Two-dimensional PBM for simultaneous modelling of drying and breakage of pharmaceutical granules

S.T.F.C. **Mortier**[*,1,2], K.V. **Gernaey**[3], T. **De Beer**[**,2], I. **Nopens**[1]
[1] BIOMATH, Department of Mathematical Modelling, Statistics and Bioinformatics, Faculty of Bioscience Engineering, Ghent University, Coupure Links 653, 9000 Ghent, Belgium
[2] Laboratory of Pharmaceutical Process Analytical Technology, Department of Pharmaceutical Analysis, Faculty of Pharmaceutical Sciences, Ghent University, Harelbekestraat 72, 9000 Ghent, Belgium
[3] Department of Chemical and Biochemical Engineering, Technical University of Denmark, Building 229, 2800 Kgs. Lyngby, Denmark
* Severine.mortier@ugent.be
** Shared last authorship

The production of pharmaceutical tablets is the result of different subprocesses. The use of a wet granulation technique during tablet production requires subsequent drying of the wet granules, which can be achieved using several techniques. This choice potentially influences the properties of the granules and, hence, their further downstream processing. Here, a fluidized bed dryer is studied, which is part of a full continuous from-powder-to-tablet line, i.e. the ConsiGma™.

The development of mechanistic models is increasingly important, for example due to the ongoing transition from batch to continuous production processes and its accompanied need for improved process understanding. Models play a significant role in the latter, and, moreover, they facilitate process optimization and the development of control strategies.

During drying the fluidizing granules are prone to break up potentially resulting in smaller sized granules. The combination of breakage and drying can be modeled using a Population Balance Model (PBM). A PBM is a tool to analyse particles that are interacting with each other and the continuous phase. A one-dimensional PBM describing the evolution of the moisture content distribution during drying was developed in previous research. In this contribution, this model has been extended towards a two-dimensional PBM. The model now allows predicting the evolution of the granule size distribution as well as the moisture content distribution during drying. Several breakage mechanisms have been implemented. A differentiation can be made between granule breakage and surface erosion. Whereas in the first case two or more smaller particles are formed with a noticeable size, in the latter case fine dust is formed while the size of the mother particle remains almost identical. Several mechanisms have been theoretically investigated, i.e. erosion, the formation of two equal fragments, etc. Another important aspect is the rate of breakage. Both the breakage rate and the breakage mechanism will be influenced by several variables. The gas velocity during fluidization will have an impact on the breakage rate, where a higher gas velocity will increase the breakage rate. Furthermore, it can be expected that dryer particles will be more subjected to erosion compared to wetter particles. The form and the size of the particles will both influence the rate and the mechanism of breakage. Spherical particles are less prone to breakage compared to elongated particles.

In this study, the breakage behaviour during drying has been investigated theoretically by simulating the PBM for different breakage mechanisms and rates. The effect of the parameters in the kernels has been analysed in detail.