toy_reactor_model_3compartments

January 14, 2018

1 Three-compartment model

Three compartments: * Gas (g) * Liquid (l) * Cell (c)

1.1 Variables

- u: volumetric flow rate; $[u] = \frac{L}{h}$
- c: input concentration of X; $[c] = \frac{mmol}{L}$
- X and Y: amount; $[X] = [Y] = mmol$
- x and y: concentration; $[x] = [y] = \frac{mmol}{L}$
- V: volume; $[V] = L$
- v: reaction rate; $[v] = \frac{mmol}{h}$
- J: transport rate; $[J] = \frac{mmol}{h}$
- Q: equlibrium constant; dimension-less
- A: area; $[A] = m^2$

1.1.1 Some realtionships between variables

- $V_c \propto Z$ (proportionality constant assumed known)
- $A_c \propto V_c^{\frac{2}{3}} \propto Z^{\frac{2}{3}}$

1.2 Rate equations:

1. Flow rate of X into gas: $J_{T_{x,in}} = uc$
2. Transport rate of X from gas to liquid: $J_{T_{x,gl}} = k_{T_{x,gl}} A_l \left(x_g - \frac{x_l}{Q_{T_{x,gl}}} \right) \approx k'_{T_{x,gl}} u \left(\frac{X_g}{V_g} - \frac{X_l}{V_l} \frac{1}{Q_{T_{x,gl}}} \right)$
3. Transport rate of X from liquid to cell: $J_{T_{x,lc}} = k_{T_{x,lc}} A_c \left(x_l - \frac{x_c}{Q_{T_{x,lc}}} \right) = k'_{T_{x,lc}} Z^{\frac{2}{3}} \left(\frac{X_l}{V_l} - \frac{X_c}{V_c} \frac{1}{Q_{T_{x,lc}}} \right) = k'_{T_{x,lc}} Z^{\frac{2}{3}} \left(\frac{X_l}{V_l} - \frac{X_c}{Z} \frac{1}{Q'_{T_{x,lc}}} \right)$

4. Reaction rate of $X \leftrightarrow Y$: $v_{R_{xy}} = k_{R_{xy}} Z \left(x_c - \frac{y_c}{Q_{R_{xy}}} \right) = k_{R_{xy}} Z \left(\frac{X_c}{V_c} - \frac{Y_c}{V_c} \frac{1}{Q_{R_{xy}}} \right) = k'_{R_{xy}} \left(X_c - \frac{Y_c}{Q_{R_{xy}}} \right)$
5. Reaction rate of $X \rightarrow Z$: $v_{R_{xz}} = k_{R_{xz}} Z x_c \left(1 - \frac{Z}{Z_{max}} \right) = k_{R_{xz}} Z \frac{X_c}{V_c} = k'_{R_{xz}} X_c \left(1 - \frac{Z}{Z_{max}} \right)$
6. Transport rate of Y from cell to liquid: $J_{T_{y,cl}} = k_{T_{y,cl}} A_c \left(y_c - \frac{y_l}{Q_{T_{y,cl}}} \right) = k'_{T_{y,cl}} Z^{\frac{2}{3}} \left(\frac{Y_c}{V_c} - \frac{Y_l}{V_l} \frac{1}{Q_{T_{y,cl}}} \right) = k''_{T_{y,cl}} Z^{\frac{2}{3}} \left(\frac{Y_c}{Z} - \frac{Y_l}{V_l} \frac{1}{Q'_{T_{y,cl}}} \right)$
7. Transport rate of Y from liquid to gas: $J_{T_{y,lg}} = k_{T_{y,lg}} A_l \left(y_l - \frac{y_g}{Q_{T_{y,lg}}} \right) = k'_{T_{y,lg}} \left(\frac{Y_l}{V_l} - \frac{Y_g}{V_g} \frac{1}{Q_{T_{y,lg}}} \right)$
8. Flow rate of X out of gas: $J_{T_{x,out}} = u x_g = u \frac{X_g}{V_g}$
9. Flow rate of Y out of gas: $J_{T_{y,out}} = u y_g = u \frac{Y_g}{V_g}$

1.2.1 Notes

- For rate equation #2, we treat $A_l \propto u$ here to model the dependence of A_l on u via bubbling.
- For rate equation #5, logistic growth of biomass is used, otherwise Z will grow indefinitely and the system will not settle to steady state.

1.3 Parameters

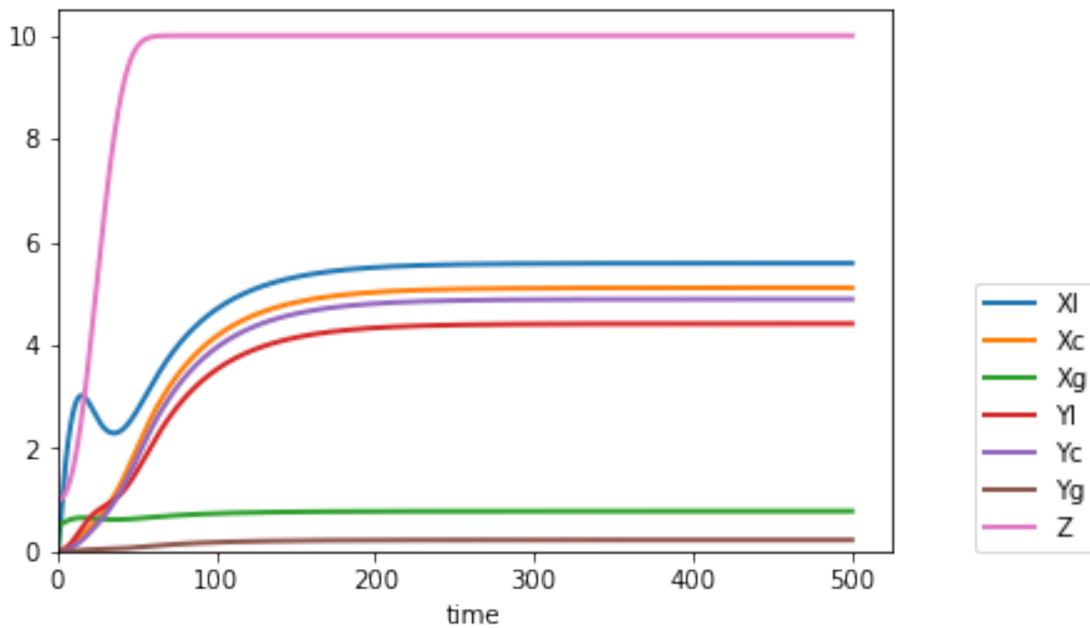
1. u
2. c
3. $k'_{T_{x,gl}}$
4. $k'_{T_{x,lc}}$
5. $k'_{R_{xy}}$
6. $k'_{R_{xz}}$
7. $k''_{T_{y,cl}}$
8. $k'_{T_{y,lg}}$
9. Z_{max}

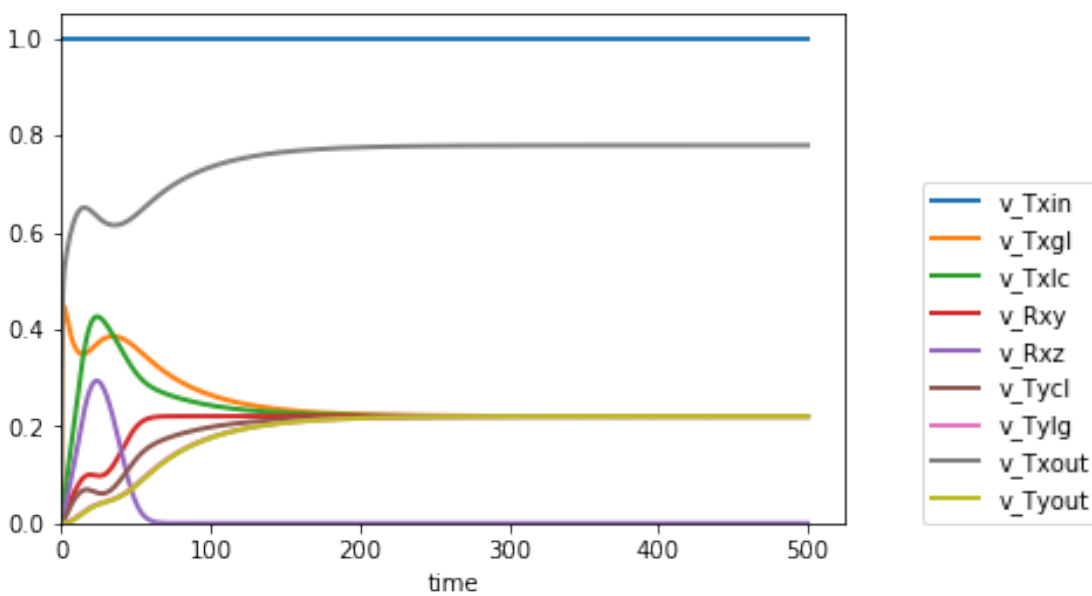
In [1]:
```
# build the model

from __future__ import absolute_import, division, print_function

import numpy as np

from rxnnet import network, experiments, mca
from infotopo import residual, fitting, sampling
```

```
In [3]: reactor = network.Network('reactor')

        reactor.add_compartment('liquid', 1)
        reactor.add_compartment('gas', 1)
        reactor.add_compartment('cell', 1)

        reactor.add_species('Xl', 'liquid', 0)
        reactor.add_species('Xc', 'cell', 0)
        reactor.add_species('Xg', 'gas', 0)
        reactor.add_species('Yl', 'liquid', 0)
        reactor.add_species('Yc', 'cell', 0)
        reactor.add_species('Yg', 'gas', 0)
        reactor.add_species('Z', 'cell', 1)

        reactor.add_parameter('Vl', 10, is_optimizable=False)
        reactor.add_parameter('Vg', 1, is_optimizable=False)

        for rxnid in ['Txgl', 'Txlc', 'Tycl', 'Tylg', 'Rxy']:
            reactor.add_parameter('KE_%s'%rxnid, 1, is_optimizable=False)

        reactor.add_parameter('u', 1, is_optimizable=True)
        reactor.add_parameter('c', 1, is_optimizable=True)
        for rxnid in ['Txgl', 'Txlc', 'Rxy', 'Rxz', 'Tycl', 'Tylg']:
            reactor.add_parameter('kf_%s'%rxnid, 1, is_optimizable=True)
        reactor.add_parameter('Zmax', 10, is_optimizable=True)

        reactor.add_reaction('Txin', eqn='->Xg', ratelaw='u*c')
        reactor.add_reaction('Txgl', eqn='Xg<->Xl', ratelaw='kf_Txgl * u * (Xg/Vg - Xl/Vl/KE_T
        reactor.add_reaction('Txlc', eqn='Xl<->Xc', ratelaw='kf_Txlc * Z**(2/3) * (Xl/Vl - Xc/
        reactor.add_reaction('Rxy', eqn='Xc<->Yc', ratelaw='kf_Rxy * (Xc - Yc/KE_Rxy)')
        reactor.add_reaction('Rxz', eqn='Xc<->Z', ratelaw='kf_Rxz * Xc * (1- Z/Zmax)')
        reactor.add_reaction('Tycl', eqn='Yc<->Yl', ratelaw='kf_Tycl * Z**(2/3) * (Yc/Z - Yl/V
        reactor.add_reaction('Tylg', eqn='Yl<->Yg', ratelaw='kf_Tylg * u * (Yl/Vl - Yg/Vg/KE_T
        reactor.add_reaction('Txout', eqn='Xg->', ratelaw='u*Xg/Vg')
        reactor.add_reaction('Tyout', eqn='Yg->', ratelaw='u*Yg/Vg')

        reactor.add_ratevars()
        reactor.compile()

In [4]: print(reactor.xids)
        print(reactor.rxnids)
        print(reactor.pids)

['Xl', 'Xc', 'Xg', 'Yl', 'Yc', 'Yg', 'Z']
['Txin', 'Txgl', 'Txlc', 'Rxy', 'Rxz', 'Tycl', 'Tylg', 'Txout', 'Tyout']
['u', 'c', 'kf_Txgl', 'kf_Txlc', 'kf_Rxy', 'kf_Rxz', 'kf_Tycl', 'kf_Tylg', 'Zmax']

In [5]: # integrate to get the time course
```

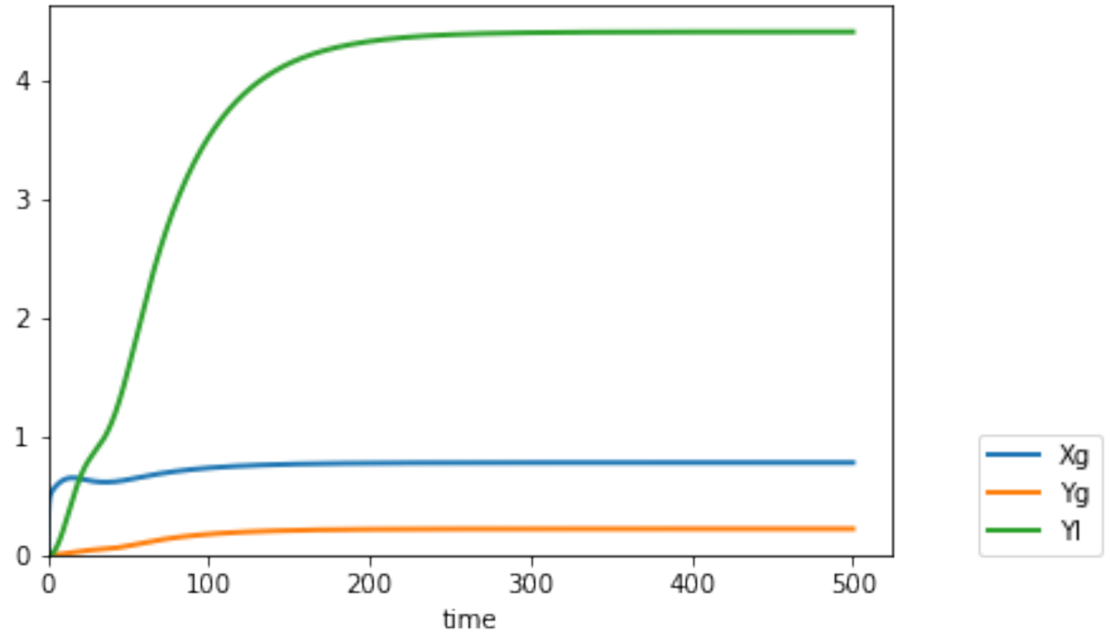
```
traj = reactor.get_traj((0,500))
```

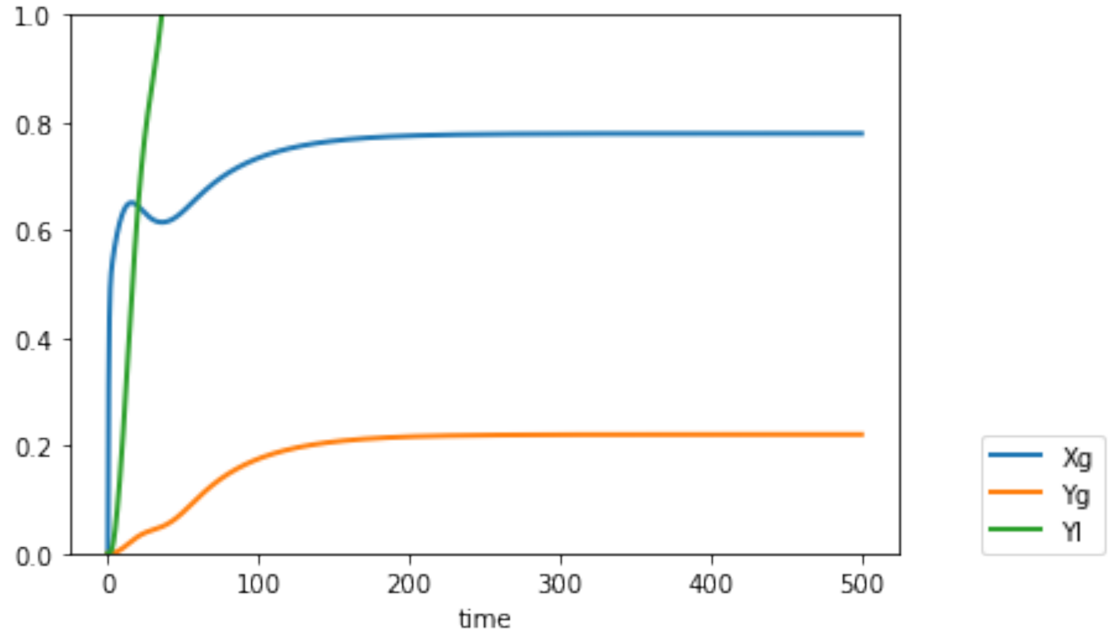
In [6]:
```
traj.plot(varids=reactor.xids, legendloc=(1.1,0))

traj.plot(varids=reactor.vids, legendloc=(1.1,0))
```





In [7]:
```
# plotting the trajectories of three variables (Xg, Yg, Yl) which we assume we can mea

datvarids = ['Xg', 'Yg', 'Yl']
traj.plot(varids=datvarids, legendloc=(1.1,0))
traj.plot(varids=datvarids, xylims=[None, [0,1]], legendloc=(1.1,0))
```



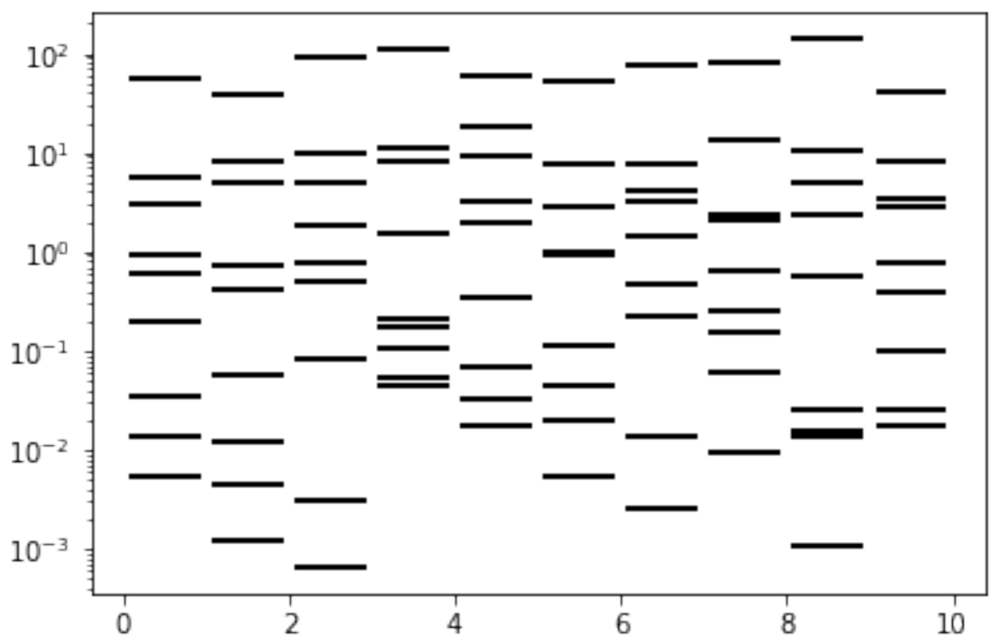


In [8]:
```
expts = experiments.Experiments()
expts.add_experiment(None, datvarids, np.linspace(0,200,101))

expts
```

Out[8]:
```
                 condition        varids  \
experiment
1                     None  [Xg, Yg, Yl]

                                                           times
experiment
1            [0.0, 2.0, 4.0, 6.0, 8.0, 10.0, 12.0, 14.0, 16...
```

In [9]:
```
pred = reactor.get_predict(expts)
```

In [10]:
```
# inspecting the spectrum (list of singular values of the Jacobian) to see if the fun

pred.plot_spectra(ps=[pred.p0.randomize(seed=i) for i in range(10)], figsize=(6,4))
```



1.4 Generate simulation data and use them for fitting

In [11]:
```
dat = pred.get_dat()

dat
```

Out[11]:
```
                           Y  sigma
None, Xg, 0.0     0.000000    1.0
```

```
None, Xg, 2.0    0.514710    1.0
None, Xg, 4.0    0.561191    1.0
None, Xg, 6.0    0.592145    1.0
None, Xg, 8.0    0.615826    1.0
None, Xg, 10.0   0.632907    1.0
None, Xg, 12.0   0.643948    1.0
None, Xg, 14.0   0.649655    1.0
None, Xg, 16.0   0.650928    1.0
None, Xg, 18.0   0.648832    1.0
None, Xg, 20.0   0.644492    1.0
None, Xg, 22.0   0.638969    1.0
None, Xg, 24.0   0.633144    1.0
None, Xg, 26.0   0.627667    1.0
None, Xg, 28.0   0.622957    1.0
None, Xg, 30.0   0.619241    1.0
None, Xg, 32.0   0.616611    1.0
None, Xg, 34.0   0.615078    1.0
None, Xg, 36.0   0.614608    1.0
None, Xg, 38.0   0.615148    1.0
None, Xg, 40.0   0.616633    1.0
None, Xg, 42.0   0.618987    1.0
None, Xg, 44.0   0.622126    1.0
None, Xg, 46.0   0.625949    1.0
None, Xg, 48.0   0.630346    1.0
None, Xg, 50.0   0.635194    1.0
None, Xg, 52.0   0.640368    1.0
None, Xg, 54.0   0.645747    1.0
None, Xg, 56.0   0.651222    1.0
None, Xg, 58.0   0.656699    1.0
...                   ...    ...
None, Yl, 142.0  4.089939    1.0
None, Yl, 144.0  4.105158    1.0
None, Yl, 146.0  4.119662    1.0
None, Yl, 148.0  4.133486    1.0
None, Yl, 150.0  4.146660    1.0
None, Yl, 152.0  4.159216    1.0
None, Yl, 154.0  4.171183    1.0
None, Yl, 156.0  4.182588    1.0
None, Yl, 158.0  4.193458    1.0
None, Yl, 160.0  4.203817    1.0
None, Yl, 162.0  4.213690    1.0
None, Yl, 164.0  4.223100    1.0
None, Yl, 166.0  4.232068    1.0
None, Yl, 168.0  4.240615    1.0
None, Yl, 170.0  4.248761    1.0
None, Yl, 172.0  4.256524    1.0
None, Yl, 174.0  4.263923    1.0
None, Yl, 176.0  4.270975    1.0
```

```
None, Yl, 178.0  4.277695    1.0
None, Yl, 180.0  4.284101    1.0
None, Yl, 182.0  4.290205    1.0
None, Yl, 184.0  4.296023    1.0
None, Yl, 186.0  4.301568    1.0
None, Yl, 188.0  4.306853    1.0
None, Yl, 190.0  4.311889    1.0
None, Yl, 192.0  4.316689    1.0
None, Yl, 194.0  4.321264    1.0
None, Yl, 196.0  4.325624    1.0
None, Yl, 198.0  4.329779    1.0
None, Yl, 200.0  4.333740    1.0

[303 rows x 2 columns]
```

```
In [12]: res = residual.Residual(pred, dat)
```

```
In [13]: # confirm that fitting recovers the parameters used for generating the simulated data

         fit = fitting.fit_lm_scipy(res, p0=pred.p0.randomize(seed=3), in_logp=True)

         print(fit.cost, '\n')
         print(fit.p - pred.p0)
```

```
3.36696262548e-28

u          -5.218048e-15
c           4.440892e-16
kf_Txgl    -4.218847e-15
kf_Txlc     2.264855e-14
kf_Rxy     -6.628031e-14
kf_Rxz     -1.254552e-14
kf_Tycl     2.997602e-14
kf_Tylg     2.220446e-16
Zmax       -1.065814e-14
dtype: float64
```

1.5 Construct parameter ensemble

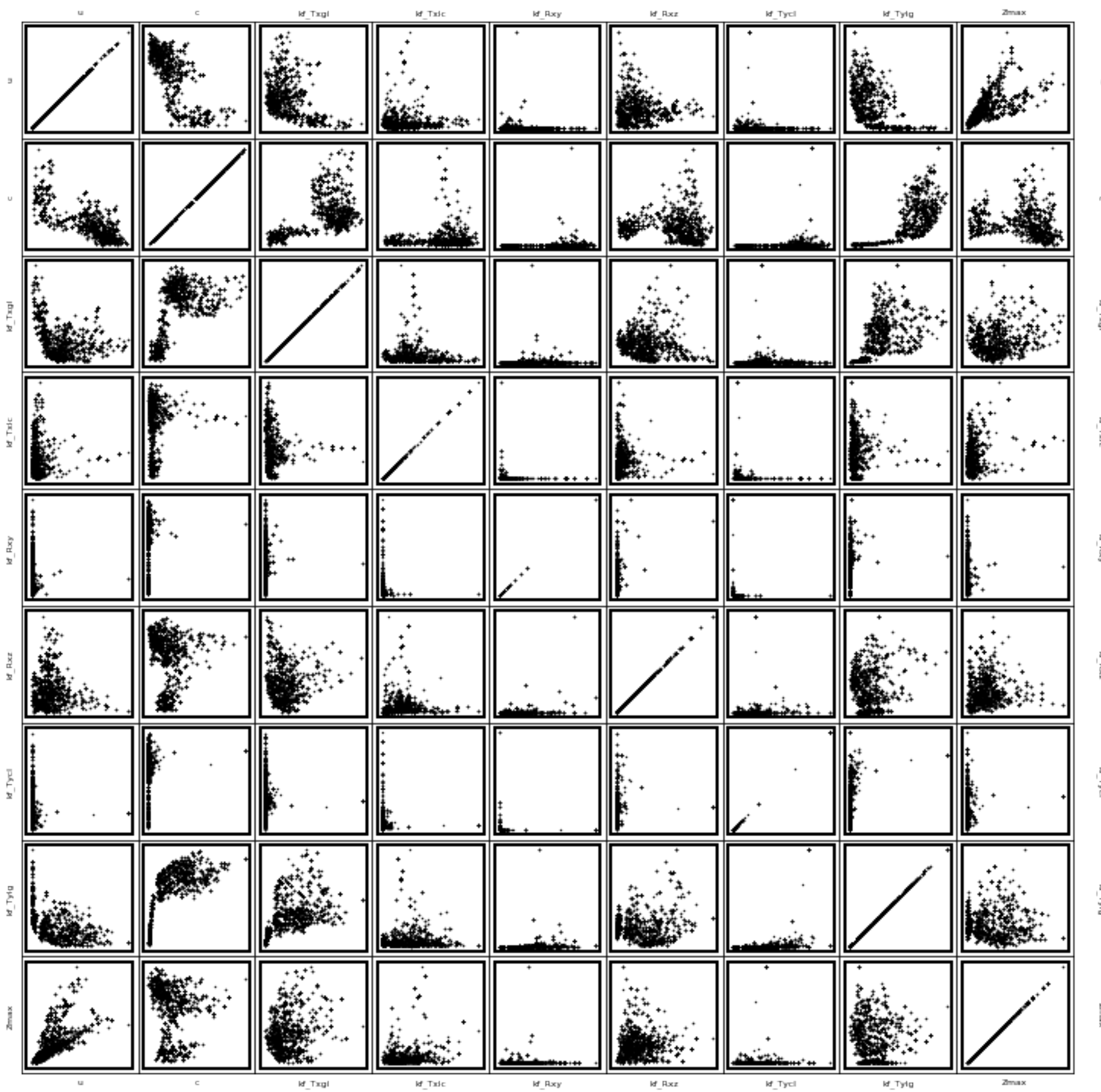
Below we construct the parameter ensemble by sampling the (posterior) distribution which captures "how data constrain the model".

```
In [15]: ens = sampling.sampling(res, nstep=5000, p0=fit.p, in_logp=True, seed=1,
                                 interval_print_step=1000, stepscale=0.5)
```

```
1000
2000
3000
```

```
4000
5000
```

In [16]:
```python
ens.p.scatter(figsize=(12,12))
```



In [21]:
```python
# get the thinned/decorrelated parameter ensemble

pens = ens.p.iloc[::10]
```

In [22]:
```python
pens.describe()
```

Out[22]:

	u	c	kf_Txgl	kf_Txlc	kf_Rxy	\
count	501.000000	501.000000	501.000000	501.000000	501.000000	

mean	0.841109	1.024061	1.580624	1.810114	475.611162
std	0.461313	0.196507	0.841520	2.775020	3990.654710
min	0.213448	0.676267	0.424507	0.314164	0.110405
25%	0.466277	0.789775	0.905508	0.731345	0.789914
50%	0.723165	1.105590	1.444329	1.094758	1.919323
75%	1.084448	1.181394	1.906769	1.685933	16.359342
max	2.675515	1.347755	4.600355	22.876072	81419.264323

	kf_Rxz	kf_Tycl	kf_Tylg	Zmax
count	501.000000	501.000000	501.000000	501.000000
mean	1.021195	19.408758	4.021468	8.751104
std	0.629017	163.897781	3.836689	4.325823
min	0.154526	0.232653	0.110408	1.819985
25%	0.619225	0.748445	0.380317	5.736048
50%	0.919878	1.261584	2.864933	7.612013
75%	1.271829	2.788570	6.852556	11.405430
max	5.017487	2526.284991	19.448108	26.242215

1.6 Sensitivity calculation

Next we compute the parameter sensitivity of two quantities:

1. Steady-state concentration of Y in liquid Y_l: it is chosen to represent the liquid **titer** of the product.
2. Steady-state flux of Y in the off-gas $J_{T_{y,out}}$: it is chosen to represent the **productivity** of the product (in the off-gas).

Why are we interested in the parameter sensitivity of these two quantities?

Let's take Y_l as an example. $\dfrac{\partial Y_l}{\partial p}$ indicates if we change parameter p, how responsive is Y_l. Since we have nine parameters in this model, we can examine which parameters should be tuned and in what way if we want to increase Y_l.

Such concepts are inspired by **Metabolic Control Analysis** (MCA), and formalize **rate-limiting steps**. For example, if $\dfrac{\partial J_{T_{Y,out}}}{\partial k_{T_{x,gl}}} \gg 0$ then we may conclude that "the productivity of Y in the off-gas is substrate-transport-limited (from gas to liquid)".

Plotting the sensitivities over the parameter ensemble constructed above, which results in *histograms* of sensitivities, gives us a sense of how tight the sensitivity predictions are: if our data is able to contrain our model and makes it preditive, sensitivity histograms should have a clear pattern and conveys a clear message.

```
In [23]: # Define functions that takes in a parameter vector and computes the parameter sensit
         # select quantities, Yl and JTyout

         def get_Yl_sens(p):
             try:
                 return mca.get_concentration_response_matrix(reactor, p=p, normed=1).loc['Yl']
             except:
                 pass
```

```
def get_JTyout_sens(p):
    try:
        return mca.get_flux_response_matrix(reactor, p=p, normed=1).loc['Tyout']
    except:
        pass
```

In [24]:
```
# Compute the sensivity ensembles (can take a couple of mins depending on ensemble si

sens_Yl = pens.apply(get_Yl_sens, axis=1)
sens_JTyout = pens.apply(get_JTyout_sens, axis=1)
```

By inspecting the sensitivity ensembles below, one can see that: * $\frac{\partial Y_l}{\partial c}$ and $\frac{\partial J_{T_{Y,out}}}{\partial c}$ are always 1 * $\frac{\partial Y_l}{\partial kf_{R_{xz}}}$ and $\frac{\partial J_{T_{Y,out}}}{\partial kf_{R_{xz}}}$ are always 0

This makes sense: the quantities scale linearly with c in our model and reaction R_{xz} always goes to 0 in steady state (all carbon goes to product conversion and none goes to cell growth).

In [25]:
```
sens_Yl.describe()
```

Out[25]:
```
                u             c     kf_Txgl     kf_Txlc        kf_Rxy  \
count  501.000000  5.010000e+02  501.000000  501.000000  5.010000e+02
mean    -0.110142  1.000000e+00    0.176309    0.048145  2.028101e-02
std      0.051737  1.801589e-10    0.045852    0.036003  2.950067e-02
min     -0.263825  1.000000e+00    0.073899    0.001829  2.460964e-07
25%     -0.136453  1.000000e+00    0.147047    0.024452  1.519378e-03
50%     -0.103509  1.000000e+00    0.175266    0.036909  1.183742e-02
75%     -0.073056  1.000000e+00    0.206849    0.061586  2.465435e-02
max     -0.013214  1.000000e+00    0.308542    0.188738  1.674451e-01

             kf_Rxz     kf_Tycl     kf_Tylg        Zmax
count  5.010000e+02  501.000000  501.000000  501.000000
mean   3.656924e-19    0.041716   -0.178681    0.080188
std    1.038243e-17    0.036408    0.102984    0.039334
min   -4.982050e-17    0.000016   -0.347658    0.009276
25%    0.000000e+00    0.016130   -0.295220    0.053094
50%    0.000000e+00    0.034322   -0.156139    0.073516
75%    0.000000e+00    0.056932   -0.080413    0.098818
max    4.751860e-17    0.200989   -0.029672    0.211287
```

In [26]:
```
sens_JTyout.describe()
```

Out[26]:
```
                u             c     kf_Txgl     kf_Txlc        kf_Rxy  \
count  501.000000  5.010000e+02  501.000000  501.000000  5.010000e+02
mean     0.889858  1.000000e+00    0.176309    0.048145  2.028101e-02
std      0.051737  1.817843e-10    0.045852    0.036003  2.950067e-02
min      0.736175  1.000000e+00    0.073899    0.001829  2.460964e-07
25%      0.863547  1.000000e+00    0.147047    0.024452  1.519378e-03
```

```
50%      0.896491  1.000000e+00    0.175266    0.036909  1.183742e-02
75%      0.926944  1.000000e+00    0.206849    0.061586  2.465435e-02
max      0.986786  1.000000e+00    0.308542    0.188738  1.674451e-01

             kf_Rxz     kf_Tycl     kf_Tylg        Zmax
count  5.010000e+02  501.000000  501.000000  501.000000
mean   3.656924e-19    0.041716    0.202783    0.080188
std    1.038243e-17    0.036408    0.189498    0.039334
min   -4.982050e-17    0.000016    0.019233    0.009276
25%    0.000000e+00    0.016130    0.046338    0.053094
50%    0.000000e+00    0.034322    0.105710    0.073516
75%    0.000000e+00    0.056932    0.406152    0.098818
max    4.751860e-17    0.200989    0.636473    0.211287
```

```
In [27]: # a detailed look at the sensivities corresponding to one particular parameter

         import pandas as pd
         pd.options.display.width = 200
         pd.options.display.precision = 4

         print(mca.get_concentration_response_matrix(reactor, p=pens.iloc[0], normed=1), '\n')
         print(mca.get_flux_response_matrix(reactor, p=pens.iloc[0], normed=1))
```

```
            u           c     kf_Txgl     kf_Txlc      kf_Rxy      kf_Rxz     kf_Tycl     kf_T
Xl  9.2593e-02  1.0000e+00  2.2071e-01 -3.7576e-02 -1.7441e-02  1.4997e-17 -3.7576e-02 -1.7441e
Xc  1.9064e-02  1.0000e+00  2.2071e-01  4.7550e-02 -2.1118e-02 -2.1766e-16 -4.5496e-02 -2.1118e
Xg  3.3184e-02  1.0000e+00 -6.2508e-02 -1.3467e-02 -6.2508e-03  5.3749e-18 -1.3467e-02 -6.2508e
Yl -1.1717e-01  1.0000e+00  2.2071e-01  4.7550e-02  2.2071e-02 -1.8978e-17  4.7550e-02 -2.7929e
Yc -1.9924e-02  1.0000e+00  2.2071e-01  4.7550e-02  2.2071e-02 -2.2663e-16 -4.9696e-02 -2.3067e
Yg -1.1717e-01  1.0000e+00  2.2071e-01  4.7550e-02  2.2071e-02 -1.8978e-17  4.7550e-02  2.2071e
Z  -4.2330e-18 -2.2204e-16 -4.9007e-17 -1.0558e-17  4.6890e-18 -2.2204e-16  1.0102e-17  4.6890e

                u           c     kf_Txgl     kf_Txlc      kf_Rxy      kf_Rxz     kf_Tycl     I
Txin   1.0000e+00  1.0000e+00  0.0000e+00  0.0000e+00  0.0000e+00  0.0000e+00  0.0000e+00  0.00
Txgl   8.8283e-01  1.0000e+00  2.2071e-01  4.7550e-02  2.2071e-02 -1.8978e-17  4.7550e-02  2.20
Txlc   8.8283e-01  1.0000e+00  2.2071e-01  4.7550e-02  2.2071e-02 -1.8978e-17  4.7550e-02  2.20
Rxy    8.8283e-01  1.0000e+00  2.2071e-01  4.7550e-02  2.2071e-02 -1.8978e-17  4.7550e-02  2.20
Rxz    5.6179e-17  5.9201e-17 -8.9457e-18  8.2227e-17 -5.2156e-17 -0.0000e+00 -6.9468e-17  2.60
Tycl   8.8283e-01  1.0000e+00  2.2071e-01  4.7550e-02  2.2071e-02 -1.8978e-17  4.7550e-02  2.20
Tylg   8.8283e-01  1.0000e+00  2.2071e-01  4.7550e-02  2.2071e-02 -1.8978e-17  4.7550e-02  2.20
Txout  1.0332e+00  1.0000e+00 -6.2508e-02 -1.3467e-02 -6.2508e-03  5.3749e-18 -1.3467e-02 -6.25
Tyout  8.8283e-01  1.0000e+00  2.2071e-01  4.7550e-02  2.2071e-02 -1.8978e-17  4.7550e-02  2.20
```

```
In [29]: # one can verify that they follow the Summation Theorem of MCA (except the one for Rx
         # confirming our computation results

         print(mca.get_concentration_control_matrix(reactor, p=pens.iloc[0], normed=1).sum(axis
         print(mca.get_flux_control_matrix(reactor, p=pens.iloc[0], normed=1).sum(axis=1))
```

```
Xl     5.8053e-11
Xc     6.6853e-11
Xg     2.1058e-11
Yl     7.3316e-11
Yc     6.9873e-11
Yg     7.4209e-11
Z     -2.2204e-16
dtype: float64

Txin      1.0000e+00
Txgl      1.0000e+00
Txlc      1.0000e+00
Rxy       1.0000e+00
Rxz       1.6782e-17
Tycl      1.0000e+00
Tylg      1.0000e+00
Txout     1.0000e+00
Tyout     1.0000e+00
dtype: float64
```

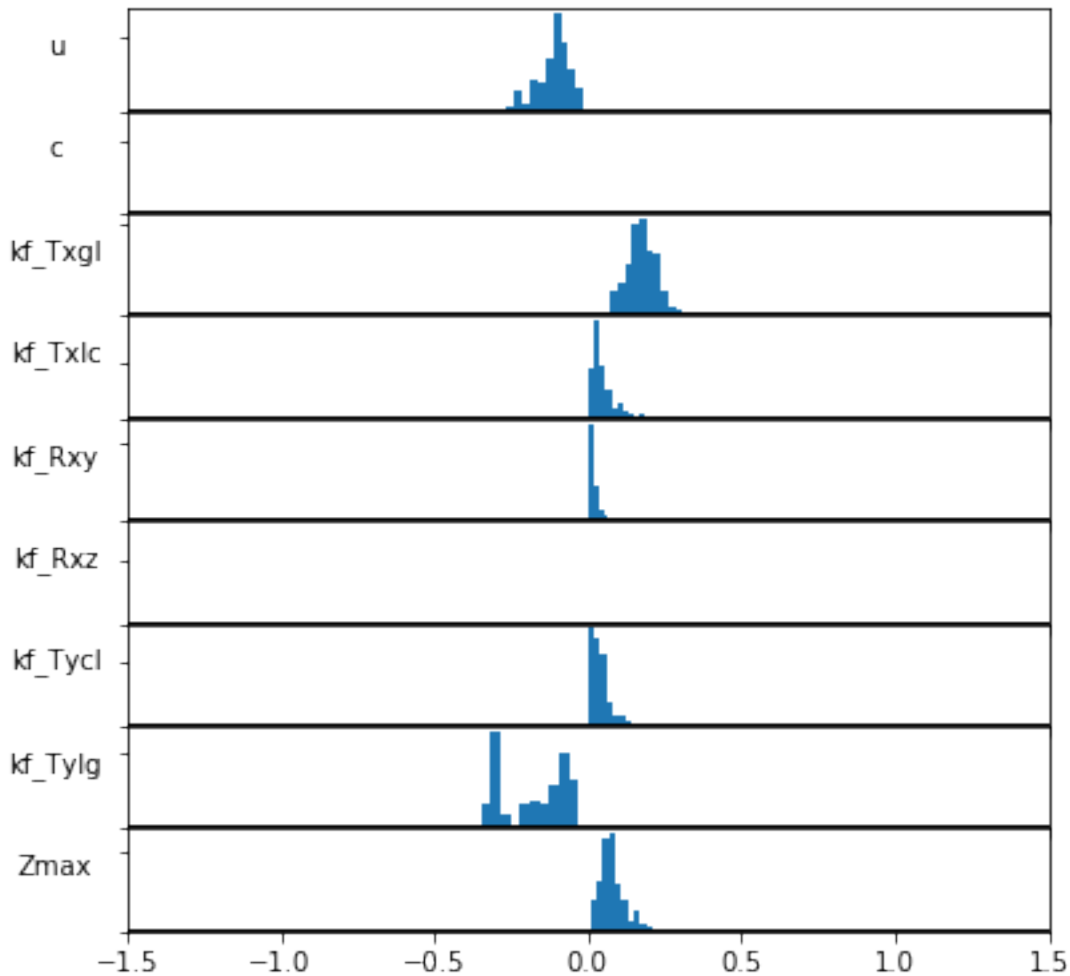
```
In [30]: sens_Yl = sens_Yl.dropna()
         sens_JTyout = sens_JTyout.dropna()

         print(sens_Yl.shape)
         print(sens_JTyout.shape)
```

```
(501, 9)
(501, 9)
```

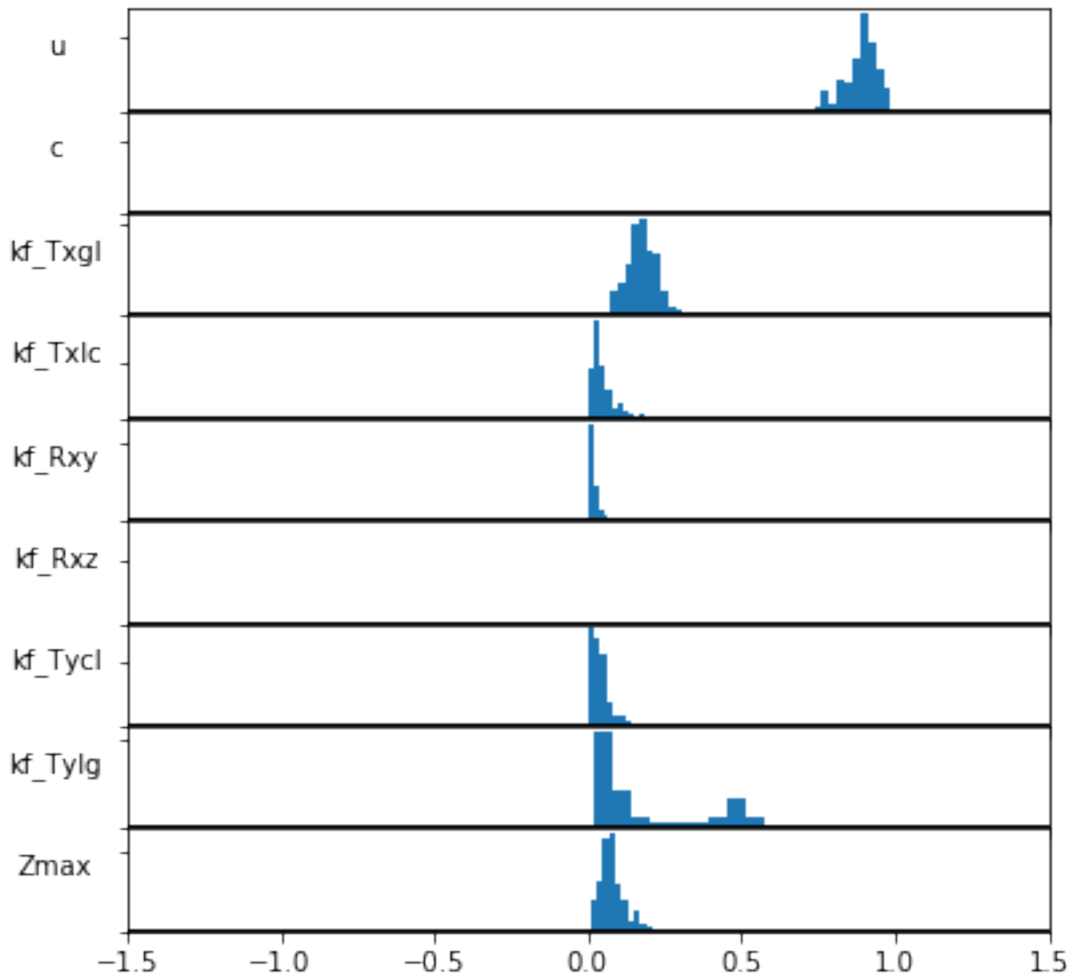
From the following two histogram plots, one can conclude that:

1. In order to increase the steady-state liquid titer Y_l, one could:
   - *Decrease* the substrate concentration in the gas feed c?? (One needs to double check this result and investigate the matter in more depth)
   - Increase the transport rate of X from gas to liquid
   - *Decrease* the transport rate of Y from liquid to gas
2. Changing other things will not affect Y_l much.
3. In order to increase the steady-state flux of Y in the off-gas, one could:
   - Increase u
   - Increase c
   - Increase the transport rate of X from gas to liquid
   - Increase the transport rate of Y from liquid to gas
4. Changing other things will not affect $J_{T_{Y,out}}$ much.

```
In [31]: sens_Yl.hist(xlims=[[-1.5,1.5]]*9, figsize=(6,6))
```




```
In [32]: sens_JTyout.hist(xlims=[[-1.5,1.5]]*9, figsize=(6,6))
```


u
c
kf_Txgl
kf_Txlc
kf_Rxy
kf_Rxz
kf_Tycl
kf_Tylg
Zmax
−1.5
−1.0
−0.5
0.0
0.5
1.0
1.5

```
In [ ]:
```