# NOVEL ELECTROSTATIC CHARACTERIZATION OF PHARMACEUTICAL POWDERS

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# NOVEL ELECTROSTATIC CHARACTERIZATION OF PHARMACEUTICAL POWDERS

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## DECLARATION

I hereby declare that the thesis is my original work and it has been written by me in its entirety. I have duly acknowledged all the sources of information which have been used in this thesis.

This thesis has also not been submitted for any degree in any university previously.

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KWEK Jin Wang

12 May 2014

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#### Summary

Triboelectrification of powders is an event in which accumulation of electrostatic charges can occur through the frictional contact between particles themselves and the walls. Besides the potential explosive hazards that can arise from the charged powders, the powder cohesiveness could encourage deposition on walls of dry powder inhalers, and the formation of agglomerated structures can promote mixture segregation, disrupt smooth flow as well as hinder particle dispersion. Applications such as electrophotography, dry powder coatings and electrostatic separation, however, specifically charge powders to each of their individual advantage. Nevertheless, the electrostatic charging phenomenon of powders would first need to be characterized before the performance of the powder processing operations can be optimized.

The traditional method of measuring the electrostatic charge of powders is the Faraday cage and its variants. The simple dispensing of powders into a measuring cup electrically shielded from external interferences induces equal and opposite charges on the cup that can be quantified by an electrometer. However, operator dependency of the cage that often resulted in inconsistency and reproducibility of the measurements has prompted the need to develop alternative techniques. The aim of this project is thus to source for alternative methods of electrostatic charge quantification both at the single particle and bulk powder levels.

A parallel plate condenser on the atomic force microscope (AFM) has been fabricated from conducting indium tin oxide electrodes to study the various contributions to the net electrostatic force acting on a micron sized glass particle functionalized AFM

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cantilever in an applied electric field. The position of the microparticle can be freely positioned between the electrodes and the electric field strength adjusted accordingly. The electrostatic force, linearly proportional to the electric field strength, can be evaluated for the particle net charge when the particle is in the middle of the plates. The condenser has been demonstrated for its capability in rapidly evaluating a single microparticle net charge, its polarizability and electro-charging properties through varying its hydrophobicity.

In addition, a nonintrusive vibrating capacitive probe connected to an electrostatic voltmeter has been used to analyze the particle size effects on the triboelectric charging properties of lactose and adipic acid. Presence of either fine particles that coat the walls or large particles can obstruct effective charge transfer and diminish the surface potential measured. The results obtained were in agreement with the Faraday cage measurements. The probe has also been effective in determining the particle surface roughness effects on the electrostatic charge contributions to the impaction behaviour after aerosolization. A rough surface with high dispersive surface energy and moisture sorption capability encourages the formation of strong agglomerates that charge more readily and do not break up easily upon impaction. However, the roughness effect on the electrostatic charge was shown to be diminished using the Faraday cage and AFM if the powders were not agitated. Therefore, the nonintrusive vibrating capacitive probe and the parallel plate condenser offer potential alternative techniques worth exploring by industries in characterizing the electrostatic behaviours of powders in their processes.

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## List of Symbols

 $\Delta q_{tr}$  : Specific charge transferred per unit area (condenser model) [C/m<sup>2</sup>]

 $\Delta t$  : Contact time of particle on plate (condenser model) [s]

- $\Delta X$  : Deflection of cantilever (Hooke's Law) [V]
- α, β, γ : Dimensionless coefficients depending on factors such as particle dielectric constant, electrode overloading, particle charge distribution and geometric configuration of system (AFM) [-]
- $\epsilon_o$  : Dielectric permittivity of air [F/m]
- $\epsilon_m$ : Relative electric permittivity of material between vibrating capacitive probe surface and test surface [-]
- $\epsilon_r$  : Relative dielectric permittivity of pipe (vibrating capacitive probe) [-]
- $\eta$  : Viscosity of fluid (E-SPART) [Pa·s]
- $\phi_f$  : Phase lag in the superimposed field (E-SPART) [rad]
- $\rho_p$  : Particle density [kg/m<sup>3</sup>]

- $\sigma_{o,c}$  : Equilibrium charge density (continuous charging) [C/m<sup>2</sup>]
- $\tau$  : Time constant (condenser model) [s]
- $\tau_a$  : Aerodynamic relaxation time (E-SPART) [s]
- $\tau_{C}$  : Residence time (continuous charging) [s]
- $\omega_e$  : Circular frequency of vibrations of the electrode in the vibrating capacitive probe [rad/s]
- $\omega_f$  : Angular frequency of field (E-SPART) [rad/s]
- $\psi$  : Impaction rate of particles on plate (condenser model) [s<sup>-1</sup>]
- $A_C$  : Contact area between particle and surface (continuous charging)  $[m^2]$
- $A_e$  : Surface area of electrode exposed in the vibrating capacitive probe configuration  $[m^2]$
- $A_s$  : Total specific surface area of powders (vibrating capacitive probe)  $[m^2/g]$
- C<sub>c</sub> : Cunningham correction factor [-]

- C<sub>e</sub> : Capacitance of electrode in the vibrating capacitive probe configuration [F]
- C<sub>p</sub> : Capacitance of plate (condenser model) [F]
- C<sub>s</sub> : Capacitance of system (continuous charging) [F]
- d : Particle to substrate separation distance (AFM) [m]
- d<sub>a</sub> : Aerodynamic diameter of particle in the superimposed field (E-SPART) [m]
- $\frac{dq_{imp}}{dt}$ : Rate of charge transferred to target plate via impaction (condenser model) [C/s]

 $\frac{dq_{out}}{dt}$  : Rate of charge lost through conduction (condenser model) [C/s]

 $\frac{dQ_c}{dt_c}$  : Rate of charge transfer during dynamic contact charging process [C/s]

 $\frac{dv_{p,a}}{dt_f}$ : Rate of change of particle acoustic velocity in the superimposed field (E-

SPART) [m/s<sup>2</sup>]

E<sub>a</sub> : Applied electric field strength (E-SPART, AFM) [V/m]

- $f_R$  : Surface roughness by BET and geometric surface area ratio [-]
- F : Force calculated from cantilever deflection (Hooke's Law) [N]
- F<sub>C</sub> : Coulombic force on a single particle (AFM) [nN]
- $F_E$  : Net electrostatic force on a single particle (AFM) [nN]
- $F_{Inet}$  : Force due to image charges on a single particle (AFM) [nN]
- $F_{Ipol}$  : Force due to field induced dipoles (AFM) [nN]
- I<sub>e</sub> : Current detected by the vibrating capacitive probe [A]
- k<sub>p</sub> : Constant in condenser model [-]
- k<sub>tr</sub> : Efficiency of charge transfer via impaction (condenser model) [C/V]
- K<sub>N</sub> : Cantilever normal spring constant [N/m]
- m<sub>P</sub> : Mass of powders (vibrating capacitive probe) [g]
- n : Number of experimental measurements [-]
- q : Charge of powders measured by Faraday cage [nC]

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- $q_{def}$  : Particle net charge from deflection of cantilever in electric field (AFM) [C]
- q<sub>e</sub> : Equilibrium charge independent of work function of metal plate [C]
- $q_p$  : Charge on plate (condenser model) [C]
- Q : Net charge on particle placed between the parallel plate condenser [C]
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- Q<sub>e</sub> : Charge accumulated on the electrode in the vibrating capacitive probe [C]
- Q<sub>ind</sub> : Charge on flowing particles (vibrating capacitive probe) [C]
- $Q_p$  : Specific charge of powders calculated from Faraday cage measurements [nC/g]
- R : Particle radius (AFM) [m]
- $R_o$  : Equivalent circuit resistance (continuous charging) [ $\Omega$ ]

- $R_p$  : Net resistance in an equivalent electric circuit where the resistors are in parallel (condenser model) [ $\Omega$ ]
- $R_{pl}$  : Electrical resistance of target plate (condenser model) [ $\Omega$ ]
- $R_s$  : Net resistance in an equivalent electric circuit where the resistors are in series (condenser model) [ $\Omega$ ]
- S : Photodiode sensitivity [nm/V]
- t : Time taken for the transfer of charge from particle to plate (condenser model)
  [s]
- t<sub>C</sub> : Contact time between particle and surface (continuous charging) [s]
- te : Time at which a specific amount of charge is taken away or delivered to the vibrating capacitive probe [s]
- $t_{\rm f}$  : Time of motion of particle in the superimposed field (E-SPART) [s]
- v : Initial surface potential of powders (vibrating capacitive probe) [kV]
- v<sub>p</sub> : Sinusoidal oscillatory velocity of particle in the superimposed electrical field on acoustic field (E-SPART) [m/s]

- v<sub>p,a</sub> : Particle velocity due to acoustic excitation (E-SPART) [m/s]
- v<sub>p,e</sub> : Particle velocity due to electrical migration (E-SPART) [m/s]
- *V* : Voltage applied to electrodes in a parallel plate condenser [V]
- $V_c$  : Potential difference between electrode of the vibrating capacitive probe and the test surface [kV]
- V<sub>e</sub> : Electrical drift velocity of particle (E-SPART) [m/s]
- V<sub>eff</sub> : Potential difference based on work function, image charge, and space charge (condenser model) [V]
- V<sub>o</sub> : Normalized initial surface potential or chargeability of powders (vibrating capacitive probe) [kV]
- V<sub>p</sub> : Potential difference due to charge on plate (condenser model) [V]
- $V_R$  : Induced electric potential of ring electrode on dielectric pipe (vibrating capacitive probe) [kV]
- V<sub>s</sub> : Potential difference in equivalent electric circuit when resistances are in series (condenser model) [V]

- $V_T$  : Total potential difference between particle and plate (condenser model) [V]
- $\frac{w}{w_o}$  : Particle-to-wall adhesion expressed as a percentage [-]
- w<sub>o</sub> : Total mass of powder loaded in bottles [mg]
- $w_1$  : Mass of powder in bottle before pouring [mg]
- w<sub>2</sub> : Mass of powder in bottle after pouring [mg]
- y : Sinusoidal vertical displacement of vibrating capacitive probe [m]
- y<sub>o</sub> : Initial vertical displacement of vibrating capacitive probe [m]
- y<sub>1</sub> : Vertical displacement of vibrating capacitive probe at time t<sub>e</sub>[m]
- Y<sub>g</sub> : Amplitude of gas motion in acoustic field (E-SPART) [m]

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#### Chapter 1

## Introduction

#### **1.1 Project Motivation and Aims**

The central aim of this thesis is to explore alternative novel techniques in the electrostatic characterization of powders with particular reference to pharmaceutically relevant powders. Ever since the Greeks discovered the electrostatic phenomenon back in 600 B.C., there has been limited number of techniques available for industries to characterize the powder electrostatic phenomenon often encountered during powder processing and handling. At present, the conventional method of powder electrostatic characterization is by depositing charged powdered samples into a shielded metallic Faraday Cage connected to an electrometer and then measuring the induced charge. Problems associated with the conventional electrostatic characterization include inconsistent charge measurements, operator dependencies, adhesion of particles on the walls of the Cage, and long discharge times in between measurements. The inadequacies of the Cage in measuring dynamic charge during aerosolization or pneumatic processes have led to its modification to an open-ended configuration for continuous flow of particles as well as the development of other advanced devices such as electrical impactors or modified phase Doppler particle analyzer. However, these devices are rather sophisticated and require specialized knowledge in analyzing the results obtained. In this project, a nonintrusive vibrating capacitive probe technique is introduced as a monitoring sensor and the potential to analyze various influencing factors such as particle size, morphology, and surface roughness on the electrostatic behaviour of bulk pharmaceutical powders is evaluated.

On the other hand, a single particle technique using a fabricated parallel plate condenser coupled with the atomic force microscope (AFM) capable of determining the electrostatic chargeability of discrete particles under an applied electric field is developed. Both the bulk powder and single particle techniques could provide potential alternatives to the Faraday Cage to provide a better mechanistic understanding on the charging behaviour of powders.

### **1.2 Thesis Outline**

The thesis begins, in the following section, with a background on the origins of electrostatics and its importance in various powder handling processes. The Faraday cage, being the conventional method adopted by many industries, is described in the last section of this chapter. The mechanisms in triboelectric charging, often encountered during frictional contact with surfaces causing electrostatic charge buildup, are discussed in Chapter 2 with its influencing factors and characterizations both at single particle and bulk powder level. Alternative novel methods of electrostatic characterizations both at the single particle and bulk powder levels using the parallel plate condenser on the atomic force microscope (AFM) and the nonintrusive vibrating capacitive probe technique are introduced in Chapters 3 and 4 respectively. In Chapter 5, the nonintrusive electrostatic monitoring technique is combined with high speed imaging in visualizing the effects of particle surface roughness on the electrostatic charges of model inhalant agglomerates upon aerosolization and the subsequent impaction behaviours in a tube model simulating the human throat. The thesis ends with proposed future work illustrating the potential in using the nonintrusive technique in detecting crystallinity changes and its implementation in industrial powder handling processes.

## **1.3 Origins of Electrostatics**

Thales of Miletus was the first who discovered electrostatics in *ca*. 600B.C. by noting that straw was attracted to a piece of rubbed amber (Staniforth and Rees, 1981; Voldman, 2012). This electrostatic phenomenon was subsequently associated with the Greek word for amber, ελεχτρον (or electron). However, it was not only until the seventeenth century, that Sir William Gilbert (1893) also observed the same phenomenon by rubbing a glass rod against silk and he started to compile the earliest list of materials for the tribo-electrification (or charging by friction) events. The concept of categorizing materials according to the nature of "removing" or "sustaining" electrification was emphasized in the list by Stepen Gray (1731) with the ability to generate charges on a ball of rotating sulfur termed as "static electricity" demonstrated by Otto von Guericke (1672). Charles du Fay (1733) further suggested, in his triboelectrification experiments with glass, silk, amber and fur, that there were two kinds of electricity: attractive as "vitreous", and repulsive as "resinous". However, contrary to the "two-fluid" idea, Benjamin Franklin (Jenson, 2005) believed, in the eighteenth century, that there was only one electrical fluid but can have opposing existence. The one-fluid idea turned out to be false as electrons were found to be the main cause behind the positive and negative polarities found on rubbed materials. While scientists continued to build on the tribo-electric list of materials, Charles-Augustin de Coulomb (1785) related the electric force between two point charges as inversely proportional to the square of the distance between them, and Michael Faraday (1844), in his "ice-pail" experiments, showed that positive and negative charges always appear in equal quantities. Further understanding of electrical forces

and electricity was achieved based on the modern formulation of electricity and magnetism by James Clerk Maxwell (1865).

### **1.4 Phenomenon of Powder Electrostatics and its Importance**

In any powder handling process, collisions of the particles between themselves or the walls are inevitable. Frictional contacts through sliding and / or separation of surfaces collectively known as triboelectrification often left the surfaces electrostatically charged. The resultant polarity and magnitude of the accumulated surface charges were believed to depend very much on the material work functions amongst other factors such as particle properties (morphology, particle size, roughness, crystallinity and chemical functionalities) and environmental conditions (temperature and relative humidity). Dissipation of the surface charges are particularly slow in insulating powders such as polymeric and pharmaceutical particles with highly adhesive or cohesive particles and the undesired outcomes could range from poor flowability to more hazardous conditions such as arc discharge precedent to a potential powder explosion. Nevertheless, powder electrostatics still finds its usefulness in several applications such as electrostatic precipitation (White, 1963), powder coating (Hughes, 1984), toner transfer in paper prints (Schein, 1992), pharmaceutical inhalation applications (Bailey et al., 1998), and creating homogeneous powder blends with electrostatic corona charging (Pu et al., 2009; Staniforth and Rees, 1981). The phenomenon and importance of powder electrostatics in various powder handling processes have also been well documented.

The performance of gas-solid systems such as pneumatic conveying depends very much on the pressure drops across the channel which in turn reflects the powder flowability (LaMarche *et al.*, 2009). Potential powder choking in the channel due to powder adhesion to the walls is the cause of the high pressure drops. It was observed that a direct link between the generated electrostatic charges on the powders to the high pressure drops can be established (Ally and Klinzing, 1985; Joseph and Klinzing, 1983; LaMarche *et al.*, 2009; Smeltzer *et al.*, 1982). The pressure drop is a function of the combination of the particle number density and the maximum charging ability or chargeability of the particles. A major contributor to both the factors is the mean particle size. Smaller particles usually displayed larger electrostatic effects due to increased particle number density and particle interactions (Gajewski, 1989; Smeltzer *et al.*, 1982). In contrast, electrostatic charging can also increase with particle size increase as observed by Guardiola and co-workers (1996) during fluidization.

Attrition that can occur during the gas or mechanical agitation of powders such as milling, sieving or blending can result in particles of various morphologies leading to higher charge variations (Yao and Wang, 2006; Unger et al., 2004; Swaminathan and Kildsig, 2000). In addition, depending on the material composition of powders and the surrounding walls, bipolarity in blends could cause particle agglomeration and segregation (Muzzio and Alexander, 2005; Lachiver *et al.*, 2006; Šupuk *et al.*, 2011). Grounding of the equipment walls to reduce the charge accumulation in the blends proved futile (Pu *et al.*, 2009) and using a high relative humidity that dissipates the accumulated surface charges can induce attraction through capillary forces instead (Zhu *et al.*, 2008). In dry powder inhalers, it is necessary to detach the drug from carrier particles while minimizing particle-wall adhesion that were significantly influenced by the presence of electrostatic charges so as to ensure consistent dosage to the lungs (Byron *et al.*, 1997; Chow *et al.*, 2008).Analogous to the migration of

charged toner particles to paper in electrophotography (Hays, 2001), the subsequent deposition of the drug particles in targeted areas in the lung would depend on the space charge field in the alveoli and more importantly on the induced charge at the upper respiratory airways (Bailey, 1998; Wilson, 1947).

As a first step to control electrostatic charging, a reliable means of characterizing the charge would need to be developed. The Faraday cage connected to an electrometer has often been used to measure the charge of powders (Colver, 1999). However, the reliability of the Faraday cage to provide consistent measurements would depend on the systems it is monitoring (Taylor, 2001). As a result, modifications to the Faraday cage (Kulvanich and Stewart, 1987; Lee and Weser, 1979; Schein and Cranch, 1975) as well as other charge measuring devices (Balachandran, 2003; Hoe *et al.*, 2009; Noras, 2006; Singh and Hearn, 1985) have been developed over the years to systematically study and understand the charge generation process.

#### **1.5 Conventional Method – The Faraday Cage**

The Faraday cage has always been the standard in charge measurements of powders probably due to the relative ease of sampling. Powder samples are taken from the processing equipment in weighed amounts and transferred into a highly conductive cup that is shielded from external electrical fields via a grounded metallic enclosure. Opposite and equal charges are induced on the inner walls of the conductive cup which in turn induce opposite charges on the outer walls. The charge is fed to a high impedance circuit in the electrometer from which the value should be normalized against the mass of the powder in the cup. A schematic diagram of the Faraday cage is shown in Fig. 1.1. Unfortunately, the ability of the Faraday cage to consistently deliver reproducible measurements has been poor as the coefficient of variations between measurements has been reported to be between 20% to as high as 50% (Zhao *et al.*, 2002). The likely cause behind the inconsistent measurements could be the adhesion of particles on the walls of the cage upon repeated measurements that led to obscuration of the induced charges (Carter *et al.*, 1998; Eilbeck *et al.*, 2000).



**Fig. 1.1:** A Faraday cage or pail connected to a monitoring high impedance circuit (Secker and Chubb, 1984).

## Chapter 2

## **Concept of Triboelectric Charging and Characterizations**

### 2.1 Discrete Particle Charging

#### 2.1.1 Contact Charge Transfer

Contact charging involves dissimilar surfaces coming together and the separation of which results in the generation of opposite charges on the surfaces (Bailey, 1993). However, it should be noted that the above-mentioned triboelectrification process is far from simple as rolling, sliding and surface deformations could occur during impact that can cause the observed results to deviate from theoretical models. Nevertheless, charges on the surfaces before and after impact were characterized and analyzed using models with appropriate assumptions as a first step in understanding the charge transfer mechanism between insulator-metal and/or insulator-insulator contacts.

The approach is to study the contact charge transfer between single insulating particles and a metal target prior to extending the mechanism to an ensemble of particles. The earliest experiments (Masui and Murata, 1983; 1984) were designed such that single polymeric particles can be directed onto a metal plate at various velocities. A typical experimental apparatus used by Matsuyama's group (1994) aimed to measure the charge generated on the particle before and after impaction is shown in Fig. 2.1. A pneumatic gun would propel the particle towards the metal plate that can be inclined at certain angles  $\theta$ . The initial charge of the particle was determined by a double cylindrical Faraday cage connected to an oscilloscope as it

passed through before colliding onto the metal plate. The impaction velocity was calculated by measuring the time required to pass through the cage from the width of the voltage waveform. Insulation of the metal plate from the support was necessary to eliminate charge leakage to the environment. The plate was connected to an electrometer to capture the charge transfer upon impact. A force transducer can also be attached to the plate to measure the contact force.



**Fig. 2.1:** Schematic diagram of experimental setup to study contact charge transfer via impaction of insulating particles on metal target plate (Matsuyama and Yamamoto, 2006).

The impact charge of the particle on the plate was measured, plotted against the initial charge and the linear relationship between the two parameters is termed the "charging line" (Matsuyama and Yamamoto, 2006). As the line is extrapolated towards the horizontal axis, the intersection of which is the "equilibrium charge" whereby no net

charge transfer occurs (Fig. 2.2). The impact velocity that is normal to the plane of the plate was found to influence the impact charge (Watanabe *et al.*, 2007) and as shown in Fig. 2.2a, the impact charge of spherical sugar granules colliding stainless steel plate increased with increasing velocity.



**Fig. 2.2:** (a) Impact charge of sugar granules on stainless steel plate increased with increasing impact velocity (Watanabe *et al.*, 2007), and (b) Impact charge of Teflon particles on Aluminium plate increased with increasing impaction angle (Matsuyama and Yamamoto, 1994).

The impact charge also increases with the increase in the impaction angle (Fig. 2.2b) which in turn affects the contact area between the particle and the plate. Ema and coworkers (2003) showed that the increase was not indefinite but reached a maximum at impact angle of 60° depending on the effective contact area (Watanabe *et al.*, 2007) between the particle and the plate that is, in turn, described by the contact efficiency (Matsuyama and Yamamoto, 1994) due to rolling and slipping on the surface. However, the impact velocity and angle are not the only factors that affect the impact charge. The charge generated was also dependent on the particle material, particle size and plate material. For instance, Yamamoto and Scarlett (1986) showed that, in Fig. 2.3, nylon particles of diameter 2.8 mm were charged positively while similarly sized polystyrene particles charged negatively upon collision with brass plate. Smaller sized particles colliding with plate of same material will acquire less charge than larger particles.



**Fig. 2.3:** Particles of different materials charge differently. Nylon particles charged positively on brass plate as compared to polystyrene particles (Yamamoto and Scarlett, 1986).

The results obtained by Matsuyama's group, as shown earlier in Fig. 2.2, generally follows the simple condenser model as illustrated in Fig. 2.4. A double layer of charge develops between the particle and the surface of the plate as the particle approaches the plate. Charge transfer would be driven by the effective potential difference between the particle and the plate, and influenced further by the capacitance at the double layer.


**Fig. 2.4:** Simple condenser model is depicted as an equivalent electrical circuit consisting of the capacitance, resistance and the driving effective potential difference for charge transfer.

Assuming that the contact time is short but sufficient for charge transfer, the condenser model starts from the following equation (Matsusaka *et al.*, 2003):

$$\Delta q_{tr} = k_{tr} V_T \tag{2.1}$$

Where,  $\Delta q_{tr}$  is the specific charge transferred per unit area,  $k_{tr}$  is the efficiency of charge transfer via impaction, and  $V_T$  is the total potential difference between particle and plate.

The total potential difference would depend on the work function, image charge, and space charge of the particles. As the charge on the plate increases, the total potential difference decreases, hence the efficiency of charge transfer decreases. The total potential difference,  $V_T$ , can therefore be expressed as the difference between the potential difference,  $V_{eff}$ , based on work function, image charge and space charge, and the potential difference,  $V_p$ , that arises due to the charge on the plate.

$$V_T = V_{eff} - \frac{k_p q_p}{C_p}$$
(2.2)

Where,  $k_p$  is a constant and  $C_p$  is the capacitance of the plate.

The rate of charge transferred to target plate via impaction is directly proportional to the frequency of particles hitting the plate and is given as:

$$\frac{dq_{imp}}{dt} = \Delta q_{tr} \psi \tag{2.3}$$

Where,  $\psi$  is the impaction rate of particles on the plate.

Charge can also be lost through conduction from the plate and assuming it obeys Ohm's law, the following equation for charge conducted per unit time is:

$$\frac{dq_{out}}{dt} = \frac{q_p}{C_p R_{p_l}} \tag{2.4}$$

Where,  $R_{pl}$  is the electrical resistance of the target plate.

From the conservation of charges, the rate of charge generated on the plate can be found from the difference between the charge transfer via impaction and the charge conducted.

$$\frac{dq_p}{dt} = \frac{dq_{imp}}{dt} - \frac{dq_{out}}{dt}$$
(2.5)

The differential equation is solved and the result relation is shown:

$$q_{p} = \frac{C_{p}V_{s}R_{p}}{R_{s} + R_{p}} \left[ 1 - \exp\left(-\frac{R_{s} + R_{p}}{CR_{s}R_{p}}t\right) \right]$$
(2.6)

The expressions for  $V_s$  and  $R_s$  are given below:

$$V_s = \frac{V_{eff}}{k_p} \tag{2.7}$$

$$R_s = \frac{1}{\psi k_{tr} k_p} \tag{2.8}$$

It is noted from the equation (2.6), the equivalent electric circuit consists of the resistance  $R_s$  is connected in series while  $R_p$  is parallel to the capacitance  $C_p$ . When  $R_p$  is much greater than  $R_s$ , all the charges are transferred onto the plate, and the equation (2.6) would be written as:

$$q_{p} = C_{p} V_{s} \left[ 1 - \exp\left(-\frac{t}{C_{p} R_{s}}\right) \right]$$
(2.9)

With the substitution of the time constant, the equation (2.10) summarizes the condenser model (Yamamoto and Scarlett, 1986):

$$q_p = C_p V_s \left( 1 - \exp\left(-\frac{\Delta t}{\tau}\right) \right)$$
(2.10)

Where,  $\Delta t$  is the contact time of the particle on the plate, and  $\tau (= R_s C_p)$  is the time constant.

The difficulty in the condenser model is that it could not explain the equilibrium charge, q<sub>e</sub>, being independent of the work function of the metal target plate (Fig. 2.5a) when it is obvious from Eq. (2.1), the charge would depend on the total potential difference arising from the work function (Eq. (2.2)). To address the inadequacy of the condenser model, the charge relaxation model was proposed by Matsuyama and Yamamoto (1997) in which the charge observed on the plate surface was the residual if conditions suffice for gaseous discharge across the gap between the impacting particle and the plate surface. When a particle approaches a metal plate, the charge transferred on the particle could cause the potential to meet the Paschen curve (Fig. 2.5b). Charge relaxation occurs due to gaseous breakdown while the potential will leave the Paschen curve with the residual charge on the particle being larger than its initial charge. If the charge on the particle is large, an excess of the charge will be released during the gas breakdown before impact, and the initial charge is the equilibrium charge. The equilibrium (or maximum limiting) charge was found to be dependent on the particle (insulator) dielectric constant and particle diameter (Fig. 2.6).



**Fig. 2.5:** (a) Equilibrium charge is found to be independent of the work function of the metal target that does not follow the condenser model (Matsuyama and Yamamoto, 1995), and (b) Paschen curve of gaseous discharge for charge relaxation model is shown to explain the remaining charge on the surface after relaxation process (Matsuyama and Yamamoto, 1997).



**Fig. 2.6:** Dependency curve of equilibrium (maximum limiting) charge on (**a**) particle relative dielectric constant, and (**b**) particle diameter (Matsuyama and Yamamoto, 2006).

Nevertheless the condenser model still presented a simple starting approach in describing the triboelectric phenomenon in many studies (Ahuja, 1976; John *et al.*, 1980; Karner and Urbanetz, 2011; Masuda and Iinoya, 1978; Masui and Murata, 1983,

1984; Matsuyama and Yamamoto, 1989). As described earlier, the impact charge was generally affected by the contact area and driving force (or contact potential difference) between the particle and the plate. The equilibrium charge on the particle was, on the other hand, significantly influenced by the particle dielectric constant and independent of the work function of the plate. The setup (Fig. 2.1) was useful in analyzing single (or multiple) particle impacts at various conditions and ascribing them to models explaining the observed phenomenon but it was an intrusive technique that could be difficult to implement in powder handling and transport processes. The following section describes an apparatus involving a combination of optics, acoustics and electrics that has the potential to measure the charge of single particles during the powder processes.

### 2.1.2 Aerodynamic Electrical Charge Relaxation

The electrical-single particle aerodynamic relaxation time analyzer (E-SPART) was used by Mazumder and colleagues (1991) to analyze the aerodynamic size and the electrostatic charges of particles flowing in the airstream. The measured charge normalized by the particle aerodynamic diameter has direct applications in examining toner attachment and repulsion efficiencies for electrophotographic processes (Donivan and Laukaitis, 1983; Watson, 1979). The approach is to measure the aerosolized particle velocity or phase lag in an acoustic field and determine the particle aerodynamic diameter through its relaxation time. The obtained aerodynamic diameter and the measured electrical migration velocity in a simultaneously applied electric field are then used to calculate the electrostatic charge of the particles.



**Fig. 2.7:** A schematic diagram of the E-SPART analyzer with its optics, the relaxation enclosure and the data processing system (Stark *et al.*, 2008).

The main components of the E-SPART analyzer are the laser Doppler velocimeter (LDV), the relaxation enclosure and the data processing system. The laser is passed through a series of mirrors and lenses to obtain dual converging beams on the aerosol particles passing through the relaxation enclosure. The particles are excited in the enclosure by the acoustic transducers positioned symmetrically perpendicular to the plane containing the laser beams. The phase lag and / or amplitude of the particle velocity due to acoustic excitation can be measured by the LDV and can be used to calculate the aerodynamic diameter. In addition to the acoustic field, a known electrical field is also applied with the AC electrode in the same direction as the acoustic field. The particle will then have another velocity component due to the electrical field and the amplitude of which depends on the charge and particle aerodynamic size.

Due to the superimposition of the electrical field on the acoustic field, the particle has a sinusoidal oscillatory motion,  $v_p$ , and an electrical drift velocity,  $v_e$ , as illustrated in Fig. 2.8.



**Fig. 2.8:** Particle sinusoidal motion as measured by the LDV in the acoustic and superimposed electrical fields (Stark *et al.*, 2008).

It was assumed that the particle motion in the acoustic field follows Stokes' law, and it can be expressed as:

$$\tau_a \frac{dv_{p,a}}{dt_f} + v_{p,a} = Y_g \sin \omega_f t_f$$
(2.11)

Where,  $\tau_a$  is the aerodynamic relaxation time,  $v_{p,a}$  is the particle velocity due to acoustic excitation,  $Y_g$  is the amplitude of gas motion in the acoustic field,  $\omega_f$  is the angular frequency of the field.

The solution of the differential equation (2.11) gives the phase lag,  $\varphi_f$ , that can be measured and is a function of the angular frequency,  $\omega_f$ , and the aerodynamic relaxation time,  $\tau_a$ .

$$\varphi_f = \tan^{-1} \omega_f \tau_a \tag{2.12}$$

The aerodynamic relaxation time,  $\tau_a$ , is calculated from the experimentally obtained phase shift,  $\phi_f$ , and then used to determine the aerodynamic diameter,  $d_a$ , as follows:

$$d_a = \left[\frac{18\eta\tau_a}{\rho_p C_c}\right]^{1/2} \tag{2.13}$$

Where,  $\eta$  is the viscosity of the fluid,  $\rho_p$  is the particle density, and  $C_c$  is the Cunningham correction factor.

An electric field of a known strength,  $E_a$ , is applied and the electrostatic force enables the particle to move with an electrical migration velocity,  $v_{p,e}$ . Therefore, the electrostatic charge on the particle,  $q_a$ , can be determined from the calculated values of  $d_a$ ,  $\tau_a$ , and the experimental observation of  $v_{p,e}$ .

$$q_a = \frac{3\pi v_{p,e} \eta d_a}{E_a C_c} \tag{2.14}$$

By measuring the velocities of the particle in acoustic and electrical fields, the E-SPART can simultaneously measure the aerodynamic diameter and the electrostatic charge on the particle. However, if the initial charge on the particle is greater than 20  $\mu$ C/g, the particles would experience repulsive forces between themselves via space charge and attractive forces toward the wall of the sampling tube via image charge, hence causing inaccuracy in the charge measurements. On the other hand, for low charges, high voltages (1000 to 5000V) would have to be applied to initiate electrical mobility. These high voltages can sometimes cause gaseous breakdown or arcing. An alternative methodology is to reduce the distance between the two electrodes generating the required electric field strength. This will be illustrated in the next section.

### 2.1.3 Charge Induced Lever Deflection

The atomic force microscope (AFM) has been commonly used to evaluate surface features by scanning a microscopic cantilever over the sample surface. Interactions between the cantilever tip and the surface cause the cantilever to bend or deflect and the deflections are tracked using a laser reflected off the cantilever. It is hence possible to measure the force between the cantilever and the surface from the deflections captured by a position sensitive detector. In colloidal probe AFM, the tip of the cantilever is replaced by a particle of interest, and particle-particle and particle-surface interactions can then be measured at the sub-micrometer or nanometer scale. Many of the studies involving the colloidal probe technique has been conducted in liquid medium with measurements of surface and adhesive forces (Ducker and Senden, 1992; Vakarelski *et al.*, 2000), frictional interactions (Vakarelski *et al.*, 2004),

interactions between deformable particles (Vakarelski *et al.*, 2003, 2008) and living cells (McNamee *et al.*, 2006).

There are, however, few studies that examine electrostatic forces in air using the colloidal probe technique. Gady and co-workers (1998) conducted contact electrification experiments using micrometer sized polystyrene (PS) particles attached on the AFM cantilevers against flat HOPG and gold film deposited on mica. They observed that during the approach of the PS particle onto the surface, long range attractive forces were present in the force curves of HOPG surfaces after repeated contacts but were absent in those of the gold film surfaces. These forces were electrostatic in nature and the amount of charge and contact area can be quantified using a disk-to-disk interaction model (Matsuyama *et al.*, 2008). Similar long range attractive forces were also found in the approaching part of the force curves measured between triamcinolone acetonide (TAA) particles (Fig. 2.9) especially at low relative humidity of 15% (Young *et al.*, 2004). Bunker and co-workers (2007) compared the lengths of the jump in during the particle approach to surface for lactose particles at RH values ranging from 0.1 to 5% so as to study the moisture effect of charge dissipation.

An alternative electrical field detachment method measures the net electrostatic force on small (5 to 15  $\mu$ m) dielectric particles such as glass or polystyrene through the application of an external electrical field on the particle functionalized AFM cantilever (Mizes, 1994). A schematic of the experimental design on the AFM is shown in Fig. 2.10.



**Fig. 2.9:** AFM force curves of TAA particles at (**a**) 15 %RH, and (**b**) 75 %RH. It was noted that long range attractive forces were present at 15 %RH but not at 75 %RH (Young *et al.*, 2004).



**Fig. 2.10:** The removal force is measured by deflection of the particle functionalized cantilever as the particle pulls away from the substrate in the presence of the applied electrical field shown here in the setup with the AFM (Mizes, 1994).

The electrical field detachment technique has found important applications in electrophotography. The net electrostatic force required for dielectric particle removal is a result of two major competing forces, the applied Coulombic force and the electrostatic adhesion force that holds the particle onto the surface. The net electrostatic force,  $F_E$ , would be the combination of the Coulombic force,  $F_C$ , the force due image force due the particle charges,  $F_{Inet}$ , and the field induced dipole force,  $F_{Ipol}$ , as given in Eq. (2.15).

$$F_E = F_C + F_{lnet} + F_{lool} \tag{2.15}$$

(a) **E** Net charges

A schematic of the forces is shown in Fig. 2.11.



**Fig. 2.11:** Schematics of the electrostatic forces acting on a charged dielectric particle (**a**) in a uniform electric field, and (**b**) near the electrode.

The Coulombic force,  $F_C$ , depends on the particle net charge,  $q_{def}$ , and the applied electrical field strength,  $E_a$ . Particles with higher net charges would thus require

higher Coulombic forces. The expression that relates the Coulombic force with the particle net charge and applied electrical field is given in Eq. (2.16).

$$F_c = \alpha q_{def} E_a \tag{2.16}$$

Any charges on the particle would induce image charges on the substrate attracting the particle and giving rise to an electrostatic adhesion force,  $F_{Inet}$ , due to the image charges. This image force is proportional to the square of the net charge on the particle which meant that a stronger electrical field would be required to remove the particle. Expressed as a function of the net charge,  $q_{def}$ , the separation, d, of the particle from the substrate surface and the dielectric permittivity,  $\varepsilon_0$ , of air, the force due to its image charges is given in Eq. (2.17) in which a negative sign is applied for adhesive forces opposing the direction of the electrical field used for particle removal.

$$F_{Inet} = -\frac{\beta q_{def}^{2}}{16\pi\varepsilon_{0}d^{2}}$$
(2.17)

Additional adhesive force,  $F_{Ipol}$ , is exerted on the particle through the interaction of the electrical field and the dipoles on the particle. The field induced dipole results in image dipole charges that pull the particle towards the substrate. The expression (Eq. 2.18) for the induced image dipole force depends on the square of the applied electric field,  $E_a$ , and the particle radius, R.

$$F_{lpol} = -\gamma \pi \varepsilon_0 R^2 E_a^2 \tag{2.18}$$

The dimensionless coefficients,  $\alpha$ ,  $\beta$ , and  $\gamma$  that are shown in Eqs. 2.16 to 2.18 depend on factors such as particle dielectric constant, electrode overcoating, particle charge distribution and the geometric configuration of the system (Feng and Hays, 1998). As the thickness of the dielectric overcoating increases, the adhesion force due to net particle charge decreases since the primary image charge in the conductive electrode is further away from the particle, hence leading to a reduced  $\beta$ . The field induced polarization also decreases with increase in overcoating and appears to be more rapid than the monopole effect in  $\beta$ , resulting in diminished  $\alpha$  and  $\gamma$ . The increase in the particle dielectric constant would, on the other hand, amplify the image charge effects and increase the values of  $\alpha$ ,  $\beta$ , and  $\gamma$ . If the modifications in the geometric configuration were made in bringing the electrodes closer to each other and the distance is comparable with the size of the particle, competitive interactions between the dipole and image charges in the counter and supporting electrodes would cause  $\gamma$ to have a maximum. On the other hand,  $\alpha$  would increase and  $\beta$  decrease monotonically respectively with the decrease in the spacing of the electrodes due to the effects of the monopole image charges and the enhanced interactions with the dipoles. If non-uniformity in the distribution of surface charges occurs, the contribution of  $\beta$  would be greater than it was for uniform distribution of charges. Although it is possible to numerically determine the Coulombic force and the attractive forces due to image charges, it would be equally interesting, as a first step, to analyze qualitatively the contributions of each of these forces to the net electrostatic force of discrete particles.

## 2.2 Particle Ensemble Charging

### 2.2.1 Continuous Particulate Flows on Surfaces

Having discussed the various techniques to analyze the electrostatic charges on discrete particles in various instances, it is also essential to investigate the triboelectric charging phenomenon of a group of particles on continuous surfaces so as to gain deeper understanding of the interactions with these surfaces. The interactions during which charge is transferred across bodies can be in the form of sliding, rolling, bouncing or a mixture of these forms. Ireland (2010) carried out a series of experiments using irregularly shaped silica (~ 1 mm) on stainless steel surfaces. The relationship between contact time, velocity and mode of contact was evaluated.

A typical experimental setup (Fig. 2.12) would consist of a regulated funnel, a sliding trough made of polished stainless steel, and a Faraday cage at the end of the trough to record the charge gained by the particles. The trough can be tilted to different angles so as to control the particle velocities.



**Fig. 2.12:** An experimental setup to investigate electrostatic charging via continuous particulate flows (Ireland, 2010).

Assuming the charge transfer during the dynamic contact charging process follows the condenser model as illustrated in Fig. 2.4, the rate of charge transfer,  $dQ_c/dt_c$ , is derived from Eq. (2.4) and is expressed as (Ireland, 2010):

$$\frac{dQ_c}{dt_c} = \frac{1}{\tau_c} (A_c \sigma_{o,c} - Q_c)$$
(2.19)

Where,  $\tau_c$  (=  $R_oC_s$ ) is the residence time of continuous charging, and  $\sigma_{o,c}$  is the equilibrium charge density,  $C_s$  is the capacitance of the system,  $R_o$  is the equivalent circuit resistance,  $A_c$  is the contact area between particle and surface, and  $Q_c$  is the charge on the particle at contact time,  $t_c$ .

Integration of Eq. (2-19) would give the following expression from which the values of  $A_c$ ,  $\sigma_{o,c}$ , and  $\tau_c$  are assumed to be constant.

$$Q_{c} = A_{c}\sigma_{o,c} \left[ 1 - \exp\left(\frac{-t_{c}}{\tau_{c}}\right) \right]$$
(2.20)

However, from the experimental results (Ireland, 2010), it was observed that the measured charge did not follow an exponential relationship with contact time. This could mean that  $A_c$ ,  $\sigma_{o,c}$ , and / or  $\tau_c$  are not constants. Even though the contact time,  $t_c$ , can be determined from the particle velocity along the axis of the slide, and the velocity in turn affects the values of  $A_c$ ,  $\sigma_{o,c}$ , and  $\tau_c$ , it was noted that the velocity was not the only significant parameter that affects the charging process. In fact, it was

demonstrated that the contact area, A<sub>c</sub>, which is a function of the mode of contact, also greatly influences the charge accumulated. Ireland (2010) has proposed a model that considers the contribution of the contact area to the generated charge arising from various modes of contact. For instance, for pure sliding contact, the charge accumulated in a manner consistent with the condenser model. However, if the particle rolls on the surface, the contact surface area would be continuously changing and an orientation-averaged contact surface area would have to be used for charge calculations. Since the total surface area available for contact for rolling particles is greater than that for sliding particles, the ability to hold more charges for rolling particles would also be larger than sliding particles. For bouncing particles, a charge limiting mechanism due to separation discharge from gas breakdown at separations of  $\sim 1 \,\mu m$  is postulated. This resulted in a lower charge magnitude observed than it was predicted. Furthermore, saturation of charge would occur more readily if the surface and / or the particle were non-conducting. The model for the calculation of the accumulated charge would become increasingly complex if the particle number density increases and / or a range of particle sizes with random charging were involved. Nevertheless the experimental setup involving the slide and the Faraday cage as shown in Fig. 2.12 proved to be useful in investigating particulate flows on surfaces.

### 2.2.2 Charging of Powder Aerosols

Powders can be charged when they are dispersed into the air prior to transport and these particles can remain charged for a long time regardless of the conductivity of the particles (Zhang, 2012). One of the earlier methods to measure the surface charges of the powder aerosols was to incorporate an open-ended or flow through Faraday cage

to the air stream carrying the particles. An air stream Faraday cage such as the one shown in Fig. 2.13 directs compressed air flow through the cage at known velocity so as to separate a powder mixture, usually consisting of the smaller particles adhered onto the larger carrier particles, in the cage. The air would carry the powder mixture through a mesh at the other end and separate the smaller particles from the larger carriers. Schein and Cranch (1975) first used the cage to study the electrification behavior between insulating toner and carrier particles at incremental detachment. Later, Kulvanich and Stewart (1987) extended the concept to analyze the electrostatic charges on pharmaceutical carrier particles after the drug particles were detached from the carrier surfaces. The method was found to be useful in providing detailed information on the triboelectric properties of powder mixtures and hence in assessing the stability of the drug-carrier interactive system. However, a larger force would be required to detach highly charged smaller drug particles from the carrier particles, resulting in charge induction from the mechanical vibration of the mesh.



**Fig. 2.13:** A schematic diagram showing an air stream Faraday cage for measuring the electrostatic charges of powder aerosols (Kulvanich and Stewart, 1987).

By removing the mesh and enclosing a pharmaceutical dry powder inhaler (DPI) in a well shielded Faraday cage (Fig. 2.14), Chow and co-workers (2008) studied the dynamic charging of aerosolized lactose at different flow rates and relative humidity (RH) levels respectively. The dynamic charge was found to increase linearly with air flow rate and RH. The propensity of collisions between particles and inhaler wall increased with increasing frictional forces while at higher RH the amount of hydrated ions increased to facilitate charge transfer. Repeated use of the inhaler was also found to have significant influence on the charges acquired by the lactose particles. Karner and Urbanetz (2013), using the same setup by Chow's team, added that carrier fines, carrier particle sizes and the presence of active pharmaceutical ingredient (API) could significantly affect the charge acquired.



**Fig. 2.14:** An experimental setup by Chow and co-workers (2008) that enclosed the inhaler in a well-shielded Faraday cage for dynamic charging studies of lactose.

Murtomaa and co-workers (2003) demonstrated an alternative method of measuring the charge of aerosolized powders by placing an induction grid probe directly at the mouth of the inhaler (Fig. 2.15). As the particles passed through the grid, electrostatic charges were induced on the grid which were then measured by an electrometer connected to a computer. The earthed grids prevented the electric field from coupling with the induction grid. From the measured signals using the grid probe technique, the authors could observe opposing polarities resulting from the separation of the drug from the carrier particles. However, interpretation of the results should be handled with care since possible particle interactions with the grid could exchange and leave residual charges.



**Fig. 2.15:** An induction grid probe was placed near the mouth of the DPI to measure the charge from the aerosolized powders (Murtomaa et al., 2003).

To minimize interactions between the charge sensing device and the aerosolized particles, Gajewski (1989) attached a metal ring electrode on a dielectric pipe. Charges induced in the ring with a capacitance would create an electric potential proportional to the charges on the flowing particles. Noras (2006) showed in his setup (Fig. 2.16) that by measuring the induced electric potential of the ring,  $V_R$  with a non-contact vibrating capacitive probe (Noras, 2002) placed in close proximity to the ring, the charge on the particles,  $Q_{ind}$  could be approximated via the following equation:

$$Q_{ind} \approx 4\pi\varepsilon_0\varepsilon_r V_R \tag{2.21}$$



Where,  $\varepsilon_r$  is the relative dielectric permittivity of the pipe.

**Fig. 2.16:** Electrostatic charge of the aerosolized particles was measured via the noncontact vibrating capacitive probe placed near the copper tape that served as electrode (Noras, 2006).

The powders, either alumina or toner particles, were pneumatically transported from Faraday cup 1 with an air pump. Initial and final charges were recorded by the Faraday cups 1 and 2 respectively. Simultaneously, the electrostatic voltmeter that connects the non-contact vibrating capacitive probe recorded the potential change of the copper tape electrode over time as the particles flow through the dielectric pipe. The charge of the flowing particles was calculated from the integration of the potential change over time and was found to be in good agreement with that measured in the Faraday cup 2. Hence the non-contact vibrating capacitive probe can be used as a potential method without interfering with the aerosol charging process.

## 2.3 Influencing Factors

### 2.3.1 Particle Characteristics and Processes

Powders can often acquire charge through triboelectrification during processes such as sieving, pouring, micronization, pneumatic transfer and fluidization. The extent of charge gained for organic powders in various industrial powder handling operations is illustrated in Table 2.1.

**Table 2.1** Specific charge gained by organic powders during various powder handling operations (Colver, 1999).

Operation	Specific charge [C/kg]
Sieving	$10^{-11} - 10^{-9}$
Pouring	$10^{-9} - 10^{-7}$
Scroll feed transfer	$10^{-8} - 10^{-6}$
Grinding	$10^{-7} - 10^{-6}$
Micronizing	$10^{-7} - 10^{-4}$
Pneumatic transfer	$10^{-6} - 10^{-4}$
Fluidization	$10^{-6} - 10^{-5}$

Collisions between the powder particles and the walls during these processes can cause particle attrition and led to a distribution of particle shapes and sizes. As mentioned briefly in section 2.1.1, the level of charging for these particles could be very much dependent on the particle shape and size. Unger and co-workers (2004) found that there was an increase in the saturation charge for cubic NaCl particles than micron-sized spherical di ethyl hexyl sebacat (DEHS) particles apparently due to a local electric field enhancement. Fragmented or irregularly shaped granules that have faces formed with more shearing actions recorded higher measured charge variations (Yao and Wang, 2006; Moughrabiah et al., 2013). A reversal in charge polarity could also occur with change in particle morphology (Murtomaa et al., 2004). The type of motion (sliding, rolling or a combination) that these granules of various shapes adopt over the surfaces governs the different charge generation levels. Ireland (2012) suggested that if the particle roundness ratio is low (or highly flattened), the particles would just slide without rolling or tumbling. As the ratio exceeds a critical value and reaches unity, the whole of the particle surface is made available for contact charging and hence increases the limiting acquired charge. On the other hand, the dependency of electrostatic charge on particle size is met with controversies. The electrification of smaller particles was shown to be higher than that of the larger particles (Masuda and Iinoya, 1978) with Smeltzer and co-workers (1982), Ally and Klinzing (1985) attributing the observation to the higher particle number density and a subsequent increase in the particle to wall interactions. Rowley (2001) added that the relationship might become complicated if the particles were to adhere to the walls. In contrast, Marra Jr. et al. (2009) observed a weak dependence between particle size and charge using laboratory generated aerosol particles while Armour-Chélu and Woodhead (2002) did not find any dependence between particle size and charge using aluminium hydroxide particles in a pneumatic pipeline. Other particle surface characteristics such as roughness and crystallinity could play a significant role on the generated charge. For instance, Adi et al. (2008 a, b) reasoned that the decreased drug-carrier contact areas with corrugated spray dried carrier particles could have reduced cohesive forces while a higher concentration of asperities on coarse carriers would serve as potential high adhesion sites (Swaminathan and Kildsig, 2000). In addition, increasing the amorphous contents on carrier lactose particles would increase the generated charges with a higher charge variation (Murtomaa et al., 2002; 2004).

#### 2.3.2 Surfaces on Contact

The charge transfer behaviour between two surfaces in contact, as described in section 2.1.1, is believed to be affected by the differences in the surface work functions. The work function is defined as the amount of energy required to remove the weakest bound electron from its orbital to infinity (Bailey, 1984). Studies have shown that the polarity of the charge gained by contact with one surface could exhibit a reversal if the same powders were tribocharged with another surface (Carter *et al.*, 1992; Eilbeck *et al.*, 1999; Elajnaf *et al.*, 2006). For example, salbutamol sulphate, an active ingredient in dry powder inhalers, gained positive charge when in contact with walls of polypropylene and acetal while tests on other surfaces resulted in negative charges on the powder as shown in Fig. 2.17 (Elajnaf *et al.*, 2006). Based on the relative charge polarity and magnitude that depend on the type of surfaces in contact, one could obtain a triboelectric series as a reference that ranked materials with low work function (positive) at the top and high work function (negative) at the bottom (Table 2.2).



**Fig. 2.17:** Effect of surfaces on the charge gained with salbutamol sulphate at ambient laboratory conditions of 20 °C, 45 %RH (Elajnaf *et al.*, 2006).

**Table 2.2** A proposed triboelectric series for ipratropium bromide monohydrate, salbutamol sulphate, and alpha lactose monohydrate powders as well as various contact surfaces (Elajnaf *et al.*, 2006).

Material	Relative strengths in work function
Ipratropium bromide monohydrate Stainless steel Salbutamol sulphate Acetal Alpha lactose monohydrate (63 – 90 μm) Polypropylene	Increasing work function (Polarity of materials becomes more negative (-))

#### 2.3.3 Environmental Conditions

Besides particle characteristics, processes and surfaces on contact, the environmental conditions such as relative humidity and temperature are also important considerations that can affect the triboelectric charging properties of powders. Electrostatic charges generated on the surfaces of the powders at low humidity can generally be dissipated by increasing the relative humidity of the system (Elajnaf et al., 2007; Grosvenor and Staniforth, 1996; Nguyen and Nieh, 1989; Nomura et al., 2003). Moisture layers that are formed on the surfaces of the powders at relative humidity greater than 50% reduce the surface areas in contact and increase the surface electrical conductivity (Kwok and Chan, 2008; Zhu et al., 2008; Young et al., 2007). However, the relative humidity has negligible effects on the electrostatic charge dissipation if the powders were non-hygroscopic (Christie et al., 2009; Rowley and Mackin, 2003) and there could even be an increase in electrostatic charge generation with an increase in relative humidity if surface functional groups were present that facilitates charge distribution and transfer (Wiles et al., 2004; Yao et al., 2002). On the other hand, increasing the temperature could cause a decrease in charge generated (Greason, 2000) with reversal in polarity (Moughrabiah, 2013).

## Chapter 3

# **Parallel Plate Condenser on AFM**

### 3.1 Approach

To study the electrostatic force contributions during toner particle detachment in an electric field, Mizes (1994) modified the Atomic Force Microscope (AFM) cantilever holder so that as an electric field was applied on the AFM cantilever functionalized with a single particle, the deflection of which can be used to determine the quantity of charge on the particle surface. A transparent counter electrode Indium Tin Oxide (ITO) was fixed above the cantilever while a metallic substrate such as aluminium was positioned below the cantilever. The electric field was then generated by applying a bias voltage between the metallic substrate and the counter electrode. By capturing the particle loading curves on the substrate in the presence of an electric field, the dependence of the adhesion and attractive forces on the electric field can be measured.

However, the modified AFM cantilever holder with the ITO electrode proposed by Mizes (1994) did not allow for independent positioning of the cantilever so that the charge on the particle can be quantified. In this study, a further modification to the AFM was attempted by using a small parallel plate condenser that consists of ITO coated glass as electrodes which can be mounted independently on the AFM piezo stage (Fig. 3.1). The separation between the parallel plates is substantially larger than the particle attached to the cantilever and the position of the particle can be adjusted freely between the condenser electrodes. Force measurements

with the particle positioned in the middle of the condenser in a known electric field are used to estimate the particle net charge whereas force measurements with particle placed near to the bottom electrode are used to estimate the contributions from induced and image charges representative of the polarizability properties of the particle.



**Fig. 3.1:** The experimental setup is depicted in the schematics (a), and in the photograph showing the parallel plate condenser (enlarged) with Indium Tin Oxide (ITO) coated glass covers as electrodes (b). A bright laser dot seen in the photograph marks the position of the glass particle attached on the AFM cantilever which in turn is positioned between the electrodes.

## **3.2 The Parallel Plate Condenser**

The parallel plate condenser to be mounted onto the AFM piezo stage was tested with model dielectric glass beads (Polysciences, Inc, USA), 105 to 150  $\mu$ m, attached to the AFM cantilevers. The electrodes used in the condenser were conductive Indium Tin-Oxide (ITO) coated (one-side) glass covers purchased from SPI supplies, USA. In addition, experiments were also carried out by using trichloro(1H,1H,2H,2H-perfluoro-octyl)silane (97%, Sigma-Aldrich) to hydrophobize the glass particles and the cantilevers.

The parallel plate condenser was designed to have conductive ITO coated glass covers as the electrodes and the fabricated prototype is shown in the schematics in Fig. 3.1a and the photograph in Fig. 3.1b. Measuring 7 mm long, 4 mm wide and 0.13 to 0.17 mm thick, the ITO coated glass covers were inserted into the condenser so that the conductive surfaces faced each other with a gap of 1.5 mm for the positioning of the AFM cantilever. The function of the conductive ITO glass covers is to allow the deflection of the cantilever to be measured from laser reflected off the cantilever onto the AFM photodetector. The ITO glass covers were electrically connected to a DC voltage source (R4K-80, Matsusada Precision, Japan). An electric field was generated across the cantilever and attached particle by applying a potential difference across the ITO glass covers. Using the condenser mounted on the AFM piezo stage, the cantilever with the attached particle can be positioned between the ITO glass covers (Fig. 3.1b).

## **3.3 Particle Attachment**

Particles that were comparatively large with respect to the AFM cantilever were used for the colloidal probe in order to capture the electrostatic forces. The colloidal probe with the glass particle is shown in the optical microscopy image in Fig. 3.2. Prior to attachment, the glass bead particles (105 to 150  $\mu$ m) were first boiled in water and then in ethanol and subsequently washed in water, filtered and dried in vacuum. Clean single particles were attached to AFM tipless silicon cantilevers (CSC12, MikroMasch) using epoxy resin and then plasma-cleaned for 10 minutes prior to AFM measurements. The rectangular cantilevers used had nominal dimensions of 350  $\mu$ m in length, 35  $\mu$ m in width and 1  $\mu$ m in thickness. Correspondingly from the dimensions, the cantilever was calculated to have a surface area of 24,500  $\mu$ m<sup>2</sup> which is lesser than the particle surface area of 34,636 to 70,686  $\mu$ m<sup>2</sup>. In addition, considering that the particle is end-loading the cantilever, the relative contribution of the electrostatic force acting on the cantilever itself as compared to the bending of particle functionalized cantilever is expected to be small. This was verified by conducting reference measurements with bare cantilevers.

In order to examine the effects of surface conductivity, the glass particle loaded cantilever was hydrophobized by treatment with saturated trichloro(1H, 1H, 2H, 2H-perfluoro-octyl) silane vapor for 30 minutes. Glass covers treated in an identical manner exhibited water contact angles of ~  $108^{\circ}$ . A separate cantilever was hydrophobized as a reference before sticking a clean glass particle to it.



**Fig. 3.2:** Optical microscopic image showing the glass particle attached on the AFM cantilever.

### **3.4 Measurement Procedures**

The Nanoscope IV MultiMode (Veeco, USA) atomic force microscope (AFM) was used for all force measurements under ambient laboratory conditions (22  $^{\circ}$ C, 65% RH). A customized cantilever holder was used to provide sufficient clearance for the mounting of the small condenser on the piezo stage as shown in Fig. 3.1b. The stepmotor function of the MultiMode AFM was used to move the cantilever probe to a desired position, *d/D*, between the condenser electrodes (Fig. 3.1a).

At a fixed d/D position, the following procedures to measure the cantilever deflection vs. condenser applied voltage are described. By operating the MultiMode AFM in "Force Calibration" mode, the cantilever deflection was recorded during a "blank" approach-retraction Z scan cycle that was, in turn, synchronized with a known voltage ramp applied between the condenser electrodes. A scan size of 10 nm (d >> 10 nm in all cases) and a scan frequency of 0.1 Hz corresponding to 10 seconds in monitoring cantilever deflection were used. The scan cycle was synchronized with a linear voltage ramp of 80 Volts in 2 seconds with a specific polarity, e.g. negative on the bottom plate electrode and positive on the top plate electrode, following which the same linear voltage ramp of opposite polarity was applied and the cantilever deflections recorded. The dependence of the functionalized cantilever deflection on the voltage ramp time was found to be independent of the ramp time by increasing the ramp time to 20 seconds and measuring the cantilever deflection. This justifies the conversion of the deflection vs. time recorded to deflection vs. voltage by scaling the ramp time with the ramp voltage. An example of applied voltage vs. time and its corresponding deflection vs. time dependence were shown in Fig. 3.3 from which the force vs. applied voltage dependence can be determined.

Hooke's Law was used to calculate the force on the particle, *F* [N] from the cantilever deflection  $\Delta X$  [Volt]:

$$F = K_{\rm N} S \Delta X \tag{3.1}$$

where  $K_N$  is the cantilever spring constant [N/m], and *S* is the photodiode sensitivity [nm/Volt]. With the nominal spring constant of the cantilevers used being  $K_N = 0.03$  N/m, the exact value was determined using a modification of the frequency method that accounts for the particle loading position (Cleveland *et al.*, 1993; Vakarelski *et al.*, 2007).



**Fig. 3.3:** Applied voltage on the condenser electrode vs. time (a), and corresponding cantilever deflection vs. time (b).

The particle was discharged of any charges that could be present on its surface by leaving overnight in contact with the grounded bottom electrode. To charge the particle positively or negatively, the uncharged particle was brought into contact with the bottom electrode and a known voltage for a fixed duration, e.g. voltage of + 30 or -30 Volts for 120 seconds, was applied. The particle was then separated from the electrode and it was charged with the same polarity as the electrode. It was found that the particle did not lose its charge significantly as long as the experiment was

conducted within 20 minutes by measuring the deflection of the cantilever with applied voltage over a period of time.

## 3.5 Quantifying Electrostatic Charge

The capability of the parallel plate condenser on the AFM was evaluated by measuring the deflections of the glass particle loaded cantilever in the electric field. As the hydrophilicity or hydrophobicity of the colloidal probe could affect the electrostatic response, the deflection response of the cantilever with respect to the hydrophilicity or hydrophobicity of the probe was checked first. The probe was plasma cleaned before use which implied that both the particle and the silicon cantilever were hydrophilic (Donose *et al.*, 2006). The convention adopted was that positive force, F was directed toward the bottom electrode and for a positive voltage, V the bottom electrode was negatively charged. The forces were measured with the same particle probe regardless of whether the probe was uncharged, positively or negatively charged. Positive or negative charging was done by bringing the uncharged probe in contact with the bottom electrode and then a positive or negative potential of 30 volts for about 2 minutes was applied before separating the probe from the electrode.

Fig. 3.4a shows the force vs. voltage dependence for uncharged, positively and negatively charged particle placed in the middle of the condenser, or d/D = 0.5. The data showed a linear force vs. voltage dependence for the charged particle and close to zero force for the uncharged particle. This result is well expected as in a uniform electric field, the net contribution due to the induced charge is null and the image force contributions will be also null with an equal balance of forces from the image

charges in the bottom and top electrodes. As illustrated in Fig. 2.11a, the sole nonzero contribution is the Coulombic force acting on the particle net charge,  $F_{\rm C} = QE \sim V$ , so the force on the charged particle in the middle of the condenser increases linearly with the applied voltage.



Fig. 3.4: Force vs. applied voltage dependence for uncharged, positively and negatively charged 120  $\mu$ m hydrophilic glass particle (a) in the middle of the condenser, d/D = 0.5, and (b) near the bottom electrode, d/D = 0.1.

Fig. 3.4b shows the force vs. voltage dependence for the particle placed near the bottom electrode, or d / D = 0.1. In this case, the particle near to the electrode shows a more complex dependence from the interplay of forces due to net particle charge, induced and image charges as shown in Fig. 2.11b. The force on the uncharged particle is due to the image force component  $F_{Ipol}$ , of the induced charge, which is always attractive to the electrode. In accordance with Eq. (2.18), the experimentally measured force follows a parabolic dependence on the applied voltage, i.e.  $F_{\rm Ipol}$  ~  $E_a^2 \sim V^2$ . In the case of the charged particle, the interplay between the attractive image force and the Coulombic force that changes direction with the change in voltage polarity caused the observed transitions between repulsive and attractive regions. Since  $F_{\rm C} \sim V$  and  $F_{\rm Ipol} \sim V^2$ ,  $F_{\rm Ipol}$  component will become dominant for high values of V and this can be seen in the experimentally measured asymmetric parabolic dependence in the charged particle case. The exact solutions to the problem for the total electric force acting on a dielectric sphere near the bottom electrode are complicated by the fact that the image charges are in reverse changing the field around the particle. Related procedures for the numerical calculations of the total electrostatic force can be found elsewhere (Davis, 1969; Mizes, 1994).




**Fig. 3.5:** Force at V = +80 volts and V = -80 volts vs. particle position between the condenser electrodes d / D measured for 120 µm hydrophilic glass particle (a) uncharged, (b) negatively charged, and (c) Force on the negatively charged particle minus the force on the uncharged particle ((b) minus (a) data).

The effect of particle position on the force measurements was shown in Fig. 3.5a for the uncharged particle and Figure 3.5b for the negatively charged particle. The force acting on the particle with applied voltages of V = +80 volts and V = -80 volts vs. the particle position d / D are plotted in the graphs. In the case of the uncharged particle, the positive and negative applied voltages gave almost identical force values that were

directed towards the closer electrode at all particle positions. There is a gradual decrease in the force as the uncharged particle was moved away from the bottom electrode where the force was zero in the middle of the condenser. As for the charged particle, the magnitude of the force is observed to change with a change in voltage polarity, reflecting a reversal in the direction of the Coulombic force component. Due to the interplay between the polarized and image charges on the force acting on the particle, a full reversal in the direction of the force, i.e. purely Coulombic force, was noted only in the middle of the condenser.

In most of the previous AFM studies on the electrostatic force (Bunker *et al.*, 2007; Burnham *et al.*, 1992; Gady *et al.*, 1997, 1998; Matsuyama *et al.*, 2008; Mizes, 1994; Young *et al.*, 2004), the interactions between the particle probe and the substrate were measured at short separation distances (0 to 1000 nm) so the cantilever interaction with the substrate can be neglected. However, in our measurements, it was important to use a comparatively large particle with respect to the cantilever dimensions (Fig. 3.2). Measurements with bare cantilever positioned at the same distance from the substrate as the cantilever with particle probe at d / D = 0.1 confirmed that the force on the bare cantilever was less than 10% of the force acting on the particle loaded cantilever and even more insignificant at larger d / D values.

Another important consideration is the effect of the conductivity of the cantilever on the measurements. The silicon cantilevers used in the studies were non-conductive but it is suspected that water adsorbed on the surface can make the surface of the cantilever slightly conductive resulting in possible charge drainage from the probe (Mizes, 1994). This speculation is well supported from the strong dependence of the electrostatic interaction on the relative humidity (Bunker *et al.*, 2007; Young *et al.*, 2004). To evaluate the possibility of charge drainage, the force acting on a freshly charged particle probe positioned in the middle of the condenser was monitored. It was found that for the first half an hour the force of the particle fluctuated less than 10 % from its initial value. This indicates that within the time scale of the experimental measurements the cantilever can be considered as non-conductive. The cantilever and the particle surface conductivity effect were investigated with reference measurements using hydrophobized cantilever and particle probes.

Fig. 3.6a shows the force vs. voltage dependence measured in the middle of the condenser using a clean (hydrophilic) particle and hydrophobized cantilever and the data in Fig. 3.6b was obtained for the hydrophobized particle and cantilever. The range of the force measured with the clean particle and hydrophobized cantilever was similar to the range measured with the plasma cleaned particle and cantilever hence confirming the negligible effect of the surface conductivity of the cantilever due to water layer adsorption on the force measurements. On the other hand, forces measured with the hydrophobized particle were significantly smaller indicating that the hydrophobic layer and its related change of particle surface conductivity has substantially affected the contact charging capability of the particle. It also seemed that the particle has attained an inherent tendency to charge negatively rather than positively. At the same time, the force vs. voltage dependence of uncharged hydrophobized particle near the bottom electrode shown in Fig. 3.7 appeared to be similar to that for the case of the hydrophilic particle indicating that the polarization charging of the particle was unaffected by the hydrophobization.

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**Fig. 3.6:** Force vs. applied voltage dependence measured with uncharged, positively and negatively charged particle placed in the middle of the condenser, d / D = 0.5, for the case of (a) hydrophilic glass particle attached on a hydrophobized cantilever, and (b) hydrophobized glass particle on a hydrophobized cantilever.



Fig. 3.7: Force vs. applied voltage dependence measured with uncharged, hydrophobized glass particle placed near the bottom electrode, d/D = 0.1.

Analyses of the data in Fig. 3.4 and 3.5 showed that the force on the uncharged particle is due to the field induced polarized and image charges, the Coulombic force on the charged particle in the middle of the condenser is due to the particle net charge, and at other particle positions, a combination of the forces acts on the particle. It should be noted that the image force due to the particle net charge, acting between the particle and the near conducting surface,  $F_{\text{Inet}}$  was not registered, as the cantilever deflection at zero applied voltage was taken as the baseline for all measurements. The net force measured is then the combination of  $F_{\text{C}}$  and  $F_{\text{Ipol}}$  only, that is, for any given position and applied voltage,  $F = F_{\text{C}} + F_{\text{Ipol}}$ . In Fig. 3.5c we plotted the net force by subtracting the force data of the uncharged particle in Figure 3.5a from the force data of the charged particle in Figure 3.5b. This resulted in almost constant force values at all particle positions which are equal to the contributions of the Coulombic force on

the charged particle in the middle of the condenser. Therefore, for any particle position, the Coulombic force component,  $F_{\rm C}$  (+*V*) and the polarization induced image force component,  $F_{\rm Ipol}$  (+*V*) can be estimated by measuring the forces at the same potential with opposite polarities, F (+*V*) and F (-*V*):

$$F_{\rm C}(+V) = (F(+V) - F(-V)) / 2 \tag{3.2}$$

$$F_{\text{Ipol}}(+V) = (F(+V) + F(-V)) / 2$$
(3.3)

The slightly larger  $F_{\rm C}$  values estimated for particle close to the electrode (Fig. 3.4 and Fig. 3.5c) would probably be due to the slightly stronger electric field near the electrode as a consequence of the condenser edge effect being more pronounced in the middle of the condenser. If condenser edge effects were to be ignored, the electric field inside the condenser equals -V/D, and the particle net charge can be estimated as:

$$Q = -F_{\rm C} D / V \tag{3.4}$$

From the force data of the charged particle shown in Figure 3.5c,  $Q = -1.87 \times 10^{-13}$  C and the charge density is  $4 \times 10^{-6}$  C/m<sup>2</sup>. If the explicit form of Eq. (2.18) is known, the estimated value of  $F_{\text{Ipol}}$  can be used to quantify the polarizability of the particle.

As explained above in the measurements, the image force due to the particle net charge, acting between the particle and the near conducting surface,  $F_{\text{Inet}}$  was not registered directly. Nevertheless the values of  $F_{\text{Inet}}$  near the conducting plate could be found using the estimated Q value as:

$$F_{\rm Inet} = Q^2 / (16\pi\epsilon_0 d^2)$$
(3.5)

Eq. (3.5) is indeed the same as Eq. (2.17) by taking  $\beta = -1$  for the case of infinite conducting plates. At the closest separation of d/D = 0.1,  $F_{\text{Inet}}$  is estimated to be equal to 3.5 nN. Because of the inverse square dependence on the separation d/D, the image force contribution will decrease rapidly with an increase in *d*. The reverse is true with decreasing *d*.

#### 3.6 Concluding Remarks

A parallel plate condenser consisting of transparent ITO glass slides as electrodes fitted onto the atomic force microscope stage was developed and tested with a single glass particle of diameter between 105 to 150  $\mu$ m. Unlike Mizes' (1994) single electrode configuration to investigate the detachment of charged toner particle from a metal substrate, the condenser in this study allowed the particle to be maneuvered freely between the electrodes and the forces on the particle can be determined from the cantilever deflection at various positions in the presence of an applied electric field. A procedure was formulated that examined the contributions such as the Coulombic and image polarization forces to the net electrostatic force and subsequently, the charge of the particle on the cantilever can be quantified. In addition, the experimental results in this study were recently shown to be in good agreement with the approximate closed form solutions to the particle detachment developed by Kemp and Whitney (2013).

# Chapter 4

# **Development of Nonintrusive Bulk Technique**

#### 4.1 Approach

As described in Section 1.5, inconsistent results with large coefficients of variation are often obtained from using the Faraday cage to measure the bulk powder electrostatic charge. The intrusive nature of the Faraday cage manifests itself in particles adhering to the walls of the cup during measurements that reduce sufficient contacts between the particles and the wall leading to lesser amount of charge recorded. On the other hand, a vibrating capacitive probe connected to an electrostatic voltmeter when placed in close proximity to the charged surface, the surface potential of which can be monitored in real time without interaction with the system of interest. The probe has been used with much success in studying the charge carrier transport phenomenon in corona charged highly resistive solids or films (Carter *et al.*, 1998; Grosvenor and Staniforth, 1996).

When the probe was placed close to the spacer wall of dry powder inhaler before and after aerosolisation, Kwok and co-workers (2006) found that coating the spacer wall with detergent resulted in a better aerosol performance and less particle to wall adhesion from the lower surface potential of the detergent coated wall. Noras (2006) demonstrated that the charge of flowing particles in a dielectric pipe can be calculated from the surface potential measured by the probe on the external surface using a mathematical model developed by Gajewski (1989) and the calculated values were later verified with a Faraday cage in the same experimental setup. In this study, the

feasibility of using the vibrating capacitive probe in a setup involving a hang down wire and a sample pan to measure the surface potential of triboelectrically charged loose bulk powders was investigated. The particle size effect on the triboelectrification of pharmaceutically relevant powders such as alpha lactose monohydrate and adipic acid through manual agitation on acetal (polyoxymethylene) surfaces was examined and the findings of which will put forward the vibrating capacitive probe as a potential addition in analytical and powder processing equipment whereby non-intrusive and real-time electrostatic monitoring is desirable.

# 4.2 Materials, Processing and Characterizations

The capability of the vibrating capacitive probe was first demonstrated in detecting the triboelectric charge in non-agitated and agitated sample powders to various extents using alpha lactose monohydrate (ALM-1), which was supplied by a major pharmaceutical company based in UK. The probe was then used to examine the particle size effects on the triboelectric charging properties of adipic acid (AA) and alpha lactose monohydrate (ALM-2) purchased from Sigma Aldrich. The AA and ALM powders were both pharmaceutical excipients used as an acidulent in effervescent tablets (Chow *et al.*, 1984) as carriers for active ingredient drug particles in inhalation therapy respectively (Kærger, *et al.*, 2006).

The powder samples were passed through a series of mechanical sieves on a sonic sifter (Model L3P, Sonic Sifter Separator, USA) to obtain various particle size fractions. The sonic amplitude was set at "6" for duration of 2 min in sift/pulse mode. Sieve fractions  $250 - 500 \mu m$ ,  $212 - 250 \mu m$ , and  $106 - 125 \mu m$  were selected for this

study as the quantity retrieved was found to be sufficient for electrostatic and other characterizations.

There is a need to compare the various degrees with which the powders were triboelectrically charged on a similar basis. One basis is by normalizing the measured charge with the mass of powders added. Another basis would be to calculate the total surface area of the powder particles in contact with the charging surface. The total contact surface area can be approximated from obtaining the specific surface areas of the powder samples using the multipoint BET surface area analyser (ASAP<sup>®</sup> 2420, Micromeritics, USA). Prior to analysis, the powder samples were degassed under liquid nitrogen at 25 °C for 16 hours.

The laser diffraction method (Mastersizer MS-2000, Malvern, UK) was used to measure the particle size distributions of the powders. The samples were dispersed dry in a sample plate vibrating at 50% intensity with a dispersing pressure of 3.5 bar. Particle morphology was captured using a high resolution scanning electron microscope (SEM JSM-6700F, JEOL, Japan) at an accelerating voltage of 2 kV with the powder samples sputtered with gold for 2 min using the sputter coater (Sputter Coater 208HR, Cressington, UK) for the analysis.

# 4.3 Vibrating Capacitive Probe Setup

The configuration of the vibrating capacitive probe is such that it consists of a voltage sensitive electrode with a surface oriented towards an aperture and vibrated perpendicularly to the plane of the aperture (Williams and Hare, 1974). The probe is positioned in close proximity from the test surface and the surface potential of which

is the voltage applied to the vibrating probe when the current is zero (Noras, 2002). Since the probe nullifies the electric field between the test surface and the probe (Llovera *et al.*, 2009), it has to be positioned within certain limits from the surface so as to measure accurately the true voltage on the surface without external electrical influence. The deviation of the surface potential from the true voltage applied on the test surface as a function of probe to surface distance was verified by using a brass surface connected to a DC voltage regulator (R4K-80, Matsusada Precision, Japan). A commercially available vibrating capacitive probe connected to an electrostatic voltmeter (Model 347, Trek Inc., USA) was positioned at varying distances from the brass surface to record the potential supplied.

The experimental setup in Fig. 4.1 was devised to include a hang-down pan on which the electrostatic behaviours of triboelectrically charged pharmaceutical powders at controlled relative humidity and temperature can be monitored using the non-contact vibrating capacitive probe. The hang-down pan mode was adopted as it served as a sample vessel that is connected to a sensitive microbalance, such as in the gravimetric vapour sorption analyser, and the instrument measures accurately mass changes of solid samples during sorption and desorption cycles with humidity. The measurements can be affected significantly due to the buildup of static charges in the sample (Kim *et al.*, 2008). The setup proposed in this study could thus have the potential in incorporating the probe in the instrument for powder electrostatic studies. As shown in Fig. 4.1, the supporting legs of the aluminium sample pan on the grounded hang-down wire were made of highly insulating polyvinylidene fluoride (PVDF) to prevent quick discharge of any electrostatic charges so that charges induced on the sample pan by the powders can be recorded.



**Fig. 4.1:** Experimental setup (25 °C, 40 %RH) on grounded stainless steel stand (e) showing the vibrating capacitive probe (c) connected to the electrostatic voltmeter (d) and placed within 3 mm from the base of the aluminium sample pan (b) hung from the wire (a).

Acetal or polyoxymethylene bottles of 2 ml capacity as well as the sample pan were first washed with water, then ethanol and dried with compressed air before each measurement. Grounding of the aluminium sample pan was done by tapping it briefly with an earthed wire and then zero-ing the electrostatic voltmeter against the empty metal pan. The surface potential of the empty pan was monitored for about 2 hours and was found to be within 2 V. Approximately 50 mg of powder samples were weighed in the bottles and stored overnight at 25 °C and 40 %RH. To charge up the powders, the samples were agitated by shaking the bottles manually at a rate of 120 to 240 per minute for duration of 1 minute. Non-agitated powders in the acetal bottles were also sampled to verify the contributions of pouring on the surface potential

measured. Care was taken in dispensing the powders in a reproducible manner using a stainless steel spatula onto the pan so that not any part of the spatula touched the pan or the legs of the pan, and scrapping of the charged powders from the acetal bottles was avoided. As a further precaution, the charged powders were carefully poured onto the center of the pan to minimise capacitance coupling effects. Charges were induced on the underside of the loaded pan and the surface potential of which was immediately captured using the vibrating capacitive probe and a data logging software in the 24-bit data acquisition system (QuantumX MX840A, HBM, Germany) that was connected to the electrostatic voltmeter. It was important to place the probe within a certain distance from the base of the pan as mentioned earlier so that the induced surface potential can be closely followed and is representative of the charges on the particles. The total surface area of the loaded powders was calculated by multiplying the mass of powders in pan,  $m_p$ , and the BET specific surface area, A<sub>S</sub>. The initial surface specific potential or chargeability,  $V_o$ , of the powders  $[kV/m^2]$  immediately after manual agitation was calculated by normalizing the initial surface potential, v, over the total surface area of the loaded powders (Eq. (4.1)). All surface potential measurements (n = 2 to 6) were performed in a metallic walk-in chamber which provided a controlled environment at a temperature of 25 °C and relative humidity of 40 %. The chamber also acted as a shield against any external electrical field influences.

$$V_o = \frac{v}{m_p \times A_s} \tag{4.1}$$

## 4.4 Faraday Cage Measurements

The relative magnitudes and polarities of the initial chargeabilities of triboelectrically charged AA and ALM sieved powders measured by the vibrating capacitive probe were verified using the Faraday cage method of electrostatic charge measurements. The Faraday cage and the acetal bottles were cleaned using the method described in the earlier section and the electrometer is given a virtual ground before each measurement. After agitating the powders manually in the bottles, the triboelectrically charged powders were poured in a reproducible way into the shielded Faraday cage (Model TR8031, Advantest, Japan) that was in turn connected to an electrometer (Model 6517A, Keithley, USA). The specific charge, Q<sub>p</sub>, of the powders [nC/g] was calculated by normalizing the charge, q, recorded over the mass of powders, m<sub>p</sub>, poured.

$$Q_p = \frac{q}{m_p} \tag{4.2}$$

During agitation of the particles in the acetal bottles, the adhesion of the particles to the inner walls of the bottles could have a significant effect on the charges acquired on the sample powders. To determine the particle-to-wall adhesion, the difference in the masses of the powder in the bottles before pouring,  $w_1$ , and after pouring,  $w_2$ , was expressed as a percentage of the total mass of powder loaded in the bottles,  $w_0$ .

$$\frac{w}{w_o}\% = \frac{w_1 - w_2}{w_o}$$
(4.3)

#### 4.5 Null Current Surface Potential

As mentioned earlier in Section 4.3, a voltage sensitive electrode in the vibrating capacitive probe is made to vibrate in a direction transverse to the surface oriented to the aperture. Its vibrational amplitude is proportional to the test surface potential. The operational principle that determines the surface potential that the probe is measuring starts from the basic equation that defines capacitance (Noras, 2002):

$$C_e = \frac{Q_e}{V_c} \tag{4.4}$$

where,  $C_e$  is the capacitance,  $Q_e$  is the electric charge accumulated by the capacitive probe, and  $V_c$  is the voltage difference between the electrode of the capacitor and test surface.

With the surface of the probe positioned parallel to the test surface as shown in Fig. 4.1, the capacitance is created between the probe surface and the test surface and a potential difference exists between the two surfaces. As the probe vibrates perpendicularly to the test surface, a specific amount of charge,  $dQ_e$ , is taken away or delivered to the probe surface during time interval,  $dt_e$ , such that the potential difference,  $V_c$ , remains constant. The current,  $I_e$  (=  $dQ_e/dt_e$ ), is related to the potential difference and the sinusoidal vertical displacement, y, of the probe with time,  $t_e$ , via the following equations.

$$I_e = V_c \frac{dC_e}{dt_e} \tag{4.5}$$

$$C_e = \frac{\varepsilon_m \varepsilon_o A_e}{y} \tag{4.6}$$

$$y = y_o + y_1 \sin(\omega_e t_e) \tag{4.7}$$

where,  $\varepsilon_m$ ,  $\varepsilon_o$  are the relative electric permittivity of the material between the probe surface and test surface, and electric permittivity of vacuum respectively. A<sub>e</sub> is the surface area of the probe. y<sub>o</sub> and y<sub>1</sub> are the initial vertical displacement and displacement at time, t<sub>e</sub>, of the probe surface from the test surface respectively.  $\omega_e$  is the circular frequency of vibrations.

The current can thus be written in the following form:

$$I_{e} = -V_{c}\varepsilon_{m}\varepsilon_{o}A_{e}\frac{y_{1}\omega_{e}\cos(\omega_{e}t_{e})}{\left\{y_{o} + y_{1}\sin(\omega_{e}t_{e})\right\}^{2}}$$
(4.8)

As mentioned earlier, the potential difference  $V_c$  is between the potentials on the electrode and the test surface. In order to obtain the test surface potential, the potential on the electrode has to be made equal to the test surface potential. This is done by adjusting the voltage of the electrode in the probe such that, according to Eq. (4.8), the current detected is zero or nullified. The surface potential at null current detected is hence the test surface potential.

#### 4.6 Verification Studies

The ability of the vibrating capacitive probe to measure accurately the surface potential was verified using the experimental setup in Fig. 4.1 with voltages of 5 and 80 V and voltage ramp rates of 2.5 and 40 V/s supplied by a DC voltage regulator respectively. Prior to measurements, the probe was referenced to a grounded metal plate and the voltmeter was correspondingly set to zero volts. Fig. 4.2 shows an

example result with 80 V supply voltage and the surface potential measured by the probe. The applied voltage was followed by an oscilloscope as the voltage was ramped from 0 to 80 V. As the voltage was ramped up or down, the measured surface potential followed correspondingly at the same ramp rate. Furthermore, there was good agreement to within 1 V between the applied voltage and observed surface potential when the voltage was held at 80 V.



**Fig. 4.2:** Example plot of a surface potential verification test with applied voltage of 80 V and a ramp rate of 40 V/s. Solid line represents the voltage measured by the probe while dotted line represents the voltage applied.

The positioning of the probe from the test surface was also very important as it should be within a certain distance from the surface in order to capture the true surface potential that is not affected by stray electric fields (Noras, 2002). In order to determine the limits in positioning the probe, the measured surface potential was investigated at varying probe to surface distances and compared it with the applied voltage of 80 V (Fig. 4.3). It was found that the measured surface potential was within 6% from the applied voltage at separation distances up to 5 mm (+/- 0.5 mm) and started to deviate significantly, from 8 to 38%, beyond 10 mm. For true representations of the surface potential, subsequent experiments were conducted with the probe to surface separation within 3 mm.



**Fig. 4.3:** Effect of probe to surface distance on the observed surface potential with a supply voltage of 80 V.

Charge transfer during triboelectrification occurs mainly due to the difference in the effective work functions between the particles and the walls of the container (Matsusaka *et al.*, 2010). Charges generated during the process can also be dissipated to the surroundings and the resultant charge measured on the particle surfaces is hence due to the difference between charge generation and dissipation. As the intensity of particle to wall collisions increases, the frequency with which the particles charges upon contact with the wall increases while the contact interval between successive

collisions reduces with subsequent decrease in the charge dissipated (Zhu *et al.*, 2007). As a result, the charges acquired on the particle surfaces increased with an increase in the agitation intensity. The effect of agitation intensity on the charge acquired was demonstrated using the vibrating capacitive probe setup and alpha lactose monohydrate (ALM-1) supplied by pharmaceutical company, and the results were shown in Fig. 4.4. ALM-1 charged negatively when the powders were agitated manually in the acetal bottle and the mass specific surface potential increased accordingly when the agitation intensity (defined as number of shakes per minute) increased. Saturation of charges was apparent at 420 to 480 shakes per minute with a 3 to 7% increase as compared to a 5-fold increase between 60 to 120 shakes per minute. The mass specific surface potential of the non-agitated ALM-1 was, in turn, 5 times less than agitated ALM-1 at 60 shakes per minute (data not shown). Subsequent studies with AA and ALM-2 were conducted at 120 and 240 shakes per minute respectively.



**Fig. 4.4:** Effect of agitation intensity (no. of shakes per minute) on the mass specific surface potential of ALM-1 powders.

# 4.7 Particle Size Effects with Faraday Cage Comparison

Next, the capability of the vibrating capacitive probe was demonstrated by analysing the effects of particle size on the chargeability of the AA and ALM-2 particles on acetal surfaces at controlled temperature of 25 °C and relative humidity of 40%, and then comparing the measurements with those obtained using the Faraday cage. The particles were sieved in various fractions, 106 - 125, 212 - 250, and  $250 - 500 \mu m$ , and were allowed to dissipate charge overnight at the controlled environmental conditions as mentioned. As ALM particles were found to be more difficult to acquire charge, they were agitated at 240 shakes per minute instead of 120 shakes per minute.

From the results shown in Table 4.1, it was observed that the AA particles charged negatively while ALM-2 particles charged positively. Different grades of lactose can charge differently in terms of magnitude and polarity and hence it was not surprising that ALM-1 and ALM-2 particles had opposing polarities (Hickey *et al.*, 2007; Pilcer *et al.*, 2012; Telko *et al.*, 2007). In addition, the absolute magnitude of the charge / surface potential for ALM-2 particles appeared to be lower than that of the AA particles. It is difficult to relate particle size to specific surface areas in this study as primarily the particles were not spherical non-agglomerates and furthermore, the specific surface areas obtained for each type of sample (AA and ALM) were of the same order of magnitude within experimental errors. However, as the potential measured by the vibrating capacitive probe is essentially dependent on the test surface, the surface specific potential could better illustrate the dependence of the

chargeability on the particle size than mass specific potential. Nevertheless, both mass specific and surface specific potential values were given here as comparisons. Conventional Faraday cage measurements were also carried out to confirm the trends observed with the probe.

**Table 4.1** A comparison between the measurements (n = 2 to 6) made using the vibrating capacitive probe and the Faraday cage after triboelectrically charging AA and ALM-2 at various sieve fractions on acetal surfaces (T =  $25 \,^{\circ}$ C, RH = 40%).

Sample	Specific surface area [m²/g]	Vibrating capacitive probe, surface potential		Faraday cage,	Particle-to- wall
		Mass specific, V <sub>m</sub> [kV/g]	Surface specific, V <sub>o</sub> [kV/m <sup>2</sup> ]	specific charge, Q [nC/g]	adhesion, w/wo [%]
AA	0.655	-24.4 (16.4)	-37.2 (16.5)	-17.9 (35.6)	76.2 (7.45)
(106 – 125 µm)					
AA	0.660	-55.4 (27.5)	-83.9 (27.5)	-62.8 (1.94)	46.5 (6.70)
(212 – 250 μm)					
AA	0.722	-87.6 (9.39)	-121.3 (9.39)	-74.3 (2.93)	11.2 (3.57)
(250 – 500 μm)					
ALM-2	0.274	3.99 (4.70)	14.6 (4.65)	2.37 (11.7)	7.11 (6.05)
(106 – 125 μm)					
ALM-2	0 377	3 50 (12.9)	9 31 (12 9)	1 79 (6 73)	2 19 (56 2)
(212 – 250 µm)		5.50 (12.7)	<i>(12.)</i>		2.17 (00.2)
ALM-2	0.364	2.67 (32.7)	7.33 (32.7)	1.08 (62.9)	11.0 (29.1)
(250 – 500 µm)					

Note: ALM-2 was agitated at 240 shakes per minute instead of 120 shakes per minute. Also shown are the specific surface areas and particle-to-wall adhesions. Coefficients of variation are in parentheses.

There were two contrasting effects particle size had on the chargeability of AA and ALM-2 particles. It is apparent in Table 4.1 that an increase in the sieve size fractions

of the AA particles led to an increase in the absolute magnitude of the surface potential. On the other hand, an increase in the sieve size fractions of the ALM-2 particles reduced their chargeabilities. Both these effects were also confirmed by the Faraday cage measurements. The postulates for the particle size effects are discussed in the subsequent paragraphs.

For the AA particles, Zhu and co-workers (2007) also noted, using the Faraday cage, that after triboelectrically charging the AA powders during turbula mixing in stainless steel containers, the specific charge increased with particle size. They attributed the cause to particle adhesion to the stainless steel walls during the mixing. Smeltzer *et al.* (1982) pointed out that the increased number of particle to wall collisions led to a higher generated current on the pipe walls. The number of successful collisions with the acetal walls increased as the particle to wall adhesion reduced for larger particle size as seen in the drop from 76% to 11% of the total mass of particles that was adhered to the walls (Table 4.1), hence resulting in a higher surface specific potential observed for AA particles. Particle to adhered particle collisions would imply very minimal charge transfer between surfaces since the effective surface work functions for the particles were similar if not identical.

Conversely, the reduction in the chargeability of ALM-2 as the particle size increased did not see any trend in the particle to wall adhesion with respect to the particle size (Table 4.1). On closer examination of the morphologies of both AA and ALM-2 in their respective sieve fractions, fine particles of ALM-2 existed in the larger sieve fractions (212 - 250 and  $250 - 500 \mu$ m) but not in any of the sieve fractions of AA particles (Fig. 4.5). The charge reducing effect of fines (< 10  $\mu$ m) on the coarser

crystalline lactose has been previously reported by Bennet *et al.* (1999). However, Bennet's group attributed the diminished charge to that of increasing particle adhesion to the stainless steel cyclone charger walls which there was no significant particle adhesion to the acetal walls in this study and hence, a different charging mechanism might be present.



**Fig. 4.5:** SEM micrographs of adipic acid (AA) particles [(a), (c), and (e)] and alpha lactose monohydrate (ALM-2) particles [(b), (d) and (f)] of sieve fractions 106 - 125 µm, 212 - 250 µm, and 250 - 500 µm respectively.

The ALM-2 particle size distribution shown in Fig. 4.6 revealed the increase in the amount of particles less than 20  $\mu$ m and a shift in the primary peak from 83 to 53  $\mu$ m for the sieve fractions 212 - 250 and 250 - 500 µm. Moreover, the particle size distributions for the sieve fractions 212 - 250 and  $250 - 500 \mu m$  also appeared to be very similar which could be attributed to the inability of the laser diffraction method to precisely distinguish between successive sieve fractions of the less than spherical ALM-2 particles. The presence of fines in the larger sieve fractions of the ALM-2 particles could be partly due to the inability of the fines to pass through the blocked apertures during mechanical sieving. Even though Singh and Hearn (1985) pointed out that broad particle size distributions could imply bipolar charging in the powder system, it was found that bipolar charging seemed remote for the ALM-2 particles as a separate study revealed that fine particles less than 38 µm sieve fraction were also positively charged to the same extent as particles between 106 and 125 µm. Hence there might be a possibility that the fine particles with lower densities and higher mobilities could have slid in easily between the larger particles and the acetal walls during the agitation process. This would have prevented effective charge transfer between the larger particles and the walls hence resulting in a reduced surface specific potential.



**Fig. 4.6:** Particle size distributions of alpha lactose monohydrate (ALM-2) particles in various sieve fractions.

# 4.8 Concluding Remarks

A nonintrusive vibrating capacitive probe was used successfully to analyze the static triboelectric chargeability of pharmaceutically relevant bulk powders such as adipic acid and alpha lactose monohydrate under controlled environmental conditions. Prior to the analyses, the probe was verified with standard voltages and the limits of positioning the probe to test surface were identified. The surface potential results obtained by the probe on the manually agitated powders with acetal surfaces were in good agreement with the results from the Faraday cage measurements. The particle size was found to have a significant effect on the triboelectric chargeability of the powders with particle-to-wall adhesion of fines and the interference of the larger sieve fractions for effective charge transfer between particles and wall being the two possible mechanisms to the observed trends.

# Dynamic Charging and Impaction Behaviours of Aerosolized Powders

# 5.1 Approach

The preceding chapter has demonstrated the nonintrusive vibrating capacitive probe in measuring the static surface potential of the manually agitated bulk powders. In this chapter, the application of the probe is extended to investigating the dynamic charging process of aerosolized pharmaceutically relevant powders. Noras (2006), as discussed in Chapter 2, has already shown that the probe has potential in observing the electrostatic charging of aerosolized particles and the surface potential can be correlated to the amount of charge gained in the process. This is particularly useful in studying the electrostatic contributions to the de-agglomeration behaviour in dry powder inhalers (DPI) whereby the nonintrusive nature of the probe can minimize disturbances to the system it is measuring.

The extent of the electrostatic contributions on the cohesive forces holding the particles together and preventing its de-agglomeration depended on particle surface properties such as particle size, surface roughness, morphology and surface functionalities (Adi *et al.*, 2008a; Carvajal, 2008; Rowley, 2001; Shur *et al.*, 2008) as well as environmental conditions (Greason, 2000; Podczeck *et al.*, 1996; Rowley and Mackin, 2003). The surface roughness of the DPI particles, in particular, has been significant in determining the aerosol performance (Chew and Chan, 2001; Ganderton,

1992; Podczeck, 1998). Adi and co-workers (2008b) postulated that corrugated spray dried bovine serum albumin (BSA) particles would have a much reduced drug-carrier contact area than smooth BSA particles, thus reducing the cohesiveness of the particles and resulting in higher fine particle fractions upon dispersion. On the other hand, Swaminathan and Kildsig (2000) argued that the distribution of surface asperities with higher surface free energies on coarse carriers could enhance the cohesiveness between the particles. A similar controversy for moisture present on the surface is that it could either enhance the dissipation of charges via improved conductivity (Elajnaf *et al.*, 2007; Grosvenor and Staniforth, 1996; Kwok and Chan, 2008; Nomura *et al.*, 2003) or an increase in electrostatic charges generated due to surface groups providing conduits for charge accumulation (Boschung and Glor, 1980; Wiles *et al.*, 2004; Yao *et al.*, 2002).

In consideration of the possible effects of the particle surface roughness on the electrostatic contributions to the subsequent de-agglomeration of the DPI particles, a combinatorial technique of electrostatic monitoring using the vibrating capacitive probe and visualization of the subsequent impaction behaviour using the high speed camera is adopted with an impaction tube setup simulating the throat (Adi *et al.*, 2010). Understanding the interplay between particle surface roughness, moisture adsorption and electrostatic forces with subsequent de-agglomeration of DPI particles upon impaction would be useful in the design of inhaler formulations.

# 5.2 Materials and Characterizations

Mannitol (Pearlitol<sup>®</sup> 160C, Roquette, France) particles commonly used in dry powder inhalers (DPI) were selected for the experiments. The particle surface roughness was

varied via spray drying aqueous solutions through a 0.7 mm two-fluid pneumatic nozzle in a Büchi B-290 mini spray dryer (Büchi Labortechnik AG, Switzerland). The feed concentrations and parameters for spray drying were shown in Table 5.1.

Propossing Paramotors	Mannitol Particles			
Frocessing Farameters —	Rough	Smooth		
Feed Concentration [w/v%]	10	10		
Feed Rate [ml/min]	2.2	2.1		
Atomizing Rate [Nl/min]	670	357		
Inlet Temperature [°C]	145	170		
Outlet Temperature [°C]	71	82		
Aspirator Rate [%]	90	60		

**Table 5.1** Spray drying conditions to produce rough and smooth mannitol particles.

Agglomeration of the spray dried mannitol was done by setting them on a roller (BTR10-12V, Ratek Instruments, Australia) for 10 minutes at 40 rpm in stainless steel bottles and passed through a series of sieves in a separator (L3P Sonic Sift Separator, USA) at amplitude of "6" for 5 minutes in sift mode. The sieve fraction of 212 to 300  $\mu$ m was chosen for the impaction studies as the amount of powders left on the sieve was sufficient for repeats. Any electrostatic charges were dissipated prior to impaction tests by keeping the sieved agglomerates in the stainless steel bottles in vacuum overnight at 25 °C.

A high resolution scanning electron microscope (SEM JSM-6700F, JEOL, Japan) was used to image the surfaces of the spray dried agglomerates at an accelerating voltage of 2kV. The agglomerates were sputter coated with gold (Sputter Coater 208HR, Cressington, UK) for 2 minutes before imaging. Differences in the surface roughness could be identified from the images and verified by defining a ratio,  $f_R$ , of the BET surface area ( $A_s$ ) to the geometrical surface area ( $A_g$ ) of a single particle (Ono-Ogasawara and Kohyama, 1999). In order to measure the particle size, the powder samples were dispersed dry in a sample plate vibrating at 50% intensity with a dispersing pressure at 3.5 bars and subsequently sampled via the laser diffraction method (Mastersizer MS 2000, Malvern, UK).

Differences in the surface roughness of the spray dried samples could likely affect the specific surface areas. The multipoint BET surface area analyser (ASAP<sup>®</sup> 2420, Micromeritics, USA) was used particularly to evaluate differences in the specific surface areas. The powder samples were degassed under liquid nitrogen for 16 h at 25 °C prior to analyses.

Moisture that is adsorbed on the powder surfaces could affect the impaction and electrostatic behaviours. The DVS Advantage 1 (Surface Measurement Systems, UK) can quantify and compare the extents of moisture sorption and desorption due to surface roughness differences via gravimetric vapour sorption. The relative humidity from 0 to 90% in steps of 10% at 25 °C was varied and changes in mass of the sample during sorption / desorption were captured. The system has reached equilibrium at a particular relative humidity level when the percentage rate of mass change, dm%/dt, remains at 0.002% / min or less within an interval of 5 min. Sample masses were kept between 20 and 25 mg for all gravimetric vapour sorption measurements.

The inverse gas chromatography technique (iGC, Surface Measurement Systems, UK) is employed to evaluate differences in dispersive surface energy. Samples were packed into 4 mm bore diameter silanized glass columns and glass wool was used to

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cap the ends. The carrier gas was helium while methane was passed through the columns as reference gas during the experiments. The conditions for experiments were set at 10 ml/min, 0 %RH, and a column temperature of 303 K. In order to remove any adsorbed moisture or organic contaminants present on the surface, the sample column was conditioned at 0 %RH for 7 hours before the analyses. Hydrocarbon probes such as heptane, octane, nonane and decane of at least 99.9% purity (Sigma Aldrich) were then injected as vapours sequentially through the sample column. Each organic probe will have a unique retention time through the sample and this was determined by detecting its presence with a flame ionisation detector (FID). From the retention time, the net retention volume was calculated for each probe after correcting for the dead volume. Using the Schultz approach (1987), the dispersive surface energy was obtained in a correlation plot between the net retention volume and the surface properties of each organic probe.

There could be changes in the crystallinity and / or polymorphic contents after spray drying and these surface phase changes can be picked by the powder X-ray diffractometer (D8 Advance, Bruker AXS GmbH, Germany) equipped with a PSD Vantec-1 detector. The diffraction patterns were obtained by performing measurements with a standard reference material SRM1976 and using CuK<sub> $\alpha$ </sub> radiation over the angular range from 4 < 2 $\theta$  < 50° with a step size of 0.02° and a scan rate of 1°/min. The diffraction patterns were then allowed to undergo Rietveld refinements using commercial software, TOPAS version 4.2, with the Partial Or No Known Crystal Structures (PONKCS) approach (Scarlett *et al.*, 2006; Schreyer *et al.*, 2011).

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# 5.3 Impaction Tube Setup

All impaction studies were carried out in a  $90^{\circ}$  impaction throat model (Fig. 5.1) that is identical to the one designed by Adi and co-workers (2010). The throat model consists of two clear acrylic tubes of internal diameter 11 mm and lengths 600 and 200 mm respectively jointed at right angle to each other. A sliding sampling port for the powders is positioned 300 mm from the joint such that the powder flow is fully developed prior to impaction. Powder agglomerates were pre-weighed and then loaded using a funnel via the sampling port into the tube. The other end of the tube was connected to a vacuum pump (Model HCP5, High Capacity Pump, Copley Scientific, UK) and the flow was generated with its rate verified using a flow meter (Model 4000 Series, Mass Flow Meter, TSI Inc., USA). Impaction of the agglomerates occurred at the joint (boxed area in Fig. 5.1) and the behaviour was visualized using a high speed camera (Photron FASTCAM SA1.1, Photron, USA) that is capable of capturing images at 30,000 frames per second. Electrostatic charges induced by the aerosolized particles before impaction were simultaneously monitored by placing a non-contact vibrating capacitive probe connected to an electrostatic voltmeter (Model 347 Electrostatic Voltmeter, Trek Inc., USA) within 3 mm from the surface of the copper ring or grid (~ 12 mm in thickness). The ring was joined with the tube with part of it (~ 3 mm) exposed to the interior of the tube. Powder particles passing through the grid or ring would induce equal and opposite charges that were captured by the voltmeter as the surface potential (Noras, 2002). The measured surface potential was referenced to the common ground shared by one of the copper rings and the voltmeter.



**Fig. 5.1:** An electrostatically configured 90° impaction throat model showing the relative positions of the sample port, copper grids or rings, and the area (boxed) for high speed imaging during impaction.

The tube model was rinsed with ultrapure water, air dried, and the copper grids or rings were touched with a ground wire so to dissipate any residual charges beforehand. The electrostatic voltmeter was next switched on to first obtain a stable baseline. After a steady baseline was reached, approximately 30 mg (+/- 2 mg) of spray dried powders was loaded into the throat model via the sampling port. A turbulent flow with a Reynolds number of 7660 and a flow rate at 60 L/min was generated by the pump (Adi *et al.*, 2010). The high speed camera was started simultaneously to record the impaction process. Recorded high speed images were referenced to the frame in which the agglomerates were seen coming into the camera's view. A jump in the measured surface potential in either polarity indicated the absolute induced charges by the flowing agglomerates. As mentioned earlier in Chapter 4, the surface specific potential values,  $V_o$  [kV/m<sup>2</sup>] were calculated by normalizing the initial surface potential, v, over the total surface area of the loaded powders (Eq. (4.1)). The total

surface area was obtained by multiplying the mass,  $m_p$ , of powders loaded with the specific surface area,  $A_s$ , as measured by the BET method. All experiments were conducted in triplicates at ambient laboratory conditions.

Differences in the flowing charge behaviours were verified for rough and smooth agglomerates with a shielded Faraday cage (Model TR8031, Advantest, Japan) connected to an electrometer (Model 6517A, Keithley, USA) whereby separate series of experiments were conducted to measure the electrostatic charges of agitated and non-agitated agglomerates. The results obtained with the Faraday cage could possibly support any postulates that can explain the flowing charge differences. About 50 mg of agglomerates were weighed in stainless steel bottles and used in each of the Faraday cage experiments (n = 3). The agglomerates experience inter-particle and / or particle to wall collisions prior to impaction in the throat model and acquire charge via triboelectric charging. Similarly, the weighed agglomerates were manually agitated at 120 shakes per minute in the stainless steel bottles before dispensing them in the Faraday cage in a reproducible way. The specific charge, Q [nC/g], of the powders was calculated by normalizing the charge, q, recorded over the mass of powders, m<sub>p</sub>, poured (Eq. (4.2)).

# 5.4 Varying Surface Properties Via Spray Drying

Fig. 5.2 shows the clear differences in surface roughness of the mannitol particles produced by spray drying with different conditions as described in Table 5.1.



**Fig. 5.2:** SEM images showing distinctly (a) rough, and (b) smooth spray dried mannitol particles with spherical morphologies at 8000x magnification.

It was apparent that the surfaces of the spray dried particles consisted of "grains" that arose from the growth of acicular crystals when water evaporates from the droplets during spray drying (Maas et al., 2011). From the images in Fig. 5.2a, the "grains" on the surfaces of the rougher particles appeared to be distinctively larger with the presence of holes or orifices. Spray dried mannitol particles have been reported to be highly porous (Elversson and Millqvist-Fureby, 2005; Heng et al., 2007) and orifices were evident on the surfaces of rougher spray dried mannitol particles (Maas et al., 2011). In the latter study, rough particles were produced using a high outlet temperature of 120 °C, whereas in our studies, they were obtained at a lower outlet temperature of 71 °C. This fundamental difference originates from the interplay between the droplet size, evaporation rate of water from the droplets, and surface recrystallization events during drying. Our spray dryer configuration favours the formation of larger crystals from the slow drying of the droplets at low outlet temperatures whereas in Maas' case, droplet was formed from the rotary atomizer via dripping and the presence of seed crystals early in the drying stage could have spurred the formation of large crystals on the particle surfaces. As the surfaces were drying up during the spray drying process, a thin solid crust was formed that had the potential of trapping any liquid in the core. Any evaporation of the liquid from the core would have to traverse through the crust and can lead to the occurrence of orifices or holes (Maas *et al.*, 2011). On the other hand, the drying of smaller droplets for our two-fluid pneumatic nozzle could have been quickened when a higher outlet temperature of 82 <sup>o</sup>C was used and when the drying was coupled with the high solids-to-surface diffusional rate (Vehring, 2008), small crystals could have been formed in the process (Fig. 5.2b). One could see the differences in the crystal size as well as the surface roughness values for rough and smooth particles shown in Table 5.2.

**Table 5.2** Values of surface roughness (by BET and geometric surface area ratio), particle size, BET specific surface area and dispersive surface free energy values for rough and smooth mannitol particles.

<b>Particle Properties</b>	Rough	Smooth	
Surface Roughness by	1.73 (0.05)	1.41 (0.03)	
Ratio f <sub>R</sub>			
d <sub>0.1</sub> [µm]	0.92 (0.05)	1.34 (0.02)	
d <sub>0.5</sub> [µm]	2.70 (0.02)	4.60 (0.03)	
d <sub>0.9</sub> [µm]	5.74 (0.26)	10.65 (0.15)	
BET Specific Surface	2.54 (0.05)	1.21 (0.01)	
Area, $A_s [m^2/g]$			
Dispersive Surface Free	56.16 (0.79)	34.63 (0.76)	
Energy [mJ/m <sup>2</sup> ]			

Note: Standard deviations are in parentheses.

A further observation is that as the particle size decreased, the surfaces became rougher. Small amounts of fines (< 1  $\mu$ m) were inherent in the particle size distributions and the mean diameters, d<sub>0.5</sub>, for both rough and smooth particles were reported as 2.70  $\mu$ m (+/- 0.02  $\mu$ m) and 4.60  $\mu$ m (+/- 0.03  $\mu$ m) respectively (Table 5.2). A higher atomizing rate combined with a higher aspirator rate during the spray drying
process could probably account for the smaller rough primary particles. Intuitively, smaller particles would imply a higher specific surface area as shown in the BET results in Table 5.2 whereby the specific surface area for the rough particles (2.54  $m^2/g$ ) was about two times higher than the smooth particles (1.21  $m^2/g$ ).

A higher dispersive surface energy was also noted for the rough particles (56.16  $mJ/m^2$ ) shown in Table 5.2 as compared to the smooth particles (34.63  $mJ/m^2$ ) and a possible explanation would be due to the surface heterogeneity of spray dried mannitol (Ho et al., 2009, 2010). Just as milling could preferentially expose certain facets of the crystal (Ho et al., 2012), so can spray drying in orientating specific crystallographic planes during droplet evaporation. A higher proportion of exposed planes having high surface energy could have formed on the rough particles. The deagglomeration and electrostatic properties of mannitol was known to be influenced by the crystallinity of the spray dried particles (Murtomaa et al., 2002; Ward and Schultz, 1995; Young et al., 2009). Spray drying could possibly induce amorphous contents on the surfaces and further promote polymorphic changes (Buckton et al., 2002; Hulse et al., 2009). In order to verify the crystallinity and polymorphic contents, the PONKCS (Partial Or No Known Crystal Structures) approach in Rietveld refinements was adopted in the analyses of the powder X-ray diffraction (pXRD) patterns for rough and smooth particles (Fig. 5.3). Within the limits of the pXRD technique, all spray dried particles were crystalline and consist of mainly the beta  $(\beta)$  form.



**Fig. 5.3:** Powder X-ray diffraction patterns of (a) rough, and (b) smooth spray dried particles.

The gravimetric vapour sorption isotherms shown in Fig. 5.4 confirmed the crystallinity of spray dried mannitol whereby the detection limit for amorphous content using the gravimetric vapour sorption can be better than 1% (Young *et al.*, 2007). The isotherms for both rough and smooth particles showed absence of any recrystallization events (Mackin *et al.*, 2002) that could have occurred if there were traces of amorphous contents on the particle surfaces. Rough particles could adsorb moisture on the surfaces approximately 2 times that of the smooth particles.



Fig. 5.4: Sorption-desorption isotherms for rough and smooth mannitol particles.

Moreover, there was about 7.58% by mass of the alpha ( $\alpha$ ) form found on the surfaces of the smooth particles while none of the  $\alpha$ -form was detectable on the rough particles. Littringer and co-workers (2012) also discovered a small amount (< 5% by mass) of a second polymorph,  $\alpha$  form, in an otherwise one-polymorph dominated spray dried mannitol agglomerates. It is important to note at this point that the configuration of the spray dryer atomizer used in this study was different from the rotary atomizer used in Littringer's group. Previous works (Dong *et al.*, 2002; Carvajal and Staniforth, 2006; Schmidt *et al.*, 2006; Mathlouthi *et al.*, 2012) have shown that the presence of polymorphs can potentially influence the water affinity of the particles. However, when the amount of sorbed moisture as shown in Fig. 5.4 was normalized against the total available surface area, there was no significant difference between the sorption capacity of the rough (2.99 mg/m<sup>2</sup>) and the smooth (2.97 mg/m<sup>2</sup>) particles. Therefore, the contribution of the  $\alpha$  polymorph can be eliminated and the difference in the sorption capacity attributed to the specific surface area.

#### 5.5 Surface Effects on Dynamic Charging and Impaction Behaviours

When the agglomerates were aerosolized from rest in the tube at 60 L/min under ambient laboratory conditions, they passed through the grounded copper ring and the sensing copper grid prior to impaction at the  $90^{\circ}$  joint of the throat model. The start of aerosolization was synchronized with the high speed recordings and subsequent impaction behaviours of the agglomerates were captured at 30,000 frames per second. The differences in the impaction behaviours were visualized in the video grabs in Fig. 5.5 and 5.6.



**Fig. 5.5:** High speed images showing aerosolized smooth spray dried agglomerates (a) before impaction, (b) at impaction, (c) after impaction, and (d) re-entrainment about 40 ms after impaction. Arrows indicate the direction of flow.

It can be observed that when the smooth particles were aerosolized, few large agglomerates were seen in the flow. They were easily broken up upon impaction resulting in a 'plume-like' re-entrainment into the horizontal before traversing down the vertical. In contrast, more large agglomerates were seen in the flow for the rough particles and they would just rebound off the joint upon impaction with little or no apparent breakup. Re-entrainment was significantly less with most agglomerates flowing down the vertical after the rebound.



**Fig. 5.6:** High speed images showing aerosolized rough spray dried agglomerates (a) before impaction, (b) at impaction, (c) after impaction, and (d) re-entrainment about 40 ms after impaction. Arrows indicate the direction of flow.

Surface specific potential measurements recorded by the non-contact vibrating capacitive probe showed that both rough and smooth agglomerates charged negatively after aerosolization (Table 5.3). Similarly, the negative polarity of single mannitol particles can be observed in Fig. 5.7 when the parallel plate condenser on the AFM, as previously described in Fig. 3.1, was used. The application of a positive potential (V = -80 volts) on the bottom plate resulted in a greater downward electrostatic force on the mannitol functionalized cantilever than the force exerted when the bottom plate had a negative potential (V = +80V).

In addition, the rough agglomerates had significantly higher surface potential (~ -5.91  $kV/m^2$ ) as compared to smooth agglomerates (~ -1.42  $kV/m^2$ ) after aerosolization.

This four-fold increase in the tribocharging ability of the rough agglomerates could also be observed when the agglomerates were first agitated in stainless steel bottles before dispensing into the Faraday cage connected to an electrometer. Agitating by shaking the agglomerates in stainless steel bottles can generate surface charges via frictional contact with the walls. Comparing the specific charge of the rough to the smooth agglomerates in Table 5.3, it was found that agitation increased the specific charge of the rough agglomerates by as much as 8-fold. On the other hand, the increase was not as significant for the smooth agglomerates. Without any agitation, there were no significant differences either in the specific charge at the bulk level (Table 5.3) or in the electrostatic force at the single particle level (Fig. 5.7) between the rough and smooth particles. It has to be noted that in the case of the Faraday cage measurements, the agglomerates were triboelectrically charged manually in stainless steel bottles instead of aerosolizing in an acrylic 90 degree impaction tube. Since there is a clear difference in work functions between acrylic and stainless steel, it is not unexpected that the polarity of the charged agglomerates in stainless steel bottles was reversed (Eilbeck et al., 1999; Rowley, 2001; Rowley and Mackin, 2003).

**Table 5.3** Specific surface potential and specific charge of rough and smooth spray

 dried mannitol particle measured by a non-contact vibrating capacitive probe and

 Faraday cage respectively. Standard deviations are in parentheses.

Particle Type	e Specific Surface	Specific Charge [nC/g]	
	Potential [kV/m <sup>2</sup> ]	Uncharged <sup>1</sup>	Charged <sup>2</sup>
Rough	-5.91 (0.91)	0.361 (0.18)	3.23 (0.54)
Smooth	-1.42 (0.15)	0.232 (0.12)	1.35 (0.30)

Note: <sup>1</sup>Uncharged particles implied that the particles were directly poured into the Faraday cage while <sup>2</sup>charged particles meant that the particles are triboelectrically charged by the shaking of the sample in a stainless steel container prior to charge characterization.



Fig. 5.7: Force at V = +80 volts and V = -80 volts vs. particle position between the condenser electrodes d / D measured for single mannitol particle that was (a) rough, (b) smooth.

High speed images, in Fig. 5.5 and 5.6, showed that the rough agglomerates rebounded at impaction without much significant breakup, while the smooth agglomerates were not only broken up but formed a 'plume-like' re-entrainment into the horizontal of the 90 degree throat model after impaction. The impaction behavioural differences seemed to imply that the inter-particle forces depended on the

surface roughness of the primary particles in the agglomerates. Several authors (Adi *et al.*, 2008a, b; Walton, 2008) suggested that increasing the corrugation of primary particles could diminish the inter-particle forces due to reduced contact area resulting in effective de-agglomeration. However, the results from the present study seemed to suggest otherwise. In the first instance, the geometry of the asperities on the surfaces of the spray dried particles used in the present study was visually different from past experiments. From Fig. 5.2, the surfaces of the particles consisted of "grains" that have larger areas exposed for particulate interactions than the limited contact area on the wave-like surfaces of the particles used in their studies. Roughening the particle surfaces by increasing the grain sizes would increase the agglomerate strength, which was demonstrated by the more regular agglomerates (consisting of the rough primary particles) obtained after subjecting to sieving (Fig. 5.8). Secondly, the formation of strong agglomerates from the smaller rough particles can be further reasoned by the higher specific surface area and dispersive surface free energy as shown in Table 5.2 (Das *et al.*, 2010).



**Fig. 5.8:** SEM images of (a) rough particles forming regular agglomerates, and (b) smooth particles with less tendency to form regular agglomerates.

It was described earlier that the adsorbed moisture on particle surfaces could play a role in the tribocharging of the particles with some authors suggesting that the moisture could dissipate the accumulated charge (Elajnaf et al., 2007; Grosvenor and Staniforth, 1996; Kwok and Chan, 2008; Nomura et al., 2003) while others contending that moisture could increase the contact charging rate with enhanced mobility in the surface groups (Yao et al., 2002; Wiles et al., 2004). From the surface specific potential results in this study, there were clear differences in the flowing charges between rough and smooth particles prior to impaction which in turn have different moisture sorption capabilities. Rough and smooth surfaces adsorbed up to 0.8% and 0.3% of its dry mass respectively due to the differences in specific surface area. It is postulated that the increase in the moisture adsorbed with surface roughness facilitated the movement and distribution of surface charges (Wiles et al., 2004). Since the rate of charge dissipation was likely to be low due to the fast movement of the aerosol powders through the tube and the poor conductivity of the acrylic tube, the charge generation would far dominate the dissipation component. This was also observed in the Faraday cage measurements even though a conductive stainless steel container was used to generate the charges by agitation. Furthermore, the increased chargeability of rough surfaces could contribute to the cohesiveness of the primary particles, hence leading to stronger agglomerates. Therefore, the surface roughness induced de-agglomeration upon impaction and the associated electrostatic characteristics could be an important consideration in the dispersion and delivery of drug particles to the lungs.

#### 5.6 Concluding Remarks

A further extension of the non-contact vibrating capacitive probe in combination with high speed imaging has been successfully developed to monitor the dynamic electrostatic charge contributions to the impaction behaviours of spray dried mannitol powders in a impaction tube setup simulating the throat. The effect of surface roughness on the electrostatic charge and the subsequent de-agglomeration behaviour upon impaction was clearly shown with the combinatorial method. Rough surfaces produced by spray drying formed strong agglomerates that could not be easily broken up and it has resulted in the rebound of agglomerates from the wall upon impaction. In contrast, smooth particles were broken up upon impaction with significant reentrainment. The higher dispersive surface energy due to the surface heterogeneity of rough particles coupled with the high specific area of the particles could have led to the formation of strong agglomerates. The higher surface specific potential observed on rough agglomerates could be explained by the increased moisture sorption on the surfaces of the rough particles enhancing the mobility and distribution of generated surface charges. However, it is interesting to note that the observed differences in the electrostatic chargeability between rough and smooth surfaces were not obvious if the particles were not agitated as shown in the measurements by the Faraday cage and the single particle parallel plate condenser. It is, therefore, essential to give due consideration to particle morphology design as the surfaces could significantly affect, for instance, the de-agglomeration efficiency of the particles required for effective respiratory drug delivery.

### Chapter 6

## Conclusion

The industry standard for powder electrostatic charge measurements has always been the Faraday cage since the sampling procedures are relatively straightforward. Even though the Faraday cage has been used to formulate several physical triboelectric charging models, it is still a challenge to obtain reproducible and consistent results. Initially a technique used to quantify static charges, the Faraday cage has been modified so as to capture dynamic electrostatic charging events. However, the enhanced cage has to be an integral part of the process to monitor the real-time electrostatic charging phenomenon and this could potentially interfere with the process it is monitoring. As such, other devices such as the electrical-single particle aerodynamic relaxation time analyzer (E-SPART) using noninvasive laser techniques were introduced. Unfortunately, the analyses of the results obtained by these devices were too complex and therefore, alternative techniques, both at single particle and bulk level, should be sourced and validated to further our understanding on the powder electrostatic charging phenomenon.

It is often advantageous, sometimes given the limited sample quantity, to be able to investigate the electrostatic charging behaviour of single discrete particles so as to predict the different effects on charge acquisition during powder handling processes arising from changes in the particle surface properties at an early stage. The atomic force microscope (AFM) has been selected as the platform on which a parallel plate condenser was fabricated to measure the electrostatic forces of a micron-sized glass particle attached to the cantilever in the presence of an electric field. Experiments done on the effects of hydrophobicity of the particle indicated that the surface conductivity of the particle affected the contact charging ability of the particle and hence the net electrostatic force measured. Analyses of the contributions to the net electrostatic force have enabled the electrostatic charge on a single particle to be calculated.

On the other hand, the nonintrusive vibrating capacitive probe was introduced and validated with the Faraday cage as a potential method for observing the triboelectric chargeability of bulk pharmaceutically relevant powders in various sieve size fractions. The probe has demonstrated to be effective in determining the influence of particle size on the surface specific potential measured. Presence of fine particles that adhere themselves to the walls of the agitating container or large particles that are relatively immobile could interfere with the charge transfer process and can lead to a diminished surface potential. By positioning the probe in close proximity to the impaction tube setup simulating the throat and combining with a high speed camera, the dynamic charging process of the aerosolized mannitol particles with varying degrees of process induced surface roughness can be visualized together with subsequent impaction behaviours. It was found that rough particles charged up more than smooth ones and they were able to form strong agglomerates that resisted break up upon impaction. High dispersive surface energy and a greater moisture adsorption capability for the rough surfaces were likely indicators for the observed phenomenon. It was also interesting to note that static charge measurements by the AFM parallel plate condenser and the Faraday cage did not reveal the observed dynamic differences. As compared to Mizes' (1994) configuration on the AFM, the parallel plate condenser fabricated in this study allowed the particle on the cantilever to be positioned freely between the two electrodes so that the force contributions on the particle can be analyzed and the charge gained by the particle can be directly quantified. The vibrating capacitive probe connected to an electrostatic voltmeter offered a versatile, nonintrusive, simple and fast approach in determining the various electrostatic behaviours of both bulk static and flowing pharmaceutical powders which the E-SPART, induction grid probe and static / modified Faraday cage cannot quite achieve. The nonintrusive capacitive probe also has the potential of being easily adapted in industrial powder flow processes to check on the electrostatic contributions to any significant flow issues. The combination of the two techniques would further enhance the understanding of the electrostatic behaviours both at the single particle and bulk powder levels so as to improve on powder formulation design strategy.

#### Chapter 7

## **Future Work**

#### 7.1 Detecting Crystallinity Changes in Powder Mixtures

Triboelectrification could serve as a potential tool in studying amorphous powders. Murtomaa and co-workers (2002) found that when the spray dried lactose particles were charged via sliding on polypropylene surfaces, the charge generated increased as a function of the amorphous content. In addition, amorphous content less than 1% could be detected. However, a higher variability in the specific charge measurements was observed in the amorphous spray dried lactose than crystalline lactose when the powders, actuated from different inhalers, had varying particle size and morphology (Murtomaa et al., 2004). Therefore, in order to use triboelectrification as a technique in detecting amorphous changes in powders, it is essential to take into consideration the effect of changes in the specific surface area on the charge acquired due to particle size and morphology changes. Possible future work would involve developing the nonintrusive vibrating capacitive probe technique described in Chapter 4 to study the effects of varying amorphous contents in a physical powder mixture on the charge acquired from triboelectrification by normalizing the surface potential measured with the specific surface area of the powders. Some preliminary work has been done in using the nonintrusive vibrating capacitive probe to detect amorphous changes in physical powder mixtures and the results are described in subsequent paragraphs.

Fully amorphous, characterized by powder X-ray diffraction, lactose was obtained by spray drying the powders with a 2.5 % (w/v) aqueous lactose solution fed into a mini

spray dryer (B-290, Büchi Labortechnik, Switzerland) at a rate of 2 ml/min, with inlet temperature of 180 °C, and the atomizing rate and aspirator ratio set at 0.452 m<sup>3</sup>/h and 80% respectively. The spray dried amorphous lactose was then mechanically blended in a mixer (T2F, Willy A. Bachofen AG Maschinenfabrik, Switzerland) with crystalline sieved (< 38  $\mu$ m) lactose at various mass ratios to obtain amorphous contents of 70, 50, 40, 35, 32.5, 30 and 10 %. Charges were induced on the powder mixtures by manual agitating a sample mass of 50 mg in a polypropylene (PP) bottle at 240 shakes per minute. The tribocharged powder mixture was then carefully loaded onto the metal pan in a setup shown in Fig. 4.1. The surface potential was measured using the nonintrusive vibrating capacitive probe attached to an electrostatic voltmeter and the value of which was normalized by the total specific surface area of the powders measured by the BET method. All measurements were made in triplicates at 25 °C and 40 %RH.

The result on the effects of amorphous contents on the electrostatic behaviour of the lactose blends was illustrated in Fig. 7.1 as a plot of the average surface specific potential [ $kV/m^2$ ] against the amorphous contents [wt.%]. Fully amorphous spray dried lactose charged positively on PP surfaces while crystalline lactose (< 38 µm) charged negatively. The average surface specific potential became less negative as the amorphous content increased. A sharp four-fold increase in the surface potential to more than 30 kV/m<sup>2</sup> with a reversal in polarity was noted when the amorphous content in the mixture was between 30 to 32.5 wt.%. Engers and co-workers (2007) also noticed the abrupt rise in the specific charge with a polarity reversal as the concentration of pseudoephedrine went beyond 50% in the powder mixture of pseudoephedrine hydrochlroide and dicalcium phosphate dihydrate.



Fig. 7.1: Graph shows the average surface specific potential versus the amorphous contents in the lactose physical powder mixtures. A representation of the approximated point at 31.8 wt.% amorphous is shown in the checked box whereby the positive and negative charging effects of spray dried lactose and crystalline lactose (<  $38 \mu$ m) respectively canceled or neutralized each other.

Assuming the surface potential of the mixture is the result of the additive contributions from the surface potential of both amorphous and crystalline lactose, a first approximation to the concentration of the amorphous lactose in the mixture that gives a nullifying effect can be calculated. The calculated mass fraction of the amorphous lactose was 26 wt.%. From the plot in Fig. 7.1, the estimated value was 31.8 wt.% amorphous content. This discrepancy from the calculated value could be due to the non-additive effect of interacting electrical fields from the electrostatically charged amorphous and crystalline surfaces. The net electrical field is thus a function of the change in energy level for charge transfer as well as the effective surface work

functions that gave its energetically favourable equilibrium surface charge distribution (Engers *et al.*, 2007).

Further increasing the amorphous contents from 32.5 to 100 wt.% will lead to a decrease and a final saturation of the surface specific potential to approximately 18  $kV/m^2$ . It is not clear as to the possible cause of the decrease but it is assumed that since amorphous materials were softer than crystalline ones (Karner *et al.*, 2011), the vigorous mixing could result in significant collisions between the amorphous and crystalline particles that in turn initiated re-crystallization of some of the amorphous lactose particles on the surfaces of the crystalline ALM particles (Wittmann *et al.*, 2010).

The preliminary results has shown that the nonintrusive vibrating capacitive probe technique has the potential to detect crystallinity changes in powder mixtures. As a first step towards developing this potential, and if the powders can charge both positively and negatively on the same surface depending on the crystallinity as in the case above, a quick detection would then be an obvious distinction between positive and negative polarities. In order to have a more quantitative perspective on crystallinity changes using the probe, a next step would involve carefully calibrating the probe to the crystallinity content of the mixtures to determine its detection sensitivity and then a functional relationship between the crystallinity content and the measuring parameter (such as the surface specific potential or differential change in surface specific potential) can be evaluated.

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#### 7.2 Implementation of the Nonintrusive Method in Powder Processes

The nonintrusive method has provided us some preliminary insights in the particle size and crystallinity effects on the triboelectric charging properties of pharmaceutical powders. It has also proven to be useful in dynamic powder aerosol process coupled with high speed imaging in examining the differences in surface roughness on the electrostatic charge and impaction behaviours. The challenge is to implement the nonintrusive method in real-time powder processes to study the change in particle properties through electrostatic charge monitoring. Attempts have been made to explore using inductive ring probes in pneumatic processes to investigate the charging tendencies of experimental dust particles such as PMMA, saccharose and PVC against the volume of particles, range of particle diameters and their velocities (Gajewski, 1984; Gajewski and Szaynok, 1981). Noras (2006) has calculated the charge from integrating the voltage induced in the electrodes during aluminium oxide powder aerosolization in a dielectric pipe. The sensitivity of the nonintrusive electrostatic charge measurement system can be carefully calibrated with model equations that relate changes in particle properties such as crystallinity, particle size and surface roughness to the change in charge measured under various environmental conditions.

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