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Tutorial: Flux Balance Analysis in MATLAB

Setting up COBRA and loading a model

1. Download the latest version of the COBRA Toolbox (found here: https://github.com/opencobra/cobratoolbox).
2. Extract the cobratoolbox ZIP archive in your directory of choice.
3. Launch MATLAB and navigate to the cobratoolbox directory.
4. Add the cobratoolbox directory to the MATLAB search path using `addpath(genpath('filepath'));` followed by `savepath()`.
5. Check the path has been added using `path`.
6. Run `initCobraToolbox` to initialise the Cobra Toolbox.
7. Type `model = readCbModel([ 'filename.mat']);` to load a COBRA-compliant model into MATLAB.

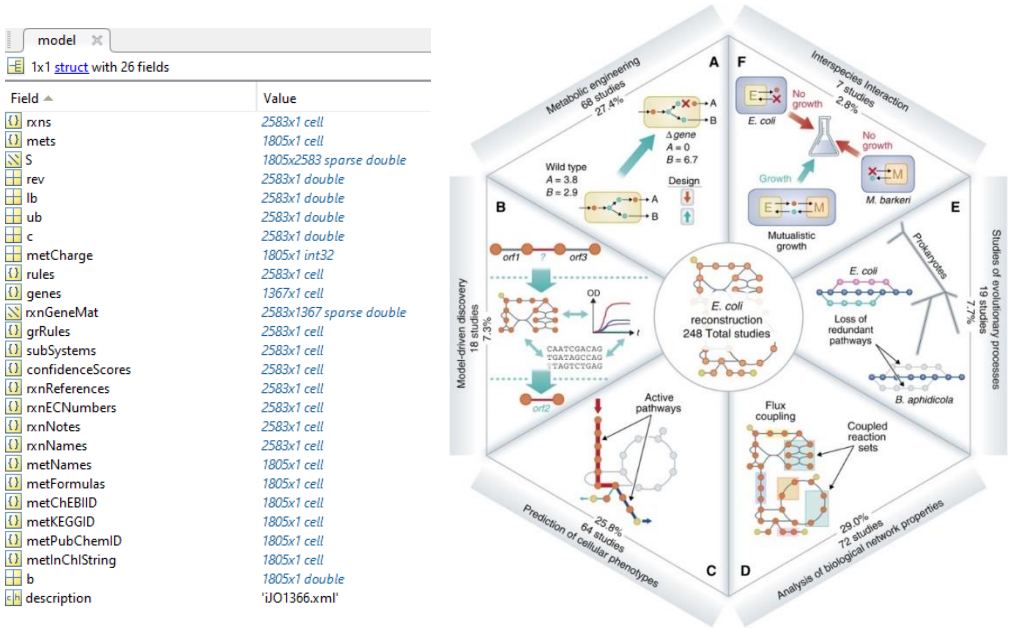

Fig 1. (Left) Fields used to describe a genome-scale metabolic model in MATLAB. (Right) available studies around flux balance analysis and omic-integration in genome-scale metabolic models

Model navigation and flux balance analysis

1. Check the index of the default reaction set as cellular objective
   ```
   ix_obj = find(model.c==1)
   ```
2. Find the name of the reaction set as objective
   ```
   model.rxns(ix_obj)
   model.rxnNames(ix_obj)
   ```

3. Predict the default cellular growth rate
```
FBA_solution = optimizeCbModel(model)
```
4. Identify the reaction allowing glucose uptake and its lower bound (what is maximum uptake?)
```
ix_glucose = find(strcmp('EX_glc(e) ',model.rxns))
model.lb(ix_glucose)
```
5. Change the glucose import to -5 mmol/(h gdW) and re-run the model
```
model.lb(ix_glucose) = -5;
FBA_solution_2 = optimizeCbModel(model)
```
6. Find the names of all exchange reactions in the model and their respective lower and upper flux bounds
```
indices_ex_rxns = strmatch('EX_',model.rxns);
ex_rxns = model.rxns(indices_ex_rxns);
names_ex_rxns = model.rxnNames(indices_ex_rxns);
lb_ex_rxns = model.lb(indices_ex_rxns);
ub_ex_rxns = model.ub(indices_ex_rxns);
```
7. List all genes in the model
```
genes = model.genes
```
8. Perform sequential single gene knockout of the first 100 genes, viewing the growth rate after each gene is knocked out
```
for i = 1 : length (genes(1:100))
       disp(['I''m knocking out ' genes{i}]);
        modelDel = deleteModelGenes(model,genes{i});
        temp = optimizeCbModel(modelDel);
        FBA_growth_after_KO(i)= temp.f;
        disp (['The growth rate is '
num2str(FBA_growth_after_KO(i))]);
end
```

References and Further Reading

Heirendt, L., Arreckx, S., Pfau, T., Mendoza, S. N., Richelle, A., Heinken, A., ... & Magnusdottir, S. (2017). Creation and analysis of biochemical constraint-based models: the COBRA Toolbox v3. 0. arXiv preprint arXiv:1710.04038.

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Orth, J. D., Conrad, T. M., Na, J., Lerman, J. A., Nam, H., Feist, A. M., & Palsson, B. Ø. (2011). A comprehensive genome-scale reconstruction of Escherichia coli metabolism—2011. Molecular systems biology, 7(1), 535.

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