NUMERICAL SIMULATIONS FOR TABLETING AND COATING

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Solid dose tablet manufacturing processes often lack reliability and robustness as a result of errors in production and a shortfall in process control. Facing unprecedented economic pressures, pharmaceutical manufacturing companies are continuously looking to improve on the quality of their products and the productivity of their processes. Multi-physics numerical simulation is emerging as a game-changing technology to help step up efficiency, enhance quality, and shorten time-to-market through virtual prototyping and optimization.

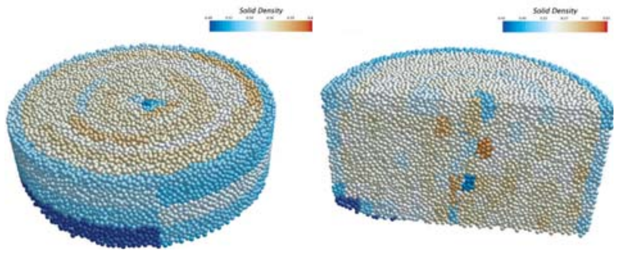

FIGURE 1: STAR-CCM+ simulation with DEM showing a pharmaceutical powder packed and compressed inside a tablet die. Variations in color reflect the non-uniformity of the granule distribution.

CHALLENGES OF SOLID DOSE TABLET MANUFACTURING

Tableting (compression from a powder into a solid dose tablet) and tablet coating are two vitally important steps in the tablet manufacturing process that ultimately determine the weight, thickness, density, hardness and coating of the final solid dosage form. Variability in any of these attributes not only negatively impacts the release profile and therapeutic efficacy of the medicine, it alters the disintegration and dissolution properties of the tablet, leads to tablet defects and causes breakage during bulk packaging and transport. With the adoption of novel manufacturing processes such as non-stop end-to-end processing, and the push to build quality and efficiency into production, solid dose tablet manufacturers have a challenging road ahead of them because they must pinpoint the key factors and requirements that will lead to robust and repeatable processes, resulting in superior products.

WHY NUMERICAL SIMULATIONS?

Multi-physics Computational Fluid Dynamics (CFD) is a numerical method for predicting the coupled behavior of fluid, gas and particulate flows including heat and mass transport. A significant advantage of using numerical simulations is that it allows for the validation of a design or process before physical tests need to be carried out. For example, the development of a new tablet shape or coating material calls for performing an extensive number of costly and time-consuming experiments to avoid unexpected variations, identify unpredictable process parameters and address scale-up problems. Studying these effects through numerical simulations can greatly reduce time, material and development costs. In addition, numerical visualization tools offer a wealth of detailed information, not always readily available from experimental tests. This not only results in an increased level of insight into the details of what is going on inside the processes, it enables innovation.

STAR-CCM+ PROVIDES THE SOLUTIONS

With its automated polyhedral meshing technology and comprehensive range of physics models, STAR-CCM+ is a complete multi-disciplinary simulation toolkit to tackle a wide range of applications in the pharmaceutical industry. One capability in STAR-CCM+ that is particularly well-suited for the simulation of tablet manufacturing processes is Discrete Element Modeling (DEM), fully coupled with numerical flow simulations and delivered in a single software environment.

Tableting and coating involve a large number of discrete particles that interact with each other and the fluids surrounding them. DEM accurately tracks these interactions and models contact forces and energy transfer due to collision and heat transfer between particles and fluids. The DEM capability in STAR-CCM+ can predict dense particle

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flows with more than one million particles in a reasonable time, making it practical for analyzing real-world tablet manufacturing processes such as filling, compressing/compacting, coating and drying.

Figure 1 shows the results obtained from a STAR-CCM+ simulation of pre-compression in a tablet press to determine how to overcome common tablet defects such as capping (splitting of the tablet's upper cap) that often occur as a result of entrapment of air and migration of fine particles during the compression process. DEM is used to track the interaction of the particles with each other and with the die as they are re-arranged and move into the empty spaces during pre-compression. This simulation offers a detailed look at the uniformity of the granule distribution and can help determine the optimal pre-compression force and dwell time required to ensure that fine particles will be locked in place before compression starts, greatly reducing the risk of incurring common tablet defects during production.

DEM simulations with particle-fluid interactions also provide realistic solutions to assess the uniformity of film coating thickness, a critical parameter for tablet quality. Figure 2 depicts a simulation performed with STAR-CCM+ for the coating process in a fluidized bed where DEM is used to analyze the random movement of particles as their trajectories change while layers of coating are applied. Parameters such as particle velocities, residence time and coating thickness are monitored during the simulation. These can be fed as objective functions into Optimate, a module in STAR-CCM+ that enables intelligent design, to help identify the important factors for equipment design (e.g. nozzle spacing) and to determine optimal equipment operating conditions.

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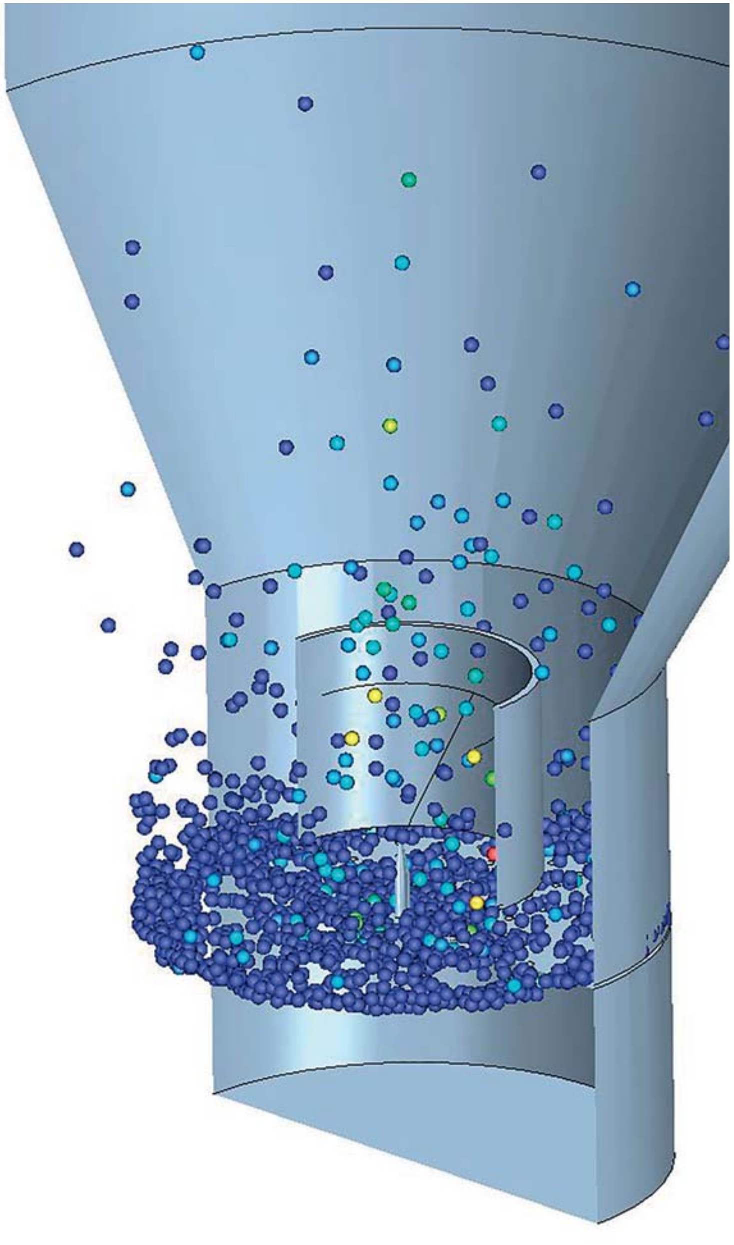

FIGURE 2: STAR-CCM+ simulation of the coating process performed in a fluidized bed

In today's competitive climate, manufacturing of solid dose tablets must have a focus on building quality and efficiency into the processes. This can be accomplished through rapid prototyping and optimization using multi-physics simulation.

passive scalar capability, enabling the user to easily monitor the coating thickness and other features of tablets. Figure 3 illustrates a case where 70,000+ tablets are tumbled in an industrial coater. The goal of the study is to improve on inter-particle coating uniformity by determining optimal spraying equipment settings in the tumbler. Two Lagrangian passive scalars representing coating thickness are defined: one with source volume confined to one cone above the surface, another with source volume confined to two cones and with an effective spray area identical to the one of the first passive scalar. Using this approach, a single simulation allows for a comparison of the inter-particle coating uniformity for two different spray zones and the result indicates that the two-spray configuration provides a more uniform coating distribution.

CONCLUSION

In today's competitive climate, manufacturing of solid dose tablets must have a focus on building quality and efficiency into processes, and multi-physics CFD simulations offer a cost-effective way to achieve this through rapid prototyping and optimization. The complex flow-fields associated with tableting and coating can be addressed with ease by using the high-end physics models delivered by STAR-CCM+, including the powerful DEM and novel passive scalar capabilities. Users in the pharmaceutical industry are fully leveraging these state-of-the art technologies as it opens the door to explore innovative ways to improve quality, reduce cost and shorten time-to-market.

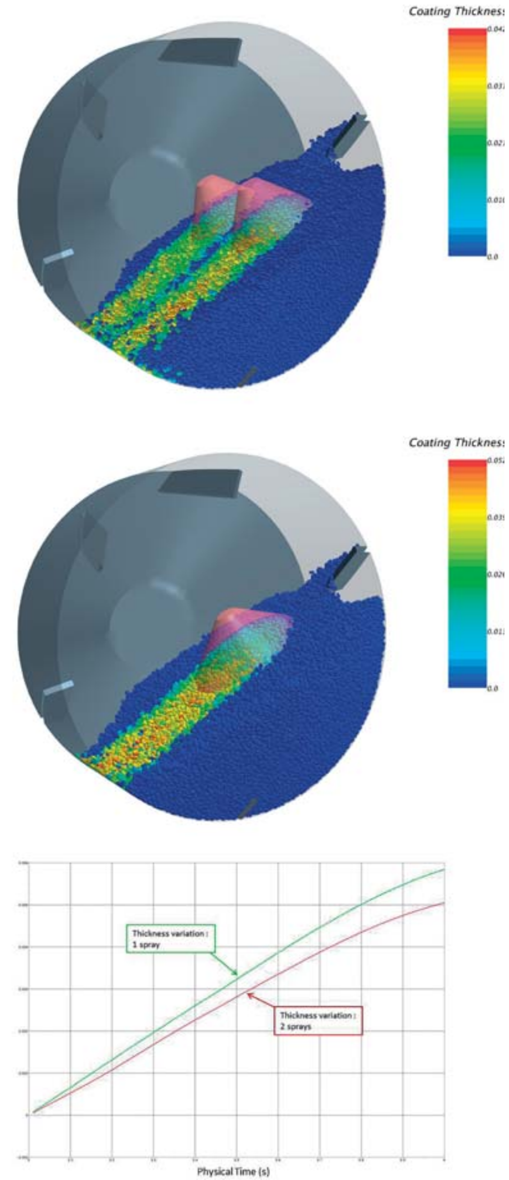

FIGURE 3: Simulation with STAR-CCM+ comparing coating thickness variation of one and two sprays in a tumbler