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Design and Synthesis of Light Activated Biomimetic Peptide-Based Soft Materials

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BEaTS

Abstract:

Naturally derived biomaterials offer biocompatibility but may lack batch-to-batch consistency and precise chemical tunability, limiting their use in advanced applications like drug delivery and tissue repair. Synthetic biomimetic peptides can address these limitations by producing consistent, peptide-only hydrogels that are both biocompatible and tunable in their properties at the atomic level.

Using optimized solid-phase peptide synthesis, we produced high-purity biomimetic peptides engineered with light responsive functional groups for rapid, light-triggered crosslinking. The peptides were purified by RP-HPLC, with identify verified by mass spectrometry, and analyzed for stable conformation and supramolecular assembly through circular dichroism. To leverage the spatial and temporal control offered by light activation, we introduced alkene and thiol moieties, enabling rapid thiol-ene reactions that allow for controlled material assembly. By systematically varying the peptide structure, we investigated how functional group configuration impacts the physical properties of hydrogels.

Our custom-designed biomimetic peptides formed strong hydrogels with finely tunable mechanical properties. Rheometry demonstrated that increasing reactive group density enhanced gel elastic modulus (G') up to the solubility limit. Allowing time for peptide folding of 1 hour before activation further strengthened the hydrogels, especially at lower concentrations.

Keywords: hydrogels; biomimetic peptides; light activation; solid-phase peptide synthesis

Natural vs Synthetic Biomaterials

Natural Biomaterials

(e.g., chitosan, collagen)

✓ Biocompatible

✓ Biodegradable

✗ Batch-to-batch consistency

✗ Chemical tunability

Synthetic Collagen-Like Peptides (CLPs)

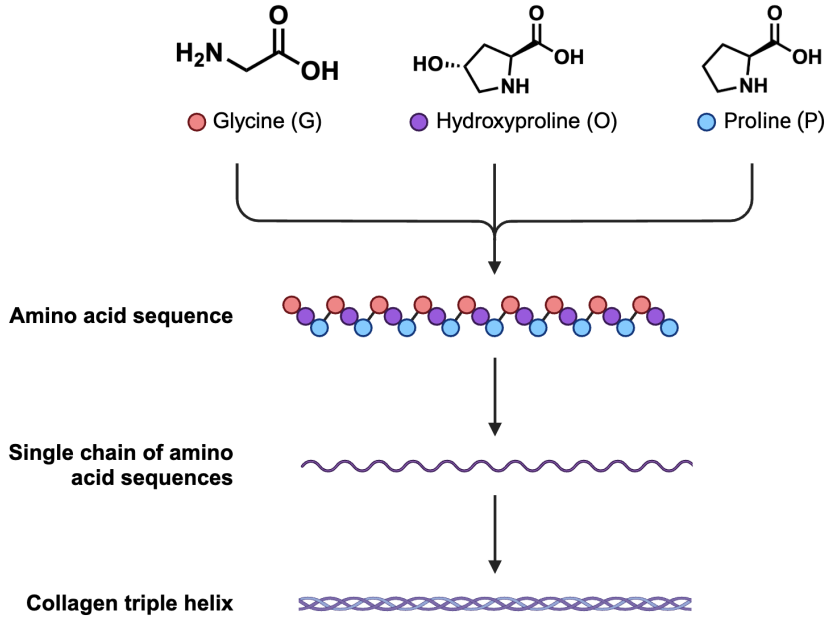
✓ Hybrid material (mimics collagen structure)

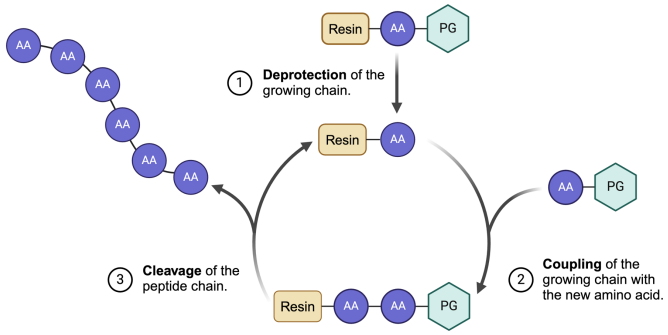
✓ Biocompatible

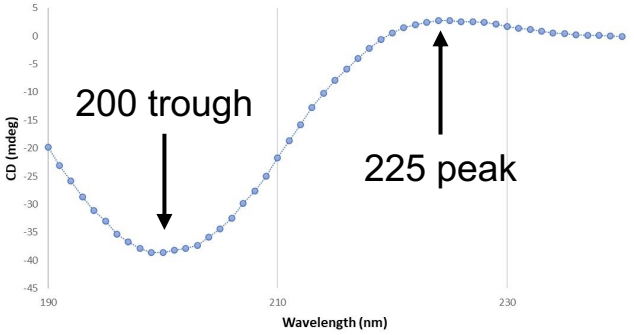
✓ Biodegradable

✓ Consistent

✓ Control over structure (peptide sequence)

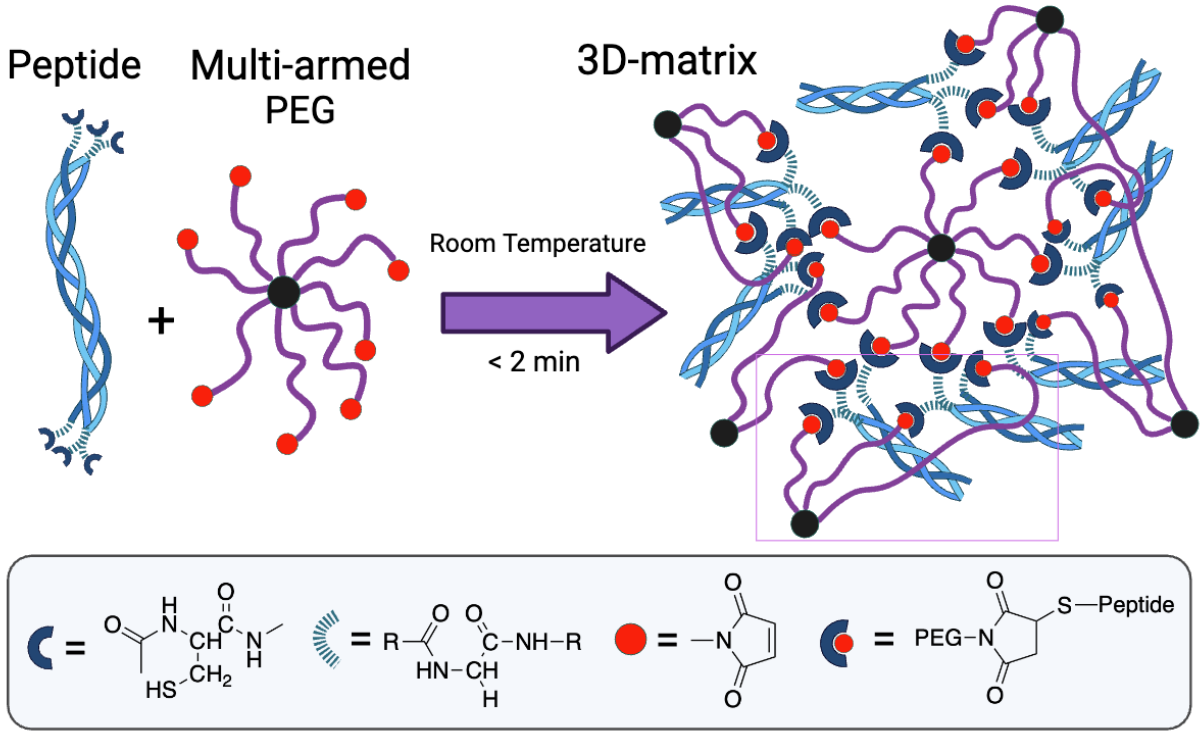






$$R_{pn} = \frac{\lambda_{225}}{\lambda_{200}}$$

Previous Work: PEG-based 3D matrix formation



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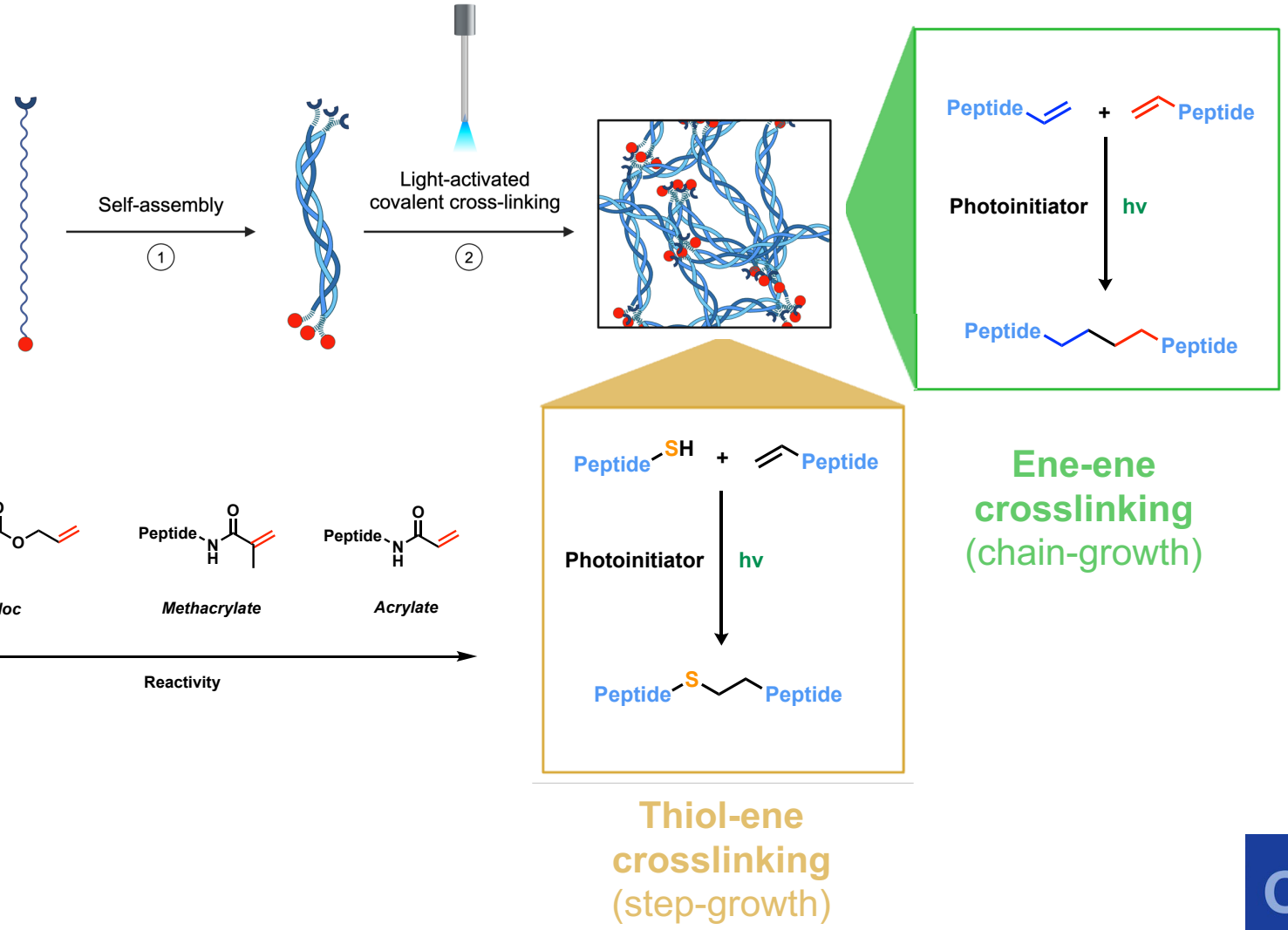
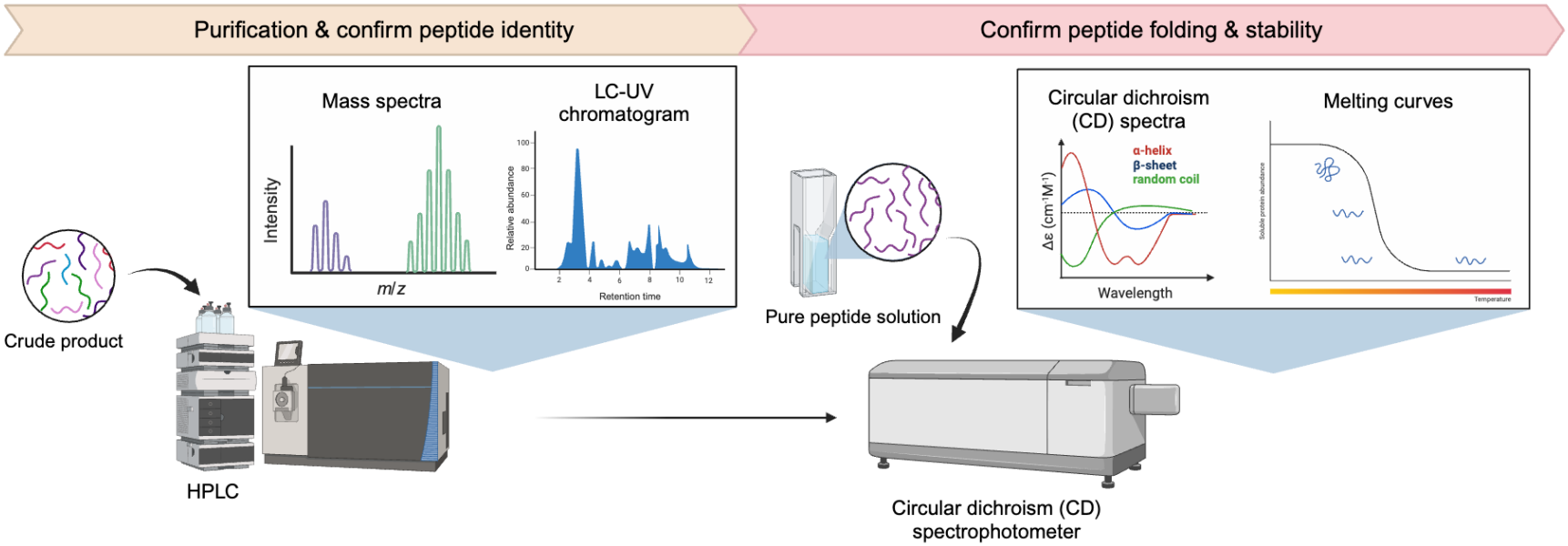
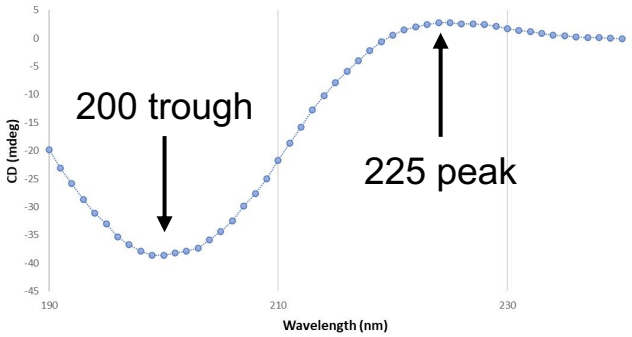
Peptide-only 3D matrix forms by light-activated crosslinking



Peptide Purification and Characterization

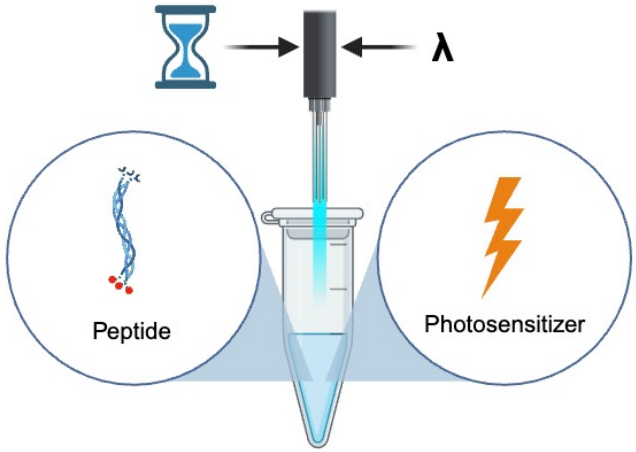


$$R_{pn} = \frac{\lambda_{225}}{\lambda_{200}}$$

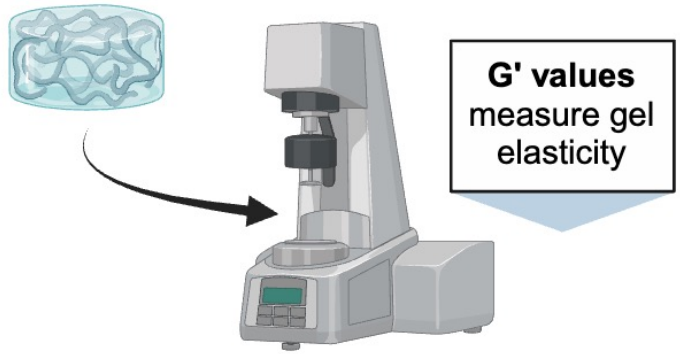


Hydrogel Assembly and Characterization

1 Optimize hydrogel assembly



2 Characterize hydrogel



Rheometer

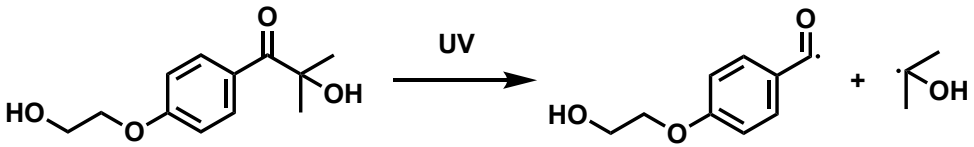
Current conditions

Peptide: 5% w/v

Photoinitiator: Irgacure 2959 (Type 1, 365 nm)

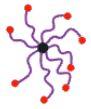
Wavelength: UVA

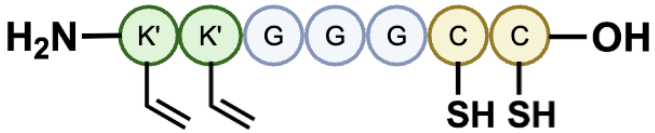
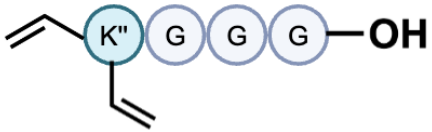
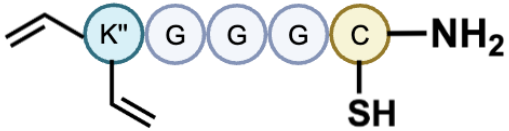
Buffer: 1x PBS (pH 7.4)



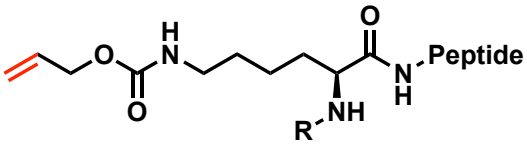
Irgacure 2959

Short peptides were insoluble

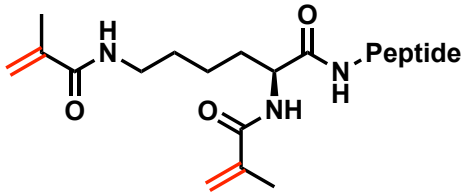
Compound	Gelation?
8-arm PEG acrylate 20k 	Yes

Short Peptide	Gelation?
	Insoluble
	Insoluble
	Insoluble

K' = Lys(alloc)



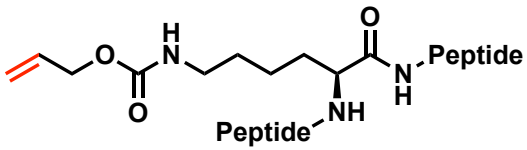
K" = MA-Lys(ε-MA)



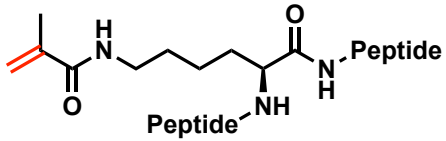
Ene-ene CLPs did not form hydrogels

Collagen-Like Peptides (CLPs)	Gelation?
	No
	No
	No

K' = Lys(alloc)



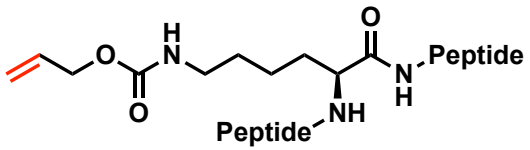
K'' = Lys(ε-MA)



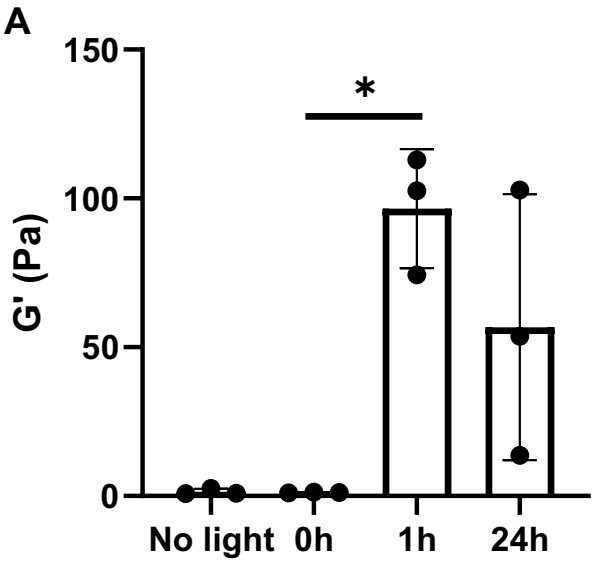
Thiol-ene CLPs formed soft gels

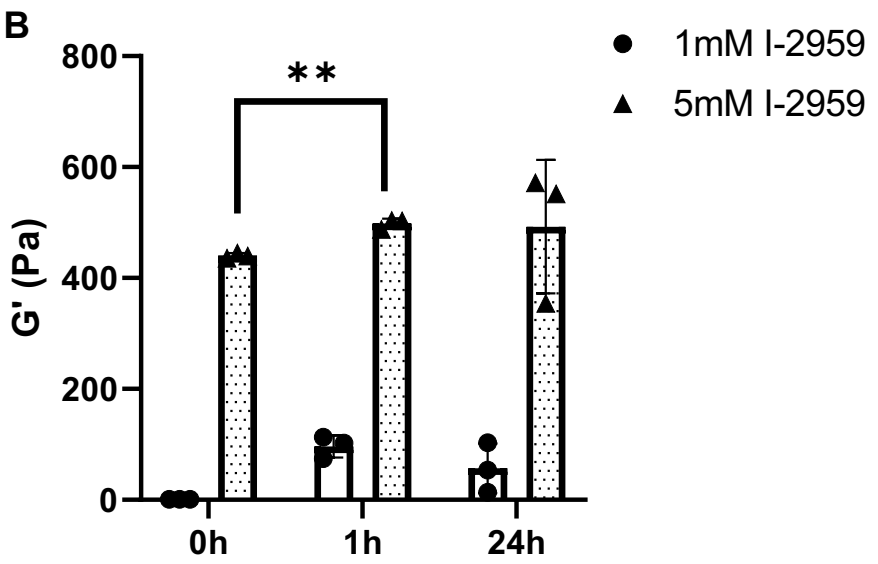
Collagen-Like Peptides (CLPs)	Gelation?
	Yes
	Yes
	Yes
	Yes
	Yes
	Insoluble

K' = Lys(alloc)

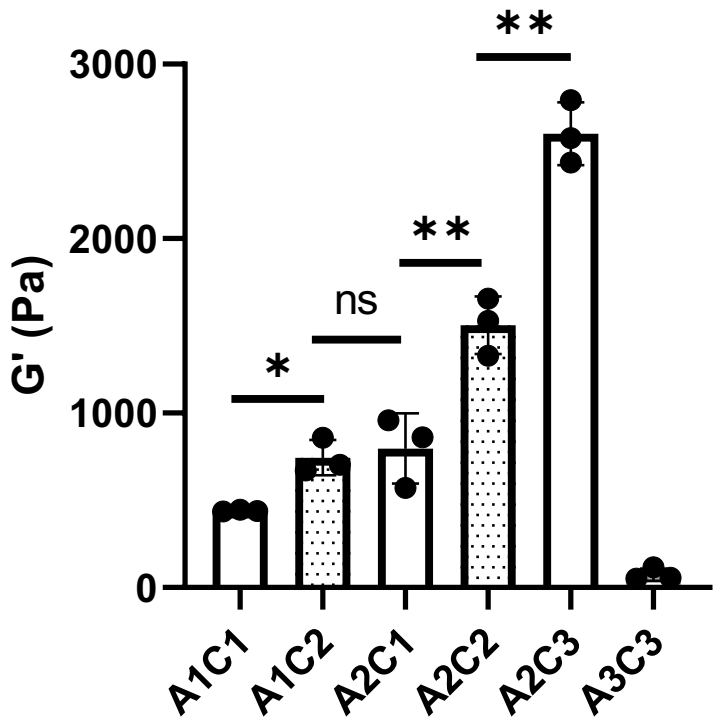


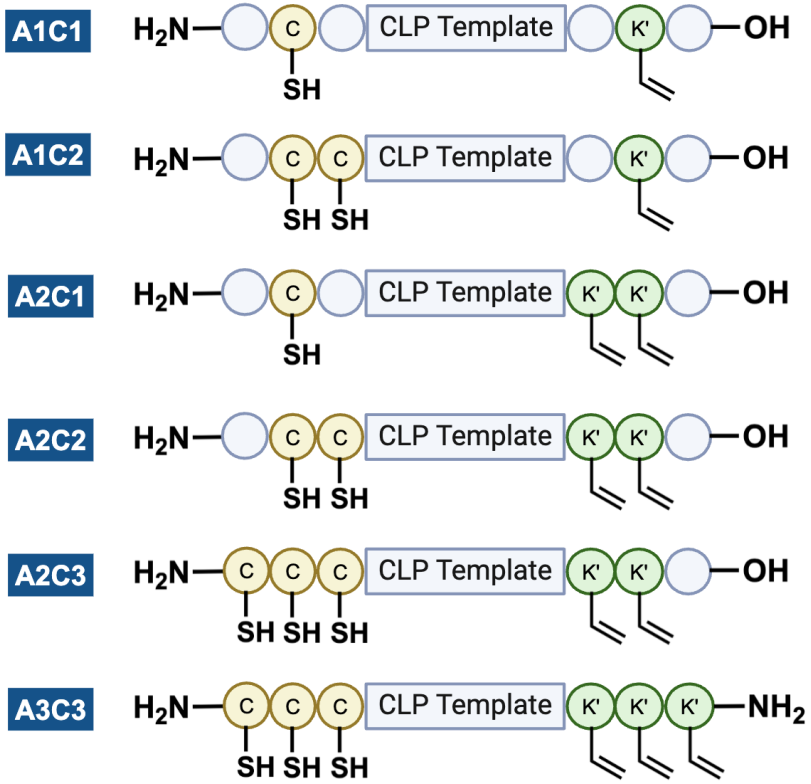
Gel mechanical properties improve after 1h folding



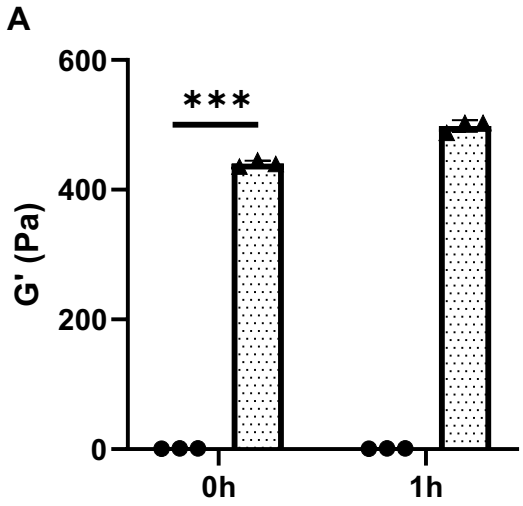


Increasing junction functionality (f) strengthens gels

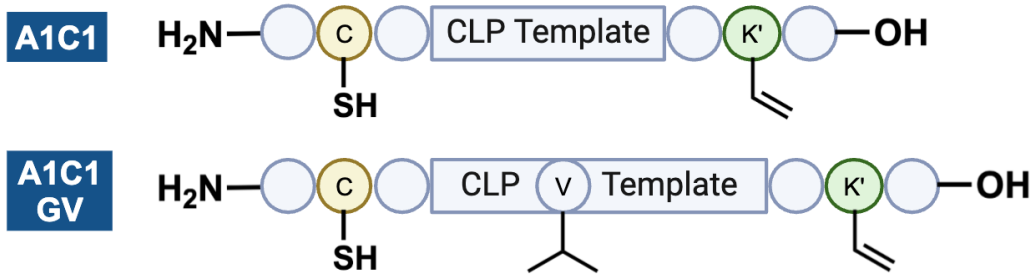


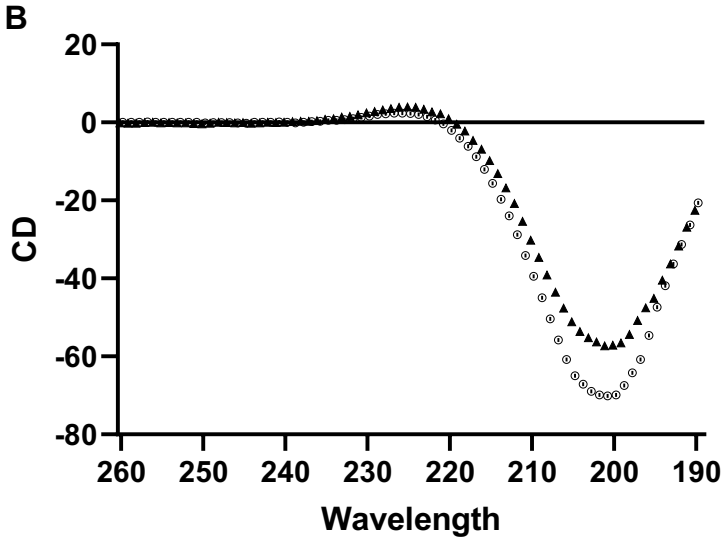


No hydrogel forms when CLP folding is disrupted



● A1C1 GV
▲ A1C1



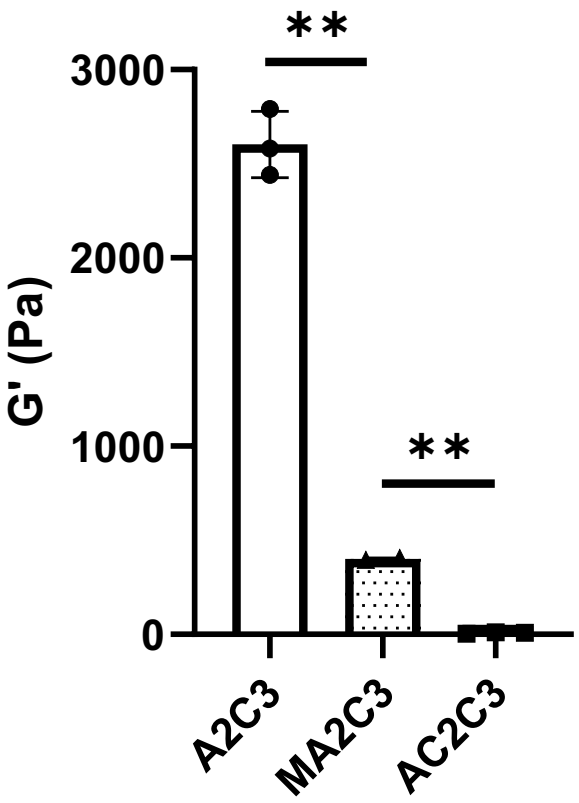


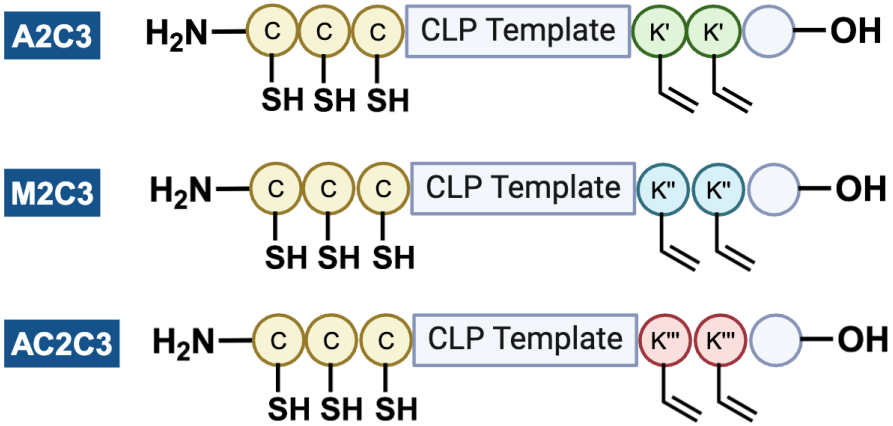
▲ A1C1 Rpn = 0.109
○ A1C1 GV Rpn = 0.034

$$R_{pn} = \frac{\lambda_{225}}{\lambda_{200}}$$

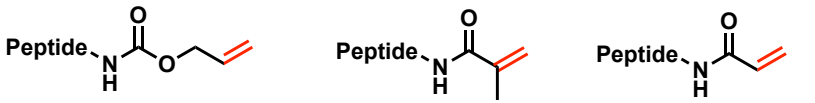
Poly(Pro)-II helix:	<0.005	R_{pn}
Collagen:	~0.12	R_{pn}

MA and Ac CLPs form weak to no gels





K' = Alloc
K'' = Methacrylate
K''' = Acrylate



Alloc *Methacrylate* *Acrylate*

Reactivity

Future Directions

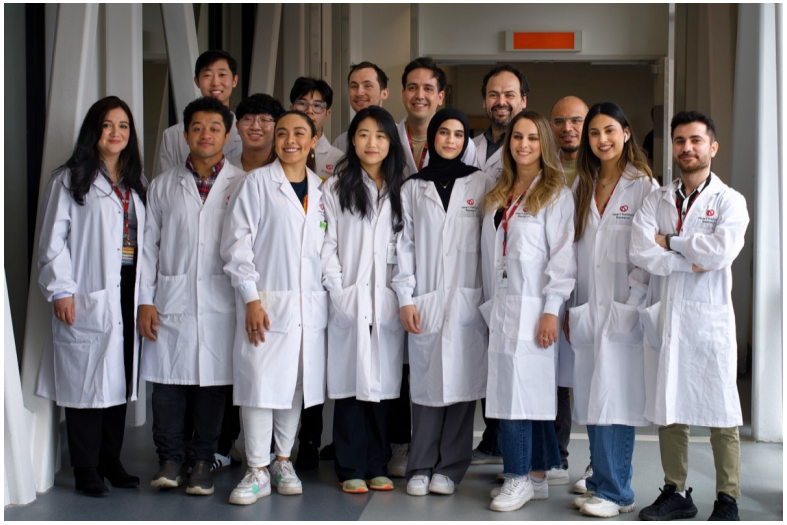
- Explore alternative visible light photoinitiators
- Investigate covalently linking photoinitiators to peptides
- Further optimize peptide concentration to find critical gel points
- Evaluate adhesive and tensile strength of hydrogels

Conclusions

- We successfully synthesized a library of light-activated CLPs capable of forming hydrogels
- We identified critical factors influencing hydrogel properties:
  - Peptide folding (collagen-like triple helix)
  - Photoinitiator conditions (higher concentration improves gel strength)
  - Chemical reactivity (Alloc groups are more effective than methacrylate or acrylate for forming strong hydrogels

Thank you!

Alex Ross
Aidan MacAdam
Dr. Erik Suuronen
Dr. Emilio Alarcon
And the BEaTS lab!



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