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Generic flowsheet model for early inventory estimates of industrial microbial processes. II. Downstream processing

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ABSTRACT

To ensure optimal process flowsheet selection it is valuable to conduct environmental and economic comparisons at an early stage of technology selection and process design. However, the data that is needed to perform these studies are not available at this stage of process development. This is also true for bioprocess systems. To overcome the lack of data, the CeBER (Centre for Bioprocess Engineering Research, University of Cape Town) Bioprocess Modeller was developed to provide material and energy values for industrial microbial processes.

This paper presents the downstream processing portion of this flowsheet. The model allows for solid–liquid separation, cell disruption, concentration and formulation units as required. The model allows section of appropriate downstream processing units include, amongst others, centrifugation, filtration, precipitation and freeze-drying. At each downstream processing stage, non-reacting and reacting chemicals can be added. The model provides both a material inventory as well as the calculation of the energy input required and waste heat generated.

Additionally, the model includes a database of values (including constants, operating conditions and others), drawn from various industrial norms and academic sources. Should specific information not be known, the model selects the most appropriate values based on other decisions made through the model.

1. Introduction

For microbial bioprocesses, it is accepted that the relative economic importance of the production and downstream stages is highly dependent on the product value and purity required. The relative importance of these stages with respect to environmental burden has yet to be addressed. Process flexibility decreases as the level of definition increases in the system; hence it is valuable to be able to analyse the potential for combined process sustainability as well as technical and environmental feasibility during the early stages of design. To achieve this, estimates of the material and energy inventories are required.

In order to obtain easy access to accurate material and energy inventory data for the modelling of industrial bioprocesses at the early stages of process design, a Microsoft®

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Table 1 – Literature review of commonly used downstream process units.

Product (Microorganism)	Separation[a]	Concentration and Purification[b]	Formulation[c]	Reference
Anthracycline antibiotics (*Streptomyces* sp., *E. coli*)	Broth filtration, solvent extraction ($CHCl_3$, butanol) centrifugation	Precipitation (dissolved with *n*-butanol. Acetone added)	Freeze drying	(Flickinger, 1985)
Cephalosporins	Filtration (rotary drum), solvent extraction (methyl isobutyl ketone)	Precipitation (acetone added), adsorption (Activated carbon, non-polar resins), enzyme treatment		(Smith, 1985)
Cephamycin	Solvent extraction (acetone (aq.), 50% v/v.)	Evaporation		(Omstead et al., 1985)
Citric Acid (*Aspergillus niger*, yeasts)	Filtration, solvent extraction (butan-2-ol, tributyl phosphate), centrifugation	Precipitation (calcium citrate)		(Milsom and Meers, 1985a)
Glycerol (*Aspergillus niger*)	Broth filtration, centrifugation	Precipitation, evaporation, ion exchange	Spray drying	(Milsom and Meers, 1985b)
Itaconic acid (*Aspergillus terreus*)	Broth filtration, centrifugation	Precipitation, evaporation		(Milsom and Meers, 1985b)
Lactic acid (*Lactobacillus* sp.)	Filtration, solvent extraction, distillation	Precipitation, evaporation		(Vickroy, 1985)
Lincomycin (*Streptomyces* sp.)	Filtration (4.0% filter aid before filtration. Water washed), solvent extraction (activated carbon, *n*-butanol)	Ion exchange (cationic resins), partition chromatography (cyclohexane, methyl ethyl ketone)	Freeze drying	(Gonzales and Miller, 1985)
Penicillin G or V (*Penicillium* sp.)	Filtration (rotary vacuum drum), solvent extraction (amyl acetate, butyl acetate, cyclic ketones)	Precipitation (potassium or sodium added), centrifugation or filtration	Drying (pre-dried with anhydrous isopropyl alcohol, butyl alcohol. Dried with warm air, vacuum or radiant heat)	(Swartz, 1985)
Polysaccharides (*Xanthamonas campestris*, *Pseudomonas aeruginosa*)	Centrifugation, milling	Precipitation (alcohol, salt and acid)	Forced air or vacuum drying	(Margaritis and Pace, 1985)
Streptomycin	Broth filtration	Precipitation, adsorption (activated carbon, non-ionic resins, alcohol, acid)		(Florent, 1985)
Thienamycin (*Streptomyces* sp.)	Pressure rotary filtration	Adsorption (Dowex 1 × 2 (HCO_3^-) resin)		(Buckland et al., 1985)
Yeasts (Bakers') (*Saccharomyces cerevisiae*, *S. uvarum*, *S. carlsbergensis*)			Freeze-, Roto-Louvre-, through circulation-, air-lift- and spray drying	(Chen and Chiger, 1985)
Yeast (*Saccharomyces cerevisiae*)	Filtration (plate and frame), centrifugation			(Smith, 1985)

[a] Separation is defined as solid liquid separation.

[b] Concentration and purification are meant as the same thing here. This is the increase in product purity by any means of downstream processing. Strictly speaking, this may also include the unit operations defined in separation and formulation.

[c] Formulation is defined as the final stage in downstream processing. It includes processes aimed at reducing the moisture content of the product. Typical examples include oven drying, freeze drying and spray drying.