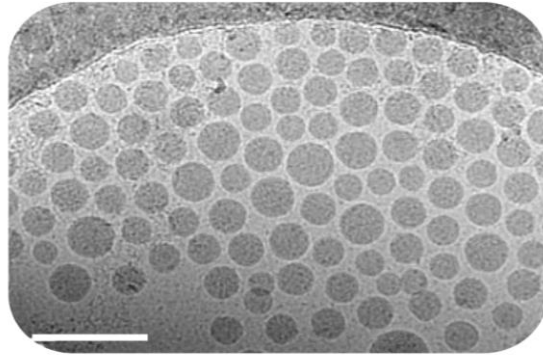


The lipid nanoparticle shape and morphology affect the efficiency and duration of mRNA transfection

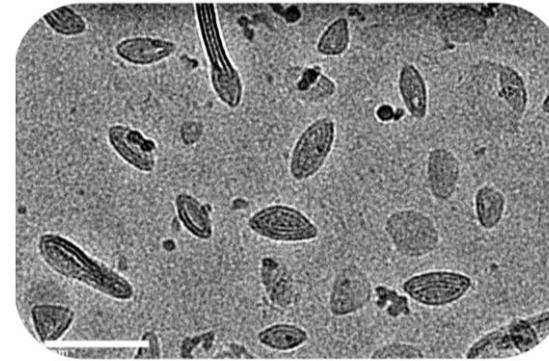
Sara Elsafy, MSc.

16.07.2025

Morphological deviations from spherical LNP detected by Cryo-TEM



Spherical LNP

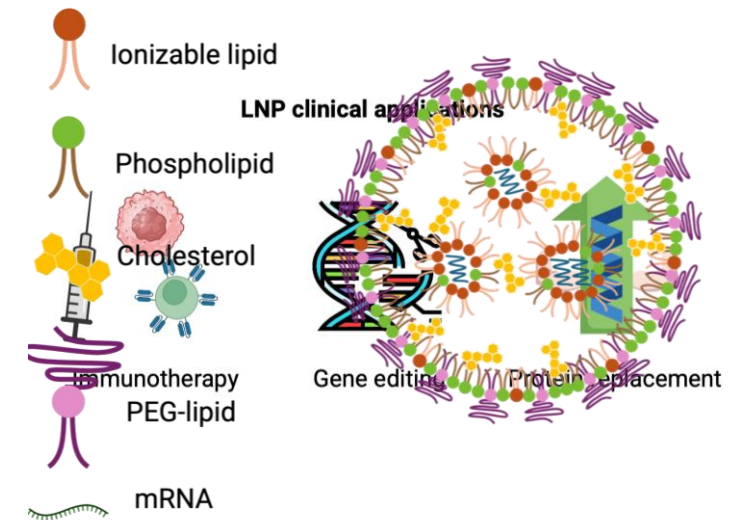


Non-spherical LNP

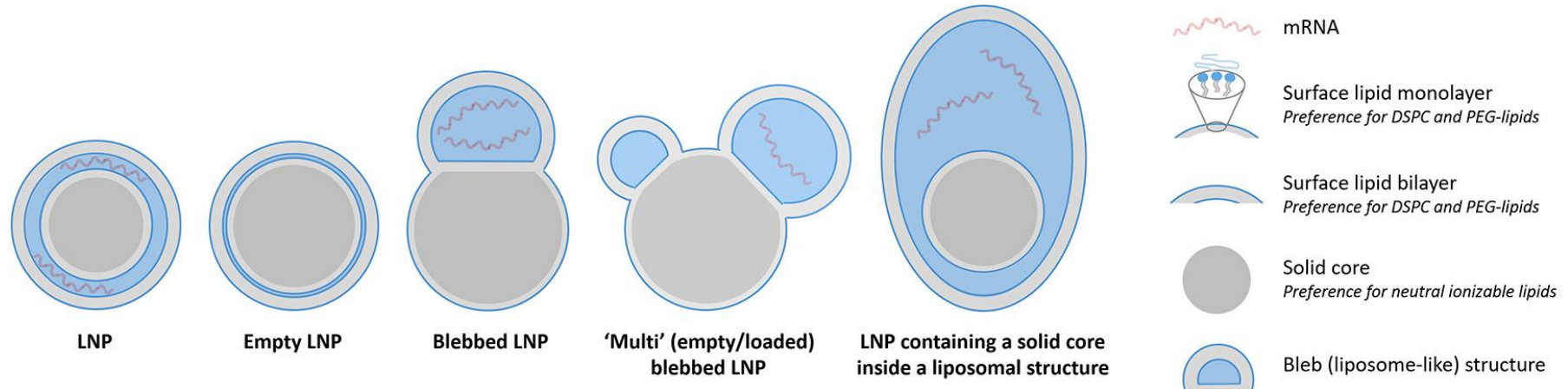
“Shape isn’t just form—it’s function.”

LNP offer a flexible platform for RNA delivery

1. LNP enabled mRNA vaccines and siRNA therapies (e.g., Onpattro, Comirnaty).
2. Now being explored for cancer therapy, protein replacement, and gene editing.
3. Key focus has been on lipid composition, PEGylation, and charge.



Why shape matters?

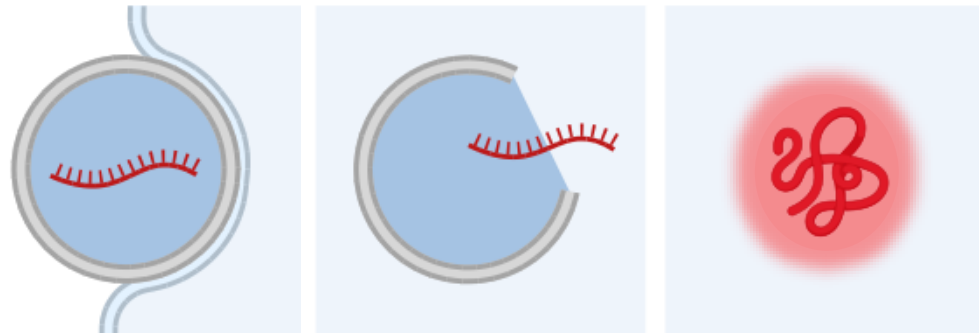


Shape affects:

1. Uptake

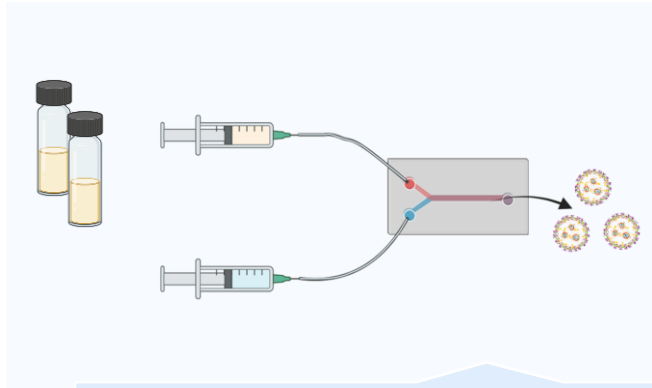
2. Release

3. Potency



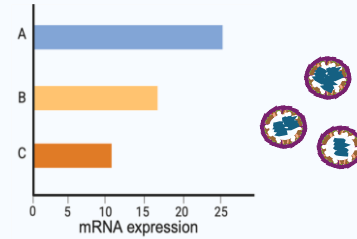
What defines shape, and what does shape define?

What factors govern LNP shape?



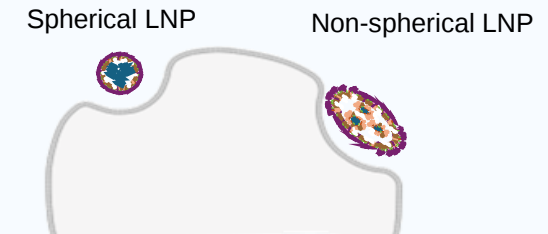
 **Formulation & Process**

Does particle shape affect RNA loading?



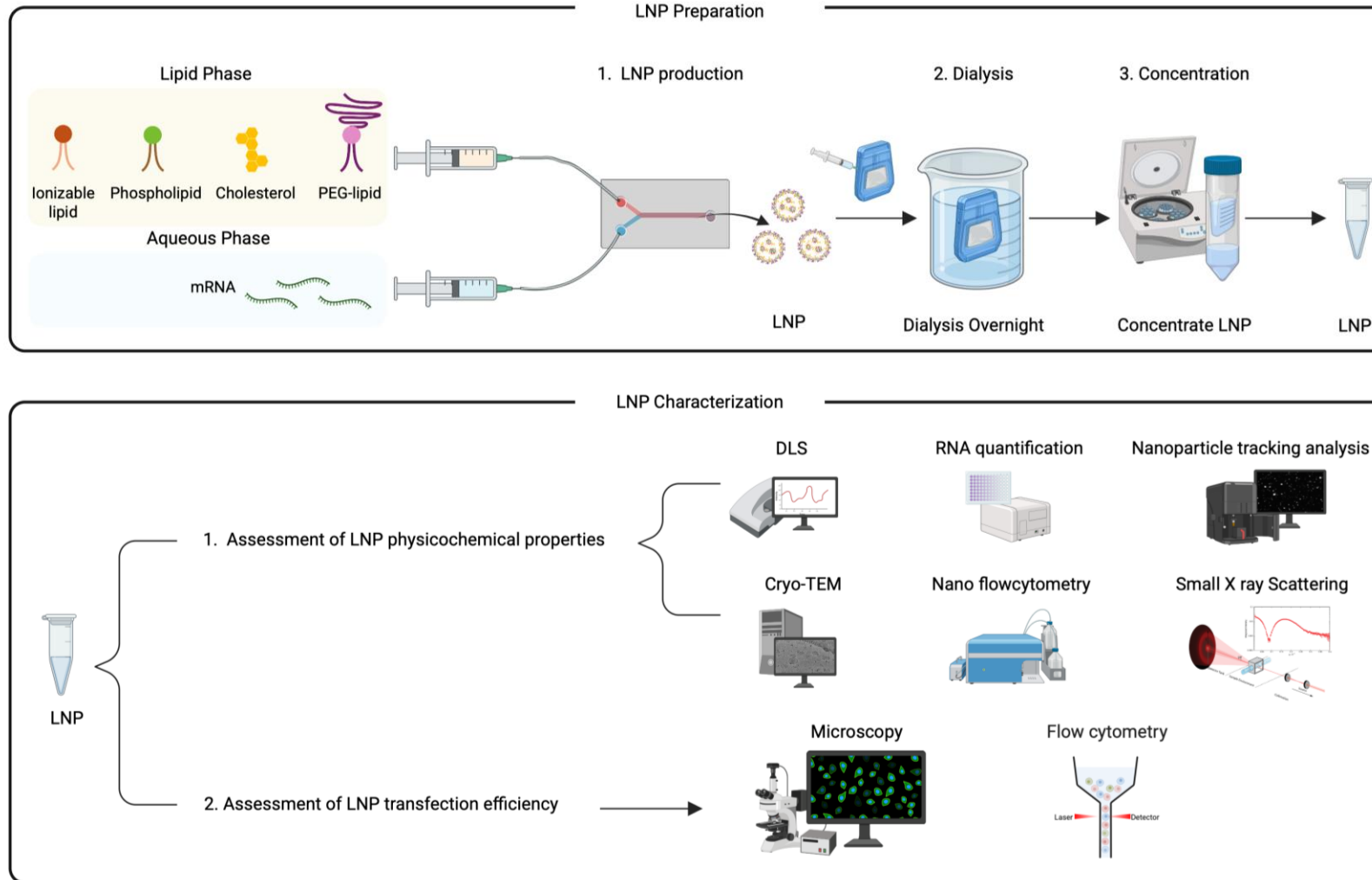
 **Payload**

Does shape impact transfection efficiency?

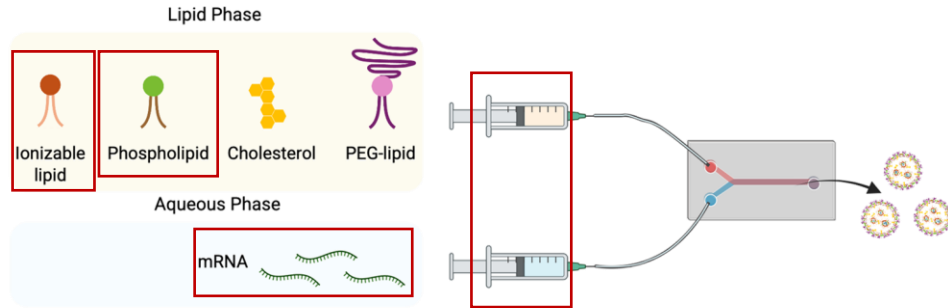


 **Delivery**

Workflow: From formulation to expression

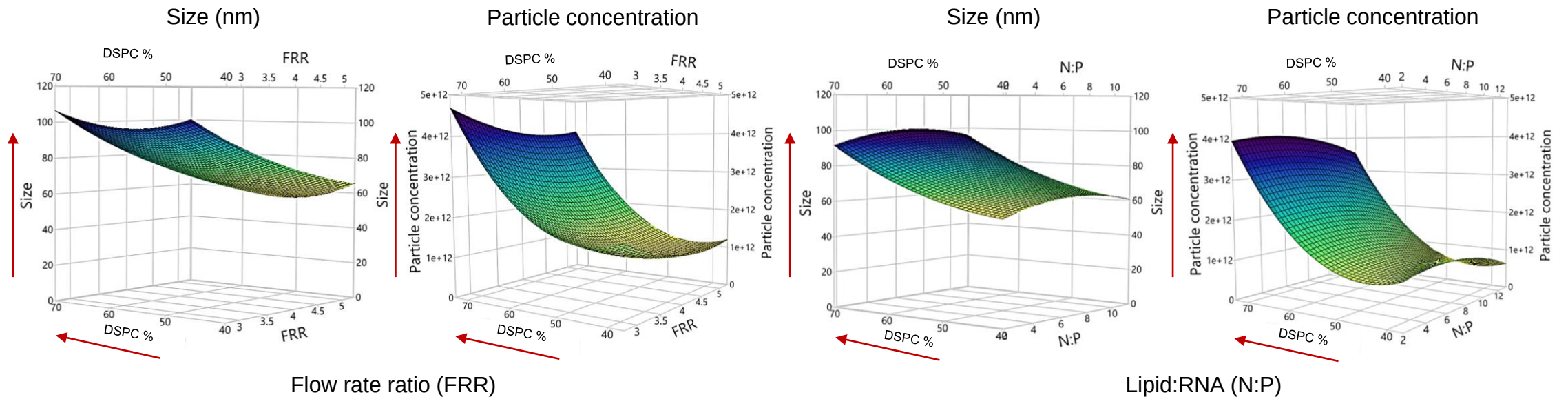


Design of experiment reveals DSPC dependent particle features

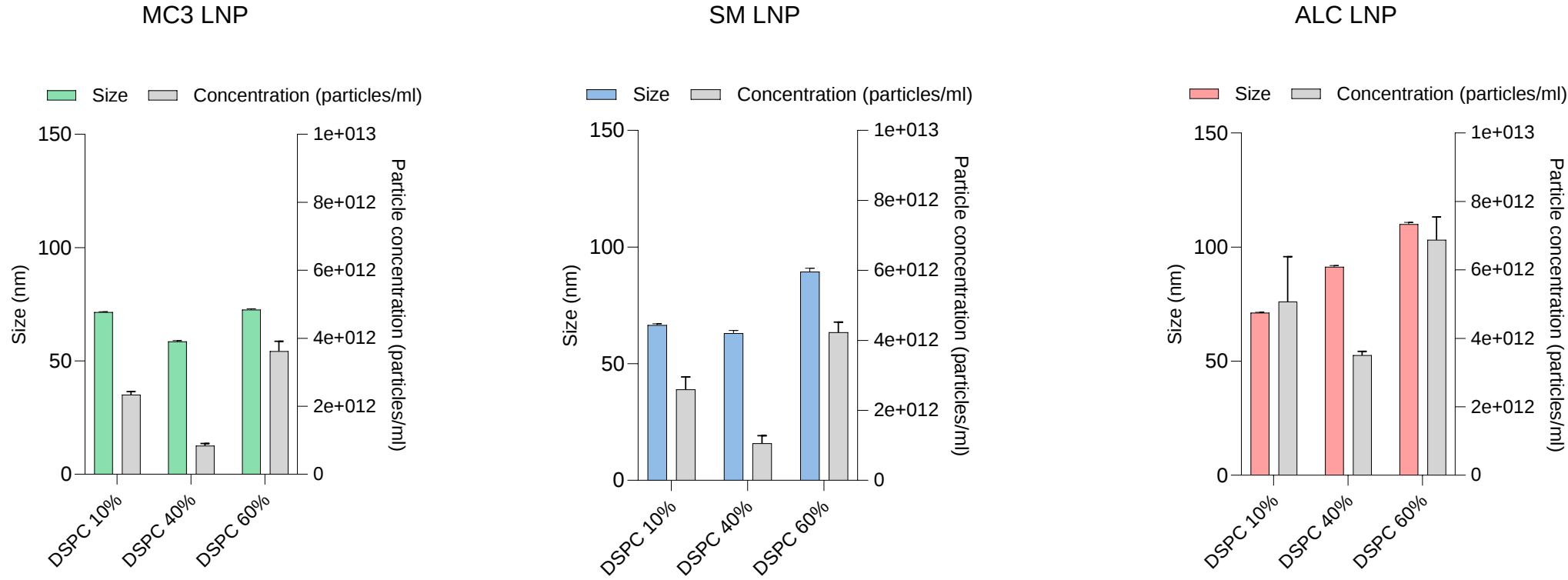


Design Space

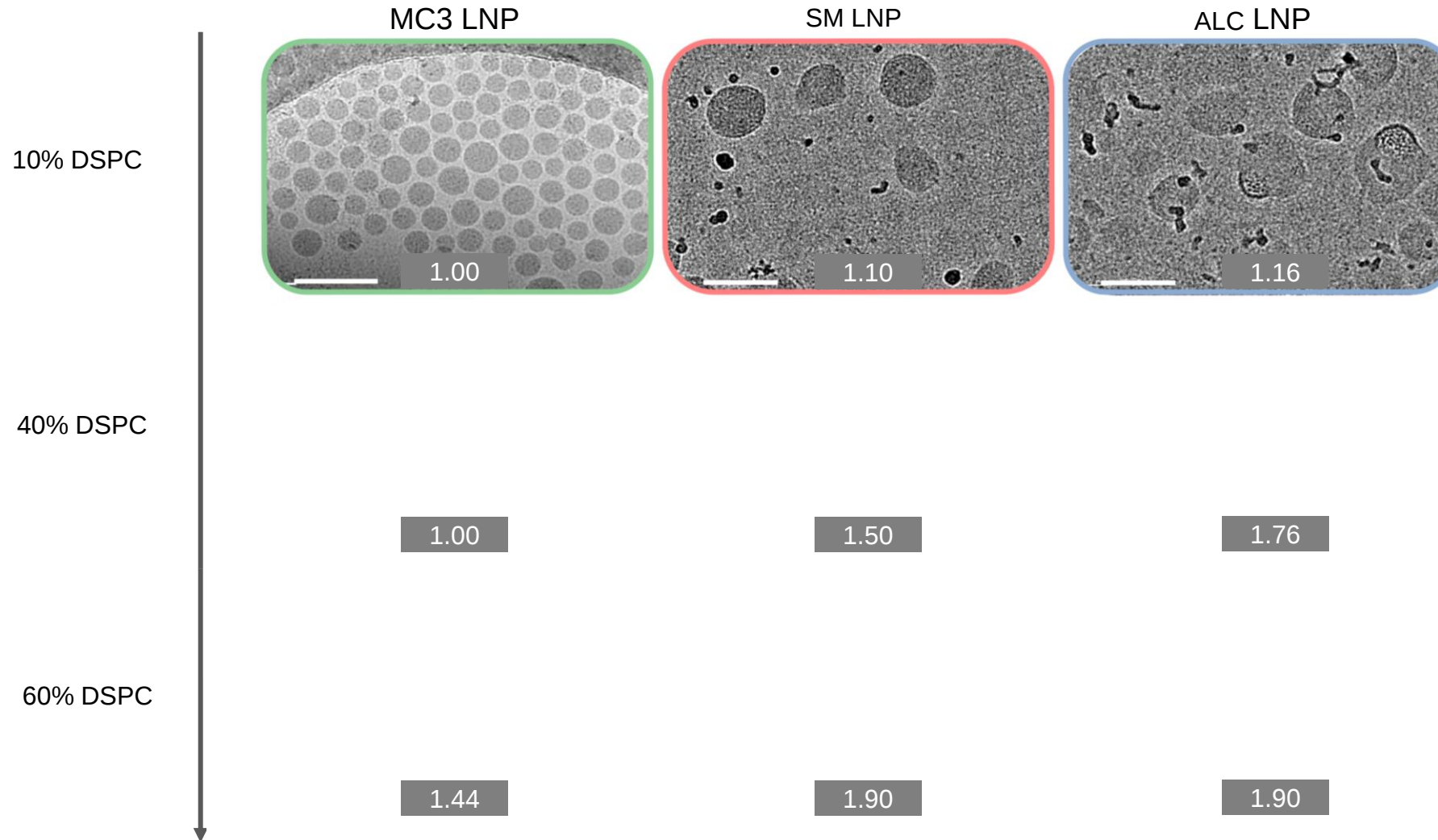
Phospholipid% (DSPC%)	Lipid:RNA (N:P)	Flow rate ratio (FRR)
10–70%	3–12	3–5



Validating the impact of DSPC on LNP size and particle count in clinically relevant ionizable lipids



Cryo-TEM confirms non-spherical structures



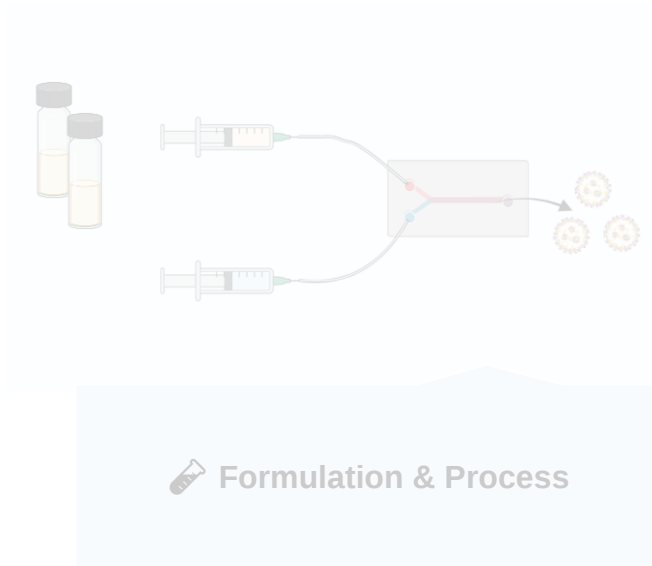
Morphological features:

1. Size
2. Particle concentration
3. Presence of bilayer
4. Aspect ratio (AR)

AR = 1 Spherical
AR > 1 Non-spherical

What defines shape, and what does shape define?

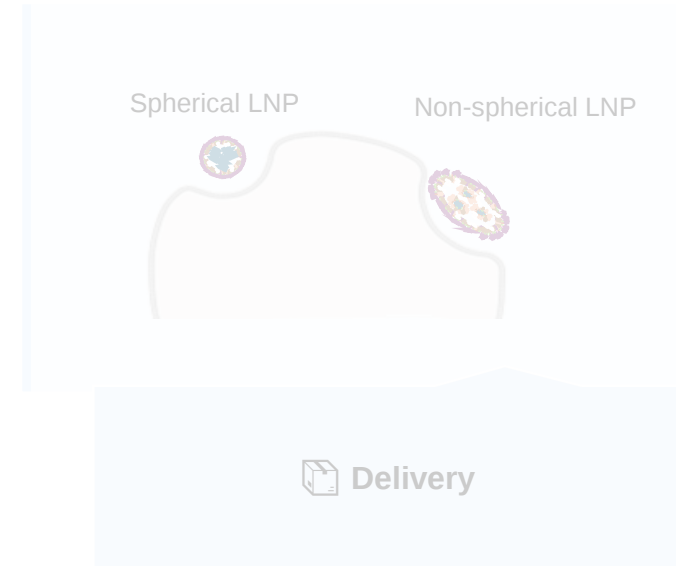
What factors govern LNP shape?



Does particle shape affect RNA loading?

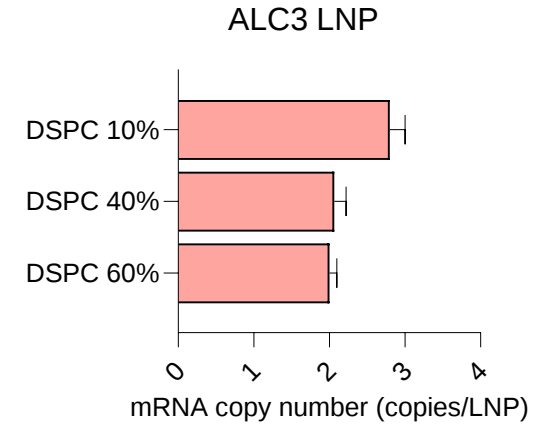
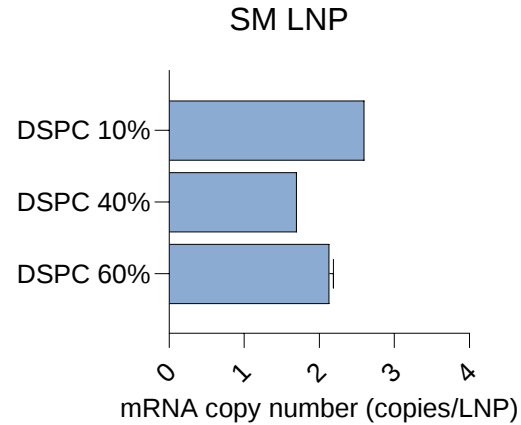
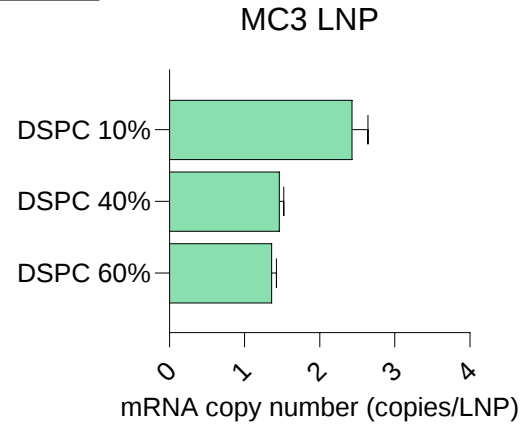


Does shape impact transfection efficiency?

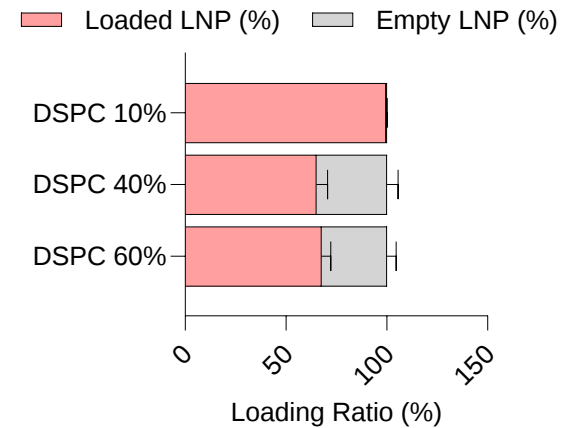
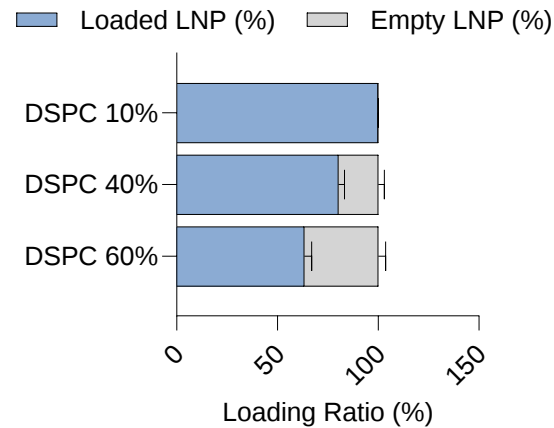
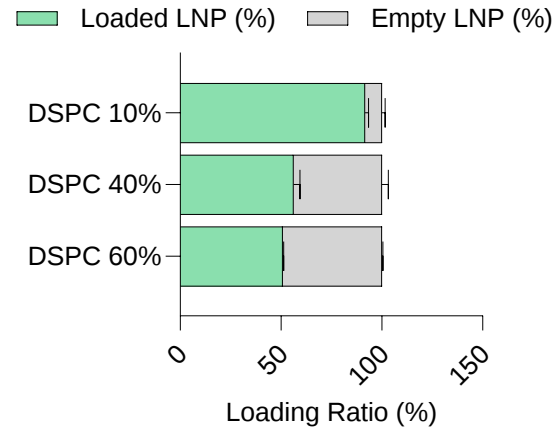


LNP shape influences RNA loading

Copies of mRNA/LNP

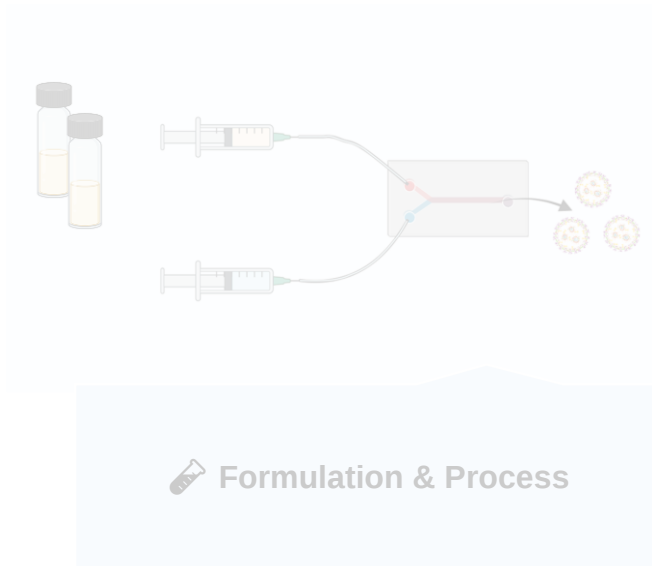


Portion of empty LNP

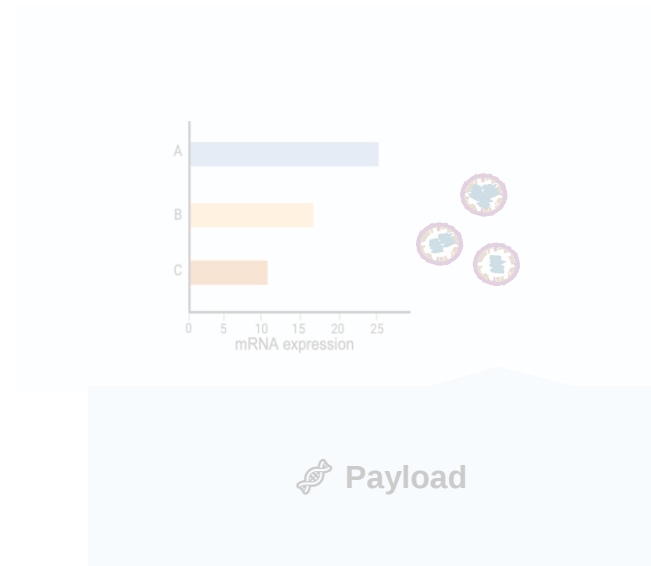


What defines shape, and what does shape define?

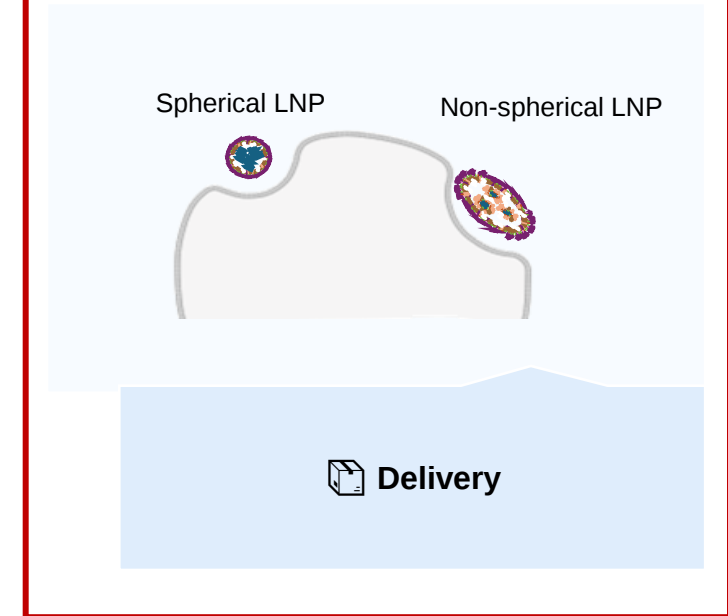
What factors govern LNP shape?



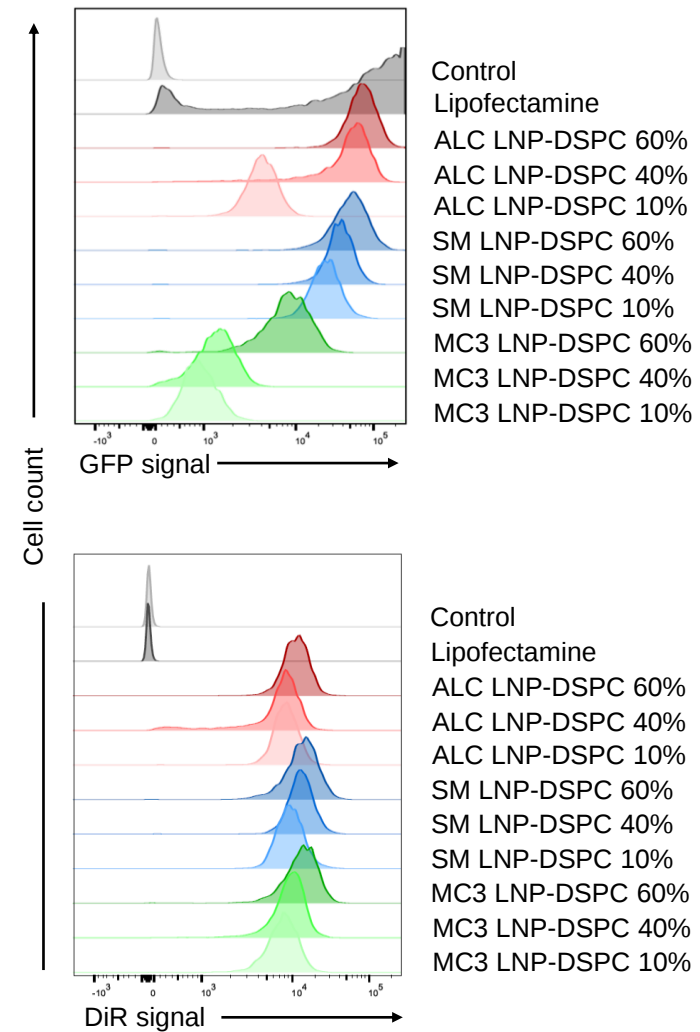
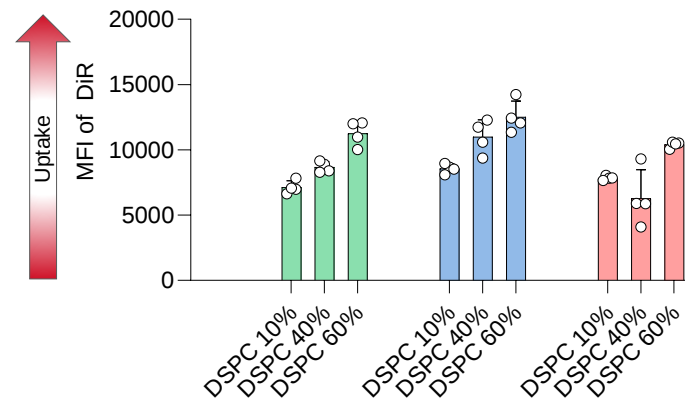
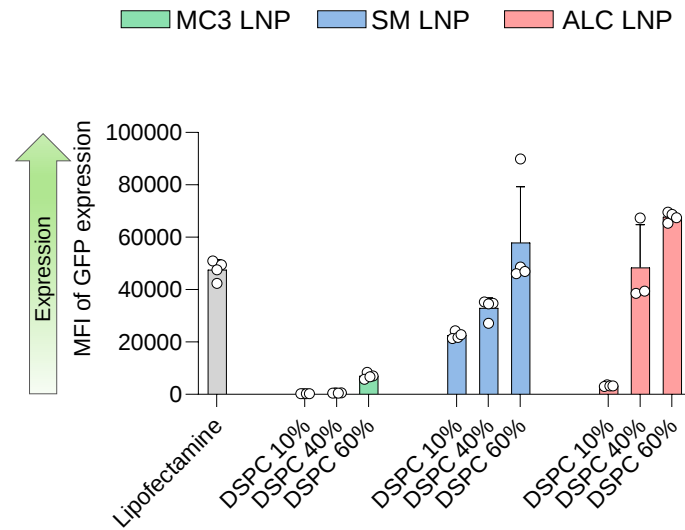
Does particle shape affect RNA loading?



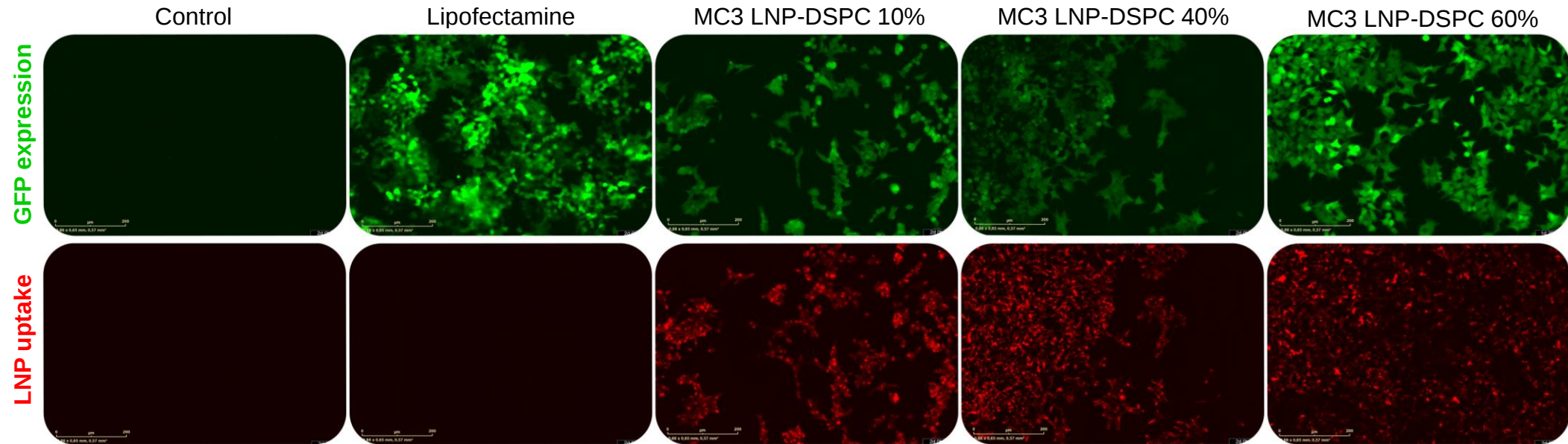
Does shape impact transfection efficiency?



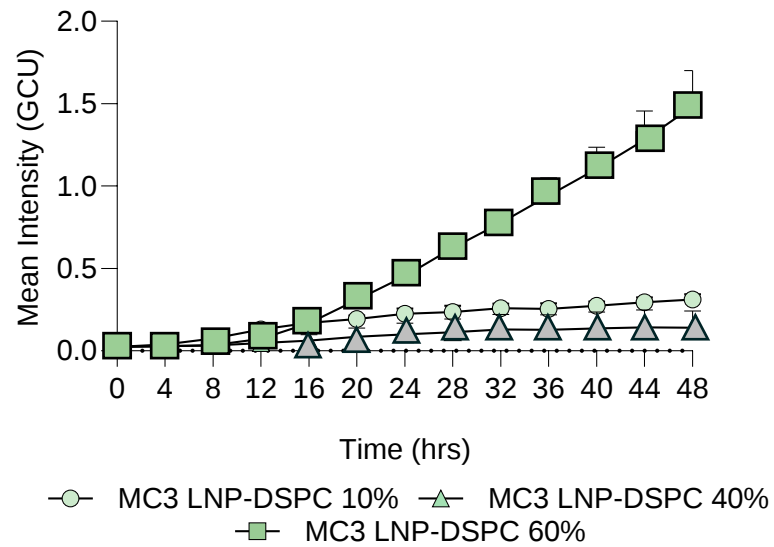
Non-spherical LNP drive higher expression



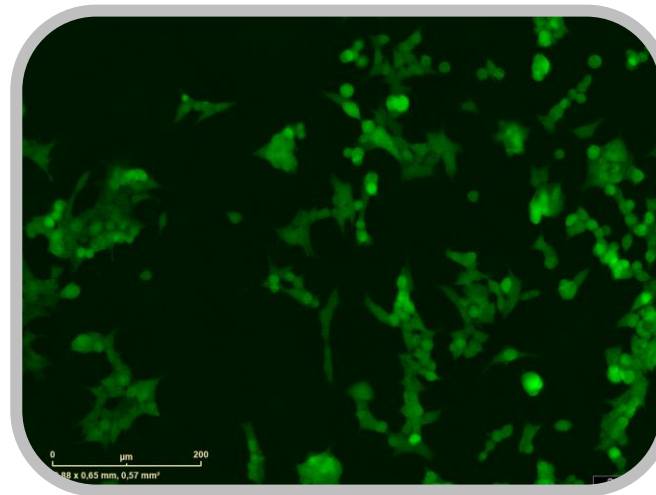
Imaging confirms enhanced expression by non-spherical LNP



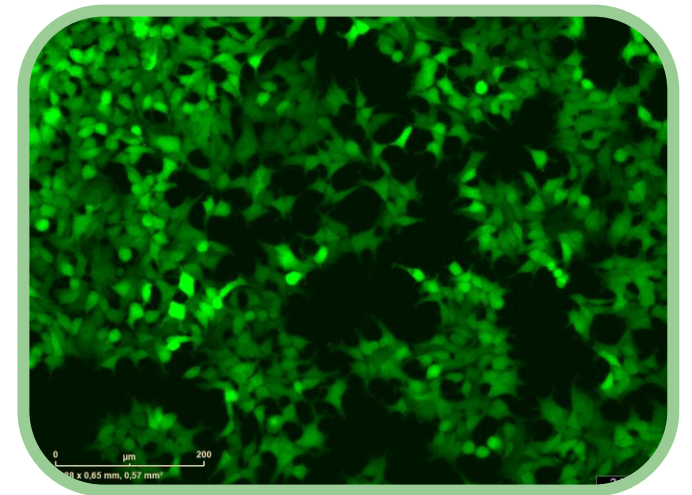
LNP shape alters GFP expression kinetics



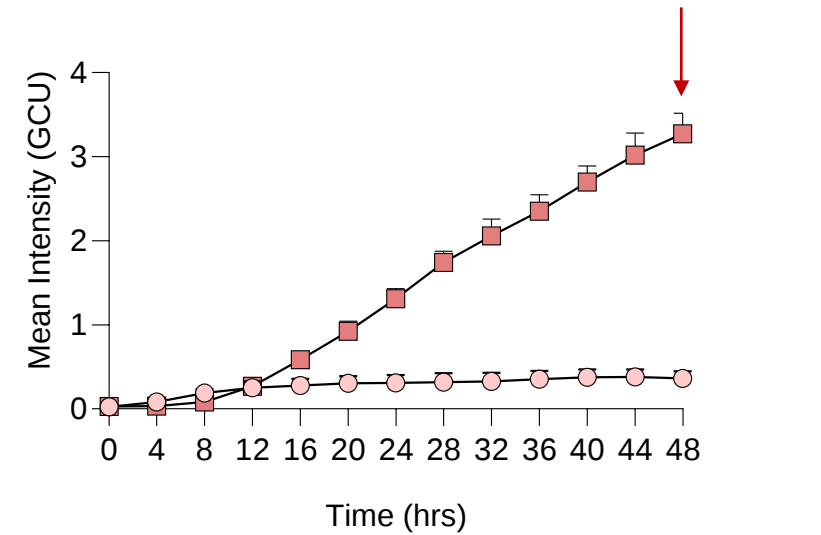
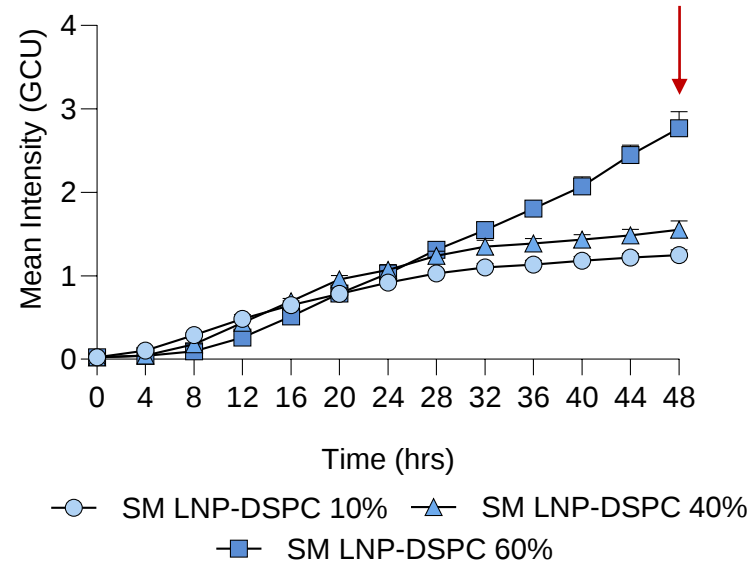
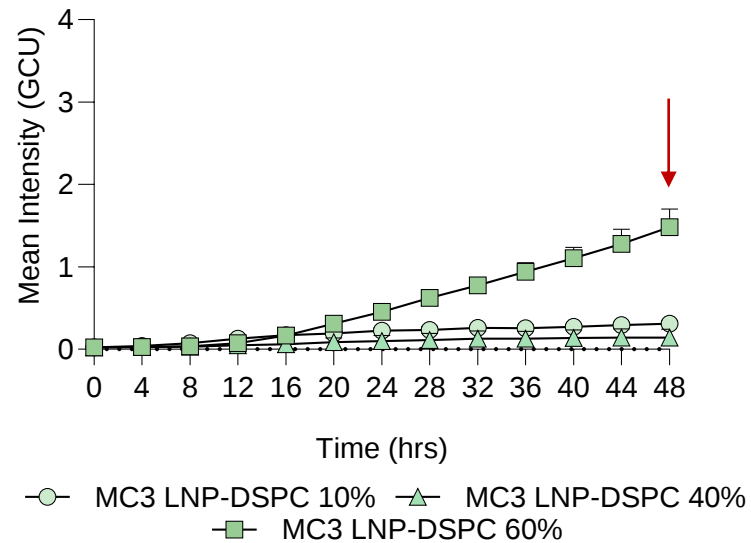
MC3 LNP-DSPC 10%



MC3 LNP-DSPC 60%

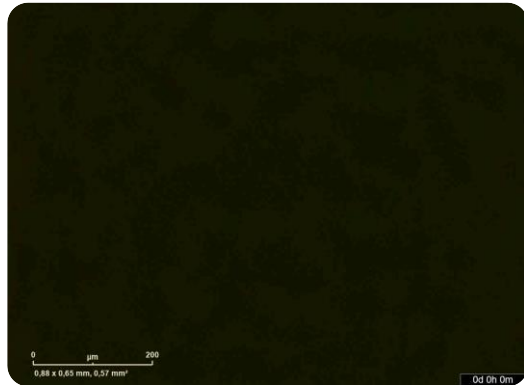


Non-spherical LNP exhibit conserved expression behavior across ionizable lipids

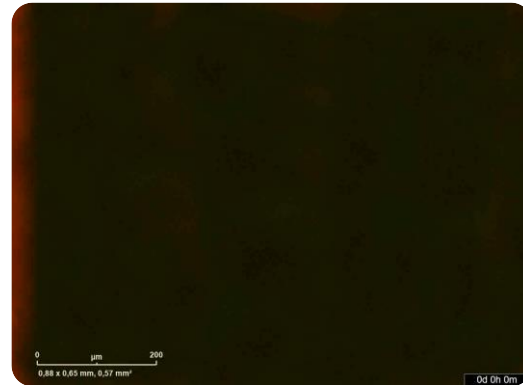


Non-spherical LNP exhibit conserved expression behavior across cell lines

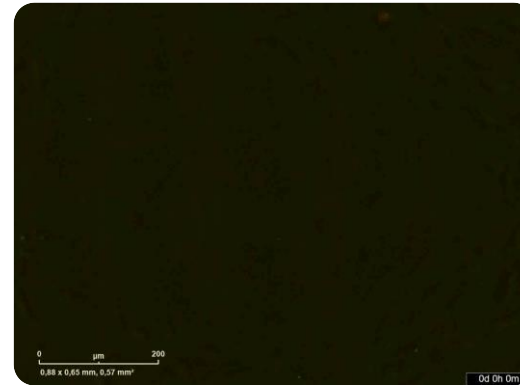
MC3 LNP-DSPC 10%



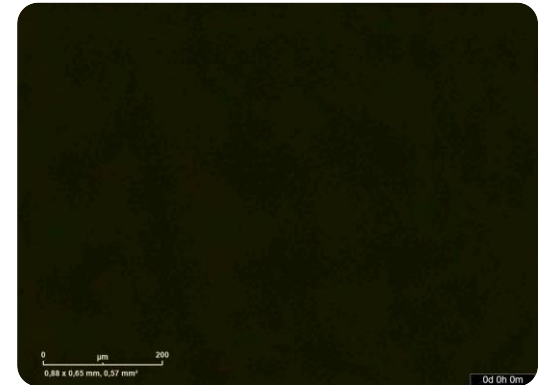
MC3 LNP-DSPC 60%



ALC LNP-DSPC 10%



ALC LNP-DSPC 60%

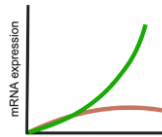


GFP expression LNP uptake

Summary and key takeaways



DSPC content affects LNP shape and aspect ratio.



Non-spherical LNP alter GFP expression kinetics.



Understanding morphology allows smarter LNP design.

Acknowledgment

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