

Fibrin and Fibrinogen in Photocurable Biofabrication: Enzymatic–Photo Dual Networks, Contraction and Remodelling

Separating thrombin-driven fibrin assembly from light-driven stabilisation in printed living constructs

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ER-324 · Engineering Review · Version 0.5 · 28 September 2026

Abstract

Fibrin is biologically familiar and strongly cell-remodelable, but its rapid enzymatic assembly and low pre-gel shape fidelity complicate additive manufacturing. Photocurable fibrin or fibrinogen-derived systems address this limitation through dual-network strategies: thrombin-driven fibrin formation provides a native fibrous matrix, while light-reactive groups or a second photocurable polymer provide additional geometric stabilisation. These mechanisms should not be conflated. This review distinguishes fibrinogen state, enzymatic conversion, covalent photochemistry, matrix contraction and proteolytic remodelling as separate state variables. It examines methacrylated fibrinogen and fibrin-containing hybrid bioinks, and it proposes measurements that can determine whether a printed construct is stabilised by fibrin architecture, the photocured network, or both. Particular emphasis is placed on contraction, because cell-mediated compaction can be biologically meaningful while simultaneously destroying geometric fidelity. The qualification objective is therefore not maximal stiffness but controlled evolution of structure under cell-driven remodelling.

Keywords: fibrin; fibrinogen; methacrylated fibrinogen; dual network; photocrosslinking; contraction; remodelling

1. Significance and scope

Fibrin forms when thrombin converts soluble fibrinogen into fibrin that assembles into a fibrous network. This biological gelation supports cell adhesion and remodelling but is difficult to synchronise with printing because ungelled fibrinogen has limited shape retention and gelled fibrin can be difficult to extrude [1]. Photocurable modifications and hybrid matrices add a second stabilisation mechanism [2-4].

1.1 Corpus boundary

ER-324 owns fibrin/fibrinogen biofabrication in which enzymatic fibrin formation and light-driven stabilisation are combined or compared. ER-322 owns GelMA chemistry even when gelatin is blended with fibrin, and ER-330 owns vascular-network architecture and perfusion qualification. Other bioink families remain with ER-321, ER-323 and ER-325 to ER-327.

2. Enzymatic network formation

Thrombin concentration, fibrinogen concentration, calcium and temperature influence fibrin assembly kinetics and microstructure. The resulting network can be highly remodelable and susceptible to proteolysis. For printing, gelation must be timed relative to deposition or generated after patterning. Process records should therefore distinguish the soluble precursor state from the fibrin network state. [1]

3. Photocurable fibrinogen and hybrid stabilisation

Methacrylated fibrinogen provides one route to direct light-driven covalent crosslinking while retaining cell-interactive protein features [2]. Other systems combine fibrin with a separate photocurable macromer such as gelatin derivatives [4]. These are mechanistically different. The fraction of mechanical load carried by the photopolymer network versus fibrin should be tested using matched controls that omit thrombin or omit the light-reactive component.

4. Contraction as a coupled biological-mechanical output

Cells can contract fibrin networks substantially. Contraction may indicate active matrix interaction, but in a dimensionally specified construct it is also a manufacturing drift. External dimensions, channel dimensions and local strain should therefore be followed over time, together with cell density and matrix composition. A single day-zero print-fidelity image is insufficient. [1,4]

5. Remodelling and degradation

Fibrinolysis and cell-secreted proteases can change mass, modulus and permeability. Photocrosslinking may slow or spatially constrain this remodelling. Qualification should include a time axis and, where relevant, protease challenge. Loss of modulus with retained shape can indicate a different mechanism from gross geometric collapse. [1,2]

6. Optical and chemical compatibility

Protein-rich matrices can alter optical transmission, and added photoinitiators may affect cells. Spectral dose should be reported together with fibrinogen and photocurable-polymer concentrations. In dual networks, the sequence of thrombin treatment and light exposure can change diffusion and microstructure, so sequence is part of the process definition. [2,5]

7. Qualification strategy

A minimum evidence set separates precursor composition, enzymatic conversion, photochemical conversion, early mechanics and time-dependent remodelling. This prevents a hybrid bioink from being described as fibrin-based when most of its dimensional stability is actually supplied by a second polymer network. [1-5]

7.1 Evidence hierarchy and transfer

Fibrin systems require the enzymatic state and the photo-crosslinked state to be measured separately. Thrombin/factor-XIII-driven fibrin formation, methacrylated fibrinogen or secondary photochemistry can each contribute to stiffness, contraction and degradation, so a final modulus alone cannot identify which network carries load [1-5].

7.2 Research priorities

Priority experiments should vary enzymatic and photo-crosslinking contributions independently, then follow contraction, remodelling and cell function over time. Spatial stiffening studies show that local light-driven modification is feasible, but the biological consequences of heterogeneous reinforcement require direct measurement [2-4].

7.3 Coupled state variables

The central coupling is between a remodelable fibrin network and any added covalent stabilisation. More photo-crosslinking can preserve geometry while reducing contraction or cell-mediated reorganisation; too little can leave the construct unable to resist handling or perfusion loads [1-4].

7.4 Decision logic for qualification

Qualification should therefore define an allowed trajectory, not just an initial stiffness: early handling stability, subsequent contraction, degradation/remodelling and the intended cell function must all be acceptable. The acceptable balance is application-specific and cannot be inferred from cure dose alone [1,2,4].

Table 1. Minimum qualification matrix for fibrin and fibrinogen in photocurable biofabrication.

State	Measurement	Purpose
Fibrinogen precursor	concentration and rheology	defines printable starting state
Enzymatic conversion	thrombin/calcium conditions and gelation time	defines fibrin assembly
Photocure	reactive-group identity, dose and conversion	defines covalent stabilisation
Mechanics	early modulus and stress relaxation	separates initial support mechanisms
Contraction	time-resolved geometry	captures cell-mediated compaction
Remodelling	mass/mechanics under culture or protease challenge	captures evolving matrix state

8. Interpretation matrix

Fibrin failure analysis should ask whether the enzymatic network, the photo-network or cell-driven remodelling dominates the observed change. Matched controls without the photo-step and without the enzymatic step are especially informative [1-5].

Table 2. Diagnostic interpretation matrix for fibrin dual-network remodelling.

Observation	Interpretation	Control
Construct shrinks while cells remain viable	cell-mediated fibrin contraction	acellular and protease-modulated controls
Thrombin-free sample still holds shape	photocured network dominates geometry	compare mechanical fractions
Light-only sample is weak	fibrin assembly carries load	matched enzymatic network
Channels narrow over culture	contraction/remodelling, not printing error alone	time-resolved channel imaging
Same dose cures differently at higher protein	optical/chemical attenuation changed	transmission and conversion profile

9. Limitations and evidence gaps

Comparisons are limited by variation in fibrinogen source, thrombin/calcium conditions, methacrylation, photochemistry and cell-mediated contraction. Long-term studies that quantify both network contributions and relate them to remodelling are relatively scarce [1-5].

10. Conclusions

Photocurable fibrin biofabrication is best treated as a dual-network problem. Engineering control comes from balancing rapid geometric stabilisation against the native fibrin network's capacity to contract, degrade and remodel; that balance must be demonstrated with time-resolved mechanical and biological evidence [1-5].

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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.