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Experimental and model-based investigation of twin screw granulation

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FACULTY OF PHARMACEUTICAL SCIENCES
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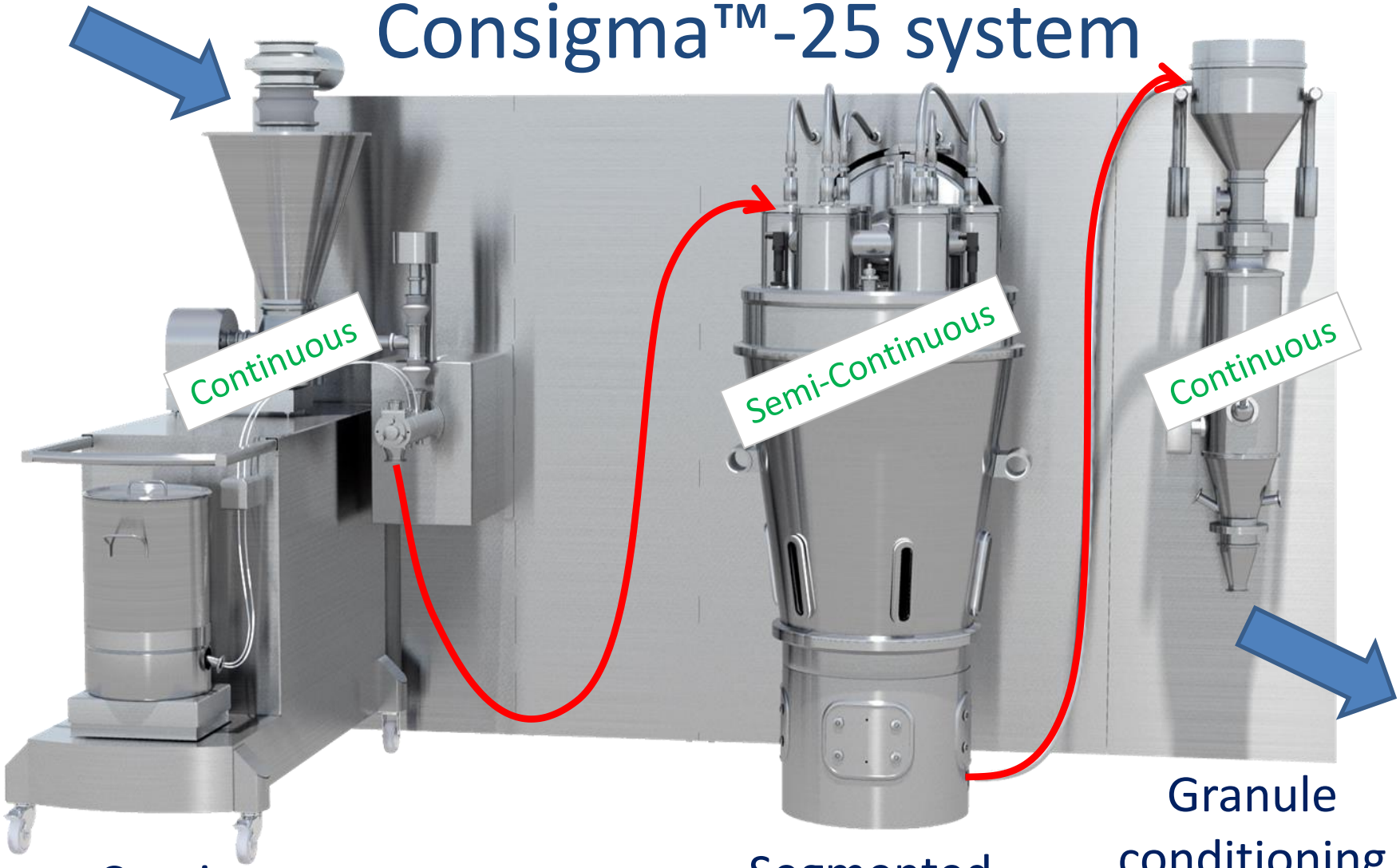
FACULTY OF BIOSCIENCE ENGINEERING

Continuous manufacturing line Consigma™-25 system

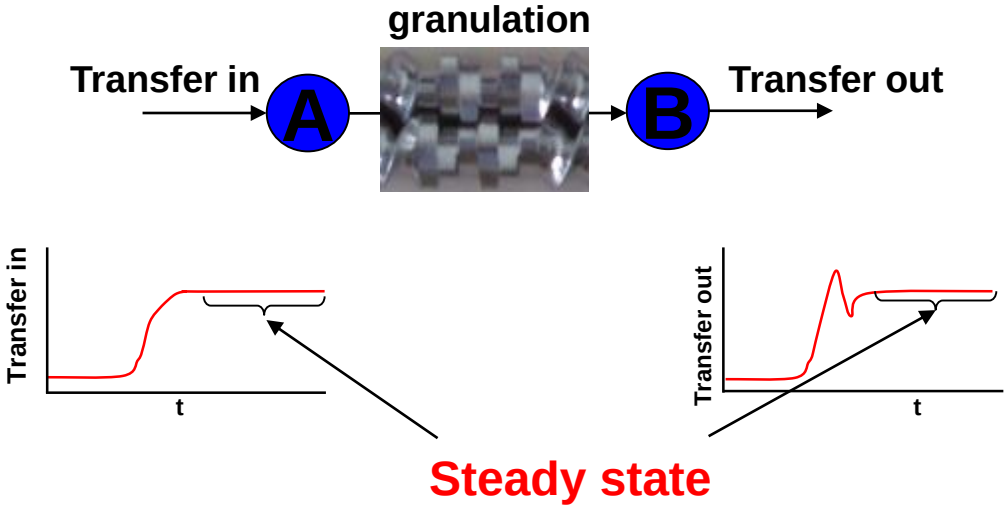


Continuous twin-screw granulator

Segmented Fluid bed dryer

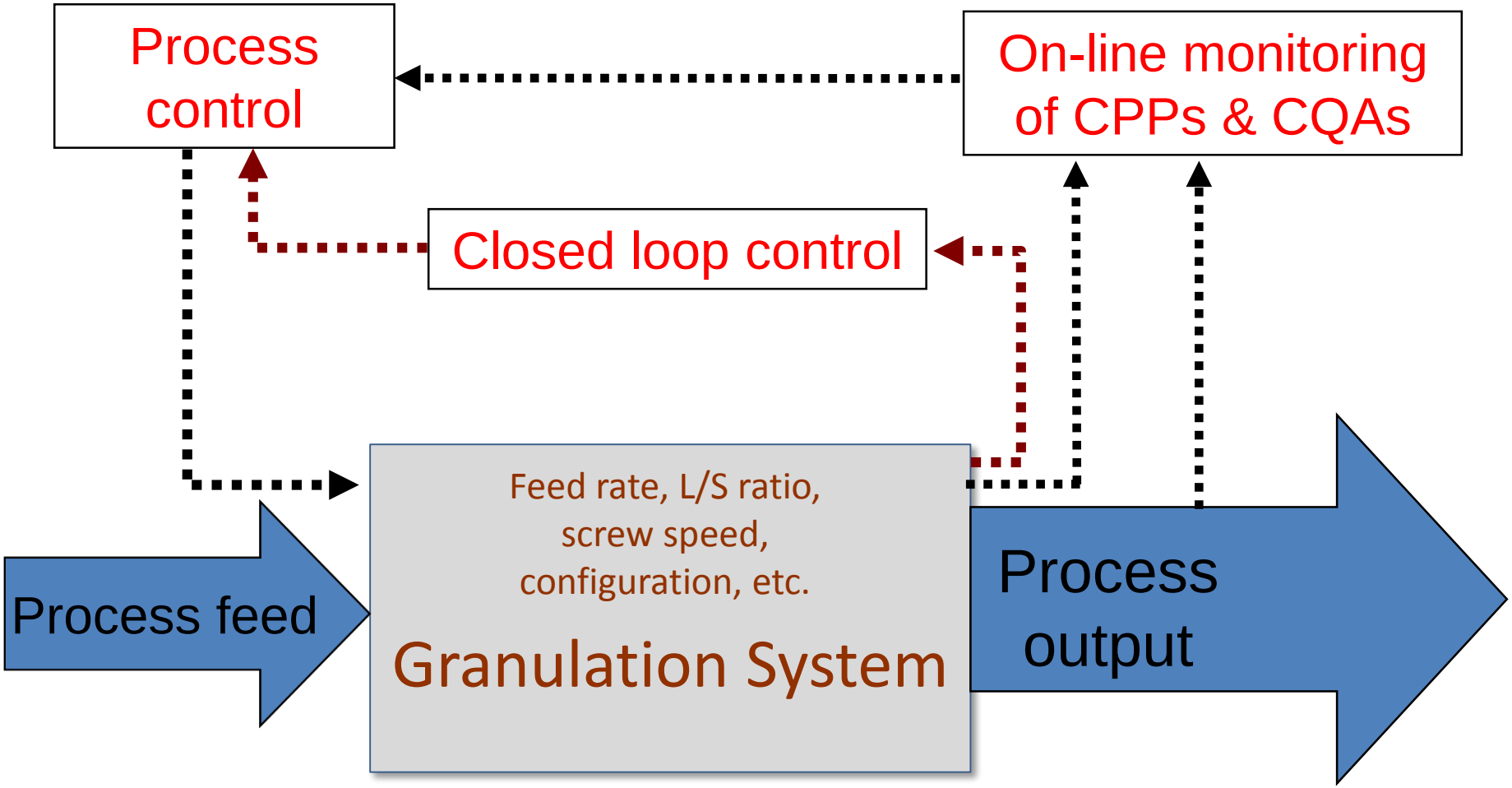
Granule conditioning module

At appropriate time-scales and conditions, granulation is in steady state

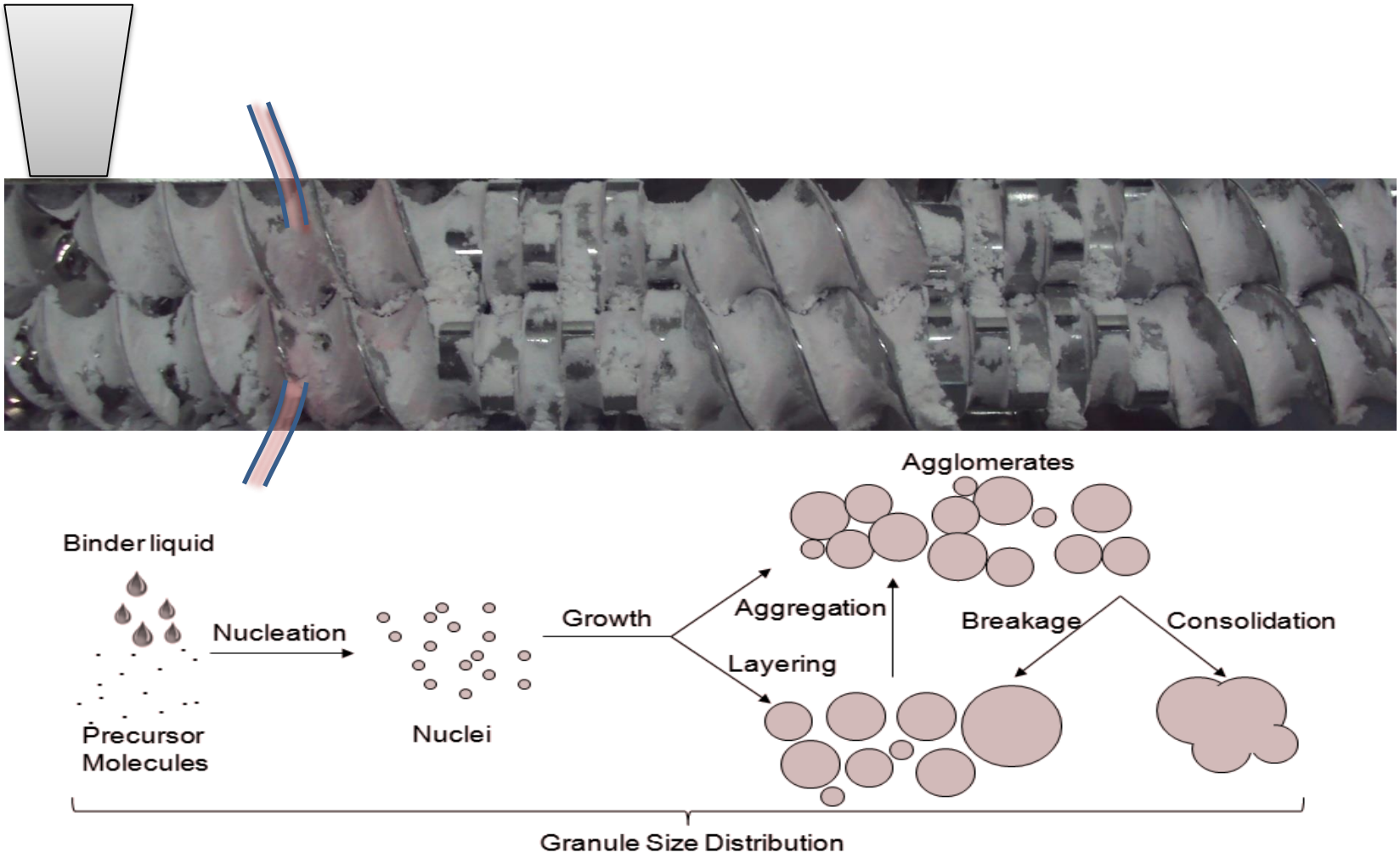


Two key implications

1. Fluxes are roughly constant (Dynamics are transient)
2. If feed is constant, product quality is consistent!


Process control
On-line monitoring of CPPs & CQAs
Closed loop control
Process feed
Feed rate, L/S ratio,
screw speed,
configuration, etc.
Granulation System
Process output

Twin-Screw Granulator applies High Shear Wet Granulation



Twin-screw granulation process development

Areas under study:

- Granulation time and mixing.
- Aggregation and breakage rates.

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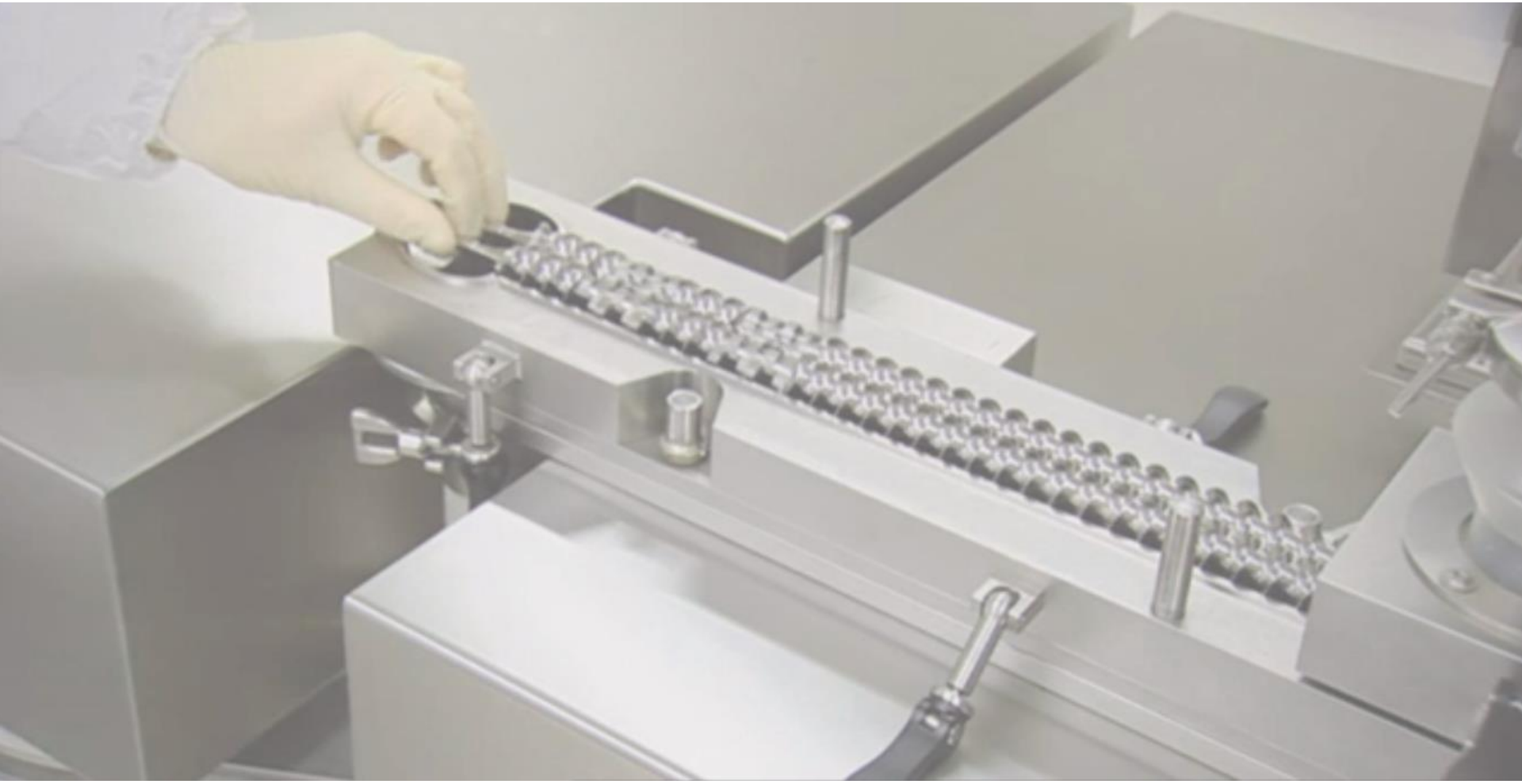
Consigma™-1 system

(GEA pharma systems, Collette)

Open barrel of a twin screw granulator

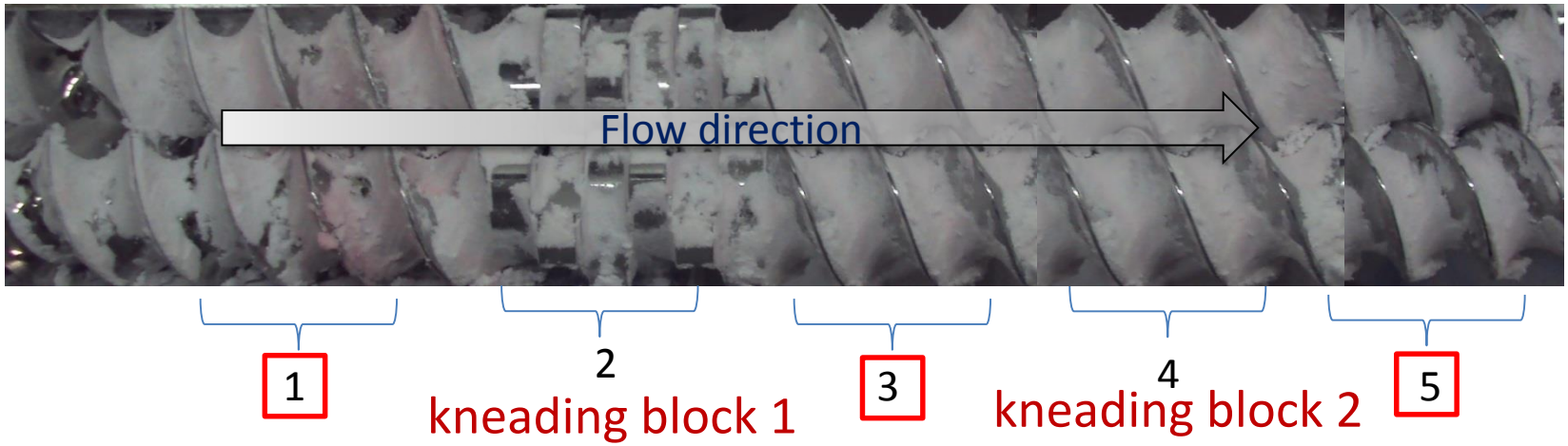


Consigma™- 1 experiments

Lactose/PVP (97.5/2.5) premix was granulated with distilled water

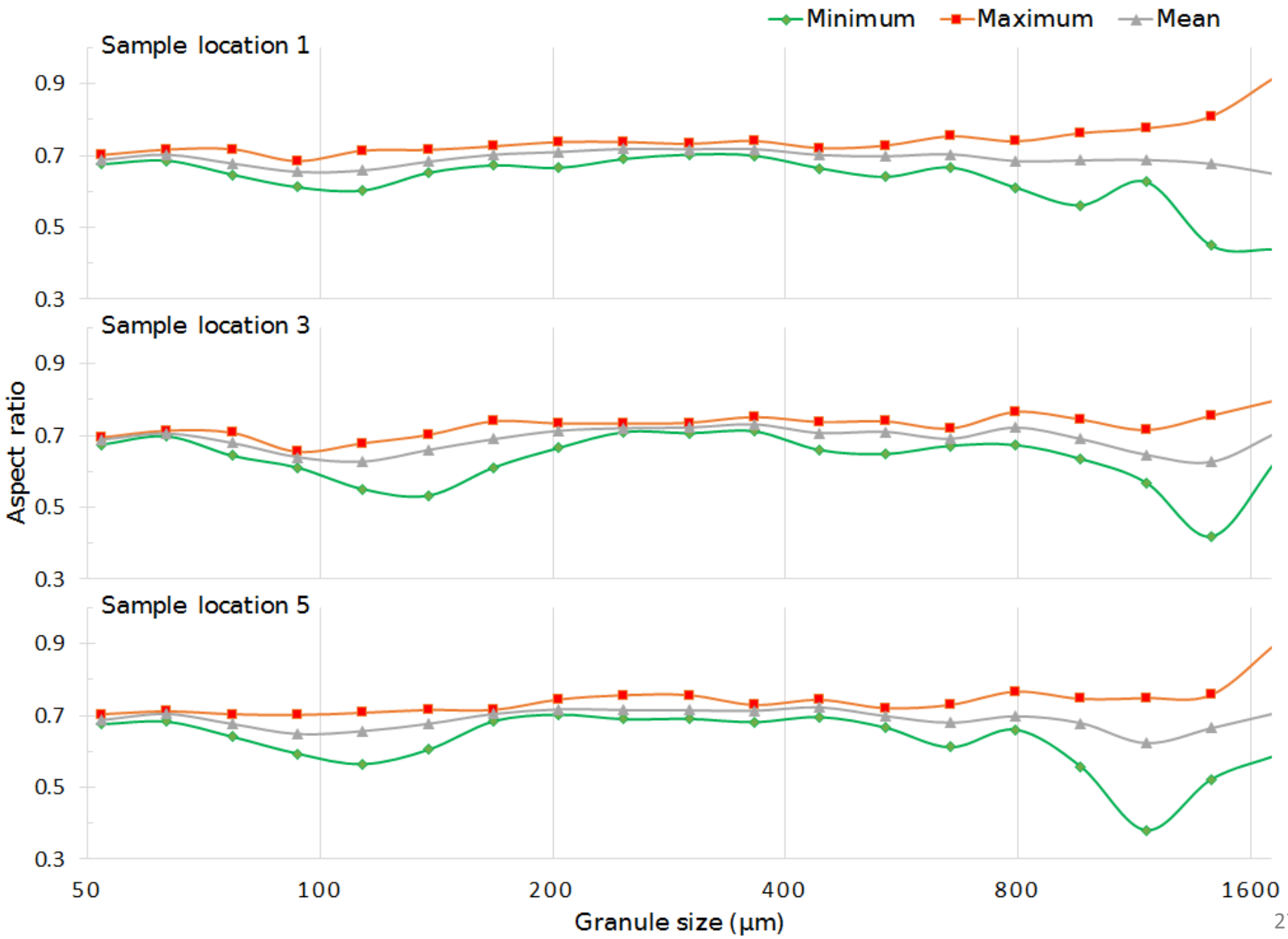
Factors:

Parameters	Low	High
Throughput	10 Kg/h	25 Kg/h
Liquid-solid ratio	4.58 %	6.52%
Screw speed	500 RPM	900 RPM

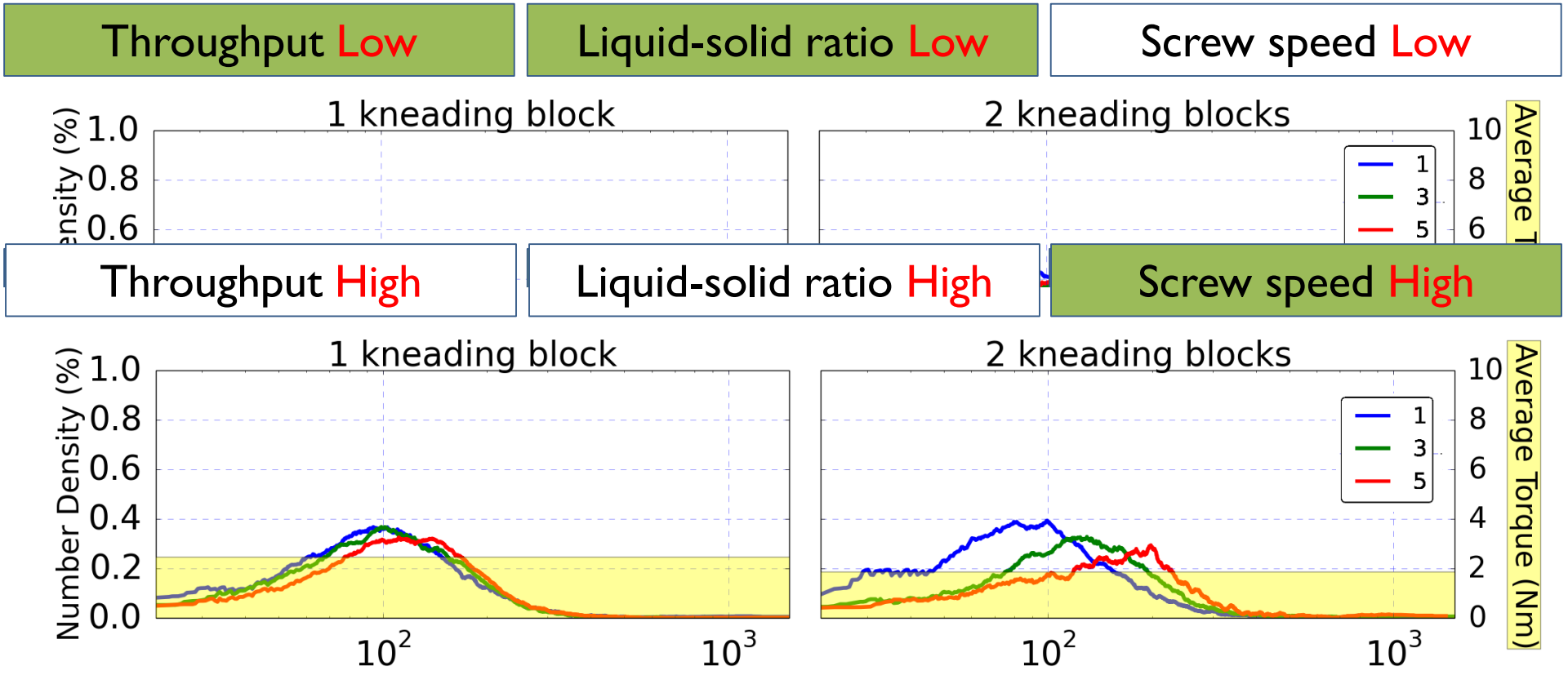


Responses: Particle characterization by Dynamic Image Analysis (Location 1, 3, 5)

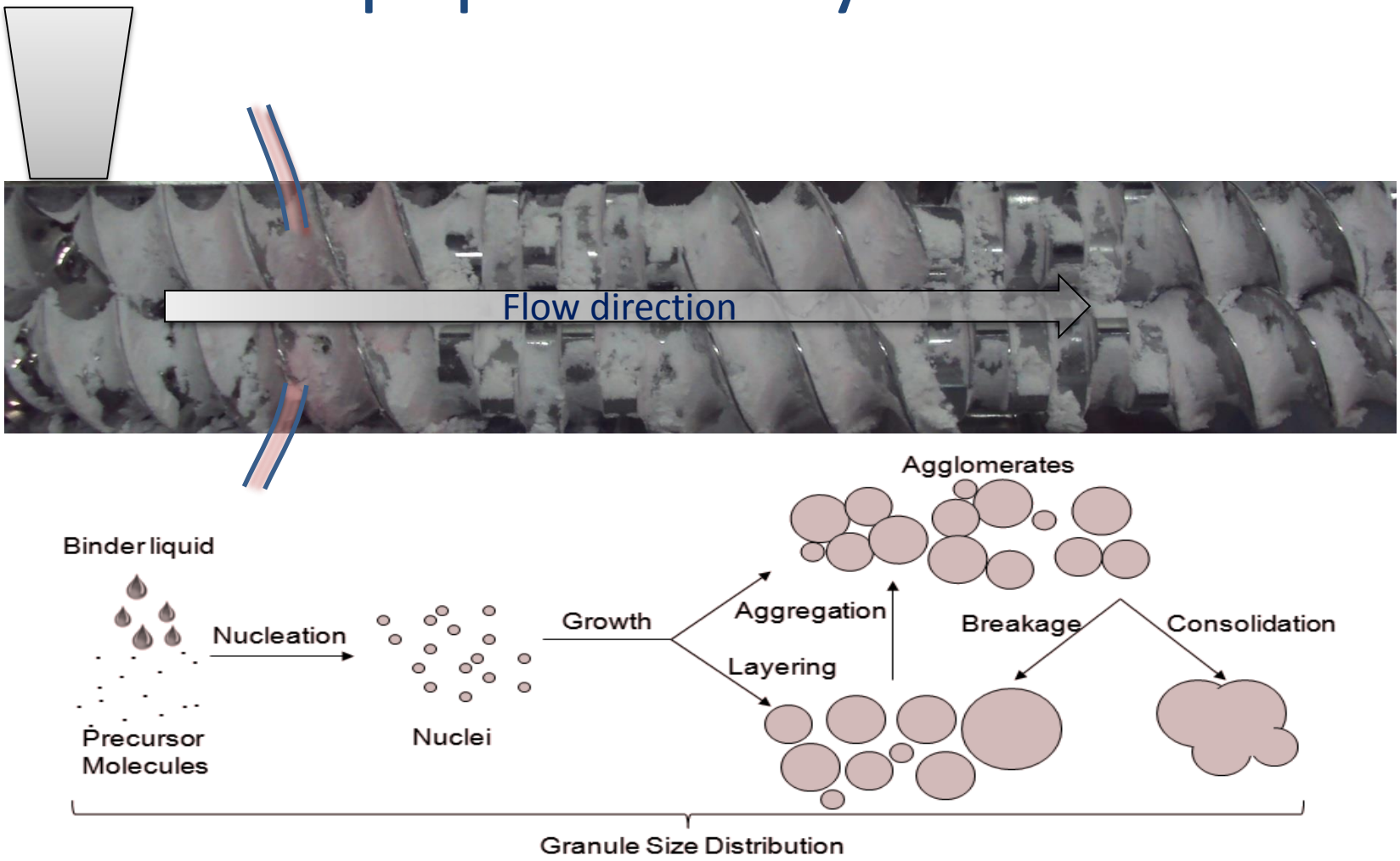
Average Feret diameter vs Aspect ratio



Comparing average Feret diameter



Granulation is result of particle population dynamics



Population balance equation

$$\frac{\partial n(t,x)}{\partial t} = \frac{Q_{in}}{\tilde{V}} n_{in}(x) - \frac{Q_{out}}{\tilde{V}} n_{out}(x)$$

GSD balance

Aggregation term

$$+\frac{1}{2}\int_0^x \beta(t, x-\varepsilon, \varepsilon)\, n(t, x-\varepsilon)\, n(t,\varepsilon)\, d\varepsilon$$

$$-n(t,x)\int_0^\infty \beta(t,x,\varepsilon)\, n(t,\varepsilon)\, d\varepsilon$$

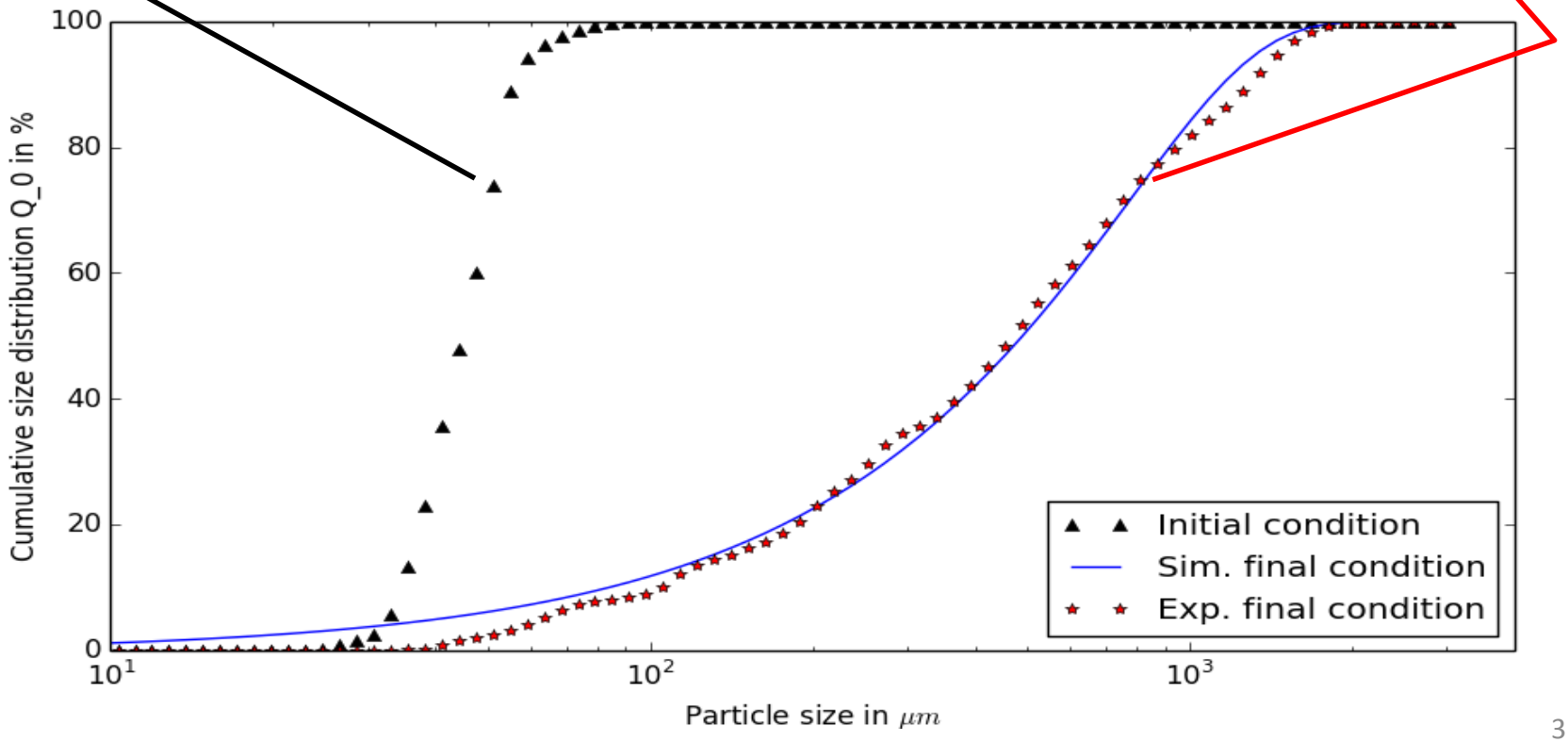
Breakage term

$$+\int_0^\infty b(x,\varepsilon) S(\varepsilon) n(t,\varepsilon)\, d\varepsilon$$

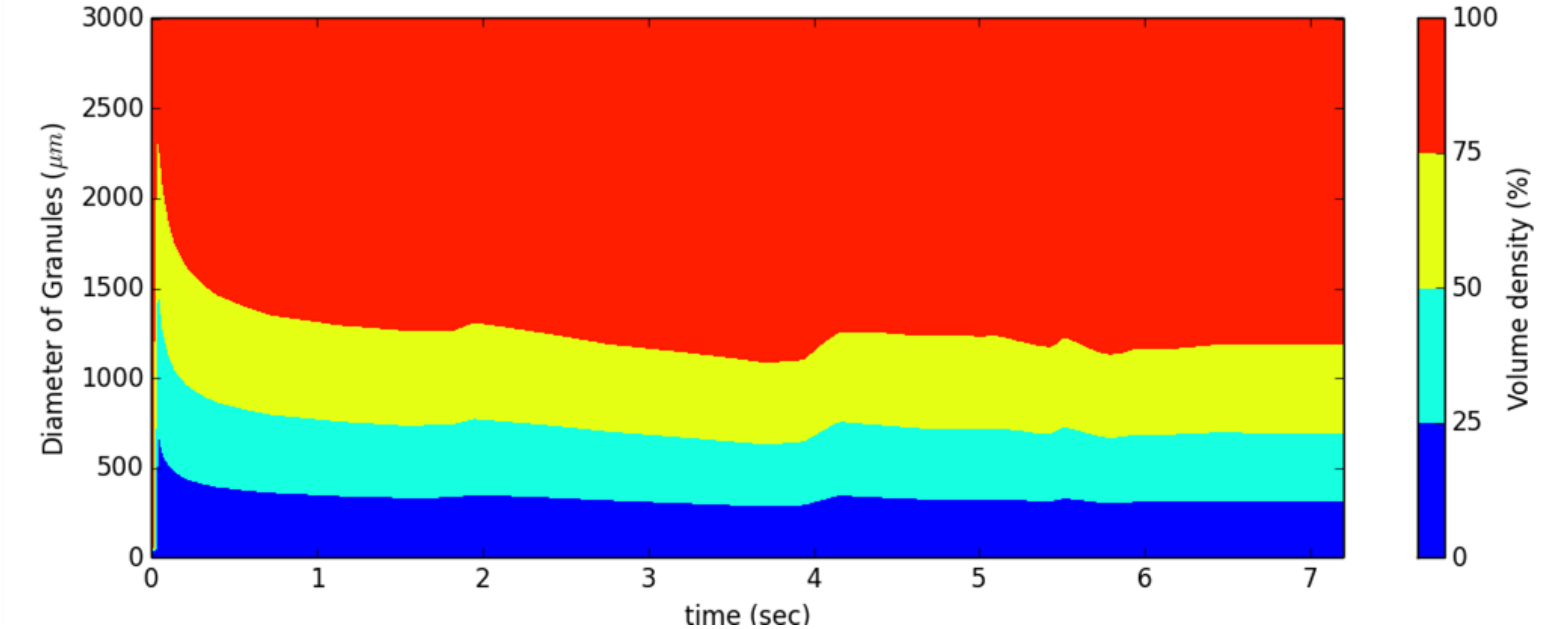
$$-S(x) n(t,x)$$

β = aggregation rate
S = selection rate
b = breakage function

Experimental and simulated data have a good agreement



Particle population dynamics during granulation



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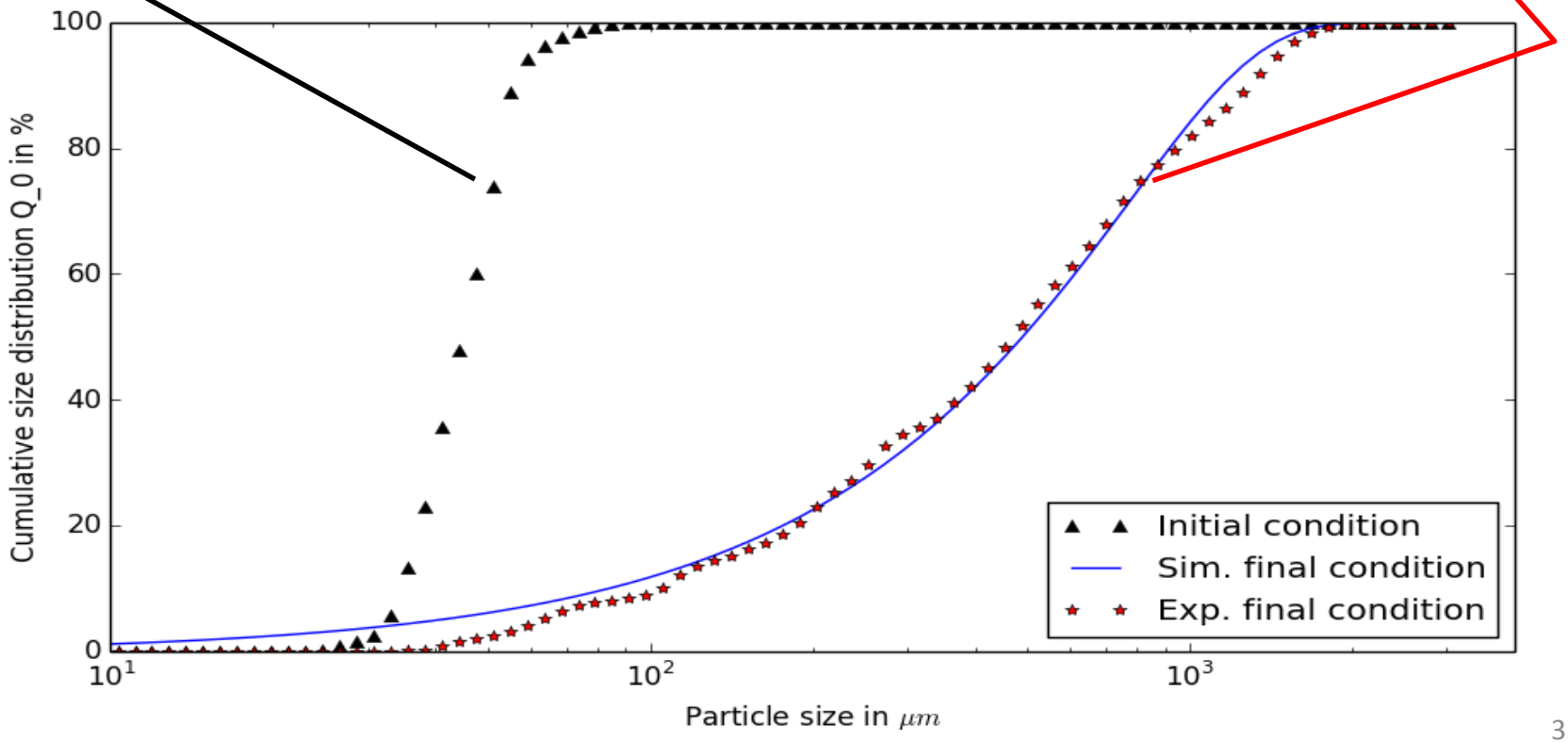
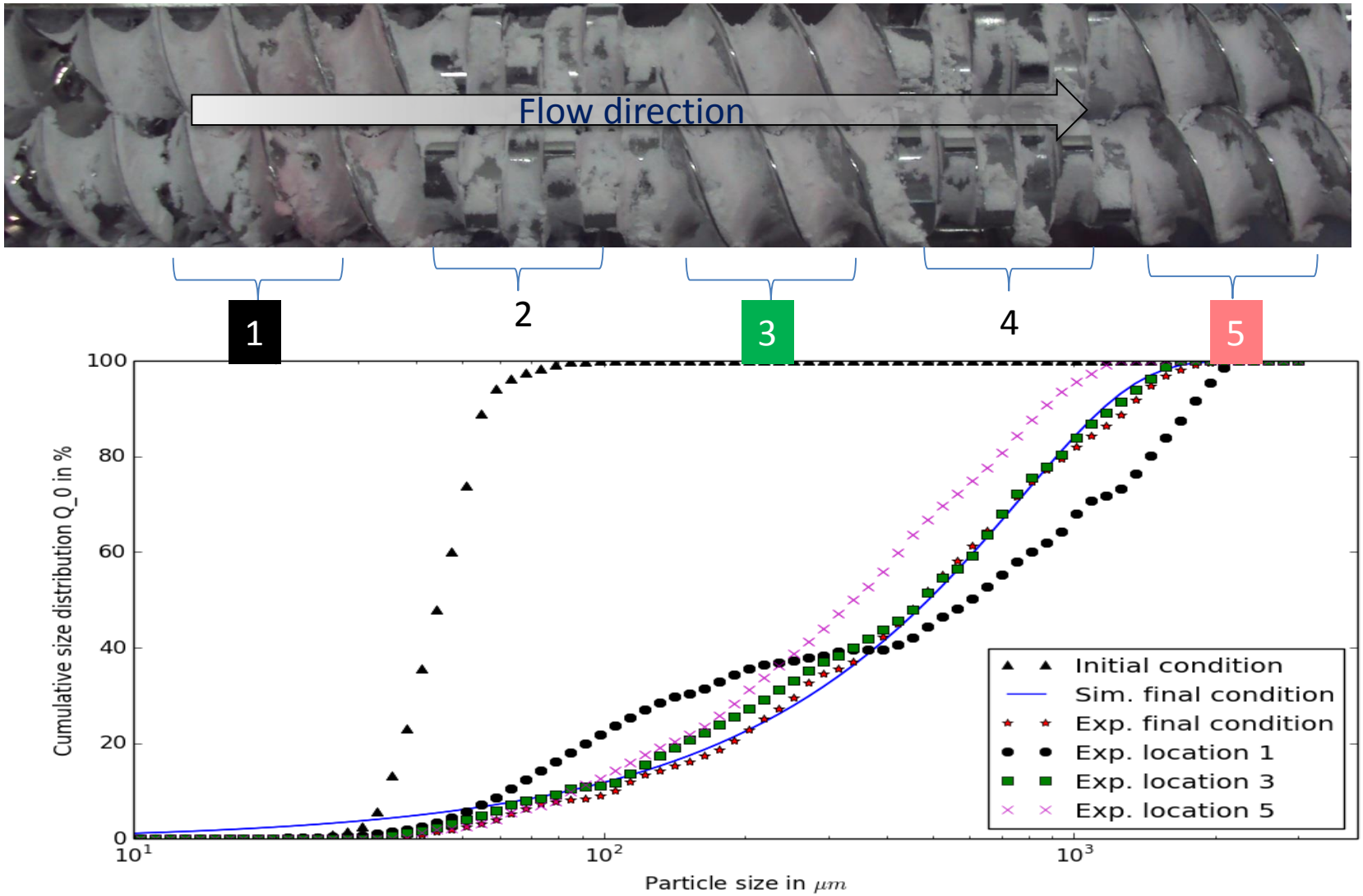


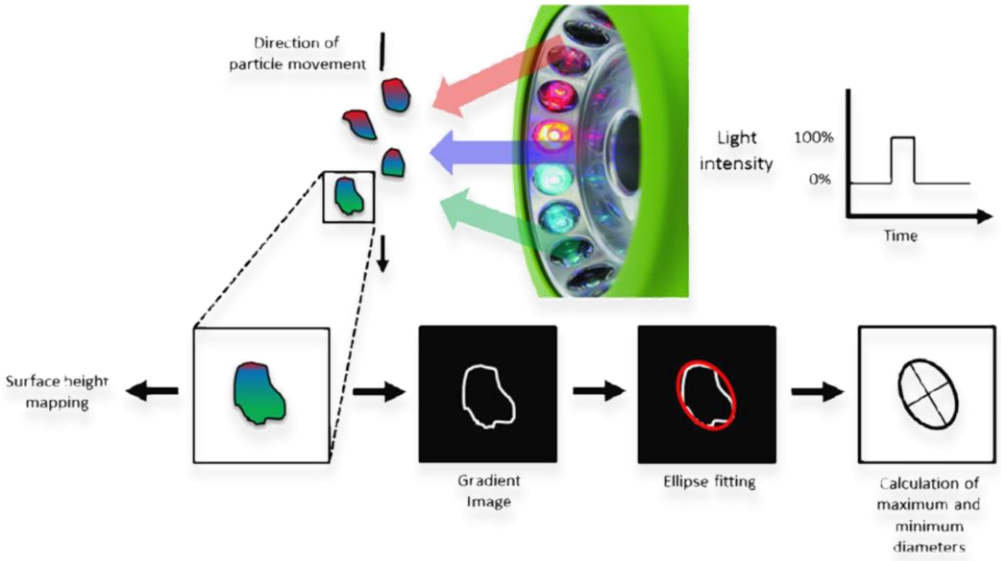
Including effect of granulator design on granule size distribution



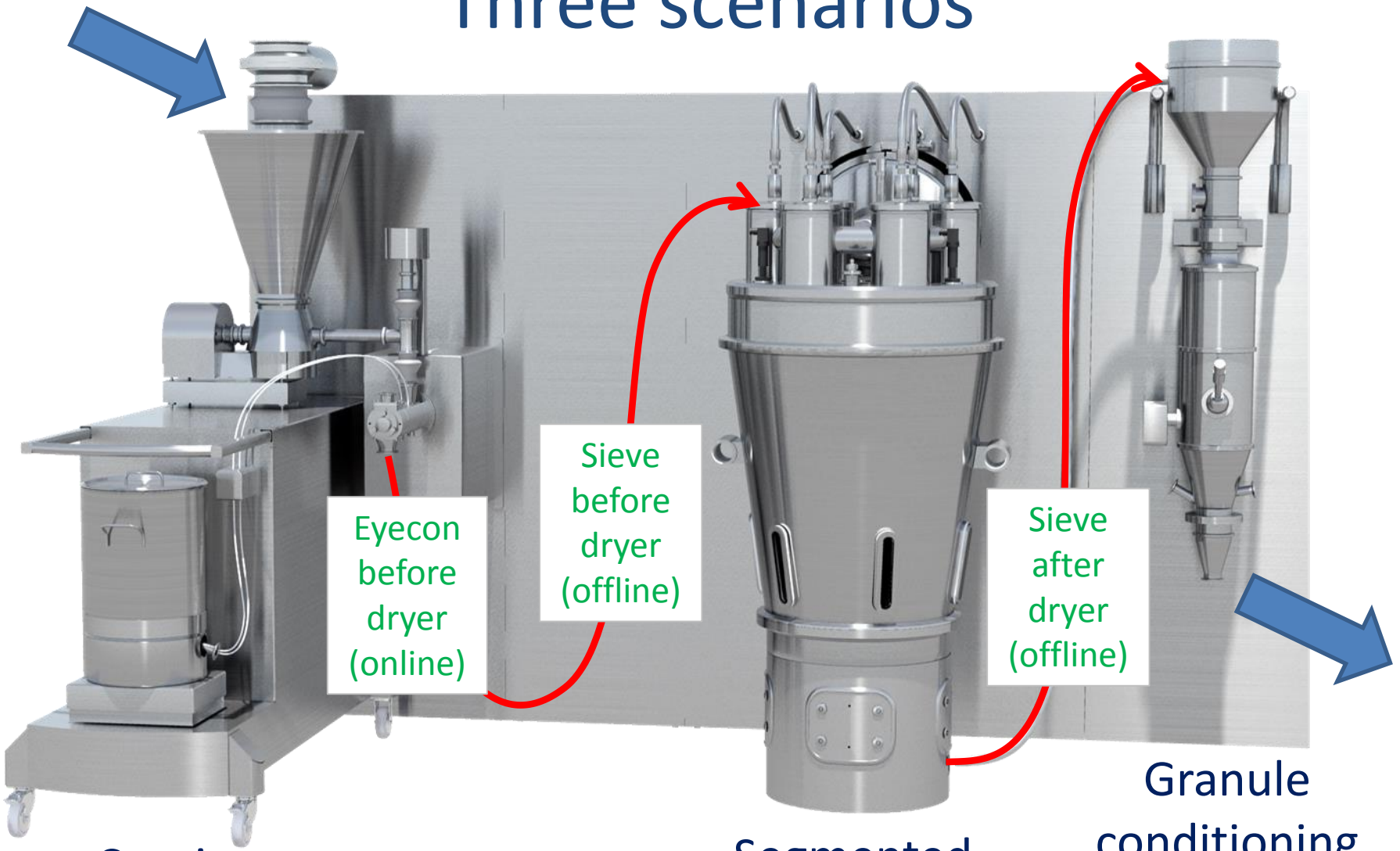
IS IT EYECON RESULTS USEABLE?

Comparison of PSD analysis methods

- Sieve analysis
- 3D imaging techniques (Eyecon™)



Three scenarios



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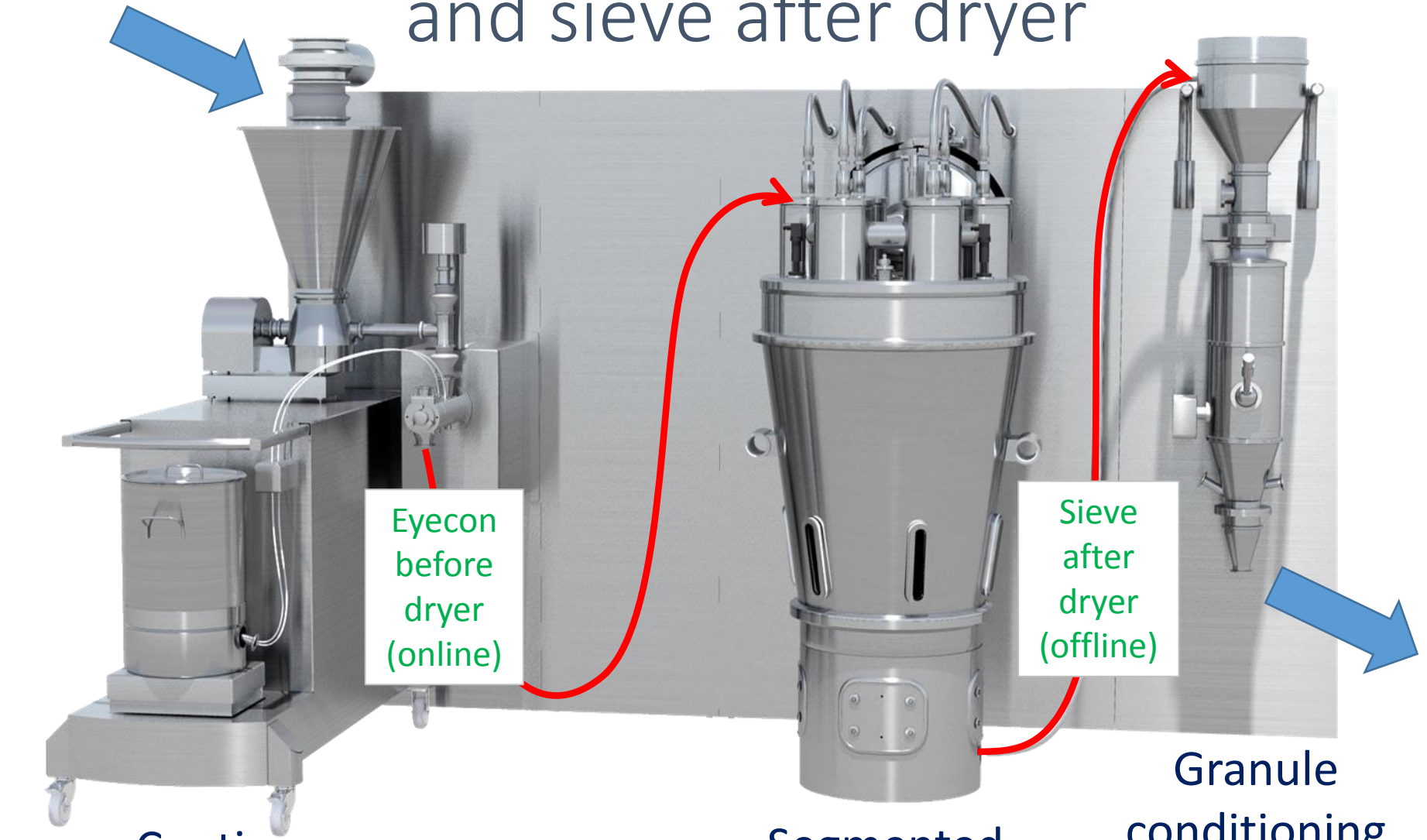
Segmented Fluid bed dryer

Granule conditioning module

Process settings for the runs

	Run 1	Run 2	Run 3	Run 4
Throughput (kg/h)	25	10	10	25
Liquid addition (%)	9	9	8	9
Screw	1x6	1x6	2x6	2x6
Screw Speed (RPM)	500	900	900	900
Stagger angle (°)	60	60	60	60
Temperature (°C)	25	25	25	25
Binder Addition	Wet	Wet	Wet	Wet

Difference between Eyecon before dryer and sieve after dryer



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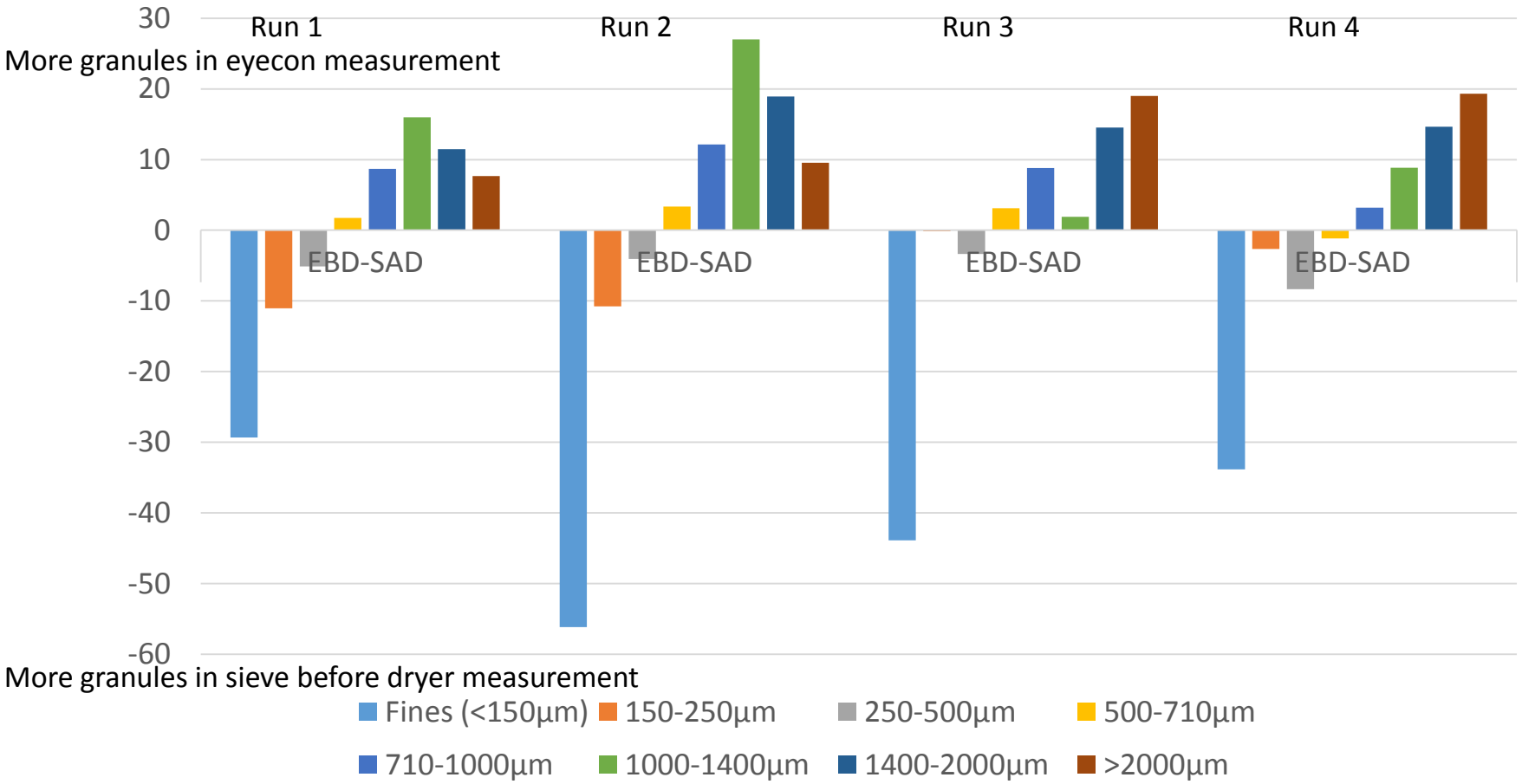

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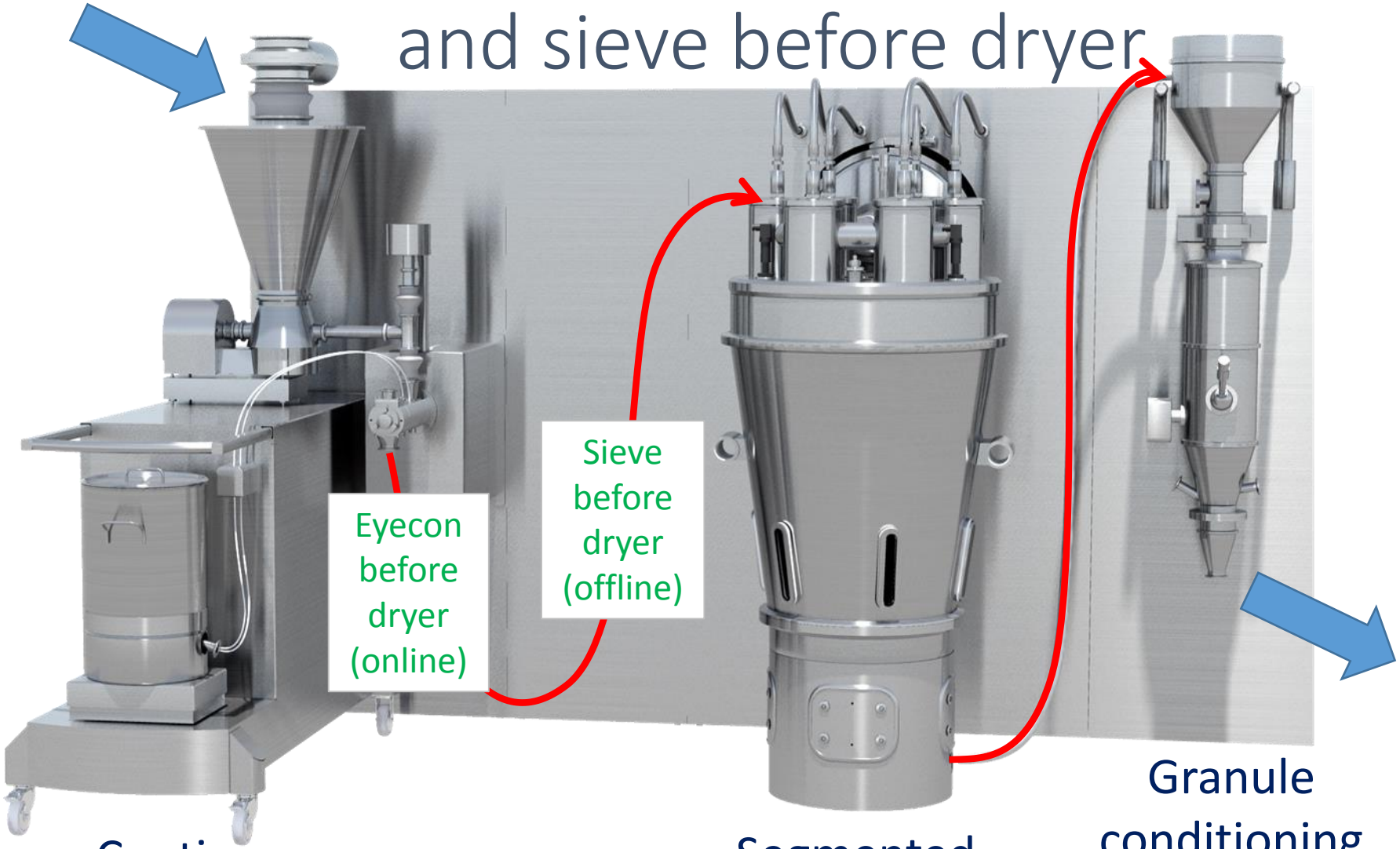
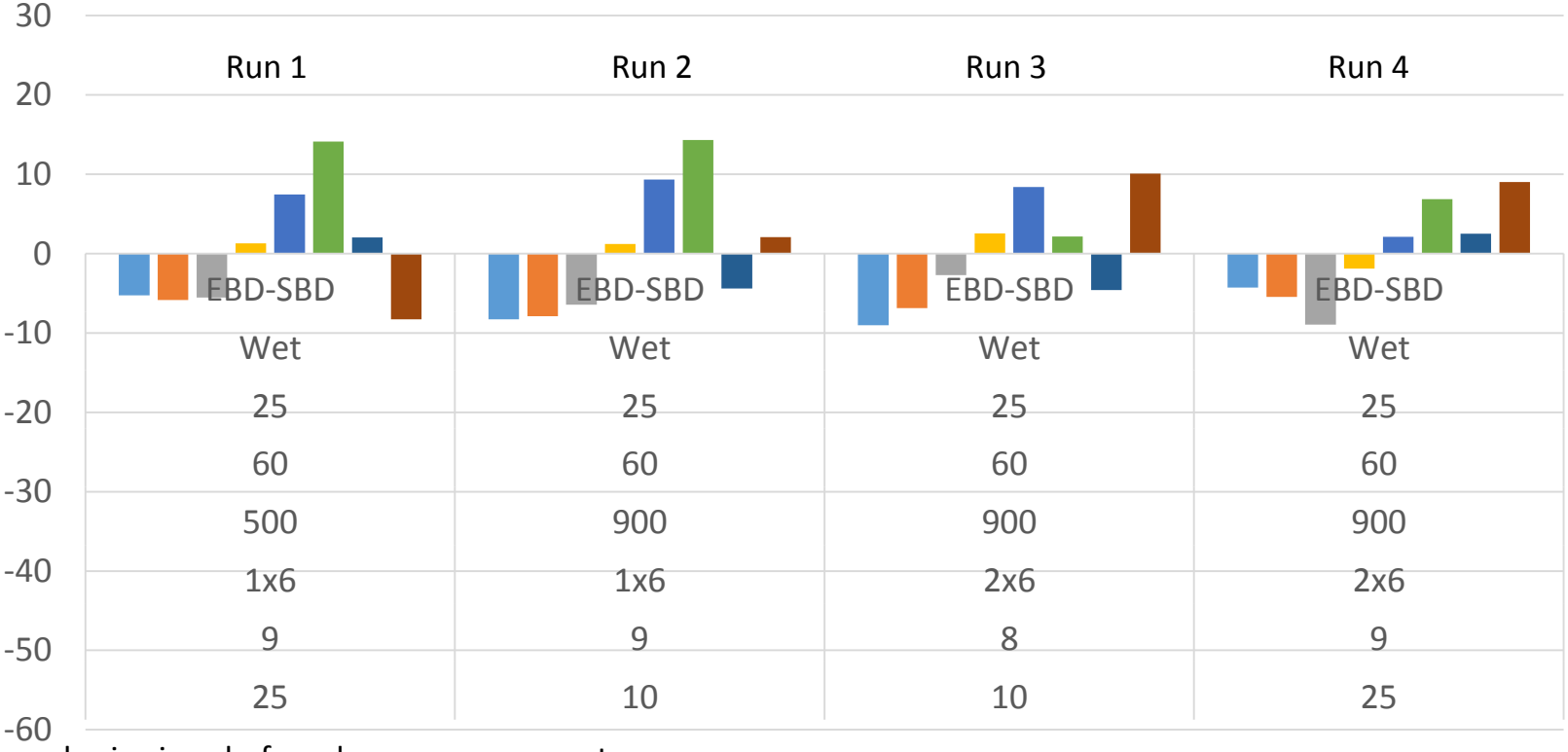


Difference between Eyecon before dryer and sieve before dryer

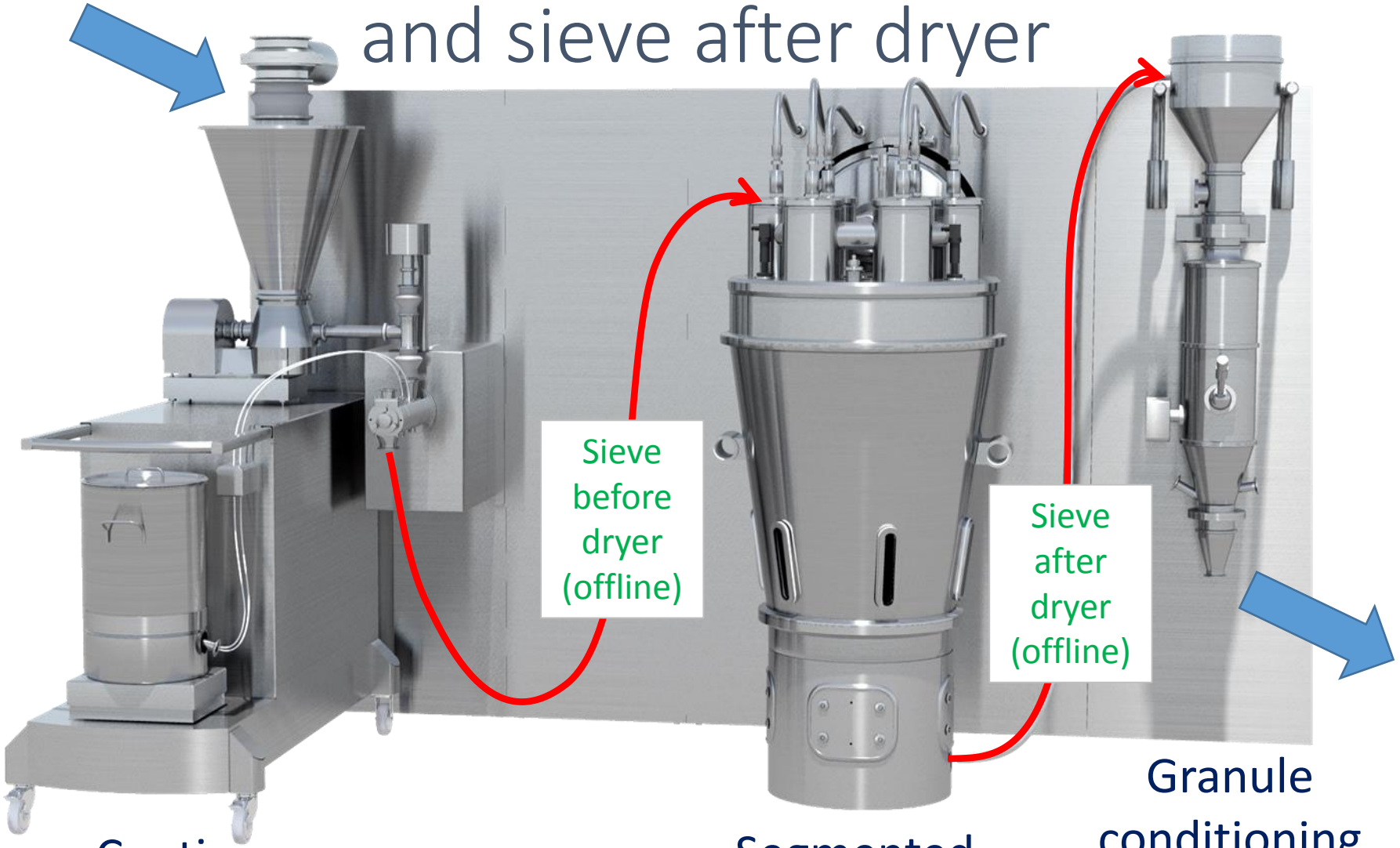
More granules in eyecon measurement



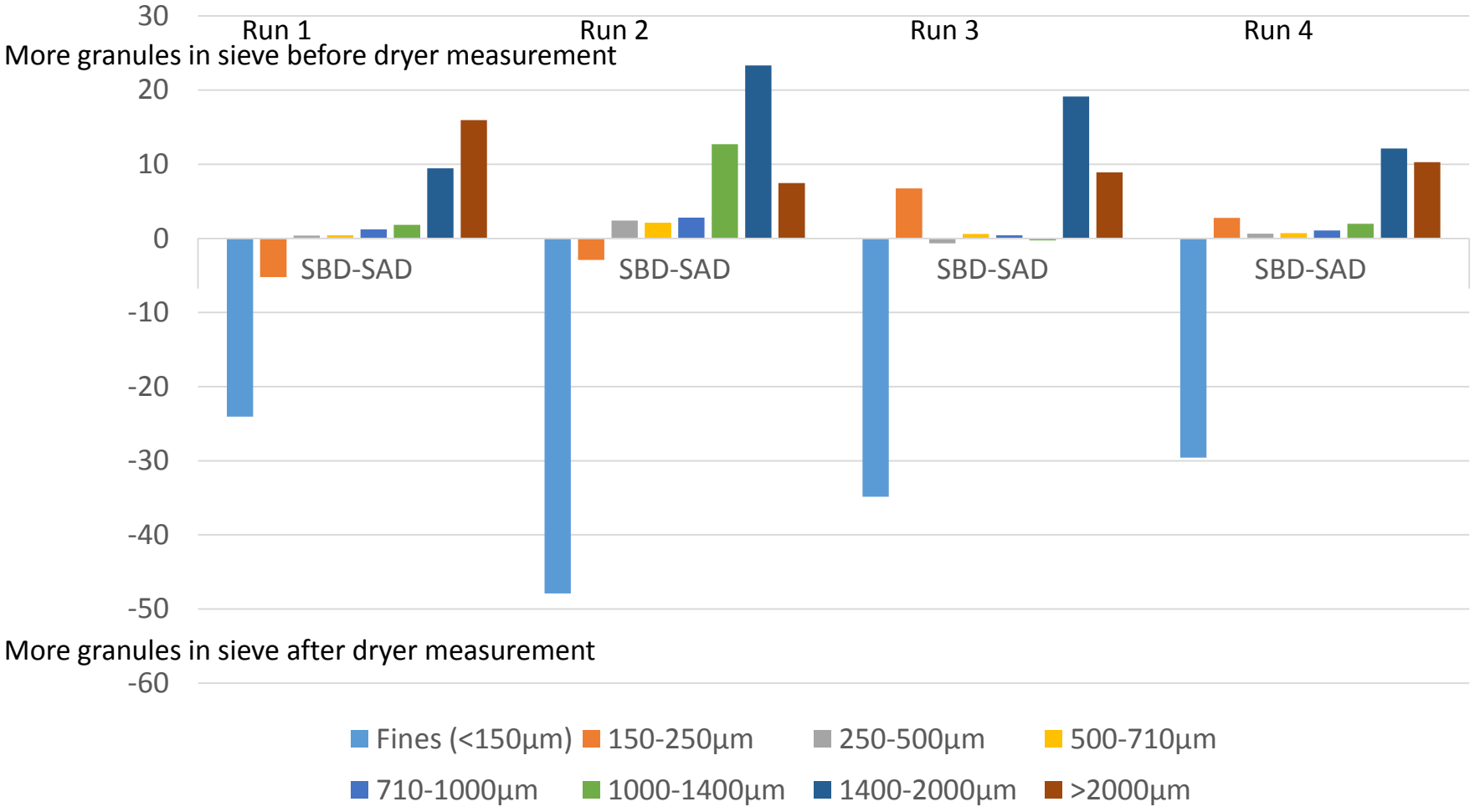
More granules in sieve before dryer measurement

Fines (<150µm) 150-250µm 250-500µm 500-710µm
710-1000µm 1000-1400µm 1400-2000µm >2000µm

Difference between sieve before dryer and sieve after dryer



Difference between sieve before dryer and sieve after dryer



Conclusions

Along with experimental study, an improved insight can be obtained by model-based analysis.

High throughput processing can be achieved by increasing the liquid-solid ratio and screw speed.

PBM requires further development to include screw geometry effect and validation.

Eyecon is showing some promising results, and can be used for studies in future.

Aknowledgements

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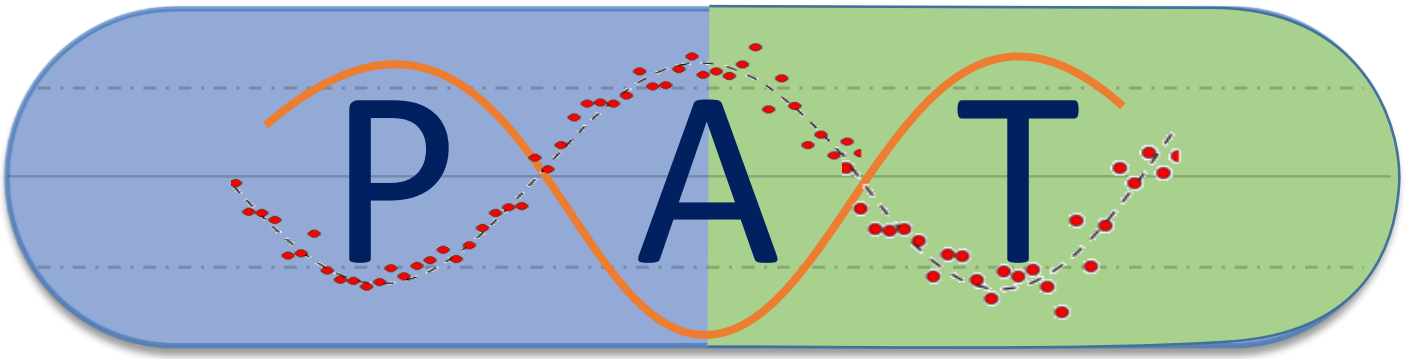

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- Extra slides