OSCILLATORY FLOW REACTOR: A SOLUTION FOR CONTINUOUS BIOPROCESSING

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The usage of aqueous two-phase extraction (ATPE) and precipitation have been proven as efficient operations for the clarification and purification of biological products. ATPE has had limited use at a large scale and the majority of the ATPE studies are still done in batchwise mode. Few existing studies of continuous ATPE report problems such as flooding, emulsification, backmixing and low separation efficiency of the phases that are responsible for a decrease in operation yield compared with batch systems. Continuous precipitation also appears to be an attractive alternative to improve the current purification platform and reduce its high costs since it is low-cost, high yield and easily scalable. However, this process has been done using stirred tank and continuous tubular reactor, raising disadvantages as shear forces and low mixing efficiency, in the former, and high superficial velocities, in the latter.
Oscillatory flow reactor (OFR) (Figure 1) is a type of tubular/channel reactor that has been used in processes as liquid-liquid reaction, polymerization, flocculation and crystallization. One of the most important features of this type of reactor is the uniform mixing that is provided by the combination of the periodically spaced restrictions and the oscillatory motion of the fluid. Therefore, the continuous mode and the particular characteristics of OFR could be the answer to more cost-competitive continuous ATPE and precipitation.

a) b)

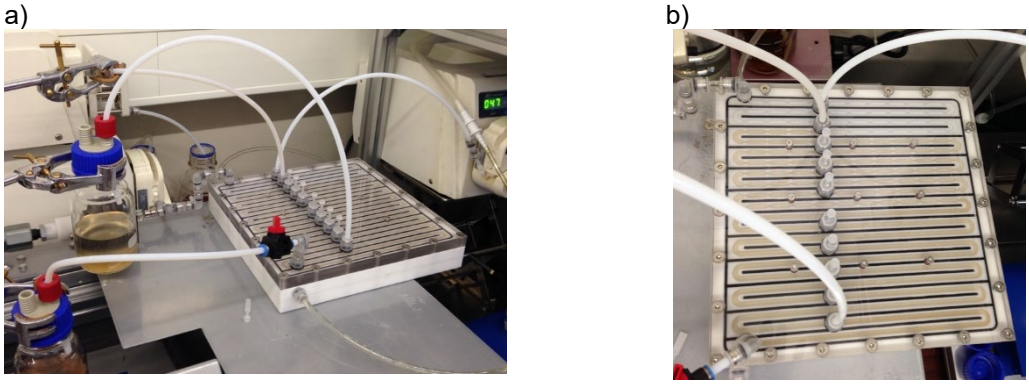

Figure 1 – Continuous ATPE apparatus (a) and oscillatory flow reactor detail (b).

This work can be divided into two sections. In the first one, the partition of a pure industrial enzyme – α-amylase from *Aspergillus oryzae* – in different polyethylene glycol (PEG)/phosphate systems was studied in batch, and the compositions presenting the highest yield of partition to the top phase were transferred to OFR, where different conditions for frequency and amplitude of oscillation, and total mass flow were evaluated. Using a system composed of 20% (w/w) PEG1500 and 9% (w/w) potassium phosphate, pH 7.4, the yield of partition to the top phase in the batch systems was 86%, while in the continuous ATPE in the OFR these values were between 77% and 95% for three different frequencies (1, 3 and 5 Hz), amplitudes (1, 2 and 3 mm) and total mass flows (4, 32 and 60 g/min). In the second section, it was studied the PEG/zinc chloride ($ZnCl_2$) precipitation of antibodies from an artificial mixture mimicking the supernatant of antibody-producing cells. The process was first optimized in batch and further implemented in the OFR under continuous operation, where the influence of mixing intensity was investigated. Continuous precipitation carried out in the OFR with 14% PEG6000 and 4 mM ZnCl2 enabled the recovery of over 99% of antibodies with 90% purity. These results show that OFR can be successfully used for continuous ATPE and precipitation, opening a door to their widespread use by industry.