

Gelatin-Methacryloyl Bioinks: Gelatin Source, Degree of Functionalisation, Thermal State, Photocure and Cell Response

Controlling GelMA as a coupled macromer, thermal gel and light-reactive cell carrier

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Abstract

Gelatin methacryloyl (GelMA) is one of the most widely used photocrosslinkable bioinks, yet the name GelMA hides several material variables that can materially change printing and biological outcomes. Gelatin source and bloom strength influence chain length and thermal gelation; degree of functionalisation controls the density of reactive groups; concentration and temperature define the pre-cure physical state; and photoinitiation determines the conversion history experienced by encapsulated cells. This review treats these variables as a coupled state description. It distinguishes printability gained from reversible gelatin gelation from final network properties created by light, and it emphasises that identical nominal GelMA concentration does not imply identical macromolecular or biological state. A qualification framework is proposed around source identity, functionalisation, thermal history, rheology, spectral dose, conversion, swelling, mechanics and cell response. The central objective is to make GelMA results transferable without assuming that a single concentration and exposure time define the material.

Keywords: GelMA; gelatin methacryloyl; degree of functionalisation; photocrosslinking; bioink; thermal gelation; cell response

1. Significance and scope

GelMA combines gelatin-derived cell-interactive motifs with covalent photocrosslinking and has become a reference bioink for extrusion and light-based biofabrication [1–4]. Its apparent simplicity can lead to under-reporting. Gelatin source, bloom strength, methacryloyl substitution and thermal state all influence the response before the photochemical step begins.

1.1 Corpus boundary

ER-322 owns GelMA-specific variation arising from gelatin source and bloom strength, degree of functionalisation, thermal state and photocure. ER-321 owns dECM provenance; ER-323 owns PEG-based architectures; ER-324 owns fibrin/fibrinogen networks; ER-325 owns elastin/tropoelastin materials; ER-326 owns gelatin-norbornene thiol-ene chemistry; ER-327 owns sequence-defined recombinant proteins; ER-328 to ER-330 own process- and construct-level biofabrication questions.

2. Gelatin source and bloom strength

Gelatin is produced by partial collagen hydrolysis, and source plus processing history affect molecular-weight distribution, gel strength and thermoreversible behaviour. A 2026 study showed that bloom strength and degree of functionalisation both influence DLP and extrusion bioprinting performance [2]. Source identity should therefore be part of the material record rather than treated as an interchangeable commodity attribute.

3. Degree of functionalisation

Methacryloyl substitution changes the number of groups available for network formation and can alter gel fraction, swelling, stiffness and residual unreacted functionality. The degree of functionalisation should be measured using a defined analytical method and reported with uncertainty. Comparing GelMA materials only by mass concentration can confound polymer concentration with network functionality. [1,3]

4. Thermal state before light exposure

GelMA can undergo reversible physical gelation as temperature decreases. This behaviour can provide extrusion fidelity before photocuring, but it also changes viscosity, diffusion and the initial microstructure presented to the light-driven reaction. Temperature at loading, printing and exposure should therefore be controlled. A material printed below its physical gel point can behave differently from the same composition exposed while fully fluid. [1,3]

5. Photoinitiation and dose

Photoinitiator identity and concentration affect radical generation, required dose and cell-compatible process windows [3]. Dose should be described spectrally and, where possible, linked to conversion rather than only to exposure time. Higher substitution does not guarantee superior constructs if increased cure density reduces cell spreading, transport or degradability.

6. Cell response is not a single endpoint

Acute viability is necessary but insufficient. Cell spreading, proliferation, matrix deposition and phenotype can depend on stiffness, mesh size, degradability and residual reactive species. The mechanical state and cell assay should be paired in the same specimens whenever possible, because a biologically favorable response may arise from a different network state rather than from an intrinsic effect of GelMA chemistry. [1,4]

7. Transfer and minimum reporting

A transferable GelMA record includes gelatin source, bloom or equivalent grade, solids concentration, degree of functionalisation, thermal history, photoinitiator system, wavelength, irradiance, dose, cure endpoint, swelling or gel fraction, modulus and a specified cell assay. These descriptors define the actual material state more accurately than the shorthand GelMA alone. [1-5]

7.1 Evidence hierarchy and transfer

GelMA results transfer only when gelatin grade, bloom strength, degree of functionalisation, concentration, thermal history and photoinitiation conditions are reported together. Similar nominal GelMA concentrations can produce different rheological, degradation and cell-response states when those variables differ [1-5].

7.2 Research priorities

The highest-value studies are factorial rather than one-variable optimisations: gelatin source and bloom strength should be crossed with degree of functionalisation, temperature and dose so that main effects are separated from interactions. Photoinitiator identity and wavelength should be treated as part of the material-process state, not as incidental machine settings [2,3,5].

7.3 Coupled state variables

GelMA couples physical gelation before exposure with covalent network formation during exposure. Temperature therefore changes the starting microstructure seen by light, while degree of functionalisation changes the available reactive-group density; both can alter stiffness, transport and cell behaviour even at the same nominal dose [1,3,4].

7.4 Decision logic for qualification

Qualification should accept a GelMA state only when rheology before exposure, conversion or gel state after exposure, geometry and the intended cell endpoint remain inside declared limits. A strong construct with altered degradation or cell proliferation is not an equivalent state merely because it prints well [1,2,4].

Table 1. Minimum qualification matrix for gelatin-methacryloyl bioinks.

Variable	Why it matters	Minimum report
Gelatin source	changes molecular distribution and biological motifs	species/type and supplier grade
Bloom/gel strength	affects thermal gelation and extrusion	bloom or equivalent characterisation
Functionalisation	sets reactive-group density	analytical degree of functionalisation
Temperature	controls physical gelation before cure	loading, printing and exposure temperatures
Light field	controls network conversion	spectrum, irradiance and dose
Cell state	defines biological compatibility	cell type, density and assay timing

8. Interpretation matrix

GelMA troubleshooting requires matched controls for gelatin grade, functionalisation, thermal history and dose. Apparent printer effects can instead be polymer-state effects, particularly near the physical-gel transition or when different photoinitiation systems are compared [1-5].

Table 2. Diagnostic interpretation matrix for GelMA state and cell response.

Observation	Possible interpretation	Control
High fidelity but poor spreading	network too dense or low degradability	lower conversion or degradable control
Same concentration, different modulus	source or functionalisation differs	molecular/functionalisation comparison
Nozzle pressure drifts	thermal state changes during printing	temperature-controlled rheology
Viability falls with longer cure	photochemical dose burden	iso-conversion spectral/dose study
Soft construct despite high substitution	insufficient conversion or dilution	conversion and gel-fraction measurement

9. Limitations and evidence gaps

Published GelMA studies use different gelatin sources, functionalisation assays, thermal conditioning, initiators and biological endpoints. This limits numerical transfer of exposure or stiffness values. Interaction data among bloom strength, functionalisation, temperature and dose remain much thinner than single-factor comparisons [1-5].

10. Conclusions

GelMA is not one material state. Its engineering behaviour emerges from gelatin provenance, chemical functionalisation, temperature-dependent physical association and light-driven covalent network formation. Reliable transfer therefore requires those state variables to be declared and verified together rather than reduced to a polymer concentration and an exposure time [1-5].

References

1. Yue K, Trujillo-de Santiago G, Alvarez MM, Tamayol A, Annabi N, Khademhosseini A. Synthesis, properties, and biomedical applications of gelatin methacryloyl (GelMA) hydrogels. *Biomaterials*. 2015;73:254-271. doi:10.1016/j.biomaterials.2015.08.045.
2. Ajgaonkar B, Menon L, Jerry N, Jain RD, Dandekar P. Exploring the impact of gelatin bloom strength and degree of functionalization in gelatin methacryloyl bioinks for optimum digital light processing and extrusion 3D bioprinting. *International Journal of Biological Macromolecules*. 2026;338(Pt 1):149458. doi:10.1016/j.ijbiomac.2025.149458.
3. Duymaz D, Karaoğlu IC, Kizilel S. Effect of Photoinitiation Process on Photo-Crosslinking of Gelatin Methacryloyl Hydrogel Networks. *Macromolecular Rapid Communications*. 2025;46(20):e00376. doi:10.1002/marc.202500376.
4. Rajabi N, Rezaei A, Kharaziha M, Bakhsheshi-Rad HR, Luo H, RamaKrishna S, Berto F. Recent Advances on Bioprinted Gelatin Methacrylate-Based Hydrogels for Tissue Repair. *Tissue Engineering Part A*. 2021;27(11-12):679-702. doi:10.1089/ten.TEA.2020.0350.
5. Lim KS, Galarraga JH, Cui X, Lindberg GCJ, Burdick JA, Woodfield TBF. Fundamentals and Applications of Photo-Cross-Linking in Bioprinting. *Chemical Reviews*. 2020;120(19):10637-10669. doi:10.1021/acs.chemrev.9b00812.

Competing interests

The author is Founder, CEO and CTO of 3Dresyns by Resyner Technologies S.L. No comparative product recommendation is made.

Data availability

No new experimental dataset was generated for this review. The analysis is based on the cited literature and the stated engineering scope.