Exam plus Solutions

Pan American Advanced Studies Institute
Emerging Trends in Process Systems Engineering

Name: _____

You need to answer at <u>one question</u> of each of the following topics listed below. Each is worth 10 points

1. Biosystems Engineering I. _____
2. Biosystems Engineering II. _____
3. Multiscale Design of New Materials I. _____
4. Multiscale Design of New Materials II. _____
5. Analysis of complex reaction networks _____
6. Complex distillation systems _____
7. Crystal Engineering _____
8. Sustainability _____
9. Energy Systems Analysis _____
10. Enterprise-wide Optimization _____
11. Batch Scheduling _____

TOTAL (110 pts) _____

1. Biosystems Engineering I. (Prof. Floudas)

Answer ONE of the 3 questions.

1. Secondary Structure Prediction Problems

a) Purely α – helical protein

Problem: Predict the secondary structure of the following purely α – helical protein (PDB: 1R69, Number of residues = 63)

SISSRVKSKRIQLGLNQAELAQKVGTTQQSIEQLENGKTKRPRFLPELASALGVSV
DWLLNGT

b) Purely β – protein

Problem: Predict the secondary structure of the following purely β – protein (PDB: 1TEN, Number of residues: 89)

LDAPSQIEVKDVTDTTALITWFKPLAEIDGIELTYGIKDVPGDRTTIDLTEDENQYS
IGNLKPDTEYEVSLISRRGDMSSNPAKETFTT

c) Mixed α/ β protein

Problem: Predict the secondary structure of the following mixed α/ β protein (PDB: 121P, Number of residues = 166)

MTEYKLVVVGAGGVGKSALTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDI
LDTAGQEEYSAMRDQYMRTGEGFLCVFAINNTKSFEDIHQYREQIKRVKDSDDV
PMVLVGNKCDLAARTVESRQAQDLARSYGIPYIETSAKTRQGVEDAFYTLVREI
RQH

Hint: EVASEC (http://cubic.bioc.columbia.edu/eva/doc/intro_sec.html) is a portal, which automatically analyses protein secondary structure prediction servers in 'real time'. A number of online secondary structure prediction methods can be found here. Some of the top – most servers from here can be used for secondary structure prediction. The predictions from the servers can be used in a consensus evaluation of the final secondary structure of the protein.

2. β – sheet Topology Prediction Problems

BPTI is a small globular protein found in many tissues of the human body. BPTI inhibits several of the serine protease proteins such as trypsin, kallikrein, chymotrypsin and plasmin, and is a part of the family of serine protease inhibitors. These proteins usually have conserved cysteine residues that participate in the formation of disulphide bonds.

a) Predict the sheet topology for the BPTI protein presented below. The actual secondary structure has also been presented:

RPDFCLEPPYTGPCKARIIRYFYNAKAGLCQTFVYGGCRAKRNNFKSAED
CMRTCGGA

The secondary structure is:

Helix 1:	3 to 6
Strand 1:	18 to 24
Strand 2:	29 to 35
Strand 3:	42 to 43
Helix 2:	48 to 55

b) Predict the β – sheet topology for BPTI, using the strand – wise and the residue – wise hydrophobicity maximization Integer programming model (ILP).

3. Tertiary Structure Prediction Problems

The prediction of the tertiary structure of a protein, given its amino acid sequence (primary sequence) is considered as one of the "holy grails" of computational biology. Numerous methods have been suggested towards this end, including homology based, fold recognition based and *ab initio* prediction methods.

The TPR2A domain (PDB: 1elr, Number of residues = 128) of the HOP complex is an important chaperone protein, which is a critical element in the assembly of the Hsp70-Hsp90 multi-chaperone machine in the body. The amino acid of this purely α – helical domain is:

GKQALKEKELGNDAYKKKDFDTALKHYDKAKELDPTNMTYITNQAAVY
FEKGDYNKCRELCEKAIEVGRENREDYRQIAKAYARIGNSYFKEEKYKD
AIHFYNKSLAEHRTPDVLKKCQQAEKILKEQ

Servers like SAM (http://www.soe.ucsc.edu/research/compbio/SAM_T06/T06-query.html) and 3DPro (http://scratch.proteomics.ics.uci.edu/) provide online facility to submit amino acid sequences to get back the final 3-d structures of proteins. The response is provided in PDB format, and can be viewed using commonly available molecular viewers.

Predict the structure of 1ELR, and compare the predicted structures with the actual native structure of the protein. The native structure of 1ELR can be got from the Protein Data Bank (http://www.rcsb.org/pdb/home/home.do). One of the common ways to compare structures is to evaluate the root mean squared deviation (RMSD) between the two structures.

Hint: In order to compare the outputs, the outputs can be viewed on the free, open – source molecular viewer PYMOL (available at www.pymol.org). The older, freely available version of PYMOL can execute RMSD evaluations. After installing PYMOL, run the pymol executable. Load the predicted protein structure, along with the native protein structure onto pymol. Once this is done, you can click on the action button corresponding to either one of them (the 'A' button next to the structure name), and align it to the other structure. The RMSD value between the two shall show up on the supporting text screen.

SOLUTIONS

1. Secondary Structure Prediction: Solutions

a) Using the Dictionary of secondary structure of proteins (DSSP), the assigned secondary structure for 1R69 is:

Helix 1:	2 to 12
Helix 2:	17 to 24
Helix 3:	28 to 35
Helix 4:	45 to 51
Helix 5:	56 to 61

A number of secondary structure prediction servers are available online, which can be used for this purpose. The accuracies of these servers can be seen at: http://cubic.bioc.columbia.edu/eva/doc/intro_sec.html

The predicted secondary structure output from one of the popular secondary structure prediction servers (PSIPRED) is:

Helix 1:	2 to 12
Helix 2:	17 to 24
Helix 3:	28 to 35
Helix 4:	42 to 52
Helix 5:	56 to 61

b) The DSSP Output for the secondary structure assignment of 1TEN:

Strand 1:	5 to 10
Strand 2:	17 to 22

Strand 3:	30 to 37
Strand 4:	45 to 50
Strand 5:	55 to 58
Strand 6:	66 to 75
Strand 7:	78 to 79
Strand 8:	83 to 88

The PSIPRED prediction for 1TEN is:

Strand 1:	8 to 12
Strand 2:	16 to 22
Strand 3:	30 to 37
Strand 4:	44 to 48
Strand 5:	55 to 58
Strand 6:	66 to 75
Strand 7:	83 to 88

As can be seen, prediction of β – strands is a much more difficult problem than predicting α – helices, since strands join together to form β – sheets, using tertiary contacts in the process.

c) The DSSP Output for secondary structure assignment for 121P is:

Strand 1:	2 to 9
Helix 1:	16 to 25
Strand 2:	37 to 46
Strand 3:	49 to 58
Helix 2:	65 to 74
Strand 4:	77 to 83
Helix 3:	87 to 103
Strand 5:	111 to 116
Helix 4:	127 to 137
Strand 6:	141 to 143
Helix 5:	152 to 164

The PSIPRED prediction for 121P is:

Strand 1:	2 to 9
Helix 1:	16 to 25
Strand 2:	38 to 46
Strand 3:	49 to 57
Helix 2:	62 to 73
Strand 4:	77 to 83
Helix 3:	87 to 103
Strand 5:	111 to 116
Helix 4:	127 to 136

Strand 6:	141 to 143
Helix 5:	152 to 165

2. β – sheet Topology Prediction: Solutions

The ILP model to predict the sheet topology for BPTI contains Integer cut constraints. These constraints allow the additional feature of not only getting the optimal solution, but to get a rank – ordered list of solutions, by eliminating the current solution at each iteration.

The top 3 predicted tertiary contacts for BPTI are:

Solution 1:

Contact between:	5 – 55	Cys – Cys
	14 – 38	Cys – Cys
	30 – 51	Cys – Cys
	18 – 34	Ile – Val
	19 – 33	Ile – Phe
	23 – 29	Tyr – Leu
	22 – 45	Phe – Phe

Solution 2:

Contact between:	5 – 51	Cys – Cys
	14 – 38	Cys – Cys
	30 – 55	Cys – Cys
	18 – 34	Ile – Val
	19 – 33	Ile – Phe
	23 – 29	Tyr – Leu
	21 – 45	Tyr – Phe

Solution 3:

Contact between:	5 – 38	Cys – Cys
	14 – 55	Cys – Cys
	30 – 51	Cys – Cys
	18 – 34	Ile – Val
	19 – 33	Ile – Phe
	23 – 29	Tyr – Leu
	10 – 22	Tyr – Phe

3. Tertiary Structure Prediction: Solutions

The RMSD value between the native 1ELR and the 5 models received from SAM-T06 are:

1.495 A, 6.276 A, 1.267 A, 2.029 A and 7.213 A

2. Biosystems Engineering II. (Prof. Doyle)

Answer ONE of the 3 questions.

1) The following questions refer to the lambda-phage toggle switch (see Figure in lecture notes you were handed out in class).

i) What would be the consequences if CI degradation were more prevalent than CI dimerization? How does Cro_2 affect the ability of CII to switch λ from lytic to lysogenic?

ii) If the PL promoter were inactivated, would this change the outcome of the toggle switch for lysogenic vs. lytic lifestyles? Explain your answer.

iii) Which of the three regulatory regions (boxes) in the figure given in the lecture notes would be subject to the most noise? Hypothesize why tolerance of noise in this area of the λ life cycle may be advantageous.

iv) Stepping back, and thinking about "reliability" in a more general context: if you were designing a biological network to be as reliable as possible, would you design:

- fewer components that could multitask (each one performing multiple roles), or
- more components, each with a specialized function? Explain your answer.

2) Using one of the biological examples from lecture (or from the reading), describe the following:

i) How is a "systems" method of analysis likely to yield more insight for this problem than a classical "reductionist" approach?

ii) What computational methods would be most appropriate, given the characteristics of the chosen system?

iii) Likewise, what are the most appropriate experimental approaches (e.g., microarray, proteomic, etc.) that would yield insight for this system?

3) A patient with type I diabetes needs an automated scheme to maintain her blood sugar within acceptable range (54 mg/dL < glucose < 144 mg/dL). She has just eaten a large meal disturbance) that you estimate will introduce glucose into her bloodstream according to $D(t) = 9.0$ $^{0.05t}$, where t is in minutes and $D(t)$ is in mg/dL-min. She has a subcutaneous insulin pump that c release insulin up to 115 mU/min (mU = 10^{-3} Units of Insulin). The flowrate of insulin is t manipulated variable.

A simple model of her blood glucose level is given by (Bequette, 2002):

$$\frac{dG}{dt} = -p_1 G - X(G + G_{Basal}) + D$$

$$\frac{dX}{dt} = -p_2 X + p_3 I$$

$$\frac{dI}{dt} = -n(I + I_{Basal}) + \frac{U}{V_1}$$

Where the constants are defined as follows: p_1=0.028735, p_2=0.028344, p_3=5.035E-5, V_1=12, and n=.0926. G, X, and I are values for glucose concentration (deviation) in the blood (mg/dL), insulin concentration (deviation) in the body (mU/L), and plasma insulin concentration (deviation), respectively. Basal values refer to the initial or baseline values for each variable (G_{basal} = 81 mg/dL and I_{basal} = 15 mU/L). D is the rate of glucose release into the blood (mg/dL-min) as the disturbance. U is the flowrate of insulin (mU/min) as the manipulated variable.

(a) What will happen to her blood glucose level if the pump is shut off initially?

(b) What will happen to her blood glucose level if the pump injects at a constant rate of 15 mU/min?

(c) Is there a constant infusion rate of insulin that will help her stay within an acceptable glucose range (54mg/dL < G < 170mg/dL) for the next 400 minutes?

SOLUTIONS

i)

If CI were degraded more rapidly, fewer dimers would be formed, which is the functional unit of CI. With less functional CI_2, less CIII would be produced which would result in less CII dimer formation due to increased CII degradation. Loss of CI_2 and CII would result in more Cro production and Cro_2 formation, which switches λ from a lysogenic to a lytic lifestyle. Therefore, by changing a simple characteristic such as the CI degradation rate, you can switch the virus from lysogenic to lytic.

Cro does not directly influence CII production. However, Cro_2 blocks the production of CI and CIII, which help promote CII. Therefore, Cro reduces the production of CII by reducing the production of CI and CIII.

ii)

Similar to the question above, reducing the amount of CIII would eventually result in a switch to lytic lifestyle. This question is not intended to be redundant but to illustrate how different components of a circuit can be altered separately and influence the outcome of the entire circuit. This helps set the stage for more complex circuits later in this chapter.

iii)

Noise in this case is probably due to irregular bursts of protein production and protein-protein interactions. It is impossible to know for sure, but based on what we have read so far, it appears that R1 and R2 might experience the most noise since protein dimerization is required. CIII does not have to dimerize before inhibiting CII degradation.

iv)

If you add more components, with each performing a specialized role, then there are more places where the circuit can fail. This is similar to buying a car with all the options versus a car with few luxuries (e.g., nonpower windows). If you design a system with parts that can perform redundant functions, then if one part fails, there may be a redundancy that can fill the gap and permit the entire circuit to be completed. The increased reliability may explain why we have so many isozymes and other apparent redundancies in our genomes.

3. Multiscale Design of New Materials I. (Prof. Venkatsubramanian)

Read and write a review (1-2 pages each) of ONE of the following two articles from http://cepac.cheme.cmu.edu/pasi2008/slides/venkat/index.htm

1. Design of Fuel Additives Using Neural Networks and Evolutionary Algorithms
Anantha Sundaram, Prasenjeet Ghosh, James M. Caruthers, and Venkat Venkatasubramanian

2. An Intelligent System for Reaction Kinetic Modeling and Catalyst Design
Santhoji Katare,† James M. Caruthers, W. Nicholas Delgass, and Venkat Venkatasubramanian*

4. Multiscale Design of New Materials I. (Prof. Grover Gallivan)

Answer ONE of the 3 questions.

1. Perform 3 iterations of the stochastic simulation algorithm for the following system.

   Reaction 1: $A \leftrightarrow B$ $\quad k_1 = 10\ s^{-1}$, $k_{-1} = 1\ s^{-1}$
   Reaction 2: $2B \rightarrow C$ $\quad k_2 = 5\ s^{-1}$
   Initially, there are 5 molecules of *A*. There is no *B* or *C* in the system, and $t = 0$ s. At the end of each iteration, compute the time and the number of each species present. Use the list of pseudorandom numbers below.
   x_r: 0.9501 0.2311 0.6068 0.4860 0.8913 0.7621

2. Consider the model

$$\hat{y}(x_1, x_2) = \theta_1 + \theta_2 x$$

   and the experimental design

x
-1
1
a

   a. Compute the D-optimal value of a (the third experiment).

   b. Is the 3^k factorial design equivalent to D-optimal?

3. Given the data (one "repetition" only)

x	*y*
-1	-3
0	0
1	1

   a. Compute the best fit parameters for the model $\hat{y}_1(x) = \theta_1 x^2$.

   b. Compute the best fit parameters for the model $\hat{y}_2(x) = \theta_1 x^2 + \theta_2 x$.
   c. Compute the probabilities of both models, assuming that their *a priori* initial probabilities are equal. Which one is more probable, given the data?
   d. At what point on the interval $-1 \le x \le 1$ do the models maximally disagree?

SOLUTION

1. Perform 2 iterations of the stochastic simulation algorithm for the following system.

   Reaction 1: $A \leftrightarrow B$ $\quad k_1 = 10\ s^{-1}$, $k_{-1} = 1\ s^{-1}$

   Reaction 2: $2B \rightarrow C$ $\quad k_2 = 5\ s^{-1}$

   Initially, there are 5 molecules of *A*. There is no *B* or *C* in the system, and *t* = 0 s. At the end of each iteration, compute the time and the number of each species present. Use the list of pseudorandom numbers below.

   x_r: 0.9501 0.2311 0.6068 0.4860 0.8913 0.8621

   Solution:

   The forward reaction for Reaction 1 is labeled 1, the backward reaction is 2, and Reaction 2 is labeled as 3. Initially, there are 5 A's, 0 B's, and 0 C's.

Iteration	1	2	3
$k_1 N_1$	10(5) = 50	10(4) = 40	10(3) = 30
$k_2 N_2$	1(0) = 0	1(1) = 1	1(2) = 2
$k_3 N_3$	5(0) = 0	5(0) = 0 (no pairs of B)	5(1) = 5 (one pair of B)
$\Sigma k_i N_i$	50	41	37
Δt (s)	-ln(0.9501)/50 = 0.0010	-ln(0.6068)/41 = 0.0122	-ln(0.8913)/37 = 0.0031
t (s)	0	0.0010+0.0122 = 0.0132	0.0132+0.0031 = 0.0163
$k_1 N_1 / \Sigma k_i N_i$	$1 > x_r = 0.2311$	40/41 = 0.9756 > 0.4860	30/37 = 0.8108 < 0.8621
$(k_1 N_1 + k_2 N_2)/ \Sigma k_i N_i$	1	41/41 = 1	32/37 = 0.8649 > 0.8621
Event selected	Event 1	Event 1	Event 2
A	4	3	4
B	1	2	1
C	0	0	0

I did three iterations here. The problem asked for two only. You could add the third or not depending on length of exam.

2. Consider the model

$\hat{y}(x_1, x_2) = \theta_1 + \theta_2 x$

and the experimental design

x
-1
1
a

a. Compute the D-optimal value of a (the third experiment). Restrict your experiments to $-1 \leq x \leq 1$. Hint: you may wish to substitute $\alpha = \alpha^2$ at some point to help with the calculations.

b. Is the 3^k factorial design equivalent to D-optimal?

Solution:

$$X = \begin{bmatrix} 1 & -1 \\ 1 & 1 \\ 1 & \alpha^2 \end{bmatrix}$$

$$X^T X = \begin{bmatrix} 3 & \alpha^2 \\ \alpha^2 & 2 + \alpha^4 \end{bmatrix} = \begin{bmatrix} 3 & 2 + \alpha \\ 2 + \alpha & 2 + \alpha^2 \end{bmatrix}$$

$$|X^T X| = 3(2 + \alpha^2) - (2 + \alpha)^2 = 2 - 4\alpha + 2\alpha^2 = 2 - 4\alpha^2 + 2\alpha^4$$

This function is largest when $\alpha = 0$. For this model, D-optimal is equivalent to 3^k factorial.

3. Given the data (one "repetition" only)

x	*y*
-1	3
0	0
1	1

a. Compute the best fit parameters for the model $\hat{y}_1(x) = \theta_1 x^2$.

b. Compute the best fit parameters for the model $\hat{y}_2(x) = \theta_1 x^2 + \theta_2 x$.

c. Compute the probabilities of both models, assuming that their *a priori* initial probabilities are equal. Which one is more probable, given the data?

d. At what point on the interval $-1 \le x \le 1$ do the models maximally disagree?

Solution:

a. $X = \begin{bmatrix} 1 \\ 0 \\ 1 \end{bmatrix}, X^T X = 1 + 0 + 1 = 2, X^T y = 3 + 0 + 1 = 4, \theta_1 = \frac{4}{2} = 2$

$y_1(x) = 2x^2$

b. $X = \begin{bmatrix} 1 & -1 \\ 0 & 0 \\ 1 & 1 \end{bmatrix}, X^T X = \begin{bmatrix} 2 & 0 \\ 0 & 2 \end{bmatrix} = 2, X^T y = \begin{bmatrix} 4 \\ -2 \end{bmatrix}, \theta_1 = \frac{4}{2} = 2, \theta_2 = \frac{-2}{2} = -1$

$y_2(x) = 2x^2 - x$

c.

x	*y*	y_1	y_2
-1	3	2	3
0	-1	0	0
1	1	2	1

$\hat{S}_{res1} = 1 + 0 + 1 = 2, \hat{S}_{res2} = 0 + 1 + 0 = 1$

$p(M_1|y,\theta) = 0.5\left((2\pi)^{-\frac{1}{2}}(\square)3^{-\frac{1}{2}}\right) = 0.20$

$p(M_2|y,\theta) = 0.5\left((2\pi)^{-1}(\square)1^{-\frac{1}{2}}\right) = 0.25$

Model 2 is more probable.

d. The models disagree most at $x = 1$. This might be the best point to do the next experiment, although we should also take into account the uncertainties in the predictions when doing formal model discrimination.

5. Analysis of complex reaction networks (Prof. Ierapetritou)

Answer ONE of the 3 questions.

1. Bi-level Optimization

Solve the following bi-level problem using any suitable method (discuss the suitability of your selected method):

$$
\begin{aligned}
&\underset{x \in X}{Min} F_1(x,y) = x - 4y \\
&st. \quad -x - y \le -3, \\
&\quad -3x + 2y \ge -4, \\
&\underset{y \in Y}{Min} F_2(x,y) = x + y \\
&st. \quad -2x + y \le 0, \\
&\quad 2x + y \le 12.
\end{aligned}
$$

Sketch the feasible space of the problem and point in the figure the inducible region and the bi-level optimal solution. (Hint: use geometrical arguments to find the solution)

2. Flexibility evaluation

For the following problem formulate the mathematical model to evaluate the flexibility index. Reformulate the problem using the active set strategy as a MINLP.

Consider a "shower" problem, where the inputs are streams of cold ($0 \le q_1 \le 4$ gal/min) and hot water ($0 \le q_2 \le 3$ gal/min) ($u_1 = q_1$ and $u_2 = q_2$). Assume initially that the cold and hot water temperatures are fixed at $T_1 = 60^0$F and $T_2 = 120^0$F, respectively. These temperatures could be subject to disturbances or uncertainties. The total flow (F) obtained from the mixture of the two streams and the outlet water temperature (T) are considered as the process outputs ($y_1 = F$ and $y_2 = T$). Moreover, the following non-linear model relates process outputs and inputs:

$$F = q_1 + q_2 \quad \text{and} \quad T = \frac{q_1 T_1 + q_2 T_2}{q_1 + q_2}$$

Furthermore, assume that the desired ranges of the shower total flow and temperature are $3 \le F \le 7$ gal/min and $74 \le T \le 94$ ^{0}F, respectively. Also consider that the hot water temperature can vary between $T_2 = 110^o$F and $T_2 = 130^o$F, which characterizes a

disturbance of $-10 \le d \le 10^{o}$F.

3. Network analysis

(a) In the following formulation if λ_j is a binary variable corresponding to the presence or absence of reaction (j) in the network, what will be the outcome of the optimization with respect to the network analysis?

$$\min_{\lambda_j} \Phi = \sum_{j=1}^{N} \lambda_j$$

$$\text{subject to: } \sum_{j=1}^{N} S_{ij} v_j = b_i, \quad i = 1,...,M$$

$$v_j^{min} \lambda_j \le v_j \le v_j^{max} \lambda_j, \quad j = 1,...,N$$

(b) For the following general LP

$$\mathbf{min}\, Z = \alpha^T z$$

$$\text{s.t.} Bz = q$$

$$z \ge 0$$

The following optimization expresses the problem that has to be solved iteratively in order to obtain all the optimal solutions of the previous LP.

$$\mathbf{min}\, Z^K = \alpha^T z$$

$$\text{s.t.} Bz = q$$

$$\sum_{i \in NZ^{K-1}} y_i \ge 1$$

$$\sum_{i \in NZ^k} w_i \le \left| NZ^k \right| - 1, k = 1,2,...,K-1$$

$$0 \le z_i \le U w_i, i \in I$$

$$y_i + w_i \le 1, i \in NZ^{K-1}$$

$$z \ge 0$$

Explain the use of each constraint in this formulation.

SOLUTION

1. The main idea of the Kuhn–Tucker approach for linear BLP is that it replaces the follower problem (F_2) with its Kuhn–Tucker conditions and appends the resultant system to the leader's problem (F_1).

$$
\begin{aligned}
&\underset{x \in X}{Min} F_1(x, y) = x - 4y \\
&st. \quad -x - y \le -3, \\
&\quad -3x + 2y \ge -4, \\
&\quad \underset{y \in Y}{Min} F_2(x, y) = x + y \\
&\quad st. \quad -2x + y \le 0, \\
&\qquad 2x + y \le 12. \\
&\qquad y \ge 0
\end{aligned}
$$

According to the extended Kuhn–Tucker approach, let us write all the inequalities of the above problem as follows:

$$
\begin{aligned}
&g_1(x, y) = x + y - 3 \ge 0, \\
&g_2(x, y) = -3x + 2y + 4 \ge 0, \\
&g_3(x, y) = 2x - y \ge 0, \\
&g_4(x, y) = -2x - y - 12 \ge 0, \\
&g_5(x, y) = y \ge 0.
\end{aligned}
$$

Let u_1, u_2, u_3, u_4, u_5 be the corresponding dual variables for constraints g_1, g_2, g_3, g_4, g_5 respectively. Applying KKT condition we obtain the following single level problem:

$$
\begin{aligned}
&\underset{x, y \in X, Y}{Min} F_1(x, y) = x - 4y \\
&st. \qquad x + y - 3 \ge 0, \\
&\qquad -3x + 2y + 4 \ge 0, \\
&\qquad 2x - y \ge 0, \\
&\qquad -2x - y + 12 \ge 0 \\
&\qquad -u_1 - 2u_2 + u_3 + u_4 - u_5 = -1 \\
&\qquad u_1 g_1(x, y) + u_2 g_2(x, y) + u_3 g_3(x, y) \\
&\qquad + u_4 g_4(x, y) + u_5 g_5(x, y) = 0 \\
&\qquad x, y, u_1, u_2, u_3, u_4, u_5 \ge 0
\end{aligned}
$$

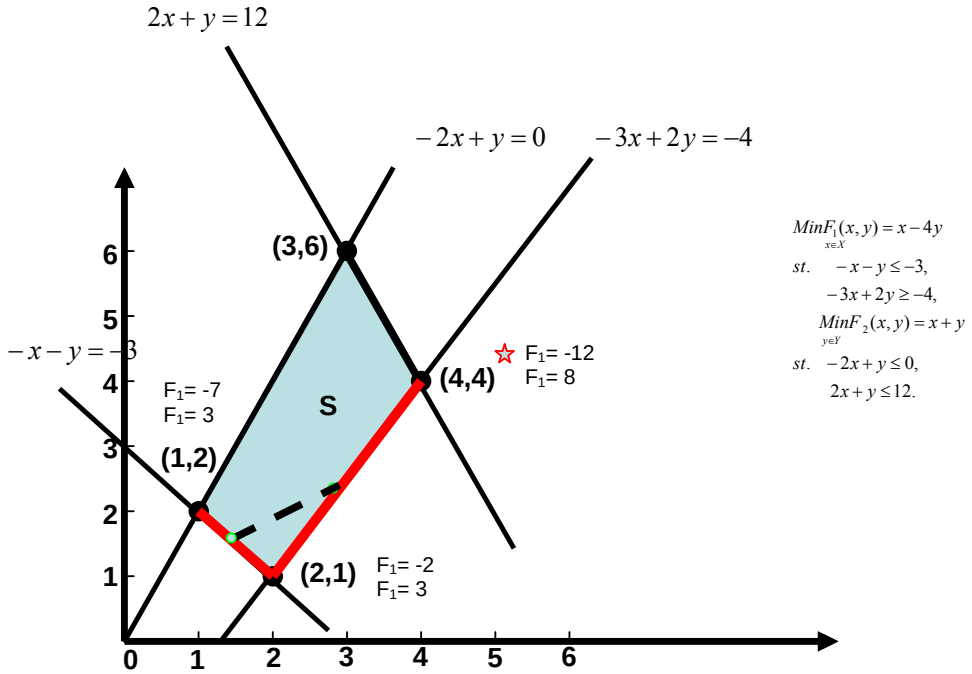
For the solution of the above nonlinear single level problem we can use the active set strategy.

We replace the last nonlinear constraints using auxiliary binary variables:

$$\underset{x,y\in X,Y}{Min} F_1(x,y) = x - 4y$$

$$\begin{aligned}
st. \quad & x + y - 3 \geq 0, \\
& -3x + 2y + 4 \geq 0, \\
& 2x - y \geq 0, \\
& -2x - y + 12 \geq 0, \\
& -u_1 - 2u_2 + u_3 + u_4 - u_5 = -1, \\
& u_1 \leq Mv_1, \\
& g_1(x,y) \leq M(1 - v_1), \\
& u_2 \leq Mv_2, \\
& g_2(x,y) \leq M(1 - v_2), \\
& u_3 \leq Mv_3, \\
& g_3(x,y) \leq M(1 - v_3), \\
& u_4 \leq Mv_4 \\
& g_4(x,y) \leq M(1 - v_4) \\
& u_5 \leq Mv_5 \\
& g_5(x,y) \leq M(1 - v_5) \\
& x, y, u_1, u_2, u_3, u_4, u_5 \geq 0
\end{aligned}$$

The solution of the above problem gives the bi-level optimal solution and for the linear continuous case is an extreme point of region defined by the constraints of the upper and lower level. The bi-level solution is between all the extreme points belonging to the inducible region which is a nonconvex region, red line in the following figure:



$$\underset{x\in X}{Min} F_1(x,y) = x - 4y$$

$$\begin{aligned}
st. \quad & -x - y \leq -3, \\
& -3x + 2y \geq -4,
\end{aligned}$$

$$\underset{y\in Y}{Min} F_2(x,y) = x + y$$

$$\begin{aligned}
st. \quad & -2x + y \leq 0, \\
& 2x + y \leq 12.
\end{aligned}$$

2. The flexibility index can be determined with the following formulation.

$$FI = \min \delta$$

$$s.t.\ \ (q_1 - q_{1ss}) + (q_2 - q_{2ss}) + F_{ss} - 7 + s_1 = 0,\ \ -[(q_1 - q_{1ss}) + (q_2 - q_{2ss}) + F_{ss}] + 3 + s_2 = 0$$

$$(q_1 - q_{1ss})T_1 + (q_2 - q_{2ss})(T_2 - T_{2ss}) + T_{ss}((q_1 - q_{1ss}) + (q_2 - q_{2ss})) - 94((q_1 - q_{1ss}) + (q_2 - q_{2ss})) +$$

$$-[(q_1 - q_{1ss})T_1 + (q_2 - q_{2ss})(T_2 - T_{2ss}) + T_{ss}((q_1 - q_{1ss}) + (q_2 - q_{2ss}))] + 74((q_1 - q_{1ss}) + (q_2 - q_{2ss})) -$$

$$q_1 - 4.0 + s_5 = 0,\ q_2 - 3.0 + s_6 = 0,\ \ -q_1 + s_7 = 0,\ q_2 + s_8 = 0$$

$$\sum_{j=1}^{8} \lambda_j = 1,\ \sum_{j=1}^{8} y_j \le 3$$

$$\lambda_1 - \lambda_2 + \lambda_3(T_1 + T_{ss} - 94) + \lambda_4(-T_1 - T_{ss} + 74) + \lambda_5 - \lambda_7 = 0$$

$$\lambda_1 - \lambda_2 + \lambda_3(T_2 + T_{ss} - 94) + \lambda_4(-T_2 - T_{ss} + 74) + \lambda_6 - \lambda_8 = 0$$

$$\lambda_j - y_j \le 0, j = 1,...,8,\ s_j - U(1 - y_j) \le 0, j = 1,...,8$$

$$120 - 10\delta \le T_2 \le 120 + 10\delta,\ y_j = \{0,1\},\ \lambda_j, s_j \ge 0, j = 1,...,8$$

In these equations q_{1ss}, q_{2ss}, T_{2ss}, F_{ss}, and T_{ss} are steady-state values of q_1, q_2, T_2, F, and T. The above formulation is non-linear and non-convex because of the bilinear term q_2T_2 in the original constraints and bilinear term λ_jT_2 in the gradient KKT constraints

3. Answer:

(a) The solution of this problem will provide the list of most important reactions in the network. You can use this model to reduce the size of kinetic network given specific conditions.

(b) The answer to this question is straight from the paper Lee et al. 2000 attached in the supplement material.

6. Complex distillation systems (Prof. Aguirre)

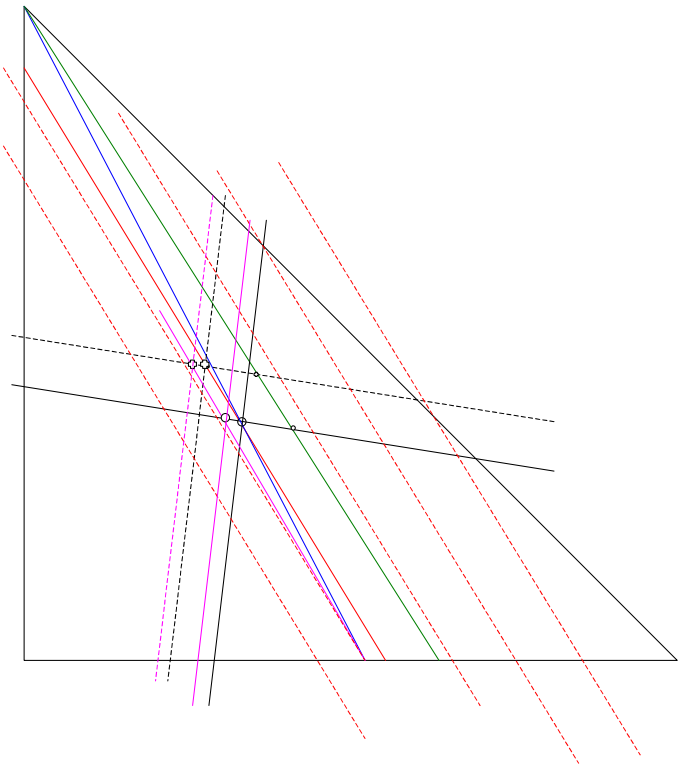
Answer ONE of the 3 questions.

1) Compute reversible distillations for different feeds of the three component mixture n-butane/isopentane/n-pentane (use the Gams file: rev_dist_nin_pasi08.gms).

2) Analyze saddle pinch and feed composition in a triangle diagram for different feed compositions (use excel).

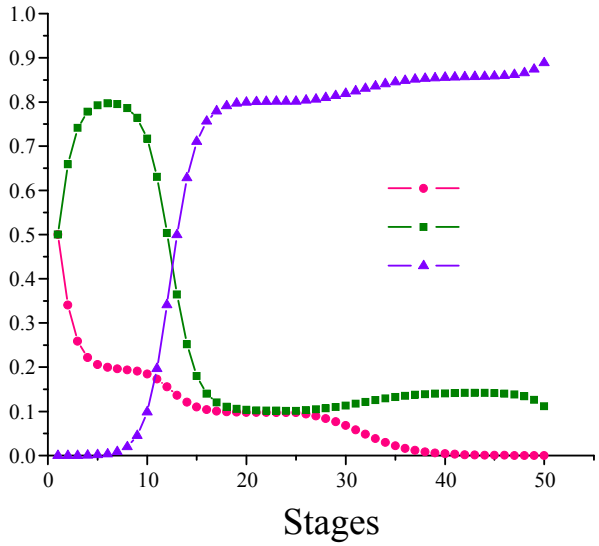
3) Select a feed composition and simulate (Aspen, Hysys) the reversible separation. Use Nstages>40 and tray to detect saddle pinchs. Initialize with values obtained previously. Show results: liquid composition vs. stages. Compare results. (Hint: specify a product flow rate and a reflux ratio)

SOLUTION
The triangle diagram should look like the following.
Saddle pinchs are on straight lines with feed (results from Gams file).



Liquid composition profiles should look like this (results from hysys simulation):

Liquid composition



Pinch composition and energy values from the rigorous simulation are predicted with error < 15 % by the reversible model.

7. Crystal Engineering for Product and Process Design (Prof. Doherty)

Answer ONE of the 3 questions.

(1) Derive a dynamic model to describe the shape evolution of faceted crystals undergoing (a) growth, and (b) dissolution. What are the algebraic conditions that define the steady-state shapes? Are these steady-states stable or unstable? Draw a sketch (roughly to scale) of the steady-state shape of a 2-dimensional plate-like crystal growing with only two principal faces which are perpendicular to each other (by symmetry there are four faces in total) and which have absolute face growth rates of 10nm/s and 2 nm/s, respectively.

Is the faster growing face larger or smaller than the slower growing face?

(2) Crystal shapes are normally modified by *chemical* means using such techniques as adding small amounts of growth inhibitors or by changing the solvent, or both. You would like to modify the shape of crystals grown in your process but for regularity reasons (e.g., FDA regulations) you are not allowed to change the solvent or to add any foreign substances (such as growth inhibitors) into your process. Being an engineer, you recognize that chemical engineers have been able to "beat" chemistry with clever processing tricks in the past - for example, using a plug flow reactor in place of a stirred tank reactor in order to get better product selectivity when certain by-product forming reactions occur. Inspired by past successes of chemical engineers you have given the crystal shape manipulation problem some thought and you believe that you have come up with a clever processing solution for changing their shapes. Your processing solution involves growing crystals in a batch crystallizer for a certain period of time then dissolving them for a further period of time. By repeating this cycle several times you think that you will be able to manipulate the shape of crystals produced by this process such that they will have shapes that are different than either the growth shape or the dissolution shape.

Before you build an experiment to test your idea you want to develop a simple model of the crystal shape evolution under these cycling conditions so as to have a better understanding of what is likely to happen in the experiment (and thereby you will be able to build a better apparatus right from the outset).

For the case of constant (but not necessarily equal) growth and dissolution rates, develop a discrete dynamical system to relate the shape of a crystal at the end of cycle "$j+1$" to the shape at the end of cycle "j." One cycle corresponds to one growth period and one dissolution period. Use the dimensionless perpendicular distance to face i at the end of cycle "j" (denoted by $x_{i,j}$) as the appropriate measure of crystal shape.

On the basis of your model, determine under what conditions such cycling produces no change in crystal shape, and under what conditions this cycling procedure produces greatest changes in shape.

Solution

1. All the elements of the solution can be found in the papers

> Zhang, Sizemore and Doherty, "Shape Evolution of 3-Dimensional Faceted Crystals," *AIChEJ, 52*, 1906 (2006)
>
> Snyder and Doherty, "Faceted Crystal Shape Evolution During Dissolution or Growth," *AIChEJ, 53*, 1377 (2007)

I can give you some additional guidance at the summer school.

On the basis of your model, determine under what conditions such cycling produces no change in crystal shape, and under what conditions this cycling procedure produces greatest changes in shape.

2. All the elements of the solution can be found in the paper

> Snyder, Studener and Doherty, "Manipulation of Crystal Shape by Cycles of Growth and Dissolution," *AIChEJ, 53*, 1510 (2007)

I can give you some additional guidance at the summer school.

8. Sustainability in the Chemical and Energy Industries (Dr. Siirola)

Answer ONE of the 3 questions.

Question 1: What are some of the expected energy impacts that may result from switching from traditional oil- and natural gas-based feedstocks to coal or biomass-based raw materials for the chemical industries?

Possible answers:
1. The average reaction energy will change from net exothermic to net endothermic.
2. Reaction energy will not likely be available for recovery and use within the process for separation and purification.
3. Reaction selectivity is likely to decrease (because of the likely higher average temperatures likely required to achieve satisfactory reaction equilibria, and the fundamental asymmetry between removing heat from a reaction site and its environment and adding heat to a reaction site).
4. If the raw material is biomass, additional energy may be required to dry it and remove water of reaction .
5. Average utility requirements may triple (because reactions will be net endothermic and all separation and purification requirements will be driven by utilities (not exothermic reactions)).

Question 2: Can biomass be expected to meet society's energy needs? Elaborate.

Possible answers:
1. Today's worldwide biomass production (60GTC/yr) exceeds the dry biomass energy equivalent of total fossil fuel consumption (10GTC/yr) so it would be possible if 1/6 of all annual biomass were so harvested, dried, and so employed. However, 50% more must be harvested if biomass energy is to be used to dry and dehydrate the biomass or the resulting fuel product. This totals 15GTC/yr biomass which might be compared to 6GTC/yr for all cultivated crops worldwide. Within fifty years, the total energy need is expected increase by about 350% which would equal the entire annual worldwide biomass production (including the 9GTC/yr that would by then be required for agricultural crops). Further, given that half of the world biomass production occurs in the tropical rainforest and tropical savannah, and that harvest of the annual biomass production in non-agricultural areas is extremely difficult, the conclusion would be that only a very small fraction of energy needs can be derived from solar via biomass.

Question 3a: What fraction of current carbon dioxide emissions (7GTC/yr) must be captured and sequestered to return the atmosphere to preindustrial CO2 concentrations (280ppm)?
3b: What fraction of projected 2050 carbon dioxide emissions if all coal-based (37GTC/yr) must be captured to hold the atmospheric CO2 concentration at today's level (380ppm)?
3c: What level will the atmospheric CO2 concentration rise to if we hold worldwide emissions at today's level (7GTC/yr)
3d: What level will the atmospheric CO2 concentration rise to by 2050 is all energy is coal-based and no CO2 is captured or sequestered (37GTC/yr CO2 emissions)?
3e: At what atmospheric CO2 concentration do adverse climatic, geophysical, or biological impacts begin?

Answers:
3a: 100%
3b: 93%
3c: 460ppm
3d: about 1650ppm
3e: unknown, but some may already be occurring at 380ppm

Question 4: What does carbon capture and sequestration cost?

Answer: Unknown, but current estimates are about $125/ton CO2 ($450/TC). It may prove to be significantly higher.

9. Energy Systems Analysis (Prof. Agrawal)

Answer ONE of the 3 questions.

1. Consider a scenario where the current gasoline driven cars are to be replaced with H_2 powered fuel cell vehicles. Furthermore, all the H_2 is produced using coal gasification.

    a. Will the use of coal in such a scenario lead to an increase in CO_2 emissions?

    b. Will well to wheels energy consumption using H_2 from coal be higher for the H_2 fuel cell vehicles when compared to gasoline driven cars.

2. What is the most efficient way to use solar energy to drive a car? What are the hurdles in the implementation of this efficient method?

3. In your opinion, why is it necessary to improve the yield of liquid fuel production from a given quantity of biomass? Suggest a method to accomplish this task.

SOLUTIONS

1. (a.) Due to the high efficiency of H2 fuel cells, there will not be an overall increase in CO2 release even when H2 is produced from coal when compared to gasoline driven cars. This is indeed a surprising result.

(b.) Actually the overall well to wheel efficiency is expected to be slightly improved with the use of H2 from coal in the H2 fuel cell vehicles. This result is shown in the slide on well to wheel energy use.

2. The most efficient way to drive a car using solar energy is through the use of electricity from solar energy. Conversion of solar energy to electricity is at least an order of magnitude more efficient than growing biomass.

Two important hurdles in the use of electricity driven cars are: (i) availability of battery with high enough energy density. (ii) the cost of batteries is too high for this application.

3. Since solar energy is converted to biomass at low efficiencies, the carbon contained in the biomass is ‘precious’. Therefore, in order to minimize land use, it is essential that biomass to liquid fuel conversion by maximized.

The biomass to liquid fuel conversion can be maximized by treating biomass primarily as a source of carbon and supplementing the liquid fuel conversion process with an alternate energy that is recovered at a much higher efficiency. This energy could come as heat and/or hydrogen from sun, nuclear or other carbon-free energy sources.

10. Enterprise-wide Optimization (Prof. Grossmann)

Answer ONE of the 3 questions.

1. Given the Integer Programming problem (P):

$$Z = \max \quad cx$$
$$st \quad Ax \le b$$
$$Dx \le e$$
$$x \in Z_+^n$$

prove that the Lagrangean Relaxation for the above problem given by the subproblem for fixed Lagrange multipliers u, provides an upper bound to the optimal solution of problem (P):

$$Z = \max \quad cx + u(b - Ax)$$
$$st \quad Dx \le e$$
$$x \in Z_+^n$$

ANSWER
(P) is a relaxation of original problem because:
1. Removing the constraint $Ax \le b$ relaxes the original feasible space,
2. $Z_{LR}(u) \ge Z$ always holds as in the original space since $(b - Ax) \ge 0$
and Lagrange multiplier is always $u \ge 0$

2. Determine an analytical expression for the optimal number of replenishments per year, n, for inventory control, when minimizing the annual costs of ordering, shipping and working inventory from a supplier to the distribution centers as given by:

$$Fn + \beta(g + a\frac{D}{n})n + \theta\frac{hD}{2n}$$

The first term Fn is the total ordering cost per year. The second term is the annual transportation costs times the weighted factor (β), where (D/n) is the expected shipment size, D is the annual demand, and the shipping cost is given by a linear function $g + aD/n$. The third term is the annual working inventory costs times the weighted factor (θ), where $D/(2n)$ is the average inventory level on hand.

Solution:

$$n = \sqrt{\theta hD / (2(F + \beta g))}$$

3. A company is considering to produce a chemical C which can be manufactured with either process II or process III, both of which use as raw material chemical B. B can be purchased from another company or else manufactured with process I which uses A as a raw material. Given the specifications below, formulate an MILP model and solve it with GAMS to decide:
   a) Which process to build (II and III are exclusive)?
   b) How to obtain chemical B?
   c) How much should be produced of product C?
   The objective is to maximize profit.

   Consider the two following cases:

   1. Maximum demand of C is 10 tons/hr with a selling price of $1800/ton.

   2. Maximum demand of C is 15 tons/hr; the selling price for the first 10 ton/hr is $1800/ton, and $1500/ton for the excess.

Data:

Investment and Operating Costs

	Fixed ($/hr)	Variable($/ton raw mat)
Process I	1000	250
Process II	1500	400
Process III	2000	550

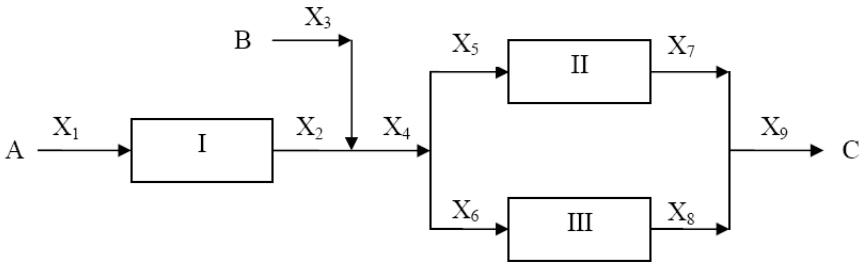
Prices: A: $500/ton
B: $950/ton

Conversions:
Process I	90% of A to B
Process II	82% of B to C
Process III	95% of B to C

Maximum supply of A: 16 tons/hr

NOTE: You may want to scale your cost coefficients (e.g. divide them by 100).

SOLUTION



Case I)

$$\textbf{Max} \quad \text{Profit} = -10y_1 - 15y_2 - 20y_3 + 18x_9 - (5 + 2.5)x_1 - 9.5x_3 - 4x_5 - 5.5x_6$$

$$\textbf{s.t.}$$

$$x_2 - 0.90x_1 = 0$$

$$x_7 - 0.82x_5 = 0$$

$$x_8 - 0.95x_6 = 0$$

$$x_4 - x_5 - x_6 = 0$$

$$x_9 - x_7 - x_8 = 0$$

$$x_4 - x_2 - x_3 = 0$$

$$x_1 - 16y_1 = 0$$

$$x_5 - 12.2y_2 = 0$$

$$x_6 - 10.6y_3 = 0$$

$$1 - y_1 + y_2 + y_3 \geq 1$$

$$x_1 \leq 16$$

$$x_9 \leq 10$$

$$x_i \geq 0 \qquad i = 1,\ldots,9$$

$$y_j = 0,1 \quad j = 1,2,3$$

Solution:

$$\text{Profit} = \$459.3/\text{hr}$$

$$x_1 = 13.55 \; tons/hr$$

$$x_2 = x_4 = x_5 = 12.20 \; tons/hr$$

$$x_7 = x_9 = 10 \; tons/hr$$

$$x_3 = x_6 = x_8 = 0 \; tons/hr$$

* Select processes I and II to produce chemical C.
* Chemical B is obtained from process I.
* Production rate of chemical C is 10 tons/hr.

11. Short-term Batch Scheduling (Prof. Mendez)

Answer ONE of the 3 questions.

1. Develop a MILP-based formulation to the scheduling of a multiproduct single-stage batch plant involving a single processing unit. Use the total tardiness criterion as the objective function to be minimized. Define and briefly describe main decision variables and equations using the following nomenclature for sets and parameters.

O	Set of production orders to be scheduled
pt_o	processing time of order o
$cl_{oo'}$	cleaning time between orders o and o'
dd_o	due date of order o
H	scheduling horizon

2. Classify the main features of the scheduling problem given above by using the 13 categories defined in the road map for scheduling problems of batch plants presented in the review paper by Méndez et al. (2006).

3. Let us consider that four consecutive processing tasks (reaction, mixing, filtering and stripping) are required to obtain a certain product "Prod" in a multistage batch plant. The Blend state produced from the mixing stage is synthesized from a (60:40)-mix of states R-prod and Add1. Also, it is known that the batch plant is always scheduled to meet minimum production targets over a one-week scheduling horizon. Data related to processing units and states are given below.

Unit	Capacity	Suitability	Processing time
Mixer 1	20	Mixing	4.0
Mixer 2	20	Mixing	4.0
Reactor 1	20	Reaction	13.0
Reactor 2	20	Reaction	13.0
Filter	20	Filtering	6.0
Strip tank 1	20	Stripping	10.0
Strip tank 2	20	Stripping	10.0
State	Storage capacity	Initial amount	
Feed	Unlimited	Unlimited	
Add 1	Unlimited	Unlimited	
R-prod (from reaction)	100	0.0	
Blend (from mixing)	100	0.0	
Filt (from filtering)	100	0.0	
Prod (from stripping)	Unlimited	0.0	

a. Generate the corresponding STN and RTN diagrams of the batch production process.
b. Classify the main features of this scheduling problem according to the road map presented by Méndez et al. (2006).

Answers.

1. *The proposed solution is based on the notion of general precedence. Other solutions lying on alternative basic ideas may be developed.*

Variable definition

Ts_o Starting time of order o

Tf_o End time of order o

$X_{oo'}$ Binary variable denoting that order o is processed before ($X_{oo'}=1$) or after ($X_{oo'}=0$) than order o'

TA_o Tardiness of order o

Constraint definition

Timing constraints: The starting and ending time for each order is defined.

$$Tf_o = Ts_o + tp_o \quad \forall o \qquad (1)$$

Sequencing constraints: If order o is processed earlier than o', then $X_{oo'}$ is equal to one and the constraint (2) is enforced to guarantee that order o' will begin after completing both the order o and the subsequent cleaning operation. Moreover, constraint (3) becomes redundant. In case that order o' is run earlier, constraint (2) is applied and constraint (3) is relaxed.

$$Ts_{o'} \geq Tf_o + cl_{oo'} - H\left(1 - X_{oo'}\right) \quad \forall o,o' \qquad (2)$$

$$Ts_o \geq Tf_{o'} + cl_{o'o} - HX_{oo'} \quad \forall o,o' \qquad (3)$$

Tardiness definition: Compute the order tardiness with respect to the promised due date.

$$TA_o \geq Tf_o - dd_o \quad \forall o \qquad (4)$$

Objective function: Generate the schedule with minimum total tardiness

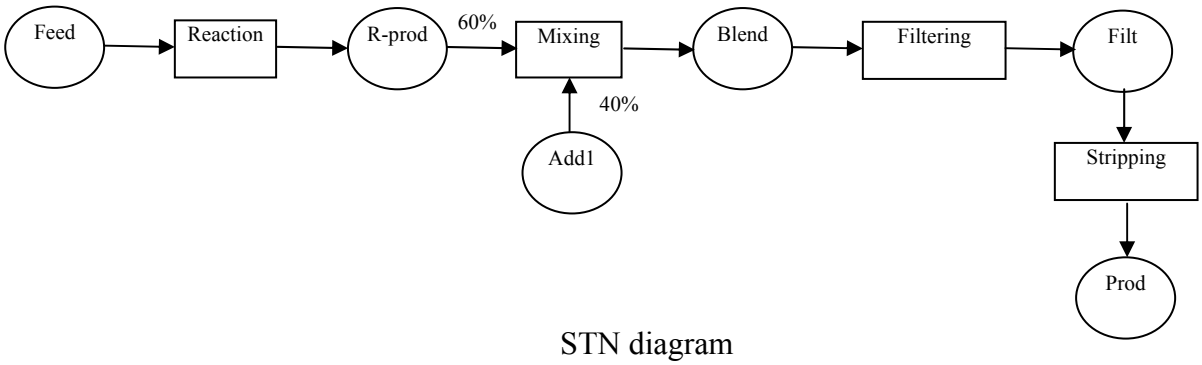
$$Min \quad \sum_o TA_o \qquad (5)$$

2.

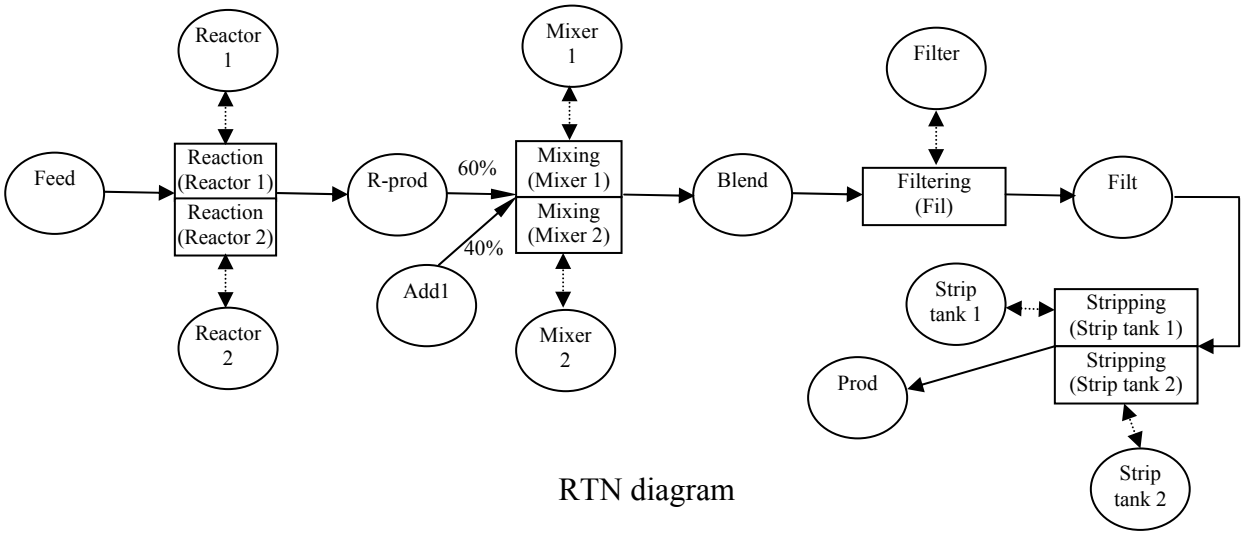
Feature	Exercise 2
Process topology	Sequential – Single stage – Single unit
Equipment assignment	Fixed
Equipment connectivity	-
Inventory storage policies	UIS
Material transfer	-
Batch size	Fixed
Batch processing time	Fixed
Demand patterns	Due dates
Changeovers	Sequence dependent
Resource constraints	None (Only equipment)
Time constraints	None
Costs	-
Degree of certainty	Deterministic

3.

a.



STN diagram



RTN diagram

b.

Feature	Exercise 3
Process topology	Sequential – Multiple stages - Multiproduct
Equipment assignment	Variable
Equipment connectivity	Full
Inventory storage policies	UIS and FIS
Material transfer	Instantaneous
Batch size	Variable
Batch processing time	Fixed
Demand patterns	Scheduling horizon
Changeovers	None
Resource constraints	None
Time constraints	None
Costs	None
Degree of certainty	Deterministic