Matlab Homework #2
ChE 231
Spring 2019

Problem 1:

Cells convert nutrients such as glucose and oxygen into stored energy and basic cellular building blocks such as amino and nucleic acids through a complex network of metabolic reactions. The stoichiometry of each reaction is often known from basic biochemistry. Steady-state mass balances on each intracellular species (reactants and products of these reactions) yield a linear algebraic system $Ax = b$ where A is a known matrix of stoichiometric coefficients, x is an unknown vector of reaction rates (also known as fluxes) and membrane transport rates for nutrients and product, and b is a known vector of measured transport rates. Each row of the matrix A corresponds to an intracellular species and each column corresponds to a particular reaction between these species. Solution of the stoichiometric model yields the unknown fluxes.

The stoichiometric model used in this assignment accounts for primary metabolism in a yeast cell. The model was originally published in a research paper that is available on the course webpage. The dimension of the A matrix in the published model is 21 x 19, but this model assumes some known reaction rates. We have added some additional fluxes to this model to represent unknown rates for O_2, CO_2 and ethanol transport as well as biomass growth. With only the glucose transport rate specified, the dimension of the A matrix becomes 21 x 23 with the last four columns corresponding to CO_2 transport, biomass growth, O_2 transport and ethanol transport. The stoichiometric matrix for this adjusted model is available on the course webpage.

A nonzero element in the b vector corresponds to a species with a measured (known) transport rate, while a zero element corresponds to a species that is not transported across the cell membrane or has an unknown transport rate (the last 4 elements corresponding to CO_2 transport, biomass growth, O_2 transport and ethanol transport). When a measurement of a previously unknown transport rate becomes available, the corresponding column is removed from the A matrix and the known rate is entered into the corresponding element of the b vector.

All calculations are based on a normalized glucose transport rate of 100. The b vector should be constructed such that b(10)=-100 to represent this uptake flux. Because the A matrix and b vector will be modified throughout this problem, we suggest that you save different versions denoted $\{A_1, \ldots, A_4\}, \{b_1, \ldots, b_4\}$. The A_1 matrix is stored in file available on the course webpage, `A1.dat`. After downloading and placing the matrix in the Matlab working directory, the matrix can be loaded into Matlab with the following command: `load A1.dat`. Make sure that you save all your variables in the Matlab workspace throughout the assignment to perform the analysis of your results for the last part. We recommend that you write Matlab scripts for solving the problems in this assignment.

1. Underdetermined stoichiometric model (21x 22): CO_2 measured.

   a) Load the matrix of coefficients to create A_1, load **A1.dat**;.
   b) Form the vector b_1, `b1 = zeros(size(A1,1),1); b1(10) = -100;`.
   c) Reformulate the A matrix and the b vector to account for an additional measurement, $b_{CO_2} = 140$. The last column of the A matrix needs to be removed and the element of the b vector corresponding to CO_2 needs to be changed from 0 to 140, `A2 = A1(:,1:end-1); b2 = b1; b2(4) = 140;`.
   d) Compute the rank of the matrix A_2.
   e) Compute the determinant of ($A_2 A^T_2$).
   f) Compute x_2.

2. Completely defined stoichiometric model (21 x 21): CO_2 and Biomass measured.

   a) Reformulate the A matrix and b vector based on the presence of biomass and CO_2 measurements. The last two columns of the original A matrix should now be removed. The measured rates for biomass and CO_2 are `bBiomass = b3(3) = 30` and `bCO2 = b3(4) = 140`, respectively.
   b) Compute the rank of the A_3 matrix.
   c) Compute the determinant of A_3.
   d) Compute x_3.

3. Overdetermined stoichiometric model (21 x 19): CO_2, biomass, O_2 and ethanol measured.

   a) Reformulate the A matrix and b vector accounting for the measurements. The last four columns of the original A matrix should be removed. The measured rates are `bBiomass = b4(3) = 30, bCO2=b4(4) = 140, bO2 = b4(15) = -47, and bEtOH = b4(5) = 60`.
   b) Compute the rank of the A_4 matrix.
   c) Compute the determinant of $A^T_4 A_4$.
   d) Compute x_4.

4. Analysis of the results.

   a) Create a bar graph of the first 19 fluxes in x_2, x_3, and x_4: `bar([x2(1:19) x3(1:19) x4(1:19)]`, and add a legend and labels for the axes. Identify the fluxes that exhibit significant differences.

   b) Compute the 2-norm of the difference between the first 19 fluxes for x_2 and x_3, x_2 and x_4, and x_3 and x_4. For instance `norm(x2(1:19)-x3(1:19))`.

5. Comprehension.

a) The method used to resolve the fluxes of the underdetermined system in part 1 calculates a solution that minimizes norm of the fluxes. Does such a strategy seem biologically plausible?

b) Provide insight on the following statement: The overdetermined system in part 4 was solved by determining fluxes that approximately satisfy the species balances in a least-squares sense. The problem with this method is that reaction stoichiometry may be violated.

c) What does the 2-norm you calculated for the difference in fluxes represent?

Problem 2 starts on the next page...

Problem 2:

Assuming ideal behavior in the gas phase, vapor-liquid equilibrium in a miscible binary mixture can be described by the following set of equations:

$$y_1 P \;=\; x_1 \gamma_1 P_1^{sat} \text{ and } y_2 P \;=\; x_2 \gamma_2 P_2^{sat}$$

Where y_1, y_2 are the vapor fractions of each component, P is the overall equilibrium pressure, x_1, x_2 are the liquid fractions of each component, P_1^{sat}, P_2^{sat} are the vapor pressures of each component as functions of temperature, and are the γ_1, γ_2 liquid activity coefficients for each component. The liquid activity coefficients for a binary mixture are functions of the liquid composition and the temperature as denoted by the Van Laar equations:

$$ln(\gamma_1) = \frac{\alpha}{\left(1 + \frac{\alpha}{\beta}\frac{x_1}{x_2}\right)^2}$$

$$ln(\gamma_2) = \frac{\beta}{\left(1 + \frac{\beta}{\alpha}\frac{x_2}{x_1}\right)^2}$$

Where α, β are functions of temperature and other parameters. A binary mixture of acetone (component 1) and water (component 2) exists at a temperature of 25°C and an overall equilibrium pressure of 180 mmHg. At this temperature, the vapor pressures of the components are $P_1^{sat} = 229.47$; $P_2^{sat} = 23.69$ (mmHg) and the parameters from the Van Laar equation are $\alpha = 1.89$, $\beta = 1.66$ (unitless). In this problem, you will numerically solve a system of nonlinear equations for the missing vapor-liquid equilibrium information.

1. Nonlinear system formulation. Use the equations and information given above to formulate a system of 4 equations with 4 unknowns to describe the vapor-liquid equilibrium of n-pentanol and n-hexane. The unknowns of your final system should be the two liquid fractions and the two liquid activity coefficients. Explicitly show your final system of equations once formulated. (*Hint: The mass balances for both the vapor and liquid fractions are needed to formulate the system. See the "Nonlinear Algebraic System Example" from the lecture slides.*)

2. Nonlinear system function in Matlab. Use your system of equations formulated in the previous part, as well as the given parameters, to write a Matlab function suitable for use with an iterative equation solving method (i.e. all 4 equations should be written in the form f(x) = 0). Complete the blank template function file, `nonlinear_sys.m`, and show the final code. (NOTE: do not change the name or header of the template function m-file)

3. Solving the nonlinear system in Matlab. Use a Matlab function capable of solving a nonlinear system of equations (`fsolve`) to solve your system for all unknowns (x_1, x_2, γ_1, γ_2). To implement `fsolve`, you will need to create an initial guess vector and pressure parameter and use them with your function from the previous part, e.g. `x0=[1 2 3 4]; P=10; x= fsolve(@(X) nonlinear_sys(X,P), x0);`. Use the solution to your system and the two VLE equations to find y_1 and y_2 and report all final answers.

4. Passing a parameter vector into a function calling the nonlinear solver. Create and show a plot by creating a vector of pressure values and running `VLE_plot.p`. The function will run the pressure values into the nonlinear system function created earlier, `nonlinear_sys.m`, and plot pressure (mm Hg) vs. liquid fractions and activity coefficients. Make sure to choose an appropriate pressure range and comment on the maximum in the range of pressures.