```
function [TICs,Direction] = OptFillTFP(model,database,mTFP)
% Enumerates all the Thermodynamically infeasible cycles in a given model
% using OptFill's algorithm. This code is adapted based on codes written in
% GAMS and python in the paper "OptFill: A Tool for Infeasible Cycle-Free
% Gapfilling of Stoichiometric Metabolic Models"
% USAGE:
응
    [TICs,Direction] = OptFillTFP(model,database,mTFP)
응
% INPUTS:
응
                 COBRA model structure defining the actual model
     model:
응
      database: COBRA model structure defining the database
      mTFP:
                 boolean value indicating whether to work on modified-TIC
응
응
                 finding problem (1) or TIC finding problem (0). In TIC
응
                 finding problem, atleast one reaction in a TIC will be
응
                 from the database.
응
응
 OUTPUTS:
                  List of all the Thermodynamically infeasible cycles in
응
      TICs:
응
                  the given input model-database pair
응
     Direction: Relative flux coefficients for reactions
응
                  in the corresponding TICs
% .. Author:
응
        - Pavan Kumar S, BioSystems Engineering and control (BiSECt) lab,
IIT Madras
응
        - Based on: Schroeder, W. L., & Saha, R. (2020). OptFill: a tool
                    for infeasible cycle-free gapfilling of stoichiometric
응
                    metabolic models. IScience, 23(1).
m_Db = mergeTwoModels(model,database); % the combined model
m_Db.origin = ismember(m_Db.rxns, model.rxns); % boolean vector indicating if
a reaction is from model (1) or the database (0)
% parameters used were taken from the OptFill paper
epsilon=0.001;
M=1000;
tolerance=1e-6;
changeCobraSolverParams('LP', 'feasTol', tolerance);
[~,max_phi] = size(m_Db.S); % number of reactions in the model-database pair
IrR = m_Db.ub<=0; % reactions irreversible in reverse direction</pre>
temp = m_Db.ub(IrR);
m_Db.S(:,IrR) = -m_Db.S(:,IrR);
m_Db.ub(IrR) = -1*m_Db.lb(IrR);
m_Db.lb(IrR) = -1*temp;
rev = ones(n,1);
rev(m_Db.1b >= 0) = 0;
m_Db.rev=rev;
```

```
% converting all the positive lower bounds to zero lower bounds
m_Db.lb(m_Db.lb>0)=0;
% normalising the bounds to max of M
temp1 = max(abs(m_Db.lb));
temp2 = max(abs(m_Db.ub));
m_Db.lb(abs(m_Db.lb)==temp1) = sign(m_Db.lb(abs(m_Db.lb)==temp1))*M;
m_Db.ub(abs(m_Db.ub)==temp2) = sign(m_Db.ub(abs(m_Db.ub)==temp2))*M;
ind = findExcRxns(m_Db); % indices of the exchange reactions
% blocking all the exchange reactions
m_Db.lb(ind) = 0;
m_Db.ub(ind) = 0;
TICs={}; Direction = {}; % empty cell to store the TICs and their respective
direction
for phi = 2:max_phi % minimum size of a TIC has to be two
    found_all = false;
   while ~found_all
        [flux,stat] = findTIC(m_Db,phi,mTFP);
    end
end
end
```

```
function [flux,stat] = findTIC(model,phi,mTFP)
end
```