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Evaluation of plasma-induced surface modification in PLA-alginate biocomposites and their dielectric response: a review

Evaluación de la modificación superficial inducida por plasma en biocompuestos de PLA- alginato y su respuesta dielectrica: una revisión

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Abstract

Surface engineering is fundamental for advancing biomaterials in regenerative medicine. Biocomposites fabricated from polylactic acid (PLA) and alginate combine the mechanical strength of PLA with the hydrophilic and crosslinkable properties of alginate. However, their intrinsic hydrophobicity limits early tissue integration. Plasma modification offers a selective and non-destructive method to improve surface chemistry, wettability, and biological response through nanolayer surface functionalization. This research examines plasma-induced modifications in PLA–alginate biocomposites and their dielectric behavior, focusing on hydration, ionic mobility, and interfacial polarization. Non-thermal plasma introduces oxygen- and nitrogen-based functional groups (e.g., hydroxyl, carboxyl, carbonyl), increases surface energy, and generates nanoscale roughness, thereby enhancing protein adsorption, fibroblast adhesion, and osteogenic activity. Dielectric spectroscopy measures these changes through parameters such as relative permittivity (ε'), dielectric loss (ε''), loss tangent (tan δ), AC conductivity (σ_ac), and Maxwell–Wagner–Sillars (MWS) relaxation, which reflect water uptake and interfacial behavior. This review consolidates findings on plasma-functionalized biomedical scaffolds and plasma activation of PLA.

Keywords: polylactic acid, alginate, non-thermal plasma, dielectric spectroscopy, tissue engineering, biomaterial

Resumen

La ingeniería de superficies es fundamental para el avance de los biomateriales en la medicina regenerativa. Los biocompuestos fabricados con ácido poliláctico (PLA) y alginato combinan la resistencia mecánica del PLA con las propiedades hidrófilas y reticulables del alginato. Sin embargo, su hidrofobicidad intrínseca limita su integración temprana en los tejidos. La modificación por plasma ofrece un método selectivo y no destructivo para mejorar la química superficial, la humectabilidad y la respuesta biológica mediante la funcionalización de la nanocapa superficial. Esta investigación estudia las modificaciones inducidas por plasma en los biocompuestos PLA-alginato y su comportamiento dieléctrico, centrándose en la hidratación, la movilidad iónica y la polarización interfacial. El plasma no térmico introduce grupos funcionales basados en oxígeno y nitrógeno (p. ej., hidroxilo, carboxilo, carbonilo), aumenta la energía superficial y genera rugosidad a nanoescala, mejorando así la adsorción de proteínas, la adhesión de fibroblastos y la actividad osteogénica. La espectroscopia dieléctrica mide los cambios mediante parámetros como la permitividad relativa (ε'), la pérdida dieléctrica (ε''), la tangente delta (tan δ), la conductividad de CA (σac) y la relajación de Maxwell-Wagner-Sillars (MWS), que reflejan la absorción de agua y el comportamiento interfacial. Esta revisión consolida los hallazgos sobre los andamios biomédicos funcionalizados con plasma y la activación del PLA mediante plasma.

Palabra clave: ácido poliláctico, alginato, plasma no térmico, espectroscopia dieléctrica, ingeniería de tejidos, biomaterial

1 Introducción

Over the past years, we have observed the growing concern of having the loss of tissue or end-stage organ failure, living with the demand of not having enough donors to prioritize the patient's life (Velázquez et al., 2025). Research into biocompatible and biodegradable polymers, both natural and synthetic, has emerged as a vital area for biomedical applications, tissue engineering, and environmental sustainability (Rondón et al., 2023). Furthermore, these materials have been evolving, focusing on replacing or restoring the function of human tissues and organs that have been damaged or lost (Abdulsalam et al., 2025).

PLA is a biodegradable polymer, used as a biomaterial for biomedical applications, tissue engineering, scaffolds, and bone fixation devices (Abdulsalam et al., 2025). The physical properties of PLA vary with molecular weight. Therefore, it degrades through simple hydrolysis of ester bonds; the degradation rate can be influenced by the isomer ratio, oxygen, and temperature of hydrolysis, pH, burial time, humidity, and shape and sample size. Unfortunately, PLA applications are limited due to several disadvantages, such as excessive brittleness, poor osteointegration, low cell adhesion, and biological inertness. In fact, depending on the PLA applications, it has a low degradation rate (Velázquez et al., 2025).

Poly(lactic acid)- based systems have been developed to deliver a variety of payloads, from small drug molecules to nucleic acids and large proteins, in a sustained-release manner. Usually, the polymer is blended with another biodegradable polymer or agent to avoid disadvantages. Furthermore, PLA can be combined with alginate, once combined forms PLA-Alginate. Alginate is a natural anionic linear biopolymer commonly obtained from brown algae and certain bacteria. However, there are challenges related to reproducibility and standards, as it varies across species, seasons, and geographic origins. It has poor mechanical properties; it may be improved by crosslinking with multivalent cations. The degradation rate is fast at high temperatures, and a key limitation is the difficulty of customization. The combination of PLA and Alginate is highly beneficial, as it increases surface wettability and hydrophilicity, thereby promoting cell adhesion and biocompatibility. Due to its high moisture-absorbance capacity, the alginate-chitosan composite is typically developed to reduce moisture permeability (Bodaghi et al., 2019). Additionally, it provides antimicrobial activity and improves mechanical properties (Abdulsalam et al., 2025; Popelka et al., 2020). The NTP (non-thermal plasma) promotes the controlled incorporation of polar functional groups, increases surface energy, modifies dielectric behavior, and generates micro-roughness (Rondón et al., 2025; Rajasekar et al., 2025).

However, there are challenges due to reproductive and standard variations, as they vary across species, seasons, and geographic origins. It has poor mechanical properties; these may be improved by crosslinking with multivalent cations. The degradation rate is fast at high temperatures, and a key limitation is the difficulty of customization. Even alginate exhibits beneficial properties, including biodegradability, non-toxicity, and high water absorption, for various biomedical applications (Hurtado-Fernández et al., 2026). The combination of PLA and alginate is highly beneficial, as it increases surface wettability and hydrophilicity, thereby promoting cell adhesion and biocompatibility. Due to the high moisture absorbance capacity, an alginate/chitosan composite is typically developed not only to reduce moisture permeability but also to bestow it with additional antimicrobial and enhanced mechanical properties (Yadav et al., 2025). The NTP (non-thermal plasma) promotes the controlled incorporation of polar functional groups, increases surface energy, modifies dielectric behavior, and generates micro roughness (Walden et al., 2024; Nayak et al., 2023).

2 Methodology

The methodology used in this research will be document- exploratory following the PRISMA guidelines (Page et al., 2021; Moher et al., 2009), based on:

a. Data search strategy and compilation: A comprehensive literature search was conducted across academic databases including PubMed, MDPI, Scopus, Web of Science, Science Direct and Research Gate. The search will be limited to the period from 2010-2026.

b. Information Selection and refinement: To organize the information, it was performed by the bibliographic manager Mendeley. Organizing into 6 databases: types of plasma and parameters, surface physicochemical changes, effects on wettability, adhesion, and degradation in SBF, dielectric properties/impedance, and their relationship to interface chemistry and implications for tissue engineering (cell adhesion /proliferation), characterization guidelines, and future applications. Relevant research articles and reviews will be prioritized.

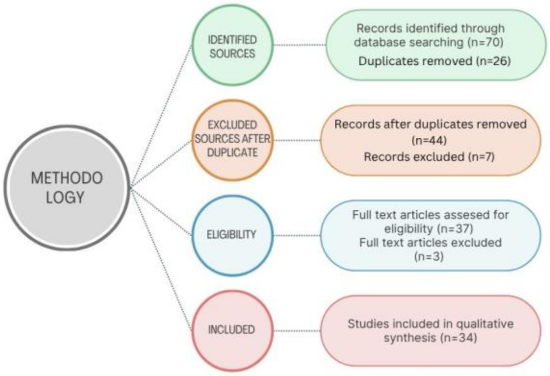

Figure 1. Study selection methodology flowchart for the research.

c. Subtopic Selection: The subtopic obtained information is analyzed to identify properties and physicochemical advances and their relevance to the growing field of regenerative medicine and tissue engineering.

d. Analysis of Results: The analysis performed of results leads to organizing information into a structured analysis review, highlighting its relevance to tissue engineering applications and future advances.

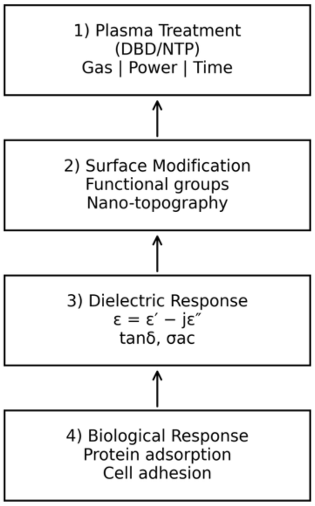

Figure 2. Plasma–surface–dielectric–biological interaction framework. Plasma treatment modifies surface chemistry and nano-topography, altering complex permittivity ($\varepsilon = \varepsilon' - j\varepsilon''$), dielectric loss (tanδ), and AC conductivity (σ_ac), which subsequently influence protein adsorption and cellular response.

3 Results and Discussions

3.1 Types of plasma and parameters

The plasmas generated under low pressure or atmospheric pressure conditions enables the cleavage of surface bonds, the introduction of oxidative functional groups, and the formation of micro-roughness factors that collectively increase surface free energy and enhance cell material interactions (Rondón et al., 2025; Yehia, 2024). As a matter of fact, non-thermal plasmas can reconfigure surface chemistry through the incorporation of polar functional groups and the generation of micro-roughness. As if these two mechanisms significantly enhance wettability and interfacial compatibility (Kamalov et al., 2022).

Recent literature on polymer surface modification has established plasma treatment as one of the most versatile and effective strategies for improving adhesion in thermoplastics, thermosetting, and elastomeric materials (Rajasekar et al., 2025; Walden et al., 2024; Nayak et al., 2023; Yadav et al., 2025). In addition, a comparative analysis of various experimental works consistently reported notable reductions in water contact angles and increases in surface energy, directly indicating improved adhesion and chemical anchoring (Rondón et al., 2025). These physicochemical transformations are recognized as optimizing the bonding of coatings, adhesives, and functional layers, extending the impact of plasma treatment to diverse biomedical engineering, tissue engineering, and microelectronics (Rondón et al., 2025; Rajasekar et al., 2025). The DBD dielectric barrier discharge plasma consists mostly of two parallel plates, and they are characterized by presence of the dielectric layer covering at least the internal surface of one the two discharge electrodes or both (Yehia, 2024). In Addition, the system operates only on high-voltage AC power supplies. It can be used to form non–thermal plasma under different operating conditions. Furthermore, the DBD has unprecedented flexibility with respect to operating conditions. It is possible to generate different electrode systems, each with dielectric layers made from materials such as glass, ceramic, epoxy, and others. This system can be operated at high voltage and fed with different gases and mixtures at high flow rates at atmospheric pressure and room temperature (Yehia, 2024; Gershman et al., 2021). Ensuring effectiveness of plasma surface modification strongly depends on both the operating parameters and the plasma type. Following the parameters ensures effective enhancement of cell adhesion and hydrophilicity promoting an effective biomedical application (Jacobs et al., 2013; Rondón et al., 2025; Fernandes et al., 2026).

3.2 Surface physicochemical changes

Bioactive scaffolds represent an evolution from purely structural support toward dynamically instructive biomaterials. In fact, they are engineered to modulate cell adhesion, proliferation, differentiation, and ECM deposition through tailored surface chemistry, nano/micro architecture, and controlled presentation of biochemical signals. Furthermore, scaffolds can be designed from natural and synthetic polymers, ceramics, and composite systems, increasing attention to the interplay between material composition, degradation behavior, and host responses. A key strategy for scaffold-enhanced performance is functionalization, involving deliberate modifications of the scaffold's bulk or surface to introduce specific physicochemical, biological, and topographical features that promote the desired cellular response (Aponte-López et al., 2025).

Polylactic acid (PLA) is among the most promising materials for tissue engineering due to its favorable biocompatibility and biodegradability. On the other hand, its relatively long degradation time of 2 to 5.5 years limits its suitability for applications. PLA is degraded by enzymatic activity or hydrolysis, forming lactic acid, which is usually present in the body. In this way, inflammatory reactions are prevented, and the by-products are expelled through normal cell activity and urine. Copolymers of PLA and polyglycolic acid (PGA) offer a more adaptable degradation profile based on their composition ratios, with opportunities to develop resorbable membranes capable of supporting complex bone regeneration scenarios (Zernitckaia et al., 2025).

Another critical step is the sterilization of PLA for clinical use. Due to PLA's thermal sensitivity, autoclaving is not suitable; it is possible to deform the material and alter its properties, potentially affecting both degradation behavior and osteoinductive potential (Pérez-Dávila et al., 2021) Besides, gamma irradiation is widely employed for sterilizing PLA-based materials with doses up to 25kGy that have been shown to be effective without compromising material safety or performance (Zernitckaia et al., 2025; Pérez-Dávila et al., 2021). This sterilization method is considered optimal for thermally sensitive medical devices that require both internal and surface sterility. The biodegradable plates were analyzed using Fourier-transform infrared spectroscopy on a Shimadzu IRTracer –100 spectrometer, *the spectra* recorded range of 500-400cm^-1 for the evaluation of structural changes in the materials resulting from both biodegradation and sterilization processes. Indeed, the irradiation performance was a linear pulsed electron accelerator (Ee=10MeV), there are studies that have shown that this dose of ionizing radiation does not damage the structural integrity of PLA and its composites, preserving their mechanical and physicochemical properties. At 25kGy, the composites such as hydroxyapatite/PLLA remain structurally stable. However, at higher doses, surface damage has been observed, negatively affecting performance, substantially reducing tensile strength and elongation at break in PLA concerns over excessive irradiation (Zernitckaia et al., 2025; Pérez-Dávila et al., 2021). In addition, changes were found indicating degradation on PLA by irradiations, such as a decrease in molecular weight, other changes in mechanical, thermal, and permeability properties (Pérez-Dávila et al., 2021). UV irradiation affects the diblock copolymer of Me.PEG-PLA, at different radiation times (0,2,5,10 and 25h). In two hours, it was observed that irradiation required properties nor the cell adhesion was altered, compared with the control. However, once the radiation time was further increased, the copolymer surface changes occurred affecting cell/protein-polymer interactions. The hydrogen peroxide plasma, which has shown electro spun biodegradable matrices without altering their chemical composition or surface morphology. In addition, the electron beam parameters are gaining traction due to its efficiency, speed, and compatibility with thermally sensitive materials (Pérez-Dávila et al., 2021). As with gamma radiation, the morphology and alignment of the fibers were not affected, nor the mechanical or thermal properties; only a slight increase in wettability was observed, and like gamma radiation, the membranes had a good cellular response (Zernitckaia et al., 2025; Pérez-Dávila et al., 2021).

The clinical potential of biodegradable polymers lies in their ability to serve as customized, resorbable scaffolds. PLA, PLGA and its copolymers have been explored for applications ranging from jawbone reconstruction to tendon repair, biocompatibility and long-term in vivo safety remain key focus areas for ongoing investigations (Aponte-López et al., 2025). In surgical applications, the mechanical performance of bioresorbable materials is as critical as their biocompatibility. For instance, adequate strength, stiffness, and controlled degradation are essential for maintaining implant stability through the healing process. To continue, the potential of PLA and copolymers is reliable biodegradable membrane materials for clinical and medical use. The analysis of physicochemical and biodegradation properties revealed material specific differences in stability (Zernitckaia et al., 2025).

3.3 Effects on Wettability, Adhesion, and Degradation in SBF

3.3.1 Impact of Plasma Treatment on Surface Wettability

The surface properties of PLA-based biomaterials undergo substantial changes upon non-thermal plasma surface modification using a dielectric barrier discharge (DBD), thereby affecting their wettability. PLA surfaces treated with plasma become more water-absorbing as their contact angles decrease from above 80° to 50°-70° (Rondón & Gonzalez-Lizardo, 2025; Hergelová et al., 2015). This change results from the addition of polar oxygen- and nitrogen-containing functional groups (such as hydroxyl, carbonyl, and carboxyl groups) and from nanoscale surface irregularities induced by plasma treatment (Hergelová et al., 2015; Pillai & Mohan, 2025).

The PLA–alginate system benefits from plasma-induced wettability enhancement due to the hydrophilic and ionic properties of alginate. Alginate domains enable water absorption and ion exchange, strengthening plasma activation results and producing a water-rich surface that promotes biological responses (Sun & Tan, 2013). This method has shown equivalent wettability enhancements in various polymeric biomaterials for orthopedic, dental, and cardiovascular applications (Pillai & Mohan, 2025; Ferreira et al., 2023).

3.3.2 Cell Adhesion and Biological Interactions

Surface wettability significantly influences cell attachment because it controls protein binding to material surfaces. Plasma treatment of PLA and PLA-based composites enhances protein adsorption, particularly extracellular matrix proteins like fibronectin and vitronectin, which facilitate cell attachment through integrin receptors (Rondón & Gonzalez-Lizardo, 2025; Krutty et al., 2016). Plasma-modified surfaces yield better fibroblast cell spreading, stronger focal adhesions, and improved cytoskeletal structure compared to untreated surfaces (Rondón & Gonzalez-Lizardo, 2025; Hergelová et al., 2015). This is crucial in tissue engineering, as early cell attachment determines the success of regenerative procedures.

Moreover, plasma surface activation combined with bioactive components enhances cell-material interactions. PLA functionalization and bioactive scaffold studies show that plasma treatment facilitates the attachment of biomolecules or nanoparticles, promoting cell attachment, growth, and tissue formation (Abdulsalam et al., 2025; Świerczyńska et al., 2024; Aponte-López et al., 2025). The ionic bonds between PLA and alginate in these composites create bioactive interfaces, maintaining stable focal adhesions and functional signaling pathways essential for tissue healing (Lopes et al., 2012).

3.3.3 Dielectric Properties and Their Role in Biomaterial Functionality

The dielectric properties of plasma-treated surfaces are influenced by their water-attracting properties and their ability to form bonds with other materials. Dielectric spectroscopy studies reveal that plasma treatment increases relative permittivity (ε'), dielectric losses, and Maxwell–Wagner–Sillars (MWS) polarization effects in PLA materials and composites (Spinelli et al., 2020; Dichtl et al., 2017; Kremer & Tress, 2025; Walker et al., 2019). These dielectric signatures reflect elevated water levels and enhanced ionic movement at the interface, supporting nutrient transport, metabolic processes, and overall cellular function. Dielectric parameters serve as secondary indicators of how plasma treatment affects surface bioactivation and biological performance (Abdelhamid, 2022).

3.3.4 Degradation Patterns in Simulated Body Fluid (SBF)

Plasma modification alters the degradation pattern of PLA-based biomaterials during exposure to simulated body fluid. Increased surface hydrophilicity allows water to penetrate the top polymer layers, accelerating surface hydrolysis without compromising the material's core structural strength (Abdulsalam et al., 2025; Kurowiak et al., 2023; Zernitckaia et al., 2025). Studies on PLA membranes and composites immersed in SBF show that improved membrane wettability enhances ionic bonding with calcium and phosphate ions, promoting bioactivity and the formation of apatite-like minerals for bone tissue engineering (Castro et al., 2022; Kudzin et al., 2021; Zernitckaia et al., 2025). The PLA–alginate system gains additional benefits from ionically active alginate, which supports Ca^{2+}-mediated crosslinking and surface mineralization (Sun & Tan, 2013).

3.3.5 Advantages of Dielectric Barrier Discharge (DBD) Plasma Treatment

The DBD plasma treatment process mitigates the risks of uncontrolled material breakdown and thermal damage. The dielectric barrier limits energy transfer, preventing overheating and confining plasma-induced surface modifications to the top nanolayers without harming the internal structure (Yehia, 2024; Subedi et al., 2017). This combination of surface reactivity and structural stability is critical for developing biomaterials that degrade in a controlled manner while maintaining long-term functionality.

3.4 Dielectric properties/impedance and their relationship to interface chemistry

Plasma-induced surface modification of polylactic acid (PLA)–alginate biocomposites results in pronounced changes in dielectric behavior and impedance response, directly linked to alterations in interfacial chemistry. In heterogeneous biodegradable polymer systems, dielectric spectroscopy and electrical impedance spectroscopy (EIS) provide sensitive probes of interfacial polarization, ionic mobility, and hydration phenomena, all of which are governed by surface functionalization and interphase structure (Kremer & Tress, 2025; Abdelhamid, 2022).

3.4.1 Interface Chemistry Induced by Plasma Treatment

Non-thermal plasma treatments, particularly dielectric barrier discharge (DBD), introduce polar oxygen- and nitrogen-containing functional groups (e.g., –OH, –COOH, –C=O) onto PLA surfaces without affecting bulk properties (Hergelová et al., 2015; Rondón et al., 2025). These chemical modifications increase surface energy, reduce hydrophobicity, and promote interfacial compatibility with hydrophilic and ionically active biopolymers such as alginate (Sun & Tan, 2013; Kudzin et al., 2021).

The efficiency of plasma-induced functionalization is strongly dependent on discharge energetics and thermal losses, as Yehia (2024) described, underscoring the importance of controlling plasma parameters to achieve stable surface activation. Reviews on polymer functionalization further highlight that plasma-generated interfaces are dynamic and susceptible to aging effects, which can influence long-term dielectric stability (Abdulsalam et al., 2025; Pillai & Mohan, 2025).

3.4.2 Dielectric Permittivity and Interfacial Polarization Mechanisms

Across PLA-based composites and nanocomposites, plasma-induced changes in interface chemistry are consistently reflected in the real part of the dielectric permittivity (ε′), particularly in the low-frequency region. Studies on PLA reinforced with carbon-based particles, cellulose nanofibrils, nanobioglass, and alginate report increased ε′ values associated with enhanced interfacial polarization (Spinelli et al., 2020; Ranakoti et al., 2022; Castro et al., 2022; Kudzin et al., 2021).

This behavior is commonly attributed to Maxwell–Wagner–Sillars (MWS) polarization, which arises from charge accumulation at interfaces between phases of differing conductivity and permittivity (Walker et al., 2019). Plasma functionalization intensifies this effect by increasing dipole density and enabling stronger coupling between the PLA surface and the alginate-rich interphase. Dielectric spectroscopy theory confirms that such interfacial contributions dominate the dielectric response of heterogeneous polymers at low frequencies (Kremer & Tress, 2025).

Dielectric Losses, Conductivity, and Ionic Mobility

The imaginary component of permittivity (ε″) and dielectric loss tangent (tan δ) provide insight into energy dissipation mechanisms linked to dipolar relaxation and ionic conduction. Plasma-treated PLA systems exhibit increased dielectric losses due to enhanced molecular mobility and water uptake within the modified interphase (Dichtl et al., 2017; Abdelhamid, 2022). In PLA–alginate composites, alginate's ionic character further amplifies these effects by facilitating ion hopping and polarization under alternating electric fields (Sun & Tan, 2013).

The observed increase in AC conductivity (σ_ac) following plasma treatment reflects improved ionic displacement and interfacial charge transport. These findings align with reports on biodegradable polymer nanocomposites, where surface chemistry and interphase hydration strongly influence electrical conductivity and dielectric relaxation behavior (Spinelli et al., 2020; Abdelhamid, 2022).

3.4.3 Impedance Spectroscopy and Interfacial Resistance

Electrical impedance spectroscopy complements dielectric measurements by quantifying resistive and capacitive elements associated with the polymer interphase. Plasma-treated PLA-based biomaterials consistently exhibit reduced impedance magnitude and lower interfacial resistance, as evidenced by smaller semicircle diameters in Nyquist plots and increased interfacial capacitance (Kudzin et al., 2021; Ferreira et al., 2023).

In PLA–alginate systems, plasma activation of the PLA surface promotes stronger physicochemical interactions at the interface, enabling more efficient ionic continuity across phases. Equivalent circuit analyses reported in polymer electrolyte and hydrogel systems suggest that these changes correspond to the formation of a more hydrated, polar, and charge-supportive interphase (Abdelhamid, 2022; Walker et al., 2019).

3.4.4 Biological and Functional Implications

The strong correlation between dielectric response and interface chemistry has direct implications for biomedical applications. Plasma-induced increases in dielectric permittivity and reductions in impedance are consistently associated with enhanced protein adsorption, fibroblast adhesion, and biocompatibility in PLA-based scaffolds and films (Rondón et al., 2025; Rondón & Gonzalez-Lizardo, 2025; Krutty et al., 2016). These effects are particularly relevant for PLA–alginate constructs used in bone and soft tissue regeneration, where interfacial hydration and ionic signaling play critical roles (Sun & Tan, 2013; Kudzin et al., 2021; Aponte-López et al., 2025).

Furthermore, dielectric and impedance measurements offer a powerful means of monitoring the stability of plasma-induced modifications during sterilization, aging, and biodegradation processes (Pérez-Dávila et al., 2021; Zernitckaia et al., 2025). As such, dielectric spectroscopy emerges as both a diagnostic and predictive tool for evaluating interface-driven performance in plasma-modified PLA–alginate biomaterials (Table 1).

3.5. Implications for tissue engineering (cell adhesion/proliferation) and characterization of guidelines.

3.5.1 Tissue Engineering

Tissue Engineering aims to review native tissue or organ function and identify replacements when damaged or diseased tissues and organs are present. It is composed of living cells, scaffolds, and signals. The scaffolds used are widely diverse, including synthetic and natural polymers (Velázquez et al., 2025). Therefore, scaffolds must provide a favorable environment for cell growth, proliferation, infiltration, differentiation, and migration, and they must have properties such as biocompatibility, good mechanical properties, degradability, and a porous morphology (Parangusan et al., 2025). However, the emergence of scaffold-free processes has expanded the field's capabilities. For instance, it has been successfully used in engineering musculoskeletal, cardiovascular, metabolic, and corneal tissues. Supporting this, scaffold-free approaches, has two primary, thermodynamically driven modalities of self-organization and selfassembly. Although the preparation methods for synthetic and biologically active scaffolds with the capacity to induce regenerative healing are three-dimensional printing, bioprinting, and electrospinning (Velázquez et al., 2025).

3.5.2 Strategies to replace damaged organs or tissues

All tisues in the human body are integrated by animal cells, which are grouped and organized to work in spectacular precision to form organs in the body. Similarly, all cells in the body are components of four tissues, such as connective tissue, epithelial tissue, nervous tissue, and muscle tissue. Therefore, strategies to replace damaged organ or tissue involve a cyclic process beginning with the donor or patient, followed by incorporating cells and growth factors into biomaterials to construct a functional graft (Velázquez et al., 2025).

Table 1. Summary of Plasma Types, Dielectric Effects, and Biological Responses Reported in Included Studies

Plasma type	**Key parameters**	**Dielectric effects**	**Biological response**
Dielectric barrier discharge (DBD)	Atmospheric pressure; AC high voltage (kV); air, O_2, N_2 or Ar; short exposure times	Increase in ε′ and tan δ at low frequencies; enhanced Maxwell–Wagner–Sillars polarization due to a hydrated interphase	Enhanced protein adsorption; improved fibroblast and osteoblast adhesion and proliferation
Atmospheric pressure plasma jet (APPJ)	Moderate voltage; controlled gas flow; room-temperature operation	Increase in AC conductivity (σ_ac) and interfacial permittivity due to higher ionic mobility	Improved cell spreading and early cell–material interactions
Low-pressure RF plasma	Vacuum environment; longer treatment times; uniform energy distribution	More homogeneous dielectric response with reduced interfacial variability	Highly reproducible cell adhesion and stable surface activation
Oxidative plasma (O_2/air)	High density of reactive oxygen species	Higher dielectric losses due to increased surface dipole density	Significant improvement in wettability and overall surface bioaffinity

3.5.3 Poly (lactic acid) Production for tissue engineering applications.

Polylactic acid is one of the most promising polymers due to its being obtained from nontoxic monomers obtained from renewables. The monomer employed in the production of PLA is the lactic acid (2-hydroxypropinic acid), a chiral molecule, which exists in two enantiomers, L-lactic acid an L-lactic acid, this acid can be produced by fermentative or chemical synthesis.

On the other hand, PLA is the reference of a family of polymers: poly (L-lactic acid) (PLLA), poly (D-lactic acid) (PDLA), and poly (D, L-lactic acid) (PDLLA). However, the stereoisomers PLLA and PDLA have similar physicochemical properties, PDLLA has different characteristics due to its structure. Additionally, PLA can be prepared through different polymerization techniques from lactid acid by indirect processes such as polycondensation, ring-opening polymerization and direct method such as azotropic dehydration and enzymatic polymerization. Among this, enzymatic polymerization and ROP are the most used techniques.

Ring-opening polymerization (ROP) is the method used to produce PLA with controlled molecular weight. This consists of three main steps: polycondensation, depolymerization, and ring-opening polymerization. However, this process requires purification of products, causing elevation of costs. Furthermore, degradation of PLA mechanisms mare hydrolytic, oxidative, thermal, microbial, enzymatic, photo-degradative, and chemical processes (Velázquez et al., 2025).

3.5.4 PLA for Skin Tissue Engineering

Skin is the largest organ in the human body, and when it is damaged, a series of complex physicochemical and biological processes are activated to restore tissue integrity (Abdelhakim & Ogawa, 2025). The development of materials that promote tissue regeneration has emerged as an innovative alternative for the treatment of skin injuries and wound healing (Mamun et al., 2024). Furthermore, Xu et al. (2023) fabricated a three-layer bandage composed of a MXene coating (top), a PLA/polyvinyl pyrrolidone (PLA/PVP) Kirigami structure (middle), and an integrated f-sensor (bottom), capable of sensing microenvironmental changes caused by wound infection in real time. This system demonstrated high extensibility (up to 831% increase over the original structure), flexibility, and biocompatibility. Similarly, recent advances in smart wound dressings enable the creation of adaptive, comfortable environments for wounds in dynamic body regions while enabling continuous monitoring and effective treatment of infections (Xue et al., 2021).

Moreover, recent studies have reported the development of nanofibrous scaffolds incorporating metal-based nanoparticles with good biocompatibility and suitable mechanical properties for wound healing applications. Electrospun nanofiber scaffolds loaded with nanoparticles such as ZnO exhibit antibacterial, anti-inflammatory, and regenerative capabilities, making them promising candidates for tissue engineering (Dang et al., 2024). In particular, the incorporation of ZnO nanoparticles enhances antibacterial activity, improves cell viability, and accelerates wound healing processes (Athamneh et al., 2025). Additionally, nanofibrous aerogel scaffolds with interconnected porous structures facilitate wound exudate absorption, air exchange, and nutrient transport, while supporting cell proliferation and migration (Mao et al., 2021). Furthermore, ZnO-containing systems have been shown to promote angiogenesis, further enhancing tissue regeneration.

3.5.5 Cartilage Regeneration

Cartilage is a specialized connective tissue responsible for supporting the body and transmitting mechanical stress. The most common types found in the human body are hyaline cartilage and fibrocartilage, each with distinct structural and functional properties (Sophia Fox et al., 2009). In recent years, innovative strategies have focused on the development of bilayer composite scaffolds that mimic the hierarchical structure of native cartilage. For instance, bilayer systems combining a hydrogel layer, such as gelatin methacrylate (GelMA), with a fibrous scaffold layer based on polymers like PLA and silk fibroin have demonstrated promising results in cartilage tissue engineering (Huang et al., 2022). These scaffolds exhibit high porosity (around 90%), suitable mechanical properties in the MPa range, and excellent cell viability. Furthermore, ex vivo studies using mesenchymal stem cells, chondrocytes, and meniscal cells suggest their strong potential for cartilage regeneration and implantation.

However, recent advances in 3D bioprinting have enabled the fabrication of polymer-based scaffolds, including PLA-based systems, for cartilage tissue engineering. These scaffolds have been extensively evaluated for their ability to support cell growth, viability, and tissue formation. In particular, 3D-printed porous scaffolds with large pore sizes (in the range of hundreds of micrometers, e.g., ~500–700 μm) have demonstrated enhanced cell infiltration, proliferation, and chondrogenic differentiation (Zhang Y et al., 2022). Furthermore, bioprinted constructs have shown high cell viability and the ability to promote extracellular matrix deposition, including proteoglycans and type II collagen, which are key components of cartilage tissue (Jang et al., 2017; Li et al., 2022; Zhang et al., 2022). These findings highlight the potential of 3D-printed scaffolds with adequate mechanical stability and controlled porosity for cartilage regeneration.

3.5.6 Bone Tissue

Bone tissue can regenerate and repair itself when experiencing minor damage, it is not sufficient repairing large defects caused by trauma, cancer, osteoporosis and congelital disorders, which significantly impart the life quality and very often require clinical interventions (Akderya et al., 2025). Furthermore, in bone tissue regeneration PLA is a biopolymer exceptional for bone applications because there is no need of other surgeries. Eventhough, it can promote a foreign body reaction, hence PLA implant is eventually encapsulated by fibrous tissues. However, the osseointegration is not reached and PLA implant failure (Velázquez et al., 2025).

Currently, clinical procedures such as autografts, allografts, and xenografts are widely used to repair large-scale bone defects; however, they present significant limitations and risks, including donor shortage, immune rejection, infection, and variability in biological performance (Grayson et al., 2022). As an alternative, the combination of polylactic acid (PLA) with bioactive ceramic materials such as hydroxyapatite, calcium phosphates, and other apatite-based compounds has been extensively explored to improve the bioactivity and osteoconductivity of implants (Zhang et al., 2019). In particular, PLA/hydroxyapatite composite scaffolds have demonstrated promising results for bone regeneration, exhibiting enhanced mechanical properties, cell proliferation, and osteogenic potential (Shuai et al., 2025). Moreover, the development of advanced scaffolds fabricated through 3D printing technologies allows precise control of pore architecture and mechanical performance, making them suitable candidates for the treatment of large bone defects (Zhang et al., 2021).

Eventhough, PLA has a poor cellular adhesion on its surface and brittleness that limits its use, mixing it with other biomaterials has benefits that provide solutions to these disadvantages. With surface modification on the hydrophobic surface of PLA, can achive to make it hydrophylic adjusting production techniques and incorporating other biomaterials. Also, the lactic acid byproduct resulting form PLA degradation, is metabolized in vivo without cytotoxic effects on living tissues. Despite the inadequacies in PLA's mechanical strength, being. Reinforced or coated by biomaterials, enhance a better durability (Akderya et al., 2025).

3.5.7 Fenugreek-enriched electrospun PLA scaffold

Electrospun nanofibrous scaffolds have been under analysis and have presented great potential as materials for tissue regeneration. The use of medicinal plant components for biomedical and wound-healing applications promotes improved performance and enhances shared positive outcomes. In addition, the electrospinning technique for fabricating fenugreek-incorporated PLA scaffolds was analysed using X-ray diffraction, Fourier transform infrared spectroscopy, mechanical testing, contact angle measurement, swelling measurement, and weight loss assessment. Moreover, the MTT aasay evaluated the scaffold's in vitro cell viability and biocompatibility using NIH/3 T3 fibroblast cells. Furthermore, the properties of polymeric based materials are determined by their cristalinity. The pure PLA and PLA/fenugreek scaffolds had a smooth, bead-free, randomly arranged surface, and, because of their porous nanostructure and surface area, they can mimic the native extracellular matrix and provide an ideal environment for cell attachment and growth (Parangusan et al., 2025).

The mechanical properties of pure PLA and PLA/fenugreek composites analyzed showed higher tensile stress in PLA/Fenugreek than in PLA scaffolds. However, swelling behavior of PLA/Fenugreek scaffolds obtained a higher water absorption rate than pure PLA. Equally important, cell attachment to tissue engineering is directly modified by surface wettability. Comparing pure PLA exhibited a higher contact angle, being that said, the Fenugreek incorportation resulted in a decrease of contact angle, which indicates an enhanced surface wettability. This MTT cell viability and in-vitro wound healing assay demonstrated that fenugreek could enhance cell migration and wound repair combining it with PLA, promoting skin cells proliferation. Another point to consider, is their excellent properties, good biocompatibility and ability to accelerate wound healing, promoting excellent candidates for tissue engineering implementation (Parangusan et al., 2025).

3.5.8 Future applications on Tissue Engineering

Tissue engineering is a constant emerging area of innovation, which looks forward to next-generation regener ative platforms which relys on the emerging technologies such as 4D bioprinting, gene-activated scaffolds, bioelectronic interfaces and AI- guided material designs. Furthermore, these innovations compromise to deliver more dynamic, adaptive and patient-specific developments that can respond to physiological stimuli promoting robust functional tissue regeneration (Aponte-López et al., 2025) (Table 2).

Table 2. PLA for skin tissue engineering and wound healing

Studies	**Composites**	**Potential applications**	**Key Properties**
In vitro cellular experiment performed on the back of a rat	Mxene/PLA/PVP bandage	Surgical Wound Care	Satisfactory stretching, bending and biocompatibility properites
In vivo studies that promote skin infection' wound healing and enhance angiogenesis	PLA/Gelatin/ZnO nanofibrous aerogel	Wound healing	Adequate antibacterial properties, biocompatibility absorption and permeability.
In vitro experiment proving biocompatibility of material, while in vivo experiment demonstrated good healing enhance of wound healing and no signs of infection.	PCL/PLA/gelatic biomimedic 3D scaffold	Skin Regeneration	Elevated surface area to volume ratio to cell adhesion, stronger mechanical properties and good hydrophilicity.
In vivo and in vitro biocompatibility 3T3-PMS/PLA interaction	PMS/PLA nanofibrous scaffolds	Skin tissue engineering	Excelent elasticity, stiffness and strength, as well as degradation rate is appropriate for soft tissues.

4 Conclusion

This study established a structured relationship between plasma surface modification, dielectric behavior, and biological response through a systematic PRISMA-based analysis of the literature. Evidence indicates that plasma treatment (DBD/NTP) induces controlled changes in surface chemistry and nano-topography, resulting in increased surface energy and altered interfacial charge distribution. These modifications directly affect the complex permittivity ($\varepsilon = \varepsilon' - j\varepsilon''$), dielectric loss (tanδ), and AC conductivity (σ_ac), reflecting changes in polarization mechanisms at the material–environment interface.

The reviewed studies consistently demonstrate that dielectric properties correlate with protein adsorption dynamics and subsequent cellular adhesion behavior. Interfacial polarization effects appear to mediate electrostatic interactions that influence early biological events at the biomaterial surface, suggesting that dielectric characterization may serve as a quantitative engineering parameter for predicting biological performance. Additionally, surface aging and biofouling were identified as variables that can modulate dielectric stability, highlighting the importance of time-dependent characterization under physiologically relevant conditions.

A primary limitation of this review is the heterogeneity in plasma parameters, dielectric measurement protocols, and biological assay methodologies across studies, which restricts direct quantitative comparison and limits the potential for meta-analytic standardization.

Overall, the proposed plasma–surface–dielectric–biological framework provides an engineering-based approach for biomaterial optimization. Integrating dielectric spectroscopy with surface functionalization strategies may enhance predictive control over biological outcomes and support the rational design of next-generation biomedical materials.

PLA applications in tissue engineering make it one of the most versatile biopolymers due to its biocompatibility and biodegradability. Several studies have demonstrated its good interaction with other biopolymers, even fusing with natural plants to create beneficial possibilities. It demonstrates its ability to emulate key functions as extracellular matrix, cell behaviour and physicochemical processes which ensure an excellent ability for wound healing acceleration and skin cell proliferation. Some of the analyses included in vitro, in vivo, and 3D electrospinning techniques, relying on and looking forward to next-generation regenerative technologies.

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