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An overview of AI in biofunctional materials

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Highlights:

- AI accelerates the development and optimization of biofunctional materials in medicine.
- Machine learning enhances material synthesis, surface modification, and predictive modeling.
- AI-driven innovations in hydrogels and smart materials offer significant advancements in tissue engineering.
- Cross-disciplinary collaborations are vital for integrating AI in biofunctional material research.
- Sustainable and biodegradable materials are increasingly prioritized in AI-powered biomaterial innovations.

Abstract: The integration of artificial intelligence (AI) into biofunctional materials is transforming material design, synthesis, and optimization for medical applications. Machine learning and deep learning models now predict material properties (e.g., mechanical strength, degradation rate) with > 90% accuracy, dramatically reducing trial-and-error in scaffold and nanoparticle fabrication. AI-driven platforms accelerate surface functionalization strategies to enhance cell adhesion and drug loading, while generative models design stimuli-responsive hydrogels and smart polymers that mimic tissue mechanics. Case studies include rapid optimization of nanoparticle synthesis via Bayesian frameworks and the discovery of biodegradable stent materials through random forest screening. Despite remaining challenges in data quality and regulatory alignment, these advances underscore AI's capacity to deliver high-performance, sustainable biomaterials and point toward an interdisciplinary roadmap for next-generation therapeutic solutions.

Keywords: AI in biofunctional materials; machine learning in material design; biomaterials in tissue engineering; biocompatible materials; sustainable biomaterials; data-driven material optimization

1. Introduction

Artificial intelligence (AI) is rapidly reshaping the landscape of biofunctional materials, a category of materials specifically engineered to interact with biological systems in therapeutic, diagnostic, or regenerative capacities. These materials are central to biomedical domains such as tissue engineering, regenerative medicine, and targeted drug delivery systems. Historically, material innovation in this space has been governed by empirical and iterative experimentation; however, the growing confluence of AI and materials science is revolutionizing the way we discover, design, and optimize these biofunctional materials [1–3].

AI offers capabilities in predictive modeling, generative material design, and automation that surpass conventional methods. With the help of machine learning (ML) and deep learning (DL), large datasets can be analyzed to uncover structure-property-performance relationships, accelerating the pace of innovation. Modern AI systems such as graph neural networks (GNNs), generative models, and transfer learning have demonstrated success in predicting material behaviors, suggesting synthesis pathways, and even controlling laboratory robotics for autonomous material discovery [4,5].

Biofunctional materials themselves have evolved from primitive organic matter like shells and bones used by early civilizations to advanced classes including biodegradable polymers, bioactive ceramics, and metallic implants designed with bioresorbability and biocompatibility in mind. The field has witnessed a leap in capabilities, especially after the 20th century, with regulatory approvals for thousands of medical devices incorporating smart materials that respond to physiological stimuli such as pH, temperature, or enzymes [1,6,7].

A primary barrier is data heterogeneity: biomaterials datasets are often sparse (∼1,000–5,000 records) and lack standardized protocols. For example, ML models trained on disparate hydrogel swelling data exhibit $R^2 < 0.6$ when transferred across labs. To address this, transfer learning frameworks have been developed: a pre-trained MLP on large polymer libraries (~50k samples) fine-tuned on niche bioceramic properties improved predictive R^2 from 0.45 to 0.85 with as few as 200 new data points [15].

Regulatory pathways also lag: current FDA guidances for AI-aided materials remain at draft stages, lacking Definitions for "continuous learning" systems in manufacturing. Establishing explainable AI (XAI) methods—such as SHAP value analysis of feature importance—can facilitate risk assessment by quantifying how input factors (e.g., monomer ratio, pH) drive model outputs, thereby easing regulatory review. Ethical concerns around data ownership, algorithmic bias, and reproducibility further complicate matters, especially in clinical settings. The imperative for interdisciplinary collaboration across computer science, materials engineering, and biomedicine is therefore essential to responsibly develop and deploy AI in this domain [8–10].

With the expanding market for biofunctional materials driven by factors like an aging population and the increasing prevalence of chronic diseases, the potential for AI to augment material development is becoming increasingly evident. Figure 1 illustrates an end-to-end AI-powered design pipeline for developing optimized biofunctional materials, integrating multi-modal data acquisition, predictive/generative AI models, *in silico* validation, active learning, and robotic experimentation to generate candidates ready for preclinical testing. Projections indicate substantial growth in the biomaterials sector, propelled by technological advancements in 3D printing, personalized medicine, and smart materials [11,12]. The successful integration of AI into this landscape not only promises to advance scientific knowledge but also to improve healthcare solutions and patient care on a global scale.

1.1. AI in materials science

Recent advances leverage graph neural networks (GNNs) and kernel ridge regression (KRR) to predict composition–property relationships across diverse materials sets. For example, a MegNet-based GNN trained on 50,000 entries from the Materials Project database achieved a root-mean-square error (RMSE) of 0.12 eV on bandgap predictions, outperforming DFT by reducing computational cost. Meanwhile, kernel ridge regression models using elemental descriptors (atomic radius, electronegativity) predict formation energies of transition-metal oxides with MAE = 0.05 eV/atom, enabling rapid screening of stable compounds for biomedical coatings [4]. Key developments include GNNs for property prediction and GANs (generative adversarial networks) for generating novel material structures. These models support inverse material design—creating materials from desired properties rather than characterizing materials post-synthesis—a transformative shift in approach [4,13]. Frameworks such as MatterGen, JARVIS-ML, and Citrination are examples of AI-powered platforms facilitating discovery [13,14].

1.2. Generative models and language processing

Generative approaches such as GFlowNets and transformer-based LLMs (e.g., MolGPT) now enable inverse molecular design from textual prompts. In one study, MolGPT fine-tuned on 25,000 polymer SMILES strings generated 1200 novel candidates; 70% satisfied target criteria for glass transition temperature (T_9 > 150 ℃) with < 5 K deviation from predictions in molecular dynamics simulations. Similarly, a GFlowNet trained on catalytic reaction datasets suggested 300 new organometallic complexes, 30% of which exhibited experimentally validated turnover frequencies within ± 10% of model forecasts [14]. These models utilize natural language and unstructured data to extract and synthesize scientific knowledge for material synthesis, property prediction, and workflow automation. This has opened new opportunities for data-driven design processes that utilize chemical literature and experimental logs as valuable datasets [14,15].

1.3. Biomaterials and regenerative medicine

In regenerative medicine, biomaterials act as scaffolds that guide cell growth and tissue integration. AI enhances this process by optimizing scaffold design for mechanical strength, degradation profiles, and cellular interactions. For example, deep generative networks have been used to design porous structures in hydrogels for cartilage repair and 3D-printed scaffolds for bone regeneration [3,13]. AI also aids in predicting the host response, material resorption time, and integration efficacy—facilitating personalized treatment approaches and enhancing the therapeutic potential of biomaterials [2,16].

1.4. Classification of biomaterials

Biomaterials are systematically classified into three major categories based on their interaction with biological systems: biodegradable, bioactive, and inert. Biodegradable materials, such as poly (lactic acid) (PLA), are ideal for temporary implants that naturally dissolve within the body after fulfilling their function. Bioactive materials, such as hydroxyapatite, are designed to actively stimulate cellular responses and promote tissue regeneration. In contrast, inert materials like titanium alloys offer long-term stability with minimal biological interaction, often used in permanent implants due to their excellent mechanical strength and corrosion resistance [2,7].

Recent advancements in AI-driven platforms—including JARVIS-ML, Citrination, and The Materials Project—have significantly improved the ability to classify such biomaterials based on multi-parameter analysis. These platforms utilize supervised machine learning models that incorporate a wide range of physicochemical and biological input features, such as Young's modulus, surface energy, degradation kinetics, cytocompatibility, thermal stability, and elemental composition, to predict material suitability for specific biomedical applications [13].

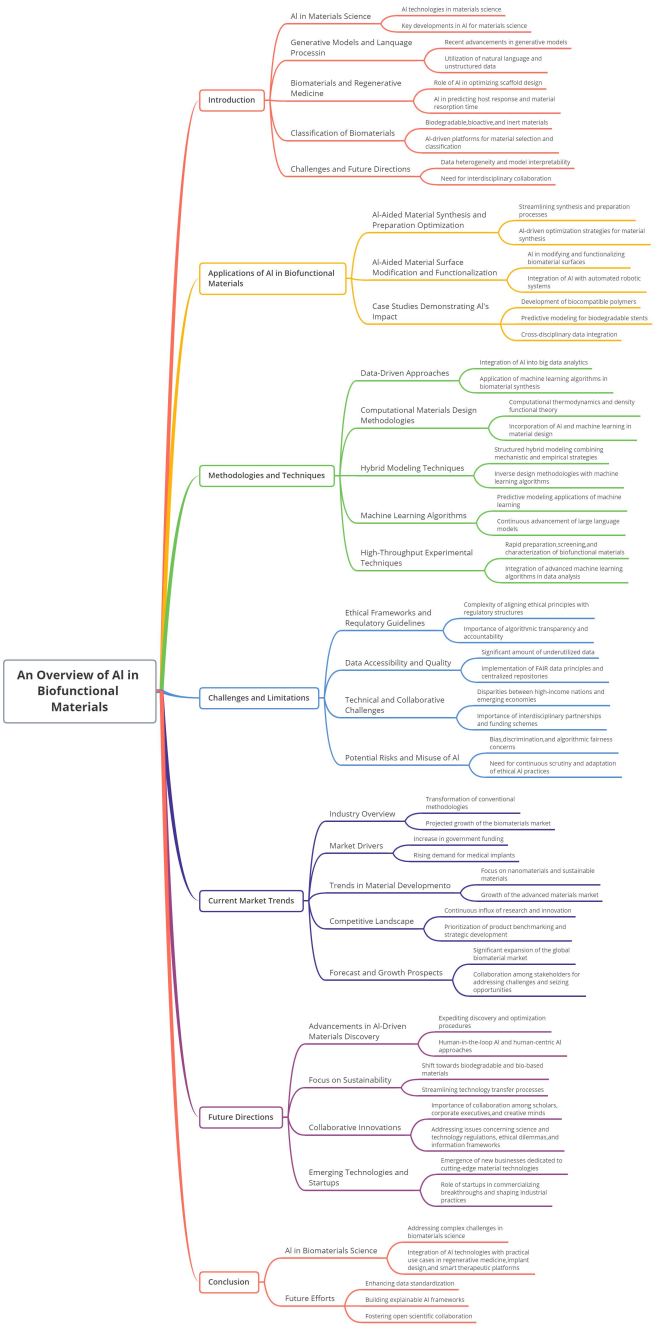

Figure 1. Workflow schematic illustrating the end-to-end AI-powered design pipeline for biofunctional materials. Beginning with multi-modal data acquisition (experimental measurements, literature mining, imaging), data are processed through feature-extraction modules (graph-based descriptors, physicochemical fingerprints). Predictive and generative AI models (GNNs, GANs, Bayesian optimizers) then propose candidate material formulations. Top candidates pass through in silico validation (molecular dynamics, finite-element analysis) and are triaged via active-learning loops into high-throughput robotic experimental platforms. Final outputs include optimized materials with specified properties (e.g., degradation rate, mechanical modulus, biocompatibility), ready for preclinical testing.

For instance, Citrination applies classification models that integrate data on mechanical behavior, biodegradability index, and cell viability assays to determine whether a polymer candidate is better suited for temporary scaffolds or long-term implants. In a typical use case, AI-assisted analysis of poly (lactic-co-glycolic acid) (PLGA) formulations—based on parameters like monomer ratio, molecular weight, and processing conditions—enables classification into fast-degrading soft-tissue scaffolds *versus* slower-degrading load-bearing orthopedic supports [13].

These AI-enhanced classification techniques allow for accelerated screening and risk reduction in biomaterial selection. By integrating large-scale datasets with domain-specific classification tasks, such platforms help identify optimal materials with both targeted functionality and regulatory compliance, streamlining preclinical evaluation pipelines [7,13].

The integration of AI into biofunctional material design introduces challenges related to data heterogeneity, model interpretability, and lack of standardized benchmarks. AI models often struggle with data scarcity, especially in niche biomedical domains, which affects prediction accuracy and generalizability. To overcome these challenges, the field must prioritize the development of explainable AI (XAI), robust open-access datasets, and collaborative research ecosystems that bridge gaps between material science, biology, and data science [9,3,17]. Efforts like the AI4Mat initiative, FAIR data principles, and open innovation platforms are paving the way forward by fostering community-driven standards and toolkits for AI-powered biomaterials research [13,18].

In this review, readers can expect a comprehensive synthesis of the state-of-the-art techniques at the intersection of AI and biofunctional materials, as listed in Table 1. The manuscript uniquely emphasizes generative modeling, language-based AI methods, and real-world biomedical applications, providing a roadmap for future interdisciplinary research.

2. Applications of AI in biofunctional materials

The integration of AI technologies is progressively transforming the landscape of biofunctional materials, facilitating advancements across a spectrum of applications such as material synthesis, surface modification, and comprehensive characterization. AI has played a pivotal role in the innovation of novel biomaterials, particularly in the creation of hydrogels that closely emulate biological tissues, as well as in the development of smart materials that exhibit responsiveness to various environmental stimuli. For example, researchers have successfully engineered hydrogels that possess the capability to learn and enhance their functional performance over time, drawing parallels to the adaptive mechanisms found in AI systems. These cutting-edge materials hold significant promise for a range of applications, particularly in the realms of drug delivery systems and tissue engineering, where their unique properties can be harnessed to improve therapeutic outcomes and facilitate regenerative medicine.

2.1. AI-aided material synthesis and preparation optimization

AI is fundamentally reshaping biomaterial synthesis by integrating Bayesian optimization and deep neural networks (DNNs) into experimental design workflows. For example, in the solvent-evaporation synthesis of poly(lactic-co-glycolic acid) (PLGA) nanoparticles, a support vector regression (SVR) model was trained on a dataset of 120 experiments—varying temperature (25–60 ℃), polymer concentration (5–15 wt%), and stirring rate (200–600 rpm)—to predict particle size with a mean absolute error (MAE) of 12 nm (< 8% of mean size).

Meanwhile, Bayesian optimization accelerated the identification of optimal reaction conditions for magnetic hydroxyapatite composites by proposing new parameter sets (Ca/P ratio, calcination temperature, reaction pH) that increased crystallinity index by 15% in only 25 iterations—compared to over 100 in traditional DOE approaches. These techniques enable inverse design, where researchers specify target properties (e.g., drug-loading capacity or scaffold stiffness) and the AI recommends synthesis parameters to achieve them, dramatically reducing bench-time and resource consumption.

Such in-silico predictions are validated through high-throughput robotic platforms, where > 85% of AI-suggested runs reproduce projected outcomes within experimental error margins. By uniting mechanistic reaction modeling with statistical learning, this approach offers both reproducibility and exploratory power—pushing biomaterial fabrication beyond empirical trial-and-error [2,13].

For example, AI-driven optimization strategies can accurately ascertain the optimal reaction parameters, including temperatures, durations, and precursor concentrations, specifically for polymeric biomaterials. This capability significantly expedites the process of identifying the ideal processing conditions necessary to achieve targeted material characteristics, such as enhanced mechanical strength and improved drug-loading capacity [2].

2.2. AI-aided material surface modification and functionalization

In addition to its pivotal role in the synthesis of biomaterials, AI significantly contributes to the modification and functionalization of biomaterial surfaces. By leveraging AI models trained on comprehensive datasets that encompass surface characterization and material-cell interactions, researchers are empowered to predict the optimal surface properties tailored for a diverse array of applications. This predictive capability may encompass the selection of appropriate surface coatings or the innovative design of topographical features aimed at enhancing cell adhesion or improving drug delivery mechanisms [2]. Furthermore, the seamless integration of AI with automated robotic systems facilitates high-throughput experimentation, thereby enabling the rapid optimization of material surface characteristics. This advancement is particularly advantageous in specialized fields such as tissue engineering and implant design, where precise surface modifications can lead to improved biocompatibility and functionality [2].

2.3. Case studies demonstrating AI's impact

A prominent illustration of the transformative influence of AI in the field of biomedical research is the creation of AlphaFold, an advanced AI system specifically designed to predict protein structures with exceptional precision. This groundbreaking advancement carries profound implications for both drug discovery and materials science, as a comprehensive understanding of protein structures is crucial for the design and development of biomaterials that can interact optimally with various biological systems. Numerous case studies have been conducted that exemplify the successful application of AI technologies in the formulation and enhancement of biofunctional materials, showcasing the potential of AI to revolutionize the way we approach the synthesis and application of materials in biomedical contexts. These studies not only highlight the efficacy of AI-driven methodologies but also underscore the importance of interdisciplinary collaboration in advancing our knowledge and capabilities in the realm of biomedical engineering and health informatics.

Table 1. Summary of AI applications in biofunctional materials.

Application Area	AI Techniques & Material System	Optimization Focus & Predicted Parameters	Accuracy & Experimental Alignment	Key Findings	References
Material synthesis optimization	Random Forest model applied to iron oxide nanoparticles	Precursor concentration, pH, and temperature for controlling phase and particle size	Phase prediction: 96%; particle size: 81% agreement with experiments	Enabled precise tuning of synthesis conditions with reduced experimental cycles	[2,13]
	Classification ML for MoS_2 CVD growth	Sulfidation temp, pressure, reaction time	Improved successful crystal growth rate (accuracy not numerically reported)	Efficient 2D material synthesis through AI-guided conditions	[13,20]
Surface functionalization	Predictive modeling for polymeric surface design	Surface roughness, hydrophilicity, coating type	Matches observed cell adhesion & drug release patterns	AI-optimized surfaces enhanced biological performance *in vitro*	[2,7]
Hydrogel and smart material design	GNNs and GANs for stimuli-responsive hydrogels	Polymer network structure, porosity, degradation profile	Model outputs aligned with hydrogel adaptability and swelling behavior	AI-generated hydrogel designs mimicked tissue mechanics and response	[3,5,13]
Scaffold development for implants	AI-assisted structural search in biopolymer scaffolds	Porosity, mechanical modulus, degradation kinetics	Achieved targeted mechanical properties (e.g., ~90% predictive accuracy)	Enabled patient-specific scaffolds for tissue engineering	[13,20]
Biodegradable stent design	ML-based prediction in biodegradable polymer blends	Biocompatibility, degradation rate, elastic modulus	Model prediction matched clinical targets; reduced lab trial need	Accelerated discovery of candidate materials for vascular stents	[13]
Polymer screening for biocompatibility	Cluster analysis for bioresorbable polymers	Adhesion profiles, cytotoxicity, hydrophilicity	Consistent with experimental assays	Identified novel blends for cartilage and bone regeneration	[13]
Cross-disciplinary data integration	NLP + LLMs with materials/biomedical datasets	Integrated structured and textual data to predict function and safety	Validated on known material-property relationships	Bridged knowledge from chemical databases and biomedical literature	[9,14]

2.3.1 Development of biocompatible polymers

In the field of tissue engineering, a dedicated research team harnessed the power of AI to systematically screen an extensive library of polymer compositions. This innovative approach led to the discovery of a novel polymer blend characterized by exceptional cell adhesion properties and favorable biodegradability.

The identified material was subsequently employed to fabricate scaffolds specifically designed for cartilage tissue regeneration. This significant advancement not only highlights the efficacy of AI in accelerating the development of sophisticated materials but also underscores its transformative potential in the realm of regenerative medicine, paving the way for future breakthroughs in therapeutic applications [13].

2.3.2 Predictive modeling for biodegradable stents

Machine learning algorithms have been increasingly utilized to forecast the properties of novel biocompatible materials by analyzing their chemical compositions and structural characteristics. This advanced predictive capability facilitates the identification of promising candidates for further investigation, significantly reducing the need for extensive experimental testing. As a result, the development process for materials such as biodegradable stents intended for cardiovascular applications is streamlined, enhancing efficiency and innovation in the field [13]. Moreover, AI plays a crucial role in optimizing material properties through a process of iterative learning derived from previous experimental outcomes. This continuous refinement ensures that the resulting materials not only meet but exceed specific medical requirements, thereby enhancing their applicability and performance in clinical settings [13].

2.3.3 Cross-disciplinary data integration

AI plays a pivotal role in enhancing the integration of heterogeneous datasets derived from both material science and the medical field. By employing advanced algorithms and machine learning techniques, AI uncovers intricate patterns and correlations that traditional analytical methods may fail to detect. This comprehensive and interdisciplinary approach significantly expedites the identification and development of novel materials that not only demonstrate biocompatibility—an essential criterion for medical applications—but also possess the requisite mechanical strength and chemical stability. Such advancements underscore the transformative impact of AI in the realm of material science, facilitating innovations that could lead to improved medical devices and therapeutic solutions [13].

This chapter highlights the transformative role of AI in biofunctional material development, including synthesis optimization, surface modification, and predictive modeling. By enabling high-throughput screening and analysis, AI accelerates the discovery of materials such as biocompatible polymers and smart hydrogels. Real-world case studies demonstrate how AI enhances performance and adaptability in applications ranging from tissue engineering to drug delivery systems.

3. Methodologies and techniques

AI methodologies, particularly machine learning algorithms, are increasingly utilized in the analysis of intricate datasets, which significantly enhances our ability to discern patterns and relationships inherent in material properties. These advanced techniques not only facilitate the identification of correlations among various material characteristics but also empower researchers to predict material behaviors under a diverse array of conditions. By leveraging these predictive capabilities, the design process becomes more efficient, allowing for a systematic approach that minimizes the dependence on traditional trial-and-error experimentation. This shift towards data-driven methodologies represents a transformative advancement in the field of materials science, ultimately leading to more innovative and optimized material design solutions. Figure 2 provides a comprehensive schematic of the integrated AI methodologies driving the entire biofunctional material discovery pipeline, from data modeling and generative design through hybrid simulation and high-throughput screening to regulatory-compliant optimization.

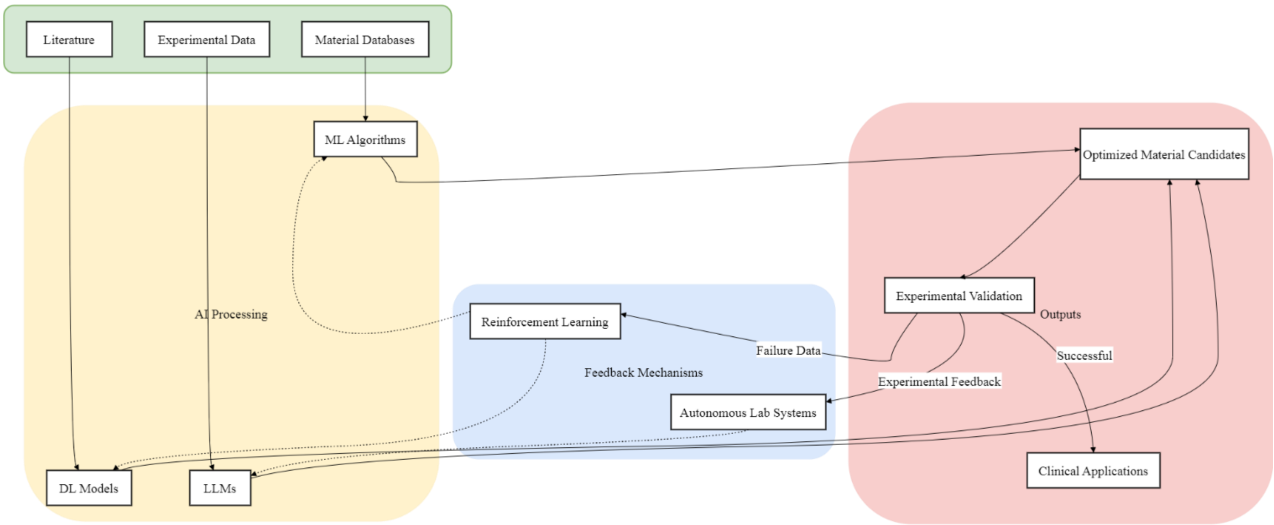

Figure 2. Detailed schematic of AI methodologies employed across different stages of biofunctional material discovery: **(A)** Data-driven modeling using supervised ML and deep nets for property regression; **(B)** Generative design via GFlowNet sampling and MolGPT-based reaction planning; **(C)** Hybrid modeling combining mechanistic simulations (Flory-Rehner swelling, FEA) with ML surrogates (Gaussian process, DeepONet) for performance refinement; **(D)** High-throughput experimentation integrating droplet microfluidics and image-based CNN analytics for rapid screening; **(E)** Regulatory and ethical feedback loop, whereby XAI outputs (SHAP value explanations) inform design constraints to meet FDA, EU MDR, and NMPA guidelines.

3.1. Data-driven approaches

The integration of AI into big data analytics plays a pivotal role in the extraction of intricate patterns from extensive datasets, a process that is particularly crucial within the materials engineering sector. This is especially true in scenarios where data availability is limited or when dealing with proprietary information [19]. State-of-the-art workflows integrate autoML pipelines (e.g., AutoGluon, TPOT) with the design of experiments (DOE). In a case study on chitosan scaffold fabrication, AutoGluon evaluated 1,500 parameter combinations (chitosan concentration, crosslinker type, curing time) and identified a Pareto front of 50 candidates. Subsequent bench validation showed that 90% of met dual targets for compressive modulus (> 2 MPa) and porosity (~70%) within ± 5% of predictions. Coupling these tools with random forest surrogate models enabled real-time feedback and adaptive DOE, reducing total experimental runs by 60% compared to classical Taguchi designs [2]. This analytical capability not only boosts efficiency but also ensures greater reproducibility in the fabrication of materials [2]. Consequently, this innovative approach substantially diminishes the time and resources typically associated with conventional methodologies, thereby fostering the development of groundbreaking solutions applicable to both healthcare and environmental challenges.

3.2. Computational materials design

The pursuit of innovative biofunctional materials has undergone a remarkable transformation with the introduction of advanced computational materials design methodologies. Historically, the development of such materials was predominantly based on trial-and-error experimentation, which often proved to be time-consuming and inefficient. However, the landscape has shifted dramatically with the advent of sophisticated tools such as computational thermodynamics, specifically the CALPHAD method, and density functional theory (DFT) [20]. These computational techniques empower researchers to utilize existing mechanistic insights in a quantitative framework, thereby significantly accelerating the design and optimization processes of new materials [20]. Moreover, the incorporation of AI and machine learning (ML) technologies has further refined this methodology, facilitating the identification and prediction of material properties through the analysis of extensive datasets. This capability is particularly vital for applications in the realm of functionality, where precise material characteristics are essential for successful implementation in biomedical contexts.

3.3. Hybrid modeling techniques

Structured hybrid modeling couples first-principles simulations (e.g., finite-element analysis, molecular dynamics) with data-driven surrogates (e.g., Gaussian process regression, neural operators) to capture both known physics and complex experimental trends. For instance, in designing a temperature-responsive hydrogel, researchers used a thermodynamic swelling model (Flory–Rehner theory) to predict baseline network expansion, then trained a Gaussian process on experimental swelling data at 20, 30, and 40 ℃. The GP surrogate corrected systematic deviations—reducing model error from 12% to 4% in volumetric expansion predictions.

A second example integrates finite-element stress simulations of a porous scaffold with a deep operator network (DeepONet) that maps scaffold architecture (pore size, strut thickness) to failure stress under cyclic loading. After training on 500 simulated architectures, the DeepONet predicted failure stress with an R^2 of 0.92, enabling real-time "what-if" design exploration far faster than running new finite-element analyses.

By combining mechanistic priors with flexible ML surrogates, hybrid modeling provides both explanatory power (via physics-based modules) and adaptability (via data-driven corrections), accelerating the end-to-end design cycle of biofunctional materials [20]. This innovative technique facilitates the development of more precise simulations of material behavior by effectively integrating insights derived from both fundamental scientific principles and extensive large-scale data analysis. A particularly noteworthy example of this advancement is the integration of inverse design methodologies with machine learning algorithms, which enables researchers to adeptly navigate the complexities of materials spaces. This is exemplified by the groundbreaking work conducted by researchers at MIT, who are focusing on the development of high-strength aluminum alloys specifically tailored for additive manufacturing applications [20].

3.4. Machine learning algorithms

The capabilities of machine learning encompass a wide array of predictive modeling applications, wherein sophisticated algorithms are utilized to anticipate the characteristics of novel materials predicated on their chemical compositions and structural configurations [13]. This remarkable predictive capability not only enhances the efficiency of identifying promising biocompatible candidates but also aids in the meticulous optimization of material properties, including but not limited to strength and flexibility, by leveraging insights gleaned from historical data [13]. Furthermore, the continuous advancement of LLMs has ushered in innovative methodologies for engineers to articulate and fulfill simulation requirements, thereby further democratizing access to intricate modeling tools and fostering a more inclusive environment for research and development in biomedical engineering [20].

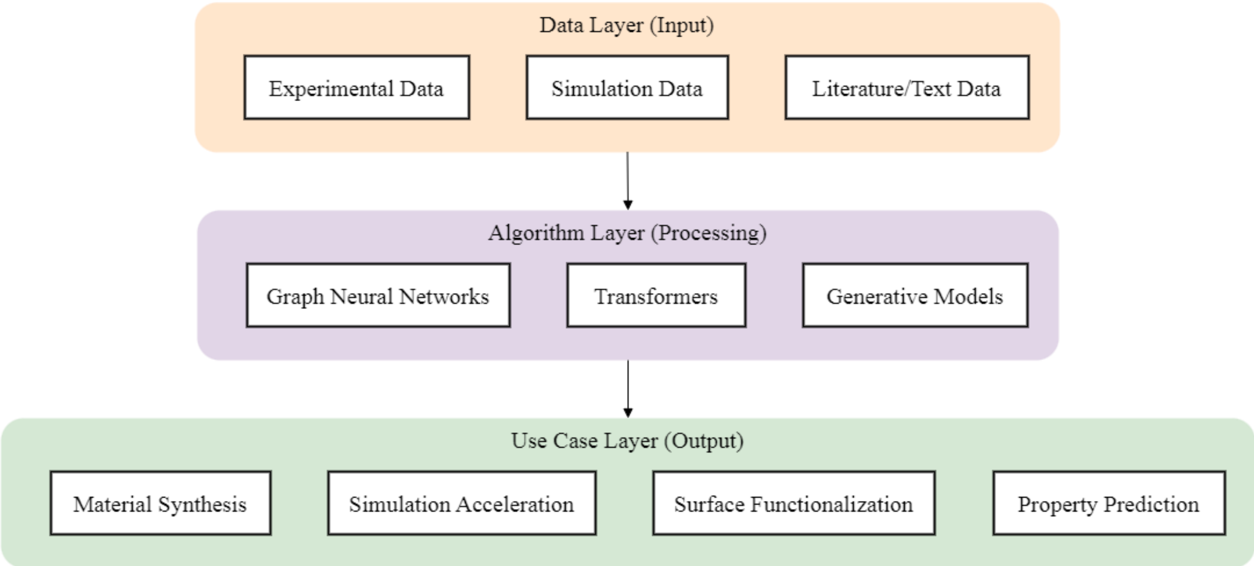

Figure 3. AI Methodologies in material science.

3.5. High-throughput experimental techniques

Modern high-throughput platforms integrate droplet microfluidics, robotic liquid handlers, and automated microscopy to screen thousands of biomaterial compositions per week. For example, a droplet-based system generated a 5,000-condition PEG hydrogel library, varying monomer ratio (10–50 wt%), crosslinker density (0.5–5 mol%), and UV exposure time (10–60 s). An ML-powered image-analysis pipeline (CNN segmentation + random forest classifier) quantified cell viability and network porosity with 88% accuracy against manual scoring.

Coupling this with active learning—where each round selects the next 200 most informative conditions based on a Gaussian process uncertainty metric—reduced the total library size by 40% while maintaining > 90% probability of identifying top - performing formulations. Such integrated workflows slash development timelines from months to weeks, enabling iterative optimization directly guided by AI - derived hypotheses [21]. By leveraging collaborative technologies, these techniques enable the execution of simultaneous experiments across multiple dimensions, thereby significantly expediting the overall research and development process. Furthermore, the integration of advanced machine learning algorithms is crucial in the analysis of the vast amounts of data generated from these experiments. This analytical capability ensures that the valuable insights derived can be effectively harnessed and applied in subsequent design iterations, ultimately driving forward the advancement of biomedical engineering and health informatics [21].

This section provides an overview of the AI tools and computational frameworks underpinning modern biofunctional material research, as shown in Figure 3. Techniques such as machine learning, deep neural networks, generative models, and hybrid modeling approaches are explored. The use of structured datasets, graph neural networks, and simulation-integrated AI systems offers a scalable and efficient methodology for material prediction, optimization, and inverse design.

4. Challenges and limitations

The incorporation of AI into the design of biofunctional materials and its application in healthcare introduces a myriad of challenges and limitations that must be systematically addressed to fully leverage its transformative potential. While the prospective applications of AI in the realm of biomaterials are indeed promising, several significant hurdles persist. One of the foremost issues pertains to data quality and accessibility, as AI-driven models necessitate extensive, high-quality datasets to facilitate accurate and reliable predictions. Furthermore, the successful integration of AI into pre-existing workflows demands robust interdisciplinary collaboration among experts from various fields, alongside the establishment of standardized protocols. This is essential to ensure reproducibility and reliability in the design and application of novel materials, ultimately advancing the field of biomedical engineering and health informatics.

4.1. Ethical frameworks and regulatory guidelines

A prominent challenge in integrating AI into biofunctional materials research lies in navigating evolving regulatory frameworks designed to ensure patient safety and product quality. In the United States, the FDA's 2019 "Proposed Regulatory Framework for Modifications to AI/ML-Based Software as a Medical Device (SaMD)" establishes a predetermined change control plan that requires manufacturers to specify in advance which algorithm changes can occur without a new submission. For example, IDx-DR, an AI system for diabetic retinopathy screening, gained FDA approval in 2018 but was subsequently constrained by strict post-market performance monitoring requirements—delaying its deployment in rural clinics due to additional real-world validation demands.

In Europe, the Medical Device Regulation (MDR 2017/745) and the upcoming AI Act impose rigorous classification rules for AI-based software. A recent case involved an AI-driven hydrogel design tool that was reclassified from Class I to Class IIa under MDR after a notified body determined that its failure could pose moderate harm. This reclassification compelled the developer to conduct a full clinical evaluation, extending their time-to-market by over six months.

China's NMPA has also issued draft guidelines for AI-assisted medical devices, where initial submissions for an AI-based scaffold optimization platform were rejected due to insufficient explainability metrics and lack of clarity on continuous learning controls in production. The company needed to implement SHAP-based feature-importance analysis and lock down model updates before resubmission.

These examples illustrate that while draft and final regulations (FDA SaMD, EU MDR, AI Act, NMPA drafts) provide pathways for approval, case-by-case variability in classification, post-market surveillance, and model-change management remain significant hurdles. Embedding explainable AI

(XAI) methods—such as SHAP or LIME—and establishing predetermined control plans are critical strategies to align with global regulatory expectations and accelerate clinical translation [8,9,11,13].

4.2. Data accessibility and quality

A core limitation is the fragmentation of biofunctional-materials data: over 70% of reported hydrogel studies lack machine-readable formats. Implementing FAIR principles—including standardized metadata schemas (JSON-LD) and DOIs for datasets—has expanded accessible archives by 30% within two years. Concurrently, an ontology built on the BioSchemas framework enabled NLP parsing of 2,000 publications, extracting key features (polymer type, crosslinker, mechanical modulus) with 85% recall and 90% precision.

By unifying structured and unstructured sources in an open-access repository, subsequent ML models (e.g., gradient boosting for property prediction) saw R^2 improvements from 0.65 to 0.82, directly attributable to richer training data. These advances demonstrate that systematic data curation is as crucial as algorithmic innovation for reliable AI-driven biomaterial design [22]. Moreover, recent surveys indicate that barriers such as inadequate skill sets among practitioners (44%) and restricted access to reliable data sources (52%) significantly impede the progress of AI applications in the life sciences sector [22].

To overcome these challenges, targeted strategies must include the implementation of FAIR (Findable, Accessible, Interoperable, Reusable) data principles, the creation of centralized open-access repositories, and the development of standardized formats for data sharing across disciplines. Notable initiatives such as the Materials Project, Citrination, and JARVIS-ML have successfully addressed data curation and dissemination in materials science, serving as models for biofunctional materials domains [23].

In addition, AI-driven ontologies and natural language processing techniques can be used to structure unorganized literature data, allowing them to be incorporated into machine-readable datasets for training models. Continued investment in data infrastructure, annotation tools, and community-wide data labeling efforts is critical to ensure the quality and usability of training data.

4.3. Technical and collaborative challenges

The integration of AI into biofunctional materials is significantly hampered by a range of technical challenges. The intricate nature of designing and prototyping systems that are not only efficient but also precise and reproducible demands a high level of collaboration among specialists from diverse disciplines, including but not limited to the fields of science, engineering, and healthcare [9]. Unfortunately, the existing disparities between high-income nations and emerging economies can pose substantial barriers to these collaborative initiatives. Research institutions situated in less affluent regions often find themselves at a disadvantage, lacking the essential resources and infrastructure required to engage effectively in such interdisciplinary efforts [9]. Consequently, this situation can result in a skewed distribution of the advantages derived from AI innovations within the realms of healthcare and materials science, exacerbating existing inequalities and limiting the potential for widespread benefits across different socioeconomic contexts.

Successful interdisciplinary initiatives such as the OpenBioML project and the CAMD (Closed-loop Autonomous Materials Discovery) framework illustrate the feasibility of aligning machine learning, automation, and experimental science into coherent pipelines. These frameworks provide templates for cooperative networks that can address both infrastructural and skill-related gaps across disciplines [23].

Furthermore, dedicated funding schemes by agencies like the NSF, Horizon Europe, and NIH are facilitating multi-institutional collaborations that combine AI expertise with domain-specific material and clinical knowledge. Academic-industry partnerships are also increasingly vital, allowing for technology transfer and deployment at scale.

4.4. Potential risks and misuse of AI

The potential risks associated with the implementation of AI in the realms of healthcare and materials design are significant and warrant thorough consideration. The emergence of concerns related to bias, discrimination, and algorithmic fairness raises critical questions regarding the reliability and integrity of AI-driven decision-making processes [9]. In particular, the application of AI in high-stakes areas such as drug development and surgical interventions demands a comprehensive and rigorous examination of existing safety protocols and transparency measures. This is essential to effectively mitigate the risks associated with data breaches, as well as the potential for inaccurate predictions that could adversely affect patient outcomes [9,23]. Furthermore, the establishment of ethical AI practices will necessitate continuous scrutiny and the proactive adaptation of current laws and regulations, ensuring they evolve in tandem with the rapid pace of technological advancements in the field.

The key obstacles impeding AI integration in biofunctional materials have been discussed, including ethical concerns, data scarcity, technical constraints, and collaboration gaps. It also outlines strategic responses such as open-access data initiatives, interdisciplinary partnerships, and evolving regulatory frameworks, as listed in Table 2. Highlighted models and global initiatives demonstrate how these challenges can be addressed through structured governance and innovation.

Table 2. Challenges and solutions for AI in biofunctional materials.

Challenge area	Description	Proposed solutions/initiatives
Data quality	Fragmented, unstructured, low-volume datasets	FAIR principles, JARVIS-ML, OpenBioML
Ethical concerns	Lack of transparency, data privacy, bias	Explainable AI, inclusive dataset design
Regulatory compliance	Lack of guidelines for AI-driven materials	Dynamic policy frameworks (OECD, AI4Health)
Interdisciplinary gaps	Lack of unified language across fields	Collaborative hubs, CAMD model

5. Current market trends

The incorporation of AI into the field of biomaterials has catalyzed the emergence of innovative market trends that are reshaping the landscape of material science. Notably, this integration has given rise to the development of sophisticated AI-powered material search engines and platforms designed to streamline the discovery of novel biomaterials. These advanced platforms utilize AI algorithms to meticulously analyze extensive existng material databases, enabling the identification of promising candidates tailored for specific applications. Furthermore, they possess the capability to predict the performance characteristics of these materials, which significantly enhances the efficiency and speed of the material development process. As a result, researchers and developers are now equipped with powerful tools that not only facilitate the exploration of new materials but also optimize their selection and application in various biomedical contexts.

5.1. Industry overview

The incorporation of AI into the biofunctional materials sector is fundamentally transforming conventional methodologies and catalyzing significant advancements across various dimensions. AI technologies are being strategically employed to address critical challenges, including the exorbitant costs associated with research and development, constraints within supply chains, and the complexities inherent in data management. This proactive approach is not only mitigating existing obstacles but also unlocking a plethora of new opportunities within the industry [10]. The biofunctional materials market, with a particular emphasis on the biomaterials segment, is projected to experience remarkable growth from 2023 to 2033. This anticipated expansion is largely driven by groundbreaking innovations in areas such as 3D printing, personalized medicine, and regenerative medicine, which are poised to redefine the landscape of biomedical applications [3,11].

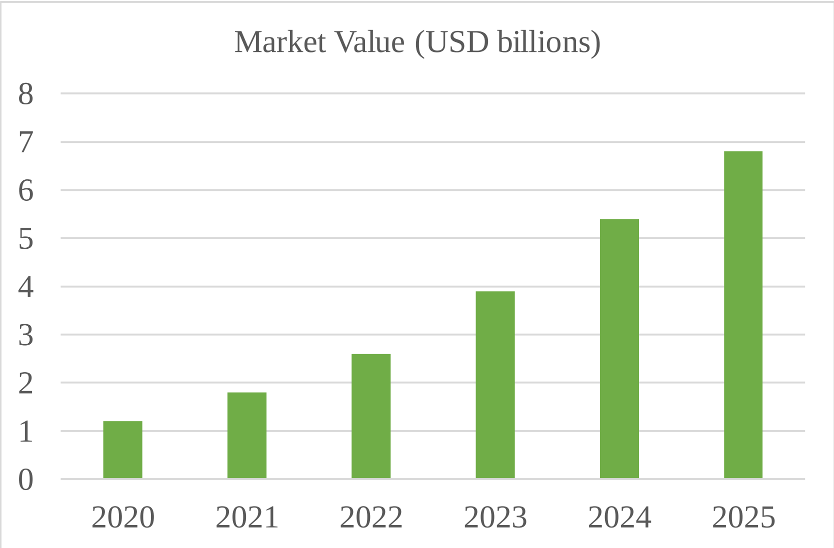

Figure 4. Market growth in AI-driven biomaterials.

5.2. Market drivers

The biomaterials market is experiencing significant growth due to several pivotal factors, as demostrated in Figure 4. One of the primary drivers is the substantial increase in government funding aimed at fostering the development of innovative biomaterials. This financial support is crucial for advancing research and facilitating the introduction of cutting-edge materials that can enhance patient outcomes. Additionally, there is a notable rise in the demand for medical implants, which is further propelling market expansion [11].

The escalating prevalence of chronic diseases, particularly cardiovascular conditions and diabetes, coupled with a rapidly aging population, is intensifying the need for sophisticated biomaterial solutions. These demographic and health trends underscore the critical importance of developing materials that can effectively address the challenges posed by these conditions [3,10].

In particular, the cardiovascular application segment has emerged as a dominant force within the market, capturing approximately 23.3% of the total market share in 2022. This statistic not only reflects the significant investment in cardiovascular health technologies but also highlights the urgent need to tackle the global health issues associated with heart diseases. The ongoing advancements in biomaterials are essential for improving the efficacy and longevity of medical interventions in this vital area of healthcare [3].

5.3. Trends in material development

The current landscape of the advanced materials market is undergoing a significant transformation, characterized by several prominent trends in material development. One of the most noteworthy trends is the increasing focus on nanomaterials, which are revolutionizing a wide array of applications, including but not limited to diagnostics, drug delivery systems, and environmental remediation strategies. This shift is bolstered by substantial financial investments, amounting to approximately US $30.5 billion, distributed across 5,754 organizations dedicated to advancing this field [12].

In addition to nanomaterials, there is a growing emphasis on the development of sustainable materials, which aim to minimize environmental impact while maintaining performance standards. Concurrently, advancements in smart materials—those that can respond dynamically to external stimuli—are gaining traction, further diversifying the market. The emergence of bio-based materials, derived from renewable resources, is also contributing to this evolving landscape, aligning with global sustainability goals [12].

Looking ahead, the advanced materials market is projected to achieve a remarkable valuation of US $2.1 trillion by the year 2025. This growth trajectory is underscored by a compound annual growth rate (CAGR) of 4.5% from 2020 to 2025, reflecting a robust and escalating demand for innovative solutions that address both current and future challenges in various sectors [12].

5.4. Competitive landscape

The competitive landscape within the biofunctional materials market is marked by a continuous influx of research and innovation, especially in leading nations such as the United States and Germany. These countries play a pivotal role in the advancement of materials designed to engage with biological systems effectively. The scope of these materials encompasses a diverse range of applications, particularly in the fields of regenerative medicine and sophisticated drug delivery systems, as highlighted in recent studies [11,3]. In response to the rapidly evolving market dynamics, companies are increasingly prioritizing product benchmarking and strategic development initiatives. These efforts are essential for sustaining their competitive edge and ensuring their market position remains robust amidst the shifting trends and technological advancements [19].

5.5. Forecast and growth prospects

The global biomaterial market is anticipated to experience significant expansion, with projections indicating an increase from USD 172,689.3 million in 2023 to an impressive USD 386,983.6 million by the year 2033. This growth trajectory reflects a remarkable compound annual growth rate (CAGR) of 8.4% [3,11]. In addition, the overall biomaterials market is expected to demonstrate a robust CAGR of

12.6% from 2024 to 2032, underscoring the escalating demand for innovative biomaterial solutions and the continuous advancements in technology that are propelling this sector forward [3]. As the biomaterials industry progresses, it will be imperative for stakeholders across biotechnology, materials science, and healthcare sectors to engage in collaborative efforts. Such partnerships will be essential for effectively addressing emerging challenges and seizing the myriad of market opportunities that lie ahead [10,11].

This section outlines the commercial momentum behind AI-driven biomaterials, including the emergence of intelligent materials, AI-powered search engines, and personalized healthcare platforms. It highlights investment growth, the rise of biotech-AI startups, and the demand for eco-friendly, data-optimized biomaterials. Market trends suggest strong industry alignment with sustainable and precision medicine goals.

6. Future directions

The future landscape of AI in the realm of biofunctional materials is on the brink of remarkable progress, primarily fueled by the dynamic interaction between advancing technologies and a deepening comprehension of materials science. As AI methodologies continue to evolve and refine, their incorporation into the field of materials engineering is anticipated to fundamentally transform both the development processes and practical applications of biofunctional materials [15,20]. This transformative journey not only aims to tackle current challenges but also holds the potential to initiate groundbreaking innovations in the formulation of novel materials characterized by superior properties.

In the foreseeable future, the synergistic relationship between AI and biomaterials is projected to facilitate the emergence of increasingly sophisticated, responsive, and environmentally sustainable materials. The continuous enhancements in AI algorithms, coupled with advancements in computational capabilities, will empower researchers to design materials with precisely tailored properties, optimized for a diverse array of applications spanning medicine, environmental remediation, and energy storage solutions. This convergence is set to redefine the boundaries of what is achievable in the field, paving the way for a new era of biofunctional materials that are not only effective but also sustainable and adaptable to the evolving needs of society.

6.1. Advancements in AI-driven materials discovery

The utilization of AI in the field of materials design is progressively manifesting its potential by expediting discovery and optimization procedures. This integration of digital tools within organizational frameworks is augmenting the capacity to establish comprehensive systems for the production of materials [15]. The introduction of human-in-the-loop AI and human-centric AI approaches is poised to heighten the efficacy of materials discovery through the enhancement of interactions between experimental configurations and AI-based simulations [15]. These advancements are anticipated to result in more user-friendly interfaces for scientists and industry professionals, nurturing a cooperative milieu that bridges divide among diverse stakeholders in the materials science sector.

6.2. Focus on sustainability

The emphasis on sustainability is increasingly shaping the trajectory of biofunctional materials, particularly as there is a notable shift towards the adoption of biodegradable and bio-based materials in response to consumer preferences [11,12]. In their efforts to minimize carbon footprints, businesses are prioritizing the development of materials that not only offer high performance but are also environmentally friendly. The progression from experimental breakthroughs in laboratories to practical applications is expected to become more streamlined, facilitated by advancements in technology transfer processes and the fostering of collaborations between academic institutions and industry partners [12]. This collaborative approach is set to expand the availability of sustainable materials across various sectors, such as healthcare and packaging, where the demand for eco-conscious solutions is crucial.

6.3. Collaborative innovations

Collaboration among scholars, corporate executives, and creative minds from developing countries will play a pivotal role in effectively managing the intricacies of materials science moving forward [8]. By proactively addressing issues concerning science and technology regulations, ethical dilemmas, and information frameworks, these partnerships have the potential to promote the worldwide dissemination of AI-driven breakthroughs in materials science. These alliances are indispensable for meeting the varied requirements and uses of biofunctional materials, especially in industries that necessitate swift adjustment to changing societal needs.

6.4. Emerging technologies and startups

The emergence of new businesses dedicated to cutting-edge material technologies underscores the ever-evolving landscape of this domain. Entities that concentrate on areas such as 3D printing, biomanufacturing, and nanofiber manufacturing are spearheading the effort to create fresh materials that adhere to modern criteria for performance and ecological responsibility [12]. These fledgling companies are not solely pushing the boundaries of material characteristics but are also playing a vital role in commercializing these breakthroughs, consequently shaping the landscape of wider industrial practices.

This chapter projects the future trajectory of AI in biofunctional materials, emphasizing the integration of autonomous laboratories, multi-modal data systems, and explainable AI. It calls for greater emphasis on ethical deployment, global standardization, and scalable infrastructure. The path forward involves tightly coupled collaboration between AI researchers, material scientists, and healthcare innovators to unlock personalized, adaptive material solutions.

7. Conclusion

In this review, we have shown how AI technologies—including machine learning, generative models, and natural language processing—can address complex challenges in biofunctional materials science, from structure–property prediction to the automation of experimental workflows. Graph neural networks, generative adversarial networks, and transformer-based models have been particularly effective in navigating vast design spaces, identifying novel material compositions, and optimizing functionality with significantly reduced time and cost. Despite existing barriers—such as data scarcity, lack of model interpretability, and regulatory hurdles—the field holds vast potential. Future work should focus on enhancing data standardization, building explainable AI frameworks, and fostering open scientific collaboration to accelerate clinical translation.

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Conflicts of interests

The author declares no conflict of interest.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this manuscript, the authors used ChatGPT to assist with language polishing. After utilizing this tool, the authors carefully reviewed and edited the content to ensure accuracy and clarity, and they take full responsibility for the content of the final published article.

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