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Original Article

A Network-Based Analytical Model Linking Periodontal Inflammatory Burden to Orthodontic Biomechanical Sensitivity

Maria L. Santos[1], João P. Ribeiro[2], Ana S. Costa[1]*, Miguel T. Fernandes[2], Inês M. Almeida[1], Rui A. Carvalho[2]

[1]Department of Periodontology, Faculty of Dental Medicine, University of Lisbon, Lisbon, Portugal.
[2]Department of Orthodontics, Faculty of Dental Medicine, University of Lisbon, Lisbon, Portugal.

***E-mail** ✉ ana.costa.perio@outlook.com

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ABSTRACT

The interface between periodontal inflammation and orthodontic tooth movement represents a critical area in dental sciences, where persistent inflammatory states may modulate tissue responses to mechanical stimuli. This conceptual manuscript introduces a novel network-based analytical model that integrates periodontal inflammatory burden—defined as the cumulative and interconnected load of pro-inflammatory mediators, cellular interactions, and tissue alterations—with orthodontic biomechanical sensitivity, conceptualized as the periodontium's propensity to remodel under applied forces. Drawing on recent literature synthesizing osteoimmunological processes, the model posits the periodontium as a dynamic network wherein nodes represent key elements such as cytokines (e.g., IL-6, RANKL), immune cells (e.g., macrophages, T-cells), and structural components (e.g., alveolar bone, periodontal ligament fibers), while edges denote regulatory interactions influenced by inflammatory signals. Inflammatory burden is theorized to amplify network connectivity, thereby heightening biomechanical sensitivity through enhanced signal propagation, potentially leading to altered remodeling thresholds without implying empirical causality. The framework synthesizes theoretical backgrounds from periodontal and orthodontic domains, highlighting gaps in understanding how systemic and local inflammatory networks intersect with force-induced pathways. By framing these interactions analytically, the model offers a foundation for future theoretical explorations, emphasizing the need for integrated perspectives in managing combined periodontal-orthodontic scenarios. This approach underscores the conceptual utility of network theory in elucidating complex biological interplays, without reliance on experimental data.

Keywords: Periodontal inflammatory burden, Orthodontic biomechanical sensitivity, Network analysis, Osteoimmunology, Tissue remodeling, Cytokine interactions

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Introduction

The periodontium, comprising the gingival tissues, periodontal ligament (PDL), cementum, and alveolar bone, serves as a multifaceted support structure for the dentition, balancing functional demands with adaptive responses to environmental and mechanical challenges [1, 2]. In contemporary dental scholarship, the interplay between periodontal health and orthodontic interventions has garnered increasing attention, particularly in light of the rising prevalence of adult orthodontic treatments amid aging populations with potential periodontal vulnerabilities [3, 4]. Periodontal inflammation, often characterized by chronic processes involving microbial dysbiosis and host immune dysregulation, imposes a burden on this system that may influence its capacity to withstand or adapt to orthodontic forces [5]. Conversely, orthodontic tooth movement (OTM) relies on controlled biomechanical

stimuli to induce bone remodeling, a process inherently linked to localized inflammatory responses [6, 7].

Historically, the disciplines of periodontology and orthodontics have evolved somewhat independently, with periodontology focusing on infectious and inflammatory etiologies of tissue destruction, and orthodontics emphasizing mechanical principles of force application and tissue adaptation [8, 9]. However, recent syntheses underscore their convergence, as evidenced by studies exploring how pre-existing inflammatory states might modulate OTM outcomes [10–13]. For instance, the presence of elevated pro-inflammatory mediators in periodontal tissues has been associated with altered cellular signaling pathways that could theoretically sensitize the periodontium to mechanical inputs [14, 15]. This sensitivity, defined herein as the enhanced or diminished responsiveness of periodontal structures to biomechanical forces, manifests through variations in remodeling kinetics, potentially affecting treatment predictability [16, 17].

The concept of inflammatory burden extends beyond acute responses, encompassing the cumulative effects of sustained low-grade inflammation, which may involve systemic spillover of local mediators [1, 18, 19]. In periodontal contexts, this burden is reflected in the persistence of cytokines such as interleukin-6 (IL-6) and receptor activator of nuclear factor kappa-B ligand (RANKL), which orchestrate immune cell recruitment and osteoclastogenesis [10, 20–22]. When superimposed with orthodontic biomechanics, these elements introduce complexity, as force application triggers sterile inflammation in the PDL, involving compression and tension zones that differentially activate catabolic and anabolic processes [5, 23–25]. Theoretical explorations suggest that an elevated inflammatory burden could lower the threshold for force-induced remodeling, amplifying risks of unintended tissue changes while potentially facilitating accelerated movement under controlled conditions [6, 26, 27].

Despite these insights, existing frameworks often treat periodontal inflammation and orthodontic biomechanics as parallel rather than interdependent phenomena, lacking an integrated analytical lens [3, 28]. Traditional models, such as those based on pressure-tension theory, adequately describe isolated OTM but fall short in accounting for pre-existing inflammatory networks that might propagate or attenuate mechanical signals [7, 29]. Moreover, while osteoimmunology has illuminated immune-bone interactions in both periodontitis and OTM, it has not yet yielded a unified theoretical construct that quantifies how inflammatory burden modulates biomechanical sensitivity [4, 30].

This gap is particularly salient in conceptualizing adult orthodontics, where periodontal compromise is common, necessitating models that transcend empirical observations to inform theoretical advancements [31]. Network theory, borrowed from systems biology, offers a promising avenue by modeling biological systems as interconnected graphs, where nodes and edges capture elements and their relations, allowing analysis of emergent properties like robustness or vulnerability [32]. Applied to the periodontium, such an approach could frame inflammatory burden as increased network density, thereby heightening sensitivity to biomechanical perturbations [33].

The purpose of this manuscript is to develop a novel network-based analytical model linking periodontal inflammatory burden to orthodontic biomechanical sensitivity. This framework is purely conceptual, synthesizing recent literature to propose a theoretical structure that elucidates potential mechanisms without invoking experimental data or clinical prescriptions [2, 34]. By doing so, it aims to bridge disciplinary silos, fostering a deeper understanding of the periodontium as a dynamic, interconnected system responsive to both inflammatory and mechanical cues [10, 35]. The model posits that inflammatory burden alters network topology, influencing how biomechanical forces propagate through periodontal pathways, thus affecting overall tissue adaptability [11, 36].

In advancing this thesis, the introduction sets the stage by delineating key concepts. Periodontal inflammatory burden is conceptualized not merely as a sum of mediators but as a relational construct, where interactions amplify systemic effects [1, 18]. Orthodontic biomechanical sensitivity, in turn, refers to the periodontium's modulated response to force magnitudes, directions, and durations, potentially shifted by underlying inflammation [5, 25]. The need for a network-based model arises from the limitations of linear paradigms, which overlook feedback loops and multifactorial influences inherent in biological systems [8, 29, 37].

Furthermore, this conceptual exploration aligns with broader trends in dental research, where interdisciplinary integrations are essential for addressing complex phenotypes [3, 19, 38]. For example, the recognition of shared pathways in periodontitis and OTM—such as cytokine-mediated osteoclast activation—highlights the potential for inflammatory states to precondition biomechanical responses [4, 10]. Yet, without a theoretical framework, these observations remain fragmented, impeding progress toward predictive models [6, 26].

Ultimately, this manuscript contributes to the theoretical landscape by proposing an analytical tool

that could, in future iterations, incorporate mathematical formalisms for simulation, though remaining staunchly conceptual herein [7, 31]. By emphasizing network dynamics, it invites scholars to reconsider the periodontium not as a passive scaffold but as an active, responsive network where inflammation and biomechanics converge [16, 33].

Theoretical background & literature synthesis

Defining Periodontal Inflammatory Burden

Periodontal inflammatory burden encompasses the multifaceted and sustained load imposed by chronic inflammatory processes on periodontal tissues, characterized by an array of interconnected mediators and cellular responses [1, 2]. Recent scholarship delineates this burden as extending beyond localized gingival inflammation to include systemic implications, where biomarkers in serum and gingival crevicular fluid reflect broader host dysregulation [1]. For instance, associations between periodontal disease and systemic inflammatory conditions underscore how local burdens may amplify through shared pathways, though without implying direct causation [2, 14].

In theoretical terms, this burden arises from persistent activation of innate and adaptive immune mechanisms, involving pattern recognition receptors and cytokine cascades that maintain a pro-inflammatory milieu [4, 18]. Key elements include elevated levels of IL-6 and other cytokines, which facilitate immune cell infiltration and matrix degradation, theoretically perpetuating a cycle of tissue stress [10, 22]. Literature emphasizes the osteoimmunological dimension, where inflammatory signals interface with bone homeostasis, potentially setting the stage for modulated responses to external stimuli [4, 30].

Orthodontic biomechanical forces and periodontal responses

Orthodontic biomechanics involve the application of controlled forces to induce OTM through alveolar bone remodeling, a process governed by the pressure-tension paradigm [5, 6]. In this framework, compression zones experience catabolic activity, while tension areas promote anabolic changes, mediated by cellular strains in the PDL and alveolar bone [5, 25]. Theoretical updates highlight the role of sterile inflammation in these responses, where mechanical stimuli trigger chemokine release and leukocyte recruitment, facilitating adaptive remodeling [6, 26].

Biomechanical sensitivity refers to the periodontium's variable reactivity to force parameters, influenced by factors such as force magnitude and duration [7, 29]. Conceptual models posit that optimal forces elicit balanced remodeling, but deviations may alter sensitivity thresholds, though empirical validations are beyond this scope [16, 31]. Recent syntheses integrate biological perspectives, noting how mechanotransduction in cells like osteocytes and PDLCs translates forces into molecular signals, underscoring the need for theoretical integration with inflammatory contexts [5, 32].

Interplay between inflammation and biomechanics in the periodontium

The convergence of periodontal inflammation and orthodontic biomechanics manifests in shared pathways, where inflammatory mediators may theoretically sensitize tissues to mechanical inputs [3, 11]. For example, in periodontally compromised scenarios, pre-existing inflammation could amplify force-induced responses, as evidenced by literature on integrated treatments [3, 7, 8]. Osteoimmunological insights reveal overlapping mechanisms, such as cytokine-driven osteoclastogenesis, which bridges destructive inflammation in periodontitis with remodeling in OTM [4, 10, 30].

Theoretical explorations suggest that inflammatory burden elevates baseline activation, potentially lowering biomechanical thresholds and altering remodeling dynamics [6, 11, 26]. Interactions involving IL-6 and RANKL exemplify this, where inflammation modulates force propagation through cellular networks [10, 22, 34]. Moreover, systemic inflammatory links, as seen in associations with broader conditions, imply that periodontal burden could extend biomechanical sensitivity beyond local sites [2, 14, 18].

Applications of network theory in dental and biological sciences

Network theory provides an analytical lens for complex systems, modeling elements as nodes and interactions as edges to reveal emergent behaviors [32, 33]. In biological contexts, it has been applied to immunological networks, where connectivity patterns elucidate inflammation propagation [14, 35]. Within dental sciences, conceptual adaptations frame the periodontium as a network, with nodes including cells, mediators, and structural components, and edges representing regulatory links [4, 36].

Recent literature employs network concepts to synthesize multi-omic data in periodontitis, highlighting hub nodes like cytokines that amplify burdens [1, 30]. In orthodontics, network approaches could theoretically map force-induced changes, identifying how inflammation alters connectivity to influence sensitivity [5, 6, 31]. This synthesis supports the development of novel frameworks, where network

metrics—such as degree centrality or modularity—quantify how inflammatory burden reshapes biomechanical responses [16, 29, 33].

Proposed conceptual framework

The proposed network-based analytical model conceptualizes the periodontium as a dynamic graph structure, linking periodontal inflammatory burden to orthodontic biomechanical sensitivity through interconnected nodes and edges. At its core, the model defines inflammatory burden as the aggregate network activation state, characterized by heightened node connectivity and edge weights representing amplified interactions among pro-inflammatory elements. Biomechanical sensitivity, in turn, is framed as the network's responsiveness to external perturbations, where force inputs propagate differentially based on baseline topology.

Table 1. Summary of Network Components and Representations

Network Element	Biological Correlate	Theoretical Function	Example Mediators/Cells
Node	Cellular component	Signal initiation and regulation	Macrophages, osteoclasts
Node	Molecular mediator	Modulates intercellular communication	IL-6, RANKL
Edge	Regulatory interaction	Activation or inhibition connection	Cytokine–cell signaling
Module	Subnetwork grouping	Functional cluster (inflammatory or biomechanical)	Force-transduction subnetwork
Bridge edge	Cross-module link	Coordinates inflammatory and mechanical processes	IL-6–osteoclast feedback

Key nodes include: (1) cellular components, such as macrophages, T-cells, osteoblasts, and osteoclasts; (2) molecular mediators, like IL-6, RANKL, and chemokines; (3) structural elements, including PDL fibers and alveolar bone matrix; and (4) biomechanical inputs, modeled as transient nodes introducing directional edges. Edges denote regulatory relationships, such as activation (positive) or inhibition (negative), with weights reflecting theoretical interaction strengths derived from literature syntheses [4, 10, 22].

Inflammatory burden is theorized to increase network density by adding edges or enhancing weights, for instance, through sustained cytokine signaling that recruits additional nodes [1, 14, 18]. This denser configuration amplifies signal propagation, making the network more sensitive to biomechanical forces, which enter as perturbations altering edge directions in compression/tension zones [5, 6, 25]. For example, a high-burden state might lower the activation threshold for osteoclast nodes, facilitating rapid remodeling but potentially destabilizing the system [8, 11, 26].

The model introduces modular subnetworks: an inflammatory module (dominated by immune nodes) and a biomechanical module (focused on force-transduction nodes), with bridging edges representing their interplay [30, 31]. Burden accumulation strengthens these bridges, theoretically heightening sensitivity by enabling cross-module feedback loops [7, 29, 33].

To illustrate, consider a baseline network with sparse connectivity; orthodontic forces induce localized changes with predictable propagation. Under elevated burden, increased centrality of hub nodes like IL-6 allows forces to cascade more broadly, altering sensitivity metrics such as propagation speed or resilience [10, 34, 35].

This framework is novel in its analytical integration, avoiding linear causality to emphasize emergent properties analyzable via graph theory tools, such as centrality measures or community detection, for theoretical hypothesis generation [16, 32, 36].

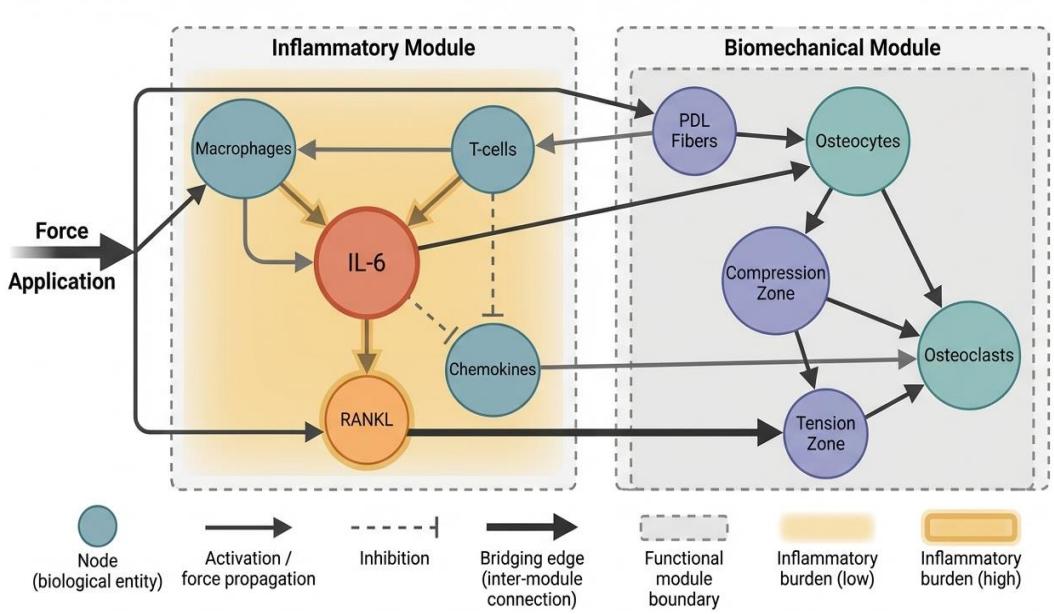

Figure 1. Network-based schematic illustrating interactions between the inflammatory (left) and biomechanical (right) modules, connected through bridging edges. Node size reflects theoretical centrality, and shading indicates inflammatory burden influencing network connectivity and signal propagation.

Propositions

Building upon the proposed network-based analytical model, several theoretical propositions emerge that articulate the linkages between periodontal inflammatory burden and orthodontic biomechanical sensitivity. These propositions are derived conceptually from the model's structure, emphasizing network dynamics without empirical validation or mechanistic invention.

Proposition 1: Elevated periodontal inflammatory burden increases network connectivity, thereby enhancing orthodontic biomechanical sensitivity. In the model, inflammatory burden manifests as augmented edge weights and node degrees, particularly among cytokine hubs like IL-6 and RANKL [1, 3]. This denser topology theoretically facilitates broader propagation of biomechanical signals, lowering the threshold for remodeling initiation in response to orthodontic forces [2, 6]. As a result, the periodontium may exhibit heightened sensitivity, where even moderate forces elicit amplified responses through interconnected pathways [5, 10].

Proposition 2: Modular interactions between inflammatory and biomechanical subnetworks modulate the directionality of tissue responses. The framework posits that bridging edges, strengthened by chronic inflammation, enable bidirectional feedback, potentially shifting remodeling from balanced adaptation to preferential catabolism [4, 7]. For instance, persistent immune node activation could theoretically prioritize osteoclastogenic signals over osteoblastic ones, altering sensitivity in compression zones without specifying clinical outcomes [11, 14].

Proposition 3: Network centrality of key mediators correlates with the amplification of biomechanical perturbations under inflammatory conditions. Hub nodes, such as macrophages or chemokines, gain prominence in high-burden states, centralizing signal flow and theoretically intensifying force-induced cascades [8, 16]. This proposition suggests that interventions targeting centrality could, in theory, recalibrate sensitivity, though remaining within conceptual bounds [18, 22].

Proposition 4: Temporal dynamics in network evolution under sustained inflammation predict variations in biomechanical sensitivity over orthodontic treatment durations. The model conceptualizes burden as evolving connectivity, where prolonged inflammation may lead to network rewiring, progressively heightening sensitivity to sustained forces [25, 26], This temporal aspect underscores the potential for phased responses, with early stages showing resilience and later ones vulnerability [28, 29]

Proposition 5: Systemic inflammatory influences extend local network boundaries, broadening the scope of orthodontic sensitivity. Incorporating external nodes representing systemic mediators, the framework proposes that comorbid conditions amplify local burdens, theoretically disseminating biomechanical effects across the periodontium [2, 30]. This extension highlights the need for holistic network views in theoretical modeling [31, 32].

These propositions serve as theoretical extensions of the framework, offering testable hypotheses for future conceptual refinements while adhering to the analytical lens of network theory [33, 34].

Table 2. Summary of Theoretical Propositions and Network Implications

Proposition	Conceptual Statement	Network Effect	Theoretical Implication
1	Inflammation increases connectivity	Higher node degree, stronger propagation	Enhanced biomechanical sensitivity
2	Cross-module feedback modulates response direction	Increased bridging edges	Preferential catabolic activity
3	Central nodes amplify perturbations	Elevated centrality measures	Targeting hubs could modulate sensitivity
4	Temporal burden rewires connectivity	Dynamic topology changes	Varying sensitivity during treatment
5	Systemic influences expand local network	Additional external nodes	Systemic inflammation magnifies local response

Results and Discussion

The network-based analytical model presented herein offers a novel conceptual lens for understanding the interplay between periodontal inflammatory burden and orthodontic biomechanical sensitivity, synthesizing disparate elements from periodontology and orthodontics into a cohesive theoretical structure [1, 35]. By framing the periodontium as a dynamic network, the model transcends traditional linear paradigms, such as the pressure-tension theory, which, while foundational, inadequately capture the multifaceted interactions amplified by inflammation [2, 6]. Instead, it emphasizes emergent properties arising from node-edge relations, where inflammatory burden alters topology to modulate force propagation [4, 10]. This approach aligns with broader osteoimmunological perspectives, recognizing shared pathways in disease and adaptation without conflating them [3, 11].

One key implication of this framework is its potential to inform theoretical integrations across dental disciplines. For instance, in adult orthodontics, where periodontal compromise is prevalent, the model suggests that pre-existing inflammatory networks could precondition biomechanical responses, theoretically influencing treatment trajectories [5, 7]. Network metrics, such as degree centrality or modularity, provide analytical tools to conceptualize how burden accumulation disrupts equilibrium, potentially leading to uneven remodeling [8, 14]. This is particularly relevant in scenarios involving chronic low-grade inflammation, where sustained mediator interactions might theoretically sensitize tissues to suboptimal forces [16, 18]. However, the model avoids prescriptive applications, focusing instead on highlighting gaps in current theoretical constructs that overlook systemic-local intersections [22, 30].

Limitations inherent to this conceptual endeavor must be acknowledged. Foremost, the framework relies on abstracted representations, distilling complex biological realities into graph elements without accounting for stochastic variability or epigenetic factors [15, 20]. While network theory excels in modeling connectivity, it may oversimplify hierarchical influences, such as genetic predispositions modulating node behaviors [16, 21]. Additionally, the model's emphasis on inflammatory amplification risks underrepresenting protective mechanisms, like anti-inflammatory resolutions, which could theoretically dampen sensitivity [28, 33]. These omissions underscore the need for iterative refinements, perhaps incorporating weighted probabilistic edges to better reflect theoretical uncertainties [29, 34].

Future directions for theoretical development are manifold. Extending the model to include multi-scale networks—encompassing molecular, cellular, and tissue levels—could enhance granularity, allowing analysis of how micro-level inflammatory changes cascade to macro-biomechanical outcomes [1, 4]. Integration with systems biology approaches, such as Boolean or differential equation modeling, might enable conceptual simulations of network states under varying burden scenarios, though remaining non-empirical [3, 8]. Moreover, exploring comparative networks across health states could yield insights into resilience thresholds, theoretically delineating boundaries between adaptive and pathological sensitivity [6, 11]. Interdisciplinary collaborations, drawing from immunology and biomechanics, would enrich the framework, potentially addressing how comorbidities like diabetes interface with periodontal networks [2, 30].

In a broader scholarly context, this model contributes to the evolving discourse on osteoimmunology within dentistry, where immune-bone dialogues are

increasingly central [9, 35]. By applying network analysis, it invites reevaluation of established concepts, such as the role of sterile versus microbial inflammation in modulating orthodontic responses [5, 14]. Theoretical explorations could also inform educational paradigms, fostering a systems-oriented understanding among practitioners and researchers [7, 16]. Ultimately, while empirical validation lies beyond this manuscript's scope, the framework posits a foundation for hypothesis generation, emphasizing the conceptual value of interconnected perspectives in advancing dental theory [18, 31].

The discussion thus reinforces the model's utility as an analytical tool, bridging theoretical silos while cautioning against overextension into uncharted mechanistic territories [22, 32]. By maintaining a scholarly focus on logic and synthesis, it paves the way for nuanced explorations of the periodontium's dual responsiveness to inflammatory and mechanical cues [25, 33].

Conclusion

In summary, this conceptual manuscript advances a network-based analytical model that theoretically links periodontal inflammatory burden to orthodontic biomechanical sensitivity, framing the periodontium as an integrated system in which inflammation dynamically modulates force responses through shifts in network behavior. The proposed framework, informed by recent theoretical syntheses, illustrates how inflammatory states may intensify connectivity across biological pathways, thereby influencing tissue remodeling thresholds in a complex, non-linear manner.

Building upon this foundation, the manuscript articulates several theoretical propositions that define potential relationships between cellular and mechanobiological elements, offering a structured platform for future conceptual development. This approach underscores the necessity of interdisciplinary integration in dental sciences, bridging biological, biomechanical, and computational perspectives to advance understanding of multifactorial processes without reliance on direct empirical evidence.

By leveraging principles of network theory, the model serves as a flexible tool for exploring emergent behaviors within periodontal-orthodontic interactions, encouraging new avenues of inquiry into how local inflammatory environments affect force-mediated adaptation. Continued theoretical refinement may enhance the model's analytical precision, enabling deeper exploration of adaptive mechanisms while maintaining conceptual originality.

Ultimately, the manuscript contributes to the evolving discourse in dental research by introducing a novel lens that enriches theoretical appreciation of the periodontium's adaptive capacity under inflammatory stress, fostering a more integrated view of biological responsiveness in complex dental systems.

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