**NovaFlow – Novel applications of a state-of-the-art oscillatory flow platform: hydroxyapatite production and its use in bone extracellular matrix growth**

Bioengineering Systems PhD  
University of Minho

**Background:** MSc. Biological Engineering, University of Minho, Portugal  
Portugal

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**Supervisors:** José Teixeira and António Vicente (UMinho)

**Research team:** F. Castro, A. Ferreira, A. Vicente, JA. Teixeira (CEB-IBB, UMinho); F. Rocha (LEPAE-Uporto); A.P. Marques (3B’s-IBB, Uminho)

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**Objectives**

The present project aims at synthesizing hydroxyapatite (HAp) crystals with a carefully controlled size, with a controlled and narrow size distribution and with a high purity. Thus HAp crystals shall be produced with a high specific surface area, i.e. small crystals, and a high biocompatibility, making them suitable for application in bone substitution.

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**Work Plan**

**Hydroxyapatite (HAp) production**
Characterization of the HAp precipitation process; optimization of the operation conditions; modelling of the HAp crystallization process

**Use of HAp particles in bone extracellular matrix growth**
Biological validation of the processes and the products developed

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**Results**

Initial experiments were performed in the reactor presented in Figure 1a. A saturated solution of calcium was mixed with a solution of phosphate with a molar ratio Ca/P=1.67 and T=37°C. The pH was continuously measured during HAp precipitation (Fig2), revealing the occurrence of three stages. In those stages the product was characterized through SEM analysis. As it is shown in Figure 2, the particles formed are very small (in the order of nanometers) and have the tendency to aggregate. Further, they have different morphologies during the process, passing through spherical form to needle-like form. The final product was analyzed by X-ray diffraction which confirmed it to be hydroxyapatite (Fig3).

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**Fig. 1.** a) Experimental crystallization apparatus, b) OFR developed by CEB-UMinho.  
**Fig. 2.** pH evolution during HAp precipitation and SEM images of the product developed at the different pH stages.  
**Fig. 3.** X-ray diffraction diagram corresponding to the final product of HAp precipitation.