Introduction

This supplementary material was developed by the CNPEM.Brazil Bioinformatics group, where were inserted missing reactions to the E.coli Core Model. These reactions are related to the HWLS pathway, as a synthetic way of consumption of CO2. By exporting to a .json file, the team tried to fit the reactions added in the E.coli Core Model through Escher online software.

```
!pip install cobra
!pip install escher

"""# **Adding Reactions to the E.coli Core Model**"""

import cobra
import cobra.test
model = cobra.test.create_test_model('textbook')
from cobra import Model, Reaction, Metabolite

model.metabolites.get_by_id('co2_e')

model.reactions.get_by_id('EX_co2_e')

reaction = Reaction('R_adc_1')
reaction.name='R_adc_1'
reaction.subsystem="Cell growth"
reaction.lower_bound=0
reaction.upper_bound=1000

co2_e = Metabolite(
    'cpd00011_e',
    formula='CO2',
    name='CO2',
    compartment='e')

for_c = Metabolite(
    'cpd00047_c',
    formula='CH1O2',
    name='Formate',
    compartment='c')

nadh_c = Metabolite(
    'cpd00004_c',
    formula='C21H27N7O14P2',
    name='Nicotinamide adenine dinucleotide - reduced',
    compartment='c')

# Adding metabolites into a reaction
reaction.add_metabolites({
    co2_e:-1.0,
    nadh_c:-1.0,
    for_c: 1.0
})

model.add_reactions([reaction])
```

```
print(f'{len(model.reactions)} reactions')
print(f'{len(model.metabolites)} metabolites')
print(f'{len(model.genes)} genes')

reaction = Reaction('R_adc_2')
reaction.name='R_adc_2'
reaction.subsystem="Cell growth"
reaction.lower_bound=0
reaction.upper_bound=1000

for_c = Metabolite(
    'cpd00047_c',
    formula='CH1O2',
    name='Formate',
    compartment='c')

atp_c = Metabolite(
    'cpd00002_c',
    formula='C10H13N5O13P3',
    name='ATP',
    compartment='c')

forTHF_c = Metabolite(
    'cpd_forTHF',
    formula='C20H23N7O7',
    name='10-Formyltetrahydrofolate',
    compartment='c')

# Adding metabolites into a reaction
reaction.add_metabolites({
    for_c: -1.0,
    atp_c: -1.0,
    forTHF_c: 1.0
})

model.add_reactions([reaction])
print(f'{len(model.reactions)} reactions')
print(f'{len(model.metabolites)} metabolites')
print(f'{len(model.genes)} genes')

reaction = Reaction('R_adc_3')
reaction.name='R_adc_3'
reaction.subsystem="Cell growth"
reaction.lower_bound=0
reaction.upper_bound=1000

forTHF_c = Metabolite(
    'cpd_forTHF',
    formula='C20H23N7O7',
    name='10-Formyltetr ahydrofolate',
    compartment='c')

methenylTHF_c = Metabolite(
    'cpd28667_c',
    formula='C20H21N7O6',
    name='5,10-Methenyltetrahydrofolate',
    compartment='c')
```

```
# Adding metabolites into a reaction
reaction.add_metabolites({
    forTHF_c: -1.0,
    methenylTHF_c: 1.0
})

model.add_reactions([reaction])
print(f'{len(model.reactions)} reactions')
print(f'{len(model.metabolites)} metabolites')
print(f'{len(model.genes)} genes')

reaction = Reaction('R_adc_4')
reaction.name='R_adc_4'
reaction.subsystem="Cell growth"
reaction.lower_bound=0
reaction.upper_bound=1000

methenylTHF_c = Metabolite(
    'cpd28667_c',
    formula='C20H21N7O6',
    name='5,10-Methenyltetrahydrofolate',
    compartment='c')

nadh_c = Metabolite(
    'cpd00004_c',
    formula='C21H27N7O14P2',
    name='Nicotinamide adenine dinucleotide - reduced',
    compartment='c')

methyleneTHF_c = Metabolite(
    'cpd27449_c',
    formula='C20H21N7O5R',
    name='METHYLENE-THF-GLU-N',
    compartment='c')

# Adding metabolites into a reaction
reaction.add_metabolites({
    methenylTHF_c: -1.0,
    nadh_c: -1.0,
    methyleneTHF_c: 1.0
})

model.add_reactions([reaction])
print(f'{len(model.reactions)} reactions')
print(f'{len(model.metabolites)} metabolites')
print(f'{len(model.genes)} genes')

reaction = Reaction('R_adc_5')
reaction.name='R_adc_5'
reaction.subsystem="Cell growth"
reaction.lower_bound=0
reaction.upper_bound=1000

methyleneTHF_c = Metabolite(
    'cpd27449_c',
    formula='C20H21N7O5R',
    name='METHYLENE-THF-GLU-N',
    compartment='c')
```

```
formaldehyde_c = Metabolite(
    'cpd00055_c',
    formula='CH2O',
    name='Formaldehyde',
    compartment='c')

# Adding metabolites into a reaction
reaction.add_metabolites({
    methenylTHF_c: -1.0,
    formaldehyde_c: 1.0
})

model.add_reactions([reaction])
print(f'{len(model.reactions)} reactions')
print(f'{len(model.metabolites)} metabolites')
print(f'{len(model.genes)} genes')

reaction = Reaction('R_adc_6')
reaction.name='R_adc_6'
reaction.subsystem="Cell growth"
reaction.lower_bound=0
reaction.upper_bound=1000

formaldehyde_c = Metabolite(
    'cpd00055_c',
    formula='CH2O',
    name='Formaldehyde',
    compartment='c')

dihydroxyacetone_c = Metabolite(
    'cpd35267_c',
    formula='C9H15O10S',
    name='sulfoquinovosyl-1-O-dihydroxyacetone',
    compartment='c')

# Adding metabolites into a reaction
reaction.add_metabolites({
    formaldehyde_c: -1.0,
    dihydroxyacetone_c: 1.0
})

model.add_reactions([reaction])
print(f'{len(model.reactions)} reactions')
print(f'{len(model.metabolites)} metabolites')
print(f'{len(model.genes)} genes')

reaction = Reaction('R_adc_7')
reaction.name='R_adc_7'
reaction.subsystem="Cell growth"
reaction.lower_bound=0
reaction.upper_bound=1000

dihydroxyacetone_c = Metabolite(
    'cpd35267_c',
    formula='C9H15O10S',
    name='sulfoquinovosyl-1-O-dihydroxyacetone',
    compartment='c')
```

```
atp_c = Metabolite(
    'cpd00002_c',
    formula='C10H13N5O13P3',
    name='ATP',
    compartment='c')

dihydroxyacetone_phosphate_c = Metabolite(
    'cpd_dihydro_phosphate_c',
    formula='C3H7O6P',
    name='1,3-diidroxi-2-propanona fosfato',
    compartment='c')

# Adding metabolites into a reaction
reaction.add_metabolites({
    dihydroxyacetone_c: -1.0,
    atp_c: -1.0,
    dihydroxyacetone_phosphate_c: 1.0
})

model.add_reactions([reaction])
print(f'{len(model.reactions)} reactions')
print(f'{len(model.metabolites)} metabolites')
print(f'{len(model.genes)} genes')

reaction = Reaction('R_adc_8')
reaction.name='R_adc_8'
reaction.subsystem="Cell growth"
reaction.lower_bound=0
reaction.upper_bound=1000

dhp_c = Metabolite(
    'cpd_dhp_c',
    formula='C3H7O6P',
    name='1,3-diidroxi-2-propanona fosfato',
    compartment='c')

glyceraldehyde_phosphate_c = Metabolite(
    'cpd00102_c',
    formula='C3H9O6P',
    name='Glyceraldehyde 3-phosphate',
    compartment='c'
)

# Adding metabolites into a reaction
reaction.add_metabolites({
    dihydroxyacetone_phosphate_c: -1.0,
    glyceraldehyde_phosphate_c: 1.0
})

model.add_reactions([reaction])
print(f'{len(model.reactions)} reactions')
print(f'{len(model.metabolites)} metabolites')
print(f'{len(model.genes)} genes')

model.reactions.EX_glc__D_e.knock_out()
model.reactions.EX_glu__L_e.knock_out()
model.reactions.EX_co2_e.lower_bound = -10.0
```

```
model.reactions.EX_glc__D_e.upper_bound = 1

model.optimize()
model.summary()

import cobra.test
import os
from os.path import join

data_dir = '/content/E coli core.Core metabolism.json'

model = cobra.io.load_json_model(join(data_dir, "mini.json"))

model.optimize()

model.summary()

with model:
    medium = model.medium
    medium["EX_glc__D_e"] = 0.0
    medium["EX_co2_e"] = -20.0
    model.medium = medium
    print(model.slim_optimize())
print(model.slim_optimize())
model.medium

model.reactions

model.metabolites.get_by_id('co2_e')

model.reactions.EX_co2_e.flux_expression

model.optimize()

biomass_rxn = model.reactions.get_by_id("Biomass_Ecoli_core")
biomass_rxn

model.optimize()
model.summary()

carb_uptake = model.problem.Constraint(
    model.reactions.EX_co2_e.flux_expression -
    model.reactions.EX_glc__D_e.flux_expression - carb,
    lb=-10,
    ub=0)
model.add_cons_vars(carb_uptake)

model.objective = 'EX_co2_e'

print(model.objective.expression)
print(model.objective.direction)

from cobra import Model, Reaction, Metabolite
import cobra.test
from cobra.flux_analysis import production_envelope
model = cobra.test.create_test_model("textbook")
model.objective = 'EX_co2_e'
```

```
model.summary()

cobra.io.save_json_model(model, "ecoli.json")
```

Original file is located at:
https://colab.research.google.com/drive/1tY8LJbU7DAUWb7ivwT9kBDLNhmstFeNV