RCSI Leading the world to better health

Nanoparticles *via* SET-LR-PISA

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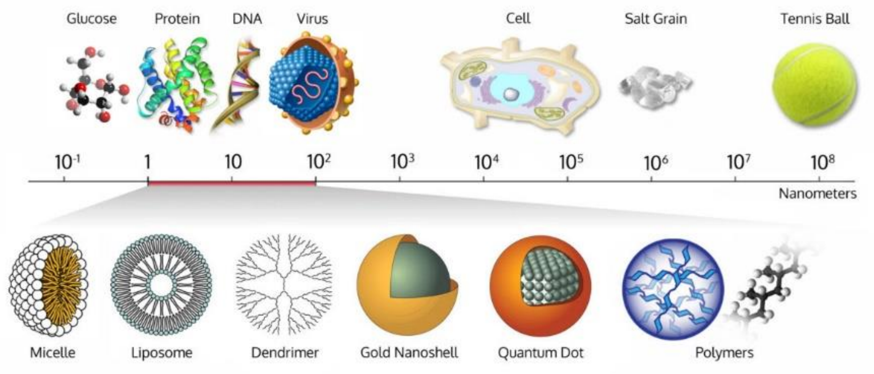
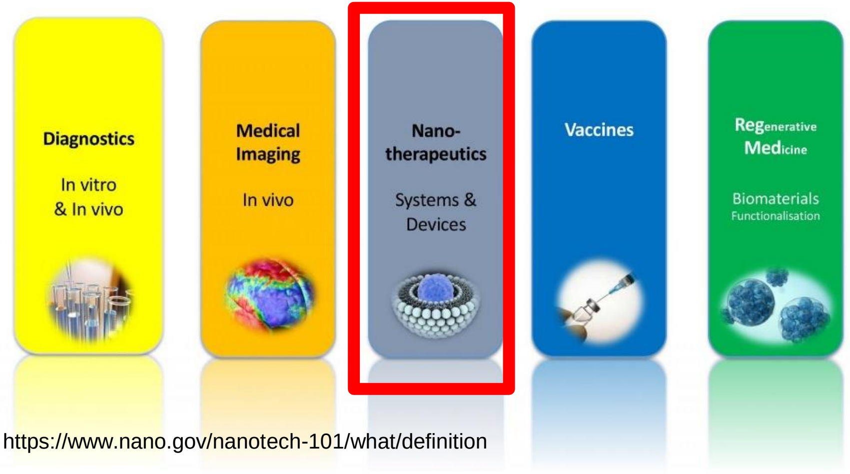
Supervisor A. Heise

Nanomedicine

"Nanotechnology is the science conducted at the nanoscale, about 1 to 100 nm"



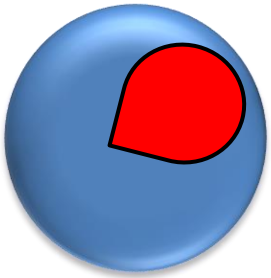


"Nanomedicine is the application of nanotechnology for medical purposes"

https://www.nano.gov/nanotech-101/what/definition

NPs in biological fluid

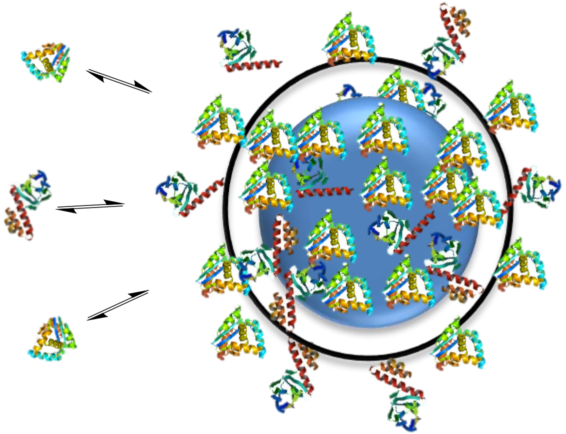
Polymeric NPs



Classified in terms of

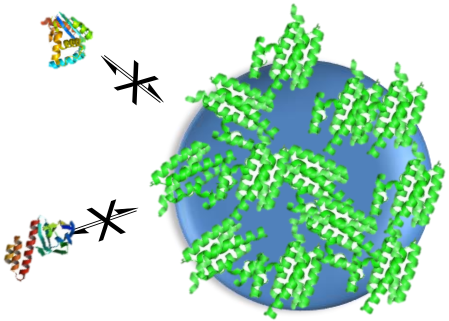
- Type of polymers
- Surface functionalisation
- morphology

Biological environment



- Formation of protein corona layer.
- New biological identity.
- Poor biodistribution.

Surface modification



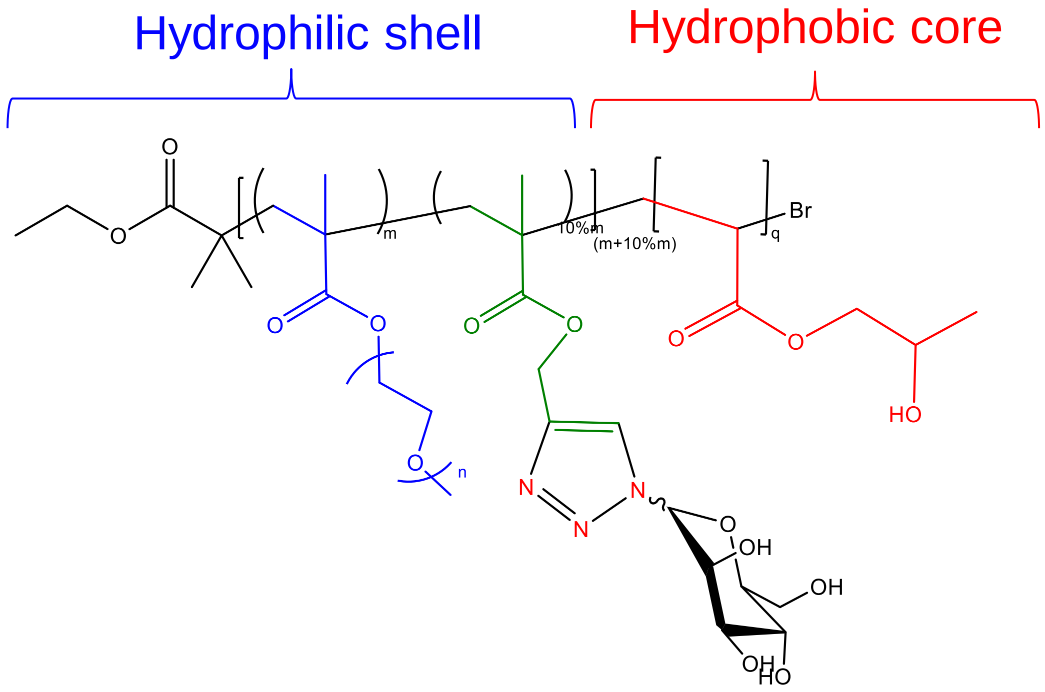
- Creation of artificial corona layer.
- **Glycopolymers.**

Monopoli, M. P., et al. (2012). "Biomolecular coronas provide the biological identity of nanosized materials." Nature Nanotechnology **7**(12): 779-786.

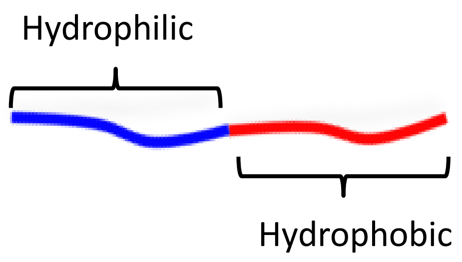
Project goal

1. Develop a facile procedure for the synthesis of a glycosylated polymer nanoparticle using block copolymer self-assembly, specifically PISA technology.

2. Test the biological interaction of glycosylated polymer nanoparticles.



Amphiphilic block copolymer

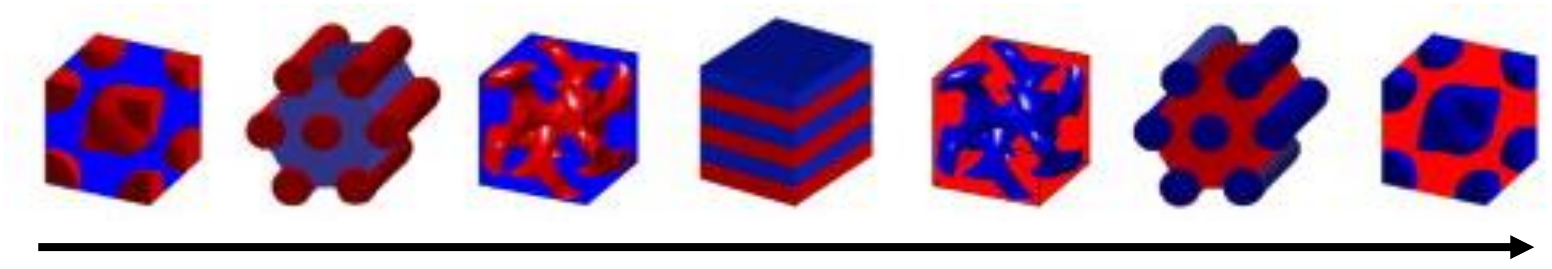


Amphiphilic block copolymers comprise of discrete immiscible hydrophobic and hydrophilic blocks which undergo phase separation in aqueous conditions.

Microphase separation promoted by;

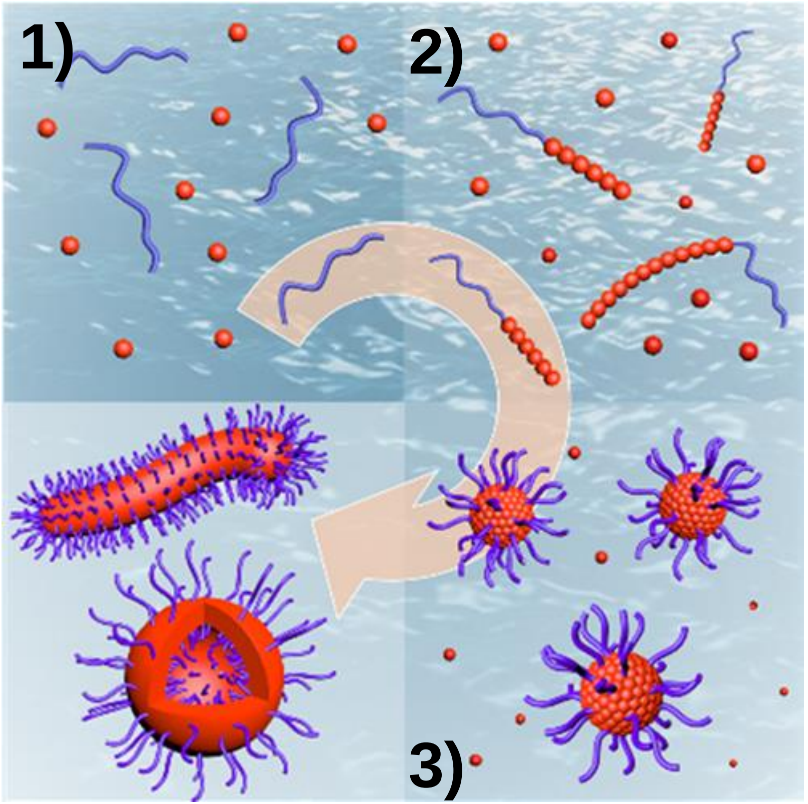
Hydrophilic repulsion → increase hydrophilic interactions with water

Hydrophobic attractions → decrease hydrocarbon water interface



f_{red}

NPs synthesis by Polymerisation-induced self-assembly (PISA)

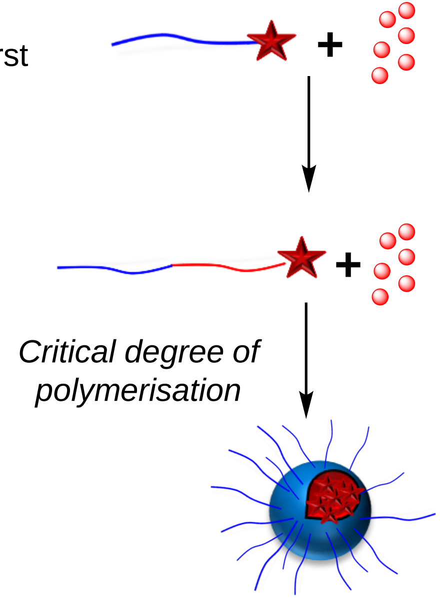


Carried out *via* controlled living radical polymerisation (*i.e*. RAFT, ATRP).

1) Synthesis of macro initiator (first block).

2) Chain extension.

3) *In situ* self-assemble.

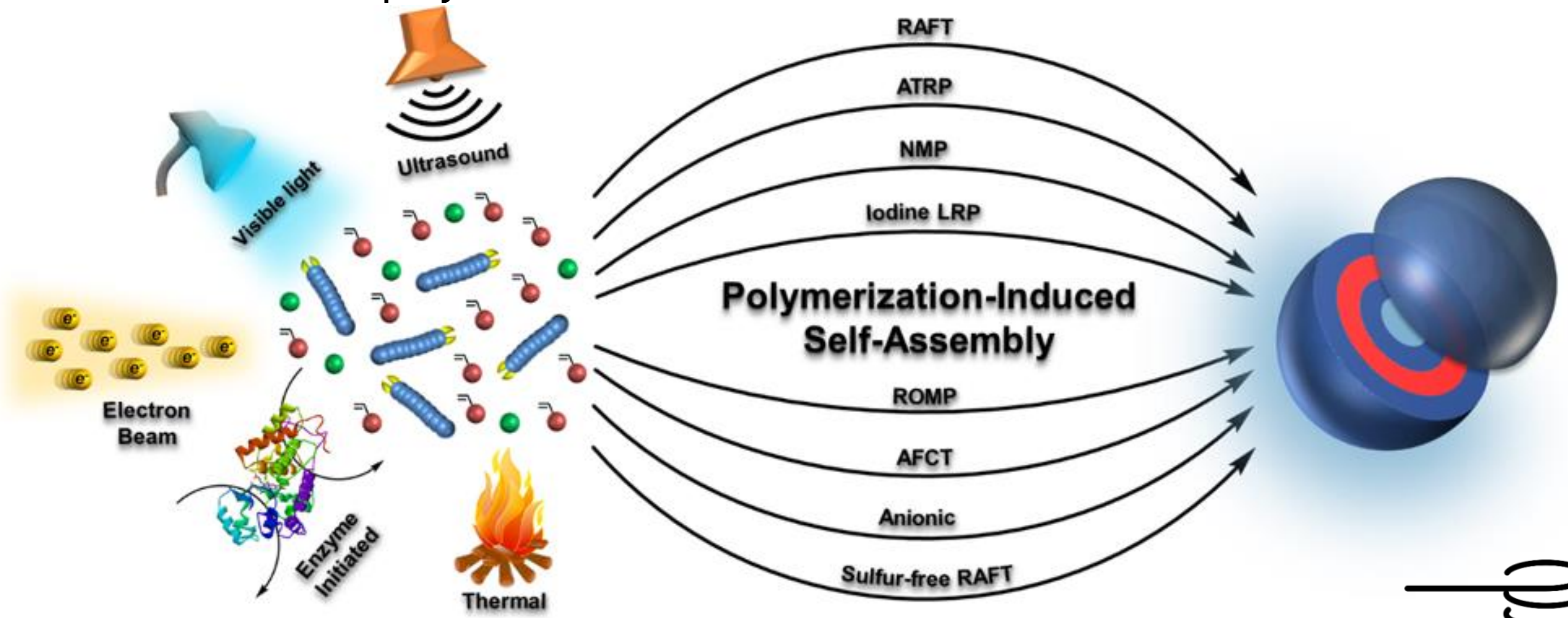


- Up to 50 w/w% solid concentration.
- Good candidate for industrial scale up.
- Nano-object of controlled size and morphology without further processing steps.

Principles and Characteristics of Polymerization-Induced Self-Assembly with Various Polymerization Techniques, Volume: 3, Issue: 4, Pages: 2104-2125.

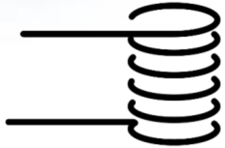
Polymerisation methods for PISA

All controlled radical polymerization methods suitable



"Single-electron-transfer living-radical polymerisation"

SET-LRP



Cu(0)

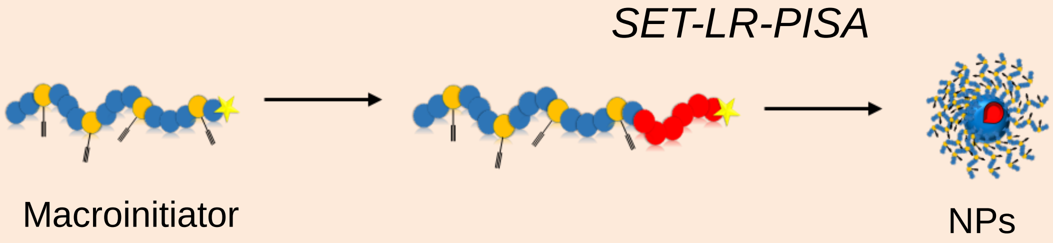
Penfold, N. J. W., *et al*. (2019). "Emerging Trends in Polymerization-Induced Self-Assembly." ACS Macro Letters **8**(8): 1029-1054.

Project stages

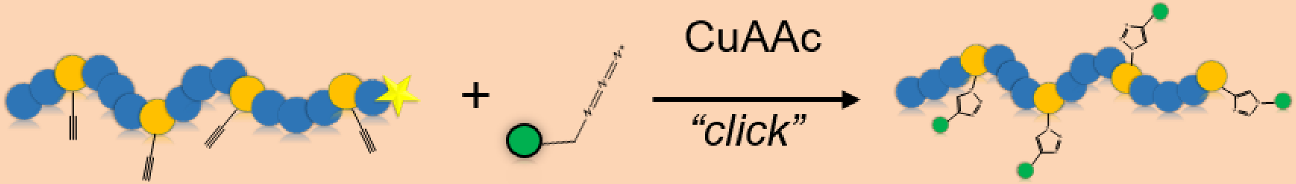
A) Preparation of NPs *via* aqueous dispersion SET-LR-PISA

Morphology evaluation:

- Core forming monomer concentration $[M]_0$
- Solvent

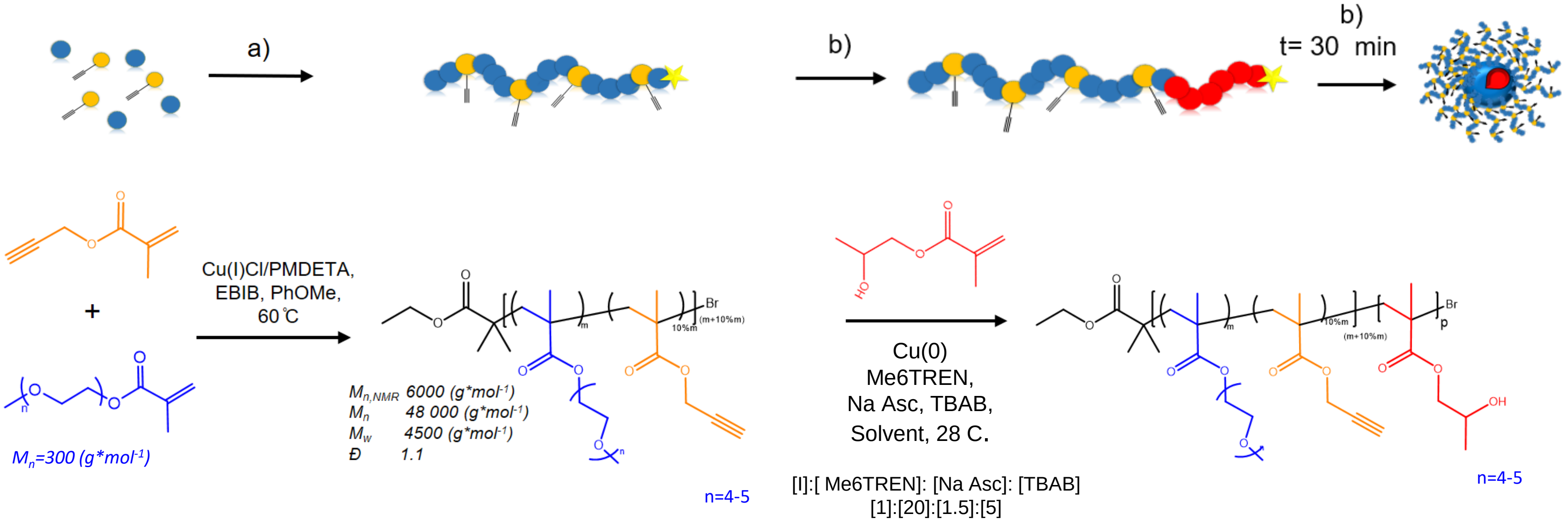


B) Macroinitiator functionalisation with mannosides via alkyne-azide copper catalysed cycloaddition:



Optimisation of NPs via aqueous dispersion SET-LR-PISA

SYNTHESIS MACROINITIATOR	*SET-LR-PISA*



a) Conventional ATRP

- DP_{PEGMA}= 20
- DP_{PgMA}=5

b) SET-LR-PISA

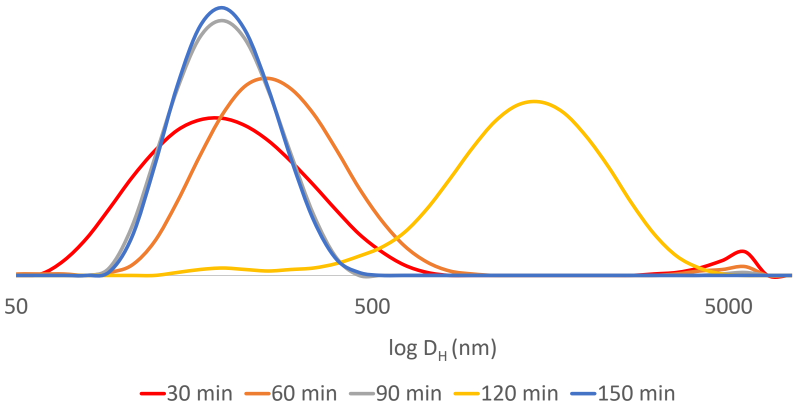
- DP_{HPMA}= 150; 300
- Solid content (SC)=10%

Followed by: DLS, TEM

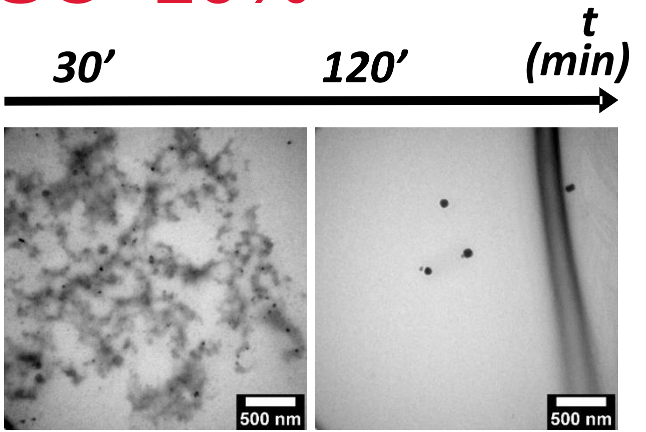
Parameters:
- Solvent (H_2O vs. PBS buffer)
- Monomer concentration

Influence of solvent: DP_{HPMA}=150 SC=10%

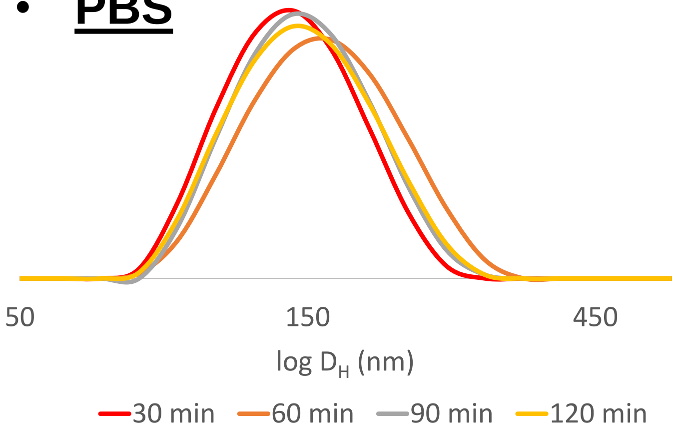
- **H_2O**



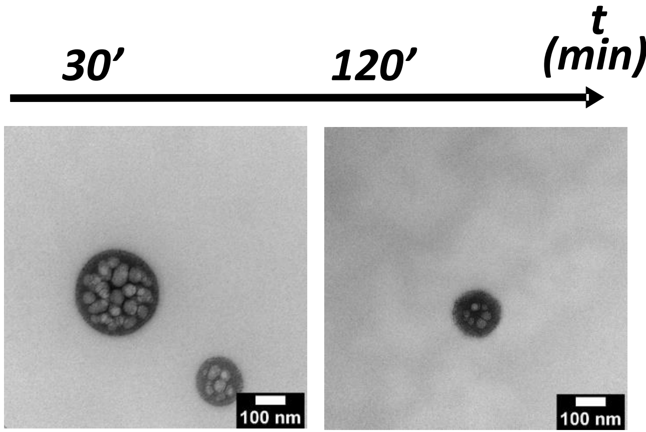
Time (min)	D_H (nm)	PDI
30	186.6	0.33
60	254.2	0.20
90	185.6	0.11
120	1100	0.27
150	188.8	0.14



- **PBS**

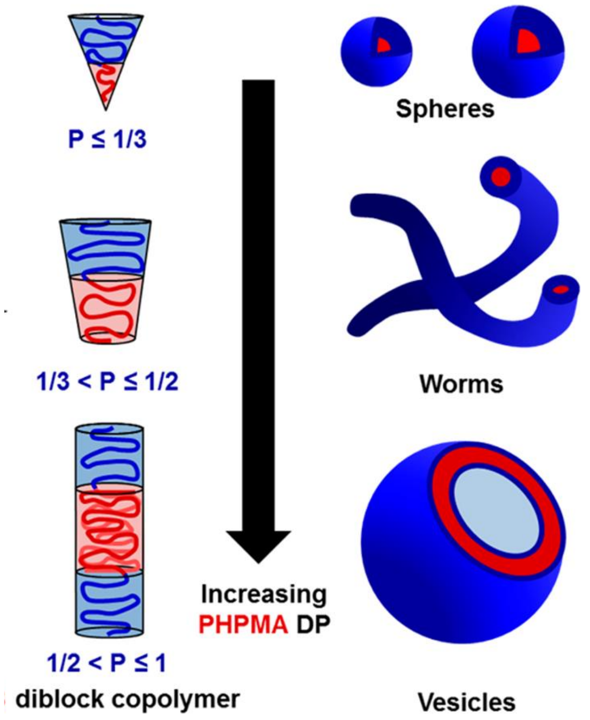


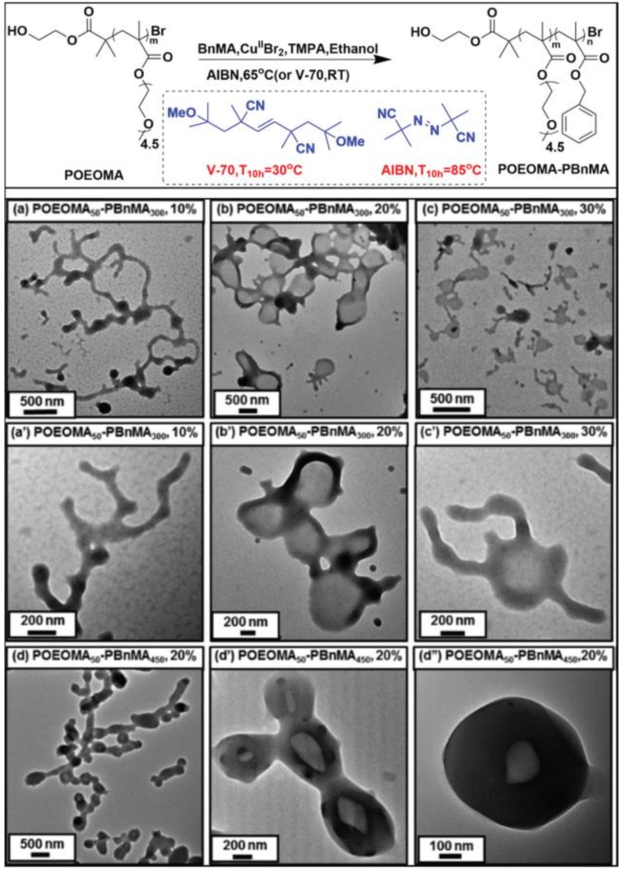
Time (min)	D_H (nm)	PDI
30	136.9	0.04
60	153.2	0.06
90	143.1	0.08
120	142.3	0.06



Influence of monomer concentration

- <u>Traditional morphology evolution</u>





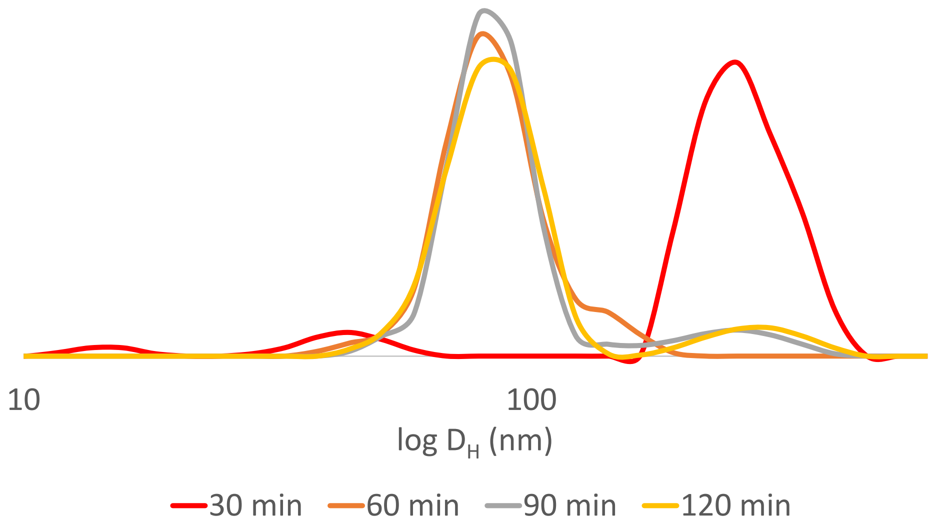
Warren, N. J.; Armes, S. P., Polymerization-induced self-assembly of block copolymer nano-objects via RAFT aqueous dispersion polymerization. *J Am Chem Soc* **2014,** *136* (29), 10174-85.

Wang, G.; Schmitt, M.; Wang, Z.; Lee, B.; Pan, X.; Fu, L.; Yan, J.; Li, S.; Xie, G.; Bockstaller, M. R.; Matyjaszewski, K., Polymerization-Induced Self-Assembly (PISA) Using ICAR ATRP at Low Catalyst Concentration. *Macromolecules* **2016,** *49* (22), 8605-8615.

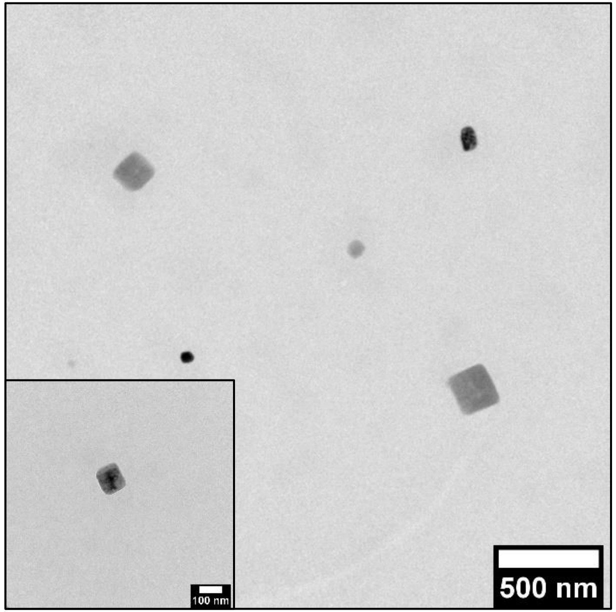
Influence of monomer concentration

- H_2O
- DP_{HPMA}= 300
- SC=10%

Time (min)	D_H (nm)	PDI
30	565.1	0.53
60	398.4	0.50
90	400.7	0.51
120	409.2	0.45

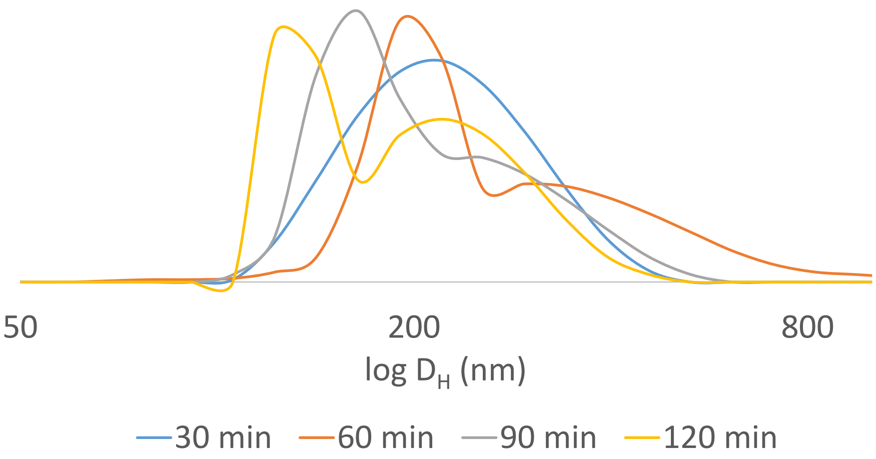


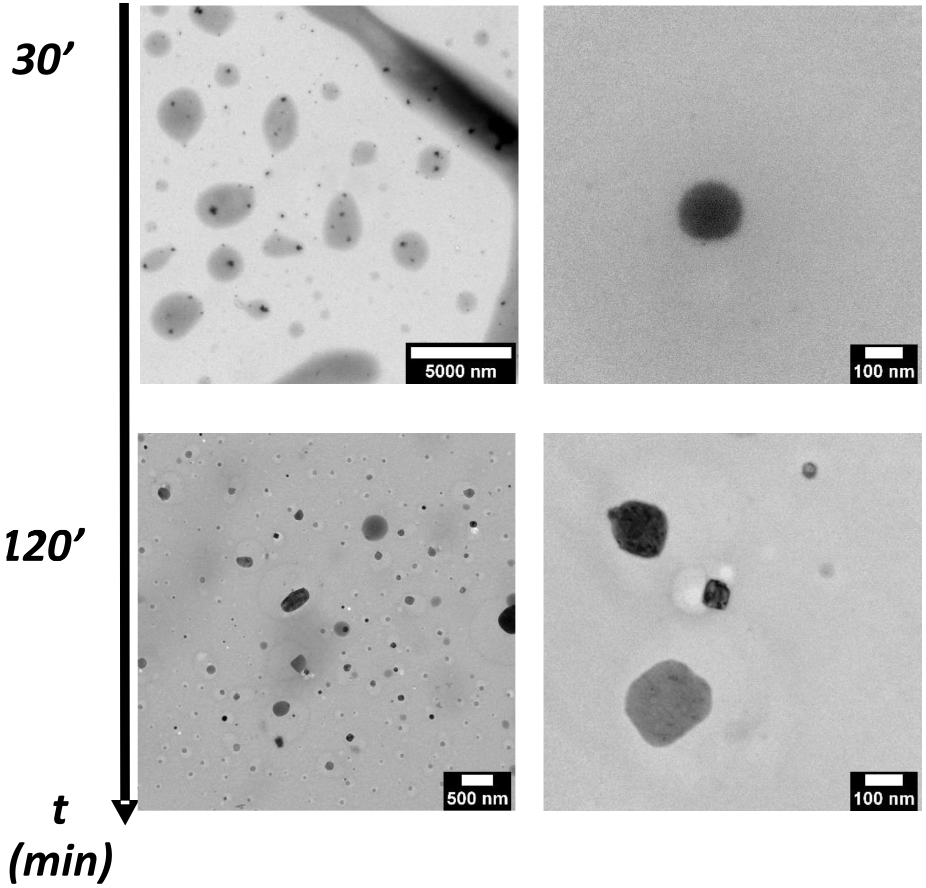
- 120 min



Influence of monomer concentration

- **PBS**
- **DP_{HPMA}= 300**
- **SC=10%**





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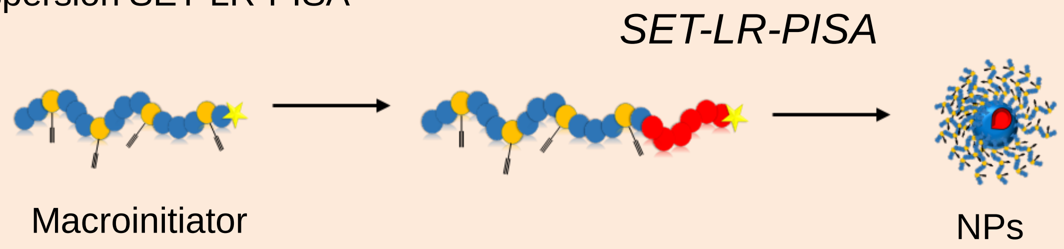
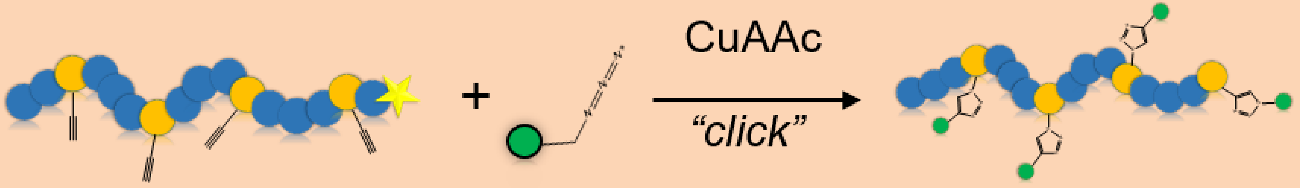
Morphology evaluation:

- Core forming monomer concentration $[M]_0$
- Solvent

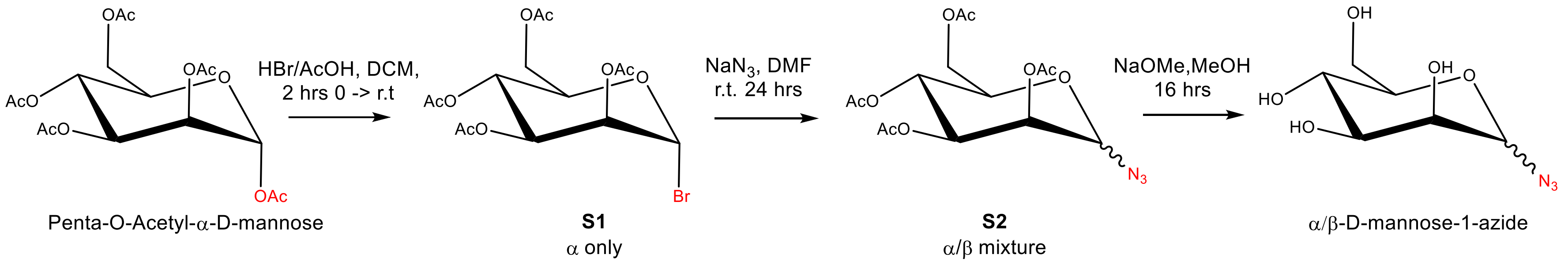


B) Macroinitiator functionalisation with mannosides via alkyne-azide copper catalysed cycloaddition:

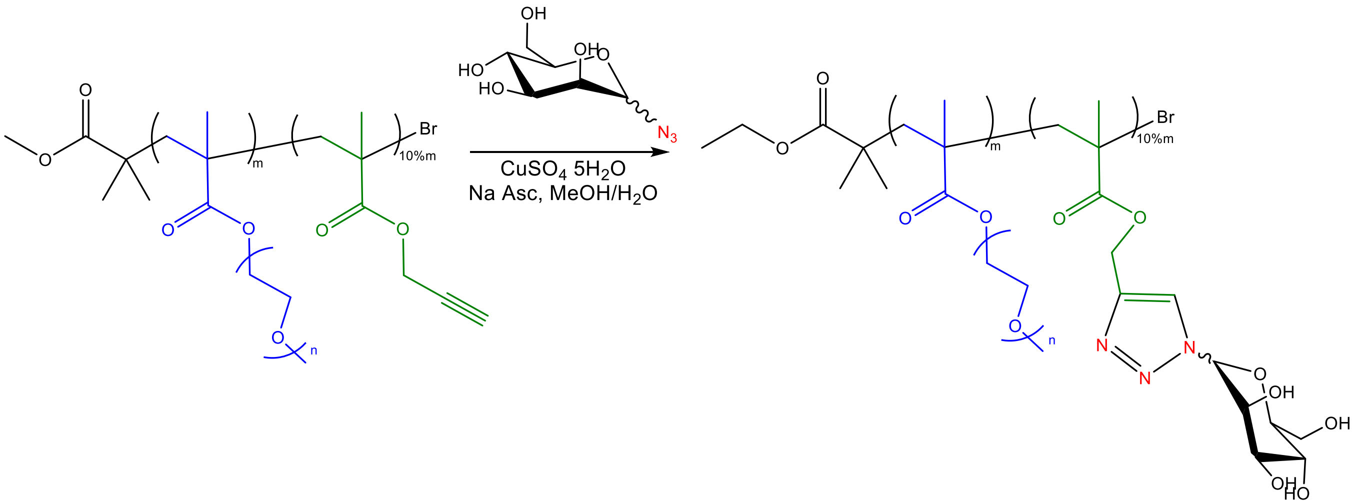


Glycosylated macroinitiator for SET-LR-PISA system

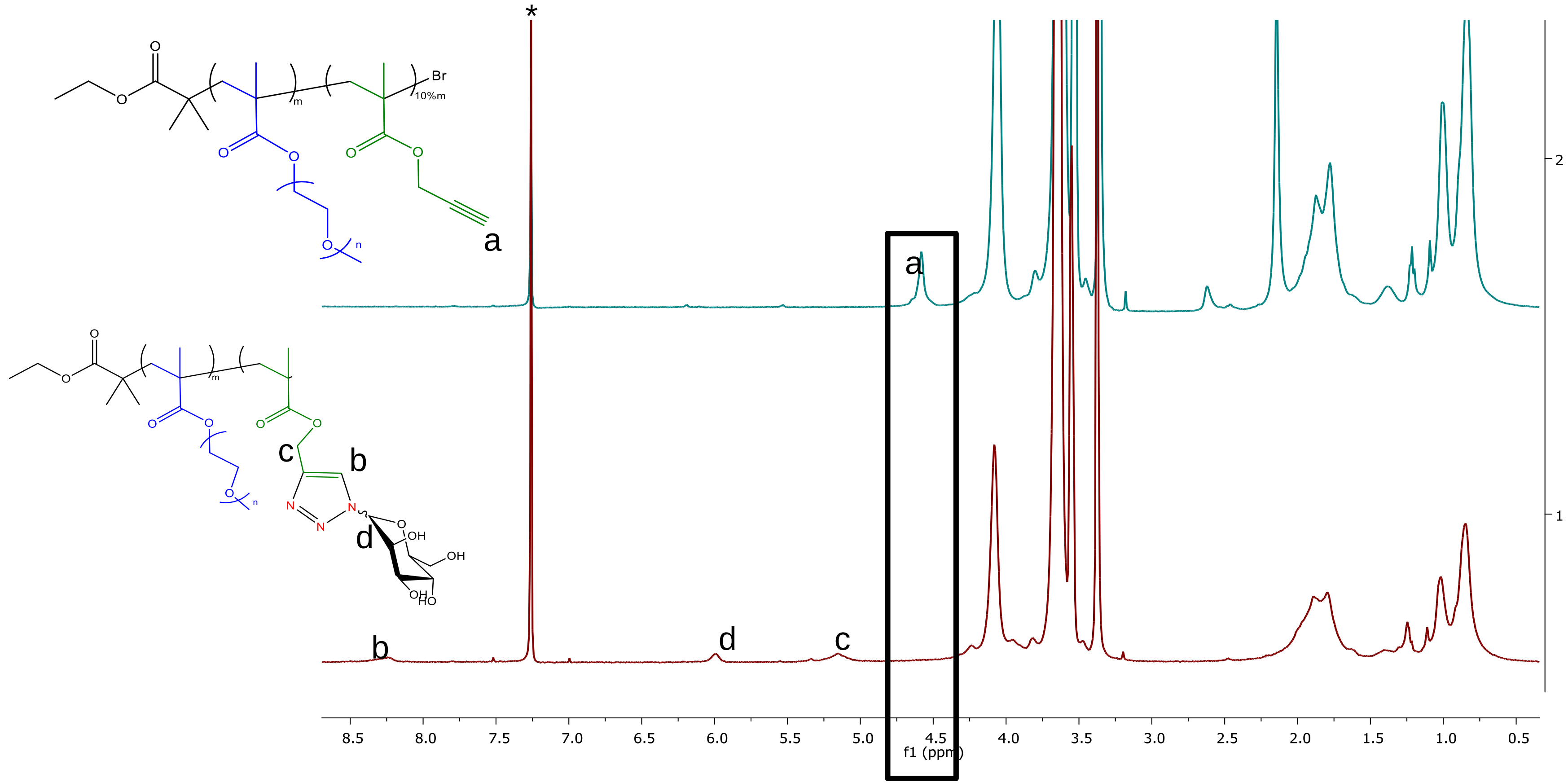
1)



2)

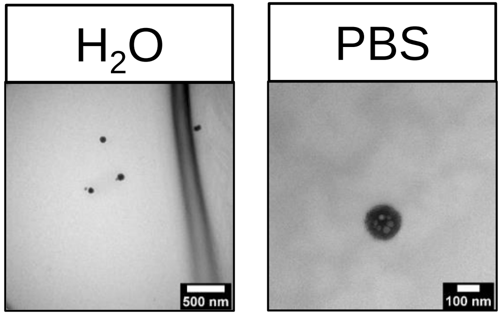


Glycosylated macroinitiator: racemic mixture

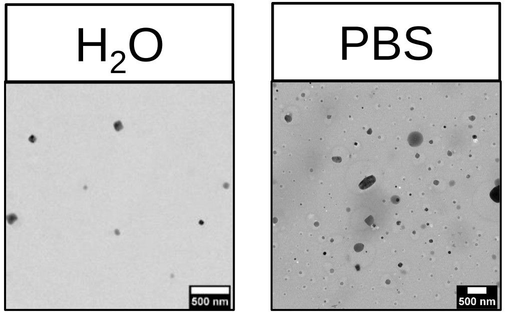


Conclusion

✓ Spherical morphology obtained when targeting DP_{HPMA}=150 after 120 min



✓ PBS provides more stable system



✓ Mixture of cubosomes and spherical NPs obtained when targeting DP_{HPMA}=300

✓ Macroinitiator suitable for glycosylation with mannosides

NanoCarb

Polymer Chemistry and Biopolymer Laboratory

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Dr Bing Wu
Dr Christopher Burke
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Dr Rafał Bielas

Smiljana Stefanovic
Nicola Judge

Thank you for your kind attention

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MARIE CURIE ACTIONS

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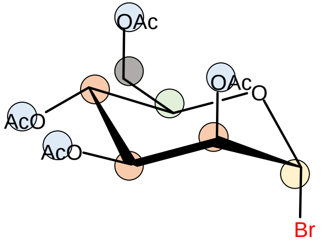
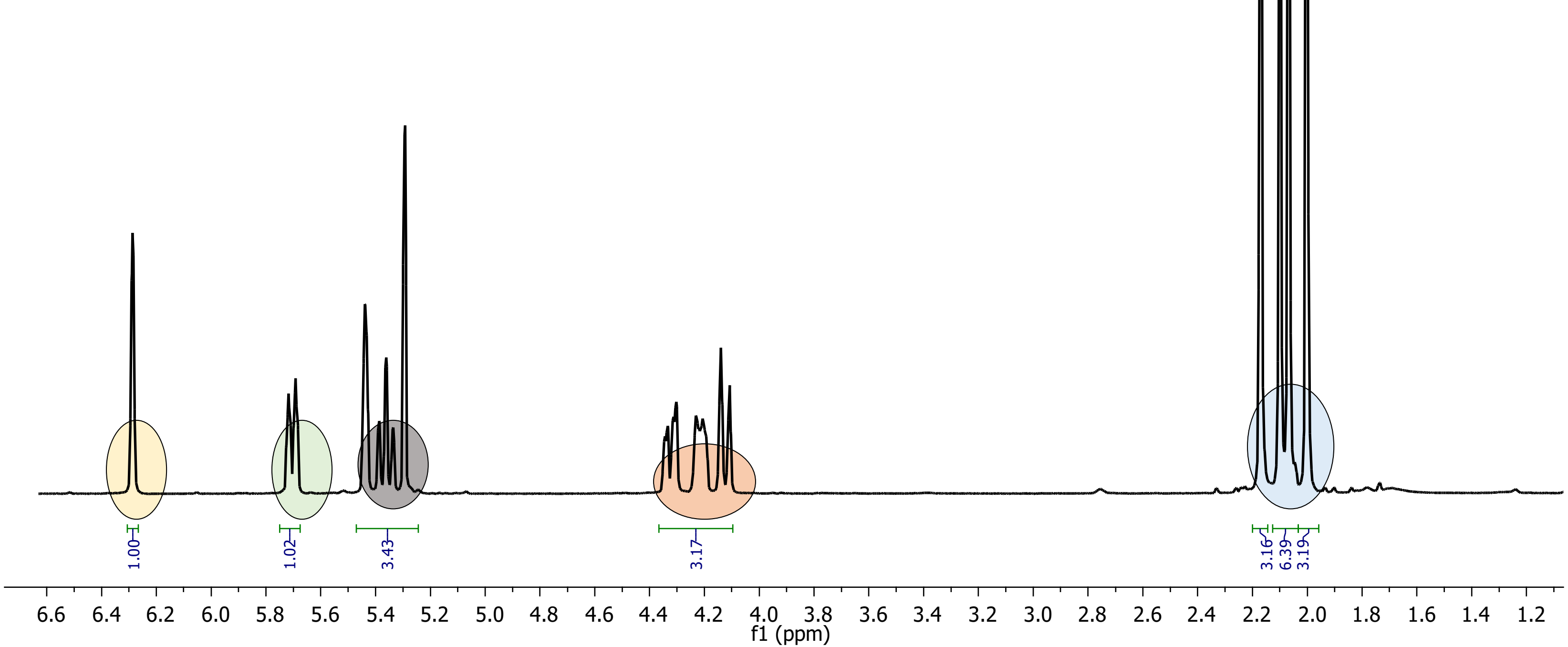
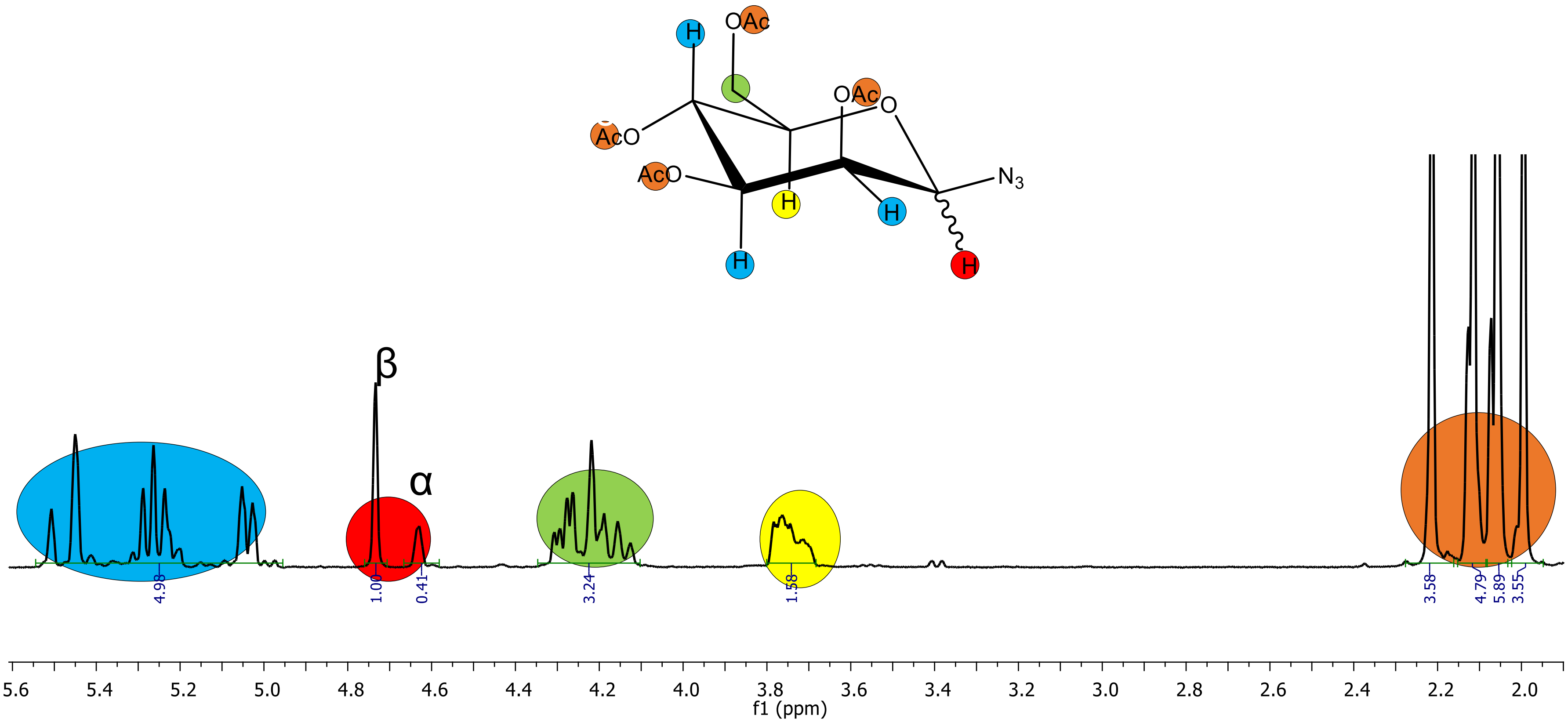
Thank you

S1 ^{1}H-NMR spectra



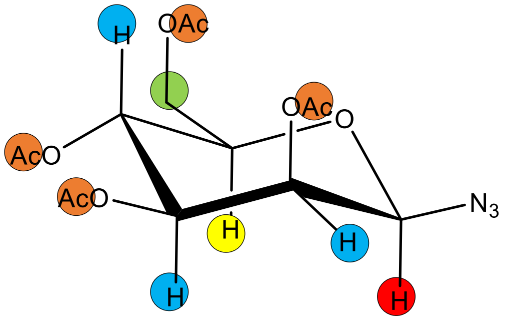


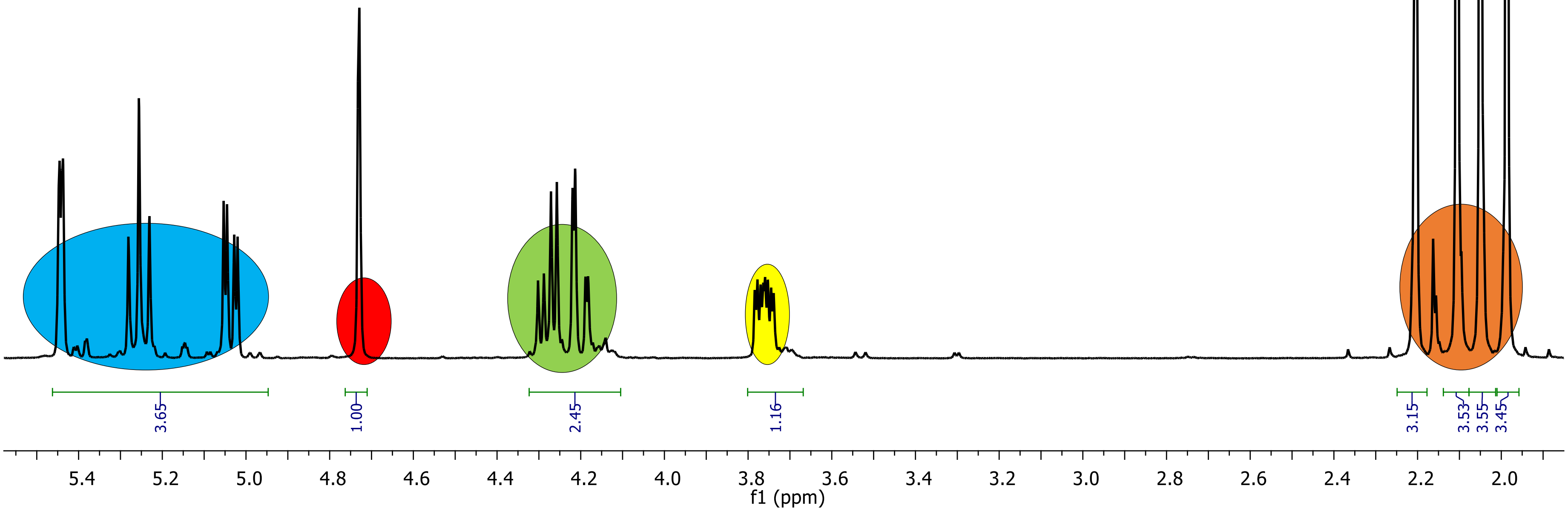
S2 ^{1}H-NMR spectra



S2 ^{1}H-NMR spectra

Reaction carried out at 70 ℃





^{1}H-NMR spectra β-D-mannose-1-azide