Application of Global Sensitivity Analysis As Preparatory Step for Reduction of a Drying Model of Pharmaceutical Granules

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Publication date:
2012

Document Version
Publisher's PDF, also known as Version of record

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Citation (APA):
A shift from batch towards continuous manufacturing is nowadays gaining interest in the pharmaceutical industry (Leuenberger, 2001). However, this transition requires detailed knowledge of all consecutive unit operations in a continuous manufacturing line in order to design adequate control strategies for guaranteeing product quality at all time. One hereby relies on in-process measurements of critical process and product parameters and real-time adjustment of input variables. Given the complexity of the system, the knowledge development can be facilitated by developing mechanistic models of the multi-phase systems in the process (Mortier et al., 2011). The need for a method of using the obtained model to systematically explore the sensitivity of the system’s output to the degrees of freedom according to their sensitivity has an influence on both drying time and behaviour. The output of the MC was further processed using a linear regression analysis at different time instants in both drying periods using the so-called Standardized Regression Coefficients (SRC) method (Saltelli et al., 2004; Saltelli et al., 2008).

Comparing the different sets of degrees of freedom it is obvious that the chosen combination of degrees of freedom for the sensitivity analysis has an influence on both drying time and behaviour. The output of the MC was further processed using a linear regression analysis at different time instants in both drying periods using the so-called Standardized Regression Coefficients (SRC) method (Saltelli et al., 2004; Saltelli et al., 2008).

As the regression analysis reaches no steady state, the moisture content for both drying phases has to be compared after a certain time has elapsed. The average moisture content for one simulation would be another way of selecting an output to perform the sensitivity analysis. The SRC of the gas temperature was found to be 0.93, clearly higher than the SRCs for the other degrees of freedom (ranging between 0-0.29). This indicates that gas temperature is by far the most influential degree of freedom in the first drying phase regardless of the values of the other degrees of freedom. For the second drying phase two time instants were selected: respectively 1 and 11 seconds after the start of the second drying phase. After 1 s the R was 0.75, while after 11 s the R dropped to 0.54 indicating strong non-linear behavior for which the applied GSA method is no longer valid (other GSA techniques should be used here, but this was considered to be outside the scope of this work). For this reason, the output after 1 s was used to rank the degrees of freedom. The gas temperature with an SRC of 0.87 was again found to be the most sensitive degree of freedom.
variable was selected to perform the reduction of the full drying model.


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