

## PERSPECTIVE ARTICLE

# Stimuli-responsive biomaterials for 3D bioprinting: Bioprinting biomaterials classification (BBC)

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## Abstract

Stimuli-responsive biomaterials have progressively developed over the last decade in three-dimensional (3D) bioprinting, enabling dynamic regulation of bioink rheological and processing properties, printing fidelity, and the functional maturation of printed constructs. However, the rapid expansion of responsive materials and bioprinting technologies has led to fragmented and non-standardized definitions of biomaterials and bioinks, resulting in inconsistent classification approaches and complicating the analysis, comparison, and design of emerging systems. This highlights the lack of a unified framework for biomaterial selection for bioprinting. This perspective introduces the bioprinting biomaterials classification (BBC) as a conceptual framework that provides a structured and design-oriented basis for biomaterial selection for bioprinting by linking stimuli-responsive behavior with stage-specific functional requirements across the bioprinting process. The BBC framework classifies biomaterials according to two complementary dimensions: stimulus category (physical, chemical, and biological stimuli) and functional roles across the bioprinting lifecycle (bioink preparation, printing process, post-printing maturation, and in vivo function). This two-level biofunctional classification connects material responsiveness with biofabrication processes and enables a systematic approach to selecting and applying responsive biomaterials based on their stage-specific functional roles. It provides a systematic framework for positioning responsive biomaterials within the biofabrication context and supports a more structured and application-driven approach to biomaterial selection and design in bioprinting systems. By addressing the current lack of structured strategies for biomaterial selection for bioprinting, the BBC framework offers a foundational step toward a more rational and consistent design of responsive biomaterials in advanced biofabrication systems.

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**Citation:** Saeb MR. Stimuli-responsive biomaterials for 3D bioprinting: Bioprinting biomaterials classification (BBC). *Int J Bioprint.* 2026;12(3):026170147.  
doi: 10.36922/IJB026170147

**Received:** March 24, 2026

**Revised:** April 17, 2026

**Accepted:** April 27, 2026

**Published online:** May 1, 2026

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**Keywords:** 3D bioprinting; Stimuli-responsive biomaterials; Bioinks; Biofabrication; Bioprinting biomaterials classification; Biomaterials selection

## 1. Introduction

Three-dimensional (3D) bioprinting has rapidly developed over the last decade as a robust, transformative biofabrication technology for engineering complex biological constructs with controlled architecture and functionality.<sup>1</sup> By enabling the spatially

precise deposition of cells, biomaterials, and bioactive components, 3D bioprinting provides powerful design and fabrication paradigms for producing tissue-like systems and biotechnological products.<sup>2</sup> Central to this progress is the formulation of advanced bioinks and biomaterials capable of supporting both the printing process and the subsequent biological performance of printed constructs.<sup>3</sup> Nevertheless, despite these advances, the process of biomaterial selection for bioprinting remains insufficiently structured and standard, often relying on fragmented norms and protocols rather than a unified design logic that connects material properties with biofabrication requirements. Among these materials, stimuli-responsive biomaterials have attracted increasing attention due to their ability to dynamically adjust their physicochemical and biological properties in response to external stimuli, thereby enabling adaptive control over material behavior during and after printing.<sup>4</sup> Such responsiveness can influence multiple stages of the bioprinting lifecycle, which include bioink preparation,<sup>5</sup> printing fidelity,<sup>6</sup> post-printing maturation,<sup>7</sup> and in vivo function,<sup>8</sup> while also shaping critical interactions among processing conditions, biomaterial properties, and cell–material responses.<sup>9</sup> Although the diversity of responsive biomaterials reported in the literature is rapidly increasing, their conceptual organization and categorization across different stages of the bioprinting process—where material properties can change significantly from one stage to another—remain insufficiently structured.<sup>10</sup>

The limitations of biomaterial selection for bioprinting processes and their classification arise mainly because conventional classifications are primarily based on the type of stimulus that activates material behavior, which does not explicitly account for how such responsiveness functions across different stages of the bioprinting process.<sup>11</sup> In practical biofabrication environments, however, the functional characteristics one would expect from biomaterials are stage-dependent, encompassing requirements for bioink preparation, printing fidelity, post-printing maturation, and in vivo performance.<sup>12</sup> From this perspective, materials that share similar stimulus mechanisms may serve fundamentally different roles depending on when their responsiveness is activated within the bioprinting workflow.<sup>13</sup> Moreover, definitions and classification logics for responsive biomaterials often vary across studies and frequently reflect author-specific interpretations shaped by material chemistry, specific stimuli, or application-oriented perspectives. Additional inconsistencies, conflicting interpretations, and even regulatory challenges may arise when comparing systems and understanding their roles in the broader biofabrication process.<sup>14</sup> In many cases, the lack of clear definition and

classification of stimuli-responsive biomaterials has become more apparent as the field of bioprinting expands across multiple technological and biological areas.<sup>15</sup> Moreover, the classification of printing technologies for cell-compatible bioprinting—such as material jetting, vat photopolymerization, material extrusion, and free-form spatial printing—cannot effectively support biomaterial selection for biofabrication.<sup>16</sup> Although such classifications are frequently used by experts, they do not explicitly capture how biomaterials' functionality contributes to material functions across the sequential stages of bioprinting processes.

Advances in bioink formulation have resulted in a wide range of natural biomaterials, each designed and tailored to meet specific requirements for printability, structural stability, and biological performance.<sup>17</sup> At the same time, the rapid evolution of bioprinting technologies—including extrusion, inkjet, laser-assisted, and photopolymerization-based approaches—has further diversified the processing environments in which these materials operate.<sup>18</sup> Consequently, the selection and design of stimuli-responsive biomaterials are no longer determined solely by stimulus mechanisms or material chemistry, but also by the degree of their compatibility with specific printing strategies, processing conditions, and the maturation requirements of printed constructs.<sup>19</sup> This increasing complexity expands the design matrix and makes it practically difficult to compare responsive systems across studies and to position newly born biofunctional materials within the broader landscape of bioprinting research. For example, a material may be considered a biomaterial based on well-established definitions,<sup>20</sup> but it may not meet the requirements for printability or structural stability during bioprinting,<sup>21</sup> highlighting the importance of involving compatibility at different processing stages together with intrinsic material properties. To address this challenge and inspired by the classification of biofunctional materials,<sup>22</sup> this perspective introduces a framework to classify stimuli-responsive biomaterials, aiming to provide a more structured basis for biomaterial selection for 3D bioprinting. The proposed framework arranges responsive biomaterials through a two-level biofunctional classification in accordance with their stimulus category and functional roles across the bioprinting lifecycle, providing a structured basis for comparing materials, optimizing bioink design, and integrating responsive functionality into evolving bioprinting strategies.

## 2. Stimuli-responsive biomaterials in 3D bioprinting

Stimuli-responsive biomaterials are important

## BOX I

**What the BBC framework helps to clarify in bioprinting**

The bioprinting biomaterials classification (BBC) framework is introduced to support a more structured and context-oriented understanding of how stimuli-responsive biomaterials function within bioprinting systems. In particular, it helps clarify several conceptual and practical challenges that arise when materials are interpreted primarily based on stimulus type or composition.

**1. Limited stage-specific interpretation of biomaterial function**

Responsive biomaterials are commonly described based on their sensitivity to physical, chemical, or biological stimuli. However, this perspective does not clearly indicate how such responsiveness is utilized at different stages of the bioprinting process, where functional requirements can vary significantly.

**2. Predominant use of stimulus-based classification**

Stimulus categories provide a useful basis for grouping materials, but they do not fully capture how materials behave during biofabrication. Materials sharing the same type of responsiveness may serve different roles depending on how and when that responsiveness is activated.

**3. Lack of a structured link between material behavior and bioprinting workflow**

Bioprinting involves multiple sequential stages, including bioink preparation, printing, post-printing maturation, and in vivo function. Existing descriptions often do not systematically connect material properties with these stages, which can limit the clarity of design decisions, particularly when transitioning between stages of the bioprinting lifecycle.

**4. Ambiguity in comparing material systems across studies**

Similar materials are often used under different conditions and for different purposes, making direct comparison challenging across different studies, applications, and processing conditions. Without a framework that accounts for both responsiveness and application context, interpreting and comparing reported systems remains difficult.

**5. Gap between material design and functional application**

Material development is frequently guided by composition and responsiveness, while functional requirements are defined by the intended application. The absence of a structured connection between these aspects can lead to fragmented design strategies.

**6. Need for a design-oriented perspective in biomaterial selection**

As the diversity of responsive biomaterials continues to expand, selecting appropriate materials for specific bioprinting applications becomes increasingly complex. A framework that integrates stimulus mechanisms with stage-specific requirements can support more transparent, consistent, and application-relevant biomaterial selection in bioprinting.

**7. Context-dependent functional role of biomaterials**

The same material system may exhibit different functional roles depending on how it is formulated, processed, and applied. Recognizing this context-dependency is important for understanding that biomaterials are not fixed entities, but dynamic components within biofabrication systems.

Overall, these considerations highlight the need for a framework that connects material responsiveness with process-specific functionality, which forms the basis of the BBC approach.

components of modern bioprinting processes because of their adaptability and functionality during biofabrication or under post-printing conditions.<sup>23</sup> Although their diversity has been progressively developed, it has not

been accompanied by a comparable development in their structural definition and classification. Therefore, strategies available for selection and implementation remain unclear, limiting the ability to systematically align their

responsiveness with specific biofabrication requirements. In bioprinting environments, these functional materials can regulate main features of the biofabrication process, including bioink rheology during preparation, structural fidelity during printing, and the functional maturation of printed constructs.<sup>24</sup> Their adaptability is based on physicochemical or biological changes in response to environmental stimuli, allowing them to interact with both processing conditions and biological systems.<sup>25</sup> In bioprinting, responsive biomaterials are commonly grouped into three main stimulus categories: physical stimuli, such as temperature, light, and mechanical forces; chemical stimuli, such as pH, ionic conditions, and redox environments; and biological stimuli, such as enzymatic activity and cell-mediated processes.<sup>26</sup> These mechanisms enable materials to function across multiple stages of the bioprinting lifecycle, thereby enabling material design to combine with fabrication strategies and the evolving biological environment of the printed constructs. This further complicates the understanding of their role in bioprinting and their clear classification as bioprinting biomaterials. For example, thermo-responsive hydrogels may be designed to regulate viscosity during bioink preparation,<sup>27</sup> while similar systems can also be utilized after printing to enable structural transformation or adaptive behavior of printed constructs.<sup>28</sup>

Although the classification of responsive biomaterials according to stimulus category provides a convenient conceptual starting point, it does not fully capture the functional complexity of these materials within bioprinting systems. This limitation becomes particularly critical in biomaterial selection for bioprinting, as stimulus-based classification alone does not provide sufficient guidance for choosing or engineering materials for specific stages of the biofabrication process. In many studies, responsive biomaterials are described solely in terms of the external or internal stimuli that activate them, such as temperature, pH, light, and enzymatic activity.<sup>29</sup> However, in practical bioprinting settings, the behavior of these materials is influenced not only by the actuating stimulus but also by their interaction with bioink formulation, printing technologies, and the changing biological environment of printed constructs.<sup>30</sup> For instance, responsive materials may be engineered to regulate rheological properties during bioink preparation, maintain structural fidelity during deposition, enable structural transformation during post-printing maturation, or respond to biological signals in the *in vivo* environment.<sup>31</sup> Accordingly, the functional significance of biomaterial responsiveness depends strongly on the stage of the bioprinting process at which it occurs, yet this aspect is often overlooked in the selection of responsive biomaterials.

When responsive biomaterials are considered only through stimulus categories, these process-dependent contributions become difficult to explicitly compare and systematically organize across different studies. For instance, ionically crosslinked systems may be used during the printing stage to achieve rapid gelation and structural stabilization,<sup>32</sup> whereas enzyme-responsive matrices may be more relevant for post-printing maturation or *in vivo* environments where biological triggers govern material behavior.<sup>33</sup> This stage-dependent variability in the role of biomaterials in bioprinting processes shows a conceptual and practical gap that requires a structured framework to position stimuli-responsive biomaterials within the broader bioprinting process and to link stimulus mechanisms with their functional roles in biofabrication. From this perspective, incorporating the lifecycle dimension into the decision-making process enables a more realistic interpretation of biomaterial functionality, where material behavior is not only defined by how it responds but also by when and for what functional purpose such responsiveness is required. This distinction in the terminology of biomaterial selection and the decision-making framework is particularly important for differentiating between materials suitable for processing, structural stabilization, or biological interaction, even when similar stimulus mechanisms are involved.

### 3. Bioprinting biomaterials classification

The growing diversity of stimuli-responsive biomaterials and the expanding range of bioprinting technologies have created a need for a systematic approach to classify biomaterials according to their functional roles in biofabrication.<sup>34</sup> In practice, responsive biomaterials are designed not only to respond to specific stimuli but also to perform distinct functions at different stages of the bioprinting process, from bioink preparation to the biological performance of printed constructs.<sup>35</sup> To capture the multidimensional relationship between stimulus mechanisms and biofabrication stages, this work introduces the bioprinting biomaterials classification (BBC) framework, a conceptual structure for classifying stimuli-responsive biomaterials in 3D bioprinting. Within the BBC framework, biomaterials are positioned according to two complementary dimensions. The first dimension reflects the category of stimulus that activates the responsive behavior of the biomaterial, i.e., physical, chemical, or biological stimuli. The second dimension relates to the bioprinting lifecycle, which includes bioink preparation, printing process, post-printing maturation, and *in vivo* function. Considering these two dimensions together allows responsive biomaterials to be interpreted not only in terms of their activation mechanism but also

in relation to the stage of the bioprinting process in which their functionality becomes relevant and applicable. In this sense, the same material may exhibit different functional significance depending on whether the responsiveness is utilized during bioink preparation, printing, post-printing maturation, or in vivo application.

The interaction pattern of these two dimensions, which forms the BBC matrix concept, is illustrated in [Figure 1](#). This simplified two-dimensional classification structure integrates stimulus categories and stages of the bioprinting lifecycle within a unified conceptual framework. In other words, the BBC is a two-level classification matrix that not only organizes responsive biomaterials but also provides a structured conceptual basis for biomaterial selection in bioprinting by linking material responsiveness to stage-dependent functional requirements. This two-dimensional structure highlights that classification based solely on stimulus categories is insufficient to describe the operational role of biomaterials in bioprinting, as it does not capture how functional requirements change across different stages of the biofabrication process. By incorporating the lifecycle dimension, the BBC framework enables a more application-relevant interpretation of responsive biomaterials, in which materials with similar activation mechanisms may serve fundamentally different roles depending on when their responsiveness is utilized. Primarily, the BBC framework provides a structured perspective for positioning responsive biomaterials within the broader landscape of bioprinting research, while also offering a practical reference for guiding biomaterial selection for bioprinting through systematic comparison of materials based on both stimulus mechanisms and functional roles. Therefore, [Figure 1](#) communicates a conceptual structure in a simplified visual form, while the more detailed material examples, design logic, and application-oriented interpretation of the framework are further elaborated in [Table 1](#) and the corresponding discussions.

Beyond the core matrix structure illustrated in [Figure 1](#), the BBC framework also involves additional design considerations that influence how responsive biomaterials are selected, designed, and implemented in bioprinting. These considerations provide complementary perspectives for interpreting responsive material systems and should be understood as design-related factors that extend the practical use of the BBC framework beyond its primary two-dimensional classification structure. First, responsive biomaterials can be classified by their origin, which commonly includes natural biomaterials,<sup>36</sup> synthetic polymers,<sup>37</sup> hybrid systems,<sup>38</sup> and extracellular matrix-derived matrices,<sup>39</sup> as this factor influences the

practical selection and design of materials for different biofabrication contexts. The origin of biomaterials influences not only their intrinsic responsiveness but also their biocompatibility, degradation behavior, and interaction with cells.<sup>40</sup> Second, the selection and behavior of responsive biomaterials are closely associated with bioprinting technologies, including extrusion bioprinting,<sup>41</sup> inkjet bioprinting,<sup>42</sup> laser-assisted bioprinting,<sup>43</sup> and vat photopolymerization.<sup>44</sup> Different printing approaches impose distinct processing environments and material requirements, which in turn shape how responsive mechanisms are utilized during fabrication.<sup>45</sup> Third, responsive biomaterials can also be interpreted in relation to their biological functions within printed constructs, including structural support,<sup>46</sup> cell guidance,<sup>47</sup> drug delivery,<sup>48</sup> and tissue maturation objectives,<sup>49</sup> reflecting the diverse biological objectives that responsive biomaterials support in bioprinting applications.<sup>50</sup> Overall, these complementary dimensions reinforce the role of the BBC framework not only as a multidimensional classification structure but also as a conceptual tool for addressing the complexity of biomaterial selection for bioprinting, where material properties, processing conditions, and biological functions must be considered simultaneously within a unified framework.

#### 4. Applying the bioprinting biomaterials classification framework for biomaterial selection in bioprinting

Viewed through the lens of the BBC classification matrix, biomaterial selection in bioprinting emerges as a layered and decision-driven process that extends beyond stimulus mechanisms alone. In practical biofabrication environments, biomaterials must operate within complex systems involving material composition, printing technologies, processing conditions, and biological interactions.<sup>51</sup> Therefore, biomaterial selection requires consideration of multiple interconnected factors, including biomaterial origin, compatibility with specific printing methods, stage-dependent functional requirements, and the biological functions that printed constructs are expected to achieve. A responsive biomaterial should be primarily engineered to support the mechanical, structural, and biological requirements imposed by different stages of the bioprinting process. Within this context, the BBC framework provides a practical guide for integrating responsive behavior into biomaterial design strategies for next-generation bioprinting systems. Practically, the BBC framework can be applied as a stepwise guide for biomaterial selection in bioprinting systems.

Rather than relying on unstructured or intuitive

## BOX II

**Applying the bioprinting biomaterials classification (BBC) framework in biomaterial selection for bioprinting**

The BBC framework can be applied as a structured guide to support biomaterial selection and design in bioprinting systems. Rather than suggesting consolidated material choices, it provides a stepwise approach to interpret how stimuli-responsive behavior can be aligned with stage-specific functional requirements across the bioprinting lifecycle.

**1. Define the target stage of the bioprinting lifecycle**

The first step involves identifying the stage at which the biomaterial is expected to perform its primary function, such as bioink preparation, printing, post-printing maturation, or in vivo application. This step establishes the functional framework in which material behavior should be interpreted.

**2. Identify stage-specific functional requirements**

Each stage of the bioprinting process is associated with distinct functional demands, including rheological control, structural stability, biological compatibility, or adaptive functionality. Defining these requirements helps to clarify what type of material response is needed.

**3. Select relevant stimuli-responsive mechanisms**

Based on the identified functional requirements, appropriate stimuli-responsive mechanisms can be considered, including physical, chemical, or biological triggers. This step connects material responsiveness to the intended functional outcome.

**4. Match candidate biomaterial systems**

Material systems can then be selected based on their ability to exhibit the desired responsiveness under the defined conditions. At this stage, commonly used systems and representative examples, as summarized in Table 1, can be used as guidance.

**5. Evaluate compatibility with bioprinting techniques and biological context**

Selected materials should be assessed in relation to the intended bioprinting method (e.g., extrusion, inkjet, or light-based printing) and the biological environment. This ensures that material performance remains consistent with both processing and application constraints.

**6. Consider context-dependent functional variation**

The same biomaterial may exhibit different functional roles depending on formulation, processing conditions, or stage of use. Recognizing this variability is important for understanding that material selection is not fixed, but may evolve across the bioprinting process.

Overall, through this stepwise approach, the BBC framework supports a more structured and interpretable pathway for biomaterial selection in bioprinting, linking stimuli-responsive behavior with stage-specific functionality in a practical and context-aware manner.

biomaterial selection, the BBC framework enables sequential consideration of the main variables that determine whether a responsive biomaterial is suitable for a given application. In this regard, one should consider and define the following steps in identifying and selecting biomaterials that guarantee their applicability for bioprinting processes, including (i) the target stage of the bioprinting lifecycle; (ii) the functional requirements associated with that stage; (iii) the appropriate stimuli-responsive mechanisms; and (iv) the compatibility

with printing technologies and biological objectives. Through this stepwise logic, the BBC framework can function and support a more structured and transparent approach to biomaterial selection for bioprinting. [Table 1](#) provides a direct representation of this mapping, where the progression from stimuli-responsive mechanisms to stage-specific applications is organized within the two-dimensional BBC structure. For example, a researcher designing a bioink for extrusion bioprinting may need to select a shear-responsive or thermo-responsive system to

<b>Stimulus Category</b>	<b>Physical Stimuli</b>	Thermo-responsive Hydrogels (Rheology Tuning)	Shear-responsive Bioinks (Print Fidelity)	Shape-morphing Bioinks (4D Construct)	Mechano-responsive Scaffolds (Mechanical Signaling)
	<b>Chemical Stimuli</b>	pH-responsive Hydrogels	Ionic Crosslinking Bioinks	Controlled Biodegradation	Stimuli-triggered Drug Release
	<b>Biological Stimuli</b>	Enzyme-triggered Matrices	Cell-mediated Gelation	ECM Remodeling	Adaptive Tissue Response
		<b>Bioink Preparation</b>	<b>Printing Process</b>	<b>Post-printing Maturation</b>	<b>In Vivo Function</b>
<b>Bioprinting Lifecycle</b>					

**Figure 1.** Two-dimensional representation of the bioprinting biomaterials classification (BBC) framework. The figure illustrates the two defining dimensions of the BBC: stimulus categories (physical, chemical, and biological) and stages of the bioprinting lifecycle (bioink preparation, printing process, post-printing maturation, and in vivo function). This matrix structure provides a simplified and explicit visualization of the core BBC concept, showing how responsive biomaterials can be classified according to both their activation mechanisms and their stage-specific functional roles in bioprinting. Abbreviation: ECM: Extracellular matrix.

ensure appropriate flow behavior during deposition, while incorporating rapid crosslinking or biologically responsive components to maintain structural fidelity and support post-printing maturation. The proposed framework and methodology illustrate how material selection can be guided by both stimulus type and stage-specific functional requirements.

In practice, the design considerations highlighted by the BBC approach can be translated into practical guidelines for the development of responsive biomaterials used in bioprinting systems. Since responsive materials operate at different stages of the biofabrication workflow, their design objectives often vary depending on the bioprinting stage and the stimulus mechanisms involved. In this regard, decision-making in biomaterial selection can be supported using the BBC framework. For example, materials intended for bioink preparation may prioritize rheological control and printability, whereas those used during construct maturation or in vivo application may be engineered for structural transformation, degradation behavior, or biological responsiveness.<sup>52</sup> In this context, thermo-responsive polymers, such as those based on poly(*N*-isopropylacrylamide) (PNIPAM), may be selected

to tune viscosity and facilitate extrusion during printing,<sup>53,54</sup> while biodegradable or enzyme-responsive hydrogels may be designed to support matrix remodeling and biological integration at later stages.<sup>55,56</sup> This highlights how material selection is guided by stage-specific functional requirements across the bioprinting lifecycle, consistent with the stepwise design logic of the BBC framework.

To summarize these relationships in a more structured and design-oriented manner, Table 1 presents representative considerations for stimuli-responsive biomaterials across stimulus categories and bioprinting stages, while also integrating design objectives, functional roles in bioprinting, representative systems, example materials, typical bioprinting techniques, and the underlying design rationale that supports biomaterial selection for bioprinting. In this structure, stimulus categories and stages of the bioprinting lifecycle explicitly define the two-dimensional organization of the BBC framework. Each row in the table represents a specific intersection between a stimulus category and a stage of the bioprinting lifecycle, thereby directly reflecting the core two-dimensional logic of the BBC framework. This table is proposed as an illustrative rather than comprehensive



representation of the field, and to visualize the applicability of the BBC concept, where the included examples were selected based on their relevance to stage-specific functional roles, their representativeness within widely studied classes of responsive systems, and their practical relevance to bioprinting applications. Besides Figure 1, which introduces the conceptual structure of the BBC framework, Table 1 provides a detailed and application-

oriented representation that supports practical biomaterial selection and design. In this sense, the table serves as a practical extension of the BBC guide by illustrating how the framework supports biomaterial selection in specific biofabrication contexts, thereby translating the interaction between stimulus categories and bioprinting stages into a structured decision-making tool.

As summarized in Table 1, the design of responsive

**Table 1. Design-oriented representation of the bioprinting biomaterials classification (BBC) framework for stimuli-responsive biomaterials in 3D bioprinting, structured according to stimulus categories and stages of the bioprinting lifecycle**

Stimulus category	Bioprinting stage	Design objective	Functional role in bioprinting	Representative systems	Example materials	Typical bioprinting technique	Design rationale	References
Physical stimuli	Bioink preparation	Rheological control, printability	Enables shear-thinning, viscosity tuning	Thermo-responsive systems	PNIPAM, Pluronic F127, methylcellulose-based systems	Extrusion	Temperature-dependent sol-gel transition allows controlled flow during printing	57-59
	Printing process	Shape fidelity, stabilization	Maintains structure during deposition	Photo- and thermo-responsive systems	GelMA, alginate blends, nanocellulose-containing bioinks	Extrusion, light-based	Rapid crosslinking or viscosity increase ensures structural integrity	60-62
	Post-printing maturation	Structural transformation	Enables dynamic reshaping or stiffening	Thermo- and light-responsive scaffolds	Shape-memory polymers, responsive hydrogels, PEG-based smart polymers	Extrusion, stereolithography	External stimuli enable post-printing tuning of properties	63-65
	In vivo function	Adaptive mechanical response	Responds to physiological conditions	Mechanically responsive systems	Stress-responsive hydrogels, elastin-like polypeptides	Implantation-based	Materials adapt to in vivo mechanical cues	66,67
Chemical stimuli	Bioink preparation	Controlled crosslinking potential	Provides support for ionic or chemical activation	Ion-sensitive systems	Alginate, gellan gum, carrageenan-based systems, chitosan, poly(acrylic acid)	Extrusion	Ionic interactions enable rapid gelation after extrusion	68-72
	Printing process	Rapid gelation	Stabilizes printed filaments	Ionically crosslinked systems	Alginate-Ca <sup>2+</sup> systems	Extrusion	Immediate crosslinking maintains print fidelity	73

(cont'd...)



Table 1. (Continued)

Stimulus category	Bioprinting stage	Design objective	Functional role in bioprinting	Representative systems	Example materials	Typical bioprinting technique	Design rationale	References
Biological stimuli	Post-printing maturation	Degradation, controlled release	Enables controlled breakdown or release	pH- and enzyme-responsive systems	Biodegradable networks, such as PEGDA and PEG-based hydrogels	Extrusion, inkjet	Chemical triggers regulate degradation and drug release	74,75
	In vivo function	Environmental responsiveness	Reacts to biochemical conditions	Dynamic covalent systems	Self-healing hydrogels	Implantation	Chemical environment triggers adaptive responses	76,77
	Bioink preparation	Bioactivity incorporation	Introduces cell-interactive components	ECM-derived systems	Collagen, gelatin, decellularized ECM	Extrusion	Provides a biologically relevant microenvironment	78-80
	Printing process	Cell compatibility	Maintains cell viability	Cell-laden bioinks	GelMA–cell systems	Extrusion, inkjet	Mild conditions preserve cell function	81,82
	Post-printing maturation	Tissue development	Supports cell differentiation and remodeling	Cell-responsive matrices	ECM hydrogels, MMP-responsive matrices	Extrusion	Cells actively remodel material structure	83,84
	In vivo function	Biological integration	Enables tissue interaction	Adaptive biomaterials	Dynamic covalent hydrogels, cell-instructive matrices	Implantation	Materials respond to biological signals in vivo	85,86

Notes: The table organizes representative biomaterial systems by stimulus category and their functional roles across the different stages of the bioprinting lifecycle, including bioink preparation, printing process, post-printing maturation, and in vivo function. For each category, corresponding design objectives, functional roles, representative systems, example materials, and typical bioprinting techniques are summarized, together with the underlying design rationale that governs their selection and application. This framework provides a structured, design-oriented perspective on how responsive biomaterials can be selected and engineered in accordance with both stimulus mechanisms and stage-specific functional requirements. The listed examples are representative rather than exhaustive and are intended to illustrate the practical implementation of the BBC framework in guiding biomaterial design in bioprinting systems, as supported by selected key references. Each row corresponds to a specific intersection in the BBC matrix, illustrating how stimuli-responsive mechanisms align with stage-specific functional requirements to support biomaterial selection.

Abbreviations: ECM: Extracellular matrix; GelMA: Gelatin methacryloyl; MMP: Matrix metalloproteinases; PEG: Polyethylene glycol; PEGDA: Polyethylene glycol diacrylate; PNIPAM: Poly(*N*-isopropylacrylamide).

biomaterials for bioprinting is inherently linked to both the type of stimulus that activates material behavior and the stage of the bioprinting process in which this behavior is utilized.<sup>87</sup> In view of the inclusion of representative examples of material systems in the established literature, the table should be interpreted as a structured and illustrative guide to the application of the BBC framework. In addition to the two-dimensional classification, it further

integrates design objectives, functional roles in bioprinting, representative systems, example materials, and typical bioprinting techniques, along with their corresponding design rationales, providing a more structured basis for interpreting and applying the BBC framework in practice. Physical stimuli are frequently exploited to regulate rheological properties, structural stability, and mechanical adaptation of printed constructs. Chemical stimuli enable

environmentally responsive processes, such as ionic crosslinking, degradation control, and stimulus-triggered molecular release, which are particularly relevant for scaffold stabilization and therapeutic delivery. In contrast, biological stimuli introduce dynamic interactions with the living microenvironment, allowing biomaterials to respond to enzymatic activity, cell-mediated processes, and extracellular matrix remodeling.<sup>88</sup>

Within the provided context, the inclusion of representative material systems and processing techniques illustrates how similar stimulus mechanisms can be used differently at different stages of the bioprinting lifecycle, thereby providing practical guidance for material selection and design. These examples were selected to highlight commonly studied and design-relevant material strategies rather than to provide a comprehensive listing of all available systems. Viewed through the BBC framework, these stimulus–function relationships highlight how biomaterial design must integrate material composition, printing strategy, and biological function. It is also important to note that incorporating design rationale in [Table 1](#) enables a clearer understanding of why specific materials are positioned within particular categories, linking material properties to stage-specific functional requirements and processing conditions. As a result, responsive biomaterials for bioprinting should be developed not merely as stimulus-sensitive materials, but as integrated components of biofabrication systems that evolve across the entire bioprinting lifecycle, with material selection guided by both activation mechanisms and application-oriented design considerations.

## 5. Conclusion and future perspectives

The rapid development of 3D bioprinting has expanded the possibilities for engineering complex biological structures, but it has also posed challenges in the selection and design of biomaterials for biofabrication. In particular, the increasing diversity of stimuli-responsive biomaterials offers new opportunities for dynamic and adaptive functions, but it also creates a fragmented understanding of how these materials should be interpreted, compared, and selected for specific bioprinting applications. In this work, the BBC framework has been introduced as a conceptual and design-oriented approach to address this challenge. By integrating stimuli-responsive mechanisms with stage-specific functional roles across the bioprinting lifecycle, the BBC framework provides a structured perspective that extends beyond conventional stimulus-based classification. Instead of inspecting biomaterials solely in terms of their activation triggers, the BBC framework emphasizes when and for what functional purpose responsiveness is utilized within biofabrication processes. In this sense,

the BBC framework contributes to a more context-based interpretation of biomaterials, where material behavior is understood in relation to both processing stages and biological objectives. A key contribution of this work is the shift from a purely conceptual classification to a more application-oriented design approach. By integrating structured explanatory elements with design-oriented representation, the framework establishes a clearer link between conceptual understanding and practical implementation.

In particular, the stepwise approach outlined for applying the BBC framework highlights how biomaterial selection can be guided through sequential consideration of bioprinting stages, functional requirements, stimuli-responsive mechanisms, and compatibility with fabrication and biological conditions. This perspective supports a more transparent and interpretable pathway for biomaterial selection, which is increasingly important as bioprinting systems become more complex and multifunctional. Of note, the BBC framework also underscores the context-dependent nature of biomaterial functionality. The same material system may perform distinct roles depending on its formulation, processing conditions, and stage of application within the bioprinting workflow. Recognizing this dynamic behavior shifts the interpretation of biomaterials from static entities toward adaptive components of biofabrication systems that evolve throughout the lifecycle of printed constructs. This shift is particularly relevant for the development of next-generation responsive biomaterials, where functionality is defined not only by composition but also by interactions with processing environments and biological systems. Looking forward, the BBC framework has the potential to serve as a conceptual foundation for advancing the rational design of stimuli-responsive biomaterials in emerging bioprinting technologies. As the field progresses toward increasingly sophisticated applications—such as adaptive bioinks, programmable scaffolds, 4D bioprinting systems, and biofabrication strategies that incorporate real-time feedback and dynamic environmental interactions—the need for structured and integrative design frameworks will become more pronounced. In this context, the BBC framework may contribute to guiding the development of materials that are not only responsive but also functionally synchronized with the evolving requirements of biofabrication processes and biological systems.

Furthermore, the framework may improve comparability across studies by providing a common reference for interpreting the responsiveness of biomaterials throughout the bioprinting lifecycle. This could support more consistent reporting practices and enable a more systematic

accumulation of knowledge across different material systems, printing technologies, and application domains. In the longer term, such structured approaches may help bridge gaps among materials science, bioengineering, and regenerative medicine, where interdisciplinary integration is essential for translating bioprinting technologies into practical biomedical solutions. Overall, the BBC framework represents a step toward a more structured, application-oriented, and context-oriented approach to biomaterial classification and selection in bioprinting. By connecting material responsiveness with biofabrication processes, it provides a foundation for interpreting and designing responsive biomaterials in a more systematic and meaningful way. As the field continues to evolve, such conceptual frameworks may play an increasingly important role in shaping the development of advanced biomaterials and enabling the next generation of biofabrication strategies.

## Acknowledgments

None.

## Funding

None.

## Conflict of interest

The author declares he has no competing interests.

## Author contributions

This is a single-authored article.

## Ethics approval and consent to participate

Not applicable.

## Consent for publication

Not applicable.

## Availability of data

Not applicable.

## Further disclosure

OpenAI's ChatGPT, accessed through a licensed institutional service, was used solely to assist with proofreading and correcting grammatical issues. It did not influence the underlying scientific concepts, data interpretation, or conclusions of the article. The author independently conceptualized, prepared, reviewed, and verified all content in both the initial and revised versions of the manuscript to ensure its accuracy and integrity, and assumes full responsibility for the work, including any

errors or interpretations.

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