

Logic-Degradable Nanogels for Therapeutic Delivery



Eric Yang

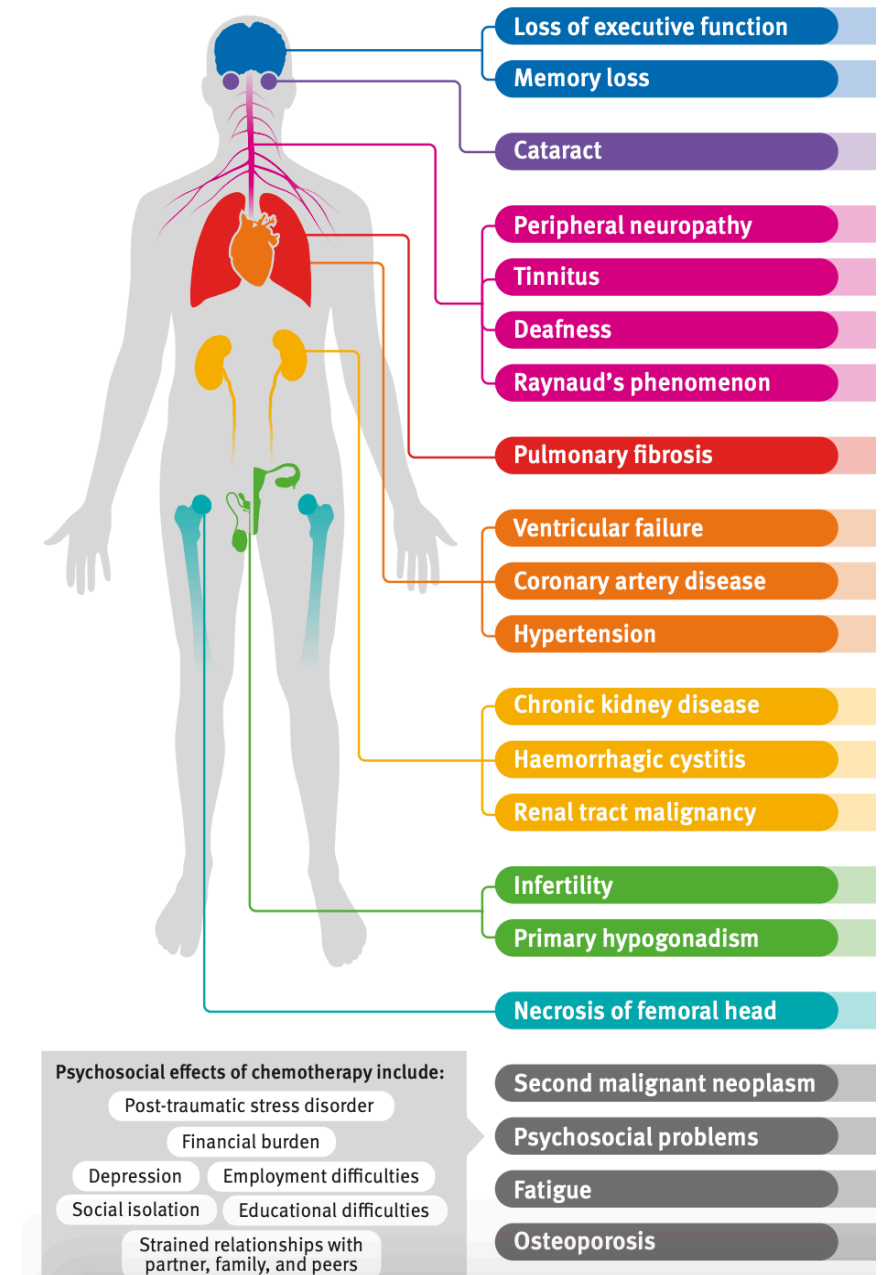
DeForest Research Group

UW BioE Capstone Symposium

06/01/20

Current chemotherapeutics delivery lack specificity for target sites

- > Single-input responsive biomaterials are the basis of many drug delivery systems
- > Many drug delivery systems triggered by nonspecific biomarkers in the body
- > Specific deployment to disease sites challenging
- > Significant harmful off-target side effects
- > Treatment dosage, efficacy and efficiency compromised

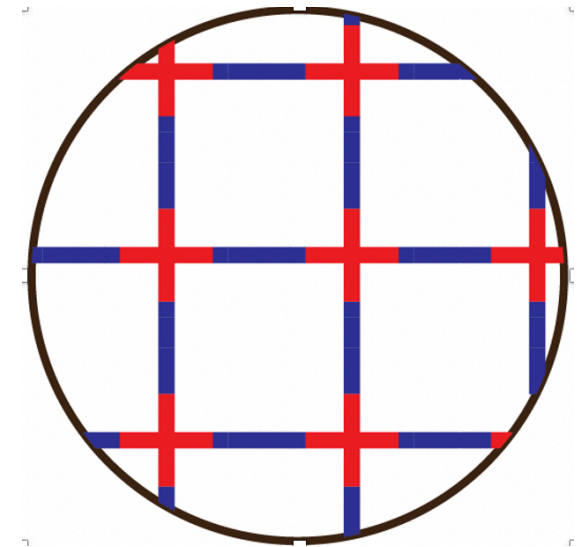
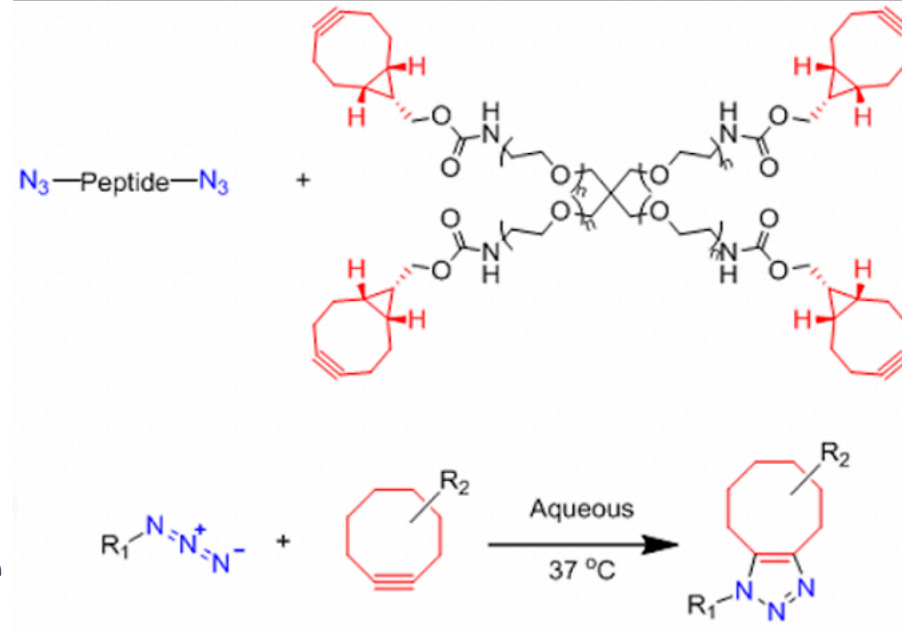


Hydrogels can be controlled in time and space to release molecules

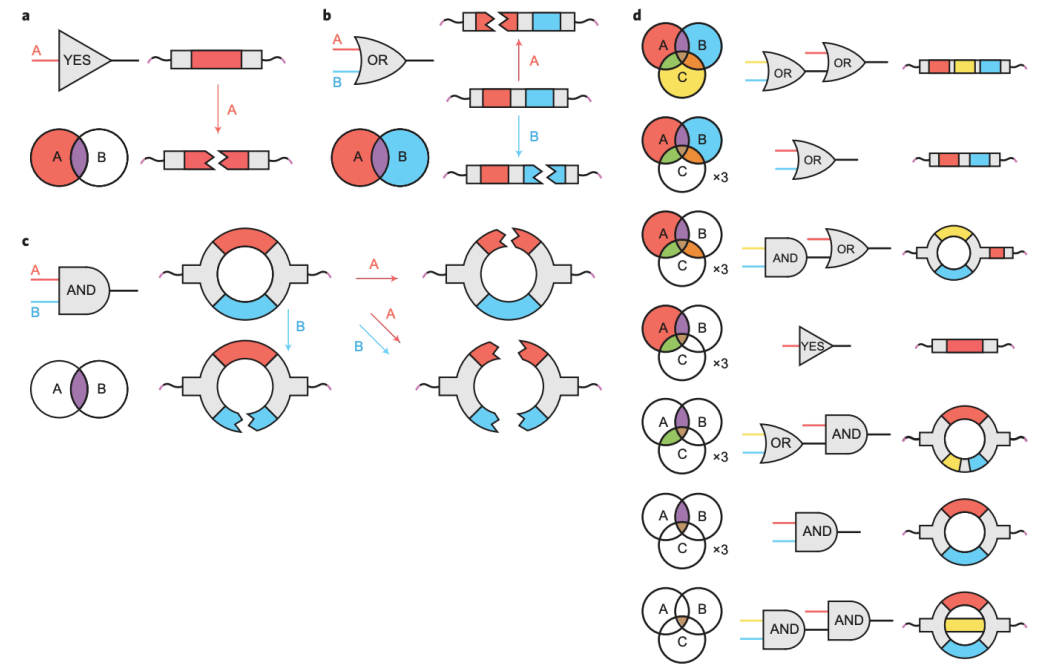
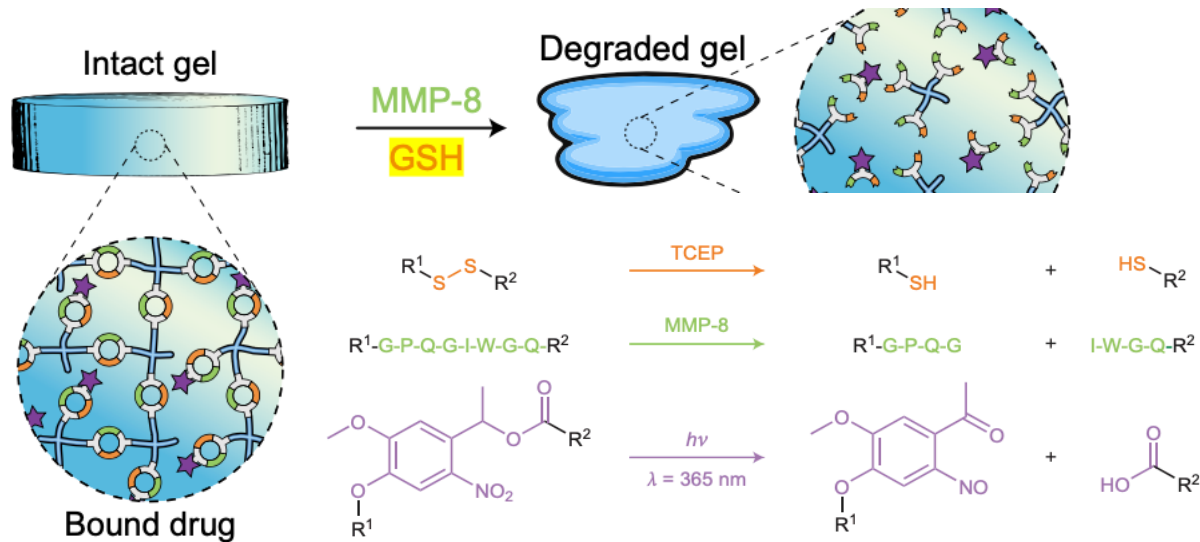
> Modular click chemistry

- Non-toxic, biorthogonal reaction
- Conjugated linkers tune molecule release rate

PEG-tetra BCN Hydrogel Synthesis



Logic-degradable hydrogels promising for drug delivery applications



- > Hydrogels degrade in response to precise combinations of multiple environmental cues
- > Currently formulated only as macroscopic hydrogels

Nanogels with physiologically relevant geometry



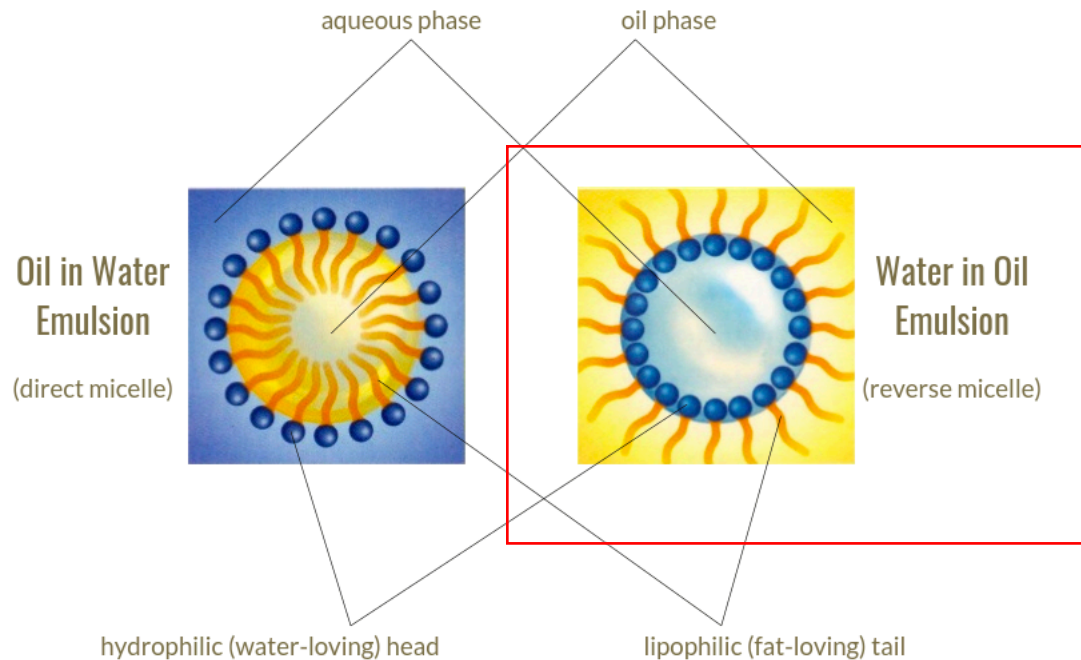
> Size: 50-250 nm

- Travel and circulate in blood stream
- Leaky tumor vasculature – enhanced permeability and retention effect
- Scalable with varying formulation conditions

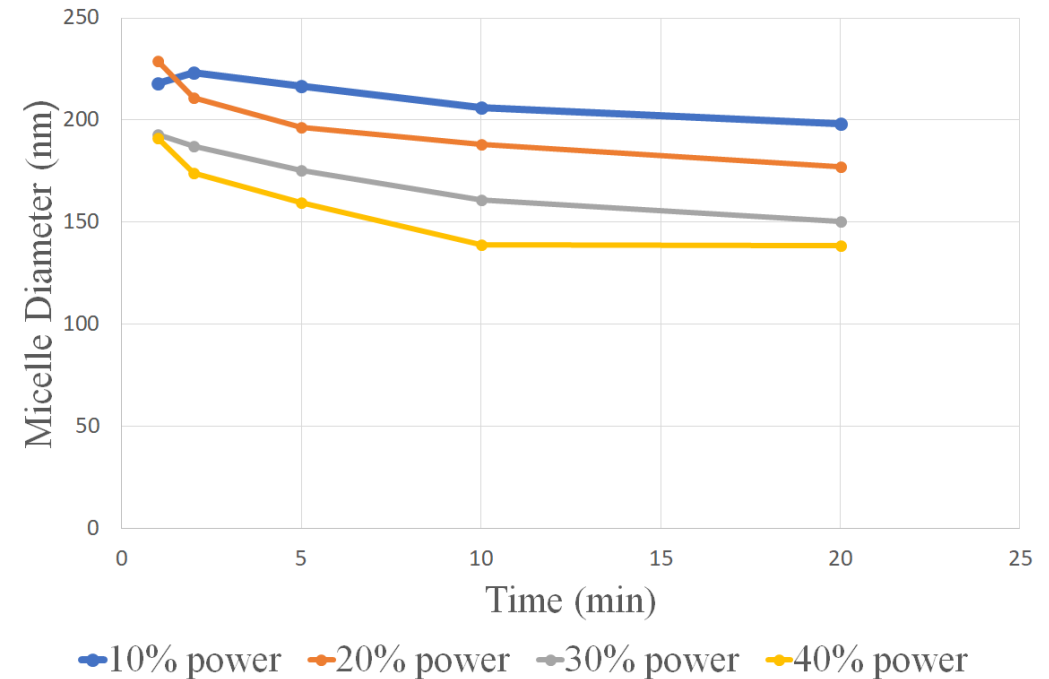
> Modular linkers

- Selective degradability

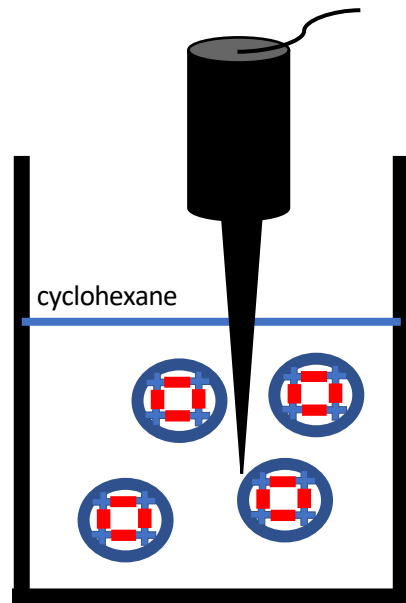
Emulsion size dictated by sonication duration and agitation power



Effect of Sonication Duration and Power on Micelle Diameter

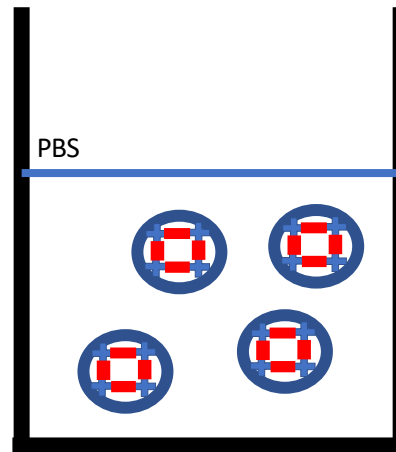


Nanogels formed by ultrasonic agitation, purified by rotary evaporation and physical mesh filter



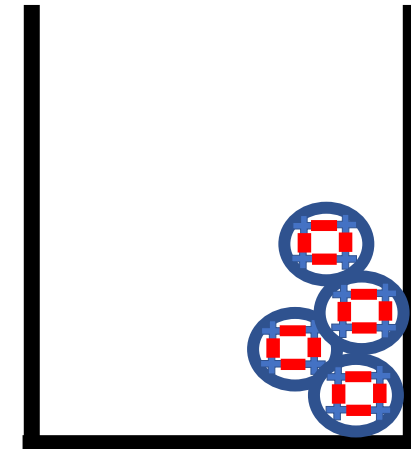
PBS in cyclohexane emulsion, 4 arm PEG-BCN, PEG diazide, Span 80 surfactant

→
RotoVap with
excess PBS



Nanogels now sit in PBS, this can be modified depending on the application

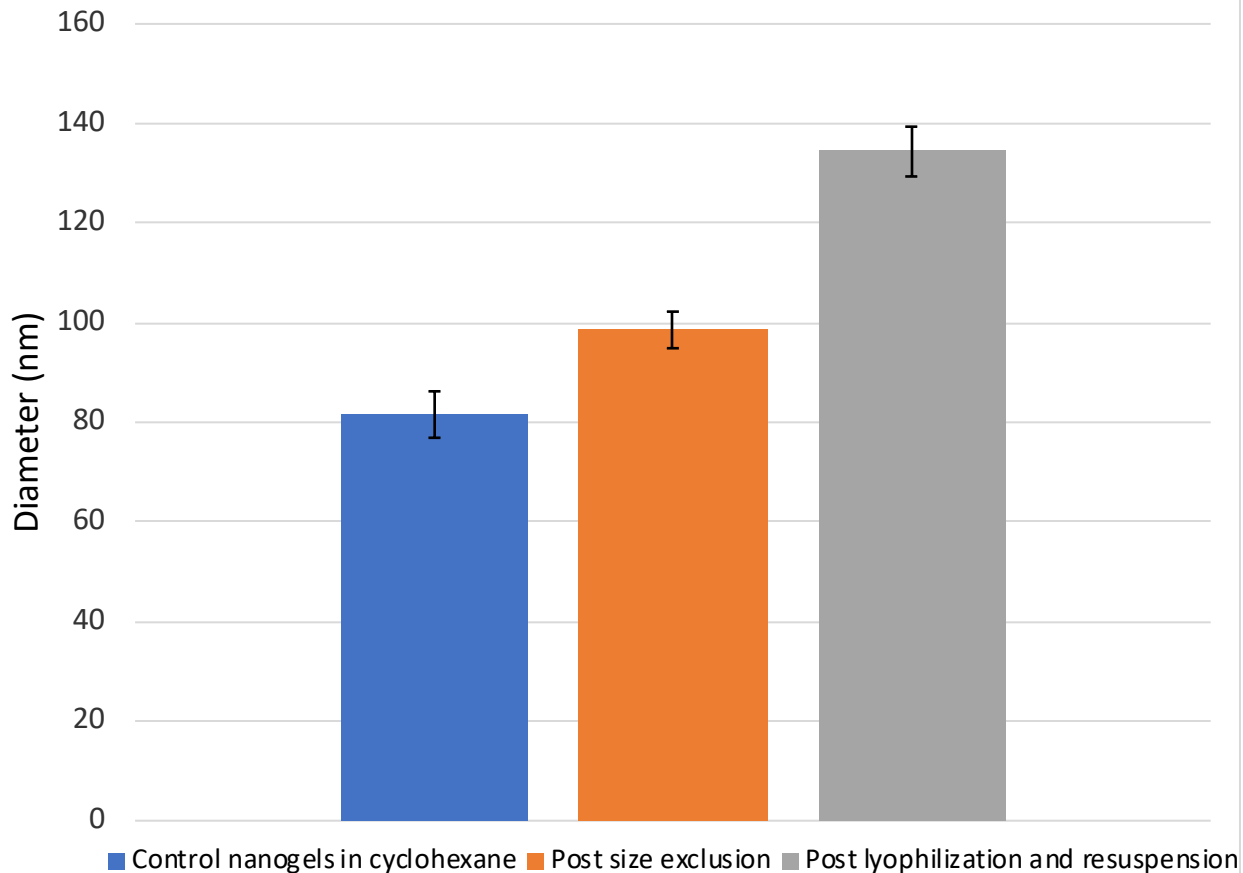
→
Size exclusion
with 220 um
cell filter,
lyophilize for
storage



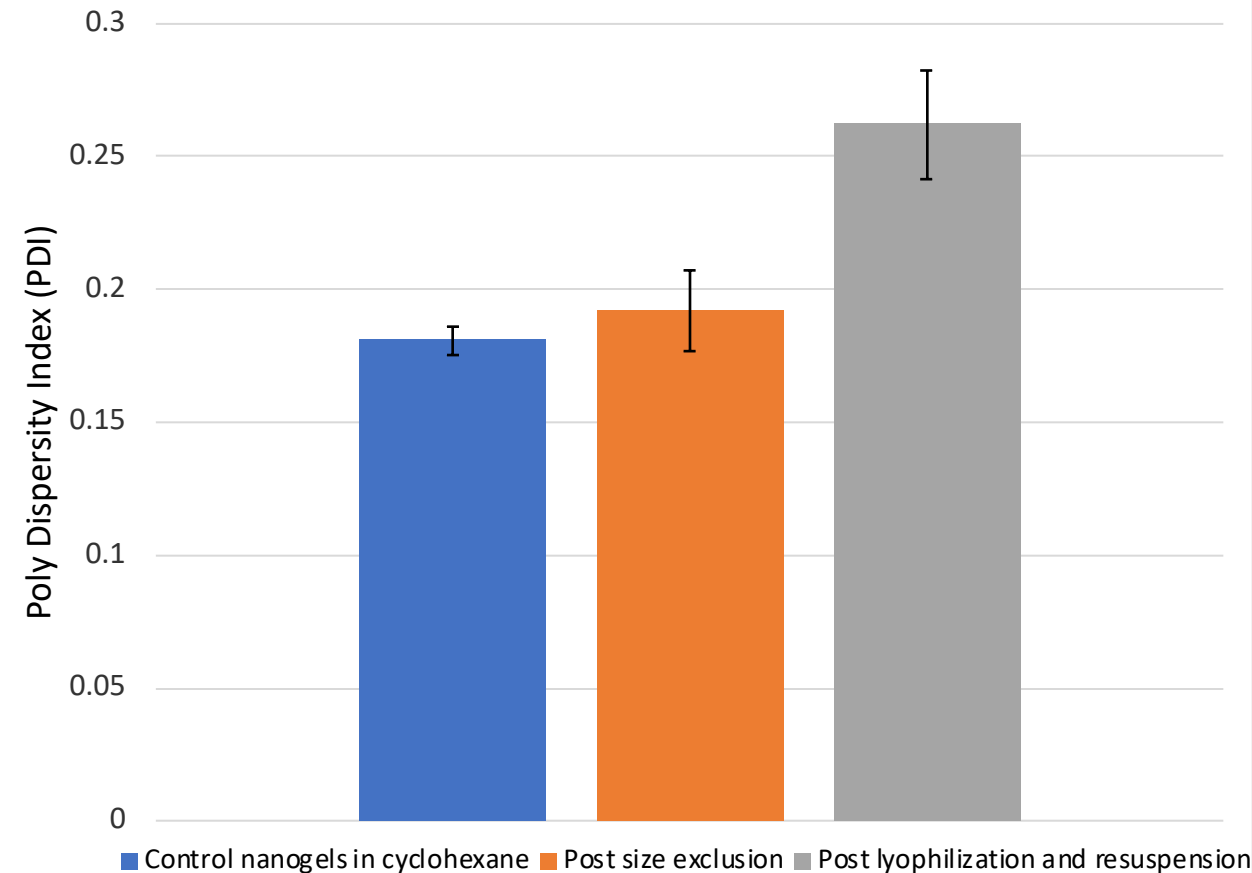
Lyophilization for long-term storage, resuspension in PBS when needed

Nanogels retain desired geometry and monodispersity over purification and time

Nanogel Size via DLS



Nanogel PDI via DLS



Nanogel size dictated by sonication duration, agitation power

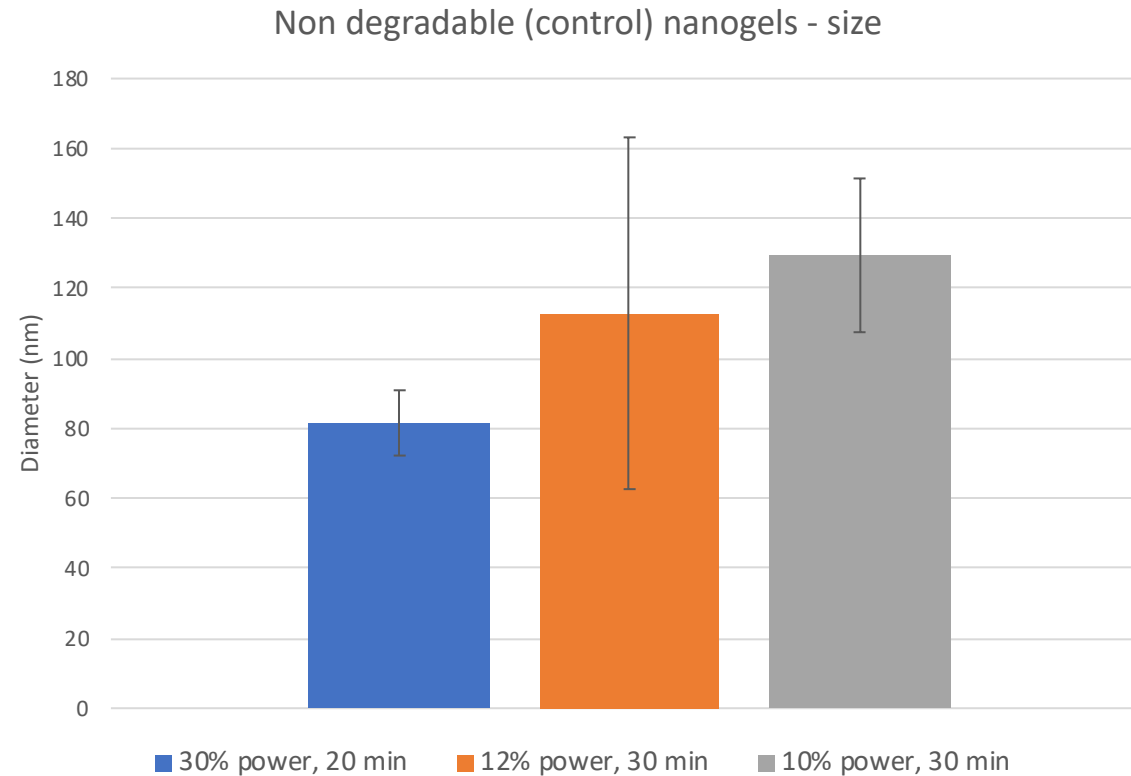
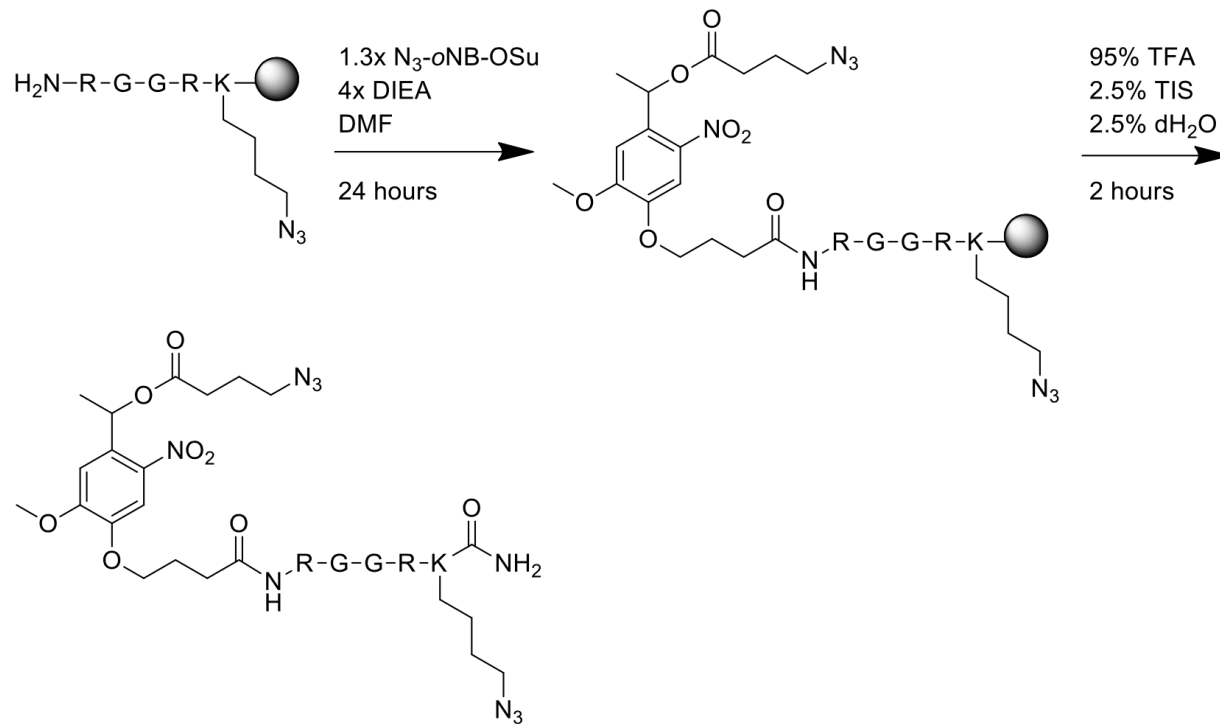


Photo-degradable YES crosslinker synthesis



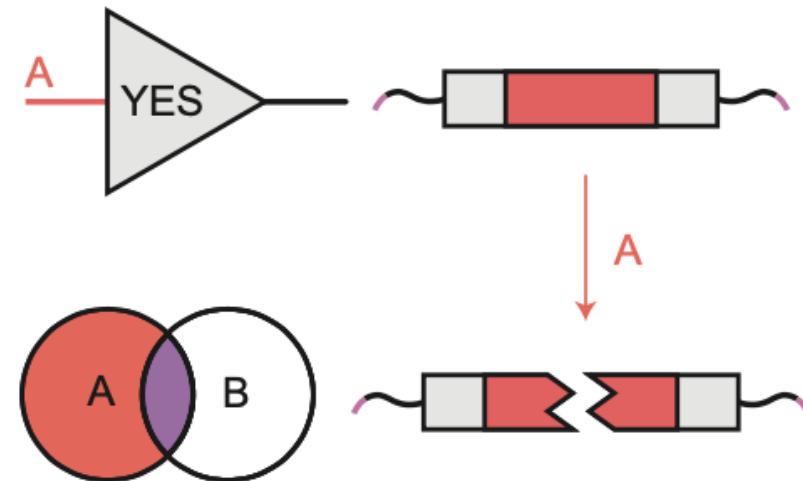
Final Product:

N_3 -oNB- RGGRK(N₃)-NH₂

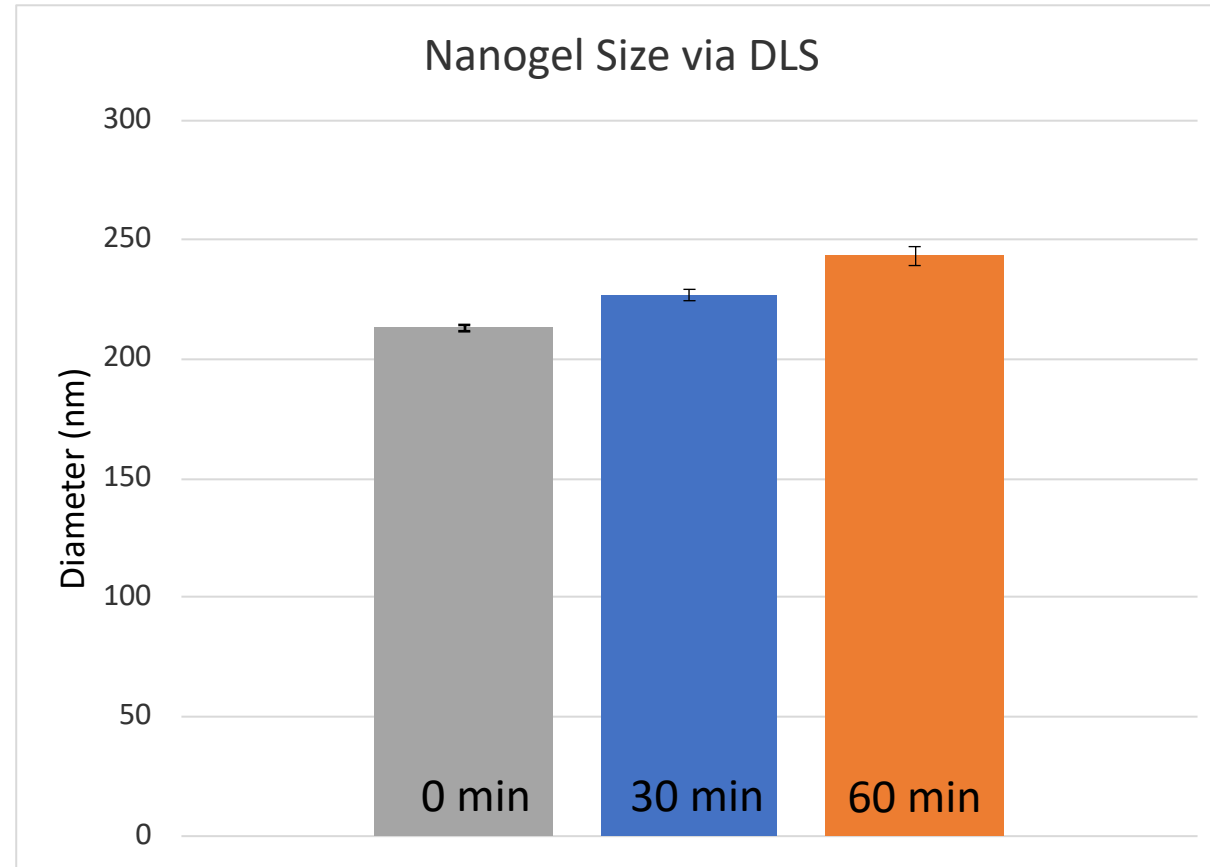
Click

Click

Photodegradable



$\lambda = 365$ nm near-UV light disrupts photo-degradable nanogels in emulsion

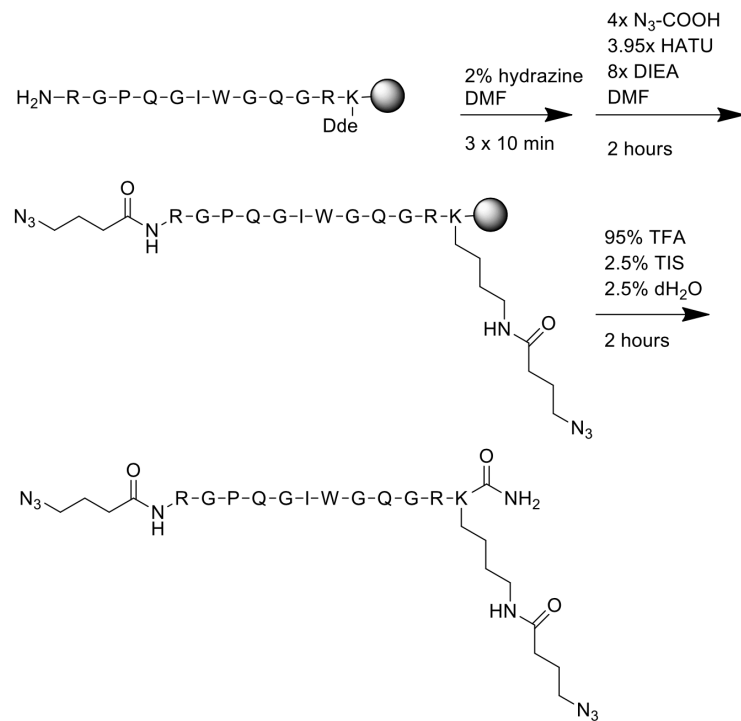


- Nanogels completely degraded at 90min

Duration of light exposure

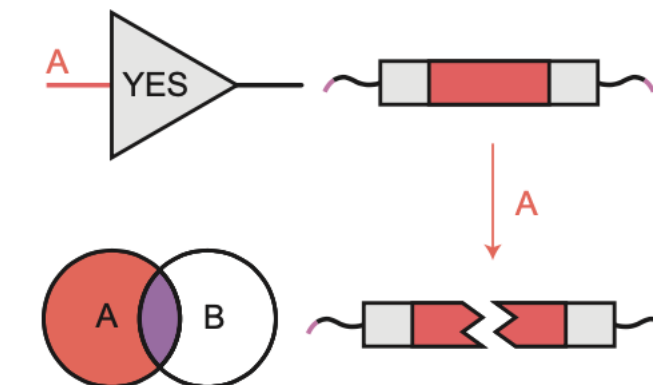
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MMP (E) YES condition degradable crosslinker



$\text{R}^1\text{-G-P-Q-G-I-W-G-Q-R}^2$

MMP-8

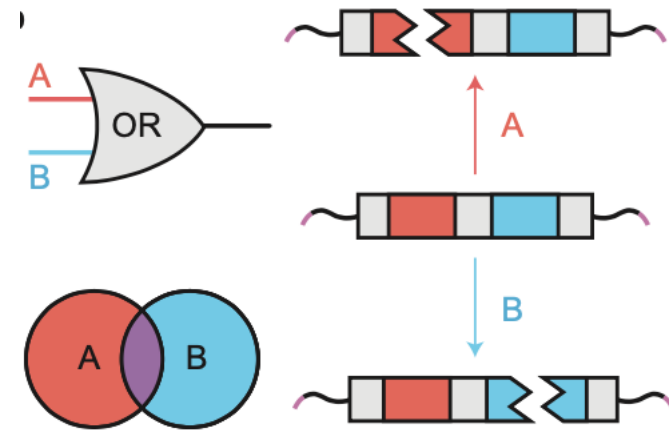
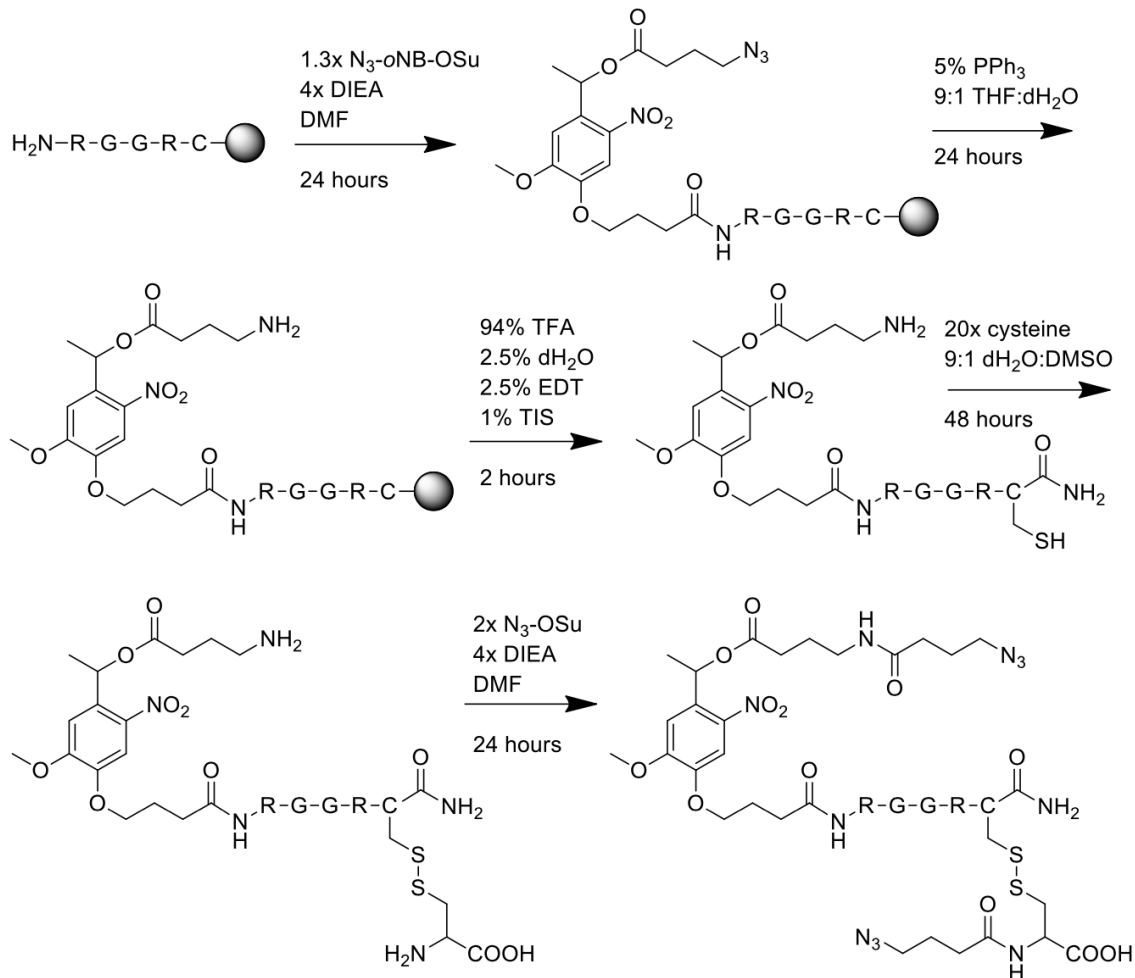


$\text{R}^1\text{-G-P-Q-G}$

+

I-W-G-Q-R^2

Light OR reducing (PUR) condition degradable crosslinker



Final Product:

$\text{N}_3\text{-oNB-RGGRC(N}_3\text{-C-OH)-NH}_2$

Click

Click

Photodegradable

cysteines linked *via* disulfide bond

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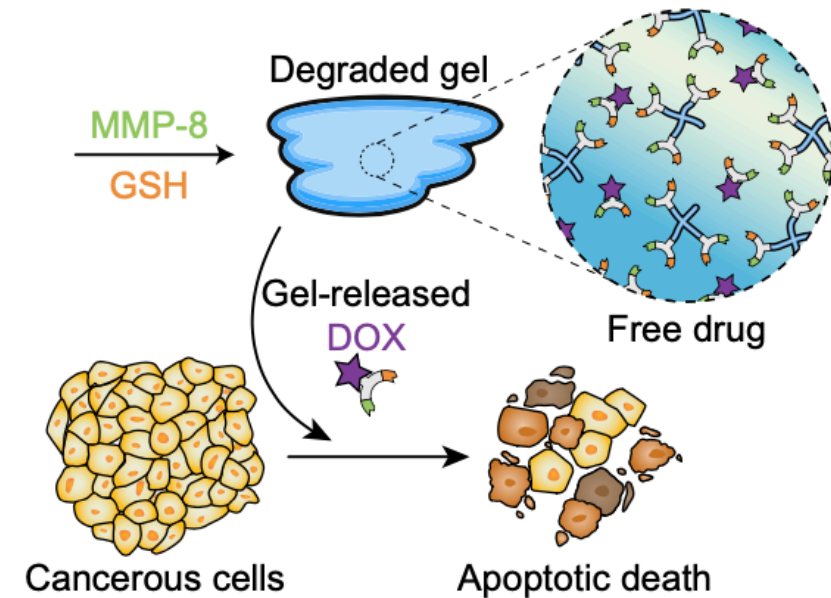
In Summary



- > Identified material components most suitable for nanogel formation
- > Optimized nanogel synthesis and purification protocols
- > Achieved desired nanogel geometry, dispersity and tuning
- > Demonstrated specific nanogel degradation in simple/complex systems

Future Work

- > Analyze nanogels with complex linkers
 - Geometry, dispersity, degradability
- > Apply nanogels to biological systems
 - Treat cancer-derived cells with chemotherapeutics released by nanogel platform based on varying inputs



Acknowledgements

- > UW Bioengineering and Chemical Engineering
- > DeForest Research Group
- > Undergraduate Research Program
- > CoMotion/Mary Gates Innovation Scholarship
- > Levinson Emerging Scholar Award



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C O M O T I O N

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