

Sensor-Integrated Organ-on-Chip Platforms Made with Photopolymers: Materials, Signals, Drift and Biological Interpretation

Engineering photopolymer microfluidics, embedded sensing and interpretation of time-dependent biological signals

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ER-439 · Engineering Review · Version 0.1 · 8 October 2026

Abstract

Photopolymer additive manufacturing can create organ-on-chip housings, microfluidic geometries and integrated sensor features, but measurement quality depends on optical, chemical and biological stability over time. This review treats sensor output as a coupled function of the photopolymer platform, calibration, flow, cell state and environmental drift. It distinguishes material autofluorescence and sensor drift from genuine biological change and defines qualification of geometry, leachables, calibration, temporal response and biological interpretation.

Keywords: organ-on-chip; stereolithography; photopolymer; integrated sensor; microfluidics; calibration; drift; biological interpretation

1. Significance and scope

SLA and related photopolymer processes allow rapid fabrication of complex microfluidic architectures for organ-on-chip systems, but resin transparency, surface chemistry and cell adhesion remain limiting factors [1]. Sensor integration adds another layer: a measured change must be assigned correctly to biology rather than to the chip material or instrument. Organ-on-chip measurements are especially sensitive to materials because small fluid volumes create large surface-area-to-volume ratios.

A low absolute amount of leachable species or absorbed drug can therefore produce a large concentration error. Material qualification should include extraction/adsorption controls at the same surface-area-to-volume ratio used in the biological experiment whenever quantitative concentration or dose is important.

2. Material optical and chemical state affect the signal

Photopolymer absorbance, autofluorescence, extractables and surface adsorption can influence optical and electrochemical measurements. Post-cure and washing conditions therefore belong in the sensor calibration record. A calibration performed in a clean buffer may not transfer to protein-rich culture medium if the sensing surface fouls or the polymer background shifts.

Optical transparency should be specified at the imaging wavelength and after the complete post-cure/sterilisation sequence.

Autofluorescence that is negligible to the eye can dominate a weak fluorescent reporter. Likewise, adsorption of hydrophobic compounds to the photopolymer can distort pharmacological exposure.

Blank chips and mass-balance controls should be included before attributing concentration-dependent responses to cells.

3. Printed geometry defines the biological forcing function

Channel dimensions, build orientation and dimensional error determine flow, shear and residence time. A biological response can therefore change when geometry changes even if the nominal flow rate is identical. SLA organ-on-chip studies have demonstrated that build orientation and channel design can influence dimensional fidelity and predicted flow fields [2].

Flow qualification should use the fabricated geometry rather than the CAD geometry alone. Machla and co-workers showed that build orientation influenced dimensional fidelity and predicted flow behaviour in an SLA-fabricated oral-mucosa chip [2]. For narrow channels, small dimensional deviations can substantially alter shear, so metrology and fluid modelling should be linked to the actual printed device.

4. Integrated sensing requires in-device calibration

Antonelli and co-workers integrated optical pH sensing into a stereolithographically fabricated lab-on-chip and calibrated the sensing approach before applying it to three-dimensional cell culture [3]. This is the correct hierarchy: sensor transfer function first, biological interpretation second. Calibration uncertainty should be carried into any derived biological conclusion.

The sensing layer can itself perturb the biological system through stiffness, surface chemistry, electrode products, optical heating or obstruction of flow. Controls should therefore compare an otherwise equivalent chip with and without the active sensor, not just calibrate the sensor in buffer. This is particularly important for electrical barrier measurements, oxygen sensors and fluorescent reporters where the measurement interface can alter the microenvironment it is intended to observe.

Sensor calibration should be repeated in the complete medium because ionic strength, proteins, pH indicators and optical turbidity can alter sensor response. Calibration performed in water is not automatically transferable to serum-containing culture medium. If a sensor is sterilised together with the chip, the sterilised state is the one that must be calibrated.

5. Drift can arise from material, sensor and biology

Long experiments combine photobleaching, dye leaching, electrode drift, fouling, medium changes and evolving cell metabolism.

Reference channels or repeated calibration points can help distinguish these mechanisms. A stable sensor baseline in an acellular chip is necessary but not sufficient because cell-secreted proteins and metabolites alter the interfacial environment.

A reference channel or acellular control can separate sensor drift from biological change. Baseline movement caused by photobleaching, electrode polarization, protein fouling or polymer swelling can otherwise be misread as metabolism or barrier failure. Long experiments should report recalibration strategy, reference stability and any correction applied to the raw signal. A corrected trace without the uncorrected baseline can hide the magnitude of instrumental drift.

Biological interpretation requires spatial context. A sensor near an inlet, outlet or tissue surface does not necessarily represent the whole construct. Sampling location, flow direction and diffusion distance should therefore be reported with the biological endpoint.

Spatial representativeness is another limit. A sensor positioned near an inlet, wall or cell-free region may report a local state that differs from the tissue average. Sensor placement, sampling volume and flow direction should therefore be documented alongside biological endpoints. When several sensors are integrated, disagreement between them can be informative evidence of gradients rather than a reason to average signals into one number.

Where multiple sensing modalities are used, their clocks and spatial registration should be synchronized before correlations are interpreted mechanistically.

Axis	Measurement	Failure mode
Photopolymer state	post-cure, wash, optical background	material signal mistaken for biology
Geometry/flow	dimensions, shear/flow verification	nominal pump rate used as local flow proxy
Sensor	calibration, response time, hysteresis	uncalibrated signal treated quantitatively
Drift	acellular and time-course controls	baseline movement interpreted as metabolism
Interpretation	sensor location and biological endpoint	local signal generalized to whole tissue

Table 1. Domain-specific qualification matrix for sensor-integrated organ-on-chip platforms made with photopolymers.

6. Device-level verification

Test dimensional accuracy, flow, leakage, sensor calibration, response time, hysteresis and drift before adding cells. Then repeat relevant calibration checks during or after biological operation. Sterilisation and repeated-use cycles should be included if claimed.

If multiple sensors are integrated, cross-talk and sampling location relative to the tissue model should be documented. ER-438 owns the material-immune interaction problem, whereas ER-439 focuses on a measurement platform in which material background, flow and sensor drift can confound biological conclusions. A chip result can support mechanism development, but the engineering qualification here is traceability of the measurement chain rather than proof of clinical performance.

Long-duration chips should additionally track evaporation, bubble formation and bonding integrity because each can alter flow and sensor response without a biological cause. Bubble traps or degassing methods should be treated as part of the device architecture if they are required for stable operation. When chips are bonded from multiple printed or nonprinted materials, the interface and adhesive become part of the chemical-exposure and leakage qualification.

7. Minimum qualification framework

Report resin and cure history, geometry and dimensional verification, surface treatment, medium compatibility, sensor type, calibration model, spatial location, response time, drift, blank controls and biological endpoint. Data processing or machine-learning models should be versioned and validated independently from the biological hypothesis. A minimum qualification package should include CAD-to-part dimensional error, surface condition, channel flow verification, leakage, material extractables or adsorption where relevant, sensor calibration, drift and response time, sterilisation state, biological viability and a predeclared interpretation model.

If the platform is used to compare treatments, randomisation and device-to-device variation should be included so that manufacturing variability is not mistaken for a biological treatment effect.

8. Engineering conclusions

A sensor-integrated organ-on-chip is simultaneously a microfluidic device, a biomaterial environment and a measurement system. The strongest designs treat calibration, material background and flow as part of biological interpretation rather than as separate engineering preliminaries. The qualification objective is traceable measurement: a signal change should remain attributable to a defined biological variable after material and instrument drift have been bounded.

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Competing interest

Juan Segurola is founder, CEO and CTO of 3Dresyns by Resyner Technologies S.L., which develops and commercialises photopolymer materials and related additive-manufacturing technologies. This review is an engineering analysis and does not constitute a product-performance claim or a device qualification.