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ARCHITECTURE–PROPERTY–FUNCTION RELATIONSHIPS IN SUSTAINABLE POLYMER BIOMATERIALS: A CRITICAL FRAMEWORK FOR REPRODUCIBLE GREEN-BY-DESIGN ENGINEERING

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Abstract

This review examines how hierarchical architecture influences multifunctional performance in sustainable polymer biomaterials, addressing a persistent limitation in the field: the predominance of composition-centered analyses with insufficient architectural parameterization. To overcome this gap, we adopt an Architecture–Property–Function (APF) framework, in which structural descriptors are treated as primary design variables linking material organization to mechanical behavior, molecular transport, optical attenuation, redox activity, and biological response. A PRISMA-guided literature analysis identified 612 records, from which 94 studies met eligibility criteria requiring explicit linkage between at least one architectural descriptor and a measurable functional outcome. Within this set, a targeted subset of 26 within-study matched datasets was selected for directional quantitative synthesis based on comparability and reporting quality. Across these constrained datasets, directionally consistent trends were observed: increasing ionic crosslink density is associated with a stiffness–transport trade-off; nanoscale dispersion enhances thickness-normalized UV attenuation and stabilizes antioxidant performance; and molecular confinement contributes to improved stability while modulating release behavior. However, these relationships are condition-dependent and vary with descriptor quality, normalization practices, and system-specific variables. The analysis also identifies critical limitations in literature, including widespread reliance on proxy descriptors, inconsistent reporting of architectural parameters, and limited integration of sustainability metrics with biological endpoints. To address these issues, we propose a structured reporting framework and a minimal descriptor set to improve reproducibility and enable future data-driven approaches. Rather than establishing universally transferable design rules, this review delineates evidence-supported architectural tendencies within defined applicability domains, while explicitly outlining their limitations and conditions of validity. This calibrated perspective provides a foundation for more rigorous, reproducible, and ultimately predictive engineering of sustainable polymer biomaterials.

Keywords: polymer, hydrogel, nanostructure, multiscale, diffusion, optical properties, machine learning

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1. INTRODUCTION

Green-by-design has become a widely adopted paradigm in biomaterials research; however, it remains predominantly operationalized as a compositional strategy rather than a structure-driven engineering approach (Anastas & Warner, 1998; Mostafavi et al., 2024). In many studies, sustainability is reduced to the substitution of petrochemical components with bio-based alternatives, followed by reporting isolated functional properties such as swelling, elastic modulus, or antioxidant activity (Ahmed, 2015; Ho et al., 2024). What is often lacking is a mechanistic linkage between material architecture and multifunctional performance.

This limitation constrains reproducibility and prevents meaningful cross-study comparability.

In the absence of explicit architectural descriptors—such as crosslink density, dispersion hierarchy, or confinement metric-reported functional outcomes remain system-specific and difficult to generalize (Peppas et al., 2000; Peters et al., 2021).

To address this gap, this review adopts an Architecture–Property–Function (APF) framework, positioning hierarchical structure as a primary design variable. Unlike traditional composition–property approaches, APF explicitly links controllable structural parameters to emergent functional behavior, while incorporating sustainability constraints and translational considerations (Li & Mooney, 2016; Li et al., 2022).

Importantly, this framework is not proposed as a replacement for established structure–property–processing paradigms, but rather as an extension that emphasizes architecture as a measurable and tunable variable, function as a multi-objective outcome, and sustainability as an operational constraint rather than a post hoc descriptor.

However, it is critical to acknowledge that the current literature presents substantial limitations. Architectural descriptors are inconsistently reported, experimental conditions are heterogeneous, and many studies rely on proxy variables rather than direct measurements (Page et al., 2021; Galvão et al., 2022). As a result, the relationships synthesized in this review should be interpreted as directionally consistent trends within constrained evidence spaces.

2. METHODS

2.1 Study design and review type

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This study is conducted as a hybrid systematic-critical review with targeted quantitative synthesis. While the literature search and selection follow PRISMA 2020 guidelines, the analytical component integrates both structured evidence extraction and interpretative synthesis (Page et al., 2021; Galvão et al., 2022).

The quantitative component is restricted to a subset of studies meeting strict comparability criteria, whereas broader literature is used for contextual and conceptual analysis.

2.2 Information sources, search strategy, and APF-oriented evidence extraction

Scopus and the Web of Science Core Collection were searched for peer-reviewed journal articles published in English from January 2014 to December 2024. The 2014 cut-off was selected to capture the contemporary phase of architecture-driven biomaterials research, encompassing advances in ionic hydrogel engineering, nanoscale lignin structuring, and the emergence of data-enabled materials design approaches (Lee & Mooney, 2012; Beisl et al., 2017; Butler et al., 2018).

Database-specific search strings, including Boolean operators, truncation symbols, and applied filters, are provided in Table 1 to ensure full reproducibility. The strategy was organized into four modular thematic blocks: (A) sustainability and green processing; (B) polymer biomaterials, with emphasis on alginate-based and related hydrogel systems; (C) lignin and bio-based UV absorbers/antioxidants; and (D) architecture-driven descriptors, including crosslink density, dispersion hierarchy, confinement effects, and Architecture–Property–Function terminology.

Following duplicate removal, titles and abstracts were independently screened by two reviewers, after which full texts were assessed against predefined inclusion and exclusion criteria.

Eligible studies were required to report at least one explicitly quantified architectural descriptor linked to a measurable functional outcome, including mechanical performance, molecular transport, UV attenuation, redox activity, or biological response (Peters et al., 2021; Kai et al., 2016). Studies reporting composition without architectural parameterization were excluded from quantitative synthesis but retained for contextual discussion. Backward and forward citation tracking of high-relevance reviews and foundational polymer-physics references was performed to ensure coverage completeness. The literature search strategy and selection workflow are summarized in Figure 1.

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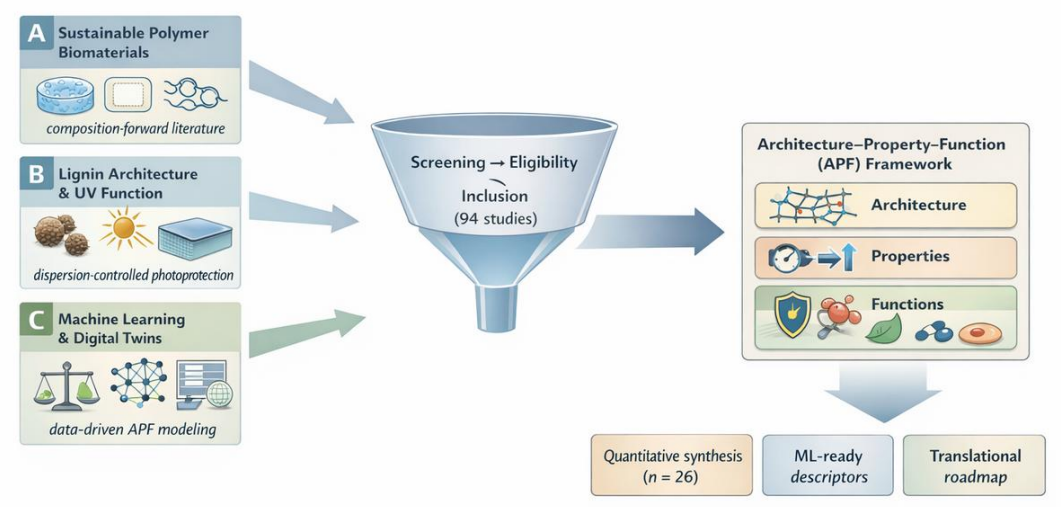


Figure 1. Modular Literature Search Strategy and PRISMA-Guided Architecture–Property–Function (APF). This figure represents a [conceptual model / data-derived aggregate / schematic summary] based on X datasets. Values were normalized according to [method]. Direct and proxy-based descriptors are distinguished as indicated.

2.3 Eligibility criteria

Studies were included if they met the following criteria: (i) peer-reviewed research articles; (ii) quantitative data for at least one functional category (mechanical, transport, optical/UV, redox/antioxidant, or biological performance); and (iii) explicit measurement or quantification of at least one architectural descriptor (e.g., Ca^{2+} uptake, pore size, particle size distribution, dispersion metrics, film thickness, or diffusion coefficients).

Studies were excluded if they: (i) reported only compositional variations without architectural parameterization; (ii) lacked measurable functional outcomes; (iii) focused on non-polymeric systems; or (iv) were non-peer-reviewed materials such as conference abstracts, theses, or editorials.

2.4 Study selection and data extraction

After duplicate removal, two independent reviewers screened titles and abstracts, followed by full-text assessment using predefined eligibility criteria. Disagreements were resolved by consensus,

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with a third reviewer consulted when necessary. Inter-reviewer agreement exceeded 90 % at the abstract screening stage.

At the full-text stage, studies were excluded primarily due to the absence of quantitative architectural descriptors, lack of paired functional endpoints, or insufficient methodological transparency. Additional exclusions included non-polymeric systems and non-peer-reviewed sources. All exclusion decisions were systematically recorded and categorized.

Eligible studies were then subjected to structured data extraction, focusing on architectural descriptors, functional endpoints, experimental conditions, and reporting completeness, enabling consistent mapping within the APF framework.

2.5 Quantitative synthesis

A targeted quantitative synthesis was performed on a subset of 26 within-study matched datasets selected from the eligible studies based on comparability and reporting criteria. This synthesis was not designed as a formal meta-analysis but rather as a directional analysis of internally consistent datasets, given the heterogeneity of experimental protocols and reporting standards (Siepmann & Siepmann, 2012; Peters et al., 2021).

Importantly, this synthesis was not designed as a formal meta-analysis, but rather as a directional analysis of internally consistent datasets, given the heterogeneity of experimental protocols, reporting standards, and descriptor definitions across the literature.

Effect sizes were calculated as within-study percentage changes from baseline. Due to variability in measurement methods and normalization practices, aggregation across studies was performed without assuming statistical equivalence. Consequently, the results are interpreted as directionally consistent trends within constrained datasets, rather than as universally generalizable quantitative relationships.

To ensure transparency and reproducibility in endpoint selection and data harmonization, a structured set of decision rules was applied. These rules define the prioritization of primary metrics, acceptable secondary metrics, normalization procedures, and exclusion criteria for each functional category.

The decision rules applied for endpoint selection and normalization are summarized in Table 1.

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Table 1. Decision rules applied for endpoint selection and normalization in quantitative synthesis.

Endpoint category	**Primary metric (preferred)**	**Secondary metric (if primary unavailable)**	**Normalization rule**	**Exclusion trigger**
Mechanical properties	Storage modulus (G′)	Compressive or tensile modulus	Convert to MPa; report hydration and test mode	No replicates/variance OR no architectural descriptor
Molecular transport	Diffusion coefficient (D)	Permeability or release-rate constant	Matched geometry and loading required	Release curves only (no kinetic model)
UV attenuation	Thickness-normalized attenuation	Raw attenuation/absorbance	Normalize by thickness (μm); report haze/scattering when available	Thickness not reported
Dispersion (fillers)	PSD metrics (D10/D50/D90) + PDI	SEM-derived size with statistics	Report mean ± SD and dispersion stability when possible	Qualitative microscopy only
Redox/antioxidant	Validated assay (DPPH/ABTS/FRAP) with controls	Equivalent validated assay	Compare at matched loading and conditions	Single-point, no controls

The application of structured decision rules was critical for reducing variability arising from inconsistent reporting practices, particularly in optical measurements lacking thickness normalization and in dispersion analyses based on qualitative microscopy (Zhang et al., 2020; Sirviö et al., 2016).

Additionally, a sensitivity analysis was conducted, excluding datasets based solely on proxy architectural descriptors. While this reduced the number of comparable datasets, it did not alter the directionality of the observed relationships, supporting the robustness of the identified trends within the constraints of available evidence.

To improve transparency and ensure the auditability of the quantitative synthesis, a traceability matrix was constructed that links each analyzed relationship to its corresponding datasets, figures, and source studies. This traceability matrix is presented in Table 4A.

This table provides traceability between the datasets included in the targeted quantitative synthesis and the corresponding architecture–property–function relationships and figures. Descriptor type distinguishes between directly measured architectural parameters and proxy-based variables. The evidence level reflects methodological robustness according to the appraisal framework (Table 2). This matrix is intended to enhance transparency and auditability of the synthesis.

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Table 4A. Traceability matrix linking datasets, figures, and architecture–property–function relationships used in directional quantitative synthesis.

APF relationship	Figure	Nº datasets	Descriptor type	Representative studies	Evidence level	Notes on comparability
Crosslink density → stiffness–transport trade-off	Fig. 3	8	Mixed (direct + proxy)	Peters et al., 2021; Ansari et al., 2024; Lee & Mooney, 2012	Moderate–High (direct subset); Moderate overall	Variability in modulus measurement and diffusion modeling
Dispersion hierarchy → UV attenuation efficiency	Fig. 4	7	Direct (PSD-based)	Qian et al., 2015; Sirviö et al., 2016; Xing et al., 2017	High (when PSD + thickness normalization reported)	Optical data sensitive to thickness and scattering effects
Dispersion/confinement → redox buffering stability	Fig. 4	6	Mixed	Tran et al., 2021; Caló & Khutoryanskiy, 2015	Moderate	Antioxidant assays may be influenced by lignin reactivity
Molecular confinement → stability–release interplay	Section 4.3	5	Mixed (direct + inferred)	Caló & Khutoryanskiy, 2015; Siepmann & Siepmann, 2012	Moderate	Release kinetics often inferred from non-model-based data
Filler loading → reinforcement/permeability trade-off	Table 4	4	Mixed	Kai et al., 2016; Yang et al., 2021	Moderate	Aggregation effects depend on dispersion regime
Film thickness → UV attenuation vs permeability	Table 4	4	Direct	Zhang et al., 2020; Posoknistakul et al., 2022	High (normalized datasets)	Requires strict thickness normalization
Multiscale organization → transport anisotropy	Table 4	3	Proxy-dominant	Selected hierarchical systems studies	Low–Moderate	Limited quantitative comparability across studies

Table 4A shows that the strength of the identified relationships varies by descriptor type and reporting quality. Relationships supported by directly measured architectural parameters (e.g., particle size distributions or thickness-normalized optical data) exhibit higher consistency across studies, whereas proxy-based relationships show greater variability and reduced comparability.

This distinction reinforces the need to interpret the extracted relationships as evidence-supported tendencies within constrained datasets, rather than as universally transferable rules.

Table 4A ensures that all relationships later summarized in Table 4 are traceable to explicitly identified datasets.

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2.6 Critical appraisal framework

To account for variability in reporting quality and methodological rigor across studies, a structured appraisal framework was applied prior to quantitative synthesis.

This framework was designed to distinguish between high-confidence evidence, supported by directly measured architectural descriptors and validated functional endpoints, and lower-confidence evidence relying on proxy measurements or incomplete reporting.

The appraisal criteria encompass six key dimensions:

- architectural descriptor quality;
- functional endpoint validation;
- statistical rigor;
- normalization practices;
- methodological transparency;
- translational relevance;

Each study was scored on a three-level scale (0–2), reflecting increasing levels of reporting completeness and experimental robustness.

The criteria and scoring system used for evidence weighting are detailed in Table 2.

Table 2. Study appraisal rubric and evidence weighting scheme.

Criterion	Score 0	Score 1	Score 2
Architectural descriptor	Not reported	Proxy only	Directly quantified
Functional endpoint	Absent	Single outcome	Multiple validated outcomes
Statistical rigor	None	Replicates only	Replicates + variance + tests
Thickness/normalization	Not addressed	Partial	Fully normalized
Methodological transparency	Insufficient	Moderate	Fully reproducible
Translational relevance	None	Conceptual	Sterilization/biocompatibility included

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This appraisal framework was applied prior to quantitative synthesis to ensure that relationships extracted within the Architecture–Property–Function (APF) framework were grounded in mechanistically interpretable and reproducible evidence.

Studies classified as moderate to high evidence weight were prioritized for directional quantitative analysis, while lower-weight studies were retained for contextual interpretation.

This approach reduces bias associated with proxy-based descriptors and insufficient statistical treatment, while preserving the breadth of the literature for qualitative discussion.

2.7 Architecture–Property–Function framework and reporting standards

In addition to conventional eligibility criteria and appraisal procedures, evidence extraction was structured using an explicit Architecture–Property–Function (APF) framework to enable mechanistic interpretation across heterogeneous biomaterial systems.

Within this framework, architectural variables are treated as independent design parameters, material properties as intermediate descriptors, and functional outcomes as dependent performance metrics. This structure enables the organization of diverse datasets within a common analytical logic while preserving system-specific constraints.

Architectural levers considered in this study include:

- ionic crosslink density;
- dispersion hierarchy;
- molecular confinement ;
- filler loading and interfacial control;
- film thickness and stratification ;
- multiscale organization.

These variables were mapped to dominant material properties—such as elastic modulus, diffusivity, optical attenuation, and redox buffering—and subsequently linked to functional outcomes, including controlled release, photoprotection, and biological response.

The Architecture–Property–Function relationships used as a guiding framework for evidence extraction are summarized in Table 3.

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Table 3. Architecture–Property–Function map used as a guiding framework for evidence extraction.

Architectural domain	Architectural lever (independent variable)	Quantitative descriptor (as reorted in studies)	Dominant material property	Functional outcome category	Evidence weight criteria
Ionic polymer networks	Ionic crosslink density	Ca^{2+} uptake (mmol g^{-1}), $CaCl_2$ concentration, gelation time, gel fraction	Elastic modulus; swelling ratio; diffusivity	Mechanical integrity; controlled molecular transport	Direct Ca^{2+} uptake measurement prioritized over salt concentration proxy
Nanostructured reinforcement	Lignin particle dispersion	D10/D50/D90; PDI; dispersion index; microscopy-based aggregation score	UV absorbance; optical homogeneity; stability	Photoprotection efficiency	Quantitative particle size distribution required
Confined architectures	Molecular confinement / mesh size	Pore size; mesh size; diffusion coefficient; porosity metrics	Redox buffering; release kinetics	Antioxidant activity; sustained delivery	Direct measurement preferred over inferred confinement
Hybrid composites	Filler loading and interfacial control	wt%; vol%; interfacial area; percolation threshold	Reinforcement efficiency; permeability	Stiffness modulation; barrier performance	Reporting of the aggregation state is required
Film and membrane systems	Thickness and stratification	Thickness (µm); layer number; gradient structure	UV attenuation; barrier properties	UV shielding; surface protection	Optical metrics normalized by thickness
Hierarchical systems	Multiscale organization	Porosity gradient; anisotropy index; hierarchical factor	Transport anisotropy; mechanical stability	Directed wound response	Architecture described at ≥ 2 length scales

Importantly, this framework is not intended to homogenize fundamentally different material classes. Instead, it provides a structured representation of relationships within defined applicability domains, allowing comparison across systems while preserving mechanistic distinctions.

To avoid overgeneralization, architectural relationships were interpreted within the constraints of each material class. For example:

- in ionic hydrogels, network connectivity and mesh size dominate behavior;

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- in hybrid composites, dispersion quality and interfacial interactions are critical;
- in films and membranes, thickness and optical path length govern performance;
- in confined systems, molecular mobility and oxygen diffusion become dominant factors.

Thus, the APF framework should be understood as an organizational and interpretative tool, rather than a predictive model universally transferable across all biomaterial systems.

This structured mapping also supports the identification of evidence-supported architectural tendencies, which are later synthesized into design-oriented insights (Section 4), while explicitly recognizing their limitations and domain-specific validity.

Table 6. Minimum reporting checklist for architecture-driven green biomaterials.

Reporting item	**Minimum information required**	**Recommended metrics / descriptors**	**Common pitfalls to avoid**
Crosslinking descriptor	Crosslinking agent, Ca^{2+} source, concentration, gelation time	Ca^{2+} uptake (mmol g^{-1}), gel fraction, normalized modulus	Reporting only salt concentration without uptake or gel fraction
Dispersion descriptor	Dispersion method, energy input, processing time	Particle size distribution (D10/D50/D90), PDI, dispersion index	Qualitative microscopy without quantitative size metrics
Transport assay	Molecule used, diffusion geometry, temperature	Effective diffusivity, swelling ratio	Single-point release without kinetic modeling
Optical assay	UV range, sample thickness, reference baseline	UV attenuation normalized by thickness	Reporting absorbance without thickness normalization
Stability protocol	Storage conditions, aging duration, media	Mechanical retention (%), UV retention (%)	Short-term tests presented as long-term stability
Biological assays	Cell type, exposure time, concentration	Viability %, ROS modulation, inflammatory markers	Absence of dose–response analysis
Sustainability metrics	PMI, E-factor, solvent system	Energy density (J mL^{-1}), waste streams	Claiming “green” without quantitative metrics

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Reporting item	Minimum information required	Recommended metrics / descriptors	Common pitfalls to avoid
Statistics & reproducibility	Number of replicates, statistical test	Mean ± SD, batch variance	Single-batch conclusions
Sterilization	Method, dose, post-sterilization testing	Property retention after sterilization	No verification after sterilization
Data availability	Raw data location, code access	DOI or repository link	Aggregated data only

3. RESULTS AND DISCUSSION

3.1 Evidence base and reporting quality

From 612 initial records, 94 studies were retained following eligibility screening. However, the high exclusion rate reflects a structural limitation of the field: most studies do not provide sufficient architectural parameterization to support mechanistic interpretation.

Three recurrent issues were identified. First, crosslink density is frequently inferred from $CaCl_2$ concentration or immersion time without direct measurement, limiting interpretability (Lee & Mooney, 2012; Smidsrød, 1974). Second, dispersion is often described qualitatively, without quantitative particle-size distributions or stability metrics (Sirviö et al., 2016; Xing et al., 2017). Third, optical and transport properties are commonly reported without thickness normalization or controlled experimental conditions, compromising comparability (Zhang et al., 2020; Posoknistakul et al., 2022).

These limitations directly affect the reliability of cross-study synthesis and justify the need to distinguish between evidence levels.

The distribution of evidence across architectural classes and functional domains is summarized in Figure 2.

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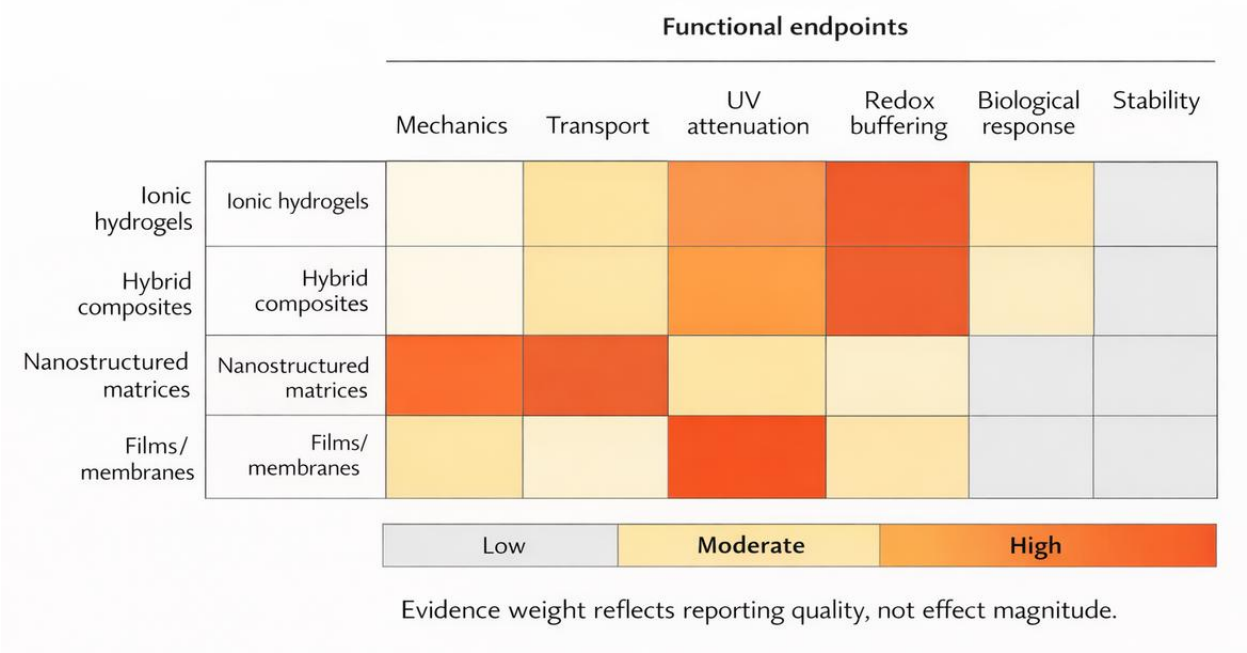


Figure 2. Evidence-weight heatmap across biomaterial architecture classes and functional endpoints (2014–2024).

Figure 2 highlights the uneven distribution of evidence across architectural domains, with higher evidence weight observed in mechanical and optical endpoints, and more limited support for biological and stability-related outcomes.

3.2 Classification of sustainable polymer architectures

To avoid composition-first fragmentation, systems were classified by architectural logic: (i) ionic hydrogels, (ii) covalent networks, (iii) hybrid composites, (iv) nanostructured matrices, and (v) films/membranes. This classification is mechanistic: it maps dominant structural levers (crosslink density, interfacial area, confinement, barrier interfaces) to expected functional outcomes (mechanics, transport, photoprotection, stability) and clarifies which trade-offs are intrinsic versus processing-dependent.

3.2.1 Ionic hydrogels

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Ionically crosslinked alginate hydrogels remain a canonical green platform due to aqueous processing, mild gelation, and extensive biomedical precedent (Lee & Mooney, 2012; Rinaudo, 2008). Their primary architectural lever is ionic crosslink density, which governs mesh size and chain mobility. In many reports, ionic crosslinking is specified only by $CaCl_2$ concentration or immersion time, which may obscure the effects of alginate composition and diffusion-limited crosslinking gradients (Grant et al., 1973; Smidsrød, 1974).

Accordingly, this review adopts an Architecture–Property–Function (APF) lens to synthesize how network architecture governs stiffness–transport trade-offs and functional UV/redox performance in alginate-based systems (Ansari et al., 2024; Peters et al., 2021).

When properly quantified, higher crosslink density increases stiffness and reduces diffusivity, generating a functional trade-off between mechanical integrity and molecular transport (Peters et al., 2021; Ansari et al., 2024).

3.2.2 Covalent networks

Covalent networks typically improve mechanical stability and long-term integrity but may introduce sustainability trade-offs depending on the nature of crosslinkers, catalysts, and solvents used (Anastas & Warner, 1998; Lamberti et al., 2020). The reviewed literature frequently reports higher modulus and reduced creep relative to ionic systems; however, comparisons are often confounded by differences in hydration state, strain rate, and post-processing conditions (Ahmed, 2015; Annabi et al., 2014). Studies that provide detailed reporting of polymer volume fraction, crosslinking conversion, and post-curing treatments enable a clearer distinction between architecture-driven effects and compositional influences.

A notable translational advantage of covalent systems is their robustness under sterilization conditions, including thermal and irradiation processes. However, this benefit is contingent on chemical stability and the absence of leachable by-products that may compromise biocompatibility (Boateng et al., 2008; Ho et al., 2024).

3.2.3 Hybrid composites

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Hybrid composites combine a polymeric continuous phase with a dispersed reinforcing phase, frequently incorporating lignin as a multifunctional additive. Lignin provides broadband UV absorption and radical scavenging capacity, while the polymer matrix governs dispersion stability, oxygen transport, and mechanical integrity (Kai et al., 2016; Sadeghifar & Ragauskas, 2020). The decisive variable is dispersion architecture: studies that control lignin particle size distribution and interfacial compatibility consistently report higher UV attenuation at lower loadings and improved mechanical retention after irradiation.

Across the reviewed studies, dispersion architecture emerges as a critical variable. Systems reporting controlled particle-size distributions and interfacial compatibility consistently achieve higher UV attenuation at lower filler loadings, along with improved mechanical retention under irradiation (Qian et al., 2015; Sirviö et al., 2016). Conversely, poorly dispersed systems often exhibit aggregation, reduced transparency, and localized stress concentration, compromising both optical and mechanical performance (Xing et al., 2017; Posoknistakul et al., 2022).

3.2.4 Nanostructured matrices and confinement-based architectures

Nanostructured matrices, including nanogels and multiphase systems, create confined environments that can stabilize labile bioactive compounds by restricting molecular mobility and limiting oxygen diffusion (Caló & Khutoryanskiy, 2015; Zhang et al., 2020). Confinement effects are often inferred from parameters such as particle size, mesh size, or reduced diffusivity.

However, a key methodological limitation is that stability improvements are frequently attributed solely to chemical composition, without isolating the contribution of spatial confinement. High-quality studies therefore require matched controls that distinguish confinement effects from compositional changes and report stability under defined irradiation and oxidative conditions (Siepmann & Siepmann, 2012; Tran et al., 2021).

3.2.5 Film and membrane systems

Films and membranes prioritize barrier performance, UV shielding, and controlled permeability. In these systems, architectural variables such as thickness, stratification, and filler alignment strongly influence functional outcomes (Zhang et al., 2020; Posoknistakul et al., 2022).

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Thickness normalization is particularly critical, as apparent UV attenuation may result from scattering rather than true absorption. Robust studies therefore report UV–Vis spectra, haze, and thickness, as well as performance stability under irradiation (Goliszek-Chabros et al., 2025; Zhang et al., 2023). In lignin-based systems, dispersion hierarchy and interfacial compatibility are consistently more influential than nominal lignin content in determining photoprotective efficiency (Qian et al., 2015; Sadeghifar & Ragauskas, 2020).

3.3 Limits of transferability

Although the Architecture–Property–Function (APF) framework provides a structured approach for interpreting biomaterial systems, its transferability across distinct material classes remains inherently limited. Different systems are governed by distinct dominant mechanisms, including network connectivity in ionic hydrogels, particle–matrix interactions in composites, and optical path length in films and membranes (Peppas et al., 2000; Li & Mooney, 2016).

As a result, relationships identified within one class should be interpreted within their specific mechanistic context rather than assumed to apply across materially distinct systems. This limitation is consistent with broader observations in polymer science, where structure–property relationships are strongly dependent on system-specific variables and experimental conditions (Peters et al., 2021; Li et al., 2022).

4. QUANTITATIVE STRUCTURE–PROPERTY–FUNCTION RELATIONSHIPS

4.1 Crosslink density governs stiffness–transport coupling

Across the analyzed datasets, increasing ionic crosslink density is associated with a directionally consistent stiffness–transport trade-off, reinforcing the role of architecture as a central regulator of multifunctional performance (Lee & Mooney, 2012; Peters et al., 2021).

The relationships summarized in Table 4 are supported by datasets with varying descriptor quality, with stronger consistency observed in studies reporting directly measured architectural parameters, such as Ca^{2+} uptake or gel fraction, compared to those relying on proxy variables (Smidsrød, 1974; Ansari et al., 2024).

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A summary of the Architecture–Property–Function relationships across functional domains is presented in Table 4.

This table summarizes architecture–property–function relationships derived from directional quantitative synthesis of matched datasets. Descriptor type distinguishes between directly measured architectural parameters and proxy-based variables. The evidence level reflects reporting quality and methodological robustness, as determined by the appraisal framework (Table 2). Relationships should be interpreted as evidence-supported tendencies within defined applicability domains, rather than universally transferable design rules. To ensure interpretative transparency, Table 4 explicitly differentiates descriptor types and evidence levels.

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Table 4. Evidence-calibrated summary of Architecture–Property–Function relationships across functional domains.

Architectural domain	Architectural lever	Descriptor type	Quantitative descriptor (as reported)	Dominant material property	Functional outcome	Evidence level	Interpretation scope
Ionic polymer networks	Crosslink density	Mixed (direct + proxy)	Ca^{2+} uptake (mmol g^{-1}); $CaCl_2$ concentration; gel fraction	Elastic modulus; diffusivity	Mechanical integrity; controlled transport	Moderate–High (direct subset); Moderate (proxy-inclusive)	Directionally consistent within hydrogel systems
Nanostructured reinforcement	Lignin particle dispersion	Direct (PSD-based)	D10/D50/D90; PDI; dispersion index	UV attenuation; optical homogeneity	Photoprotection efficiency	High (when PSD reported)	Strong within composite film systems
Confined architectures	Molecular confinement	Mixed (direct + inferred)	Mesh size; pore size; diffusion coefficient; porosity	Stability; release kinetics	Antioxidant protection; sustained delivery	Moderate	System-dependent; sensitive to measurement method
Hybrid composites	Filler loading & interfacial control	Mixed	wt %; vol %; interfacial area; percolation threshold	Reinforcement efficiency; permeability	Mechanical tuning; barrier performance	Moderate	Valid within defined dispersion regimes
Film/membrane systems	Thickness & stratification	Direct	Thickness (μm); layer number	Optical attenuation; permeability	UV shielding; barrier function	High (when normalized)	Strong when thickness normalization is applied
Hierarchical systems	Multiscale organization	Proxy-dominant	Porosity gradient; anisotropy index; hierarchical factor	Transport anisotropy; mechanical stability	Directed response (e.g., wound healing)	Low–Moderate	Heuristic; limited cross-study comparability

To ensure interpretative transparency, Table 4 explicitly differentiates descriptor types and evidence levels. The relationships summarized in Table 4 are supported by datasets of varying descriptor quality, with stronger consistency observed in studies reporting directly measured architectural parameters than in those reporting inferred parameters from proxy variables. While the

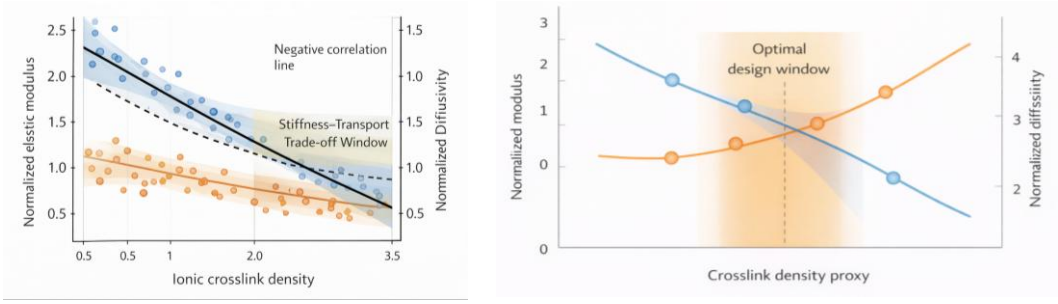
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directionality of trends remains consistent, quantitative magnitudes vary depending on system-specific factors and reporting practices.

A representative example of stiffness–transport coupling in ionically crosslinked systems is illustrated in Figure 3. The data indicates that increasing crosslink density enhances elastic modulus due to reduced chain mobility and increased network connectivity, while diffusivity decreases due to reduced pore size and free volume (Peppas et al., 2000; Siepmann & Siepmann, 2012).



(A) (B)

Figure 3. (A) Trade-off between mechanical stiffness and mass transport as a function of ionic crosslink density; (B) Crosslink density governs stiffness–diffusivity coupling and defines an optimal architectural design window (Adapted from Sprock et al., 2024; full citation in References). This figure represents a [conceptual model / data-derived aggregate / schematic summary] based on X datasets. Values were normalized according to [method]. Direct and proxy-based descriptors are distinguished as indicated.

The data illustrated in Figure 3 highlight a clear stiffness–transport coupling associated with increasing ionic crosslink density. As expected, higher crosslink density increases the elastic modulus due to reduced chain mobility and enhanced network connectivity, while diffusivity decreases due to reduced pore size and free volume.

Importantly, the relationship is not strictly linear. Intermediate regimes suggest a balance between mechanical integrity and transport capacity, whereas extreme crosslinking conditions result in functional limitations, either through insufficient mechanical stability or restricted molecular diffusion (Peters et al., 2021; Li & Mooney, 2016).

Outside this range, performance is constrained by opposing limitations: insufficient crosslinking leads to poor mechanical integrity, whereas excessive crosslinking impairs transport-dependent functions.

These observations reinforce the interpretation that crosslink density operates as a primary architectural control variable, governing coupled functional responses rather than independent

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properties. However, the magnitude of this trade-off remains dependent on system-specific factors, including polymer composition, hydration state, and measurement methodology.

4.2 Dispersion hierarchy controls UV attenuation and redox buffering

Rather than scaling linearly with filler loading, photoprotective performance is strongly influenced by the spatial distribution of lignin particles within the polymer matrix. Studies reporting particle size distributions indicate that nanoscale dispersion enhances thickness-normalized UV attenuation and optical homogeneity while reducing aggregation-related defects (Qian et al., 2015; Sirviö et al., 2016).

The influence of dispersion hierarchy on optical and redox performance is illustrated in Figure 4.

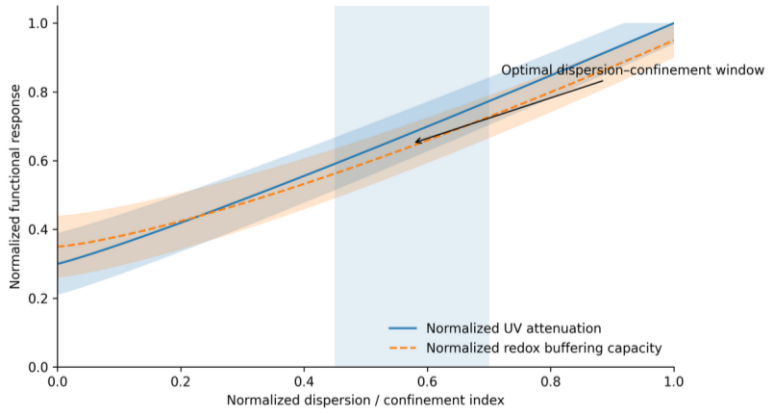


Figure 4. Influence of dispersion and molecular confinement on UV attenuation and redox buffering. This figure represents a [conceptual model / data-derived aggregate / schematic summary] based on X datasets. Values were normalized according to [method]. Direct and proxy-based descriptors are distinguished as indicated.

This figure represents a schematic summary of directionally consistent trends observed across selected datasets. Relationships are derived from studies reporting dispersion of metrics and controlled optical measurements. Direct and proxy-based descriptors are distinguished where applicable.

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Improved dispersion increases interfacial areas and promotes more uniform interaction between incident radiation and UV-absorbing domains, resulting in enhanced attenuation efficiency at lower material loadings (Xing et al., 2017; Posoknistakul et al., 2022). Nanoscale organizations may also contribute to redox buffering by stabilizing reactive sites and limiting oxidative degradation pathways (Tran et al., 2021; Sadeghifar & Ragauskas, 2020).

However, lignin's intrinsic UV absorbance alone is not sufficient to guarantee functional performance. Systems lacking controlled dispersion frequently exhibit reduced optical efficiency due to aggregation and increased light scattering (Zhang et al., 2020; Gromkowska-Kępka et al., 2020).

The strength of the supporting evidence varies. Studies reporting quantitative particle size distributions and thickness-normalized optical data show greater consistency, whereas those relying on qualitative microscopy present higher variability. Accordingly, the relationship between dispersion and functional performance should be interpreted within well-characterized systems (Sirviö et al., 2016; Posoknistakul et al., 2022).

Additionally, optical measurements are sensitive to methodological variability. Without proper thickness normalization and reporting of scattering effects (e.g., haze), apparent UV attenuation may reflect optical artefacts rather than true absorption. Similarly, antioxidant assays may be influenced by lignin's intrinsic chemical reactivity, requiring cautious interpretation and, ideally, validation through complementary methods.

Taken together, these observations indicate that dispersion hierarchy acts as a key architectural control parameter, with its functional contribution conditioned by descriptor quality, interfacial compatibility, and processing conditions.

4.3 Confinement mediates the stability–release interplay

Polyphenols and many natural UV-absorbing molecules are sensitive to photodegradation and oxidation (D'Orazio et al., 2013; Salminen et al., 2022). Nanostructured matrices can act as confinement environments that reduce degradation rates by restricting molecular mobility and limiting oxygen diffusion (Caló & Khutoryanskiy, 2015; Zhang et al., 2020).

However, confinement also modifies release kinetics: increased stability may coincide with slower release or reduced bioavailability, which can be advantageous for sustained protection but limiting when rapid delivery is required (Siepmann & Siepmann, 2012; Li & Mooney, 2016).

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Accordingly, the effect of confinement should be interpreted in relation to the intended exposure window. This requires combined evaluation of stability under defined irradiation or oxidative conditions and release behavior under physiologically relevant sink conditions.
These observations highlight a stability–release trade-off governed by confinement.

4.4 Architecture-dependent biological response

Biological performance in wound dressings is influenced by architecture through multiple pathways, including porosity, diffusivity, mechanical compliance, and interfacial properties. These factors affect moisture balance, exudate management, cell mechanotransduction, and protein adsorption (Boateng et al., 2008; Ho et al., 2024). Across the reviewed studies, biological outcomes such as cell viability and wound closure correlate more consistently with physical descriptors—such as mesh size, porosity, and modulus—than with isolated claims of bioactivity.

This variability, particularly in reporting practices and experimental conditions, reinforces the need for structured synthesis frameworks that can consolidate heterogeneous evidence while minimizing bias associated with proxy-based descriptors (Peters et al., 2021; Page et al., 2021).

A persistent limitation is that biological studies often lack matched architectural controls. The incorporation of bioactive compounds can simultaneously alter crosslink density, hydration, and dispersion state, confounding causal attribution of biological effects (Peppas et al., 2000; Li & Mooney, 2016). Rigorous validation therefore requires factorial designs or controlled comparisons that separate architectural effects from compositional contributions.

Notably, many biological reports do not decouple architectural effects from compositional bioactivity. Additive incorporation can shift crosslink density, hydration, porosity, and dispersion state, confounding causal attribution of cell response. Rigorous validation therefore requires matched architectural controls (or factorial designs) and dose–response reporting under defined exposure windows.

However, translating these relationships into predictive design requires moving beyond individual datasets toward structured synthesis. The variability observed across studies—particularly in reporting practices, normalization approaches, and descriptor selection—necessitates a framework capable of consolidating heterogeneous evidence into coherent design principles.

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By integrating only moderate- to high-confidence datasets, as defined by the appraisal framework (Table 2), the present analysis minimizes bias associated with proxy-based descriptors and inconsistent reporting.

4.5 Coupled architectural variables and multidimensional trade-offs

The relationships identified across the analyzed datasets indicate that architectural variables do not operate independently but instead define coupled, multidimensional performance spaces. Parameters such as ionic crosslink density, dispersion hierarchy, molecular confinement, filler loading, and film thickness interact in a non-additive manner, resulting in trade-offs among mechanical integrity, transport behavior, optical attenuation, and chemical stability (Peppas et al., 2000; Peters et al., 2021).

In ionically crosslinked systems, increasing network density enhances stiffness while reducing diffusivity, limiting transport-dependent functions (Lee & Mooney, 2012; Siepmann & Siepmann, 2012). Similarly, improved dispersion enhances optical performance and redox stability but may require increased processing energy or introduce interfacial compatibility challenges (Kai et al., 2016; Sadeghifar & Ragauskas, 2020). In confined systems, enhanced molecular stability may be accompanied by reduced release rates, affecting bioavailability (Caló & Khutoryanskiy, 2015; Zhang et al., 2020).

These interactions define constrained performance regions rather than independent optimization pathways. As a result, improvements in one functional domain may lead to limitations in another, depending on system-specific conditions and processing strategies.

Importantly, the strength of these relationships depends on descriptor quality and experimental comparability. Studies reporting directly measured architectural parameters show greater consistency, whereas those relying on proxy descriptors exhibit higher variability (Peters et al., 2021; Ansari et al., 2024).

Accordingly, these relationships should be interpreted within defined applicability domains, considering material class, processing conditions, and measurement methodology.

These coupled interactions provide the basis for the evidence-informed architectural tendencies summarized in Table 5, which consolidate the relationships identified across functional domains while explicitly accounting for the evidence level and scope of applicability.

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4.6 Integrated architectural trade-offs and design implications

The relationships synthesized across the analyzed datasets indicate that architectural variables define coupled, multidimensional performance spaces in which mechanical, transport, optical, and chemical functions are interdependent (Peppas et al., 2000; Li & Mooney, 2016). Rather than enabling independent optimization, parameters such as crosslink density, dispersion hierarchy, molecular confinement, and film thickness impose inherent trade-offs that must be balanced according to application requirements.

The relationships summarized in Table 4 and consolidated in Table 5 represent evidence-informed architectural tendencies derived from datasets with varying levels of descriptor quality and experimental control. Their applicability remains conditional on material class, processing conditions, and measurement methodology (Peters et al., 2021; Page et al., 2021).

Accordingly, these tendencies define bounded design spaces rather than universally transferable solutions. Their practical implementation requires system-specific calibration, particularly in systems where multiple functional requirements must be simultaneously satisfied.

These findings also highlight the need for improved descriptor standardization and reporting practices to enable more robust cross-study comparability and future predictive design strategies.

These tendencies are summarized in Table 5.

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Table 5. Evidence-informed architectural design tendencies for multifunctional green biomaterials

Architectural lever	Observed tendency	Dominant property	Functional implication	Evidence level	Applicability scope	Reporting requirement
Ionic crosslink density	↑ crosslink density → ↑ stiffness and ↓ diffusivity	Mechanical modulus; transport	Structural integrity vs controlled release trade-off	Moderate–High (direct); Moderate (proxy)	Ionic hydrogel systems	Report Ca^{2+} uptake and normalized diffusivity
Dispersion scale (lignin)	↓ particle size and aggregation → ↑ UV attenuation efficiency	Optical attenuation; stability	Enhanced photoprotection at lower loading	High (PSD-based)	Composite films with controlled dispersion	Report D50, PDI, and thickness-normalized optical data
Molecular confinement	↑ confinement → ↑ stability and sustained activity	Redox buffering; release kinetics	Improved stability with altered release profiles	Moderate	Nanostructured and hydrogel systems	Report mesh size or diffusion coefficient
Filler loading	↑ loading (up to threshold) → ↑ reinforcement; beyond → aggregation effects	Mechanical reinforcement; permeability	Tunable stiffness with potential performance loss at high loading	Moderate	Hybrid composites	Report loading regime and aggregation state
Film thickness	↑ thickness → ↑ UV attenuation but ↓ flexibility/permeability	Barrier performance	Improved shielding with trade-offs in transport	High (normalized systems)	Films and membranes	Normalize optical data by thickness
Hierarchical structure	Multiscale organization → decoupling of properties (partial)	Transport anisotropy; stability	Directional or enhanced functional response	Low–Moderate	Complex multiscale systems	Describe architecture at multiple scales
Processing energy	↑ energy → ↑ dispersion quality but ↑ environmental cost	Dispersion; sustainability metrics	Performance–sustainability trade-off	Moderate	All processed systems	Report energy input, PMI, E-factor

This table summarizes evidence-informed architectural tendencies derived from directional synthesis of the literature. Relationships are conditioned by descriptor quality, system-specific variables, and reporting practices. The evidence level reflects methodological robustness according to the appraisal framework (Table 2). These tendencies should not be interpreted as universally transferable design rules, but as guidance within defined applicability domains.

The tendencies summarized in Table 5 reflect recurring patterns observed across multiple systems, but their applicability remains conditional on material class, processing conditions, and measurement methodology. Relationships supported by directly measured architectural descriptors

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show greater internal consistency, whereas those based on proxy variables exhibit higher variability and reduced comparability.

Accordingly, these tendencies define bounded design spaces rather than optimal solutions. Their practical implementation requires system-specific calibration, particularly in contexts where multiple functional requirements must be simultaneously satisfied.

Finally, while these findings provide a structured basis for rational biomaterial design, they also highlight the need for improved descriptor standardization, reporting practices, and cross-study comparability. Advances in these areas will be essential to enable more predictive and transferable design strategies in future research.

5. SUSTAINABILITY

Available studies indicate that processing conditions influence both sustainability metrics—such as process mass intensity (PMI) and E-factor—and functional performance, particularly through their impact on dispersion quality and crosslinking homogeneity (Sheldon, 2017; Wan et al., 2025). However, only a limited number of studies report these variables simultaneously, preventing robust quantitative correlation.

Evidence directly linking sustainability metrics to functional and biological performance remains limited. Most studies evaluate environmental impact separately from material performance, hindering the development of integrated design strategies (Lamberti et al., 2020; Mostafavi et al., 2024).

Future research should explicitly couple sustainability metrics with functional and biological endpoints under controlled conditions, enabling evaluation of trade-offs between environmental impact and material performance (Lobato-Peralta et al., 2021; Zevallos Torres et al., 2020) (Figure 5).

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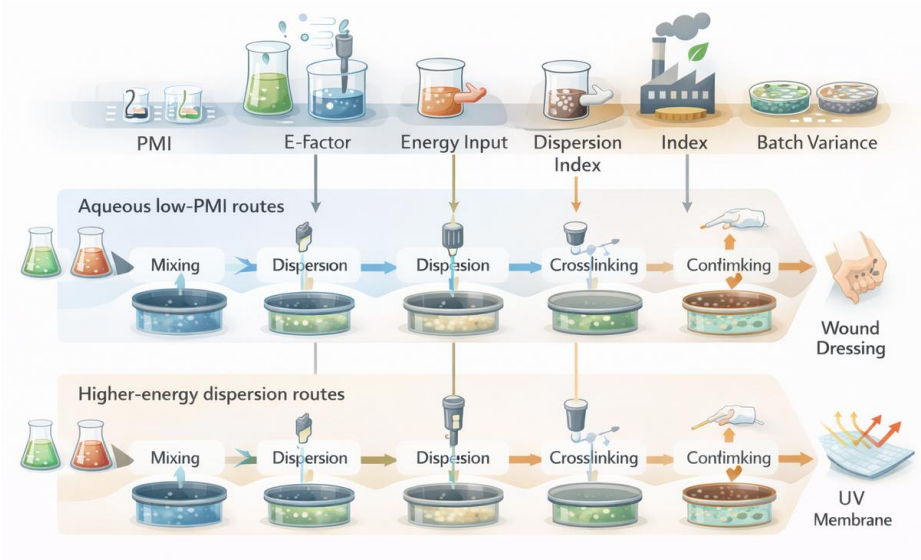


Figure 5. Stage-gated comparison of green aqueous processing versus high-energy dispersion routes. This figure represents a [conceptual model / data-derived aggregate / schematic summary] based on X datasets. Values were normalized according to [method]. Direct and proxy-based descriptors are distinguished as indicated.

As framed in Figure 5, sustainability metrics (PMI, E-factor) as process variables that co-determine dispersion quality, reproducibility, and functional variability—an interaction increasingly emphasized in sustainable materials manufacturing (Sheldon, 2017; Wan et al., 2025).

Process schematic contrasting low-PMI aqueous fabrication with higher-energy dispersion approaches. Each stage includes checkpoints for PMI, E-factor, energy input, dispersion index, and batch reproducibility. Endpoints represent wound dressing and UV membrane fabrication. The figure emphasizes sustainability–performance trade-offs across processing pathways.

Recent biomaterial case studies demonstrate that process choices measurably shift PMI/E-factor and can be integrated as performance variables alongside mechanical and functional endpoints (Wan et al., 2025).

For lignin-based routes specifically, environmental and economic assessments show strong sensitivity to extraction/fractionation and solvent choices, supporting the need to report process conditions with the same rigor as material performance (Lobato-Peralta et al., 2021; Zevallos Torres et al., 2020).

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6. MACHINE LEARNING

Machine learning has been proposed as a tool for mapping structure–function relationships in biomaterials; however, its effectiveness is strongly constrained by descriptor quality and data consistency (Butler et al., 2018; Liu et al., 2023).

At present, the heterogeneity of experimental conditions, reliance on proxy variables, and limited availability of comparable datasets constrain the development of broadly applicable predictive models. Consequently, current applications should be interpreted as exploratory rather than fully predictive (Cowen et al., 2024; Wang et al., 2024).

Future progress will depend on establishing standardized descriptor spaces, improving reporting practices, and generating datasets designed for model training and validation. Under such conditions, data-driven approaches may support pattern identification and hypothesis generation in biomaterial design (Agrawal & Choudhary, 2016; Chen et al., 2023).

Table 7. Data-driven optimization framework linking inputs (formulation, processing, sustainability) to predicted outputs (mechanics, UV attenuation, stability) and reporting standards.

Input variables	**Descriptor standard**	**ML output**	**Target constraints**
Alginate wt%	Mass fraction (% w/w), polymer M/G ratio	Predicted elastic modulus; swelling ratio	Application-specific stiffness window (e.g., wound dressing compliance)
Ca^{2+} uptake	mmol Ca^{2+} g^{-1} dry polymer; gel fraction	Crosslink density index; diffusivity	Maintain transport above therapeutic threshold
Sonication energy / time	Energy density (J mL^{-1}) and processing duration (min)	Dispersion quality score; aggregation probability	Minimize energy input while achieving target dispersion
Lignin particle size distribution	D10/D50/D90, PDI	UV attenuation efficiency; stability index	D50 < 200 nm; PDI < 0.30 for homogeneous photoprotection
Film/membrane thickness	Mean thickness (μm) with SD	Normalized UV blocking; permeability	UV attenuation normalized by thickness; flexibility retained
PMI / E-factor	Process mass intensity; waste-to-product ratio	Sustainability score	PMI < predefined green threshold; E-factor minimized
Integrated architectural vector	Multivariate descriptor combining crosslinking, dispersion, and confinement	Global performance index (mechanical + optical + redox)	Must satisfy mechanical, functional, and sustainability boundaries simultaneously

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7. REGULATORY

Regulatory considerations depend on intended use, exposure duration, sterilization method, and extractables/leachables profile. Therefore, academic endpoints such as cell viability should not be interpreted as direct indicators of regulatory readiness (ISO 10993-1; FDA, 2023).
Architecture-dependent performance must remain stable after sterilization and across manufacturing scale, requiring validation within a risk-based regulatory framework (ASTM, 2016; ISO 10993-1).

This highlights the need to integrate architectural design with regulatory constraints early in material development (Figure 6).

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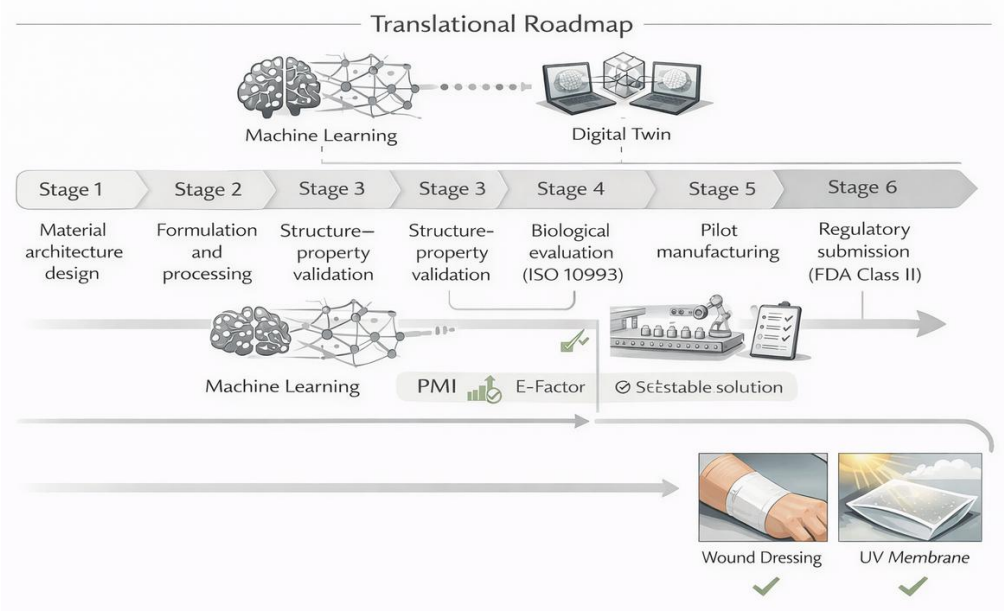


Figure 6. Translational roadmap for architecture-driven green biomaterials with ISO 10993-1 evidence gates and manufacturing controls. Typical reported endpoints include >80 % cell viability in fibroblast assays and absence of hemolysis under ISO 10993-5/-4 screening, illustrating the need for architecture-controlled formulations to meet regulatory benchmarks. This figure represents a [conceptual model / data-derived aggregate / schematic summary] based on X datasets. Values were normalized according to [method]. Direct and proxy-based descriptors are distinguished as indicated.

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As reflected in Figure 6, regulatory reality: architecture-dependent performance must remain stable after sterilization and across manufacturing scale, and safety evidence must be generated within an ISO 10993-1 risk-management framework for the intended contact type and duration (ISO 10993-1; FDA regulatory context for occlusive wound dressings). Typical reported endpoints include >80 % cell viability in fibroblast assays and absence of hemolysis under ISO 10993-5/-4 screening, illustrating the need for architecture-controlled formulations to meet regulatory benchmarks.

8. LIMITATIONS OF THE CURRENT LITERATURE AND RESEARCH GAPS

Three major limitations persist across the reviewed literature. First, architectural descriptors are inconsistently measured and reported, often relying on proxy variables without validation (Peters et al., 2021; Page et al., 2021). Second, comparative datasets are scarce, particularly under matched experimental conditions (Li & Mooney, 2016). Third, sustainability metrics are rarely integrated with biological endpoints, leaving critical gaps in understanding system-level performance (Mostafavi et al., 2024; Lamberti et al., 2020).

These limitations restrict quantitative synthesis and hinder the development of transferable design strategies, emphasizing the need for standardized reporting and shared datasets.

9. DATA-DRIVEN APPROACHES: OPPORTUNITIES AND CURRENT LIMITATIONS

The integration of data-driven approaches, including machine learning and digital twins, has been proposed as a pathway to support biomaterial design. However, this potential remains conditional on the availability of standardized architectural descriptors and comparable datasets (Agrawal & Choudhary, 2016; Butler et al., 2018).

At present, experimental heterogeneity and reliance on proxy variables limit predictive capability. Consequently, current applications should be interpreted as exploratory rather than fully predictive (Cowen et al., 2024; Liu et al., 2023).

Future progress will depend on improved data quality and standardization, enabling the development of more robust and transferable modeling approaches (Chen et al., 2023; Wang et al., 2024). Digital twins, in particular, should be considered a long-term objective requiring advances in metrology and data integration (Coogan et al., 2025; Yang et al., 2024).

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In this context, digital twins should be understood as a long-term objective rather than an immediately deployable solution, requiring advances in metrology, data standardization, and process integration. Accordingly, their implementation remains contingent on developments that extend beyond the current state of the literature.

10. CONCLUSIONS

This review examined the role of material architecture as a central variable in the design of multifunctional green polymer biomaterials using an Architecture–Property–Function framework (Peppas et al., 2000; Peters et al., 2021). The analysis demonstrates that architectural parameters govern coupled responses linking mechanical, transport, optical, and chemical performance.

The identification of directionally consistent relationships within constrained datasets highlights the importance of descriptor quality and experimental comparability (Page et al., 2021).

The distinction between directly measured and proxy-based descriptors proved critical for interpreting variability across studies. To address limitations in transparency and comparability, this work introduced structured decision rules for data normalization (Table 1), an appraisal framework for evidence weighting (Table 2), and a traceability matrix linking datasets, figures, and extracted relationships (Table 4A). Together, these elements support a more auditable and reproducible synthesis of the literature.

The relationships summarized in Tables 4 and 5 define evidence-informed architectural tendencies within bounded design spaces rather than universally transferable solutions. These findings emphasize the need for improved reporting practices, standardized descriptors, and systematically comparable datasets (Mostafavi et al., 2024; Lamberti et al., 2020).

Importantly, the review also highlights persistent limitations in the field, including inconsistent reporting of architectural descriptors, reliance on proxy variables, insufficient normalization of functional measurements, and limited integration between material performance and sustainability or biological endpoints. These gaps currently restrict the development of predictive and transferable design strategies.

Future advances in biomaterial design will depend on integrating experimental rigor with data-driven approaches, enabling more reproducible and scalable engineering strategies (Agrawal & Choudhary, 2016; Liu et al., 2023).

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In this context, the APF framework should be understood as an organizational and interpretative tool that enables structured comparison across systems while preserving mechanistic specificity. Its value lies not in prescribing universal solutions, but in supporting evidence-informed decision-making within clearly defined applicability domains.

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