Proposition de sujet de thèse – 2022

Title: AMACOP - Multiscale Approach to Adhesion during Pharmaceutical Compression

Supervisor(s): Pr. Eric Lesniewska / Dr. Eric Bourillot
Laboratory / Department / Team: ICB UMR CNR 6303 / Dept. Nanosciences / Team OSNC
Collaborations: Institut I2M u. Bordeaux (Pierre Tchoreloff)

Challenge

AMACOP project addresses a **new and crucially important question**, the development of a Multiscale Approach to Adhesion during Pharmaceutical Compression.

Understanding and predicting the cohesion that a pharmaceutical tablet acquires during the process, knowing the properties of the powders used, is currently a challenge for several reasons.

The first reason is the structure of the tablet itself. It is indeed a porous medium, containing pores of different sizes, shapes, and orientations. The distribution of mechanical stresses inside the material, subjected to compression loading in a matrix, is therefore complex with the existence, at the microscopic level, of stress concentrations and gradients (Plassard et al., 2004) which will play a major role in the cracking phenomena.

The second reason comes from the mechanisms at play during compression, involving both elastic and plastic deformations of the grains. These deformations will create the contact surfaces between the grains and allow the implementation of the phenomena of adhesion. Nevertheless, now of stress relaxation, the influence of the relaxation of the elastic stresses greatly complicates the behaviour of the compact (Hiestand, 1991). Moreover, due to the nature of the materials used in the pharmaceutical field, and the speed at which the compression of the powder is carried out (the duration of the compression/decompression cycle is, at most, a few tens of milliseconds), viscous components intervene in the deformations (viscoelasticity, viscoplasticity) which have an important effect on the development and evolution of the stress fields at the microscopic level. Viscoelastic effects have a strong impact on the local stresses at the time of decompression and until after the ejection phase and thus play an important role in the appearance of defects.

The third reason is related to the development of adhesion itself. Indeed, the surface energy at the interface between the powder particles depends on physical phenomena at the molecular level (crystalline conformation, specific surface for example). These phenomena are influenced not only by temperature and water content, but also and above all by the stress state itself, which naturally depends on the compression cycle. Moreover, a pharmaceutical tablet always consists of a mixture of products with different mechanical and physico-chemical properties, which further complicates the interactions at the microscopic level.

The aim of this PhD project is therefore to develop a multi-scale approach, both analytical and numerical, in order to advance in the construction of a numerical twin of the compression process by characterizing the acquisition and maintenance of cohesion in the pharmaceutical tablet during the whole compression cycle and until the ejection of the matrix.

From an economic point of view, developing a methodology that would allow upstream, during formulation, to predict the cohesion of tablets to prevent (the aspect of predictivity is extremely important here) these phenomena could allow important gains in both quality and productivity.

Our approach is part of the current implementation of the "quality by design" approach in the pharmaceutical industry which consists in guaranteeing the quality through the construction of the process and not through a control at the end of the process. Our project must allow to define critical parameters for the product/process couple in connection with critical quality attributes for the tablets to allow the production of tablets of satisfactory mechanical resistance.

This project is in line with the priorities of the PowderON regional research and economic development plan supported by Dijon Metropole.

Knowledges required: Physics, nanoscale characterization, numerical simulation, open for multidisciplinary collaboration

Contacts: Eric Lesniewska (lesniew@u-bourgogne.fr) - Eric Bourillot (eric.bourillot@u-bourgogne.fr)