

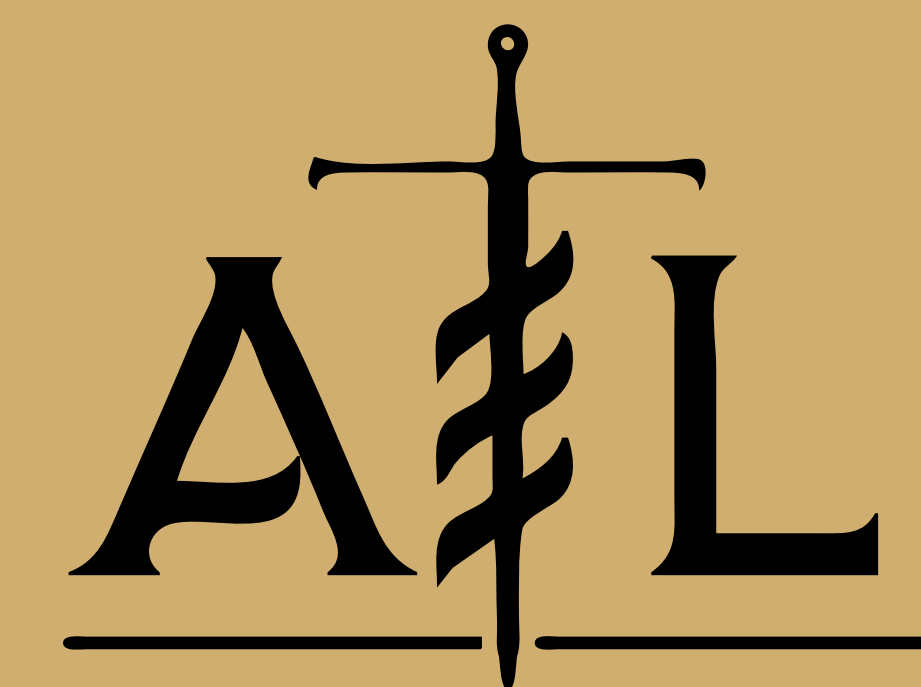


# Optimization of Polymeric Nanoparticles for siRNA Delivery

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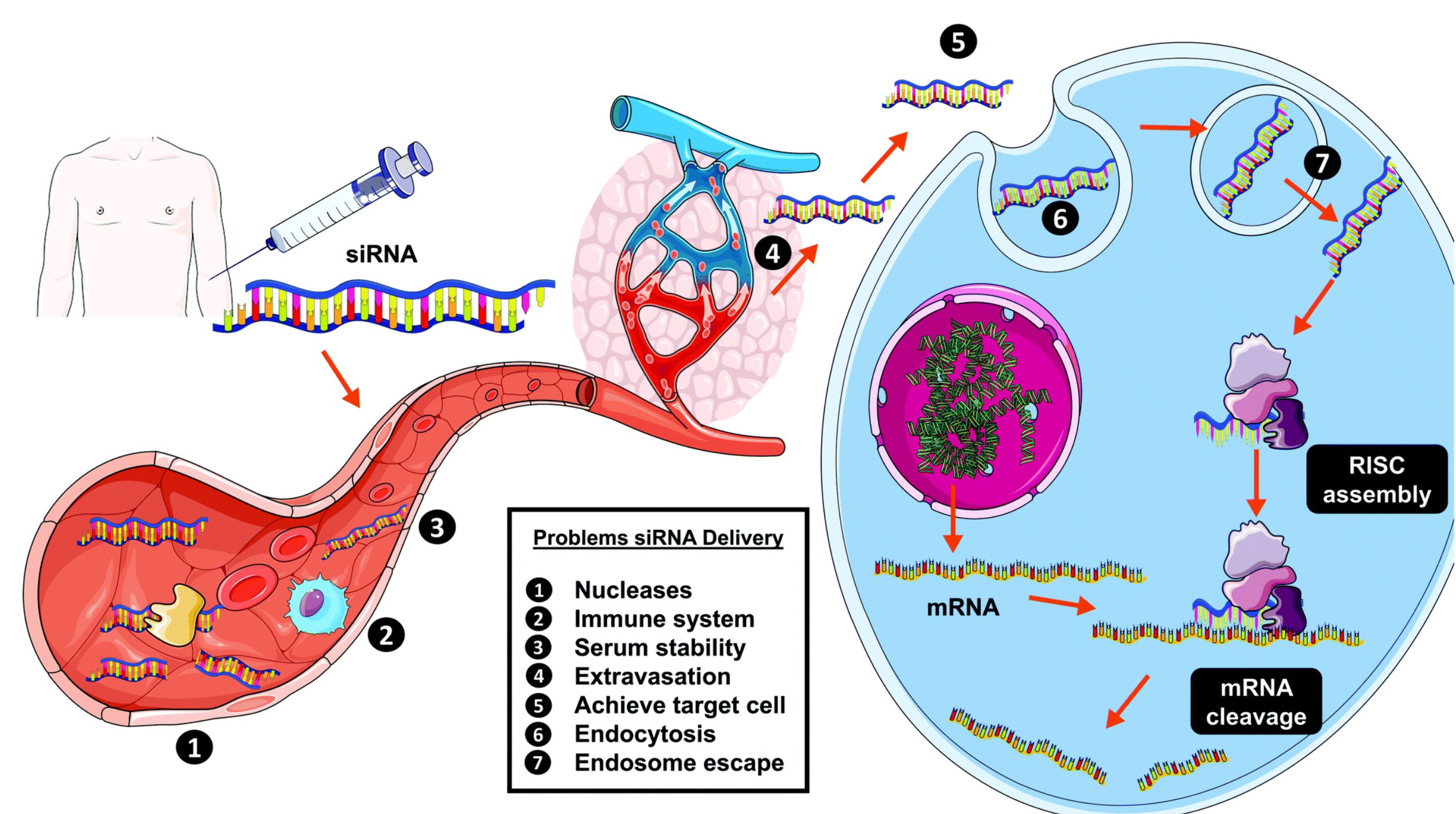
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## Background

- Small interfering RNA (siRNA) can be used to selectively target and degrade mRNA to enable gene silencing



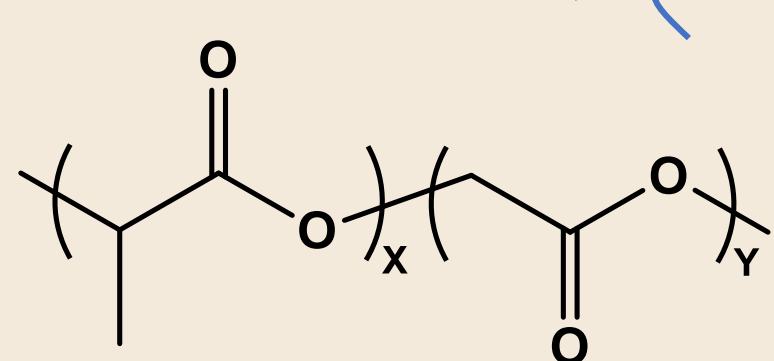
## Objective

To optimize polymeric nanoparticles for stability, gene silencing activity, and cytocompatibility.

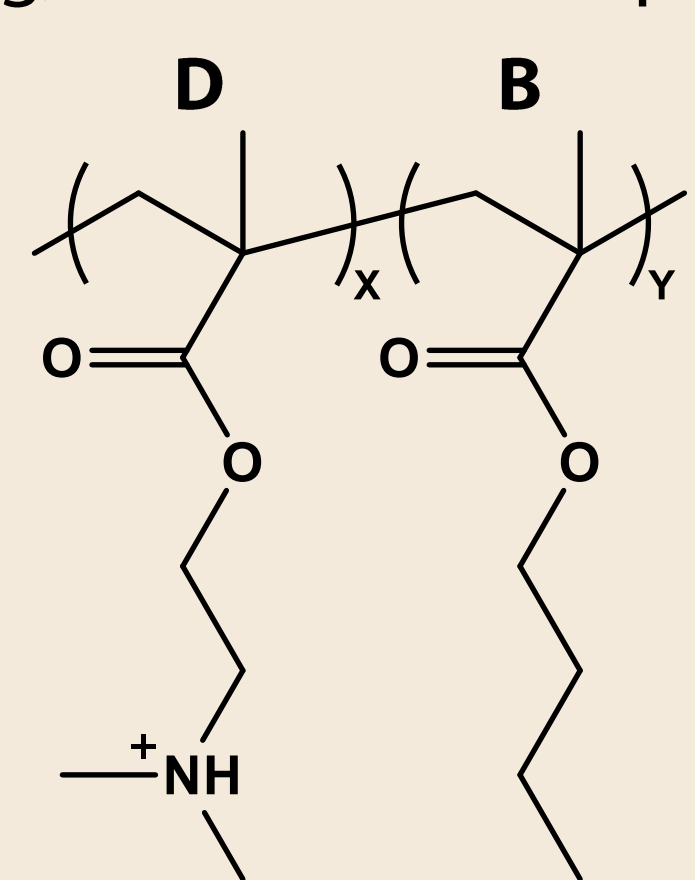
## Polymeric Nanoparticles (si-NPs)

NP system components:

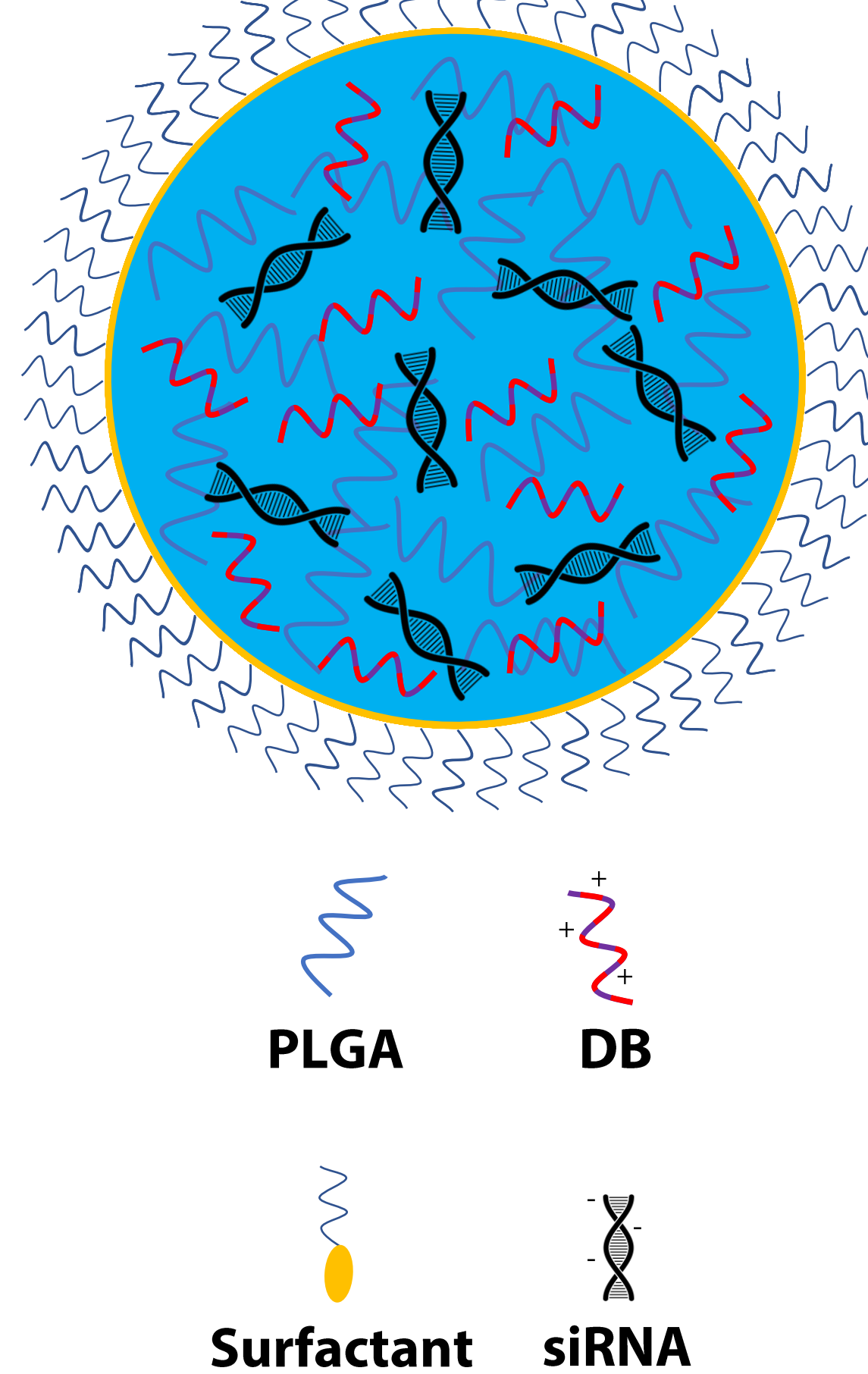
- (1) **PLGA** to improve stability



- (2) **DMAEMA-co-BMA (DB)** for packaging, endosome escape

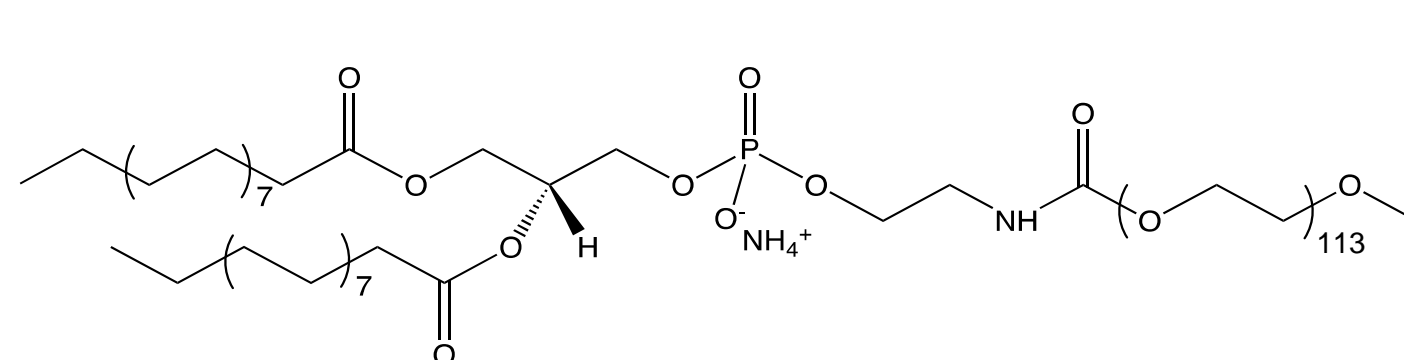


- (3) **Surfactant** for biocompatibility, colloidal stability



## NP Surfactants

### DSPE-PEG



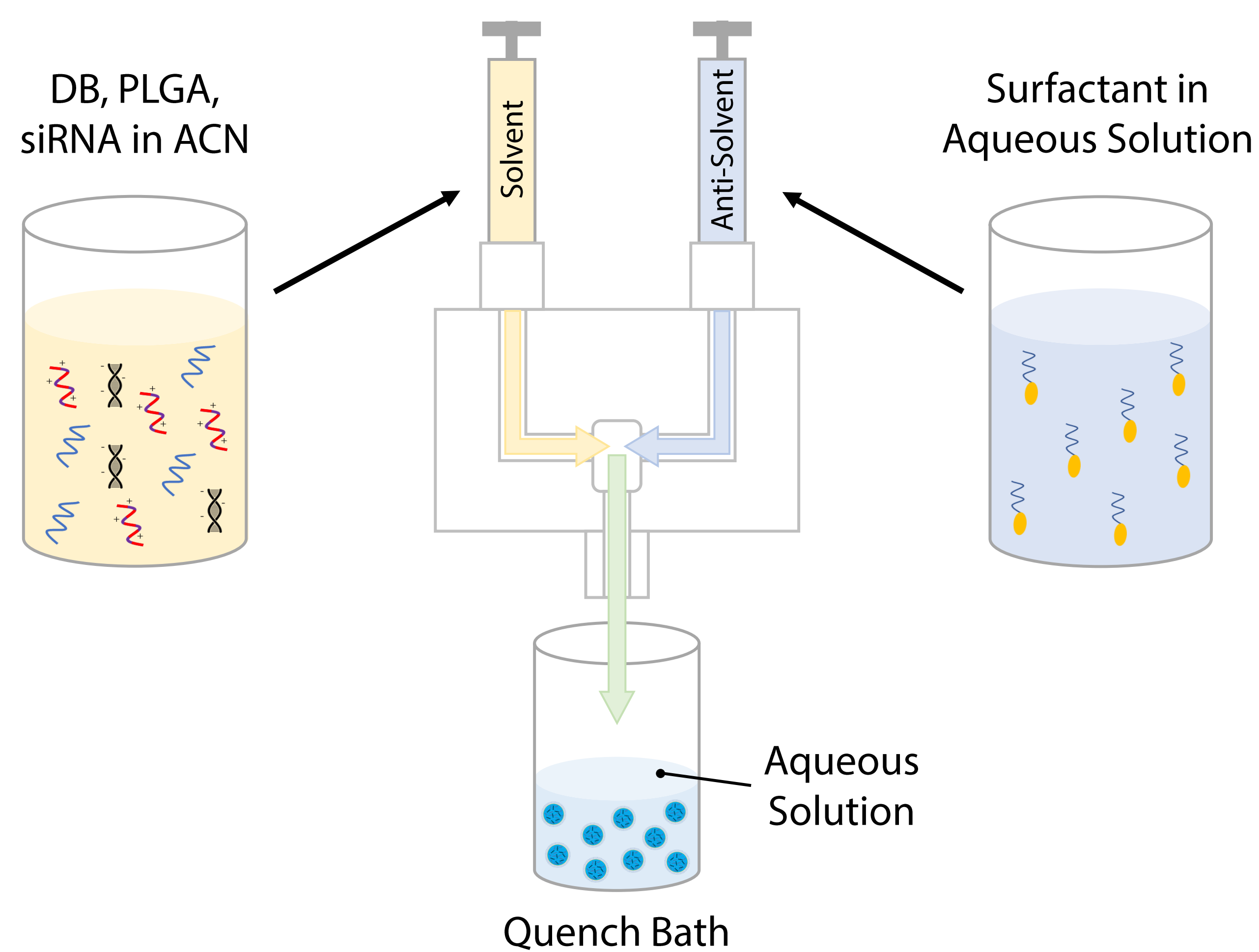
### Custom polymeric surfactants



si-NP aggregation, better anchor to si-NP core needed

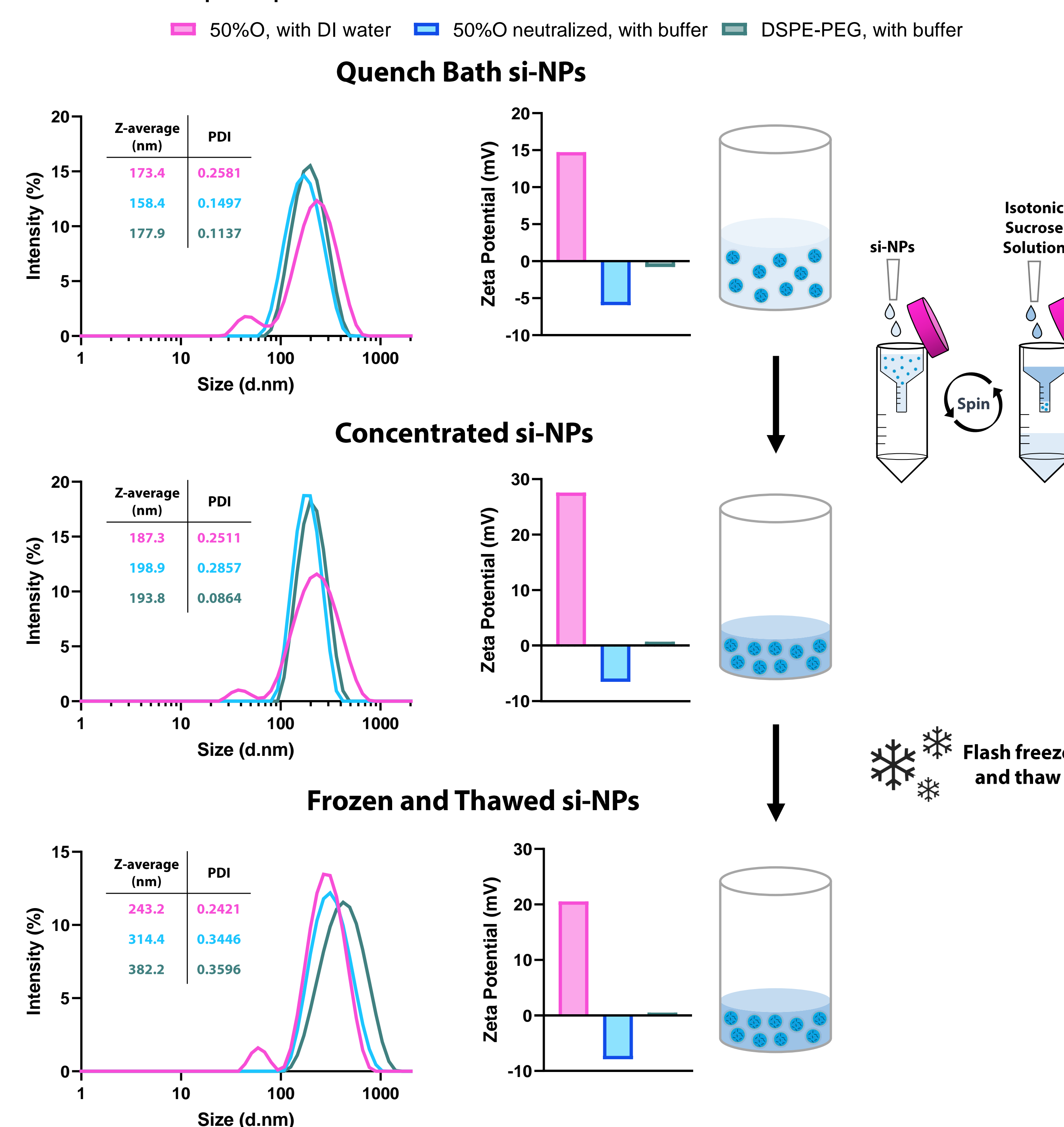
Anchors to si-NP core with alkyl side groups and electrostatic interactions

## Confined Impinging Jets (CIJ) Mixer



## Dynamic Light Scattering (DLS) Characterization of si-NPs

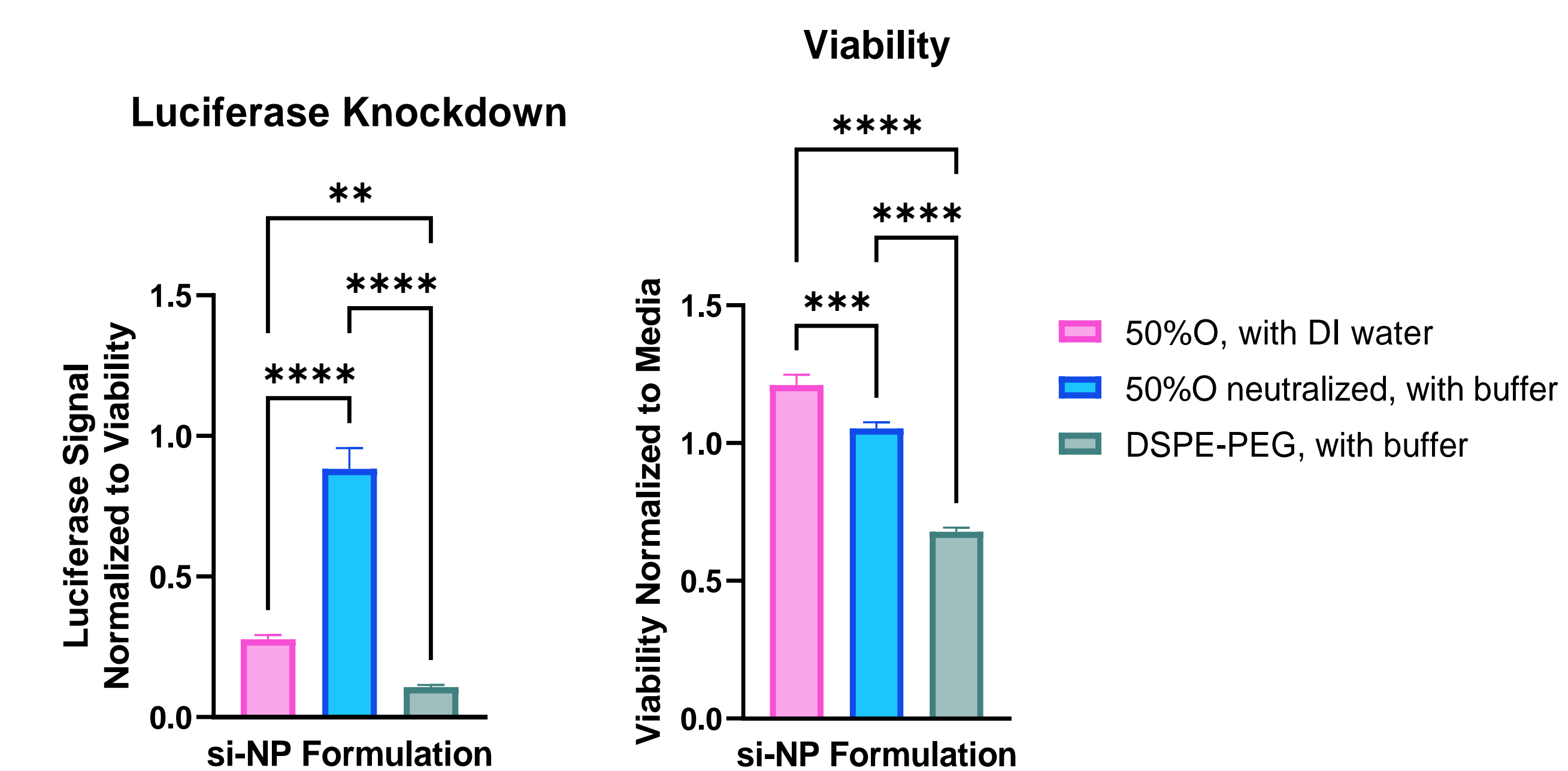
- Formulated si-NPs with a core composition of 50% PLGA and 50% DB, with amines to phosphates ratio (N:P) of 10



Neutralization of the 50%O surfactant and the use of sodium phosphate buffer prevented the formation of micelles and lowered the zeta potential of the si-NPs.

## Luciferase Knockdown and Cell Viability

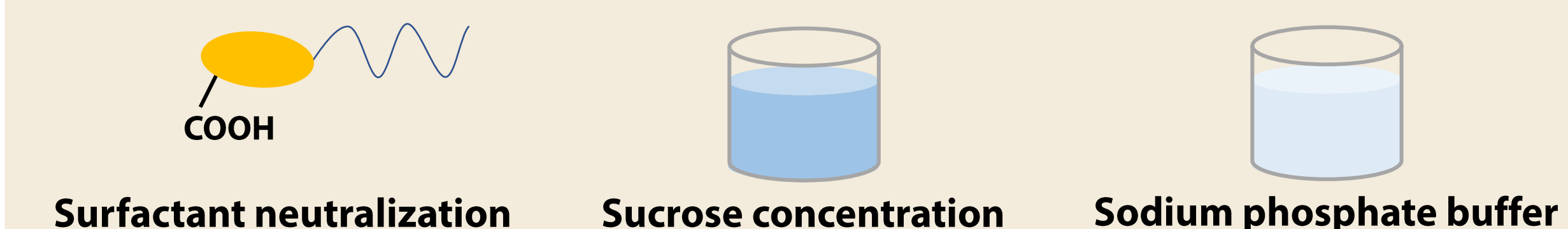
- Assessed luciferase knockdown and cell viability in luciferase-expressing MDA-MB-231 cells 48h after a 50 nM treatment



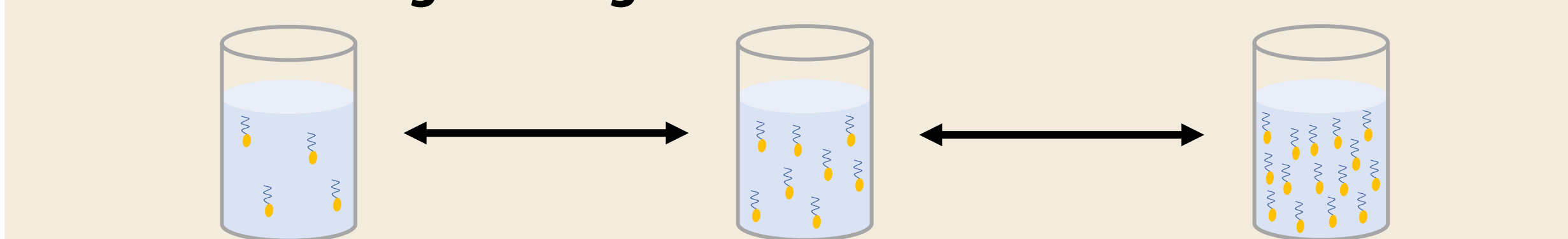
The si-NPs with the non-neutralized 50%O custom polymeric surfactant achieved around 70% luciferase knockdown, and both of the 50%O surfactants enabled significantly better viability than DSPE-PEG.

## Future Work

### Optimize formulation conditions

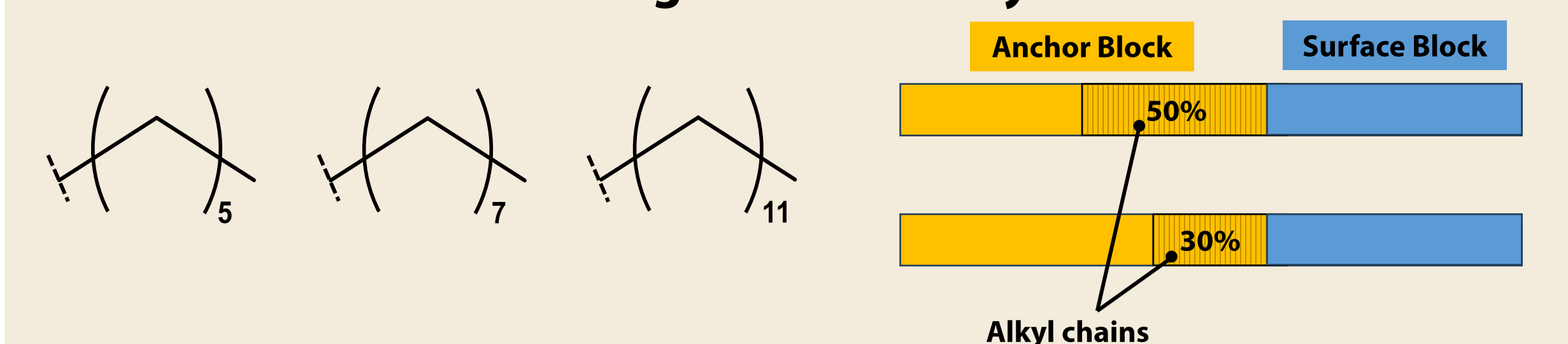


### Investigate range of surfactant concentrations



- Vary surfactant concentration above and below 4 mg/ml

### Evaluate custom polymeric surfactants with varied alkyl chain length and density



## Acknowledgements

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## References

1. Kanasty et al. Nature Materials, 2013.
2. Artiga et al. J. Mat. Chem B, 2019.
3. Han et al. J Pharm Sci, 2012.
4. Created with Biorender.com