THE UNIVERSITY OF RHODE ISLAND

Universidad Zaragoza

1542

Gold Nanoparticles Synthesis and Assembly in Continuous Flow Processes.

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University of Rhode Island.

And Universidad de Zaragoza.

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1. INTRODUCTION

"Creating complex, multicomponent nanoparticles in batch mode, test tubes, often yields heterogeneous structures. This is primarily due to changes in concentration as one solution is added stepwise to another, as well as insufficient mixing. We have observed this when creating layersomes (liposomes coated with one or more layers of polyelectrolytes) and nanoparticle-decorated liposomes (nanoparticles adsorbed onto the surface of liposomes) – both of which are potential approaches to designing nanoparticle-based therapeutics that can combine multiple therapeutic objectives such as drug delivery, diagnostics, and imaging in a single platform. Continuous flow processes offer advantages over batch mode for creating homogenous structures including the ability to work with small reaction volumes and to control shear, mixing, and reaction, residence time. Investigate synthesis and assembly mechanisms, and the effects of operating conditions Reynolds Number, Angle, Radius". (Dr. Bothun, 2017).

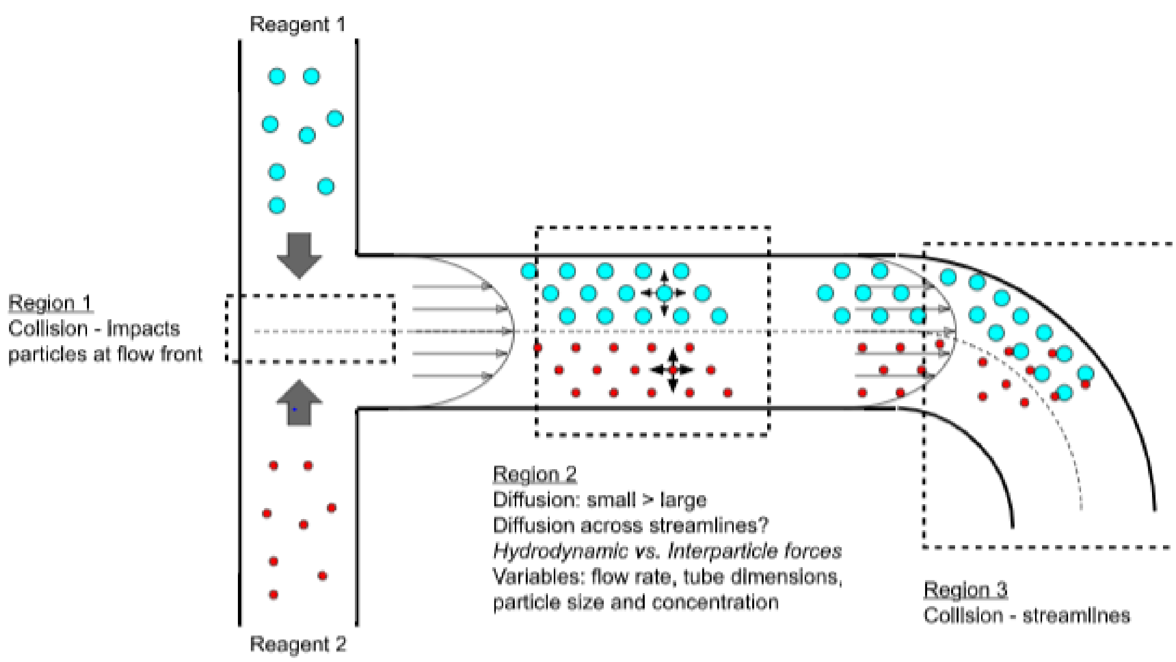


Figure 1.1. Nanoparticles synthesis through a small tube with turn. (Dr. Bothun, 2017)

2. FOOD COLORANT EXPERIMENTS

Quality of mixture depending on 3 main parameters:

- Radius
- Angle
- Reynolds Number (By Changing Flow Rates)

Constant Parameters:

- Length of the tube
- Diameter of the tube

Green spots - Points where mixing is appreciated.

2.1. Comparison of Radius.

- Constant Angle: 180º
- Constant Flow Rate: 10 mL/min
- Radii used: 4” and 9"

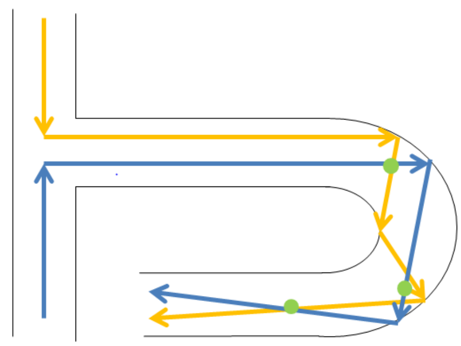


Figure 2.1.1. Tube: 180º angle, 10 mL/min, 4" Radius.

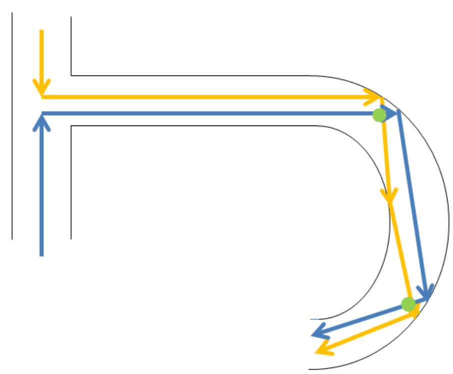


Figure 2.1.2 Tube: 180º angle, 10 mL/min, 9" Radius.

2.2. Comparison of Angle.

- Constant Radius: 4”
- Constant Flow Rate: 10 mL/min
- Angles used: 180º and 360º

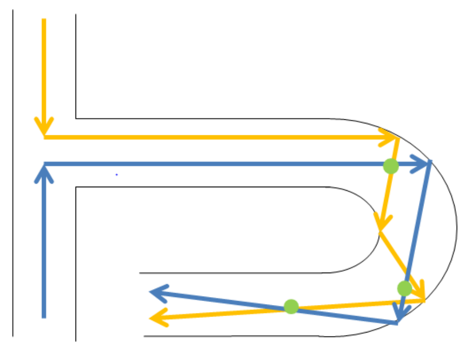


Figure 2.2.1. Tube: 180º angle, 10 mL/min, 4" Radius.

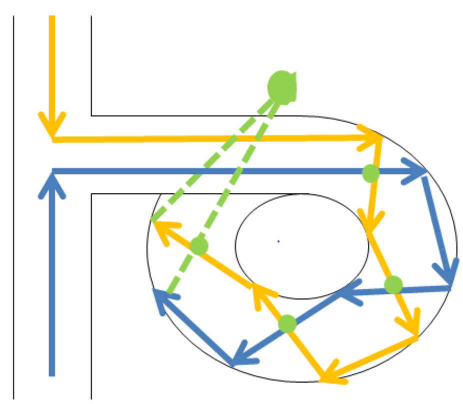


Figure 2.2.2. Tube: 360º angle, 10 mL/min, 4" Radius.

2.3. Comparison of Reynolds Number. By Changing Flow Rates

- Constant Radius: 4”
- Constant Angle: 180º
- Flow Rates used: 10 mL/min, 5 mL/min, 2 mL/min

$$\mathrm{Re}(D) = \frac{V_1 D}{\nu_1} = \frac{4 q_m}{\pi \mu_1 D}$$

Figure 2.3.1. Reynolds Number Formula for tubes. (Wikipedia, 2017).

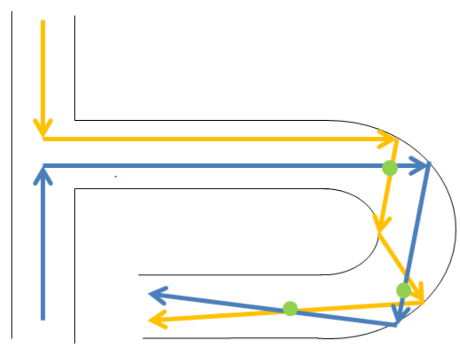


Figure 2.3.2. Tube: 180º angle, 10 mL/min, 4" Radius.

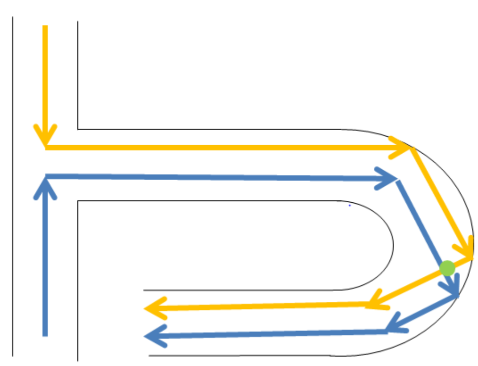


Figure 2.3.3. Tube: 180º angle, 5 mL/min, 4" Radius.

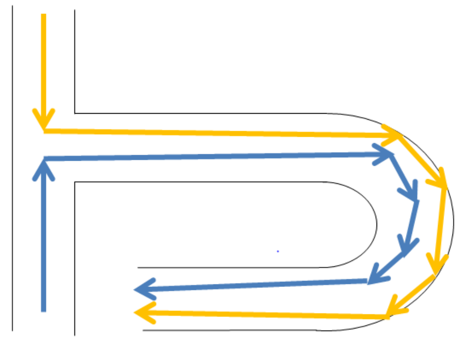


Figure 2.3.4. Tube: 180º angle, 2 mL/min, 4" Radius.

2.4. Comparison of Residence Time. By Changing Volumes

- Constant Angle: 180º
- Constant Flow Rate: 10 mL/min
- Constant Diameter
- Radius used: 4”
- Length of the Tube used: 19" and 38"

$$\tau = \frac{V}{v_0}$$

Figure 2.4.1. Reynolds Number Formula for tubes. (Wikipedia, 2017).

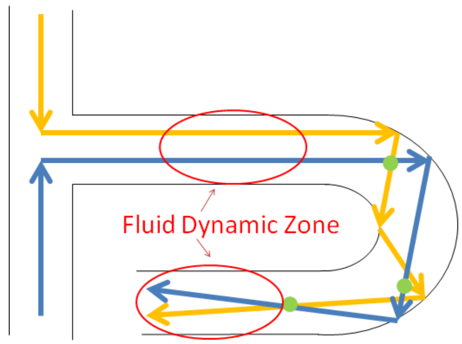


Figure 2.4.2. Tube: 180º angle, 10 mL/min, 4" Radius, 19" length.

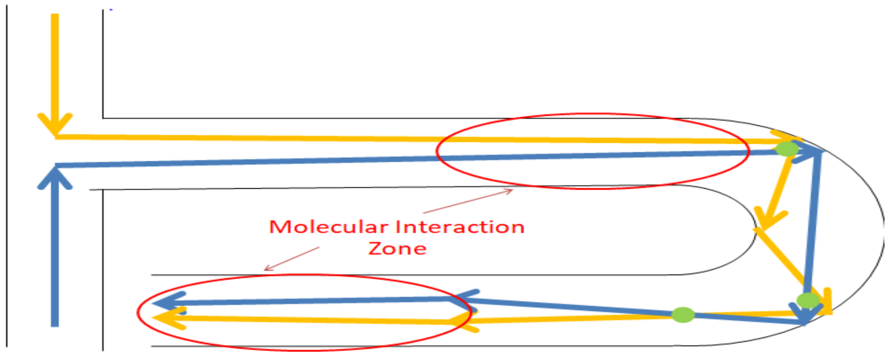


Figure 2.4.3. Tube: 180º angle, 10 mL/min, 4" Radius, 38" length.

2.5. Conclusion.

- **Radius:**

The smaller the Radius, the better the mixing

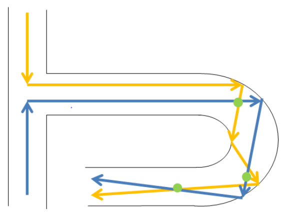


Figure 2.1.1

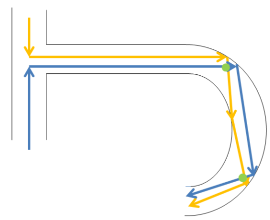


Figure 2.1.2

- **Angles:**

The greater the angle, the better the mixing.

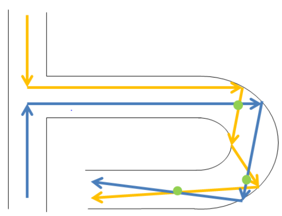


Figure 2.2.1.

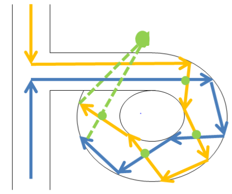


Figure 2.2.2.

- **Reynolds number:**

A greater Reynolds number results in better mixing. However, this causes the residence time to be smaller. We are not sure if this results in better mixing.

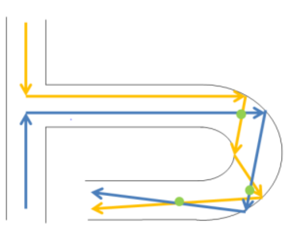


Figure 2.3.2.

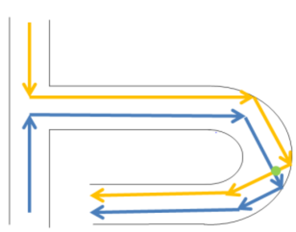


Figure 2.3.3.

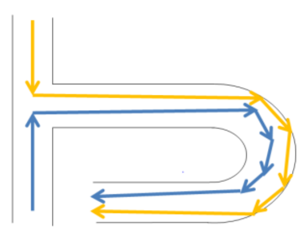


Figure 2.3.4.

- **Residence Time:**

The greater the Residence Time, the better the mixing.

Residence Time can be changed by Flow Rate as we saw before, or by the Length of the Tube. In any case, the greater the Residence Time is, the greater are the interaction effects.

If Residence Time is great enough, Fluid Dynamics are not so important. Particles begin to lose their flow line, and instead of that, they start to interact witch each other. (Van der Waals forces).

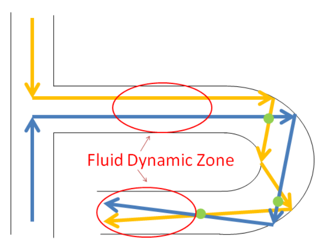


Figure 2.4.2.

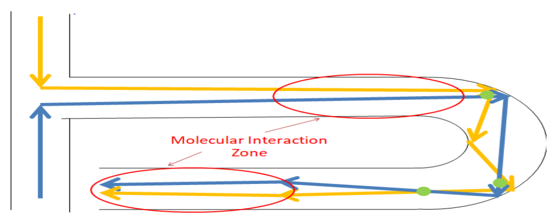


Figure 2.4.3.

3. 3D MODELS

Quality of mixture depending on 3 main parameters:

- Radius
- Angle
- Reynolds Number (By Changing Velocity)

Constant Parameters:

- Diameter of the tube

3.1. Comparison of Radius.

- Constant Angle: 180º
- Constant Velocity
- Greatest Radius = 3 · Smallest Radius

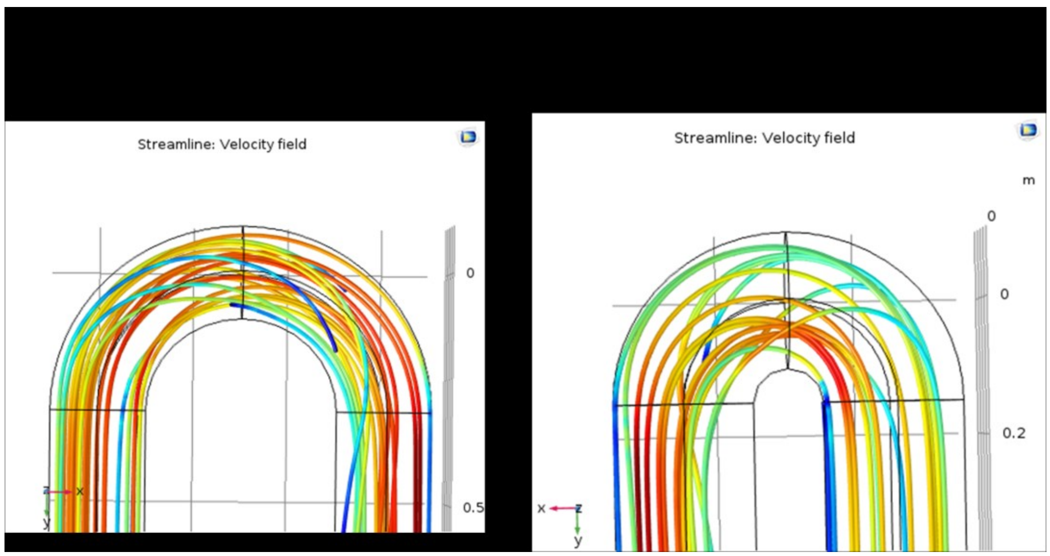


Figure 3.1.1. Comparison Streamlines Changing Radius.

Comparison Radius 

Conclusion from experiments:

- Radius:

  The smaller the Radius, the better the mixing.

Conclusion from 3D Model:

- Radius:

  The smaller the Radius, the better the mixing.

3.2. Comparison of Angle.

- Constant Radius
- Constant Velocity
- Angles used: 90º, 180º, 360º Loop.

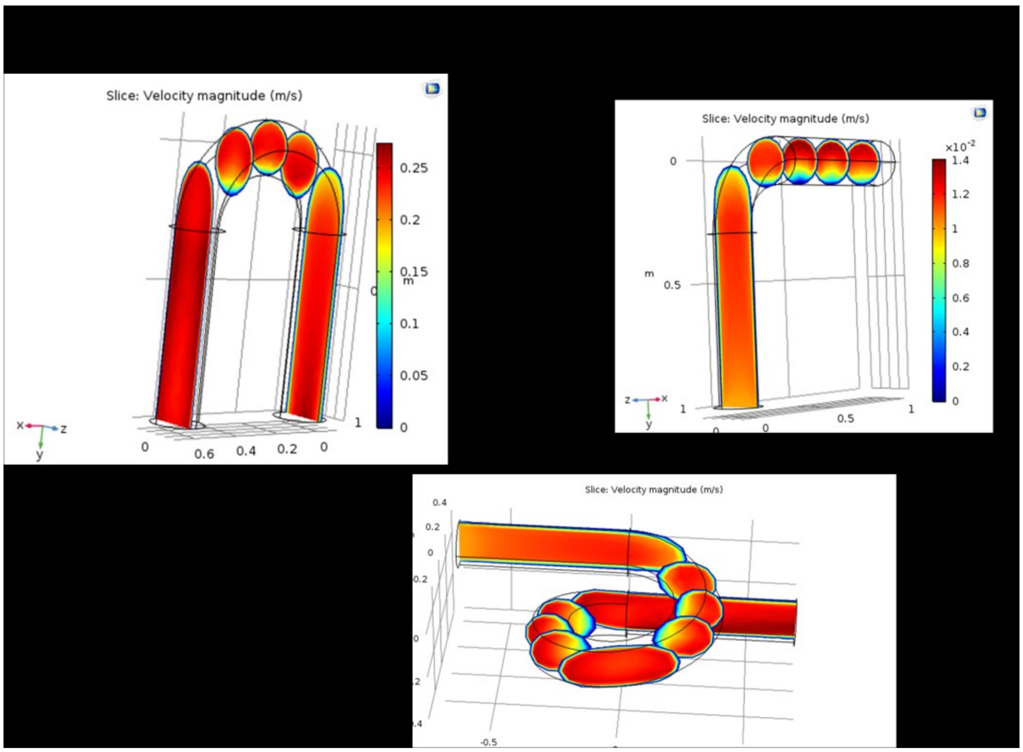


Figure 3.2.1. Comparison Velocity Profile Changing Angle.

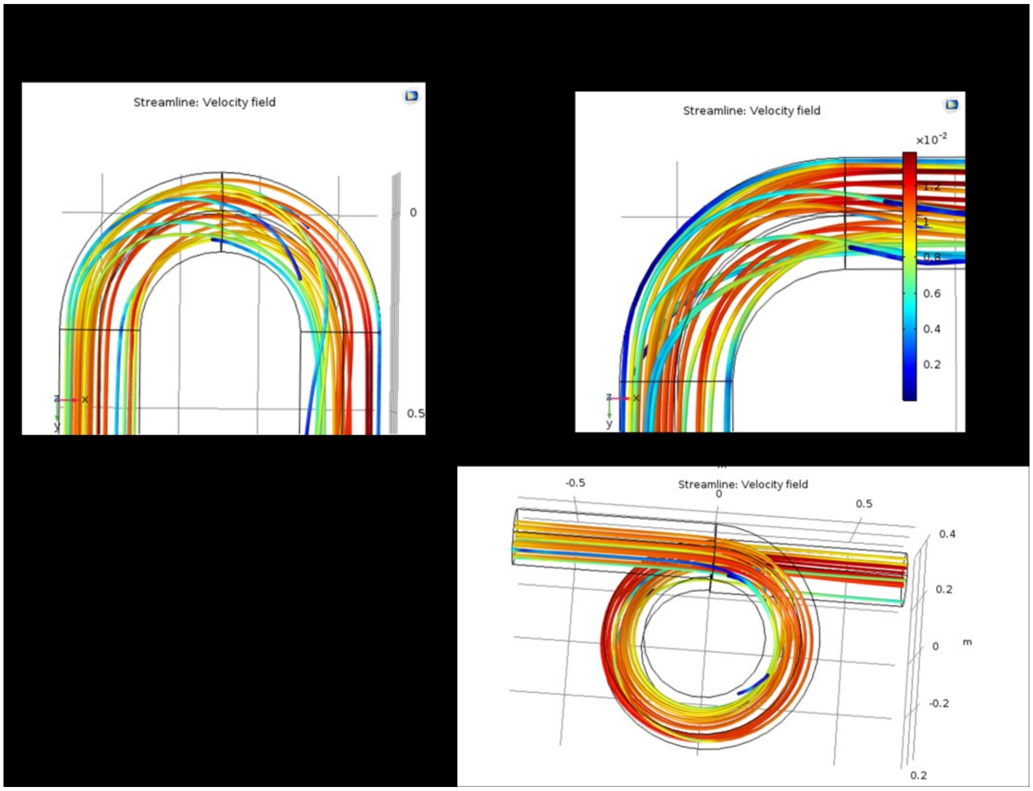


Figure 3.2.2. Comparison Streamlines Changing Angle.

Comparison Angle

Conclusion from experiments:

- Angle:

  The grater the Angle, the better the mixing.

Conclusion from 3D Model:

- Angle:

  The grater the Angle, the better the mixing.

3.3. Comparison of Reynolds Number. By Changing Flow Rates

- Constant Radius
- Constant Angle
- Velocities: Greatest Reynolds Number = 10 x Smallest Reynolds Number

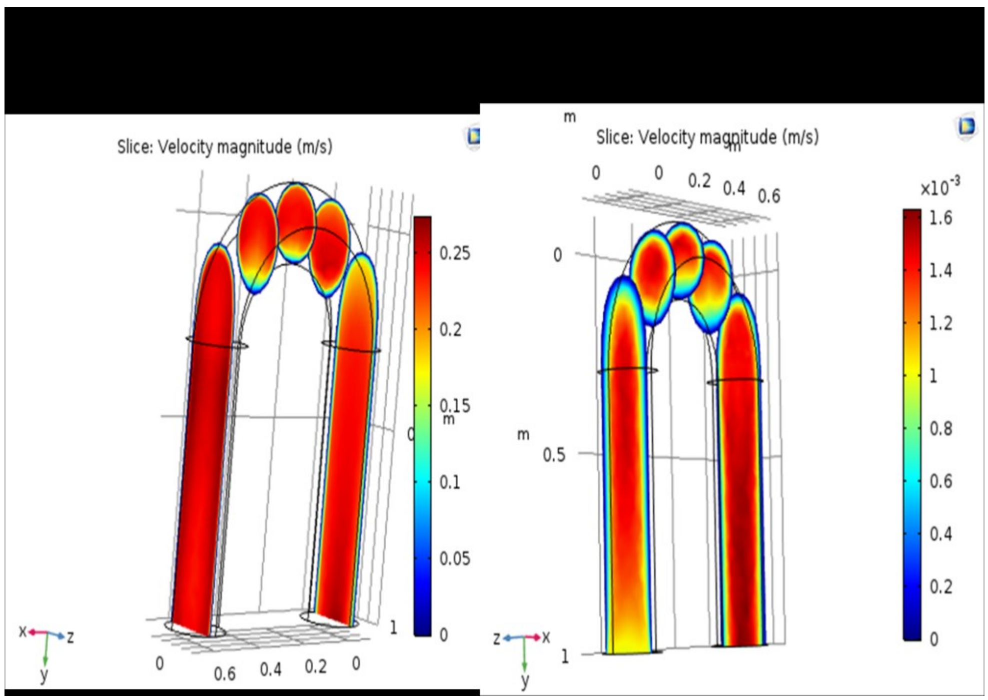


Figure 3.3.1. Comparison Velocity Profile Changing Reynolds Number.

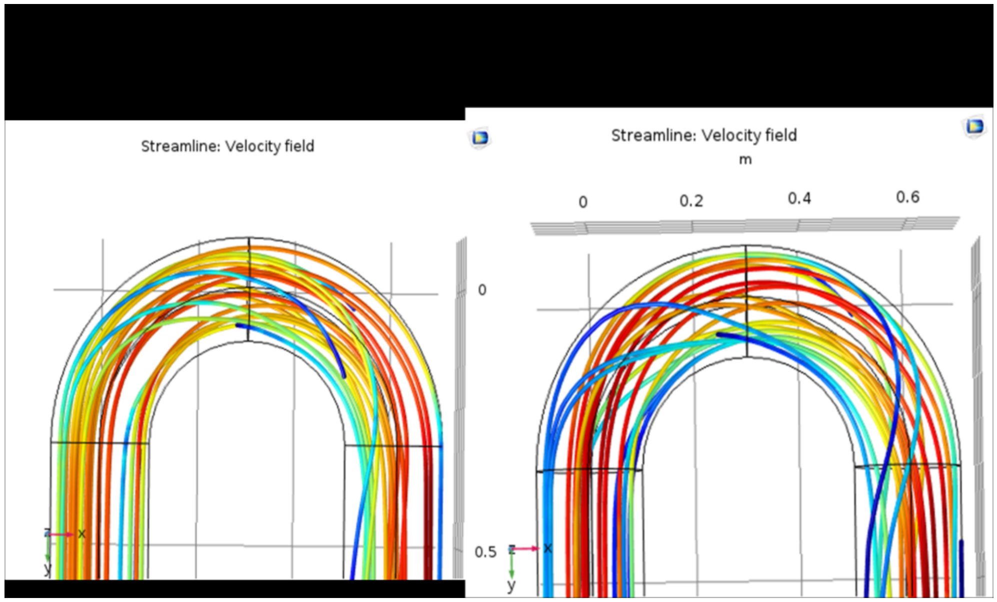


Figure 3.3.2. Comparison Streamlines Changing Reynolds Number.

Comparison of Reynolds Number

- Conclusion from experiments:

  A greater Reynolds number results in better mixing.

- Conclusion from 3D Model:

  The grater the Angle, the better the mixing.

Small Reynolds Numbers make huge velocity loss in the walls. Streamlines tend to turn randomly, what would make a better mixing but in a random way.

4. GOLD NANOPARTCILES SYNTHESIS

Comparison of Gold Nanoparticles using the PUMP vs. The BATCH process.

The Pump is set up with the same parameters that gave us the best mixing results:

- Greater Angle
- Smaller Radius
- Greater Reynolds Number
- Greater Residence Time

4.1. Batch Process

Gold Nanoparticles

- Made 0.5 mM Gold Solution by adding 30 µL of 50 mM $HAuCl_4$ to 2.97 mL Water.
- Made 0.75 mM Ascorbic Acid Solution.
- Add 1 mL of each to get 2 mL Solution.

Mixed by hand-shaking

PLL + GNPs

- Made Gold + PLL Solution by adding 30 uL of 50 mM $HAuCl_4$, 100 µL PLL Stock Solution to 2.87 mL Water.
- Made 0.75 mM Ascorbic Acid Solution.
- Add 1 mL of each to get 2 mL Solution.

Mixed by hand-shaking

4.2. Continuous Process with Pump and different configurations.

Gold Nanoparticles

- Syringe 1 3 mL of 0.75 mM Ascorbic Acid Solution.
- Syringe 2 3 mL of 0.5 mM Gold Solution.
- Pump is operated at a Flow Rate of 2.021 mL/min

PLL + GNPs

- Syringe 1 3 mL of 0.75 mM Ascorbic Acid Solution.
- Syringe 2 3 mL of Gold + PLL Solution.
- Pump is operated at a Flow Rate of 2.021 mL/min

4.2.1. Continuous Pump Set Up 1/16" inner diameter tube wrapped around a 4" diameter Bottle Cap 1 time, 360º.

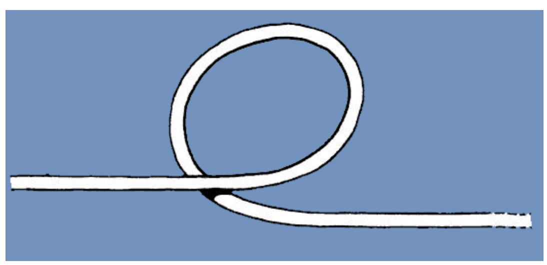


Figure 4.2.1.1. 360º Loop (Survival World, 2017)

Figure 4.2.1.2. 1/16" inner diameter tube wrapped around a 4" diameter Bottle Cap, 360º.

Table 4.2.1.1. DLS Results Continuous Pump Set Up 1/16" inner diameter tube wrapped around a 4" diameter Bottle Cap 1 time, 360º vs. Batch Process by hand-shaking.

Type of Process	Size (nm)	PDI	Zeta Potential (mV)
GNPs (Batch)	32.23	0.326	-29.0
GNPs + PLL (Batch)	74.03	0.272	39.5
GNPs (Pump)	101.5	0.204	-20.5
GNPs + PLL (Pump)	102.2	0.167	37.2

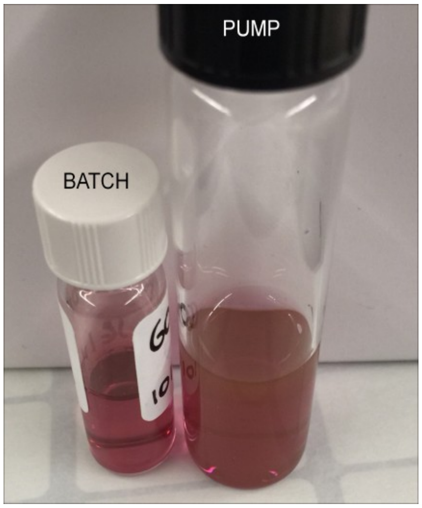


Figure 4.2.1.3. Comparison of color between Pump and Batch Process.

BATCH SOLUTIONS

Type of Process	Size (nm)	PDI	Zeta Potential (mV)
GNPs (Batch)	32.23	0.326	-29.0
GNPs + PLL (Batch)	74.03	0.272	39.5

Batch Solutions

- Expected Color and Transparent Reddish Pink for GNPs and Dark Blue for GNPs + PLL
- Ideal Size
- Ideal Charge
- PDI large due to small intensity peak at 10 nm

- The Batch Process had a mysterious intensity peak at a size about 10 nm.
- We have to repeat these experiments to see if the small peak goes away
- In the future, we will try centrifuging the sample to see if the small peak goes away.

Figure 4.2.1.4. Batch Solutions

CONTINUOUS SOLUTIONS

Type of Process	Size (nm)	PDI	Zeta Potential (mV)
GNPs (Pump)	101.5	0.204	-20.5
GNPs + PLL (Pump)	102.2	0.167	37.2

Continuous Solutions

- Translucent Suggesting that there are aggregates
- High Size Average Which suggests particles are sticking together
- Charge for GNPs is above -25mV Suggesting that it will aggregate

- We think that the pump set up did not allow for “good enough” mixing.
- We will repeat with just gold (no PLL) with a different set up.

Figure 4.2.1.5. Continuous Solutions

4.2.2. Three Different Continuous Configurations.

1. Continuous Pump Set Up 1/16" inner diameter Tube wrapped around a 2" diameter Bottle Cap 1.75 times = 630º.

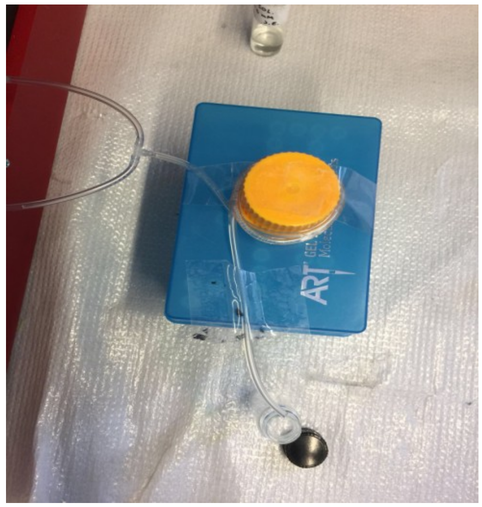


Figure 4.2.2.1. 1/16" inner diameter Tube wrapped around a 2" diameter Bottle Cap 1.75 times = 630º.

2. Continuous Pump Set Up 1/16" inner diameter Tube wrapped around a 2" diameter Bottle Cap 4 times = 1440º.

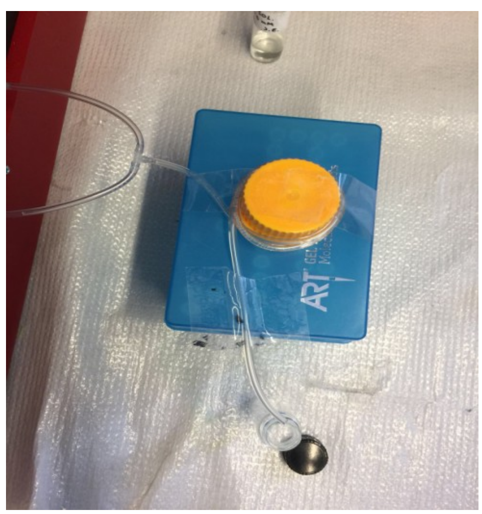


Figure 4.2.2.2. 1/16" inner diameter Tube wrapped around a 2" diameter Bottle Cap 1.75 times = 630º.

3. Continuous Pump Set Up 1/16" Tube made 3 loops (like a W)

Figure 4.2.2.3. 1/16" Tube made 3 loops (like a W)

Table 4.2.2.1. DLS Results Continuous Pump with different configurations just made.

Type of Process	Size (nm)	PDI	Zeta Potential (mV)
GNPs (Batch)	31.50	0.448	- 29.0
GNPs (Pump) Loop 630º	43.2	0.302	- 24.1
GNPs (Pump) Loop 1440º	45.55	0.317	- 20.8
GNPs (Pump) W	39.67	0.383	- 24.3

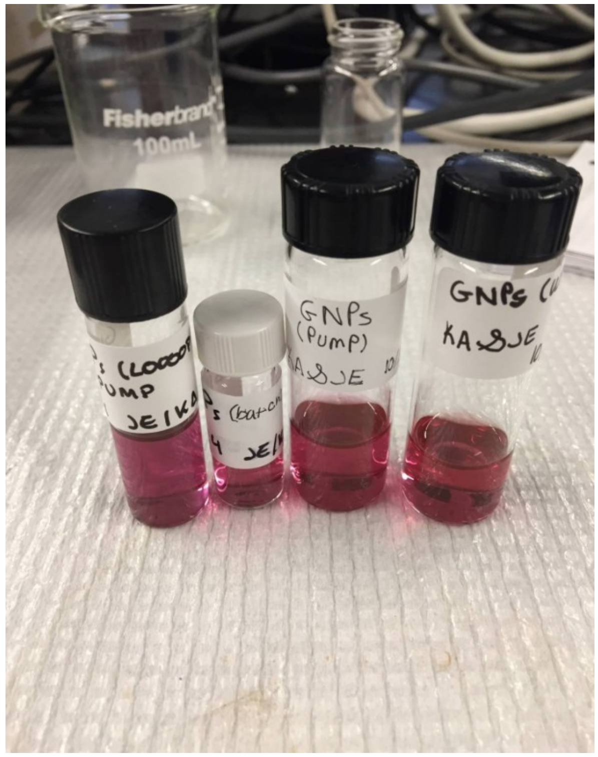


Figure 4.2.2.4. Comparison of color between Continuous Pump with different configurations just made.

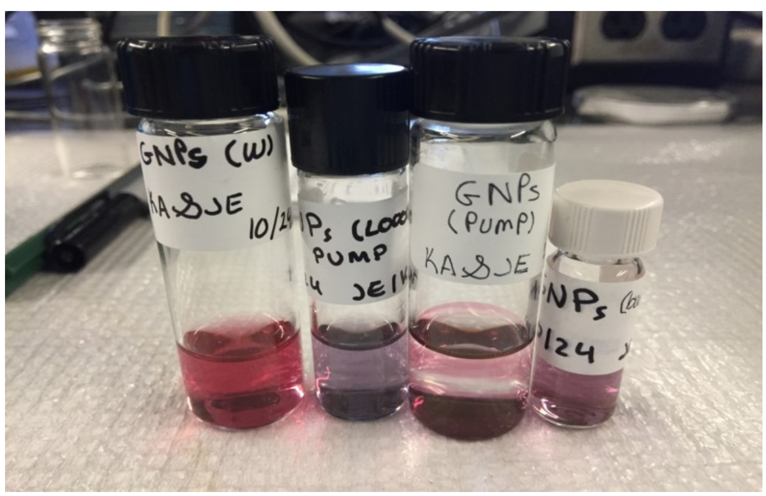


Figure 4.2.2.5. Comparison of color between Continuous Pump with different configurations 1 Week After.

Table 4.2.2.2. DLS Results Continuous Pump with different configurations After 1 Week.

Type of Process	Size (nm)	PDI	Zeta Potential (mV)
GNPs (Batch) 10/24	31.50	0.448	- 29.0
GNPs (Batch) 10/31	28.69	0.449	-25.1
GNPs (Pump) W 10/24	45.55	0.317	- 20.8
GNPs (Pump) W 10/31	44.56	0.316	-26.1

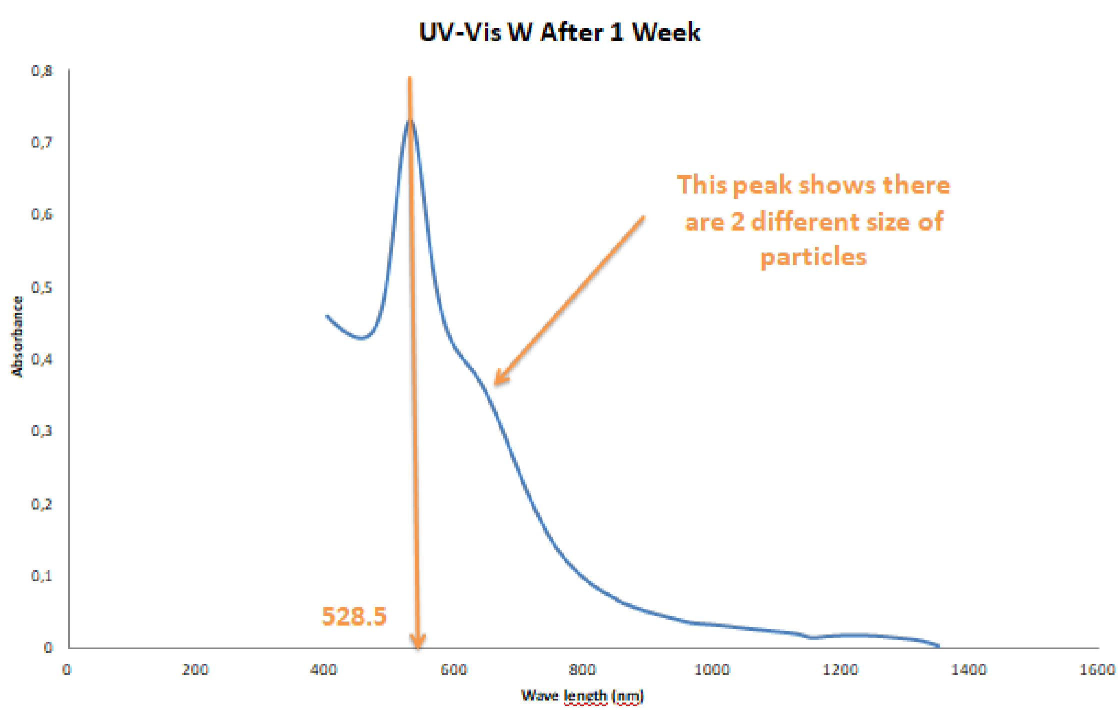


Figure 4.2.2.6. UV-Vis W configuration 1 Week After.

4.3. Continuous Process with Pump through Sonicator

4.3.1. Pump through Sonicator.

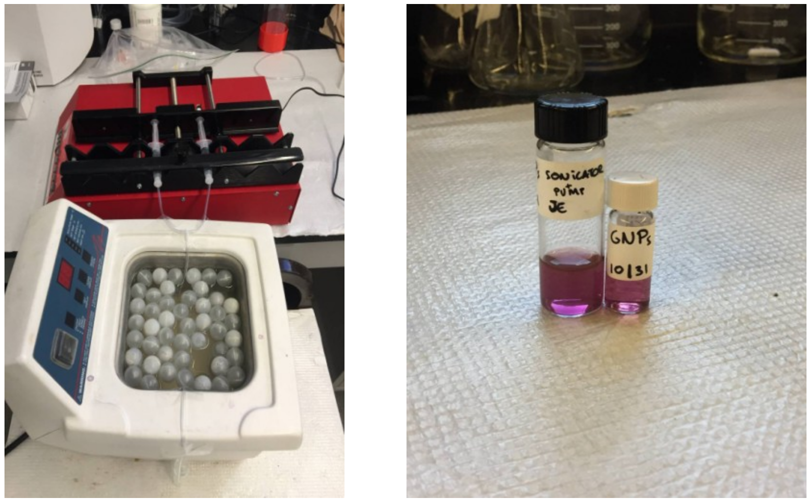


Figure 4.3.1.1. Pump through Sonicator. Configuration and results.

Table 4.3.1.1. Comparison DLS Results Pump through sonicator and Batch Mode.

Type of Process	Size (nm)	PDI	Zeta Potential (mV)
GNPs Pump + Sonicator	56.57	0.285	-23.8
GNPs Batch	25.86	0.567	-31.1

4.3.2. Pump through Sonicator + Loop configuration.

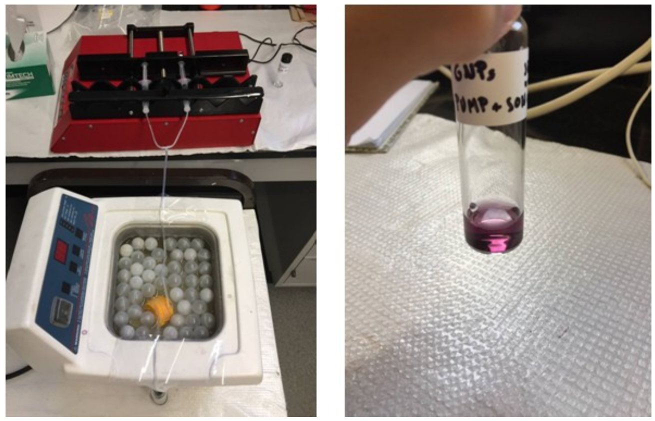


Figure 4.3.2.1. Pump through Sonicator + Loop Configuration and result.

4.3.3. Pump through Sonicator + W configuration.

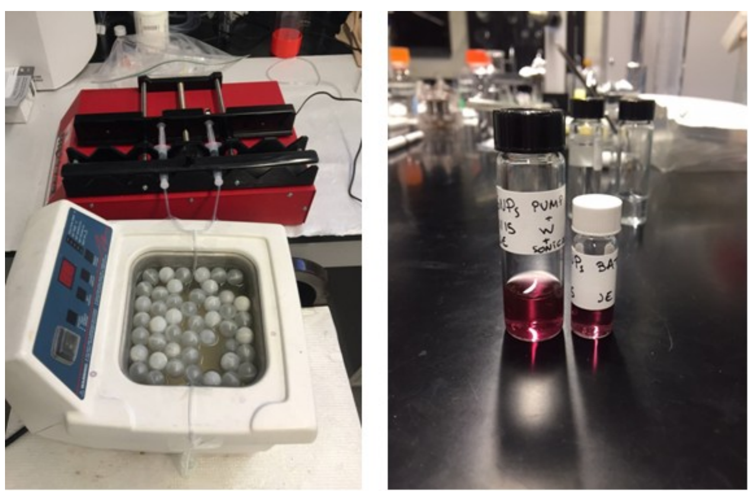


Figure 4.3.3.1. Pump through Sonicator + W Configuration and result.

Table 4.3.3.1. Comparison DLS Results Pump through Sonicator + W configuration and Batch Mode.

Type of Process	Size (nm)	PDI	Zeta Potential (mV)
GNPs (Batch)	26.12	0.504	-37.5
GNPs (Pump) + Sonicator + W	33.51	0.493	-23.9
GNPs (Batch) After 1 Day	29.10	0.398	-36.9
GNPs (Pump) + Sonicator + W After 1 Day	234.5	0.619	-24.8

4.4. Continuous Process with Pump and Mixer

Table 4.4.1. Comparison DLS Results Pump with Mixer and Batch Mode. Just made and After 1 Day.

Type of Process	Size (nm)	PDI	Zeta Potential (mV)
GNPs (Batch)	220.8	0.472	-20.6
GNPs (Batch) NEXT DAY	1389	0.703	-13.7
GNPs (Pump + Mixer)	31.31	0.491	-30.6
GNPs (Pump + Mixer) NEXT DAY	33.42	0.449	-25.8

↓ There is a PEAK about 5 nm (10%)

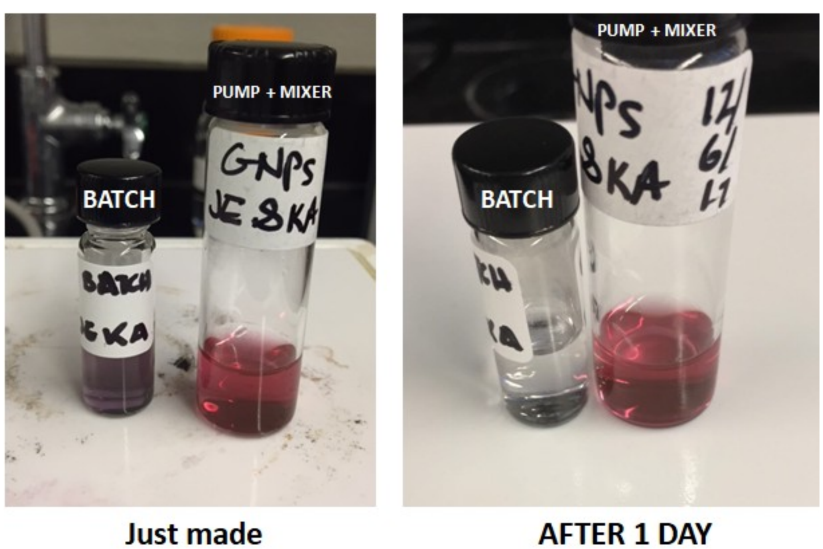


Figure 4.4.1. Pump with Mixer and Batch Mode. Just made and after 1 day.

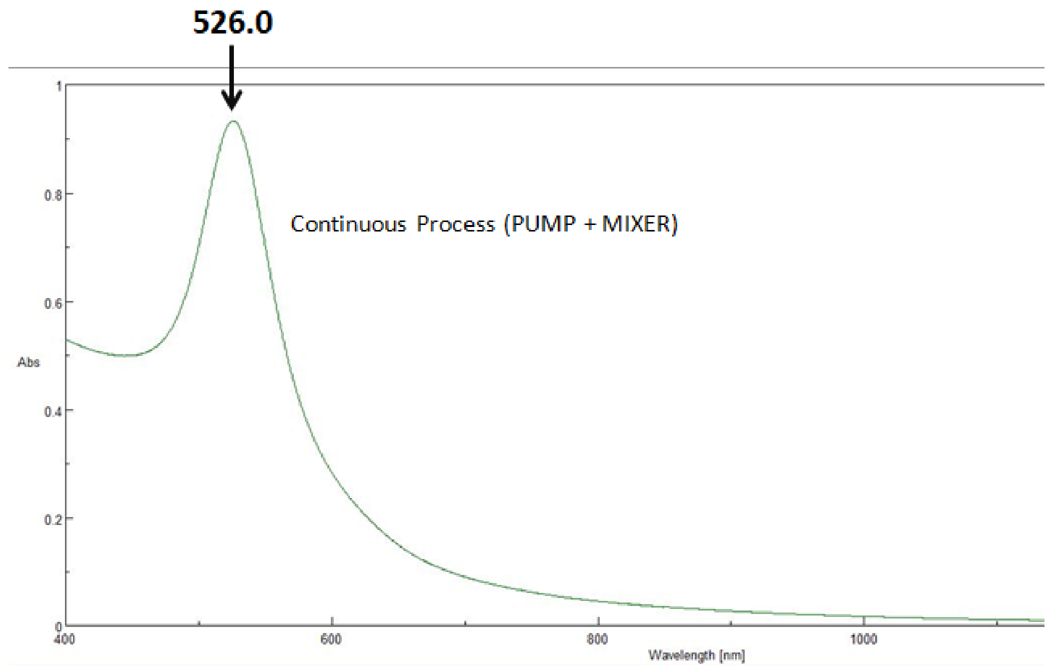


Figure 4.4.2. UV-Vis Result Pump with Mixer. Just made.

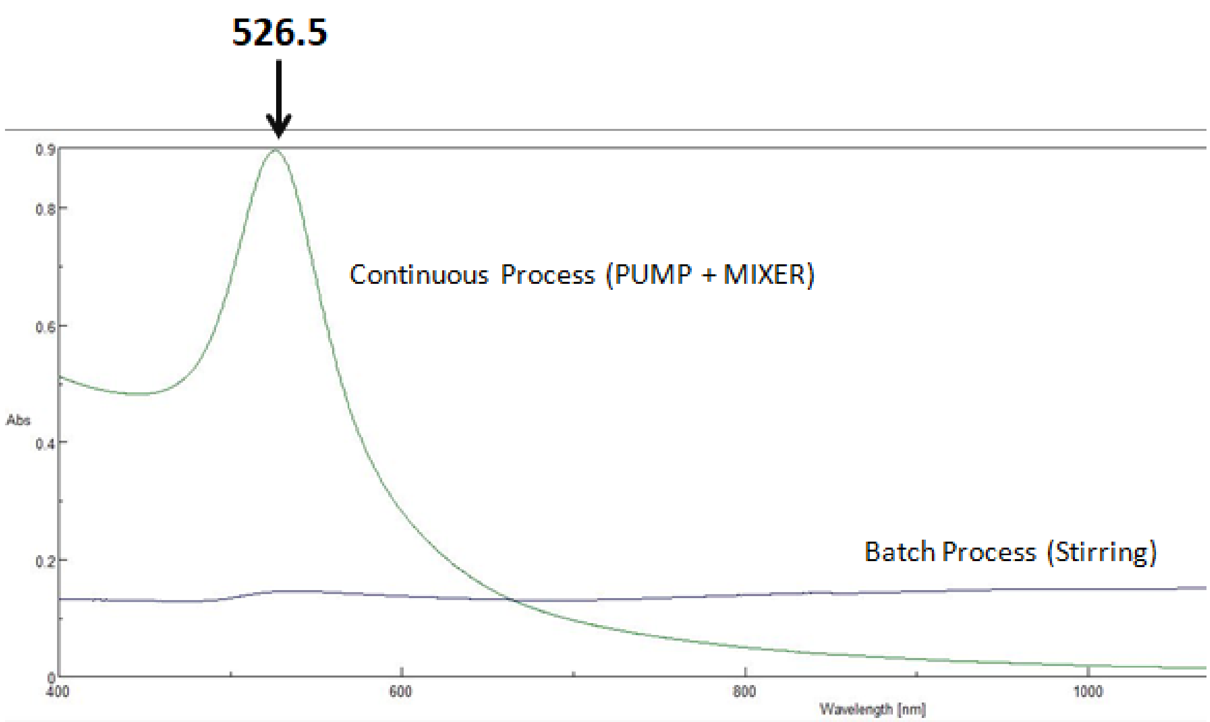
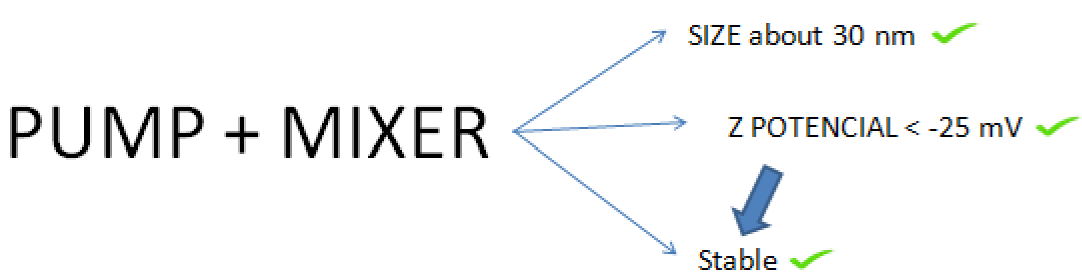


Figure 4.4.3. UV-Vis Result Pump with Mixer and Batch Mode. After 1 day.

Table 4.4.2. Comparison DLS Results Pump with Mixer and Batch Mode. Just made, after 1 day and after 2 days.

Type of Process	Size (nm)	PDI	Zeta Potential (mV)
GNPs (Pump + Mixer)	31.31	0.491	-30.6
GNPs (Pump + Mixer) NEXT DAY	33.42	0.449	-25.8
GNPs (Pump + Mixer) After 2 Days	33.89	0.498	-28.4

There is a PEAK about 5 nm (10%)



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