Sensitivity Analysis of Biochemical Systems Using Bond Graphs: Additional Material for Pentose Phosphate Pathway

Peter Gawthrop. *peter.gawthrop@unimelb.edu.au*

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Contents

1 Introduction

This notebook generates the figures for the paper: Sensitivity Analysis of Biochemical Systems Using Bond Graphs - Pentose Phosphate Pathway Example

2 Set up the code

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
import time

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

# ## For path etc: sys.path
import sys
sys.path.append("/home/peterg/WORK/Research/SystemsBiology/lib/python")

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

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

[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
```

[3]:
```
## High frequency gain function (initial response to step)
def hfgain(sys):

    tf = con.ss2tf(sys)
    num = tf.num[0][0]
    den = tf.den[0][0]
    n = len(den)
    m = len(num)
#     print(den)
#     print(num)
#     print(n,m)

    if n==m:
        g = num[0]/den[0]
    elif n>m:
        g = 0
    elif n<m:
        g = float('inf')

    return g


# g = hfgain(sys)
# print(g)
```

[4]:
```
## Optional plotting
def Savefig(name):
    if Plotting:
        plotname = 'Figs/'+name+'.pdf'
        print('Saving',plotname)
        plt.rcParams.update({'font.size': 20})
        plt.tight_layout()
        plt.savefig(plotname)
        plt.clf()
```

2.2 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
```

2.3 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
```

2.4 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
```

2.5 Extract subsystem from linear system

[8]:
```
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,tol=1e-3,order=None,minreal=False,quiet=False):
 ↪

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

```
    ## 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)
        i_outp = Index(species,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=True)

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

    return sys
```

2.6 Plotting

[9]:
```
def␣
↪plotSensitivity(dat,reactions=['r1','r2'],plotSim=True,name=None,labeling=True):
↪

    if plotSim:
        plt.plot(t,y_step,color='black')
```

```
    else:
        plt.plot(t,y_step,label=label)

    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)))
            if labeling:
                label = f'{reac} ({pc}%)'
            else:
                label = None
            plt.plot(t,(dat['V'][:,i]-V_ss[i])/(lam-1),
                     lw=5,ls='dashed',label=label)

    plt.grid()
    if labeling:
        plt.legend()
    plt.xlabel('$t$')
    plt.ylabel(r'$\tilde{v}/\tilde{\lambda}$')
#     plt.ylim(bottom=0)
#     plt.xlim(left=0)
#     plt.tight_layout()
```

[10]:
```
def␣
↪plotSensitivitydX(dat,species=['A','C'],plotSim=True,name=None,labeling=True,setZero=False
↪
    if plotSim:
        plt.plot(t,y_step,color='black')
    else:
        plt.plot(t,y_step,label=label)

    for spec in species:
        print(spec)
        i_s = s['species'].index(spec)
        if plotSim:
            pc = int(round(100*(lam-1)))
            if labeling:
                label = f'{spec} ({pc}%)'
            else:
                label=None
            plt.plot(t,(dat['dX'][:,i_s]-dX_ss[i_s])/(lam-1),
                     lw=5,ls='dashed',label=label)

    plt.grid()
    if labeling:
        plt.legend()
    plt.xlabel('$t$')
    plt.ylabel(r'$\Delta \mathbf{f} /\Delta \lambda$')
```

```
    #plt.ylabel(r'$\tilde{\dot{x}}/\tilde{\lambda}$')
    if setZero:
        plt.ylim(bottom=0)
        plt.xlim(left=0)
#     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_step.flatten()),1.1*max(y_step.
 ↪flatten()),color='black',ls=ls,lw=lw)
```

3 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
```

4 Stoichiometric approach

[13]:
```
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,tol=None):

    ## Extract sensitivity system
```

```
    sys = extractSubsystem(Sys,sc,sf,inp=inp,outp=outp,order=order,tol=tol)

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

    ## Sensitivity step response
    step = con.step_response(sys,T=t)
    y_step = step.y[:,0,:].T

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

    if inComp in chemostats:
        ## Perturb state
        iComp = s['species'].index(inComp)
        X_ss_1[iComp] = lam*X_ss_1[iComp]
    else:
        ## Perturb parameter
        if inComp in s['species']:
            parname = 'K_'+inComp
        else:
            parname = 'kappa_'+inComp

        print(parname)

        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)

    return dat,y_step,t,sys
```

5 Import Pentose Phosphate Pathway information from:

Peter J. Gawthrop, Michael Pan, and Edmund J. Crampin. *Modular dynamic biomolecular modelling with bond graphs: the unification of stoichiometry, thermodynamics*, kinetics and data. Journal of The Royal Society Interface, 18(181):20210478, 2021. doi:10.1098/rsif.2021.0478.

[14]:
```
## Load data
import pickle
filename = 'GlyPPP.pic'
datafile = open(filename, 'rb')
GlyPPP = pickle.load(datafile)

s0 = GlyPPP['s']
```

```python
parameter = GlyPPP['parameter']
print(parameter)

sc0 = GlyPPP['sc']
chemostats = sc0['chemostats']
print(chemostats)

conc = GlyPPP['conc']

import json
print(json.dumps(parameter,indent=2))
```

```
{'kappa_PGI': 154.38997002578546, 'kappa_PFK': 54.85043355391926, 'kappa_FBA':
160.07691981318658, 'kappa_TPI': 353.9323765134668, 'kappa_G6PDH2R':
4.667672687418436, 'kappa_PGL': 291.6414393949941, 'kappa_GND':
1.2695594575280742, 'kappa_RPI': 4206.975085828208, 'kappa_TKT2':
9.170830408091838, 'kappa_TALA': 1.6563170906188465, 'kappa_TKT1':
8.819978413932159, 'kappa_RPE': 96.07053469867635, 'K_6PGC': 6.233520699319548,
'K_6PGL': 1.0397283862123778, 'K_ADP': 5.154605959675528, 'K_ATP':
2.2539233202427162, 'K_CO2': 33.794182951886775, 'K_DHAP': 1.778985981513151,
'K_E4P': 57.93534155565906, 'K_F6P': 1.41401983409913, 'K_FDP':
0.38795235349448437, 'K_G3P': 14.902044199279699, 'K_G6P': 0.8377378837717493,
'K_H': 0.3491739027654742, 'K_H2O': 1.0397283862123778, 'K_NADP':
11747.063287701598, 'K_NADPH': 21.002665768445333, 'K_R5P': 12.241945837528652,
'K_RU5PD': 86.15506601742248, 'K_S7P': 21.751324335743256, 'K_XU5PD':
51.68293204643235}
['ADP', 'ATP', 'CO2', 'G6P', 'H', 'H2O', 'NADP', 'NADPH', 'R5P', 'G3P']
{
  "kappa_PGI": 154.38997002578546,
  "kappa_PFK": 54.85043355391926,
  "kappa_FBA": 160.07691981318658,
  "kappa_TPI": 353.9323765134668,
  "kappa_G6PDH2R": 4.667672687418436,
  "kappa_PGL": 291.6414393949941,
  "kappa_GND": 1.2695594575280742,
  "kappa_RPI": 4206.975085828208,
  "kappa_TKT2": 9.170830408091838,
  "kappa_TALA": 1.6563170906188465,
  "kappa_TKT1": 8.819978413932159,
  "kappa_RPE": 96.07053469867635,
  "K_6PGC": 6.233520699319548,
  "K_6PGL": 1.0397283862123778,
  "K_ADP": 5.154605959675528,
  "K_ATP": 2.2539233202427162,
  "K_CO2": 33.794182951886775,
  "K_DHAP": 1.778985981513151,
  "K_E4P": 57.93534155565906,
  "K_F6P": 1.41401983409913,
  "K_FDP": 0.38795235349448437,
  "K_G3P": 14.902044199279699,
  "K_G6P": 0.8377378837717493,
```

```
  "K_H": 0.3491739027654742,
  "K_H2O": 1.0397283862123778,
  "K_NADP": 11747.063287701598,
  "K_NADPH": 21.002665768445333,
  "K_R5P": 12.241945837528652,
  "K_RU5PD": 86.15506601742248,
  "K_S7P": 21.751324335743256,
  "K_XU5PD": 51.68293204643235
}
```

[15]:
```
## Reactions
disp.Latex(st.sprintrl(s0,chemformula=True))
```

[15]:

$$\mathrm{G_6P} \rightleftharpoons[\mathrm{PGI}] \mathrm{F_6P} \tag{1}$$

$$\mathrm{ATP} + \mathrm{F_6P} \rightleftharpoons[\mathrm{PFK}] \mathrm{ADP} + \mathrm{FDP} + \mathrm{H} \tag{2}$$

$$\mathrm{FDP} \rightleftharpoons[\mathrm{FBA}] \mathrm{DHAP} + \mathrm{G_3P} \tag{3}$$

$$\mathrm{DHAP} \rightleftharpoons[\mathrm{TPI}] \mathrm{G_3P} \tag{4}$$

$$\mathrm{G_6P} + \mathrm{NADP} \rightleftharpoons[\mathrm{G_6PDH_2R}] {}_6\mathrm{PGL} + \mathrm{H} + \mathrm{NADPH} \tag{5}$$

$${}_6\mathrm{PGL} + \mathrm{H_2O} \rightleftharpoons[\mathrm{PGL}] {}_6\mathrm{PGC} + \mathrm{H} \tag{6}$$

$${}_6\mathrm{PGC} + \mathrm{NADP} \rightleftharpoons[\mathrm{GND}] \mathrm{CO_2} + \mathrm{NADPH} + \mathrm{RU_5PD} \tag{7}$$

$$\mathrm{RU_5PD} \rightleftharpoons[\mathrm{RPI}] \mathrm{R_5P} \tag{8}$$

$$\mathrm{E_4P} + \mathrm{XU_5PD} \rightleftharpoons[\mathrm{TKT_2}] \mathrm{F_6P} + \mathrm{G_3P} \tag{9}$$

$$\mathrm{G_3P} + \mathrm{S_7P} \rightleftharpoons[\mathrm{TALA}] \mathrm{E_4P} + \mathrm{F_6P} \tag{10}$$

$$\mathrm{R_5P} + \mathrm{XU_5PD} \rightleftharpoons[\mathrm{TKT_1}] \mathrm{G_3P} + \mathrm{S_7P} \tag{11}$$

$$\mathrm{RU_5PD} \rightleftharpoons[\mathrm{RPE}] \mathrm{XU_5PD} \tag{12}$$

[16]:
```
## Pathway reactions
sp0 = st.path(s0,sc0)
disp.Latex(st.sprintrl(sp0,chemformula=True))
```

[16]:

$$\mathrm{ATP} + \mathrm{G_6P} \rightleftharpoons[\mathrm{pr_1}] \mathrm{ADP} + 2\,\mathrm{G_3P} + \mathrm{H} \tag{13}$$

$$\mathrm{G_6P} + \mathrm{H_2O} + 2\,\mathrm{NADP} \rightleftharpoons[\mathrm{pr_2}] \mathrm{CO_2} + 2\,\mathrm{H} + 2\,\mathrm{NADPH} + \mathrm{R_5P} \tag{14}$$

$$2\,\mathrm{H_2O} + 4\,\mathrm{NADP} + \mathrm{R_5P} \rightleftharpoons[\mathrm{pr_3}] 2\,\mathrm{CO_2} + \mathrm{G_3P} + 4\,\mathrm{H} + 4\,\mathrm{NADPH} \tag{15}$$

5.1 Repeat simulations for sanity check

[17]:
```
def setPath(s,path='R5P'):

    print('\n Path =', path)

    if path == 'R5P':
        chemostats = ['ADP', 'ATP', 'CO2', 'G6P', 'H', 'H2O', 'NADP',␣
↪'NADPH', 'R5P']
        flowstats =['G6PDH2R']
        dX_G6P = 5
    elif path == 'NADPH':
        chemostats = ['ADP', 'ATP', 'CO2', 'G6P', 'H', 'H2O', 'NADP', 'NADPH']
        flowstats = []
        dX_G6P = 1
    elif path == 'both':
        chemostats = ['ADP', 'ATP', 'CO2', 'G6P', 'H', 'H2O', 'NADP',␣
↪'NADPH', 'R5P']
        flowstats =  ['PGI', 'TKT2']
        dX_G6P = 1
    elif path == 'all':
        chemostats = ['ADP', 'ATP', 'CO2', 'G6P', 'H', 'H2O', 'NADP',␣
↪'NADPH', 'R5P','G3P']
        flowstats = []
        dX_G6P = 10
    elif path == 'all_e4p':
        chemostats = ['ADP', 'ATP', 'CO2', 'G6P', 'H', 'H2O', 'NADP',␣
↪'NADPH', 'R5P','G3P','E4P']
        flowstats = []
        dX_G6P = 10

    sc = st.statify(s,chemostats=chemostats)
    sf = st.statify(s,flowstats=flowstats)

    return sc,sf,dX_G6P
```

[18]:
```
## Data normalisation
c_0 = 7.88 # mM
f_0 = 0.9916666666666667 # mM/sec
t_0 = 7.946218487394957 # sec
```

[19]:
```
## Simulate for each path
s = copy.copy(s0) ## for compatibility
spec = s['species']
approximateFlowstats = True

Spec = ['G6P','R5P','NADPH','ADP','CO2','H','H2O']
#paths = ['all','both','R5P','NADPH']
#paths = ['R5P']
#paths = ['all','both','NADPH','R5P']
paths = ['both','NADPH','R5P','all_e4p','all']
```

```
RATIO = {}
for path in paths:
    Ratio = {}
    normalisedRatio = {}

    ## Set up pathway
    sc,sf,dX_G6P_0 = setPath(s,path=path)

    ## Print pathway
    sp = st.path(s,sc)
    print(st.sprintrl(sp))

    ## Set up parameters
    par = copy.copy(parameter)
    if approximateFlowstats:
        small = 1e-3
        par = copy.copy(parameter)
        for fs in sf['flowstats']:
            par['kappa_'+fs] = small
        sf = None

    ## Simulate
    t = np.linspace(0,3*t_0,1000)

#     ## Find steady-state with no flowstats
#     dat_ss = st.sim(s,sc=sc,sf=sf,t=t,parameter=parameter,X0=conc)
#     X_ss = dat_ss['X'][-1,:]

    dat = st.sim(s,sc=sc,sf=sf,t=t,parameter=par,X0=conc)
    #st.plot(s,dat,species=[])
#     st.plot(s,dat,reaction=[],species=Spec,dX=True)

    ## Extract some external flows
    DX = dat['dX']
    dX = {}
    for Sp in Spec:
        dX[Sp] = DX[:,spec.index(Sp)]
        Ratio[Sp] = -dX[Sp]/dX['G6P']
        normalisedRatio[Sp] =  -dX_G6P_0*dX[Sp]/dX['G6P']

    RATIO[path] = normalisedRatio


    ## Print steady-state values
    for Sp in Spec:
        ratio = Ratio[Sp][-1]
        print(f'{Sp}:\t{dX[Sp][0]:3.1f} \t{dX[Sp][-1]:3.
↪1f}\t{(dX_G6P_0*ratio):3.1f}\t{100*ratio:3.1f}%')
```

```
Path = both
```

```
\begin{align}
G6P + H2O + 2 NADP  &\Leftrightarrow CO2 + 2 H + 2 NADPH + R5P \\
ADP + 4 H2O + 8 NADP + 2 R5P  &\Leftrightarrow ATP + 4 CO2 + G6P + 7 H + 8 NADPH
\end{align}

G6P:    -11.6   -11.6   -1.0    -100.0%
R5P:    6.2     11.5    1.0     99.4%
NADPH:  23.2    23.2    2.0     200.0%
ADP:    63.1    0.0     0.0     0.4%
CO2:    11.6    11.6    1.0     100.0%
H:      86.3    23.2    2.0     200.4%
H2O:    -11.6   -11.6   -1.0    -100.0%

 Path = NADPH
\begin{align}
ADP + G6P + 6 H2O + 12 NADP  &\Leftrightarrow ATP + 6 CO2 + 11 H + 12 NADPH
\end{align}

G6P:    -71.1   -1.9    -1.0    -100.0%
R5P:    6.2     0.0     0.0     0.0%
NADPH:  23.2    23.1    12.0    1200.0%
ADP:    63.1    -1.9    -1.0    -100.0%
CO2:    11.6    11.6    6.0     600.0%
H:      86.3    21.2    11.0    1100.0%
H2O:    -11.6   -11.6   -6.0    -600.0%

 Path = R5P
\begin{align}
G6P + H2O + 2 NADP  &\Leftrightarrow CO2 + 2 H + 2 NADPH + R5P \\
ADP + 4 H2O + 8 NADP + 2 R5P  &\Leftrightarrow ATP + 4 CO2 + G6P + 7 H + 8 NADPH
\end{align}

G6P:    -59.5   -2.4    -5.0    -100.0%
R5P:    6.2     2.9     6.0     120.0%
NADPH:  11.6    0.0     0.0     0.2%
ADP:    63.1    0.5     1.0     20.0%
CO2:    11.6    0.0     0.0     0.1%
H:      74.7    0.5     1.0     20.2%
H2O:    -11.6   -0.0    -0.0    -0.1%

 Path = all_e4p
\begin{align}
ATP + G6P  &\Leftrightarrow ADP + 2 G3P + H \\
G6P + H2O + 2 NADP  &\Leftrightarrow CO2 + 2 H + 2 NADPH + R5P \\
G3P + R5P  &\Leftrightarrow 2 E4P \\
E4P + H2O + 2 NADP  &\Leftrightarrow CO2 + G3P + 2 H + 2 NADPH
\end{align}

G6P:    -71.1   -71.1   -10.0   -100.0%
R5P:    6.2     6.2     0.9     8.7%
NADPH:  23.2    23.2    3.3     32.6%
```

```
ADP:    63.1    63.1    8.9     88.8%
CO2:    11.6    11.6    1.6     16.3%
H:      86.3    86.3    12.1    121.3%
H2O:    -11.6   -11.6   -1.6    -16.3%

 Path = all
\begin{align}
ATP + G6P  &\Leftrightarrow ADP + 2 G3P + H \\
G6P + H2O + 2 NADP  &\Leftrightarrow CO2 + 2 H + 2 NADPH + R5P \\
2 H2O + 4 NADP + R5P  &\Leftrightarrow 2 CO2 + G3P + 4 H + 4 NADPH
\end{align}

G6P:    -71.1   -71.1   -10.0   -100.0%
R5P:    6.2     6.2     0.9     8.7%
NADPH:  23.2    23.2    3.3     32.6%
ADP:    63.1    63.1    8.9     88.8%
CO2:    11.6    11.6    1.6     16.3%
H:      86.3    86.3    12.1    121.3%
H2O:    -11.6   -11.6   -1.6    -16.3%
```

[20]:
```python
## Set up chemostats to correspond to above path
chemostats = sc['chemostats']
Chemostats = copy.copy(sc['chemostats'])
print(path)
print(chemostats)
```

```
all
['ADP', 'ATP', 'CO2', 'G6P', 'H', 'H2O', 'NADP', 'NADPH', 'R5P', 'G3P']
```

[21]:
```python
## Plot ratios
plottingRatios = False
if plottingRatios:
    name = ['i','ii','iii']
    for sp in ['R5P','NADPH']:
        BigFont = 24
        plt.rcParams.update({'font.size': BigFont})
        for i,path in enumerate(['both','R5P','NADPH']):
            Ratio = RATIO[path]
            label = f'Path {name[i]} ({path})'
            plt.plot(t/t_0,Ratio[sp],label=label,linewidth=5)
        if sp=='R5P':
            ylim = 8
        else:
            ylim=15
        plt.ylim((0,ylim))
        ylabel = r'$\rho_{'+sp+'}$'
        plt.ylabel(ylabel)
        plt.xlabel('$t/t_0$')
        plt.legend()
        plt.grid()
    #     if SaveFig:
```

```
    #         plt.savefig(f'Figs/{sp}.pdf',bbox_inches='tight')

        # plt.show()
```

6 Sensitivity System

[22]:
```
## Create sensitivity system
s = copy.copy(s0)
extra = st.stoichSensitivity(s)
chemostats += extra
sc = st.statify(s,chemostats=chemostats)
```

[23]:
```
## Reactions
disp.Latex(st.sprintrl(s,all=True,chemformula=True))
```

[23]:

$$G_6P + sG_6P + sPGI \xrightleftharpoons{PGI} F_6P + sF_6P + sPGI \tag{16}$$

$$ATP + F_6P + sATP + sF_6P + sPFK \xrightleftharpoons{PFK} ADP + FDP + H + sADP + sFDP + sH + sPFK \tag{17}$$

$$FDP + sFDP + sFBA \xrightleftharpoons{FBA} DHAP + G_3P + sDHAP + sG_3P + sFBA \tag{18}$$

$$DHAP + sDHAP + sTPI \xrightleftharpoons{TPI} G_3P + sG_3P + sTPI \tag{19}$$

$$G_6P + NADP + sG_6P + sNADP + sG_6PDH_2R \xrightleftharpoons{G_6PDH_2R} {}_6PGL + H + NADPH + s_6PGL + sH + sNAI \tag{20}$$

$${}_6PGL + H_2O + s_6PGL + sH_2O + sPGL \xrightleftharpoons{PGL} {}_6PGC + H + s_6PGC + sH + sPGL \tag{21}$$

$${}_6PGC + NADP + s_6PGC + sNADP + sGND \xrightleftharpoons{GND} CO_2 + NADPH + RU_5PD + sCO_2 + sNADPH + \tag{22}$$

$$RU_5PD + sRU_5PD + sRPI \xrightleftharpoons{RPI} R_5P + sR_5P + sRPI \tag{23}$$

$$E_4P + XU_5PD + sE_4P + sXU_5PD + sTKT_2 \xrightleftharpoons{TKT_2} F_6P + G_3P + sF_6P + sG_3P + sTKT_2 \tag{24}$$

$$G_3P + S_7P + sG_3P + sS_7P + sTALA \xrightleftharpoons{TALA} E_4P + F_6P + sE_4P + sF_6P + sTALA \tag{25}$$

$$R_5P + XU_5PD + sR_5P + sXU_5PD + sTKT_1 \xrightleftharpoons{TKT_1} G_3P + S_7P + sG_3P + sS_7P + sTKT_1 \tag{26}$$

$$RU_5PD + sRU_5PD + sRPE \xrightleftharpoons{RPE} XU_5PD + sXU_5PD + sRPE \tag{27}$$

[24]:
```
## Initial conditions
X0 = np.hstack((conc,np.ones(s0['n_X']),np.ones(s0['n_V'])))
# print(X0)
print(X0.shape)
```

```
(50,)
```

[25]:
```
## Linearise
# Sys,X_ss,V_ss,dX_ss = Linear(s,sc,X0=X0)
# Sys,X_ss,V_ss,dX_ss = Linear(s,sc,parameter=parameter,X0=X0, invar='X',␣
 ↪outvar = 'V', quiet=False)
```

[26]:
```
# species = s['species']
# reaction = s['reaction']
```

[27]:
```
# print(chemostats)
# print(reaction)
# print(species)
# # print(s0['Z'])
```

[28]:
```
# sys = extractSubsystem(Sys,sc,sf,inp=['sG6P'],outp=['RPI'],order=3)
```

6.1 Linearise sensitivity system

[29]:
```
## Linearise dX as outvar
Sys,X_ss,V_ss,dX_ss = Linear(s,sc,parameter=parameter,X0=X0, invar='X',␣
 ↪outvar = 'dX', quiet=False)
```

```
Steady-state finder error: 2.10e-14
V_ss = [59.52330023 63.11688312 63.11688312 63.11688312 11.57830405 11.57830405
 11.57830405  7.98472116  1.79679144  1.79679144  1.79679144  3.59358289]
Setting K_6PGC to 6.233520699319548
Setting K_6PGL to 1.0397283862123778
Setting K_ADP to 5.154605959675528
Setting K_ATP to 2.2539233202427162
Setting K_CO2 to 33.794182951886775
Setting K_DHAP to 1.778985981513151
Setting K_E4P to 57.93534155565906
Setting K_F6P to 1.41401983409913
Setting K_FDP to 0.38795235349448437
Setting K_G3P to 14.902044199279699
Setting K_G6P to 0.8377378837717493
Setting K_H to 0.3491739027654742
Setting K_H2O to 1.0397283862123778
Setting K_NADP to 11747.063287701598
Setting K_NADPH to 21.002665768445333
Setting K_R5P to 12.241945837528652
Setting K_RU5PD to 86.15506601742248
Setting K_S7P to 21.751324335743256
Setting K_XU5PD to 51.68293204643235
Setting kappa_PGI to 154.38997002578546
```

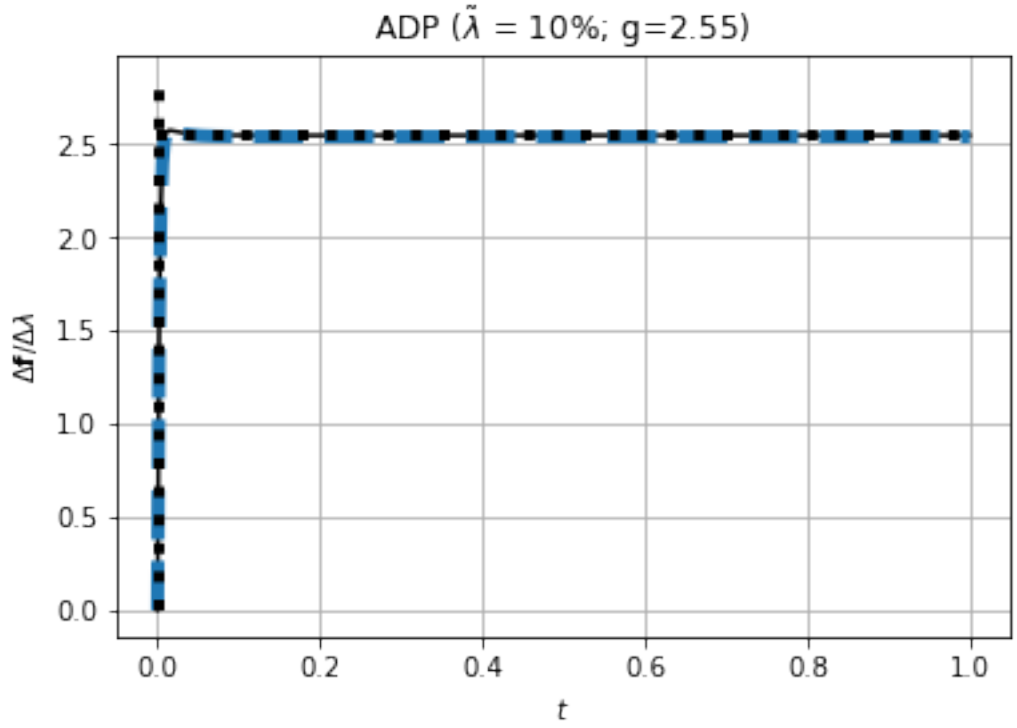
```
Setting kappa_PFK to 54.85043355391926
Setting kappa_FBA to 160.07691981318658
Setting kappa_TPI to 353.9323765134668
Setting kappa_G6PDH2R to 4.667672687418436
Setting kappa_PGL to 291.6414393949941
Setting kappa_GND to 1.2695594575280742
Setting kappa_RPI to 4206.975085828208
Setting kappa_TKT2 to 9.170830408091838
Setting kappa_TALA to 1.6563170906188465
Setting kappa_TKT1 to 8.819978413932159
Setting kappa_RPE to 96.07053469867635
```

6.2 Compute chemostat sensitivities

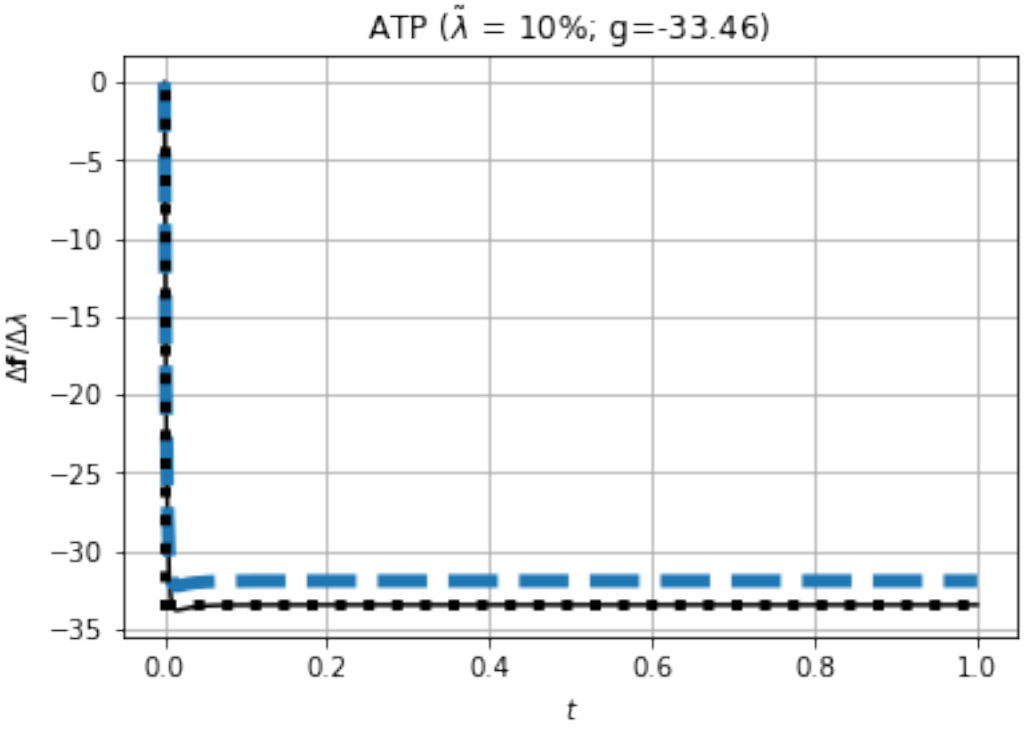
[30]:
```
## Chemostat sensitivities
# Inp = ['sG6P','sR5P','sNADPH','sG3P']
Outp = ['G6P','R5P','NADPH','G3P']
Inp = []
for chemo in sc['chemostats']:
    if not chemo[0] in ['s','H']:
        Inp.append('s'+chemo)
print(Inp)
Inp_chemo = Inp
# Inp = []
# for reac in s['reaction']:
#     Inp.append('s'+reac)
# Inp = ['sG6PDH2R']

t_last=1
lam = 1.1 # Perturbation parameter

dcgain = {}
Tau = {}
for outp in Outp:
    for inp in Inp:
        print('Doing:',inp)
        sf = None
        order = None
        dat,y_step,t,sys =␣
↪simSensitivity(s,sc,sf,Sys,X_ss,V_ss,dX_ss,chemostats=Chemostats,parameter=parameter,
                                                    ␣
↪inp=[inp],outp=[outp],lam=lam,t_last=t_last,order=order)


        g = con.dcgain(sys)
        g,tau = tfProps(sys)
        print('g =',g)
        name = inp[1:]

        if outp=='G6P':
            dcgain[name] = -g
```

```
            ylabel = '$-g_{\infty}$'
        else:
            dcgain[name] = g
            ylabel = '$g_{\infty}$'

        Tau[name] = tau

        dlam = int((lam-1)*100)
        print('dlam =',dlam)
        if Titles:
            plt.title(f'{name}'+r' ($\tilde\lambda$ = ' + f'{dlam}%; g={g:.
 ↪2f})')
        plotSensitivitydX(dat,species=[outp],labeling=False)
#         plt.hlines(g,min(t),max(t),color='black',ls='dashed')
        plotLines()
        Savefig('PPPdX_'+name+'_'+outp)
        plt.show()

    ## Barcharts
    ## DC gain
    if Titles:
        plt.title(outp)
    plt.tick_params(axis='x', rotation=90)
    plt.grid()
    plt.bar(range(len(dcgain)), dcgain.values(), align='center')
    plt.xticks(range(len(dcgain)), list(dcgain.keys()))
    plt.ylabel(ylabel)
    Savefig(f'PPPdX_{outp}_chem_bar')
    plt.show()

    ## Time constant
    if Titles:
        plt.title(outp)
    plt.tick_params(axis='x', rotation=90)
    plt.grid()
    plt.bar(range(len(Tau)), Tau.values(), align='center')
    plt.xticks(range(len(Tau)), list(Tau.keys()))
    plt.ylabel(r'$\tau$')
    Savefig(f'PPPdX_{outp}_chem_tau_bar')
    plt.show()
```

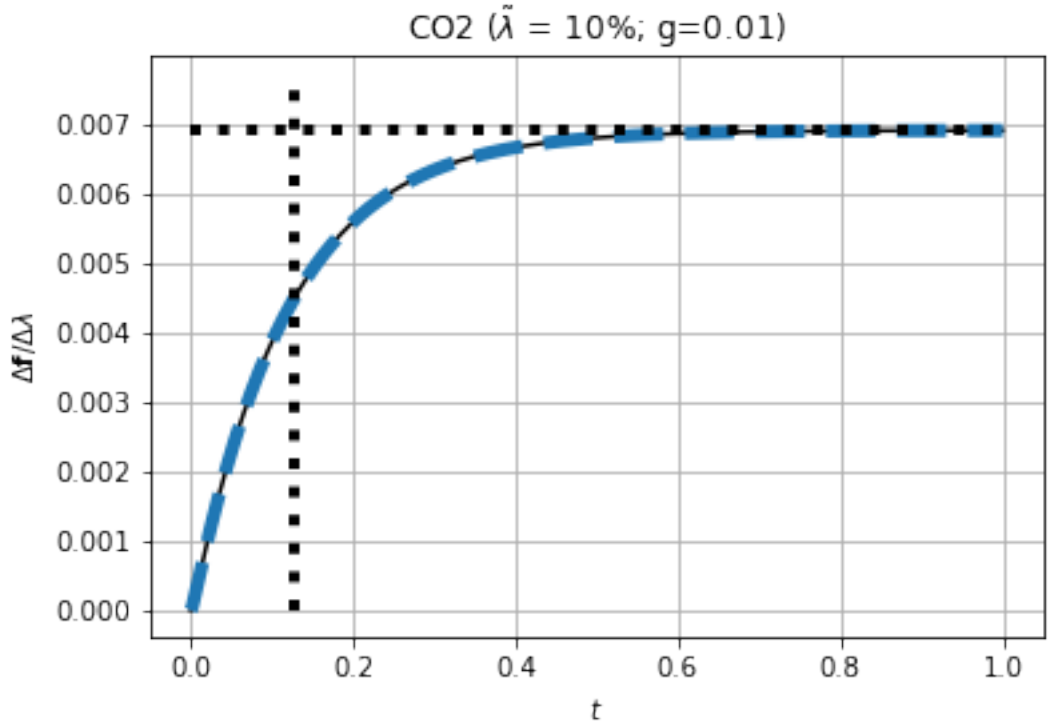
```
['sADP', 'sATP', 'sCO2', 'sG6P', 'sNADP', 'sNADPH', 'sR5P', 'sG3P']
Doing: sADP
g = 2.5484963469688147
dlam = 10
G6P
```



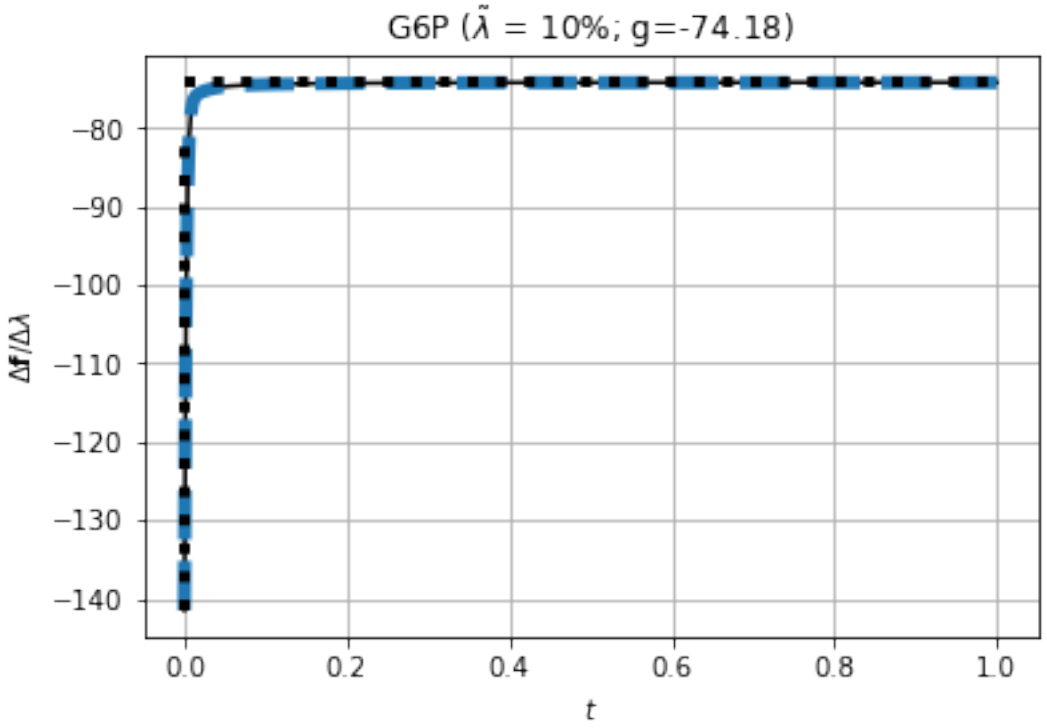

```
Doing: sATP
g = -33.46210603034223
dlam = 10
G6P
```



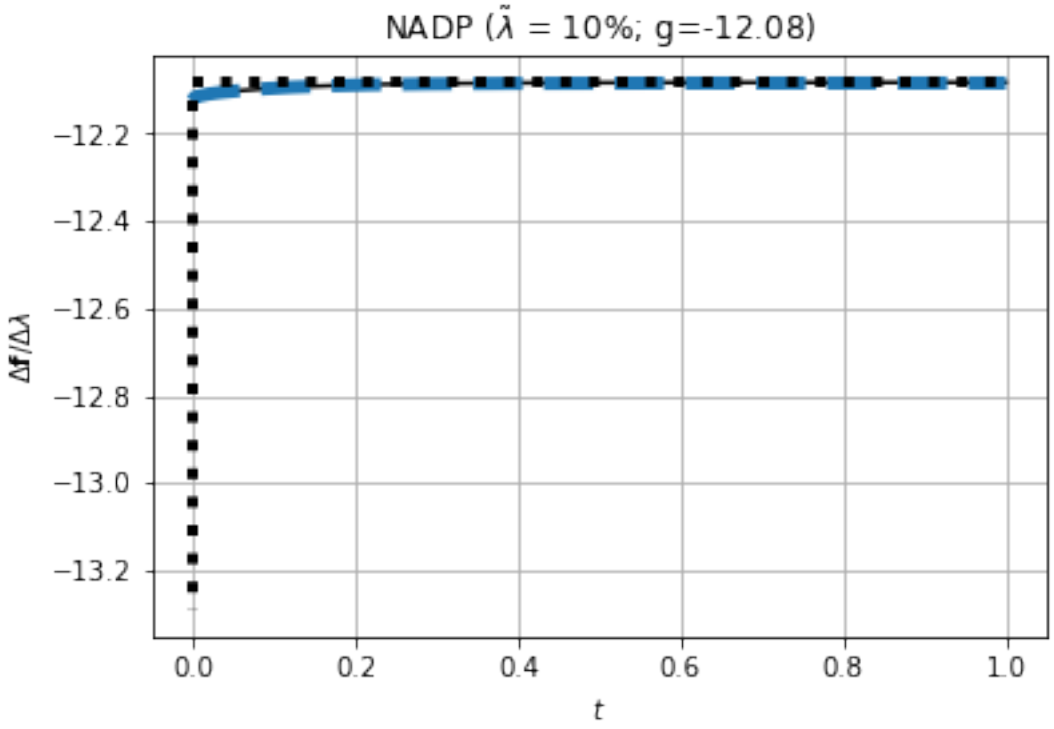
```
Doing: sCO2
g = 0.006924942429813596
dlam = 10
G6P
```



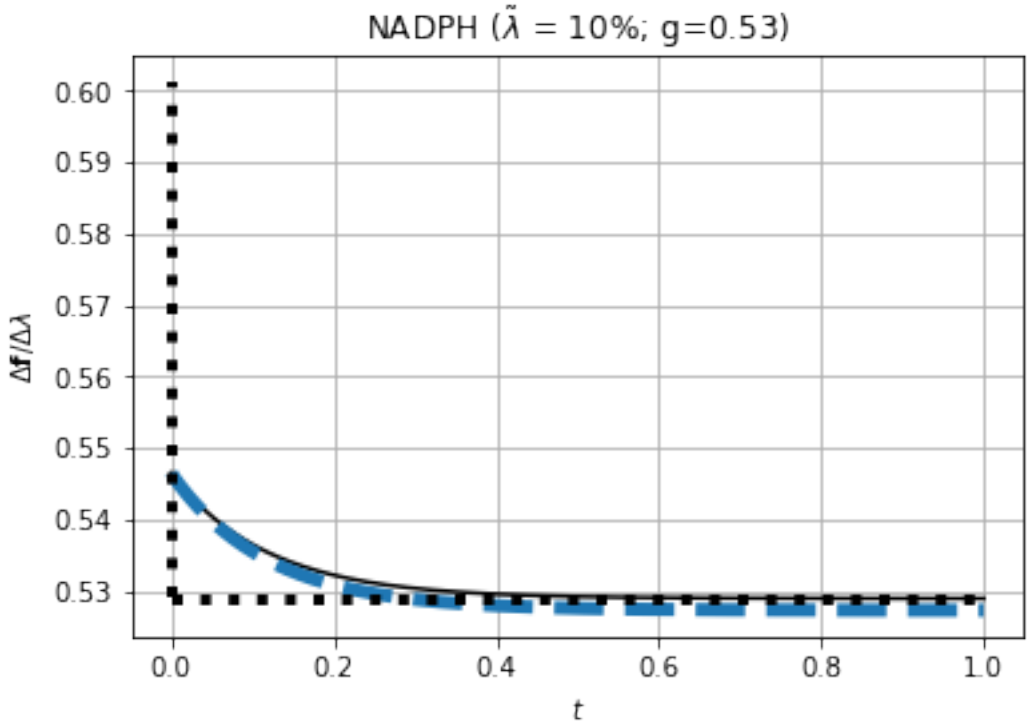

```
Doing: sG6P
g = -74.1814457534691
dlam = 10
G6P
```



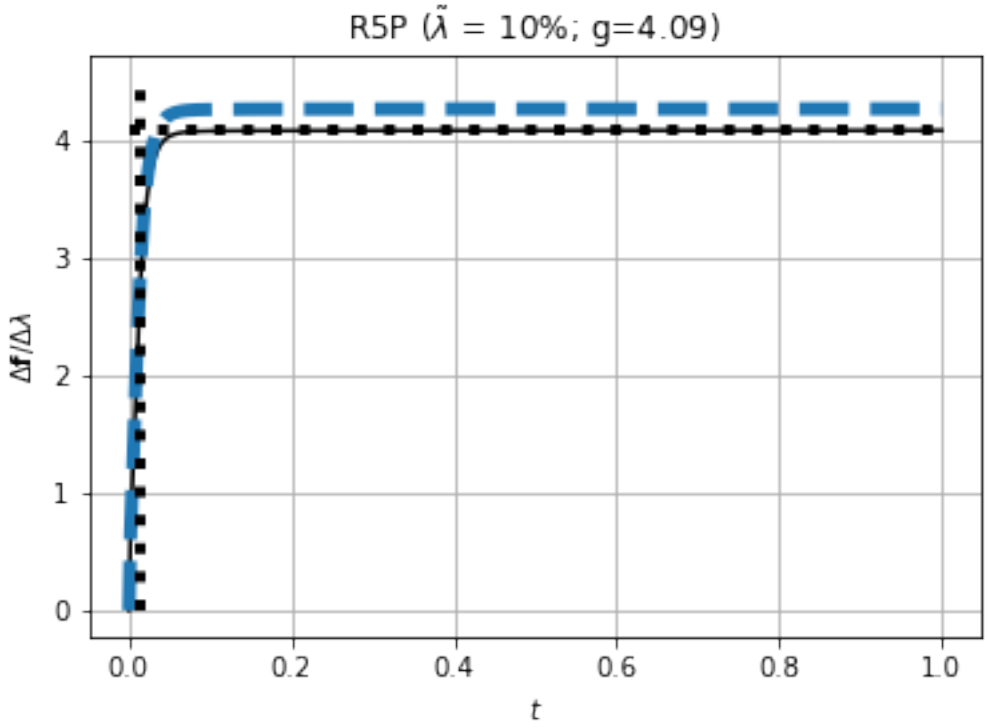

```
Doing: sNADP
g = -12.083105188911864
dlam = 10
G6P
```



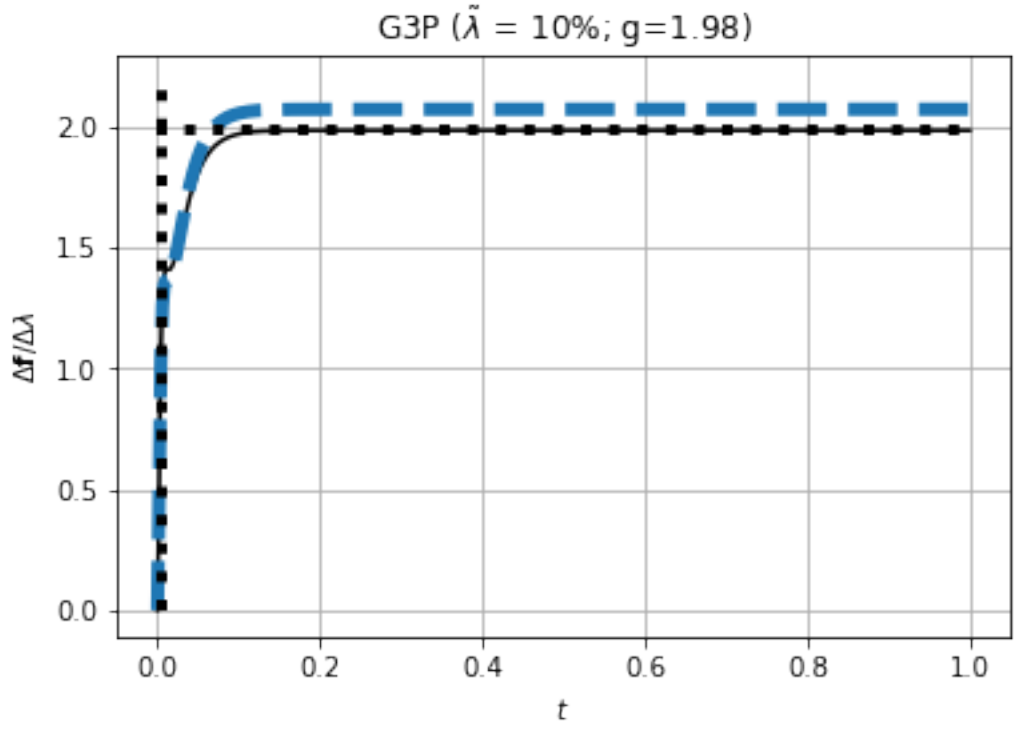
```
Doing: sNADPH
g = 0.5288892968979394
dlam = 10
G6P
```

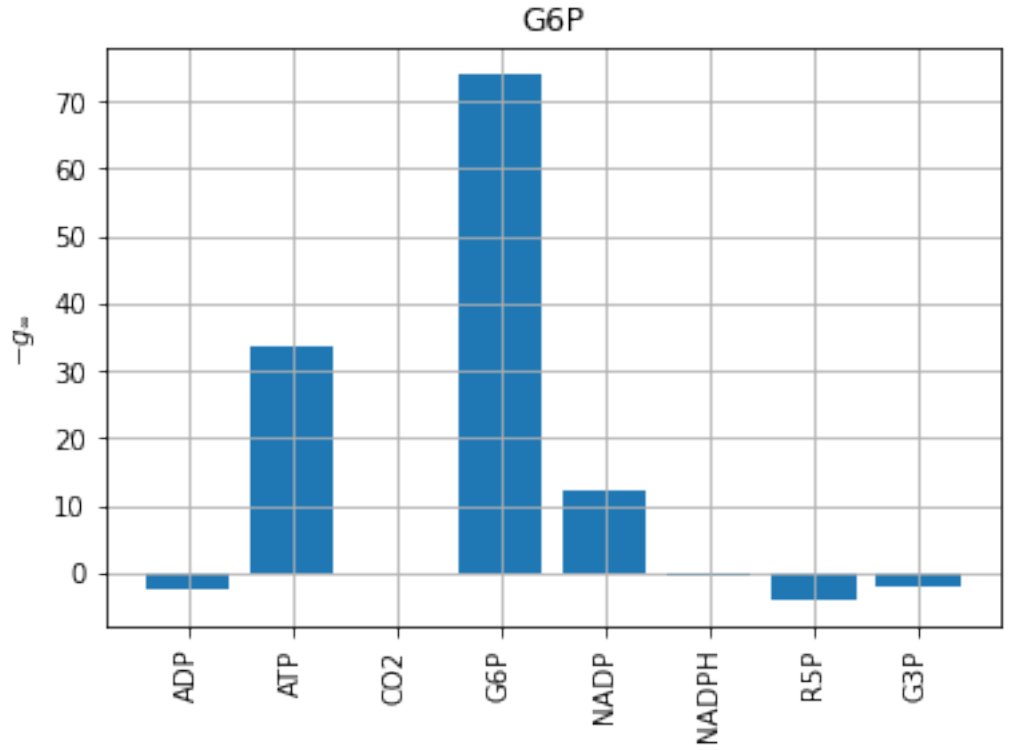


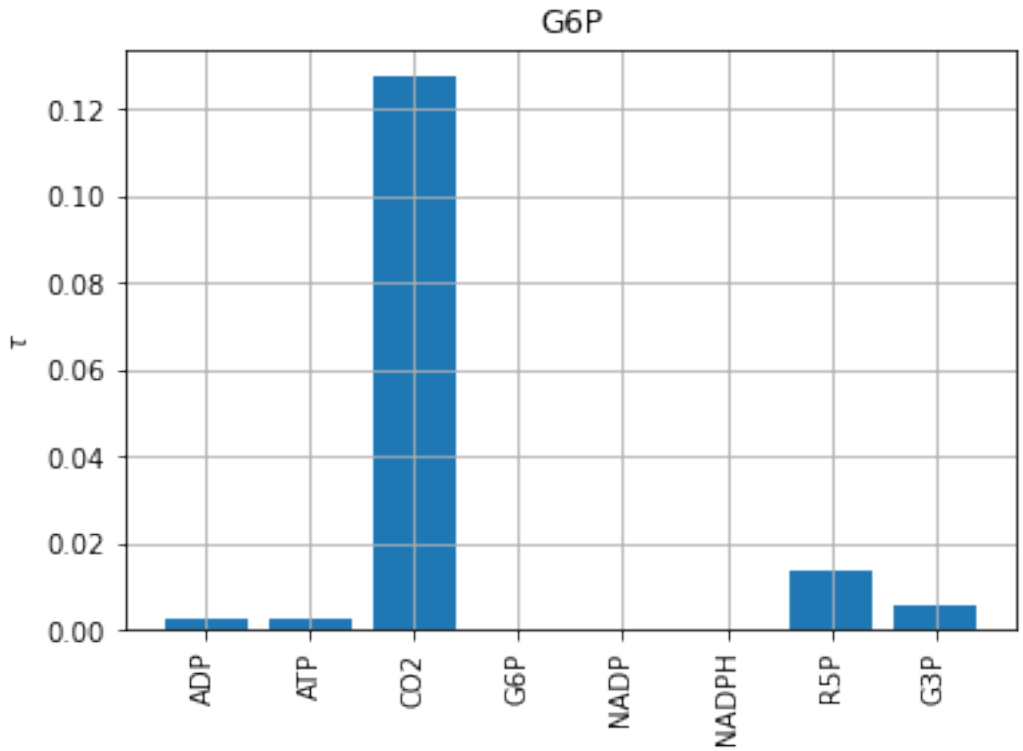

```
Doing: sR5P
g = 4.08711120268265
dlam = 10
G6P
```




```
Doing: sG3P
g = 1.984521369029551
dlam = 10
G6P
```

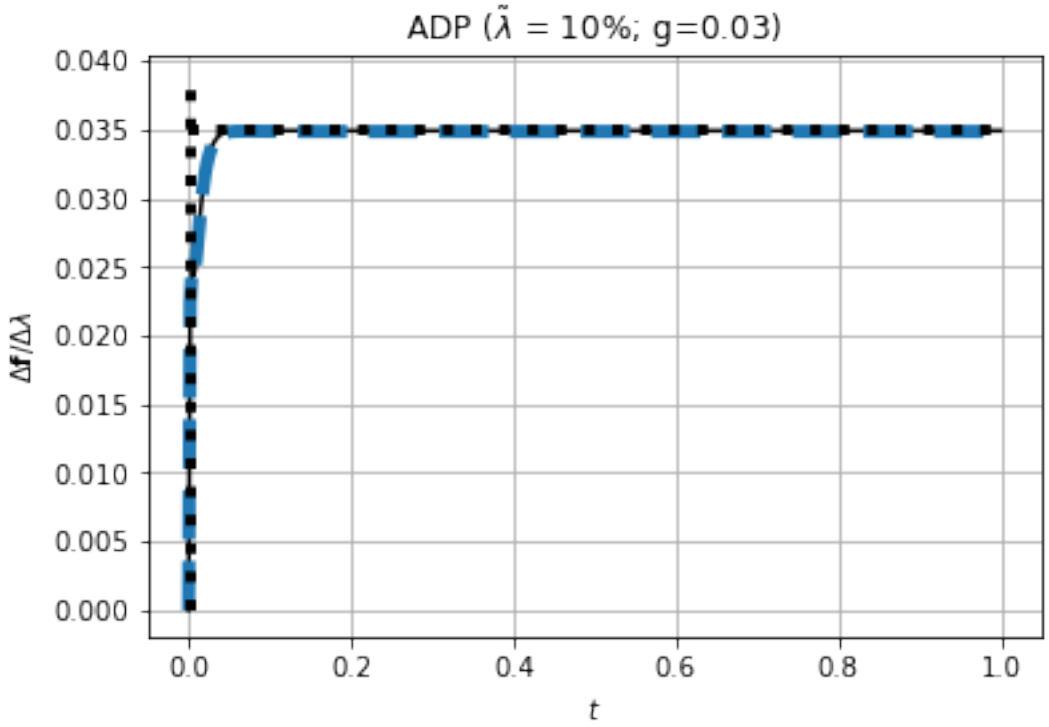



G6P
70
60
50
40
30
20
10
0
$-g_\infty$
ADP
ATP
CO2
G6P
NADP
NADPH
R5P
G3P

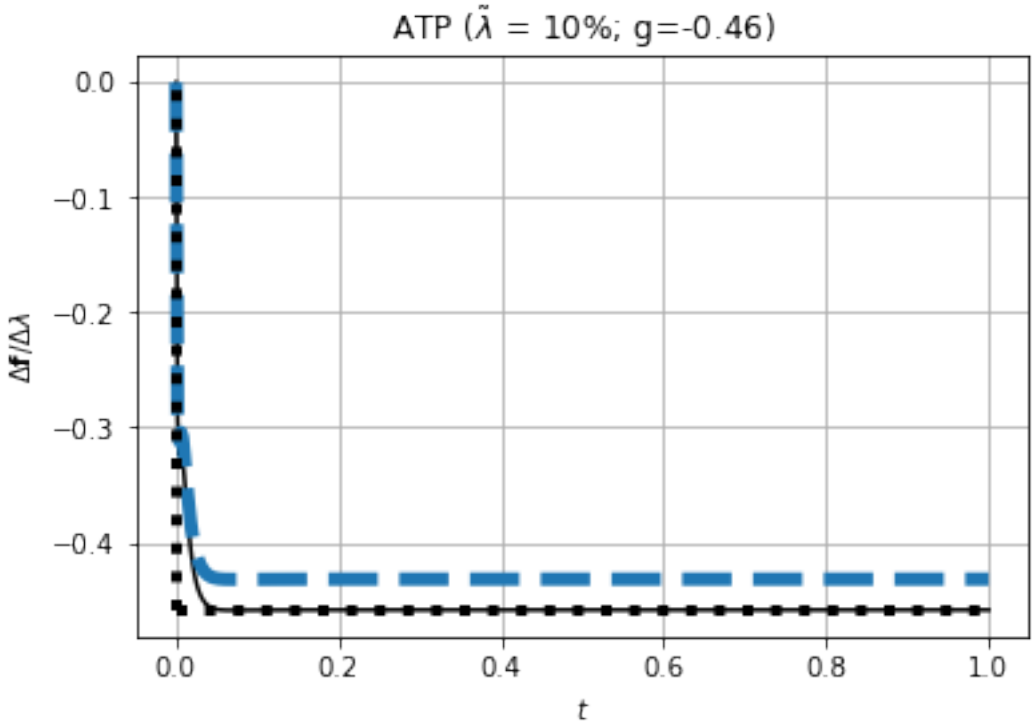

G6P
0.12
0.10
0.08
0.06
0.04
0.02
0.00
τ
ADP
ATP
CO2
G6P
NADP
NADPH
R5P
G3P

```
Doing: sADP
```

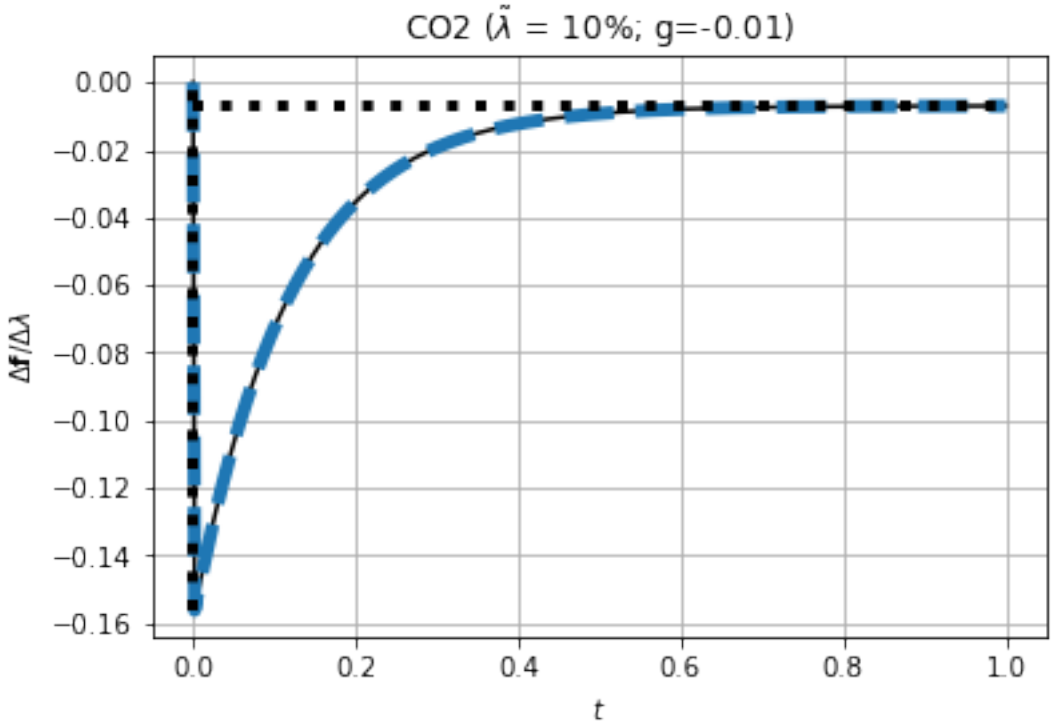
```
g = 0.0349248023890647
dlam = 10
R5P
```



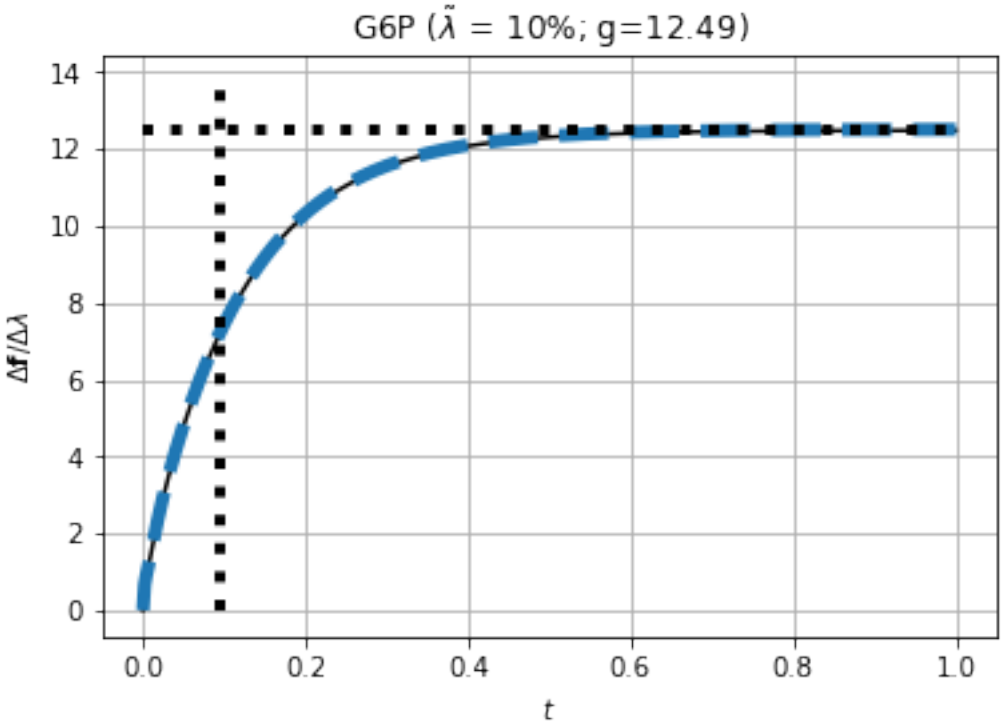

```
Doing: sATP
g = -0.4585674380195499
dlam = 10
R5P
```



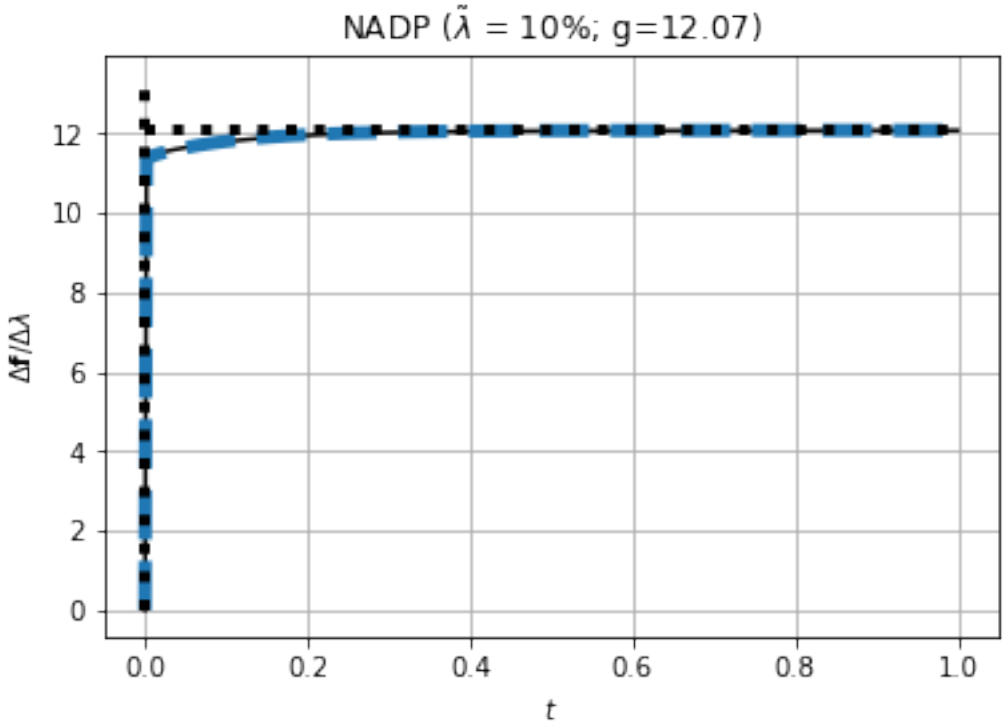

```
Doing: sCO2
g = -0.006919387119948707
dlam = 10
R5P
```



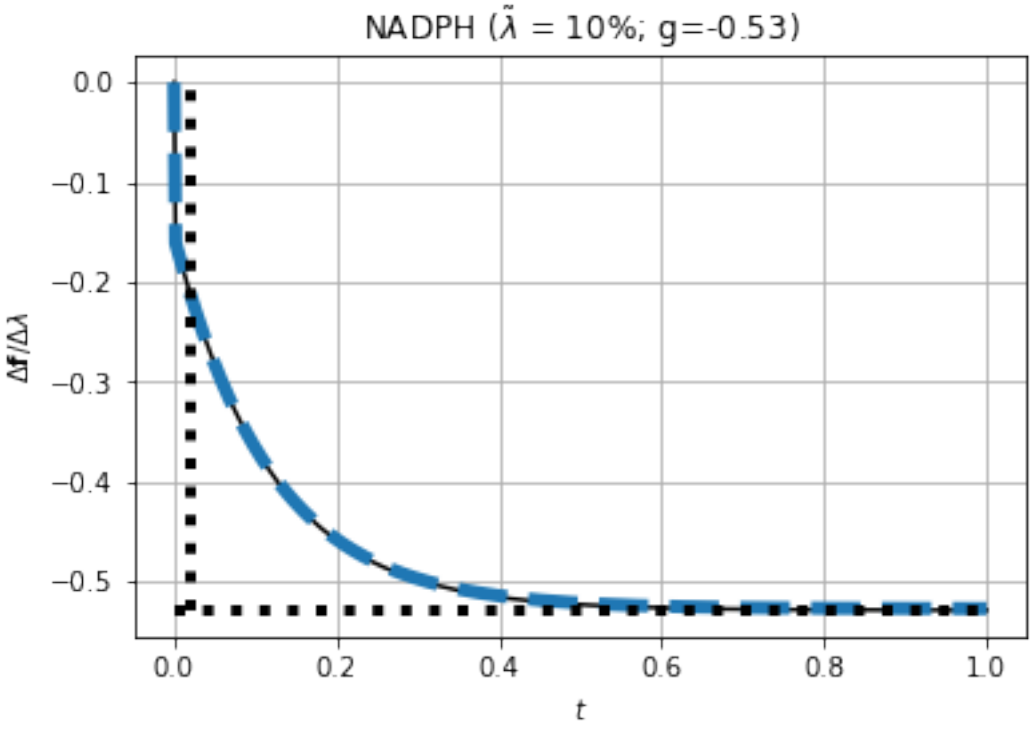
```
Doing: sG6P
g = 12.485591708850293
dlam = 10
R5P
```



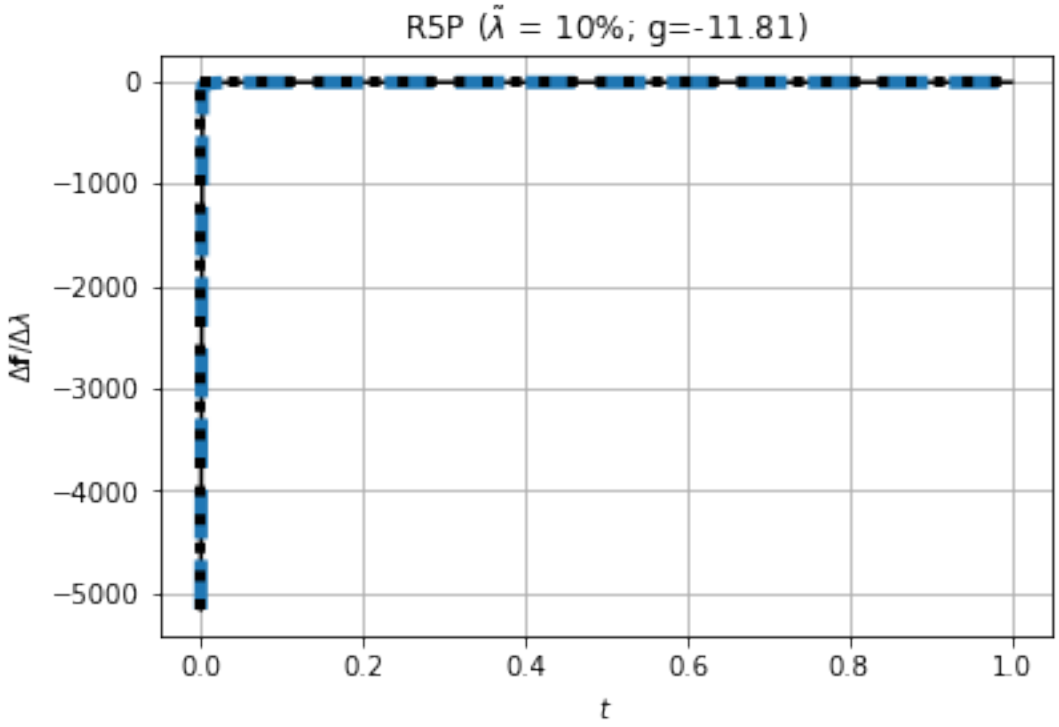

```
Doing: sNADP
g = 12.07341191065308
dlam = 10
R5P
```



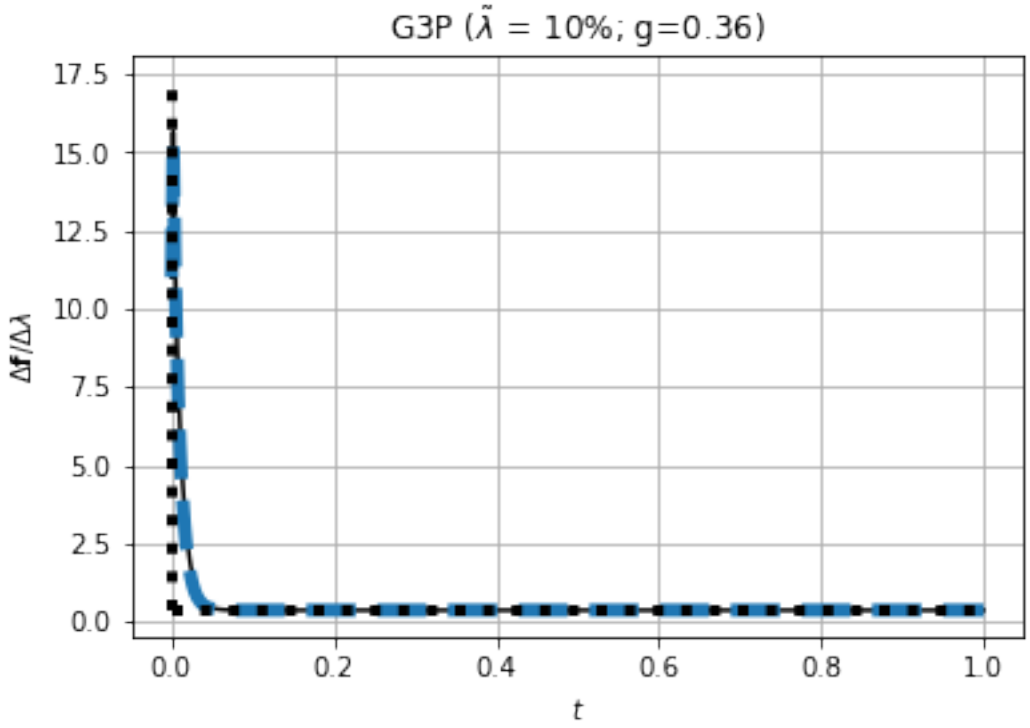

```
Doing: sNADPH
g = -0.5284650126561967
dlam = 10
R5P
```

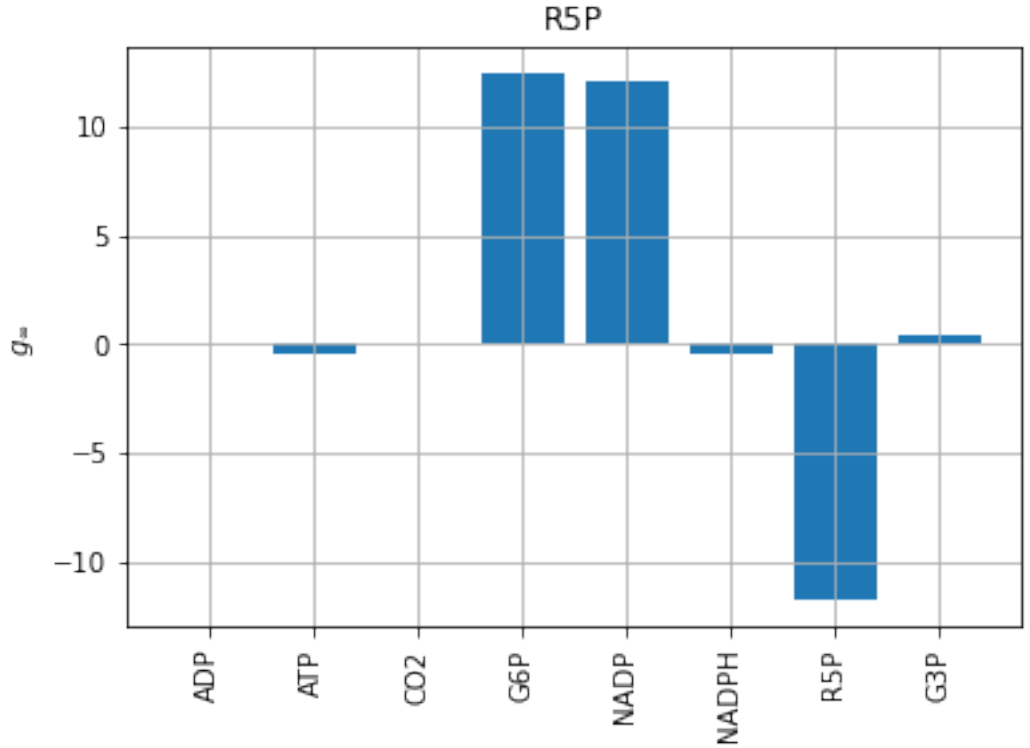


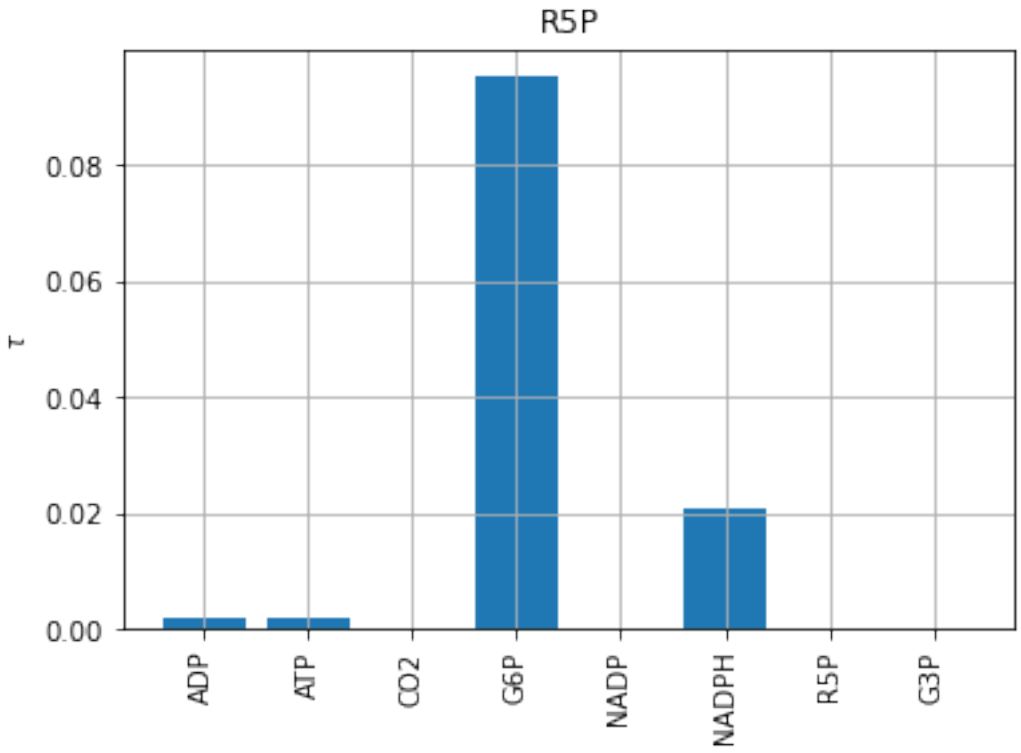
```
Doing: sR5P
g = -11.81229752462059
dlam = 10
R5P
```



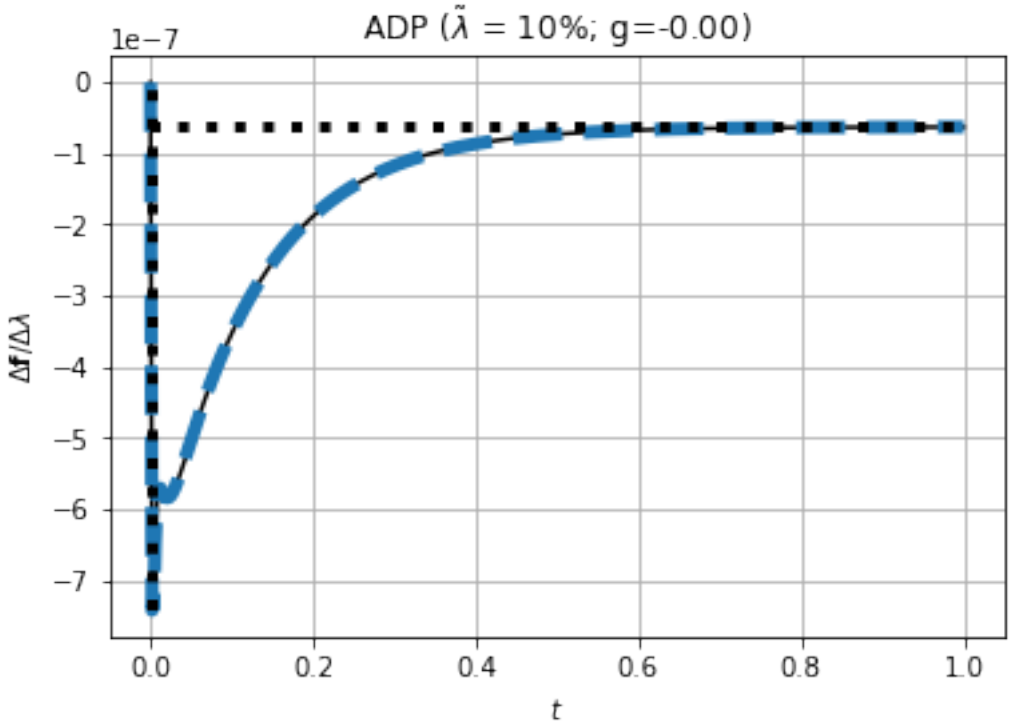

```
Doing: sG3P
g = 0.3634389561691993
dlam = 10
R5P
```


G3P ($\tilde{\lambda}$ = 10%; g=0.36)
17.5
15.0
12.5
10.0
7.5
5.0
2.5
0.0
$\Delta f/\Delta\lambda$
0.0
0.2
0.4
0.6
0.8
1.0
t

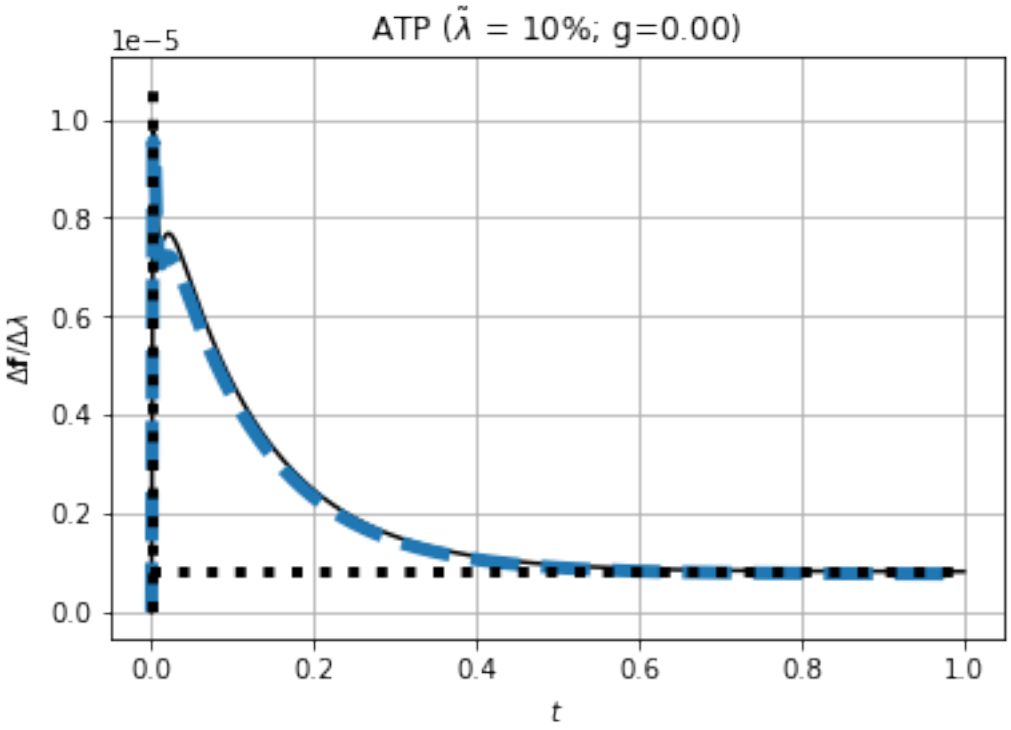

R5P
10
5
0
−5
−10
$g_=$
ADP
ATP
CO2
G6P
NADP
NADPH
R5P
G3P



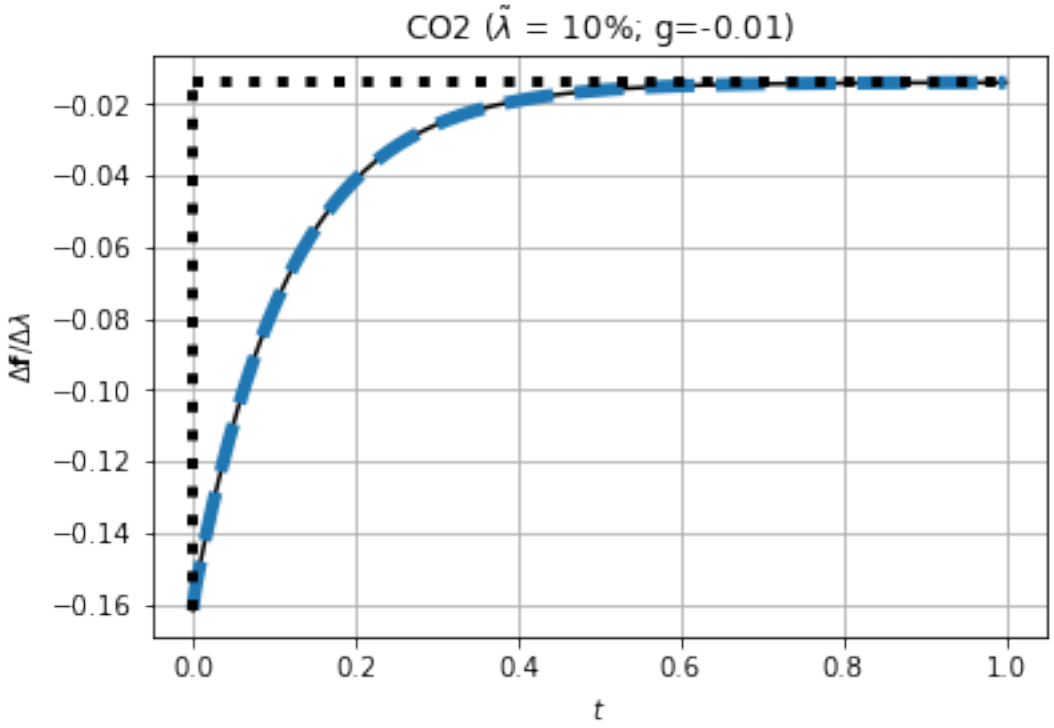

```
Doing: sADP
g = -6.262253882820029e-08
dlam = 10
NADPH
```



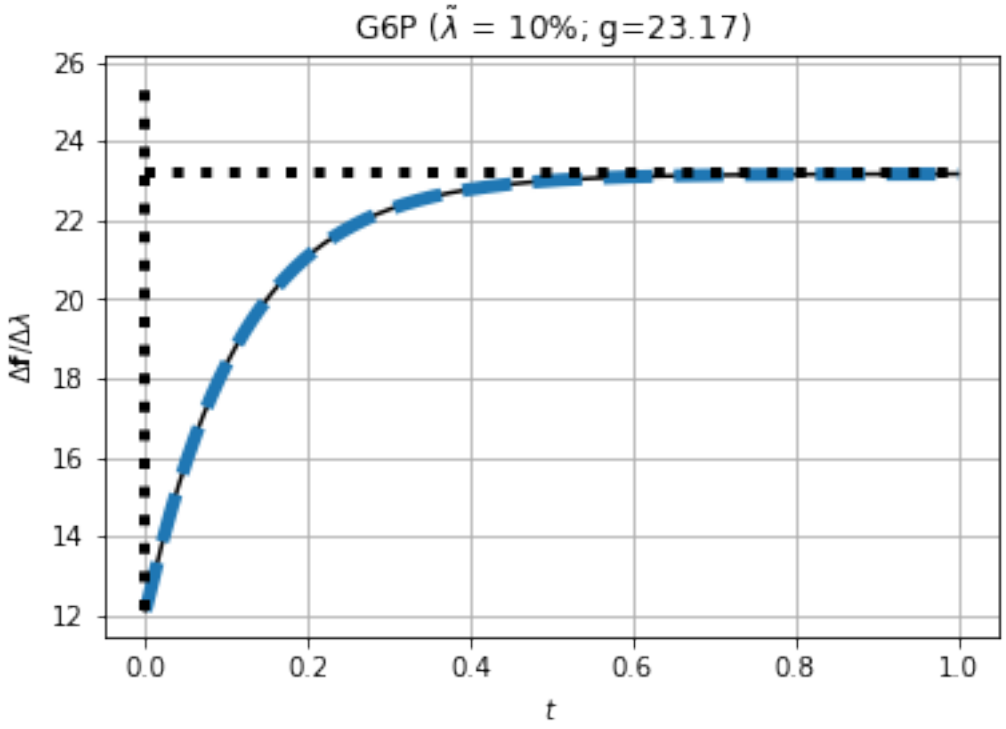
```
Doing: sATP
g = 8.22242510439288e-07
dlam = 10
NADPH
```



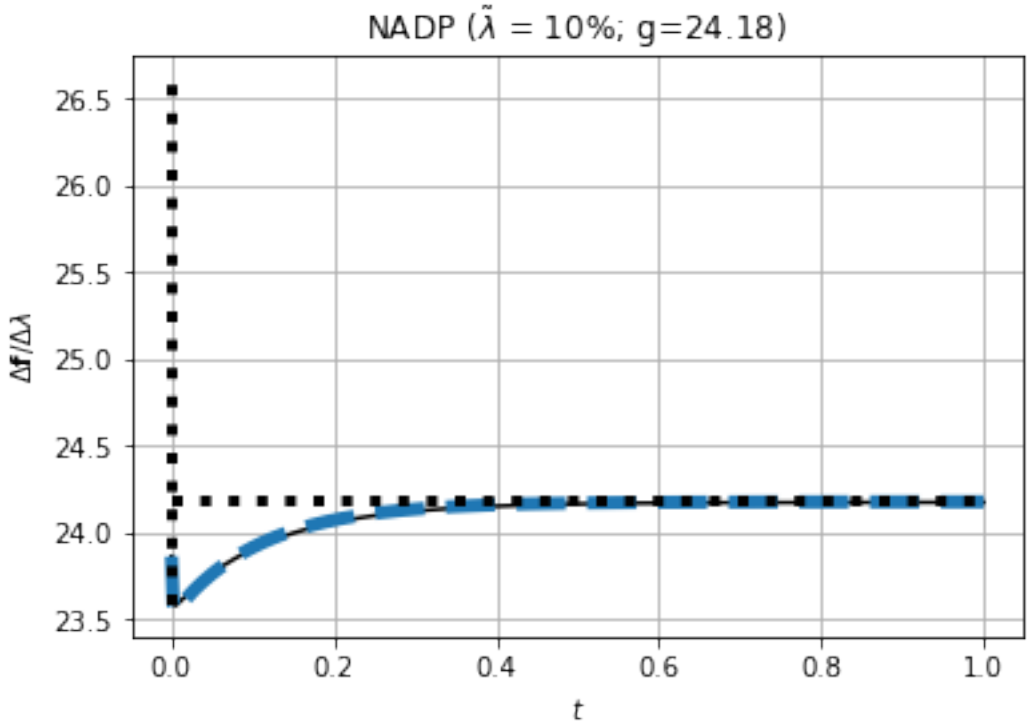

```
Doing: sCO2
g = -0.013855753145603666
dlam = 10
NADPH
```



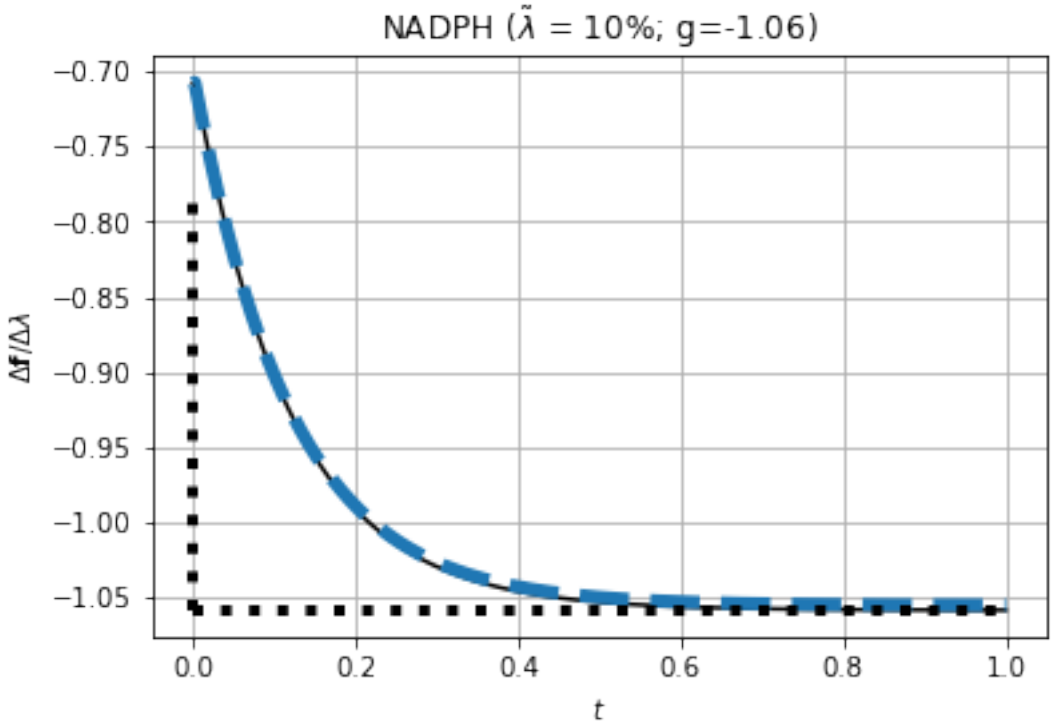

```
Doing: sG6P
g = 23.170431095483337
dlam = 10
NADPH
```



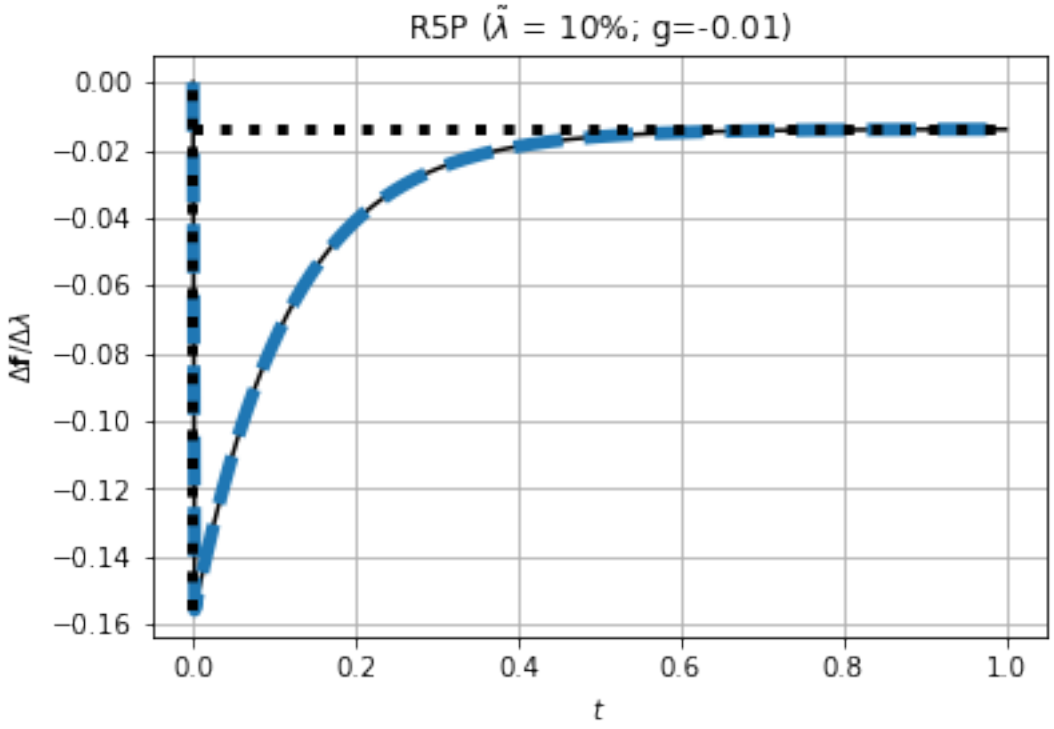
```
Doing: sNADP
g = 24.176449757783388
dlam = 10
NADPH
```



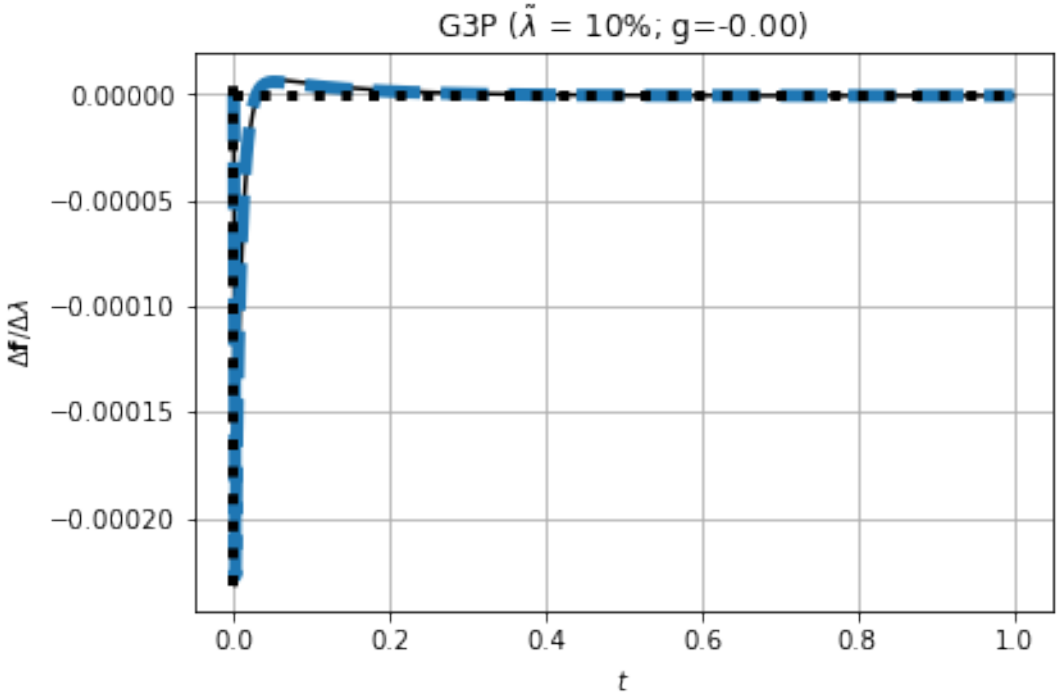

```
Doing: sNADPH
g = -1.058226781441594
dlam = 10
NADPH
```

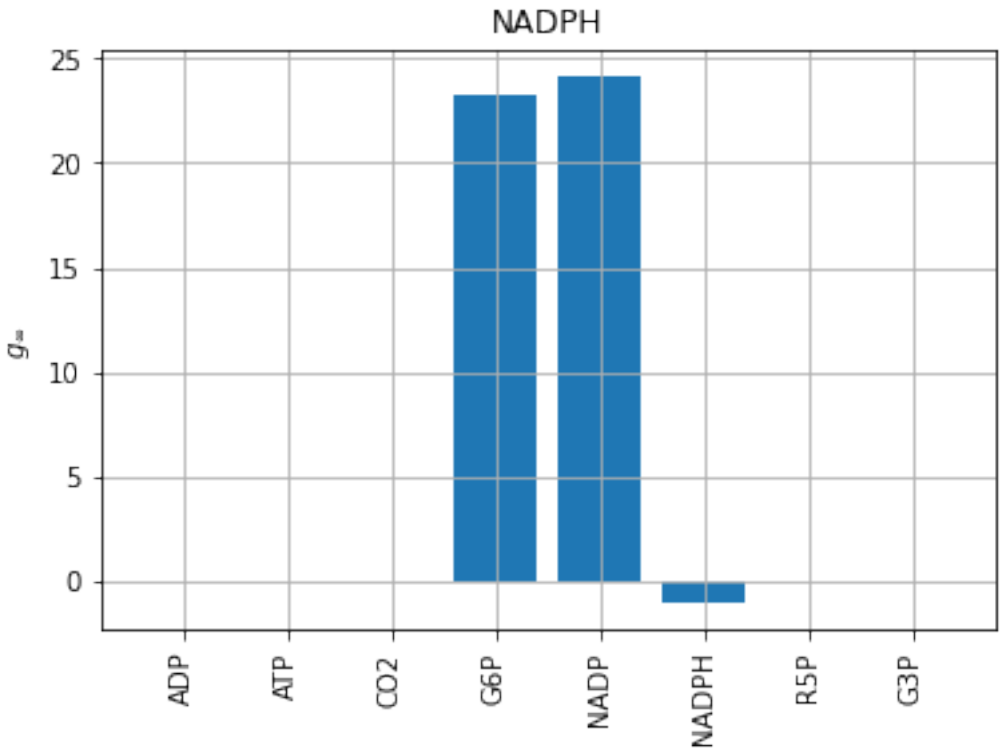


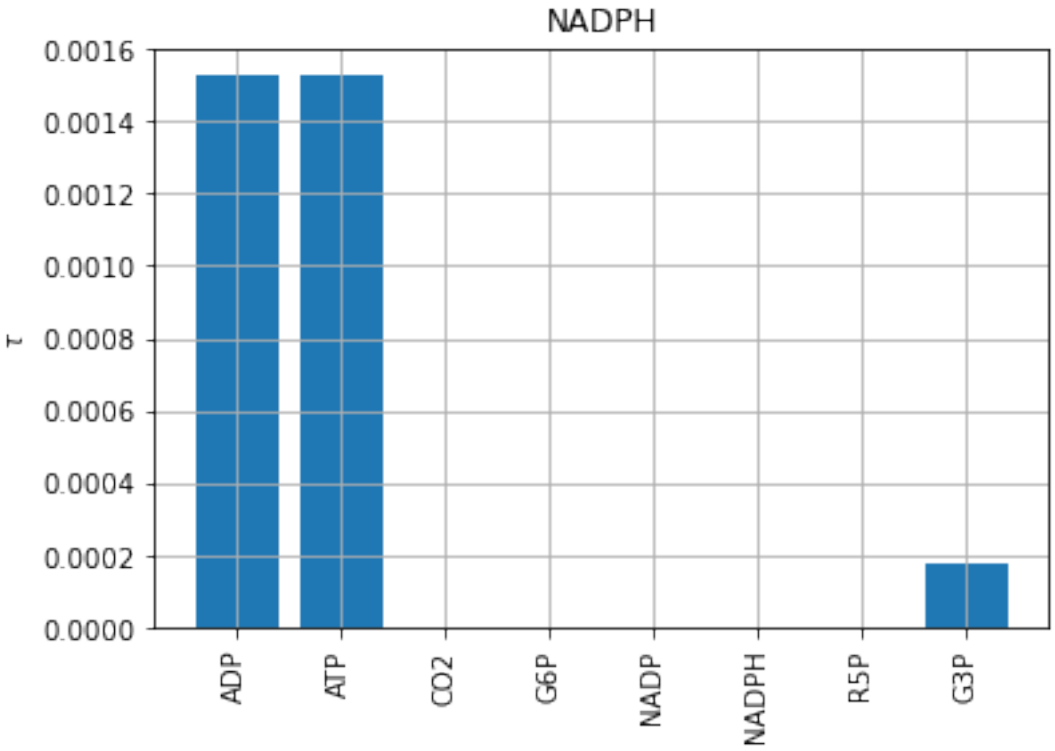

```
Doing: sR5P
g = -0.013813109583456041
dlam = 10
NADPH
```



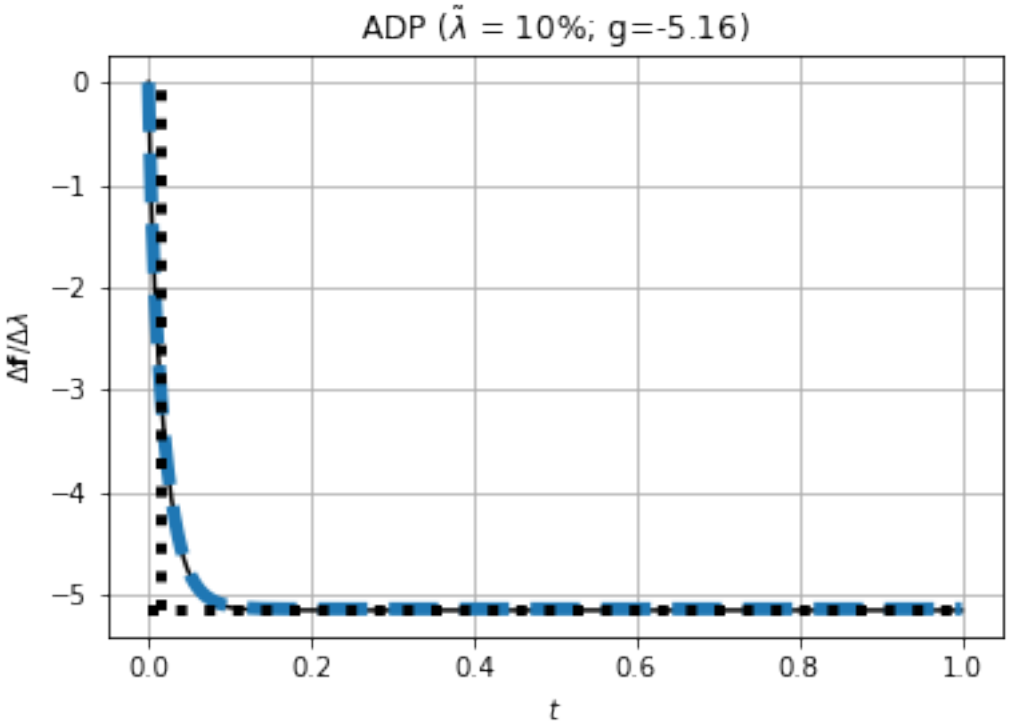
```
Doing: sG3P
g = -6.516705662261944e-07
dlam = 10
NADPH
```



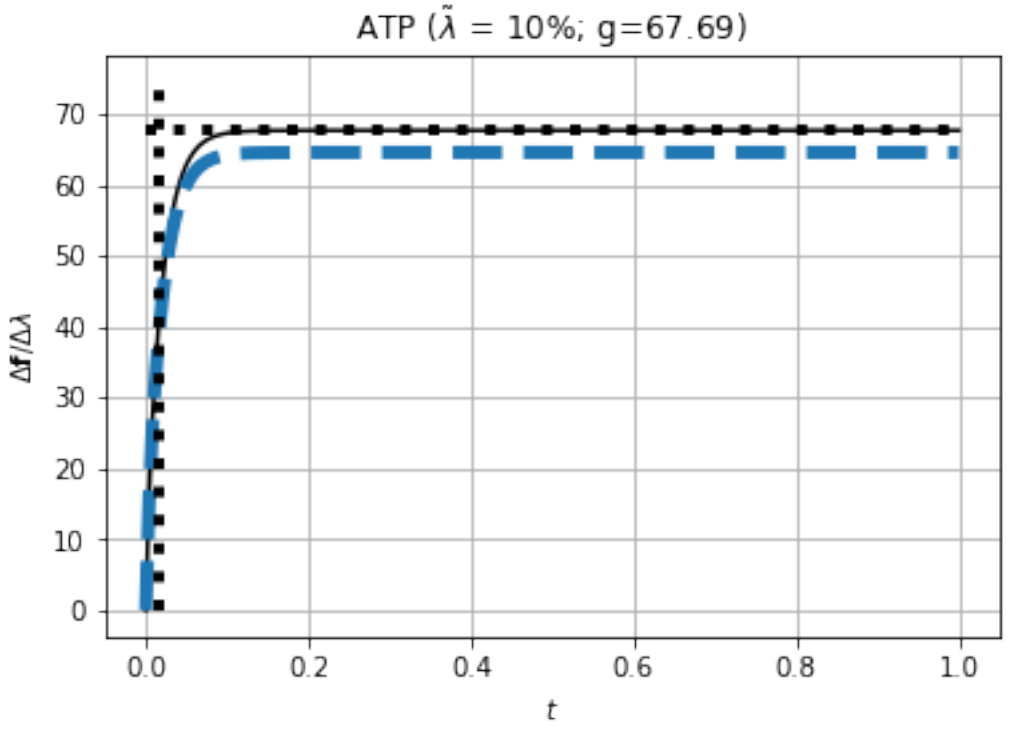




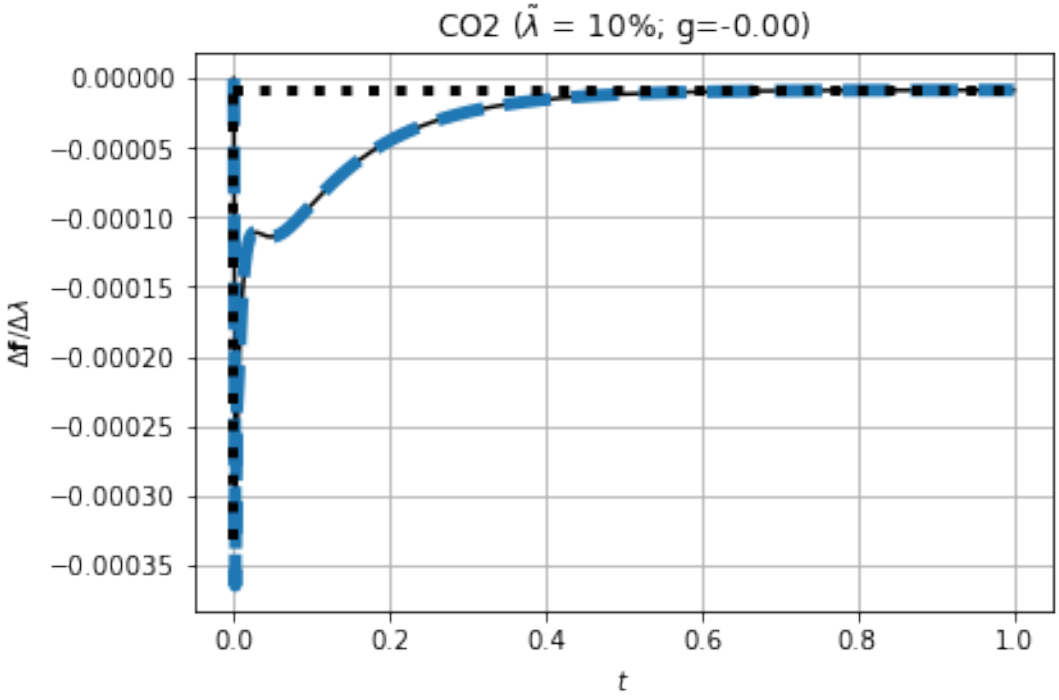

```
Doing: sADP
g = -5.155200687482189
dlam = 10
G3P
```



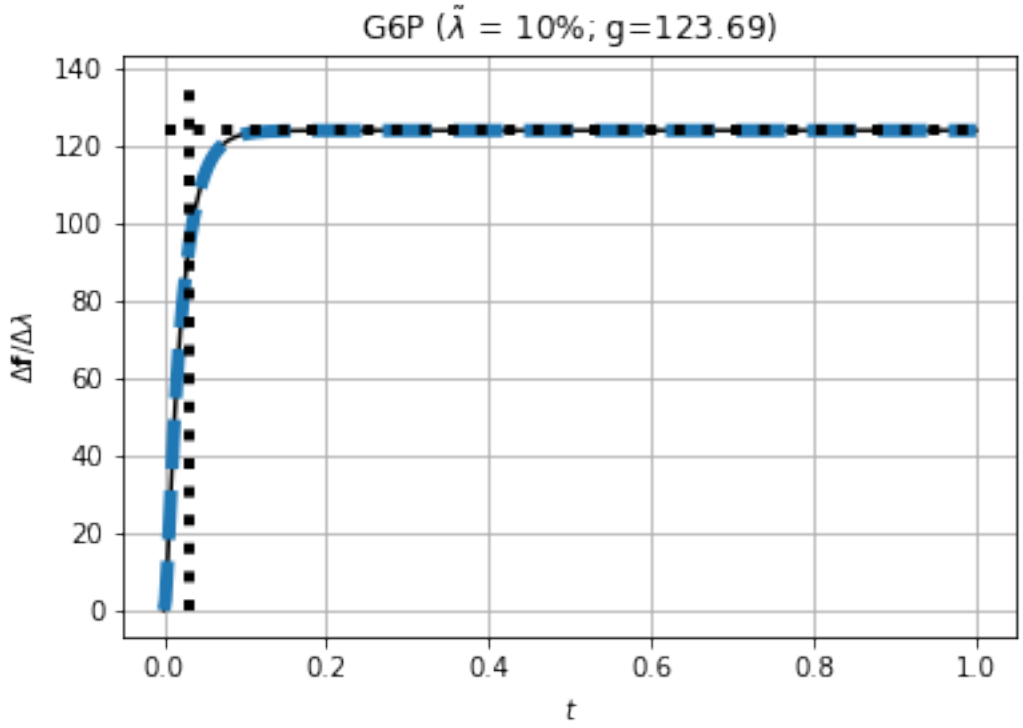

```
Doing: sATP
g = 67.68849098700832
dlam = 10
G3P
```



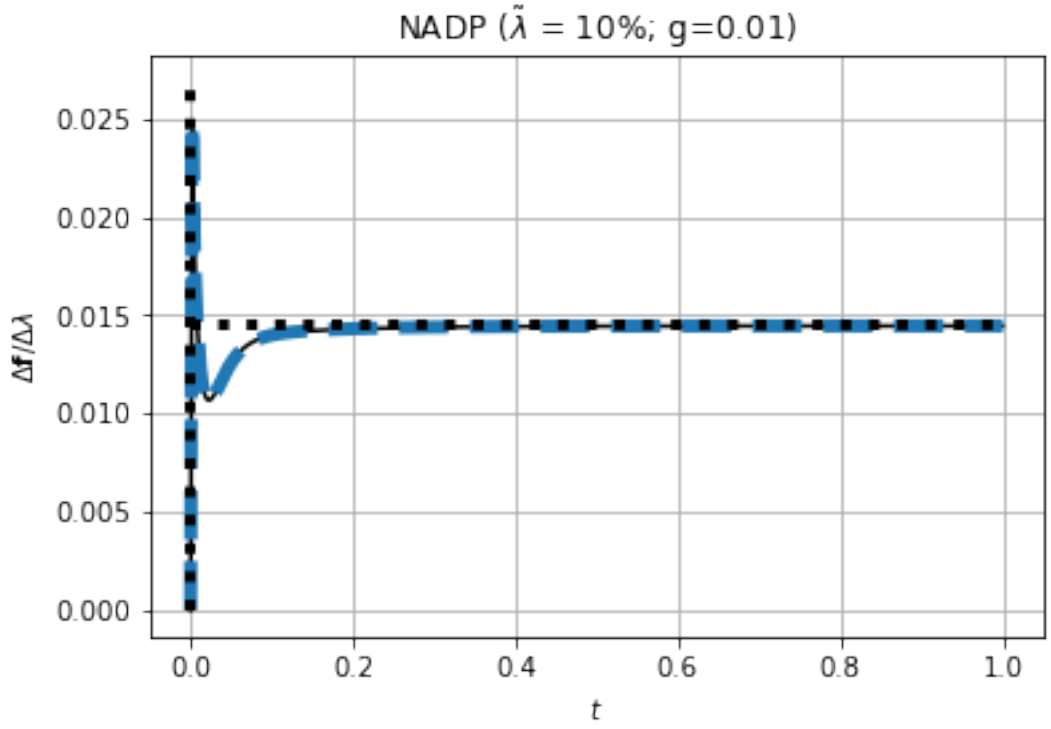
```
Doing: sCO2
g = -8.280802207064823e-06
dlam = 10
G3P
```



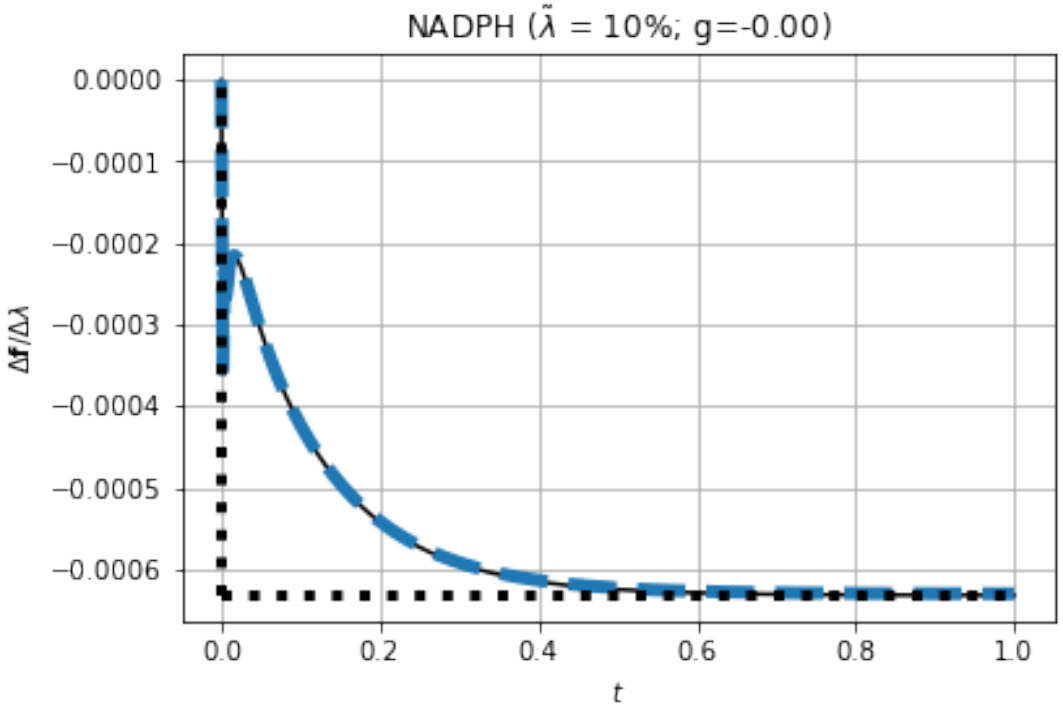

```
Doing: sG6P
g = 123.69183347627043
dlam = 10
G3P
```



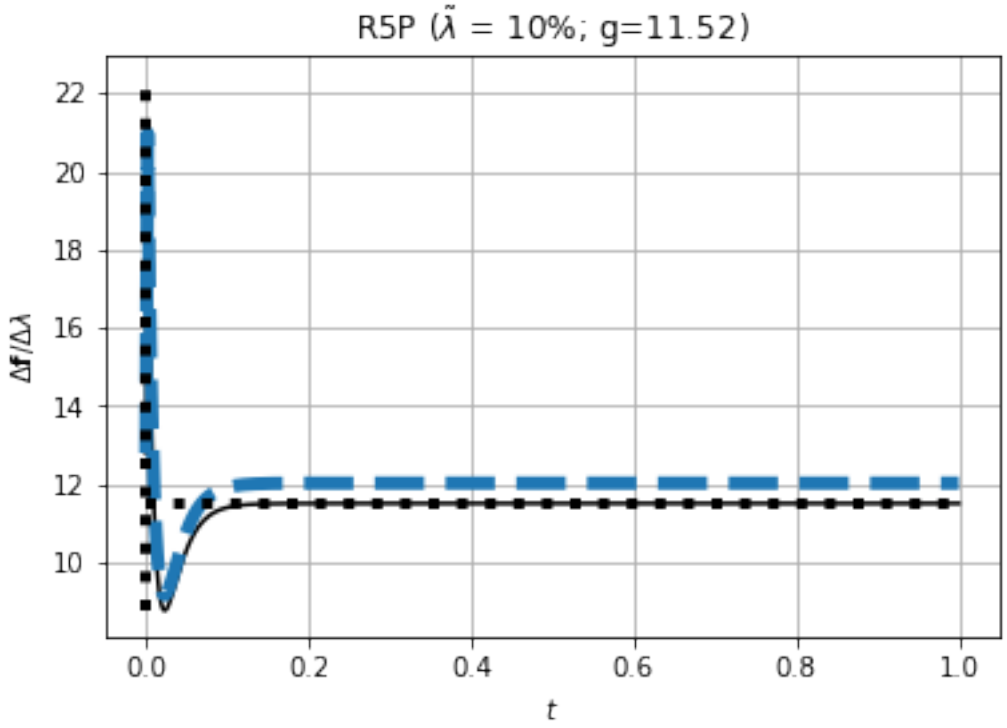

```
Doing: sNADP
g = 0.014448900437827383
dlam = 10
G3P
```



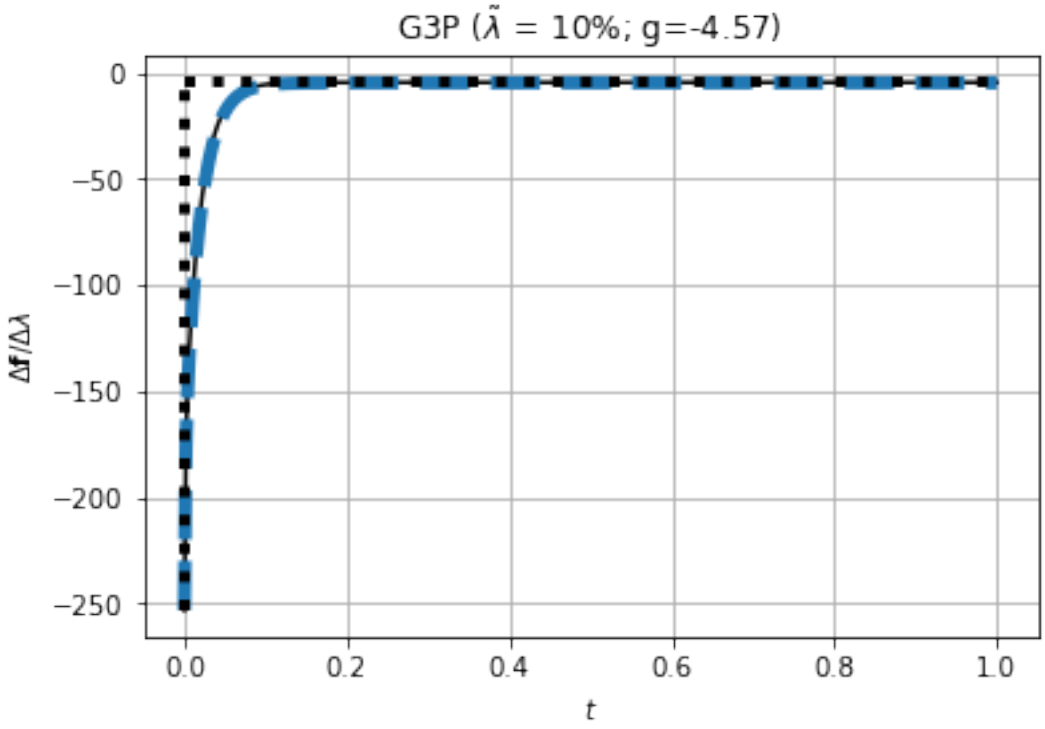
```
Doing: sNADPH
g = -0.0006324424618591407
dlam = 10
G3P
```

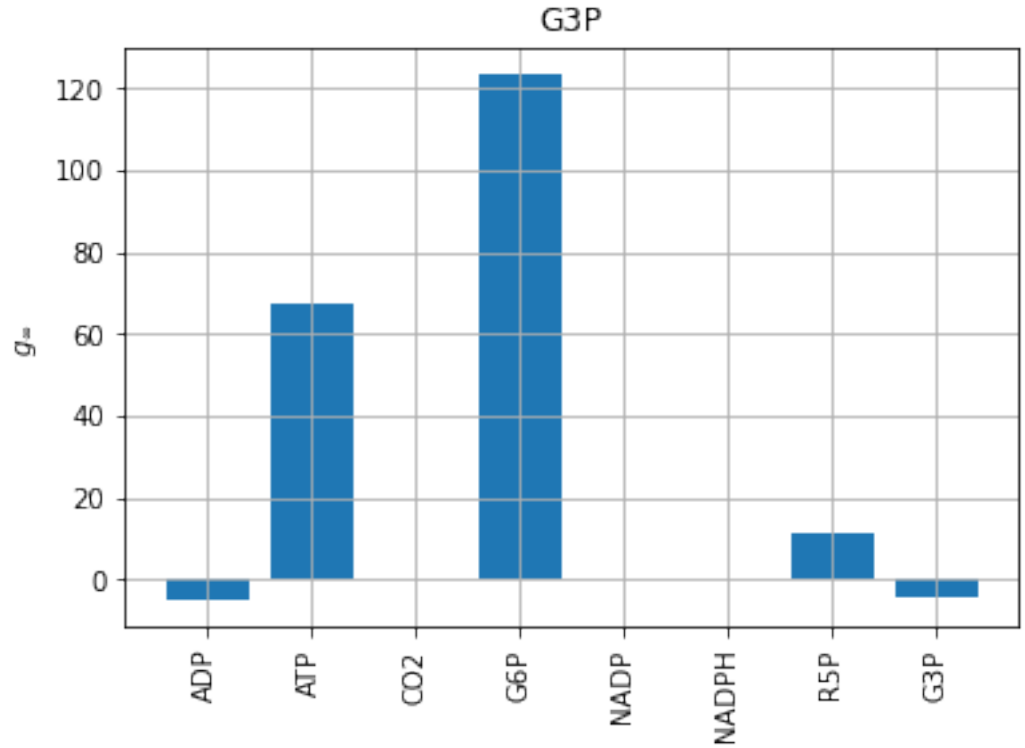


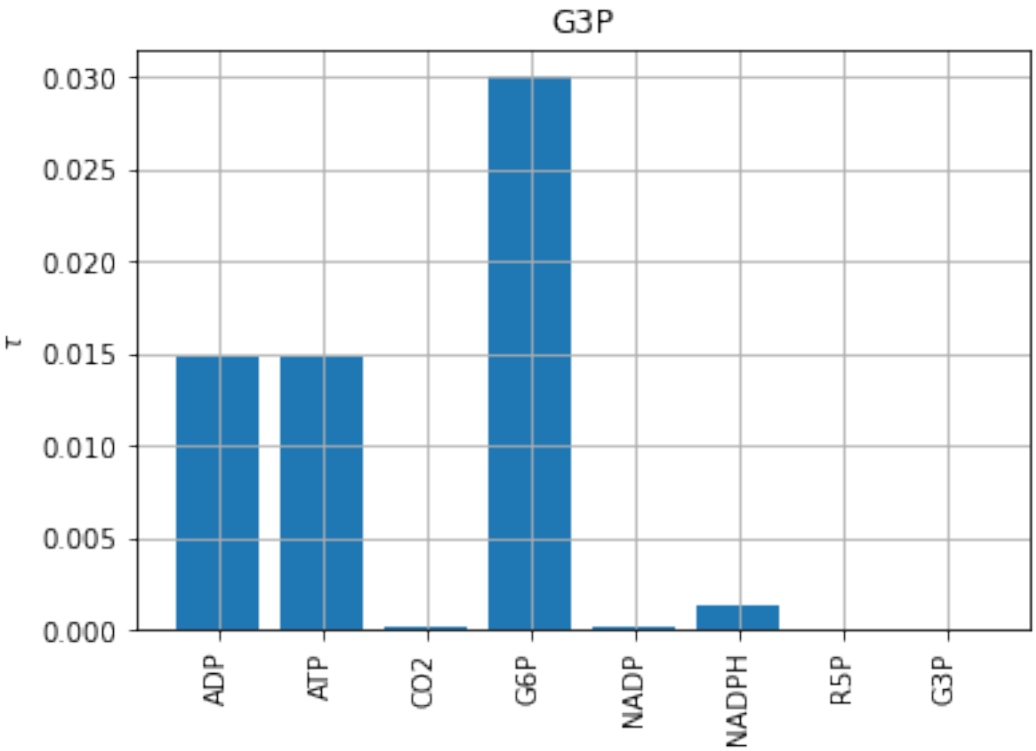

```
Doing: sR5P
g = 11.515242320596151
dlam = 10
G3P
```




```
Doing: sG3P
g = -4.574774223072097
dlam = 10
G3P
```



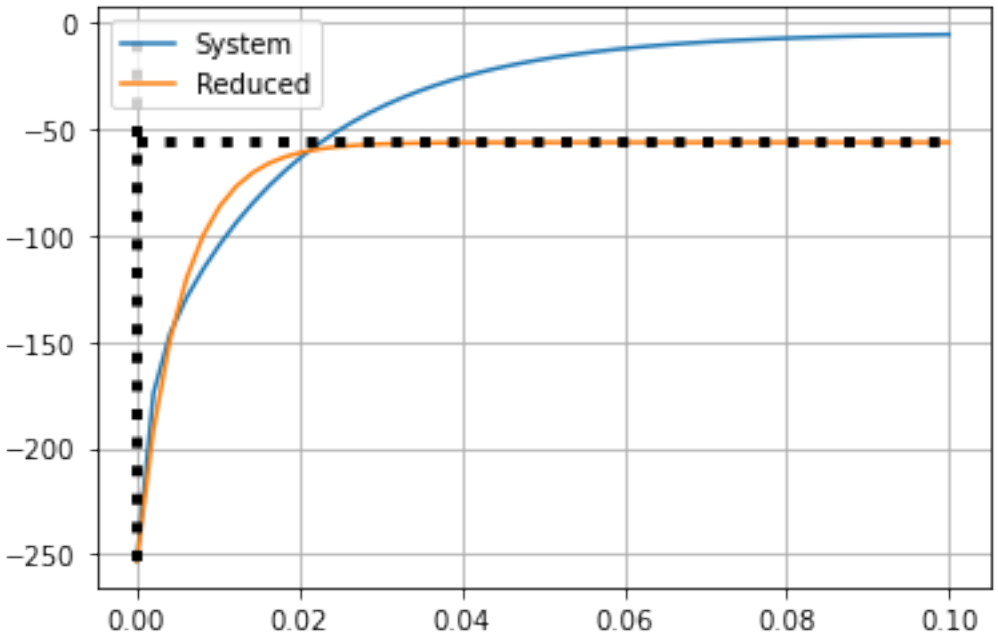

G3P
120
100
80
60
40
20
0
g_∞
ADP
ATP
CO2
G6P
NADP
NADPH
R5P
G3P


G3P
0.030
0.025
0.020
0.015
0.010
0.005
0.000
τ
ADP
ATP
CO2
G6P
NADP
NADPH
R5P
G3P

6.3 Test model reduction

[31]:
```
## Test model reduction
g,tau = tfProps(sys)
print(f'g = {g:.2f}, tau = {tau:.2f}')
sys1 = con.balred(sys,orders=1,method='truncate')
# 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(0,0.1)
step = con.step_response(sys,T=t)
step1 = con.step_response(sys1,T=t)
plt.plot(t,step.outputs.T,label='System')
plt.plot(t,step1.outputs.T,label='Reduced')
plt.legend()
plt.grid()
plotLines()
```

```
g = -4.57, tau = 0.00
g = -56.31, tau = 0.00
```



[32]:
```
print(Tau)
```

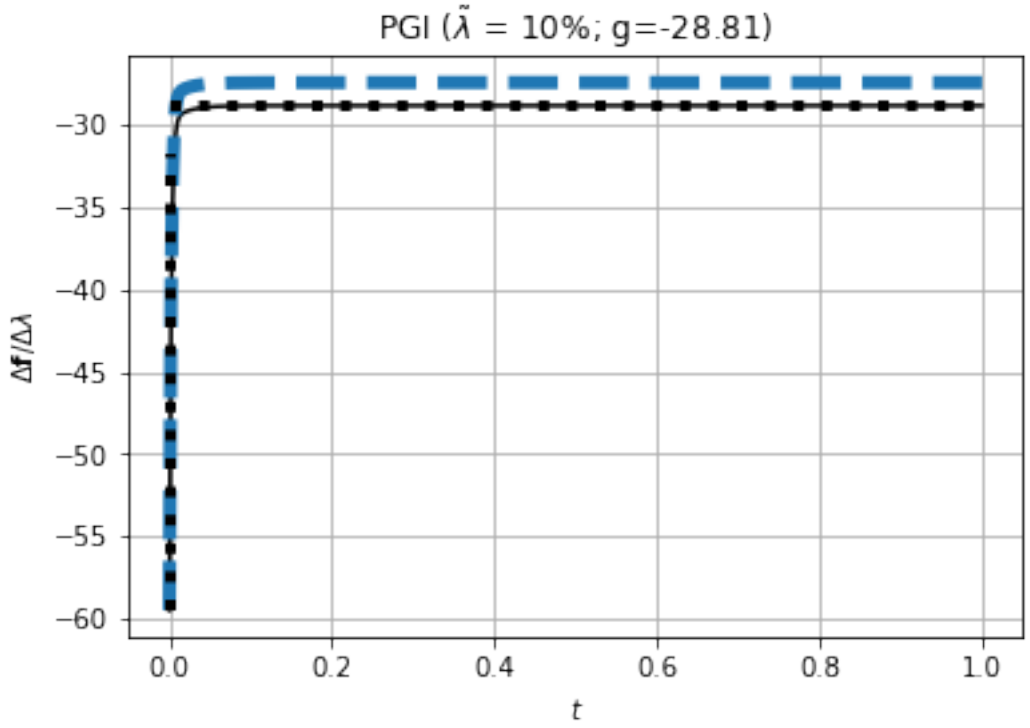
```
{'ADP': 0.014866156765752257, 'ATP': 0.01486615676575225, 'CO2':
0.00017684665624202378, 'G6P': 0.03004139008090118, 'NADP':
0.00017642871957648497, 'NADPH': 0.0013662874711383617, 'R5P': 0, 'G3P': 0}
```

6.4 Compute reaction sensitivities

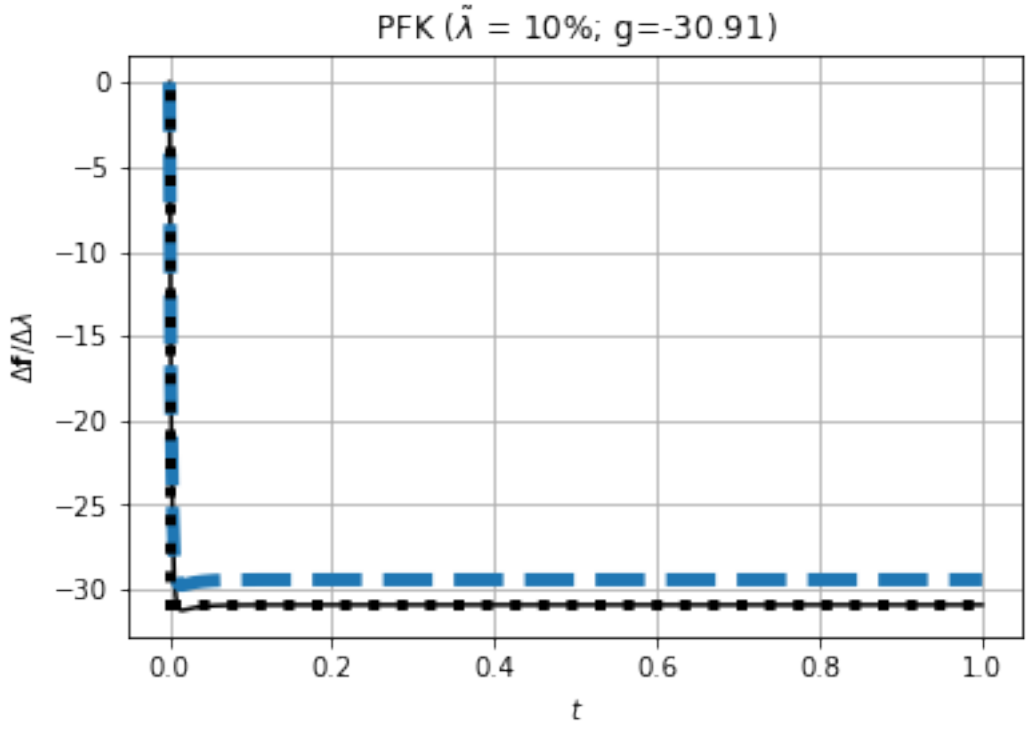
[33]:
```
## Reaction sensitivities
Outp = ['G6P','R5P','NADPH','G3P']
Inp = []
for reac in s['reaction']:
    Inp.append('s'+reac)

Inp_reac = Inp
# Inp = []
# for reac in s['reaction']:
#     Inp.append('s'+reac)
# Inp = ['sG6PDH2R']

t_last=1
lam = 1.1 # Perturbation parameter

dcgain = {}
Tau = {}
for outp in Outp:
    for inp in Inp:
        print('Doing:',inp)
        sf = None
        order = None
        dat,y_step,t,sys =␣
↪simSensitivity(s,sc,sf,Sys,X_ss,V_ss,dX_ss,chemostats=Chemostats,parameter=parameter,
                                                    ␣
↪inp=[inp],outp=[outp],lam=lam,t_last=t_last,order=order,tol=None)

#         g = con.dcgain(sys)
        g,tau = tfProps(sys)
        print('g =',g, 'tau =',tau)
        poles = con.poles(sys)
#         print('Poles:', poles)
#         print('Zeros:', con.zeros(sys))
#         print(con.ss2tf(sys))
        name = inp[1:]
        if name == 'G6PDH2R':
            name = 'G6PD.'
        if outp=='G6P':
            dcgain[name] = -g
            ylabel = '$-g_{\infty}$'
        else:
            dcgain[name] = g
            ylabel = '$g_{\infty}$'

        Tau[name] = tau

        dlam = int((lam-1)*100)
        print('dlam =',dlam)
        plt.title(f'Order = {poles.size}')
```

```
        if Titles:
            plt.title(f'{name}'+r' ($\tilde\lambda$ = ' + f'{dlam}%; g={g:.
↪2f})')
        plotSensitivitydX(dat,species=[outp],labeling=False)
#         plt.hlines(g,min(t),max(t),color='black',ls='dashed')
        plotLines()
        Savefig('PPPdX_'+name+'_'+outp)

        plt.show()
        #print(con.tf(sys))


    ## Bar chart of gains
    if Titles:
        plt.title(outp)
    plt.tick_params(axis='x', rotation=90)
    plt.grid()
    plt.bar(range(len(dcgain)), dcgain.values(), align='center')
    plt.xticks(range(len(dcgain)), list(dcgain.keys()))
    plt.ylabel(ylabel)
    Savefig(f'PPPdX_{outp}_reac_bar')
    plt.show()

    ## Time constant
    if Titles:
        plt.title(outp)
    plt.tick_params(axis='x', rotation=90)
    plt.grid()
    plt.bar(range(len(Tau)), Tau.values(), align='center')
    plt.xticks(range(len(Tau)), list(Tau.keys()))
    plt.ylabel(r'$\tau$')
    Savefig(f'PPPdX_{outp}_reac_tau_bar')
    plt.show()
```

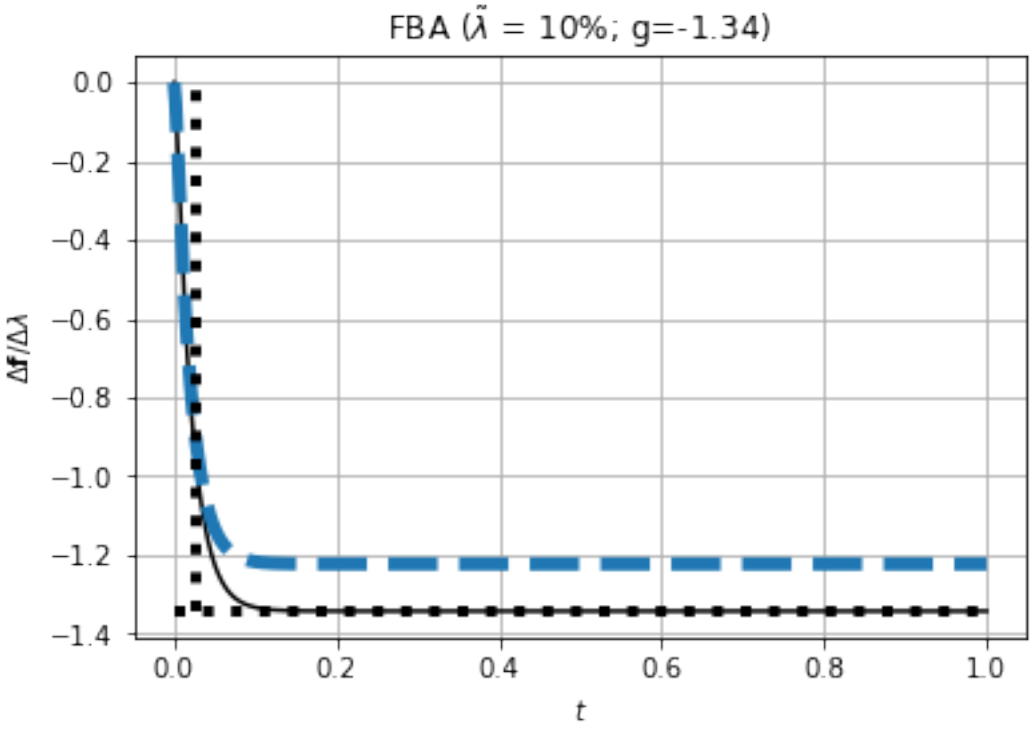
```
Doing: sPGI
kappa_PGI
g = -28.80991511396469 tau = 0
dlam = 10
G6P
```



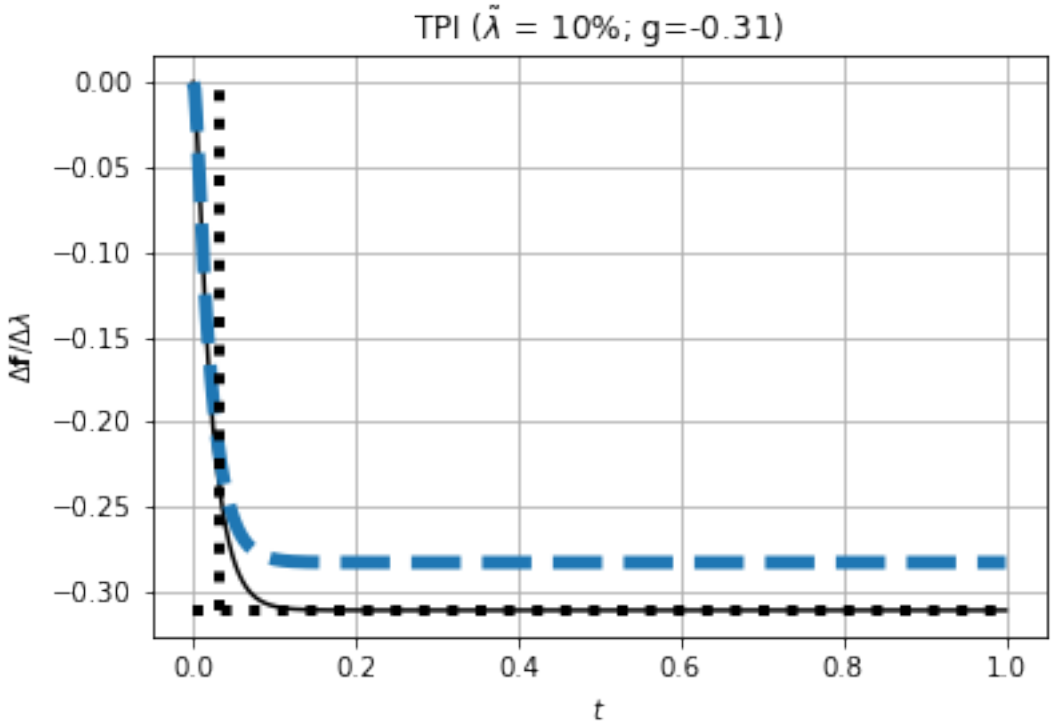

```
Doing: sPFK
kappa_PFK
g = -30.913609683373416 tau = 0.002278015825776077
dlam = 10
G6P
```



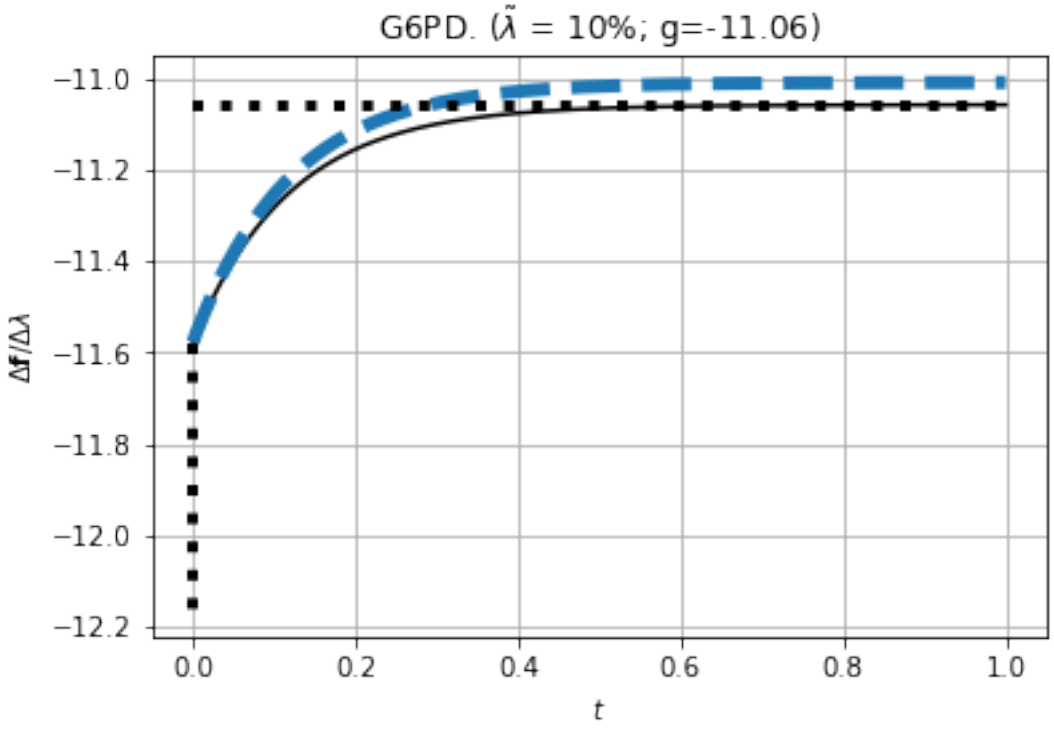
```
Doing: sFBA
kappa_FBA
g = -1.3427806651016105 tau = 0.026921154867136633
dlam = 10
G6P
```



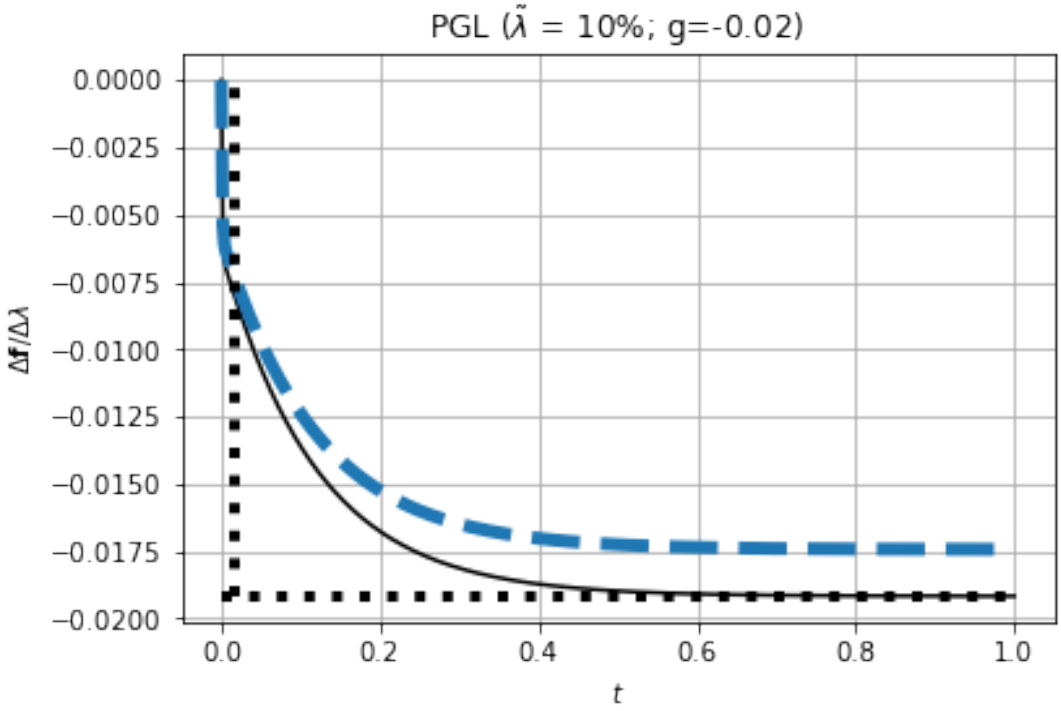

```
Doing: sTPI
kappa_TPI
g = -0.31124503089893363 tau = 0.03292616976551729
dlam = 10
G6P
```



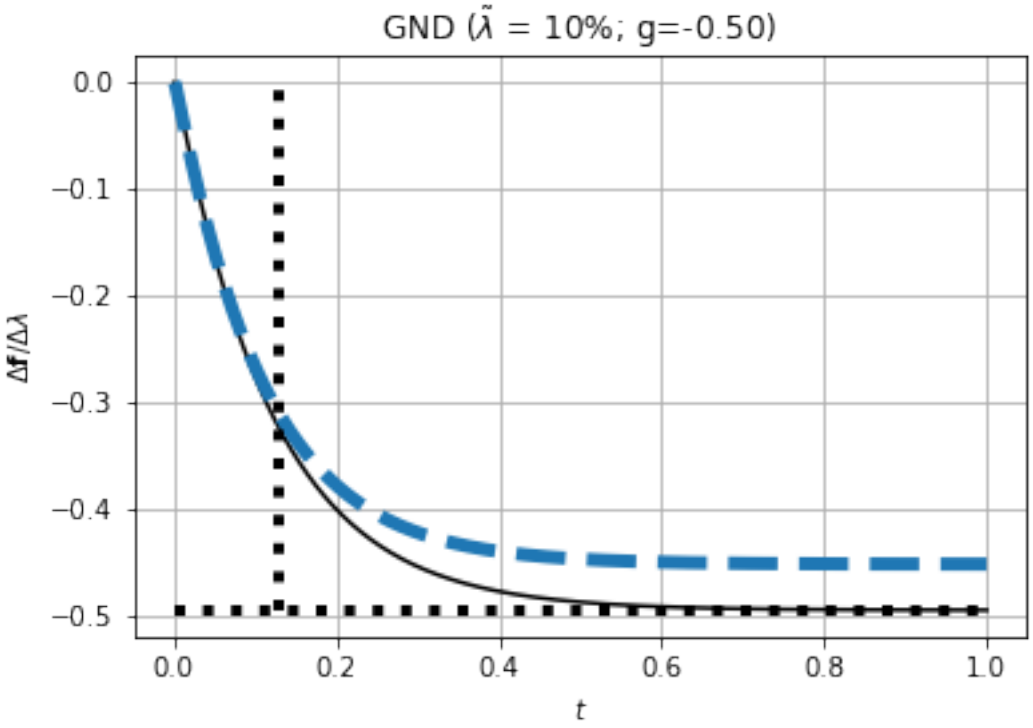

```
Doing: sG6PDH2R
kappa_G6PDH2R
g = -11.05834536093916 tau = 0
dlam = 10
G6P
```



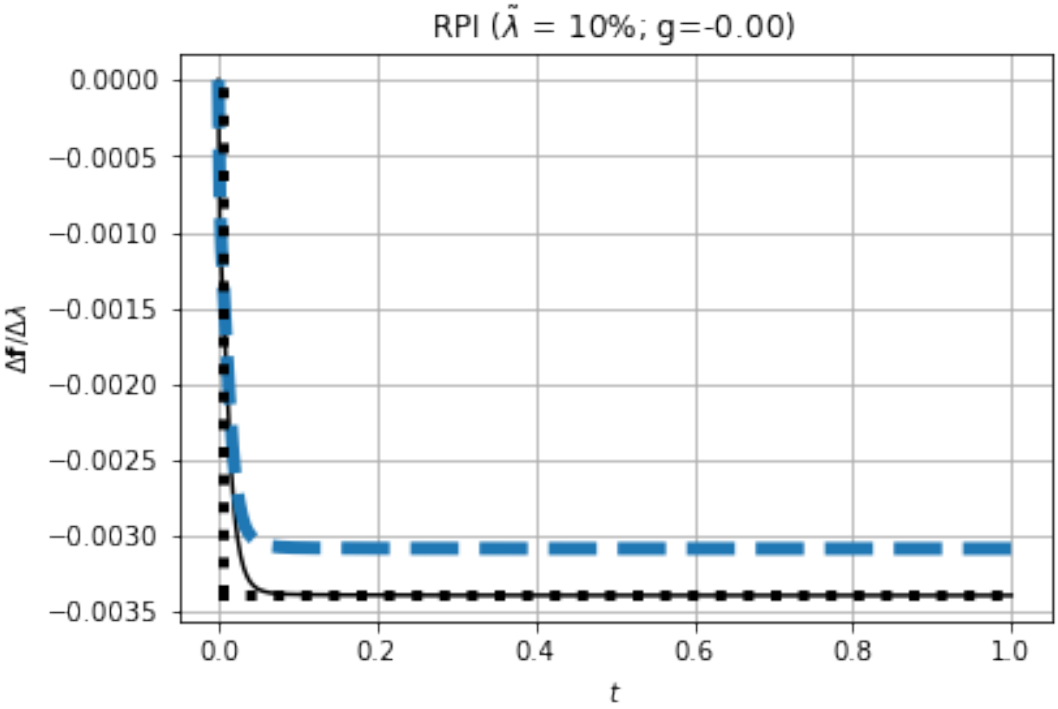
```
Doing: sPGL
kappa_PGL
g = -0.019168880963538627 tau = 0.016293783108219457
dlam = 10
G6P
```



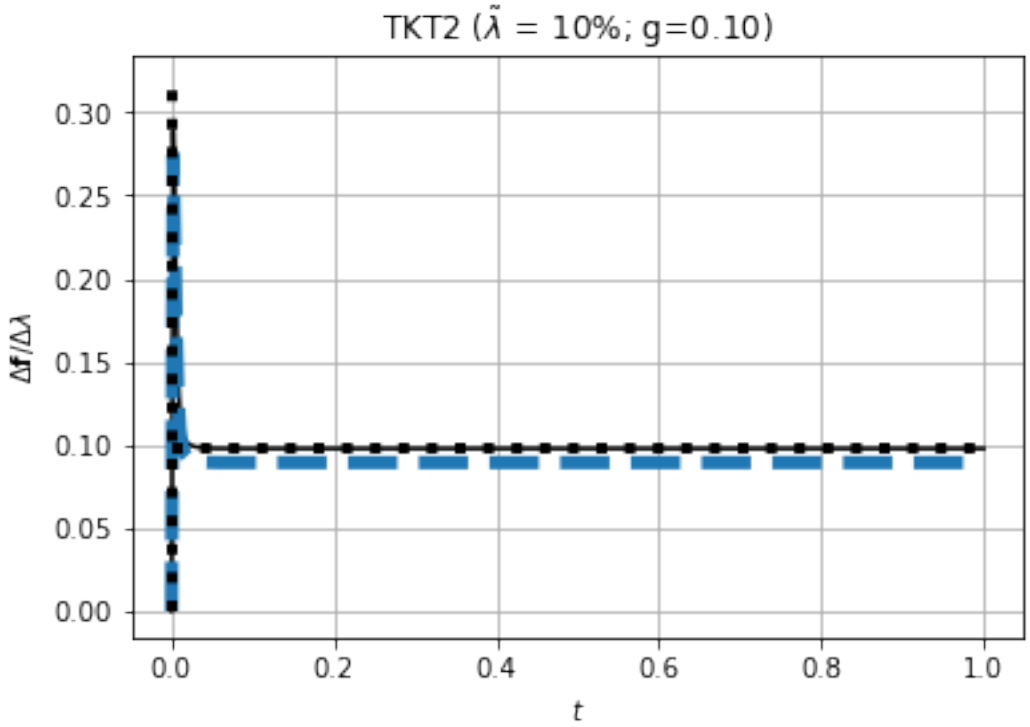

```
Doing: sGND
kappa_GND
g = -0.4958705310747634 tau = 0.12751609732062125
dlam = 10
G6P
```



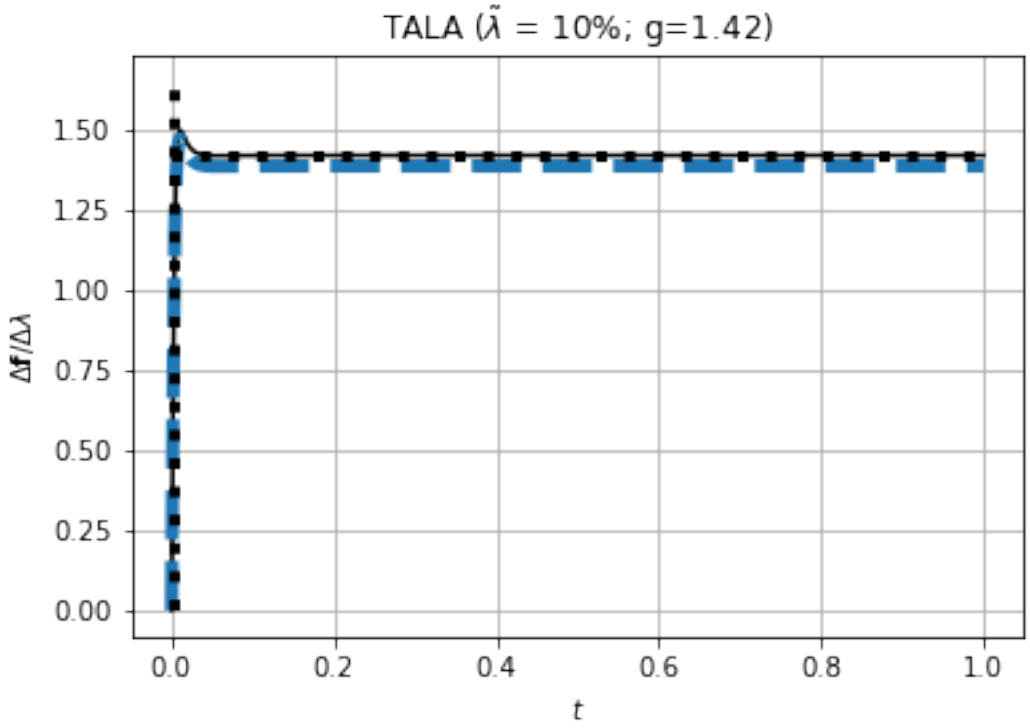

```
Doing: sRPI
kappa_RPI
g = -0.00339246977181743 tau = 0.00824443541241612
dlam = 10
G6P
```



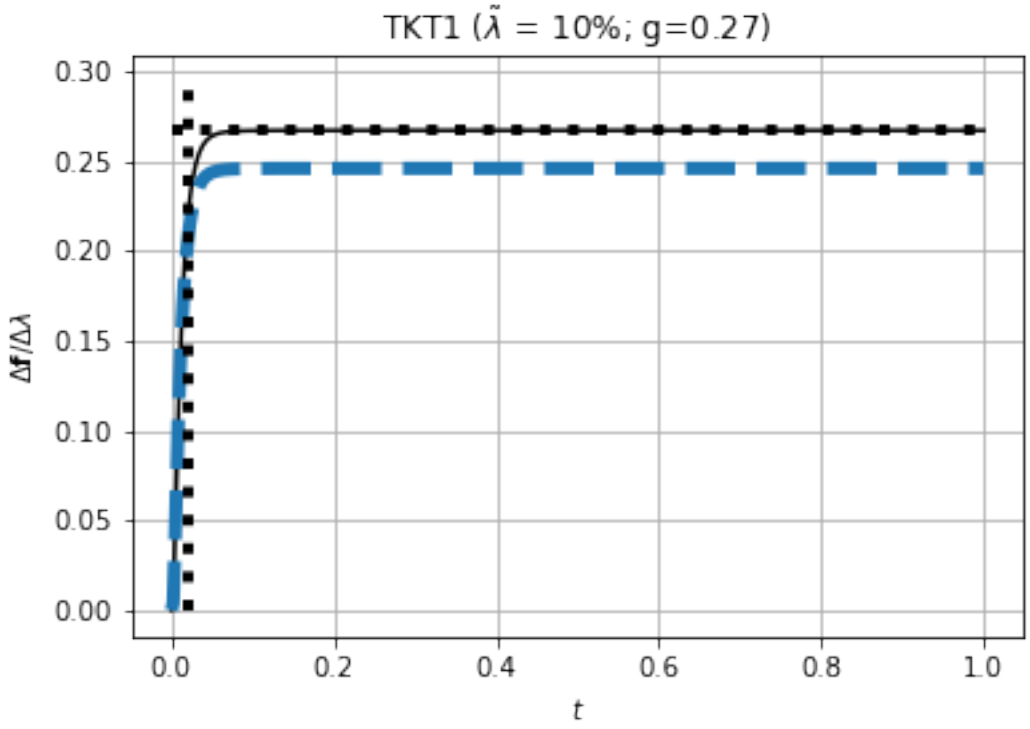
```
Doing: sTKT2
kappa_TKT2
g = 0.09778496614281532 tau = 0.0009111118563853957
dlam = 10
G6P
```



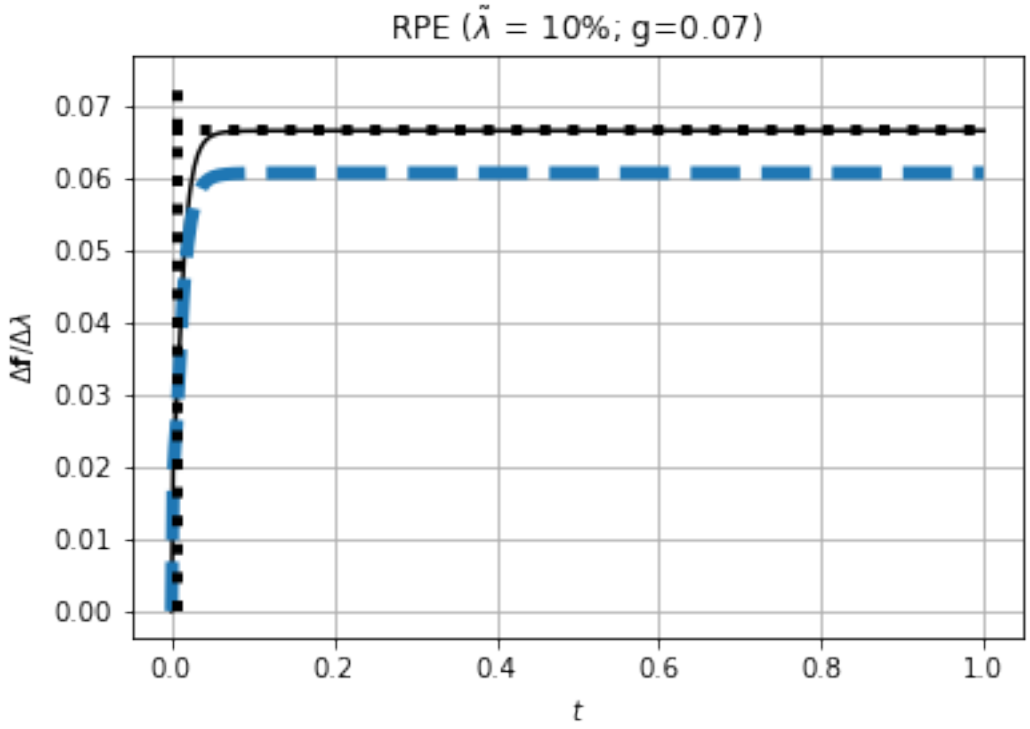

```
Doing: sTALA
kappa_TALA
g = 1.4213693479775253 tau = 0.0033987149739030348
dlam = 10
G6P
```

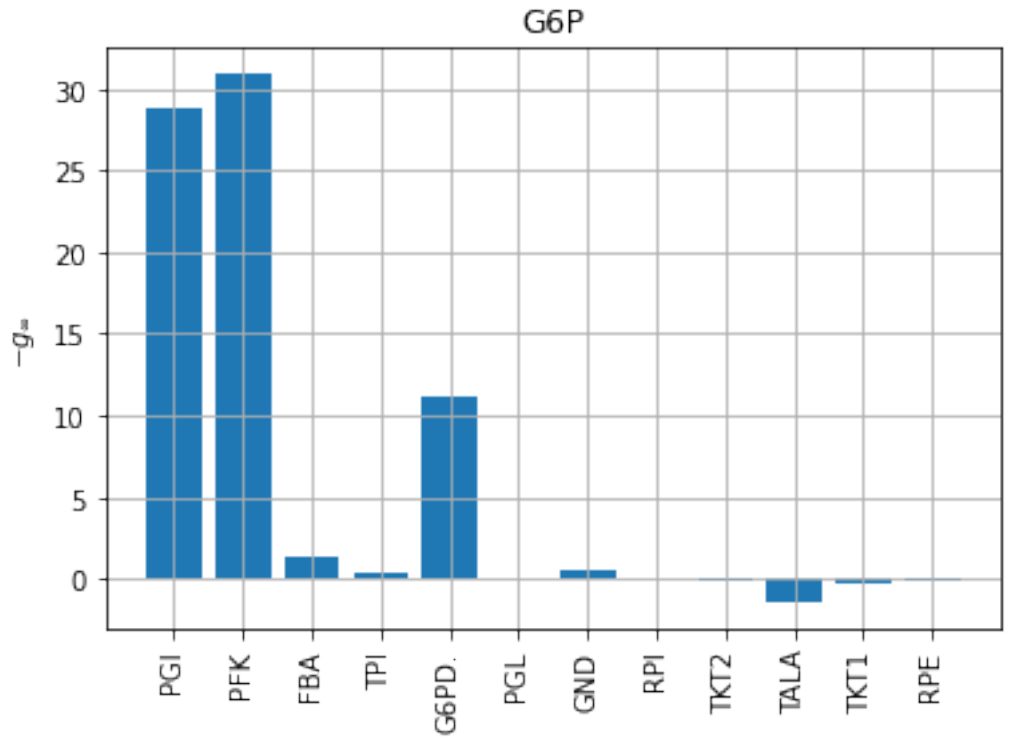


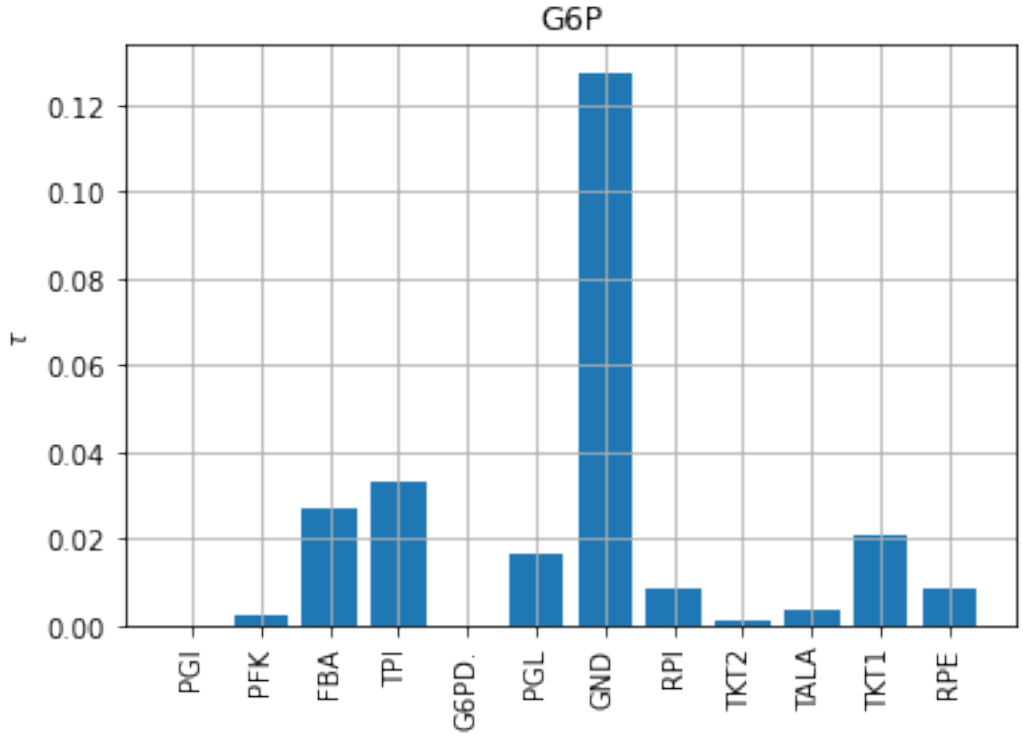

```
Doing: sTKT1
kappa_TKT1
g = 0.2669211003303768 tau = 0.021001174006396915
dlam = 10
G6P
```



```
Doing: sRPE
kappa_RPE
g = 0.06664804356236037 tau = 0.008221010075271595
dlam = 10
G6P
```

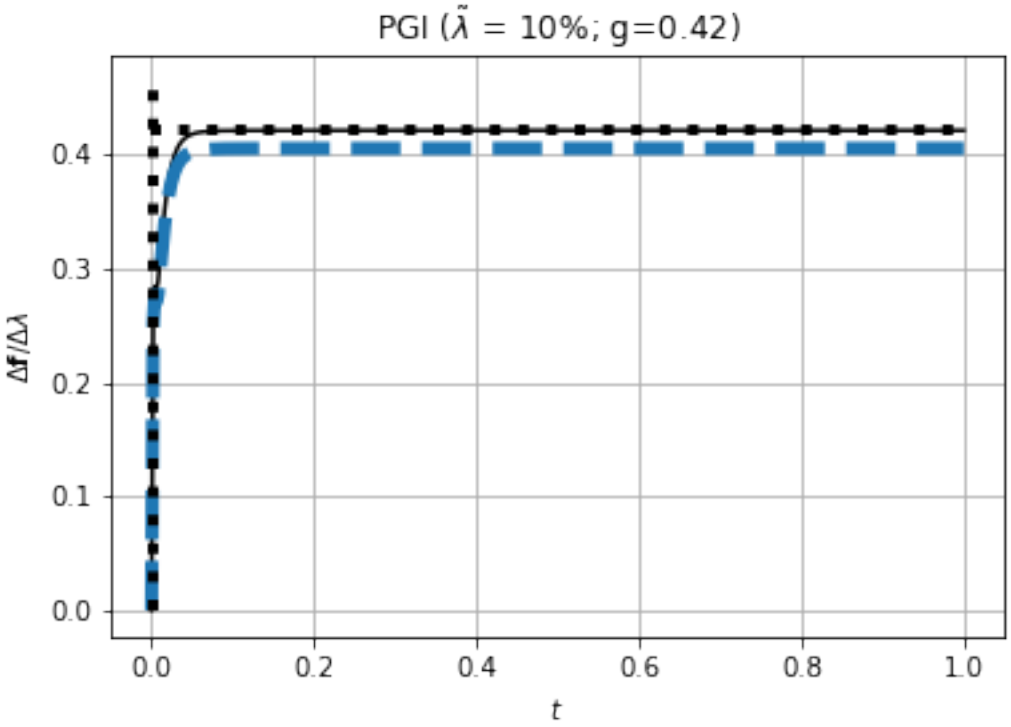




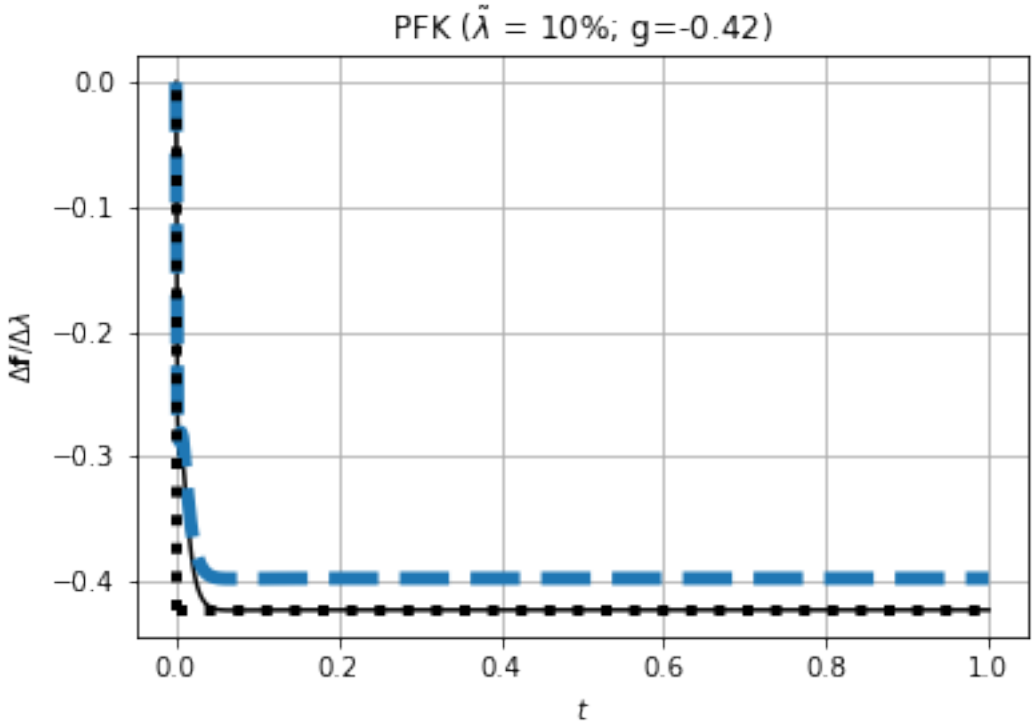



```
Doing: sPGI
kappa_PGI
g = 0.4208987417694914 tau = 0.001784019116768216
```

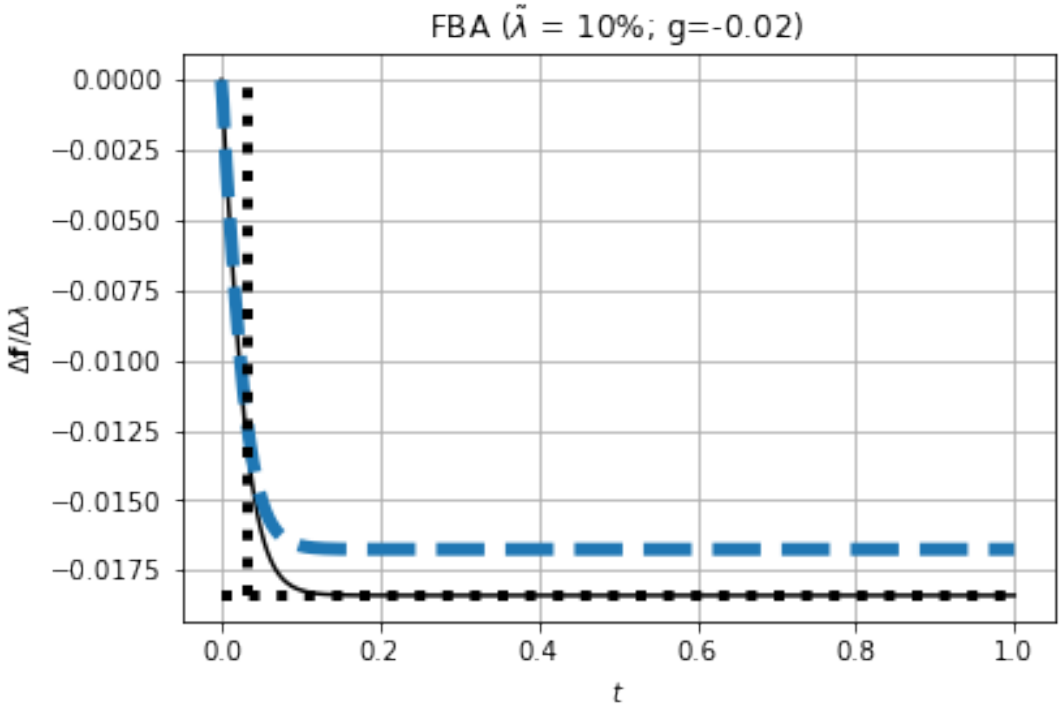
```
dlam = 10
R5P
```



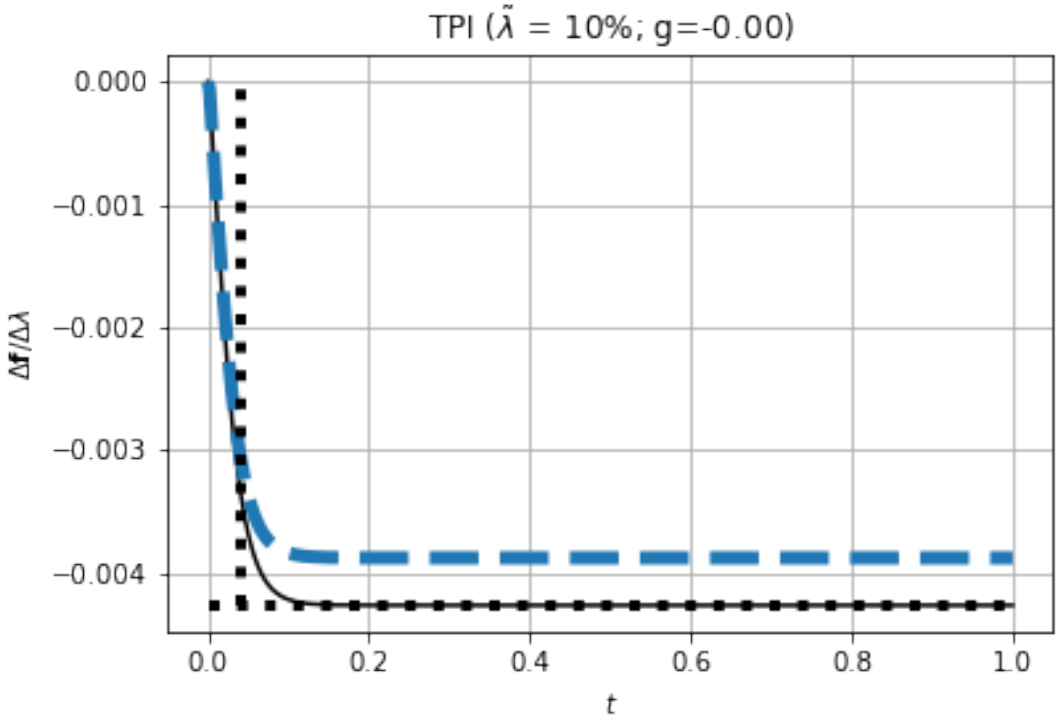

```
Doing: sPFK
kappa_PFK
g = -0.42364263563046833 tau = 0.001717964990211834
dlam = 10
R5P
```



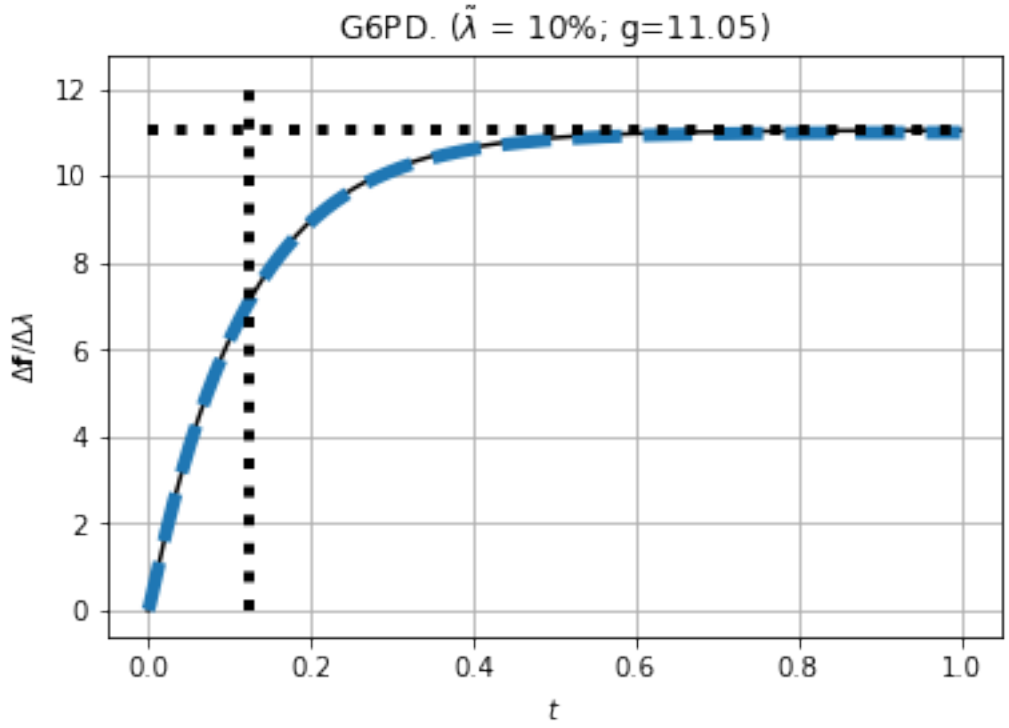

```
Doing: sFBA
kappa_FBA
g = -0.018401576065215863 tau = 0.033394801269318826
dlam = 10
R5P
```



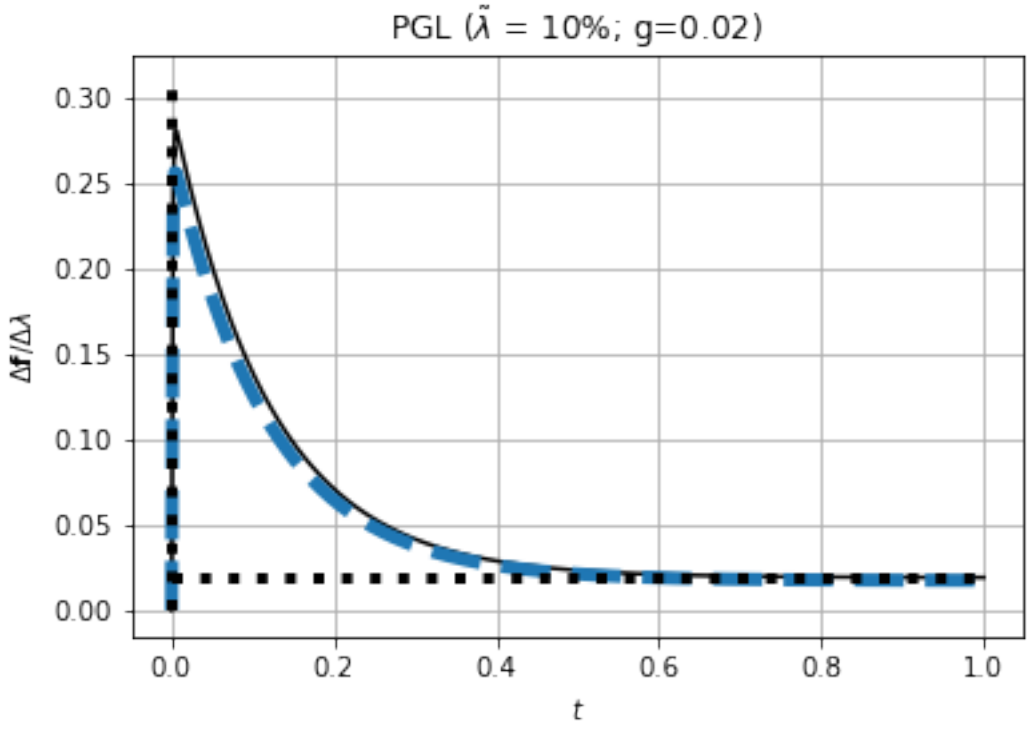
```
Doing: sTPI
kappa_TPI
g = -0.004265327359156856 tau = 0.039469568172793866
dlam = 10
R5P
```



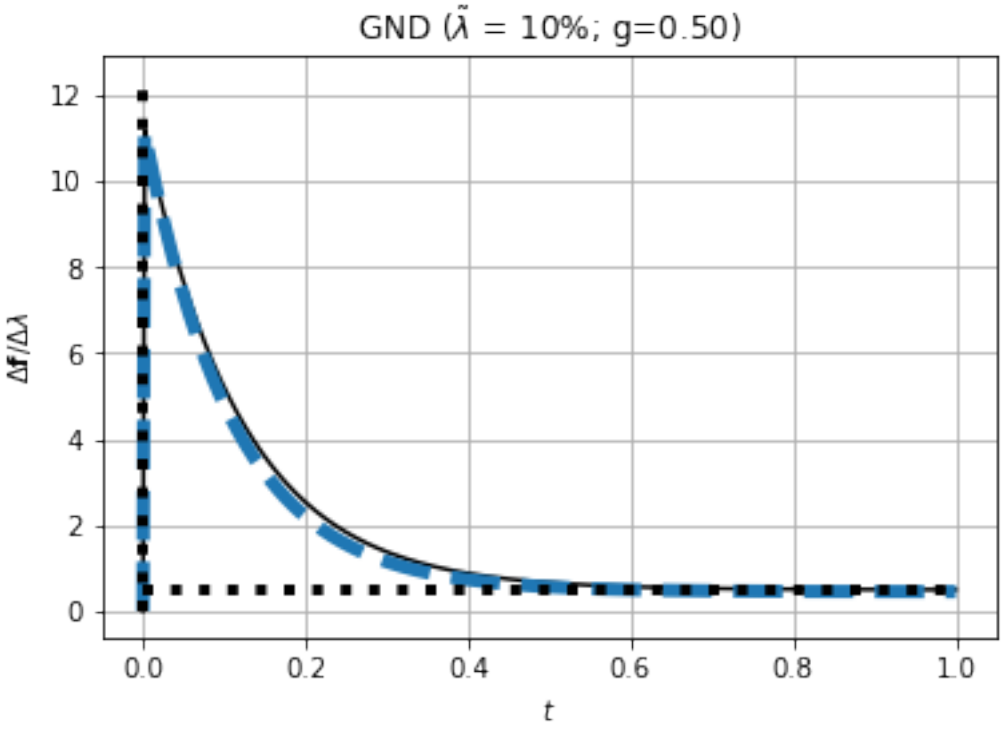

```
Doing: sG6PDH2R
kappa_G6PDH2R
g = 11.049474162931 tau = 0.12364579561293719
dlam = 10
R5P
```



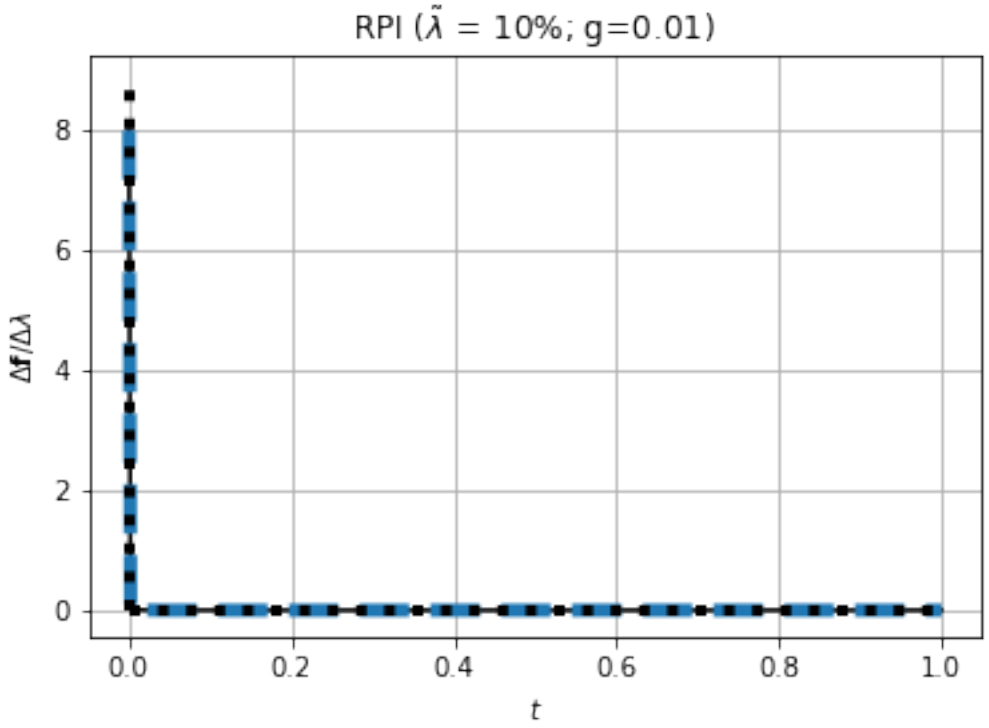

```
Doing: sPGL
kappa_PGL
g = 0.01915350335214014 tau = 0.0010470596032330958
dlam = 10
R5P
```



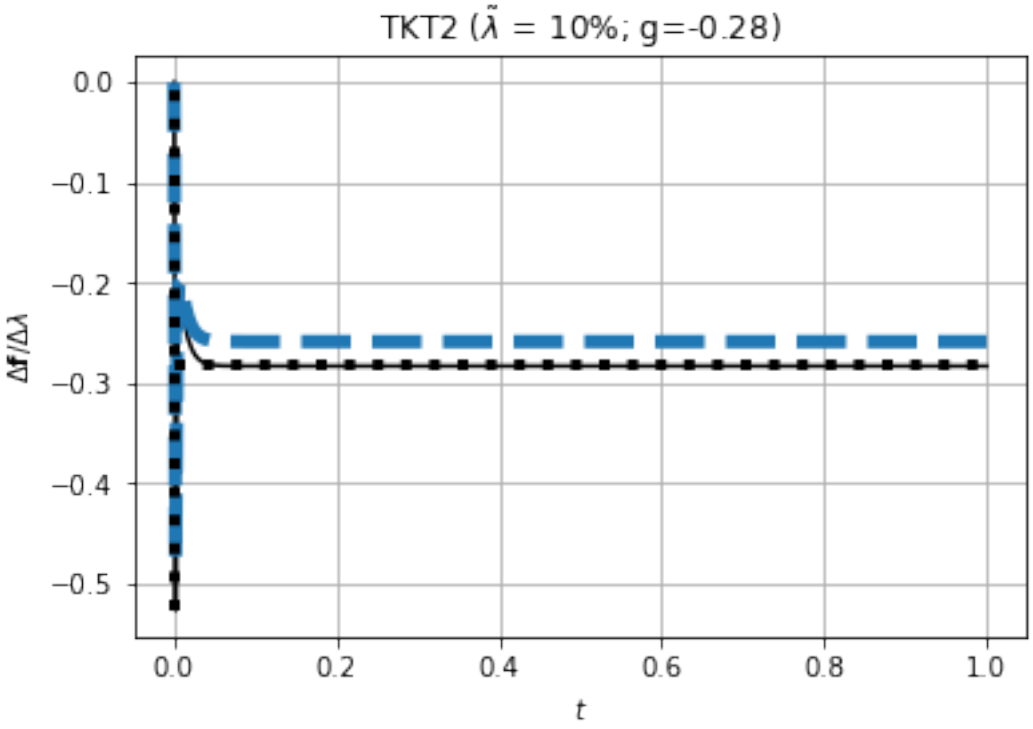
```
Doing: sGND
kappa_GND
g = 0.4954727350638917 tau = 2.6988194236854497e-06
dlam = 10
R5P
```



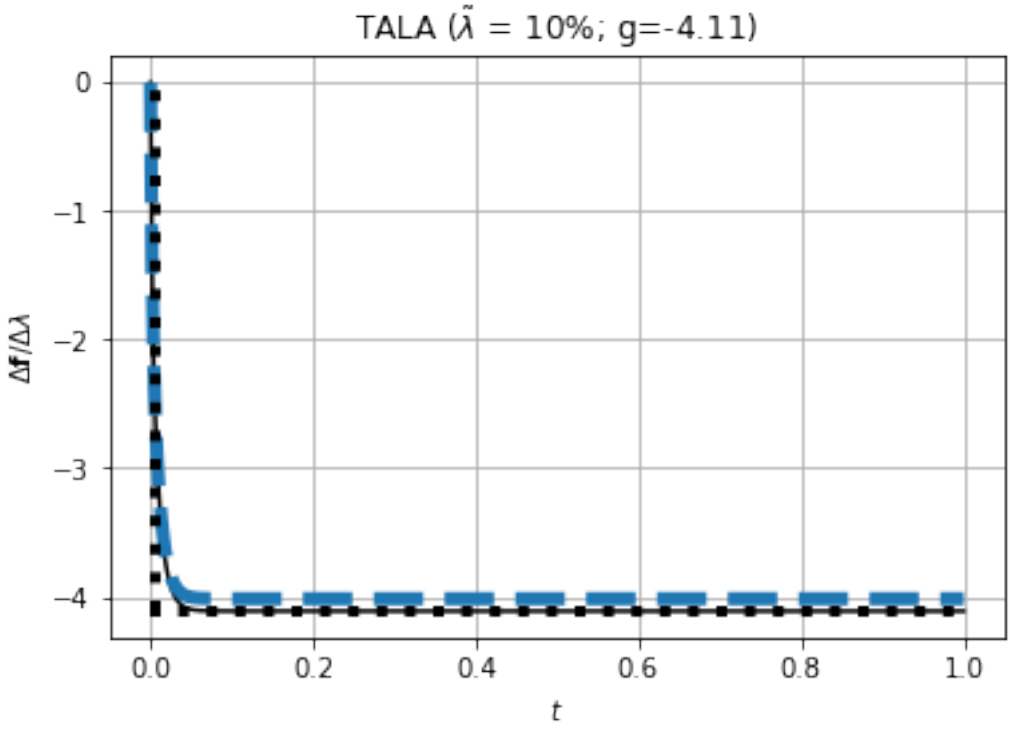

```
Doing: sRPI
kappa_RPI
g = 0.009795231203673538 tau = 0
dlam = 10
R5P
```



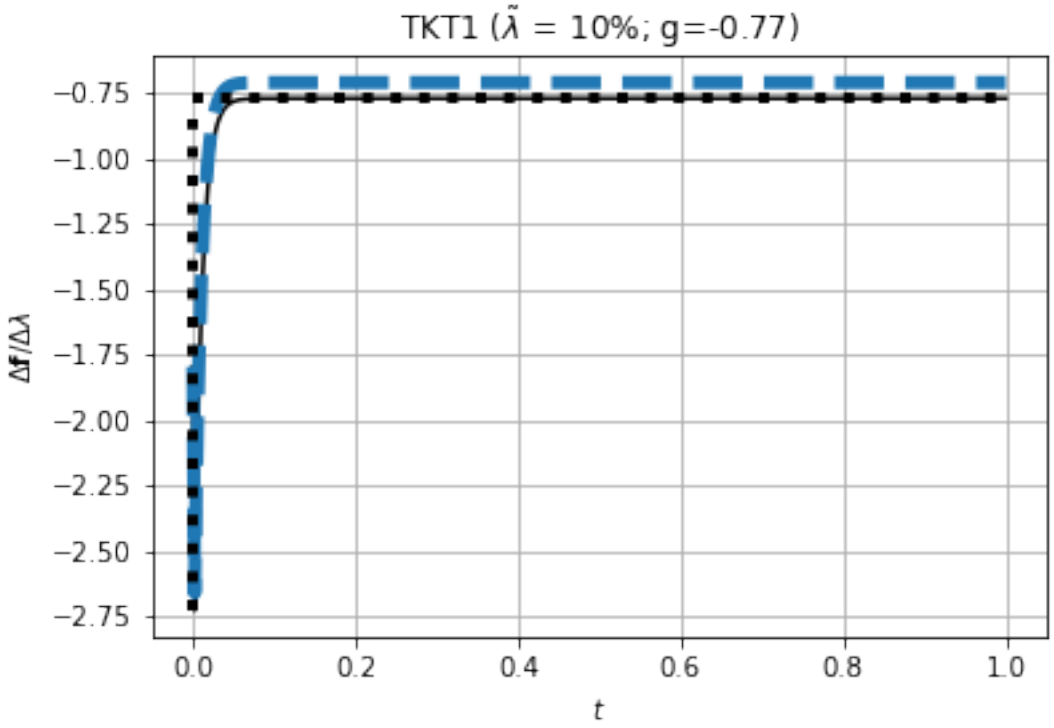

```
Doing: sTKT2
kappa_TKT2
g = -0.282924954852798 tau = 0.00017126550296392315
dlam = 10
R5P
```



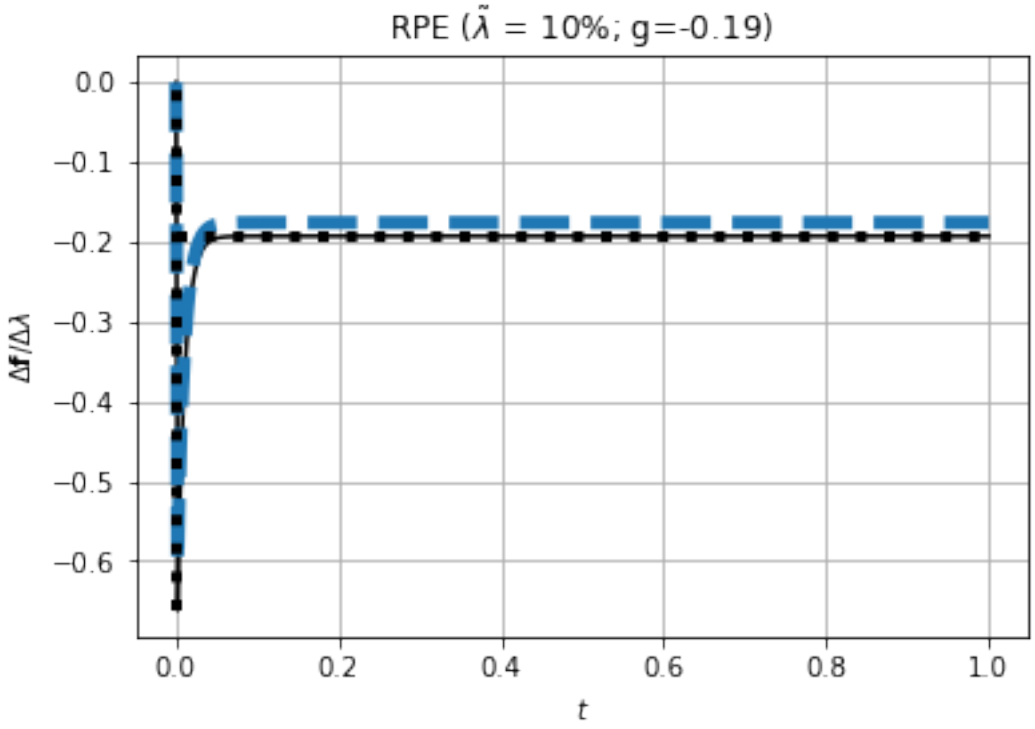
```
Doing: sTALA
kappa_TALA
g = -4.1125018954178 tau = 0.0045160996928807215
dlam = 10
R5P
```

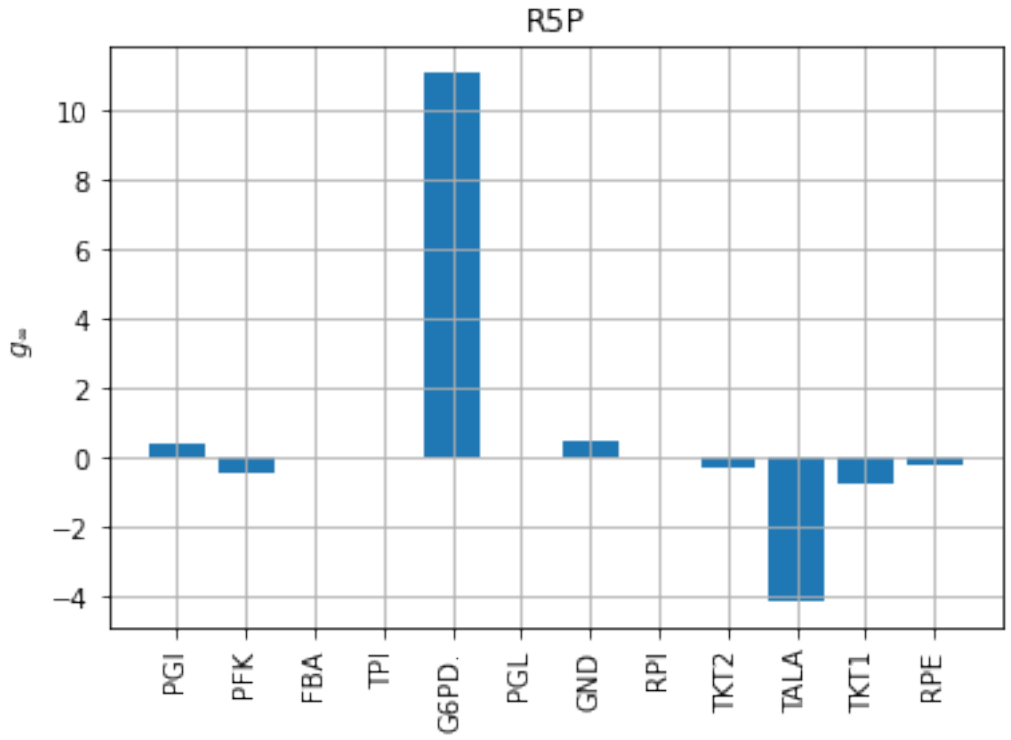


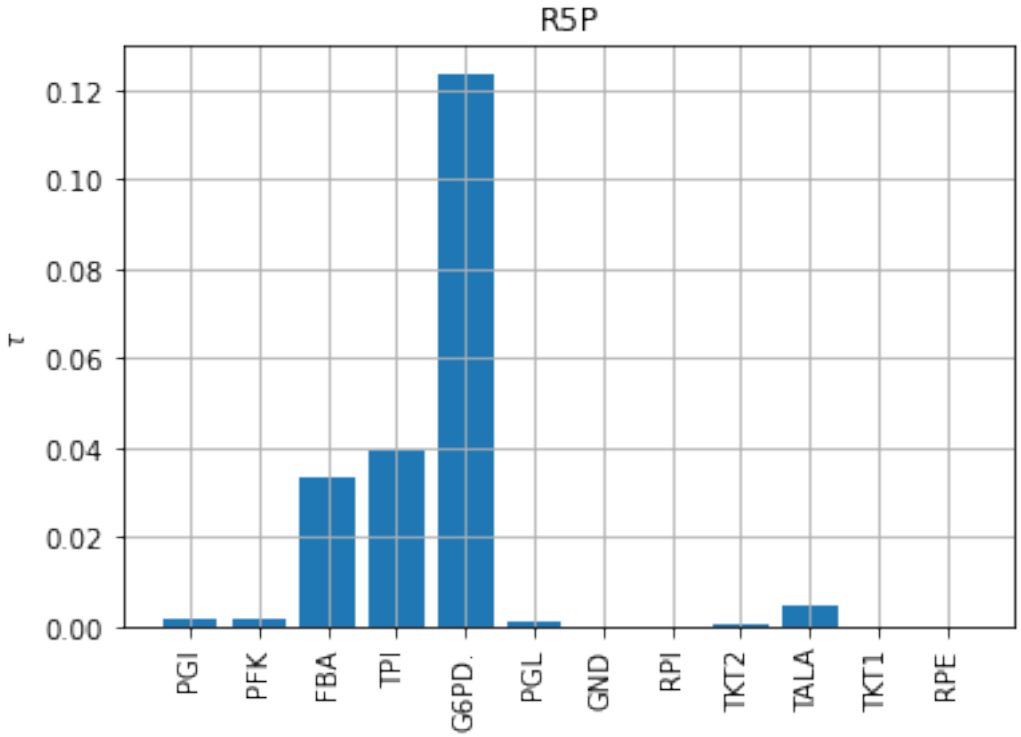

```
Doing: sTKT1
kappa_TKT1
g = -0.7722929529876414 tau = 0
dlam = 10
R5P
```



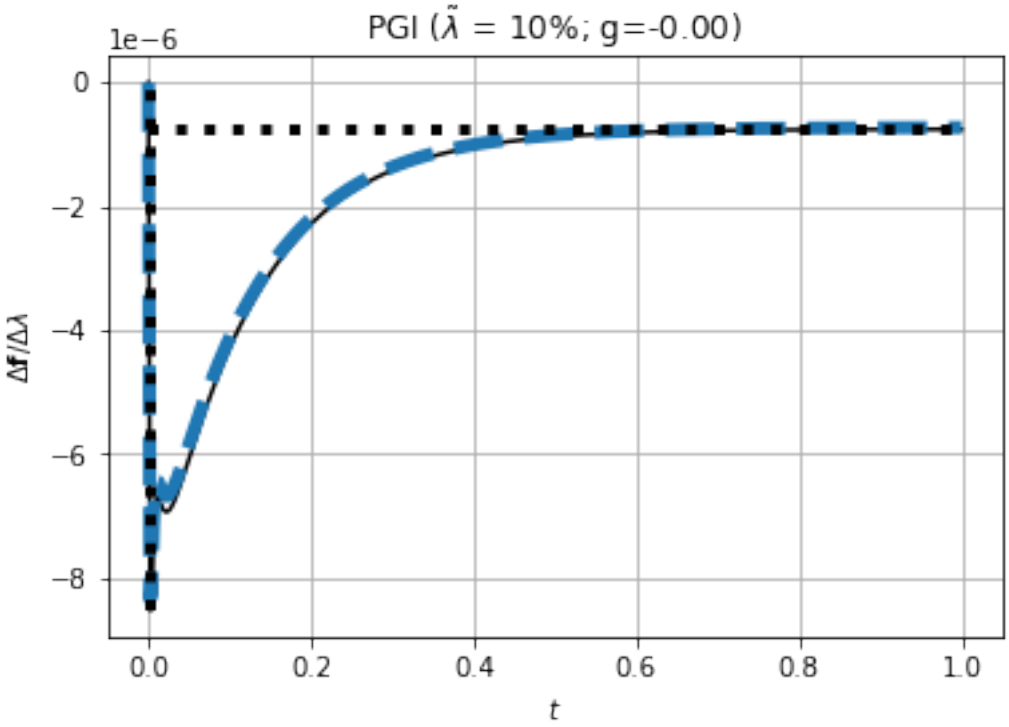

```
Doing: sRPE
kappa_RPE
g = -0.19283531466757647 tau = 2.6571744064148927e-06
dlam = 10
R5P
```



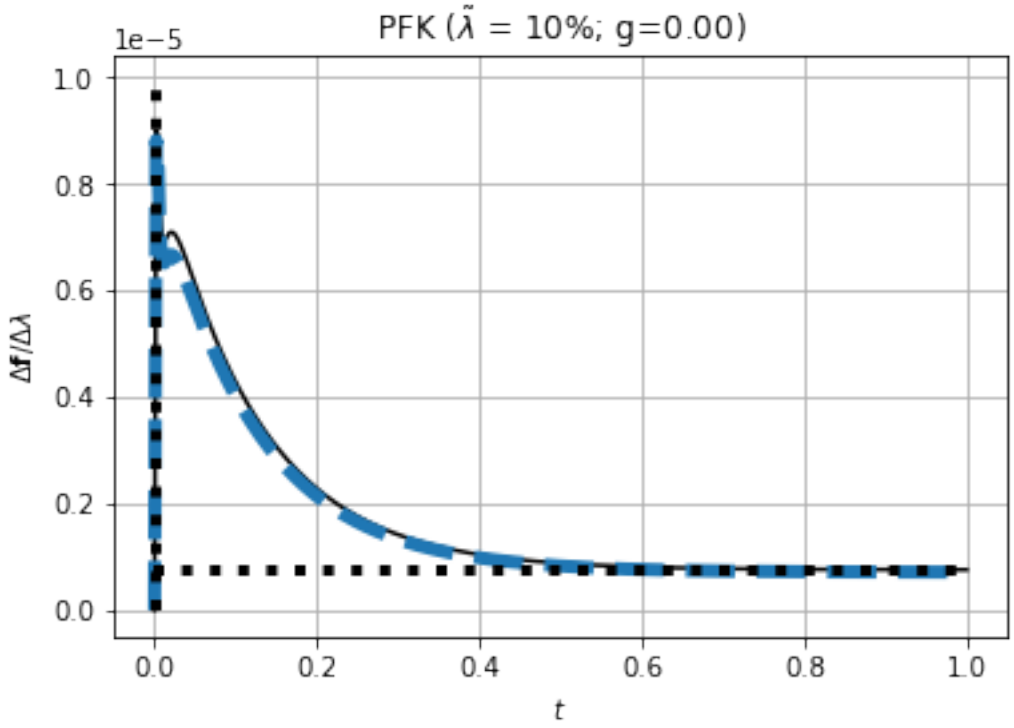

R5P
g_∞
10
8
6
4
2
0
−2
−4
PGI
PFK
FBA
TPI
G6PD.
PGL
GND
RPI
TKT2
TALA
TKT1
RPE


R5P
τ
0.12
0.10
0.08
0.06
0.04
0.02
0.00
PGI
PFK
FBA
TPI
G6PD.
PGL
GND
RPI
TKT2
TALA
TKT1
RPE

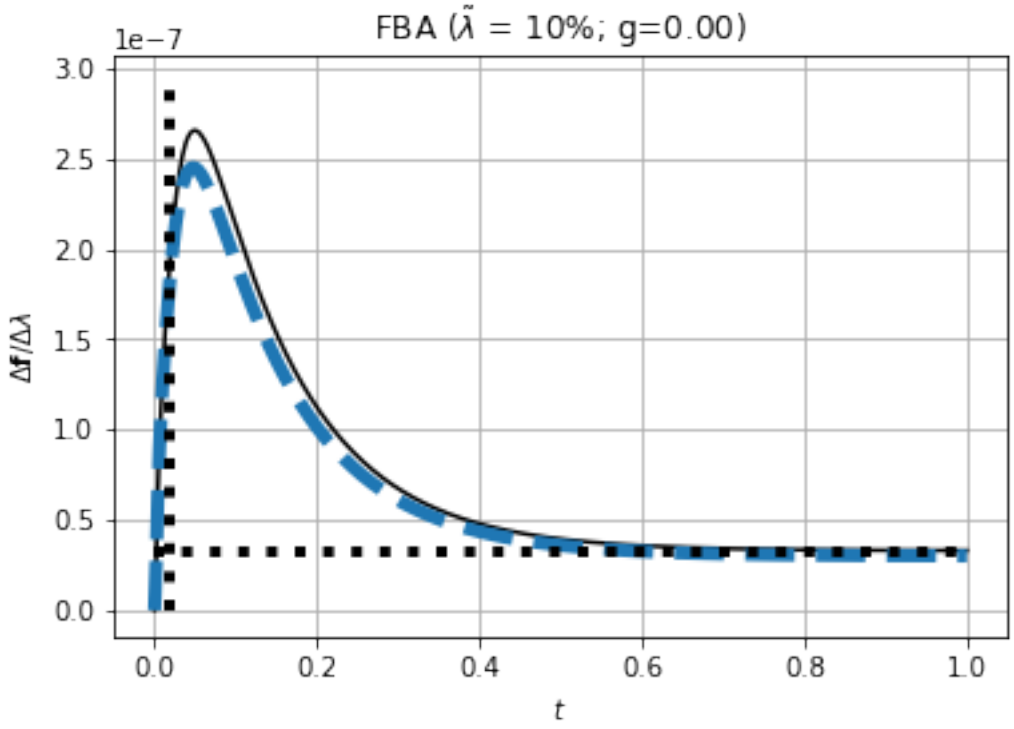
```
Doing: sPGI
kappa_PGI
g = -7.546999477333997e-07 tau = 0.0015271411542531847
dlam = 10
NADPH
```



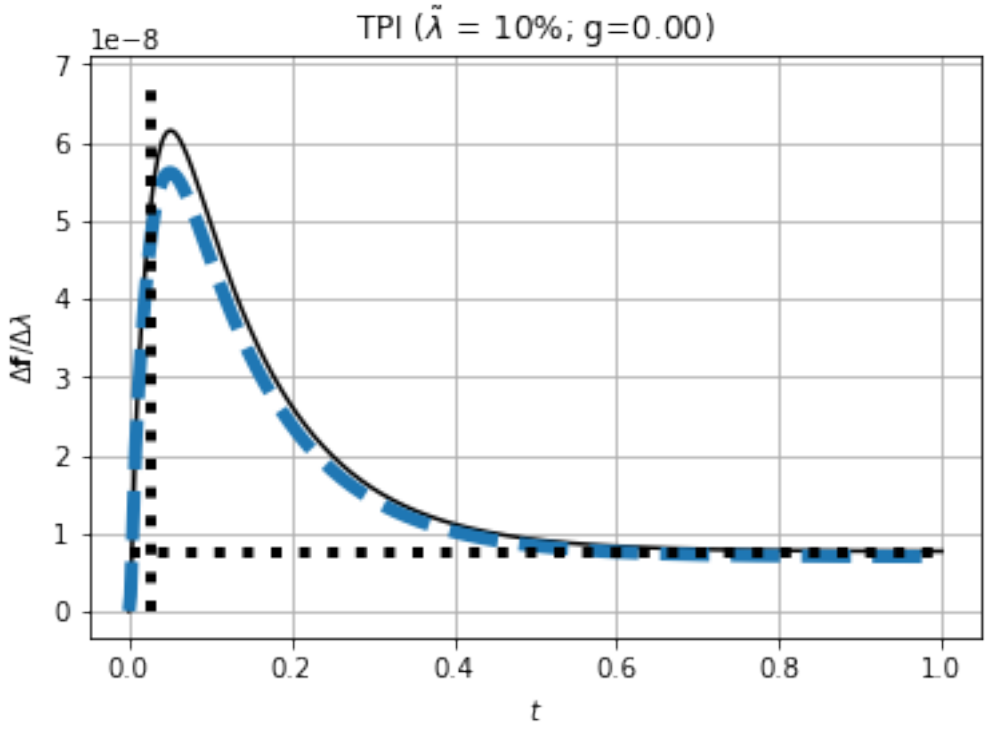

```
Doing: sPFK
kappa_PFK
g = 7.596199715986058e-07 tau = 0.0015261943288164277
dlam = 10
NADPH
```



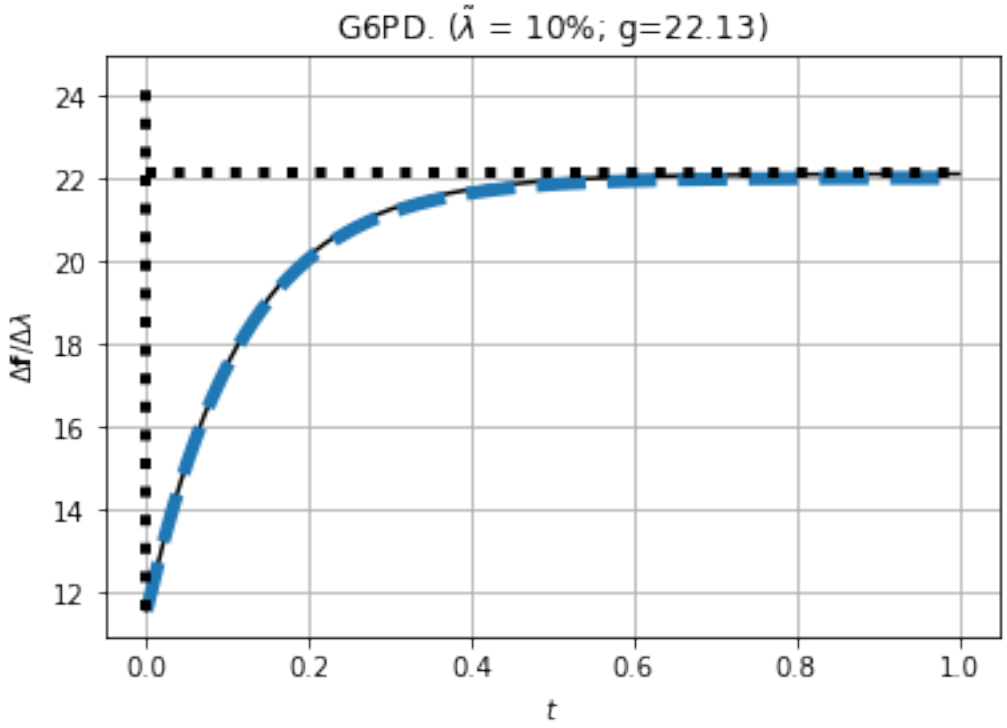

```
Doing: sFBA
kappa_FBA
g = 3.299527434456363e-08 tau = 0.019527507142779787
dlam = 10
NADPH
```



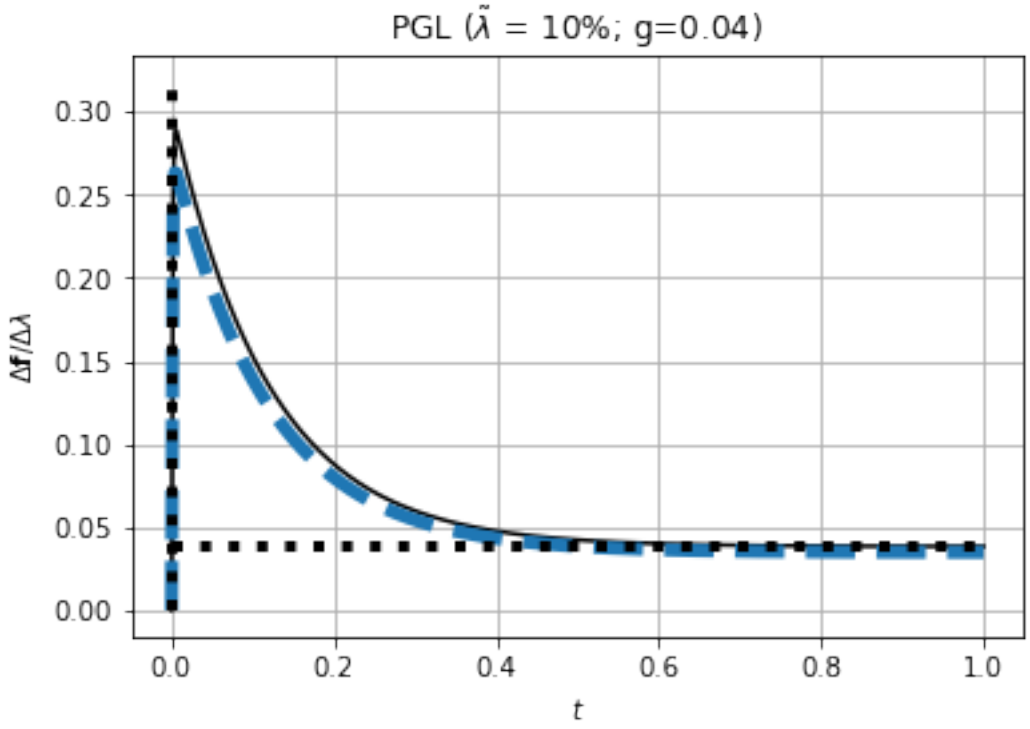
```
Doing: sTPI
kappa_TPI
g = 7.647982183374511e-09 tau = 0.02541572981821223
dlam = 10
NADPH
```



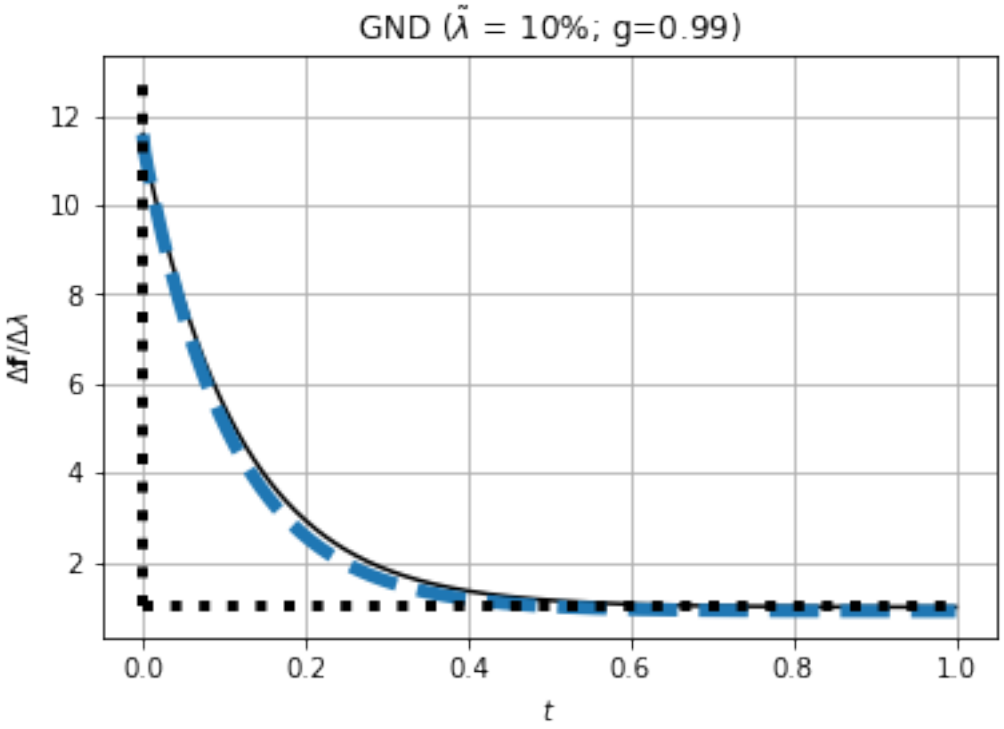

```
Doing: sG6PDH2R
kappa_G6PDH2R
g = 22.126061707076737 tau = 0
dlam = 10
NADPH
```



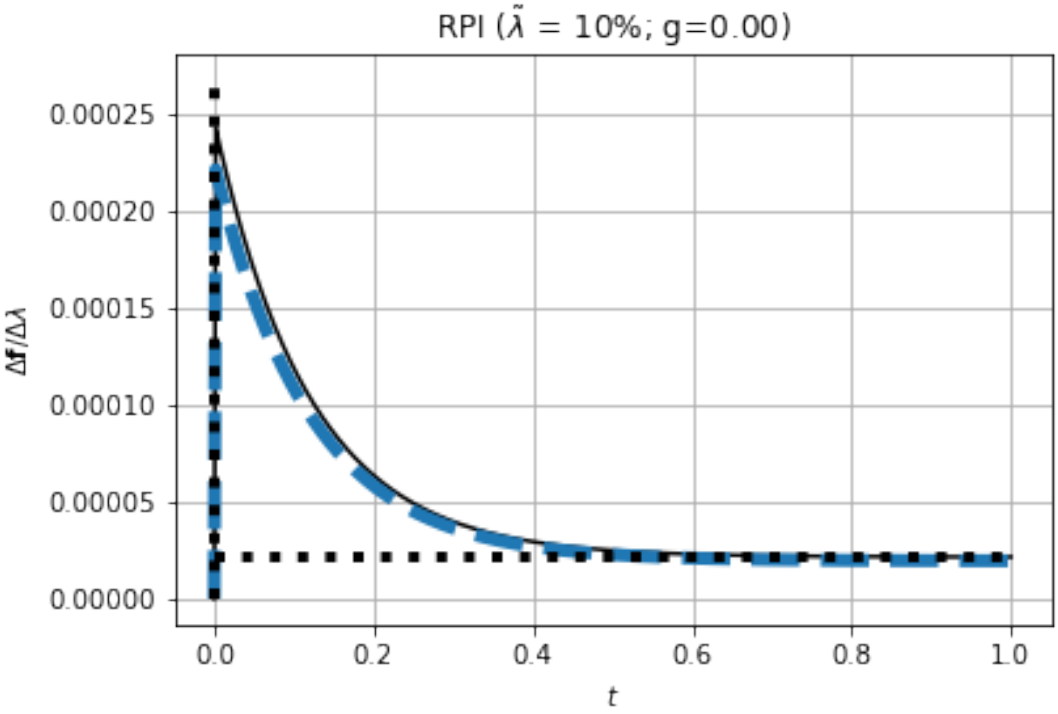

```
Doing: sPGL
kappa_PGL
g = 0.03835400588527368 tau = 0.001025533527882495
dlam = 10
NADPH
```



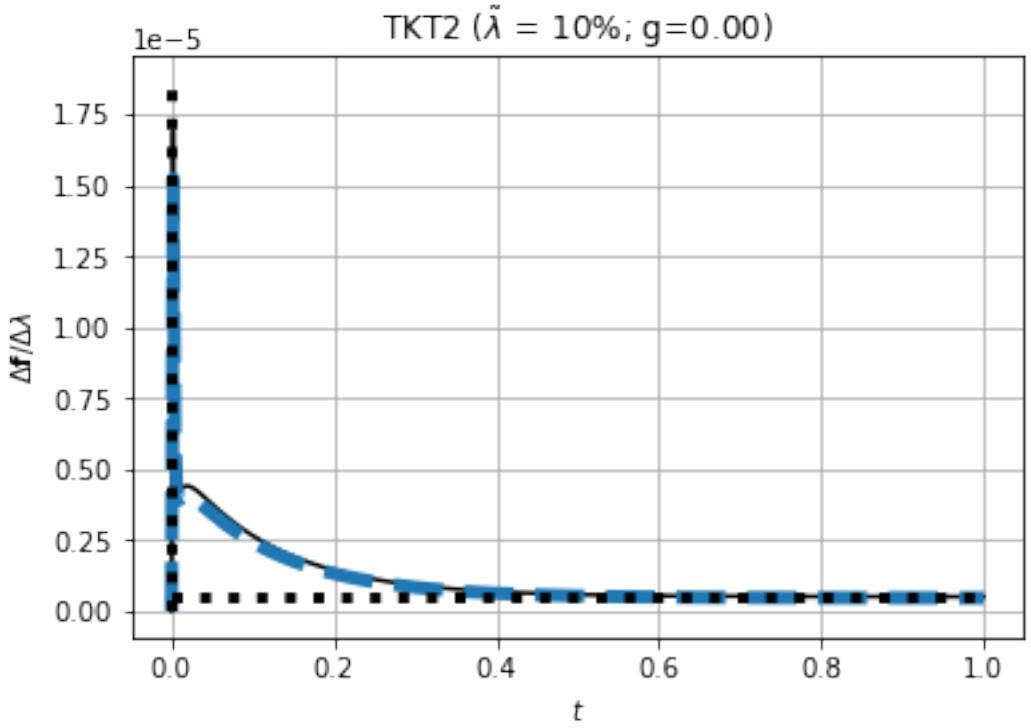
```
Doing: sGND
kappa_GND
g = 0.9921612692650577 tau = 0
dlam = 10
NADPH
```



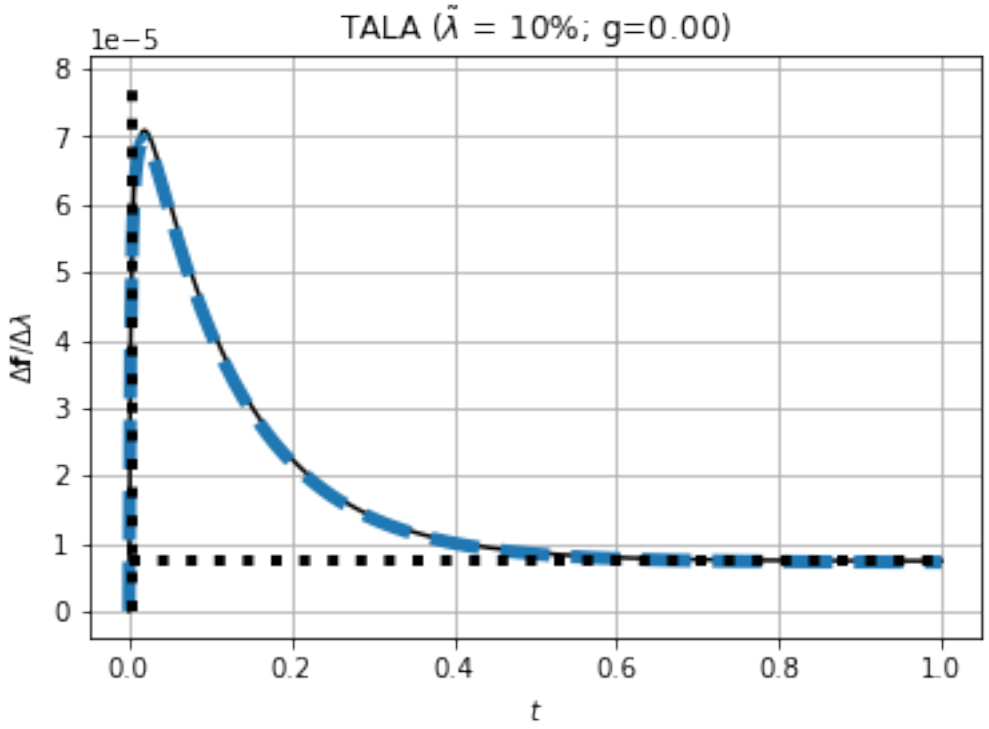

```
Doing: sRPI
kappa_RPI
g = 2.1458155641420664e-05 tau = 2.699186974424081e-06
dlam = 10
NADPH
```



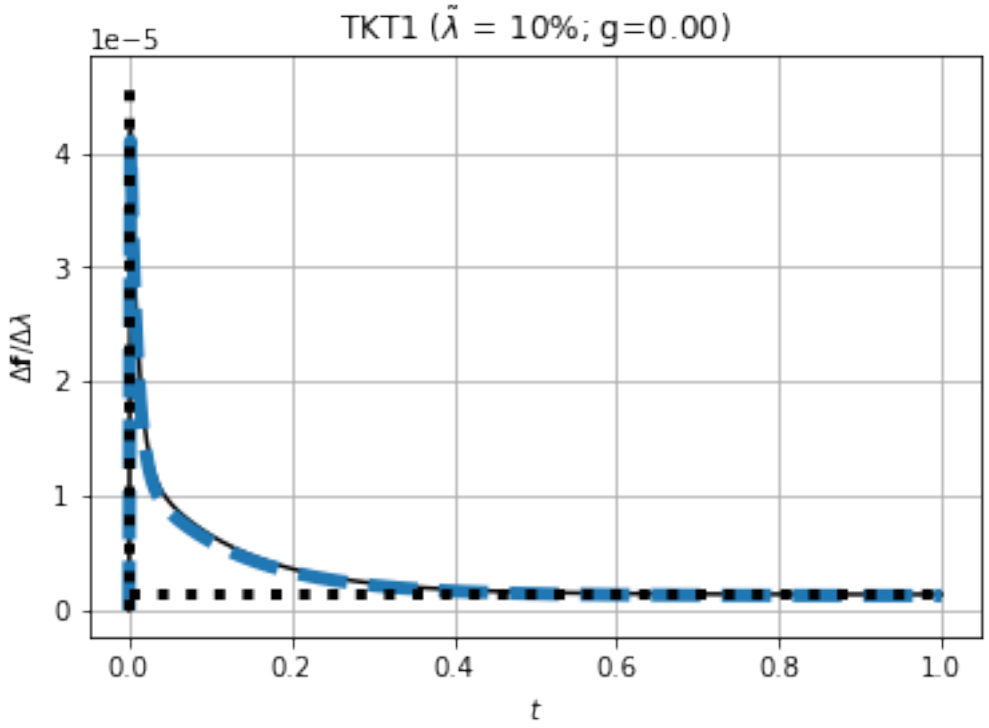

```
Doing: sTKT2
kappa_TKT2
g = 5.073036156607876e-07 tau = 0.00016943022110076314
dlam = 10
NADPH
```



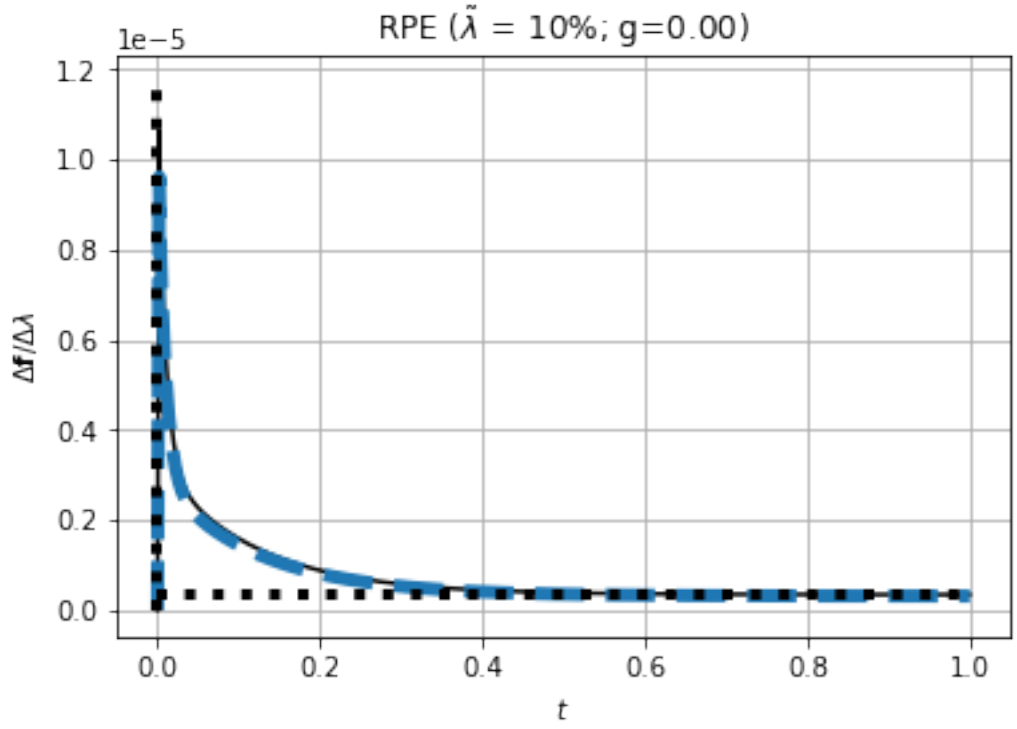
```
Doing: sTALA
kappa_TALA
g = 7.373994570839489e-06 tau = 0.0028552247467929955
dlam = 10
NADPH
```

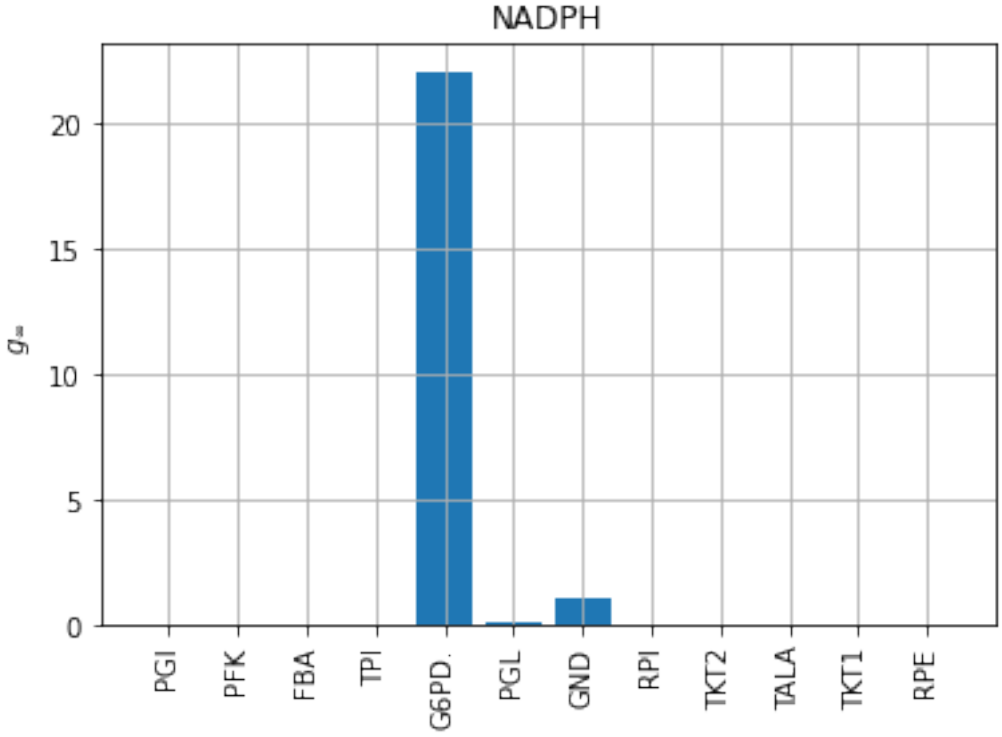


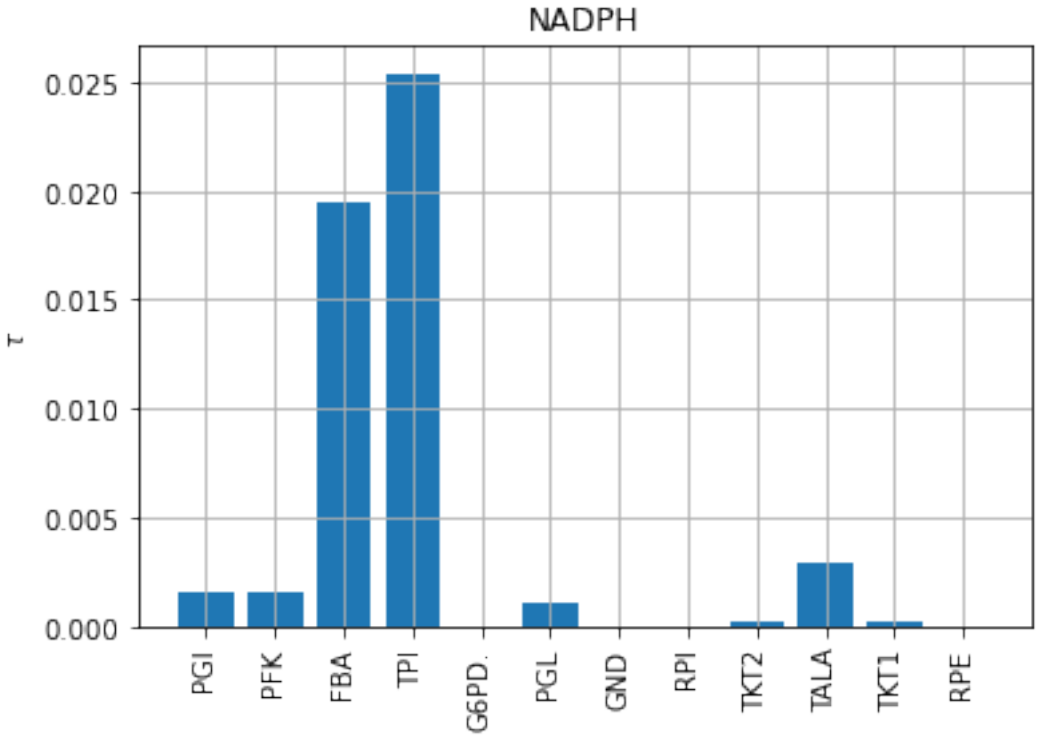

```
Doing: sTKT1
kappa_TKT1
g = 1.3847735970665945e-06 tau = 0.00018475667332612674
dlam = 10
NADPH
```



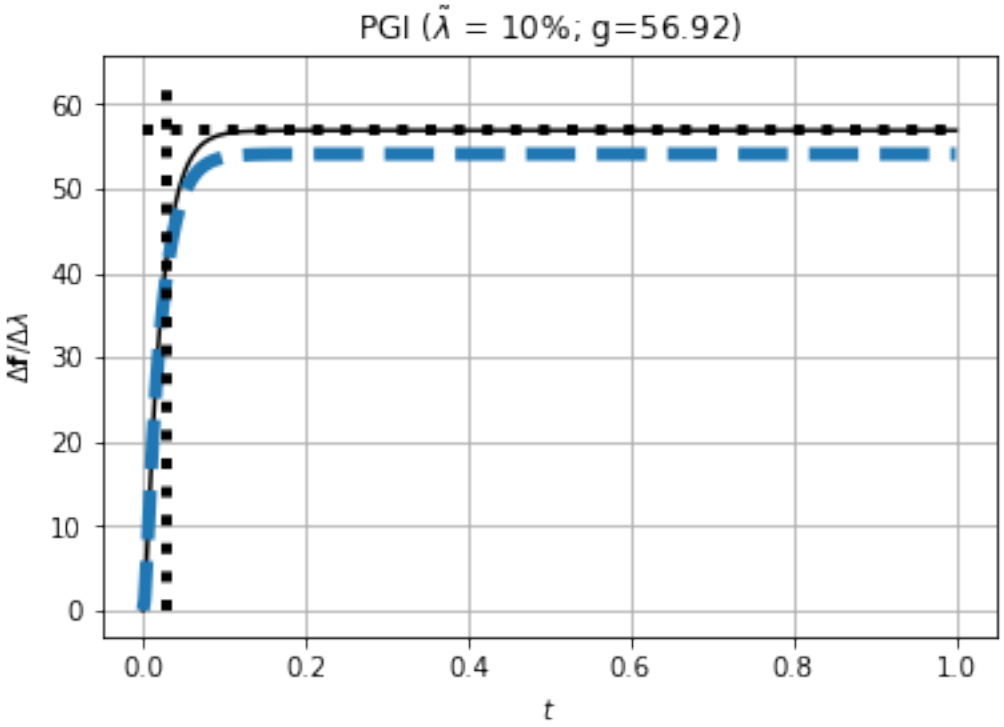

```
Doing: sRPE
kappa_RPE
g = 3.457667861388965e-07 tau = 2.6565945344600007e-06
dlam = 10
NADPH
```



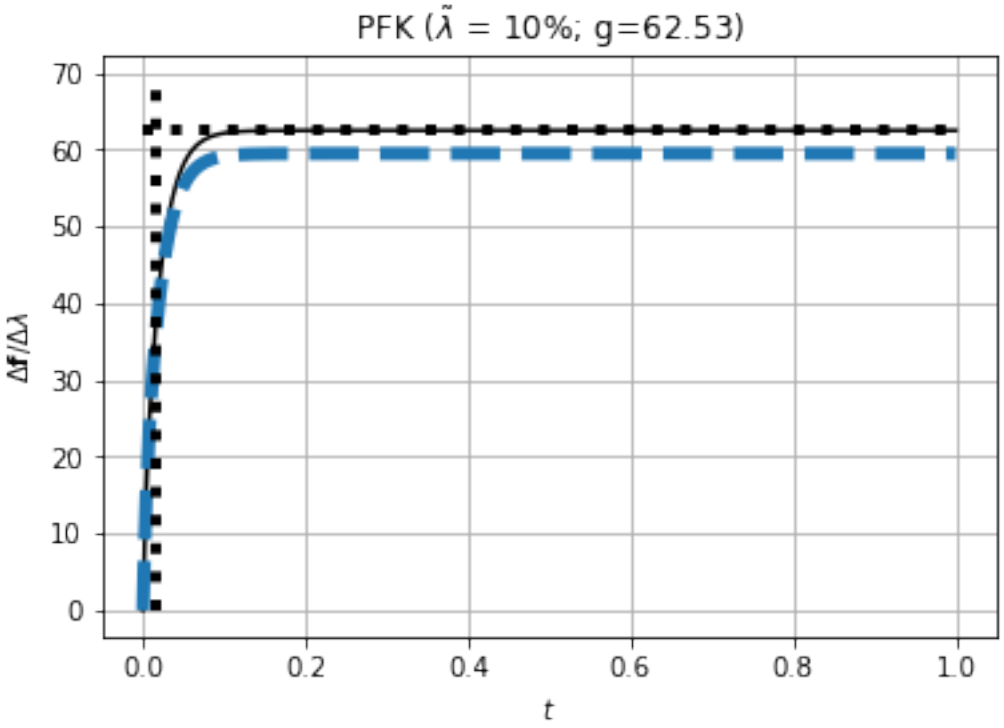

NADPH
g_∞
0
5
10
15
20
PGI
PFK
FBA
TPI
G6PD.
PGL
GND
RPI
TKT2
TALA
TKT1
RPE


NADPH
τ
0.000
0.005
0.010
0.015
0.020
0.025
PGI
PFK
FBA
TPI
G6PD.
PGL
GND
RPI
TKT2
TALA
TKT1
RPE

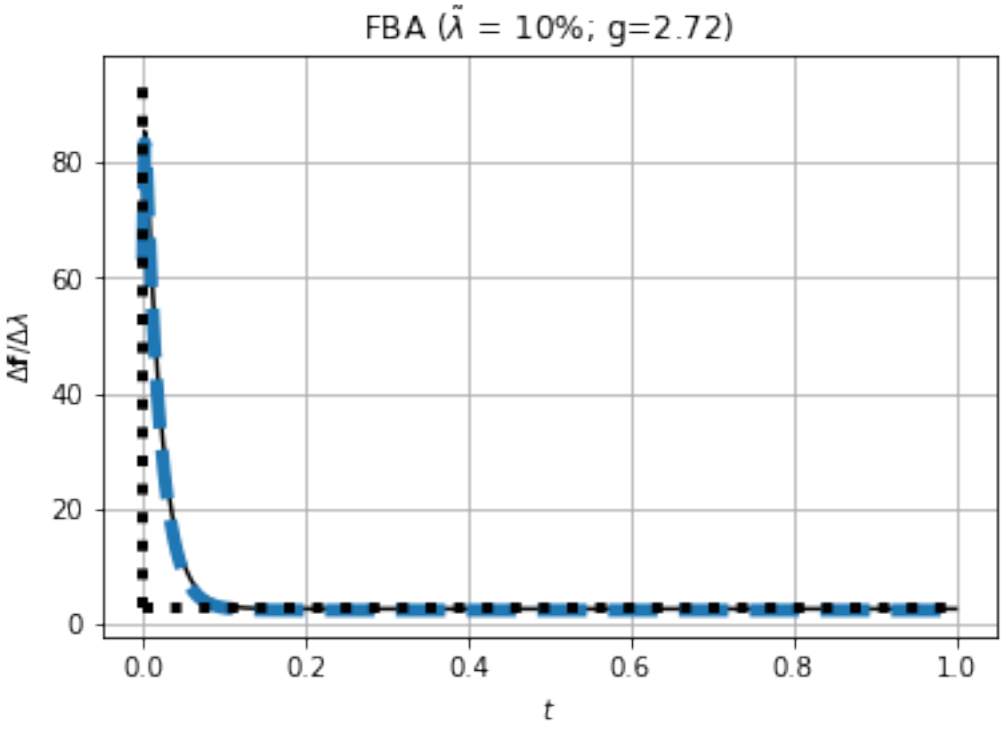
```
Doing: sPGI
kappa_PGI
g = 56.91833245076208 tau = 0.030041038107083886
dlam = 10
G3P
```



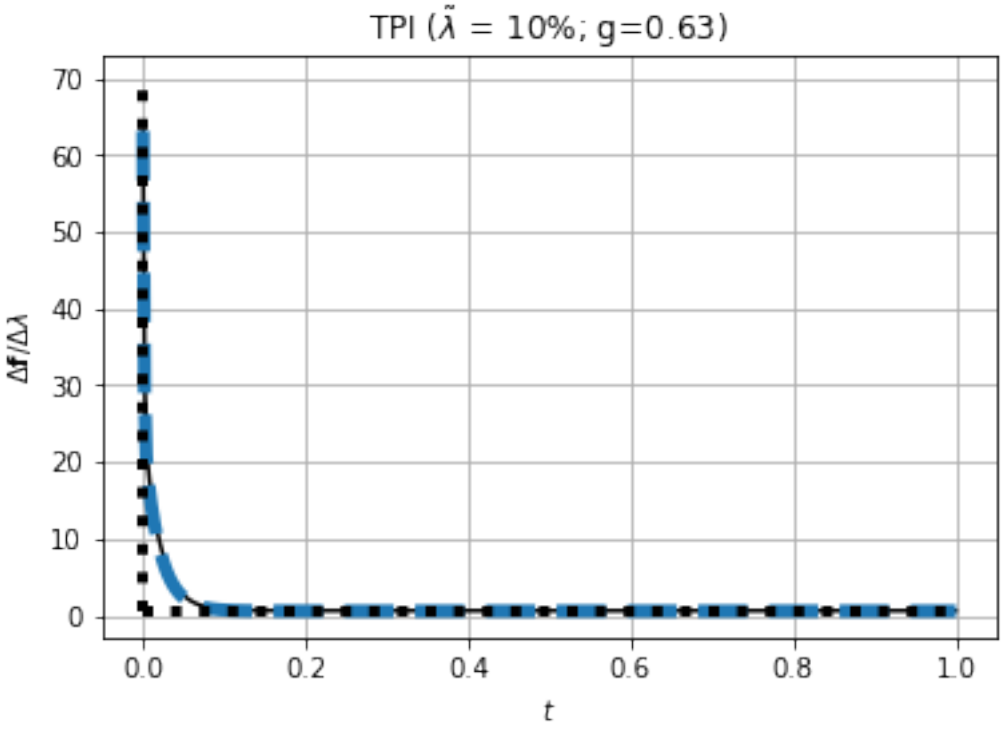

```
Doing: sPFK
kappa_PFK
g = 62.533290299526094 tau = 0.014866156765752257
dlam = 10
G3P
```



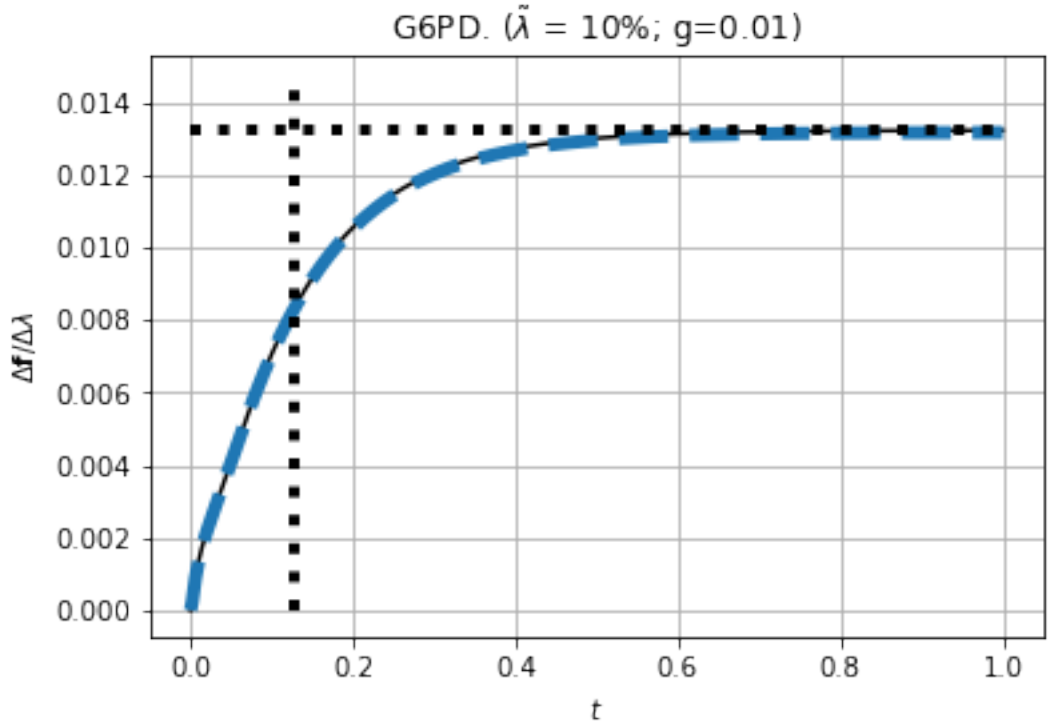

```
Doing: sFBA
kappa_FBA
g = 2.7162306181456373 tau = 0
dlam = 10
G3P
```



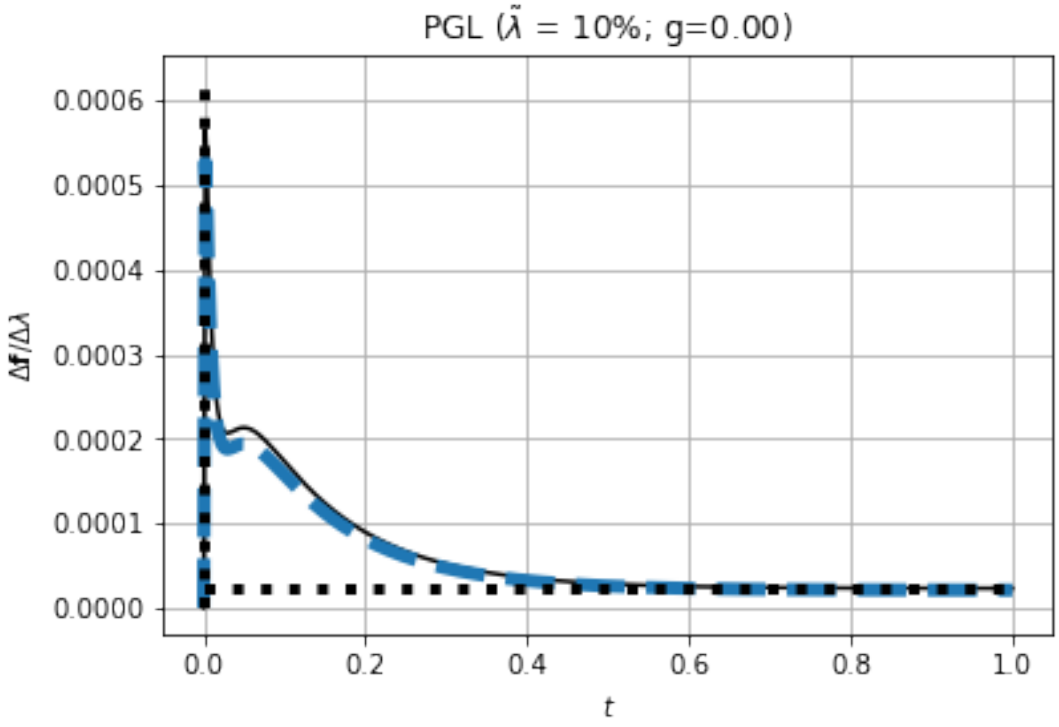
```
Doing: sTPI
kappa_TPI
g = 0.6295989394585817 tau = 0
dlam = 10
G3P
```



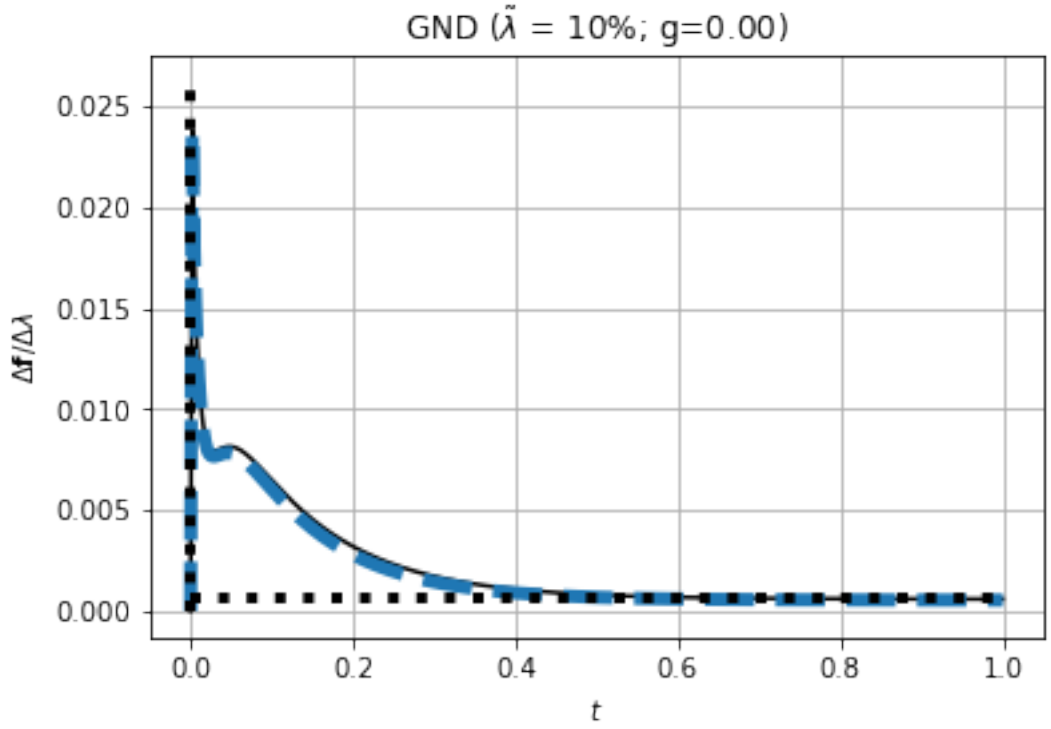

```
Doing: sG6PDH2R
kappa_G6PDH2R
g = 0.01322349914204985 tau = 0.12800864302389323
dlam = 10
G3P
```



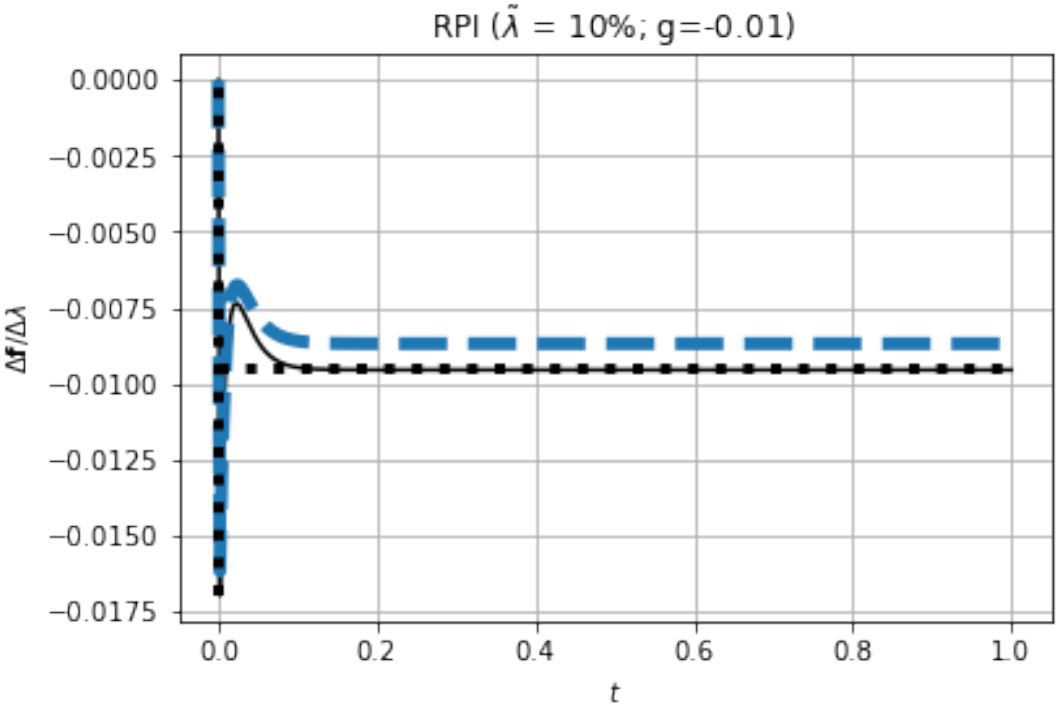

```
Doing: sPGL
kappa_PGL
g = 2.2922026197106206e-05 tau = 0.0014045237898896985
dlam = 10
G3P
```



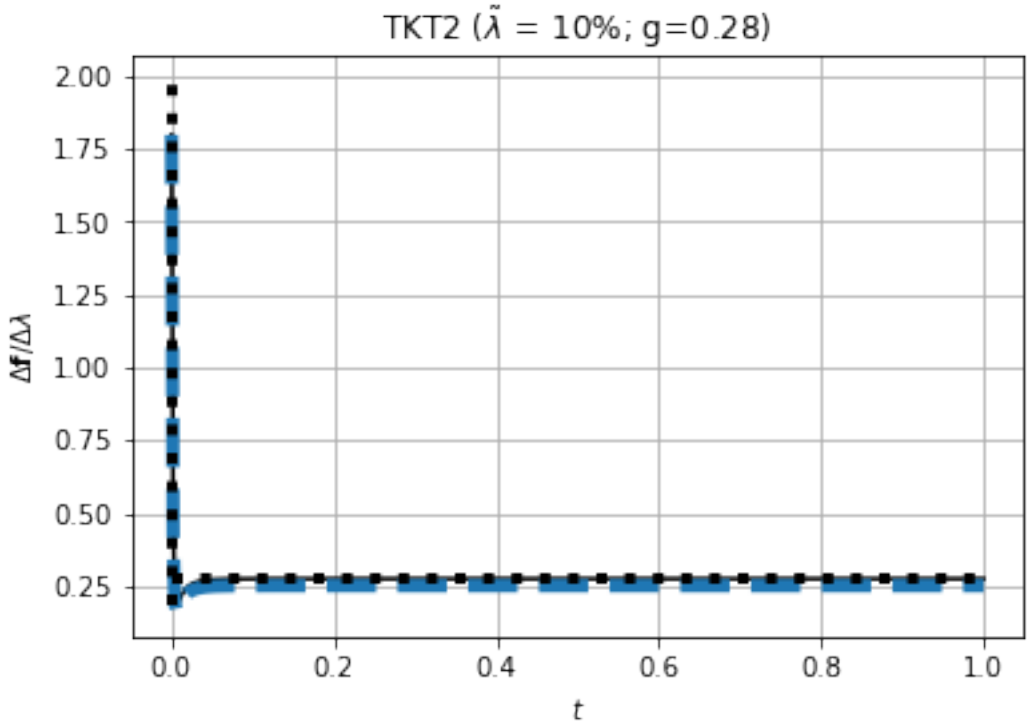
```
Doing: sGND
kappa_GND
g = 0.0005929588339176166 tau = 0.00017684665624202348
dlam = 10
G3P
```



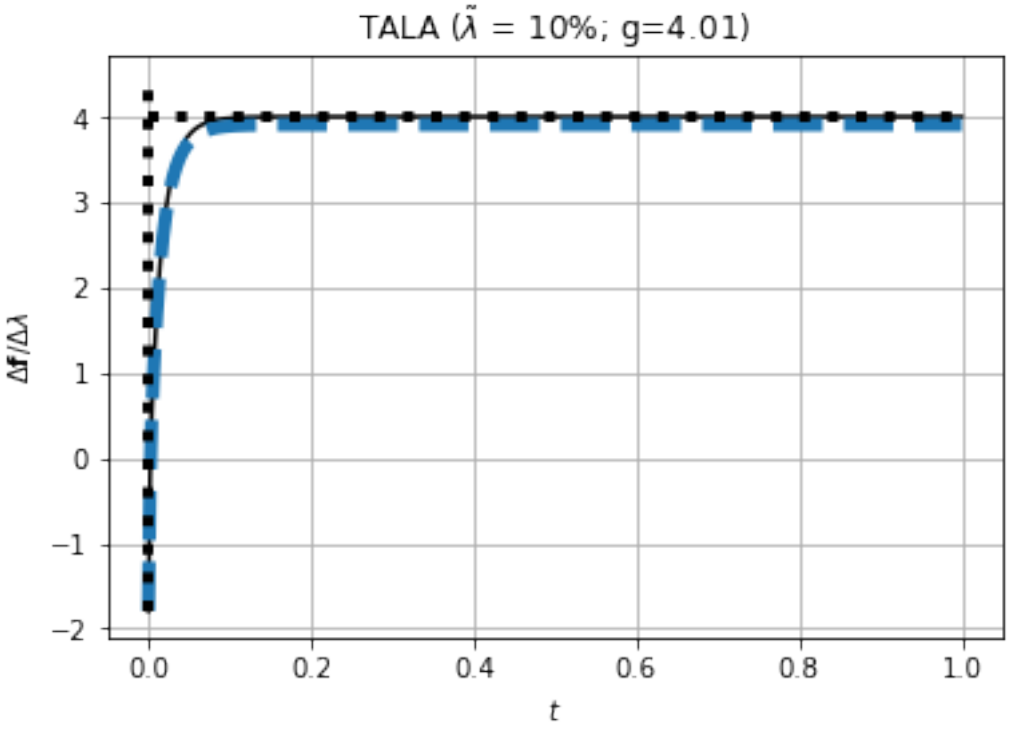

```
Doing: sRPI
kappa_RPI
g = -0.009544022155095424 tau = 0.00017769464683751047
dlam = 10
G3P
```



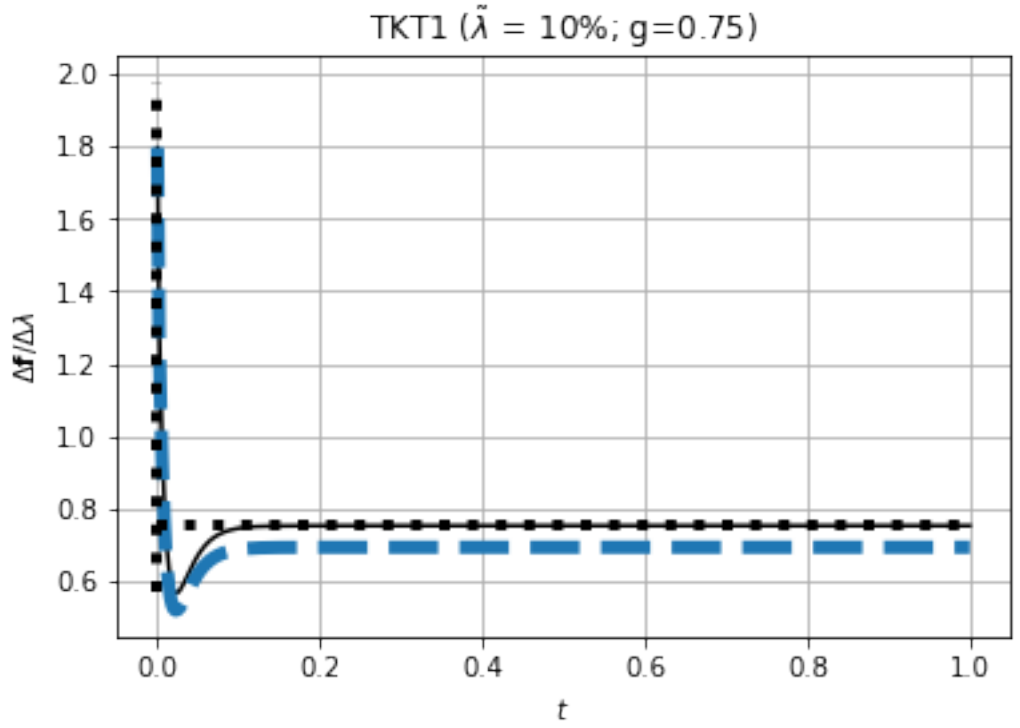

```
Doing: sTKT2
kappa_TKT2
g = 0.2759715745850926 tau = 0
dlam = 10
G3P
```



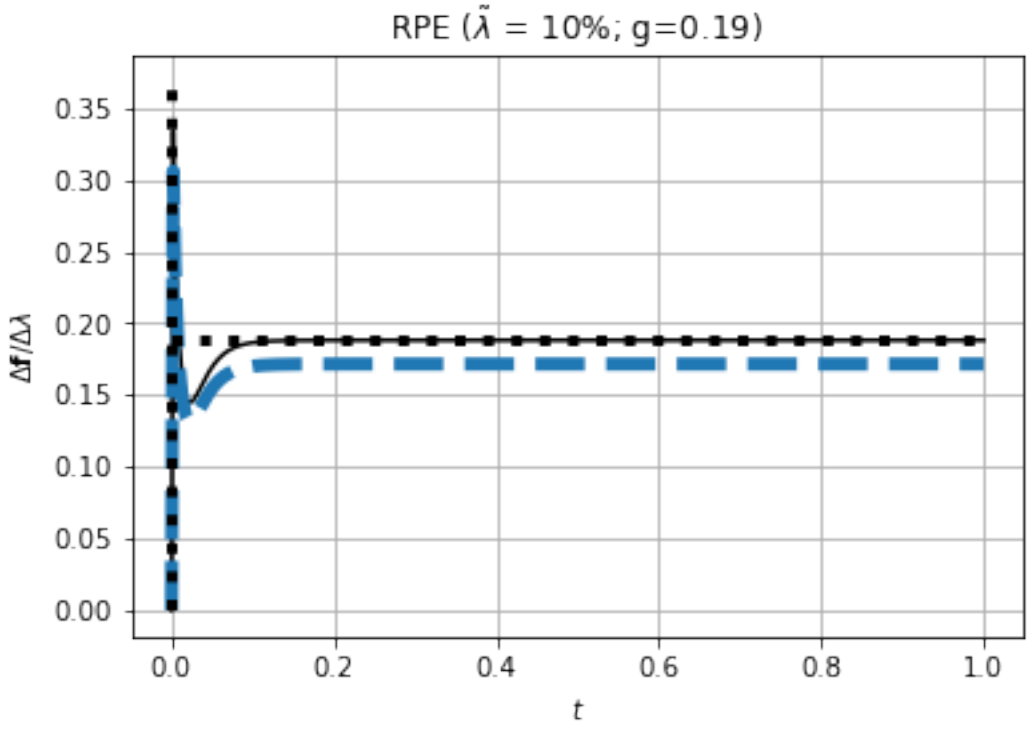
```
Doing: sTALA
kappa_TALA
g = 4.011429900742118 tau = 0
dlam = 10
G3P
```

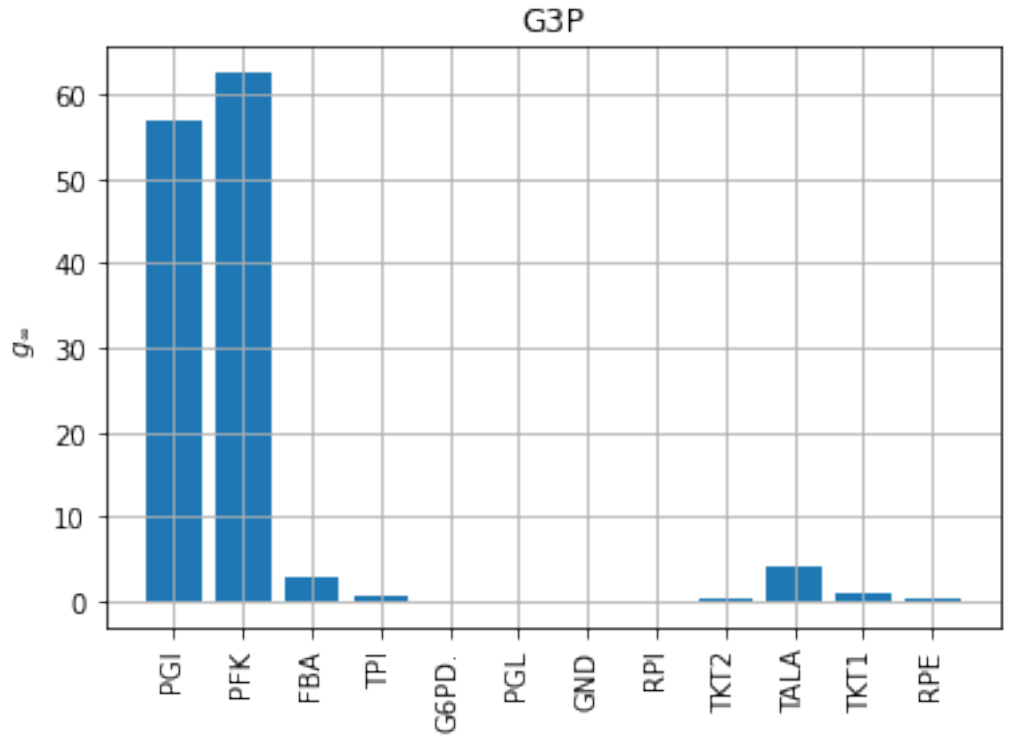


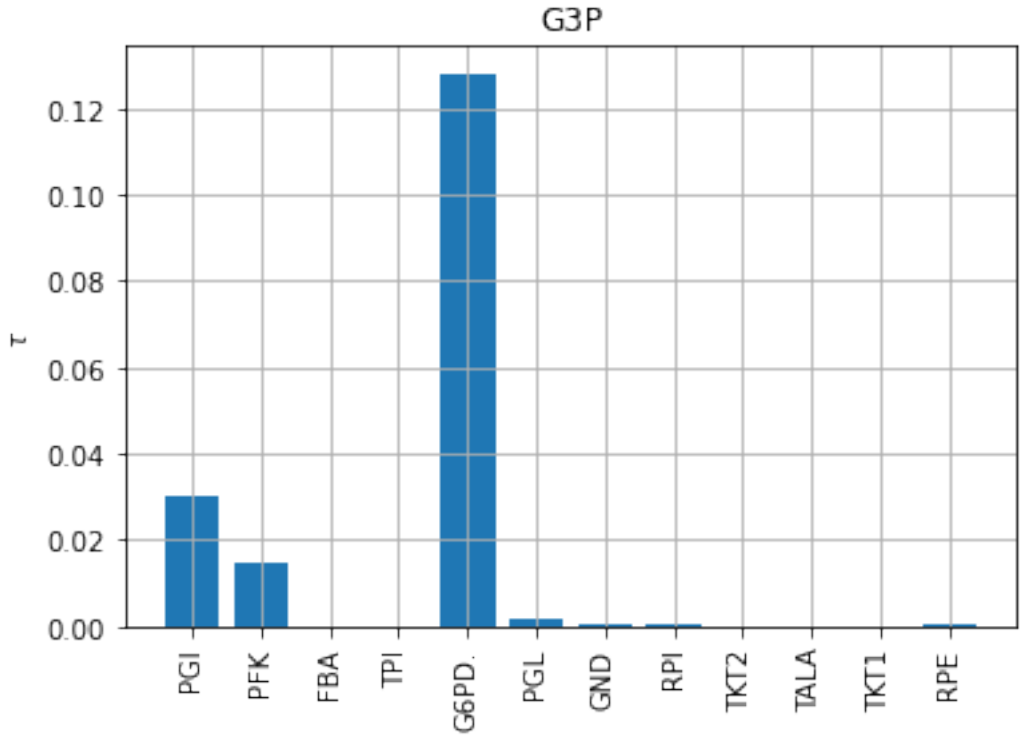

```
Doing: sTKT1
kappa_TKT1
g = 0.7533124901897006 tau = 0
dlam = 10
G3P
```




```
Doing: sRPE
kappa_RPE
g = 0.18809604636010738 tau = 0.00016682574714716445
dlam = 10
G3P
```




G3P
60
50
40
30
20
10
0
PGI
PFK
FBA
TPI
G6PD.
PGL
GND
RPI
TKT2
TALA
TKT1
RPE

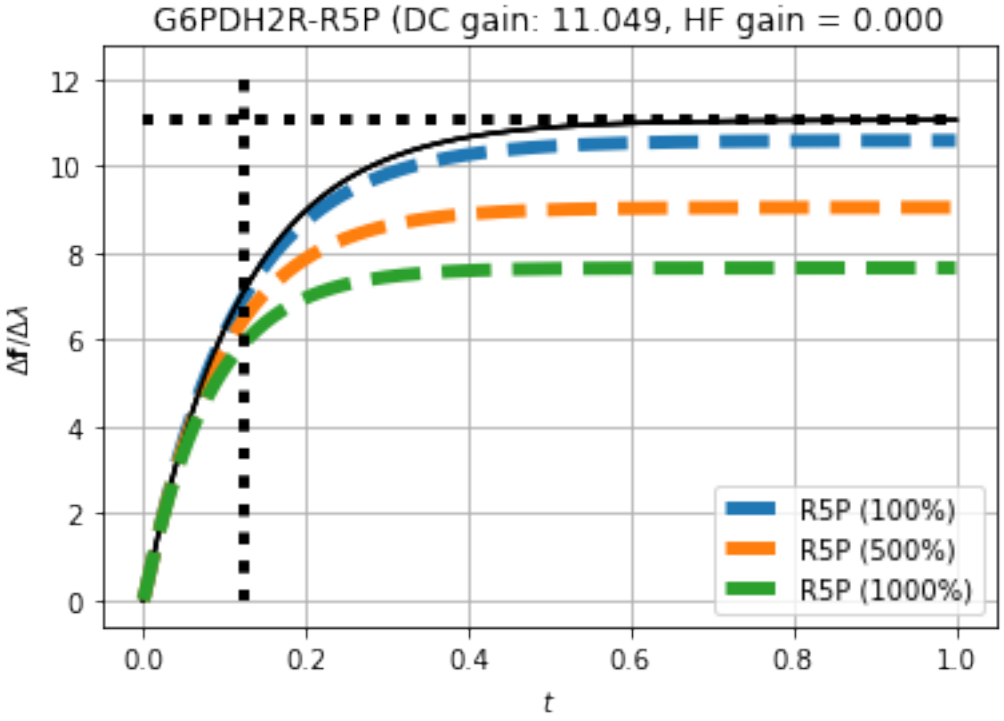

G3P
0.12
0.10
0.08
0.06
0.04
0.02
0.00
PGI
PFK
FBA
TPI
G6PD.
PGL
GND
RPI
TKT2
TALA
TKT1
RPE

6.5 Vary Lambda

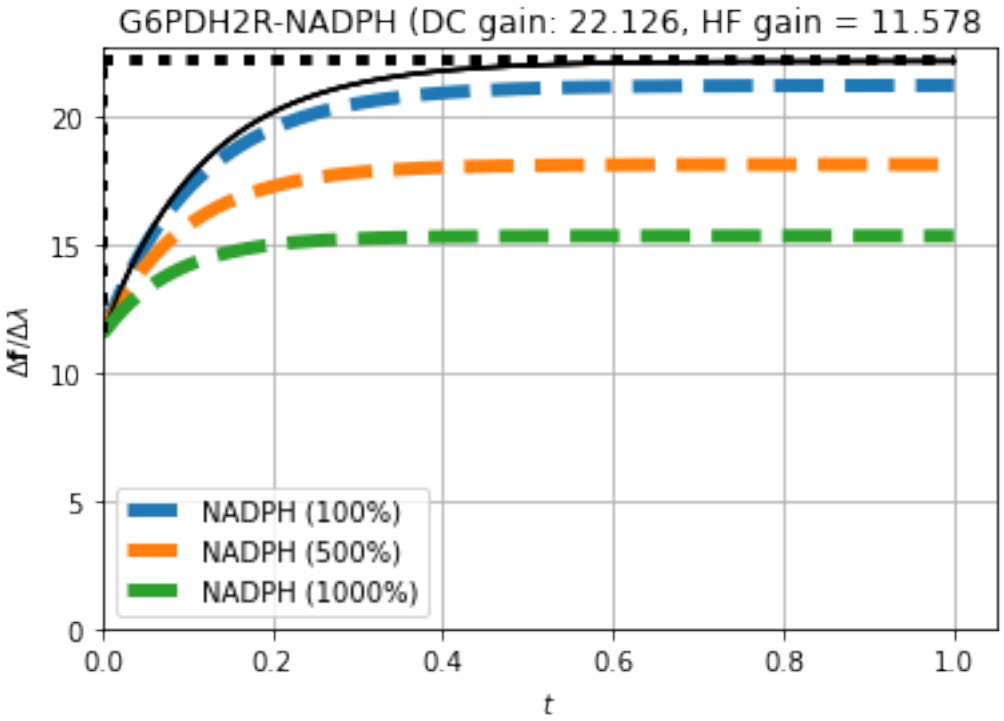
[34]:
```
## Vary Lambda

# inp = 'sG6PDH2R'
# outp = ['R5P']
Lin = {}
Nlin = {}
Lam = [1.1,2,6,11]
species = s['species']
for inp in ['sG6PDH2R','sG6P']:
    for outp in ['R5P','NADPH']:
        lin = []
        nlin = []
        for lam in Lam:
            dat,y_step,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)
#             g = con.dcgain(sys)
            g,tau = tfProps(sys)
            g_hf = hfgain(sys)

            lin.append(g)
            i = species.index(outp)
            dX = dat['dX'][-1,i]
            ng = (dX-dX_ss[i])/(lam-1)
            nlin.append(ng)

            name = inp[1:]
            Name = f'{name}-{outp}'
            print(f'{Name} (DC gain: {g:.3f}, HF gain = {g_hf:.3f}')
            if Titles:
                plt.title(f'{Name} (DC gain: {g:.3f}, HF gain = {g_hf:.3f}')
            if lam>1.5:
                setZero = outp in ['NADPH']
                plotSensitivitydX(dat,species=[outp],setZero=setZero)
                plotLines()
        Lin[Name] = lin
        Nlin[Name] = nlin
        Savefig(f'PPPdX_{name}_{outp}_lambda')
        plt.show()
# print(Lin)
# print(Nlin)
```

```
kappa_G6PDH2R
G6PDH2R-R5P (DC gain: 11.049, HF gain = 0.000
kappa_G6PDH2R
G6PDH2R-R5P (DC gain: 11.049, HF gain = 0.000
R5P
kappa_G6PDH2R
G6PDH2R-R5P (DC gain: 11.049, HF gain = 0.000
```

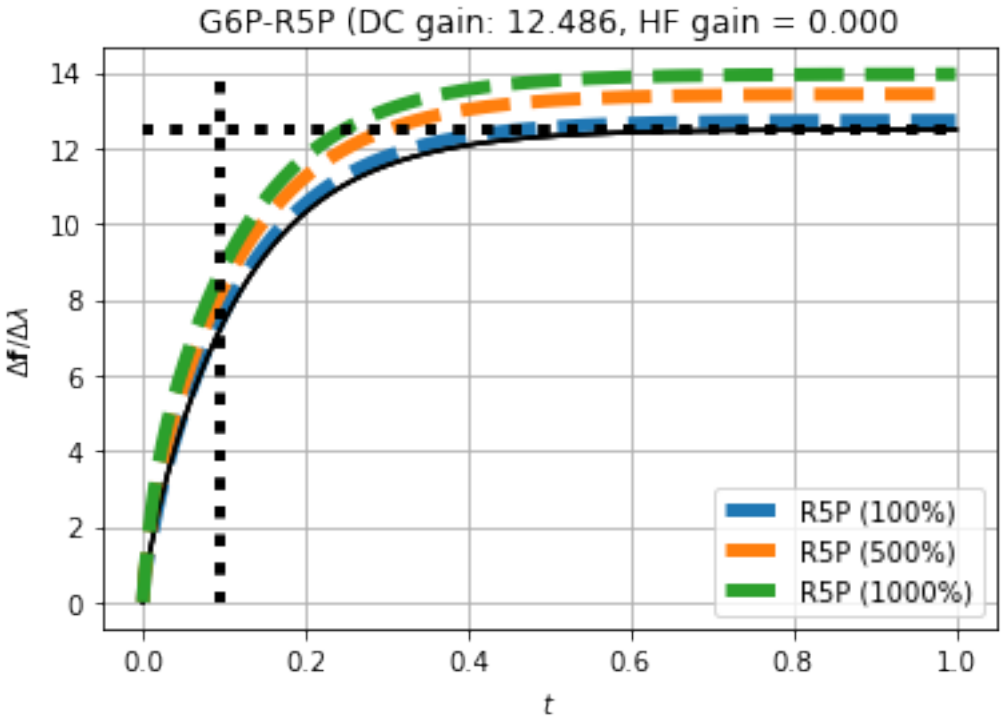
```
R5P
kappa_G6PDH2R
G6PDH2R-R5P (DC gain: 11.049, HF gain = 0.000
R5P
```



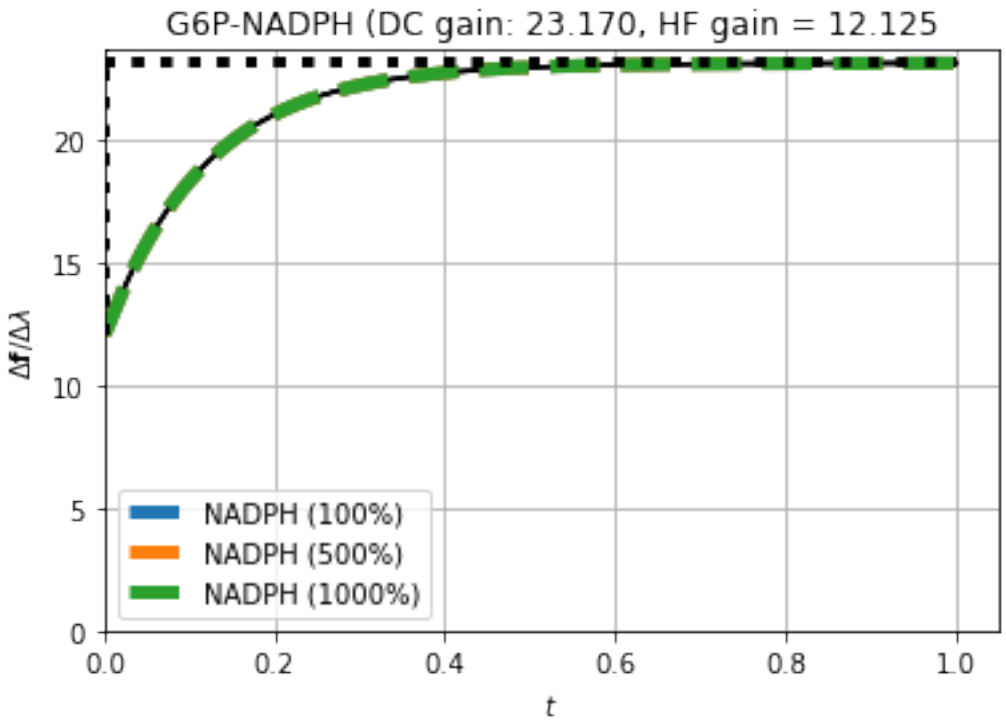

```
kappa_G6PDH2R
G6PDH2R-NADPH (DC gain: 22.126, HF gain = 11.578
kappa_G6PDH2R
G6PDH2R-NADPH (DC gain: 22.126, HF gain = 11.578
NADPH
kappa_G6PDH2R
G6PDH2R-NADPH (DC gain: 22.126, HF gain = 11.578
NADPH
kappa_G6PDH2R
G6PDH2R-NADPH (DC gain: 22.126, HF gain = 11.578
NADPH
```




```
K_G6P
G6P-R5P (DC gain: 12.486, HF gain = 0.000
K_G6P
G6P-R5P (DC gain: 12.486, HF gain = 0.000
R5P
K_G6P
G6P-R5P (DC gain: 12.486, HF gain = 0.000
R5P
K_G6P
G6P-R5P (DC gain: 12.486, HF gain = 0.000
R5P
```



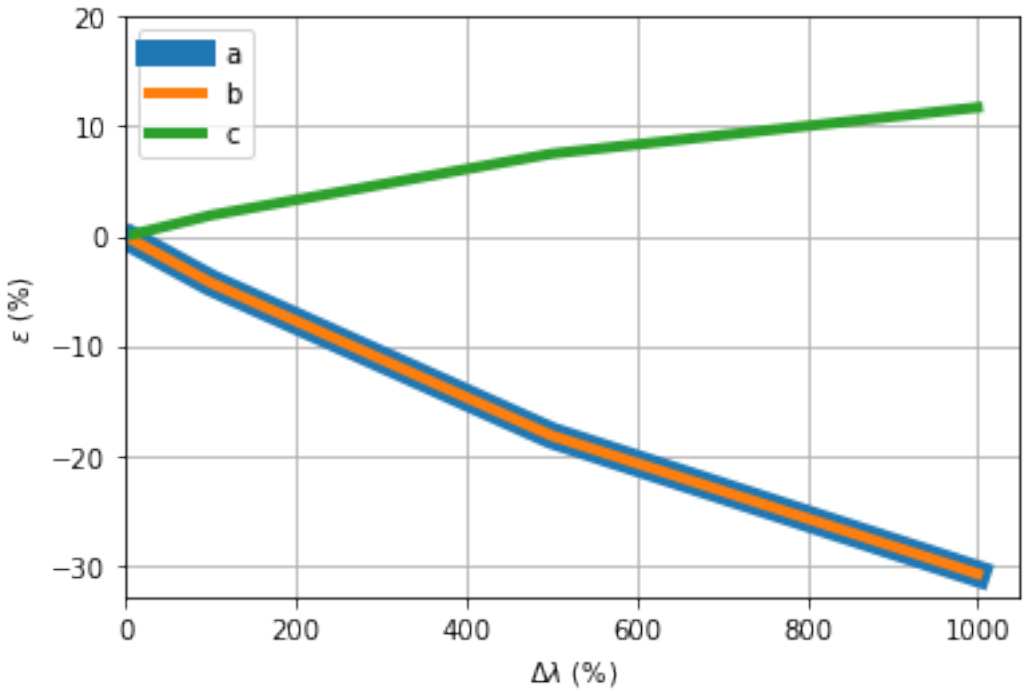

```
K_G6P
G6P-NADPH (DC gain: 23.170, HF gain = 12.125
K_G6P
G6P-NADPH (DC gain: 23.170, HF gain = 12.125
NADPH
K_G6P
G6P-NADPH (DC gain: 23.170, HF gain = 12.125
NADPH
K_G6P
G6P-NADPH (DC gain: 23.170, HF gain = 12.125
NADPH
```



[35]:
```
## Plot error curves
name = ['a','b','c','d']
lw = [10,4,4,4]
for i,Name in enumerate(Nlin):
    print(Name)
    G = np.array(Lin[Name])
    NG = np.array(Nlin[Name])
    Err = (NG-G)/G
    ErrPC = 100*Err
    LamPC = (Lam-np.ones(len(Lam)))*100

    ## Just plot the first 3
    if i<3:
        plt.plot(LamPC,ErrPC,label=name[i],lw=lw[i])

plt.legend()
plt.grid()
plt.ylim(top=20)
plt.xlim(left=0)
plt.xlabel(r'$\Delta \lambda$ (%)')
# plt.ylabel(r'$\tilde{\dot{x}}/\tilde{\lambda}-g$ (%)')
plt.ylabel(r'$\epsilon$ (%)')
Savefig(f'PPPdX_lambda')
plt.show()
```

```
G6PDH2R-R5P
G6PDH2R-NADPH
```

```
G6P-R5P
G6P-NADPH
```



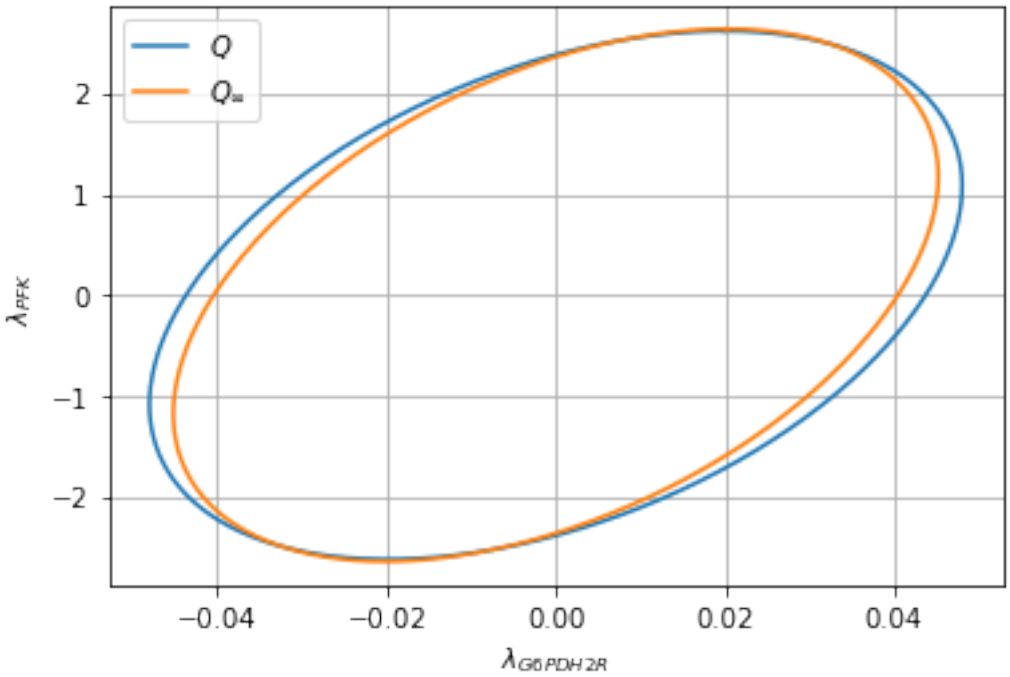
7 Sloppy parameter analysis

[36]:
```
imp.reload(slp)
def sloppy(Sys,inp,outp,t=None):

    sys = extractSubsystem(Sys,sc,sf,inp,outp)
    #print(sys)
    H,eig,eigv,t = slp.Sloppy(sys,t=t)
    cond = np.linalg.cond(H)
    print(f'Log10 condition number: {np.log10(cond):.1f}')
    slp.SloppyPrint(eig,eigv,inp)
    slp.SloppyPlot(eig,eigv,inp,square=False)
    #slp.SloppyPlotData(t,y,inp,outp)


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

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

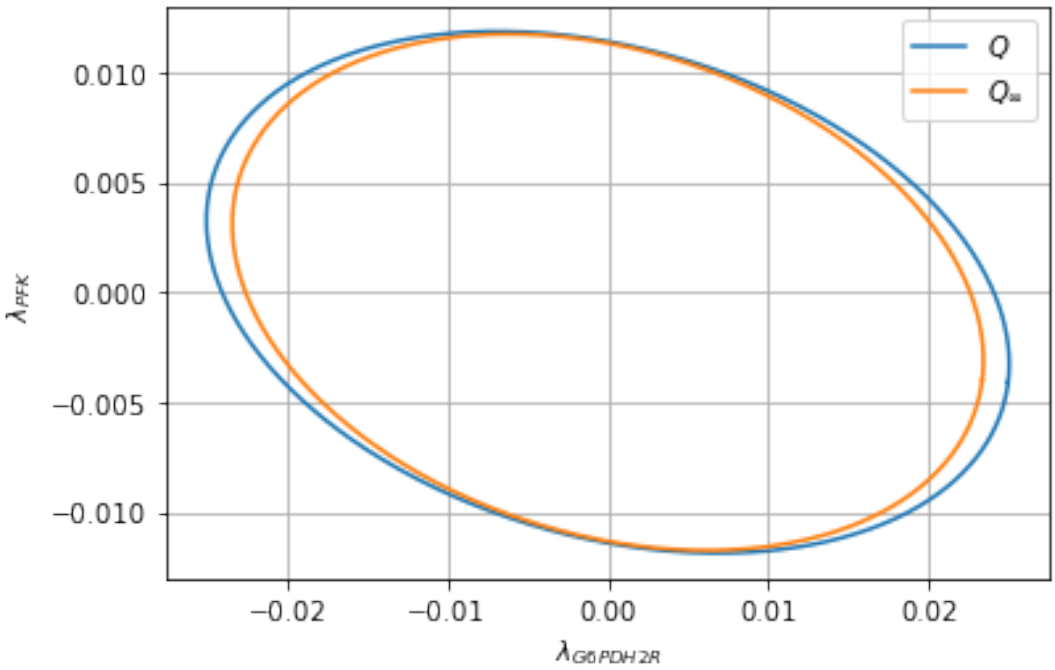
```
        name = f'{SysName}_sloppy_{inp[0]}_long'

    #print(sys)
    H,eig,eigv,t = slp.Sloppy(sys,t=t,GainOnly=False)
    print('H:\n',H)
    slp.SloppyPrint(eig,eigv,inp,min_eig=0)
    H,Eig,Eigv,t = slp.Sloppy(sys,t=t,GainOnly=True)
    print('H_ss:\n',H)
    slp.SloppyPrint(Eig,Eigv,inp,min_eig=0)
    slp.SloppyPlot(eig,eigv,inp,Eig=Eig,Eigv=Eigv)

    Savefig(name)
    plt.show()


for t_last in [0,1e1]:
    if t_last==0:
        t = None
    else:
        t = np.linspace(0,t_last,100)

    SysName = 'GlyPPP_PFK_2'
    inp = ['sG6PDH2R','sPFK']
    outp = ['NADPH','R5P']
    sloppyBoth(Sys,inp,outp,t=t)

    SysName = 'GlyPPP_PFK_all'
    Outp = []
    for chemo in sc['chemostats']:
        if not chemo[0] in ['s']:
            Outp.append(chemo)
    print(Outp)
    sloppyBoth(Sys,inp,Outp,t=t)

    SysName = 'GlyPPP_PGI_all'
    inp = ['sG6PDH2R','sPGI']
    sloppyBoth(Sys,inp,Outp,t=t)
```

```
******************************
 GlyPPP_PFK_2
******************************

H:
 [[ 5.23558279e+02 -3.97898795e+00]
 [-3.97898795e+00  1.76090966e-01]]
\sqrt\sigma_1 &= 23 & V_1\Lambda &= + 1.00 \lambda_{G6PDH2R} - 0.01
\lambda_{PFK}
\sqrt\sigma_2 &= 0.38 & V_2\Lambda &= + 1.00 \lambda_{PFK} + 0.01
\lambda_{G6PDH2R}
H_ss:
```

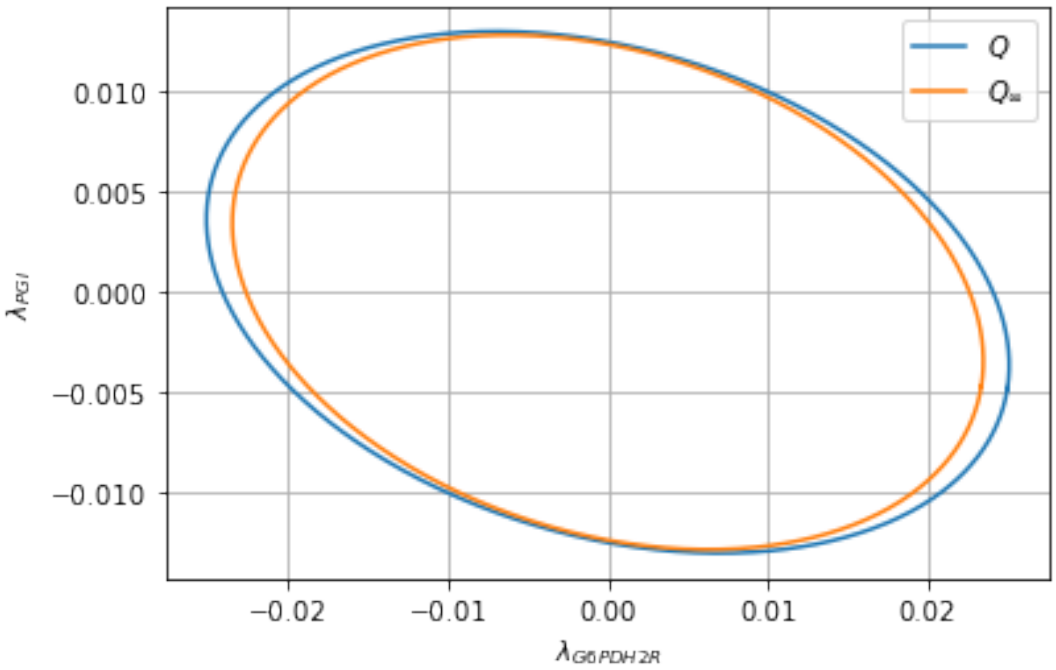
```
 [[ 6.12e+02 -4.68e+00]
 [-4.68e+00  1.79e-01]]
\sqrt\sigma_1 &= 25 & V_1\Lambda &= + 1.00 \lambda_{G6PDH2R} - 0.01
\lambda_{PFK}
\sqrt\sigma_2 &= 0.38 & V_2\Lambda &= + 1.00 \lambda_{PFK} + 0.01
\lambda_{G6PDH2R}
```



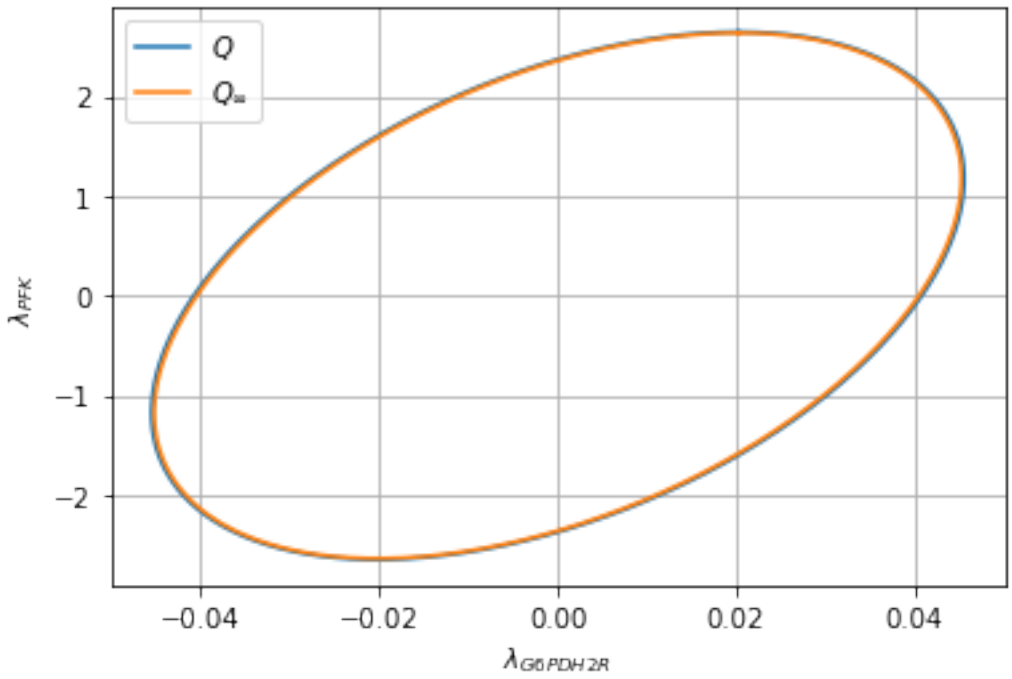

```
['ADP', 'ATP', 'CO2', 'G6P', 'H', 'H2O', 'NADP', 'NADPH', 'R5P', 'G3P']

******************************
 GlyPPP_PFK_all
******************************

H:
 [[1726.16 1001.12]
 [1001.12 7677.69]]
\sqrt\sigma_1 &= 89 & V_1\Lambda &= + 0.99 \lambda_{PFK} + 0.16
\lambda_{G6PDH2R}
\sqrt\sigma_2 &= 40 & V_2\Lambda &= + 0.99 \lambda_{G6PDH2R} - 0.16
\lambda_{PFK}
H_ss:
 [[1958.04 1028.65]
 [1028.65 7785.82]]
\sqrt\sigma_1 &= 89 & V_1\Lambda &= + 0.99 \lambda_{PFK} + 0.17
\lambda_{G6PDH2R}
\sqrt\sigma_2 &= 42 & V_2\Lambda &= + 0.99 \lambda_{G6PDH2R} - 0.17
\lambda_{PFK}
```



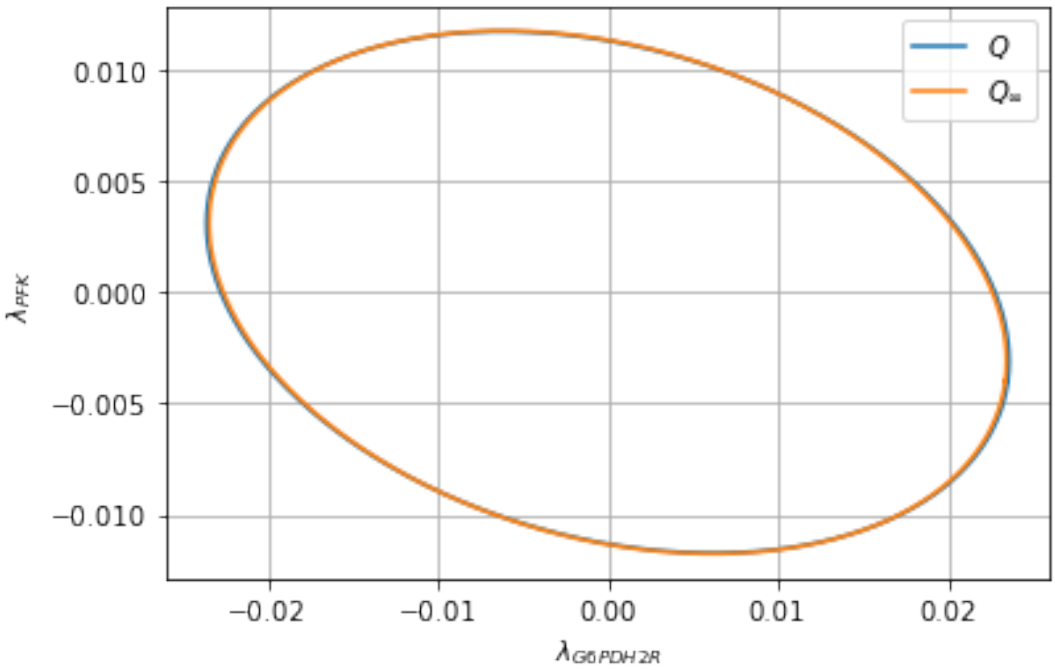

```
*******************************
 GlyPPP_PGI_all
*******************************

H:
 [[1726.16  928.88]
 [ 928.88 6383.28]]
\sqrt\sigma_1 &= 81 & V_1\Lambda &= + 0.98 \lambda_{PGI} + 0.19
\lambda_{G6PDH2R}
\sqrt\sigma_2 &= 39 & V_2\Lambda &= + 0.98 \lambda_{G6PDH2R} - 0.19
\lambda_{PGI}
H_ss:
 [[1958.04  955.61]
 [ 955.61 6511.65]]
\sqrt\sigma_1 &= 82 & V_1\Lambda &= + 0.98 \lambda_{PGI} + 0.20
\lambda_{G6PDH2R}
\sqrt\sigma_2 &= 42 & V_2\Lambda &= + 0.98 \lambda_{G6PDH2R} - 0.20
\lambda_{PGI}
```



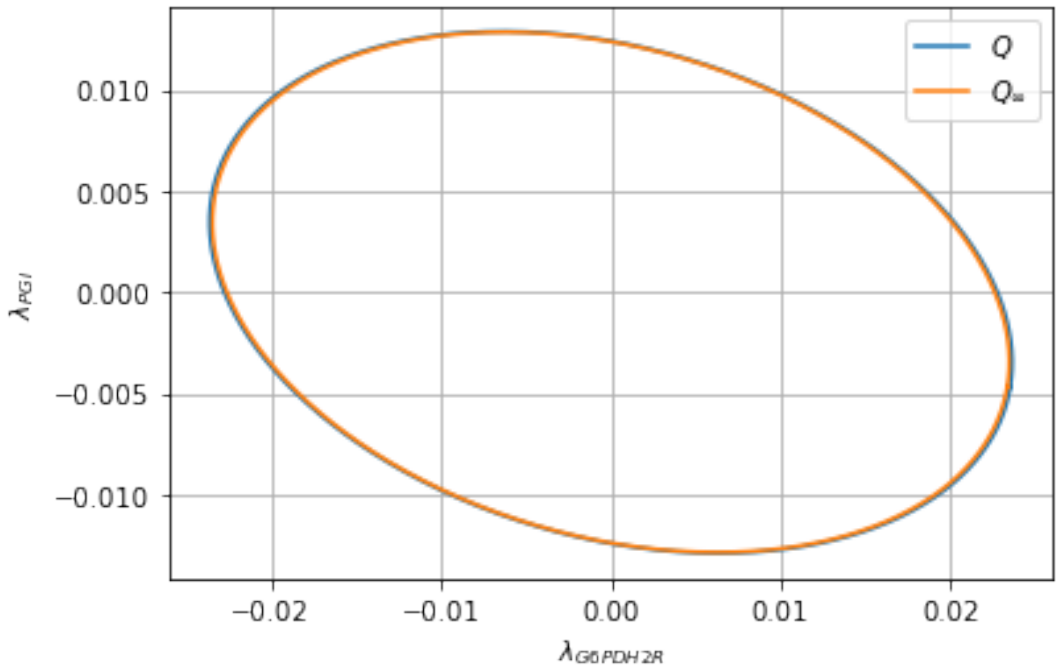

```
*******************************
 GlyPPP_PFK_2
*******************************

H:
 [[ 6.02e+02 -4.60e+00]
 [-4.60e+00  1.78e-01]]
\sqrt\sigma_1 &= 25 & V_1\Lambda &= + 1.00 \lambda_{G6PDH2R} - 0.01
\lambda_{PFK}
\sqrt\sigma_2 &= 0.38 & V_2\Lambda &= + 1.00 \lambda_{PFK} + 0.01
\lambda_{G6PDH2R}
H_ss:
 [[ 6.12e+02 -4.68e+00]
 [-4.68e+00  1.79e-01]]
\sqrt\sigma_1 &= 25 & V_1\Lambda &= + 1.00 \lambda_{G6PDH2R} - 0.01
\lambda_{PFK}
\sqrt\sigma_2 &= 0.38 & V_2\Lambda &= + 1.00 \lambda_{PFK} + 0.01
\lambda_{G6PDH2R}
```




```
['ADP', 'ATP', 'CO2', 'G6P', 'H', 'H2O', 'NADP', 'NADPH', 'R5P', 'G3P']

******************************
 GlyPPP_PFK_all
******************************

H:
 [[1930.92 1024.22]
 [1024.22 7827.07]]
\sqrt\sigma_1 &= 89 & V_1\Lambda &= + 0.99 \lambda_{PFK} + 0.17
\lambda_{G6PDH2R}
\sqrt\sigma_2 &= 42 & V_2\Lambda &= + 0.99 \lambda_{G6PDH2R} - 0.17
\lambda_{PFK}
H_ss:
 [[1958.04 1028.65]
 [1028.65 7785.82]]
\sqrt\sigma_1 &= 89 & V_1\Lambda &= + 0.99 \lambda_{PFK} + 0.17
\lambda_{G6PDH2R}
\sqrt\sigma_2 &= 42 & V_2\Lambda &= + 0.99 \lambda_{G6PDH2R} - 0.17
\lambda_{PFK}
```




```
*******************************
 GlyPPP_PGI_all
*******************************

H:
 [[1930.92  951.55]
 [ 951.55 6481.53]]
\sqrt\sigma_1 &= 82 & V_1\Lambda &= + 0.98 \lambda_{PGI} + 0.20
\lambda_{G6PDH2R}
\sqrt\sigma_2 &= 42 & V_2\Lambda &= + 0.98 \lambda_{G6PDH2R} - 0.20
\lambda_{PGI}
H_ss:
 [[1958.04  955.61]
 [ 955.61 6511.65]]
\sqrt\sigma_1 &= 82 & V_1\Lambda &= + 0.98 \lambda_{PGI} + 0.20
\lambda_{G6PDH2R}
\sqrt\sigma_2 &= 42 & V_2\Lambda &= + 0.98 \lambda_{G6PDH2R} - 0.20
\lambda_{PGI}
```



[37]:
```
imp.reload(slp)
Outp = ['R5P','NADPH','G3P']
# Outp = ['R5P']
def PrintSloppy(Inp,Outp,GainOnly=True):
    blurb = '\n*********\n'
    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)
        slp.SloppyPrint(eig,eigv,Inp,min_eig=0.01,min_eigv=0.1,max_eigs=5)
        if GainOnly:
            print('Direct')
            slp.SloppyPrint([norm],np.array([ngain]).T,Inp,min_eig=0.
 ↪01,min_eigv=0.1,max_eigs=5)
#         print(eigv[:,0])
#         print(ngain)

## Reactions
for GainOnly in [True,False]:
    print('\nGainOnly =',GainOnly)
    PrintSloppy(Inp_reac,Outp,GainOnly=GainOnly)
```

```
GainOnly = True
```

```
*********
 R5P
*********

\sqrt\sigma_1 &= 12 & V_1\Lambda &= + 0.93 \lambda_{G6PDH2R} - 0.35
\lambda_{TALA}
Direct
\sqrt\sigma_1 &= 12 & V_1\Lambda &= + 0.93 \lambda_{G6PDH2R} - 0.35
\lambda_{TALA}

*********
 NADPH
*********

\sqrt\sigma_1 &= 22 & V_1\Lambda &= + 1.00 \lambda_{G6PDH2R}
Direct
\sqrt\sigma_1 &= 22 & V_1\Lambda &= + 1.00 \lambda_{G6PDH2R}

*********
 G3P
*********

\sqrt\sigma_1 &= 85 & V_1\Lambda &= + 0.74 \lambda_{PFK} + 0.67 \lambda_{PGI}
Direct
\sqrt\sigma_1 &= 85 & V_1\Lambda &= + 0.74 \lambda_{PFK} + 0.67 \lambda_{PGI}

GainOnly = False

*********
 R5P
*********

\sqrt\sigma_1 &= 11 & V_1\Lambda &= + 0.91 \lambda_{G6PDH2R} - 0.38
\lambda_{TALA} + 0.15 \lambda_{GND}
\sqrt\sigma_2 &= 3 & V_2\Lambda &= + 0.94 \lambda_{GND} - 0.25 \lambda_{G6PDH2R}
- 0.21 \lambda_{TALA}

*********
 NADPH
*********

\sqrt\sigma_1 &= 21 & V_1\Lambda &= + 0.99 \lambda_{G6PDH2R} + 0.11
\lambda_{GND}
\sqrt\sigma_2 &= 2.7 & V_2\Lambda &= + 0.99 \lambda_{GND} - 0.11
\lambda_{G6PDH2R}

*********
 G3P
*********
```

```
\sqrt\sigma_1 &= 76 & V_1\Lambda &= + 0.74 \lambda_{PFK} + 0.65 \lambda_{PGI} +
0.16 \lambda_{FBA}
\sqrt\sigma_2 &= 26 & V_2\Lambda &= + 0.94 \lambda_{FBA} + 0.29 \lambda_{TPI} -
0.17 \lambda_{PGI}
```

[38]:
```
## Chemostats
for GainOnly in [True,False]:
    print('\nGainOnly =',GainOnly)
    PrintSloppy(Inp_chemo,Outp,GainOnly=GainOnly)
```

```
GainOnly = True

*********
 R5P
*********

\sqrt\sigma_1 &= 21 & V_1\Lambda &= + 0.59 \lambda_{G6P} + 0.57 \lambda_{NADP} -
0.56 \lambda_{R5P}
Direct
\sqrt\sigma_1 &= 21 & V_1\Lambda &= + 0.59 \lambda_{G6P} + 0.57 \lambda_{NADP} -
0.56 \lambda_{R5P}

*********
 NADPH
*********

\sqrt\sigma_1 &= 34 & V_1\Lambda &= + 0.72 \lambda_{NADP} + 0.69 \lambda_{G6P}
Direct
\sqrt\sigma_1 &= 34 & V_1\Lambda &= + 0.72 \lambda_{NADP} + 0.69 \lambda_{G6P}

*********
 G3P
*********

\sqrt\sigma_1 &= 1.4e+02 & V_1\Lambda &= + 0.87 \lambda_{G6P} + 0.48
\lambda_{ATP}
Direct
\sqrt\sigma_1 &= 1.4e+02 & V_1\Lambda &= + 0.87 \lambda_{G6P} + 0.48
\lambda_{ATP}

GainOnly = False

*********
 R5P
*********

\sqrt\sigma_1 &= 1.5e+03 & V_1\Lambda &= + 1.00 \lambda_{R5P}

*********
 NADPH
```

```
*********

\sqrt\sigma_1 &= 32 & V_1\Lambda &= + 0.74 \lambda_{NADP} + 0.67 \lambda_{G6P}

*********
 G3P
*********

\sqrt\sigma_1 &= 1.3e+02 & V_1\Lambda &= + 0.86 \lambda_{G6P} + 0.48
\lambda_{ATP} - 0.16 \lambda_{G3P}
\sqrt\sigma_2 &= 48 & V_2\Lambda &= + 0.98 \lambda_{G3P} + 0.17 \lambda_{G6P}
```

[39]:
```
## Three outputs
Outp = ['R5P','NADPH','G3P']
sys = extractSubsystem(Sys,sc,sf,Inp,Outp)
for GainOnly in [True,False]:
    print('\nGainOnly =',GainOnly)
    H,eig,eigv,t = slp.Sloppy(sys,GainOnly=GainOnly,small=1e-10)
    slp.SloppyPrint(eig,eigv,Inp,min_eig=1e-3,min_eigv=0.1,max_eigs=4)
```

```
GainOnly = True
\sqrt\sigma_1 &= 85 & V_1\Lambda &= + 0.74 \lambda_{PFK} + 0.67 \lambda_{PGI}
\sqrt\sigma_2 &= 25 & V_2\Lambda &= + 1.00 \lambda_{G6PDH2R}
\sqrt\sigma_3 &= 3.8 & V_3\Lambda &= + 0.97 \lambda_{TALA} + 0.18 \lambda_{TKT1}
- 0.14 \lambda_{PGI}

GainOnly = False
\sqrt\sigma_1 &= 83 & V_1\Lambda &= + 0.74 \lambda_{PFK} + 0.67 \lambda_{PGI}
\sqrt\sigma_2 &= 23 & V_2\Lambda &= + 0.99 \lambda_{G6PDH2R} + 0.12
\lambda_{GND}
\sqrt\sigma_3 &= 11 & V_3\Lambda &= + 0.95 \lambda_{FBA} + 0.29 \lambda_{TPI}
\sqrt\sigma_4 &= 4.3 & V_4\Lambda &= + 0.73 \lambda_{GND} - 0.64 \lambda_{TALA}
- 0.14 \lambda_{G6PDH2R} - 0.14 \lambda_{TKT1}
```

[40]:
```
## All outputs
for chemo in sc['chemostats']:
    if not chemo[0] in ['s']:
        Outp.append(chemo)
print(Outp)
sys = extractSubsystem(Sys,sc,sf,Inp,Outp)

for GainOnly in [True,False]:
    print('\nGainOnly =',GainOnly)
    H,eig,eigv,t = slp.Sloppy(sys,GainOnly=GainOnly,small=1e-10)
    slp.SloppyPrint(eig,eigv,Inp,min_eig=0.001,min_eigv=0.1,max_eigs=4)
```

```
['R5P', 'NADPH', 'G3P', 'ADP', 'ATP', 'CO2', 'G6P', 'H', 'H2O', 'NADP', 'NADPH',
'R5P', 'G3P']

GainOnly = True
\sqrt\sigma_1 &= 1.5e+02 & V_1\Lambda &= + 0.74 \lambda_{PFK} + 0.67
```

```
\lambda_{PGI}
\sqrt\sigma_2 &= 50 & V_2\Lambda &= + 0.99 \lambda_{G6PDH2R}
\sqrt\sigma_3 &= 6.3 & V_3\Lambda &= + 0.97 \lambda_{TALA} + 0.18 \lambda_{TKT1}
- 0.13 \lambda_{PGI}

GainOnly = False
\sqrt\sigma_1 &= 1.5e+02 & V_1\Lambda &= + 0.74 \lambda_{PFK} + 0.67
\lambda_{PGI}
\sqrt\sigma_2 &= 47 & V_2\Lambda &= + 0.99 \lambda_{G6PDH2R} + 0.11
\lambda_{GND}
\sqrt\sigma_3 &= 16 & V_3\Lambda &= + 0.95 \lambda_{FBA} + 0.29 \lambda_{TPI}
\sqrt\sigma_4 &= 7.4 & V_4\Lambda &= + 0.92 \lambda_{GND} - 0.35 \lambda_{TALA}
- 0.12 \lambda_{G6PDH2R}
```

[ ]: