Visualise conserved moieties in dopaminergic neuronal metabolism

```
tutorial_initConservedMoietyPaths
```

```
modelName = 
'DAS'
projectDir = 
'/home/rfleming/work/sbgCloud/code/fork-COBRA.tutorials/analysis/conservedMoieties'
dataDir = 
'/home/rfleming/work/sbgCloud/code/fork-COBRA.tutorials/analysis/conservedMoieties/data/models/'
softwareDir = 
'/home/rfleming/work/sbgCloud/code/fork-COBRA.tutorials/analysis/conservedMoieties/software/'
visDataDir = 
'/home/rfleming/work/sbgCloud/code/fork-COBRA.tutorials/analysis/conservedMoieties/data/visualisation/'
resultsDir = 
'/home/rfleming/work/sbgCloud/code/fork-COBRA.tutorials/analysis/conservedMoieties/results/DAS_ConservedMo
rxnfileDir = 
'/home/rfleming/work/sbgCloud/code/fork-COBRA.tutorials/analysis/conservedMoieties/data/mini-ctf/rxns/atom
```

```
% if ~recompute
%     load([resultsDir  modelName '_ConservedMoietiesAnalysis.mat'])
%     return
% end
```

Load the dopaminergic neuronal metabolic model

```
load([dataDir modelName '.mat'])
```

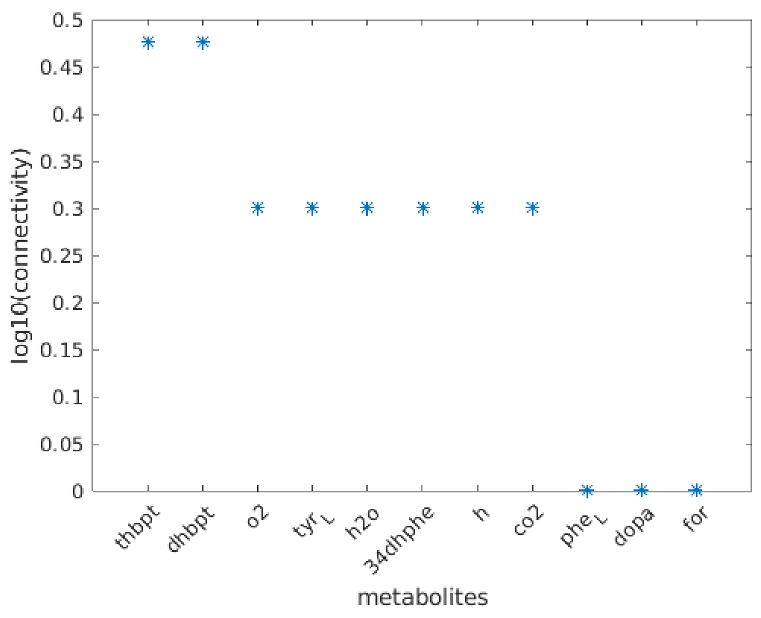
Identify the stoichiometrically consistent subset of the model

```
massBalanceCheck=1;
printLevel=1;
[SConsistentMetBool, SConsistentRxnBool, SInConsistentMetBool, SInConsistentRxnBool, un
    = findStoichConsistentSubset(model,massBalanceCheck,printLevel);
```

```
--- findStoichConsistentSubset START ----
--- Summary of stoichiometric consistency ----
    11        11     totals.
     0         7     heuristically external.
    11         4     heuristically internal:
    11         4     ... of which are stoichiometrically consistent.
     0         0     ... of which are stoichiometrically inconsistent.
     0         0     ... of which are of unknown consistency.
---
     0         0     heuristically internal and stoichiometrically inconsistent or unknown consistency.
     0         0     ... of which are elementally imbalanced (inclusively involved metabolite).
     0         0     ... of which are elementally imbalanced (exclusively involved metabolite).
    11         4     Confirmed stoichiometrically consistent by leak/siphon testing.
--- findStoichConsistentSubset END ----
Warning: Model did not contain a genes field. Building it along with the rules field
Warning: This function can be only be used on a model that has grRules field!\n
```

Metabolite connectity

```
param.n=20;
[rankMetConnectivity,rankMetInd,rankConnectivity] = rankMetabolicConnectivity(model,par
```



Load atomically resolved models & conserved moiety analysis

Load the atomically resolved models derived from identifyConservedMoieties.m

```
if 0
    load([resultsDir 'iDopaMoieties_noChecks.mat'])
else
    load([resultsDir  modelName '_ConservedMoietiesAnalysis.mat'])
end
```

Transitive moiety, of sufficient mass, with moderate incidence

```
isTransititiveMoiety= strcmp('Transitive',moietyTypes);
isModerateIncidence = moietyIncidence>=10 & moietyIncidence<=100;
isSufficientMass = moietyMasses > 2;
isSufficientMinimalMassFraction = minimalMassFraction > 0.1;
interestingMoiety = isTransititiveMoiety & isModerateIncidence & isSufficientMass & isS
C = cell(nnz(interestingMoiety),9);
n=1;
for i=1:size(arm.L,1)
    if interestingMoiety(i)
        ind = find(strcmp(minimalMassMetabolite{i},model.mets));
        C(n,1:9) = {i,nnz(arm.L(i,:)),nnz(model.S((arm.L(i,:)~=0)',:)~=0),moietyFormula
        n=n+1;
    end
end

C=sortrows(C,9,'descend');
T=cell2table(C);
T.Properties.VariableNames={'index','metabolites','rxns','moiety_formula','mass','Minim
size(T,1)
```

```
ans = 0
```

```
disp(T)
```

Recon3Map

Import Recon3Map

```
if ~exist('Recon3xml','var')
    [Recon3xml, Recon3map] = transformXML2Map([visDataDir 'reconMap3d_allin.xml']);
end
if 0
    transformMap2XML(Recon3xml,Recon3map,[resultsDir 'Recon3map.xml']);
end
```

Compare the reactions in the specified metabolic model and Recon3Map

The function `checkCDerrors` gives four outputs summarising all possible discrepancies between model and map.

```
printLevel=0;
[diffReactions, diffMetabolites, diffReversibility, diffFormula] = checkCDerrors(Recon3
```

Four outputs are obtained from this function:

"`diffReactions`" summarises present and absent reactions between model and map.

Display the internal reactions in the model that are not present in the map.

```
bool=ismember(diffReactions.extraRxnModel,model.rxns(model.SConsistentRxnBool));
nnz(bool)
```

```
ans = 4
```

```
disp(diffReactions.extraRxnModel(bool))
```

```
    {'R1'}
    {'R2'}
    {'R3'}
    {'R4'}
```

"`diffMetabolites`" summarises present and absent metabolites.

NOTE! *Note that having more metabolites and reactions in the COBRA model is normal since the model can contain more elements than the map. On the other hand, the map should only contain elements present in the model.*

"`diffReversibility`" summarises discrepancies in defining the reversibility of reactions.

The last output "`diffFormula`" summarises discrepancies in reactions formulae (kinetic rates) and also lists duplicated reactions.

Create a map of the model

Remove some reactions from the map

```
rxnRemoveList = diffReactions.extraRxnsMap;
```

Remove non-dopaminergic neuronal reactions from the map

```
[modelNameXml,modelNameMap] = removeMapReactions(Recon3xml, Recon3map,rxnRemoveList);
```

Remove pathway labels from the map

```
specRemoveType='UNKNOWN';
specRemoveList=[];
printLevel=0;
[modelNameXml,modelNameMap,specNotInMap] = removeMapSpecies(modelNameXml,modelNameMap,s
```

Remove highly connected metabolites from the map

```
specRemoveList={'h[c]';'h[l]';'h[e]';'h[r]';'h2o[c]';'h2o[l]';'h20[e]';'pi[c]';'adp[c]'
[xmlStruct,map,specNotInMap] = removeMapSpeciesOnly(modelNameXml,modelNameMap,specRemov
```

Export the model map

```
transformMap2XML(modelNameXml,modelNameMap,[resultsDir modelName '_CD.xml']);
```

```
Elapsed time is 0.030606 seconds.
```

Nicotinate moiety

```
ind = 9;% Nicotinate moiety
mBool=arm.L(min(ind,size(arm.L,1)),:)~=0;
nnz(mBool)
```

```
ans = 5
```

```
rBool = getCorrespondingCols(model.S, mBool, true(size(model.S,2),1), 'inclusive');
nnz(rBool)
```

```
ans = 6
```

Metabolites

```
bool=mBool;
C = cell(nnz(bool),5);
n=1;
for i=1:size(model.S,1)
    if bool(i)
        C(n,1:5) = {i,model.mets{i},model.metNames{i},model.metFormulas{i},metMasses(i)
        n=n+1;
    end
end
C=sortrows(C,5,'descend');
T=cell2table(C);
T.Properties.VariableNames={'index','met','name','formula','mass'};
disp(T)
```

```
index        met             name            formula          mass
_____    ___________    ___________    ____________    ______

  7      {'34dhphe'}    {'34dhphe'}    {'C9H11NO4'}    197.07
  4      {'tyr_L'  }    {'tyr_L'  }    {'C9H11NO3'}    181.07
  9      {'dopa'   }    {'dopa'   }    {'C8H12NO2'}    154.09
  3      {'o2'     }    {'o2'     }    {'O2'      }     31.99
  6      {'h2o'    }    {'h2o'    }    {'H2O'     }    18.011
```

Reactions

```
formulas = printRxnFormula(model, model.rxns(rBool));
```

```
R1     phe_L + thbpt + o2     ->     tyr_L + dhbpt + h2o
R2     thbpt + o2 + tyr_L     ->     dhbpt + h2o + 34dhphe
R3     34dhphe + h     ->     dopa + co2
EX_o2     o2     <=>
EX_h2o     h2o     ->
EX_dopa     dopa     ->
```

Map of nicotinate subnetwork

This code is specific to the dopaminergic neuronal metabolic model. Export the dopaminergic neuronal model as an sbml file

```
if 0
    nicotinateRxnRemoveList=model.rxns(~rBool);
    [iDopaNicotinateXml,iDopaNicotinateMap] = removeMapReactions(iDopaXml,iDopaMap,nico
    transformMap2XML(iDopaNicotinateXml,iDopaNicotinateMap,[resultsDir modelName '_Nico
    outmodel = writeCbModel(model, 'format','sbml','fileName', [resultsDir 'iDopaNeuro_
end
```

Generate a set of submodels of the interesting moieties

Get abbreviations, without compartments for each metabolite in the model, then generate a results directory for each interesting moiety

```
[compartments, uniqueCompartments, minimalMassMetaboliteAbbr, uniqueAbbr]= getCompartme
extractSubnetwork=1;
matFile=0;
sbmlFile=1;
moietyData=1;
CDFile=0;
n=1;
for i=1:size(arm.L,1)
    if interestingMoiety(i)
        metSampleName = minimalMassMetaboliteAbbr{i};
        disp(metSampleName)
        [SUCCESS,MESSAGE,MESSAGEID] = mkdir(resultsDir,metSampleName);
        cd([resultsDir filesep metSampleName])
        mBool = arm.L(i,:)~=0;
        rBool = getCorrespondingCols(model.S, mBool, true(size(model.S,2),1), 'inclusiv
        if extractSubnetwork
            modelNameInterestingSubModel{n,1} = extractSubNetwork(model, model.rxns(rBo
        end
        mBoolModel = ismember(model.mets,modelNameInterestingSubModel{n,1}.mets);
        modelNameInterestingSubModel{n,2}=i;
        modelNameInterestingSubModel{n,3}=minimalMassMetabolite{i};

        if matFile
            outmodel = writeCbModel(modelNameInterestingSubModel{n,1}, 'format','mat','
        end

        if sbmlFile
            outmodel = writeCbModel(modelNameInterestingSubModel{n,1}, 'format','sbml',
        end

        if moietyData

            moietyIncidence = arm.L(modelNameInterestingSubModel{n,2},ismember(model.me

            fileName = [resultsDir metSampleName filesep modelName '_' metSampleName '_
            param.name = [modelName '_' metSampleName 'MoietySubnetwork'];
            param.description = [modelName '_' metSampleName ' moiety incidence'];
            param.color.minValue = -1;
            param.color.minColor = '#FF0000';
            param.color.zeroValue = 0;
            param.color.zeroColor = '#FFFFFF';
            param.color.maxValue =  full(max(moietyIncidence));
            param.color.maxColor = '#87CEFA';
            writeNewtExperiment(modelNameInterestingSubModel{n,1},moietyIncidence,metSa
        end

        if CDFile
            [modelNameInterestingXml{n},modelNameInterestingMap{n},modelNameRxnNotInMap
            transformMap2XML(modelNameInterestingXml{n},modelNameInterestingMap{n},[res
        end
        n=n+1;
        cd('../')
    end
end
```