Laser and Optical Diagnostics for Characterization of DPIs

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https://www.sydney.edu.au/engineering/schools/school-of-aerospace-mechanical-and-mechatronic-engineering.html

Brief Outline of the Talk

- Motivation for our Research Program

- Case Study 1. High Speed Shadowgraph Imaging of Dry Powder Inhaler Flows
- Case Study 2. Optical Coherence Tomography for Deposition Measurement
- Case Study 3. Simple Laser Extinction Methods Applied to Airway Flows

- Summary and Outlook

Motivation

- Develop new capabilities to characterize the behaviour of dry powder inhalers, in real-time, **at the appropriate resolution.**

- Develop methods that can give you a **quick answer early**-that can be used to discount ideas that are not promising, early in the DPI design process.

- **Validate computational models**, it is not adequate to validate based on a final output. A variety of different processes can all lead to the same output.

- New metrics to define inhaler efficacy/bioequivalence

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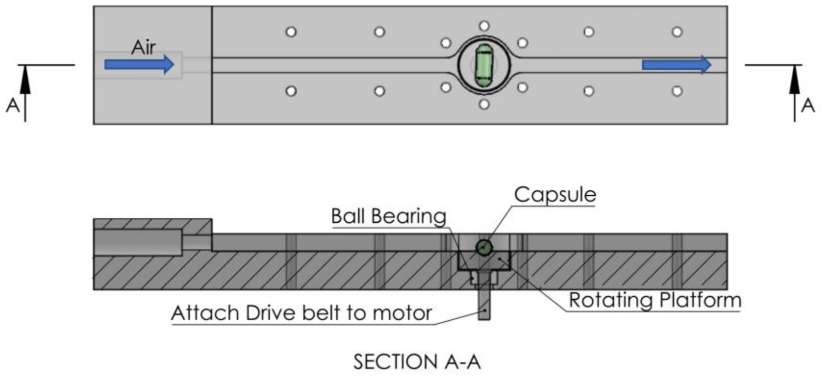
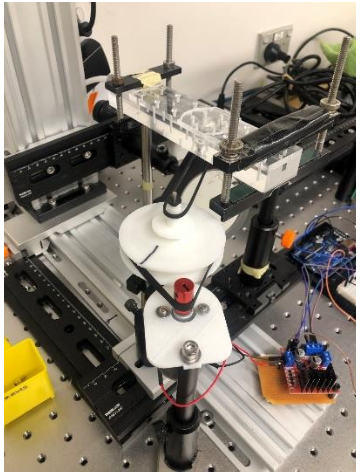
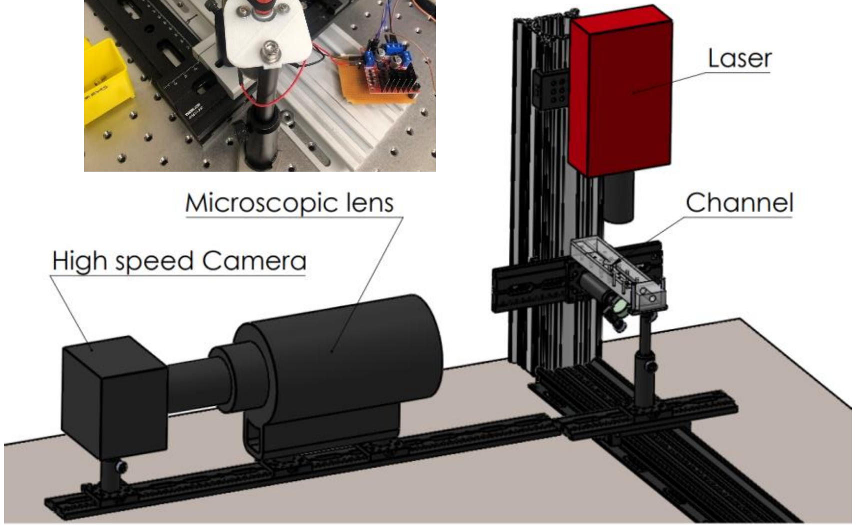
Capsule Rotation Experiment

- Aim: decouple the effects of rotation and flow rate on powder evacuation from a capsule
- Using highspeed microscopic imaging of powder evacuation from an actively spun capsule

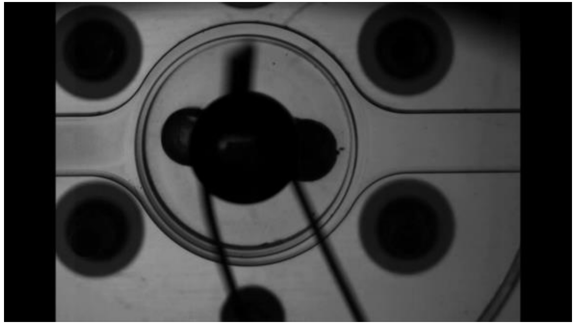




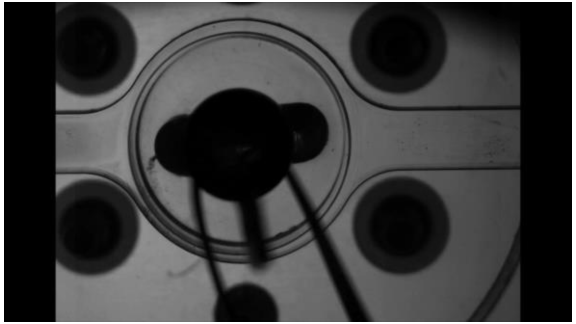


Comparison of Evacuation Behaviour

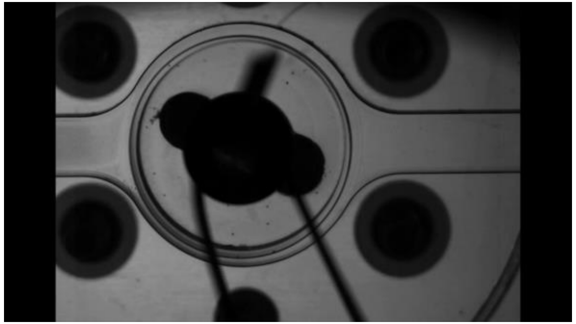
- Macroscopic imaging provides context of overall evacuation behaviour
- Figures below demonstrate the interaction of the capsule rotation and airflow



No Air Flow



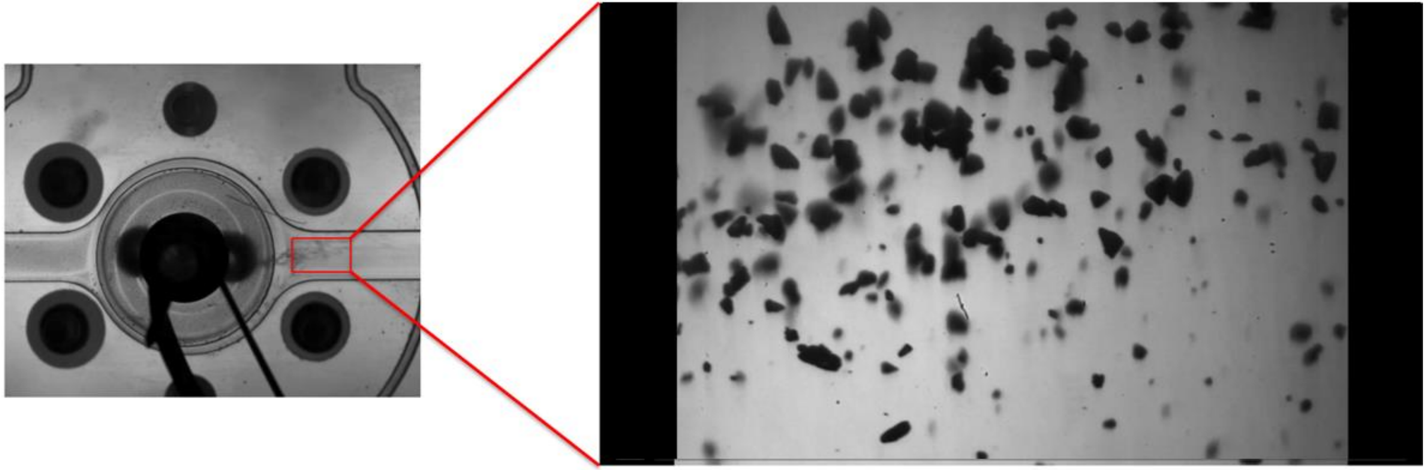
30 SLPM



60 SLPM

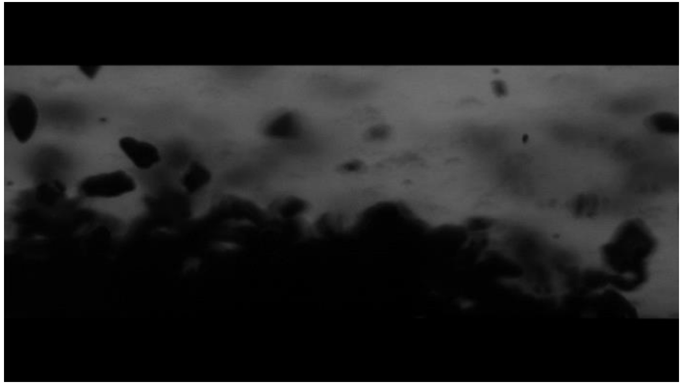
Evacuation of SV010 from capsule at High rotational speed under various flow conditions

Micro HS Shadowgraph



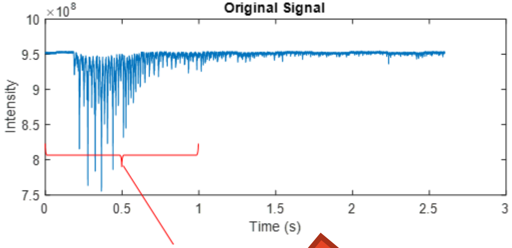
Relevant references:

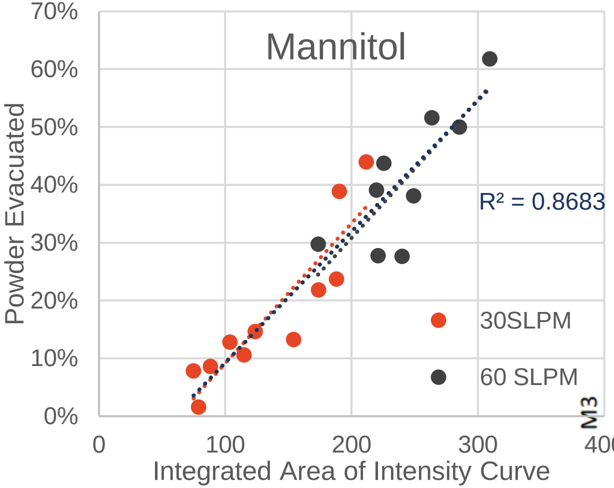
Elserfy et al., IJP, vol. 578, 2020
Elserfy et al., Adv. Powd. Tech., vol. 32(9), 2021
Singh et al., IJP, vol. 608, 2021
Singh et al., IJP, vol. 616, 2022
Azeem et al., Pharm. Res., vol. 40(1), 2023

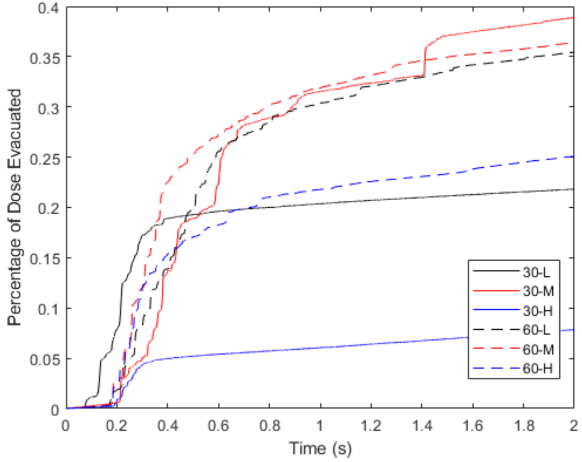


What can you do with these images?

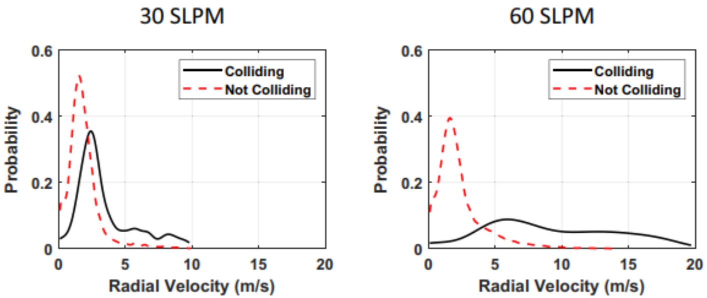
With appropriate calibration:
Size, velocity, dose, various dynamic characteristics







From capsule expt



From an optically accessible inhaler

The University of Sydney

Azeem et al., Pharm. Res.,vol. 40(1), 2023
Azeem et al., AFMC Conference, 2022

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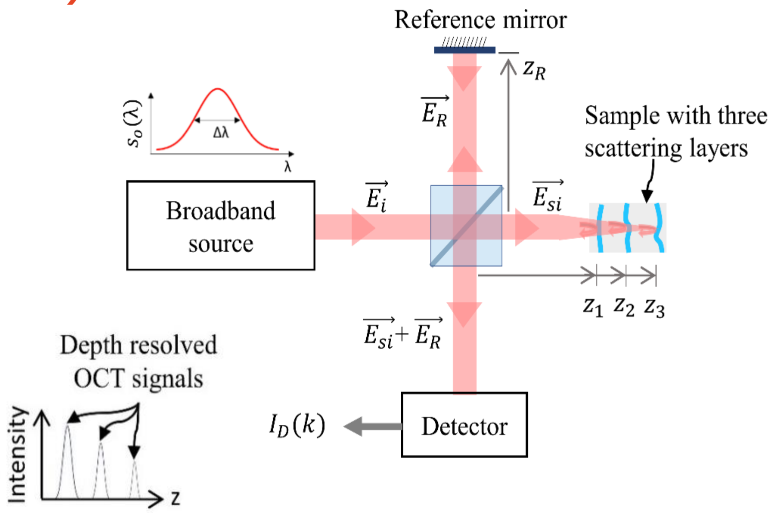
Optical Coherence Tomography (OCT)

- OCT is a tomographic imaging modality commonly used in biomedical imaging and industrial non-destructive testing.

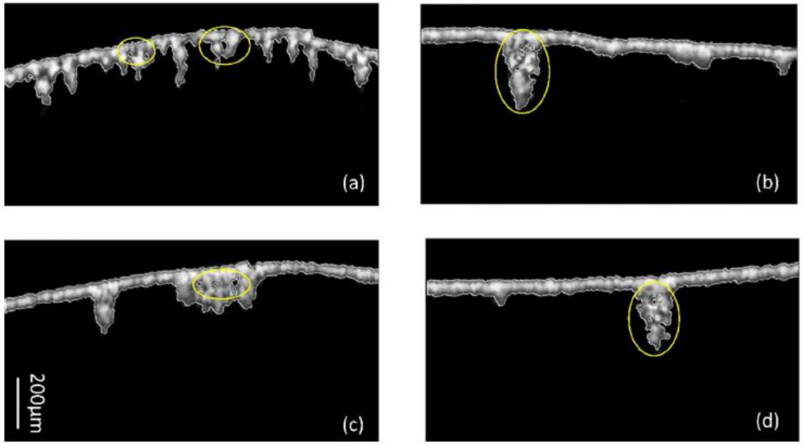
- Analogous to ultrasound imaging - relies on echo-time delay for depth information.

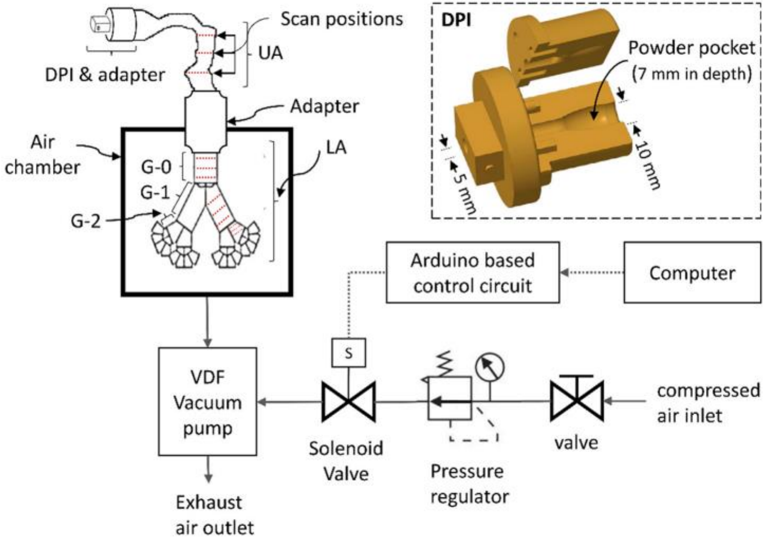


Imaging modality	Resolution	Depth field of view	Speed
Single photon emission computed tomography	10 mm	>50 cm	~ 30mins
Positron emission tomography	4 mm	>50 cm	15- 30 mins
Magnetic resonance imaging	1 mm	>50 cm	5-10 min
X-ray computed tomography	300 µm	>50 cm	1-2 sec
Ultrasound	150 µm	~15 cm	Video rate
Optical Coherence tomography	1-10 µm	2-3 mm	Video rate
Confocal Microscopy	1 µm	200-500 µm	Video rate

Multi-Channel OCT/Time Resolved OCT

- Can we resolve the formation of a particle layer in real-time?
- How uniform is the deposition pattern?
- Are there any agglomerates?
- Can we distinguish between API and carrier in real-time?



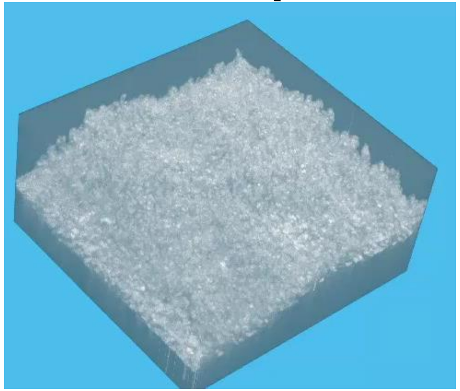


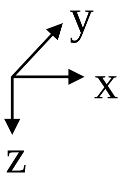
Mekonnen et al., Int.J.Pharm.,vol. 582, 2020
Mekonnen et al., Meas. Sci. Tech., vol. 31, 2020

Tomographic reconstruction of Mannitol and Lactose Carrier using the OCT method

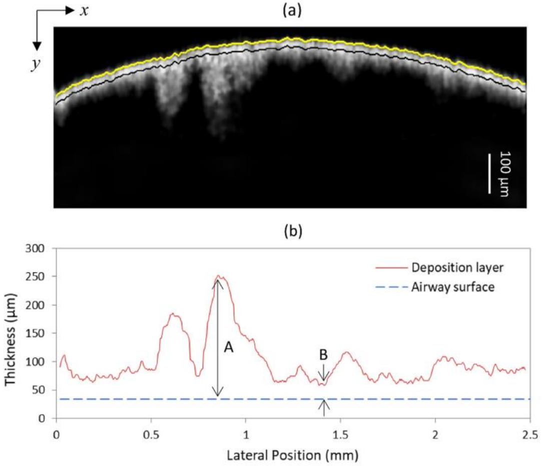
M3 (cohesive)

LH100 (coarse carrier)





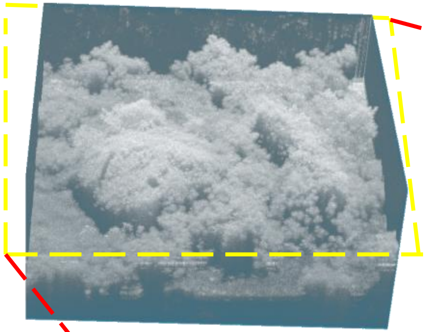
- Applied to in-vitro silicone model (OCT through curved surface)



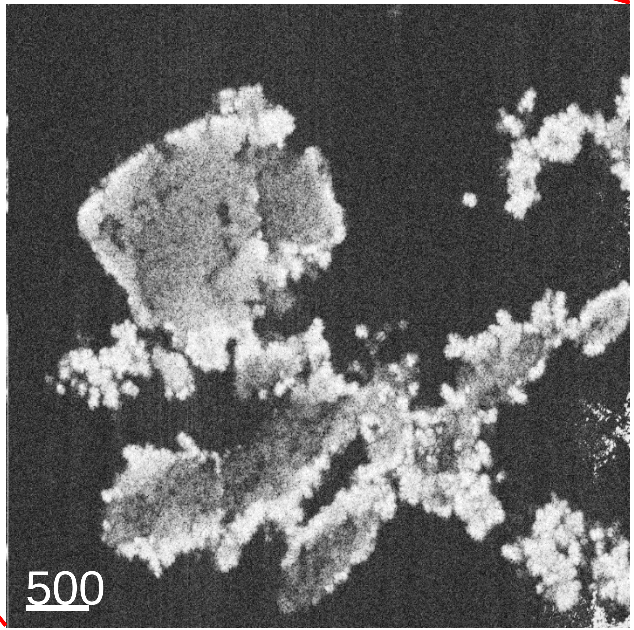
Mekonnen et al., Int.J.Pharm.,vol. 582, 2020

En-face slice of powder bed in-situ

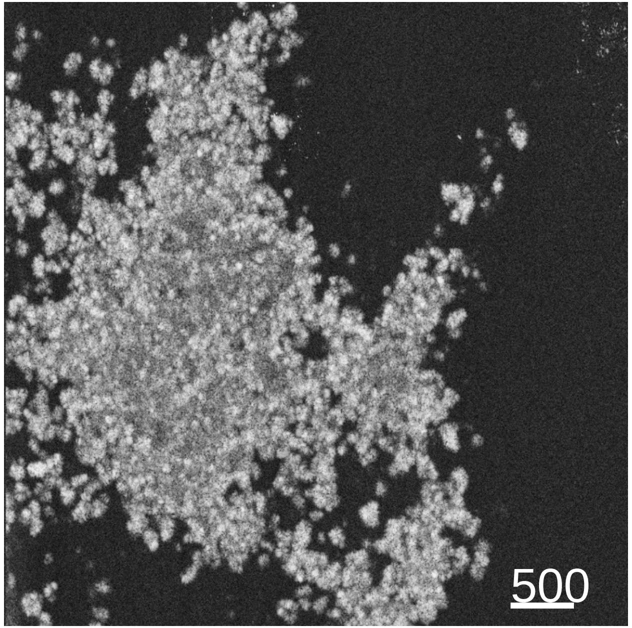
Next is to Expand capability for appropriate time resolution



M3



LH100



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1.Experiment setup (part of larger program with Proveris Scientific Corporation)

- Each laser diode will connect to the power supply
- Photo diode connect to the DAQ board with BNC cable before sending signal into computer
- Able to capture four channel signal simultaneously

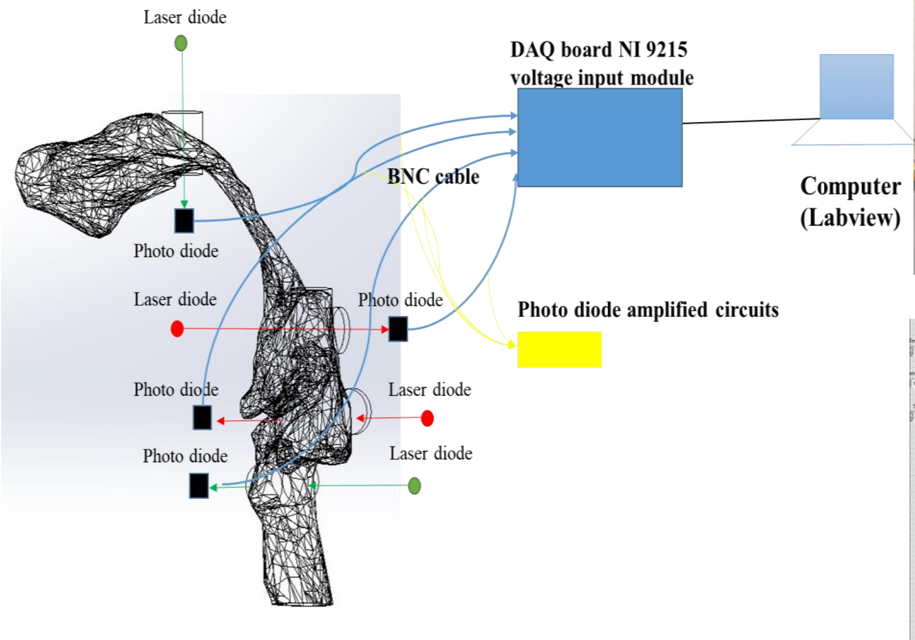


Figure 1. Schematic

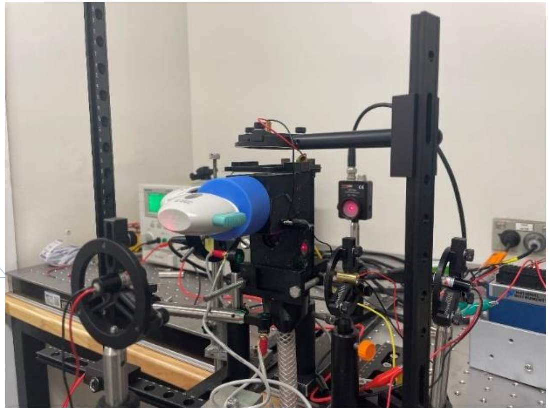


Figure 2. experiment setup (four channels)

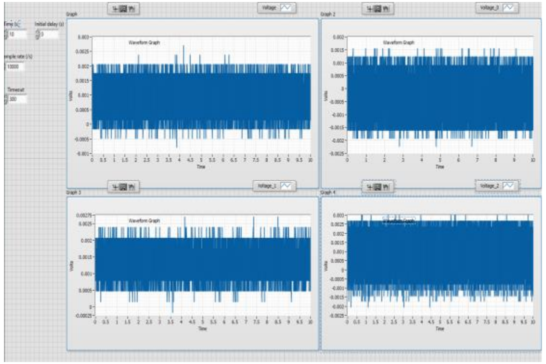
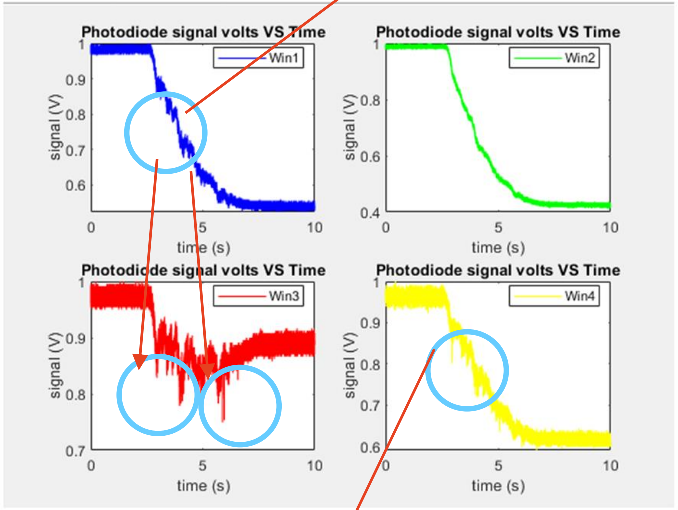


Figure 3. Labview panel

(20LPM, Aerolizer-3um mannitol)

- The powder is gradually released from the Aerolizer under 20LPM condition.
- The powder will accumulate on windows 1,2,4 and the powder release process will last around 3 seconds.
- Unique behaviour noticed in window 3, more unstable flow behaviour after the epiglottis.
- Transmissivity values indicative of local aerosol concentration

Residual powder released from inhaler



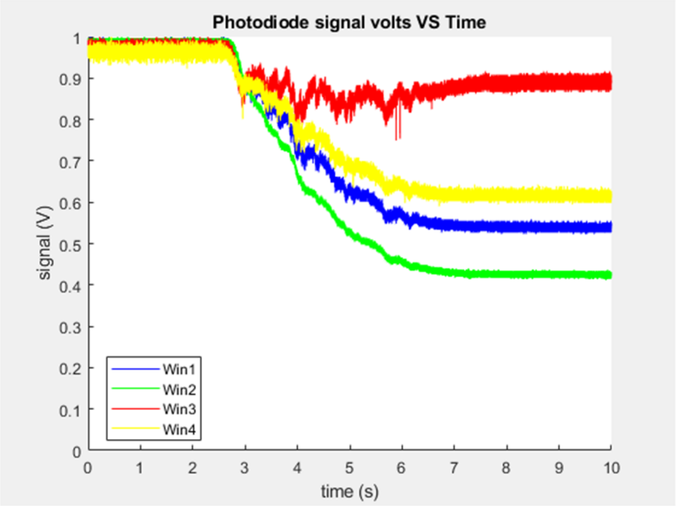


Fig.8. Aerolizer 20L/min

Powder accumulates on the window

Outlook

- Potential to drive the use of more optical and laser diagnostic methods in the characterization of DPIs

- These provide data much faster, and in real-time, but they **need to be made more "user friendly" for wide uptake**, and they need to be better standardized.

- CFD is widely used with minimal validation leading to inconsistent results. This is because of **lack of experiments with well defined boundary and initial conditions**.

- A key focus must be on converting data extracted from these methods **to markers of efficacy.**

People closely involved in this work

- Ms. Athiya Azeem (PhD Candidate-School of AMME, USyd)

- Dr. Taye Mekonnen (Postdoctoral Researcher-School of AMME, USyd)

- Dr. Liam Milton-McGurk (Postdoctoral Researcher-School of AMME, USyd)

- Mr. Zhaoqi Ma (PhD Candidate-School of AMME, USyd)

- Dr. Gajendra Singh (Research Affiliate, School of AMME, USyd)

- Prof. Hak-Kim Chan (School of Pharmacy, USyd)
- A/Prof. Shaokoon Cheng (School of Engineering, Macquarie U.)
- Dino Farina (Proveris Scientific Corporation)

- **Australian Research Council** (Discovery and Linkage Programs)
- **US-Food and Drug Administration**
- **Proveris Scientific Corporation**