# S1 Appendix to Personalized computational model quantifies heterogeneity in postprandial responses to oral glucose challenge

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## 1 E-DES Model structure

**Glucose in the gut**

$$\frac{dM_G^{gut}}{dt} = m_G^{meal}(D^{meal}, t) - m_G^{pl}(M_G^{gut}) \tag{1}$$

$$m_G^{meal} = \sigma k_1^{\sigma} t^{\sigma-1} exp(-(k_1 t)^{\sigma}) D^{meal} \tag{2}$$

$$m_G^{pl} = k_2 M_G^{gut} \tag{3}$$

**Glucose in the plasma**

$$\frac{dG^{pl}}{dt} = g^{liv}(G^{pl}, I^{pl}) + g^{gut}(M_G^{gut}) - g^{non-it}(G^{pl}) - g^{it}(G^{pl}, I^{pl}) - g^{ren}(G^{pl}) \tag{4}$$

$$g^{liv} = g_b^{liv} - k_3(G^{pl} - G_b^{pl}) - k_4\beta(I^{pl} - I_b^{pl}) \tag{5}$$

$$g^{gut} = \frac{f}{V_G M^b} m_G^{pl} = k_2 \frac{f}{V_G M^b} M_G^{gut} \tag{6}$$

$$c_2 = g_b^{liv}\left(\frac{K_M + G_b^{pl}}{G_b^{pl}}\right) - k_5\beta I_b^{pl} \tag{7}$$

$$g^{non-it} = c_2 \frac{G^{pl}}{K_M + G^{pl}} \tag{8}$$

$$g^{it} = k_5\beta I^{pl} \frac{G^{pl}}{K_M + G^{pl}} \tag{9}$$

$$g^{ren} = \begin{cases} \frac{c_1}{V_G M^b}(G^{pl} - G_{th}^{pl}), & \text{if } G^{pl} > G_{th}^{pl} \quad (10) \\ 0, & \text{if } G^{pl} \leq G_{th}^{pl} \quad (11) \end{cases}$$

**Insulin in the plasma**

$$\frac{dI^{pl}}{dt} = i^{pnc}(G^{pl}) - i^{liv}(I^{pl}) - i^{if}(I^{pl}) \tag{12}$$

$$i^{pnc} = \beta^{-1}\left(k_6(G^{pl} - G_b^{pl}) + \left(\frac{k_7}{\tau_i}\right)\int (G^{pl} - G_b^{pl})dt + \left(\frac{k_7}{\tau_i}\right) G_b^{pl} + (k_8\tau_d)\frac{dG^{pl}}{dt}\right) \tag{13}$$

$$c_3 = k_7 \frac{G_b^{pl}}{\beta\tau_i I_b^{pl}} \tag{14}$$

$$i^{liv} = c_3 I^{pl} \tag{15}$$

$$i^{if} = k_9(I^{pl} - I_b^{pl}) \tag{16}$$

## 2 E-DES model inputs, fluxes, parameters and constants

Table A: Overview of the E-DES model (input) variables

| Name | Description | Units |
|---|---|---|
| $t$ | Time | min |
| $M_G^{gut}(t)$ | Glucose mass in the gut | mg |
| $G^{pl}(t)$ | Plasma glucose concentration | mmol/L |
| $I^{pl}(t)$ | Plasma insulin concentration | mU/L |
| $D^{meal}$ | Glucose intake | mg |
| $M^b$ | Body mass | kg |

Glucose intake was set to 75g and body mass was set to 70kg.

Table B: Overview of the E-DES model fluxes

| Name | Description | Units |
|---|---|---|
| $m_G^{meal}(t)$ | Glucose mass entering from stomach | mg/min |
| $m_G^{pl}(t)$ | Glucose mass leaving to plasma | mg/min |
| $g^{liv}(t)$ | Glucose production by the liver (EGP) | mmol/L/min |
| $g^{gut}(t)$ | Glucose entering from the gut | mmol/L/min |
| $g^{non-it}(t)$ | Glucose uptake by insulin-independent tissue | mmol/L/min |
| $g^{it}(t)$ | Glucose uptake by insulin-dependent tissue | mmol/L/min |
| $g^{ren}(t)$ | Renal glucose elimination | mmol/L/min |
| $i^{pnc}(t)$ | Pancreas insulin secretion | mU/L/min |
| $i^{if}(t)$ | Insulin flowing into interstitial fluid | mU/L/min |
| $i^{liv}(t)$ | Insulin uptake by the liver | mU/L/min |

Table C: Overview of the E-DES model parameters

| Name | Description | Units | Value |
|---|---|---|---|
| $k1$ | Rate constant of glucose appearance in the gut | 1/min | 1.35e-2 |
| $k2$ | Rate constant of gut emptying | 1/min | 6.33e-1 |
| $k3$ | Rate constant of $\Delta$G suppression of EGP when $G^{pl} > G_b$ | 1/min | 5.00e-5 |
| $k4$ | Rate constant of insulin-dependent suppression of EGP | 1/min | 1.00e-3 |
| $k5$ | Rate constant of insulin-dependent glucose uptake | 1/min | 3.80e-3 |
| $k6$ | Rate constant of $\Delta$G dependant insulin production | 1/min | 5.82e-1 |
| $k7$ | Rate constant of $\int G$ dependant insulin production | 1/min | 2.20e-2 |
| $k8$ | Rate constant of $\frac{dG}{dt}$ dependant insulin production | 1/min | 4.71 |
| $k9$ | Rate constant of insulin outflow from plasma to interstitial fluid | 1/min | 1.08e-2 |
| $\sigma$ | Shape factor | - | 1.35 |
| $K_M$ | Michaelis-Menten constant for glucose uptake | mmol/L | 0.63 |

Table D: Overview of the E-DES model constants

| Name | Description | Units | Value |
|---|---|---|---|
| $G_b^{pl}$ | Basal plasma glucose | mmol/L | $G^{pl}(0)$ |
| $I_b^{pl}$ | Basal plasma Insulin | mU/L | $I^{pl}(0)$ |
| $g_b^{liv}$ | Basal endogenous glucose production | mmol/L/min | 0.043 |
| $G_{th}^{pl}$ | Renal threshold | mmol/L | 9 |
| $V_G$ | Glucose distribution volume in plasma | L/kg | 17/70 |
| $\beta$ | Unit conversion factor from glucose to insulin | (mmol/L)/(mU/L) | 1 |
| $f$ | Unit conversion factor from mmol to mg glucose | mmol/mg | 0.005551 |
| $\tau_i$ | Integral time constant | min | 31 |
| $\tau_d$ | Derivative time constant | min | 3 |
| $c1$ | Rate constant of glomerular filtration | 1/min | 0.1 |
| $c2$ | Rate constant of glucose uptake by the non-insulin dependent tissue | 1/min | - |
| $c3$ | Rate constant of liver insulin clearance | 1/min | - |

## Model changes from published version

The current model has been adapted from [1]. Changes include:
1. Short and long-acting exogenous insulin inflow, c-peptide, and the parameter accounting for complex carbohydrates were removed in the model.
2. The baseline glucose ($G_b$) and insulin ($I_b$) concentrations were adjusted in model constants c2 and c3 to account for individual values.
3. Parameter k10 was removed in the model.

# References

[1] Maas, A. (2017). *Playing with numbers: the development of an educational diabetes game*. Technische Universiteit Eindhoven.