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HUMAN TISSUES AS PIEZOELECTRIC BIOMATERIALS: REVIEW AND PERSPECTIVES FOR BIOSENSORS

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ABSTRACT: Piezoelectricity is the ability of certain materials to generate an electrical charge when mechanical pressure is applied to them and, conversely, to deform when subjected to an electric field. Although traditionally associated with inorganic crystals such as quartz, this phenomenon is also present in various biological materials in the human body, thanks to the non-centrosymmetric organization of structural proteins such as collagen and keratin. This paper presents a comprehensive review of recent advances in the study of piezoelectric biomaterials present in bone, dental enamel and dentin, and keratinous tissues, particularly nails. Piezoelectricity in these tissues plays a key role in physiological processes such as bone adaptation and remodeling. The effects of various systemic pathologies, including diabetes, are also analyzed, as they can alter the structure, hydration, and molecular organization of tissues, significantly modifying their electromechanical behavior. Current evidence suggests that these alterations reduce the functional efficiency of piezoelectric tissues and open up new possibilities for early diagnosis, non-invasive monitoring, and the development of piezoelectricity-based biosensors.

Introduction

Piezoelectricity is a physical phenomenon discovered in 1880 by brothers Pierre and Jacques Curie, who observed that certain crystals (such as quartz and tourmaline) generated an electrical potential when subjected to mechanical pressure. This discovery opened up a new area of study in materials physics, which later expanded into engineering, electronics, and biomedicine (Curie & Curie, 1880; Jaffe et al., 1971).

In the mid-20th century, scientific interest expanded to biopiezoelectricity, driven by the pioneering work of Fukada and Yasuda (1957), who demonstrated for the first time that human bone exhibits piezoelectric properties. This finding revealed that nature also employs this phenomenon in various hierarchical tissues, such as collagen, tendons, tooth enamel, dentin, and keratin. These biological matrices have a non-centrosymmetric molecular organization that facilitates the alignment of electric dipoles and, consequently, the generation of charges under mechanical stress (Marino, 1989; Kamel et al., 2022).

In recent years, it has been experimentally confirmed that various human tissues—including bone, enamel, dentin, dental cementum, and nails—possess measurable piezoelectric or triboelectric properties. This has prompted a new line of research at the frontier between biophysics and bioengineering, where even non-mineralized materials, such as keratin, have been shown to generate electrical signals with potential for integration into biosensors and low-power nanogenerators (Marzec, 2013; Galindo-Mentle & Blas-Sánchez, 2025).

The present article aims to systematically review the scientific literature on piezoelectricity in biomaterials. It examines the physical fundamentals of the phenomenon, the experimental methods used, the values reported in the literature, and emerging applications in health, tissue regeneration, and implantable energy harvesting devices. The aim is to provide a comprehensive overview of the role that piezoelectricity plays as a bridge between biological mechanisms and energy generation, highlighting its potential impact on the medicine of the future.

Theoretical foundations of the piezoelectric effect

The piezoelectric effect is the ability of certain materials to convert mechanical energy into electrical energy and vice versa. It manifests itself when a non-centrosymmetric material generates electrical polarization when subjected to mechanical deformation (direct piezoelectric effect), or when it undergoes mechanical deformation when an electric field is applied (inverse piezoelectric effect) (Jaffe, Cook & Jaffe, 1971; Nye, 1985).

Linear piezoelectric behavior is described by constitutive equations that relate mechanical stress (T), strain (S), electric field (E), and electric displacement (D):

$$D_i = d_{ij}T_j + \epsilon_{ij}E_j$$

$$S_i = s_{ij}^E T_j + D_{ij}E_j$$

Definition of parameters

Symbol	Description	Unit
D_i	Electrical displacement	C/m ²
T_j	Mechanical stress	N/m ²
S_i	Mechanical deformation	dimensionless
E_j	Electric field	V/m
d_{ij}	Piezoelectric coefficient (piezoelectric modulus)	C/N or m/V
s_{ij}^E	Elastic coefficient at constant electric field	m ² /N
ϵ_{ij}	Dielectric permittivity	F/m

The d_{ij} coefficient is one of the most important parameters, as it quantifies the amount of electrical charge generated per unit of force applied in a specific direction.

Piezoelectric modulus under static conditions

Under quasi-static conditions (low frequencies), the effective piezoelectric modulus can be obtained from the relationship between the charge generated and the force applied:

$$d = \frac{Q}{F} = \frac{\Delta V \cdot C}{F}$$

or equivalently, in terms of voltage and material thickness:

$$d = \frac{V \cdot \epsilon_0 \epsilon_r}{t \cdot \sigma}$$

where:

Symbol	Description	Unit
Q	generated electric charge	C (Coulomb)
F	Mechanical force applied	N (Newton)
V	induced voltage	V (Volt)
ϵ_0	permittivity of vacuum	(8.854×10 ⁻¹² F/m)
ϵ_r	relative dielectric constant of the material	C/N or m/V
r	material thickness	(m)
σ	mechanical stress	(Pa)

This approach is common in the measurement of biological materials such as bone, dentin, or nails, where a controlled load is applied and the generated surface electrical potential is measured (Fukada & Yasuda, 1957; Marino, 1989).

Dynamic determination of the piezoelectric modulus

Under dynamic conditions, when the material is subjected to vibrations or harmonic excitations (e.g., in ultrasound or nanogenerators), the piezoelectric modulus can be calculated from the electrical and mechanical resonances of the system. The dynamic coefficient d_{yn} is obtained from the alternating current response (I) to a sinusoidal stress

$$T(t) = T_0 \sin(\omega t)$$

$$d_{dyn} = \frac{I}{\omega A T_0}$$

where:

Symbol	Description	Unit
I	piezoelectric current generated	A (Amperes)
ω	Excitation angular frequency	(rad/s)
A	effective electrode area	(m ²)
T_0	amplitude of mechanical stress	(Pa)

This method is widely used in electrical impedance characterization or dynamic mechanical analysis, and allows the dependence of the coefficient d_{33} or d_{31} on frequency to be obtained (Damjanovic, 1998; Safari & Akdoğan, 2008).

In piezoelectric biomaterials such as collagen, keratin, or dentin, measuring the piezoelectric coefficient (piezoelectric modulus) is more complex due to their heterogeneous nature, high water content, and low electrical conductivity. Therefore, specialized methods are used:

1. Piezoelectric force microscopy (PFM): This allows the local modulus d_{33} to be measured in micro- and nanodomains. Used for bone, collagen, and keratin (Reyes-Gasga et al., 2019).
2. FTIR with mechanical stress: Relates molecular orientation (C–O, N–H, C=O modes) to changes in polarization.
3. Hybrid piezo/triboelectric methods: Useful when friction contributes to the signal (Fu et al., 2020).

Methodology

This work uses the principle of piezoelectricity in static conditions using an analog force sensor that allows pressure to be exerted in a range from 0N to 500N. The force is applied by means of a helical crank that moves the z-axis, and the biological samples are prepared and placed on a fixed surface which applies pressure with the helical crank.

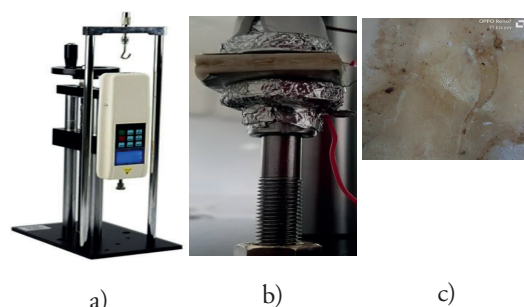


Figure 1: Analog force sensor. B) Biological sample subjected to pressure force c) Biological sample: beef bone.

The electrical potential generated by the biological samples is measured using an amplification system consisting of three stages based on 741 operational amplifiers. The electrodes placed on the surface of each sample capture very low amplitude signals, which are directed to the first stage of the amplifier. Each stage uses a non-inverting configuration with feedback and input resistors that determine the individual gain. Together, the circuit provides a total amplification of approximately 10 times, allowing the biological signal level to be raised to values suitable for visualization and analysis. The three cascaded stages ensure stable amplification, reduce noise, and improve the quality of the signal obtained.

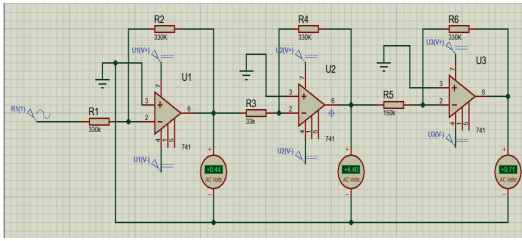


Figure 2. Three-stage amplifier circuit based on 741 operational amplifiers used to increase the electrical signal generated by biological samples.

The electrodes placed on the surface of each sample () are connected to the input of the first amplifier, and the signal is progressively increased through stages with resistors configured for a total gain of approximately 10 \times . This arrangement allows a voltage high enough for recording and experimental analysis to be obtained.

Figure 3 shows the voltage generated by two biological samples subjected to different forces. Sample 1 (beef bone) exhibits high voltages, between 3 and 6 V, with noticeable increases as the applied force increases. This behavior reflects the piezoelectric nature of bone tissue, mainly associated with the orientation and deformation of mineralized collagen, which generates an electrical charge when subjected to mechanical stress.

In contrast, Sample 2 (nails) generates very low voltages, less than 0.4 V, with a minimal increase at higher forces. Although nails also have piezoelectric properties due to keratin, their response is significantly lower, suggesting that their structure produces a weaker mechanical-electrical coupling.

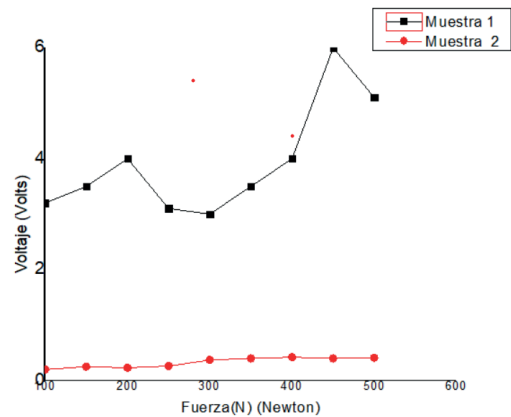


Figure 3. Voltage generated by biological samples as a function of applied force. Sample 1 (beef bone) shows a notable increase in electrical potential, attributable to the piezoelectric response of the collagen present in bone tissue. Sample 2 (nails) shows low voltages, less than 0.4 V, consistent with the lower piezoelectric activity of keratin.

Analysis and discussion of results

The pioneering study by Fukada and Yasuda (1957) marked a turning point in the modern understanding of biological piezoelectricity. Through experiments conducted on cortical bone, they demonstrated that the application of compressive, bending, or tensile forces produces reproducible electrical signals. This finding, published in *the Journal of the Physical Society of Japan*, revealed that piezoelectricity was not a phenomenon exclusive to inorganic crystals, but was also present in organized protein matrices of biological origin. The physical explanation was attributed to the highly ordered structure of type I collagen, whose triple helix and fibrillar orientation generate polar domains capable of undergoing polarization induced by mechanical deformation. This discovery opened up a new area of research in bioelectromechanics and provided the first molecular model for understanding piezoelectricity in living tissues.

Decades later, the theoretical synthesis presented by Marino (1989) reinforced the idea that mechanical electrification is a widely distributed phenomenon in mineralized tissues such as bone, dentin, and dental cementum. Marino compiled data reporting piezoelectric coefficients in the range of 0.027–0.028 pC/N for dentin and cementum, and around 0.22 pC/N for bone, establishing that the electromechanical properties of these tissues are the result of the interaction between organic (collagen) and inorganic (hydroxyapatite) phases. Their review also highlighted the physiological role of piezoelectricity in mechanotransduction processes, including bone remodeling, healing, mechanical adaptation, and intracellular signaling. This consolidated the concept that biological piezoelectricity has functional and regulatory roles, in addition to physical interest.

The work of Wang et al. (2006/2007) delved into the factors that modulate piezoelectricity in human dentin. Their experiments demonstrated that the electromechanical response is strongly dependent on moisture content and dentin tubule orientation, with a significant increase in signal observed when dentin is rehydrated. This is attributed to water restoring the molecular mobility of collagen, promoting dipole polarization, and improving coupling between the organic matrix and the mineral phase. The greater response when applying forces parallel to the tubule axis reflects the hierarchical anisotropy of the tissue. These results explain discrepancies between measurements reported in the literature and offer a robust biophysical and *hy* model for understanding both the mechanoelectrical function of the tooth and its potential use in biomedical devices.

In the field of keratinous tissues, Marzec (2013) conducted a detailed analysis of the dielectric properties of the keratin-water system in human nails using spectroscopy from 20 Hz to 3 MHz. His results showed clear differences between healthy individuals and people with diabetes: healthy nails had a higher dielectric constant, higher conductivity, and more efficient polarization, associated with greater hydration and dipole mobility. In contrast, the nails of diabetic patients exhibited slower dielectric relaxations, higher activation energies, and an overall reduction in polarization, probably due to advanced protein glycation, loss of molecular order, and decreased moisture content. This study demonstrated that molecular structure and the water microenvironment directly influence the electrical behavior of keratin, providing a fundamental conceptual framework for further research on piezoelectricity in nails.

Research by Reyes-Gasga et al. (2019) using piezoelectric force microscopy (PFM) and mechanical testing confirmed that dentin and enamel possess piezoelectric activity at both the macroscale and nanoscale. Local d_{33} values ranged from 15 to 40 pC/N (with an average of approximately 22.5 pC/N in dentin and 15.8 pC/N in enamel), while macroscopic values barely reach ~0.03 pC/N. This disparity demonstrates that, although individual hydroxyapatite nanocrystals are highly piezoactive, the three-dimensional organization and heterogeneity of the tissue reduce the overall response. A notable finding was that piezoelectricity persists even after collagen is removed, demonstrating that the inorganic phase also possesses electromechanical activity. These results open the door to the design of biomimetic materials and sensors based on the natural electrical properties of dental tissue.

Finally, the recent study by Galindo Mentle and Blas Sánchez (2025) makes a significant contribution by clearly demonstrating the presence of piezoelectricity in human nails, a keratinous tissue that has historically been little explored in this context () (Figure 1). The authors show that the nail generates reproducible electrical charges under mechanical compression, consistent with the piezoelectricity observed in other tissues rich in fibrillar proteins. The structure of α -keratin, with partially ordered regions, appears sufficient to sustain induced polarization. One of the most relevant findings is the comparison between healthy and diabetic individuals: diabetic samples show a 30–60% reduction in the piezoelectric signal. This decrease is consistent with what was reported by Marzec (2013) regarding dielectric alterations associated with advanced glycation, loss of hydration, and molecular disorganization.

This set of studies establishes that the piezoelectricity of biological tissues is not a constant phenomenon, but rather a property that is highly sensitive to structural alterations induced by systemic diseases. In mineralized tissues such as bone and dentin, classic research by Fukada and Yasuda (1957) and Marino (1989), as well as nanometric analyses by Wang et al. (2006/2007) and Reyes-Gasga et al. (2019), show that the generation of electrical charges is closely dependent on collagen organization and the degree of mineralization. This suggests that pathologies affecting these parameters—such as osteoporosis, osteopenia, aging, or metabolic disorders—could reduce the electromechanical efficiency necessary for tissue remodeling and repair processes. Similarly, in keratinous tissues such as nails, recent studies (Marzec, 2013; Galindo-Mentle

& Blas-Sánchez, 2025) show that diabetes mellitus alters the hydration, stiffness, and molecular orientation of keratin, causing a significant reduction in the piezoelectric response. Table 1 presents the studies conducted and the evidence suggesting promising clinical potential for the measurement of piezoelectric signals for early diagnosis, non-invasive monitoring of metabolic diseases, and assessment of the structural health of bone and keratinous tissues.

Author / Year	Property studied	Main findings
Marino (1989)	Mechanical structure	Microfibril arrangement, water-keratin interaction
Marzec (2013)	Dielectric properties	Reduced conductivity and slower relaxation in diabetic nails
Reyes-Gasga (2019)	Piezoelectric properties	Piezoelectric coefficient in enamel and dentin
Galindo Mentle & Blas Sánchez (2025)	Optical and piezoelectric response	Decreased piezoelectric signal in diabetic nails

Table 1: Comparison of relevant findings on human nail properties

Conclusion

The evidence presented in this review confirms that piezoelectricity is an intrinsic phenomenon of multiple biological tissues, particularly those formed by fibrillar proteins and hierarchical structures such as collagen, hydroxyapatite, and keratin. The studies analyzed show that the piezoelectric and dielectric properties of these tissues depend critically on structural, environmental, and pathophysiological factors. Among these, hydration, molecular orientation, and protein matrix integrity stand out as deter-

mining variables of the magnitude of the electromechanical response. This allows us to understand why healthy tissues exhibit more efficient piezoelectric activity compared to those affected by metabolic disorders such as diabetes, in which advanced glycation and loss of molecular order significantly reduce dipole mobility and the ability to generate electrical charge.

Keratin, due to its accessibility, stability, and ability to reflect the physiometabolic state of the organism, is positioned as a strategic material for the development of non-invasive biosensors. The reviewed results highlight that piezoelectricity in the human body not only represents a fundamental link between the molecular structure and physiological functions of tissues, but also an emerging platform for biomedical innovation. Future integration between biophysics, materials engineering, and clinical sciences will enable progress toward more sensitive, personalized, and high- r technologies capable of harnessing the body's mechanical energy to produce diagnostic information and high-impact therapeutic solutions.

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