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Master Thesis subjects 2020-2021 proposed by *TIPs – Benoit Haut*

1. Towards a better understanding of the dynamics of bronchial mucus, in healthy and unhealthy people.

Summary:
Human bronchi are covered with a thin layer of mucus. This layer acts as a trap for inspired fine particles and microorganisms. The bronchial epithelium is also covered with cilia that, by their beating, move the mucus along the bronchial tree towards the trachea, where it is finally swallowed. The presence of this mucus and its displacement by the cilia is therefore fundamental to prevent lung infections. However, today, the dynamics of the bronchial mucus is still poorly understood. In addition, it is known that, in the context of certain diseases such as asthma and cystic fibrosis, this dynamics is significantly impaired. In collaboration with the pulmonology department of the Erasme Hospital, the aim of this Master thesis is to improve the understanding of the bronchial mucus dynamics by combining *in silico* (modelling and simulation) and *in vitro* (laboratory experiments) studies. A specific objective could be to analyse the coupling, potentially very important, between the rheology of the mucus and the respiratory conditions (respiration frequency, breathing air temperature and humidity…). This will be achieved by laboratory measurements performed on synthetic/real mucus (rheological measurements and drying experiments under controlled conditions), as well as through the development of mathematical models of water vapor and heat transport phenomena in the first generations of the bronchial tree.

Supervisor: Benoit Haut (bhaut@ulb.ac.be) and Alexandra Buess

2. New insights in exhaled NO in future space environments.

Summary:
In the lungs, nitric oxide (NO) is produced by the airway epithelium and is a well-known marker of lung inflammation. The molar fraction of NO in the exhaled air (FENO) is very easy to measure with small devices and, therefore, is ideal to monitor inflammatory status (for instance in asthmatic patients). In a space context, the NO could be used to monitor pulmonary airway inflammation after, for example, toxic dust inhalation on the Moon or Mars. Accordingly, with our partners from the Karolinska Institute (Sweden), we have performed experiments, which will be analysed during this Master thesis, on the International Space Station (ISS), in order to measure the FENO of astronauts in altered conditions (gravity, ambient pressure), independently from an inflammatory state. Indeed, it is well known that NO is also a marker of non-inflammatory changes in the lungs, as airway calibre modifications. Such changes might occur in microgravity or reduced pressure conditions. Therefore, they have to be precisely characterized to be able to accurately estimate changes in the exhaled NO actually due to an inflammation process in the frame of long-term space missions. Comparisons will be made with ground controls at normal and reduced gas density. The NO results will be interpreted through mathematical modelling of NO transport incorporating molecular diffusion, a realistic axial NO production and gravity-dependent alveolar diffusion rate. The results of this study are expected to provide new insights in exhaled NO in future space environments and, more generally, in the NO turnover in the lungs.

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2. Movements of the arterial system induced by blood circulation. Towards a better understanding of the effect of prolonged low gravity conditions of the cardiac system.

Summary:
Ballistocardiography (BCG) is a medical technique consisting in measuring, thanks to sensors, the small movements of the body induced by the blood circulation. It is used in particular on the International Space

Station, to monitor the time evolution of the heart health of astronauts. Measured signals have been shown to be good indicators of the heart function. In this Master thesis, in collaboration with the cardiology department of the Erasme Hospital, we propose to develop the fundamental scientific knowledge behind BCG. For this purpose, a mathematical model of the body movements induced by the circulation of blood in the arteries will be established, by the combination of fluid mechanics and rational mechanics approaches. In this model, the very specific flow of blood in the aorta could be characterized by the combination of MRI Imaging and Computational Fluid Dynamics (CFD). Then, this model will be simulated and challenged against BCG signals obtained on Earth, under bed rest conditions (i.e., simulating microgravity), and on astronauts in the International Space Station. This should provide new insights into this promising technique for the monitoring of the heart function, as well as applied results related to space research.

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4. Instrumented nasal cast for nose-to-brain drug delivery.

Context:

Nose-to-brain drug delivery is a very promising way to deliver drugs. For this purpose, the airflow generated by a spray device must convey the drug particles through the nose and deposit them in the so-called olfactive area. Since each patient nose anatomy is different, this process must be optimized to become patient specific. This work would be the follow up of two ongoing master theses. These theses allowed to develop a new nasal cast which is intended to be used for the study of drug deposition. Together with this experimental approach, numerical simulations will be carried on to get precise knowledge about the mechanisms driving nasal drug delivery.

Goals:

According to the student profile, we can consider two different theses (the topic can be duplicated):

Experimental

- Measure of drug deposition as a function of different parameters
- Draw the first guiding lines to optimise nasal drug delivery.

Computational

- Model the nasal cavity using a CFD software (Ansys-Fluent or OpenFOAM).
- Analyse the flow in the cavity under different breath patterns

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5. Microencapsulation of pharmaceutical active compounds by spray drying. A numerical and experimental optimization of the process.

Summary:

Microencapsulation is a formulation operation commonly encountered in the pharmaceutical industry. It typically consists of adding an "encapsulating" agent to a liquid solution containing a dissolved pharmaceutical active ingredient. Then, the solution is dispersed as fine drops in a hot air stream (in a device called a spray dryer). The subsequent evaporation of the solvent generates an increase of the encapsulating agent concentration within the drops (especially at the liquid-gas interface), until the onset of a sol-gel transition. The finished product is therefore a powder, with each particle composed of a "shell" of the encapsulating agent, containing the active ingredient, thus protected from the environment. Although used for a long time in industry, the physical and chemical mechanisms taking place during microencapsulation are still poorly understood today. Therefore, the goal of this Master thesis is to improve this understanding, through experimental studies (at different scales) and mathematical modelling. The aim is also to use, in a combined way, the experimental and modelling results in order to optimize the microencapsulation operation in a specific case: the encapsulation of gallic acid, a polyphenol with anti-oxidant and anti-oxidative properties.

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6. Intermittent drying of Baker's yeast pellets. A new way to improve the quality of the dried product?

Summary:

Yeasts are microorganisms widely used in the food industry (e.g. in the making of bread and beer). Yeasts are produced by fermentation. At the end of the fermentation, the culture medium is filtered and the filtration cake obtained is converted into small cylindrical or spherical pellets of one or two millimetres in diameter. Each of these pellets is an agglomeration of yeast cells, with water between them. In order to extend the shelf life of this product, the yeast pellets can be dried. However, this drying should be done with caution, as exposure to too high temperatures or too much removal of water can have a significant negative impact on the quality of the product (e.g. the ability of the yeasts to release CO_2, as part of bread making). In collaboration with the Puratos company, the aim of this Master thesis is to analyse the impact of an intermittent realization of the drying of yeast pellets on the kinetics of this drying and on the quality of the end product. By "intermittent", it is understood that the drying is carried out by successive phases of drying at high rate and drying at low (or zero) rate. It has already been shown for several products that such an intermittent drying can have beneficial effects on the quality of the end product. This analysis will be performed by the combination of drying experiments, at different scales (scale of a part of the porous medium, pellet scale and dryer scale), and mathematical modelling. The comparison of the experimental and modelling results should make it possible to highlight the key phenomena involved during an intermittent drying of yeast pellets and to understand their impact on the kinetics of the drying and on the quality of the end product.

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