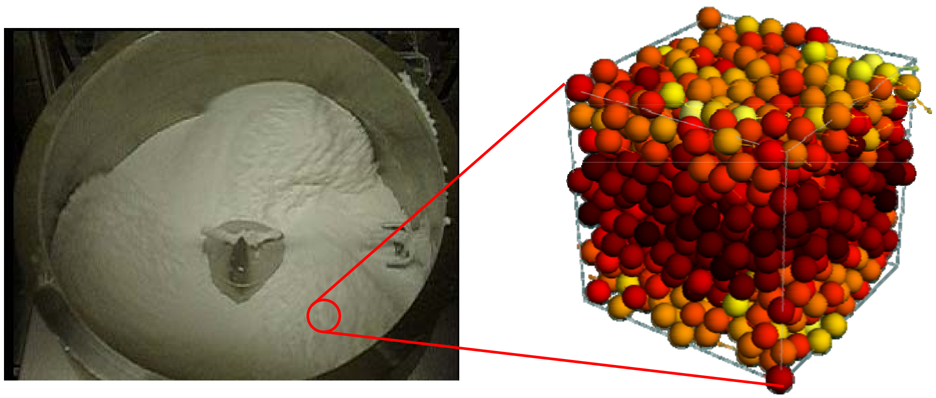
Discrete element model (DEM) simulations of High Shear Wet Granulation (HSWG)

Ben Freireich, Vince Hoon, and Prof. Carl Wassgren

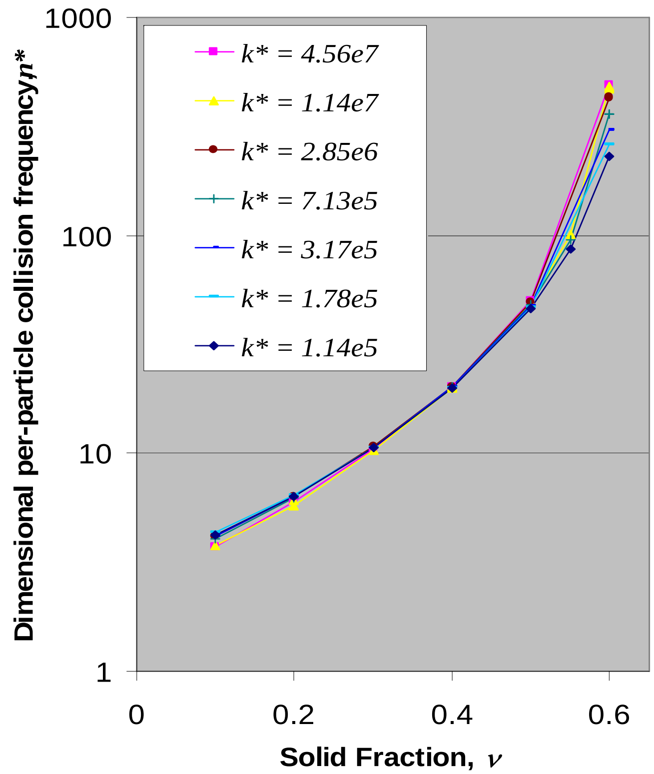
Sponsored by the Consortium for the Advancement of Manufacturing of Pharmaceuticals (CAMP)

Motivation: HSWG is a common particle size enlargement pharmaceutical processing operation that improves powder handling, uniformity, and reduces dust hazards. HSWG involves the mixing of powder while simultaneously spraying a binder solution on the powder bed. There currently is no first principles method for accurately modeling the process. The goal of this project is to develop relations for collision frequencies and coalescence and breakage probabilities for a HSWG system. These relations will be used to predict the particle size distribution evolution in a HSWG operation.



Above: A "point" within the granulator is modeled using DEM as a cell of particles in a uniform shear field with periodic boundary conditions.

Right: Average collision frequency, *n*, made dimensionless using the shear rate, γ, plotted as a function of the solid fraction, ν, and dimensionless stiffness, $k^* = k/(\rho d^3 \gamma^2)$.

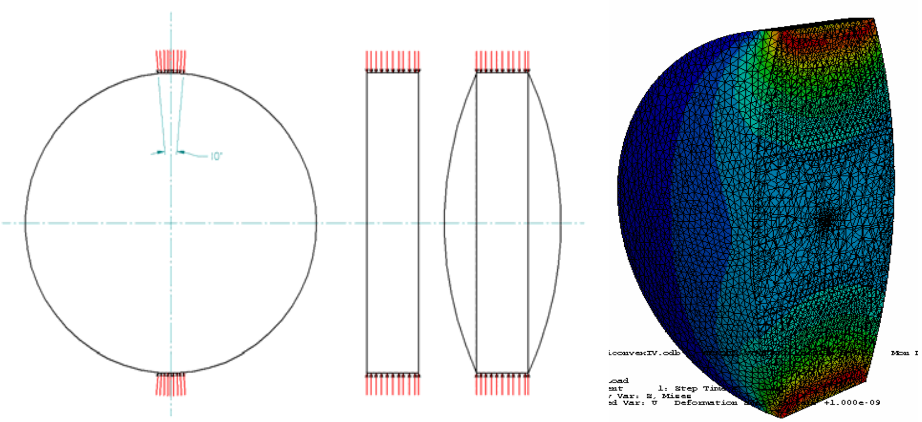


Stress distributions in pharmaceutical tablets

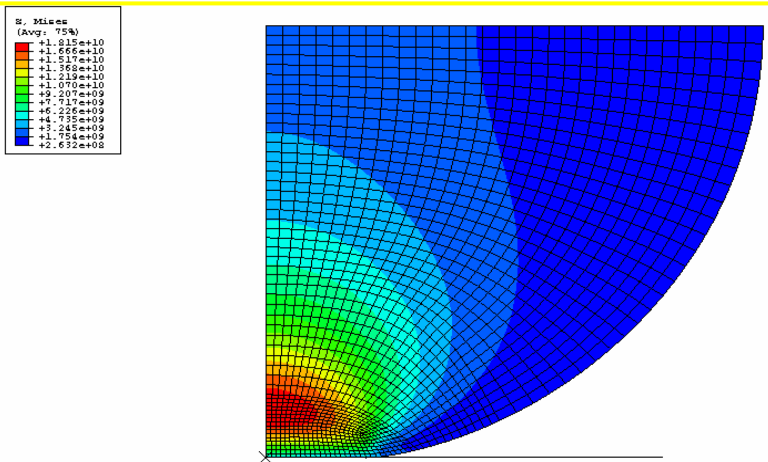
Tuhin Sinha and Prof. Carl Wassgren

Sponsored by the National Science Foundation GOALI program and Pfizer, Inc.

Motivation: Stresses developed during the production and handling of pharmaceutical tablets can result in broken and damaged tablets. The goal of the current work is to predict the stress distribution within a tablet during tableting (tablet compression) and tablet coating operations using the Finite Element Method. These predictions will be used to design tablets such that breakage and surface damage are minimized.



Stresses generated during the diametrical compression of a uniform-property, bi-convex tablet.



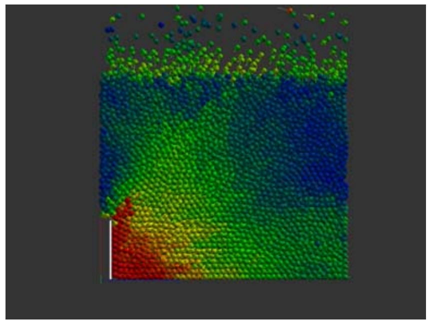
Stresses developed in a two-dimensional, contact stress analysis.

Blade optimization for powder blending

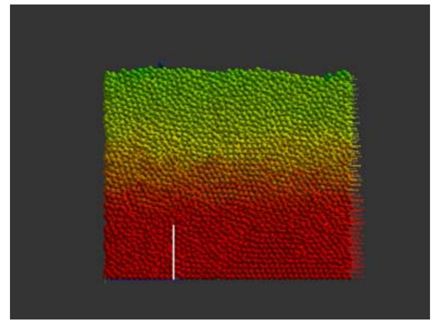
Avik Sarkar and Prof. Carl Wassgren

Sponsored by the NSF Engineering Research Center for Structured Organic Particulate Systems

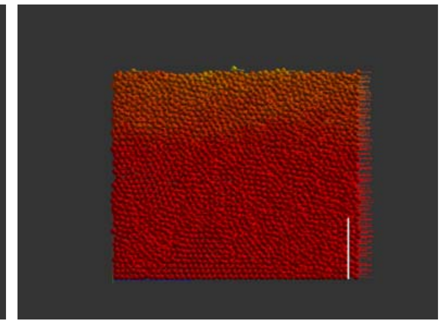
- The goal of this project is to determine how a mixing blade's characteristics influence powder blending.
- These studies will be used to design a blade that will generate the greatest degree of blending in the least number of passes (or time).
- Discrete Element Modeling (DEM) is used to predict the bed behavior. DEM is a particle-based method in which the dynamics of every powder particle is simulated.



starting

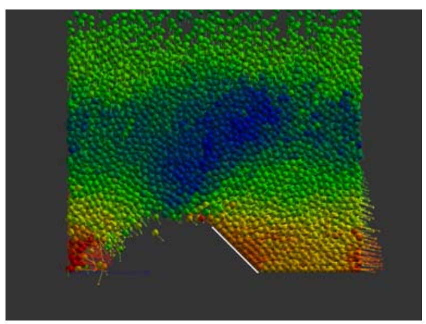


during second pass

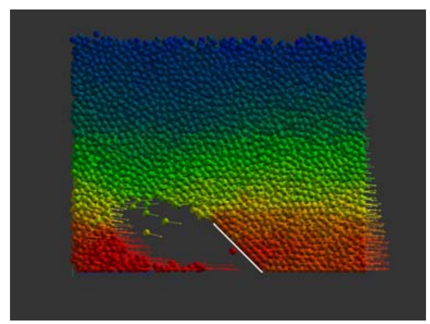


after second pass

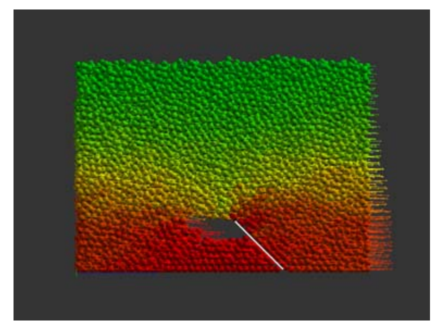
Straight blade, blade velocity is 0.5 m/s (particles colored by speed)



during first pass



during second pass



during sixth pass

Inclined blade (45 degrees), blade velocity is 1.5 m/s

Inter- and Intra-Tablet Coating Variability

Arjun Kalbag and Prof. Carl R. Wassgren

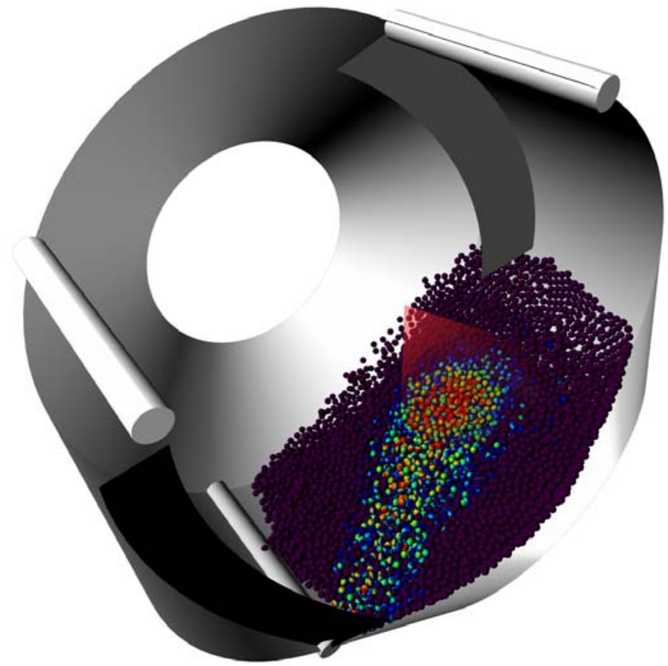
Sponsored by the Consortium for the Advancement of Manufacturing of Pharmaceuticals (CAMP)

- Tablets are coated for a number of reasons most important of which is controlling the release profiles and bioavailability of the active ingredient. The amount of coating on the surface of a tablet is critical to the effectiveness of the oral dosage form.

- Tablet are usually coated in horizontal rotating pans with the coating sprayed onto the free surface of the tablet bed. Tablets must have a coating mass that lies within a prescribed range with very little inter- and intra-tablet coating variability.

- Using the Discrete Element Method (DEM), tablet coating can be simulated on the computer. Simulation data provide the position, velocity, and orientation of each tablet within the coater allowing accurate measurements of the time and orientation that each tablet spends exposed to the coating spray. Video-based experiments provide a validation of the simulation results.

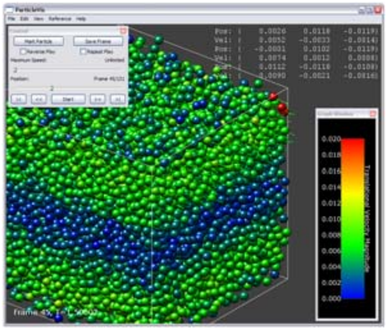
- The effect of process variables in tablet coating such as pan speed, fill level, spray pattern, spray mass flow rate can be analyzed using the DEM model.

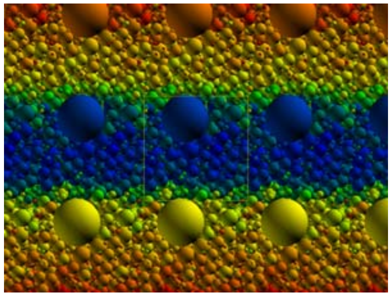


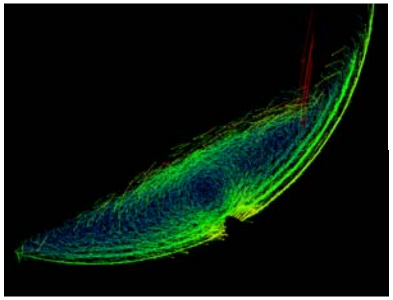
A simulated pan coater with spherical tablets used for studying inter-tablet coating variability. Continued work focuses on the intra-tablet variability, specifically the variation of coating between the caps and bands of biconvex tablets.

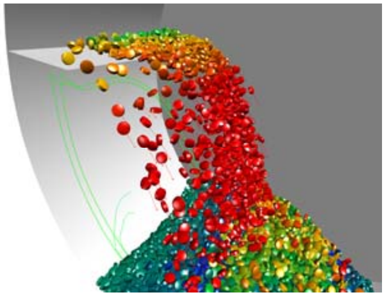
Visualization of Particle-Based Computer Data

Vince Hoon and Prof. Carl Wassgren

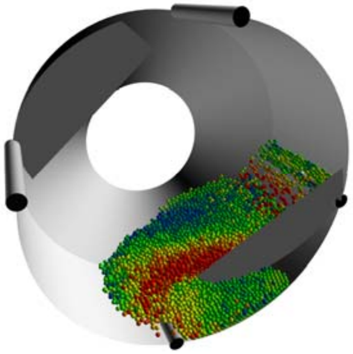








- The goal of this project is to design a software system for full-featured visualization of discrete element method (DEM) computer data.
- The resulting software is known as *ParticleVis*. It is written in C++ and OpenGL.
- *ParticleVis* capabilities:
  - real-time 3D rendering of large sets of particle states
  - adjustable lighting conditions and camera viewing characteristics
  - display translational velocity, rotational velocity, and orientation vectors along with particle pathlines
  - color mapped particles based on external data (*e.g.* speed, force information, residence tie, etc.)
  - external vector and scalar fields (*e.g.* display electromagnetic fields, temperatures, etc.)
  - transparent and textured particles
  - XML-based particle shape files
  - CAD file rendering
  - output individual frames and movies

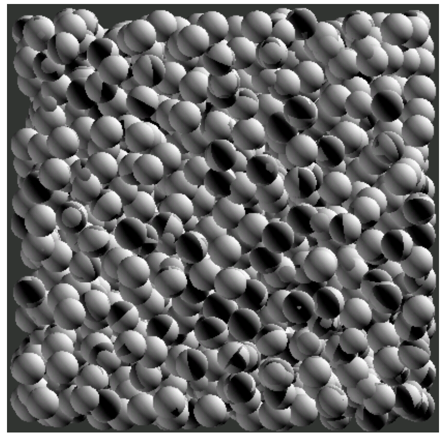


Modeling of inter-particle cohesion

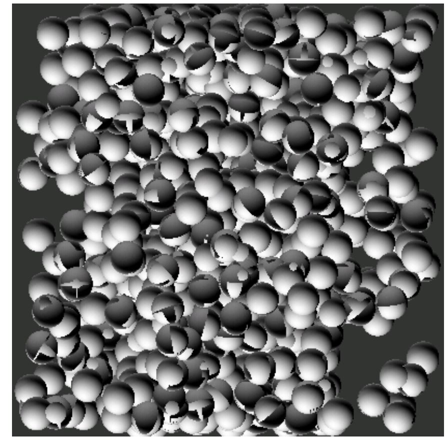
Andrew Otte, Profs. Carl Wassgren and Teresa Carvajal

Sponsored by the Dane O. Kildsig Center for Pharmaceutical Processing Research

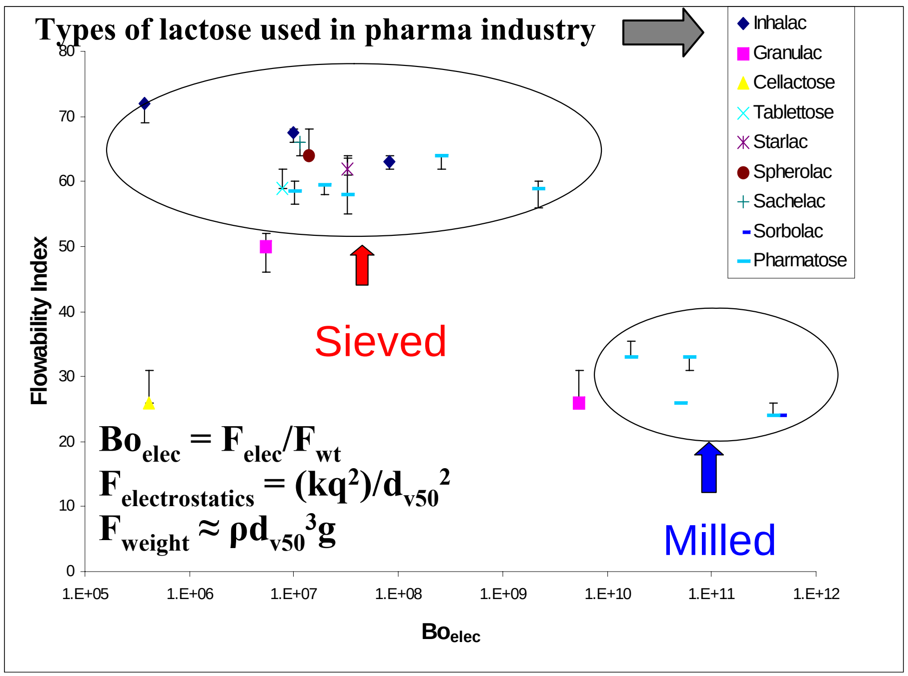
- Inter-particle cohesion is a significant factor when handling powders. Cohesion can be detrimental to the performance of many manufacturing operations and can lead to failed products.
- Having a better understanding of how to model cohesion and how cohesion affects powder flow should lead to better process design and operation
- This project utilizes experiments to measure inter-particle cohesive forces and discrete element method (DEM) computer simulations to model cohesive powder flow.

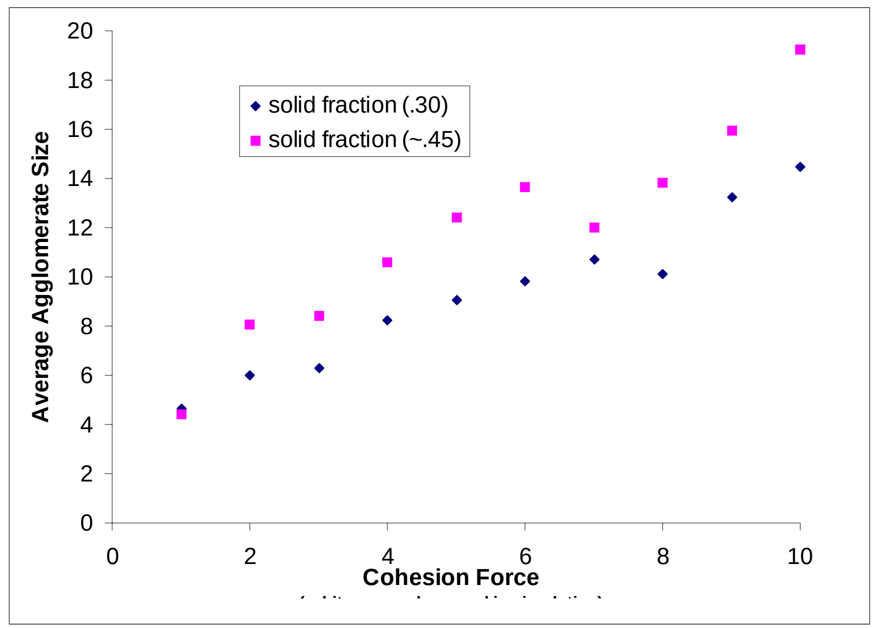


simulation with no cohesive forces



simulation with cohesive forces





Impact of non-Newtonian drops on pharmaceutical tablet surfaces

Alexis Dechelette, Prof. Paul Sojka, and Prof. Carl Wassgren

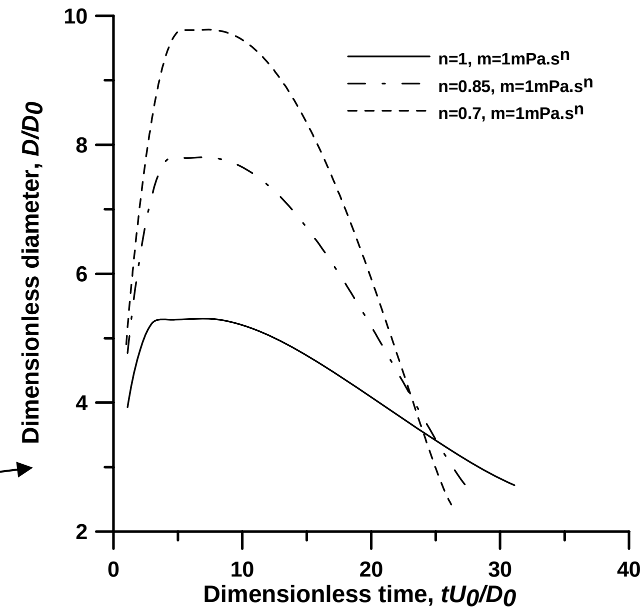
Sponsored by the Consortium for the Advancement of Manufacturing of Pharmaceuticals (CAMP)

Motivation: The quality of pharmaceutical coatings is often critical to the performance of the dosage form. Not only are coatings used for aesthetic and taste masking purposes, but they are frequently used to control the rate of disintegration and sometimes contain active ingredients. Understanding how coating sprays cover and bond to a surface is important for ensuring the effectiveness of pharmaceutical coatings.

Objectives: To predict the spreading diameter of non-Newtonian drops on surfaces as a function of the spray and surface properties.

Peeling (Image from Julian Vincent, GSK Harlow)

Diameter prediction for three non-Newtonian liquids (U=2m/s, D=5mm)



Xanthan Gum drop at t=5.5ms, (U=3.5m/s, D=3.5mm)

Xanthan Gum drop at t=75ms, (U=3.5m/s, D=3.5mm)

Attrition of pharmaceutical tablets

Madhusudhan Kodam and Prof. Carl Wassgren

Sponsored by Pfizer, Inc.

Motivation: Attrition and breakage of pharmaceutical tablets and granules occurs frequently during their handling and processing. As a result, the materials may require additional processing or must be discarded. Current methods for estimating the degree of surface damage of pharmaceutical products are purely empirical and qualitative. It is desired that a more fundamental method for predicting the degree of surface damage be developed.

Objectives: Develop experimentally validated analytical models for predicting tablet attrition and particle damage as a function of the surface loading conditions and material properties. These models will be combined with 3D discrete element method (DEM) computer simulations of coating and blending operations to predict the degree of attrition as a function of the system parameters. This information will be used to develop recommendations for modifying system designs to reduce attrition.

Tablets damaged during friability testing

Tester for determining the friability of tablets.

Liquid transfer during particle collisions

Craig Bradshaw and Prof. Carl Wassgren

- Motivation: Powder flow behavior is a strong function of the cohesive forces acting between particles. In many cases, these cohesive forces are the result of liquid bridges that form on the surface of wetted particles. An important factor in determining these liquid bridge force is the volume of liquid present in the bridge.
- The goal of this work is to experimentally measure the amount of liquid transferred between particles when a collision occurs. In particular, the effects of particle size, liquid viscosity, film thickness, separation distance, and contact duration are investigated.