# The Discrete Element Method: An Overview, Case Studies, and Linkages with Population Balance Models

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Pfizer Worldwide R&D, Groton, CT  USA

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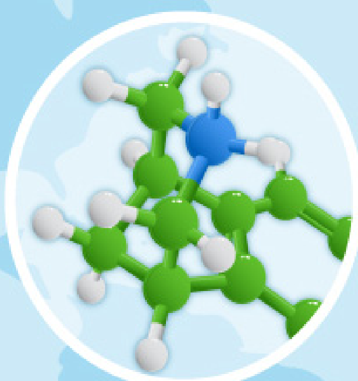
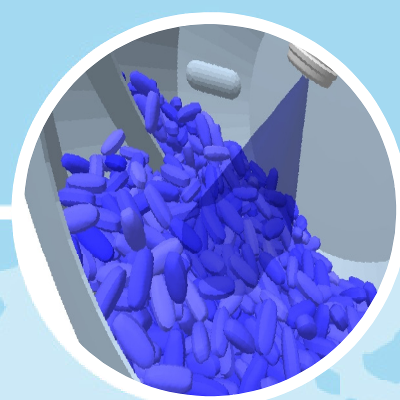


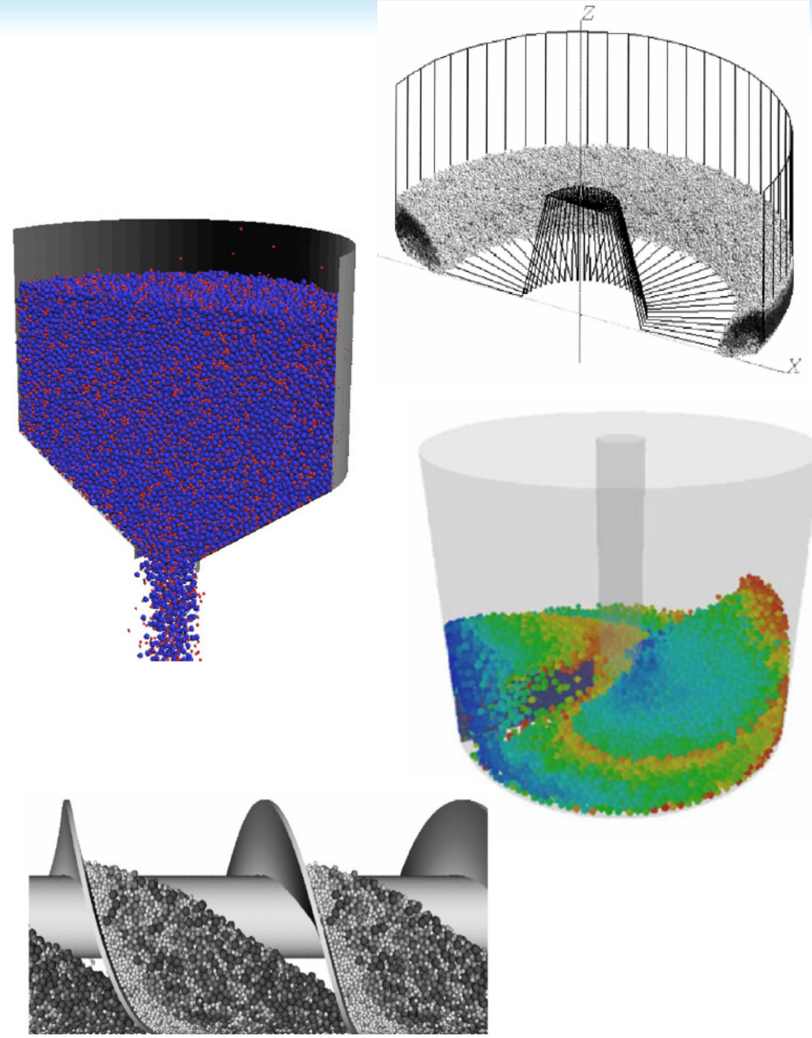


# Outline

- Discrete element method (DEM)
  - – Overview of DEM
  - – Case studies
    - Batch powder blending process
    - Tablet film coating uniformity
  - – Linking DEM and PBM approaches

# Discrete Element Method (DEM)

- The Discrete Element Method
  - Computational model for particulate-based systems
  - Tracks the state of each particle
    - Forces, position, velocities, etc.
    - In contrast to continuum models:
      - Computational fluid dynamics (CFD)
      - Finite element method (FEM)
  - Key advantage:
    Wealth of particle-level information
    - Monitor mixing & segregation, velocity profiles, bulk density, stresses, etc.
    - Difficult/expensive to measure experimentally
  - Key disadvantage:
    Long computational run times required
    - Typical simulations require 1-7 days



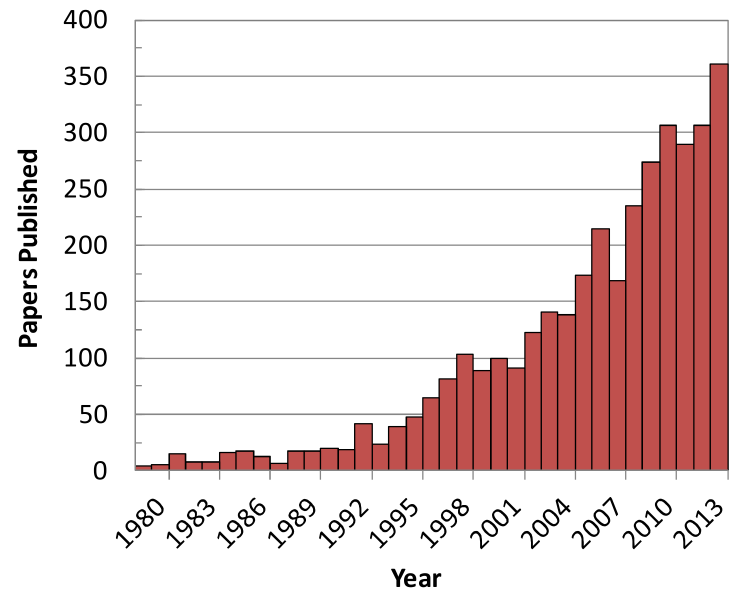

*Ketterhagen, et al. 2009 J Pharm Sci 98(2):442 - 470*

# History & Growth

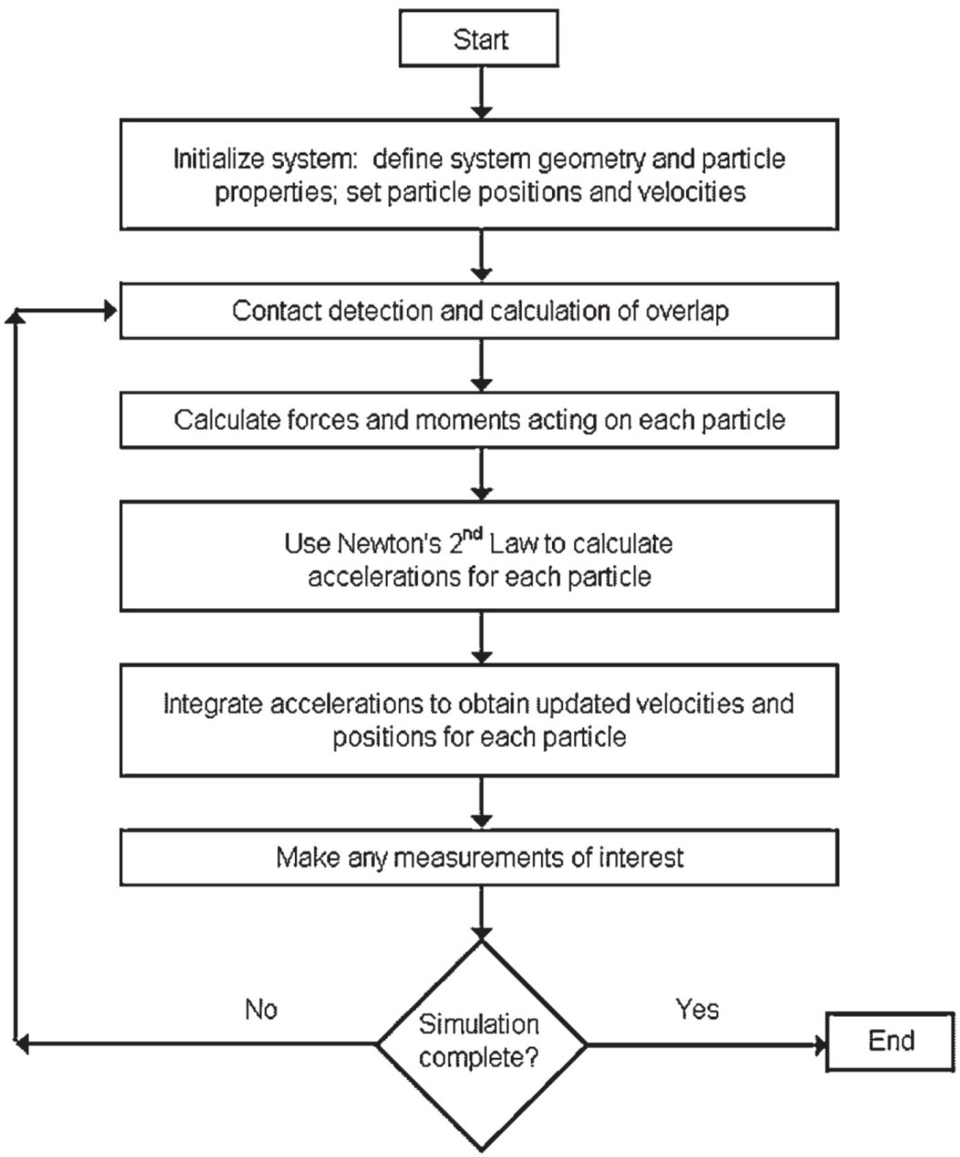
- Peter Cundall and Otto Strack
  - 1970’s, University of Minnesota
  - Rock mechanics

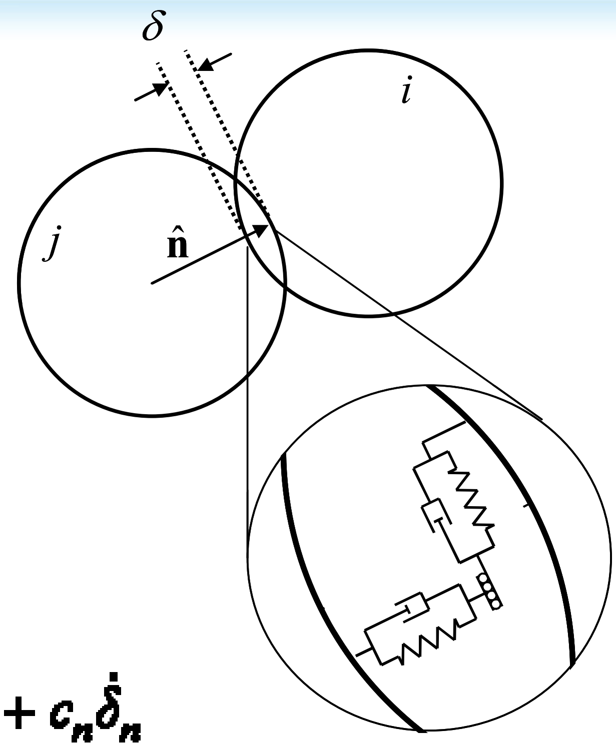
- Growth to broader application
  - Geomechanical
    - Landslides/soil stability, rock fracture
  - Material handling applications
    - Hopper discharge, mixing drums
  - Process industries (chemicals, food, ceramics, pharmaceuticals)
    - Mixing, drying, milling, coating, granulation
    - Fluidized beds, pneumatic conveying [when coupled with CFD]

SciFinder search using terms “discrete element method” OR “distinct element method”



# DEM Computational Flowchart




$$F_n = k_n \delta_n^{\frac{3}{2}} + c_n \dot{\delta}_n$$

$$F_t = \min\left[ -S_t \delta_t - 2\sqrt{\frac{5}{6}}\beta\sqrt{S_t m^*}\,\dot{\delta}_t, \mu F_n \right]$$

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# Required Inputs

- Material properties
  - Density,  Poisson's ratio, and Young's modulus
  - Particle size distribution, Particle shape
- Contact parameters
  - Coefficient of restitution, $e$
  - Coefficient of sliding friction, $\mu$
  - Coefficient of rolling friction, $\mu_R$
  - Surface energy, $\gamma$
- Equipment geometry
  - Electronic CAD file for complex geometries
- Process conditions
  - Rotation speed, mass in the system, etc.

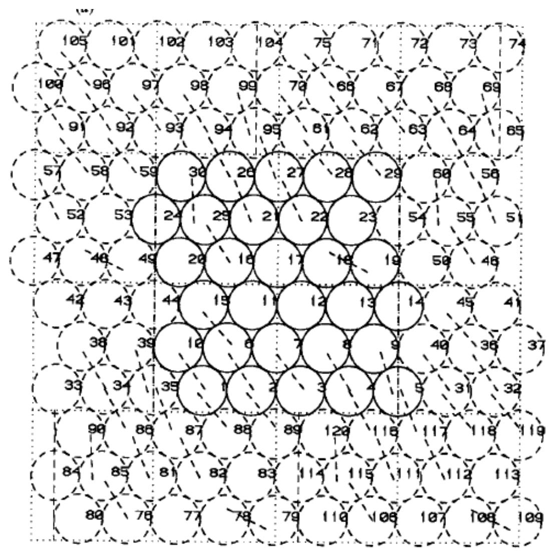
# Outputs

- Base data available from DEM
  - Particle data: velocity, forces, torques, orientation, etc.
  - Geometry data: force, torque, position, etc.
  - Contact data: collision rate, collision energy distributions

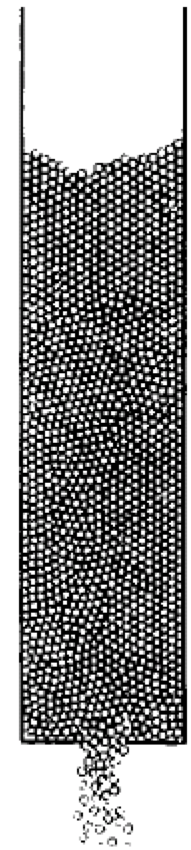
- Additional calculations or post-processing
  - Mixing indices, segregation
  - Particle residence times
  - Stresses / work done on particles
  - Many others

# Early DEM models

- Early DEM models tended to be limited to:
  - Spherical particles
  - Non-cohesive
  - Gravitational force
  - Simple geometry
  - Neglect air/fluid flows



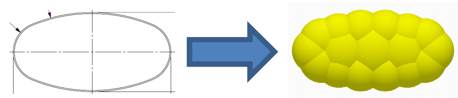
Babic *et al.*, J. Fluid. Mech. **219** (1990) 81.

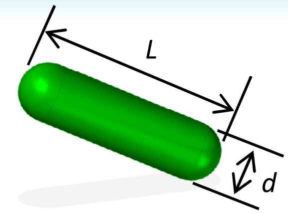


Langston *et al.*, Chem. Eng. Sci. **50** (1995) 967.

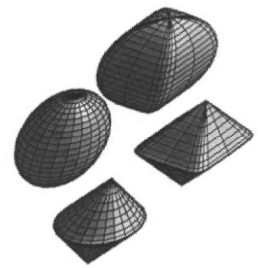
# Model Extensions

- Non-spherical particles
  - "glued-spheres" approach
  - mathematical representation
    - Ellipsoids, superquadrics
  - CAD geometries



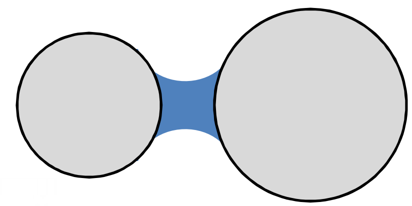



Hua *et al.*, Chem. Eng. Sci. **101** (2013) 144.

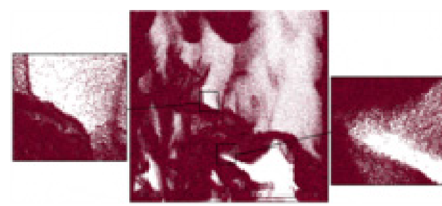


Hogue, Engrg. Comput. **15** (1998) 374.

- Cohesive particles
  - e.g. JKR model, capillary liquid bridge model

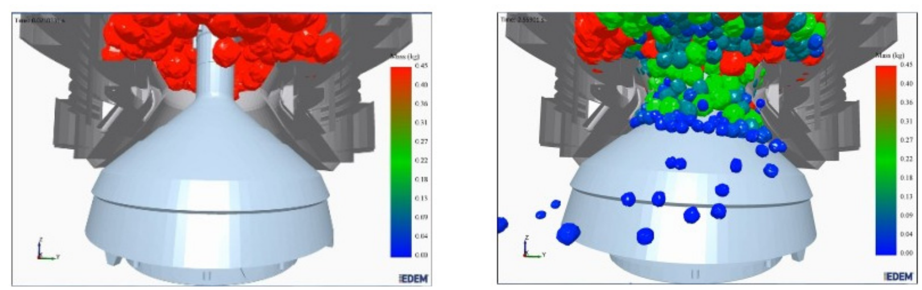


- Electrostatics
- Fluid effects
  - Fluidized beds, pneumatic conveying



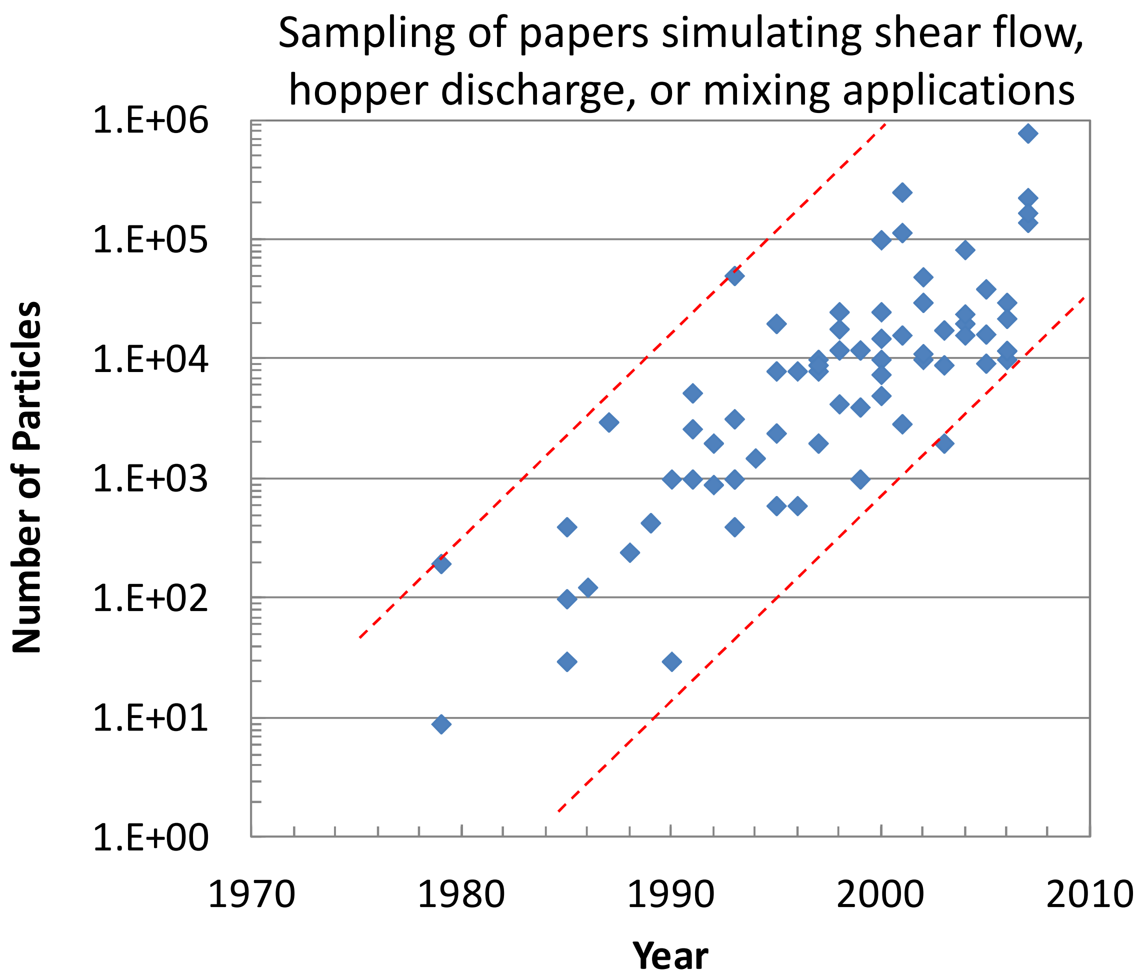
RCPE Website (www.rcpe.at)

- Particle agglomeration, breakage
  - Granulation, milling



DEM Solutions, Ltd. Website

# Growth of Computing Power



# Outline

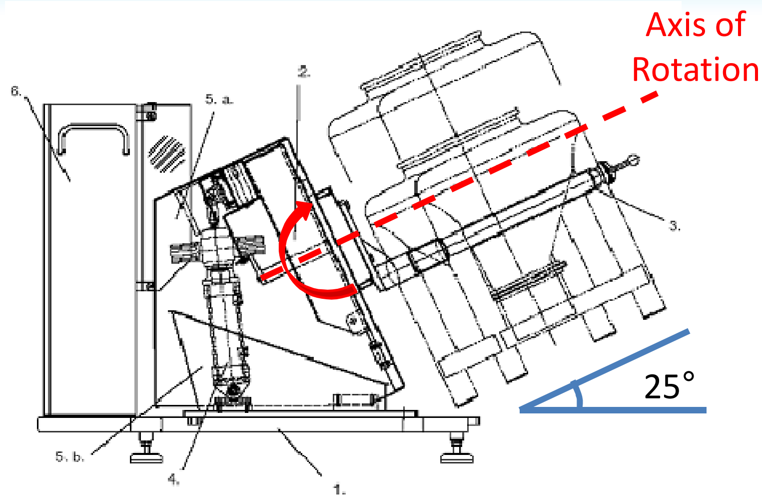
- Discrete element method (DEM)
  - Overview of DEM
  - Case studies
    - Batch powder blending process
    - Tablet film coating uniformity
  - Linking DEM and PBM approaches

# Introduction

- Powder blending is an important process in manufacture of solid dosage forms
- Achieving a uniform blend is requisite to reach content uniformity specifications
- Blend uniformity (BU) internal spec
  - Individuals: ± 10% of mean
  - RSD ≤ 5%


(Images from www.servo-lift.com and www.epmmagazine.com)

# Pilot Scale Blending Process




- Final Blend Uniformity (% label claim)
  - Sub-potent regions observed with large RSD

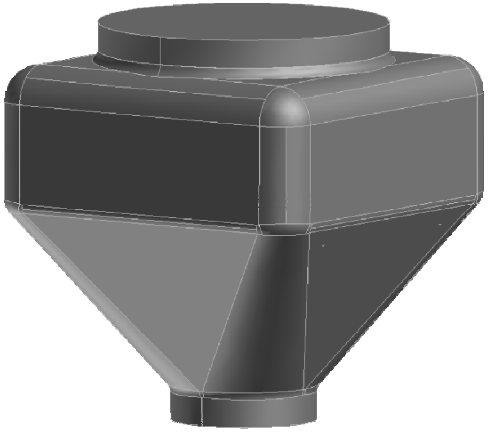
| Dose | 0.25 mg | 0.25 mg | 1 mg | 1 mg |
|---|---|---|---|---|
| **Mean** | **103.82** | **97.54** | **96.55** | **90.93** |
| **Min** | **101.42** | **77.25** | **95.38** | **38.25** |
| **Max** | **105.48** | **106.21** | **99.72** | **99.96** |
| **Std. Dev.** | **1.50** | **10.66** | **1.33** | **19.31** |
| **% RSD** | **1.45** | **10.93** | **1.38** | **21.24** |

Why?

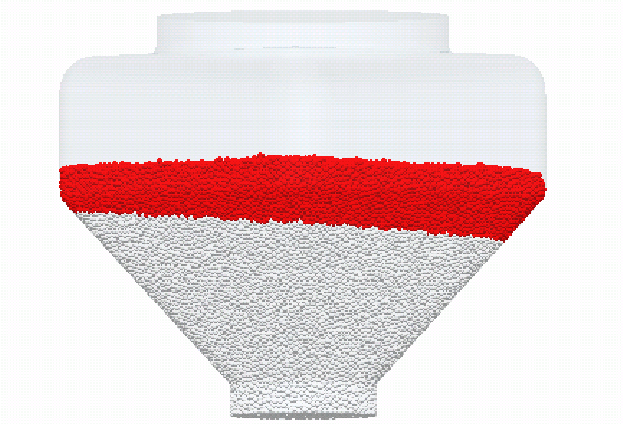
Sampling error?
Analytical problem?
Poor mixing?

# DEM Model

- Simulation procedure set to match experimental procedure
  - Layered fill with 55% “active” granulation, 45% extra-granular excipients
  - Bin tilted up 25° and rotated at 12 RPM



Initial Condition



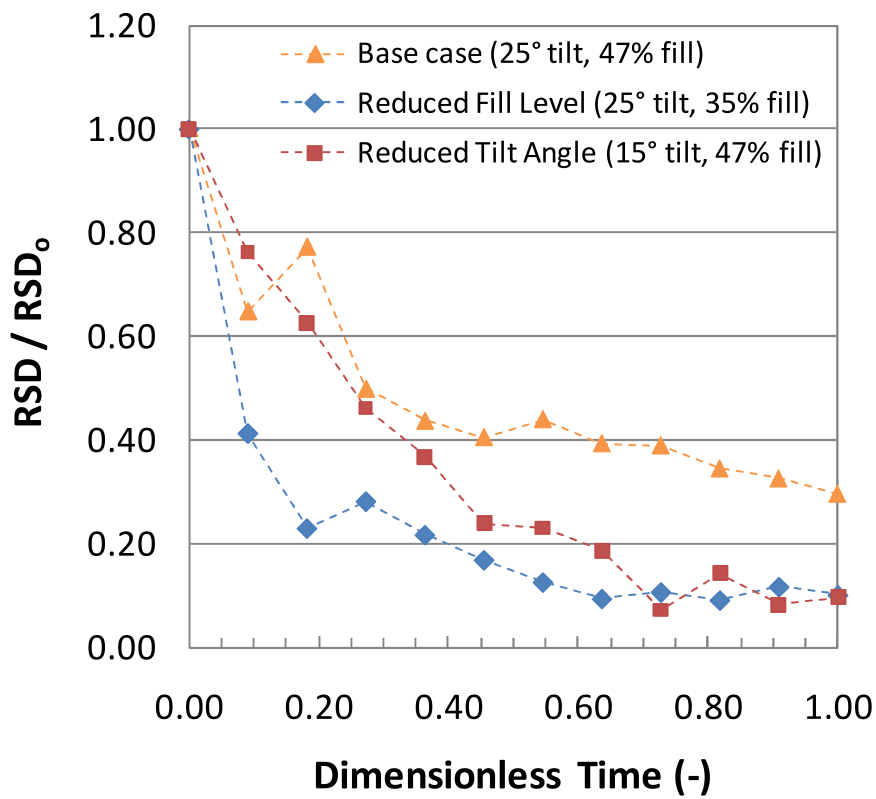
# DEM Simulation of Pilot Scale Bin Blender

Initial State

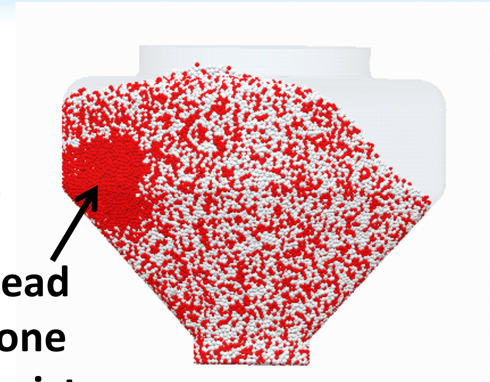
Simulation Video

Predicted
Final State

# DEM Simulation of Pilot Scale Bin Blender

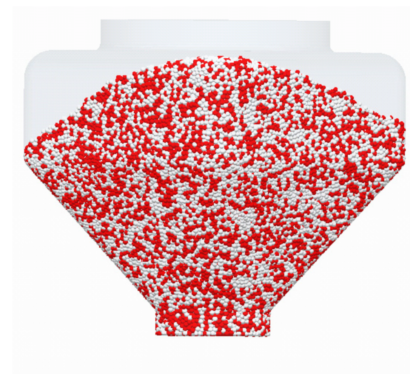



Base Case

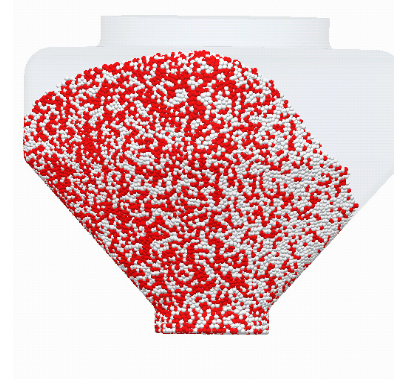


**Dead zone persists**

Reduced Tilt Angle



Reduced Fill Level



- Potential process improvements:
  - Reduce fill level
  - Reduce bin tilt angle

Pfizer

# DEM Predictions of Film Coating Uniformity

- Pharmaceutical tablets are film coated for a variety of reasons
  - Cosmetic coatings:
    - Elegance, Taste masking, Improve stability
  - Functional coatings:
    - Controlled release dosage forms
    - Active coatings containing API


- Coating uniformity, or variability, is a quality attribute
  - Inter-tablet coating variability - Variation in thickness from tablet-to-tablet
  - Intra-tablet coating variability - Variation in thickness from side to side of a given tablet

- Consequences of poor coating uniformity
  - Cosmetic coatings: process inefficiencies
    - Longer processing times to ensure all tablets have a minimum weight gain
  - Functional coatings: variable release rates or potency variation
    - Release rates or potency may differ from tablet-to-tablet

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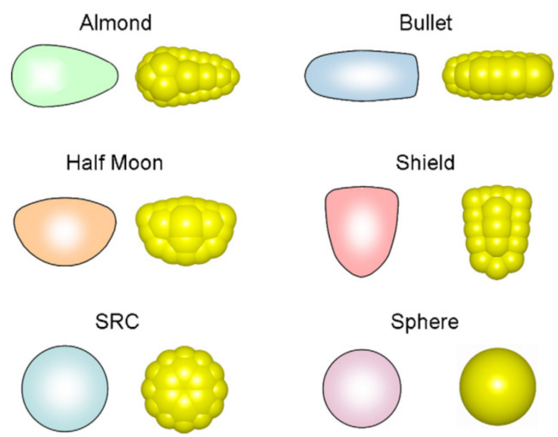
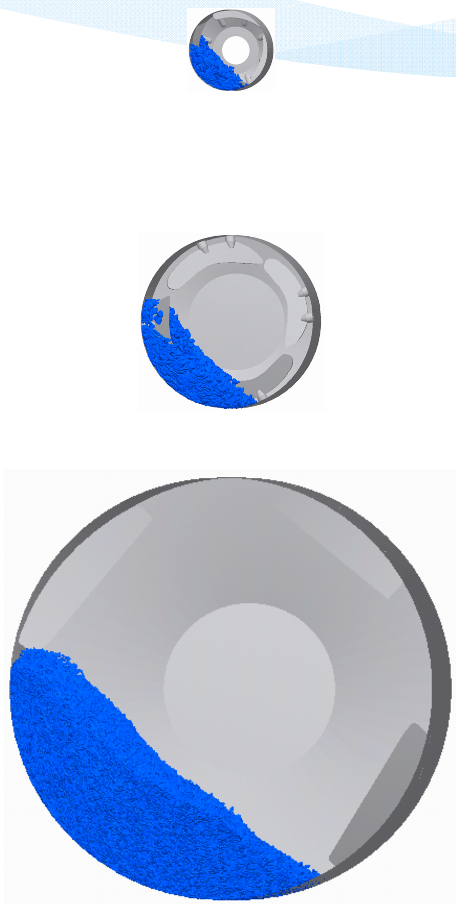
# DEM Model

- Coating pans
  - Effect of process scale (lab, pilot, production)
- Tablets
  - Effect of tablet shape
  - Glued-spheres approach

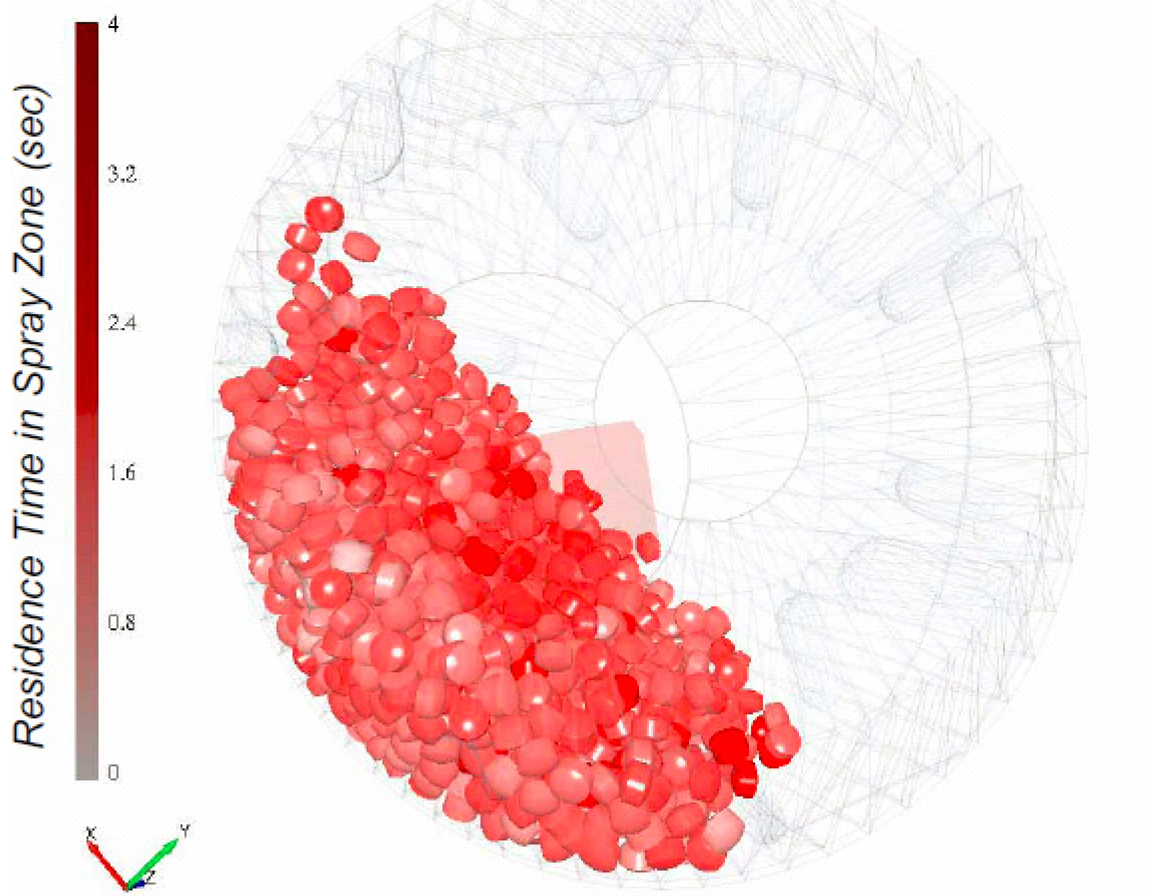



Ketterhagen, Int. J. Pharm. **409** (2011) 137.




Ketterhagen, Proc. DEM 6 Conference, Golden, CO, 2013.

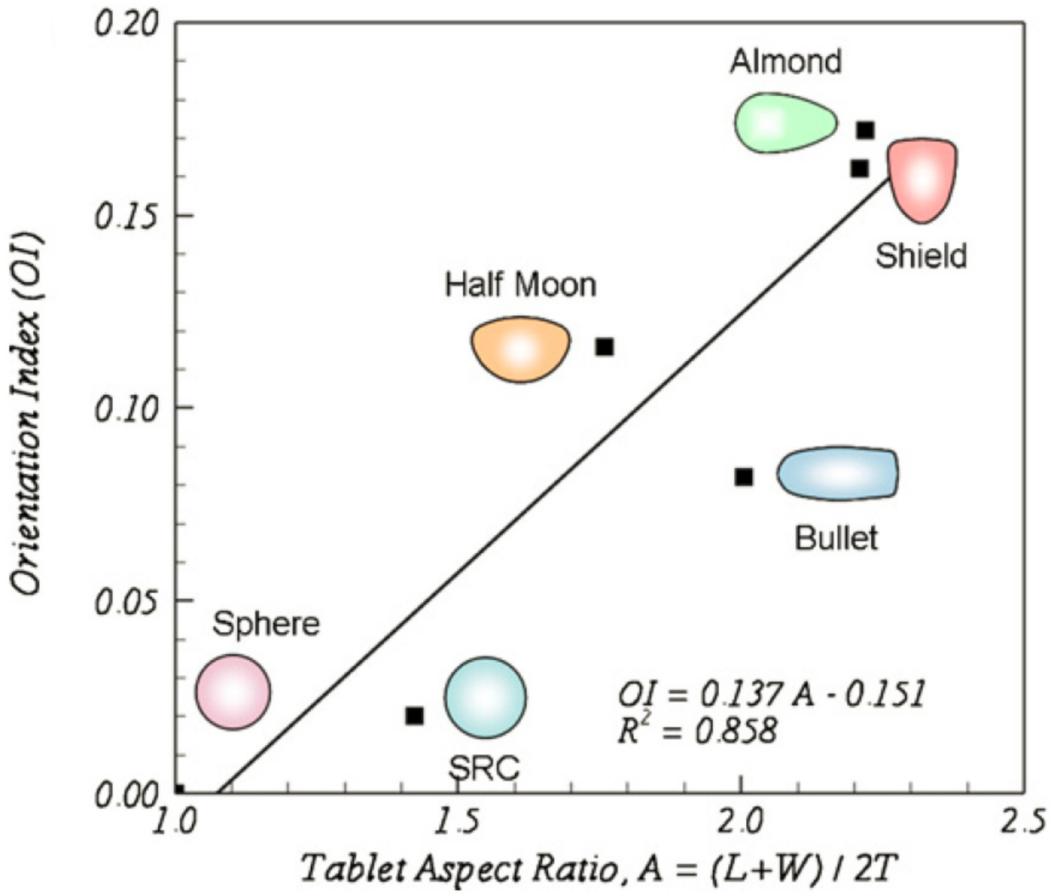
# Simulation Video



# Intra-Tablet Coating Variability

Large $CoV_{intra}$

Small $CoV_{intra}$

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# Multi-scale Modelling

- Multi-scale models are useful for systems with a large disparity in length or time scales
- Macro-scale:
  - model equations may not be completely known or at sufficient resolution
- Micro-scale:
  - model is available, but too expensive to use for entire macro-scale system
- One example:  linking DEM-PBM

# Value in Linking Models

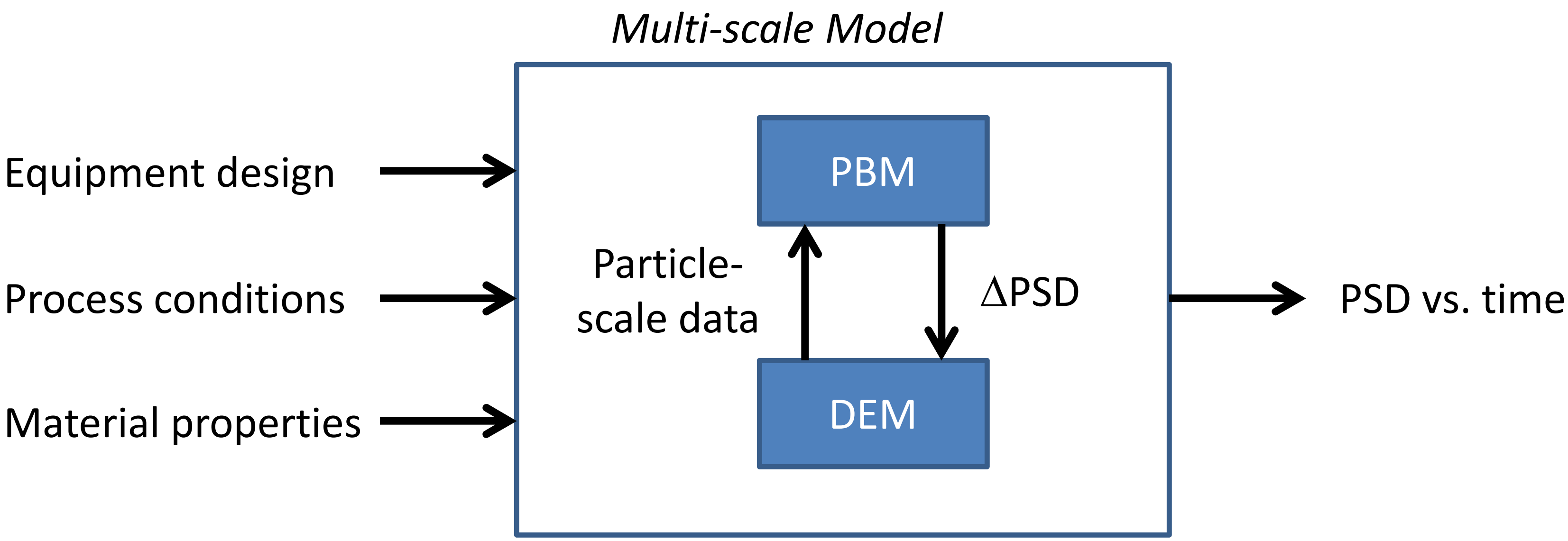
- Bridge multiple scales within complex processes
  - Process-scale (PBM)
  - Particle-scale (DEM)
- Leverage vast information at particle-scale from DEM simulations
  - Attain greater levels of detail within the model
  - Improved physical understanding of particle-scale phenomena
  - Leverage DEM capabilities for process design/equipment design
    - Relate process parameters to kernel parameters
- Conduct fewer experiments

# Literature Snapshot

- Use DEM to determine kernels
  - Extract particle collision rates and collision velocities
  - For example:
    - Wet granulation – coalescence
      - Goldschmidt (2001), Tan *et al*. (2004), Ingram (2005), Gantt *et al*. (2006)
    - Milling – breakage
      - Datta *et al*. (2002), Herbst (2004), Concas *et al*. (2006)

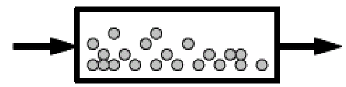
# Linking Frameworks

- Schematic of one possible linking framework:

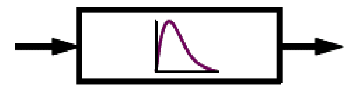


# Linking Frameworks

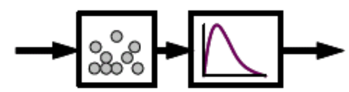
- Other frameworks possible (e.g. Ingram and Cameron (2005))
- Integration frameworks for a continuous drum granulator
  - Simultaneous – use DEM to model entire granulator



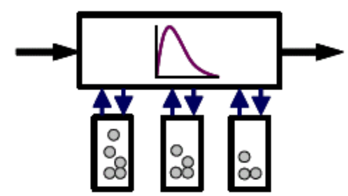
  - Serial – offline DEM simulations to create a constitutive equation



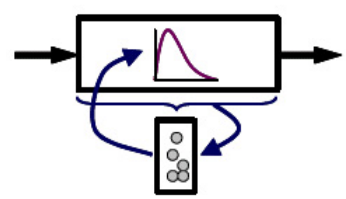
  - Multi-domain – DEM and PBM model separate domains



  - Embedded – PBM calls DEM model to supply kernel parameters for each sub-domain of process



  - Parallel – PBM calls a single DEM model to supply kernel parameters for entire process domain



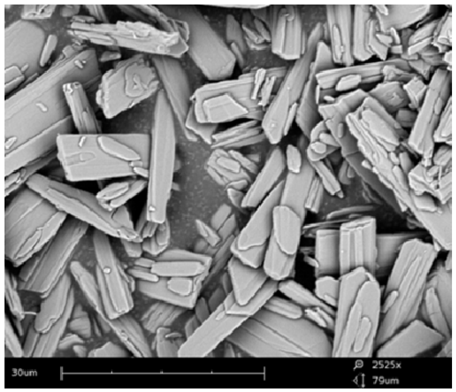
# Optimal Framework

- Optimal framework may be dependent on several factors
  - Goals of model
    - output of interest, assumptions willing to make, desired resolution of output
  - System design
    - batch vs continuous, domain heterogeneity
  - Computational constraints

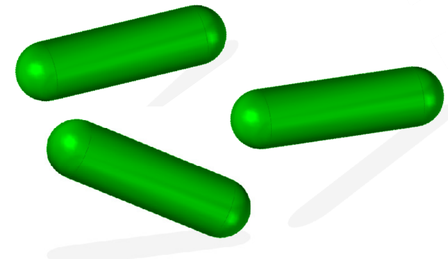
# Challenges

- Calibration of DEM

"Pharmaceutical Powder"
(www.teachnano.com)



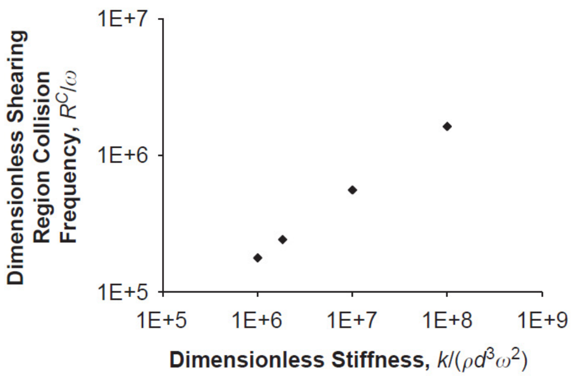
Assumptions
of particle PSD, shape, properties, etc.

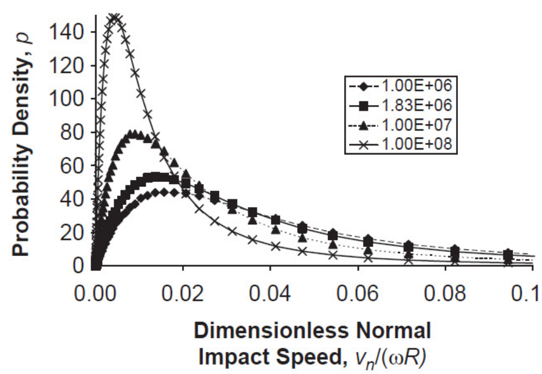


Hua *et al.*, Chem. Eng. Sci. **101** (2013) 144.

  - Without proper calibration, results are usually qualitative

- Collision rate, impact velocity measurements are sensitive to material properties (Freireich, 2009)



# Outlook

- DEM is a useful computational tool for particulate systems
  - Insight into particle and bulk-scale flow phenomena
- Significant potential in linking DEM-PBM in multi-scale framework
- Design of framework may vary based on system of interest
  - Goals of model, system design, computational constraints
- Some challenges do exist
  - Calibration  of DEM is likely required and can be difficult
  - Particle-scale data are sensitive to some material properties

# Thank you for your attention!

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