Sorensen 01.01.43LaTeX Companion

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Annotated Variable formulas (the updated MoSpec rules)

[Variable 0]

t **time in minutes (min)**

Time is considered an algebraic variable, correctly unassigned

```
Definition: Time =
undefined


Initial value: Time(t0) =
Tzero
```

[Variable 1]

G_{BV} **Glucose concentration in Brain Vascular space (mM)**

Glucose concentration in Brain Vascular space

$$\frac{dG_{BV}}{dt} = \frac{Q_B^G}{V_{BV}^G}(G_H - G_{BV}) - \frac{V_{BI}}{T_B V_{BV}^G}(G_{BV} - G_{BI}), \quad G_{BV}(0) = G_{BV0}$$

```
Definition: d GlucBV /dt =
(GlucH - GlucBV) * QfloGB / VolGBV - VolBI / (TdifB * VolGBV) * (GlucBV - GlucBI)


Initial value: GlucBV(t0) =
GlucBV0
```

[Variable 2]

G_{BI} **Glucose concentration in Brain Interstitial space (mM)**

Glucose concentration in Brain Interstitial space

$$\frac{dG_{BI}}{dt} = \frac{1}{T_B}(G_{BV} - G_{BI}) - \frac{\Gamma_{\texttt{BGU}}}{V_{BI}}, \quad G_{BI}(0) = G_{BI0}$$

BGU: Brain Glucose Uptake.

```
Definition: d GlucBI /dt =
1 / TdifB * (GlucBV - GlucBI) - GammaBGU / VolBI


Initial value: GlucBI(t0) =
GlucBI0
```

[Variable 3]

G_H **Glucose concentration in Heart-Lung space (mM)**

Glucose concentration in Heart-Lung space

$$\frac{dG_H}{dt} = \frac{Q_B^G G_{BV} + Q_L^G G_L + Q_K^G G_K + Q_P^G G_{PV} - Q_H^G G_H - \Gamma_{\texttt{RBCU}}}{V_H^G}, \quad G_H(0) = G_{H0}$$

```
Definition: d GlucH /dt =
(QfloGB * GlucBV + QfloGL * GlucL +  QfloGK * GlucK + QfloGP * GlucPV +
- QfloGH * GlucH - GammaRBCU + GammaIVG) / VolGH

Initial value: GlucH(t0) =
GlucH0
```

[Variable 4]

G_H^N **Normalized Glucose concentration in Heart-Lung space (#)**

Normalized Glucose concentration in Liver space

$$G_H^N = \frac{G_H}{G_{H0}}, \quad G_H^N(0) = 1$$

```
Definition: GlucNH =
GlucH / GlucH0

Initial value: GlucNH(t0) =
1
```

[Variable 5]

G_J **Glucose concentration in gut (Jejunal) space (mM)**

Glucose conrcentration in gut (Jejunal) space

$$\frac{dG_J}{dt} = \frac{Q_J^G}{V_J^G}(G_H - G_J) - \frac{\Gamma_{\texttt{JGU}} + R_{oga}}{V_J^G}, \quad G_J(0) = G_{J0}$$

JGU: Jejunal (Gut) Glucose Uptake or Utilization

Note: we have substituted the original "G" suffix in Chee&Fernando with "J" (Jejunum) for legibility.

```
Definition: d GlucJ /dt =
(GlucH - GlucJ) * QfloGJ / VolGJ - GammaJGU / VolGJ
```

```
Initial value: GlucJ(t0) =
GlucJ0
```

[Variable 6]

G_L **Glucose concentration in Liver space (mM)**

Glucose concentration in Liver space

$$\frac{dG_L}{dt} = \frac{Q_A^G G_H + Q_J^G G_J - Q_L^G G_L + \Gamma_{\texttt{HGP}} - \Gamma_{\texttt{HGU}}}{V_L^G}, \quad G_L(0) = G_{L0}$$

HGP: Hepatic Glucose Production
HGU: Hepatic Glucose Uptake

```
Definition: d GlucL /dt =
(QfloGA * GlucH + QfloGJ * GlucJ - QfloGL * GlucL + GammaHGP - GammaHGU) / VolGL

Initial value: GlucL(t0) =
GlucL0
```

[Variable 7]

G_L^N **Normalized Glucose concentration in Liver space (#)**

Normalized Glucose concentration in Liver space

$$G_L^N = \frac{G_L}{G_{L0}}, \quad G_L^N(0) = 1$$

```
Definition: GlucNL =
GlucL / GlucL0

Initial value: GlucNL(t0) =
1
```

[Variable 8]

G_K **Glucose concentration in Kidney space (mM)**

Glucose concentration in Kidney space

$$\frac{dG_K}{dt} = \frac{Q_K^G}{V_K^G}(G_H - G_K) - \frac{\Gamma_{\texttt{KGE}}}{V_K^G}, \quad G_K(0) = G_{K0}$$

KGE: Kidney Glucose Excretion

```
Definition: d GlucK /dt =
(GlucH - GlucK) * QfloGK / VolGK - GammaKGE / VolGK

Initial value: GlucK(t0) =
GlucK0
```

[Variable 9]

G_{PV} **Glucose concentration in Peripheral Vascular space (mM)**

Glucose concentration in Peripheral Vascular space

$$\frac{dG_{PV}}{dt} = \frac{Q_P^G}{V_{PV}^G}(G_H - G_{PV}) - \frac{V_{PI}}{T_P^G V_{PV}^G}(G_{PV} - G_{PI}), \quad G_{PV}(0) = G_{PV0}$$

```
Definition: d GlucPV /dt =
QfloGP / VolGPV * (GlucH - GlucPV) - VolPI / (TdifGP * VolGPV) * (GlucPV - GlucPI)

Initial value: GlucPV(t0) =
GlucPV0
```

[Variable 10]

G_{PI} **Glucose concentration in Peripheral Interstitial space (mM)**

Glucose concentration in Peripheral Interstitial space

$$\frac{dG_{PI}}{dt} = \frac{1}{T_P^G}(G_{PV} - G_{PI}) - \frac{\Gamma_{\texttt{PGU}}}{V_{PI}}, \quad G_{PI}(0) = G_{PI0}$$

PGU: Peripheral Glucose Uptake

```
Definition: d GlucPI /dt =
(GlucPV - GlucPI) / TdifGP - GammaPGU / VolPI

Initial value: GlucPI(t0) =
GlucPI0
```

[Variable 11]

G_{PI}^N **Normalized Glucose concentration in Peripheral Interstitial space (#)**

Normalized Glucose concentration in Peripheral Interstitial space

$$G_{PI}^N = \frac{G_{PI}}{G_{PI0}}, \quad G_{PI}^N(0) = 1$$

```
Definition: GlucNPI =
GlucPI / GlucPI0


Initial value: GlucNPI(t0) =
1
```

[Variable 12]

$\Gamma_{\texttt{PGU}}$ **Rate of Peripheral Glucose Uptake (mmol/min)**

Rate of (insulinemia- and glycemia-dependent) Peripheral Glucose Uptake:

$$\Gamma_{\texttt{PGU}} = \Gamma^{B}_{\texttt{PGU}} \cdot M^{G}_{PGU} \cdot M^{I}_{PGU}, \quad \Gamma_{\texttt{PGU}}(0) = \Gamma_{\texttt{PGU0}}$$

```
Definition: GammaPGU =
GammaBPGU * GlucNPI * MIPGU


Initial value: GammaPGU(t0) =
GammaBPGU
```

[Variable 13]

$M^{I}_{\texttt{HGP}}$ **Insulin Action on glucose uptake (#)**

Insulin Action on glucose uptake:

$$M^{I}_{\texttt{PGU}} = \beta^{0}_{\texttt{PGU}} + \beta^{1}_{\texttt{PGU}} \tanh\left[\beta^{2}_{\texttt{PGU}} \cdot (I^{N}_{PI} - \beta^{3}_{\texttt{PGU}})\right] \tag{1}$$

```
Definition: MIPGU =
beta0PGU + beta1PGU * tanh(beta2PGU * (InsuNPI - beta3PGU))


Initial value: MIPGU(t0) =
MIPGU0
```

[Variable 14]

$\Gamma_{\texttt{HGP}}$ **Hepatic Glucose Production (mmol/min)**

Rate of (glycemia-dependent) Hepatic Glucose Production

$$\Gamma_{\texttt{HGP}} = \Gamma^{B}_{\texttt{HGP}} \cdot M^{I}_{\texttt{HGP}} \cdot M^{C}_{\texttt{HGP}} \cdot M^{G}_{\texttt{HGP}}, \quad \Gamma_{\texttt{HGP}}(0) = \Gamma_{\texttt{HGP0}}$$

```
Definition: GammaHGP =
GammaHGP0 * MIHGP * MCHGP * MGHGP


Initial value: GammaHGP(t0) =
GammaHGP0
```

[Variable 15]

$M^I_{\texttt{HGP}}$ **Insulin suppression of Hepatic Glucose Production** (#)

Insulin suppression of Hepatic Glucose Production

$$\frac{dM^I_{\texttt{HGP}}}{dt} = \frac{M^I_{\texttt{HGPinf}} - M^I_{\texttt{HGP}}}{\tau_I}, \quad M^I_{\texttt{HGP}}(0) = M^I_{\texttt{HGP0}}$$

```
Definition: d MIHGP /dt =
(MIHGPinf - MIHGP) / tauInsu


Initial value: MIHGP(t0) =
MIHGP0
```

[Variable 16]

$M^I_{\texttt{HGPinf}}$ **Steady State Insulin suppression of Hepatic Glucose Production** (#)

Steady State Insulin suppression of Hepatic Glucose Production

$$M^I_{\texttt{HGPinf}} = \beta^2_{\texttt{HGP}} - \beta^3_{\texttt{HGP}} \tanh\left[\beta^4_{\texttt{HGP}}(I^N_L - \beta^5_{\texttt{HGP}})\right], \quad M^I_{\texttt{HGPinf}}(0) = M^I_{\texttt{HGPinf0}}$$

```
Definition: MIHGPinf =
beta2HGP - beta3HGP * tanh(  beta4HGP*( InsuNL - beta5HGP ) )


Initial value: MIHGPinf(t0) =
MIHGPinf0
```

[Variable 17]

$M^C_{\texttt{HGP}}$ **gluCagon contribution to Hepatic Glucose Production** (#)

gluCagon contribution to Hepatic Glucose Production

$$M^C_{\texttt{HGP}} = M^{C0}_{\texttt{HGP}} - f_2, \quad M^C_{\texttt{HGP}}(0) = M^C_{\texttt{HGP0}} = 1$$

```
Definition: MCHGP =
MC0HGP - Fun2


Initial value: MCHGP(t0) =
MCHGP0
```

[Variable 18]

$M^{C0}_{\texttt{HGP}}$ **gluCagon contribution to Hepatic Glucose Production at baseline** (#)

gluCagon contribution to Hepatic Glucose Production at baseline

$$M^{C0}_{\texttt{HGP}} = \beta^{0}_{\texttt{HGP}} \tanh(\beta^{1}_{\texttt{HGP}} C^{N}), \quad M^{C0}_{\texttt{HGP}}(0) = M^{C0}_{\texttt{HGP0}}$$

```
Definition: MC0HGP =
beta0HGP * tanh(beta1HGP * CgonN)


Initial value: MC0HGP(t0) =
MC0HGP0
```

[Variable 19]

f_2 **Damping of gluCagon contribution to Hepatic Glucose Production** (#)

Damping of gluCagon contribution to Hepatic Glucose Production

$$\frac{df_2}{dt} = \frac{1}{\tau_C}[(\frac{M^{C0}_{\texttt{HGP}} - 1}{2}) - f_2], \quad f_2(0) = f_{20} = 0$$

```
Definition: d Fun2 /dt =
((MC0HGP - 1.0) / 2.0 - Fun2) / tauCgon


Initial value: Fun2(t0) =
Func20
```

[Variable 20]

$M^{G}_{\texttt{HGP}}$ **Glucose contribution to Hepatic Glucose Production** (#)

Glucose contribution to Hepatic Glucose Production

$$M^{G}_{\texttt{HGP}} = \left\{\beta^{6}_{\texttt{HGP}} - \beta^{7}_{\texttt{HGP}} \tanh\left[\beta^{8}_{\texttt{HGP}} (G^{N}_{L} - \beta^{9}_{\texttt{HGP}})\right]\right\}, \quad M^{G}_{\texttt{HGP}}(0) = M^{G}_{\texttt{HGP0}} = 1$$

```
Definition: MGHGP =
 (beta6HGP - beta7HGP * tanh(beta8HGP * (GlucNL - beta9HGP)))


Initial value: MGHGP(t0) =
MGHGP0
```

[Variable 21]

$\Gamma_{\texttt{HGU}}$ **Hepatic Glucose Uptake** (**mmol/min**)

Hepatic Glucose Uptake

$$\Gamma_{\texttt{HGU}} = \Gamma^{B}_{\texttt{HGU}} \cdot M^{I}_{\texttt{HGU}} \cdot M^{G}_{\texttt{HGU}}, \quad \Gamma_{\texttt{HGU}}(0) = \Gamma_{\texttt{HGU0}}$$

```
Definition: GammaHGU =
GammaHGU0 * MIHGU * MGHGU


Initial value: GammaHGU(t0) =
GammaHGU0
```

[Variable 22]

$M^{I}_{\texttt{HGU}}$ **Insulin acceleration of Hepatic Glucose Uptake** (#)

Insulin acceleration of Hepatic Glucose Uptake

$$\frac{dM^{I}_{\texttt{HGU}}}{dt} = \frac{M^{I}_{\texttt{HGUinf}} - M^{I}_{\texttt{HGU}}}{\tau_I}, \quad M^{I}_{\texttt{HGU}}(0) = M^{I}_{\texttt{HGU0}}$$

```
Definition: d MIHGU /dt =
(MIHGUinf - MIHGU) / tauInsu


Initial value: MIHGU(t0) =
MIHGU0
```

[Variable 23]

$M^{I}_{\texttt{HGUinf}}$ **Steady State Insulin acceleration of Hepatic Glucose Uptake** (#)

Steady State Insulin acceleration of Hepatic Glucose Uptake

$$M^{I}_{\texttt{HGUinf}} = \beta^{0}_{\texttt{HGU}} \tanh(\beta^{1}_{\texttt{HGU}} I^{N}_{L}), \quad M^{I}_{\texttt{HGUinf}}(0) = M^{I}_{\texttt{HGUinf0}}$$

```
Definition: MIHGUinf =
beta0HGU * tanh(beta1HGU *  InsuNL)

Initial value: MIHGUinf(t0) =
MIHGUinf0
```

[Variable 24]

$M^G_{\texttt{HGU}}$ **Glucose acceleration of Hepatic Glucose Uptake (#)**

Glucose acceleration of Hepatic Glucose Uptake

$$M^G_{\texttt{HGU}} = \beta^2_{\texttt{HGU}} + \beta^3_{\texttt{HGU}} \tanh\left[\beta^4_{\texttt{HGU}} \left(G^N_L - \beta^5_{\texttt{HGU}}\right)\right], \quad M^G_{\texttt{HGU}}(0) = M^G_{\texttt{HGU0}}$$

```
Definition: MGHGU =
beta2HGU + beta3HGU * tanh(beta4HGU * (GlucNL -  beta5HGU))

Initial value: MGHGU(t0) =
MGHGU0
```

[Variable 25]

$\Gamma_{\texttt{KGE}}$ **Kidney Glucose Excretion (mmol/min)**

Kidney Glucose Excretion

$$\begin{aligned} \Gamma_{\texttt{KGE}} &= \begin{cases} \beta^0_{\texttt{KGE}} + \beta^1_{\texttt{KGE}} \tanh\left[\beta^2_{\texttt{KGE}} \left(G_K - \beta^3_{\texttt{KGE}}\right)\right] & , \quad 0 \le G_K < \beta^3_{\texttt{KGE}} \\ -\beta^4_{\texttt{KGE}} + \beta^5_{\texttt{KGE}} G_K & , \quad G_K \ge \beta^3_{\texttt{KGE}} \end{cases} \\ \Gamma_{\texttt{KGE}}(0) &= \Gamma_{\texttt{KGE0}} \end{aligned}$$

```
Definition: GammaKGE =
(GlucK < beta3KGE)   *  (beta0KGE + beta1KGE * tanh(beta2KGE*( GlucK - beta3KGE )))
+ (GlucK >= beta3KGE)   *  (- beta4KGE + beta5KGE * GlucK)

Initial value: GammaKGE(t0) =
GammaKGE0
```

[Variable 26]

I_B **Insulin concentration in Brain space (pM)**

Insulin concentration in Brain space

$$\frac{dI_B}{dt} = \frac{Q^I_B}{V^I_B}\left(I_H - I_B\right), \quad I_B(0) = I_{B0}$$

```
Definition: d InsuB /dt =
QfloIB / VolIB * (InsuH - InsuB)

Initial value: InsuB(t0) =
InsuB0
```

[Variable 27]

I_H **Insulin concentration in Heart/lung space (pM)**

Insulin concentration in Heart/lung space

$$\frac{dI_H}{dt} = \frac{Q_B^I I_B + Q_L^I I_L + Q_K^I I_K + Q_P^I I_{PV} - Q_H^I I_H}{V_H^I}, \quad I_H(0) = I_{H0}$$

```
Definition: d InsuH /dt =
(QfloIB * InsuB + QfloIL * InsuL + QfloIK * InsuK + QfloIP * InsuPV +
- QfloIH * InsuH +GammaIVI) / VolIH

Initial value: InsuH(t0) =
InsuH0
```

[Variable 28]

I_H^N **Normalized Insulin concentration in Heart/lung space (#)**

Normalized Insulin concentration in Liver space

$$I_H^N = \frac{I_H}{I_{H0}}, \quad I_H^N(0) = 1$$

```
Definition: InsuNH =
InsuH / InsuH0

Initial value: InsuNH(t0) =
1
```

[Variable 29]

I_J **Insulin concentration in gut (Jejunal) space (pM)**

Insulin concentration in gut (Jejunal) space

$$\frac{dI_J}{dt} = \frac{Q_J^I}{V_J^I}\left(I_H - I_J\right), \quad I_J(0) = I_{J0}$$

Note: we have substituted the original "G" suffix in Chee&Fernando with "J" (Jejunum) for legibility.

```
Definition: d InsuJ /dt =
QfloIJ / VolIJ * (InsuH - InsuJ)


Initial value: InsuJ(t0) =
InsuJ0
```

[Variable 30]

I_L **Insulin concentration in Liver space (pM)**

Insulin concentration in Liver space

$$\frac{dI_L}{dt} = \frac{Q_A^I I_H + Q_J^I I_J - Q_L^I I_L + \Gamma_{\texttt{PIR}} - \Gamma_{\texttt{LIC}}}{V_L^I}, \quad I_L(0) = I_{L0}$$

PIR: Peripheral Insulin Release, Pancreatic Insulin Release
LIC: Liver Insulin Clearance

```
Definition: d InsuL /dt =
(QfloIA * InsuH + QfloIJ * InsuJ - QfloIL * InsuL + GammaPIR - GammaLIC) / VolIL


Initial value: InsuL(t0) =
InsuL0
```

[Variable 31]

I_K **Insulin concentration in Kidney space (pM)**

Insulin concentration in Kidney space

$$\frac{dI_K}{dt} = \frac{Q_K^I}{V_K^I}(I_H - I_K) - \frac{\Gamma_{\texttt{KIC}}}{V_K^I}, \quad I_K(0) = I_{K0}$$

```
Definition: d InsuK /dt =
(QfloIK / VolIK) * (InsuH - InsuK) - GammaKIC / VolIK


Initial value: InsuK(t0) =
InsuK0
```

[Variable 32]

I_{PV} **Insulin concentration in Peripheral Vascular space (pM)**

Insulin concentration in Peripheral Vascular space

$$\frac{dI_{PV}}{dt} = \frac{Q_P^I}{V_{PV}^I}(I_H - I_{PV}) - \frac{V_{PI}}{V_{PV}^I T_P^I}(I_{PV} - I_{PI}), \quad I_{PV}(0) = I_{PV0}$$

```
Definition: d InsuPV /dt =
(QfloIP/VolIPV) * (InsuH - InsuPV) - VolPI / (VolIPV * TdifIP) * (InsuPV - InsuPI)

Initial value: InsuPV(t0) =
InsuPV0
```

[Variable 33]

I_{PI} **Insulin concentration in Peripheral Interstitial space (pM)**

Insulin concentration in Peripheral Interstitial space

$$\frac{dI_{PI}}{dt} = \frac{1}{T_P^I}(I_{PV} - I_{PI}) - \frac{\Gamma_{\texttt{PIC}}}{V_{PI}}, \quad I_{PI}(0) = I_{PI0}$$

PIC: Peripheral Insulin Clearance

```
Definition: d InsuPI /dt =
(1 / TdifIP) * (InsuPV - InsuPI) - GammaPIC / VolPI

Initial value: InsuPI(t0) =
InsuPI0
```

[Variable 34]

I_{PI}^N **Normalized Insulin concentration in Peripheral Interstitial space (#)**

Normalized Insulin concentration in Peripheral Interstitial space

$$I_{PI}^N = \frac{I_{PI}}{I_{PI0}}, \quad I_{PI}^N(0) = 1$$

```
Definition: InsuNPI =
InsuPI / InsuPI0

Initial value: InsuNPI(t0) =
1
```

[Variable 35]

I_L^N **Normalized Insulin concentration in Liver space** (#)

Normalized Insulin concentration in Liver space

$$I_L^N = \frac{I_L}{I_{L0}}, \quad I_L^N(0) = 1$$

```
Definition: InsuNL =
InsuL / InsuL0
```

```
Initial value: InsuNL(t0) =
1
```

[Variable 36]

$\Gamma_{\mathtt{LIC}}$ **Liver Insulin Clearance** (**pmol/min**)

Liver Insulin Clearance

$$\Gamma_{\mathtt{LIC}} = F_{\mathtt{LIC}} \left\{ Q_A^I I_H + Q_J^I I_J + \Gamma_{\mathtt{PIR}} \right\}, \quad \Gamma_{\mathtt{LIC}}(0) = \Gamma_{\mathtt{LIC0}}$$

```
Definition: GammaLIC =
FracLIC * (QfloIA * InsuH + QfloIJ * InsuJ + GammaPIR)
```

```
Initial value: GammaLIC(t0) =
GammaLIC0
```

[Variable 37]

$\Gamma_{\mathtt{KIC}}$ **Kidney Insulin Clearance** (**pmol/min**)

Kidney Insulin Clearance

$$\Gamma_{\mathtt{KIC}} = F_{\mathtt{KIC}}(Q_K^I \, I_H)$$

with $F_{\mathtt{KIC}} = 0.30$

```
Definition: GammaKIC =
FracKIC * (QfloIK * InsuH)
```

```
Initial value: GammaKIC(t0) =
GammaKIC0
```

[Variable 38]

$\Gamma_{\texttt{PIC}_{\texttt{NC}}}$ **Peripheral Insulin Clearance (pmol/min)**

Peripheral Insulin Clearance

$$\Gamma_{\texttt{PIC}} = \frac{I_{PI}}{\left[\left(\frac{1-F_{\texttt{PIC}}}{F_{\texttt{PIC}}}\right)\left(\frac{1}{Q_P^I}\right) - \left(\frac{T_P^I}{V_{PI}}\right)\right]}$$

with $F_{\texttt{PIC}} = 0.15$

```
Definition: GammaPIC =
InsuPI / (((1.0 - FracPIC  ) / FracPIC) * (1 / QfloIP) - (TdifIP / VolPI))

Initial value: GammaPIC(t0) =
GammaPIC0
```

[Variable 39]

$\Gamma_{\texttt{SerPIR}}$ **Pancreatic Insulin Release according to Sorensen (pmol/min)**

Pancreatic Insulin Release according to Sorensen

$$\Gamma_{PIR} = \frac{S_{ecr}}{S_{ecr}^B}\Gamma_{PIR}^B = S_{ecr}^N\Gamma_{PIR}^B, \quad \Gamma_{PIR}(0) = \Gamma_{PIR}^B$$

```
Definition: GammaPIR =
SecrN * GammaBPIR

Initial value: GammaPIR(t0) =
GammaBPIR
```

[Variable 40]

P_{otn} **Potentiator (#)**

Potentiator

$$\frac{dP_{otn}}{dt} = \alpha(P_{tgt} - P_{otn}), \quad P_{otn}(0) = P_{otn0}$$

```
Definition: d Potn /dt =
KappaPotnPtgt * (Ptgt - Potn)

Initial value: Potn(t0) =
Potn0
```

[Variable 41]

P_{inh} **Inhibitor (#)**

Inhibitor

$$\frac{dP_{inh}}{dt} = K_{PinhPprp}(P_{prp} - P_{inh}), \quad P_{inh}(0) = P_{inh0} = P_{prp0}$$

```
Definition: d Pinh /dt =
KappaPinhPrp * (Pprp - Pinh)

Initial value: Pinh(t0) =
Pinh0
```

[Variable 42]

R_{insu} **Labile or granular insulin (pmol)**

Labile or granular insulin

$$\frac{dR_{insu}}{dt} = K_{Rinsu}(R_{insu0} - R_{insu}) + K_{RinsuPotn}P_{otn} - S_{ecr}, \quad R_{insu}(0) = InitialR_{insu0}$$

```
Definition: d Rinsu /dt =
KappaRinsu * (Rinsu0 - Rinsu) + KappaRinsuPotn * Potn - Secr

Initial value: Rinsu(t0) =
InitialRinsu0
```

[Variable 43]

S_{ecr} **Secretion rate (pmol/min)**

Secretion rate

$$S_{ecr} = [M1P_{tgt} + M2(P_{prp} - P_{inh})^{+}]R_{insu}, \quad S_{ecr}(0) = S_{ecr0}$$

```
Definition: Secr =
(Pprp > Pinh)   *   ((EMME1 * Ptgt + EMME2 * (Pprp - Pinh)) * Rinsu)
+ (Pprp <= Pinh) * (EMME1 * Ptgt * Rinsu)

Initial value: Secr(t0) =
Secr0
```

[Variable 44]

S^N_{ecr} **Normalized secretion rate** (#)

Normalized Insulin secretion rate

$$S^N_{ecr} = \frac{S_{ecr}}{S_{ecr0}}, \quad S^N_{ecr}(0) = 1$$

```
Definition: SecrN =
Secr / Secr0
```

```
Initial value: SecrN(t0) =
1
```

[Variable 45]

P_{prp} **Potentiator glucose proportional factor** (#)

Potentiator glucose proportional factor

$$P_{prp} = \frac{G_H^{\beta^1_{PIR}}}{(\beta^2_{PIR})^{\beta^1_{PIR}} + \beta^3_{PIR} G_H^{\beta^4_{PIR}}}, \quad P_{prp}(0) = P_{prp0} = \frac{G_{H0}^{\beta^1_{PIR}}}{(\beta^2_{PIR})^{\beta^1_{PIR}} + \beta^3_{PIR} G_{H0}^{\beta^4_{PIR}}}$$

```
Definition: Pprp =
pow(GlucH,beta1PIR)/(pow(beta2PIR,beta1PIR)+beta3PIR*pow(GlucH,beta4PIR))
```

```
Initial value: Pprp(t0) =
Pprp0
```

[Variable 46]

P_{tgt} **Potentiator target** (#)

Potentiator target

$$P_{tgt} = P_{prp}^{\beta^5_{PIR}}, \quad P_{tgt}(0) = P_{tgt0} = P_{prp0}^{\beta^5_{PIR}}$$

```
Definition: Ptgt =
pow(Pprp,beta5PIR)
```

```
Initial value: Ptgt(t0) =
Ptgt0
```

[Variable 47]

C **gluCagon plasma concentration (pM)**

GluCagon plasma concentration

$$\frac{dC}{dt} = \frac{\Gamma_{\mathtt{PCR}} - \Gamma_{\mathtt{PCC}}}{V_C}, \quad C(0) = C_0$$

```
d Cgon /dt =  GammaPCR - GammaPCC ) / VolC;

Cgon (Tzero) = Cgon0;
```

```
Definition: d Cgon /dt =
(GammaPCR - GammaPCC) / VolC

Initial value: Cgon(t0) =
Cgon0
```

[Variable 48]

C^N **Normalized gluCagon plasma concentration (#)**

Normalized gluCagon plasma concentration

$$C^N = \frac{C}{C_0}, \quad C^N(0) = 1$$

```
Definition: CgonN =
Cgon / Cgon0

Initial value: CgonN(t0) =
1
```

[Variable 49]

$\Gamma_{\mathtt{PCC}}$ **Peripheral gluCagon Clearance (pmol/min)**

Peripheral gluCagon Clearance

$$\Gamma_{\mathtt{PCC}} = \Gamma_{\mathtt{MCC}} C$$

with $\Gamma_{\mathtt{MCC}} = 910\, ml/min$
MCC: Metabolic gluCagon Clearance

```
Definition: GammaPCC =
GammaMCC * Cgon

Initial value: GammaPCC(t0) =
GammaPCC0
```

[Variable 50]

$\Gamma_{\texttt{PCR}}$ **Pancreatic gluCagon Release (pmol/min)**

Pancreatic gluCagon Release

$$\Gamma_{\texttt{PCR}} = \Gamma^{B}_{\texttt{PCR}} M^{G}_{PCR} M^{I}_{PCR}, \quad \Gamma_{\texttt{PCR}}(0) = \Gamma_{\texttt{PCR0}}$$

with $V_C = 11.310\,L$

```
Definition: GammaPCR =
GammaBPCR * MGPCR * MIPCR

Initial value: GammaPCR(t0) =
GammaBPCR
```

[Variable 51]

$M^{G}_{\texttt{PCR}}$ **Glucose effect on gluCagon clearance (#)**

Glucose effect on Glucagone clearance

$$M^{G}_{\texttt{PCR}} = \beta^{0}_{\texttt{PCR}} - \beta^{1}_{\texttt{PCR}} \tanh(\beta^{2}_{\texttt{PCR}}(G^{N}_{H} - \beta^{3}_{\texttt{PCR}})), \quad M^{G}_{\texttt{PCR}}(0) = M^{G}_{\texttt{PCR0}}$$

```
Definition: MGPCR =
beta0PCR - beta1PCR * tanh(beta2PCR * (GlucNH - beta3PCR))

Initial value: MGPCR(t0) =
MGPCR0
```

[Variable 52]

$M^{I}_{\texttt{PCR}}$ **Insulin effect on gluCagon clearance (#)**

Insulin effect on Glucagone clearance

$$M^{I}_{\texttt{PCR}} = \beta^{4}_{\texttt{PCR}} - \beta^{5}_{\texttt{PCR}} \tanh\left[\beta^{6}_{\texttt{PCR}}\left(I^{N}_{H} - \beta^{7}_{\texttt{PCR}}\right)\right], \quad M^{I}_{\texttt{PCR}}(0) = M^{I}_{\texttt{PCR0}}$$

```
Definition: MIPCR =
beta4PCR - beta5PCR * tanh(beta6PCR * (InsuNH - beta7PCR))


Initial value: MIPCR(t0) =
MIPCR0
```

[Variable 53]

$\Gamma_{\texttt{IVG}}$ **Intravenous Glucose Infusion (mmol/min)**

Intravenous Glucose infusion

$$\Gamma_{\texttt{IVG}} = \begin{cases} 0 & t < Time_{\texttt{IVG}} \\ GammaIVGin & Time_{\texttt{IVG}} \leq t < Time_{\texttt{IVGend}} \\ 0 & t \geq Time_{\texttt{IVGend}} \end{cases} \tag{2}$$

```
Definition: GammaIVG =
GammaIVG0+(GammaIVGin)*(Time>=TimeIVG)*(Time<=TimeIVGend)


Initial value: GammaIVG(t0) =
GammaIVG0
```

[Variable 54]

$\Gamma_{\texttt{IVI}}$ **Intravenous Insulin Infusion (pmol/min)**

Intravenous Insulin infusion

$$\Gamma_{\texttt{IVI}} = \begin{cases} 0 & t < Time_{\texttt{IVI}} \\ GammaIVIin & Time_{\texttt{IVI}} \leq t < Time_{\texttt{IVIend}} \\ 0 & t \geq Time_{\texttt{IVIend}} \end{cases} \tag{3}$$

```
Definition: GammaIVI =
GammaIVI0+(GammaIVIin)*(Time>=TimeIVI)*(Time<=TimeIVIend)


Initial value: GammaIVI(t0) =
GammaIVI0
```

Annotated Parameter formulas (the updated MoSpec rules)

[Parameter 0]

t_0 **Starting time for numerical integration**
(-30 min)

MUST be present and MASKED: Gemini reserved keyword

[Parameter 1]

t_{end} **Final time for numerical integration**
(200 min)

MUST be present and MASKED: Gemini reserved keyword

[Parameter 2]

t_{Δ} **Time integration step**
(0.1 min)

MUST be present and MASKED: Gemini reserved keyword

[Parameter 3]

Q_B^G **Vascular blood water flow rate for Brain (glucose-related)**
(0.59 L/min)

[Parameter 4]

V_{BV}^G **Distribution Volume of Glucose in Brain Vascular space**
(0.35 L)

[Parameter 5]

V_{BI} **Volume of Brain Interstitial space**
(0.45 L)

[Parameter 6]

T_B **Trans-capillary diffusion rate for Brain**
(2.1 min)

[Parameter 7]

G_{H0} **Baseline value of G_H at initial time (t_0)**
(5.07333 mM)

[Parameter 8]

$\Gamma_{\texttt{BGU}}$ **Brain Glucose Uptake rate**
(0.388889 mmol/min)

[Parameter 9]

Q_L^G **Vascular blood water flow rate for Liver (glucose-related)**
(1.26 L/min)

[Parameter 10]

Q_K^G **Vascular blood water flow rate for Kidney (glucose-related)**
(1.01 L/min)

[Parameter 11]

Q_P^G **Vascular blood water flow rate for Peripheral tissues (glucose-related)**
(1.51 L/min)

[Parameter 12]

Q_H^G **Vascular blood water flow rate for Heart/lung (glucose-related)**
(4.37 L/min)

[Parameter 13]

$\Gamma_{\texttt{RBCU}}$ **Red Blood cell Glucose Uptake rate**
(0.0555556 mmol/min)

[Parameter 14]

V_H^G **Distribution Volume of Glucose in Heart/lung Vascular space**
(1.38 L)

[Parameter 15]

Q_J^G **Vascular blood water flow rate for Gut/Jejunum (glucose-related)**
(1.01 L/min)

[Parameter 16]

V_J^G **Distribution Volume of Glucose in Gut/Jejunum Vascular space**
(1.12 L)

[Parameter 17]

$\Gamma_{\texttt{JGU}}$ **Gut/Jejunal Glucose Uptake or utilization rate**
(0.111111 mmol/min)

[Parameter 18]

Q_A^G **Vascular blood water flow rate in hepatic Artery (glucose-related)**
(0.25 L/min)

[Parameter 19]

V_L^G **Distribution Volume of Glucose in Liver space**
(2.51 L)

[Parameter 20]

V_K^G **Distribution Volume of Glucose in Kidney space**
(0.66 L)

[Parameter 21]

V_{PV}^G **Distribution Volume of Glucose in Peripheral Vascular space**
(1.04 L)

[Parameter 22]

V_{PI} **Volume of Peripheral Interstitial space**
(6.74 L)

[Parameter 23]

T_P^G **Trans-capillary diffusion rate for Peripheral tissues (glucose-related)**
(5 min)

[Parameter 24]

$\Gamma_{\mathtt{PGU}}^B$ **Baseline rate of Peripheral Glucose Uptake**
(0.194444 mmol/min)

[Parameter 25]

$\beta_{\mathtt{PGU}}^0$ **PGU Insulin effect midpoint**
(7.03 #)

[Parameter 26]

$\beta_{\mathtt{PGU}}^1$ **PGU Insulin effect half-amplitude**
(6.52 #)

[Parameter 27]

$\beta^2_{\texttt{PGU}}$ **PGU Insulin effect steepness**
(0.338 #)

[Parameter 28]

$\beta^3_{\texttt{PGU}}$ **PGU Insulin effect shift**
(5.82 #)

[Parameter 29]

$\beta^0_{\texttt{HGP}}$ **HGP gluCagon effect scale**
(2.7 #)

[Parameter 30]

$\beta^1_{\texttt{HGP}}$ **HGP gluCagon scale**
(0.388852 #)

[Parameter 31]

τ_C **Inverse of the decay rate for the glucagon-driven intensification of f_2 Hepatic Glucose Uptake suppression**
(65 min)

[Parameter 32]

$\beta^2_{\texttt{HGP}}$ **HGP Insulin effect midpoint**
(1.21 #)

[Parameter 33]

$\beta^3_{\texttt{HGP}}$ **HGP Insulin effect half-amplitude**
(1.14 #)

[Parameter 34]

$\beta^4_{\texttt{HGP}}$ **HGP Insulin effect steepness**
(1.66 #)

[Parameter 35]

$\beta^5_{\texttt{HGP}}$ **HGP Insulin effect shift**
(0.887748 #)

[Parameter 36]

τ_I **Inverse of the decay rate for the insulin-driven intensification of $M^I_{\texttt{HGP}}$ and $M^I_{\texttt{HGU}}$ (same for both)**
(25 min)

[Parameter 37]

$\beta^6_{\texttt{HGP}}$ **HGP Glucose effect midpoint**
(1.42 #)

[Parameter 38]

$\beta^7_{\texttt{HGP}}$ **HGP Glucose effect half-amplitude**
(1.41 #)

[Parameter 39]

$\beta^8_{\texttt{HGP}}$ **HGP Glucose effect steepness**
(0.62 #)

[Parameter 40]

$\beta^9_{\texttt{HGP}}$ **HGP Glucose effect shift**
(0.504543 #)

[Parameter 41]

$\Gamma_{\texttt{HGP0}}$ **Baseline value of $\Gamma_{\texttt{HGP}}$ at initial time (t_0)**
(0.861111 mmol/min)

[Parameter 42]

$\beta^0_{\texttt{HGU}}$ **HGU Insulin effect half-amplitude**
(2 #)

[Parameter 43]

$\beta^1_{\texttt{HGU}}$ **HGU Insulin effect steepness**
(0.549306 #)

[Parameter 44]

$\beta^2_{\texttt{HGU}}$ **HGP Glucose effect midpoint**
(5.66 #)

[Parameter 45]

$\beta^3_{\texttt{HGU}}$ **HGP Glucose effect half-amplitude**
(5.66 #)

[Parameter 46]

$\beta^4_{\texttt{HGU}}$ **HGP Glucose effect steepness**
(2.44 #)

[Parameter 47]

$\beta^5_{\texttt{HGU}}$ **HGP Glucose effect shift**
(1.4783 #)

[Parameter 48]

$\Gamma_{\texttt{HGU0}}$ **Baseline value of $\Gamma_{\texttt{HGU}}$ at initial time (t_0)**
(0.111111 mmol/min)

[Parameter 49]

$\beta^0_{\texttt{KGE}}$ **KGE Glucose effect midpoint**
(0.394444 mmol/min)

[Parameter 50]

$\beta^1_{\texttt{KGE}}$ **KGE Glucose effect half-amplitude**
(0.394444 mmol/min)

[Parameter 51]

$\beta^2_{\texttt{KGE}}$ **KGE Glucose effect steepness**
(0.198 /mM)

[Parameter 52]

$\beta^3_{\texttt{KGE}}$ **KGE Glucose effect shift, point of transition between tanh and linear regime**
(25.5556 mM)

[Parameter 53]

$\beta^4_{\texttt{KGE}}$ **KGE Glucose linear effect intercept**
(1.834 mmol/min)

[Parameter 54]

$\beta^5_{\texttt{KGE}}$ **KGE Glucose linear effect slope**
(0.0872 mmol/min/mM)

[Parameter 55]

Q_B^I **Vascular blood water flow rate for Brain (insulin-related)**
(0.45 L/min)

[Parameter 56]

V_B^I **Distribution Volume of Insulin in Brain vascular space**
(0.26 L)

[Parameter 57]

V_H^I **Distribution Volume of Insulin in Heart/lung vascular space**
(0.99 L)

[Parameter 58]

Q_L^I **Vascular blood water flow rate for Liver (insulin-related)**
(0.9 L/min)

[Parameter 59]

Q_K^I **Vascular blood water flow rate for Kidney (insulin-related)**
(0.72 L/min)

[Parameter 60]

Q_P^I **Vascular blood water flow rate for Periphery (insulin-related)**
(1.05 L/min)

[Parameter 61]

Q_H^I **Vascular blood water flow rate for Heart and Lungs (insulin-related)**
(3.12 L/min)

[Parameter 62]

V_J^I **Distribution Volume of Insulin in Gut Vascular space**
(0.94 L)

[Parameter 63]

Q_J^I **Vascular blood water flow rate for Gut (insulin-related)**
(0.72 L/min)

[Parameter 64]

V_L^I **Distribution Volume of Insulin in Liver Vascular space**
(1.14 L)

[Parameter 65]

Q_A^I **Vascular blood water flow rate in hepatic Artery (insulin-related)**
(0.18 L/min)

[Parameter 66]

$F_L IC$ **Fraction of insulin Liver clearance**
(0.4 #)

[Parameter 67]

$F_K IC$ **Fraction of insulin Kidney clearance**
(0.3 #)

[Parameter 68]

V_K^I **Distribution Volume of Insulin in Kidney Vascular space**
(0.51 L)

[Parameter 69]

V_{PV}^{I} **Distribution Volume of Insulin in Peripheral Vascular space**
(0.74 L)

[Parameter 70]

T_{P}^{I} **Trans-capillary diffusion rate for Peripheral tissues (insulin-related)**
(20 min)

[Parameter 71]

$F_P IC$ **Fraction of insulin Periphery clearance**
(0.15 #)

[Parameter 72]

$\beta_{\mathtt{PIR}}^{1}$ **PIR Glucose effect parameter 1**
(3.27 #)

[Parameter 73]

$\beta_{\mathtt{PIR}}^{2}$ **PIR Glucose effect parameter 2**
(7.33333 mmol/l)

[Parameter 74]

$\beta_{\mathtt{PIR}}^{3}$ **PIR Glucose effect parameter 3**
(2.879 #)

[Parameter 75]

$\beta_{\mathtt{PIR}}^{4}$ **PIR Glucose effect parameter 4**
(3.02 #)

[Parameter 76]

$\beta^5_{\texttt{PIR}}$ **Potentiator parameter**
(1.11 #)

[Parameter 77]

$K_{\texttt{Rinsu}}$ **Rate of labile Insulin secretion**
(0.00794 /min)

[Parameter 78]

$R_{\texttt{insu0}}$ **Labile Insulin for Glucose=0**
(44310 pmol)

[Parameter 79]

$K_{\texttt{RinsuPotr}}$ **Rate of Potentiator effect on labile insulin**
(4025 pmol/min)

[Parameter 80]

$K_{\texttt{RinsuPtgt}}$ **Rate at which Potentiator reachs its target value**
(0.0482 /min)

[Parameter 81]

$K_{\texttt{pinhPrp}}$ **Rate at which Inhibitor reaches the proportional insulin response function**
(0.931 /min)

[Parameter 82]

M_1 **Late rate of increase in insulin secretion**
(0.00747 /min)

[Parameter 83]

M_2 **Rate of insulin response**
(0.0958 /min)

[Parameter 84]

I_{PV0} **Baseline value of I_{PV} at initial time (t_0)**
(91 pM)

[Parameter 85]

Γ_{MCC} **Starting value for gluCagon**
(11.48 pM)

[Parameter 86]

Γ_{MCC} **Rate constant of gluCagon clearance**
(0.91 L/min)

[Parameter 87]

V_C **gluCagon distribution volume**
(11.31 L)

[Parameter 88]

$\beta^0_{\mathtt{PCR}}$ **PCR Glucose effect midpoint**
(2.93 #)

[Parameter 89]

$\beta^1_{\mathtt{PCR}}$ **PCR Glucose effect half-amplitude**
(2.1 #)

[Parameter 90]

$\beta^2_{\mathtt{PCR}}$ **PCR Glucose effect steepness**
(4.18 #)

[Parameter 91]

$\beta^3_{\mathtt{PCR}}$ **PCR Glucose effect shift**
(0.621325 #)

[Parameter 92]

$\beta^4_{\mathtt{PCR}}$ **PCR Insulin effect midpoint**
(1.31 #)

[Parameter 93]

$\beta^5_{\mathtt{PCR}}$ **PCR Insulin effect half-amplitude**
(0.61 #)

[Parameter 94]

$\beta^5_{\mathtt{PCR}}$ **PCR Insulin effect steepness**
(1.06 #)

[Parameter 95]

$\beta^5_{\mathtt{PCR}}$ **PCR Insulin effect shift**
(0.471419 #)

[Parameter 96]

f_{20} **Baseline value of f_2 at initial time (t_0)**
(0 #)

[Parameter 97]

$\Gamma_{\texttt{IVG}}$ **Intravenous Glucose Infusion starting value**
(0 mmol/min)

[Parameter 98]

$\Gamma_{\texttt{IVGin}}$ **Intravenous Glucose Infusion**
(64.81 mmol/min)

[Parameter 99]

$Time_{\texttt{IVG}}$ **Start time of intravenous Glucose Infusion**
(-3 min)

[Parameter 100]

$Time_{\texttt{IVGend}}$ **End time of intravenous Glucose Infusion**
(0 min)

[Parameter 101]

$\Gamma_{\texttt{IVI}}$ **Intravenous Insulin Infusion starting value**
(0 pmol/min)

[Parameter 102]

$\Gamma_{\texttt{IVIin}}$ **Intravenous Insulin Infusion**
(0 pmol/min)

[Parameter 103]

$time_{\texttt{IVI}}$ **Starting time of Instravenous Insulin Infusion**
(0 min)

[Parameter 104]

$time_{\texttt{IVIend}}$ **End time of Instravenous Insulin Infusion**
(0 min)

[Parameter 105]

I_{H0} **Baseline value of I_H at initial time (t_0)**
(107.059 pM)

Baseline value for I_H at time 0:

$$I_{H0} = \frac{I_{PV0}}{1 - F_{PIC}}$$

```
Definition: InsuH0 =
InsuPV0/(1-FracPIC)
```

[Parameter 106]

I_{K0} **Baseline value of I_K at initial time (t_0)**
(74.9412 pM)

Baseline value for I_K at time 0:

$$I_{K0} = I_{H0}(1 - F_{KIC})$$

```
Definition: InsuK0 =
InsuH0*(1-FracKIC)
```

[Parameter 107]

I_{B0} **Baseline value of I_B at initial time (t_0)**
(107.059 pM)

Baseline value for I_B at time 0:

$$I_{B0} = I_{H0}$$

```
Definition: InsuB0 =
InsuH0
```

[Parameter 108]

I_{G0} **Baseline value of I_G at initial time (t_0)**
(107.059 pM)

Baseline value for I_J at time 0:

$$I_{J0} = I_{H0}$$

```
Definition: InsuJ0 =
InsuH0
```

[Parameter 109]

I_{PI0} **Baseline value of I_{PI} at initial time (t_0)**
(40.9651 pM)

Baseline value for i_{pi} at time 0:

$$I_{PI0} = I_{PV0} - (I_{H0} - I_{PV0})\frac{Q_P^I T_P}{V_P^I}$$

```
Definition: InsuPI0 =
InsuPV0-((QfloIP*TdifIP/VolPI)*(InsuH0-InsuPV0))
```

[Parameter 110]

I_{L0} **Baseline value of I_L at initial time (t_0)**
(151.488 pM)

Baseline value for I_L at time 0:

$$I_{L0} = \frac{1}{Q_L^I}(Q_H^I I_{H0} - Q_B^I I_{B0} - Q_K^I I_{K0} - Q_P^I I_{PV0})$$

```
Definition: InsuL0 =
1/QfloIL*(QfloIH*InsuH0-QfloIB*InsuB0-QfloIK*InsuK0-QfloIP*InsuPV0)
```

[Parameter 111]

$\Gamma_{\mathtt{PIR0}}$ **Baseline value of $\Gamma_{\mathtt{PIR}}$ at initial time (t_0)**
(130.879 pmol/min)

Baseline value for Γ_{BPIR} at time 0:

$$\Gamma_{BPIR} = \frac{Q_L^I}{1 - F_{LIC}} I_{L0} - Q_J^I I_{J0} - Q_A^I I_{H0}$$

```
Definition: GammaBPIR =
QfloIL/(1-FracLIC)*InsuL0 - QfloIJ*InsuJ0-QfloIA*InsuH0
```

[Parameter 112]

$\Gamma_{\texttt{PIC0}}$ **Baseline value of $\Gamma_{\texttt{PIC}}$ at initial time (t_0)**
(16.8618 pmol/min)

Baseline value for Γ_{PIC} at time 0:

$$\Gamma_{PIC0} = \frac{I_{PI0}}{\frac{1-F_{PIC}}{F_{PIC}}} - \frac{T_{IP}}{V_{PI}}$$

```
Definition: GammaPIC0 =
InsuPI0/(((1-FracPIC)/FracPIC)*(1/QfloIP)-TdifIP/VolPI)
```

[Parameter 113]

$P_{\texttt{prp0}}$ **Baseline value of $P_{\texttt{prp}}$ at initial time (t_0)**
(0.19032 #)

Baseline value for P_{prp} at time 0:

$$P_{prp0} = \frac{(G_{H0})^{\beta^1_{PIR}}}{(\beta^2_{PIR})^{\beta^1_{PIR}} + \beta^3_{PIR}(G_{H0})^{\beta^4_{PIR}}}$$

```
Definition: Pprp0 =
pow((GlucH0),beta1PIR) /( pow((beta2PIR),beta1PIR)+beta3PIR*pow((GlucH0),beta4PIR) )
```

[Parameter 114]

$P_{\texttt{tgt0}}$ **Baseline value of $P_{\texttt{tgt}}$ at initial time (t_0)**
(0.158572 #)

Baseline value for P_{tgt} at time 0:

$$P_{tgt0} = P_{prp0}^{\beta_{5PIR}}$$

```
Definition: Ptgt0 =
pow(Pprp0,beta5PIR)
```

[Parameter 115]

$P_{\texttt{inh0}}$ **Baseline value of** $P_{\texttt{inh}}$ **at initial time** (t_0)
(0.19032 #)

Baseline value for P_{inh} at time 0:

$$P_{inh0} = P_{prp0}$$

```
Definition: Pinh0 =
Pprp0
```

[Parameter 116]

$P_{\texttt{otn0}}$ **Baseline value of** $P_{\texttt{otn}}$ **at initial time** (t_0)
(0.158572 #)

Baseline value for P_{otn} at time 0:

$$P_{otn0} = P_{tgt0}$$

```
Definition: Potn0 =
Ptgt0
```

[Parameter 117]

$InitialRinsu_0$ **Baseline value of** $Rinsu$ **at initial time** (t_0)
(108507 pmol)

Baseline value for $Initial_{Rinsu}$ at time 0:

$$Initial_{Rinsu0} = \frac{K_{Rinsu} R_{insu0} + K_{RinsuPotn} P_{otn0}}{K_{Rinsu} + M_1 P_{otn0}}$$

```
Definition: InitialRinsu0 =
((KappaRinsu*Rinsu0)+ KappaRinsuPotn * Potn0)/(KappaRinsu+EMME1* Potn0)
```

[Parameter 118]

S_{ecr0} **Baseline value of** S_{ecr} **at initial time** (t_0)
(128.53 pmol/min)

Baseline value for S_{ecr} at time 0:

$$S_{ecr0} = M_1 P_{tgt0} Initial_{Rinsu0}$$

```
Definition: Secr0 =
EMME1*Ptgt0*InitialRinsu0
```

[Parameter 119]

G_{PV0} **Baseline value of G_{PV} at initial time (t_0)**
(4.94456 mM)

Baseline value for G_{PV} at time 0:

$$G_{PV0} = G_{H0} - \frac{\Gamma_{BPGU}}{Q_P^G}$$

```
Definition: GlucPV0 =
GlucH0 - GammaBPGU/QfloGP
```

[Parameter 120]

G_{K0} **Baseline value of G_K at initial time (t_0)**
(5.07333 mM)

Baseline value for G_K at time 0:

$$G_{K0} = G_{H0}$$

```
Definition: GlucK0 =
GlucH0
```

[Parameter 121]

G_{BV0} **Baseline value of G_{BV} at initial time (t_0)**
(4.4142 mM)

Baseline value for G_{BV} at time 0:

$$G_{BV0} = G_{H0} - \frac{\Gamma BPGU}{Q_B^G}$$

```
Definition: GlucBV0 =
GlucH0 - GammaBGU/QfloGB
```

[Parameter 122]

G_{J0} **Baseline value of G_J at initial time (t_0)**
(4.96332 mM)

Baseline value for G_J at time 0:

$$G_{J0} = G_{H0} - \frac{\Gamma JGU}{Q_J^G}$$

```
Definition: GlucJ0 =
GlucH0-GammaJGU/QfloGJ
```

[Parameter 123]

G_{L0} **Baseline value of G_L at initial time (t_0)**
(5.58039 mM)

Baseline value for G_L at time 0:

$$G_{L0} = \frac{Q_A^G G_{H0} + Q_J^G G_{J0} + \Gamma_{HGP0} - \Gamma HGU0}{Q_L^G}$$

```
Definition: GlucL0 =
(QfloGA*GlucH0+QfloGJ*GlucJ0+GammaHGP0-GammaHGU0)/QfloGL
```

[Parameter 124]

G_{BI0} **Baseline value of G_{BI} at initial time (t_0)**
(2.59938 mM)

Baseline value for G_{BI} at time 0:

$$G_{BI0} = G_{BV0} - \frac{\Gamma_{BPGU} T_B}{V_{BI}}$$

```
Definition: GlucBI0 =
GlucBV0-(GammaBGU*TdifB)/VolBI
```

[Parameter 125]

G_{PI0} **Baseline value of G_{PI} at initial time (t_0)**
(4.80032 mM)

Baseline value for G_{PI} at time 0:

$$G_{PI0} = G_{PV0} - \frac{\Gamma_{BPGU} T_{GP}}{V_{PI}}$$

```
Definition: GlucPI0 =
GlucPV0-GammaBPGU*TdifGP/VolPI
```

[Parameter 126]

$M_{\texttt{PGU0}}$ **Baseline value of** $M_{\texttt{PGU}}$ **at initial time** (t_0)
(0.992859 #)

Baseline value for M^I_{PGU} at time 0:

$$M^I_{PGU0} = \beta^0_{PGU} + \beta^1_{PGU} tanh[\beta^2_{PGU}(1 - \beta^3_{PGU})]$$

```
Definition: MIPGU0 =
beta0PGU+beta1PGU*tanh(beta2PGU*(1-beta3PGU))
```

[Parameter 127]

$M^C_{\texttt{HGP0}}$ **Baseline value of** $M^C_{\texttt{HGP}}$ **at initial time** (t_0)
(1 #)

Baseline value for M^C_{HGP} at time 0:

$$M^C_{HGP0} = \beta^0_{HGP} tanh(\beta^1_{HGP}) - F_{20}$$

```
Definition: MCHGP0 =
beta0HGP   * tanh(beta1HGP * 1) - Func20
```

[Parameter 128]

$M^{C0}_{\texttt{HGP0}}$ **Baseline value of** $M^{C0}_{\texttt{HGP}}$ **at initial time** (t_0)
(1 #)

Baseline value for M^{C0}_{HGP} at time 0:

$$M^{C0}_{HGP0} = \beta^0_{HGP} tanh(\beta^1_{HGP})$$

```
Definition: MC0HGP0 =
beta0HGP   * tanh(beta1HGP * 1)
```

[Parameter 129]

$M^I_{\texttt{HGP0}}$ **Baseline value of $M^I_{\texttt{HGP}}$ at initial time (t_0)**
(1 #)

Baseline value for M^I_{HGP} at time 0:

$$M^I_{HGP0} = \beta^2_{HGP} - \beta^3_{HGP} tanh[\beta^4_{HGP}(1 - \beta^5_{HGP})]$$

```
Definition: MIHGP0 =
beta2HGP - beta3HGP * tanh(beta4HGP * (1-beta5HGP))
```

[Parameter 130]

$M^I_{\texttt{HGPinf0}}$ **Steady state of MIHGP**
(1 #)

Baseline value for M^I_{HGPinf} at time 0:

$$M^I_{HGPinf0} = M^I_{HGP0}$$

```
Definition: MIHGPinf0 =
MIHGP0
```

[Parameter 131]

$M^G_{\texttt{HGP0}}$ **Baseline value of $M^G_{\texttt{HGP}}$ at initial time (t_0)**
(1 #)

Baseline value for M^G_{HGP} at time 0:

$$M^G_{HGP0} = \beta^6_{HGP} - \beta^7_{HGP} tanh[\beta^8_{HGP}(1 - \beta^9_{HGP})]$$

```
Definition: MGHGP0 =
beta6HGP-beta7HGP*tanh(beta8HGP*(1-beta9HGP))
```

[Parameter 132]

$M^I_{\texttt{HGU0}}$ **Baseline value of $M^I_{\texttt{HGU}}$ at initial time (t_0)**
(1 #)

Baseline value for M^I_{HGU} at time 0:

$$M^I_{HGU0} = \beta^0_{HGU} tanh(\beta^1_{HGU})$$

```
Definition: MIHGU0 =
beta0HGU * tanh(beta1HGU)
```

[Parameter 133]

$M^I_{\texttt{HGUinf0}}$ **Steady state of** $M^I_{\texttt{HGU}}$
(1 #)

Baseline value for M^I_{HGUinf} at time 0:

$$M^I_{HGUinf0} = M^I_{HGU0}$$

```
Definition: MIHGUinf0 =
MIHGU0
```

[Parameter 134]

$M^G_{\texttt{HGU0}}$ **Baseline value of** $M^G_{\texttt{HGU}}$ **at initial time** (t_0)
(1 #)

Baseline value for M^G_{HGU} at time 0:

$$M^G_{HGU0} = \beta^2_{HGU} + \beta^3_{HGU} tanh[\beta^4_{HGU}(1 - \beta^5_{HGU})]$$

```
Definition: MGHGU0 =
beta2HGU+beta3HGU*tanh(beta4HGU*(1-beta5HGU))
```

[Parameter 135]

$\Gamma_{\texttt{KGE0}}$ **Baseline value of** $\Gamma_{\texttt{KGE}}$ **at initial time** (t_0)
(0.000236777 mmol/min)

Baseline value for Γ_{KGE} at time 0:

$$\Gamma_{KGE0} = \begin{cases} \beta^0_{KGE} + \beta^1_{KGE} tanh[\beta^2_{KGE}(G_{K0} - \beta^3_{KGE})] & 0 \le G_K < \beta^3_{KGE} \\ -\beta^4_{KGE} + \beta^5_{KGE} G_{K0} & G_{K0} \ge \beta^3_{KGE} \end{cases} \tag{4}$$

(5)

```
Definition: GammaKGE0 =
(GlucK0<beta3KGE) * (beta0KGE+beta1KGE*tanh(beta2KGE*(GlucK0-beta3KGE)))
+ (GlucK0 >= beta3KGE) * (-beta4KGE+beta5KGE*GlucK0)
```

[Parameter 136]

$\Gamma_{\texttt{LIC0}}$ **Baseline value of $\Gamma_{\texttt{LIC}}$ at initial time (t_0)**
(90.8929 pmol/min)

Baseline value for Γ_{LIC} at time 0:

$$\Gamma_{LIC0} = F_{LIC}(Q_A^I I_{H0} + Q_J^I I_{J0} + \Gamma BPIR)$$

```
Definition: GammaLIC0 =
FracLIC*(QfloIA*InsuH0+QfloIJ*InsuJ0+GammaBPIR)
```

[Parameter 137]

$\Gamma_{\texttt{KIC0}}$ **Baseline value of $\Gamma_{\texttt{KIC}}$ at initial time (t_0)**
(23.1247 pmol/min)

Baseline value for Γ_{KIC} at time 0:

$$\Gamma_{KIC0} = F_{KIC} Q_K^I I_{H0}$$

```
Definition: GammaKIC0 =
FracKIC*(QfloIK*InsuH0)
```

[Parameter 138]

$M^G_{\texttt{PCR0}}$ **Baseline value of $M^G_{\texttt{PCR}}$ at initial time (t_0)**
(1 #)

Baseline value for M^G_{PCR} at time 0:

$$M^G_{PCR0} = \beta^0_{PCR} - \beta^1_{PCR} tanh[\beta^2_{PCR}(1 - \beta^3_{PCR})]$$

```
Definition: MGPCR0 =
beta0PCR - beta1PCR * tanh(beta2PCR * (1-beta3PCR))
```

[Parameter 139]

$M^I_{\texttt{PCR0}}$ **Baseline value of $M^I_{\texttt{PCR}}$ at initial time (t_0)**
(1 #)

Baseline value for M^I_{PCR} at time 0:

$$M^I_{PCR0} = \beta^4_{PCR} - \beta^5_{PCR} tanh[\beta^6_{PCR}(1 - \beta^7_{PCR})]$$

```
Definition: MIPCR0 =
beta4PCR - beta5PCR * tanh(beta6PCR * (1-beta7PCR))
```

[Parameter 140]

$\Gamma_{\texttt{PCC0}}$ **Baseline value of $\Gamma_{\texttt{PCC}}$ at initial time (t_0)**
(10.4468 pM)

Baseline value for Γ_{PCC} at time 0:

$$\Gamma_{PCC0} = C_0 \Gamma_{MCC}$$

```
Definition: GammaPCC0 =
Cgon0*GammaMCC
```

[Parameter 141]

$\Gamma^B_{\texttt{PCR0}}$ **Baseline value of $\Gamma^B_{\texttt{PCR}}$ at initial time (t_0)**
(10.4468 pM)

Baseline value for Γ_{BPCR} at time 0:

$$\Gamma_{BPCR0} = \Gamma_{PCC0}$$

```
Definition: GammaBPCR =
GammaPCC0
```

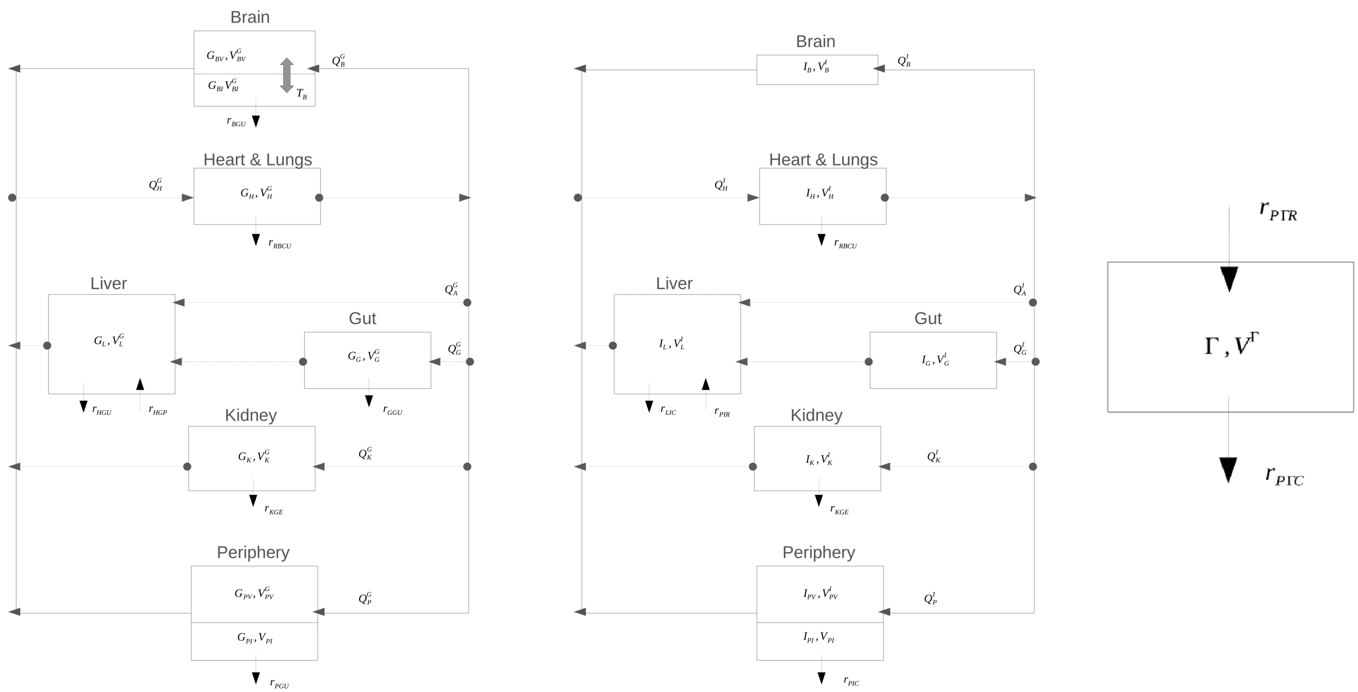

Figure 1. Block Diagram

Table 1. Model Variables

VarID	Variable	Units	Meaning
0	t	min	time in minutes
1	G_{BV}	mM	Glucose concentration in Brain Vascular space
2	G_{BI}	mM	Glucose concentration in Brain Interstitial space
3	G_H	mM	Glucose concentration in Heart-Lung space
4	G_H^N	#	Normalized Glucose concentration in Heart-Lung space
5	G_J	mM	Glucose concentration in gut (Jejunal) space
6	G_L	mM	Glucose concentration in Liver space
7	G_L^N	#	Normalized Glucose concentration in Liver space
8	G_K	mM	Glucose concentration in Kidney space
9	G_{PV}	mM	Glucose concentration in Peripheral Vascular space
10	G_{PI}	mM	Glucose concentration in Peripheral Interstitial space
11	G_{PI}^N	#	Normalized Glucose concentration in Peripheral Interstitial space
12	$\Gamma_{\texttt{PGU}}$	mmol/min	Rate of Peripheral Glucose Uptake
13	$M^I_{\texttt{HGP}}$	#	Insulin Action on glucose uptake
14	$\Gamma_{\texttt{HGP}}$	mmol/min	Hepatic Glucose Production
15	$M^I_{\texttt{HGP}}$	#	Insulin suppression of Hepatic Glucose Production
16	$M^I_{\texttt{HGPinf}}$	#	Steady State Insulin suppression of Hepatic Glucose Production
17	$M^C_{\texttt{HGP}}$	#	gluCagon contribution to Hepatic Glucose Production
18	$M^{C0}_{\texttt{HGP}}$	#	gluCagon contribution to Hepatic Glucose Production at baseline
19	f_2	#	Damping of gluCagon contribution to Hepatic Glucose Production
20	$M^G_{\texttt{HGP}}$	#	Glucose contribution to Hepatic Glucose Production
21	$\Gamma_{\texttt{HGU}}$	mmol/min	Hepatic Glucose Uptake
22	$M^I_{\texttt{HGU}}$	#	Insulin acceleration of Hepatic Glucose Uptake
23	$M^I_{\texttt{HGUinf}}$	#	Steady State Insulin acceleration of Hepatic Glucose Uptake
24	$M^G_{\texttt{HGU}}$	#	Glucose acceleration of Hepatic Glucose Uptake
25	$\Gamma_{\texttt{KGE}}$	mmol/min	Kidney Glucose Excretion
26	I_B	pM	Insulin concentration in Brain space
27	I_H	pM	Insulin concentration in Heart/lung space
28	I_H^N	#	Normalized Insulin concentration in Heart/lung space
29	I_J	pM	Insulin concentration in gut (Jejunal) space
30	I_L	pM	Insulin concentration in Liver space
31	I_K	pM	Insulin concentration in Kidney space

Table 1. Model Variables

VarID	Variable	Units	Meaning
32	I_{PV}	pM	Insulin concentration in Peripheral Vascular space
33	I_{PI}	pM	Insulin concentration in Peripheral Interstitial space
34	I_{PI}^{N}	#	Normalized Insulin concentration in Peripheral Interstitial space
35	I_{L}^{N}	#	Normalized Insulin concentration in Liver space
36	$\Gamma_{\texttt{LIC}}$	pmol/min	Liver Insulin Clearance
37	$\Gamma_{\texttt{KIC}}$	pmol/min	Kidney Insulin Clearance
38	$\Gamma_{\texttt{PIC}_{\texttt{NC}}}$	pmol/min	Peripheral Insulin Clearance
39	$\Gamma_{\texttt{SerPIR}}$	pmol/min	Pancreatic Insulin Release according to Sorensen
40	P_{otn}	#	Potentiator
41	P_{inh}	#	Inhibitor
42	R_{insu}	pmol	Labile or granular insulin
43	S_{ecr}	pmol/min	Secretion rate
44	S_{ecr}^{N}	#	Normalized secretion rate
45	P_{prp}	#	Potentiator glucose proportional factor
46	P_{tgt}	#	Potentiator target
47	C	pM	gluCagon plasma concentration
48	C^{N}	#	Normalized gluCagon plasma concentration
49	$\Gamma_{\texttt{PCC}}$	pmol/min	Peripheral gluCagon Clearance
50	$\Gamma_{\texttt{PCR}}$	pmol/min	Pancreatic gluCagon Release
51	$M_{\texttt{PCR}}^{G}$	#	Glucose effect on gluCagon clearance
52	$M_{\texttt{PCR}}^{I}$	#	Insulin effect on gluCagon clearance
53	$\Gamma_{\texttt{IVG}}$	mmol/min	Intravenous Glucose Infusion
54	$\Gamma_{\texttt{IVI}}$	pmol/min	Intravenous Insulin Infusion

Table 2. Model Parameters

ParID	Parameter	Units	Meaning
1	t_0	min	Starting time for numerical integration
2	t_{end}	min	Final time for numerical integration
3	t_Δ	min	Time integration step
4	Q_B^G	L/min	Vascular blood water flow rate for Brain (glucose-related)
5	V_{BV}^G	L	Distribution Volume of Glucose in Brain Vascular space
6	V_{BI}	L	Volume of Brain Interstitial space
7	T_B	min	Trans-capillary diffusion rate for Brain
8	G_{H0}	mM	Baseline value of G_H at initial time (t_0)
9	$\Gamma_{\texttt{BGU}}$	mmol/min	Brain Glucose Uptake rate
10	Q_L^G	L/min	Vascular blood water flow rate for Liver (glucose-related)
11	Q_K^G	L/min	Vascular blood water flow rate for Kidney (glucose-related)
12	Q_P^G	L/min	Vascular blood water flow rate for Peripheral tissues (glucose-related)
13	Q_H^G	L/min	Vascular blood water flow rate for Heart/lung (glucose-related)
14	$\Gamma_{\texttt{RBCU}}$	mmol/min	Red Blood cell Glucose Uptake rate
15	V_H^G	L	Distribution Volume of Glucose in Heart/lung Vascular space
16	Q_J^G	L/min	Vascular blood water flow rate for Gut/Jejunum (glucose-related)
17	V_J^G	L	Distribution Volume of Glucose in Gut/Jejunum Vascular space
18	$\Gamma_{\texttt{JGU}}$	mmol/min	Gut/Jejunal Glucose Uptake or utilization rate
19	Q_A^G	L/min	Vascular blood water flow rate in hepatic Artery (glucose-related)
20	V_L^G	L	Distribution Volume of Glucose in Liver space
21	V_K^G	L	Distribution Volume of Glucose in Kidney space
22	V_{PV}^G	L	Distribution Volume of Glucose in Peripheral Vascular space
23	V_{PI}	L	Volume of Peripheral Interstitial space
24	T_P^G	min	Trans-capillary diffusion rate for Peripheral tissues (glucose-related)
25	$\Gamma_{\texttt{PGU}}^B$	mmol/min	Baseline rate of Peripheral Glucose Uptake
26	$\beta_{\texttt{PGU}}^0$	#	PGU Insulin effect midpoint
27	$\beta_{\texttt{PGU}}^1$	#	PGU Insulin effect half-amplitude
28	$\beta_{\texttt{PGU}}^2$	#	PGU Insulin effect steepness
29	$\beta_{\texttt{PGU}}^3$	#	PGU Insulin effect shift
30	$\beta_{\texttt{HGP}}^0$	#	HGP gluCagon effect scale

Table 2. Model Parameters

ParID	Parameter	Units	Meaning
31	$\beta^1_{\texttt{HGP}}$	#	HGP gluCagon scale
32	τ_C	min	Inverse of the decay rate for the glucagon-driven intensification of f_2 Hepatic Glucose Uptake suppression
33	$\beta^2_{\texttt{HGP}}$	#	HGP Insulin effect midpoint
34	$\beta^3_{\texttt{HGP}}$	#	HGP Insulin effect half-amplitude
35	$\beta^4_{\texttt{HGP}}$	#	HGP Insulin effect steepness
36	$\beta^5_{\texttt{HGP}}$	#	HGP Insulin effect shift
37	τ_I	min	Inverse of the decay rate for the insulin-driven intensification of $M^I_{\texttt{HGP}}$ and $M^I_{\texttt{HGU}}$ (same for both)
38	$\beta^6_{\texttt{HGP}}$	#	HGP Glucose effect midpoint
39	$\beta^7_{\texttt{HGP}}$	#	HGP Glucose effect half-amplitude
40	$\beta^8_{\texttt{HGP}}$	#	HGP Glucose effect steepness
41	$\beta^9_{\texttt{HGP}}$	#	HGP Glucose effect shift
42	$\Gamma_{\texttt{HGP0}}$	mmol/min	Baseline value of $\Gamma_{\texttt{HGP}}$ at initial time (t_0)
43	$\beta^0_{\texttt{HGU}}$	#	HGU Insulin effect half-amplitude
44	$\beta^1_{\texttt{HGU}}$	#	HGU Insulin effect steepness
45	$\beta^2_{\texttt{HGU}}$	#	HGP Glucose effect midpoint
46	$\beta^3_{\texttt{HGU}}$	#	HGP Glucose effect half-amplitude
47	$\beta^4_{\texttt{HGU}}$	#	HGP Glucose effect steepness
48	$\beta^5_{\texttt{HGU}}$	#	HGP Glucose effect shift
49	$\Gamma_{\texttt{HGU0}}$	mmol/min	Baseline value of $\Gamma_{\texttt{HGU}}$ at initial time (t_0)
50	$\beta^0_{\texttt{KGE}}$	mmol/min	KGE Glucose effect midpoint
51	$\beta^1_{\texttt{KGE}}$	mmol/min	KGE Glucose effect half-amplitude
52	$\beta^2_{\texttt{KGE}}$	/mM	KGE Glucose effect steepness
53	$\beta^3_{\texttt{KGE}}$	mM	KGE Glucose effect shift, point of transition between tanh and linear regime
54	$\beta^4_{\texttt{KGE}}$	mmol/min	KGE Glucose linear effect intercept
55	$\beta^5_{\texttt{KGE}}$	mmol/min/mM	KGE Glucose linear effect slope
56	Q^I_B	L/min	Vascular blood water flow rate for Brain (insulin-related)
57	V^I_B	L	Distribution Volume of Insulin in Brain vascular space
58	V^I_H	L	Distribution Volume of Insulin in Heart/lung vascular space
59	Q^I_L	L/min	Vascular blood water flow rate for Liver (insulin-related)
60	Q^I_K	L/min	Vascular blood water flow rate for Kidney (insulin-related)

Table 2. Model Parameters

ParID	Parameter	Units	Meaning
61	Q_P^I	L/min	Vascular blood water flow rate for Periphery (insulin-related)
62	Q_H^I	L/min	Vascular blood water flow rate for Heart and Lungs (insulin-related)
63	V_J^I	L	Distribution Volume of Insulin in Gut Vascular space
64	Q_J^I	L/min	Vascular blood water flow rate for Gut (insulin-related)
65	V_L^I	L	Distribution Volume of Insulin in Liver Vascular space
66	Q_A^I	L/min	Vascular blood water flow rate in hepatic Artery (insulin-related)
67	$F_L IC$	#	Fraction of insulin Liver clearance
68	$F_K IC$	#	Fraction of insulin Kidney clearance
69	V_K^I	L	Distribution Volume of Insulin in Kidney Vascular space
70	V_{PV}^I	L	Distribution Volume of Insulin in Peripheral Vascular space
71	T_P^I	min	Trans-capillary diffusion rate for Peripheral tissues (insulin-related)
72	$F_P IC$	#	Fraction of insulin Periphery clearance
73	$\beta^1_{\texttt{PIR}}$	#	PIR Glucose effect parameter 1
74	$\beta^2_{\texttt{PIR}}$	mmol/l	PIR Glucose effect parameter 2
75	$\beta^3_{\texttt{PIR}}$	#	PIR Glucose effect parameter 3
76	$\beta^4_{\texttt{PIR}}$	#	PIR Glucose effect parameter 4
77	$\beta^5_{\texttt{PIR}}$	#	Potentiator parameter
78	$K_{\texttt{Rinsu}}$	/min	Rate of labile Insulin secretion
79	$R_{\texttt{insu0}}$	pmol	Labile Insulin for Glucose=0
80	$K_{\texttt{RinsuPotr}}$	pmol/min	Rate of Potentiator effect on labile insulin
81	$K_{\texttt{RinsuPtgt}}$	/min	Rate at which Potentiator reachs its target value
82	$K_{\texttt{pinhPrp}}$	/min	Rate at which Inhibitor reaches the proportional insulin response function
83	M_1	/min	Late rate of increase in insulin secretion
84	M_2	/min	Rate of insulin response
85	I_{PV0}	pM	Baseline value of I_{PV} at initial time (t_0)
86	Γ_{MCC}	pM	Starting value for gluCagon
87	Γ_{MCC}	L/min	Rate constant of gluCagon clearance
88	V_C	L	gluCagon distribution volume
89	$\beta^0_{\texttt{PCR}}$	#	PCR Glucose effect midpoint
90	$\beta^1_{\texttt{PCR}}$	#	PCR Glucose effect half-amplitude

Table 2. Model Parameters

ParID	Parameter	Units	Meaning
91	$\beta^2_{\texttt{PCR}}$	#	PCR Glucose effect steepness
92	$\beta^3_{\texttt{PCR}}$	#	PCR Glucose effect shift
93	$\beta^4_{\texttt{PCR}}$	#	PCR Insulin effect midpoint
94	$\beta^5_{\texttt{PCR}}$	#	PCR Insulin effect half-amplitude
95	$\beta^5_{\texttt{PCR}}$	#	PCR Insulin effect steepness
96	$\beta^5_{\texttt{PCR}}$	#	PCR Insulin effect shift
97	f_{20}	#	Baseline value of f_2 at initial time (t_0)
98	$\Gamma_{\texttt{IVG}}$	mmol/min	Intravenous Glucose Infusion starting value
99	$\Gamma_{\texttt{IVGin}}$	mmol/min	Intravenous Glucose Infusion
100	$Time_{\texttt{IVG}}$	min	Start time of intravenous Glucose Infusion
101	$Time_{\texttt{IVGend}}$	min	End time of intravenous Glucose Infusion
102	$\Gamma_{\texttt{IVI}}$	pmol/min	Intravenous Insulin Infusion starting value
103	$\Gamma_{\texttt{IVIin}}$	pmol/min	Intravenous Insulin Infusion
104	$time_{\texttt{IVI}}$	min	Starting time of Instravenous Insulin Infusion
105	$time_{\texttt{IVIend}}$	min	End time of Instravenous Insulin Infusion
106	I_{H0}	pM	Baseline value of I_H at initial time (t_0)
107	I_{K0}	pM	Baseline value of I_K at initial time (t_0)
108	I_{B0}	pM	Baseline value of I_B at initial time (t_0)
109	I_{G0}	pM	Baseline value of I_G at initial time (t_0)
110	I_{PI0}	pM	Baseline value of I_{PI} at initial time (t_0)
111	I_{L0}	pM	Baseline value of I_L at initial time (t_0)
112	$\Gamma_{\texttt{PIR0}}$	pmol/min	Baseline value of $\Gamma_{\texttt{PIR}}$ at initial time (t_0)
113	$\Gamma_{\texttt{PIC0}}$	pmol/min	Baseline value of $\Gamma_{\texttt{PIC}}$ at initial time (t_0)
114	$P_{\texttt{prp0}}$	#	Baseline value of $P_{\texttt{prp}}$ at initial time (t_0)
115	$P_{\texttt{tgt0}}$	#	Baseline value of $P_{\texttt{tgt}}$ at initial time (t_0)
116	$P_{\texttt{inh0}}$	#	Baseline value of $P_{\texttt{inh}}$ at initial time (t_0)
117	$P_{\texttt{otn0}}$	#	Baseline value of $P_{\texttt{otn}}$ at initial time (t_0)
118	$InitialRinsu_0$	pmol	Baseline value of $Rinsu$ at initial time (t_0)
119	S_{ecr0}	pmol/min	Baseline value of S_{ecr} at initial time (t_0)
120	G_{PV0}	mM	Baseline value of G_{PV} at initial time (t_0)
121	G_{K0}	mM	Baseline value of G_K at initial time (t_0)
122	G_{BV0}	mM	Baseline value of G_{BV} at initial time (t_0)
123	G_{J0}	mM	Baseline value of G_J at initial time (t_0)

Table 2. Model Parameters

ParID	Parameter	Units	Meaning
124	G_{L0}	mM	Baseline value of G_L at initial time (t_0)
125	G_{BI0}	mM	Baseline value of G_{BI} at initial time (t_0)
126	G_{PI0}	mM	Baseline value of G_{PI} at initial time (t_0)
127	$M_{\mathtt{PGU0}}$	#	Baseline value of $M_{\mathtt{PGU}}$ at initial time (t_0)
128	$M^{C}_{\mathtt{HGP0}}$	#	Baseline value of $M^{C}_{\mathtt{HGP}}$ at initial time (t_0)
129	$M^{C0}_{\mathtt{HGP0}}$	#	Baseline value of $M^{C0}_{\mathtt{HGP}}$ at initial time (t_0)
130	$M^{I}_{\mathtt{HGP0}}$	#	Baseline value of $M^{I}_{\mathtt{HGP}}$ at initial time (t_0)
131	$M^{I}_{\mathtt{HGPinf0}}$	#	Steady state of MIHGP
132	$M^{G}_{\mathtt{HGP0}}$	#	Baseline value of $M^{G}_{\mathtt{HGP}}$ at initial time (t_0)
133	$M^{I}_{\mathtt{HGU0}}$	#	Baseline value of $M^{I}_{\mathtt{HGU}}$ at initial time (t_0)
134	$M^{I}_{\mathtt{HGUinf0}}$	#	Steady state of $M^{I}_{\mathtt{HGU}}$
135	$M^{G}_{\mathtt{HGU0}}$	#	Baseline value of $M^{G}_{\mathtt{HGU}}$ at initial time (t_0)
136	$\Gamma_{\mathtt{KGE0}}$	mmol/min	Baseline value of $\Gamma_{\mathtt{KGE}}$ at initial time (t_0)
137	$\Gamma_{\mathtt{LIC0}}$	pmol/min	Baseline value of $\Gamma_{\mathtt{LIC}}$ at initial time (t_0)
138	$\Gamma_{\mathtt{KIC0}}$	pmol/min	Baseline value of $\Gamma_{\mathtt{KIC}}$ at initial time (t_0)
139	$M^{G}_{\mathtt{PCR0}}$	#	Baseline value of $M^{G}_{\mathtt{PCR}}$ at initial time (t_0)
140	$M^{I}_{\mathtt{PCR0}}$	#	Baseline value of $M^{I}_{\mathtt{PCR}}$ at initial time (t_0)
141	$\Gamma_{\mathtt{PCC0}}$	pM	Baseline value of $\Gamma_{\mathtt{PCC}}$ at initial time (t_0)
142	$\Gamma^{B}_{\mathtt{PCR0}}$	pM	Baseline value of $\Gamma^{B}_{\mathtt{PCR}}$ at initial time (t_0)

Table 3. Model Parameter Configurations

ParID	Parameter	Units	Intravenous Glucose Tolerance Test: Variable Dose 0.05g/kg	Intravenous Glucose Tolerance Test: Variable Dose 0.2g/kg	Intravenous Glucose Tolerance Test: Variable Dose 0.75g/kg	Intravenous Insulin Tolerance Test 0.04U/kg	Continuous Intravenous Insulin Infusion 0.4mU/kg/min
1	t_0	min	-10	-10	-10	-30	-20
2	t_{end}	min	60	60	60	120	150
3	t_Δ	min	0.1	0.1	0.1	0.1	0.1
4	Q_B^G	L/min	0.59	0.59	0.59	0.59	0.59
5	V_{BV}^G	L	0.35	0.35	0.35	0.35	0.35
6	V_{BI}	L	0.45	0.45	0.45	0.45	0.45
7	T_B	min	2.1	2.1	2.1	2.1	2.1
8	G_{H0}	mM	5.12889	5.24	4.90667	5.73333	5.40667
9	$\Gamma_{\texttt{BGU}}$	mmol/min	0.388889	0.388889	0.388889	0.388889	0.388889
10	Q_L^G	L/min	1.26	1.26	1.26	1.26	1.26
11	Q_K^G	L/min	1.01	1.01	1.01	1.01	1.01
12	Q_P^G	L/min	1.51	1.51	1.51	1.51	1.51
13	Q_H^G	L/min	4.37	4.37	4.37	4.37	4.37
14	$\Gamma_{\texttt{RBCU}}$	mmol/min	0.0555556	0.0555556	0.0555556	0.0555556	0.0555556
15	V_H^G	L	1.38	1.38	1.38	1.38	1.38
16	Q_J^G	L/min	1.01	1.01	1.01	1.01	1.01
17	V_J^G	L	1.12	1.12	1.12	1.12	1.12
18	$\Gamma_{\texttt{JGU}}$	mmol/min	0.111111	0.111111	0.111111	0.111111	0.111111
19	Q_A^G	L/min	0.25	0.25	0.25	0.25	0.25
20	V_L^G	L	2.51	2.51	2.51	2.51	2.51
21	V_K^G	L	0.66	0.66	0.66	0.66	0.66
22	V_{PV}^G	L	1.04	1.04	1.04	1.04	1.04
23	V_{PI}	L	6.74	6.74	6.74	6.74	6.74
24	T_P^G	min	5	5	5	5	5
25	$\Gamma_{\texttt{PGU}}^B$	mmol/min	0.194444	0.194444	0.194444	0.194444	0.194444
26	$\beta_{\texttt{PGU}}^0$	#	7.03	7.03	7.03	7.03	7.03
27	$\beta_{\texttt{PGU}}^1$	#	6.52	6.52	6.52	6.52	6.52
28	$\beta_{\texttt{PGU}}^2$	#	0.338	0.338	0.338	0.338	0.338

Table 3. Model Parameter Configurations

ParID	Parameter	Units	Intravenous Glucose Tolerance Test: Variable Dose 0.05g/kg	Intravenous Glucose Tolerance Test: Variable Dose 0.2g/kg	Intravenous Glucose Tolerance Test: Variable Dose 0.75g/kg	Intravenous Insulin Tolerance Test 0.04U/kg	Continuous Intravenous Insulin Infusion 0.4mU/kg/min
29	$\beta^3_{\mathtt{PGU}}$	#	5.82	5.82	5.82	5.82	5.82
30	$\beta^0_{\mathtt{HGP}}$	#	2.7	2.7	2.7	2.7	2.7
31	$\beta^1_{\mathtt{HGP}}$	#	0.388852	0.388852	0.388852	0.388852	0.388852
32	τ_C	min	65	65	65	65	65
33	$\beta^2_{\mathtt{HGP}}$	#	1.21	1.21	1.21	1.21	1.21
34	$\beta^3_{\mathtt{HGP}}$	#	1.14	1.14	1.14	1.14	1.14
35	$\beta^4_{\mathtt{HGP}}$	#	1.66	1.66	1.66	1.66	1.66
36	$\beta^5_{\mathtt{HGP}}$	#	0.887748	0.887748	0.887748	0.887748	0.887748
37	τ_I	min	25	25	25	25	25
38	$\beta^6_{\mathtt{HGP}}$	#	1.42	1.42	1.42	1.42	1.42
39	$\beta^7_{\mathtt{HGP}}$	#	1.41	1.41	1.41	1.41	1.41
40	$\beta^8_{\mathtt{HGP}}$	#	0.62	0.62	0.62	0.62	0.62
41	$\beta^9_{\mathtt{HGP}}$	#	0.504543	0.504543	0.504543	0.504543	0.504543
42	$\Gamma_{\mathtt{HGP0}}$	mmol/min	0.861111	0.861111	0.861111	0.861111	0.861111
43	$\beta^0_{\mathtt{HGU}}$	#	2	2	2	2	2
44	$\beta^1_{\mathtt{HGU}}$	#	0.549306	0.549306	0.549306	0.549306	0.549306
45	$\beta^2_{\mathtt{HGU}}$	#	5.66	5.66	5.66	5.66	5.66
46	$\beta^3_{\mathtt{HGU}}$	#	5.66	5.66	5.66	5.66	5.66
47	$\beta^4_{\mathtt{HGU}}$	#	2.44	2.44	2.44	2.44	2.44
48	$\beta^5_{\mathtt{HGU}}$	#	1.4783	1.4783	1.4783	1.4783	1.4783
49	$\Gamma_{\mathtt{HGU0}}$	mmol/min	0.111111	0.111111	0.111111	0.111111	0.111111
50	$\beta^0_{\mathtt{KGE}}$	mmol/min	0.394444	0.394444	0.394444	0.394444	0.394444
51	$\beta^1_{\mathtt{KGE}}$	mmol/min	0.394444	0.394444	0.394444	0.394444	0.394444
52	$\beta^2_{\mathtt{KGE}}$	/mM	0.198	0.198	0.198	0.198	0.198
53	$\beta^3_{\mathtt{KGE}}$	mM	25.5556	25.5556	25.5556	25.5556	25.5556
54	$\beta^4_{\mathtt{KGE}}$	mmol/min	1.834	1.834	1.834	1.834	1.834
55	$\beta^5_{\mathtt{KGE}}$	mmol/min/mM	0.0872	0.0872	0.0872	0.0872	0.0872
56	Q^I_B	L/min	0.45	0.45	0.45	0.45	0.45
57	V^I_B	L	0.26	0.26	0.26	0.26	0.26

Table 3. Model Parameter Configurations

ParID	Parameter	Units	Intravenous Glucose Tolerance Test: Variable Dose 0.05g/kg	Intravenous Glucose Tolerance Test: Variable Dose 0.2g/kg	Intravenous Glucose Tolerance Test: Variable Dose 0.75g/kg	Intravenous Insulin Tolerance Test 0.04U/kg	Continuous Intravenous Insulin Infusion 0.4mU/kg/min
58	V_H^I	L	0.99	0.99	0.99	0.99	0.99
59	Q_L^I	L/min	0.9	0.9	0.9	0.9	0.9
60	Q_K^I	L/min	0.72	0.72	0.72	0.72	0.72
61	Q_P^I	L/min	1.05	1.05	1.05	1.05	1.05
62	Q_H^I	L/min	3.12	3.12	3.12	3.12	3.12
63	V_J^I	L	0.94	0.94	0.94	0.94	0.94
64	Q_J^I	L/min	0.72	0.72	0.72	0.72	0.72
65	V_L^I	L	1.14	1.14	1.14	1.14	1.14
66	Q_A^I	L/min	0.18	0.18	0.18	0.18	0.18
67	$F_L IC$	#	0.4	0.4	0.4	0.4	0.4
68	$F_K IC$	#	0.3	0.3	0.3	0.3	0.3
69	V_K^I	L	0.51	0.51	0.51	0.51	0.51
70	V_{PV}^I	L	0.74	0.74	0.74	0.74	0.74
71	T_P^I	min	20	20	20	20	20
72	$F_P IC$	#	0.15	0.15	0.15	0.15	0.15
73	$\beta_{\texttt{PIR}}^1$	#	3.27	3.27	3.27	3.27	3.27
74	$\beta_{\texttt{PIR}}^2$	mmol/l	7.33333	7.33333	7.33333	7.33333	7.33333
75	$\beta_{\texttt{PIR}}^3$	#	2.879	2.879	2.879	2.879	2.879
76	$\beta_{\texttt{PIR}}^4$	#	3.02	3.02	3.02	3.02	3.02
77	$\beta_{\texttt{PIR}}^5$	#	1.11	1.11	1.11	1.11	1.11
78	$K_{\texttt{Rinsu}}$	/min	0.00794	0.00794	0.00794	0.00794	0.00794
79	$R_{\texttt{insu0}}$	pmol	44310	44310	44310	44310	44310
80	$K_{\texttt{RinsuPotr}}$	pmol/min	4025	4025	4025	4025	4025
81	$K_{\texttt{RinsuPtgt}}$	/min	0.0482	0.0482	0.0482	0.0482	0.0482
82	$K_{\texttt{pinhPrp}}$	/min	0.931	0.931	0.931	0.931	0.931
83	M_1	/min	0.00747	0.00747	0.00747	0.00747	0.00747
84	M_2	/min	0.0958	0.0958	0.0958	0.0958	0.0958
85	I_{PV0}	pM	126	133	147	91	56
86	Γ_{MCC}	pM	11.48	11.48	11.48	34.44	31.57

Table 3. Model Parameter Configurations

ParID	Parameter	Units	Intravenous Glucose Tolerance Test: Variable Dose 0.05g/kg	Intravenous Glucose Tolerance Test: Variable Dose 0.2g/kg	Intravenous Glucose Tolerance Test: Variable Dose 0.75g/kg	Intravenous Insulin Tolerance Test 0.04U/kg	Continuous Intravenous Insulin Infusion 0.4mU/kg/min
87	Γ_{MCC}	L/min	0.91	0.91	0.91	0.91	0.91
88	V_C	L	11.31	11.31	11.31	11.31	11.31
89	$\beta^0_{\texttt{PCR}}$	#	2.93	2.93	2.93	2.93	2.93
90	$\beta^1_{\texttt{PCR}}$	#	2.1	2.1	2.1	2.1	2.1
91	$\beta^2_{\texttt{PCR}}$	#	4.18	4.18	4.18	4.18	4.18
92	$\beta^3_{\texttt{PCR}}$	#	0.621325	0.621325	0.621325	0.621325	0.621325
93	$\beta^4_{\texttt{PCR}}$	#	1.31	1.31	1.31	1.31	1.31
94	$\beta^5_{\texttt{PCR}}$	#	0.61	0.61	0.61	0.61	0.61
95	$\beta^5_{\texttt{PCR}}$	#	1.06	1.06	1.06	1.06	1.06
96	$\beta^5_{\texttt{PCR}}$	#	0.471419	0.471419	0.471419	0.471419	0.471419
97	f_{20}	#	0	0	0	0	0
98	$\Gamma_{\texttt{IVG}}$	mmol/min	0	0	0	0	0
99	$\Gamma_{\texttt{IVGin}}$	mmol/min	6.481	25.926	97.222	0	0
100	$Time_{\texttt{IVG}}$	min	-3	-3	-3	0	0
101	$Time_{\texttt{IVGend}}$	min	0	0	0	0	0
102	$\Gamma_{\texttt{IVI}}$	pmol/min	0	0	0	0	0
103	$\Gamma_{\texttt{IVIin}}$	pmol/min	0	0	0	6533.33	196
104	$time_{\texttt{IVI}}$	min	0	0	0	0	0
105	$time_{\texttt{IVIend}}$	min	0	0	0	3	150
106	I_{H0}	pM	148.235	156.471	172.941	107.059	65.8824
107	I_{K0}	pM	103.765	109.529	121.059	74.9412	46.1176
108	I_{B0}	pM	148.235	156.471	172.941	107.059	65.8824
109	I_{G0}	pM	148.235	156.471	172.941	107.059	65.8824
110	I_{PI0}	pM	56.7209	59.8721	66.1744	40.9651	25.2093
111	I_{L0}	pM	209.753	221.406	244.712	151.488	93.2235
112	$\Gamma_{\texttt{PIR0}}$	pmol/min	181.218	191.285	211.421	130.879	80.5412
113	$\Gamma_{\texttt{PIC0}}$	pmol/min	23.3471	24.6441	27.2382	16.8618	10.3765
114	$P_{\texttt{prp0}}$	#	0.194841	0.203904	0.176821	0.244086	0.217518
115	$P_{\texttt{tgt0}}$	#	0.16276	0.171184	0.146138	0.209013	0.183916

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ParID	Parameter	Units	Intravenous Glucose Tolerance Test: Variable Dose 0.05g/kg	Intravenous Glucose Tolerance Test: Variable Dose 0.2g/kg	Intravenous Glucose Tolerance Test: Variable Dose 0.75g/kg	Intravenous Insulin Tolerance Test 0.04U/kg	Continuous Intravenous Insulin Infusion 0.4mU/kg/min
116	$P_{\mathtt{inh0}}$	#	0.194841	0.203904	0.176821	0.244086	0.217518
117	$P_{\mathtt{otn0}}$	#	0.158572	0.158572	0.158572	0.158572	0.158572
118	$InitialRinsu_0$	pmol	108507	108507	108507	108507	108507
119	S_{ecr0}	pmol/min	131.924	138.753	118.452	169.415	149.072
120	G_{PV0}	mM	5.00012	5.11123	4.7779	5.60456	5.2779
121	G_{K0}	mM	5.12889	5.24	4.90667	5.73333	5.40667
122	G_{BV0}	mM	4.46976	4.58087	4.24753	5.0742	4.74753
123	G_{J0}	mM	5.01888	5.12999	4.79666	5.62332	5.29666
124	G_{L0}	mM	5.63594	5.74705	5.41372	6.24039	5.91372
125	G_{BI0}	mM	2.65494	2.76605	2.43272	3.25938	2.93272
126	G_{PI0}	mM	4.85587	4.96698	4.63365	5.46032	5.13365
127	$M_{\mathtt{PGU0}}$	#	0.992859	0.992859	0.992859	0.992859	0.992859
128	$M^{C}_{\mathtt{HGP0}}$	#	1	1	1	1	1
129	$M^{C0}_{\mathtt{HGP0}}$	#	1	1	1	1	1
130	$M^{I}_{\mathtt{HGP0}}$	#	1	1	1	1	1
131	$M^{I}_{\mathtt{HGPinf0}}$	#	1	1	1	1	1
132	$M^{G}_{\mathtt{HGP0}}$	#	1	1	1	1	1
133	$M^{I}_{\mathtt{HGU0}}$	#	1	1	1	1	1
134	$M^{I}_{\mathtt{HGUinf0}}$	#	1	1	1	1	1
135	$M^{G}_{\mathtt{HGU0}}$	#	1	1	1	1	1
136	$\Gamma_{\mathtt{KGE0}}$	mmol/min	0.000242043	0.000252927	0.000221659	0.000307474	0.000270177
137	$\Gamma_{\mathtt{LIC0}}$	pmol/min	105.716	108.681	114.611	90.8929	76.0694
138	$\Gamma_{\mathtt{KIC0}}$	pmol/min	32.0188	33.7976	37.3553	23.1247	14.2306
139	$M^{G}_{\mathtt{PCR0}}$	#	1	1	1	1	1
140	$M^{I}_{\mathtt{PCR0}}$	#	1	1	1	1	1
141	$\Gamma_{\mathtt{PCC0}}$	pM	10.4468	10.4468	10.4468	31.3404	28.7287
142	$\Gamma^{B}_{\mathtt{PCR0}}$	pM	10.4468	10.4468	10.4468	10.4468	10.4468