A Mathematical Model for the Flow of Carbon Through th Asparate, Threonine and the Branched Chain Amino Acid Pathways of *Escherichia coli* K12.

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(* call Cellerator and kMech into Mathematica Kernel *)
<< cellerator.m;
<< kMech.m;
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Cellerator™ 1.4.6 (30-July-2004) loaded 27-Aug-2005 17:01
  using Mathematica Version 5.0 for Microsoft Windows (June 11, 2003)
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kMech is loaded
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(* kMech Input of Enzyme Mechanisms for the Mathematical Modeling
  of Threonine (Thr), L-isoleucine (ILE), L-valine (VAL),
 and L-leucine (LEU) Biosynthesis *)

Asp$Thr$Synthesis = Union[
   {{{AKI} ⟹(ASA, {{},{},{}}) {HDHI},
     GMWC[cGMWC → cASA, LGMWC → LASA, nGMWC → nASA, KGMWC → {KmHDHIASA},
      kcatGMWC → kcat$AKI$HDHI]}},
   {{{HDHI} ⟹(Asp, {{},{},{}}) {AKI},
     GMWC[cGMWC → cAsp, LGMWC → LAsp, nGMWC → nAsp, KGMWC → {KmAKIAsp},
      kcatGMWC → kcat$HDHI$AKI]}},
   {{{Asp} ⟹(AKI, {{},{Thr},{}}) {AspP},
     GMWC[cGMWC → cAKI, LGMWC → LAKI, nGMWC → nAKI, KGMWC → {KmAKIAsp, KiAKIAspThr},
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    kcatGMWC → kcat$AKI$Asp]}},
  Enz[{Asp, ATP} ⇄(AKII) {AspP, ADP}, BiBi[kfAKIIAsp, krAKIIAsp, kcat$AKII$Asp]],
  {{{Asp} ⟹({{},{Lys},{}}) {AspP},
    GMWC[cGMWC → cAKIII, LGMWC → LAKIII, nGMWC → nAKIII,
     KGMWC → {KmAKIIIAsp, KiAKIIIAspLys}, kcatGMWC → kcat$AKIII$Asp]}},
  Enz[{AspP, NADPH} ⇄(ASD) {ASA, NADP, Phosphate}, BiTri[kfASDAspP, krASDAspP, kcat$ASD$A
  Enz[{ASA, NADP, Phosphate} ⇄(ASD) {AspP, NADPH}, TriBi[kfASDASA, krASDASA, kcat$ASD$AS
  {{{ASA} ⟹({{},{Thr},{}}) {Hse},
    GMWC[cGMWC → cHDHI, LGMWC → LHDHI, nGMWC → nHDHI, KGMWC → {KmHDHIASA, KiHDHIASAT
     kcatGMWC → kcat$HDHI$ASA]}},
  {{ASA → ∅, kfASA}},
  {{Hse → ∅, kfHse}},
  Enz[{ASA, NADPH} ⇄(HDHII) {Hse, NADP}, BiBi[kfHDHIIASA, krHDHIIASA, kcat$HDHII$ASA]],
  Enz[{Hse, ATP} ⇄(HSK) {HseP, ADP}, BiBi[kfHSKHse, krHSKHse, kcat$HSK$Hse],
   CI[Thr, kfiHSKHseThr, kriHSKHseThr]],
  {{HseP ⇄(TS) Thr, kfTSHseP, krTSHseP, kcat$TS$HseP}}
 ];

ILESynthesis = Union[
  {{{Thr} ⟹({{Val},{Ile}}) {aKB, NH3},
    GMWC[nGMWC → nTDA, cGMWC → cTDA, LGMWC → L0TDA, kcatGMWC → kcat$TDA,
     KGMWC → {KmThr, KaVal, KiIle}]}},
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{{          aKB ⇄(KDC) propionylCoA, kfKDCaKB, krKDCaKB, kcat$KDC$aKB}},

Enz[{Pyr, aKB} ⇄(AHASI,AHASICH3CO) {CO2, aAHB}, PingPong[kfAHASIPyr, krAHASIPyr, kcat$AHASI$Pyr,
  kfAHASIaKB, krAHASIaKB, kcat$AHASI$aKB],
 NCI[Val, kfiAHASIPyrVal, kriAHASIPyrVal, kfiAHASIaKBVal, kriAHASIaKBVal,
  residualRateAHASIValaKB]],

Enz[{Pyr, aKB} ⇄(AHASII,AHASIICH3CO) {CO2, aAHB}, PingPong[kfAHASIIPyr, krAHASIIPyr, kcat$AHASII$Pyr,
  kfAHASIIaKB, krAHASIIaKB, kcat$AHASII$aKB]],

Enz[{Pyr, aKB} ⇄(AHASIII,AHASIIICH3CO) {CO2, aAHB}, PingPong[kfAHASIIIPyr, krAHASIIIPyr, kcat$AHASIII$Py
  kfAHASIIIaKB, krAHASIIIaKB, kcat$AHASIII$aKB],
 NCI[Val, kfiAHASIIIPyrVal, kriAHASIIIPyrVal, kfiAHASIIIaKBVal, kriAHASIIIaKBVal
  residualRateAHASIIIValaKB]],

Enz[{aAHB, NADPH} ⇄(IR) {aDMV, NADP}, BiBi[kfIRaAHB, krIRaAHB, kcat$IR$aAHB]],

{{aDMV ⇄(DAD) aKMV, kfDADaDMV, krDADaDMV, kcat$DAD$aDMV}},

Enz[{Glu, aKMV} ⇄(TB,TBNH2) {aKG, Ile}, PingPong[fkfTBGlu, fkrTBGlu, fkcat$TB$Glu, fkfTBaKMV
  fkrTBaKMV, fkcat$TB$aKMV]],
Enz[{Ile, aKG} ⇄(TB,TBNH2) {aKMV, Glu}, PingPong[rkfTBIle, rkrTBIle, rkcat$TB$Ile, rkfTBaKG,
  rkrTBaKG, rkcat$TB$aKG]],
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  {{exIle ⇄(LIVI) Ile, kfLIVIexIle, krLIVIexIle, kcat$LIVI$exIle}},
  {{exIle ⇄(LIVII) Ile, kfLIVIIexIle, krLIVIIexIle, kcat$LIVII$exIle}},

  {{aKMV → acetylCoA, kcat$aKMV}},

  {{Ile → protein, kcat$Ile}}];

VALSynthesis = Union[
  Enz[{Pyr, Pyr} ⇄(AHASI,AHASICH3CO) {CO2, aAL}, PingPong[kfAHASIPyr, krAHASIPyr, kcat$AHASI$Pyr,
    kfAHASIPyr2, krAHASIPyr2, kcat$AHASI$Pyr2],
   NCI[Val, kfiAHASIPyrVal, kriAHASIPyrVal, kfiAHASIPyr2Val, kriAHASIPyr2Val,
    residualRateAHASIValPyr2]],

  Enz[{Pyr, Pyr} ⇄(AHASII,AHASIICH3CO) {CO2, aAL}, PingPong[kfAHASIIPyr, krAHASIIPyr, kcat$AHASII$Pyr,
    kfAHASIIPyr2, krAHASIIPyr2, kcat$AHASII$Pyr2]],

  Enz[{Pyr, Pyr} ⇄(AHASIII,AHASIIICH3CO) {CO2, aAL}, PingPong[kfAHASIIIPyr, krAHASIIIPyr, kcat$AHASIII$Pyr
    kfAHASIIIPyr2, krAHASIIIPyr2, kcat$AHASIII$Pyr2],
   NCI[Val, kfiAHASIIIPyrVal, kriAHASIIIPyrVal, kfiAHASIIIPyr2Val, kriAHASIIIPyr2V
    residualRateAHASIIIValPyr2]],

  Enz[{aAL, NADPH} ⇄(IR) {aDHIV, NADP}, BiBi[kfIRaAL, krIRaAL, kcat$IR$aAL]],

  {{aDHIV ⇄(DAD) aKIV, kfDADaDHIV, krDADaDHIV, kcat$DAD$aDHIV}},
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  Enz[{Ala, aKIV} ⇄^{TC,TCNH2} {Pyr, Val}, PingPong[fkfTCAla, fkrTCAla, fkcat$TC$Ala, fkfTCaKIV
    fkrTCaKIV, fkcat$TC$aKIV]],
  Enz[{Val, Pyr} ⇄^{TC,TCNH2} {aKIV, Ala}, PingPong[rkfTCVal, rkrTCVal, rkcat$TC$Val, rkfTCPyr,
    rkrTCPyr, rkcat$TC$Pyr]],

  Enz[{Glu, aKIV} ⇄^{TB,TBNH2} {aKG, Val}, PingPong[fkfTBGlu, fkrTBGlu, fkcat$TB$Glu, fkfTBaKIV
    fkrTBaKIV, fkcat$TB$aKIV]],
  Enz[{Val, aKG} ⇄^{TB,TBNH2} {aKIV, Glu}, PingPong[rkfTBVal, rkrTBVal, rkcat$TB$Val, rkfTBaKG,
    rkrTBaKG, rkcat$TB$aKG]],

  {{exVal ⇄^{LIVI} Val, kfLIVIexVal, krLIVIexVal, kcat$LIVI$exVal}},
  {{exVal ⇄^{LIVII} Val, kfLIVIIexVal, krLIVIIexVal, kcat$LIVII$exVal}},

  {{aKIV → pantothenate, kcat$aKIV}},

  {{Val → protein, kcat$Val}}];

LEUSynthesis = Union[
  Enz[{acetylCoA, aKIV} ⇄^{IPMS,IPMSacetyl} {CoA, aIPM},
   PingPong[kfIPMSacetylCoA, krIPMSacetylCoA, kcat$IPMS$acetylCoA, kfIPMSaKIV,
    krIPMSaKIV, kcat$IPMS$aKIV], CI[Leu, kfiIPMSLeu, kriIPMSLeu],
   NCI[Leu, kfiIPMSacetylLeu, kriIPMSacetylLeu]],
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```
  {{aIPM IPMI⇄ bIPM, kfIPMIaIPM, krIPMIaIPM, kcat$IPMI$aIPM}},
  {{bIPM IPMI⇄ aIPM, kfIPMIbIPM, krIPMIbIPM, kcat$IPMI$bIPM}},

  Enz[{bIPM, NAD} IPMDH⇄ {aKIC, NADH}, BiBi[kfIPMDHbIPM, krIPMDHbIPM, kcat$IPMDH$bIPM]],

  Enz[{Glu, aKIC} TB,TBNH2⇄ {aKG, Leu}, PingPong[fkfTBGlu, fkrTBGlu, fkcat$TB$Glu, fkfTBaKIC
    fkrTBaKIC, fkcat$TB$aKIC]],
  Enz[{Leu, aKG} TB,TBNH2⇄ {aKIC, Glu}, PingPong[rkfTBLeu, rkrTBLeu, rkcat$TB$Leu, rkfTBaKG,
    rkrTBaKG, rkcat$TB$aKG]],

  {{aKIC → glutarylCoA, kcat$aKIC}},

  {{exLeu LIVI⇄ Leu, kfLIVIexLeu, krLIVIexLeu, kcat$LIVI$exLeu}},
  {{exLeu LIVII⇄ Leu, kfLIVIIexLeu, krLIVIIexLeu, kcat$LIVII$exLeu}},
  {{exLeu LS⇄ Leu, kfLSexLeu, krLSexLeu, kcat$LS$exLeu}},

  {{Leu → protein, kcat$Leu}}];

THR$ILE$VAL$LEU$Synthesis = Union[Asp$Thr$Synthesis, ILESynthesis, VALSynthesis,
   LEUSynthesis];
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(* Cellerator-interpreted Ordinary Differential Equations (ODEs) and
   Equations for the MWC Model and Substrate Generators . *)

interpret[THR$ILE$VAL$LEU$Synthesis];
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(*
 Modifications for Substrate Generators:
   The generated ODEs require some modifications to include the
    constant substrate fluxes for the steady state simulation

  1. Substrate Generators:
         Set the first derivatives of the following substrates to 0
     to simulate constant flux,
 Asp'[t]==0, ATP'[t]==0, NADP'[t]==0, NADPH'[t]==0, Phosphate'[t]==0,
 Pyr'[t]==0, Glu'[t]==0, Ala'[t]==0, exIle'[t]==0, exVal'[t]==0,
 exLeu'[t]==0, acetylCoA'[t]==0, NAD'[t]==0,
 *)

{myODEs, myVars} =
 {{aAHB'[t] == -kfIRaAHB aAHB[t] IR[t] NADPH[t] + kcat$AHASI$aKB $Complex$aKB$AHASICH3C
     kcat$AHASI$aKB residualRateAHASIValaKB $Complex$aKB$AHASICH3CO$Val$[t] +
     kcat$AHASII$aKB $Complex$aKB$AHASIICH3CO$[t] +
     kcat$AHASIII$aKB $Complex$aKB$AHASIIICH3CO$[t] +
     kcat$AHASIII$aKB residualRateAHASIIIValaKB $Complex$aKB$AHASIIICH3CO$Val$[t] +
     krIRaAHB $Complex$IR$aAHB$NADPH$[t],
   aAL'[t] == -kfIRaAL aAL[t] IR[t] NADPH[t] + krIRaAL $Complex$IR$aAL$NADPH$[t] +
     kcat$AHASI$Pyr2 $Complex$Pyr$AHASICH3CO$[t] +
     kcat$AHASI$Pyr2 residualRateAHASIValPyr2 $Complex$Pyr$AHASICH3CO$Val$[t] +
     kcat$AHASII$Pyr2 $Complex$Pyr$AHASIICH3CO$[t] +
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  kcat$AHASIII$Pyr2 $Complex$Pyr$AHASIIICH3CO$[t] +
  kcat$AHASIII$Pyr2 residualRateAHASIIIValPyr2 $Complex$Pyr$AHASIIICH3CO$Val$[t]
acetylCoA'[t] == 0,
aDHIV'[t] == -kfDADaDHIV aDHIV[t] DAD[t] + krDADaDHIV $Complex$aDHIV$DAD$[t] +
  kcat$IR$aAL $Complex$IR$aAL$NADPH$[t],
aDMV'[t] == -kfDADaDMV aDMV[t] DAD[t] + krDADaDMV $Complex$aDMV$DAD$[t] +
  kcat$IR$aAHB $Complex$IR$aAHB$NADPH$[t],
ADP'[t] == kcat$AKII$Asp $Complex$AKII$Asp$ATP$[t] + kcat$HSK$Hse $Complex$HSK$Hse$
AHASI'[t] == -kfAHASIPyr AHASI[t] Pyr[t] - kfiAHASIPyrVal AHASI[t] Val[t] +
  kriAHASIPyrVal $Complex$AHASI$Val$[t] + kcat$AHASI$aKB $Complex$aKB$AHASICH3CO$
  kcat$AHASI$Pyr2 $Complex$Pyr$AHASICH3CO$[t] + krAHASIPyr $Complex$Pyr$AHASI$[t]
AHASICH3CO'[t] == -kfAHASIaKB AHASICH3CO[t] aKB[t] - kfAHASIPyr2 AHASICH3CO[t] Pyr[t
  kfiAHASIaKBVal AHASICH3CO[t] Val[t] + kriAHASIaKBVal $Complex$AHASICH3CO$Val$[t
  krAHASIaKB $Complex$aKB$AHASICH3CO$[t] + krAHASIPyr2 $Complex$Pyr$AHASICH3CO$[t
  kcat$AHASI$Pyr $Complex$Pyr$AHASI$[t],
AHASII'[t] == -kfAHASIIPyr AHASII[t] Pyr[t] + kcat$AHASII$aKB $Complex$aKB$AHASIICH
  kcat$AHASII$Pyr2 $Complex$Pyr$AHASIICH3CO$[t] + krAHASIIPyr $Complex$Pyr$AHASII
AHASIICH3CO'[t] == -kfAHASIIaKB AHASIICH3CO[t] aKB[t] - kfAHASIIPyr2 AHASIICH3CO[t]
  krAHASIIaKB $Complex$aKB$AHASIICH3CO$[t] + krAHASIIPyr2 $Complex$Pyr$AHASIICH3C
  kcat$AHASII$Pyr $Complex$Pyr$AHASII$[t],
AHASIII'[t] == -kfAHASIIIPyr AHASIII[t] Pyr[t] - kfiAHASIIIPyrVal AHASIII[t] Val[t]
  kriAHASIIIPyrVal $Complex$AHASIII$Val$[t] +
  kcat$AHASIII$aKB $Complex$aKB$AHASIIICH3CO$[t] +
  kcat$AHASIII$Pyr2 $Complex$Pyr$AHASIIICH3CO$[t] + krAHASIIIPyr $Complex$Pyr$AHA
AHASIIICH3CO'[t] == -kfAHASIIIaKB AHASIIICH3CO[t] aKB[t] -
  kfAHASIIIPyr2 AHASIIICH3CO[t] Pyr[t] - kfiAHASIIIaKBVal AHASIIICH3CO[t] Val[t] +
  kriAHASIIIaKBVal $Complex$AHASIIICH3CO$Val$[t] +
  krAHASIIIaKB $Complex$aKB$AHASIIICH3CO$[t] +
  krAHASIIIPyr2 $Complex$Pyr$AHASIIICH3CO$[t] + kcat$AHASIII$Pyr $Complex$Pyr$AHA
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$$
\begin{aligned}
&\text{aIPM}'[t] == -\text{kfIPMIaIPM}\,\text{aIPM}[t]\,\text{IPMI}[t] + \text{krIPMIaIPM}\,\$\text{Complex}\$\text{aIPM}\$\text{IPMI}\$[t] + \\
&\quad \text{kcat}\$\text{IPMS}\$\text{aKIV}\,\$\text{Complex}\$\text{aKIV}\$\text{IPMSacetyl}\$[t] + \text{kcat}\$\text{IPMI}\$\text{bIPM}\,\$\text{Complex}\$\text{bIPM}\$\text{IPMI} \\
&\text{aKB}'[t] == -\text{kfAHASIaKB}\,\text{AHASICH3CO}[t]\,\text{aKB}[t] - \text{kfAHASIIaKB}\,\text{AHASIICH3CO}[t]\,\text{aKB}[t] - \\
&\quad \text{kfAHASIIIaKB}\,\text{AHASIIICH3CO}[t]\,\text{aKB}[t] - \text{kfKDCaKB}\,\text{aKB}[t]\,\text{KDC}[t] + \\
&\quad \left(\text{kcat}\$\text{TDA}\,\text{TDA}[t]\left(\frac{\text{cTDA}\,\text{L0TDA}\left(1+\frac{\text{Ile}[t]}{\text{KiIle}}\right)^{\text{nTDA}}\text{Thr}[t]\left(1+\frac{\text{cTDA}\,\text{Thr}[t]}{\text{KmThr}}\right)^{-1+\text{nTDA}}}{\text{KmThr}} + \right.\right. \\
&\qquad \left.\left.\frac{\text{Thr}[t]\left(1+\frac{\text{Thr}[t]}{\text{KmThr}}\right)^{-1+\text{nTDA}}\left(1+\frac{\text{Val}[t]}{\text{KaVal}}\right)^{\text{nTDA}}}{\text{KmThr}}\right)\right) \Big/ \\
&\quad \left(\text{L0TDA}\left(1+\frac{\text{Ile}[t]}{\text{KiIle}}\right)^{\text{nTDA}}\left(1+\frac{\text{cTDA}\,\text{Thr}[t]}{\text{KmThr}}\right)^{\text{nTDA}} + \left(1+\frac{\text{Thr}[t]}{\text{KmThr}}\right)^{\text{nTDA}}\left(1+\frac{\text{Val}[t]}{\text{KaVal}}\right)^{\text{nTDA}}\right) - \\
&\quad \text{kfAHASIaKB}\,\text{aKB}[t]\,\$\text{Complex}\$\text{AHASICH3CO}\$\text{Val}\$[t] - \\
&\quad \text{kfAHASIIIaKB}\,\text{aKB}[t]\,\$\text{Complex}\$\text{AHASIIICH3CO}\$\text{Val}\$[t] + \\
&\quad \text{krAHASIaKB}\,\$\text{Complex}\$\text{aKB}\$\text{AHASICH3CO}\$[t] + \text{krAHASIaKB}\,\$\text{Complex}\$\text{aKB}\$\text{AHASICH3CO}\$\text{Val} \\
&\quad \text{krAHASIIaKB}\,\$\text{Complex}\$\text{aKB}\$\text{AHASIICH3CO}\$[t] + \text{krAHASIIIaKB}\,\$\text{Complex}\$\text{aKB}\$\text{AHASIIICH3} \\
&\quad \text{krAHASIIIaKB}\,\$\text{Complex}\$\text{aKB}\$\text{AHASIIICH3CO}\$\text{Val}\$[t] + \text{krKDCaKB}\,\$\text{Complex}\$\text{aKB}\$\text{KDC}\$[t], \\
&\text{aKG}'[t] == -\text{rkfTBaKG}\,\text{aKG}[t]\,\text{TBNH2}[t] + \text{rkrTBaKG}\,\$\text{Complex}\$\text{aKG}\$\text{TBNH2}\$[t] + \\
&\quad \text{fkcat}\$\text{TB}\$\text{Glu}\,\$\text{Complex}\$\text{Glu}\$\text{TB}\$[t], \\
&\text{AKI}'[t] == \\
&\quad -\left(\text{kcat}\$\text{AKI}\$\text{HDHI}\left(\frac{\text{AKI}[t]\left(1+\frac{\text{AKI}[t]}{\text{KmHDHIASA}}\right)^{-1+\text{nASA}}}{\text{KmHDHIASA}} + \frac{\text{cASA}\,\text{LASA}\,\text{AKI}[t]\left(1+\frac{\text{cASA}\,\text{AKI}[t]}{\text{KmHDHIASA}}\right)^{-1+\text{nA}}}{\text{KmHDHIASA}}\right.\right. \\
&\qquad \left.\left.\text{ASA}[t]\right) \Big/ \left(\left(1+\frac{\text{AKI}[t]}{\text{KmHDHIASA}}\right)^{\text{nASA}} + \text{LASA}\left(1+\frac{\text{cASA}\,\text{AKI}[t]}{\text{KmHDHIASA}}\right)^{\text{nASA}}\right) +
\end{aligned}
$$

$$\left(\text{kcat\$HDHI\$AKI}\,\text{Asp}[t]\left(\frac{\text{HDHI}[t]\left(1+\frac{\text{HDHI}[t]}{\text{KmAKIAsp}}\right)^{-1+\text{nAsp}}}{\text{KmAKIAsp}}+\frac{\text{cAsp}\,\text{LAsp}\,\text{HDHI}[t]\left(1+\frac{\text{cAsp}\,\text{HDHI}[t]}{\text{KmAKIAsp}}\right)^{-1+\text{nAsp}}}{\text{KmAKIAsp}}\right)\right)\Big/$$

$$\left(\left(1+\frac{\text{HDHI}[t]}{\text{KmAKIAsp}}\right)^{\text{nAsp}}+\text{LAsp}\left(1+\frac{\text{cAsp}\,\text{HDHI}[t]}{\text{KmAKIAsp}}\right)^{\text{nAsp}}\right),$$

$$\text{aKIC}'[t] == -\text{kcat\$aKIC}\,\text{aKIC}[t]-\text{fkfTBaKIC}\,\text{aKIC}[t]\,\text{TBNH2}[t]+\text{fkrTBaKIC}\,\text{\$Complex\$aKIC\$TBNH2\$}[t]+\text{kcat\$IPMDH\$bIPM}\,\text{\$Complex\$IPMDH\$bIPM\$NAD\$}[t]\text{rkcat\$TB\$Leu}\,\text{\$Complex\$Leu\$TB\$}[t],$$

$$\text{AKII}'[t] == -\text{kfAKIIAsp}\,\text{AKII}[t]\,\text{Asp}[t]\,\text{ATP}[t]+\text{kcat\$AKII\$Asp}\,\text{\$Complex\$AKII\$Asp\$ATP\$}|\text{krAKIIAsp}\,\text{\$Complex\$AKII\$Asp\$ATP\$}[t],\ \text{AKIII}'[t] == 0,$$

$$\text{aKIV}'[t] == -\text{kcat\$aKIV}\,\text{aKIV}[t]-\text{kfIPMSaKIV}\,\text{aKIV}[t]\,\text{IPMSacetyl}[t]-\text{fkfTBaKIV}\,\text{aKIV}[t]\,\text{TBNH2}[t]-\text{fkfTCaKIV}\,\text{aKIV}[t]\,\text{TCNH2}[t]+\text{kcat\$DAD\$aDHIV}\,\text{\$Complex\$aDHIV\$DAD\$}[t]+\text{krIPMSaKIV}\,\text{\$Complex\$aKIV\$IPMSacetyl\$}[t]\text{krIPMSaKIV}\,\text{\$Complex\$aKIV\$IPMSacetyl\$Leu\$}[t]+\text{fkrTBaKIV}\,\text{\$Complex\$aKIV\$TBNH2\$}[t]\text{fkrTCaKIV}\,\text{\$Complex\$aKIV\$TCNH2\$}[t]-\text{kfIPMSaKIV}\,\text{aKIV}[t]\,\text{\$Complex\$IPMSacetyl\$Leu\$}\text{rkcat\$TB\$Val}\,\text{\$Complex\$Val\$TB\$}[t]+\text{rkcat\$TC\$Val}\,\text{\$Complex\$Val\$TC\$}[t],$$

$$\text{aKMV}'[t] == -\text{kcat\$aKMV}\,\text{aKMV}[t]-\text{fkfTBaKMV}\,\text{aKMV}[t]\,\text{TBNH2}[t]+\text{kcat\$DAD\$aDMV}\,\text{\$Complex\$aDMV\$DAD\$}[t]+\text{fkrTBaKMV}\,\text{\$Complex\$aKMV\$TBNH2\$}[t]+\text{rkcat\$TB\$Ile}\,\text{\$Complex\$Ile\$TB\$}[t],$$

$$\text{Ala}'[t] == 0,$$

$$\text{ASA}'[t] == -\text{kfASA}\,\text{ASA}[t]-\text{kfHDHIIASA}\,\text{ASA}[t]\,\text{HDHII}[t]\,\text{NADPH}[t]-\text{kfASDASA}\,\text{ASA}[t]\,\text{ASD}[t]\,\text{NADP}[t]\,\text{Phosphate}[t]-\left(\text{kcat\$HDHI\$ASA}\,\text{HDHI}[t]\right.$$

$$\left(\frac{\text{ASA}[t]\left(1+\frac{\text{ASA}[t]}{\text{KmHDHIASA}}\right)^{-1+\text{nHDHI}}}{\text{KmHDHIASA}}+\frac{\text{cHDHI}\,\text{LHDHI}\,\text{ASA}[t]\left(1+\frac{\text{cHDHI}\,\text{ASA}[t]}{\text{KmHDHIASA}}\right)^{-1+\text{nHDHI}}\left(1+\frac{\text{Thr}[t]}{\text{KiHDHIASAThr}}\right)^{\text{nHDHI}}}{\text{KmHDHIASA}}\right)\Bigg/$$

$$\left(\left(1+\frac{\text{ASA}[t]}{\text{KmHDHIASA}}\right)^{\text{nHDHI}}+\text{LHDHI}\left(1+\frac{\text{cHDHI}\,\text{ASA}[t]}{\text{KmHDHIASA}}\right)^{\text{nHDHI}}\left(1+\frac{\text{Thr}[t]}{\text{KiHDHIASAThr}}\right)^{\text{nHDHI}}\right)+$$

$$\text{krASDASA}\,\$\text{Complex}\$\text{ASD}\$\text{ASA}\$\text{NADP}\$\text{Phosphate}\$[t]+$$

$$\text{kcat}\$\text{ASD}\$\text{AspP}\,\$\text{Complex}\$\text{ASD}\$\text{AspP}\$\text{NADPH}\$[t]+\text{krHDHIIASA}\,\$\text{Complex}\$\text{HDHII}\$\text{ASA}\$\text{NADPH}$$

$$\text{ASD}'[t]==-\text{kfASDAspP}\,\text{ASD}[t]\,\text{AspP}[t]\,\text{NADPH}[t]-\text{kfASDASA}\,\text{ASA}[t]\,\text{ASD}[t]\,\text{NADP}[t]\,\text{Phosph}$$

$$\text{kcat}\$\text{ASD}\$\text{ASA}\,\$\text{Complex}\$\text{ASD}\$\text{ASA}\$\text{NADP}\$\text{Phosphate}\$[t]+$$

$$\text{krASDASA}\,\$\text{Complex}\$\text{ASD}\$\text{ASA}\$\text{NADP}\$\text{Phosphate}\$[t]+$$

$$\text{kcat}\$\text{ASD}\$\text{AspP}\,\$\text{Complex}\$\text{ASD}\$\text{AspP}\$\text{NADPH}\$[t]+\text{krASDAspP}\,\$\text{Complex}\$\text{ASD}\$\text{AspP}\$\text{NADPH}\$[$$

$$\text{Asp}'[t]==0,$$

$$\text{AspP}'[t]==$$

$$\left(\text{kcat}\$\text{AKIII}\$\text{Asp}\,\text{AKIII}[t]\right.$$

$$\left(\frac{\text{Asp}[t]\left(1+\frac{\text{Asp}[t]}{\text{KmAKIIIAsp}}\right)^{-1+\text{nAKIII}}}{\text{KmAKIIIAsp}}+\frac{1}{\text{KmAKIIIAsp}}\right.$$

$$\left.\left(\text{cAKIII}\,\text{LAKIII}\,\text{Asp}[t]\left(1+\frac{\text{cAKIII}\,\text{Asp}[t]}{\text{KmAKIIIAsp}}\right)^{-1+\text{nAKIII}}\left(1+\frac{\text{Lys}[t]}{\text{KiAKIIIAspLys}}\right)^{\text{nAKIII}}\right)\right.$$

$$\left(\left(1+\frac{\text{Asp}[t]}{\text{KmAKIIIAsp}}\right)^{\text{nAKIII}}+\text{LAKIII}\left(1+\frac{\text{cAKIII}\,\text{Asp}[t]}{\text{KmAKIIIAsp}}\right)^{\text{nAKIII}}\left(1+\frac{\text{Lys}[t]}{\text{KiAKIIIAspLys}}\right)^{\text{nAKI}}\right.$$

$$
\begin{aligned}
&\quad \text{kfASDAspP}\,\text{ASD}[t]\,\text{AspP}[t]\,\text{NADPH}[t] + \\
&\quad \left(\text{kcat\$AKI\$Asp}\,\text{AKI}[t]\right. \\
&\qquad \left(\frac{\text{Asp}[t]\left(1+\frac{\text{Asp}[t]}{\text{KmAKIAsp}}\right)^{-1+\text{nAKI}}}{\text{KmAKIAsp}} + \right. \\
&\qquad \left.\left.\frac{\text{cAKI}\,\text{LAKI}\,\text{Asp}[t]\left(1+\frac{\text{cAKI}\,\text{Asp}[t]}{\text{KmAKIAsp}}\right)^{-1+\text{nAKI}}\left(1+\frac{\text{Thr}[t]}{\text{KiAKIAspThr}}\right)^{\text{nAKI}}}{\text{KmAKIAsp}}\right)\right) \Big/ \\
&\quad \left(\left(1+\frac{\text{Asp}[t]}{\text{KmAKIAsp}}\right)^{\text{nAKI}} + \text{LAKI}\left(1+\frac{\text{cAKI}\,\text{Asp}[t]}{\text{KmAKIAsp}}\right)^{\text{nAKI}}\left(1+\frac{\text{Thr}[t]}{\text{KiAKIAspThr}}\right)^{\text{nAKI}}\right) + \\
&\quad \text{kcat\$AKII\$Asp}\,\text{\$Complex\$AKII\$Asp\$ATP\$}[t] + \\
&\quad \text{kcat\$ASD\$ASA}\,\text{\$Complex\$ASD\$ASA\$NADP\$Phosphate\$}[t] + \\
&\quad \text{krASDAspP}\,\text{\$Complex\$ASD\$AspP\$NADPH\$}[t], \\
&\text{ATP}'[t] == 0, \\
&\text{bIPM}'[t] == -\text{kfIPMIbIPM}\,\text{bIPM}[t]\,\text{IPMI}[t] - \text{kfIPMDHbIPM}\,\text{bIPM}[t]\,\text{IPMDH}[t]\,\text{NAD}[t] + \\
&\quad \text{kcat\$IPMI\$aIPM}\,\text{\$Complex\$aIPM\$IPMI\$}[t] + \text{krIPMIbIPM}\,\text{\$Complex\$bIPM\$IPMI\$}[t] + \\
&\quad \text{krIPMDHbIPM}\,\text{\$Complex\$IPMDH\$bIPM\$NAD\$}[t], \\
&\text{CO2}'[t] == \text{kcat\$AHASIII\$Pyr}\,\text{\$Complex\$Pyr\$AHASIII\$}[t] + \\
&\quad \text{kcat\$AHASIII\$Pyr}\,\text{residualRateAHASIIIValaKB}\,\text{\$Complex\$Pyr\$AHASIII\$Val\$}[t] + \\
&\quad \text{kcat\$AHASII\$Pyr}\,\text{\$Complex\$Pyr\$AHASII\$}[t] + \text{kcat\$AHASI\$Pyr}\,\text{\$Complex\$Pyr\$AHASI\$}[t] \\
&\quad \text{kcat\$AHASI\$Pyr}\,\text{residualRateAHASIValaKB}\,\text{\$Complex\$Pyr\$AHASI\$Val\$}[t], \\
&\text{CoA}'[t] == \text{kcat\$IPMS\$acetylCoA}\,\text{\$Complex\$acetylCoA\$IPMS\$}[t], \\
&\text{DAD}'[t] == -\text{kfDADaDHIV}\,\text{aDHIV}[t]\,\text{DAD}[t] - \text{kfDADaDMV}\,\text{aDMV}[t]\,\text{DAD}[t] + \\
&\quad \text{kcat\$DAD\$aDHIV}\,\text{\$Complex\$aDHIV\$DAD\$}[t] + \text{krDADaDHIV}\,\text{\$Complex\$aDHIV\$DAD\$}[t] + \\
&\quad \text{kcat\$DAD\$aDMV}\,\text{\$Complex\$aDMV\$DAD\$}[t] + \text{krDADaDMV}\,\text{\$Complex\$aDMV\$DAD\$}[t], \\
&\text{exIle}'[t] == 0,
\end{aligned}
$$

$$
\begin{aligned}
&\text{exLeu}'[t] == 0,\\
&\text{exVal}'[t] == 0,\\
&\text{Glu}'[t] == 0,\\
&\text{glutarylCoA}'[t] == \text{kcat\$aKIC}\ \text{aKIC}[t],\\
&\text{HDHI}'[t] ==\\
&\left(\text{kcat\$AKI\$HDHI}\left(\frac{\text{AKI}[t]\left(1+\frac{\text{AKI}[t]}{\text{KmHDHIASA}}\right)^{-1+\text{nASA}}}{\text{KmHDHIASA}}+\frac{\text{cASA LASA AKI}[t]\left(1+\frac{\text{cASA AKI}[t]}{\text{KmHDHIASA}}\right)^{-1+\text{nASA}}}{\text{KmHDHIASA}}\right)\right.\\
&\qquad\left.\text{ASA}[t]\right)\Big/\left(\left(1+\frac{\text{AKI}[t]}{\text{KmHDHIASA}}\right)^{\text{nASA}}+\text{LASA}\left(1+\frac{\text{cASA AKI}[t]}{\text{KmHDHIASA}}\right)^{\text{nASA}}\right)-\\
&\quad\left(\text{kcat\$HDHI\$AKI}\ \text{Asp}[t]\right.\\
&\qquad\left.\left(\frac{\text{HDHI}[t]\left(1+\frac{\text{HDHI}[t]}{\text{KmAKIAsp}}\right)^{-1+\text{nAsp}}}{\text{KmAKIAsp}}+\frac{\text{cAsp LAsp HDHI}[t]\left(1+\frac{\text{cAsp HDHI}[t]}{\text{KmAKIAsp}}\right)^{-1+\text{nAsp}}}{\text{KmAKIAsp}}\right)\right)\Big/\\
&\quad\left(\left(1+\frac{\text{HDHI}[t]}{\text{KmAKIAsp}}\right)^{\text{nAsp}}+\text{LAsp}\left(1+\frac{\text{cAsp HDHI}[t]}{\text{KmAKIAsp}}\right)^{\text{nAsp}}\right),\\
&\text{HDHII}'[t] == -\text{kfHDHIIASA ASA}[t]\ \text{HDHII}[t]\ \text{NADPH}[t]+\\
&\quad\text{kcat\$HDHII\$ASA \$Complex\$HDHII\$ASA\$NADPH\$}[t]+\text{krHDHIIASA \$Complex\$HDHII\$ASA\$NAI}\\
&\text{Hse}'[t] == -\text{kfHse Hse}[t]-\text{kfHSKHse ATP}[t]\ \text{Hse}[t]\ \text{HSK}[t]+\\
&\quad\left(\text{kcat\$HDHI\$ASA HDHI}[t]\right.
\end{aligned}
$$

$$\left(\frac{\text{ASA}[t]\left(1+\frac{\text{ASA}[t]}{\text{KmHDHIASA}}\right)^{-1+\text{nHDHI}}}{\text{KmHDHIASA}}+\frac{\text{cHDHI LHDHI ASA}[t]\left(1+\frac{\text{cHDHI ASA}[t]}{\text{KmHDHIASA}}\right)^{-1+\text{nHDHI}}\left(1+\frac{\text{Thr}[t]}{\text{KiHDHIASAThr}}\right)^{\text{nHDHI}}}{\text{KmHDHIASA}}\right)\Bigg/$$

$$\left(\left(1+\frac{\text{ASA}[t]}{\text{KmHDHIASA}}\right)^{\text{nHDHI}}+\text{LHDHI}\left(1+\frac{\text{cHDHI ASA}[t]}{\text{KmHDHIASA}}\right)^{\text{nHDHI}}\left(1+\frac{\text{Thr}[t]}{\text{KiHDHIASAThr}}\right)^{\text{nHDHI}}\right)+$$

```
  kcat$HDHII$ASA $Complex$HDHII$ASA$NADPH$[t] + krHSKHse $Complex$HSK$Hse$ATP$[t]
HseP'[t] == -kfTSHseP HseP[t] TS[t] + krTSHseP $Complex$HseP$TS$[t] +
  kcat$HSK$Hse $Complex$HSK$Hse$ATP$[t],
HSK'[t] == -kfHSKHse ATP[t] Hse[t] HSK[t] - kfiHSKHseThr HSK[t] Thr[t] +
  kcat$HSK$Hse $Complex$HSK$Hse$ATP$[t] + krHSKHse $Complex$HSK$Hse$ATP$[t] +
  kriHSKHseThr $Complex$HSK$Thr$[t],
Ile'[t] == -kcat$Ile Ile[t] - rkfTBIle Ile[t] TB[t] + fkcat$TB$aKMV $Complex$aKMV$TBN
  kcat$LIVII$exIle $Complex$exIle$LIVII$[t] + kcat$LIVI$exIle $Complex$exIle$LIVI
  rkrTBIle $Complex$Ile$TB$[t],
IPMDH'[t] == -kfIPMDHbIPM bIPM[t] IPMDH[t] NAD[t] +
  kcat$IPMDH$bIPM $Complex$IPMDH$bIPM$NAD$[t] + krIPMDHbIPM $Complex$IPMDH$bIPM$N
IPMI'[t] == -kfIPMIaIPM aIPM[t] IPMI[t] - kfIPMIbIPM bIPM[t] IPMI[t] +
  kcat$IPMI$aIPM $Complex$aIPM$IPMI$[t] + krIPMIaIPM $Complex$aIPM$IPMI$[t] +
  kcat$IPMI$bIPM $Complex$bIPM$IPMI$[t] + krIPMIbIPM $Complex$bIPM$IPMI$[t],
IPMS'[t] == -kfIPMSacetylCoA acetylCoA[t] IPMS[t] - kfiIPMSLeu IPMS[t] Leu[t] +
  krIPMSacetylCoA $Complex$acetylCoA$IPMS$[t] +
  kcat$IPMS$aKIV $Complex$aKIV$IPMSacetyl$[t] + kriIPMSLeu $Complex$IPMS$Leu$[t],
IPMSacetyl'[t] == -kfIPMSaKIV aKIV[t] IPMSacetyl[t] - kfiIPMSacetylLeu IPMSacetyl[t
  kcat$IPMS$acetylCoA $Complex$acetylCoA$IPMS$[t] +
  krIPMSaKIV $Complex$aKIV$IPMSacetyl$[t] + kriIPMSacetylLeu $Complex$IPMSacetyl$
IR'[t] == -kfIRaAHB aAHB[t] IR[t] NADPH[t] - kfIRaAL aAL[t] IR[t] NADPH[t] +
```

```
  kcat$IR$aAHB $Complex$IR$aAHB$NADPH$[t] + krIRaAHB $Complex$IR$aAHB$NADPH$[t] +
  kcat$IR$aAL $Complex$IR$aAL$NADPH$[t] + krIRaAL $Complex$IR$aAL$NADPH$[t],
KDC'[t] == -kfKDCaKB aKB[t] KDC[t] + kcat$KDC$aKB $Complex$aKB$KDC$[t] +
  krKDCaKB $Complex$aKB$KDC$[t],
Leu'[t] == -kcat$Leu Leu[t] - kfiIPMSLeu IPMS[t] Leu[t] -
  kfiIPMSacetylLeu IPMSacetyl[t] Leu[t] - rkfTBLeu Leu[t] TB[t] +
  fkcat$TB$aKIC $Complex$aKIC$TBNH2$[t] -
  kfiIPMSacetylLeu Leu[t] $Complex$aKIV$IPMSacetyl$[t] +
  kriIPMSacetylLeu $Complex$aKIV$IPMSacetyl$Leu$[t] +
  kcat$LIVII$exLeu $Complex$exLeu$LIVII$[t] + kcat$LIVI$exLeu $Complex$exLeu$LIVI
  kcat$LS$exLeu $Complex$exLeu$LS$[t] + kriIPMSacetylLeu $Complex$IPMSacetyl$Leu$
  kriIPMSLeu $Complex$IPMS$Leu$[t] + rkrTBLeu $Complex$Leu$TB$[t],
LIVI'[t] == -kfLIVIexIle exIle[t] LIVI[t] - kfLIVIexLeu exLeu[t] LIVI[t] -
  kfLIVIexVal exVal[t] LIVI[t] + kcat$LIVI$exIle $Complex$exIle$LIVI$[t] +
  krLIVIexIle $Complex$exIle$LIVI$[t] + kcat$LIVI$exLeu $Complex$exLeu$LIVI$[t] +
  krLIVIexLeu $Complex$exLeu$LIVI$[t] + kcat$LIVI$exVal $Complex$exVal$LIVI$[t] +
  krLIVIexVal $Complex$exVal$LIVI$[t],
LIVII'[t] == -kfLIVIIexIle exIle[t] LIVII[t] - kfLIVIIexLeu exLeu[t] LIVII[t] -
  kfLIVIIexVal exVal[t] LIVII[t] + kcat$LIVII$exIle $Complex$exIle$LIVII$[t] +
  krLIVIIexIle $Complex$exIle$LIVII$[t] + kcat$LIVII$exLeu $Complex$exLeu$LIVII$[
  krLIVIIexLeu $Complex$exLeu$LIVII$[t] + kcat$LIVII$exVal $Complex$exVal$LIVII$[
  krLIVIIexVal $Complex$exVal$LIVII$[t],
LS'[t] == -kfLSexLeu exLeu[t] LS[t] + kcat$LS$exLeu $Complex$exLeu$LS$[t] +
  krLSexLeu $Complex$exLeu$LS$[t],
Lys'[t] == 0,
NAD'[t] == 0,
NADH'[t] == kcat$IPMDH$bIPM $Complex$IPMDH$bIPM$NAD$[t],
NADP'[t] == 0,
NADPH'[t] == 0,
```

$$NH3'[t] == \left(kcat\$TDA\ TDA[t]\left(\frac{cTDA\ L0TDA\left(1+\frac{Ile[t]}{KiIle}\right)^{nTDA}\ Thr[t]\left(1+\frac{cTDA\ Thr[t]}{KmThr}\right)^{-1+nTDA}}{KmThr}+\frac{Thr[t]\left(1+\frac{Thr[t]}{KmThr}\right)^{-1+nTDA}\left(1+\frac{Val[t]}{KaVal}\right)^{nTDA}}{KmThr}\right)\right)\Big/\left(L0TDA\left(1+\frac{Ile[t]}{KiIle}\right)^{nTDA}\left(1+\frac{cTDA\ Thr[t]}{KmThr}\right)^{nTDA}+\left(1+\frac{Thr[t]}{KmThr}\right)^{nTDA}\left(1+\frac{Val[t]}{KaVal}\right)^{nTDA}\right),$$

$$pantothenate'[t] == kcat\$aKIV\ aKIV[t],$$

$$Phosphate'[t] == 0,$$

$$propionylCoA'[t] == kcat\$KDC\$aKB\ \$Complex\$aKB\$KDC\$[t],$$

$$protein'[t] == kcat\$Ile\ Ile[t] + kcat\$Leu\ Leu[t] + kcat\$Val\ Val[t],$$

$$Pyr'[t] == 0,$$

$$TB'[t] == -fkfTBGlu\ Glu[t]\ TB[t] - rkfTBIle\ Ile[t]\ TB[t] - rkfTBLeu\ Leu[t]\ TB[t] - rkfTBVal\ TB[t]\ Val[t] + rkcat\$TB\$aKG\ \$Complex\$aKG\$TBNH2\$[t] + fkcat\$TB\$aKIC\ \$Complex\$aKIC\$TBNH2\$[t] + fkcat\$TB\$aKIV\ \$Complex\$aKIV\$TBNH2\$[t] + fkcat\$TB\$aKMV\ \$Complex\$aKMV\$TBNH2\$[t] + fkrTBGlu\ \$Complex\$Glu\$TB\$[t] + rkrTBIle\ \$Complex\$Ile\$TB\$[t] + rkrTBLeu\ \$Complex\$Leu\$TB\$[t] + rkrTBVal\ \$Complex\$Val\$TB\$[t],$$

$$TBNH2'[t] == -rkfTBaKG\ aKG[t]\ TBNH2[t] - fkfTBaKIC\ aKIC[t]\ TBNH2[t] - fkfTBaKIV\ aKIV[t]\ TBNH2[t] - fkfTBaKMV\ aKMV[t]\ TBNH2[t] + rkrTBaKG\ \$Complex\$aKG\$T$$
$$fkrTBaKIC\ \$Complex\$aKIC\$TBNH2\$[t] + fkrTBaKIV\ \$Complex\$aKIV\$TBNH2\$[t] + fkrTBaKMV\ \$Complex\$aKMV\$TBNH2\$[t] + fkcat\$TB\$Glu\ \$Complex\$Glu\$TB\$[t] + rkcat\$TB\$Ile\ \$Complex\$Ile\$TB\$[t] + rkcat\$TB\$Leu\ \$Complex\$Leu\$TB\$[t] + rkcat\$TB\$Val\ \$Complex\$Val\$TB\$[t],$$

$$TC'[t] == -fkfTCAla\ Ala[t]\ TC[t] - rkfTCVal\ TC[t]\ Val[t] + fkcat\$TC\$aKIV\ \$Complex\$aKIV\$TCNH2\$[t] + fkrTCAla\ \$Complex\$Ala\$TC\$[t] + rkcat\$TC\$Pyr\ \$Complex\$Pyr\$TCNH2\$[t] + rkrTCVal\ \$Complex\$Val\$TC\$[t],$$

$$
\begin{aligned}
&\text{TCNH2}'[t] == -\text{fkfTCaKIV}\,\text{aKIV}[t]\,\text{TCNH2}[t] - \text{rkfTCPyr}\,\text{Pyr}[t]\,\text{TCNH2}[t] + \\
&\quad \text{fkrTCaKIV}\,\$\text{Complex}\$\text{aKIV}\$\text{TCNH2}\$[t] + \text{fkcat}\$\text{TC}\$\text{Ala}\,\$\text{Complex}\$\text{Ala}\$\text{TC}\$[t] + \\
&\quad \text{rkrTCPyr}\,\$\text{Complex}\$\text{Pyr}\$\text{TCNH2}\$[t] + \text{rkcat}\$\text{TC}\$\text{Val}\,\$\text{Complex}\$\text{Val}\$\text{TC}\$[t],\ \text{TDA}'[t] == 0, \\
&\text{Thr}'[t] == -\text{kfiHSKHseThr}\,\text{HSK}[t]\,\text{Thr}[t] - \\
&\quad \left(\text{kcat}\$\text{TDA}\,\text{TDA}[t]\left(\frac{\text{cTDA}\,\text{L0TDA}\left(1+\frac{\text{Ile}[t]}{\text{KiIle}}\right)^{\text{nTDA}}\text{Thr}[t]\left(1+\frac{\text{cTDA}\,\text{Thr}[t]}{\text{KmThr}}\right)^{-1+\text{nTDA}}}{\text{KmThr}} + \right.\right. \\
&\qquad \left.\left.\frac{\text{Thr}[t]\left(1+\frac{\text{Thr}[t]}{\text{KmThr}}\right)^{-1+\text{nTDA}}\left(1+\frac{\text{Val}[t]}{\text{KaVal}}\right)^{\text{nTDA}}}{\text{KmThr}}\right)\right) \Big/ \\
&\quad \left(\text{L0TDA}\left(1+\frac{\text{Ile}[t]}{\text{KiIle}}\right)^{\text{nTDA}}\left(1+\frac{\text{cTDA}\,\text{Thr}[t]}{\text{KmThr}}\right)^{\text{nTDA}} + \left(1+\frac{\text{Thr}[t]}{\text{KmThr}}\right)^{\text{nTDA}}\left(1+\frac{\text{Val}[t]}{\text{KaVal}}\right)^{\text{nTDA}}\right) + \\
&\quad \text{kcat}\$\text{TS}\$\text{HseP}\,\$\text{Complex}\$\text{HseP}\$\text{TS}\$[t] + \text{kriHSKHseThr}\,\$\text{Complex}\$\text{HSK}\$\text{Thr}\$[t], \\
&\text{TS}'[t] == -\text{kfTSHseP}\,\text{HseP}[t]\,\text{TS}[t] + \text{kcat}\$\text{TS}\$\text{HseP}\,\$\text{Complex}\$\text{HseP}\$\text{TS}\$[t] + \\
&\quad \text{krTSHseP}\,\$\text{Complex}\$\text{HseP}\$\text{TS}\$[t], \\
&\text{Val}'[t] == -\text{kcat}\$\text{Val}\,\text{Val}[t] - \text{kfiAHASIPyrVal}\,\text{AHASI}[t]\,\text{Val}[t] - \\
&\quad \text{kfiAHASIaKBVal}\,\text{AHASICH3CO}[t]\,\text{Val}[t] - \text{kfiAHASIIIPyrVal}\,\text{AHASIII}[t]\,\text{Val}[t] - \\
&\quad \text{kfiAHASIIIaKBVal}\,\text{AHASIIICH3CO}[t]\,\text{Val}[t] - \text{rkfTBVal}\,\text{TB}[t]\,\text{Val}[t] - \text{rkfTCVal}\,\text{TC}[t]\,\text{V} \\
&\quad \text{kriAHASIaKBVal}\,\$\text{Complex}\$\text{AHASICH3CO}\$\text{Val}\$[t] + \\
&\quad \text{kriAHASIIIaKBVal}\,\$\text{Complex}\$\text{AHASIIICH3CO}\$\text{Val}\$[t] + \\
&\quad \text{kriAHASIIIPyrVal}\,\$\text{Complex}\$\text{AHASIII}\$\text{Val}\$[t] + \text{kriAHASIPyrVal}\,\$\text{Complex}\$\text{AHASI}\$\text{Val}\$[\\
&\quad \text{kfiAHASIaKBVal}\,\text{Val}[t]\,\$\text{Complex}\$\text{aKB}\$\text{AHASICH3CO}\$[t] + \\
&\quad \text{kriAHASIaKBVal}\,\$\text{Complex}\$\text{aKB}\$\text{AHASICH3CO}\$\text{Val}\$[t] - \\
&\quad \text{kfiAHASIIIaKBVal}\,\text{Val}[t]\,\$\text{Complex}\$\text{aKB}\$\text{AHASIIICH3CO}\$[t] + \\
&\quad \text{kriAHASIIIaKBVal}\,\$\text{Complex}\$\text{aKB}\$\text{AHASIIICH3CO}\$\text{Val}\$[t] + \\
&\quad \text{fkcat}\$\text{TB}\$\text{aKIV}\,\$\text{Complex}\$\text{aKIV}\$\text{TBNH2}\$[t] + \text{fkcat}\$\text{TC}\$\text{aKIV}\,\$\text{Complex}\$\text{aKIV}\$\text{TCNH2}\$[t] + \\
&\quad \text{kcat}\$\text{LIVII}\$\text{exVal}\,\$\text{Complex}\$\text{exVal}\$\text{LIVII}\$[t] + \text{kcat}\$\text{LIVI}\$\text{exVal}\,\$\text{Complex}\$\text{exVal}\$\text{LIV} \\
&\quad \text{kfiAHASIPyr2Val}\,\text{Val}[t]\,\$\text{Complex}\$\text{Pyr}\$\text{AHASICH3CO}\$[t] + \\
&\quad \text{kriAHASIPyr2Val}\,\$\text{Complex}\$\text{Pyr}\$\text{AHASICH3CO}\$\text{Val}\$[t] -
\end{aligned}
$$

```
  kfiAHASIIIPyr2Val Val[t] $Complex$Pyr$AHASIIICH3CO$[t] +
  kriAHASIIIPyr2Val $Complex$Pyr$AHASIIICH3CO$Val$[t] -
  kfiAHASIIIPyrVal Val[t] $Complex$Pyr$AHASIII$[t] +
  kriAHASIIIPyrVal $Complex$Pyr$AHASIII$Val$[t] -
  kfiAHASIPyrVal Val[t] $Complex$Pyr$AHASI$[t] + kriAHASIPyrVal $Complex$Pyr$AHAS
  rkrTBVal $Complex$Val$TB$[t] + rkrTCVal $Complex$Val$TC$[t],
$Complex$acetylCoA$IPMS$'[t] == kfIPMSacetylCoA acetylCoA[t] IPMS[t] -
  kcat$IPMS$acetylCoA $Complex$acetylCoA$IPMS$[t] -
  krIPMSacetylCoA $Complex$acetylCoA$IPMS$[t],
$Complex$aDHIV$DAD$'[t] == kfDADaDHIV aDHIV[t] DAD[t] -
  kcat$DAD$aDHIV $Complex$aDHIV$DAD$[t] - krDADaDHIV $Complex$aDHIV$DAD$[t],
$Complex$aDMV$DAD$'[t] == kfDADaDMV aDMV[t] DAD[t] - kcat$DAD$aDMV $Complex$aDMV$DA
  krDADaDMV $Complex$aDMV$DAD$[t],
$Complex$AHASICH3CO$Val$'[t] == kfiAHASIaKBVal AHASICH3CO[t] Val[t] -
  kriAHASIaKBVal $Complex$AHASICH3CO$Val$[t] -
  kfAHASIaKB aKB[t] $Complex$AHASICH3CO$Val$[t] -
  kfAHASIPyr2 Pyr[t] $Complex$AHASICH3CO$Val$[t] +
  krAHASIaKB $Complex$aKB$AHASICH3CO$Val$[t] +
  kcat$AHASI$aKB residualRateAHASIValaKB $Complex$aKB$AHASICH3CO$Val$[t] +
  krAHASIPyr2 $Complex$Pyr$AHASICH3CO$Val$[t] +
  kcat$AHASI$Pyr2 residualRateAHASIValPyr2 $Complex$Pyr$AHASICH3CO$Val$[t],
$Complex$AHASIIICH3CO$Val$'[t] ==
 kfiAHASIIIaKBVal AHASIIICH3CO[t] Val[t] - kriAHASIIIaKBVal $Complex$AHASIIICH3CO
  kfAHASIIIaKB aKB[t] $Complex$AHASIIICH3CO$Val$[t] -
  kfAHASIIIPyr2 Pyr[t] $Complex$AHASIIICH3CO$Val$[t] +
  krAHASIIIaKB $Complex$aKB$AHASIIICH3CO$Val$[t] +
  kcat$AHASIII$aKB residualRateAHASIIIValaKB $Complex$aKB$AHASIIICH3CO$Val$[t] +
  krAHASIIIPyr2 $Complex$Pyr$AHASIIICH3CO$Val$[t] +
  kcat$AHASIII$Pyr2 residualRateAHASIIIValPyr2 $Complex$Pyr$AHASIIICH3CO$Val$[t
```

```
$Complex$AHASIII$Val$'[t] == kfiAHASIIIPyrVal AHASIII[t] Val[t] -
  kriAHASIIIPyrVal $Complex$AHASIII$Val$[t] - kfAHASIIIPyr Pyr[t] $Complex$AHASII
  krAHASIIIPyr $Complex$Pyr$AHASIII$Val$[t] +
  kcat$AHASIII$Pyr residualRateAHASIIIValaKB $Complex$Pyr$AHASIII$Val$[t],
$Complex$AHASI$Val$'[t] == kfiAHASIPyrVal AHASI[t] Val[t] -
  kriAHASIPyrVal $Complex$AHASI$Val$[t] - kfAHASIPyr Pyr[t] $Complex$AHASI$Val$[t
  krAHASIPyr $Complex$Pyr$AHASI$Val$[t] +
  kcat$AHASI$Pyr residualRateAHASIValaKB $Complex$Pyr$AHASI$Val$[t],
$Complex$aIPM$IPMI$'[t] == kfIPMIaIPM aIPM[t] IPMI[t] -
  kcat$IPMI$aIPM $Complex$aIPM$IPMI$[t] - krIPMIaIPM $Complex$aIPM$IPMI$[t],
$Complex$aKB$AHASICH3CO$'[t] == kfAHASIaKB AHASICH3CO[t] aKB[t] -
  kcat$AHASI$aKB $Complex$aKB$AHASICH3CO$[t] - krAHASIaKB $Complex$aKB$AHASICH3CO
  kfiAHASIaKBVal Val[t] $Complex$aKB$AHASICH3CO$[t] +
  kriAHASIaKBVal $Complex$aKB$AHASICH3CO$Val$[t],
$Complex$aKB$AHASICH3CO$Val$'[t] ==
 kfAHASIaKB aKB[t] $Complex$AHASICH3CO$Val$[t] +
  kfiAHASIaKBVal Val[t] $Complex$aKB$AHASICH3CO$[t] -
  krAHASIaKB $Complex$aKB$AHASICH3CO$Val$[t] -
  kriAHASIaKBVal $Complex$aKB$AHASICH3CO$Val$[t] -
  kcat$AHASI$aKB residualRateAHASIValaKB $Complex$aKB$AHASICH3CO$Val$[t],
$Complex$aKB$AHASIICH3CO$'[t] ==
 kfAHASIIaKB AHASIICH3CO[t] aKB[t] - kcat$AHASII$aKB $Complex$aKB$AHASIICH3CO$[t]
  krAHASIIaKB $Complex$aKB$AHASIICH3CO$[t],
$Complex$aKB$AHASIIICH3CO$'[t] ==
 kfAHASIIIaKB AHASIIICH3CO[t] aKB[t] - kcat$AHASIII$aKB $Complex$aKB$AHASIIICH3CO
  krAHASIIIaKB $Complex$aKB$AHASIIICH3CO$[t] -
  kfiAHASIIIaKBVal Val[t] $Complex$aKB$AHASIIICH3CO$[t] +
  kriAHASIIIaKBVal $Complex$aKB$AHASIIICH3CO$Val$[t],
$Complex$aKB$AHASIIICH3CO$Val$'[t] ==
```

```
 kfAHASIIIaKB aKB[t] $Complex$AHASIIICH3CO$Val$[t] +
  kfiAHASIIIaKBVal Val[t] $Complex$aKB$AHASIIICH3CO$[t] -
  krAHASIIIaKB $Complex$aKB$AHASIIICH3CO$Val$[t] -
  kriAHASIIIaKBVal $Complex$aKB$AHASIIICH3CO$Val$[t] -
  kcat$AHASIII$aKB residualRateAHASIIIValaKB $Complex$aKB$AHASIIICH3CO$Val$[t],
$Complex$aKB$KDC$'[t] == kfKDCaKB aKB[t] KDC[t] - kcat$KDC$aKB $Complex$aKB$KDC$[t]
  krKDCaKB $Complex$aKB$KDC$[t],
$Complex$aKG$TBNH2$'[t] == rkfTBaKG aKG[t] TBNH2[t] - rkcat$TB$aKG $Complex$aKG$TBN
  rkrTBaKG $Complex$aKG$TBNH2$[t],
$Complex$aKIC$TBNH2$'[t] == fkfTBaKIC aKIC[t] TBNH2[t] -
  fkcat$TB$aKIC $Complex$aKIC$TBNH2$[t] - fkrTBaKIC $Complex$aKIC$TBNH2$[t],
$Complex$AKII$Asp$ATP$'[t] == kfAKIIAsp AKII[t] Asp[t] ATP[t] -
  kcat$AKII$Asp $Complex$AKII$Asp$ATP$[t] - krAKIIAsp $Complex$AKII$Asp$ATP$[t],
$Complex$aKIV$IPMSacetyl$'[t] ==
 kfIPMSaKIV aKIV[t] IPMSacetyl[t] - kcat$IPMS$aKIV $Complex$aKIV$IPMSacetyl$[t] -
  krIPMSaKIV $Complex$aKIV$IPMSacetyl$[t] -
  kfiIPMSacetylLeu Leu[t] $Complex$aKIV$IPMSacetyl$[t] +
  kriIPMSacetylLeu $Complex$aKIV$IPMSacetyl$Leu$[t],
$Complex$aKIV$IPMSacetyl$Leu$'[t] ==
 kfiIPMSacetylLeu Leu[t] $Complex$aKIV$IPMSacetyl$[t] -
  kriIPMSacetylLeu $Complex$aKIV$IPMSacetyl$Leu$[t] -
  krIPMSaKIV $Complex$aKIV$IPMSacetyl$Leu$[t] +
  kfIPMSaKIV aKIV[t] $Complex$IPMSacetyl$Leu$[t],
$Complex$aKIV$TBNH2$'[t] == fkfTBaKIV aKIV[t] TBNH2[t] -
  fkcat$TB$aKIV $Complex$aKIV$TBNH2$[t] - fkrTBaKIV $Complex$aKIV$TBNH2$[t],
$Complex$aKIV$TCNH2$'[t] == fkfTCaKIV aKIV[t] TCNH2[t] -
  fkcat$TC$aKIV $Complex$aKIV$TCNH2$[t] - fkrTCaKIV $Complex$aKIV$TCNH2$[t],
$Complex$aKMV$TBNH2$'[t] == fkfTBaKMV aKMV[t] TBNH2[t] -
  fkcat$TB$aKMV $Complex$aKMV$TBNH2$[t] - fkrTBaKMV $Complex$aKMV$TBNH2$[t],
```

```
$Complex$Ala$TC$'[t] == fkfTCAla Ala[t] TC[t] - fkcat$TC$Ala $Complex$Ala$TC$[t] -
  fkrTCAla $Complex$Ala$TC$[t],
$Complex$ASD$ASA$NADP$Phosphate$'[t] ==
 kfASDASA ASA[t] ASD[t] NADP[t] Phosphate[t] -
  kcat$ASD$ASA $Complex$ASD$ASA$NADP$Phosphate$[t] -
  krASDASA $Complex$ASD$ASA$NADP$Phosphate$[t],
$Complex$ASD$AspP$NADPH$'[t] == kfASDAspP ASD[t] AspP[t] NADPH[t] -
  kcat$ASD$AspP $Complex$ASD$AspP$NADPH$[t] - krASDAspP $Complex$ASD$AspP$NADPH$[
$Complex$bIPM$IPMI$'[t] == kfIPMIbIPM bIPM[t] IPMI[t] -
  kcat$IPMI$bIPM $Complex$bIPM$IPMI$[t] - krIPMIbIPM $Complex$bIPM$IPMI$[t],
$Complex$exIle$LIVII$'[t] == kfLIVIIexIle exIle[t] LIVII[t] -
  kcat$LIVII$exIle $Complex$exIle$LIVII$[t] - krLIVIIexIle $Complex$exIle$LIVII$[
$Complex$exIle$LIVI$'[t] == kfLIVIexIle exIle[t] LIVI[t] -
  kcat$LIVI$exIle $Complex$exIle$LIVI$[t] - krLIVIexIle $Complex$exIle$LIVI$[t],
$Complex$exLeu$LIVII$'[t] == kfLIVIIexLeu exLeu[t] LIVII[t] -
  kcat$LIVII$exLeu $Complex$exLeu$LIVII$[t] - krLIVIIexLeu $Complex$exLeu$LIVII$[
$Complex$exLeu$LIVI$'[t] == kfLIVIexLeu exLeu[t] LIVI[t] -
  kcat$LIVI$exLeu $Complex$exLeu$LIVI$[t] - krLIVIexLeu $Complex$exLeu$LIVI$[t],
$Complex$exLeu$LS$'[t] == kfLSexLeu exLeu[t] LS[t] - kcat$LS$exLeu $Complex$exLeu$L
  krLSexLeu $Complex$exLeu$LS$[t],
$Complex$exVal$LIVII$'[t] == kfLIVIIexVal exVal[t] LIVII[t] -
  kcat$LIVII$exVal $Complex$exVal$LIVII$[t] - krLIVIIexVal $Complex$exVal$LIVII$[
$Complex$exVal$LIVI$'[t] == kfLIVIexVal exVal[t] LIVI[t] -
  kcat$LIVI$exVal $Complex$exVal$LIVI$[t] - krLIVIexVal $Complex$exVal$LIVI$[t],
$Complex$Glu$TB$'[t] == fkfTBGlu Glu[t] TB[t] - fkcat$TB$Glu $Complex$Glu$TB$[t] -
  fkrTBGlu $Complex$Glu$TB$[t],
$Complex$HDHII$ASA$NADPH$'[t] == kfHDHIIASA ASA[t] HDHII[t] NADPH[t] -
  kcat$HDHII$ASA $Complex$HDHII$ASA$NADPH$[t] - krHDHIIASA $Complex$HDHII$ASA$NAD
$Complex$HseP$TS$'[t] == kfTSHseP HseP[t] TS[t] - kcat$TS$HseP $Complex$HseP$TS$[t]
```

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  krTSHseP $Complex$HseP$TS$[t],
$Complex$HSK$Hse$ATP$'[t] == kfHSKHse ATP[t] Hse[t] HSK[t] -
  kcat$HSK$Hse $Complex$HSK$Hse$ATP$[t] - krHSKHse $Complex$HSK$Hse$ATP$[t],
$Complex$HSK$Thr$'[t] == kfiHSKHseThr HSK[t] Thr[t] - kriHSKHseThr $Complex$HSK$Thr
$Complex$Ile$TB$'[t] == rkfTBIle Ile[t] TB[t] - rkcat$TB$Ile $Complex$Ile$TB$[t] -
  rkrTBIle $Complex$Ile$TB$[t],
$Complex$IPMDH$bIPM$NAD$'[t] == kfIPMDHbIPM bIPM[t] IPMDH[t] NAD[t] -
  kcat$IPMDH$bIPM $Complex$IPMDH$bIPM$NAD$[t] - krIPMDHbIPM $Complex$IPMDH$bIPM$N
$Complex$IPMSacetyl$Leu$'[t] == kfiIPMSacetylLeu IPMSacetyl[t] Leu[t] +
  krIPMSaKIV $Complex$aKIV$IPMSacetyl$Leu$[t] -
  kriIPMSacetylLeu $Complex$IPMSacetyl$Leu$[t] -
  kfIPMSaKIV aKIV[t] $Complex$IPMSacetyl$Leu$[t],
$Complex$IPMS$Leu$'[t] == kfiIPMSLeu IPMS[t] Leu[t] - kriIPMSLeu $Complex$IPMS$Leu$
$Complex$IR$aAHB$NADPH$'[t] == kfIRaAHB aAHB[t] IR[t] NADPH[t] -
  kcat$IR$aAHB $Complex$IR$aAHB$NADPH$[t] - krIRaAHB $Complex$IR$aAHB$NADPH$[t],
$Complex$IR$aAL$NADPH$'[t] == kfIRaAL aAL[t] IR[t] NADPH[t] -
  kcat$IR$aAL $Complex$IR$aAL$NADPH$[t] - krIRaAL $Complex$IR$aAL$NADPH$[t],
$Complex$Leu$TB$'[t] == rkfTBLeu Leu[t] TB[t] - rkcat$TB$Leu $Complex$Leu$TB$[t] -
  rkrTBLeu $Complex$Leu$TB$[t],
$Complex$Pyr$AHASICH3CO$'[t] == kfAHASIPyr2 AHASICH3CO[t] Pyr[t] -
  kcat$AHASI$Pyr2 $Complex$Pyr$AHASICH3CO$[t] - krAHASIPyr2 $Complex$Pyr$AHASICH3
  kfiAHASIPyr2Val Val[t] $Complex$Pyr$AHASICH3CO$[t] +
  kriAHASIPyr2Val $Complex$Pyr$AHASICH3CO$Val$[t],
$Complex$Pyr$AHASICH3CO$Val$'[t] ==
 kfAHASIPyr2 Pyr[t] $Complex$AHASICH3CO$Val$[t] +
  kfiAHASIPyr2Val Val[t] $Complex$Pyr$AHASICH3CO$[t] -
  krAHASIPyr2 $Complex$Pyr$AHASICH3CO$Val$[t] -
  kriAHASIPyr2Val $Complex$Pyr$AHASICH3CO$Val$[t] -
  kcat$AHASI$Pyr2 residualRateAHASIValPyr2 $Complex$Pyr$AHASICH3CO$Val$[t],
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```
$Complex$Pyr$AHASIICH3CO$'[t] == kfAHASIIPyr2 AHASIICH3CO[t] Pyr[t] -
  kcat$AHASII$Pyr2 $Complex$Pyr$AHASIICH3CO$[t] -
  krAHASIIPyr2 $Complex$Pyr$AHASIICH3CO$[t],
$Complex$Pyr$AHASIIICH3CO$'[t] ==
 kfAHASIIIPyr2 AHASIIICH3CO[t] Pyr[t] - kcat$AHASIII$Pyr2 $Complex$Pyr$AHASIIICH3
  krAHASIIIPyr2 $Complex$Pyr$AHASIIICH3CO$[t] -
  kfiAHASIIIPyr2Val Val[t] $Complex$Pyr$AHASIIICH3CO$[t] +
  kriAHASIIIPyr2Val $Complex$Pyr$AHASIIICH3CO$Val$[t],
$Complex$Pyr$AHASIIICH3CO$Val$'[t] ==
 kfAHASIIIPyr2 Pyr[t] $Complex$AHASIIICH3CO$Val$[t] +
  kfiAHASIIIPyr2Val Val[t] $Complex$Pyr$AHASIIICH3CO$[t] -
  krAHASIIIPyr2 $Complex$Pyr$AHASIIICH3CO$Val$[t] -
  kriAHASIIIPyr2Val $Complex$Pyr$AHASIIICH3CO$Val$[t] -
  kcat$AHASIII$Pyr2 residualRateAHASIIIValPyr2 $Complex$Pyr$AHASIIICH3CO$Val$[t]
$Complex$Pyr$AHASIII$'[t] == kfAHASIIIPyr AHASIII[t] Pyr[t] -
  kcat$AHASIII$Pyr $Complex$Pyr$AHASIII$[t] - krAHASIIIPyr $Complex$Pyr$AHASIII$[
  kfiAHASIIIPyrVal Val[t] $Complex$Pyr$AHASIII$[t] +
  kriAHASIIIPyrVal $Complex$Pyr$AHASIII$Val$[t],
$Complex$Pyr$AHASIII$Val$'[t] == kfAHASIIIPyr Pyr[t] $Complex$AHASIII$Val$[t] +
  kfiAHASIIIPyrVal Val[t] $Complex$Pyr$AHASIII$[t] -
  krAHASIIIPyr $Complex$Pyr$AHASIII$Val$[t] -
  kriAHASIIIPyrVal $Complex$Pyr$AHASIII$Val$[t] -
  kcat$AHASIII$Pyr residualRateAHASIIIValaKB $Complex$Pyr$AHASIII$Val$[t],
$Complex$Pyr$AHASII$'[t] == kfAHASIIPyr AHASII[t] Pyr[t] -
  kcat$AHASII$Pyr $Complex$Pyr$AHASII$[t] - krAHASIIPyr $Complex$Pyr$AHASII$[t],
$Complex$Pyr$AHASI$'[t] == kfAHASIPyr AHASI[t] Pyr[t] -
  kcat$AHASI$Pyr $Complex$Pyr$AHASI$[t] - krAHASIPyr $Complex$Pyr$AHASI$[t] -
  kfiAHASIPyrVal Val[t] $Complex$Pyr$AHASI$[t] + kriAHASIPyrVal $Complex$Pyr$AHAS
$Complex$Pyr$AHASI$Val$'[t] == kfAHASIPyr Pyr[t] $Complex$AHASI$Val$[t] +
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    kfiAHASIPyrVal Val[t] $Complex$Pyr$AHASI$[t] - krAHASIPyr $Complex$Pyr$AHASI$Va
    kriAHASIPyrVal $Complex$Pyr$AHASI$Val$[t] -
    kcat$AHASI$Pyr residualRateAHASIValaKB $Complex$Pyr$AHASI$Val$[t],
  $Complex$Pyr$TCNH2$'[t] == rkfTCPyr Pyr[t] TCNH2[t] - rkcat$TC$Pyr $Complex$Pyr$TCN
    rkrTCPyr $Complex$Pyr$TCNH2$[t],
  $Complex$Val$TB$'[t] == rkfTBVal TB[t] Val[t] - rkcat$TB$Val $Complex$Val$TB$[t] -
    rkrTBVal $Complex$Val$TB$[t],
  $Complex$Val$TC$'[t] == rkfTCVal TC[t] Val[t] - rkcat$TC$Val $Complex$Val$TC$[t] -
    rkrTCVal $Complex$Val$TC$[t]},
 {aAHB, aAL, acetylCoA, aDHIV, aDMV, ADP, AHASI, AHASICH3CO, AHASII, AHASIICH3CO,
  AHASIII, AHASIIICH3CO, aIPM, aKB, aKG, AKI, aKIC, AKII, AKIII, aKIV, aKMV, Ala,
  ASA, ASD, Asp, AspP, ATP, bIPM, CO2, CoA, DAD, exIle, exLeu, exVal, Glu, glutarylCo
  HDHI, HDHII, Hse, HseP, HSK, Ile, IPMDH, IPMI, IPMS, IPMSacetyl, IR, KDC, Leu,
  LIVI, LIVII, LS, Lys, NAD, NADH, NADP, NADPH, NH3, pantothenate, Phosphate,
  propionylCoA, protein, Pyr, TB, TBNH2, TC, TCNH2, TDA, Thr, TS, Val,
  $Complex$acetylCoA$IPMS$, $Complex$aDHIV$DAD$, $Complex$aDMV$DAD$,
  $Complex$AHASICH3CO$Val$, $Complex$AHASIIICH3CO$Val$, $Complex$AHASIII$Val$,
  $Complex$AHASI$Val$, $Complex$aIPM$IPMI$, $Complex$aKB$AHASICH3CO$,
  $Complex$aKB$AHASICH3CO$Val$, $Complex$aKB$AHASIICH3CO$, $Complex$aKB$AHASIIICH
  $Complex$aKB$AHASIIICH3CO$Val$, $Complex$aKB$KDC$, $Complex$aKG$TBNH2$,
  $Complex$aKIC$TBNH2$, $Complex$AKII$Asp$ATP$, $Complex$aKIV$IPMSacetyl$,
  $Complex$aKIV$IPMSacetyl$Leu$, $Complex$aKIV$TBNH2$, $Complex$aKIV$TCNH2$,
  $Complex$aKMV$TBNH2$, $Complex$Ala$TC$, $Complex$ASD$ASA$NADP$Phosphate$,
  $Complex$ASD$AspP$NADPH$, $Complex$bIPM$IPMI$, $Complex$exIle$LIVII$,
  $Complex$exIle$LIVI$, $Complex$exLeu$LIVII$, $Complex$exLeu$LIVI$, $Complex$exLe
  $Complex$exVal$LIVII$, $Complex$exVal$LIVI$, $Complex$Glu$TB$, $Complex$HDHII$AS
  $Complex$HseP$TS$, $Complex$HSK$Hse$ATP$, $Complex$HSK$Thr$, $Complex$Ile$TB$,
  $Complex$IPMDH$bIPM$NAD$, $Complex$IPMSacetyl$Leu$, $Complex$IPMS$Leu$,
  $Complex$IR$aAHB$NADPH$, $Complex$IR$aAL$NADPH$, $Complex$Leu$TB$,
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   $Complex$Pyr$AHASICH3CO$, $Complex$Pyr$AHASICH3CO$Val$, $Complex$Pyr$AHASIICH3C
   $Complex$Pyr$AHASIIICH3CO$, $Complex$Pyr$AHASIIICH3CO$Val$, $Complex$Pyr$AHASII
   $Complex$Pyr$AHASIII$Val$, $Complex$Pyr$AHASII$, $Complex$Pyr$AHASI$,
   $Complex$Pyr$AHASI$Val$, $Complex$Pyr$TCNH2$, $Complex$Val$TB$, $Complex$Val$TC$
```

```
(*
  Inputs for Values of Km , Ki and kcat for each Enzyme.
   Lambda Approximation Functions:Kf[],Kf2S[] for kf,
                                  Kr[] for kr
   Omega Approximation Functions: Kfi[] for kfi,
                                  Kri[] for kri.
 *)

Lambda = 100;
Omega = 1;
myKs = {

   cASA = 1;
   LASA = 1;
   nASA = 4;
   KmHDHIASA = 80;
   kcat$AKI$HDHI = 10000;

   cAsp = 1;
   LAsp = 1;
   nAsp = 4;
   KmAKIAsp = 220;
   kcat$HDHI$AKI = 10000;
```

```
cAKI = 0.0001;
LAKI = 10000;
nAKI = 4;
KmAKIAsp = 220;
KiAKIAspThr = 135;
kcat$AKI$Asp = 100;

cAKIII = 0.00005;
LAKIII = 1000;
nAKIII = 2;
KmAKIIIAsp = 30;
KiAKIIIAspLys = 15;
kcat$AKIII$Asp = 20;

cHDHI = 0.008;
LHDHI = 3000;
nHDHI = 4;
KmHDHIASA = 80;
KiHDHIASAThr = 120;
kcat$HDHI$ASA = 800;

kfHDHIAKI = 1000;
kfAKIHDHI = 1000;

KmAKIIAsp = 100; kcat$AKII$Asp = 100;
kfAKIIAsp → Kf[KmAKIIAsp, kcat$AKII$Asp, Lambda],
krAKIIAsp → Kr[kcat$AKII$Asp, Lambda],

kmASDAspP = 22; kcat$ASD$AspP = 40;
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```
kfASDAspP → Kf[kmASDAspP, kcat$ASD$AspP, Lambda],
krASDAspP → Kr[kcat$ASD$AspP, Lambda],

KmASDASA = 110; KmASDNADP = 140; KmASDPhosphate = 10200; kcat$ASD$ASA = 80;
kfASDASA → Kf3S[KmASDASA, KmASDNADP, KmASDPhosphate, kcat$ASD$ASA, Lambda],
krASDASA → Kr[kcat$ASD$ASA, Lambda],

KmHDHIIASA = 100; kcat$HDHII$ASA = 100;
kfHDHIIASA → Kf[KmHDHIIASA, kcat$HDHII$ASA, Lambda],
krHDHIIASA → Kr[kcat$HDHII$ASA, Lambda],

KmHSKHse = 110; kcat$HSK$Hse = 60;
kfHSKHse → Kf[KmHSKHse, kcat$HSK$Hse, Lambda],
krHSKHse → Kr[kcat$HSK$Hse, Lambda],

KiHSKHseThr = 1000;
kfiHSKHseThr → Kfi[KmHSKHse, kcat$HSK$Hse, Lambda, Omega],
kriHSKHseThr → Kri[KmHSKHse, kcat$HSK$Hse, Lambda, Omega, KiHSKHseThr],

kfASA = 0.05;
kfHse = 0.05;

KmTSHseP = 310; kcat$TS$HseP = 60;
kfTSHseP → Kf[KmTSHseP, kcat$TS$HseP, Lambda],
krTSHseP → Kr[kcat$TS$HseP, Lambda],

nTDA → 4,
cTDA → 0.013,
L0TDA → 1.05,
```

```
kcat$TDA → 6000,
KmThr → 2700,
KaVal → 550,
KiIle → 15,                    (* TDA feedback resistant mutant, KiIle=100000 *)

KmKDCaKB = 1000; kcat$KDC$aKB = 3000;
kfKDCaKB → Kf[KmKDCaKB, kcat$KDC$aKB, Lambda],
krKDCaKB → Kr[kcat$KDC$aKB, Lambda],

KmAHASIPyr = 10; kcat$AHASI$Pyr = 7000;
kfAHASIPyr → Kf[KmAHASIPyr, kcat$AHASI$Pyr, Lambda],
krAHASIPyr → Kr[kcat$AHASI$Pyr, Lambda],

KmAHASIaKB = 5000; kcat$AHASI$aKB = 7000;
kfAHASIaKB → Kf[KmAHASIaKB, kcat$AHASI$aKB, Lambda],
krAHASIaKB → Kr[kcat$AHASI$aKB, Lambda],
residualRateAHASIValaKB → 0,

KiAHASIVal = 200;
kfiAHASIPyrVal → Kfi[KmAHASIPyr, kcat$AHASI$Pyr, Lambda, Omega],
kriAHASIPyrVal → Kri[KmAHASIPyr, kcat$AHASI$Pyr, Lambda, Omega, KiAHASIVal],
kfiAHASIaKBVal → Kfi[KmAHASIaKB, kcat$AHASI$aKB, Lambda, Omega],
kriAHASIaKBVal → Kri[KmAHASIaKB, kcat$AHASI$aKB, Lambda, Omega, KiAHASIVal],

KmAHASIIPyr = 10; kcat$AHASII$Pyr = 7000;
kfAHASIIPyr → Kf[KmAHASIIPyr, kcat$AHASII$Pyr, Lambda],
krAHASIIPyr → Kr[kcat$AHASII$Pyr, Lambda],

KmAHASIIaKB = 150; kcat$AHASII$aKB = 7000;
```

```
kfAHASIIaKB → Kf[KmAHASIIaKB, kcat$AHASII$aKB, Lambda],
krAHASIIaKB → Kr[kcat$AHASII$aKB, Lambda],

KmAHASIIIPyr = 10; kcat$AHASIII$Pyr = 7000;
kfAHASIIIPyr → Kf[KmAHASIIIPyr, kcat$AHASIII$Pyr, Lambda],
krAHASIIIPyr → Kr[kcat$AHASIII$Pyr, Lambda],

KmAHASIIIaKB = 150; kcat$AHASIII$aKB = 7000;
kfAHASIIIaKB → Kf[KmAHASIIIaKB, kcat$AHASIII$aKB, Lambda],
krAHASIIIaKB → Kr[kcat$AHASIII$aKB, Lambda],
residualRateAHASIIIValaKB → 0.15,

KiAHASIIIVal = 20;
kfiAHASIIIPyrVal → Kfi[KmAHASIIIPyr, kcat$AHASIII$Pyr, Lambda, Omega],
kriAHASIIIPyrVal → Kri[KmAHASIIIPyr, kcat$AHASIII$Pyr, Lambda, Omega, KiAHASIIIVa
kfiAHASIIIaKBVal → Kfi[KmAHASIIIaKB, kcat$AHASIII$aKB, Lambda, Omega],
kriAHASIIIaKBVal → Kri[KmAHASIIIaKB, kcat$AHASIII$aKB, Lambda, Omega, KiAHASIIIVa

KmIRaAHB = 780; KmIRNADPH = 15; kcat$IR$aAHB = 4700;
kfIRaAHB → Kf2S[KmIRaAHB, KmIRNADPH, kcat$IR$aAHB, Lambda],
krIRaAHB → Kr[kcat$IR$aAHB, Lambda],

KmDADaDMV = 750; kcat$DAD$aDMV = 24000;
kfDADaDMV → Kf[KmDADaDMV, kcat$DAD$aDMV, Lambda],
krDADaDMV → Kr[kcat$DAD$aDMV, Lambda],

KmTBGlu = 1000; fkcat$TB$Glu = 2000;
fkfTBGlu → Kf[KmTBGlu, fkcat$TB$Glu, Lambda],
fkrTBGlu → Kr[fkcat$TB$Glu, Lambda],
```

```
KmTBaKMV = 200; fkcat$TB$aKMV = 1500;
fkfTBaKMV → Kf[KmTBaKMV, fkcat$TB$aKMV, Lambda],
fkrTBaKMV → Kr[fkcat$TB$aKMV, Lambda],

KmTBIle = 600; rkcat$TB$Ile = 3000;
rkfTBIle → Kf[KmTBIle, rkcat$TB$Ile, Lambda],
rkrTBIle → Kr[rkcat$TB$Ile, Lambda],

KmTBaKG = 2500; rkcat$TB$aKG = 2100;
rkfTBaKG → Kf[KmTBaKG, rkcat$TB$aKG, Lambda],
rkrTBaKG → Kr[rkcat$TB$aKG, Lambda],

KmLIVIexIle = 7; kcat$LIVI$exIle = 200;
kfLIVIexIle → Kf[KmLIVIexIle, kcat$LIVI$exIle, Lambda],
krLIVIexIle → Kr[kcat$LIVI$exIle, Lambda],

KmLIVIIexIle = 1; kcat$LIVII$exIle = 1;
kfLIVIIexIle → Kf[KmLIVIIexIle, kcat$LIVII$exIle, Lambda],
krLIVIIexIle → Kr[kcat$LIVII$exIle, Lambda],

kcat$aKMV → 5,
kcat$Ile → 0.2,

KmAHASIPyr = 10; kcat$AHASI$Pyr = 7000;
kfAHASIPyr → Kf[KmAHASIPyr, kcat$AHASI$Pyr, Lambda],
krAHASIPyr → Kr[kcat$AHASI$Pyr, Lambda],

KmAHASIPyr2 = 1000; kcat$AHASI$Pyr2 = 7000;
```

```
kfAHASIPyr2 → Kf[KmAHASIPyr2, kcat$AHASI$Pyr2, Lambda],
krAHASIPyr2 → Kr[kcat$AHASI$Pyr2, Lambda],
residualRateAHASIValPyr2 → 0,

KiAHASIVal = 200;
kfiAHASIPyrVal → Kfi[KmAHASIPyr, kcat$AHASI$Pyr, Lambda, Omega],
kriAHASIPyrVal → Kri[KmAHASIPyr, kcat$AHASI$Pyr, Lambda, Omega, KiAHASIVal],
kfiAHASIPyr2Val → Kfi[KmAHASIPyr2, kcat$AHASI$Pyr2, Lambda, Omega],
kriAHASIPyr2Val → Kri[KmAHASIPyr2, kcat$AHASI$Pyr2, Lambda, Omega, KiAHASIVal],

KmAHASIIPyr = 10; kcat$AHASII$Pyr = 7000;
kfAHASIIPyr → Kf[KmAHASIIPyr, kcat$AHASII$Pyr, Lambda],
krAHASIIPyr → Kr[kcat$AHASII$Pyr, Lambda],

KmAHASIIPyr2 = 10000; kcat$AHASII$Pyr2 = 7000;
kfAHASIIPyr2 → Kf[KmAHASIIPyr2, kcat$AHASII$Pyr2, Lambda],
krAHASIIPyr2 → Kr[kcat$AHASII$Pyr2, Lambda],

KmAHASIIIPyr = 10; kcat$AHASIII$Pyr = 7000;
kfAHASIIIPyr → Kf[KmAHASIIIPyr, kcat$AHASIII$Pyr, Lambda],
krAHASIIIPyr → Kr[kcat$AHASIII$Pyr, Lambda],

KmAHASIIIPyr2 = 7000; kcat$AHASIII$Pyr2 = 7000;
kfAHASIIIPyr2 → Kf[KmAHASIIIPyr2, kcat$AHASIII$Pyr2, Lambda],
krAHASIIIPyr2 → Kr[kcat$AHASIII$Pyr2, Lambda],
residualRateAHASIIIValPyr2 → 0.15,

KiAHASIIIVal = 20;
kfiAHASIIIPyrVal → Kfi[KmAHASIIIPyr, kcat$AHASIII$Pyr, Lambda, Omega],
```

```
kriAHASIIIPyrVal → Kri[KmAHASIIIPyr, kcat$AHASIII$Pyr, Lambda, Omega, KiAHASIIIVa
kfiAHASIIIPyr2Val → Kfi[KmAHASIIIPyr2, kcat$AHASIII$Pyr2, Lambda, Omega],
kriAHASIIIPyr2Val → Kri[KmAHASIIIPyr2, kcat$AHASIII$Pyr2, Lambda, Omega, KiAHASII

KmIRaAL = 290; KmIRNADPH = 15; kcat$IR$aAL = 1100;
kfIRaAL → Kf2S[KmIRaAL, KmIRNADPH, kcat$IR$aAL, Lambda],
krIRaAL → Kr[kcat$IR$aAL, Lambda],

KmDADaDHIV = 2800; kcat$DAD$aDHIV = 24000;
kfDADaDHIV → Kf[KmDADaDHIV, kcat$DAD$aDHIV, Lambda],
krDADaDHIV → Kr[kcat$DAD$aDHIV, Lambda],

KmTBGlu = 1000; fkcat$TB$Glu = 2000;
fkfTBGlu → Kf[KmTBGlu, fkcat$TB$Glu, Lambda],
fkrTBGlu → Kr[fkcat$TB$Glu, Lambda],

KmTBaKIV = 300; fkcat$TB$aKIV = 930;
fkfTBaKIV → Kf[KmTBaKIV, fkcat$TB$aKIV, Lambda],
fkrTBaKIV → Kr[fkcat$TB$aKIV, Lambda],

KmTBVal = 2700; rkcat$TB$Val = 2000;
rkfTBVal → Kf[KmTBVal, rkcat$TB$Val, Lambda],
rkrTBVal → Kr[rkcat$TB$Val, Lambda],

KmTBaKG = 2500; rkcat$TB$aKG = 2100;
rkfTBaKG → Kf[KmTBaKG, rkcat$TB$aKG, Lambda],
rkrTBaKG → Kr[rkcat$TB$aKG, Lambda],

KmTCAla = 100; fkcat$TC$Ala = 2000;
```

```
fkfTCAla → Kf[KmTCAla, fkcat$TC$Ala, Lambda],
fkrTCAla → Kr[fkcat$TC$Ala, Lambda],

KmTCaKIV = 100; fkcat$TC$aKIV = 1500;
fkfTCaKIV → Kf[KmTCaKIV, fkcat$TC$aKIV, Lambda],
fkrTCaKIV → Kr[fkcat$TC$aKIV, Lambda],

KmTCVal = 3000;  rkcat$TC$Val = 3000;
rkfTCVal → Kf[KmTCVal, rkcat$TC$Val, Lambda],
rkrTCVal → Kr[rkcat$TC$Val, Lambda],

KmTCPyr = 2000; rkcat$TC$Pyr = 3000;
rkfTCPyr → Kf[KmTCPyr, rkcat$TC$Pyr, Lambda],
rkrTCPyr → Kr[rkcat$TC$Pyr, Lambda],

KmLIVIexVal = 2; kcat$LIVI$exVal = 500;
kfLIVIexVal → Kf[KmLIVIexVal, kcat$LIVI$exVal, Lambda],
krLIVIexVal → Kr[kcat$LIVI$exVal, Lambda],

KmLIVIIexVal = 1; kcat$LIVII$exVal = 1;
kfLIVIIexVal → Kf[KmLIVIIexVal, kcat$LIVII$exVal, Lambda],
krLIVIIexVal → Kr[kcat$LIVII$exVal, Lambda],

kcat$aKIV → 70,
kcat$Val → 0.2,

KmIPMSacetylCoA = 200 ; kcat$IPMS$acetylCoA = 1000;
kfIPMSacetylCoA → Kf[KmIPMSacetylCoA, kcat$IPMS$acetylCoA, Lambda],
krIPMSacetylCoA → Kr[kcat$IPMS$acetylCoA, Lambda],
```

```
KmIPMSaKIV = 60; kcat$IPMS$aKIV = 1000;
kfIPMSaKIV → Kf[KmIPMSaKIV, kcat$IPMS$aKIV, Lambda],
krIPMSaKIV → Kr[kcat$IPMS$aKIV, Lambda],

KiIPMSLeu = 200;
kfiIPMSLeu → Kfi[KmIPMSacetylCoA, kcat$IPMS$acetylCoA, Lambda, Omega],
kriIPMSLeu → Kri[KmIPMSacetylCoA, kcat$IPMS$acetylCoA, Lambda, Omega, KiIPMSLeu],

KiIPMSacetylLeu = 500;
kfiIPMSacetylLeu → Kfi[KmIPMSaKIV, kcat$IPMS$aKIV, Lambda, Omega],
kriIPMSacetylLeu → Kri[KmIPMSaKIV, kcat$IPMS$aKIV, Lambda, Omega, KiIPMSacetylLeu

KmIPMIaIPM = 100; kcat$IPMI$aIPM = 1000;
kfIPMIaIPM → Kf[KmIPMIaIPM, kcat$IPMI$aIPM, Lambda],
krIPMIaIPM → Kr[kcat$IPMI$aIPM, Lambda],

KmIPMIbIPM = 100; kcat$IPMI$bIPM = 1000;
kfIPMIbIPM → Kf[KmIPMIbIPM, kcat$IPMI$bIPM, Lambda],
krIPMIbIPM → Kr[kcat$IPMI$bIPM, Lambda],

KmIPMDHbIPM = 105; KmIPMDHNAD = 320; kcat$IPMDH$bIPM = 4000;
kfIPMDHbIPM → Kf2S[KmIPMDHbIPM, KmIPMDHNAD, kcat$IPMDH$bIPM, Lambda],
krIPMDHbIPM → Kr[kcat$IPMDH$bIPM, Lambda],

KmTBGlu = 1000; fkcat$TB$Glu = 2000;
fkfTBGlu → Kf[KmTBGlu, fkcat$TB$Glu, Lambda],
fkrTBGlu → Kr[fkcat$TB$Glu, Lambda],
```

```
 KmTBaKIC = 200; fkcat$TB$aKIC = 3600;
 fkfTBaKIC → Kf[KmTBaKIC, fkcat$TB$aKIC, Lambda],
 fkrTBaKIC → Kr[fkcat$TB$aKIC, Lambda],

 KmTBLeu = 4400; rkcat$TB$Leu = 2800;
 rkfTBLeu → Kf[KmTBLeu, rkcat$TB$Leu, Lambda],
 rkrTBLeu → Kr[rkcat$TB$Leu, Lambda],

 KmTBaKG = 2500; rkcat$TB$aKG = 2100;
 rkfTBaKG → Kf[KmTBaKG, rkcat$TB$aKG, Lambda],
 rkrTBaKG → Kr[rkcat$TB$aKG, Lambda],

 KmLIVIexLeu = 4; kcat$LIVI$exLeu = 100;
 kfLIVIexLeu → Kf[KmLIVIexLeu, kcat$LIVI$exLeu, Lambda],
 krLIVIexLeu → Kr[kcat$LIVI$exLeu, Lambda],

 KmLIVIIexLeu = 1; kcat$LIVII$exLeu = 1;
 kfLIVIIexLeu → Kf[KmLIVIIexLeu, kcat$LIVII$exLeu, Lambda],
 krLIVIIexLeu → Kr[kcat$LIVII$exLeu, Lambda],

 KmLSexLeu = 0.5; kcat$LS$exLeu = 100;
 kfLSexLeu → Kf[KmLSexLeu, kcat$LS$exLeu, Lambda],
 krLSexLeu → Kr[kcat$LS$exLeu, Lambda],

 kcat$aKIC → 25,
 kcat$Leu → 0.01
};
```

```
(*
  Inputs for Values of Substrate and Enzyme Concentrations (μM)
  { note: NADP[0]=0 in yang's pathway}
*)

myICs = {
   AKI[0] == 8.1,
   AKII[0] == 0,
   AKIII[0] == 9.5,
   ASD[0] == 6.2,
   HDHI[0] == 8.1,
   HDHII[0] == 0,
   HSK[0] == 5.6,
   TS[0] == 8.3,

   Asp[0] == 3600,
   AspP[0] == 0,
   ASA[0] == 0,
   Hse[0] == 0,
   HseP[0] == 0,
   Lys[0] == 1000,
   Thr[0] == 0,

   ATP[0] == 1000,
   ADP[0] == 0,
   NADP[0] == 1000,
   NADPH[0] == 1000,
   Phosphate[0] == 1000,
```

```
    $Complex$AKII$Asp$ATP$[0] == 0,
    $Complex$ASD$ASA$NADP$Phosphate$[0] == 0,
    $Complex$ASD$AspP$NADPH$[0] == 0,
    $Complex$HDHII$ASA$NADPH$[0] == 0,
    $Complex$HseP$TS$[0] == 0,
    $Complex$HSK$Hse$ATP$[0] == 0,
    $Complex$HSK$Thr$[0] == 0,

    Pyr[0] == 1000,
    Leu[0] == 0,
    Ala[0] == 2000,
    Glu[0] == 2000,
    Ile[0] == 0,
    Val[0] == 0,
    aKB[0] == 0,
    NH3[0] == 0,
    aAHB[0] == 0,
    aDMV[0] == 0,
    aKMV[0] == 0,
    aKG[0] == 0,
    aAL[0] == 0,
    aDHIV[0] == 0,
    aKIV[0] == 0,
    aIPM[0] == 0,
    bIPM[0] == 0,
    aKIC[0] == 0,

    propionylCoA[0] == 0,
    glutarylCoA[0] == 0,
```

```
    pantothenate[0] == 0,
    acetylCoA[0] == 1000,
    CoA[0] == 0,
    NAD[0] == 1000,
    NADH[0] == 0,
    CO2[0] == 0,
    protein[0] == 0,

    TDA[0] == 3,
    KDC[0] == 2,

    AHASI[0] == 10,
    AHASICH3CO[0] == 0,
    AHASII[0] == 0,          (* E. coli K12 has no active AHASII *)
    AHASIICH3CO[0] == 0,
    AHASIII[0] == 2,
    AHASIIICH3CO[0] == 0,

    IR[0] == 13.5,
    DAD[0] == 7,

    TB[0] == 2.5,
    TBNH2[0] == 0,
    TC[0] == 2,
    TCNH2[0] == 0,

    IPMS[0] == 5,
    IPMSacetyl[0] == 0,
    IPMI[0] == 6,
```

```
IPMDH[0] == 5,

LIVI[0] == 10,
LIVII[0] == 0,
LS[0] == 8,
                          (* extracellular amino acid treatment *)
exVal[0] == 0,            (* 1000 for valine growth inhibition *)
exIle[0] == 0,            (* 500 for isoleucine rescue *)
exLeu[0] == 0,


$Complex$aKB$KDC$[0] == 0, $Complex$Pyr$AHASI$[0] == 0,
$Complex$AHASI$Val$[0] == 0, $Complex$Pyr$AHASI$Val$[0] == 0,
$Complex$AHASICH3CO$Val$[0] == 0, $Complex$aKB$AHASICH3CO$[0] == 0,
$Complex$aKB$AHASICH3CO$Val$[0] == 0, $Complex$Pyr$AHASICH3CO$[0] == 0,
$Complex$Pyr$AHASICH3CO$Val$[0] == 0, $Complex$Pyr$AHASII$[0] == 0,
$Complex$aKB$AHASIICH3CO$[0] == 0, $Complex$Pyr$AHASIICH3CO$[0] == 0,
$Complex$Pyr$AHASIII$[0] == 0, $Complex$AHASIII$Val$[0] == 0,
$Complex$Pyr$AHASIII$Val$[0] == 0, $Complex$AHASIICH3CO$Val$[0] == 0,
$Complex$aKB$AHASIIICH3CO$[0] == 0, $Complex$aKB$AHASIIICH3CO$Val$[0] == 0,
$Complex$Pyr$AHASIIICH3CO$[0] == 0, $Complex$Pyr$AHASIIICH3CO$Val$[0] == 0,
$Complex$IR$aAHB$NADPH$[0] == 0, $Complex$IR$aAL$NADPH$[0] == 0,
$Complex$aDHIV$DAD$[0] == 0, $Complex$aDMV$DAD$[0] == 0,
$Complex$Glu$TB$[0] == 0, $Complex$aKMV$TBNH2$[0] == 0,
$Complex$aKIV$TBNH2$[0] == 0, $Complex$Ile$TB$[0] == 0,
$Complex$Val$TB$[0] == 0, $Complex$aKG$TBNH2$[0] == 0,
$Complex$Ala$TC$[0] == 0, $Complex$aKIV$TCNH2$[0] == 0,
$Complex$Val$TC$[0] == 0, $Complex$Pyr$TCNH2$[0] == 0,
$Complex$exIle$LIVI$[0] == 0, $Complex$exIle$LIVII$[0] == 0,
```

```
   $Complex$exVal$LIVI$[0] == 0, $Complex$exVal$LIVII$[0] == 0,
   $Complex$acetylCoA$IPMS$[0] == 0, $Complex$aKIV$IPMSacetyl$[0] == 0,
   $Complex$IPMS$Leu$[0] == 0, $Complex$IPMSacetyl$Leu$[0] == 0,
   $Complex$aKIV$IPMSacetyl$Leu$[0] == 0, $Complex$aIPM$IPMI$[0] == 0,
   $Complex$bIPM$IPMI$[0] == 0, $Complex$IPMDH$bIPM$NAD$[0] == 0,
   $Complex$aKIC$TBNH2$[0] == 0, $Complex$Leu$TB$[0] == 0,
   $Complex$exLeu$LIVI$[0] == 0, $Complex$exLeu$LIVII$[0] == 0,
   $Complex$exLeu$LS$[0] == 0};
```

```
(*
 Call the Mathematica NDSolve Function to Solve the ODEs with Given
  Values of Kinetic Parameters and Substrate and Enzyme Concentrations
  Listed Above.
 *)

tmax = 100;  (* minutes *)
mySolution = NDSolve[Join[myODEs /. myKs, myICs], myVars, {t, 0, tmax}, AccuracyGoal →
   PrecisionGoal → 3, MaxSteps → 30000];
```

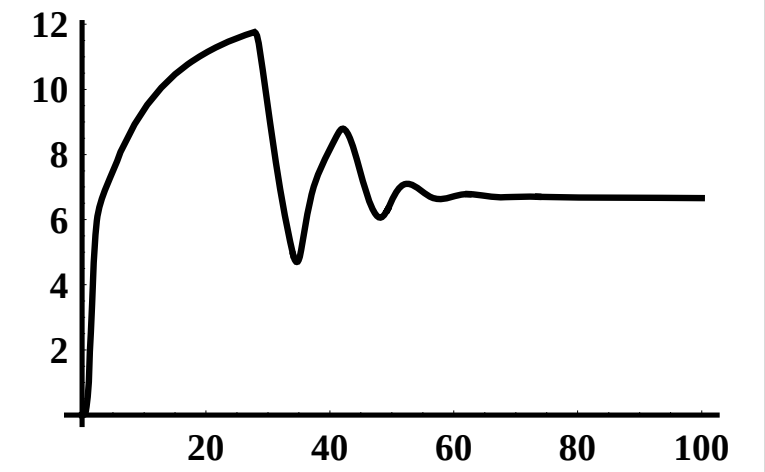
```
(* List of Substrates, Intermediates and Products for Graphic Outputs
  Displayed Below *)

metabolites = {
   Asp, AspP, ASA, Hse, HseP, HSK,
   Thr, Pyr, aKB, aAHB, aAL, NADPH, aDMV, aDHIV, aKMV, aKIV, acetylCoA, aIPM, bIPM,
   NAD, aKIC, Glu, Ala, aKG, Ile, Val, Leu
  };
```

```
TBTCdistribution = {
   TB, TBNH2, $Complex$Glu$TB$, $Complex$aKMV$TBNH2$, $Complex$aKIV$TBNH2$,
   $Complex$aKIC$TBNH2$,
   $Complex$Ile$TB$, $Complex$Val$TB$, $Complex$Leu$TB$, $Complex$aKG$TBNH2$,
   TC, TCNH2, $Complex$Ala$TC$, $Complex$aKIV$TCNH2$,
   $Complex$Val$TC$, $Complex$Pyr$TCNH2$};
```

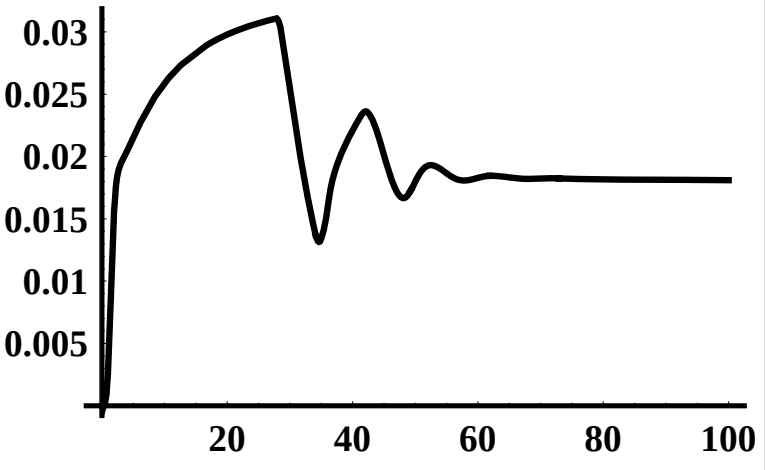
```
(* Define some plotting functions *)
FormalPlot[varName_, displayTime_, YplotRange_] :=
  Plot[varName[t] /. mySolution, {t, 0, displayTime}, PlotRange → YplotRange,
   Background → GrayLevel[1],
   TextStyle → {FontWeight → "Bold", FontSize → 14, FontFamily → "Times New Roman"},
   PlotStyle → {Thickness[0.01]}, AxesStyle → {Thickness[0.008]}];
DashPlot[varName_, displayTime_, YplotRange_] :=
  Plot[varName[t] /. mySolution, {t, 0, displayTime}, PlotRange → YplotRange,
   Background → GrayLevel[1],
   TextStyle → {FontWeight → "Bold", FontSize → 12, FontFamily → "Times New Roman"},
   PlotStyle → {Thickness[0.008], Dashing[{0.02, 0.025}]}, AxesStyle → {Thickness[0.
DotPlot[varName_, displayTime_, YplotRange_] :=
  Plot[varName[t] /. mySolution, {t, 0, displayTime}, PlotRange → YplotRange,
   Background → GrayLevel[1],
   TextStyle → {FontWeight → "Bold", FontSize → 12, FontFamily → "Times New Roman"},
   PlotStyle → {Thickness[0.008], Dashing[{0.001, 0.001, 0.001, 0.015}]},
   AxesStyle → {Thickness[0.0006]}];
```

```
(*
  Display Results of Simulation of Branched Chain Amino Acid
  Simulation: Rates of Production of Metabolic Intermediates and End-
    products.

      X axis is Time (min), and Y axis is Concentration (μM)
 *)

displayTime = 100;
Show[
  GraphicsArray[
   Partition[
    Map[Plot[#[t] /. mySolution, {t, 0, displayTime}, PlotLabel → #, PlotRange → All,
       DisplayFunction → Identity] &, metabolites], 3]
  ]
 ];
```

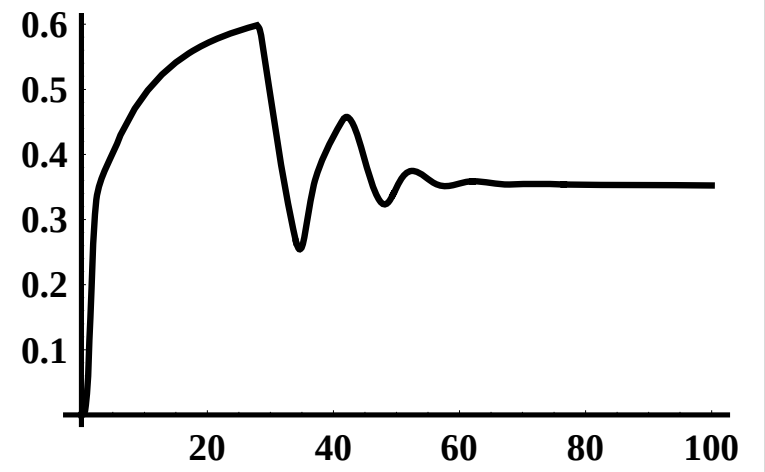
```
FormalPlot[aKB, 100, All];
```



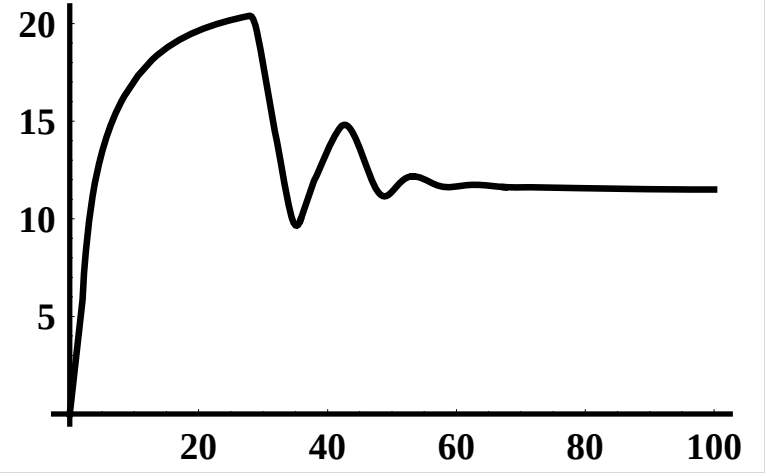

```
FormalPlot[aAHB, 100, All];
```



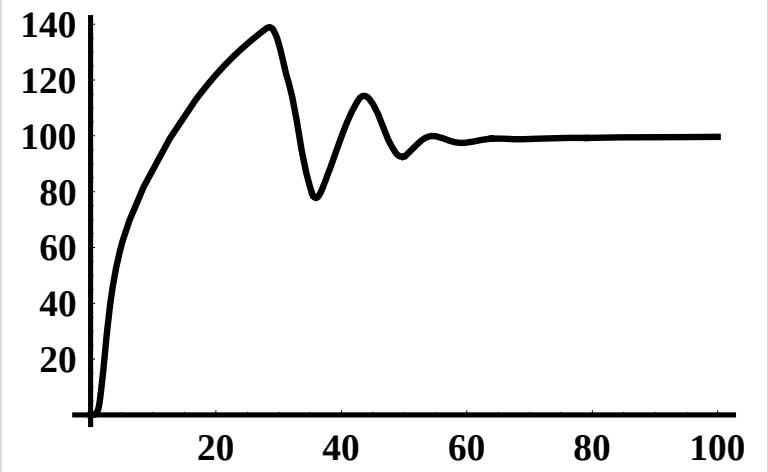
```
FormalPlot[aDMV, 100, All];
```



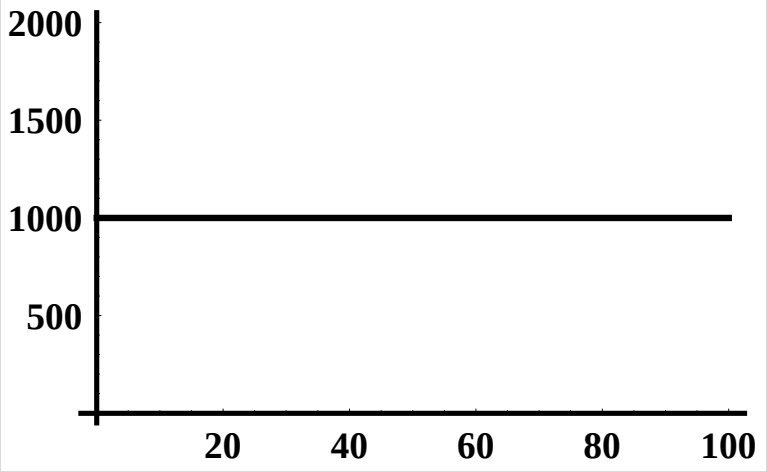

```
FormalPlot[aKMV, 100, All];
```



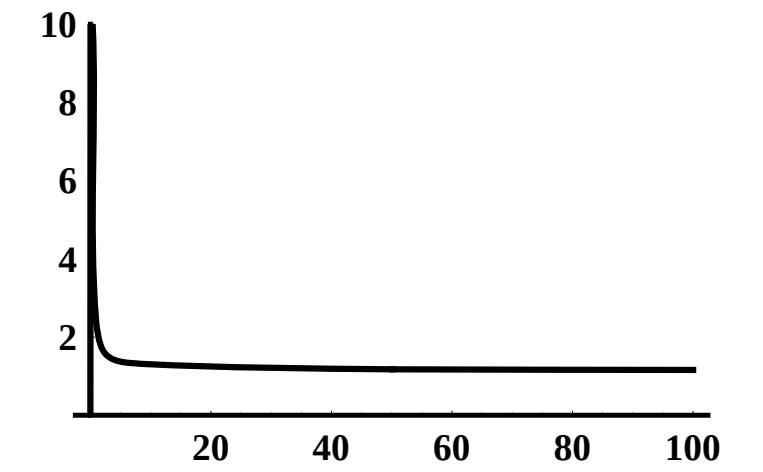
```
FormalPlot[Ile, 100, All];
```



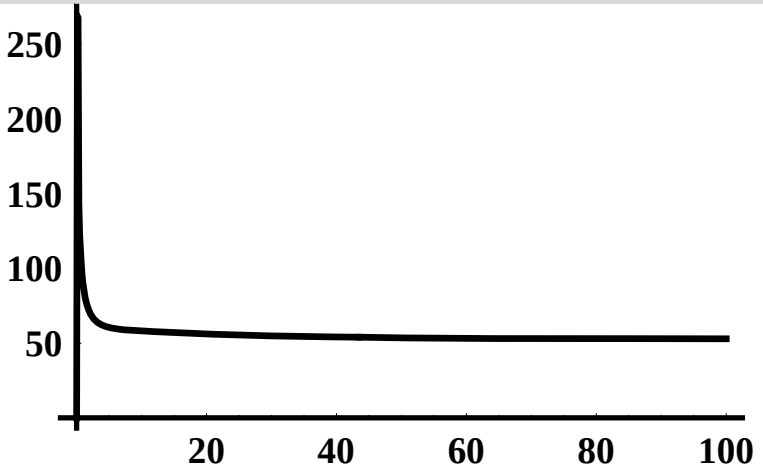

```
FormalPlot[Pyr, 100, All];
```



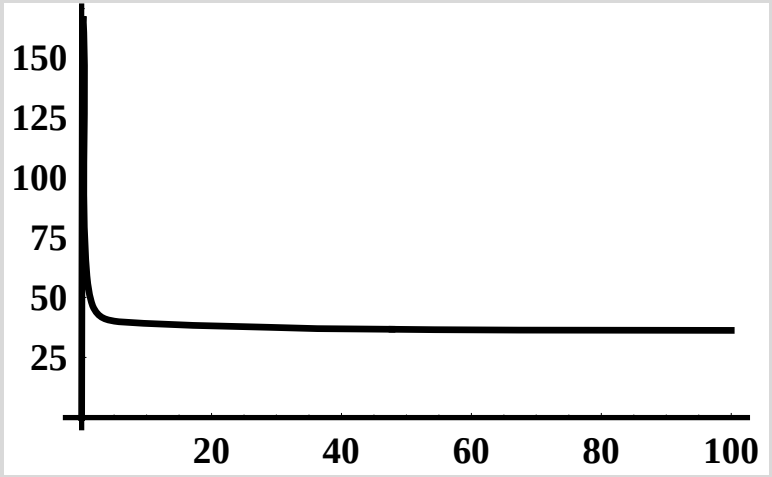
```
FormalPlot[aAL, 100, {0, 10}];
```



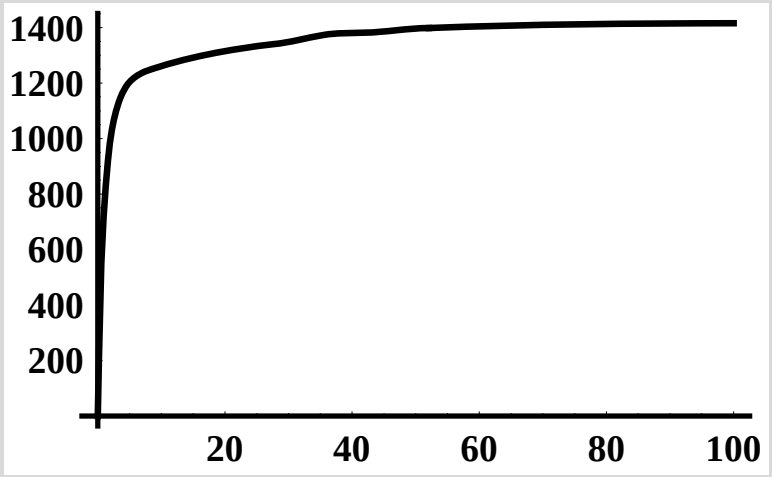

```
FormalPlot[aDHIV, 100, All];
```



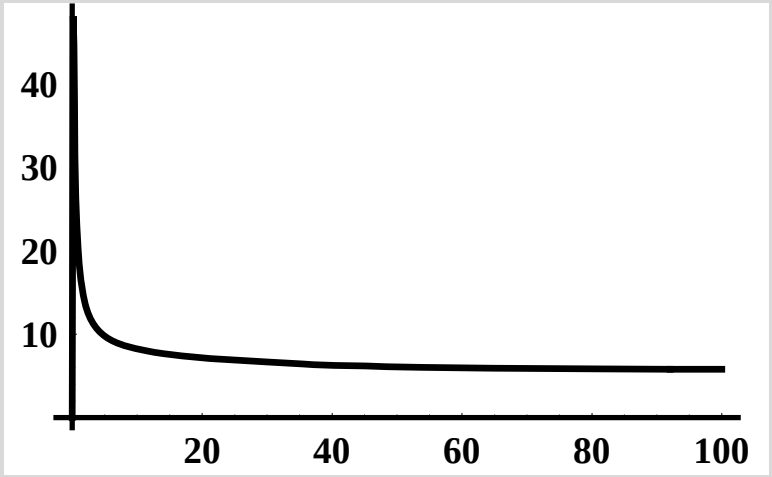
```
FormalPlot[aKIV, 100, All];
```



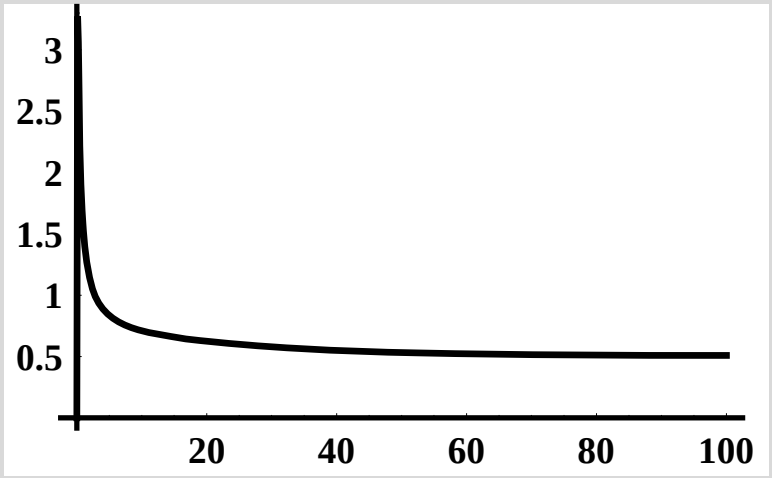

```
FormalPlot[Val, 100, All];
```



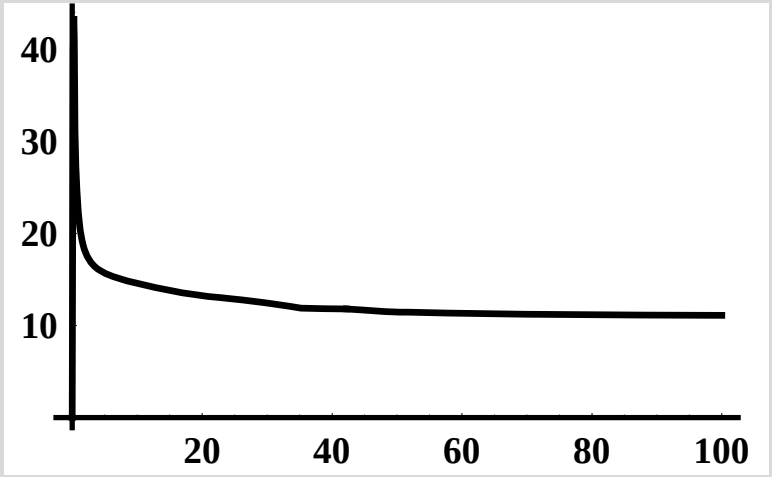
```
FormalPlot[aIPM, 100, All];
```



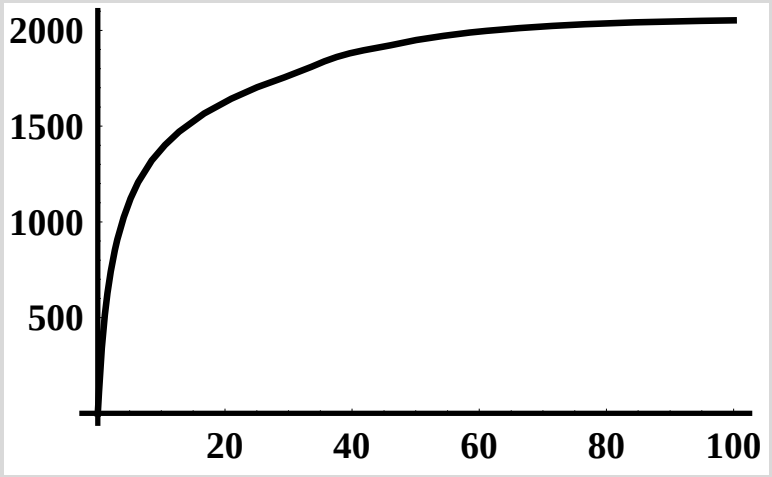

```
FormalPlot[bIPM, 100, All];
```



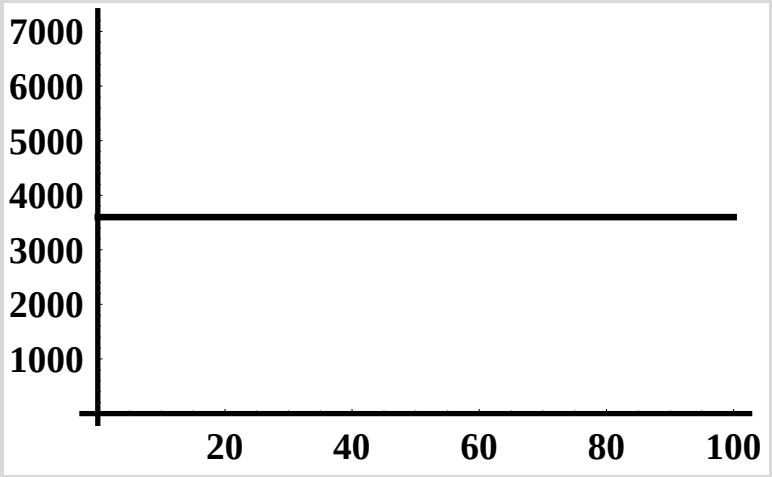
```
FormalPlot[aKIC, 100, All];
```



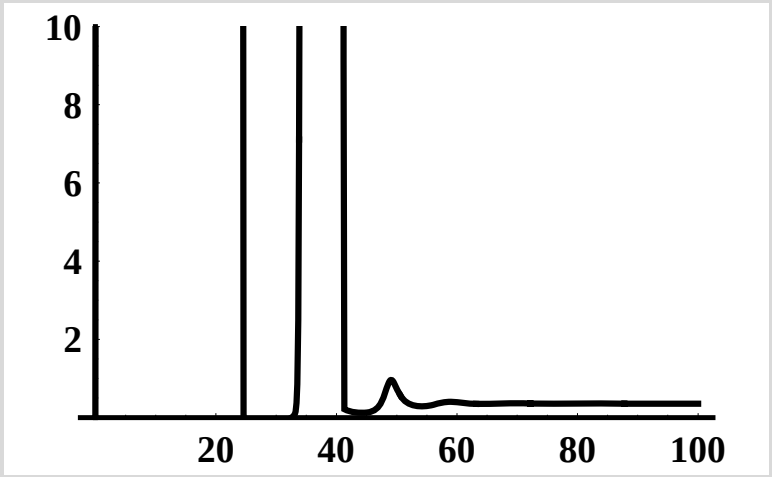

```
FormalPlot[Leu, 100, All];
```



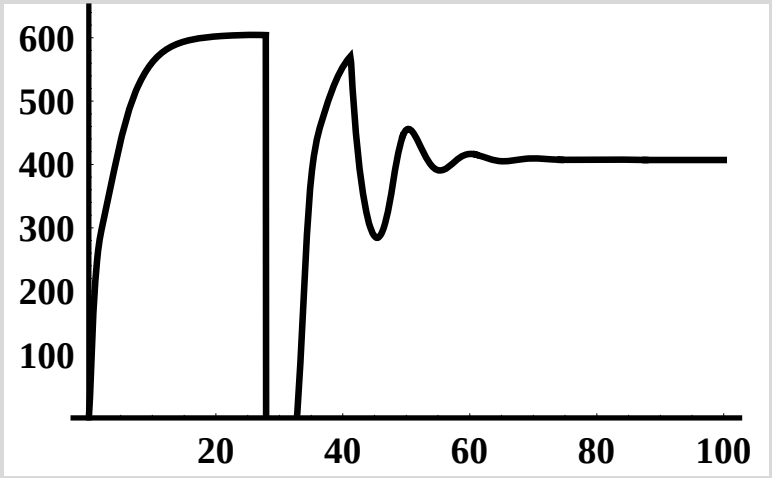
```
FormalPlot[Asp, 100, All];
```



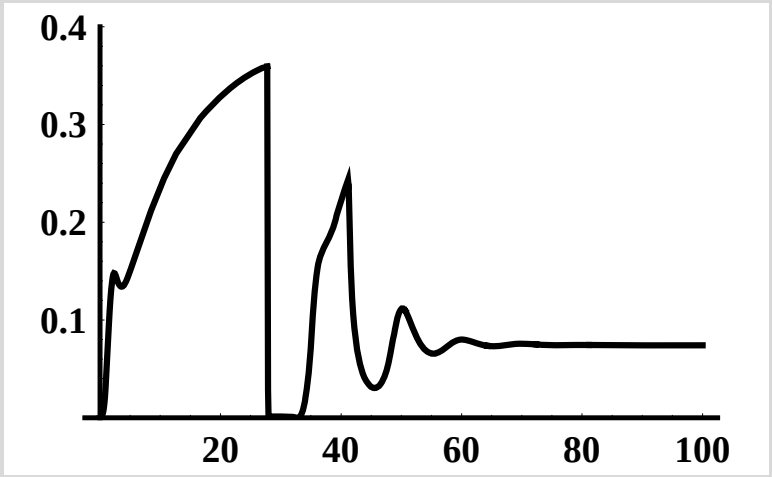

```
FormalPlot[AspP, 100, {0, 10}];
```



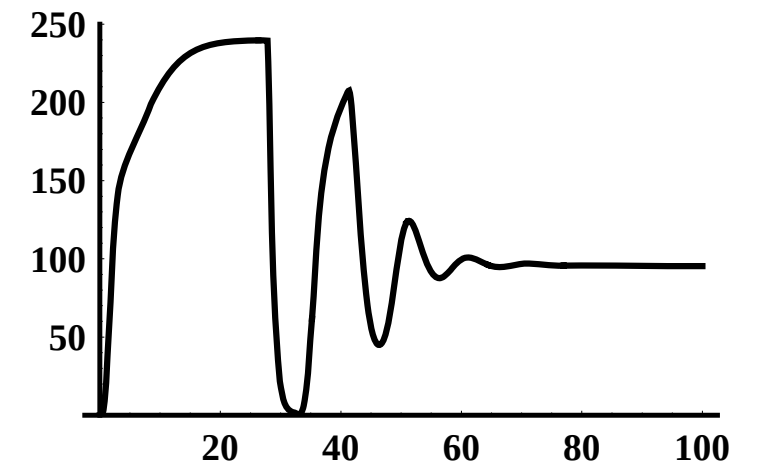
```
FormalPlot[ASA, 100, {0, 650}];
```



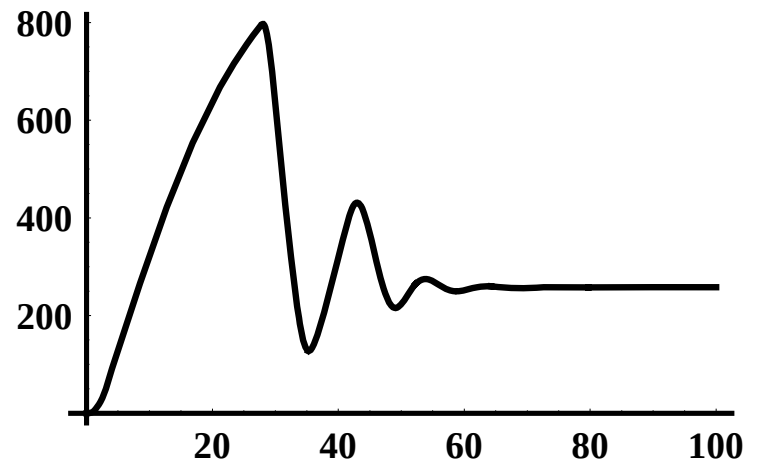

```
FormalPlot[Hse, 100, {0, 0.4}];
```



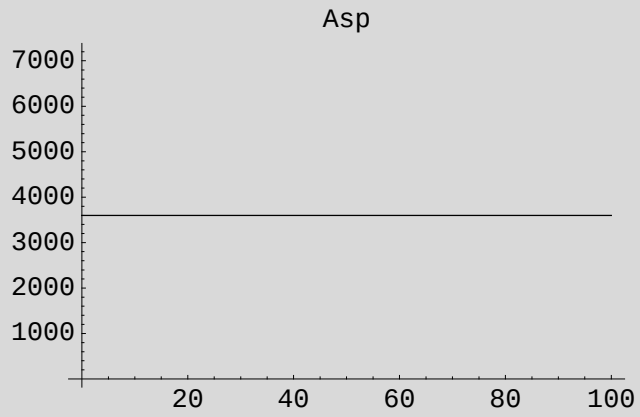
```
FormalPlot[HseP, 100, {0, 250}];
```

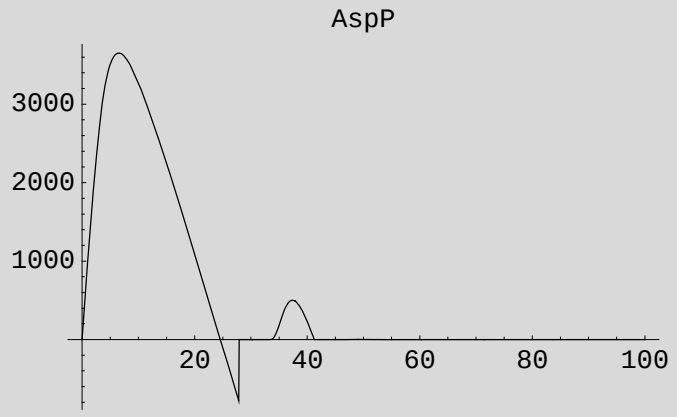


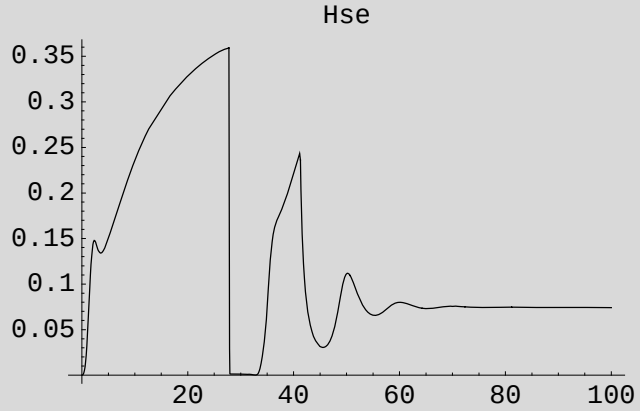

```
FormalPlot[Thr, 100, All];
```

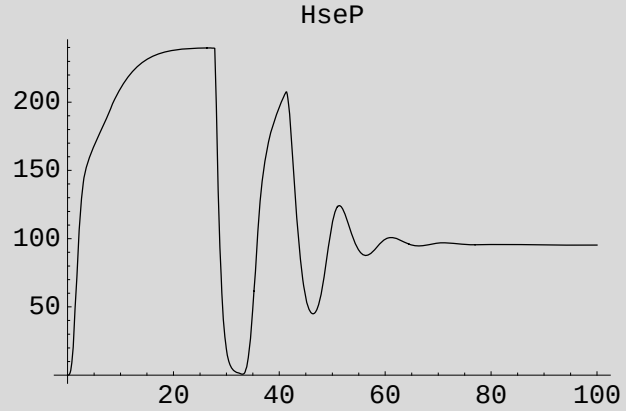


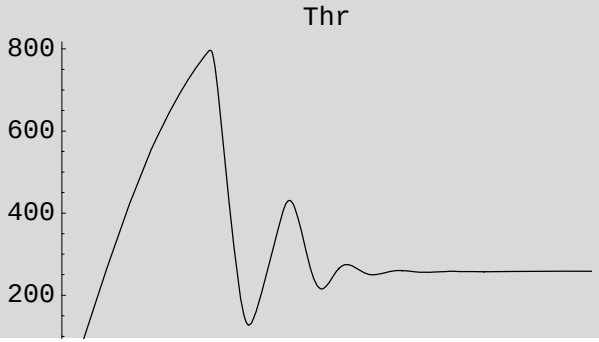

```
(* Pyr[0]= 1,000 *)
```

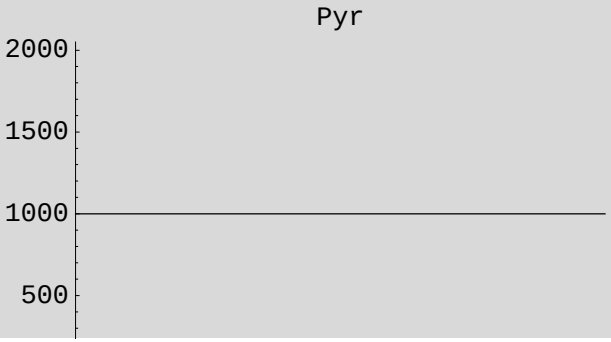

Asp
7000
6000
5000
4000
3000
2000
1000
20
40
60
80
100

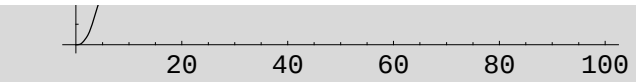

AspP
3000
2000
1000
20
40
60
80
100

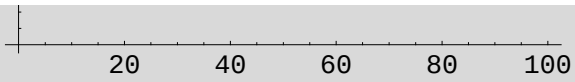

Hse
0.35
0.3
0.25
0.2
0.15
0.1
0.05
20
40
60
80
100


HseP
200
150
100
50
20
40
60
80
100

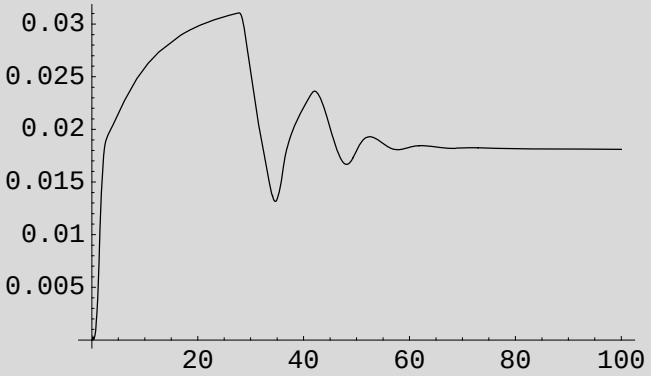

Thr
800
600
400
200


Pyr
2000
1500
1000
500

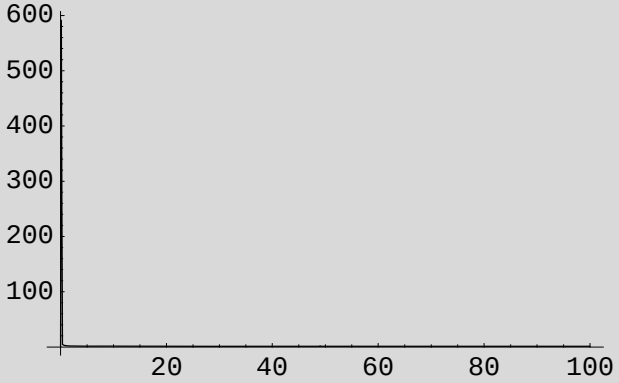




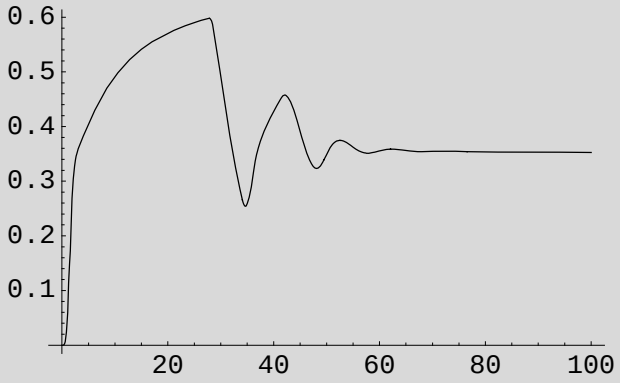
aAHB



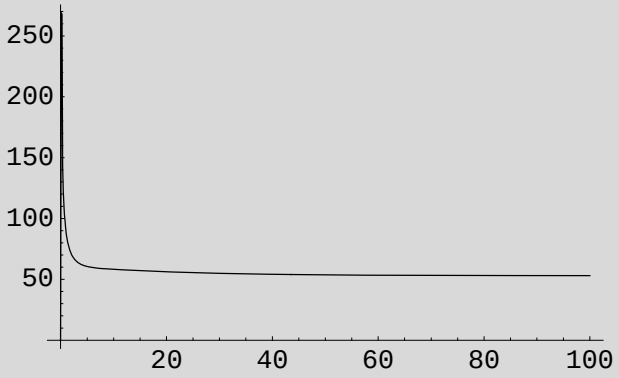
aAL



aDMV

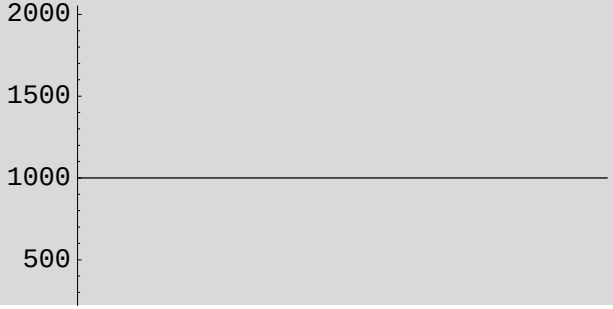


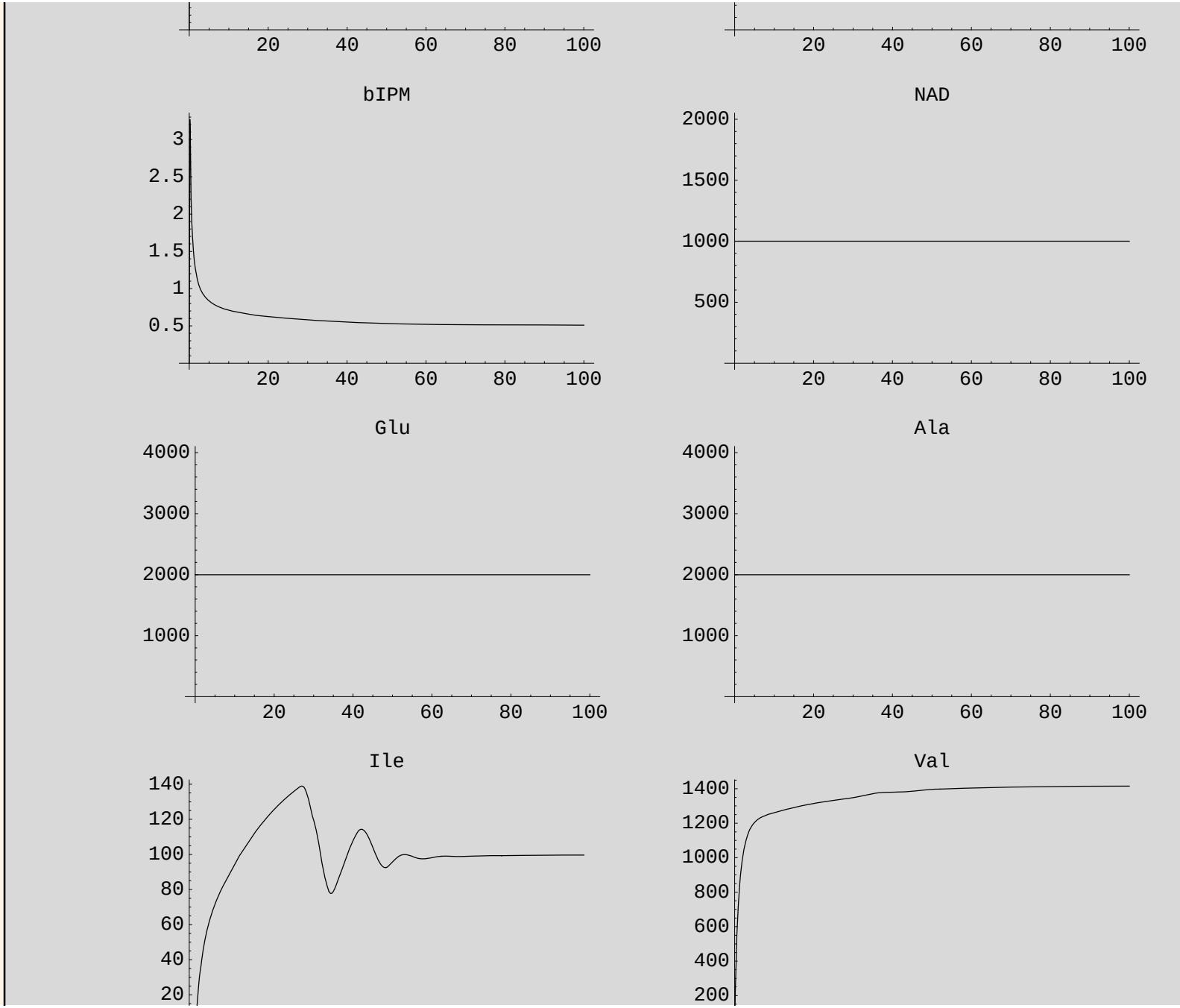
aDHIV

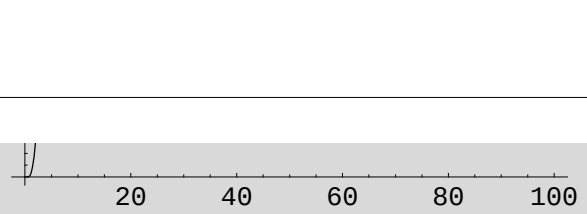


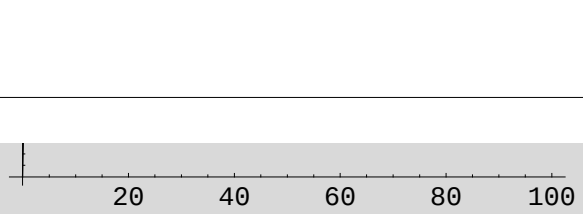
aKIV

acetylCoA

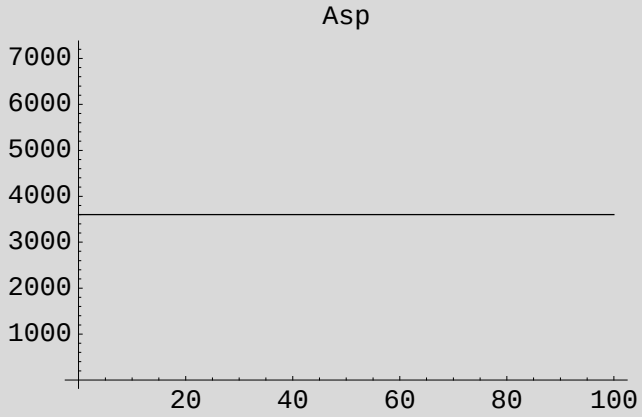


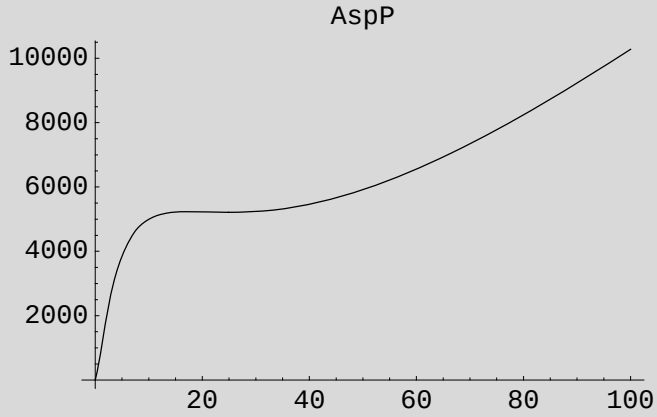

20
40
60
80
100
bIPM
3
2.5
2
1.5
1
0.5
NAD
2000
1500
1000
500
Glu
4000
3000
2000
1000
Ala
Ile
140
120
100
80
60
40
20
Val
1400
1200
1000
800
600
400
200

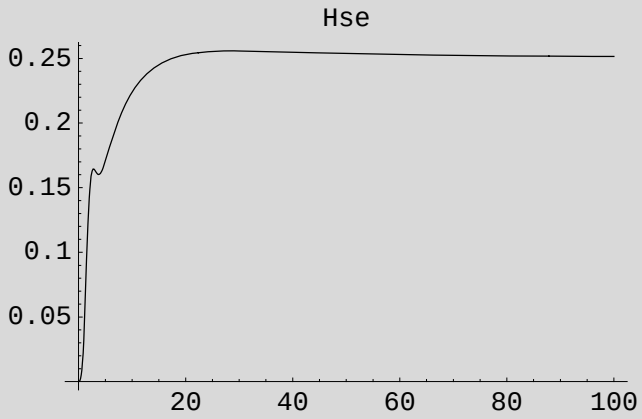

20
40
60
80
100

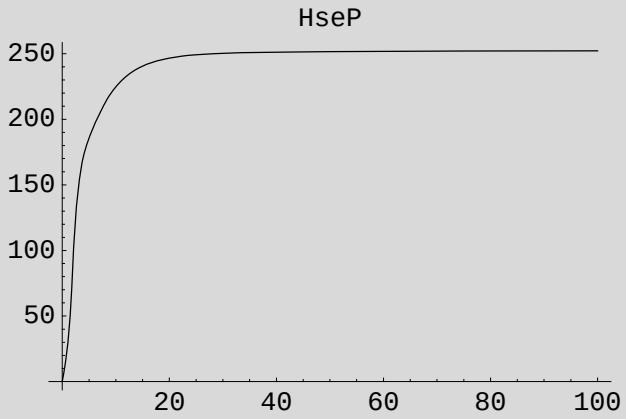

20
40
60
80
100

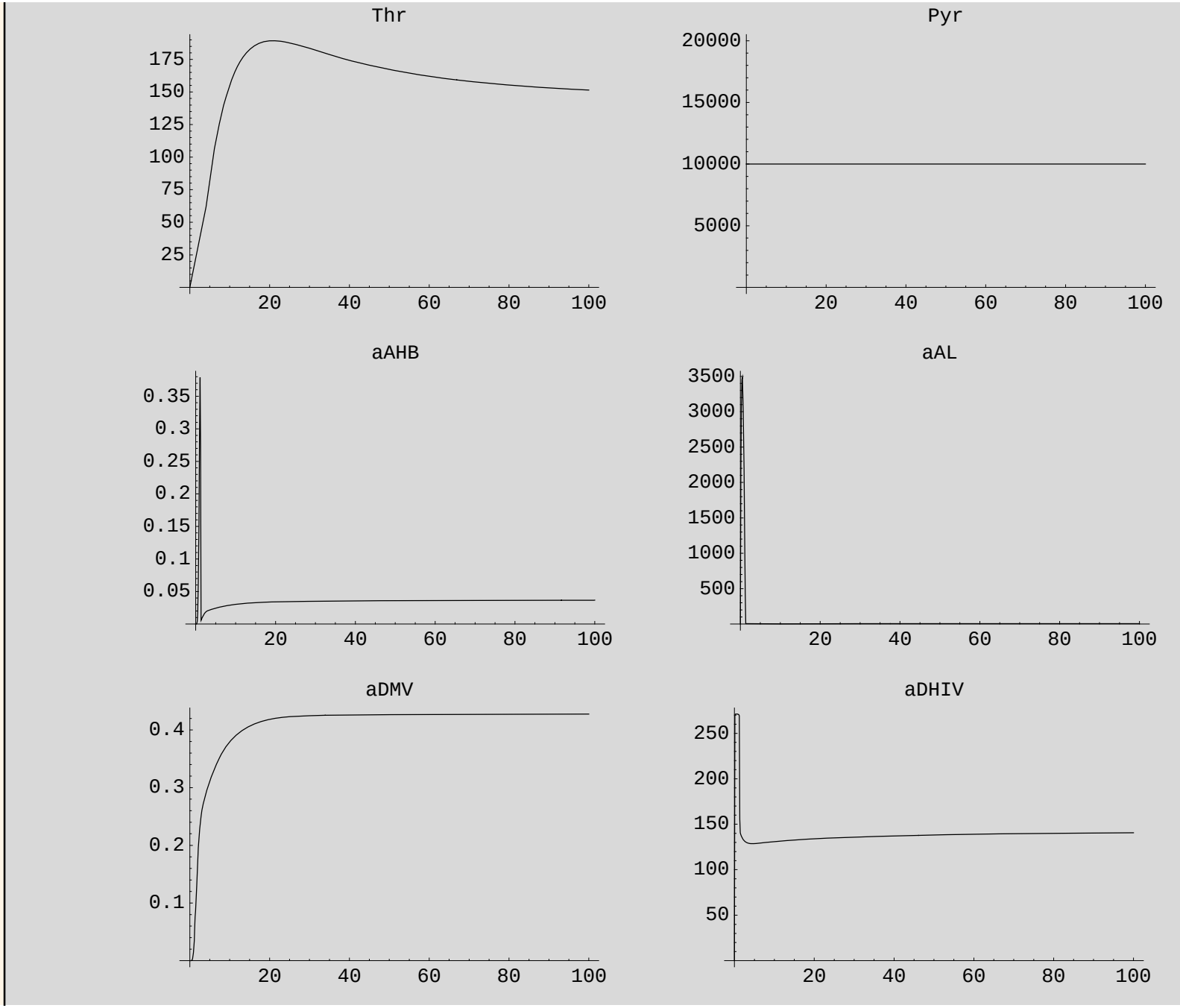
```
(* Pyr[0]= 10,000 *)
```

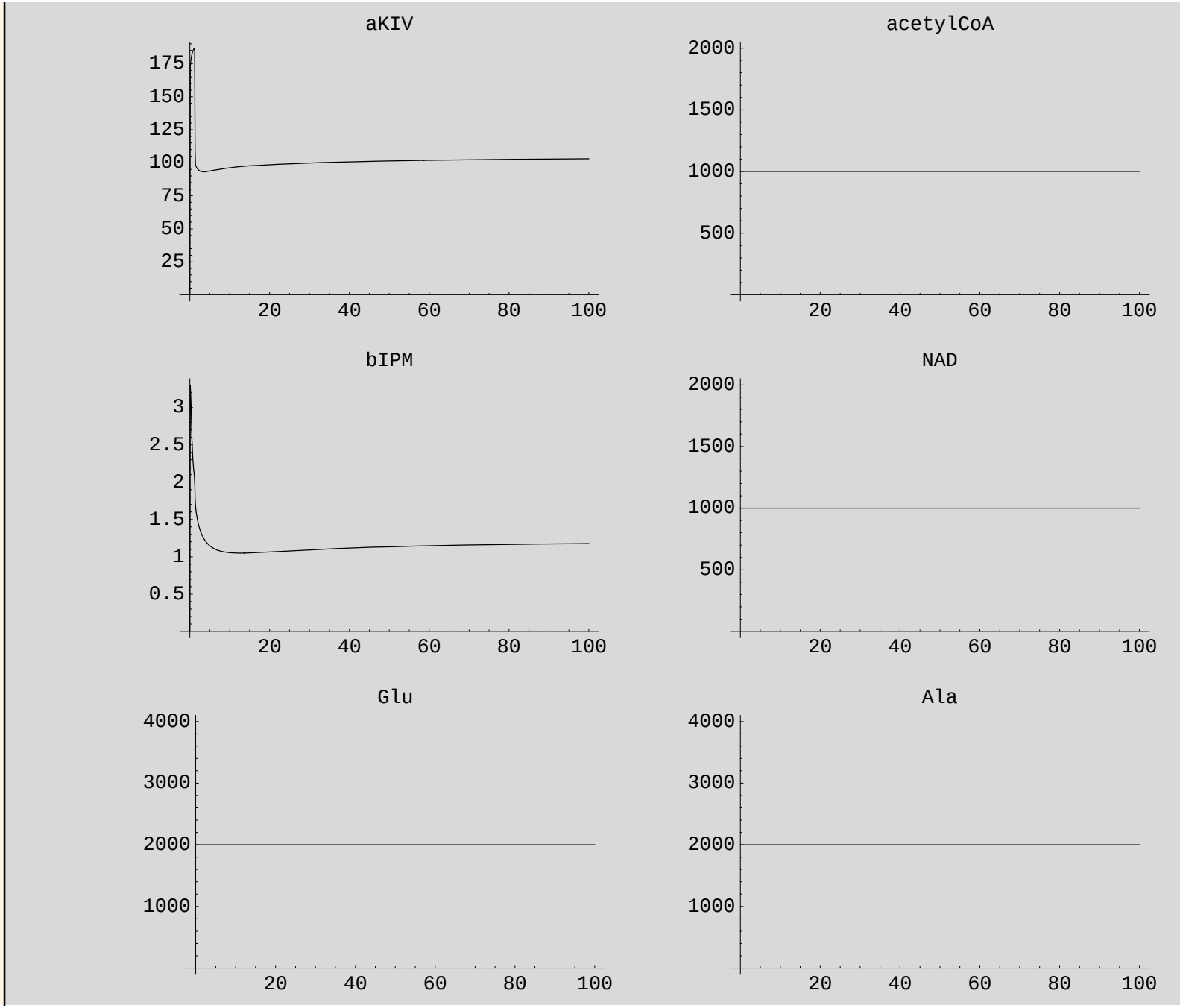

Asp
7000
6000
5000
4000
3000
2000
1000
20
40
60
80
100

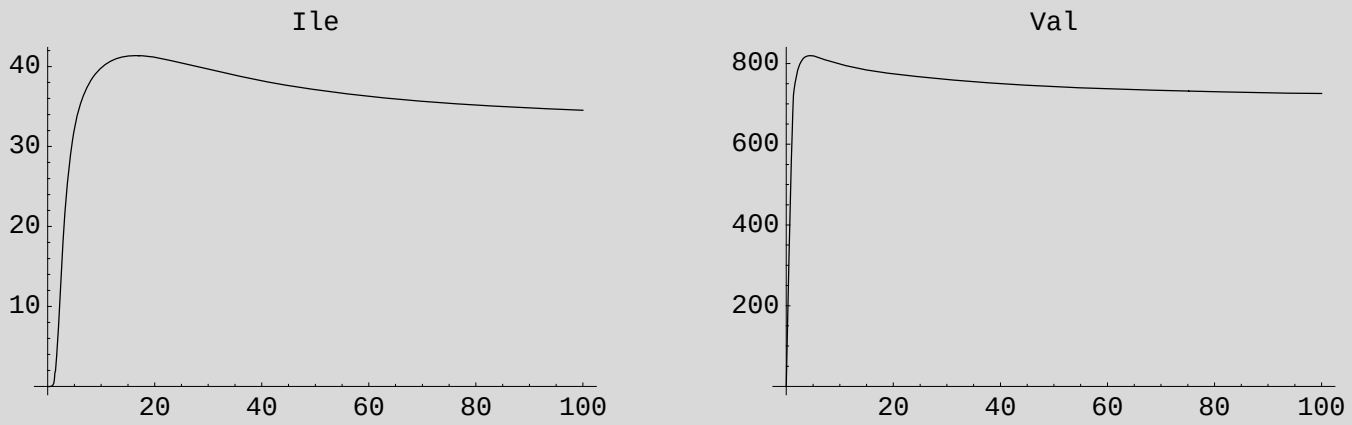

AspP
10000
8000
6000
4000
2000
20
40
60
80
100


Hse
0.25
0.2
0.15
0.1
0.05
20
40
60
80
100


HseP
250
200
150
100
50
20
40
60
80
100

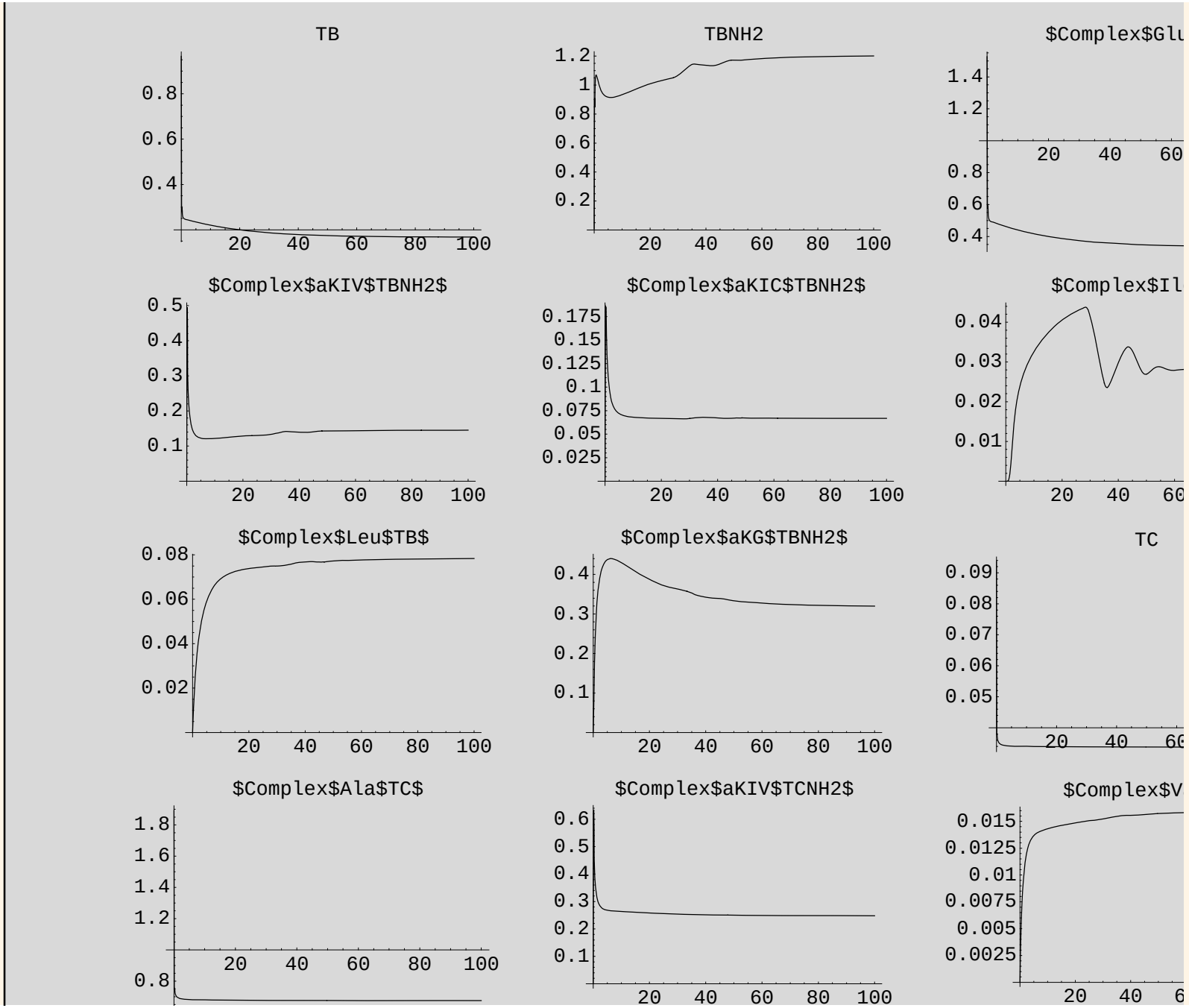

Thr
175
150
125
100
75
50
25
20
40
60
80
100
Pyr
20000
15000
10000
5000
20
40
60
80
100
aAHB
0.35
0.3
0.25
0.2
0.15
0.1
0.05
20
40
60
80
100
aAL
3500
3000
2500
2000
1500
1000
500
20
40
60
80
100
aDMV
0.4
0.3
0.2
0.1
20
40
60
80
100
aDHIV
250
200
150
100
50
20
40
60
80
100


aKIV
175
150
125
100
75
50
25
20
40
60
80
100
acetylCoA
2000
1500
1000
500
20
40
60
80
100
bIPM
3
2.5
2
1.5
1
0.5
20
40
60
80
100
NAD
2000
1500
1000
500
20
40
60
80
100
Glu
4000
3000
2000
1000
20
40
60
80
100
Ala
4000
3000
2000
1000
20
40
60
80
100

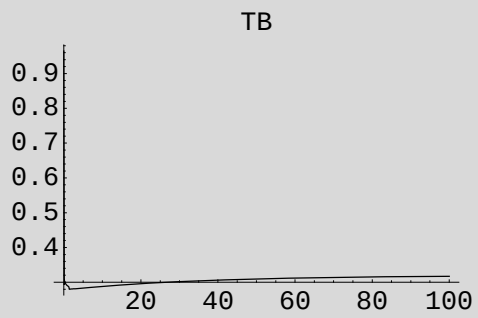


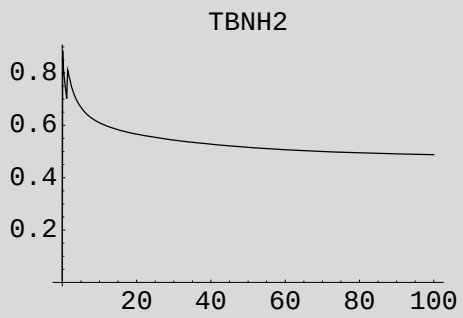

```
(*
  Display Simulations of Partition of Transaminase B and C
 X axis is Time (min), and Y axis is Concentration (μM)
 *)

displayTime = 100;
Show[
  GraphicsArray[
   Partition[
    Map[Plot[#[t] /. mySolution, {t, 0, displayTime}, PlotLabel → #, PlotRange → All,
       DisplayFunction → Identity] &, TBTCdistribution], 4]
  ]
 ];
```

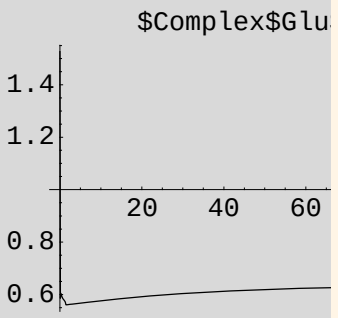
```
(* Pyr[0]= 1,000 *)
```

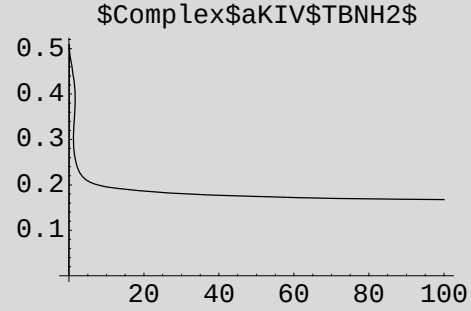

TB
TBNH2
$Complex$Glu
$Complex$aKIV$TBNH2$
$Complex$aKIC$TBNH2$
$Complex$Il
$Complex$LeuTB
$Complex$aKG$TBNH2$
TC
$Complex$AlaTC
$Complex$aKIV$TCNH2$
$Complex$V

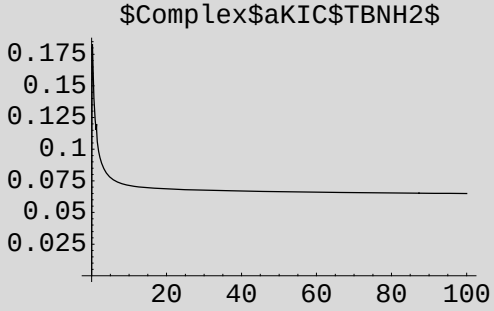
```
(* Pyr[0]= 10,000 *)
```

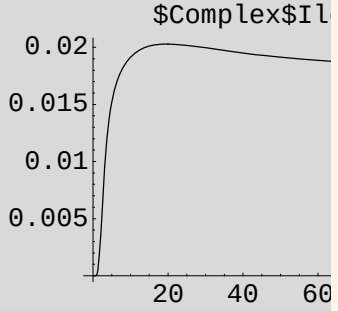

TB
0.9
0.8
0.7
0.6
0.5
0.4
20
40
60
80
100

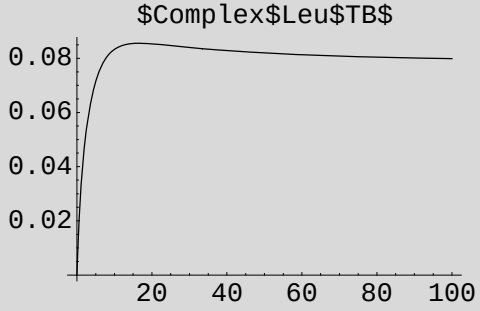

TBNH2
0.8
0.6
0.4
0.2
20
40
60
80
100

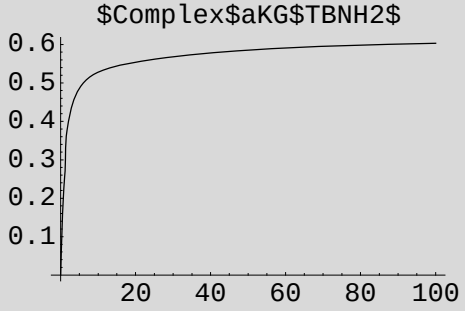

$Complex$Glu
1.4
1.2
0.8
0.6
20
40
60

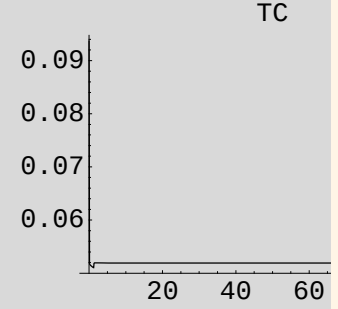

$Complex$aKIV$TBNH2$
0.5
0.4
0.3
0.2
0.1
20
40
60
80
100

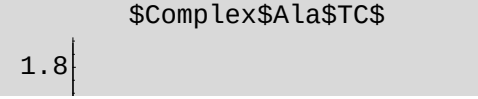

$Complex$aKIC$TBNH2$
0.175
0.15
0.125
0.1
0.075
0.05
0.025
20
40
60
80
100

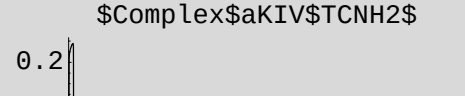

$Complex$Il
0.02
0.015
0.01
0.005
20
40
60


$Complex$LeuTB
0.08
0.06
0.04
0.02
20
40
60
80
100

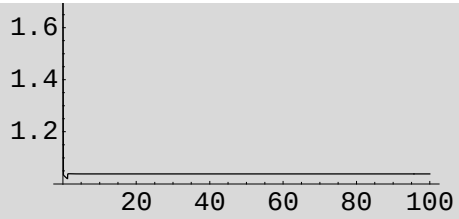

$Complex$aKG$TBNH2$
0.6
0.5
0.4
0.3
0.2
0.1
20
40
60
80
100

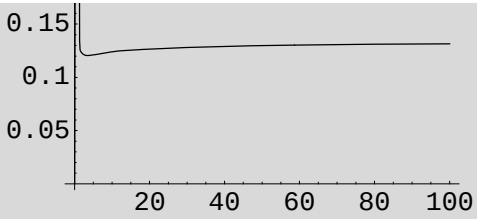

TC
0.09
0.08
0.07
0.06
20
40
60


$Complex$AlaTC
1.8


$Complex$aKIV$TCNH2$
0.2


$Complex$Va
0.014
0.012


1.6
1.4
1.2
20
40
60
80
100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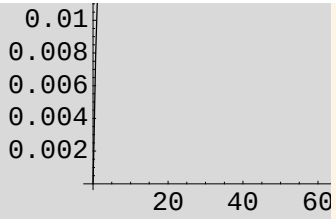
0.1
0.05
20
40
60
80
100


0.01
0.008
0.006
0.004
0.002
20
40
60