Optimising DPI Formulations

The influence of surface energy on the suitability of additional fines

DDL 2020
Christmas Lectures

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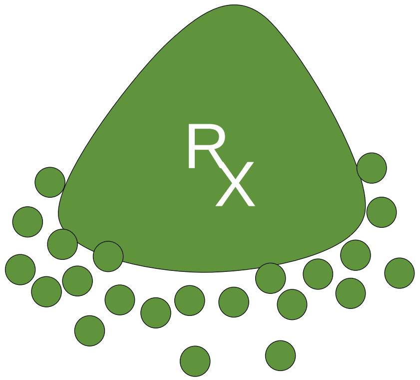
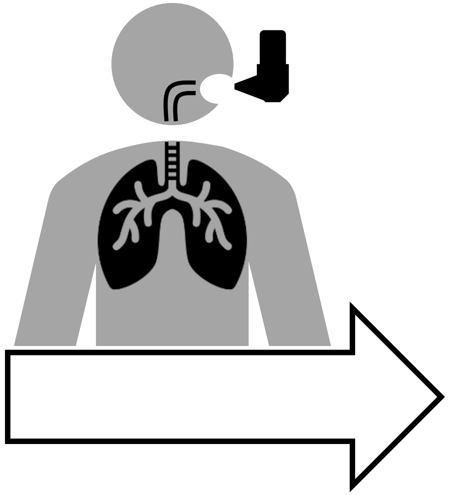
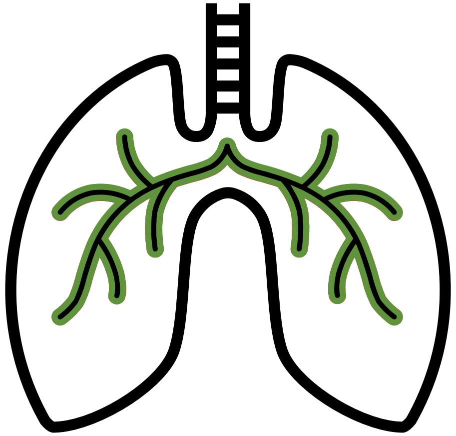
Introduction – Formulation development

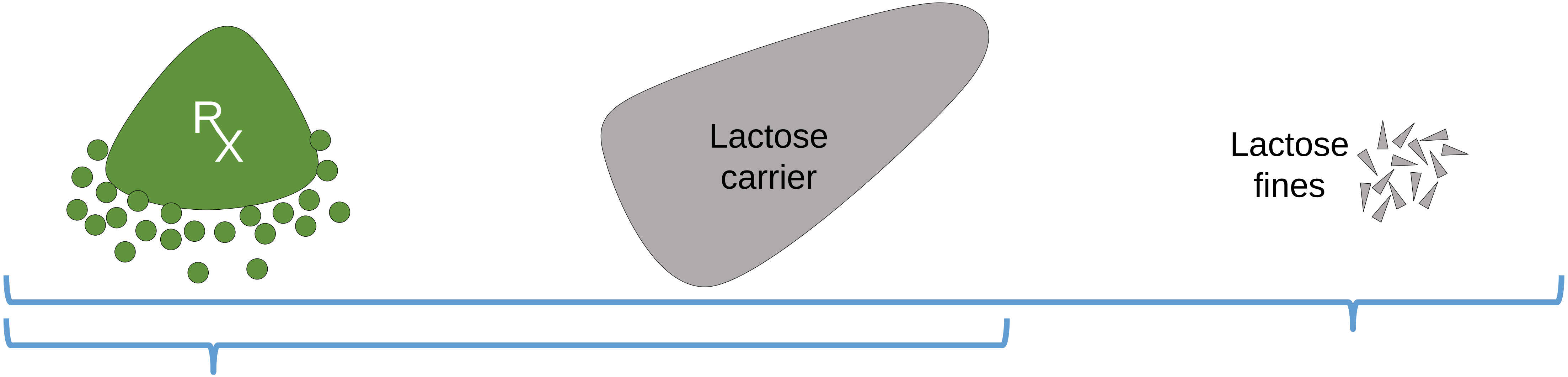


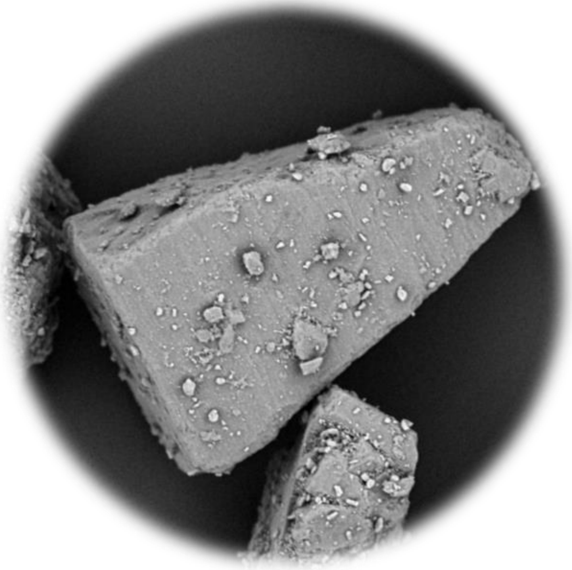




→ Making drugs accessible via inhalation

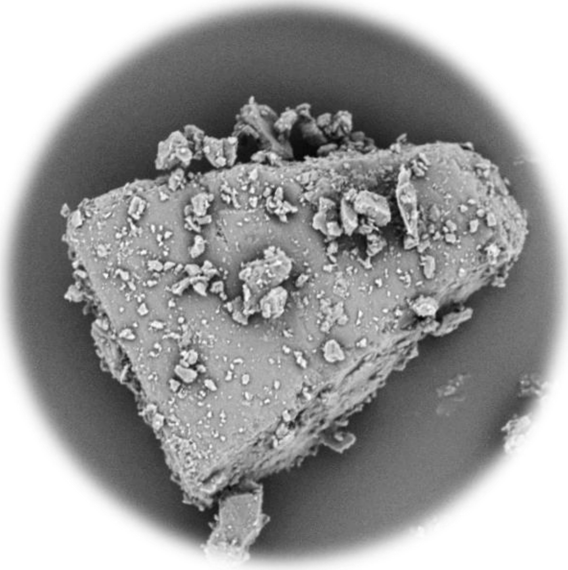
Interactive blends – Addition of fines



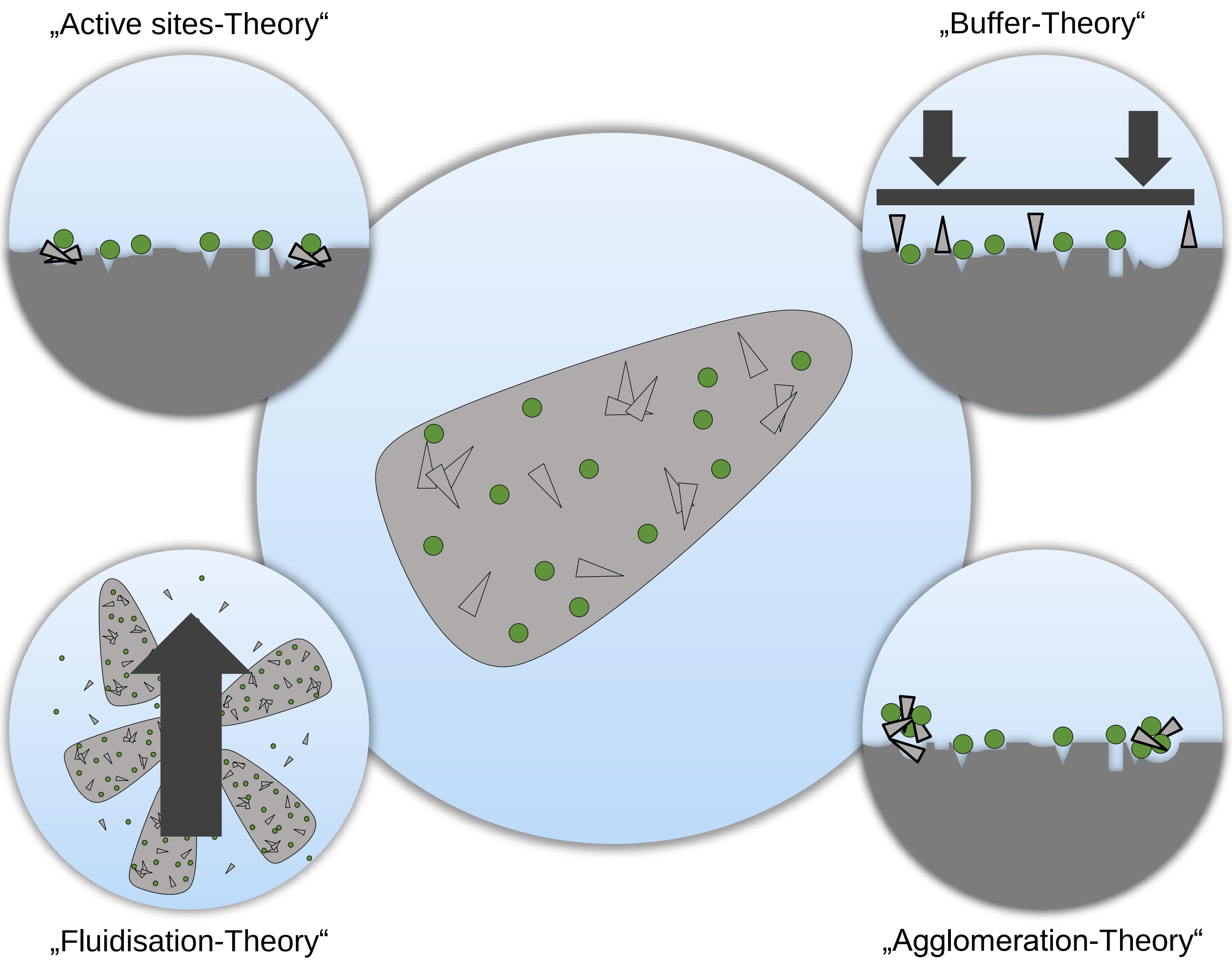


Fine particle fraction

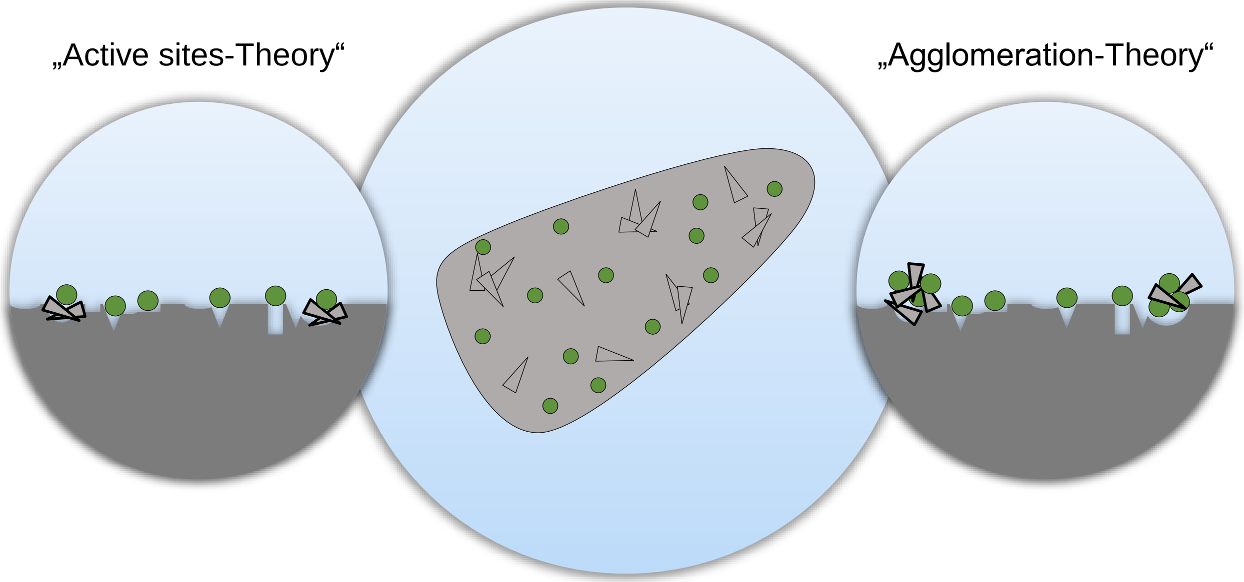
<



Operating principles of additional fines



Operating principles
Fundamentally based on adhesion strength

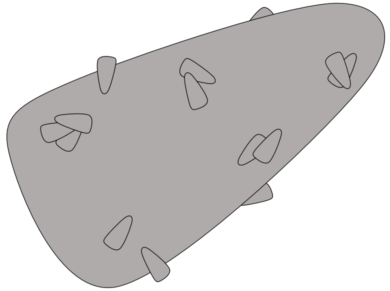


$$W_{adh}^{Total} = W_{adh}^{d} + W_{adh}^{ab} = 2 \times \sqrt{\gamma_{s1}^{d} \times \gamma_{s2}^{d}} + 2 \times \left[\sqrt{\gamma_{s1}^{-} \times \gamma_{s2}^{+}} + \sqrt{\gamma_{s1}^{+} \times \gamma_{s2}^{-}}\right]$$

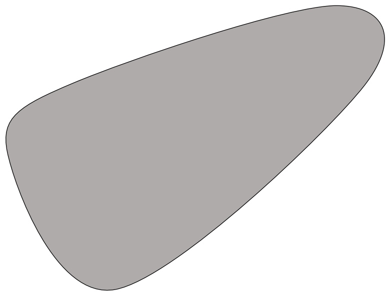
$\gamma_s^d = Dispersive\ surface\ energy$ $\gamma_s^+ = Lewis - Acid$ $\gamma_s^- = Lewis - Base$

Which surface energy works best for fines?

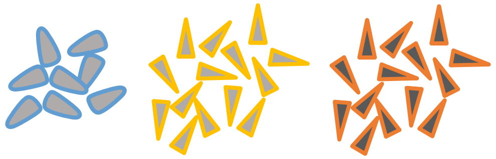
Experimental setup



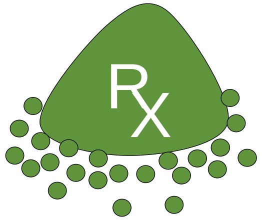
InhaLac 230 (IH 230)



InhaLac 230 without intrinsic fines (IH 230rf)

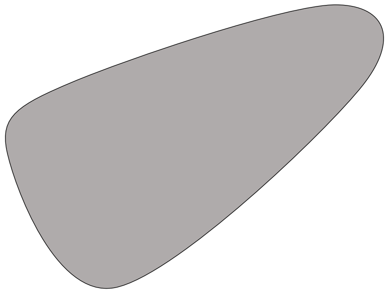


Intrinsic fines of IH 230 (IH 230if)
InhaLac 400 (IH 400)
Expired InhaLac 400 (IH 400ex)

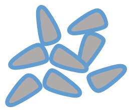


Ipratropium bromide (IP)

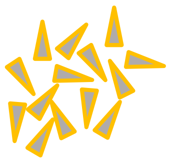
Particle size distributions



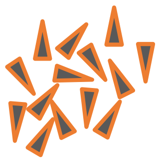
IH 230rf



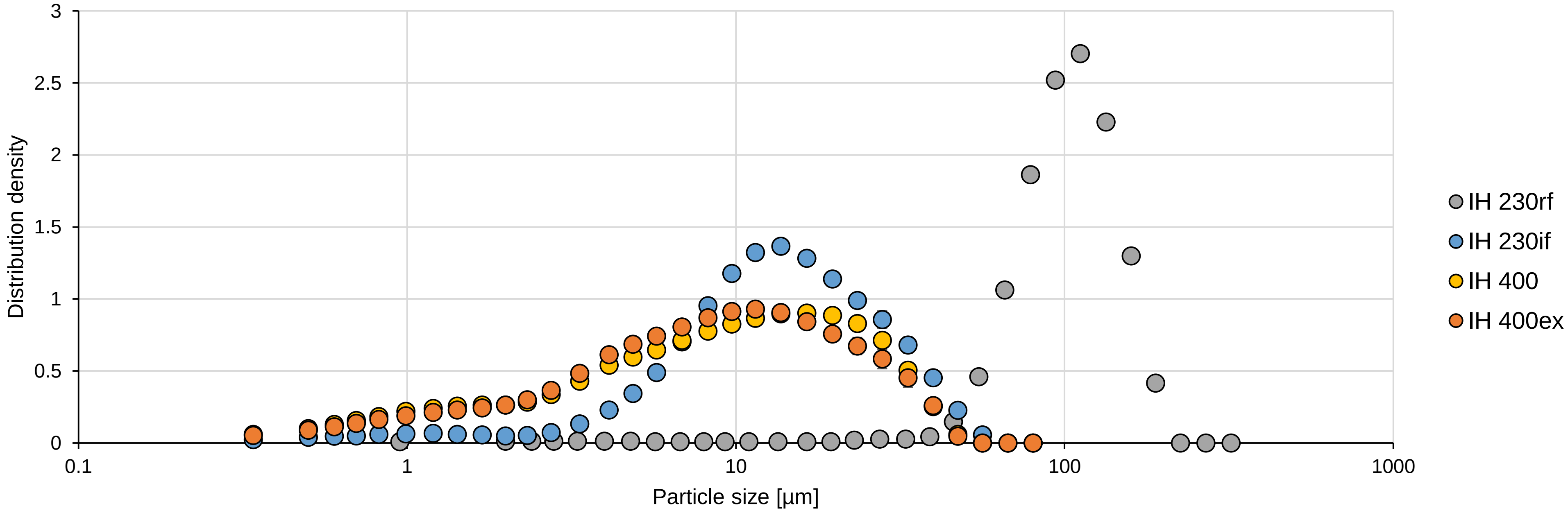
IH 230if



IH 400

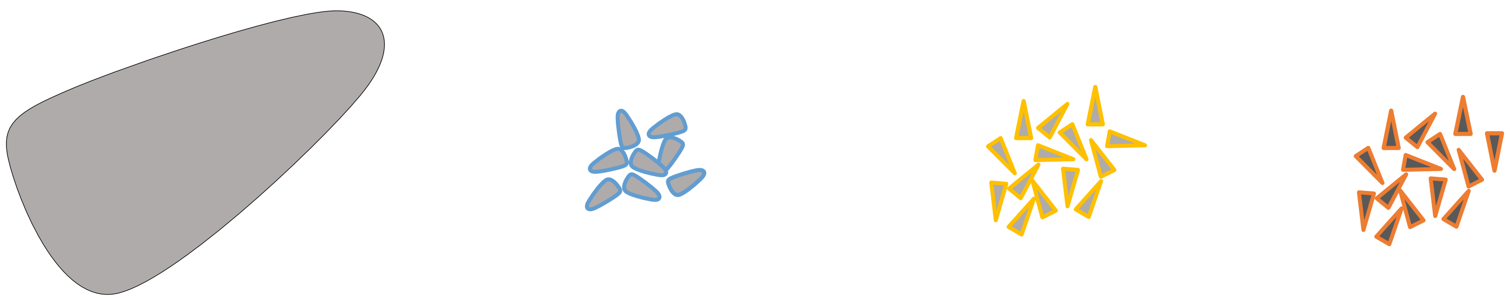


IH 400ex



Data displayed as average of three measurements
SD displayed by error bars

Surface energy data

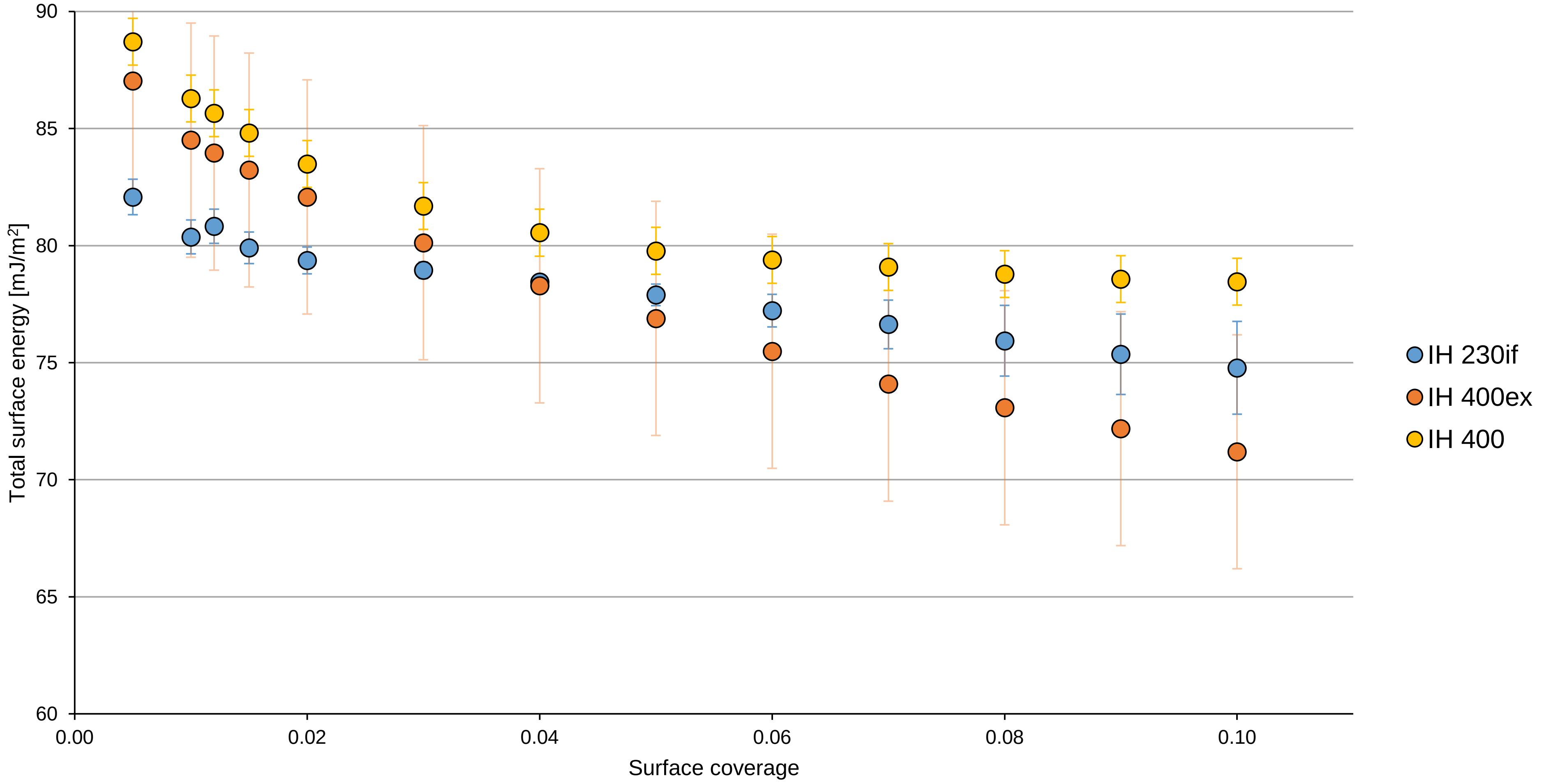


IH 230rf | IH 230if | IH 400 | IH 400ex

	γ_s^D [mJ/m^2]		γ_s^{AB} [mJ/m^2]		γ_s^{Total} [mJ/m^2]	
	Min	Max	Min	Max	Min	Max
IH 230rf	34.3	43.0	22.6	32.6	56.9	75.6
IH 230if	37.3	44.4	27.0	37.7	63.7	82.1
IH 400	44.1	45.6	33.9	43.1	78.2	88.7
IH 400ex	36.0	44.9	24.9	42.1	60.1	87.0
IP	26.6	42.3	23.4	46.8	50.1	89.1

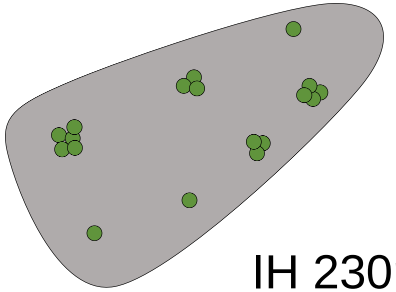
Data displayed as average of three measurements

Surface energy distributions

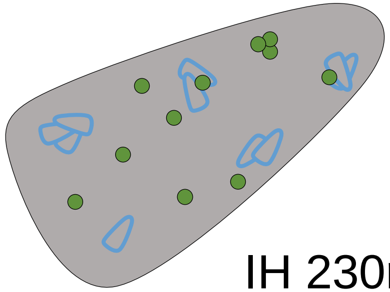


Data displayed as average of three measurements
SD displayed by error bars

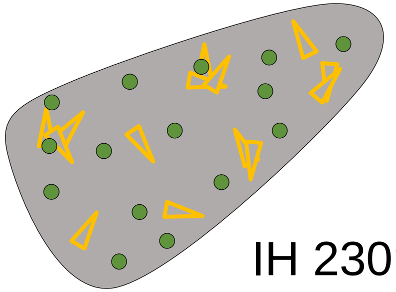
Experimental setup



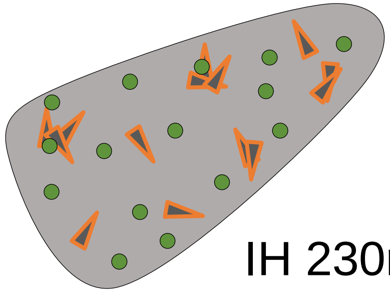
IH 230rf +1 % IP



IH 230rf + 7.5 % IH 230if +1 % IP



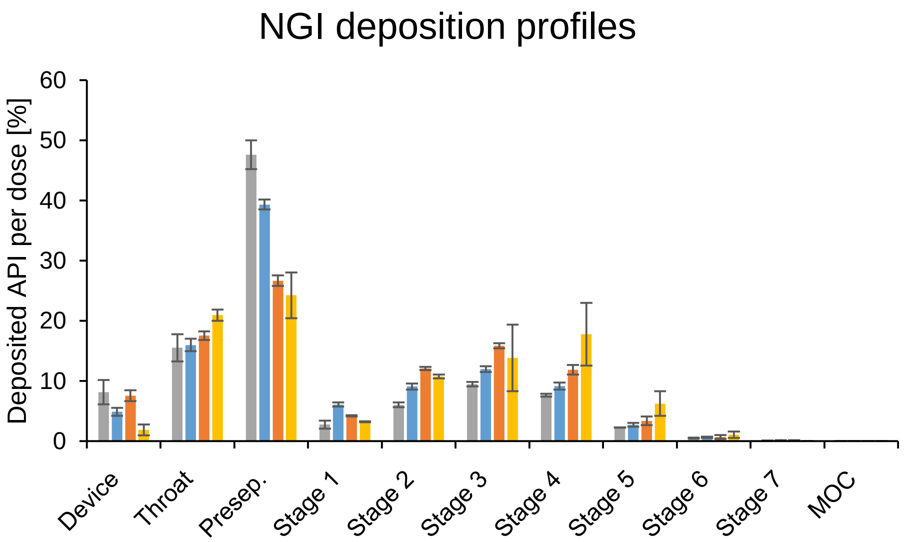
IH 230rf + 7.5 % IH 400 +1 % IP



IH 230rf + 7.5 % IH 400ex +1 % IP

Blends were prepared using the Picomix high-shear mixer and conditioned for one week at 20 °C and 45 % RH

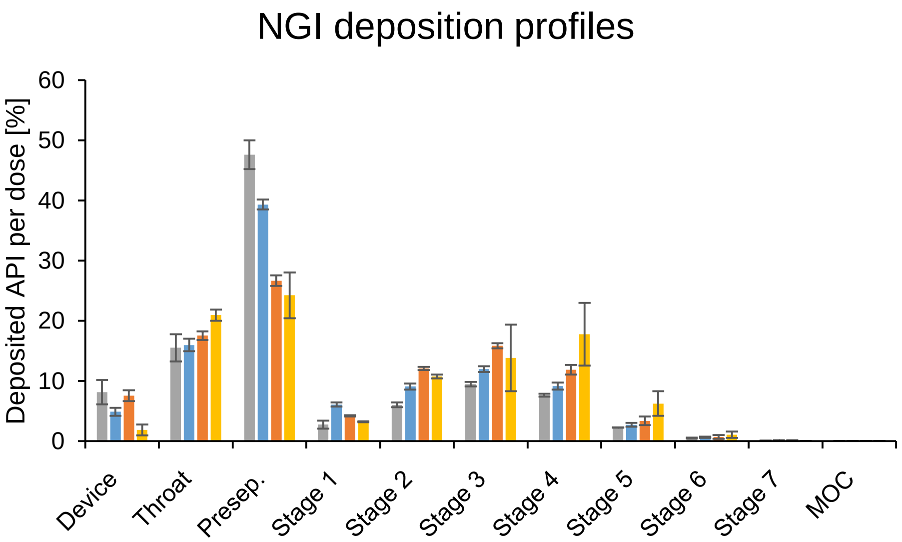
Aerodynamic assessment



Blend	FPF < 5 µm	FPF < 3 µm	FPF < 1 µm
IH 230rf – IP	25.2 %	15.9 %	1.2 %
IH 230rf – IH 230if – IP	30.6 %	18.6 %	1.5 %
IH 230rf – IH 400ex – IP	41.5 %	24.7 %	1.7 %
IH 230rf – IH 400 – IP	45.7 %	31.9 %	2.3 %

Data displayed as average of three measurements using the Novolizer
SD displayed by error bars

Aerodynamic assessment



Blend	FPF < 5 µm	FPF < 3 µm	FPF < 1 µm
IH 230rf – IP	25.2 %	15.9 %	1.2 %
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IH 230rf – IH 400ex – IP	41.5 %	24.7 %	1.7 %
IH 230rf – IH 400 – IP	45.7 %	31.9 %	2.3 %

+ 21.6 %*

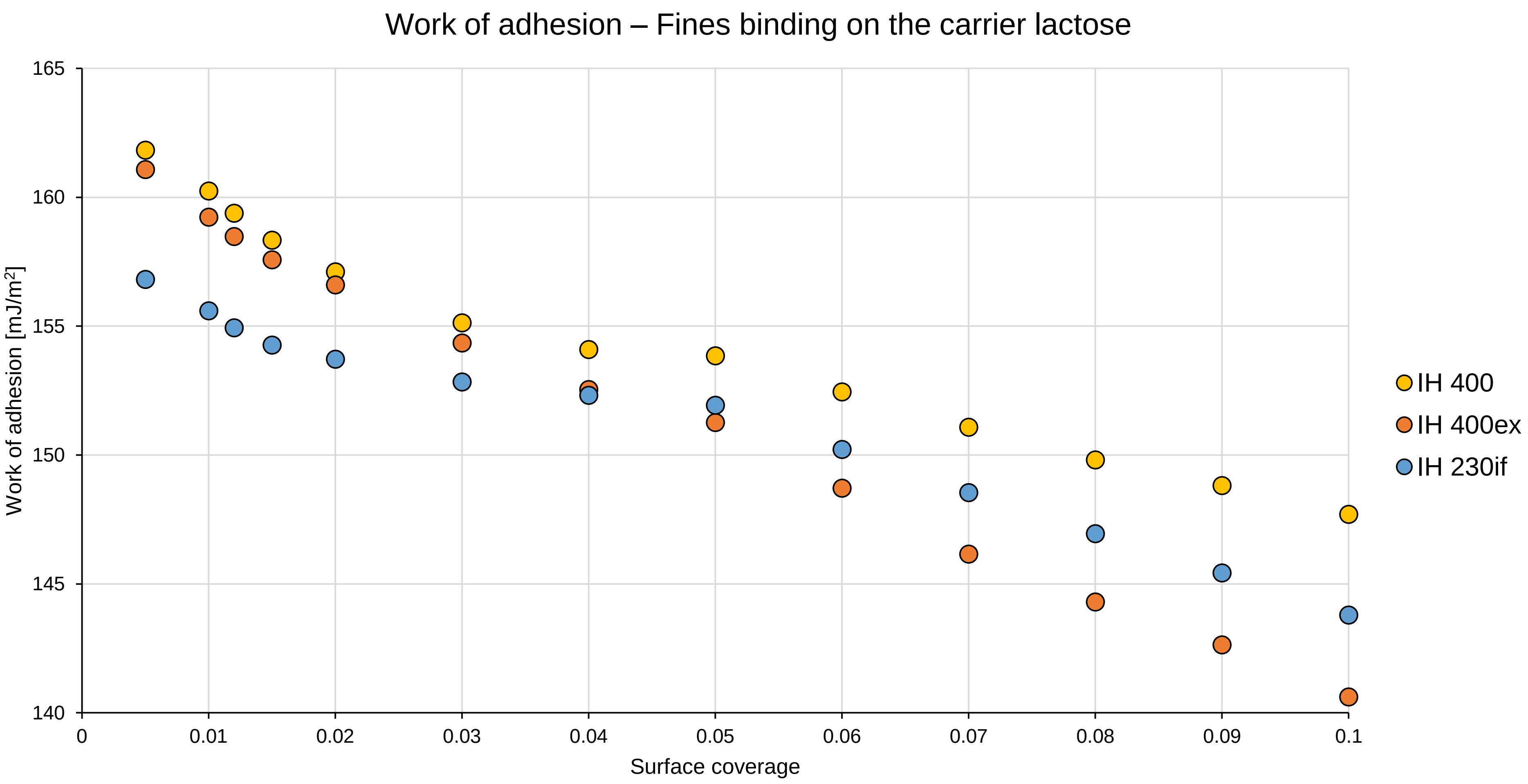
+ 64.9 %***

+ 81.7 %***

* p-value ≤ 0.05; *** p-value ≤ 0.001

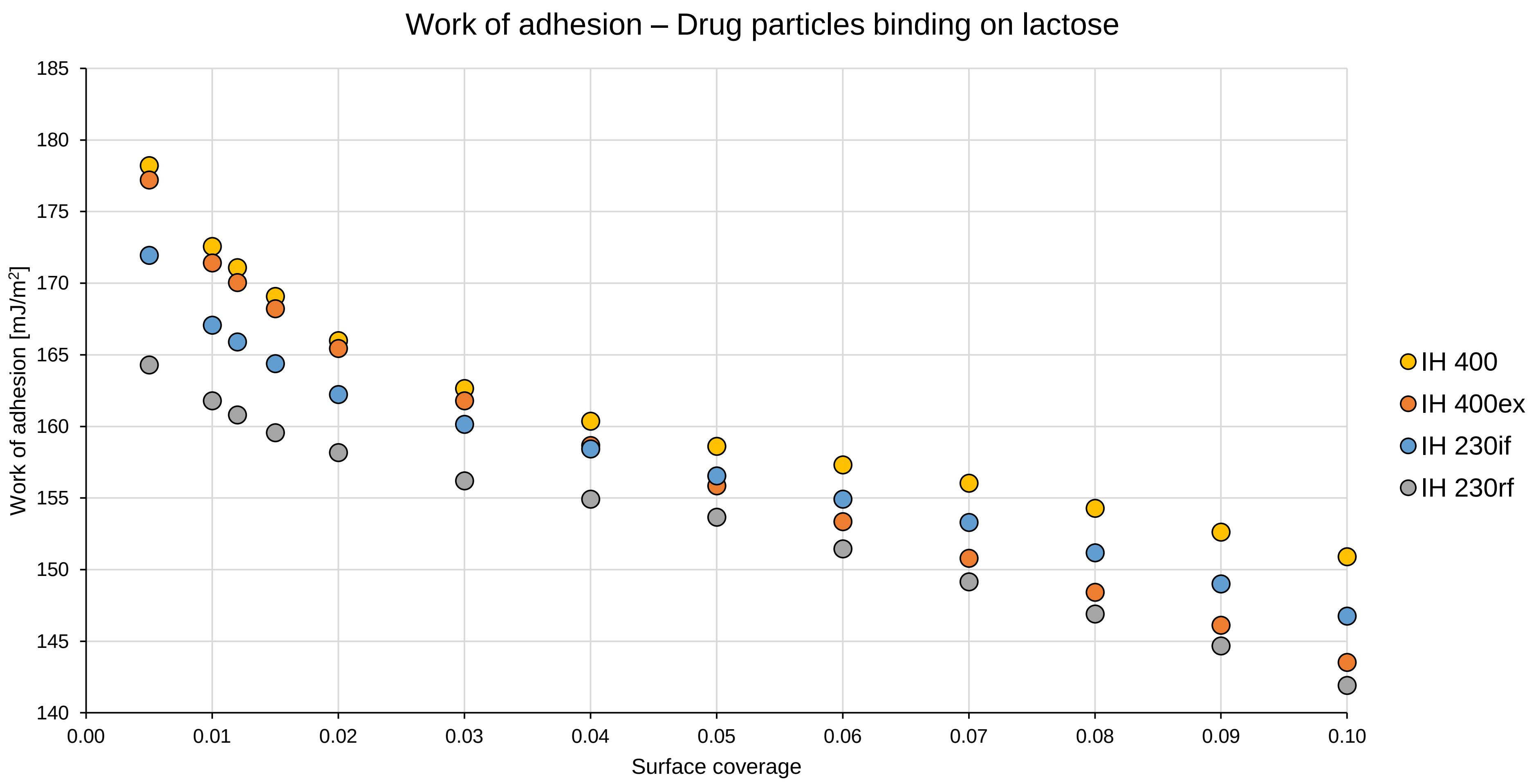
Data displayed as average of three measurements using the Novolizer
SD displayed by error bars

Work of adhesion – Saturation of active sites



All calculations are based on mean values of three measurements

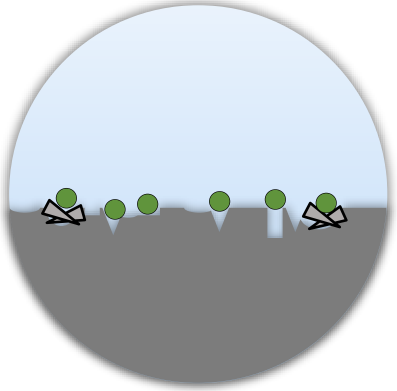
Work of adhesion – Formation of agglomerates



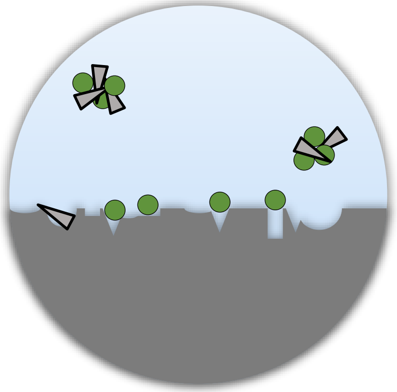
All calculations are based on mean values of three measurements

Conclusion

Stronger active site saturation



Formation of stronger agglomerates



Higher surface energies of fines lead to higher FPF of the respective blend

Thank you for your attention!

Please do not hesitate to get in touch:

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