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Bimodal MEMS Sensor Cartridge for Prediagnostic Evaluation of Pleural Effusion

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Summary:
This paper presents the design, fabrication, and integration of a compact (45x34x6 mm) bimodal microfluidic cartridge for the prediagnostic screening of pleural effusion. The system successfully integrates a MEMS-based sensor layer, featuring capacitive pressure and electrochemical LDH sensors, with a high-precision thermoformed styrenic block copolymer microfluidic layer. Adhering to ISO 22916 standards for inlet/outlet positioning and utilizing custom 3D-printed clamps for mechanical sealing, the platform demonstrates a robust and compact solution for multimodal biomarker detection.

Keywords: MEMS integration, Microfluidic cartridge, Bimodal sensing, Flexdym thermoforming, Prediagnostic platform

Background, Motivation and Objective

The accurate diagnosis of pleural effusion relies on the simultaneous analysis of multiple biomarkers, such as lactate dehydrogenase (LDH) activity and fluid viscosity, to distinguish between malignant and inflammatory conditions. Clinical studies indicate that viscosity levels above 1.6 mPa.s often signal severe infection, while levels below 1.4 mPa.s are associated with malignancy [1]. However, traditional in vitro diagnostic methods are time-consuming, require significant sample volumes, and typically assess a single biomarker at a time. This work addresses these limitations by developing a prediagnostic cartridge for the simultaneous measurement of LDH and viscosity from a small volume of pleural effusion sample, combining MEMS-based bimodal sensing with a compact microfluidic cartridge architecture.

Description of the New Method or System

The cartridge utilizes a four-layer architecture: a polymethyl methacrylate (PMMA) top cover, a thermoformed Flexdym microfluidic layer, a MEMS-produced sensor chip, and a PMMA support base. Each layer serves a distinct functional role, enabling delivery of pleural effusion samples to both sensing regions within a single integrated platform.

Integrated Sensor Layer: The core of the system is a bimodal sensor chip fabricated on a glass substrate using a specialized 10-step MEMS fabrication flow, integrating a Parylene-C based capacitive pressure sensor and gold/silver-based electrodes for electrochemical LDH activity measurement. Viscosity is assessed by measuring the pressure drop induced by sample flow through the serpentine microchannel, which is analytically related to fluid viscosity via the Hagen-Poiseuille framework and converted to a capacitance signal by the Parylene-C diaphragm [2]. Analytical modeling of the diaphragms was performed to ensure high sensitivity and linearity within the target 1.0-1.8 mPa.s viscosity range [3]. Electrochemical LDH detection is based on amperometric measurement of NADH oxidation, facilitated by a conducting polymer-modified electrode surface [4].

Microfluidic Channel Layer: The microfluidic network is produced from Flexdym, a biocompatible styrenic block copolymer (SBC), via a high-precision thermoforming process. This material provides excellent replication fidelity and inherent self-sealing properties when compared to traditional PDMS [5]. The channel layer features 100 µm wide serpentine geometries optimized for controlled sample delivery and the detection of viscosity-induced pressure drops. To ensure reliable electrochemical detection, phaseguide structures are incorporated into the reaction chambers to facilitate bubble-free wetting of the sensor electrodes, preventing signal artifacts. The channel geometry is replicated using a high-temperature Stereolithography (SLA) 3D-printed polymer insert as the thermoforming mold, enabling rapid tooling and precise feature transfer without the need for metal tooling.

Packaging and Integration: The entire assembly is secured by custom 3D-printed clamps that provide uniform mechanical pressure for leak-proof sealing without the need for permanent bonding or adhesives, as illustrated in Fig. 1. Precision alignment between layers is achieved through dedicated pockets machined into the PMMA layers via CNC milling. For fluidic operation, a magnetic interface integrates a Flexible Hydraulic Reservoir (FHR) pump, enabling dead-volume-free sample loading and precise flow control [6]. Port positions follow the ISO 22916 standard to ensure compatibility with other analysis platforms that conform to the same standard.

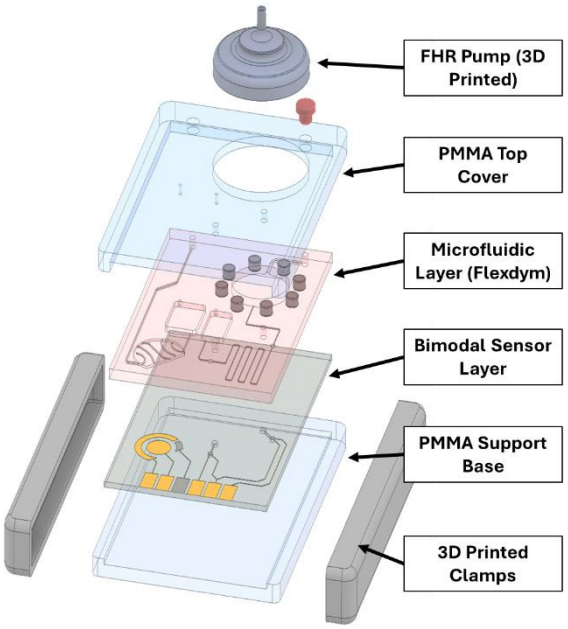


Fig. 1. Exploded view of the four-layer bimodal sensor cartridge architecture.

Results

The MEMS bimodal sensor chip, comprising the Parylene-C pressure sensor and electrochemical electrodes, was successfully fabricated and verified to be electrically functional prior to cartridge integration. The integration process successfully yielded a fully functional prediagnostic cartridge with portable dimensions of 45x34x6 mm, as shown in Fig. 2. Fabrication of the 100 µm microchannels in the Flexdym layer was verified using profilometry and electron microscopy, confirming high geometric fidelity with a mean surface roughness (Ra) of approximately 1.9 µm on channel walls. Sealing performance, facilitated by the elastic properties of the SBC layer and the mechanical pressure from the 3D-printed clamps, was confirmed to be completely leak-proof during operational flow tests. Furthermore, integrated phaseguide structures effectively ensured bubble-free filling of the sensor chambers, enabling reliable wetting of the electrodes even at varying flow rates. These results demonstrate a robust bimodal cartridge architecture capable of simultaneous multimodal biomarker detection from a single low-volume clinical sample.



Fig. 2. Photograph of the assembled bimodal sensor cartridge.

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