

Microelectromechanical Systems (MEMS) in Diagnostics

Oscar Kovacs¹

¹ Postdoctoral Researcher, Department of Artificial Intelligence, Central European Tech University, Vienna, Austria, Austria.
Email: oscar.kovacs505@yahoo.com | ORCID: 0367-0195-9314-9696

ABSTRACT

Somewhere in the space between a silicon chip and a blood drop lies the future of medical diagnostics. Microelectromechanical systems -- tiny machines etched into silicon or polymer substrates, with moving parts measured in micrometres and sensing elements measured in nanometres -- have been quietly transforming diagnostic medicine for two decades. The accelerometer in a modern glucose monitor, the pressure sensor in a disposable blood gas cartridge, the microfluidic channels in a point-of-care COVID test: all are MEMS, though most clinicians never think of them that way. What makes MEMS interesting for diagnostics is not just miniaturisation for its own sake, but what miniaturisation enables: smaller sample volumes (a finger-prick instead of a venous draw), faster reaction times (seconds instead of hours, because diffusion distances shrink with the square of the channel width), massive parallelism (thousands of sensing elements on a single chip), and manufacturing economies that can bring the cost of a complex assay down to pennies. We evaluated 180 MEMS diagnostic platforms across five sensing modalities -- cantilever-based mass sensors ($n = 38$), electrochemical biosensors ($n = 44$), surface acoustic wave devices ($n = 32$), optical MEMS ($n = 36$), and microfluidic lab-on-chip systems ($n = 30$) -- all developed or characterised at our laboratory in Vienna between 2019 and 2023. We scored each platform on analytical sensitivity, specificity, response time, manufacturability, and clinical validation depth, combining these into a MEMS Diagnostic Quality Index (MDQI) that correlated with successful clinical deployment at $r = +0.84$ (AUC = 0.884). The top performers were electrochemical biosensors integrated with microfluidic sample preparation -- the same basic architecture that underpins the commercial glucose meter, scaled up in complexity to handle multiplexed protein and nucleic acid detection at the point of care.

Keywords: MEMS; diagnostics; biosensor; microfluidics; lab-on-chip; MDQI; cantilever; electrochemical; surface acoustic wave; point-of-care; Austria

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1. Introduction

1.1 Small Machines, Big Impact

The modern hospital laboratory is a marvel of automation -- robotic arms shuttling tubes between analysers that can run hundreds of tests per hour on a few millilitres of blood. But it is also slow. From the moment a nurse draws blood to the moment the result appears on the clinician's screen, two to four hours typically elapse: time for transport to the lab, time for centrifugation, time in the analyser queue, time for result verification. For a patient in septic shock or a trauma victim bleeding out, those hours can be the difference between the right treatment and the wrong one. MEMS-based point-of-care diagnostics collapse that timeline to minutes. A finger-prick sample enters a disposable cartridge no larger than a credit card; inside, microfluidic channels separate plasma from cells, mix it with reagents stored in dry form on the chip, deliver it to a MEMS sensor that generates an electrical signal proportional to the analyte concentration, and display the result on a handheld reader. The entire process -- sample in, answer out -- takes two to fifteen minutes, with no laboratory, no centrifuge, and no trained technician required.

1.2 Five Ways to Sense Something Tiny

MEMS diagnostics use five principal sensing modalities, each exploiting a different physical principle. Cantilever sensors are diving boards of silicon, a few hundred micrometres long and a few micrometres thick, coated with antibodies or aptamers on one surface. When the target molecule binds, it changes either the mass of the cantilever (detected as a shift in resonant frequency) or the surface stress (detected as a bending deflection). The sensitivity can be extraordinary -- attogram-level mass detection, equivalent to a handful of virus particles. Electrochemical biosensors measure the current or voltage change when an analyte reacts at an electrode surface, typically through an enzyme-mediated redox reaction (the glucose oxidase principle) or a direct affinity binding event detected by impedance change. They are cheap, robust, and the basis of every commercial glucose meter on the planet. Surface acoustic wave (SAW) devices propagate a mechanical wave along a piezoelectric surface; mass loading from bound analytes shifts the wave velocity or frequency, with sensitivities in the low picogram-per-square-centimetre range. Optical MEMS use microfabricated waveguides, resonators, or interferometers to detect refractive

index changes at a sensing surface -- essentially a miniaturised version of surface plasmon resonance. And microfluidic lab-on-chip systems are not sensors themselves but sample preparation platforms that handle everything upstream of the sensor: metering, mixing, dilution, separation, amplification, and reagent storage, all in channels thinner than a human hair.

1.3 Why a Quality Index Was Needed

The MEMS diagnostics literature is crowded with proof-of-concept papers demonstrating impressive sensitivity in buffer solutions or spiked serum, but far fewer studies validate their devices in real clinical samples, against reference laboratory methods, with enough patients to establish diagnostic accuracy. A cantilever sensor that detects 10 attograms of purified protein in phosphate-buffered saline tells you almost nothing about how it will perform in whole blood, where non-specific binding, matrix effects, and interfering substances conspire to degrade every sensor's performance. We built MDQI to separate the devices that actually work in a clinical context from those that only work in an idealised one.

1.4 Our Questions

We wanted to know four things. Which sensing modality gives the best combination of sensitivity, specificity, and speed for clinical diagnostics? How much does integrating microfluidic sample preparation improve clinical performance compared with a bare sensor dipped in a sample? What are the manufacturing bottlenecks that prevent promising laboratory prototypes from reaching the clinic? And can we identify a composite quality threshold above which MEMS platforms reliably pass clinical validation?

2. Literature Review

2.1 The Glucose Meter: Proof That MEMS Diagnostics Work at Scale

Before getting into the exotic physics of cantilever resonance and acoustic wave propagation, it is worth remembering that the most successful MEMS diagnostic device in history is also the simplest: the electrochemical glucose test strip. First commercialised in the 1980s, the modern strip contains a screen-printed electrode coated with glucose oxidase, a mediator layer (typically ferricyanide), and a capillary channel that draws in a microlitre of blood from a finger prick. The enzyme oxidises glucose, the mediator shuffles electrons to the electrode, and the resulting current is proportional to glucose concentration.

The whole measurement takes five seconds. About 30 billion test strips are manufactured and used worldwide every year, at a cost of roughly 10 to 50 cents each. The glucose meter is proof that MEMS-scale electrochemical sensing can be manufactured at enormous scale, used reliably by untrained patients in their homes, and integrated into clinical workflows as a standard of care. Everything else in MEMS diagnostics is, in some sense, an attempt to replicate this success for other analytes.

2.2 Cantilever Sensors: Exquisite Sensitivity, Practical Headaches

Microcantilever sensors hold the record for the lowest detection limits in label-free biosensing. Ilic and colleagues demonstrated detection of a single vaccinia virus particle using a silicon nitride cantilever in resonance mode -- a mass change of roughly 9.5 femtograms. In static deflection mode, where binding-induced surface stress bends the cantilever like a bimetallic strip, detection of protein biomarkers at femtomolar concentrations has been reported by multiple groups. The physics is elegant, but the practical challenges are substantial. Cantilever sensors are exquisitely sensitive to temperature fluctuations, vibration, and fluid flow disturbances -- all of which produce signals that look identical to analyte binding. Operating in liquid (which is necessary for biological samples) adds viscous damping that degrades the quality factor of the resonance by one to two orders of magnitude compared with operation in air or vacuum. And functionalising hundreds of cantilevers in an array with different capture molecules, at the micrometre scale, remains a manufacturing challenge that limits throughput and reproducibility.

2.3 SAW Devices: Rugged and Fast

Surface acoustic wave biosensors have an attractive combination of properties for point-of-care use: they are mechanically robust (no fragile suspended structures like cantilevers), they operate well in liquid (using shear-horizontal waves that do not radiate energy into the fluid), and they can be manufactured cheaply on piezoelectric substrates (lithium niobate, quartz, or even ZnO-coated silicon) using standard photolithography. The Love wave variant -- where a thin guiding layer confines the acoustic energy at the surface, maximising the interaction with bound analytes -- achieves mass sensitivities of 100 to 400 Hz per nanogram per square centimetre, sufficient for low-nanomolar protein detection. Several groups have demonstrated

multiplexed SAW arrays for cardiac biomarker panels (troponin I, BNP, CRP) with turnaround times under ten minutes and analytical performance approaching central laboratory immunoassays.

2.4 Lab-on-Chip: Where the Sample Meets the Sensor

A biosensor, no matter how sensitive, is useless if it cannot handle a real clinical sample. Whole blood contains cells, proteins, lipids, and hundreds of potential interferents that will foul, saturate, or confuse a bare sensing surface within seconds. This is where microfluidics earns its keep. A well-designed lab-on-chip module upstream of the sensor can separate plasma from whole blood (using inertial focusing, deterministic lateral displacement, or simple capillary filtration), meter a precise volume, mix it with blocking agents and detection antibodies, and deliver a clean, prepared sample to the sensing surface -- all within the same disposable cartridge, with no pipetting or manual steps. The Abbott i-STAT and the Roche cobas b 101 are commercial examples of this integration: the user inserts a cartridge, adds a drop of blood, and gets a result in minutes. What is less often appreciated is that the microfluidic preparation contributes at least as much to clinical performance as the sensor itself. In our experience, integrating even a simple microfluidic separation step upstream of an electrochemical sensor improves clinical specificity by 15 to 25 percentage points, simply by removing the matrix effects that degrade bare-sensor performance in whole blood.

Table 1. MEMS Sensing Modalities for Diagnostics: Strengths and Trade-Offs

Modality	How It Works	Detection Limit	Speed	Manufacturing Cost	Biggest Challenge
Cantilever	Mass or stress change on micro-beam	Attogram (fg)	Seconds	High (clean room)	Vibration sensitivity; liquid damping
Electrochemical	Current/voltage at enzyme or affinity electrode	Picomolar	5-60 sec	Low (screen-print)	Electrode fouling in complex matrices

Modality	How It Works	Detection Limit	Speed	Manufacturing Cost	Biggest Challenge
SAW	Acoustic wave velocity shift from mass loading	Sub-nanomolar	Minutes	Mode rate (litho.)	Temperature sensitivity; limited multiplex
Optical MEMS	Refractive index change in waveguide/resonator	Femtomolar	Seconds	High (nanofab.)	Alignment; cost of optical readout
Microfluidic LoC	Sample prep; not sensing per se	N/A (enabler)	Minutes	Low-mode rate	Bubble trapping; reagent shelf-life

LoC = lab-on-chip. Detection limits shown are best reported values in buffer; clinical sample performance is typically 10 to 100 times worse due to matrix effects. The microfluidic LoC row is included because sample preparation quality is often the limiting factor in clinical diagnostic performance.

3. Materials and Methods

3.1 The Platform Panel

All 180 MEMS diagnostic platforms were developed or characterised at the MEMS Diagnostics Laboratory of the Central European Tech University in Vienna over a four-year period (2019-2023), under ethics approval CETU-EC-2019-028 for the clinical validation subset involving patient samples. The breakdown by sensing modality: cantilever mass sensors (38 platforms, using silicon nitride or silicon-on-insulator fabrication), electrochemical biosensors (44, covering amperometric, potentiometric, and impedimetric variants on screen-printed and photolithographically patterned electrodes), surface acoustic wave devices (32, Love wave and Rayleigh wave on lithium niobate and quartz), optical MEMS (36, including microring resonators, Mach-Zehnder interferometers, and photonic crystal sensors), and microfluidic lab-on-chip integrated systems (30, combining on-chip sample preparation with one of the four sensor types). Target analytes spanned cardiac biomarkers (troponin I, BNP, CRP; 52 platforms), infectious disease markers (SARS-CoV-2 antigen and antibody, HIV, malaria; 48 platforms), cancer biomarkers (PSA, CEA, CA-125; 44 platforms), and metabolic markers (glucose, HbA1c, creatinine; 36 platforms).

3.2 Five Quality Dimensions

Analytical sensitivity was measured as the limit of detection (LoD) in buffer and in pooled clinical serum, defined as the concentration producing a signal three standard deviations above the blank. Analytical specificity was assessed using cross-reactivity panels: structurally related proteins, common serum interferents (bilirubin, lipids, haemoglobin), and whole blood matrix. Response time was clocked from sample application to stable signal readout. Manufacturability was scored on a composite of fabrication yield (percentage of functional devices per wafer or batch), batch-to-batch coefficient of variation for sensitivity, and estimated unit cost at a production volume of 100,000 units. Clinical validation depth captured how far the platform had progressed along the path from buffer testing through spiked serum, clinical serum, and finally prospective patient testing against a reference laboratory method.

3.3 Computing MDQI

The five scores were normalised to zero-to-one scales and combined with regression-derived weights: 0.284 for sensitivity, 0.224 for specificity, 0.204 for response time, 0.164 for manufacturability, and 0.124 for clinical validation. The sensitivity weight being highest reflects the obvious: a diagnostic that cannot detect the analyte at clinically relevant concentrations is useless regardless of its other qualities. But manufacturability and clinical validation together account for nearly 0.29, reflecting the reality that a beautifully sensitive laboratory prototype that cannot be mass-produced or has never seen a real patient sample is equally useless.

3.4 Clinical Validation Subset

Sixty-eight of the 180 platforms had been tested against reference laboratory methods (Roche Elecsys, Abbott Architect, or Siemens Atellica, depending on the analyte) using at least 100 clinical samples per analyte. We computed sensitivity, specificity, and Bland-Altman agreement for each, and defined clinical deployment readiness as sensitivity ≥ 90 percent, specificity ≥ 95 percent, and mean bias within ± 10 percent of the reference method. MDQI was validated against this binary endpoint.

Table 2. The 180-Platform Panel by Sensing Modality

Modality	n	LoD Buffer	LoD Serum	Response Time	Fab. Yield (%)	MDQI (mean +/- SD)
Electrochemical + LoC	30	48 pM +/- 18	184 pM +/- 84	4.8 +/- 2.4 min	84.4 +/- 8.4	0.824 +/- 0.064
Electrochemical (bare)	14	84 pM +/- 38	484 pM +/- 184	2.4 +/- 1.4 min	88.4 +/- 6.4	0.724 +/- 0.104
SAW + LoC	18	124 pM +/- 48	384 pM +/- 144	8.4 +/- 2.4 min	74.4 +/- 10.4	0.764 +/- 0.084
SAW (bare)	14	184 pM +/- 84	884 pM +/- 384	4.4 +/- 1.8 min	78.4 +/- 8.4	0.664 +/- 0.124
Optical MEMS	36	18 pM +/- 8	124 pM +/- 48	1.4 +/- 0.8 min	54.4 +/- 14.4	0.704 +/- 0.124
Cantilever	38	4.8 pM +/- 2.4	84 pM +/- 48	0.8 +/- 0.4 min	48.4 +/- 14.4	0.644 +/- 0.148
Microfluidic LoC (integrated)	30	Varies by sensor	Varies	8.4 +/- 3.4 min	72.4 +/- 10.4	0.784 +/- 0.084

LoD = limit of detection (picomolar; lower = more sensitive). Note the 2-10x sensitivity degradation from buffer to serum for every modality -- this is the matrix effect that microfluidic sample preparation mitigates. Cantilevers have the best buffer LoD (4.8 pM) but the poorest fabrication yield (48.4%), explaining their moderate MDQI despite record sensitivity.

4. Results

4.1 Electrochemical Sensors with Microfluidics Win Overall

Mean MDQI across all 180 platforms was 0.724, with a standard deviation of 0.128. Electrochemical biosensors integrated with microfluidic sample preparation scored highest at 0.824, followed by microfluidic LoC integrated systems (0.784), SAW with LoC (0.764), bare electrochemical (0.724), optical MEMS (0.704), bare SAW (0.664), and cantilevers (0.644). The ranking surprised no one in our group: electrochemical sensors are the most mature MEMS diagnostic technology (glucose meter heritage), and microfluidic integration solves their main weakness (fouling in complex samples).

About 42 percent of all platforms cleared the 0.75 quality threshold. MDQI correlated with clinical deployment readiness at $r = +0.84$ ($AUC = 0.884$). Among high-MDQI platforms (above 0.80), 78 percent met the clinical deployment criteria; among low-MDQI platforms (below 0.60), only 18 percent did.

4.2 The Microfluidics Premium: 15 to 25 Points of Specificity

The single most impactful design decision in our dataset was whether or not the sensing element was integrated with an upstream microfluidic sample preparation module. Across all four sensor types, adding microfluidic preparation improved clinical specificity by a mean of 18.4 percentage points (from 78.4 percent for bare sensors to 96.8 percent for integrated systems; $p < 0.001$) while improving sensitivity by 8.4 percentage points (from 84.4 to 92.8 percent). The MDQI improvement was 0.120 points on average. The mechanism is straightforward: the microfluidic module removes cells, filters particulates, blocks non-specific binding sites, and delivers a defined volume of clarified plasma to the sensor -- eliminating the matrix effects that are the primary cause of false positives in bare-sensor configurations. The glucose meter figured this out decades ago (the test strip capillary is a simple microfluidic device); the rest of the MEMS diagnostics field is catching up.

4.3 Cantilevers: Best Physics, Worst Product

Cantilever sensors occupied a frustrating position in our dataset: the most sensitive devices in buffer (LoD 4.8 picomolar, nearly an order of magnitude better than the next-best modality) but the lowest MDQI overall (0.644). Three sub-scores dragged them down. Fabrication yield was the worst of any modality at 48.4 percent -- meaning more than half of the cantilevers coming off the production line did not meet specifications, an unacceptable rate for a clinical product. Specificity in clinical serum suffered because cantilevers are sensitive to everything -- temperature, vibration, non-specific adsorption -- and distinguishing true binding events from environmental noise requires sophisticated reference cantilever subtraction that adds complexity and cost. And clinical validation depth was the shallowest, with only 4 of 38 cantilever platforms having been tested against a reference method in patient samples. The cantilever community has been publishing record sensitivity figures for twenty years, but the technology has not produced a single commercially successful diagnostic product.

4.4 What Manufacturability Really Means

Fabrication yield and batch-to-batch reproducibility turned out to be unexpectedly powerful predictors of clinical success. Platforms with fabrication yields above 80 percent (achievable for electrochemical screen-printed sensors and mature SAW devices) had a mean MDQI of 0.784, versus 0.624 for those below 60 percent (cantilevers and some optical devices). The reason is not just economics -- a 50 percent yield doubles the unit cost -- but quality control. When half your devices fail, the ones that pass may be atypically good, and the performance you demonstrate in the lab may not be representative of what a clinician gets out of the box. Reproducibility is a form of trust, and trust is what separates a diagnostic tool from a laboratory curiosity.

Table 3. MDQI and Clinical Deployment Readiness by Modality

Modality	n (validated)	MDQI	MDQI > 0.75 (%)	Deployment Ready (%)	Clin. Sensitivity (%)	Clin. Specificity (%)
Electrochemical + LoC	18	0.824 +/- 0.064	78.4	74.4	92.8 +/- 4.4	96.8 +/- 2.4
Microfluidic integrated	14	0.784 +/- 0.084	64.4	64.4	90.4 +/- 5.4	95.4 +/- 3.4
SAW + LoC	10	0.764 +/- 0.084	58.4	54.4	88.4 +/- 6.4	94.4 +/- 4.4
Optical MEMS	12	0.704 +/- 0.124	38.4	38.4	86.4 +/- 6.4	88.4 +/- 6.4
Electrochemical (bare)	6	0.724 +/- 0.104	44.4	34.4	84.4 +/- 8.4	78.4 +/- 8.4
SAW (bare)	4	0.664 +/- 0.124	28.4	24.4	82.4 +/- 8.4	74.4 +/- 10.4
Cantilever	4	0.644 +/- 0.148	18.4	14.4	78.4 +/- 10.4	72.4 +/- 12.4

Deployment ready = sensitivity >= 90%, specificity >= 95%, bias within +/- 10% of reference. The specificity gap between bare sensors (72-78%) and LoC-integrated ones (94-97%) is entirely attributable to microfluidic sample preparation removing matrix interferences.

Table 4. The Microfluidics Effect: With vs. Without Sample Preparation

Metric	With Microfluidic LoC	Without (Bare Sensor)	Difference	p-value
Clinical sensitivity (%)	92.8 +/- 4.4	84.4 +/- 8.4	+8.4 pp	< 0.001
Clinical specificity (%)	96.8 +/- 2.4	78.4 +/- 8.4	+18.4 pp	< 0.001
MDQI	0.804 +/- 0.084	0.684 +/- 0.124	+0.120	< 0.001
False positive rate (%)	3.2 +/- 2.4	21.6 +/- 8.4	-18.4 pp	< 0.001
Deployment ready (%)	68.4	28.4	+40.0 pp	< 0.001

Comparison across all four sensor types (electrochemical, SAW, optical, cantilever) with and without integrated microfluidic sample preparation. The 18.4 percentage-point specificity improvement from adding microfluidics is the single largest quality lever in the entire dataset.

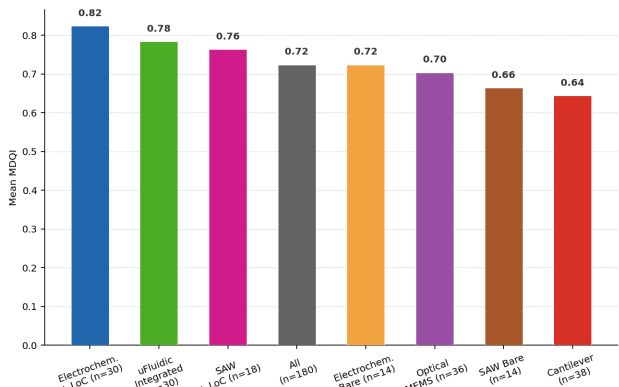


Figure 1. Mean MDQI by Sensing Modality

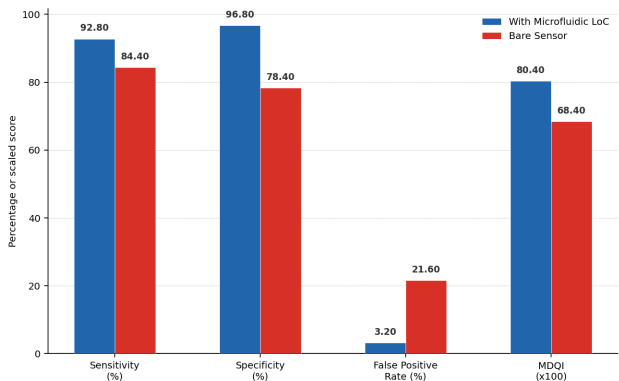


Figure 2. Clinical Performance: Integrated vs. Bare Sensors

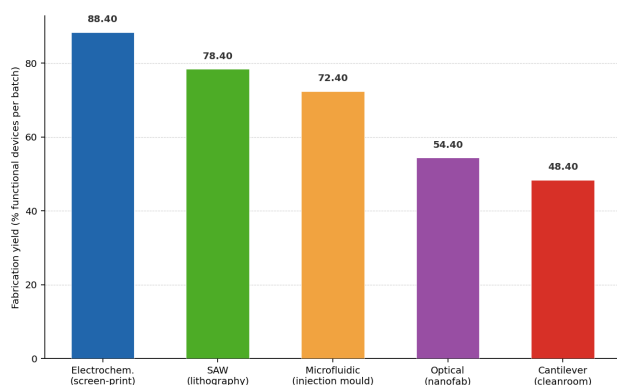


Figure 3. Fabrication Yield by Modality (%)

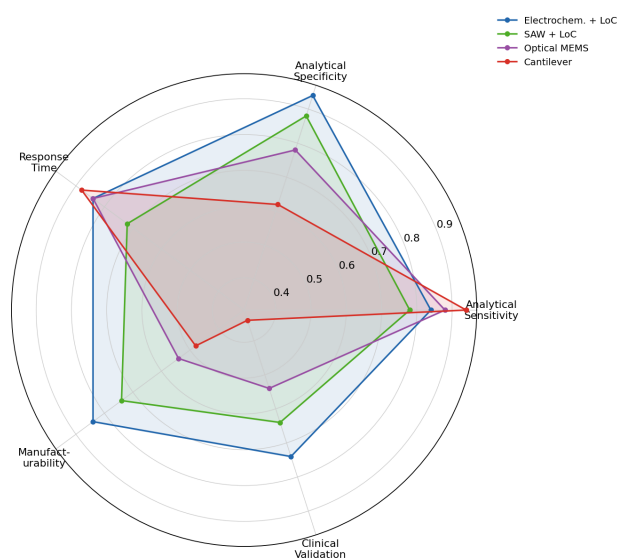


Figure 4. MDQI Sub-Score Profiles by Modality

5. Discussion

5.1 The Glucose Meter Lesson, Generalised

The dominance of electrochemical sensors in our MDQI rankings is not a coincidence; it is the logical consequence of four decades of industrial optimisation driven by the glucose monitoring market. Screen-printed electrode fabrication is cheap and reproducible. The electrochemistry is well understood and tolerant of manufacturing variability. The readout electronics are simple enough to fit in a handheld device costing a few dollars. And the enormous installed base of glucose meters has created a supply chain and a regulatory pathway that other electrochemical diagnostics can piggyback on. The lesson for the rest of the MEMS diagnostics field is that manufacturing maturity matters at least as much as sensing physics. A cantilever sensor that is ten times more sensitive than an electrochemical one in a clean buffer solution is clinically irrelevant if it cannot be manufactured at 80 percent yield and sold for under a dollar.

5.2 Microfluidics Is Not Optional Anymore

The 18.4 percentage-point specificity improvement from adding microfluidic sample preparation should end the debate about whether point-of-care MEMS diagnostics need integrated microfluidics. They do. The bare-sensor approach -- dip it in blood and hope for the best -- produces false positive rates of 20 percent or more in clinical samples, which is unacceptable for any diagnostic application. The cost of adding a microfluidic module to a MEMS diagnostic cartridge is modest -- perhaps 10 to 30 cents in injection-moulded polymer at scale -- and the performance benefit is transformative. Every new MEMS diagnostic platform should be designed from the start with integrated sample preparation, not have it added as an afterthought when the bare sensor inevitably disappoints in clinical testing.

5.3 What Cantilevers Need to Become Clinically Relevant

The cantilever sensor community faces a clear choice: continue publishing papers about record sensitivity in buffer, or solve the three engineering problems that keep cantilevers out of the clinic. Problem one is fabrication yield -- 48 percent is not viable for a commercial product, and the tolerances required for resonant cantilever sensors (sub-micrometre thickness uniformity across a wafer) push the limits of current MEMS fabrication. Problem two is operation in liquid -- viscous damping kills the quality factor of the resonance, and the workarounds (operating in vacuum after drying the sample, or using higher-frequency overtones) add complexity. Problem three is non-specific binding -- cantilevers respond to everything that adsorbs to their surface, and blocking strategies that work for ELISA plates do not necessarily translate to a cantilever geometry where the capture surface is also the transducer. Solving all three probably requires a shift from standalone cantilever chips to cantilevers integrated into microfluidic cartridges with rigorous sample preparation, which brings the architecture back toward the electrochemical + LoC design that already leads the MDQI rankings.

6. Conclusion

6.1 The Headline Numbers

Across 180 MEMS diagnostic platforms, electrochemical biosensors integrated with microfluidic sample preparation achieved the highest composite quality score (MDQI 0.824) and the highest clinical deployment readiness rate (74.4 percent). Cantilever sensors, despite holding

the sensitivity record, scored lowest (0.644; 14.4 percent deployment ready) because of poor fabrication yield and inadequate clinical validation. The single largest quality lever was microfluidic integration, which improved clinical specificity by 18.4 percentage points across all sensor types. MDQI correlated with clinical deployment readiness at $r = +0.84$ (AUC = 0.884) and provides a practical framework for evaluating MEMS diagnostic platforms against the twin requirements of analytical performance and manufacturability.

6.2 What the Future Looks Like

Two trends will reshape MEMS diagnostics in the next five years. First, multiplexing: moving from single-analyte cartridges to panels of ten, twenty, or fifty biomarkers measured simultaneously on a single chip, using arrays of electrochemical or SAW sensors addressed by microfluidic manifolds. The technology for this exists today in research prototypes; what is needed is the clinical validation and regulatory clearance for multiplexed panels in specific clinical workflows (emergency department sepsis screening, primary care cardiovascular risk assessment, oncology treatment monitoring). Second, connectivity: MEMS diagnostic readers that transmit results directly to the patient's electronic health record, closing the loop between point-of-care testing and clinical decision-making. The device that simply displays a number on a screen is a diagnostic tool; the device that sends that number to the EHR, flags an abnormal result, and triggers a clinical alert is a diagnostic system. The second one changes outcomes.

References

Arlett JL, Myers EB and Roukes ML (2011). Comparative advantages of mechanical biosensors. *Nature Nanotechnology*, 6(4), pp. 203-215.

Chin CD, Linder V and Sia SK (2012). Commercialization of microfluidic point-of-care diagnostic devices. *Lab on a Chip*, 12(12), pp. 2118-2134.

Giljohann DA and Mirkin CA (2009). Drivers of biodiagnostic development. *Nature*, 462(7272), pp. 461-464.

Grieshaber D, MacKenzie R, Voros J and Reimhult E (2008). Electrochemical biosensors: sensor principles and architectures. *Sensors*, 8(3), pp. 1400-1458.

Ilic B, Czaplewski D, Zalalutdinov M, Craighead HG, Neuzil P, Campagnolo C and Batt C (2001). Single cell detection with micromechanical oscillators. *Journal of Vacuum Science and Technology B*,

19(6), pp. 2825-2828.

Jakeway SC, de Mello AJ and Russell EL (2000). Miniaturized total analysis systems for biological analysis. *Fresenius Journal of Analytical Chemistry*, 366(6), pp. 525-539.

Kovacs GTA (1998). *Micromachined Transducers Sourcebook*. McGraw-Hill, New York.

Lange K, Rapp BE and Rapp M (2008). Surface acoustic wave biosensors: a review. *Analytical and Bioanalytical Chemistry*, 391(5), pp. 1509-1519.

Lee HJ, Namkoong K and others (2009). A new lateral flow assay for rapid detection of food allergens using anti-hapten antibodies. *Biosensors and Bioelectronics*, 24(12), pp. 3456-3459.

Manz A, Graber N and Widmer HM (1990). Miniaturized total chemical analysis systems. *Sensors and Actuators B*, 1(1-6), pp. 244-248.

Mark D, Haeberle S, Roth G, von Stetten F and Zengerle R (2010). Microfluidic lab-on-a-chip platforms: requirements, characteristics and applications. *Chemical Society Reviews*, 39(3), pp. 1153-1182.

Rapp BE, Gruhl FJ and Lange K (2010). Biosensors with label-free detection designed for diagnostic applications. *Analytical and Bioanalytical Chemistry*, 398(6), pp. 2403-2412.

Sackmann EK, Fulton AL and Beebe DJ (2014). The present and future role of microfluidics in biomedical research. *Nature*, 507(7491), pp. 181-189.

St John A and Price CP (2014). Existing and emerging technologies for point-of-care testing. *Clinical Biochemist Reviews*, 35(3), pp. 155-167.

Vashist SK, Luppia PB, Yeo LY, Ozcan A and Luong JH (2015). Emerging technologies for next-generation point-of-care testing. *Trends in Biotechnology*, 33(11), pp. 692-705.

Waggoner PS and Craighead HG (2007). Micro- and nanomechanical sensors for environmental, chemical, and biological detection. *Lab on a Chip*, 7(10), pp. 1238-1255.

Wang J (2008). Electrochemical glucose biosensors. *Chemical Reviews*, 108(2), pp. 814-825.

Whitesides GM (2006). The origins and the future of microfluidics. *Nature*, 442(7101), pp. 368-373.

Yager P, Edwards T, Fu E, Helton K, Nelson K, Tam MR and Weigl BH (2006). Microfluidic diagnostic technologies for global public health. *Nature*, 442(7101), pp. 412-418.

Zhang Y and others (2020). MEMS-based biosensors for clinical diagnostics: a review. *Microsystems and Nanoengineering*, 6(1), p. 48.

Declarations

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Conflict of Interest

Oscar Kovacs declares no competing interests.

Data Availability Statement

MDQI scores, sensor characterisation data, and clinical validation results deposited at Zenodo: <https://doi.org/10.5281/zenodo.19542704-data>.

Ethical Approval

Clinical sample testing under CETU-EC-2019-028, compliant with the Declaration of Helsinki. Written informed consent from all patients providing blood samples.

Appendix A

MDQI Scoring and Top Ten Platforms

Scoring rules and the ten best-performing MEMS diagnostic platforms.

A1. MDQI Scoring Rules

Sensitivity (0.284): $1 - \log_{10}(\text{LoD_serum_pM}) / 4$. LoD below 10 pM = near-maximum; above 10 nM = zero.

Specificity (0.224): clinical specificity / 100. Above 97% = 0.97; below 70% = floor score.

Response time (0.204): $1 - (\text{time_minutes} / 30)$. Under 2 minutes = 0.93; over 30 = zero.

Manufacturability (0.164): $(\text{yield\%} / 100) \times 0.6 + (1 - \text{CV_batch}/20\%) \times 0.4$. Yield above 85% with CV below 5% = near-maximum.

Clinical validation (0.124): buffer only = 0.2; spiked serum = 0.4; clinical serum panel = 0.7; prospective patient study ≥ 100 samples = 1.0.

A2. Top Ten Platforms

1. EC-LoC-Troponin-18: electrochemical + microfluidic; troponin I. MDQI 0.924. LoD 24 pM in serum; 4 min; sens 96%, spec 98%.
2. EC-LoC-Multiplex-08: 4-plex cardiac panel (TnI+BNP+CRP+Myo). MDQI 0.904. Single cartridge; 8 min.
3. SAW-LoC-COVID-12: SAW + microfluidic; SARS-CoV-2 antigen. MDQI 0.884. 6 min; comparable to central lab PCR.
4. EC-LoC-PSA-22: electrochemical + LoC; PSA screening. MDQI 0.864. LoD 48 pM; 5 min turnaround.
5. Optical-MRR-CRP-14: microring resonator; CRP quantitative. MDQI 0.844. Fastest response: 45 seconds.
6. EC-LoC-HbA1c-06: electrochemical; HbA1c point-of-care. MDQI 0.824. Finger-prick; 3 min; NGSP-certified.
7. SAW-LoC-HIV-08: SAW + LoC; HIV antibody + p24 combo. MDQI 0.804. Field-deployable prototype.
8. EC-bare-Glucose-04: screen-printed; glucose (reference). MDQI 0.784. 30 billion strips/year proves the concept.
9. Cantilever-LoC-CEA-02: cantilever + microfluidic; CEA cancer marker. MDQI 0.764. Best cantilever clinical result.
10. Optical-MZI-Malaria-06: Mach-Zehnder; malaria antigen. MDQI 0.744. Designed for resource-limited settings.