

Controlling Size of PEG-PLGA Nanoparticles by Flash Nano Precipitation (FNP) Using a Confined Impinging Jet Device

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Introduction

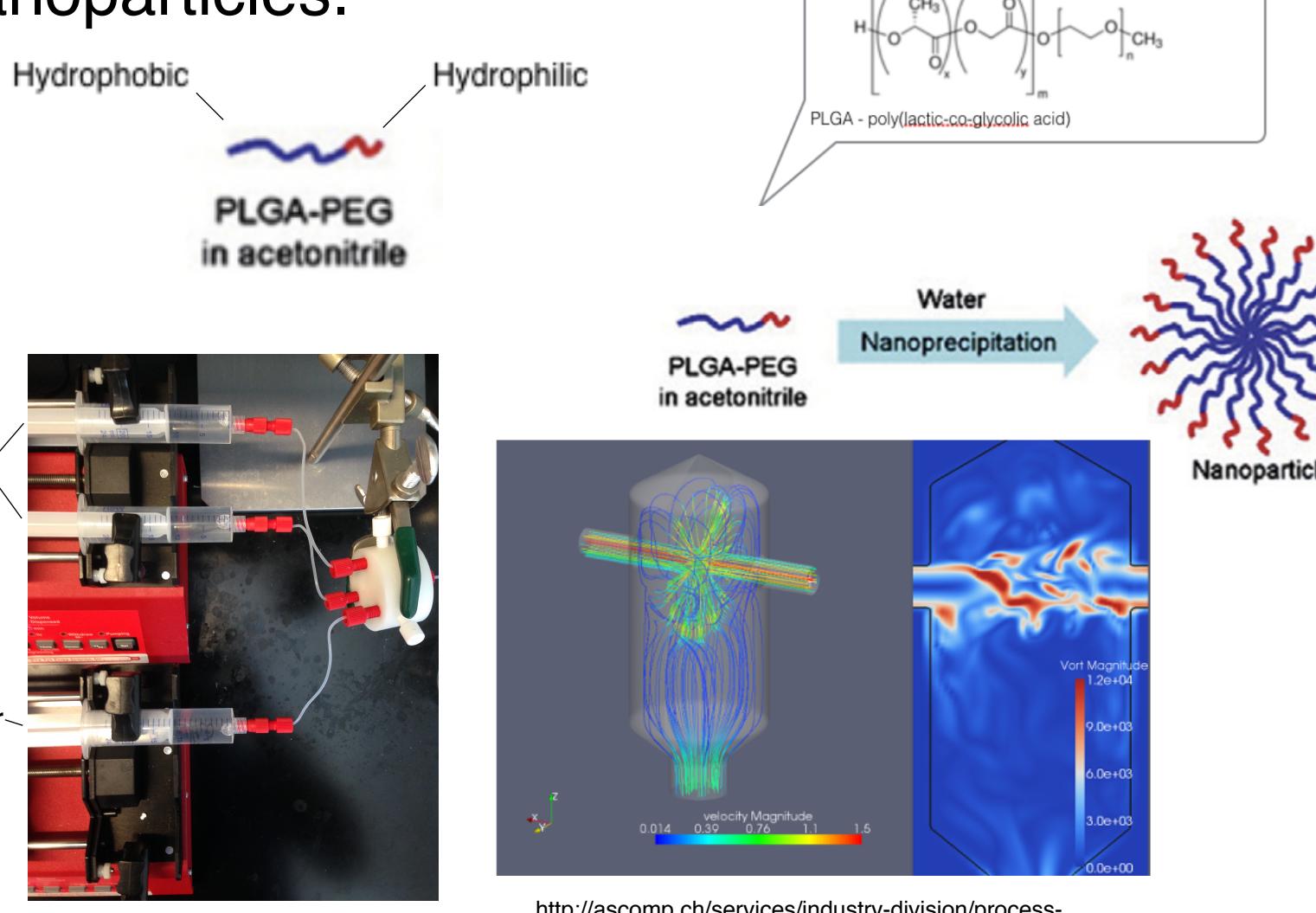
Polymeric nanoparticles (NPs) are used for a variety of biomedical applications as result of inexpensive production costs and the wide range of physicochemical properties offered by different polymers. Adjustable parameters of NPs include shape, size, charge, hydrophobicity, etc. By optimizing specific parameters, NPs can serve as effective delivery platforms. In the Mao Lab (of Johns Hopkins University's INBT), NPs are optimized to deliver a malaria transmission blocking vaccine antigen directly to lymph node-resident dendritic cells via the lymphatic system. Size control is imperative as dendritic uptake is optimal at specific sizes. Controlled NP synthesis will optimize particle size for these studies.

PEG-PLGA Biodegradable Nanoparticles.

The PEG-PLGA polymer is comprised of a hydrophobic block (polylactic-co-glycolic acid) and a hydrophilic block (polyethylene glycol). Through the FNP system, PEG-PLGA in organic solvent (this case acetonitrile) mixes with distilled water (DI H₂O) to synthesize nanoparticles. PEG-PLGA is biodegradable and its low toxicity makes it a viable material for NP fabrication. PEG-PLGA easily allows ligands to conjugate to the surface of the particle.

FNP Method

FNP has been developed as a method for the fabrication of nanoparticles. Scaling up our nanoparticle production process is simple— inexpensive and efficient. With distilled water and polymer in organic solvent, particles are produced through the confined impinging jet device which channels H₂O and polymer through a chamber to produce sizes ranging from 29 nanometers to 111 nanometers. Amphiphilic PEG-PLGA remains as free polymer in organic solvent. In the FNP method, the hydrophobicity of PEG-PLGA and the mixing of polymer and water synthesizes nanoparticles.



<http://ascomp.ch/services/industry-division/process/>

Varying FNP Parameters to Adjust Particle Size

- Here we investigate the effects of polymeric and aqueous flow rates on the sizes of NP's. Varied rates result in a wide range of NP diameter and PDI.
- General flow rates with optimal size/PDI shown to the right
- PDI (polydispersity index)—size distribution

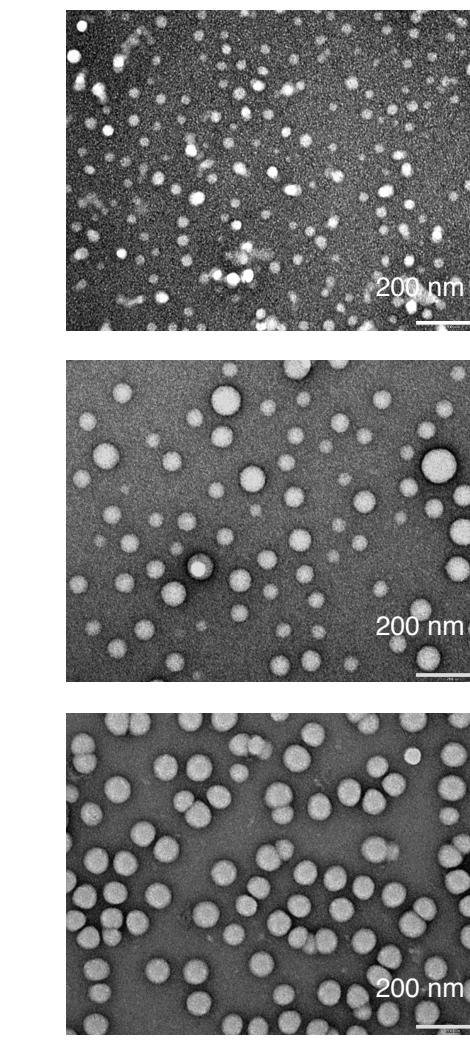
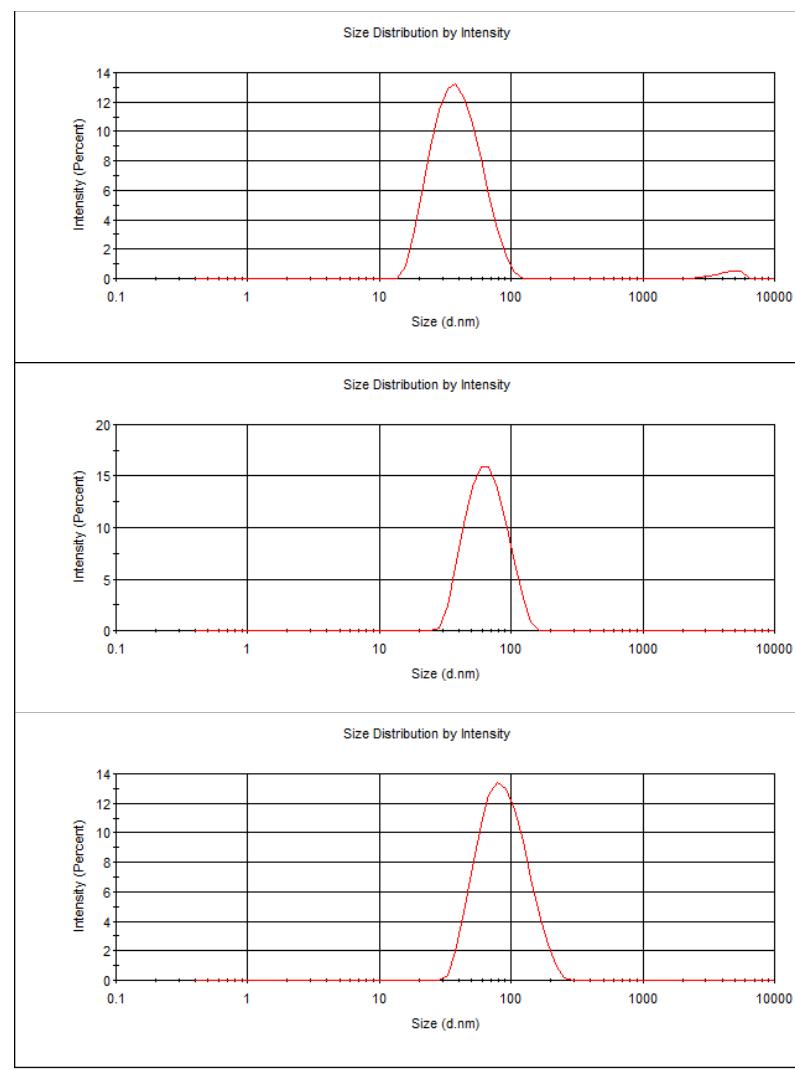
$$PDI = \frac{M_w}{M_n}$$

Mw= molecular weight
Mn= number avg. molecular weight

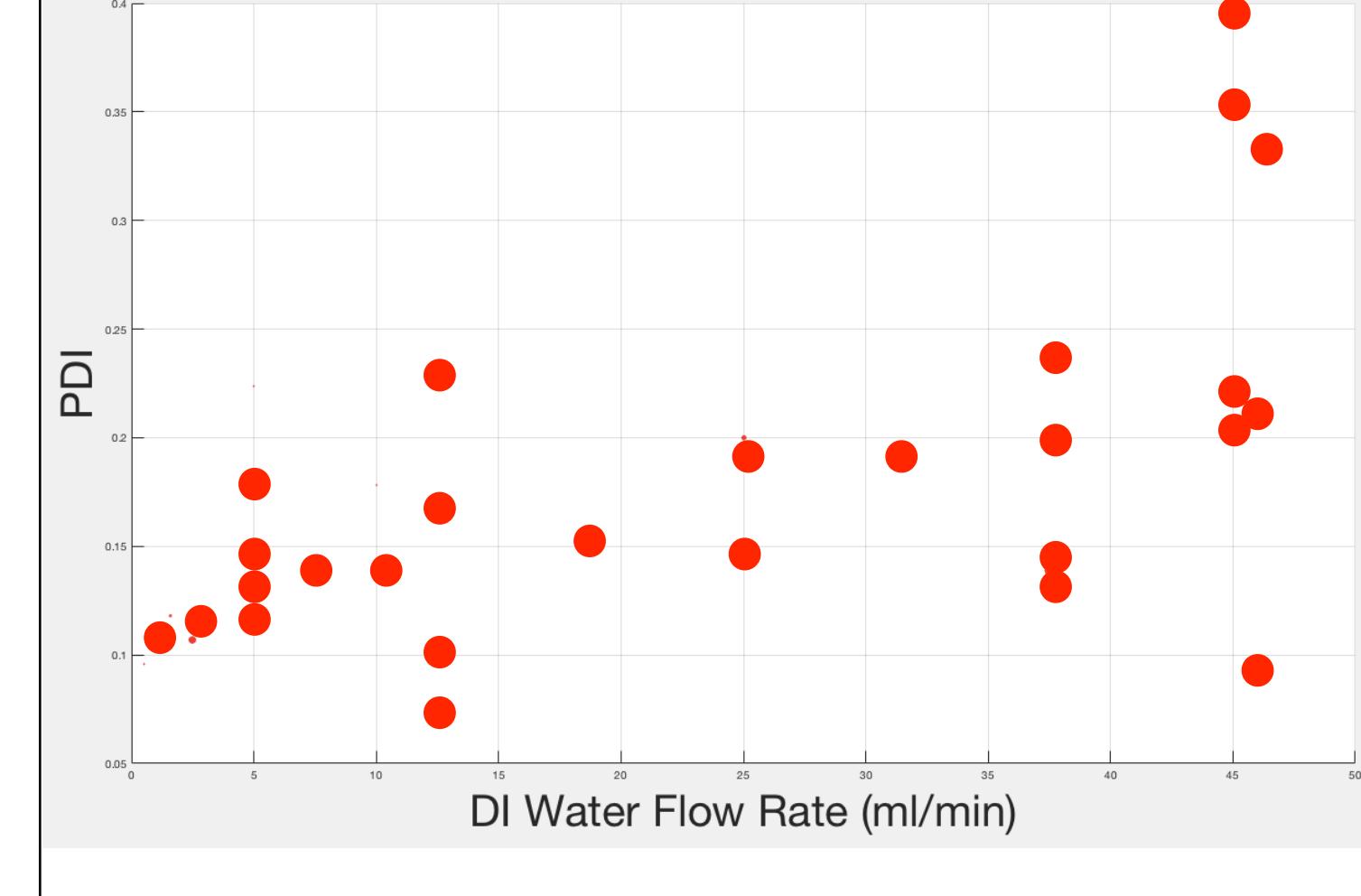
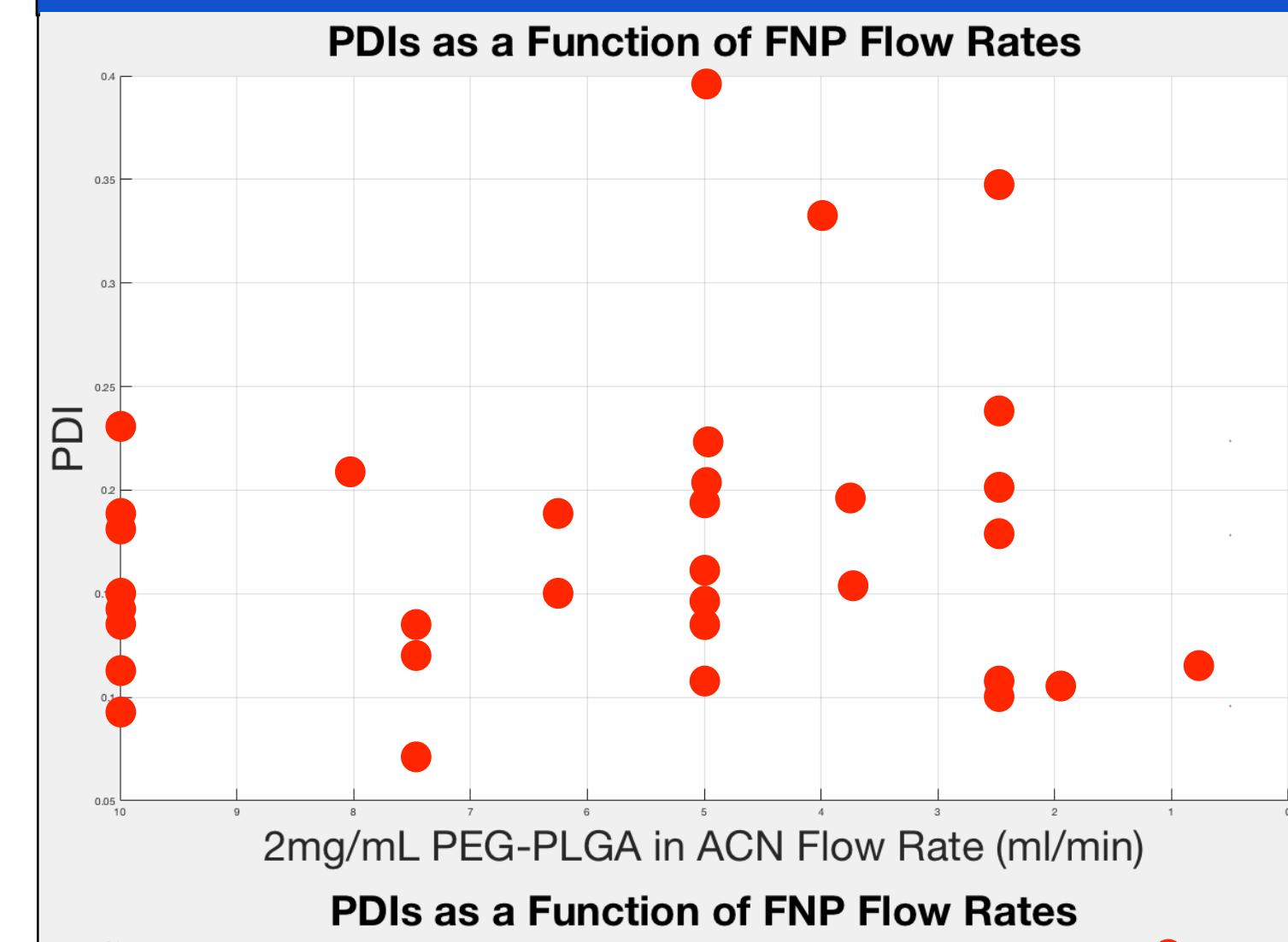
35 nm
PDI: .19

57 nm
PDI: .17

77 nm
PDI: .11

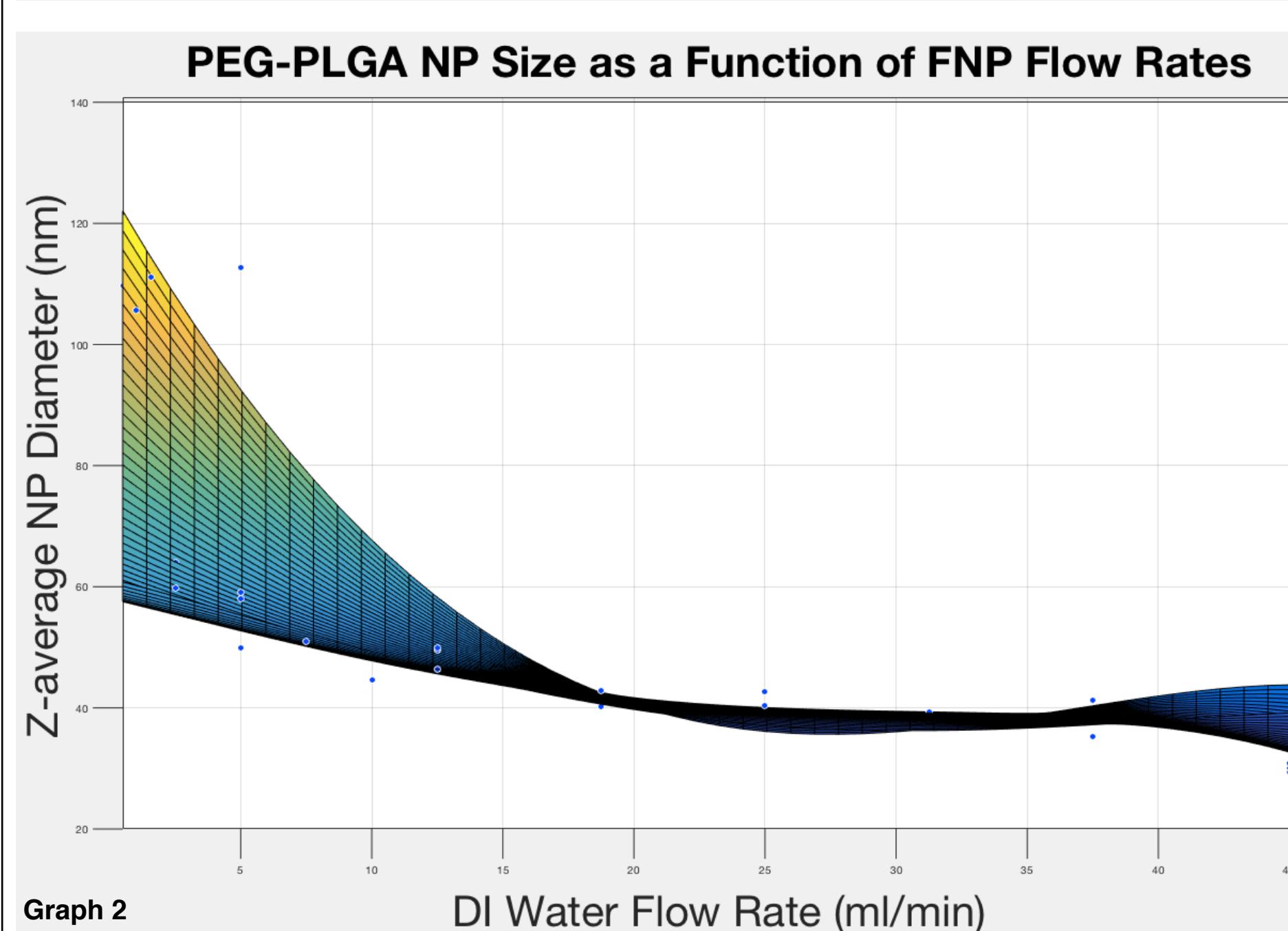
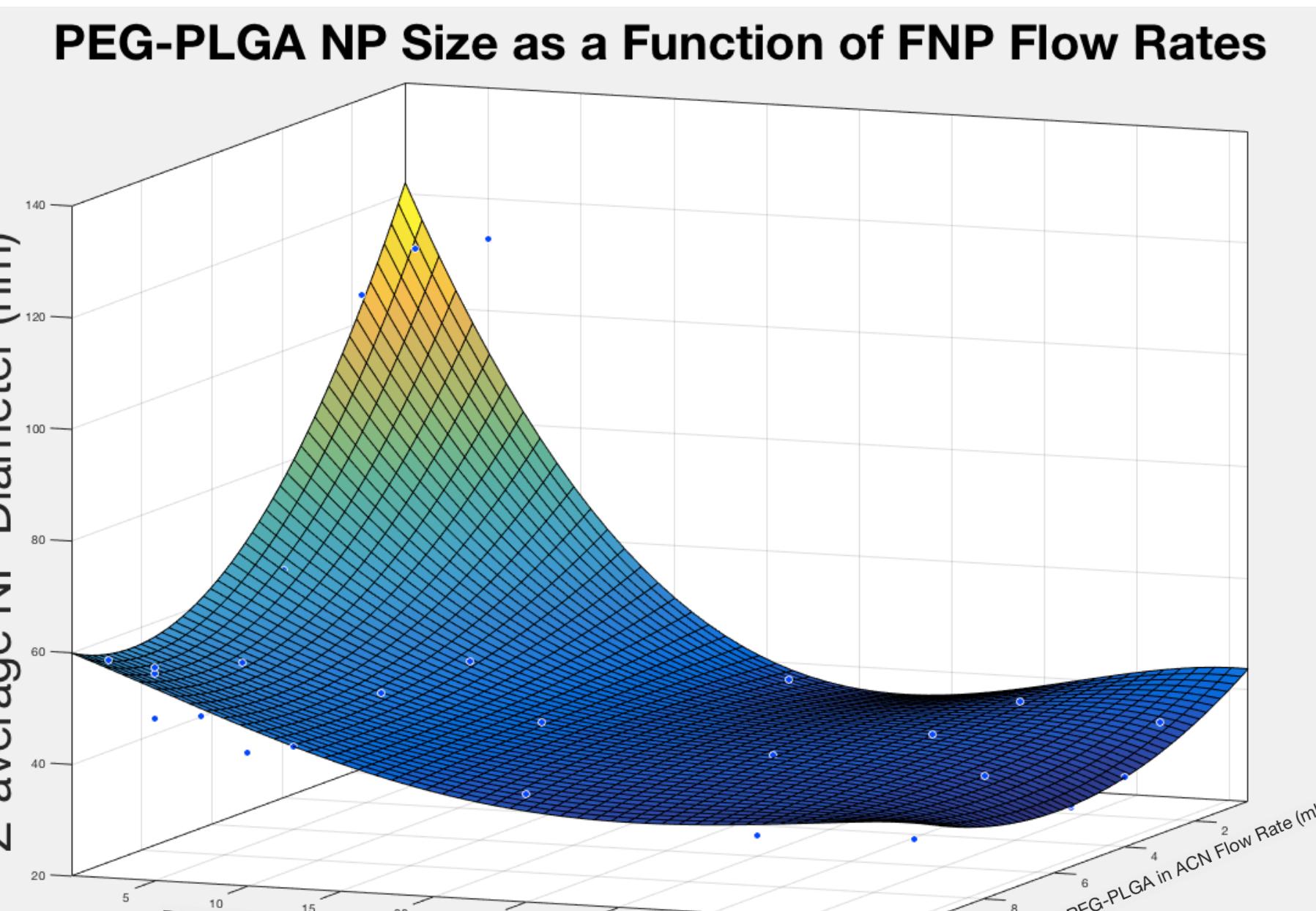


Data/Charts

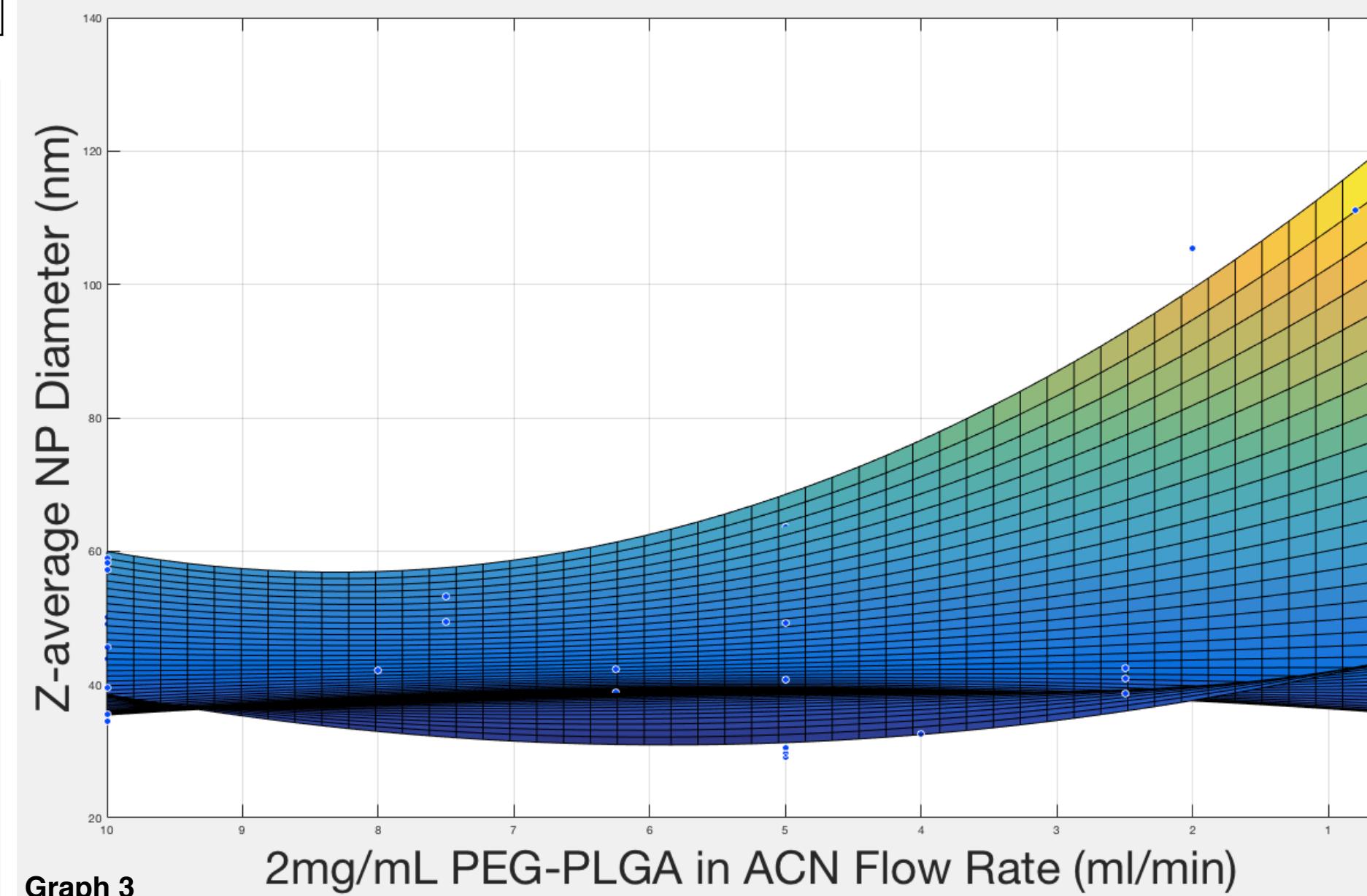


Size as a Function of Flow Rates

In the three dimensional graph, the X-axis represents the DI H₂O flow rate, Y-axis the 2 mg/ml PEG-PLGA flow rate, and Z axis is the Z-average size (intensity-weighted avg. hydrodynamic size) of the particles created post-FNP. As indicated by Graph 2, the NPs maintain an average size of 40nm after a 15 ml/min flow rate of DI H₂O, which suggests particle stability. Graph 3 depicts larger particle size with a low polymer flow rate and a range of sizes for NPs with a higher polymer flow rate, implying a more significant impact with the DI H₂O flow rates. General trend of data displays that higher polymer flow rates and higher DI H₂O flow rates produce particles with a smaller size. Conversely, lower polymer flow rates and lower DI H₂O flow rates produce particles with larger size.



Graph 1: PEG-PLGA NP Size as a Function of FNP Flow Rates



Graph 2: PEG-PLGA NP Size as a Function of FNP Flow Rates

Graph 3: PEG-PLGA NP Size as a Function of FNP Flow Rates

Conclusion

Polymer and water flow rates are significant parameters for controlling size with the FNP fabrication system. Manipulating these factors can result in the creation of NPs with specific diameters for biomedical applications. Further optimization of mixing kinetics will enable controlled NP size formation with minimal size distribution (PDI).

Future Work

- Optimizing the FNP fabrication process to generate nanoparticles with a smaller size distribution to determine optimal nanoparticle size for delivery platforms
- Retesting the data points for more accurate size and PDI measurements.

Acknowledgements

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