IE400 PROJECT
2021-2022 Fall

Deadline: 30.12.2021, 23:59

Doctor Who, who works at the XYZ Medical Center, decided to find a personalized way to improve the treatment of breast cancer patients. Chemotherapy, where one or more anti-cancer drugs are used as part of a standardized regimen, is known to be one of the most effective cancer treatments. Chemotherapy may be given with a curative intent, or it may aim to prolong life and improve quality of life by reducing symptoms. Quality of Life (Q-score) is an important health metric that is used in the medical literature to summarize important information pertaining to many different aspects of a patient's health outcomes. A higher Q-score indicates better health condition for a patient.

One of the main challenges of chemotherapy is finding an effective combination of anti-cancer drugs since any combination is expected to have a different impact on the quality of life of different patients, depending on the demographics and the current health condition of the patients. Thanks to her years of expertise and data collected from the past patients, Dr. Who narrowed the most effective anti-cancer drugs down to 7 drugs (ingredients): *Melphalan, Oxaliplatin, Decitabine, Pentostatin, Epirubicin, Lomustine, Thiotepa*. A unit of an acceptable chemotherapy regimen is 100 centiliters (cl) and must include one or more of these drugs. The minimum and maximum allowed dosages of each drug in a unit of chemotherapy regimen are given below:

Index (i)	**Drug**	**Min Dose (cl)**	**Max Dose (cl)**
1	Melphalan	20	80
2	Oxaliplatin	10	50
3	Decitabine	20	100
4	Pentostatin	10	100
5	Epirubicin	10	70
6	Lomustine	20	90
7	Thiotepa	20	50

Moreover, she also identified 9 important factors regarding a patient's demographics and current health conditions that have an impact on how effective a given chemotherapy regimen will be on the health outcome of a patient. We will call these factors *patient features* which are listed below:

Index (j)	Feature	Description
1	Age	indicates if the patient is over 65
2	Gender	indicates if the patient is Male
3	Cancer	indicates if there is any history of cancer in the family
4	Diabetes	indicates if the patient has diabetes
5	Infectious Diseases	indicates if the patient has any infectious disease
6	Blood Diseases	indicates if the patient has any blood disease
7	Allergies	indicates if the patient has any allergies
8	Smoke	indicates if the patient is a smoker
9	Alcohol	indicates if the patient is a regular alcohol user

After rigorous clinical trials, Dr. Who was able to propose a formula that can effectively predict the impact of a given chemotherapy regimen (defined as the set of different drugs used and their respective dosages) on the *Quality of Life* (Q-score) of a given patient. The formula to predict Q-score given a patient's characteristics $\mathbf{p} = (p_1, p_2, ..., p_9)$, the drugs included in the chemotherapy regimen $\mathbf{y} = (y_1, y_2, ..., y_7)$ and their dosages $\mathbf{x} = (x_1, x_2, ..., x_7)$ is shown below:

$$\begin{aligned} Q(\mathbf{p}, \mathbf{y}, \mathbf{x}) = &- 5p_1 - 0.5p_2 - 12p_3 - 8p_4 - 5p_5 - 5p_6 - 1p_7 - 3p_8 - 2p_9 \\ &- 5y_1 - 6y_2 - 4y_3 - 4y_4 - 8y_5 - 6y_6 - 7y_7 \\ &+ 0.28x_1 + 0.30x_2 + 0.25x_3 + 0.17x_4 + 0.31x_5 + 0.246x_6 + 0.40x_7 \end{aligned} \tag{1}$$

where $\mathbf{p} = (p_1, p_2, ..., p_9)$ are the binary variables indicating (for each patient feature j described in Table 2) whether the j^{th} feature exists in the given patient, $\mathbf{y} = (y_1, y_2, ..., y_7)$ are the binary variables indicating (for each drug listed in Table 1) whether the i^{th} drug is included in the chemotherapy regimen, and $\mathbf{x} = (x_1, x_2, ..., x_7)$ are the continuous variables indicating the dosage of the i^{th} drug in the chemotherapy regimen.

Another challenge with the chemotherapy is the possible side effects. As a chemotherapy regimen typically consists of very strong drugs/chemicals, one must be very careful to make sure that secondary systems are not harmed while trying to treat the cancer. Based on clinical trials, Dr. Who identified a chemotherapy regimen that has an acceptable level of side effects on an average patient. The regimen, which we will call the *base regimen* is given below:

Index (i)	Drug	Is Included (y_i)	Dosage (x_i)
1	Melphalan	1	20
2	Oxaliplatin	0	0
3	Decitabine	1	30
4	Pentostatin	1	15
5	Epirubicin	0	0
6	Lomustine	0	0
7	Thiotepa	1	35

It can be assumed that the more you deviate from this base regimen, the more likely it is to have a side effect. Therefore, the goal of a *personalized chemotherapy* can be summarized as follows: **for a given patient, identify a chemotherapy regimen that will result in a desired level of quality of life (Q-score) while deviating minimally from the *base regimen* in order to reduce the risk of side effects.**

In this project, each group will be given a single patient described by his/her *patient features* (check Patients.xlsx file to find out your patient's **p** vector).

(a) Assume that you are only allowed to make changes in the dosages of the existing ingredients in the base regimen, i.e., you cannot add a new ingredient or completely remove an existing ingredient. Which ingredients would you change, and by how much, to maximize the patient's quality of life? Model this problem as an LP/IP problem, write down the decision variables, parameters, objective function, and constraints explicitly. Then, solve the problem using an mathematical optimization solver (e.g., Gurobi, CPLEX, XPRESS, etc.)

(b) Now, assume that in addition to being able to change the dosages of the existing ingredients, you are also allowed to make changes in the composition of the regimen, i.e., you can add a new ingredient or remove an existing one. To quantify the risk of potential side effects of any change from the *base regimen* by adding/removing an ingredient, as well as changing the dosages, the following table of cost coefficients is given:

Index (i)	**Drug**	**Fixed Cost of Adding/Removing**	**Unit Cost of Dosage Change**
1	Melphalan	25	1
2	Oxaliplatin	50	2
3	Decitabine	10	1
4	Pentostatin	25	3
5	Epirubicin	20	2
6	Lomustine	30	1
7	Thiotepa	40	1

Your goal is to find the combination that will achieve a desired level of Q-score (given in **patient_data.xlsx**) with the minimum cost. Model this problem as an LP/IP problem, write down the decision variables, parameters, objective function, and constraints explicitly. Then, solve the problem using an mathematical optimization solver (e.g., Gurobi, CPLEX, XPRESS, etc.)

(c) After her experiments are over Doctor Who realized that there are certain problems that should be taken into consideration when a personalized chemotherapy regimen is prepared. They are listed below:

- Melphalan and Oxaliplatin, when combined in wrong amounts, decrease the effect of the therapy. Hence, when combined, the total amount of these two chemicals should be less than 70 cl and greater than 50cl in any regimen.
- Either Epirubicin should be included in the regimen or the dosage of Decitabine should be less than 25cl.
- If both Pentostatin and Lomoustine are included in the regimen, then at least one of the Thiotepa and Epirubicin should also be chosen.

Make the necessary changes in your model in Part (b) to determine the personalized chemotherapy regimen for your patient considering these issues while still achieving the desired level of Q-score with the minimum cost.

Instructions

Please read the following instructions carefully:

(1) Formulate the models in each part separately.

(2) Solve the models using Gurobi or any other solver (CPLEX, Xpress, GAMS etc.)

(3) Prepare a written document including your precise mathematical models. Explain your objective values, constraints, decision variables and parameters explicitly.

(4) Submit your report (including members full names and ID's) as well as your Gurobi model (or your choice of solver) and all of your codes as a .zip file to busra.bayrak@bilkent.edu.tr. The name of the .zip file should be your group number (Do not add names, ID's etc. to the file name).

(5) There will be a presentation session where you will be asked questions about your models and the project.