakage or structural damage to the underlying electronic array. This invention improves upon the design in WO2025024652A1 by introducing a multi-part mechanical assembly. By clamping a dedicated base to the exterior of the commercial well ring and using a separate screw or clamp mechanism to compress the gasketed insert downward, the sealing forces are safely distributed away from the delicate sensor surface. This mechanical adaptation allows the closed, non-evaporative fluidic principles of the parent patent to be safely retrofitted onto standard commercial hardware.

RELATED MATERIALS

RELATED TECHNOLOGIES

- Dual Gasket System For Gas-Tight But Biocompatible Cell Culture Vessel Sealing
- "Incubator-Free" Vessels For Cell Culture Which Do Not Use An Air Intermediate For Gas Regulation
- Fiber Optic Light Source Scheme For Modular Remote Illumination Of Incubator-Based Live-Cell Microscopy
- Method Of Media Exchange In A Sealed, Fixed Volume Bioreactor
- Perfusion Of A Semi-Permeable Tissue-Containing Block By Means Of A Pressure Gradient In A Circulatory Bioreactor

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Dual Gasket System For Gas-Tight But Biocompatible Cell Culture Vessel Sealing
- Perfusion Of A Semi-Permeable Tissue-Containing Block By Means Of A Pressure Gradient In A Circulatory Bioreactor
- "Incubator-Free" Vessels For Cell Culture Which Do Not Use An Air Intermediate For Gas Regulation
- Fiber Optic Light Source Scheme For Modular Remote Illumination Of Incubator-Based Live-Cell Microscopy

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