YAPE (Yet Another Programming Environment): ZIB_RubyExt

Thomas Dierkes[1]

Zuse Institute Berlin (ZIB), Computational Systems Biology Group[1]

Aug 26, 2015

Why?

PRO

- Improved handling of SBML models
- Provides a user-friendly interfaces to (legacy) `FORTRAN` routines
- Ready for easy integration to WEB services (i.e. ReST API)
- Fast!
- ...

CONTRA

- Yet another programming/scripting language (i.e. Ruby)
- `Ruby` infrastructure not (yet!) as rich as other environments
- e.g. a `Modelica` pipeline still pending; in fact, not yet started
- ...

How!

Installing the Ruby package:

```
[path]$ git clone https://github.com/CSB-at-ZIB/ZIB_RubyExt
Cloning into 'ZIB_RubyExt'...
remote: Counting objects: 726, done.
remote: Compressing objects: 100% (6/6), done.
remote: Total 726 (delta 0), reused 0 (delta 0), pack-reused 719
Receiving objects: 100% (726/726), 36.65 MiB | 4.26 MiB/s, done.
Resolving deltas: 100% (461/461), done.
Checking connectivity... done.

[path]$ cd ZIB_RubyExt

[path/ZIB_RubyExt]$ make clean; make

      ... wait! ... [lots of output] ...

[path/ZIB_RubyExt]$ cd tst
```

And now for something completely different: a real crash course in Ruby!

How!

Installing the Ruby package:

```
[path]$ git clone https://github.com/CSB-at-ZIB/ZIB_RubyExt
Cloning into 'ZIB_RubyExt'...
remote: Counting objects: 726, done.
remote: Compressing objects: 100% (6/6), done.
remote: Total 726 (delta 0), reused 0 (delta 0), pack-reused 719
Receiving objects: 100% (726/726), 36.65 MiB | 4.26 MiB/s, done.
Resolving deltas: 100% (461/461), done.
Checking connectivity... done.

[path]$ cd ZIB_RubyExt

[path/ZIB_RubyExt]$ make clean; make

      ... wait! ... [lots of output] ...

[path/ZIB_RubyExt]$ cd tst
```

And now for something completely different: a real crash course in Ruby!

Preliminary Example 1

prelimex1.rb

```ruby
#! /usr/bin/env ruby
require 'Nlscon'
#-----------------------------------------------------------------
q = 3
mTotal = mFit = 10     # def fcn(n,m,mcon,x) [z0, ..., z9] end

nlscon = Nlscon.new [q, mTotal, mFit]

nlscon.f = method(:fcn)                          # nlscon.df = ...
nlscon.x = [ 1.0, 2.0, 3.0 ]                     # nlscon.xscal = ...
nlscon.fobs = [ 6.28, -3.7, 2E-5, ..., 42 ]      # nlscon.fscal = ...
nlscon.rtol = 1.0E-3                             # nlscon.iopt = ...

status = -1     # nlscon.iopt = { "nonlin" => 3, "jacgen" => 3 }
iter = 0        # nlscon.iwk  = { "nitmax" => 35 }

while status == -1 && iter < nlscon.iwk["nitmax"] do
  iter += 1
  status = nlscon.iterate
end

printf "Done! Final result: x = #{nlscon.x}\n" if status == 0
```

Example 2

simulex2.rb

```
#! /usr/bin/env ruby
require_relative '../../lib/Model'    # uses Ruby ext. 'Limex'!
#-------------------------------------------------------------
def predator_prey( t, y, par )
  a, b, c, d = par                                  # [ prey, pred ]
  [ y[0]*(a - b*y[1] , -y[1]*(c - d*y[0]) ]    # [  dy0,  dy1 ]
end
#-------------------------------------------------------------
initvar = {      t0: 1900.0,
                 y0: [  30.0 ,   4.0  ],
            y0label: [ "n1_0", "n2_0" ],
                par: [    0.5 ,  0.02 ,    1.0 ,   0.02  ],
             plabel: [ "alpha", "beta", "gamma", "delta" ]   }

model = Model.new :predator_prey, initvar

tspan = [ model.t0, model.t0 + 20.0 ]
t, sol = model.solve_ode tspan
#-------------------------------------------------------------
fout = File.open("predator_prey_solution.dat", "w")
model.save_current_solution fout
fout.close

printf "Time steps t = #{t}\n"
printf "Solution   y = #{sol}\n"
```

Cont'd Example 2

Result: predator_prey_solution.dat

```
Timepoint                 1                 2
1.900000e+03 3.000000e+01 4.000000e+00
1.900000e+03 3.000126e+01 3.999840e+00
1.900010e+03 3.012758e+01 3.983924e+00
```

... [lots of numbers!] ...

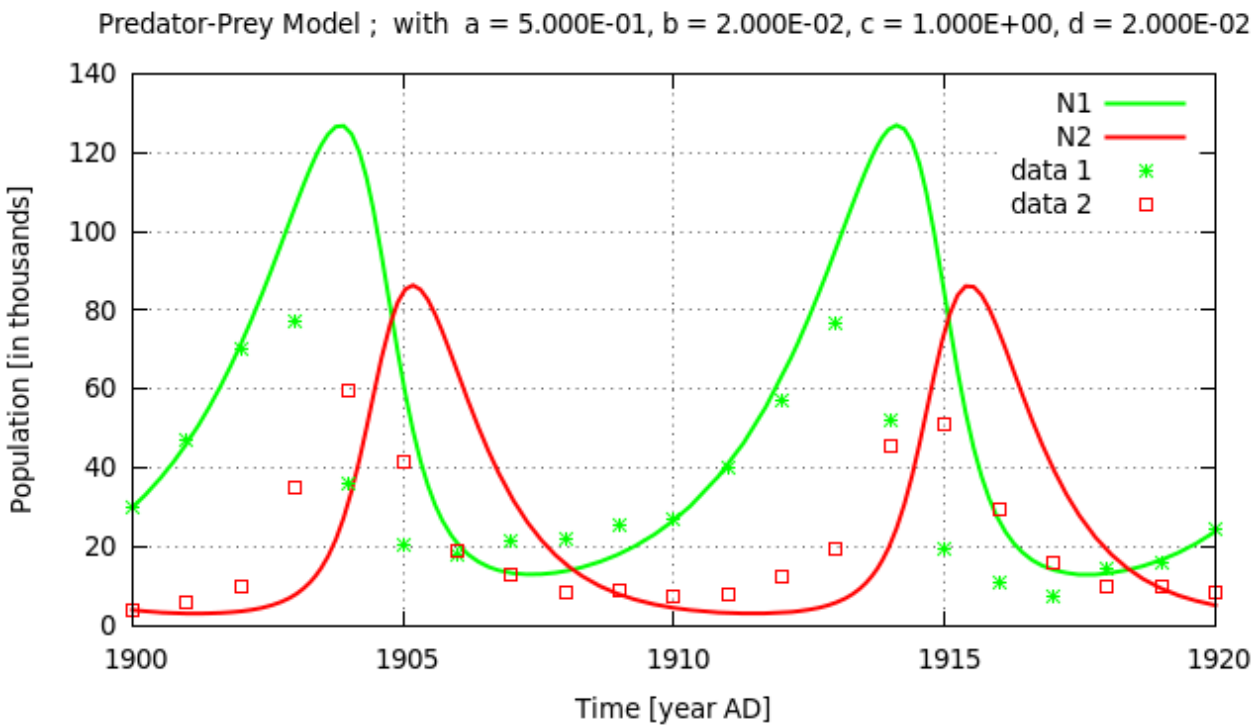


Figure : Simulation result and some data (plotted with gnuplot).

Cont'd Example 2

Combining the Ruby objects Nlscon and Model, we can readily perform the parameter identification task on dynamical models given by ODE systems.

(cf. the Ruby script "check_Nlscon_with_PredPrey_model.rb")

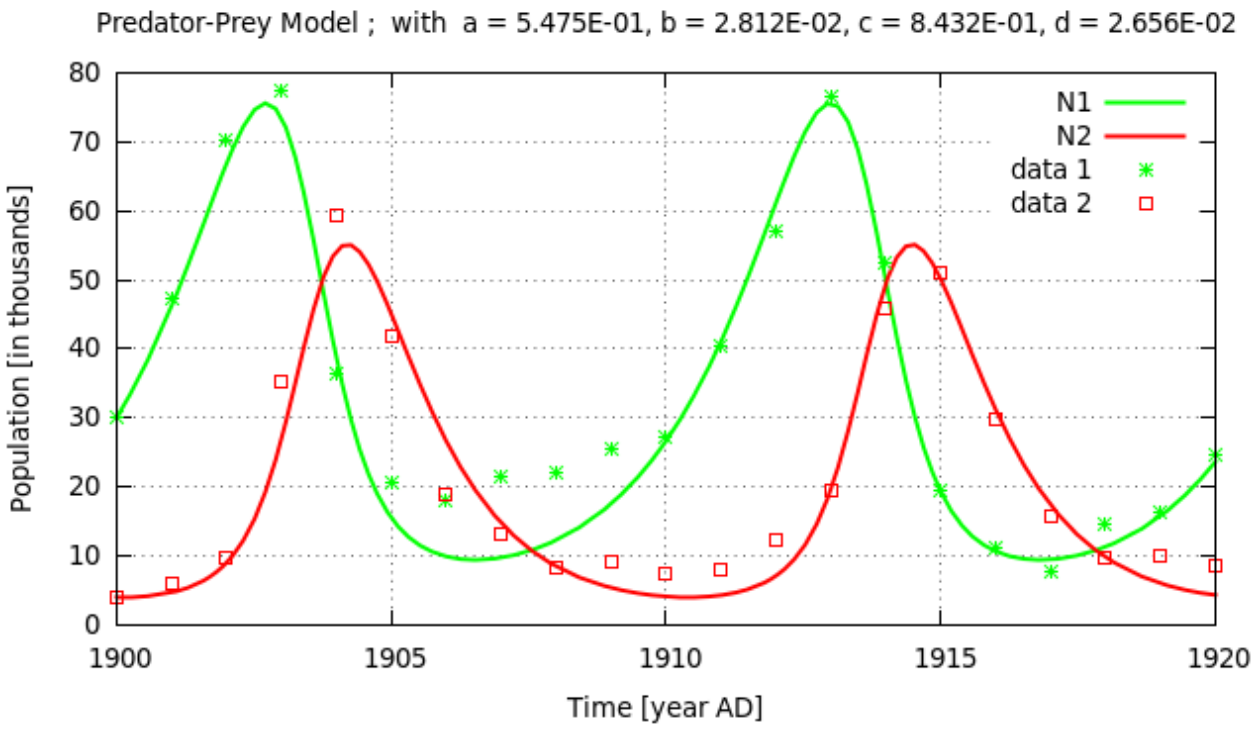


Figure : Fitting result and data after 8 iterations (plotted with gnuplot).

SBML Example 3

Now, we head for SBML models! At last.

Short-hand SBML: reacAB.mod

```
@model:3.1.1=ReactionAB

@species
  default:[A]     =     1.0        "Initial Concentration A"
  default:[B]     =     0.0        "Initial Concentration B"

@parameters
             k1   =     2.0        "Reaction Rate A -> B"
             k_1  =     0.003      "Reaction Rate B -> A"

@reactions
#
  @r=re001                          "Reaction A -> B"
     A -> B
     k1 * A
#
  @r=r002                           "Reaction B -> A"
     B -> A
     k_1 * B
#
```

Cont'd SBML Example 3

1. Conversion of sh-SBML and *pure* SBML (and vice versa).
2. Compiling into a dynamic link library (.so files in LINUX).
3. Using libODEydot.so with Ruby object ModelDL.

```
[.../GynCycle]$ cd Model_ODE
[.../GynCycle/Model_ODE]$ ./sbml2mod.py GynCycle.xml >myGyn.mod
[.../GynCycle/Model_ODE]$ vi myGyn.mod

[.../MyReacAB/Model_ODE]$ ./mod2sbml.py reacAB.mod >reacAB.xml
[.../MyReacAB/Model_ODE]$ make clean
```

.

.

.

Cont'd SBML Example 3

1. Conversion of sh-SBML and *pure* SBML (and vice versa).
2. Compiling into a dynamic link library (.so files in LINUX).
3. Using libODEydot.so with Ruby object ModelDL.

```
[.../GynCycle]$ cd Model_ODE
[.../GynCycle/Model_ODE]$ make clean; make GynCycle.so
/bin/rm -f *.so *.o
./sbml2adolc GynCycle.xml >ydot_LIMEXcpp.cpp
g++ -I. -I../../../pkg/include -fexceptions -O3 -fPIC
-c ydot_LIMEXcpp.cpp
g++ -shared -s ydot_LIMEXcpp.o -o GynCycle.so
-Wl,-init,set_adolc_num_dir
-Wl,-rpath,/home/tom/Work/Programs/ZIB_RubyExt/pkg/lib
-L/home/tom/Work/Programs/ZIB_RubyExt/pkg/lib -ladolc
-lColPack -lm
cp GynCycle.so ../libODEydot.so
[.../GynCycle/Model_ODE]$ cd ..
```

Cont'd SBML Example 3: *libODEydot.so*

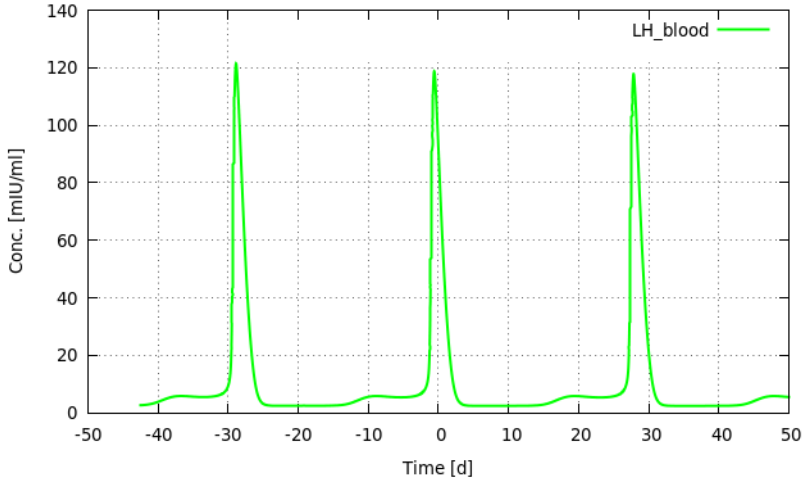
1. Conversion of sh-SBML and *pure* SBML (and vice versa).
2. Compiling into a dynamic link library (.so files in LINUX).
3. Using libODEydot.so with Ruby object ModelDL.

sbmlex3.rb

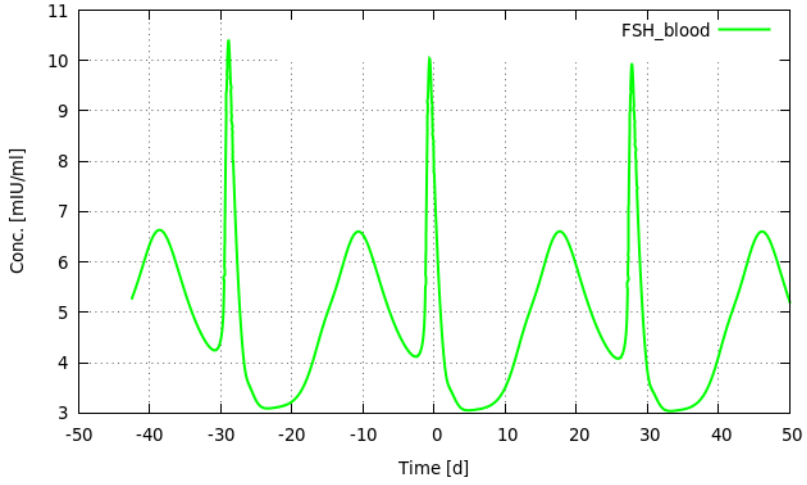
```
#! /usr/bin/env ruby
require_relative '../../lib/ModelDL' # uses Ruby ext.'LimexDL'
#-------------------------------------------------------------
#           !!! no 'def fcn()' nor 'initvar = {}' !!!
#-------------------------------------------------------------
model = ModelDL.new    # loads automagically './libODEydot.so'
model.t0 = -42.5
tspan = [model.t0, model.t0 + 100.0]
t, sol = model.solve_ode tspan
#-------------------------------------------------------------
fout = File.open("#{model.version[0]}_solution.dat","w")
model.save_current_solution fout
fout.close
printf "Saved Solution: Model #{model.version}"
```

Cont'd SBML Example 3: Graphs with *gnuplot*

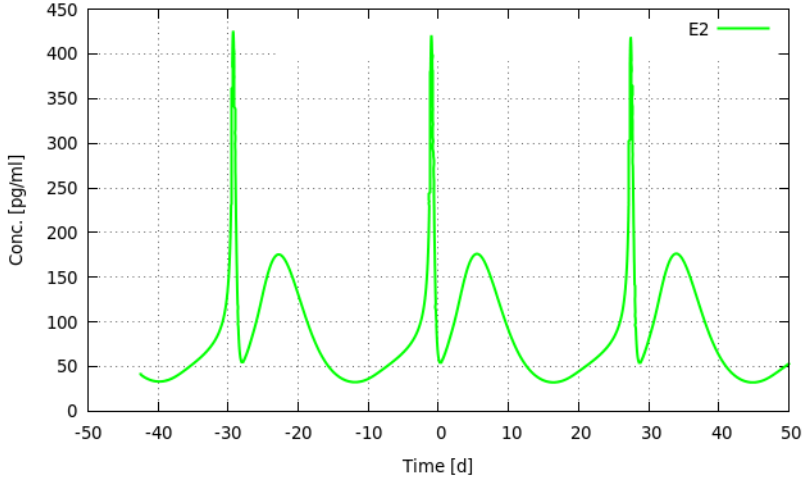
a) LH



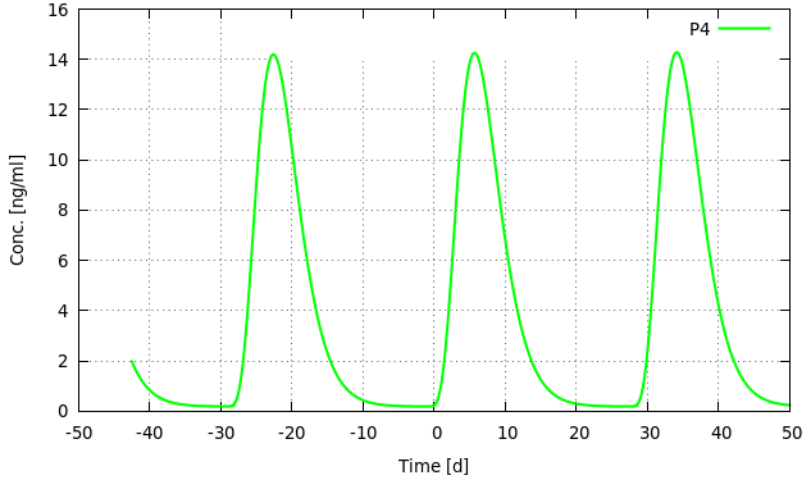
b) FSH



c) Estradiol (E2)



d) Progesterone (P4)



Full Example 4

fullex4.rb

```
#! /usr/bin/env ruby
require_relative '../../lib/ModelDL'
require_relative '../../lib/Experiment'
require_relative '../../lib/SysBioFit' # uses Ruby ext.'Nlscon'
#-------------------------------------------------------------
$fndata = "rb_Nlscon_with_PAEON_V2_data.dat"
#-------------------------------------------------------------
# Model/dynamic-load ODE

model = ModelDL.new

model.t0 = -42.5
model.hmax = 0.0
model.inistep = 1.0E-4
# model.monitor = 1
#-------------------------------------------------------------
# Measurement/Experiment Data:  Timepoint sId1 SD sId2 SD ...

ex1 = Experiment.new

ex1.load_data $fndata          #  reads data _with_ weights!
#-------------------------------------------------------------
# [...]
```

Full Example 4: CSV Format

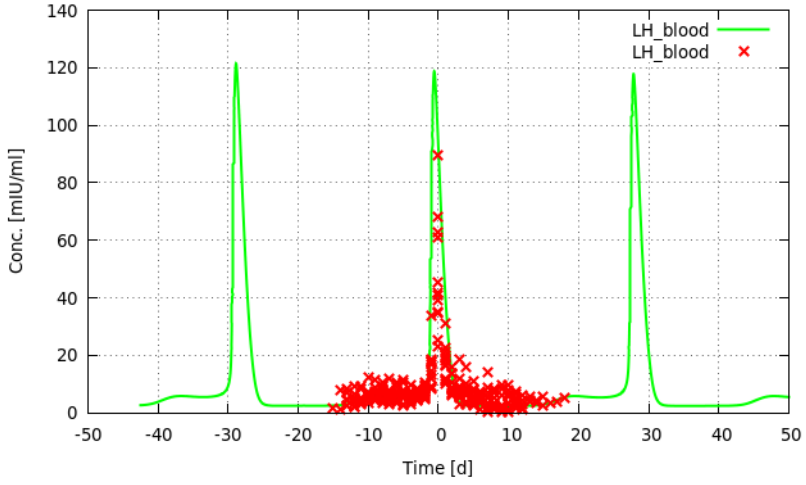
- All data shall come in two (!) columns.
- Graphs done by prepackaged (shell) script './showPreparation'.

Data CSV: rb_NIscon_with_PAEON_V2_data.dat

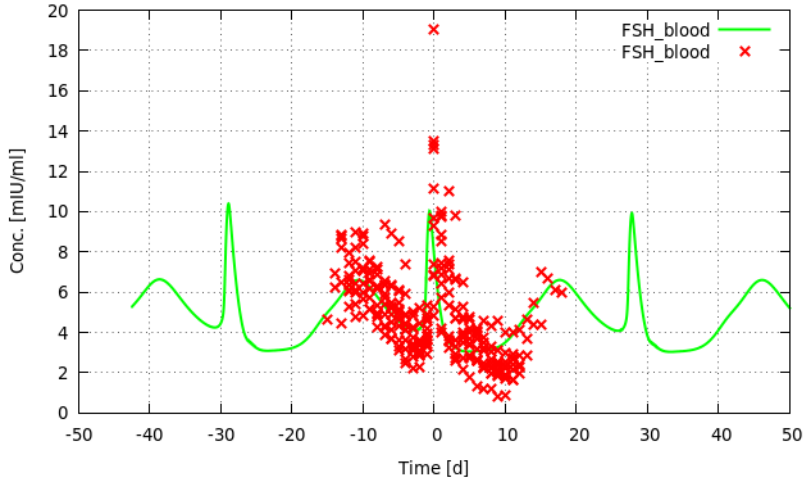
Timepoint	E2	SD	P4	SD	LH_blood	SD
-1.50e+01	n/a	n/a	n/a	n/a	n/a	n/a
-1.50e+01	n/a	n/a	n/a	n/a	n/a	n/a
-1.50e+01	n/a	n/a	n/a	n/a	n/a	n/a
-1.50e+01	n/a	n/a	n/a	n/a	n/a	n/a
-1.50e+01	1.60e+01	1.0e+00	2.69e-01	1.0e+00	1.67e+00	1.0e+00
-1.50e+01	n/a	n/a	n/a	n/a	n/a	n/a
-1.40e+01	n/a	n/a	n/a	n/a	n/a	n/a
-1.40e+01	n/a	n/a	n/a	n/a	n/a	n/a
-1.40e+01	n/a	n/a	n/a	n/a	n/a	n/a
.						
.						
.						

Cont'd Full Example 4: Data with Simulation

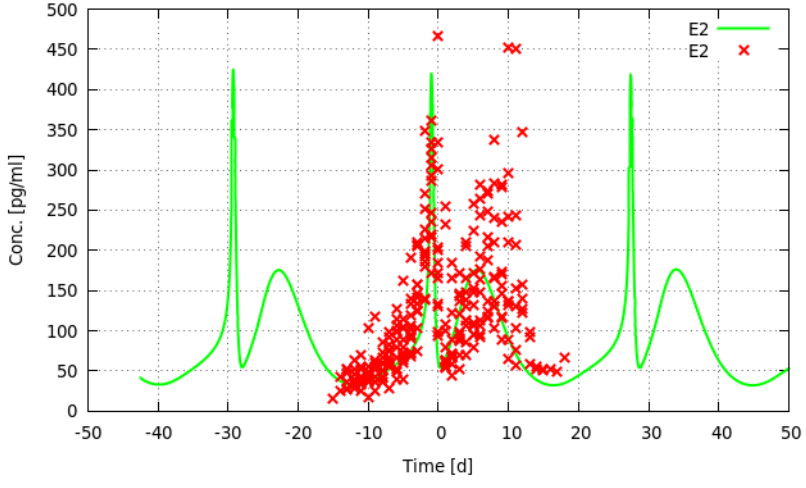
a) LH



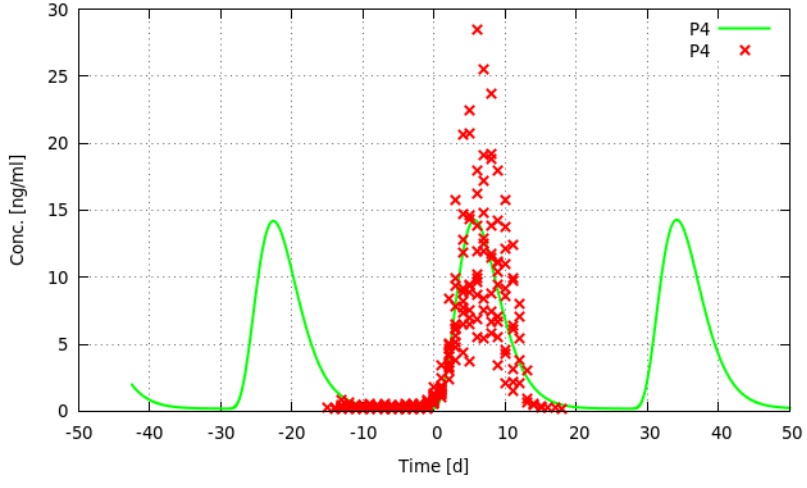
b) FSH



c) Estradiol (E2)



d) Progesterone (P4)



Cont'd Full Example 4

cont'd fullex4.rb

```
# [...]
#-------------------------------------------------------------
# Parameter Estimation/Identification
pIniGuess = {
  "global_p_019_001" => [ 0.958 , 1.0 ],   # GynCycle Param 61
  "global_p_020_001" => [ 0.925 , 1.0 ],   # GynCycle Param 62
  "global_p_021_001" => [ 0.7576, 1.0 ]    # GynCycle Param 63
}
#-------------------------------------------------------------
# ... computing nPar, mTotal, mFit from 'ex1' (left out here)
#-------------------------------------------------------------
nlscon = SysBioFit.new [nPar,mTotal,mFit]

nlscon.rtol     =  1.0E-2
nlscon.pfname   =  "rb_Nlscon_with_PAEON_V2_parameter.dat"
nlscon.sfname   =  "rb_Nlscon_with_PAEON_V2_solution.dat"
nlscon.jacgen   =  1 # 3
nlscon.rwk      =  { "cond" => 1.0E+4 }

current_task    =  { model: model, data: ex1, guess: pIniGuess }

estim = nlscon.identify_par current_task
#-------------------------------------------------------------
# [...]
```

Cont'd Full Example 4

cont'd fullex4.rb

```
# [...]
#-------------------------------------------------------------
# Result Output
if estim.has_key?("par") then
  printf "\n"
  printf "   %22s      %12s       %12s      %12s\n",
         "Parameter", "confid_lo", "*p_estim*", "confid_up"
  printf "   %22s      %12s       %12s      %12s\n",
         "---------", "---------", "---------", "---------"

  estim["pidx"].each_with_index do |j,idx|
    label = (j > 0) ? model.pId[j-1] : model.y0Id[-j-1]
    printf "  %22s      % 12.6f     % 12.6f     % 12.6f\n",
           label[0..21],
           estim["rwk"]["xl"][idx],
           estim["par"][idx],
           estim["rwk"]["xr"][idx]
  end

  printf "\n\n"
  printf "incomp. kappa:  % .4e\n" , estim["rwk"]["skap"]
  printf "achieved rtol:  % .4e\n" , estim["rwk"]["prec"]
  printf "\n"
  printf "Done!  (Model: #{model.version})\n"
```

Cont'd Full Example 4: Output *NLSCON*

```
[...]

Correlation coefficients
------------------------

      1      2      3      4      5
1   1.00
2  -0.05   1.00
3  -0.22   0.84   1.00
4  -0.03  -0.98  -0.89   1.00
5  -0.16  -0.88  -0.70   0.83   1.00


Standard deviation of parameters
--------------------------------
  No.  Estimate              sigma(X)
   1   0.150D+01   +/-   0.681D+00      =   45.58 %
   2   0.487D+00   +/-   0.213D+00      =   43.74 %
   3   0.125D+01   +/-   0.119D+01      =   94.93 %
   4   0.468D+00   +/-   0.232D+00      =   49.62 %
   5   0.447D+00   +/-   0.403D-01      =    9.01 %

[...]
```

Cont'd Full Example 4: Output *NLSCON*

```
[...]

Independent confidence intervals
--------------------------------
   (on 95%-probability level using F-distribution
                                          F(alfa,1,m-n)=  3.88)

   1  (  0.153D+00 ,  0.284D+01 )
   2  (  0.674D-01 ,  0.907D+00 )
   3  ( -0.109D+01 ,  0.360D+01 )
   4  (  0.105D-01 ,  0.924D+00 )
   5  (  0.367D+00 ,  0.526D+00 )

******  Statistics * NLSCON   *******
***  Gauss-Newton iter.:      13  ***
***  Corrector steps   :      12  ***
***  Rejected rk-1 st. :       4  ***
***  Jacobian eval.    :      13  ***
***  Function eval.    :      26  ***
***  ...  for Jacobian :       0  ***
************************************

[...]
```

Cont'd Full Example 4: Output *NLSCON*

```
   [...]

12
         Parameter   confid_lower    *p_estim*    confid_upper
         ---------   ------------    ---------    ------------
 global_p_019_001       0.152736     1.495117       2.837498
 global_p_020_001       0.067438     0.486973       0.906507
 global_p_021_001      -1.089967     1.252936       3.595838
 global_p_022_001       0.010549     0.467514       0.924479
 global_p_023_001       0.367445     0.446749       0.526052


incomp. kappa:  -1.0000e+00
achieved rtol:  -1.0000e+00


["PAEON_V2__OvF_ne_0", "Mon Aug 24 09:18:13 2015",
        "001440400693", "PAEON_V2__OvF_ne_0.xml", "with vareq"]
```

- Again, plots by a (shell) script ./showSolutionIter "0 10"

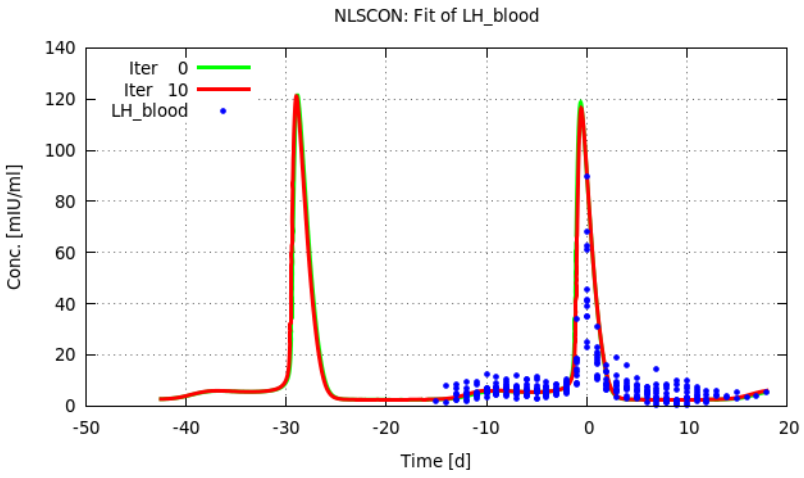
Cont'd Full Example 4: Output *NLSCON*

```
   [...]

12
         Parameter   confid_lower    *p_estim*    confid_upper
         ---------   ------------    ---------    ------------
 global_p_019_001       0.152736     1.495117       2.837498
 global_p_020_001       0.067438     0.486973       0.906507
 global_p_021_001      -1.089967     1.252936       3.595838
 global_p_022_001       0.010549     0.467514       0.924479
 global_p_023_001       0.367445     0.446749       0.526052


incomp. kappa:  -1.0000e+00
achieved rtol:  -1.0000e+00


["PAEON_V2__OvF_ne_0", "Mon Aug 24 09:18:13 2015",
        "001440400693", "PAEON_V2__OvF_ne_0.xml", "with vareq"]
```

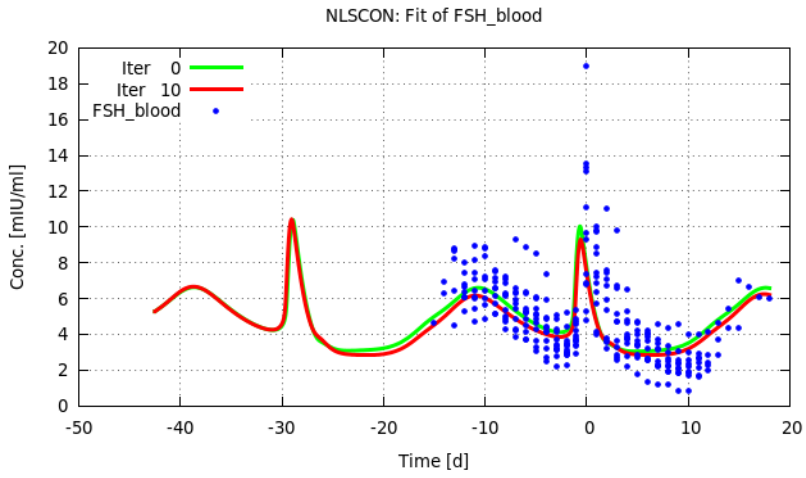
- Again, plots by a (shell) script ./showSolutionIter "0 10"

Cont'd Full Example 4: Fit with Data (*10th iter.*)

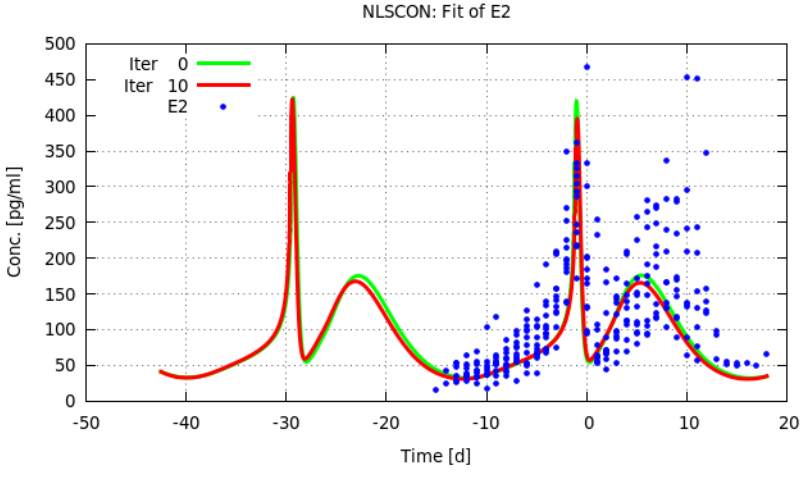
a) LH



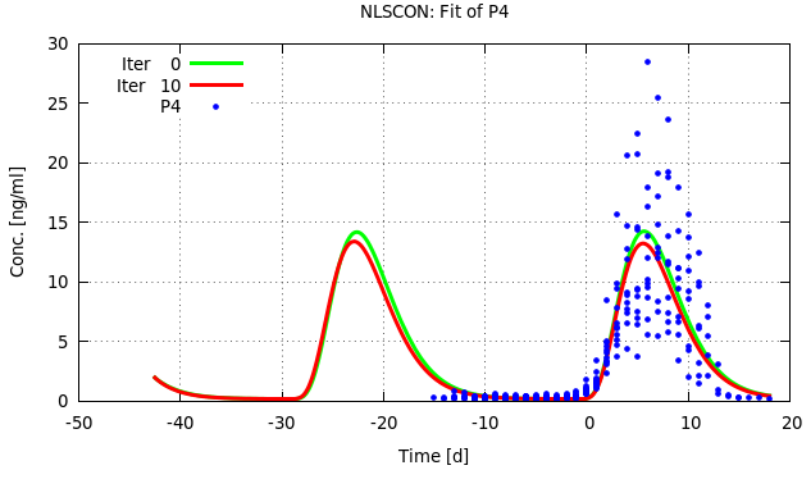
b) FSH



c) Estradiol (E2)



d) Progesterone (P4)



Cont'd Full Example 4: Fitted Parameters vs. Iteration

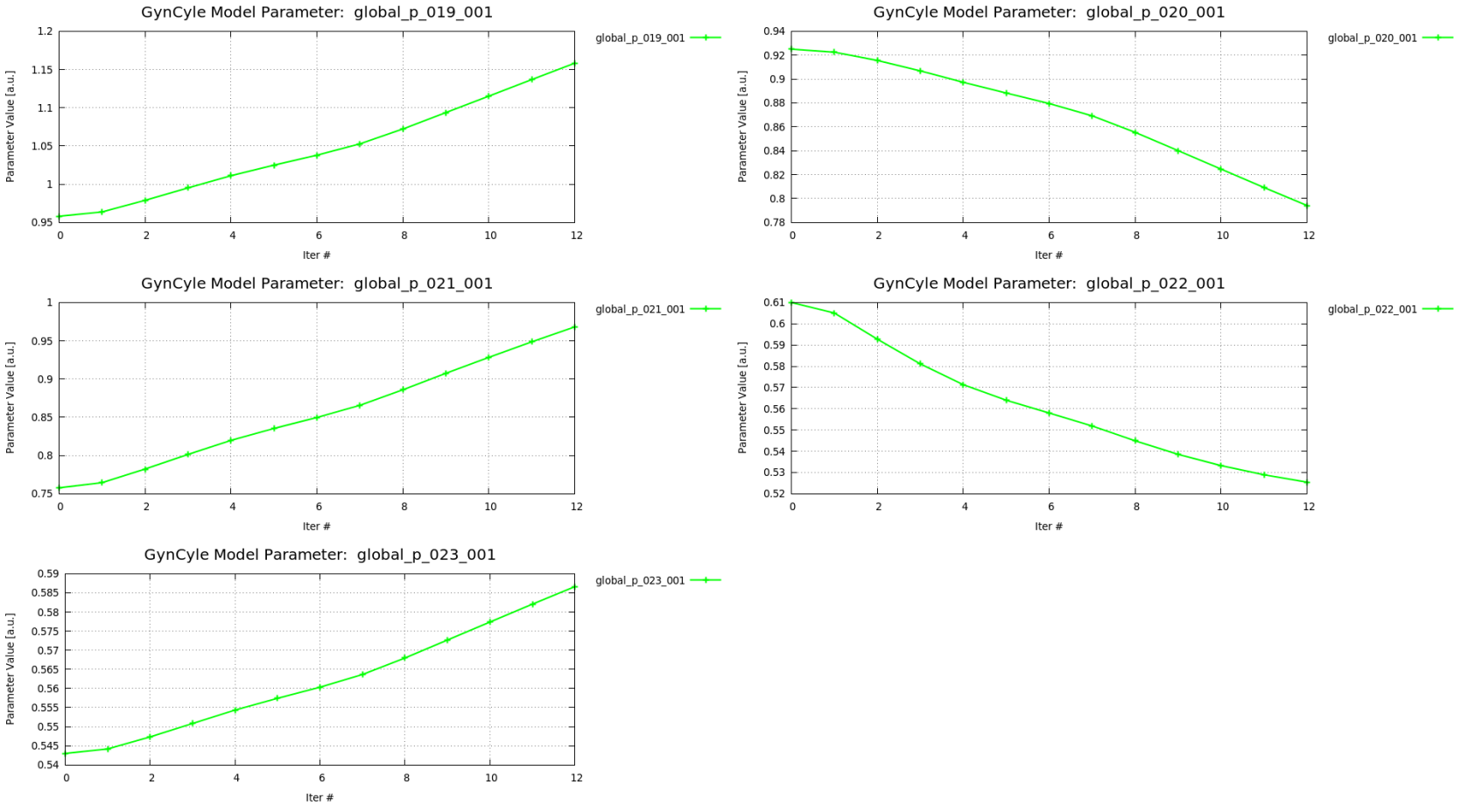


Figure : Evolution of parameter values w.r.t. iteration number.