Auto-activation

Example of a self-activating transcriptional system where x_1 is the mRNA and x_2 is the protein:

$$\frac{dx_1}{dt} = \alpha \frac{x_2^n}{K + x_2^n} - \beta x_1$$

$$\frac{dx_2}{dt} = \gamma x_1 - \delta x_2$$

The null-clines of this system are:

$$x_1 = \frac{\alpha}{\beta} \frac{x_2^n}{K + x_2^n}$$

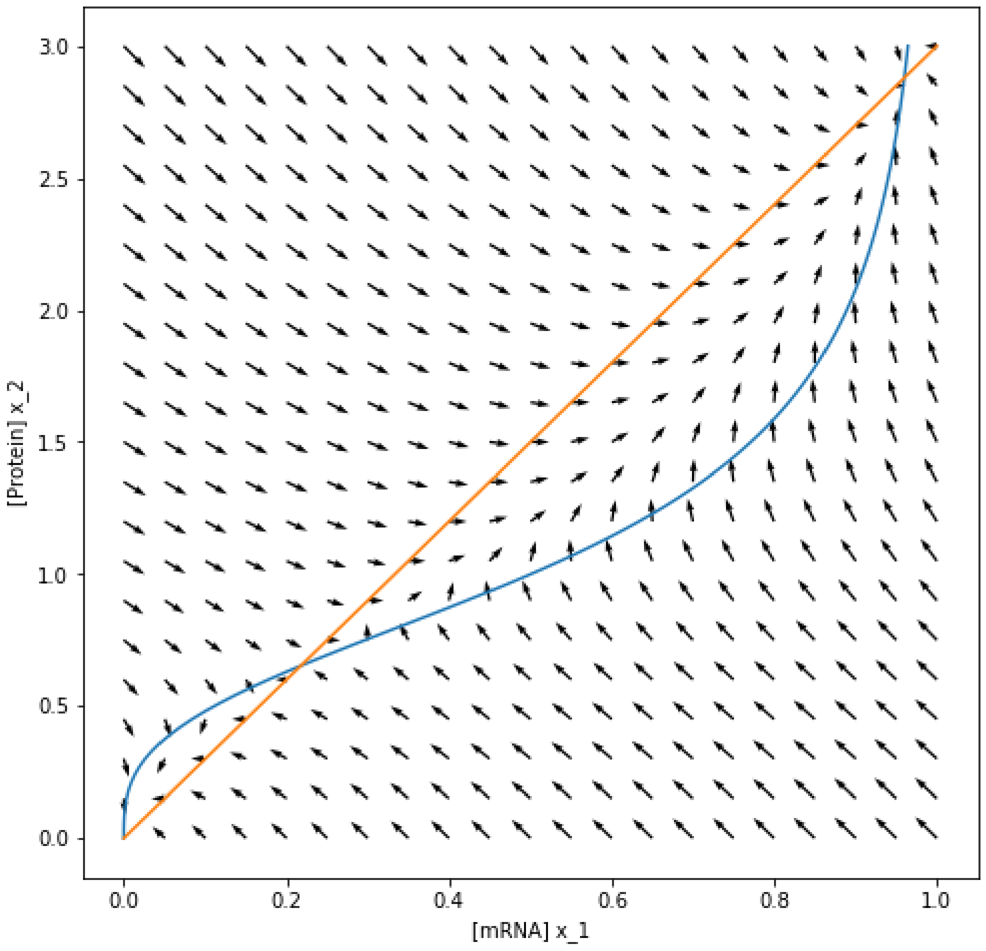
$$x_1 = \frac{\delta}{\gamma} x_2$$

In [1]:

```
import numpy as np
import matplotlib.pyplot as plt
from scipy.integrate import odeint

def dxdt(x,t, a,b,c,d,K,n):
    return [a*x[1]**n/(K+x[1]**n) - b*x[0], c*x[0] - d*x[1]]

b=1
d=1
a=1
c=3
K=1
n=3

plt.figure(figsize=(8,8))
x_2 = np.linspace(0,3,101)
plt.plot(a/b*x_2**n/(K+x_2**n), x_2)
plt.plot(d/c*x_2, x_2)
plt.xlabel('[mRNA] x_1')
plt.ylabel('[Protein] x_2')

grid = np.meshgrid(np.linspace(0,1,21), np.linspace(0,3,21))
arrows = dxdt(grid,0, a,b,c,d,K,n)
arrow_length = np.sqrt(arrows[0]**2 + arrows[1]**2)+1e-10
plt.quiver(grid[0], grid[1], arrows[0]/arrow_length**0.8, arrows[1]/arrow_length
**0.8, angles='xy')
```

Out[1]:

```
<matplotlib.quiver.Quiver at 0x7fa2074c6d10>
```

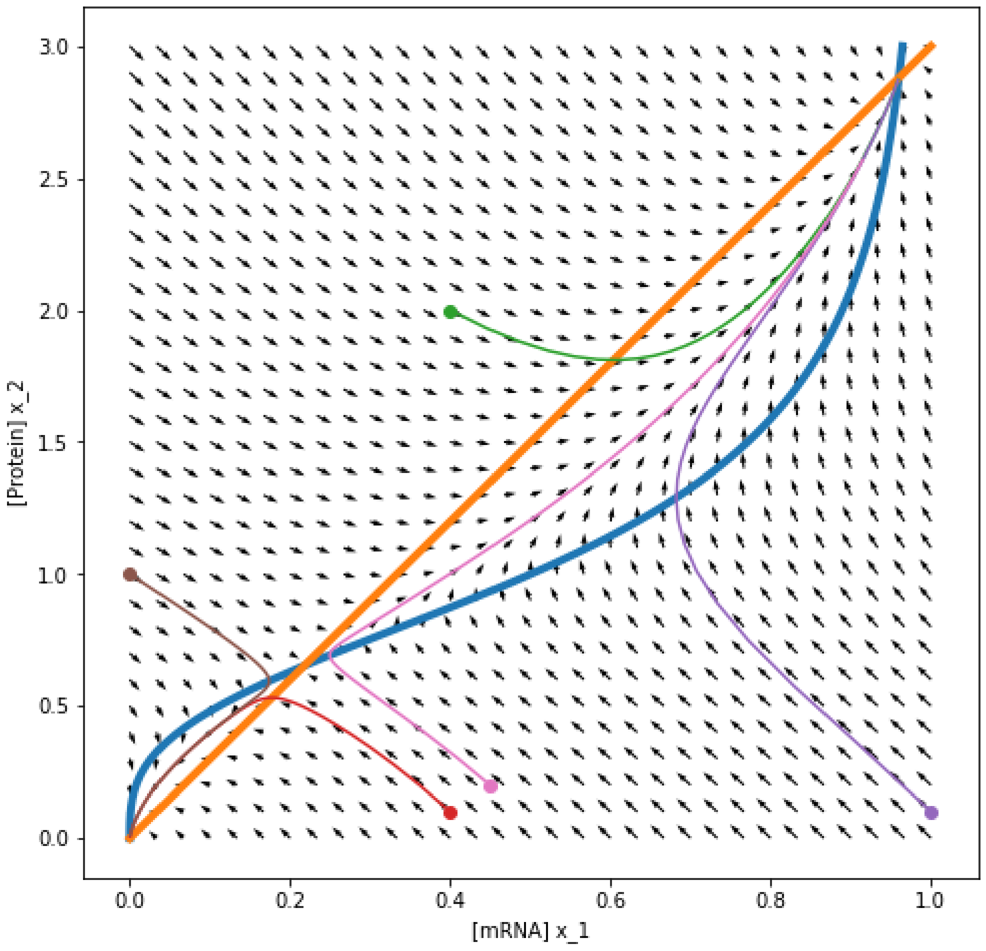


In [2]:

```
plt.figure(figsize=(8,8))
plt.plot(a/b*x_2**n/(K+x_2**n), x_2, lw=4)
plt.plot(d/c*x_2, x_2, lw=4)
plt.xlabel('[mRNA] x_1')
plt.ylabel('[Protein] x_2')

t = np.linspace(0,10,101)

grid = np.meshgrid(np.linspace(0,1,31), np.linspace(0,3,31))
arrows = dxdt(grid,0, a,b,c,d,K,n)
arrow_length = np.sqrt(arrows[0]**2 + arrows[1]**2)+1e-10
plt.quiver(grid[0], grid[1], arrows[0]/arrow_length**0.8, arrows[1]/arrow_length
**0.8, angles='xy')

x0 = [0.4, 2.0]
sol = odeint(dxdt, x0, t, args=(a,b,c,d,K,n))
plt.scatter([x0[0]], [x0[1]], c="C2")
plt.plot(sol[:,0], sol[:,1], c="C2")


x0 = [0.4, 0.1]
sol = odeint(dxdt, x0, t, args=(a,b,c,d,K,n))
plt.scatter([x0[0]], [x0[1]], c="C3")
plt.plot(sol[:,0], sol[:,1], c="C3")

x0 = [1.0, 0.1]
sol = odeint(dxdt, x0, t, args=(a,b,c,d,K,n))
plt.scatter([x0[0]], [x0[1]], c="C4")
plt.plot(sol[:,0], sol[:,1], c="C4")


x0 = [0.0, 1.0]
sol = odeint(dxdt, x0, t, args=(a,b,c,d,K,n))
plt.scatter([x0[0]], [x0[1]], c="C5")
plt.plot(sol[:,0], sol[:,1], c="C5")


x0 = [0.45, 0.2]
sol = odeint(dxdt, x0, t, args=(a,b,c,d,K,n))
plt.scatter([x0[0]], [x0[1]], c="C6")
plt.plot(sol[:,0], sol[:,1], c="C6")
```

Out[2]:

```
[<matplotlib.lines.Line2D at 0x7fa207438810>]
```



The above example is a case of self-activation:

- the protein at concentration x_2 increases transcription
- mRNA x_1 translates into protein x_2
- both quantities decay

This behavior results in three fixed points:

- A stable fixed point at (0,0): no protein, no transcription and no mRNA, no translation
- A stable fixed point at $\approx (1, 2.9)$: degradation and production balance each other for both mRNA and protein
- An unstable fixed point around $(0.2, 0.6)$: marks the point at which the system either goes to (0,0) or the high fixed point.

Self-repression

Next, we will discuss another useful example of gene regulation: auto-repression. The system of ODEs for this case is:

Example of a self-activating transcriptional system where x_1 is the mRNA and x_2 is the protein:

$$\frac{dx_1}{dt} = \alpha \frac{K}{K + x_2^n} - \beta x_1$$

$$\frac{dx_2}{dt} = \gamma x_1 - \delta x_2$$

and the corresponding null-clines are

$$x_1 = \frac{\alpha}{\beta} \frac{K}{K + x_2^n}$$

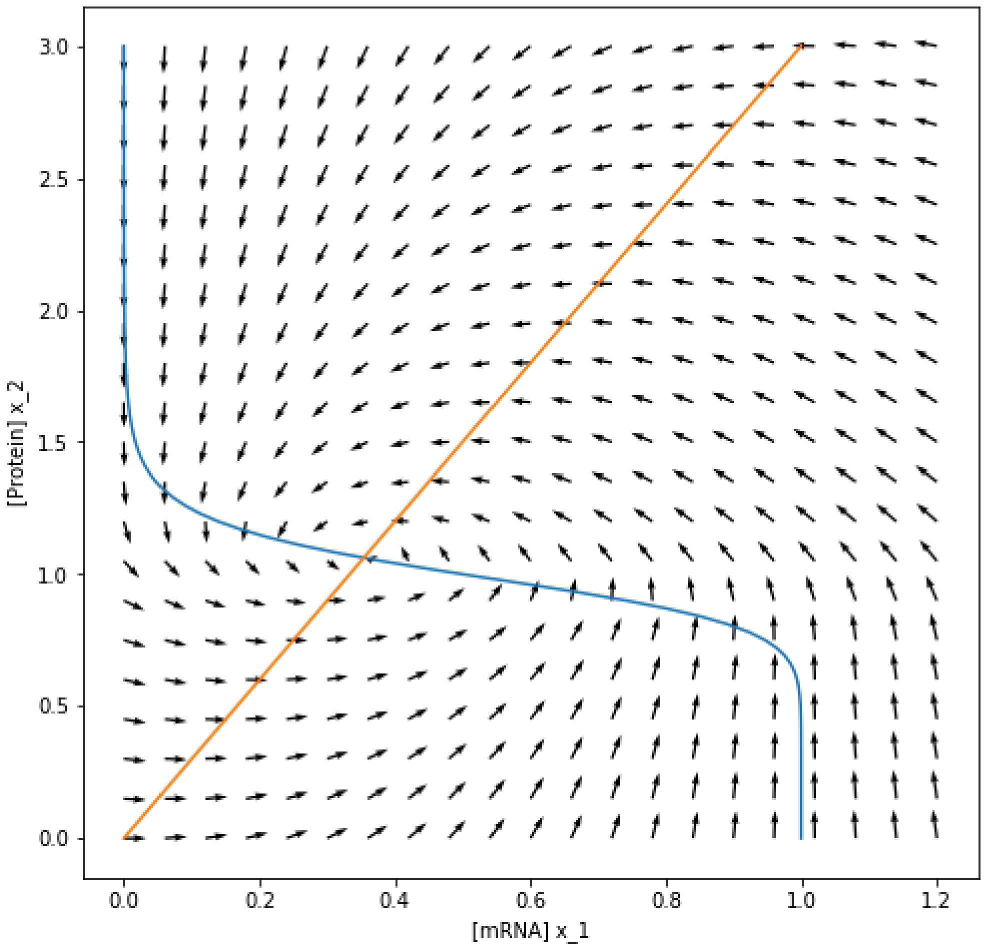
$$x_1 = \frac{\delta}{\gamma} x_2$$

In [3]:

```
def dxdt(x,t, a,b,c,d,K,n):
    return [a*K/(K+x[1]**n) - b*x[0], c*x[0] - d*x[1]]

x_2 = np.linspace(0,3,101)

b=1
d=1
a=1
c=3
K=1
n=10

plt.figure(figsize=(8,8))
plt.plot(a/b*K/(K+x_2**n), x_2)
plt.plot(d/c*x_2, x_2)
plt.xlabel('[mRNA] x_1')
plt.ylabel('[Protein] x_2')

grid = np.meshgrid(np.linspace(0,1.2,21), np.linspace(0,3,21))
arrows = dxdt(grid,0, a,b,c,d,K,n)
arrow_length = np.sqrt(arrows[0]**2 + arrows[1]**2)+1e-10
plt.quiver(grid[0], grid[1], arrows[0]/arrow_length**0.8, arrows[1]/arrow_length
**0.8, angles='xy')
```

Out[3]:

```
<matplotlib.quiver.Quiver at 0x7fa2073f8dd0>
```

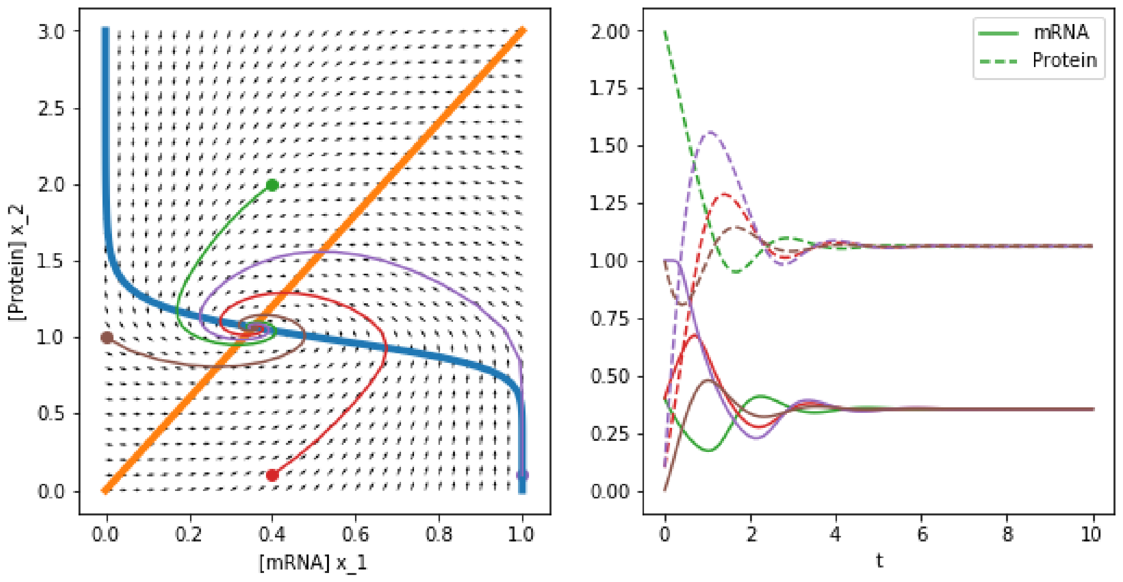


In [4]:

```
fig, axs = plt.subplots(1,2, figsize=(10,5))
axs[0].plot(a/b*K/(K+x_2**n), x_2, lw=4)
axs[0].plot(d/c*x_2, x_2, lw=4)
axs[0].set_xlabel('[mRNA] x_1')
axs[0].set_ylabel('[Protein] x_2')

grid = np.meshgrid(np.linspace(0,1,31), np.linspace(0,3,31))
arrows = dxdt(grid,0, a,b,c,d,K,n)
arrow_length = np.sqrt(arrows[0]**2 + arrows[1]**2)+1e-10
axs[0].quiver(grid[0], grid[1], arrows[0]/arrow_length**0.8, arrows[1]/arrow_len
gth**0.8, angles='xy')

x0 = [0.4, 2.0]
sol = odeint(dxdt, x0, t, args=(a,b,c,d,K,n))
axs[0].scatter([x0[0]], [x0[1]], c="C2")
axs[0].plot(sol[:,0], sol[:,1], c="C2")
axs[1].plot(t, sol[:,0], c="C2", label="mRNA")
axs[1].plot(t, sol[:,1], c="C2", ls='--', label="Protein")


x0 = [0.4, 0.1]
sol = odeint(dxdt, x0, t, args=(a,b,c,d,K,n))
axs[0].scatter([x0[0]], [x0[1]], c="C3")
axs[0].plot(sol[:,0], sol[:,1], c="C3")
axs[1].plot(t, sol[:,0], c="C3")
axs[1].plot(t, sol[:,1], c="C3", ls='--')

x0 = [1.0, 0.1]
sol = odeint(dxdt, x0, t, args=(a,b,c,d,K,n))
axs[0].scatter([x0[0]], [x0[1]], c="C4")
axs[0].plot(sol[:,0], sol[:,1], c="C4")
axs[1].plot(t, sol[:,0], c="C4")
axs[1].plot(t, sol[:,1], c="C4", ls='--')


x0 = [0.0, 1.0]
sol = odeint(dxdt, x0, t, args=(a,b,c,d,K,n))
axs[0].scatter([x0[0]], [x0[1]], c="C5")
axs[0].plot(sol[:,0], sol[:,1], c="C5")
axs[1].plot(t, sol[:,0], c="C5")
axs[1].plot(t, sol[:,1], c="C5", ls='--')

axs[1].set_xlabel('t')
axs[1].legend()
```

Out[4]:

```
<matplotlib.legend.Legend at 0x7fa20735fdd0>
```



Dig deeper

- Chance the cooperativity parameter n of the repressor (range 1 to 20). How does the behavior of the system change?
- Solve the system with the forward Euler approach that we used in the beginning of the course? (You should see the same behavior)
- Explore how stochasticity chances the dynamics of the auto-repressor! (use the forward Euler way of solving it and implement stochastic increments)