Supplementary material

The mechanism descibed by Scheme 1 is solved using the King-Altman method. Some additional *Mathematica* commands that were required to enable the input below to be evaluated are not shown but are available on request. The main body of the paper demonstrates the numerical capabilities of *Mathematica*. Below the symbolic capabilities are demonstrated. We begin by defining the matrix and vector:

In[1]:=
```
Clear[Γ_Ox, Γ_HR, Γ_Red, Γ_Red.S, Γ_T, mat, b, res];

mat = -{{-k^F_E1, k^B_E1, 0, k_2}, {k^F_E1, -(k^B_E1 + k^F_E2), k^B_E2, 0},
    {0, k^F_E2, -(k_+1 * S_y=0 + k^B_E2), k_-1}, {0, 0, k_+1 * S_y=0, -(k_-1 + k_2)}};

b = {Γ_Ox, Γ_HR, Γ_Red, Γ_Red.S};

MatrixForm[mat].MatrixForm[b] == MatrixForm[{0, 0, 0, 0}]
```

Out[4]=
$$\begin{pmatrix} k^F_{E1} & -k^B_{E1} & 0 & -k_2 \\ -k^F_{E1} & k^B_{E1} + k^F_{E2} & -k^B_{E2} & 0 \\ 0 & -k^F_{E2} & k^B_{E2} + k_{+1}\, S_{y=0} & -k_{-1} \\ 0 & 0 & -k_{+1}\, S_{y=0} & k_2 + k_{-1} \end{pmatrix} \cdot \begin{pmatrix} \Gamma_{Ox} \\ \Gamma_{HR} \\ \Gamma_{Red} \\ \Gamma_{Red.S} \end{pmatrix} == \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

Check that the equations are correct and agree with eqn (1).

In[5]:=
```
TableForm[mat.{Γ_Ox, Γ_HR, Γ_Red, Γ_Red.S}]
```

Out[5]//TableForm=

$$-k^B_{E1}\,\Gamma_{HR} + k^F_{E1}\,\Gamma_{Ox} - k_2\,\Gamma_{Red.S}$$
$$(k^B_{E1} + k^F_{E2})\,\Gamma_{HR} - k^F_{E1}\,\Gamma_{Ox} - k^B_{E2}\,\Gamma_{Red}$$
$$-k^F_{E2}\,\Gamma_{HR} + (k^B_{E2} + k_{+1}\,S_{y=0})\,\Gamma_{Red} - k_{-1}\,\Gamma_{Red.S}$$
$$-k_{+1}\,S_{y=0}\,\Gamma_{Red} + (k_2 + k_{-1})\,\Gamma_{Red.S}$$

Find King-Altman solution to the problem.

In[6]:=
```
size = 4; (*size of the matrix*)
res = Table[Minors[mat, size - 1][[size - i + 1, size - i + 1]], {i, size}];
TableForm[MapThread[#1 == #2 &, {b, res}]]
Γ_T = Tr[res];
```

Out[7]//TableForm=

$$\Gamma_{Ox} == k_2\,k^B_{E1}\,k^B_{E2} + k_{-1}\,k^B_{E1}\,k^B_{E2} + k_2\,k_{+1}\,k^B_{E1}\,S_{y=0} + k_2\,k_{+1}\,k^F_{E2}\,S_{y=0}$$
$$\Gamma_{HR} == k_2\,k^F_{E1}\,k^B_{E2} + k_{-1}\,k^F_{E1}\,k^B_{E2} + k_2\,k_{+1}\,k^F_{E1}\,S_{y=0}$$
$$\Gamma_{Red} == k_2\,k^F_{E1}\,k^F_{E2} + k_{-1}\,k^F_{E1}\,k^F_{E2}$$
$$\Gamma_{Red.S} == k_{+1}\,k^F_{E1}\,k^F_{E2}\,S_{y=0}$$

Check that the derivation agrees with that of Armstrong et al:

In[9]:= $\mathbf{Clear}[\Gamma_{Ox}, \Gamma_{HR}, \Gamma_{Red}, \Gamma_{Red.S}];$

$\{\Gamma_{Ox}, \Gamma_{HR}, \Gamma_{Red}, \Gamma_{Red.S}\} = \mathbf{res}$

Out[10]= $\{k_2\, k_{E1}^B\, k_{E2}^B + k_{-1}\, k_{E1}^B\, k_{E2}^B + k_2\, k_{+1}\, k_{E1}^B\, S_{y=0} + k_2\, k_{+1}\, k_{E2}^F\, S_{y=0},$
$k_2\, k_{E1}^F\, k_{E2}^B + k_{-1}\, k_{E1}^F\, k_{E2}^B + k_2\, k_{+1}\, k_{E1}^F\, S_{y=0},\ k_2\, k_{E1}^F\, k_{E2}^F + k_{-1}\, k_{E1}^F\, k_{E2}^F,\ k_{+1}\, k_{E1}^F\, k_{E2}^F\, S_{y=0}\}$

Evaluate $\Gamma_{Red} / \Gamma_{Red.S}$ and substitute in the definition of K_m.

In[11]:= $\mathbf{Simplify}[\Gamma_{Red} / \Gamma_{Red.S}]\ /.\ \frac{k_{-1} + k_2}{k_{+1}} \to K_m$

Out[11]= $\frac{K_m}{S_{y=0}}$

Evaluate $\Gamma_{HR} / \Gamma_{Red}$. Convert to partial fractions. Substitute the definition of K_m and ϵ_2.

In[12]:= $\mathbf{Apart}[\Gamma_{HR} / \Gamma_{Red}]\ /.\ \left\{\frac{k_{+1}}{k_{-1} + k_2} \to \frac{1}{K_m},\ \frac{k_{E2}^B}{k_{E2}^F} \to \epsilon_2\right\}$

Out[12]= $\frac{k_2\, S_{y=0}}{K_m\, k_{E2}^F} + \epsilon_2$

Evaluate $\Gamma_{Ox} / \Gamma_{HR}$. Convert to partial fractions.

In[13]:= $\mathbf{temp} = \mathbf{Apart}\ /@\ \mathbf{Apart}[\Gamma_{Ox} / \Gamma_{HR}]$

Out[13]= $\frac{k_{E1}^B}{k_{E1}^F} + \frac{k_{E2}^F}{k_{E1}^F} - \frac{(k_2 + k_{-1})\, k_{E2}^B\, k_{E2}^F}{k_{E1}^F\, (k_2\, k_{E2}^B + k_{-1}\, k_{E2}^B + k_2\, k_{+1}\, S_{y=0})}$

Take the second and third terms and multiply top and bottom by $\Gamma_{HR} / \Gamma_{Red}$. Force one occurence of $\Gamma_{HR} / \Gamma_{Red}$ to be unevaluated so that a comparison can be made with eqn (B4c) of Armstrong et al. Then substitute the definition of K_m.

In[14]:= $\mathbf{temp2} = \mathbf{Simplify}[\mathbf{temp}[[\{2, 3\}]] * (\Gamma_{HR} / \Gamma_{Red}) * \mathbf{Hold}[(\Gamma_{Red} / \Gamma_{HR})]]\ /.$
$\frac{k_{+1}}{k_2 * x_ + k_{-1} * x_} \to \frac{1}{K_m * x}$

Out[14]= $$\frac{k_2\ S_{y=0}\ \text{Hold}\left[\frac{\Gamma_{Red}}{\Gamma_{HR}}\right]}{K_m\ k_{E1}^F}$$

Add the two parts together and substitute the definition of ϵ_2 .

In[15]:= $$\text{temp}[[1]] + \text{temp2}\ /.\ \frac{k_{E1}^B}{k_{E1}^F} \to \epsilon_1$$

Out[15]= $$\epsilon_1 + \frac{k_2\ S_{y=0}\ \text{Hold}\left[\frac{\Gamma_{Red}}{\Gamma_{HR}}\right]}{K_m\ k_{E1}^F}$$

Double check.

In[16]:= $$\text{Simplify}\left[\frac{\Gamma_T}{\Gamma_{Red.S}} == 1 + \frac{\Gamma_{Red}}{\Gamma_{Red.S}} * \left(1 + \frac{\Gamma_{HR}}{\Gamma_{Red}} * \left(1 + \frac{\Gamma_{Ox}}{\Gamma_{HR}}\right)\right)\right]$$

Out[16]= True

Obtain the King-Altman result for $x_{\text{Red.S}}$.

In[17]:= $$\text{FullSimplify}\left[\frac{\Gamma_{Red.S}}{\Gamma_T}\right]$$

Out[17]= $$\left(k_{+1}\ k_{E1}^F\ k_{E2}^F\ S_{y=0}\right) / \left(\left(k_2 + k_{-1}\right)\left(k_{E1}^B\ k_{E2}^B + k_{E1}^F\left(k_{E2}^B + k_{E2}^F\right)\right) + k_{+1}\left(k_{E1}^F\ k_{E2}^F + k_2\left(k_{E1}^B + k_{E1}^F + k_{E2}^F\right)\right) S_{y=0}\right)$$

Obtain the King-Altman result for x_{Red} .

In[17]:= $$\text{FullSimplify}\left[\frac{\Gamma_{Red}}{\Gamma_T}\right]$$

Out[17]= $$\left(\left(k_2 + k_{-1}\right) k_{E1}^F\ k_{E2}^F\right) / \left(\left(k_2 + k_{-1}\right)\left(k_{E1}^B\ k_{E2}^B + k_{E1}^F\left(k_{E2}^B + k_{E2}^F\right)\right) + k_{+1}\left(k_{E1}^F\ k_{E2}^F + k_2\left(k_{E1}^B + k_{E1}^F + k_{E2}^F\right)\right) S_{y=0}\right)$$

Obtain the King-Altman result for x_{HR} .

In[18]:= $$\text{FullSimplify}\left[\frac{\Gamma_{HR}}{\Gamma_T}\right]$$

Out[18]= $$\left(\left(k_2 + k_{-1}\right) k_{E1}^{F} k_{E2}^{B} + k_2 k_{+1} k_{E1}^{F} S_{y=0}\right) / \left(\left(k_2 + k_{-1}\right) \left(k_{E1}^{B} k_{E2}^{B} + k_{E1}^{F} \left(k_{E2}^{B} + k_{E2}^{F}\right)\right) + k_{+1} \left(k_{E1}^{F} k_{E2}^{F} + k_2 \left(k_{E1}^{B} + k_{E1}^{F} + k_{E2}^{F}\right)\right) S_{y=0}\right)$$

Obtain the King-Altman result for x_{Ox} .

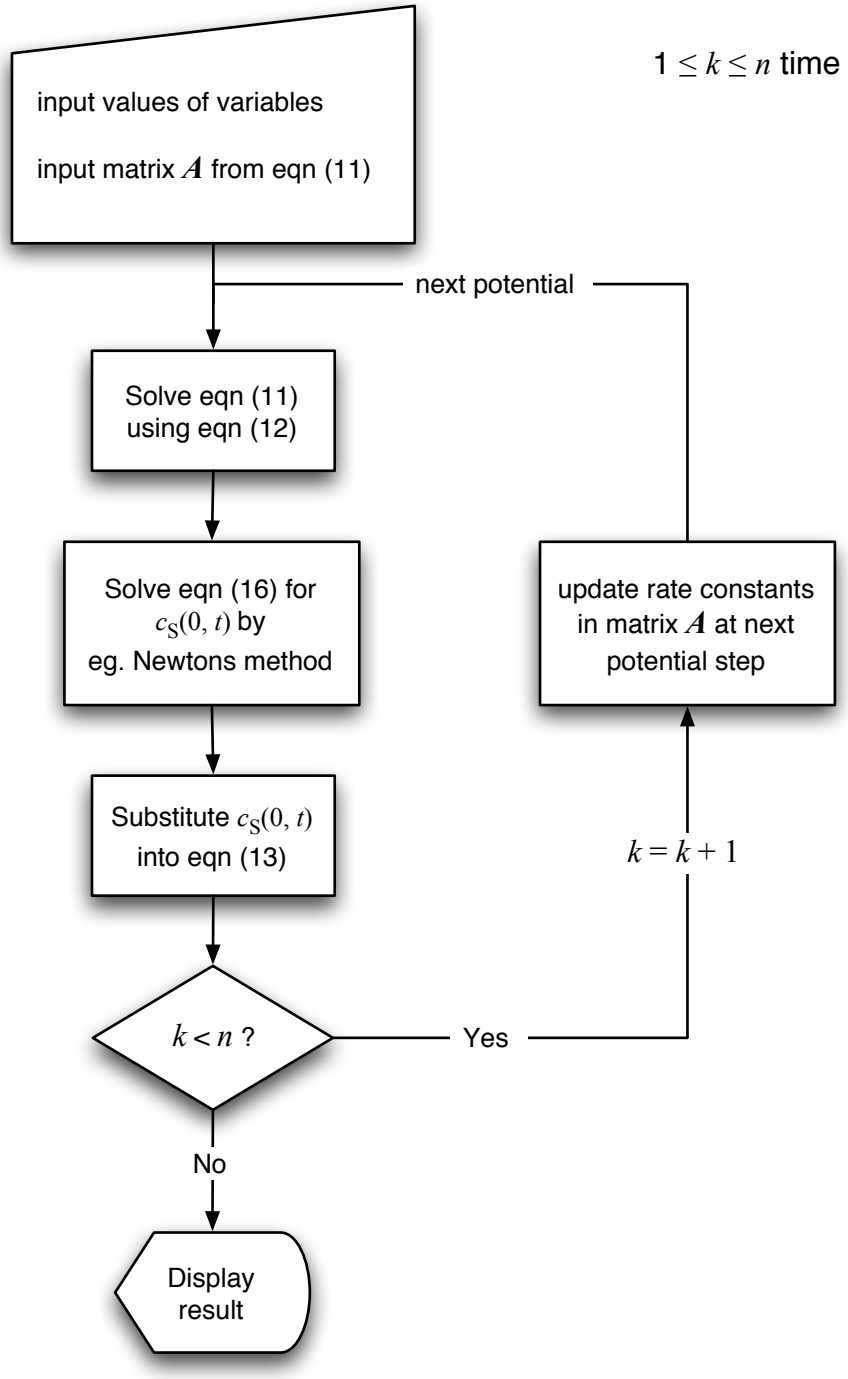
In[19]:= $$\mathbf{FullSimplify}\left[\frac{\Gamma_{\mathrm{Ox}}}{\Gamma_{\mathrm{T}}}\right]$$

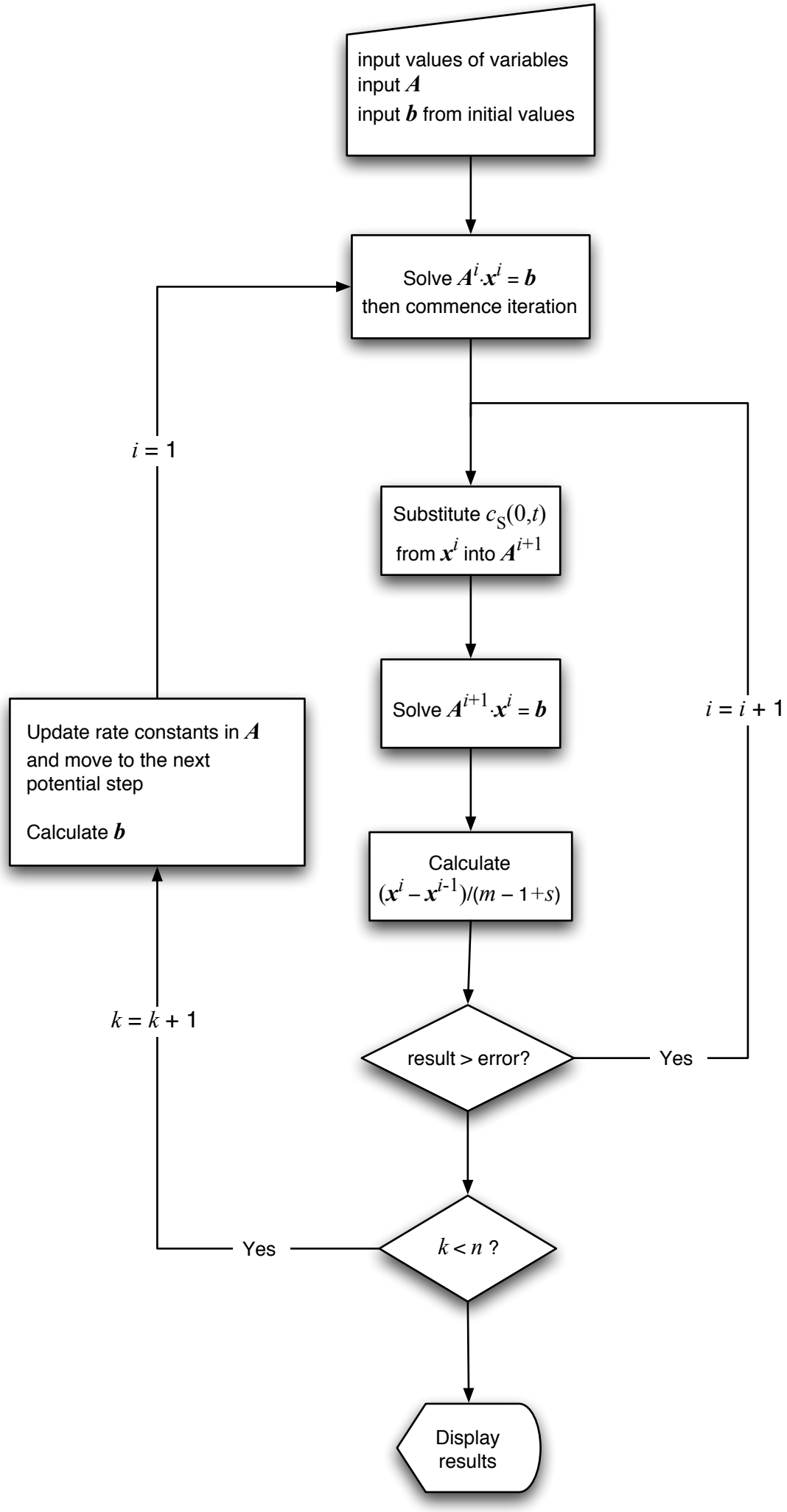
Out[19]= $$\left(\left(k_2 + k_{-1}\right) k_{E1}^{B} k_{E2}^{B} + k_2 k_{+1} \left(k_{E1}^{B} + k_{E2}^{F}\right) S_{y=0}\right) / \left(\left(k_2 + k_{-1}\right) \left(k_{E1}^{B} k_{E2}^{B} + k_{E1}^{F} \left(k_{E2}^{B} + k_{E2}^{F}\right)\right) + k_{+1} \left(k_{E1}^{F} k_{E2}^{F} + k_2 \left(k_{E1}^{B} + k_{E1}^{F} + k_{E2}^{F}\right)\right) S_{y=0}\right)$$

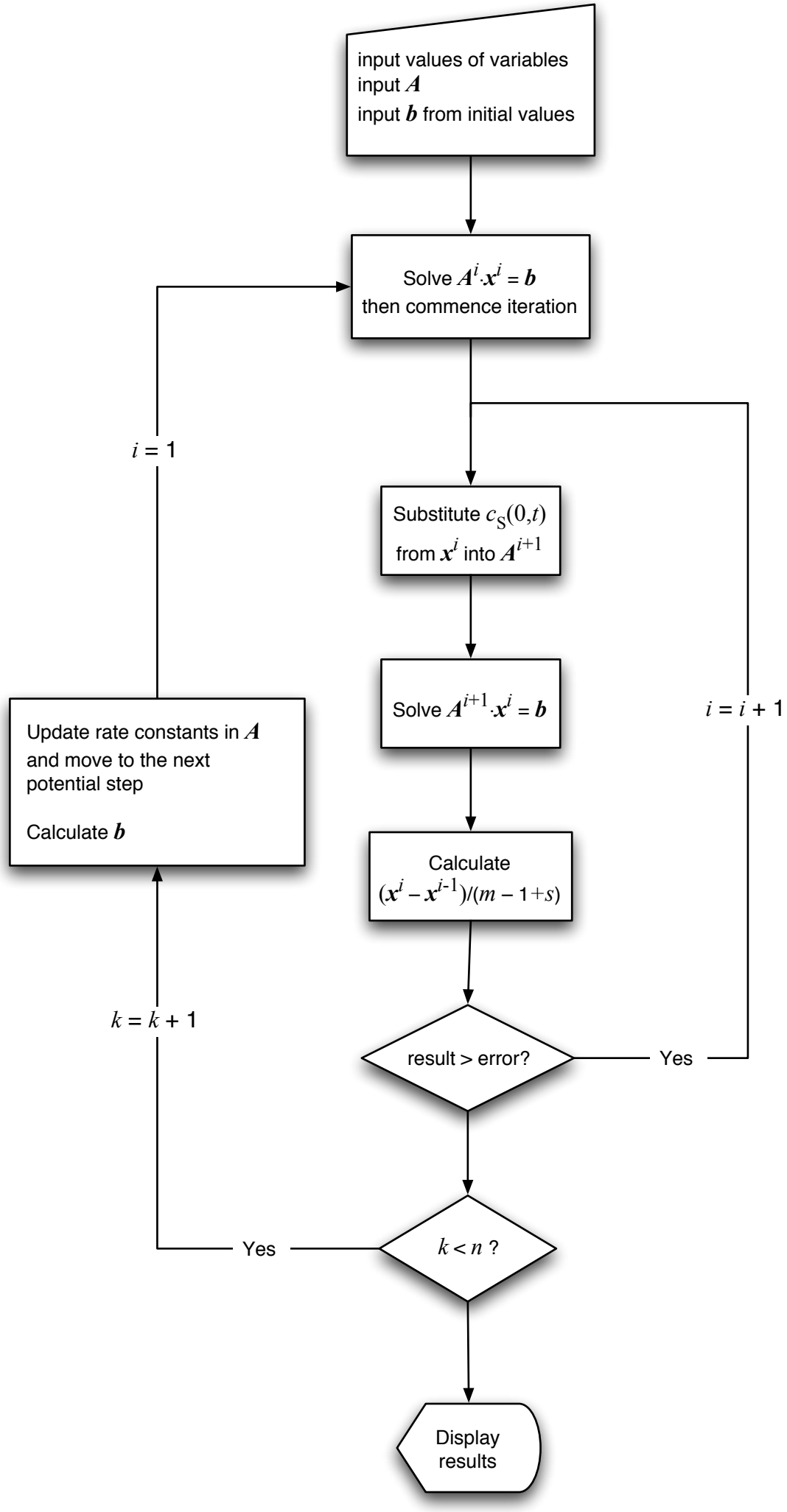
Flow chart for the King-Altman simulation

Simulation involving:

$1 \leq k \leq n$ time steps.




input values of variables
input $\boldsymbol{A}$
input $\boldsymbol{b}$ from initial values
Solve $\boldsymbol{A}^i \cdot \boldsymbol{x}^i = \boldsymbol{b}$
then commence iteration
$i = 1$
Substitute $c_S(0,t)$
from $\boldsymbol{x}^i$ into $\boldsymbol{A}^{i+1}$
Solve $\boldsymbol{A}^{i+1} \cdot \boldsymbol{x}^i = \boldsymbol{b}$
$i = i + 1$
Update rate constants in $\boldsymbol{A}$
and move to the next
potential step
Calculate $\boldsymbol{b}$
Calculate
$(\boldsymbol{x}^i - \boldsymbol{x}^{i-1})/(m - 1 + s)$
$k = k + 1$
result > error?
Yes
Yes
$k < n$?
Display
results


input values of variables
input $\boldsymbol{A}$
input $\boldsymbol{b}$ from initial values
Solve $\boldsymbol{A}^i \cdot \boldsymbol{x}^i = \boldsymbol{b}$
then commence iteration
$i = 1$
Substitute $c_S(0,t)$
from $\boldsymbol{x}^i$ into $\boldsymbol{A}^{i+1}$
Solve $\boldsymbol{A}^{i+1} \cdot \boldsymbol{x}^i = \boldsymbol{b}$
$i = i + 1$
Update rate constants in $\boldsymbol{A}$
and move to the next
potential step
Calculate $\boldsymbol{b}$
Calculate
$(\boldsymbol{x}^i - \boldsymbol{x}^{i-1})/(m - 1 + s)$
$k = k + 1$
result > error?
Yes
Yes
$k < n$?
Display
results