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DRUG DELIVERY TO THE LUNGS

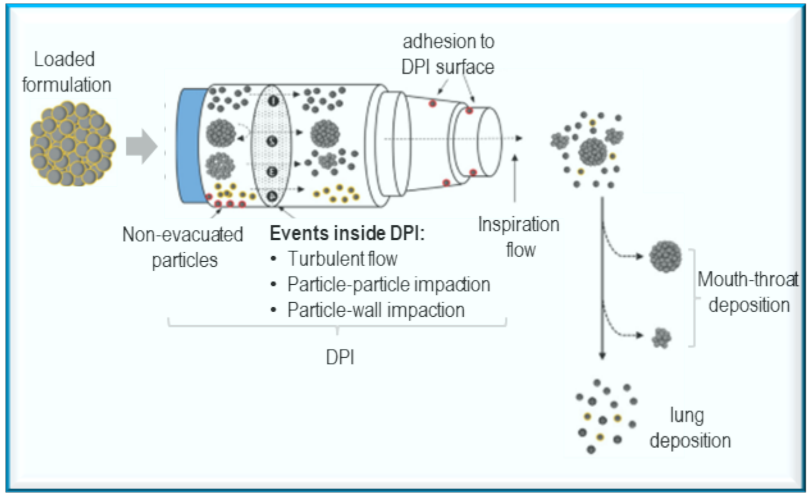
Characterizing Deposition Inside an Optically Accessible Dry Powder Inhaler using Optical Coherence Tomography

TT. Mekonnen, *L. Milton-McGurk, S. Cheng, W. Tai, HK. Chan, S. Boc, G. Singh & A. Kourmatzis*

THE UNIVERSITY OF SYDNEY
MACQUARIE University
FDA U.S. FOOD & DRUG ADMINISTRATION

Deposition inside Dry Powder Inhalers (DPIs)

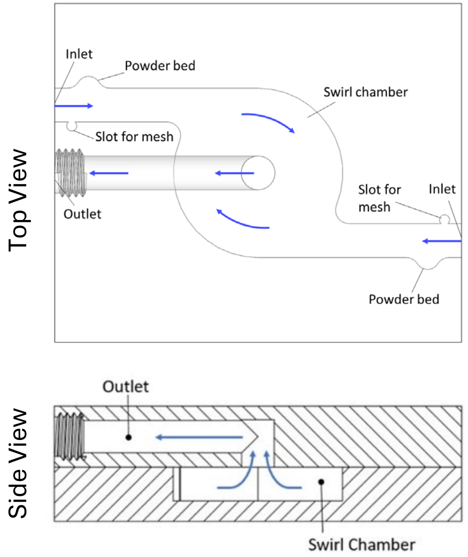
- Limited understanding of local aerosol dynamics in DPIs impacts:
  - inhaler design
  - Computational Fluid Dynamics model validation
- Total DPI deposition alone does not fully capture the in-device dispersion and deposition characteristics.
- Local deposition provides insights into airflow pattern and particle dispersion.

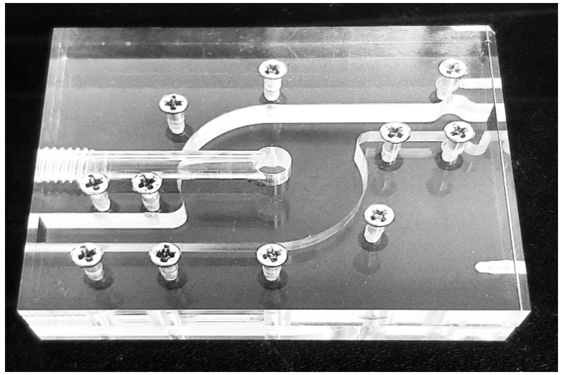


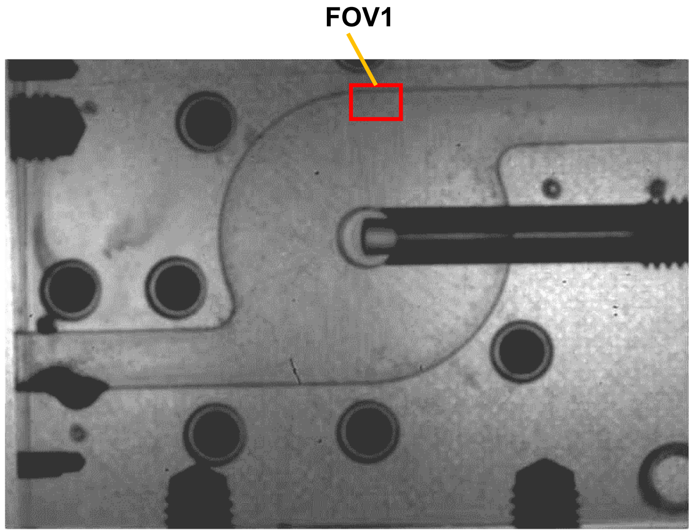
- Challenges of measuring local deposition:
  - access to DPI's inner surfaces
  - lack of suitable technique

Unique ‘Optically Accessible’ DPI (OA-DPI)

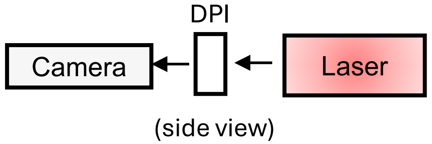
- Simulates flow conditions of typical commercial inhalers.
  - dual inlets & swirl chamber (like Aerolizer® & Osmohaler®)
  - matching resistance & dimensions

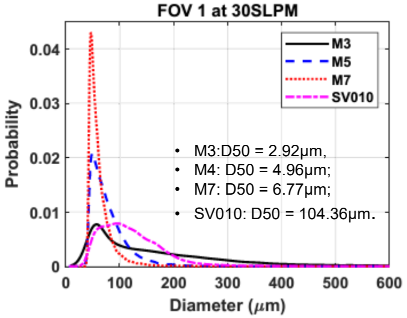






Microscopic high-speed imaging





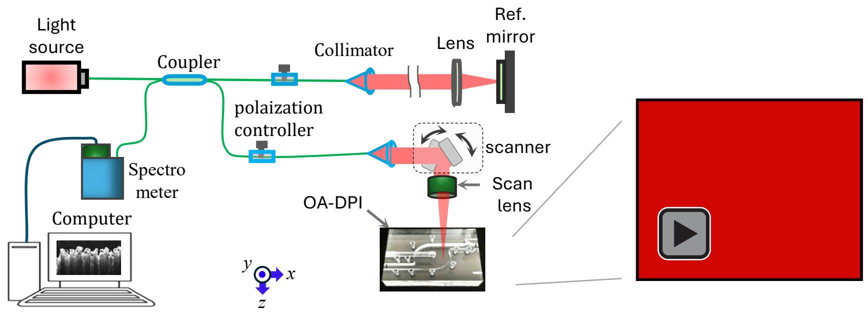
- Allows inhaler performance evaluation applicable across various DPI designs and IFRs.
  - fluidization and particle dynamics
  - particle deposition

Azeem et al.(2023), *Pharm Res;* Singh et al.(2022), *Int. J. Pharm.*

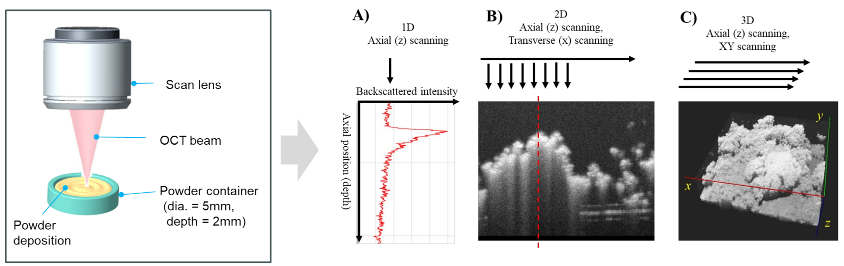
Deposition imaging inside OA-DPI

- Inner wall of DPIs is one of the crucial contributing factors impacting aerosol retention.
- OA-DPI enables 'through-wall deposition imaging'
- We develop & integrate an innovative **optical coherence tomography (OCT)** method to the OA-DPI.
  - provides tomographic images at high-resolution (~ 1 to 10 μm).
  - non-destructive structural imaging.

In-house OCT setup

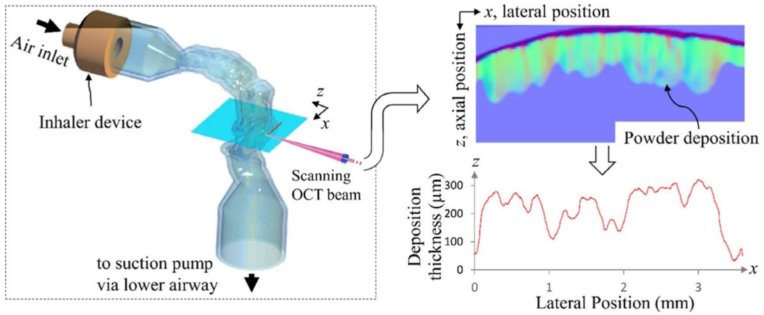


Demo. scanning & image reconstruction



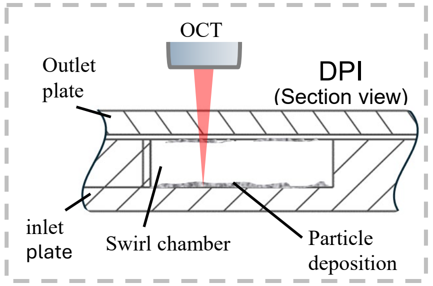
OCT solutions for deposition measurement

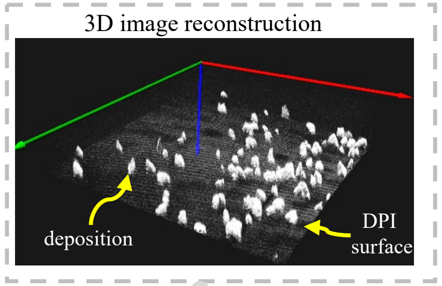
- ***Previously***, we introduced OCT for through wall deposition imaging in realistic airways.
  - regional deposition at high spatial resolution
    - Morphology (e.g., thickness)
    - sub-surface micro-pores



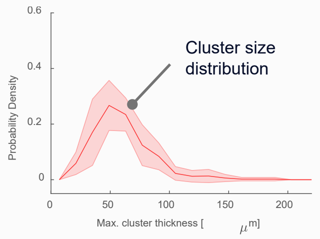
Mekonnen et. al (2020), *Int. J. Pharm.*

- *In the **current study***,
  - OA-DPI tailored OCT system for deposition.
  - Quantitative analysis of deposition

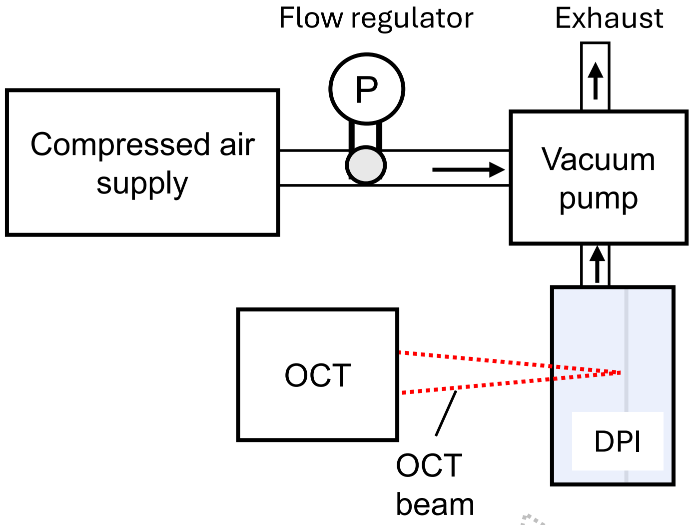


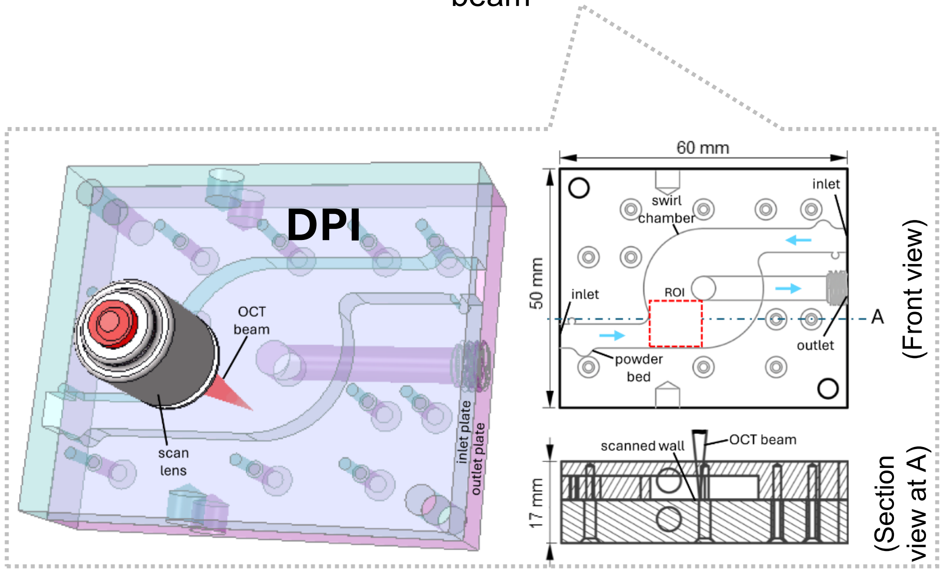


- Segmentation
- Quantifying thickness
- Thickness distribution



Method: OCT-based deposition imaging

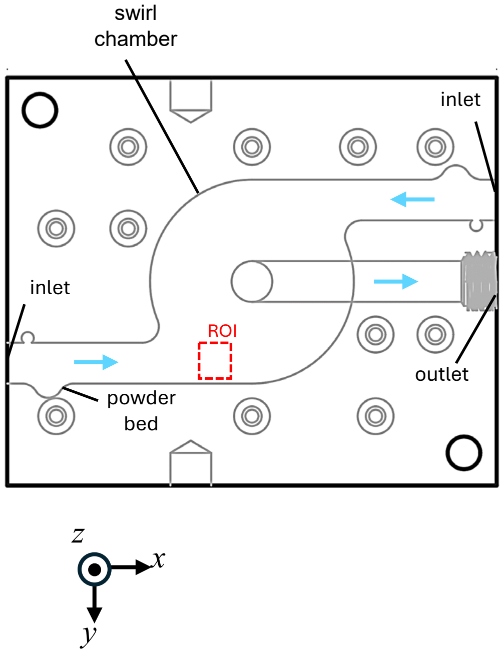




- OCT scan performed after evacuation process.
  - Flow rate & durations: 30LPM & 4.37s, resp.
- OCT system & imaging:
  - Depth resolution (in air): 7.6 µm.
  - 3D scan at 40 frames/s, ROI: 10.5x9.8 mm.
- Formulations:
  - **API**: Salbutamol sulfate (SS, Dv50 = 4 µm)
  - **Excipients**: Coarse lactose (SV010, Dv50 = 109 µm); Fine lactose (LH300, Dv50 = 5 µm).
  - Loaded dose: 20 ± 0.6 mg

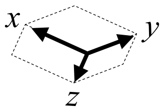
Formulation	% SS	% LH300	%SV010
SV010	0.00	0.00	100
F1	2.75	0.00	97.25
F2	2.75	10.0	87.25
F3	1.00	0.00	99
F4	2.75	2.50	94.75
F5	4.50	0.00	95.5

Results: OCT images of deposition



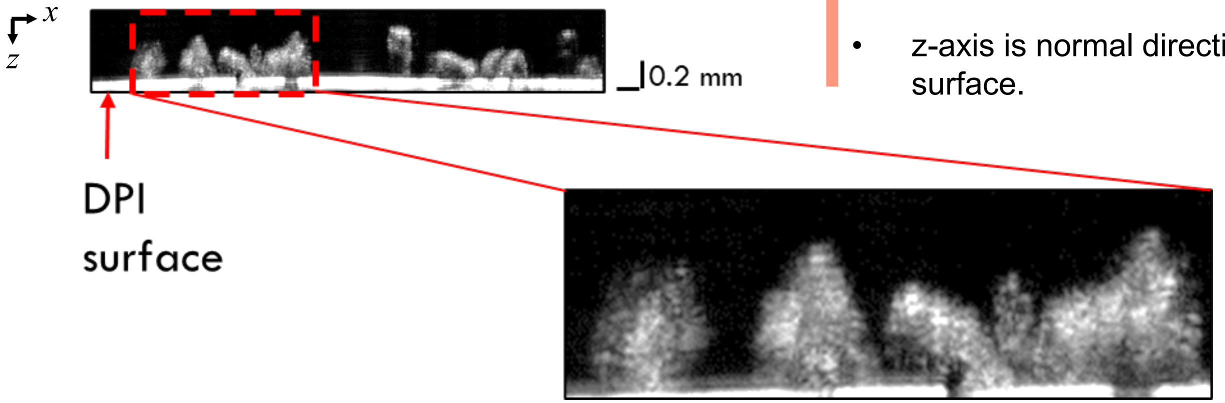
SV010, 30LPM

Sectional view



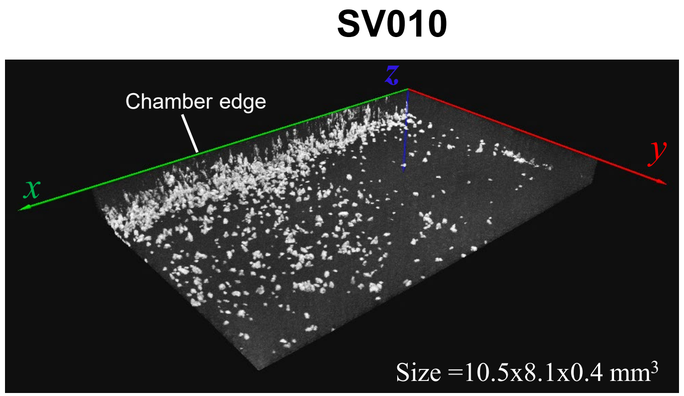
Volumetric view

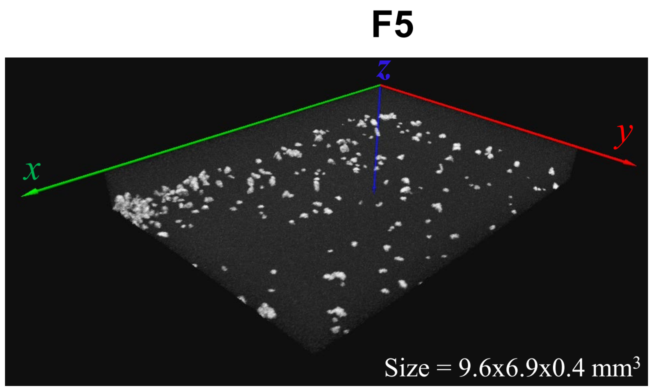
Depth cross-section



- *x-y* plane aligns with the DPI surface.
- z-axis is normal direction to the DPI surface.

Results: Deposition morphology & distribution





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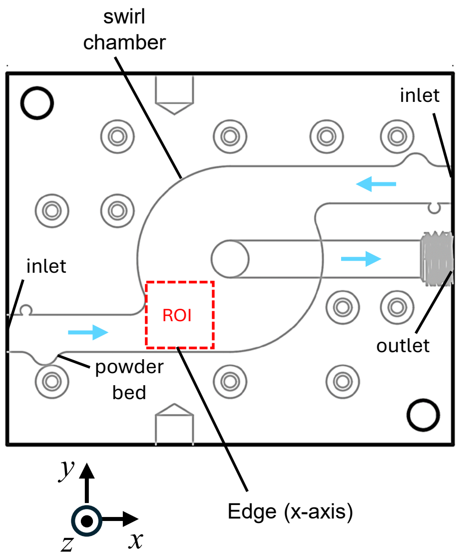
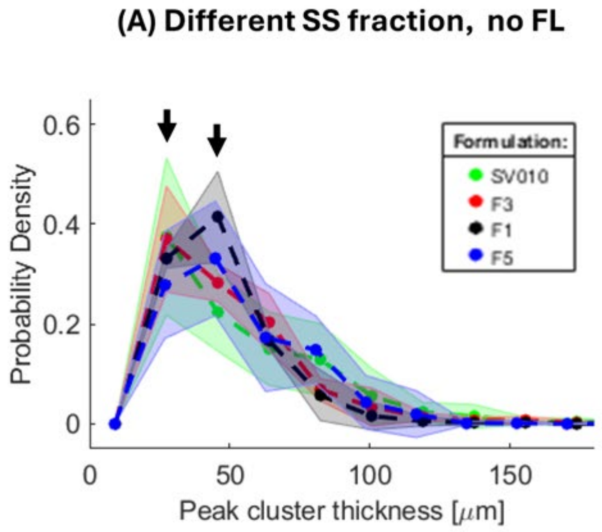
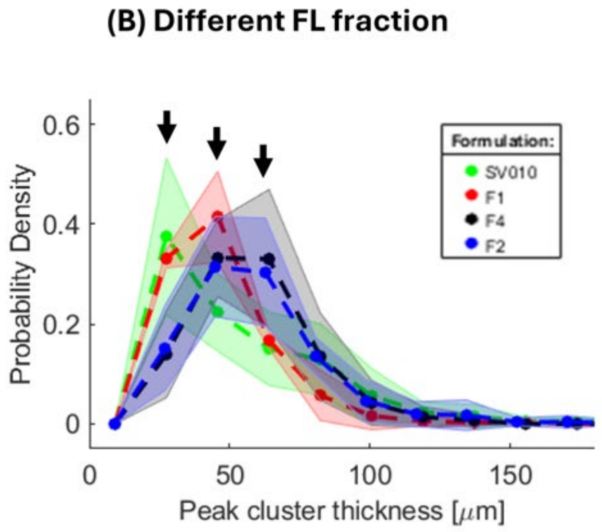


- Deposition forms clusters scattered across the inner surface of the DPI.
  - higher concentration of clusters near the edges (x-axis) of the swirl chamber.
- Deposition cluster thickness corresponds to its height along the z-axis.
  - F1-F5 exhibited thicker but sparser cluster populations than SV010.

Results: Deposition thickness





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*Salbutamol sulfate (SS, Dv50 = 4 μm).

*Fine lactose, FL (LH300, Dv50 = 5 μm).

*Coarse lactose (SV010, Dv50 = 109 μm).

- Change in SS fraction appears to influence the peak thickness of deposition.
- Increase in the mass fraction of fine lactose (FL) correlates with increased deposition thickness.

Summary

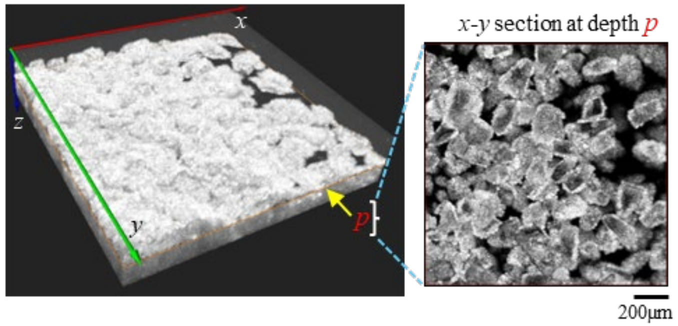
- OCT successfully characterizes particle deposition in OA-DPI.
- Deposition forms localized clusters.
- Denser clusters observed near edges of DPI swirl chamber.
- Formulation compositions affect deposition patterns and cluster sizes.
  - i.e., mass fraction of fine excipients and API.

Outlook

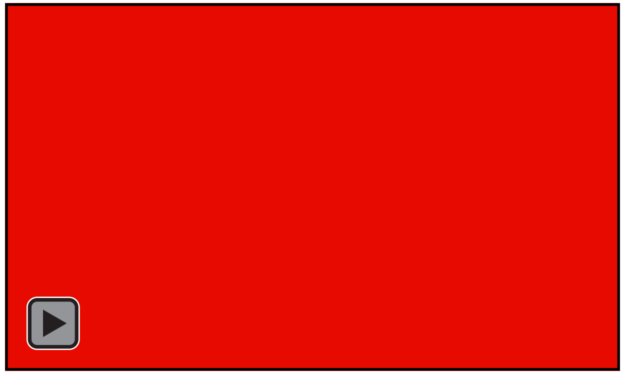
- Volumetric and spatial analyses could further enhance deposition understanding.
- OCT's potential in characterizing the mechanics, accumulation, and intrinsic optical properties of particles presents promising opportunities for advancing DPI performance testing.

Subsurface microstructure	Time-resolved deposition	Spectroscopic analysis

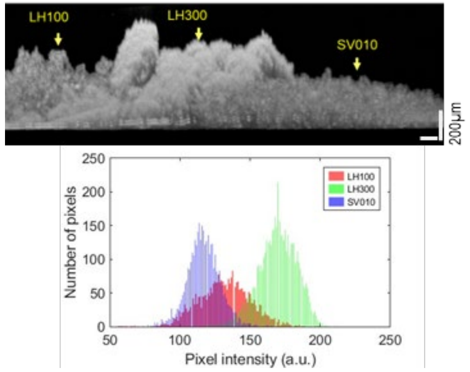
Subsurface microstructure



Time-resolved deposition



Spectroscopic analysis



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