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Biofunctional materials: fundamentals and classification

Mohammad Reza Saeb

Department of Pharmaceutical Chemistry, Medical University of Gdańsk, 80-416 Gdańsk, Poland;
E-mail: mr.saeb@gumed.edu.pl.

Abstract: The term biomaterial is widely used to describe materials associated with biological systems, but often fails to distinguish whether a material merely exists within a biological environment or actively participates in regulating biological processes. This ambiguity has created a subtle conceptual gap, making it difficult to distinguish passive materials from those deliberately engineered to trigger biological responses. This Editorial addresses this gap by introducing a foundational framework for defining and classifying biofunctional materials. Accordingly, biofunctional materials are defined as deliberately engineered material systems designed to engage biological environments and produce measurable and reproducible biological outcomes. To conceptualize this concept, biofunctionality is defined and described as a multidimensional continuum governed by four foundational pillars including structural, physicochemical, biological signaling, and adaptive functionality. Together, these pillars form a conceptual biofunctionality landscape, enabling materials to be interpreted according to the maturity of their functional mechanisms and the degree of integration across domains. By clarifying the distinction between passive biomaterials and actively biofunctional systems, this framework aims to provide a milestone, thereby to support clearer terminology, more rigorous evaluation, and more rational design of materials that decisively interact with living systems.

Keywords: biofunctional materials; advanced materials; biofunctionality; biomaterials; materials selection; materials classification; biofunctionality landscape

1. Beyond biomaterials: a conceptual gap

The term biomaterial has long been employed by researchers as descriptor for a general class of materials associated with biological systems. In a classic definition, biomaterial usually refers to materials derived from biological sources, materials compatible with living tissues, or materials applied within medical contexts [1]. Nevertheless, despite its widespread use, the term does not inherently indicate whether a material merely exists within a biological environment or actively performs a biological function. For instance, a metallic implant, an inert polymer coating, or a ceramic scaffold may each be considered a biomaterial, even if their role is limited to structural support or passive presence within a biological system. In many cases, however, such a designation reflects proximity to biology rather than active participation of the material in a defined biological system. In contemporary literature, it is common to encounter statements such as “a novel biomaterial was designed for tissue engineering” or “a new biomaterial was developed for regenerative medicine”. Nevertheless, such descriptions often fail to

address and distinguish whether the material merely provides a permissive environment for cells or whether it is engineered to direct, modulate, or instruct biological behavior. The corresponding most frequently asked questions remaining for biologists and materials researchers to ask are: Does the material actively influence cell differentiation, immune response, or molecular signaling? Does it simply serve as a substrate upon which biological processes occur independently? Is the material merely tolerated by the biological system, or is it designed to induce an identified biological response? Does the material present specific biochemical or physicochemical signals triggering cellular behavior? The terminology rarely addresses these functions explicitly [1].

When it comes to their origin, an additional ambiguity extends to materials described as green biomaterials, i.e., those derived from renewable sources, mainly obtained from plants, algae, and agricultural wastes. To name but a few examples, a so-called green class of materials referred to as biomaterials include but are not principally limited to bio-based, biodegradable, renewable, sustainable, or environmentally friendly materials [2]. These labels adhered to such materials are attributes related to their origin, lifecycle, or ecological responsibility, but they do not fundamentally demonstrate their specific functional engagement with biological systems. Moreover, these terms are often used interchangeably to describe a broad range of biomaterials without specifying their roles and most critically their functions in biological systems. Such segregated terminology, rather than a universal and coherent conceptual standard, has contributed to misunderstandings and occasionally unreliable interpretations. Furthermore, one should pay attention to the fact that a biodegradable polymer may gradually resorb *in vivo* without altering cellular pathways. Likewise, a scaffold fabricated from natural polymers may support tissue ingrowth without actively modulating biochemical signaling. From a practical standpoint, an advanced material used in biomedical devices may be optimized for mechanical strength, manufacturability, or degradation kinetics, yet still remain biologically passive. These examples illustrate that biological origin does not guarantee a biological function, or compatibility does not equate to responsiveness. In a similar manner, the presence of cells on a material surface does not solely indicate that the material participates in a biological process. Likewise, the ability of a material to exist within a living system is distinct from its capacity to function through that system.

In light of these considerations and highlighted uncertainties, the overlap between terminology and the functional intent of materials in biological environments reflects a deeper conceptual gap. To clarify this distinction, the term biofunctional may be introduced to describe materials intentionally designed to perform defined functions within biological systems. However, introducing such a distinction also invites a closer look at what is actually meant by the term. Before adopting it as a meaningful descriptor, it is important to consider how a biofunctional material is expected to operate within a biological environment and what characteristics would justify such a designation. These considerations obviously feature some fundamental questions to be answered, like: When a material is described as biofunctional, what precisely is being claimed? Does the term biofunctional denote a four-in-one concept encompassing safety, material origin, application domain, and genuine biological performance? By what principles, conditions or evidence can such biofunctionality be demonstrated or verified? Accordingly, it can be inferred that without a well-defined distinction, materials that merely coexist with biological environments are prone to being mistakenly grouped with those deliberately engineered to engage, modulate, and direct biological processes in measurable and predictable ways. Clarifying this distinction is not merely semantic refinement; it is necessary for distinguishing materials that operate within

biological systems from those purposefully designed to function through them. Therefore, a foundational definition of biofunctional materials is required to resolve these ambiguities and to establish a conceptual framework capable of guiding future research, evaluation, and rational design in this emerging domain.

2. The multidimensional foundations of biofunctionality

The conceptual gap outlined earlier requires more than terminological refinement; it requires it calls for a structured framework capable of distinguishing materials that merely reside within biological environments from those intentionally designed to function through them. To move beyond ambiguity, biofunctionality must be treated and classified in terms of fundamental design principles and their measurable biological behavior. In this framework, a biofunctional material is defined as a deliberately engineered material system designed to engage biological environments through defined structural and physicochemical mechanisms, thereby producing measurable and reproducible biological outcomes [3]. This definition emphasizes the intended function, mechanism, and performance of materials. From this perspective, biofunctionality is not an incidental attribute arising from biological proximity, nor a consequence of material origin, but a characteristic emerging from deliberate integration between material design and biological response. Notably, such combination does not manifest as a binary condition. In other words, a material does not simply become biofunctional at a predefined threshold. In contrast, biofunctionality develops progressively as functional mechanisms mature and as interactions across biological dimensions become more coherent and controlled. Thus, biofunctionality should be regarded as a multidimensional continuum.

To provide a conceptual structure for this continuum, biofunctionality can be organized around four foundational pillars that collectively describe how materials engage biological systems. Accordingly, four foundational pillars are proposed to describe the mechanisms of biofunctionality: structural biofunctionality, physicochemical biofunctionality, biological signaling functionality, and adaptive or dynamic biofunctionality. Structural biofunctionality considers architecture, hierarchy, and interfacial topology of materials. Physicochemical biofunctionality mirrors the contributions of materials arising from surface chemistry, charge, degradation, and molecular interactions. Biological signaling functionality addresses the modulation of cellular and molecular pathways. Eventually, adaptive or dynamic biofunctionality reflects time-dependent, stimuli-responsive, or self-regulating behavior. These pillars represent distinct yet interrelated domains through which materials can intentionally engage and regulate biological systems. The integration and maturity of these four pillars are conceptualized within a multidimensional biofunctionality landscape, illustrated in **Figure 1**. The horizontal axis represents the maturation of functional mechanisms—from incidental interaction to predictive and tunable engagement—while the vertical axis reflects the degree of cross-pillar integration within a material system. Together, these dimensions define a continuous landscape in which materials occupy positions corresponding to their level of functional maturity and multidimensional coherence.

It should be emphasized that the proposed framework is intended as a foundation rather than a definitive or exhaustive taxonomy. As the field progresses, additional dimensions and more rigorous quantitative metrics may emerge through continued scientific investigations and experimental validation. Therefore, the four pillars and their landscape representation constitute an initial structural platform intended to stimulate dialogue, comparison, and progressive refinement within the emerging domain of biofunctional materials. In this sense, the landscape is not a closed classification scheme but

a conceptual means for organizing thought and guiding inquiry. It is also believed that the landscape presented here enables positioning of materials within a multidimensional space of biological engagement. Nonetheless, by doing so, it simultaneously raises deeper and more technical questions. For instance: What specific design parameters govern progression along each axis? How do structural, physicochemical, signaling, and adaptive dimensions interact to elevate a material ranking or biofunctionality position from isolated functionality to multidimensional coherence? Can the maturation of one pillar compensate for the immaturity of another, or does robust biofunctionality require balanced integration across domains? To what extent can these dimensions be intentionally orchestrated rather than empirically observed? These questions underline that defining biofunctional materials and the biofunctionality landscape in this work may solely help to pave the first steps in an innovative avenue. Achieving this objective requires a deeper understanding of how the foundational pillars of biofunctionality are constructed, parameterized, and interconnected in order to translate conceptual positioning into rational material design.

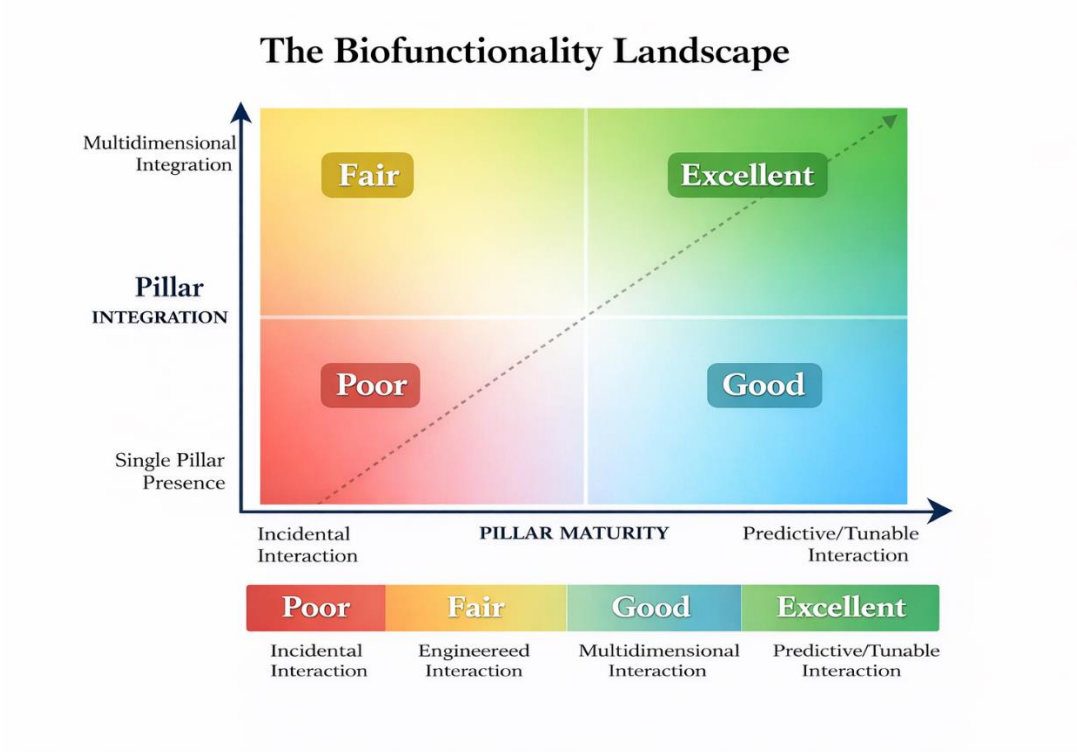

Figure 1. ***The biofunctionality landscape: a multidimensional continuum for the qualification of biofunctional materials.*** The diagram conceptualizes biofunctionality as a categorized functional state defined by two controlling dimensions. The horizontal axis (Pillar Maturity) represents the progression from incidental biological interaction to engineered, mechanistically validated, and ultimately predictive or tunable functionality. However, the vertical axis (Pillar Integration) reflects the extent to which multiple functional pillars—structural, physicochemical, biological signaling, and adaptive/dynamic—are coherently coupled within a material system. Color transitions from Poor to Excellent denote increasing levels of functional maturity and multidimensional integration. Notably, the diffuse boundaries between regions emphasize that biofunctionality is not a binary label but a continuum emerging from the depth and breadth of biological engagement. Therefore, the position of a material within biofunctionality landscape represents the degree to which material passes biofunctional sophistication. This milestone may provide researchers with a structured yet non-arbitrary basis for comparative classification of biofunctional materials across diverse applications.

The biofunctionality landscape illustrated in **Figure 1** is grounded in four foundational pillars that collectively define how materials engage biological systems. Each pillar represents a distinct mechanistic domain through which materials may influence biological behavior. Though structural biofunctionality addresses the spatial and architectural organization of materials, physicochemical biofunctionality deals with the interfacial and molecular properties governing material–biological interactions. Moreover, biological signaling functionality refers to the ability of materials to modulate cellular and molecular pathways, while adaptive or dynamic biofunctionality reflects time-dependent or stimuli-responsive behavior that enables materials to interact with evolving biological environments. For clarity, the four pillars and their primary mechanistic domains are summarized in **Table 1**.

Table 1. ***Foundational pillars of biofunctionality and their mechanistic domains.*** The four foundational pillars provide the conceptual structure underlying the biofunctionality landscape illustrated in **Figure 1**. Each pillar represents a distinct yet interconnected domain through which materials may engage biological systems. Structural biofunctionality deals with spatial architecture and hierarchical organization governing cell–material interactions. Moreover, physicochemical biofunctionality reflects interfacial and molecular properties regulating communication between materials and biological environments. Biological signaling functionality addresses the ability of materials to influence cellular pathways through engineered biochemical or biophysical cues. Adaptive or dynamic biofunctionality extends these interactions into the temporal domain, enabling stimuli-responsive or evolving material behavior within biological systems.

Biofunctionality Pillar	Mechanistic Domain	Representative Design Parameters	Typical Biological Influence
Structural biofunctionality	Spatial architecture and material topology	Hierarchical structure, porosity, surface topology, anisotropy	Cell adhesion, migration, tissue organization
Physicochemical biofunctionality	Interfacial and molecular material properties	Surface chemistry, charge distribution, degradation kinetics, ion release	Protein adsorption, molecular signaling gradients
Biological signaling functionality	Regulation of cellular and molecular pathways	Ligand presentation, bioactive motifs, immunomodulatory cues	Gene expression, inflammatory modulation, lineage specification
Adaptive or dynamic biofunctionality	Time-dependent or stimuli-responsive behavior	Shape transformation, stimuli responsiveness, self-regulation	Feedback interaction with biological processes

3. Mechanistic architecture of biofunctionality

Having established the multidimensional foundations of biofunctionality, the discussion now advances from conceptual positioning toward mechanistic construction. Although the biofunctionality landscape introduced earlier describes where a material resides within a multidimensional space of biological engagement, there is a need foe mechanistic architecture to explain why it occupies that position and how it may transition within the landscape. Biofunctionality does not arise from isolated attributes or incidental properties; rather, it emerges from a structure–function–response relationship governed by controllable design parameters [4]. Within this framework, structural organization, physicochemical characteristics, biological signaling capacity, and dynamic adaptability operate as interdependent layers in a causally linked system whose coordinated modulation determines the depth and predictability of biological response. Structural biofunctionality constitutes the spatial control layer of this architecture, governing how materials physically interact with cells and tissues. Architectural hierarchy, porosity engineering, interfacial topology, and multiscale organization collectively determine how biological entities perceive and respond to material surfaces [5]. At the nanoscale, surface roughness influences protein adsorption kinetics; at the microscale, pore size and connectivity regulate cell infiltration and nutrient

transport; and at the macroscale, structural anisotropy can direct tissue alignment and organization [6]. Through these mechanisms, structural design translates geometric parameters into quantifiable biological outcomes, transforming biofunctionality from a descriptive label into a design-governed property.

Beyond spatial architecture, biofunctionality also arises from molecular and biochemical interactions at the material–biology interface. Physicochemical biofunctionality governs these processes by regulating surface chemistry, charge distribution, ion release kinetics, and degradation behavior, all of which influence protein adsorption dynamics, ionic signaling gradients, and local microenvironmental conditions. Variations in functional group density or electrostatic potential can therefore alter integrin binding, cytokine release, and stem cell fate decisions, demonstrating how interfacial properties translate material composition into controlled biochemical influence [7]. Building upon this layer, biological signaling functionality represents a deeper level of mechanistic engagement in which materials actively modulate cellular and molecular pathways through engineered biochemical or biophysical cues. Such mechanisms include regulated cell–material communication, engineered protein adsorption patterns, immunomodulation strategies, and tissue-inductive interactions that influence gene expression, inflammatory cascades, angiogenic signaling, or lineage specification [8,9]. The most advanced expression of this architecture emerges through adaptive or dynamic biofunctionality, where materials operate within the temporal dimension. Stimuli-responsive behavior, self-regulation, shape transformation, and time-dependent evolution—including four-dimensional (4D) material responses—enable materials to respond to biochemical gradients, mechanical loading, enzymatic activity, or environmental changes [10]. Through this feedback-informed adaptability, biofunctional materials transition from passive substrates to dynamic systems capable of evolving alongside biological processes, reinforcing the integrated and multidimensional nature of biofunctionality.

The progression from Poor to Excellent regions in the biofunctionality landscape (**Figure 1**), together with the mechanistic domains summarized in **Table 1**, highlights that the four pillars of biofunctionality do not operate as independent modules but as interdependent layers of biological engagement. Structural topology influences protein adsorption, physicochemical gradients regulate signaling cascades, and adaptive transformations continuously reshape both spatial and biochemical environments. Consequently, biofunctionality emerges from coordinated integration across pillars rather than isolated optimization. Materials engineered within this framework may therefore be interpreted according to the coherence and maturity of their underlying mechanisms. Through this lens, application domains such as regenerative medicine, drug delivery, antimicrobial coatings, biosensing, and smart implants represent functional manifestations of different pillar configurations. Regenerative systems typically require strong structural hierarchy and signaling integration, while drug delivery platforms rely on physicochemical modulation and dynamic responsiveness. Recognizing these relationships transforms biofunctional materials from empirically optimized constructs into purposefully engineered systems whose performance can be conceptually defined before fabrication.

4. Contextual qualification within the biofunctionality landscape

As illustrated in the biofunctionality landscape (**Figure 1**), materials may occupy different regions representing increasing levels of biofunctional maturity, qualitatively described as Poor, Fair, Good, and Excellent. These regions should not be interpreted as rigid boundaries but as conceptual zones within a continuous multidimensional space defined by the four pillars of biofunctionality. Thus, the descriptors

are intentionally qualitative, reflecting progressive degrees of mechanistic maturity and cross-pillar integration rather than numerical thresholds. Materials situated in the Poor region typically exhibit incidental biological interaction with limited intentional design. Fair biofunctionality reflects engineered interaction producing measurable biological responses but with partial mechanistic understanding or limited pillar coherence. Good biofunctionality emerges when structure–function–response relationships are mechanistically validated across multiple pillars, enabling reproducible biological outcomes. At the highest level, Excellent biofunctionality denotes predictive or tunable performance achieved through coordinated integration of structural, physicochemical, biological signaling, and adaptive mechanisms. To clarify these distinctions without imposing arbitrary scoring systems, qualitative maturity descriptors across each pillar are summarized in **Table 2**.

Table 2. ***Qualitative maturity descriptors within the biofunctionality landscape***. Non-numerical criteria are defined to provide milestone for rigorous thinking and graded biofunctional maturity across foundational pillars. Indeed, this table reflects a rationalized image of biofunctionality maturation within materials characteristics, necessitating continued update and conceptual revision.

Biofunctionality Pillar	Incidental Interaction	Engineered Interaction	Mechanistically Validated	Predictive/Tunable
Structural biofunctionality	Passive geometry or limited hierarchical control	Designed porosity or topology with intended biological influence	Demonstrated causal linkage between structure and biological outcome	Hierarchically optimized architecture providing controlled and tunable spatial bioresponse
Physicochemical biofunctionality	Uncontrolled surface chemistry or degradation behavior	Modified surface properties to induce measurable biological effect	Quantified structure–chemistry–bioresponse relationships	Precisely tuned interfacial and degradation parameters providing predictable molecular modulation
Biological signaling functionality	Indirect or nonspecific cellular interaction	Engineered cues affecting measurable cellular pathways	Verified modulation of defined signaling mechanisms	Targeted and controllable pathway regulation with reproducible biological outcomes
Adaptive or dynamic biofunctionality	Static behavior without environmental responsiveness	Stimuli-responsive or time-dependent features	Validated adaptive behavior linked to biological triggers	Programmable, feedback-informed, and tunable dynamic interaction

The maturity descriptors summarized in **Table 2** provide a qualitative framework for positioning materials within the biofunctionality landscape. Rather than relying on numerical scores, the framework emphasizes causal validation and cross-pillar coherence as indicators of advancement. Materials categorized as Poor typically exhibit largely incidental biological interaction with minimal intentional design or mechanistic verification. Fair biofunctionality reflects engineered interaction within one or more pillars but with limited integration or incomplete causal understanding. Good biofunctionality emerges when structure–function–response relationships are mechanistically validated across multiple pillars, enabling reproducible and controllable biological outcomes. At the highest level, Excellent biofunctionality is characterized by predictive or tunable behavior resulting from coordinated integration of structural, physicochemical, signaling, and adaptive mechanisms. Importantly, these classifications represent multidimensional maturity profiles rather than fixed stages; progression across the landscape may occur unevenly across pillars. This graded interpretation therefore provides a conceptual basis for evaluating materials and contextualizing application-specific biofunctional expectations. Although the biofunctionality landscape provides a graded framework for qualification, the interpretation of maturity remains inherently contextual. Thus, biofunctional excellence is not universally defined but relative to

the intended biological objective and application domain. Different technologies aid prioritizing distinct configurations of the four pillars and their integration patterns. For example, biosensing platforms may require high physicochemical maturity to ensure selective molecular recognition, stable interfacial transduction, and reliable signal modulation, while only moderate structural hierarchy or adaptive functionality may be necessary. In contrast, regenerative scaffolds typically demand coordinated structural organization and biological signaling coherence, coupled with strong cross-pillar integration to guide tissue formation, vascularization, and immune compatibility. Drug delivery systems often rely more heavily on adaptive or dynamic biofunctionality, where tunable degradation kinetics, stimuli responsiveness, and temporally programmed release profiles determine therapeutic precision. Antimicrobial coatings, by comparison, may primarily depend on physicochemical modulation and targeted biological signaling control without extensive structural hierarchy. These examples illustrate that applications correspond not to fixed maturity thresholds but to characteristic multidimensional regions within the biofunctionality landscape. Recognizing this contextual dependency transforms the landscape from a descriptive taxonomy into a strategic design framework, enabling researchers to conceptually define the desired biofunctional region and align pillar-specific design parameters before material synthesis.

5. Challenges and future perspectives

The development of advanced materials, referred to in this Editorial as biofunctional materials, toward predictive and application-specific maturity is accompanied by intertwined conceptual, methodological, and systemic challenges. The multidimensional nature of biofunctionality—spanning structural hierarchy, physicochemical modulation, biological signaling, and adaptive dynamics—renders its rigorous evaluation inherently complex. Biological systems are inherently nonlinear, context-dependent, and temporally evolving, which complicates the isolation of causal relationships between design parameters and biological outcomes. Moreover, translating mechanistic validation into predictive reliability across biological and engineering scales remains an open scientific frontier. Beyond technical considerations, future developments must also align with broader societal and environmental priorities. Sustainable material sourcing, energy-efficient manufacturing, circular lifecycle strategies, and decarbonization of productionprocesses will increasingly define boundary conditions within which biofunctional innovation must operate. Therefore, further advancement will require harmonizing functional sophistication with environmental responsibility, ensuring that improvements in biological performance are pursued alongside ecological stewardship.

Looking ahead, the evolution of biofunctional materials is likely to be profoundly governed by data-centric and immersive digital technologies. Artificial intelligence, multiscale simulation, high-throughput experimentation, and digital twin modeling may collectively transform the biofunctionality landscape from a conceptual map into an interactive design environment. In particular, emerging metaverse-based research platforms—integrating virtual laboratories, shared simulation ecosystems, immersive data visualization, and collaborative digital twin infrastructures—have the potential to transform how materials are conceived, visualized, parameterized, and repositioned within the landscape prior to physical synthesis. Such environments could facilitate and expand inverse design windows and strategies, where target regions of biofunctionality are specified in advance and material architectures are computationally optimized to approach them. In this paradigm, qualification precedes

fabrication, experimentation becomes guided rather than exploratory, and the landscape evolves into a predictive compass for rational innovation. Therefore, the future challenge is not merely to refine definitions or classifications, but to operationalize this multidimensional framework within sustainable, digitally integrated, and globally collaborative research infrastructures capable of anticipatory and responsible biofunctional innovation.

Data availability statement

No datasets were generated or analyzed during the current study.

Declaration of generative AI and AI-assisted technologies

I used OpenAI's ChatGPT, accessed through a licensed institutional service, to assist with proofreading and graphical preparation based on my own conceptual design and scientific framework. The tool was used to improve readability, clarity, and visual presentation, without influencing the underlying scientific concepts, data interpretation, or conclusions of the article. I reviewed and verified all textual and graphical content to ensure its accuracy and integrity and take full responsibility for the manuscript, including any possible errors or interpretations.

Authors' contribution

Mohammad Reza Saeb: conceptualization, writing—original draft, methodology, writing—review and editing, supervision.

Conflicts of interest

The author declares that there are no conflicts of interest.

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