A sample for numerical method of DFBA

Reference:
Constructed metabolic network of *Escherichia coli* (85 reactions, 54 metabolites from central carbon metabolism)
Fig 1 Simplified metabolic network. The network identified after pathway analysis with glucose, acetate, and oxygen as the input and biomass as the output and selection is based on biomass yield.

Stoichiometric matrix

\[
\begin{bmatrix}
1 & 1 & 1 & 1 \\
-39.43 & 0 & 1.24 & 12.12 \\
0 & -9.46 & -9.48 & -19.23 \\
-35 & -12.92 & -12.73 & 0 \\
\end{bmatrix}
\]
\[
\begin{align*}
\frac{dGlcx}{dt} &= A^{Glcx}vx \\
\frac{dAc}{dt} &= A^{Ac}vx \\
\frac{dO_2}{dt} &= A^{O_2}vx + k_L\alpha(0.21-O_2) \\
\frac{dx}{dt} &= (v_1 + v_2 + v_3 + v_4)x
\end{align*}
\]

- The equations of the dynamic model. Where \(A^{Glcx}, A^{Ac}, A^{O_2}\) are the rows of the stoichiometric matrix associated with glucose, acetate, and oxygen, respectively, \(k_L\alpha\) is the mass transfer coefficient for oxygen.
The dynamic optimization problem was solved by parameterizing the dynamic equations through the use of orthogonal collocation on finite elements.

-- The time period was divided into a finite number of intervals (finite elements). In this example, the number of intervals is 5.

-- The fluxes, the metabolite levels, and the biomass concentration were parameterized at the roots of an orthogonal polynomial within each finite element.
Step 1: Use fifth-order Legendre polynomial on each normalized finite element to receive their roots. The number of the roots in each element is 5 in this example.

\[ P_5(x) = \frac{1}{8} (63x^5 - 70x^3 + 15x) \]

Fifth-order Legendre polynomial

- 5 roots : T=[0.0469101, 0.23076535, 0.5, 0.76923465, 0.9530899]
Step 2: Use Fifth–order Lagrange polynomials to parameterize the 5 roots in each finite element.

\[ L_5(x) = \sum_{k=0}^{5} y_k L_k(x) \]

Where \( y_k \) is the coefficient, and

\[ L_k(x) = \frac{(x - x_0) \cdots (x - x_{k-1})(x - x_{k+1}) \cdots (x - x_n)}{(x_k - x_0) \cdots (x_k - x_{k-1})(x_k - x_{k+1}) \cdots (x_k - x_n)} \]
Get the differential coefficient of the fifth–order Lagrange polynomials, the Matlab codes of which are listed as follows:

For $i=1:5$

```matlab
for i=1:5
    t = T(i);
    a(i)=(1*(t-T(3))*(t-T(4))*(t-T(5)))*1*(t-T(2))*(t-T(5))*(t-T(3))*(t-T(5))*1*(t-T(2))*(t-T(3))*(t-T(5))/(((t-1)-T(2))*(T(1)-T(3))*(T(1)-T(4))*(T(1)-T(5)));
    b1(i)=(1*(t-T(3))*(t-T(4))*(t-T(5))+1*(t-T(1))*(t-T(4))*(t-T(5)))*1*(t-T(1))*(t-T(3))*(t-T(5))+1*(t-T(1))*(t-T(3))*(t-T(5))/((t-2)-T(1))*(T(2)-T(3))*(T(2)-T(4))*(T(2)-T(5));
    c1(i)=(1*(t-T(2))*(t-T(4))*(t-T(5))+1*(t-T(1))*(t-T(4))*(t-T(5)))*1*(t-T(1))*(t-T(2))*(t-T(5))+1*(t-T(1))*(t-T(2))*(t-T(5))/((t-3)-T(1))*(T(3)-T(2))*(T(3)-T(4))*(T(3)-T(5));
    d(i)=(1*(t-T(2))*(t-T(3))*(t-T(5))+1*(t-T(1))*(t-T(3))*(t-T(5))+1*(t-T(1))*(t-T(2))*(t-T(5))+1*(t-T(1))*(t-T(2))*(t-T(5))/((t-4)-T(1))*(T(4)-T(2))*(T(4)-T(3))*(T(4)-T(5));
    e(i)=(1*(t-T(2))*(t-T(3))*(t-T(4))+1*(t-T(1))*(t-T(3))*(t-T(4))+1*(t-T(1))*(t-T(2))*(t-T(4))+1*(t-T(1))*(t-T(2))*(t-T(4))/((t-5)-T(1))*(T(5)-T(2))*(T(5)-T(3))*(T(5)-T(4));
end
```
• Step 3: Parameterizing the dynamic equations

Take the following equation as an example:

$$\frac{dX}{dt} = (v_1 + v_2 + v_3 + v_4)X,$$
- In the first finite element, the five variables (X, V1, V2, V3, V4) are represented by novel parameters at each orthogonal root.

- \[ \begin{array}{c|c|c|c|c|c}
\text{X} & X(1) & X(2) & X(3) & X(4) & X(5) \\
\text{V1} & X(6) & X(7) & X(8) & X(9) & X(10) \\
\text{V2} & X(11) & X(12) & X(13) & X(14) & X(15) \\
\text{V3} & X(16) & X(17) & X(18) & X(19) & X(20) \\
\text{V4} & X(21) & X(22) & X(23) & X(24) & X(25) \\
\end{array} \]
Then we can receive the equation of the five variables by the novel parameters at each orthogonal root of each finite element. The equation of variable $X$ at first and second orthogonal roots in first finite element as described as follows:

\[ X(t) = X(1) \times a(1) + X(2) \times b1(1) + X(3) \times c1(1) + X(4) \times d(1) + X(5) \times e(1) \]

\[ X(t) = X(1) \times a(2) + X(2) \times b1(2) + X(3) \times c1(2) + X(4) \times d(2) + X(5) \times e(2) \]
\[
\frac{dX}{dt} = (\nu_1 + \nu_2 + \nu_3 + \nu_4) X,
\]

The upper equation was parameterized at the roots of the orthogonal polynomial within the first finite element.

\[
[(a(1) \cdot x(1) + b(1) \cdot x(2) + c(1) \cdot x(3) + d(1) \cdot x(4) + e(1) \cdot x(5) - 2 \cdot (x(6) + x(11) + x(16) + x(21)) \cdot x(1)), ...
(a(2) \cdot x(1) + b(2) \cdot x(2) + c(2) \cdot x(3) + d(2) \cdot x(4) + e(2) \cdot x(5) - 2 \cdot (x(7) + x(12) + x(17) + x(22)) \cdot x(2)), ...
(a(3) \cdot x(1) + b(3) \cdot x(2) + c(3) \cdot x(3) + d(3) \cdot x(4) + e(3) \cdot x(5) - 2 \cdot (x(8) + x(13) + x(18) + x(23)) \cdot x(3)), ...
(a(4) \cdot x(1) + b(4) \cdot x(2) + c(4) \cdot x(3) + d(4) \cdot x(4) + e(4) \cdot x(5) - 2 \cdot (x(9) + x(14) + x(19) + x(24)) \cdot x(4)), ...
(a(5) \cdot x(1) + b(5) \cdot x(2) + c(5) \cdot x(3) + d(5) \cdot x(4) + e(5) \cdot x(5) - 2 \cdot (x(10) + x(15) + x(20) + x(25)) \cdot x(5)), ...
\]
• Constraints must be added to guarantee the continuity of the state profiles at the element limits. Therefore, the polynomials are extrapolated to generate the initial point of the next element.
\[
\begin{align*}
&\cdot \frac{(0-T(1))*(0-T(3))*(0-T(4))*(0-T(5))*x(42))/((T(2)-T(1))*(T(2)-T(3))*(T(2)-T(4))*(T(2)-T(5)))+...
&\cdot \frac{(0-T(1))*(0-T(2))*(0-T(4))*(0-T(5))*x(43))/((T(3)-T(1))*(T(3)-T(2))*(T(3)-T(4))*(T(3)-T(5)))+...
&\cdot \frac{(0-T(1))*(0-T(2))*(0-T(3))*(0-T(5))*x(44))/((T(4)-T(1))*(T(4)-T(2))*(T(4)-T(3))*(T(4)-T(5)))-...
&\cdot \frac{(1-T(2))*(1-T(3))*(1-T(4))*(1-T(5))*x(1))/((T(1)-T(2))*(T(1)-T(3))*(T(1)-T(4))*(T(1)-T(5)))-...
&\cdot \frac{(1-T(1))*(1-T(3))*(1-T(4))*(1-T(5))*x(2))/((T(2)-T(1))*(T(2)-T(3))*(T(2)-T(4))*(T(2)-T(5)))-...
&\cdot \frac{(1-T(1))*(1-T(2))*(1-T(4))*(1-T(5))*x(3))/((T(3)-T(1))*(T(3)-T(2))*(T(3)-T(4))*(T(3)-T(5)))-...
&\cdot \frac{(1-T(1))*(1-T(2))*(1-T(3))*(1-T(5))*x(4))/((T(4)-T(1))*(T(4)-T(2))*(T(4)-T(3))*(T(4)-T(5)))-...
&\cdot \frac{(1-T(1))*(1-T(2))*(1-T(3))*(1-T(4))*x(5))/((T(5)-T(1))*(T(5)-T(2))*(T(5)-T(3))*(T(5)-T(4))),...
\end{align*}
\]

\[
\text{The continuity constraints of } X \text{ at mesh point between finite element 1 and finite element 2}
\]
For the purpose of satisfying the systemic initial conditions, the initial point constraints are added into the system after parameterizing.
• \((0-T(2))(0-T(3))(0-T(4))(0-T(5))x(1)/((T(1)-T(2))(T(1)-T(3))(T(1)-T(4))(T(1)-T(5))) + ...\)

• \((0-T(1))(0-T(3))(0-T(4))(0-T(5))x(2)/((T(2)-T(1))(T(2)-T(3))(T(2)-T(4))(T(2)-T(5))) + ...\)

• \((0-T(1))(0-T(2))(0-T(4))(0-T(5))x(3)/((T(3)-T(1))(T(3)-T(2))(T(3)-T(4))(T(3)-T(5))) + ...\)

• \((0-T(1))(0-T(2))(0-T(3))(0-T(5))x(4)/((T(4)-T(1))(T(4)-T(2))(T(4)-T(3))(T(4)-T(5))) + ...\)

• \((0-T(1))(0-T(2))(0-T(3))(0-T(4))x(5)/((T(5)-T(1))(T(5)-T(2))(T(5)-T(3))(T(5)-T(4))) - x_{chuzhi}, ... \%

• The initial point constraints of x
Thanks

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