Modeling and Control of Biomimetic Cilia

NSF Grant CMII 0624597

Control Systems Program

Graduate Students in Project

1. **Kieseok Oh**, Microfabricated Bio-mimetic Cilia for Resonance-Enhanced Mixing and Reaction of Biomolecules, PhD Thesis (December 2009)
2. **Dhanakorn Iamratanakul**, Pre-Actuation and Post-Actuation in Control Applications, PhD Thesis (July 2007)
3. **Brandon Smith**, An Experimental Examination of Improved Micromixing Using Bio-Mimetic Synthetic Cilia, Master's Thesis (December 2009)
4. **Beren McKay**, Masters (Non-thesis) Degree, developed initial experiments for the cilia models (2006)
5. **Jiradech Kongthon**, Modeling and Control of Bio-mimetic Cilia-based Devices for Micro-fluidic Applications, PhD Thesis (December 2012)

Outline of the talk at ACC*

1) **Motivation and context**
2) Large Cilia motions with Fluid Damping
3) Can Cilia improve mixing?
    3.1 Will choice of trajectory affect mixing?
    3.2 Precision control of excitation trajectory
    3.3 Experimental Results
4) Conclusions

*** Following Slides are based on Jiradech Kongthon's PhD Thesis**

1) Motivation and Context

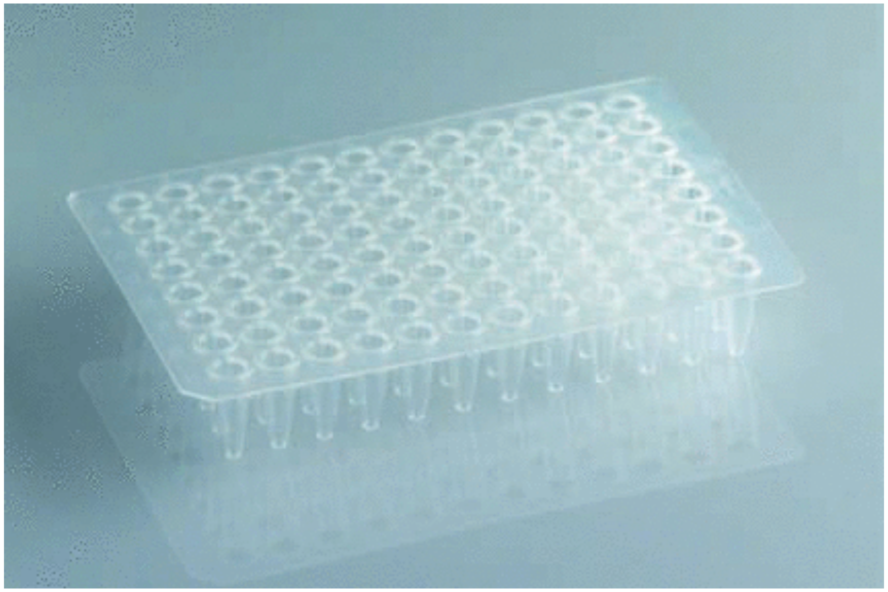
Fluid Manipulation at nano and micro-scale is important in a variety of problems

Example 1:

Mixing and Reaction
in large-arrays of wells
(Micro-plates)

Example 2:

Movement and/or
Pumping of fluid
in micro-channels



www.labmate-online.com/

What is the challenge?

❖ In general, mixing is not difficult in macroscale.

Turbulent Flow

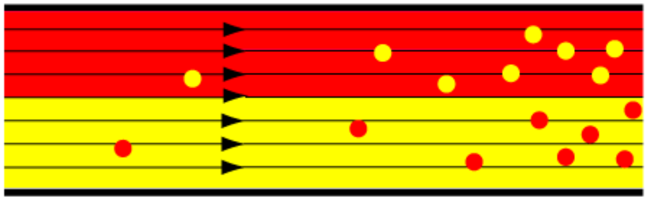
What is the challenge?

❖ In general, mixing is not difficult in macroscale.

Turbulent Flow

❖ Mixing can be very difficult in microscale due to laminar flows (low Reynolds number)

Laminar Flow



❖ In laminar flows, mixing is possible by diffusion only.

❖ But!!!, diffusion can be too slow for larger molecules …

Micro-Nano Fluid Manipulation

Variety of approaches are available

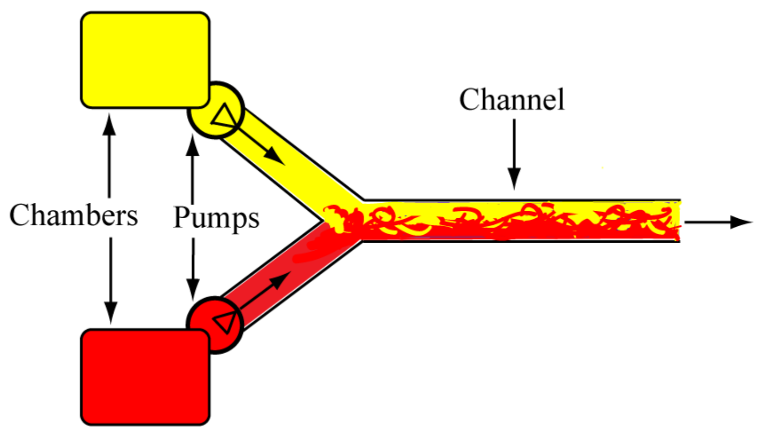
mixing area: there are two broad classes

Micro-Nano Fluid Manipulation

Variety of approaches are available

mixing area: there are two broad classes

1) **<u>Mixing of Flows:</u>** Example: Herringbone when two flows are to be mixed (Whitesides and co-workers)



Micro-Nano Fluid Manipulation

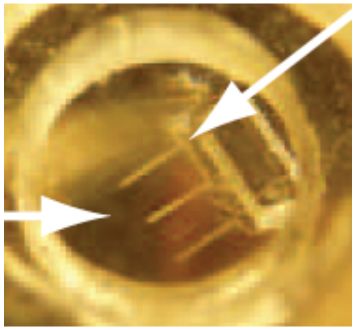
Variety of approaches are available

mixing area: there are two broad classes

1) <u>**Mixing of Flows:**</u> Example: Herringbone when two flows are to be mixed (Whitesides and co-workers)

2) <u>Mixing in a micro-wells.</u> **No flow (sample size)** Examples: Shakers, magnetic elements, ultrasound

Chamber = 3mm (diameter)
Fluid Height = 1.66mm



Micro-Nano Fluid Manipulation

Variety of approaches are available

Broadly two classes in the mixing area:

1) **Mixing of Flows:** Example: Herringbone when two flows are to be mixed (Whitesides and co-workers)
2) **Mixing in a micro-wells.** No flow. Examples: Shakers, magnetic elements, ultrasound

Typical Research Issues:

1) Increase rate of mixing (increase throughput)
2) Avoid damage to biosamples due to large electrical, magnetic, mechanical forces.

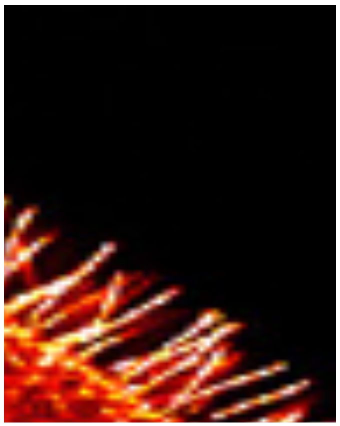
Proposed Approach

Cilia-based approach to fluid
Manipulation

Why?

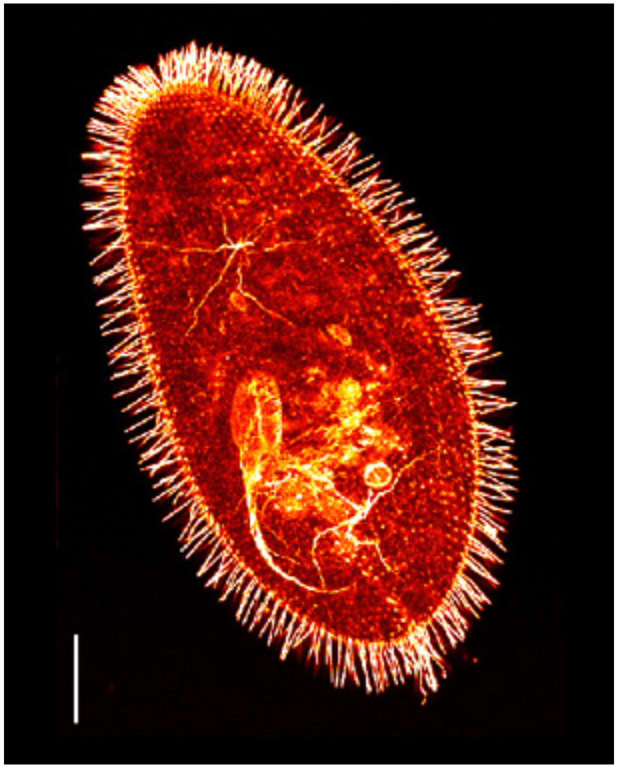
Biomimetic --- similar to biological systems and therefore, hopefully, less damage to samples

What are Cilia?



Cilia are Fine, hair like (micron scale) structures that beat in a Rythmic manner **(10-100 Hz)**

What are Cilia?



Cilia are Fine, hair like (micron scale) structures

Rythmic beating (10-100 Hz) is used

1) To generate motion, e.g, paramecium swimming

Paramecium --- thousands of cilia

Photo by Anne Fleury, Michael Laurent and Andre Adoutte, Universite Paris-Sud, France http://www.zeiss.de/

What are Cilia?

Cilia are Fine, hair like (micron scale) structures

Rythmic beating (10-100 Hz) is used to

1) Generate motion, e.g, paramecium swimming

2) To move fluid and particles (Lungs)

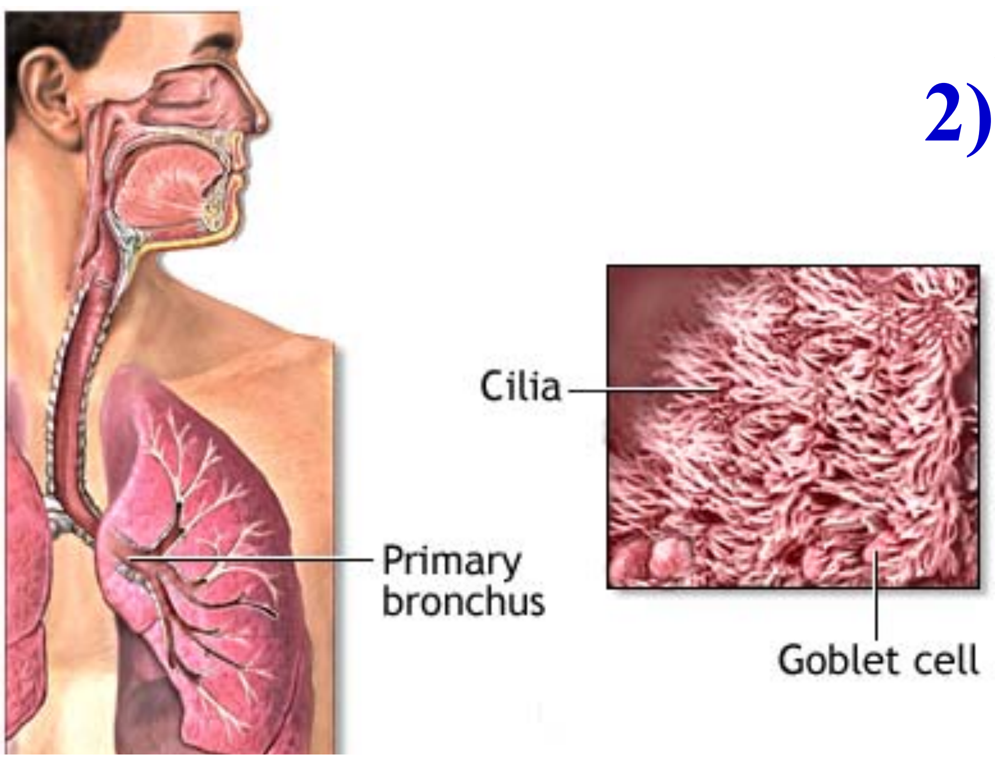


Photo From
http://www.mdconsult.com

Approaches to Artificial Cilia

Several Approaches to Artificial Cilia

Each with its advantages and challenges

Approaches to Artificial Cilia

1)Self-oscillating Polymer Gel:

Advantage --- soft material

Challenge --- Low frequency (0.0055Hz)

2) **PDMS (**polydimethylsiloxane**) Pillars actuated by cardio-myocytes:**

Advantage --- soft cilia

Challenges --- control of the actuation, cell attachment

3) **Ferrofluid-PDMS Composite Nanorod arrays:**

Advantage --- easy to control

Challenges --- fabrication

4) Electro-static actuation of artificial cilia:

Advantage --- easy to control

Challenges --- minimize damage due to high fields

Proposed Approach

Mechanical Resonance

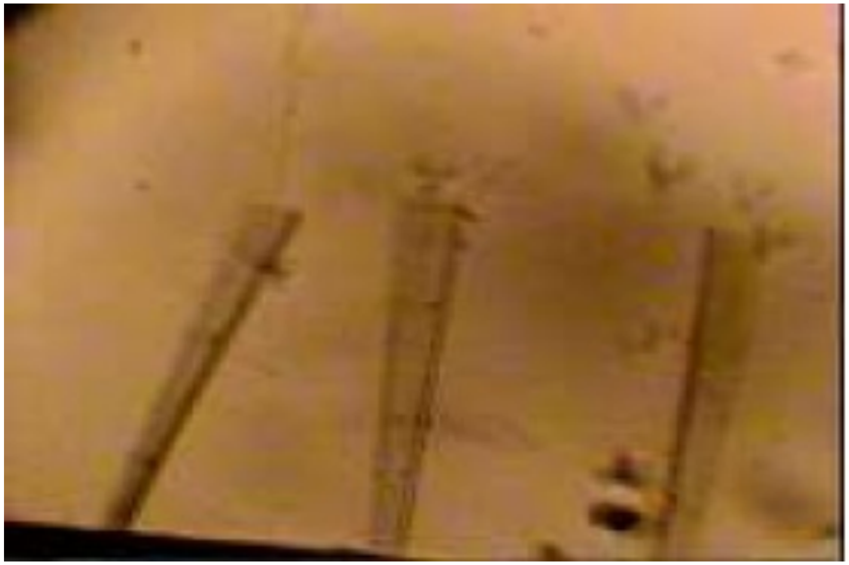
Proposed Approach

Mechanical Resonance

Base motion (with piezo) generates motion of the cilia

Length = 400-700 μ; Width = 10 μ; Height = 45-75 μ
B (Motion) about 20μ

Similarities and Differences



Similarities with Bio-Cilia (1) soft material, (2) similar beat frequency (10-100Hz) as bio-samples --- less damage to soft samples

Differences from Bio-Cilia : Not self actuated

Outline of the talk

1) Motivation and context
2) **Large Cilia motions with Fluid Damping**
3) Can Cilia improve mixing?
    3.1 Will choice of trajectory affect mixing?
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Are Large Cilia Oscillations Possible?

Main Concern

1) Typically, damping ratio can be large in liquids

2) This can prevent large oscillations in fluid

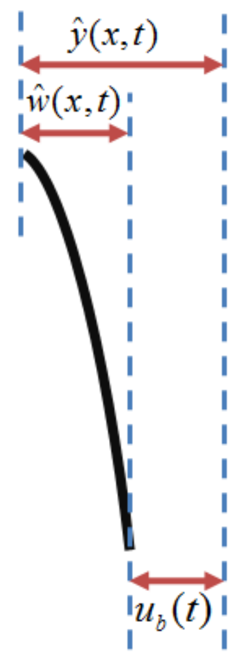
3) Especially since our cilia are not self actuated

Model: Standard Beam Eqs

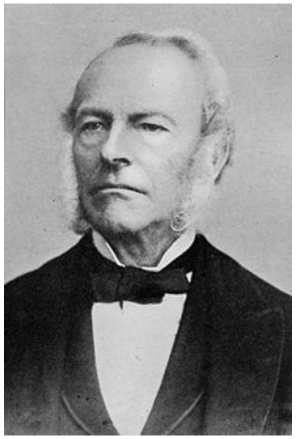
Damping (Fluid, structural) **Stiffness** **Forcing**

$$\frac{\partial^2 \hat{w}(x,t)}{\partial t^2} + \frac{(B_f + B_i)}{\rho_b A_b} \frac{\partial \hat{w}(x,t)}{\partial t} + \frac{EI}{\rho_b A_b} \frac{\partial^4 \hat{w}(x,t)}{\partial x^4} = r(t)$$

Mass



Brief History: Added Mass



Sir George Gabriel Stokes (1819–1903)
Photo from http://en.wikipedia.org/wiki/George_Gabriel_Stokes

- Dubuat oscillation of pendulums in water in 1786
- History written by Stokes in 1850

- The added-mass effect arises because of the need to accelerate the fluid around an object when it is accelerated through a fluid – increase in inertia!

Added Mass

Damping (Fluid, structural) **Stiffness** **Forcing**

$$\frac{\partial^2 \hat{w}(x,t)}{\partial t^2} + \frac{(B_f + B_i)}{\rho_b A_b} \frac{\partial \hat{w}(x,t)}{\partial t} + \frac{EI}{\rho_b A_b} \frac{\partial^4 \hat{w}(x,t)}{\partial x^4} = r(t)$$

Mass

$$\frac{\partial^2 \hat{w}(x,t)}{\partial t^2} + \frac{(B_f + B_i)}{\rho_b A_b (1 + C_m)} \frac{\partial \hat{w}(x,t)}{\partial t} + \frac{EI}{\rho_b A_b (1 + C_m)} \frac{\partial^4 \hat{w}(x,t)}{\partial x^4} = r^*(t)$$

Added Mass

Additional Details in Paper

ASME J of Vibration and Acoustics, 2010

Damping (Fluid, structural) **Stiffness** **Forcing**

$$\frac{\partial^2 \hat{w}(x,t)}{\partial t^2} + \frac{(B_f + B_i)}{\rho_b A_b}\frac{\partial \hat{w}(x,t)}{\partial t} + \frac{EI}{\rho_b A_b}\frac{\partial^4 \hat{w}(x,t)}{\partial x^4} = r(t)$$

Mass

$$\frac{\partial^2 \hat{w}(x,t)}{\partial t^2} + \frac{(B_f + B_i)}{\rho_b A_b (1 + C_m)}\frac{\partial \hat{w}(x,t)}{\partial t} + \frac{EI}{\rho_b A_b (1 + C_m)}\frac{\partial^4 \hat{w}(x,t)}{\partial x^4} = r^*(t)$$

Added Mass

Main Effects ---
resonance freq reduces by third

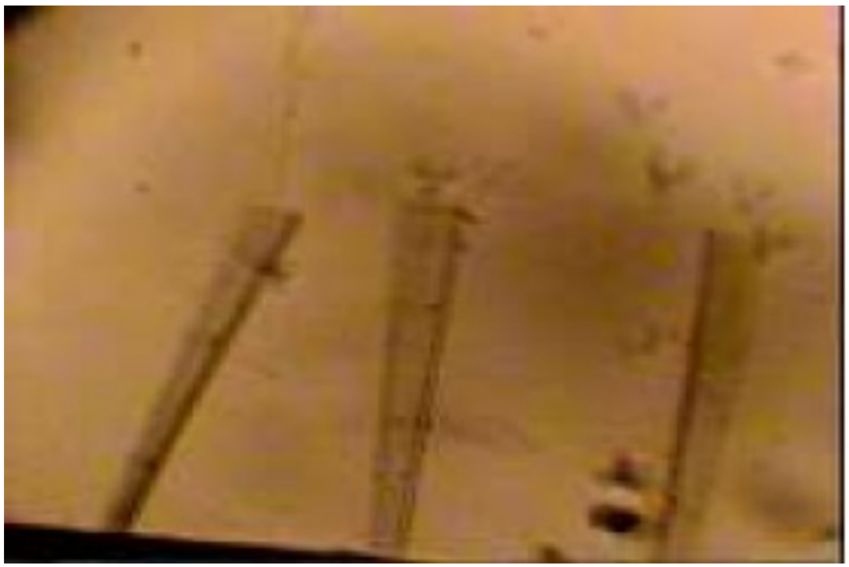
Added Mass Effect Reduces Natural Frequency, and therefore reduces resonance frequency

$$\frac{\omega_n^*}{\sqrt{(1+C_m)}}$$

$$\frac{\partial^2 \hat{w}(x,t)}{\partial t^2} + \frac{(B_f + B_i)}{\rho_b A_b (1+C_m)} \frac{\partial \hat{w}(x,t)}{\partial t} + \frac{EI}{\rho_b A_b (1+C_m)} \frac{\partial^4 \hat{w}(x,t)}{\partial x^4} = r^*(t)$$

Also reduces damping by a third!

Added Mass effect reduces the damping ratio (overdamped → underdamped)



$$\frac{\zeta_f^*}{\sqrt{(1+C_m)}}.$$

$$\frac{\partial^2 \hat{w}(x,t)}{\partial t^2} + \frac{(B_f + B_i)}{\rho_b A_b (1+C_m)} \frac{\partial \hat{w}(x,t)}{\partial t} + \frac{EI}{\rho_b A_b (1+C_m)} \frac{\partial^4 \hat{w}(x,t)}{\partial x^4} = r^*(t)$$

Outline of the talk

1) Motivation and context
2) Large Cilia motions with Fluid Damping
3) **Can Cilia improve mixing?**
    3.1 Will choice of trajectory affect mixing?
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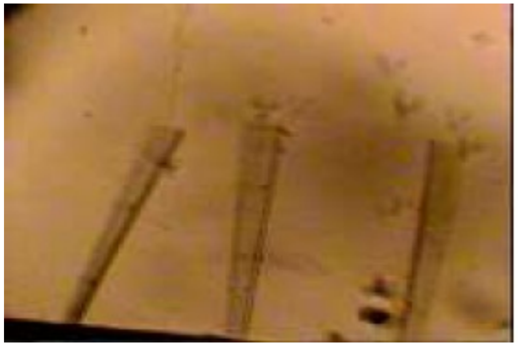
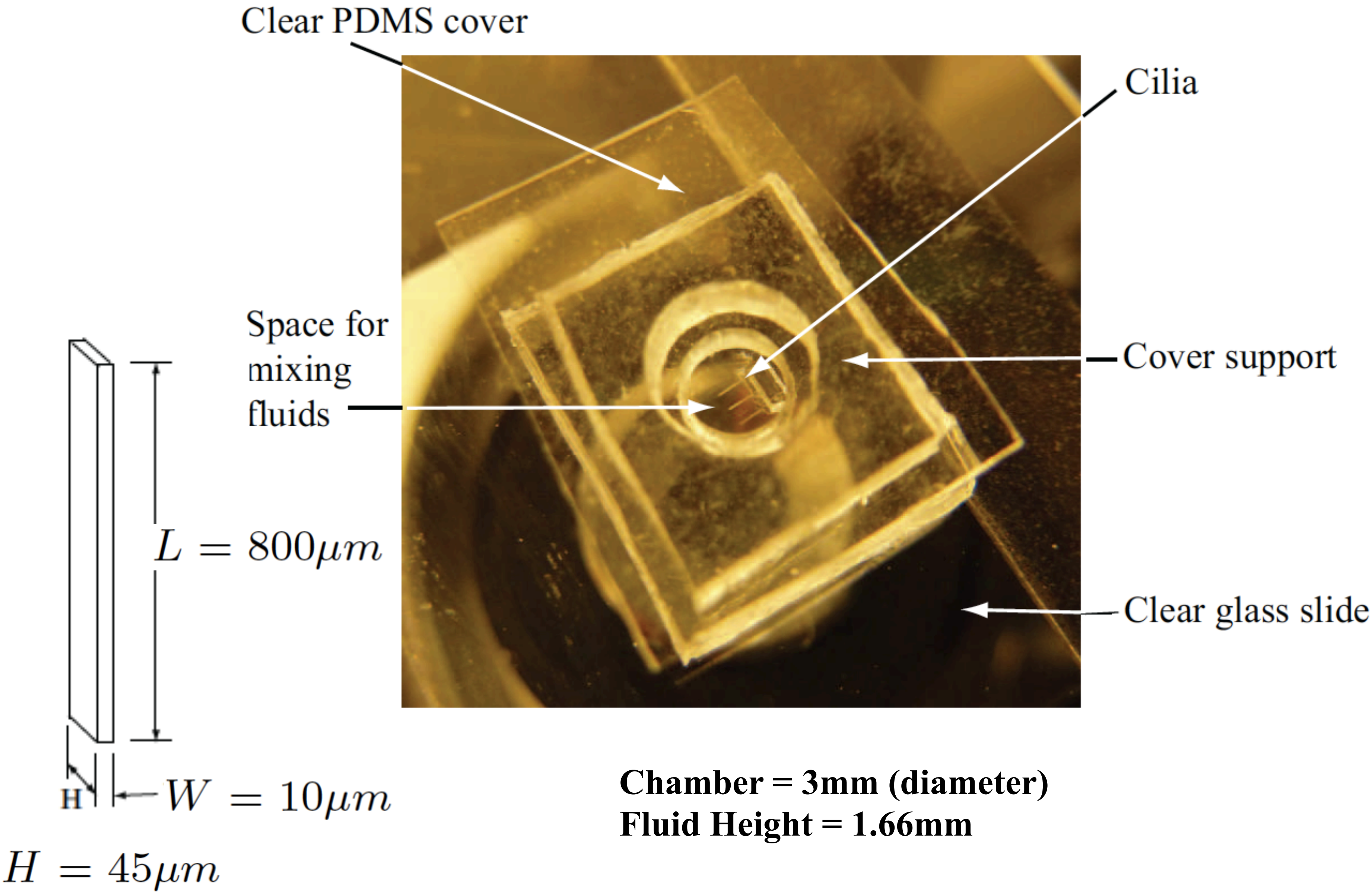
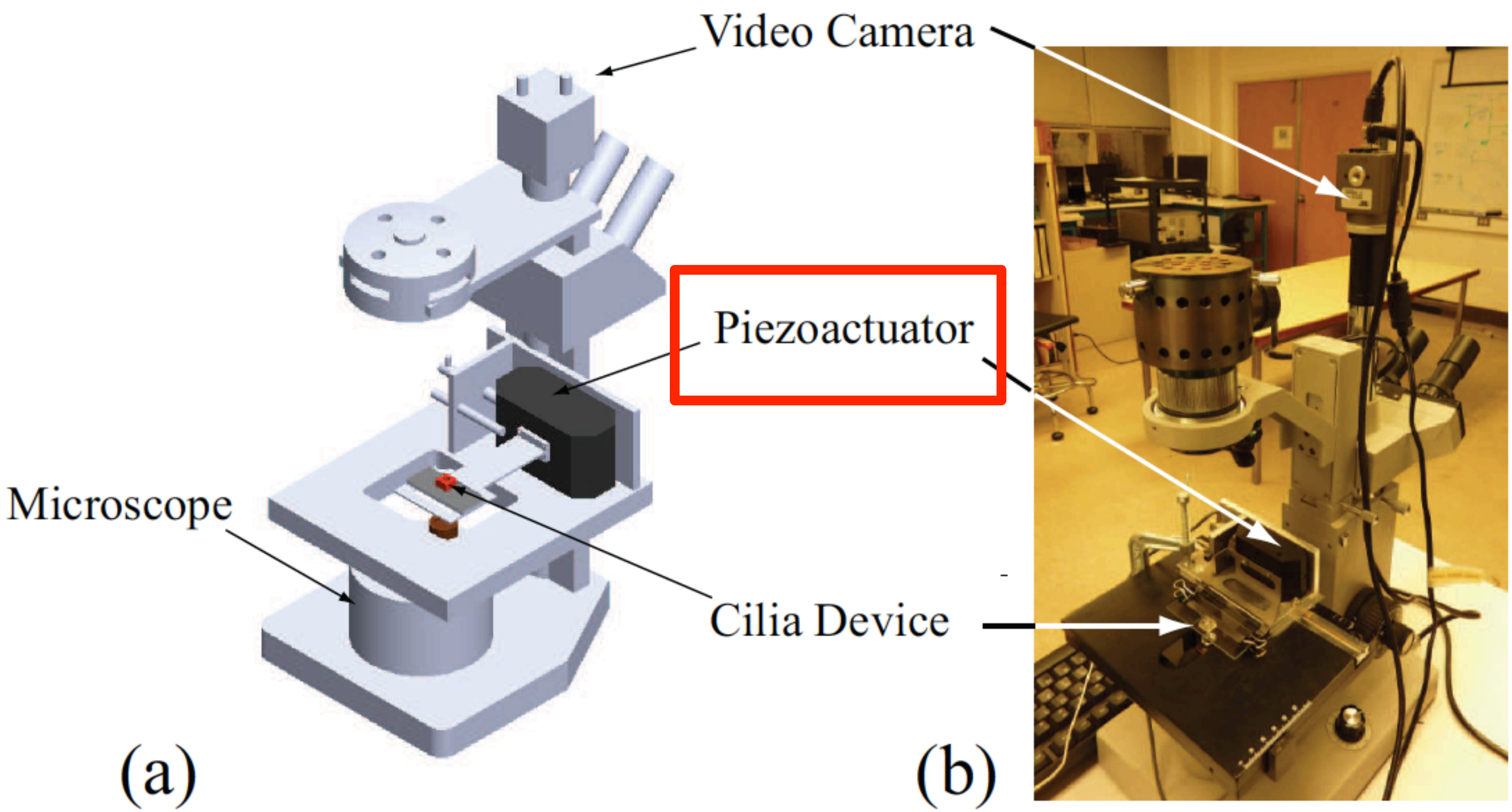


Experimental System: Mixing Chamber



Chamber = 3mm (diameter)
Fluid Height = 1.66mm

Piezo Positioner for exciting motion



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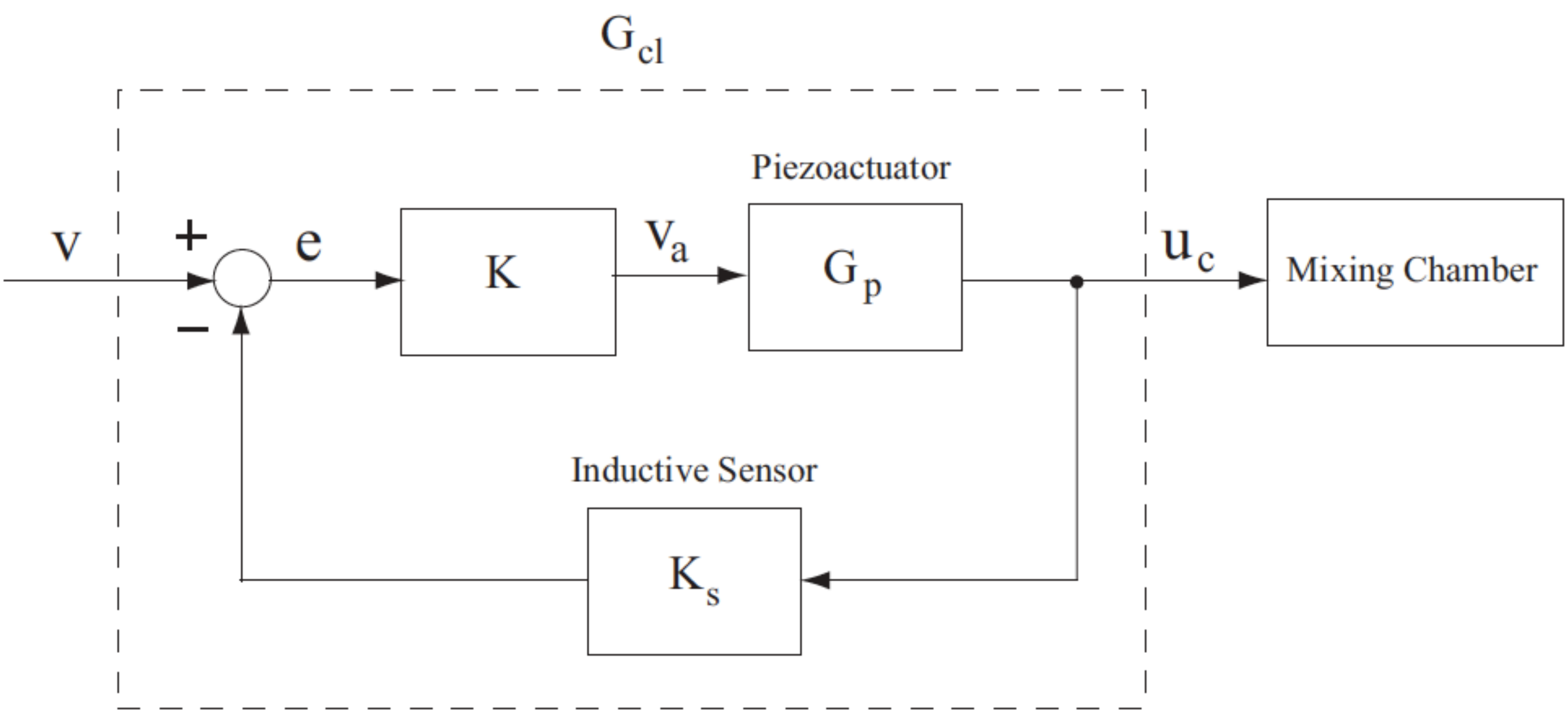
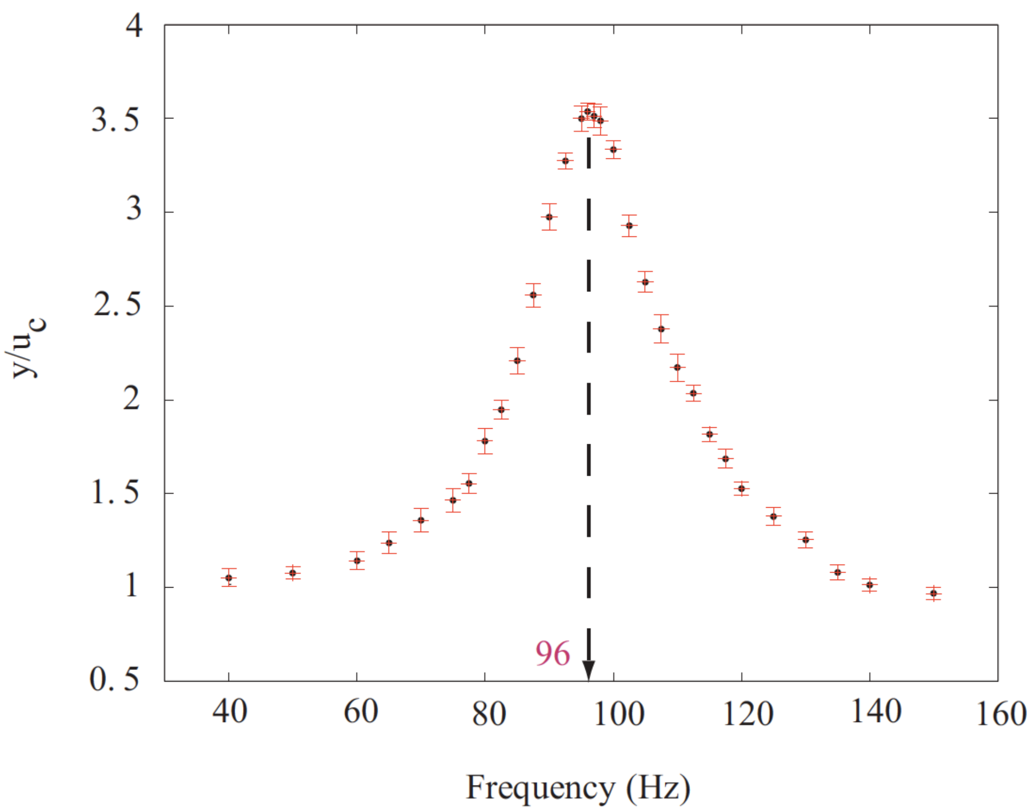
Positioning System Model



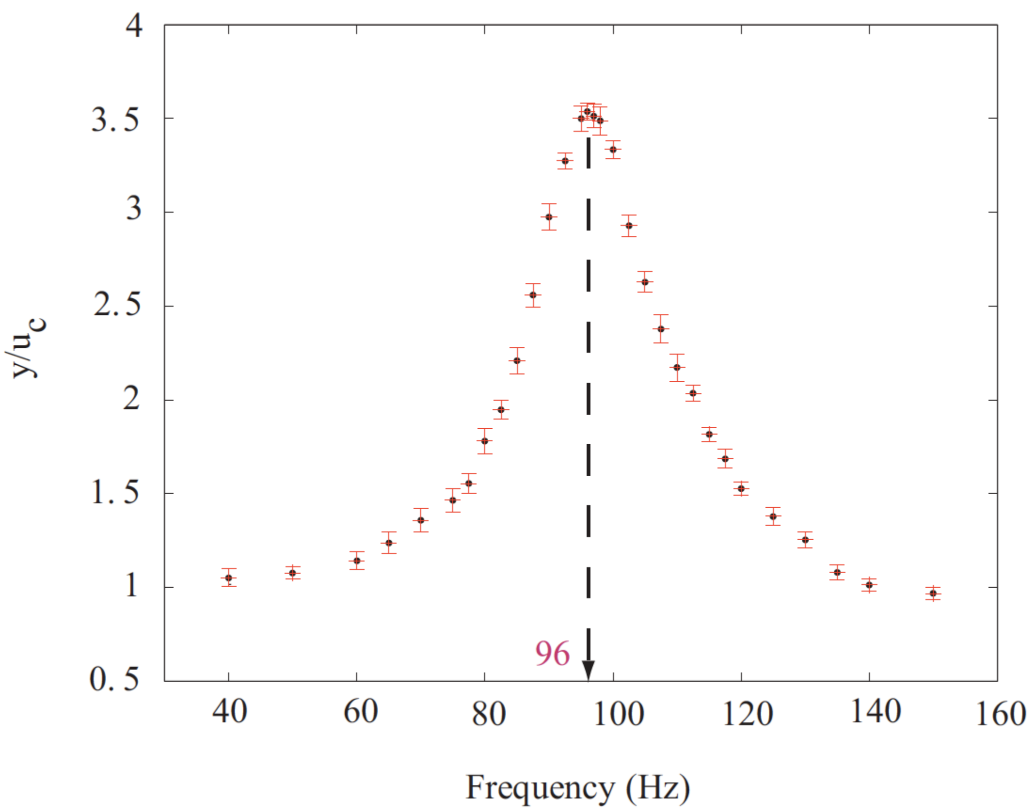
Question: What is a good input trajectory Uc for the cilia chamber for mixing?

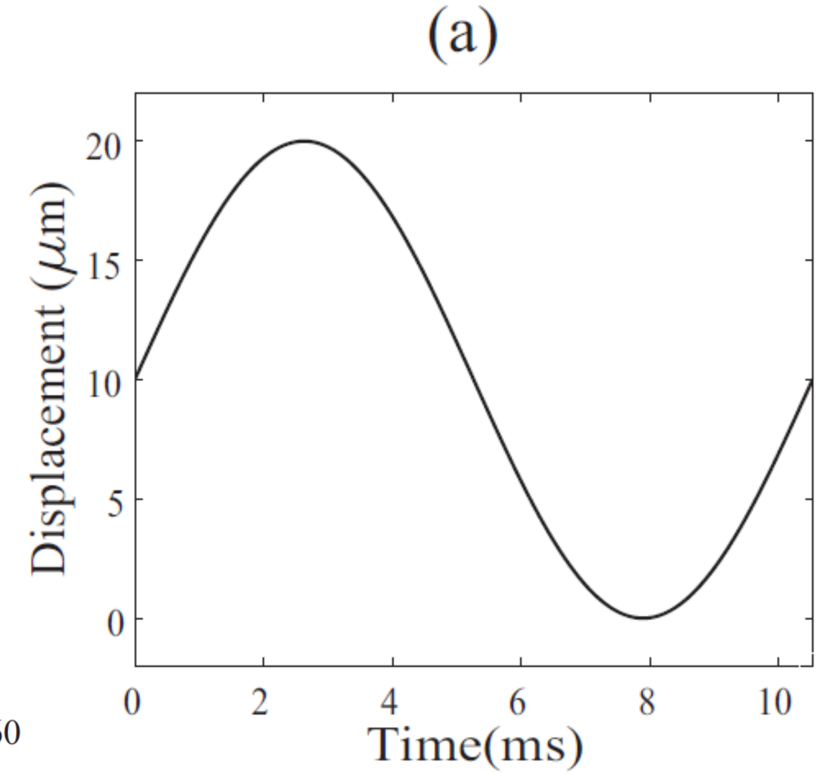
Issue: Choice of Cilia Chamber Trajectories



resonance of cilia in chamber (about 96 Hz)
What is a good chamber positioning trajectory?

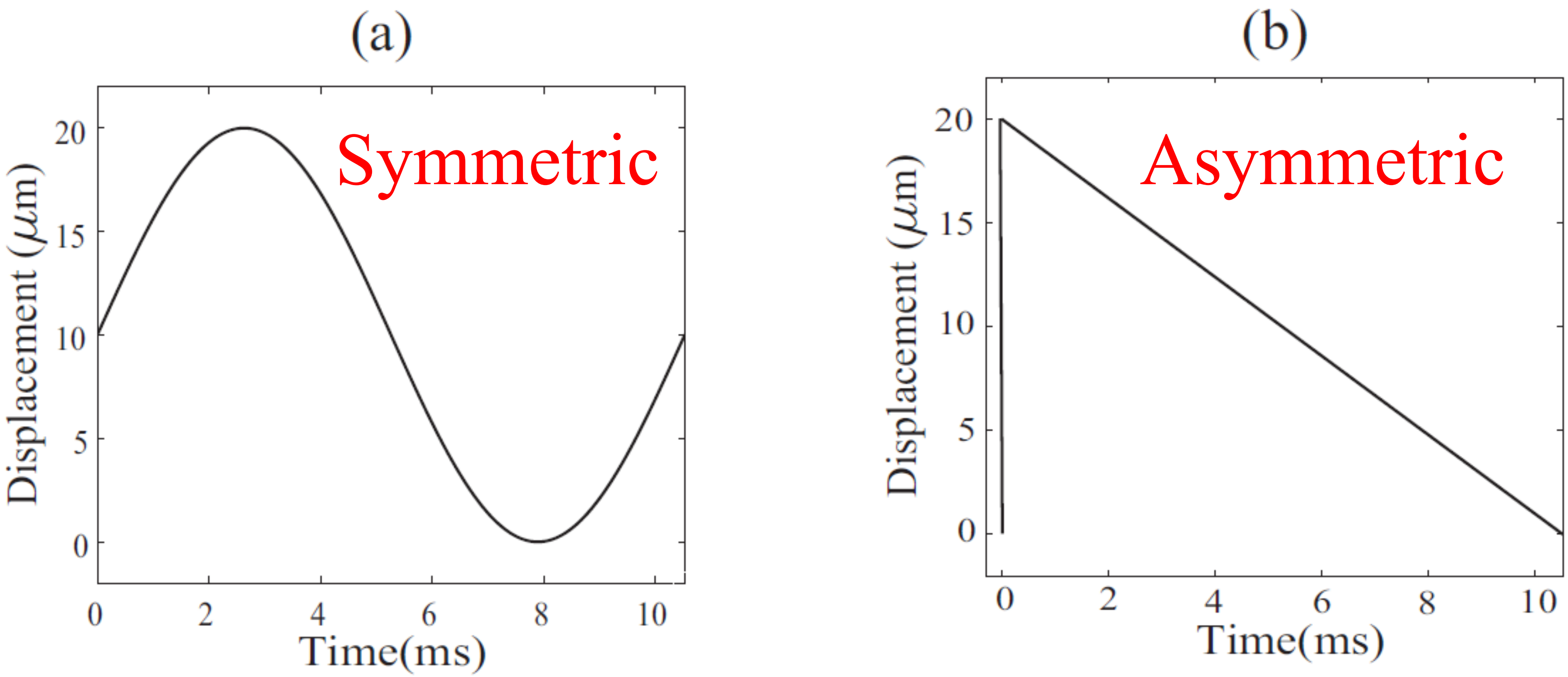
Issue: Choice of Cilia Chamber Trajectories





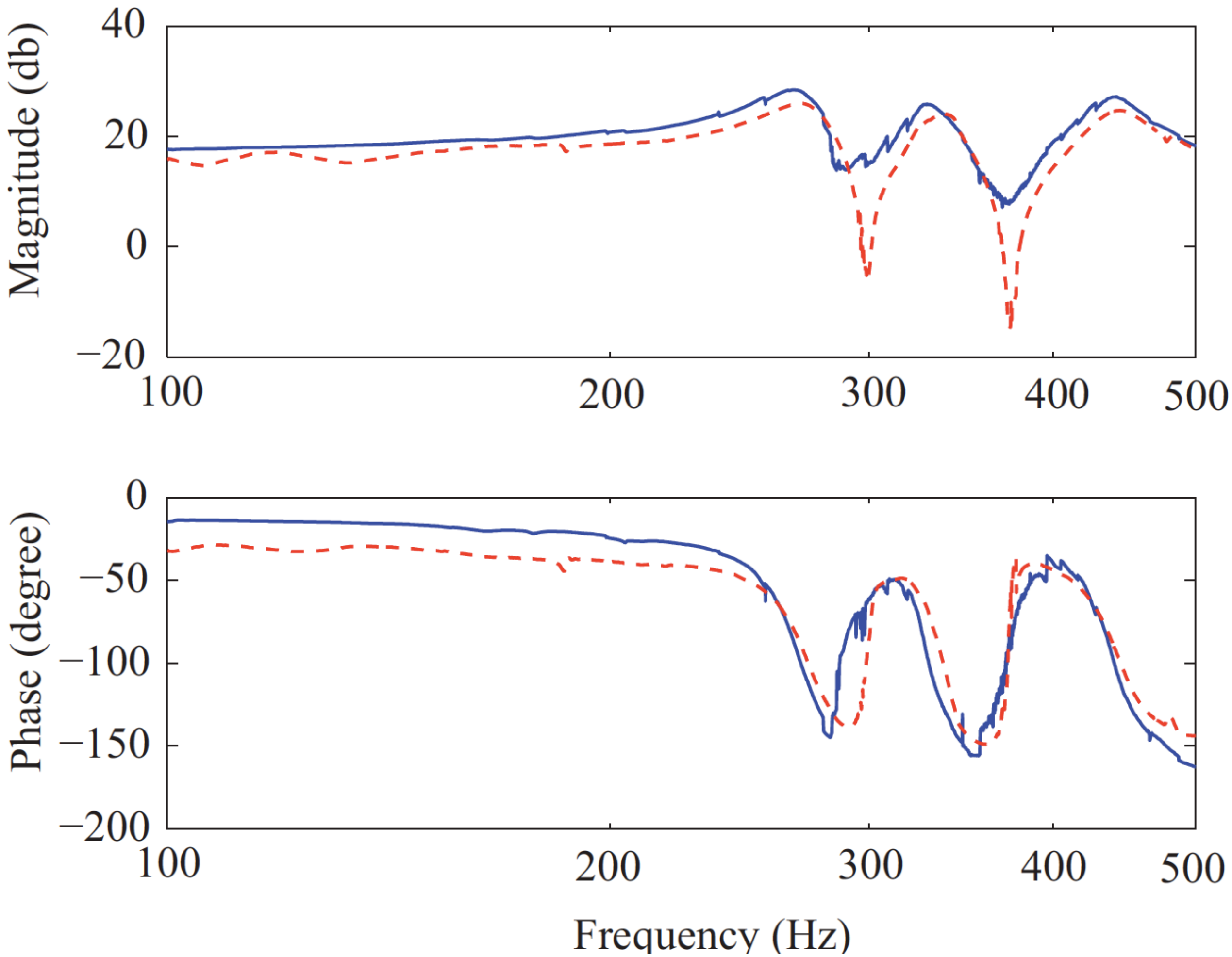
E.g., sinusoidal?
With main frequency = resonance of cilia in chamber
Other chamber positioning trajectories?

Example study: Symmetric vs Asymmetric



Will Asymmetry improve mixing speed?
Such studies require good positioning control !

Challenge in such studies ---Positioning (hysteresis)



Small Amplitude (dashed)

Large Amplitude (solid)
More damping

Amplitude dependent dynamics in closed-loop system due to hysteresis effects (more damped)

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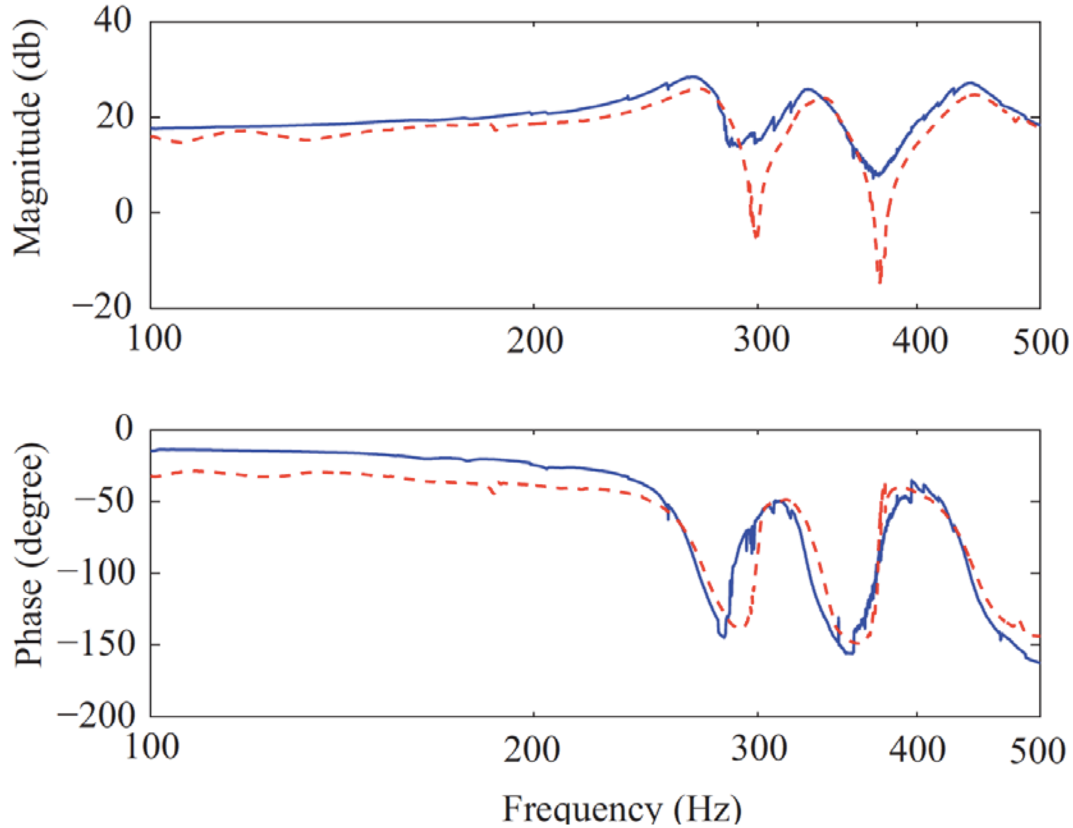
Challenge

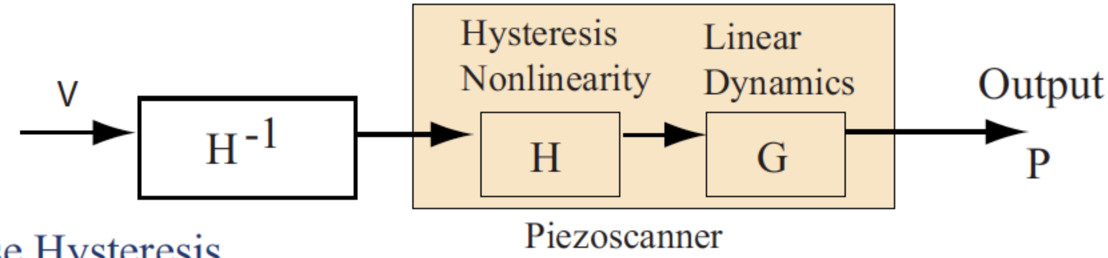


Small Amplitude (dashed)

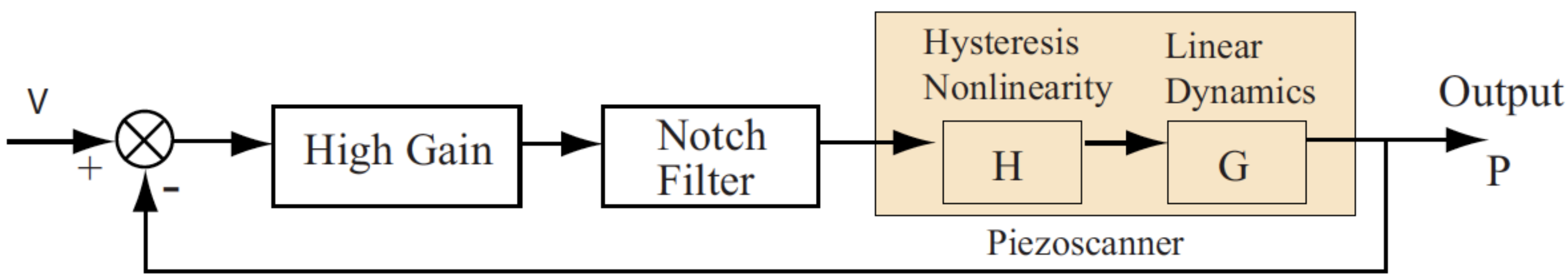
Large Amplitude (solid)
More damping

Positioning error makes it difficult to evaluate different mixing strategies.
We need to correct such dynamics effects to evaluate different vibration schemes

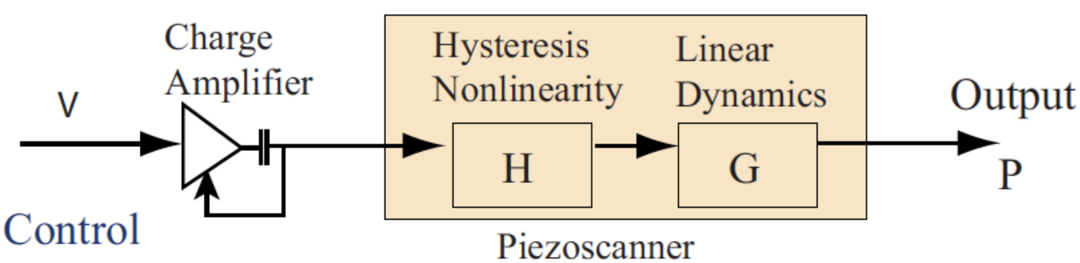
Approaches to correct hysteresis



(a) Inverse Hysteresis



(b) High-gain Feedback Control



(c) Charge Control

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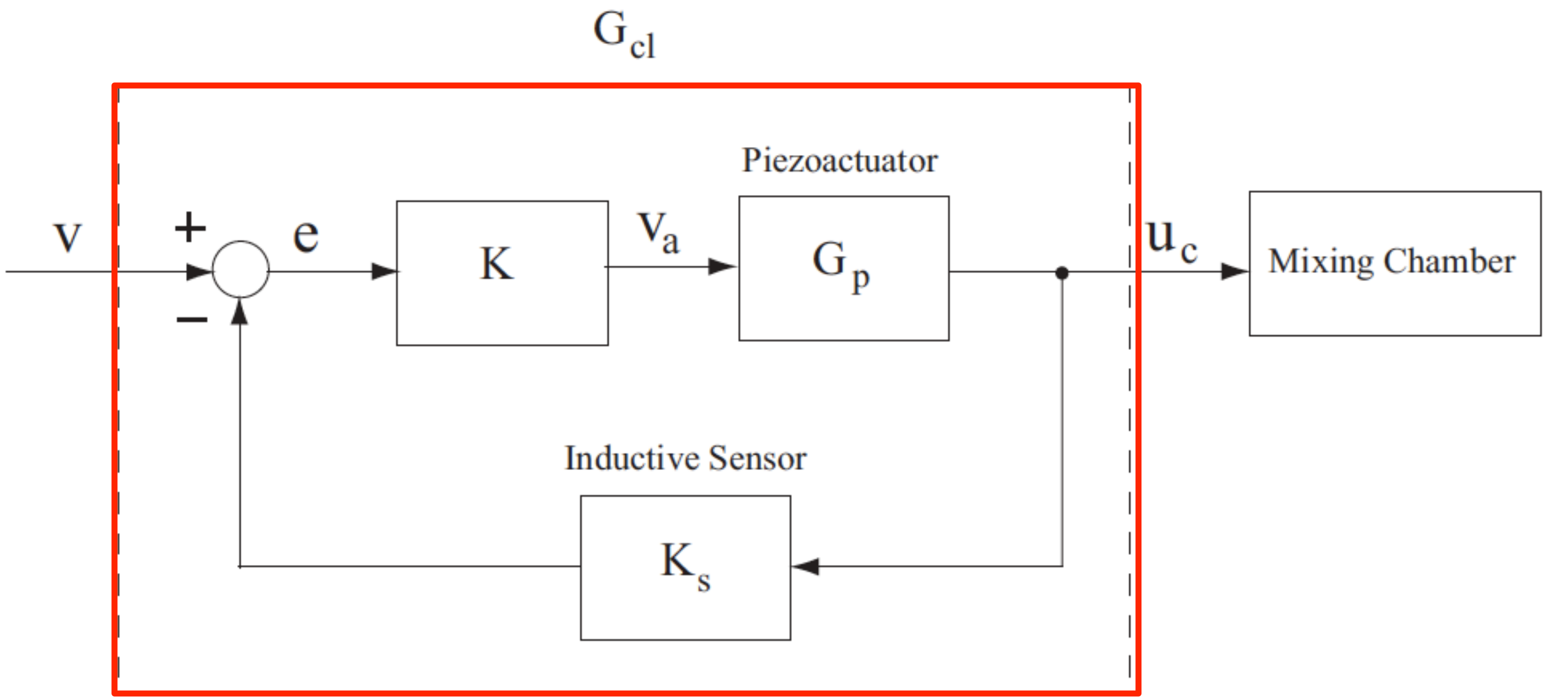
Our approach --- iterative correction



$$V_{opt,k}(\omega) = V_{opt,k-1}(\omega) + \rho(\omega) G_{cl,opt}^{-1}(\omega) \left[u_{c,p}(\omega) - u_{c,k-1}(\omega) \right]$$

Our approach --- iterative correction

We can usually track within 2*(noise level) with such an iterative approach

$$V_{opt,k}(\omega) = V_{opt,k-1}(\omega) + \rho(\omega) G_{cl,opt}^{-1}(\omega) \left[u_{c,p}(\omega) - u_{c,k-1}(\omega) \right]$$

Need to worry about convergence

$$V_{ff,k+1}(j\omega) = V_{ff,k}(j\omega) + \rho(j\omega)\left[G^{-1}(j\omega)\right]\left[E_k(j\omega)\right].$$

1) the magnitude of phase variation is less than $\pi/2$ $|\Delta_\theta(\omega)| < \pi/2$, at frequency ω; and
2) the iteration coefficient $\rho(\omega)$ in (9) is chosen as

$$0 < \rho(\omega) < \frac{2\cos\left(\Delta_\theta(\omega)\right)}{\Delta_r(\omega)}.$$

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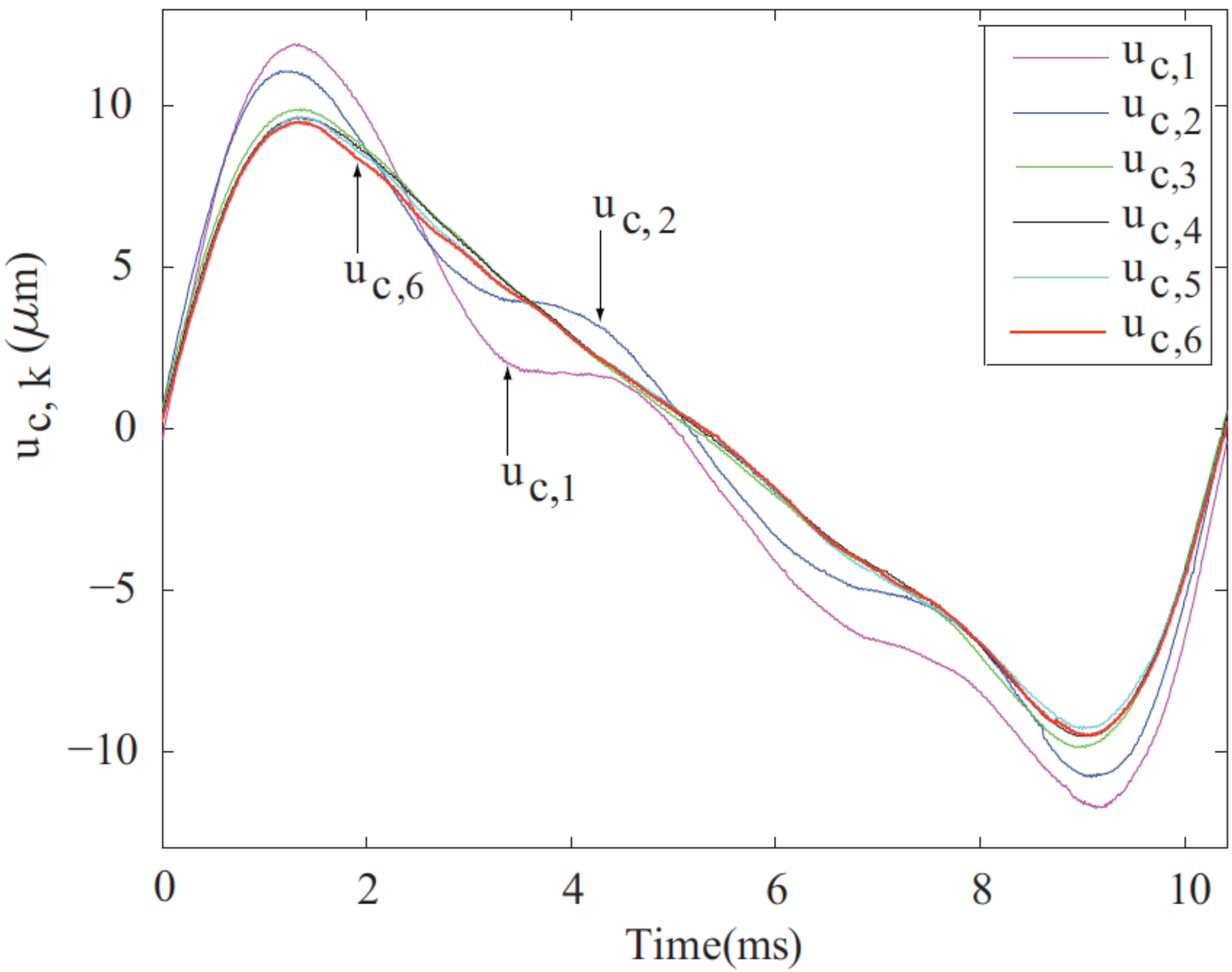
Tracking Results

Reduction in tracking error



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Quantify: Reduction in tracking error

Iteration Step k	$E_{k,max}$ μm	$E_{k,rms}$ μm
1	2.71	82.82
2	2.17	47.98
3	0.90	21.01
4	0.81	14.27
5	0.66	11.45
6	0.37	8.51

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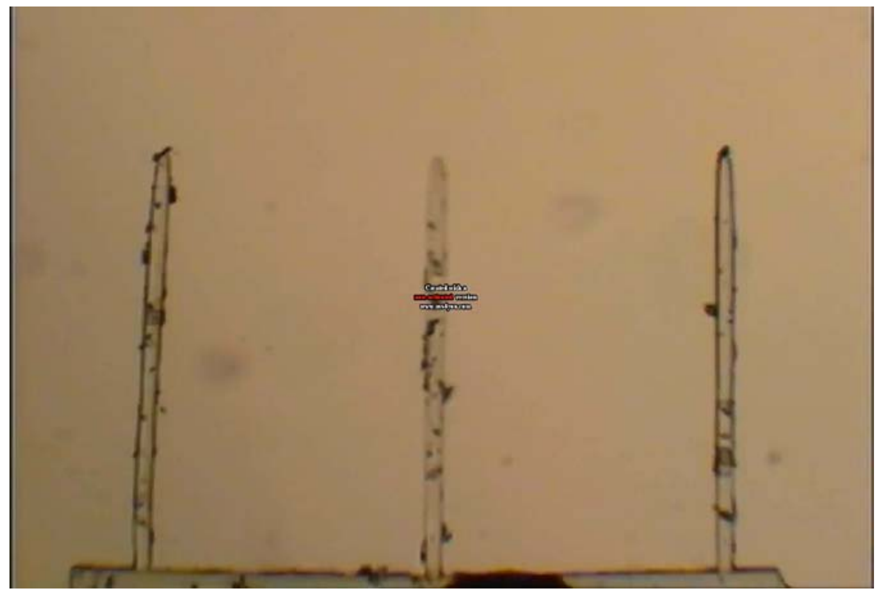
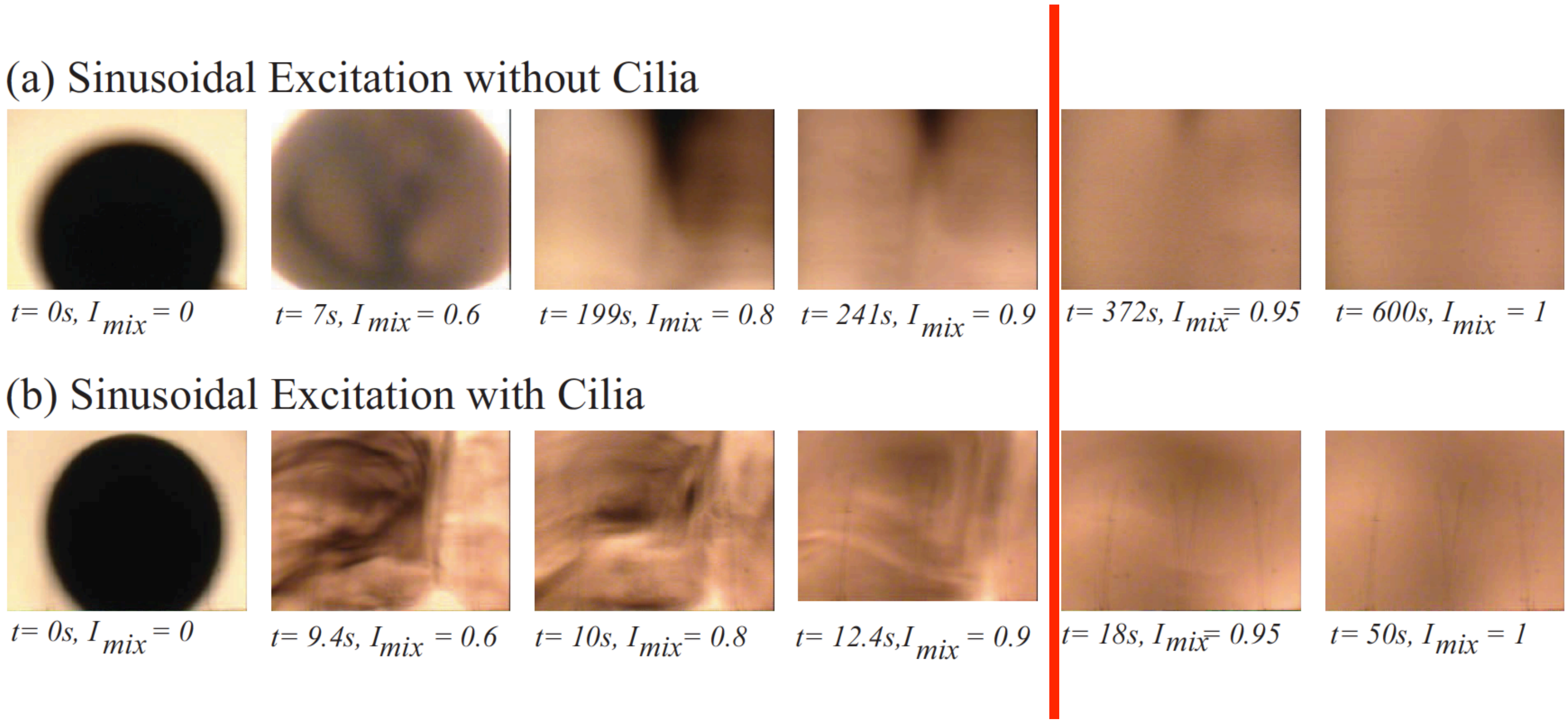
Videos – Example results

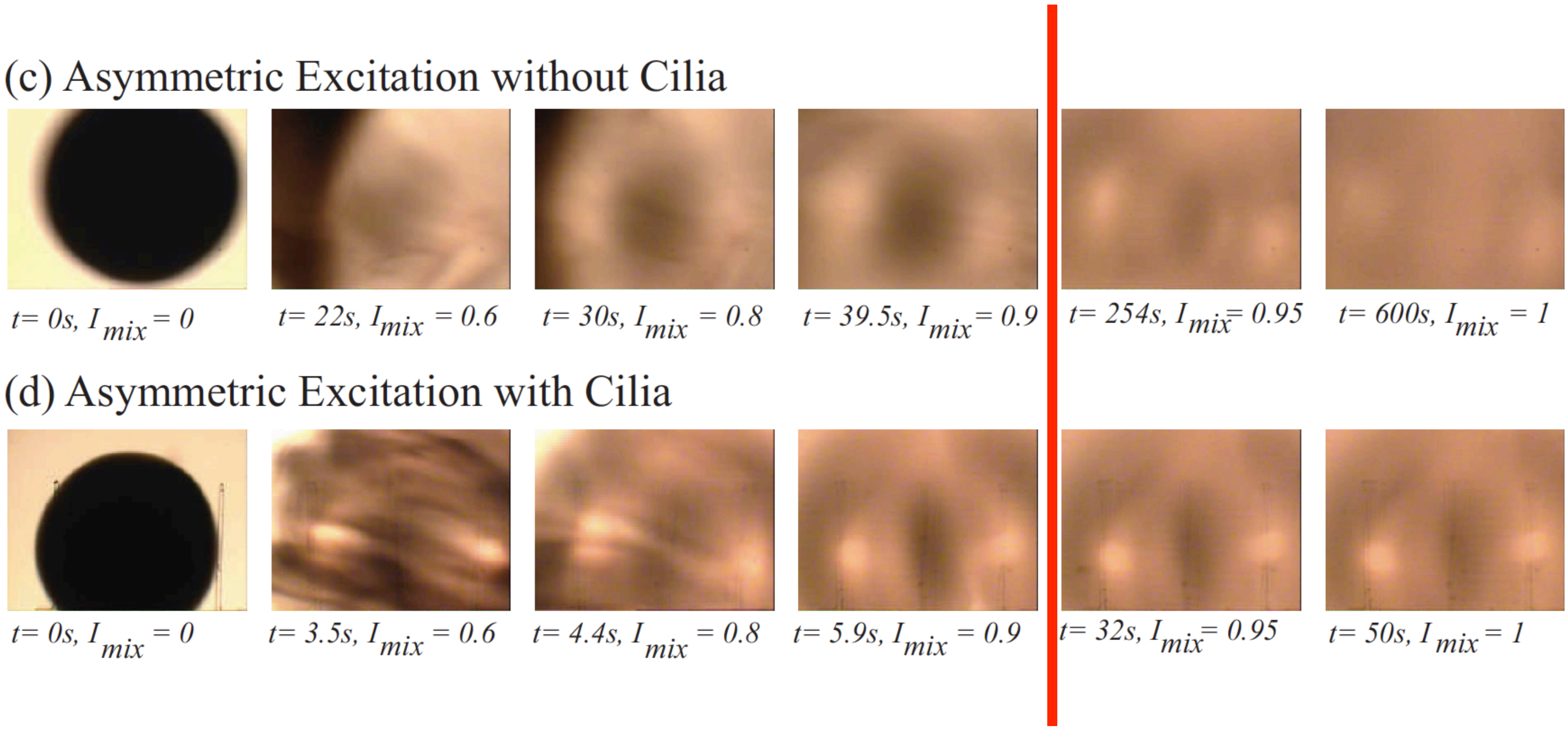


Sinusoidal case -- with/without cilia



Mixing (90%) without cilia completed in about 241 seconds
Mixing (90%) with cilia completed in about 12.4 seconds

Asymmetric case -- with/without cilia



Mixing (90%) without cilia completed in about 39 seconds
Mixing (90%) with cilia completed in about 5.9 seconds

Quantifying the mixing

before ink drop | *t= 0s* | *t= 3.5s* | *t=50s* | *t=69.7s* | *t=72s*

Note: final image at 72 seconds is dark when compared to initial image before ink drop --- addition of ink

Spots can appear due to reflections of lights when surface is sloshing

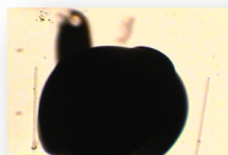
Need to look for image to reach steady state (even with the spots)

Quantifying the mixing

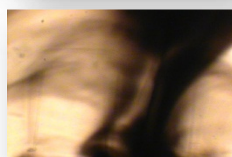
- Approach: use a "mixing index" that can describe the amount of mixing that has occurred at a given time.

$$I^*_{mix} = \left(1 - \frac{\int_A |c_i - c_\infty| dA}{\int_A |c_0 - c_\infty| dA}\right)$$

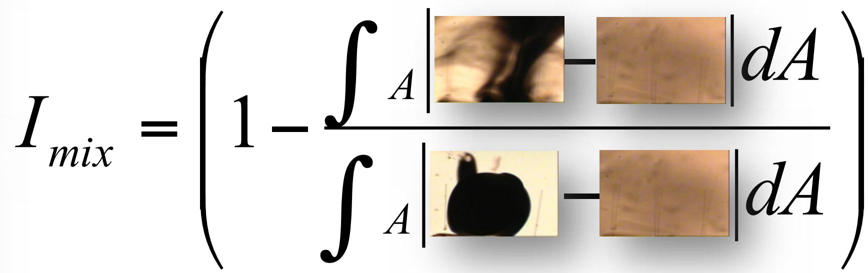
  - C_o is the first frame



  - C_i is the current frame

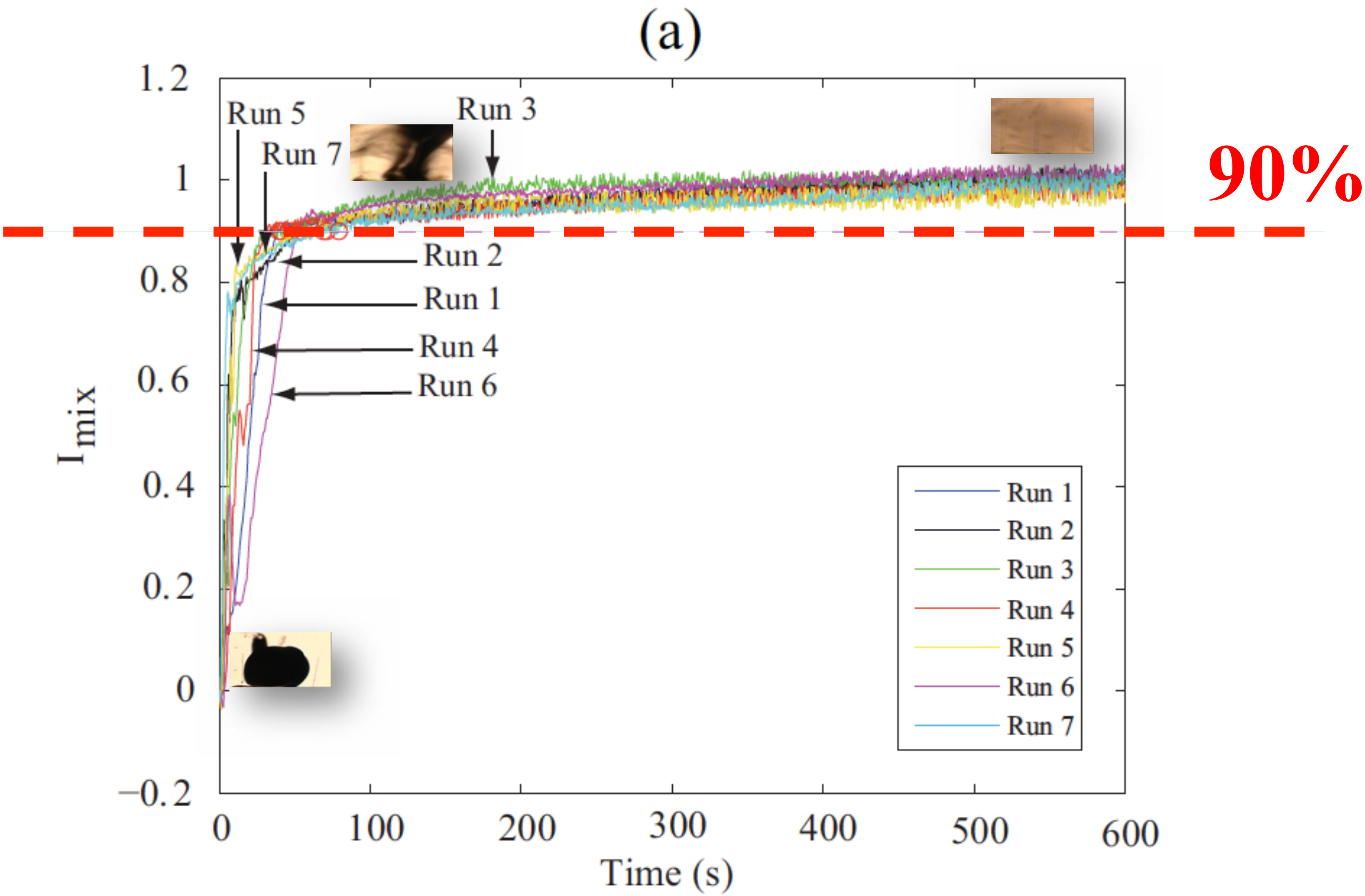


  - C_∞ is the last frame



Implies that if the last image is fully mixed and the first is unmixed, the mixing index will go from 0 to 1 as the fluids become fully mixed.

90% mixing --- Typical results (average of 7 runs)



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Sinusoidal & Asymmetric cases

Sinusoidal

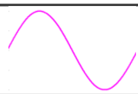
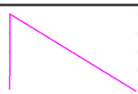
Run Number	No: Mixing Time without Cilia (s)	Yes: Mixing Time with Cilia (s)
1	241.0	12.4
2	182.5	12.2
3	122.0	13.0
4	155.5	14.8
5	230.0	17.3
6	157.0	13.5
7	137.0	11.7
Mean	175.0	13.56
σ	45.45	1.94

Asymmetric

Run Number	No: Mixing Time without Cilia (s)	Yes: Mixing Time with Cilia (s)
1	39.5	5.9
2	69.0	5.0
3	48.0	5.4
4	41.0	5.2
5	71.0	4.4
6	52.5	4.3
7	79.0	6.0
Mean	57.14	5.17
σ	15.74	0.67

Comparison of results

Mixing Time in Second (mean value from 7 runs)

Excitation Wave Form	With Cilia	Without Cilia
 Symmetric	13.56	175
 Asymmetric	5.17	57.14

- **Mixing time can be reduced using cilia**
- **Further reduced using asymmetry**
- **Net reduction --- 175 seconds to 5.17 seconds !**

Conclusions

Mixing Time in Second (mean value from 7 runs)

Excitation Wave Form	With Cilia	Without Cilia
Symmetric	13.56	175
Asymmetric	5.17	57.14

- **Mixing time can be reduced using cilia**
- **Further reduced using asymmetry**
- **Net reduction --- 175 seconds to 5.17 seconds !**
- **Thus, trajectory optimization can be important**
- **The study was facilitated by iterative control**

Overall Accomplishments

1. Design and fabrication of soft Silicone cilia with substantial resonance excitation in an oscillating fluid-chamber
2. Used added mass effect to explain the substantial reduction in the resonance frequency of the cilia
3. Characterized the mixing of fluids with the cilia
4. Developed fluid-structure interaction models to explain the large-amplitude cilia vibrations and mixing improvements
5. Used control techniques to track waveforms for evaluating the effect of different excitation waveforms for mixing
6. Demonstrated more than an order-of-magnitude reduction in the mixing time with the use of cilia when compared to the case without cilia