(P2) Mixed Integer Non-Linear model for route selection

Objective function

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$$\begin{aligned}\min\ \text{cost} = & \sum_{j\in E^1} \mathbf{z_j^2} c_j^1 \exp\left(\mathbf{x_j^1} + \mathbf{x_j^2} + \mathbf{y_j^1}\gamma_j^1\right) \\ & + \sum_{j\in(E^2\cup E^3)} \mathbf{z_j^2}\left[c_j^1 \exp\left(\mathbf{x_j^2} + \mathbf{y_j^1}\gamma_j^1\right) + c_j^3 \exp\left(\mathbf{x_j^1} + \mathbf{x_j^2} + \mathbf{y_j^3}\gamma_j^3\right)\right] \\ & + \sum_{j\in(E^{2\prime}\cup E^3)} \mathbf{z_j^2} c_j^2 \exp\left(\mathbf{x_j^2} + \mathbf{y_j^2}\gamma_j^2\right) + \mathbf{r}\rho\delta \quad (1)\end{aligned}$$

Restrictions

Batch stages

$$\mathbf{y_j^1 z_j^2} + \mathbf{x_j^1 z_j^2} \geq \mathbf{z_{ih}^1} s_{ihj}^1 + \mathbf{y_{ih}^4 z_{ih}^1} \qquad \forall i \in I, j \in E^1 \quad (2)$$

$$\mathbf{y_{ih}^5 z_{ih}^1} + \mathbf{x_j^2 z_j^2} \geq \mathbf{z_{ih}^1} t_{ihj}^0 \qquad \forall i \in I, j \in E^1 \quad (3)$$

Semi-continuous stages

$$\mathbf{y_j^1 z_j^2} \geq \mathbf{z_{ih}^1} s_{ihj}^1 + \mathbf{y_{ih}^4 z_{ih}^1} \qquad \forall i \in I, j \in E^2 \quad (4)$$

$$\mathbf{y_j^2 z_j^2} \geq \mathbf{z_{ih}^1} s_{ihj}^2 + \mathbf{y_{ih}^4 z_{ih}^1} \qquad \forall i \in I, j \in E^{2\prime} \quad (5)$$

$$\mathbf{y_{ih}^5 z_{ih}^1} + \mathbf{x_j^2 z_j^2} \geq \mathbf{z_{ih}^1} t_{ihj}^1 + \mathbf{y_{ih}^4 z_{ih}^1} - \mathbf{x_j^1 z_j^2} - \mathbf{y_j^3 z_j^2} \qquad \forall i \in I, j \in E^2 \quad (6)$$

Chromatographic stages

$$\mathbf{y_j^1 z_j^2} \geq \mathbf{z_{ih}^1} s_{ihj}^1 + \mathbf{y_{ih}^4 z_{ih}^1} \qquad \forall i \in I, j \in E^3 \quad (7)$$

$$\mathbf{y_j^2 z_j^2} \geq \mathbf{z_{ih}^1} s_{ihj}^2 + \mathbf{y_{ih}^4 z_{ih}^1} \qquad \forall i \in I, j \in E^3 \quad (8)$$

$$\mathbf{y_j^3 z_j^2} + \mathbf{x_j^1 z_j^2} \geq \mathbf{z_{ih}^1} s_{ihj}^3 + \mathbf{y_{ih}^4 z_{ih}^1} \qquad \forall i \in I, j \in E^3 \quad (9)$$

$$\mathbf{y_{ih}^5 z_{ih}^1} + \mathbf{x_j^2 z_j^2} \geq \mathbf{z_{ih}^1} \ln\left[\exp\left(t_{ij}^0\right) + \exp\left(t_{ij}^1 + \mathbf{y_i^4} - \mathbf{x_j^1} - \mathbf{y_j^3}\right)\right] \qquad \forall i \in I, j \in (E^3 \setminus E^{3\prime}) \quad (10)$$

$$\mathbf{y_{ih}^5 z_{ih}^1} + \mathbf{x_j^2 z_j^2} \geq t_{ihj}^0 \mathbf{z_{ih}^1} \qquad \forall i \in I, j \in E^{3\prime} \quad (11)$$

Planning horizon

$$\sum_{i \in I} \mathbf{z^1_{ih}} \frac{d_i}{\delta} \exp\left(\mathbf{y^5_{ih}} - \mathbf{y^4_{ih}}\right) \leq 1 + \mathbf{r} \tag{12}$$

Binary variables for duplication of units

$$\mathbf{x^1_j} = \sum_{k \in K} \mathbf{y^6_{jk}} \ln(k) \qquad \forall j \in E \tag{13}$$

$$\sum_{k \in K} \mathbf{y^6_{jk}} = \mathbf{z^2_j} \qquad \forall j \in E \tag{14}$$

$$\mathbf{x^2_j} = \sum_{k \in K} \mathbf{y^7_{jk}} \ln(k) \qquad \forall j \in E \tag{15}$$

$$\sum_{k \in K} \mathbf{y^7_{jk}} = \mathbf{z^2_j} \qquad \forall j \in E \tag{16}$$

Binary variables for selection of hosts and stages

$$\sum_{(i,h) \in I \times H} \mathbf{z^1_{ih}} \leq 1 \tag{17}$$

$$\mathbf{z^1_{ih}} \leq \mathbf{z^2_j} \qquad \forall (i,h,j) \in R \tag{18}$$

Variable bounds Each variable has upper and lower bounds set by the user.

$$\mathbf{z^2_j} y_j^{1,lo} \leq \mathbf{y^1_j} \leq \mathbf{z^2_j} y_j^{1,up} \qquad \forall j \in E \tag{19}$$

$$\mathbf{z^2_j} y_j^{2,lo} \leq \mathbf{y^2_j} \leq \mathbf{z^2_j} y_j^{2,up} \qquad \forall j \in (E^{2'} \cup E^3) \tag{20}$$

$$\mathbf{z^2_j} y_j^{3,lo} \leq \mathbf{y^3_j} \leq \mathbf{z^2_j} y_j^{3,up} \qquad \forall j \in (E^2 \cup E^3) \tag{21}$$

$$\mathbf{z^2_j} x_j^{1,lo} \leq \mathbf{x^1_j} \leq \mathbf{z^2_j} x_j^{1,up} \qquad \forall j \in E \tag{22}$$

$$\mathbf{z^2_j} x_j^{2,lo} \leq \mathbf{x^2_j} \leq \mathbf{z^2_j} x_j^{2,up} \qquad \forall j \in E \tag{23}$$

$$\mathbf{z^1_{ih}} y_{ih}^{4,lo} \leq \mathbf{y^4_{ih}} \leq \mathbf{z^1_{ih}} y_{ih}^{4,up} \qquad \forall (i,j) \in I \times H \tag{24}$$

$$\mathbf{z^1_{ih}} y_{ih}^{5,lo} \leq \mathbf{y^5_{ih}} \leq \mathbf{z^1_{ih}} y_{ih}^{5,up} \qquad \forall (i,j) \in I \times H \tag{25}$$

Using constraints (2) to (10) we can refine y_{ih}^{4} upper bound and y_{ih}^{5} lower bound.

$$y_i^{4,up} = \min \Bigg[\min_{(i,h,j)\in I\times H\times E^1} \left(y_j^{1,up} + x_j^{1,up} - s_{ihj}^1\right), \min_{(i,h,j)\in I\times H\times (E^2\cup E^3)} \left(y_j^{1,up} - s_{ihj}^1\right), \min_{(i,h,j)\in I\times H\times (E^{2'}\cup E^3)} \left(y_j^{2,up} - s_{ihj}^2\right), \min_{(i,h,j)\in I\times H\times E^3} \left(y_j^{3,up} + x_j^{1,up} - s_{ihj}^3\right) \Bigg] \quad (26)$$

$$y_i^{5,lo} = \max \Bigg[\max_{(i,h,j)\in I\times H\times (E^1\cup E^{3'})} \left(t_{ihj}^0 - x_j^{2,up}\right), \max_{(i,h,j)\in I\times H\times (E^3\setminus E^{3'})} \left(\ln\left(T_{ihj}^0 + \exp\left(t_{ihj}^1 - y_j^{3,up} - x_j^{1,up}\right)\right) - x_j^{2,up}\right) \Bigg] \quad (27)$$

Notations

Indices and sets

I	Set of products i
H	Set of hosts h
E	Set of stages j
E^1	Set of batch stages j
E^2	Set of semicontinuous stages j
$E^{2'}$	Subset of semicontinuous stages j with permeate units
E^3	Set of chromatographic stages j
$E^{3'}$	Subset of gel filtration chromatographic stages j
K	Set of available units operating in-phase or out-of-phase

Variables

y_j^1	logarithmic volumetric capacity for tanks in batch stages and retentate or feed tanks for semicontinuous and chromatographic stages
y_j^2	logarithmic volumetric capacity for permeate or product tanks for semicontinuous and chromatographic stages
y_j^3	logarithmic size of the semicontinuous or chromatographic unit which can be, for example, a processing rate in the case of an homogenizer or an area in the case of a filter
y_{ih}^4	logarithmic final batch size, in mass units, of product i synthesized by host h
y_{ih}^5	logarithmic cycle time of product i synthesized by host h
x_j^1	number of units operating in-phase
x_j^2	number of units operating out-of-phase
y_{jk}^6	binary variables to account for a discrete number of units duplicated and operating in-phase
y_{jk}^7	binary variables to account for a discrete number of units duplicated and operating out-of-phase
z_{ih}^1	binary variable that is 1 if product i is synthesized by host h
z_j^2	binary variable that is 1 if stage j is part of the production path
r	Slack variable

Parameters

s^1_{ihj}	Constant size factor for batch stages or retentate/feed tank in semicontinuous or chromatographic stages for product i that was synthesized by host h and processed in stage j
s^2_{ihj}	Constant size factor for permeate/product tanks in semicontinuous or chromatographic stages for product i that was synthesized by host h and processed in stage j
s^3_{ihj}	Constant size factor for chromatographic columns for product i that was synthesized by host h and processed in stage j
t^0_{ihj}	Constant time factor for batch and chromatographic stages for product i that was synthesized by host h and processed in stage j
t^1_{ihj}	Constant time factor for semicontinuous and chromatographic stages for product i that was synthesized by host h and processed in stage j
c^1_j	cost coefficient for batch stage j of for retentate/feed tank of semicontinuos or chromatographic stage j
c^2_j	cost coefficient for permeate/product tank of semicontinuous of chromatographic stage j
c^3_j	cost coefficient for chromatographic column in stage j
γ^1_j	cost coefficient for batch stage j of for retentate/feed tank of semicontinuos or chromatographic stage j
γ^2_j	cost coefficient for permeate/product tank of semicontinuous of chromatographic stage j
γ^3_j	cost coefficient for chromatographic column in stage j
ρ	appropriate constant comparable to c_j parameters
d_i	overall amount of product i to be made within the time horizon δ
δ	time horizon