Miniaturized Experimental Toolbox for -Transaminase Technology (BIOINTENSE)

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Introduction:

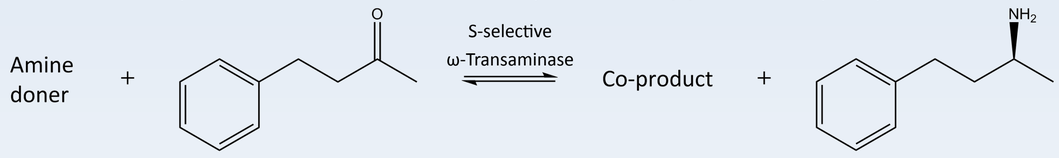
The next generation biocatalytic processes in industry face new challenges, e.g. high concentration operation, unfavourable reaction equilibrium, complex molecule formation, minimum environmental impact, etc. [1]. Significant work is therefore required for development of the biocatalyst and process to fit commercial requirements. It is quite demanding to find the best biocatalyst and process combination to fit industrial requirements, especially with respect to the limited resource availability at an early stage of development.

BIOINTENSE, an EC FP7 funded program, has focus on developing toolboxes capable of accelerating biocatalyst and process development through the use of modular microsystem platforms. Operation at micro-scale enable better process control, low consumption of resources, fast process evaluation, as well as rapid mass and heat transfer [2, 3].

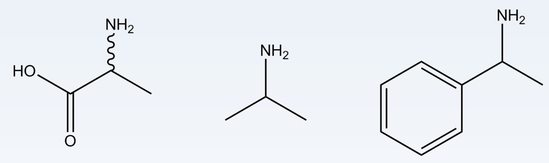
BIOINTENSE will deliver 3 types of platforms (figure 1): 1) High data content biocatalyst screening platforms, 2) generic process development platforms operated by the plug-and-play principle, 3) production platforms for product synthesis.

The platforms will be developed for ω-transaminase-catalysed reaction systems, scheme 1. These systems are quite interesting due to the highly unfavourable equilibrium of such reactions and the severe inhibiting effects of both substrates and products, although there are also systems enabling complete conversion. [4, 5, 6, 7].

Scheme 1: Example of reaction scheme from benzylacetone to (S)-3-amino-1-phenylbutane



Different amine donors: alanine, isopropylamine, and methylbenzylamine



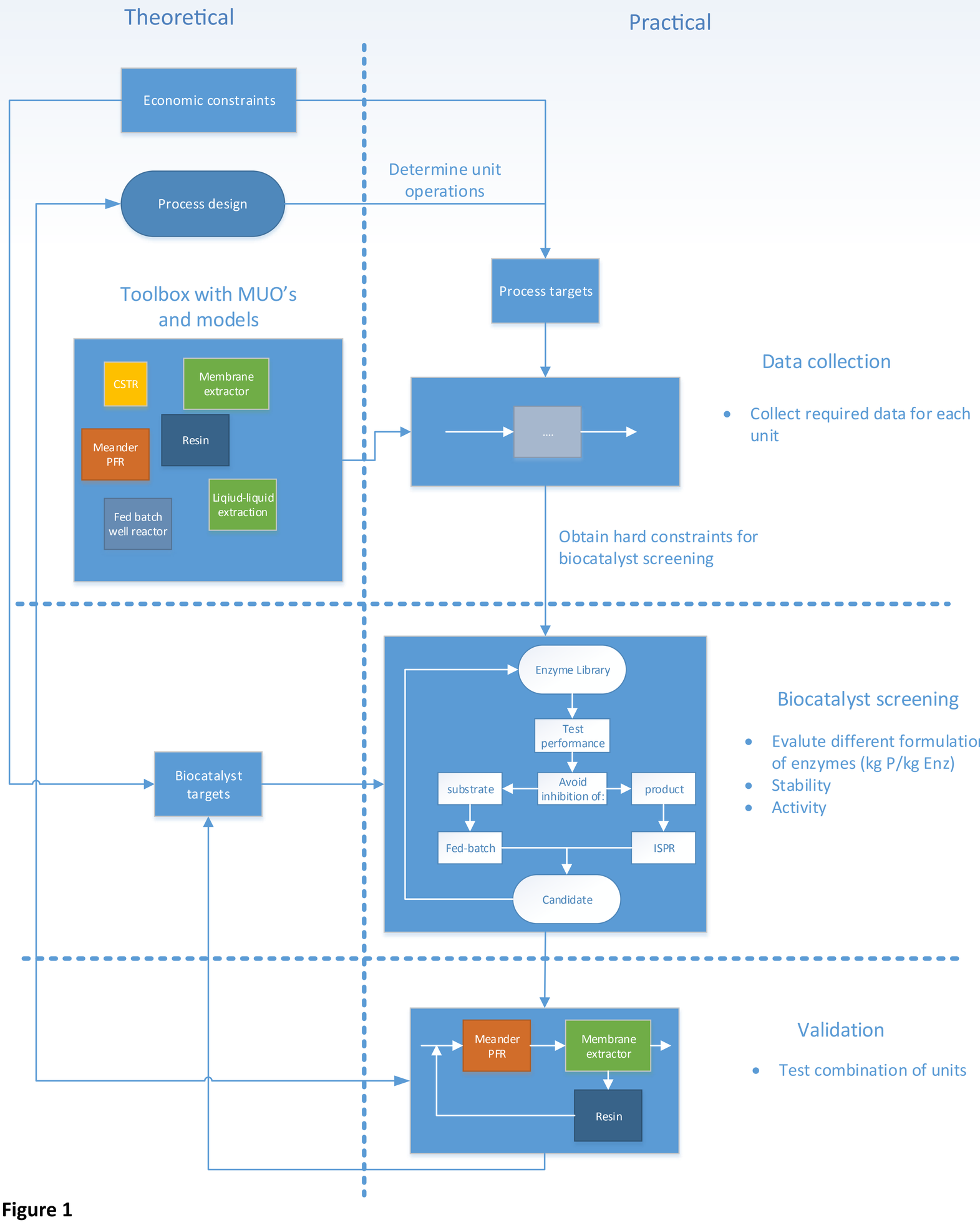


Figure 1

Platform 1

As a result of the theoretical process design unit operations (MUO's—Miniaturized Unit Operations) are chosen for data collection, constrained by economic assessment. The collected data will provide hard constraints for the biocatalyst performance.

Platform 2

The target from platform 1 will be reached by development of the biocatalyst through protein engineering. The mutants will be evaluated by high content screening methods.

Platform 3

By combining the process design and developed biocatalysts, system validation of the production platforms is performed by synthesis of the product-in-the-bottle as final evaluation.

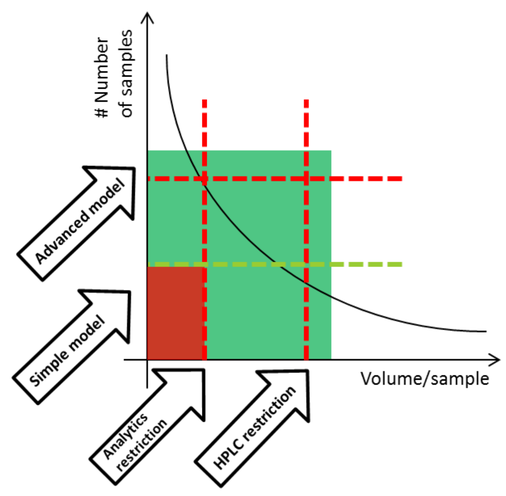


Figure 2

The quality of models is to a large extent determined by the number of experimental data points available (Figure 2). Conventional analytics require certain sample quantities, limiting the number of samples that can be collected. Micro-scale operations can offer solutions to these requirements.

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