roadrunner_complete

February 27, 2018

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

1 Roadrunner Methoden

1.1 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/BIOMD0000000

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/biomodel
         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";
  Reaction9 is "degradation of CI";
  Reaction10 is "transcription of LacI";
  Reaction11 is "transcription of TetR";
  Reaction12 is "transcription of CI";
end
```

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";
  Reaction9 is "degradation of CI";
  Reaction10 is "transcription of LacI";
  Reaction11 is "transcription of TetR";
  Reaction12 is "transcription of CI";
end
```

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

1.2 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()
```

1.3 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
[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]
```

1.4 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
```

2 Roadrunner and your model as an object in Python

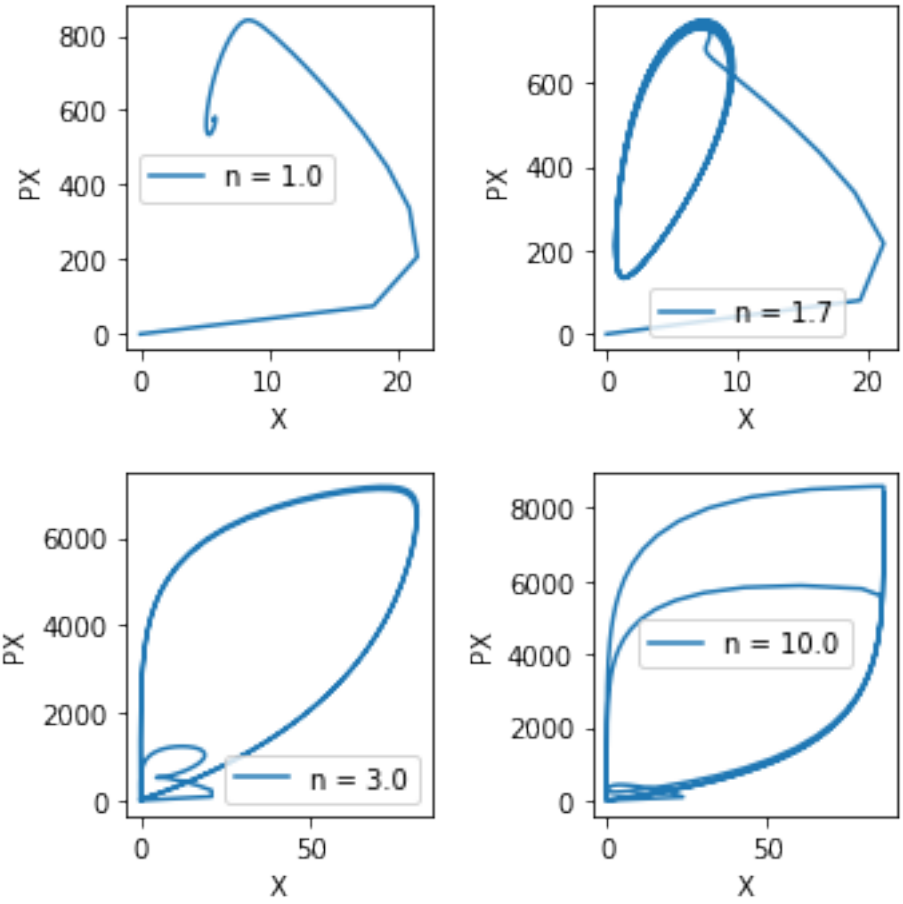
From loading a model with loada() an instance of roadrunner is generated. Additionally, the roadrunner object contains a the model as a python-object. Hence, there are i) specific methods for that .model object but also the content of the model can be manipulated. Try it out!

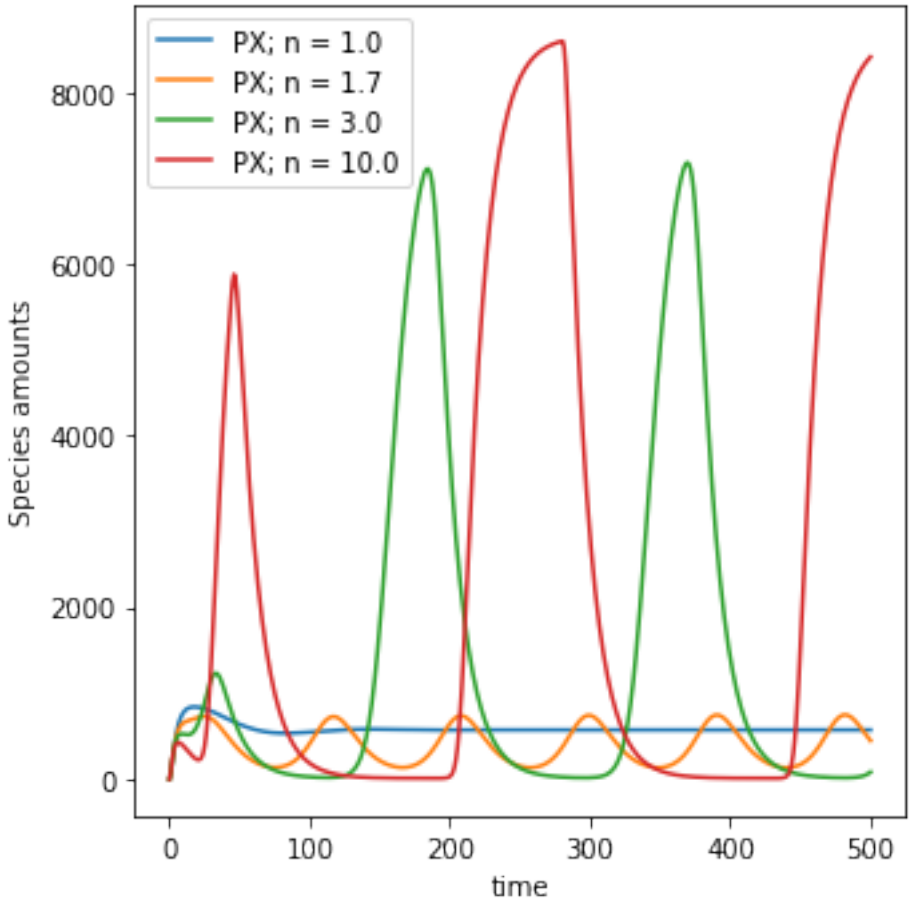
```
In [83]: rr = te.loada(Repressilator)
         print(type(rr))
         print(type(rr.model))
```

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

2.1 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()
```


n = 1.0
n = 1.7
n = 3.0
n = 10.0
PX
X

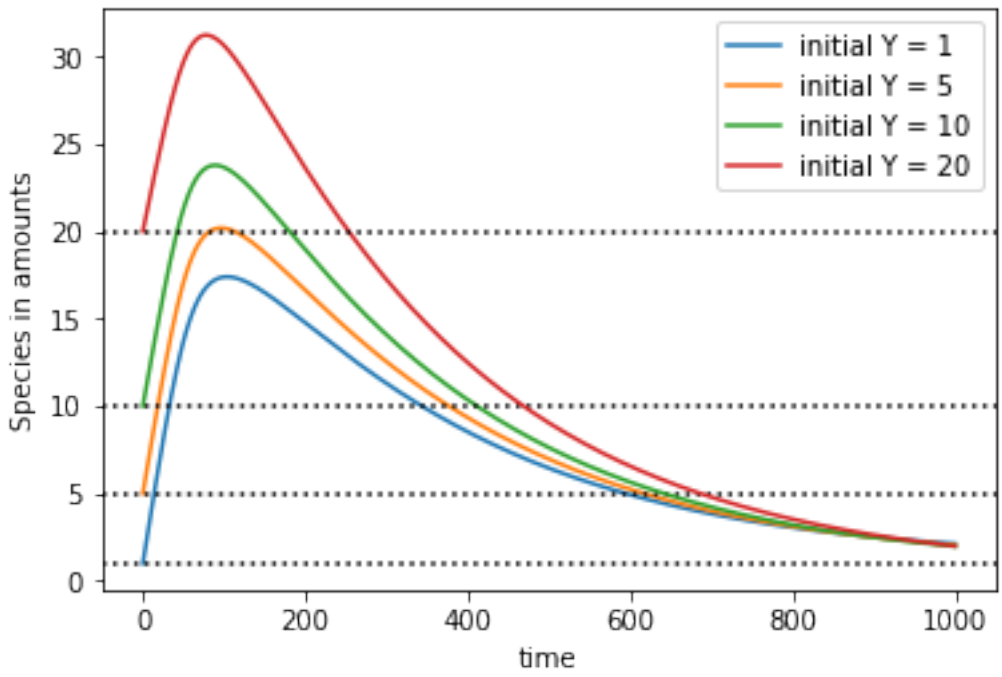


2.2 Example - (Initial value)-scan:

```
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 [ ]:
```