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A superstructure-based framework for bio-separation network synthesis

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ABSTRACT

Modern biotechnologies enable the production of chemicals using engineered microorganisms. However, the cost of downstream recovery and purification steps is high, which means that the feasibility of bio-based chemicals production depends heavily on the synthesis of cost-effective separation networks. To this end, we develop a superstructure-based framework for bio-separation network synthesis. Based on general separation principles and insights obtained from industrial processes for specific products, we first identify four separation stages: cell treatment, product phase isolation, concentration and purification, and refinement. For each stage, we systematically implement a set of connectivity rules to develop stage-superstructures, all of which are then integrated to generate a general superstructure that accounts for all types of chemicals that can be produced using microorganisms. We further develop a superstructure reduction method to solve specific instances, based on product attributes, technology availability, case-specific considerations, and final product stream specifications. A general optimization model, including short-cut models for all technologies, is formulated. The proposed framework enables preliminary synthesis and analysis of bio-separation networks, and thus estimation of separation costs.

1. Introduction

The last decade has seen significant progress in metabolic engineering and synthetic biology (Tee et al., 2014; Angermayr et al., 2015; Knoop and Steuer, 2015; Jullesson et al., 2015; Liao et al., 2016). These advances enable the use of engineered microorganisms such as *E.coli*, yeast and algae for the production of chemicals that are currently derived mainly from fossil fuel feedstocks (Gavrilescu and Chisti, 2005; Wilson and Roberts, 2014; Clark et al., 2014; Bornscheuer and Nielsen, 2015; Zhang et al., 2016). Advantages of bio-processes include mild production conditions and good selectivity toward a specific product (Kiss et al., 2015). However, the effluent of the bioreactor is typically dilute (containing less than 20 wt% product), and thus the downstream separation tends to be expensive, typically accounting for 60–80% of the total production cost (Kiss et al., 2015; Brandt and Schembecker, 2016). Thus, the synthesis of an effective downstream process is one of the major challenges (Nishida et al., 1981; Siirola, 1996; Barnicki and Siirola, 2004; Westerberg, 2004; Li and Kraslawski, 2004; Noble and Agrawal, 2005; Grossmann and Guillen-Gosalbez, 2010; Kravanja, 2010; Cremaschi, 2015).

The synthesis of bio-separation processes is challenging for the following reasons: (1) multiple technologies are usually available for a given separation task, and thus a large number of alternative process configurations exists; (2) many bio-based chemicals require processing under mild conditions, and thus certain separation technologies (e.g., distillation) are sometimes excluded; and (3) the product physical properties and the bioreactor effluent composition are not uniform across chemicals, but rather specific. Methods used for process synthesis generally include enumeration of alternatives, evolutionary modification, and superstructure optimization (Biegler et al., 1997). In enumeration of alternatives, alternative designs are generated and evaluated, which is only feasible when the number of alternatives is relatively small. In evolutionary modification, designers make changes to known flowsheets for similar processes to meet new objectives and constraints (King et al., 1972; Douglas, 1985, 1988; Smith and Linnhoff, 1988). Superstructure optimization is a model-based approach that compares alternative processes simultaneously (Grossmann and Daichendt, 1996; Biegler et al., 1997; Barnicki and Siirola, 2004; Liu et al., 2010; Cremaschi, 2015). A superstructure incorporates a

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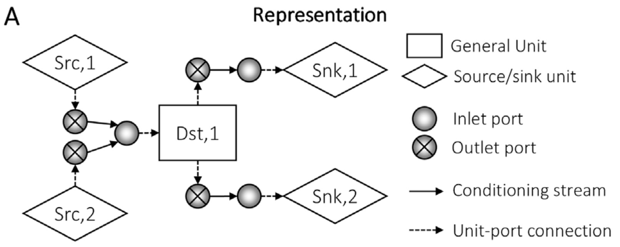

B Generation

- **Four basic sets**

$\mathbf{C}_p^{\mathrm{F}}/\mathbf{C}_p^{\mathrm{M}}$: feasible/minimal component of inlet port $p \in \mathbf{P}_{\mathrm{in}}$
$\mathbf{C}_{p'}^{\mathrm{F}}/\mathbf{C}_{p'}^{\mathrm{M}}$: feasible/minimal component of outlet port $p' \in \mathbf{P}_{\mathrm{out}}$

- **Four connectivity rules**

Rule 1: $\mathbf{C}_{p'}^{\mathrm{M}} \subseteq \mathbf{C}_p^{\mathrm{F}} \quad \forall\, p \in \mathbf{P}_{\mathrm{in}}, p' \in \mathbf{P}_p$; Rule 3: $\mathbf{C}_p^{\mathrm{M}} \cap \mathbf{C}_{p'}^{\mathrm{F}} \neq \emptyset \quad \forall\, p \in \mathbf{P}_{\mathrm{Rct,in}}, p' \in \mathbf{P}_p$;
Rule 2: $\mathbf{C}_p^{\mathrm{M}} \subseteq \bigcup_{p' \in \mathbf{P}_p} \mathbf{C}_{p'}^{\mathrm{F}} \quad \forall\, p \in \mathbf{P}_{\mathrm{in}}$; Rule 4: $\mathbf{C}_p^{\mathrm{M}} \cap \mathbf{C}_{p'}^{\mathrm{F}} = \mathbf{C}_p^{\mathrm{M}} \quad \forall\, p \in \mathbf{P}_{\mathrm{Spr,in}}, p' \in \mathbf{P}_p$

Fig. 1. Superstructure representation and generation methods developed by Wu et al. (A) Representation; (B) generation. “Src”=source; “Snk”=sink. In (B), $\mathbf{P}_{\mathrm{in}}/\mathbf{P}_{\mathrm{out}}$ denotes inlet/outlet port; $p' \in \mathbf{P}_p$ indicates that port p' is connected to port p.

large number of alternative units and relevant interconnections. It has been proposed for the synthesis of separation networks (Novak et al., 1993; Eden et al., 2004; Marquardt et al., 2008; Dowling and Biegler, 2015), and the development of bio-refineries and bioprocesses (Kokossis et al., 2010; Kokossis and Yang, 2010; Schaber et al., 2011; Rizwan et al., 2013; Yuan et al., 2013; Kelloway and Daoutidis, 2013; Kim et al., 2013; Mascia et al., 2013; Gonzalez-Delgado et al., 2015; Kong et al., 2016). However, these studies were mostly performed for specific products, on a case-by-case basis. The work presented herein focuses on the development of a general framework for bio-separation network synthesis.

In terms of superstructure representation, which is the first step in addressing the process synthesis problem, there are multiple approaches: State Task Network (STN) (Kondili et al., 1993); State Equipment Network (SEN) (Smith, 1996; Yeomans and Grossmann, 1999); P-Graph (Friedler et al., 1992, 1993); R-Graph (Farkas et al., 2005); and the recently proposed Unit-Port-Conditioning Stream (UPCS) approach (Wu et al., 2016).

Based on the selected representation approach, a superstructure is then generated, often by combining specific processes, or subsystem superstructures (e.g. reaction networks, separation networks, heat recovery networks, etc.) each pre-designed via system-specific methodologies (Stephanopoulos and Westerberg, 1975; Kocis and Grossmann, 1989; Yee and Grossmann, 1990; Kravanja and Grossmann, 1990, 1993; Lakshmanan and Biegler, 1996; Schweiger and Floudas, 1999). There are also general rule-based systematic approaches that aim to generate simple superstructures containing all relevant structural alternatives (Friedler et al., 1992, 1993; Tula et al., 2015; Wu et al., 2016).

Based on this superstructure, an optimization model is then formulated. In general, this model includes sets of equations describing units, their interconnections, equations for thermodynamic property calculations, etc. The model is often formulated as a mixed integer non-linear programming (MINLP) problem. The modeling of units can be performed in various ways, generally using simplifications, such as shortcut models (e.g. Fenske-Underwood equations for distillation columns) (Vausa and Marquardt, 2000; Caballero and Grossmann, 2001; Bao et al., 2011) and surrogate models (Caballero and Grossmann, 2008a,b; Henao and Maravelias, 2011; Zhang and Sahinidis, 2012; Boukouvala and Ierapetritou, 2013; Agarwal and Biegler, 2013; Eason and Cremaschi, 2014; Cozad et al., 2014; Biegler et al., 2014; Yu et al., 2015; Rogers and Ierapetritou, 2015). Also, in pharmaceutical product and process development, ontologies have been used for efficient model development and management (Venkatasubramanian et al., 2006; Suresh et al., 2010; Hailemariam and Venkatasubramanian, 2010). The solution of the optimization model identifies the best process along with the optimal operating conditions for all units. For a review of MINLP and global optimization solution algorithms, the reader is pointed to past works (Arora et al., 1995; Tawarmalani and Sahinidis, 2004; Floudas and Chrysanthos, 2009; Burer and Letchford, 2012; Horst and Pardalos, 2013; Nallasivam et al., 2013; Trespalacios and Grossmann, 2014; Boukouvala et al., 2016).

In this work, we develop a framework for bio-separation network synthesis, which allows the generation of the optimal separation processes for liquid and solid chemicals that can be produced using microorganisms. The framework provides guidance on the preliminary synthesis of separation networks, thereby aiding the analysis of bio-based chemical production technologies.

The remaining of the paper is structured as follows. In the next section, we present our superstructure representation and generation approaches. In Section 3, we provide a general overview of our framework. In Section 4, we discuss the generation of stage-superstructures. In Section 5, we present the stage-superstructures. In Section 6, we discuss the general superstructure. In Section 7, we present methods to generate a reduced superstructure for specific instances. In Section 8, we discuss our modeling approach, and in Section 9, we present three case studies.

2. Background

In this work, we adopt the superstructure representation and generation methods developed by Wu et al. (Wu et al., 2016), which are briefly summarized in Fig. 1. In terms of representation (“UPCS”), three basic elements are adopted (Fig. 1A): units (u), ports (p), and conditioning streams (s). A unit is indexed by a unit type (ut) and a unit number (un), e.g. “Dst,1” refers to the unit of unit type “Dst (distillation)” and unit number “1”. We also refer to unit type as “technology” hereafter. In addition to general units, source units and sink units are included as auxiliary elements whose functions are to provide raw materials and collect the final product stream and wastes. Every unit type has a predefined set of inlet and outlet ports, e.g. membrane units have one inlet port- for the feed stream, and two outlet ports- one for the permeate stream and the other for the concentrate stream. The inlet ports are generally treated as mixers, and the outlet ports are treated as splitters. Thus, a port is indexed by a unit, a port type (pt: in/out) and a port number (pn). Conditioning streams (referred to as “streams” hereafter) act as connections between outlet and inlet ports, while also performing temperature and pressure conditioning tasks. A stream is indexed by an inlet and an outlet port. Since the focus of this work is on preliminary synthesis and analysis of separation networks, we adopt simple models. Specifically, we neglect the conditioning function of streams and regard them as simple connections instead. Calculation of the stream conditioning duties is incorporated into the unit models, with simplifying assumptions. For example, the reboiler heating duty of a distillation unit is approximated as the latent heat of vapor in the column plus the energy required to heat up the feed stream from the feed temperature (usually 25 °C) to its boiling point (see Supplementary material for example). Since each connection between ports represents a stream, we use the terms “connection” and “stream” interchangeably hereafter.

In terms of generation (see Fig. 1B), four connectivity rules based on “minimal” and “feasible” component sets (components that are “required” and “allowed”, respectively, to be present in the ports during the normal operation of their units) are implemented for the generation of simple superstructures (Wu et al., 2016).