BioSorSimo 01.01.45LaTeX Companion

Marcello Pompa, Simona Panunzi, Andrea De Gaetano

CNR-IASI BioMatLab (National Research Council of Italy - Institute of Systems Analysis and Computer Science - Biomathematics Laboratory), UCSC Largo A. Gemelli 8, 00168 Rome, Italy

“BioSorSimo ”is Sorensen model + Simo model for OGTT simulations

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

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

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

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

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

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

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 + Roga / VolGJ
```

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

[Variable 6] ————————————————————————————————

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

Glucose concentration in Liver space

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

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

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

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:

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

```
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] ————————————————————————————————

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

Insulin suppression of Hepatic Glucose Production

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

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

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

[Variable 16] ————————————————————————————————

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

Steady State Insulin suppression of Hepatic Glucose Production

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

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

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

[Variable 17] ————————————————————————————————

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

gluCagon contribution to Hepatic Glucose Production

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

```
Definition: MCHGP =
MC0HGP - Fun2
```

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

[Variable 18] ————————————————————————————————————

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

gluCagon contribution to Hepatic Glucose Production at baseline

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

```
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

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

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

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

[Variable 20] ————————————————————————————————————

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

Glucose contribution to Hepatic Glucose Production

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

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

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

[Variable 21] ————————————————————————————————

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

Hepatic Glucose Uptake

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

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

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

[Variable 22] ————————————————————————————————

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

Insulin acceleration of Hepatic Glucose Uptake

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

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

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

[Variable 23] ————————————————————————————————

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

Steady State Insulin acceleration of Hepatic Glucose Uptake

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

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

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

[Variable 24] ————————————————————————————————

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

Glucose acceleration of Hepatic Glucose Uptake

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

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

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

[Variable 25] ————————————————————————————————

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

Kidney Glucose Excretion

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

```
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) / 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

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

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

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

```
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

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

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] ——————————————————————————————————————

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

Liver Insulin Clearance

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

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

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

[Variable 37] ——————————————————————————————————————

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

Kidney Insulin Clearance

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

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

```
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

$$S_{ecr} = [M_1 P_{tgt} + M_2(P_{prp} - P_{inh})^+]R_{insu}, \quad S_{ecr}(0) = S_{ecr0}$$

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

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

[Variable 44] ————————————————————————————————

S_{ecr}^{N} **Normalized secretion rate** (#)

Normalized Insulin secretion rate

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

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

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

[Variable 45] ————————————————————————————————

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

Potentiator glucose proportional factor

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

```
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

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

```
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] ————————————————————————————————————

S **Glucose into the Stomach (mmol)**

Glucose into the stomach

$$\frac{dS}{dt} = -k_{\mathtt{js}}S + D\,\delta(t), S(0) = S_0 \tag{2}$$

```
Definition: d Sto /dt =
- kjs * Sto
```

```
Diracs:
if  (Time==0)     Sto = Sto + Dose  end
```

check correct programming of Diracs in `BioSorSimoComputeDiracs.m` *and* `Gemini.autogenerated.cpp`

```
Initial value: Sto(t0) =
Sto0
```

[Variable 54] ————————————————————————————————————

J **Glucose into the Jejunum (mmol)**

Glucose into the Jejunum

$$\frac{dJ}{dt} = k_{\mathtt{js}}S - k_{\mathtt{gj}}J - k_{\mathtt{rj}}J, J(0) = J_0 \tag{3}$$

```
Definition: d Jej /dt =
kjs * Sto - kgj  *Jej - krj * Jej
```

```
Initial value: Jej(t0) =
Jej0
```

[Variable 55] ——————————————————————————————

R **Glucose into the Delay compartment (mmol)**

Glucose into the Delay compartment

$$\frac{dR}{dt} = -k_{\mathtt{lr}} * R + k_{\mathtt{rj}} J, R(0) = R_0 \tag{4}$$

```
Definition: d Rit /dt =
- klr * Rit + krj * Jej
```

```
Initial value: Rit(t0) =
Rit0
```

[Variable 56] ——————————————————————————————

L **Glucose into the Ileum (mmol)**

Glucose into the ileum

$$\frac{dL}{dt} = k_{\mathtt{lr}} R - k_{\mathtt{gl}} L, L(0) = L_0 \tag{5}$$

```
Definition: d Ile /dt =
klr * Rit - kgl * Ile
```

```
Initial value: Ile(t0) =
Ile0
```

[Variable 57] ——————————————————————————————

$R_{\mathtt{oga}}$ **Glucose Gut absorption rate (mmol/min)**

Gut oral glucose absorption rate

$$R_{\mathtt{oga}} = k_{\mathtt{gj}} J + k_{\mathtt{gl}} I, R_{oga}(0) = R_{oga0} \tag{6}$$

```
Definition: Roga =
frac * (kgj * Jej + kgl * Ile)
```

```
Initial value: Roga(t0) =
Roga0
```

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**
(300 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] ————————————————————————————————

$\Gamma_{\mathtt{BGU}}$ **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] ————————————————————————————————

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

[Parameter 28] ————————————————————————————————

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

[Parameter 29] ————————————————————————————————

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

[Parameter 30] ————————————————————————————————

$\beta^{1}_{\mathtt{HGP}}$ **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] ————————————————————————————————

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

[Parameter 33] ————————————————————————————————

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

[Parameter 34] ————————————————————————————————————

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

[Parameter 35] ————————————————————————————————————

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

[Parameter 36] ————————————————————————————————————

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

[Parameter 37] ————————————————————————————————————

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

[Parameter 38] ————————————————————————————————————

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

[Parameter 39] ————————————————————————————————————

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

[Parameter 40] ————————————————————————————————————

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

[Parameter 41] ————————————————————————————————

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

[Parameter 42] ————————————————————————————————

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

[Parameter 43] ————————————————————————————————

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

[Parameter 44] ————————————————————————————————

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

[Parameter 45] ————————————————————————————————

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

[Parameter 46] ————————————————————————————————

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

[Parameter 47] ————————————————————————————————

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

[Parameter 48] ——————————————————————————————

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

[Parameter 49] ——————————————————————————————

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

[Parameter 50] ——————————————————————————————

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

[Parameter 51] ——————————————————————————————

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

[Parameter 52] ——————————————————————————————

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

[Parameter 53] ——————————————————————————————

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

[Parameter 54] ——————————————————————————————

$\beta^5_{\mathtt{KGE}}$ **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_{LIC} **Fraction of insulin Liver clearance**
(0.4 #)

[Parameter 67] ——————————————————————————————

F_{KIC} **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_{PIC} **Fraction of insulin Periphery clearance**
(0.15 #)

[Parameter 72] ——————————————————————————————————

$\beta_{\mathtt{PIR}}^{1}$ **PIR Glucose effect parameter 1**
(6.51625 #)

[Parameter 73] ——————————————————————————————————

$\beta_{\mathtt{PIR}}^{2}$ **PIR Glucose effect parameter 2**
(4.13532 mmol/l)

[Parameter 74] ——————————————————————————————————

$\beta_{\mathtt{PIR}}^{3}$ **PIR Glucose effect parameter 3**
(4.34599 #)

[Parameter 75] ——————————————————————————————————

$\beta_{\mathtt{PIR}}^{4}$ **PIR Glucose effect parameter 4**
(5.57083 #)

[Parameter 76] ————————————————————————————————————

$\beta^5_{\mathtt{PIR}}$ **Potentiator parameter**
(2.28432 #)

[Parameter 77] ————————————————————————————————————

$K_{\mathtt{Rinsu}}$ **Rate of labile Insulin secretion**
(0.0137576 /min)

[Parameter 78] ————————————————————————————————————

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

[Parameter 79] ————————————————————————————————————

$K_{\mathtt{RinsuPotr}}$ **Rate of Potentiator effect on labile insulin**
(3300.71 pmol/min)

[Parameter 80] ————————————————————————————————————

$K_{\mathtt{RinsuPtgt}}$ **Rate at which Potentiator reachs its target value**
(0.0169775 /min)

[Parameter 81] ————————————————————————————————————

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

[Parameter 82] ————————————————————————————————————

M_1 **Late rate of increase in insulin secretion**
(0.000241686 /min)

[Parameter 83] ——————————————————————————————

M_2 **Rate of insulin response**
(**0.304906** **/min**)

[Parameter 84] ——————————————————————————————

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

[Parameter 85] ——————————————————————————————

C_0 **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] ————————————————————————————

D **Glucose dose for the oral challenge**
(555.56 mmol)

[Parameter 98] ————————————————————————————

S_0 **Baseline value of S at initial time (t_0)**
(0 mmol)

[Parameter 99] ————————————————————————————

$k_{\mathtt{js}}$ **Glucose transfer rate from Stomach to Jejunum compartment**
(0.0365887 1/min)

[Parameter 100] ————————————————————————————

J_0 **Baseline value of J at initial time (t_0)**
(0 mmol)

[Parameter 101] ————————————————————————————

$k_{\mathtt{gj}}$ **Glucose transfer rate from Jejunum to Gut compartment**
(0.0245626 1/min)

[Parameter 102] ————————————————————————————

$k_{\mathtt{rj}}$ **Glucose transfer rate from Jejunum to Delay compartment**
(0.0277149 1/min)

[Parameter 103] ————————————————————————————

Rit_0 **Baseline value of R at initial time (t_0)**
(0 mmol)

[Parameter 104] ——————————————————————————————————

$k_{\mathtt{lr}}$ **Glucose transfer rate from Delay to Ileum compartment**
(**0.0248468** **1/min**)

[Parameter 105] ——————————————————————————————————

Ile_0 **Baseline value of L at initial time (t_0)**
(**0** **mmol**)

[Parameter 106] ——————————————————————————————————

$k_{\mathtt{gl}}$ **Glucose transfer rate from Ileum to Gut compartment**
(**0.0261629** **1/min**)

[Parameter 107] ——————————————————————————————————

f **Fraction of Glucose absorbed**
(**1** **#**)

[Parameter 108] ——————————————————————————————————

$R_{\mathtt{oga0}}$ **Baseline value of R_{oga} at initial time (t_0)**
(**0** **mmol/min**)

[Parameter 109] ——————————————————————————————————

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 110] ————————————————————————————————

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 111] ————————————————————————————————

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 112] ————————————————————————————————

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 113] ————————————————————————————————

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 114] ————————————————————————————————

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 115] ————————————————————————————————

$\Gamma_{\mathtt{PIR0}}$ **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 116] ————————————————————————————————

$\Gamma_{\mathtt{PIC0}}$ **Baseline value of $\Gamma_{\mathtt{PIC}}$ 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 117] ————————————————————————————————————

$P_{\mathtt{prp0}}$ **Baseline value of $P_{\mathtt{prp}}$ at initial time (t_0)**
(**0.833373** #)

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 118] ————————————————————————————————————

$P_{\mathtt{tgt0}}$ **Baseline value of $P_{\mathtt{tgt}}$ at initial time (t_0)**
(**0.659434** #)

Baseline value for P_{tgt} at time 0:

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

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

[Parameter 119] ————————————————————————————————————

$P_{\mathtt{inh0}}$ **Baseline value of $P_{\mathtt{inh}}$ at initial time (t_0)**
(**0.833373** #)

Baseline value for P_{inh} at time 0:

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

```
Definition: Pinh0 =
Pprp0
```

[Parameter 120] ————————————————————————————————————

$P_{\mathtt{otn0}}$ **Baseline value of $P_{\mathtt{otn}}$ at initial time (t_0)**
(**0.659434** #)

Baseline value for P_{otn} at time 0:

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

```
Definition: Potn0 =
Ptgt0
```

[Parameter 121] ————————————————————————————————————

$InitialRinsu_0$ **Baseline value of $Rinsu$ at initial time (t_0)**
(200202 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 122] ————————————————————————————————————

S_{ecr0} **Baseline value of S_{ecr} at initial time (t_0)**
(31.9073 pmol/min)

Baseline value for S_{ecr} at time 0:

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

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

[Parameter 123] ————————————————————————————————————

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 124] ————————————————————————————————————

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 125] ————————————————————————————————————

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 126] ————————————————————————————————————

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 127] ————————————————————————————————————

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 128] ————————————————————————————————

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 129] ————————————————————————————————

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 130] ————————————————————————————————

$M^I_{\mathtt{PGU0}}$ **Baseline value of $M^I_{\mathtt{PGU}}$ 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 131] ————————————————————————————————————

$M^C_{\mathtt{HGP0}}$ **Baseline value of $M^C_{\mathtt{HGP}}$ 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 132] ————————————————————————————————————

$M^{C0}_{\mathtt{HGP0}}$ **Baseline value of $M^{C0}_{\mathtt{HGP}}$ 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 133] ————————————————————————————————————

$M^I_{\mathtt{HGP0}}$ **Baseline value of $M^I_{\mathtt{HGP}}$ 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 134] ————————————————————————————————————

$M^I_{\mathtt{HGPinf0}}$ **Steady state of MIHGP**

(1 #)

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

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

```
Definition: MIHGPinf0 =
MIHGP0
```

[Parameter 135] ————————————————————————————————

$M^{G}_{\mathtt{HGP0}}$ **Baseline value of $M^{G}_{\mathtt{HGP}}$ 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 136] ————————————————————————————————

$M^{I}_{\mathtt{HGU0}}$ **Baseline value of $M^{I}_{\mathtt{HGU}}$ 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 137] ————————————————————————————————

$M^{I}_{\mathtt{HGUinf0}}$ **Steady state of $M^{I}_{\mathtt{HGU}}$**
(1 #)

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

$$M^{I}_{HGUinf0} = M^{I}_{HGU0}$$

```
Definition: MIHGUinf0 =
MIHGU0
```

[Parameter 138] ———————————————————————————————

$M^G_{\mathtt{HGU0}}$ **Baseline value of $M^G_{\mathtt{HGU}}$ 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 139] ———————————————————————————————

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

Baseline value for Γ_{KGE} at time 0:

$$\Gamma_{KGE0} = \begin{cases} \beta^0_{KGE} + \beta^1_{KGE} tanh[\beta^2_{KGE}(G_{K0} - \beta^3_{KGE})] & 0 \leq G_K < \beta^3_{KGE} \\ -\beta^4_{KGE} + \beta^5_{KGE} G_{K0} & G_{K0} \geq \beta^3_{KGE} \end{cases} \quad (7)$$

(8)

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

[Parameter 140] ———————————————————————————————

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

Baseline value for Γ_{LIC} at time 0:

$$\Gamma_{LIC0} = F_{LIC}(Q^I_A I_{H0} + Q^I_J I_{J0} + \Gamma BPIR)$$

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

[Parameter 141] ———————————————————————————————

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

Baseline value for Γ_{KIC} at time 0:

$$\Gamma_{KIC0} = F_{KIC} Q^I_K I_{H0}$$

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

[Parameter 142] ————————————————————————————————

$M^G_{\mathtt{PCR0}}$ **Baseline value of $M^G_{\mathtt{PCR}}$ 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 143] ————————————————————————————————

$M^I_{\mathtt{PCR0}}$ **Baseline value of $M^I_{\mathtt{PCR}}$ 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 144] ————————————————————————————————

$\Gamma_{\mathtt{PCC0}}$ **Baseline value of $\Gamma_{\mathtt{PCC}}$ 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 145] ————————————————————————————————————

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

Baseline value for Γ_{BPCR} at time 0:

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

```
Definition: GammaBPCR =
GammaPCC0
```

Dynamic constraints on the Parameters (the updated MoSpec rules)

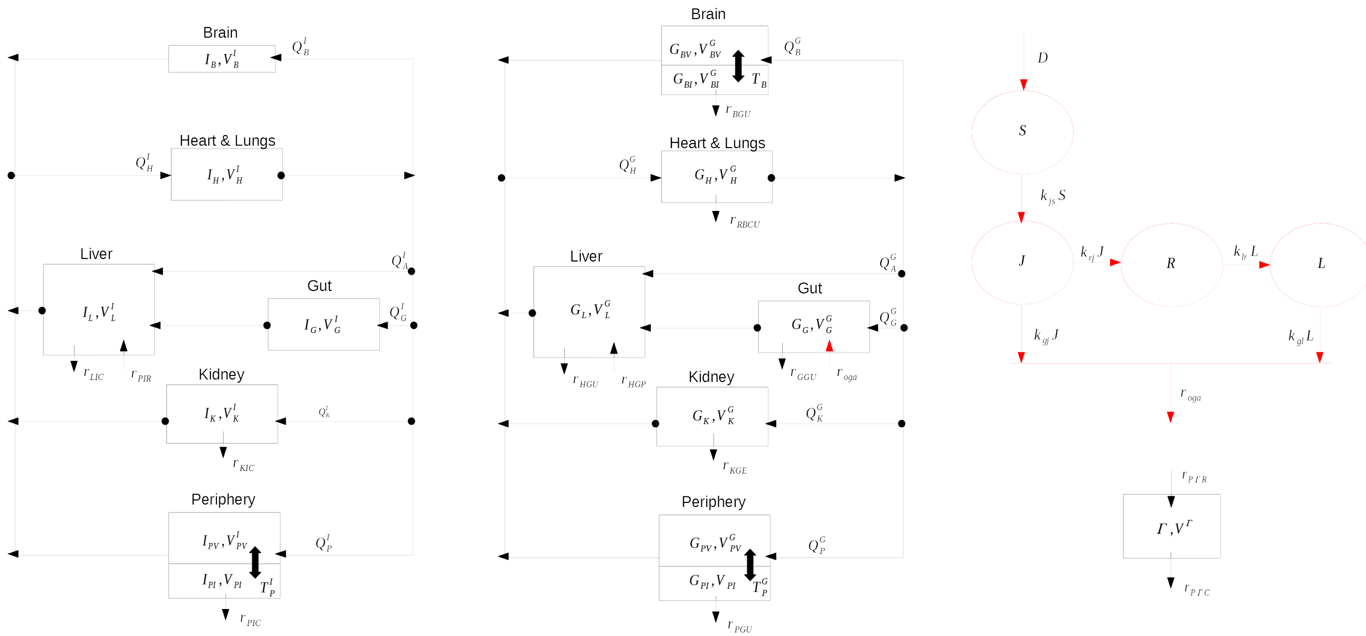

Figure 1. Block Diagram

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	$M_{\texttt{HGP}}^I$	#	Insulin Action on glucose uptake
14	$\Gamma_{\texttt{HGP}}$	mmol/min	Hepatic Glucose Production
15	$M_{\texttt{HGP}}^I$	#	Insulin suppression of Hepatic Glucose Production
16	$M_{\texttt{HGPinf}}^I$	#	Steady State Insulin suppression of Hepatic Glucose Production
17	$M_{\texttt{HGP}}^C$	#	gluCagon contribution to Hepatic Glucose Production
18	$M_{\texttt{HGP}}^{C0}$	#	gluCagon contribution to Hepatic Glucose Production at baseline
19	f_2	#	Damping of gluCagon contribution to Hepatic Glucose Production
20	$M_{\texttt{HGP}}^G$	#	Glucose contribution to Hepatic Glucose Production
21	$\Gamma_{\texttt{HGU}}$	mmol/min	Hepatic Glucose Uptake
22	$M_{\texttt{HGU}}^I$	#	Insulin acceleration of Hepatic Glucose Uptake
23	$M_{\texttt{HGUinf}}^I$	#	Steady State Insulin acceleration of Hepatic Glucose Uptake
24	$M_{\texttt{HGU}}^G$	#	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	$\Gamma_{\mathtt{LIC}}$	pmol/min	Liver Insulin Clearance
37	$\Gamma_{\mathtt{KIC}}$	pmol/min	Kidney Insulin Clearance
38	$\Gamma_{\mathtt{PIC_{NC}}}$	pmol/min	Peripheral Insulin Clearance
39	$\Gamma_{\mathtt{SerPIR}}$	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	$\Gamma_{\mathtt{PCC}}$	pmol/min	Peripheral gluCagon Clearance
50	$\Gamma_{\mathtt{PCR}}$	pmol/min	Pancreatic gluCagon Release
51	$M_{\mathtt{PCR}}^{G}$	#	Glucose effect on gluCagon clearance
52	$M_{\mathtt{PCR}}^{I}$	#	Insulin effect on gluCagon clearance
53	S	mmol	Glucose into the Stomach
54	J	mmol	Glucose into the Jejunum
55	R	mmol	Glucose into the Delay compartment
56	L	mmol	Glucose into the Ileum
57	$R_{\mathtt{oga}}$	mmol/min	Glucose Gut absorption rate

Table 2. Model Parameters

ParID	Parameter	Units	Meaning	Value
1	t_0	min	starting time for numerical integration	- 30
2	t_{end}	min	final time for numerical integration	300
3	t_{Δ}	min	time integration step	0.1
4	Q_B^G	L/min	Vascular blood water flow rate for Brain (glucose-related)	0.59
5	V_{BV}^G	L	Distribution Volume of Glucose in Brain Vascular space	0.35
6	V_{BI}	L	Volume of Brain Interstitial space	0.45
7	T_B	min	Trans-capillary diffusion rate for Brain	2.1
8	G_{H0}	mM	Baseline value of G_H at initial time (t_0)	5.07333
9	$\Gamma_{\mathtt{BGU}}$	mmol/min	Brain Glucose Uptake rate	0.388889
10	Q_L^G	L/min	Vascular blood water flow rate for Liver (glucose-related)	1.26
11	Q_K^G	L/min	Vascular blood water flow rate for Kidney (glucose-related)	1.01
12	Q_P^G	L/min	Vascular blood water flow rate for Peripheral tissues (glucose-related)	1.51
13	Q_H^G	L/min	Vascular blood water flow rate for Heart/lung (glucose-related)	4.37
14	$\Gamma_{\mathtt{RBCU}}$	mmol/min	Red Blood cell Glucose Uptake rate	0.0555556
15	V_H^G	L	Distribution Volume of Glucose in Heart/lung Vascular space	1.38
16	Q_J^G	L/min	Vascular blood water flow rate for Gut/Jejunum (glucose-related)	1.01
17	V_J^G	L	Distribution Volume of Glucose in Gut/Jejunum Vascular space	1.12
18	$\Gamma_{\mathtt{JGU}}$	mmol/min	Gut/Jejunal Glucose Uptake or utilization rate	0.111111
19	Q_A^G	L/min	Vascular blood water flow rate in hepatic Artery (glucose-related)	0.25
20	V_L^G	L	Distribution Volume of Glucose in Liver space	2.51
21	V_K^G	L	Distribution Volume of Glucose in Kidney space	0.66
22	V_{PV}^G	L	Distribution Volume of Glucose in Peripheral Vascular space	1.04
23	V_{PI}	L	Volume of Peripheral Interstitial space	6.74
24	T_P^G	min	Trans-capillary diffusion rate for Peripheral tissues (glucose-related)	5
25	$\Gamma_{\mathtt{PGU}}^B$	mmol/min	Baseline rate of Peripheral Glucose Uptake	0.194444
26	$\beta_{\mathtt{PGU}}^0$	#	PGU Insulin effect midpoint	7.03
27	$\beta_{\mathtt{PGU}}^1$	#	PGU Insulin effect half-amplitude	6.52
28	$\beta_{\mathtt{PGU}}^2$	#	PGU Insulin effect steepness	0.338
29	$\beta_{\mathtt{PGU}}^3$	#	PGU Insulin effect shift	5.82

Table 2. Model Parameters

ParID	Parameter	Units	Meaning	Value
30	$\beta^0_{\mathtt{HGP}}$	#	HGP gluCagon effect scale	2.7
31	$\beta^1_{\mathtt{HGP}}$	#	HGP gluCagon scale	0.388852
32	τ_C	min	Inverse of the decay rate for the glucagon-driven intensification of f_2 Hepatic Glucose Uptake suppression	65
33	$\beta^2_{\mathtt{HGP}}$	#	HGP Insulin effect midpoint	1.21
34	$\beta^3_{\mathtt{HGP}}$	#	HGP Insulin effect half-amplitude	1.14
35	$\beta^4_{\mathtt{HGP}}$	#	HGP Insulin effect steepness	1.66
36	$\beta^5_{\mathtt{HGP}}$	#	HGP Insulin effect shift	0.887748
37	τ_I	min	Inverse of the decay rate for the insulin-driven intensification of $M^I_{\mathtt{HGP}}$ and $M^I_{\mathtt{HGU}}$ (same for both)	25
38	$\beta^6_{\mathtt{HGP}}$	#	HGP Glucose effect midpoint	1.42
39	$\beta^7_{\mathtt{HGP}}$	#	HGP Glucose effect half-amplitude	1.41
40	$\beta^8_{\mathtt{HGP}}$	#	HGP Glucose effect steepness	0.62
41	$\beta^9_{\mathtt{HGP}}$	#	HGP Glucose effect shift	0.504543
42	$\Gamma_{\mathtt{HGP0}}$	mmol/min	Baseline value of $\Gamma_{\mathtt{HGP}}$ at initial time (t_0)	0.861111
43	$\beta^0_{\mathtt{HGU}}$	#	HGU Insulin effect half-amplitude	2
44	$\beta^1_{\mathtt{HGU}}$	#	HGU Insulin effect steepness	0.549306
45	$\beta^2_{\mathtt{HGU}}$	#	HGP Glucose effect midpoint	5.66
46	$\beta^3_{\mathtt{HGU}}$	#	HGP Glucose effect half-amplitude	5.66
47	$\beta^4_{\mathtt{HGU}}$	#	HGP Glucose effect steepness	2.44
48	$\beta^5_{\mathtt{HGU}}$	#	HGP Glucose effect shift	1.4783
49	$\Gamma_{\mathtt{HGU0}}$	mmol/min	Baseline value of $\Gamma_{\mathtt{HGU}}$ at initial time (t_0)	0.111111
50	$\beta^0_{\mathtt{KGE}}$	mmol/min	KGE Glucose effect midpoint	0.394444
51	$\beta^1_{\mathtt{KGE}}$	mmol/min	KGE Glucose effect half-amplitude	0.394444
52	$\beta^2_{\mathtt{KGE}}$	/mM	KGE Glucose effect steepness	0.198
53	$\beta^3_{\mathtt{KGE}}$	mM	KGE Glucose effect shift, point of transition between tanh and linear regime	25.5556
54	$\beta^4_{\mathtt{KGE}}$	mmol/min	KGE Glucose linear effect intercept	1.834
55	$\beta^5_{\mathtt{KGE}}$	mmol/min/mM	KGE Glucose linear effect slope	0.0872
56	Q^I_B	L/min	Vascular blood water flow rate for Brain (insulin-related)	0.45
57	V^I_B	L	Distribution Volume of Insulin in Brain vascular space	0.26
58	V^I_H	L	Distribution Volume of Insulin in Heart/lung vascular space	0.99
59	Q^I_L	L/min	Vascular blood water flow rate for Liver (insulin-related)	0.9

Table 2. Model Parameters

ParID	Parameter	Units	Meaning	Value
60	Q^I_K	L/min	Vascular blood water flow rate for Kidney (insulin-related)	0.72
61	Q^I_P	L/min	Vascular blood water flow rate for Periphery (insulin-related)	1.05
62	Q^I_H	L/min	Vascular blood water flow rate for Heart and Lungs (insulin-related)	3.12
63	V^I_J	L	Distribution Volume of Insulin in Gut Vascular space	0.94
64	Q^I_J	L/min	Vascular blood water flow rate for Gut (insulin-related)	0.72
65	V^I_L	L	Distribution Volume of Insulin in Liver Vascular space	1.14
66	Q^I_A	L/min	Vascular blood water flow rate in hepatic Artery (insulin-related)	0.18
67	F_{LIC}	#	Fraction of insulin Liver clearance	0.4
68	F_{KIC}	#	Fraction of insulin Kidney clearance	0.3
69	V^I_K	L	Distribution Volume of Insulin in Kidney Vascular space	0.51
70	V^I_{PV}	L	Distribution Volume of Insulin in Peripheral Vascular space	0.74
71	T^I_P	min	Trans-capillary diffusion rate for Peripheral tissues (insulin-related)	20
72	F_{PIC}	#	Fraction of insulin Periphery clearance	0.15
73	$\beta^1_{\mathtt{PIR}}$	#	PIR Glucose effect parameter 1	6.51625
74	$\beta^2_{\mathtt{PIR}}$	mmol/l	PIR Glucose effect parameter 2	4.13532
75	$\beta^3_{\mathtt{PIR}}$	#	PIR Glucose effect parameter 3	4.34599
76	$\beta^4_{\mathtt{PIR}}$	#	PIR Glucose effect parameter 4	5.57083
77	$\beta^5_{\mathtt{PIR}}$	#	Potentiator parameter	2.28432
78	$K_{\mathtt{Rinsu}}$	/min	Rate of labile Insulin secretion	0.0137576
79	$R_{\mathtt{insu0}}$	pmol	Labile Insulin for Glucose=0	44310
80	$K_{\mathtt{RinsuPotr}}$	pmol/min	Rate of Potentiator effect on labile insulin	3300.71
81	$K_{\mathtt{RinsuPtgt}}$	/min	Rate at which Potentiator reachs its target value	0.0169775
82	$K_{\mathtt{pinhPrp}}$	/min	Rate at which Inhibitor reaches the proportional insulin response function	15.212
83	M_1	/min	Late rate of increase in insulin secretion	0.000241686
84	M_2	/min	Rate of insulin response	0.304906
85	I_{PV0}	pM	Baseline value of I_{PV} at initial time (t_0)	91
86	C_0	pM	Starting value for gluCagon	11.48
87	Γ_{MCC}	L/min	Rate constant of gluCagon clearance	0.91
88	V_C	L	gluCagon distribution volume	11.31
89	$\beta^0_{\mathtt{PCR}}$	#	PCR Glucose effect midpoint	2.93

Table 2. Model Parameters

ParID	Parameter	Units	Meaning	Value
90	$\beta^1_{\mathtt{PCR}}$	#	PCR Glucose effect half-amplitude	2.1
91	$\beta^2_{\mathtt{PCR}}$	#	PCR Glucose effect steepness	4.18
92	$\beta^3_{\mathtt{PCR}}$	#	PCR Glucose effect shift	0.621325
93	$\beta^4_{\mathtt{PCR}}$	#	PCR Insulin effect midpoint	1.31
94	$\beta^5_{\mathtt{PCR}}$	#	PCR Insulin effect half-amplitude	0.61
95	$\beta^5_{\mathtt{PCR}}$	#	PCR Insulin effect steepness	1.06
96	$\beta^5_{\mathtt{PCR}}$	#	PCR Insulin effect shift	0.471419
97	f_{20}	#	Baseline value of f_2 at initial time (t_0)	0
98	D	mmol	Glucose dose for the oral challenge	555.56
99	S_0	mmol	Baseline value of S at initial time (t_0)	0
100	$k_{\mathtt{js}}$	1/min	Glucose transfer rate from Stomach to Jejunum compartment	0.0365887
101	J_0	mmol	Baseline value of J at initial time (t_0)	0
102	$k_{\mathtt{gj}}$	1/min	Glucose transfer rate from Jejunum to Gut compartment	0.0245626
103	$k_{\mathtt{rj}}$	1/min	Glucose transfer rate from Jejunum to Delay compartment	0.0277149
104	Rit_0	mmol	Baseline value of R at initial time (t_0)	0
105	$k_{\mathtt{lr}}$	1/min	Glucose transfer rate from Delay to Ileum compartment	0.0248468
106	Ile_0	mmol	Baseline value of L at initial time (t_0)	0
107	$k_{\mathtt{gl}}$	1/min	Glucose transfer rate from Ileum to Gut compartment	0.0261629
108	f	#	Fraction of Glucose absorbed	1
109	$R_{\mathtt{oga0}}$	mmol/min	Baseline value of R_{oga} at initial time (t_0)	0
110	I_{H0}	pM	Baseline value of I_H at initial time (t_0)	107.059
111	I_{K0}	pM	Baseline value of I_K at initial time (t_0)	74.9412
112	I_{B0}	pM	Baseline value of I_B at initial time (t_0)	107.059
113	I_{G0}	pM	Baseline value of I_G at initial time (t_0)	107.059
114	I_{PI0}	pM	Baseline value of I_{PI} at initial time (t_0)	40.9651
115	I_{L0}	pM	Baseline value of I_L at initial time (t_0)	151.488
116	$\Gamma_{\mathtt{PIR0}}$	pmol/min	Baseline value of $\Gamma_{\mathtt{PIR}}$ at initial time (t_0)	130.879
117	$\Gamma_{\mathtt{PIC0}}$	pmol/min	Baseline value of $\Gamma_{\mathtt{PIC}}$ at initial time (t_0)	16.8618
118	$P_{\mathtt{prp0}}$	#	Baseline value of $P_{\mathtt{prp}}$ at initial time (t_0)	0.833373
119	$P_{\mathtt{tgt0}}$	#	Baseline value of $P_{\mathtt{tgt}}$ at initial time (t_0)	0.659434
120	$P_{\mathtt{inh0}}$	#	Baseline value of $P_{\mathtt{inh}}$ at initial time (t_0)	0.833373
121	$P_{\mathtt{otn0}}$	#	Baseline value of $P_{\mathtt{otn}}$ at initial time (t_0)	0.659434
122	$InitialRinsu_0$	pmol	Baseline value of $Rinsu$ at initial time (t_0)	200202

Table 2. Model Parameters

ParID	Parameter	Units	Meaning	Value
123	S_{ecr0}	pmol/min	Baseline value of S_{ecr} at initial time (t_0)	31.9073
124	G_{PV0}	mM	Baseline value of G_{PV} at initial time (t_0)	4.94456
125	G_{K0}	mM	Baseline value of G_K at initial time (t_0)	5.07333
126	G_{BV0}	mM	Baseline value of G_{BV} at initial time (t_0)	4.4142
127	G_{J0}	mM	Baseline value of G_J at initial time (t_0)	4.96332
128	G_{L0}	mM	Baseline value of G_L at initial time (t_0)	5.58039
129	G_{BI0}	mM	Baseline value of G_{BI} at initial time (t_0)	2.59938
130	G_{PI0}	mM	Baseline value of G_{PI} at initial time (t_0)	4.80032
131	$M^I_{\mathtt{PGU0}}$	#	Baseline value of $M^I_{\mathtt{PGU}}$ at initial time (t_0)	0.992859
132	$M^C_{\mathtt{HGP0}}$	#	Baseline value of $M^C_{\mathtt{HGP}}$ at initial time (t_0)	1
133	$M^{C0}_{\mathtt{HGP0}}$	#	Baseline value of $M^{C0}_{\mathtt{HGP}}$ at initial time (t_0)	1
134	$M^I_{\mathtt{HGP0}}$	#	Baseline value of $M^I_{\mathtt{HGP}}$ at initial time (t_0)	1
135	$M^I_{\mathtt{HGPinf0}}$	#	Steady state of MIHGP	1
136	$M^G_{\mathtt{HGP0}}$	#	Baseline value of $M^G_{\mathtt{HGP}}$ at initial time (t_0)	1
137	$M^I_{\mathtt{HGU0}}$	#	Baseline value of $M^I_{\mathtt{HGU}}$ at initial time (t_0)	1
138	$M^I_{\mathtt{HGUinf0}}$	#	Steady state of $M^I_{\mathtt{HGU}}$	1
139	$M^G_{\mathtt{HGU0}}$	#	Baseline value of $M^G_{\mathtt{HGU}}$ at initial time (t_0)	1
140	$\Gamma_{\mathtt{KGE0}}$	mmol/min	Baseline value of $\Gamma_{\mathtt{KGE}}$ at initial time (t_0)	0.000236777
141	$\Gamma_{\mathtt{LIC0}}$	pmol/min	Baseline value of $\Gamma_{\mathtt{LIC}}$ at initial time (t_0)	90.8929
142	$\Gamma_{\mathtt{KIC0}}$	pmol/min	Baseline value of $\Gamma_{\mathtt{KIC}}$ at initial time (t_0)	23.1247
143	$M^G_{\mathtt{PCR0}}$	#	Baseline value of $M^G_{\mathtt{PCR}}$ at initial time (t_0)	1
144	$M^I_{\mathtt{PCR0}}$	#	Baseline value of $M^I_{\mathtt{PCR}}$ at initial time (t_0)	1
145	$\Gamma_{\mathtt{PCC0}}$	pM	Baseline value of $\Gamma_{\mathtt{PCC}}$ at initial time (t_0)	10.4468
146	$\Gamma^B_{\mathtt{PCR0}}$	pM	Baseline value of $\Gamma^B_{\mathtt{PCR}}$ at initial time (t_0)	10.4468