Decoding Pentapeptide Self-Assembly Using Molecular Dynamics: from Aggregation to Architecture

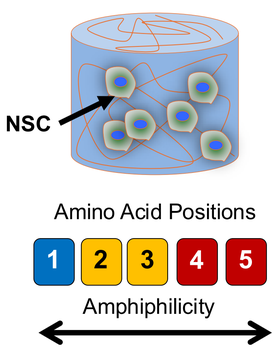
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Background

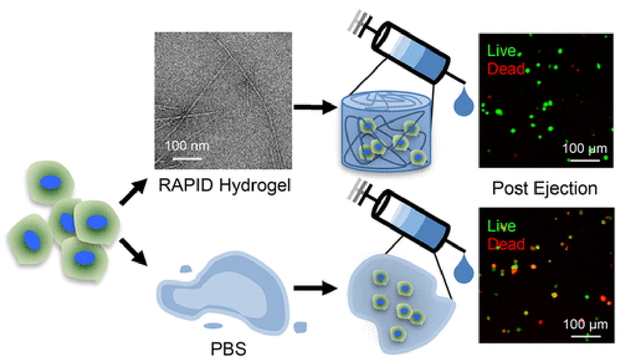
Injectable hydrogels are promising for neural stem cell (NSC) delivery and tissue engineering, requiring shear-thinning and self-healing properties.



- **Pentapeptides** can **self-assemble** into RAPID hydrogels, **mimicking** the **extracellular matrix** to support cell growth and differentiation.
- Understanding **peptide sequence effects** on self-assembly **permits designer gelation** and **mechanical properties** for biomedical applications.

Computational modeling provides insights into **peptide self-assembly**, guiding experimental peptide design.

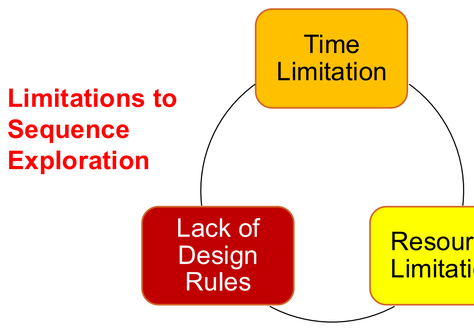
Experimental Motivation



Tang et al.[1]

Using RAPID hydrogel increases cell viability significantly.

(Rapidly Assembling Pentapeptides for Injectable Delivery)

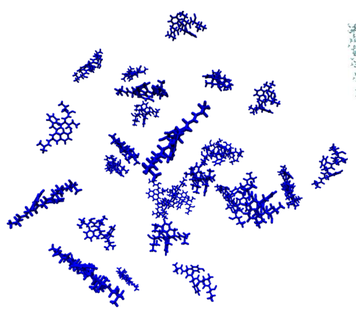


Limitations to Sequence Exploration

Even for a peptide with five amino acids
The total number of sequences possible is
3,200,000

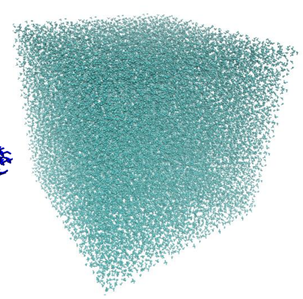
Molecular Dynamics Setup

30 Peptides



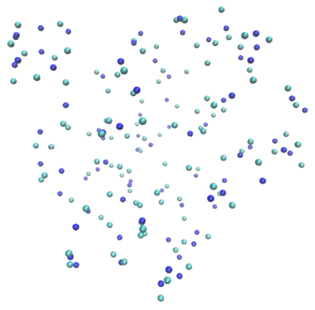
Protein Force Field
FF19SB

Water Box

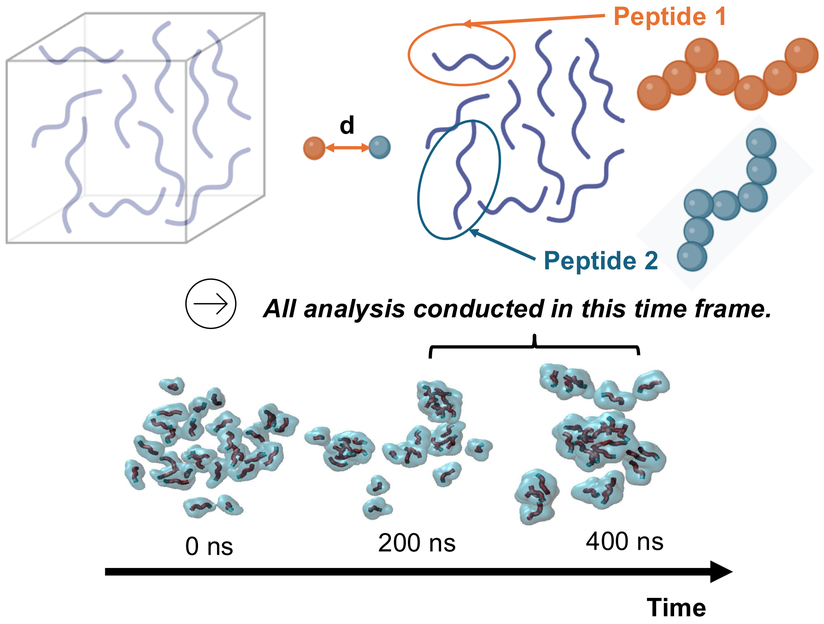


Water Force Field
Optimal Point Charge (OPC)

150 mM Salt



Additional ions were added to neutralize the system



All analysis conducted in this time frame.

Acknowledgments

Lampe Biomaterials Group

Bilodeau Group

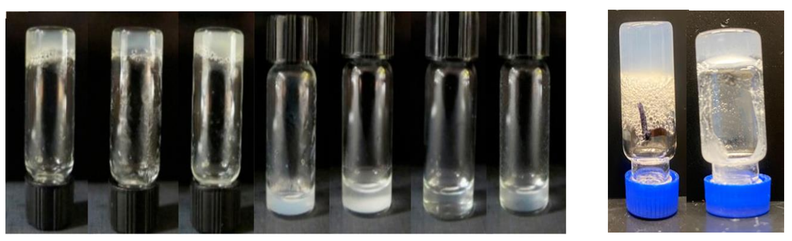
RESEARCH COMPUTING

NSF

Molecular Dynamics Outcome Matches Experimental Results

KYFIL
- **A**YFIL / K**A**FIL / KY**A**IL / KYF**A**L/
- KYFI**A** / KYFI**V**/ KFFFL / KYYYL

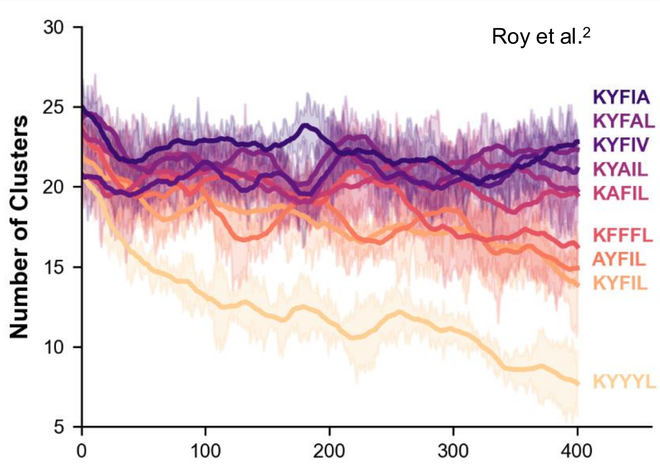
Test Sequence



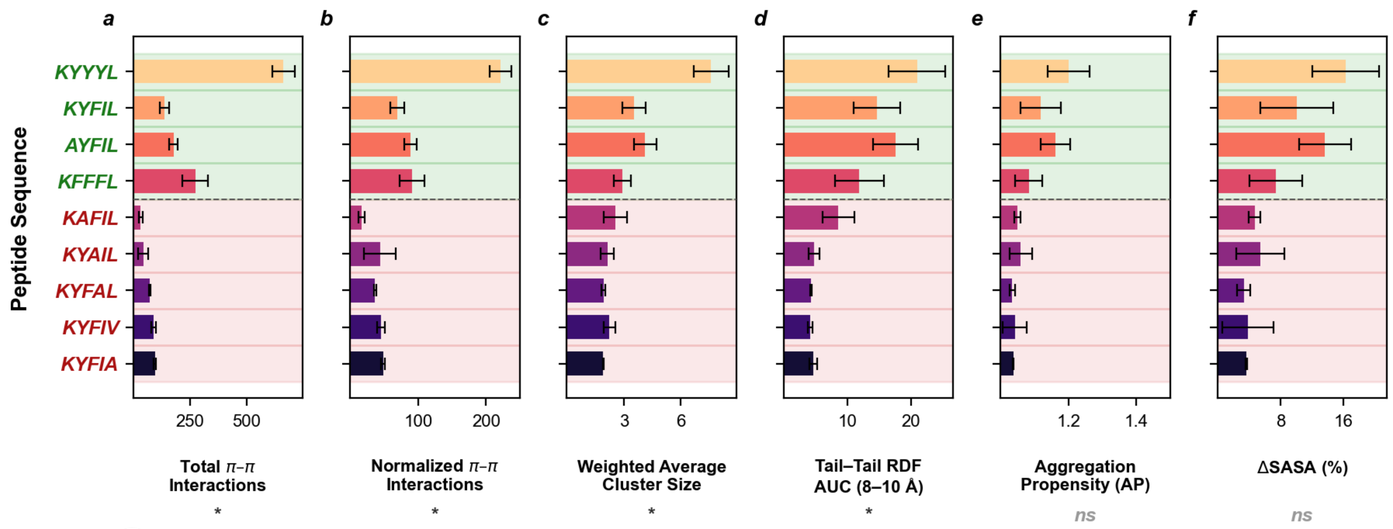
KYFIL AYFIL KYFAL KYFIV KYFIA KAFIL KYAIL

KFFFL KYYYL

Gelling → Non-Gelling



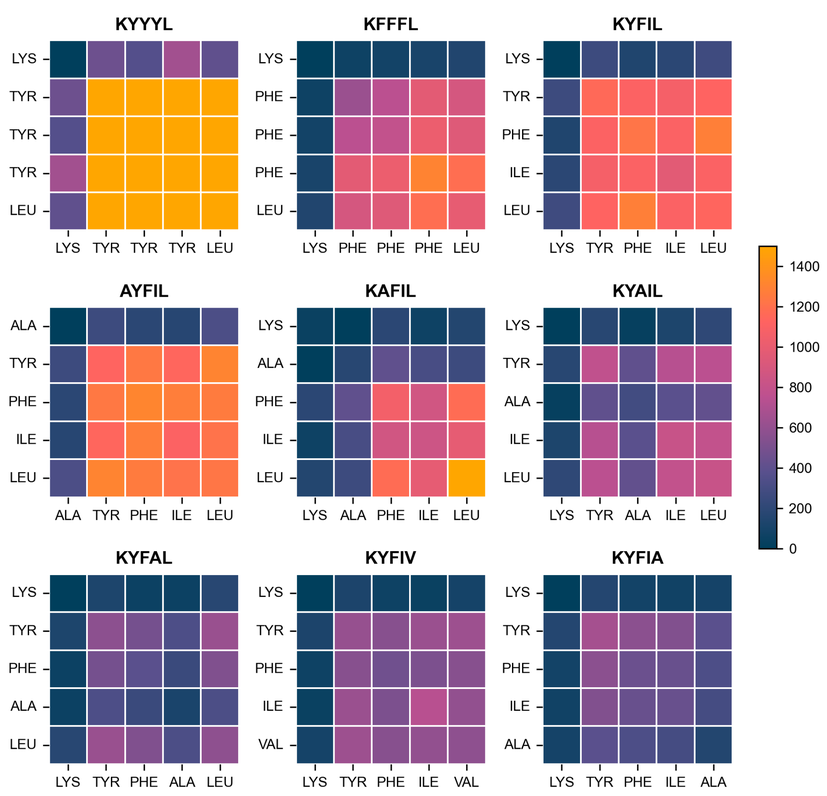
Lower number of clusters indicate higher assembly of peptides.



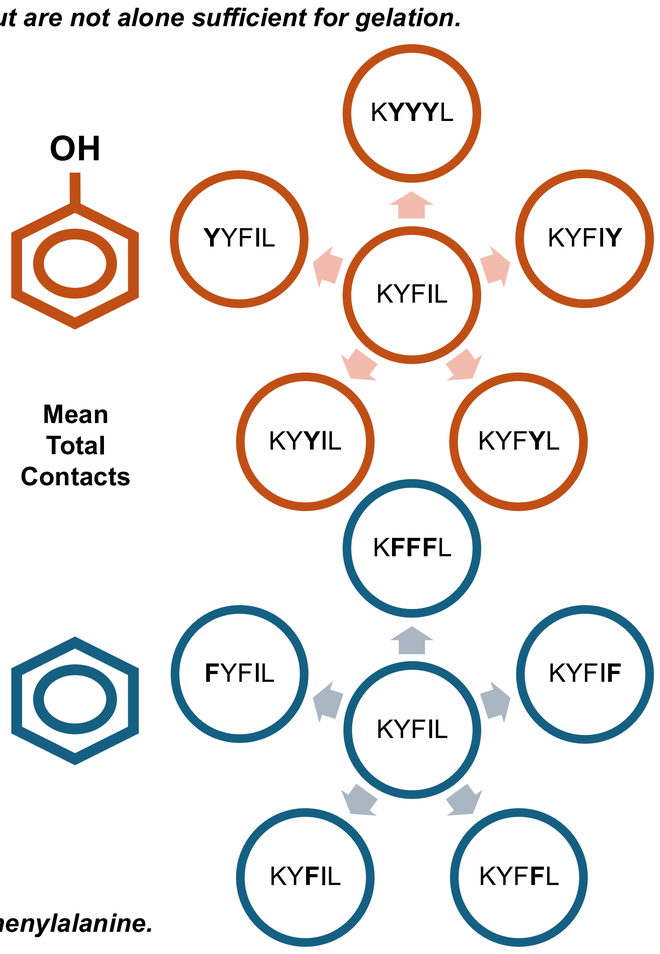
Order Parameters derived from MD simulation can differentiate Self-Assembly.

Aromatic-biased Contact Pattern

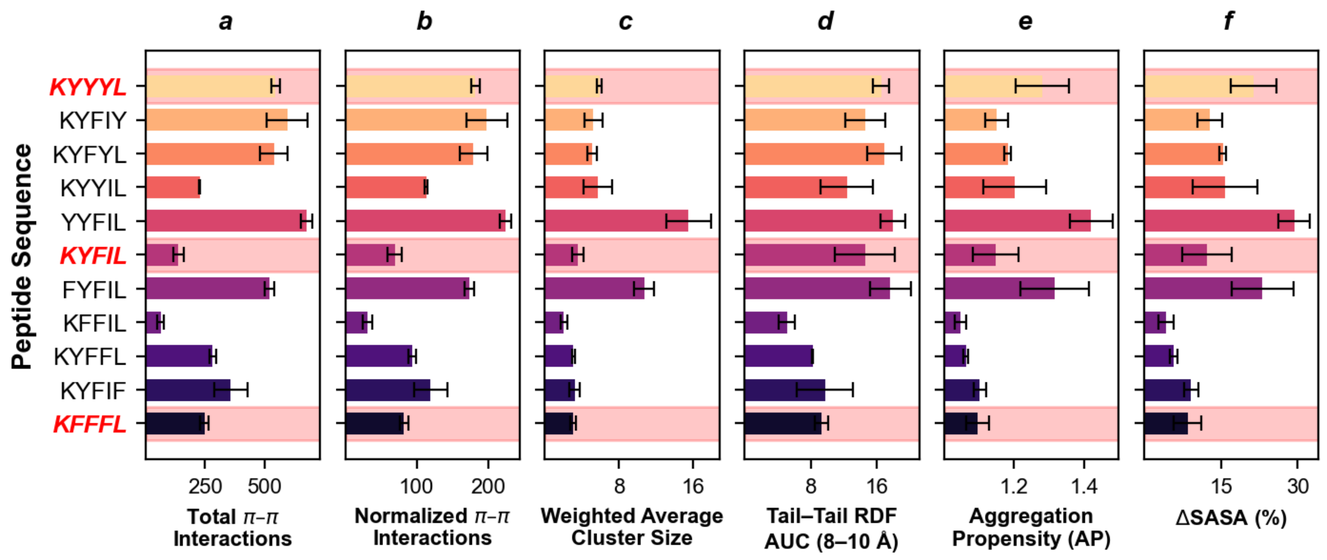
Aromatic residues play crucial role in self-assembly but are not alone sufficient for gelation.



Mean Total Contacts



Tyrosine has a greater influence on self-assembly than Phenylalanine.



References

1. Tang, J. D.; Mura, C.; Lampe, K. J. (2019). A Stimuli-Responsive, Pentapeptide, Nanofiber Hydrogel for Tissue Engineering. Journal of American Chemical Society.
2. Roy, S., Hur, R. K., McAllister, L. C., Lampe, K. J., & Bilodeau, C. L. (2026). A methodological approach to relate pentapeptide sequence, Atomistic Self-Assembly, and gelation behavior. ACS Biomaterials Science & Engineering.