Sensitivity Analysis of Biochemical Systems Using Bond Graphs: Additional Material.

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Contents

1 Introduction

This notebook generates the figures for the paper: Sensitivity Analysis of Biochemical Systems Using Bond Graphs. The companion notebook Sensitivity_PPP.ipynb contains the Pentose Phosphate Pathway example.

2 Supporting software

2.1 Import packages

[1]:
```
## Some useful imports
import BondGraphTools as bgt
import numpy as np
import sympy as sp
import matplotlib.pyplot as plt
import control as con
import copy
import importlib

## For reimporting: use imp.reload(module)
import importlib as imp

## Stoichiometric analysis
import stoich as st

## SVG
import svgBondGraph as sbg
```

```
## Stoichiometry to BG
import stoichBondGraph as stbg

## Modularity
# import modular as bgm

## Sloppy parameters
import sloppy as slp

## Display (eg disp.SVG(), disp.
import IPython.display as disp

##
quiet = True
Titles = True
Plotting = False
```

```
Warning - scikit.odes not found. Simulations are disabled.
```

2.2 Transfer function properties

[2]:
```
def tfProps(tf,method='truncate'):

    ## Steady-state gain
    g = con.dcgain(tf)

    if not con.issiso(tf):
        g = g[0][0]

    ## Time constant
    ## Check if direct link
    direct_link = np.any(tf.D)
    ## Only set tau=0 if siso
    if direct_link and con.issiso(tf):
        ## Instant response
        tau = 0
    else:
        ## Reduce to first-order to estimate time constant
        ## Note that method='matchdc' can give a kernel crash - use 'truncate'
        tf1  = con.balred(sys,orders=1,method=method)
        poles = con.poles(tf1)
        realPoles = np.real(poles)
        tau = -1/min(realPoles)

    return g,tau
```

2.3 Plotting and printing

[3]:
```
## Optional plotting
def Savefig(name):
    if Plotting:
        plt.rcParams.update({'font.size': 14})
        plotname = 'Figs/'+name+'.pdf'
        print('Saving',plotname)
        plt.savefig(plotname)
```

[4]:
```
def latex(m,name):
    lm = sp.latex(sp.Matrix(m),mat_delim="(")
    return name+' &= '+lm

## Optional print latex for the paper
printing = True
def printLatex(s,sc=None):
    if printing:
        ## System properties in LaTeX
        AA = Sys.A; print(latex(AA,'A'))
        BB = Sys.B; print(latex(BB,'B'))
        CC = Sys.C; print(latex(CC,'C'))
        DD = Sys.D; print(latex(DD,'D'))


        for m in ['species','reaction','Nf','Nr','N']:
            print(st.sprintl(s,m))

        if not (sc==None):
            print('%% Nc matrix')
            print(st.sprintl(sc,'N'))

        print(st.sprintrl(s,all=True,chemformula=True))
        print(st.sprintvl(s))
```

2.4 Steady-state by simulation

[5]:
```
## Steady-state by simulation
def SteadyState(s,sc,sf=None,parameter={},X0=None,t_ss=1000):
    t = np.linspace(0,t_ss)
    dat = st.
↪sim(s,sc=sc,sf=sf,t=t,parameter=parameter,X0=X0,tol=1e-4,quiet=quiet)
    X_ss = dat['X'][-1]
    V_ss = dat['V'][-1]
    #dX_ss = sc['N']@V_ss
    dX_ss = dat['dX'][-1]
    dXc_ss = dat['dXc'][-1]
    print(f'Steady-state finder error: {np.linalg.norm(dXc_ss):.2e}')
    return X_ss,V_ss
```

2.5 Stoichiometry

[6]:
```
def␣
↪Stoichiometry(model,chemostats=[],flowstats=[],CommonSpecies=None,sensitivity=False):
↪

    ## Stoichiometry
    s = st.stoich(model,quiet=quiet)

    ## Unify species
    if not (CommonSpecies is None):
        commonSpecies = st.merge(s,CommonSpecies=CommonSpecies)
#          print(commonSpecies)
        st.unify(s,commonSpecies=commonSpecies)

    ## Sensitivity
    if sensitivity:
        extra = st.stoichSensitivity(s)
    else:
        extra = []

#      print(chemostats+extra)

    ## Chemostats and flowstats
    sc = st.statify(s,chemostats=chemostats+extra)
    sf = st.statify(s,flowstats=flowstats)

    return s,sc,sf
```

2.6 Linearisation

[7]:
```
def Linear(s,sc,sf=None,parameter={},X0=None, invar='X', outvar = 'V',␣
↪quiet=False):

    ## Steady state
    if X0 is None:
        X0 = np.ones(s['n_X'])
#      print(len(X0))

    X_ss,V_ss = SteadyState(s,sc,sf=sf,parameter=parameter,X0=X0)
    dX_ss = s['N']@V_ss
    print('X_ss =',X_ss)
    print('V_ss =', V_ss)
#      print('dX_ss =', dX_ss)

    ## Linearise
    sys = st.lin(s,sc,sf=sf,x_ss=X_ss,parameter=parameter,
                 invar=invar,outvar=outvar,quiet=quiet)

    return sys,X_ss,V_ss,dX_ss
```

[8]:
```
def linStep(sc,sys,T=None,X0=None):
    """ Linearised response: step (X0 is None) or initial conditions␣
↪(otherwise)
    """

    if X0 is None:
        resp = con.step_response(sys,T)
        y = resp.y[:,0,:].T
    else:
        L_xX = sc['L_xX']
        G_X = sc['G_X']
        resp = con.initial_response(sys,T,X0=L_xX@X0)
        y = resp.y.T


    return y
```

2.7 Extract subsystem from linear system

[9]:
```
def Index(A,a):

    I = []
    for aa in a:
        i = A.index(aa)
        I.append(i)
    return np.array(I)

def zapSmall(x,tol=1e-10,quiet=True):

    xx = np.zeros(len(x))
    for i,val in enumerate(x):
        if abs(val)>tol:
            xx[i] = x[i]
        else:
            if not quiet:
                print(f'Setting {i}th coefficient {val:.2} to zero')
    return xx

def␣
↪extractSubsystem(SYS,sc,sf,inp,outp,minreal=False,tol=None,order=None,quiet=False):
↪

    Sys = copy.copy(SYS)
    chemostats = sc['chemostats']
    if sf is None:
        flowstats = []
    else:
        flowstats = sf['flowstats']
    species = sc['species']
    reaction = sc['reaction']
```

```python
    ## Index of input and output
    if inp[0] in chemostats:
        i_inp = Index(chemostats,inp)
#           print('Input:',i_inp,chemostats[i_inp[0]])
    else:
        i_inp = Index(flowstats,inp)+len(chemostats)

#       print(i_inp)

    if outp[0] in chemostats:
        i_outp = Index(chemostats,outp)
    elif outp[0] in species:
        i_outp = Index(species,outp)
    else:
        if outp[0] in reaction:
            i_outp = Index(reaction,outp)
        else:
            print(f'Output {outp} does not exist')

    ## Extract tf
    n_y = len(i_outp)
    n_u = len(i_inp)
    nn = Sys.A.shape
    n_x = nn[0]
#       print(n_x)

    sys = con.ss(Sys.A,
                 Sys.B[:,i_inp].reshape(n_x,n_u),
                 Sys.C[i_outp,:].reshape(n_y,n_x),
                 Sys.D[i_outp][:,i_inp].reshape(n_y,n_u))
    if minreal:
        sys = con.minreal(sys,tol=tol,verbose=False)

    ## Reduce order
    if not (order is None):
        sys = con.balred(sys,order,method='matchdc')

    return sys
```

2.8 Plotting

[10]:
```python
def plotSensitivity(dat,reactions=['r1','r2'],plotSim=True,name=None):

    if plotSim:
        plt.plot(t,y_lin,color='black',lw=3)
    else:
        plt.plot(t,y_lin,label=label,lw=3)

    for reac in reactions:
```

```
        i = s['reaction'].index(reac)
        if plotSim:
            label = reac + r' ($\tilde\lambda$ = ' + f'{lam-1:0.2f})'
            pc = int(round(100*(lam-1)))
            label = f'{reac} ({pc}%)'
            plt.plot(t,(dat['V'][:,i]-V_ss[i])/(lam-1),
                     lw=5,ls='dashed',label=label)

    plt.grid()
    plt.legend()
    plt.xlabel('$t$')
    plt.ylabel(r'$\Delta {v}/\Delta{\lambda}$')
#     plt.tight_layout()
```

[11]:
```
def plotLines(lw=4,ls='dotted'):
        plt.hlines(g,min(t),max(t),color='black',ls=ls,lw=lw)
        plt.vlines(tau,min(y_lin.flatten()),max(y_lin.
 ↪flatten()),color='black',ls=ls,lw=lw)
```

2.9 Normalisation constants

[12]:
```
T_human = 37 # Human body temperature
K_0 = 273.15
print(f'T_human = {T_human} degC = {T_human+K_0} K')

mu_0 = RT = st.RT(T_cent=T_human)
print(f'mu_0 = {mu_0*1e-3:0.3f} kJ/mol')

F = st.F() # Faraday's constant
print(f'F = {F*1e-3:0.2f} kC/mol')

V_0 = RT/F
print(f'V_0 = {V_0*1e3:0.2f} mV')

P_0 = 1e-3

v_0 = P_0/mu_0
print(f'v_0 = {v_0*1e6:0.4f} micro mol /s')

i_0 = F*v_0
print(f'i_0 = {i_0*1e3:0.2f} mA')
```

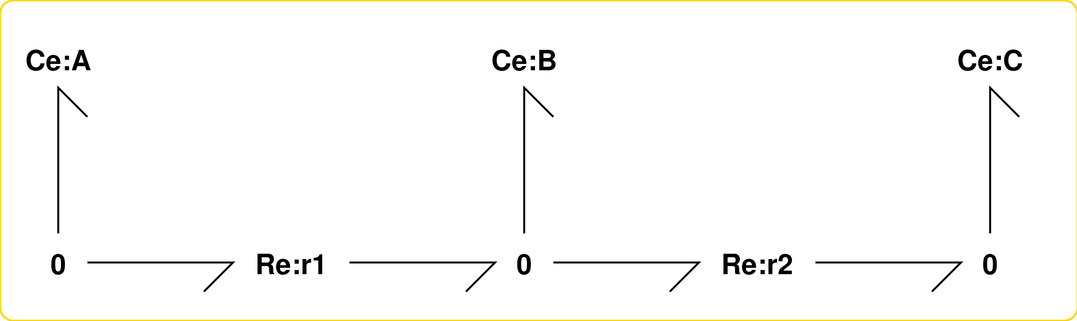
```
T_human = 37 degC = 310.15 K
mu_0 = 2.579 kJ/mol
F = 96.49 kC/mol
V_0 = 26.73 mV
v_0 = 0.3878 micro mol /s
i_0 = 37.42 mA
```

3 Simple example A = B = C revisited.

3.1 Bond Graph

[13]:
```python
# Simple example A = B = C
sbg.model('ABC_abg.svg')
import ABC_abg
disp.SVG('ABC_abg.svg')
```

[13]:



[14]:
```python
## BG generated equations
# model = ABC_abg.model()
# for cr in model.constitutive_relations:
#     print(cr)
#     #print(sp.diff(cr,'x_0'))
```

3.2 Parameters

[15]:
```python
## Parameters
parameter = {}
parameter['K_A'] = 1
parameter['K_B'] = 1
parameter['kappa_r1'] = 1
parameter['kappa_r2'] = 9
print(parameter)

## Initial states
X_A_0 = 2
```

```
{'K_A': 1, 'K_B': 1, 'kappa_r1': 1, 'kappa_r2': 9}
```

3.3 Stoichiometry & linearisation

[16]:
```python
## Stoichiometry
s,sc,sf = Stoichiometry(ABC_abg.model(),chemostats=['A','C'],flowstats=[])
```

[17]:
```python
## Linearise
Parameter = copy.copy(parameter)
Parameter['K_A'] = X_A_0*parameter['K_A']
```

```
Sys,X_ss,V_ss,dX_ss =␣
↪Linear(s,sc,parameter=parameter,X0=[X_A_0,1,1],quiet=quiet)
i_A = s['species'].index('A')
X_A_ss = X_ss[i_A]


## Show transfer function
con.tf(Sys)

## Lambda for comparison
lam = 1.1
```

```
Steady-state finder error: 8.88e-16
X_ss = [2.  1.1 1. ]
V_ss = [0.9 0.9]
```

[18]:

```
printLatex(s,sc=sc)
```

```
A &= \left(\begin{matrix}-10.0\end{matrix}\right)
B &= \left(\begin{matrix}1.0 & 9.0\end{matrix}\right)
C &= \left(\begin{matrix}-1.0\\9.0\end{matrix}\right)
D &= \left(\begin{matrix}1.0 & 0\\0 & -9.0\end{matrix}\right)
\begin{align}
X&= \begin{pmatrix}
    X_{A}\\
    X_{B}\\
    X_{C}\\
\end{pmatrix}
\end{align}

\begin{align}
V&= \begin{pmatrix}
    V_{r1}\\
    V_{r2}\\
\end{pmatrix}
\end{align}

\begin{align}
Nf &=
\left(\begin{matrix}1 & 0\\0 & 1\\0 & 0\end{matrix}\right)
\end{align}

\begin{align}
Nr &=
\left(\begin{matrix}0 & 0\\1 & 0\\0 & 1\end{matrix}\right)
\end{align}

\begin{align}
N &=
\left(\begin{matrix}-1 & 0\\1 & -1\\0 & 1\end{matrix}\right)
\end{align}
```

```
%% Nc matrix
\begin{align}
N &=
\left(\begin{matrix}0 & 0\\1 & -1\\0 & 0\end{matrix}\right)
\end{align}

\begin{align}
\ch{A & <> [ r1 ] B }\\
\ch{B & <> [ r2 ] C }
\end{align}

\begin{align}
v_{r1} &= \kappa_{r1} \left(K_{A} x_{A} - K_{B} x_{B}\right)\\
v_{r2} &= \kappa_{r2} \left(K_{B} x_{B} - K_{C} x_{C}\right)
\end{align}
```

[19]:
```
## Show dc gain
print('DC gain: \n', con.dcgain(Sys))
```

```
DC gain:
 [[ 0.9 -0.9]
 [ 0.9 -0.9]]
```

3.4 Sensitivity Bond Graph – change chemostats

[20]:
```
## Extract sensitivity system
inp = ['A']
outp = ['r1','r2']
sys = extractSubsystem(Sys,sc,sf,inp,outp)

## Include factor X_A_0 into the linarised system
sys.B = sys.B*X_A_0
sys.D = sys.D*X_A_0
```

[21]:
```
## Show transfer function
con.tf(sys)
```

[21]:

$$\begin{bmatrix} \frac{2s+18}{s+10} \\ \frac{18}{s+10} \end{bmatrix}$$

[22]:
```
## System matrix
sys
```

[22]:

$$\left(\begin{array}{r|l} -10 & 2 \\ \hline -1 & 2 \\ 9 & 0 \end{array}\right)$$

[23]:
```
## Show dc gain
print('DC gain: \n', con.dcgain(sys))
```

```
DC gain:
 [[1.8]
 [1.8]]
```

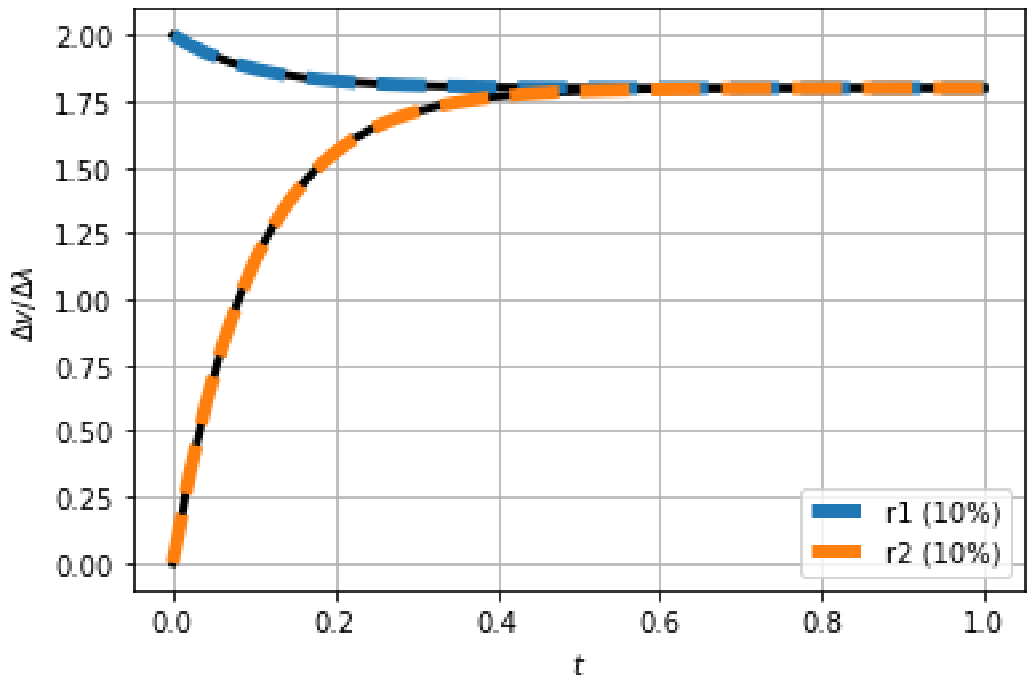
3.4.1 Compare sensitivity with exact simulation

[24]:
```
## Exact Simulate with changed x_A
X_ss_1 = copy.copy(X_ss)
X_ss_1[i_A] = lam*X_A_ss
print(X_ss)
t = np.linspace(0,1)
dat = st.sim(s,sc=sc,t=t,parameter=parameter,X0=X_ss_1,quiet=quiet)
print(parameter)
```

```
[2.  1.1 1. ]
{'K_A': 1, 'K_B': 1, 'kappa_r1': 1, 'kappa_r2': 9}
```

[25]:
```
## Step response to change in A
y_lin = linStep(sc,sys,T=t)
```

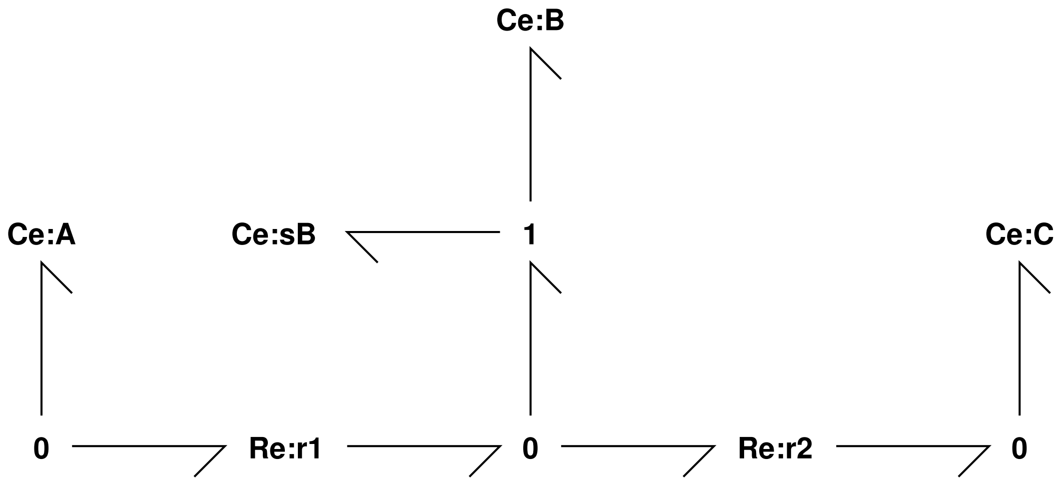
[26]:
```
## Plot
plotSensitivity(dat,)
```



3.5 Sensitivity Bond Graph – change K_B

[27]:
```
# Simple example A = B = C: sensitivity
sbg.model('sKABC_abg.svg')
import sKABC_abg
disp.SVG('sKABC_abg.svg')
```

[27]:



3.5.1 Stoichiometry & linearisation

[28]:
```
## Stoichiometry
s,sc,sf = Stoichiometry(sKABC_abg.
 ↪model(),chemostats=['A','C','sB'],flowstats=[])

## Linearise
Sys,X_ss,V_ss,dX_ss =␣
 ↪Linear(s,sc,parameter=parameter,X0=[2,1,1,1],quiet=quiet)

## Extract sensitivity system
inp = ['sB']
outp = ['r1','r2']
sys = extractSubsystem(Sys,sc,sf,inp,outp)

## Species and reactions
print(s['species'])
print(s['reaction'])
```

```
Steady-state finder error: 8.88e-16
X_ss = [2.  1.1 1.  1. ]
V_ss = [0.9 0.9]
['A', 'B', 'C', 'sB']
['r1', 'r2']
```

[29]:
```
## Show transfer function
con.tf(sys)
```

[29]:

$$\begin{bmatrix} \frac{-1.1s}{s+10} \\ \frac{9.9s}{s+10} \end{bmatrix}$$

[30]:
```
## System matrix
sys
```

[30]:

$$\left(\begin{array}{c|c} -10 & -11 \\ \hline -1 & -1.1 \\ 9 & 9.9 \end{array}\right)$$

[31]:
```
## Show dc gain
print('DC gain: \n', con.dcgain(sys))
```

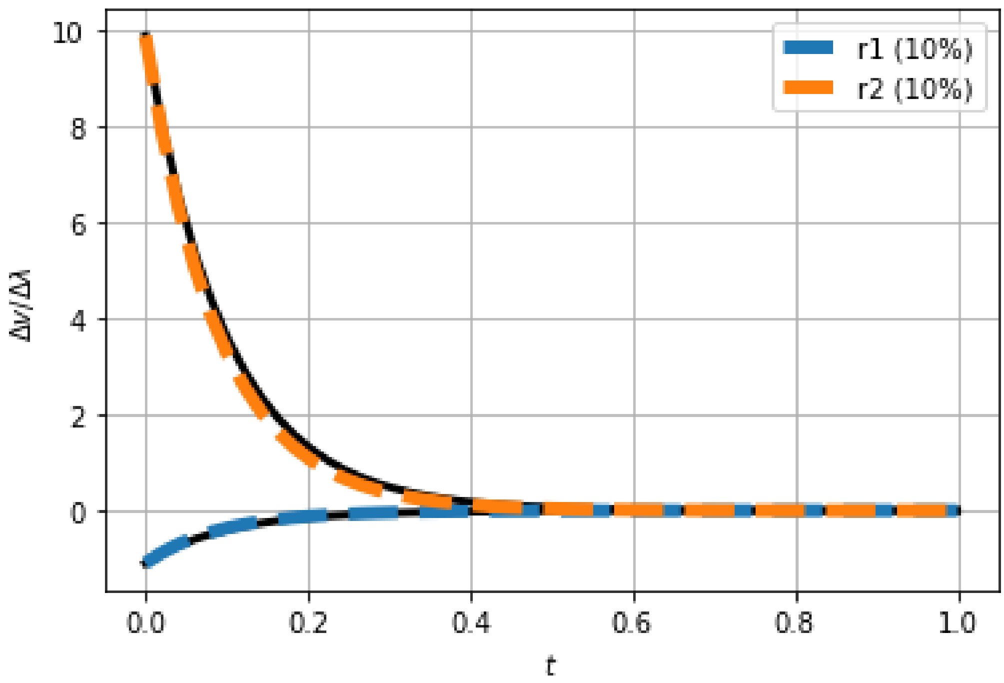
```
DC gain:
 [[0.]
 [0.]]
```

3.5.2 Compare sensitivity with exact simulation

[32]:
```
## Exact Simulate with changed K
parameter1 = copy.copy(parameter)
parameter1['K_B'] *= lam
t = np.linspace(0,1)
dat = st.sim(s,sc=sc,t=t,parameter=parameter1,X0=X_ss,quiet=quiet)
```

[33]:
```
## Step response to sB
y_lin = linStep(sc,sys,T=t)
```

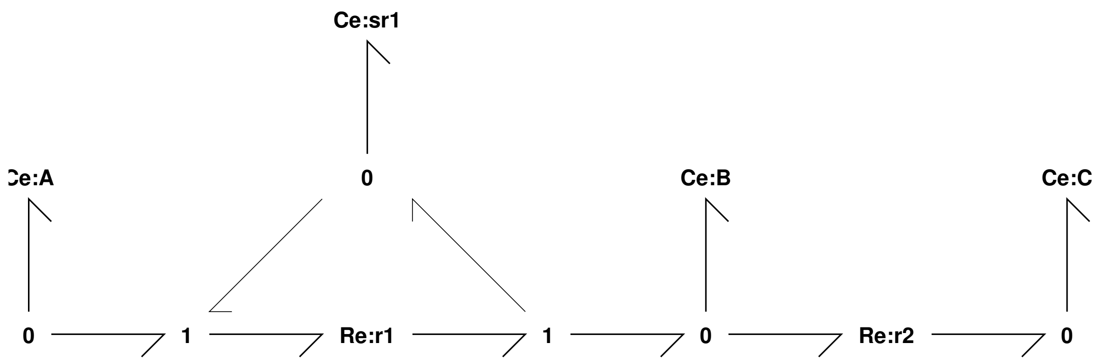
[34]:
```
## Plot
plotSensitivity(dat,)
```



3.6 Sensitivity Bond Graph – change κ_1

[35]:
```
# Simple example A = B = C: sensitivity
sbg.model('sKapABC_abg.svg')
import sKapABC_abg
disp.SVG('sKapABC_abg.svg')
```

[35]:



[36]:
```
## BG generated equations
model = sKapABC_abg.model()
for cr in model.constitutive_relations:
    print(cr)
    #print(sp.diff(cr,'x_0'))
```

```
K_A*K_sr1*kappa_r1*x_0*x_3 - K_B*K_sr1*kappa_r1*x_1*x_3 + dx_0
-K_A*K_sr1*kappa_r1*x_0*x_3 + K_B*K_sr1*kappa_r1*x_1*x_3 + K_B*kappa_r2*x_1 -
```

```
K_C*kappa_r2*x_2 + dx_1
-K_B*kappa_r2*x_1 + K_C*kappa_r2*x_2 + dx_2
dx_3
```

3.6.1 Stoichiometry & linearisation

[37]:
```
print(s['reaction'])
## Stoichiometry
s,sc,sf = Stoichiometry(sKapABC_abg.model(),chemostats=['A','C','sr1'])
print(sf['flowstats'])

## Linearise
Sys,X_ss,V_ss,dX_ss =␣
↪Linear(s,sc,parameter=parameter,X0=[2,1,1,1],quiet=quiet)

## Extract sensitivity system
inp = ['sr1']
outp = ['r1','r2']
sys = extractSubsystem(Sys,sc,sf,inp,outp)

## Show transfer function
con.tf(sys)
```

```
['r1', 'r2']
[]
Steady-state finder error: 8.88e-16
X_ss = [2.  1.1 1.  1. ]
V_ss = [0.9 0.9]
```

[37]:

$$\begin{bmatrix} \frac{0.9s+8.1}{s+10} \\ \frac{8.1}{s+10} \end{bmatrix}$$

[38]:
```
## System matrix
sys
```

[38]:

$$\left(\begin{array}{c|c} -10 & 0.9 \\ \hline -1 & 0.9 \\ 9 & 0 \end{array}\right)$$

[39]:
```
## Show dc gain
print('DC gain: \n', con.dcgain(sys))
```

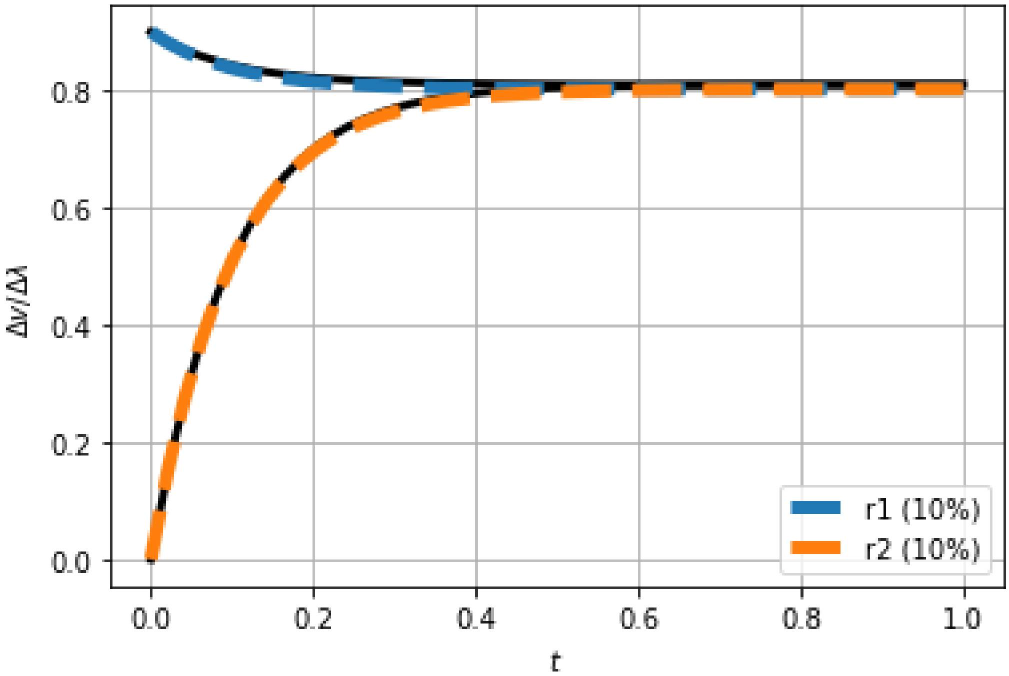
```
DC gain:
 [[0.81]
 [0.81]]
```

3.6.2 Compare sensitivity with exact simulation

[40]:
```
## Exact Simulate with changed K
lam = 1.1
parameter1 = copy.copy(parameter)
parameter1['kappa_r1'] *= lam
t = np.linspace(0,1)
dat = st.sim(s,sc=sc,sf=sf,t=t,parameter=parameter1,X0=X_ss,quiet=quiet)
```

[41]:
```
## Step response to sB
y_lin = linStep(sc,sys,T=t)
```

[42]:
```
## Plot
plotSensitivity(dat,)
```



[43]:
```
sys
```

[43]:

$$\left(\begin{array}{c|c} -10 & 0.9 \\ \hline -1 & 0.9 \\ 9 & 0 \end{array}\right)$$

[44]:
```
disp.Latex(st.sprintvl(s))
```

[44]:

$$v_{r1} = K_{sr1}\kappa_{r1}x_{sr1}\left(K_Ax_A - K_Bx_B\right) \quad (1)$$

$$v_{r2} = \kappa_{r2}\left(K_Bx_B - K_Cx_C\right) \quad (2)$$

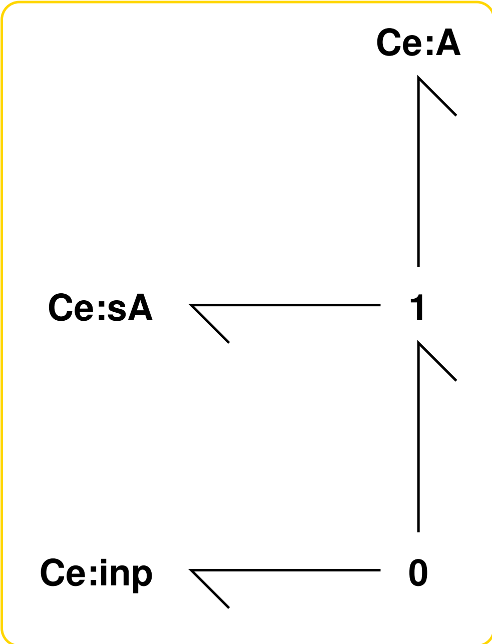
4 Sensitivity components

4.1 sCe

4.1.1 Bond Graph

[45]:
```
# sCe
sbg.model('sCe_abg.svg')
import sCe_abg
disp.SVG('sCe_abg.svg')
```

[45]:

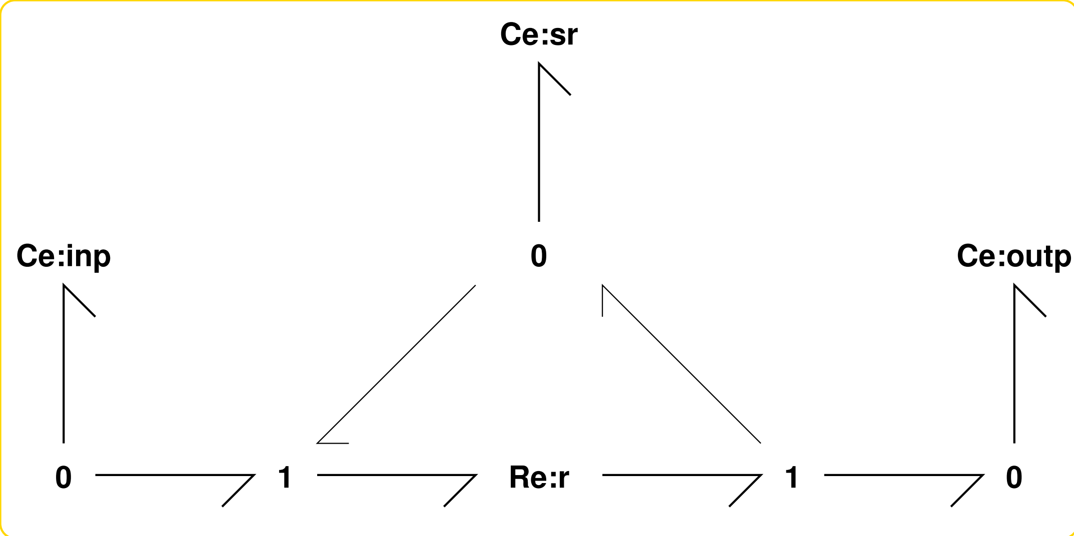


4.2 sRe

4.2.1 Bond Graph

[46]:
```
# sRe
sbg.model('sRe_abg.svg')
import sRe_abg
disp.SVG('sRe_abg.svg')
```

[46]:

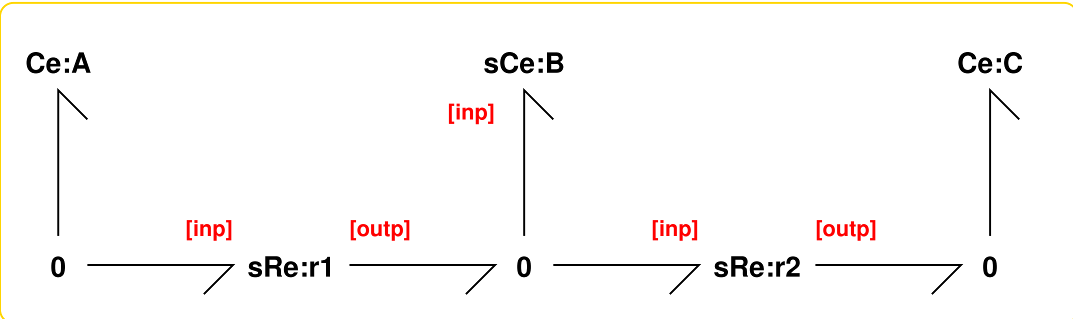


4.3 Simple system revisited

[47]:
```
# Simple example A = B = C with sensitivity components
sbg.model('sABC_abg.svg')
import sABC_abg
disp.SVG('sABC_abg.svg')
```

```
Creating subsystem: sCe:B
Creating subsystem: sRe:r1
Creating subsystem: sRe:r2
```

[47]:



4.3.1 Parameters

[48]:
```
## Parameters
parameter = {}
parameter['K_A'] = 1
parameter['K_B_A'] = 1
parameter['kappa_r1'] = 0.1
parameter['kappa_r2'] = 0.9
print(parameter)
```

```
## Initial states
X_A_0 = 2
```

```
{'K_A': 1, 'K_B_A': 1, 'kappa_r1': 0.1, 'kappa_r2': 0.9}
```

[49]:
```
## Parameters
parameter = {}
parameter['K_A'] = 1
parameter['K_B_A'] = 1
parameter['kappa_r1'] = 1
parameter['kappa_r2'] = 9
print(parameter)

## Initial states
X_A_0 = 2
```

```
{'K_A': 1, 'K_B_A': 1, 'kappa_r1': 1, 'kappa_r2': 9}
```

4.3.2 Stoichiometry & linearisation

[50]:
```
## Stoichiometry
s,sc,sf = Stoichiometry(sABC_abg.
 ↪model(),chemostats=['A','C','B_sA','r1_sr','r2_sr'],flowstats=[])

## Species
print(s['species'])

## Reactions
print(s['reaction'])

## Linearise
Sys,X_ss,V_ss,dX_ss =␣
 ↪Linear(s,sc,parameter=parameter,X0=[X_A_0,1,1,1,1,1],quiet=quiet)


## Lambda for comparison
lam = 1.1
```

```
['A', 'C', 'B_A', 'B_sA', 'r1_sr', 'r2_sr']
['r1', 'r2']
Steady-state finder error: 8.88e-16
X_ss = [2.  1.  1.1 1.  1.  1. ]
V_ss = [0.9 0.9]
```

[51]:
```
## Show reactions
disp.Latex(st.sprintrl(s,all=True,chemformula=True))
```

[51]:

$$\mathrm{A} + \mathrm{r_{1s}r} \xrightleftharpoons{\mathrm{r_1}} \mathrm{B_A} + \mathrm{B_sA} + \mathrm{r_{1s}r} \tag{3}$$

$$\mathrm{B_A} + \mathrm{B_sA} + \mathrm{r_{2s}r} \xrightleftharpoons{\mathrm{r_2}} \mathrm{C} + \mathrm{r_{2s}r} \tag{4}$$

[52]:
```
## Show system
Sys
```

[52]:

$$\left(\begin{array}{r|rrrrr} -10 & 1 & 9 & -11 & 0.9 & -0.9 \\ \hline -1 & 1 & 0 & -1.1 & 0.9 & 0 \\ 9 & 0 & -9 & 9.9 & 0 & 0.9 \end{array}\right)$$

[53]:
```
## Show transfer function
con.tf(Sys)
```

[53]:

$$\begin{bmatrix} \frac{s+9}{s+10} & \frac{-9}{s+10} & \frac{-1.1s}{s+10} & \frac{0.9s+8.1}{s+10} & \frac{0.9}{s+10} \\ \frac{9}{s+10} & \frac{-9s-9}{s+10} & \frac{9.9s}{s+10} & \frac{8.1}{s+10} & \frac{0.9s+0.9}{s+10} \end{bmatrix}$$

4.3.3 Stoichiometric matrix

[54]:
```
disp.Latex(st.sprintl(s,'N'))
```

[54]:

$$N = \begin{pmatrix} -1 & 0 \\ 0 & 1 \\ 1 & -1 \\ 1 & -1 \\ 0 & 0 \\ 0 & 0 \end{pmatrix} \tag{5}$$

[55]:
```
disp.Latex(st.sprintl(s,'Nf'))
```

[55]:

$$Nf = \begin{pmatrix} 1 & 0 \\ 0 & 0 \\ 0 & 1 \\ 0 & 1 \\ 1 & 0 \\ 0 & 1 \end{pmatrix} \tag{6}$$

[56]:
```
disp.Latex(st.sprintl(s,'Nr'))
```

[56]:

$$Nr = \begin{pmatrix} 0 & 0 \\ 0 & 1 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 0 & 1 \end{pmatrix} \tag{7}$$

[57]:
```
## Show dc gain
print('DC gain: \n', con.dcgain(Sys))
```

```
DC gain:
 [[ 0.9  -0.9   0.    0.81  0.09]
 [ 0.9  -0.9   0.    0.81  0.09]]
```

4.4 Sensitivity Bond Graph – change B

[58]:
```
## Extract sensitivity system
inp = ['B_sA']
outp = ['r1','r2']
sys = extractSubsystem(Sys,sc,sf,inp,outp)
```

[59]:
```
## Show transfer function
con.tf(sys)
```

[59]:

$$\begin{bmatrix} \frac{-1.1s}{s+10} \\ \frac{9.9s}{s+10} \end{bmatrix}$$

[60]:
```
## System matrix
sys
```

[60]:

$$\left(\begin{array}{c|c} -10 & -11 \\ \hline -1 & -1.1 \\ 9 & 9.9 \end{array}\right)$$

[61]:
```
## Show dc gain
print('DC gain: \n', con.dcgain(sys))
```

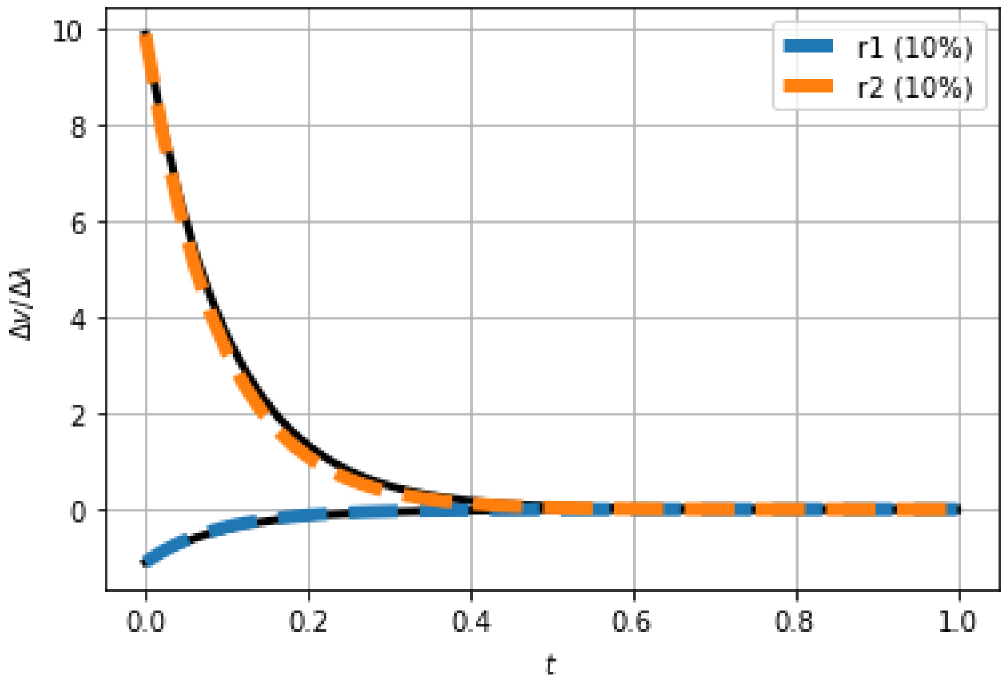
```
DC gain:
 [[0.]
 [0.]]
```

4.4.1 Compare sensitivity with exact simulation

[62]:
```
## Exact Simulate with changed K
parameter1 = copy.copy(parameter)
parameter1['K_B_A'] *= lam
t = np.linspace(0,1)
dat = st.sim(s,sc=sc,t=t,parameter=parameter1,X0=X_ss,quiet=quiet)
```

[63]:
```
## Step response to sB
y_lin = linStep(sc,sys,T=t)
```

[64]:
```
## Plot
plotSensitivity(dat,)
```



4.5 Sensitivity Bond Graph – change r1

[65]:
```
## Extract sensitivity system
inp = ['r1_sr']
outp = ['r1','r2']
sys = extractSubsystem(Sys,sc,sf,inp,outp)
```

[66]:
```
## Show transfer function
con.tf(sys)
```

[66]:

$$\begin{bmatrix} \frac{0.9s+8.1}{s+10} \\ \frac{8.1}{s+10} \end{bmatrix}$$

[67]:
```
## System matrix
sys
```

[67]:

$$\left(\begin{array}{c|c} -10 & 0.9 \\ \hline -1 & 0.9 \\ 9 & 0 \end{array}\right)$$

[68]:
```
## Show dc gain
print('DC gain: \n', con.dcgain(sys))
```

```
DC gain:
 [[0.81]
 [0.81]]
```

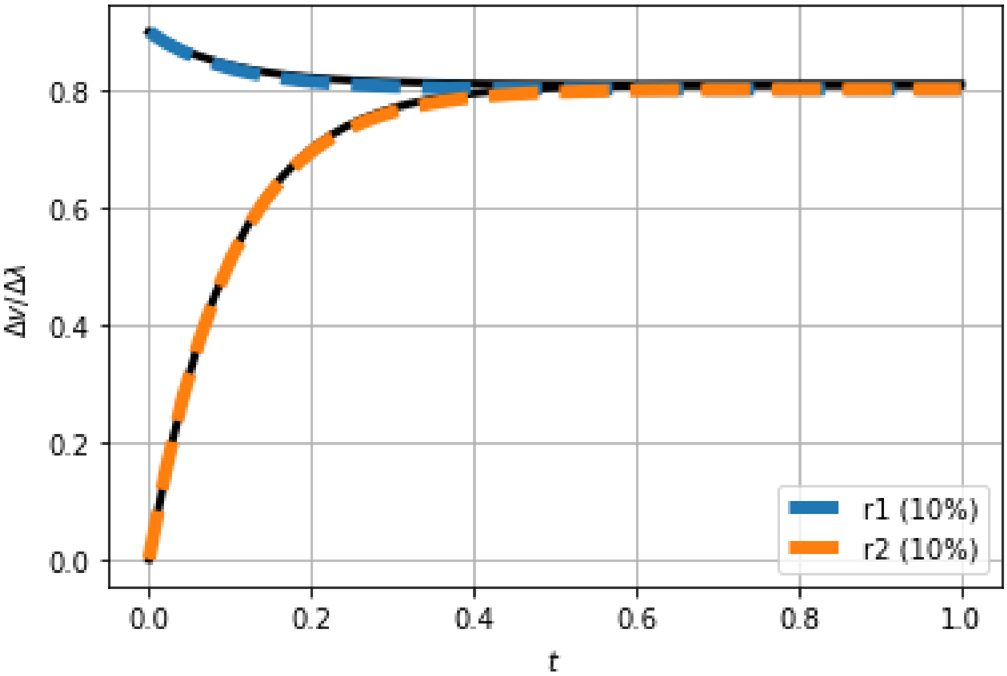
4.5.1 Compare sensitivity with exact simulation

[69]:
```
## Exact Simulate with changed r1
parameter1 = copy.copy(parameter)
parameter1['kappa_r1'] *= lam
t = np.linspace(0,1)
dat = st.sim(s,sc=sc,t=t,parameter=parameter1,X0=X_ss,quiet=quiet)
print(parameter1)
```

```
{'K_A': 1, 'K_B_A': 1, 'kappa_r1': 1.1, 'kappa_r2': 9}
```

[70]:
```
## Step response to sr1
y_lin = linStep(sc,sys,T=t)
```

[71]:
```
## Plot
plotSensitivity(dat,)
```



4.6 Sensitivity Bond Graph – change r2

[72]:
```
## Extract sensitivity system
inp = ['r2_sr']
outp = ['r1','r2']
sys = extractSubsystem(Sys,sc,sf,inp,outp)
```

[73]:
```
## Show transfer function
con.tf(sys)
```

[73]:

$$\begin{bmatrix} \frac{0.9}{s+10} \\ \frac{0.9s+0.9}{s+10} \end{bmatrix}$$

[74]:
```
## System matrix
sys
```

[74]:

$$\left(\begin{array}{c|c} -10 & -0.9 \\ \hline -1 & 0 \\ 9 & 0.9 \end{array}\right)$$

[75]:
```
## Show dc gain
print('DC gain: \n', con.dcgain(sys))
```

```
DC gain:
 [[0.09]
 [0.09]]
```

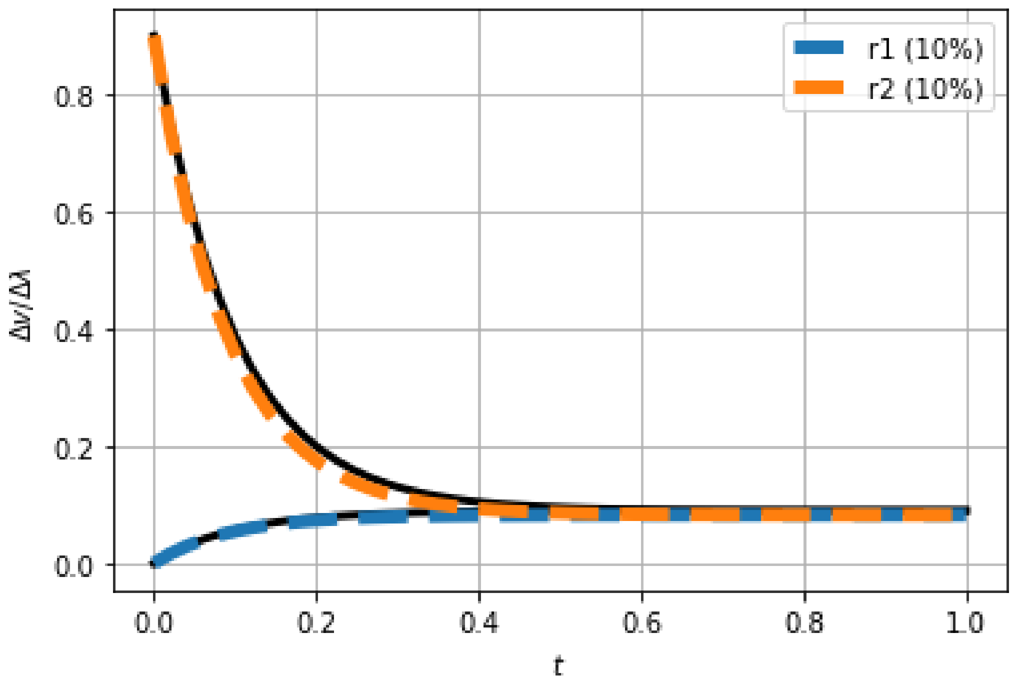
4.6.1 Compare sensitivity with exact simulation

[76]:
```
## Exact Simulate with changed r2
parameter1 = copy.copy(parameter)
parameter1['kappa_r2'] *= lam
t = np.linspace(0,1)
dat = st.sim(s,sc=sc,t=t,parameter=parameter1,X0=X_ss,quiet=quiet)
print(parameter1)
print(X_ss)
```

```
{'K_A': 1, 'K_B_A': 1, 'kappa_r1': 1, 'kappa_r2': 9.9}
[2.  1.  1.1 1.  1.  1. ]
```

[77]:
```
## Step response to sr2
y_lin = linStep(sc,sys,T=t)
```

[78]:
```
## Plot
plotSensitivity(dat,)
```



5 Stoichiometric approach

5.1 Supporting software

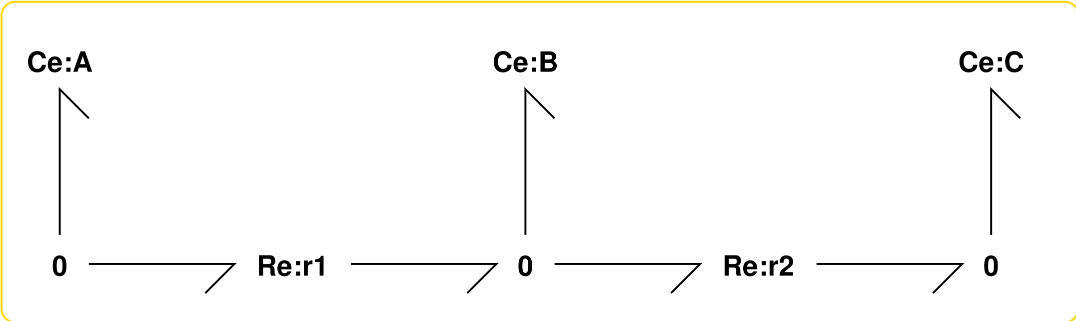
[79]:
```
def stoichSensitivity(model,chemostats=['A','C'],␣
↪parameter={},X0=None,CommonSpecies=None):
    """Sensitivity analysis  via stoichiometric approach """

    ## Stoichiometry
    s,sc,sf =␣
↪Stoichiometry(model,chemostats=chemostats,CommonSpecies=CommonSpecies,sensitivity=True)

    ## Linearise
    if X0 is None:
        X0 = np.ones(s['n_X'])
        i_chem = s['species'].index(chemostats[0])
        X0[i_chem] = 2

    Sys,X_ss,V_ss,dX_ss = Linear(s,sc,parameter=parameter,X0=X0,quiet=quiet)

    return s,sc,sf,Sys,X_ss,V_ss,dX_ss


def simSensitivity(s,sc,sf,Sys,X_ss,V_ss,dX_ss,chemostats=['A','C'],
                   inp=['sr1'],outp=['r1','r2'],t_last=2,parameter={},lam=1.
↪2,order=None,sX0=None):
```

```
    ## Extract sensitivity system
    sys = extractSubsystem(Sys,sc,sf,inp=inp,outp=outp,order=order)

    ## Time
    t = np.linspace(0,t_last,500)

    ## Sensitivity step response
#     step = con.step_response(sys,T=t)
#     y_lin = step.y[:,0,:].T
    y_lin = linStep(sc,sys,T=t,X0=sX0)

    ## Exact simulation with changed parameter or state
    X_ss_1 = copy.copy(X_ss)
    parameter1 = copy.copy(parameter)
    inComp = inp[0][1:]

    if sX0 is None:
        ## Parameter or chemostat perturbation
        if inComp in chemostats:
            ## Perturb state
            iComp = s['species'].index(inComp)
            X_ss_1[iComp] = lam*X_ss_1[iComp]
    #         y_lin *= X_ss_1[iComp]
        else:
            ## Perturb parameter
            if inComp[0].isupper():
                parname = 'K_'+inComp
            else:
                parname = 'kappa_'+inComp

            if parname in list(parameter.keys()):
                parameter1[parname] = lam*parameter[parname]
            else:
                parameter1[parname] = lam

        dat = st.
↪sim(s,sc=sc,sf=sf,t=t,parameter=parameter1,X0=X_ss_1,quiet=quiet)
    else:
        ## Initial condition perturbation.
        X_ss_1 += (lam-1)*sX0
        dat = st.
↪sim(s,sc=sc,sf=sf,t=t,parameter=parameter1,X0=X_ss_1,quiet=quiet)

    return dat,y_lin,t,sys
```

5.2 Simple example A = B = C

[80]:
```
# Simple example A = B = C
sbg.model('ABC_abg.svg')
import ABC_abg
disp.SVG('ABC_abg.svg')
```

[80]:



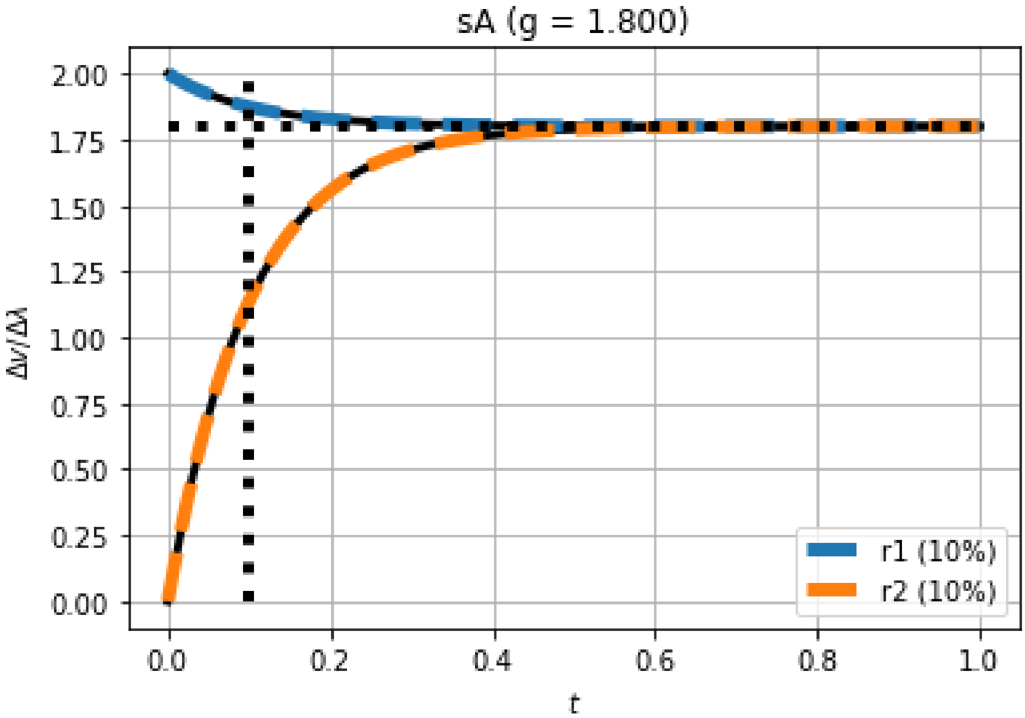
[81]:
```
## Parameters
parameter = {}
parameter['K_A'] = 1
parameter['K_B'] = 1
parameter['kappa_r1'] = 1
parameter['kappa_r2'] = 9
print(parameter)

## Initial states
X_A_0 = 2
```

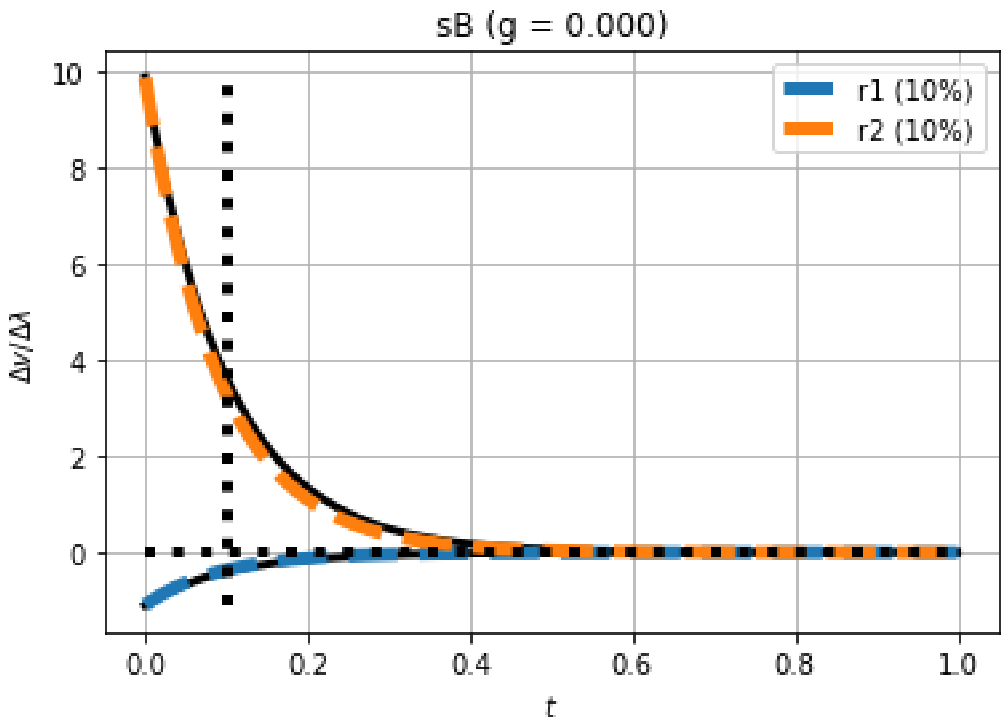
```
{'K_A': 1, 'K_B': 1, 'kappa_r1': 1, 'kappa_r2': 9}
```

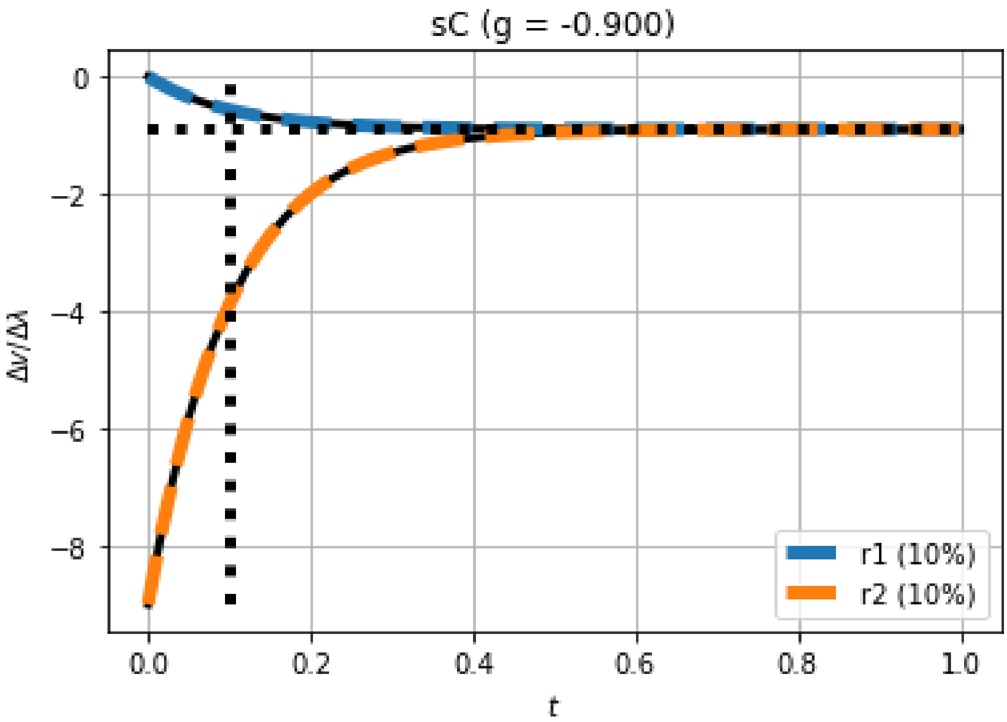
[82]:
```
## ABC model
dcgain = {}
s,sc,sf,Sys,X_ss,V_ss,dX_ss = stoichSensitivity(ABC_abg.
 ↪model(),parameter=parameter)
lam = 1.1
outp = ['r1','r2']
for inp in ['sA','sB','sC','sr1','sr2']:
    dat,y_lin,t,sys = simSensitivity(s,sc,sf,Sys,X_ss,V_ss,dX_ss,
                                                        ␣
 ↪parameter=parameter,inp=[inp],outp=outp,lam=lam,t_last=1)
#     g = con.dcgain(sys)[0][0]

    g,tau = tfProps(sys)
    dcgain[inp] = g
    if Titles:
        plt.title(f'{inp} (g = {g:.3f})')
    plotSensitivity(dat,reactions=outp)
    plotLines()
#     plt.hlines(g,min(t),max(t),color='black',ls='dashed')
```

```
    Savefig('ABC_'+inp)
    plt.show()
```

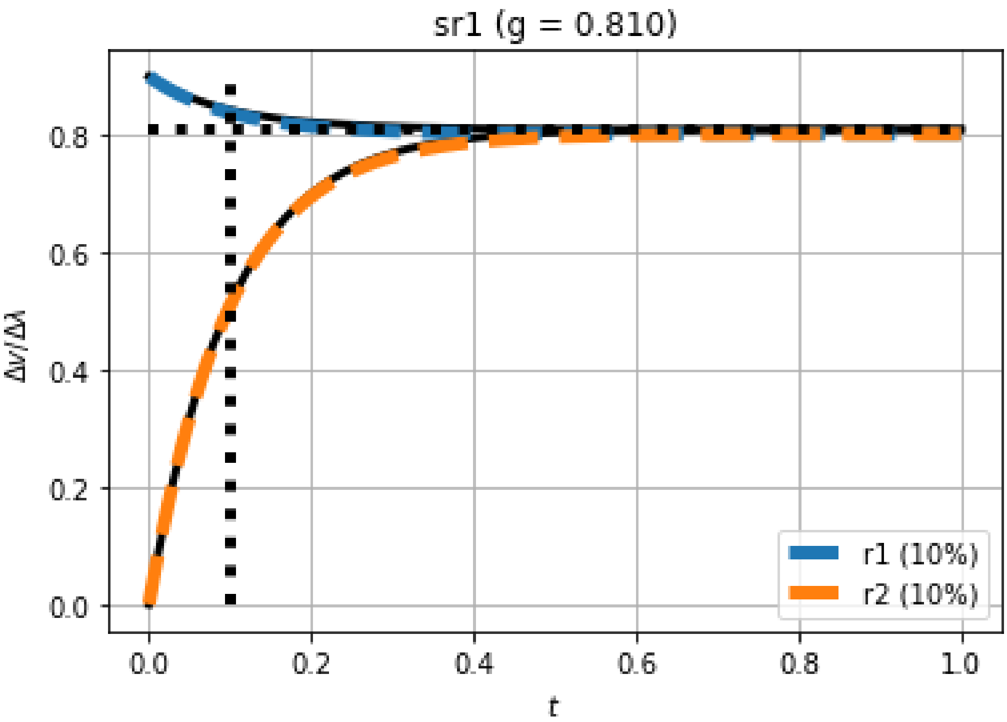
```
Steady-state finder error: 8.88e-16
X_ss = [2.  1.1 1.  1.  1.  1.  1.  1. ]
V_ss = [0.9 0.9]
```



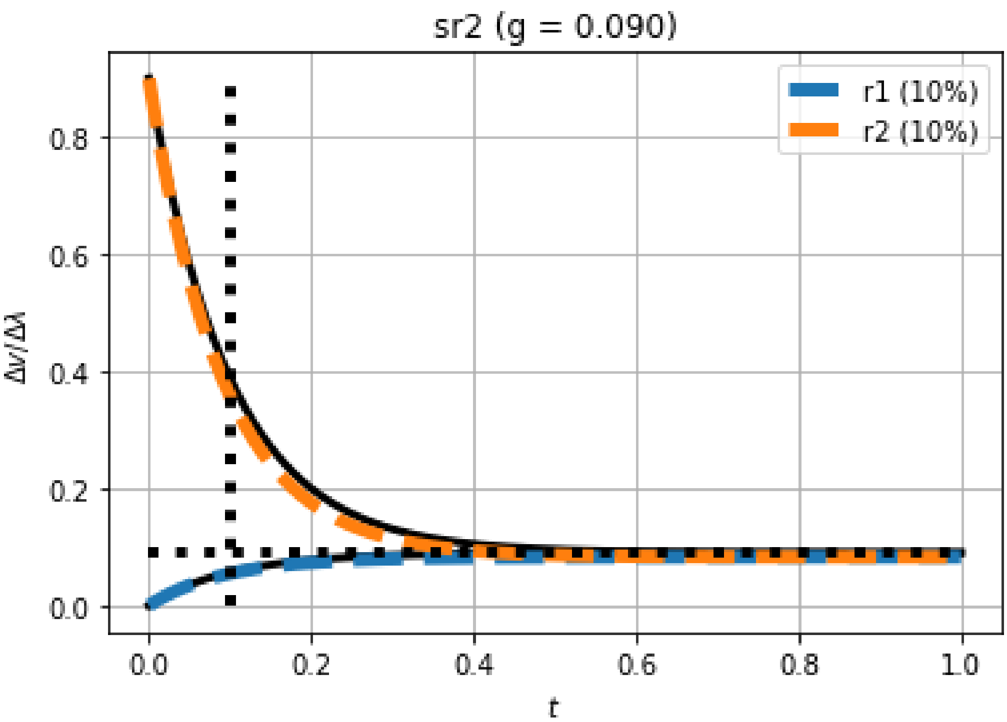




sC (g = -0.900)
0
−2
−4
−6
−8
Δv/Δλ
r1 (10%)
r2 (10%)
0.0
0.2
0.4
0.6
0.8
1.0
t



sr1 (g = 0.810)
0.8
0.6
0.4
0.2
0.0
Δv/Δλ
r1 (10%)
r2 (10%)
0.0
0.2
0.4
0.6
0.8
1.0
t



[83]:
```
printLatex(s,sc=sc)
```

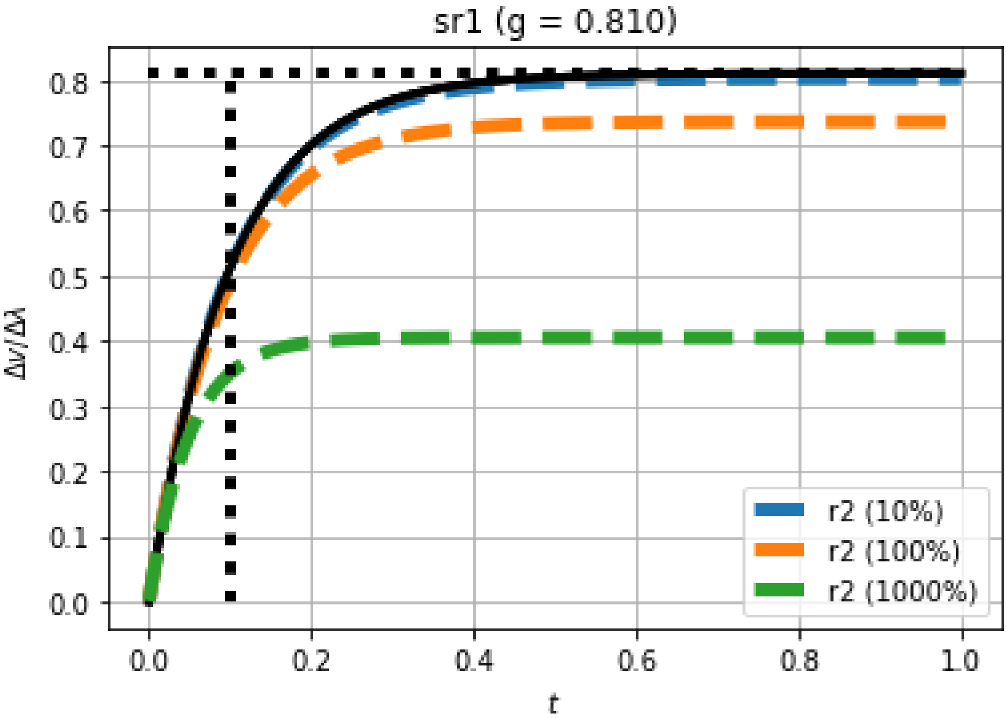
```
A &= \left(\begin{matrix}-10.0\end{matrix}\right)
B &= \left(\begin{matrix}1.0 & 9.0 & 2.0 & -11.0 & 9.0 & 0.9 &
-0.900000000000001\end{matrix}\right)
C &= \left(\begin{matrix}-1.0\\9.0\end{matrix}\right)
D &= \left(\begin{matrix}1.0 & 0 & 2.0 & -1.1 & 0 & 0.9 & 0\\0 & -9.0 & 0 & 9.9
& -9.0 & 0 & 0.900000000000001\end{matrix}\right)
\begin{align}
X&= \begin{pmatrix}
    X_{A}\\
    X_{B}\\
    X_{C}\\
    X_{sA}\\
    X_{sB}\\
    X_{sC}\\
    X_{sr1}\\
    X_{sr2}\\
\end{pmatrix}
\end{align}

\begin{align}
V&= \begin{pmatrix}
    V_{r1}\\
    V_{r2}\\
\end{pmatrix}
\end{align}
```

```
\begin{align}
Nf &=
\left(\begin{matrix}1.0 & 0\\0 & 1.0\\0 & 0\\1.0 & 0\\0 & 1.0\\0 & 0\\1.0 & 0\\0
& 1.0\end{matrix}\right)
\end{align}

\begin{align}
Nr &=
\left(\begin{matrix}0 & 0\\1.0 & 0\\0 & 1.0\\0 & 0\\1.0 & 0\\0 & 1.0\\1.0 & 0\\0
& 1.0\end{matrix}\right)
\end{align}

\begin{align}
N &=
\left(\begin{matrix}-1.0 & 0\\1.0 & -1.0\\0 & 1.0\\-1.0 & 0\\1.0 & -1.0\\0 &
1.0\\0 & 0\\0 & 0\end{matrix}\right)
\end{align}

%% Nc matrix
\begin{align}
N &=
\left(\begin{matrix}0 & 0\\1.0 & -1.0\\0 & 0\\0 & 0\\0 & 0\\0 & 0\\0 & 0\\0 &
0\end{matrix}\right)
\end{align}

\begin{align}
\ch{A + sA + sr1 & <> [ r1 ] B + sB + sr1 }\\
\ch{B + sB + sr2 & <> [ r2 ] C + sC + sr2 }
\end{align}

\begin{align}
v_{r1} &= \kappa_{r1} \left(K_{sr1} x_{sr1}\right)^{1.0} \left(\left(K_{A}
x_{A}\right)^{1.0} \left(K_{sA} x_{sA}\right)^{1.0} - \left(K_{B}
x_{B}\right)^{1.0} \left(K_{sB} x_{sB}\right)^{1.0}\right)\\
v_{r2} &= \kappa_{r2} \left(K_{sr2} x_{sr2}\right)^{1.0} \left(\left(K_{B}
x_{B}\right)^{1.0} \left(K_{sB} x_{sB}\right)^{1.0} - \left(K_{C}
x_{C}\right)^{1.0} \left(K_{sC} x_{sC}\right)^{1.0}\right)
\end{align}
```

5.2.1 Vary λ

[84]:
```
inp = 'sr1'
outp = ['r2']
for lam in [1.1,2,11]:
    dat,y_lin,t,sys = simSensitivity(s,sc,sf,Sys,X_ss,V_ss,dX_ss,
 ↪parameter=parameter,inp=[inp],outp=outp,lam=lam,t_last=1)
#     print(con.dcgain(sys))
    g = con.dcgain(sys)
```

```
    if Titles:
        plt.title(f'{inp} (g = {g:.3f})')
    plotSensitivity(dat,reactions=outp)
    plotLines()
Savefig('ABC_lambda')
```



[85]:
```
## Show system
Sys
```

[85]:

$$\left(\begin{array}{c|ccccccc} -10 & 1 & 9 & 2 & -11 & 9 & 0.9 & -0.9 \\ \hline -1 & 1 & 0 & 2 & -1.1 & 0 & 0.9 & 0 \\ 9 & 0 & -9 & 0 & 9.9 & -9 & 0 & 0.9 \end{array}\right)$$

[86]:
```
## Show system TF
print(sc['chemostats'])
con.tf(Sys)
```

```
['A', 'C', 'sA', 'sB', 'sC', 'sr1', 'sr2']
```

[86]:

$$\begin{bmatrix} \frac{s+9}{s+10} & \frac{-9}{s+10} & \frac{2s+18}{s+10} & \frac{-1.1s}{s+10} & \frac{-9}{s+10} & \frac{0.9s+8.1}{s+10} & \frac{0.9}{s+10} \\ \frac{9}{s+10} & \frac{-9s-9}{s+10} & \frac{18}{s+10} & \frac{9.9s}{s+10} & \frac{-9s-9}{s+10} & \frac{8.1}{s+10} & \frac{0.9s+0.9}{s+10} \end{bmatrix}$$

[87]:
```
## Show DC gain
con.dcgain(Sys)
```

[87]: array([[0.9 , -0.9 , 1.8 , 0. , -0.9 , 0.81, 0.09],
       [0.9 , -0.9 , 1.8 , 0. , -0.9 , 0.81, 0.09]])

[88]:
```
## Show initial reponse
print(Sys.D)
```

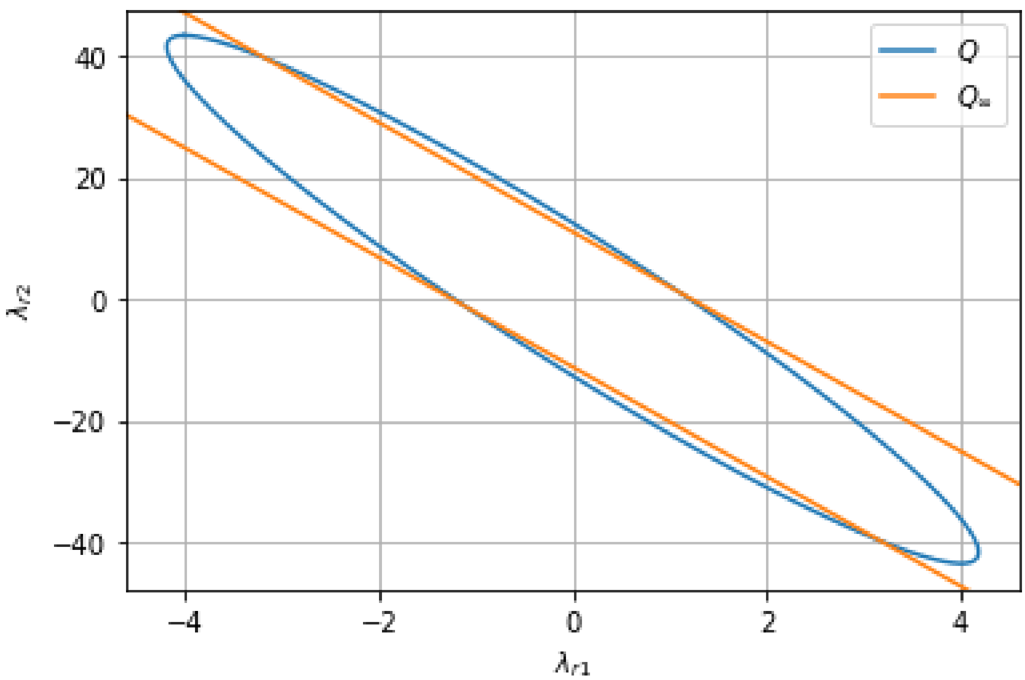
```
[[ 1.   0.   2.  -1.1  0.   0.9  0. ]
 [ 0.  -9.   0.   9.9 -9.   0.   0.9]]
```

5.2.2 Sloppy parameters

[89]:
```
imp.reload(slp)

def sloppy(Sys,inp,outp,t=None,GainOnly=False):
    sys = extractSubsystem(Sys,sc,sf,inp,outp)
    #print(sys)
    H,eig,eigv,t = slp.Sloppy(sys,t=t,GainOnly=GainOnly)
    print(H)
    slp.SloppyPlot(eig,eigv,inp)
    slp.SloppyPrint(eig,eigv,inp,min_eig=0)
#     if not GainOnly:
#         slp.SloppyPlotData(t,y,inp,outp)

def sloppyBoth(Sys,inp,outp,t=None):

    sys = extractSubsystem(Sys,sc,sf,inp,outp)
    SysName = sc['name']
    print(SysName)
    if (t is None):
        name = f'{SysName}_sloppy_{inp[0]}'
    else:
        name = f'{SysName}_sloppy_{inp[0]}_long'

    #print(sys)
    H,eig,eigv,t = slp.Sloppy(sys,t=t,GainOnly=False)
    print(f'\n t_f = {max(t):0.2f}')
    print('H:')
    slp.SloppyPrint(eig,eigv,inp,min_eig=0)

    H,Eig,Eigv,t = slp.Sloppy(sys,t=t,GainOnly=True)
    print('H_ss:')
    slp.SloppyPrint(Eig,Eigv,inp,min_eig=0)

    ## Direct computation
    print('Direct:')
    gain = con.dcgain(sys)[0]
    norm = np.sum(gain*gain)
    ngain = gain/np.sqrt(norm)
    slp.SloppyPrint([norm],np.array([ngain]).T,inp,min_eig=0.0,min_eigv=0.
↪05,max_eigs=2)
```

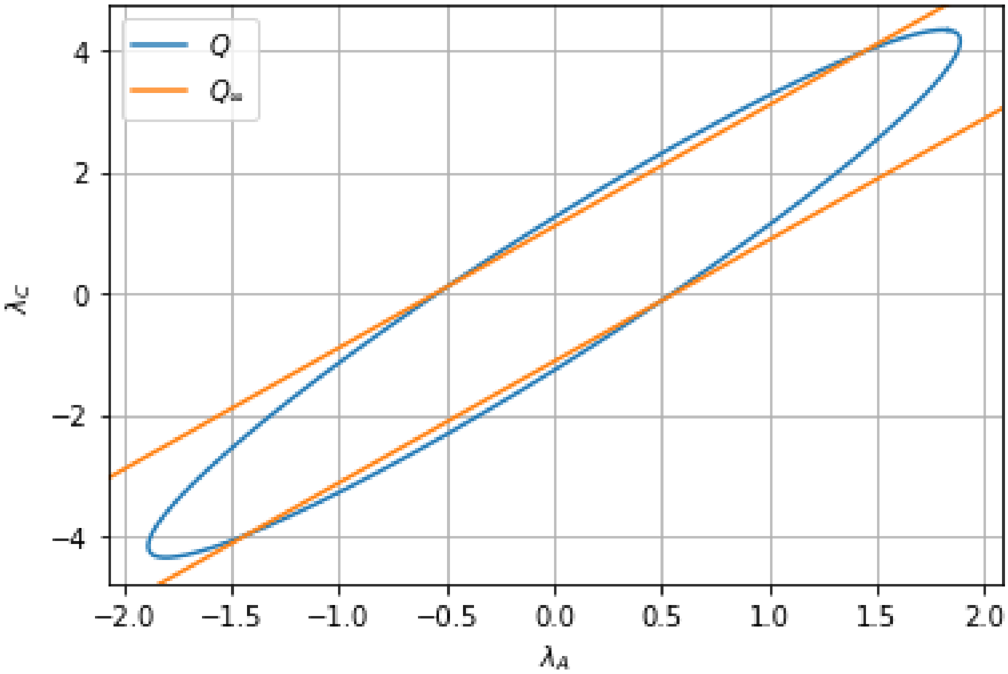
```
    ## Plot
    slp.SloppyPlot(eig,eigv,inp,Eig=Eig,Eigv=Eigv)

    Savefig(name)
    plt.show()

for t_last in [0,1e6]:
    if t_last==0:
        t = None
    else:
        t = np.linspace(0,t_last,100)
    sloppyBoth(Sys,['sr1','sr2'],['r1'],t=t)
    sloppyBoth(Sys,['sA','sC'],['r1'],t=t)
```

```
ABC

 t_f = 0.69
H:
\sqrt\sigma_1 &= 0.83 & V_1\Lambda &= + 1.00 \lambda_{r1} + 0.09 \lambda_{r2}
\sqrt\sigma_2 &= 0.023 & V_2\Lambda &= + 1.00 \lambda_{r2} - 0.09 \lambda_{r1}
H_ss:
\sqrt\sigma_1 &= 0.81 & V_1\Lambda &= + 0.99 \lambda_{r1} + 0.11 \lambda_{r2}
\sqrt\sigma_2 &= 3.2e-05 & V_2\Lambda &= + 0.99 \lambda_{r2} - 0.11 \lambda_{r1}
Direct:
\sqrt\sigma_1 &= 0.81 & V_1\Lambda &= + 0.99 \lambda_{r1} + 0.11 \lambda_{r2}
```



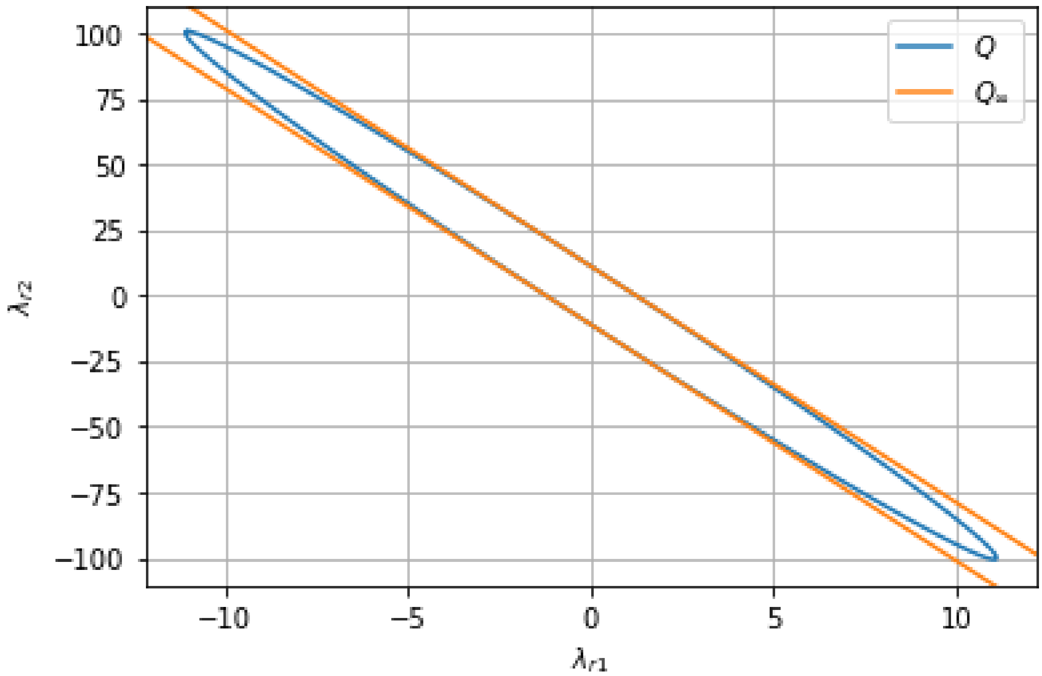

```
ABC
```

t_f = 0.69
H:
```
\sqrt\sigma_1 &= 2 & V_1\Lambda &= + 0.92 \lambda_{A} - 0.39 \lambda_{C}
\sqrt\sigma_2 &= 0.21 & V_2\Lambda &= + 0.92 \lambda_{C} + 0.39 \lambda_{A}
```
H_ss:
```
\sqrt\sigma_1 &= 2 & V_1\Lambda &= + 0.89 \lambda_{A} - 0.45 \lambda_{C}
\sqrt\sigma_2 &= 3.2e-05 & V_2\Lambda &= + 0.89 \lambda_{C} + 0.45 \lambda_{A}
```
Direct:
```
\sqrt\sigma_1 &= 2 & V_1\Lambda &= + 0.89 \lambda_{A} - 0.45 \lambda_{C}
```

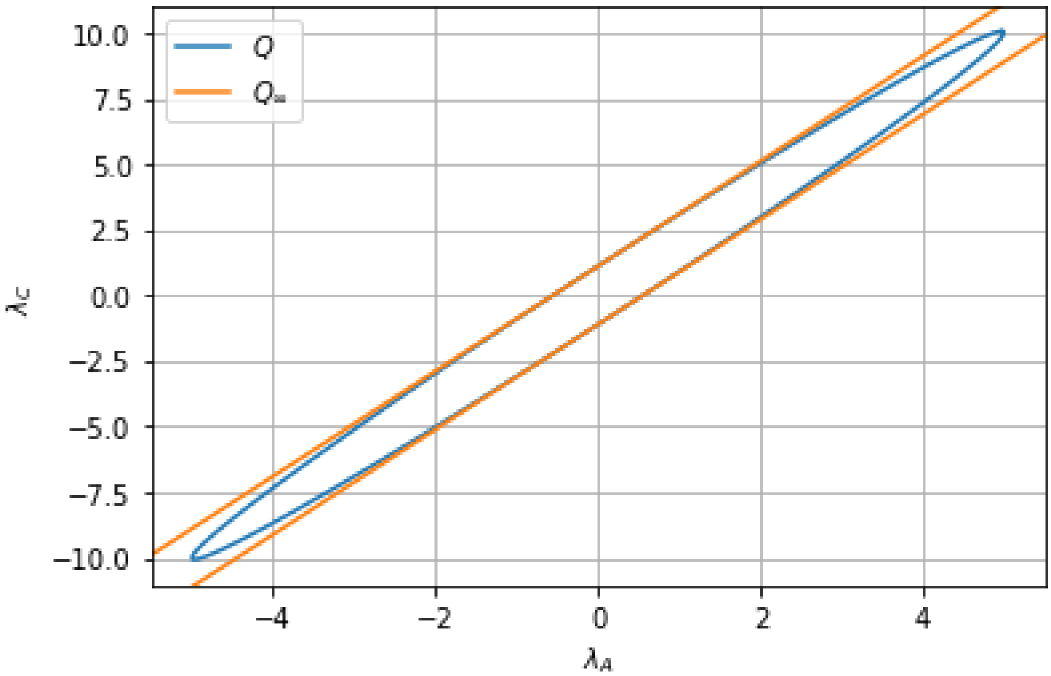


ABC

t_f = 1000000.00
H:
```
\sqrt\sigma_1 &= 0.82 & V_1\Lambda &= + 0.99 \lambda_{r1} + 0.11 \lambda_{r2}
\sqrt\sigma_2 &= 0.0099 & V_2\Lambda &= + 0.99 \lambda_{r2} - 0.11 \lambda_{r1}
```
H_ss:
```
\sqrt\sigma_1 &= 0.81 & V_1\Lambda &= + 0.99 \lambda_{r1} + 0.11 \lambda_{r2}
\sqrt\sigma_2 &= 3.2e-05 & V_2\Lambda &= + 0.99 \lambda_{r2} - 0.11 \lambda_{r1}
```
Direct:
```
\sqrt\sigma_1 &= 0.81 & V_1\Lambda &= + 0.99 \lambda_{r1} + 0.11 \lambda_{r2}
```



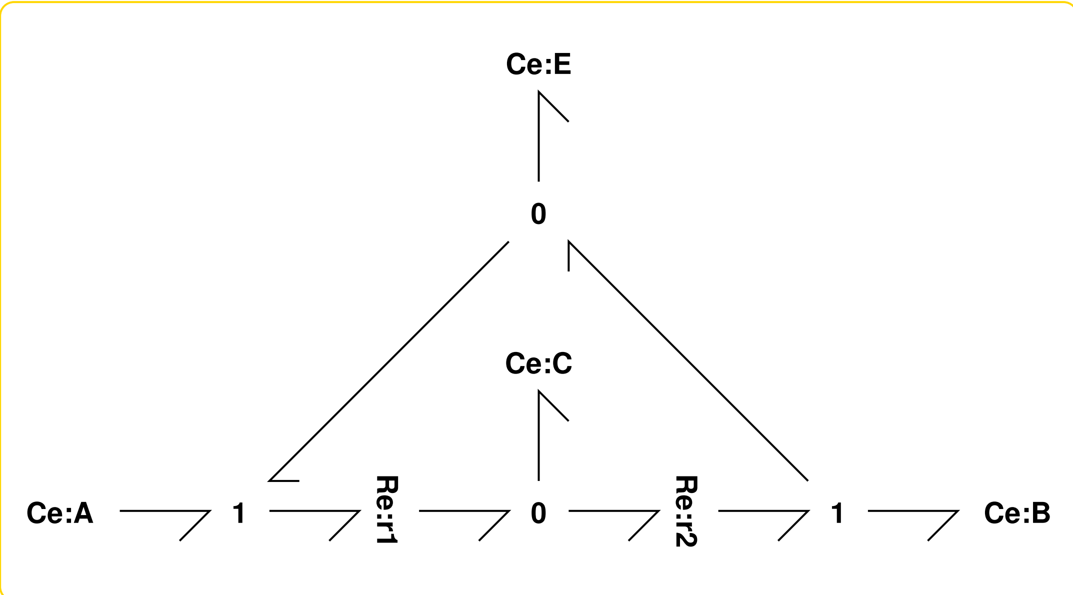

```
ABC

 t_f = 1000000.00
H:
\sqrt\sigma_1 &= 2 & V_1\Lambda &= + 0.90 \lambda_{A} - 0.44 \lambda_{C}
\sqrt\sigma_2 &= 0.089 & V_2\Lambda &= + 0.90 \lambda_{C} + 0.44 \lambda_{A}
H_ss:
\sqrt\sigma_1 &= 2 & V_1\Lambda &= + 0.89 \lambda_{A} - 0.45 \lambda_{C}
\sqrt\sigma_2 &= 3.2e-05 & V_2\Lambda &= + 0.89 \lambda_{C} + 0.45 \lambda_{A}
Direct:
\sqrt\sigma_1 &= 2 & V_1\Lambda &= + 0.89 \lambda_{A} - 0.45 \lambda_{C}
```



5.3 Example: Enzyme-catalysed reaction

[90]:
```
sbg.model('ECR_abg.svg')
import ECR_abg
imp.reload(ECR_abg)
disp.SVG('ECR_abg.svg')
```

[90]:



[91]:
```python
## Stoichiometry
s0 = st.stoich(ECR_abg.model(),quiet=quiet)
species = s0['species']
reaction=s0['reaction']
n_X = s0['n_X']
n_V = s0['n_V']
```

[92]:
```python
## Initial states (for sensitivity system)
e0 = 10 ## Total bound and unbound enzyme
XX0 = {}
# XX0['A'] = 1
XX0['E'] = e0/2
XX0['C'] = e0/2
X0 = np.ones(2*n_X+n_V)

for spec in XX0:
    X0[species.index(spec)] = XX0[spec]
```

[93]:
```python
## Parameters
kappa_1 = 1
K_B = 1e-3

parameter = {}
parameter['K_A'] = 1
parameter['K_B'] = K_B
parameter['kappa_r1'] = kappa_1
parameter['kappa_r2'] = 1
print(parameter)
```

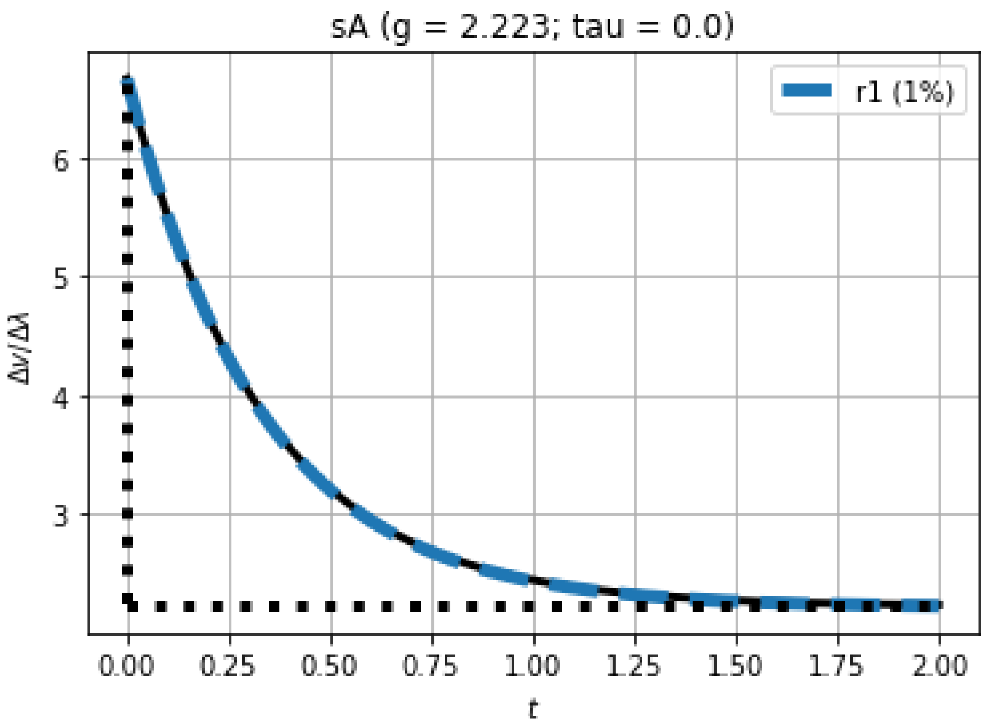
```
{'K_A': 1, 'K_B': 0.001, 'kappa_r1': 1, 'kappa_r2': 1}
```

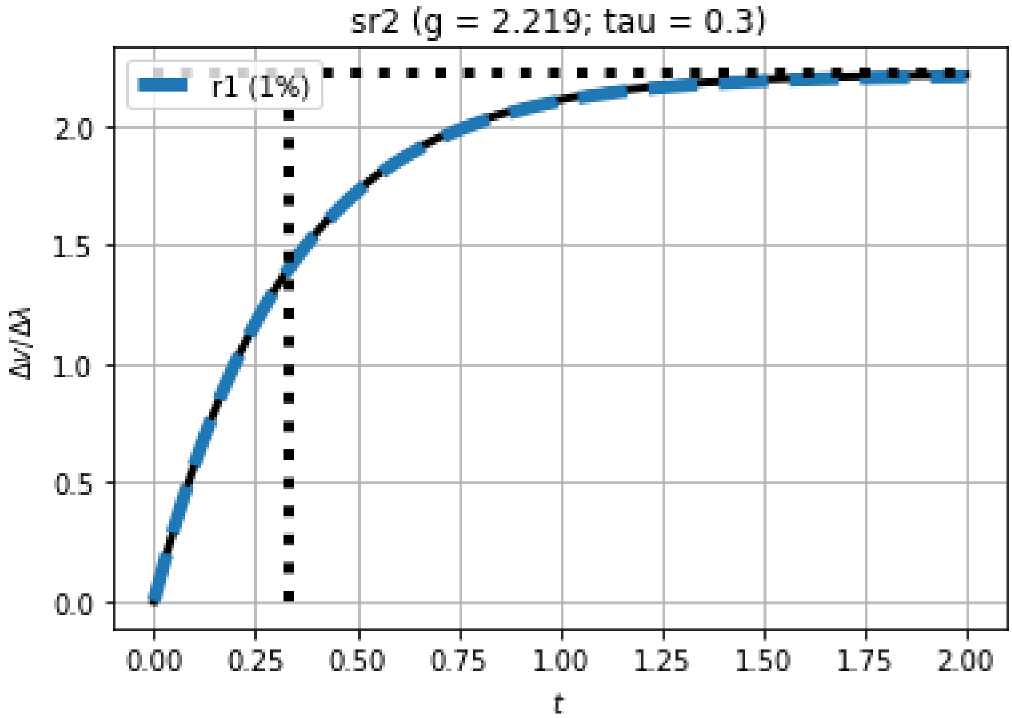
[94]:
```python
## Chemostats
chemostats = ['A','B']
```

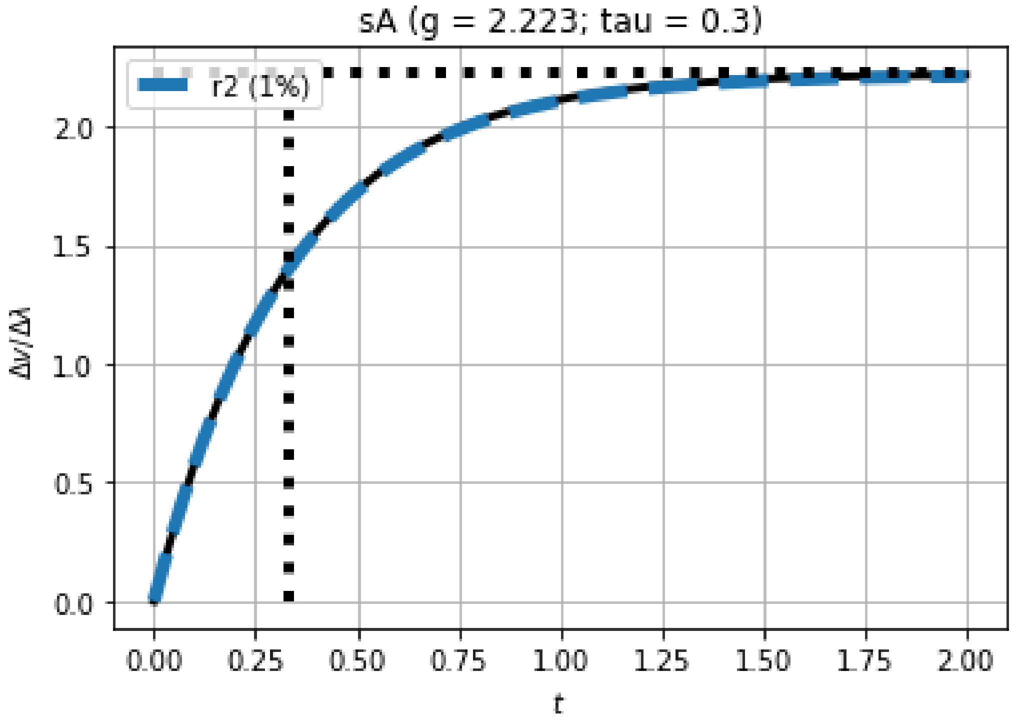
[95]:
```python
dcgain = {}
syss = {}
s,sc,sf,Sys,X_ss,V_ss,dX_ss = stoichSensitivity(ECR_abg.
 ↪model(),parameter=parameter,chemostats=chemostats,X0=X0)
lam = 1.01
Outp = ['r1','r2']
Inp = ['sA','sr2']
t_last = 2/kappa_1
for outp in Outp:
    for inp in Inp:
        dat,y_lin,t,sys = simSensitivity(s,sc,sf,Sys,X_ss,V_ss,dX_ss,
                                                              ␣
 ↪parameter=parameter,inp=[inp],outp=[outp],lam=lam,t_last=t_last)
        syss[inp] = sys
#          g = con.dcgain(sys)
        g,tau = tfProps(sys)
        dcgain[inp] = g
```

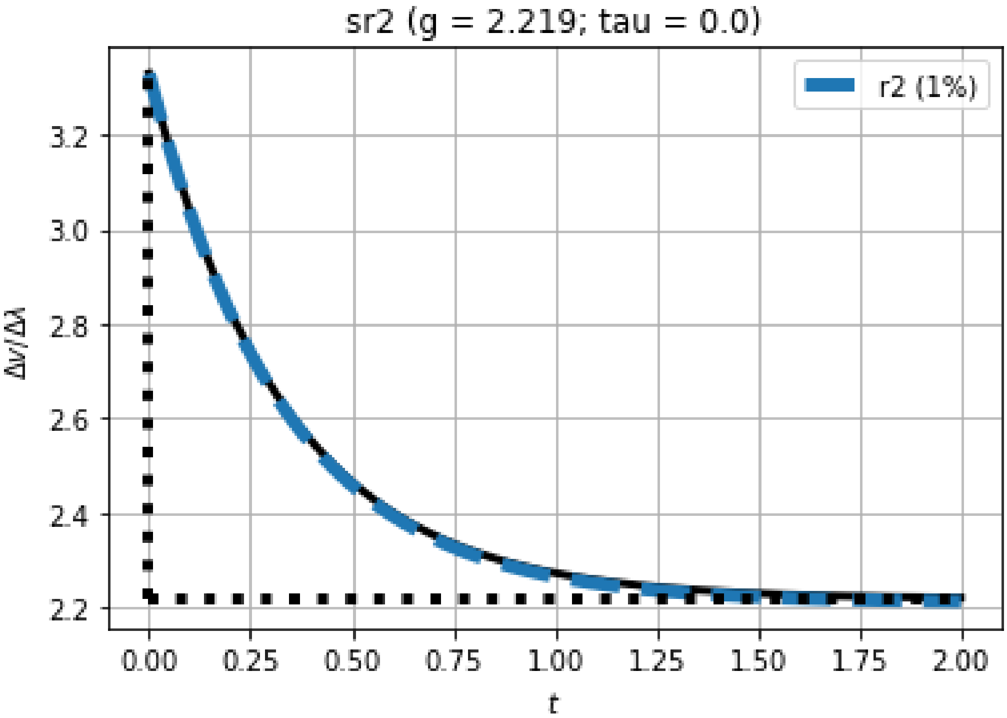
```python
        #print(g)
        if Titles:
            plt.title(f'{inp} (g = {g:.3f}; tau = {tau:0.1f})')
        plotSensitivity(dat,reactions=[outp])
        plotLines()
        Savefig('ECR_'+inp+'_'+outp)
        plt.show()
```

```
Steady-state finder error: 1.26e-15
X_ss = [1.   1.   3.34 6.66 1.   1.   1.   1.   1.   1.  ]
V_ss = [3.33 3.33]
```



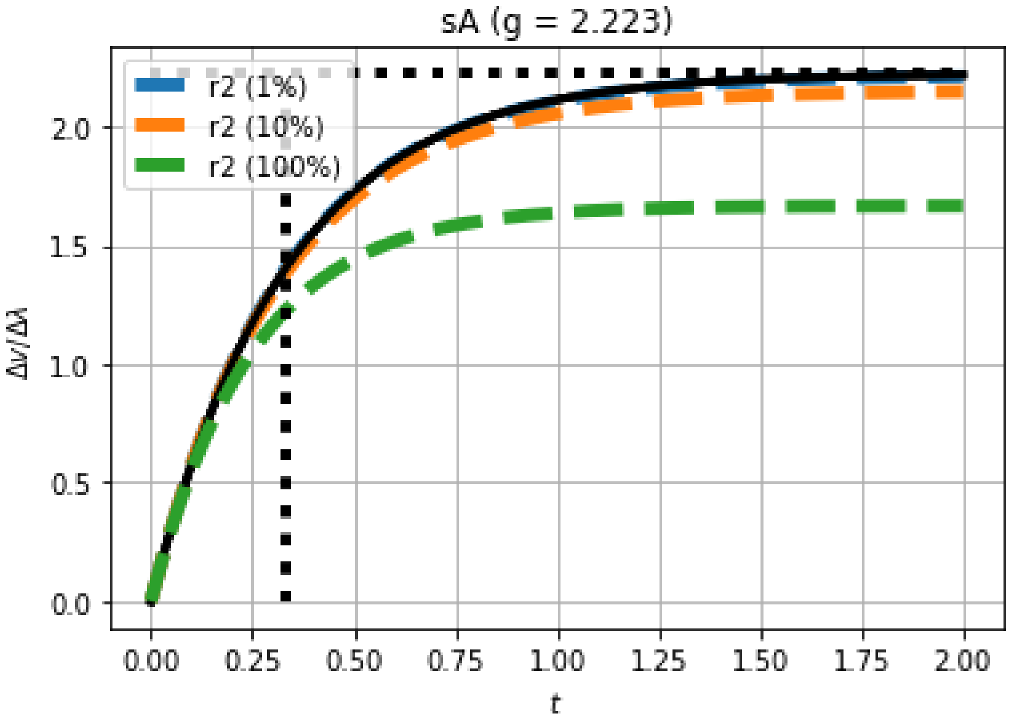

sr2 (g = 2.219; tau = 0.3)
r1 (1%)
Δv/Δλ
0.0
0.5
1.0
1.5
2.0
0.00
0.25
0.50
0.75
1.00
1.25
1.50
1.75
2.00
t


sA (g = 2.223; tau = 0.3)
r2 (1%)
Δv/Δλ
0.0
0.5
1.0
1.5
2.0
0.00
0.25
0.50
0.75
1.00
1.25
1.50
1.75
2.00
t



5.3.1 Vary λ

[96]:
```
inp = 'sA'
outp = ['r2']
for lam in [1.01,1.1,2]:
    dat,y_lin,t,sys = simSensitivity(s,sc,sf,Sys,X_ss,V_ss,dX_ss,
                                                    ␣
 ↪parameter=parameter,inp=[inp],outp=outp,lam=lam,t_last=t_last)
#     print(con.dcgain(sys))
    g,tau = tfProps(sys)
    if Titles:
        plt.title(f'{inp} (g = {g:.3f})')
    plotSensitivity(dat,reactions=outp)
    plotLines()
Savefig('ECR_lambda')
```



[97]:
```
## Show system
#Sys
```

[98]:
```
## Show system TFs
con.tf(syss['sA'])
```

[98]:

$$\frac{6.671}{s+3.001}$$

[99]:
```
con.tf(syss['sr2'])
```

[99]:

$$\frac{3.329s+6.658}{s+3.001}$$

5.3.2 Simulate over flow range - quasi steady-state. Supporting software

[100]:
```
def QuasiSteadyState(Inp=['sAct','sInh'],points=10,x_max=100):

    ## Extract info
    species = s['species']
    reaction = s['reaction']

    ### Simulate over flow range.
    ## Slow ramp for x_A
    X_chemo = {}
    t_d = 1e3
```

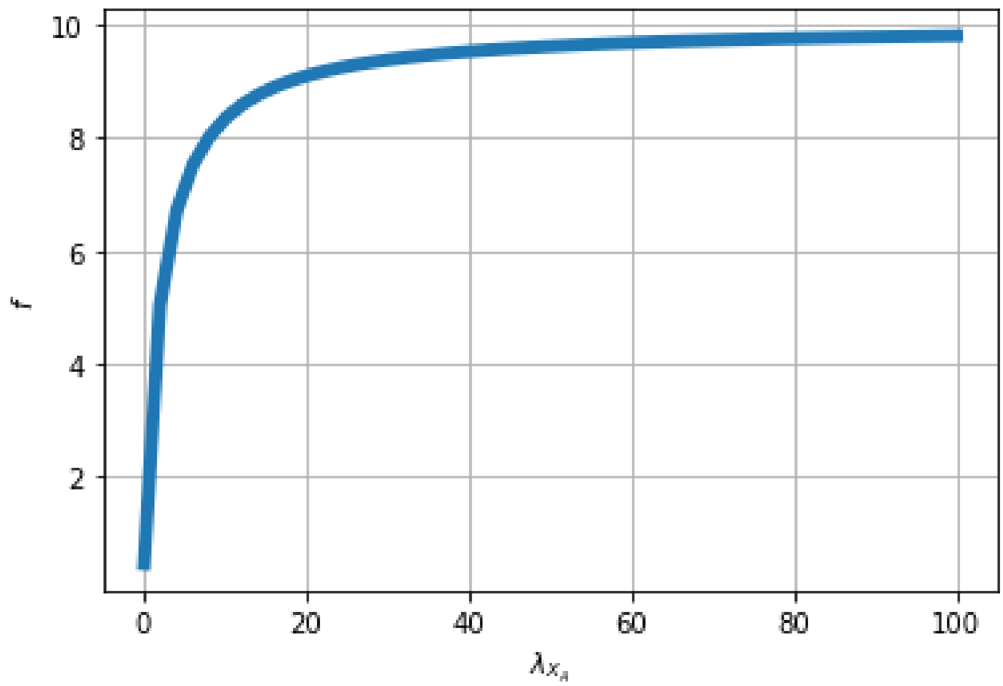
```
    t_last = 1e6
#     points = 50
    t = np.linspace(0,t_last,points)
    x_0 = 0.1
    X0[species.index('A')] = x_0
    slope = (x_max-x_0)/(t_last-t_d)
    X_chemo['A'] = f'({x_0} + {slope}*(t-{t_d})*(1*(t>{t_d})))'
    print(X_chemo)

    ## Steady-state
    X_ss,V_ss = SteadyState(s,sc,parameter=parameter,X0=X0)

    ## Simulate
    ndat = st.
↪sim(s,sc=sc,t=t,parameter=parameter,X0=X_ss,X_chemo=X_chemo,quiet=quiet)

    ## Plot
#     st.plot(s,ndat,species=['E0','E','C'],reaction=['r2'])

    ## Plot flow v X_A
    ylabel = r'$\Delta f_2/\Delta \lambda}$'
    X_A = ndat['X'][:,species.index('A')]
    V_2 = ndat['V'][:,reaction.index('r2')]
    plt.plot(X_A,V_2,lw=5)
    plt.grid()
    plt.xlabel('$\lambda_{X_A}$')
    plt.ylabel('$f$')

    sysname = s['name']
    plotname = f'{sysname}_flow'
    Savefig(plotname)
    plt.show()
    plt.clf()

    ## Compute sensitivity gain for each steady-state
    X = ndat['X']
    DCgain = {}
    Tau = {}

    for inp in Inp:
        DCgain[inp] = []
        Tau[inp] = []
        for x in X:
            ## Linearise about this steady-state
            Sys = st.lin(s,sc,x_ss=x,parameter=parameter,
                         quiet=quiet)

            ## Extract relevant subsystems
            outp = ['r1']
            sys = extractSubsystem(Sys,sc,sf,inp=[inp],outp=outp)
#             dcgain = con.dcgain(sys)
```

```
            dcgain,tau = tfProps(sys)
    #           print(dcgain)
            DCgain[inp].append(dcgain)
            Tau[inp].append(tau)

    # plt.plot(X_A,V_2,lw=6,label='flow')
    INP = ''
    for inp in Inp:
        plt.plot(X_A,DCgain[inp],label=inp[1:],lw=5)
        INP += inp+'_'
    plt.legend()
    plt.grid()
    plt.xlabel('$X_A$')
    plt.ylabel(ylabel)
    plotname = f'{sysname}_{INP}X'
    Savefig(plotname)
    plt.show()

    # plt.plot(X_A,V_2,lw=6,label='flow')
    ## Plot DC gain v flow
    for inp in Inp:
        plt.plot(V_2,DCgain[inp],label=inp[1:],lw=5)

    plt.legend()
    plt.grid()
    plt.xlabel('$f$')
    ylabel = '$g_\infty$'
    plt.ylabel(ylabel)
    plotname = f'{sysname}_{INP}f'
    Savefig(plotname)
    plt.show()

    ## Plot time-constant v flow
    for inp in Inp:
        plt.plot(V_2,Tau[inp],label=inp[1:],lw=5)

    plt.legend()
    plt.grid()
    plt.xlabel('$f$')
    plt.ylabel(r'$\tau$')
    plotname = f'{sysname}_{INP}f_tau'
    Savefig(plotname)
    plt.show()
```

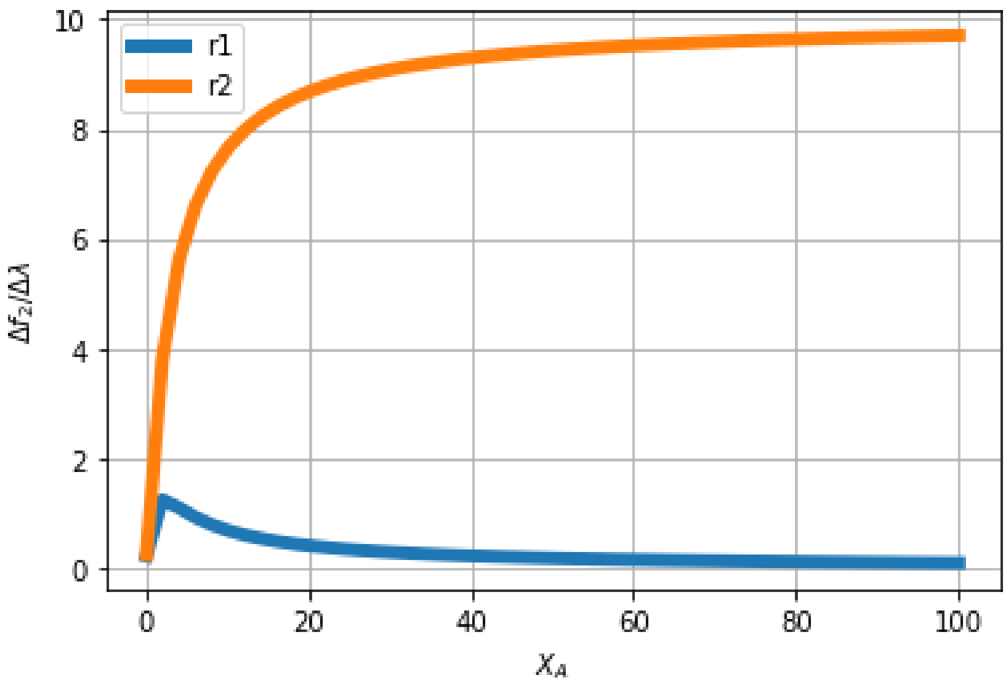
5.3.3 Simulate over flow range - quasi steady-state. Vary Re components.

[101]:
```
QuasiSteadyState(Inp=['sr1','sr2'],points=50)
```

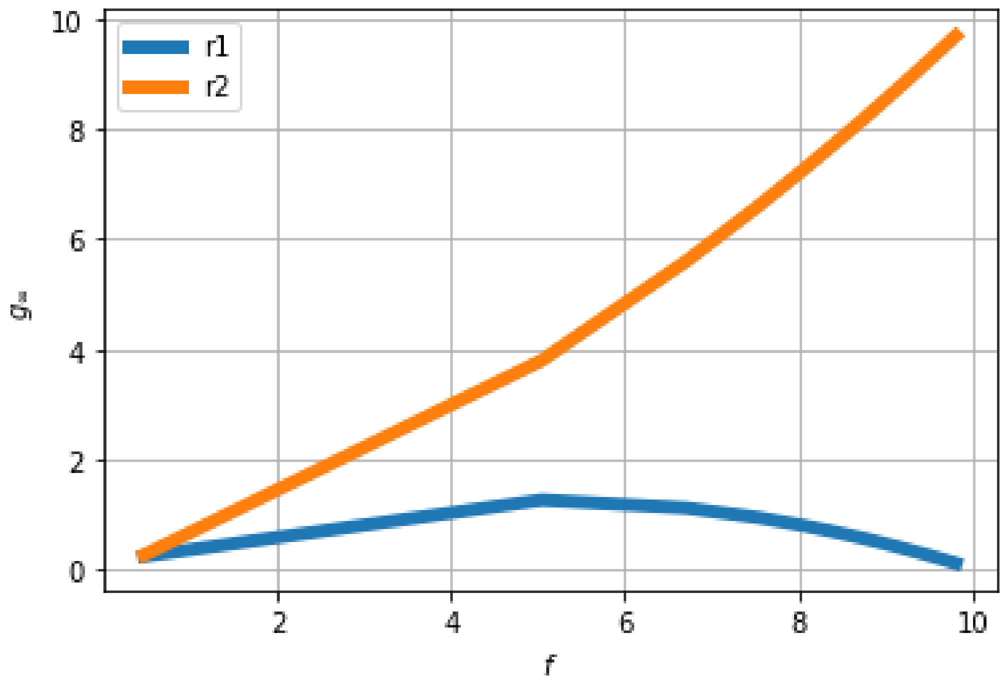
```
{'A': '(0.1 + 0.0001*(t-1000.0)*(1*(t>1000.0)))'}
Steady-state finder error: 7.85e-17
```

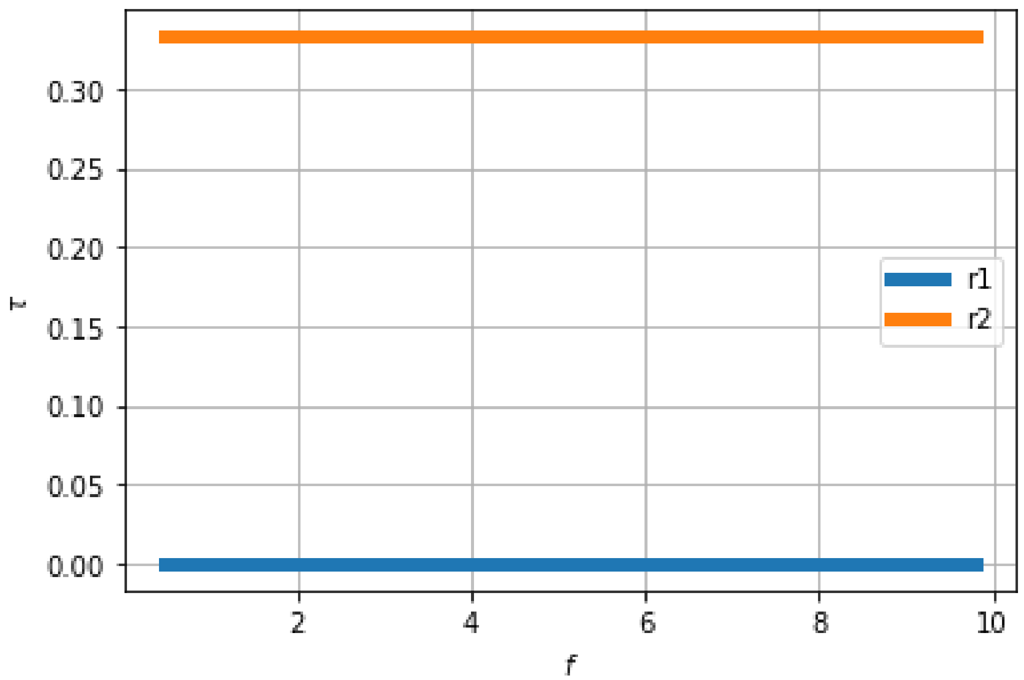


10
8
6
4
2
f
0
20
40
60
80
100
λ_{X_A}



r1
r2
10
8
6
4
2
0
$\Delta f_2/\Delta\lambda$
0
20
40
60
80
100
X_A



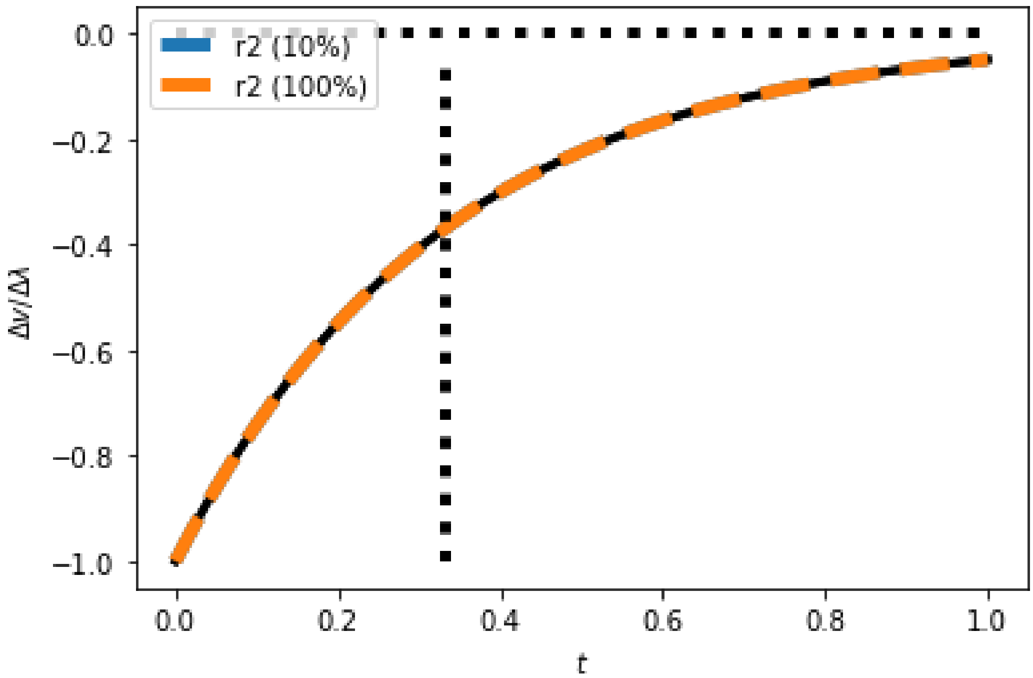


5.3.4 Initial condition sensitivity.

[102]:
```
## Set up deviation state for full system
n_X = sc['n_X']
sX0 = np.zeros(n_X)
```

```
spec = sc['species']
i_C = spec.index('C')
i_E = spec.index('E')
sX0[i_E] = 1
sX0[i_C] = -1

## Test conserved moiety compatability
G_c = sc['G']
error = np.linalg.norm(G_c@sX0)
print('Compatibility error =',error)

## Compare linear and non-linear
inp = 'sr1'
outp = ['r2']
for lam in [1.1,2,]:
    dat,y_lin,t,sys = simSensitivity(s,sc,sf,Sys,X_ss,V_ss,dX_ss,
                                          sX0=sX0,
                                        ␣
 ↪parameter=parameter,inp=[inp],outp=outp,lam=lam,t_last=1)
#     print(con.dcgain(sys))
    g = con.dcgain(sys)
#     if Titles:
#         plt.title(f'{inp} (g = {g:.3f})')
    plotSensitivity(dat,reactions=outp)
    g=0;plotLines()
Savefig('ECR_IC')
```

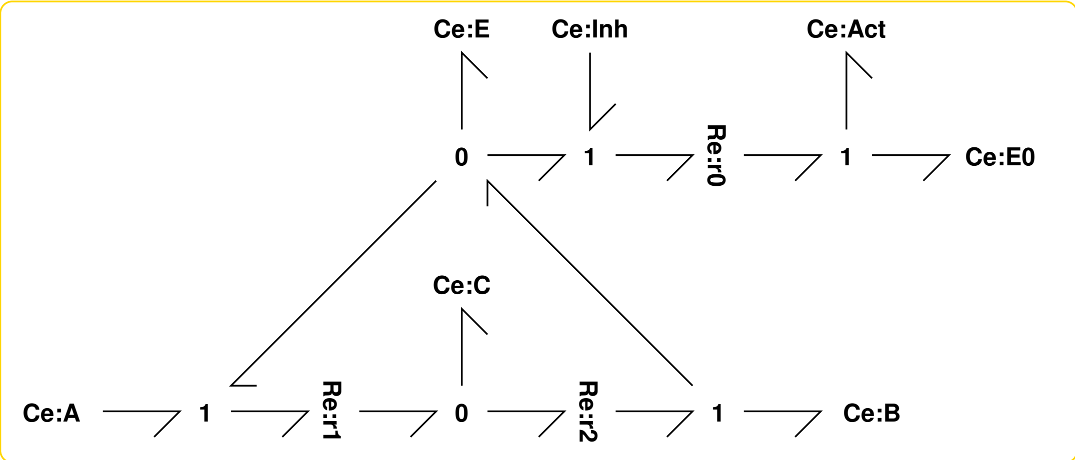
```
Compatibility error = 0.0
```



5.4 Example: Modulated Enzyme-catalysed reaction

[103]:
```
sbg.model('ecr_abg.svg')
import ecr_abg
imp.reload(ecr_abg)
disp.SVG('ecr_abg.svg')
```

[103]:



[104]:
```
## Stoichiometry
s0 = st.stoich(ecr_abg.model(),quiet=quiet)
species = s0['species']
n_X = s0['n_X']
n_V = s0['n_V']
```

[105]:
```
## Initial states (for sensitivity system)
# e0 = 10
XX0 = {}
# XX0['A'] = 1
XX0['E'] = e0/3
XX0['E0'] = e0/3
XX0['C'] = e0/3
XX0['Inh'] = 1
X0 = np.ones(2*n_X+n_V)

for spec in XX0:
    X0[species.index(spec)] = XX0[spec]
```

[106]:
```
## Parameters
parameter = {}
parameter['K_A'] = 1
parameter['K_B'] = K_B
# parameter['K_F'] = 1
# parameter['K_G'] = 1
parameter['kappa_r0'] = 1
parameter['kappa_r1'] = kappa_1
parameter['kappa_r2'] = 1
```

```
parameter['K_E0'] = 1
print(parameter)
```

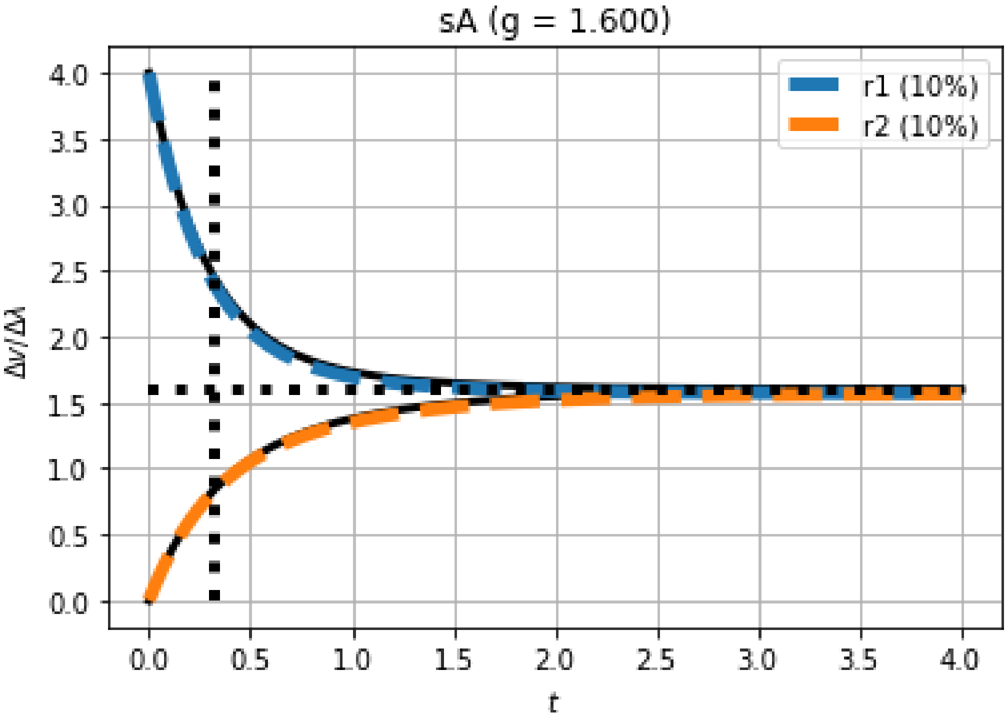
```
{'K_A': 1, 'K_B': 0.001, 'kappa_r0': 1, 'kappa_r1': 1, 'kappa_r2': 1, 'K_E0': 1}
```

[107]:
```
## Chemostats
chemostats = ['A','B','Act','Inh']
```

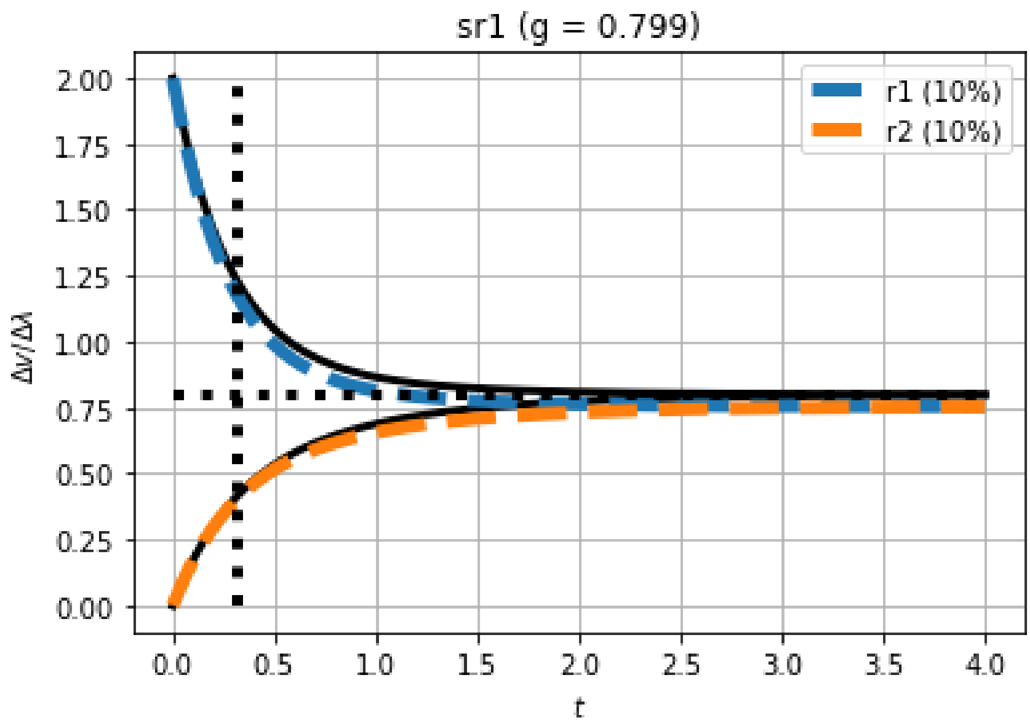
[108]:
```
dcgain = {}
syss = {}
print(s['species'])
s,sc,sf,Sys,X_ss,V_ss,dX_ss = stoichSensitivity(ecr_abg.
↪model(),parameter=parameter,chemostats=chemostats,X0=X0)
lam = 1.1
outp = ['r1','r2']
Inp = ['sA','sr1','sr2','sAct','sInh']
#Inp = ['sAct','sInh','sA','sB']
t_last = 4
for inp in Inp:
    dat,y_lin,t,sys = simSensitivity(s,sc,sf,Sys,X_ss,V_ss,dX_ss,
                                                        ␣
↪parameter=parameter,inp=[inp],outp=outp,lam=lam,t_last=t_last)
    syss[inp] = sys
    print(sys)
#     g = con.dcgain(sys)[0][0]
    g,tau = tfProps(sys)
    dcgain[inp] = g
    print(f'g = {g:0.2f}, tau = {tau:0.2f}')
    if Titles:
        plt.title(f'{inp} (g = {g:.3f})')
    plotSensitivity(dat,reactions=outp)
    plotLines()
#     plt.hlines(g,min(t),max(t),color='black',ls='dashed')
    Savefig('ecr_'+inp)
    plt.show()
```

```
['A', 'B', 'C', 'E', 'sA', 'sB', 'sC', 'sE', 'sr1', 'sr2']
Steady-state finder error: 1.66e-15
X_ss = [1. 1. 1. 2. 4. 4. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1.]
V_ss = [-8.88e-16  2.00e+00  2.00e+00]
<LinearIOSystem>: sys[315]
Inputs (1): ['u[0]']
Outputs (2): ['y[0]', 'y[1]']
States (2): ['x[0]', 'x[1]']

A = [[-2.  1.]
     [ 1. -3.]]

B = [[ 4.]
     [-4.]]
```

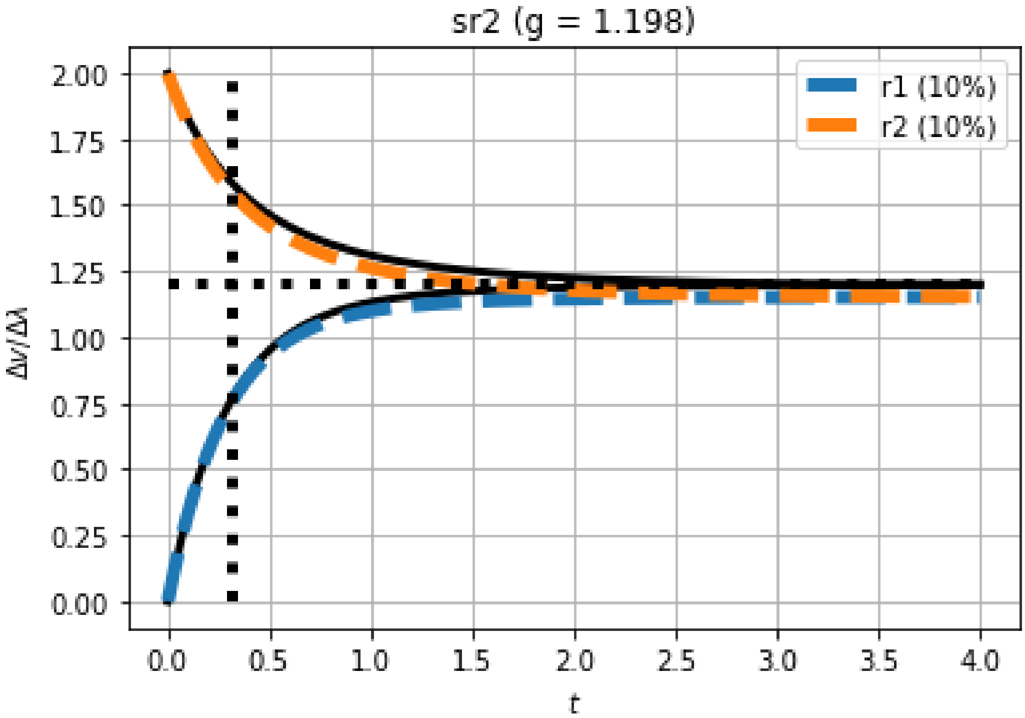
```
C = [[-1.  1.]
     [ 1. -0.]]

D = [[4.]
     [0.]]

g = 1.60, tau = 0.32
```



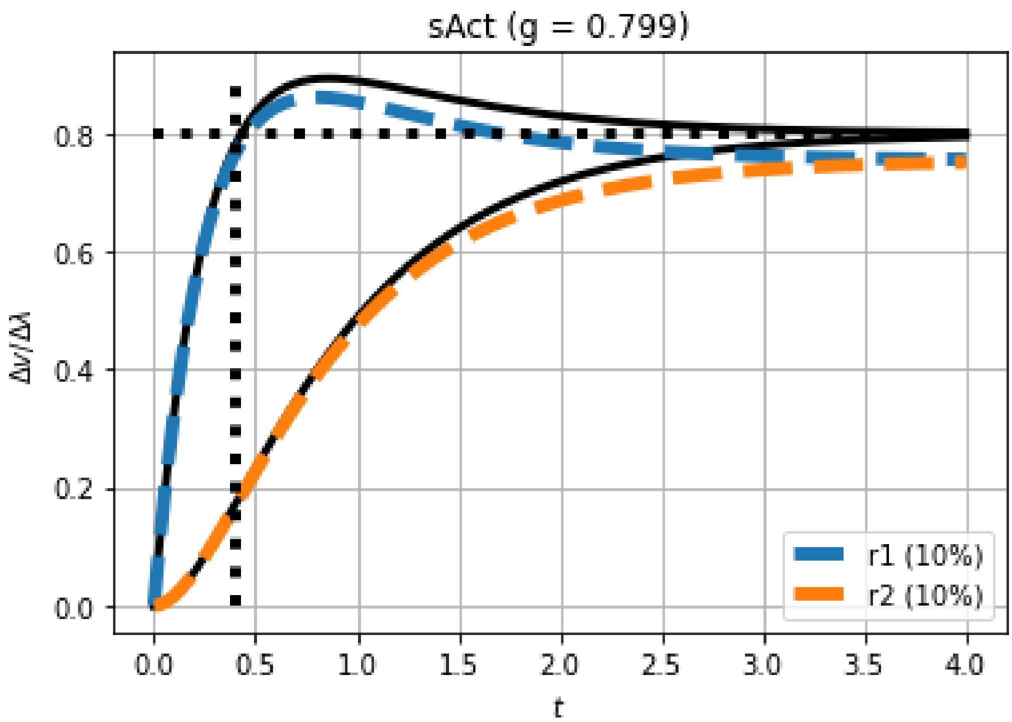

```
<LinearIOSystem>: sys[317]
Inputs (1): ['u[0]']
Outputs (2): ['y[0]', 'y[1]']
States (2): ['x[0]', 'x[1]']

A = [[-2.  1.]
     [ 1. -3.]]

B = [[ 2.]
     [-2.]]

C = [[-1.  1.]
     [ 1. -0.]]

D = [[2.]
     [0.]]

g = 0.80, tau = 0.32
```



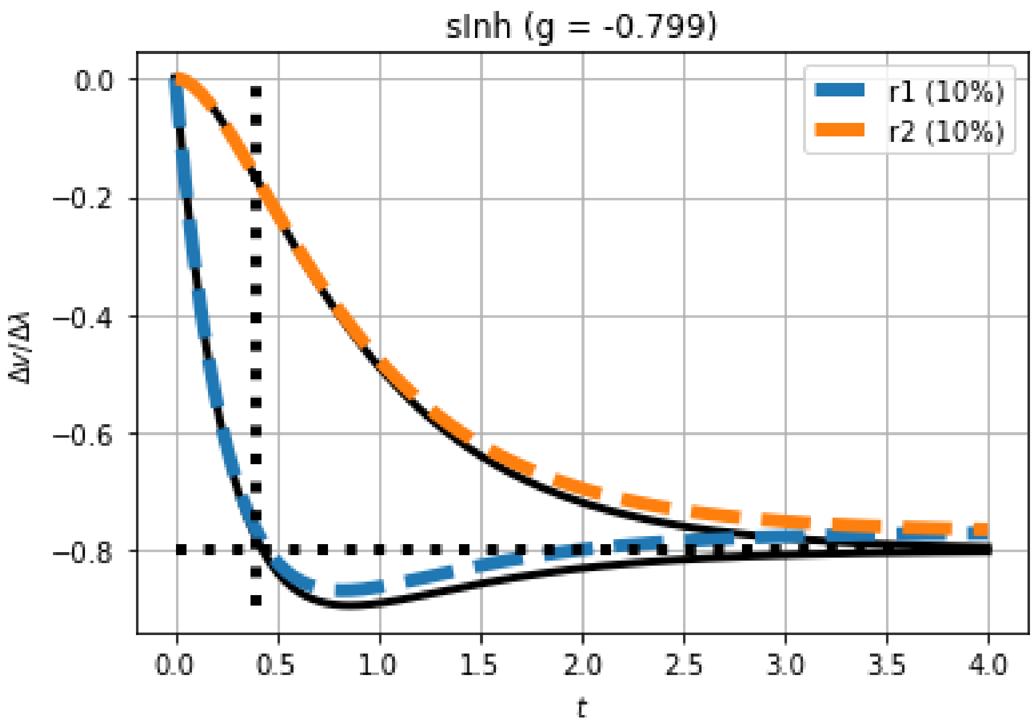

```
<LinearIOSystem>: sys[319]
Inputs (1): ['u[0]']
Outputs (2): ['y[0]', 'y[1]']
States (2): ['x[0]', 'x[1]']

A = [[-2.  1.]
     [ 1. -3.]]

B = [[-2.]
     [ 2.]]

C = [[-1.  1.]
     [ 1. -0.]]

D = [[0.]
     [2.]]

g = 1.20, tau = 0.32
```




```
<LinearIOSystem>: sys[321]
Inputs (1): ['u[0]']
Outputs (2): ['y[0]', 'y[1]']
States (2): ['x[0]', 'x[1]']

A = [[-2.  1.]
     [ 1. -3.]]

B = [[0.]
     [4.]]

C = [[-1.  1.]
     [ 1. -0.]]

D = [[0.]
     [0.]]

g = 0.80, tau = 0.40
```




```
<LinearIOSystem>: sys[323]
Inputs (1): ['u[0]']
Outputs (2): ['y[0]', 'y[1]']
States (2): ['x[0]', 'x[1]']

A = [[-2.  1.]
     [ 1. -3.]]

B = [[ 0.]
     [-4.]]

C = [[-1.  1.]
     [ 1. -0.]]

D = [[0.]
     [0.]]

g = -0.80, tau = 0.40
```

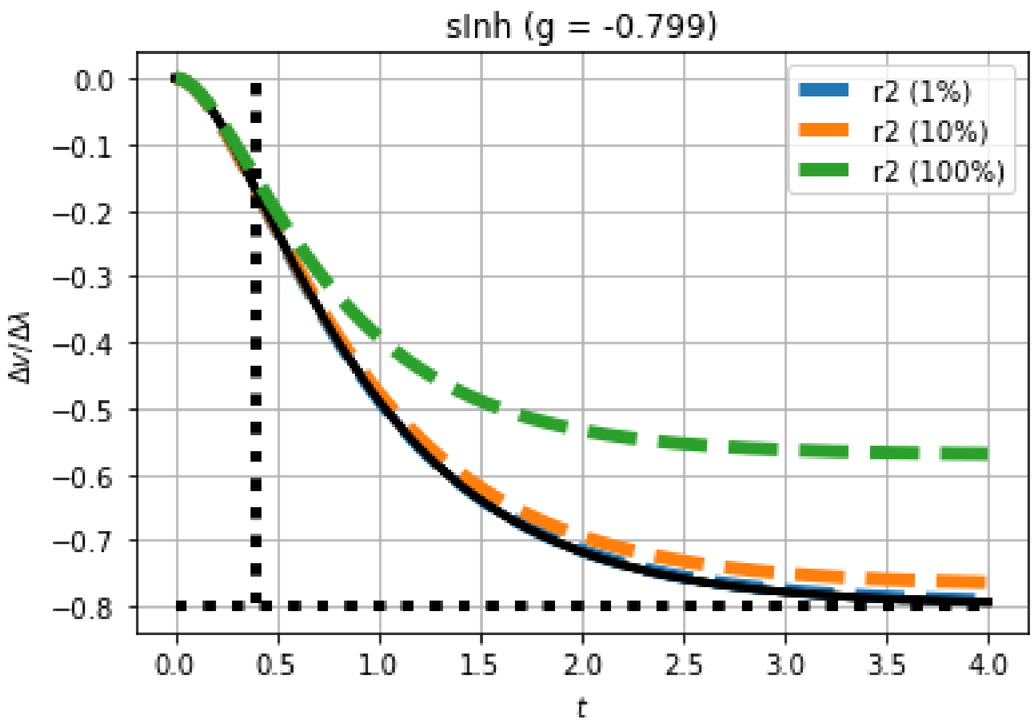


5.4.1 Vary λ

[109]:
```
tau
```

[109]: 0.39992001599680055

[110]:
```
inp = 'sInh'
outp = ['r2']
for lam in [1.01,1.1,2]:
    dat,y_lin,t,sys = simSensitivity(s,sc,sf,Sys,X_ss,V_ss,dX_ss,
                                                        ␣
 ↪parameter=parameter,inp=[inp],outp=outp,lam=lam,t_last=t_last)
#     print(con.dcgain(sys))
    g = con.dcgain(sys)
    if Titles:
        plt.title(f'{inp} (g = {g:.3f})')
    plotSensitivity(dat,reactions=outp)
    plotLines()
Savefig('ecr_lambda')
```



5.4.2 Show system transfer functions

[111]:
```
## Show system TFs
con.tf(syss['sAct'])
```

[111]:

$$\begin{bmatrix} \frac{3.999s+3.995}{s^2+5.001s+5.001} \\ \frac{-0.003999s+3.995}{s^2+5.001s+5.001} \end{bmatrix}$$

[112]:
```
con.tf(syss['sInh'])
```

[112]:

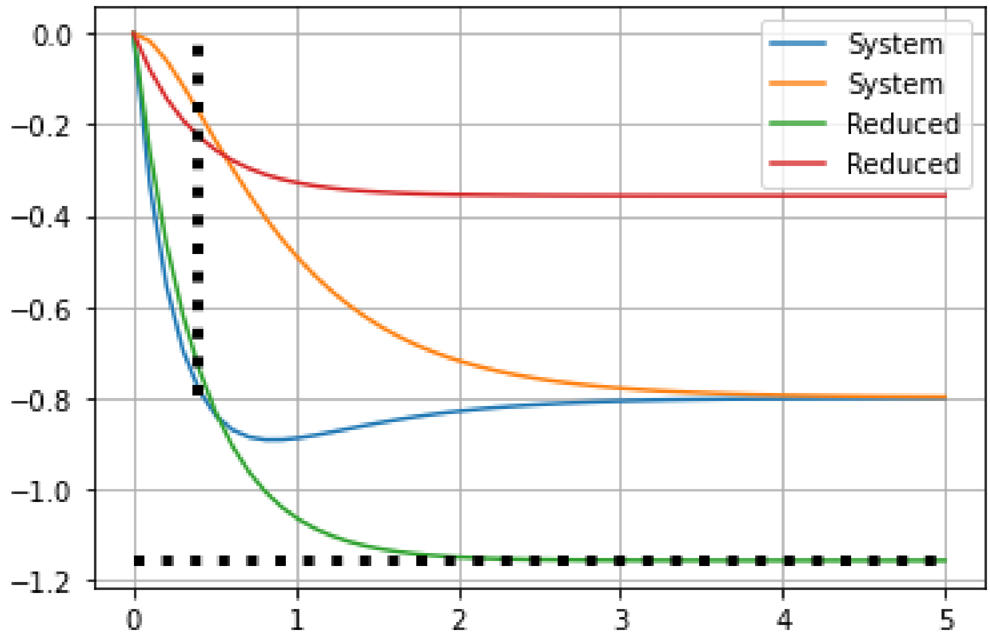
$$\begin{bmatrix} \frac{-3.999s-3.995}{s^2+5.001s+5.001} \\ \frac{0.003999s-3.995}{s^2+5.001s+5.001} \end{bmatrix}$$

5.4.3 Test model reduction

[113]:
```
## Test model reduction - truncate
method = 'truncate'
sys = syss['sInh']
g,tau = tfProps(sys)
print(f'g = {g:.2f}, tau = {tau:.2f}')
sys1 = con.balred(sys,orders=1,method=method)
# print(con.dcgain(sys))
# print(con.dcgain(sys1))
con.tf(sys1)
g,tau = tfProps(sys1)
```

```
print(f'g = {g:.2f}, tau = {tau:.2f}')

t = np.linspace(0,5)
step = con.step_response(sys,T=t)
step1 = con.step_response(sys1,T=t)
plt.plot(t,step.outputs[:,0,:].T,label='System')
plt.plot(t,step1.outputs[:,0,:].T,label='Reduced')
plt.legend()
plt.grid()
plotLines()
```

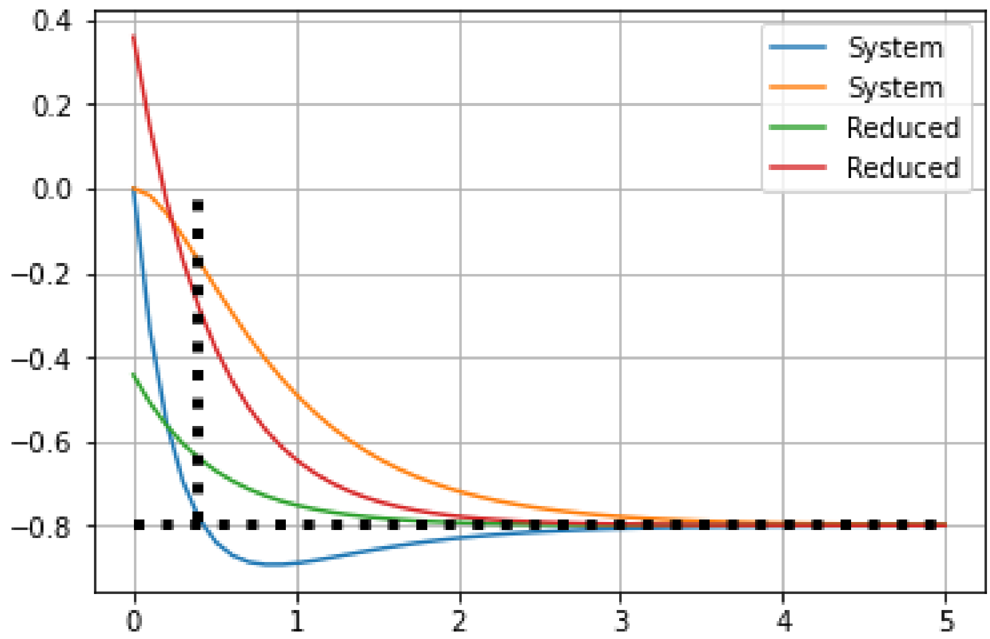
```
g = -0.80, tau = 0.40
g = -1.16, tau = 0.40
```



[114]:
```
## Test model reduction - matchdc
method = 'matchdc'
sys = syss['sInh']
g,tau = tfProps(sys)
print(f'g = {g:.2f}, tau = {tau:.2f}')
sys1 = con.balred(sys,orders=1,method=method)
# print(con.dcgain(sys))
# print(con.dcgain(sys1))
con.tf(sys1)
g,tau = tfProps(sys1)
print(f'g = {g:.2f}, tau = {tau:.2f}')

t = np.linspace(0,5)
step = con.step_response(sys,T=t)
step1 = con.step_response(sys1,T=t)
```

```
plt.plot(t,step.outputs[:,0,:].T,label='System')
plt.plot(t,step1.outputs[:,0,:].T,label='Reduced')
plt.legend()
plt.grid()
plotLines()
```

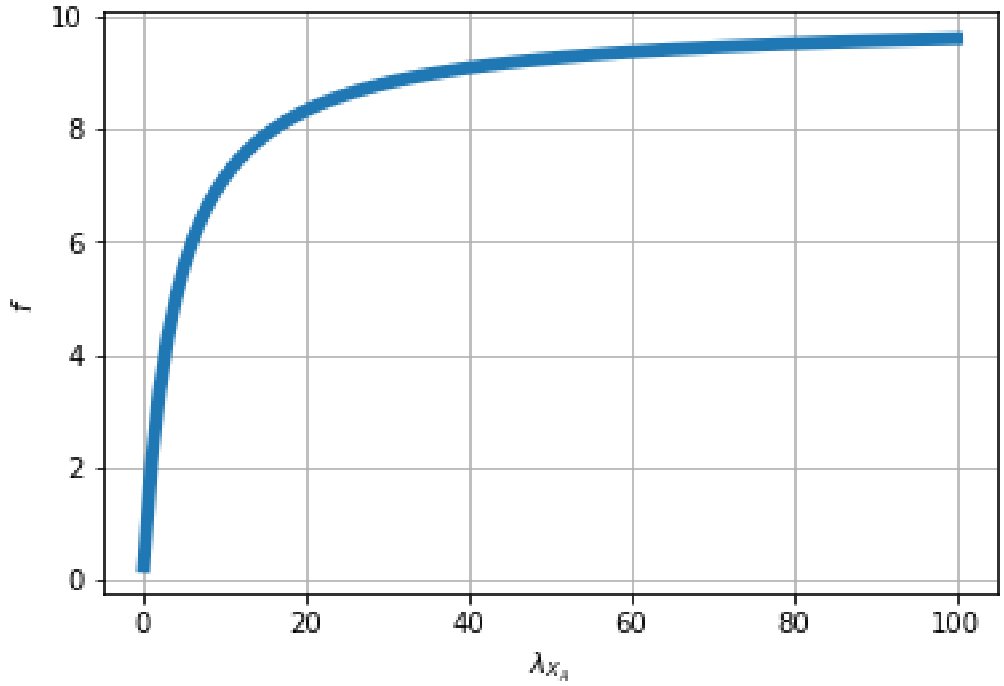
```
g = -0.80, tau = 0.40
g = -0.80, tau = 0.40
```



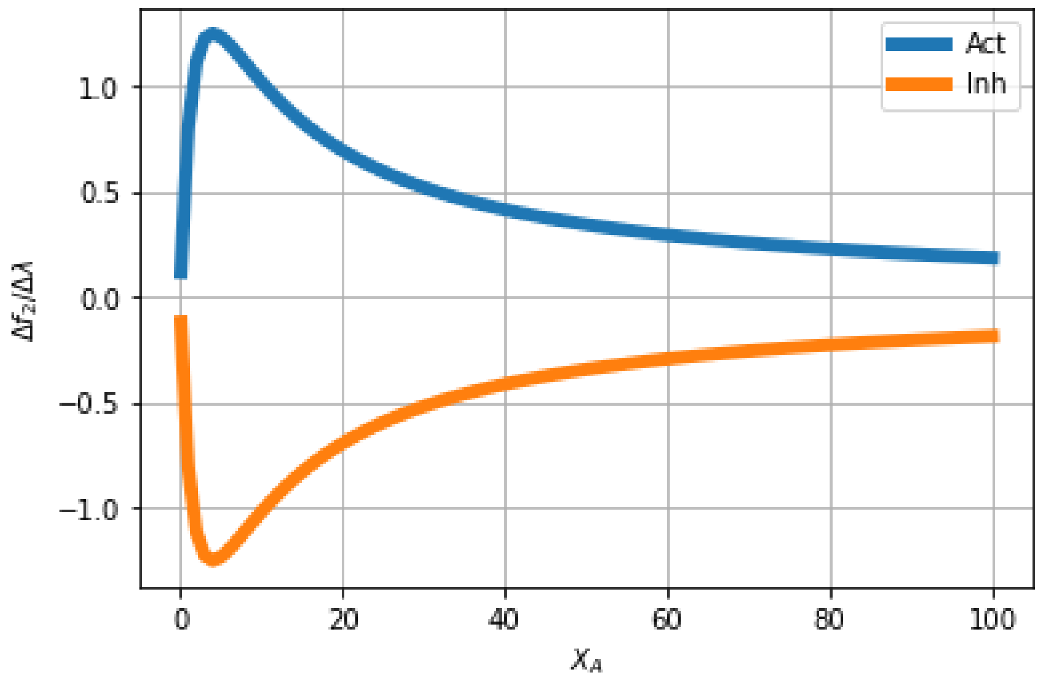
5.4.4 Simulate over flow range - quasi steady-state. Vary Activation and Inhibition.

[115]:
```
QuasiSteadyState(Inp=['sAct','sInh'],points=100)
```

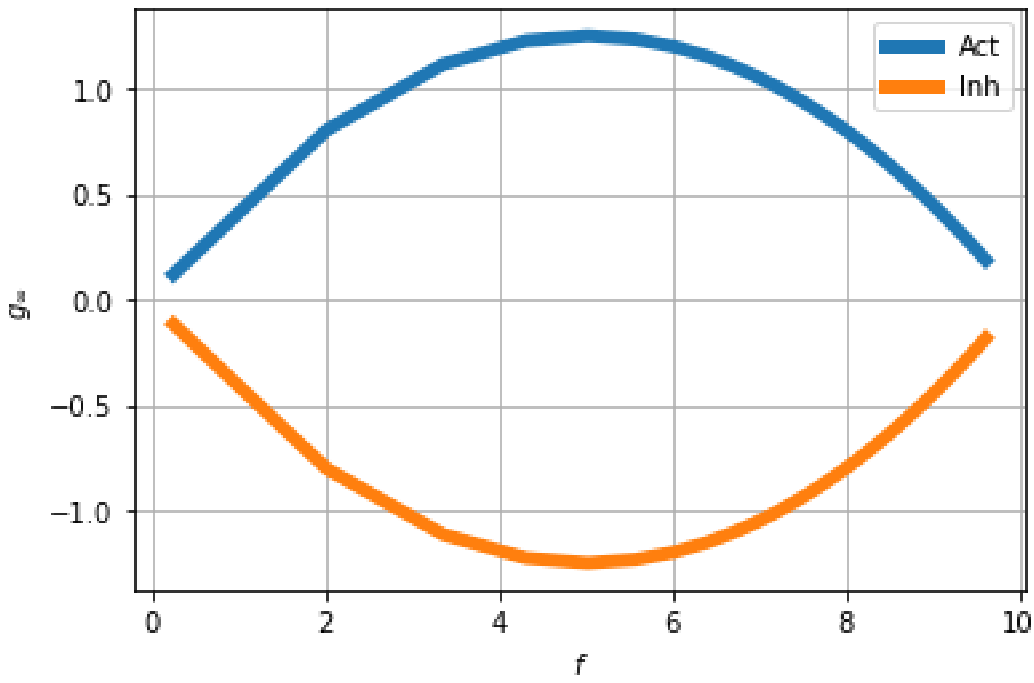
```
{'A': '(0.1 + 0.0001*(t-1000.0)*(1*(t>1000.0)))'}
Steady-state finder error: 7.85e-17
```

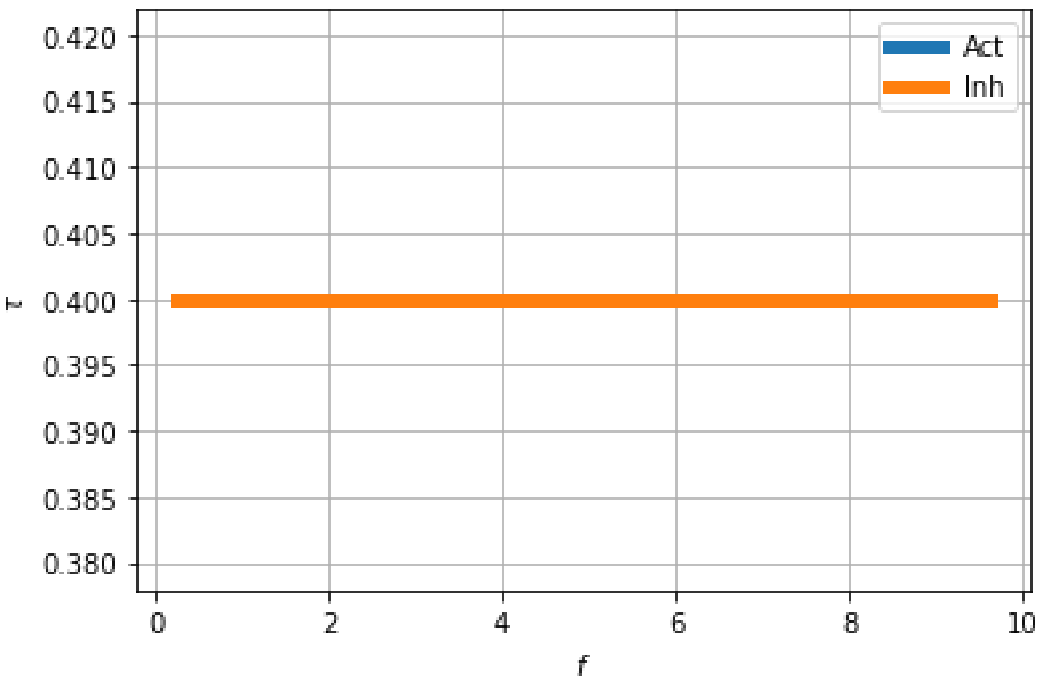


10
8
6
4
2
0
f
0
20
40
60
80
100
λ_{X_A}



Act
Inh
1.0
0.5
0.0
−0.5
−1.0
$\Delta f_2/\Delta\lambda$
0
20
40
60
80
100
X_A

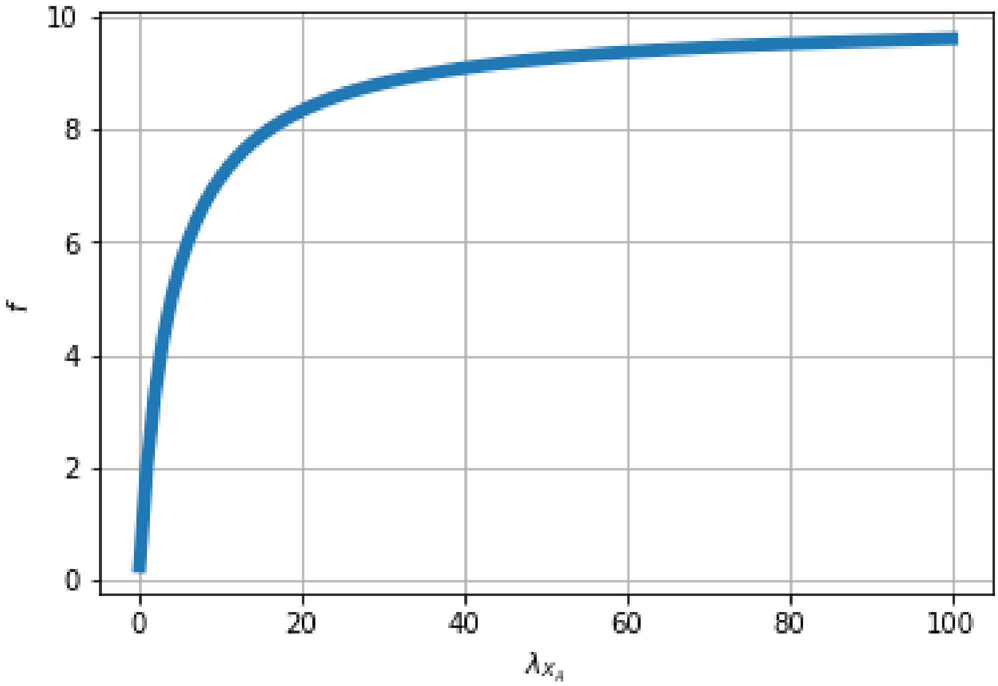




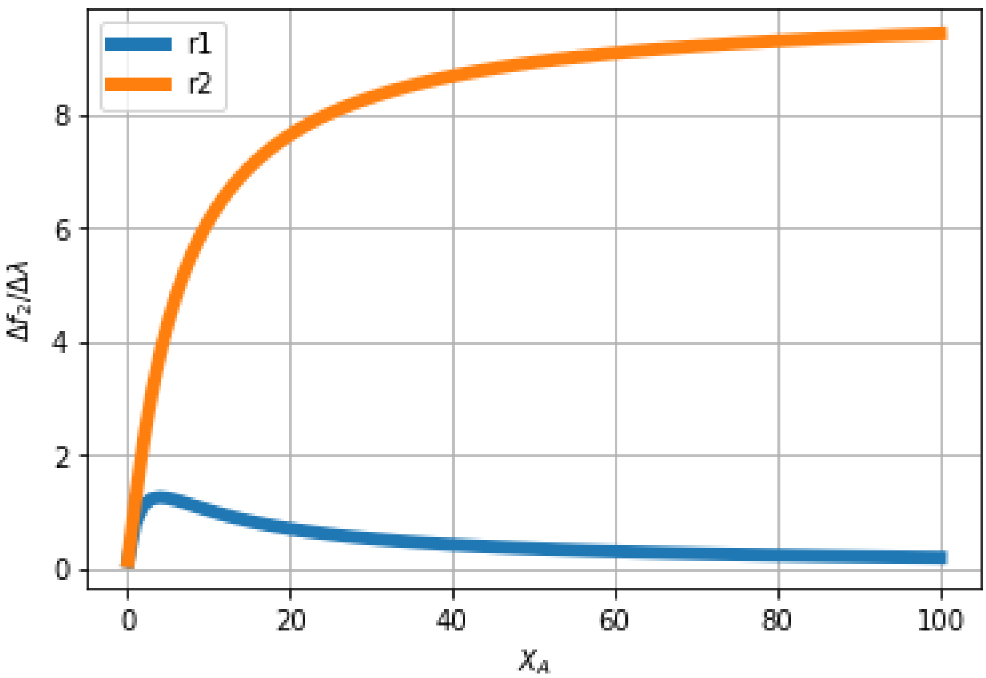
5.4.5 Simulate over flow range - quasi steady-state. Vary Re components

[116]:
```
QuasiSteadyState(Inp=['sr1','sr2'],points=100)
```

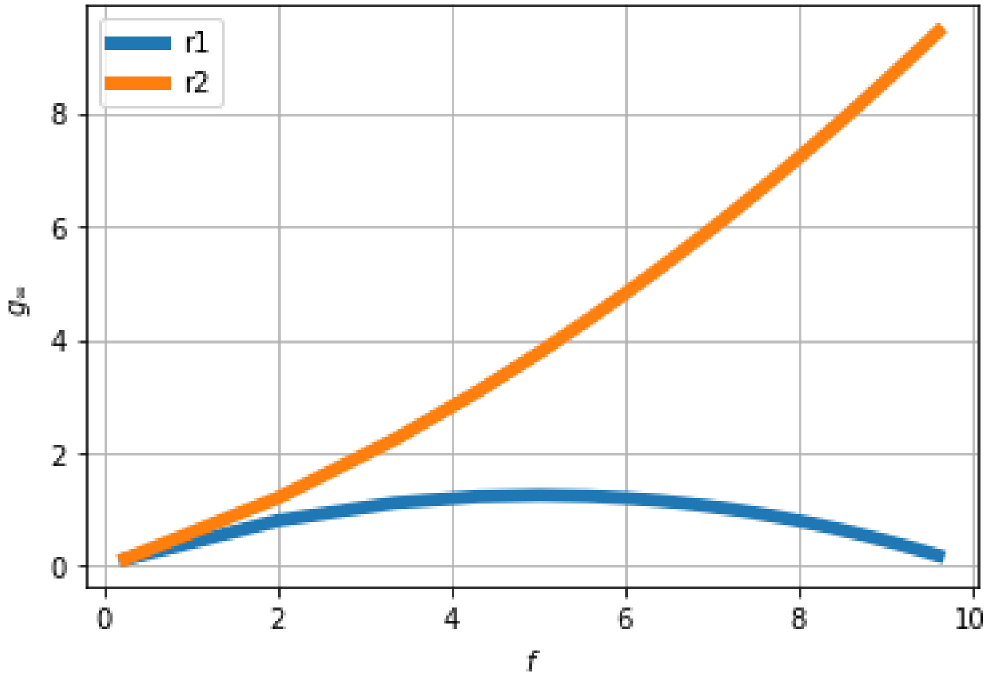
```
{'A': '(0.1 + 0.0001*(t-1000.0)*(1*(t>1000.0)))'}
Steady-state finder error: 7.85e-17
```

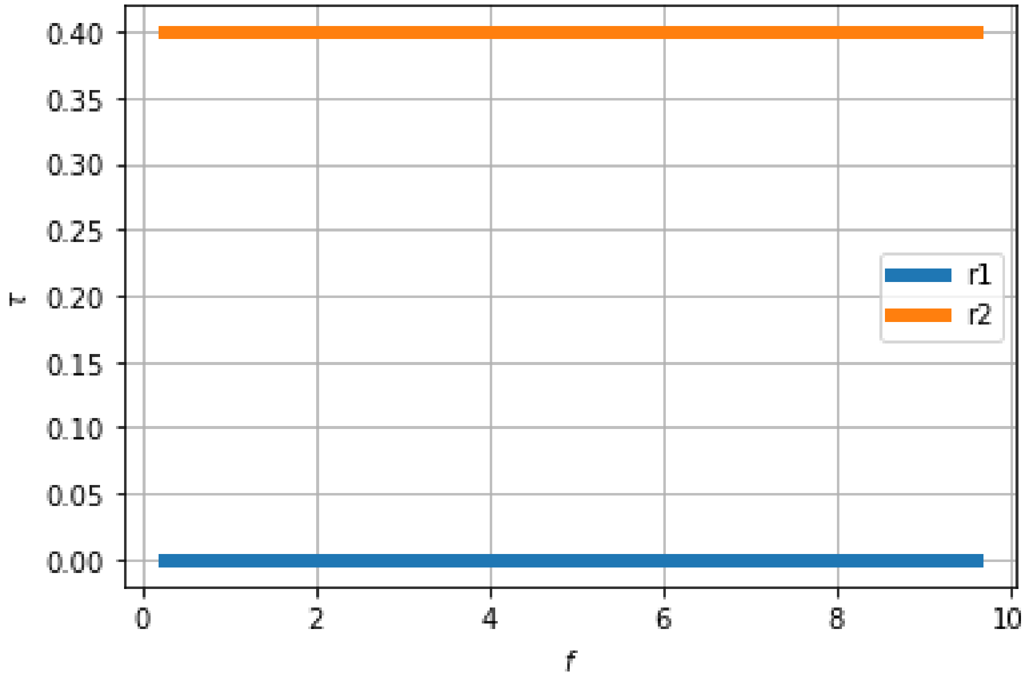


10
8
6
4
2
0
f
0
20
40
60
80
100
λ_{X_A}



r1
r2
8
6
4
2
0
$\Delta f_2/\Delta\lambda$
0
20
40
60
80
100
X_A

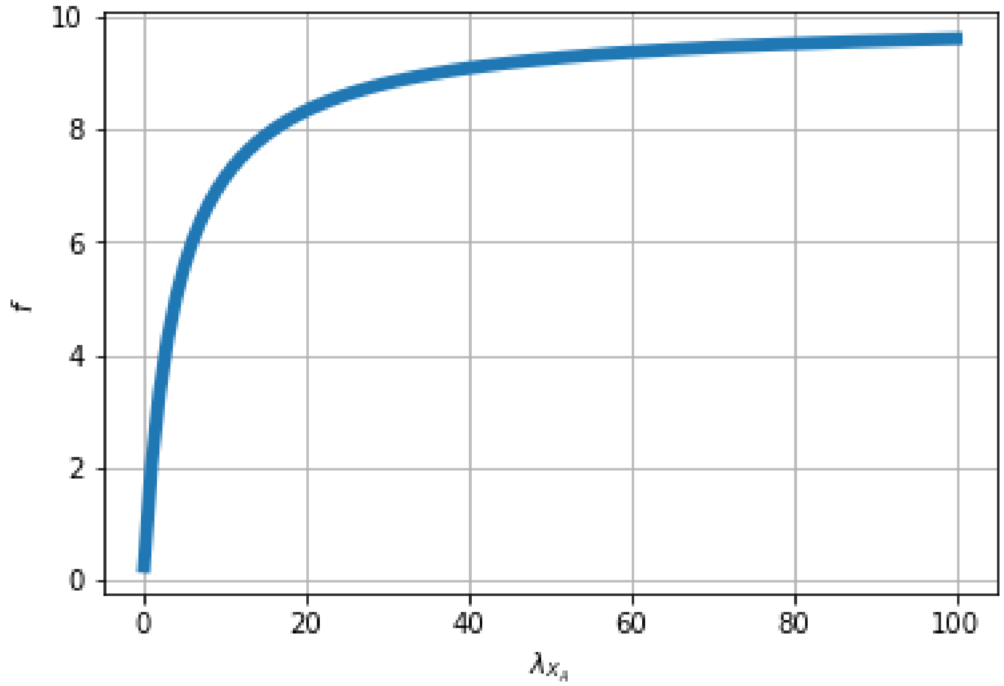




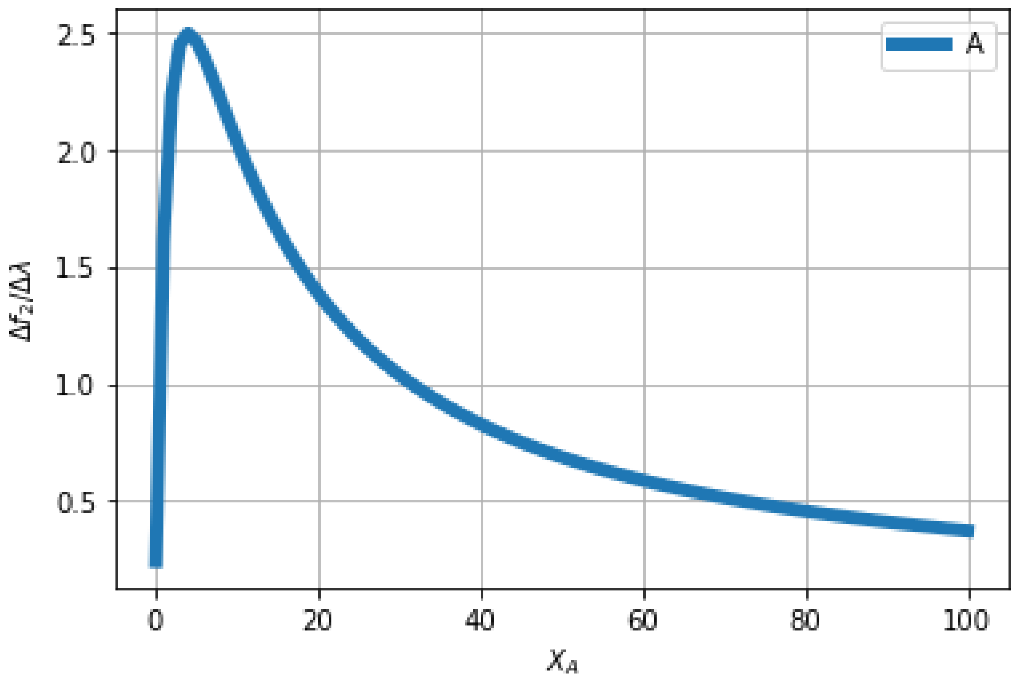
5.4.6 Simulate over flow range - quasi steady-state. Vary substrate concentration.

[117]:
```
QuasiSteadyState(Inp=['sA'],points=100)
```

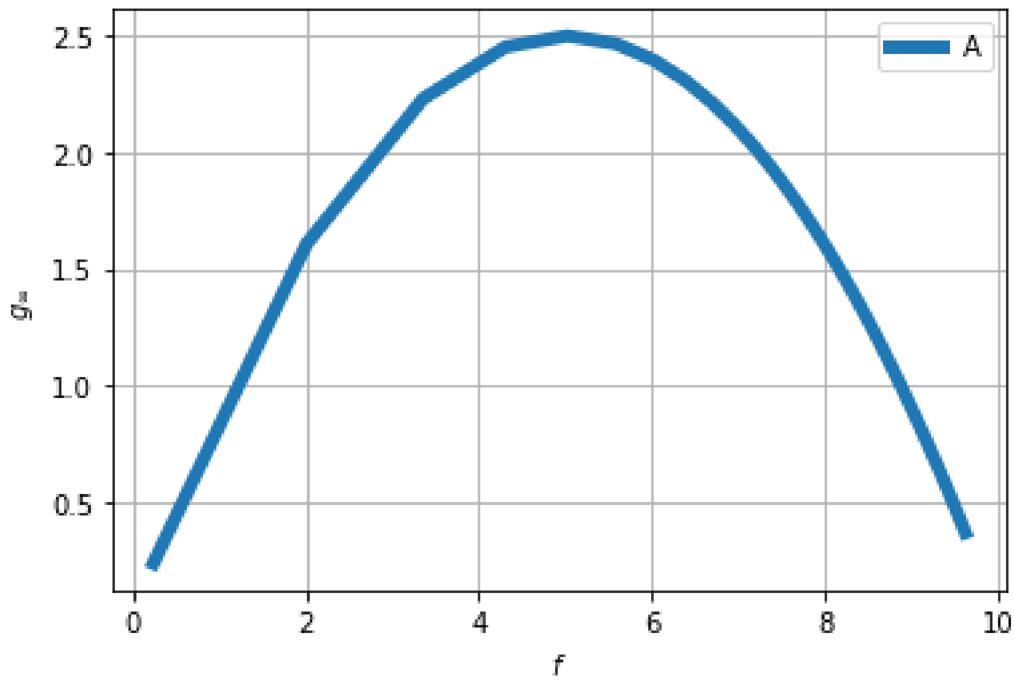
```
{'A': '(0.1 + 0.0001*(t-1000.0)*(1*(t>1000.0)))'}
Steady-state finder error: 7.85e-17
```

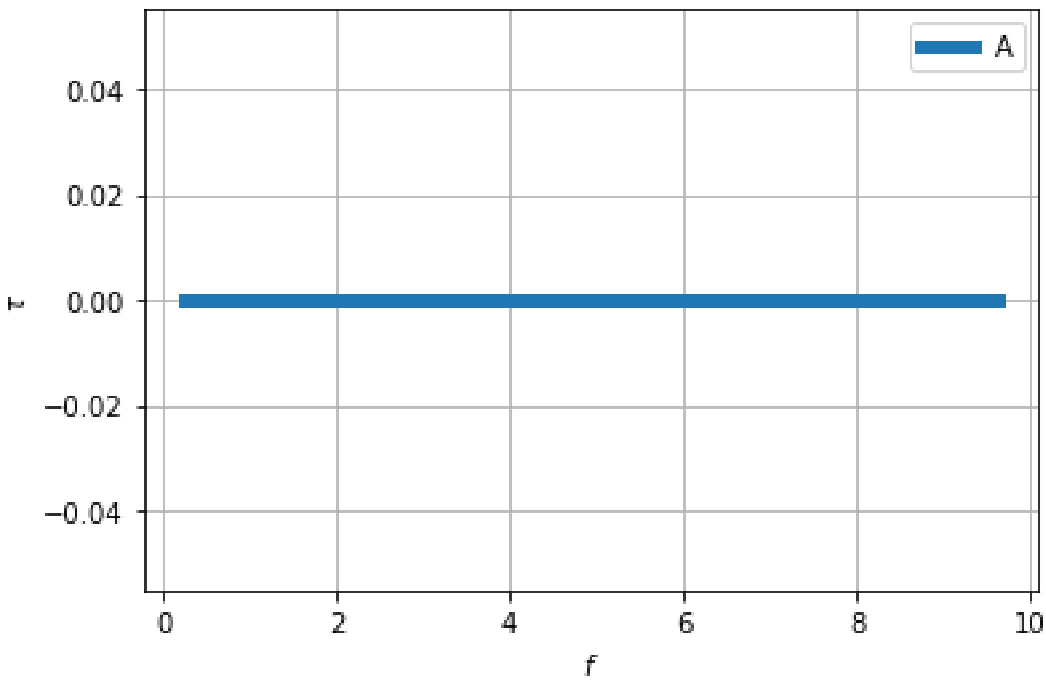


10
8
6
4
2
0
f
0
20
40
60
80
100
λ_{X_A}



2.5
2.0
1.5
1.0
0.5
$\Delta f_2/\Delta\lambda$
0
20
40
60
80
100
X_A
A



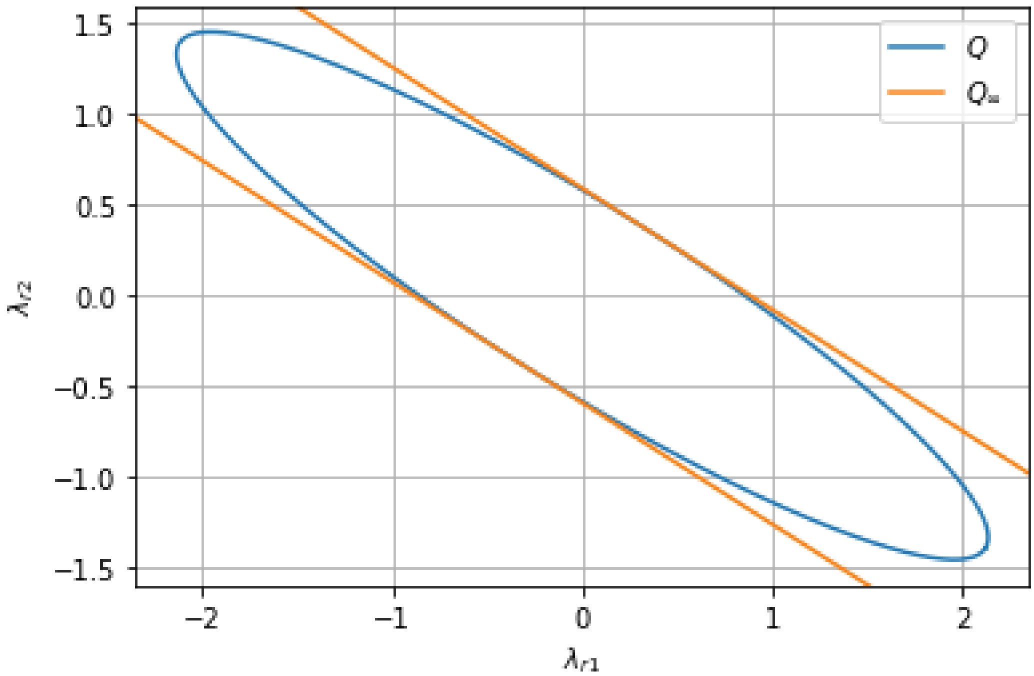


5.4.7 Sloppy parameters

[118]:
```
imp.reload(slp)

for t_last in [0,1e2]:
```

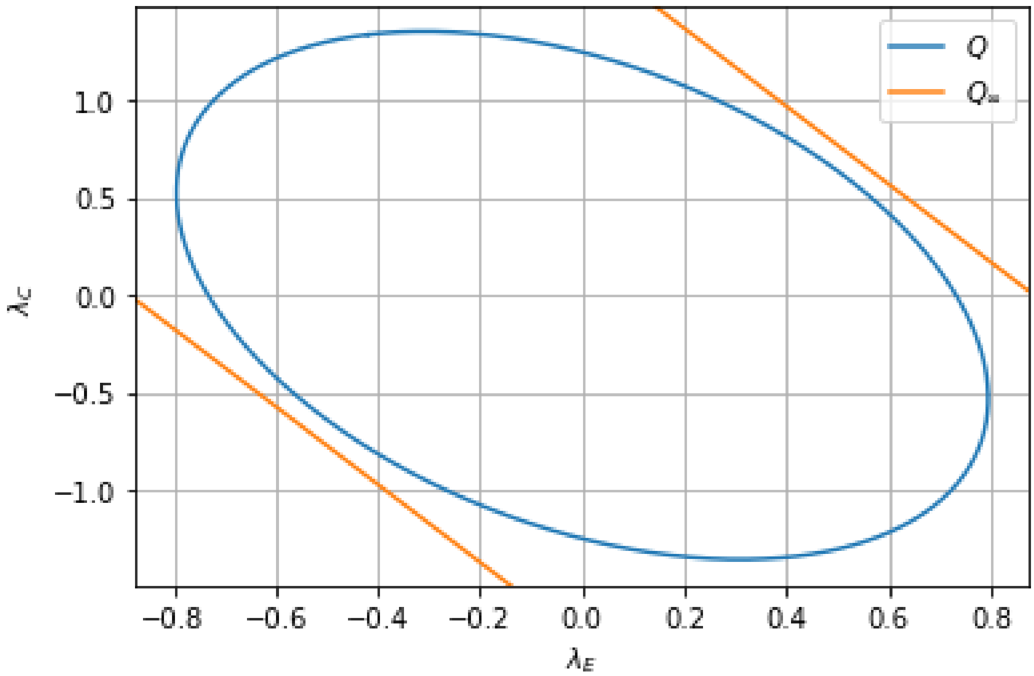
```
    if t_last==0:
        t = None
    else:
        t = np.linspace(0,t_last,100)

    sloppyBoth(Sys,['sr1','sr2'],['r1','r2'],t=t)
    sloppyBoth(Sys,['sE','sC'],['r1','r2'],t=t)
    sloppyBoth(Sys,['sA','sB'],['r1','r2'],t=t)
```

```
ecr

 t_f = 5.00
H:
\sqrt\sigma_1 &= 2 & V_1\Lambda &= + 0.84 \lambda_{r2} + 0.55 \lambda_{r1}
\sqrt\sigma_2 &= 0.39 & V_2\Lambda &= + 0.84 \lambda_{r1} - 0.55 \lambda_{r2}
H_ss:
\sqrt\sigma_1 &= 2 & V_1\Lambda &= + 0.83 \lambda_{r2} + 0.55 \lambda_{r1}
\sqrt\sigma_2 &= 3.2e-05 & V_2\Lambda &= + 0.83 \lambda_{r1} - 0.55 \lambda_{r2}
Direct:
\sqrt\sigma_1 &= 1.4 & V_1\Lambda &= + 0.83 \lambda_{r2} + 0.55 \lambda_{r1}
```

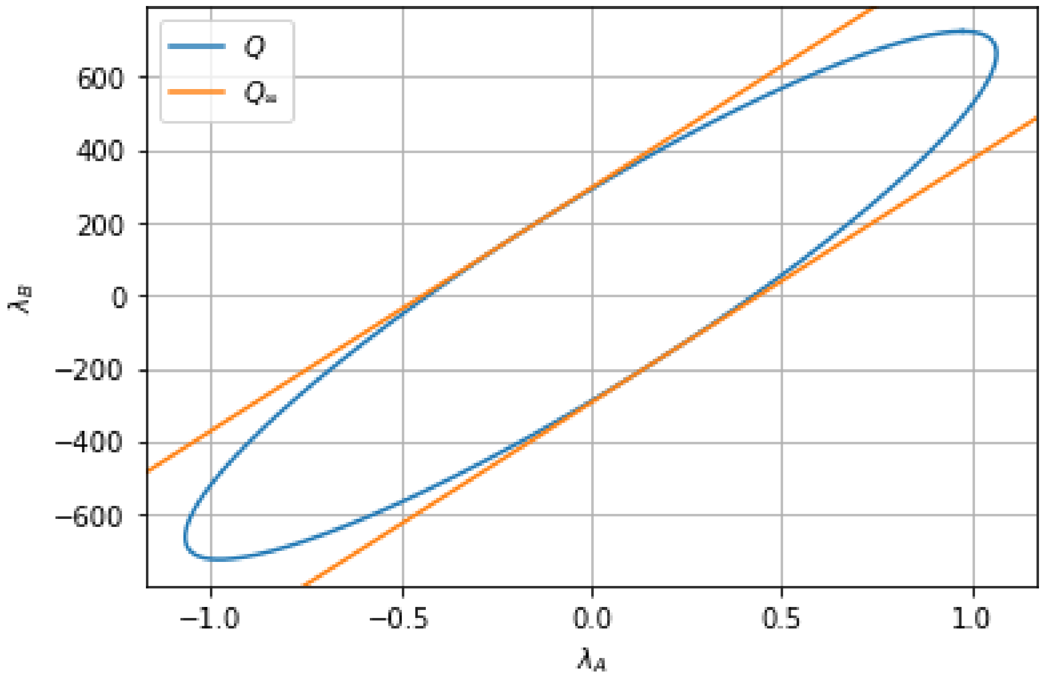



```
ecr

 t_f = 5.00
H:
\sqrt\sigma_1 &= 1.4 & V_1\Lambda &= + 0.95 \lambda_{E} + 0.30 \lambda_{C}
\sqrt\sigma_2 &= 0.71 & V_2\Lambda &= + 0.95 \lambda_{C} - 0.30 \lambda_{E}
```

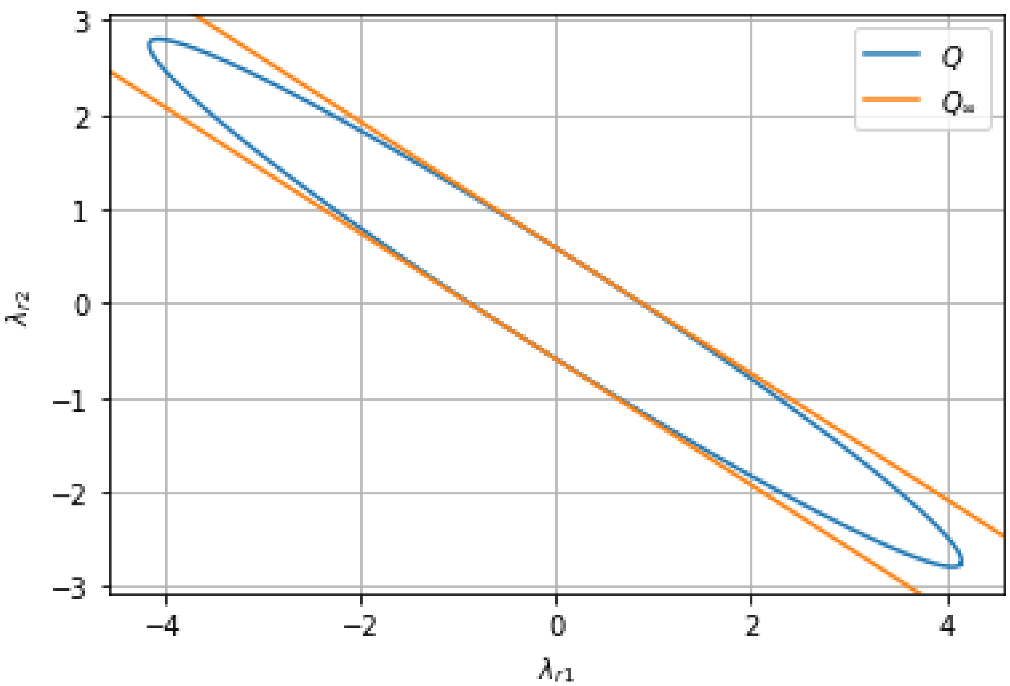
```
H_ss:
\sqrt\sigma_1 &= 1.3 & V_1\Lambda &= + 0.89 \lambda_{E} + 0.45 \lambda_{C}
\sqrt\sigma_2 &= 3.2e-05 & V_2\Lambda &= + 0.89 \lambda_{C} - 0.45 \lambda_{E}
Direct:
\sqrt\sigma_1 &= 0.89 & V_1\Lambda &= + 0.89 \lambda_{E} + 0.45 \lambda_{C}
```



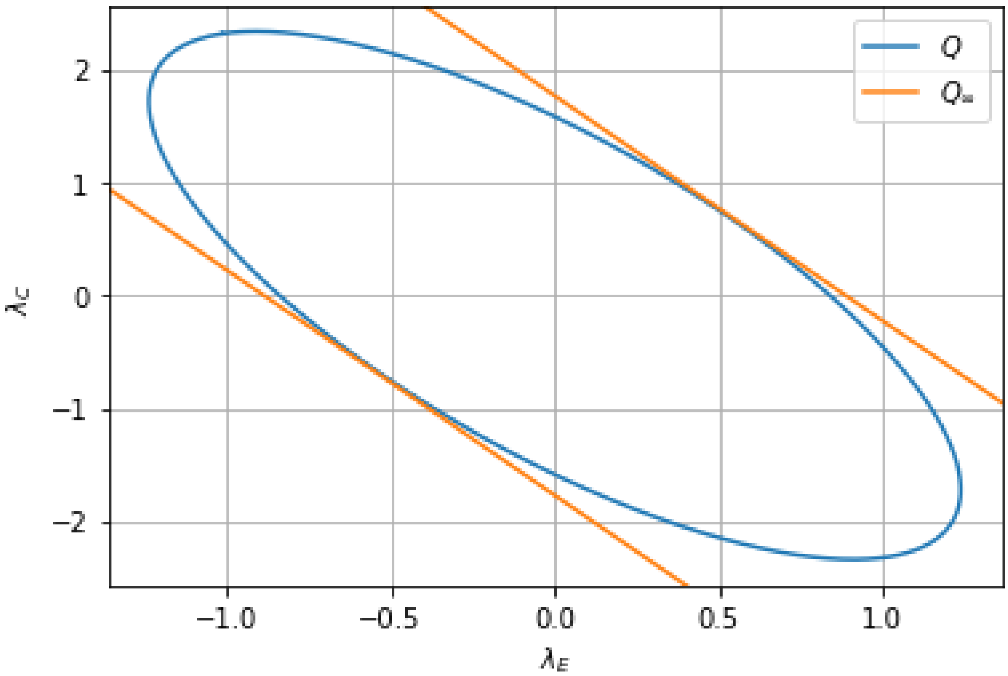

```
ecr

 t_f = 5.00
H:
\sqrt\sigma_1 &= 2.3 & V_1\Lambda &= + 1.00 \lambda_{A} - 0.00 \lambda_{B}
\sqrt\sigma_2 &= 0.0014 & V_2\Lambda &= + 1.00 \lambda_{B} + 0.00 \lambda_{A}
H_ss:
\sqrt\sigma_1 &= 2.3 & V_1\Lambda &= + 1.00 \lambda_{A} - 0.00 \lambda_{B}
\sqrt\sigma_2 &= 3.2e-05 & V_2\Lambda &= + 1.00 \lambda_{B} + 0.00 \lambda_{A}
Direct:
\sqrt\sigma_1 &= 1.6 & V_1\Lambda &= + 1.00 \lambda_{A}
```



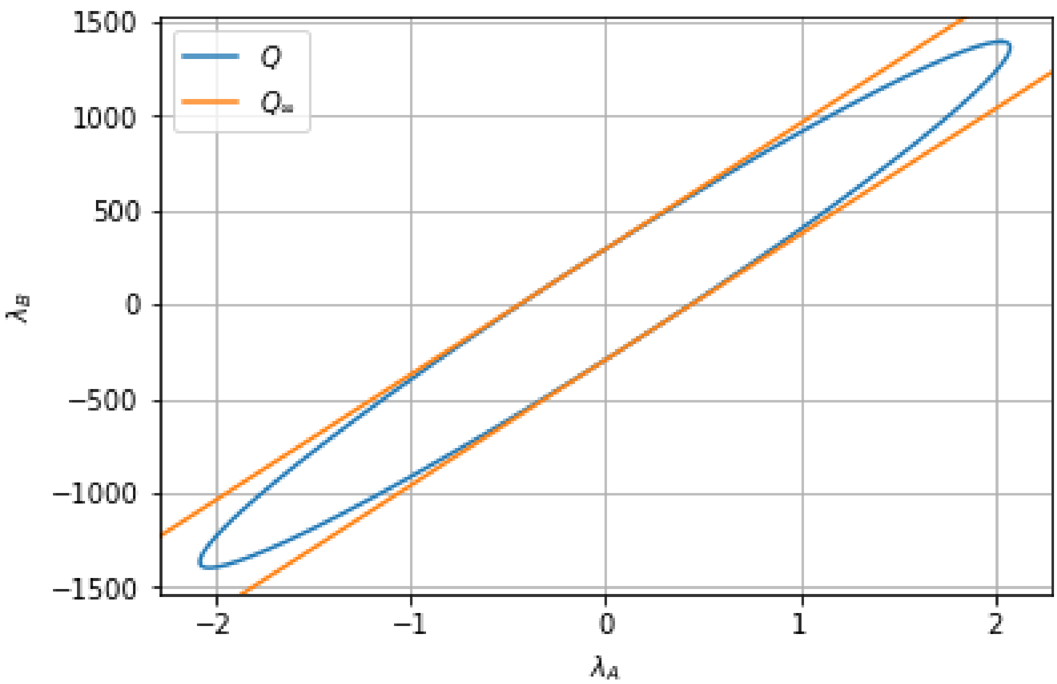

```
ecr

 t_f = 100.00
H:
\sqrt\sigma_1 &= 2 & V_1\Lambda &= + 0.83 \lambda_{r2} + 0.55 \lambda_{r1}
\sqrt\sigma_2 &= 0.2 & V_2\Lambda &= + 0.83 \lambda_{r1} - 0.55 \lambda_{r2}
H_ss:
\sqrt\sigma_1 &= 2 & V_1\Lambda &= + 0.83 \lambda_{r2} + 0.55 \lambda_{r1}
\sqrt\sigma_2 &= 3.2e-05 & V_2\Lambda &= + 0.83 \lambda_{r1} - 0.55 \lambda_{r2}
Direct:
\sqrt\sigma_1 &= 1.4 & V_1\Lambda &= + 0.83 \lambda_{r2} + 0.55 \lambda_{r1}
```




```
ecr

 t_f = 100.00
H:
\sqrt\sigma_1 &= 1.3 & V_1\Lambda &= + 0.92 \lambda_{E} + 0.40 \lambda_{C}
\sqrt\sigma_2 &= 0.4 & V_2\Lambda &= + 0.92 \lambda_{C} - 0.40 \lambda_{E}
H_ss:
\sqrt\sigma_1 &= 1.3 & V_1\Lambda &= + 0.89 \lambda_{E} + 0.45 \lambda_{C}
\sqrt\sigma_2 &= 3.2e-05 & V_2\Lambda &= + 0.89 \lambda_{C} - 0.45 \lambda_{E}
Direct:
\sqrt\sigma_1 &= 0.89 & V_1\Lambda &= + 0.89 \lambda_{E} + 0.45 \lambda_{C}
```




```
ecr

 t_f = 100.00
H:
\sqrt\sigma_1 &= 2.3 & V_1\Lambda &= + 1.00 \lambda_{A} - 0.00 \lambda_{B}
\sqrt\sigma_2 &= 0.00072 & V_2\Lambda &= + 1.00 \lambda_{B} + 0.00 \lambda_{A}
H_ss:
\sqrt\sigma_1 &= 2.3 & V_1\Lambda &= + 1.00 \lambda_{A} - 0.00 \lambda_{B}
\sqrt\sigma_2 &= 3.2e-05 & V_2\Lambda &= + 1.00 \lambda_{B} + 0.00 \lambda_{A}
Direct:
\sqrt\sigma_1 &= 1.6 & V_1\Lambda &= + 1.00 \lambda_{A}
```



[119]:

```
imp.reload(slp)
Outp = ['r1']
Inp_reac = ['sr1','sr2']
def PrintSloppy(Inp,Outp,GainOnly=True,tf=None):
    blurb = '\n*********\n'

    if tf is None:
        t = None
    else:
        t = np.linspace(0,tf)

    for outp in Outp:
        print(blurb,outp,blurb)
        sys = extractSubsystem(Sys,sc,sf,Inp,[outp])
#         print(con.dcgain(sys))
        gain = con.dcgain(sys)[0]
        norm = np.sum(gain*gain)
        ngain = gain/np.sqrt(norm)
#         print(norm,gain/np.sqrt(norm))
        H,eig,eigv,t = slp.Sloppy(sys,GainOnly=GainOnly,small=1e-10,t=tf)
        slp.SloppyPrint(eig,eigv,Inp,min_eig=0.0,min_eigv=0.05,max_eigs=2)
        if GainOnly:
            print('Direct')
            slp.SloppyPrint([norm],np.array([ngain]).T,Inp,min_eig=0.
↪0,min_eigv=0.05,max_eigs=2)
#         print(eigv[:,0])
#         print(ngain)
```

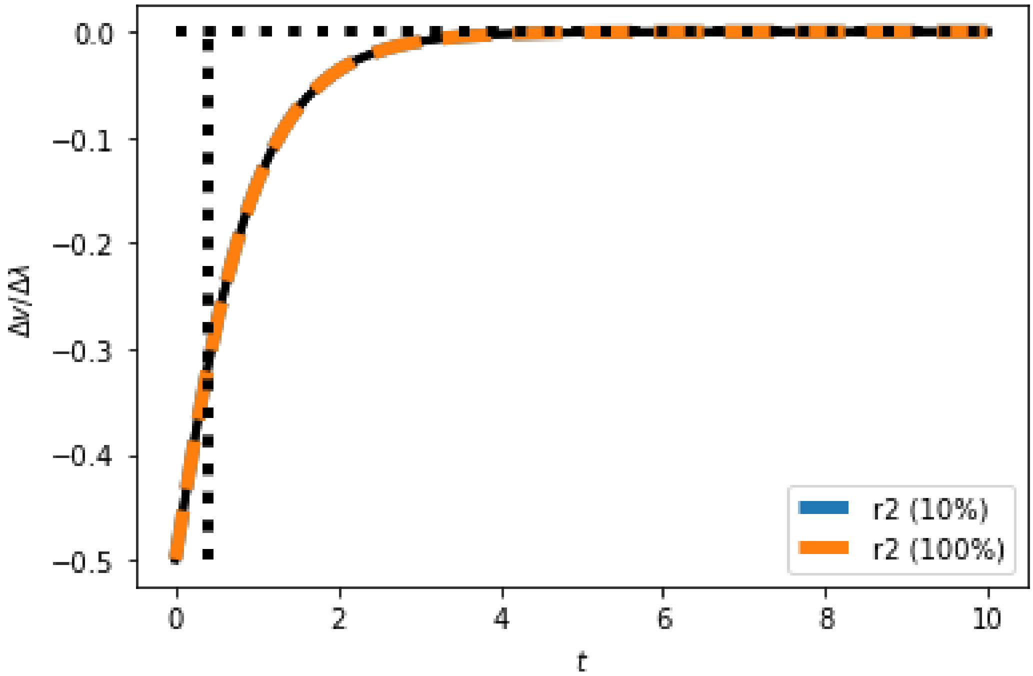
```python
## Reactions
for tf in [None,1e2]:
    for GainOnly in [True,False]:
        print('\nGainOnly =',GainOnly,'; tf =',tf)
        PrintSloppy(Inp_reac,Outp,GainOnly=GainOnly,tf=tf)
```

```
GainOnly = True ; tf = None

*********
 r1
*********

\sqrt\sigma_1 &= 1.4 & V_1\Lambda &= + 0.83 \lambda_{r2} + 0.55 \lambda_{r1}
\sqrt\sigma_2 &= 1e-05 & V_2\Lambda &= + 0.83 \lambda_{r1} - 0.55 \lambda_{r2}
Direct
\sqrt\sigma_1 &= 1.4 & V_1\Lambda &= + 0.83 \lambda_{r2} + 0.55 \lambda_{r1}

GainOnly = False ; tf = None

*********
 r1
*********

\sqrt\sigma_1 &= 1.4 & V_1\Lambda &= + 0.79 \lambda_{r2} + 0.62 \lambda_{r1}
\sqrt\sigma_2 &= 0.29 & V_2\Lambda &= + 0.79 \lambda_{r1} - 0.62 \lambda_{r2}

GainOnly = True ; tf = 100.0

*********
 r1
*********

\sqrt\sigma_1 &= 1.4 & V_1\Lambda &= + 0.83 \lambda_{r2} + 0.55 \lambda_{r1}
\sqrt\sigma_2 &= 1e-05 & V_2\Lambda &= + 0.83 \lambda_{r1} - 0.55 \lambda_{r2}
Direct
\sqrt\sigma_1 &= 1.4 & V_1\Lambda &= + 0.83 \lambda_{r2} + 0.55 \lambda_{r1}

GainOnly = False ; tf = 100.0

*********
 r1
*********

\sqrt\sigma_1 &= 1.4 & V_1\Lambda &= + 0.83 \lambda_{r2} + 0.56 \lambda_{r1}
\sqrt\sigma_2 &= 0.069 & V_2\Lambda &= + 0.83 \lambda_{r1} - 0.56 \lambda_{r2}
```

5.4.8 Initial condition sensitivity.

[120]:
```
## Set up deviation state for full system
n_X = sc['n_X']
sX0 = np.zeros(n_X)
spec = sc['species']
i_C = spec.index('C')
i_E = spec.index('E')
i_E0 = spec.index('E0')

sX0[i_E0] = 1
sX0[i_E] = -0.5
sX0[i_C] = -0.5

## Test conserved moiety compatability
G_c = sc['G']
error = np.linalg.norm(G_c@sX0)
print('Compatibility error =',error)

## Compare linear and non-linear
inp = 'sr1'
outp = ['r2']
for lam in [1.1,2,]:
    dat,y_lin,t,sys = simSensitivity(s,sc,sf,Sys,X_ss,V_ss,dX_ss,
                                        sX0=sX0,
                                                                    ␣
 ↪parameter=parameter,inp=[inp],outp=outp,lam=lam,t_last=10)
#     print(con.dcgain(sys))
    g = con.dcgain(sys)
#     if Titles:
#         plt.title(f'{inp} (g = {g:.3f})')
    plotSensitivity(dat,reactions=outp)
    g=0;plotLines()
Savefig('ecr_IC')
```

```
Compatibility error = 0.0
```




```
[ ]:
```

```
[ ]:
```

References