In [69]:
```
import tellurium as te
from urllib.request import urlopen
%matplotlib inline
```

Roadrunner Methoden

Query an antimony model from model db's:

Load the "Repressilator". Therefore use urlopen() and the methods read().decode('utf-8').

The URL for the repressilator reads: http://antimony.sourceforge.net/examples/biomodels/BIOMD0000000012.txt (http://antimony.sourceforge.net/examples/biomodels/BIOMD0000000012.txt)

Elowitz, M. B., & Leibler, S. (2000). A synthetic oscillatory network of transcriptional regulators. Nature, 403(6767), 335-338.

In [70]:
```
Repressilator = urlopen('http://antimony.sourceforge.net/examples/biomodels/BIOMD0000000012.txt').read().decode('ut
f-8')
print(Repressilator)
```

```
// Created by libAntimony v2.8.0
model *BIOMD0000000012()

  // Compartments and Species:
  compartment cell;
  substanceOnly species PX in cell, PY in cell, PZ in cell, X in cell, Y in cell;
  substanceOnly species Z in cell;

  // Assignment Rules:
  beta := tau_mRNA/tau_prot;
  alpha0 := (a0_tr*eff*tau_prot)/(ln(2)*KM);
  a0_tr := ps_0*60;
  alpha := (a_tr*eff*tau_prot)/(ln(2)*KM);
  a_tr := (ps_a - ps_0)*60;
  t_ave := tau_mRNA/ln(2);
  kd_mRNA := ln(2)/tau_mRNA;
  kd_prot := ln(2)/tau_prot;
  k_tl := eff/t_ave;

  // Reactions:
  Reaction1: X => ; kd_mRNA*X;
  Reaction2: Y => ; kd_mRNA*Y;
  Reaction3: Z => ; kd_mRNA*Z;
  Reaction4:  => PX; k_tl*X;
  Reaction5:  => PY; k_tl*Y;
  Reaction6:  => PZ; k_tl*Z;
  Reaction7: PX => ; kd_prot*PX;
  Reaction8: PY => ; kd_prot*PY;
  Reaction9: PZ => ; kd_prot*PZ;
  Reaction10:  => X; a0_tr + (a_tr*KM^n)/(KM^n + PZ^n);
  Reaction11:  => Y; a0_tr + (a_tr*KM^n)/(KM^n + PX^n);
  Reaction12:  => Z; a0_tr + (a_tr*KM^n)/(KM^n + PY^n);

  // Species initializations:
  PX = 0;
  PY = 0;
  PZ = 0;
  X = 0;
  Y = 20/cell;
  Z = 0;

  // Compartment initializations:
  cell = 1;

  // Variable initializations:
  tau_mRNA = 2;
  tau_prot = 10;
  eff = 20;
  KM = 40;
  n = 2;
  ps_a = 0.5;
  ps_0 = 0.0005;

  // Other declarations:
  var beta, alpha0, a0_tr, alpha, a_tr, t_ave, kd_mRNA, kd_prot, k_tl;
  const cell, tau_mRNA, tau_prot, eff, KM, n, ps_a, ps_0;

  // Unit definitions:
  unit volume = 1e-15 litre;
  unit substance = item;
  unit time_unit = 60 second;

  // Display Names:
  volume is "cubic microns";
  substance is "item";
  time_unit is "minute";
  PX is "LacI protein";
  PY is "TetR protein";
  PZ is "cI protein";
  X is "LacI mRNA";
  Y is "TetR mRNA";
  Z is "cI mRNA";
  tau_mRNA is "mRNA half life";
  tau_prot is "protein half life";
  eff is "translation efficiency";
  t_ave is "average mRNA life time";
  ps_a is "tps_active";
  ps_0 is "tps_repr";
  Reaction1 is "degradation of LacI transcripts";
  Reaction2 is "degradation of TetR transcripts";
  Reaction3 is "degradation of CI transcripts";
  Reaction4 is "translation of LacI";
  Reaction5 is "translation of TetR";
  Reaction6 is "translation of CI";
  Reaction7 is "degradation of LacI";
  Reaction8 is "degradation of TetR";
```

By loading a model you similarly generate a roadrunner object. Use loada() from tellurium.

In [71]:
```
rr = te.loada(Repressilator)
```

The following section illustrates several methods of roadrunner. For example you can print a model in different formats such as antimony or SBML. For this use getAntimony() or getSBML().

In [72]:
```
print(rr.getAntimony())
```

```
// Created by libAntimony v2.9.4
model *BIOMD0000000012()

  // Compartments and Species:
  compartment cell;
  substanceOnly species PX in cell, PY in cell, PZ in cell, X in cell, Y in cell;
  substanceOnly species Z in cell;

  // Assignment Rules:
  beta := tau_mRNA/tau_prot;
  alpha0 := a0_tr*eff*tau_prot/(ln(2)*KM);
  a0_tr := ps_0*60;
  alpha := a_tr*eff*tau_prot/(ln(2)*KM);
  a_tr := (ps_a - ps_0)*60;
  t_ave := tau_mRNA/ln(2);
  kd_mRNA := ln(2)/tau_mRNA;
  kd_prot := ln(2)/tau_prot;
  k_tl := eff/t_ave;

  // Reactions:
  Reaction1: X => ; kd_mRNA*X;
  Reaction2: Y => ; kd_mRNA*Y;
  Reaction3: Z => ; kd_mRNA*Z;
  Reaction4:  => PX; k_tl*X;
  Reaction5:  => PY; k_tl*Y;
  Reaction6:  => PZ; k_tl*Z;
  Reaction7: PX => ; kd_prot*PX;
  Reaction8: PY => ; kd_prot*PY;
  Reaction9: PZ => ; kd_prot*PZ;
  Reaction10:  => X; a0_tr + a_tr*KM^n/(KM^n + PZ^n);
  Reaction11:  => Y; a0_tr + a_tr*KM^n/(KM^n + PX^n);
  Reaction12:  => Z; a0_tr + a_tr*KM^n/(KM^n + PY^n);

  // Species initializations:
  PX = 0;
  PY = 0;
  PZ = 0;
  X = 0;
  Y = 20/cell;
  Z = 0;

  // Compartment initializations:
  cell = 1;

  // Variable initializations:
  tau_mRNA = 2;
  tau_prot = 10;
  eff = 20;
  KM = 40;
  ps_0 = 0.0005;
  ps_a = 0.5;
  n = 2;

  // Other declarations:
  var beta, alpha0, a0_tr, alpha, a_tr, t_ave, kd_mRNA, kd_prot, k_tl;
  const cell, tau_mRNA, tau_prot, eff, KM, ps_0, ps_a, n;

  // Unit definitions:
  unit volume = 1e-15 litre;
  unit substance = item;
  unit time_unit = 6e1 second;

  // Display Names:
  volume is "cubic microns";
  substance is "item";
  time_unit is "minute";
  PX is "LacI protein";
  PY is "TetR protein";
  PZ is "cI protein";
  X is "LacI mRNA";
  Y is "TetR mRNA";
  Z is "cI mRNA";
  tau_mRNA is "mRNA half life";
  tau_prot is "protein half life";
  eff is "translation efficiency";
  ps_0 is "tps_repr";
  ps_a is "tps_active";
  t_ave is "average mRNA life time";
  Reaction1 is "degradation of LacI transcripts";
  Reaction2 is "degradation of TetR transcripts";
  Reaction3 is "degradation of CI transcripts";
  Reaction4 is "translation of LacI";
  Reaction5 is "translation of TetR";
  Reaction6 is "translation of CI";
  Reaction7 is "degradation of LacI";
  Reaction8 is "degradation of TetR";
```

In [2]:
```
#print(rr.getSBML())
```

Solver Methoden

Attention: resetToOrigin() resets the model somewhat similar to to loada(). But integrator settings are not affected by this. Hence, always use te.loada() for a hard reset!

Use getIntegrator() to display the solver algorithm and solver settings.

In [73]:
```
rr = te.loada(Repressilator)
print(rr.getIntegrator())
```

```
< roadrunner.Integrator() >
  name: cvode
  settings:
      relative_tolerance: 0.000001
      absolute_tolerance: 0.000000000001
                   stiff: true
       maximum_bdf_order: 5
     maximum_adams_order: 12
       maximum_num_steps: 20000
       maximum_time_step: 0
       minimum_time_step: 0
       initial_time_step: 0
          multiple_steps: false
      variable_step_size: false
```

Change the solver method from 'CVODE' to 'rk45' and print the settings again. You may notice the default parameters are solver specific. Use methods setIntegrator() and getIntegrator().

In [74]:
```
rr = te.loada(Repressilator)
rr.setIntegrator('rk45')
print(rr.getIntegrator())
```

```
< roadrunner.Integrator() >
  name: rk45
  settings:
      variable_step_size: true
       minimum_time_step: 0.000000000001
       maximum_time_step: 1
                 epsilon: 0.000000000001
```

For example, use 'CVODE' and plot the model trajectories for different values for the 'relative_tolerance'-parameter.

Change the solver parameters via roadrunner.getIntegrator().setValue().

```
In [78]: rr = te.loada(Repressilator)
         rr.getIntegrator().setValue('relative_tolerance',1)
         rr.simulate(0,1000,1000)
         rr.plot()
```

Steady-State Analysis

In [80]:
```
rr = te.loada(Repressilator)

print(rr.model.getGlobalParameterIds())
rr.model.setGlobalParameterValues([6],[1])
print(rr.model.getGlobalParameterValues())
rr.reset()
rr.simulate(0,1000,1000)
rr.plot()

rr.conservedMoietyAnalysis = True
rr.model.setGlobalParameterValues([6],[1])
print(rr.model.getGlobalParameterValues())


print('Convergence estimator:', rr.steadyState())
print(rr.steadyStateSelections)
print(rr.getSteadyStateValues())
```

```
['tau_mRNA', 'tau_prot', 'eff', 'KM', 'ps_0', 'ps_a', 'n', 'beta', 'alpha0', 'a0_tr', 'alpha', 'a_tr', 't_ave', 'kd
_mRNA', 'kd_prot', 'k_tl']
[2.00000000e+00 1.00000000e+01 2.00000000e+01 4.00000000e+01
 5.00000000e-04 5.00000000e-01 1.00000000e+00 2.00000000e-01
 2.16404256e-01 3.00000000e-02 2.16187852e+02 2.99700000e+01
 2.88539008e+00 3.46573590e-01 6.93147181e-02 6.93147181e+00]
```

```
[2.00000000e+00 1.00000000e+01 2.00000000e+01 4.00000000e+01
 5.00000000e-04 5.00000000e-01 1.00000000e+00 2.00000000e-01
 2.16404256e-01 3.00000000e-02 2.16187852e+02 2.99700000e+01
 2.88539008e+00 3.46573590e-01 6.93147181e-02 6.93147181e+00]
Convergence estimator: 1.181171963772573e-07
['[PX]', '[PY]', '[PZ]', '[X]', '[Y]', '[Z]']
[572.96415158 572.96415158 572.96415158   5.72964152   5.72964152
   5.72964152]
```

Control Analysis

In [82]:
```
rr = te.loada(Repressilator)
rr.conservedMoietyAnalysis = True
#print(rr.getAntimony())
print('Control coef.:',rr.getCC('Reaction10','n'))
print('Control coef.:',rr.getCC('X','n'))
print('Elasticiy coef.:',rr.getEE('Reaction10','PZ'))
```

```
Control coef.: -0.032516447220156626
Control coef.: -1.1721672329544974
Elasticiy coef.: -1.876229798902059
```

Roadrunner and your model as an object in Python

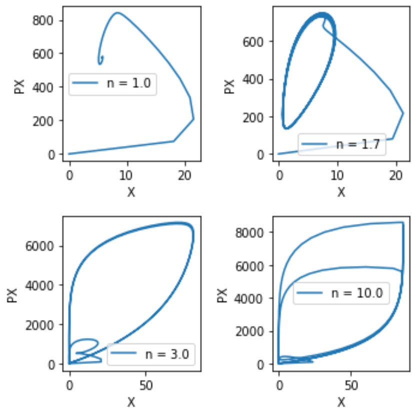
From loading a model with loada() an instance of roadrunner is generated. Additionally, the roadrunner object contains a the model as a python-object. Hence, there are i) specific methods for that .model object but also the content of the model can be manipulated. Try it out!

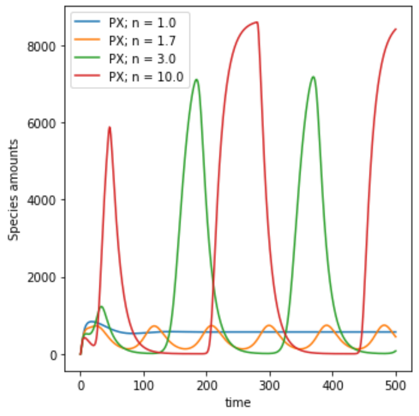
In [83]:
```
rr = te.loada(Repressilator)
print(type(rr))
print(type(rr.model))
```

```
<class 'tellurium.roadrunner.extended_roadrunner.ExtendedRoadRunner'>
<class 'roadrunner.roadrunner.ExecutableModel'>
```

Example - Parameterscan:

In [84]:
```
import matplotlib.pyplot as plt
import numpy as np

fig_phase = plt.figure(figsize=(5,5))

rr = te.loada(Repressilator)
for l,i in enumerate([1.0,1.7,3.0,10.]):

    fig_phase.add_subplot(2,2,l+1)

    rr.n = i
    rr.reset()
    result = rr.simulate(0,500,500,selections=['time','X','PX'])

    plt.plot(result['X'],result['PX'],label='n = %s' %i)

    plt.xlabel('X')
    plt.ylabel('PX')
    plt.legend()

plt.tight_layout()

fig_timecourse= plt.figure(figsize=(5,5))

rr = te.loada(Repressilator)
for l,i in enumerate([1.0,1.7,3.0,10.]):

    rr.n = i
    rr.reset()
    result = rr.simulate(0,500,500,selections=['time','X','PX'])

    plt.plot(result['time'],result['PX'],label='PX; n = %s' %i)

    plt.xlabel('time')
    plt.ylabel('Species amounts')
    plt.legend()



plt.tight_layout()
```

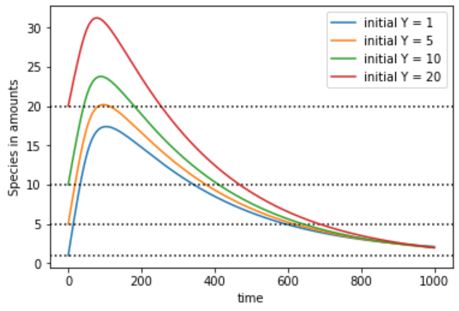




Example - (Initial value)-scan:

In [87]:
```
import matplotlib.pyplot as plt
import numpy as np

rr = te.loada(Repressilator)
print(rr.model.getFloatingSpeciesInitAmountIds())
print(rr.model.getFloatingSpeciesInitAmounts())

for l,i in enumerate([1,5,10,20]):

    # There are many possibilites to implement this:
    # First - wrong
    #rr.Y=i

    # Second - wrong
    #rr.Y=i
    #rr.reset()

    # Third - correct, but there are more possibilites...
    rr.model["init(Y)"] = i
    rr.reset()


    result = rr.simulate(0,10,1000,selections=['Y','PY'])

    #plt.plot(result[:,0],result['PY'],label='n = %s' %i)
    plt.plot(result['Y'],label='initial Y = %s' %i)
    plt.xlabel('time')
    plt.ylabel('Species in amounts')
    plt.axhline(y=i,linestyle = ':',color='black')
    plt.legend()
```

```
['init(PX)', 'init(PY)', 'init(PZ)', 'init(X)', 'init(Y)', 'init(Z)']
[ 0.  0.  0.  0. 20.  0.]
```



In [ ]: