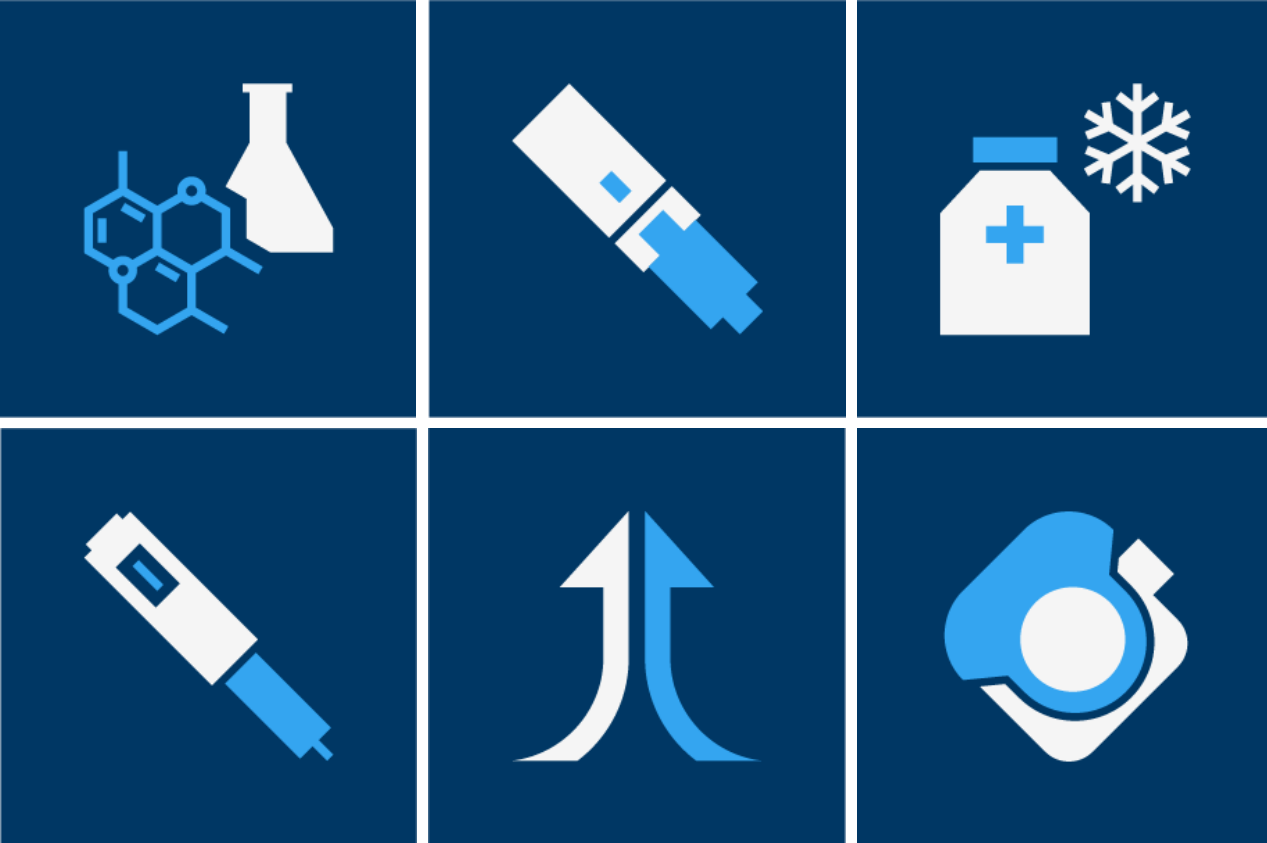




ASYMMETRIC CYCLONIC FLOW AND POWDER TRANSPORT IN A DRY POWDER INHALER

Baudouin Géraud

September 24, 2026

Phillips
Medisize
a **molex** company

Bringing Possibilities to Life

AGENDA

- Introduction
- Flow Visualisations
- Asymmetric Cyclonic Flow Modelling
- Powder Transport
- Device Performance
- Conclusions



INTRODUCTION



DRY POWDER INHALERS

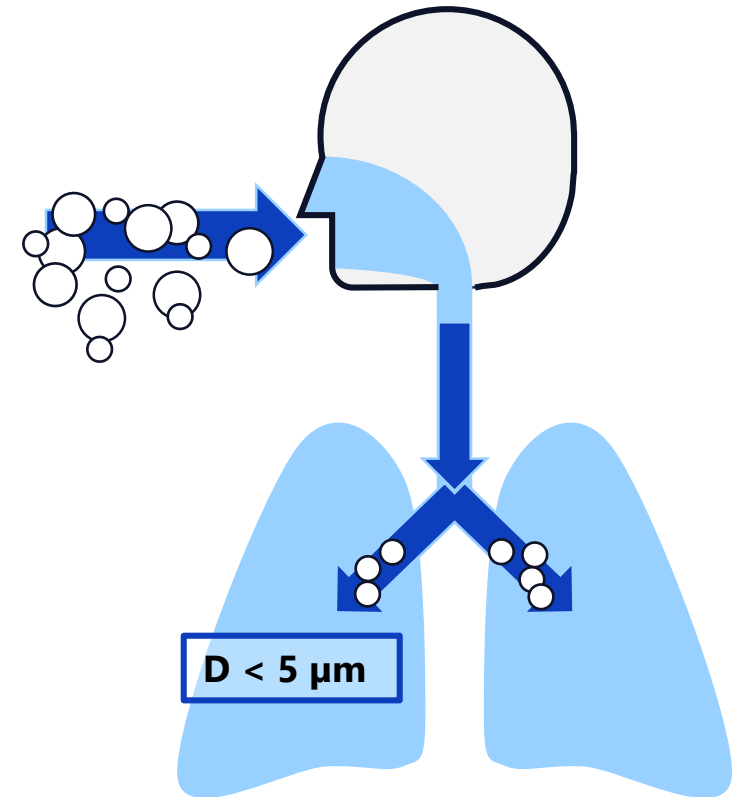
Introduction

Dry powder inhalers (DPIs) are well established in the treatment of respiratory disease (asthma and COPD in particular), mainly requiring the delivery of small doses of potent active pharmaceutical ingredients (APIs).

These therapies critically depend on powder aerosolisation and deagglomeration to reach **deep lung deposition**:

Respirable sizes are generally defined as $< 5 \mu\text{m}$ in diameter

The trends in inhalation drug delivery are for more systemically acting products for a broader set of indications and molecule types (including molecules of lower potency or requiring large amounts of stabilising excipients).



THE O1 CONCEPT DEVICE

AN INCREASING NEED FOR HIGH PAYLOAD DRY POWDER INHALERS (DPIs)

O1 is a concept device designed to deliver **large amounts of formulations*** filled into a blister (> 20mg – 100mg fill weight).

Most of the data shown today was established for a formulation which was predominantly micronized API, intended to be delivered for a systemic indication as an acute rescue therapy requiring a large dose.

The tolerability aspects associated with the inhalation of large amounts of powder (e.g. cough and irritation) will not be covered in this presentation

Dose ranging studies as part of early clinical development usually require ranges of dosing from sub to supra therapeutic doses.



THE O1 CONCEPT DEVICE

O1's DEAGGLOMERATION ENGINE

The delivery and deagglomeration of large amounts of formulations are ensured by **key components**:

- Large blister – Approximately 2.4 mL
- **Cruciform ball**



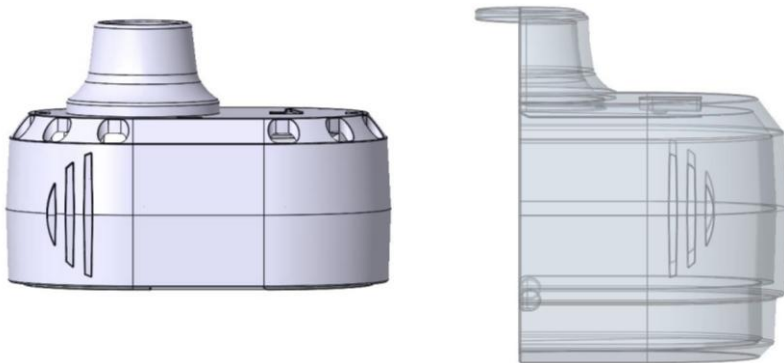
Opening the mouthpiece pierces the blister
Single-dose concept: **1** inhalation required

THE O1 CONCEPT DEVICE

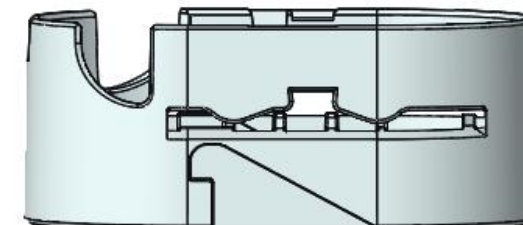
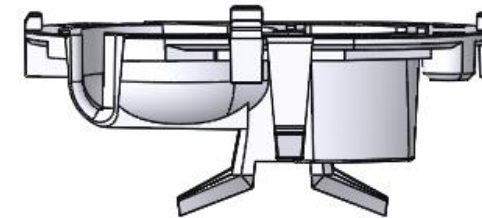
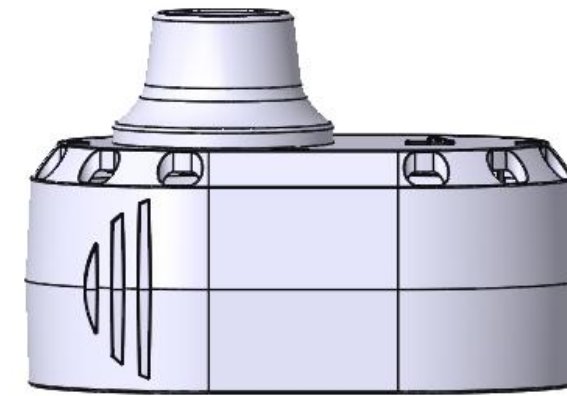
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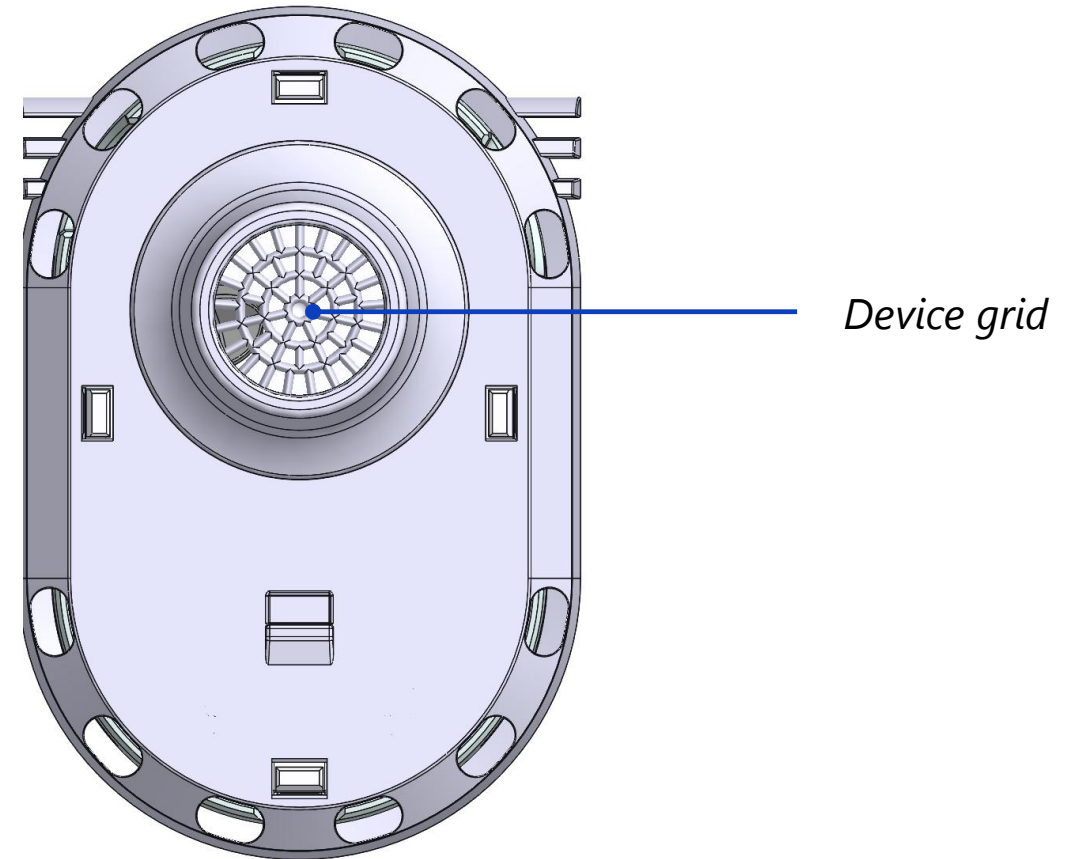


THE O1 CONCEPT DEVICE

O1's DEAGGLOMERATION ENGINE

The delivery and deagglomeration of large amounts of formulations are ensured by **key components**:

- Large blister – Approximately 2.4 mL
- **Cruciform ball**
- Device grid

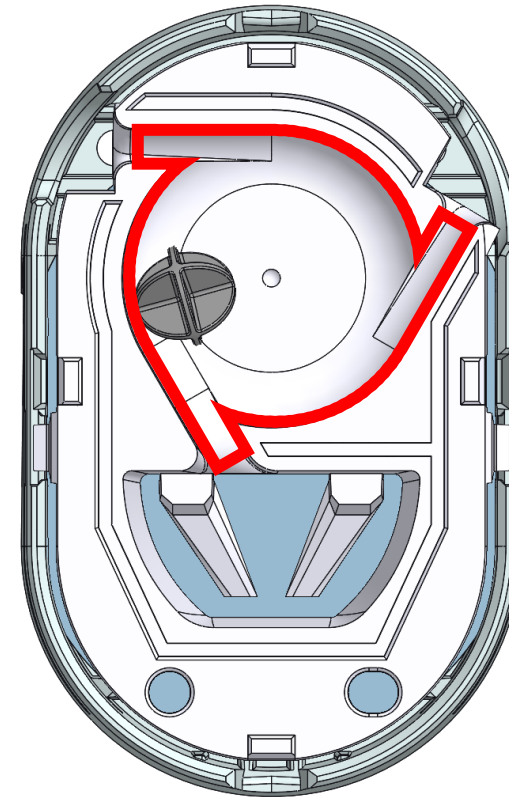


THE O1 CONCEPT DEVICE

O1's DEAGGLOMERATION ENGINE

The delivery and deagglomeration of large amounts of formulations are ensured by **key components**:

- Large blister – Approximately 2.4 mL
- **Cruciform ball**
- Device grid
- **Cyclonic chamber**
 - 1 powder inlet**
 - + 2 air inlets**



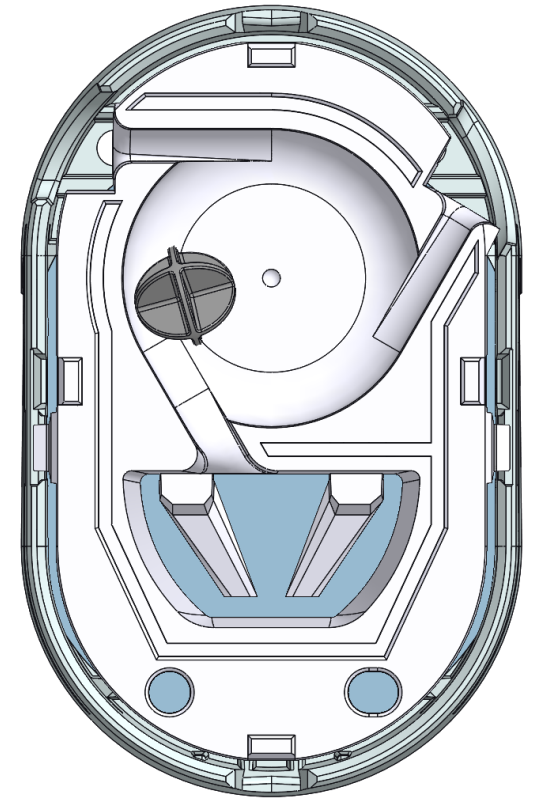
THE O1 CONCEPT DEVICE

O1's DEAGGLOMERATION ENGINE

How do the cruciform ball and the cyclonic chamber contribute to the device performance?

- How do they deagglomerate the powder?
- How is the powder dispersed in the flow?
- How is the cruciform ball interacting with the flow?
- How does the device react to different types of formulations?

Investigations in high-speed imaging (HSI) and *Computational Fluid Dynamics (CFD) simulations*





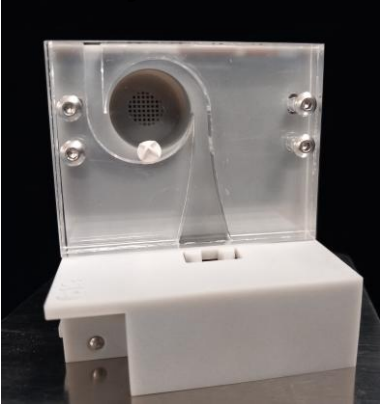
FLOW VISUALISATIONS



CYCLONIC FLOW IN TRANSPARENT GEOMETRIES

HSI INVESTIGATION

2-inlet cyclone



3-inlet cyclone



Experiments performed in transparent geometries

- 2-inlet and 3-inlet cyclones present similar flow phenomenology

Recordings at 10,000 frames per seconds (100 μ s time interval) using a Photron Nova S9 high-speed camera.

Observation through the cyclonic chamber, along the mouthpiece axis

- Curvature of internal geometry causes a slight distortion at the edges of the cyclone

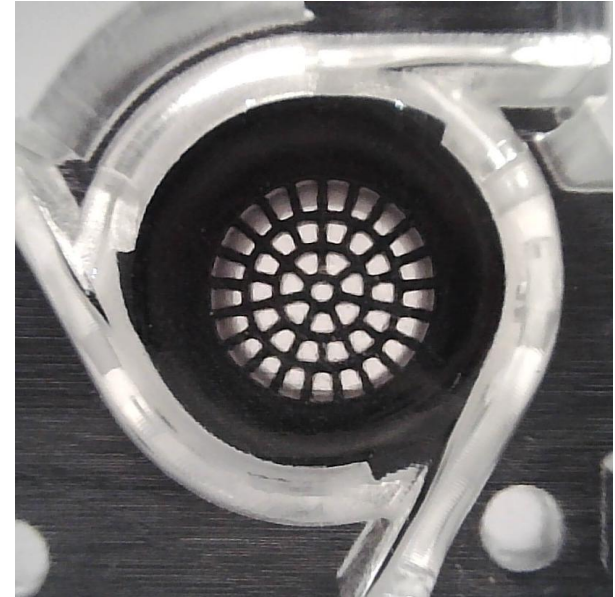
Large payloads used for these experiments

- Approximately 100 mg of micronized formulation
- Powder tapped density 0.3 g.mL⁻¹

Triple comparison: Spherical ball, no ball and cruciform ball

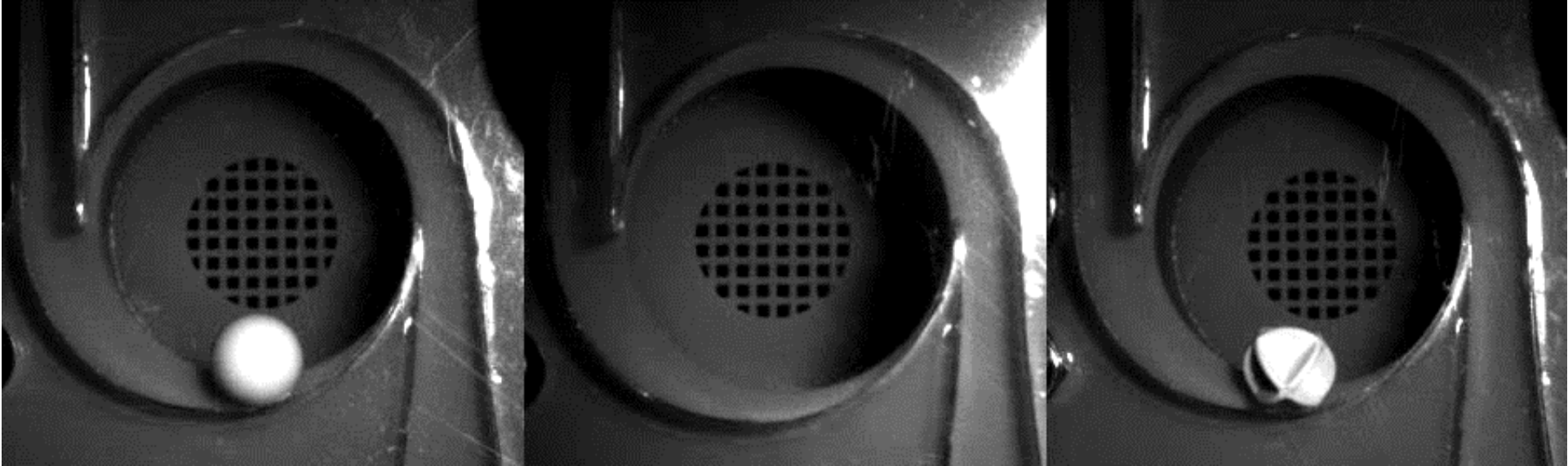
- Identical flow conditions
- Flows generated by Copley TPK2100 at 60 L.min⁻¹, device resistance ≈ 0.023 kPa^{0.5}.min.L⁻¹

Field of view: cyclonic chamber



HIGH-SPEED IMAGING

IMPACT OF THE BALL SHAPE ON THE FLOW



- High-velocity rotary flow:
 - Accumulation of large particles on the walls by centrifugal forces
 - Smaller particles are conveyed towards the grid and mouthpiece
- The cyclone eye shows different dynamics depending on the ball shape.

HIGH-SPEED IMAGING

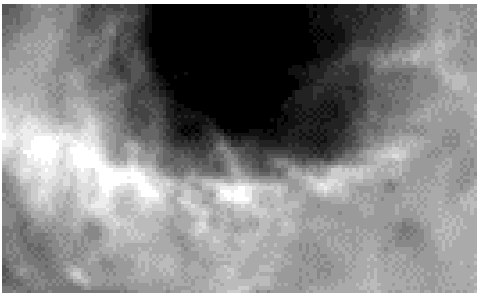
IMPACT OF THE BALL SHAPE ON THE FLOW

Multiple deagglomeration mechanisms observed:

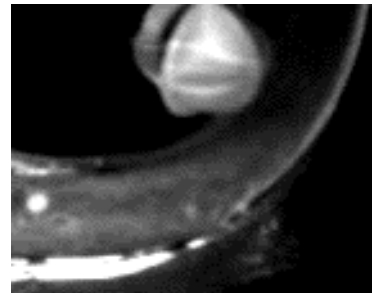
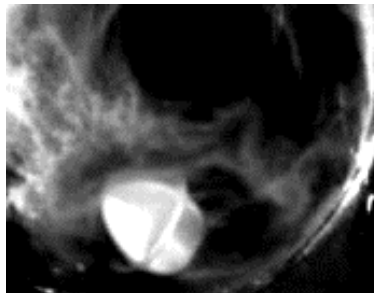
- Shear in the cyclonic flow
- Impacts against the ball
- Impacts against the walls

The cyclone eye seems destabilised by the irregular dynamics of the cruciform ball.

Shear

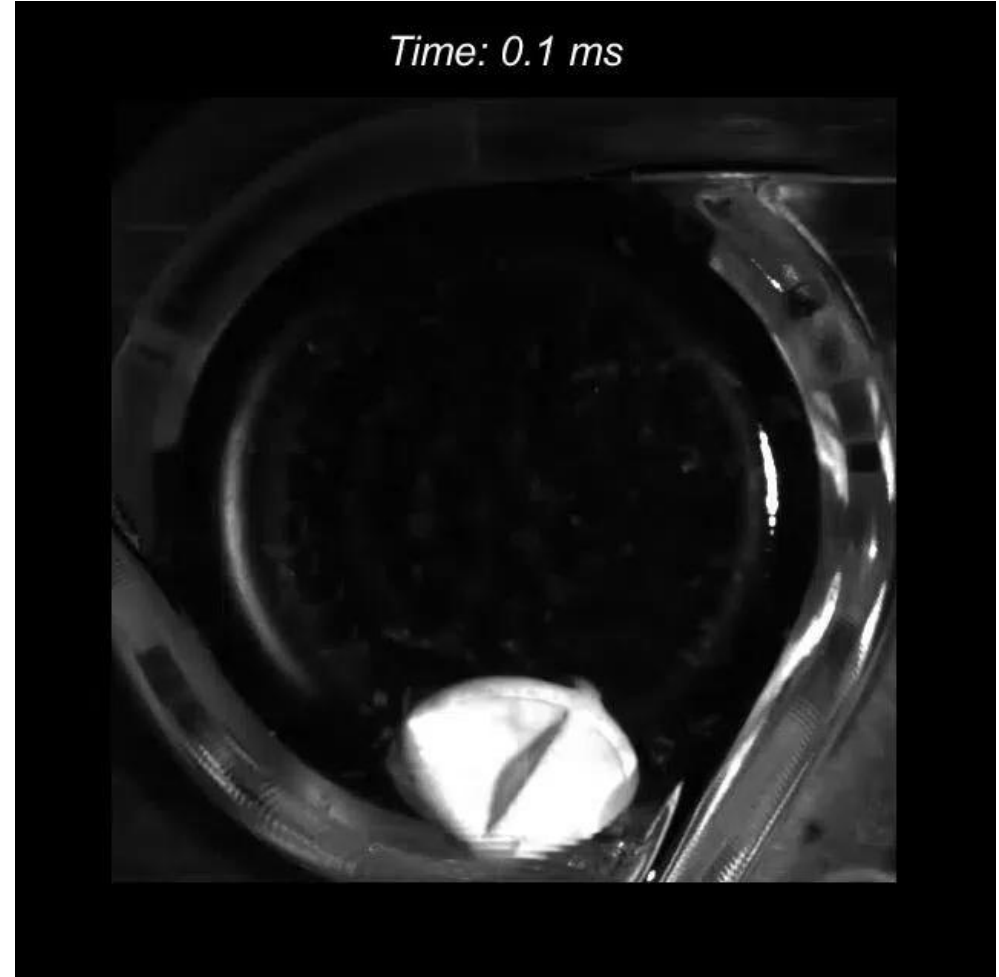


Impacts against the ball and the walls



Micronized Formulation – 110mg – 4kPa

Time: 0.1 ms



DEAGGLOMERATION IN A CHAOTIC FLOW

CONCLUSIONS

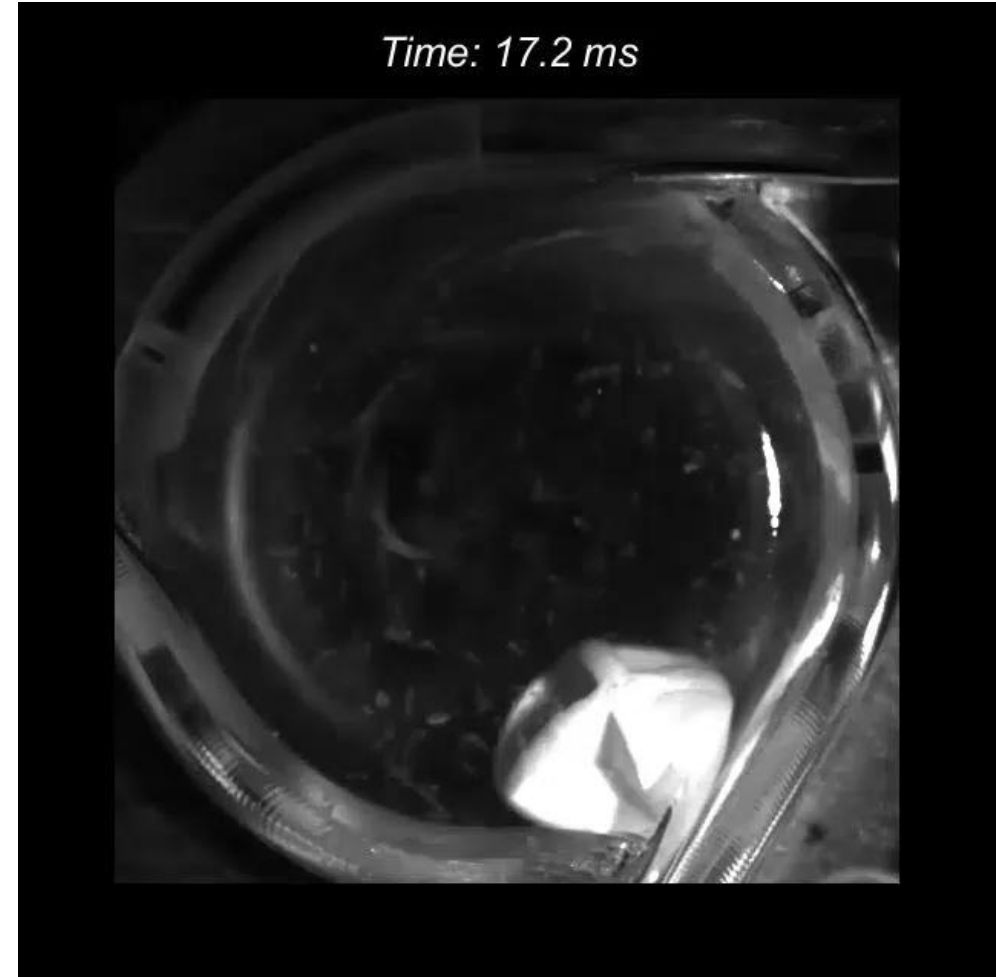
Observations in transparent geometries show different deagglomeration mechanisms:

- Shear within the cyclonic flow
- Impacts against the ball (large differences of velocities between the ball and the flow)
- Impacts against the walls

The cruciform ball exhibits a chaotic dynamic that promotes deagglomeration by destabilising the cyclonic flow:

- Maintains the cyclone in an unsteady state and results in an increase of pressure fluctuations and shear stresses on particles.

These observations do not however explain the better performance of the device with the cruciform ball in aerosol testing and need to be further rationalised.





ASYMMETRIC CYCLONIC FLOW MODELLING



MODELING APPROACH

CFD SETUP

Computational fluid dynamics (CFD) simulations were performed to further investigate the interaction between the flow and the particles.

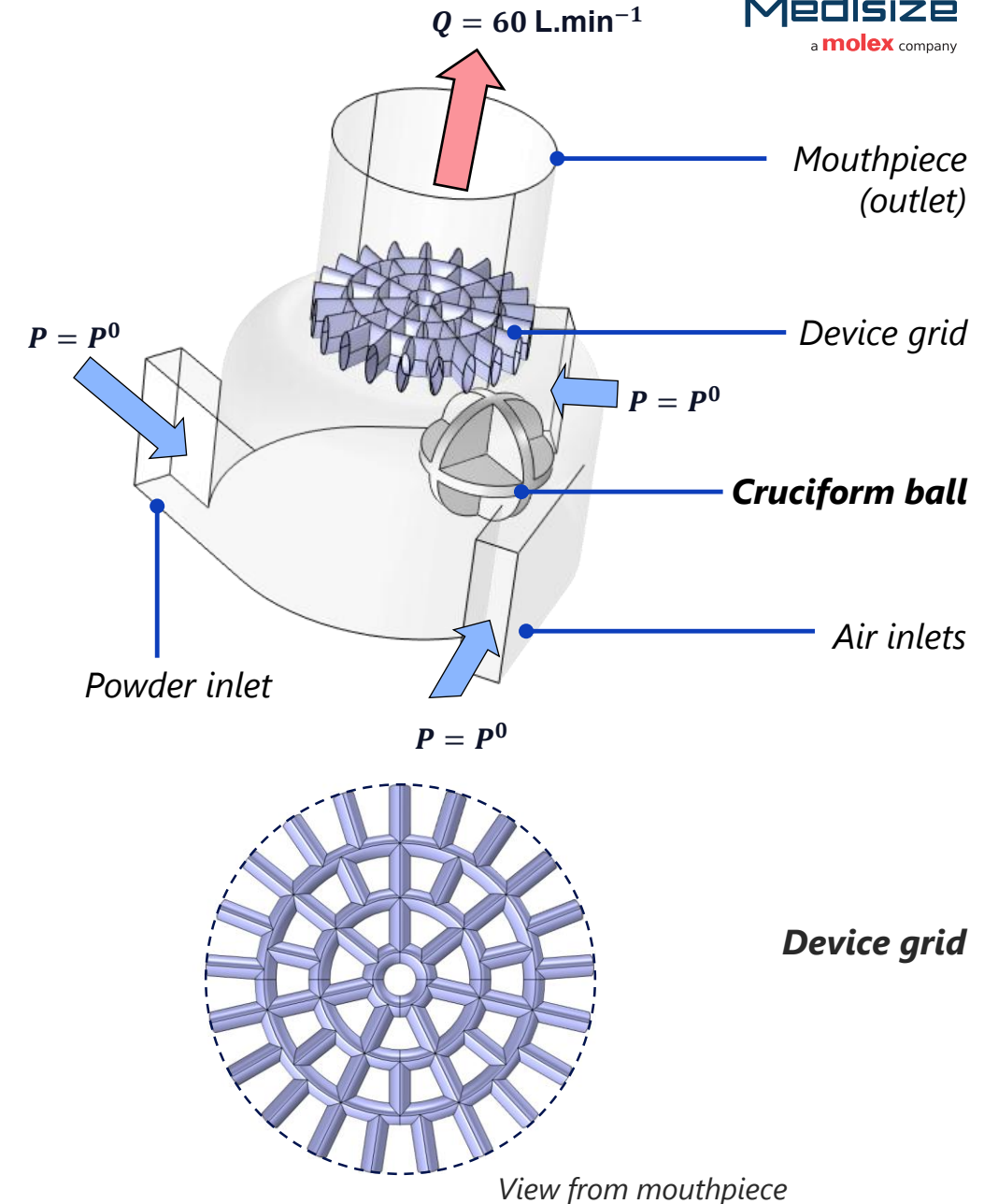
- Solves the equations of fluid motion using a discretisation of space and time
- Provides insights on the flow phenomenology and its dependency with design parameters

Stationary k- ϵ turbulent model with a static ball

- Quasi-static approximation, confirmed by high-speed imaging (HSI) observations

Model boundary conditions

- Driven by USP <601> standard test requirements
- 3 inlet channels set at atmospheric pressure $P = P^0$
- Outlet flow rate set by normal flow velocity boundary condition (BC), equivalent to a volumetric flow rate $Q = 60 \text{ L/min}$



MODELLING APPROACH

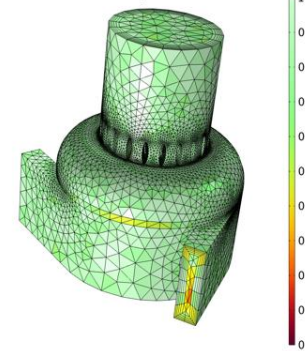
MESH REFINEMENT STUDY

Mesh refinement study conducted to assess the modelling accuracy and determine the degree of discretisation required for the mesh

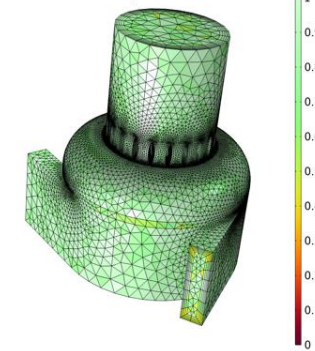
- Use of COMSOL's predefined mesh sizes (Extra Coarse → Fine)
- Mesh quality (skewness) typically of the order of $0.68 > 0.1$

The pressure drop across the device is computed for each mesh.

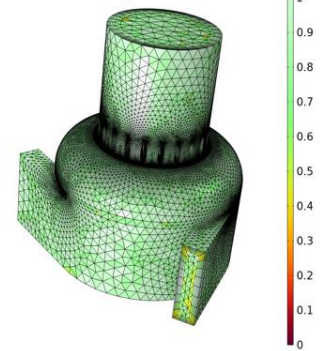
Extra Coarse
 $\langle h \rangle = 1130.2 \mu m$



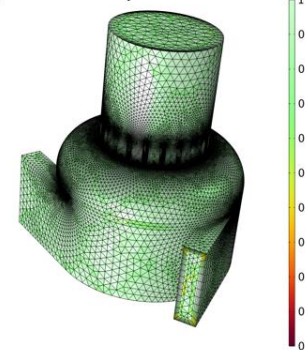
Coarser
 $\langle h \rangle = 890.9 \mu m$



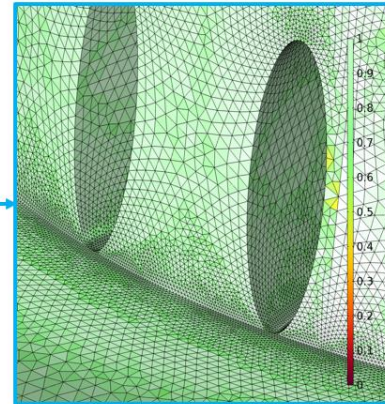
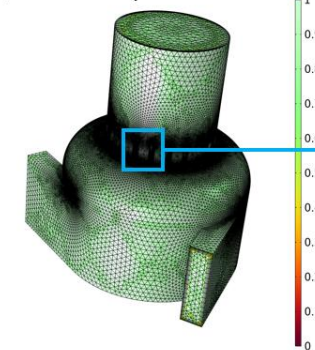
Coarse
 $\langle h \rangle = 730.3 \mu m$



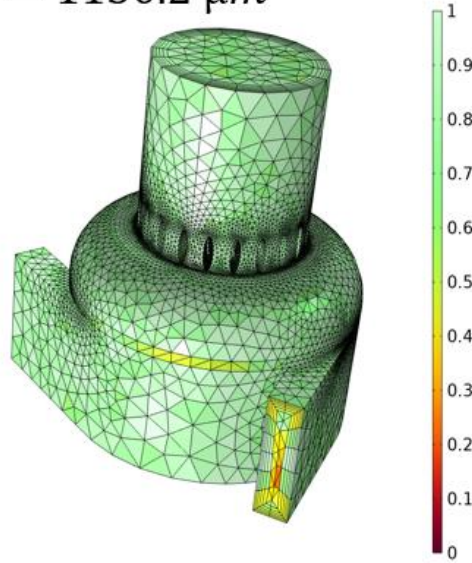
Normal
 $\langle h \rangle = 552.2 \mu m$



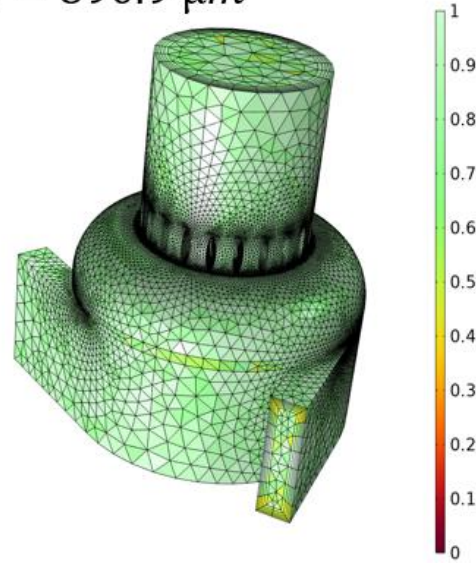
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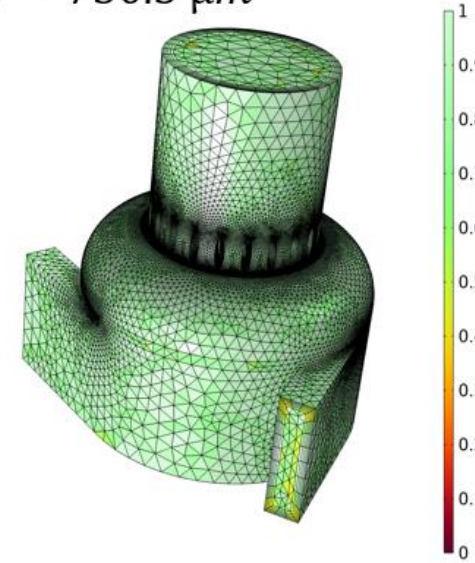
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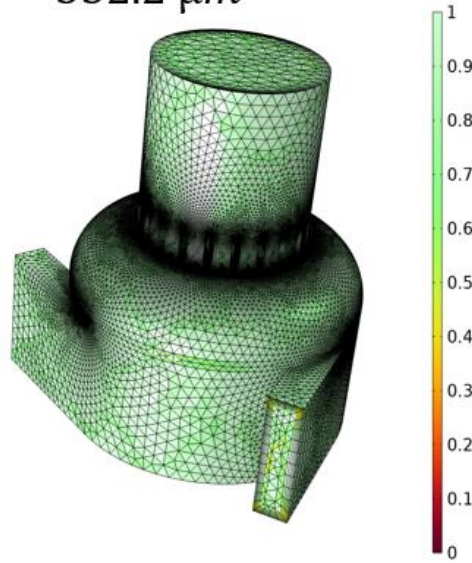
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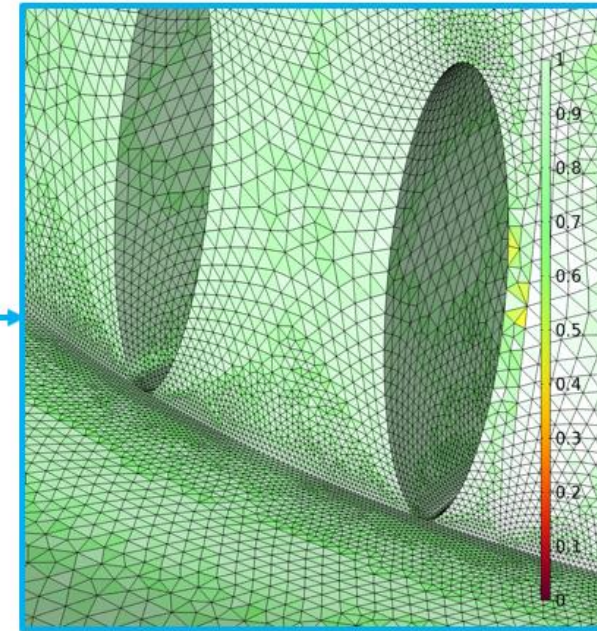
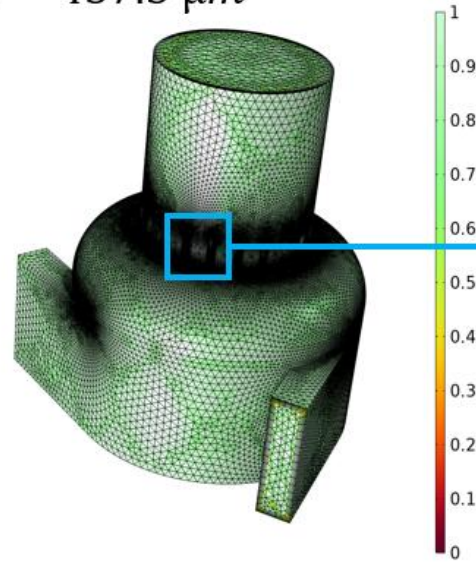
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MODELLING APPROACH

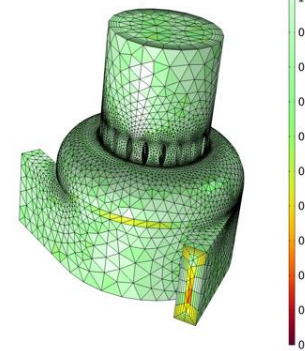
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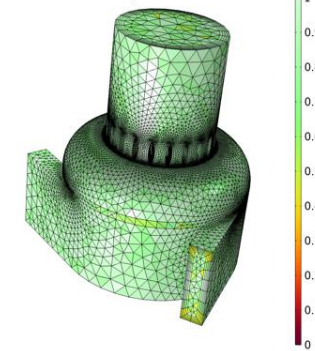
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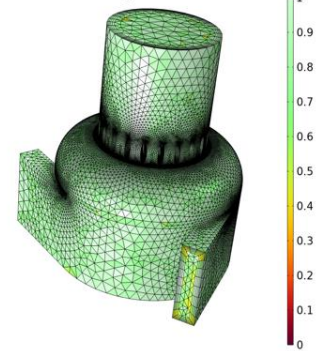
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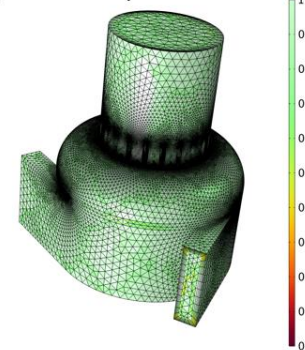
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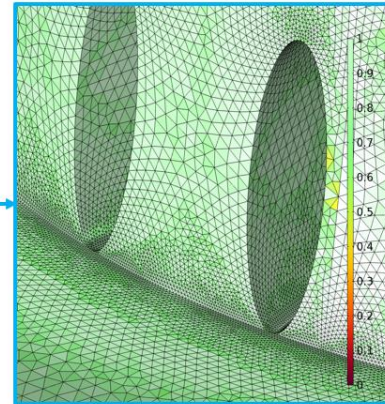
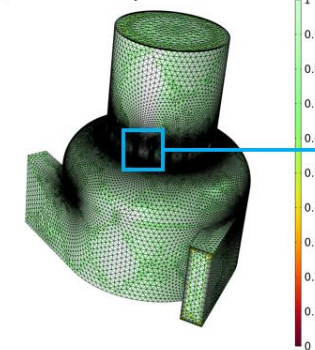
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MODELING APPROACH

NUMERICAL VALIDATION

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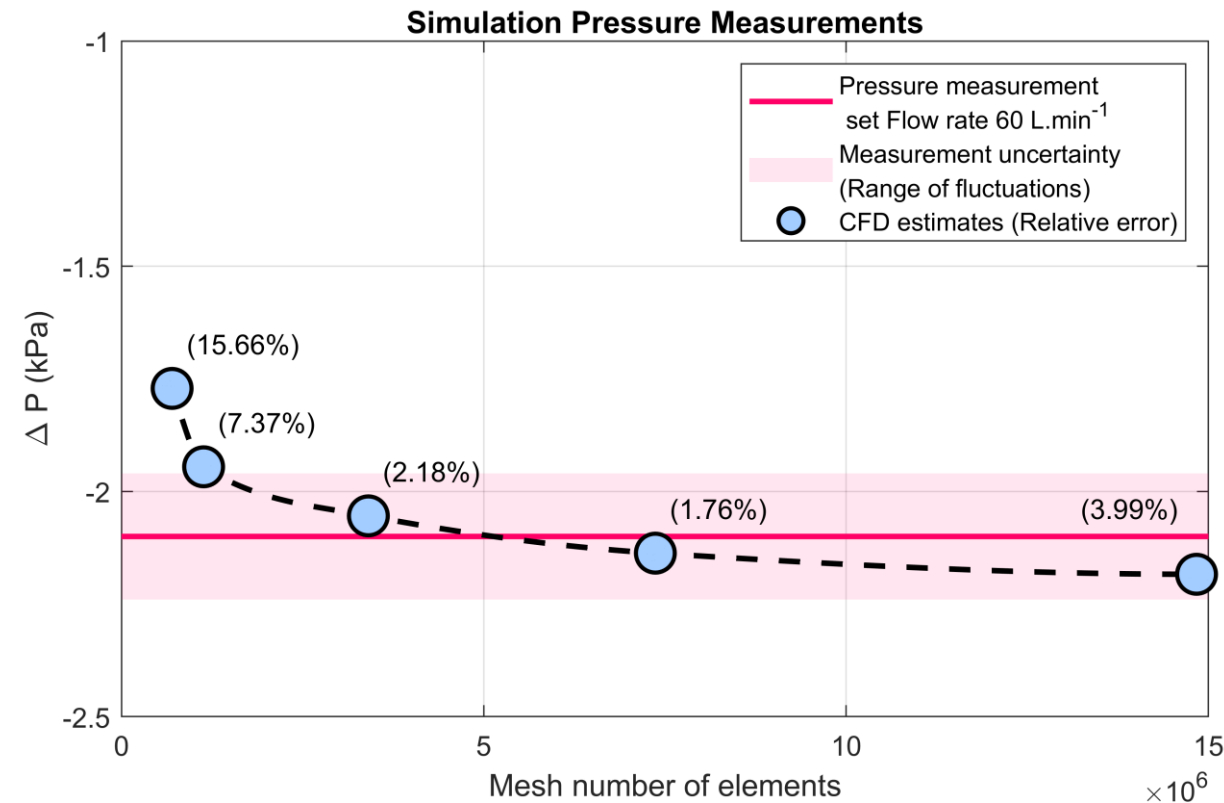
The pressure drop across the device is computed for each mesh.

CFD predictions were compared against pressure drop measurements at the same flow rate for validation purposes

- Copley TPK2100 / TSI 4040 flow sensor

Simulations show a close agreement with the experimental data

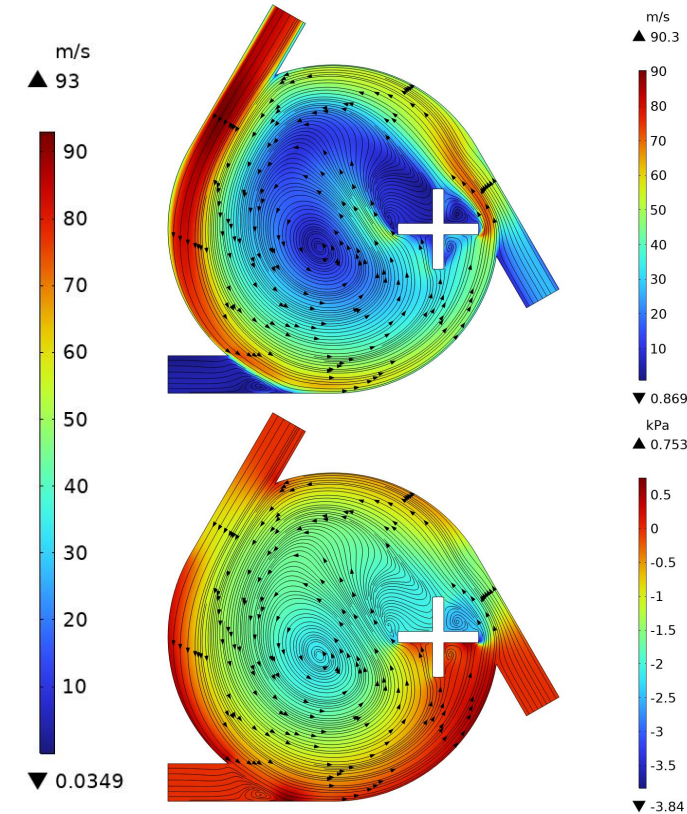
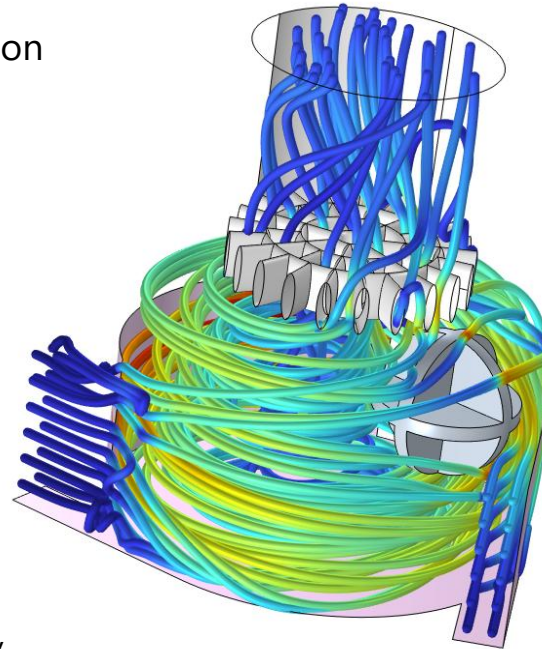
- Provides confidence in the flow phenomenology
- Confirms the adequacy of the modelling approach

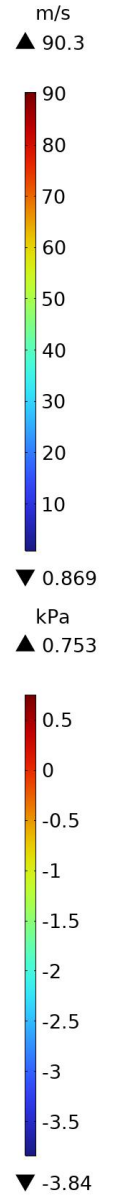
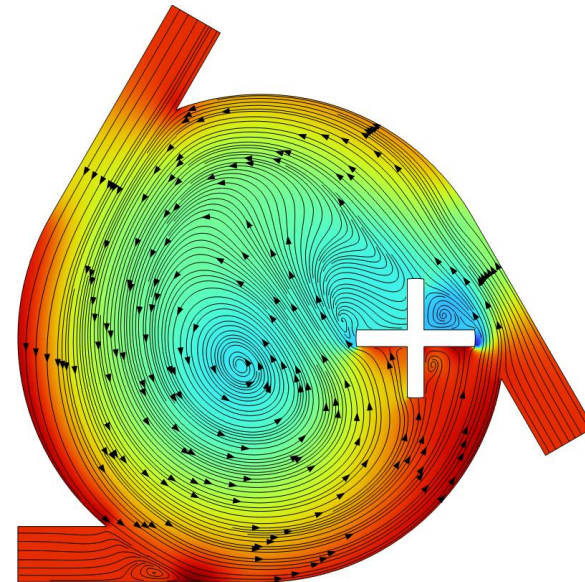
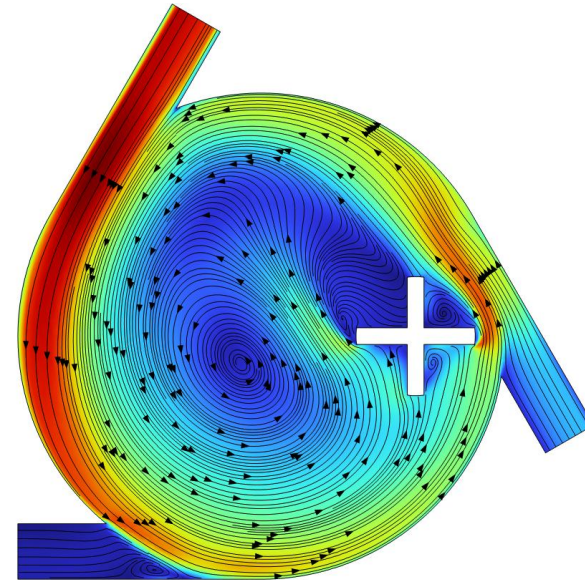
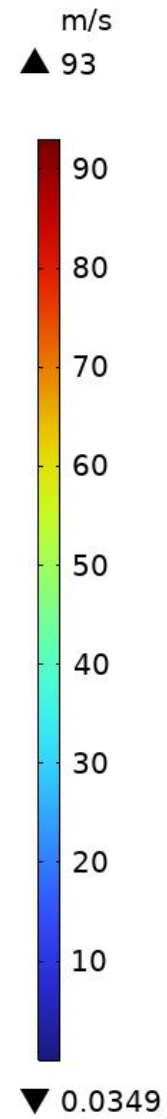
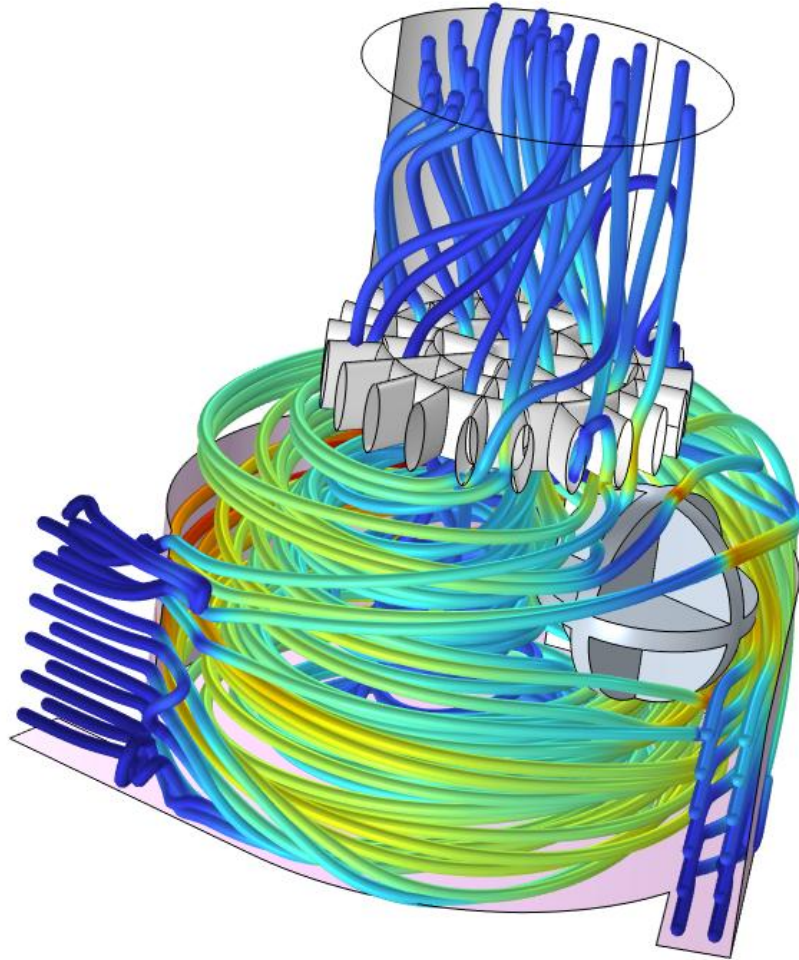


FLOW PHENOMENOLOGY

HIGH VELOCITY ROTATIONAL FLOW

- High velocity gradients contribute to powder deagglomeration by shear
- Cyclone eye off-centred by the ball
 - Confirms that observations in HSI are not an experimental artefact
- The device grid straightens the flow and contributes significantly to the device air flow resistance (AFR)
- High velocity flow unevenly spread between inlets
 - Flow heterogeneity qualitatively more pronounced than in HSI, likely due to the imposed boundary conditions (BC) and quasi-static approximation

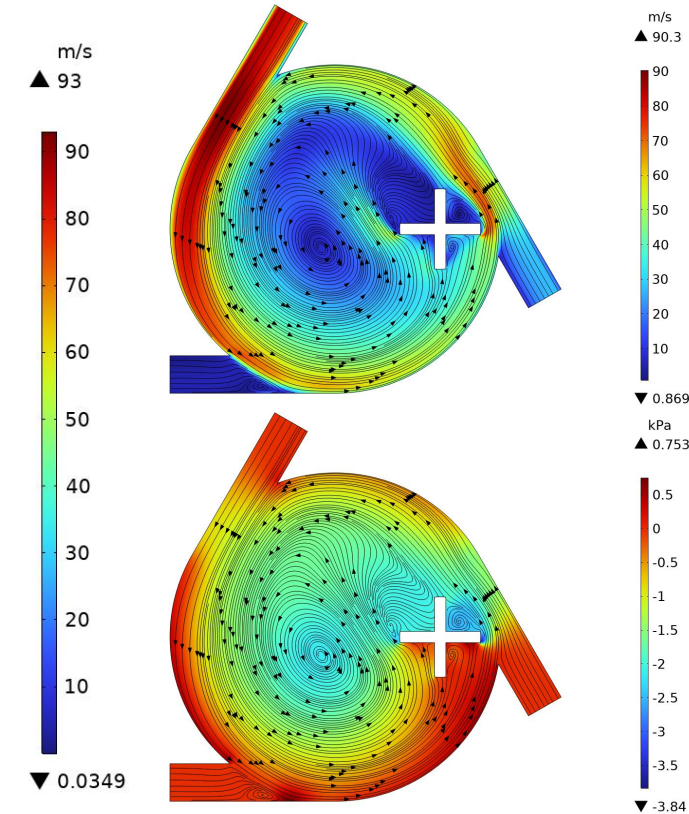
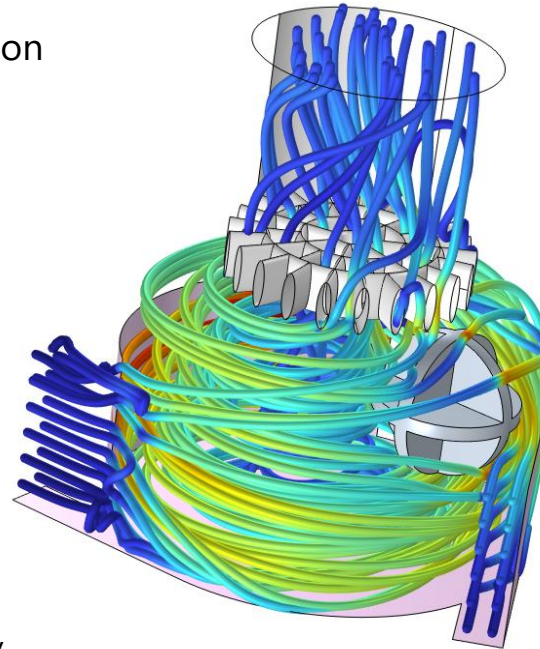




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Flow Phenomenology consistent with observations supports further simplifications to reduce computational cost and investigate Powder/Flow interaction

ASYMMETRIC FLOW STRUCTURE

MODEL SIMPLIFICATION

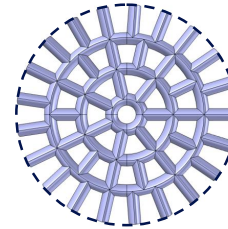
Device grid simplification enables multiple iterations at lower computational cost.

- Flat-faced boundaries that preserve the original hole positions allow for mapped swept mesh across the grid's fluid domain.
- The modification increases the device air flow resistance, inducing overestimated pressure drops and slower flow velocities accordingly.

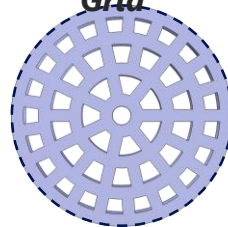
Geometry simplification preserves the internal flow structures in the cyclone mid-plane:

- Identical streamline patterns
- Same preferential inlet channel
- Preserves the location of the cyclone eye

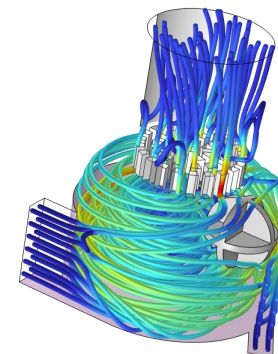
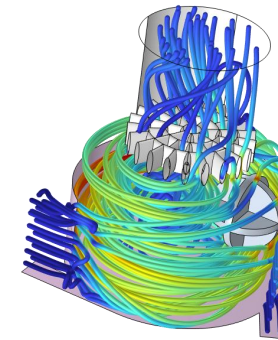
Device Grid



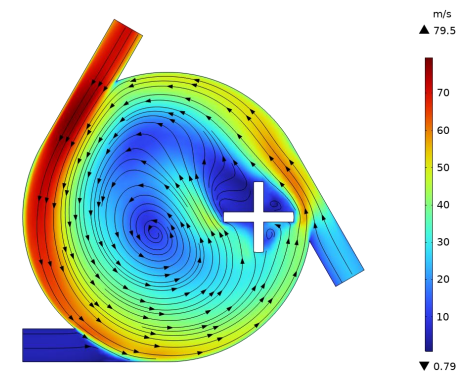
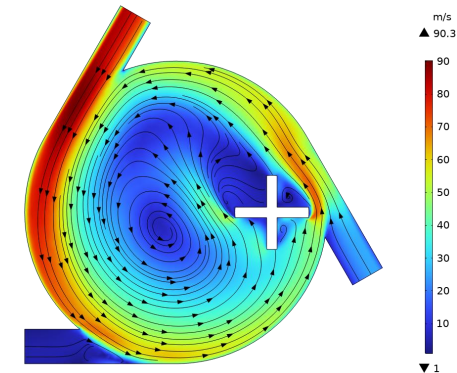
Simplified Grid



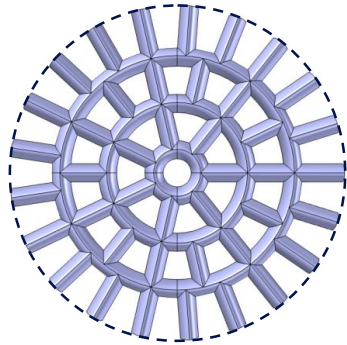
Internal Flow



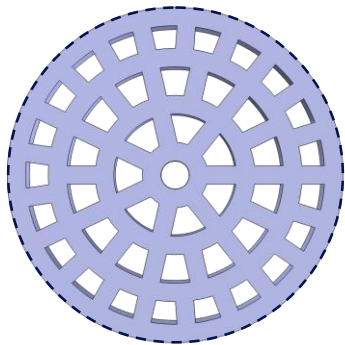
Mid-Plane Velocities



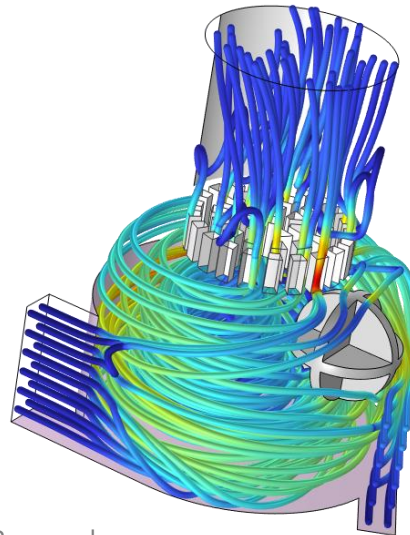
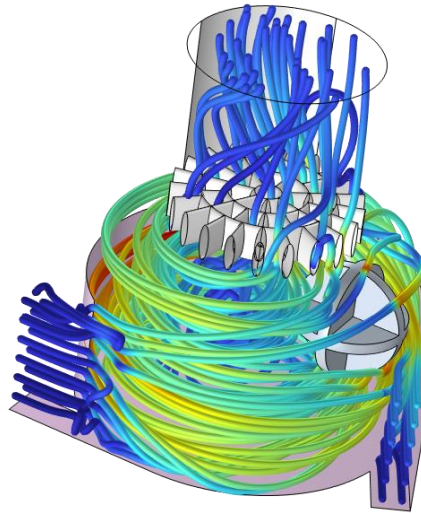
Device Grid



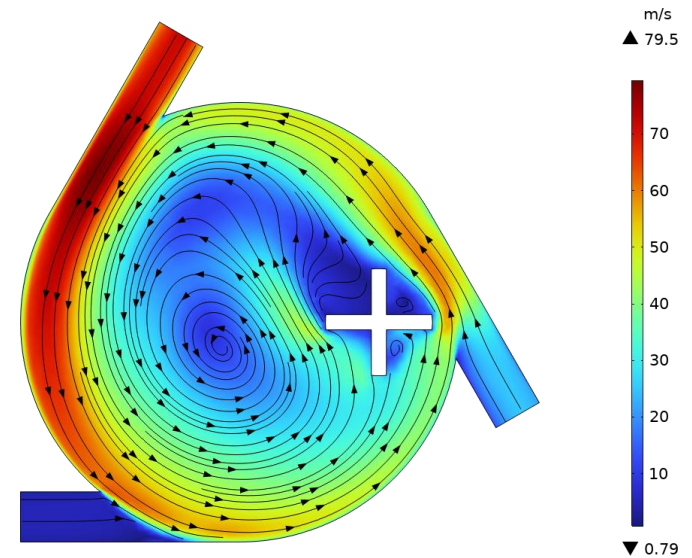
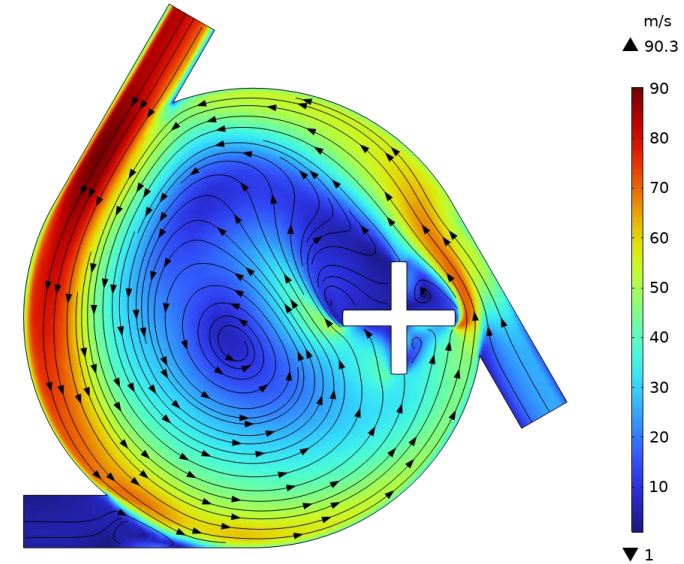
Simplified Grid



Internal Flow



Mid-plane Velocities



ASYMMETRIC FLOW STRUCTURE

CYCLONE DISRUPTION

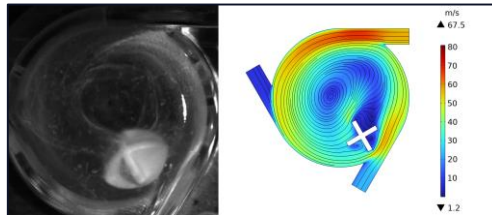
The cruciform ball distorts the velocity streamlines

Simulations without ball predict a centred cyclone eye, confirming the observations in HSI

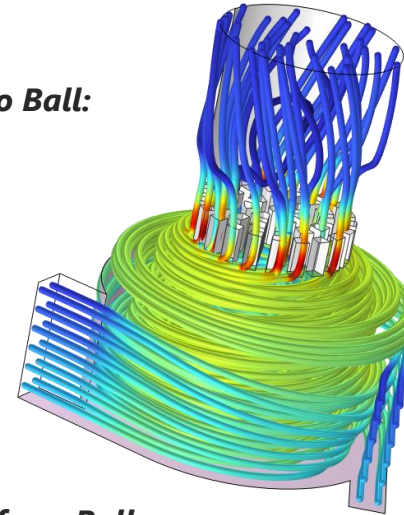
- The ball breaks the flow symmetry in the cyclonic chamber (introducing additional non-slip conditions within)
- Associated with a reduced pressure drop across the device compared with the configuration without a ball

Parametric studies show variations between preferential channels and the location of the eye according to the ball angular position

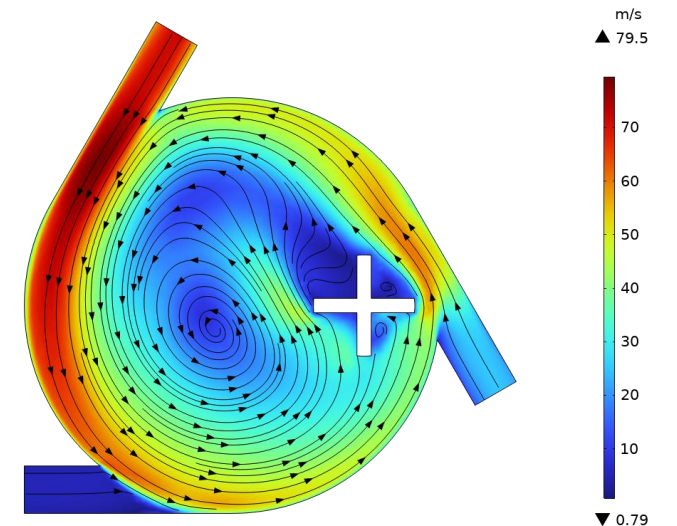
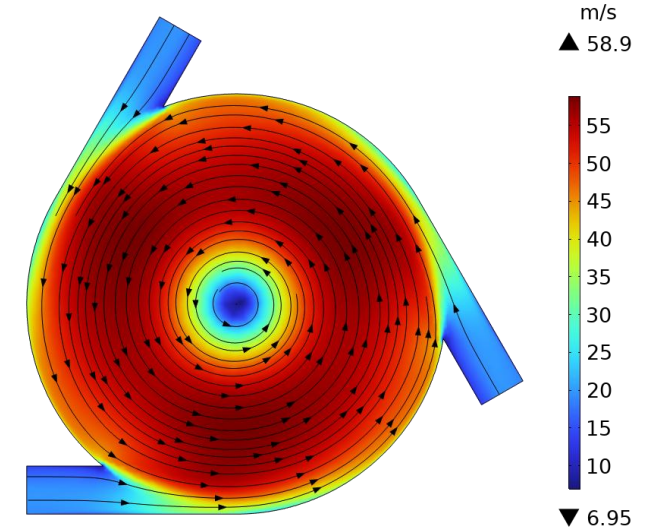
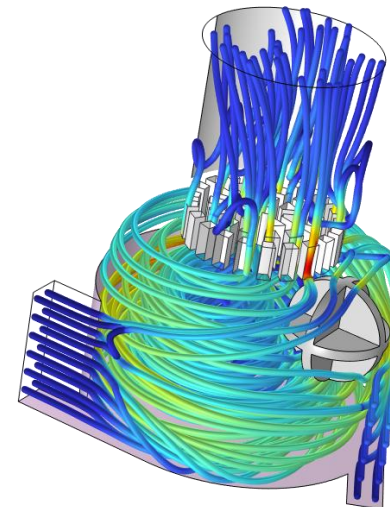
- Matches observations in HSI

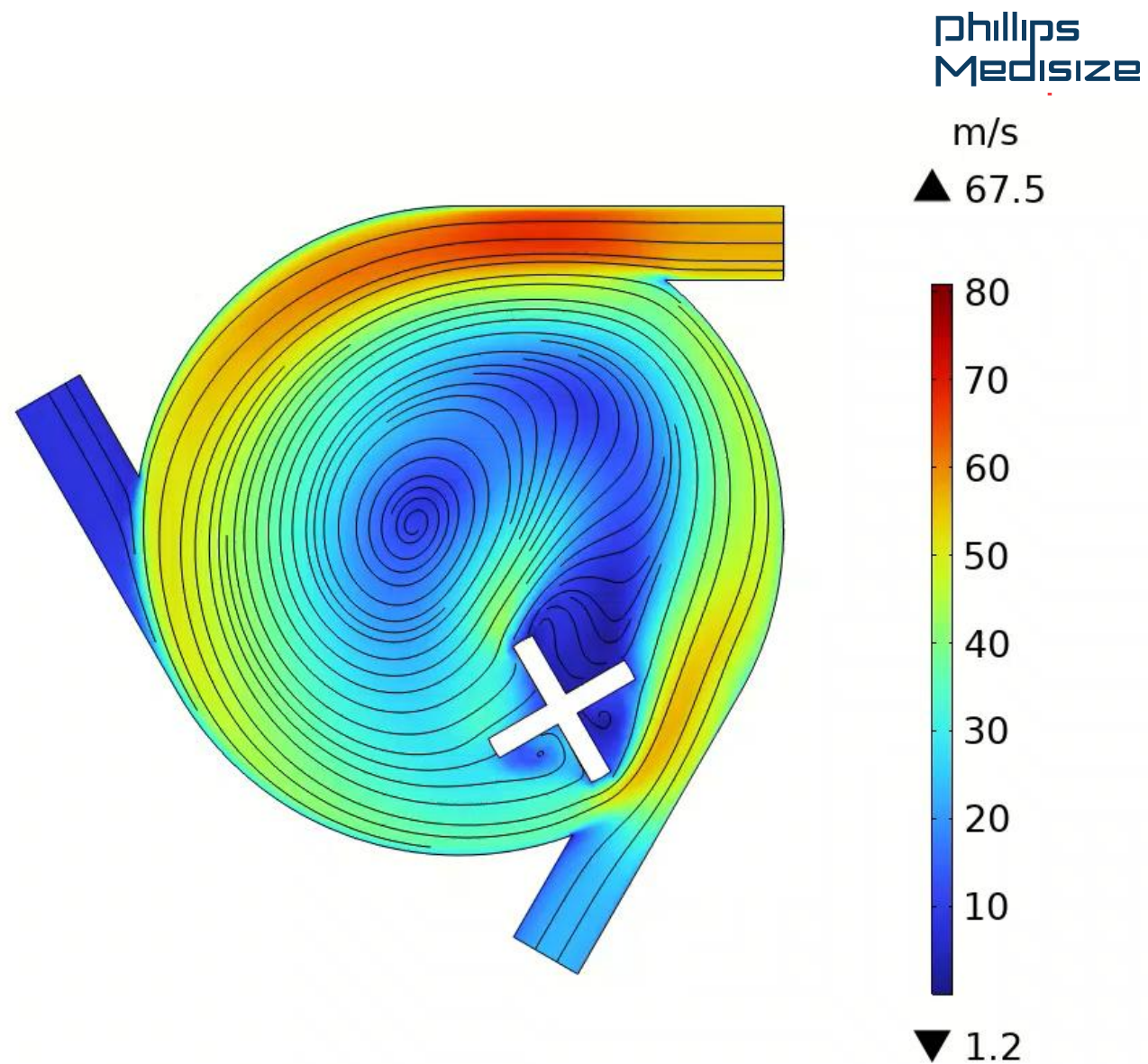


No Ball:



Cruciform Ball:







POWDER TRANSPORT



POWDER TRANSPORT

PARTICLE TRACING

BC modified as a time average approximation of the varying inlet flow by the ball motion

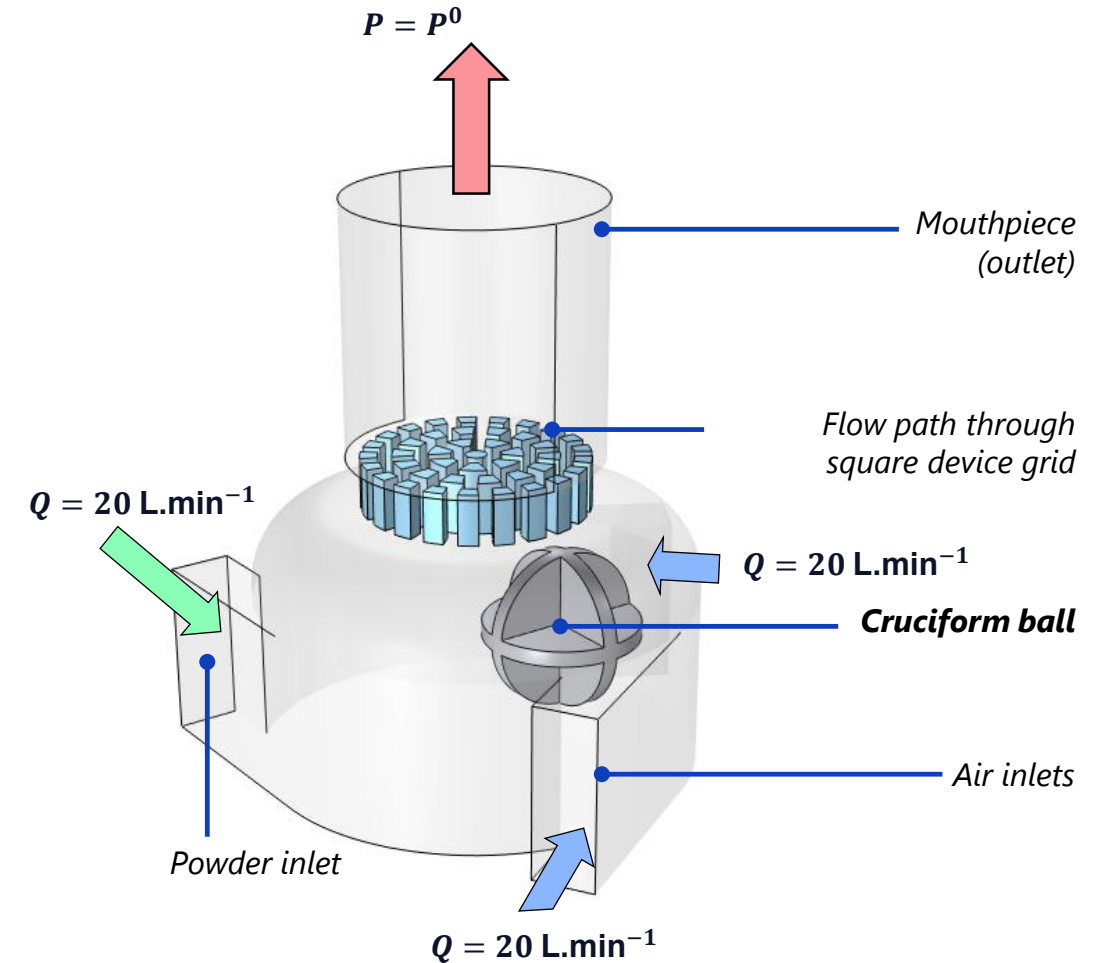
- Normal inlet velocities corresponding to 20 L.min⁻¹ in each inlet
- Outlet pressure set at atmosphere

Particles of various sizes are seeded from a surface covering the whole inlet open area

- Subject to drag forces and follow the equations of motion
- Set flow rate of 60 L.min⁻¹ allows for direct comparison of the geometry and the shape of the balls on particles recovery
- Particles bounce on walls, freeze at the outlet
- The sizes investigated are: 0.2, 0.5, 2.0, 5.0, and 10.0 μm

Simulations at set flow rate of 60 L.min⁻¹ allow for direct comparison of the geometry and the shape of the balls on particles recovery

- Focus on recovery ratio of particles at the device outlet
- Comparison between different configurations (flows with and without balls in the cyclonic chamber — cruciform and spherical)



POWDER TRANSPORT

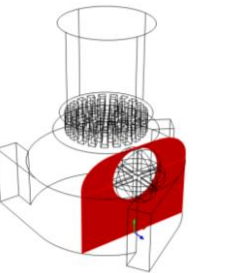
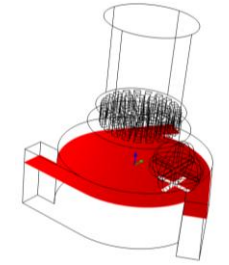
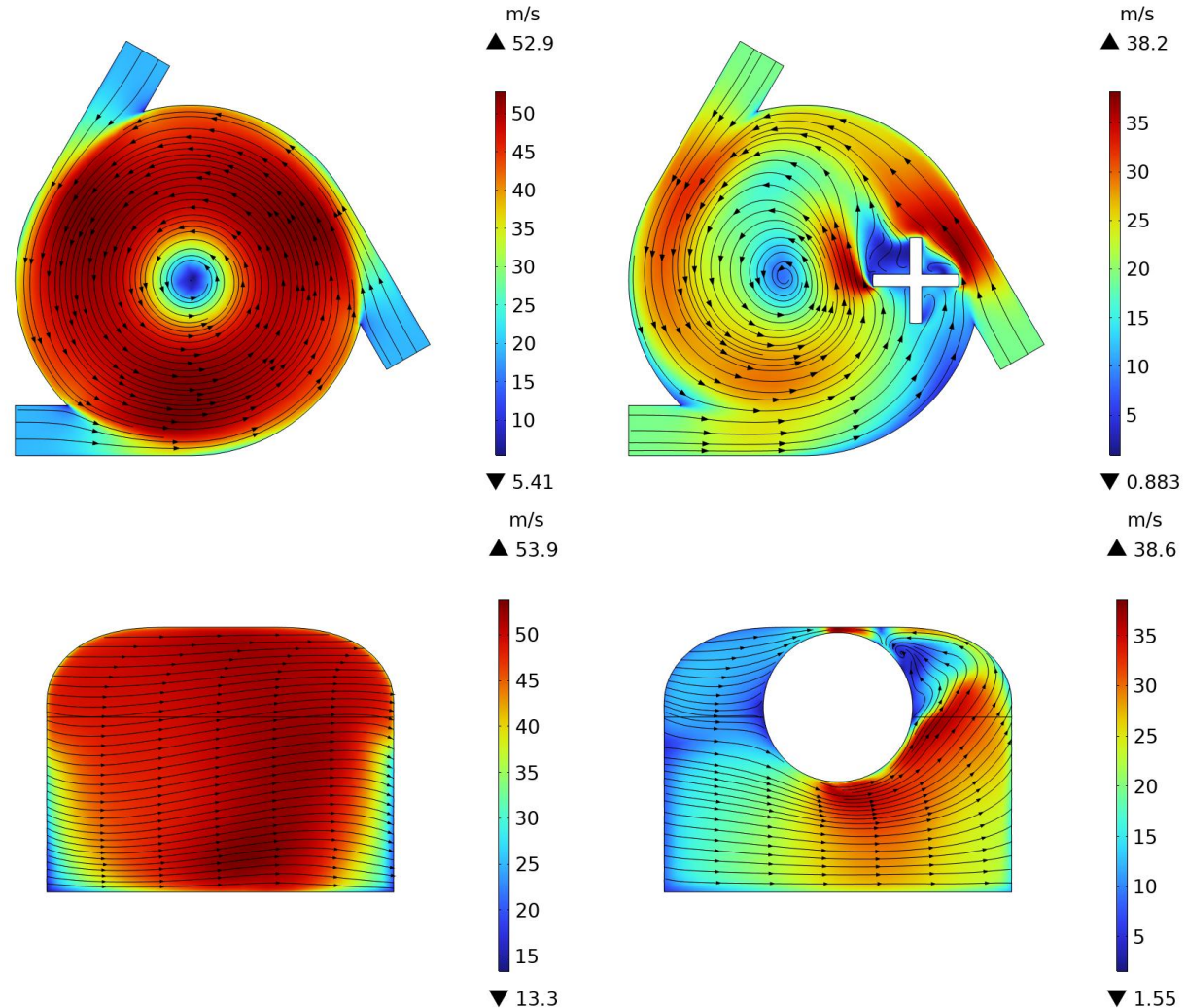
MIDPLANE FLOW VELOCITIES

The approximated flow preserves most of the features identified previously:

- Flow heterogeneities depending on the ball position
- Off-centred cyclone eye

The ball generates an uplift that promotes particles recovery

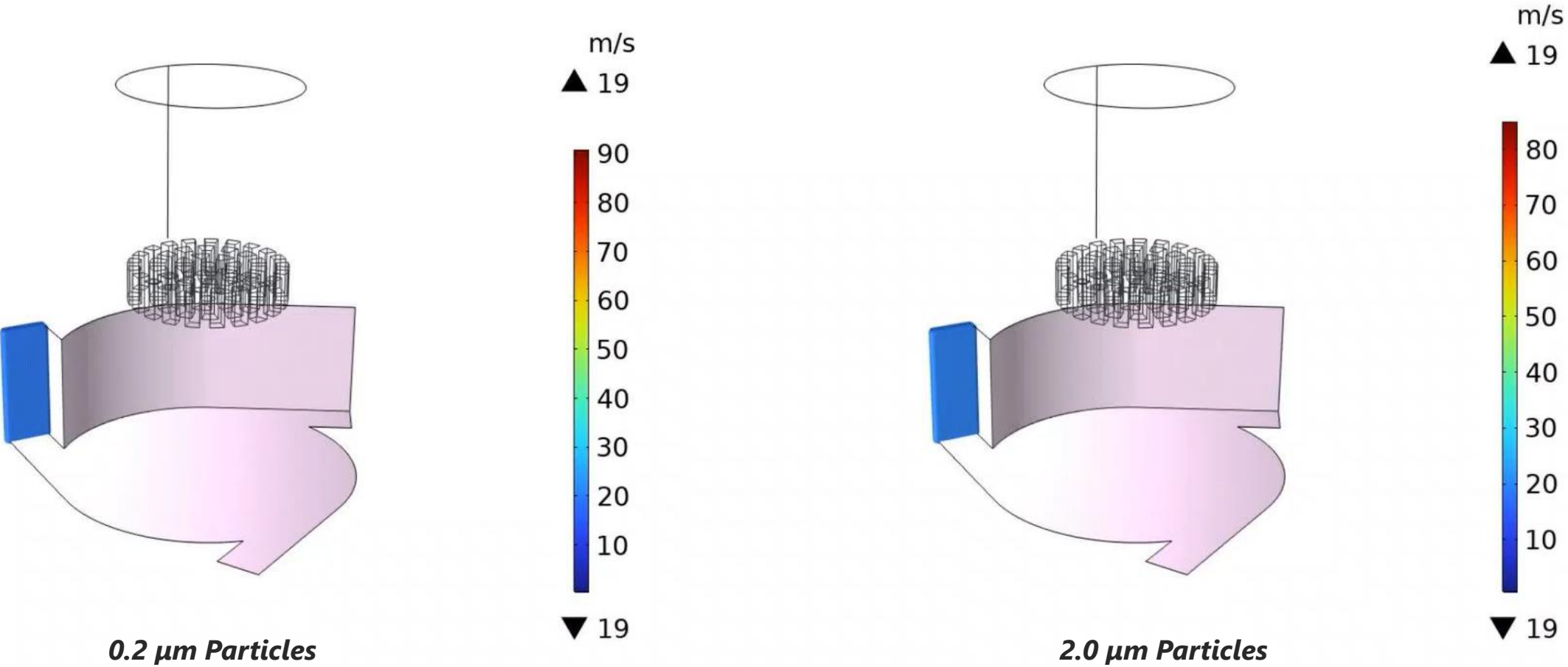
- A similar uplift was also identified with the former set of BC



PARTICLES TRACING

CENTRIFUGAL FORCES TRAP 2.0 μm PARTICLES IN THE CYCLONIC FLOW

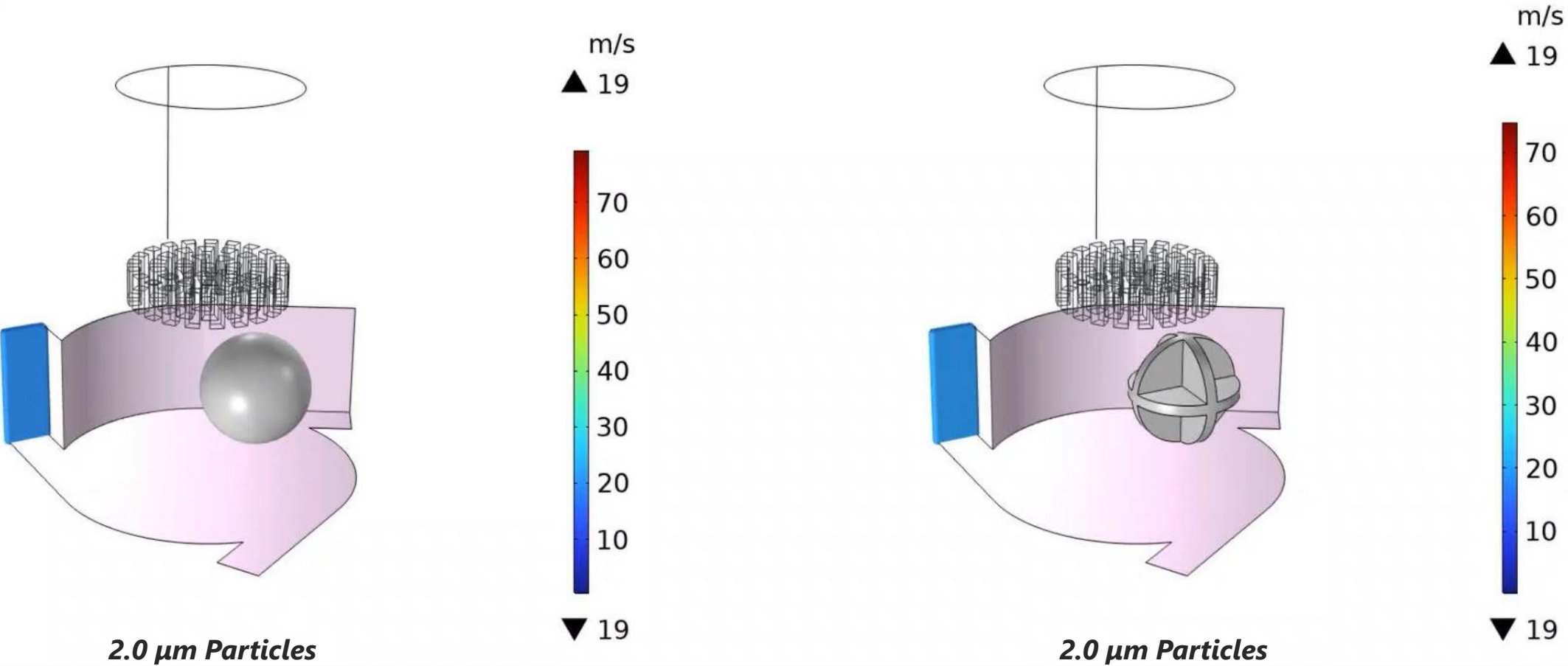
Time=0 ms



PARTICLES TRACING

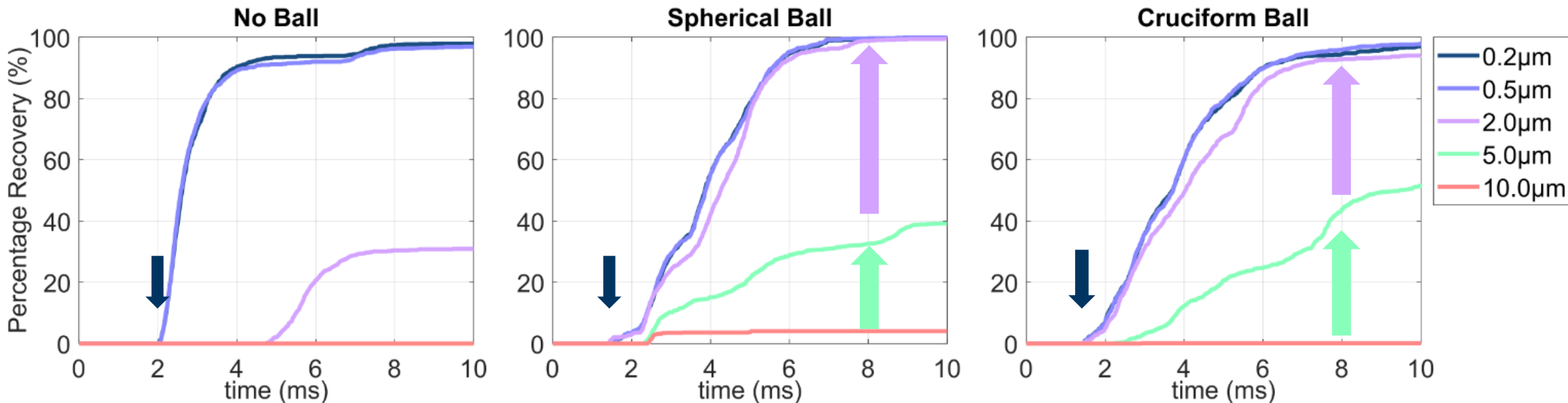
THE BALLS BREAK THE TRAP AND ALLOW RECOVERY OF A LARGER NUMBER OF PARTICLES

Time=0 ms



ENHANCED FLOW RECOVERY

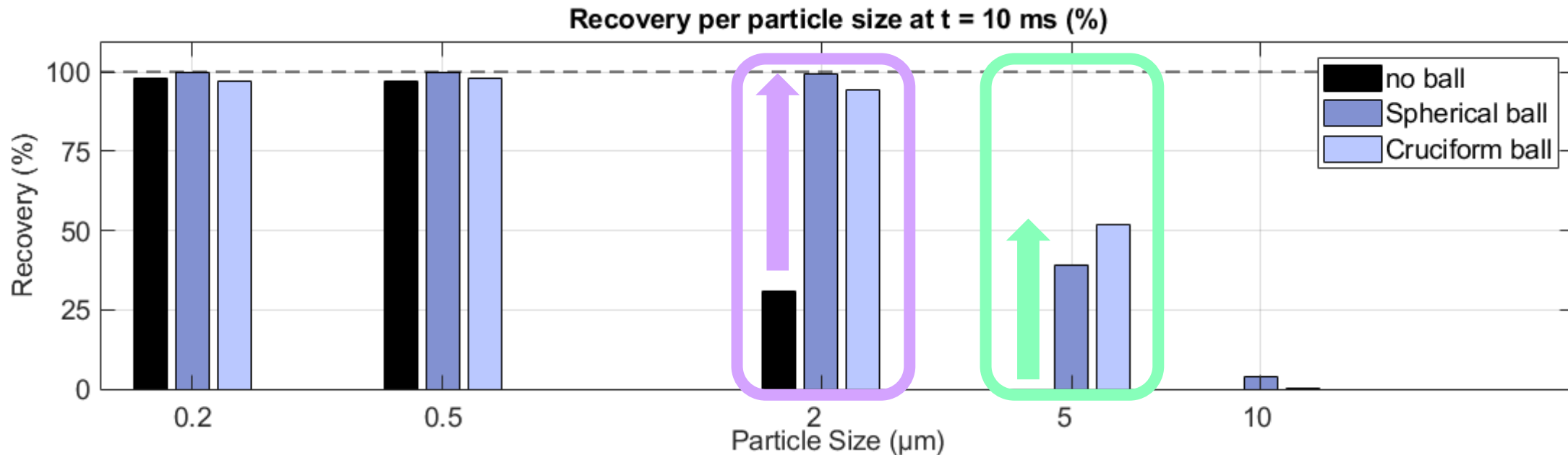
FLOW UPLIFT – RECOVERY DYNAMICS



- Both spherical and cruciform balls improve the recovery of 2 μm and 5 μm particles
- Asymmetric Flow allows an earlier pick up of the particles

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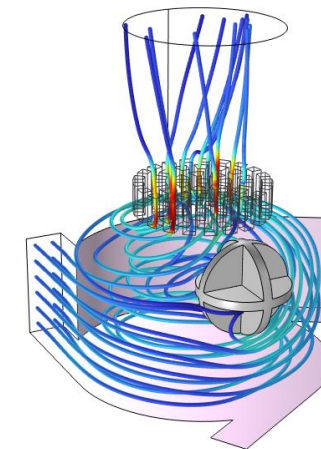
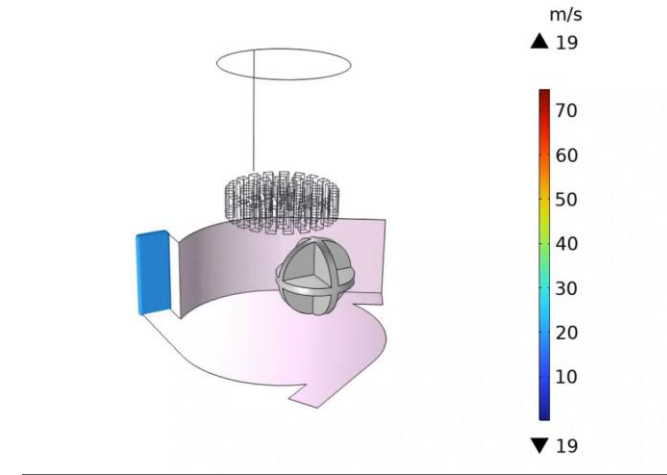
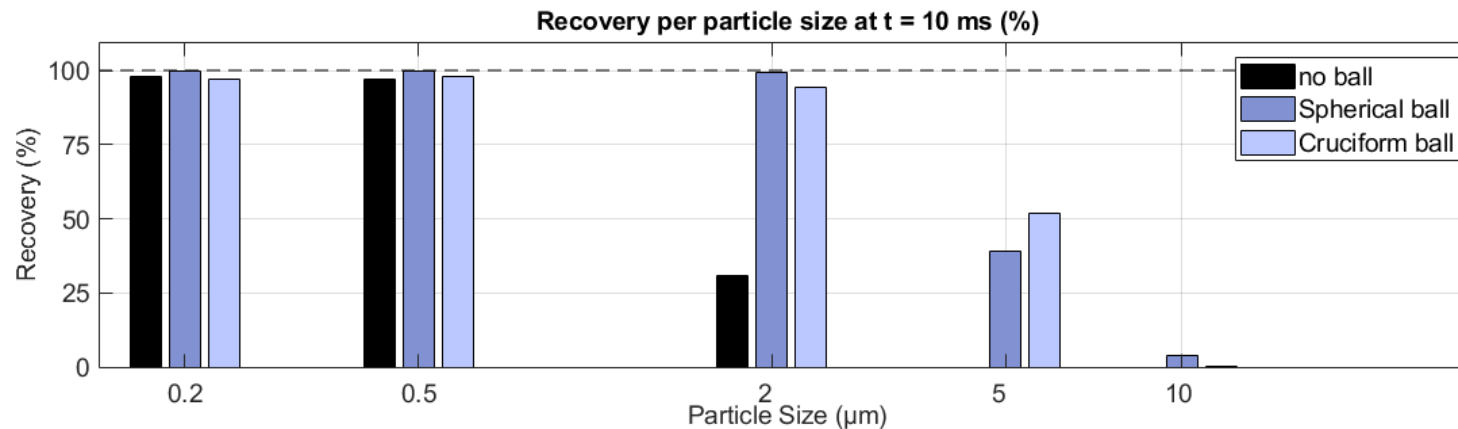
ENHANCED FLOW RECOVERY

FLOW UPLIFT

The cruciform ball creates an uplift that promotes particle recovery and lets them escape the centrifugal forces.

Additional effects such as impacts against the ball surface promote deagglomeration as well.

- The cruciform ball shape promotes impaction of particles by inducing sudden changes of flow direction near its surface





Conclusions

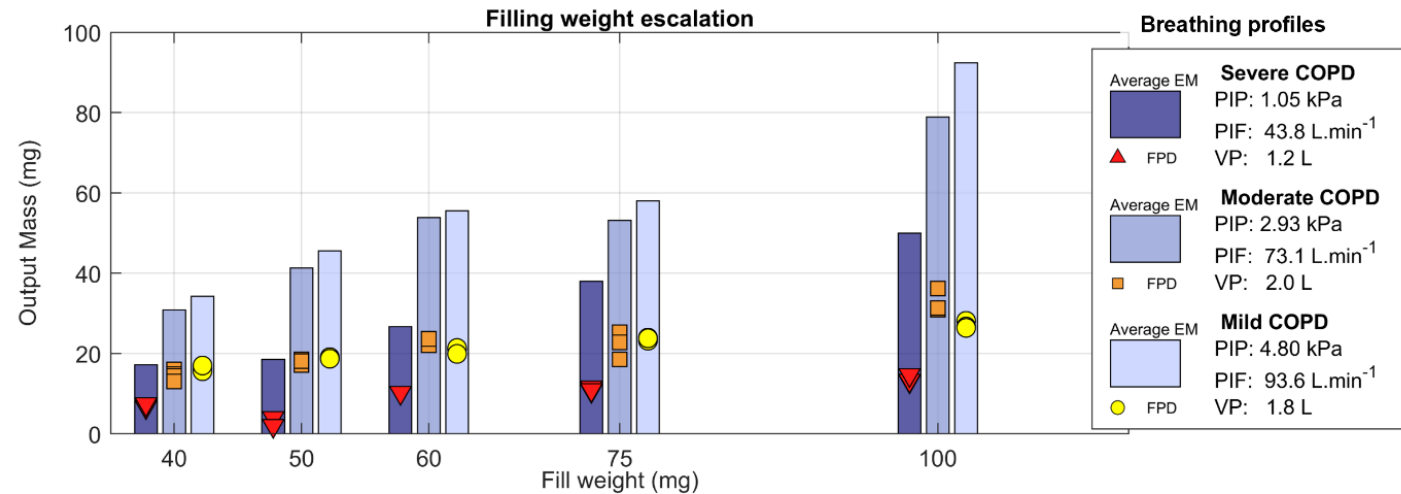


DEVICE PERFORMANCE

DEAGGLOMERATION ENGINE

O1's deagglomeration engine ensures powder aerosolization by generating a chaotic flow in a cyclone chamber.

This allows a sustained and flat performance of fine particle dose (FPD) which correlates to lung dose over a large range of powder payloads and inspiratory efforts



The disruption of the cyclone by the cruciform ball enhances the particle recovery by an uplift of the streamlines in the wake of the ball, while also promoting particles deagglomeration.

Observations of cyclonic flows of denser powders suggest potential applications for heavier formulations than the micronized API rich formulation presented here.

SIMULATIONS IN DEVELOPMENT

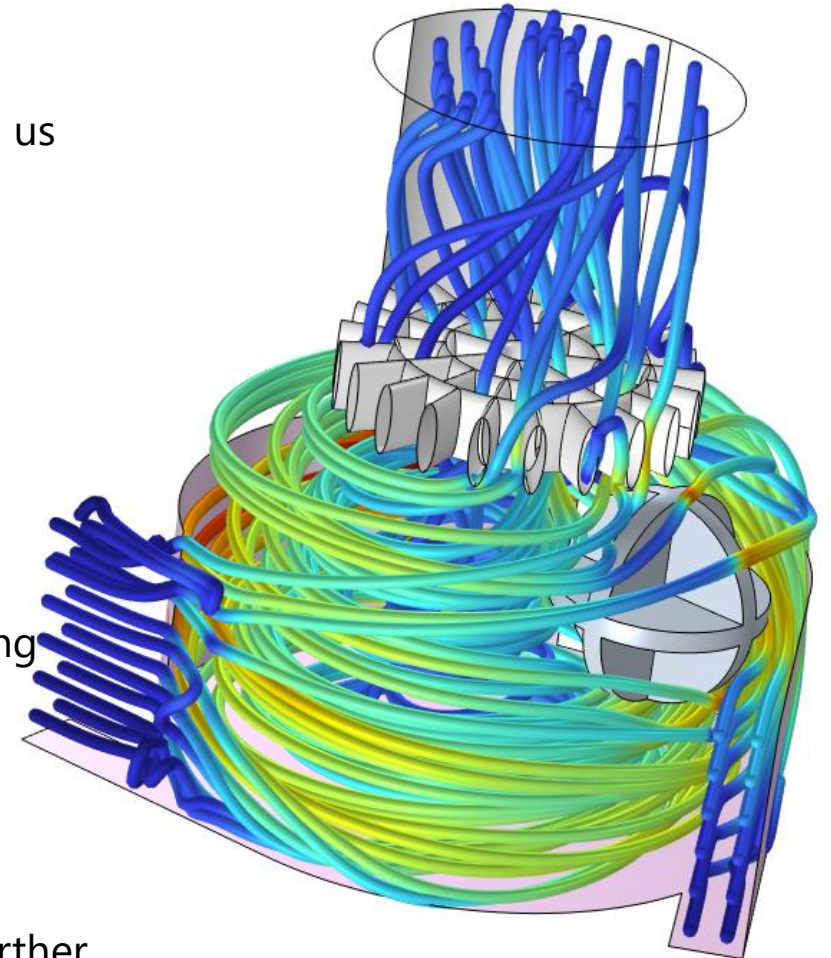
AN ASSET ALL ALONG THE JOURNEY

Simulations were a key tool for the development of this concept device, allowing us to:

- Understand, investigate and test the physics of a complex flow
- Identify rules of design to maximise performance
- Rationalise experimental results

COMSOL's multiphysics capabilities and versatility are well suited to understanding the coupling between a flow and the particle dynamics

- The particle tracing module offers more capabilities than those demonstrated here, particularly with regard to deagglomeration
- Future developments of the module will hopefully enable the modelling of further phenomena, such as fluidisation and compaction



THANKS AND ACKNOWLEDGEMENTS

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Thanks to COMSOL and moderators for giving us the opportunity to share our learnings.



Thanks to all colleagues involved for providing support and insights to conduct this development.



Thanks to everyone here for joining this session.

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