Application And Design Strategies of Piezoelectric Sensors for Blood Glucose Detection

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Abstract. Conventional blood-based assays are accurate yet episodic and invasive, under sampling day-to-day excursions. This review examined piezoelectric (PZ) platforms for wearable, non/minimally-invasive glucose monitoring, emphasizing liquid-phase behavior and system co-design. From QCM physics, frequency shifts arise from interfacial mass and viscous-inertial loading $\propto \eta \cdot \rho$, motivating parameter-stable readouts—phase/|Z| near (anti) resonance and ring-down time τ —with matched reference channels to reject bulk and thermal drift. The paper linked these choices to materials/surfaces (lead-free KNN/NKN; PVDF-based composites; Au-thiol SAMs, thin hydrogels, antifouling) and microfluidics that stabilizes the acoustic load. The paper outlined PENG-assisted architectures in which harvested motion/respiration both trickle-charge storage and act as context priors, enabling duty-cycled sensing, burst BLE/NFC, and learning-based calibration with on-device QC. Finally, the paper discussed hybridization with electrochemistry to curb false alarms under activity-dependent viscoelastic shifts, and propose reporting/validation practices (MARD, Clarke/Parkes grids, drift over wear/regeneration, controlled-sweating vs free-living robustness, and harvest-vs-consumption energy ledgers) for population-level studies across perspiration phenotypes and climates.

Keywords: Glucose monitoring; piezoelectric biosensor; microfluidics; quality control.

1. Introduction

Diabetes is a chronic metabolic disorder that involves persistently high blood glucose and, quite often, disturbances in lipid and protein metabolism. In practice, this condition usually develops because the pancreas does not release enough insulin or because cells fail to respond effectively to insulin, leaving glucose poorly utilized [1]. According to the International Diabetes Federation (IDF) Diabetes Atlas, global diabetes health expenditure reached about 1.015 trillion United States Dollars (USD) in 2024, a 338% increase over 2007; by 2050 it is projected to be around USD 1.043 trillion, approximately 11.9% of total health spending [2]. The spending levels and growth reported in the IDF Atlas argue for monitoring strategies that are efficient, broadly deployable, and capable of reducing complication-related costs. In light of these trends, the case for improving day-to-day monitoring and management is immediate.

For now, blood-based tests remain the clinical mainstay. Fasting plasma glucose (FPG) testing, the oral glucose tolerance test (OGTT), and hemoglobin A1c (HbA1c) measurement are routinely applied and widely trusted methods for the diagnosis and follow-up of diabetes [3]. Yet these tools are far from perfect. HbA1c reflects long-term exposure over several months but misses the short-term fluctuations that often matter in daily care [4]. Finger-prick tests and venous blood draws, although accurate, are invasive and uncomfortable, discouraging frequent use [5]. The cost of test strips and other consumables can also become a burden, especially for patients who need daily monitoring.

These drawbacks explain why so much attention has shifted to non-invasive, continuous monitoring. A variety of wearable systems have been tested, including devices that analyze sweat, saliva, tears, or interstitial fluid [5]. Sweat has been particularly attractive because it is easy and painless to collect and integrates naturally with on-skin microfluidic devices. Still, major challenges remain: sweat secretion varies between individuals, environmental factors interfere with readings, and strong correlations with blood glucose are not consistently achieved [6].

Against this backdrop of both promise and persistent limitations, researchers have begun to explore new sensing strategies. Among them, piezoelectric biosensors have emerged as an intriguing alternative. Instead of relying solely on enzymatic reactions or optics, they convert biochemical interactions at the sensor surface into electrical signals. This allows real-time, label-free detection and, importantly, does not require overly complex instrumentation [7]. In the following sections, the working principles of these sensors, relevant materials and design considerations, as well as their potential role in advancing non-invasive glucose monitoring from the laboratory to everyday clinical use will be outlined and discussed.

2. State of the Art and Comparative Design Strategies of Piezoelectric Biosensors for Diabetes Monitoring

2.1. Why Move beyond Blood Tests: Clinical Gaps that Shape the Sensor Briefly

Finger-stick and venous assays are accurate yet episodic and invasive, so day-to-day excursions often slip past routine follow-up. In clinic, that blind spot shows up as unexplained variability in HbA1c for the same regimen or in post-prandial spikes that never get captured during scheduled checks. Sweat is attractive because collection is painless and integrates well with soft microfluidics. Recent surveys still find no clinically accepted, fully non-invasive, calibration-free solution despite steady engineering progress in sweat, saliva, and tear sensing [8,9].

These constraints set the 'must-haves.' First, the transducer has to remain stable in soft/wet stacks whose viscoelastic properties drift over wear time. Second, drift control should be designed in (reference channels, temperature/humidity logging) rather than left to post-processing. Third, data need context: motion and sweat-rate priors materially change interpretation. Piezoelectric (PZ) platforms are compelling in this regard because they read out interface physics without a mandatory label or reagent, and because frequency/phase observables can be modeled in detail [10]. A persuasive PZ device, therefore, is as much about boundary conditions and covariates as it is about crystal cuts and electrodes.

A 'persuasive' PZ solution is not just about the crystal cut and electrode layout; it hinges on how well one manages boundary conditions and covariates and on producing evidence against clinical metrics (e.g., MARD, Clarke/Parkes error grids, long-term drift, and the energy budget).

Therefore, the next step is to lay out the operating principles in liquids: liquid loading is not a purely mass-driven effect, and static-charge readouts exhibit exponential decay drift $q(t) = Qe^{-t/RC}$— which is why, in what follows, this text prioritizes readout strategies based on phase/dissipation (or ring-down time τ) with a matched reference channel.

2.2. Operating Principles in Liquids: from Frequency to Phase and Decay

Quartz crystal microbalance (QCM) translates interfacial events into shifts of the thickness-shear resonance. For a thin, rigid film, Sauerbrey's relation captures the first order behavior.

$$\Delta f = -\frac{2f_0^2}{A\sqrt{\rho_q \mu_q}}\Delta m \tag{1}$$

Where f_0 is the unloaded resonance, A the active area, and ρ_q, μ_q the density and shear modulus of quartz. In liquids, loading is governed not only by mass but also by viscosity and density of the boundary layer; the Kanazawa-Gordon term scales as:

$$\Delta f_{liq} \propto -{f_0}^{3/2}\sqrt{\eta_\iota \rho_\iota} \tag{2}$$

reminding researchers that "frequency down" can arise from higher $\eta_\iota \rho_\iota$ even at constant Δm. This is why dissipation/phase information or a reference channel is more than a luxury in wearable environments [9, 11].

Readout strategy matters as much as the resonator. Classic oscillator loops track f_0 directly, but fixed-frequency phase/amplitude interrogation (Direct Digital Synthesis (DDS) source + phase detector) has practical advantages in small, battery-backed systems. By probing a narrow band around resonance or antiresonance, one resolves sub-ohm admittance changes with milliwatt-level power and without sweeping a network analyzer [8]. In ringdown mode, a short impulse excites the mode and the envelope decays with $\tau \approx Q/(\pi f_0)$. Measuring τ is essentially free in power terms (timers and comparators are cheap), which is helpful for long-wear scenarios.

A persistent caveat for piezo elements is their "static" behavior: charge decays as $q(t) = Qe^{-t/RC}$, so naive static-load readouts drift. Modern biosensors avoid integrating charge; they monitor parameter-stable observables—f_0, |Z|, phase near (anti)resonance, τ, or capacitance—that are tolerant of quasi-static biochemical films [9, 12]. In soft stacks (e.g., elastomer interlayers for comfort), phase/impedance near f_0 typically yields more robust behavior and fewer surprises in miniaturized electronics [9]. A conservative design pairs a sensing resonator with a matched reference under identical microfluidics to subtract bulk $\sqrt{\eta\rho}$ swings and thermal drift.

2.3. Materials-to-Surface Co-Design for Wearable Piezoelectric Biosensing

2.3.1 Materials landscape: stiffness, flexibility, and piezoelectric constants

Material and geometry choices act as filters that determine which electrode stacks and surface chemistries remain viable on skin. Once the base film is fixed, the usable range for mechanical load, thermal drift, and electromechanical headroom is largely defined.

On the ceramic track, lead zirconate titanate (PZT) is a practical yardstick, while Pb content complicates long-wear safety and end-of-life handling. Lead-free niobates (KNN/NKN) provide a middle ground and benefit from doping, texturing, and domain control. Where transparent or biocompatible interfaces are required, ZnO is serviceable; modest coupling can be balanced by series/parallel front-end layouts that trade voltage and current [13]. Substrate decisions propagate to adhesion and metallization (e.g., Ti/Cr/Au) and subsequently constrain the feasibility of thiol SAMs or silane routes.

On the polymer side, piezoelectric response arises only from β-phase PVDF. The copolymer P(VDF-TrFE) stabilizes that phase and elevates effective response around~30 mol% TrFE while maintaining skin-like compliance [13]. Composite stacks—PVDF with ZnO nano-fillers or $BaTiO_3$—recover signal without sacrificing flexibility. Flexible laminates preserve acoustic coupling to microchannels on moving skin and tolerate bending cycles that would fracture brittle films [11], [14]. Because softer and thicker stacks raise dissipation and depress Q, biofunctional over-layers added later should remain sufficiently thin to keep the phase slope and τ within a readable band.

From a broader nanomaterials view, a system-level rule remains consistent: ceramics (Barium titanate (BTO), PZT, KNN) supply coupling; PVDF/P(VDF-TrFE) supply compliance; hybrids (PVDF/BT, PVDF/ZnO) blend both for biosensing tasks [15]. Wrist-mounted prototypes in recent literature converge on the same direction: ultrathin, conformal piezo stacks that remain bend-tolerant and support self-powered or wireless operation on the wrist, arguing for micrometer-scale total thickness from the outset [16].

The wrist form factor sets two boundary checks before surface chemistry selection. First, durability under repeated bending at a curvature radius below ~15-20 mm for several-hundred-thousand cycles; stacks are retained only when the operating-tone |Z| shows no measurable drift. Second, thermal behavior near f0 ≈ 10 MHz; a drift of a few Hz/°C can be nulled by a matched reference channel, whereas an order-of-magnitude larger drift overwhelms subtraction. Material and geometry choices determine on which side of these gates a design settle. After the substrate and electrodes pass these gates, adhesion and metallization narrow feasible chemistries (thiol SAMs versus silanes), and any biofunctional layer is justified by its liquid-phase loading of the resonator.

2.3.2 Assay chemistry and surfaces on piezo platforms

Given the substrate/electrode choices above, the next layer is chemistry: it must provide selectivity without adding so much viscoelastic load that Q and phase readability suffer.

This is where "bio" meets "electromechanics." General surveys catalog enzyme (Glucose oxidase, Glucose dehydrogenase), affinity (aptamers/antibodies), and cell constructs—each with distinct lifetimes and fouling profiles [10, 17]. On gold electrodes, thiolated self-assembled monolayers (e.g., mercaptocarboxylic acids, aminothiols) provide anchors; Poly (ethylene glycol) (PEG) or zwitterionic brushes reduce nonspecific adsorption; thin hydrogels (tens of micrometers) preserve hydration and improve enzyme retention. The QCM literature's lesson is consistent: robust, regenerable chemistry plus a proper reference channel beats a heroic single-channel fit in changing fluids [14]. Because liquid loading is viscoelastic, every added surface is also a mechanical layer; hence frequency alone is insufficient for attribution.

Because liquid loading is viscoelastic, tracking both frequency and a dissipation/phase observable is safer than frequency alone. Fixed-frequency phase or ring-down timing is far easier to embed on a flex Printed Circuit Board (PCB) than a full network analyzer, which is why compact amplitude/phase meters with DDS sources and phase detectors keep showing up in prototypes [9]. This readout choice feeds back to surface design: thinner gels and well-packed SAMs keep dissipation manageable, enabling low-power phase/τ instrumentation.

Finally, the microfluidic layer is not a passive bystander: controlling evaporation and temperature, adding wicking/valving, or even using gentle iontophoresis for on-demand sweat all stabilize the acoustic load that the piezo "sees."

In short, materials-electrodes-chemistry-microfluidics is a single constraint loop; pairing a sensing resonator with a matched reference closes that loop by subtracting bulk swings and thermal drift.

2.4. Application Pathways: Sweat-First, but not Sweat-Only

Material-electrode-surface choices from Section 2.3 map directly onto the fluid pathway, because wetting behavior, ionic strength, and enzyme compatibility differ across sweat, tears, saliva, urine, and interstitial fluid (ISF). Sweat represents the most mature on-skin setting for PZ stacks. Patterned hydrophilic/hydrophobic routing with absorbent layers limits bubble entrainment, gentle heaters paired with temperature sensing curb condensation, and iontophoresis enables on-demand sampling during sedentary periods. Translation to practice hinges on population-level validation: the same patch must remain dependable across perspiration phenotypes and climates. Wearable surveys repeatedly underline the study-design implications: beyond agreement metrics, reports should document drift over wear time, the outcomes of regeneration cycles, and the cadence of calibration [8]. In short, sweat establishes the baseline for field performance and anchors the validation playbook used in other matrices.

Beyond sweat, complementary fluids extend coverage and decouple use cases. Tears allow contact-lens-like stacks (lens-compatible yet volume-limited); saliva offers easy access (chemically noisy and sensitive to meals); urine supports spot sampling (storage and timing constraints apply); ISF provides a minimally invasive route (often via microneedles with skin-interface considerations). PZ platforms have already been explored for pathogen and metabolite sensing in these matrices, so glucose layers can often re-use proven surface chemistries and packaging rather than rebuild from scratch [14], [15]. A practical architecture keeps the readout and MCU common while accepting replaceable cassettes tailored to each target fluid, and a final interface note is that cassette changes should preserve calibration context and reference channels to avoid re-training the entire signal chain.

2.5. Self-Powered, Context-Aware Piezo Sensing: from PENG to Decision

2.5.1 Self-powered operation: piezoelectric nanogenerators as power and context

Continuous radios drain coin cells; sensors that sample often but speak rarely last much longer. Piezoelectric nanogenerators (PENGs) convert gait, hand motion, and even arterial pulsation into usable power and a context signal. Lead-free KNN films and PVDF/ZnO fiber laminates are particularly skin-friendly; even partial scavenging enables duty-cycled sensing with burst telemetry [14]. A practical energy picture looks like this: sensing/processing in the milliwatt range but for milliseconds, and BLE/NFC bursts in the 1-10mW range for tens of milliseconds. If a PENG harvests tens to hundreds of microwatts averaged over a walking period, then a modest storage buffer (thin-film capacitor or microbattery) can smooth the mismatch between harvest and burst. These harvested streams therefore serve a dual role-supplying energy for duty-cycled operation and providing motion/respiration features that downstream calibration and QC pipelines can directly consume.

Meanwhile, the harvested waveform encodes motion/respiration; feeding that into the inference stack helps distinguish sweat-rate surges (which alter acoustic loading) from biochemical trends and lets the firmware trigger "read more often" windows during activity peaks [14]. In short: self-powering is not only about lifetime—it also makes the data easier to interpret. Taken together, self-powering and context sensing set up the systems problem: how to fuse PENG-derived priors with low-power readout and turn them into robust, field-grade decisions.

2.5.2 Systems integration: low-power electronics and learning-based calibration

Hardware alone will not neutralize drift, motion artifacts, or secretion spikes. Flexible piezo passives paired with machine learning pipelines already show real-time anomaly detection and artifact suppression in cardiovascular monitoring; the same ingredients—sensor-level denoising, domain-adapted calibration, online quality control-can be ported to chemical-mechanical fusion for glucose wearables [13]. The calibration story benefits from context: temperature/humidity, PENG-derived motion/respiration, and microfluidic state (filled/evaporating) are all explanatory variables rather than nuisances. In other words, the signals harvested in Section 2.5.1 power the device and also regularize the learning problem by informing when and how to trust the PZ channel.

On the circuit side, the pieces are straightforward. A DDS synthesizes a clean tone near resonance; a gain/phase detector measures the response; a microcontroller sweeps a few points or stays at a high-slope phase setpoint to maximize Signal-to-Noise Ratio (SNR). For low-duty devices, the tone can be duty-cycled, with ring-down reading τ between bursts to monitor slow drifts. Typical numbers are modest: tens of microamperes in idle, milliamperes in short active windows, and a radio that turns on only when it has to. With PENG trickle charge into a thin-film capacitor, burst-mode telemetry becomes realistic without frequent charging [9, 14]. This closes the energy loop: PENG trickle charge sustains the duty cycle, while context-gated telemetry avoids unnecessary radio use.

From a quality-control standpoint, researchers recommend building a "traffic light" into firmware: green when reference and sensing channels track expected physics; yellow when the dissipation or phase residual exceeds a threshold (microfluidic anomaly suspected); red when cross-modal disagreement (e.g., PZ vs. electrochemical) passes a clinical risk boundary. This is how a field device behaves like a cautious lab instrument.

2.6.Practical Recommendations for a Piezoelectric Glucose Wearable

Sensing and readout. The readout should not rely on static charge integration but should instead focus on stable parameters. These include the phase or magnitude of impedance (|Z|) around the (anti)resonance point, and the ring-down time (τ). These parameters can be acquired either by stabilizing the system at a high-slope phase setpoint or by performing a sparse frequency sweep across a few critical points. In situ precision targets are pragmatic rather than aspirational (e.g., phase noise $< 0.5°$ rms; τ coefficient of variation $< 5\%$ over 24-72 h wear), and a sensing channel must be paired with a geometry- and microfluidics-matched reference to achieve robust common-mode rejection under temperature and viscosity/density swings ($\geq$ 20 dB Common-Mode Rejection (CMR) across 20°C-40°C).

Materials and mechanics. Substrate and geometry should be chosen for skin safety and motion tolerance first, then piezoelectric performance. Lead-free KNN/NKN and PVDF-based composites (PVDF/ZnO, PVDF/$BaTiO_3$) offer a favorable balance; face-shear or tuning-fork-like modes preserve usable response with elastomer backing. A practical durability envelope is hundreds of thousands of bends at < 15-20 mm curvature without measurable |Z| drift near f_0, while residual thermal coefficients near 10 MHz should remain at a few Hz/°C after reference subtraction.

Surfaces and assay chemistry. Selectivity and fouling control should come from robust Au-thiol SAM anchoring, PEG/zwitterionic antifouling, and thin hydrogels that maintain hydration without excessive dissipation. Because soft, thick coatings depress Q and flatten phase slope, layer thickness should be minimized within assay constraints (e.g., ≤ 10-30 μm) and validated with frequency-plus-dissipation/phase observables rather than frequency alone; regeneration protocols should specify rinse/reprime limits and permissible drift (e.g., < 10% change in phase slope or τ over ≥ 5 cycles).

Microfluidics and environmental control. Patterned hydrophilic/hydrophobic routing, absorbent stacks, and gentle heaters with temperature sensing stabilize the acoustic load by suppressing bubbles and condensation across activity and climate windows. When sedentary, iontophoresis can provide on-demand sweat within safe current density limits. Reporting should differentiate controlled-sweating benches from free-living trials and quantify load stability (dropout-free operation during ≥ 30 min moderate activity; condensation-free across 15-35°C, 30-80% relative humidity).

Power, telemetry, and context. PENGs should be treated as both an energy source and a context channel: trickle-charging a thin-film capacitor or microbattery enables duty-cycled sensing with burst BLE/NFC (milliwatts for milliseconds; 1-10 mW for tens of milliseconds), while the harvested motion/respiration features regularize interpretation by gating transmission and triggering “read-more-often” windows during activity peaks.

Learning-based calibration and QC. Calibration should start with instrument-level compensation and proceed to domain-adapted regression/classification that maps PZ features plus context (temperature/humidity, sweat-rate proxies, PENG-derived motion/respiration, microfluidic fill/evaporation state) to capillary references. Firmware-level quality control is best expressed as a traffic-light logic: green when sensing-and-reference track expected physics; yellow when dissipation/phase residuals exceed thresholds suggesting microfluidic anomalies; red when cross-modal disagreement (e.g., PZ vs electrochemical) reaches a predefined clinical risk boundary, prompting automatic resampling or deferred decisions. Beyond bias and MARD, reports should include Clarke/Parkes grids, drift versus wear time/regenerations, robustness across perspiration phenotypes and climates, and a harvest-versus-consumption energy ledger.

2.7.Outlook

Effective governance of wrist-worn piezoelectric sensing should be organized around auditable checks. The first gate is mechanical: evaluate layer stacks on a wrist-curvature jig under long-cycle bending and retain only those that maintain a stable impedance at the operating frequency. The second gate is thermal: quantify the temperature coefficient near the operating band using a matched reference channel so that thermal drift can be subtracted during routine use. Together, these two screens define practical design bounds and keep subsequent decisions aligned with field conditions.

Within those bounds, align readout and system architecture. Prefer fixed-frequency phase/impedance interrogation or ring-down timing to preserve sensitivity near (anti) resonance while meeting wearable power budgets. Keep the total stack thickness in the micrometer range to ensure skin conformity, and introduce hybrid laminates only when electromechanical coupling must coexist with softness. After curvature cycling, verify adhesion and surface chemistry through soak-peel tests, and record any primers or barrier layers in a bill of process to maintain traceability. Manage biofunctional layers within a defined regeneration window. Assess stability using liquid-relevant observables (phase slope or decay time) rather than frequency alone, and report accuracy together with its uncertainty. Finally, document missing-data rate, motion artifacts, re-attachments, and adhesive replacements in free-living evaluations. Any route that involves restricted substances should include an explicit end-of-life plan and a validated lead-free alternative.

3. Conclusion

Piezoelectric biosensing for diabetes becomes practical when design treats the sensor as a full system. Blood tests are accurate, but they are invasive and episodic. On-skin piezoelectric stacks offer continuous and label-free signals. That format fits daily life.

Choose observables that stay stable in liquid. Phase near resonance is stable. Impedance near resonance is stable. Ring-down time is also useful. Use a matched reference so bulk effects and temperature drift can be subtracted. Prefer fixed-frequency interrogation or ring-down timing. Both methods meet tight power limits in wearables.

To ensure close contact with skin, the stack is kept thin. A hybrid laminate is introduced only when coupling must live alongside softness. After wrist-like bending is completed, adhesion is checked, followed by soak and peel tests. Primers and barrier layers are recorded in a concise process log so later changes remain traceable. Active surface chemistry is maintained, and antifouling layers are added to limit drift. Microfluidics manages wetting, bubbles, and temperature. A small piezoelectric generator supplies trickle energy and also provides motion or respiration context for the signal. With a cassette interface, a single readout and controller can serve sweat and other fluids as needed.

Translation to everyday use relies on disciplined evaluation. The device first passes a mechanical screen and then a thermal screen. Accuracy is measured during wear and reported with its uncertainty, while drift is tracked both during wear and during regeneration. Free-living trials are run, and logs include missing data, motion artifacts, re-attachments, and any changes of adhesive. Calibration is treated as ongoing work that adapts to daily routines. Reproducibility is part of the deliverable, supported by a clear process list, fixture descriptions, automation scripts, and a concise catalog of failure modes with remedies. Following these practices, piezoelectric platforms move from promising materials to practical monitors, offering quieter operation, more continuous records, and better comfort in daily care.

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