

Dynamic-Mode Microcantilever Biosensor: Detection Strategies and Recent Applications

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ABSTRACT: Microcantilever biosensors have attracted considerable attention as micro-electro-mechanical system (MEMS)-based sensing platforms because of their high mechanical sensitivity, label-free operation, and real-time detection capability. By directly converting biomolecular interactions into mechanical responses through surface stress or resonance-frequency shifts, microcantilever sensors enable highly sensitive, quantitative analysis without requiring fluorescent or enzymatic labels. This review summarizes recent advances in dynamic-mode microcantilever biosensors, focusing on their operating principles, excitation methods, and signal transduction techniques. Representative applications in nucleic acid, protein, and cell detection are discussed, highlighting recent developments in molecular recognition strategies and nanomaterial-assisted signal amplification. These advances have significantly improved analytical performance, enabling ultrasensitive detection from single-copy nucleic acids to picogram-level proteins and single-cell analysis. Despite this progress, several technical challenges still limit the practical application of microcantilever biosensors. Future advances in portable, integrated readout technologies; standardized, scalable fabrication; and multiplexed sensing are expected to facilitate the translation of microcantilever biosensors from laboratory-scale demonstrations to practical applications in clinical diagnostics, environmental monitoring, and food safety.

KEYWORDS: *Microcantilever, Biosensor, Dynamic mode, Nucleic acid detection, Protein detection, Cell detection*

1. INTRODUCTION

Cantilever structures have a long history in engineering, and cantilever beams have been widely used in mechanical and civil engineering because of their simple geometry and excellent load-bearing characteristics [1]. The rapid advancement of micro and nanofabrication technologies has profoundly influenced the development of mechanical structures with dimensions down to a few nanometers, allowing unprecedented control over geometry, mass, and mechanical properties [2]. Microcantilever structures have become attractive sensing platforms because of their simple fabrication process, high mechanical sensitivity, low power consumption, and compatibility with label-free detection [3]. Furthermore, microcantilever sensors can detect extremely

small forces, mass loading, and surface stress variations through static deflection or resonance frequency shifts [4]. Consequently, microcantilever sensors have established themselves as one of the most sensitive and versatile sensing platforms among existing sensor technologies [4].

A major advantage of microcantilever sensors is their ability to directly detect interaction forces between target analytes and the functionalized microcantilever surface [5]. Unlike electrical or optical sensors that primarily detect secondary effects such as charge transfer or refractive index changes, microcantilever sensors can directly measure surface stress and binding forces arising from molecular interactions. Recent force-sensitive cantilever studies have enabled quantitative analysis of intermolecular forces and adsorption-induced stress [6-12].

Microcantilever sensors can be operated in two modes: static and dynamic. In static mode, detection is based on surface stress-induced deflection, which is often disturbed by environmental fluctuations such as nonspecific adsorption and long-term thermal drift [4,5,13]. In contrast, dynamic-mode sensing transduces biomolecular interactions into resonance frequency shifts, enabling direct, quantitative detection of mass loading with significantly improved signal-to-noise

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ratios. The signal from a dynamic-mode microcantilever sensor is less affected by low-frequency noise and baseline drift, allowing stable and reproducible measurements compared with static mode [4,5]. Consequently, dynamic-mode operation has become a preferred sensing strategy for microcantilever-based biosensors because of its sensitivity, robustness, and quantitative reliability [5].

Microcantilever sensors can detect a wide range of biological species, from small biomolecules to whole cells. By functionalizing the cantilever surface with specific recognition elements such as DNA probes, antibodies, or aptamers, the sensors can selectively detect nucleic acids (DNA and RNA) [14-16], proteins [17-21], and even single cells [22-24]. The microcantilever sensors can measure simple presence or concentration, like other types of sensors. However, the sensors are also able to measure surface stress, binding-induced mass loading, and viscoelastic or mechanical property changes associated with biomolecular interactions, which could not be achieved with other types of sensors such as electrical and optical sensors [25]. This unique detection capability enables microcantilever-based platforms to perform biosensing across molecular-to-cellular scales, highlighting their potential for diverse biosensing applications.

In this review, we provide a comprehensive overview of recent researches of microcantilever-based biosensors published after 2020, focusing on detection strategies and representative biological applications. First, we describe the fundamental operating principles of dynamic sensing modes, followed by a discussion of mechanical excitation methods and signal transduction techniques. Finally, we discuss recent applications of microcantilever biosensors and current challenges, offering perspectives on future directions in biomedical diagnostics, environmental monitoring, and fundamental biological studies.

2. DETECTION STRATEGIES

2.1 Detection Mechanism

The resonance frequency of a microcantilever is a fundamental mechanical property determined primarily by its effective stiffness and effective mass [26]. For a simple rectangular cantilever beam with small thickness, the resonance frequency can be approximated using the classical elastic continuum model as below:

$$f_n = \frac{\lambda_n^2}{2\pi L^2} \sqrt{\frac{EI}{\rho A}} \quad (1)$$

where f_n is the resonance frequency of the n th mode, λ_n is the dimensionless eigenvalue determined by the boundary

conditions, L , E , I , ρ , and A are the length, Young's modulus, cross-sectional moment of inertia, mass density, and cross-sectional area of the microcantilever, respectively. Eq. (1) can be simplified using the effective stiffness and effective mass as below:

$$f_0 = \frac{1}{2\pi} \sqrt{\frac{k_{\text{eff}}}{m_{\text{eff}}}} \quad (2)$$

where f_0 is the fundamental resonance frequency, k_{eff} is the effective stiffness, and m_{eff} is the effective mass of the cantilever. From the equation, the resonance frequency increases with greater stiffness and decreases with increasing mass. In biosensing applications, this dependence underpins the detection mechanism of a dynamic-mode sensor. For instance, when target analytes bind to the surface of the cantilever, the additional mass leads to a measurable decreased resonance frequency (Fig. 1). Specifically, the resonance frequency scales inversely with the cantilever length and directly with its thickness, indicating that shorter cantilevers can achieve higher resonance frequencies [27]. Reducing the cantilever dimensions can also improve mass sensitivity by decreasing its effective mass. Material properties such as density and elastic modulus also influence the cantilever's dynamic behavior. However, these properties are generally fixed because microcantilevers are predominantly fabricated from silicon and silicon nitride using semiconductor manufacturing processes, as well as polymers, piezoelectric materials, and diamond-based materials compatible with semiconductor manufacturing processes.

In dynamic-mode biosensing, resonance frequency serves as the primary sensing parameter for detection in response to mass loading on the cantilever surface. When target analytes

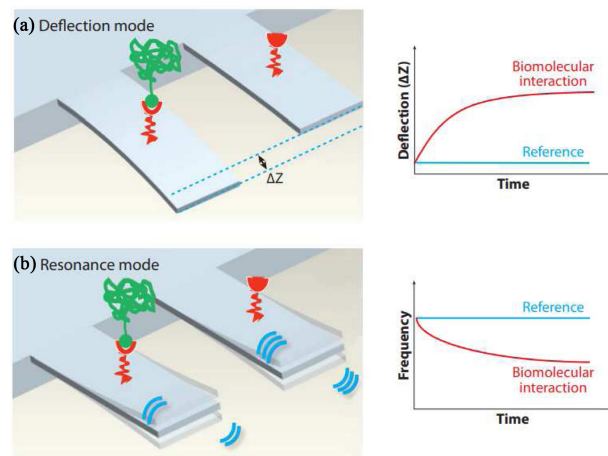


Fig. 1. Two modes of microcantilever based biomolecule detection. (a) deflection(static) mode. (b) dynamic mode. Adapted from Ref. [13].

bind to receptors immobilized on the cantilever, the effective mass increases, resulting in a measurable frequency shift that can be correlated quantitatively with the amount of bound analyte. Beyond simple mass effects, the viscoelastic properties of the adsorbed biological layer can also modify effective stiffness and damping, influencing resonance behavior [4,27].

2.2 Mechanical Excitation Method

The resonance frequency of a microcantilever is measured with controlled excitation of the cantilever and monitoring of its vibrational response. Several actuation methods are commonly employed. Piezoelectric base excitation is one of the simplest techniques, in which a piezoelectric actuator mechanically vibrates the cantilever substrate, as shown in Fig. 2 [28,30]. The substrate then transfers energy to the cantilever, causing it to oscillate near its resonance frequency. A major advantage of this method is its ease of implementation. However, this method may introduce additional substrate resonances in liquid environments, affecting the detection signal.

Electrothermal actuation relies on periodic Joule heating of an integrated resistive element within or near the cantilever [30]. The resulting thermal expansion generates bending oscillations (Fig. 3). This approach allows compact on-chip integration but may induce thermal drift, requiring careful experimental preparation and control. Magnetic actuation is achieved by coating the cantilever with a thin magnetic layer and applying an external oscillating magnetic field [31]. In detail, the magnetic torque drives cantilever oscillation without mechanically disturbing the substrate, improving performance in liquid media. The electrostatic technique uses an applied AC voltage between the cantilever and a nearby electrode to generate an oscillatory electrostatic force [32,33]. This method

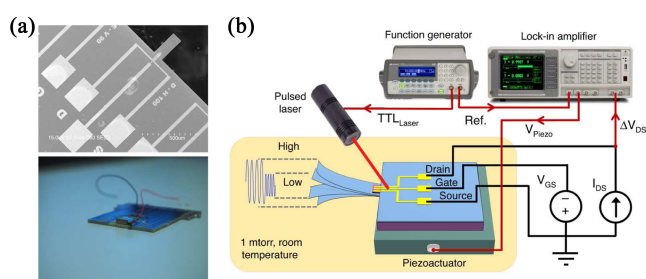


Fig. 2. Microcantilever excitation using piezoelectric base. (a) SEM image of the microcantilever (top) and photo of the piezo actuator attached underneath the microcantilever chip (bottom). (b) Schematic diagram of the experimental setup showing simultaneous piezo chip and photoacoustic excitation. Adapted from Ref. [28].

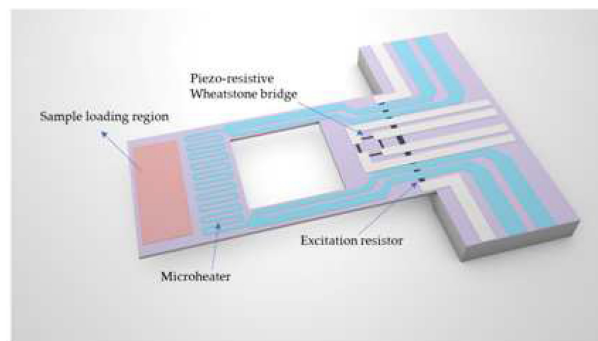


Fig. 3. Schematic diagram of a microcantilever excitation using an electrothermal actuation method. Adapted from Ref. [30].

is widely used in micro-electro-mechanical systems (MEMS) due to its low power consumption and compatibility with electronic circuit integration. Photothermal excitation employs a modulated laser beam to periodically heat the cantilever surface, inducing localized thermal expansion and vibration. This technique provides resonance excitation with minimal mechanical coupling to the environment and is particularly advantageous for liquid-phase biosensing.

2.3 Mechanical Response Measurement

For microcantilever sensors, the mechanical response readout mechanism converts the mechanical response into measurable electrical or optical signals, enabling precise measurement of resonance frequency in each state. Readout performance influences sensor characteristics such as sensitivity, resolution, and system integration. Among the various techniques, optical and electrical transduction are the most commonly used approaches. Optical beam deflection is a standard approach in laboratory-based systems [34]. In this configuration, a laser beam is focused onto the edge of the cantilever, and a position-sensitive photodetector detects the reflected beam (Fig. 4). Mechanical motion induces angular deflection of the reflected beam, which the photodetector converts into a voltage signal proportional to cantilever displacement. This technique provides high displacement sensitivity and wide bandwidth, although it requires precise optical alignment and external instrumentation.

Laser Doppler vibrometry (LDV) is another optical readout technique that measures cantilever vibration based on the Doppler frequency shift of the reflected laser beam. This non-contact method provides highly sensitive vibration measurements and enables accurate determination of the resonance frequency. Electrical transduction methods convert microcantilever response into electrical signals. Common approaches include piezoresistive, piezoelectric,

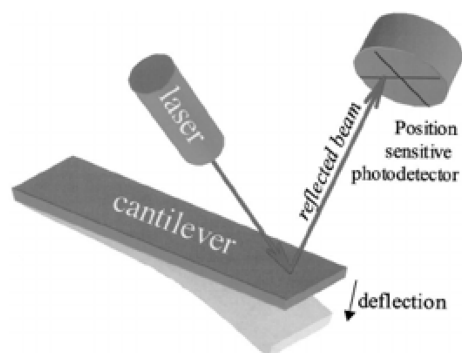


Fig. 4. Schematic diagram of a microcantilever mechanical response measurement using an optical method. Adapted from Ref. [34].

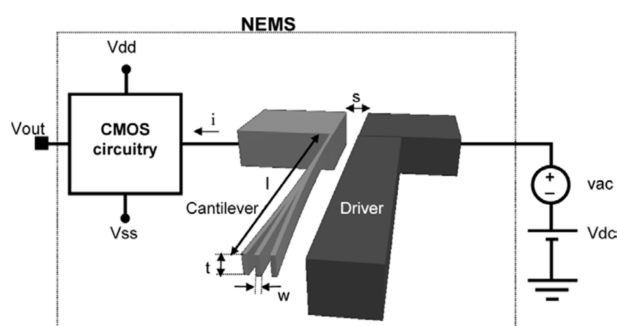


Fig. 5. Schematic diagram of a microcantilever mechanical response measurement using a capacitive method. Adapted from Ref. [37].

and capacitive-based methods [35-37]. Piezoresistive methods detect strain-induced resistance changes, piezoelectric methods generate electrical charges during deformation, and capacitive methods measure changes in electrode capacitance (Fig. 5). These methods offer advantages such as miniaturization, low-cost semiconductor integration, array compatibility, and portability compared with conventional optical readout systems. However, thermal drift, electrical noise, parasitic capacitance, and electromagnetic interference can degrade detection performance.

3. RECENT RESEARCH

Microcantilever biosensors have emerged as one of the most promising MEMS-enabled sensing platforms for the label-free, highly sensitive detection of biological species. Fritz et al. first demonstrated a microcantilever biosensor in 2000, translating DNA hybridization into measurable nanomechanical surface stress and establishing the foundation for label-free microcantilever biosensing [38]. Since then, microcantilever biosensors have evolved considerably, enabling sensitive, label-free detection of diverse biological targets, including

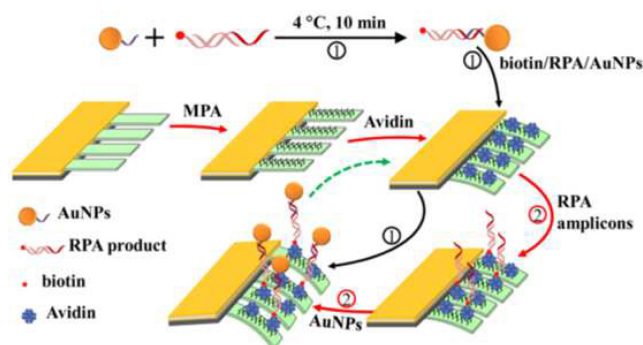


Fig. 6. Schematic diagram of DNA detection using microcantilever with AuNPs. Adapted from Ref. [40].

nucleic acids, proteins, and cells. More recently, researchers have combined microcantilever biosensors with nanomaterials such as graphene, carbon nanotubes, and gold nanoparticles to increase surface area and amplify signals [39]. Integration with molecular recognition systems has further enhanced sequence specificity and enabled ultrasensitive detection of biological targets.

Microcantilever biosensors have demonstrated excellent potential as nucleic acid detection platforms. Lei et al. developed a dynamic-mode microcantilever integrated with recombinase polymerase amplification (RPA) and gold nanoparticles (AuNPs) for ultrasensitive detection of the plant pathogen *Leptosphaeria maculans*, as shown in Fig. 6 [40]. Unlike conventional biosensors integrated with nucleic acid assays such as polymerase chain reaction (PCR) that rely on optical or electrochemical labels, microcantilever sensors directly convert biomolecular recognition events into measurable mechanical signals. Although the platform supports both static and dynamic operation, the dynamic mode was employed as the primary sensing mechanism by monitoring resonance frequency shifts induced by mass loading and stiffness changes after target binding. The cantilever was actively excited using a piezoelectric crystal, while the optical readout system tracked the cantilever motion. Sequential binding of biotin-labeled RPA amplicons and complementary DNA-functionalized 20 nm AuNPs significantly amplified the resonance frequency shift, leading to a detection limit of approximately one copy of genomic DNA, which is more sensitive than conventional fluorescence RPA. The assay also detected 57 ppm of *L. maculans* genomic DNA in field samples, demonstrating excellent sensitivity, specificity, and suitability for rapid on-site plant pathogen diagnostics.

Microcantilever biosensors have demonstrated excellent performance for protein biomarker detection. Zhao et al. developed a dynamic-mode microcantilever using AuNPs as a

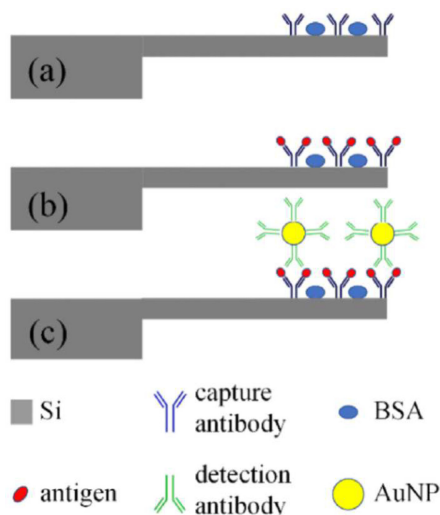


Fig. 7. Schematic diagram of protein biomarker detection using a microcantilever. (a) Microcantilever surface functionalization using capture antibodies and BSA. (b) Specific binding of target antigens to the capture antibodies. (c) AuNP-assisted target detection for signal amplification. Adapted from Ref. [41].

mass amplifier for highly sensitive detection of the protein biomarker alpha-fetoprotein (AFP) [41]. The sensor operated with a piezoelectric transducer for mechanical excitation under vacuum. The optical system measured the mechanical response. For detection, antibody probes were functionalized on the microcantilever surface to bind AFP specifically (Fig. 7). AuNP-conjugated detection antibodies were then introduced to form a sandwich immunoassay. The AuNP-assisted sandwich immunoassay enhanced the resonance frequency response from approximately 2 Hz to 140 Hz for 20 ng/mL AFP, increasing the sensor sensitivity from 7.68 Hz/nM to 412 Hz/nM and reducing the limit of detection (LOD) from 1.1 ng/mL to 21 pg/mL. Integrating microcantilevers with AuNP-based sandwich immunoassays dramatically enhanced mass-loading sensitivity while maintaining high reproducibility, demonstrating strong potential for early clinical diagnosis of protein biomarkers.

Microcantilever biosensors have demonstrated outstanding capabilities for cell detection by combining label-free sensing, high sensitivity, real-time monitoring, and compatibility with microfluidic and array-based platforms. Incaviglia et al. optimized microcantilevers for single adherent mammalian cell mass measurements by reducing cantilever inertial mass through focused ion beam (FIB) modification, as shown in Fig. 8 [42]. The redesigned cantilevers exhibited over 70% improvement in signal-to-noise ratio and picogram mass sensitivity, with significantly reduced measurement errors caused by cell migration. Fathy and Lai developed a dynamic

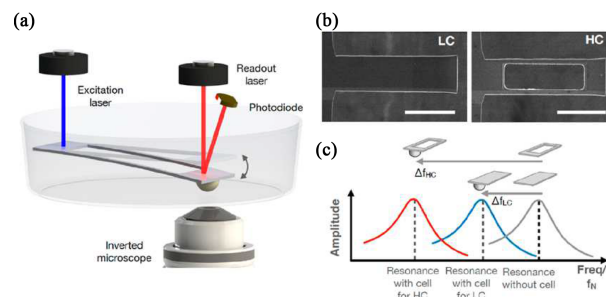


Fig. 8. Microcantilever for cell detection. (a) Schematic diagram of cell detection using microcantilever. (b) Top view SEM images of rectangular (LC) and FIB-modified (HC) microcantilevers. Scale bars, 50 μm . (c) The resonance frequency shift of each microcantilever state upon cell attachment. Adapted from Ref. [42].

V-shaped microcantilever integrated with dielectrophoretic (DEP) particle enrichment for real-time *E. coli* detection [43]. The sensor detected bacterial concentrations ranging from 10^3 to 10^5 cells/mL within 4 min, producing frequency shifts of -755 to -2264 Hz. More recently, Qiao et al. introduced a graphene oxide-assisted magnetic nanomechanical microcantilever array that substantially improved mechanical signal amplification [44]. The platform achieved single bacterial cell detection without culture, maintained a linear detection range of 1–100 CFU/mL, enabled simultaneous detection of multiple bacterial species, and demonstrated excellent specificity, reproducibility, stability, and resistance to interference in complex samples such as milk.

4. CHALLENGES AND PERSPECTIVES

Despite their high sensitivity and label-free detection capability, microcantilever biosensors have not achieved widespread adoption comparable to mature MEMS devices such as accelerometers. One major limitation, particularly for dynamic-mode sensing, is operation in liquid environments. Biological reactions generally require aqueous conditions. The surrounding liquid introduces hydrodynamic added mass and viscous damping, which decrease the resonance frequency, broaden the resonance peak, and consequently reduce frequency resolution and mass sensitivity [45]. Furthermore, variations in temperature, fluid density, and viscosity can cause resonance-frequency drift independent of target binding, resulting in false or nonspecific sensor responses. However, differential measurements using reference cantilevers and temperature compensation can reduce these effects, although these approaches increase system complexity.

The intrinsic mechanical response generated by biomolecular binding can be extremely small, particularly for

Table 1. Comparison of sensor performance of representative dynamic-mode microcantilever biosensors.

Study	Target	Excitation/ Readout method	LOD	Real-sample validation
Lei et al. (2021)	<i>Leptosphaeria maculans</i> DNA	Piezoelectric/Optical	57 ppm	plant/seed samples
Zhao et al. (2021)	Alpha-fetoprotein (AFP)	Piezoelectric/Optical	21 pg/mL	None
Incaviglia et al. (2023)	Single adherent living cells: HeLa and mouse fibroblasts	Photothermal/Optical	N/R	living HeLa cells and mouse fibroblast lines
Fathy and Lai (2022)	<i>E. coli</i> K-12	Piezoelectric/Optical	10 ³ cells/mL	None

N/R: not reported

targets with low molecular weight and low target concentrations. Recent studies have therefore increasingly employed mass amplification strategies using AuNPs, enabling approximately 70-fold improvement in the detection limit for AFP (Table 1) and significantly enhanced measurement reproducibility by increasing the specific signal above thermal noise and nonspecific adsorption [41]. Similarly, combining RPA with AuNP-assisted mass loading has enabled nucleic acid detection down to approximately a single DNA copy [40]. These approaches demonstrate the exceptional sensitivity achievable by microcantilever platforms; however, they also introduce additional labeling, reaction, and sample-preparation steps, partially compromising the inherent simplicity and label-free nature of mechanical sensing. Therefore, alternative amplification strategies that maintain simple assay procedures while ensuring sufficiently strong and reproducible mechanical responses are required.

Furthermore, conventional optical readout requires bulky instrumentation and precise alignment, limiting system miniaturization [34]. Future development should therefore focus on standardized, scalable MEMS fabrication; robust surface functionalization; integrated readout and microfluidics; and multiplexed cantilever arrays. Greater validation using complex real-world samples will also be essential to translate microcantilever biosensors into reliable clinical diagnostics, environmental monitoring, and food safety applications.

5. CONCLUSIONS

Microcantilever biosensors have emerged as highly sensitive and versatile MEMS-based sensing platforms that translate biomolecular interactions into measurable mechanical signals. Recent advances in dynamic-mode sensing and signal transduction have significantly improved the detection of diverse biological targets, including nucleic acids, proteins, and cells, enabling rapid, real-time, and quantitative analysis with high sensitivity and specificity. In particular, incorporating nanomaterials, advanced molecular recognition strategies, and array-based configurations has substantially enhanced

analytical performance. Despite these advances, several challenges remain for practical implementation, including performance degradation in liquid environments, weak mechanical responses to low-mass targets, and limitations in system integration and standardization. Signal amplification, surface functionalization, and microfluidic integration have addressed some of these limitations; however, further improvements are required to achieve robust, reproducible, and simplified sensing platforms.

In addition, conventional optical readout systems require relatively bulky and expensive instrumentation, limiting portability and point-of-care applications, whereas electrical transduction provides a compact alternative but may suffer from lower sensitivity and electrical noise. Large-scale integration, multiplexed detection, device standardization, and scalable manufacturing also remain important barriers to commercialization. Therefore, future research should focus on improving signal stability and device robustness, developing compact, integrated readout systems, integrating microfluidics and on-chip electronics, and establishing standardized, scalable fabrication processes. Advances in these areas, together with enhanced multiplexing capabilities and validation using complex real-world samples, will be essential for translating microcantilever biosensors from laboratory-scale demonstrations into practical platforms for clinical diagnostics, environmental monitoring, and food safety.

CRediT Authorship Contribution Statement

Kuewhan Jang: Writing - review & editing.

Declaration of Competing Interests

The authors declare no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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