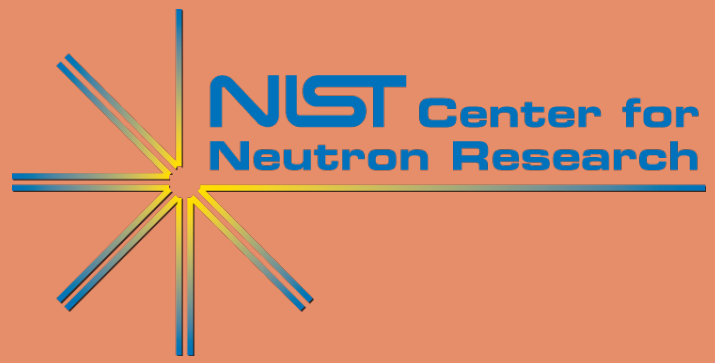
Exploring the Rheological Properties of Dense Lipid Vesicle Solutions as Models for Liposome Nanomedicines

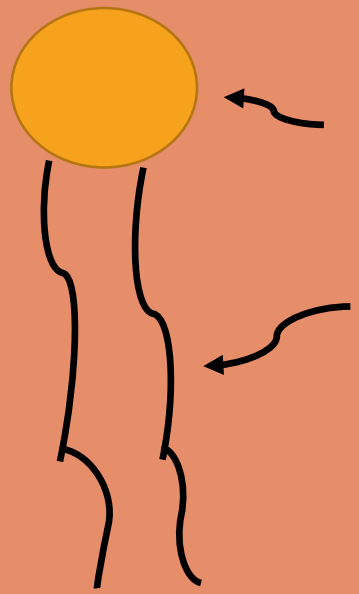
By: Emily Blick



PRESENTATION OVERVIEW

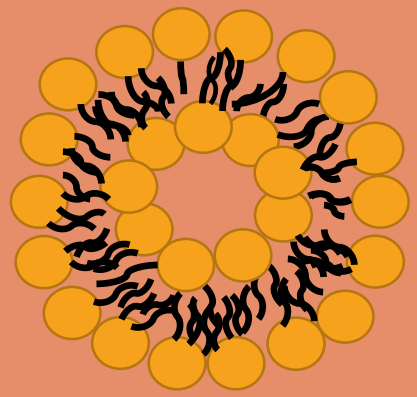
- Background
  - What are liposomes?
  - Why do we care?
- My Project
  - Rheology experiment
  - Stability experiment
- SANS
- Summary of Conclusions
- Future Work

WHAT ARE LIPOSOMES?



Hydrophilic head group

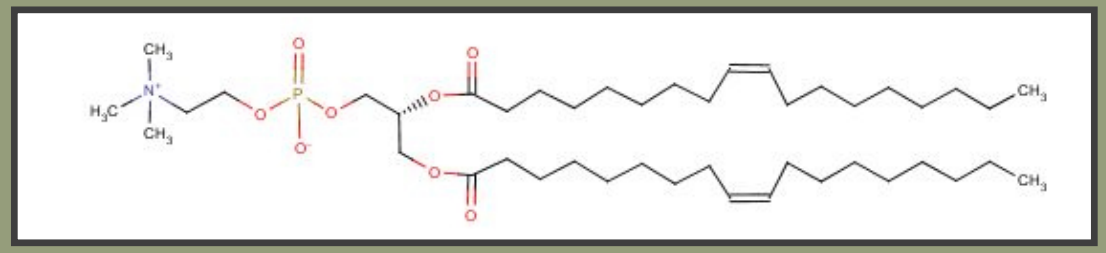
Hydrophobic tails



- Lipids are **amphiphilic** molecules
- Lipids in solution form **liposomes**
  - Enclose aqueous solutions
- Using model system 1,2-Dioleoyl-sn-glycero-3-phosphocholine **(DOPC)**
  - Commonly used lipid in research
  - Relatively inexpensive

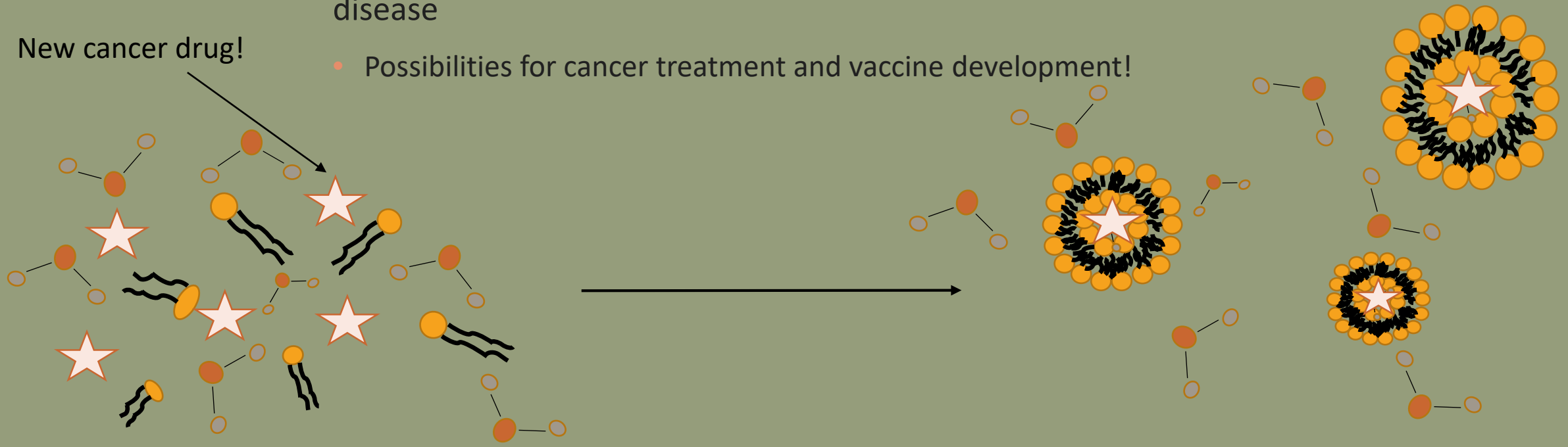
Hydrophilic

Hydrophobic

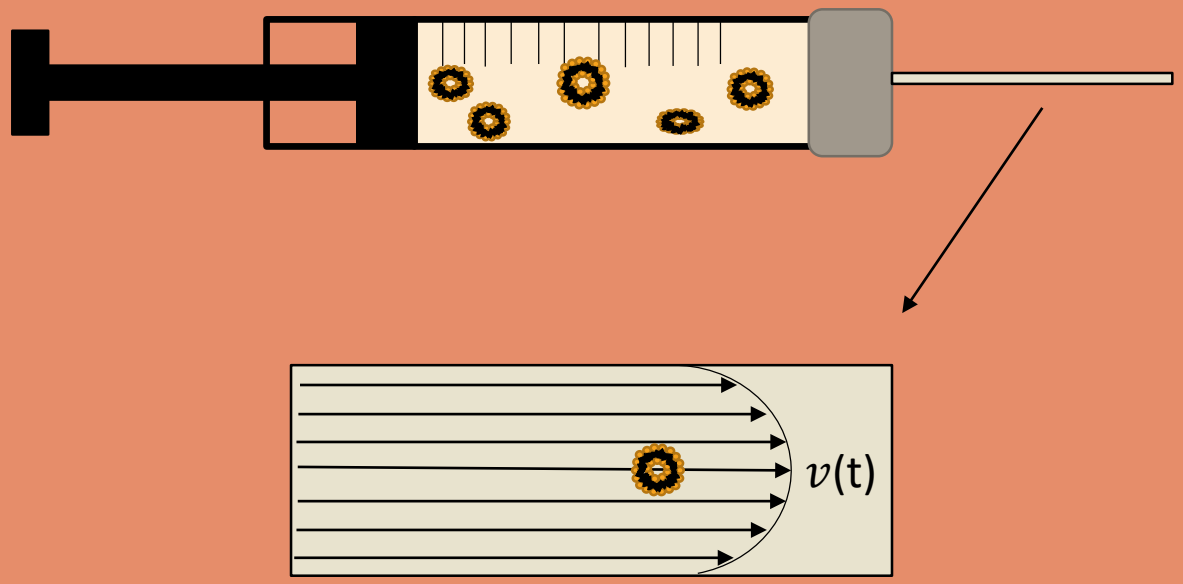


WHY LIPOSOMES?

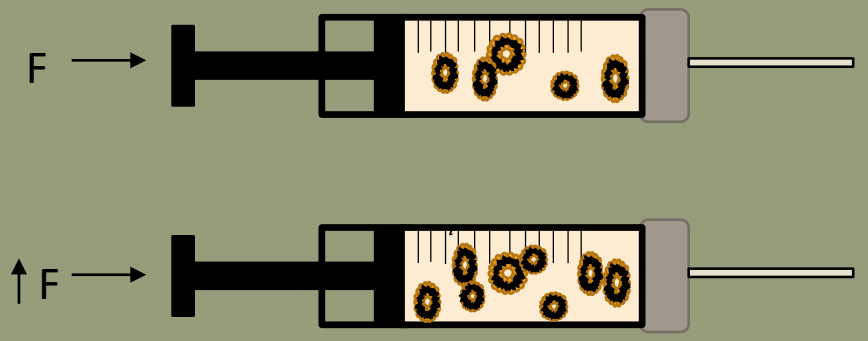
- Liposomes are promising candidates for future drug delivery applications
  - Similar morphology to the cellular membrane
  - Biocompatible, biodegradability, and low toxicity
- Nanomedicine possibilities
- Liposomal nanomedicines can be designed to accumulate at sites of disease
  - Possibilities for cancer treatment and vaccine development!



RHEOLOGY-THE STUDY OF FLOW OF MATTER

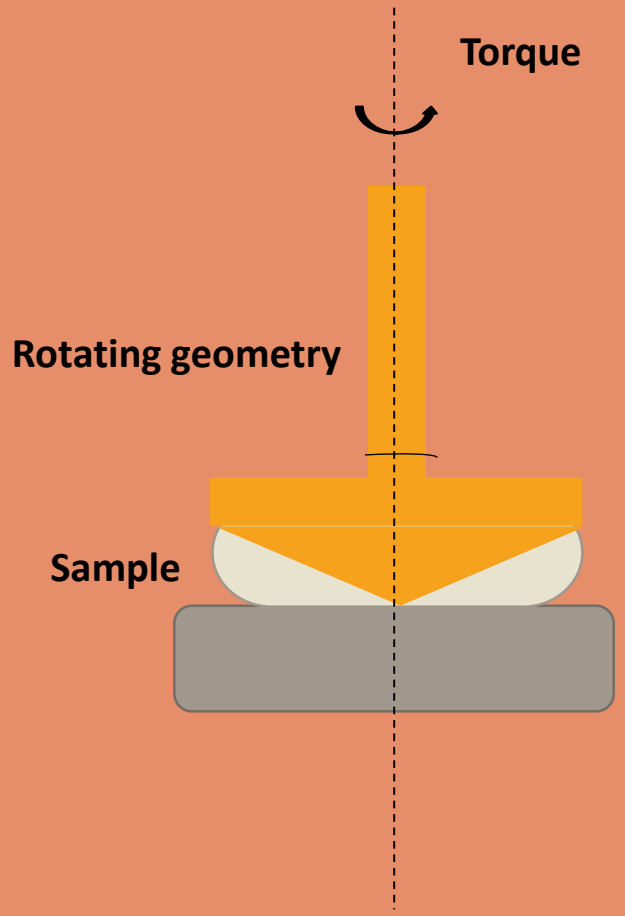


- Liposome therapeutics will likely be delivered through a syringe
  - Solution will experience shear stress going through needle
- How does concentration and shear rate affect solution viscosity?
- How can we predict volume fraction of liposomes?



More viscous sample

RHEOLOGY EXPERIMENT



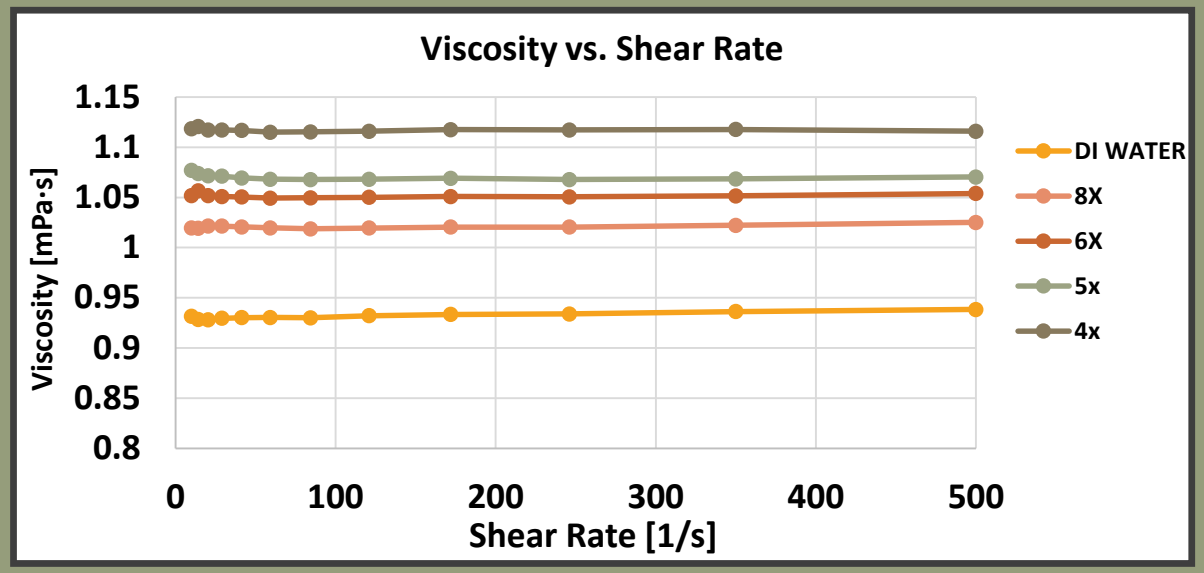
- Measurements were taken using a rheometer
  - Measures torque response of solution to an applied force
  - **Calculate viscosity**
- Made concentration series to study relationship between concentration and viscosity
  - **Better estimate volume fraction**

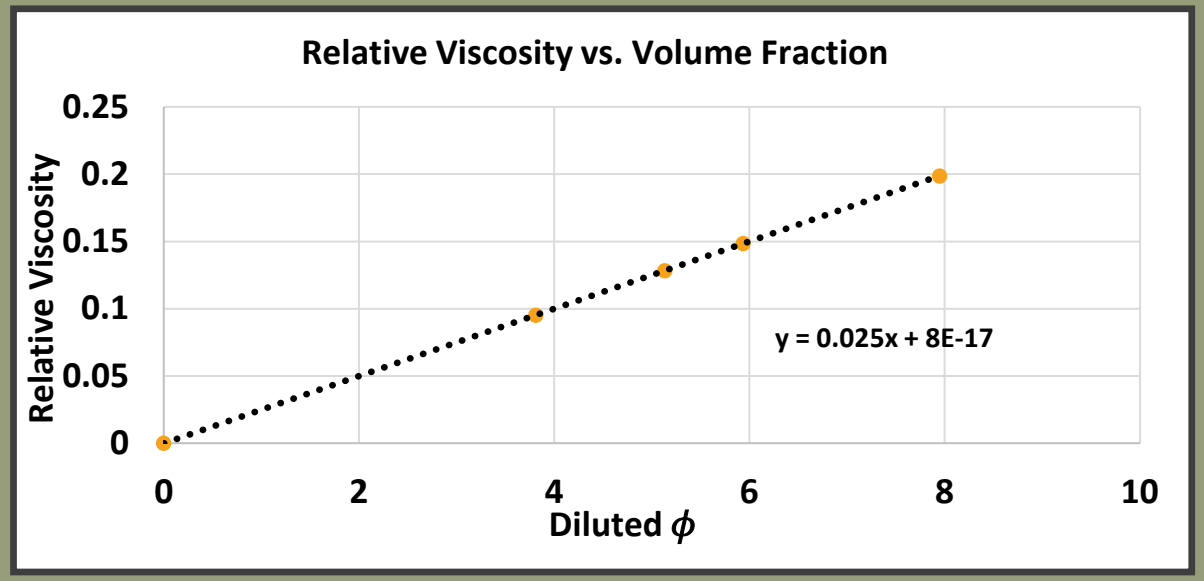
VOLUME FRACTION CALCULATIONS

Relative Viscosity $\longrightarrow \frac{\eta}{\eta_0} = 1 + 2.5\phi$

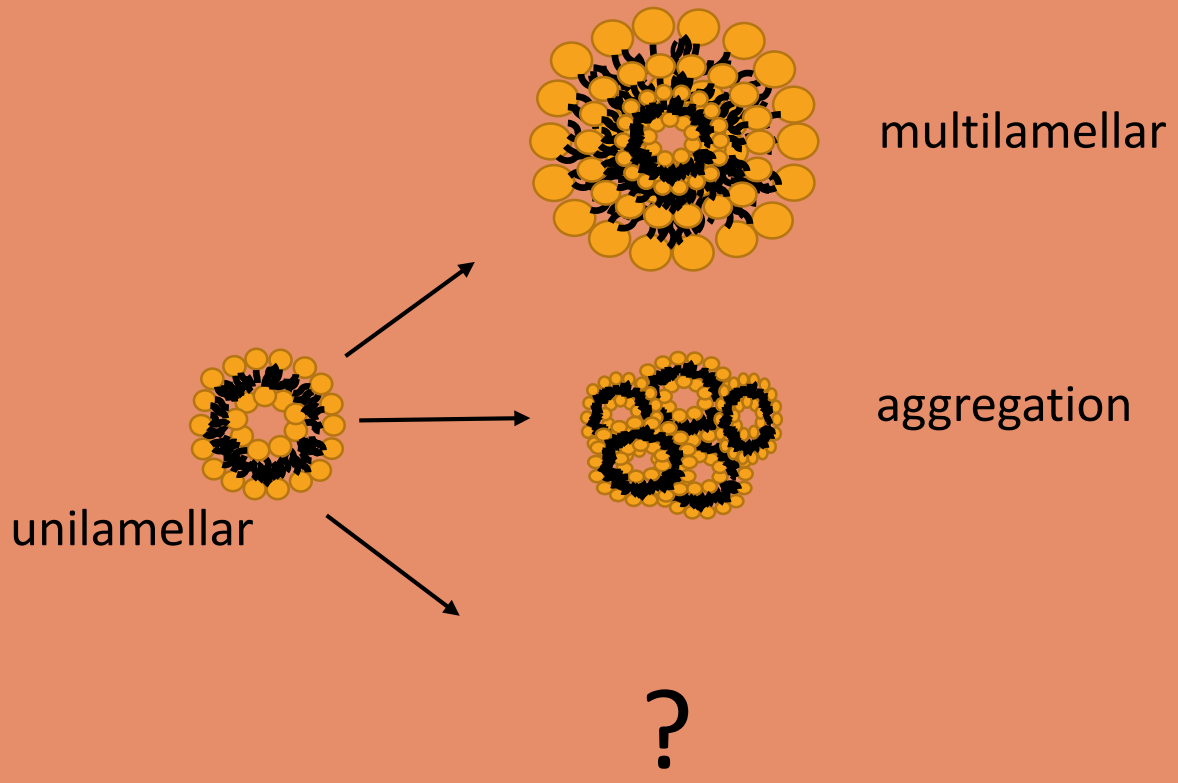
Specific Viscosity $\longrightarrow \eta_{SP} = \eta_r - 1 = 2.5\phi$

Will allow better prediction of volume fraction for future experiments!



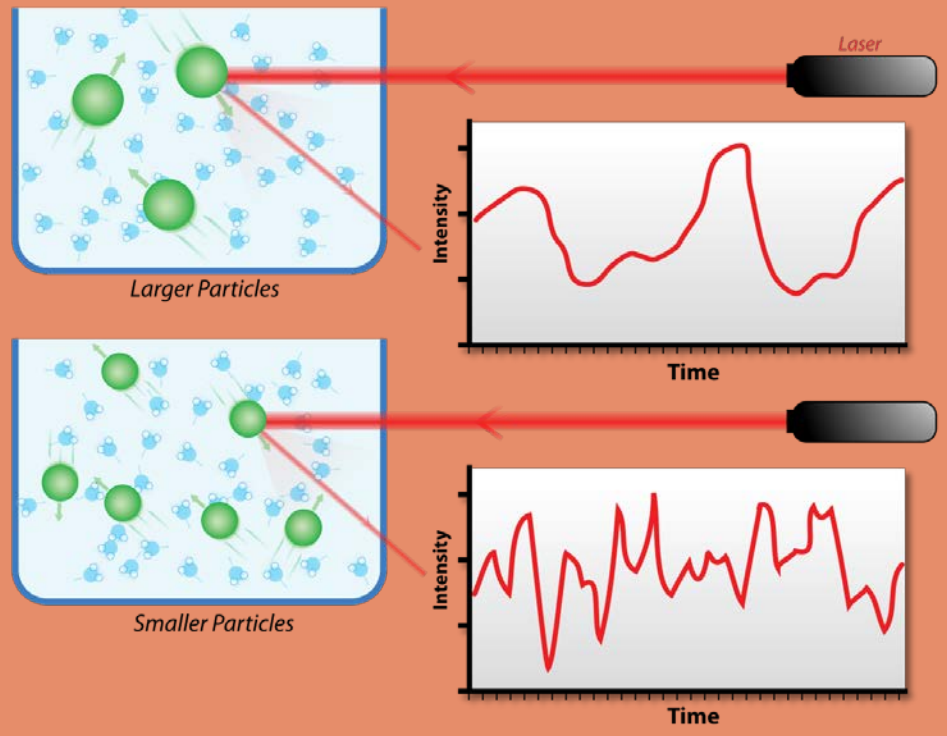


STABILITY



- What factors impact long term stability of vesicle system?
  - Temperature?
  - Size?
  - Concentration?
- What happens to DOPC liposomes when they become unstable at different conditions?
  - Multilamellar?
  - Aggregation?
  - ?
- What are the consequences for drug delivery?
- Generally assumed DOPC stable at high concentration for about 2 weeks
  - No known data supporting

DYNAMIC LIGHT SCATTERING



- Popular light scattering technique
- Laser beam shot at sample and detector senses changes in scattering light
  - Particles scattered at known angle
- Can provide diffusion coefficient
  - Can be related to particle size
- Only valid at low concentrations

$$D = \frac{kT}{6\pi\eta R}$$

Radius!

STABILITY EXPERIMENTS

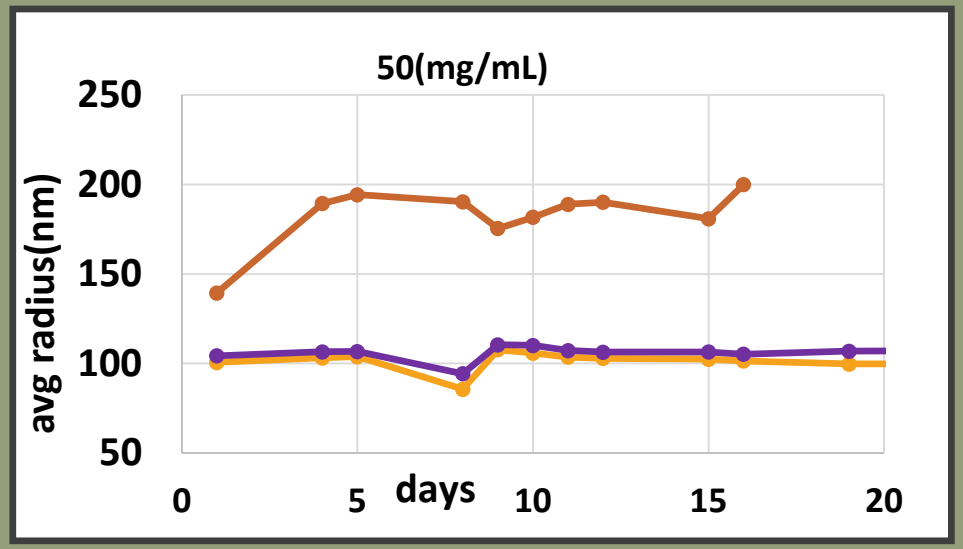
- Set up 5 vials at different concentrations at three different temperatures
  - Concentrations: 50, 25, 12.5, 5, 1 (mg/mL)
- Set up conditions with a diameter of 60, 100, 120, 200 nm
- Took frequent DLS measurements
  - Each sample under the same conditions during measurement

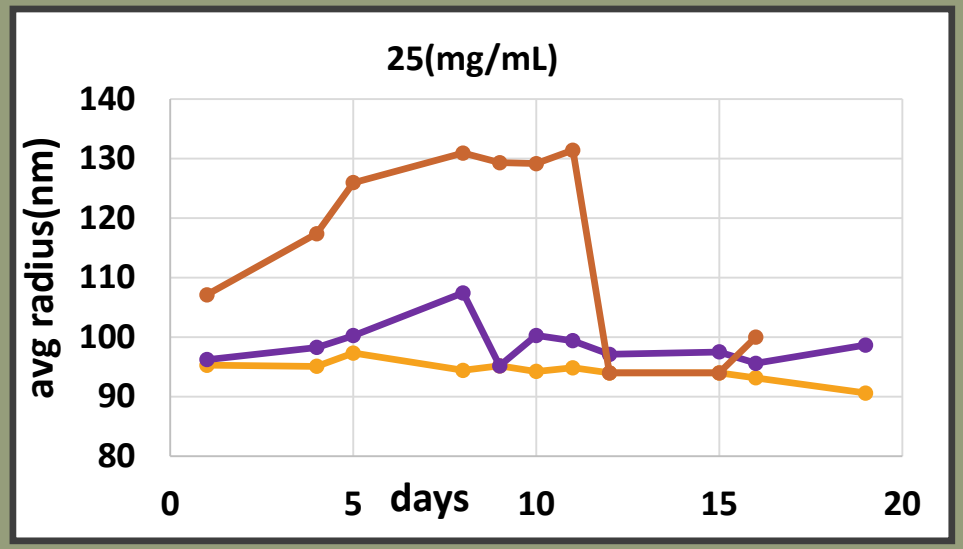
4° C

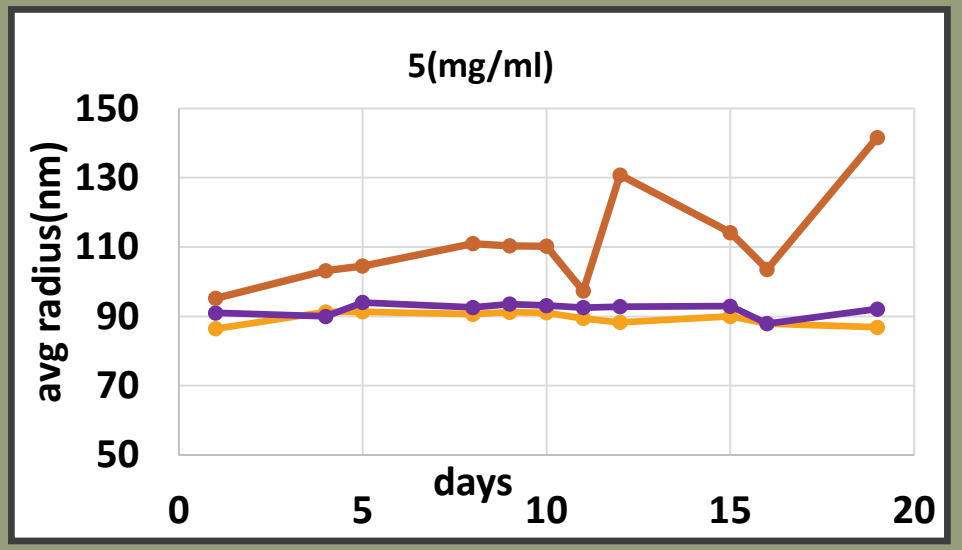
22° C

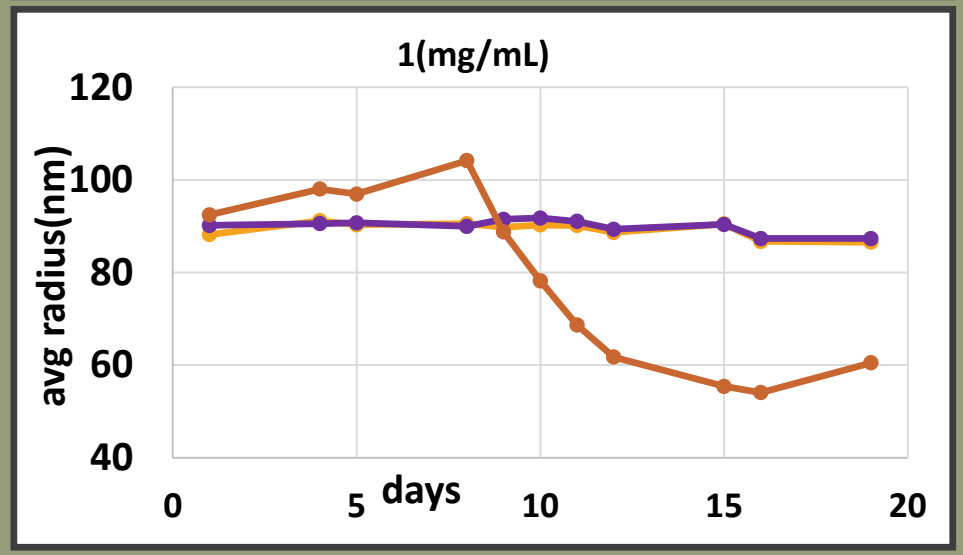
55° C

STABILITY RESULTS FOR 200 NANOMETER VESICLES







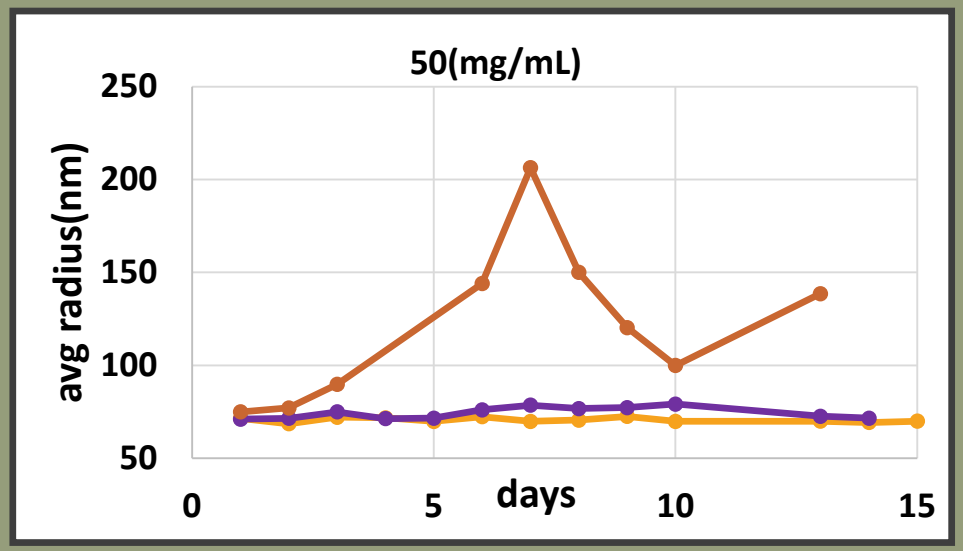


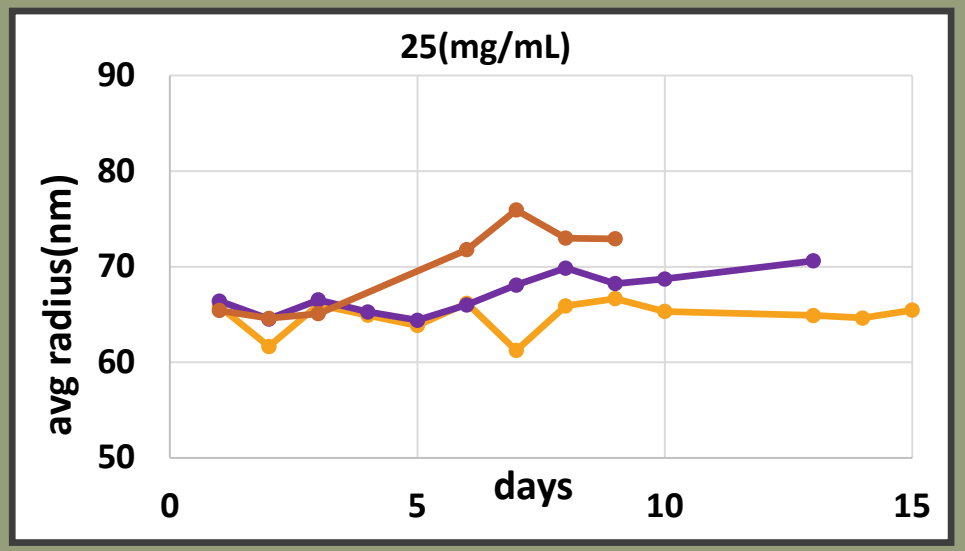
22 ° C
4 ° C
55 ° C

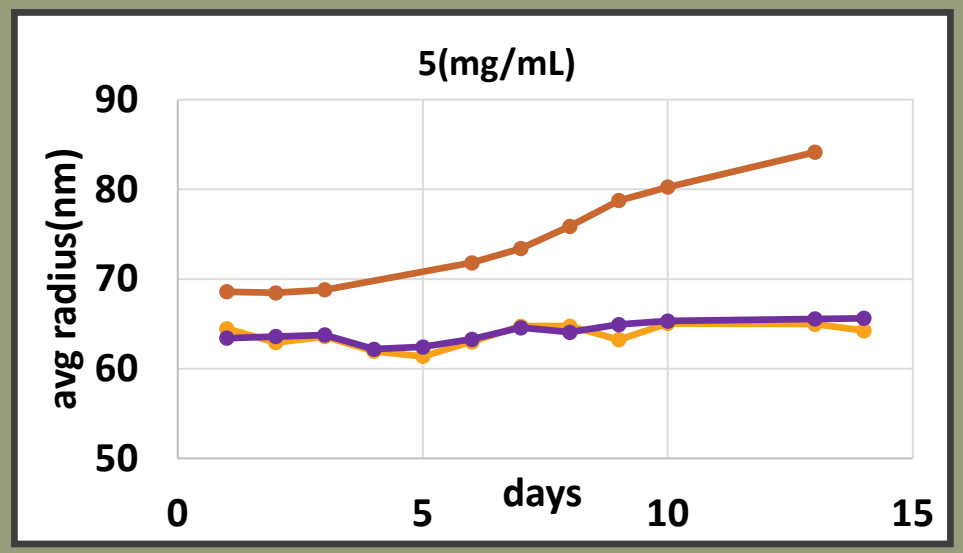
Summary:

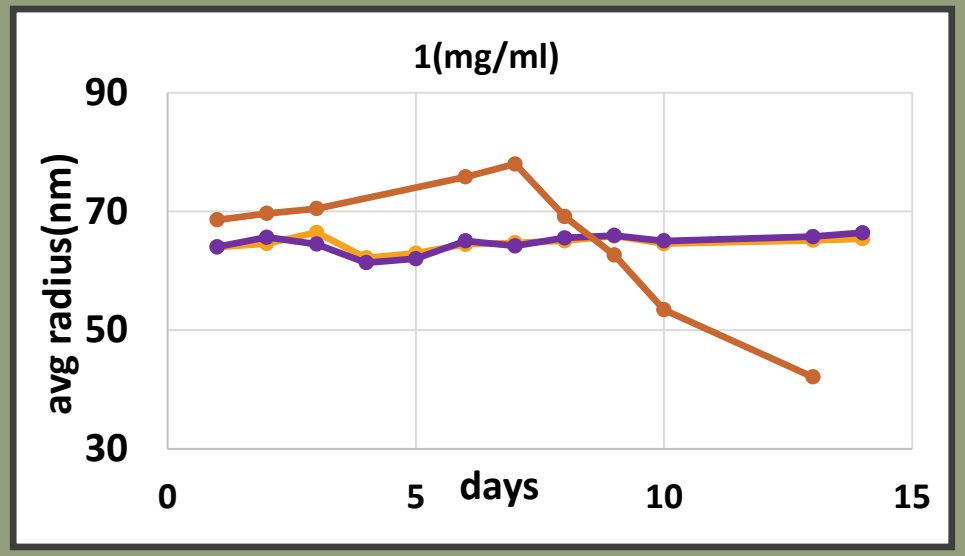
- **Samples at lower temperature:**
  - Follow similar mostly flat path
- **Samples at high temperature:**
  - Show unpredictable pattern

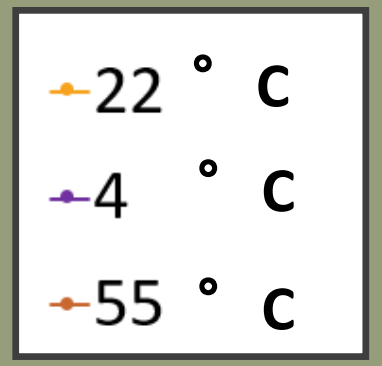
STABILITY RESULTS FOR 120 NANOMETER VESICLES











Summary:

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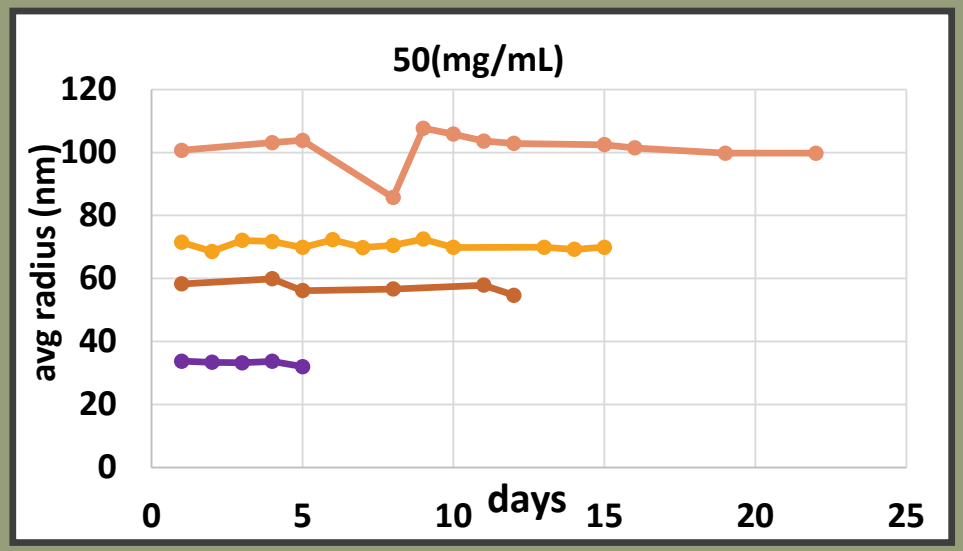
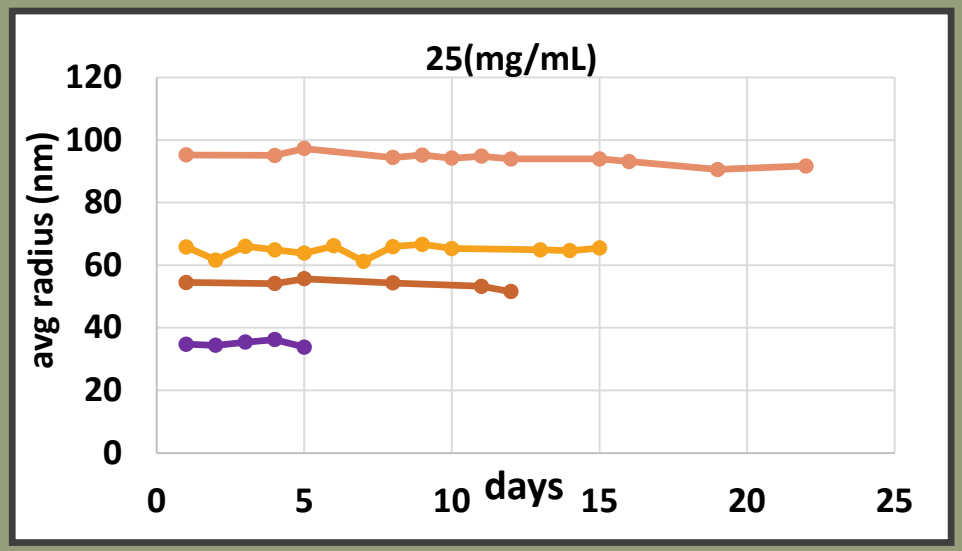
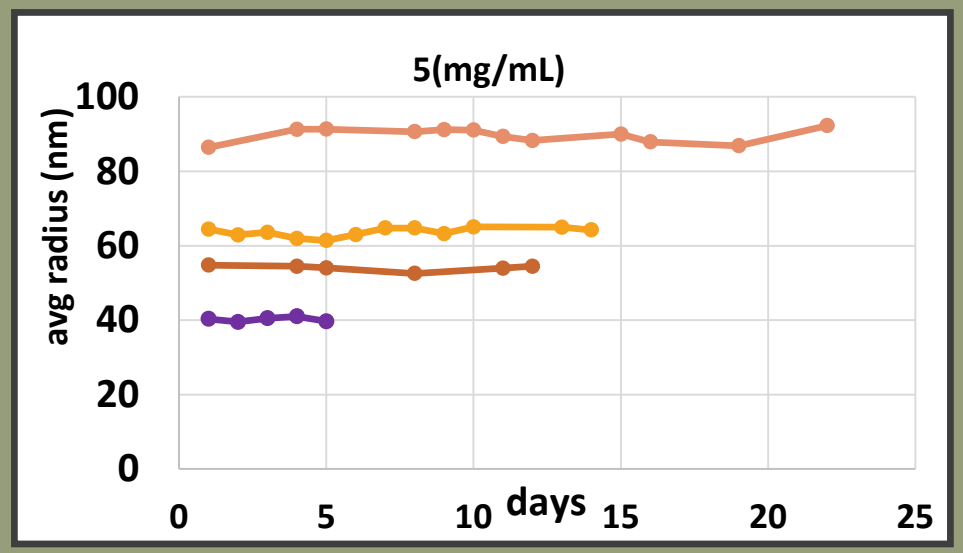
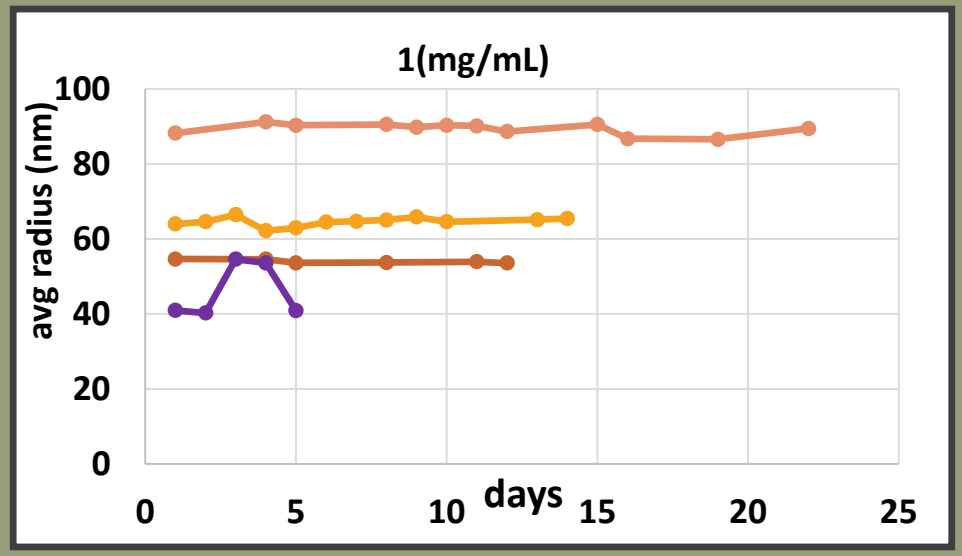
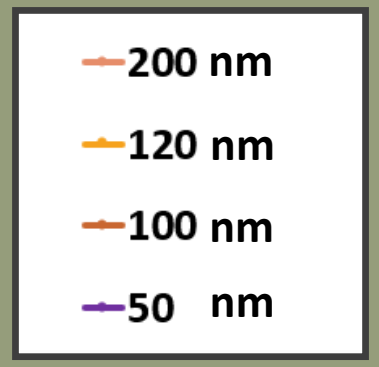
STABILITY RESULTS FOR ROOM TEMPERATURE







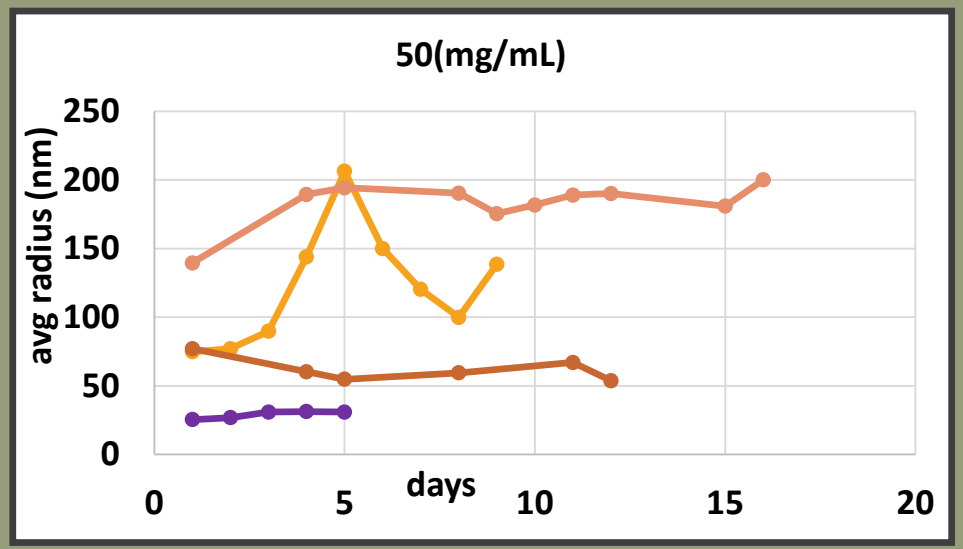


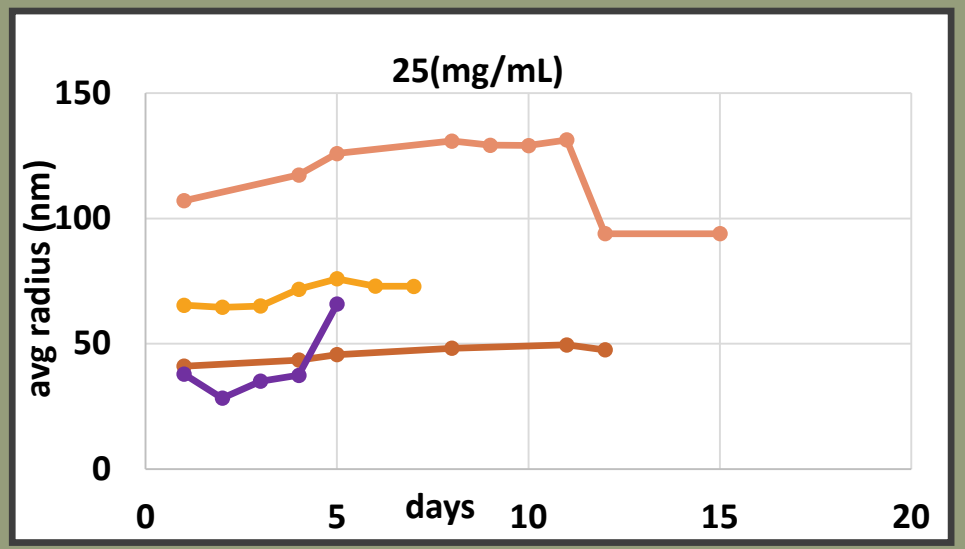


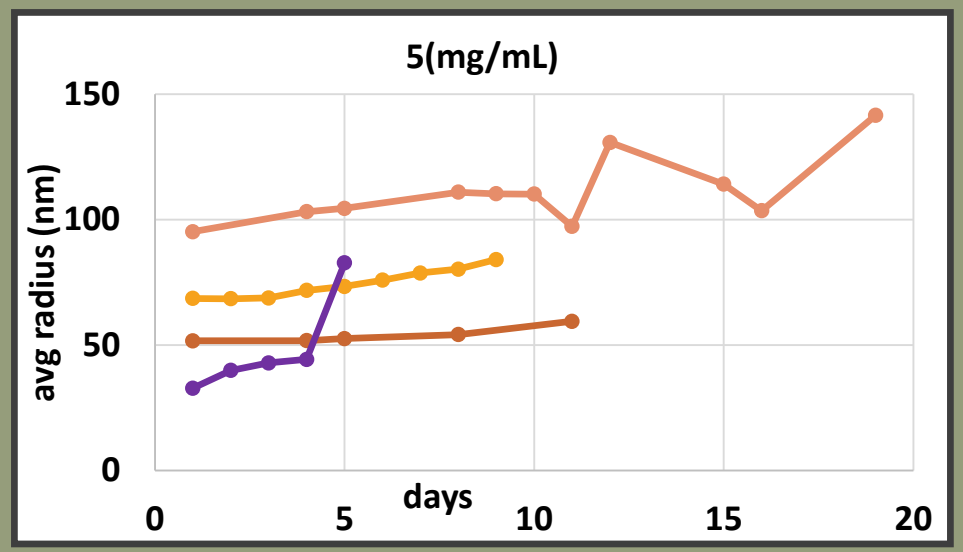
Summary:

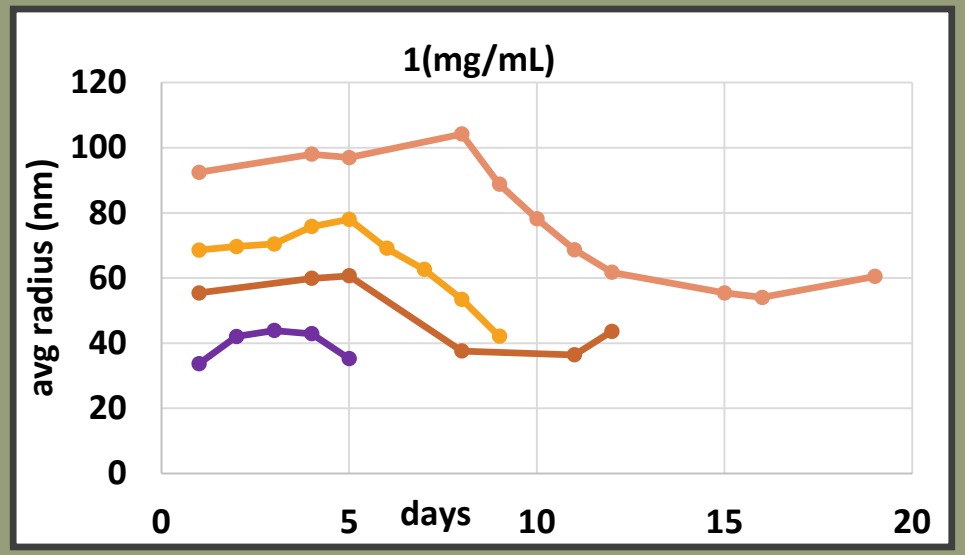
- **Samples at room temperature:**
  - Follow same path at 22° C and 4° C
  - Path continues almost flat for all vesicle sizes

STABILITY RESULTS FOR 55° C









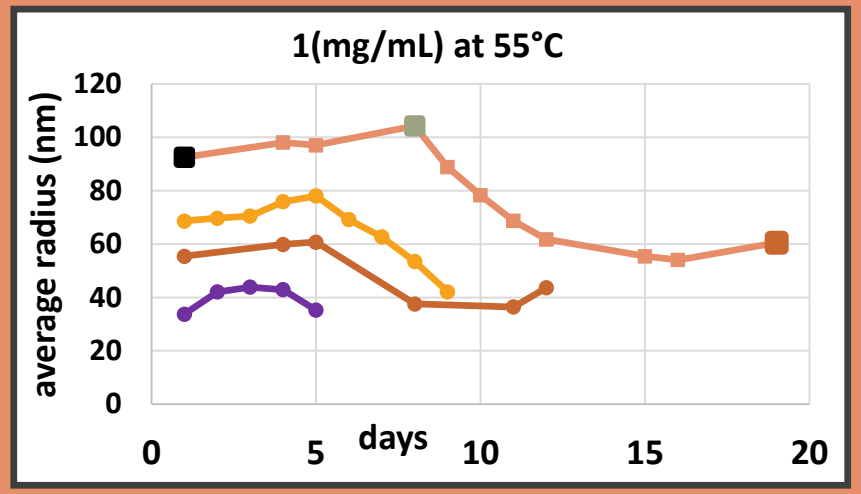
Summary:

- **Samples at 55° C :**
  - Different and unpredictable
  - Maintain unpredictability at all vesicle sizes
  - **Lower concentration of 1(mg/mL) shows pattern of decreasing vesicle size**

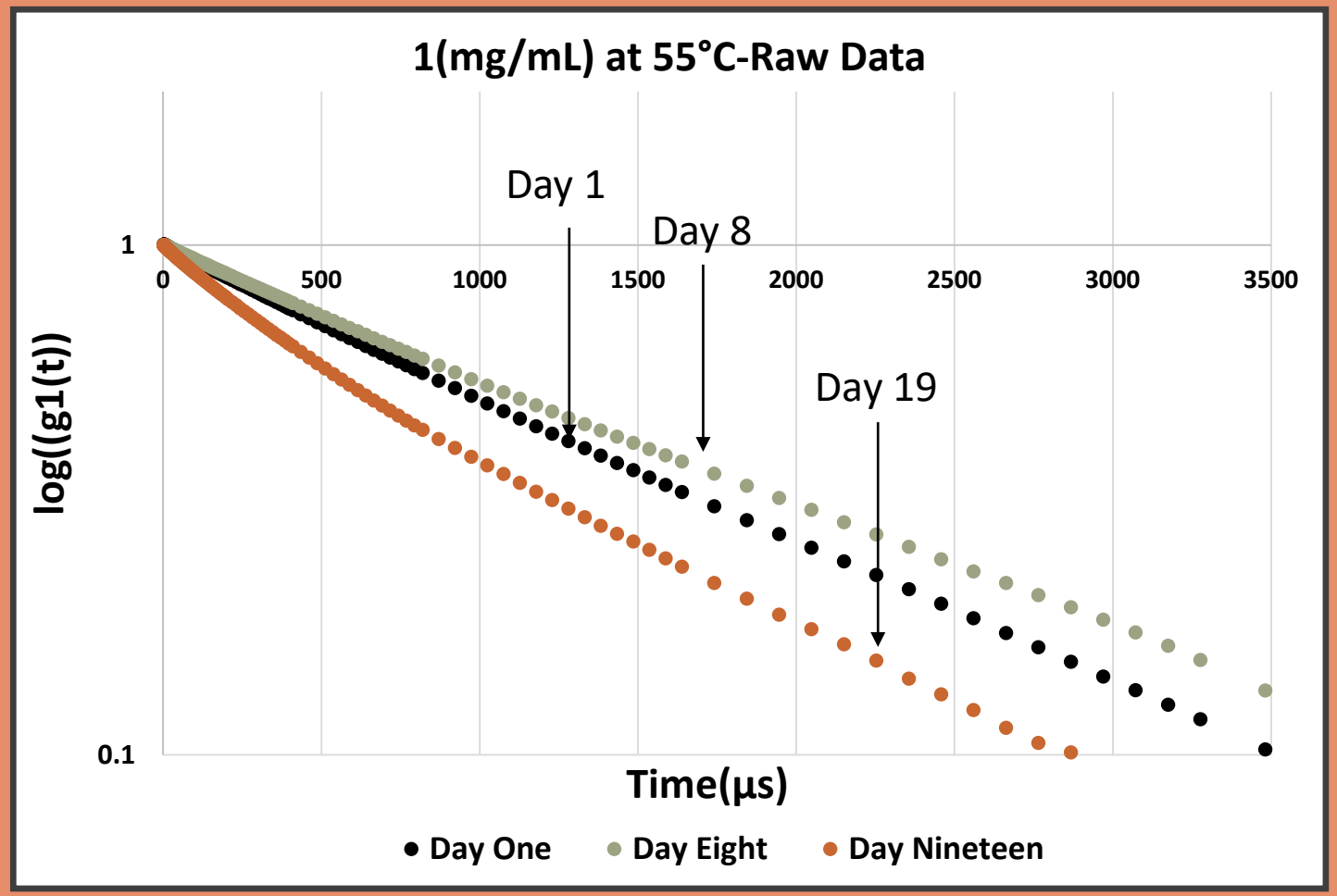
Type equation here.

nm
nm
nm
nm

RAW DATA

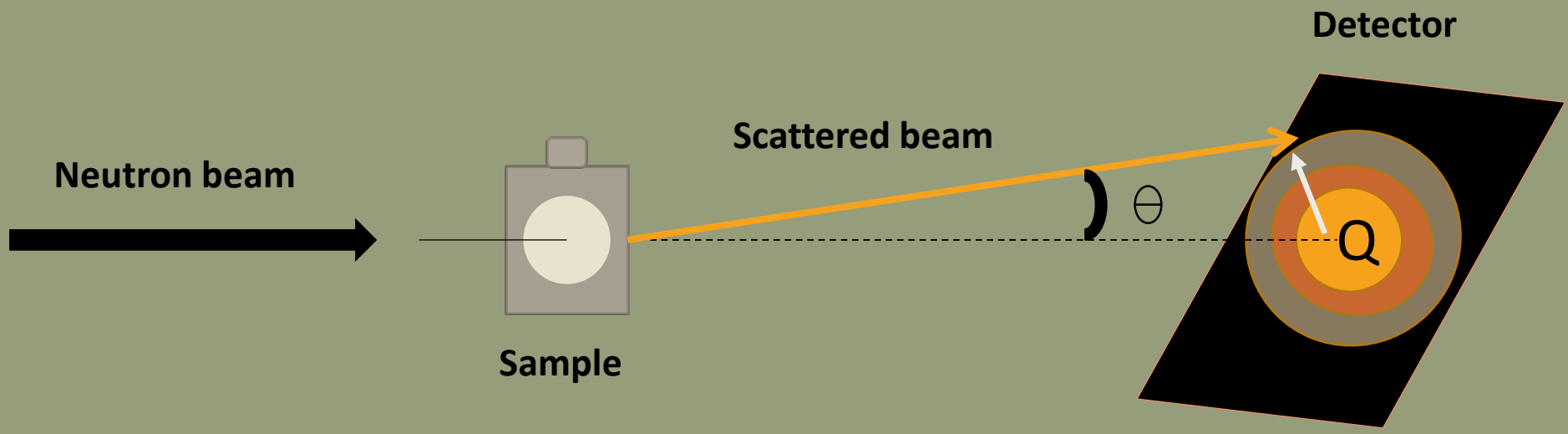


$$g_1(t) = e^{-Dq^2t}$$

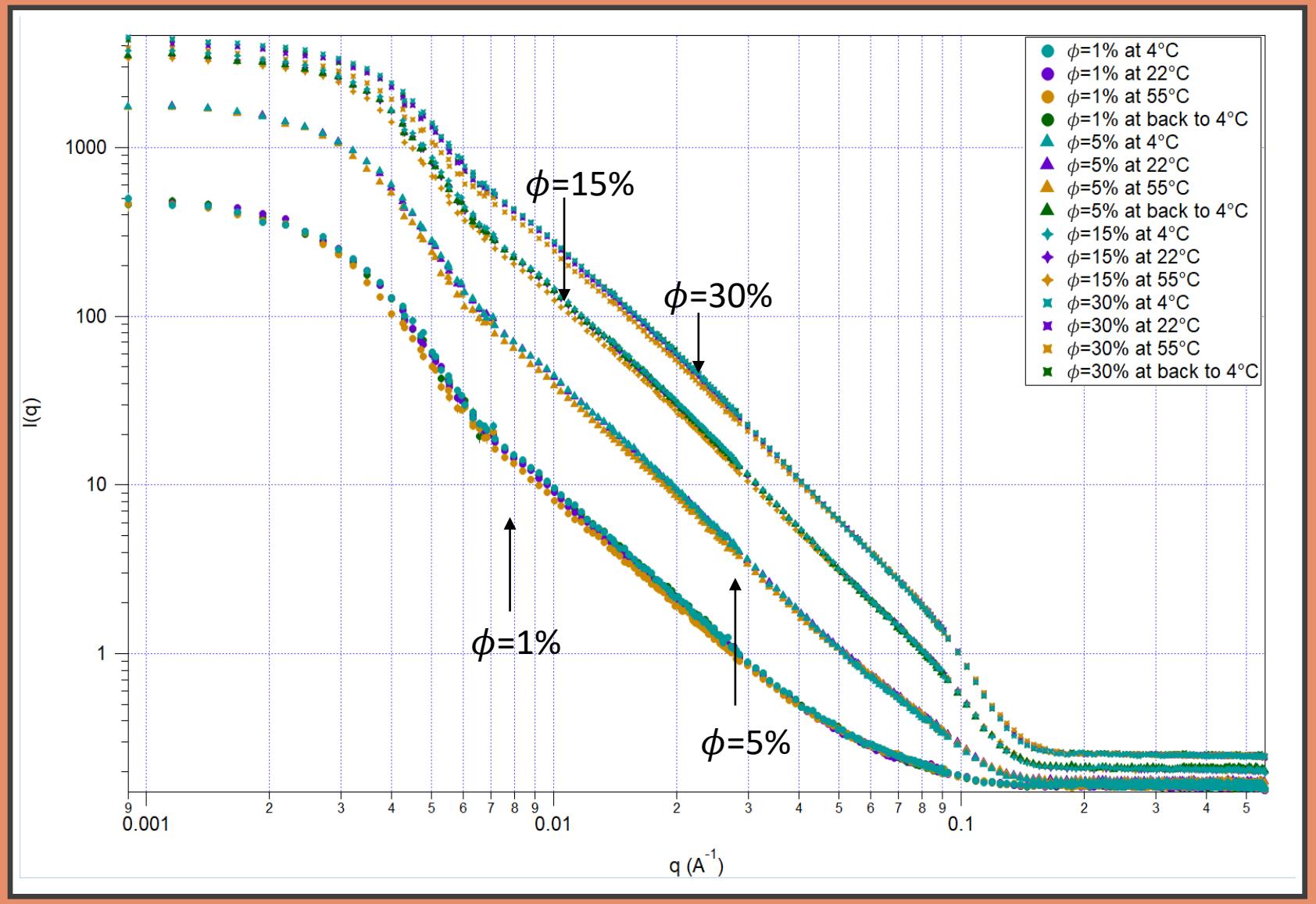


SMALL ANGLE NEUTRON SCATTERING

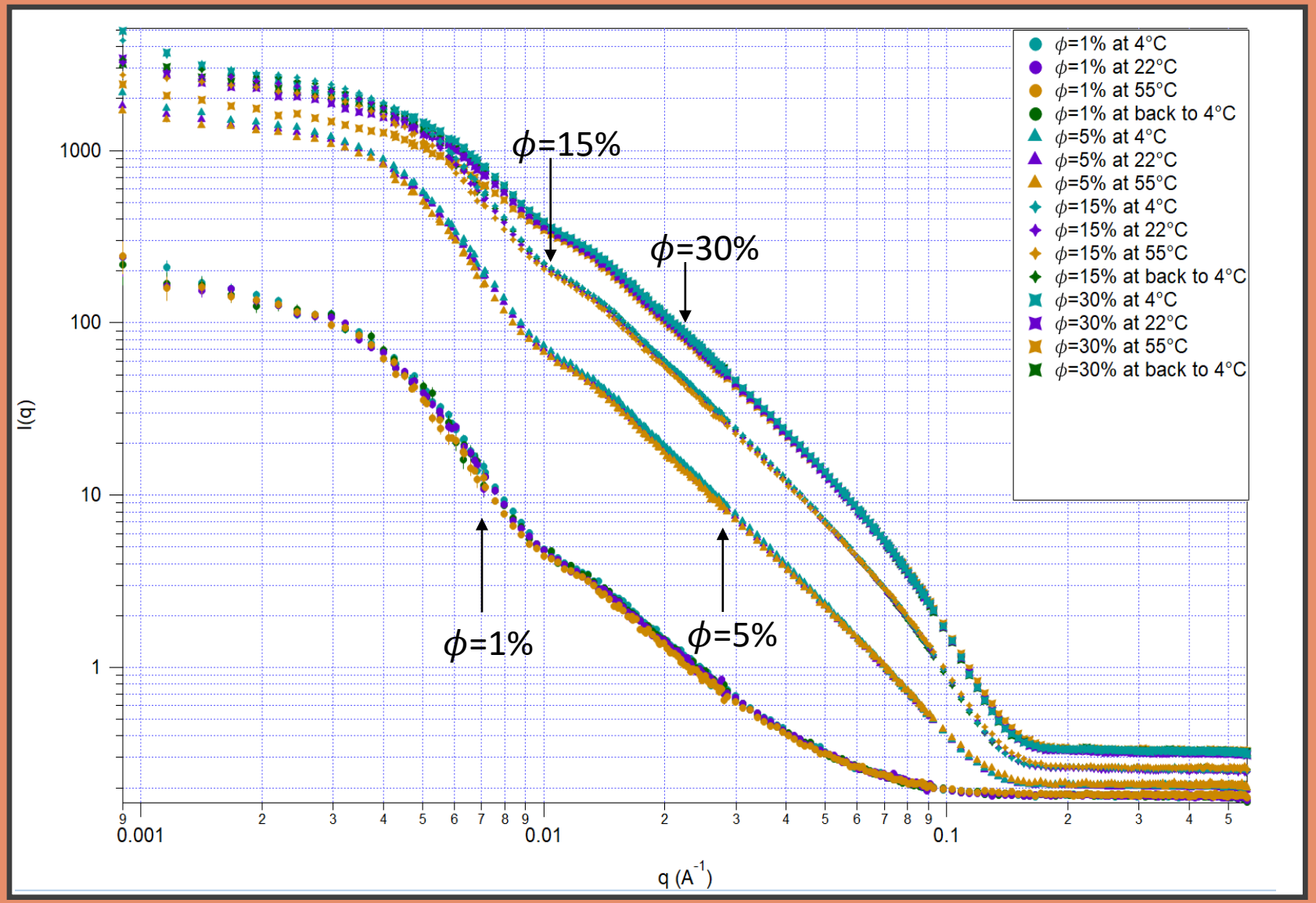
- Probes material structures by interacting with nucleus in sample
- Neutron scattering occurs due to the scattering length density components in sample
- Scattering vector Q can tell us about structures in our sample



SANS 100 NANOMETER RESULTS



SANS 50 NANOMETER RESULTS



CONCLUSION

- **The possibility of liposomes for nanomedicines is dependent on vesicle stability and rheological properties**
- What I completed:
  - Created a model to estimate volume fraction based on sample viscosity to improve future experiments
  - Ran multiple stability tests showing DOPC instability at high temperatures
  - Completed SANS experiment showing temperature dependence
    - Defies what is generally assumed

FUTURE WORK

- Study the possibility of chemical decomposition
- Analyze spin echo data
- Continue trials on smaller vesicles
- Continue trials in higher concentrations but dilute right before measurements
- Run RheoSANS experiment in relation to future injection applications
- Run SANS experiments on samples after duration of time at different temperatures

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- My fellow NCNR SURFers

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