

Acetylation ODEs

Ac-CoA1

PDHA1 + ACSS1 - CS

$$\begin{aligned} \frac{dAc-CoA1}{dt} = & \frac{K_{cat,PDHA1} \times [PDHA1] \times [Pyruvate] \times [NAD^+] \times [CoA1]}{(K_{m,PDHA1,Pyruvate} + [Pyruvate])(K_{m,PDHA1,NAD^+} + [NAD^+])(K_{m,PDHA1,CoA1} + [CoA1])(1 + \frac{[Ac-CoA1]}{K_i})^3} \\ & + \frac{K_{cat,ACSS1} \times [ACSS1] \times [Acetate] \times [CoA1]}{(K_{m,ACSS1,Acetate} + [Acetate])(K_{m,ACSS1,CoA1} + [CoA1])(1 + \frac{[Ac-CoA1]}{K_i})^2} \\ & - \frac{K_{cat,CS} \times [CS] \times [OXA] \times [Ac-CoA1]}{(K_{m,CS,OXA} + [OXA])(K_{m,CS,Ac-CoA1} + [Ac-CoA1])(1 + \frac{[Citrate1]}{K_i})^2} \end{aligned}$$

Citrate1

CS - ACO2 - CTP

$$\begin{aligned} \frac{dCitrate1}{dt} = & \frac{K_{cat,CS} \times [CS] \times [Oxaloacetate] \times [Ac-CoA1]}{(K_{m,CS,Oxaloacetate} + [Oxaloacetate])(K_{m,CS,Ac-CoA1} + [Ac-CoA1])(1 + \frac{[Citrate1]}{K_i})^2} \\ & - \left(\frac{K_{cat,ACO21} \times [ACO2] \times [Citrate1]}{(K_{m,ACO2,Citrate} + [Citrate1])(1 + \frac{[Isocitrate]}{K_i})} - \frac{K_{cat,ACO22} \times [ACO2] \times [Isocitrate]}{(K_{m,ACO2,Isocitrate} + [Isocitrate])(1 + \frac{[Citrate1]}{K_i})} \right) \\ & - \frac{K_{cat,CTP} \times [CTP] \times [Citrate1]}{(K_{m,CTP,Citrate} + [Citrate1])(1 + \frac{[Citrate2]}{K_i})} \end{aligned}$$

Citrate2

CTP - ACLY

$$\begin{aligned} \frac{dCitrate2}{dt} = & \frac{K_{cat,CTP} \times [CTP] \times [Citrate1]}{(K_{m,CTP,Citrate} + [Citrate1])(1 + \frac{[Citrate2]}{K_i})} \\ & - \frac{K_{cat,ACLY} \times [ACLY] \times [Citrate2]}{(K_{m,ACLY,Citrate} + [Citrate2])(1 + \frac{[Ac-CoA2]}{K_i})} \end{aligned}$$

Isocitrate

ACO2 - IDH2

$$\begin{aligned} \frac{dIsocitrate}{dt} = & \left(\frac{K_{cat,ACO21} \times [ACO2] \times [Citrate]}{(K_{m,ACO2,Citrate} + [Citrate])(1 + \frac{[Isocitrate]}{K_i})} - \frac{K_{cat,ACO22} \times [ACO2] \times [Isocitrate]}{(K_{m,ACO2,Isocitrate} + [Isocitrate])(1 + \frac{[Citrate1]}{K_i})} \right) \\ & - \frac{K_{cat,IDH2} \times [IDH2] \times [Isocitrate] \times [NAD^+]}{(K_{m,IDH2,Isocitrate} + [Isocitrate])(K_{m,IDH2,NAD^+} + [NAD^+])(1 + \frac{[Alpha-KG]}{K_i})^2} \end{aligned}$$

Alpha-KG

IDH2 - OGDH

$$\begin{aligned} \frac{dAlphaKG}{dt} = & \frac{K_{cat,IDH2} \times [IDH2] \times [Isocitrate] \times [NAD^+]}{(K_{m,IDH2,Isocitrate} + [Isocitrate])(K_{m,IDH2,NAD^+} + [NAD^+])(1 + \frac{[Alpha-KG]}{K_i})^2} \\ & - \frac{K_{cat,OGDH} \times [OGDH] \times [AlphaKG] \times [NAD^+]}{(K_{m,OGDH,AlphaKG} + [AlphaKG])(K_{m,OGDH,NAD^+} + [NAD^+])(1 + \frac{[Succinyl-CoA]}{K_i})^2} \end{aligned}$$

Succinyl-CoA

OGDH - SUDG1

$$\frac{d\text{Succinyl-CoA}}{dt} = \frac{K_{cat,OGDH} \times [OGDH] \times [\text{Alpha-KG}] \times [NAD^+]}{(K_{m,OGDH,\text{Alpha-KG}} + [\text{Alpha-KG}])(K_{m,OGDH,NAD^+} + [NAD^+])(1 + \frac{[\text{Succinyl-CoA}]}{K_i})^2} - \frac{K_{cat,SUDG1} \times [SUDG1] \times [\text{Succinyl-CoA}]}{(K_{m,SUDG1,\text{Succinyl-CoA}} + [\text{Succinyl-CoA}])(1 + \frac{[\text{Succinate}]}{K_i})}$$

Succinate

SUDG1 - SDHA

Did NOT take FAD^+ and $FADH_2$ into account!

$$\frac{d\text{Succinate}}{dt} = \frac{K_{cat,SUDG1} \times [SUDG1] \times [\text{Succinyl-CoA}]}{(K_{m,SUDG1,\text{Succinyl-CoA}} + [\text{Succinyl-CoA}])(1 + \frac{[\text{Succinate}]}{K_i})} - \frac{K_{cat,SDHA} \times [SDHA] \times [\text{Succinate}]}{(K_{m,SDHA,\text{Succinate}} + [\text{Succinate}])(1 + \frac{[\text{Fumarate}]}{K_i})}$$

Fumarate

SDHA - FH

$$\frac{d\text{Fumarate}}{dt} = \frac{K_{cat,SDHA} \times [SDHA] \times [\text{Succinate}]}{(K_{m,SDHA,\text{Succinate}} + [\text{Succinate}])(1 + \frac{[\text{Fumarate}]}{K_i})} - \frac{K_{cat,FH} \times [FH] \times [\text{Fumarate}]}{(K_{m,FH,\text{Fumarate}} + [\text{Fumarate}])(1 + \frac{[\text{Malate}]}{K_i})}$$

Malate

FH - MDH2

$$\frac{d\text{Malate}}{dt} = \frac{K_{cat,FH} \times [FH] \times [\text{Fumarate}]}{(K_{m,FH,\text{Fumarate}} + [\text{Fumarate}])(1 + \frac{[\text{Malate}]}{K_i})} - \frac{K_{cat,MDH2} \times [MDH2] \times [\text{Malate}]}{(K_{m,MDH2,\text{Malate}} + [\text{Malate}])(1 + \frac{[\text{Oxaloacetate}]}{K_i})}$$

Oxaloacetate

MDH2 + PC - CS

$$\begin{aligned} \frac{d\text{Oxaloacetate}}{dt} = & \frac{K_{cat,MDH2} \times [MDH2] \times [\text{Malate}]}{(K_{m,MDH2,\text{Malate}} + [\text{Malate}])(1 + \frac{[\text{Oxaloacetate}]}{K_i})} \\ & + \frac{K_{cat,PC} \times [PC] \times [\text{Pyruvate}] \times [HCO_3^-]}{(K_{m,PC,\text{Pyruvate}} + [\text{Pyruvate}])(K_{m,PC,HCO_3^-} + [HCO_3^-])(1 + \frac{[\text{Oxaloacetate}]}{K_i})^2} \\ & - \frac{K_{cat,CS} \times [CS] \times [\text{Oxaloacetate}] \times [Ac-CoA]}{(K_{m,CS,\text{Oxaloacetate}} + [OXA])(K_{m,CS,\text{Ac-CoA}} + [Ac-CoA])(1 + \frac{[\text{Citrate}]}{K_i})^2} \end{aligned}$$

Ac-CoA2

ACLY + ACSS2 - ACOT12 - FASN - HMGCS1 - KAT2A

No product inhibition for reactions going into end products (pools).

$$\begin{aligned} \frac{dAc - CoA2}{dt} = & \frac{K_{cat,ACLY} \times [ACLY] \times [Citrate2] \times [CoA2]}{(K_{m,ACLY,Citrate} + [Citrate2])(K_{m,ACLY,CoA2} + [CoA2])(1 + \frac{[Ac-CoA2]}{K_i})^2} \\ & + \frac{K_{cat,ACSS2} \times [ACSS2] \times [Acetate] \times [CoA2]}{(K_{m,ACSS2,Acetate} + [Acetate])(K_{m,ACSS2,CoA} + [CoA2])} \\ & - \frac{K_{cat,ACOT12} \times [ACOT12] \times [Ac - CoA2]}{(K_{m,ACOT12,Ac-CoA2} + [Ac - CoA2])(1 + \frac{[Acetate]}{K_i})(1 + \frac{[CoA2]}{K_i})} \\ & - 2 \times \frac{k_{cat,FASN} \times [FASN] \times [Ac - CoA2]^2 \times [HCO_3^-] \times [NADPH]^2}{(K_{m,FASN,AcCoA2} + [Ac - CoA2])^2 (K_{m,FASN,HCO_3^-} + [HCO_3^-])(K_{m,FASN,NADPH} + [NADPH])^2} \\ & - 3 \times \frac{K_{cat,HMGCS1} \times [HMGCS1] \times [Ac - CoA2]^3}{(K_{m,ACAT2,Ac-CoA2} + [Ac - CoA2])^2 (K_{m,HMGCS1,Ac-CoA2} + [Ac - CoA2])} \\ & - \frac{K_{cat,KAT2A} \times [KAT2A] \times [Ac - CoA2]}{K_{m,KAT2A,Ac-CoA2} + [Ac - CoA2]} \end{aligned}$$

Acetate

SLC16A3 + HDAC1 + HDAC2 + HDAC3 + ACOT12 - ACSS1 - ACSS2

HDACs still need some changes.

$$\begin{aligned} \frac{dAcetate}{dt} = & V_{max,SLC16A3} \times \left[\frac{[Acetate]_{blood}}{[Acetate]_{blood} + K_{T,Acetate}} - \frac{[Acetate]}{[Acetate] + K_{T,Acetate}} \right] \\ & + \frac{K_{cat,HDAC1} \times [HDAC1]}{\frac{[Acetate]}{K_i}} \\ & + \frac{K_{cat,HDAC2} \times [HDAC2]}{\frac{[Acetate]}{K_i}} \\ & + \frac{K_{cat,HDAC3} \times [HDAC3]}{\frac{[Acetate]}{K_i}} \\ & + \frac{K_{cat,ACOT12} \times [ACOT12] \times [Ac - CoA2]}{(K_{m,ACOT12,Ac-CoA2} + [Ac - CoA2])(1 + \frac{[Acetate]}{K_i})} \\ & - \frac{K_{cat,ACSS1} \times [ACSS1] \times [Acetate] \times [CoA1]}{(K_{m,ACSS1,Acetate} + [Acetate])(K_{m,ACSS1,CoA} + [CoA1])(1 + \frac{[Ac-CoA1]}{K_i})^2} \\ & - \frac{K_{cat,ACSS2} \times [ACSS2] \times [Acetate] \times [CoA2]}{(K_{m,ACSS2,Acetate} + [Acetate])(K_{m,ACSS2,CoA} + [CoA2])(1 + \frac{[Ac-CoA2]}{K_i})^2} \end{aligned}$$

NAD^+

v_NAD - PDHA1 - IDH2 - OGDH - MDH2

$$\begin{aligned}
 \frac{dNAD^+}{dt} = & \frac{V_{ATP,ss}}{n_{ATP:NAD^+}} \times \frac{[NADH]}{[NADH]_{ss}} \\
 & - \frac{K_{cat,PDHA1} \times [PDHA1] \times [Pyruvate] \times [NAD^+] \times [CoA1]}{(K_{m,PDHA1,Pyruvate} + [Pyruvate])(K_{m,PDHA1,NAD^+} + [NAD^+])(K_{m,PDHA1,CoA1} + [CoA1])(1 + \frac{[Ac-CoA1]}{K_i})^3} \\
 & - \frac{K_{cat,IDH2} \times [IDH2] \times [Isocitrate] \times [NAD^+]}{(K_{m,IDH2,Isocitrate} + [Isocitrate])(K_{m,IDH2,NAD^+} + [NAD^+])(1 + \frac{[Alpha-KG]}{K_i})^2} \\
 & - \frac{K_{cat,OGDH} \times [OGDH] \times [AlphaKG] \times [NAD^+]}{(K_{m,OGDH,AlphaKG} + [AlphaKG])(K_{m,OGDH,NAD^+} + [NAD^+])(1 + \frac{[Succinyl-CoA]}{K_i})^2} \\
 & - \frac{K_{cat,MDH2} \times [MDH2] \times [Malate]}{(K_{m,MDH2,Malate} + [Malate])(1 + \frac{[Oxaloacetate]}{K_i})}
 \end{aligned}$$