

$$\begin{aligned}
\frac{d([InR] \cdot V_{\text{cellsurface}})}{dt} &= - (k1 \cdot [Ins] \cdot V_{\text{extracellular}} \cdot [InR] \cdot V_{\text{cellsurface}}) \\
&+ (kminus1 \cdot [Ins_InR] \cdot V_{\text{cellsurface}}) \\
&+ V_{\text{cellsurface}} \cdot (kminus3 \cdot [PTP1B] \cdot V_{\text{cytoplasm}} \cdot [Ins_InR_P]) \\
&- (k4 \cdot [InR] \cdot V_{\text{cellsurface}}) \\
&+ (kminus4 \cdot [cytoplasm_InR] \cdot V_{\text{cytoplasm}}) \\
\frac{d([Ins_InR] \cdot V_{\text{cellsurface}})}{dt} &= + (k1 \cdot [Ins] \cdot V_{\text{extracellular}} \cdot [InR] \cdot V_{\text{cellsurface}}) \\
&- (kminus1 \cdot [Ins_InR] \cdot V_{\text{cellsurface}}) \\
&- V_{\text{cellsurface}} \cdot (k3 \cdot [Ins_InR]) \\
\frac{d([Ins_InR_P] \cdot V_{\text{cellsurface}})}{dt} &= - (k4prime \cdot [Ins_InR_P] \cdot V_{\text{cellsurface}}) \\
&+ (kminus4prime \cdot [cytoplasm_Ins_InR_P] \cdot V_{\text{cytoplasm}}) \\
&+ V_{\text{cellsurface}} \cdot (k3 \cdot [Ins_InR]) \\
&- (k2 \cdot [Ins] \cdot V_{\text{extracellular}} \cdot [Ins_InR_P] \cdot V_{\text{cellsurface}}) \\
&+ (kminus2 \cdot [Ins_2_InR_P] \cdot V_{\text{cellsurface}}) \\
&- V_{\text{cellsurface}} \cdot (kminus3 \cdot [PTP1B] \cdot V_{\text{cytoplasm}} \cdot [Ins_InR_P]) \\
\frac{d([Ins_2_InR_P] \cdot V_{\text{cellsurface}})}{dt} &= + (k2 \cdot [Ins] \cdot V_{\text{extracellular}} \cdot [Ins_InR_P] \cdot V_{\text{cellsurface}}) \\
&- (kminus2 \cdot [Ins_2_InR_P] \cdot V_{\text{cellsurface}}) \\
&- (k4prime \cdot [Ins_2_InR_P] \cdot V_{\text{cellsurface}}) \\
&+ (kminus4prime \cdot [cytoplasm_Ins_2_InR_P] \cdot V_{\text{cytoplasm}}) \\
\frac{d([cytoplasm_InR] \cdot V_{\text{cytoplasm}})}{dt} &= + V_{\text{cytoplasm}} \cdot (k6 \cdot [PTP1B] \cdot [cytoplasm_Ins_2_InR_P] \cdot V_{\text{cytoplasm}}) \\
&+ V_{\text{cytoplasm}} \cdot (k6 \cdot [PTP1B] \cdot [cytoplasm_Ins_InR_P] \cdot V_{\text{cytoplasm}}) \\
&+ V_{\text{cytoplasm}} \cdot ([cytoplasm_RNA_InR] \cdot 2.46) \\
&- V_{\text{cytoplasm}} \cdot (0.0044 \cdot [cytoplasm_InR]) \\
&+ (k4 \cdot [InR] \cdot V_{\text{cellsurface}}) \\
&- (kminus4 \cdot [cytoplasm_InR] \cdot V_{\text{cytoplasm}}) \\
\frac{d([cytoplasm_Ins_2_InR_P] \cdot V_{\text{cytoplasm}})}{dt} &= - V_{\text{cytoplasm}} \cdot (k6 \cdot [PTP1B] \cdot [cytoplasm_Ins_2_InR_P] \cdot V_{\text{cytoplasm}}) \\
&+ (k4prime \cdot [Ins_2_InR_P] \cdot V_{\text{cellsurface}}) \\
&- (kminus4prime \cdot [cytoplasm_Ins_2_InR_P] \cdot V_{\text{cytoplasm}}) \\
\frac{d([cytoplasm_Ins_InR_P] \cdot V_{\text{cytoplasm}})}{dt} &= + (k4prime \cdot [Ins_InR_P] \cdot V_{\text{cellsurface}}) \\
&- (kminus4prime \cdot [cytoplasm_Ins_InR_P] \cdot V_{\text{cytoplasm}}) \\
&- V_{\text{cytoplasm}} \cdot (k6 \cdot [PTP1B] \cdot [cytoplasm_Ins_InR_P] \cdot V_{\text{cytoplasm}}) \\
[InR_tot] &= \frac{InR.ParticleNumber + Ins_InR.ParticleNumber + Ins_InR_P.ParticleNumber + Ins_2_InR_P.ParticleNumber}{V_{\text{cytoplasm}}} \\
&+ \frac{cytoplasm_InR.ParticleNumber + cytoplasm_Ins_2_InR_P.ParticleNumber + cytoplasm_Ins_InR_P.ParticleNumber}{V_{\text{cytoplasm}}} \\
[InR_bound] &= \frac{Ins_2_InR_P.ParticleNumber + Ins_InR_P.ParticleNumber + Ins_InR.ParticleNumber}{V_{\text{cytoplasm}}} \\
[InR_active] &= \frac{Ins_2_InR_P.ParticleNumber + Ins_InR_P.ParticleNumber}{V_{\text{cytoplasm}}} \\
\frac{d([IRS1] \cdot V_{\text{cytoplasm}})}{dt} &= - V_{\text{cytoplasm}} \cdot \left(\text{cyto_vol} \cdot \frac{k7 \cdot [IRS1] \cdot ([Ins_2_InR_P] \cdot V_{\text{cellsurface}} + [Ins_InR_P] \cdot V_{\text{cellsurface}})}{IRp} \right) \\
&+ V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot kminus7a \cdot [PTP1B] \cdot [IRS1_TyrP] \cdot V_{\text{cytoplasm}}) \\
&- V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot k2psp \cdot [IRS1] \cdot [PKC_P] \cdot V_{\text{cytoplasm}}) \\
&+ V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot kminus7b \cdot [PP2A] \cdot [IRS1_PolySerP] \cdot V_{\text{cytoplasm}}) \\
&+ V_{\text{cytoplasm}} \cdot \left(\frac{k_irs1_basal_syn}{V_{\text{cytoplasm}}} \right) \\
&- V_{\text{cytoplasm}} \cdot (k_irs1_basal_degr \cdot [IRS1]) \\
&- V_{\text{cytoplasm}} \cdot \left(\frac{kcat51 \cdot [IRS1] \cdot [IKK_P] \cdot V_{\text{cytoplasm}}}{Km51 + [IRS1] \cdot V_{\text{cytoplasm}}} \right) \\
&- V_{\text{cytoplasm}} \cdot \left(\frac{kcat52 \cdot [IRS1] \cdot [JNK_P] \cdot V_{\text{cytoplasm}}}{Km52 + [IRS1] \cdot V_{\text{cytoplasm}}} \right) \\
\frac{d([IRS1_TyrP] \cdot V_{\text{cytoplasm}})}{dt} &= + V_{\text{cytoplasm}} \cdot \left(\text{cyto_vol} \cdot \frac{k7 \cdot [IRS1] \cdot ([Ins_2_InR_P] \cdot V_{\text{cellsurface}} + [Ins_InR_P] \cdot V_{\text{cellsurface}})}{IRp} \right) \\
&- V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot kminus7a \cdot [PTP1B] \cdot [IRS1_TyrP] \cdot V_{\text{cytoplasm}}) \\
&- V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot k2psp \cdot [IRS1_TyrP] \cdot [PKC_P] \cdot V_{\text{cytoplasm}}) \\
&+ V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot kminus7b \cdot [PP2A] \cdot [IRS1_TyrP_PolySerP] \cdot V_{\text{cytoplasm}}) \\
&- V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot k8 \cdot [IRS1_TyrP] \cdot [PI3K] \cdot V_{\text{cytoplasm}}) \\
&+ V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot kminus8 \cdot [IRS1_TyrP_PI3K]) \\
&- V_{\text{cytoplasm}} \cdot (k_irs1_basal_degr \cdot [IRS1_TyrP]) \\
\frac{d([IRS1_PolySerP] \cdot V_{\text{cytoplasm}})}{dt} &= + V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot k2psp \cdot [IRS1] \cdot [PKC_P] \cdot V_{\text{cytoplasm}}) \\
&- V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot kminus7b \cdot [PP2A] \cdot [IRS1_PolySerP] \cdot V_{\text{cytoplasm}}) \\
&- V_{\text{cytoplasm}} \cdot (k_irs1_polyserp_degr \cdot [IRS1_PolySerP]) \\
&+ V_{\text{cytoplasm}} \cdot \left(\frac{kcat51 \cdot [IRS1] \cdot [IKK_P] \cdot V_{\text{cytoplasm}}}{Km51 + [IRS1] \cdot V_{\text{cytoplasm}}} \right) \\
&+ V_{\text{cytoplasm}} \cdot \left(\frac{kcat52 \cdot [IRS1] \cdot [JNK_P] \cdot V_{\text{cytoplasm}}}{Km52 + [IRS1] \cdot V_{\text{cytoplasm}}} \right) \\
\frac{d([IRS1_TyrP_PolySerP] \cdot V_{\text{cytoplasm}})}{dt} &= + V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot k2psp \cdot [IRS1_TyrP] \cdot [PKC_P] \cdot V_{\text{cytoplasm}}) \\
&- V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot kminus7b \cdot [PP2A] \cdot [IRS1_TyrP_PolySerP] \cdot V_{\text{cytoplasm}}) \\
&- V_{\text{cytoplasm}} \cdot (k_irs1_polyserp_degr \cdot [IRS1_TyrP_PolySerP]) \\
[IRS_total] &= \frac{IRS1.ParticleNumber + IRS1_TyrP.ParticleNumber + IRS1_PolySerP.ParticleNumber + IRS1_TyrP_PolySerP.ParticleNumber}{V_{\text{cytoplasm}}} \\
\frac{d([PI3K] \cdot V_{\text{cytoplasm}})}{dt} &= - V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot k8 \cdot [IRS1_TyrP] \cdot [PI3K] \cdot V_{\text{cytoplasm}}) \\
&+ V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot kminus8 \cdot [IRS1_TyrP_PI3K]) \\
\frac{d([IRS1_TyrP_PI3K] \cdot V_{\text{cytoplasm}})}{dt} &= + V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot k8 \cdot [IRS1_TyrP] \cdot [PI3K] \cdot V_{\text{cytoplasm}}) \\
&- V_{\text{cytoplasm}} \cdot (\text{cyto_vol} \cdot kminus8 \cdot [IRS1_TyrP_PI3K]) \\
\frac{d([PI345P3] \cdot V_{\text{cytoplasm}})}{dt} &= + V_{\text{cytoplasm}} \cdot ((k9_basal + k9 \cdot [IRS1_TyrP_PI3K] \cdot V_{\text{cytoplasm}}) \cdot [PIP2]) \\
&- V_{\text{cytoplasm}} \cdot ((kminus9_basal + kminus9 \cdot [PTEN] \cdot V_{\text{cytoplasm}}) \cdot [PI345P3])
\end{aligned}$$

$$\begin{aligned}
\frac{d([PIP2] \cdot V_{cytoplasm})}{dt} &= -V_{cytoplasm} \cdot ((k9_{basal} + k9 \cdot [IRS1.TyrP.PI3K] \cdot V_{cytoplasm}) \cdot [PIP2]) \\
&\quad + V_{cytoplasm} \cdot ((kminus9_{basal} + kminus9 \cdot [PTEN] \cdot V_{cytoplasm}) \cdot [PI345P3]) \\
[PI345P3_{mol}] &= \frac{sc_{pip} \cdot PI345P3.ParticleNumber}{V_{cytoplasm}} \\
[PIP2_{mol}] &= \frac{sc_{pip} \cdot PIP2.ParticleNumber}{V_{cytoplasm}} \\
\frac{d([Akt] \cdot V_{cytoplasm})}{dt} &= -V_{cytoplasm} \cdot \left(k11 \cdot [Akt] \cdot \begin{cases} [PI345P3] \cdot V_{cytoplasm} - pip3_{basal} & \text{if } [PI345P3] \cdot V_{cytoplasm} > pip3_{basal} \\ 0 & \text{otherwise} \end{cases} \right) \\
&\quad + V_{cytoplasm} \cdot (kminus11 \cdot [PP2A] \cdot [Akt.P2] \cdot V_{cytoplasm}) \\
\frac{d([Akt.P2] \cdot V_{cytoplasm})}{dt} &= +V_{cytoplasm} \cdot \left(k11 \cdot [Akt] \cdot \begin{cases} [PI345P3] \cdot V_{cytoplasm} - pip3_{basal} & \text{if } [PI345P3] \cdot V_{cytoplasm} > pip3_{basal} \\ 0 & \text{otherwise} \end{cases} \right) \\
&\quad - V_{cytoplasm} \cdot (kminus11 \cdot [PP2A] \cdot [Akt.P2] \cdot V_{cytoplasm}) \\
\frac{d([PKC] \cdot V_{cytoplasm})}{dt} &= -V_{cytoplasm} \cdot \left(k12 \cdot [PKC] \cdot \begin{cases} [PI345P3] \cdot V_{cytoplasm} - pip3_{basal} & \text{if } [PI345P3] \cdot V_{cytoplasm} > pip3_{basal} \\ 0 & \text{otherwise} \end{cases} \right) \\
&\quad + V_{cytoplasm} \cdot (kminus12 \cdot [PP2A] \cdot [PKC.P] \cdot V_{cytoplasm}) \\
\frac{d([PKC.P] \cdot V_{cytoplasm})}{dt} &= +V_{cytoplasm} \cdot \left(k12 \cdot [PKC] \cdot \begin{cases} [PI345P3] \cdot V_{cytoplasm} - pip3_{basal} & \text{if } [PI345P3] \cdot V_{cytoplasm} > pip3_{basal} \\ 0 & \text{otherwise} \end{cases} \right) \\
&\quad - V_{cytoplasm} \cdot (kminus12 \cdot [PP2A] \cdot [PKC.P] \cdot V_{cytoplasm}) \\
\frac{d([AS160] \cdot V_{cytoplasm})}{dt} &= -V_{cytoplasm} \cdot (kr16a \cdot [Akt.P2] \cdot [AS160] \cdot V_{cytoplasm}) \\
&\quad + V_{cytoplasm} \cdot (kminusr16a \cdot [PP2A] \cdot [AS160.P] \cdot V_{cytoplasm}) \\
\frac{d([AS160.P] \cdot V_{cytoplasm})}{dt} &= +V_{cytoplasm} \cdot (kr16a \cdot [Akt.P2] \cdot [AS160] \cdot V_{cytoplasm}) \\
&\quad - V_{cytoplasm} \cdot (kminusr16a \cdot [PP2A] \cdot [AS160.P] \cdot V_{cytoplasm}) \\
\frac{d([cellsurface_GLUT4] \cdot V_{cellsurface})}{dt} &= +((k13_{basal} + k13 \cdot [AS160.P] \cdot V_{cytoplasm}) \cdot [cytoplasm_GLUT4] \cdot V_{cytoplasm}) \\
&\quad - (kminus13 \cdot [cellsurface_GLUT4] \cdot V_{cellsurface}) \\
\frac{d([cytoplasm_GLUT4] \cdot V_{cytoplasm})}{dt} &= -((k13_{basal} + k13 \cdot [AS160.P] \cdot V_{cytoplasm}) \cdot [cytoplasm_GLUT4] \cdot V_{cytoplasm}) \\
&\quad + (kminus13 \cdot [cellsurface_GLUT4] \cdot V_{cellsurface}) \\
\frac{d([PTEN] \cdot V_{cytoplasm})}{dt} &= -V_{cytoplasm} \cdot (k31f \cdot [PTEN] \cdot [ROS] \cdot V_{cytoplasm}) \\
&\quad + V_{cytoplasm} \cdot (k31r \cdot [PTEN_{ox}] \cdot [GSH] \cdot V_{cytoplasm}) \\
\frac{d([PTP1B_{ox}] \cdot V_{cytoplasm})}{dt} &= +V_{cytoplasm} \cdot (k30f \cdot [PTP1B] \cdot [ROS] \cdot V_{cytoplasm}) \\
&\quad - V_{cytoplasm} \cdot (k30r \cdot [PTP1B_{ox}] \cdot [GSH] \cdot V_{cytoplasm}) \\
[PTP1B_{plus_PTP1B_{ox}}] &= \frac{PTP1B.ParticleNumber + PTP1B_{ox}.ParticleNumber}{V_{cytoplasm}} \\
\frac{d([PTEN_{ox}] \cdot V_{cytoplasm})}{dt} &= +V_{cytoplasm} \cdot (k31f \cdot [PTEN] \cdot [ROS] \cdot V_{cytoplasm}) \\
&\quad - V_{cytoplasm} \cdot (k31r \cdot [PTEN_{ox}] \cdot [GSH] \cdot V_{cytoplasm}) \\
\frac{d([PTP1B] \cdot V_{cytoplasm})}{dt} &= -V_{cytoplasm} \cdot (k30f \cdot [PTP1B] \cdot [ROS] \cdot V_{cytoplasm}) \\
&\quad + V_{cytoplasm} \cdot (k30r \cdot [PTP1B_{ox}] \cdot [GSH] \cdot V_{cytoplasm}) \\
[PTEN_{plus_PTEN_{ox}}] &= \frac{PTEN.ParticleNumber + PTEN_{ox}.ParticleNumber}{V_{cytoplasm}} \\
\frac{d([ROS] \cdot V_{cytoplasm})}{dt} &= +V_{cytoplasm} \cdot (k35f \cdot [NOX]) \\
&\quad - V_{cytoplasm} \cdot (k35r \cdot [ROS] \cdot [cytoplasm_SOD2] \cdot V_{cytoplasm}) \\
&\quad + V_{cytoplasm} \cdot (k36f \cdot [Mt]) \\
&\quad + (k_{ros_perm} \cdot [extracellular_ROS] \cdot V_{extracellular}) \\
&\quad - \left(k_{ros_perm} \cdot \frac{V_{extracellular}}{V_{cytoplasm}} \cdot [ROS] \cdot V_{cytoplasm} \right) \\
\frac{d([GSH] \cdot V_{cytoplasm})}{dt} &= -V_{cytoplasm} \cdot (k38f \cdot [GSH] \cdot [ROS] \cdot V_{cytoplasm}) \\
&\quad + V_{cytoplasm} \cdot (k38r \cdot [GSSG]) \\
\frac{d([GSSG] \cdot V_{cytoplasm})}{dt} &= +V_{cytoplasm} \cdot (k38f \cdot [GSH] \cdot [ROS] \cdot V_{cytoplasm}) \\
&\quad - V_{cytoplasm} \cdot (k38r \cdot [GSSG]) \\
\frac{d([cytoplasm_SOD2] \cdot V_{cytoplasm})}{dt} &= +V_{cytoplasm} \cdot ([cytoplasm_RNA_SOD2] \cdot 1.23) \\
&\quad - V_{cytoplasm} \cdot (0.0019 \cdot [cytoplasm_SOD2]) \\
\frac{d([NOX_{inact}] \cdot V_{cytoplasm})}{dt} &= - (k34f \cdot [NOX_{inact}] \cdot V_{cytoplasm} \cdot [Ins] \cdot V_{extracellular}) \\
&\quad + V_{cytoplasm} \cdot (k34r2 \cdot [NOX]) \\
&\quad + V_{cytoplasm} \cdot (k34r3 \cdot [NOX_{deact}] \cdot [NOX_{deact}] \cdot V_{cytoplasm}) \\
\frac{d([NOX] \cdot V_{cytoplasm})}{dt} &= + (k34f \cdot [NOX_{inact}] \cdot V_{cytoplasm} \cdot [Ins] \cdot V_{extracellular}) \\
&\quad - V_{cytoplasm} \cdot (k34r1 \cdot [NOX] \cdot [NOX] \cdot V_{cytoplasm}) \\
&\quad - V_{cytoplasm} \cdot (k34r2 \cdot [NOX]) \\
\frac{d([NOX_{deact}] \cdot V_{cytoplasm})}{dt} &= +V_{cytoplasm} \cdot (k34r1 \cdot [NOX] \cdot [NOX] \cdot V_{cytoplasm}) \\
&\quad - V_{cytoplasm} \cdot (k34r3 \cdot [NOX_{deact}] \cdot [NOX_{deact}] \cdot V_{cytoplasm}) \\
[NOX_{total}] &= \frac{NOX_{inact}.ParticleNumber + NOX.ParticleNumber + NOX_{deact}.ParticleNumber}{V_{cytoplasm}} \\
\frac{d([JNK.P] \cdot V_{cytoplasm})}{dt} &= +V_{cytoplasm} \cdot (k42f \cdot \alpha_{ox} \cdot [JNK] \cdot [ROS] \cdot V_{cytoplasm}) \\
&\quad - V_{cytoplasm} \cdot (k42r \cdot [JNK.P] \cdot [DUSP] \cdot V_{cytoplasm}) \\
\frac{d([IKK.P] \cdot V_{cytoplasm})}{dt} &= +V_{cytoplasm} \cdot (k43f \cdot [IKK] \cdot [ROS] \cdot V_{cytoplasm}) \\
&\quad - V_{cytoplasm} \cdot (k43r \cdot [IKK.P] \cdot [DUSP] \cdot V_{cytoplasm}) \\
\frac{d([JNK] \cdot V_{cytoplasm})}{dt} &= -V_{cytoplasm} \cdot (k42f \cdot \alpha_{ox} \cdot [JNK] \cdot [ROS] \cdot V_{cytoplasm}) \\
&\quad + V_{cytoplasm} \cdot (k42r \cdot [JNK.P] \cdot [DUSP] \cdot V_{cytoplasm}) \\
[JNK_{plus_JNK.P}] &= \frac{JNK.ParticleNumber + JNK.P.ParticleNumber}{V_{cytoplasm}} \\
\frac{d([IKK] \cdot V_{cytoplasm})}{dt} &= -V_{cytoplasm} \cdot (k43f \cdot [IKK] \cdot [ROS] \cdot V_{cytoplasm}) \\
&\quad + V_{cytoplasm} \cdot (k43r \cdot [IKK.P] \cdot [DUSP] \cdot V_{cytoplasm}) \\
[IKK_{plus_IKK.P}] &= \frac{IKK.ParticleNumber + IKK.P.ParticleNumber}{V_{cytoplasm}} \\
\frac{d([DUSP] \cdot V_{cytoplasm})}{dt} &= -V_{cytoplasm} \cdot (k32f \cdot [DUSP] \cdot [ROS] \cdot V_{cytoplasm}) \\
&\quad + V_{cytoplasm} \cdot (k32r \cdot [DUSP_{ox}] \cdot [GSH] \cdot V_{cytoplasm})
\end{aligned}$$

