Metabolic multi-stability and hysteresis in a model aerobe-anaerobe microbiome community

In order to run the code in MATLAB, the COBRA TOOLBOX must be installed. The main file is **main_CSTR.m**. In this main file, the path that calls the genome scale models should be adjusted to the location stored in local computer. The genome scale models are included in the folder called **Genome Scale Models**.

Note: FBA solutions for every time point are stored in the variables: BTFBAS, BTFBAS_time, KPFBAS, and KPFBAS_time. To not track these values and reduce simulation time the variables can be uncommented in **main_CSTR.m** and in all of the files named **parameters_BtKp_two_CSTR_*.m** (there should be 4 total).

For Figure 3A: glucose simulations at a constant input oxygen flow rate of 1.7 mL/min

- For simulating the state switch, glucose was varied from 0.25mM to 6mM at 0.25mM intervals, while input oxygen was kept constant at 1.7mL/min. For these simulations, each glucose concentration simulation started with the same initial conditions.
    - The folder containing the code for running this simulation: **Analytical-BTKP-CSTRGlucoseSimulations-FIG3A**
    - In the script main_CSTR, make sure the section labeled "For hysteresis run this section" is commented and the section labeled "For state switch run this section" is uncommented.
- For simulating hysteresis, glucose was varied from 6mM back to 0mM at 0.25mM intervals. For these simulations, the starting condition for each glucose value was the final value of the previous glucose concentration to mimic changing input glucose concentration in a continuously stirred tank reactor.
    - The folder containing the code for running this simulation: **Analytical-BTKP-CSTRGlucoseSimulations-FIG3A**
- Each glucose condition is run for a tspan of 50 hours.

For Figure 3B: oxygen simulations at a constant glucose concentration in the feed of 3mM

- For simulating the state switch oxygen was varied from 6mL/min to 1mL/min at 0.25mL/min time intervals, while glucose input was kept constant at 3mM. For these simulations, each oxygen flowrate simulation started with the same initial conditions.
    - The folder containing the code for running this simulation: **Analytical-BTKP-CSTROxygenSimulations-FIG3B**
- For simulating hysteresis, input glucose was varied from 1mL/min back to 6mL/min at 0.25mL/min intervals. For these simulations, the starting condition for each oxygen value was the final value of the previous glucose concentration to mimic changing input glucose concentration in a continuously stirred tank reactor.
    - The folder containing the code for running this simulation: **Analytical-BTKP-CSTROxygenSimulations-FIG3B**
    - Each oxygen condition is run for a tspan of 50 hours.

For Figure 3C: heat-map of oxygen and glucose variations

- We ran oxygen variation simulations at constant glucose (similar to Figure 3B) for all the glucose concentrations. The oxygen variation ranges from 6 to 0.5 (for state switch) and from 0.5 back to 6 for hysteresis, in 0.5 mL/min intervals. The glucose concentrations we ran this are 1 to 6 at 0.5mM intervals. For simulating state-switch run the **main_CSTR.m** file. For simulating hysteresis we ran the main_CSTR_hysteresis.m file. The folder containing the code for running this simulation: **Analytical-BTKP-CSTR-HeatMap-FIG3C**

Michaelis Menten Constants

For the simulations presented in the paper we used Michaelis Menton values for substrate uptake presented in the table below. These values were guided by MCMC fitting of batch experiments in Table S1.

Species	Carbon Source	K (mM)	Vmax (mmol/gCDW×h)
K. pneumoniae	Glucose	0.012	19.3
B. *thetaiotaomicron*	Glucose	0.6	11
B. *thetaiotaomicron*	Dextran	0.003	0.65