

Table S1. ODE system for the integrative model*

$$\begin{aligned}
\frac{d \text{ H}^+}{dt} &= -J_{Pma1} + \frac{3}{2} \cdot J_{Nha1,Na} + \frac{3}{2} \cdot J_{Nha1,K} + J_{H_uptake} + J_{H_production} \\
\frac{d \text{ Na}^+}{dt} &= -J_{Ena1,Na} - J_{Nha1,Na} + J_{Trk,Na} + J_{NSC1,Na} + J_{diff,Na} \\
\frac{d \text{ K}^+}{dt} &= -J_{Ena1,K} - J_{Nha1,K} + J_{Trk,K} + J_{NSC1,K} - J_{Tok1} + J_{diff,K} \\
\frac{d[Pbs2]}{dt} &= -\frac{K_{pho}^{Pbs2} \cdot [Pbs2]}{1 + \left(\frac{P_{tur}}{\alpha_{Hog1}} \right)^8} + K_{depho}^{Pbs2} \cdot [Pbs2PP] - [Pbs2] \cdot V_{ratio} \\
\frac{d[Pbs2PP]}{dt} &= \frac{K_{pho}^{Pbs2} \cdot [Pbs2]}{1 + \left(\frac{P_{tur}}{\alpha_{Hog1}} \right)^8} - K_{depho}^{Pbs2} \cdot [Pbs2PP] - [Pbs2PP] \cdot V_{ratio} \\
\frac{d[Hog1c]}{dt} &= -K_{pho}^{Hog1} \cdot [Pbs2PP] \cdot [Hog1c] + K_{depho}^{Hog1PPc} \cdot [Hog1PPc] \\
&\quad - K_{imp}^{Hog1c} \cdot [Hog1c] + \frac{K_{exp}^{Hog1n} \cdot [Hog1n] \cdot V_{nuc}}{V_{cyt}} - [Hog1c] \cdot V_{ratio} \\
\frac{d[Hog1PPc]}{dt} &= K_{pho}^{Hog1} \cdot [Pbs2PP] \cdot [Hog1c] - K_{depho}^{Hog1PPc} \cdot [Hog1PPc] \\
&\quad - K_{imp}^{Hog1PPc} \cdot [Hog1PPc] + \frac{K_{exp}^{Hog1PPn} \cdot [Hog1PPn] \cdot V_{nuc}}{V_{cyt}} \\
&\quad - [Hog1PPc] \cdot V_{ratio} \\
\frac{d[Hog1n]}{dt} &= \frac{K_{imp}^{Hog1c} \cdot [Hog1c] \cdot V_{cyt}}{V_{nuc}} - K_{exp}^{Hog1n} \cdot [Hog1n] + K_{depho}^{Hog1PPn} \cdot [Hog1PPn] \\
&\quad - [Hog1n] \cdot V_{ratio} \\
\frac{d[Hog1PPn]}{dt} &= \frac{K_{imp}^{Hog1PPc} \cdot [Hog1PPc] \cdot V_{cyt}}{V_{nuc}} - K_{exp}^{Hog1PPn} \cdot [Hog1PPn] \\
&\quad - K_{depho}^{Hog1PPn} \cdot [Hog1PPn] - [Hog1PPn] \cdot V_{ratio}
\end{aligned}$$

$$\frac{d[Gly_{int}]}{dt} = K_{s0}^{Glyc} + \frac{K_{s1}^{Glyc} \cdot (totalHog1PP)^4}{\beta_{Hog1}^4 (totalHog1PP)^4} + K_{s2}^{Glyc} \cdot [Yt] \\ - \left(K_{exp0}^{Glyc} + \frac{K_{exp1}^{Glyc} \cdot (P_{tur})^{12}}{(\gamma_{Hog1})^{12} + (P_{tur})^{12}} \right) \cdot [Gly_{int}] - [Gly_{int}] \cdot V_{ratio}$$

$$\frac{d[Yt]}{dt} = K_{s0}^{Yt} + K_{s1}^{Yt} \cdot [z4] - K_t^{Yt} \cdot [Yt] - [Yt] \cdot V_{ratio}$$

$$\frac{d[z1]}{dt} = \frac{4 \cdot ([Hog1PPn] - [z1])}{\tau}$$

$$\frac{d[z2]}{dt} = \frac{4 \cdot ([z1] - [z2])}{\tau}$$

$$\frac{d[z3]}{dt} = \frac{4 \cdot ([z2] - [z3])}{\tau}$$

$$\frac{d[z4]}{dt} = \frac{4 \cdot ([z3] - [z4])}{\tau}$$

$$\frac{d[Ca^{2+}]}{dt} = C_{Ca} - d_{Ca} \cdot [Ca^{2+}] + k_{Ca, cyt} \cdot \frac{[Na^+]_{Cyt}^{h_{-Na_cyt}}}{[Na^+]_{Cyt}^{h_{-Na_cyt}} + Km_{Ca, cyt}^{h_{-Na_cyt}}} \\ + k_{Ca, ext} \cdot \frac{[Na^+]_{ext}^{h_{-Na_ext}}}{[Na^+]_{ext}^{h_{-Na_ext}} + Km_{Ca, ext}^{h_{-Na_ext}}} + k_{Ca, pH} \cdot (pH_{ext} - 6.5) \\ - 3 \cdot k_{CN,a} \cdot [Ca^{2+}]^3 \cdot [CN_{off}] + 3 \cdot k_{CN,da} \cdot [CN] - [Ca^{2+}] \cdot V_{ratio}$$

$$\frac{d[CN_{off}]}{dt} = -k_{CN,a} \cdot [Ca^{2+}]^3 \cdot [CN_{off}] + k_{CN,da} \cdot [CN] + k_{CN_Ppz,da} \cdot [Ppz] \cdot [CN] - [CN_{off}] \cdot V_{ratio}$$

$$\frac{d[CN]}{dt} = k_{CN,a} \cdot [Ca^{2+}]^3 \cdot [CN_{off}] - k_{CN,da} \cdot [CN] - k_{CN_Ppz,da} \cdot [Ppz] \cdot [CN] - [CN] \cdot V_{ratio}$$

$$\frac{d[Crz1]}{dt} = C_{Crz1} - d_{Crz1} \cdot [Crz1] + k_{Crz1} \cdot [CN] - [Crz1] \cdot V_{ratio}$$

$$\frac{d[Nrg1]}{dt} = C_{Nrg1} \cdot \frac{Km_{Nrg1,pH}}{Km_{Nrg1,pH} + k_{pHext}} - d_{Nrg1} \cdot [Nrg1] - [Nrg1] \cdot V_{ratio}$$

$$\frac{d[ENAA1_{mRNA}]}{dt} = C_{ENAA1,Nrg1} \cdot \frac{Km_{ENAA1,Nrg1}^{h_{-ENAA1Nrg1}}}{Km_{ENAA1,Nrg1}^{h_{-ENAA1Nrg1}} + [Nrg1]^{h_{-ENAA1Nrg1}}} \\ + k_{ENAA1,Crz1} \cdot [Crz1] + k_{ENAA1,Hog1} \cdot [z2] - d_{ENAA1mRNA} \cdot [ENAA1_{mRNA}]$$

$$\frac{d[Ena1]}{dt} = kt_{Ena1} \cdot [ENAA1_{mRNA}] - d_{Ena1} \cdot [Ena1] - [Ena1] \cdot V_{ratio}$$

$$\frac{d \text{ Volume}_{\text{cyt}}}{dt} = -G_{EK} \cdot Lp \cdot D_{\text{Pressure}}$$

* For expressions of the transporter activities and volume changes, see Section 2-4 in the Supporting text (Text S1).