

# Pharmaceutical Surface Science: Probing Interparticulate Forces

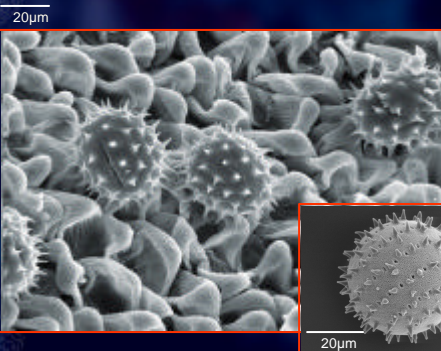
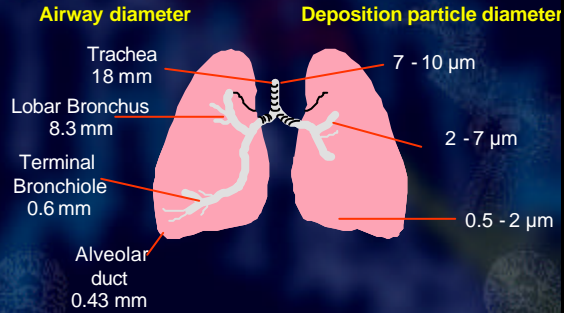
Applications to Dry Powder Inhaler Systems (DPIs)

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# Targeting by deposition



# Dry Powder Inhalers (DPIs)

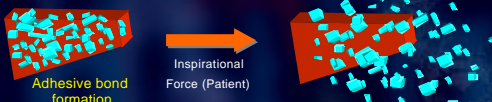
## Key issues:

- Drug Particles must reach the deep lung.
- Particle size must be below 5  $\mu\text{m}$ .
- Powders must be micronised.
- Micronised powders are very cohesive

Less than 25% of the emitted dose reaches the deep lung!

# Dry Powder Aerosols: Formulation Strategies

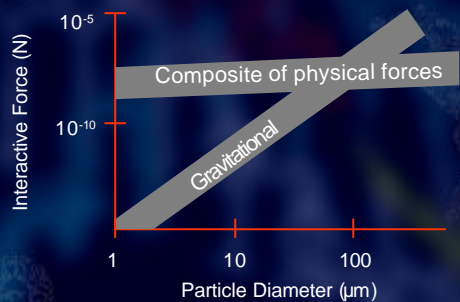
## Carrier - Based Systems



## Agglomerated Systems



# Particle size and powder interactions



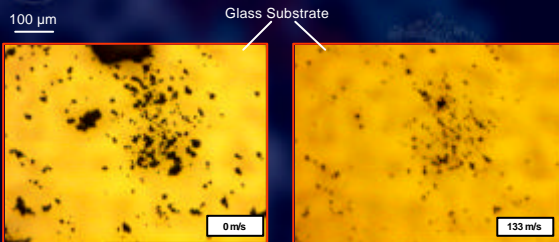
## A composite of Interparticulate Forces

Particle interactions are primarily dictated by:

- van der Waals Forces
- Electrostatic Forces
- Capillary Forces

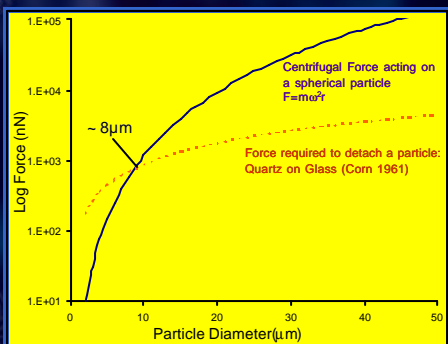
The relative contribution of these components to the total adhesion/cohesion depends on the interacting materials and relative humidity.

## Entrainment Inefficiencies



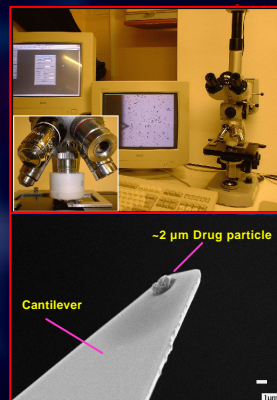
Unable to elutriate respirable sized drug particles

## Centrifugal Force (60,000 rev/min)

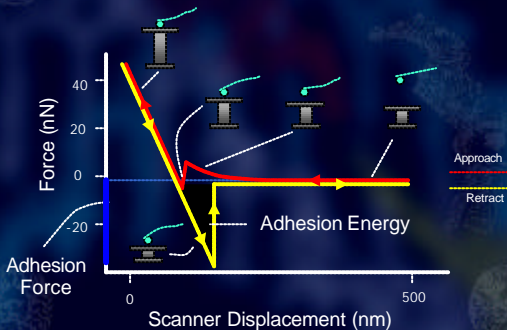


## Attaching individual drug particles

1. Drawing of Glue using Tipped Cantilever
2. Creation of micron-sized protrusions
3. Deposition of glue on Tip-less cantilever
4. Selection of drug Particle
5. Attachment of drug particle
6. High Mag. image of Particle



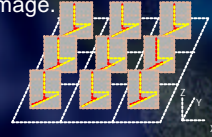
## Anatomy of a Force Curve



## Force Volume (FV) Imaging

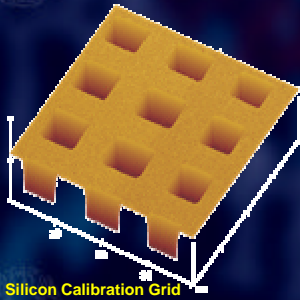
Collecting an array of force curves provides:

- A 3D laterally resolved description of the volume of forces above and upon contact with a sample surface.
- A low resolution topographic image.

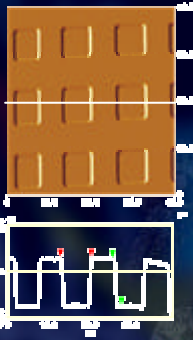




### 1. Topographical Image



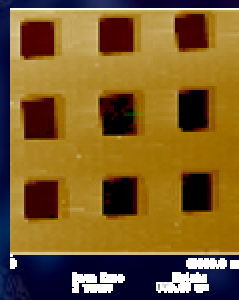
Silicon Calibration Grid



Horizontal Distance = 7.500  $\mu$ m  
Vertical Distance = 202.92 nm



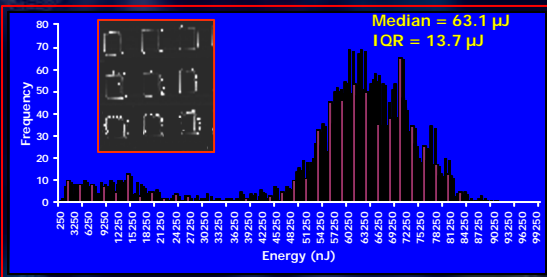
### 2. Force Volume Image (with drug probe)



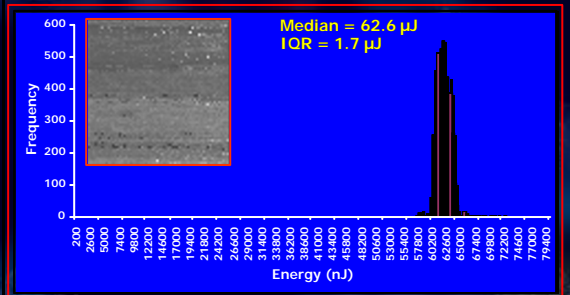
FV Image



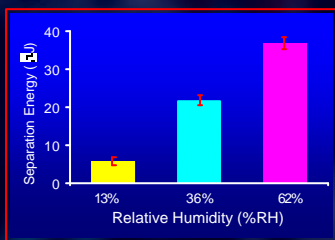
### 3. Separation Energy Analysis



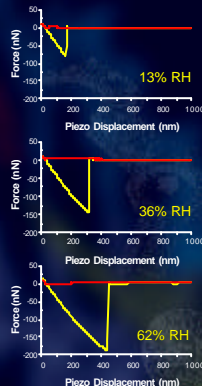
### Separation Energy Histogram & Map Particle removal from atomically flat Mica



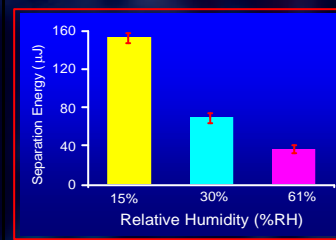
### Variation in Particle Adhesion due to Capillary Forces



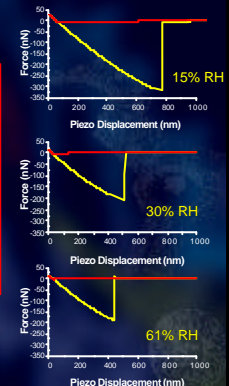
Separation energy of Drug particle (A) from an atomically flat Mica, as a function of relative humidity



### Variation in Particle Adhesion due to Electrostatic Forces



Separation energy of Drug particle (B) from an atomically flat Mica, as a function of relative humidity



## Conclusion

- AFM-based force spectroscopy allows the interactive and adhesive forces of particles  $<10\mu\text{m}$  to be measured.
- In the absence of contact electrification, surface tensional forces play a dominant role in particle adhesion.
- Due to the high resistivity of organic drug crystals, the build of electrostatic forces will have a dramatic effect on aerolisation.

## Acknowledgements



**Paul Young**  
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100 $\mu\text{m}$