UCI Samueli School of Engineering

Engineering Stimuli-Responsive Macromolecular Bioconjugates for Cardiac Tissue Engineering

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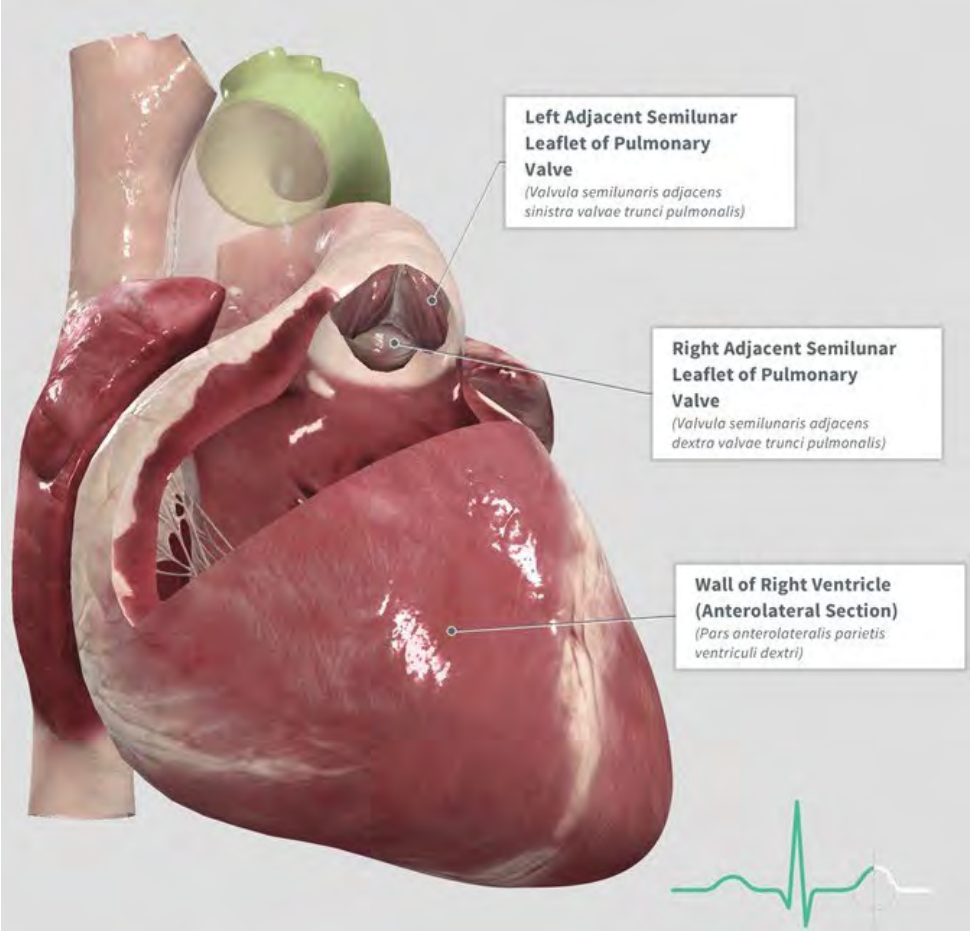
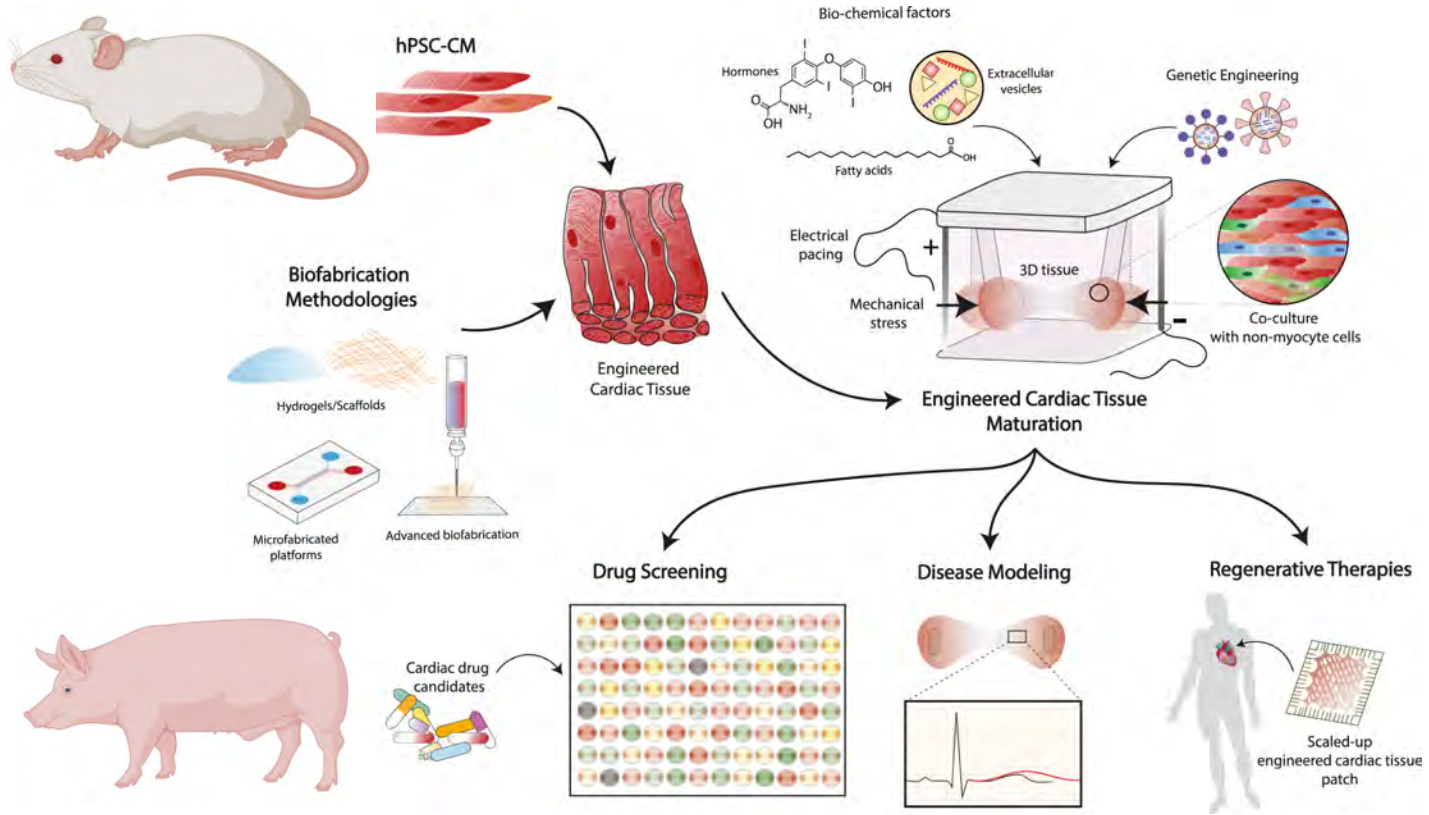
Biophysical Signal Transduction in Cardiac System



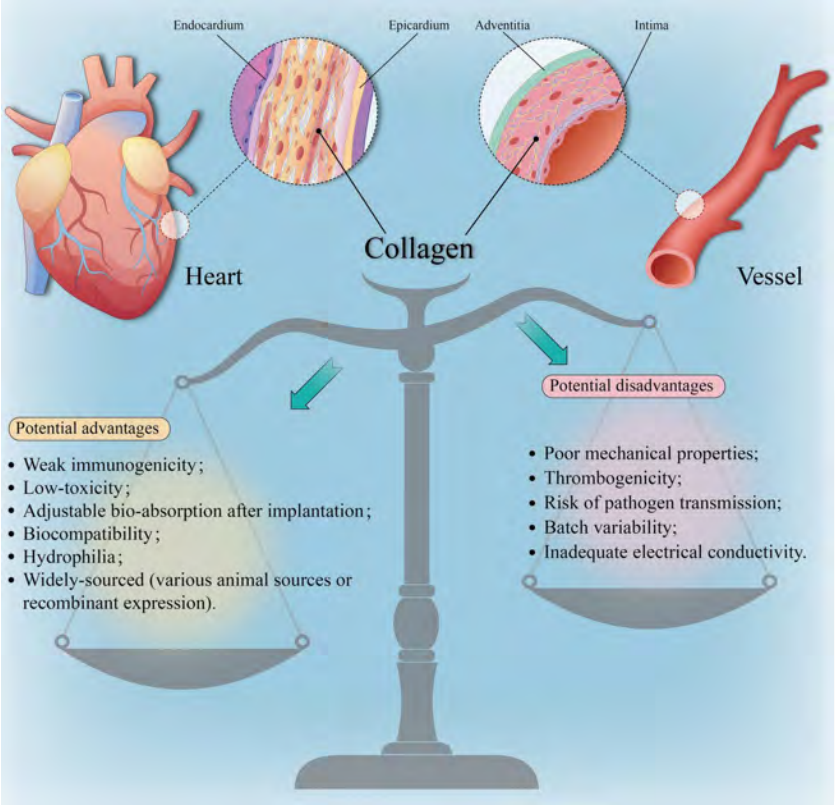
A healthy heart depends on **cardiomyocyte contraction force** and **electrophysiology signaling**.

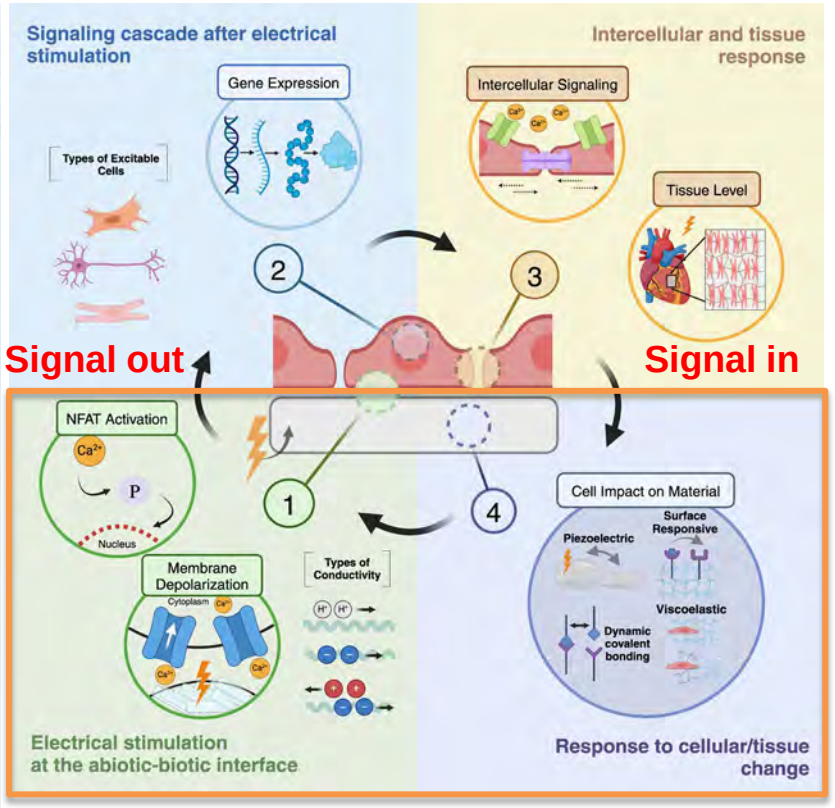


Creates **physiologically relevant cardiac tissues** to replicate specific aspects of myocardial physiology in a scalable and cost-effective way

Iacobellis Nat. Rev. Cardiol. 2022; Chien et al., Science 2008.

Macromolecular Bioconjugates for Cardiac Tissue Engineering





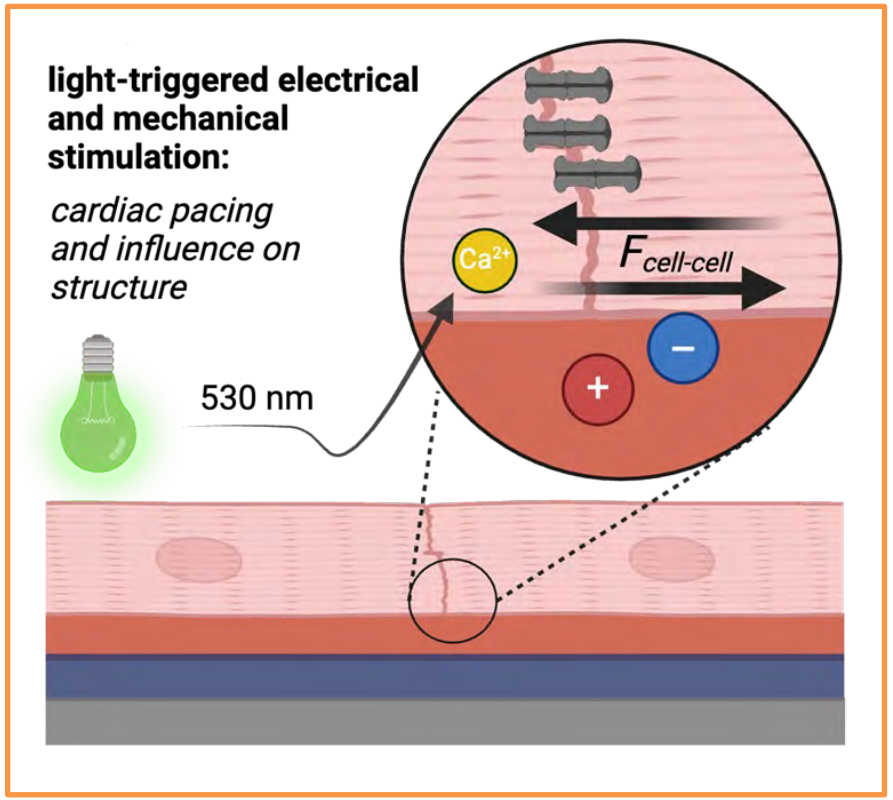
Natural and classical synthetic biomolecules failing to replicate the reciprocal signaling loops of native myocardium

Macromolecular bioconjugates constructed from *stimuli-responsive polymers and biomolecular assemblies enable the control and monitoring of signal transduction in cardiac tissue*.

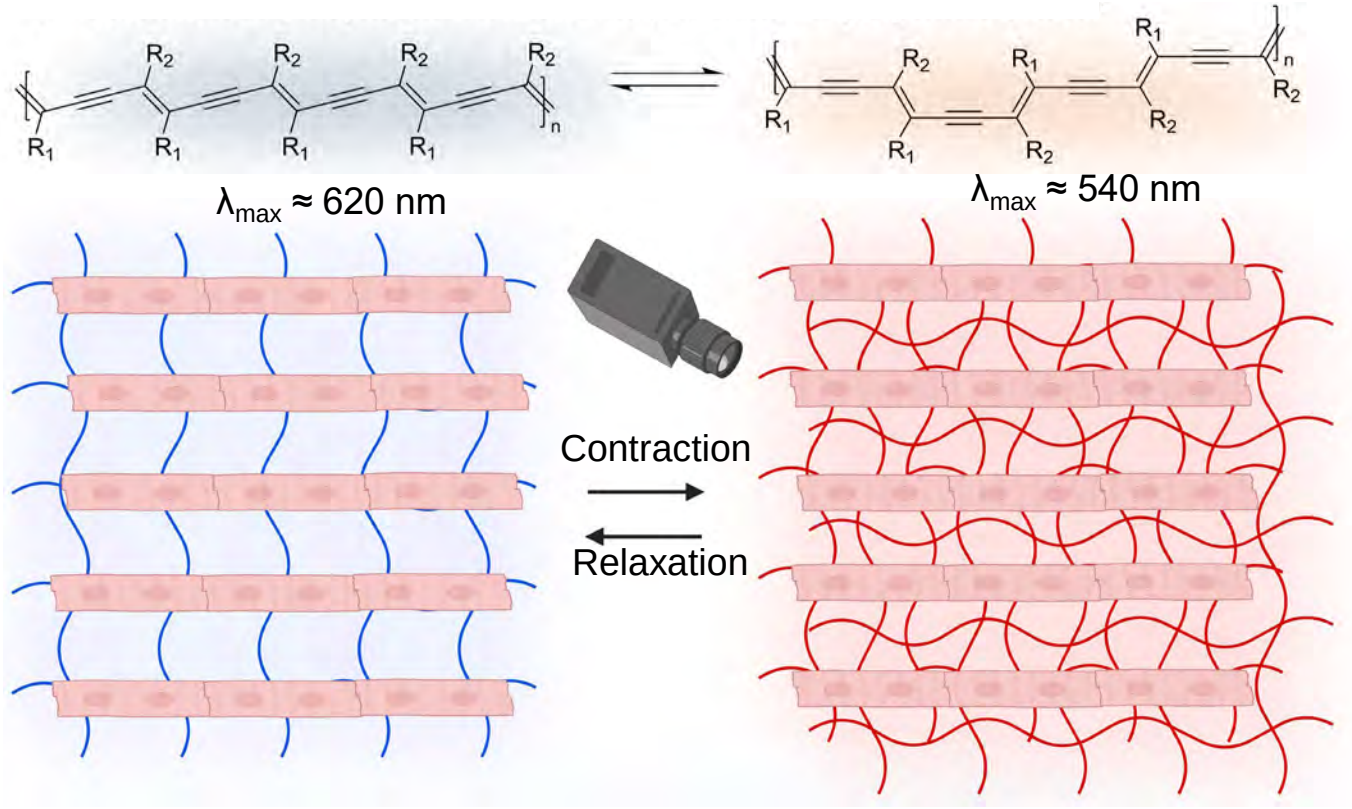
- Convert light into electrical or electromechanical stimuli for local biological stimulation applications
- Translate mechanical forces into optical signals for real-time sensing.

Lee & Celt et al., Biophysics Reviews, 2024.

Engineering Stimuli-Responsive Macromolecular Bioconjugates for Cardiac Tissue Engineering



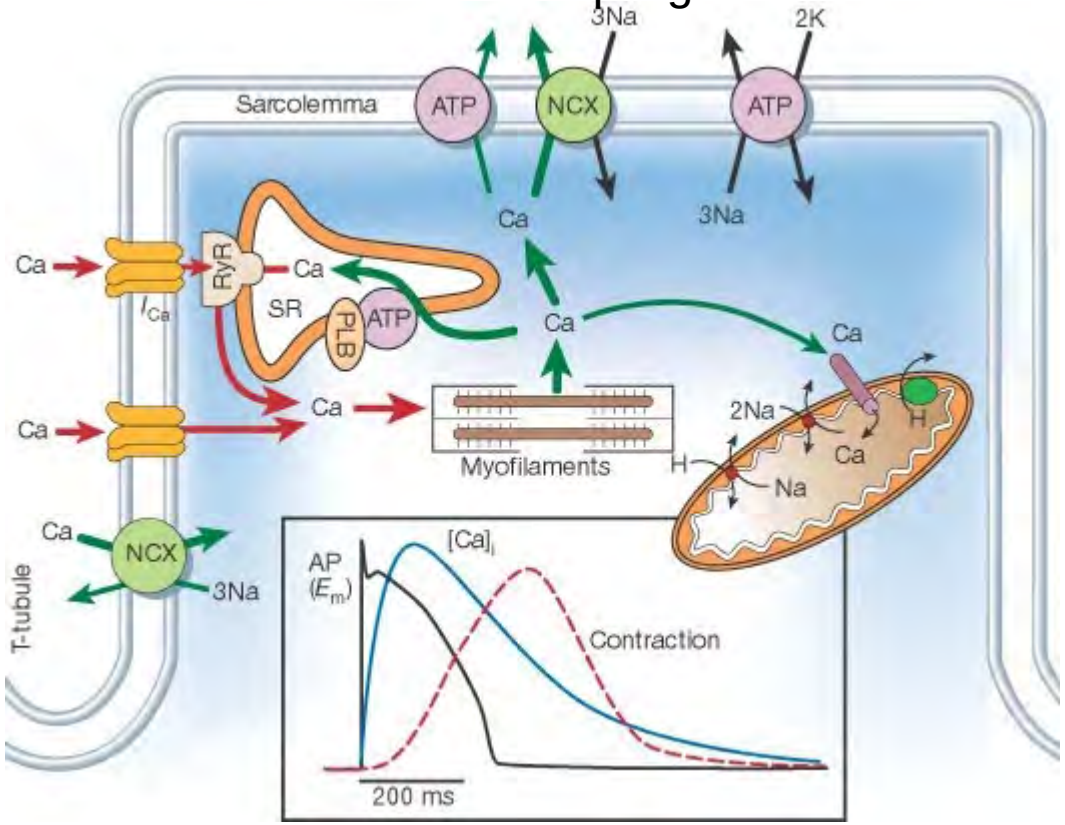
Providing stimulatory cues for cardiac function regulation

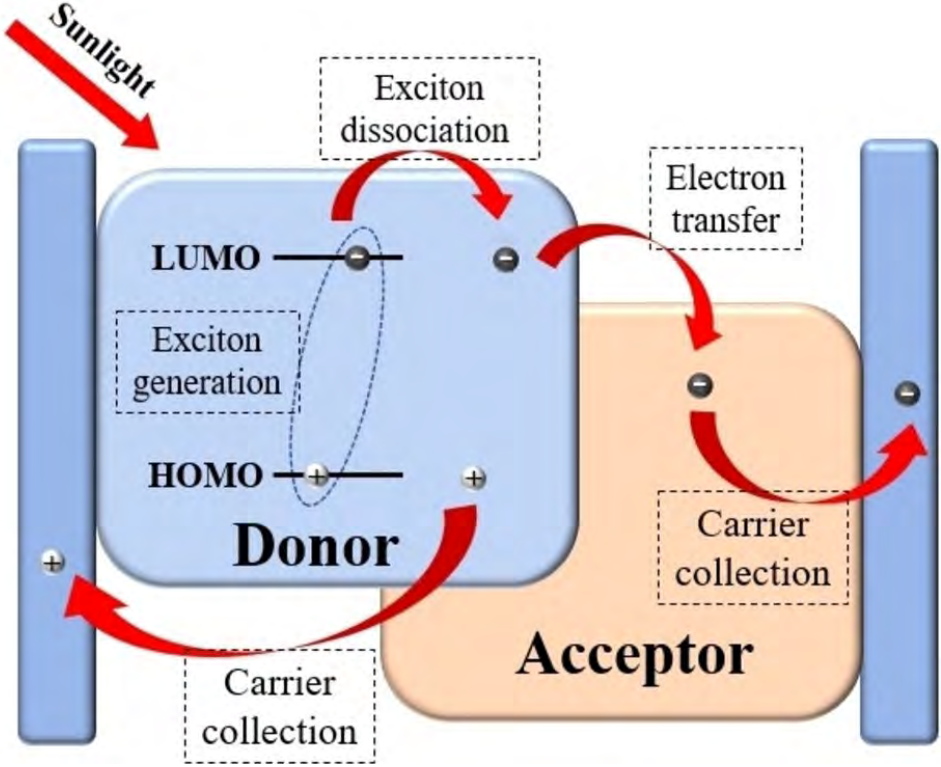


Biological process sensing

Optoelectronic Biohybrid Platform Enables Light-Controlled Cardiac Structural and Functional Feedback

Excitation-contraction coupling: ion flux drives rhythmic heartbeats



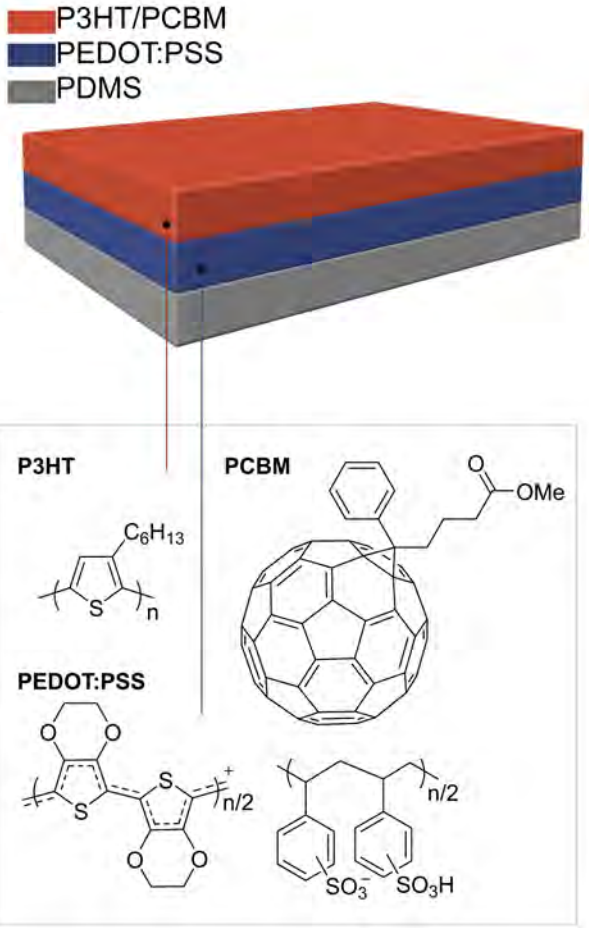


Challenges of current cardiac stimulation methods:
Lack of spatial resolution down to µm~nm & clinical translation challenges

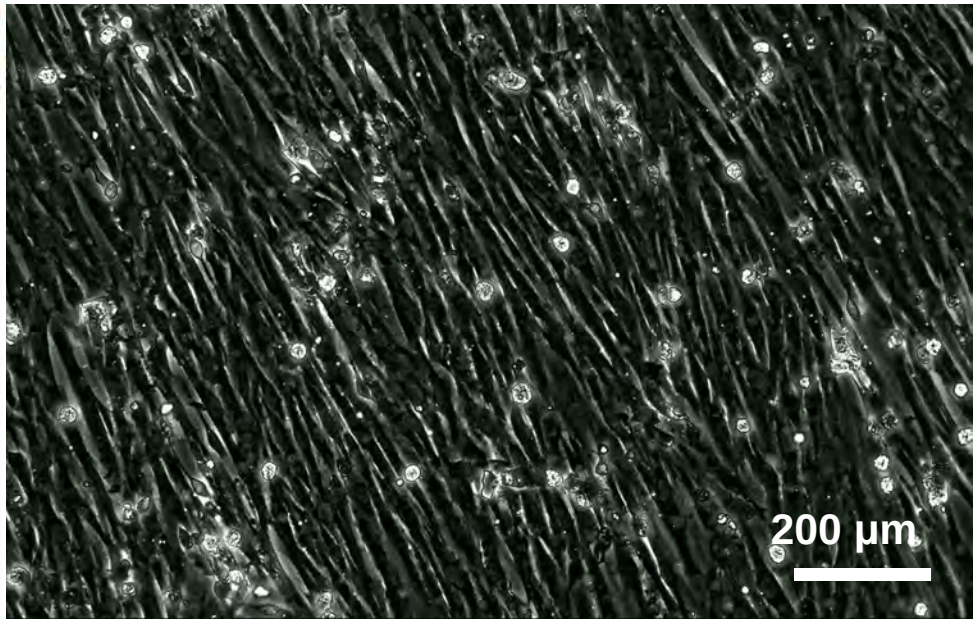
Transduce light signal to currents to direct interfacial ion transport for cardiac pacing

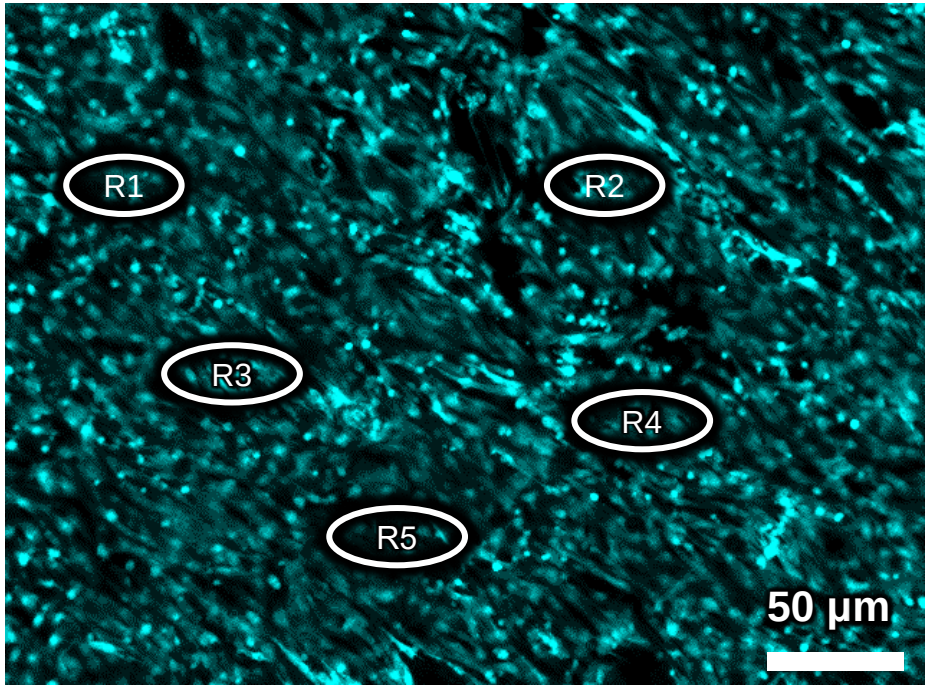
Mayo Clinic Website; Chien et al., Science 2008; The New York Times; Sunet al., Chemistry–An Asian Journal, 2023.

Interfacing of the Fabricated Optoelectronic Platform with Cardiomyocytes



2 Hz, 530 nm light stimulation of neonatal rat ventricular myocytes (NRVMs, Day 5)



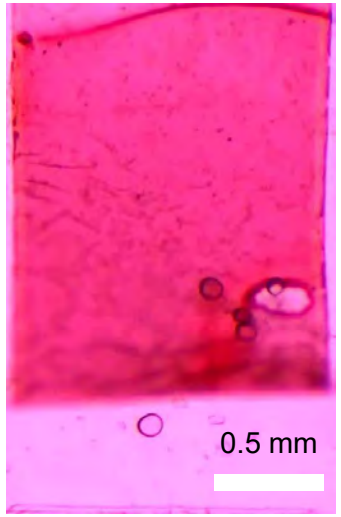


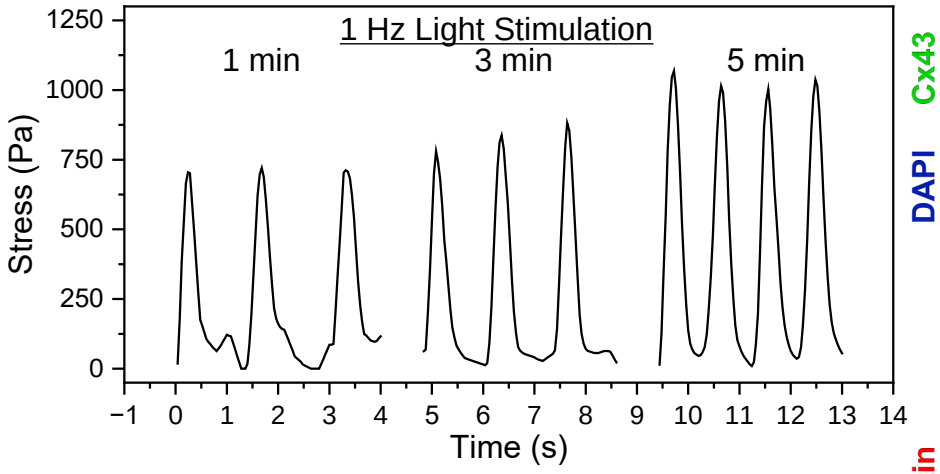
Pulsed light irradiation paces NRVMs to exhibit synchronous contractions

Kuang, Y., et al., Optoelectronic biohybrid platform enables light-controlled cardiac structural and functional feedback, Cell Biomaterials, accepted with front cover selection.

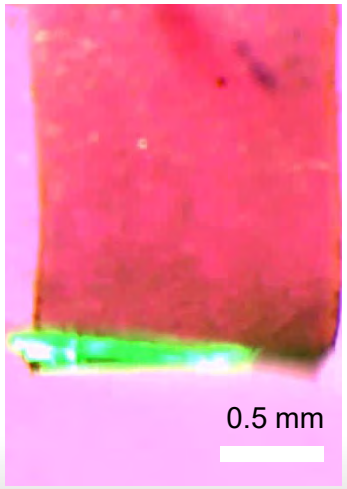
Light-Based Pacing of Cardiac Biohybrid Actuators

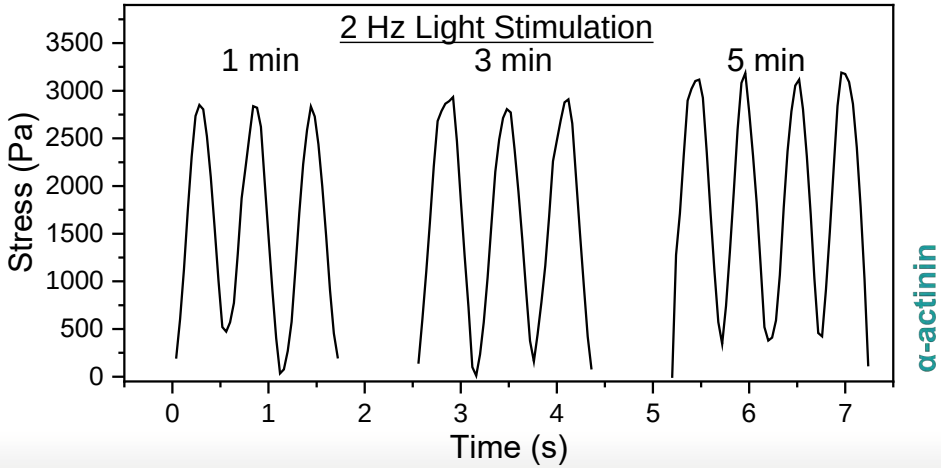
1 Hz, 530 nm light stimulation

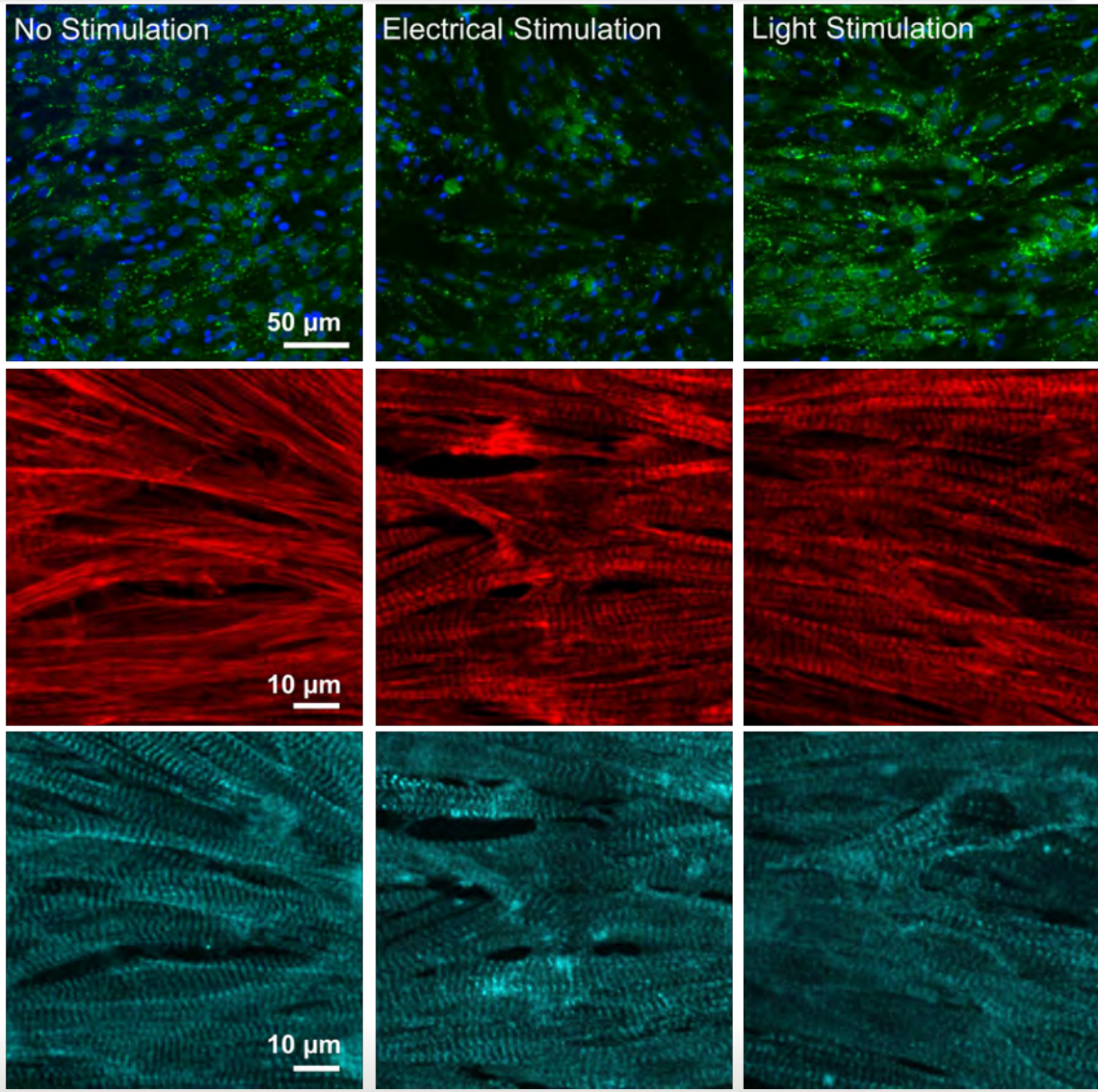




2 Hz, 530 nm light stimulation

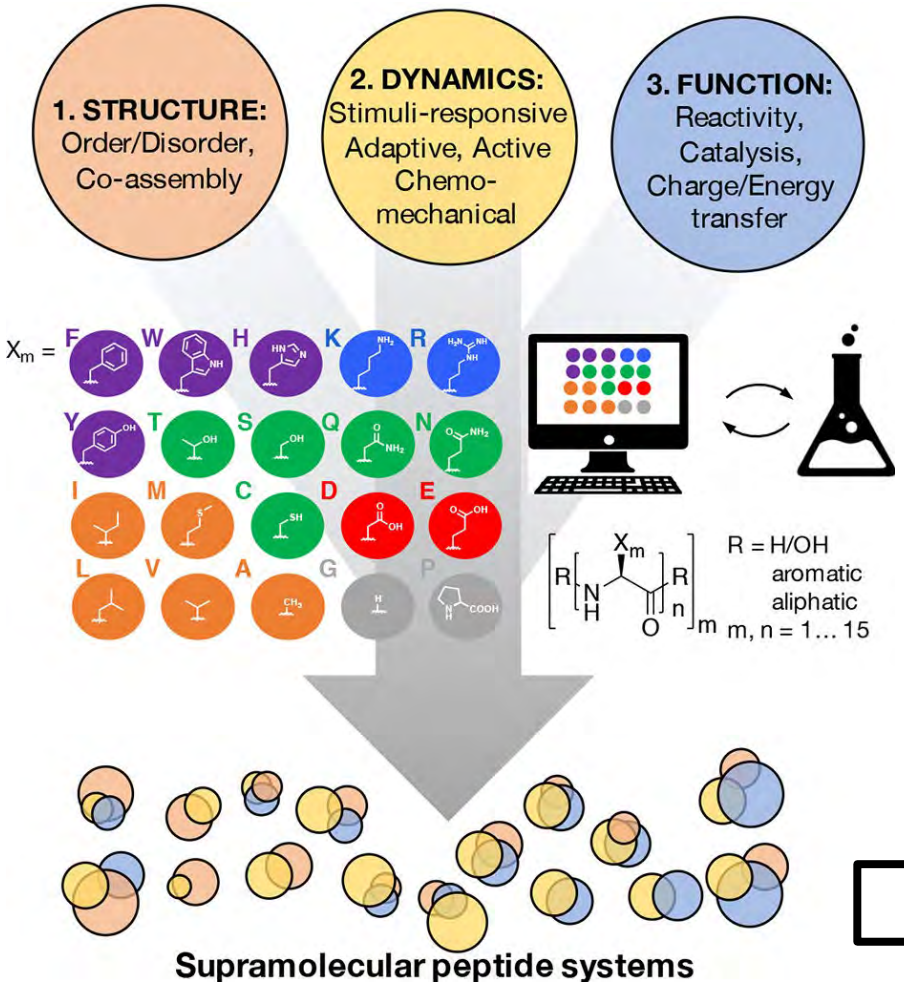


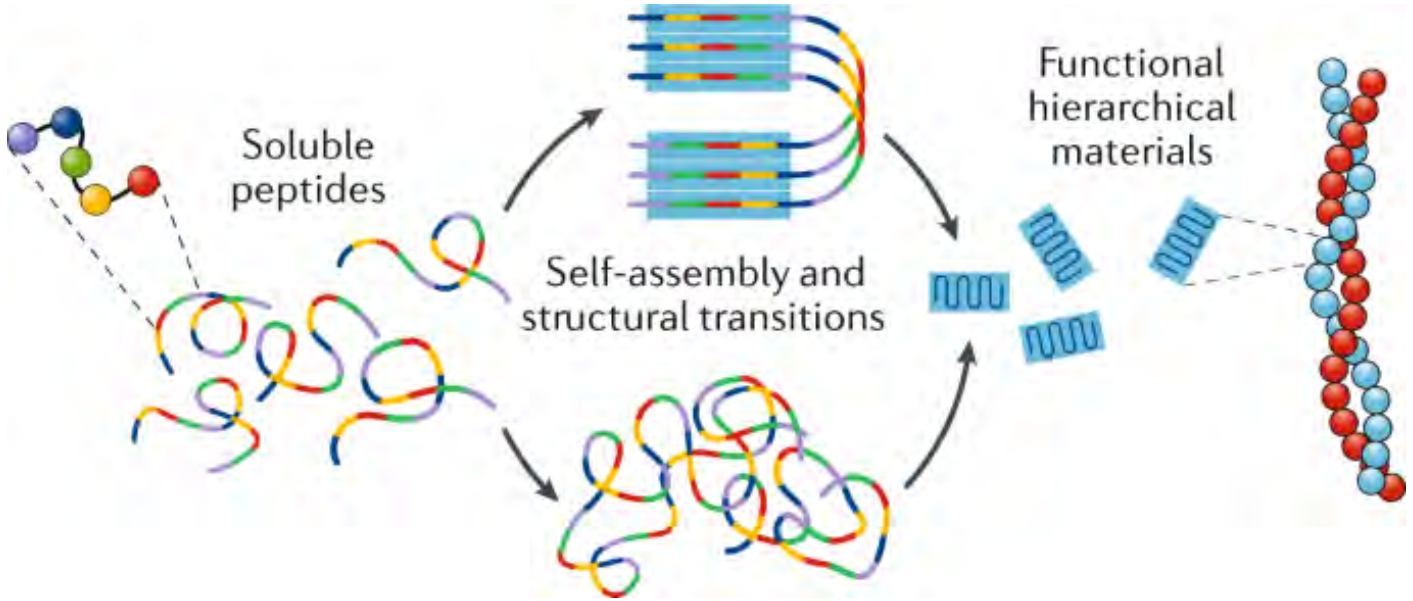




Kuang, Y., et al., Optoelectronic biohybrid platform enables light-controlled cardiac structural and functional feedback, Cell Biomaterials, accepted with front cover selection.

Designing Peptide-based Supramolecular Systems



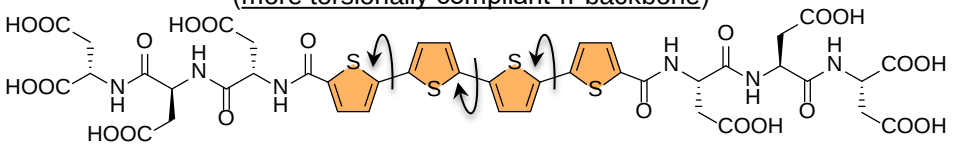


Programmable structures and supramolecular interactions

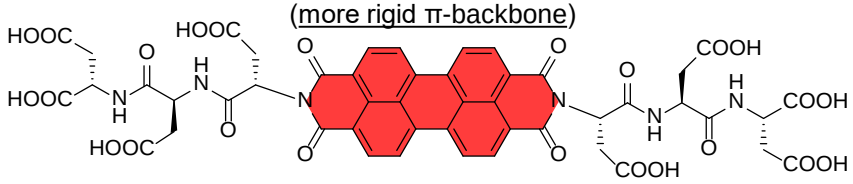
Sheehan et al., Chemical Reviews, 2021; Levin Nature Reviews Chemistry, 2020.

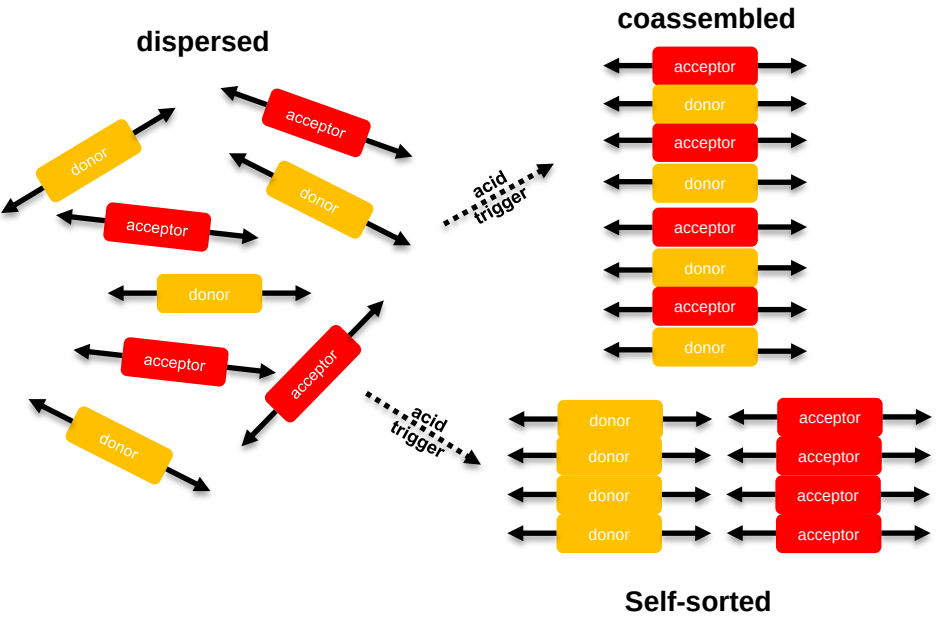
Coassembly of π-Conjugated Peptidic Donor Acceptor Bioconjugates

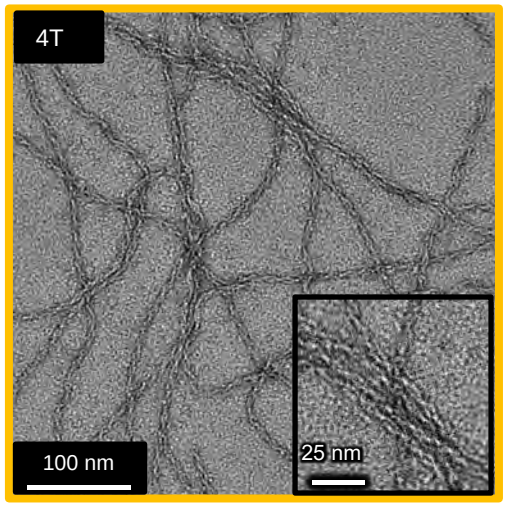
DDD-4T, *donor*
(more torsionally compliant π-backbone)

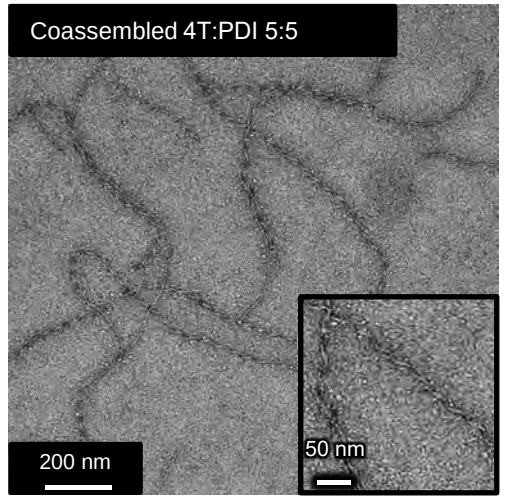


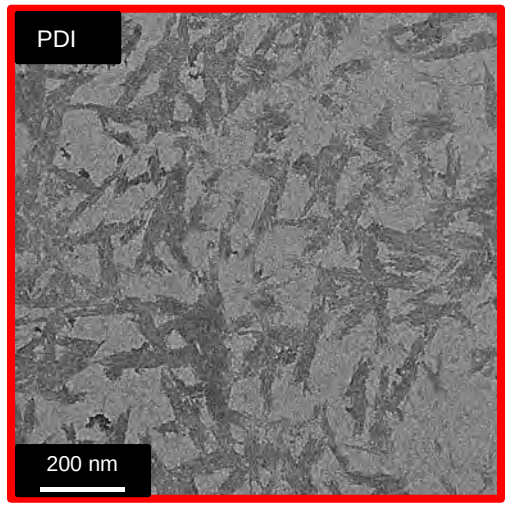
DDD-PDI, *acceptor*
(more rigid π-backbone)

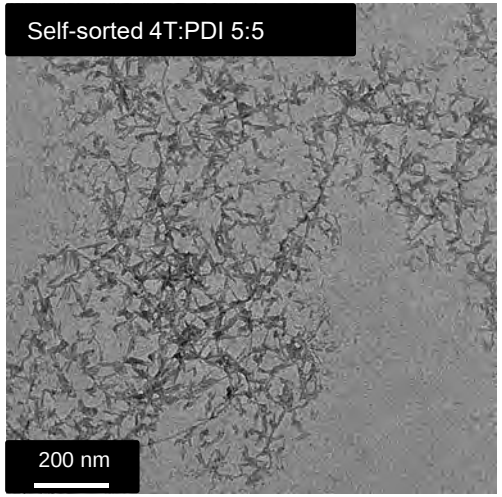


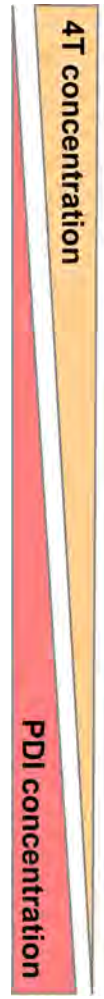


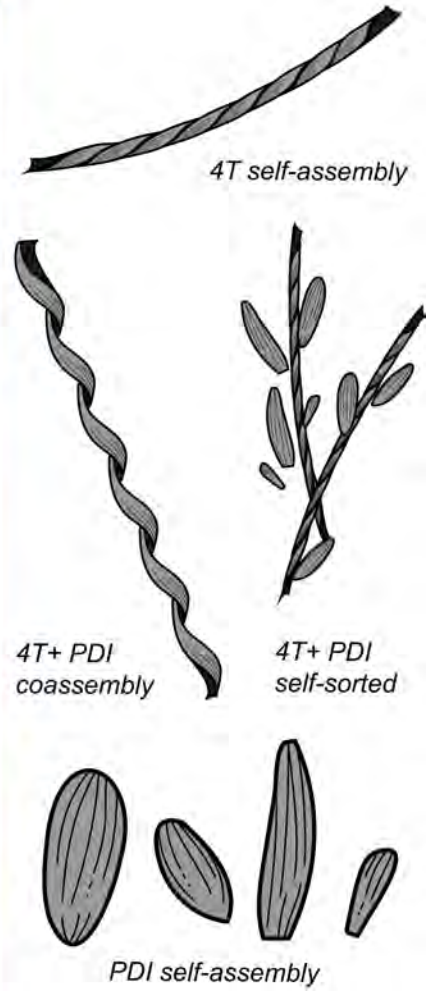








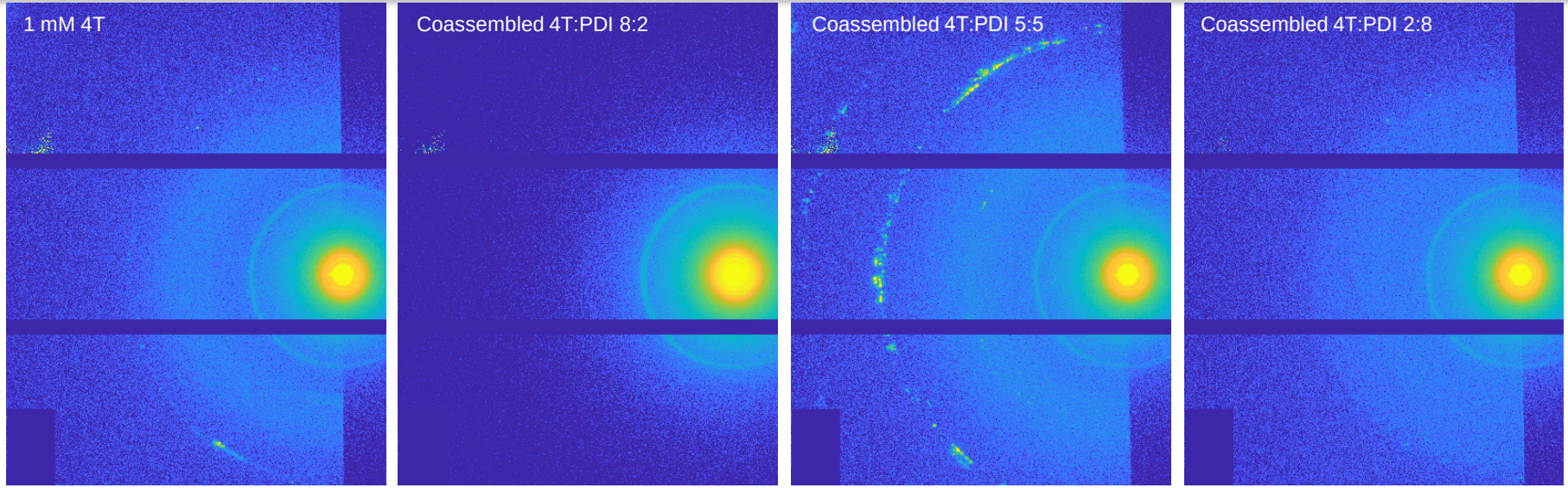


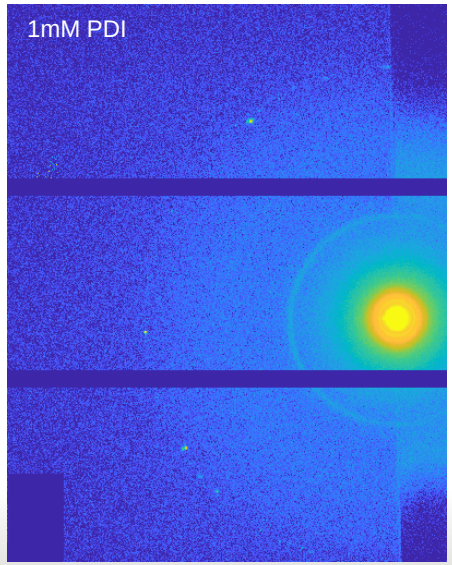


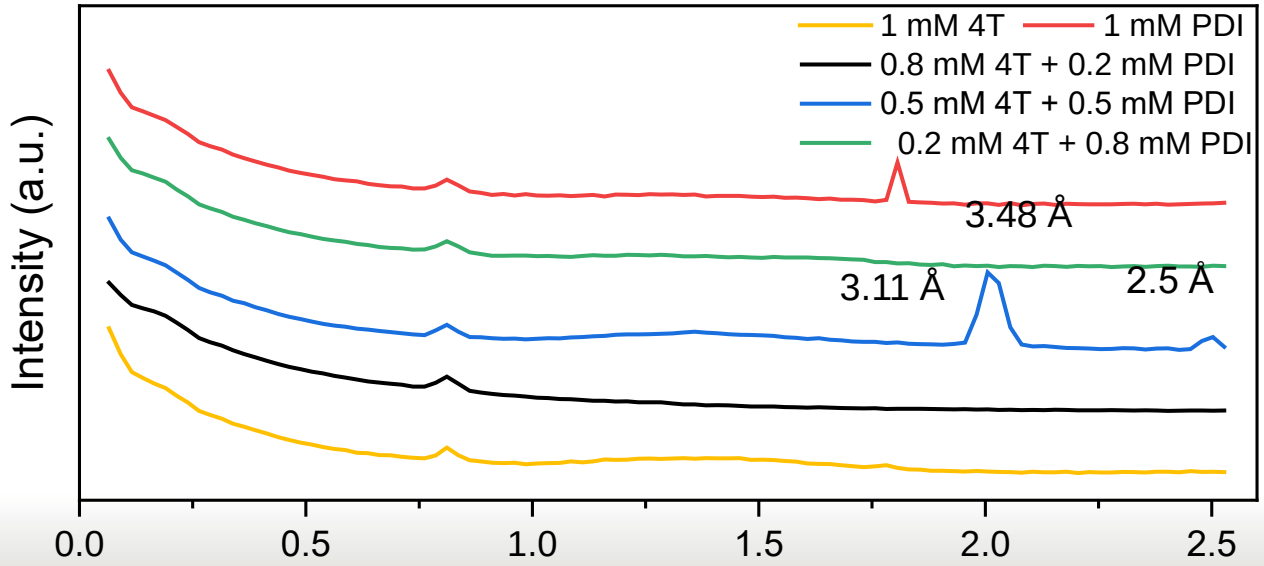
Coassembled DDD-4T and DDD-PDI formed new hybrid nanostructures distinct from their individual assemblies

Kuang, Y., et al., Geometric divergence in nanostructural fates of coassembled peptides leads to broadening of morphology-based optoelectronic property outcomes, Chem, in revision.

Local Molecular Ordering Changes



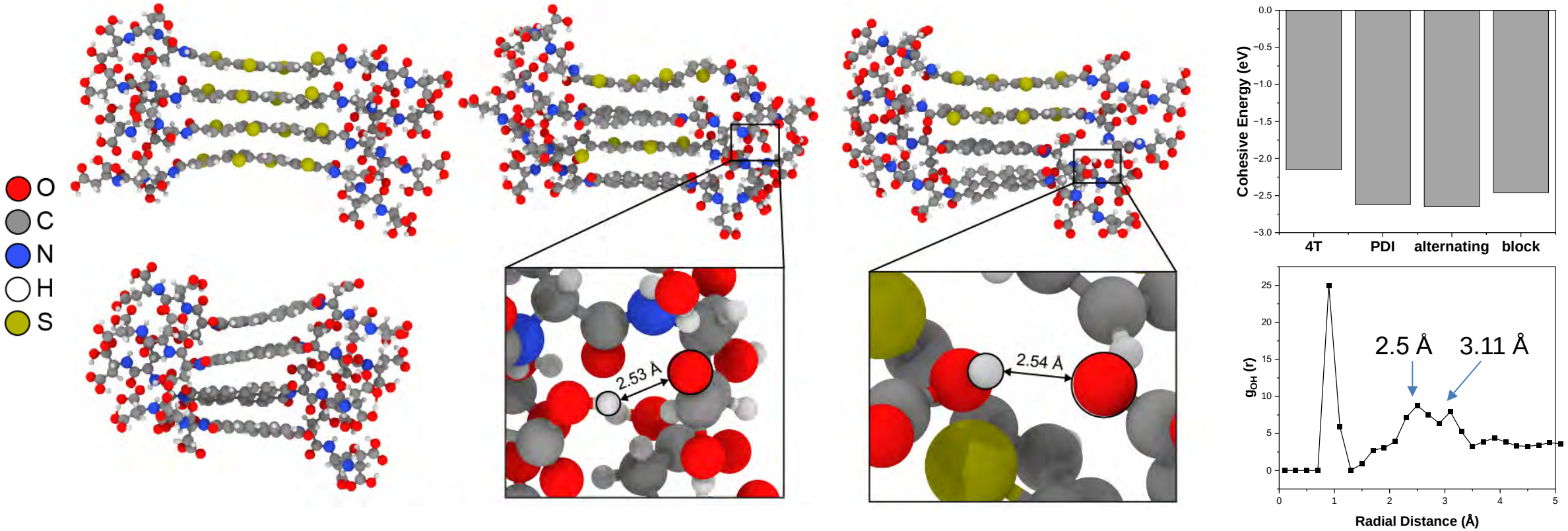




Coassembled DDD-4T and DDD-PDI lead to tighter molecular packing

Kuang, Y., et al., Geometric divergence in nanostructural fates of coassembled peptides leads to broadening of morphology-based optoelectronic property outcomes, Chem, in revision.

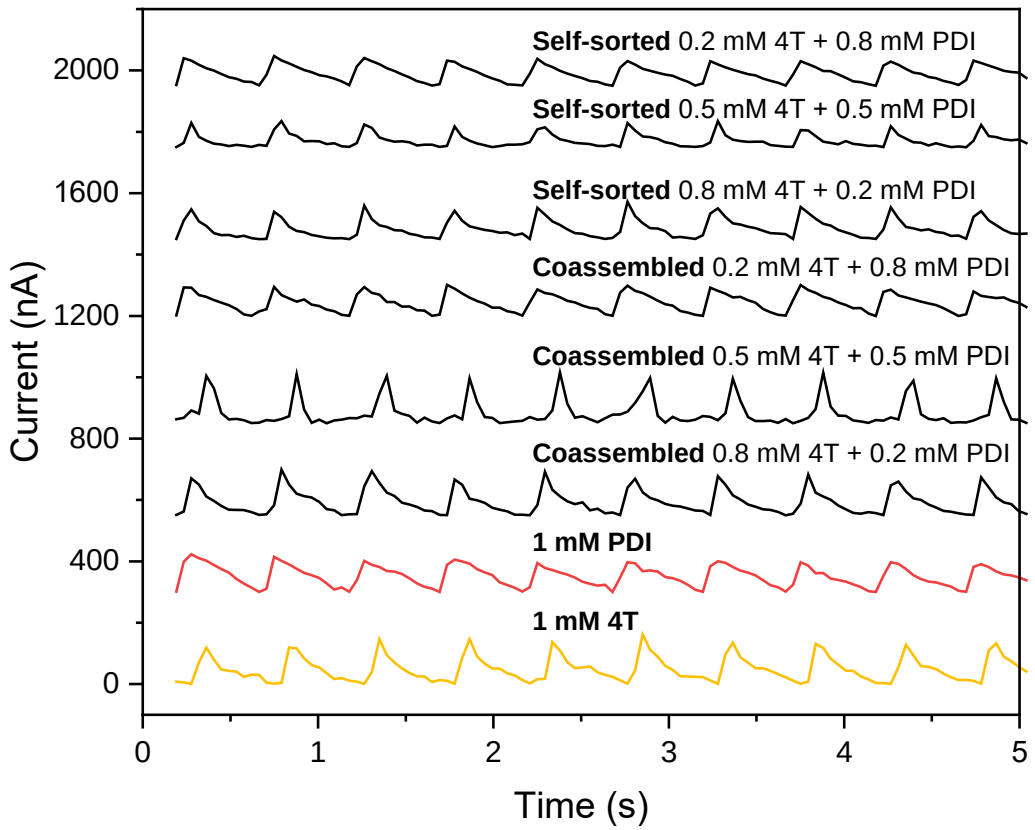
Investigating Thermodynamic Stability Using DFT + MD Simulations

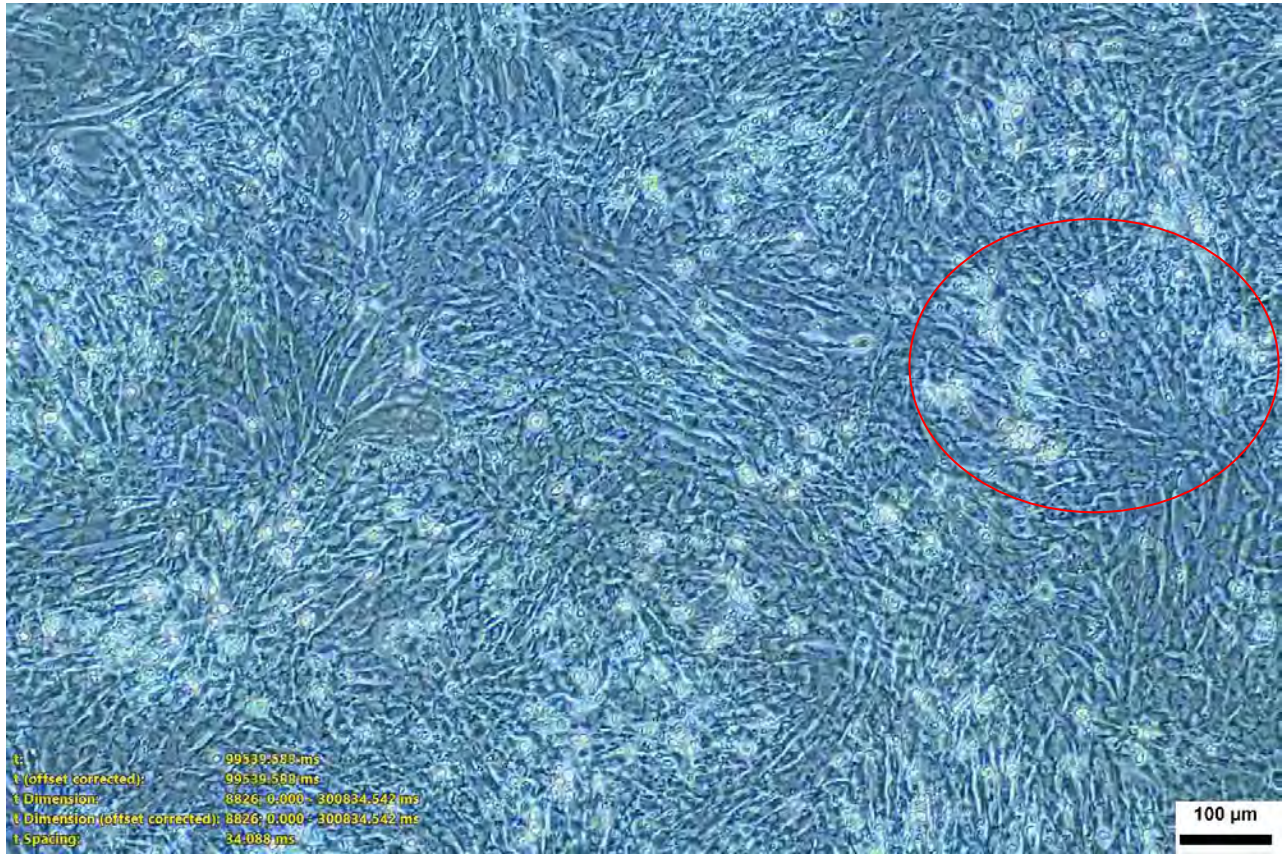


Peptidic segments, along with the alternating configuration of the π-units, stabilize the coassembly formation

Kuang, Y., et al., Geometric divergence in nanostructural fates of coassembled peptides leads to broadening of morphology-based optoelectronic property outcomes, Chem, in revision.

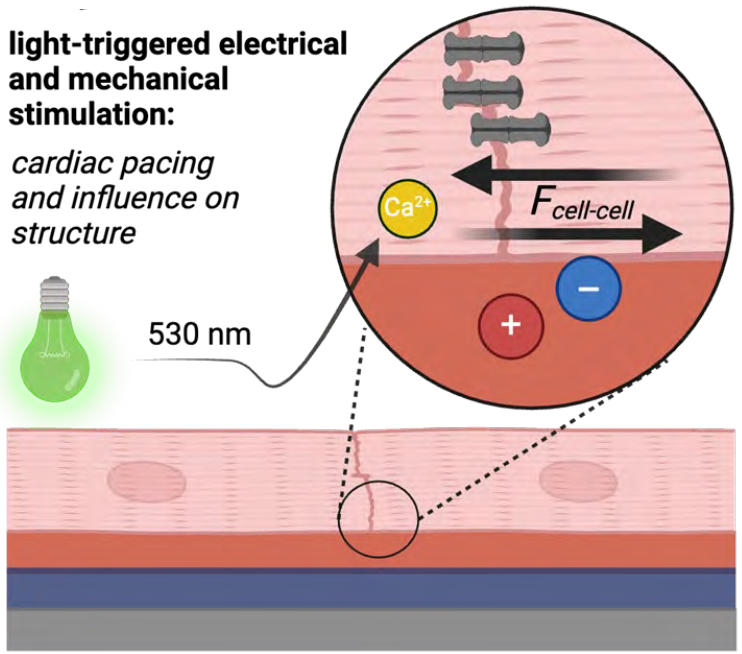
Photocurrent Responses for a light-driven pacing of cardiac contractions



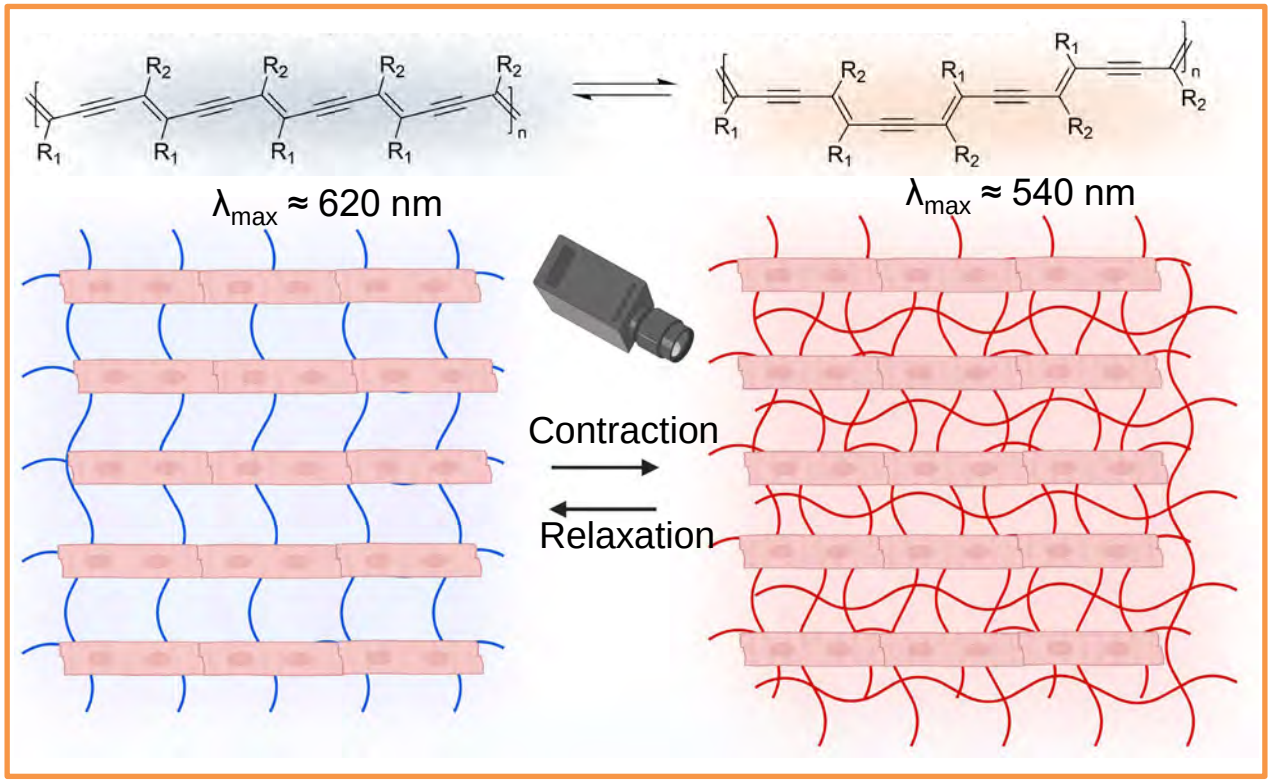


Kuang, Y., et al., Geometric divergence in nanostructural fates of coassembled peptides leads to broadening of morphology-based optoelectronic property outcomes, Chem, in revision.
Yao, Z.-F.*, Lim, S.*, **Kuang, Y.,** et al., Complementary biomolecular coassemblies direct energy transport for cardiac photostimulators, PNAS, 2025.

Engineering Macromolecular Bioconjugates for Cardiac Evaluation



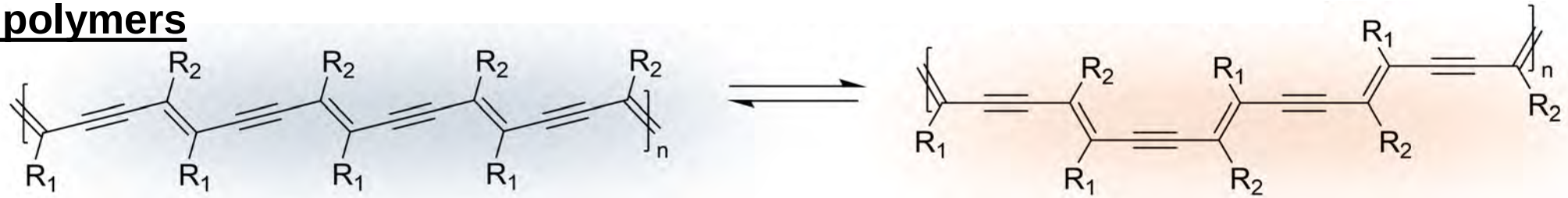
provide stimulatory cues for cardiac function regulation



Enable biological process sensing

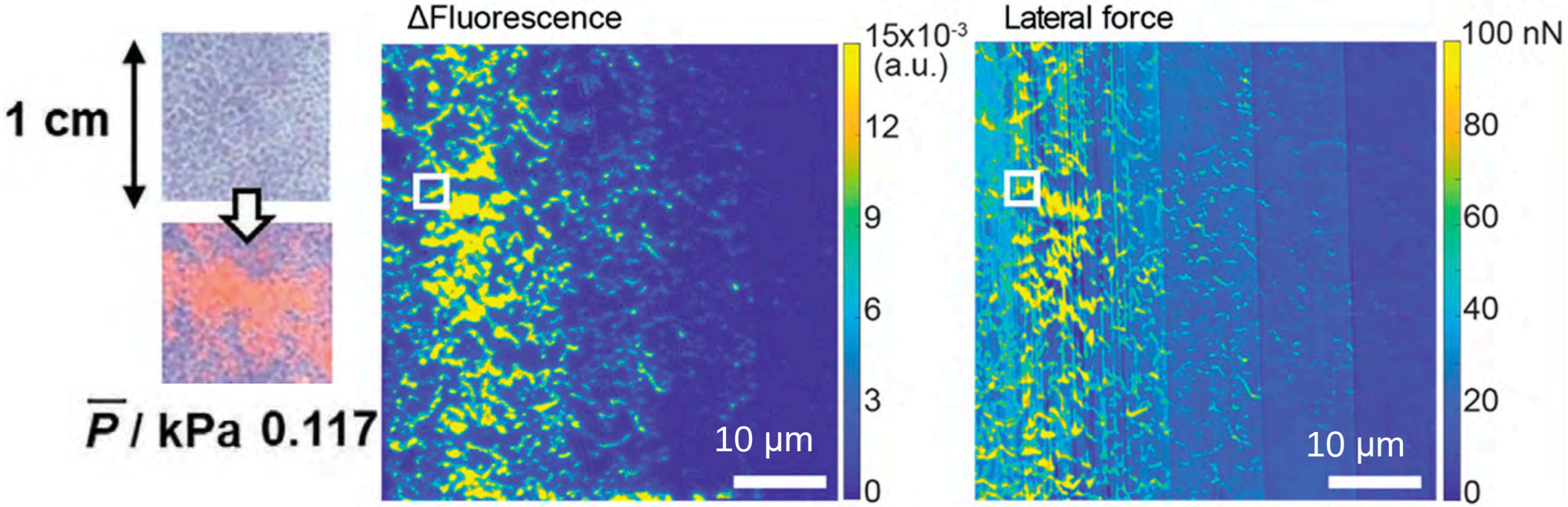
Mechanoresponsive Macromolecular Bioconjugates

PDA-based polymers



$\lambda_{max} \approx 620$ nm

$\lambda_{max} \approx 540$ nm



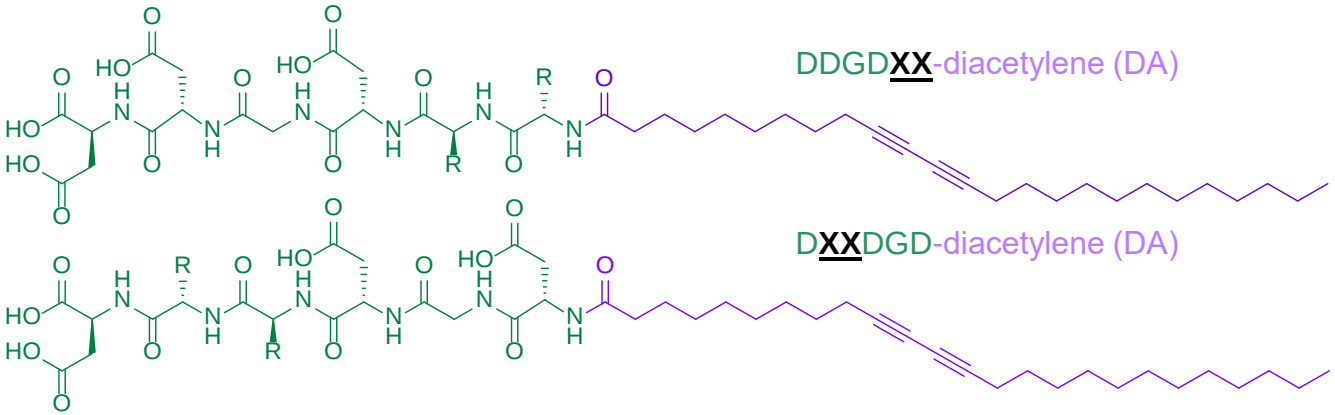
Cellular traction force: ~1 μN

Cardiomyocyte contraction force: ~10 μN

Photophysical property variation induced by conjugated backbone conformation change

Juhasz et al., Nano Letters, 2020; Nakamitsu et al, Advanced Materials, 2021.

Investigation of Molecular Polarity and Residue Size Impact on PDA Properties



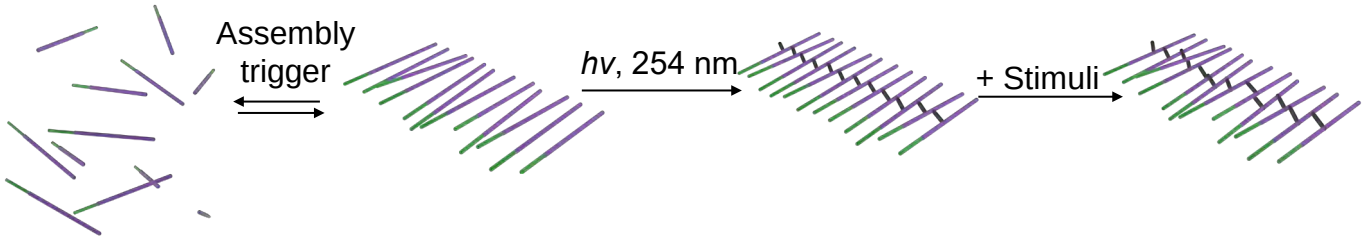
R = H, , OH, , , OH

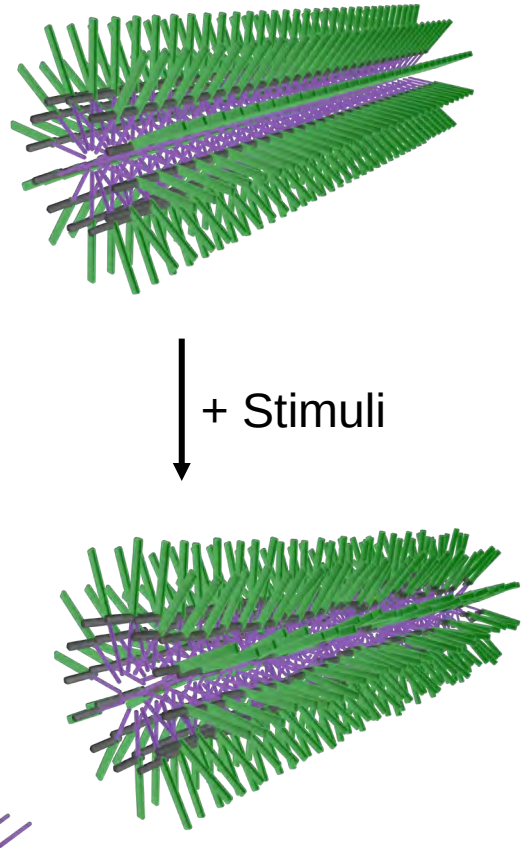
X = G V T F Y

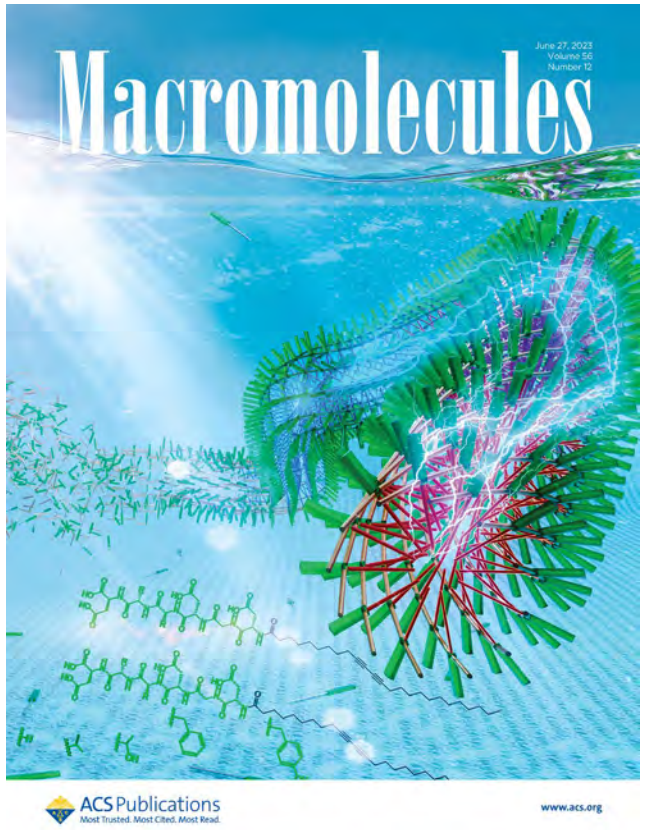
Peptide

Conjugated backbone

Alkyl chain

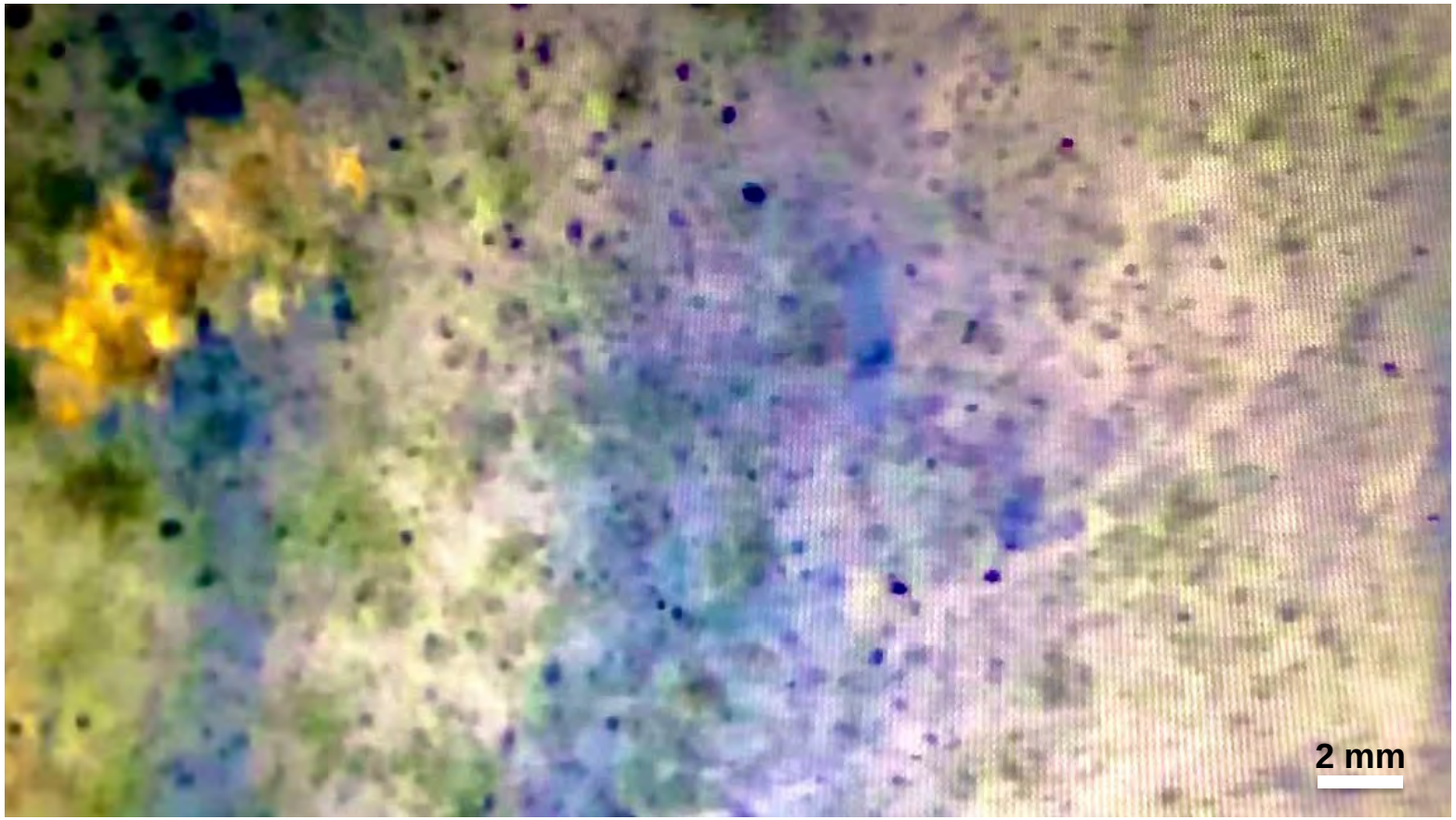






Kuang, Y., et al., Biomimetic sequence-templating approach toward a multiscale modulation of chromogenic polymer properties. Macromolecules, front cover, 2023.

Hybrid Mechanochromic Substrate Enables Optical Signal Variation Induced by Cellular/Tissue Contraction

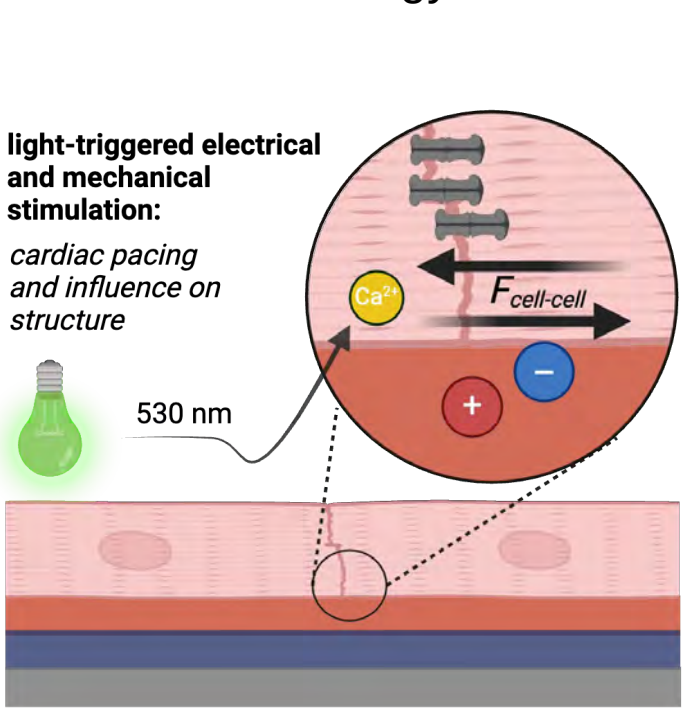


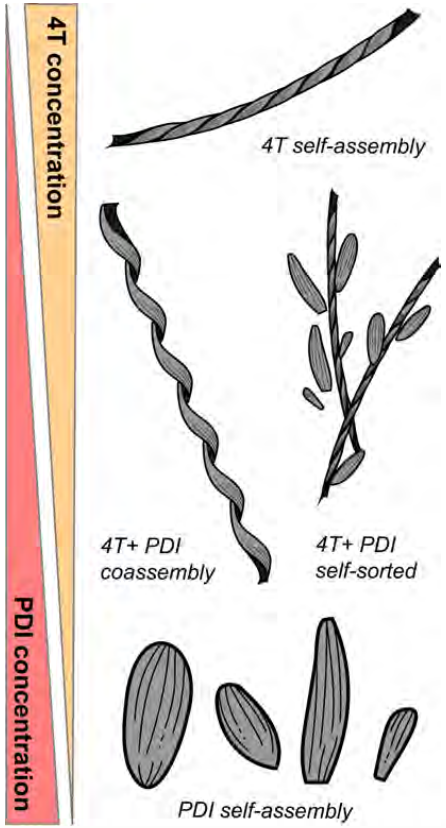
Potentiate the high throughput cardiac evaluation based on optical signals

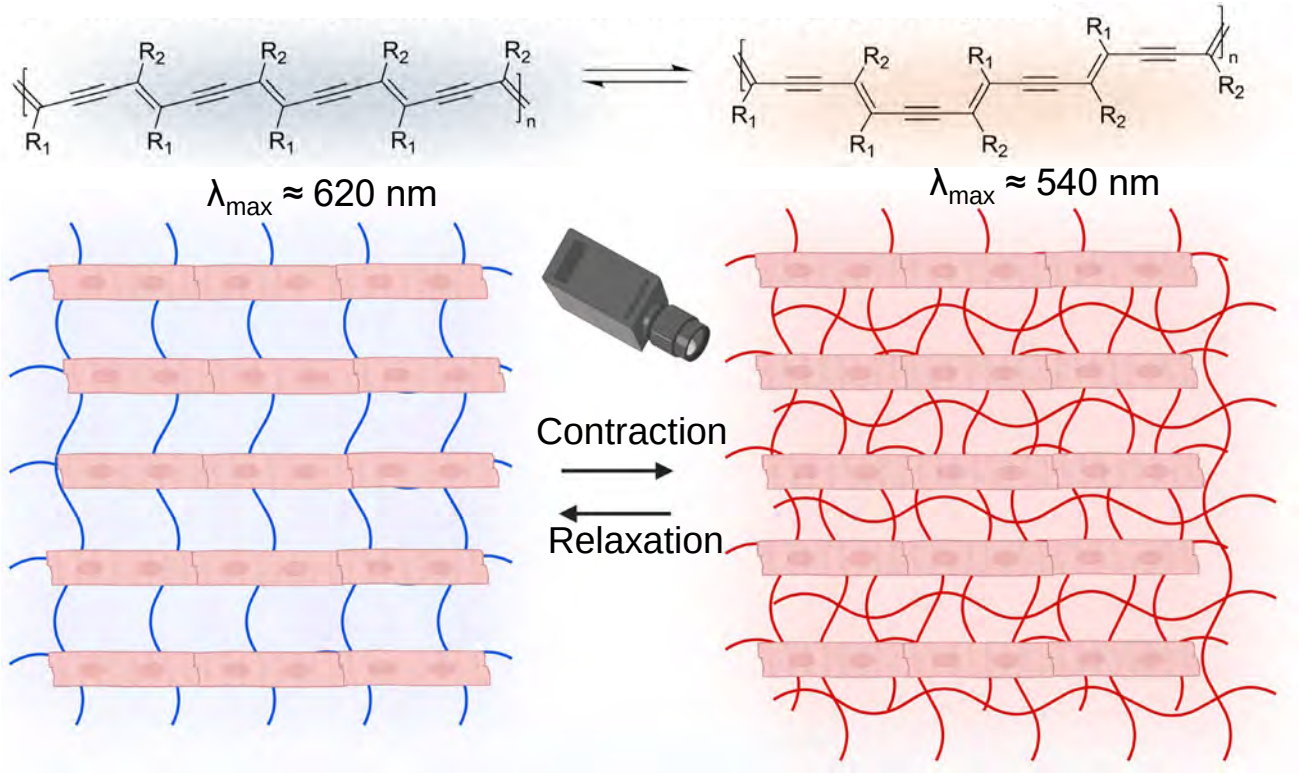
Kuang, Y., Celt, N., et al., in preparation

Engineering Stimuli-Responsive Macromolecular Bioconjugates for Cardiac Tissue Engineering

- Light-to-electrical transduction for cardiac biointerfaces: engineering a polymeric transducer for excitable tissues functional control and structure remodeling
- Mechanical-to-optical transduction for cardiac biointerfaces: Force-sensitive polymers for probing cardiac mechanobiology

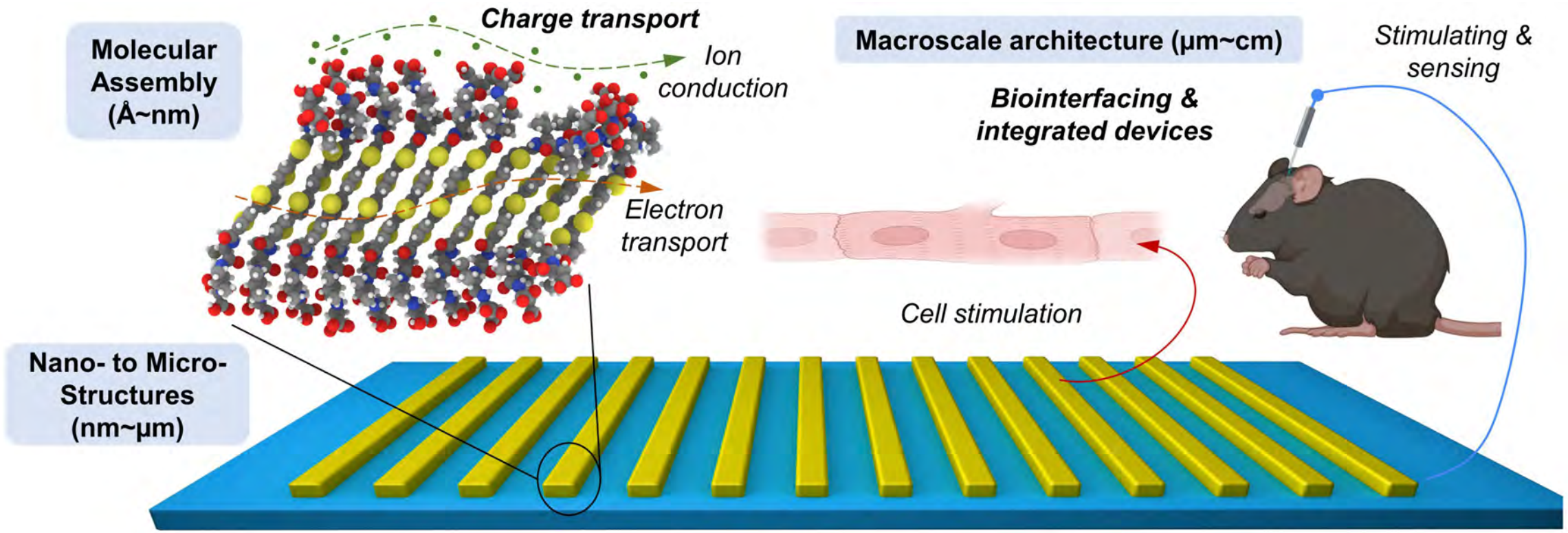






Kuang, Y., et al., Biomimetic sequence-templating approach toward a multiscale modulation of chromogenic polymer properties. Macromolecules, front cover, 2023;
Kuang, Y., et al., Geometric divergence in nanostructural fates of coassembled peptides leads to broadening of morphology-based optoelectronic property outcomes, Chem, in revision;
Kuang, Y., et al., in preparation

Future Outlook



Molecular Structure → Supramolecular Assembly → Micro(Nano) Patterns → Biointerfacing

Yao, Z.-F. Lundqvist, E.M., **Kuang, Y.**, Ardoña, H.A.M., Advanced Science, 2023.

Publications & Patents during Ph.D. Training

Published

1. **Kuang, Y.**, et al., Optoelectronic biohybrid platform enables light-controlled cardiac structural and functional feedback. Cell Biomaterials, accepted, front cover.
2. Yao, Z.F.*, Lim, S.*, **Kuang, Y.**, et al., Complementary biomolecular coassemblies direct energy transport for cardiac photostimulators. PNAS, e2509467122.
3. Lundqvist, E.M., …, **Kuang, Y.**, et al., Micropatterning photoconductive peptide assemblies on stiff and soft biomaterial substrates. ACS AMI, 17 (22), 31982-31992.
4. Jeong, H.C**, Kuang, Y.**, et al., Supramolecular peptidic dopants for inducing photoconductivity and mechanical tunability in digital light processable hydrogels. Faraday Discussions.
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Patents

1. Photoactive organic material blends as cardiac photostimulators, U.C. Case No. 2025-800-1
2. Biological force-responsive chromogenicity of polymeric hydrogels, U.C. Case No. 2026-626

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- **Purification and analytical analysis**: NMR, HPLC/UHPLC, GPC/SEC, LC-MS, MALDI, UV-Vis, CD, FTIR, Raman, DLS, PL, SEM, AFM, TEM, Cryo-TEM, XRD, SAXS, GiWAXS, XRPD, DSC, TGA.
- Molecular biology, protein engineering, and mammalian cell line functional study
- **Biomedical platform fabrication**: hydrogel formulation, cleanroom operation, photolithography, field-effect transistors, nanoimprinting, surface treatment, coating chemistry, rheometer, nanoindentation.
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