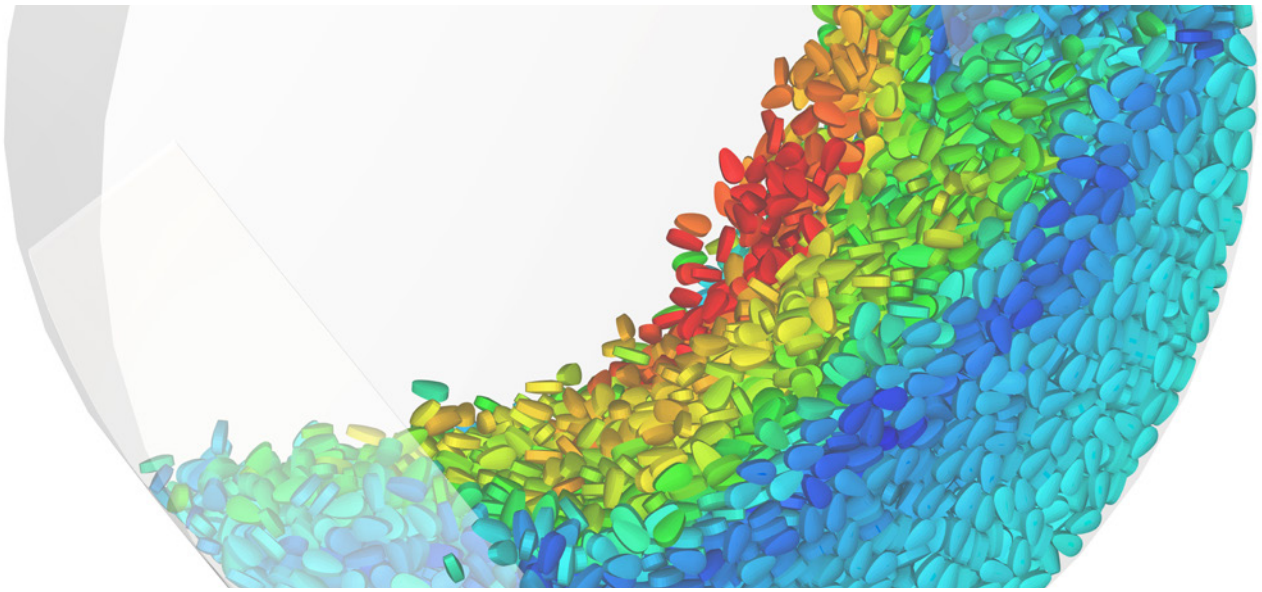
CASE STUDY

PURDUE UNIVERSITY

ROCKY

Purdue University Investigates Pharmaceutical Tablet Coating Variability



"Rocky DEM was our tool of choice, with its capability to model tablet shapes using polyhedral elements that accurately predict real-world particle behavior. Traditional DEM software uses bonded-sphere elements, which can produce artificial roughness that significantly affects the accuracy of tablet dynamics simulation."

Carl Wassgren

Professor, School of Mechanical Engineering and Department of Industrial and Physical Pharmacy
Director, Center for Particulate Products and Processes
Purdue University

In the pharmaceutical industry, tablet coating is a standard process that addresses a number of issues, from patient compliance (pill taste and odor) to drug efficacy (delayed or sustained delivery) to product perishability. The coating on a tablet's surface can be crucial to the drug product's effectiveness. Tablets are usually coated during the manufacturing process in a horizontal rotating pan, with the coating solution sprayed onto the free surface of the tablet bed.

Controlling process parameters is important to good tablet coating; a suboptimal coating process may result in defects. Pharmaceutical research that investigates tablet coating tracks the motion of tablets within the coating pan, considering variables such as circulation times, residence times of tablets in the spray zone, projected surface areas and tablet bed surface velocities. The objective is to ensure good mixing so that each and every tablet gets sprayed with the same coating mass (inter-tablet), with a uniform thickness of coating solution (intra-tablet).

Once a coating process is developed at a small scale in the lab, it must be scaled up for the manufacturing plant. Prof. Carl Wassgren and his student, Siddhartha Agarwal, at Purdue's School of Mechanical Engineering and Department of Industrial and Physical Pharmacy, relied on discrete element modeling (DEM) and simulation software to study intra-tablet coating variability related to scale-up.

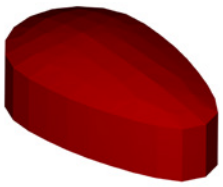


Figure 1. High Fidelity Tablet Shape

The small-scale lab study used a 1-foot coating pan, the pilot-plant-scale pan was a few feet in diameter, and manufacturing scale used a 60-inch pan. "Our investigation studied intra-tablet coating variability changes with scale," explained Wassgren. "Does it get better, does it get worse, does it stay the same as the scale changes?

A pharmaceutical tablet coating pan has baffles that mix and tumble the tablets as the nozzle sprays the coating solution. Wassgren's team used Rocky DEM software to model the movement of almond-shaped tablets in pans of varying size for extended time periods. "Rocky DEM uses polyhedral elements for modeling objects that compact, settle, and behave just like real-world particles," Wassgren said. "The ability to model complex tablet shapes using polyhedral elements is important, since the more-common bonded-sphere approach introduces artificially bumpy surfaces that can significantly affect tablet dynamics."

The number of tablets ranged from approximately 1,300 in the smallest pan to nearly 87,000 tablets in the largest pan. A GPU-based ray-tracing algorithm was applied in post-processing to determine the exposure time of each tablet's surface area elements in a simulated spray. From these exposure times, the variability in coating thickness over the surface of individual tablets was predicted and used to investigate how scale affects intra-tablet coating variability. (See Figures 2 and 3.)

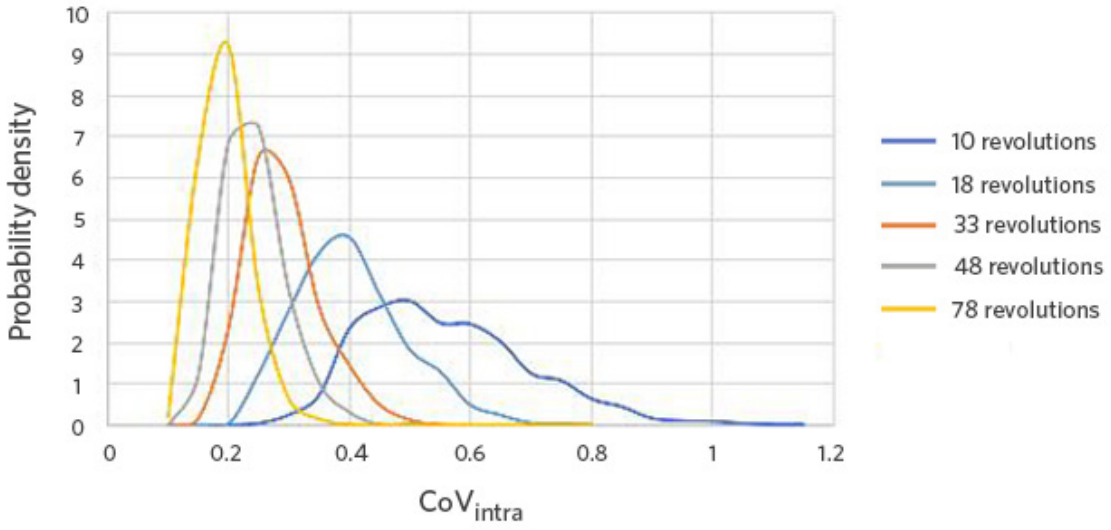


Figure 2. Probability distributions of individual tablet intra-tablet coating variabilities plotted for different numbers of pan revolutions. As the number of pan revolutions increases, the mean coating variability decreases along with the standard deviation in variability.

The team used discrete element method simulation since corresponding experiments would have been impractical to perform. And although DEM simulations themselves may take a lot of time, they require little oversight from the operator while the simulations run. Wassgren noted, "It is impractical, perhaps impossible, to measure the coating thickness variation over the entire surface of every tablet – at each instant throughout the whole spraying process. Simulation readily traces the interaction of particles with each other and system boundaries at every time step of the simulation. But more significantly, we can glean much more information from these studies compared to physical experiments."

Wassgren and his team found that intra-tablet coating variability correlated very well with the angular displacement of tablets as they pass through the spray zone. "The more a tablet tumbles in the spray zone of the coating pan, the better the coating. That finding will give us some ideas on how to improve the overall pharmaceutical coating process – such as agitating tablets just before the spray zone," Wassgren concluded. "Our research project was designed to improve the coating process, which in turn can improve overall product quality in the pharmaceutical industry."

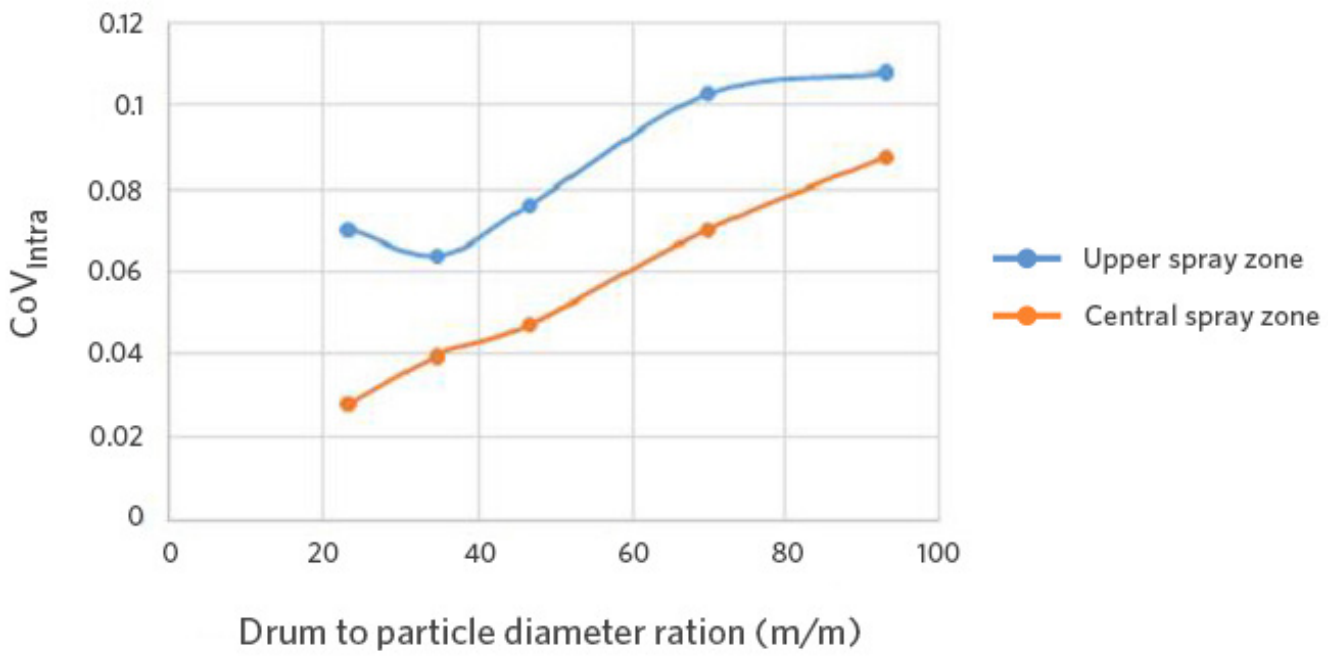


Figure 3. Asymptotic intra-tablet coating variability over all tablets as a function of drum-to-tablet diameter ratio for two different spray zone locations. Increasing pan scale results in tablets with larger asymptotic intra-tablet coating variability.

PROBLEM

To improve pharmaceutical industry processes related to spray-coating tablets, Purdue University researchers needed to identify how scale-up affects complex tablet dynamics in a coating pan. The goal was to identify intra-tablet coating variability.

SOLUTION

The team at Purdue University used Rocky DEM's polyhedral element capability to model tablets in coating pans of various sizes. A GPU-based algorithm was applied to determine exposure time of each tablet's surface area elements in a simulated spray.

BENEFITS

Rocky DEM simulations offered insight into how tablet mixing affects spray coating, a scenario that is impractical to accomplish with experimental studies. The software's GPU processing capability reduced the time needed to complete these lengthy simulations.

