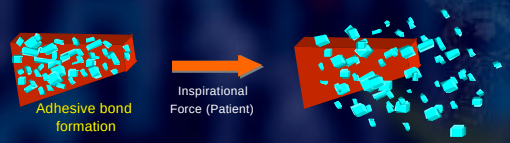
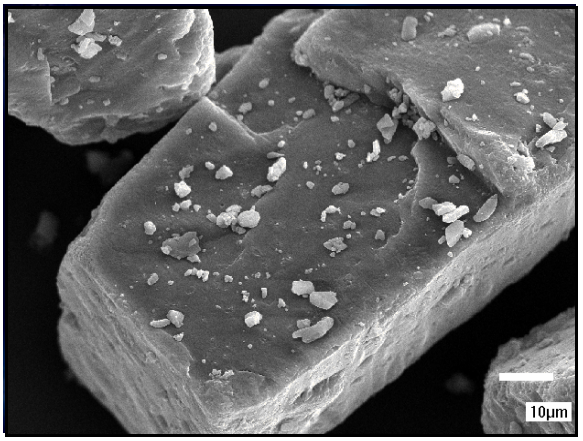
# DPI Powder Adhesion Properties: The Power of AFM

Dr Robert Price




University of Bath,
Pharmaceutical Technology Research Group.






## A composite of Interparticulate Forces

Particle interactions are primarily dictated by:

- van der Waals Forces
- Electrostatic Forces
- Capillary Forces

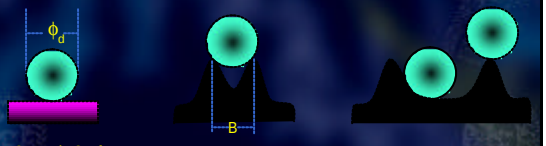
The relative contribution of these components to the total adhesion/cohesion depends on the interacting materials and relative humidity.






## Additional factors that influence particle adhesion

| | | |
|---|---|---|
| Surface Energy | - | Intrinsic "free" energy |
| Surface Roughness | - | Contact Area |
| Mechanical Properties | - | Hardness |
| Environmental Conditions | - | Temp. & %RH |



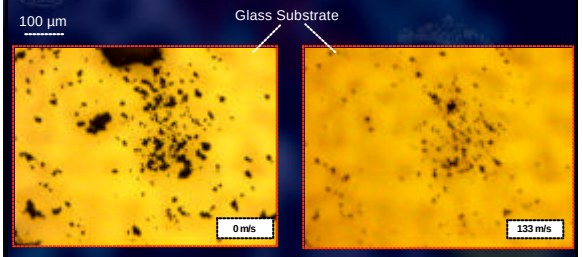

i. Smooth Surface

ii. $\phi_d$ > B

iii. $\phi_d$ < B

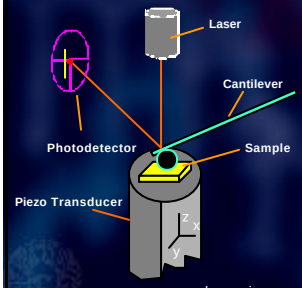


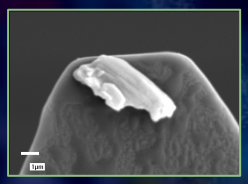
## Entrainment Inefficiencies




Unable to elutriate respirable sized drug particles

# Atomic Force Microscope (AFM)



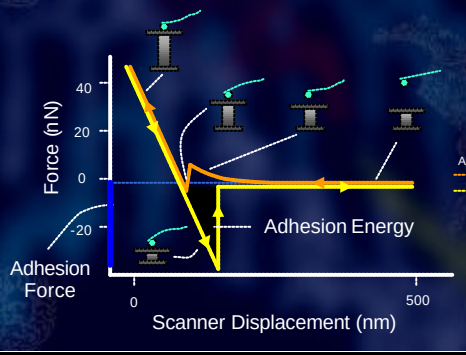
Model salbutamol sulphate drug probe

$F = kdx$

k = spring constant (N/m)
dx = cantilever deflection

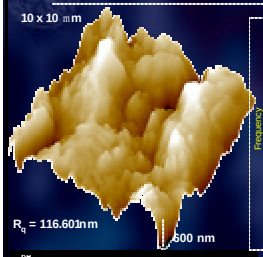


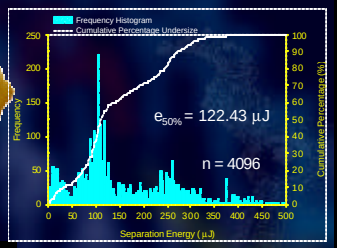
# Anatomy of a Force Curve

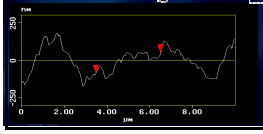





# Commercial Grade Lactose



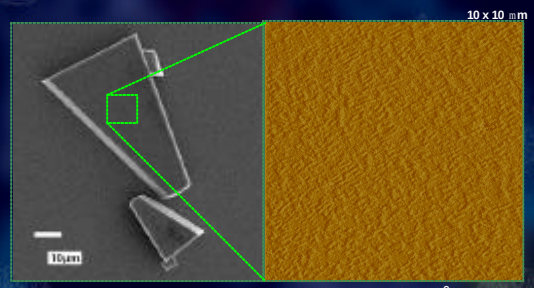



- Approaches a log-normal separation energy distribution
- Statistical analysis and effect of surface roughness rather onerous.



# Modified α-lactose surfaces

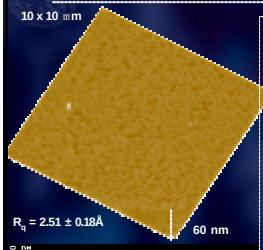


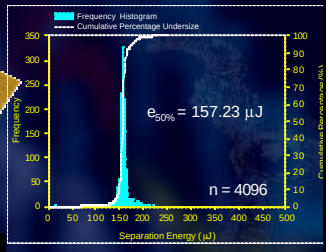

dominant $\{0\bar{1}1\}$ face

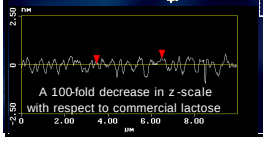
$R_q$ = 2.51Å



# Atomically Smooth Lactose



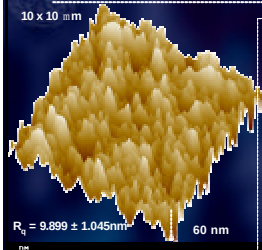



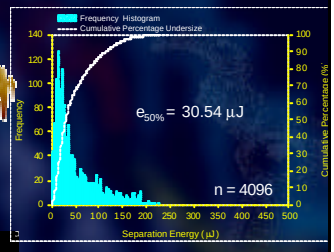



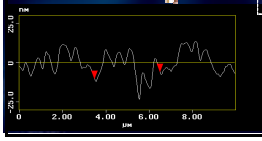

- Normally distributed data
- Statistical analysis (mean and standard deviation).



# Nanometre smooth Lactose

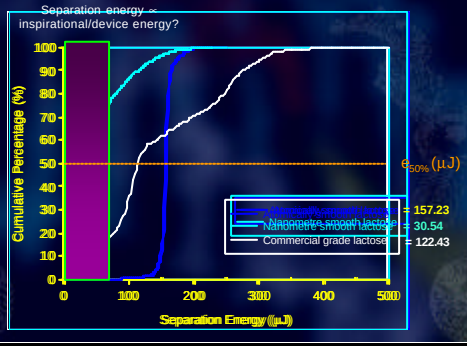


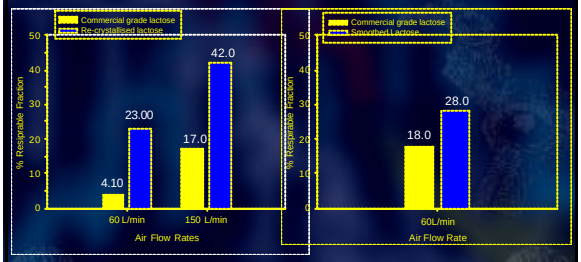
- Significant decrease in separation energy.
- Positively skewed distribution.

## The role of surface roughness on particle adhesion






## The effect of surface rugosity on %FPF

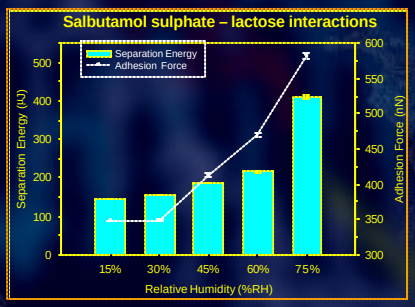



Dose: 400μg Salbutamol sulphate Device: Rotohaler®
D. Ganderton, (1992) J.Biopharm. Sci., 3 101-105.
Patent: US 5,376,386

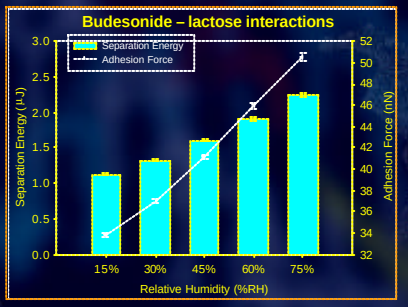
Dose: 200μg BDP Device: Pulvinal®
P. Colombo et al. (2000) RDD VII, 629 – 631.
Patent: WO 01/05429



## The Role of RH on drug-lactose interactions

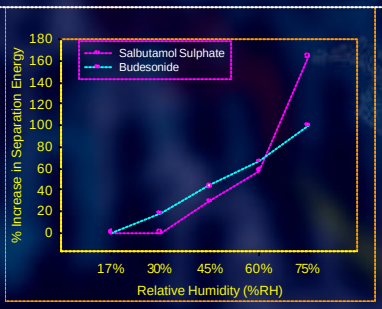







## Normalised Separation Energy




Hydrophobic, water insoluble budesonide more susceptible to capillary interactions at low RH



## General conclusions

- AFM provides a fundamental insight into the microscopic interactions which govern bulk properties of a DPI formulation.
- Variation in exipient surface roughness at the nanometre-Ångstrom scale dramatically influences drug-lactose interactions.
- Environmental conditions may play a critical role in the aerolisation efficiency and therapeutic efficacy of respirable particles.
- In combination with bulk techniques, AFM may potentially play a pivotal role in the design and modifications of DPI formulations.