Exercise for Constraint-based Modeling of Cellular Networks
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Homework should be sent to Anika (ankueken@uni-potsdam.de)

Exercise

Writing functions in MATLAB

Write a Matlab function *[minimum_flux,maximum_flux] = FluxRange(M,w)* that takes as input arguments

1. *M* - a metabolic model in cobra format
2. *w* - a numeric vector indicating reaction indices for which min/max flux should be calculated

The function returns *minimum_*flux and maximum*_flux* the minimum and maximum flux a reaction can have, i.e. the feasible flux range. Hence, the function has to solve the following two LP for each reaction specified in *w*

```
for each j in w
      do solve min/max FBA:
      minimum_flux(j) =  min v_j
                         s.t.
                         Nv=0
                         lb<=v<=ub
      maximum_flux(j) =  max v_j
                         s.t.
                         Nv=0
                         lb<=v<=ub
end
```

Use function *FluxRange* to calculate feasible flux ranges for reactions in the *E. coli* core model.

Use the result to check if there are blocked reactions!

[homework see next page]

Homework

1. (1 point) Use function *FluxRange* from the exercise to calculate the operational flux range of reactions in the *E. coli* core model.

2. (1 point) Given model M, suppose we use the following two LPs to find blocked reactions, with z^* being the optimal biomass for model M

$$\begin{aligned} &\min/\max\ v_j \\ &\text{s.t.} \\ &Nv=0 \qquad\qquad (LP1) \\ &lb<=v<=ub \end{aligned}$$

$$\begin{aligned} &\min/\max\ v_j \\ &\text{s.t.} \\ &Nv=0 \qquad\qquad (LP2) \\ &V_{bio}=z^* \\ &lb<=v<=ub \end{aligned}$$

Which statement is correct?

a) The set of blocked reactions for model M identified from LP1 and LP2 must be the same.
b) The set of blocked reactions obtained from LP1 must be a subset of blocked reactions obtained from LP2.
c) The set of blocked reactions obtained from LP2 must be a subset of blocked reactions obtained from LP1.

3. (8 points) Write function *C = essentiality_check(M,target)* that classifies the relationship of each model reaction on target trait production into three groups: *essential*, *dispensable* and *redundant.* A reaction is called *essential*, if its removal causes zero production of the target of interest. The removal of a *dispensable* reaction decreases the production of target compared to its optimum production. In the case of a *redundant* reaction its removal has no effect on the target production.

Follow the steps specified below!

Input:

M a model struct
target a reaction index that represents maximum target production (e.g. maximum flux through a reaction exporting metabolite A will represent maximizing production of A)

Output:

C Table having a column indicating the reaction and a column showing the classification.

The reaction maximized for optimal target production should be indicated in the second column as well.

Example output:

Reaction name	classification
R1	Redundant
R2	Essential
R3	Essential
R4	Target production

Function body:

1. Split each reversible reaction into two irreversible once
2. Find the maximum production rate of target, i.e. $z = max\ v(target)$
3. Find the minimum sum over all fluxes at the optimal flux through $v(target)$

$$\begin{gathered} min \sum v \\ s.t \\ Nv = 0 \\ v(target) = z \\ 0 <= v <= ub \end{gathered}$$

4. Use the solution of step 3. to classify some redundant reaction(s) already
5. Categorize the remaining reactions in the model by solving the following LP for each reaction i

$$\begin{gathered} \max v_{target} \\ s.t \\ Nv = 0 \\ v_i = 0 \\ 0 <= v <= ub \end{gathered}$$

The final table has n rows, equal to number of reactions in the input model (**before reversible reaction split!**)

To check if your function is working correctly you can compare your results with those given in tcacycle_results.mat on moodle obtained from running essentiality_check on a small model of TCA cycle.

```
>> C_tca = essentiality_check(model, strcmp(model.rxnNames,'ex_G6P'))
```