# Complex patterns of metabolic and $Ca^{2+}$ entrainment in pancreatic islets by oscillatory glucose
# Supporting Material

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## Model equations

The model is as in Bertram et al. (2007), ref. 9 in the manuscript, except for the expression of the glucokinase rate $J_{\rm GK}$. We refer to the original article for details on the rate expressions.

### Glycolytic model

The glycolytic model describes the time evolution of glucose 6-phosphate ($G6P$, in $\mu$M) and fructose 1,6-bisphosphate ($FBP$, in $\mu$M) concentrations:

$$\frac{dG6P}{dt} = J_{\rm GK} - J_{\rm PFK}, \quad (1)$$

$$\frac{dFBP}{dt} = J_{\rm PFK} - \frac{1}{2}J_{\rm GPDH}, \quad (2)$$

where

$$J_{\rm GK} = V_{\rm GK}\frac{G^{n{\rm GK}}}{G^{n{\rm GK}} + K_{\rm GK}^{n{\rm GK}}}, \quad (3)$$

$$J_{\rm GPDH} = k_{\rm GPDH}\sqrt{FBP/(1\mu{\rm M})}, \quad (4)$$

$$J_{\rm PFK} = V_{\max}\frac{w_{1110} + \lambda\sum_{ijl} w_{ij1l}}{\sum_{ijkl} w_{ijkl}}, \quad (5)$$

with $i, j, k, l \in \{0, 1\}$ and

$$w_{ijkl} = \frac{1}{f_{13}^{ik} f_{23}^{jk} f_{41}^{il} f_{42}^{jl} f_{43}^{kl}}\left(\frac{AMP}{K_1}\right)^i \left(\frac{FBP}{K_2}\right)^j \left(\frac{(0.3\,G6P)^2}{K_3}\right)^k \left(\frac{(ATP)^2}{K_4}\right)^l. \quad (6)$$

## Mitochondrial model

The mitochondrial model describes the time evolution of mitochondrial membrane potential ($\Psi_m$, in mV) and mitochondrial concentrations of NADH ($NADH_m$, in mM), Ca$^{2+}$ ($Ca_m$, in $\mu$M) and ADP ($ADP_m$, in mM):

$$\frac{d\Psi_m}{dt} = (J_{\rm H,res} - J_{\rm H,atp} - J_{\rm ANT} - J_{\rm H,leak} - J_{\rm NaCa} - 2J_{\rm uni})/C_{mito}, \tag{7}$$

$$\frac{dNADH_m}{dt} = \gamma(J_{\rm PDH} - J_{\rm O}), \tag{8}$$

$$\frac{dCa_m}{dt} = -f_m(J_{\rm NaCa} - J_{\rm uni}), \tag{9}$$

$$\frac{dADP_m}{dt} = \gamma(J_{\rm ANT} - J_{\rm F1F0}), \tag{10}$$

where

$$J_{\rm H,res} = \left(\frac{p_8 NADH_m}{p_9 + NADH_m}\right)\left(\frac{1}{1+\exp((\Psi_m - p_{10})/p_{11})}\right), \tag{11}$$

$$J_{\rm F1F0} = \left(\frac{p_{13}}{p_{13} + ATP_m}\right)\left(\frac{p_{16}}{1+\exp(-(\Psi_m - p_{14})/p_{15})}\right), \tag{12}$$

$$J_{\rm H,atp} = 3J_{\rm F1F0}, \tag{13}$$

$$J_{\rm ANT} = p_{19}\frac{ATP_m}{ATP_m + p_{20}ADP_m}\exp(0.5\Psi_m F/(RT)), \tag{14}$$

$$J_{\rm H,leak} = p_{17}\Psi_m + p_{18}, \tag{15}$$

$$J_{\rm NaCa} = p_{23}\exp(p_{24}\Psi_m)Ca_m/Ca_c, \tag{16}$$

$$J_{\rm uni} = (p_{21}\Psi_m - p_{22})Ca_c^2, \tag{17}$$

$$J_{\rm PDH} = \left(\frac{p_1 NAD_m}{p_2 NAD_m + NADH_m}\right)\left(\frac{Ca_m}{p_3 + Ca_m}\right)(J_{\rm GPDH} + J_{\rm GPDHbas}), \tag{18}$$

$$J_{\rm O} = \left(\frac{p_4 NADH_m}{p_5 + NADH_m}\right)\left(\frac{1}{1+\exp((\Psi_m - p_6)/p_7)}\right), \tag{19}$$

$$ATP_m = ATP_{m,tot} - ADP_m, \tag{20}$$

$$NAD_m = NAD_{m,tot} - NADH_m. \tag{21}$$

## Electical/calcium model

The electrical/calcium model describes the time evolution of plasma membrane potential ($V$, in mV), a gating variable of the delayed rectifier K$^+$ (Kv) current ($n$, unitless), Ca$^{2+}$ concentrations in the cytosol ($Ca_c$, in $\mu$M) and the endoplasmic reticulum ($Ca_{er}$, in $\mu$M), and cytosolic ADP concentration ($ADP_c$, in $\mu$M):

$$\frac{dV}{dt} = -(I_K + I_{Ca} + I_{K(Ca)} + I_{K(ATP)})/C_m, \tag{22}$$

$$\frac{dn}{dt} = (n_\infty(V) - n)/\tau_n, \tag{23}$$

$$\frac{dCa_c}{dt} = f_c(J_{\text{mem}} + (J_{\text{leak}} - J_{\text{SERCA}}) + \kappa(J_{\text{NaCa}} - J_{\text{uni}})), \tag{24}$$

$$\frac{dCa_{er}}{dt} = -f_{er}(V_c/V_{er})(J_{\text{leak}} - J_{\text{SERCA}}), \tag{25}$$

$$\frac{dADP_c}{dt} = (k_{hyd}Ca_c + k_{hyd,bas})ATP_c - \kappa J_{\text{ANT}}, \tag{26}$$

where

$$I_K = \bar{g}_K n(V - V_K), \tag{27}$$

$$I_{Ca} = \bar{g}_{Ca} m_\infty(V)(V - V_{Ca}), \tag{28}$$

$$I_{K(Ca)} = \bar{g}_{K(Ca)} \frac{Ca_c^2}{Ca_c^2 + K_D^2}(V - V_K), \tag{29}$$

$$I_{K(ATP)} = \bar{g}_{K(ATP)} o_\infty(ADP_c, ATP_c)(V - V_K), \tag{30}$$

and

$$n_\infty(V) = 1/(1 + \exp(-(V + 16\text{mV})/5\text{mV})), \tag{31}$$

$$m_\infty(V) = 1/(1 + \exp(-(V + 20\text{mV})/12\text{mV})), \tag{32}$$

$$o_\infty(ADP_c, ATP_c) = \frac{0.08\,(1 + 2MgADP^*) + 0.89(MgADP^*)^2}{(1 + MgADP^*)^2(1 + ADP^* + ATP^*)}, \tag{33}$$

$$ATP_c = ATP_{c,tot} - ADP_c. \tag{34}$$

Here, $MgADP^* = 0.165ADP_c/17\mu$M, $ADP^* = 0.135ADP_c/26\mu$M, and $ATP^* = 0.05ATP_c/1\mu$M. Finally,

$$J_{\text{mem}} = -\alpha I_{Ca} - k_{\text{PMCA}}(Ca - Ca_b), \tag{35}$$

$$J_{\text{leak}} = p_{\text{leak}}(Ca_{er} - Ca_c), \tag{36}$$

$$J_{\text{SERCA}} = k_{SERCA}Ca_c. \tag{37}$$

**Parameters**

$V_{GK} = 0.001\ \mu M/ms$, $K_{GK} = 7\ \mu M$, $nGK = 4$, $k_{GPDH} = 0.0005\ \mu M/ms$,
$V_{max} = 0.005\ \mu M/ms$, $\lambda = 0.06$, $f_{13} = 0.02$, $f_{23} = 0.2$,
$f_{41} = 20$, $f_{42} = 20$, $f_{43} = 20$, $K_1 = 30\ \mu M$,
$K_2 = 1\ \mu M$, $K_3 = 50000\ \mu M$, $K_4 = 220\ \mu M$, $AMP_c = 500\ \mu M$.

$C_{mito} = 1.8\ \mu M/mV$, $\gamma = 0.001\ mM/\mu M$, $f_m = 0.01$, $p_1 = 400$,
$p_2 = 1$, $p_3 = 0.01\ \mu M$, $p_4 = 0.6\ \mu M/ms$, $p_5 = 0.1\ mM$,
$p_6 = 177\ mV$, $p_7 = 5\ mV$, $p_8 = 7\ \mu M/ms$, $p_9 = 0.1\ mM$,
$p_{10} = 177\ mV$, $p_{11} = 5\ mV$, $p_{13} = 10\ mM$, $p_{14} = 190\ mV$,
$p_{15} = 8.5\ mV$, $p_{16} = 35\ \mu M/ms$, $p_{17} = 0.002\ \mu M/(ms \cdot mV)$, $p_{18} = -0.03\ \mu M/ms$,
$p_{19} = 0.35\ \mu M/ms$, $p_{20} = 2$, $p_{21} = 0.04\ (\mu M \cdot ms \cdot mV)^{-1}$, $p_{22} = 1.1\ (\mu M \cdot ms)^{-1}$,
$p_{23} = 0.01\ \mu M/ms$, $p_{24} = 0.016\ mV^{-1}$, $ATP_{m,tot} = 15\ mM$, $NAD_{m,tot} = 10\ mM$,
$F/(RT) = 96480/(310.16 \cdot 8315)\ mV^{-1} = 0.0374\ mV^{-1}$, $J_{GPDHbas} = 0.0005\ \mu M/ms$.

$C_m = 5300\ fF$, $\tau_n = 20\ ms$, $f_c = 0.01$, $\kappa = 0.0733$,
$f_{er} = 0.01$, $V_c/V_{er} = 31$, $k_{hyd} = 5 \cdot 10^{-5}\ (\mu M \cdot ms)^{-1}$, $k_{hyd,bas} = 5 \cdot 10^{-5}\ ms^{-1}$,
$\bar{g}_K = 2700\ pS$, $\bar{g}_{Ca} = 1000\ pS$, $\bar{g}_{K(Ca)} = 100\ pS$, $\bar{g}_{K(ATP)} = 12000\ pS$,
$V_K = -75\ mV$, $V_{Ca} = 25\ mV$, $K_D = 0.5\ \mu M$, $ATP_{c,tot} = 2500\ \mu M$,
$k_{PMCA} = 0.1\ ms^{-1}$, $Ca_b = 0.05\ \mu M$, $p_{leak} = 0.0002\ ms^{-1}$, $k_{SERCA} = 0.4\ ms^{-1}$,
$\alpha = 4.50 \cdot 10^{-6}\ \mu M/(ms \cdot fA)$.