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Simultaneous optimization of scheduling, equipment dimensions and operating conditions of sequential multi-purpose batch plants

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ABSTRACT

The design of multi-purpose batch plants is a challenging task, because the number of degrees of freedom for optimization is high. Important optimization variables are the scheduling, operating conditions and the sizes of the equipment items. Since all factors interact, a simultaneous consideration would be beneficial in order to reduce capital and operating costs. In this article, this complex task is tackled for a new case study of a sequential plant for protein production. The case study contains comprehensive models of the unit operations to evaluate equipment dimensions, mass balances and operating times. Variable changeover times and semicontinuous unit operations are considered. For optimization, a MINLP model is used that consists of smaller NLP and MILP submodels in order to simplify modeling. Simulation runs for different product demands are performed and it is shown that good solutions can be found in an adequate time.

1. Introduction

Multi-purpose batch plants are used in industry, when the amount of product to be produced is small and the added value of the product is high. In this case they offer advantages like higher capacity utilization and more flexibility allowing the consideration of fluctuations in product demand. One example is the production of pharmaceutical ingredients (Sanden, 1998).

Compared to mono-product plants, the design of multi-purpose plants is more challenging and complex because the number of degrees of freedom for optimization is higher. Besides the fact that several processes take place in one plant that have to be optimized instead of one only, also a completely new degree of freedom arises: the scheduling of the different products. Some important factors that influence the operating and capital costs of a multi-purpose plant are presented in Fig. 1. They can be grouped into three categories. The first one is the plant design in the form of the physical dimensions of the different equipment items, like for example the volume of a fermenter or the area of a filter. Also the number of parallel equipment items belongs to this group. The second category is the process design. In contrast to the plant design, here the design of the unit operations is meant. In this case the operating conditions are optimized. These are variables that can influence the operating time of a unit operation, like for example the temperature or the concentration at which a unit operation is performed. The third group covers decisions concerning the scheduling, which means the allocation of the equipment items with the different tasks and the sequencing of the different products. Also the batch size, which correlates with the batch number necessary to fulfill the demand, belongs to this group. All the different factors interact and often there are trade-offs between them, so it seems obvious that they should be optimized simultaneously. In industrial application the scheduling problem is regarded only after the design of the plant and the process has been fixed. However, for designing new production facilities, the consideration of the scheduling during the design phase of the process simultaneous with the plant design bears potential for a better capacity utilization of the plant and thus for saving capital and operating costs.

The main reason for this optimization potential is the trade-off between the operating time and the costs of a unit operation that processes a batch. The operating time often can be influenced by altering the plant or process design while mostly it is valid that the shorter the operating time becomes, the higher the operating

Abbreviations: AEX, anion exchange chromatography; CIP, cleaning in place; CVI, chemical virus inactivation; DF, diafiltration; HIC, hydrophobic interaction chromatography; mab, monoclonal antibody; PAC, protein A chromatography; RP, recombinant protein; SIP, sterilization in place; STN, state-task network; UF, ultrafiltration; VF, virusfiltration; WFI, water for injection.

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Nomenclature

Indices

i	Batch tasks
j	Batch processing units
n	Eventpoints
r	Resources
s	States

Sets

I	Batch tasks
I_i^{con}	Consecutive task of task i
I^{fp}	Tasks which produce final products
I_i^p	Parallel operation belonging to parallel task i
I_i^t	Transfer time belonging to task i
I_j	Tasks that can be processed in unit j
I^p	Tasks which are parallel tasks
I_r	Tasks consuming resource r
I_s^c	Tasks consuming state s
I_s^p	Tasks producing state s
I^{st}	Storage tasks
I^{start}	First tasks of a sequential processes
I^t	Tasks that have a transfer time included in their extra time
J	Processing units
J_i	Units that can perform task i
N	Eventpoints
R	Resources
S	States
S^0	States which are raw materials
S^{fp}	States which are final products
S^{st}	States without intermediate storage

Parameters

$cap_{i,j}$	Capacity for task i in unit j
$c_i^{cells,0}$	Initial cell concentration of fermentation i
$c_i^{cells,max}$	Final cell concentration of fermentation i
c_i^{cont}	Concentration of contaminations of task i
c_i^{gel}	Gel concentration of task i
c_m	Frictional coefficient
c_i^{subs}	Substrate concentration of fermentation medium for fermentation i
D_s	Demand for state s at the end of horizon H
DV_i	Diafiltration volumes of task i
exp_j	Degression exponent of unit j
F	Lang factor
f_i^{eff}	Efficiency factor of centrifuge j
f_j^{safety}	Safety factor for the dimensioning of unit j
$Flux_i^{max}$	Maximal flux i allowed in unit j to perform task i
$Flux_i^{initial}$	Initial flux of filtration task i
H	Time horizon
IC_j^0	Reference investment costs of unit j
K_1	Coefficient for objective function
K_2	Coefficient for objective function
k_i	Mass transfer coefficient of task i
L_j	Bed length of chromatography column j
$m_i^{oxygen,spec}$	Specific oxygen consumption of fermentation i
N^{max}	Maximum number of eventpoints in horizon H
n_i^{cv}	Number of column volumes of chromatography task i
n_j^{discs}	Number of discs of centrifuge j
$price_r$	Price per unit of resource r
Q_i^{spec}	Specific heat production of cells of fermentation i
r_j^{inner}	Inner diameter of centrifuge j
S_j^0	Reference size for investment costs of unit j
$S_i^{intrinsic}$	Intrinsic sieving factor of concentration task i
$S_i^{solvent}$	Sieving factor of solvent of task i
T^{DPR}	Depreciation period
T^{OH}	Operating hours
$V_{i,j}^{spec,hold-up}$	Specific hold-up volume of filter j for task i
$V_j^{spec,rec}$	Specific recovery volume of unit j
v_i	Flow velocity of chromatography task i
$v_i^{s,cells}$	Settling velocity of cells of centrifugation task i
w_i^{solid}	Mass fraction of solids of task i
$w_i^{solvent}$	Mass fraction of solvent of diafiltration task i
Y_i	Yield losses of task i
$Y_i^{x/s}$	Yield of cells on substrate of fermentation i
$Y_i^{p/s}$	Yield of product on substrate of fermentation i
η_j^{el}	Electric efficiency of unit j
θ_i	Moisture of the sediment of centrifugation task i
μ_i	Growth rate of cells of fermentation i
φ_j	Disc angle of centrifuge j
δ	Density

Continuous variables

A_j	Filter area of unit j
$am_{r,i,j}$	Amount of resource r consumed by task i in unit j
c_i^{bulk}	Bulk concentration of task i
c_i^{conc1}	Concentration after the first concentration step of DF/UF task i
c_i^{final}	Final concentration after ultrafiltration i
c_i^{out}	End concentration after task i
$c_i^{out,centri}$	Concentration of output stream after centrifugation task i
cap_i	Capacity of task i
CF_i	Concentration factor of task i
D_j	Diameter of chromatography column j
$Flux_i$	Membrane flux of task i
$m_i^{cells,in}$	Amount of cells that enter centrifugation task i
m_i^{subs}	Mass of substrate fed for fed batch fermentation of fermentation i
$\dot{m}_i$	Mass flow that enters centrifugation task i
n_i	Cycle number of chromatography task i
$P_{i,j}$	Power consumption of centrifugation task i in unit j
$pt_{i,j}$	Operating time of task i in unit j
$pt_{i,j}^{co}$	Changeover time connected with task i in unit j
$pt_{i,j}^{DF}$	Operating time of diafiltration step in UF/DF operation
$pt_{i,j}^{conc}$	Operating time of concentration step in UF/DF operation
r_j^{outer}	Outer diameter of centrifuge j
$R_i^{observed}$	Retaining factor of task i
rpm_i	Rotational speed of centrifugation i
$S_i^{observed}$	Sieving factor of task i
$slack_s$	Slack variable for underproduction of state s
$ST0_s$	Initial amount of state s at the beginning of horizon H
STF_s	Final amount of state s at the end of horizon H
$ST_{s,n}$	Amount of state s at eventpoint n
S_i	Characteristic size needed for task i