

Sparse Linear Optimisation

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INTRODUCTION

In this tutorial, we will show how to use the sparse LP solver. This solver aims to solve the following optimisation problem

$$\begin{aligned} \min \quad & \|x\|_0 \\ \text{s.t.} \quad & A_{eq}x = b_{eq} \\ & A_{ineq}x \leq b_{ineq} \\ & l \leq x \leq u \end{aligned}$$

It has been proved that zero-norm is a non-convex function and the minimisation of zero-norm is a NP-hard problem. Non-convex approximations of zero-norm extensively developed. For a complete study of non-convex approximations of zero-norm, the reader is referred to Le Thie et al. (2015)¹.

The method is described in Le Thie et al. (2015)¹. The sparse LP solver contains one convex (one-norm) and 6 non-convex approximation of zero-norms

- Capped-L1 norm
- Exponential function
- Logarithmic function
- SCAD (Smoothly Clipped Absolute Deviation) function
- p norm with $p < 0$
- p norm with $0 < p < 1$

The tutorial consist of two parts. Part 1 shows a basic usage of the solver. In part 2 provides an application of the code for finding the minimal set of reactions subject to a LP objective. Ready-made scripts are provided for both parts.

EQUIPMENT SETUP

Initialize the COBRA Toolbox.

If necessary, initialize The Cobra Toolbox using the `initCobraToolbox` function.

```
initCobraToolbox(false) % false, as we don't want to update
```

COBRA model.

In this tutorial, the model used is the generic reconstruction of human metabolism, the Recon 2.04², which is provided in the COBRA Toolbox. The Recon 2.04 model can also be downloaded from the [Virtual Metabolic Human](#) webpage. You can also select your own model to work with. Before proceeding with the simulations, the path for the model needs to be set up:

```
global CBTDIR
modelFileName = 'Recon2.v04.mat';
modelDirectory = getDistributedModelFolder(modelFileName); %Look up the folder for the
modelFileName= [modelDirectory filesep modelFileName]; % Get the full path. Necessary t
model = readCbModel(modelFileName);
```

NOTE: The following text, code, and results are shown for the Recon 2.04 model

PROCEDURE

Example of using sparseLP solver on randomly generated data

One randomly generates a matrix $A \in \mathcal{R}^{m \times n}$ and a vector $x_0 \in \mathcal{R}^n$. The right hand side vector $b = A \cdot x_0$. There are three optional inputs for the method.

```
n = 100;
m = 50;
x0 = rand(n,1);
constraint.A = rand(m,n);
constraint.b = constraint.A*x0;
constraint.lb = -1000*ones(n,1);
constraint.ub = 1000*ones(n,1);
constraint.csense = repmat('E', m, 1);
```

The two first: maximum number of iterations (*nbMaxIteration*) and threshold (*epsilon*) are stopping criterion conditions. *theta* is the parameter of zero-norm approximation. The greater the value of *theta*, the better the approximation of the zero-norm. However, the greater the value of *theta*, the more local solutions the problem has. If the value of *theta* is not given then the algorithm will use a default value and update it gradually.

```
params.nbMaxIteration = 100;    % stopping criteria
params.epsilon = 1e-6;        % stopping criteria
params.theta = 2;             % parameter of l0 approximation
```

Call the solver with a chosen approximation

```
solution = sparseLP('cappedL1',constraint,params);
```

or with default parameter

```
%solution = sparseLP('cappedL1',constraint);
```

Finding the minimal set of reactions subject to a LP objective

Set the tolerance to distinguish between zero and non-zero flux, based on the numerical tolerance of the currently installed optimisation solver.

```
feasTol = getCobraSolverParams('LP', 'feasTol');
```

Select the biomass reaction to optimise

```
model.biomassBool=strcmp(model.rxns, 'biomass_reaction');  
model.c(model.biomassBool)=1;
```

We will firstly find the optimal value subject to a LP objective

```
%% Solve FBA  
% max c'v  
% s.t Sv = b  
% l <= v <= u  
% Define the LP structure  
[c,S,b,lb,ub,csense] = deal(model.c,model.S,model.b,model.lb,model.ub,model.csense);  
[m,n] = size(S);  
LPproblem = struct('c',-c,'osense',1,'A',S,'csense',csense,'b',b,'lb',lb,'ub',ub);  
% Call solveCobraLP to solve the LP  
LPsolution = solveCobraLP(LPproblem);  
vFBA = LPsolution.full;
```

We will now find the minimum number of reactions needed to achieve the same max objective found previously.

Then one will add one more constraint: $c^T v = c^T v_{FBA} =: f_{FBA}$.

```
constraint.A = [S ; c'];  
constraint.b = [b ; c'*vFBA];  
constraint.csense = [csense; 'E'];  
constraint.lb = lb;  
constraint.ub = ub;
```

Call the sparseLP solver to solve the problem

$$\begin{aligned} \min \quad & \|v\|_0 \\ \text{s.t.} \quad & Sv = b \\ & c^T v = f_{FBA} \\ & l \leq v \leq u \end{aligned}$$

```
% Try all non-convex approximations of zero norm and take the best result  
approximations = {'cappedL1', 'exp', 'log', 'SCAD', 'lp-', 'lp+'};  
bestResult = n;  
bestAprox = '';  
for i=1:length(approximations)  
    solution = sparseLP(char(approximations(i)),constraint);  
    if solution.stat == 1  
        if bestResult > length(find(abs(solution.x)>eps))  
            bestResult=length(find(abs(solution.x)>eps));  
            bestAprox = char(approximations(i));  
            solutionL0 = solution;  
        end  
    end  
end
```

```

        end
    end
end

```

Now we call the sparse linear step function approximations

```

bestResult = n;
bestAprox = '';
for i=1:length(approximations)
    solution = sparseLP(char(approximations(i)),constraint);
    if solution.stat == 1
        nnzSol=nnz(abs(solution.x)>feasTol);
        fprintf('%u%s',nnzSol,' active reactions in the sparseFBA solution with ', char
        if bestResult > nnzSol
            bestResult=nnzSol;
            bestAprox = char(approximations(i));
            solutionL0 = solution;
        end
    end
end
end

```

Select the most sparse flux vector, unless there is a numerical problem.

```

if ~isequal(bestAprox, '')
    vBest = solutionL0.x;
else
    vBest = [];
    error('Min L0 problem error !!!!!')
end

```

Report the best approximation

```

display(strcat('Best step function approximation: ',bestAprox))

```

Report the number of active reactions in the most sparse flux vector

```

fprintf('%u%s',nnz(abs(vBest)>feasTol),' active reactions in the best sparse flux balan

```

Warn if there might be a numerical issue with the solution

```

feasError=norm(constraint.A * solutionL0.x - constraint.b,2);
if feasError>feasTol
    fprintf('%g\t%s\n',feasError, ' feasibily error.')
    warning('Numerical issue with the sparseLP solution')
end

```

REFERENCES

[1] Le Thi, H.A., Pham Dinh, T., Le, H.M., and Vo, X.T. (2015). DC approximation approaches for sparse optimization. European Journal of Operational Research 244, 26–46.

[2] Thiele, I., Swainston, N., Fleming, R.M., Hoppe, A., Sahoo, S., Aurich, M.K., Haraldsdottir, H., Mo, M.L., Rolfsson, O., Stobbe, M.D., et al. (2013). A community-driven global reconstruction of human metabolism. *Nat Biotechnol* 31, 419-425.