

PROCESS DESIGN AND CONTROL

Holistic Approach to Process Retrofitting: Application to Downstream Process for Biochemical Production of Organics

Jiahong Liu and L. T. Fan*

Department of Chemical Engineering, Kansas State University, Manhattan, Kansas 66506

Paul Seib

Department of Grain Science and Industry, Kansas State University, Manhattan, Kansas 66506

Ferenc Friedler and Botond Bertok

Department of Computer Science, University of Veszprém, Veszprém, Egyetem u. 10 H-8200, Hungary

A novel holistic approach is proposed for process retrofitting. Unlike conventional approaches, the proposed approach totally resynthesizes the entire process by incorporating the operating units with enhanced performances. As such, it can take into account all possible outcomes, including the inevitable restructuring of the flowsheet's network structure. Naturally, the proposed approach can be executed by resorting to the efficient graph-theoretic method based on P-graphs that have been originally devised for synthesizing virgin processes; nevertheless, the approach does not require the enormous effort involved in exhaustively identifying plausible operating units in synthesizing virgin processes. With the combinatorial feasibility of most operating units largely predetermined, the approach detects, with extraordinary speed, any changes in the flowsheet's network structure incurred by retrofitting. The efficacy of the approach is demonstrated by applying it to the retrofitting of a conventional downstream process for the biochemical production of butanol through the incorporation of newly identified adsorbing units.

Introduction

Most, if not all, existing processes must be continually retrofitted during their lifetime to remain competitive and sustainable.^{1–5} The goals of retrofitting can be expansion of the production capacity, enhancement of the product quality, or reduction of the operating costs to improve the profit margin;^{3,6–8} another goal could be the minimization of environmental impact to meet ever-tightening regulations.^{1,7,9} The identification and evaluation of retrofit options to attain one or more of these goals have been performed either heuristically or algorithmically.^{3,6,8,10}

Most of the available approaches for retrofitting focus on some specific operations, aspects, or segments of the processes with fixed flowsheet structures. Instances of such operations, aspects, or segments are waste reduction,^{1,7,9} mass-exchange networks,¹⁰ heat-exchange networks,^{11,12} reactor systems,⁸ and entrainer selection.¹² These approaches are indeed viable when the operations, aspects, or segments of concern can be unequivocally isolated from the remainder of the processes; more often than not, this is the case. As such, the approaches would result in optimally retrofitted processes when they can be implemented algorithmically and rigorously, as presented by Fraser and Hallale,¹⁰ and by Ciric and Floudas,¹¹ for example. For various processes or systems, however, situations can arise such that the effects of upgrading or modifying any operation,

or segment propagate throughout these processes or systems. This is indeed the case when the downstream-processing system of a biochemical manufacturing process is upgraded, i.e., retrofitted, at the upper or initial segment immediately following the fermenter. The downstream-processing system essentially comprises sequences of separation trains, interlocked mainly in the upper segment of the systems.^{13–17} Moreover, the components in the feed to the system are separated most extensively in the upper segment from the viewpoint of the quantities involved, implying that the maximum benefit can possibly be derived from retrofitting when an operating unit or units in that segment of the system is upgraded. However, the effects of such upgrading inevitably propagate measurably throughout the system. This necessitates totally reconfiguring the system's network structure (flowsheet) through re-synthesis for the retrofitted system to remain optimal in its performance, thereby entailing the development of a holistic approach for process retrofitting.

The issue of combinatorial feasibility is largely resolved for all the operating units in the original flowsheet that must be taken into account in re-synthesis for retrofitting. Nevertheless, it would still be daunting to circumvent the combinatorial complexity involved in the total re-synthesis of a flowsheet containing a multitude of operating units for which a robust, rigorous, and highly efficient algorithmic method is required. The current work resorts to the rigorous graph-theoretic method based on process graphs (P-graphs) to perform re-synthesis and simultaneous generation of the optimal and near optimal retrofit

* To whom correspondence should be addressed. Tel: (785) 532-5584. Fax: (785) 532-7372. Email: fan@ksu.edu.

Table 1. Candidate Adsorbents for the Downstream Processing in Biochemical Production of Butanol, Ethanol, and Acetone

adsorbent	comments		ref(s)
	adsorption capacity	adsorption of nutrients?	
zeolite and silicalite	80–90 mg butanol/g resin	possible	38, 39, 47, 48
XAD series	inferior or similar to that for silicalite	possible	39, 40, 41, 43
Bonopore	similar to that for silicalite	minimal	38, 43
charcoal and activated carbon	inferior to that for silicalite	possible	40, 41
IRC-50	inferior to that for silicalite	possible	41

options in terms of the entire flowsheet cost. This method, originally developed by Friedler and his collaborators,^{18–23} has been repeatedly shown to be extraordinarily efficient in process-network synthesis since its inception.^{24–28} The method has been increasingly gaining utility in other areas. Some of these areas include representation of process structures in developing decision support systems for process operations as demonstrated by Halim and Srinivisan,^{29,30} the identification of catalytic or metabolic pathways,^{31–33} and environmentally friendly system design.³⁴ Specifically, the efficacy of the proposed holistic approach based on the P-graph is demonstrated in this paper in the retrofitting of the downstream-processing system for biochemical production of butanol, ethanol, and acetone by incorporating one of the unconventional separating units, namely, adsorption, into the upper segment of the system.

Process Description

Adsorption is ubiquitous in the laboratory-scale as well as industrial-scale separation or purification of liquid and gaseous mixtures for the manufacture of a wide variety of chemicals, biochemicals and materials.³⁵ The effectiveness of adsorption as a means of separating or purifying organics is extensively discussed by Chi.³⁶ In fact, adsorption has been the separation method of choice for the final purification and polishing of products, e.g., fuel-grade ethanol via a biochemical route.³⁷ Naturally, the potential of adopting adsorption for the same purpose in the biochemical production of butanol (B), ethanol (E), and acetone (A) has been well-recognized.^{38–43} Apparently, however, no attempt has yet been made to incorporate adsorption into an industrial plant design for the downstream processing in the biochemical production of B, E, and A.

At the outset of the downstream processing system, insoluble protein, fiber, cells, and trace chemicals are removed from the fermentation broth. The remaining aqueous stream, which contains butanol, ethanol, and acetone, in addition to water, is processed through a series of variously combined operating units that perform the separation. The system yields B, E, and A as the final products. The system for the downstream processing described in our previous papers^{13,16} consists only of the conventional operating units, including distilling, gas-stripping, and extracting units. The additional operating units to be included in the current work are two adsorbing units and one concomitant centrifuging unit. Processes that involve these newly added units are described in the following.

The fermentation broth contains 2 wt % of insoluble solids whose densities are much higher than those of the aqueous portion of the broth comprising butanol (B), ethanol (E), acetone (A), and water (W).¹⁴ Hence, the insoluble solids can be readily removed from the fermentation broth by centrifugation prior to adsorption. This prevents the adsorption of insoluble solids, including cells onto the adsorbents' surfaces, thus facilitating the adsorption of desired B, E, and A.^{44–46} It is worth noting that the cells have a tendency to form biofilms on the surfaces of the adsorbents, thereby inhibiting further adsorption of the desired products. The clear supernatant from the centrifugal unit

is passed through the first of the two adsorbing units that comprises two adsorption columns operated cyclically between the adsorption and desorption phases. In one column, the desired final products are adsorbed; in the other, these final products are thermally desorbed, thereby reactivating the adsorbents.⁴⁷ The desirable characteristics of the adsorbents include high adsorbent capacities for B, E, and A but not for sugar, acetic acid, butyric acid, or any nutrients; favorable adsorption kinetics; and effective adsorption over a broad range of solvent concentrations.³⁹ The adsorbents investigated to date are summarized in Table 1. Among them, Bonopore (which is a divinylbenzene-styrene copolymer, manufactured by Nobelkemi AB, Sweden) seems to be the most suitable adsorbent: Despite its high adsorption capacity for B, Bonopore hardly removes nutrients from the fermenting broth.⁴³ Bonopore, therefore, is used in the current work.

The biochemical production of fuel ethanol is very similar to that of B, E, and A. Thus, the adsorption of W from the vapor phase, as practiced in the former, is also considered for inclusion in the current process;³⁷ this constitutes the second of the two adsorbing units. To implement it, the fermentation broth is first concentrated in an existing gas-stripping unit, identified as Gas Stripper G1 in our previous paper,¹³ to yield the vapor phase, which comprises B, E, A, and W, and the aqueous-phase-containing solid suspensions. Subsequently, W in the vapor phase is removed in two adsorption columns that are operated cyclically between the adsorption and desorption phases, similar to those of the other adsorption unit.

Methodology

The methodology involves the following procedures: (a) identifying operating units plausible for downstream processing; (b) composing the maximal structure from the plausible operating units identified; and (c) determining the optimal and near-optimal flowsheets in the ranked order in terms of cost. The methodology as well as its implementation is detailed in our previous paper¹³ and the related appendices. What follows describes the exceptions due to the inclusion of the two aforementioned adsorbing units and concomitant centrifuging unit.

1. Identification of Operating Units. Altogether, the operating units that have been identified include the one centrifuging unit and two adsorbing units previously mentioned, as well as all the conventional operating units identified previously. Their total number is 25, comprising 38 pieces of processing equipment.

A. Centrifuging Unit. The centrifuging unit is designated as Centrifuge C1. The fermentation broth is fed to this operating unit. The clear supernatant exiting from it, free of solid suspension, is fed into the adsorbing unit. This supernatant contains 1.5 wt % butanol (B), 0.2 wt % ethanol (E), 0.6 wt % acetone (A), and 97.7 wt % water (W). The concentrated suspension that contains the solids is recycled to the fermenter.

B. Adsorbing Units. The first of the two adsorbing units, designated as Unit 24, and comprises subunits Adsorption

Table 2. Summary of Operating Units Newly Identified and Their Costs

Operating Units and Subunits					Cost (10 ³ US\$)		Annual Cost (10 ³ US\$/yr)	
number of operating units	number of subunits	equipment designation	type	function ^a	capital	annualized capital ^b	operating	total
23		C1	centrifuge	removal of suspended solids from the fermentation broth	9240	3080	1168	4248
24	24-1	B1	adsorption column	separation of B, E, and A from the liquid mixture of B, E, A and W	25107	8369	871	9240
24	24-2	B2	adsorption column	separation of B, E, and A from the liquid mixture of B, E, A and W				
25	25-1	B3	adsorption column	removal of W from the vapor mixture of B, E, A, and W	3806	1269	132	1401
25	25-2	B4	adsorption column	removal of W from the vapor mixture of B, E, A, and W				

^a B = butanol, E = ethanol, A = acetone, and W = water. ^b Based on the three-year payback period.

Column B1 and Adsorption Column B2, each of which is packed with Bonopore adsorbents. The two columns are operated cyclically between the adsorption and desorption phases, as mentioned previously. The clear supernatant from Unit 23, comprising Centrifuge C1, is fed to one of the columns, where B, E, and A are adsorbed onto the adsorbents. The adsorption capacities of the adsorbents are ~50–80 mg/g of adsorbent for the products. The equilibrium adsorption isotherms indicate that butanol can be concentrated from 0.5% (w/v) to 98% (w/v).⁴⁸ When the products saturate the adsorbents, they are thermally desorbed and subsequently recovered; meanwhile, the adsorbents are reactivated in the other column.

The second of the two adsorbing units, designated as Unit 25, and comprises Adsorption Column B3 and Adsorption Column B4, each of which is packed with multiple beds (trays) of thinly layered molecular sieves. These two columns are also operated cyclically between the adsorption and desorption phases. The vapor stream from Unit 3, which comprises Gas Stripper G1, as mentioned previously, is fed into this unit, where water is essentially completely adsorbed onto the adsorbents. Although the active column is under pressure during dehydration, where the mixture of B, E, and A is condensed, the other column, with the adsorbents saturated by water, is under vacuum for regeneration.

Table 2 summarizes the three newly added operating units that are numbered, following the operating units given in our previous paper.¹³ The three operating units consist of a total of five pieces of processing equipment.

2. P-graph Representations of Operating Units. The three operating units identified in the current work are graphically represented in conventional diagrams as well as by P-graphs in Figure 1.

3. Generation of Comprehensive Flowsheet. Based on the specifications of materials, similar to those presented in our previous paper,¹³ and the P-graph representations of the 23 operating units identified (excluding the two reacting units also listed in the table that do not come into play in the current work), algorithm MSG has constructed the comprehensive flowsheet, corresponding to the maximal structure. The total computing time consumed is <2 s on a personal computer (PC) (266 MHz and 65 MB Pentium II; Windows 95).

The comprehensive flowsheet, i.e., the maximal structure, is presented in Figure 2 by P-graph representations. It includes the operating units, which comprise 1 gas stripper, 1 extractor, 27 simple distillation columns, 2 azeotropic distillation units, 1 centrifuge, and 4 adsorption columns.

4. Generation of Optimal and Near-Optimal Flowsheets. The optimal and near-optimal flowsheets are identified by

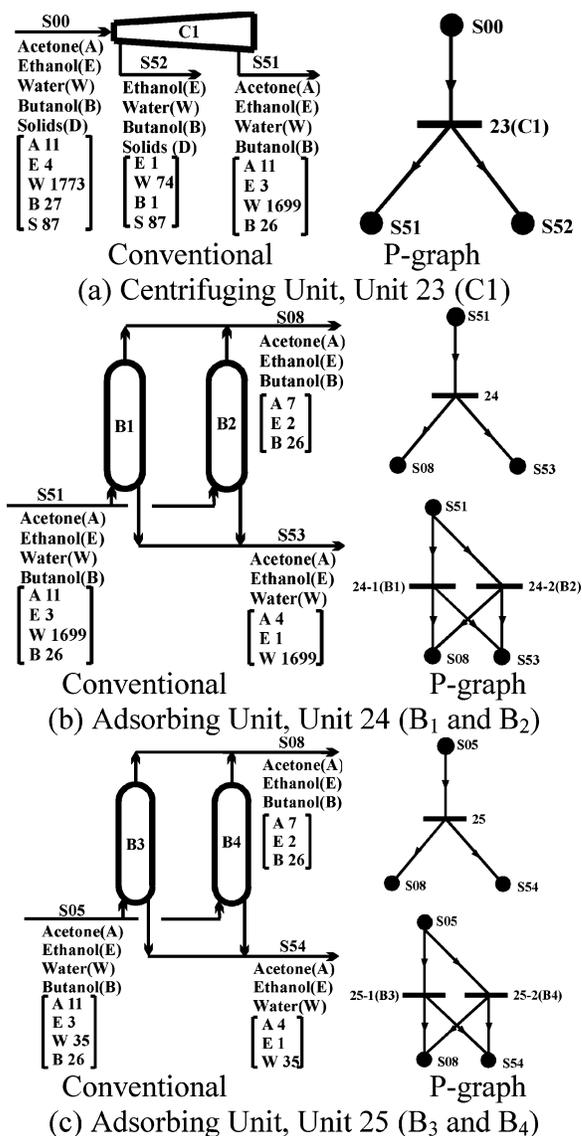


Figure 1. Conventional and process graph (P-graph) representations of newly identified operating units: (a) Centrifuging Unit 23 (Centrifuge C1), (b) Adsorbing Unit 24 (Adsorption Columns B₁ and B₂), and (c) Adsorbing Unit 25 (Adsorption Columns B₃ and B₄).

resorting to algorithm ABB,^{20,25} as presented in our previous paper.¹³ Additional details are available in Appendix 1, which is given in the Supporting Information.

A. Objective Function. As stated in the previous paper,¹³ the objective function to be minimized is the flowsheet's cost.

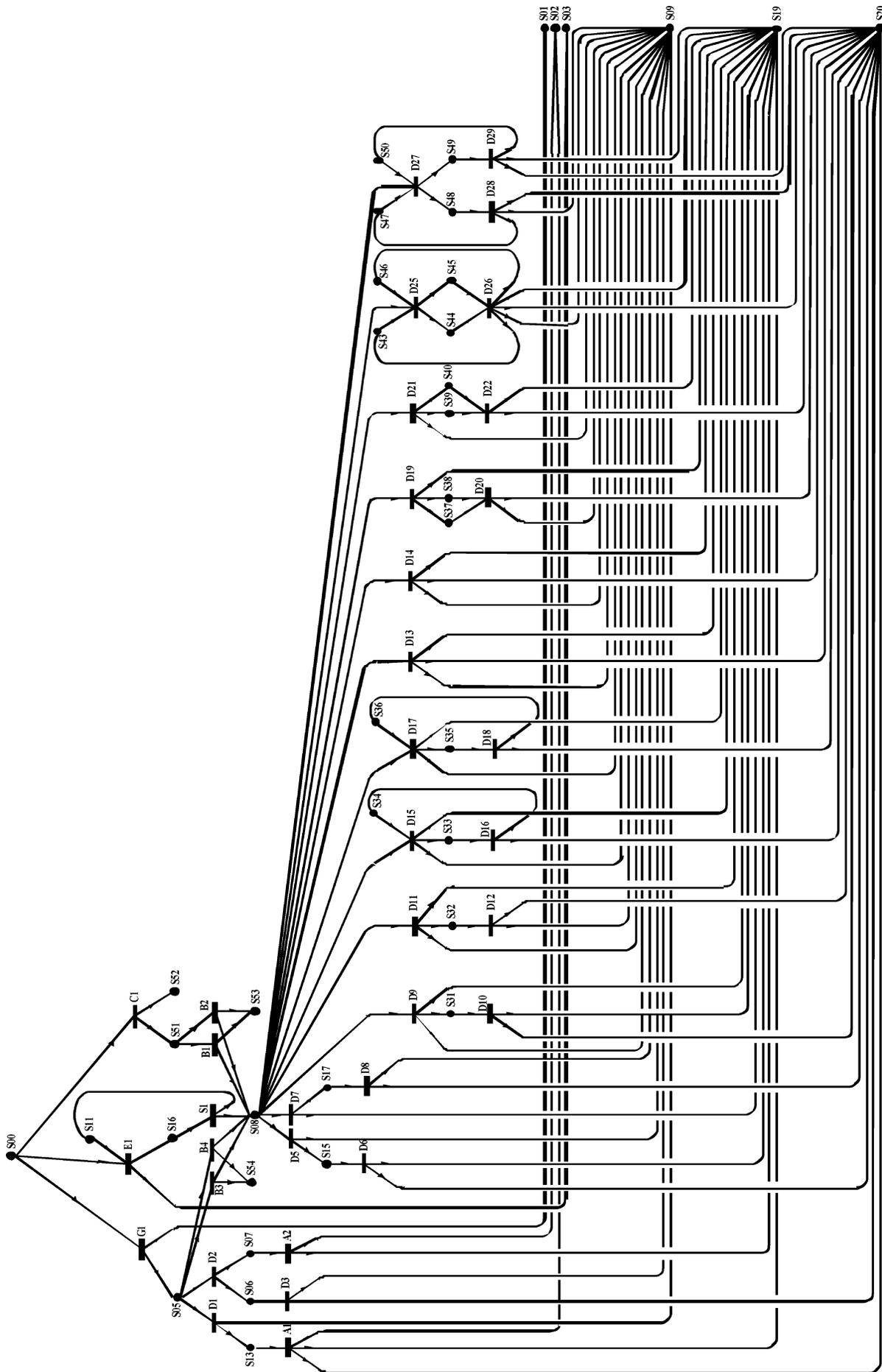


Figure 2. Comprehensive flowsheet corresponding to the maximal structure for the production of butanol, ethanol, and acetone with the inclusion of adsorption: P-graph representation. A letter followed by a numeral adjacent to a bar designates an operating unit represented by the bar; a letter followed by a numeral represented by the circle.

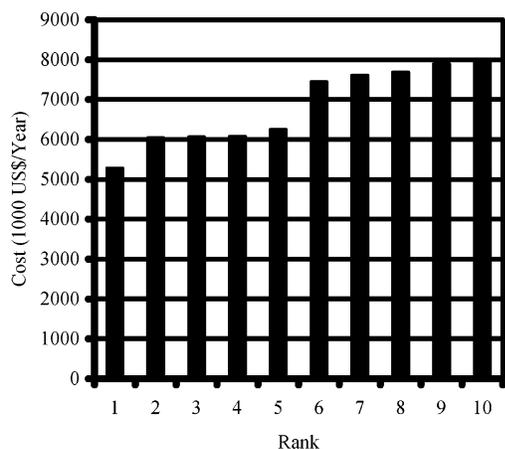


Figure 4. Comparison of the total costs of the top 10 flowsheets with the inclusion of adsorption considered.

the comprehensive flowsheet and the optimal and near-optimal flowsheets. This attests to the efficacy of the methodology that is adopted.

2. Evaluation of Generated Flowsheets. Table 3 lists, in ranked order, the top 10 flowsheets generated on the basis of their total costs. The top 10 flowsheets are also compared graphically in Figure 4. The optimal flowsheet is noticeably less expensive than the four flowsheets ranked second through fifth, which, in turn, are substantially less expensive than the five ranked sixth through tenth. Table 3 also reveals that, similar to the results obtained in our previous paper,¹³ the differences in the costs among the top 10 flowsheets can be attributed to the differences in the configurations of distillation columns downstream beyond G1, B3, and B4.

None of the top 10 flowsheets contains the extracting, centrifuging, or azeotropic-distillation units. The total cost of the optimal flowsheet—5.286 million U.S. dollars—is 756 000 U.S. dollars (12.5%) and 2.653 million U.S. dollars (33%) less than those of the second and tenth best flowsheets, respectively. Therefore, there are only slight differences between the cost of the second-best flowsheet and those of the third-best (20 000 U.S. dollars, 0.3%), fourth-best (39 000 U.S. dollars, 0.6%) and fifth-best (215 000 U.S. dollars, 3%) flowsheets. The difference between the costs of the fifth-best and sixth-best flowsheets is appreciable—1.183 million U.S. dollars, or 16%. The cost differences among the sixth-best through tenth-best flowsheets are indeed small.

The optimal flowsheet consists of Gas Stripper G1, Adsorption Columns B3 and B4, and Distillation Columns D21 and D22. The configuration of these two distillation columns for separating butanol (B), ethanol (E), and acetone (A) from each other is referenced in our previous paper¹³ as the complex-direct.⁵² The configurations of the two distillation columns in the second- and third-best flowsheets are referenced in our previous paper¹³ as complex-Petlyuk type IIIb and simple-indirect, respectively.⁵² Naturally, the cost of the complex-Petlyuk type IIIb configuration is lower than that of the simple-indirect configuration; moreover, both costs are higher than that of the complex-direct configuration of the distillation columns in the optimal flowsheet. The cost differences among the top 10 flowsheets can mainly be attributed to the difference in the configurations of the distillation columns separating B, E, and A from each other.

3. Sensitivity Analysis. A sensitivity analysis has been undertaken by perturbing the collective cost, or simply cost, of adsorbing units (adsorption columns) B3 and B4 and the

concomitant centrifuging unit, which are incorporated into the process for retrofitting. This cost can vary substantially, depending on the supplier, location, and time. Thus, the cost is perturbed widely from -20% up to as much as $+350\%$.

No changes in the structures of the optimal and near-optimal flowsheets, including the best 10 and their rankings in terms of cost, are discernible when the perturbation of the cost is $<200\%$. Only when the cost perturbation exceeds this magnitude does the existing flowsheet become barely competitive with the low-ranking near-optimal flowsheets resulting from retrofitting. These results seem to indicate that the retrofitting through the incorporation of the adsorbing units and the concomitant centrifuging unit indeed results in robust optimal and near-optimal flowsheets that are superior to even the existing flowsheet, which is optimal.

4. Comparison with Flowsheets Comprising Only Conventional Operating Units. The top 10 flowsheets listed in Table 3 are markedly different from those generated in our previous paper with only conventional operating units,¹³ i.e., without adsorbing units. The marked cost reduction of the top 10 flowsheets is attributable to the replacement of Extractor E1 and Solvent Stripper S1 with Gas Stripper G1, and Adsorption Column B3 and Adsorption Column B4. The total cost of the optimal flowsheet, 5.286 million U.S. dollars, is 4.130 million U.S. dollars (44%) less than that of the optimal flowsheet generated in our previous paper.¹³ In fact, even the total cost of the tenth-best flowsheet, 7.979 million U.S. dollars, is 1.477 million U.S. dollars (16%) lower than that of the optimal flowsheet generated in our previous paper.¹³

5. Effect of Inclusion of Adsorption. The newly generated top 10 flowsheets indicate that the incorporation of the adsorbing unit (Unit 25), which comprises Adsorption Column B3 and Adsorption Column B4, reduces the cost immeasurably. None, however, contain the adsorbing unit (Unit 24), which comprises Adsorption Column B1 and Adsorption Column B2.

Water (W) and suspended solids constitute the major fraction of the fermentation broth. Gas Stripper G1 preceding Adsorption Column B3 and Adsorption Column B4 removes the massive amount of W and almost all solids as the bottom liquid stream from the fermentation broth. The feed to Adsorption Column B3 and Adsorption Column B4 is the vapor stream from Gas Stripper G1, which is only a small fraction of the original fermentation broth, thus substantially reducing the equipment size.

In contrast to Adsorption Columns B3 and B4, the inclusion of Adsorption Columns B1 and B2 are not advantageous, from the cost standpoint. Adsorption Columns B1 and B2 receive feed at a rate of 789×10^3 kg/h, which is ~ 22 times larger than Adsorption Columns B3 and B4 (34×10^3 kg/h). Moreover, the inclusion of Adsorption Columns B1 and B2 necessitates the addition of Centrifuge C1 to remove insoluble solids from the high-volume feed, thereby incurring additional cost. Naturally, the incorporation of Adsorption Columns B1 and B2 dramatically magnifies the cost of the flowsheets; as a result, these two adsorption columns are totally excluded from the list of the optimal and near-optimal flowsheets.

Conclusions

The proposed holistic approach represents a novel and robust paradigm for optimally retrofitting the downstream processing system of a biochemical production process. This holistic approach, which requires the total re-synthesis of the system's network structure, is rooted in the highly efficient and robust graph-theoretic method for process-network synthesis based on

process graphs (P-graphs). The approach's development is dictated by the fact that any change implemented in retrofitting downstream processing systems, especially at their upper segment, has a tendency to propagate throughout the system, because of its inherent or unique sequential structural feature. Naturally, this approach is applicable to many other chemical processes that share the same structural feature.

The approach generates a set of optimal and near-optimal retrofitted flowsheets in ranked order, in light of a specific objective function (namely, cost) in the current work. The availability of multiple ranked retrofitting options is indeed advantageous: One or more of the options may be found infeasible or unsustainable if the retrofitted system is scrutinized or assessed by taking into account other criteria and constraints, such as stability, controllability, and environmental, societal, and regulatory constraints.

Acknowledgment

This is contribution No. 05-58-J, Department of Chemical Engineering, Kansas Agricultural Experiment Station, Kansas State University (Manhattan, KS), from which the first three authors received financial support.

Supporting Information Available: Appendix 1, which gives the algorithm ABB, and Appendix 2, which gives sample calculations for cost estimation (pdf). This material is available free of charge via the Internet at <http://pubs.acs.org>.

Literature Cited

- (1) Diwekar, U. M. Greener by Design. *Environ. Sci. Technol.* **2003**, *37*, 5432.
- (2) Turton, R.; Bailie, R. C.; Whiting, W. B.; Shaiwitz, J. A. *Analysis, Synthesis, and Design of Chemical Processes*; Prentice Hall: Upper Saddle River, NJ, 2003.
- (3) Uerdingen, E.; Fischer, U.; Hungerbühler, K.; Gani, R. Screening for Profitable Retrofit Options of Chemical Processes: a New Method. *AIChE J.* **2003**, *49*, 2400.
- (4) Rapoport, H.; Lavie, R.; Kehat, E. Retrofit Design of New Units into an Existing Plant: Cast Study: Adding New Units to an Aromatics Plant. *Comput. Chem. Eng.* **1994**, *18*, 743.
- (5) Fisher, W. R.; Doherty, M. F.; Douglas, J. M. Screening of Process Retrofit Alternatives. *Ind. Eng. Chem. Res.* **1987**, *26*, 2195.
- (6) Uerdingen, E.; Fischer, U.; Gani, R.; Hungerbühler, K. A New Retrofit Design Methodology for Identifying, Developing, and Evaluating Retrofit Projects for Cost-Efficiency Improvements in Continuous Chemical Processes. *Ind. Eng. Chem. Res.* **2005**, *44*, 1842.
- (7) Dantus, M. M.; High, K. A. Economic Evaluation for the Retrofit of Chemical Processes through Waste Minimization and Process Integration. *Ind. Eng. Chem. Res.* **1996**, *35*, 4566.
- (8) Guntern, C.; Keller, A. H.; Hungerbühler, K. Economic Optimization of an Industrial Semibatch Reactor Applying Dynamic Programming. *Ind. Eng. Chem. Res.* **1998**, *37*, 4017.
- (9) Van der Helm, D. U.; High, K. A. Waste Minimization by Process Modifications. *Environ. Prog.* **1996**, *15*, 56.
- (10) Fraser, D. M.; Hallale, N. Retrofit of Mass Exchange Networks Using Pinch Technology. *AIChE J.* **2000**, *45*, 2112.
- (11) Ciric, A. R.; Floudas, C. A. A Retrofit Approach for Heat Exchanger Networks. *Comput. Chem. Eng.* **1989**, *13*, 703.
- (12) Kurum, S.; Heinzle, E.; Hungerbühler, K. Plant Optimisation by Retrofitting Using a Hierarchical Method: Entrainer Selection, Recycling and Heat Integration. *J. Chem. Biotechnol.* **1997**, *70*, 29.
- (13) Liu, J.; Fan, L. T.; Seib, P.; Friedler, F.; Bertok, B. Downstream Process Synthesis for Biochemical Production of Butanol, Ethanol, and Acetone from Grains: Generation of Optimal and Near-Optimal Flowsheets with Conventional Operating Units. *Biotechnol. Prog.* **2004**, *20*, 1518.
- (14) Marlatt, J. A.; Datta, R. Acetone-Butanol Fermentation Process Development and Economic Evaluation. *Biotechnol. Prog.* **1986**, *2*, 23.
- (15) Dadgar, A. M.; Foutch, G. L. Improving the Acetone-Butanol Fermentation Process with Liquid-Liquid Extraction. *Biotechnol. Prog.* **1988**, *4*, 36.
- (16) Liu, J. Downstream process synthesis for biochemical production of butanol, ethanol, and acetone from grains. Ph.D. Dissertation, Kansas State University, Manhattan, KS, 2003.
- (17) Prokopakis, G. J.; Asenjo, J. A. *Synthesis of Downstream Processes, Separation Processes in Biotechnology, Separation Processes in Biotechnology*; Marcel Dekker: New York, 1990.
- (18) Friedler, F.; Tarjan, K.; Huang, Y. W.; Fan, L. T. Combinatorial Algorithms for Process Synthesis. *Comput. Chem. Eng.* **1992**, *16*, S313.
- (19) Friedler, F.; Tarjan, K.; Huang, Y. W.; Fan, L. T. Graph-Theoretic Approach to Process Synthesis: Axioms and Theorems. *Chem. Eng. Sci.* **1992**, *47*, 1973.
- (20) Friedler, F.; Fan, L. T. Combinatorial Acceleration of the Branch and Bound Search for Process Network Synthesis. presented at the Symposium on Applied Mathematical Programming and Modeling, Budapest, Hungary, 1993.
- (21) Friedler, F.; Tarjan, K.; Huang, Y. W.; Fan, L. T. Graph-Theoretic Approach to Process Synthesis: Polynomial Algorithm for Maximal Structure Generation. *Comput. Chem. Eng.* **1993**, *17*, 929.
- (22) Friedler, F.; Varga, J. B.; Fan, L. T. Decision Mapping: A Tool for Consistent and Complete Decisions in Process Synthesis. *Chem. Eng. Sci.* **1995**, *50*, 1755.
- (23) Brendel, M. H.; Friedler, F.; Fan, L. T. Combinatorial Foundation for Logical Formulation in Process Network Synthesis. *Comput. Chem. Eng.* **2000**, *24*, 1859.
- (24) Friedler, F.; Varga, J. B.; Fan, L. T. Algorithmic Approach to the Integration of Total Flowsheet Synthesis and Waste Minimization. *AIChE Symp. Ser.* **1995**, *303*, 86. (Also see *Chem. Eng. Prog.* **1995**, *90*.)
- (25) Imreh, B.; Friedler, F.; Fan, L. T. An Algorithm for Improving the Bounding Procedure in Solving Process Network Synthesis by a Branch-and-Bound Method. In *Nonconvex Optimization and Its Applications, Developments in Global Optimization*; Kluwer Academic Publishers: Dordrecht, The Netherlands, 1997, 315.
- (26) Partin, L. R. Combinatorial Analysis Application for Flowsheet Synthesis of Chemical Plants. *Maple Tech. Newsl.* **1998**, *5* (2-3), 15.
- (27) Keller, G. E.; Bryan, P. F. Process Engineering Moving in New Directions. *Chem. Eng. Prog.* **2000**, *96* (1), 41.
- (28) Sargent, R. Process systems engineering: A retrospective view with questions for the future. *Comput. Chem. Eng.* **2005**, *29*, 1237.
- (29) Halim, I.; Srinivisan, R. Systematic Waste Minimization in Chemical Processes. 1. Methodology. *Ind. Eng. Chem. Res.* **2002**, *41*, 196.
- (30) Halim, I.; Srinivisan, R. Systematic Waste Minimization in Chemical Processes. 2. Intelligent Decision Support System. *Ind. Eng. Chem. Res.* **2002**, *41*, 208.
- (31) Lee, D.-Y.; Fan, L. T.; Park, S.; Lee, S. Y.; Shafie, S.; Bertok, B.; Friedler, F. Complementary Identification of Multiple Flux Distributions and Multiple Metabolic Pathways. *Metab. Eng.* **2005**, *7*, 182.
- (32) Seo, H.; Lee, D.-Y.; Park, S.; Fan, L. T.; Shafie, S.; Bertok, B.; Friedler, F. Graph-Theoretical Identification of Pathways for Biochemical Reactions. *Biotechnol. Lett.* **2001**, *23*, 1551.
- (33) Rossello, R.; Valiente, G. Graph transformation in molecular biology. *Lect. Notes. Comput. Sci.* **2005**, *3393*, 116.
- (34) Xu, W.; Diwekar, U. M. Environmentally Friendly Heterogeneous Azeotropic Distillation System Design: Integration of EBS Selection and IPS Recycling. *Ind. Eng. Chem. Res.* **2005**, *44*, 4061.
- (35) Seader, J. D.; Henley, E. J. *Separation Process Principles*; Wiley: New York, 1998.
- (36) Chi, T. *Adsorption Calculations and Modeling*; Butterworth: Stoneham, U.K., 1994.
- (37) Merrick & Company. *Building a Bridge to the Corn Ethanol Industry*; Project Subcontract to National Renewable Energy Laboratory, No. ZXE-9-18080-04. National Renewable Energy Laboratory Publication: Fort Collins, CO, 2000.
- (38) Larsson, M.; Mattiasson, B. Novel Process Technology for Biotechnological Solvent Production. *Chem. Ind.—London* **1984**, *12*, 428.
- (39) Ennis, B. M.; Gutierrez, N. A.; Maddox, I. S. The Acetone-Butanol-Ethanol Fermentation: A Current Assessment. *Process Biochem.* **1986**, *21*, 131.
- (40) Groot, W. J.; Luyben, K. Ch. A. M. In situ Product Recovery by Adsorption in the Butanol/2-Propanol Batch Fermentation. *Appl. Microbiol. Biotechnol.* **1986**, *25*, 29.
- (41) Das, K.; Soni, B. K.; Ghose, T. K. Static and Column Studies on Selective Adsorption-Desorption of Butanol. In *Proceedings of the 4th European Congress on Biotechnology*; Neijssel, O. M.; van der Meer, R. R.; Luyben, K. Ch. A. M., Eds.; Elsevier: Amsterdam, The Netherlands, 1985; Vol. 15, p 611.
- (42) Ennis, B. M.; Qureshi, N.; Maddox, I. S. In-line Toxic Product Removal During Solvent Production by Continuous Fermentation Using Immobilized *Clostridium acetobutylicum*. *Enzyme Microbiol. Technol.* **1987**, *9*, 672.

- (43) Nielsen, L.; Larsson, M.; Holst, O.; Mattiasson, B. Adsorbents for Extractive Bioconversion Applied to the Acetone–Butanol Fermentation, *Appl. Microbiol. Biotechnol.* **1988**, *28*, 335.
- (44) Belter, P. A.; Cussler, E. L.; Hu, W. S. *Bioseparations: Downstream Processing for Biotechnology*; Wiley: New York, 1988.
- (45) Ladisch, M. R. Fermentation-derived butanol and scenarios for its uses in energy-related applications. *Enzyme Microbiol. Technol.* **1991**, *13*, 280.
- (46) Harrison, R. G.; Todd, P.; Rudge, S. R.; Petrides, D. P. *Bioseparations Science and Engineering*; Oxford University Press: New York, 2003.
- (47) Maddox, I. S. The Acetone–Butanol–Ethanol Fermentation: Recent Progress in Technology. *Biotechnol. Genet. Eng. Rev.* **1989**, *7*, 189.
- (48) Milestone, N. B.; Bibby, D. M. Concentration of Alcohols by Adsorption on Silicalite. *J. Chem. Technol. Biotechnol.* **1981**, *31*, 732.
- (49) Peters, M. S.; Timmerhaus, K. D.; West, R. *Plant Design and Economics for Chemical Engineers*; McGraw–Hill International: New York, 2003.
- (50) Feng, G.; Fan, L. T.; Seib, P. A.; Bertok, B.; Kalotai, L.; Friedler, F. A Graph-Theoretic Method for the Algorithmic Synthesis of Azeotropic–Distillation Systems. *Ind. Eng. Chem. Res.* **2003**, *42*, 3602.
- (51) Heckl, I.; Friedler, F.; Fan, L. T. Integrated Synthesis of Optimal Separation and Heat Exchanger Networks Involving Separations Based on Various Properties. *Heat Transfer Eng.* **2005**, *26*, 25.
- (52) Doherty, M. F.; Malone, M. F. *Conceptual Design of Distillation Systems*; McGraw–Hill: New York, 2001.

Received for review September 9, 2005
Revised manuscript received March 16, 2006
Accepted March 29, 2006

IE051014M