Poly(β-amino ester) particles with programmable shape, stiffness, and degradation for drug release

July 17, 2025

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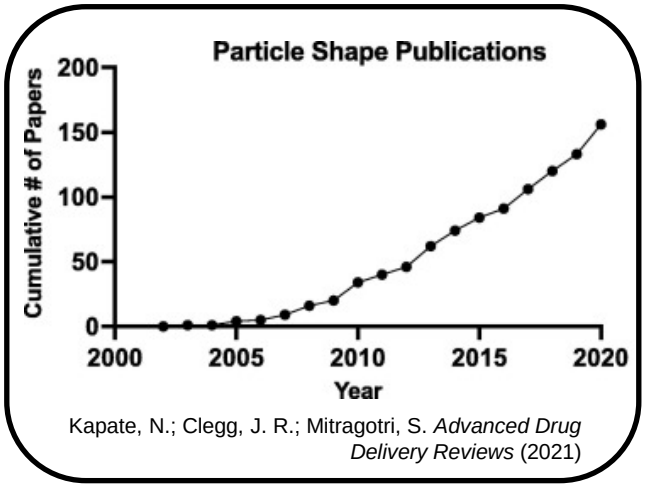
CRS 2025 ANNUAL MEETING & EXPOSITION
PHILADELPHIA, PA
JULY 13-18, 2025

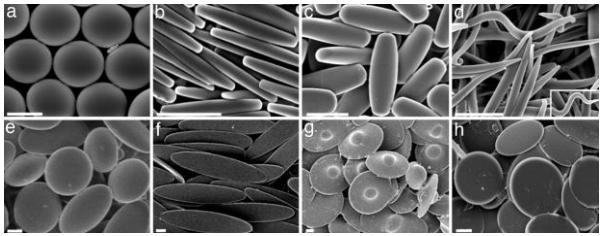
NEXT-GENERATION DELIVERY INNOVATIONS

Nonspherical, biodegradable particles possess powerful drug delivery implications

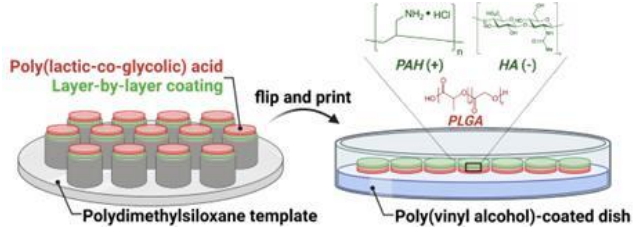


Kapate, N.; Clegg, J. R.; Mitragotri, S. *Advanced Drug Delivery Reviews* (2021)

- Cell-particle interactions
- Biodistribution
- Behavior in fluid flow
- Active particles



Champion et al. *PNAS* (2007)

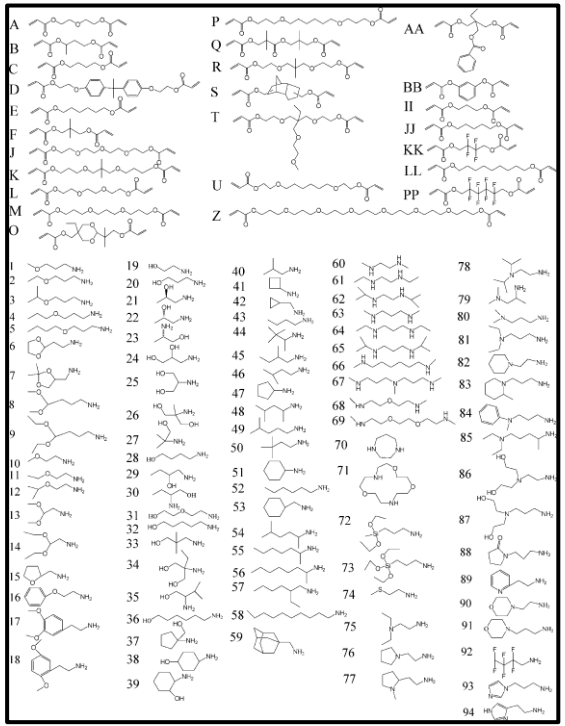


Kwan et al. *In Revision*

Poly(β-amino ester) (PBAE) as a modular biomaterial

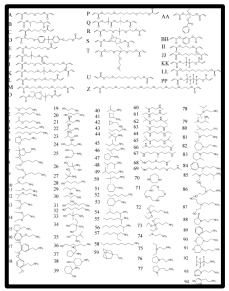
Diacrylates

Amines

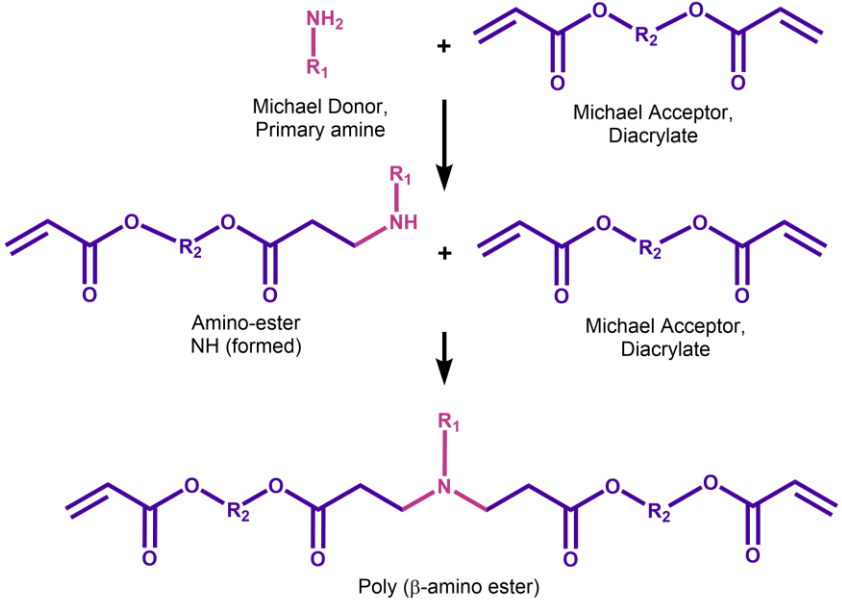


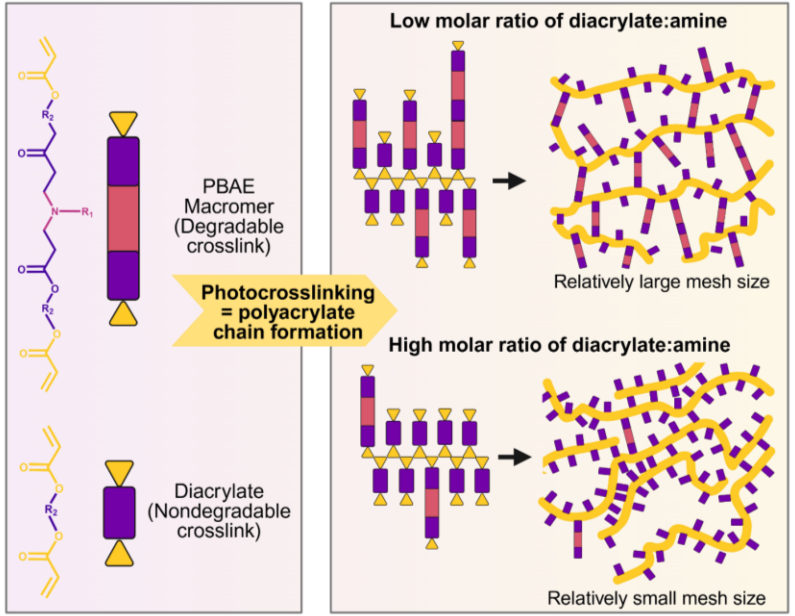
Green et al. *Acc Chem Res. (*2008)

Poly(β-amino ester) (PBAE) as a modular biomaterial

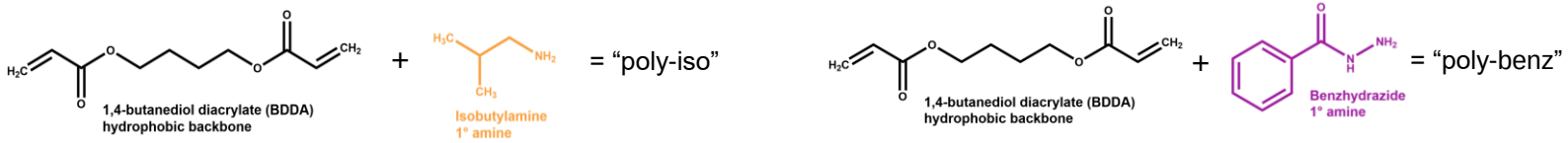


Green et al. *Acc Chem Res. (*2008)

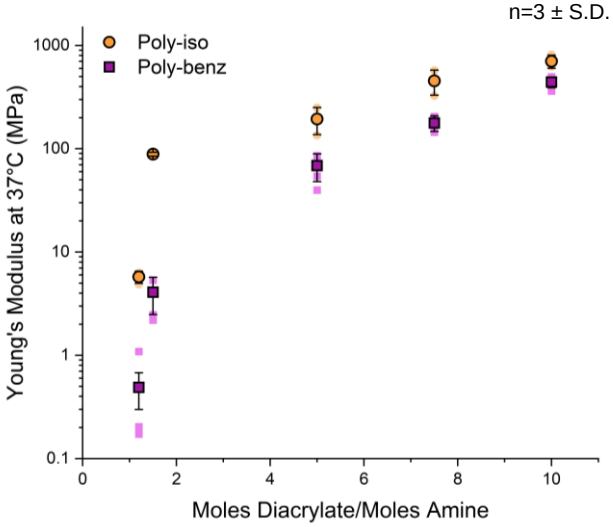


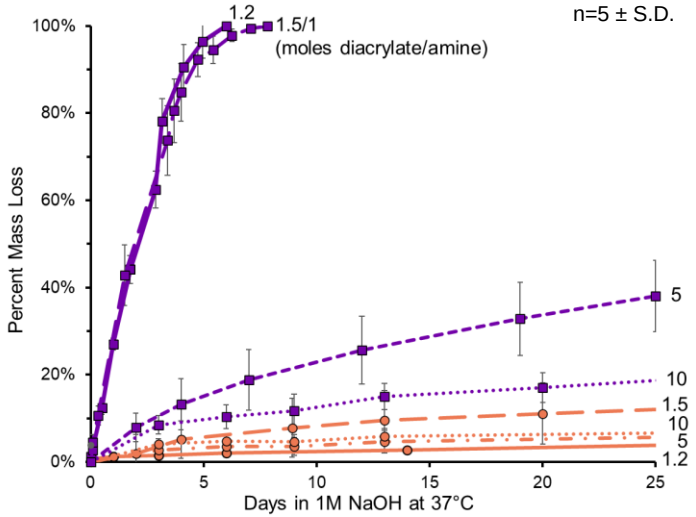


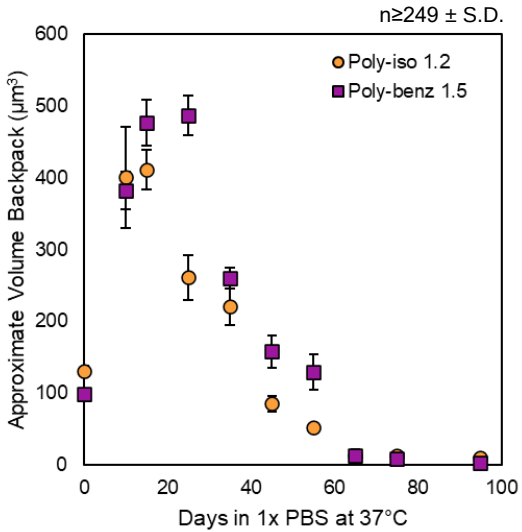
PBAE-dA elasticity and degradation can be tuned



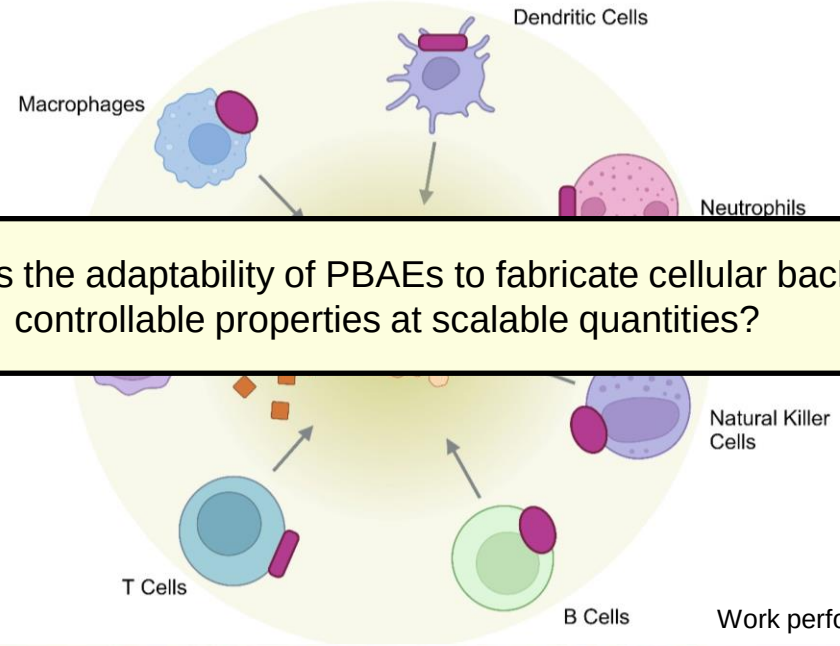
Molar ratios diacrylate:amine → 1.2:1, 1.5:1, 5:1, 10:1







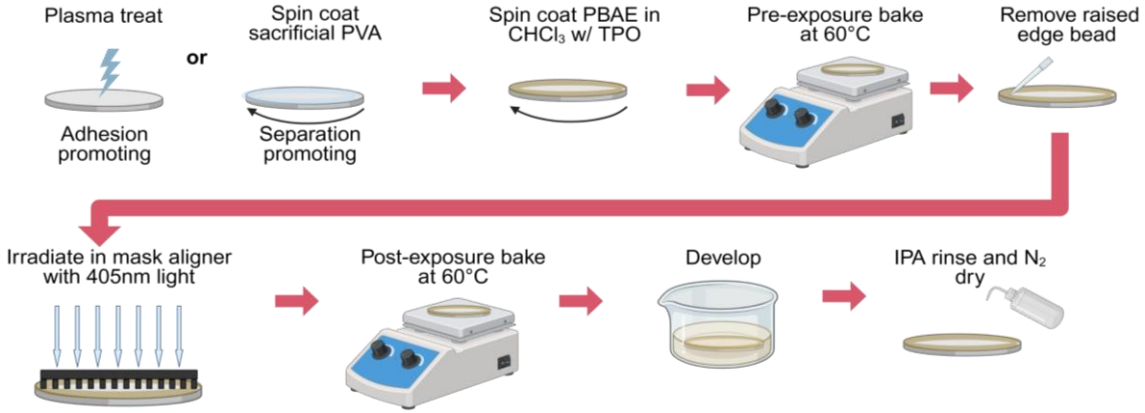
Use Case 1:
Cellular backpacks for drug delivery

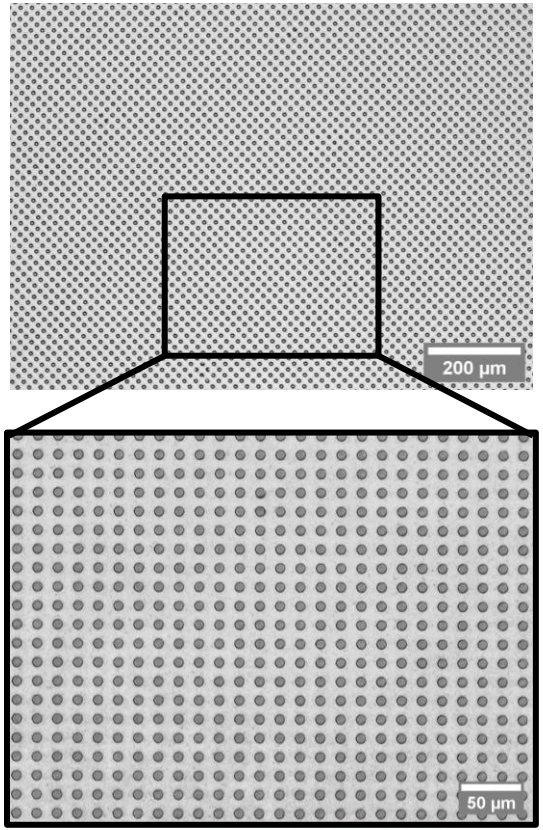


Can we harness the adaptability of PBAEs to fabricate cellular backpacks with controllable properties at scalable quantities?

Work performed in large part by the Mitragotri group

Contact photolithography

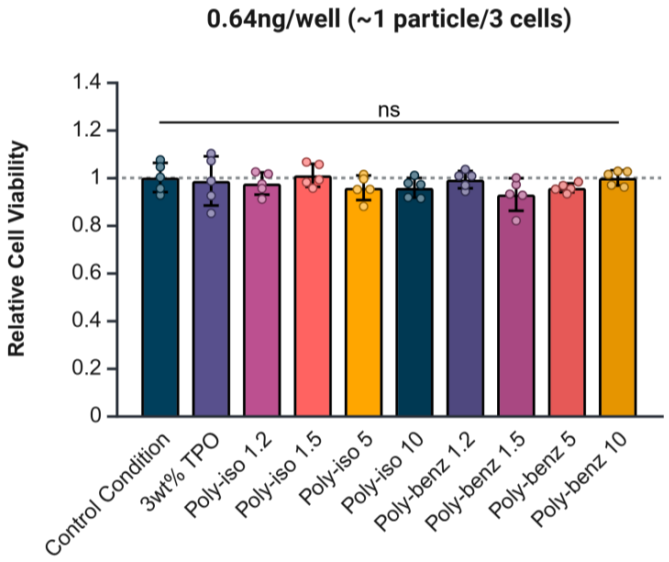


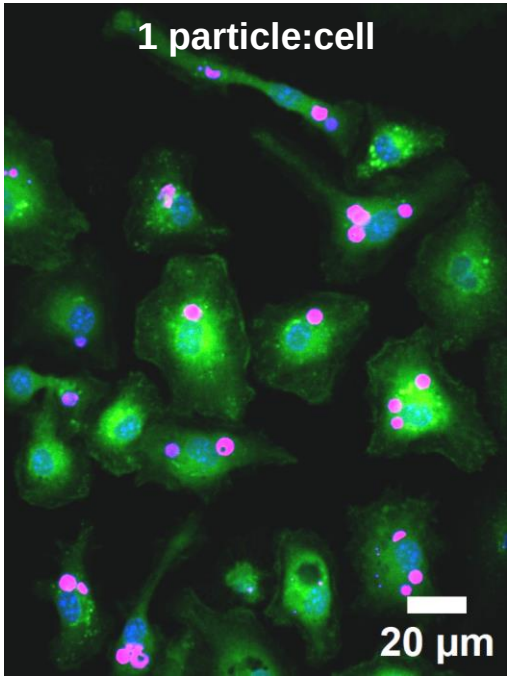


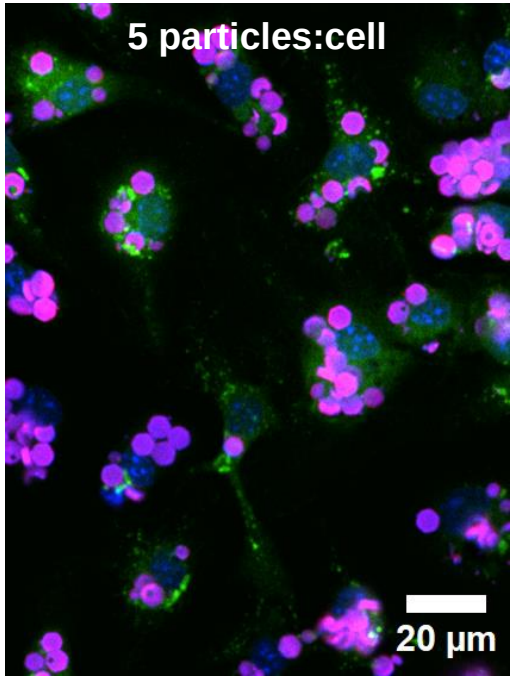
- ≥1µm 2D resolution limit*
- ~10^8 backpacks/hr

*Wu CY et al *Micromachines (Basel)* (2019)

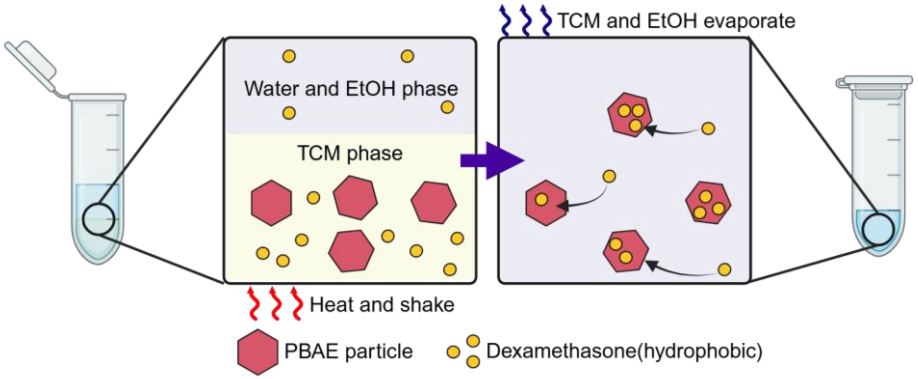
PBAE-dA backpacks are biocompatible and promote adhesion

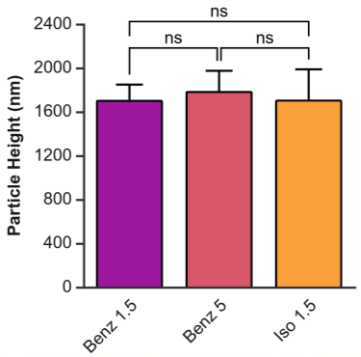


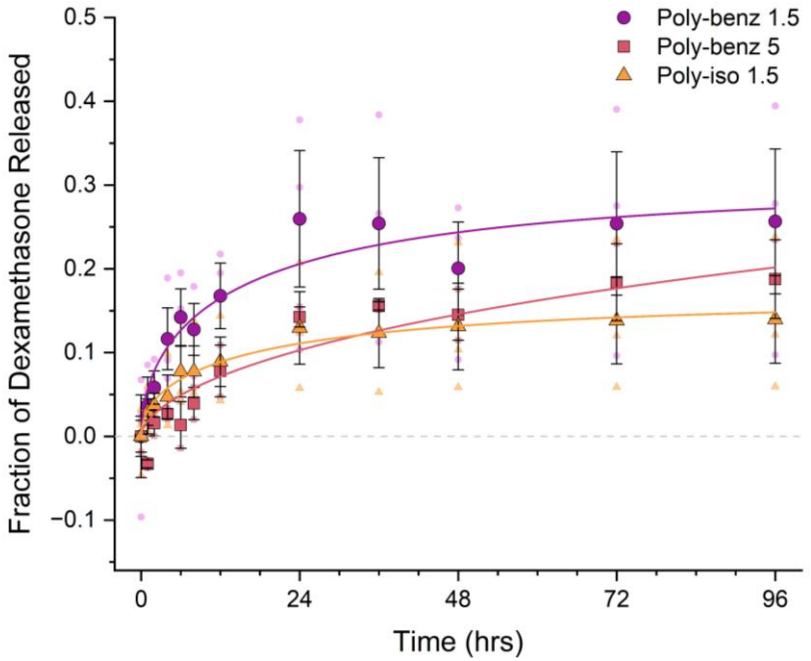




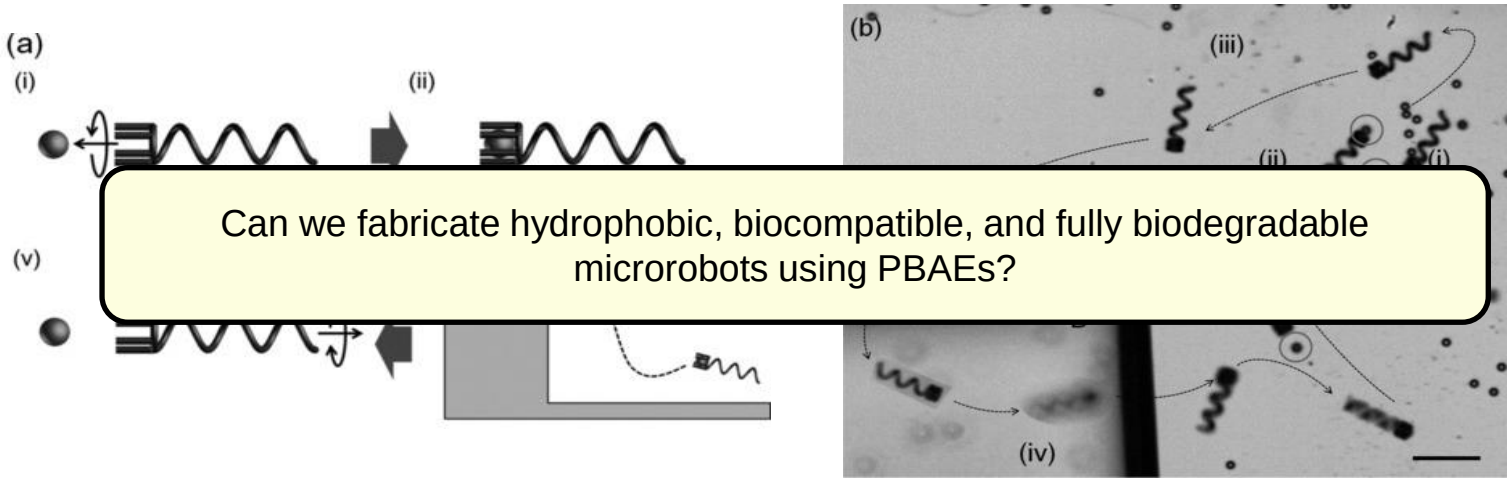
Backpacks prolong drug release of dexamethasone







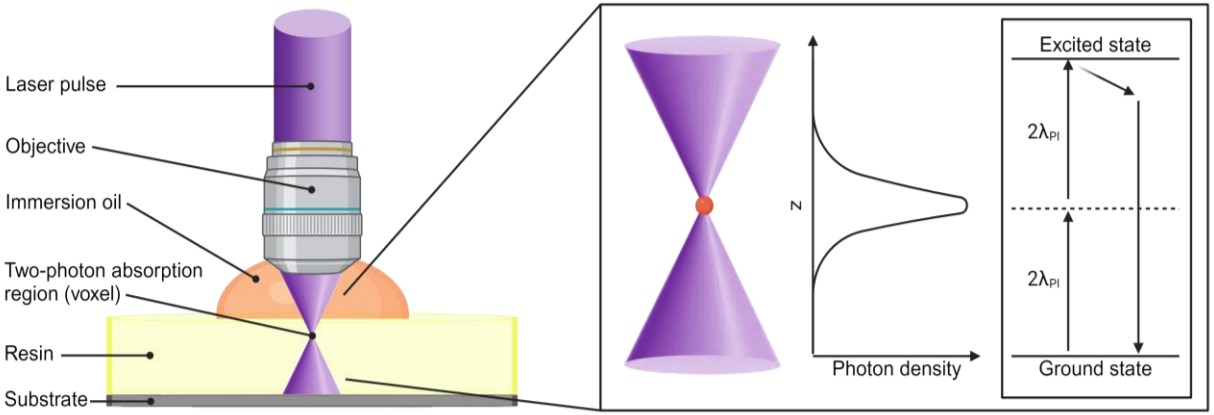
Use Case 2:
Biodegradable magnetic microrobots

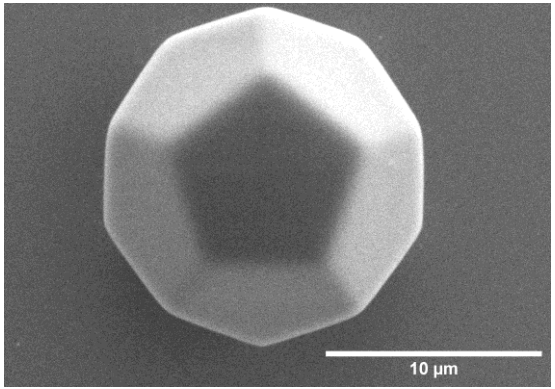


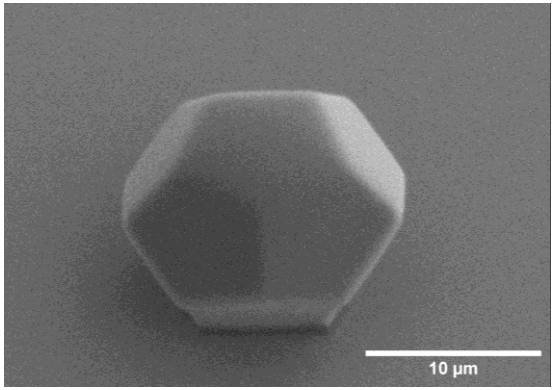
Can we fabricate hydrophobic, biocompatible, and fully biodegradable microrobots using PBAEs?

Tottori S. et al, *Adv. Mater.* (2012)

Two-photon lithography

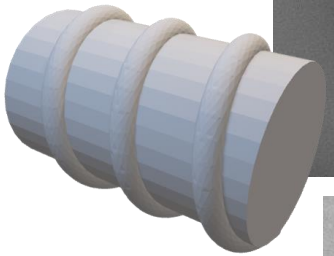


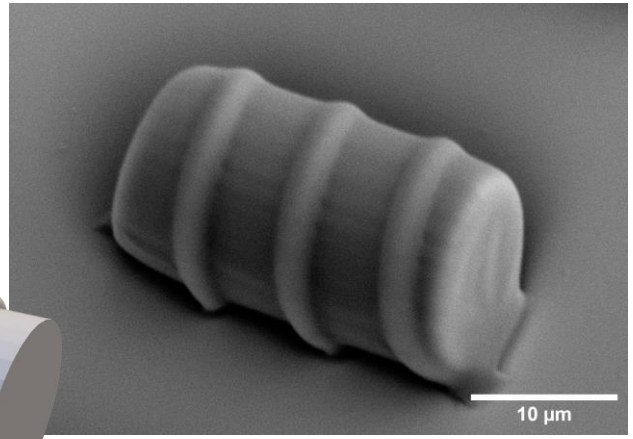


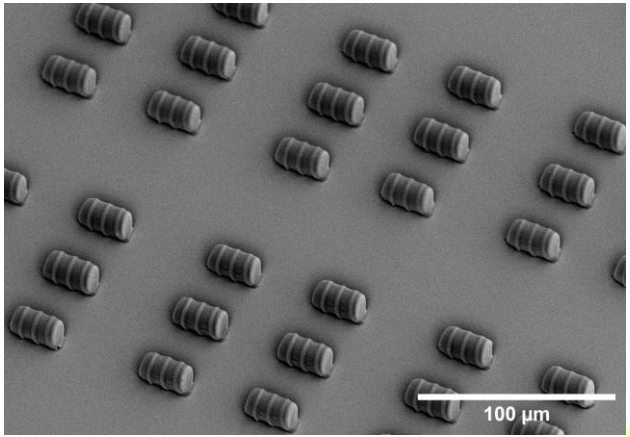


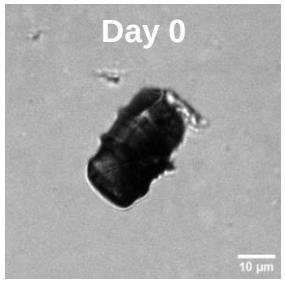
- ~200nm 3D resolution
- ~10^2 particles/hr

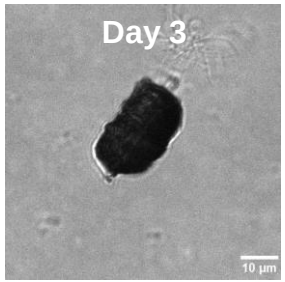
Fully biodegradable magnetic micRotinis

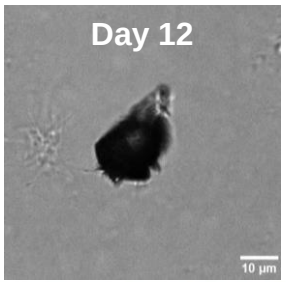


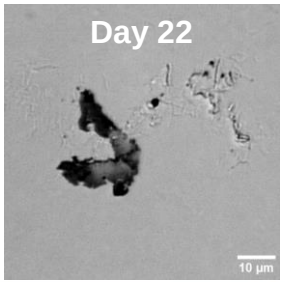




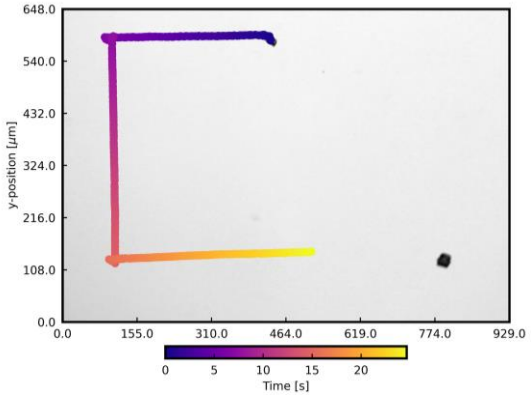


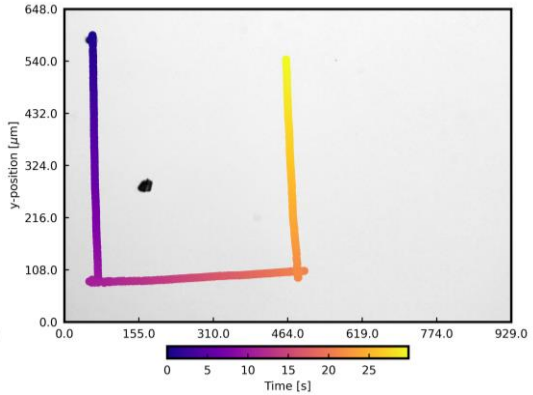


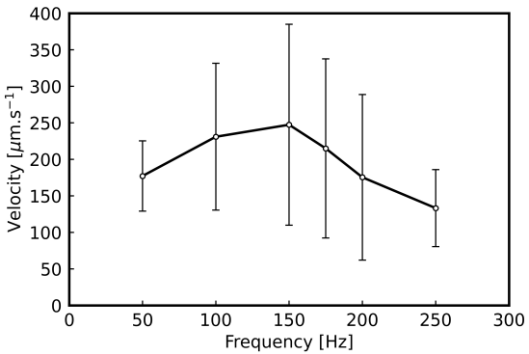




MicRotinis offer spatiotemporal control







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Leslie Radosevich M.S.
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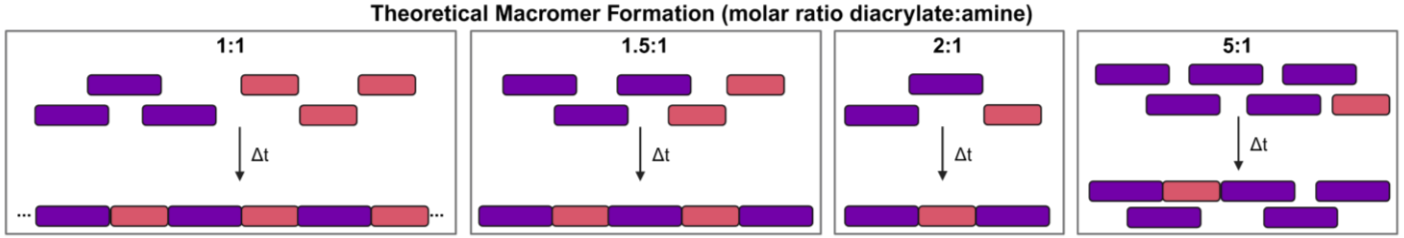
Hunter Wiese

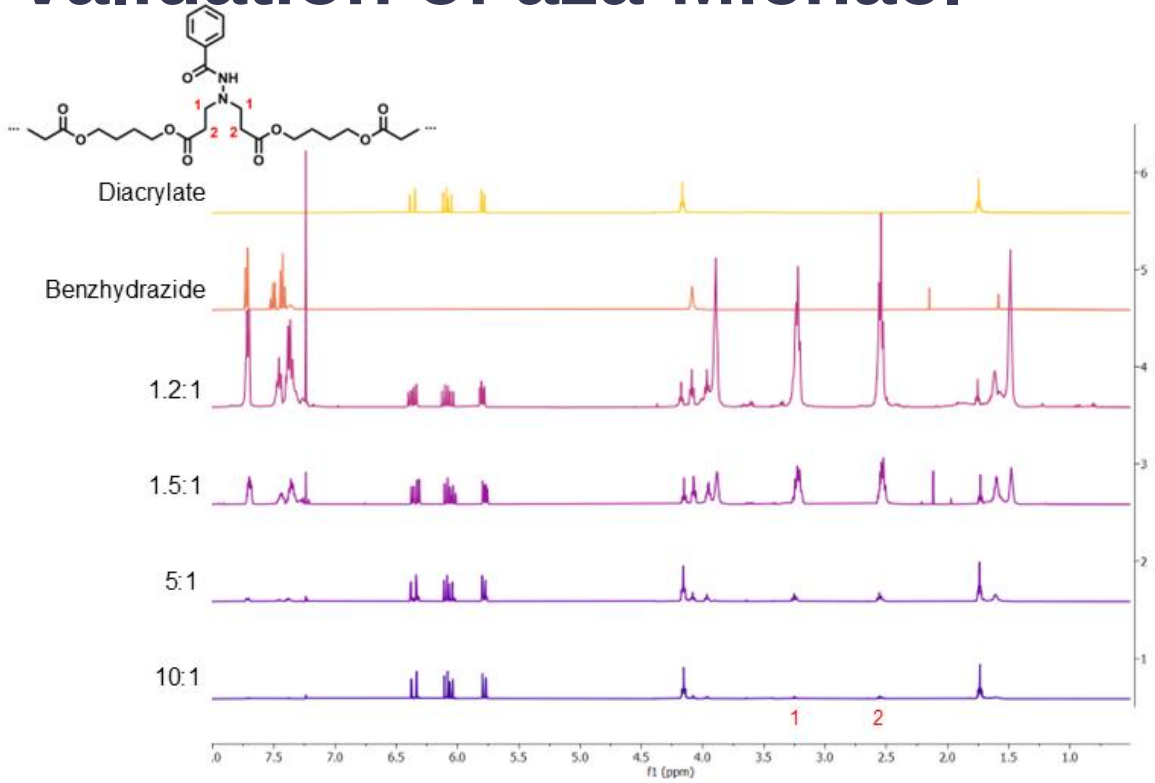
Figures produced using BioRender

Shields IV, CW; Trese, KA. U.S. Patent App. No.: 63/682,666

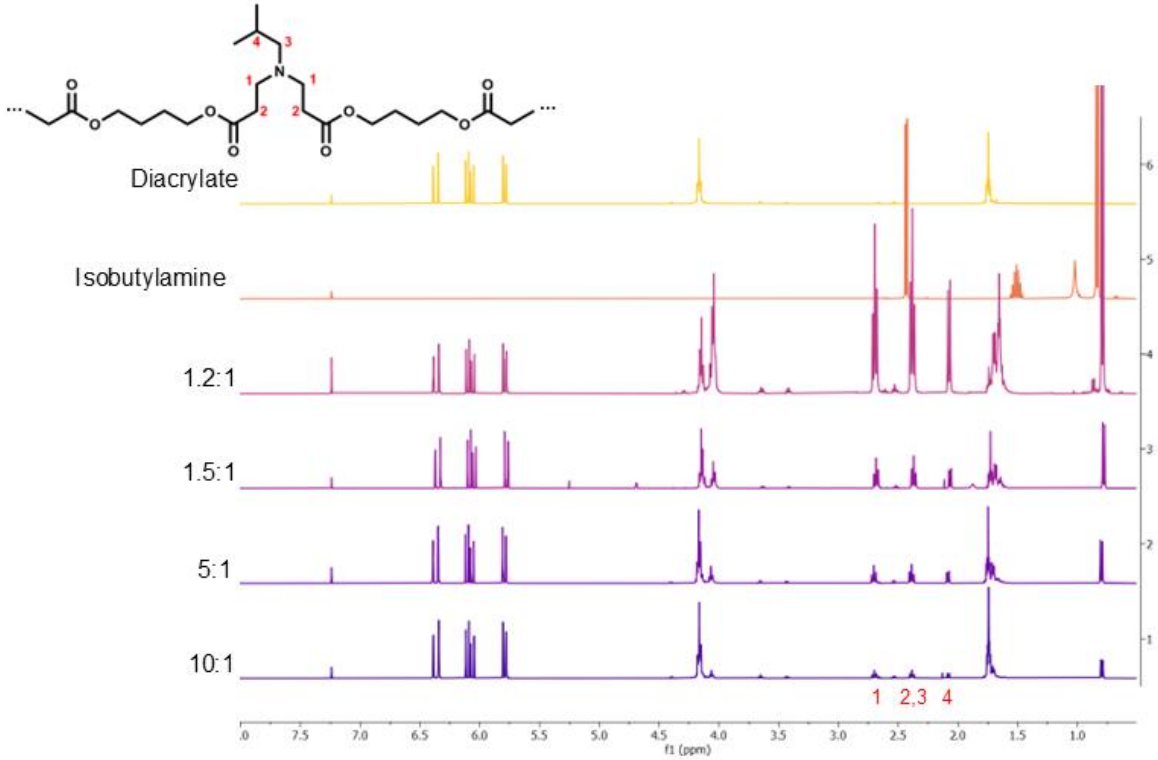
Theoretical macromer formation



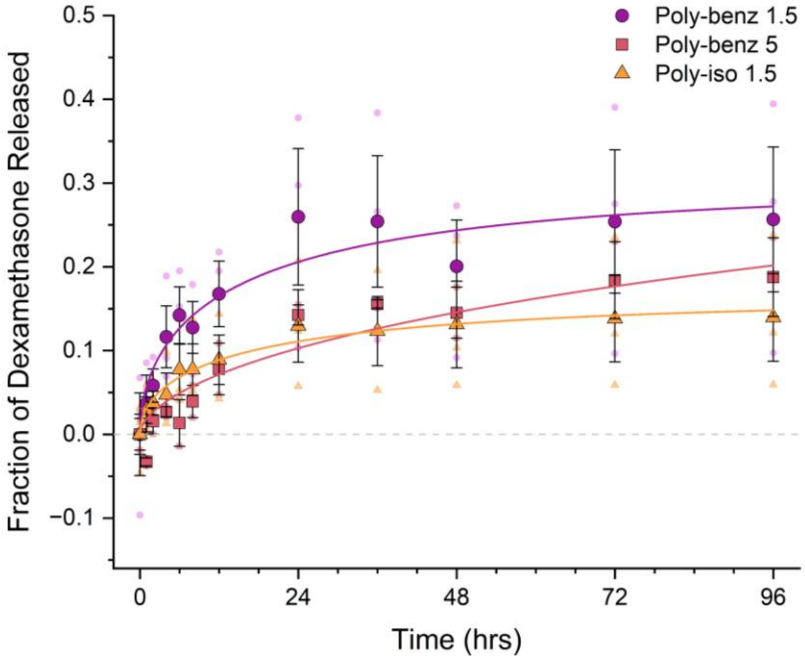
H-NMR validation of aza-Michael

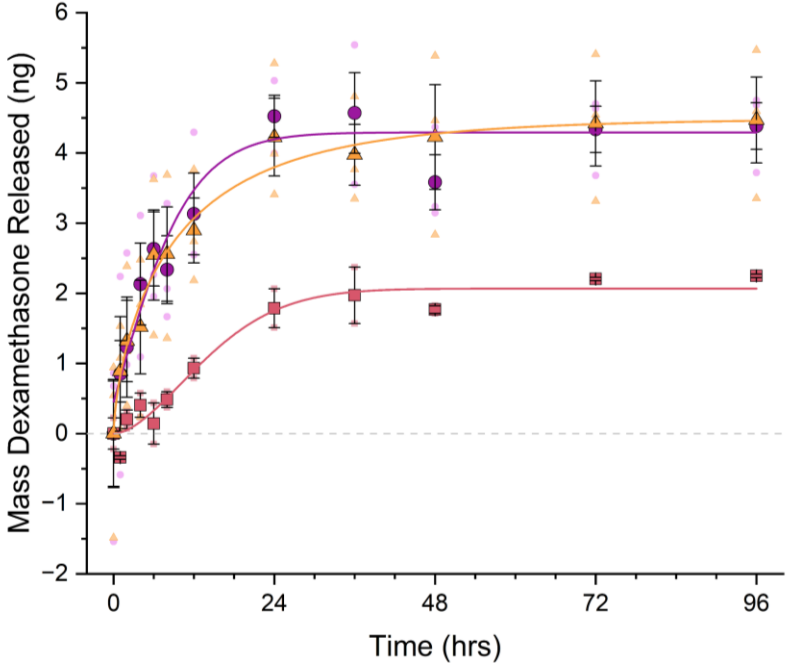


H-NMR validation of aza-Michael

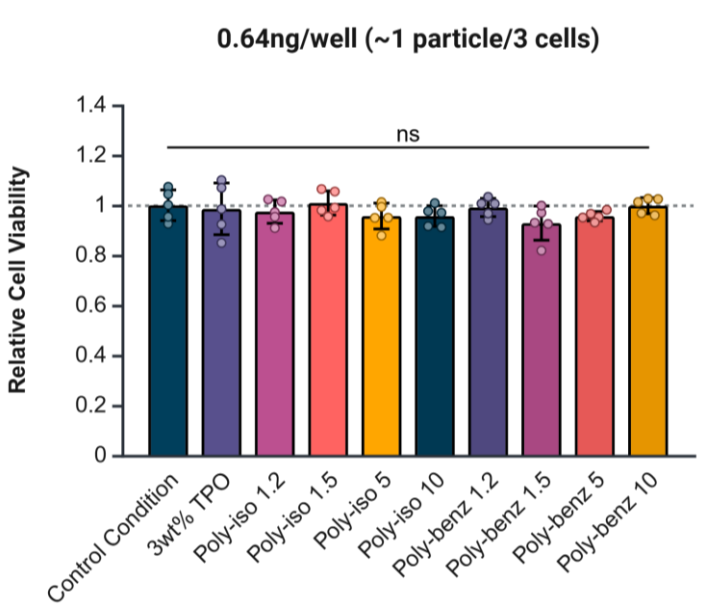


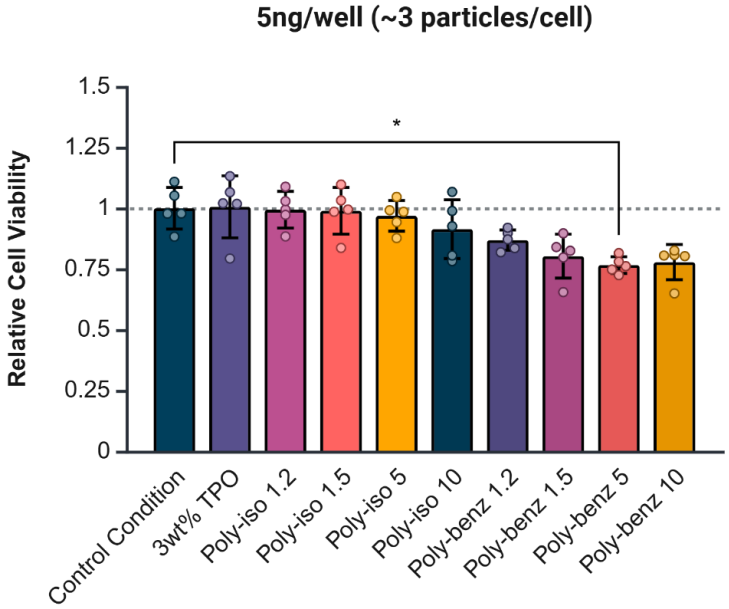
Dexamethasone release



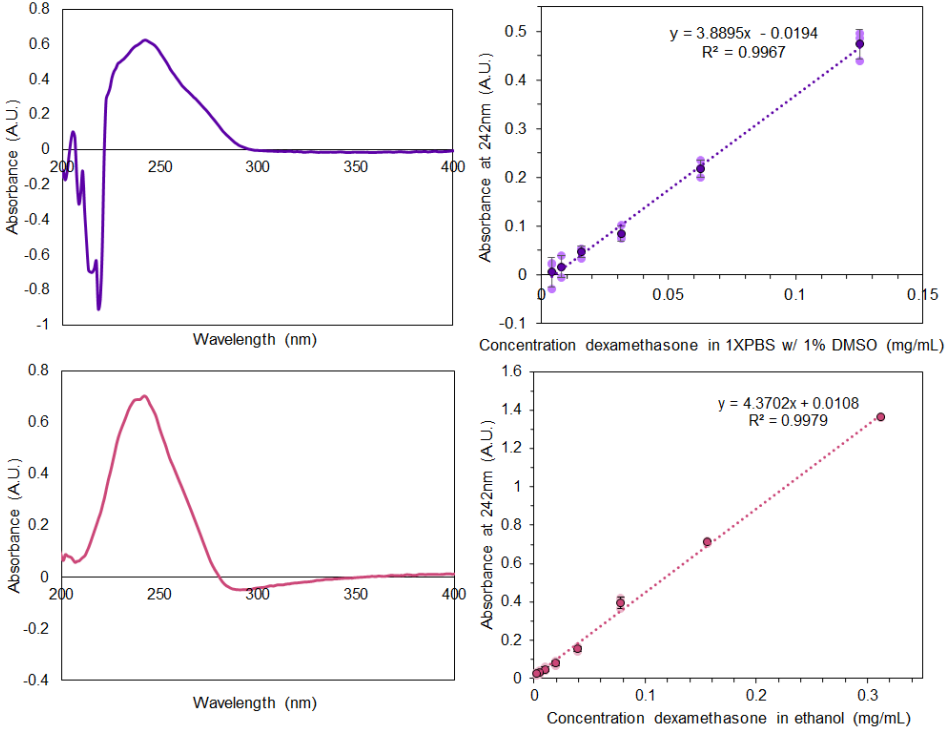


MTT assay


0.64ng/well (~1 particle/3 cells)
Relative Cell Viability
1.4
1.2
1
0.8
0.6
0.4
0.2
0
ns
Control Condition
3wt% TPO
Poly-iso 1.2
Poly-iso 1.5
Poly-iso 5
Poly-iso 10
Poly-benz 1.2
Poly-benz 1.5
Poly-benz 5
Poly-benz 10

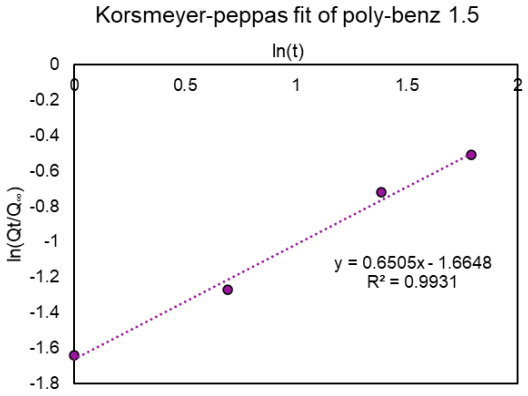

5ng/well (~3 particles/cell)
Relative Cell Viability
1.5
1.25
1
0.75
0.5
0.25
0
*
Control Condition
3wt% TPO
Poly-iso 1.2
Poly-iso 1.5
Poly-iso 5
Poly-iso 10
Poly-benz 1.2
Poly-benz 1.5
Poly-benz 5
Poly-benz 10

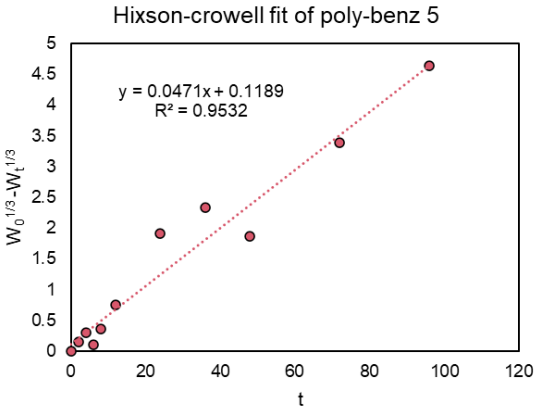
Drug release calibration curve

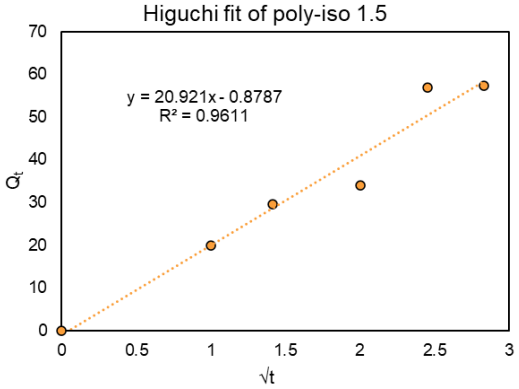


$$y = A(1 - e^{-(k(x-x_c))^d})$$

Drug release curve fits



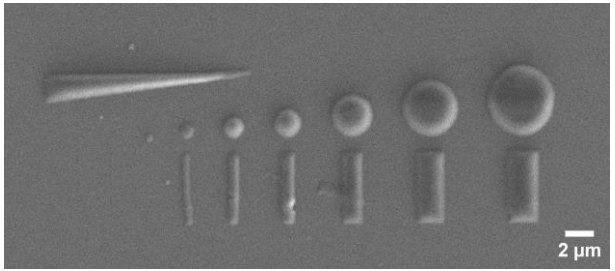


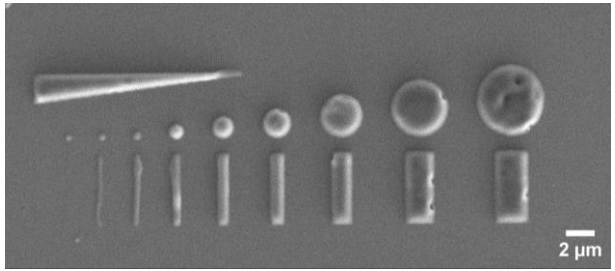


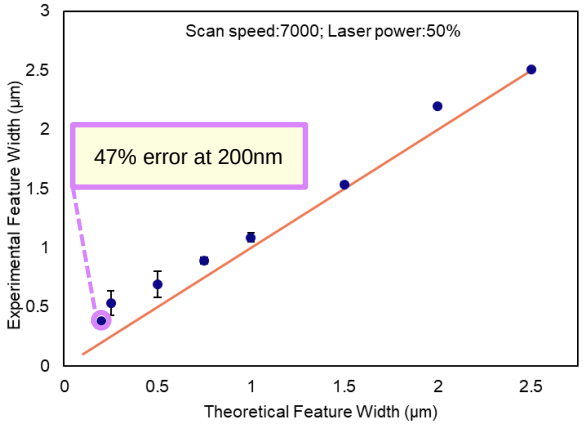
Contact photolithography parameters

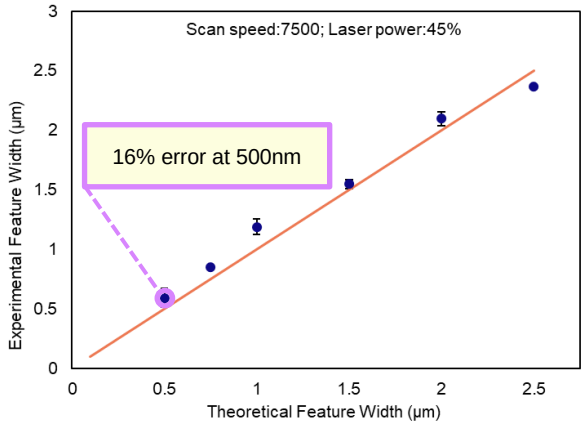
Amine	Molar ratio diacrylate:amine	TCM wt.%	TPO wt.%	Dosage 405nm light (mJ/cm^2)
Isobutylamine	1.2	10	3.00	392
Isobutylamine	1.5	10	3.00	112
Isobutylamine	5	0	0.85	154
Isobutylamine	10	0	0.85	112
Benzhydrazide	1.5	10	3.00	336
Benzhydrazide	5	0	0.85	84.0
Benzhydrazide	10	0	0.85	70.0

We can print features with submicron critical dimensions via two-photon lithography









Maskless photolithography

- ≥0.6µm 2D resolution*
- ~10^4 particles/hr

**uMLA*. Heidelberg Instruments. (2025, June 5).