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Development of regime map for steady-state granulation

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Ashish Kumar

7th International Granulation Workshop

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Continuous manufacturing line

Consigma™-25 system

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Continuous

twin-screw granulator

Segmented

Fluid bed dryer

Semi-Continuous

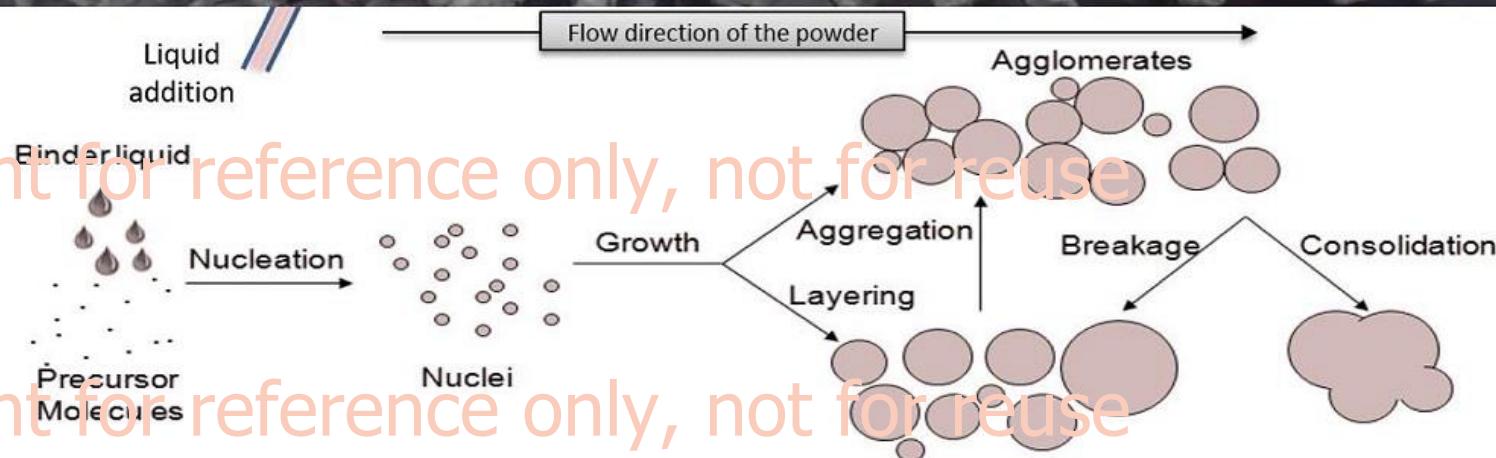
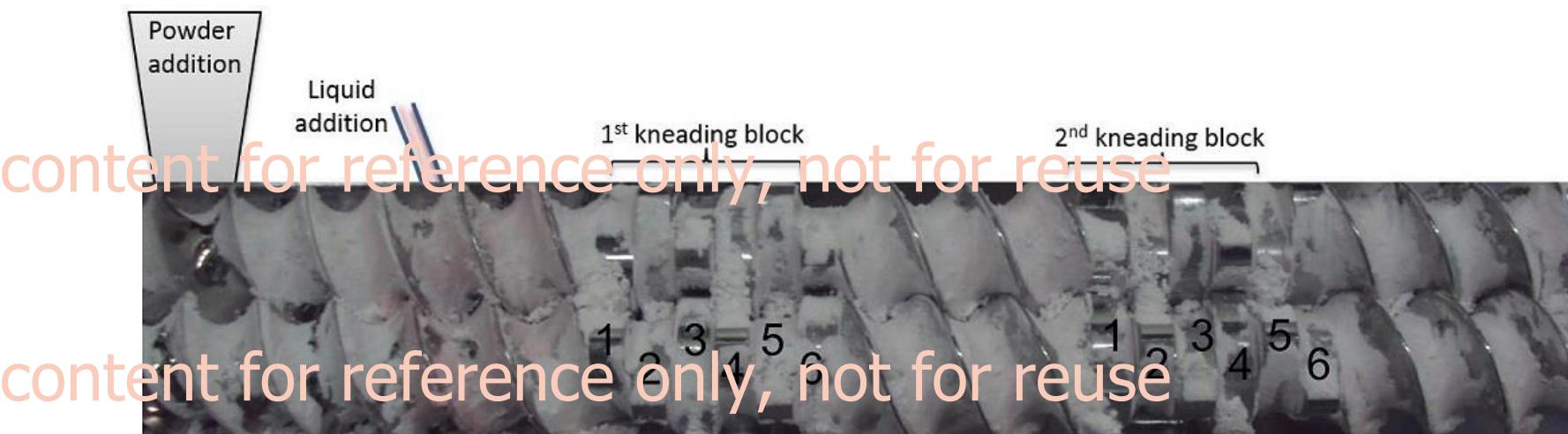
Continuous

Granule
conditioning
module

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High shear wet granulation in TSG involves
many different process and equipment variables



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Challenges in wet granulation

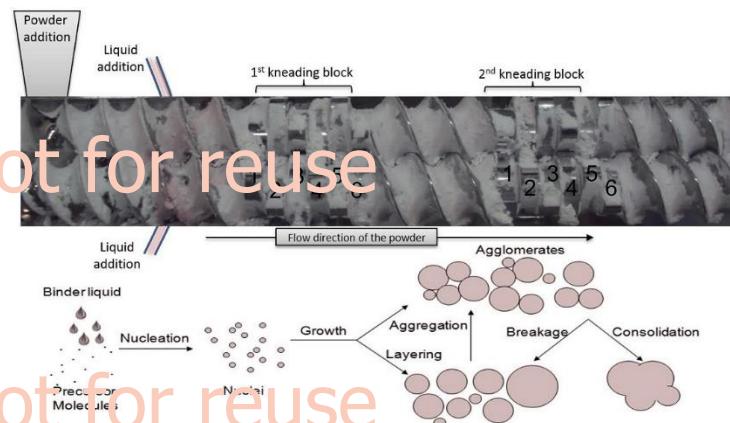
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Understanding the effect of process settings on
granulation performance

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- Process evolution

- Product quality



Mostly theoretical approaches
tracking granule attributes

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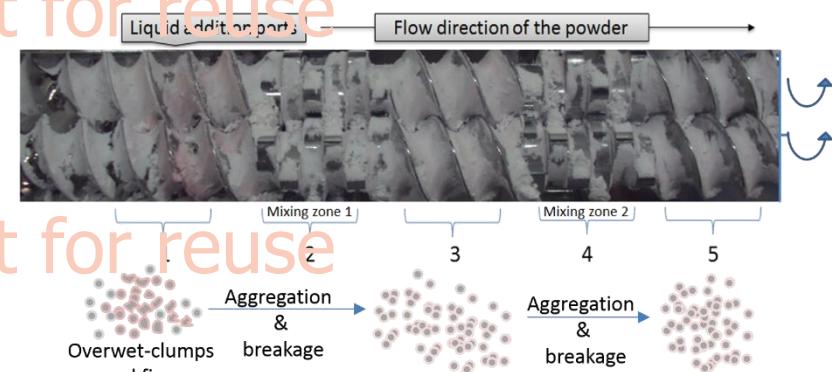
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Challenges in wet granulation

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Understanding the effect of process settings on
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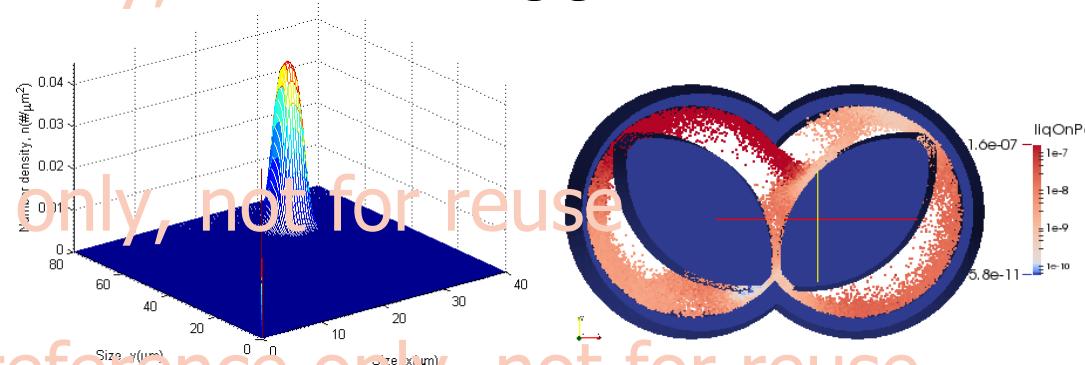


Process evolution

Mostly theoretical approaches

Product quality

tracking granule attributes



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Challenges in wet granulation

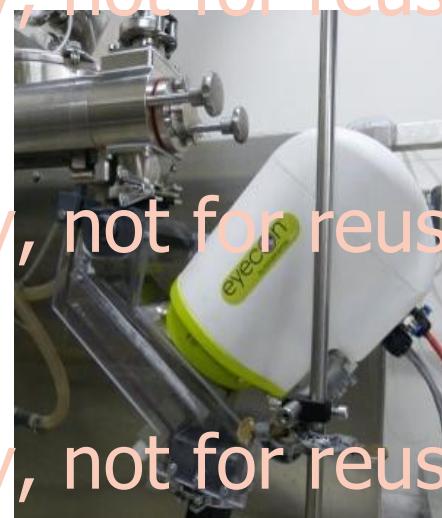
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Understanding the effect of process settings on
granulation performance

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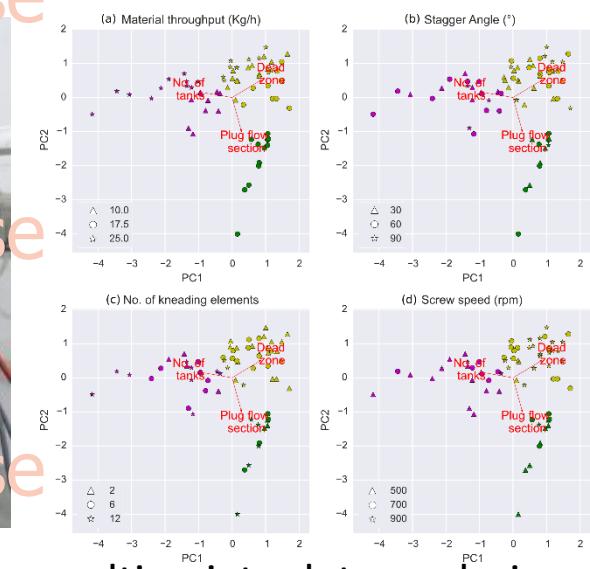
- Process evolution

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- Product quality

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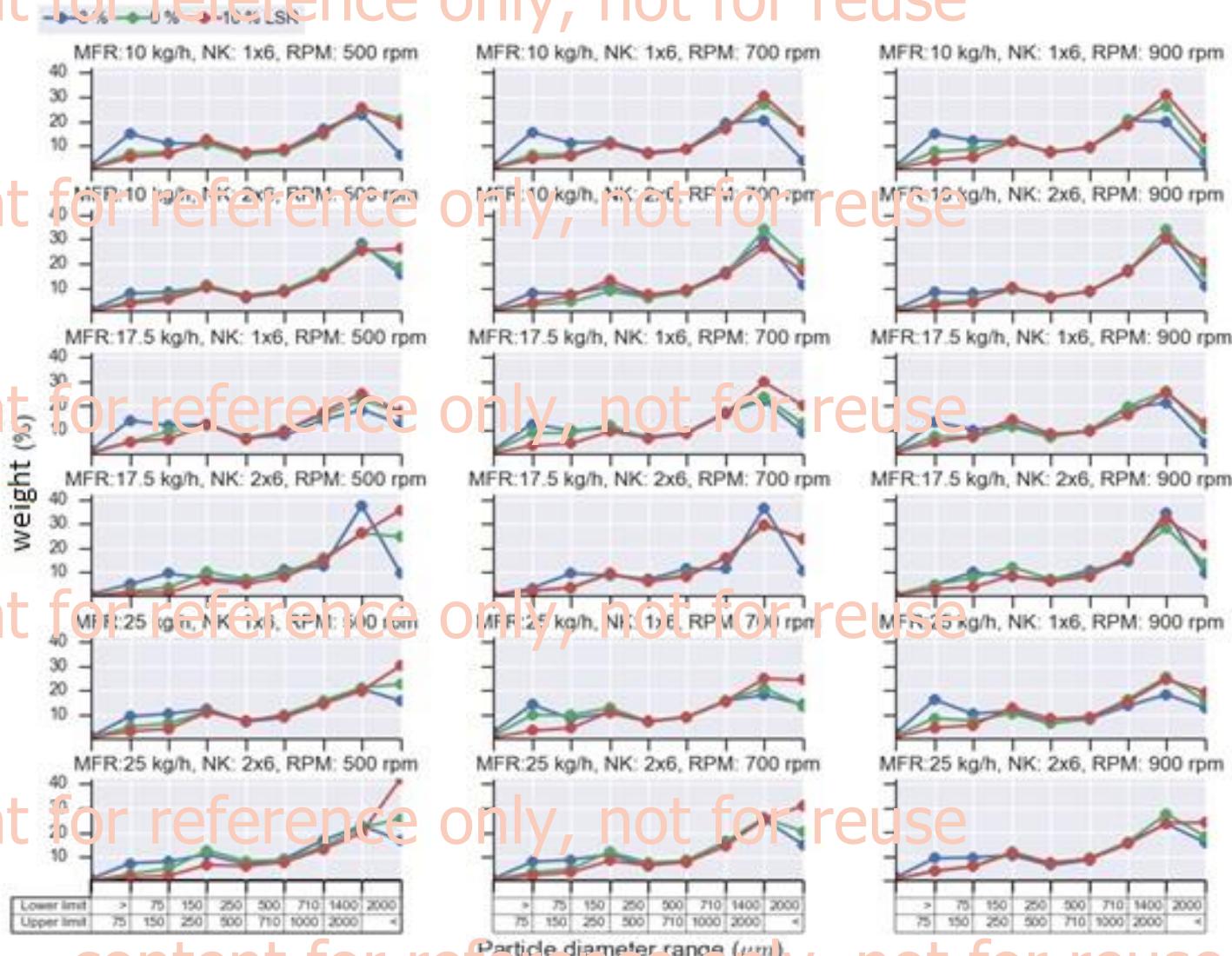
Experiments

multivariate data analysis

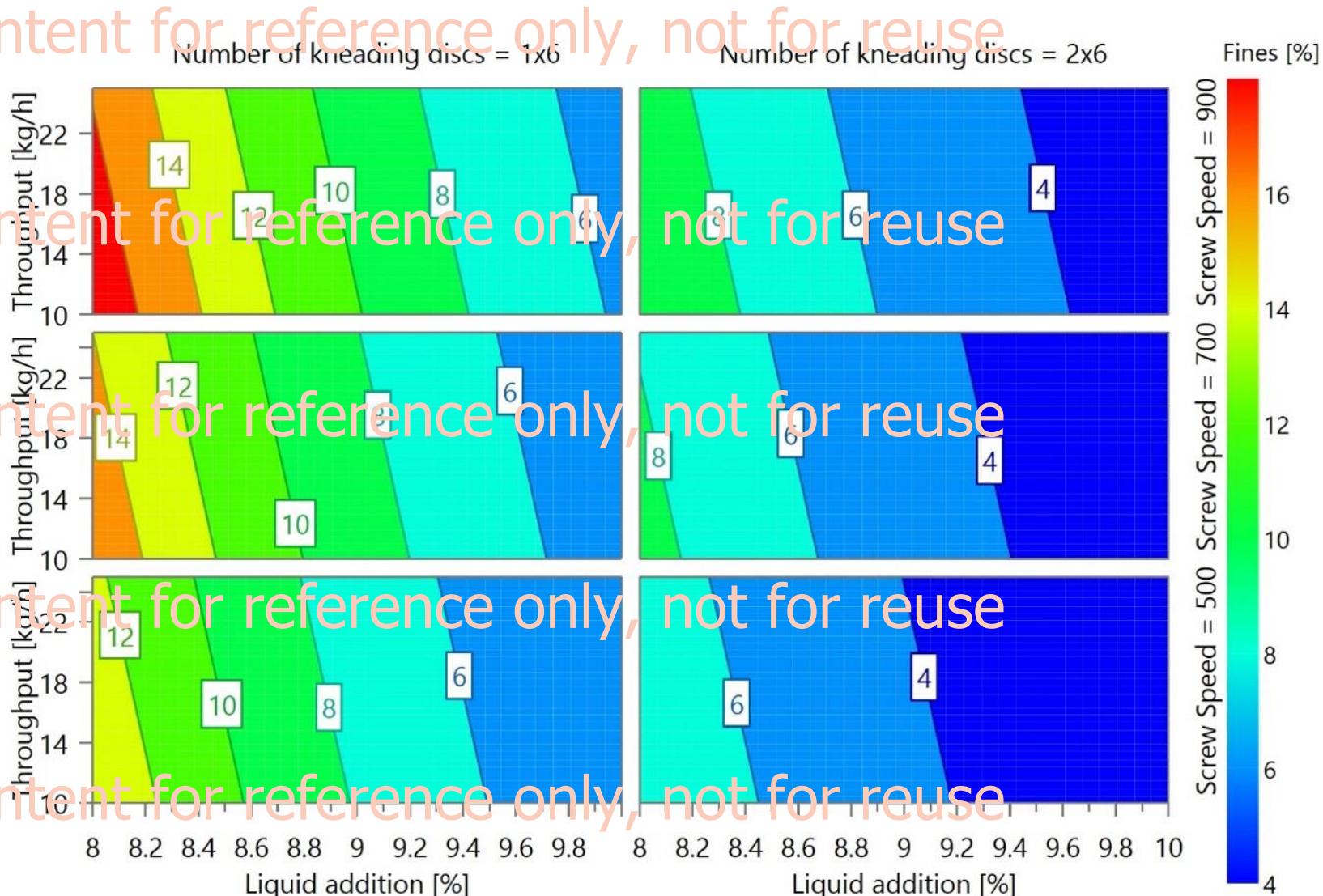
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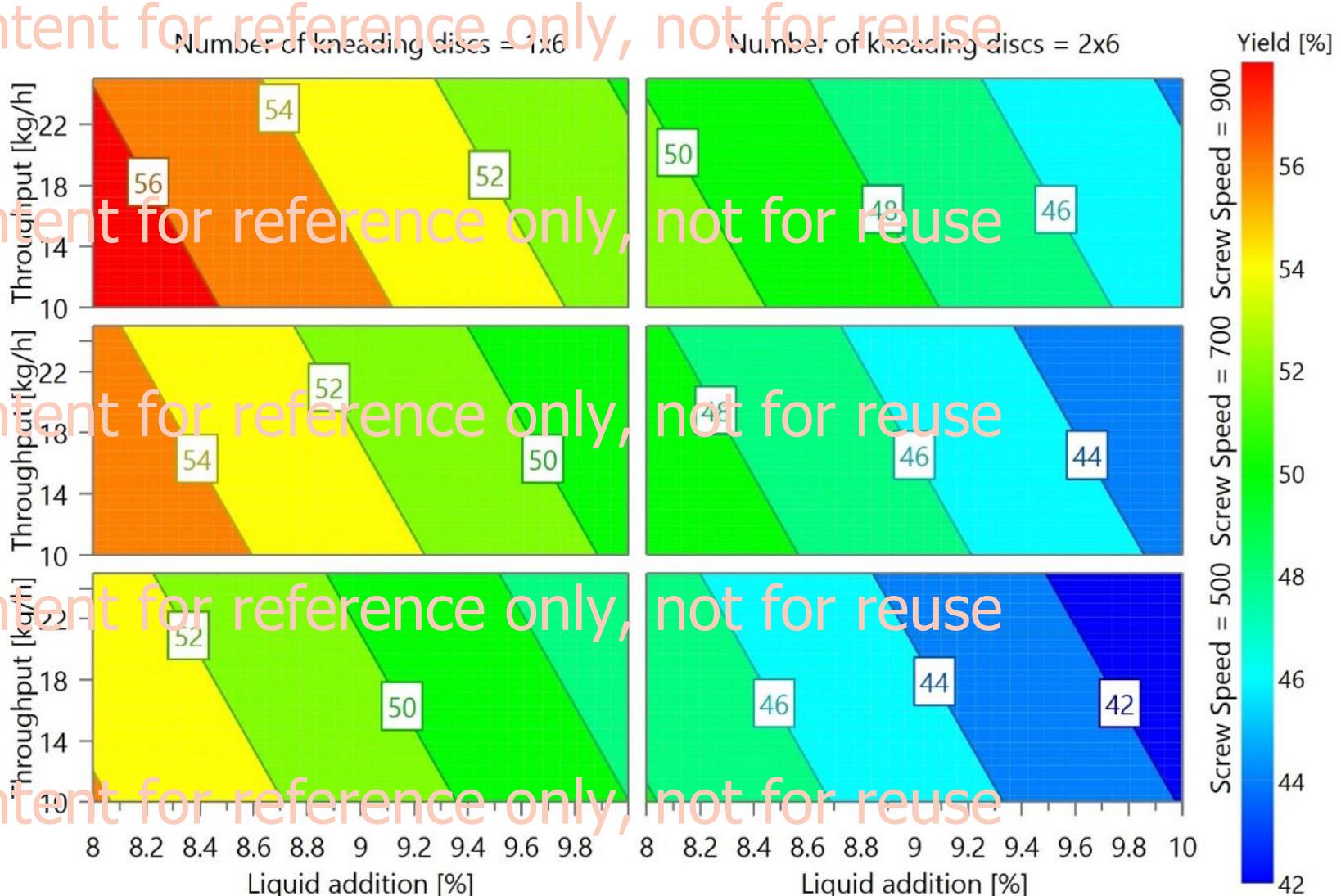
Traditional approach involves change in scale dependent process settings on PSD



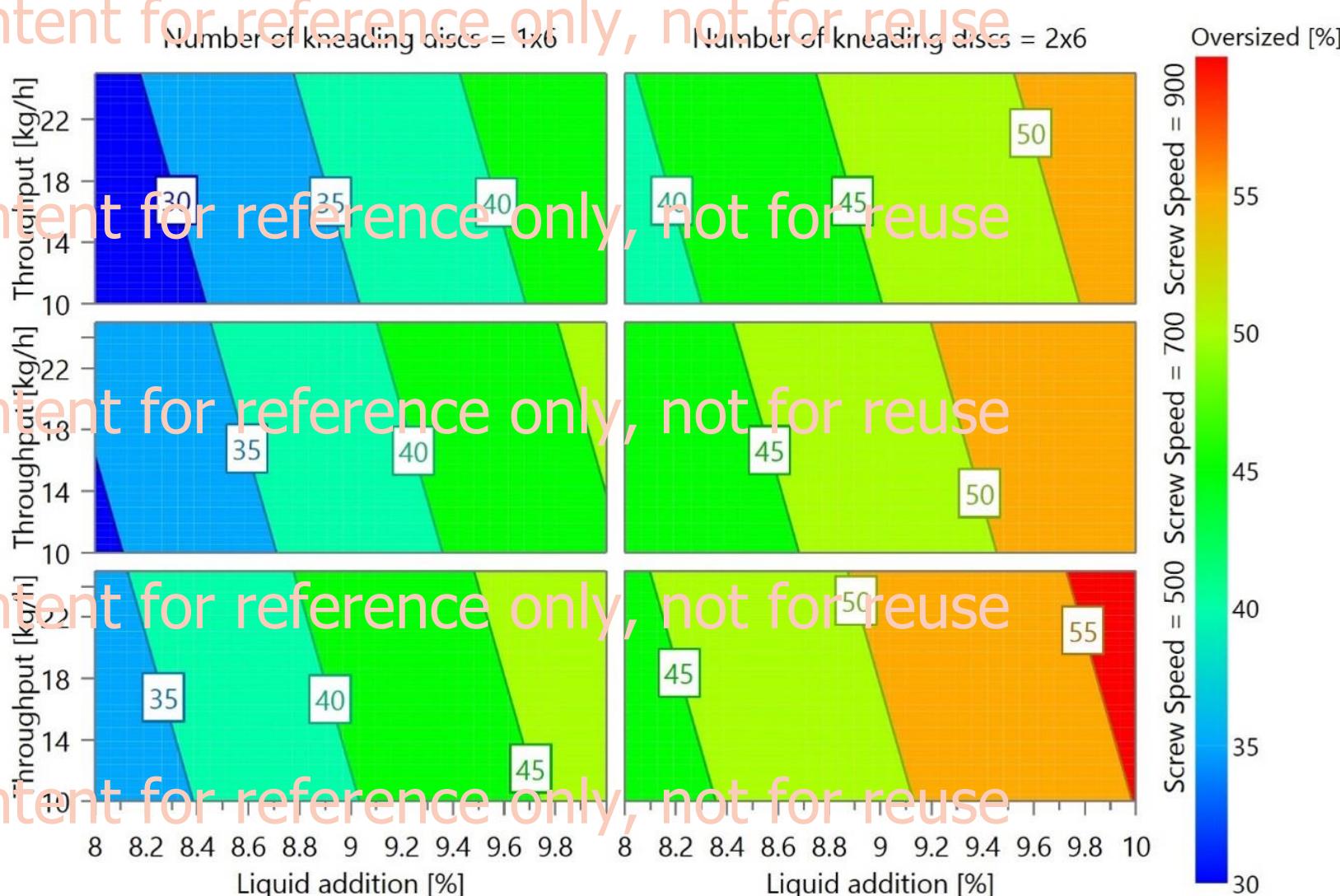
Increasing number of kneading discs and L/S reduced amount of fines



Yield fraction increases at low fill ratio and reduces with increasing L/S

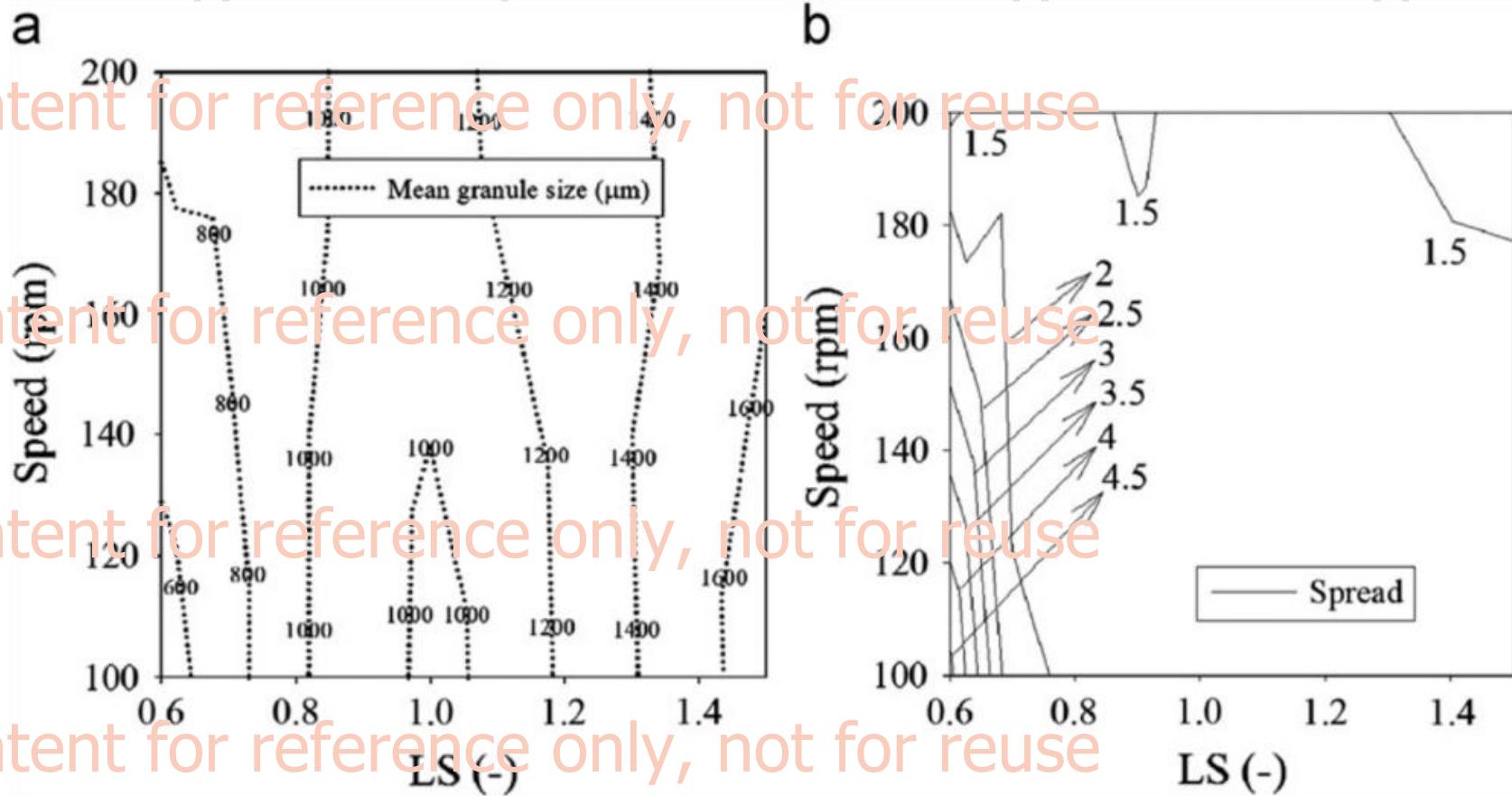


Increasing L/S produced more oversize at high fill ratio



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Regime map: consolidating knowledge

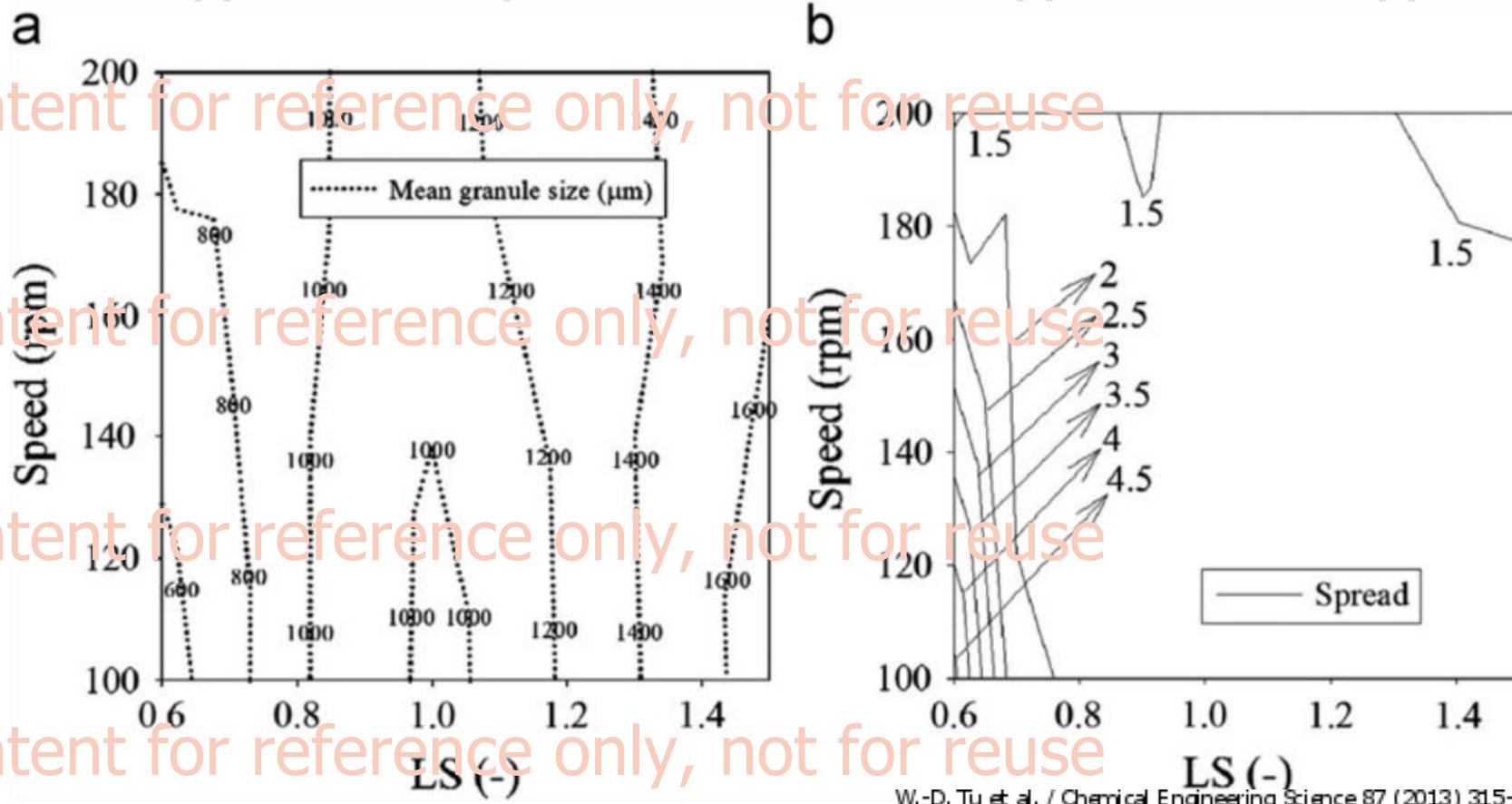


W.-D. Tu et al. / Chemical Engineering Science 87 (2013) 315–326

Boundaries were drawn to separate the growth behavior in terms of the L/S ratio and screw speed.

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Regime map: consolidating knowledge



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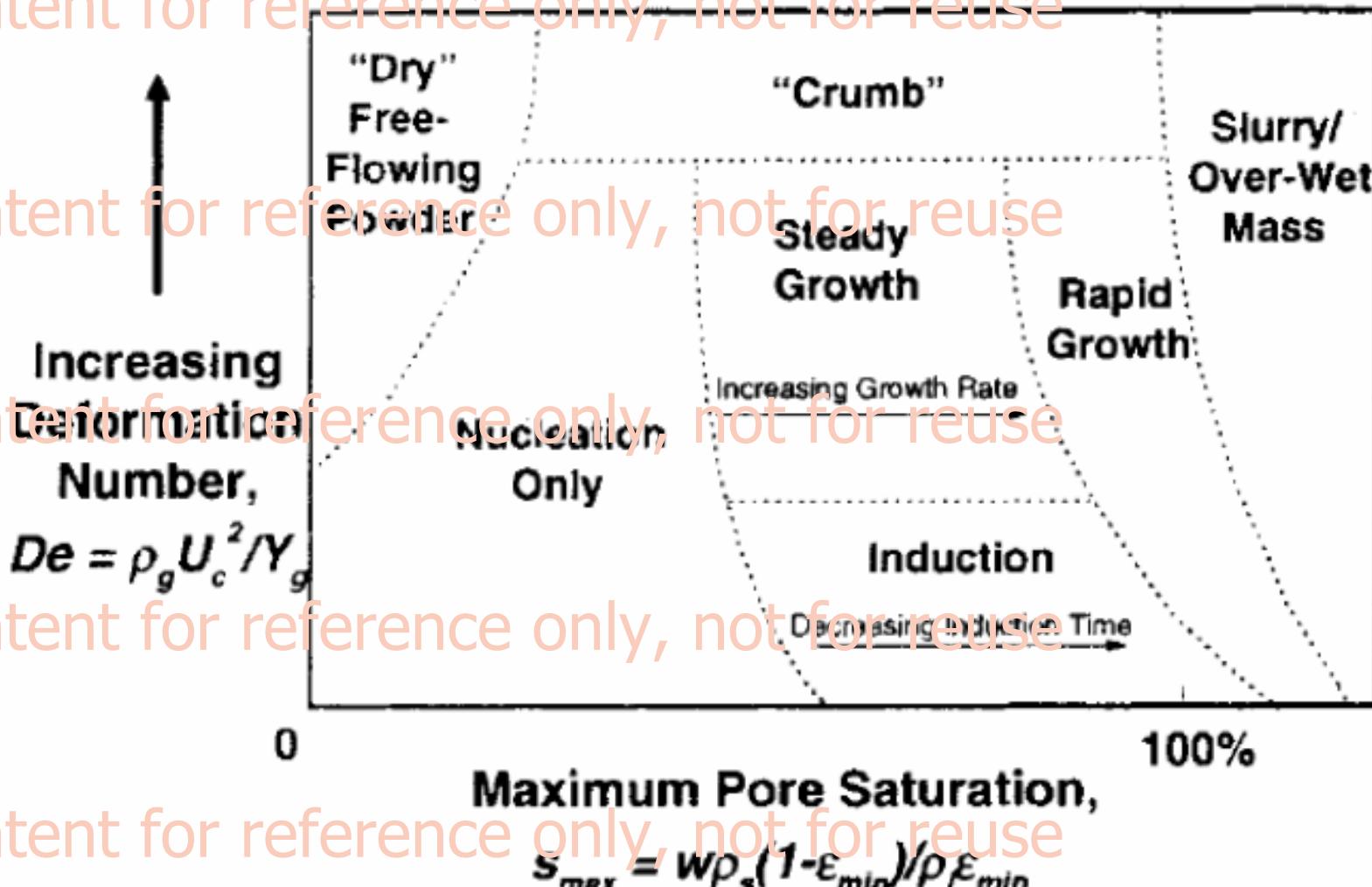
Dimensional measurements limits its applicability.

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Growth regime map for wet granulation

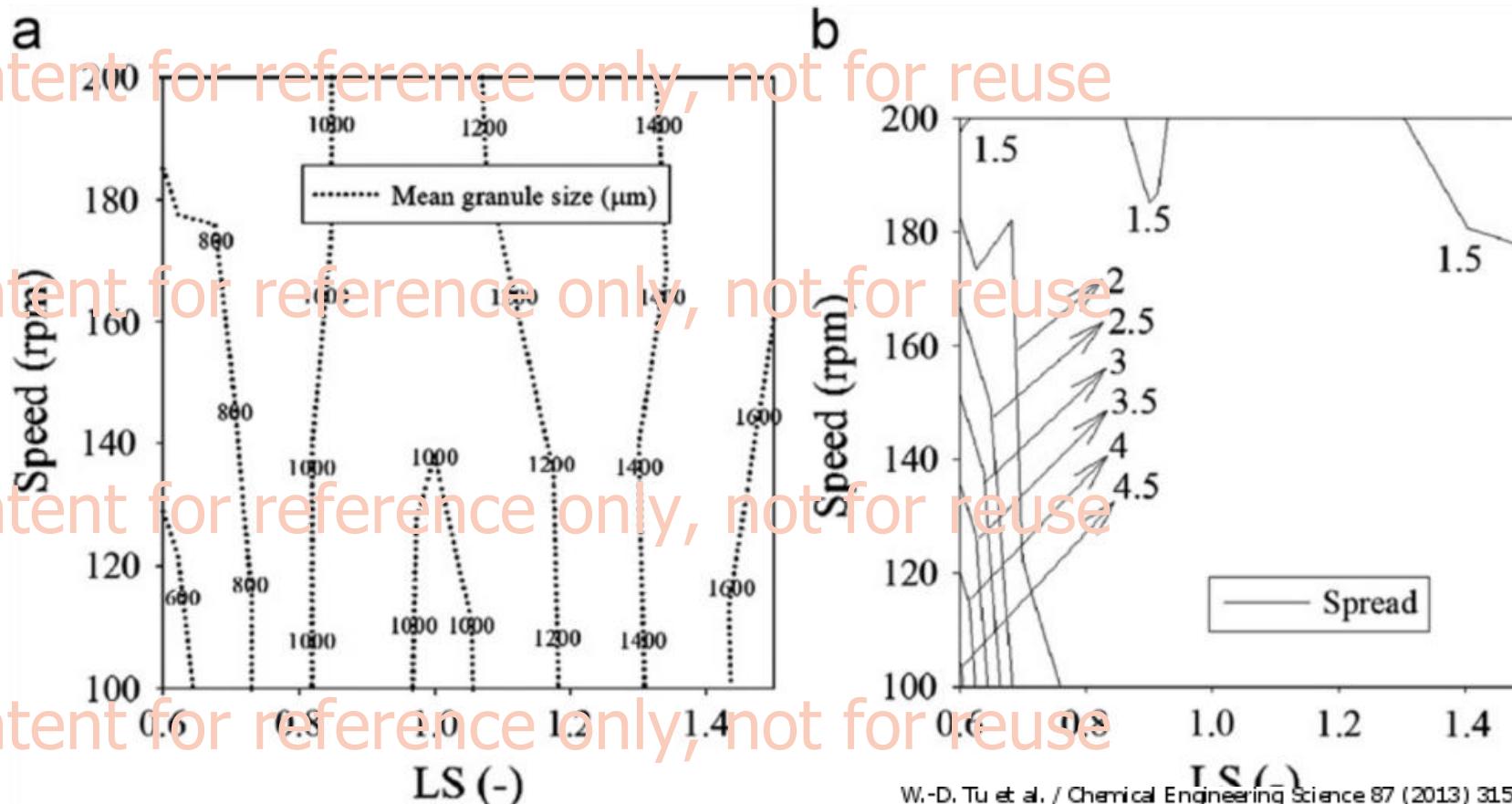
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source: Iveson et al. (1998). AIChE J., 44, 1510 - 1518

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Regime map: consolidating knowledge



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Mean of granule size distribution is not representative.

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Using scale-independent parameter and a

broad look on distribution

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Specific mechanical energy (kJ/kg)

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$$SME = \text{motor rating} \times \% \text{ torque} \times \frac{RPM_{oper.}}{RPM_{max.}} \times \frac{\text{gearbox efficiency}(0.97)}{\text{material throughput}}$$

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Liquid to solid ratio (%)

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Quartiles of distribution D25, D50, D75

Quartile ratio D75/ D25

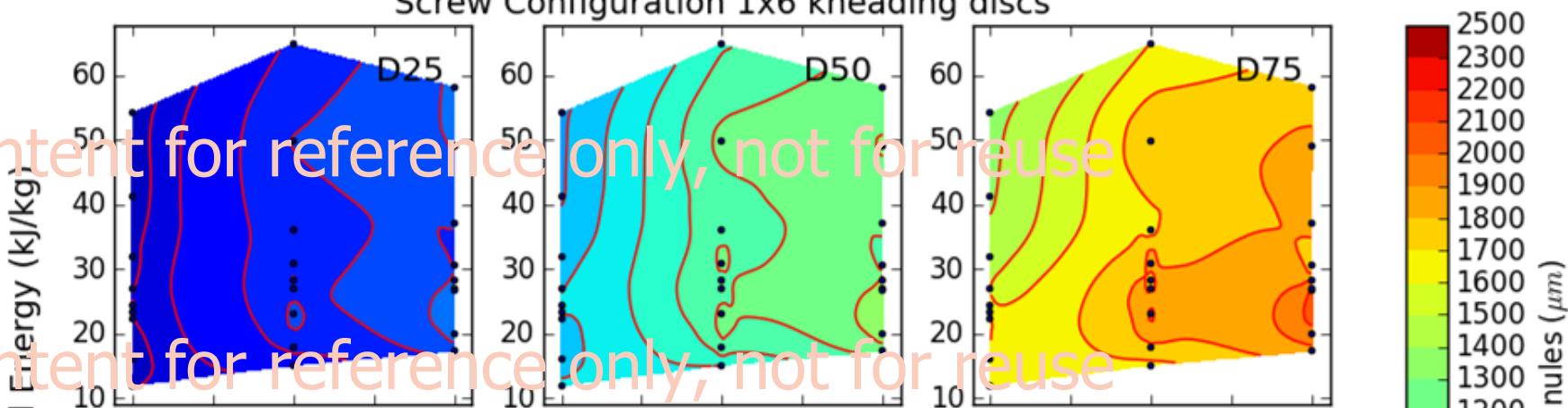
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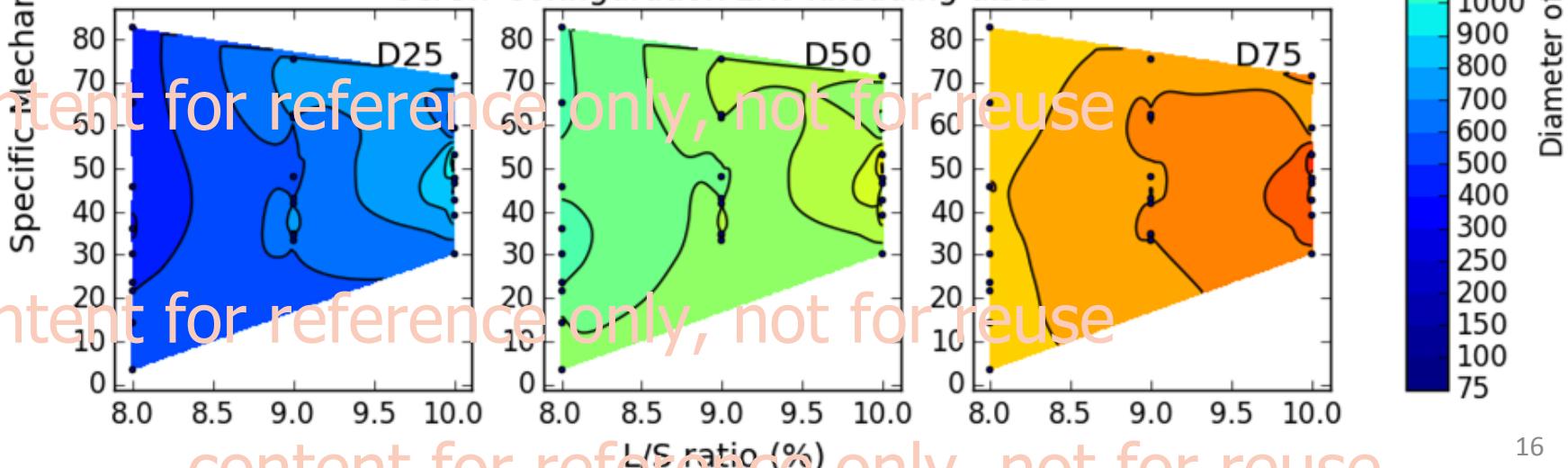
A higher L/S ratio led to formation of oversized granules instead of increasing yield

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Screw Configuration 1x6 kneading discs

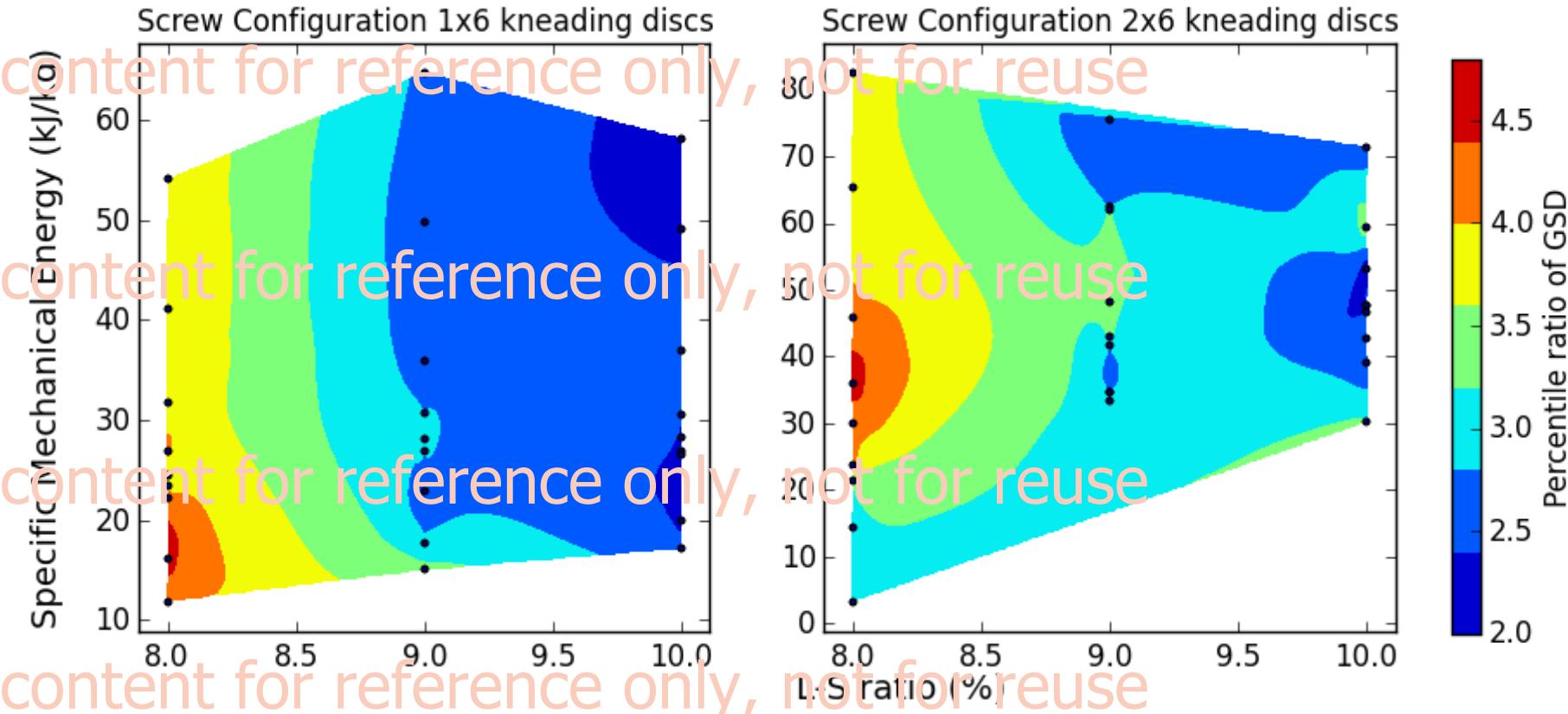


Screw Configuration 2x6 kneading discs



Width of the distribution reduced at higher L/S ratio and SME level

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Summary

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..the liquid addition should be kept at an intermediate level.

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.. the throughput and screw speed should be increased simultaneously to improve the granulation yield.

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regimens for other formulations are necessary due to the likely differences in the granulation behavior.

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Perspectives

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Formulation properties

D_p , Y, $\gamma \cos\theta$...

Process parameter
RPM, P_{input} , shear..

Propose most relevant
dimensionless groups

Generalised
regime map

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Laboratory of Pharmaceutical Process Analytical Technology

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Model-based analysis and optimization of bioprocesses

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