Tutorial 4

May 15, 2019

1 Tutorial 4 - Computational Biology

1.1 Part 1

Write down the differential equation describing the system of chemical equations (assuming a volume of 1) 1)   X at a rate 1 2) X Y at rate 2 3) 2 X + Y 3 X at rate 0.02 4) X   at rate 0.04

Systems of chemical equations are used to represent how gene regulation takes place. Converting in differential form the system shown above, the following two differential equations have been identified.

$$k_1 = 1, k_2 = 2, k_3 = 0.02, k_4 = 0.04$$

$$\frac{\partial x}{\partial t} = k_1 - k_2 \times x(t) - k_4 \times x(t) - k_3 \times x(t)^2 \times y(t)$$

$$\frac{\partial y}{\partial t} = k_2 \times x(t) - x(t)^2 \times y(t)$$

In [1]:
```
from sympy.interactive import printing
printing.init_printing(use_latex=True)
from sympy import *
import sympy as sp

k1 = 1
k2 = 2
k3 = 0.02
k4 = 0.04

t = sp.symbols('t')
y = sp.symbols('y')
#x = sp.symbols('x')
x = sp.Function('x')
# y = sp.Function('y')

eq = sp.Eq(x(t).diff(t),(k1 + k3*y(t)*(x(t)**2)) -(k4*x(t) + k2*x(t)))
display(eq)
so = dsolve(eq)
display(so)
```

```
x = sp.symbols('x')
y = sp.Function('y')

eq2 = Eq(y(t).diff(t),(k2*x(t) - k3*y(t)*(x(t)**2)))
display(eq2)
display(dsolve(eq2))
```

$$\frac{d}{dt}x(t) = 0.02x^2(t)y(t) - 2.04x(t) + 1$$

$$x(t) = t\,(0.02C_1y(0) - 2.04C_1 + 1) + \frac{t^2}{2}\left(0.02C_1\left.\frac{d}{dt}y(t)\right|_{t=0} + (C_1y(0) - 2.04)\,(0.02C_1y(0) - 2.04C_1 + 1)\right) + \frac{t^3}{6}\Bigg(0$$

$$\frac{d}{dt}y(t) = -0.02x^2(t)y(t) + 2x(t)$$

$$\left(e^{0.02\int x^2(t)\,dt} - 0.02\int x^2(t)e^{0.02\int x^2(t)\,dt}\,dt\right)y(t) + 1.0\int\left(-2.0x(t)e^{0.02\int x^2(t)\,dt}\right)dt + 1.0\int 0.02x^2(t)y(t)e^{0.02\int x^2(t)\,dt}$$

1.2 Part 2

Use a package to solve the differential equation for 500 time units starting from X(0)=Y(0)=0 (matlab will do this)

```
In [2]: import plotly
        print(plotly.__version__)
        plotly.tools.set_credentials_file(username='pierpaolo28', api_key='x6npysHAU1iZgcZMrIT
```

```
3.9.0
```

```
In [17]: import plotly.plotly as py
         import plotly.graph_objs as go

         # Create random data with numpy
         import numpy as np
         from scipy.integrate import odeint

         # function that returns dy/dt
         def model_fun(inp,t):
             k1 = 1
             k2 = 2
             k3 = 0.02
             k4 = 0.04
             x = inp[0]
             y = inp[1]
             dydt = (k2*x - k3*y*(x**2))
```

```
    dxdt = (k1 + k3*y*(x**2)) -(k4*x + k2*x)
#     dydt = (((k2*x)) - ((k3*y*(x**2))/(a**2)))
#     dxdt = ((k1*a + ((k3*y*(x**2))/(a**2))) - (((k4*x)) + ((k2*x))))
    return [dxdt,dydt]

# initial condition
z = [0,0]

# time points
t = np.linspace(0,500,500)
# solve ODEs
x1 = odeint(model_fun,z,t)

z1 = [14,20]
x2 = odeint(model_fun,z1,t)

# Create a trace
dxdt = go.Scatter(
    x = t,
    y = x1[:,0],
    name = 'dxdt'
)

# Create a trace
dydt = go.Scatter(
    x = t,
    y = x1[:,1],
    name = 'dydt'
)

# Create a trace
dxdt2 = go.Scatter(
    x = t,
    y = x2[:,0],
    name = 'dxdt x(0)=14'
)

# Create a trace
dydt2 = go.Scatter(
    x = t,
    y = x2[:,1],
    name = 'dydt y(0)=20'
)


data = [dxdt, dydt, dxdt2, dydt2]
layout = go.Layout(
    title=go.layout.Title(
```

```
                text='Differential Equations solved for 500 time units',
                xref='paper',
                x=0
            ),
            xaxis=go.layout.XAxis(
                title=go.layout.xaxis.Title(
                    text='Time',
                    font=dict(
                        family='Courier New, monospace',
                        size=18,
                        color='#7f7f7f'
                    )
                )
            ),
            yaxis=go.layout.YAxis(
                title=go.layout.yaxis.Title(
                    text='Concentration, X,Y',
                    font=dict(
                        family='Courier New, monospace',
                        size=18,
                        color='#7f7f7f'
                    )
                )
            )
        )
        fig = go.Figure(data=data, layout=layout)
        py.iplot(fig, filename='styling-names')
```

```
Out[17]: <chart_studio.tools.PlotlyDisplay object>
```

```
In [4]: k1 = 1
        k2 = 2
        k3 = 0.02
        k4 = 0.04

        xpl = np.linspace(23,26,500)
        res = (k2*xpl)/(k3*(xpl**2))
        res2 = (-k1+k2*xpl+k4*xpl)/(k3*(xpl**2))

        # Create a trace
        conc = go.Scatter(
            x = x1[:,0],
            y = x1[:,1],
            name = 'Concentration'
        )

        line1 = go.Scatter(
            x = xpl,
```

```
    y = res,
    name = 'dxdt=0'
)

line2 = go.Scatter(
    x = xpl,
    y = res2,
    name = 'dydt=0'
)

line3 = go.Scatter(
    x = [((k1)/(k4))],
    y = [((k2*k4)/(k3*k1))],
    name = 'Nullcline'
)

data = [conc, line1, line2, line3]

layout = go.Layout(
    title=go.layout.Title(
        text='X vs Y concentration',
        xref='paper',
        x=0
    ),
    xaxis=go.layout.XAxis(
        title=go.layout.xaxis.Title(
            text='Concentration, X',
            font=dict(
                family='Courier New, monospace',
                size=18,
                color='#7f7f7f'
            )
        )
    ),
    yaxis=go.layout.YAxis(
        title=go.layout.yaxis.Title(
            text='Concentration, Y',
            font=dict(
                family='Courier New, monospace',
                size=18,
                color='#7f7f7f'
            )
        )
    )
)
fig = go.Figure(data=data, layout=layout)

py.iplot(fig,filename='styling-names')
```

Out[4]: <chart_studio.tools.PlotlyDisplay object>

In [5]:
```
k1 = 1
k2 = 2
k3 = 0.02
k4 = 0.04

xpl = np.linspace(23,26,500)
res = (k2*xpl)/(k3*(xpl**2))
res2 = (-k1+k2*xpl+k4*xpl)/(k3*(xpl**2))

# Create a trace
line1 = go.Scatter(
    x = xpl,
    y = res,
    name = 'dxdt=0'
)

line2 = go.Scatter(
    x = xpl,
    y = res2,
    name = 'dydt=0'
)

line3 = go.Scatter(
    x = [((k1)/(k4))],
    y = [((k2*k4)/(k3*k1))],
    name = 'Nullcline'
)

data = [line1,line2,line3]

layout = go.Layout(
    title=go.layout.Title(
        text='Finding the intersection between dxdt=0 and dydt=0 (Nullcline)',
        xref='paper',
        x=0
    )
)
fig = go.Figure(data=data, layout=layout)

py.iplot(fig,filename='styling-names')
```

Out[5]: <chart_studio.tools.PlotlyDisplay object>

In [19]:
```
a = 6.022140857*(10**(23))
k1 = np.linspace(1,35,100)
# function that returns dy/dt
```

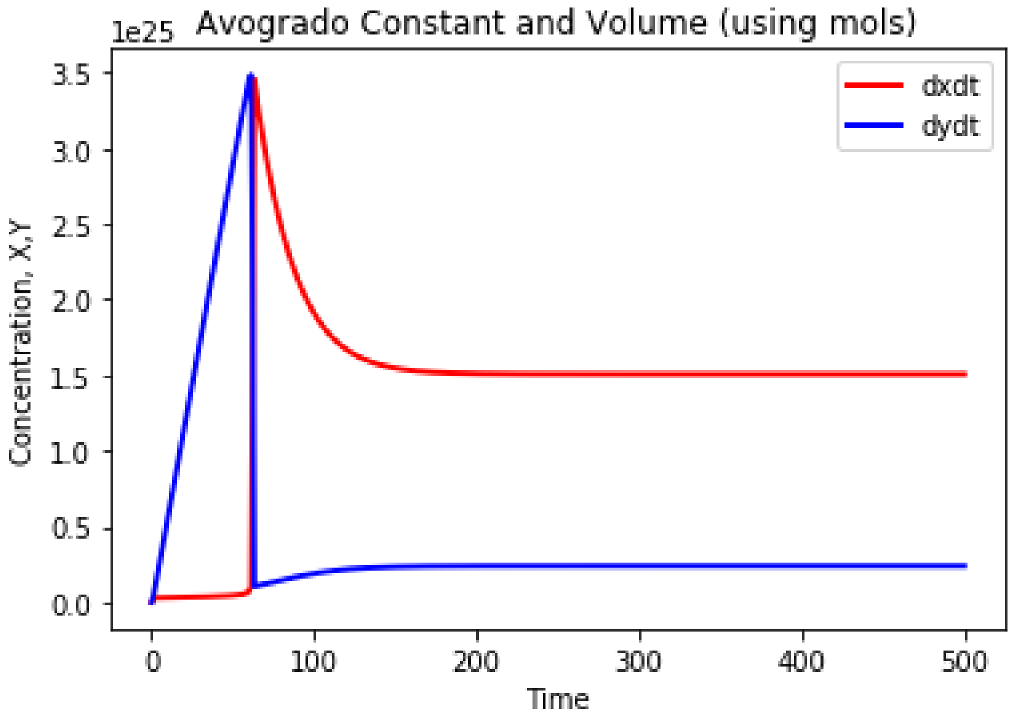
```python
def model_fun(inp,k1):
    #k1 = 1
    k2 = k1
    k3 = 0.02
    k4 = 0.04
    x = inp[0]
    y = inp[1]
    dydt = (((k2*x)) - ((k3*y*(x**2))))
    dxdt = ((k1 + ((k3*y*(x**2))) - (((k4*x)) + ((k2*x)))))
    return [dxdt,dydt]

# initial condition
z = [0,0]

# time points
t = np.linspace(0,500,500)
# solve ODEs
x1 = odeint(model_fun,z,k1)

# Create a trace
kconc = go.Scatter(
    x = k1,
    y = x1[:,0],
    name = 'Concentration, X'
)

# Create a trace
kconc2 = go.Scatter(
    x = k1,
    y = x1[:,1],
    name = 'Concentration, Y'
)


data = [kconc, kconc2]
layout = go.Layout(
    title=go.layout.Title(
        text='How the concentration of X and Y changes varying k1',
        xref='paper',
        x=0
    ),
    xaxis=go.layout.XAxis(
        title=go.layout.xaxis.Title(
            text='Varying k1 (k2)',
            font=dict(
                family='Courier New, monospace',
                size=18,
                color='#7f7f7f'
```

```
                )
            )
        ),
        yaxis=go.layout.YAxis(
            title=go.layout.yaxis.Title(
                text='Concentration of X and Y',
                font=dict(
                    family='Courier New, monospace',
                    size=18,
                    color='#7f7f7f'
                )
            )
        )
    )
    fig = go.Figure(data=data, layout=layout)
    py.iplot(fig, filename='styling-names')
```

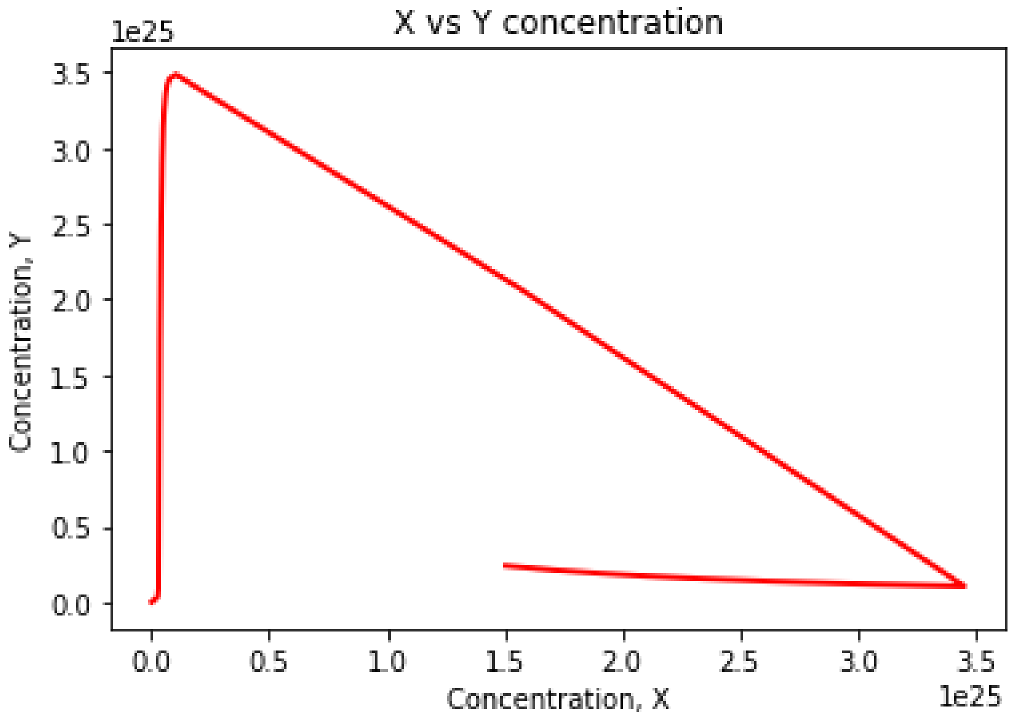
Out[19]: <chart_studio.tools.PlotlyDisplay object>

In [16]:
```
import matplotlib.pyplot as plt
from scipy.integrate import odeint
import numpy as np

a = 6.022140857*(10**(23))

# function that returns dy/dt
def model_fun(inp,t):
    k1 = 1
    k2 = 2
    k3 = 0.02
    k4 = 0.04
    x = inp[0]
    y = inp[1]
    dydt = (((k2*x)) - ((k3*y*(x**2))/(a**2)))
    dxdt = ((k1*a + ((k3*y*(x**2))/(a**2))) - (((k4*x)) + ((k2*x))))
    return [dxdt,dydt]

# initial condition
z = [0,0]

# time points
t = np.linspace(0,500,500)
# solve ODEs
x1 = odeint(model_fun,z,t)

# plot results
plt.plot(t,x1[:,0],'r-',linewidth=2,label='dxdt')
plt.plot(t,x1[:,1],'b-',linewidth=2,label='dydt')
```

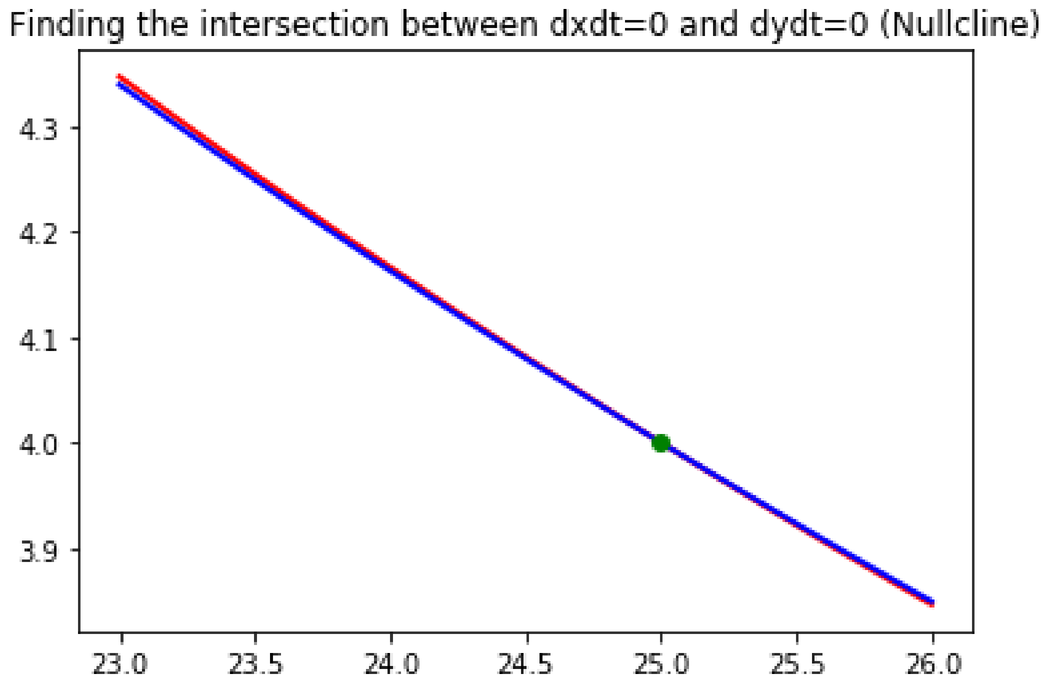
```
plt.title('Avogrado Constant and Volume (using mols)')
plt.xlabel('Time')
plt.ylabel('Concentration, X,Y')
plt.legend()
plt.show()
```




```
In [8]: k1 = 1
        k2 = 2
        k3 = 0.02
        k4 = 0.04

        plt.plot(x1[:,0], x1[:,1],'r-',linewidth=2)
        plt.xlabel('Concentration, X')
        plt.ylabel('Concentration, Y')
        plt.title('X vs Y concentration')
        plt.show()
```

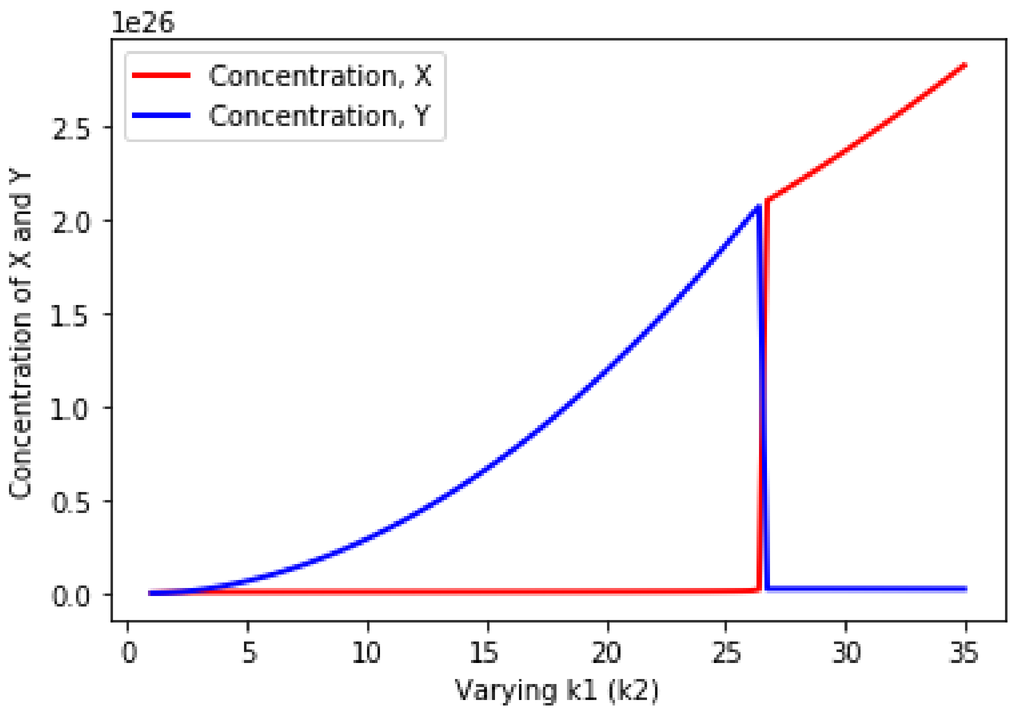



```
In [9]: xpl = np.linspace(23,26,500)
        res = (k2*xpl)/(k3*(xpl**2))
        res2 = (-k1+k2*xpl+k4*xpl)/(k3*(xpl**2))

        plt.plot(xpl, res,'r-',linewidth=2,label='y')
        plt.plot(xpl, res2,'b-',linewidth=2,label='x')
        plt.plot(((k1)/(k4)),((k2*k4)/(k3*k1)), linestyle='--', marker='o', color='g')
        plt.title('Finding the intersection between dxdt=0 and dydt=0 (Nullcline)')
        plt.show()
```



In [20]:
```
import matplotlib.pyplot as plt
from scipy.integrate import odeint
import numpy as np

a = 6.022140857*(10**(23))
k1 = np.linspace(1,35,100)
# function that returns dy/dt
def model_fun(inp,k1):
    #k1 = 1
    k2 = k1
    k3 = 0.02
    k4 = 0.04
    x = inp[0]
    y = inp[1]
    dydt = (((k2*x)) - ((k3*y*(x**2))/(a**2)))
    dxdt = ((k1*a + ((k3*y*(x**2))/(a**2))) - (((k4*x)) + ((k2*x))))
    return [dxdt,dydt]

# initial condition
z = [0,0]

# time points
t = np.linspace(0,500,500)
# solve ODEs
x1 = odeint(model_fun,z,k1)
```

```python
# plot results
plt.plot(k1,x1[:,0],'r-',linewidth=2,label='Concentration, X')
plt.plot(k1,x1[:,1],'b-',linewidth=2,label='Concentration, Y')
plt.xlabel('Varying k1 (k2)')
plt.ylabel('Concentration of X and Y')
plt.legend()
plt.show()
```

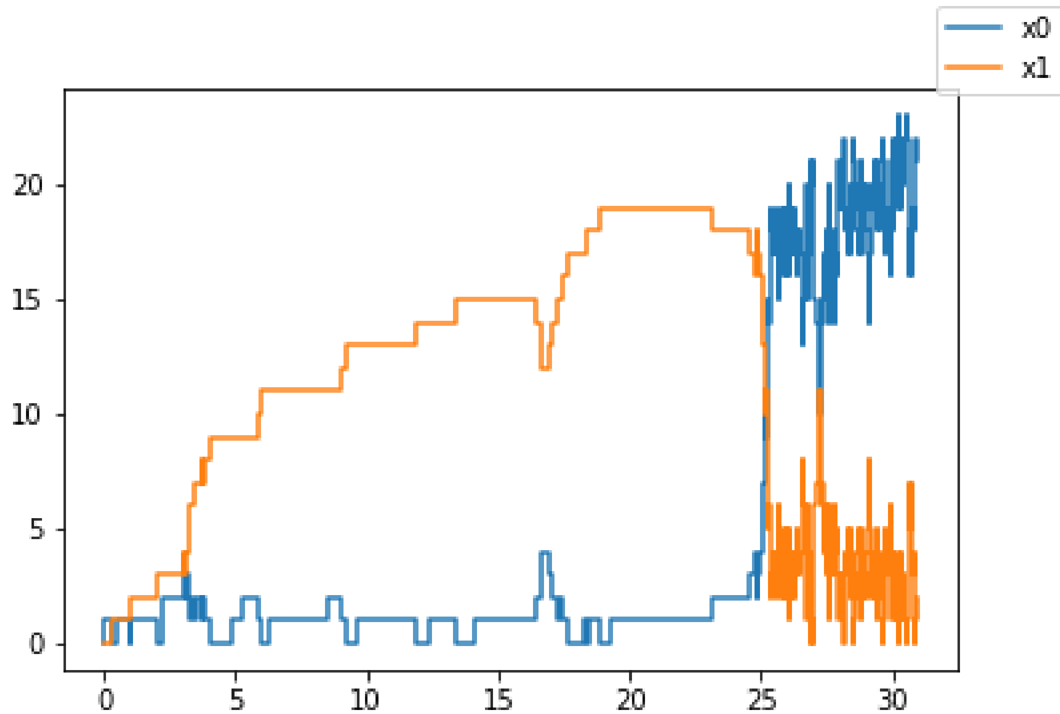


1.3 Part 3

Write a Gillespie algorithm to simulate the same four chemical equation and plot the results for 500 time units (note that this is a lot of data to plot and you might want to save and plot the data only after X or Y have changed in number by at least 5.)

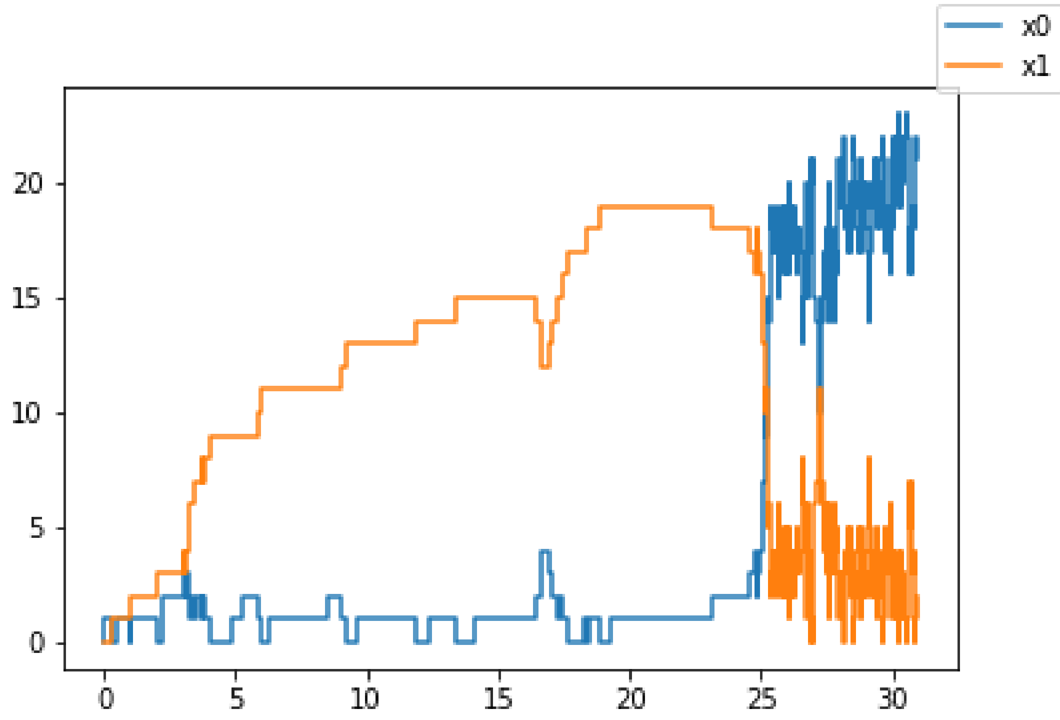
```python
In [11]: # Looking at the 4 chemical reactions, the reactant matrix can be formed by placing a
         # list of lists (V_r left side, V_p right side), and the Y values in the second eleme
         # (V_r left side, V_p right side).

         from pyssa.simulation import Simulation
         V_r = np.array([[0, 1, 2, 1], [0, 0, 1, 0]]) # Reactant matrix
         V_p = np.array([[1, 0, 3, 0], [0, 1, 0, 0]]) # Product matrix
         X0 = np.array([0,0]) # Initial state
         k1 = 1
```

```
k2 = 2
k3 = 0.02
k4 = 0.04
k = np.array([k1, k2, k3, k4]) # Rate constants
sim = Simulation(V_r, V_p, X0, k) # Declare the simulation object
# Run the simulation
sim.simulate(max_t=100, max_iter=500, chem_flag=True, n_rep=1)
sim.plot()
```




```
Out[11]: (<Figure size 432x288 with 1 Axes>,
          <matplotlib.axes._subplots.AxesSubplot at 0x178b974c588>)
```

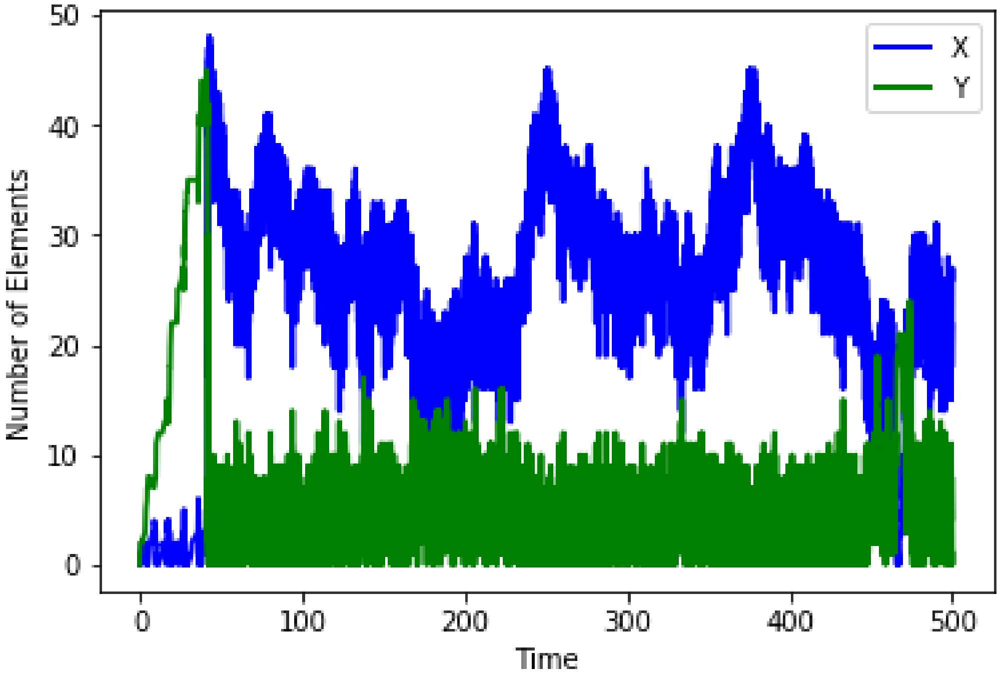
```
In [12]: sim.plot(plot_indices = [0, 1])
```




```
Out[12]: (<Figure size 432x288 with 1 Axes>,
          <matplotlib.axes._subplots.AxesSubplot at 0x178b9bc4748>)

In [13]: results = sim.results
         print(results)

<Results n_rep=1 algorithm=direct seed=[0]>


In [35]: import numpy as np
         from numpy.random import choice
         import matplotlib.pyplot as plt

         x = 0
         y = 0


         k1 = 1
         k2 = 2
         k3 = 0.02
         k4 = 0.04

         p1 = k1
         p2 = k2*x
```

```
p3 = k3*((x**2)*y)
p4 = k4*x

l2 = []
l3 = []
t = [0]

some_table = [
    [1,0],
    [-1,1],
    [1,-1],
    [-1,0],
]

psum = np.sum(p1+p2+p3+p4)

tim = np.random.exponential(1/psum)
t.append(t[-1] + tim)

while t[-1]<500:
#for f in range(0,500):
    p1 = k1
    p2 = k2*x
    p3 = k3*((x**2)*y)
    p4 = k4*x
    psum = np.sum(p1+p2+p3+p4)
    tim = np.random.exponential(1/psum)
    t.append(t[-1] + tim)
    #print(tim)
    elements = ['eq1', 'eq2', 'eq3', 'eq4']
    weights = [p1, p2, p3, p4]
    weights = [float(j)/sum(weights) for j in weights]
    reaction = np.random.choice(a=4, p=weights)
    if reaction == 0:
        x = x + 1
        l2.append(x)
        l3.append(y)
    elif reaction == 1:
        x-= 1
        l2.append(x)
        y+= 1
        l3.append(y)
    elif reaction == 2:
        x+= 1
        l2.append(x)
        y-= 1
        l3.append(y)
    elif reaction == 3:
```

```
        x-= 1
        l2.append(x)
        l3.append(y)


#xp = np.linspace(0,tim,len(l2))
#xp2 = np.linspace(0,tim,len(l3))

plt.plot(t[:-2],l2,'b-', linewidth=2.0)
plt.plot(t[:-2],l3,'g-', linewidth=2.0)
plt.xlabel("Time")
plt.ylabel("Number of Elements")
plt.legend(["X","Y"])
plt.show()
```




```
In [36]: # function that returns dy/dt
         from scipy.integrate import odeint
         import plotly.plotly as py
         import plotly.graph_objs as go
         def model_fun(inp,t2):
             k1 = 1
             k2 = 2
             k3 = 0.02
             k4 = 0.04
             x = inp[0]
```

```
    y = inp[1]
    dydt = (k2*x - k3*y*(x**2))
    dxdt = (k1 + k3*y*(x**2)) -(k4*x + k2*x)
#     dydt = (((k2*x)) - ((k3*y*(x**2))/(a**2)))
#     dxdt = ((k1*a + ((k3*y*(x**2))/(a**2))) - (((k4*x)) + ((k2*x))))
    return [dxdt,dydt]

# initial condition
z = [0,0]

# time points
t2 = np.linspace(0,500,500)
# solve ODEs
x1 = odeint(model_fun,z,t2)

# Create a trace
dxdt = go.Scatter(
    x = t2,
    y = x1[:,0],
    name = 'X (ODE)'
)

# Create a trace
dydt = go.Scatter(
    x = t2,
    y = x1[:,1],
    name = 'Y (ODE)'
)

line3 = go.Scatter(
    x = t[:-2],
    y = l2,
    name = 'X (Gillespie algorithm)'
)

line4 = go.Scatter(
    x = t[:-2],
    y = l3,
    name = 'Y (Gillespie algorithm)'
)

data = [dxdt,dydt,line3, line4]
```

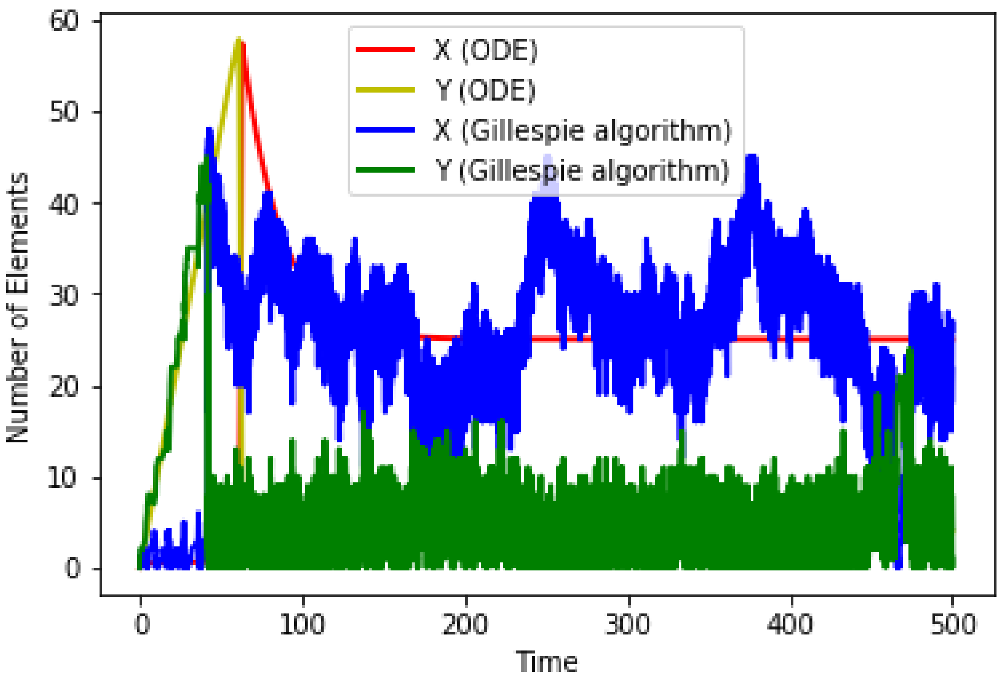
In [52]:
```
layout = go.Layout(
    title=go.layout.Title(
        text='ODE vs Gillespie algorithm',
        xref='paper',
        x=0
```

```
    ),
    xaxis=go.layout.XAxis(
        title=go.layout.xaxis.Title(
            text='Time',
            font=dict(
                family='Courier New, monospace',
                size=18,
                color='#7f7f7f'
            )
        )
    ),
    yaxis=go.layout.YAxis(
        title=go.layout.yaxis.Title(
            text='Concentration, X,Y',
            font=dict(
                family='Courier New, monospace',
                size=18,
                color='#7f7f7f'
            )
        )
    )
)

fig = go.Figure(data=data, layout=layout)

py.iplot(fig,filename='styling-names')
```

```
C:\Users\hp\Anaconda3\lib\site-packages\chart_studio\plotly\plotly.py:248: UserWarning:

Woah there! Look at all those points! Due to browser limitations, the Plotly SVG drawing functi
(1) Use the `plotly.graph_objs.Scattergl` trace object to generate a WebGl graph.
(2) Trying using the image API to return an image instead of a graph URL
(3) Use matplotlib
(4) See if you can create your visualization with fewer data points

If the visualization you're using aggregates points (e.g., box plot, histogram, etc.) you can d



The draw time for this plot will be slow for all clients.


C:\Users\hp\Anaconda3\lib\site-packages\chart_studio\api\v1\clientresp.py:44: UserWarning:

Estimated Draw Time Too Long
```

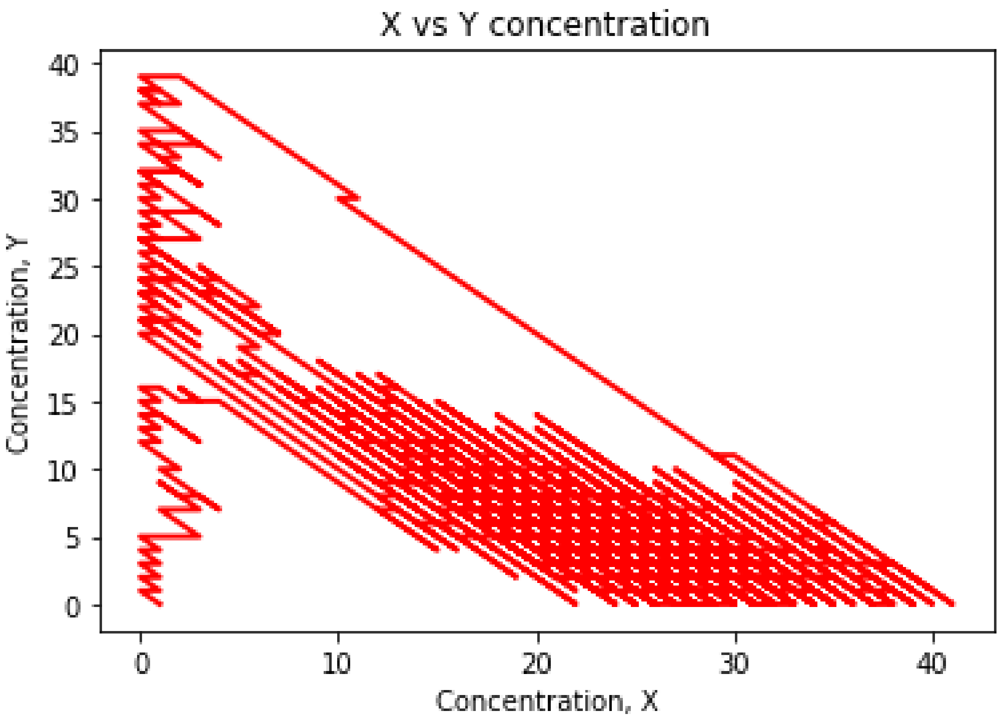
```
Out[52]: <chart_studio.tools.PlotlyDisplay object>
```

In [50]:
```
plt.plot(t2,x1[:,0],'r-', linewidth=2.0)
plt.plot(t2,x1[:,1],'y-', linewidth=2.0)
plt.plot(t[:-2],l2,'b-', linewidth=2.0)
plt.plot(t[:-2],l3,'g-', linewidth=2.0)
plt.xlabel("Time")
plt.ylabel("Number of Elements")
plt.legend(["X (ODE)","Y (ODE)",'X (Gillespie algorithm)','Y (Gillespie algorithm)'])
plt.figure(figsize=(200,200))
plt.show()
```




```
<Figure size 14400x14400 with 0 Axes>
```

In [8]:
```
plt.plot(l2, l3,'r-',linewidth=2)
plt.xlabel('Concentration, X')
plt.ylabel('Concentration, Y')
plt.title('X vs Y concentration')
plt.show()
```




```
In [9]: k1 = 1
        k2 = 2
        k3 = 0.02
        k4 = 0.04

        xpl = np.linspace(23,26,500)
        res = (k2*xpl)/(k3*(xpl**2))
        res2 = (-k1+k2*xpl+k4*xpl)/(k3*(xpl**2))

        # Create a trace
        conc = go.Scatter(
            x = x1[:,0],
            y = x1[:,1],
            name = 'ODE'
        )

        line1 = go.Scatter(
            x = l2,
            y = l3,
            name = 'Gillespie algorithm'
        )


        data = [conc, line1]
```

```python
layout = go.Layout(
    title=go.layout.Title(
        text='X vs Y concentration',
        xref='paper',
        x=0
    ),
    xaxis=go.layout.XAxis(
        title=go.layout.xaxis.Title(
            text='Concentration, X',
            font=dict(
                family='Courier New, monospace',
                size=18,
                color='#7f7f7f'
            )
        )
    ),
    yaxis=go.layout.YAxis(
        title=go.layout.yaxis.Title(
            text='Concentration, Y',
            font=dict(
                family='Courier New, monospace',
                size=18,
                color='#7f7f7f'
            )
        )
    )
)
fig = go.Figure(data=data, layout=layout)

py.iplot(fig,filename='styling-names')
```

```
C:\Users\hp\Anaconda3\lib\site-packages\chart_studio\plotly\plotly.py:248: UserWarning:

Woah there! Look at all those points! Due to browser limitations, the Plotly SVG drawing functi
(1) Use the `plotly.graph_objs.Scattergl` trace object to generate a WebGl graph.
(2) Trying using the image API to return an image instead of a graph URL
(3) Use matplotlib
(4) See if you can create your visualization with fewer data points

If the visualization you're using aggregates points (e.g., box plot, histogram, etc.) you can d



The draw time for this plot will be slow for clients without much RAM.


C:\Users\hp\Anaconda3\lib\site-packages\chart_studio\api\v1\clientresp.py:44: UserWarning:
```

```
Estimated Draw Time Slow
```

```
Out[9]: <chart_studio.tools.PlotlyDisplay object>
```