

STBRsim – A MATLAB Application for Stirred Tank Bioreactor Simulation

The screenshot displays the STBRsim MATLAB application interface, which is organized into several panels for configuring a bioreactor simulation. The main title is "STBRsim - Dynamic Simulation of Stirred Tank Bioreactors Using Genome-Scale Metabolic Models".

1 - Select Metabolic Model
 Model Folder: C:/Users/micha/OneDrive/Documents/Consulting/ISF/Matlab/ME/Project 2 0
 Selected Model: iML1515_1-2-propanediol_gene_KO_model

2 - Define Medium Nutrients
 Nutrient List: CO2 CO2
 Filter Nutrients: [Empty]
 Medium List: [Empty]

Nutrient	Uptake Bound
Ammonium	-1000
Calcium	-1000
Chloride	-1000
Co2+	-1000
Copper	-1000

3 - Define Extracellular Metabolites
 Metabolite List: O2 O2
 Filter Metabolites: [Empty]
 Metabolite Type: Substrate
 Metabolite Phase: Liquid & Gas

Metabolite	Type	Phase	Vmax	Km
D-Glucose	Substrate	Liquid Only	10.0000	0.5000
O2 O2	Substrate	Liquid & Gas	20.0000	0.0030
(R)-Propane-1,2-diol	Product	Liquid Only	0	1.0000
(S)-Propane-1,2-diol	Product	Liquid Only	0	1.0000
Acetate	Product	Liquid Only	0	1.0000
CO2 CO2	Product	Liquid & Gas	0	1.0000

4 - Simulate Steady-State Growth
 ATP Maintenance Reaction: ATPM
 ATP Maintenance Bound: 6.85
 LP Solver: gurobi
 Run Flux Analysis

Compound	Uptake Bound	FBA Flux
E. coli biomass objective function (iML1515) - core - with ...	0	0.6787
(R)-Propane-1,2-diol	0	2.4367
(S)-Propane-1,2-diol	0	0
Acetate	0	0.4727
Ammonium	-1000	-7.3301
CO2 CO2	0	23.8864
Calcium	-1000	-0.0035
Chloride	-1000	-0.0035
Co2+	-1000	-1.6968e-04
Copper	-1000	-4.8121e-04
D-Glucose	-10	-10

5 - Configure Reactor
 Reactor Temperature: 37
 Reactor Pressure: 1
 Reactor Phase: Liquid
 Flow Stage: Stage 1
 Flow Mode: Batch
 Feeding Profile: No Flow

Flow Stage	Stage 1
Start	0
End	18
Flow	N/A
Parameter	N/A
D-Glucose	N/A
O2 O2	N/A

6 - Specify Dissolved Gas Parameters

Dissolved Gas	Henry's Constant	Mass Transfer Coefficient
CO2 CO2	0.6080	100.0000
O2 O2	0.0260	100.0000

7 - Specify Extracellular Initial Conditions

Variable	Type	Phase	Initial Condition
E. coli biomass objective function...	Biomass	Liquid	0.1000
(R)-Propane-1,2-diol	Product	Liquid	0
(S)-Propane-1,2-diol	Product	Liquid	0
Acetate	Product	Liquid	0
CO2 CO2	Product	Liquid	0
D-Glucose	Substrate	Liquid	250.0000
O2 O2	Substrate	Liquid	0.2145
Liquid Volume	Volume	Liquid	80
CO2 CO2	Product	Gas	0

8 - Perform Bioreactor Simulation
 ODE Solver: ode15s
 LP Solution: Fast
 ODE Tolerance: 0.0001
 Simulation Duration: 18
 Run Simulation
 Result Name: gas_switch_4h
 Result List: gas_switch_4h

9 - Manage Case
 File Folder: C:/Users/micha/OneDrive/Documents/Consulting/ISF/Matlab/DFBA/Files
 Save Case
 Case File: case_ecoli_mutant_propanediol
 Load Case
 Case File Status: Case File Created

Example – Determine the optimal time for aerobic-to-anaerobic switch to maximize the production of R-1,2-propanediol production in engineered *Escherichia coli*

1. Select the metabolic model for the strain to be simulated. Here we select an *E. coli* strain designed for 1,2-propanediol synthesis.

2. Define the culture medium in terms of unlimited nutrients and their maximum uptake rates. The nutrients can be extracted from the model, specified manually, or loaded from a saved file.

3. Define balanced extracellular metabolites, including growth-limiting substrates and secreted products. Each metabolite is characterized by its phase(s) and uptake kinetic parameters.

1 - Select Metabolic Model

Model Folder: C:/Users/micha/OneDrive/Documents/Consulting/ISF/Matlab/ME/Project 2.0
Selected Model: iML1515_1-2-propanediol_gene_KO_model
Set Model Panel 1 Status: Selected Model Loaded

2 - Define Medium Nutrients

Nutrient List: CO2 CO2
Filter Nutrients:
Medium List:
Add Nutrient Remove Nutrient Clear Nutrients

Nutrient	Uptake Bound
Ammonium	-1000
Calcium	-1000
Chloride	-1000
Co2+	-1000
Copper	-1000

Save Medium Medium File:
Set Medium Panel 2 Status: Nutrient Removed

3 - Define Extracellular Metabolites

Metabolite List: O2 O2
Filter Metabolites:
Metabolite Type: Substrate
Metabolite Phase: Liquid & Gas
Add Metabolite Remove Metabolite Clear Metabolites

Metabolite	Type	Phase	Vmax	Km
D-Glucose	Substrate	Liquid Only	10.0000	0.5000
O2 O2	Substrate	Liquid & Gas	20.0000	0.0030
(R)-Propane-1,2-diol	Product	Liquid Only	0	1.0000
(S)-Propane-1,2-diol	Product	Liquid Only	0	1.0000
Acetate	Product	Liquid Only	0	1.0000
CO2 CO2	Product	Liquid & Gas	0	1.0000

Set Metabolites Panel 3 Status: Metabolite Uptake Parameter Changed

4 - Simulate Steady-State Growth

ATP Maintenance Reaction: ATP Maintenance Bound:
LP Solver: gurobi Run Flux Analysis

Compound	Uptake Bound	FBA Flux	Minimum Flux	Maximum Flux
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Accept FBA Panel 4 Status:

5 - Configure Reactor

Reactor Temperature: 37 Reactor Pressure: 1
Reactor Phase: Flow Stage:
Flow Mode: Feeding Profile:
Add Stage Modify Stage Remove Stage Clear Stages

Set Configuration Panel 5 Status:

4. Perform flux balance analysis to analyze steady-state growth. Maximum uptake rates can be changed to determine their effects on cellular growth, substrate uptake and product secretion rates.

5. Configure liquid and gas flow stages to implement time-based feeding strategies. The flow mode (e.g., fed-batch), feeding profile (e.g., ramp), start/end times, flow rate parameters, and feed substrate values can be specified for each stage.

STBRsim - Dynamic Simulation of Stirred Tank Bioreactors Using Genome Scale Metabolic Models

1 - Select Metabolic Model

Model Folder: C:/Users/micha/OneDrive/Documents/Consulting/ISF/Matlab/ME/Project 2.0
 Selected Model: iML1515_1-2-propanediol_gene_KO_model
 Panel 1 Status: Selected Model Loaded

2 - Define Medium Nutrients

Nutrient List: CO2 CO2
 Filter Nutrients:
 Medium List:

Nutrient	Uptake Bound
Ammonium	-1000
Calcium	-1000
Chloride	-1000
Co2+	-1000
Copper	-1000

Panel 2 Status: Nutrient Removed

3 - Define Extracellular Metabolites

Metabolite List: O2 O2
 Filter Metabolites:
 Metabolite Type: Substrate
 Metabolite Phase: Liquid & Gas

Metabolite	Type	Phase	Vmax	Km
D-Glucose	Substrate	Liquid Only	10.0000	0.5000
O2 O2	Substrate	Liquid & Gas	20.0000	0.0030
(R)-Propane-1,2-diol	Product	Liquid Only	0	1.0000
(S)-Propane-1,2-diol	Product	Liquid Only	0	1.0000
Acetate	Product	Liquid Only	0	1.0000
CO2 CO2	Product	Liquid & Gas	0	1.0000

Panel 3 Status: Extracellular Metabolites Set

4 - Simulate Steady-State Growth

ATP Maintenance Reaction: ATPM
 ATP Maintenance Bound: 6.86
 LP Solver: gurobi
 Run Flux Analysis

Compound	Uptake Bound	FBA Flux
E. coli biomass objective function (iML1515) - core - with ...	0	0.6787
(R)-Propane-1,2-diol	0	2.4367
(S)-Propane-1,2-diol	0	0
Acetate	0	0.4727
Ammonium	-1000	-7.3301
CO2 CO2	0	23.8864
Calcium	-1000	-0.0035
Chloride	-1000	-0.0035
Co2+	-1000	-1.6968e-05
Copper	-1000	-4.8121e-05
D-Glucose	-10	-10

Panel 4 Status: FBA Results Accepted

5 - Configure Reactor

Reactor Temperature: 37
 Reactor Pressure: 1
 Reactor Phase: Gas
 Flow Stage: Stage 2
 Flow Mode: Constant
 Feeding Profile: Constant

Flow Stage	Stage 1	Stage 2
Start	0	6
End	6	15
Flow	1000	0
Parameter	N/A	N/A
O2 O2	0.2100	0.2100

Panel 5 Status: Gas Flow Stage Value Changed

4 - Simulate Steady-State Growth

ATP Maintenance Reaction: ATP Maintenance Bound:

LP Solver:

Compound	Uptake Bound	FBA Flux
E. coli biomass objective function (iML1515) - core - with ...	0	0.6787
(R)-Propane-1,2-diol	0	2.4367
(S)-Propane-1,2-diol	0	0
Acetate	0	0.4727
Ammonium	-1000	-7.3301
CO2 CO2	0	23.8864
Calcium	-1000	-0.0035
Chloride	-1000	-0.0035
Co2+	-1000	-1.6968e-05
Copper	-1000	-4.8121e-05
D-Glucose	-10	-10

Panel 4 Status:

5 - Configure Reactor

Reactor Temperature: Reactor Pressure:

Reactor Phase: Flow Stage:

Flow Mode: Feeding Profile:

Flow Stage	Stage 1
Start	0
End	18
Flow	N/A
Parameter	N/A
D-Glucose	N/A
O2 O2	N/A

Panel 5 Status:

In Silico Fermentation

6 - Specify Dissolved Gas Parameters

Dissolved Gas	Henry's Constant	Mass Transfer Coefficient
CO2 CO2	0.6080	100.0000
O2 O2	0.0260	100.0000

Panel 6 Status:

7 - Specify Extracellular Initial Conditions

Variable	Type	Phase	Initial Condition
E. coli biomass objective function...	Biomass	Liquid	0.1000
(R)-Propane-1,2-diol	Product	Liquid	0
(S)-Propane-1,2-diol	Product	Liquid	0
Acetate	Product	Liquid	0
CO2 CO2	Product	Liquid	0
D-Glucose	Substrate	Liquid	250.0000
O2 O2	Substrate	Liquid	0.2145
Liquid Volume	Volume	Liquid	80
CO2 CO2	Product	Gas	0

Panel 7 Status:

8 - Perform Bioreactor Simulation

ODE Solver: LP Solution:

ODE Tolerance: Simulation Duration:

Result Name:

Result List:

Panel 8 Status:

9 - Manage Case

File Folder:

Case File:

Panel 9 Status:

6. Specify dissolution and mass transfer parameters for the dissolved gases.

7. Specify initial conditions for all extracellular variables in the liquid and gas phases.

8. Perform dynamic simulation for the current parameters. Different simulations can be stored to allow comparison through a companion visualization App.

9. Save current case to completely capture the current App state for subsequent loading.

STBRsim – Companion App for Result Visualization and Comparison

MATLAB App

STBRsim - Visualization of Stirred Tank Bioreactor Simulation Results | **In Silico Fermentation**

Extracellular Variables

Uptake and Secretion Fluxes

Plot Settings

Plot Panel: Right Panel | Variable Type: Fluxes | Start Plot Time: 0 | End Plot Time: 18

Results: gas_switch_none, gas_switch_8h, gas_switch_6h, gas_switch_4h

Variables: Growth Rate, (R)-Propane-1,2-diol exchange, (S)-Propane-1,2-diol exchange, Acetate exchange, CO2 exchange

File Format: png | Plot Folder: C:/Users/micha/OneDrive/Documents/Consulting/ISF/Matlab/DFBA/Plots

Plot File Name: | Plot Status: Panel Plots Created

Batch Production of R-1,2-propanediol in Engineered *Escherichia coli*

Gas Switch Time (h)	Total Batch Time (h)	Final R-1,2-BD Titer (mmol/L)	Volumetric Productivity (mmol BD/L/h)	Product Yield (g BD/g glucose)
None	10.3	187	18.2	0.32
8	10.8	200	18.5	0.34
6	14.4	214	14.9	0.36
4	17.0	230	13.5	0.39