

# Entropic flux balance analysis

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## INTRODUCTION

Entropic flux balance analysis [1] maximises the (unnormalised) entropy of unidirectional fluxes ( $v_f$  and  $v_r$ ) and optionally a linear function of external net fluxes  $w$ , subject to mass balance constraints, optionally coupling constraints, box constraints on net flux, and zero lower bounds on unidirectional fluxes. This ensures that predicted steady state fluxes are thermodynamically feasible, assuming one is given a model that admits a thermodynamically feasible flux. A method for finding the largest subset of a given model that admits a thermodynamically feasible flux is described in this paper [3] and this tutorial [4]. Given a generic model of metabolism and context-specific omics data, this paper [5] and this tutorial [6] explain how to extract a context-specific model that admits a thermodynamically feasible internal net flux vector, using the XomicsToModel protocol [5].

Entropic flux balance analysis is mathematically represented by the optimisation problem

$$\min_{v_f, v_r, w} v_f^T \cdot (\log(v_f) - 1) + v_r^T \cdot (\log(v_r) - 1) + c_e^T \cdot w$$

subject to

$$\begin{aligned} v &= [v_f - v_r; w] \\ N \cdot (v_f - v_r) + B \cdot w &= b, \quad : y_N \\ C \cdot (v_f - v_r) &\leq d, \quad : y_C \\ l \leq v &\leq u, \quad : z_v \\ 0 \leq v_f, & \quad : z_{v_f} \\ 0 \leq v_r, & \quad : z_{v_r} \end{aligned}$$

where  $N$  is the internal reaction stoichiometric matrix (all reactions bass balanced),  $B$  is the external reaction stoichiometric matrix (all reactions mass imbalanced),  $b$  may be used to represent any known fixed input (negative) or output (positive) of molecular species from the system, and zero otherwise. The variables to the right of the  $:$  are the corresponding dual variables to each constraint.

A variation of this is quadratically constrained entropic flux balance analysis [2], which allows one to penalise deviation of predicted net flux from experimentally measured net flux. This is represented by the following optimisation problem

$$\min_{v_f, v_r, w} v_f^T \cdot (\log(v_f) - 1) + v_r^T \cdot (\log(v_r) - 1) + c_e^T \cdot w + \frac{1}{2}(v - h)^T \cdot H \cdot (v - h)$$

subject to

$$\begin{aligned} v &= [v_f - v_r; w] \\ N \cdot (v_f - v_r) + B \cdot w &= b, \quad : y_N \\ C \cdot (v_f - v_r) &\leq d, \quad : y_C \\ l \leq v &\leq u, \quad : z_v \\ 0 \leq v_f, & \quad : z_{v_f} \\ 0 \leq v_r, & \quad : z_{v_r} \end{aligned}$$

where  $H$  may be used to add penalties, e.g.,  $H_{j,j} = \frac{1}{(1 + \sigma_{exp}^2)}$  where  $\sigma_{exp} \in \mathbb{R}_{\geq 0}^n$  is the standard deviation in measured net flux  $h$ .

## MATERIALS - EQUIPMENT SETUP

Mosek installation required

## PROCEDURE

Set the directory for results

```
basePath='~/work/sbgCloud';
resultsDirectory=[basePath '/programModelling/projects/thermoModel/results/
entropicFBA'];
```

Set the model to load

```
modelToUse='iDopaNeuro';
%modelToUse='ecoli_core';
%modelToUse = 'fork';
%modelToUse = 'single';
%modelToUse='recon3';

if ~exist('model','var')
    switch modelToUse
        case 'single'
            driver_singleModel
        case 'fork'
            driver_forkModel

        case 'ecoli_core'
            dataDirectory=[basePath '/data'];
            load([dataDirectory '/models/published/e_coli_core.mat']);
```

```

        if ~isfield(model,'SConsistentMetBool') || ~isfield(model,'SConsistentRxnBool')
            massBalanceCheck=0;
            [~,~,~,~,~,~,~,model,~] = findStoichConsistentSubset(model, massBalanceCheck, 0);
        end
        model.lb(ismember(model.rxns,'BIOMASS_Ecoli_core_w_GAM'))=0.1;

    case 'recon3'
        %COBRA.models/mat/Recon3DModel_301_xomics_input.mat
        load(which('Recon3DModel_301_xomics_input.mat'))

        %change onto uMol/gDW/hr
        model.lb = model.lb;
        model.ub = model.ub;
    case 'iDopaNeuro'
        %load('~/drive/sbgCloud/projects/iDopaNeuro/results/codeResults/iDN1/iDopaNeuroC/iDopaNeuroC.mat')
        load('~/drive/sbgCloud/projects/variationalKinetics/data/iDopaNeuro/iDopaNeuroC.mat')
        model = iDopaNeuroC;
        clear iDopaNeuroC
        model.lb(ismember(model.rxns,'ATPM')) =
        model.lb(ismember(model.rxns,'ATPM'))/2;

        %problematic reactions
        %      {'34DHPHET'}      {'3, 4-Dihydroxy-L-Phenylalanine Transport'} -0.53635 0 {'34dhphe[e] <=> 34dhphe[c]'}
        %      {'URAT'}          {'Uracil Transport via Faciliated Diffusion'} -0.0013626 0 {'ura[e] <=> ura[c]'}
        model.lb(ismember(model.rxns,'34DHPHET'))=-1e4;
        model.ub(ismember(model.rxns,'34DHPHET'))= 1e4;
        model.lb(ismember(model.rxns,'URAT'))=-1e4;
        model.ub(ismember(model.rxns,'URAT'))= 1e4;
    end
end

```

## Examine the constraints on the model

```
printConstraints(model,-1e4,1e4,model.SIntRxnBool)
```

Forward_Reaction, 0 bound	Name	lb
{'10FTHF6GLUTl'}	{'6-Glutamyl-10Fthf Transport, Lysosomal'}	0
{'1PPDCRp'}	{'Delta1-Piperideine-2-Carboxylate Reductase, Peroxisomal'}	0
{'2OXOADOXm'}	{'2-Oxoadipate:Lipoamide 2-Oxidoreductase (Decarboxylating And )'}	0
{'34DHPHAMT'}	{'3, 4-Dihydroxyphenylacetate:Amid O-Methyltransferase'}	0
{'34DHPLACOX'}	{'3, 4-Dihydroxyphenylacetate:NAD+ Oxidoreductase'}	0
{'34DHXMANDACOX'}	{'3, 4-Dihydroxymandelaldehyde:NAD+ Oxidoreductase'}	0
{'34HPLFM'}	{'3- (4-Hydroxyphenyl-)Lactate Formation'}	0
{'3DSPHR'}	{'3-Dehydrophinganine Reductase'}	0

{ '3HLYTCL'	{ '3-Hydroxy-L-Tyrosine Carboxy-Lyase'	}	0
{ '3SALACBOXL'	{ '3-Sulfino-L-Alanine Carboxy-Lyase'	}	0
{ '3SALAOX'	{ 'Cysteinesulfinic Acid Oxidase'	}	0
{ '3SALATAi'	{ '3-Sulfino-Alanine Transaminase (Irreversible)'	}	0
{ '3SPYRSP'	{ '3-Sulfinopyruvate Hydrolase (Spotaneous Reaction)'	}	0
{ '41R1H2MAE12BOOK'	{ '4-[ (1R)-1-Hydroxy-2- (Methylamino)Ethyl]-1, 2-Benzenediol:O'}	}	0
{ '42A12BOOK'	{ '4- (2-Aminoethyl)-1, 2-Benzenediol:Oxygen Oxidoreductase (De'}	}	0
{ '4HBZCOAFm'	{ '4-Hydroxybenzoyl Coenzyme A Formation'	}	0
{ '4HBZFm'	{ '4-Hydroxybenzoate Formation'	}	0
{ '4MOPt2im'	{ '4-Methyl-2-Oxopentanoate Mitochondrial Transport via Proton '	}	0
{ '7DHFTl'	{ '7-Glutamyl-Dhf Transport, Lysosomal'	}	0
{ 'AASAD3m'	{ 'L-Aminoadipate-Semialdehyde Dehydrogenase (NADH), Mitochondr'	}	0
{ 'ACACT1x'	{ 'Acetyl Coenzyme A C-Acetyltransferase'	}	0
{ 'ACGALK'	{ 'N-Acetylgalactosamine Kinase'	}	0
{ 'ACGALK2'	{ 'N-Acetylgalactosamine Kinase (ITP)'	}	0
{ 'ACGAM6Psi'	{ 'N-Acetylglucosamine-6-Phosphate Synthase'	}	0
{ 'ACGAMK'	{ 'N-Acetylglucosamine Kinase'	}	0
{ 'ACGAMtly'	{ 'N-Acetyl-Glucosamine Lysosomal Efflux'	}	0
{ 'ACITL'	{ 'ATP-Citrate Lyase'	}	0
{ 'ACNAM9PL2'	{ 'N-Acetylneuraminate 9-Phosphate Pyruvate-Lyase (Pyruvate-Pho'	}	0
{ 'ACOAD8m'	{ 'Acyl Coenzyme A Dehydrogenase (Isovaleryl Coenzyme A), Mitoc'	}	0
{ 'ACP1_FMN_'	{ 'Acid Phosphatase (FMN)'	}	0
{ 'ADMDC'	{ 'Adenosylmethionine Decarboxylase'	}	0
{ 'ADNCYC'	{ 'Adenylate Cyclase'	}	0
{ 'ADRNLPVESSEC'	{ 'Adrenaline Secretion via Secretory Vesicle (ATP Driven)'	}	0
{ 'ADSK'	{ 'Adenylyl-Sulfate Kinase'	}	0
{ 'ADSL1'	{ 'Adenylosuccinate Lyase'	}	0
{ 'ADSL2'	{ 'Adenylosuccinate Lyase'	}	0
{ 'AGPAT1'	{ '1-Acylglycerol-3-Phosphate O-Acyltransferase 1'	}	0
{ 'AGTIm'	{ 'Alanine-Glyoxylate Transaminase (Irreversible), Mitochondria'	}	0
{ 'AKGDm'	{ '2-Oxoglutarate Dehydrogenase'	}	0
{ 'ALAASNNaEx'	{ 'L-Alanine/L-Asparagine Na-Dependent Exchange (Ala-L In)'	}	0
{ 'ALAGLNNaEx'	{ 'L-Alanine/L-Glutamine Na-Dependent Exchange (Ala-L In)'	}	0
{ 'ALASm'	{ '5-Aminolevulinate Synthase'	}	0
{ 'ALAt4'	{ 'Alanine-Sodium Symporter'	}	0
{ 'ALCD21_L'	{ 'Alcohol Dehydrogenase (L-1, 2-Propanediol)'	}	0
{ 'ALDD2xm'	{ 'Aldehyde Dehydrogenase (Acetylaldehyde, NAD), Mitochondrial'	}	0
{ 'ALDD2y'	{ 'Aldehyde Dehydrogenase (Acetaldehyde, NADP)'	}	0
{ 'ALOX5'	{ 'Arachidonate 5-Lipoxygenase'	}	0
{ 'ALOX52'	{ 'Arachidonate 5-Lipoxygenase'	}	0
{ 'ALR2'	{ 'Aldose Reductase (Methylglyoxal)'	}	0
{ 'ALR3'	{ 'Aldose Reductase (Acetol)'	}	0
{ 'AMPDA'	{ 'Adenosine Monophosphate Deaminase'	}	0
{ 'APRTO2'	{ 'N-Acetylputrescine: Oxygen Oxireductase (Deaminating)'	}	0
{ 'ARGLYSex'	{ 'Arginine/Lysine Exchanger (Arg In)'	}	0
{ 'ARGSS'	{ 'Argininosuccinate Synthase'	}	0
{ 'R_group_phosphotase_1'	{ 'R Group Phosphotase 1'	}	0
{ 'R_group_phosphotase_2'	{ 'R Group Phosphotase 2'	}	0
{ 'ASAHL1'	{ 'N-Acylsphingosine Amidohydrolase'	}	0
{ 'ASNALANaEx'	{ 'L-Alanine/L-Asparagine Na-Dependent Exchange (Asn-L In)'	}	0
{ 'ASNNm'	{ 'L-Asparaginase, Mitochondrial'	}	0
{ 'ASNS1'	{ 'Asparagine Synthase (Glutamine-Hydrolysing)'	}	0
{ 'ASNT4'	{ 'L-Asparagine Transport in via Sodium Symport'	}	0
{ 'ASNtm'	{ 'L-Asparagine Transport, Mitochondrial'	}	0
{ 'ASPdt6'	{ 'D-Aspartate Transport via Na, H Symport And K Antiport'	}	0
{ 'ASPGLUm'	{ 'Aspartate-Glutamate Mitochondrial Shuttle'	}	0
{ 'ASPNATm'	{ 'Aspartate N-Acetyltransferase, Mitochondrial'	}	0
{ 'ASPt6'	{ 'L-Aspartate Transport via Na, H Symport And K Antiport'	}	0
{ 'ATPasel'	{ 'V-Type ATPase, H+ Transporting, Lysosomal'	}	0
{ 'ATPH1e'	{ 'ATP Diphosphohydrolase'	}	0
{ 'ATPtM'	{ 'ADP/ATP Transporter, Mitochondrial'	}	0
{ 'BAMPPALDOX'	{ 'Beta-Aminopropion Aldehyde:NAD+ Oxidoreductase'	}	0
{ 'BPNT2'	{ '3', 5'-Bisphosphate Nucleotidase (Paps)'	}	0
{ 'CAATPS'	{ 'Ca ATPase'	}	0

{ 'CATm'	} { 'Catalase'	}	0
{ 'CATp'	} { 'Catalase A, Peroxisomal'	}	0
{ 'CBPPer'	} { 'Carbamoyl Phosphate Phosphotransferase, Endoplasmic Reticulum'	}	0
{ 'CDS'	} { 'Phosphatidate Cytidylyltransferase'	}	0
{ 'CEPTC'	} { 'Choline Phosphotransferase'	}	0
{ 'CERK'	} { 'Ceramide Kinase'	}	0
{ 'CGLYt3_2_'	} { 'Cys-Gly Transport in via Proton Symport'	}	0
{ 'CHLPCTD'	} { 'Choline Phosphate Cytidyltransferase'	}	0
{ 'CHOLK'	} { 'Choline Kinase'	}	0
{ 'CHSTEROLtg'	} { 'Cholesterol Efflux (ATP Dependent), Golgi Apparatus'	}	0
{ 'CK'	} { 'ATP Creatine Kinase'	}	0
{ 'CKc'	} { 'ATP Creatine Kinase, Cytosolic'	}	0
{ 'CMPSAS'	} { 'CMP Sialic Acid Synthase'	}	0
{ 'COUCOAFm'	} { 'P-Coumaroyl Coenzyme A Formation'	}	0
{ 'CREATTmdiffir'	} { 'Creatine Transport To/from Mitochondria via Diffusion'	}	0
{ 'CRNCARTp'	} { 'Carnitine-Acetylcarnitine Carrier, Peroxisomal'	}	0
{ 'CRTNSyn'	} { 'Creatinine Synthase'	}	0
{ 'CSM'	} { 'Citrate Synthase'	}	0
{ 'CYSO'	} { 'Cysteine Oxidase'	}	0
{ 'CYSTGLUex'	} { 'L-Cystine/L-Glutamate Exchanger'	}	0
{ 'CYTDK1'	} { 'ATPcytidine 5-Phosphotransferase'	}	0
{ 'DAGK_hs'	} { 'Diacylglycerol Phosphate Kinase (Homo Sapiens)'	}	0
{ 'DASCBR'	} { 'Dehydroascorbate Reductase'	}	0
{ 'DESAT16_2'	} { 'Palmitoyl Coenzyme A Desaturase (N-C16:0CoA -> N-C16:1CoA)'	}	0
{ 'DESAT18_5'	} { 'Stearoyl Coenzyme A Desaturase (N-C18:0CoA -> N-C18:1CoA)'	}	0
{ 'DESAT22_1p'	} { 'Fatty Acyl Coenzyme A Desaturase (N-C22:4CoA -> N-C22:5CoA)'	}	0
{ 'DHCR242r'	} { '24-Dehydrocholesterol Reductase [Precursor]'	}	0
{ 'DHC RD1'	} { 'Dihydroceramide Desaturase'	}	0
{ 'DHC RD2'	} { 'Dihydroceramide Desaturase'	}	0
{ 'DHPR2'	} { '6, 7-Dihydropteridine Reduction'	}	0
{ 'DKMPPD'	} { '2, 3-Diketo-5-Methylthio-1-Phosphopentane Degradation React'}	0	0
{ 'DOLGLCP_Lter'	} { 'Dolichyl Beta-D-Glucosyl Phosphate Flippase (Liver)'	0	0
{ 'DOLGPP_Ler'	} { 'Dolichyl-Beta-D-Glucosyl-Phosphate Dolichylphosphohydrolase '	0	0
{ 'DOLPMT4_Ler'	} { 'Dolichyl-Phosphate-Mannose-Glycolipid Alpha-Mannosyltransfer'}	0	0
{ 'DOPABMO'	} { 'Dopamine Beta-Monooxygenase'	0	0
{ 'DOPACHRMISO'	} { 'L-Dopachrome Isomerase 1'	0	0
{ 'DOPASFT'	} { 'Transport of Dopamine 3-O-Sulfate (Diffusion)'	0	0
{ 'DOPASULT'	} { 'Dopamine Sulfotransferase'	0	0
{ 'DPGase'	} { 'Diphosphoglycerate Phosphatase'	0	0
{ 'DPMV Dx'	} { 'Diphosphomevalonate Decarboxylase'	0	0
{ 'DRPA'	} { 'Deoxyribose-Phosphate Aldolase'	0	0
{ 'DSAT'	} { 'Dihydrosphingosine N-Acyltransferase'	0	0
{ 'DUTPDPm'	} { 'DUTP Diphosphatase'	0	0
{ 'DUTPDPn'	} { 'DUTP Diphosphatase, Nuclear'	0	0
{ 'ETF'	} { 'Electron Transfer Flavoprotein'	0	0
{ 'ETFQO'	} { 'Electron Transfer Flavoprotein-Ubiquinone Oxidoreductase'	0	0
{ 'ETHAK'	} { 'Ethanolamine Kinase'	0	0
{ 'FACOAL160i'	} { 'C160 Fatty Acid Activation'	0	0
{ 'FACOAL1821'	} { 'Fatty-Acid- Coenzyme A Ligase'	0	0
{ 'FACOAL80i'	} { 'Fatty-Acid- Coenzyme A Ligase (Octanoate)'	0	0
{ 'FADH2tru'	} { 'Transport of FADH2, Endoplasmic Reticulum'}	0	0
{ 'FADtru'	} { 'Transport of FAD, Endoplasmic Reticulum'}	0	0
{ 'FAEL183'	} { 'Fatty-Acyl Coenzyme A Elongation (N-C18:3CoA)'	0	0
{ 'FAEL204'	} { 'Fatty-Acyl Coenzyme A Elongation (N-C20:4CoA)'	0	0
{ 'FAOCX160'	} { 'Beta Oxidation of Long Chain Fatty Acid'}	0	0
{ 'FAOCX16080x'	} { 'Beta Oxidation of Long Chain Fatty Acid'}	0	0
{ 'FAOCX16180m'	} { 'Beta Oxidation Fatty Acid'}	0	0
{ 'FAOCX180'	} { 'Beta Oxidation of Long Chain Fatty Acid'}	0	0
{ 'FAOCX180x'	} { 'Beta Oxidation of Long Chain Fatty Acid'}	0	0
{ 'FAOCX1811603m'	} { 'Beta Oxidation Fatty Acid'}	0	0
{ 'FAOCX183806x'	} { 'Beta Oxidation of Long Chain Fatty Acid'}	0	0
{ 'FAOCX18480x'	} { 'Beta Oxidation of Long Chain Fatty Acid'}	0	0
{ 'FAOCX200180m'	} { 'Beta Oxidation of Long Chain Fatty Acid'}	0	0
{ 'FAOCX200180x'	} { 'Beta Oxidation of Long Chain Fatty Acid'}	0	0

{ 'FAOXC204'	} { 'Beta Oxidation of Long Chain Fatty Acid'	}	0
{ 'FAOXC2051843x'	} { 'Beta Oxidation of Long Chain Fatty Acid'	}	0
{ 'FAOXC2251836x'	} { 'Beta Oxidation of Long Chain Fatty Acid'	}	0
{ 'FAOXC2252053m'	} { 'Beta Oxidation of Long Chain Fatty Acid'	}	0
{ 'FAOXC80'	} { 'Beta Oxidation of Med/Long Chain Fatty Acid'	}	0
{ 'FAS100COA'	} { 'Fatty Acyl Coenzyme A Synthase (N-C10:0CoA)'	}	0
{ 'FAS120COA'	} { 'Fatty-Acyl Coenzyme A Synthase (N-C12:0CoA)'	}	0
{ 'FAS140COA'	} { 'Fatty-Acyl Coenzyme A Synthase (N-C14:0CoA)'	}	0
{ 'FAS160COA'	} { 'Fatty-Acyl Coenzyme A Synthase (N-C16:0CoA)'	}	0
{ 'FAS180COA'	} { 'Fatty-Acyl Coenzyme A Synthase (N-C18:0CoA)'	}	0
{ 'FAS80COA_L'	} { 'Fatty Acyl Coenzyme A Synthase (N-C8:0CoA), Lumped Reaction'	}	0
{ 'FBP26'	} { 'Fructose-2, 6-Bisphosphate 2-Phosphatase'	}	0
{ 'FKYNH'	} { 'N-Formyl-L-Kynurenine Amidohydrolase'	}	0
{ 'FOLR2'	} { 'Folate Reductase'	}	0
{ 'FPGS2'	} { 'Folylpolyglutamate Synthetase'	}	0
{ 'FPGS3'	} { 'Folylpolyglutamate Synthetase'	}	0
{ 'FPGS4'	} { 'Folylpolyglutamate Synthetase (Dhf)'	}	0
{ 'FPGS5'	} { 'Folylpolyglutamate Synthetase (Dhf)'	}	0
{ 'FPGS6'	} { 'Folylpolyglutamate Synthetase (Dhf)'	}	0
{ 'FPGS8'	} { 'Folylpolyglutamate Synthetase (10Fthf)'	}	0
{ 'G5SDym'	} { 'Glutamate-5-Semialdehyde Dehydrogenase, Mitochondrial'	}	0
{ 'G6PPer'	} { 'Glucose-6-Phosphate Phosphatase, Endoplasmic Reticular'}	}	0
{ 'GALTly'	} { 'Galactose Efflux from Lysosome'}	}	0
{ 'GBA'	} { 'Glucosylceramidase'	}	0
{ 'GGH_10FTHF5GLUL'	} { 'Gamma-Glutamyl Hydrolase (10Fthf5Glu), Lysosomal'	}	0
{ 'GGH_10FTHF6GLUL'	} { 'Gamma-Glutamyl Hydrolase (10Fthf6Glu), Lysosomal'	}	0
{ 'GGH_5DHF1'	} { 'Gamma-Glutamyl Hydrolase (5Dhf), Lysosomal'	}	0
{ 'GGH_6DHF1'	} { 'Gamma-Glutamyl Hydrolase (6Dhf), Lysosomal'	}	0
{ 'GGH_7DHF1'	} { 'Gamma-Glutamyl Hydrolase (7Dhf), Lysosomal'	}	0
{ 'GLAL'	} { 'Galactosidase, Alpha'}	}	0
{ 'GLCAASE8ly'	} { 'Beta-Glucuronidase, Lysosomal'}	}	0
{ 'GLCAASE9ly'	} { 'Beta-Glucuronidase, Lysosomal'}	}	0
{ 'GLCtly'	} { 'Glucose Efflux from Lysosome'}	}	0
{ 'GLCURter'	} { 'Glucuronate Endoplasmic Reticular Transport'	}	0
{ 'GLNASNNaEx'	} { 'L-Glutamine/L-Asparagine Na-Dependent Exchange (Gln-L In)'	}	0
{ 'GLNSERNaEx'	} { 'L-Serine/L-Glutamine Na-Dependent Exchange (Gln-L In)'	}	0
{ 'GLNTHRNaEx'	} { 'L-Threonine/L-Glutamine Na-Dependent Exchange (Gln-L In)'	}	0
{ 'GLNtm'	} { 'L-Glutamine Transport via Electroneutral Transporter'	}	0
{ 'GLU5Km'	} { 'Glutamate 5-Kinase, Mitochondrial'	}	0
{ 'GLUCYS'	} { 'Gamma-Glutamylcysteine Synthetase'	}	0
{ 'GLUNm'	} { 'Glutaminase, Mitochondrial'	}	0
{ 'GLUt6'	} { 'Glutamate Transport via Na, H Symport And K Antiport'	}	0
{ 'GLUt71'	} { 'Glutamate Transport, Lysosomal'	}	0
{ 'GLUVESSEC'	} { 'L-Glutamate Secretion via Secretory Vesicle (ATP Driven)'	}	0
{ 'GLYCLTDy'	} { 'Glycolate Dehydrogenase (NADP)'	}	0
{ 'GLYOp'	} { 'Glycine Oxidase, Peroxisomal'	}	0
{ 'GLYt4'	} { 'Transport of Glycine via Sodium Symport'	}	0
{ 'GPAM_hs'	} { 'Glycerol-3-Phosphate Acyltransferase'	}	0
{ 'GTHO'	} { 'Glutathione Oxidoreductase'	}	0
{ 'GTHOm'	} { 'Glutathione Oxidoreductase'	}	0
{ 'GTHP'	} { 'Glutathione Peroxidase'	}	0
{ 'GTHPe'	} { 'Glutathione Peroxidase, Extracellular'}	}	0
{ 'GTHPm'	} { 'Glutathione Peroxidase, Mitochondria'	}	0
{ 'GTHS'	} { 'Glutathione Synthetase'	}	0
{ 'GUACYC'	} { 'Guanylate Cyclase'	}	0
{ 'GULNter'	} { 'L-Gulonate Endoplasmic Reticular Export'	}	0
{ 'H2CO3Dm'	} { 'Carboxylic Acid Dissociation'	}	0
{ 'H2O2tm'	} { 'Hydrogen Peroxide Mitochondrial Transport'	}	0
{ 'HAS1'	} { 'Hyaluronan Synthase'}	}	0
{ 'HAS2'	} { 'Hyaluronan Synthase'}	}	0
{ 'HATly'	} { 'Hyaluronan Transport, Extracellular to Lysosome'}	}	0
{ 'HISDC'	} { 'Histidine Decarboxylase'	}	0
{ 'HIST4'	} { 'L-Histidine Transport in via Sodium Symport'	}	0
{ 'HISTASE'	} { 'Histaminase'}	}	0

{ 'HISTAVESSEC'	} { 'Histamine Secretion via Secretory Vesicle (ATP Driven)'	}	0
{ 'HMGOAsi'	} { 'Hydroxymethylglutaryl Coenzyme A Synthase (Ir)'	}	0
{ 'HMGLm'	} { 'Hydroxymethylglutaryl Coenzyme A Lyase'	}	0
{ 'HMGLx'	} { 'Hydroxymethylglutaryl Coenzyme A Lyase'	}	0
{ 'HOMt4'	} { 'L-Homoserine via Sodium Symport'	}	0
{ 'HPYRRy'	} { 'Hydroxypyruvate Reductase (NADPH)'	}	0
{ 'HYPTROX'	} { 'Hypotaurine Oxidase'	}	0
{ 'ICDHxm'	} { 'Isocitrate Dehydrogenase (NAD+)'}	}	0
{ 'ICDHy'	} { 'Isocitrate Dehydrogenase (NADP)'}	}	0
{ 'KDNH'	} { '2-Keto-3Deoxy-D-Glycero-D-Galactononic Acid Phosphohydrolase'}	}	0
{ 'KYNAKGAT'	} { 'L-Kynurenine:2-Oxoglutarate Aminotransferase'	}	0
{ 'KYNATESYN'	} { '4-(2-Aminophenyl)-2, 4-Dioxobutanoate Dehydratase'}	}	0
{ 'LAPCOAL'	} { 'Lysosomal Acid Phosphorylase (CoA)'}	}	0
{ 'LCYSTCBOXL'	} { '3-Sulfoalanine Carboxy-Lyase'	}	0
{ 'LEUt4'	} { 'Transport of L-Leucine via Sodium Symport'	}	0
{ 'L_LACDcm'	} { 'L-Lactate Dehydrogenase, Cytosolic/Mitochondrial'	}	0
{ 'L_LACTcm'	} { 'Transport of L-Lactate via Diffusion, Mitochondrial'	}	0
{ 'L_LACTm'	} { 'Transport of L-Lactate, Mitochondrial'	}	0
{ 'LPASE'	} { 'Lysophospholipase'	}	0
{ 'LPS2'	} { 'Lipase'	}	0
{ 'LTA4H'	} { 'Leukotriene A-4 Hydrolase'}	}	0
{ 'LYStiDF'	} { 'Transport of L-Lysine via Diffusion'	}	0
{ 'LYStip'	} { 'Transport of L-Lysine, Peroxisomal (Irreversible)'}	}	0
{ 'MACOXO'	} { '3-Methylimidazole Acetaldehyde:NAD+ Oxidoreductase'}	}	0
{ 'MAOX'	} { 'Methylamine Oxidase'}	}	0
{ 'MDRPD'	} { '5-Methylthio-5-Deoxy-D-Ribulose 1-Phosphate Dehydratase'}	}	0
{ 'ME1m'	} { 'Malic Enzyme (NAD), Mitochondrial'	}	0
{ 'ME2'	} { 'Malic Enzyme (NADP)'}	}	0
{ 'ME2m'	} { 'Malic Enzyme (NADP), Mitochondrial'	}	0
{ 'METLEUex'	} { 'Methionine/Leucine Exchange (Met In)'}	}	0
{ 'METS'	} { 'Methionine Synthase'}	}	0
{ 'METt4'	} { 'L-Methionine Transport in via Sodium Symport'	}	0
{ 'MEVK1x'	} { 'Mevalonate Kinase (ATP)'}	}	0
{ 'MGSA'	} { 'Methylglyoxal Synthase'}	}	0
{ 'MGSA2'	} { 'Methylglyoxylate Synthase 2 (from G3P)'}	}	0
{ 'MHISOR'	} { 'N-Methylhistamine:Oxygen Oxidoreductase (Deaminating)'}	}	0
{ 'MI1345PP'	} { 'Inositol-1, 3, 4, 5-Trisphosphate 5-Phosphatase'}	}	0
{ 'MI1PS'	} { 'Myo-Inositol-1-Phosphate Synthase'}	}	0
{ 'MMSAD3m'	} { 'Methylmalonate-Semialdehyde Dehydrogenase (Malonic Semialdehyd)'}	}	0
{ 'MTAP'	} { '5'-Methylthioadenosine Phosphorylase'}	}	0
{ 'NABTNO'	} { 'N4-Acetylaminobutanal:NAD+ Oxidoreductase'}	}	0
{ 'NACASPtM'	} { 'N-Acetyl-L-Aspartate Transport (Mitochondria to Cytosol)'}	}	0
{ 'NACHEX27ly'	} { 'Beta-N-Acetylhexosaminidase, Lysosomal'}	}	0
{ 'NADHtpu'	} { 'NADH Transporter, Peroxisome'}	}	0
{ 'NADPHtru'	} { 'Transport of NADPH, Endoplasmic Reticulum'}	}	0
{ 'NADPhtxu'	} { 'Transport of NADPH, Peroxisome'}	}	0
{ 'NADPtru'	} { 'Transport of NADP, Endoplasmic Reticulum'}	}	0
{ 'NADPtxu'	} { 'Transport of NADP, Peroxisome'}	}	0
{ 'NaKt'	} { 'Na+/K+ Exchanging ATPase'}	}	0
{ 'NDP6'	} { 'Nucleoside-Diphosphatase (dCDP)'}	}	0
{ 'NDP7er'	} { 'Nucleoside-Diphosphatase (UDP), Endoplasmic Reticulum'}	}	0
{ 'NDP8'	} { 'Nucleoside-Diphosphatase (dUDP)'}	}	0
{ 'NICRNS'	} { 'Nicotinate D-Ribonucleoside Kinase'}	}	0
{ 'NMNATn'	} { 'Nicotinamide-Nucleotide Adenylyltransferase'}	}	0
{ 'NMNS'	} { 'Nicotinamide Ribotide (NMN) Synthetase'}	}	0
{ 'NORANMT'	} { 'Noradrenaline N-Methyltransferase'}	}	0
{ 'NP1'	} { 'Nucleotide Phosphatase'}	}	0
{ 'NTD2e'	} { '5'-Nucleotidase (UMP), Extracellular'}	}	0
{ 'NTD7e'	} { '5'-Nucleotidase (AMP), Extracellular'}	}	0
{ 'OCCOAtm'	} { 'Octanoyl Coenzyme A Transport, Diffusion'}	}	0
{ 'OIVD1m'	} { '2-Oxoisovalerate Dehydrogenase (Acylating)'}	}	0
{ 'ORntiDF'	} { 'Ornithine Transport via Diffusion (Extracellular to Cytosol)'}	}	0
{ 'P45027A12m'	} { '5-Beta-Cholestane-3-Alpha, 7-Alpha, 12-Alpha-Triol 27-Hydrox'}	}	0
{ 'P45027A13m'	} { '5-Beta-Cholestane-3-Alpha, 7-Alpha, 12-Alpha-Triol 27-Hydrox'}	}	0

{'P45027A15m'}	{'5-Beta-Cytochrome P450, Family 27, Subfamily A, Polypeptide '}	0
{'P45027A16m'}	{'Cytochrome P450 27'}	0
{'P45027A1m'}	{'Cytochrome P450 27'}	0
{'P450LTB4r'}	{'Cytochrome P450 Leukotriene B4'}	0
{'PAFH'}	{'Platelet-Activating Factor Acetylhydrolase'}	0
{'PAFS'}	{'Alkyl Glycerol Phosphocholine Acetyl Transferase'}	0
{'PAN4PP'}	{'Phosphatase (Pan4P)'}	0
{'PCFLOPm'}	{'Phosphatidylcholine Flippase'}	0
{'PCHOLP_hs'}	{'Choline Phosphatase'}	0
{'PCHOLPm_hs'}	{'Choline Phosphatase'}	0
{'PCREATtmddifir'}	{'Phosphocreatine Transport To/from Mitochondria via Diffusion'}	0
{'PDE1'}	{'3', 5'-Cyclic-Nucleotide Phosphodiesterase'}	0
{'PDE4'}	{'3', 5'-Cyclic-Nucleotide Phosphodiesterase'}	0
{'PEFLIPm'}	{'Phosphatidylethanolamine Flippase'}	0
{'PETOHMm_hs'}	{'Phosphatidylethanolamine N-Methyltransferase'}	0
{'PFK26'}	{'6-Phosphofructo-2-Kinase'}	0
{'PGCD'}	{'Phosphoglycerate Dehydrogenase'}	0
{'PGLer'}	{'6-Phosphogluconolactonase, Endoplasmic Reticulum'}	0
{'PHEt4'}	{'Transport of L-Phenylalanine via Sodium Symport'}	0
{'PHYQt'}	{'Transport of Phylloquinone '}	0
{'PI345P3P'}	{'Phosphatidylinositol-3, 4, 5-Trisphosphate 3-Phosphatase'}	0
{'PI345P5P'}	{'Phosphatidylinositol-3, 4, 5-Trisphosphate 5-Phosphatase'}	0
{'PI3P4K'}	{'Phosphatidylinositol 3-Phosphate 4-Kinase'}	0
{'PI3P5K'}	{'Phosphatidylinositol 3-Phosphate 5-Kinase'}	0
{'PI45P4P'}	{'Phosphatidylinositol-4, 5-Bisphosphate 4-Phosphatase'}	0
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{'PI4P3K'}	{'Phosphatidylinositol 4-Phosphate 3-Kinase'}	0
{'PI4P5K'}	{'Phosphatidylinositol 4-Phosphate 5-Kinase'}	0
{'PI4PP'}	{'Phosphatidylinositol-4-Phosphate 4-Phosphatase'}	0
{'PI5P3K'}	{'Phosphatidylinositol-5-Phosphate 3-Kinase'}	0
{'PIK5'}	{'Phosphatidylinositol 5-Kinase'}	0
{'PIPLC'}	{'Phosphatidylinositol Phospholipase C'}	0
{'PITg'}	{'Phosphate Transport, Golgi Apparatus'}	0
{'PLA2_2'}	{'Phospholipase A2'}	0
{'PMEVKx'}	{'Phosphomevalonate Kinase'}	0
{'PMI12346PH'}	{'5-Diphosphoinositol-1, 2, 3, 4, 6-Pentakisphosphate Diphosph'}	0
{'PNTOT5'}	{'Pantothenate Sodium Symporter Ii'}	0
{'PPA2'}	{'Inorganic Triphosphatase'}	0
{'PPAAer'}	{'Inorganic Diphosphatase, Endoplasmic Reticulum'}	0
{'PPAm'}	{'Inorganic Diphosphatase'}	0
{'PPAn'}	{'Inorganic Diphosphatase, Nuclear'}	0
{'PPAP'}	{'Phosphatidic Acid Phosphatase'}	0
{'PPD2CSPP'}	{'Ppd2Cspp'}	0
{'PRAGSr'}	{'Phosphoribosylglycinamide Synthase'}	0
{'PRASCS'}	{'Phosphoribosylaminoimidazolesuccinocarboxamide Synthase'}	0
{'PRDX'}	{'Peroxidase (Multiple Substrates)'}	0
{'PROt4'}	{'Na+/Proline-L Symporter'}	0
{'PSFLIPm'}	{'Phosphatidylserine Flippase'}	0
{'PTE2x'}	{'Peroxisomal Acyl Coenzyme A Thioesterase'}	0
{'PTHPS'}	{'6-Pyruvyltetrahydropterin Synthase'}	0
{'PTRCAT1'}	{'Putrescine Acetyltransferase'}	0
{'PTRCOX1'}	{'Putrescine:Oxygen Oxidoreductase (Deaminating)'}	0
{'PYRt2m'}	{'Pyruvate Mitochondrial Transport via Proton Symport'}	0
{'RDH3a'}	{'Retinol Dehydrogenase (11-Cis, NADPH)'}	0
{'SACCD3m'}	{'Saccharopine Dehydrogenase (NADP, L-Lysine Forming), Mitocho'}	0
{'SADT'}	{'Sulfate Adenylyltransferase'}	0
{'SAMHISTA'}	{'S-Adenosyl-L-Methionine:Histamine N-Tele-Methyltransferase'}	0
{'SBTD_D2'}	{'D-Sorbitol Dehydrogenase (D-Fructose Producing)'}	0
{'SBTR'}	{'D-Sorbitol Reductase'}	0
{'SERCYSNaEx'}	{'L-Serine/L-Cysteine Na-Dependent Exchange (Ser-L In)'}	0
{'SERPT'}	{'Serine C-Palmitoyltransferase'}	0
{'SERT4'}	{'L-Serine via Sodium Symport'}	0
{'SFGTH'}	{'S-Formylglutathione Hydralase'}	0
{'SMS'}	{'Sphingomyelin Synthase (Homo Sapiens)'}	0

{ 'SO4HCOTex'	} { 'Sulfate Transport via Bicarbonate Antiport'	}	0
{ 'SPODMm'	} { 'Superoxide Dismutase'	}	0
{ 'SPR'	} { 'Sepiapterin Reductase'	}	0
{ 'SPRMS'	} { 'Spermine Synthase'	}	0
{ 'SULFOX'	} { 'Sulfite Oxidase'	}	0
{ 'T4HCINNMFM'	} { '4-Hydroxycinnamate Formation'	}	0
{ 'THBPT4ACAMDASE'	} { 'Tetrahydrobiopterin-4A-Carbinolamine Dehydratase'	}	0
{ 'THD1m'	} { 'NAD (P) Transhydrogenase'	}	0
{ 'THMTP'	} { 'Thiamine-Triphosphatase'	}	0
{ 'THRALANaEx'	} { 'L-Alanine/L-Threonine Na-Dependent Exchange (Thr-L In)'	}	0
{ 'THRCYSNaEx'	} { 'L-Cysteine/L-Threonine Na-Dependent Exchange (Thr-L In)'	}	0
{ 'THRt4'	} { 'L-Threonine via Sodium Symport'	}	0
{ 'THYMDt1'	} { 'Thymd Transport'	}	0
{ 'TMDK1m'	} { 'Thymidine Kinase (ATP:Thymidine)'	}	0
{ 'TMDPPK'	} { 'Thiamine-Diphosphate Kinase'	}	0
{ 'TRDR'	} { 'Thioredoxin Reductase (NADPH)'	}	0
{ 'TRPO2'	} { 'L-Tryptophan:Oxygen 2, 3-Oxidoreductase (Decyclizing)'	}	0
{ 'TYR3MO2'	} { 'Tyrosine 3-Monooxygenase'	}	0
{ 'TYRCBOX'	} { 'L-Tyrosine Carboxy-Lyase'	}	0
{ 'UAG2EMAi'	} { 'UDP-N-Acetyl-D-Glucosamine 2-Epimerase (Hydrolysis)'	}	0
{ 'UAGALDP'	} { 'UDP-N-Acetylgalactosamine Diphosphorylase'	}	0
{ 'UDPDOLPT_L'	} { 'UDPGlucose:Dolichyl-Phosphate Beta-D-Glucosyltransferase (Li)'	}	0
{ 'UDPGD'	} { 'UDPGlucose 6-Dehydrogenase'	}	0
{ 'UDPGNP'	} { 'UDPGlucuronate Uridine-Diphosphohydrolase'	}	0
{ 'UDPGP'	} { 'UDPGlucose Pyrophosphohydrolase'	}	0
{ 'URIK1'	} { 'Uridine Kinase (ATP:Uridine)'	}	0
{ 'r0023'	} { 'NADH:Ferricytochrome-B5 Oxidoreductase'	}	0
{ 'r0047'	} { 'Adenosine 5-Monophosphate Phosphohydrolase'	}	0
{ 'r0085'	} { '2-Oxoglutaramate Amidohydrolase'	}	0
{ 'r0086'	} { '2-Oxoglutaramate Amidohydrolase'	}	0
{ 'r0119'	} { 'Guanosine 5-Triphosphate Pyrophosphohydrolase'	}	0
{ 'r0142'	} { 'Sulfite:Oxygen Oxidoreductase'	}	0
{ 'r0145'	} { 'L-Arginine, NADPH:Oxygen Oxidoreductase (Nitric-Oxide-Formin)'	}	0
{ 'r0153'	} { 'CTP:Pyruvate O2-Phototransferase'	}	0
{ 'r0156'	} { 'L-Glutamine:Pyruvate Aminotransferase'	}	0
{ 'r0157'	} { 'L-Glutamine:Pyruvate Aminotransferase'	}	0
{ 'r0160'	} { 'L-Serine:Pyruvate Aminotransferase'	}	0
{ 'r0165'	} { 'UTP:Pyruvate O2-Phototransferase'	}	0
{ 'r0166'	} { 'Uridine Triphosphate Pyrophosphohydrolase'	}	0
{ 'r0179'	} { 'Succinate-Semialdehyde:NADP+ Oxidoreductase'	}	0
{ 'r0186'	} { 'Ethanolamine-Phosphate Phospho-Lyase (Deaminating)'	}	0
{ 'r0191'	} { 'UTP:D-Fructose-6-Phosphate 1-Phototransferase'	}	0
{ 'r0280'	} { 'DATP:Pyruvate O2-Phototransferase'	}	0
{ 'r0281'	} { 'Putrescine:Oxygen Oxidoreductase (Deaminating)'	}	0
{ 'r0301'	} { 'Xanthosine-5-Phosphate:Ammonia Ligase (AMP-Forming)'	}	0
{ 'r0354'	} { 'Hexokinase'	}	0
{ 'r0357'	} { 'Hexokinase'	}	0
{ 'r0365'	} { '3-Hydroxypropanoate:NAD+ Oxidoreductase '	}	0
{ 'r0377'	} { 'ATP:Deoxycitidine 5-Phototransferase'	}	0
{ 'r0383'	} { 'Pyruvate:[Dihydrolipoyllysine-Residue Acetyltransferase]-Lip'}	}	0
{ 'r0399'	} { 'L-Phenylalanine, Tetrahydrobiopterin:Oxygen Oxidoreductase ('}	)	0
{ 'r0413'	} { 'DATP:Pyruvate O2-Phototransferase'	}	0
{ 'r0423'	} { 'Isocitrate:NADP+ Oxidoreductase (Decarboxylating)'	}	0
{ 'r0426'	} { 'Isocitrate Hydro-Lyase '	}	0
{ 'r0438'	} { 'Palmitoyl Coenzyme A:L-Carnitine O-Palmitoyltransferase'	}	0
{ 'r0451'	} { '2-Oxoacid:Lipoamide 2-Oxidoreductase (Decarboxylating And '}	)	0
{ 'r0456'	} { 'ATP:Deoxyguanosine 5-Phototransferase'	}	0
{ 'r0509'	} { 'Succinate:Ubiquinone Oxidoreductase'	}	0
{ 'r0511'	} { 'Steroyl Coenzyme A, Hydrogen-Donor:Oxygen Oxidoreductase Pol'}	)	0
{ 'r0555'	} { 'Acetyl Coenzyme A:Enzyme N6- (Dihydrolipoyl)Lysine S-Acetyl'}	)	0
{ 'r0557'	} { 'Glutaryl Coenzyme A:Dihydrolipoamide S-Succinyltransferase L'}	)	0
{ 'r0568'	} { '(5-L-Glutamyl)-L-Amino-Acid 5-Glutamyltransferase (Cyclizin)'}	)	0
{ 'r0578'	} { 'ATP:Pantothenate 4-Phototransferase'	)	0
{ 'r0594'	} { 'L-2-Aminoacid:6-Semialdehyde:NAD+ 6-Oxidoreductase Lysine'}	)	0

{'r0596'}	{'3-Hydroxyisobutyryl Coenzyme A Hydrolase'}	}	0
{'r0655'}	{'3-Methylbutanoyl Coenzyme A: (Acceptor) 2, 3-Oxidoreductase'}	}	0
{'r0666'}	{'2- (Formamido)-N1- (5-Phosphoribosyl)Acetamidine Cyclo-Ligase'}	}	0
{'r0698'}	{'Propanoyl Coenzyme A:Acetyl Coenzyme A C-Acyltransferase Bil'}	}	0
{'r0853'}	{'Facilitated Diffusion'}	}	0
{'r0924'}	{'ATP-Binding Cassette (ABC) Tcdb:3.A.1.204.5'}	}	0
{'r0986'}	{'Vesicular Transport'}	}	0
{'r1002'}	{'Facilitated Diffusion'}	}	0
{'r1078'}	{'Vesicular Transport'}	}	0
{'r1109'}	{'Citrate Oxaloacetate-Lyase ( (Pro-3S)-Ch2Coo- ->Acetate)'}	}	0
{'r1150'}	{'Facilitated Diffusion'}	}	0
{'r1164'}	{'Sterol O-Acyltransferase'}	}	0
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{'r1179'}	{'Sterol Esterase'}	}	0
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{'r1183'}	{'Sterol Esterase'}	}	0
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{'r1254'}	{'Long-Chain-Fatty-Acid---Coa Ligase'}	}	0
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{'r1298'}	{'Vesicular Transport'}	}	0
{'r1299'}	{'Vesicular Transport'}	}	0
{'r1382'}	{'Folylpolyglutamyl Synthetase'}	}	0
{'r1383'}	{'Gamma-Glutamyl Hydrolase'}	}	0
{'r1423'}	{'Facilitated Diffusion'}	}	0
{'r1434'}	{'Transport Reaction'}	}	0
{'r1435'}	{'Transport Reaction'}	}	0
{'r1455'}	{'Transport Reaction'}	}	0
{'r1493'}	{'Utilized Transport'}	}	0
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{'r1515'}	{'ATP-Binding Cassette (ABC) Tcdb:3.A.1.211.1'}	}	0
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{'r1530'}	{'ATP-Binding Cassette (ABC) Tcdb:3.A.1.208.15'}	}	0
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{'r2419'}	{'Mitochondrial Carrier (Mc) Tcdb:2.A.29.2.7'}	}	0
{'r2471'}	{'Major Facilitator (Mfs) Tcdb:2.A.18.8.1'}	}	0
{'r2473'}	{'Major Facilitator (Mfs) Tcdb:2.A.1.4.5'}	}	0
{'r2512'}	{'Utilized Transport'}	}	0
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{'RE1836X'} } {'Propionyl Coenzyme A C2-Trimethyltridecanoyltransferase'} } 0
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{'RE2717L'} } {'Galactosylceramidase'} } 0
{'RE2985M'} } {'Acyl Coenzyme A Oxidase'} } 0
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{'RE3095C'} } {'Peroxidase'} } 0
{'RE3201C'} } {'Tyrosinase'} } 0
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{'RE3346M'} } {'Aldehyde Dehydrogenase (NAD+)' } } 0
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{'RE3525R'} } {'Arachidonate 12-Lipoxygenase'} } 0
{'RE3624M'} } {'Acyl Coenzyme A Oxidase'} } 0
{'RE3637C'} } {'RE3637C'} } 0
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{'FAOXC16C14m'} } {'Fatty Acid Beta Oxidation (C16->C14), Mitochondrial'} } 0
{'FAOXC4C2m'} } {'Fatty Acid Beta Oxidation (C4->C2), Mitochondrial'} } 0
{'FAOXC5C50Hm'} } {'Fatty Acid Beta Oxidation (C5->C50h), Mitochondrial'} } 0
{'FAOXC6C4m'} } {'Fatty Acid Beta Oxidation (C6->C4), Mitochondrial'} } 0
{'FAOXC8C6m'} } {'Fatty Acid Beta Oxidation (C8->C6), Mitochondrial'} } 0
{'HEXCOAACBP'} } {'Transport of Hexanoyl Coenzyme A (N-C6:0CoA) from Mitochondr'} } 0
{'PRISTCOAtcx'} } {'Transport of Pristanoylcoa from Cytosol to Peroxisomes.' } 0
{'SCP21cx'} } {'Transport of Phytanoylcoa from Cytosol to Peroxisomes.' } 0
{'SUCCACT'} } {'Activation of Succinate'} } 0
{'TDCRNe'} } {'Transport of Myristoyl Carnitine into Extra Cellular Space'} } 0
{'34DHPHELAT1tc'} } {'Transport of 3, 4-Dihydroxy-L-Phenylalanine by Lat1 in Assoc'} } 0
{'ASCBSVCTtc'} } {'Transport of L-Ascorbate by Svct1 Or Svct2 Transporter'} } 0
{'FOLTle'} } {'Transport of Folate'} } 0
{'GLNyLATthc'} } {'Transport of Glutamine by Y+Lat1 Or Y+Lat2 with Symporter of'} } 0
{'HISyLATtc'} } {'Transport of L-Histidine by Y+Lat1 Or Y+Lat2 Transporters'} } 0
{'LEUyLAThtc'} } {'Transport of Leucine by Y+Lat1 Or Y+Lat2 with Symporter of H'} } 0
{'LINOFATPtc'} } {'Uptake of Linoleic Acid'} } 0
{'PALFATPtc'} } {'Transport of Hexadecanoate'} } 0
{'PNTORDe'} } {'Release of Pantothenate'} } 0
{'TAUPAT1c'} } {'Transport of Taurine by Pat1'} } 0
{'VITKtl'} } {'Transport of Vitamin K into Lymph'} } 0
{'4HPROLTASCT1'} } {'Transport of Hydroxy-Proline '} } 0
{'ASPPROASCT1'} } {'Aspartate Intake by System Asct-1 Transporter'} } 0
{'CHOLESACATc'} } {'Esterification of Cholesterol to Cholesterol Ester'} } 0
{'DPMVdc'} } {'Diphosphomevalonate Decarboxylase, Cytosol'} } 0
{'FADH2ETC'} } {'Complex Ii Reaction for Respiratory Chain'} } 0
{'G6PDH2c'} } {'Glucose 6-Phosphate Dehydrogenase'} } 0

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printConstraints(model,-1e4,1e4,~model.SIntRxnBool)
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{'EX_3mlda[e]'} }	{'Exchange of 3-Methylimidazoleacetic Acid '}	0	1000
{'EX_adrnl[e]'} }	{'Exchange of Adrenaline '}	0	1000
{'EX_amp[e]'} }	{'Exchange of AMP '}	0	1000
{'EX_creat[e]'} }	{'Exchange of Creatine '}	0	1000
{'EX_dag_hs[e]'} }	{'Exchange of Diglyceride'}	0	1000
{'EX_gsn[e]'} }	{'Exchange of Guanosine'}	0	1000
{'EX_gthox[e]'} }	{'Exchange of Oxidized Glutathione '}	0	1000
{'EX_histal[e]'} }	{'Exchange of Histamine '}	0	1000
{'EX_imp[e]'} }	{'Exchange of IMP '}	0	1000
{'EX_leuktrB4[e]'} }	{'Exchange of Leukotriene B4 '}	0	1000

{'EX_mag_hs[e]'	{'Exchange of Monoacylglycerol 2 (Homo Sapiens) '}	0
{'EX_no[e]'	{'Exchange of Nitric Oxide'}	0
{'EX_nrpphr[e]'	{'Exchange of Norepinephrine '}	0
{'EX_xolest2_hs[e]'	{'Exchange of Cholesterol Ester (from FullR2) '}	0
{'EX_4abutn[e]'	{'Exchange of 4-Ammoniobutanal'}	0
{'EX_fad[e]'	{'Exchange of Flavin Adenine Dinucleotide Oxidized'}	0
{'EX_fald[e]'	{'Exchange of Formaldehyde'}	0
{'EX_HC02213[e]'	{'Exchange of Prostaglandin-E3 '}	0
{'EX_4hpro[e]'	{'Exchange of Hydroxy Proline'}	0
{'EX_leuleu[e]'	{'Exchange of Leucylleucine'}	0
{'EX_34hpp[e]'	{'Exchange of 3- (4-Hydroxyphenyl)Pyruvate'}	0
{'EX_3mob[e]'	{'Exchange of 3-Methyl-2-Oxobutanoate'}	0
{'EX_3mop[e]'	{'Exchange of 3-Methyl-2-Oxopentanoate'}	0
{'EX_4mop[e]'	{'Exchange of 4-Methyl-2-Oxopentanoate'}	0
{'EX_5mta[e]'	{'Exchange of 5-S-Methyl-5-Thioadenosine'}	0
{'EX_5oxpro[e]'	{'Exchange of 5-Oxoprolinate'}	0
{'EX_ahcys[e]'	{'Exchange of S-Adenosyl-L-Homocysteine'}	0
{'EX_cbasp[e]'	{'Exchange of N-Carbamoyl-L-Aspartate'}	0
{'EX_crtn[e]'	{'Exchange of Creatinine'}	0
{'EX_cyst_L[e]'	{'Exchange of L-Cystathionine'}	0
{'EX_ethamp[e]'	{'Exchange of Ethanolamine Phosphate'}	0
{'EX_gudac[e]'	{'Exchange of Guanidinoacetic Acid'}	0
{'EX_kynate[e]'	{'Exchange of Kynurenic Acid'}	0
{'EX_xmp[e]'	{'Exchange of Xanthyllic Acid'}	0
{'EX_argsuc[e]'	{'Exchange of L-Arginosuccinic Acid'}	0
{'EX_3mtp[e]'	{'Exchange of 3-Methyl-Thio-Propionate'}	0
{'EX_34hpl[e]'	{'Exchange of 3- (4-Hydroxyphenyl)Lactate'}	0
{'EX_4aabutn[e]'	{'Exchange of 4-Acetamidobutanoate'}	0
{'EX_aclys[e]'	{'Exchange of Acetyl-Lysine'}	0
{'EX_C02712[e]'	{'Exchange of N-Acetylmethionine'}	0
{'EX_C04805[e]'	{'Exchange of 5(S)-HETE'}	0
{'EX_leuktrB4wcooh[e]'	{'Exchange of W-Carboxy Leukotriene B4'}	0
{'EX_Lpipecol[e]'	{'Exchange of L-Pipecolic Acid'}	0
{'EX_magole_hs[e]'	{'Exchange of 1-Oleoylglycerol'}	0
{'EX_milp_D[e]'	{'Exchange of Myo-Inositol 1-Phosphate'}	0
{'EX_urcan[e]'	{'Exchange of Urocanate'}	0
{'EX_dhbpt[e]'	{'Exchange of 6,7-Dihydrobiopterin'}	0
{'EX_thbpt[e]'	{'Exchange of 5,6,7,8-Tetrahydrobiopterin'}	0
{'EX_argglygly[e]'	{'Exchange of ArgGlyGly'}	0
{'EX_gluleu[e]'	{'Exchange of GluLeu'}	0
{'EX_hisglylys[e]'	{'Exchange of HisGlyLys'}	0
{'EX_leuleutrp[e]'	{'Exchange of LeuLeuTrp'}	0
{'EX_leuval[e]'	{'Exchange of LeuVal'}	0
{'EX_lysvaltrp[e]'	{'Exchange of LysValTrp'}	0
{'EX_phetrpleu[e]'	{'Exchange of PheTrpLeu'}	0
{'EX_trpglyleu[e]'	{'Exchange of TrpGlyLeu'}	0
{'EX_trpglyval[e]'	{'Exchange of TrpGlyVal'}	0
{'EX_homoval[e]'	{'Exchange of Homovanillate'}	0
{'EX_acgal[e]'	{'Exchange of N-Acetylgalactosamine '}	0
{'EX_acnam[e]'	{'Exchange of N-Acetylneuraminate '}	0
{'EX_pccreat[e]'	{'Exchange of Phosphocreatine'}	0
{'EX_2obut[e]'	{'Exchange of 2-Oxobutanoate'}	0
{'EX_glcn[e]'	{'Exchange of D-Gluconate'}	0
{'EX_adn[e]'	{'Exchange of Adenosine'}	0
{'EX_cgly[e]'	{'Exchange of Cysteinyl-Glycine '}	0
{'EX_co2[e]'	{'Exchange of Carbon Dioxide '}	0
{'EX_cytd[e]'	{'Exchange of Cytidine'}	0
{'EX_glypro[e]'	{'Exchange of Glypro'}	0
{'EX_ppi[e]'	{'Exchange of Ppi'}	0
{'EX_for[e]'	{'Exchange of Formate '}	0
{'EX_ac[e]'	{'Exchange of Acetate '}	0
{'EX_fru[e]'	{'Exchange of D-Fructose'}	0
{'EX_glcur[e]'	{'Exchange of D-Glucuronate '}	0
{'EX_xan[e]'	{'Exchange of Xanthine '}	0

{'EX_xy1_D[e]'	{'Exchange of D-Xylose '}	0	10
{'EX_4hbz[e]'	{'Exchange of 4-Hydroxybenzoate'}	0	10
{'EX_3mox4hoxm[e]'	{'Exchange of 3-Methoxy-4-Hydroxymandelate'}	0	10
{'EX_2h3mv[e]'	{'Exchange of 2-Hydroxy-3-Methyl-Valerate'}	0	10
{'EX_2hiv[e]'	{'Exchange of 2-Hydroxy-Isovalerate'}	0	10
{'EX_2m3hbu[e]'	{'Exchange of 2-Methyl-3-Hydroxy-Butyrate'}	0	10
{'EX_2m3hvac[e]'	{'Exchange of 2-Methyl-3-Hydroxy-Valerate'}	0	10
{'EX_3h3mglt[e]'	{'Exchange of 3-Hydroxy-3-Methyl-Glutarate'}	0	10
{'EX_3mglutac[e]'	{'Exchange of 3-Methyl-Glutaconate'}	0	10
{'EX_mvvlac[e]'	{'Exchange of Mevalonate-Lactone'}	0	10
{'EX_3ohglutac[e]'	{'Excahnge of 3-Hydroxy-Glutarate'}	0	10
{'EX_glutcon[e]'	{'Exchange of Glutaconate'}	0	10
{'EX_sql[e]'	{'Exchange of Squalene'}	0	10
{'EX_HC02020[e]'	{'Exchange of Cholesterol-Ester-Palm'}	0	10
{'EX_xol124oh[e]'	{'Exchange of (24S)-24-Hydroxycholesterol'}	0	10
{'EX_xol127oh[e]'	{'Exchange of 26-Hydroxycholesterol'}	0	10
{'EX_34dhoxmnd[e]'	{'Exchange of 3,4-Dihydroxymandelate'}	0	10
{'EX_C05767[e]'	{'Exchange of Uroporphyrin I'}	0	10
{'EX_C05770[e]'	{'Exchange of Coproporphyrin Iii'}	0	10
{'EX_mhista[e]'	{'Exchange of N(Tele)-Methylhistaminium'}	0	10
{'EX_ppbng[e]'	{'Exchange of Porphobilinogen'}	0	10
{'EX_ametam[e]'	{'Exchange of S-Adenosylmethioninamine'}	0	10
{'EX_xylu_D[e]'	{'Exchange of Xylu_D'}	0	10
{'EX_sphings[e]'	{'Exchange of Sphingosine'}	0	10
{'EX_im4ac[e]'	{'Exchange of Imidazol-4-Ylacetate'}	0	10
{'EX_mlthf[e]'	{'Exchange of 5,10-Methylenetetrahydrofolate'}	0	10
{'EX_CE2705[e]'	{'Exchange of Quinonoid Dihydrobiopterin'}	0	10
{'EX_fdp[e]'	{'Exchange of D-Fructose 1,6-Bisphosphate'}	0	10
{'EX_34dhpe[c]'	{'Exchange of 3, 4-Dihydroxyphenylethanol '}	0	10
{'EX_pail_hs[e]'	{'Exchange of 1-Phosphatidyl-1D-Myo-Inositol'}	0	10
{'EX_caproic[e]'	{'Exchange for Caproic Acid'}	0	10
{'EX_M01966[e]'	{'Exchange for D-Glucose 1,6-Bisphosphate'}	0	10
{'EX_kdn[e]'	{'Exchange for 2-Keto-3-Deoxy-D-Glycero-D-Galactononic Acid'}	0	10
{'DM_CE5026[c]'	{'Demand for 5-S-Glutathionyl-L-Dopa'}	0	10
{'DM_CE1261[c]'	{'Demand for 5-S-Cysteinyldopa'}	0	10
{'DM_4glu56dihdind[c]'	{'Demand for 4-S-Glutathionyl-5,6-Dihydroxyindoline'}	0	10
{'DM_CE1562[c]'	{'Demand for 5,6-Indolequinone-2-Carboxylate'}	0	10
{'DM_ind56qn[c]'	{'Demand for Indole-5,6-Quinone'}	0	10
{'DM_5cysdopa[c]'	{'Demand for 5-S-Cysteinyldopamine'}	0	10
{'DM_CE5025[c]'	{'Demand for 5-S-Glutathionyl-Dopamine'}	0	10
{'DM_CE4888[c]'	{'Demand for Dopaminochrome'}	0	10

### Reverse Reaction, 0 bound

<b>Name</b>	<b>lb</b>	<b>ub</b>	<b>equation</b>
{ 'Exchange of L-Lysine '	-100.23	0	{'lys_L[e] <=> '}
{ 'Exchange of L-Methionine '	-1.8909	0	{'met_L[e] <=> '}
{ 'Exchange of Oxugen'	-1516.9	0	{'o2[e] <=> '}
{ 'Exchange of L-Histidine'	-27.05	0	{'his_L[e] <=> '}
{ 'Exchange of L-Threonine '	-96.44	0	{'thr_L[e] <=> '}
{ 'Exchange of L-Phenylalanine'}	-47.547	0	{'phe_L[e] <=> '}
{ 'Exchange of L-Tryptophan '	-0.83573	0	{'trp_L[e] <=> '}

### Forward\_Reaction, non-0 bound

Name	1b
{ 'Exchange of 2-Hydroxybutyrate '	0.032705
{ 'Transport of (R)-3-Hydroxybutanoate via H+ Symport'	0.053865
{ 'Exchange of 3-Hydroxypropionate'	0.02363
{ 'Exchange of N-Acetyl-L-Aspartate'	0.32205
{ 'Exchange of D-Glycerate'	0.28767
{ 'Exchange of Glycolate'	0.10791
{ 'Exchange of 2-Oxoglutarate '	0.1022
{ 'Exchange of L-Asparagine'	0.48669

{'EX_fum[e]'} }	{'Exchange of Fumarate'}	}	0.06551
{'EX_lac_L[e]'} }	{'Exchange of L-Lactate'}	}	196.46
{'EX_mal_L[e]'} }	{'Exchange of L-Malate'}	}	0.054241
{'EX_orn[e]'} }	{'Exchange of Ornithine'}	}	25.366
{'EX_pro_L[e]'} }	{'Exchange of L-Proline'}	}	0.96137
{'EX_ser_L[e]'} }	{'Exchange of L-Serine'}	}	2.79
{'EX_succ[e]'} }	{'Exchange of Succinate'}	}	0.15368
{'EX_ala_L[e]'} }	{'Exchange of L-Alanine'}	}	8.6953
{'EX_cit[e]'} }	{'Exchange of Citrate'}	}	0.254
{'EX_ura[e]'} }	{'Exchange of Uracil'}	}	0.0070234
{'EX_taur[e]'} }	{'Exchange of Taurine'}	}	0.0022509
{'EX_actyrl[e]'} }	{'Exchange of N-Acetyl-Tyrosine'}	}	0.00018472
{'EX_3hivac[e]'} }	{'Exchange of 3-Hydroxy-Isovalerate'}	}	0.92259

#### Reverse\_Reaction, non-0 bound

Reverse_Reaction	Name	lb	ub
{'EX_acglu[e]'} }	{'Exchange of N-Acetyl-L-Glutamate'}	-0.27082	-0.18228
{'EX_ille_L[e]'} }	{'Exchange of L-Isoleucine'}	-19.49	-8.4975
{'EX_leu_L[e]'} }	{'Exchange of L-Leucine'}	-18.323	-8.3021
{'EX_val_L[e]'} }	{'Exchange of L-Valine'}	-11.719	-2.6654
{'EX_gly[e]'} }	{'Exchange of Glycine'}	-25.654	-14.496
{'EX_cys_L[e]'} }	{'Exchange of L-Cysteine'}	-1.6574	-0.57181
{'EX_gln_L[e]'} }	{'Exchange of L-Glutamine'}	-60.556	-3.9021
{'EX_arg_L[e]'} }	{'Exchange of L-Arginine'}	-6.0387	-1.8685
{'EX_etha[e]'} }	{'Exchange of Ethanolamine'}	-0.56504	-0.35439
{'EX_glc_D[e]'} }	{'Exchange of D-Glucose'}	-298.95	-126.74

#### Reversible\_Reaction

Reversible_Reaction	Name	lb
{'EX_34dhphe[e]'} }	{'Exchange of 3, 4-Dihydroxy-L-Phenylalanine'}	-1
{'EX_ala_B[e]'} }	{'Exchange of Beta-Alanine'}	-0.1
{'EX_arachd[e]'} }	{'Exchange of Nc20:4'}	-1
{'EX_atp[e]'} }	{'Exchange of ATP'}	-1
{'EX_chol[e]'} }	{'Exchange of Choline'}	-7.
{'EX_chsterol[e]'} }	{'Exchange of Cholesterol'}	-1
{'EX_dopa[e]'} }	{'Exchange of Dopamine'}	-1
{'EX_dopasf[e]'} }	{'Exchange of Dopamine 3-O-Sulfate'}	-1
{'EX_gthrd[e]'} }	{'Exchange of Reduced Glutathione'}	-0.2
{'EX_h2o2[e]'} }	{'Exchange of Hydrogen Peroxide'}	-1
{'EX_hco3[e]'} }	{'Exchange of Bicarbonate'}	-42
{'EX_inost[e]'} }	{'Exchange of Myo-Inositol'}	-8.
{'EX_Lcystin[e]'} }	{'Exchange of L-Cystine'}	-7.
{'EX_lneldc[e]'} }	{'Exchange of Linoelaidic Acid'}	-1
{'EX_lnlc[e]'} }	{'Exchange of Linoleic Acid (All Cis C18:2)'}	-0.01
{'EX_lnlncg[e]'} }	{'Exchange of Gamma-Linolenic Acid'}	-1
{'EX_octa[e]'} }	{'Exchange of Octanoate (N-C8:0)'}	-0.03
{'EX_strdnc[e]'} }	{'Exchange of Stearidonic Acid'}	-1
{'EX_citr_L[e]'} }	{'Exchange of L-Citrulline'}	-0.001
{'EX_Lkynr[e]'} }	{'Exchange of L-Kynurenine'}	-0.0009
{'EX_CE2028[e]'} }	{'Exchange of Beta-Hydroxy-Beta-Methylbutyrate'}	-1
{'EX_acile_L[e]'} }	{'Exchange of Acetyl Isoleucine'}	-0.009
{'EX_acleu_L[e]'} }	{'Exchange of Acetyl Leucine'}	-0.007
{'EX_asp_L[e]'} }	{'Exchange of L-Aspartate'}	-3.
{'EX_gal[e]'} }	{'Exchange of D-Galactose'}	-1
{'EX_glu_L[e]'} }	{'Exchange of L-Glutamate'}	-3.
{'EX_h[e]'} }	{'Exchange of Proton'}	-1
{'EX_h2o[e]'} }	{'Exchange of Water'}	-1
{'EX_pile[e]'} }	{'Exchange of Phosphate'}	-14
{'EX_ribflv[e]'} }	{'Exchange of Riboflavin'}	-0.1
{'EX_so4[e]'} }	{'Exchange of Sulfate'}	-31
{'EX_thymd[e]'} }	{'Exchange of Thymidine'}	-0.
{'EX_tyrr_L[e]'} }	{'Exchange of L-Tyrosine'}	-5.

{'EX_nh4[e]'	{'Exchange of Ammonia '}	}	-0.0001
{'EX_fol[e]'	{'Exchange of Folate'}	}	-1.
{'EX_ptrc[e]'	{'Exchange of 1, 4-Butanediammonium'}	}	-0.1
{'EX_34dphfa[e]'	{'Exchange of 34Dphfa'}	}	-1
{'EX_pyr[e]'	{'Exchange of Pyruvate '}	}	-0.7
{'EX_4abut[e]'	{'Exchange of 4-Aminobutanoate '}	}	-0.0002
{'EX_C09642[e]'	{'Exchange of (-)-Salsolinol'}	}	-1
{'EX_dopa4sf[e]'	{'Exchange of Dopamine 4-O-Sulfate '}	}	-1
{'EX_dopa4glcur[e]'	{'Exchange of Dopamine 4-O-Glucuronide '}	}	-1
{'EX_dopa3glcur[e]'	{'Exchange of Dopamine 3-O-Glucuronide '}	}	-1
{'EX_4glu56dihdind[e]'	{'Exchange of 4-S-Glutathionyl-5, 6-Dihydroxyindoline '}	}	-1
{'EX_5cysdopa[e]'	{'Exchange of 5-S-Cysteinyl-dopamine '}	}	-1
{'EX_CE5025[e]'	{'Exchange of 5-S-Glutathionyl-Dopamine '}	}	-1
{'EX_CE5629[e]'	{'Exchange of 6, 7-Dihydroxy-1, 2, 3, 4-Tetrahydroisoquinoline'}	}	-1
{'EX_CE5026[e]'	{'Exchange of 5-S-Glutathionyl-L-Dopa'}	}	-1
{'EX_CE1261[e]'	{'Exchange of 5-S-Cysteinyl-dopa'}	}	-1
{'EX_CE1554[e]'	{'Exchange of Acetyl-Alanine'}	}	-1
{'DM_ps_hs[c]'	{'Phosphatidylserine demand'}	}	-1

```
printCouplingConstraints(model,1);
```

### coupledRxnId

### constraints

{'Phosphatidylcholine'}	{'PCHOLP_hs + PLA2_2 + SMS >= 2.025'}
{'Adenosine Monophosphate'}	{'AMPDA + NTD7 >= 0.2265'}
{'Glutamate'}	{'- ALATA_L + GLUCYS + GLUDxm + GLUDym - ASPTA - ILETA - LEUTA - VALTA'}
{'Aspartate'}	{'ARGSS + ASPTA >= 1.1925'}
{'Serine'}	{'GHMT2r + r0060 >= 0.8625'}
{'Arginine'}	{'GLYAMDTRc + r0145 >= 0.7245'}
{'Tyrrosine'}	{'TYR3MO2 + TYRTA + HMR_6728 + HMR_6874 >= 0.55875'}
{'Histidine'}	{'HISDC + HISD >= 1.095'}
{'Leucine + Isoleucine'}	{'ILETA + LEUTA >= 1.305'}
{'Valine + Methionine'}	{'METAT + VALTA >= 0.705'}
{'Glycine'}	{'GTHS - GHMT2r >= 0.7725'}

Set the data parameters for the entropic flux balance analysis problem

Linear optimisation direction

```
model.osenseStr = 'min';
```

Reaction parameters

```
model.cf=0.1;
model.cr=0.1;
model.g=2;
if 0
    quad = zeros(size(model.S,2),1);
    quad(~model.SIntRxnBool)=1;
    model.Q=diag(quad);
end
```

## Reaction parameters

Setting the bounds on reaction direction is important, because certain bounds may be incompatible with the existence of a thermodynamically feasible steady state

```
param.internalNetFluxBounds = 'original' maintains direction and magnitude of internal net flux from model.lb & model.ub
```

```
param.internalNetFluxBounds = 'directional' maintains direction of internal net flux from model.lb & model.ub but not magnitude
```

```
param.internalNetFluxBounds = 'none' removes lower and upper bounds on internal net flux
```

```
param.internalNetFluxBounds = 'random' random internal net flux direction, replacing constraints from model.lb & model.ub
```

```
param.internalNetFluxBounds='directional';
%param.internalNetFluxBounds='original';
%param.internalNetFluxBounds='none';
```

Maximum permitted internal flux

```
param.maxUnidirectionalFlux=100;
%model.vfl = [0;0;0]
```

## Method parameters

```
param.method='fluxes';
%param.method='fluxConc'; %param.method='fluxConcNorm';
```

## Metabolite parameters (only relevant if a concentration method chosen)

Standard chemical potential

```
model.u0 = ones(1,size(model.S,1))*0;
```

Strictly positive weight on concentration entropy maximisation

```
model.f=1;
```

Scalar maximum permitted metabolite concentration

```
param.maxConc=1;
```

## Solver parameters

Set the solver

```
%param.solver='pdco';
param.solver='mosek';
```

Minimum permitted internal flux required for exponential cone reformulation

```

if strcmp(param.solver, 'mosek')
    param.minUnidirectionalFlux=0;
end

```

## Tolerances

```
param.feasTol=1e-7;
```

## Printing level

```
param.printLevel=2;
param.debug = 1;
```

## Entropic flux balance analysis

```
[solution,modelOut] = entropicFluxBalanceAnalysis(model,param);
```

Using directional internal net flux bounds only.  
 Using existing external net flux bounds without modification.

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 Platform: Linux/64-X86

MOSEK Version 10.2.5 (Build date: 2024-9-17 12:12:35)  
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 Platform: Linux/64-X86

Problem  
 Name :  
 Objective sense : minimize  
 Type : LO (linear optimization problem)  
 Constraints : 2965  
 Affine conic cons. : 0  
 Disjunctive cons. : 0  
 Cones : 0  
 Scalar variables : 3625  
 Matrix variables : 0  
 Integer variables : 0

Optimizer started.  
 Presolve started.  
 Eliminator started.  
 Freed constraints in eliminator : 1219  
 Eliminator terminated.  
 Linear dependency checker started.  
 Linear dependency checker terminated.  
 Eliminator started.  
 Freed constraints in eliminator : 141  
 Eliminator terminated.  
 Eliminator - tries : 2 time : 0.00  
 Lin. dep. - tries : 1 time : 0.00  
 Lin. dep. - primal attempts : 1 successes : 1  
 Lin. dep. - dual attempts : 0 successes : 0  
 Lin. dep. - primal deps. : 9 dual deps. : 0  
 Presolve terminated. Time: 0.02  
 Optimizer - threads : 18  
 Optimizer - solved problem : the primal

```

Optimizer - Constraints : 512
Optimizer - Cones : 0
Optimizer - Scalar variables : 1700
Optimizer - Semi-definite variables: 0
Factor - setup time : 0.01
Factor - dense det. time : 0.00
Factor - nonzeros before factor : 5040
Factor - dense dim. : 1
ITE PFEAS DFEAS GFEAS PRSTATUS POBJ DOBJ MU TIME
0 8.1e+03 1.2e+03 2.7e+04 0.00e+00 2.524651910e+04 -1.187509009e+03 1.3e+02 0.03
1 3.5e+03 5.6e-01 1.1e+04 1.01e+00 9.340150454e+03 2.546036924e+03 5.5e+01 0.05
2 1.6e+03 2.6e-01 5.4e+03 1.21e+00 5.103765843e+03 2.145030639e+03 2.6e+01 0.05
3 6.0e+02 9.6e-02 2.0e+03 1.12e+00 2.290895208e+03 1.257801880e+03 9.4e+00 0.06
4 1.2e+02 1.9e-02 3.8e+02 1.05e+00 6.891441803e+02 4.922303657e+02 1.8e+00 0.06
5 4.0e+01 6.4e-03 1.3e+02 1.02e+00 4.330729771e+02 3.656226850e+02 6.3e-01 0.06
6 5.4e+00 8.8e-04 1.8e+01 1.02e+00 3.116637492e+02 3.025822720e+02 8.6e-02 0.06
7 1.8e+00 2.9e-04 5.9e+00 1.01e+00 2.971165650e+02 2.941345150e+02 2.8e-02 0.06
8 4.7e-01 7.6e-05 1.5e+00 1.00e+00 2.918325929e+02 2.910515001e+02 7.4e-03 0.07
9 3.4e-02 5.4e-06 1.1e-01 1.00e+00 2.900752738e+02 2.900195527e+02 5.3e-04 0.07
10 1.5e-02 2.5e-06 5.1e-02 9.93e-01 2.899968569e+02 2.899711094e+02 2.4e-04 0.07
11 9.4e-04 1.5e-07 3.1e-03 9.98e-01 2.899355375e+02 2.899339714e+02 1.5e-05 0.07
12 1.6e-05 2.6e-09 5.3e-05 1.00e+00 2.899307214e+02 2.899306947e+02 2.5e-07 0.08
13 1.1e-07 1.8e-11 3.7e-07 1.00e+00 2.899306171e+02 2.899306169e+02 1.7e-09 0.08
14 2.8e-08 1.2e-11 3.3e-08 1.00e+00 2.899306168e+02 2.899306168e+02 1.8e-13 0.08
Basis identification started.
Primal basis identification phase started.
Primal basis identification phase terminated. Time: 0.00
Dual basis identification phase started.
Dual basis identification phase terminated. Time: 0.00
Basis identification terminated. Time: 0.00
Optimizer terminated. Time: 0.09

```

#### Interior-point solution summary

```

Problem status : PRIMAL_AND_DUAL_FEASIBLE
Solution status : OPTIMAL
Primal. obj: 2.8993061675e+02    nrm: 2e+02    Viol. con: 1e-07    var: 3e-09
Dual.   obj: 2.8993061677e+02    nrm: 5e+00    Viol. con: 0e+00    var: 6e-12

```

#### Basic solution summary

```

Problem status : PRIMAL_AND_DUAL_FEASIBLE
Solution status : OPTIMAL
Primal. obj: 2.8993061677e+02    nrm: 2e+02    Viol. con: 7e-13    var: 1e-14
Dual.   obj: 2.8993061677e+02    nrm: 7e+00    Viol. con: 2e-14    var: 8e-10

```

#### Optimizer summary

Optimizer	-	time: 0.09
Interior-point	- iterations : 14	time: 0.09
Basis identification	-	time: 0.00
Primal	- iterations : 37	time: 0.00
Dual	- iterations : 95	time: 0.00
Clean primal	- iterations : 0	time: 0.00
Clean dual	- iterations : 0	time: 0.00
Simplex	-	time: 0.00
Primal simplex	- iterations : 0	time: 0.00
Dual simplex	- iterations : 0	time: 0.00
Mixed integer	- relaxations: 0	time: 0.00

solveCobraEP: LP part of EPproblem is feasible according to solveCobraLP with mosek.

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Problem

Name	:
Objective sense	: minimize
Type	: CONIC (conic optimization problem)
Constraints	: 2965
Affine conic cons.	: 3420 (10260 rows)
Disjunctive cons.	: 0
Cones	: 0
Scalar variables	: 7046
Matrix variables	: 0
Integer variables	: 0

Optimizer started.

Presolve started.

Linear dependency checker started.

Linear dependency checker terminated.

Eliminator started.

Freed constraints in eliminator : 0

Eliminator terminated.

Eliminator - tries	:	1	time	:	0.00
Lin. dep. - tries	:	1	time	:	0.00
Lin. dep. - primal attempts	:	1	successes	:	1
Lin. dep. - dual attempts	:	0	successes	:	0
Lin. dep. - primal deps.	:	25	dual deps.	:	0

Presolve terminated. Time: 0.03

Optimizer - threads	:	18			
Optimizer - solved problem	:	the primal			
Optimizer - Constraints	:	1960			
Optimizer - Cones	:	3420			
Optimizer - Scalar variables	:	11264	conic	:	10260
Optimizer - Semi-definite variables	:	0	scalarized	:	0
Factor - setup time	:	0.02			
Factor - dense det. time	:	0.00	GP order time	:	0.00
Factor - nonzeros before factor	:	1.19e+04	after factor	:	2.06e+04
Factor - dense dim.	:	0	flops	:	7.95e+05

ITE	PFEAS	DFEAS	GFEAS	PRSTATUS	POBJ	DOBJ	MU	TIME
0	1.0e+04	1.2e+00	1.0e+04	0.00e+00	5.937759534e+03	-4.414972768e+03	1.0e+00	0.06
1	7.8e+03	9.2e-01	9.2e+03	-9.99e-01	8.329038595e+03	-2.020744460e+03	7.8e-01	0.08
2	7.1e+03	8.3e-01	8.7e+03	-9.96e-01	9.584261566e+03	-7.537052715e+02	7.1e-01	0.08
3	5.2e+03	6.1e-01	7.4e+03	-9.87e-01	1.460992409e+04	4.361323650e+03	5.2e-01	0.09
4	1.7e+03	2.0e-01	4.1e+03	-9.66e-01	5.216178440e+04	4.235234708e+04	1.7e-01	0.10
5	7.4e+02	8.7e-02	2.4e+03	-8.64e-01	1.028563864e+05	9.397331223e+04	7.4e-02	0.11
6	4.0e+02	4.6e-02	1.4e+03	-6.03e-01	1.076676790e+05	1.004097991e+05	4.0e-02	0.12
7	2.8e+02	3.3e-02	9.7e+02	-1.71e-01	8.893218123e+04	8.290489716e+04	2.8e-02	0.13
8	1.6e+02	1.9e-02	4.9e+02	8.31e-02	6.300096522e+04	5.880765531e+04	1.6e-02	0.13
9	1.1e+02	1.2e-02	2.7e+02	4.17e-01	4.940899724e+04	4.640012206e+04	1.1e-02	0.14
10	4.5e+01	5.3e-03	8.2e+01	6.09e-01	3.123427143e+04	2.979941887e+04	4.5e-03	0.16
11	1.4e+01	1.7e-03	1.6e+01	8.34e-01	2.194998655e+04	2.146636309e+04	1.4e-03	0.16
12	4.4e+00	5.2e-04	2.8e+00	9.56e-01	1.845528587e+04	1.830414181e+04	4.4e-04	0.17
13	1.3e+00	1.6e-04	4.8e-01	9.89e-01	1.743922038e+04	1.739390618e+04	1.3e-04	0.18
14	3.6e-01	4.3e-05	7.2e-02	9.98e-01	1.714335346e+04	1.713092359e+04	3.6e-05	0.19
15	8.7e-02	1.0e-05	8.4e-03	1.00e+00	1.705275421e+04	1.704978384e+04	8.7e-06	0.20
16	1.5e-02	1.7e-06	6.2e-04	9.99e-01	1.703018296e+04	1.702967748e+04	1.5e-06	0.21
17	2.2e-03	2.5e-07	3.4e-05	1.00e+00	1.702611788e+04	1.702604409e+04	2.2e-07	0.22
18	1.2e-03	1.5e-07	1.5e-05	1.00e+00	1.702582068e+04	1.702577846e+04	1.2e-07	0.23
19	2.1e-04	2.4e-08	1.0e-06	1.00e+00	1.702548983e+04	1.702548272e+04	2.1e-08	0.24
20	2.1e-04	2.4e-08	1.0e-06	1.00e+00	1.702548982e+04	1.702548271e+04	2.1e-08	0.25
21	2.1e-04	2.4e-08	1.0e-06	1.00e+00	1.702548968e+04	1.702548258e+04	2.1e-08	0.25
22	2.1e-04	2.4e-08	1.0e-06	1.00e+00	1.702548967e+04	1.702548258e+04	2.1e-08	0.27
23	2.1e-04	2.4e-08	1.0e-06	1.00e+00	1.702548966e+04	1.702548257e+04	2.1e-08	0.28

24	2.1e-04	2.4e-08	1.0e-06	1.00e+00	1.702548948e+04	1.702548241e+04	2.1e-08	0.28
25	2.1e-04	2.4e-08	1.0e-06	1.00e+00	1.702548946e+04	1.702548239e+04	2.1e-08	0.29
26	2.1e-04	2.4e-08	1.0e-06	1.00e+00	1.702548944e+04	1.702548238e+04	2.1e-08	0.30
27	2.1e-04	2.4e-08	1.0e-06	1.00e+00	1.702548912e+04	1.702548208e+04	2.1e-08	0.31
28	2.1e-04	2.4e-08	1.0e-06	1.00e+00	1.702548909e+04	1.702548206e+04	2.1e-08	0.32
29	2.0e-04	2.3e-08	9.3e-07	1.00e+00	1.702548550e+04	1.702547886e+04	2.0e-08	0.33
30	1.9e-04	2.3e-08	9.3e-07	1.00e+00	1.702548537e+04	1.702547873e+04	1.9e-08	0.34
31	1.9e-04	2.2e-08	8.8e-07	1.00e+00	1.702548330e+04	1.702547689e+04	1.9e-08	0.35
32	1.9e-04	2.2e-08	8.8e-07	1.00e+00	1.702548321e+04	1.702547681e+04	1.9e-08	0.36
33	1.8e-04	2.2e-08	8.5e-07	1.00e+00	1.702548189e+04	1.702547563e+04	1.8e-08	0.37
34	1.8e-04	2.1e-08	8.3e-07	1.00e+00	1.702548076e+04	1.702547461e+04	1.8e-08	0.38
35	1.8e-04	2.1e-08	8.3e-07	1.00e+00	1.702548072e+04	1.702547458e+04	1.8e-08	0.39
36	1.8e-04	2.1e-08	8.2e-07	1.00e+00	1.702548061e+04	1.702547448e+04	1.8e-08	0.40
37	1.8e-04	2.1e-08	8.2e-07	1.00e+00	1.702548053e+04	1.702547441e+04	1.8e-08	0.41
38	1.7e-04	2.0e-08	7.9e-07	1.00e+00	1.702547900e+04	1.702547305e+04	1.7e-08	0.41
39	1.7e-04	2.0e-08	7.9e-07	1.00e+00	1.702547899e+04	1.702547303e+04	1.7e-08	0.42
40	1.7e-04	2.0e-08	7.9e-07	1.00e+00	1.702547899e+04	1.702547303e+04	1.7e-08	0.43
41	1.7e-04	2.0e-08	7.9e-07	1.00e+00	1.702547899e+04	1.702547303e+04	1.7e-08	0.44
42	3.8e-05	4.4e-09	7.9e-08	1.00e+00	1.702543493e+04	1.702543364e+04	3.8e-09	0.45
43	3.8e-05	4.4e-09	7.9e-08	1.00e+00	1.702543493e+04	1.702543364e+04	3.8e-09	0.47
44	3.8e-05	4.4e-09	7.9e-08	1.00e+00	1.702543493e+04	1.702543364e+04	3.8e-09	0.49

Optimizer terminated. Time: 0.51

#### Interior-point solution summary

Problem status : PRIMAL_AND_DUAL_FEASIBLE								
Solution status : OPTIMAL								
Primal. obj: 1.7025434927e+04	nrm: 5e+02	Viol.	con: 3e-07	var: 2e-05	acc: 3e-08			
Dual. obj: 1.7025433643e+04	nrm: 8e+03	Viol.	con: 8e-08	var: 1e-07	acc: 0e+00			

#### Optimizer summary

Optimizer	-	time: 0.51
Interior-point	- iterations : 45	time: 0.50
Basis identification	-	time: 0.00
Primal	- iterations : 0	time: 0.00
Dual	- iterations : 0	time: 0.00
Clean primal	- iterations : 0	time: 0.00
Clean dual	- iterations : 0	time: 0.00
Simplex	-	time: 0.00
Primal simplex	- iterations : 0	time: 0.00
Dual simplex	- iterations : 0	time: 0.00
Mixed integer	- relaxations: 0	time: 0.00

> [mosek] Primal optimality condition in solveCobraEP satisfied.

> [mosek] Dual optimality condition in solveCobraEP satisfied.

#### Optimality conditions (biochemistry)

```

2.8e-07 || N*(vf - vr) + B*ve - b ||_inf
    Inf || C*(vf - vr) + s_C - d ||_inf, s_C = slack variable
8.8e-08 || cf + ci + N'*y_N + C'*y_C + y_vi + Qv*vf + k_vf + z_vf ||_inf
8.8e-08 || cr - ci - N'*y_N - C'*y_C - y_vi + Qv*vf + k_vr + z_vr ||_inf
7.4e-13 || ce + B'*y_N + z_ve ||_inf
        0 || k_e_1 + z_e_1 ||_inf
1.5e-07 || -g + k_e_vf + z_e_vf||_inf
1.5e-07 || -g + k_e_vr + z_e_vr||_inf
2.1e-06 || e_vf + vf*log(vf) ||_inf
3.4e-06 || e_vr + vr*log(vr) ||_inf

```

#### Derived optimality conditions (biochemistry)

```

18 || g.*log(vf) + g - k_vf ||_inf
0.0043 || g.*log(vr) + g - k_vr ||_inf
    18 || cf + ci + N'*y_N + C'*y_C + y_vi + Qv*vf + g.*log(vf) + g + z_vf ||_inf
0.0043 || cr - ci - N'*y_N - C'*y_C - y_vi + Qv*vf + g.*log(vr) + g + z_vr ||_inf

```

```

Thermo conditions
2.7e+02 || g.*log(vr/vf) - 2*N'*y_N - 2*C'*y_C ||_inf
53 || g.*log(vr/vf) + cr - cf - 2*ci - 2*N'*y_N - 2*C'*y_C - 2*y_vi ||_inf
88 || g.*log(vr/vf) + cr - cf - 2*ci - 2*N'*y_N - 2*C'*y_C - 2*y_vi - z_vr + z_vf ||_inf
-1.5e+02 min(slack)
Inf max(slack)

```

```
model=modelOut;
```

Extract the fields of the solution structure

```

if solution.stat ~=1
    disp('No solution')
    return
end
[v,vf,vr,vt,y_N,z_v,z_dx,z_vf,z_vr,stat]=...

deal(solution.v,solution.vf,solution.vr,solution.vt,solution.y_N,solution.z_v
,solution.z_dx,solution.z_vf,solution.z_vr,solution.stat);
cf = model.cf;
cr = model.cr;

g=deal(model.g);
if isfield(solution,'x')
    [x, x0, z_x, z_x0, z_dx] = deal(solution.x, solution.x0, solution.z_x,
solution.z_x0, solution.z_dx);
    [u0,f]=deal(model.u0,model.f);
    dx = x - x0;
end

```

Extract the internal (N) and exchange (B) stoichiometric matrices

```
N = model.S(:,model.SConsistentRxnBool);
B = model.S(:,~model.SConsistentRxnBool);
```

Extract the matrix of coupling constraints, if present

```

if isfield(model,'C')
    C = model.C(:,model.SConsistentRxnBool);
    y_C = solution.y_C;
end

```

Extract the objective on the internal reaction rates

```
e = ones(length(vf),1);
ci = solution.osense*model.c(model.SConsistentRxnBool);
```

Extract the net internal reaction dual variable

```
z_vi = z_v(model.SConsistentRxnBool);
```

Compute the nullspace of the internal stoichiometric matrix

```
if 0
    %get nullspace of N
    [Z,rankS]=getNullSpace(N,0);
else
    Z=[ ];
end
```

## ANTICIPATED RESULTS

Optimality conditions should be satisfied approximately to the feasibility (or optimality) tolerances of the numerical optimisation solver, typically 1e-6.

```
if param.printLevel>2 || 1
    v_detailed=1;
else
    v_detailed=0;
end
```

Biochemical optimality conditions: steady state

```
if isfield(solution,'x')
    fprintf('%.2g %s\n',norm(N*(vf - vr) - x + x0 - model.b,inf), '|| N*(vf
- vr) - x + x0 - b ||_inf');
else
    fprintf('%.2g %s\n',norm(model.S*v - model.b,inf), '|| S*v - b ||_inf');
end
```

2.8e-07 || S\*v - b ||\_inf

Optionally, display detailed properties of flux related solution vector

```
if v_detailed
    fprintf('%.2g %s\n',sum(vf)+sum(vr), 'sum(vf)+sum(vr) >= 0');
    fprintf('%.2g %s\n',norm(g.*reallog(vf),inf), '|| g*log(vf) ||_inf');
    fprintf('%.2g %s\n',norm(g.*reallog(vr),inf), '|| g*log(vr) ||_inf');
    fprintf('%.2g %s\n',norm(cr,inf), '|| cr ||_inf');
    fprintf('%.2g %s\n',norm(cf,inf), '|| cf ||_inf');
    fprintf('%.2g %s\n',norm(ci,inf), '|| ci ||_inf');
    fprintf('%.2g %s\n',norm(N'*y_N,inf), '|| N'*y_N ||_inf');
    fprintf('%.2g %s\n',norm(z_v,inf), '|| z_v ||_inf');
    fprintf('%.2g %s\n',norm(z_vf,inf), '|| z_vf ||_inf');
    fprintf('%.2g %s\n',norm(z_vr,inf), '|| z_vr ||_inf');
    if isfield(model,'C')
        fprintf('%.2g %s\n',norm(C'*y_C,inf), '|| C'*y_C ||_inf');
    end
end
```

4.1e+03 sum(vf)+sum(vr) >= 0  
31 || g\*log(vf) ||\_inf

```

13 || g*log(vr) ||_inf
0.1 || cr ||_inf
0.1 || cf ||_inf
0 || ci ||_inf
1.4e+02 || N'*y_N ||_inf
1.4e+02 || z_v ||_inf
2e-07 || z_vf ||_inf
35 || z_vr ||_inf
37 || C'*y_C ||_inf

if isfield(model,'C')
    fprintf('%8.2g %s\n',norm(g.*reallog(vf) + ci + cf + N'*y_N + C'*y_C +
z_vi + z_vf,inf), '|| g*log(vf) + ci + cf + N'*y_N + C'*y_C + z_vi + z_vf
||_inf');
    fprintf('%8.2g %s\n',norm(g.*reallog(vr) - ci + cr - N'*y_N - C'*y_C -
z_vi + z_vr,inf), '|| g*log(vr) - ci + cr - N'*y_N - C'*y_C - z_vi + z_vr
||_inf');
    fprintf('%8.2g %s\n',norm( C'*y_C + z_vi + z_vf,inf), '|| + C'*y_C +
z_vi + z_vf ||_inf');
    fprintf('%8.2g %s\n',norm( - C'*y_C - z_vi + z_vr,inf), '|| - C'*y_C -
z_vi + z_vr ||_inf');
else
    fprintf('%8.2g %s\n',norm(g.*reallog(vf) + ci + cf + N'*y_N + z_vi -
z_vf,inf), '|| g*log(vf) + ci + cf + N'*y_N + z_vi - z_vf ||_inf');
    fprintf('%8.2g %s\n',norm(g.*reallog(vr) - ci + cr - N'*y_N - z_vi -
z_vr,inf), '|| g*log(vr) - ci + cr - N'*y_N - z_vi - z_vr ||_inf');
end

16 || g*log(vf) + ci + cf + N'*y_N + C'*y_C + z_vi + z_vf ||_inf
2 || g*log(vr) - ci + cr - N'*y_N - C'*y_C - z_vi + z_vr ||_inf
1.4e+02 || + C'*y_C + z_vi + z_vf ||_inf
1.4e+02 || - C'*y_C - z_vi + z_vr ||_inf

```

### Derived biochemical optimality conditions (fluxes)

```

if isfield(model,'C')
    res = g.*reallog(vr./vf) + cr - cf - 2*ci - 2*N'*y_N - 2*C'*y_C - 2*z_vi -
z_vr + z_vf;
    fprintf('%8.2g %s\n',norm(res,inf),'|| g*log(vr/vf) + cr - cf - 2*ci -
2*N'*y_N - 2*C'*y_C - 2*z_vi - z_vr + z_vf ||_inf');
else
    res = g.*reallog(vr./vf) + cr - cf - 2*ci - 2*N'*y_N - 2*z_vi - z_vr +
z_vf;
    fprintf('%8.2g %s\n',norm(res,inf),'|| g*log(vr/vf) + cr - cf - 2*ci -
2*N'*y_N - 2*z_vi - z_vr + z_vf ||_inf');
end

88 || g*log(vr/vf) + cr - cf - 2*ci - 2*N'*y_N - 2*C'*y_C - 2*z_vi - z_vr + z_vf ||_inf

```

Optionally, display detailed properties of concentration related solution vector

```

if isfield(solution,'x')
    fprintf('\n%$s\n','Optimality conditions (concentrations)')
    if v_detailed

```

```

        fprintf('%.2g %s\n',norm(reallog(x),inf), '|| log(x)||_inf');
        fprintf('%.2g %s\n',norm(u0,inf), '|| u0 ||_inf');
        fprintf('%.2g %s\n',norm(y_N,inf), '|| y_N ||_inf');
        fprintf('%.2g %s\n',norm(z_dx,inf), '|| z_dx ||_inf');
        fprintf('%.2g %s\n',norm(z_x,inf), '|| z_x ||_inf');
        fprintf('%.2g %s\n',norm(z_x0,inf), '|| z_x0 ||_inf');
    end
    fprintf('%.2g %s\n',norm(f.*reallog(x) + u0 - y_N + z_dx + z_x,inf),
'|| f.*log(x) + u0 - y_N + z_dx + z_x ||_inf');
    fprintf('%.2g %s\n',norm(f.*reallog(x0) + u0 + y_N - z_dx +
z_x0,inf),'|| f.*log(x0) + u0 + y_N - z_dx + z_x0 ||_inf');

    fprintf('\n%s\n','Derived biochemical optimality conditions
(concentrations)')
    fprintf('%.2g %s\n',norm(f.*reallog(x./x0) - 2*y_N + 2*z_dx + z_x -
z_x0,inf),'|| f.*log(x/x0) - 2*y_N + 2*z_dx + z_x - z_x0 ||_inf');
    fprintf('%.2g %s\n',norm(f.*reallog(x.*x0) + 2*u0 + z_x + z_x0,inf),'|| 
f.*log(x.*x0) + 2*u0 + z_x + z_x0 ||_inf');

    fprintf('\n%s\n','Derived biochemical optimality conditions (fluxes and
concentrations)')
    if isfield(model,'C')
        fprintf('%.2g %s\n',norm(g.*reallog(vf) + cf + ci + N'* (u0 +
f.*reallog(x) + z_dx + z_x) + C'*y_C + z_v + z_vf,inf),'|| g*log(vf) + cf
+ ci + N'* (u0 + f*log(x) + z_dx + z_x) + C'*y_C + z_v + z_vf ||_inf');
        fprintf('%.2g %s\n',norm(g.*reallog(vr) + cr - ci - N'* (u0 +
f.*reallog(x) + z_dx + z_x) - C'*y_C - z_v + z_vr,inf),'|| g*log(vr) + cr -
ci - N'* (u0 + f*log(x) + z_dx + z_x) - C'*y_C - z_v + z_vr ||_inf');
    else
        fprintf('%.2g %s\n',norm(g.*reallog(vf) + cf + ci + N'* (u0 +
f.*reallog(x) + z_dx + z_x) + z_v + z_vf,inf),'|| g*log(vf) + cf + ci +
N'* (u0 + f*log(x) + z_dx + z_x) + z_v + z_vf ||_inf');
        fprintf('%.2g %s\n',norm(g.*reallog(vr) + cr - ci - N'* (u0 +
f.*reallog(x) + z_dx + z_x) - z_v + z_vr,inf),'|| g*log(vr) + cr - ci -
N'* (u0 + f*log(x) + z_dx + z_x) - z_v + z_vr ||_inf');
    end

    fprintf('\n%s\n','Derived biochemical optimality conditions (fluxes and
concentrations)')
    if isfield(model,'C')
        fprintf('%.2g %s\n',norm(g.*reallog(vr./vf) + cr - cf - 2*ci -
2*N'* (u0 + f.*reallog(x) + z_dx + z_x) - 2*C'*y_C - 2*z_v - z_vf +
z_vr,inf),'|| g.*reallog(vr./vf) + cr - cf - 2*(ci + N'* (u0 + f*log(x)
+ z_dx + z_x) + C'*y_C + z_v) - z_vf + z_vr ||_inf');
        fprintf('%.2g %s\n',norm(g.*reallog(vr./vf) + cr - cf - 2*ci +
2*N'* (u0 + f.*reallog(x0) - z_dx + z_x0) - 2*C'*y_C - 2*z_v - z_vf +
z_vr,inf),'|| g.*reallog(vr./vf) + cr - cf - 2*(ci - N'* (u0 + f*log(x0) -
z_dx + z_x0) + C'*y_C + z_v) - z_vf + z_vr ||_inf');
    else

```

```

        fprintf('%.2g %s\n',norm(g.*reallog(vr./vf) + cr - cf - 2*ci -
2*N'*(u0 + f.*reallog(x) + z_dx + z_x) - 2*z_v - z_vf + z_vr,inf),'|||
g.*reallog(vr./vf) + cr - cf - 2*(ci + N'*(u0 + f*log(x) + z_dx + z_x) +
z_v) - z_vf + z_vr ||_inf');
        fprintf('%.2g %s\n',norm(g.*reallog(vr./vf) + cr - cf - 2*ci +
2*N'*(u0 + f.*reallog(x0) - z_dx + z_x0) - 2*z_v - z_vf + z_vr,inf),'|||
g.*reallog(vr./vf) + cr - cf - 2*(ci - N'*(u0 + f*log(x0) - z_dx + z_x0) +
z_v) - z_vf + z_vr ||_inf');
        fprintf('%.2g %s\n',norm(g.*reallog(vr.*vf) + cr + cf - N'*(u0
+ f.*reallog(x) + z_dx + z_x) - 2*z_v - z_vf + z_vr,inf),'|||
g.*reallog(vr./vf) + cr - cf - 2*(ci + N'*(u0 + f*log(x) + z_dx + z_x) +
z_v) - z_vf + z_vr ||_inf');
        fprintf('%.2g %s\n',norm(g.*reallog(vr./vf) + cr - cf - 2*ci +
2*N'*(u0 + f.*reallog(x0) - z_dx + z_x0) - 2*z_v - z_vf + z_vr,inf),'|||
g.*reallog(vr./vf) + cr - cf - 2*(ci - N'*(u0 + f*log(x0) - z_dx + z_x0) +
z_v) - z_vf + z_vr ||_inf');
    end
end

```

```

fprintf('\n')
if isfield(solution,'v')
    vfpad = NaN*ones(size(model.S,2),1);
    vfpad(model.SConsistentRxnBool)=vf;
    vrpad = NaN*ones(size(model.S,2),1);
    vrpad(model.SConsistentRxnBool)=vr;
    zvfpad = NaN*ones(size(model.S,2),1);
    zvfpad(model.SConsistentRxnBool)=z_vr;
    zvrpad = NaN*ones(size(model.S,2),1);
    zvrpad(model.SConsistentRxnBool)=z_vr;
    T1 =
table(model.lb, v,model.ub,z_v,vfpad,zvfpad,vrpad,zvrpad,'VariableNames',
{'vl','v','vu','z_v','vf','z_vf','vr','z_vr'});
    if length(v)<=10
        disp(T1)
    end
end

```

```

if isfield(solution,'x')
    T2 =
table(model.xl,solution.x,model.xu,z_x,model.x0l,x0,model.x0u,z_x0,model.dxl,
dx,model.dxu,z_dx, ...
    'VariableNames',{ 'xl' 'x' 'xu' 'z_x' 'x0l' 'x0' 'x0u' 'z_x0' 'dxl'
'dx' 'dxu' 'z_dx'});
    if length(solution.x)<=10
        disp(T2)
    end
end

```

## TROUBLESHOOTING

### Debugging satisfaction of constraints

Entropic Flux Balance Analysis will find a thermodynamically feasible steady state, provided one exists. That is, bounds on net fluxes, for example those causing net flux around a stoichiometrically balanced cycle, can preclude the existence of a thermodynamically feasible steady state. The following plots can be used to investigate deviation from thermodynamic feasibility for certain reactions, indicated by numerical tolerances beyond that considered satisfactory (typically 1e-6 for a double precision solver). Setting the bounds on reaction direction is important, because certain bounds may be incompatible with the existence of a thermodynamically feasible steady state

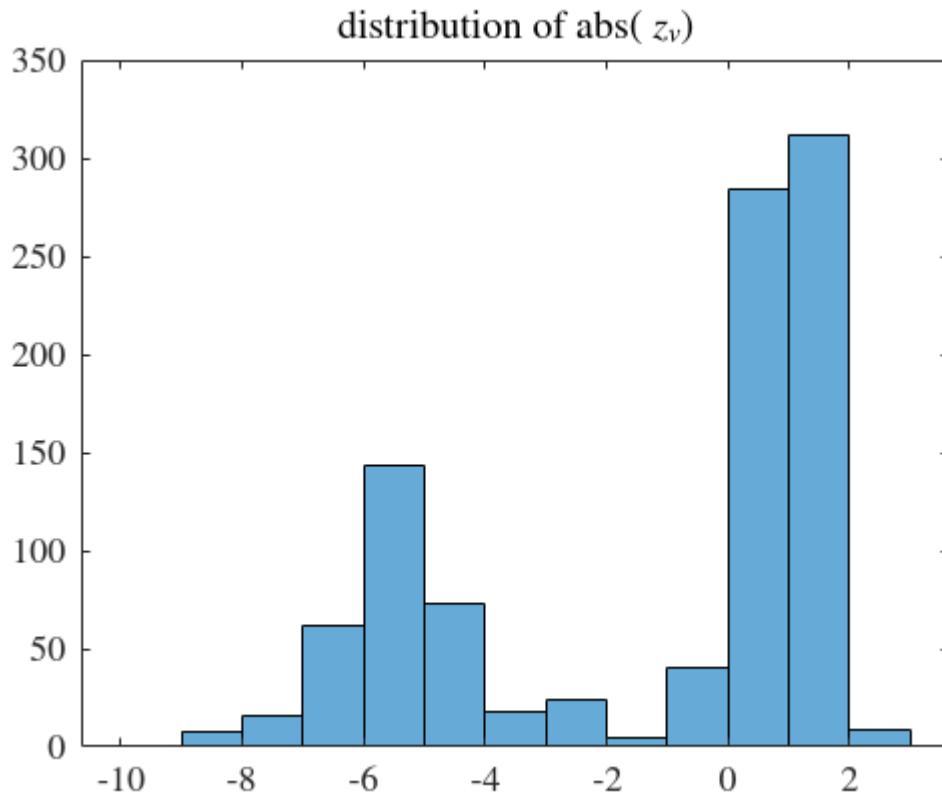
```
param.internalNetFluxBounds = 'original' maintains direction and magnitude of internal net flux  
from model.lb & model.ub
```

```
param.internalNetFluxBounds = 'directional' maintains direction of internal net flux from model.lb  
& model.ub but not magnitude
```

```
param.internalNetFluxBounds = 'none' removes lower and upper bounds on internal net flux
```

```
param.internalNetFluxBounds = 'random' random internal net flux direction, replacing constraints  
from model.lb & model.ub
```

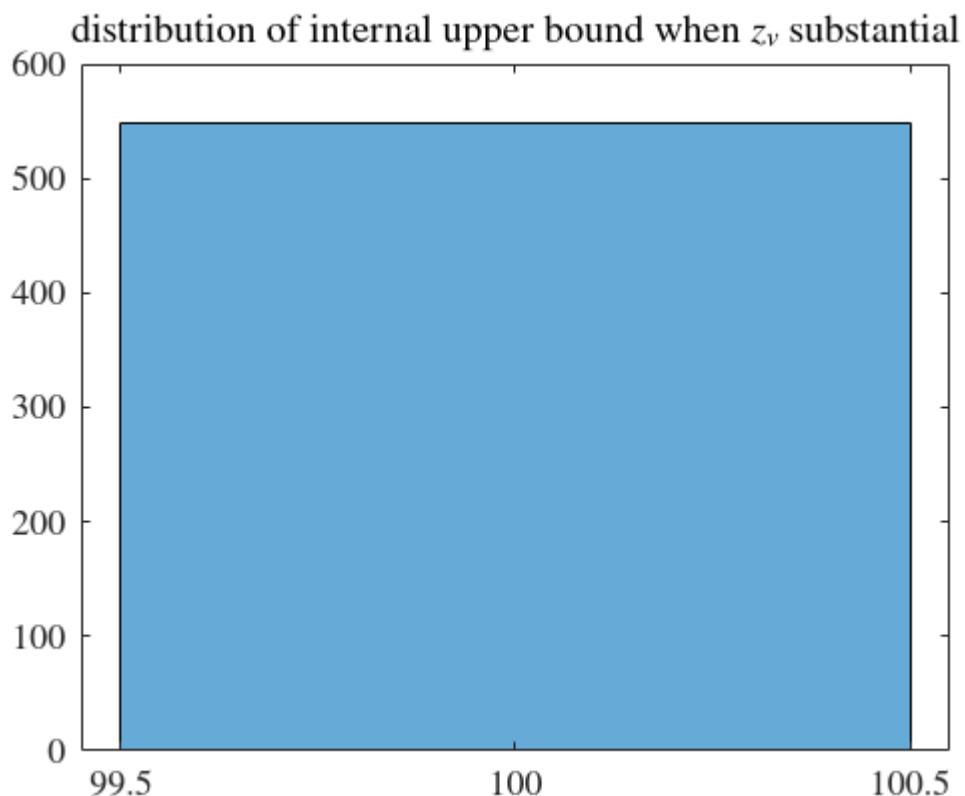
```
l = model.lb(model.SConsistentRxnBool);  
u = model.ub(model.SConsistentRxnBool);  
vi = vf - vr;  
logrvf = reallog(vr./vf);  
  
figure  
histogram(log10(abs(z_v)))  
title('distribution of abs( $z_v$ )')
```



```

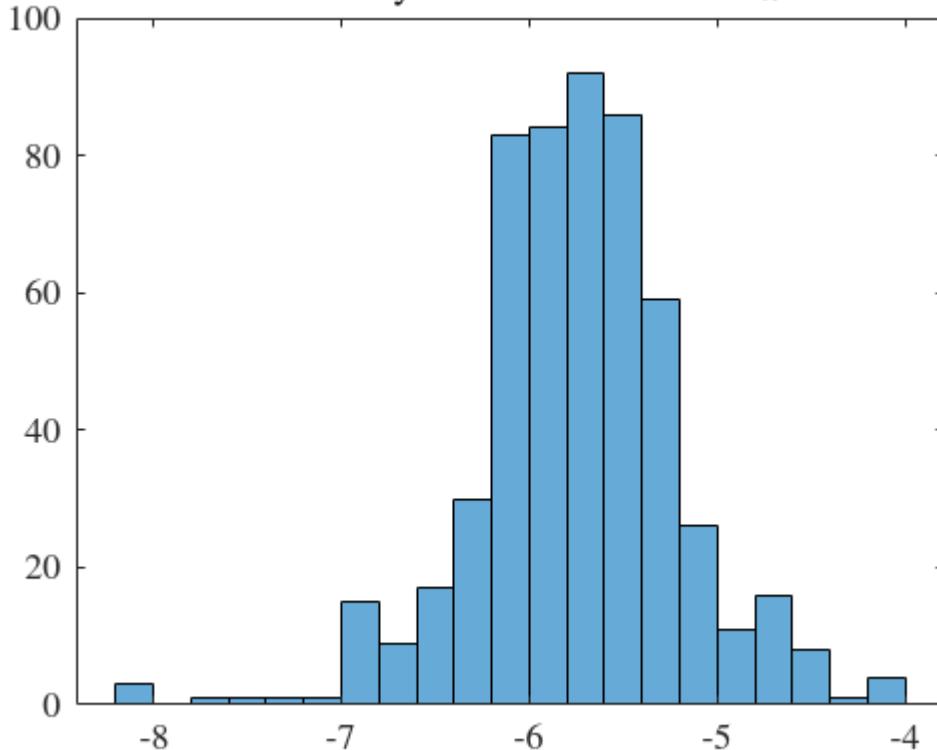
zBool = abs(z_vi)>0.1;
if any(l(zBool)~=0)
    figure
    histogram(l(zBool))
    title('distribution of internal lower bound when $z_v$ substantial')
end
if any(u(zBool)~=inf)
    figure
    histogram(u(zBool))
    title('distribution of internal upper bound when $z_v$ substantial')
end

```

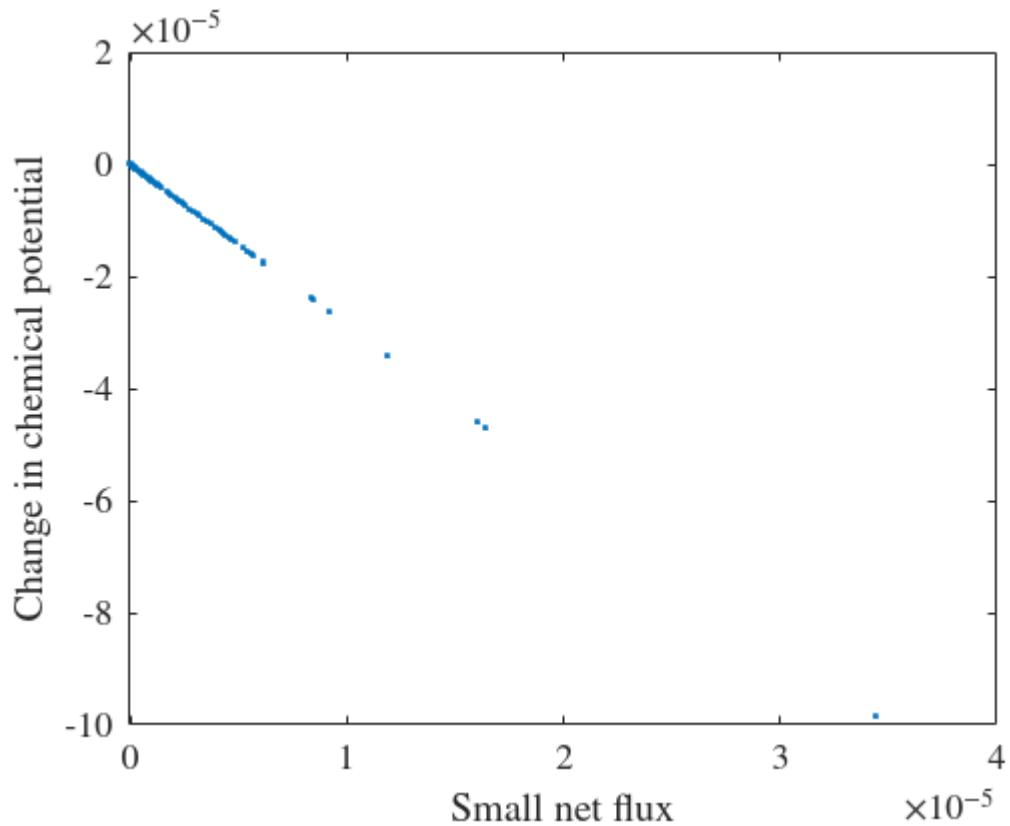


```
if any(zBool)
    figure
    histogram(log10(abs(res(zBool))))
    title('distribution of thermodynamic residual when $z_v$ is substantial')
end
```

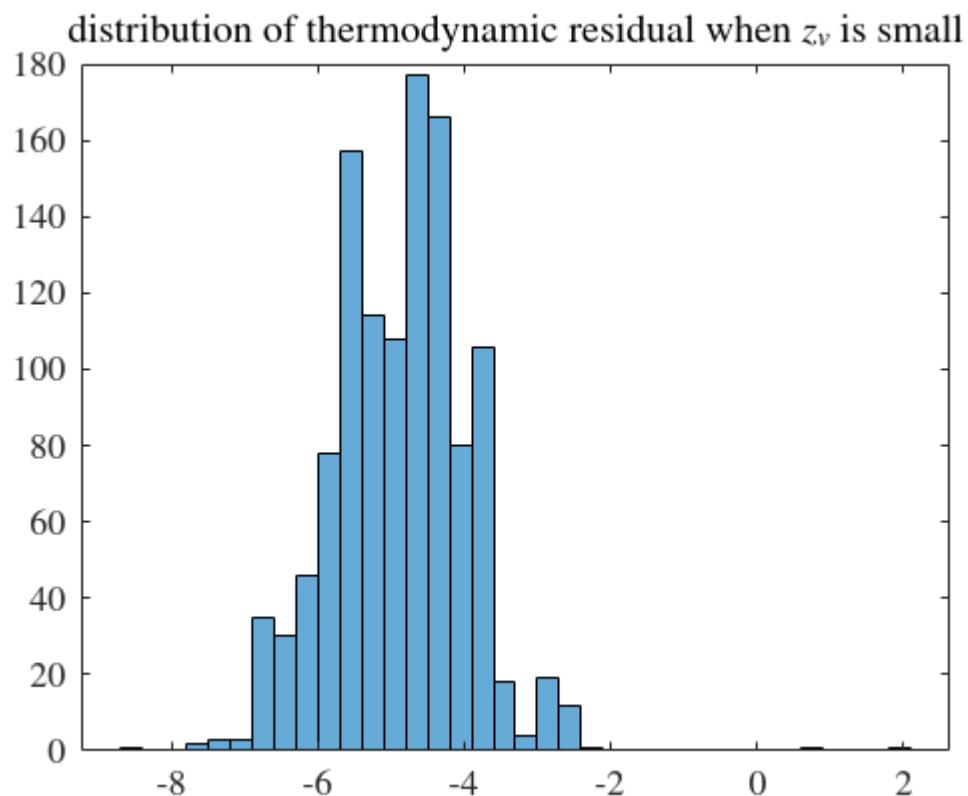
distribution of thermodynamic residual when  $z_v$  is substantial

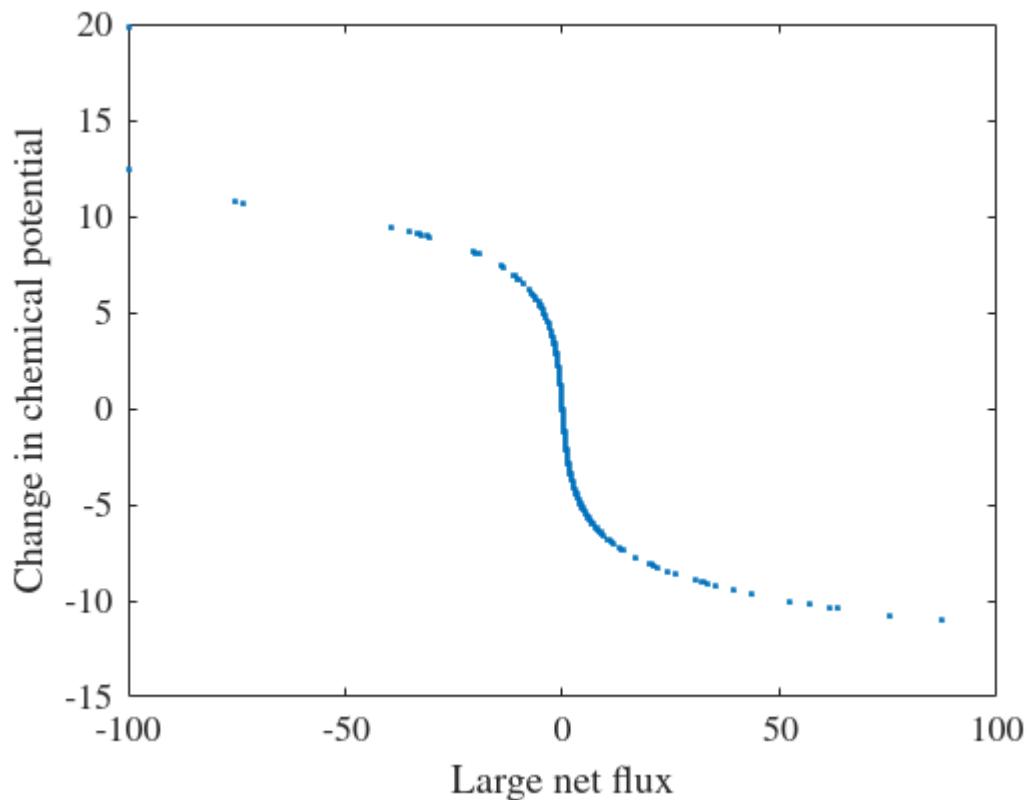


```
if any(zBool)
    figure
    plot(vi(zBool),logvrvf(zBool),'.')
    xlabel('Small net flux')
    ylabel('Change in chemical potential')
end
```

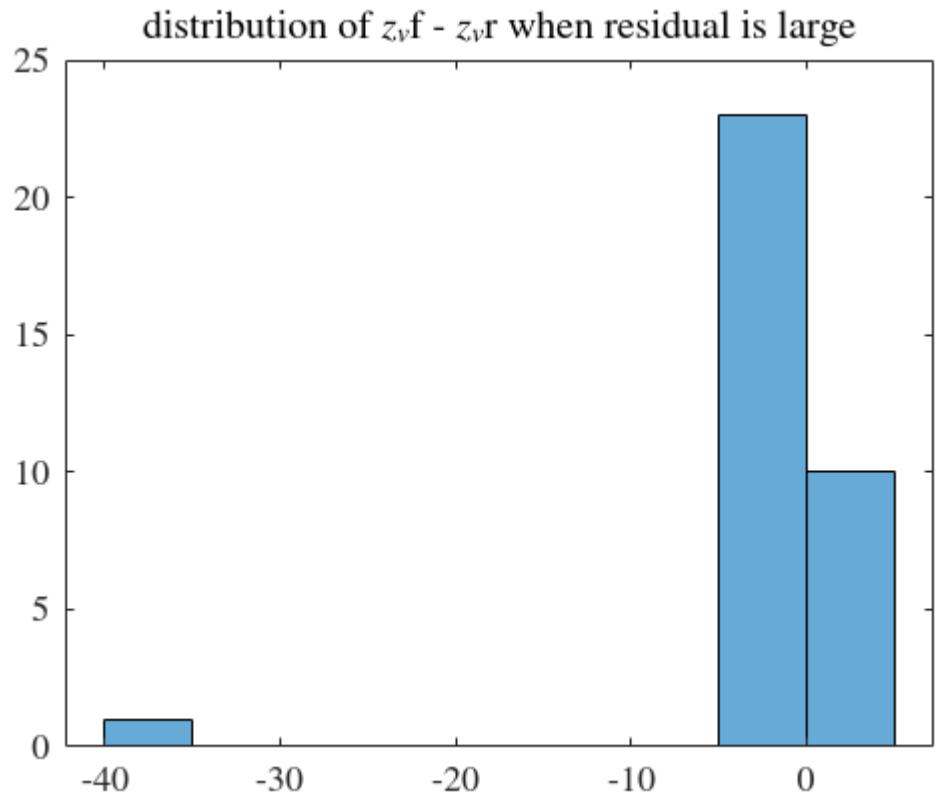


```
if any(~zBool)
    %thermo residual is large even when z_v is small
    figure
    histogram(log10(abs(res(~zBool))))
    title('distribution of thermodynamic residual when $z_v$ is small')
end
```





```
rBool = abs(res)>0.001;
fwdBool = vi>0;
if any(rBool)
    ab = z_vf - z_vr;
    figure
    histogram(ab(rBool))
    title('distribution of $z_v$f - $z_v$r when residual is large')
end
```

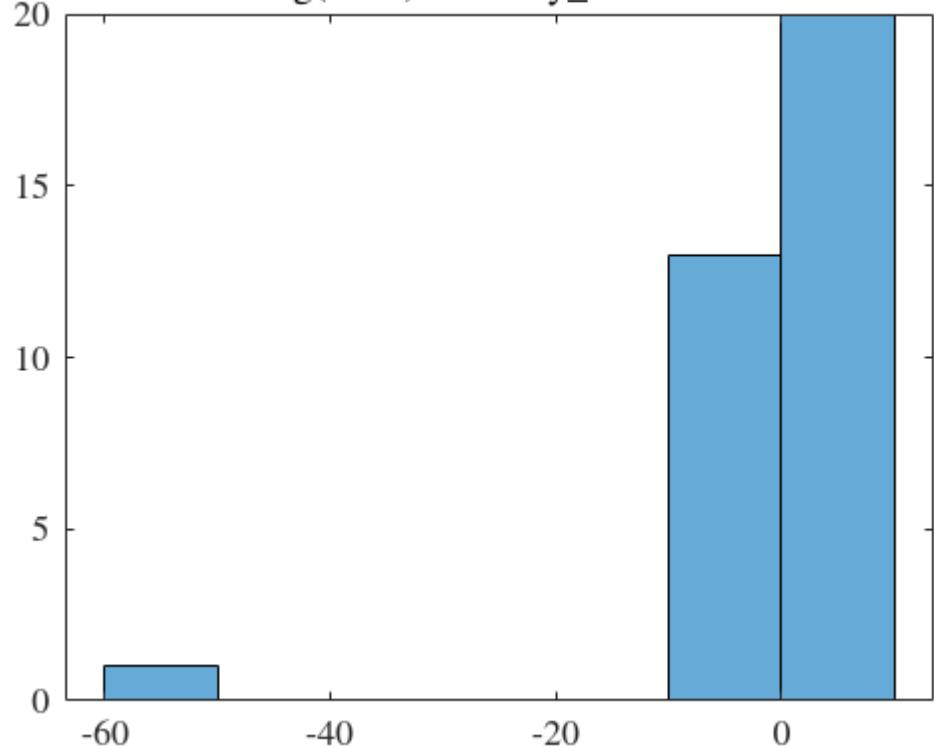


```

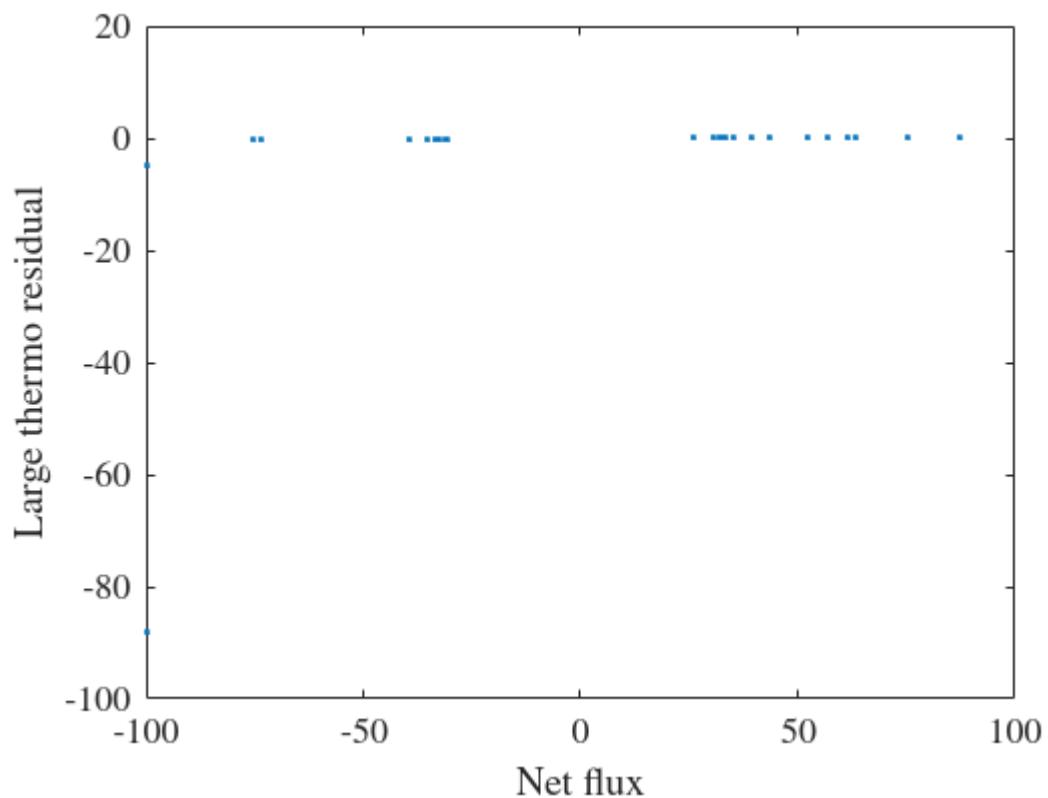
if any(rBool)
    %deviation from thermodynamic constraint occurring when net flux is
    %substantial
    figure
    res1 = g.*reallog(vr./vf) + cr - cf - 2*ci - 2*N'*y_N;
    histogram(res1(rBool))
    title('distribution of log(vr/vf) - 2*N'*y_N when residual is large')
end

```

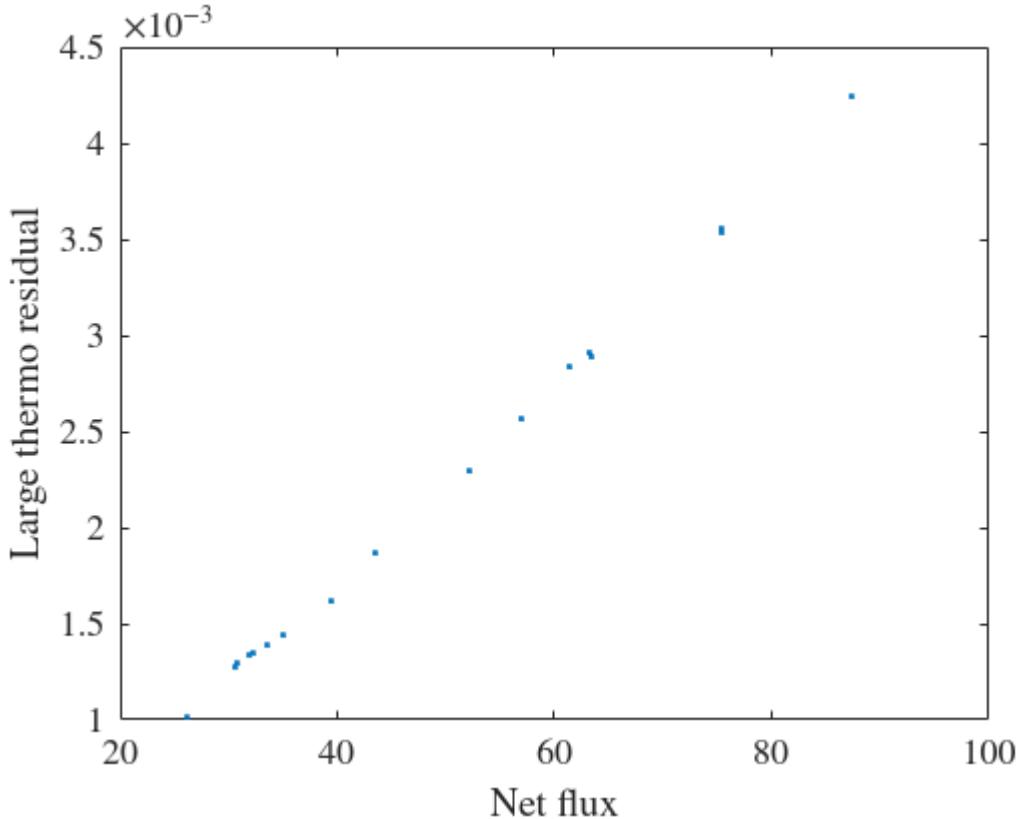
distribution of  $\log(v_r/v_f) - 2 \cdot N' \cdot y_N$  when residual is large



```
if any(rBool)
    figure
    plot(vi(rBool),res(rBool),'.')
    xlabel('Net flux')
    ylabel('Large thermo residual')
end
```



```
if any(rBool)
    figure
    plot(vi(rBool & fwdBool),res(rBool & fwdBool),'.')
    xlabel('Net flux')
    ylabel('Large thermo residual')
end
```

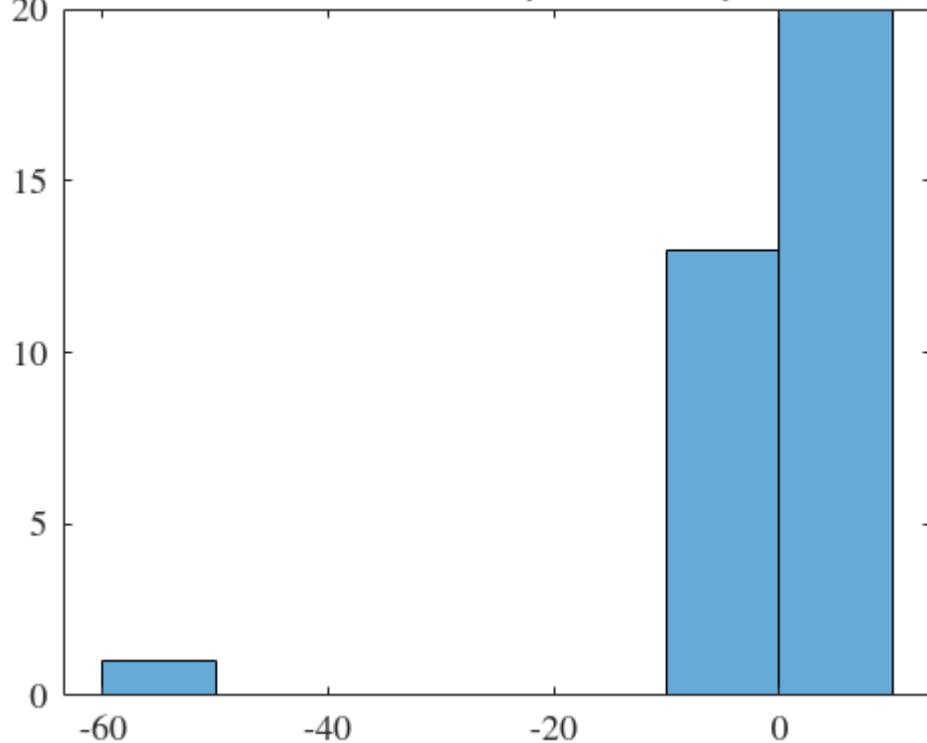


```

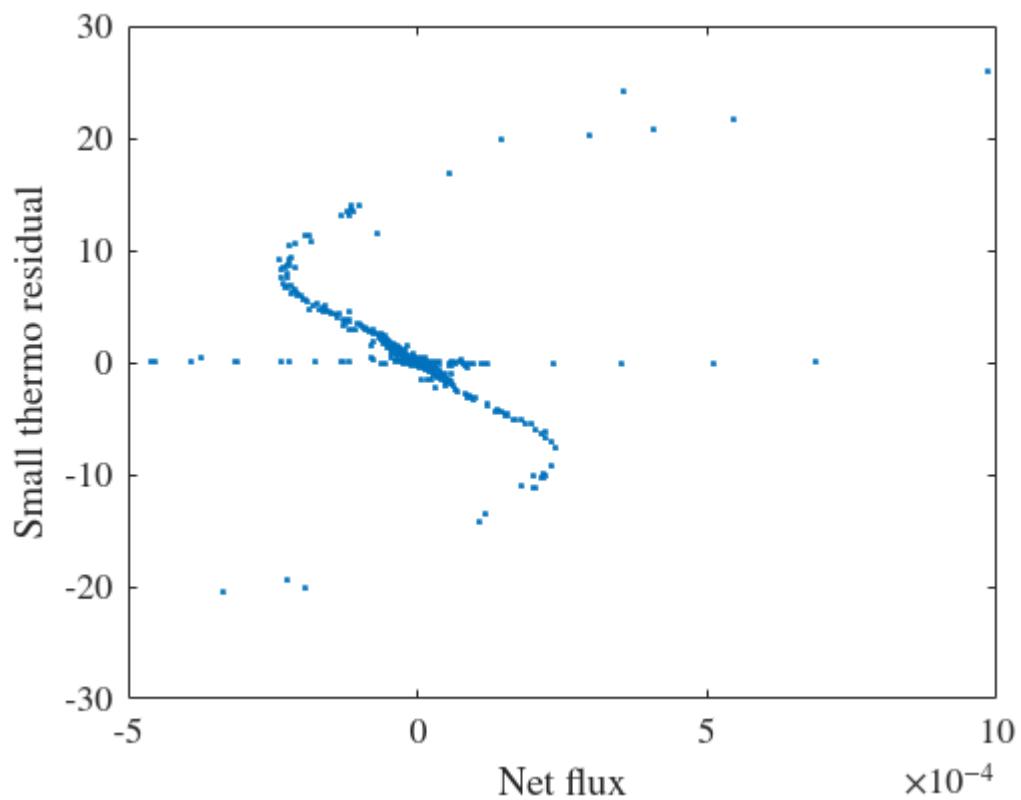
if any(rBool)
    figure
    if isfield(model,'C')
        res5 = g.*reallog(vr./vf) + cr - cf - 2*ci - 2*N'*y_N - 2*C'*y_C -
2*z_vi;
        histogram(res5(rBool))
        title('distribution of g.*log(vr/vf) + cr - cf - 2*ci - 2*N''*y\_N -
2*C''*y\_C - 2*z\_vi when residual is large')
    else
        res5 = g.*reallog(vr./vf) + cr - cf - 2*ci - 2*N'*y_N - 2*z_vi;
        histogram(res5(rBool))
        title('distribution of g.*log(vr/vf) + cr - cf - 2*ci - 2*N''*y\_N -
2*z\_vi when residual is large')
    end
end

```

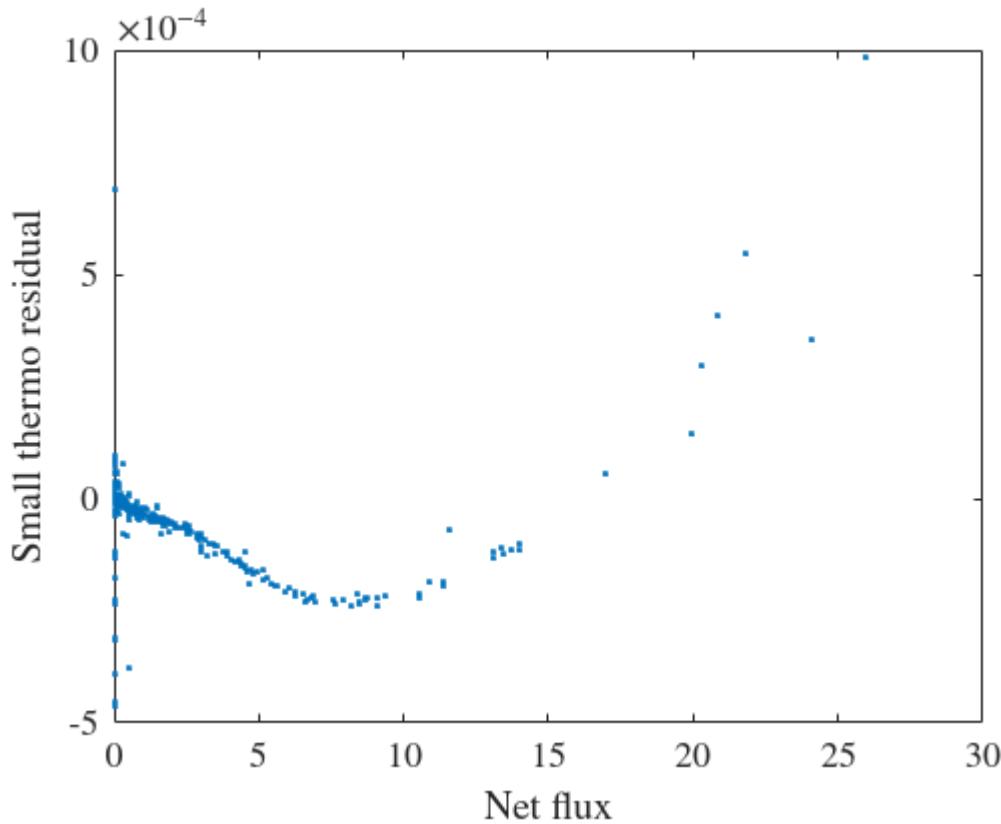
```
if g.*log(vr/vf) + cr - cf - 2*ci - 2*N'*y_N - 2*C'*y_C - 2*z_vi when
```



```
if any(~rBool)
figure
plot(res(~rBool),vi(~rBool),'.')
xlabel('Net flux')
ylabel('Small thermo residual')
end
```



```
if any(rBool)
    figure
    plot(vi(~rBool & fwdBool),res(~rBool & fwdBool),'.')
    xlabel('Net flux')
    ylabel('Small thermo residual')
end
```



```

if isequal(modelToUse,'single') && isfield(solution,'x')
    fprintf('%8.2g %s\n',norm(vf - exp(-(cf + cr - u0(1) - u0(2))/2)*x(1)),
    '|| vf - exp(-(cr + cf - u0 - u0)/2)*x1 ||')
end

```

## Quadratically constrained entropic flux balance analysis - all external reactions

Generate a random external flux vector that is a perturbation of the previously obtained external flux vector and then quadratically penalise any deviation from it.

```
model.h = (solution.v).*(rand(length(solution.v),1)+0.5)*2;
```

Do not optimise toward any internal net flux

```
model.h(model.SConsistentRxnBool)=NaN;
```

Compare the original external flux vector, with the external flux vector to penalise deviation from

```

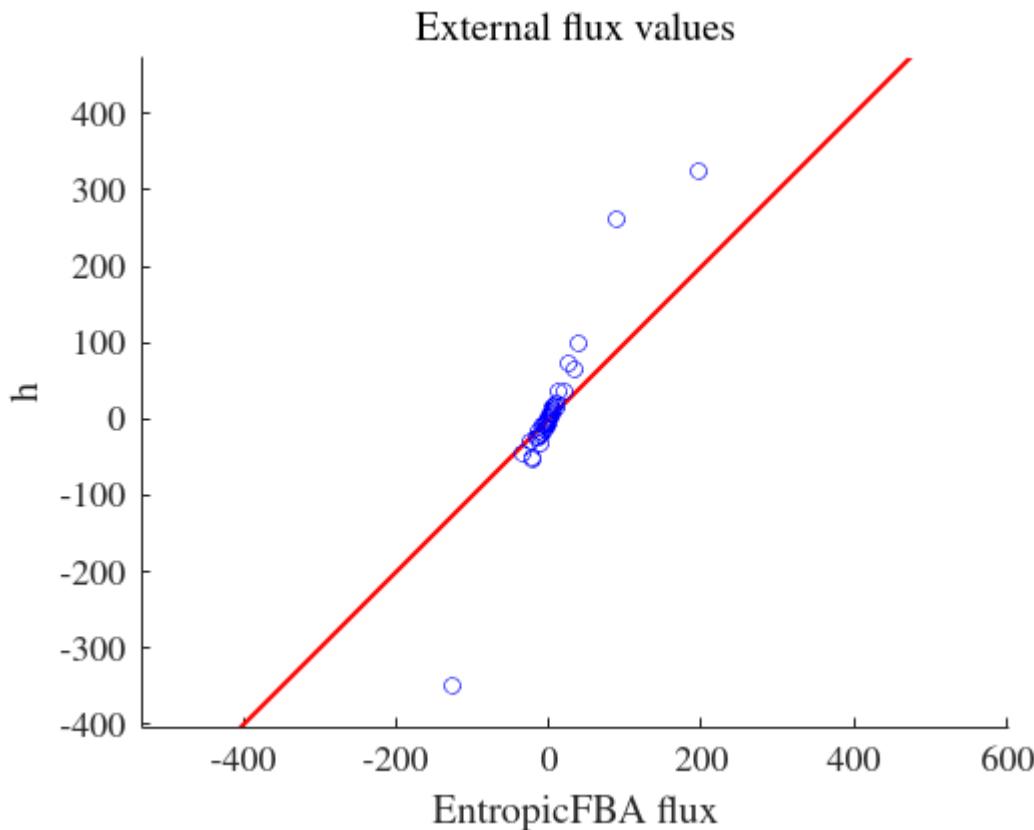
figure
hold on
fplot(@(x) x, 'LineWidth', 1.5, 'Color', 'r')
plot(solution.v(~model.SConsistentRxnBool),model.h(~model.SConsistentRxnBool),
    'o', 'Color', 'b')

```

```

xlabel('EntropicFBA flux')
ylabel('h')
title('External flux values')
axis equal

```



Set the penalty

```

HH = ones(length(solution.v),1);
HH(model.SConsistentRxnBool)=0;
model.H = spdiags(HH,0,length(solution.v),length(solution.v));

```

Run the optimisation

```
[solutionQEFBA,modelOut] = entropicFluxBalanceAnalysis(model,param);
```

Using directional internal net flux bounds only.  
Using existing external net flux bounds without modification.

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Platform: Linux/64-X86

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Platform: Linux/64-X86

Problem  
 Name :  
 Objective sense : minimize

```

Type : LO (linear optimization problem)
Constraints : 3170
Affine conic cons. : 0
Disjunctive cons. : 0
Cones : 0
Scalar variables : 3830
Matrix variables : 0
Integer variables : 0

Optimizer started.
Presolve started.
Eliminator started.
Freed constraints in eliminator : 1219
Eliminator terminated.
Linear dependency checker started.
Linear dependency checker terminated.
Eliminator started.
Freed constraints in eliminator : 141
Eliminator terminated.
Eliminator - tries : 2 time : 0.00
Lin. dep. - tries : 1 time : 0.00
Lin. dep. - primal attempts : 1 successes : 1
Lin. dep. - dual attempts : 0 successes : 0
Lin. dep. - primal deps. : 9 dual deps. : 0
Presolve terminated. Time: 0.02
GP based matrix reordering started.
GP based matrix reordering terminated.
Optimizer - threads : 18
Optimizer - solved problem : the primal
Optimizer - Constraints : 514
Optimizer - Cones : 0
Optimizer - Scalar variables : 1704 conic : 0
Optimizer - Semi-definite variables: 0 scalarized : 0
Factor - setup time : 0.01 GP order time : 0.00
Factor - dense det. time : 0.00 after factor : 1.23e+04
Factor - nonzeros before factor : 4991 flops : 5.75e+05
Factor - dense dim. : 5
ITE PFEAS DFEAS GFEAS PRSTATUS POBJ DOBJ MU TIME
0 8.1e+03 1.2e+03 2.6e+04 0.00e+00 2.566112318e+04 -8.236241217e+01 1.3e+02 0.04
1 4.0e+03 6.3e-01 1.3e+04 8.50e-01 9.850126937e+03 2.790977534e+03 6.2e+01 0.05
2 1.8e+03 2.8e-01 5.6e+03 1.00e+00 5.514031979e+03 2.486949549e+03 2.8e+01 0.05
3 3.7e+02 5.8e-02 1.2e+03 1.04e+00 1.582358312e+03 9.674172343e+02 5.8e+00 0.06
4 1.4e+02 2.2e-02 4.5e+02 1.02e+00 7.750755310e+02 5.407839174e+02 2.2e+00 0.06
5 2.4e+01 3.8e-03 7.7e+01 1.01e+00 3.840553962e+02 3.438656965e+02 3.8e-01 0.06
6 7.1e+00 1.1e-03 2.3e+01 1.01e+00 3.179179905e+02 3.061918973e+02 1.1e-01 0.06
7 2.5e+00 3.9e-04 7.8e+00 1.01e+00 2.995918221e+02 2.955633008e+02 3.8e-02 0.07
8 2.1e-01 3.3e-05 6.7e-01 1.00e+00 2.907815335e+02 2.904374570e+02 3.3e-03 0.07
9 3.1e-02 4.8e-06 9.8e-02 1.00e+00 2.900770246e+02 2.900267589e+02 4.8e-04 0.07
10 9.2e-03 1.4e-06 2.9e-02 9.99e-01 2.899745013e+02 2.899594753e+02 1.4e-04 0.07
11 1.3e-03 2.1e-07 4.3e-03 1.00e+00 2.899369219e+02 2.899347208e+02 2.1e-05 0.08
12 2.3e-05 3.7e-09 7.4e-05 1.00e+00 2.899307232e+02 2.899306850e+02 3.6e-07 0.08
13 5.3e-08 8.3e-12 1.7e-07 1.00e+00 2.899306170e+02 2.899306169e+02 8.2e-10 0.08
14 1.1e-09 2.2e-15 2.5e-10 1.00e+00 2.899306168e+02 2.899306168e+02 8.4e-14 0.08

Basis identification started.
Primal basis identification phase started.
Primal basis identification phase terminated. Time: 0.00
Dual basis identification phase started.
Dual basis identification phase terminated. Time: 0.00
Basis identification terminated. Time: 0.01
Optimizer terminated. Time: 0.11

```

Interior-point solution summary  
 Problem status : PRIMAL\_AND\_DUAL\_FEASIBLE

```

Solution status : OPTIMAL
Primal. obj: 2.8993061677e+02    nrm: 3e+02    Viol. con: 7e-10    var: 3e-11
Dual.   obj: 2.8993061677e+02    nrm: 5e+00    Viol. con: 0e+00    var: 1e-15

```

#### Basic solution summary

```

Problem status : PRIMAL_AND_DUAL_FEASIBLE
Solution status : OPTIMAL
Primal. obj: 2.8993061677e+02    nrm: 3e+02    Viol. con: 1e-12    var: 6e-14
Dual.   obj: 2.8993061677e+02    nrm: 7e+00    Viol. con: 1e-14    var: 1e-10

```

#### Optimizer summary

Optimizer	-	time: 0.11
Interior-point	- iterations : 14	time: 0.10
Basis identification	-	time: 0.01
Primal	- iterations : 37	time: 0.00
Dual	- iterations : 95	time: 0.00
Clean primal	- iterations : 0	time: 0.00
Clean dual	- iterations : 0	time: 0.00
Simplex	-	time: 0.00
Primal simplex	- iterations : 0	time: 0.00
Dual simplex	- iterations : 0	time: 0.00
Mixed integer	- relaxations: 0	time: 0.00

solveCobraEP: LP part of EPproblem is feasible according to solveCobraLP with mosek.

```

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```

```

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Platform: Linux/64-X86

```

#### Problem

Name	:
Objective sense	: minimize
Type	: CONIC (conic optimization problem)
Constraints	: 3170
Affine conic cons.	: 3625 (10875 rows)
Disjunctive cons.	: 0
Cones	: 0
Scalar variables	: 7457
Matrix variables	: 0
Integer variables	: 0

Optimizer started.

Presolve started.

Linear dependency checker started.

Linear dependency checker terminated.

Eliminator started.

Freed constraints in eliminator : 177

Eliminator terminated.

Eliminator started.

Freed constraints in eliminator : 0

Eliminator terminated.

Eliminator - tries	: 2	time	: 0.00
Lin. dep. - tries	: 1	time	: 0.00
Lin. dep. - primal attempts	: 1	successes	: 1
Lin. dep. - dual attempts	: 0	successes	: 0
Lin. dep. - primal deps.	: 25	dual deps.	: 0

Presolve terminated. Time: 0.04

Optimizer - threads	: 18
Optimizer - solved problem	: the primal
Optimizer - Constraints	: 2001

Optimizer	- Cones	: 3625						
Optimizer	- Scalar variables	: 11715	conic				: 10875	
Optimizer	- Semi-definite variables	: 0	scalarized				: 0	
Factor	- setup time	: 0.02						
Factor	- dense det. time	: 0.00	GP order time				: 0.00	
Factor	- nonzeros before factor	: 1.21e+04	after factor				: 2.08e+04	
Factor	- dense dim.	: 0	flops				: 7.99e+05	
ITE	PFEAS	DFEAS	GFEAS	PRSTATUS	POBJ	DOBJ	MU	TIME
0	3.5e+02	1.2e+00	1.1e+04	0.00e+00	6.142759534e+03	-4.414972768e+03	1.0e+00	0.07
1	2.1e+02	7.1e-01	8.1e+03	-9.69e-01	1.293676978e+04	2.486468134e+03	6.1e-01	0.10
2	8.4e+01	2.8e-01	4.9e+03	-9.48e-01	3.821773325e+04	2.819119065e+04	2.4e-01	0.11
3	3.5e+01	1.2e-01	2.8e+03	-8.52e-01	7.716914143e+04	6.825818530e+04	9.9e-02	0.12
4	2.4e+01	8.1e-02	2.0e+03	-5.23e-01	7.314062084e+04	6.533922498e+04	6.9e-02	0.12
5	1.8e+01	6.0e-02	1.4e+03	-2.41e-01	6.246633604e+04	5.578403824e+04	5.1e-02	0.13
6	1.4e+01	4.6e-02	1.0e+03	-8.27e-03	5.393114255e+04	4.825307503e+04	3.9e-02	0.14
7	5.7e+00	1.9e-02	3.4e+02	1.81e-01	3.383569036e+04	3.081079831e+04	1.6e-02	0.15
8	2.3e+00	7.8e-03	9.6e+01	6.23e-01	2.508943839e+04	2.371772103e+04	6.7e-03	0.16
9	1.3e+00	4.5e-03	4.4e+01	8.51e-01	2.236402705e+04	2.154830688e+04	3.9e-03	0.17
10	4.7e-01	1.6e-03	9.5e+00	9.18e-01	1.966955885e+04	1.937963274e+04	1.3e-03	0.18
11	1.5e-01	4.9e-04	1.7e+00	9.76e-01	1.861852162e+04	1.852707961e+04	4.2e-04	0.19
12	2.4e-02	8.0e-05	1.2e-01	9.94e-01	1.822719660e+04	1.821223790e+04	6.8e-05	0.20
13	5.6e-03	1.9e-05	1.3e-02	1.00e+00	1.817800220e+04	1.817447205e+04	1.6e-05	0.21
14	3.8e-03	1.3e-05	7.2e-03	9.92e-01	1.817193446e+04	1.816961635e+04	1.1e-05	0.22
15	4.5e-04	1.5e-06	3.0e-04	1.00e+00	1.816384080e+04	1.816356651e+04	1.3e-06	0.23
16	6.8e-05	2.3e-07	1.7e-05	1.00e+00	1.816291739e+04	1.816287632e+04	2.0e-07	0.25
17	3.9e-05	1.3e-07	7.5e-06	1.00e+00	1.816284866e+04	1.816282527e+04	1.1e-07	0.26
18	3.8e-05	1.3e-07	7.4e-06	1.00e+00	1.816284837e+04	1.816282506e+04	1.1e-07	0.27
19	9.6e-06	3.2e-08	9.7e-07	1.00e+00	1.816277947e+04	1.816277366e+04	2.8e-08	0.29
20	9.6e-06	3.2e-08	9.7e-07	1.00e+00	1.816277946e+04	1.816277366e+04	2.8e-08	0.30
21	9.5e-06	3.2e-08	9.7e-07	1.00e+00	1.816277943e+04	1.816277364e+04	2.8e-08	0.31
22	9.5e-06	3.2e-08	9.7e-07	1.00e+00	1.816277943e+04	1.816277363e+04	2.8e-08	0.32
23	9.5e-06	5.8e-08	9.6e-07	1.00e+00	1.816277929e+04	1.816277353e+04	2.8e-08	0.33
24	9.3e-06	1.5e-07	9.3e-07	1.00e+00	1.816277877e+04	1.816277312e+04	2.8e-08	0.34
25	9.3e-06	1.6e-07	9.3e-07	1.00e+00	1.816277874e+04	1.816277310e+04	2.8e-08	0.35
26	9.3e-06	1.7e-07	9.3e-07	1.00e+00	1.816277864e+04	1.816277302e+04	2.7e-08	0.36
27	9.3e-06	1.7e-07	9.3e-07	1.00e+00	1.816277864e+04	1.816277302e+04	2.7e-08	0.37
28	9.3e-06	1.8e-07	9.2e-07	1.00e+00	1.816277861e+04	1.816277300e+04	2.7e-08	0.38
29	9.2e-06	1.8e-07	9.2e-07	1.00e+00	1.816277857e+04	1.816277296e+04	2.7e-08	0.39
30	9.2e-06	1.8e-07	9.2e-07	1.00e+00	1.816277857e+04	1.816277296e+04	2.7e-08	0.39
31	9.2e-06	1.8e-07	9.2e-07	1.00e+00	1.816277856e+04	1.816277296e+04	2.7e-08	0.41
32	9.2e-06	1.9e-07	9.2e-07	1.00e+00	1.816277852e+04	1.816277293e+04	2.7e-08	0.42
33	2.3e-06	4.1e-08	1.1e-07	1.00e+00	1.816275925e+04	1.816275788e+04	6.7e-09	0.44
34	2.3e-06	4.4e-08	1.1e-07	1.00e+00	1.816275925e+04	1.816275788e+04	6.7e-09	0.45
35	2.3e-06	1.2e-07	1.1e-07	1.00e+00	1.816275923e+04	1.816275786e+04	6.7e-09	0.46
36	2.3e-06	1.2e-07	1.1e-07	1.00e+00	1.816275923e+04	1.816275786e+04	6.7e-09	0.47
37	2.3e-06	1.3e-07	1.1e-07	1.00e+00	1.816275923e+04	1.816275786e+04	6.7e-09	0.48
38	2.3e-06	1.3e-07	1.1e-07	1.00e+00	1.816275923e+04	1.816275786e+04	6.7e-09	0.49
39	2.3e-06	1.3e-07	1.1e-07	1.00e+00	1.816275923e+04	1.816275786e+04	6.7e-09	0.50
40	2.3e-06	1.3e-07	1.1e-07	1.00e+00	1.816275922e+04	1.816275785e+04	6.7e-09	0.53
41	2.3e-06	1.3e-07	1.1e-07	1.00e+00	1.816275922e+04	1.816275785e+04	6.7e-09	0.53
42	2.3e-06	1.3e-07	1.1e-07	1.00e+00	1.816275922e+04	1.816275785e+04	6.7e-09	0.54
43	2.3e-06	1.3e-07	1.1e-07	1.00e+00	1.816275922e+04	1.816275785e+04	6.7e-09	0.56
44	2.3e-06	1.3e-07	1.1e-07	1.00e+00	1.816275922e+04	1.816275785e+04	6.7e-09	0.56
45	2.3e-06	1.4e-07	1.1e-07	1.00e+00	1.816275922e+04	1.816275785e+04	6.7e-09	0.57
46	2.2e-06	1.4e-07	1.1e-07	1.00e+00	1.816275901e+04	1.816275769e+04	6.5e-09	0.59
47	2.2e-06	1.4e-07	1.1e-07	1.00e+00	1.816275901e+04	1.816275769e+04	6.5e-09	0.60
48	2.2e-06	1.6e-07	1.1e-07	1.00e+00	1.816275901e+04	1.816275768e+04	6.5e-09	0.61
49	2.2e-06	1.6e-07	1.1e-07	1.00e+00	1.816275901e+04	1.816275768e+04	6.5e-09	0.62
50	2.2e-06	1.6e-07	1.1e-07	1.00e+00	1.816275901e+04	1.816275768e+04	6.5e-09	0.63
51	2.2e-06	1.8e-07	1.1e-07	1.00e+00	1.816275900e+04	1.816275768e+04	6.5e-09	0.65
52	2.2e-06	1.5e-07	1.1e-07	1.00e+00	1.816275899e+04	1.816275767e+04	6.5e-09	0.67
53	2.2e-06	1.5e-07	1.1e-07	1.00e+00	1.816275899e+04	1.816275767e+04	6.5e-09	0.68
54	2.2e-06	1.5e-07	1.1e-07	1.00e+00	1.816275899e+04	1.816275767e+04	6.5e-09	0.70

Optimizer terminated. Time: 0.73

```

Interior-point solution summary
Problem status : PRIMAL_AND_DUAL_FEASIBLE
Solution status : OPTIMAL
Primal. obj: 1.8162758994e+04    nrm: 5e+02    Viol. con: 4e-05    var: 1e-06    acc: 3e-08
Dual.   obj: 1.8162757675e+04    nrm: 8e+03    Viol. con: 9e-08    var: 3e-06    acc: 0e+00
Optimizer summary
Optimizer          -                                time: 0.73
  Interior-point      - iterations : 55           time: 0.72
  Basis identification -                                time: 0.00
    Primal             - iterations : 0           time: 0.00
    Dual               - iterations : 0           time: 0.00
    Clean primal       - iterations : 0           time: 0.00
    Clean dual         - iterations : 0           time: 0.00
  Simplex            -                                time: 0.00
    Primal simplex     - iterations : 0           time: 0.00
    Dual simplex       - iterations : 0           time: 0.00
  Mixed integer       - relaxations: 0           time: 0.00

> [mosek] Dual optimality condition in solveCobraEP satisfied.

Optimality conditions (biochemistry)
4.4e-05 || N*(vf - vr) + B*ve - b ||_inf
  Inf || C*(vf - vr) + s_C - d ||_inf, s_C = slack variable
8.8e-08 || cf + ci + N'*y_N + C'*y_C + y_vi + Qv*vf + k_vf + z_vf ||_inf
8.8e-08 || cr - ci - N'*y_N - C'*y_C - y_vi + Qv*vf + k_vr + z_vr ||_inf
  1 || ce + B'*y_N + z_ve ||_inf
8.2e+03 || k_e_1 + z_e_1 ||_inf
8.2e+03 || -g + k_e_vf + z_e_vf ||_inf
1.5e-07 || -g + k_e_vr + z_e_vr ||_inf
1.8e-06 || e_vf + vf*log(vf) ||_inf
  3e-06 || e_vr + vr*log(vr) ||_inf
1.6e+02 || k_q_1 + z_q_1 ||_inf

Derived optimality conditions (biochemistry)
  17 || g.*log(vf) + g - k_vf ||_inf
  0.005 || g.*log(vr) + g - k_vr ||_inf
    17 || cf + ci + N'*y_N + C'*y_C + y_vi + Qv*vf + g.*log(vf) + g + z_vf ||_inf
  0.005 || cr - ci - N'*y_N - C'*y_C - y_vi + Qv*vf + g.*log(vr) + g + z_vr ||_inf

Thermo conditions
  2.6e+02 || g.*log(vr/vf) - 2*N'*y_N - 2*C'*y_C ||_inf
    52 || g.*log(vr/vf) + cr - cf - 2*ci - 2*N'*y_N - 2*C'*y_C - 2*y_vi ||_inf
    87 || g.*log(vr/vf) + cr - cf - 2*ci - 2*N'*y_N - 2*C'*y_C - 2*y_vi - z_vr + z_vf ||_inf
-1.5e+02 min(slack)
  Inf max(slack)

```

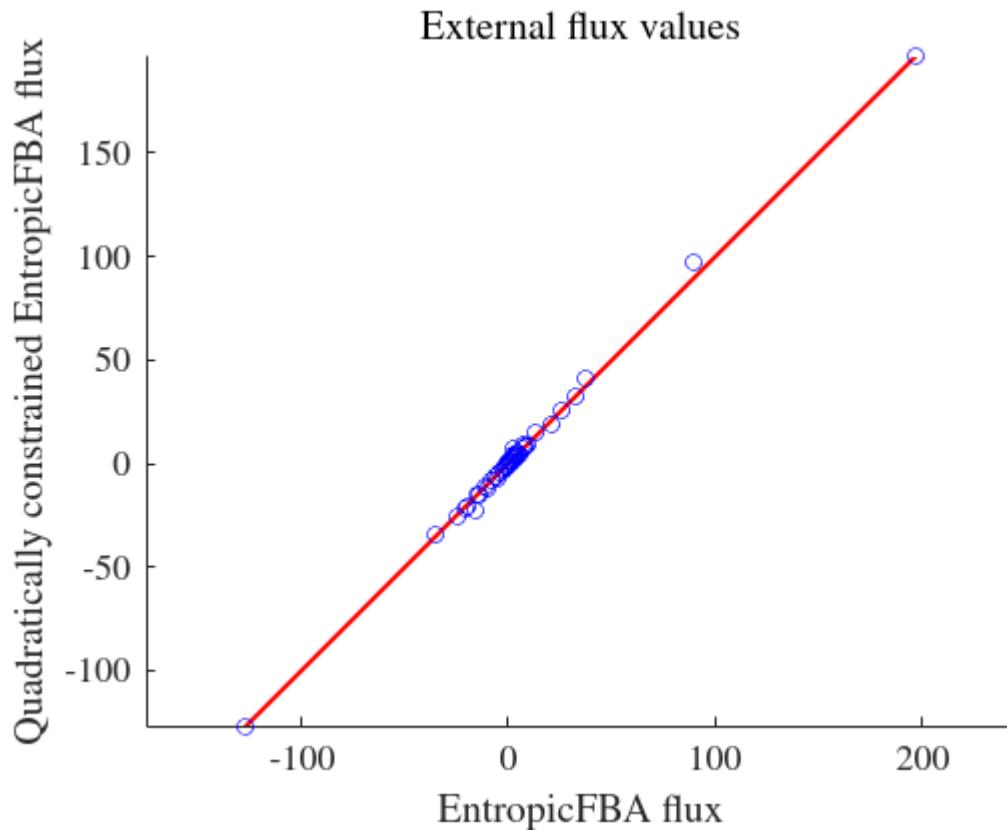
Compare the original external flux vector, with the quadratically constrained external flux vector. The values should be closer to the red line than above, but not exactly, because the quadratic penalty is trading off against entropy maximisation of internal reactions. Change H(j,j) to adjust this trade off.

```

figure
hold on
fplot(@(x) x, 'LineWidth', 1.5, 'Color', 'r')
plot(solution.v(~model.SConsistentRxnBool),solutionQEFBA.v(~model.SConsistent
RxnBool), 'o', 'Color', 'b')
xlabel('EntropicFBA flux')
ylabel('Quadratically constrained EntropicFBA flux')

```

```
title('External flux values')
axis equal
```



## Quadratically constrained entropic flux balance analysis - subset of external reactions

Generate a random given external flux vector that is a perturbation of the previously obtained external flux vector and then quadratically penalise any deviation from it.

```
model.h = (solution.v).*(rand(length(solution.v),1)+0.5)*2;
```

Do not optimise toward any internal net flux

```
model.h(model.SConsistentRxnBool)=NaN;
```

Only optimise toward the top 10 magnitude given external net flux

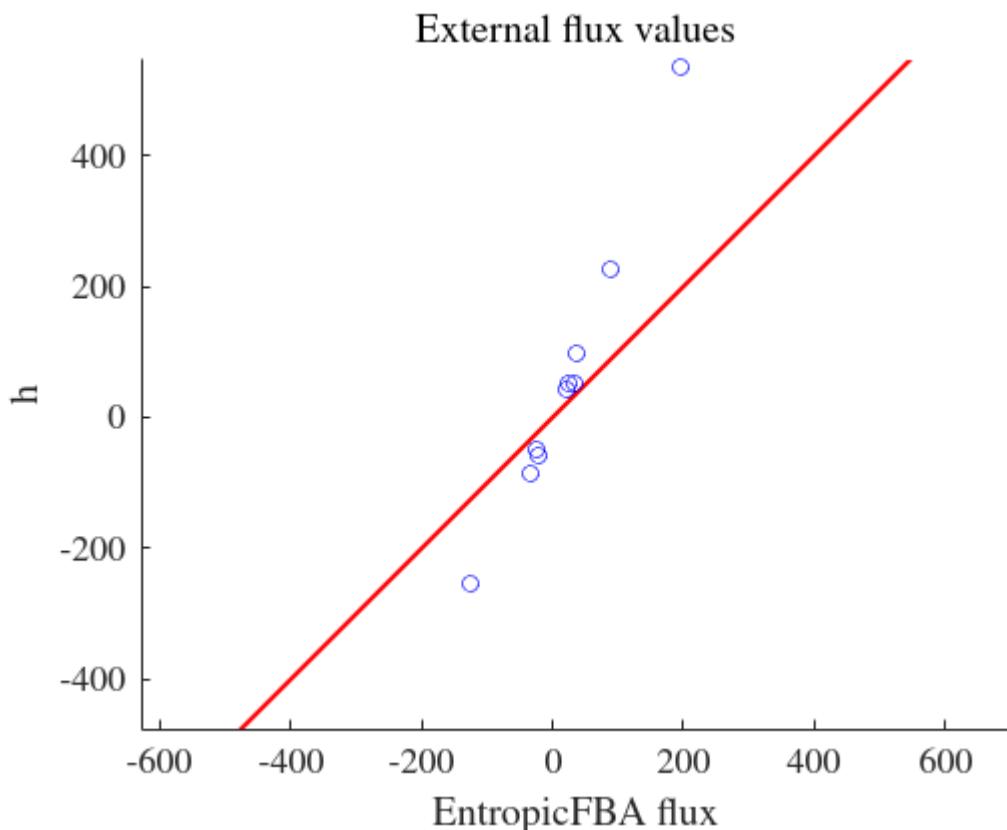
```
[sortedh,ind]=sort(abs(model.h),'descend','MissingPlacement','last');
if length(ind)>10
    model.h(ind(11:end))=NaN;
end
```

Compare the original external flux vector, with the external flux vector to penalise deviation from

```

figure
hold on
fplot(@(x) x, 'LineWidth', 1.5, 'Color', 'r')
plot(solution.v(isfinite(model.h)),model.h(isfinite(model.h)), 'o', 'Color', 'b')
)
xlabel('EntropicFBA flux')
ylabel('h')
title('External flux values')
axis equal

```



Set the penalty

```

HH = ones(length(solution.v),1);
HH(model.SConsistentRxnBool)=0;
model.H = spdiags(HH,0,length(solution.v),length(solution.v));

```

Run the optimisation

```
[solutionQEFBA,modelOut] = entropicFluxBalanceAnalysis(model,param);
```

Using directional internal net flux bounds only.  
Using existing external net flux bounds without modification.

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Problem

Name	:
Objective sense	: minimize
Type	: LO (linear optimization problem)
Constraints	: 2975
Affine conic cons.	: 0
Disjunctive cons.	: 0
Cones	: 0
Scalar variables	: 3635
Matrix variables	: 0
Integer variables	: 0

Optimizer started.

Presolve started.

Eliminator started.

Freed constraints in eliminator : 1219

Eliminator terminated.

Linear dependency checker started.

Linear dependency checker terminated.

Eliminator started.

Freed constraints in eliminator : 141

Eliminator terminated.

Eliminator - tries	: 2	time	: 0.00
Lin. dep. - tries	: 1	time	: 0.00
Lin. dep. - primal attempts	: 1	successes	: 1
Lin. dep. - dual attempts	: 0	successes	: 0
Lin. dep. - primal deps.	: 9	dual deps.	: 0

Presolve terminated. Time: 0.02

Optimizer - threads	: 18		
Optimizer - solved problem	: the primal		
Optimizer - Constraints	: 512		
Optimizer - Cones	: 0		
Optimizer - Scalar variables	: 1700	conic	: 0
Optimizer - Semi-definite variables	: 0	scalarized	: 0
Factor - setup time	: 0.01		
Factor - dense det. time	: 0.00	GP order time	: 0.00
Factor - nonzeros before factor	: 5040	after factor	: 1.19e+04
Factor - dense dim.	: 1	flops	: 5.13e+05

ITE	PFEAS	DFEAS	GFEAS	PRSTATUS	POBJ	DOBJ	MU	TIME
0	8.0e+03	1.2e+03	2.7e+04	0.00e+00	2.536209125e+04	-1.137375866e+03	1.3e+02	0.04
1	4.3e+03	7.2e-01	1.4e+04	1.01e+00	1.109112427e+04	2.131423372e+03	6.8e+01	0.05
2	1.6e+03	2.7e-01	5.2e+03	1.30e+00	5.333642613e+03	2.475579900e+03	2.5e+01	0.05
3	3.7e+02	6.2e-02	1.2e+03	1.11e+00	1.677123434e+03	1.043181022e+03	5.9e+00	0.05
4	4.5e+01	7.6e-03	1.5e+02	1.04e+00	4.494526587e+02	3.734394760e+02	7.1e-01	0.05
5	2.3e+01	3.8e-03	7.5e+01	1.01e+00	3.721136544e+02	3.336327497e+02	3.6e-01	0.06
6	4.2e+00	7.1e-04	1.4e+01	1.01e+00	3.060528620e+02	2.990462288e+02	6.7e-02	0.06
7	1.3e+00	2.3e-04	4.4e+00	1.00e+00	2.951088773e+02	2.928706595e+02	2.1e-02	0.06
8	5.7e-01	9.6e-05	1.9e+00	1.00e+00	2.921571806e+02	2.912048430e+02	9.1e-03	0.06
9	9.0e-02	1.5e-05	3.0e-01	1.00e+00	2.902963878e+02	2.901452889e+02	1.4e-03	0.07
10	2.0e-02	3.4e-06	6.6e-02	9.99e-01	2.900126991e+02	2.899790785e+02	3.2e-04	0.07
11	6.9e-03	1.2e-06	2.3e-02	1.00e+00	2.899593316e+02	2.899477152e+02	1.1e-04	0.07
12	3.9e-04	6.5e-08	1.3e-03	1.00e+00	2.899323089e+02	2.899316648e+02	6.1e-06	0.07
13	1.5e-05	2.5e-09	4.9e-05	1.00e+00	2.899306835e+02	2.899306588e+02	2.4e-07	0.08
14	3.4e-07	3.7e-10	3.5e-07	1.00e+00	2.899306169e+02	2.899306167e+02	4.6e-10	0.08

Basis identification started.

Primal basis identification phase started.

Primal basis identification phase terminated. Time: 0.00

Dual basis identification phase started.

Dual basis identification phase terminated. Time: 0.00

Basis identification terminated. Time: 0.01

Optimizer terminated. Time: 0.10

Interior-point solution summary

Problem status : PRIMAL_AND_DUAL_FEASIBLE			
Solution status : OPTIMAL			
Primal. obj: 2.8993061688e+02	nrm: 5e+02	Viol. con: 1e-06	var: 1e-07
Dual. obj: 2.8993061665e+02	nrm: 5e+00	Viol. con: 0e+00	var: 2e-10

Basic solution summary

Problem status : PRIMAL_AND_DUAL_FEASIBLE			
Solution status : OPTIMAL			
Primal. obj: 2.8993061677e+02	nrm: 5e+02	Viol. con: 8e-13	var: 3e-14
Dual. obj: 2.8993061672e+02	nrm: 6e+00	Viol. con: 6e-11	var: 4e-07

Optimizer summary

Optimizer	-	time: 0.10
Interior-point	- iterations : 14	time: 0.09
Basis identification	-	time: 0.01
Primal	- iterations : 37	time: 0.00
Dual	- iterations : 95	time: 0.00
Clean primal	- iterations : 0	time: 0.00
Clean dual	- iterations : 0	time: 0.00
Simplex	-	time: 0.00
Primal simplex	- iterations : 0	time: 0.00
Dual simplex	- iterations : 0	time: 0.00
Mixed integer	- relaxations: 0	time: 0.00

solveCobraEP: LP part of EPproblem is feasible according to solveCobraLP with mosek.

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Platform: Linux/64-X86

Problem

Name	:
Objective sense	: minimize
Type	: CONIC (conic optimization problem)
Constraints	: 2975
Affine conic cons.	: 3430 (10290 rows)
Disjunctive cons.	: 0
Cones	: 0
Scalar variables	: 7067
Matrix variables	: 0
Integer variables	: 0

Optimizer started.

Presolve started.

Linear dependency checker started.

Linear dependency checker terminated.

Eliminator started.

Freed constraints in eliminator : 7

Eliminator terminated.

Eliminator - tries	: 1	time	: 0.00
Lin. dep. - tries	: 1	time	: 0.00
Lin. dep. - primal attempts	: 1	successes	: 1
Lin. dep. - dual attempts	: 0	successes	: 0
Lin. dep. - primal deps.	: 25	dual deps.	: 0

Presolve terminated. Time: 0.03

Optimizer - threads : 18

Optimizer	- solved problem		: the primal					
Optimizer	- Constraints		: 1960					
Optimizer	- Cones		: 3430					
Optimizer	- Scalar variables		: 11284		conic		: 10290	
Optimizer	- Semi-definite variables	: 0			scalarized		: 0	
Factor	- setup time		: 0.02					
Factor	- dense det. time		: 0.00		GP order time		: 0.00	
Factor	- nonzeros before factor		: 1.19e+04		after factor		: 2.06e+04	
Factor	- dense dim.		: 0		flops		: 7.95e+05	
ITE	PFEAS	DFEAS	GFEAS	PRSTATUS	POBJ	DOBJ	MU	TIME
0	1.0e+04	1.2e+00	1.0e+04	0.00e+00	5.947759534e+03	-4.414972768e+03	1.0e+00	0.06
1	8.1e+03	9.5e-01	9.3e+03	-9.99e-01	8.037729882e+03	-2.321978061e+03	8.1e-01	0.08
2	7.3e+03	8.6e-01	8.8e+03	-9.96e-01	9.251313347e+03	-1.094838395e+03	7.3e-01	0.09
3	5.4e+03	6.3e-01	7.5e+03	-9.85e-01	1.411292582e+04	3.857496674e+03	5.4e-01	0.10
4	1.8e+03	2.1e-01	4.1e+03	-9.66e-01	5.104523733e+04	4.123658305e+04	1.8e-01	0.11
5	7.7e+02	9.1e-02	2.5e+03	-8.61e-01	9.839593865e+04	8.950761846e+04	7.7e-02	0.12
6	4.2e+02	4.9e-02	1.5e+03	-6.00e-01	1.025664394e+05	9.529333740e+04	4.2e-02	0.13
7	3.0e+02	3.5e-02	1.0e+03	-1.72e-01	8.505723708e+04	7.901253075e+04	3.0e-02	0.14
8	2.1e+02	2.5e-02	6.5e+02	8.13e-02	6.954940345e+04	6.468064026e+04	2.1e-02	0.14
9	1.2e+02	1.5e-02	3.3e+02	2.99e-01	5.111476715e+04	4.781160692e+04	1.2e-02	0.15
10	9.8e+01	1.2e-02	2.4e+02	5.63e-01	4.528535708e+04	4.256295185e+04	9.8e-03	0.16
11	3.6e+01	4.3e-03	5.9e+01	6.52e-01	2.920508427e+04	2.807972182e+04	3.6e-03	0.17
12	9.4e+00	1.1e-03	8.3e+00	8.79e-01	2.082004927e+04	2.051703883e+04	9.4e-04	0.18
13	4.4e+00	5.2e-04	2.8e+00	9.76e-01	1.924949650e+04	1.910574210e+04	4.4e-04	0.19
14	1.0e+00	1.2e-04	3.2e-01	9.90e-01	1.814985735e+04	1.811605395e+04	1.0e-04	0.20
15	2.1e-01	2.5e-05	3.0e-02	9.99e-01	1.792314815e+04	1.791624423e+04	2.1e-05	0.21
16	5.3e-02	6.2e-06	3.8e-03	1.00e+00	1.787841040e+04	1.787669859e+04	5.3e-06	0.22
17	7.0e-03	8.3e-07	1.9e-04	1.00e+00	1.786577541e+04	1.786554655e+04	7.0e-07	0.23
18	6.9e-03	8.1e-07	1.8e-04	1.00e+00	1.786575033e+04	1.786552448e+04	6.9e-07	0.24
19	6.0e-03	7.0e-07	1.5e-04	1.00e+00	1.786548486e+04	1.786529081e+04	6.0e-07	0.25
20	5.9e-03	6.9e-07	1.4e-04	1.00e+00	1.786545512e+04	1.786526463e+04	5.9e-07	0.26
21	5.8e-03	6.8e-07	1.4e-04	1.00e+00	1.786544992e+04	1.786526005e+04	5.8e-07	0.27
22	3.3e-03	3.9e-07	6.0e-05	1.00e+00	1.786475410e+04	1.786464697e+04	3.3e-07	0.28
23	3.2e-03	3.8e-07	5.8e-05	1.00e+00	1.786473323e+04	1.786462859e+04	3.2e-07	0.29
24	3.2e-03	3.8e-07	5.7e-05	1.00e+00	1.786472788e+04	1.786462387e+04	3.2e-07	0.30
25	3.2e-03	3.8e-07	5.7e-05	1.00e+00	1.786472784e+04	1.786462384e+04	3.2e-07	0.31
26	3.2e-03	3.8e-07	5.7e-05	1.00e+00	1.786472783e+04	1.786462383e+04	3.2e-07	0.32
27	2.9e-03	3.4e-07	4.9e-05	1.00e+00	1.786464169e+04	1.786454793e+04	2.9e-07	0.33
28	2.9e-03	3.4e-07	4.9e-05	1.00e+00	1.786463783e+04	1.786454452e+04	2.9e-07	0.34
29	2.9e-03	3.4e-07	4.9e-05	1.00e+00	1.786463779e+04	1.786454449e+04	2.9e-07	0.35
30	2.8e-03	3.3e-07	4.8e-05	1.00e+00	1.786462591e+04	1.786453402e+04	2.8e-07	0.36
31	2.8e-03	3.3e-07	4.8e-05	1.00e+00	1.786462415e+04	1.786453247e+04	2.8e-07	0.36
32	2.8e-03	3.3e-07	4.7e-05	1.00e+00	1.786462172e+04	1.786453033e+04	2.8e-07	0.37
33	2.8e-03	3.3e-07	4.7e-05	1.00e+00	1.786462156e+04	1.786453019e+04	2.8e-07	0.39
34	2.8e-03	3.3e-07	4.7e-05	1.00e+00	1.786462155e+04	1.786453017e+04	2.8e-07	0.40
35	2.8e-03	3.3e-07	4.7e-05	1.00e+00	1.786462154e+04	1.786453017e+04	2.8e-07	0.41
36	6.9e-04	8.1e-08	6.0e-06	1.00e+00	1.786404195e+04	1.786401940e+04	6.9e-08	0.43
37	6.9e-04	8.1e-08	6.0e-06	1.00e+00	1.786404189e+04	1.786401935e+04	6.9e-08	0.44
38	6.9e-04	8.1e-08	6.0e-06	1.00e+00	1.786404189e+04	1.786401935e+04	6.9e-08	0.45
39	6.9e-04	8.1e-08	5.9e-06	1.00e+00	1.786404177e+04	1.786401925e+04	6.9e-08	0.46
40	6.9e-04	8.1e-08	5.9e-06	1.00e+00	1.786404174e+04	1.786401922e+04	6.9e-08	0.47
41	6.9e-04	8.1e-08	5.9e-06	1.00e+00	1.786404168e+04	1.786401916e+04	6.9e-08	0.47
42	6.9e-04	8.1e-08	5.9e-06	1.00e+00	1.786404146e+04	1.786401897e+04	6.9e-08	0.48
43	6.9e-04	8.1e-08	5.9e-06	1.00e+00	1.786404146e+04	1.786401897e+04	6.9e-08	0.49
44	6.9e-04	8.1e-08	5.9e-06	1.00e+00	1.786404144e+04	1.786401895e+04	6.9e-08	0.50
45	6.3e-04	7.4e-08	5.1e-06	1.00e+00	1.786402303e+04	1.786400265e+04	6.3e-08	0.52
46	6.3e-04	7.4e-08	5.1e-06	1.00e+00	1.786402298e+04	1.786400261e+04	6.3e-08	0.53
47	6.3e-04	7.3e-08	5.1e-06	1.00e+00	1.786402288e+04	1.786400252e+04	6.3e-08	0.54
48	6.3e-04	7.3e-08	5.1e-06	1.00e+00	1.786402288e+04	1.786400251e+04	6.3e-08	0.54
49	6.1e-04	7.1e-08	4.9e-06	1.00e+00	1.786401709e+04	1.786399739e+04	6.1e-08	0.56
50	6.1e-04	7.1e-08	4.9e-06	1.00e+00	1.786401706e+04	1.786399736e+04	6.1e-08	0.57
51	6.1e-04	7.1e-08	4.9e-06	1.00e+00	1.786401704e+04	1.786399735e+04	6.1e-08	0.58
52	6.1e-04	7.1e-08	4.9e-06	1.00e+00	1.786401697e+04	1.786399728e+04	6.1e-08	0.59
53	6.0e-04	7.1e-08	4.8e-06	1.00e+00	1.786401648e+04	1.786399685e+04	6.0e-08	0.60

54	6.0e-04	7.1e-08	4.8e-06	1.00e+00	1.786401642e+04	1.786399680e+04	6.0e-08	0.61
55	6.0e-04	7.1e-08	4.8e-06	1.00e+00	1.786401641e+04	1.786399678e+04	6.0e-08	0.62
56	6.0e-04	7.1e-08	4.8e-06	1.00e+00	1.786401635e+04	1.786399673e+04	6.0e-08	0.63
57	6.0e-04	7.1e-08	4.8e-06	1.00e+00	1.786401627e+04	1.786399667e+04	6.0e-08	0.64
58	6.0e-04	7.1e-08	4.8e-06	1.00e+00	1.786401624e+04	1.786399664e+04	6.0e-08	0.65
59	6.0e-04	7.1e-08	4.8e-06	1.00e+00	1.786401613e+04	1.786399654e+04	6.0e-08	0.66
60	6.0e-04	7.1e-08	4.8e-06	1.00e+00	1.786401596e+04	1.786399639e+04	6.0e-08	0.67
61	6.0e-04	7.1e-08	4.8e-06	1.00e+00	1.786401596e+04	1.786399639e+04	6.0e-08	0.67
62	6.0e-04	7.1e-08	4.8e-06	1.00e+00	1.786401591e+04	1.786399635e+04	6.0e-08	0.68
63	6.0e-04	7.0e-08	4.8e-06	1.00e+00	1.786401513e+04	1.786399565e+04	6.0e-08	0.70
64	6.0e-04	7.0e-08	4.8e-06	1.00e+00	1.786401502e+04	1.786399556e+04	6.0e-08	0.71
65	6.0e-04	7.0e-08	4.8e-06	1.00e+00	1.786401502e+04	1.786399556e+04	6.0e-08	0.72
66	6.0e-04	7.0e-08	4.8e-06	1.00e+00	1.786401498e+04	1.786399552e+04	6.0e-08	0.73
67	6.0e-04	7.0e-08	4.8e-06	1.00e+00	1.786401498e+04	1.786399552e+04	6.0e-08	0.73
68	6.0e-04	7.0e-08	4.8e-06	1.00e+00	1.786401495e+04	1.786399550e+04	6.0e-08	0.74
69	6.0e-04	7.0e-08	4.8e-06	1.00e+00	1.786401495e+04	1.786399549e+04	6.0e-08	0.75
70	6.0e-04	7.0e-08	4.8e-06	1.00e+00	1.786401473e+04	1.786399530e+04	6.0e-08	0.77
71	5.9e-04	7.0e-08	4.7e-06	1.00e+00	1.786401388e+04	1.786399455e+04	5.9e-08	0.79
72	5.9e-04	6.9e-08	4.7e-06	1.00e+00	1.786401317e+04	1.786399392e+04	5.9e-08	0.81
73	5.9e-04	6.9e-08	4.6e-06	1.00e+00	1.786401117e+04	1.786399215e+04	5.9e-08	0.83
74	5.9e-04	6.9e-08	4.6e-06	1.00e+00	1.786401117e+04	1.786399215e+04	5.9e-08	0.84
75	5.9e-04	6.9e-08	4.6e-06	1.00e+00	1.786401115e+04	1.786399214e+04	5.9e-08	0.85
76	5.9e-04	6.9e-08	4.6e-06	1.00e+00	1.786401114e+04	1.786399212e+04	5.9e-08	0.86
77	5.9e-04	6.9e-08	4.6e-06	1.00e+00	1.786401114e+04	1.786399212e+04	5.9e-08	0.87
78	5.9e-04	6.9e-08	4.6e-06	1.00e+00	1.786401111e+04	1.786399210e+04	5.9e-08	0.88
79	5.9e-04	6.9e-08	4.6e-06	1.00e+00	1.786401109e+04	1.786399207e+04	5.9e-08	0.89
80	5.9e-04	6.9e-08	4.6e-06	1.00e+00	1.786401107e+04	1.786399206e+04	5.9e-08	0.89
81	5.8e-04	6.8e-08	4.6e-06	1.00e+00	1.786401041e+04	1.786399148e+04	5.8e-08	0.91
82	5.8e-04	6.8e-08	4.6e-06	1.00e+00	1.786401039e+04	1.786399146e+04	5.8e-08	0.93
83	5.8e-04	6.8e-08	4.6e-06	1.00e+00	1.786401037e+04	1.786399144e+04	5.8e-08	0.95
84	5.8e-04	6.8e-08	4.6e-06	1.00e+00	1.786401037e+04	1.786399144e+04	5.8e-08	0.96
85	5.8e-04	6.8e-08	4.6e-06	1.00e+00	1.786401036e+04	1.786399143e+04	5.8e-08	0.96
86	5.8e-04	6.8e-08	4.5e-06	1.00e+00	1.786400875e+04	1.786399001e+04	5.8e-08	0.98
87	5.8e-04	6.8e-08	4.5e-06	1.00e+00	1.786400874e+04	1.786399000e+04	5.8e-08	0.99
88	5.8e-04	6.8e-08	4.5e-06	1.00e+00	1.786400874e+04	1.786398999e+04	5.8e-08	1.00
89	5.8e-04	6.8e-08	4.5e-06	1.00e+00	1.786400874e+04	1.786398999e+04	5.8e-08	1.01
90	5.8e-04	6.8e-08	4.5e-06	1.00e+00	1.786400869e+04	1.786398996e+04	5.8e-08	1.03
91	5.8e-04	6.8e-08	4.5e-06	1.00e+00	1.786400869e+04	1.786398995e+04	5.8e-08	1.04
92	5.8e-04	6.8e-08	4.5e-06	1.00e+00	1.786400855e+04	1.786398983e+04	5.8e-08	1.06
93	5.8e-04	6.8e-08	4.5e-06	1.00e+00	1.786400854e+04	1.786398982e+04	5.8e-08	1.07
94	5.8e-04	6.8e-08	4.5e-06	1.00e+00	1.786400853e+04	1.786398981e+04	5.8e-08	1.08
95	5.8e-04	6.8e-08	4.5e-06	1.00e+00	1.786400852e+04	1.786398980e+04	5.8e-08	1.09
96	5.8e-04	6.8e-08	4.5e-06	1.00e+00	1.786400851e+04	1.786398980e+04	5.8e-08	1.10
97	5.8e-04	6.8e-08	4.5e-06	1.00e+00	1.786400849e+04	1.786398978e+04	5.8e-08	1.11
98	5.8e-04	6.8e-08	4.5e-06	1.00e+00	1.786400849e+04	1.786398978e+04	5.8e-08	1.14
99	5.8e-04	6.8e-08	4.5e-06	1.00e+00	1.786400849e+04	1.786398978e+04	5.8e-08	1.15
100	5.8e-04	6.7e-08	4.5e-06	1.00e+00	1.786400830e+04	1.786398960e+04	5.8e-08	1.15
101	5.8e-04	6.7e-08	4.5e-06	1.00e+00	1.786400824e+04	1.786398955e+04	5.8e-08	1.16
102	5.7e-04	6.7e-08	4.5e-06	1.00e+00	1.786400790e+04	1.786398925e+04	5.7e-08	1.17
103	5.7e-04	6.7e-08	4.5e-06	1.00e+00	1.786400770e+04	1.786398908e+04	5.7e-08	1.18
104	5.7e-04	6.7e-08	4.5e-06	1.00e+00	1.786400759e+04	1.786398898e+04	5.7e-08	1.19
105	5.7e-04	6.7e-08	4.5e-06	1.00e+00	1.786400759e+04	1.786398897e+04	5.7e-08	1.20
106	5.2e-04	6.1e-08	3.8e-06	1.00e+00	1.786399159e+04	1.786397481e+04	5.2e-08	1.23
107	5.2e-04	6.1e-08	3.8e-06	1.00e+00	1.786399156e+04	1.786397479e+04	5.2e-08	1.24
108	5.2e-04	6.1e-08	3.8e-06	1.00e+00	1.786399154e+04	1.786397477e+04	5.2e-08	1.24
109	5.1e-04	6.0e-08	3.8e-06	1.00e+00	1.786399031e+04	1.786397367e+04	5.1e-08	1.26
110	5.1e-04	6.0e-08	3.8e-06	1.00e+00	1.786399014e+04	1.786397353e+04	5.1e-08	1.28
111	5.1e-04	6.0e-08	3.8e-06	1.00e+00	1.786399012e+04	1.786397351e+04	5.1e-08	1.30
112	5.1e-04	6.0e-08	3.8e-06	1.00e+00	1.786399005e+04	1.786397344e+04	5.1e-08	1.31
113	5.1e-04	6.0e-08	3.8e-06	1.00e+00	1.786399004e+04	1.786397344e+04	5.1e-08	1.32
114	5.1e-04	6.0e-08	3.8e-06	1.00e+00	1.786399003e+04	1.786397343e+04	5.1e-08	1.33
115	5.1e-04	6.0e-08	3.8e-06	1.00e+00	1.786399003e+04	1.786397343e+04	5.1e-08	1.34
116	5.1e-04	6.0e-08	3.8e-06	1.00e+00	1.786399000e+04	1.786397340e+04	5.1e-08	1.36
117	3.0e-04	3.6e-08	1.7e-06	1.00e+00	1.786393151e+04	1.786392160e+04	3.0e-08	1.37

118	3.0e-04	3.5e-08	1.7e-06	1.00e+00	1.786393094e+04	1.786392111e+04	3.0e-08	1.39
119	3.0e-04	3.5e-08	1.7e-06	1.00e+00	1.786393094e+04	1.786392110e+04	3.0e-08	1.40
120	3.0e-04	3.5e-08	1.7e-06	1.00e+00	1.786393091e+04	1.786392108e+04	3.0e-08	1.41
121	2.9e-04	3.4e-08	1.6e-06	1.00e+00	1.786392763e+04	1.786391817e+04	2.9e-08	1.43
122	2.9e-04	3.4e-08	1.6e-06	1.00e+00	1.786392762e+04	1.786391816e+04	2.9e-08	1.45
123	2.9e-04	3.4e-08	1.6e-06	1.00e+00	1.786392762e+04	1.786391817e+04	2.9e-08	1.46
124	2.9e-04	3.4e-08	1.6e-06	1.00e+00	1.786392762e+04	1.786391817e+04	2.9e-08	1.46
125	2.9e-04	3.4e-08	1.6e-06	1.00e+00	1.786392753e+04	1.786391808e+04	2.9e-08	1.48
126	2.9e-04	3.4e-08	1.6e-06	1.00e+00	1.786392752e+04	1.786391807e+04	2.9e-08	1.50
127	2.9e-04	3.4e-08	1.6e-06	1.00e+00	1.786392752e+04	1.786391807e+04	2.9e-08	1.51
128	2.9e-04	3.4e-08	1.6e-06	1.00e+00	1.786392748e+04	1.786391804e+04	2.9e-08	1.53
129	2.9e-04	3.4e-08	1.6e-06	1.00e+00	1.786392748e+04	1.786391804e+04	2.9e-08	1.54
130	2.9e-04	3.4e-08	1.6e-06	1.00e+00	1.786392748e+04	1.786391804e+04	2.9e-08	1.55

Optimizer terminated. Time: 1.59

#### Interior-point solution summary

Problem status : PRIMAL_AND_DUAL_FEASIBLE								
Solution status : OPTIMAL								
Primal. obj: 1.7863927476e+04	nrm: 5e+02	Viol.	con: 5e-04	var: 1e-05	acc: 1e-07			
Dual. obj: 1.7863918037e+04	nrm: 8e+03	Viol.	con: 6e-07	var: 1e-06	acc: 0e+00			

#### Optimizer summary

Optimizer	-	time: 1.59
Interior-point	- iterations : 131	time: 1.57
Basis identification	-	time: 0.00
Primal	- iterations : 0	time: 0.00
Dual	- iterations : 0	time: 0.00
Clean primal	- iterations : 0	time: 0.00
Clean dual	- iterations : 0	time: 0.00
Simplex	-	time: 0.00
Primal simplex	- iterations : 0	time: 0.00
Dual simplex	- iterations : 0	time: 0.00
Mixed integer	- relaxations: 0	time: 0.00

> [mosek] Dual optimality condition in solveCobraEP satisfied.

#### Optimality conditions (biochemistry)

0.00049    N*(vf - vr) + B*ve - b   _inf								
Inf    C*(vf - vr) + s_C - d   _inf, s_C = slack variable								
6.4e-07    cf + ci + N'*y_N + C'*y_C + y_vi + Qv*vf + k_vf + z_vf   _inf								
6.4e-07    cr - ci - N'*y_N - C'*y_C - y_vi + Qv*vf + k_vr + z_vr   _inf								
1    ce + B'*y_N + z_ve   _inf								
8.2e+03    k_e_1 + z_e_1   _inf								
8.2e+03    -g + k_e_vf + z_e_vf   _inf								
1.1e-06    -g + k_e_vr + z_e_vr   _inf								
1.5e-05    e_vf + vf*log(vf)   _inf								
1.5e-05    e_vr + vr*log(vr)   _inf								
1.7    k_q_1 + z_q_1   _inf								

#### Derived optimality conditions (biochemistry)

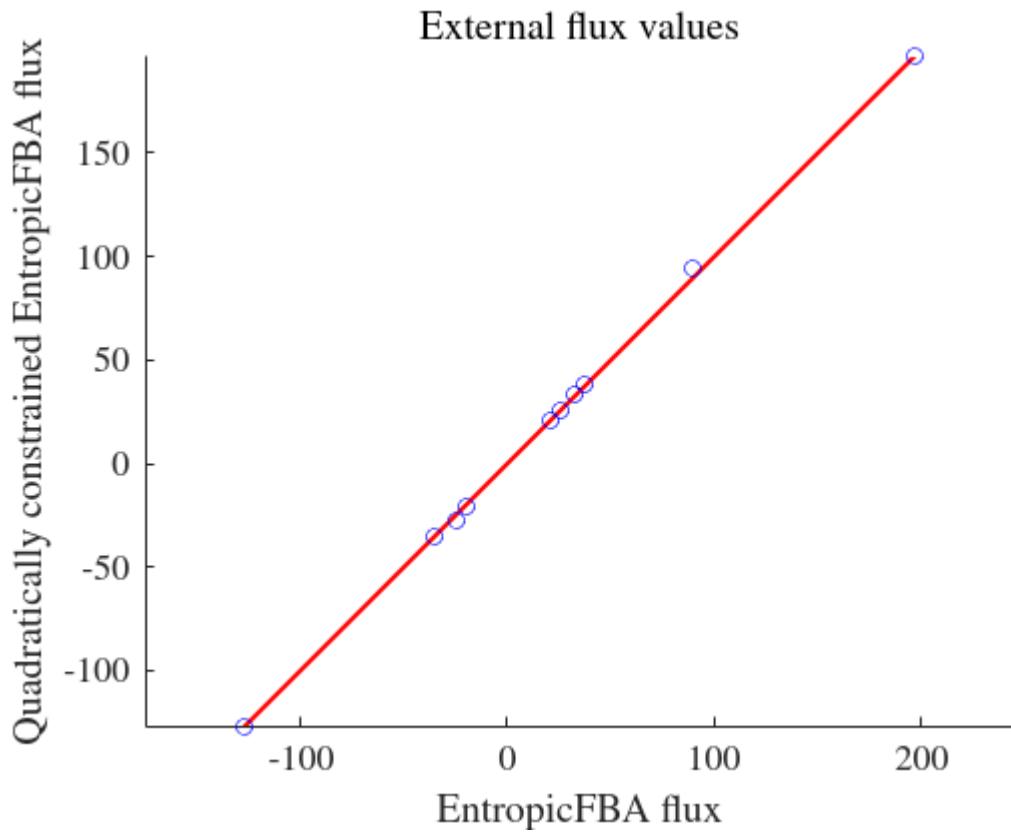
21    g.*log(vf) + g - k_vf   _inf								
0.022    g.*log(vr) + g - k_vr   _inf								
21    cf + ci + N'*y_N + C'*y_C + y_vi + Qv*vf + g.*log(vf) + g + z_vf   _inf								
0.022    cr - ci - N'*y_N - C'*y_C - y_vi + Qv*vf + g.*log(vr) + g + z_vr   _inf								

#### Thermo conditions

2.7e+02    g.*log(vr/vf) - 2*N'*y_N - 2*C'*y_C   _inf								
56    g.*log(vr/vf) + cr - cf - 2*ci - 2*N'*y_N - 2*C'*y_C - 2*y_vi   _inf								
91    g.*log(vr/vf) + cr - cf - 2*ci - 2*N'*y_N - 2*C'*y_C - 2*y_vi - z_vr + z_vf   _inf								
-1.5e+02 min(slack)								
Inf max(slack)								

Compare the original external flux vector, with the quadratically constrained external flux vector. The values should be closer to the red line than above, but not exactly, because the quadratic penalty is trading off against entropy maximisation of internal reactions. Change  $H(j,j)$  to adjust this trade off.

```
figure
hold on
fplot(@(x) x, 'LineWidth', 1.5, 'Color', 'r')
plot(solution.v(isfinite(model.h)),solutionQEFBA.v(isfinite(model.h)), 'o', 'Color', 'b')
xlabel('EntropicFBA flux')
ylabel('Quadratically constrained EntropicFBA flux')
title('External flux values')
axis equal
```



## Quadratically constrained entropic flux balance analysis - subset of external reactions and no coupling constraints

```
model = rmfield(model,{'C','d'});
```

Generate a random given external flux vector that is a perturbation of the previously obtained external flux vector and then quadratically penalise any deviation from it.

```
model.h = (solution.v).*(rand(length(solution.v),1)+0.5)*2;
```

Do not optimise toward any internal net flux

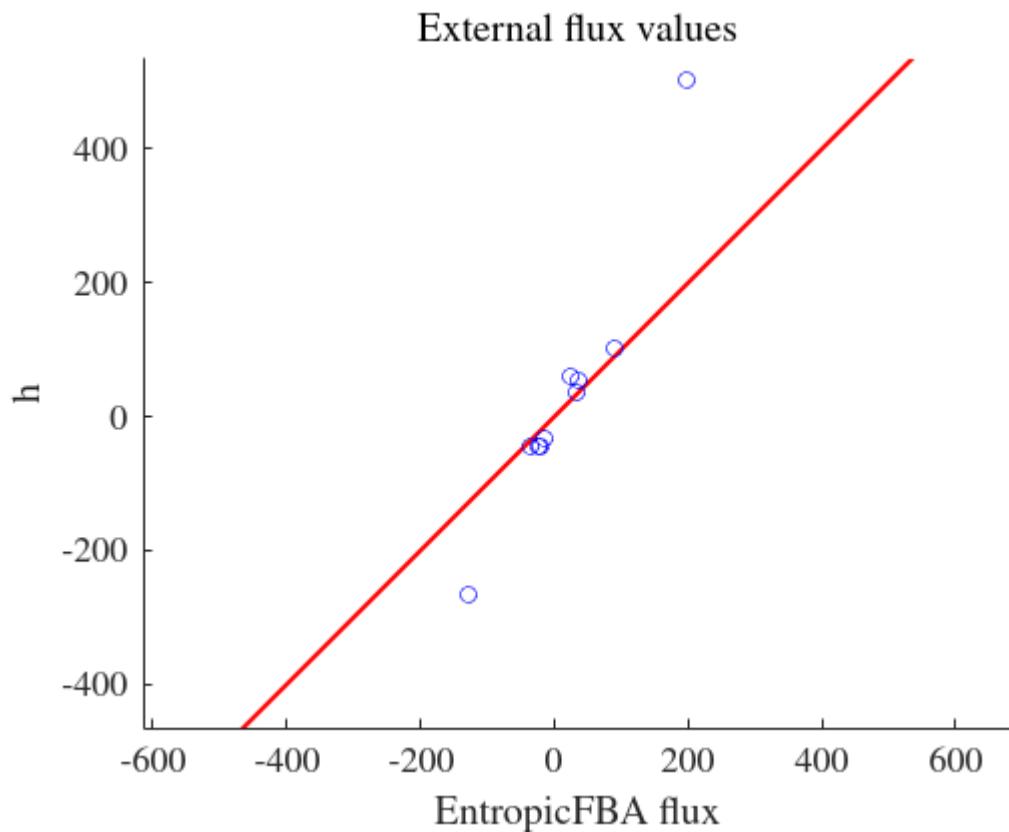
```
model.h(model.SConsistentRxnBool)=NaN;
```

Only optimise toward the top 10 magnitude given external net flux

```
[sortedh,ind]=sort(abs(model.h), 'descend', 'MissingPlacement', 'last');
if length(ind)>10
    model.h(ind(11:end))=NaN;
end
```

Compare the original external flux vector, with the external flux vector to penalise deviation from

```
figure
hold on
fplot(@(x) x, 'LineWidth', 1.5, 'Color', 'r')
plot(solution.v(isfinite(model.h)),model.h(isfinite(model.h)), 'o', 'Color', 'b')
)
xlabel('EntropicFBA flux')
ylabel('h')
title('External flux values')
axis equal
```



Set the penalty

```
HH = ones(length(solution.v),1);
```

```

HH(model.SConsistentRxnBool)=0;
model.H = spdiags(HH,0,length(solution.v),length(solution.v));

```

## Run the optimisation

```
[solutionQEFBA,modelOut] = entropicFluxBalanceAnalysis(model,param);
```

Using directional internal net flux bounds only.  
 Using existing external net flux bounds without modification.

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```

Problem
Name          :
Objective sense : minimize
Type          : LO (linear optimization problem)
Constraints   : 2964
Affine conic cons. : 0
Disjunctive cons. : 0
Cones         : 0
Scalar variables : 3635
Matrix variables : 0
Integer variables : 0

Optimizer started.
Presolve started.
Eliminator started.
Freed constraints in eliminator : 1218
Eliminator terminated.
Linear dependency checker started.
Linear dependency checker terminated.
Eliminator started.
Freed constraints in eliminator : 141
Eliminator terminated.
Eliminator - tries           : 2             time       : 0.00
Lin. dep. - tries            : 1             time       : 0.00
Lin. dep. - primal attempts : 1             successes : 1
Lin. dep. - dual attempts   : 0             successes : 0
Lin. dep. - primal deps.   : 9             dual deps. : 0
Presolve terminated. Time: 0.02
GP based matrix reordering started.
GP based matrix reordering terminated.
Optimizer - threads          : 18
Optimizer - solved problem    : the primal
Optimizer - Constraints       : 502
Optimizer - Cones             : 0
Optimizer - Scalar variables  : 1690           conic      : 0
Optimizer - Semi-definite variables: 0           scalarized : 0
Factor - setup time           : 0.01
Factor - dense det. time     : 0.00           GP order time : 0.00
Factor - nonzeros before factor : 4935         after factor  : 1.17e+04
Factor - dense dim.          : 2             flops       : 5.02e+05
ITE PFEAS    DFEAS    GFEAS    PRSTATUS   POBJ        DOBJ        MU        TIME
0  8.0e+03  1.2e+03  2.6e+04  0.00e+00  2.503116488e+04  -1.234172434e+03  1.3e+02  0.04
1  3.9e+03  6.4e-01  1.3e+04  9.99e-01  1.002253781e+04  2.316670551e+03  6.2e+01  0.05
2  1.7e+03  2.8e-01  5.6e+03  1.18e+00  5.545217022e+03  2.452230824e+03  2.7e+01  0.05

```

```

3 3.6e+02 5.9e-02 1.2e+03 1.09e+00 1.613658539e+03 9.982955221e+02 5.6e+00 0.06
4 1.5e+02 2.5e-02 4.9e+02 1.03e+00 8.264611299e+02 5.722855572e+02 2.4e+00 0.06
5 2.8e+01 4.5e-03 9.1e+01 1.01e+00 3.934480893e+02 3.467403504e+02 4.4e-01 0.06
6 5.5e+00 9.0e-04 1.8e+01 1.02e+00 3.052316807e+02 2.960376884e+02 8.6e-02 0.06
7 4.2e-01 6.9e-05 1.4e+00 1.01e+00 2.838759387e+02 2.831788041e+02 6.6e-03 0.07
8 2.4e-02 4.0e-06 7.9e-02 1.01e+00 2.820862755e+02 2.820463229e+02 3.8e-04 0.07
9 1.2e-03 1.9e-07 3.9e-03 1.01e+00 2.819644523e+02 2.819625049e+02 1.9e-05 0.07
10 2.7e-05 4.4e-09 8.8e-05 1.00e+00 2.819572914e+02 2.819572471e+02 4.2e-07 0.07
11 2.4e-06 1.9e-08 1.1e-08 1.01e+00 2.819571856e+02 2.819571856e+02 1.2e-08 0.08
12 2.4e-06 1.9e-08 1.1e-08 1.00e+00 2.819571856e+02 2.819571856e+02 1.2e-08 0.08

```

Basis identification started.

Primal basis identification phase started.

Primal basis identification phase terminated. Time: 0.00

Dual basis identification phase started.

Dual basis identification phase terminated. Time: 0.00

Basis identification terminated. Time: 0.01

Optimizer terminated. Time: 0.10

#### Interior-point solution summary

```

Problem status : PRIMAL_AND_DUAL_FEASIBLE
Solution status : OPTIMAL
Primal. obj: 2.8195718558e+02    nrm: 5e+02    Viol. con: 7e-06    var: 3e-07
Dual.   obj: 2.8195717596e+02    nrm: 5e+00    Viol. con: 0e+00    var: 9e-09

```

#### Basic solution summary

```

Problem status : PRIMAL_AND_DUAL_FEASIBLE
Solution status : OPTIMAL
Primal. obj: 2.8195718114e+02    nrm: 5e+02    Viol. con: 8e-13    var: 1e-14
Dual.   obj: 2.8195718114e+02    nrm: 8e+00    Viol. con: 0e+00    var: 8e-16

```

#### Optimizer summary

Optimizer	-	time: 0.10
Interior-point	- iterations : 12	time: 0.09
Basis identification	-	time: 0.01
Primal	- iterations : 47	time: 0.00
Dual	- iterations : 103	time: 0.00
Clean primal	- iterations : 0	time: 0.00
Clean dual	- iterations : 0	time: 0.00
Simplex	-	time: 0.00
Primal simplex	- iterations : 0	time: 0.00
Dual simplex	- iterations : 0	time: 0.00
Mixed integer	- relaxations: 0	time: 0.00

solveCobraEP: LP part of EPproblem is feasible according to solveCobraLP with mosek.

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Platform: Linux/64-X86

#### Problem

Name	:
Objective sense	: minimize
Type	: CONIC (conic optimization problem)
Constraints	: 2964
Affine conic cons.	: 3430 (10290 rows)
Disjunctive cons.	: 0
Cones	: 0
Scalar variables	: 7067
Matrix variables	: 0

```

Integer variables : 0

Optimizer started.
Presolve started.
Linear dependency checker started.
Linear dependency checker terminated.
Eliminator started.
Freed constraints in eliminator : 8
Eliminator terminated.
Eliminator - tries : 1 time : 0.00
Lin. dep. - tries : 1 time : 0.00
Lin. dep. - primal attempts : 1 successes : 1
Lin. dep. - dual attempts : 0 successes : 0
Lin. dep. - primal deps. : 25 dual deps. : 0
Presolve terminated. Time: 0.03
Optimizer - threads : 18
Optimizer - solved problem : the primal
Optimizer - Constraints : 1949
Optimizer - Cones : 3430
Optimizer - Scalar variables : 11273 conic : 10290
Optimizer - Semi-definite variables: 0 scalarized : 0
Factor - setup time : 0.02
Factor - dense det. time : 0.00 GP order time : 0.00
Factor - nonzeros before factor : 1.17e+04 after factor : 2.01e+04
Factor - dense dim. : 0 flops : 7.52e+05
ITE PFEAS DFEAS GFEAS PRSTATUS POBJ DOBJ MU TIME
0 1.0e+04 1.2e+00 1.0e+04 0.00e+00 5.947759534e+03 -4.414972768e+03 1.0e+00 0.06
1 7.9e+03 9.3e-01 9.2e+03 -9.99e-01 8.232311490e+03 -2.127371810e+03 7.9e-01 0.09
2 7.2e+03 8.4e-01 8.8e+03 -9.96e-01 9.502069016e+03 -8.439738464e+02 7.2e-01 0.10
3 5.3e+03 6.2e-01 7.5e+03 -9.85e-01 1.447239244e+04 4.217526204e+03 5.3e-01 0.15
4 1.7e+03 2.0e-01 4.1e+03 -9.66e-01 5.230892004e+04 4.250374657e+04 1.7e-01 0.33
5 7.0e+02 8.2e-02 2.4e+03 -8.61e-01 1.067632391e+05 9.800078150e+04 7.0e-02 0.34
6 4.0e+02 4.7e-02 1.4e+03 -5.59e-01 1.049141326e+05 9.770526243e+04 4.0e-02 0.35
7 2.8e+02 3.3e-02 9.6e+02 -1.56e-01 8.608338702e+04 8.013144341e+04 2.8e-02 0.36
8 1.7e+02 2.0e-02 5.3e+02 1.01e-01 6.412938836e+04 5.978465784e+04 1.7e-02 0.37
9 1.2e+02 1.4e-02 3.2e+02 3.93e-01 5.168438193e+04 4.842911750e+04 1.2e-02 0.38
10 6.6e+01 7.7e-03 1.4e+02 5.72e-01 3.786764539e+04 3.590026862e+04 6.6e-03 0.39
11 4.6e+01 5.4e-03 8.3e+01 7.65e-01 3.225068439e+04 3.083571157e+04 4.6e-03 0.40
12 1.2e+01 1.4e-03 1.2e+01 8.40e-01 2.140669702e+04 2.101253429e+04 1.2e-03 0.41
13 3.7e+00 4.3e-04 2.1e+00 9.68e-01 1.845839483e+04 1.833657509e+04 3.7e-04 0.42
14 1.0e+00 1.2e-04 3.1e-01 9.93e-01 1.755884221e+04 1.752535817e+04 1.0e-04 0.43
15 2.7e-01 3.1e-05 4.4e-02 9.99e-01 1.733318360e+04 1.732430925e+04 2.7e-05 0.44
16 6.6e-02 7.7e-06 5.4e-03 1.00e+00 1.727034946e+04 1.726816170e+04 6.6e-06 0.45
17 1.4e-02 1.6e-06 5.2e-04 1.00e+00 1.725455691e+04 1.725410508e+04 1.4e-06 0.46
18 8.8e-03 1.0e-06 2.7e-04 1.00e+00 1.725310464e+04 1.725281349e+04 8.8e-07 0.46
19 5.6e-03 6.6e-07 1.4e-04 1.00e+00 1.725214547e+04 1.725196026e+04 5.6e-07 0.48
20 5.0e-03 5.8e-07 1.1e-04 1.00e+00 1.725196013e+04 1.725179540e+04 5.0e-07 0.49
21 4.9e-03 5.8e-07 1.1e-04 1.00e+00 1.725194216e+04 1.725177942e+04 4.9e-07 0.50
22 4.8e-03 5.7e-07 1.1e-04 1.00e+00 1.725192055e+04 1.725176019e+04 4.8e-07 0.51
23 4.7e-03 5.5e-07 1.1e-04 1.00e+00 1.725188600e+04 1.725172946e+04 4.7e-07 0.52
24 4.7e-03 5.5e-07 1.1e-04 1.00e+00 1.725188038e+04 1.725172446e+04 4.7e-07 0.53
25 4.5e-03 5.3e-07 9.8e-05 1.00e+00 1.725181785e+04 1.725166884e+04 4.5e-07 0.54
26 4.5e-03 5.3e-07 9.8e-05 1.00e+00 1.725181614e+04 1.725166732e+04 4.5e-07 0.55
27 4.5e-03 5.3e-07 9.8e-05 1.00e+00 1.725181610e+04 1.725166728e+04 4.5e-07 0.56
28 4.4e-03 5.2e-07 9.7e-05 1.00e+00 1.725180155e+04 1.725165434e+04 4.4e-07 0.56
29 4.4e-03 5.2e-07 9.6e-05 1.00e+00 1.725179983e+04 1.725165281e+04 4.4e-07 0.57
30 4.4e-03 5.2e-07 9.6e-05 1.00e+00 1.725179981e+04 1.725165279e+04 4.4e-07 0.58
31 4.2e-03 4.9e-07 8.8e-05 1.00e+00 1.725171945e+04 1.725158131e+04 4.2e-07 0.59
32 4.1e-03 4.8e-07 8.6e-05 1.00e+00 1.725170588e+04 1.725156924e+04 4.1e-07 0.60
33 4.0e-03 4.7e-07 8.2e-05 1.00e+00 1.725166415e+04 1.725153212e+04 4.0e-07 0.61
34 3.9e-03 4.6e-07 8.1e-05 1.00e+00 1.725165276e+04 1.725152199e+04 3.9e-07 0.62
35 3.9e-03 4.6e-07 8.1e-05 1.00e+00 1.725165262e+04 1.725152186e+04 3.9e-07 0.63
36 3.9e-03 4.6e-07 8.1e-05 1.00e+00 1.725165254e+04 1.725152179e+04 3.9e-07 0.64
37 3.9e-03 4.6e-07 7.9e-05 1.00e+00 1.725163673e+04 1.725150773e+04 3.9e-07 0.65

```

38	3.9e-03	4.5e-07	7.9e-05	1.00e+00	1.725163234e+04	1.725150382e+04	3.9e-07	0.65
39	3.8e-03	4.5e-07	7.8e-05	1.00e+00	1.725162216e+04	1.725149476e+04	3.8e-07	0.67
40	3.8e-03	4.5e-07	7.7e-05	1.00e+00	1.725161063e+04	1.725148450e+04	3.8e-07	0.67
41	3.8e-03	4.5e-07	7.7e-05	1.00e+00	1.725160908e+04	1.725148313e+04	3.8e-07	0.68
42	3.8e-03	4.5e-07	7.7e-05	1.00e+00	1.725160845e+04	1.725148257e+04	3.8e-07	0.69
43	3.8e-03	4.5e-07	7.7e-05	1.00e+00	1.725160838e+04	1.725148251e+04	3.8e-07	0.70
44	3.0e-03	3.6e-07	5.5e-05	1.00e+00	1.725137931e+04	1.725127873e+04	3.0e-07	0.71
45	3.0e-03	3.6e-07	5.5e-05	1.00e+00	1.725137837e+04	1.725127789e+04	3.0e-07	0.72
46	3.0e-03	3.5e-07	5.4e-05	1.00e+00	1.725137662e+04	1.725127634e+04	3.0e-07	0.73
47	3.0e-03	3.5e-07	5.4e-05	1.00e+00	1.725137360e+04	1.725127365e+04	3.0e-07	0.74
48	3.0e-03	3.5e-07	5.4e-05	1.00e+00	1.725137289e+04	1.725127302e+04	3.0e-07	0.75
49	3.0e-03	3.5e-07	5.3e-05	1.00e+00	1.725136541e+04	1.725126636e+04	3.0e-07	0.76
50	3.0e-03	3.5e-07	5.3e-05	1.00e+00	1.725136508e+04	1.725126607e+04	3.0e-07	0.77
51	3.0e-03	3.5e-07	5.3e-05	1.00e+00	1.725136501e+04	1.725126601e+04	3.0e-07	0.78
52	3.0e-03	3.5e-07	5.3e-05	1.00e+00	1.725136419e+04	1.725126528e+04	3.0e-07	0.79
53	3.0e-03	3.5e-07	5.3e-05	1.00e+00	1.725136416e+04	1.725126525e+04	3.0e-07	0.80
54	3.0e-03	3.5e-07	5.3e-05	1.00e+00	1.725136391e+04	1.725126503e+04	3.0e-07	0.81
55	3.0e-03	3.5e-07	5.3e-05	1.00e+00	1.725136324e+04	1.725126444e+04	3.0e-07	0.81
56	3.0e-03	3.5e-07	5.3e-05	1.00e+00	1.725136313e+04	1.725126433e+04	3.0e-07	0.82
57	7.2e-04	8.4e-08	6.4e-06	1.00e+00	1.725068311e+04	1.725065935e+04	7.2e-08	0.84
58	7.2e-04	8.4e-08	6.4e-06	1.00e+00	1.725068310e+04	1.725065934e+04	7.2e-08	0.85
59	7.2e-04	8.4e-08	6.4e-06	1.00e+00	1.725068301e+04	1.725065926e+04	7.2e-08	0.86
60	7.2e-04	8.4e-08	6.4e-06	1.00e+00	1.725068289e+04	1.725065915e+04	7.2e-08	0.86
61	7.2e-04	8.4e-08	6.4e-06	1.00e+00	1.725068288e+04	1.725065914e+04	7.2e-08	0.87
62	7.2e-04	8.4e-08	6.4e-06	1.00e+00	1.725068253e+04	1.725065883e+04	7.1e-08	0.89
63	7.1e-04	8.4e-08	6.4e-06	1.00e+00	1.725068252e+04	1.725065882e+04	7.1e-08	0.90
64	7.1e-04	8.4e-08	6.3e-06	1.00e+00	1.725068231e+04	1.725065863e+04	7.1e-08	0.91
65	7.1e-04	8.4e-08	6.3e-06	1.00e+00	1.725068227e+04	1.725065860e+04	7.1e-08	0.92
66	7.1e-04	8.4e-08	6.3e-06	1.00e+00	1.725068226e+04	1.725065859e+04	7.1e-08	0.93
67	7.1e-04	8.4e-08	6.3e-06	1.00e+00	1.725068225e+04	1.725065858e+04	7.1e-08	0.94
68	7.1e-04	8.4e-08	6.3e-06	1.00e+00	1.725068225e+04	1.725065858e+04	7.1e-08	0.95
69	7.1e-04	8.3e-08	6.2e-06	1.00e+00	1.725067970e+04	1.725065631e+04	7.1e-08	0.97
70	7.0e-04	8.3e-08	6.2e-06	1.00e+00	1.725067928e+04	1.725065594e+04	7.0e-08	0.98
71	7.0e-04	8.3e-08	6.2e-06	1.00e+00	1.725067923e+04	1.725065589e+04	7.0e-08	0.99
72	7.0e-04	8.3e-08	6.2e-06	1.00e+00	1.725067923e+04	1.725065589e+04	7.0e-08	1.00
73	7.0e-04	8.3e-08	6.2e-06	1.00e+00	1.725067921e+04	1.725065587e+04	7.0e-08	1.01
74	6.7e-04	7.8e-08	5.7e-06	1.00e+00	1.725066747e+04	1.725064542e+04	6.6e-08	1.03
75	6.7e-04	7.8e-08	5.7e-06	1.00e+00	1.725066746e+04	1.725064542e+04	6.6e-08	1.04
76	6.4e-04	7.5e-08	5.4e-06	1.00e+00	1.725066042e+04	1.725063915e+04	6.4e-08	1.05
77	6.4e-04	7.5e-08	5.4e-06	1.00e+00	1.725066041e+04	1.725063914e+04	6.4e-08	1.06
78	6.4e-04	7.5e-08	5.4e-06	1.00e+00	1.725066041e+04	1.725063914e+04	6.4e-08	1.07
79	1.5e-04	1.8e-08	6.3e-07	1.00e+00	1.725051265e+04	1.725050760e+04	1.5e-08	1.09
80	1.5e-04	1.8e-08	6.3e-07	1.00e+00	1.725051265e+04	1.725050760e+04	1.5e-08	1.09
81	1.5e-04	1.8e-08	6.3e-07	1.00e+00	1.725051265e+04	1.725050760e+04	1.5e-08	1.11
82	1.5e-04	1.8e-08	6.2e-07	1.00e+00	1.725051262e+04	1.725050757e+04	1.5e-08	1.11
83	1.5e-04	1.8e-08	6.2e-07	1.00e+00	1.725051262e+04	1.725050757e+04	1.5e-08	1.13
84	1.5e-04	1.8e-08	6.2e-07	1.00e+00	1.725051262e+04	1.725050757e+04	1.5e-08	1.15
85	1.5e-04	1.8e-08	6.2e-07	1.00e+00	1.725051262e+04	1.725050757e+04	1.5e-08	1.17
86	1.5e-04	1.8e-08	6.2e-07	1.00e+00	1.725051260e+04	1.725050756e+04	1.5e-08	1.18
87	1.5e-04	1.8e-08	6.2e-07	1.00e+00	1.725051260e+04	1.725050756e+04	1.5e-08	1.20
88	1.5e-04	1.8e-08	6.2e-07	1.00e+00	1.725051260e+04	1.725050756e+04	1.5e-08	1.22

Optimizer terminated. Time: 1.24

#### Interior-point solution summary

Problem status : PRIMAL\_AND\_DUAL\_FEASIBLE  
 Solution status : OPTIMAL

Primal. obj: 1.7250512601e+04 nrm: 5e+02 Viol. con: 2e-04 var: 7e-06 acc: 7e-08  
 Dual. obj: 1.7250507555e+04 nrm: 8e+03 Viol. con: 3e-07 var: 6e-07 acc: 0e+00

#### Optimizer summary

Optimizer	-	time: 1.24
Interior-point	- iterations : 89	time: 1.23
Basis identification	-	time: 0.00
Primal	- iterations : 0	time: 0.00

```

Dual           - iterations : 0          time: 0.00
Clean primal   - iterations : 0          time: 0.00
Clean dual     - iterations : 0          time: 0.00
Simplex        -                      time: 0.00
Primal simplex - iterations : 0          time: 0.00
Dual simplex   - iterations : 0          time: 0.00
Mixed integer   - relaxations: 0         time: 0.00

> [mosek] Dual    optimality condition in solveCobraEP satisfied.

Optimality conditions (biochemistry)
0.00025 || N*(vf - vr) + B*ve - b ||_inf
3.4e-07 || cf + ci + N'*y_N + y_vi + Qv*vf + k_vf + z_vf ||_inf
3.4e-07 || cr - ci - N'*y_N - y_vi + Qv*vf + k_vr + z_vr ||_inf
1 || ce + B'*y_N + z_ve ||_inf
8e+03 || k_e_1 + z_e_1 ||_inf
8e+03 || -g + k_e_vf + z_e_vf||_inf
5.7e-07 || -g + k_e_vr + z_e_vr||_inf
8.2e-06 || e_vf + vf*log(vf) ||_inf
7.9e-06 || e_vr + vr*log(vr) ||_inf
1.3 || k_q_1 + z_q_1 ||_inf

Derived optimality conditions (biochemistry)
20 || g.*log(vf) + g - k_vf ||_inf
0.0082 || g.*log(vr) + g - k_vr ||_inf
20 || cf + ci + N'*y_N + y_vi + Qv*vf + g.*log(vf) + g + z_vf ||_inf
0.0082 || cr - ci - N'*y_N - y_vi + Qv*vf + g.*log(vr) + g + z_vr ||_inf

Thermo conditions
2.4e+02 || g.*log(vr/vf) - 2*N'*y_N ||_inf
54 || g.*log(vr/vf) + cr - cf - 2*ci - 2*N'*y_N - 2*y_vi ||_inf
88 || g.*log(vr/vf) + cr - cf - 2*ci - 2*N'*y_N - 2*y_vi - z_vr + z_vf ||_inf
-1.5e+02 min(slack)
2e+02 max(slack)

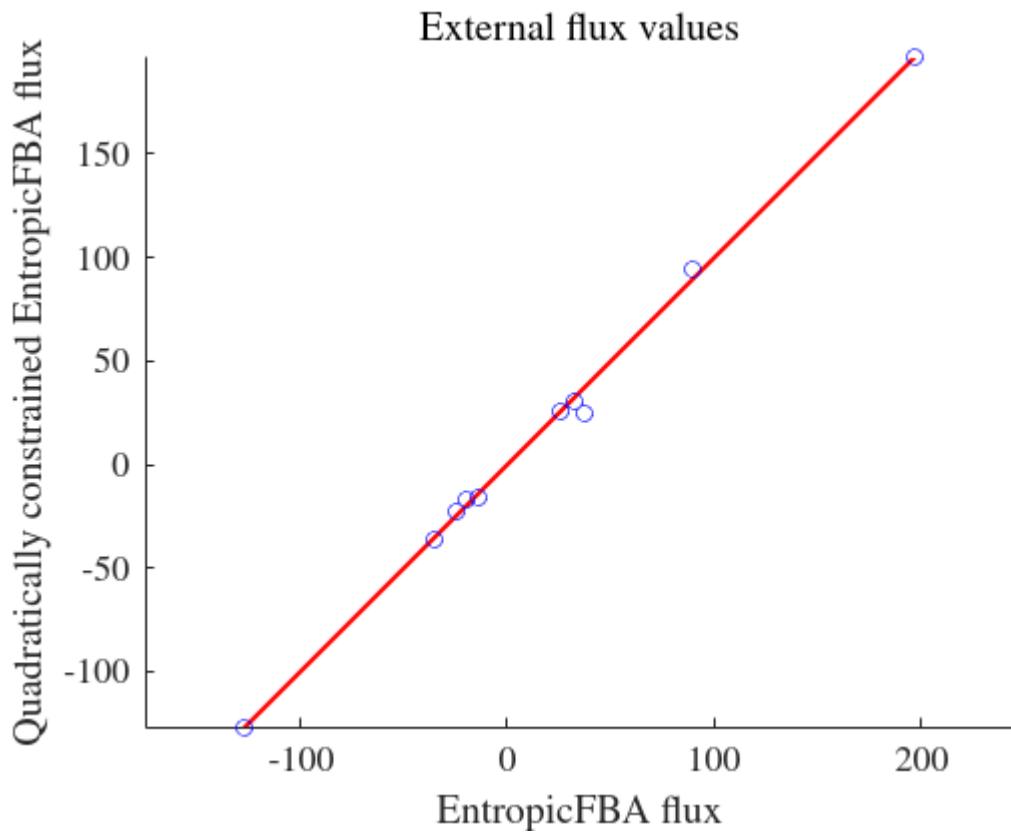
```

Compare the original external flux vector, with the quadratically constrained external flux vector. The values should be closer to the red line than above, but not exactly, because the quadratic penalty is trading off against entropy maximisation of internal reactions. Change H(j,j) to adjust this trade off.

```

figure
hold on
fplot(@(x) x, 'LineWidth', 1.5, 'Color', 'r')
plot(solution.v(isfinite(model.h)),solutionQEFBA.v(isfinite(model.h)), 'o', 'Color', 'b')
xlabel('EntropicFBA flux')
ylabel('Quadratically constrained EntropicFBA flux')
title('External flux values')
axis equal

```



## Acknowledgments

Co-funded by the European Union's Horizon Europe Framework Programme (101080997)

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