

There are 12 reactions and 9 species in the fumarase model.

The stoichiometric matrix is  $S =$

```

-1  0 -1  0  0  1  1  0  1  0  0 -1
 0  0  0  0  1 -1  0  0  0  0 -1  1
 1 -1  0  0  0  0 -1  1  0  0  0  0
 0  1  0  1 -1  0  0 -1  0 -1  1  0
 0  0  1 -1  0  0  0  0 -1  1  0  0
-1  0  0 -1  0  0  1  0  0  1  0  0
 0 -1 -1  0  0  0  0  1  1  0  0  0
 0  0  0  0 -1  0  0  0  0  0  1  0
 0  0  0  0  0 -1  0  0  0  0  0  1

```

The vector of reaction velocities is  $v$ , where

```

v( 1) = k1*x1*x6
v( 2) = k2*x3*x7
v( 3) = k3*x1*x7
v( 4) = k4*x5*x6
v( 5) = k5*x4*x8
v( 6) = k6*x2
v( 7) = k7*x3
v( 8) = k8*x4
v( 9) = k9*x5
v(10) = k10*x4
v(11) = k11*x2
v(12) = k12*x1*x9

```

The vector of mass balance equations is  $\dot{x} = S*v$ , where

```

xdot(1) = k6*x2 + k7*x3 + k9*x5 - k1*x1*x6 - k3*x1*x7 - k12*x1*x9
xdot(2) = k5*x4*x8 - k11*x2 - k6*x2 + k12*x1*x9
xdot(3) = k8*x4 - k7*x3 + k1*x1*x6 - k2*x3*x7
xdot(4) = k11*x2 - k8*x4 - k10*x4 + k2*x3*x7 + k4*x5*x6 - k5*x4*x8
xdot(5) = k10*x4 - k9*x5 + k3*x1*x7 - k4*x5*x6
xdot(6) = k7*x3 + k10*x4 - k1*x1*x6 - k4*x5*x6
xdot(7) = k8*x4 + k9*x5 - k3*x1*x7 - k2*x3*x7
xdot(8) = k11*x2 - k5*x4*x8
xdot(9) = k12*x1*x9 - k6*x2

```

Let the map  $\psi_p$  be given by

```

k1  |--> p1
k2  |--> p2
k3  |--> p3
k4  |--> p4
k5  |--> p5
k6  |--> y1
k7  |--> y2
k8  |--> y3
k9  |--> y4
k10 |--> y5
k11 |--> y6
k12 |--> p6
x1  |--> p7
x2  |--> p8
x3  |--> p9
x4  |--> p10
x5  |--> p11
x6  |--> y7
x7  |--> y8
x8  |--> y9
x9  |--> y10

```

This results in a linear velocity vector  $\psi_p(v)$ , where

```

psi_p(v( 1)) = p1*p7*y7
psi_p(v( 2)) = p2*p9*y8
psi_p(v( 3)) = p3*p7*y8
psi_p(v( 4)) = p4*p11*y7
psi_p(v( 5)) = p5*p10*y9
psi_p(v( 6)) = p8*y1
psi_p(v( 7)) = p9*y2
psi_p(v( 8)) = p10*y3
psi_p(v( 9)) = p11*y4
psi_p(v(10)) = p10*y5
psi_p(v(11)) = p8*y6
psi_p(v(12)) = p6*p7*y10

```

We can express  $\text{psi\_p}(v)$  as the product  $P*y$ , where  $y$  is the vector  $[y_1, \dots, y_{10}]^T$  and  $P =$

```

0 0 0 0 0 0 p1*p7 0 0 0
0 0 0 0 0 0 0 p2*p9 0 0
0 0 0 0 0 0 0 p3*p7 0 0
0 0 0 0 0 0 p4*p11 0 0 0
0 0 0 0 0 0 0 0 p5*p10 0
p8 0 0 0 0 0 0 0 0 0 0
0 p9 0 0 0 0 0 0 0 0 0
0 0 p10 0 0 0 0 0 0 0 0
0 0 0 p11 0 0 0 0 0 0 0
0 0 0 0 p10 0 0 0 0 0 0
0 0 0 0 0 p8 0 0 0 0 0
0 0 0 0 0 0 0 0 0 p6*p7

```

From this we calculate the coefficient matrix,  $C = S*P =$

```

p8 p9 0 p11 0 0 -p1*p7 -p3*p7 0 -p6*p7
-p8 0 0 0 0 -p8 0 0 p5*p10 p6*p7
0 -p9 p10 0 0 0 p1*p7 -p2*p9 0 0
0 0 -p10 0 -p10 p8 p4*p11 p2*p9 -p5*p10 0
0 0 0 -p11 p10 0 -p4*p11 p3*p7 0 0
0 p9 0 0 p10 0 C(6, 7) 0 0 0
0 0 p10 p11 0 0 0 -p3*p7 -p2*p9 0 0
0 0 0 0 0 p8 0 0 -p5*p10 0 0
-p8 0 0 0 0 0 0 0 0 p6*p7

```

where

$$C(6, 7) = -p1*p7 - p4*p11$$

$C$  is row equivalent to the reduced matrix  $\text{Crref} =$

```

1 0 0 0 0 0 0 0 0 -(p6*p7)/p8
0 1 0 0 p10/p9 0 Crref(2, 7) 0 0 0
0 0 1 0 1 0 Crref(3, 7) Crref(3, 8) 0 0
0 0 0 1 -p10/p11 0 p4 Crref(4, 8) 0 0
0 0 0 0 0 1 0 0 -(p5*p10)/p8 0
0 0 0 0 0 0 0 0 0 0
0 0 0 0 0 0 0 0 0 0
0 0 0 0 0 0 0 0 0 0
0 0 0 0 0 0 0 0 0 0

```

where

$$\text{Crref}(4, 8) = -(p3*p7)/p11$$

$$\text{Crref}(3, 8) = -(p2*p9)/p10$$

$$\text{Crref}(3, 7) = -(p4*p11)/p10$$

$$\text{Crref}(2, 7) = -(p1*p7 + p4*p11)/p9$$

The null space of C is spanned by the columns of N =

$$\begin{array}{cccccc}
 0 & 0 & 0 & 0 & (p_6 p_7)/p_8 & \\
 -p_{10}/p_9 & (p_1 p_7 + p_4 p_{11})/p_9 & 0 & 0 & 0 & 0 \\
 -1 & (p_4 p_{11})/p_{10} & (p_2 p_9)/p_{10} & 0 & 0 & 0 \\
 p_{10}/p_{11} & -p_4 & (p_3 p_7)/p_{11} & 0 & 0 & 0 \\
 1 & 0 & 0 & 0 & 0 & 0 \\
 0 & 0 & 0 & (p_5 p_{10})/p_8 & 0 & 0 \\
 0 & 1 & 0 & 0 & 0 & 0 \\
 0 & 0 & 1 & 0 & 0 & 0 \\
 0 & 0 & 0 & 0 & 1 & 0 \\
 0 & 0 & 0 & 0 & 0 & 1
 \end{array}$$

Let  $\bar{y} = Nq$ , where  $q$  is given by

$$\begin{aligned}
 q(1) &= q_2 \\
 q(2) &= q_4 \\
 q(3) &= (p_{10} q_1 + p_{10} q_2 - p_4 p_{11} q_4)/(p_2 p_9) \\
 q(4) &= (p_8 q_3)/(p_5 p_{10}) \\
 q(5) &= q_5
 \end{aligned}$$

This gives

$$\begin{aligned}
 \bar{y}(1) &= (p_6 p_7 q_5)/p_8 \\
 \bar{y}(2) &= (q_4 (p_1 p_7 + p_4 p_{11}))/p_9 - (p_{10} q_2)/p_9 \\
 \bar{y}(3) &= q_1 \\
 \bar{y}(4) &= (p_{10} q_2 - p_4 p_{11} q_4)/p_{11} + (p_3 p_7 (p_{10} q_1 + p_{10} q_2 - p_4 p_{11} q_4))/(p_2 p_9 p_{11}) \\
 \bar{y}(5) &= q_2 \\
 \bar{y}(6) &= q_3 \\
 \bar{y}(7) &= q_4 \\
 \bar{y}(8) &= (p_{10} q_1 + p_{10} q_2 - p_4 p_{11} q_4)/(p_2 p_9) \\
 \bar{y}(9) &= (p_8 q_3)/(p_5 p_{10}) \\
 \bar{y}(10) &= q_5
 \end{aligned}$$

From  $\bar{y}$  we construct the composite forward map  $\psi_{py}$  :

$$\begin{array}{ll}
 k_1 & | \rightarrow p_1 \\
 k_2 & | \rightarrow p_2 \\
 k_3 & | \rightarrow p_3 \\
 k_4 & | \rightarrow p_4 \\
 k_5 & | \rightarrow p_5 \\
 k_6 & | \rightarrow (p_6 p_7 q_5)/p_8 \\
 k_7 & | \rightarrow (q_4 (p_1 p_7 + p_4 p_{11}))/p_9 - (p_{10} q_2)/p_9 \\
 k_8 & | \rightarrow q_1 \\
 k_9 & | \rightarrow (p_{10} q_2 - p_4 p_{11} q_4)/p_{11} + (p_3 p_7 (p_{10} q_1 + p_{10} q_2 - p_4 p_{11} q_4))/(p_2 p_9 p_{11}) \\
 k_{10} & | \rightarrow q_2
 \end{array}$$

```

k11  |-->  q3
k12  |-->  p6
x1    |-->  p7
x2    |-->  p8
x3    |-->  p9
x4    |-->  p10
x5    |-->  p11
x6    |-->  q4
x7    |-->  (p10*q1 + p10*q2 - p4*p11*q4)/(p2*p9)
x8    |-->  (p8*q3)/(p5*p10)
x9    |-->  q5

```

The steady state reaction velocity vector  $\mathbf{vbar}$  is given by  $\mathbf{psi\_py(v)}$ , where

```

vbar( 1) = p1*p7*q4
vbar( 2) = p10*q1 + p10*q2 - p4*p11*q4
vbar( 3) = (p3*p7*(p10*q1 + p10*q2 - p4*p11*q4))/(p2*p9)
vbar( 4) = p4*p11*q4
vbar( 5) = p8*q3
vbar( 6) = p6*p7*q5
vbar( 7) = -p9*((p10*q2)/p9 - (q4*(p1*p7 + p4*p11))/p9)
vbar( 8) = p10*q1
vbar( 9) = p11*((p10*q2 - p4*p11*q4)/p11 + (p3*p7*(p10*q1 + p10*q2 - p4*p11*
      q4))/(p2*p9*p11))
vbar(10) = p10*q2
vbar(11) = p8*q3
vbar(12) = p6*p7*q5

```

The mapping function  $\mathbf{psi\_q^{-1}}$  is given by

```

q1  |-->  y3
q2  |-->  y5
q3  |-->  y6
q4  |-->  y7
q5  |-->  y10

```

The composite inverse map  $\mathbf{psi\_qp^{-1}}$ :

```

p1  |-->  k1
p2  |-->  k2
p3  |-->  k3
p4  |-->  k4
p5  |-->  k5
p6  |-->  k12

```

```

p7  |--> x1
p8  |--> x2
p9  |--> x3
p10 |--> x4
p11 |--> x5
q1  |--> k8
q2  |--> k10
q3  |--> k11
q4  |--> x6
q5  |--> x9

```

The complete steady state map  $\psi_{ss}$  is therefore

```

k1  |--> k1
k2  |--> k2
k3  |--> k3
k4  |--> k4
k5  |--> k5
k6  |--> (k12*x1*x9)/x2
k7  |--> (x6*(k1*x1 + k4*x5))/x3 - (k10*x4)/x3
k8  |--> k8
k9  |--> (k10*x4 - k4*x5*x6)/x5 + (k3*x1*(k8*x4 + k10*x4 - k4*x5*x6))/(k2*
      x3*x5)
k10 |--> k10
k11 |--> k11
k12 |--> k12
x1  |--> x1
x2  |--> x2
x3  |--> x3
x4  |--> x4
x5  |--> x5
x6  |--> x6
x7  |--> (k8*x4 + k10*x4 - k4*x5*x6)/(k2*x3)
x8  |--> (k11*x2)/(k5*x4)
x9  |--> x9

```

The unsubstituted steady state reaction velocity vector  $\mathbf{vbar} = \psi_{ss}(\mathbf{v})$  is given by

```

vbar( 1) = k1*x1*x6
vbar( 2) = k8*x4 + k10*x4 - k4*x5*x6
vbar( 3) = (k3*x1*(k8*x4 + k10*x4 - k4*x5*x6))/(k2*x3)
vbar( 4) = k4*x5*x6

```

```
vbar( 5) = k11*x2
vbar( 6) = k12*x1*x9
vbar( 7) = -x3*((k10*x4)/x3 - (x6*(k1*x1 + k4*x5))/x3)
vbar( 8) = k8*x4
vbar( 9) = x5*((k10*x4 - k4*x5*x6)/x5 + (k3*x1*(k8*x4 + k10*x4 - k4*x5*x6))/
              (k2*x3*x5))
vbar(10) = k10*x4
vbar(11) = k11*x2
vbar(12) = k12*x1*x9
```

Verify steady state.  $\dot{x} = S * vbar$ , where

```
xdot(1) = 0
xdot(2) = 0
xdot(3) = 0
xdot(4) = 0
xdot(5) = 0
xdot(6) = 0
xdot(7) = 0
xdot(8) = 0
xdot(9) = 0
```