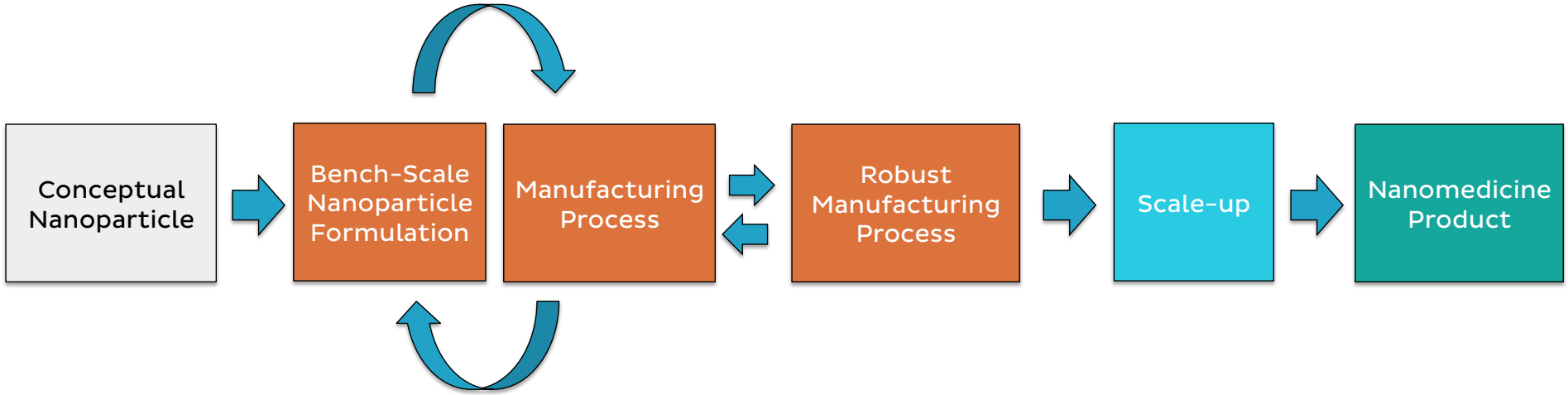
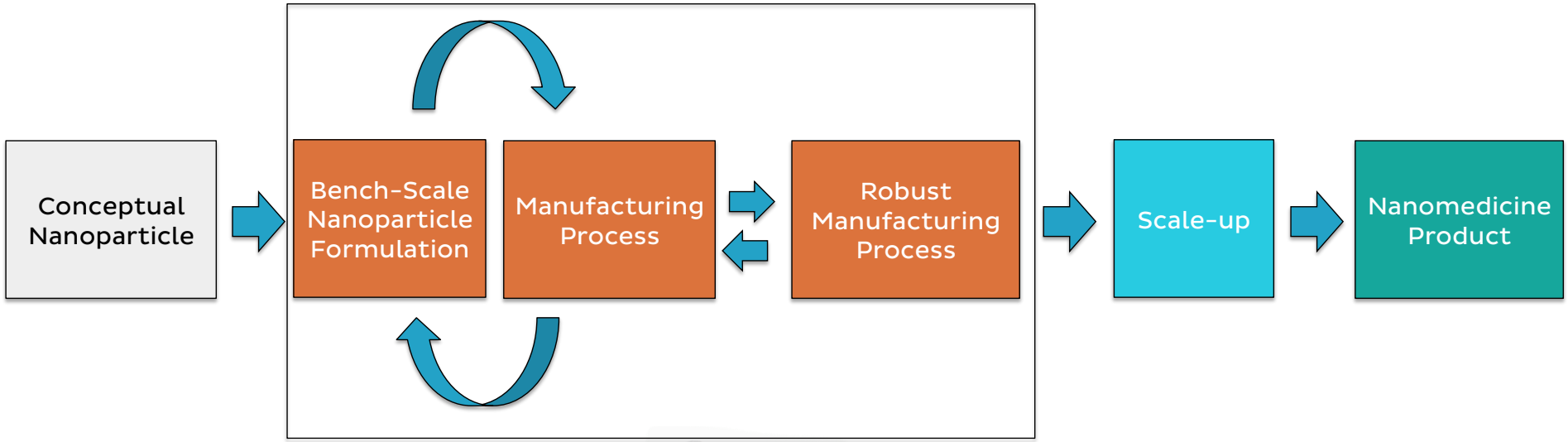
The NanoAssemblr™ Platform: Microfluidics-Based Manufacture of Nanomedicines

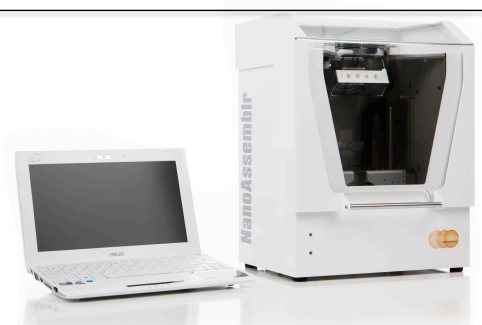
Precision NanoSystems, Inc.
September 2014

Nanoparticle Development Process



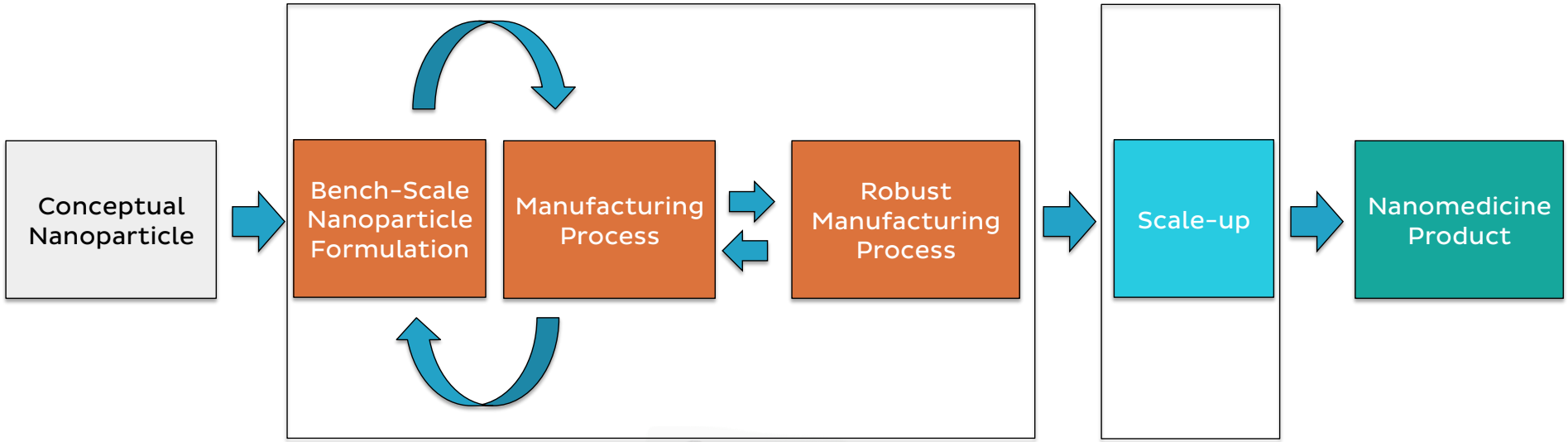
Nanoparticle Development Process

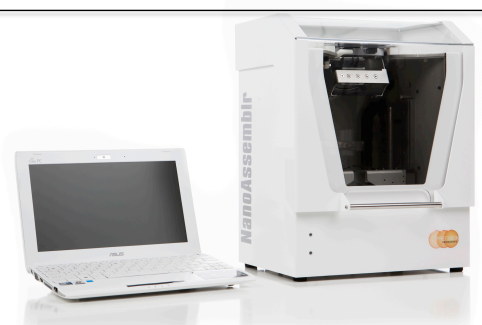




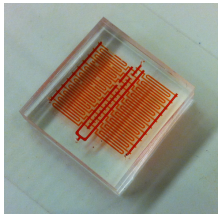
NanoAssemblr™ Benchtop Instrument

Nanoparticle Development Process





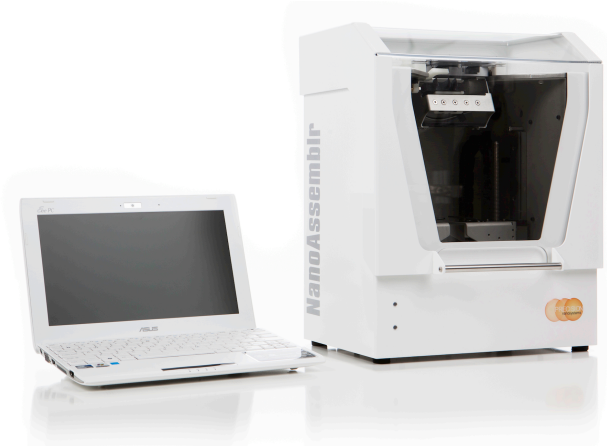
NanoAssemblr™ Benchtop Instrument



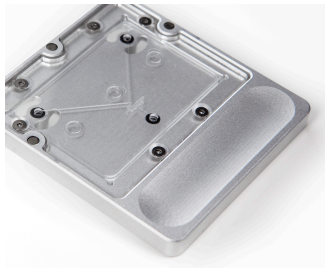
Scale-Up Platform

Accelerated Development of Nanoparticles

The NanoAssemblr™ Benchtop Instrument



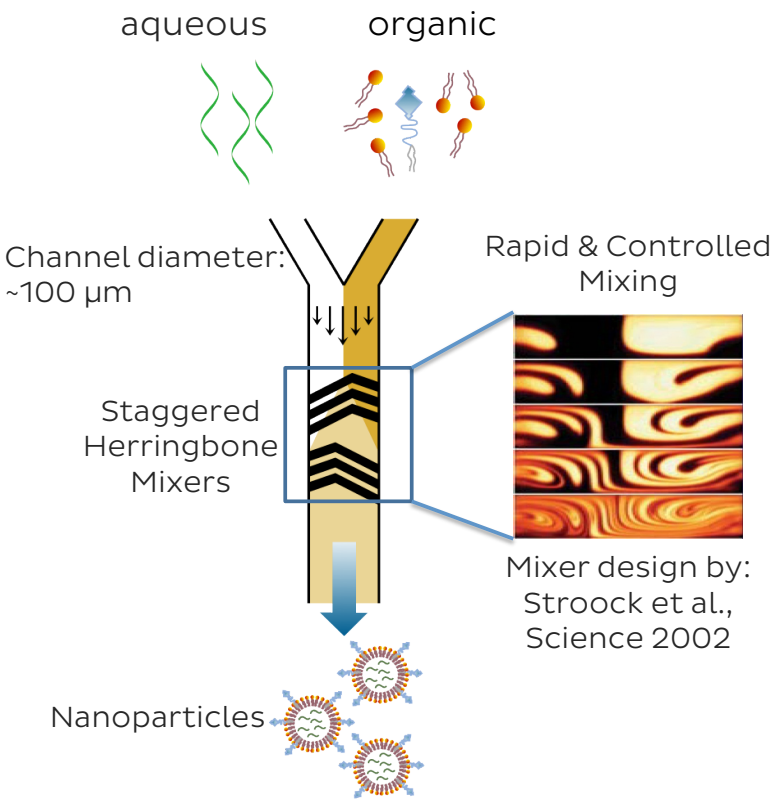
NanoAssemblr™ Benchtop Instrument



Microfluidic Cartridge

- ✓ Proprietary microfluidics-based instrument
- ✓ Rapid nanoparticle prototyping
- ✓ Single step
- ✓ Small sample volumes
- ✓ Software controlled, automated
- ✓ Intra- and inter-operator reproducibility
- ✓ Robust processing and variable manipulation

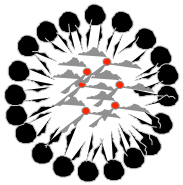
The Magic is in the Microfluidics



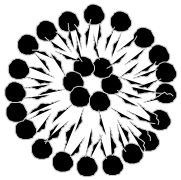
- ✓ Laminar flow – controlled mixing
- ✓ Rapid mixing (3 ms^{-1})
- ✓ Nanoliter Reaction volumes: ~ 14 nL
- ✓ Low energy input, low shear system
- ✓ Seamless scale-up

Exquisite Control Over Manufacturing Process

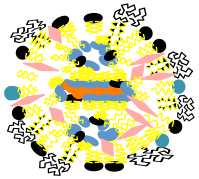
The NanoAssemblr™: Manufacture of Novel Nanoparticles



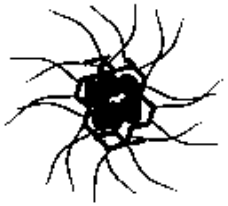
O/W Nanoemulsions



Liposomes

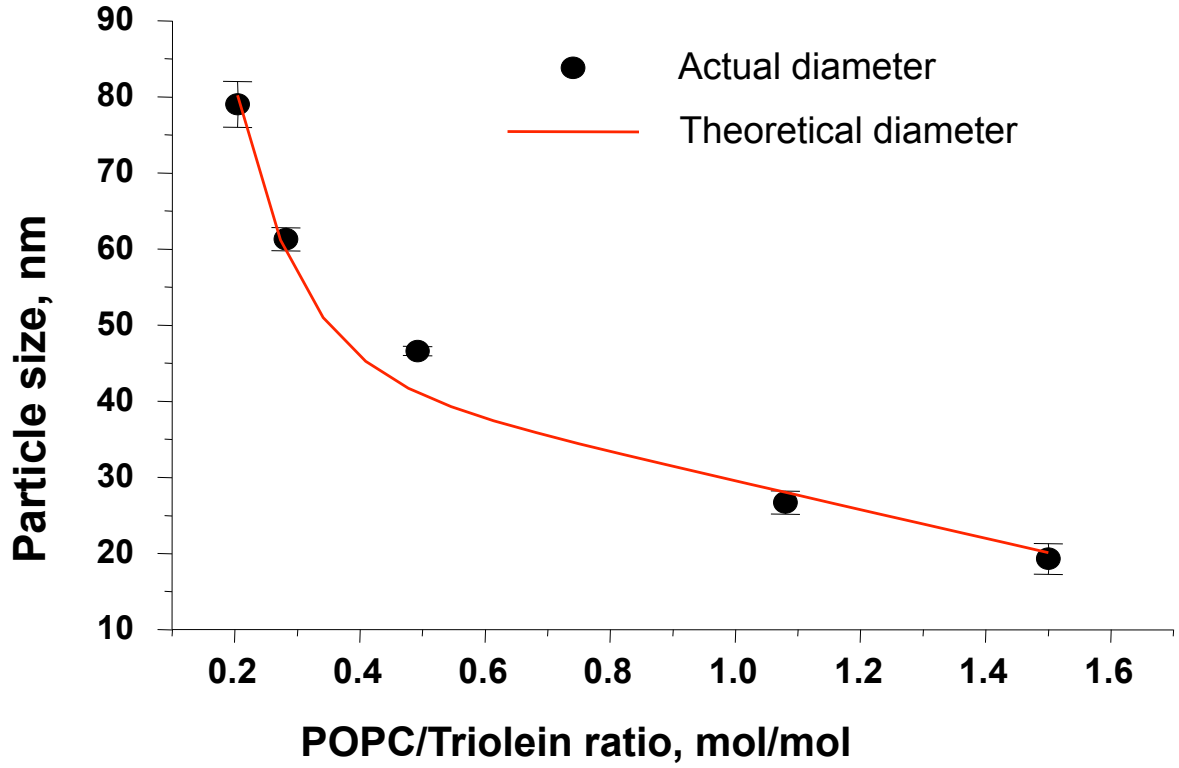


Lipid Nanoparticles



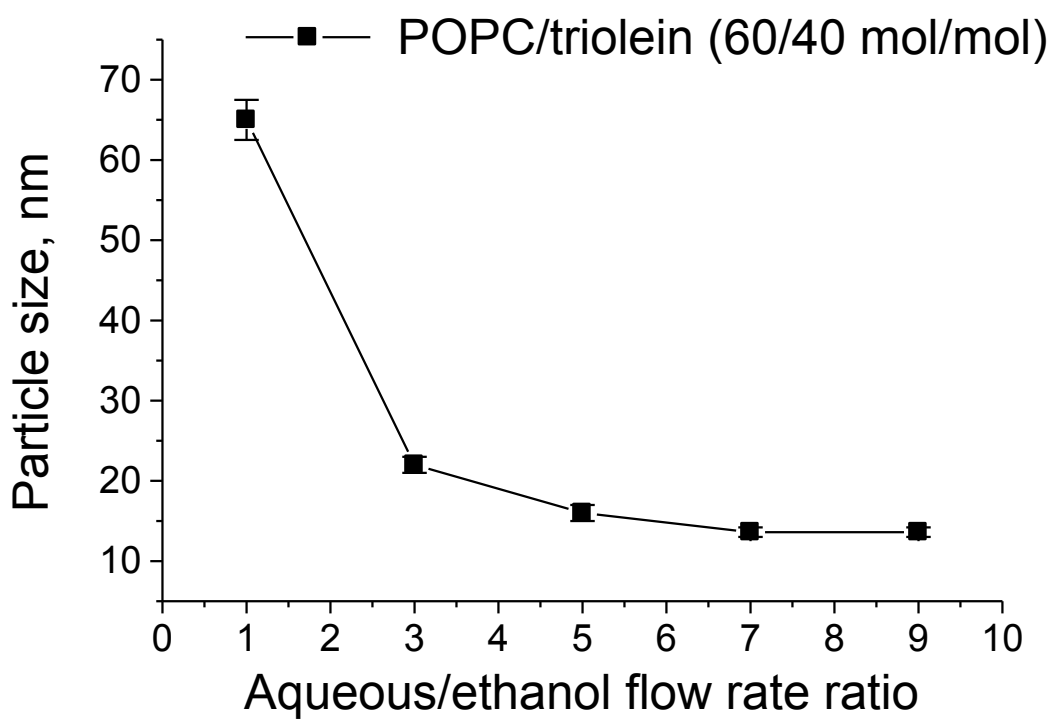
Polymer Nanoparticles

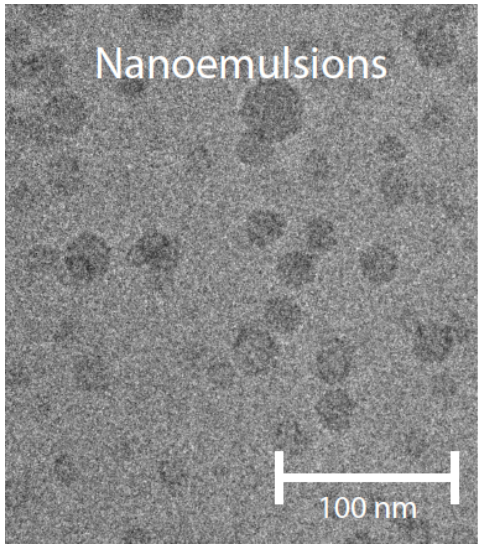
Nanoemulsion Droplet Size Dictated by Emulsion Composition



Zhigaltsev, I.V. Et al., Langmuir 2012, 28, 3633–3640

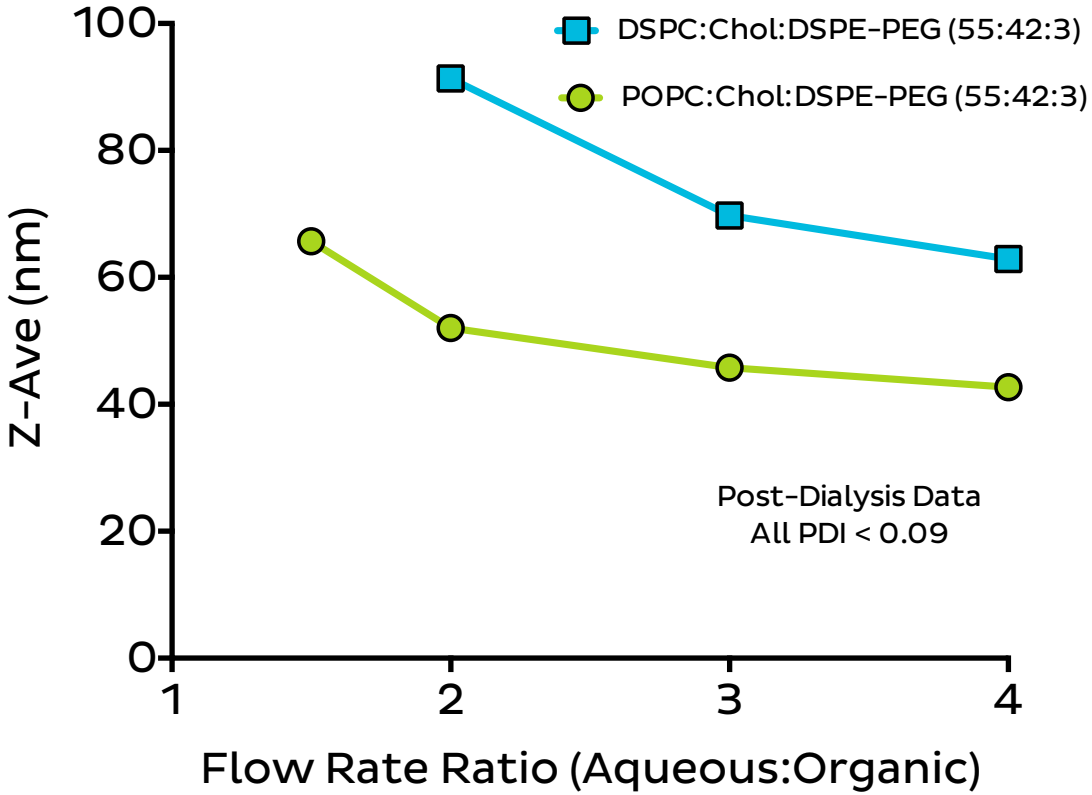
Nanoemulsion Droplet Size Dictated by Manufacturing Process



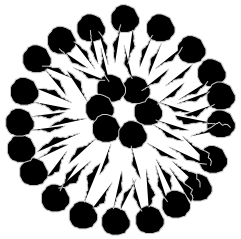


Zhigaltsev, I.V. Et al., Langmuir 2012, 28, 3633–3640

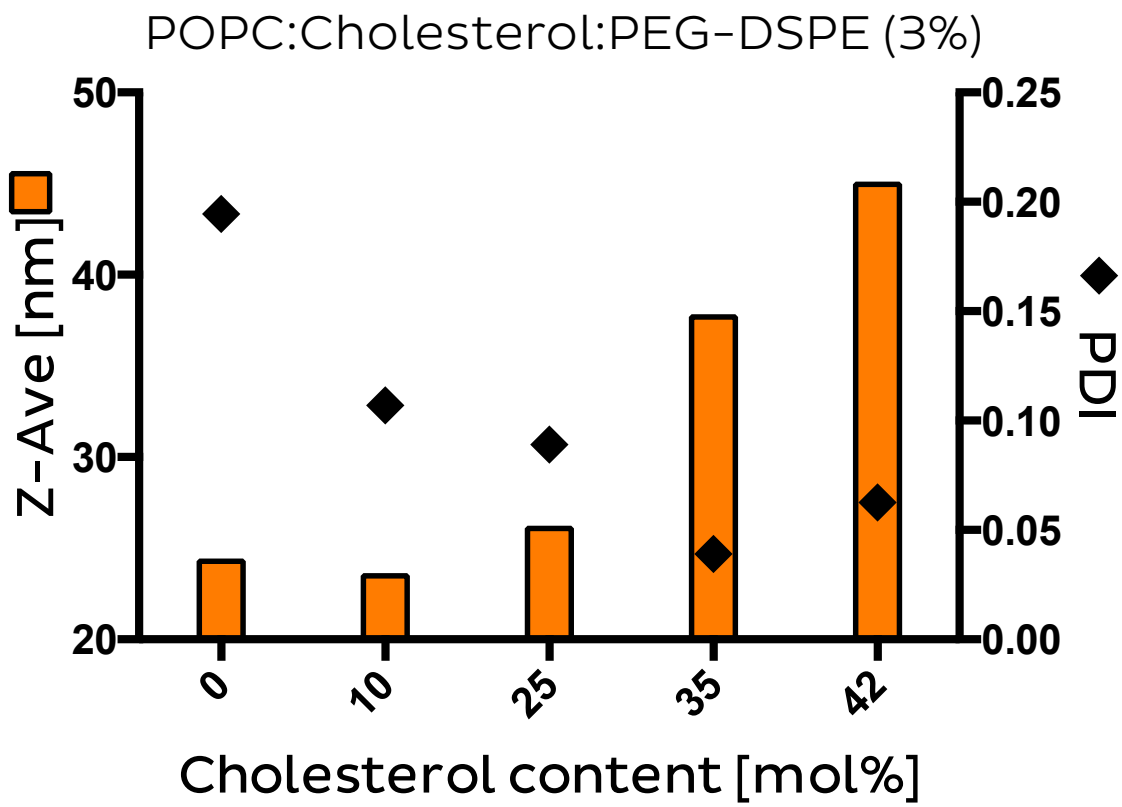
Liposome Size Dictated by Manufacturing process



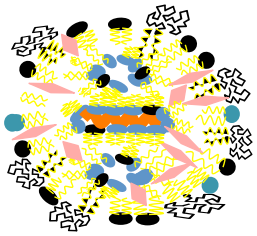
"Limit size" Liposomes are dictated by the Flow Rate Ratio



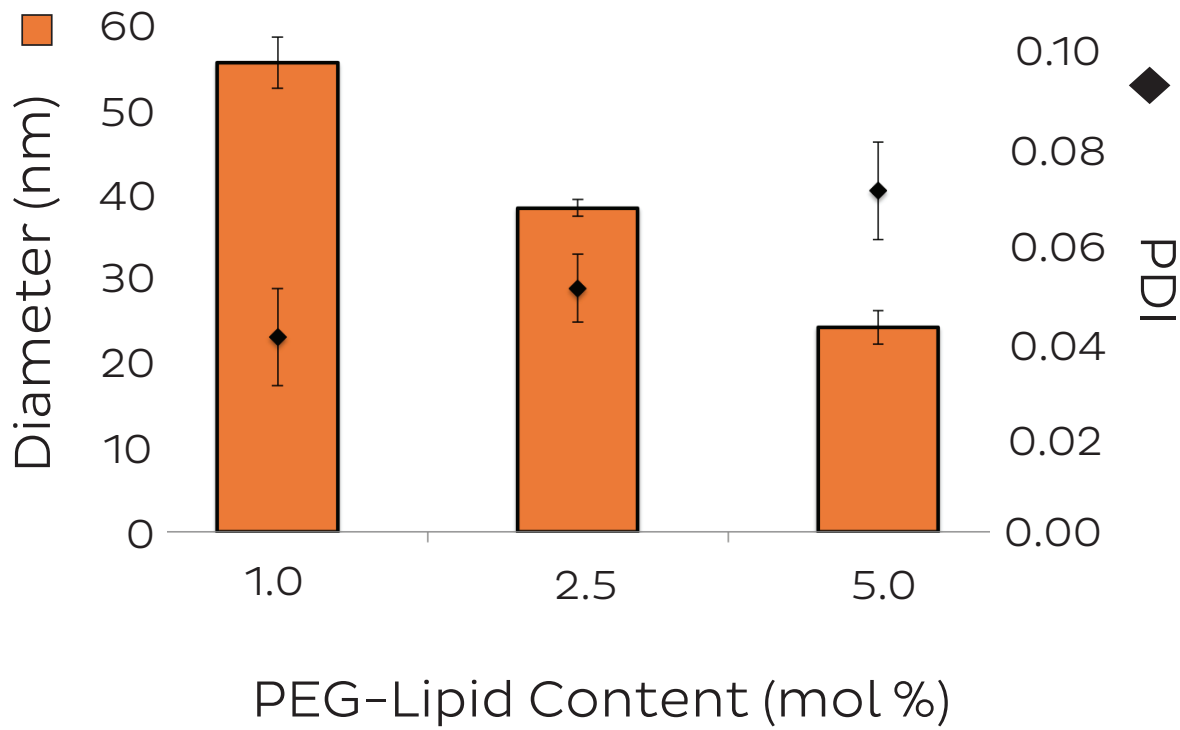
Liposome Size Dictated by Lipid Composition

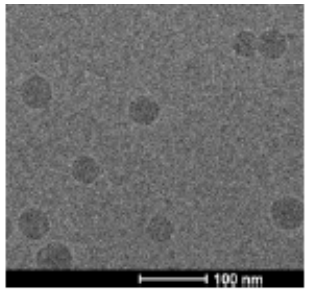


Liposome size and size distribution is dependent on Cholesterol content

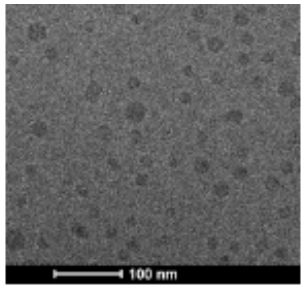


RNA-Lipid Nanoparticle Size Dictated by Lipid Composition



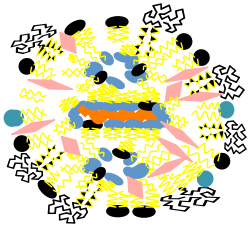


1 mol%

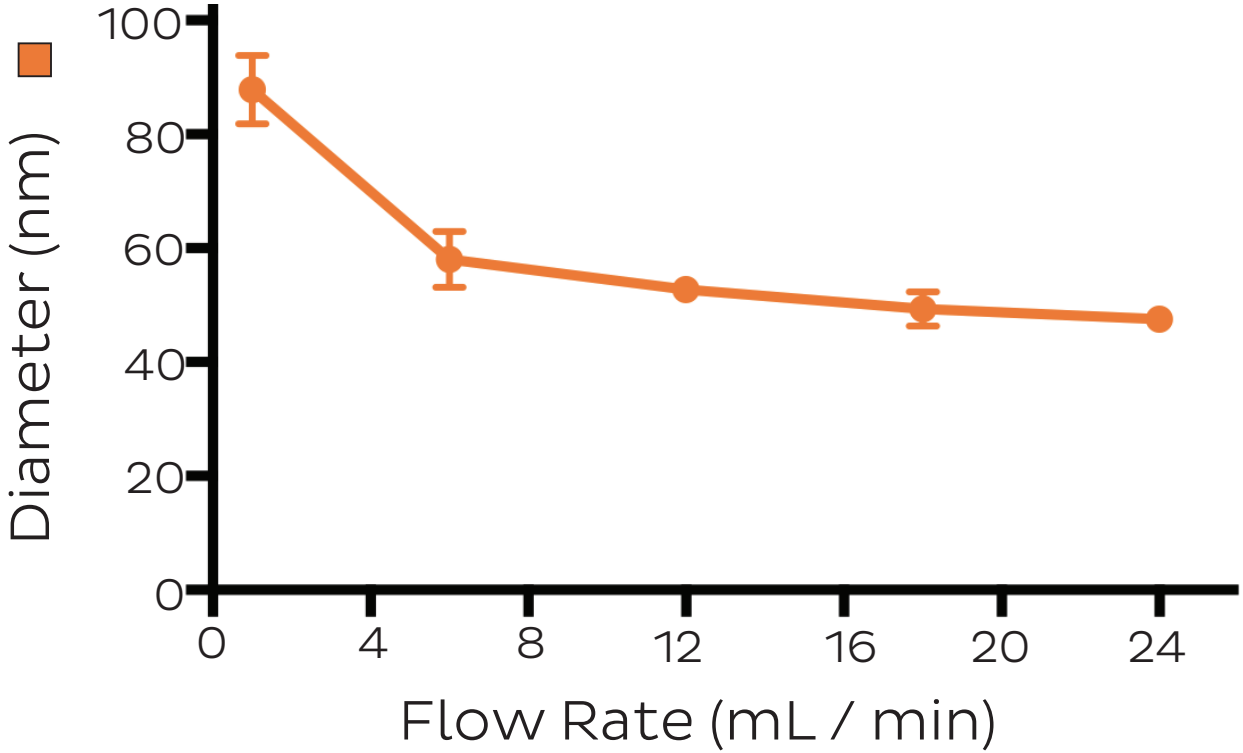


5 mol%

"Limit Size" is Dependent on RNA-Lipid Nanoparticle Composition

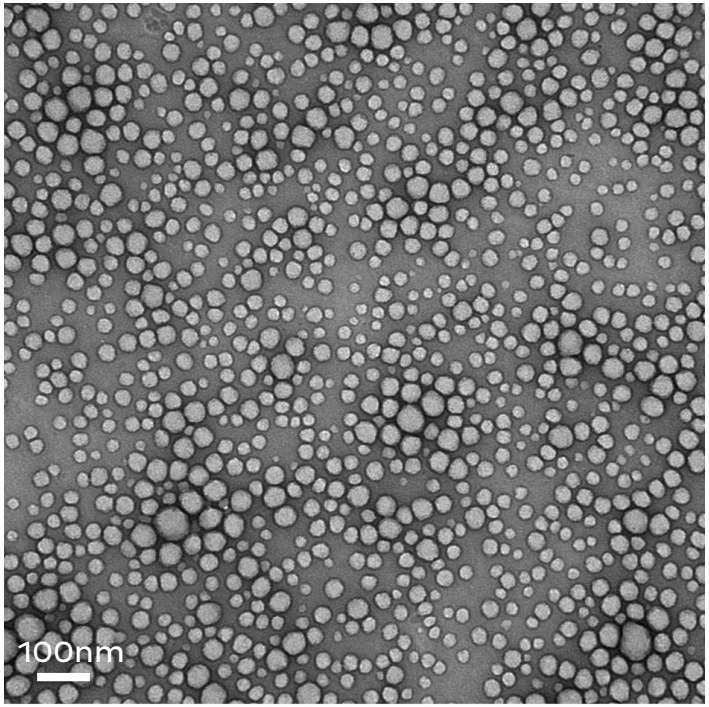


RNA-Lipid Nanoparticle Size Dictated by Manufacturing Process

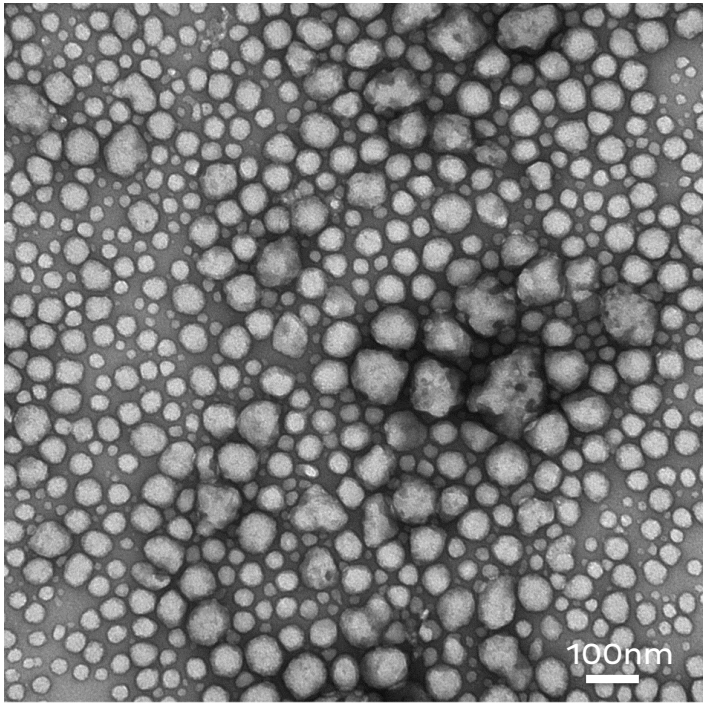


RNA-Lipid Nanoparticles Reach "Limit Size" at High Flow Rates

Cellax™ Polymer-Drug conjugates



NanoAssemblr ™

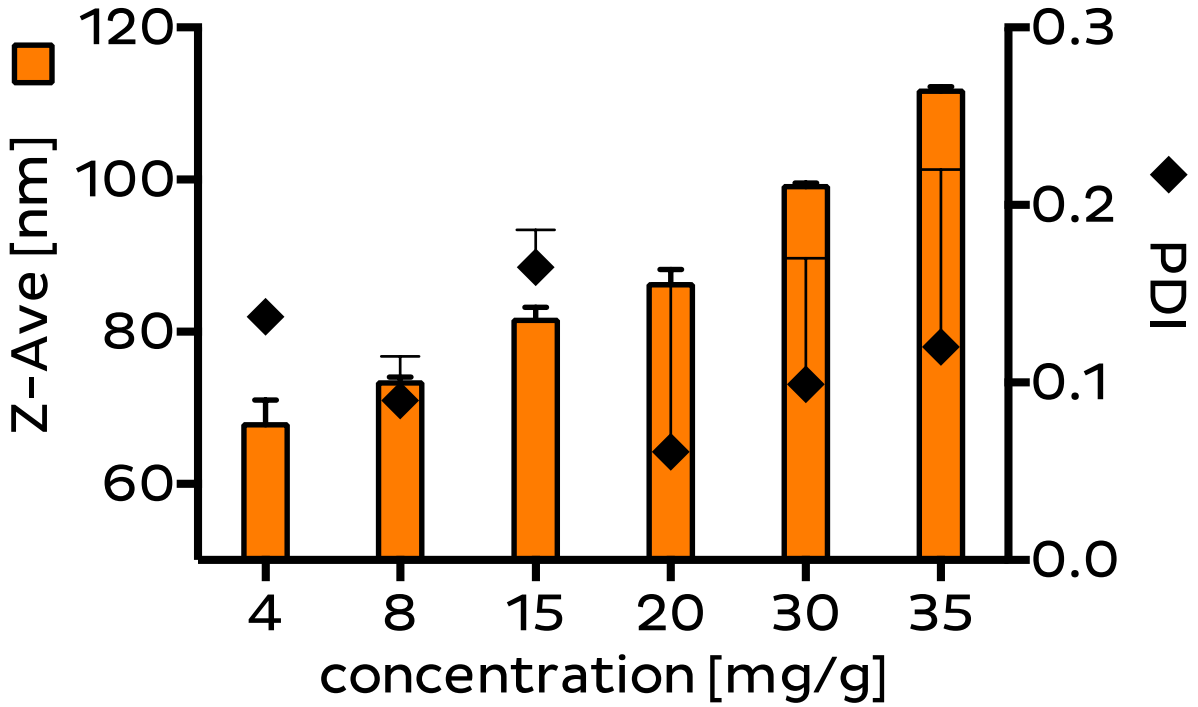


Vortex

OICR
Ontario Institute for Cancer Research

Nanoparticle Size Dictated by Polymer Concentration

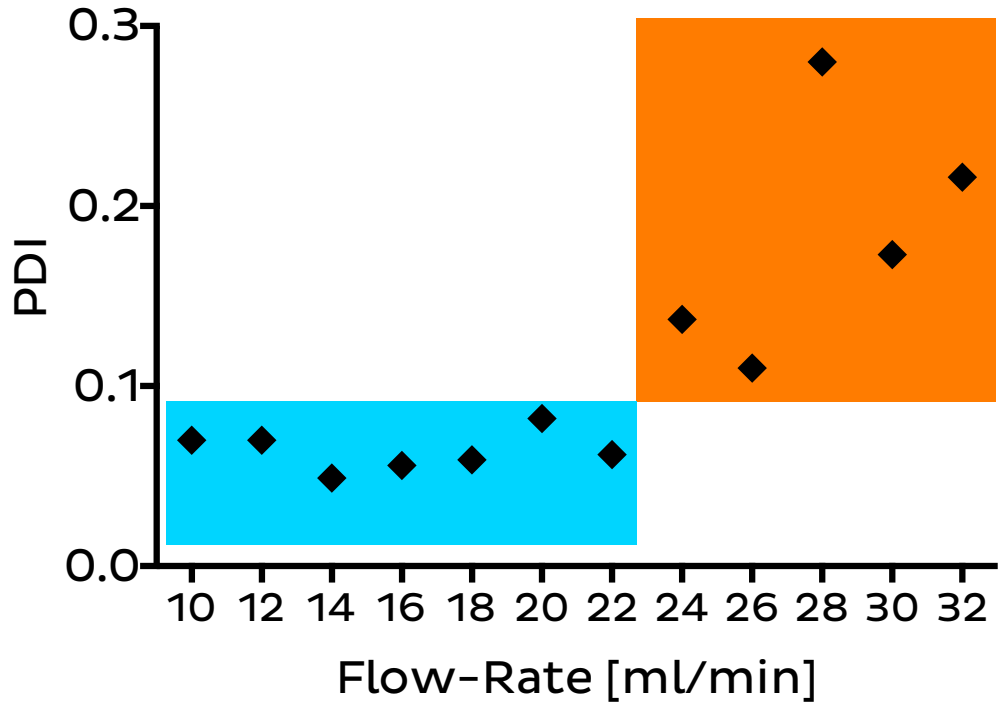
Cellax™ Polymer-Drug conjugates



Particle size is dictated by polymer concentration

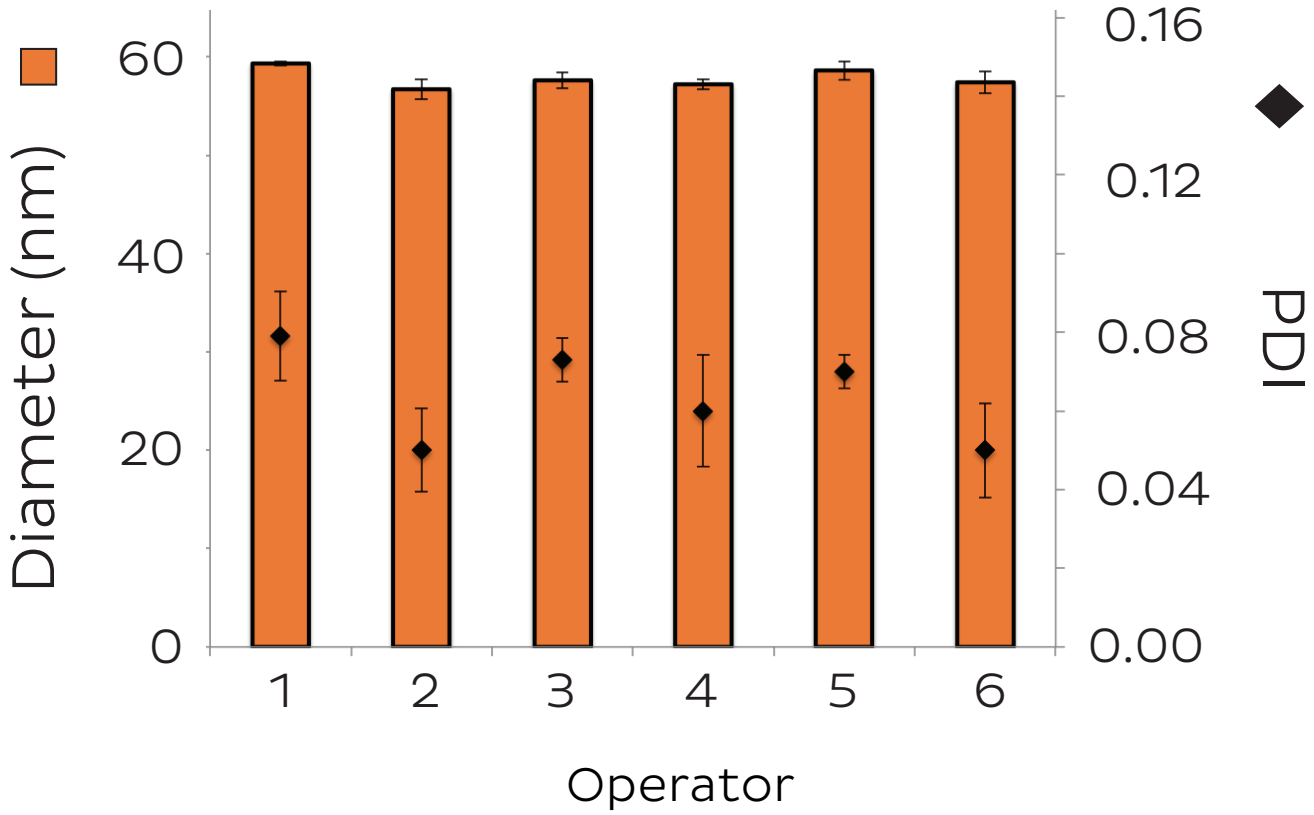
Polymer Nanoparticle Size Distribution Dictated by Manufacturing Process

Cellax™ Polymer-Drug conjugates



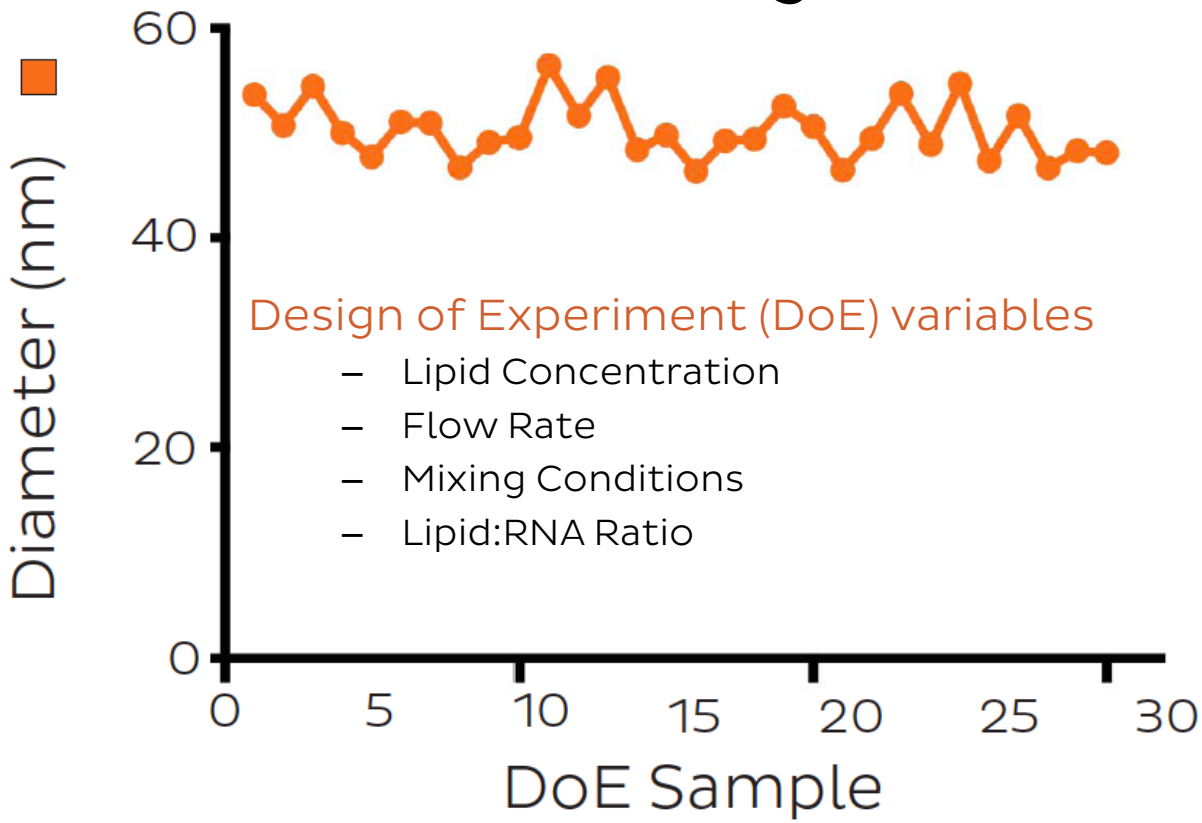
Polydispersity is dependent on flow rate

Reproducible RNA-Lipid Nanoparticles Independent of Operator or Site



Automated Instrumentation Removes Operator Variability

Assessment of the Robustness of the Manufacturing Process

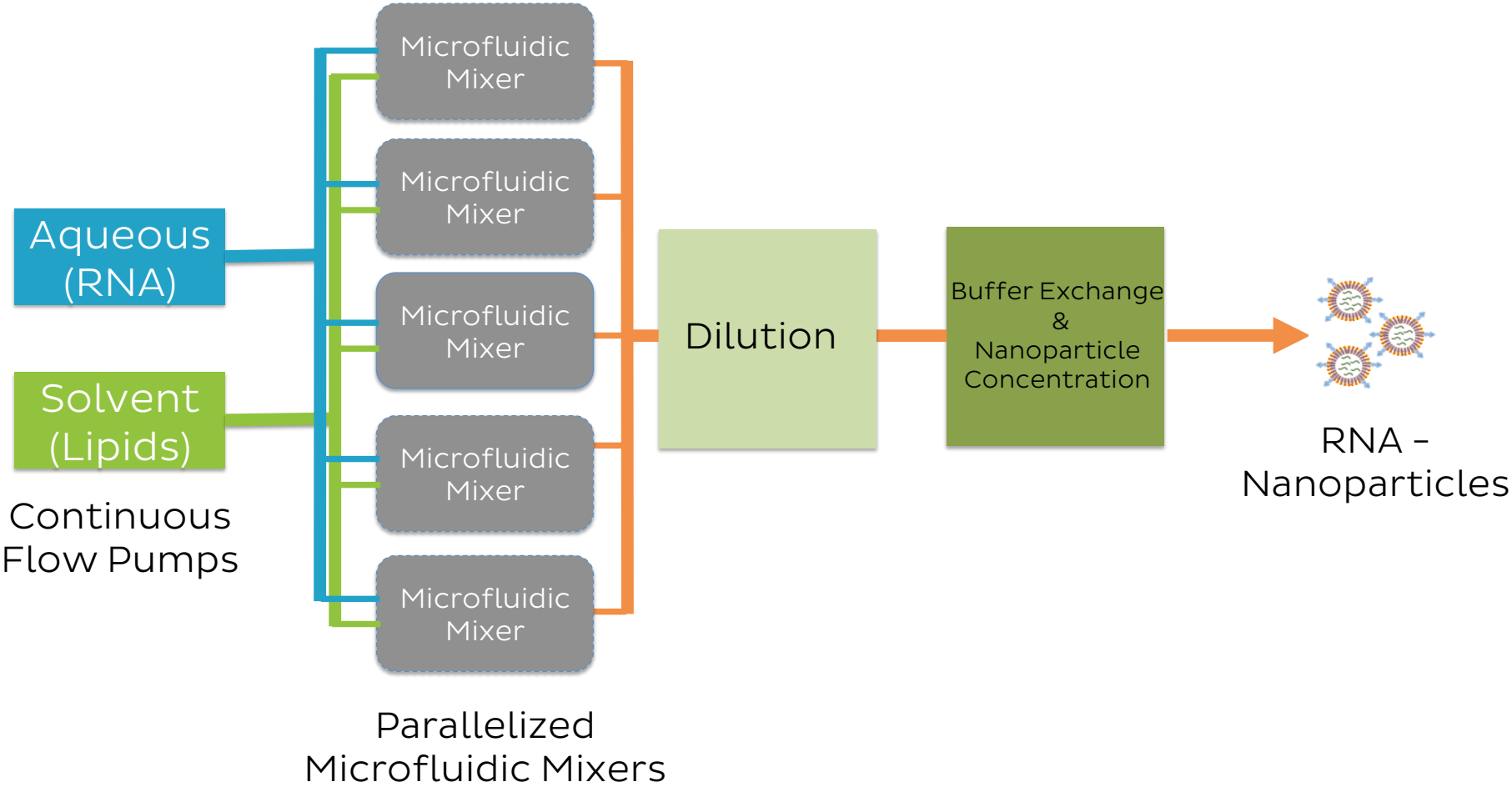


Design of Experiment (DoE) variables

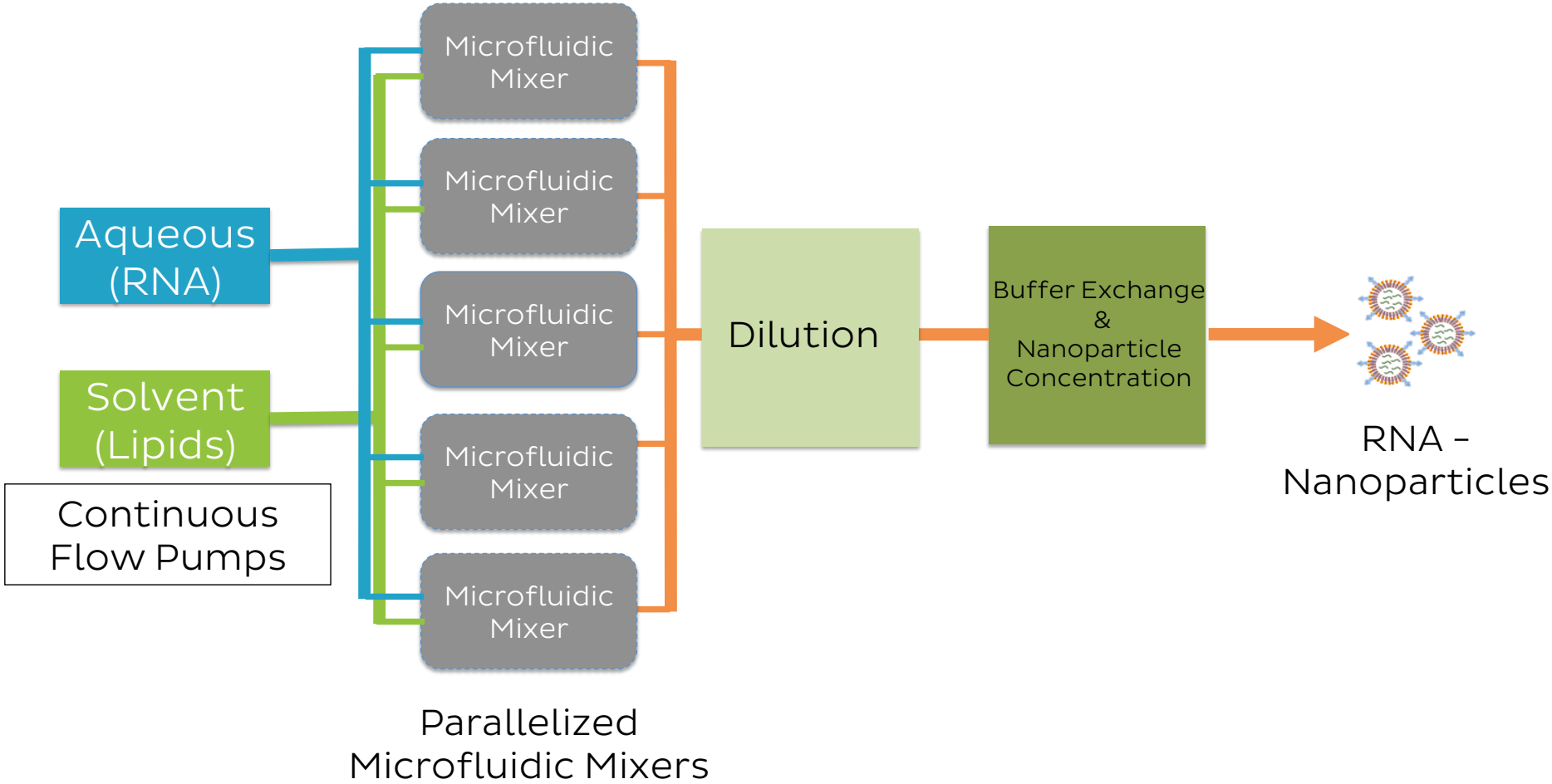
- Lipid Concentration
- Flow Rate
- Mixing Conditions
- Lipid:RNA Ratio

Stable Results = Robust Process = **Scalable Process**

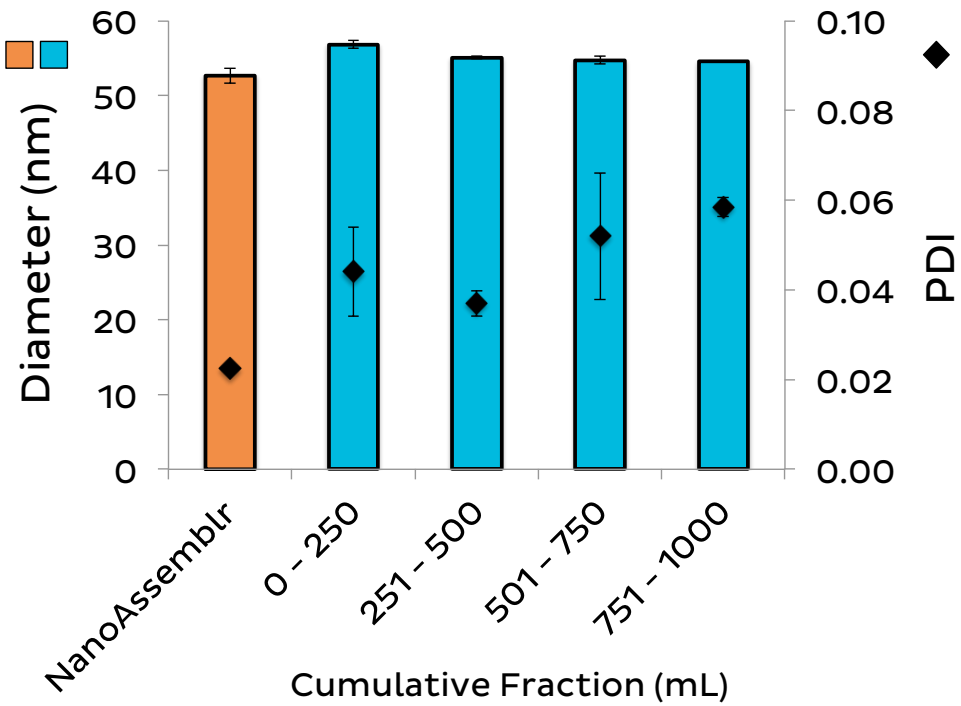
Microfluidics Enables "Seamless Scale-Up"



Microfluidics Enables "Seamless Scale-Up"

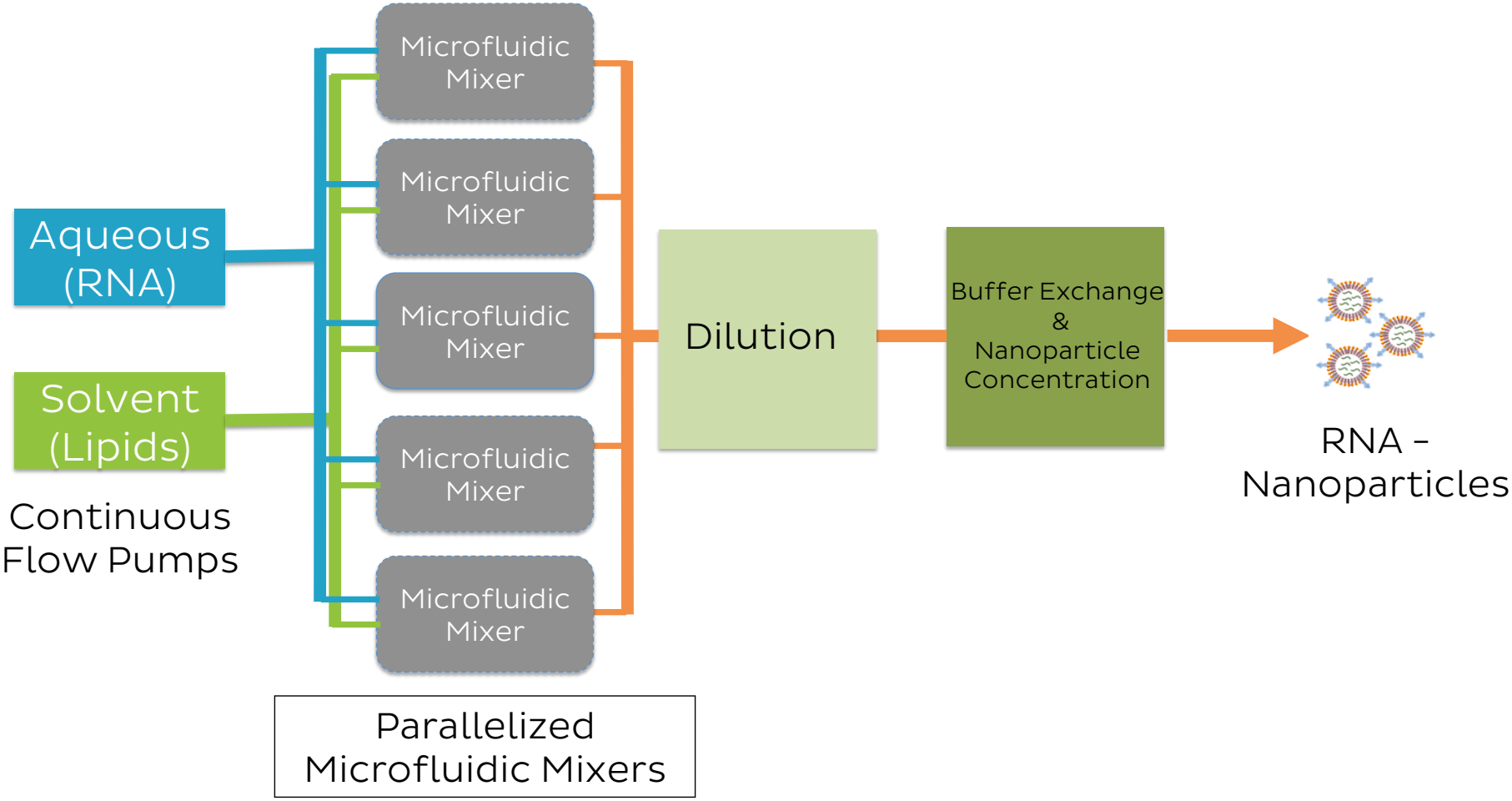


Continuous Flow Scale-up Manufacture of RNA-Lipid Nanoparticles Using Single Mixer

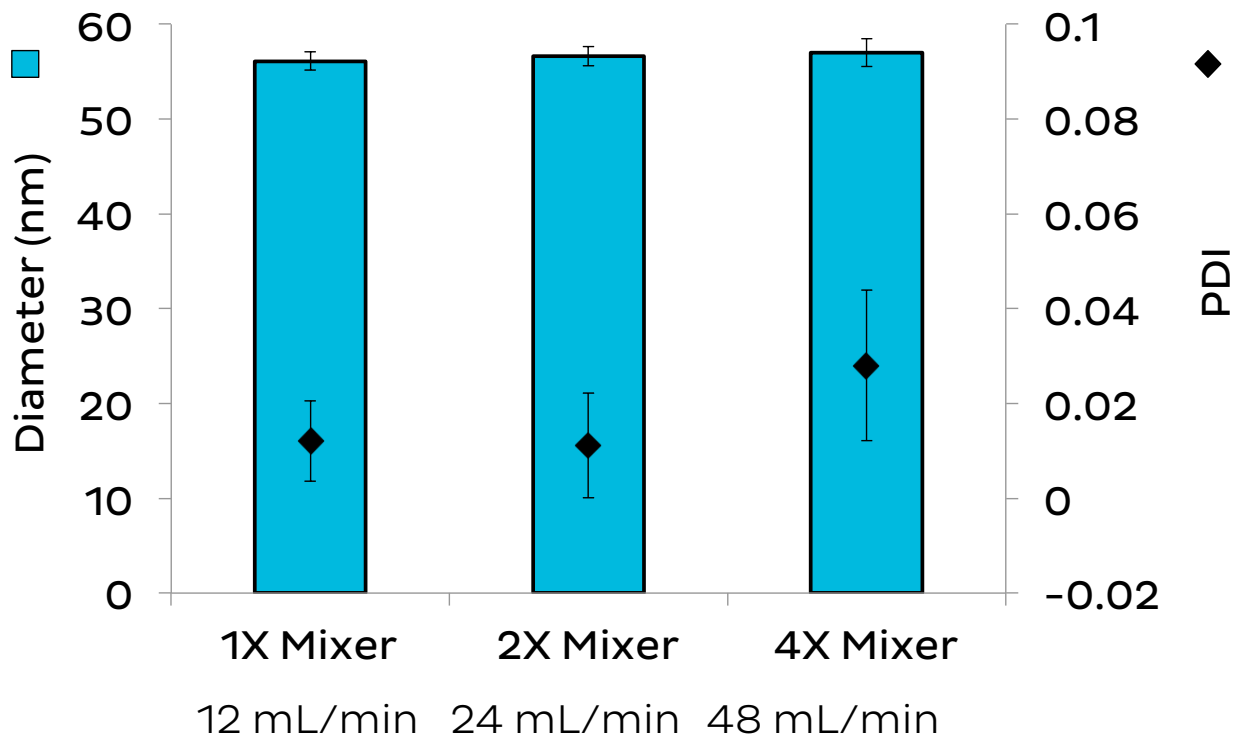


Seamless Transfer of Optimized Manufacturing Parameters

Microfluidics Enables "Seamless Scale-Up"

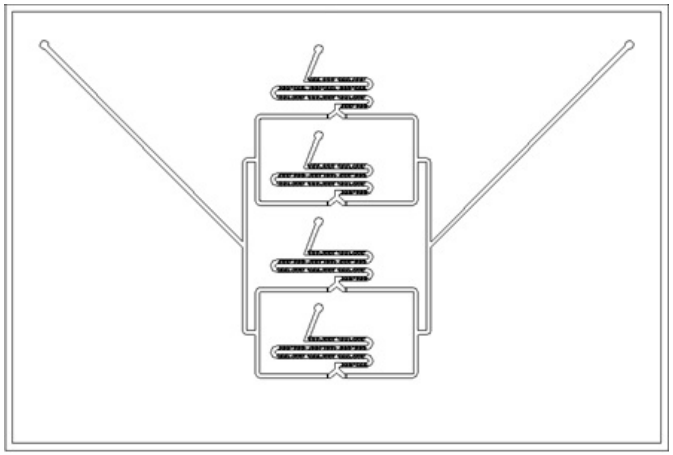


Manifold Microfluidic Parallelization Enables RNA-Lipid Nanoparticle Scale-Up Manufacture

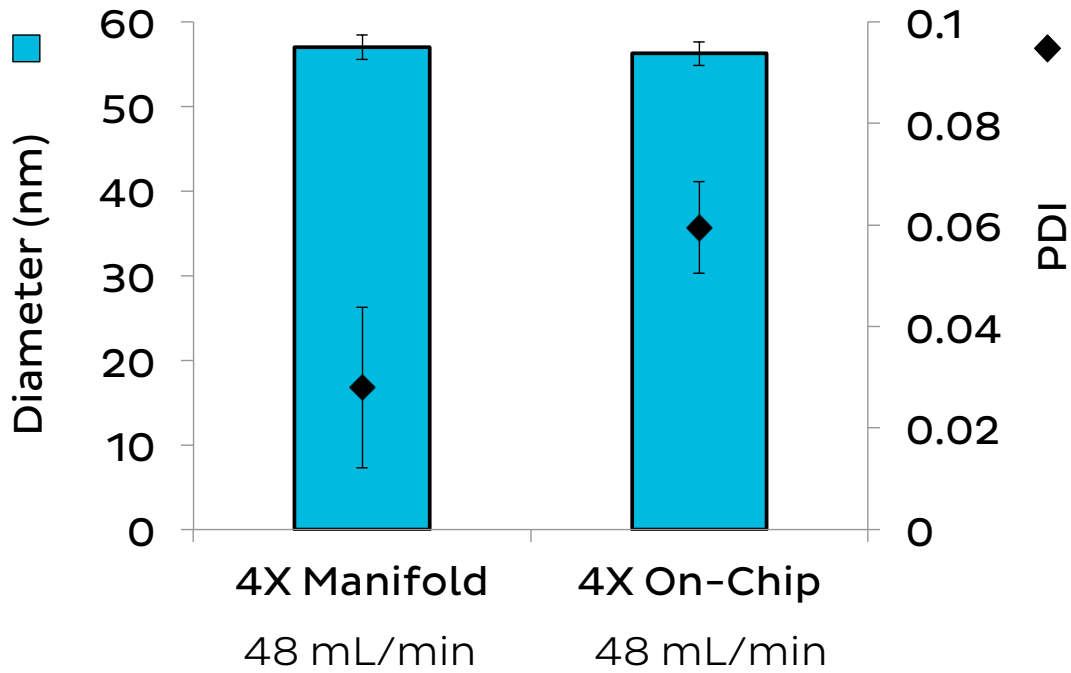


Parallelization of Microfluidic Mixers Enables Higher Throughput

On-Chip Microfluidic Parallelization Produces Equivalent RNA-LNP

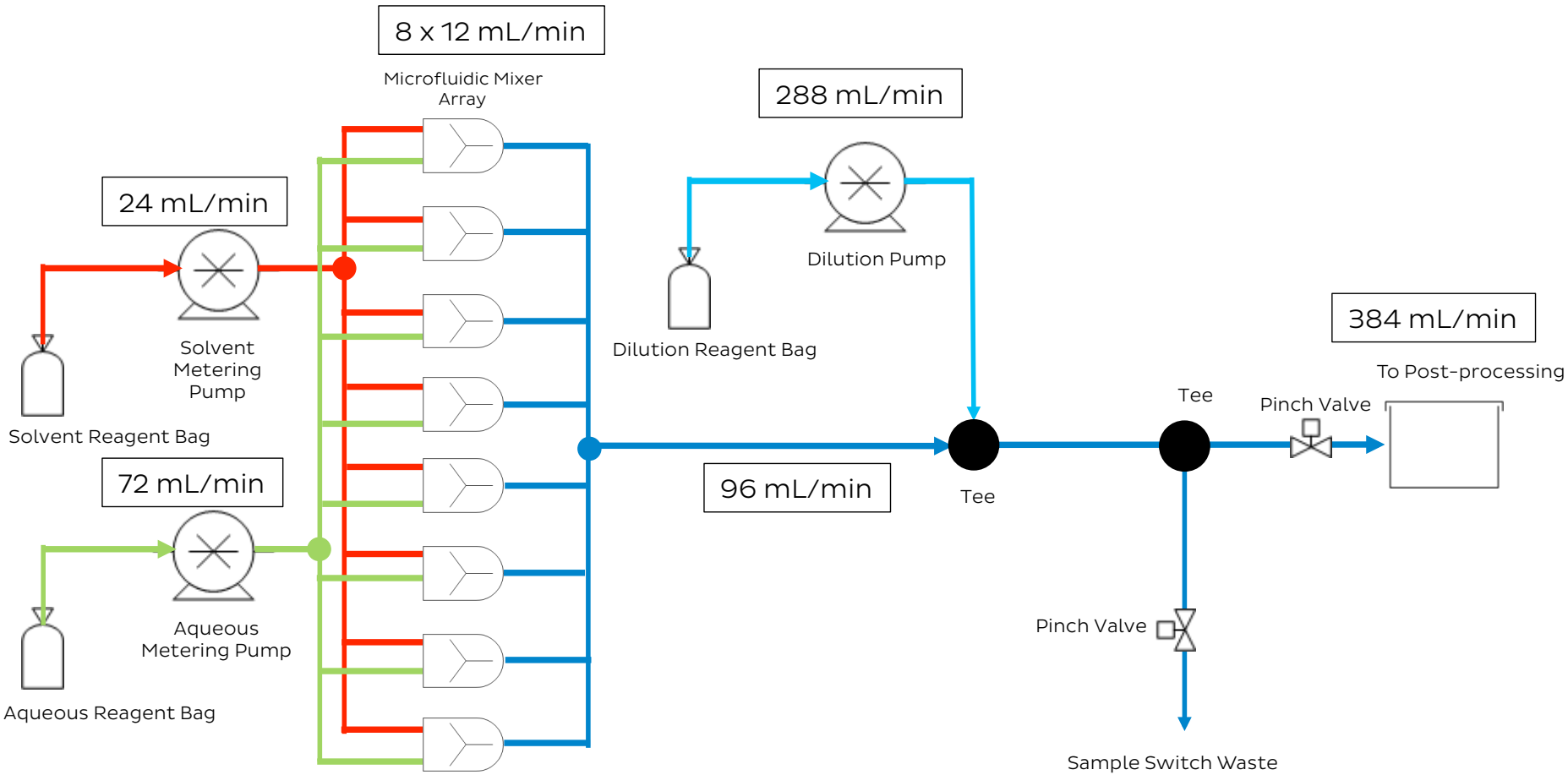


4X Mixer Chip



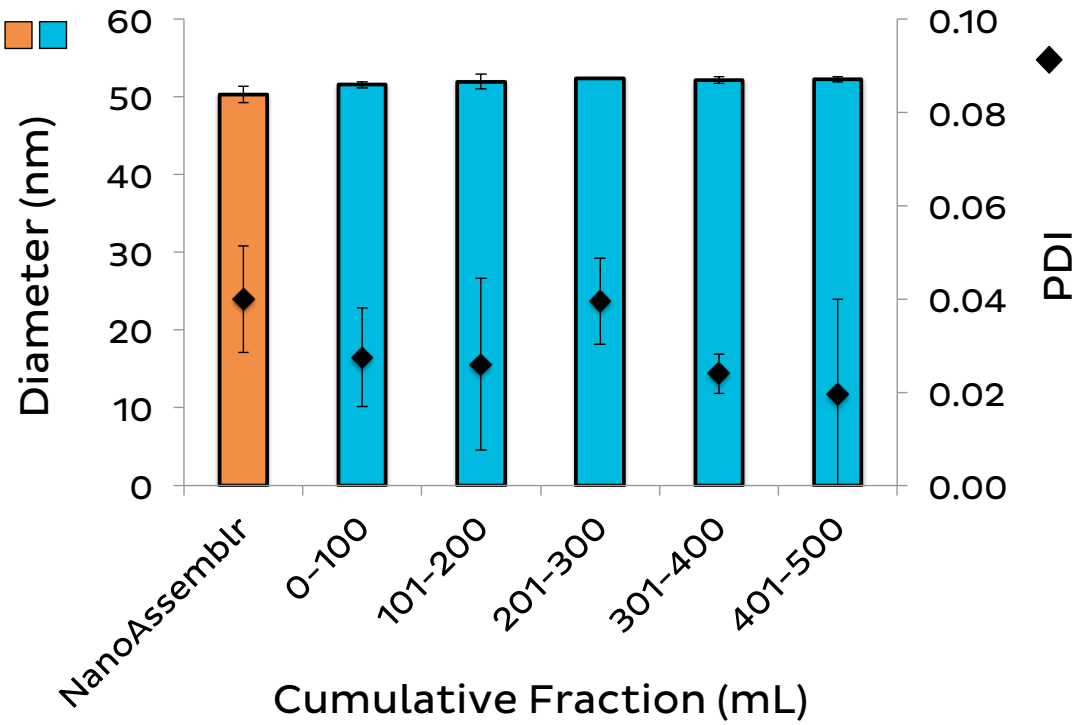
Multiple options for increased throughput by parallelization

Design for GMP Manufacturing



8X Scale-up System

8X Scale-Up Instrumentation Produces High-Quality RNA-LNP



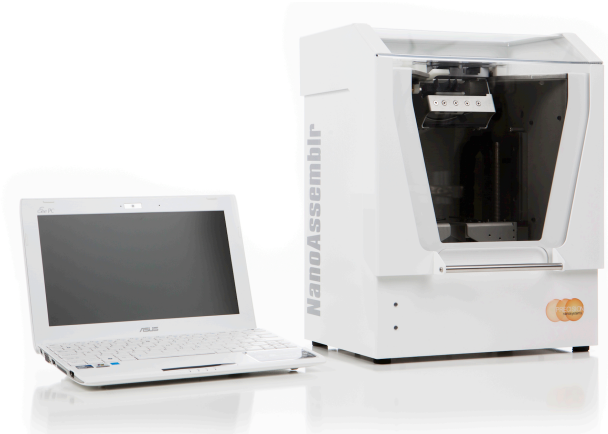
- 8X Scale-Up System Processes 5.75 L/hr
- Further parallelized systems under development

GMP Program in Development

- ✓ Prototype instrumentation developed
- ✓ Disposable COC microfluidic chips developed
- ✓ Working with drug development partner to transfer technology to CMO for scale-up and GMP manufacturing
- ✓ Fully disposable fluid path using USP Class 5/6 materials
- ✓ Working with partners and to support development and push programs forward

Try the NanoAssemblr™ for your drug development program

- ✓ Worldwide distribution
- ✓ Demo Program Available
  - ✓ Contact Colin Walsh: cwalsh@precision-nano.com
  - ✓ Contact Gesine Heuck: gheuck@precision-nano.com
- ✓ Development programs in place
  - ✓ RNA delivery systems
  - ✓ Liposomes
  - ✓ Polymers
  - ✓ Polymer-drug conjugates
  - ✓ Other nanoparticle systems



NanoAssemblr™ Benchtop Instrument