

PEG-Based Photocurable Bioinks: Architecture, Functionalisation, Mesh Size, Bioinertness and Bioactive Modification

Synthetic-network control from molecular architecture to cell-interactive printed constructs

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Abstract

Poly(ethylene glycol) (PEG)-based photocurable systems provide unusually direct control over macromer architecture, crosslink density and network chemistry, making them valuable reference materials for mechanistic biofabrication. Their reproducibility also exposes a central limitation: an unmodified PEG network is comparatively bioinert and does not automatically provide cell-adhesive or degradable cues. This review examines PEG diacrylate, PEG methacrylate and multifunctional thiol-ene/norbornene architectures as engineering platforms rather than as a single material class. It links molecular weight, functionality and concentration to mesh size, swelling, transport and stiffness, then separates these physical variables from deliberate biological modification using peptides, proteins or degradable linkers. The review also treats light dose and conversion as part of the network state. The resulting qualification framework is intended to distinguish reproducible synthetic control from apparent biological performance that actually arises from added ligands, copolymers or degradable crosslinks.

Keywords: polyethylene glycol; PEGDA; PEG-norbornene; photocrosslinking; mesh size; bioinert hydrogel; bioactive modification

1. Significance and scope

PEG-derived bioinks are attractive because molecular weight, functionality and architecture can be specified more precisely than for many natural macromers [1-4]. This enables controlled studies of network structure but also demands clear reporting: PEGDA, PEGMA and PEG-norbornene systems differ in polymerisation mechanism and in the relation between formulation and final mesh.

1.1 Corpus boundary

ER-323 owns PEG-based photocurable bioinks as synthetic-network architectures, including molecular architecture, mesh size, swelling, bioinertness and deliberate bioactive modification. ER-326 owns gelatin-norbornene thiol-ene networks; PEG-norbornene examples are used here only to discuss PEG architecture and mesh control, not to take ownership of gelatin-norbornene reaction chemistry. ER-321, ER-322 and ER-324/325/327 retain their natural-macromer families, while ER-328 to ER-330 retain process and construct applications.

2. Architecture and functionality

Linear difunctional PEGDA forms chain-growth networks, whereas multi-arm PEG-norbornene or thiol-ene systems can be designed as step-growth networks with more explicit stoichiometric control. Molecular weight between reactive groups, arm number and reactive-group conversion all affect the effective network strand length. These variables should be reported directly rather than collapsed into polymer mass fraction. [1,4]

3. Mesh size, swelling and transport

Mesh size is not a directly visible printing parameter, yet it governs diffusion of nutrients, proteins and degradation products. It is coupled to polymer concentration, crosslink functionality, conversion and swelling. A useful qualification strategy combines equilibrium swelling with modulus and, where transport matters, diffusion or permeability measurements. Stiffness alone does not uniquely specify the mesh. [1,4]

4. Bioinertness as both advantage and limitation

PEG resists nonspecific protein adsorption relative to many natural polymers. This can reduce uncontrolled interactions and make PEG useful for mechanistic experiments, but cells may require added adhesion ligands or matrix proteins. Biological performance should therefore be attributed to the complete functionalised system, not to PEG generically. [2,3]

5. Bioactive and degradable modification

Cell-adhesive peptides, enzyme-cleavable linkers and growth-factor-binding motifs can be incorporated into PEG networks. Such additions change both biology and network structure. Their density, spatial distribution and effect on conversion should be quantified. A degradable linker may increase remodelling but also lower long-term geometric stability, so biological gain and mechanical persistence should be tested together. [2,3,5]

6. Photocure and process transfer

PEG-based systems can be fabricated by extrusion followed by curing or by lithographic processes. Transfer requires matching wavelength, irradiance, optical path and oxygen environment. In step-growth systems, off-stoichiometry can leave residual functional groups even at high overall conversion; in chain-growth systems, heterogeneous kinetic chains can create a different network architecture at similar bulk modulus. [1,5]

7. Qualification logic

PEG is most useful as a controlled platform when architecture, chemistry and biological modification remain separable in the evidence. A minimum report includes molecular weight, functionality, concentration, stoichiometry where relevant, photoinitiation, dose, conversion or gel fraction, swelling, modulus, ligand density and degradation mechanism. [1-5]

7.1 Evidence hierarchy and transfer

PEG evidence should connect precursor architecture and functionality to network density, swelling, transport and biological modification. Molecular weight or wt% alone is insufficient because branch number, end-group conversion and degradable linkers can produce different meshes at the same solids content [1-5].

7.2 Research priorities

Priority studies should report precursor distributions and functional-group conversion, then test transport and cell response across independently varied mesh size and ligand density. This is particularly important when bioactive peptides or degradable sequences are introduced, because biological effects can otherwise be confounded with changes in network mechanics [1-4].

7.3 Coupled state variables

PEG systems couple network architecture, water uptake and diffusion. Increasing crosslink density can improve fidelity yet restrict macromolecular transport; adding bioactive groups can also change effective functionality and swelling. These couplings should be measured rather than inferred from nominal formulation labels [1,2,4].

7.4 Decision logic for qualification

Qualification should separate structural performance from biological modification: first establish the PEG network state and transport window, then verify that added ligands or degradable motifs deliver the intended cell interaction without invalidating the mechanical and geometric state [1-5].

Table 1. Minimum qualification matrix for PEG-based photocurable bioinks.

Design variable	Primary effect	Qualification metric
Macromer molecular weight	strand length and swelling	molecular specification plus swelling
Functionality/arm number	network connectivity	reactive-group density and conversion
Concentration	mesh and modulus	solids plus equilibrium swelling
Ligand density	cell adhesion/signalling	defined molar density or conjugation level
Degradable linker	remodelling and stability	mass loss/mechanics under defined enzyme conditions
Light dose	conversion and residual groups	spectral dose plus conversion endpoint

8. Interpretation matrix

A PEG construct that is dimensionally accurate can still be biologically unsuitable because mesh size, transport or ligand presentation differs. Interpretation therefore requires independent measurements of network state, swelling/transport and the engineered biological cue [1-4].

Table 2. Diagnostic interpretation matrix for PEG-bioink mesh and bioactivity.

Observation	Potential cause	Discriminating test
Same modulus, different cell spreading	ligand density or mesh differs	ligand assay plus swelling/diffusion
Rapid swelling	low crosslink density or conversion	gel fraction and conversion
Good acute viability, poor remodelling	network nondegradable or mesh restrictive	degradation and transport assay
Dose change alters stiffness	conversion is process-limited	conversion-dose curve
Different behaviour at same wt%	macromer MW/functionality differs	molecular specification check

9. Limitations and evidence gaps

PEG bioink literature spans PEGDA, multi-arm PEGs, degradable and norbornene-functional systems with different molecular-weight conventions and incomplete reporting of conversion. Direct comparison of mesh size and transport is therefore limited, and long-duration links between synthetic-network state and tissue maturation remain sparse [1-5].

10. Conclusions

PEG-based photocurable bioinks are valuable because architecture can be engineered deliberately, but that same design freedom makes nominal concentration a poor identifier. Qualification should track precursor architecture, conversion, swelling/mesh state and any bioactive modification as separate but coupled measurands [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.