

Decellularised-Extracellular-Matrix Photocurable Bioinks: Source Tissue, Processing, Methacrylation, Bioactivity and Variability

Tissue-specific composition, light-enabled stabilisation and evidence requirements for reproducible biofabrication

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Abstract

Decellularised extracellular matrix (dECM) bioinks combine tissue-derived biochemical complexity with the geometric control of additive biofabrication. Their central engineering difficulty is that the material is not a single polymer: source tissue, donor state, decellularisation chemistry, solubilisation, sterilisation, storage and functionalisation can all change composition before printing begins. Photocrosslinkable modification can improve shape retention and decouple deposition from slow thermal or enzymatic gelation, but it also adds new variables including substitution level, photoinitiating system, optical attenuation and light dose. This review treats photocurable dECM as a controlled-material-state problem rather than a generic bioink class. It defines the minimum characterisation needed to connect tissue source and processing history to rheology, cure response, retained bioactivity, cell response and printed geometry. Particular attention is given to the distinction between compositional variability that is intrinsic to tissue-derived materials and avoidable variability introduced by processing. The objective is to establish an evidence architecture in which photocuring improves manufacturability without obscuring the biological and chemical state of the dECM.

Keywords: decellularised extracellular matrix; dECM bioink; photocrosslinking; methacrylation; biofabrication; batch variability; tissue engineering

1. Significance and scope

dECM bioinks are attractive because decellularised tissues retain mixtures of collagens, glycosaminoglycans, basement-membrane proteins and other tissue-associated cues that are difficult to reproduce with a single synthetic macromer [1-4]. The same complexity creates a qualification burden. A printed construct can differ because the source tissue differs, because the decellularisation sequence removed or modified different fractions, or because functionalisation and light exposure changed the residual matrix. ER-321 therefore focuses on source-to-print traceability for photocurable dECM systems, not on a specific proprietary tissue recipe.

1.1 Corpus boundary

ER-321 owns the chain from source-tissue provenance through decellularisation, solubilisation and light-enabled modification of dECM to the qualified printed matrix state. ER-322 owns GelMA-specific source and functionalisation variables; ER-323 owns PEG-based bioinks; ER-324 owns fibrin/fibrinogen dual networks; ER-325 owns elastin/tropoelastin-derived materials; ER-326 owns gelatin-norbornene thiol-ene systems; ER-327 owns sequence-defined recombinant-protein materials; ER-328 to ER-330 own volumetric, organoid and vascular fabrication questions rather than dECM material identity.

2. Source tissue is part of the material specification

Species, organ, anatomical region, donor age, disease state, storage interval and pre-processing can alter matrix composition before decellularisation. Reviews of tissue-specific dECM bioinks consistently emphasise that bioactivity depends on the retained matrix rather than on the label dECM alone [1-3]. A defensible specification therefore records source provenance and defines which compositional markers are expected to survive the chosen process.

3. Decellularisation and solubilisation create coupled losses and gains

Physical, chemical and enzymatic decellularisation methods remove cells through different mechanisms and can also extract glycosaminoglycans, alter collagen ultrastructure or leave residual process chemicals. Subsequent milling, pepsin digestion, pH neutralisation and concentration adjustment change rheology and self-assembly. These steps should be recorded as a process history, while acceptance should be based on measurable residual DNA, key matrix markers, solids content, pH and rheological state rather than on recipe identity alone [1,3,4].

4. Methacrylation and other light-enabled modifications

Light-activated dECM systems introduce reactive groups so that the matrix can be stabilised rapidly after or during printing. Methacrylation is common, but thiol-ene and phenol-based strategies are also reported [5]. Degree of functionalisation affects crosslink density, swelling and accessibility of native motifs. It should therefore be measured directly, linked to cure response and interpreted alongside retained matrix composition rather than treated as a purely synthetic-polymer variable.

5. Optical dose, photoinitiation and cell exposure

The useful cure window must satisfy three simultaneous constraints: enough conversion for shape retention, limited damage to encapsulated cells, and minimal loss of biological function. dECM can scatter or absorb light, particularly at higher solids content or with residual pigments. Cure depth, conversion and viability should be measured under the same spectral and geometric conditions used for fabrication. Nominal exposure time alone is not a transferable dose metric. [2,5]

6. Variability and batch qualification

Batch variability should be partitioned into source-derived and process-derived components. A practical qualification plan uses a fixed panel of compositional, rheological, photochemical and biological measurements across multiple independent batches. Large between-batch shifts require investigation even if each batch can still be printed, because identical geometry does not prove identical matrix state. [1,2,5]

7. Minimum evidence for transfer

Transfer between laboratories or printers requires the material state and the light field to be specified together. At minimum, source provenance, decellularisation endpoint, residual DNA, solids content, functionalisation, viscosity or moduli, spectral irradiance, dose, printed fidelity and a defined cell or bioactivity assay should travel with the result. This reporting structure supports comparison without requiring disclosure of proprietary process details. [1-5]

7.1 Evidence hierarchy and transfer

For dECM, evidence transfer is credible only when tissue provenance and decellularisation history remain traceable to composition, photocurable modification and the printed biological response. A mechanical match obtained from a different tissue source is not evidence of biological equivalence, and a similar DNA-removal endpoint does not establish preservation of the same matrix cues [1-5].

7.2 Research priorities

Priority experiments should separate donor/tissue variability from processing variability, quantify what is lost during decellularisation and digestion, and measure how light-enabled modification changes both network formation and retained bioactivity. Multi-batch studies with the same analytical panel are more valuable than additional one-off demonstrations of printability [1,2,5].

7.3 Coupled state variables

The dominant coupled variables are source tissue, solids content, residual matrix composition, degree of modification, optical attenuation and delivered dose. Their covariance is consequential: increasing modification can improve geometric stability while simultaneously changing ligand accessibility, degradation and cell-matrix signalling [1,4,5].

7.4 Decision logic for qualification

A dECM transfer decision should therefore require concordance at three levels: starting-material provenance, post-processing matrix state, and application-relevant biological function. A batch that prints to the same dimensions but differs materially in matrix markers or cell response should not be treated as equivalent [1-3].

Table 1. Minimum qualification matrix for decellularised-extracellular-matrix photocurable bioinks.

Domain	Minimum measurement	Primary interpretation
Source	species, tissue, donor and storage provenance	defines starting biological variability
Decellularisation	residual DNA and selected ECM markers	separates cell removal from matrix preservation
Functionalisation	degree of modification and solids content	defines available photocurable groups
Photocure	spectrum, irradiance, dose and gel/conversion endpoint	links light field to material state
Biology	defined viability or functional assay	tests whether process-compatible is also bio-compatible
Geometry	feature fidelity, swelling and stability	tests manufacturing outcome

8. Interpretation matrix

Interpretation must discriminate source-driven variability from processing-driven variability. The same geometric symptom can arise from altered matrix composition, digestion, functionalisation or optical dose, so each diagnosis needs a control that localises the change in the material-state chain [1,2,5].

Table 2. Diagnostic interpretation matrix for decellularised-matrix bioink variability.

Observation	Plausible cause	Discriminating control
Same cure dose, different stiffness	batch composition or functionalisation differs	compare solids, substitution and conversion
Good print fidelity, weak cell response	processing or dose damaged biological function	matched unmodified/low-dose controls
Large viscosity shift between batches	source or digestion variability	source-normalised solids and molecular-state checks
Surface cure but weak interior	attenuation or oxygen/dose limitation	depth-resolved conversion and optical measurement
Sterilised batch cures differently	sterilisation changed chemistry or optics	pre/post sterilisation matched characterisation

9. Limitations and evidence gaps

The dECM literature remains difficult to compare because tissue sources, donor states, decellularisation protocols, solubilisation routes and retained-matrix assays vary widely. Quantitative dose-response data that link compositional loss to printing and long-term biological function are sparse, and many studies report viability without a source-matched functional comparator [1-5].

10. Conclusions

Photocurable dECM should be qualified as a provenance-sensitive biological material, not as a generic hydrogel. Reproducibility depends on documenting what tissue entered the process, what matrix state survived decellularisation and functionalisation, and how the selected light dose converts that state into a stable construct without erasing the biological function that motivated dECM use [1,2,5].

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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.