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Emerging innovations in 3D and 4D bioprinting

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This themed collection highlights the latest breakthroughs in 3D and 4D bioprinting of biomaterials and cells, underscoring its transformative potential as a versatile platform for tissue engineering and regenerative medicine. This collection emphasizes the profound impact of integrating advanced bioprinting techniques with innovative biomaterial-based bioinks for creating complex 3D tissues. Such constructs serve not only as sophisticated *in vitro* models for studying tissue development, disease remodeling, and cellular interactions, but also as implantable scaffolds for diverse applications in tissue engineering and regenerative medicine. The featured articles represent a wide spectrum of innovations in 3D bioprinting, focusing on both novel printing methodologies and the development of functional bioinks. The collection includes advances in digital light processing (DLP)-based printing, embedded bioprinting, chaotic bioprinting, and magnetic-assisted tissue engineering (MagTE) combined with 3D printing. Furthermore, a range of next-generation bioinks with specialized functionalities, such as angiogenic, nitric oxide (NO)-releasing, conductive, and stimuli-responsive properties, are introduced. These bioinks enable precise fabrication of 3D and 4D printed constructs for various applications including vascularization, bone tissue formation, implantable devices, strain sensors, *in vitro* thrombosis models, and stromal microenvironments. Together, these contributions highlight the rapidly evolving landscape of bioprinting technologies and their pivotal role in advancing the frontiers of tissue engineering and regenerative medicine.

Innovations in biomaterials design have led to the development of advanced bioinks for 3D bioprinting of functional tissue constructs, driving significant progress in the field of tissue engineering. For instance, Rizzo and Lewis *et al.* introduced a photoinitiator- and radical-free, light-based method for rapid crosslinking of synthetic polymers and native proteins without backbone modification (https://doi.org/10.1039/D4BM00849A). The resulting hydrogels exhibited dynamic, reversible, and bioadhesive properties, making them well-suited as bioinks for 3D bioprinting and tissue engineering applications. In a complementary study, García-Astrain *et al.* developed a library of plasmonic, surface-enhanced Raman spectroscopy (SERS)-active hydrogels from naturally derived biopolymers modified with complementary thiol and norbornene groups (https://doi.org/10.1039/D4BM01529K). Integrating these hydrogels with 3D printing provides a powerful platform for monitoring cellular metabolism, signalling, and drug responses within complex 3D environments. Similarly, Gonzalez-Fernandez *et al.* introduced a high-swelling composite hydrogel composed of gelatin methacryloyl (GelMA) and sodium polyacrylate (SPA) for advanced 4D printing (https://doi.org/10.1039/D5BM00551E). This system enabled precise and reversible swelling and shrinking triggered by ionic strength, offering dynamic control over printed constructs and broad potential for biomedical applications requiring tunable hydrogel behavior. In a comprehensive review, de Oliveira *et al.* highlighted recent advances in 3D printing of nitric oxide (NO)-releasing biomaterials, emphasizing their potential roles in tissue repair, immune modulation, and wound healing (https://doi.org/10.1039/D4BM01304B). To engineer highly vascularized tissue constructs, Huang *et al.* developed an angiogenic bioink derived from a dorsal dermal decellularized extracellular matrix, which promoted vascular network formation in 3D bioprinted tissues (https://doi.org/10.1039/D4BM00957F). For electroactive tissues such as cardiac, neural, and muscle systems, conductivity is critical. Addressing this, Chatterjee *et al.* combined 4D printing with conductive bioinks composed of alginate and acid-functionalized carbon nanotubes, generating multifunctional 4D-printed hydrogels as implantable nerve conduits and strain sensors (https://doi.org/10.1039/D5BM00166H).

Beyond bioink innovation, this themed collection also highlights significant advancements in 3D and 4D printing methodologies for fabricating complex,

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functional tissues. Berry and Chen *et al.* developed an advanced DLP-based 3D printing system to engineer the myotendinous junction (https://doi.org/10.1039/D4BM00892H). By modulating local stiffness through light exposure parameters guided by an AI-trained algorithm, they successfully recreated the graded mechanical heterogeneity of native muscle–tendon interfaces. Similarly, Veiseh *et al.* employed DLP-based bioprinting of GelMA/polyethylene glycol diacrylate (PEGDA) hydrogels with tunable internal channel architectures to fabricate vascularized 3D tissue constructs (https://doi.org/10.1039/D5BM00193E). Optimizing channel design enhanced *in vivo* vascular infiltration and integration, providing a robust platform for prevascularized scaffolds for tissue transplantation. Guvendiren *et al.* further advanced the field with an embedded bioprinting strategy that integrated a methacrylated hyaluronic acid hydrogel with bioactive bone allograft or tricalcium phosphate microparticles (https://doi.org/10.1039/D4BM01616E). This composite enabled the fabrication of dense, osteoinductive cellular constructs, with strong implications for bone regeneration. Alvarez and Trujillo-de Santiago *et al.* introduced an innovative chaotic bioprinting approach using a GelMA–alginate bioink as a novel multimaterial biofabrication strategy, enabling the creation of mechanically robust and vascularized large tissue constructs (https://doi.org/10.1039/D4BM01674B). In another paper, Choi and Jang combined magnetic-based tissue engineering (MagTE) with bioprinting to dynamically manipulate cells, biomaterials, and microenvironments, creating complex 3D tissue constructs with promising applications in tissue engineering and regenerative medicine (https://doi.org/10.1039/D5BM00160A). These innovative technologies have also facilitated the development of advanced *in vitro* models for studying disease mechanisms. For example, Zorlutuna *et al.* used 3D bioprinting to create stromal models and demonstrated that normal fibroblasts in proximity to breast tumors secreted extracellular vesicles (EVs) that enhanced cancer cell migration, tumor growth, and invasion (https://doi.org/10.1039/D4BM01569J). This study demonstrates that 3D-printed models can reveal proximity-dependent EV effects that cannot be captured in 2D systems. Finally, a comprehensive review article by Lim and Ju *et al.* discussed the evolution of *in vitro* thrombosis models, transitioning from traditional polydimethylsiloxane-based microfluidic platforms to hydrogel-based and 3D bioprinted constructs, which better mimic the native hemodynamic environment (https://doi.org/10.1039/D4BM01354A).

In conclusion, this themed collection brings together landmark advances in 3D and 4D bioprinting for applications in regenerative medicine and *in vitro* tissue modeling. Collectively, these studies demonstrate how innovations in biomaterial chemistry, bioink design, and printing methodology are addressing key challenges in creating functional 3D tissues. The interdisciplinary integration of materials science, engineering, and biology continues to advance the field of 3D bioprinting. Looking ahead, closer collaboration between tissue engineers and clinicians, combined with efforts to scale up tissue printing processes, will be essential for translating these technologies into clinical practice. Continued optimization of bioink properties and bioprinting parameters to achieve faster, higher-resolution, and more biomimetic fabrication will further accelerate the successful clinical translation of 3D and 4D bioprinting technologies.