

Size-Tunable Polymeric Nanoparticles for Drug Delivery after Traumatic Brain Injury

Dhrasti Dalal¹, David Flores-Prieto¹, Sarah Stabenfeldt¹

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Introduction

Five million people in the United States live with disabilities caused by traumatic brain injury (TBI)¹. TBI can break down the blood-brain barrier (BBB), the membrane that regulates what enters the brain. While BBB breakdown is problematic, it provides a unique opportunity to use nanoparticles for drug delivery to the injured brain. This research aims to develop a targeting nanoparticle for TBI that is between 70-100 nm since this optimizes circulation, brain delivery, and reduces MPS uptake².

Methods

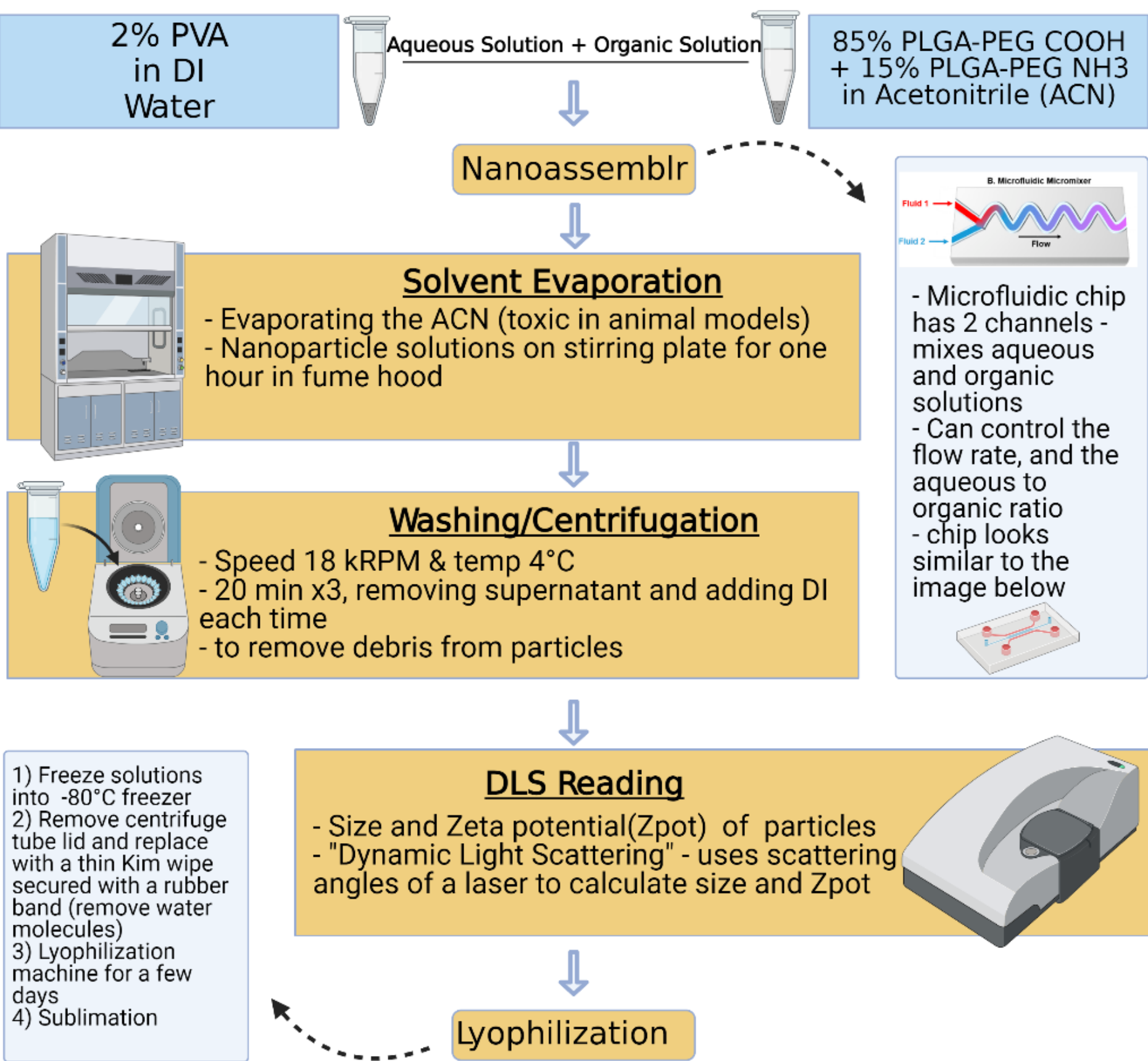


Figure 1: Materials and methods block diagram

Results

Many iterations of the experiments were conducted, and Design of Experiments was performed resulting in the following data from an optimized iteration.

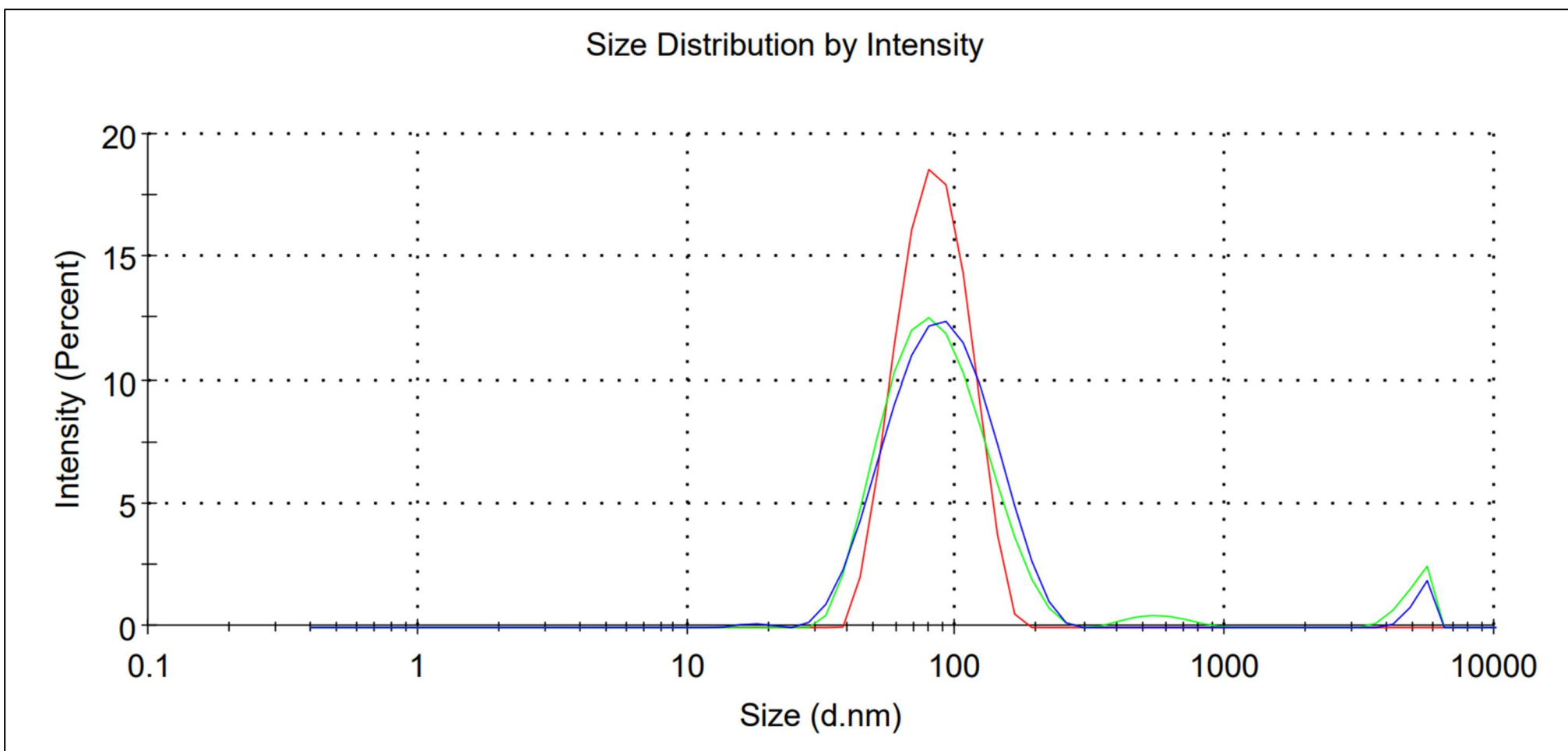


Figure 2: Representative DLS reading graph – Size of 87.4 nm and PDI of 0.19

Factor	Concentration	A:O Ratio	Flow Rate
↓ Size		+++	++
↓ PDI	++	---	-
↓ Z-pot	---	-	-
↓ St dev	-	++	--

Figure 3: Factorial plot summary table from first DOE – relationships between independent and dependent variables

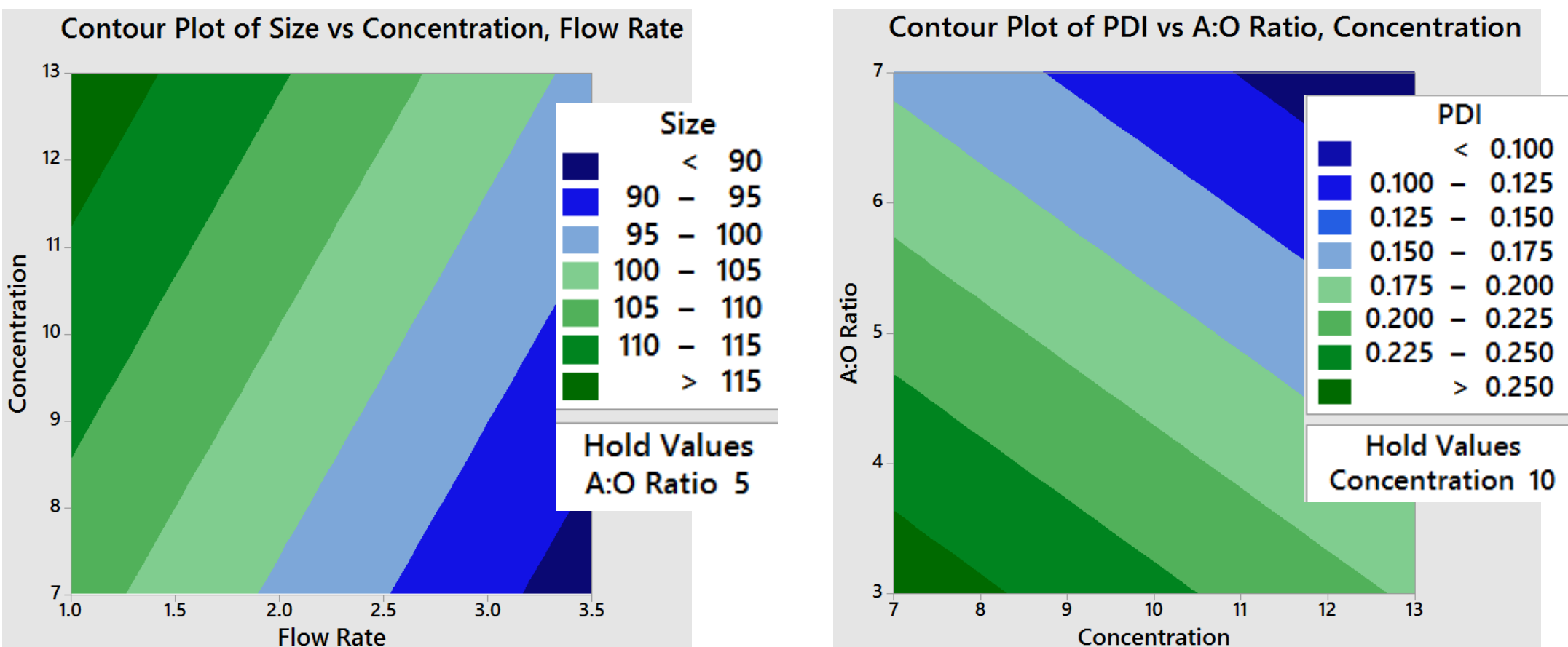


Figure 4- (a) Contour plots showing the effect that the independent variables concentration and flow rate have on size and (b) showing the effect A:O ratio and concentration have on PDI

Discussion

This project aided in the development of a protocol that allows us to obtain a nanoparticle with the desired size and PDI based on three independent variables: the concentration of polymer, the flow rate in the microfluidic device, and the aqueous to organic solution ratio. This protocol can be summarized by the following equations in which FR is flow rate, C is concentration, and AOR is aqueous to organic ratio:

$$\begin{aligned} \text{Size} &= 124 - 7.88 * FR + 1.88 * C - 4.44 * AOR \\ \text{PDI} &= 0.1575 + 0.053 * FR - 0.00458 * C - 0.00954 * AOR \\ \text{Zpot} &= -25.03 + 1.549 * FR + 0.055 * C + 0.535 * AOR \end{aligned}$$

Future research should focus on drug encapsulation and in vitro testing.

References

1) Badhiwala, J. H., Wilson, J. R., & Fehlings, M. G. (2019). Global burden of traumatic brain and spinal cord injury. *The Lancet Neurology*, 18(1), 24-25.
2) Bharadwaj, V. N., Nguyen, D. T., Kodibagkar, V. D., & Stabenfeldt, S. E. (2018). Nanoparticle-Based Therapeutics for Brain Injury. *Advanced healthcare materials*, 7(1), 1700668.

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Introduction & Methods

- Five million people in the United States live with disabilities caused by traumatic brain injury (TBI).
- Break down the blood-brain barrier (BBB), the membrane that regulates what enters the brain.
- Unique opportunity to use nanoparticles for drug delivery to the injured brain.
- **AIM:** develop a targeting nanoparticle for TBI between with size between 70-100 nm

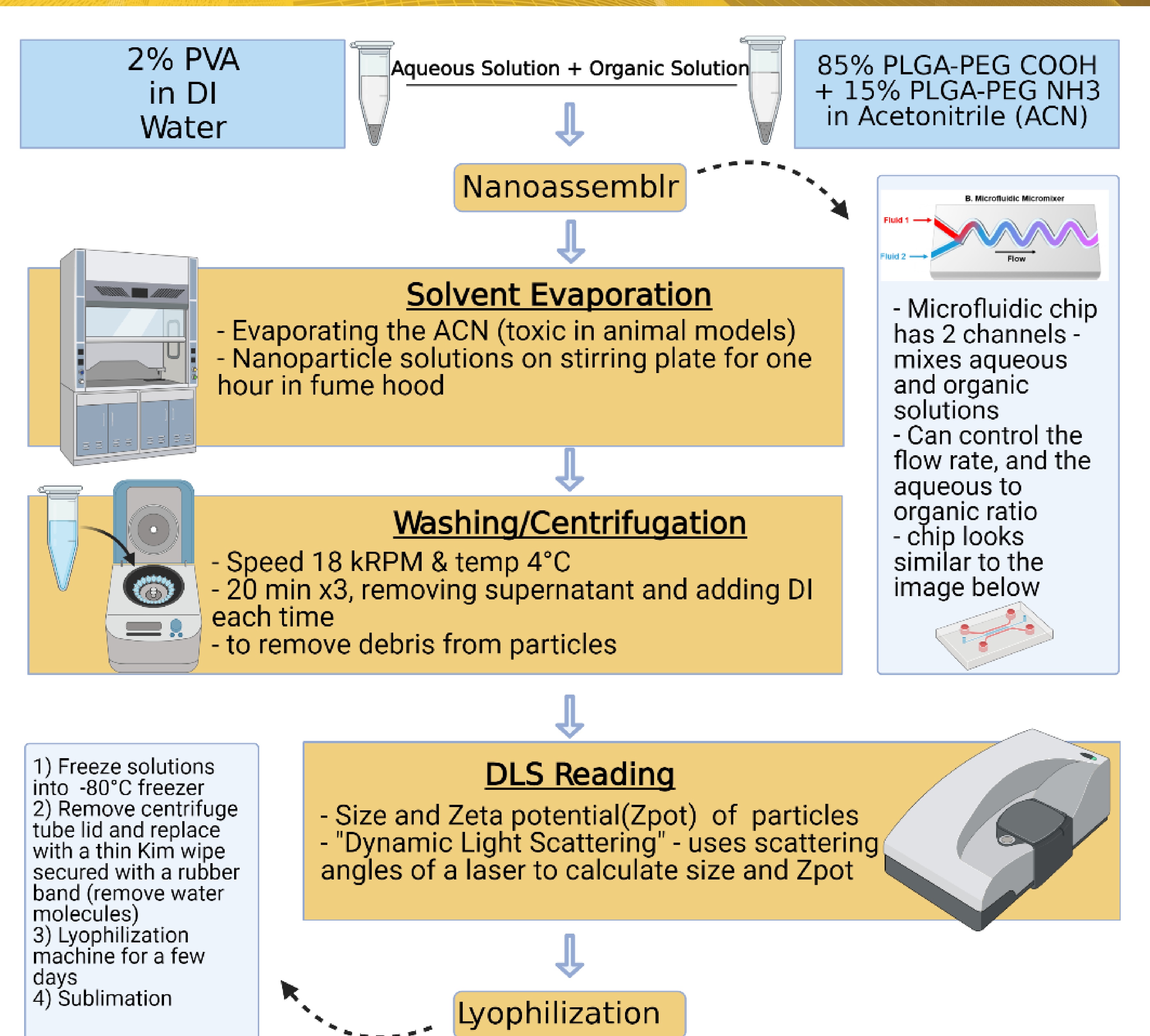


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Results

- Many iterations of the experiments were conducted
- DOE was performed resulting in the following data from an optimized iteration.
- PDI: polydispersity index – variability in size (flatter peak)
- Zpot: zeta potential – charge of the nanoparticle

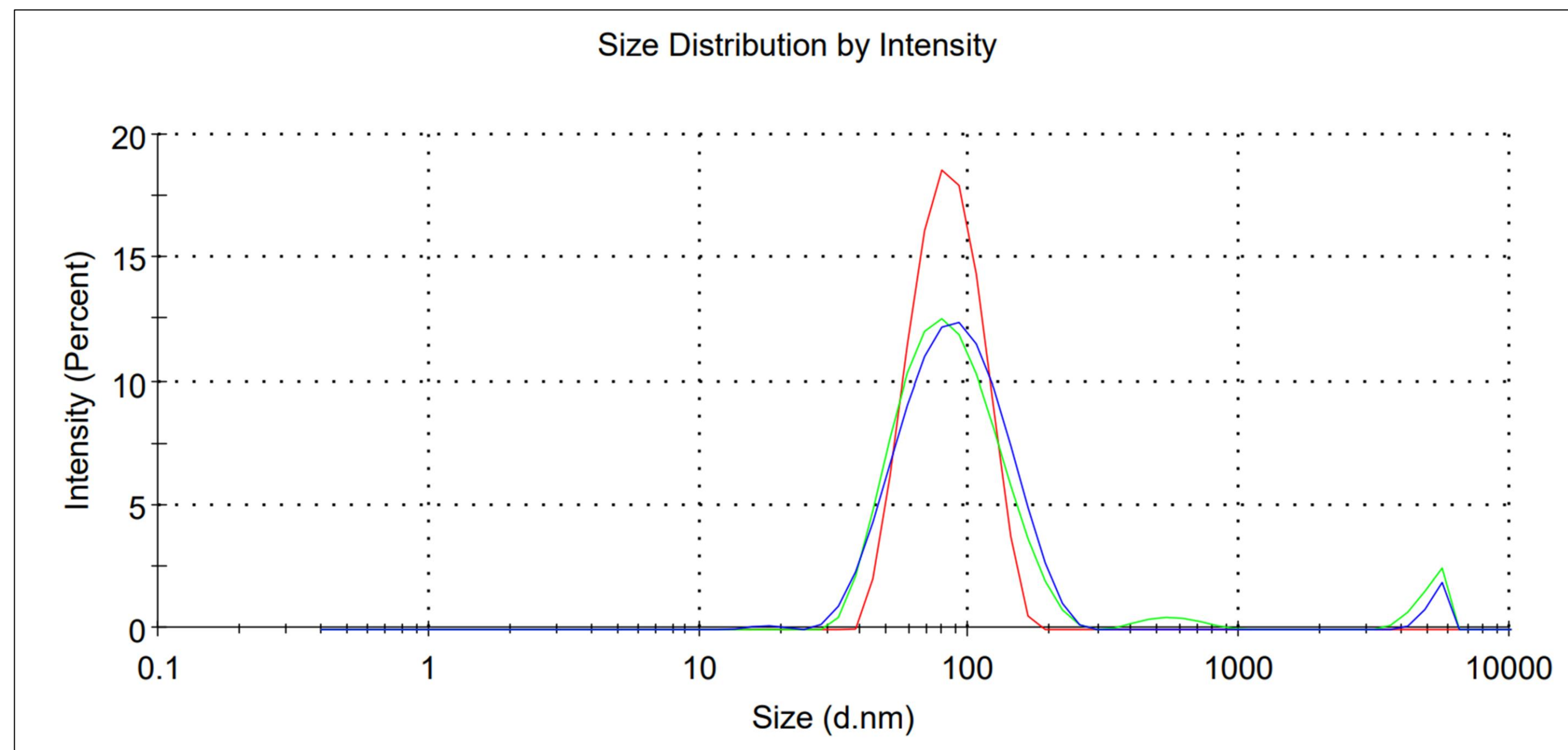


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Results

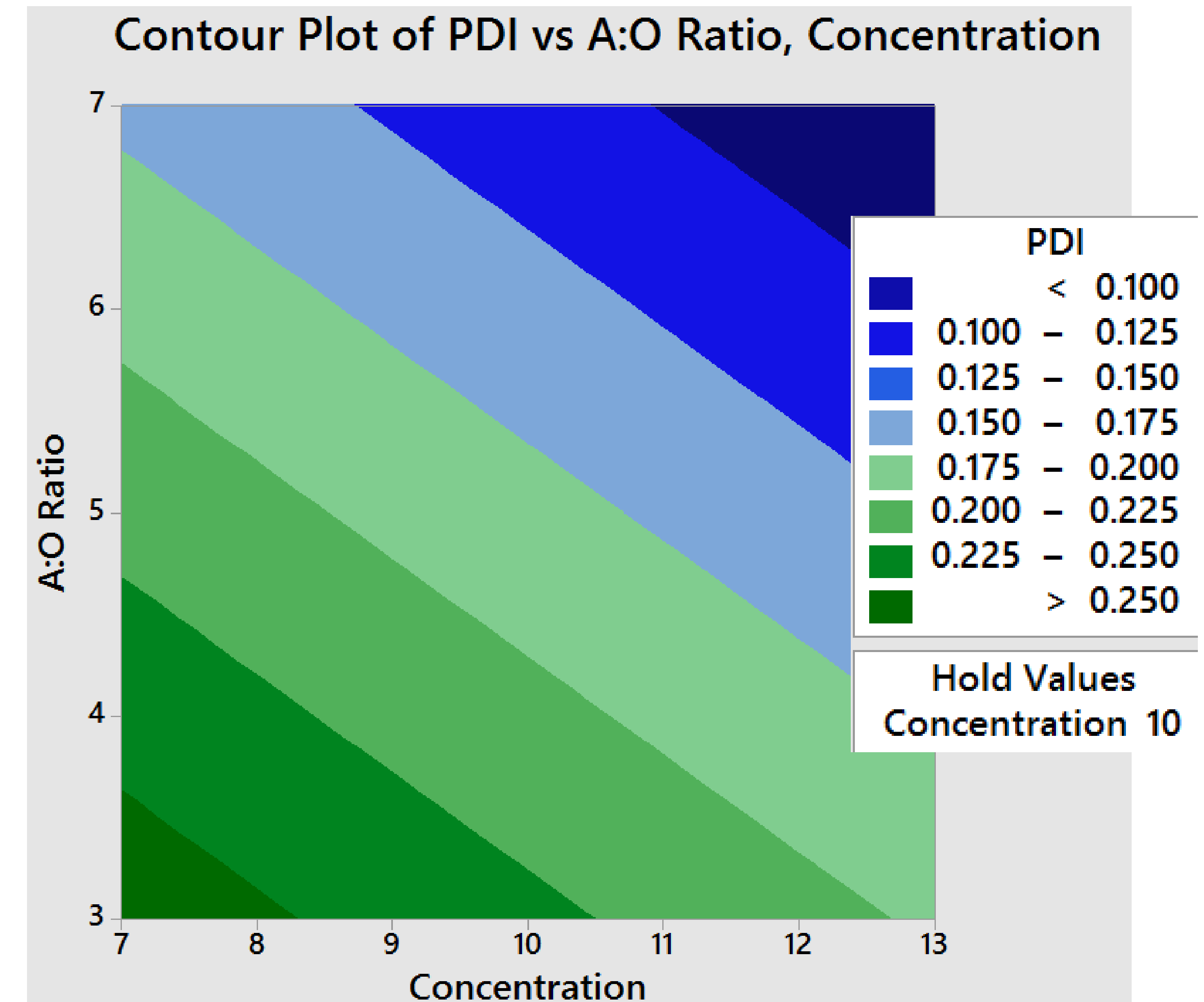
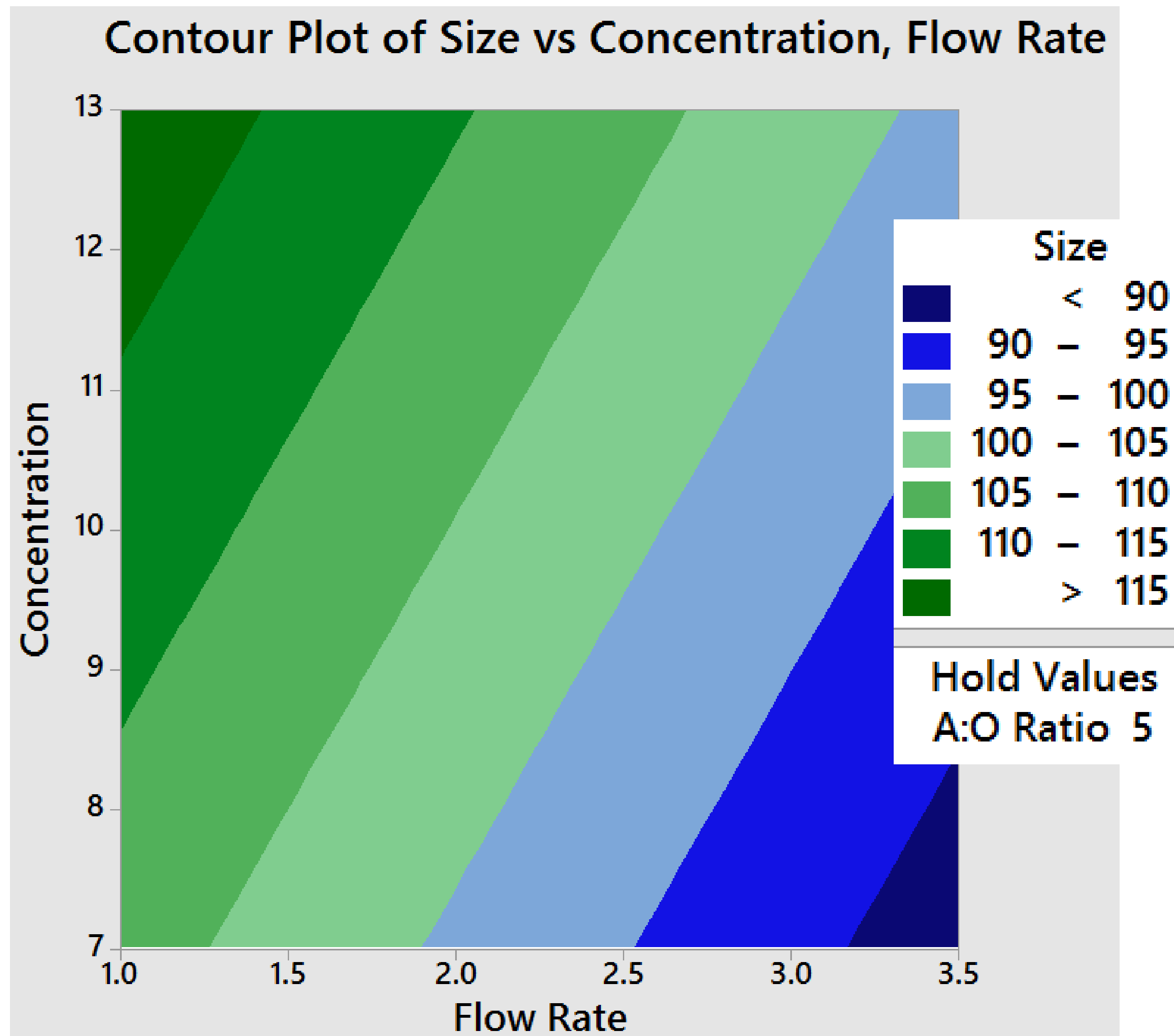


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Discussion

- Protocol that for nanoparticle with the desired size and PDI based on:
 - the concentration of polymer
 - the flow rate in the microfluidic device
 - aqueous to organic solution ratio.
- FR is flow rate, C is concentration, and AOR is aqueous to organic ratio:

$$Size = 124 - 7.88 * FR + 1.88 * C - 4.44 * AOR$$

$$PDI = 0.1575 + 0.053 * FR - 0.00458 * C - 0.00954 * AOR$$

$$Z_{pot} = -25.03 + 1.549 * FR + 0.055 * C + 0.535 * AOR$$

- Future research: drug encapsulation and in vitro testing.



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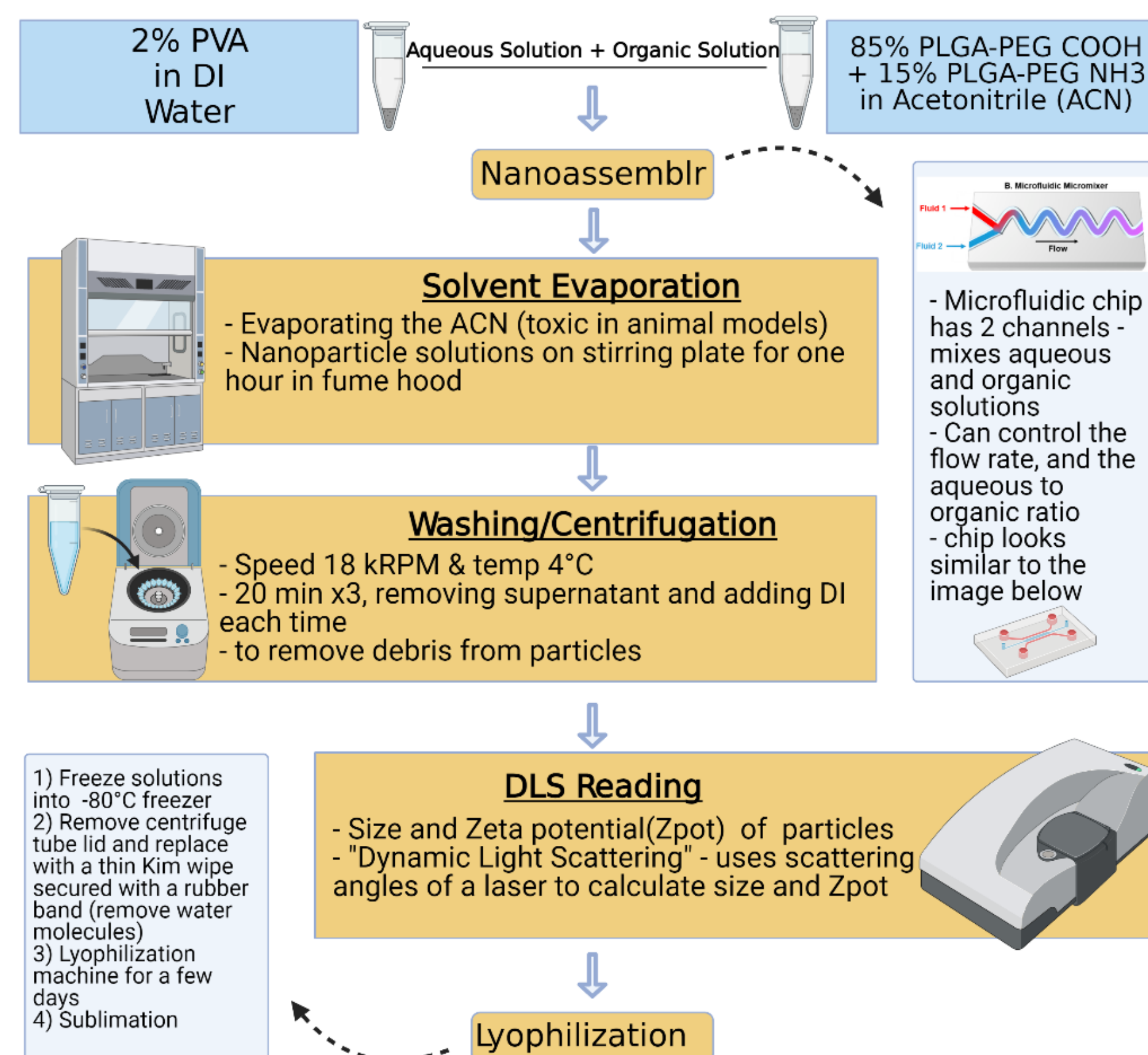


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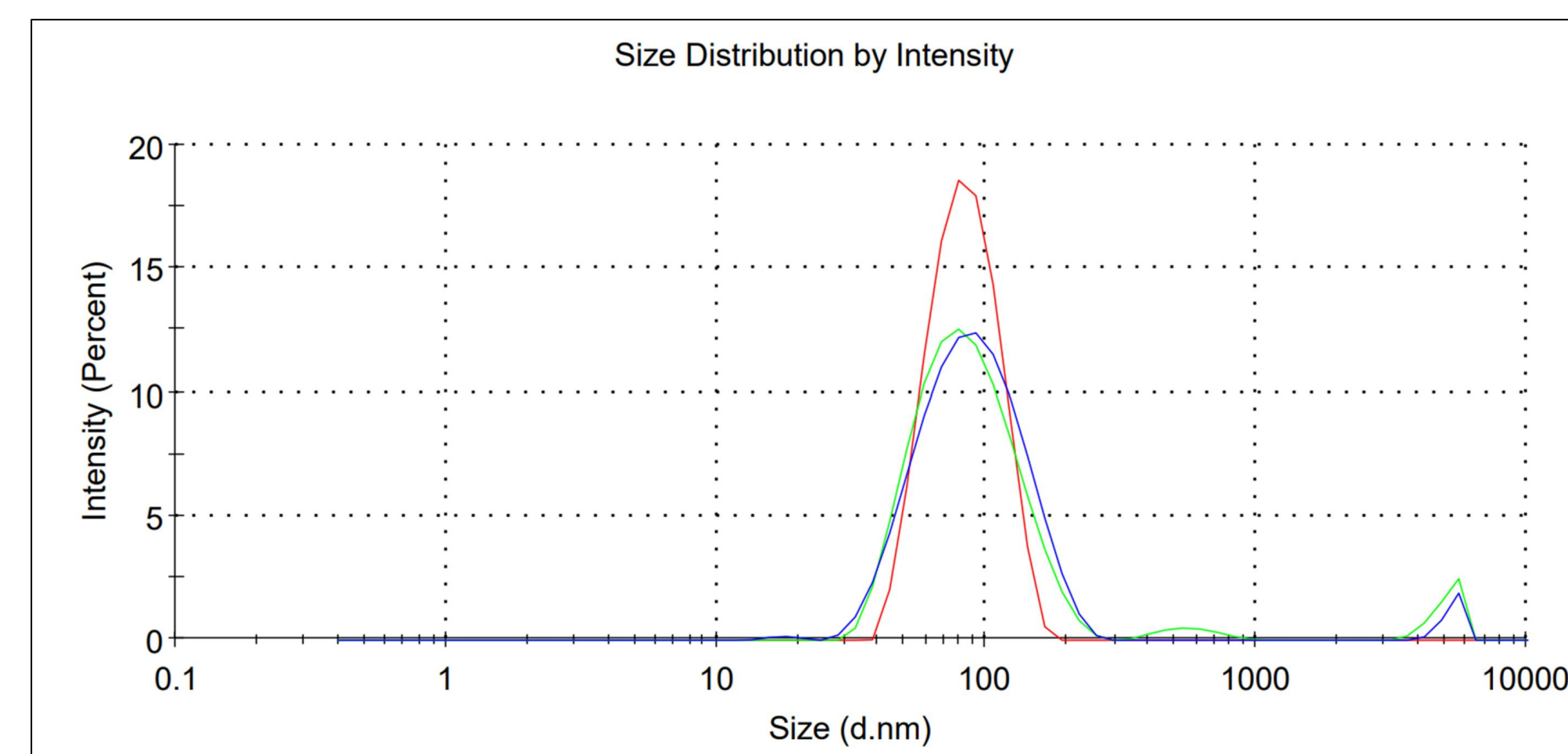


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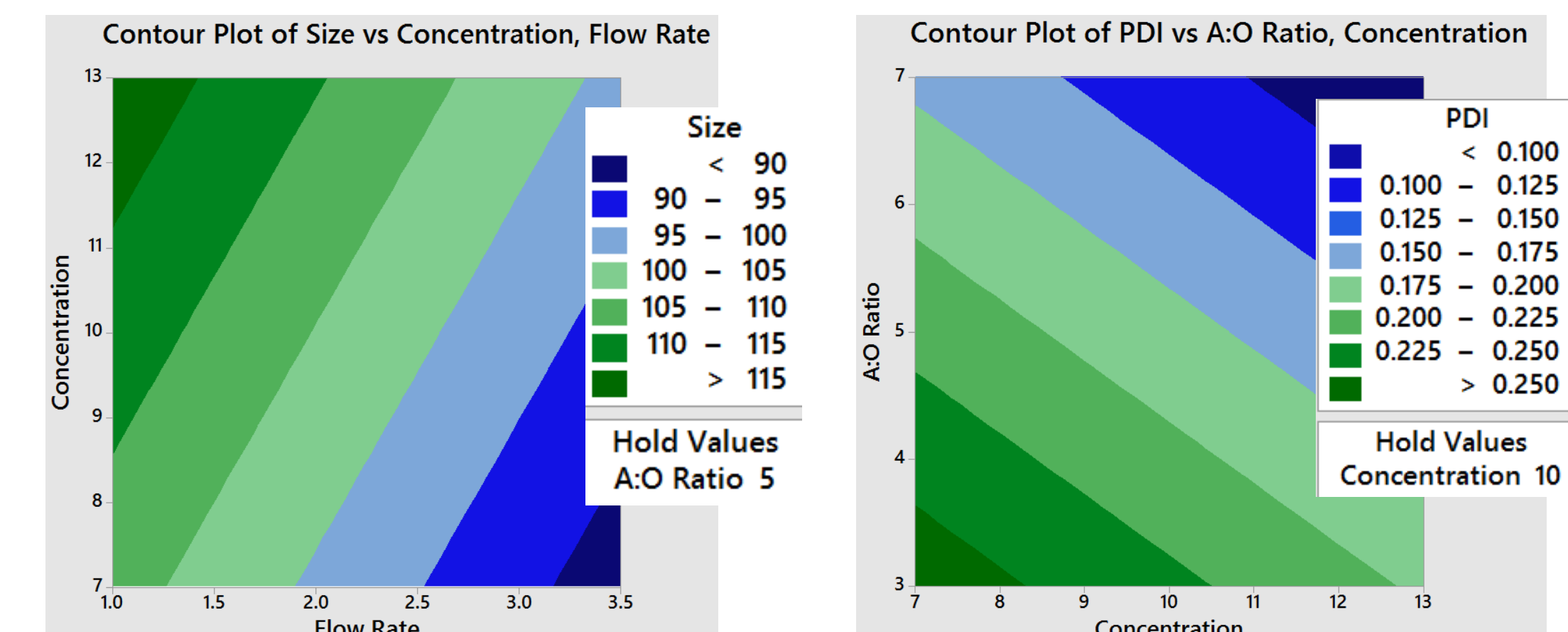


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