

# SynComSim – A MATLAB Application for Simulation of Synthetic Bacterial Communities

**1 - Select Strains**

Model Folder: C:\Users\micha\OneDrive\Documents\Consulting\ISF\Matlab\GSM\AGOR

Strain Model List: Clostridium\_difficile\_CD196

Filter Strains: diff

Strain Model	Number	Genes	Metabolites
Clostridium_difficile_CD196	1	899	1170
Enterobacter_cloacae_EcWSU1	2	1325	1414
Escherichia_coli_str_K_12_substr_MG1655	3	1190	1348
Klebsiella_pneumoniae_pneumoniae_MGH78578	4	1393	1379

**2 - Define Community Medium**

File Folder: C:\Users\micha\OneDrive\Documents\Consulting\ISF\Matlab\SteadyCom

Medium File List: Empty

Nutrient List: (R)-Pantothenate

Medium Nutrient	Uptake Bound	Transport Strains	Strain 1	Strain 2
(R)-Pantothenate	-1000	1 2 3 4	-1000	-1000
Ammonium	-1000	1 2 3 4	-1000	-1000
Chloride	-1000	1 2 3 4	-1000	-1000
Co2+	-1000	1 2 3 4	-1000	-1000
Cu2+	-1000	1 2 3 4	-1000	-1000
D-glucose	-5	1 2 3 4	-5	-5
Fe2+	-1000	1 2 3 4	-1000	-1000
Fe3+	-1000	1 2 3 4	-1000	-1000
L-leucine	-0.5000	1 2 3 4	-0.5000	-0.5000
L-tryptophan	-0.5000	1 2 3 4	-0.5000	-0.5000

**3 - Simulate Strain Monocultures**

LP Solver: gurobi

Monoculture Strains: Clostridium\_difficile\_CD196

Nutrient or Product	Strain 1	Strain 2	Strain 3	Strain 4
Biomass	0.2629	0.2600	0.2505	0.3008
(R)-Pantothenate	-0.0042	-0.0016	-0.0039	-0.0047
Ammonium	-0.8647	-1.9904	-2.0109	-2.9981
Chloride	-0.0021	-0.0008	-0.0020	-0.0023
Co2+	-0.0021	-0.0008	-0.0020	-0.0023
Cu2+	-0.0021	-0.0008	-0.0020	-0.0023
D-glucose	-5.0000	-5.0000	-5.0000	-5.0000
Diphosphate	0	0	1.8314	0
Fe2+	-0.0063	0	-0.0020	-0.0023

**4 - Define Crossfed Metabolites**

Crossfed File List: Crossfeed\_amino\_acids\_agora

Metabolite List: (R)-lactate

Crossfed Metabolite	Transport Strains	Strain 1	Strain 2	Strain 3
(R)-lactate	1 2 3 4	-1	-1	-1
(S)-lactate	1 2 3 4	-1	-1	-1
Formate	1 2 3 4	-1	-1	-1
Glycine	1 2 3 4	-1	-1	-1
L-alanine	1 2 3 4	-1	-1	-1
L-argininium(1+)	1 2 3 4	-1	-1	-1
L-aspartate(1-)	1 2 3 4	-1	-1	-1
L-cysteine	1 2 3 4	-1	-1	-1
L-glutamate(1-)	1 2 3 4	-1	-1	-1

**5 - Simulate Community**

Click Strains to Exclude: Clostridium\_difficile\_CD196, Enterobacter\_cloacae\_EcWSU1, Escherichia\_coli\_str\_K\_12\_substr\_MG1655, Klebsiella\_pneumoniae\_pneumoniae\_MGH78578

FVA Percentage: 99

Growth & Abundances	Growth Rate	Strain 1	Strain 2	Strain 3	S
FBA Solution	0.2937	0.4930	0.5070	0	0
FVA Minimum	0.2907	0.4064	0.3183	0	0
FVA Maximum	0.2907	0.6817	0.5872	0.1332	0

FBA Solution	Community	Strain 1	Strain 2	Strain 3	Strain 4
Growth rate	0.2937	0.2937	0.2937	0	0
Abundance	1.0000	0.4930	0.5070	0	0
(R)-Pantothenate	-0.0032	-0.0023	-0.0009	0	0
(R)-lactate	0	0.5070	-0.5070	0	0
(S)-lactate	0	0.5070	-0.5070	0	0
Ammonium	-1.6738	0.2904	-1.9642	0	0
Chloride	-0.0016	-0.0011	-0.0005	0	0
Co2+	-0.0016	-0.0011	-0.0005	0	0
Cu2+	-0.0016	-0.0011	-0.0005	0	0
D-glucose	-4.9998	-2.4649	-2.5349	0	0
Fe2+	-0.0034	-0.0034	0	0	0
Fe3+	-0.0030	-0.0011	-0.0018	0	0
Formate	2.0187	-0.0556	2.0743	0	0
Glycine	0	-0.4930	0.4930	0	0
Hydrogen	2.0323	0	2.0323	0	0

**6 - Manage Case**

Case Folder: C:\Users\micha\OneDrive\Documents\Consulting\ISF\Matlab\SteadyCom

Case File: State\_agora\_Clostridium\_difficile\_CD196-Three\_Er

Example – Investigate metabolite crossfeeding strategies for a 4-species community consisting of the gut pathogen *Clostridioides difficile* and three Enterobacteriaceae species

1. Select metabolic models for the strains of interest. Strains can be removed from selected simulations later in the workflow.

2. Define nutrients contained in the culture medium. Nutrients and their uptake bounds can be added individually or loaded from a medium file created with our App MediumFBA.

**SynComSim - Synthetic Bacterial Community Simulation using Genome-Scale Metabolic Models**

**1 - Select Strains**

Model Folder: C:/Users/micha/OneDrive/Documents/Consulting/ISF/Matlab/GSM/AGOR  
Strain Model List: Clostridium\_difficile\_CD196  
Filter Strains: diff

Add Strain Remove Strain Clear Strains

Strain Model	Number	Genes	Metabolites
Clostridium_difficile_CD196	1	899	1170
Enterobacter_cloacae_EcWSU1	2	1325	1414
Escherichia_coli_str_K_12_substr_MG1655	3	1190	1348
Klebsiella_pneumoniae_pneumoniae_MGH78578	4	1393	1379

Build Community Model Panel 1 Status: Community Model Build Complete

**2 - Define Community Medium**

File Folder: C:/Users/micha/OneDrive/Documents/Consulting/ISF/Matlab/SteadyCom...  
Medium File List: Growth\_medium\_agora\_Clostridium\_difficile\_CD196-Three\_Enter...  
Nutrient List: (R)-Pantothenate  
Filter Nutrients:

Add Nutrient Remove Nutrient Clear Nutrients

Medium Nutrient	Uptake Bound	Transport Strains	Strain 1	Strain 2
(R)-Pantothenate	-1000	1 2 3 4	-1000	-1000
Ammonium	-1000	1 2 3 4	-1000	-1000
Chloride	-1000	1 2 3 4	-1000	-1000
Co2+	-1000	1 2 3 4	-1000	-1000
Cu2+	-1000	1 2 3 4	-1000	-1000
D-glucose	-5	1 2 3 4	-5	-5
Fe2+	-1000	1 2 3 4	-1000	-1000
Fe3+	-1000	1 2 3 4	-1000	-1000
L-leucine	-0.5000	1 2 3 4	-0.5000	-0.5000
L-tryptophan	-0.5000	1 2 3 4	-0.5000	-0.5000

Save Medium Medium File:   
Set Medium Panel 2 Status: Loaded MediumFBA Growth Medium File

**3 - Simulate Strain Monocultures**

LP Solver: gurobi Simulate Monocultures

Monoculture Strains:

Add Strain Result Remove Strain Result Clear Strain Results

Accept Strain Results Panel 3 Status:

**4 - Define Crossfed Metabolites**

Crossfed File List:

Metabolite List:

Filter Metabolites:

Add Metabolite Remove Metabolite Clear Metabolites

Save Crossfed Crossfed File:   
Set Crossfed Panel 4 Status:

3. Perform monoculture simulations to examine strain growth behavior. Fluxes of consumed nutrients and secreted products are predicted for each strain.

4. Define metabolites allowed to be crossfed between community strains. Options include all possible metabolites, individually added metabolites, or metabolites loaded from a previously saved file.

**SynComSim - Synthetic Bacterial Community Simulation using Genome-Scale Metabolic Models**

### 1 - Select Strains

Model Folder:

Strain Model List:

Filter Strains:

Strain Model	Number	Genes	Metabolites
Clostridium_difficile_CD196	1	899	1170
Enterobacter_cloacae_EcWSU1	2	1325	1414
Escherichia_coi_str_K_12_substr_MG1655	3	1190	1348
Klebsiella_pneumoniae_pneumoniae_MGH78578	4	1393	1379

Panel 1 Status:

### 2 - Define Community Medium

File Folder:

Medium File List:

Nutrient List:

Filter Nutrients:

Medium Nutrient	Uptake Bound	Transport Strains	Strain 1	Strain 2
(R)-Pantothenate	-1000	1 2 3 4	-1000	-1000
Ammonium	-1000	1 2 3 4	-1000	-1000
Chloride	-1000	1 2 3 4	-1000	-1000
Co2+	-1000	1 2 3 4	-1000	-1000
Cu2+	-1000	1 2 3 4	-1000	-1000
D-glucose	-5	1 2 3 4	-5	-5
Fe2+	-1000	1 2 3 4	-1000	-1000
Fe3+	-1000	1 2 3 4	-1000	-1000
L-leucine	-0.5000	1 2 3 4	-0.5000	-0.5000
L-tryptophan	-0.5000	1 2 3 4	-0.5000	-0.5000

Medium File:

Panel 2 Status:

### 3 - Simulate Strain Monocultures

LP Solver:

Monoculture Strains:

Nutrient or Product	Strain 1	Strain 2	Strain 3	Strain 4
Biomass	0.2629	0.2600	0.2505	0.3008
(R)-Pantothenate	-0.0042	-0.0016	-0.0039	-0.0047
Ammonium	-0.8647	-1.9904	-2.0109	-2.9981
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Co2+	-0.0021	-0.0008	-0.0020	-0.0023
Cu2+	-0.0021	-0.0008	-0.0020	-0.0023
D-glucose	-5.0000	-5.0000	-5.0000	-5.0000
Diphosphate	0	0	1.8314	0

Panel 3 Status:

### 4 - Define Crossfed Metabolites

Crossfed File List:

Metabolite List:

Filter Metabolites:

Crossfed Metabolite	Transport Strains	Strain 1	Strain 2	Strain 3	Strain 4
(3,4-dihydroxyphenyl)acetate	1 2 4	-1	-1	NaN	NaN
(4-hydroxyphenyl)acetaldehyde	2 3 4	NaN	-1	-1	-1
(R)-3-hydroxybutyrate	1 2 4	-1	-1	NaN	NaN
(R)-Acetoin	2 4	NaN	-1	NaN	NaN
(R)-lactate	1 2 3 4	-1	-1	-1	-1
(S)-lactate	1 2 3 4	-1	-1	-1	-1
(S)-malate(2-)	2 3 4	NaN	-1	-1	-1
(S)-propane-1,2-diol	2 3 4	NaN	-1	-1	-1
1,5-Diaminopentane	3 4	NaN	NaN	-1	-1

Crossfed File:

Panel 4 Status:

### Simulation using Genome-Scale Metabolic Models

#### 3 - Simulate Strain Monocultures

LP Solver:

Monoculture Strains:

Nutrient or Product	Strain 1	Strain 2	Strain 3	Strain 4
Biomass	0.2629	0.2600	0.2505	0.3008
(R)-Pantothenate	-0.0042	-0.0016	-0.0039	-0.0047
Ammonium	-0.8647	-1.9904	-2.0109	-2.9981
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Co2+	-0.0021	-0.0008	-0.0020	-0.0023
Cu2+	-0.0021	-0.0008	-0.0020	-0.0023
D-glucose	-5.0000	-5.0000	-5.0000	-5.0000
Diphosphate	0	0	1.8314	0
Fe2+	-0.0063	0	-0.0020	-0.0023

Panel 3 Status:

#### 4 - Define Crossfed Metabolites

Crossfed File List:

Metabolite List:

Filter Metabolites:

Crossfed Metabolite	Transport Strains	Strain 1	Strain 2	Strain 3
(R)-lactate	1 2 3 4	-1	-1	-1
(S)-lactate	1 2 3 4	-1	-1	-1
Formate	1 2 3 4	-1	-1	-1
Glycine	1 2 3 4	-1	-1	-1
L-alanine	1 2 3 4	-1	-1	-1
L-argininium(1+)	1 2 3 4	-1	-1	-1
L-aspartate(1-)	1 2 3 4	-1	-1	-1
L-cysteine	1 2 3 4	-1	-1	-1
L-glutamate(1-)	1 2 3 4	-1	-1	-1

Crossfed File:

Panel 4 Status:

### In Silico Fermentation

#### 5 - Simulate Community

Click Strains to Exclude:

FVA Percentage:

Growth & Abundances	Growth Rate	Strain 1	Strain 2	Strain 3	Strain 4
FBA Solution	0.2937	0.4930	0.5070	0	0
FVA Minimum	0.2907	0.4064	0.3183	0	0
FVA Maximum	0.2907	0.6817	0.5872	0	0.1332

FBA Solution	Community	Strain 1	Strain 2	Strain 3	Strain 4
Growth rate	0.2937	0.2937	0.2937	0	0
Abundance	1.0000	0.4930	0.5070	0	0
(R)-Pantothenate	-0.0032	-0.0023	-0.0009	0	0
(R)-lactate	0	0.5070	-0.5070	0	0
(S)-lactate	0	0.5070	-0.5070	0	0
Ammonium	-1.6738	0.2904	-1.9642	0	0
Chloride	-0.0016	-0.0011	-0.0005	0	0
Co2+	-0.0016	-0.0011	-0.0005	0	0
Cu2+	-0.0016	-0.0011	-0.0005	0	0
D-glucose	-4.9998	-2.4649	-2.5349	0	0
Fe2+	-0.0034	-0.0034	0	0	0
Fe3+	-0.0030	-0.0011	-0.0018	0	0
Formate	2.0187	-0.0556	2.0743	0	0
Glycine	0	-0.4930	0.4930	0	0
Hydrogen	2.0323	0	2.0323	0	0

Result Name:

Result List:

Panel 5 Status:

#### 6 - Manage Case

Case Folder:

Case File:

Panel 6 Status:

5. Perform community simulation for the specified uptake bounds on medium nutrients and crossfed metabolites. Specific strains can be excluded from any simulation. Different simulations can be stored to allow comparison through a companion visualization App.

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

# SynComSim – Companion App for Result Visualization and Comparison

