Supplementary material

1. The chemical reactions

Here we list all of the enzymatic reactions included in the mathematical model. For brevity, we introduce the following notation.

E:	free *hexokinase I* enzyme,	G:	glucose,	T:	ATP,
$G6$:	$G6P$,	P:	P_i,	D:	ADP,

k_0 : catalytic constant rate,

k^G, k^T, k^{G6}, k^P : adsorption constant rates of glucose, ATP, $G6P$, and P_i on the N-binding sites, respectively.

$k^{-G}, k^{-T}, k^{-G6}, k^{-P}$: desorption constant rates of glucose, ATP, $G6P$, and P_i from the N-binding sites, respectively.

k_G, k_T, k_{G6}, k_P : adsorption constant rates of glucose, ATP, $G6P$, and P_i on the C-binding sites, respectively.

$k_{-G}, k_{-T}, k_{-G6}, k_{-P}$: desorption constant rates of glucose, ATP, $G6P$, and P_i from the C-binding sites, respectively.

k^P_{G6}, k^P_{-G6} : adsorption and desorption constant rates of $G6P$ on and from the C-binding site of complexes of enzyme with one P_i molecule bound at the N-binding site.

${}_yE^x_z$: an enzyme complex with an x molecule bound at its N-binding site, a y molecule bound at its C-site, and a z molecule bound at its C-site.

$$E+G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^{G}E, \qquad E+G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}_{G}E, \qquad E+T \underset{k^{-T}}{\overset{k^T}{\rightleftharpoons}} E^T, \qquad E+T \underset{k_{-T}}{\overset{k_T}{\rightleftharpoons}} E_T,$$

$$E+G6 \underset{k^{-G6}}{\overset{k^{G6}}{\rightleftharpoons}} E^{G6}, \qquad E+G6 \underset{k_{-G6}}{\overset{k_{G6}}{\rightleftharpoons}} E_{G6}, \qquad E+P \underset{k^{-P}}{\overset{k^P}{\rightleftharpoons}} E^P, \qquad E+P \underset{k_{-P}}{\overset{k_P}{\rightleftharpoons}} E_P,$$

$$\boxed{{}^{G}E}+G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^{G}_{G}E, \qquad {}^{G}E+T \underset{k^{-T}}{\overset{k^T}{\rightleftharpoons}} {}^{G}E^T, \qquad {}^{G}E+T \underset{k_{-T}}{\overset{k_T}{\rightleftharpoons}} {}^{G}E_T, \qquad {}^{G}E+G6 \underset{k^{-G6}}{\overset{k^{G6}}{\rightleftharpoons}} {}^{G}E_{G6},$$

$${}^{G}E+G6 \underset{k_{-G6}}{\overset{k_{G6}}{\rightleftharpoons}} {}^{G}E_{G6}, \qquad {}^{G}E+P \underset{k^{-P}}{\overset{k^P}{\rightleftharpoons}} {}^{G}E^P, \qquad {}^{G}E+P \underset{k_{-P}}{\overset{k_P}{\rightleftharpoons}} {}^{G}E_P, \qquad \boxed{{}_{G}E}+G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^{G}_{G}E,$$

$${}^{G}E+T \underset{k^{-T}}{\overset{k^T}{\rightleftharpoons}} {}^{G}E^T, \qquad {}^{G}E+T \underset{k_{-T}}{\overset{k_T}{\rightleftharpoons}} {}^{G}E_T, \qquad {}^{G}E+G6 \underset{k^{-G6}}{\overset{k^{G6}}{\rightleftharpoons}} {}^{G}E^{G6}, \qquad {}^{G}E+G6 \underset{k_{-G6}}{\overset{k_{G6}}{\rightleftharpoons}} {}^{G}E_{G6},$$

$${}^{G}E+P \underset{k^{-P}}{\overset{k^P}{\rightleftharpoons}} {}^{G}E^P, \qquad {}^{G}E+P \underset{k_{-P}}{\overset{k_P}{\rightleftharpoons}} {}^{G}E_P, \qquad \boxed{E^T}+G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^{G}E^T, \qquad E^T+G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}_{G}E^T,$$

$$E^T+T \underset{k_{-T}}{\overset{k_T}{\rightleftharpoons}} E^T_T, \qquad E^T+G6 \underset{k_{-G6}}{\overset{k_{G6}}{\rightleftharpoons}} E^T_{G6}, \qquad E^T+P \underset{k_{-P}}{\overset{k_P}{\rightleftharpoons}} E^T_P, \qquad \boxed{E_T}+G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^{G}E_T,$$

$$E_T + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}_GE_T, \quad E_T + T \underset{k^{-T}}{\overset{k^T}{\rightleftharpoons}} E_T^T, \quad E_T + G6 \underset{k^{-G6}}{\overset{k^{G6}}{\rightleftharpoons}} E_T^{G6}, \quad E_T + P \underset{k^{-P}}{\overset{k^P}{\rightleftharpoons}} E_T^P,$$

$$\boxed{E^{G6}} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^GE^{G6}, \quad E^{G6} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}_GE^{G6}, \quad \boxed{E_{G6}} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^GE_{G6}, \quad E_{G6} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}_GE_{G6},$$

$$E_{G6} + T \underset{k^{-T}}{\overset{k^T}{\rightleftharpoons}} E_{G6}^T, \quad E_{G6} + P \underset{k^{-P}}{\overset{k^P}{\rightleftharpoons}} E_{G6}^P, \quad \boxed{E^P} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^GE^P, \quad E^P + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}_GE^P,$$

$$E^P + T \underset{k_{-T}}{\overset{k_T}{\rightleftharpoons}} E_T^P, \quad E^P + G6 \underset{k_{-G6}^P}{\overset{k_{G6}^P}{\rightleftharpoons}} E_{G6}^P, \quad E^P + P \underset{k_{-P}}{\overset{k_P}{\rightleftharpoons}} E_P^P, \quad \boxed{E_P} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^GE_P,$$

$$E_P + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}_GE_P, \quad E_P + T \underset{k^{-T}}{\overset{k^T}{\rightleftharpoons}} E_P^T, \quad E_P + G6 \underset{k^{-G6}}{\overset{k^{G6}}{\rightleftharpoons}} E_P^{G6}, \quad E_P + P \underset{k^{-P}}{\overset{k^P}{\rightleftharpoons}} E_P^P,$$

$$\boxed{{}^GE^T} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^G_GE^T, \quad {}^GE^T + T \underset{k_{-T}}{\overset{k_T}{\rightleftharpoons}} {}^GE_T^T, \quad {}^GE^T + G6 \underset{k_{-G6}}{\overset{k_{G6}}{\rightleftharpoons}} {}^GE_{G6}^T, \quad {}^GE^T + P \underset{k_{-P}}{\overset{k_P}{\rightleftharpoons}} {}^GE_P^T,$$

$$\boxed{{}^GE^{G6}} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^G_GE^{G6}, \quad \boxed{{}^GE^P} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^G_GE^P, \quad {}^GE^P + T \underset{k_{-T}}{\overset{k_T}{\rightleftharpoons}} {}^GE_T^P, \quad {}^GE^P + G6 \underset{k_{-G6}^P}{\overset{k_{G6}^P}{\rightleftharpoons}} {}^GE_{G6}^P,$$

$${}^GE^P + P \underset{k_{-P}}{\overset{k_P}{\rightleftharpoons}} {}^GE_P^P, \quad \boxed{{}^G_GE} + T \underset{k^{-T}}{\overset{k^T}{\rightleftharpoons}} {}^G_GE^T, \quad {}^G_GE + T \underset{k_{-T}}{\overset{k_T}{\rightleftharpoons}} {}^G_GE_T, \quad {}^G_GE + G6 \underset{k^{-G6}}{\overset{k^{G6}}{\rightleftharpoons}} {}^G_GE^{G6},$$

$${}^G_GE + G6 \underset{k_{-G6}}{\overset{k_{G6}}{\rightleftharpoons}} {}^G_GE_{G6}, \quad {}^G_GE + P \underset{k^{-P}}{\overset{k^P}{\rightleftharpoons}} {}^G_GE^P, \quad {}^G_GE + P \underset{k_{-P}}{\overset{k_P}{\rightleftharpoons}} {}^G_GE_P, \quad \boxed{{}^GE_T} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^G_GE_T,$$

$${}^GE_T + T \underset{k^{-T}}{\overset{k^T}{\rightleftharpoons}} {}^GE_T^T, \quad {}^GE_T + G6 \underset{k^{-G6}}{\overset{k^{G6}}{\rightleftharpoons}} {}^GE_T^{G6}, \quad {}^GE_T + P \underset{k^{-P}}{\overset{k^P}{\rightleftharpoons}} {}^GE_T^P, \quad \boxed{{}^GE_{G6}} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^G_GE_{G6},$$

$${}^GE_{G6} + T \underset{k^{-T}}{\overset{k^T}{\rightleftharpoons}} {}^GE_{G6}^T, \quad {}^GE_{G6} + P \underset{k^{-P}}{\overset{k^P}{\rightleftharpoons}} {}^GE_{G6}^P, \quad \boxed{{}^GE_P} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^G_GE_P, \quad {}^GE_P + T \underset{k^{-T}}{\overset{k^T}{\rightleftharpoons}} {}^GE_P^T,$$

$${}^GE_P + G6 \underset{k^{-G6}}{\overset{k^{G6}}{\rightleftharpoons}} {}^GE_P^{G6}, \quad {}^GE_P + P \underset{k^{-P}}{\overset{k^P}{\rightleftharpoons}} {}^GE_P^P, \quad \boxed{{}_GE^T} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^G_GE^T, \quad {}_GE^T + T \underset{k_{-T}}{\overset{k_T}{\rightleftharpoons}} {}_GE_T^T,$$

$${}_GE^T + G6 \underset{k_{-G6}}{\overset{k_{G6}}{\rightleftharpoons}} {}_GE_{G6}^T, \quad {}_GE^T + P \underset{k_{-P}}{\overset{k_P}{\rightleftharpoons}} {}_GE_P^T, \quad \boxed{E_T^T} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^GE_T^T, \quad E_T^T + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}_GE_T^T,$$

$$\boxed{E_{G6}^T} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^GE_{G6}^T, \quad E_{G6}^T + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}_GE_{G6}^T, \quad \boxed{E_P^T} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^GE_P^T, \quad E_P^T + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}_GE_P^T,$$

$$\boxed{{}_GE^{G6}} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^G_GE^{G6}, \quad \boxed{E_T^{G6}} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^GE_T^{G6}, \quad E_T^{G6} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}_GE_T^{G6}, \quad \boxed{E_P^{G6}} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^GE_P^{G6},$$

$$E_P^{G6} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}_GE_P^{G6}, \quad \boxed{{}_GE^P} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^G_GE^P, \quad {}_GE^P + T \underset{k_{-T}}{\overset{k_T}{\rightleftharpoons}} {}_GE_T^P, \quad {}_GE^P + G6 \underset{k_{-G6}^P}{\overset{k_{G6}^P}{\rightleftharpoons}} {}_GE_{G6}^P,$$

$${}_GE^P + P \underset{k_{-P}}{\overset{k_P}{\rightleftharpoons}} {}_GE_P^P, \quad \boxed{E_T^P} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^GE_T^P, \quad E_T^P + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}_GE_T^P, \quad \boxed{E_{G6}^P} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^GE_{G6}^P,$$

$$E_{G6}^P + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}_GE_{G6}^P, \quad \boxed{E_P^P} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^GE_P^P, \quad E_P^P + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}_GE_P^P, \quad \boxed{{}_GE_T} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^G_GE_T,$$

$${}^GE_T + T \underset{k^{-T}}{\overset{k^T}{\rightleftharpoons}} {}_GE_T^T, \quad {}^GE_T + G6 \underset{k^{-G6}}{\overset{k^{G6}}{\rightleftharpoons}} {}^GE_T^{G6}, \quad {}^GE_T + P \underset{k^{-P}}{\overset{k^P}{\rightleftharpoons}} {}^GE_T^P, \quad \boxed{{}_GE_{G6}} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^G_GE_{G6},$$

$${}_GE_{G6} + T \underset{k^{-T}}{\overset{k^T}{\rightleftharpoons}} {}_GE_{G6}^T, \quad {}_GE_{G6} + P \underset{k^{-P}}{\overset{k^P}{\rightleftharpoons}} {}_GE_{G6}^P, \quad \boxed{{}_GE_P} + G \underset{k^{-G}}{\overset{k^G}{\rightleftharpoons}} {}^G_GE_P, \quad {}_GE_P + T \underset{k^{-T}}{\overset{k^T}{\rightleftharpoons}} {}_GE_P^T,$$

$$
{}_GE_P + G6 \underset{k^{-G6}}{\overset{k^{G6}}{\rightleftharpoons}} {}_GE_P^{G6}, \quad {}_GE_P + P \underset{k^{-P}}{\overset{k^{P}}{\rightleftharpoons}} {}_GE_P^{P}, \quad \boxed{{}^G_GE^T} + T \underset{k_{-T}}{\overset{k_T}{\rightleftharpoons}} {}^G_GE^T_T, \quad {}^G_GE^T + G6 \underset{k_{-G6}}{\overset{k_{G6}}{\rightleftharpoons}} {}^G_GE^T_{G6},
$$

$$
{}^G_GE^T + P \underset{k_{-P}}{\overset{k_P}{\rightleftharpoons}} {}^G_GE^T_P, \quad \boxed{{}^GE^T_T} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^G_GE^T_T, \quad \boxed{{}^GE^T_{G6}} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^G_GE^T_{G6}, \quad \boxed{{}^GE^T_P} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^G_GE^T_P,
$$

$$
\boxed{{}^GE^{G6}_T} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^G_GE^{G6}_T, \quad \boxed{{}^GE^{G6}_P} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^G_GE^{G6}_P, \quad \boxed{{}^G_GE^P} + T \underset{k_{-T}}{\overset{k_T}{\rightleftharpoons}} {}^G_GE^P_T, \quad {}^G_GE^P + G6 \underset{k^P_{-G6}}{\overset{k^P_{G6}}{\rightleftharpoons}} {}^G_GE^P_{G6},
$$

$$
{}^G_GE^P + P \underset{k_{-P}}{\overset{k_P}{\rightleftharpoons}} {}^G_GE^P_P, \quad \boxed{{}^GE^P_T} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^G_GE^P_T, \quad \boxed{{}^GE^P_{G6}} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^G_GE^P_{G6}, \quad \boxed{{}^GE^P_P} + G \underset{k_{-G}}{\overset{k_G}{\rightleftharpoons}} {}^G_GE^P_P,
$$

$$
\boxed{{}^G_GE_T} + T \underset{k^{-T}}{\overset{k^T}{\rightleftharpoons}} {}^G_GE^T_T, \quad {}^G_GE_T + G6 \underset{k^{-G6}}{\overset{k^{G6}}{\rightleftharpoons}} {}^G_GE^{G6}_T, \quad {}^G_GE_T + P \underset{k^{-P}}{\overset{k^{P}}{\rightleftharpoons}} {}^G_GE^P_T, \quad \boxed{{}^GE^T_T} + G \underset{k^{-G}}{\overset{k^{G}}{\rightleftharpoons}} {}^G_GE^T_T,
$$

$$
\boxed{{}^GE^{G6}_T} + G \underset{k^{-G}}{\overset{k^{G}}{\rightleftharpoons}} {}^G_GE^{G6}_T, \quad \boxed{{}^GE^P_T} + G \underset{k^{-G}}{\overset{k^{G}}{\rightleftharpoons}} {}^G_GE^P_T, \quad \boxed{{}^G_GE_{G6}} + T \underset{k^{-T}}{\overset{k^{T}}{\rightleftharpoons}} {}^G_GE^T_{G6}, \quad {}^G_GE_{G6} + P \underset{k^{-P}}{\overset{k^{P}}{\rightleftharpoons}} {}^G_GE^P_{G6},
$$

$$
\boxed{{}^GE^T_{G6}} + G \underset{k^{-G}}{\overset{k^{G}}{\rightleftharpoons}} {}^G_GE^T_{G6}, \quad \boxed{{}^GE^P_{G6}} + G \underset{k^{-G}}{\overset{k^{G}}{\rightleftharpoons}} {}^G_GE^P_{G6}, \quad \boxed{{}^G_GE_P} + T \underset{k^{-T}}{\overset{k^{T}}{\rightleftharpoons}} {}^G_GE^T_P, \quad {}^G_GE_P + G6 \underset{k^{-G6}}{\overset{k^{G6}}{\rightleftharpoons}} {}^G_GE^{G6}_P,
$$

$$
\boxed{{}^GE^T_P} + G \underset{k^{-G}}{\overset{k^{G}}{\rightleftharpoons}} {}^G_GE^T_P, \quad \boxed{{}^GE^{G6}_P} + G \underset{k^{-G}}{\overset{k^{G}}{\rightleftharpoons}} {}^G_GE^{G6}_P, \quad \boxed{{}^GE^P_P} + G \underset{k^{-G}}{\overset{k^{G}}{\rightleftharpoons}} {}^G_GE^P_P.
$$

Note no substrate can bind to the $\boxed{{}^G_GE^{G6}}$ complex. Here are all reactions that produce product

$$
{}_GE_T \xrightarrow{k_0} E + G6 + D, \quad {}^G_GE_T \xrightarrow{k_0} {}^GE + G6 + D, \quad {}_GE^T_T \xrightarrow{k_0} E^T + G6 + D,
$$

$$
{}_GE^{G6}_T \xrightarrow{k_0} E^{G6} + G6 + D, \quad {}_GE^P_T \xrightarrow{k_0} E^P + G6 + D, \quad {}^G_GE^T_T \xrightarrow{k_0} {}^GE^T + G6 + D,
$$

$$
{}^G_GE^{G6}_T \xrightarrow{k_0} {}^GE^{G6} + G6 + D, \quad {}^G_GE^P_T \xrightarrow{k_0} {}^GE^P + G6 + D,
$$

2. The model equations

We now list the complete set of governing equations for the model. The notation used is explained in the paper. Information on how these equations are constructed can also be found in the paper.

$$
\begin{aligned}
\frac{d[E]}{dt} = {} & k_0[{}_GE_T] + k^{-G}[{}^GE] + k_{-G}[{}_GE] + k^{-T}[E^T] + k_{-T}[E_T] + k^{-G6}[E^{G6}] \\
& + k_{-G6}[E_{G6}] + k^{-P}[E^P] + k_{-P}[E_P] - [E]\left((k^G + k_G)[G]\right. \\
& \left. +(k^T + k_T)[T] + (k^{G6} + k_{G6})[G6] + (k^P + k_P)[P]\right), \qquad (1)
\end{aligned}
$$

$$
\begin{aligned}
\frac{d[G]}{dt} &= k^{-G}([{}^{G}E] + [{}^{G}E^{T}] + [{}^{G}E^{G6}] + [{}^{G}E^{P}] + [{}^{G}E_{T}] + [{}^{G}E_{G6}] + [{}^{G}E_{P}] + [{}^{G}E_{T}^{T}] \\
&\quad + [{}^{G}E_{G6}^{T}] + [{}^{G}E_{P}^{T}] + [{}^{G}E_{T}^{G6}] + [{}^{G}E_{P}^{G6}] + [{}^{G}E_{T}^{P}] + [{}^{G}E_{G6}^{P}] + [{}^{G}E_{P}^{P}]) \\
&+ k_{-G}([{}_{G}E] + [{}_{G}E_{T}] + [{}_{G}E_{G6}] + [{}_{G}E_{P}] + [{}_{G}E^{T}] + [{}_{G}E^{G6}] + [{}_{G}E^{P}] + [{}_{G}E_{T}^{T}] \\
&\quad + [{}_{G}E_{T}^{G6}] + [{}_{G}E_{T}^{P}] + [{}_{G}E_{G6}^{T}] + [{}_{G}E_{G6}^{P}] + [{}_{G}E_{P}^{T}] + [{}_{G}E_{P}^{G6}] + [{}_{G}E_{P}^{P}]) \\
&+ (k^{-G} + k_{-G})([{}_{G}^{G}E] + [{}_{G}^{G}E^{T}] + [{}_{G}^{G}E^{G6}] + [{}_{G}^{G}E^{P}] + [{}_{G}^{G}E_{T}] + [{}_{G}^{G}E_{G6}] + [{}_{G}^{G}E_{P}] \\
&\quad + [{}_{G}^{G}E_{T}^{T}] + [{}_{G}^{G}E_{G6}^{T}] + [{}_{G}^{G}E_{P}^{T}] + [{}_{G}^{G}E_{T}^{G6}] + [{}_{G}^{G}E_{P}^{G6}] + [{}_{G}^{G}E_{T}^{P}] + [{}_{G}^{G}E_{G6}^{P}] + [{}_{G}^{G}E_{P}^{P}]) \\
&- [G]((k^{G} + k_{G})([E] + [E^{T}] + [E_{T}] + [E^{G6}] + [E_{G6}] + [E^{P}] + [E_{P}] \\
&\quad + [E_{T}^{T}] + [E_{G6}^{T}] + [E_{P}^{T}] + [E_{T}^{G6}] + [E_{P}^{G6}] + [E_{T}^{P}] + [E_{G6}^{P}] + [E_{P}^{P}]) \\
&\quad + k^{G}([{}_{G}E] + [{}_{G}E^{T}] + [{}_{G}E^{G6}] + [{}_{G}E^{P}] + [{}_{G}E_{T}] + [{}_{G}E_{G6}] + [{}_{G}E_{P}] + [{}_{G}E_{T}^{T}] \\
&\quad + [{}_{G}E_{T}^{G6}] + [{}_{G}E_{T}^{P}] + [{}_{G}E_{G6}^{T}] + [{}_{G}E_{G6}^{P}] + [{}_{G}E_{P}^{T}] + [{}_{G}E_{P}^{G6}] + [{}_{G}E_{P}^{P}]) \\
&\quad + k_{G}([{}^{G}E] + [{}^{G}E^{T}] + [{}^{G}E^{G6}] + [{}^{G}E^{P}] + [{}^{G}E_{T}] + [{}^{G}E_{G6}] + [{}^{G}E_{P}] + [{}^{G}E_{T}^{T}] \\
&\quad + [{}^{G}E_{G6}^{T}] + [{}^{G}E_{P}^{T}] + [{}^{G}E_{T}^{G6}] + [{}^{G}E_{P}^{G6}] + [{}^{G}E_{T}^{P}] + [{}^{G}E_{G6}^{P}] + [{}^{G}E_{P}^{P}])), \qquad (2)
\end{aligned}
$$

$$
\begin{aligned}
\frac{d[T]}{dt} &= k^{-T}([E^{T}] + [{}_{G}E^{T}] + [E_{G6}^{T}] + [E_{P}^{T}] + [{}_{G}^{G}E^{T}] + [{}^{G}E_{G6}^{T}] + [{}^{G}E_{P}^{T}] + [{}_{G}E_{G6}^{T}] + [{}_{G}E_{P}^{T}] \\
&\quad + [{}_{G}^{G}E_{G6}^{T}] + [{}_{G}^{G}E_{P}^{T}]) + k_{-T}([E_{T}] + [{}^{G}E_{T}] + [E_{T}^{G6}] + [E_{T}^{P}] + [{}_{G}^{G}E_{T}] + [{}_{G}E_{T}^{G6}] + [{}_{G}E_{T}^{P}] \\
&\quad + [{}^{G}E_{T}^{G6}] + [{}^{G}E_{T}^{P}] + [{}_{G}^{G}E_{T}^{G6}] + [{}_{G}^{G}E_{T}^{P}]) + (k^{-T} + k_{-T})([E_{T}^{T}] + [{}^{G}E_{T}^{T}] + [{}_{G}E_{T}^{T}] + [{}_{G}^{G}E_{T}^{T}]) \\
&\quad - [T]((k^{T} + K_{T})([E] + [{}^{G}E] + [{}_{G}E] + [{}_{G}^{G}E]) + k^{T}([E_{T}] + [E_{G6}] + [E_{P}] + [{}^{G}E_{T}] \\
&\quad + [{}^{G}E_{G6}] + [{}^{G}E_{P}] + [{}_{G}E_{T}] + [{}_{G}E_{G6}] + [{}_{G}E_{P}] + [{}_{G}^{G}E_{T}] + [{}_{G}^{G}EG6] + [{}_{G}^{G}E_{P}]) \\
&\quad + k_{T}([E^{T}] + [E^{P}] + [{}_{G}E^{T}] + [{}_{G}E^{P}] + [{}_{G}E^{T}] + [{}_{G}E^{P}] + [{}_{G}^{G}E^{T}] + [{}_{G}^{G}E^{P}])), \qquad (3)
\end{aligned}
$$

$$
\begin{aligned}
\frac{d[G6]}{dt} &= k_{0}([{}_{G}E_{T}] + [{}_{G}^{G}E_{T}] + [{}_{G}E_{T}^{T}] + [{}_{G}E_{T}^{G6}] + [{}_{G}E_{T}^{P}] + [{}_{G}^{G}E_{T}^{T}] + [{}_{G}^{G}E_{T}^{G6}] + [{}_{G}^{G}E_{T}^{P}]) \\
&\quad + k^{-G6}([E^{G6}] + [{}^{G}E^{G6}] + [{}_{G}E^{G6}] + [E_{T}^{G6}] + [E_{P}^{G6}] + [{}_{G}^{G}E^{G6}] + [{}^{G}E_{T}^{G6}] + [{}^{G}E_{P}^{G6}] \\
&\quad + [{}_{G}E_{T}^{G6}] + [{}_{G}E_{P}^{G6}] + [{}_{G}^{G}E_{T}^{G6}] + [{}_{G}^{G}E_{P}^{G6}]) + k_{-G6}([E_{G6}] + [{}_{G}E_{G6}] + [{}^{G}E_{G6}] + [E_{G6}^{T}] \\
&\quad + [{}_{G}^{G}E_{G6}] + [{}_{G}E_{G6}^{T}] + [{}^{G}E_{G6}^{T}] + [{}_{G}^{G}E_{G6}^{T}]) + k_{-G6}^{P}([E_{G6}^{P}] + [{}_{G}^{G}E_{G6}^{P}] + [{}_{G}E_{G6}^{P}] + [{}_{G}^{G}E_{G6}^{P}]) \\
&\quad - [G6]((k^{G6} + k_{G6})([E] + [{}^{G}E] + [{}_{G}E] + [{}_{G}^{G}E]) + k^{G6}([E_{T}] + [{}^{G}E_{T}] + [E_{P}] \\
&\quad + [{}^{G}E_{P}] + [{}_{G}E_{T}] + [{}_{G}E_{P}] + [{}_{G}^{G}E_{T}] + [{}_{G}^{G}EP]) + k_{G6}([E^{T}] + [{}_{G}E^{T}] + [{}^{G}E^{T}] + [{}_{G}^{G}E^{T}]) \\
&\quad + k_{G6}^{P}([E^{P}] + [{}_{G}E^{P}] + [{}^{G}E^{P}] + [{}_{G}^{G}E^{P}])), \qquad (4)
\end{aligned}
$$

$$
\begin{aligned}
\frac{d[P]}{dt} &= k^{-P}([E^{P}] + [{}^{G}E^{P}] + [{}_{G}E^{P}] + [E_{T}^{P}] + [E_{G6}^{P}] + [{}_{G}^{G}E^{P}] + [{}^{G}E_{T}^{P}] + [{}^{G}E_{G6}^{P}] + [{}_{G}E_{T}^{P}] \\
&\quad + [{}_{G}E_{G6}^{P}] + [{}_{G}^{G}E_{T}^{P}] + [{}_{G}^{G}E_{G6}^{P}]) + k_{-P}([E_{P}] + [{}_{G}E_{P}] + [{}^{G}E_{P}] + [E_{P}^{T}] + [E_{P}^{G6}] \\
&\quad + [{}_{G}^{G}E_{P}] + [{}_{G}E_{P}^{T}] + [{}_{G}E_{P}^{G6}] + [{}_{G}E_{P}^{T}] + [{}^{G}E_{P}^{G6}] + [{}_{G}^{G}E_{P}^{T}] + [{}_{G}^{G}E_{P}^{G6}]) \\
&\quad + (k^{-P} + k_{-P})([E_{P}^{P}] + [{}^{G}E_{P}^{P}] + [{}_{G}E_{P}^{P}] + [{}_{G}^{G}E_{P}^{P}]) \\
&\quad - [P](k^{P}([E_{T}] + [E_{G6}] + [E_{P}] + [{}^{G}E_{T}] + [{}^{G}E_{G}6] + [{}^{G}E_{P}] + [{}_{G}E_{T}] + [{}_{G}E_{G6}] + [{}_{G}E_{P}] \\
&\quad + [{}_{G}^{G}E_{T}] + [{}_{G}^{G}E_{G6}] + [{}_{G}^{G}E_{P}]) + k_{P}([E^{T}] + [E^{P}] + [{}_{G}E^{T}] + [{}_{G}E^{P}] + [{}^{G}E^{T}] \\
&\quad + [{}^{G}E^{P}] + [{}_{G}^{G}E^{T}] + [{}_{G}^{G}E^{P}]) + (k^{P} + k_{P})([E] + [{}^{G}E] + [{}_{G}E] + [{}_{G}^{G}E])), \qquad (5)
\end{aligned}
$$

$$
\frac{d[D]}{dt} = k_{0}([{}_{G}E_{T}] + [{}_{G}^{G}E_{T}] + [{}_{G}E_{T}^{T}] + [{}_{G}E_{T}^{G6}] + [{}_{G}E_{T}^{P}] + [{}_{G}^{G}E_{T}^{T}] + [{}_{G}^{G}E_{T}^{G6}] + [{}_{G}^{G}E_{T}^{P}]), \qquad (6)
$$

$$\frac{d[{}^{G}E]}{dt} = k_0[{}^{G}_{G}E_T] + k^{G}[G][E] + k_{-G}[{}^{G}_{G}E] + k^{-T}[{}^{G}E^{T}] + k_{-T}[{}^{G}E_T] + k^{-G6}[{}^{G}E^{G6}]$$
$$+ k_{-G6}[{}^{G}E_{G6}] + k^{-P}[{}^{G}E^{P}] + k_{-P}[{}^{G}E_P] - [{}^{G}E](k^{-G} + k_G[G]$$
$$+ (k^{T} + k_T)[T] + (k^{G6} + k_{G6})[G6] + (k^{P} + k_P)[P]), \tag{7}$$

$$\frac{d[E^{T}]}{dt} = k_0[{}_{G}E^{T}_{T}] + k^{-G}[{}^{G}E^{T}] + k_{-G}[{}_{G}E^{T}] + k_{-T}[E^{T}_{T}] + k_{-G6}[E^{T}_{G6}] + k_{-P}[E^{T}_{P}] + k^{T}[T][E]$$
$$- [E^{T}](k^{-T} + (k^{G} + k_G)[G] + k_T[T] + k_{G6}[G6] + k_P[P]), \tag{8}$$

$$\frac{d[E^{G6}]}{dt} = k_0[{}_{G}E^{G6}_{T}] + k^{-G}[{}^{G}E^{G6}] + k_{-G}[{}_{G}E^{G6}] + k_{-T}[E^{G6}_{T}] + k_{-P}[E^{G6}_{P}] + k^{G6}[G6][E]$$
$$- [E^{G6}](k^{-G6} + (k^{G} + k_G)[G]), \tag{9}$$

$$\frac{d[E^{P}]}{dt} = k_0[{}_{G}E^{P}_{T}] + k^{-G}[{}^{G}E^{P}] + k_{-G}[{}_{G}E^{P}] + k_{-T}[E^{P}_{T}] + k^{P}_{-G6}[E^{P}_{G6}] + k_{-P}[E^{P}_{P}] + k^{P}[P][E]$$
$$- [E^{P}](k^{-P} + (k^{G} + k_G)[G] + k_T[T] + k^{P}_{G6}[G6] + k_P[P]), \tag{10}$$

$$\frac{d[{}_{G}E]}{dt} = k_G[E][G] + k^{-G}[{}^{G}_{G}E] + k^{-T}[{}_{G}E^{T}] + k_{-T}[{}_{G}E_T]$$
$$+ k^{-G6}[{}_{G}E^{G6}] + k_{-G6}[{}_{G}E_{G6}] + k^{-P}[{}_{G}E^{P}] + k_{-P}[{}_{G}E_P]$$
$$- [{}_{G}E](k_{-G} + k^{G}[G] + (k^{T} + k_T)[T] + (k^{G6} + k_{G6})[G6] + (k^{P} + k_P)[P]), \tag{11}$$

$$\frac{d[E_T]}{dt} = k^{-G}[{}^{G}E_T] + k_{-G}[{}_{G}E_T] + k^{-T}[E^{T}_{T}] + k^{-G6}[E^{G6}_{T}] + k^{-P}[E^{P}_{T}] + k_T[T][E]$$
$$- [E_T](k_{-T} + (k^{G} + k_G)[G] + k^{T}[T] + k^{G6}[G6] + k^{P}[P]), \tag{12}$$

$$\frac{d[E_{G6}]}{dt} = k^{-G}[{}^{G}E_{G6}] + k_{-G}[{}_{G}E_{G6}] + k^{-T}[E^{T}_{G6}] + k^{-P}[E^{P}_{G6}] + k_{G6}[G6][E]$$
$$- [E_{G6}](k_{-G6} + (k^{G} + k_G)[G] + k^{T}[T] + k^{P}[P]), \tag{13}$$

$$\frac{d[E_P]}{dt} = k^{-G}[{}^{G}E_P] + k_{-G}[{}_{G}E_P] + k^{-T}[E^{T}_{P}] + k^{-G6}[E^{G6}_{P}] + k^{-P}[E^{P}_{P}] + k_P[P][E]$$
$$- [E_P](k_{-P} + (k^{G} + k_G)[G] + k^{T}[T] + k^{G6}[G6] + k^{P}[P]), \tag{14}$$

$$\frac{d[{}^{G}E^{T}]}{dt} = k_0[{}^{G}_{G}E^{T}_{T}] + k_{-G}[{}^{G}_{G}E^{T}] + k_{-T}[{}^{G}E^{T}_{T}] + k_{-G6}[{}^{G}E^{T}_{G6}] + k_{-P}[{}^{G}E^{T}_{P}] + k^{G}[G][E^{T}]$$
$$+ k^{T}[T][{}^{G}E] - [{}^{G}E^{T}](k^{-G} + k^{-T} + k_G[G] + k_T[T] + k_{G6}[G6] + k_P[P]), \tag{15}$$

$$\frac{d[{}^{G}E^{G6}]}{dt} = k_0[{}^{G}_{G}E^{G6}_{T}] + k_{-G}[{}^{G}_{G}E^{G6}] + k_{-T}[{}^{G}E^{G6}_{T}] + k_{-P}[{}^{G}E^{G6}_{P}] + k^{G}[G][E^{G6}] + k^{G6}[G6][{}^{G}E]$$
$$- [{}^{G}E^{G6}](k^{-G} + k^{-G6} + k_G[G]), \tag{16}$$

$$\frac{d[{}^{G}E^{P}]}{dt} = k_0[{}^{G}_{G}E^{P}_{T}] + k_{-G}[{}^{G}_{G}E^{P}] + k_{-T}[{}^{G}E^{P}_{T}] + k^{P}_{-G6}[{}^{G}E^{P}_{G6}] + k_{-P}[{}^{G}E^{P}_{P}] + k^{G}[G][E^{P}]$$
$$+ k^{P}[P][{}^{G}E] - [{}^{G}E^{P}](k^{-G} + k^{-P} + k_G[G] + k_T[T] + k^{P}_{G6}[G6] + k_P[P]), \tag{17}$$

$$\frac{d[{}^{G}_{G}E]}{dt} = k^{-T}[{}^{G}_{G}E^{T}] + k_{-T}[{}^{G}_{G}E_T] + k^{-G6}[{}^{G}_{G}E^{G6}] + k_{-G6}[{}^{G}_{G}E_{G6}] + k^{-P}[{}^{G}_{G}E^{P}] + k_{-P}[{}^{G}_{G}E_P]$$
$$+ (k^{G}[{}_{G}E] + k_G[{}^{G}E])[G] - [{}^{G}_{G}E](k^{-G} + k_{-G} + (k^{T} + k_T)[T]$$
$$+ (k^{G6} + k_{G6})[G6] + (k^{P} + k_P)[P]), \tag{18}$$

$$\frac{d[{}^{G}E_T]}{dt} = k_{-G}[{}^{G}_{G}E_T] + k^{-T}[{}^{G}E^{T}_{T}] + k^{-G6}[{}^{G}E^{G6}_{T}] + k^{-P}[{}^{G}E^{P}_{T}] + k^{G}[G][E_T] + k_T[T][{}^{G}E] - [{}^{G}E_T](k^{-G} + k_{-T} + k_G[G] + k^{T}[T] + k^{G6}[G6] + k^{P}[P]), \quad (19)$$

$$\frac{d[{}^{G}E_{G6}]}{dt} = k_{-G}[{}^{G}_{G}E_{G6}] + k^{-T}[{}^{G}E^{T}_{G6}] + k^{-P}[{}^{G}E^{P}_{G6}] + k^{G}[G][E_{G6}] + k_{G6}[G6][{}^{G}E] - [{}^{G}E_{G6}](k^{-G} + k_{-G6} + k_G[G] + k^{T}[T] + k^{P}[P]), \quad (20)$$

$$\frac{d[{}^{G}E_P]}{dt} = k_{-G}[{}^{G}_{G}E_P] + k^{-T}[{}^{G}E^{T}_{P}] + k^{-G6}[{}^{G}E^{G6}_{P}] + k^{-P}[{}^{G}E^{P}_{P}] + k^{G}[G][E_P] + k_P[P][{}^{G}E] - [{}^{G}E_P](k^{-G} + k_{-P} + k_G[G] + k^{T}[T] + k^{G6}[G6] + k^{P}[P]), \quad (21)$$

$$\frac{d[{}_{G}E^{T}]}{dt} = k^{-G}[{}^{G}_{G}E^{T}] + k_{-T}[{}_{G}E^{T}_{T}] + k_{-G6}[{}_{G}E^{T}_{G6}] + k_{-P}[{}_{G}E^{T}_{P}] + k_G[G][E^{T}] + k^{T}[T][{}_{G}E] - [{}_{G}E^{T}](k_{-G} + k^{-T} + k^{G}[G] + k_T[T] + k_{G6}[G6] + k_P[P]), \quad (22)$$

$$\frac{d[E^{T}_{T}]}{dt} = k^{-G}[{}^{G}E^{T}_{T}] + k_{-G}[{}_{G}E^{T}_{T}] + [T](k^{T}[E_T] + k_T[E^{T}]) - [E^{T}_{T}](k^{-T} + k_{-T} + (k^{G} + k_G)[G]), \quad (23)$$

$$\frac{d[E^{T}_{G6}]}{dt} = k^{-G}[{}^{G}E^{T}_{G6}] + k_{-G}[{}_{G}E^{T}_{G6}] + k^{T}[T][E_{G6}] + k_{G6}[G6][E^{T}] - [E^{T}_{G6}](k^{-T} + k_{-G6} + (k^{G} + k_G)[G]), \quad (24)$$

$$\frac{d[E^{T}_{P}]}{dt} = k^{-G}[{}^{G}E^{T}_{P}] + k_{-G}[{}_{G}E^{T}_{P}] + k^{T}[T][E_P] + k_P[P][E^{T}] - [E^{T}_{P}](k^{-T} + k_{-P} + (k^{G} + k_G)[G]), \quad (25)$$

$$\frac{d[{}_{G}E^{G6}]}{dt} = k^{-G}[{}^{G}E^{G6}_{G}] + k_{-T}[{}_{G}E^{G6}_{T}] + k_{-P}[{}_{G}E^{G6}_{P}] + k_G[G][E^{G6}] + k^{G6}[G6][{}_{G}E] - [{}_{G}E^{G6}](k_{-G} + k^{-G6} + k^{G}[G]), \quad (26)$$

$$\frac{d[E^{G6}_{T}]}{dt} = k^{-G}[{}^{G}E^{G6}_{T}] + k_{-G}[{}_{G}E^{G6}_{T}] + k^{G6}[G6][E_T] - [E^{G6}_{T}](k_{-T} + k^{-G6} + (k^{G} + k_G)[G]), \quad (27)$$

$$\frac{d[E^{G6}_{P}]}{dt} = k^{-G}[{}^{G}E^{G6}_{P}] + k_{-G}[{}_{G}E^{G6}_{P}] + k^{G6}[G6][E_P] - [E^{G6}_{P}](k^{-G6} + k_{-P} + (k^{G} + k_G)[G]), \quad (28)$$

$$\frac{d[{}_{G}E^{P}]}{dt} = k^{-G}[{}^{G}_{G}E^{P}] + k_{-T}[{}_{G}E^{P}_{T}] + k^{P}_{-G6}[{}_{G}E^{P}_{G6}] + k_{-P}[{}_{G}E^{P}_{P}] + k_G[G][E^{P}] + k^{P}[P][{}_{G}E] - [{}_{G}E^{P}](k_{-G} + k^{-P} + k^{G}[G] + k_T[T] + k^{P}_{G6}[G6] + k_P[P]), \quad (29)$$

$$\frac{d[E^{P}_{T}]}{dt} = k^{-G}[{}^{G}E^{P}_{T}] + k_{-G}[{}_{G}E^{P}_{T}] + k_T[T][E^{P}] + k^{P}[P][E_T] - [E^{P}_{T}](k_{-T} + k^{-P} + (k^{G} + k_G)[G]), \quad (30)$$

$$\frac{d[E^{P}_{G6}]}{dt} = k^{-G}[{}^{G}E^{P}_{G6}] + k_{-G}[{}_{G}E^{P}_{G6}] + k^{P}_{G6}[G6][E^{P}] + k^{P}[P][E_{G6}] - [E^{P}_{G6}](k^{P}_{-G6} + k^{-P} + (k^{G} + k_G)[G]), \quad (31)$$

$$\frac{d[E^{P}_{P}]}{dt} = k^{-G}[{}^{G}E^{P}_{P}] + k_{-G}[{}_{G}E^{P}_{P}] + (k^{P}[E_P] + k_P[E^{P}])[P] - [E^{P}_{P}](k^{-P} + k_{-P} + (k^{G} + k_G)[G]), \quad (32)$$

$$\frac{d[{}_GE_T]}{dt} = k^{-G}[{}^G_GE_T] + k^{-T}[{}_GE^T_T] + k^{-G6}[{}_GE^{G6}_T] + k^{-P}[{}_GE^P_T] + k_G[G][E_T] + k_T[T][{}_GE]$$
$$- [{}_GE_T](k_0 + k_{-G} + k_{-T} + k^G[G] + k^T[T] + k^{G6}[G6] + k^P[P]), \quad (33)$$

$$\frac{d[{}_GE_{G6}]}{dt} = k^{-G}[{}^G_GE_{G6}] + k^{-T}[{}_GE^T_{G6}] + k^{-P}[{}_GE^P_{G6}] + k_G[G][E_{G6}] + k_{G6}[G6][{}_GE]$$
$$- [{}_GE_{G6}](k_{-G} + k_{-G6} + k^G[G] + k^T[T] + k^P[P]), \quad (34)$$

$$\frac{d[{}_GE_P]}{dt} = k^{-G}[{}^G_GE_P] + k^{-T}[{}_GE^T_P] + k^{-G6}[{}_GE^{G6}_P] + k^{-P}[{}_GE^P_P] + k_G[G][E_P] + k_P[P][{}_GE]$$
$$- [{}_GE_P](k_{-G} + k_{-P} + k^G[G] + k^T[T] + k^{G6}[G6] + k^P[P]), \quad (35)$$

$$\frac{d[{}^G_GE^T]}{dt} = k_{-T}[{}^G_GE^T_T] + k_{-G6}[{}^G_GE^T_{G6}] + k_{-P}[{}^G_GE^T_P] + (k^G[{}_GE^T] + k_G[{}^GE^T])[G] + k^T[T][{}^G_GE]$$
$$- [{}^G_GE^T](k^{-G} + k_{-G} + k^{-T} + k_T[T] + k_{G6}[G6] + k_P[P]), \quad (36)$$

$$\frac{d[{}^GE^T_T]}{dt} = k_{-G}[{}^G_GE^T_T] + k^G[G][E^T_T] + (k^T[{}^GE_T] + k_T[{}^GE^T])[T]$$
$$- [{}^GE^T_T](k^{-G} + k^{-T} + k_{-T} + k_G[G]), \quad (37)$$

$$\frac{d[{}^GE^T_{G6}]}{dt} = k_{-G}[{}^G_GE^T_{G6}] + k^G[G][E^T_{G6}] + k^T[T][{}^GE_{G6}] + k_{G6}[G6][{}^GE^T]$$
$$- [{}^GE^T_{G6}](k^{-G} + k^{-T} + k_{-G6} + k_G[G]), \quad (38)$$

$$\frac{d[{}^GE^T_P]}{dt} = k_{-G}[{}^G_GE^T_P] + k^G[G][E^T_P] + k^T[T][{}^GE_P] + k_P[P][{}^GE^T]$$
$$- [{}^GE^T_P](k^{-G} + k^{-T} + k_{-P} + k_G[G]), \quad (39)$$

$$\frac{d[{}^G_GE^{G6}]}{dt} = k_{-T}[{}^G_GE^{G6}_T] + k_{-P}[{}^G_GE^{G6}_P] + (k^G[{}_GE^{G6}] + k_G[{}^GE^{G6}])[G] + k^{G6}[{}^G_GE][G6]$$
$$- [{}^G_GE^{G6}](k^{-G} + k_{-G} + k^{-G6}), \quad (40)$$

$$\frac{d[{}^GE^{G6}_T]}{dt} = k_{-G}[{}^G_GE^{G6}_T] + k^G[G][E^{G6}_T] + k^{G6}[G6][{}^GE_T]$$
$$- [{}^GE^{G6}_T](k^{-G} + k_{-T} + k^{-G6} + k_G[G]), \quad (41)$$

$$\frac{d[{}^GE^{G6}_P]}{dt} = k_{-G}[{}^G_GE^{G6}_P] + k^G[G][E^{G6}_P] + k^{G6}[G6][{}^GE_P]$$
$$- [{}^GE^{G6}_P](k^{-G} + k^{-G6} + k_{-P} + k_G[G]), \quad (42)$$

$$\frac{d[{}^G_GE^P]}{dt} = k_{-T}[{}^G_GE^P_T] + k^P_{-G6}[{}^G_GE^P_{G6}] + k_{-P}[{}^G_GE^P_P] + (k^G[{}_GE^P] + k_G[{}^GE^P])[G] + k^P[P][{}^G_GE]$$
$$- [{}^G_GE^P](k^{-G} + k_{-G} + k^{-P} + k_T[T] + k^P_{G6}[G6] + k_P[P]), \quad (43)$$

$$\frac{d[{}^GE^P_T]}{dt} = k_{-G}[{}^G_GE^P_T] + k^G[G][E^P_T] + k_T[T][{}^GE^P] + k^P[P][{}^GE_T]$$
$$- [{}^GE^P_T](k^{-G} + k_{-T} + k^{-P} + k_G[G]), \quad (44)$$

$$\frac{d[{}^GE^P_{G6}]}{dt} = k_{-G}[{}^G_GE^P_{G6}] + k^G[G][E^P_{G6}] + k^P_{G6}[G6][{}^GE^P] + k^P[P][{}^GE_{G6}]$$
$$- [{}^GE^P_{G6}](k^{-G} + k^P_{-G6} + k^{-P} + k_G[G]), \quad (45)$$

$$\frac{d[{}^{G}E_{P}^{P}]}{dt} = k_{-G}[{}_{G}^{G}E_{P}^{P}] + k^{G}[G][E_{P}^{P}] + (k^{P}[{}^{G}E_{P}] + k_{P}[{}^{G}E^{P}])[P] - [{}^{G}E_{P}^{P}](k^{-G} + k^{-P} + k_{-P} + k_{G}[G]), \quad (46)$$

$$\frac{d[{}_{G}^{G}E_{T}]}{dt} = k^{-T}[{}_{G}^{G}E_{T}^{T}] + k^{-G6}[{}_{G}^{G}E_{T}^{G6}] + k^{-P}[{}_{G}^{G}E_{T}^{P}] + (k^{G}[{}_{G}E_{T}] + k_{G}[{}^{G}E_{T}])[G] + k_{T}[T][{}_{G}^{G}E] - [{}_{G}^{G}E_{T}](k_{0} + k^{-G} + k_{-G} + k_{-T} + k^{T}[T] + k^{G6}[G6] + k^{P}[P]), \quad (47)$$

$$\frac{d[{}_{G}E_{T}^{T}]}{dt} = k^{-G}[{}_{G}^{G}E_{T}^{T}] + k_{G}[G][E_{T}^{T}] + (k^{T}[{}_{G}E_{T}] + k_{T}[{}_{G}E^{T}])[T] - [{}_{G}E_{T}^{T}](k_{0} + k_{-G} + k^{-T} + k_{-T} + k^{G}[G]), \quad (48)$$

$$\frac{d[{}_{G}E_{T}^{G6}]}{dt} = k^{-G}[{}_{G}^{G}E_{T}^{G6}] + k_{G}[G][E_{T}^{G6}] + k^{G6}[G6][{}_{G}E_{T}] - [{}_{G}E_{T}^{G6}](k_{0} + k_{-G} + k_{-T} + k^{-G6} + k^{G}[G]), \quad (49)$$

$$\frac{d[{}_{G}E_{T}^{P}]}{dt} = k^{-G}[{}_{G}^{G}E_{T}^{P}] + k_{G}[G][E_{T}^{P}] + k_{T}[T][-GE^{P}] + k^{P}[P][{}_{G}E_{T}] - [{}_{G}E_{T}^{P}](k_{0} + k_{-G} + k_{-T} + k^{-P} + k^{G}[G]), \quad (50)$$

$$\frac{d[{}_{G}^{G}E_{G6}]}{dt} = k^{-T}[{}_{G}^{G}E_{G6}^{T}] + k^{-P}[{}_{G}^{G}E_{G6}^{P}] + (k^{G}[{}_{G}E_{G6}] + k_{G}[{}^{G}E_{G6}])[G] + k_{G6}[G6][{}_{G}^{G}E] - [{}_{G}^{G}E_{G6}](k^{-G} + k_{-G} + k_{-G6} + k^{T}[T] + k^{P}[P]), \quad (51)$$

$$\frac{d[{}_{G}E_{G6}^{T}]}{dt} = k^{-G}[{}_{G}^{G}E_{G6}^{T}] + k_{G}[G][E_{G6}^{T}] + k^{T}[T][{}_{G}E_{G6}] + k_{G6}[G6][{}_{G}E^{T}] - [{}_{G}E_{G6}^{T}](k_{-G} + k^{-T} + k_{-G6} + k^{G}[G]), \quad (52)$$

$$\frac{d[{}_{G}E_{G6}^{P}]}{dt} = k^{-G}[{}_{G}^{G}E_{G6}^{P}] + k_{G}[G][E_{G6}^{P}] + k_{G6}^{P}[G6][{}_{G}E^{P}] + k^{P}[P][{}_{G}E_{G6}] - [{}_{G}E_{G6}^{P}(k_{-G} + k_{-G6}^{P} + k^{-P} + k^{G}[G]), \quad (53)$$

$$\frac{d[{}_{G}^{G}E_{P}]}{dt} = k^{-T}[{}_{G}^{G}E_{P}^{T}] + k^{-G6}[{}_{G}^{G}E_{P}^{G6}] + k^{-P}[{}_{G}^{G}E_{P}^{P}] + (k^{G}[{}_{G}E_{P}] + k_{G}[{}^{G}E_{P}])[G] + k_{P}[P][{}_{G}^{G}E] - [{}_{G}^{G}E_{P}](k^{-G} + k_{-G} + k_{-P} + k^{T}[T] + k^{G6}[G6] + k^{P}[P]), \quad (54)$$

$$\frac{d[{}_{G}E_{P}^{T}]}{dt} = k^{-G}[{}_{G}^{G}E_{P}^{T}] + k_{G}[G][E_{P}^{T}] + k^{T}[T][{}_{G}E_{P}] + k_{P}[P][{}_{G}E^{T}] - [{}_{G}E_{P}^{T}](k_{-G} + k^{-T} + k_{-P} + k^{G}[G]), \quad (55)$$

$$\frac{d[{}_{G}E_{P}^{G6}]}{dt} = k^{-G}[{}_{G}^{G}E_{P}^{G6}] + k_{G}[G][E_{P}^{G6}] + k^{G6}[G6][{}_{G}E_{P}] - [{}_{G}E_{P}^{G6}](k_{-G} + k^{-G6} + k_{-P} + k^{G}[G]), \quad (56)$$

$$\frac{d[{}_{G}E_{P}^{P}]}{dt} = k^{-G}[{}_{G}^{G}E_{P}^{P}] + k_{G}[G][E_{P}^{P}] + (k^{P}[{}_{G}E_{P}] + k_{P}[-GE^{P}])[P] - [{}_{G}E_{P}^{P}](k_{-G} + k^{-P} + k_{-P} + k^{G}[G]), \quad (57)$$

$$\frac{d[{}_{G}^{G}E_{T}^{T}]}{dt} = (k^{G}[{}_{G}E_{T}^{T}] + k_{G}[{}^{G}E_{T}^{T}])[G] + (k^{T}[{}_{G}^{G}E_{T}] + k_{T}[{}_{G}^{G}E^{T}])[T] - [{}_{G}^{G}E_{T}^{T}](k_{0} + k^{-G} + k_{-G} + k^{-T} + k_{-T}), \quad (58)$$

$$\frac{d[{}^G_G E^T_{G6}]}{dt} = (k^G[{}_G E^T_{G6}] + k_G[{}^G E^T_{G6}])[G] + k^T[T][{}^G_G E_{G6}] + k_{G6}[G6][{}^G_G E^T] - [{}^G_G E^T_{G6}](k^{-G} + k_{-G} + k^{-T} + k_{-G6}), \quad (59)$$

$$\frac{d[{}^G_G E^T_P]}{dt} = (k^G[{}_G E^T_P] + k_G[{}^G E^T_P])[G] + k^T[T][{}^G_G E_P] + k_P[P][{}^G_G E^T] - [{}^G_G E^T_P](k^{-G} + k_{-G} + k^{-T} + k_{-P}), \quad (60)$$

$$\frac{d[{}^G_G E^{G6}_T]}{dt} = (k^G[{}_G E^{G6}_T] + k_G[{}^G E^{G6}_T])[G] + k^{G6}[G6][{}^G_G E_T] - [{}^G_G E^{G6}_T](k_0 + k^{-G} + k_{-G} + k_{-T} + k^{-G6}), \quad (61)$$

$$\frac{[{}^G_G E^{G6}_P]}{dt} = (k^G[{}_P E^{G6}_P] + k_G[{}^G E^{G6}_P])[G] + k^{G6}[G6][{}^G_G E_P] - [{}^G_G E^{G6}_P](k^{-G} + k_{-G} + k^{-G6} + k_{-P}), \quad (62)$$

$$\frac{[{}^G_G E^P_T]}{dt} = (k^G[{}_G E^P_T] + k_G[{}^G E^P_T])[G] + k_T[T][{}^G_G E^P] + k^P[P][{}^G_G E_T] - [{}^G_G E^P_T](k_0 + k^{-G} + k_{-G} + k_{-T} + k^{-P}), \quad (63)$$

$$\frac{d[{}^G_G E^P_{G6}]}{dt} = (k^G[{}_G E^P_{G6}] + k_G[{}^G E^P_{G6}])[G] + k^P_{G6}[G6][{}^G_G E^P] + k^P[P][{}^G_G E_{G6}] - [{}^G_G E^P_{G6}](k^{-G} + k_{-G} + k^P_{-G6} + k^{-P}), \quad (64)$$

$$\frac{d[{}^G_G E^P_P]}{dt} = (k^G[{}_G E^P_P] + k_G[{}^G E^P_P])[G] + (k^P[{}^G_G E_P] + k_P[{}^G_G E^P])[P] - [{}^G_G E^P_P](k^{-G} + k_{-G} + k^{-P} + k_{-P}). \quad (65)$$

These equations are solved subject to the initial conditions

$$\begin{aligned}
&[E](t=0) = E_0,\\
&[G](t=0) = G_0,\\
&[T](t=0) = ATP_0,\\
&[G6](t=0) = 0,\\
&[P](t=0) = P_{i0},\\
&[D](t=0) = 0,\\
&[{}^G E](t=0) = 0,\\
&[{}_G E](t=0) = 0,\\
&[E^k](t=0) = 0, && k = T, G6, P,\\
&[E_k](t=0) = 0, && k = T, G6, P,\\
&[{}^G E^j](t=0) = 0, && j = T, G6, P,\\
&[{}_G E_j](t=0) = 0, && j = T, G6, P,\\
&[{}^G_G E](t=0) = 0,\\
&[{}^G E_j](t=0) = 0, && J = T, G6, P,\\
&[{}_G E^j](t=0) = 0, && J = T, G6, P,
\end{aligned}$$

$$
\begin{array}{lll}
[E^k_j](t=0)=0, & k=T,G6,P, & j=T,P,\\
[E^j_{G6}](t=0)=0, & j=T,P, & \\
[{}^GE^x_y](t=0)=0, & x=T,G6,P, & y=G,T,P,\\
[{}_GE^x_y](t=0)=0, & x=G,T,P, & y=T,G6,P,\\
[{}^GE^x_{G6}](t=0)=0, & x=T,P, & \\
[{}_GE^{G6}_x](t=0)=0, & x=T,P, & \\
[{}^G_GE^x_y](t=0)=0, & x=T,P, & y=T,P,\\
[{}^G_GE^{G6}_x](t=0)=0, & x=T,P, & \\
[{}^G_GE^x_{G6}](t=0)=0, & x=T,P, &
\end{array}
$$

where E_0, G_0, ATP_0, P_{i0} give the initial concentrations of enzyme, glucose, ATP, and P_i, respectively.

3. Calculations of parameters

In this section, the Λ and Ω methods discussed in [1] are used to calculate values of the model paramters.

Let $\Omega = T$ and $\Lambda = 100$. The Michaelis-Menten constant for the C binding site for glucose is

$$K_m = 53\ \mu M,$$

and the catalytic constant $k_0 = 63\ s^{-1}$. Using the formula for Λ method, we have

$$k_G = (\Lambda k_G)/K_m = 118868\ mM^{-1}s^{-1},\ \text{and}\ k_{-G} = (\Lambda – T)k_G = 6237\ s^{-1}.$$

We set $k^G = k_G$ and $k^{-G} = k_{-G}$ since there are no dissociation constant for the N binding site for glucose available in the literature. Similarly, the Λ method can be used for calculating k_T, k_{-T}, then set $k^T = k_T, k^{-T} = k_{-T}$ as well. As a result, $k^T = k_T = 9000\ mM^{-1}s^{-1}$, and $k^{-T} = k_{-T} = 6237\ s^{-1}$.

The Ω method was used to calculate the kinetic constants for P_i and $G6P$. For example, the dissociation constant for the N binding site for P_i is $K_D = 0.022\ mM$. Using the formula for the Ω method [1], we have

$$k^P = \Omega k^T = 9000\ mM^{-1}s^{-1},\ \text{and}\ k^{-G6} = 198\ s^{-1}.$$

Analogously, we can calculate the values of k^{G6}, k^{-G6}, k_{G6}, k_{-G6}, k_P, k_{-P}, k^P_{G6}, and k^P_{-G6}.

References

[1] Chin-Rang Yang, Bruce E Shapiro, Eric D Mjolsness, and G Wesley Hatfield. An enzyme mechanism language for the mathematical modeling of metabolic pathways. *Bioinformatics*, 21(6):774-780, 2004.

4. Software

The software used for the calculations of the paper can be found at the following link

`https://github.com/vinh-mai/Hexokinase-2019`