Assignment5

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Contents

1 The central dogma

1.1 Equations

1.2 Numerical simulation first model

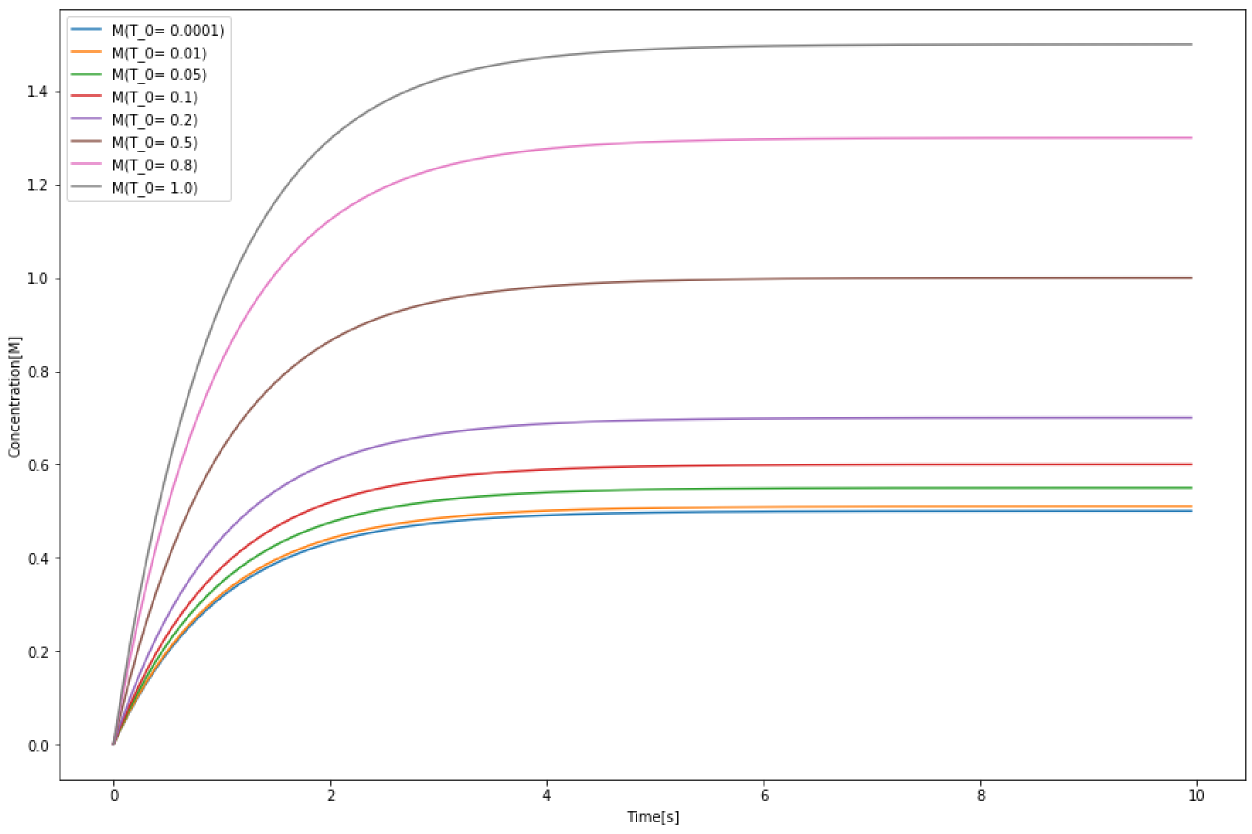
Script 1.2.1 (python)

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

# Initial conditions
M_0 = 0
P_0 = 0
Km = 1
Kp = 1
dm = 1
dp = 1
a = 0.5
T_0 = 1
D_0 = 1

total_time = 10
dt = 0.05
```

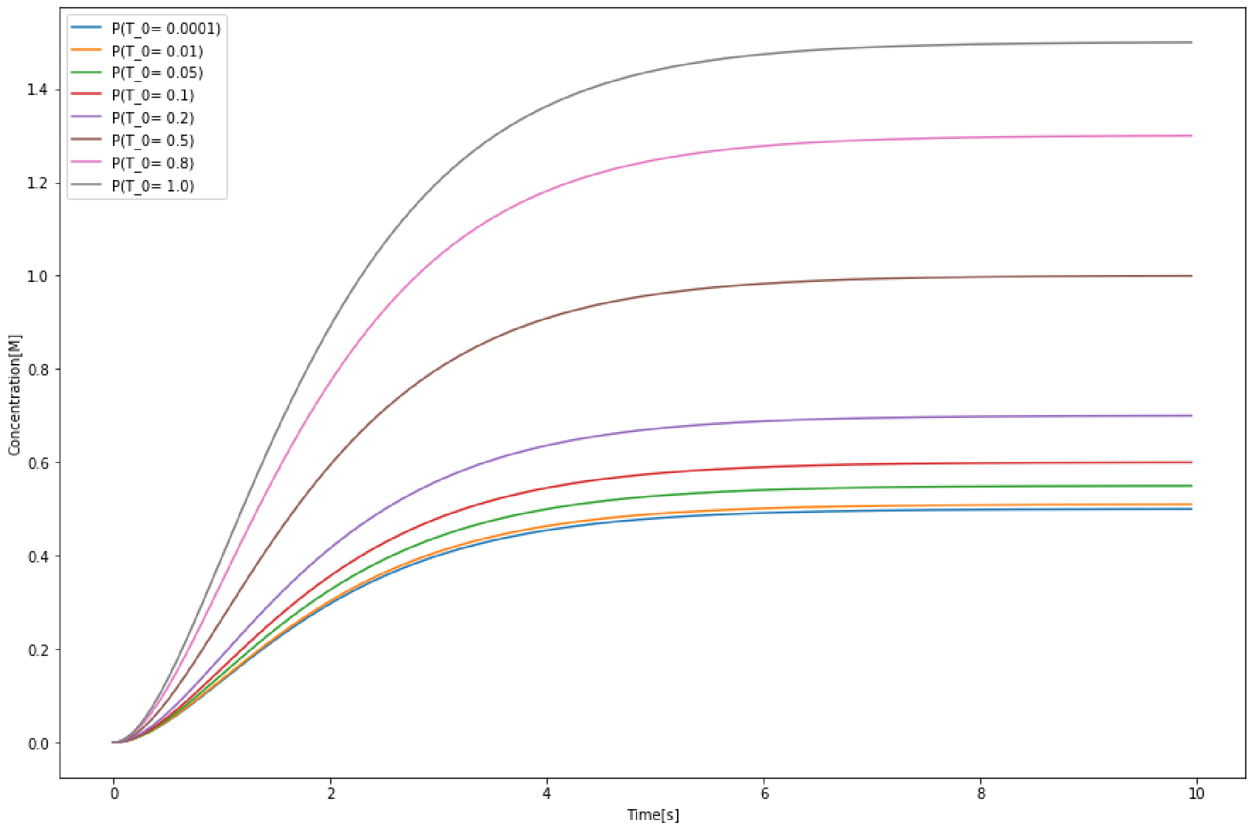
Script 1.2.2 (python)

```python
# M = mRNA
# D = DNA
# P = protein
# T = transcription factor
# Km = rate of mRNA production
# Kp = rate of protein production
# dm = rate of mRNA degradation
# dp = rate of protein degradation
# a = promoter leaking

# T + D -Km-> M + T + D, T is not consumed and nor DNA
# M -Kp-> P + M, not being consumed
# M -dm-> 0
# P -dp-> 0
# 0 -a-> M

def modelD(y, t, Km, Kp, dm, dp, a, T_0, D_0):
    [M, P] = y
    dMdt = Km*T_0*D_0 - dm*M + a
    dPdt = Kp*M - dp*P

    dydt = [dMdt, dPdt]
    return dydt

```

```python
def plot_modelD(y, t, Km, Kp, dm, dp, a, T_0, D_0, n, plot_M=True, plot_P=True):
    # initial condition
    y0 = [M_0, P_0]

    # time points
    t = np.arange(0, total_time, dt)

    # solve ODE
    y = odeint(modelD, y0, t, args=(Km, Kp, dm, dp, a, T_0, D_0))


    # plot results
    if plot_M: plt.plot(t, y[:,0], label = "M(T_0= " + str(T_0) + ")")
    if plot_P: plt.plot(t, y[:,1], label = "P(T_0= " + str(T_0) + ")")

    plt.xlabel("Time[s]")
    plt.ylabel("Concentration[M]")
    plt.legend(loc = "best")

plt.figure(figsize=(15,10))
for T_0 in [0.0001, 0.01, 0.05, 0.1, 0.2, 0.5, 0.8, 1.0]:
    plot_model(y, t, Km, Kp, dm, dp, a, T_0, D_0, n, plot_P=False)

plt.show()

plt.figure(figsize=(15,10))
for T_0 in [0.0001, 0.01, 0.05, 0.1, 0.2, 0.5, 0.8, 1.0]:
    plot_model(y, t, Km, Kp, dm, dp, a, T_0, D_0, n, plot_M=False)

plt.show()
```



M(T_0= 0.0001)
M(T_0= 0.01)
M(T_0= 0.05)
M(T_0= 0.1)
M(T_0= 0.2)
M(T_0= 0.5)
M(T_0= 0.8)
M(T_0= 1.0)
Concentration[M]
Time[s]
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
0
2
4
6
8
10

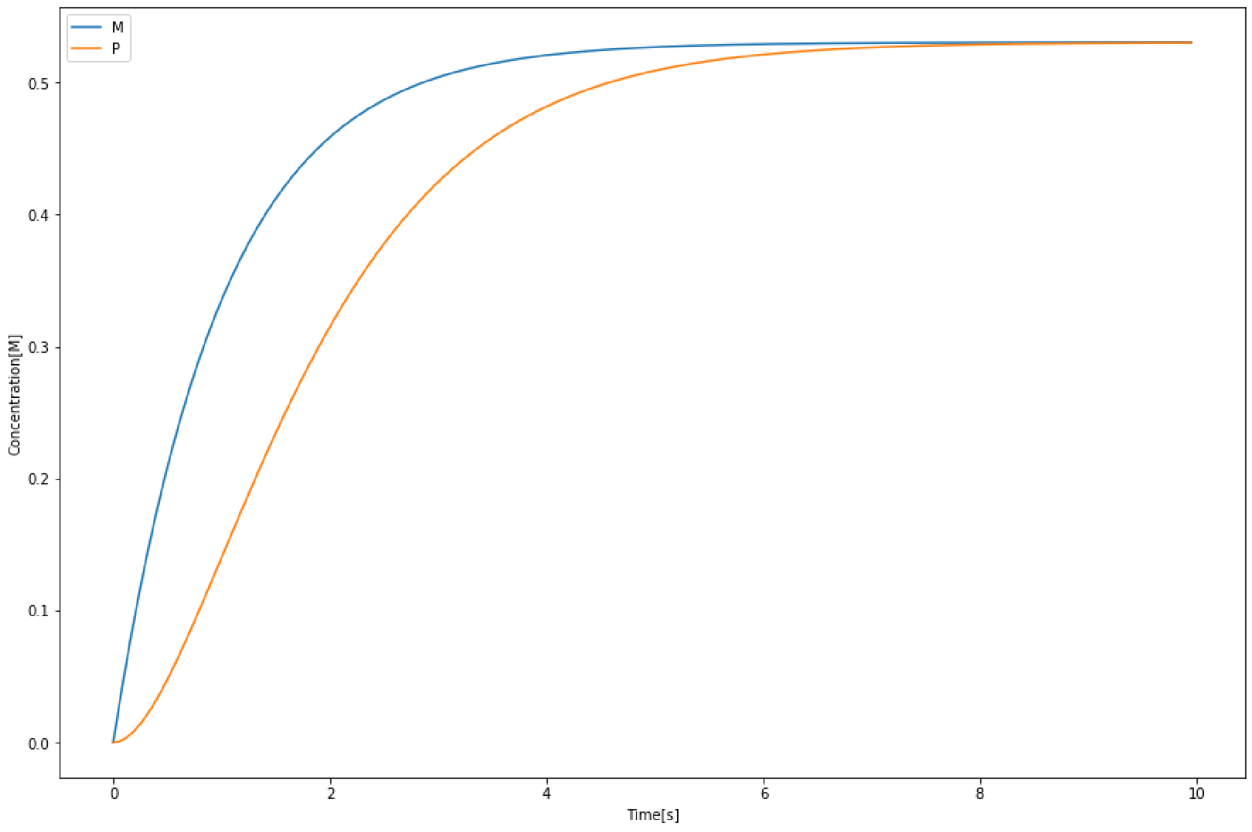


1.3 Hill function for activators

New activation equation for D_i to D_a (see python comments)

Script 1.3.1 (python)

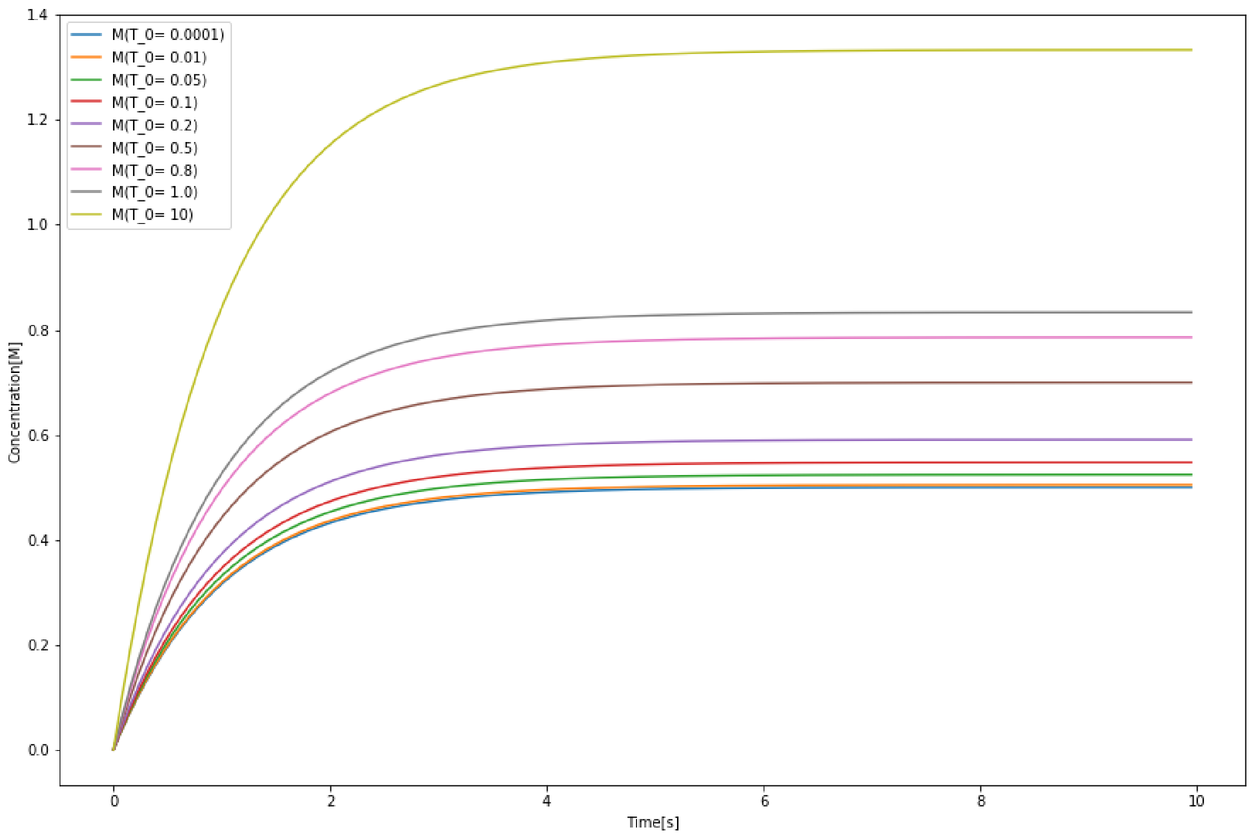
```python
# M = mRNA
# D = DNA
# P = protein
# T = transcription factor
# Km = rate of mRNA production
# Kp = rate of protein production
# dm = rate of mRNA degradation
# dp = rate of protein degradation
# a = promoter leaking

# T + D -Km-> M + T + D, T is not consumed and nor DNA
# M -Kp-> P + M, not being consumed
# M -dm-> 0
# P -dp-> 0
# 0 -a-> M

# Activation of DNA with n T
# Di + nT <-K1/K2->  K1 * Di * T**n = K2 * Da => Di * T**n = Kd * Di, where Kd = K1/K2
# Dt = Di + Da
# so
# Da/Dt = T**n/(Kd(1+Da/Di))

# Da/Dt = T**n/(K**n + T**n)

K = 2
n = 5
def hill(T, K, n):
    return T**n/(K**n + T**n)

def modelDH(y, t, Km, Kp, dm, dp, a, T_0, D_0, K, n):
    [M, P] = y
    dMdt = Km*hill(T_0, K, n)*D_0 - dm*M + a
    dPdt = Kp*M - dp*P

    dydt = [dMdt, dPdt]
    return dydt

# initial condition
y0 = [M_0, P_0]

# time points
t = np.arange(0, total_time, dt)

# solve ODE
y = odeint(modelDH, y0, t, args=(Km, Kp, dm, dp, a, T_0, D_0, K, n))

plt.figure(figsize=(15,10))

# plot results
plt.plot(t, y[:,0], label = "M")
plt.plot(t, y[:,1], label = "P")

plt.xlabel("Time[s]")
plt.ylabel("Concentration[M]")
plt.legend(loc = "best")
plt.show()
```

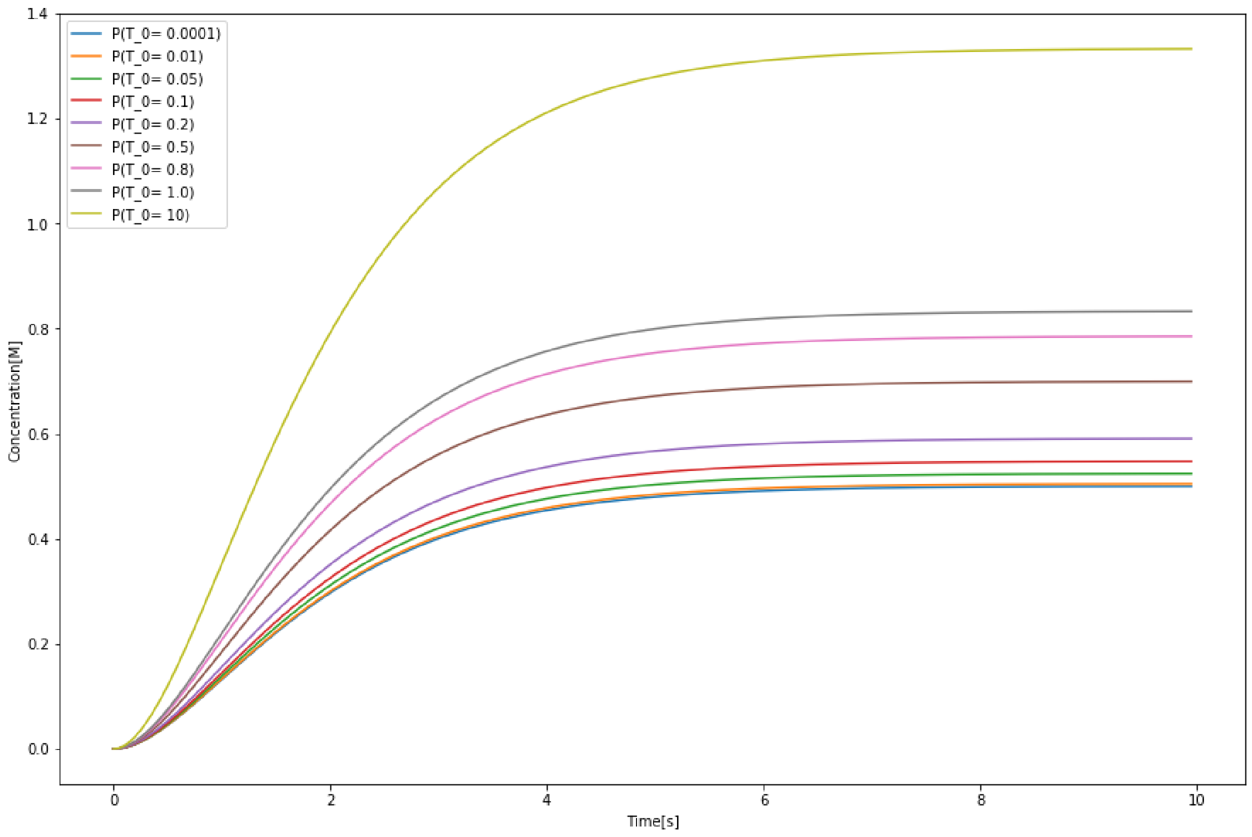


Script 1.3.2 (python)

```python
n = 1
def plot_modelDH(y, t, Km, Kp, dm, dp, a, T_0, D_0, K, n, plot_M=True, plot_P=True):
    # initial condition
    y0 = [M_0, P_0]

    # time points
    t = np.arange(0, total_time, dt)

    # solve ODE
    y = odeint(modelDH, y0, t, args=(Km, Kp, dm, dp, a, T_0, D_0, K, n))


    # plot results
    if plot_M: plt.plot(t, y[:,0], label = "M(T_0= " + str(T_0) + ")")
    if plot_P: plt.plot(t, y[:,1], label = "P(T_0= " + str(T_0) + ")")

    plt.xlabel("Time[s]")
    plt.ylabel("Concentration[M]")
    plt.legend(loc = "best")

plt.figure(figsize=(15,10))
```

```
for T_0 in [0.0001, 0.01, 0.05, 0.1, 0.2, 0.5, 0.8, 1.0, 10]:
    plot_modelDH(y, t, Km, Kp, dm, dp, a, T_0, D_0, K, n, plot_P=False)

plt.show()

plt.figure(figsize=(15,10))
for T_0 in [0.0001, 0.01, 0.05, 0.1, 0.2, 0.5, 0.8, 1.0, 10]:
    plot_modelDH(y, t, Km, Kp, dm, dp, a, T_0, D_0, K, n, plot_M=False)

plt.show()
```





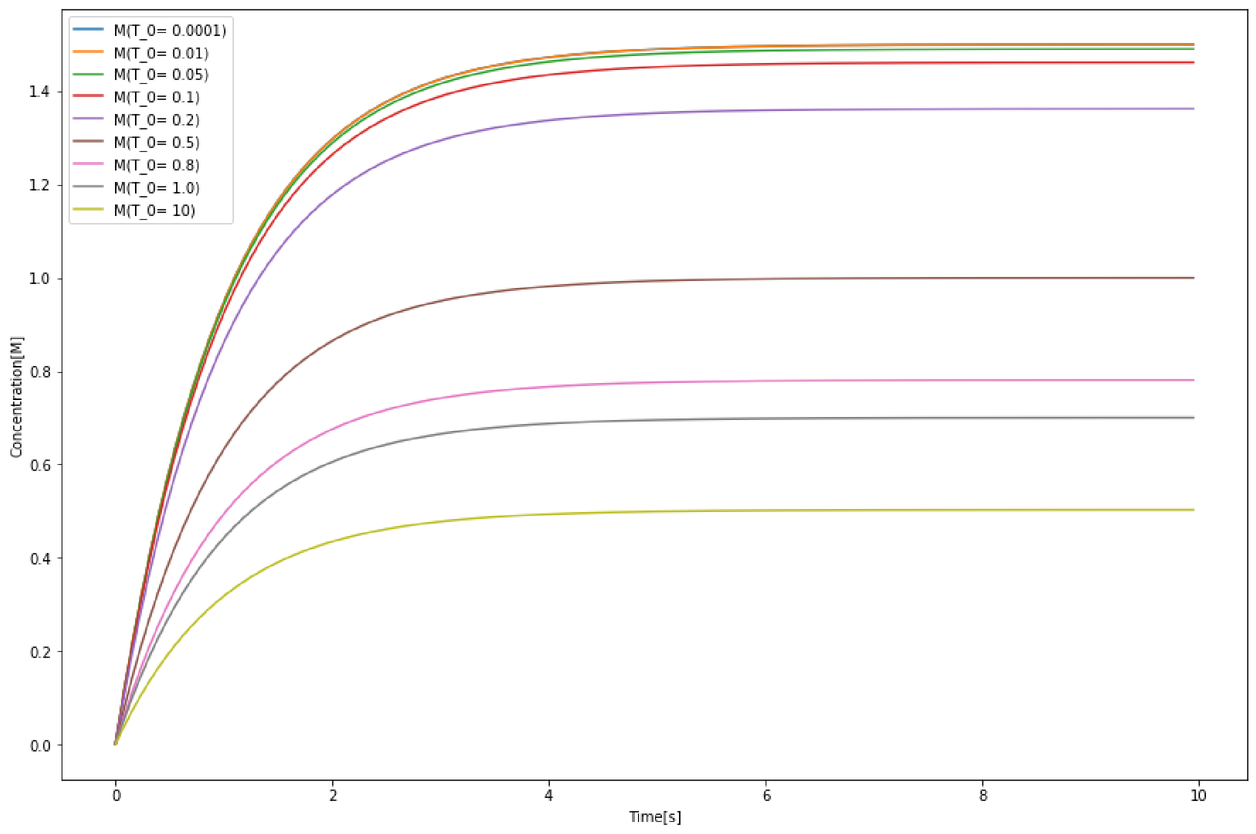
1.4 Hill function for represors

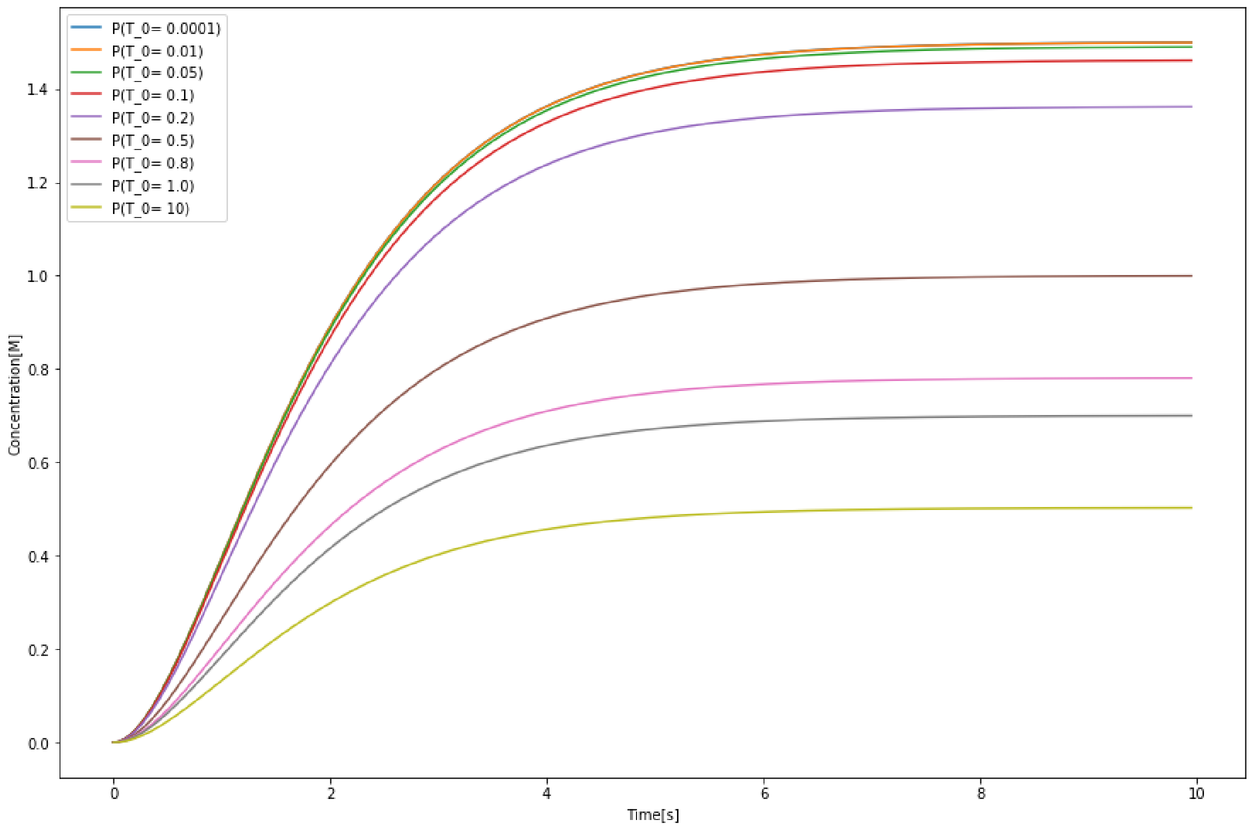
New repression equation for D_a to D_i (see python comments)

Script 1.4.1 (python)

```
# M = mRNA
# D = DNA
# P = protein
# T = transcription factor
# Km = rate of mRNA production
# Kp = rate of protein production
# dm = rate of mRNA degradation
# dp = rate of protein degradation
# a = promoter leaking

# T + D -Km-> M + T + D, T is not consumed and nor DNA
# M -Kp-> P + M, not being consumed
# M -dm-> 0
# P -dp-> 0
# 0 -a-> M

# Da + nT <-K1/K2->  Di
```

```python
# implies Da/Di = K**n/(T**n + K**n)

def hill_repress(T, K, n):
    return K**n/(K**n + T**n)

def modelDHR(y, t, Km, Kp, dm, dp, a, T_0, D_0, K, n):
    [M, P] = y
    dMdt = Km*hill_repress(T_0, K, n)*D_0 - dm*M + a
    dPdt = Kp*M - dp*P

    dydt = [dMdt, dPdt]
    return dydt

n = 2
K = 0.5
def plot_modelDHR(y, t, Km, Kp, dm, dp, a, T_0, D_0, K, n, plot_M=True, plot_P=True):
    # initial condition
    y0 = [M_0, P_0]

    # time points
    t = np.arange(0, total_time, dt)

    # solve ODE
    y = odeint(modelDHR, y0, t, args=(Km, Kp, dm, dp, a, T_0, D_0, K, n))


    # plot results
    if plot_M: plt.plot(t, y[:,0], label = "M(T_0= " + str(T_0) + ")")
    if plot_P: plt.plot(t, y[:,1], label = "P(T_0= " + str(T_0) + ")")

    plt.xlabel("Time[s]")
    plt.ylabel("Concentration[M]")
    plt.legend(loc = "best")


plt.figure(figsize=(15,10))
for T_0 in [0.0001, 0.01, 0.05, 0.1, 0.2, 0.5, 0.8, 1.0, 10]:
    plot_modelDHR(y, t, Km, Kp, dm, dp, a, T_0, D_0, K, n, plot_P=False)

plt.show()

plt.figure(figsize=(15,10))
for T_0 in [0.0001, 0.01, 0.05, 0.1, 0.2, 0.5, 0.8, 1.0, 10]:
    plot_modelDHR(y, t, Km, Kp, dm, dp, a, T_0, D_0, K, n, plot_M=False)

plt.show()
```


M(T_0= 0.0001)
M(T_0= 0.01)
M(T_0= 0.05)
M(T_0= 0.1)
M(T_0= 0.2)
M(T_0= 0.5)
M(T_0= 0.8)
M(T_0= 1.0)
M(T_0= 10)
Concentration[M]
Time[s]
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
0
2
4
6
8
10

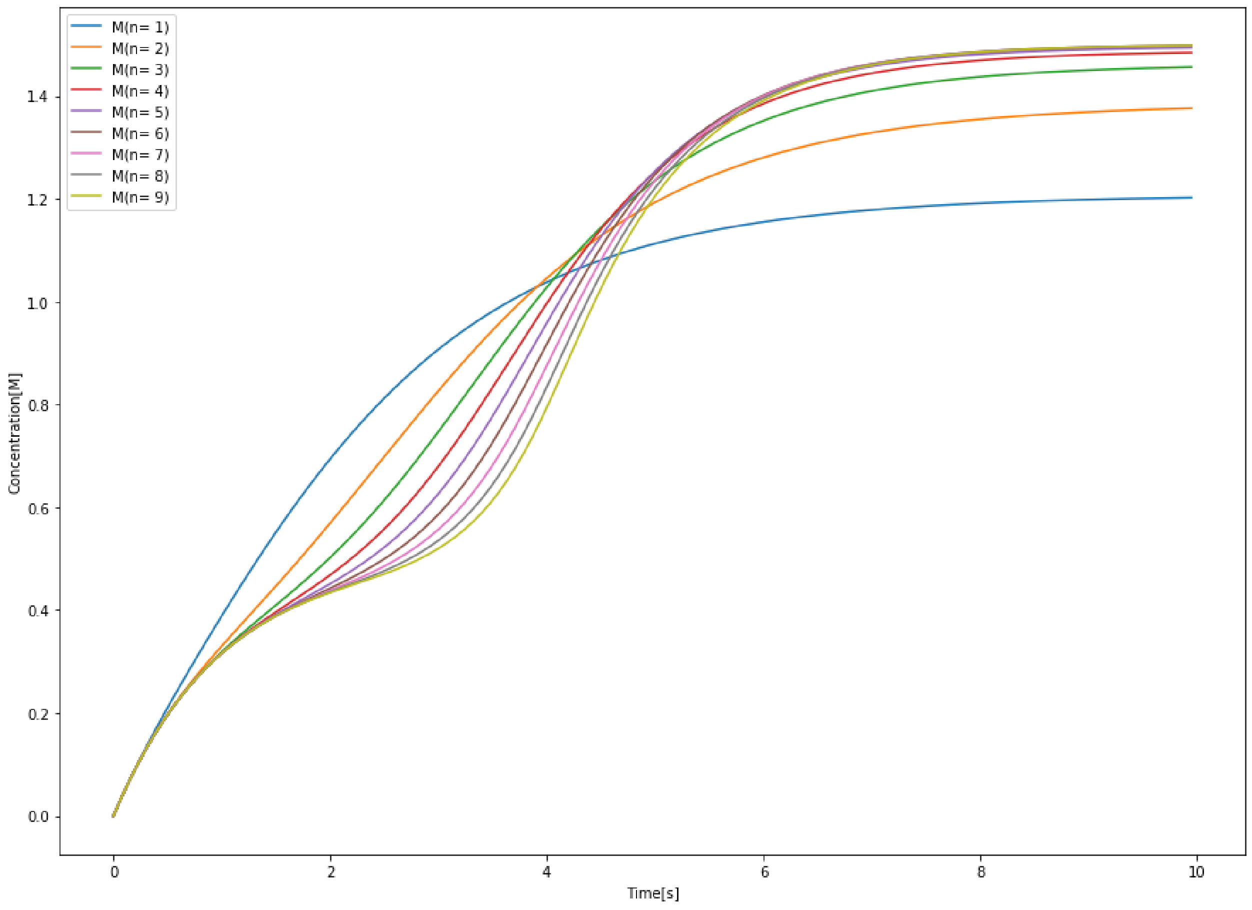


1.5 Possitive feedback

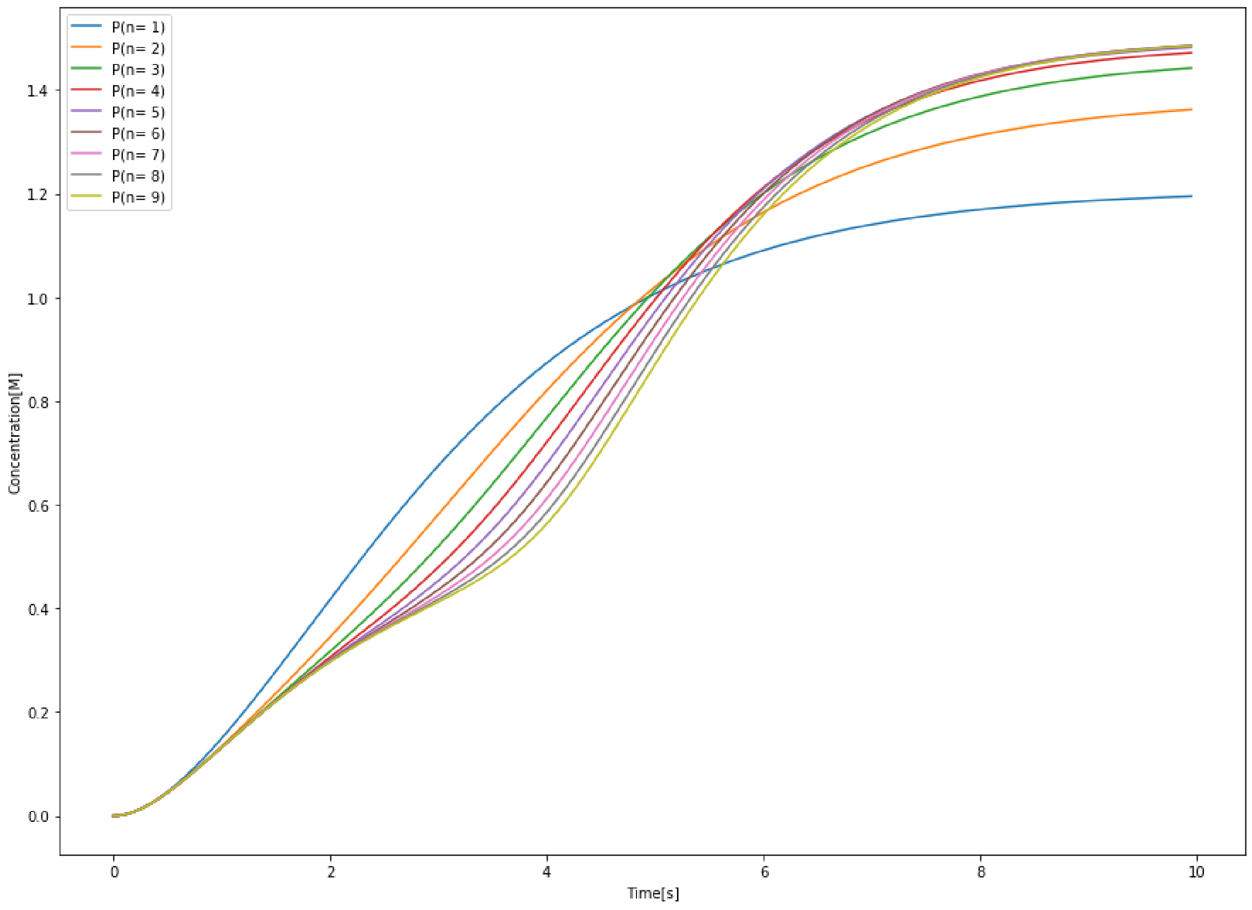
Script 1.5.1 (python)

```python
# M = mRNA
# D = DNA
# P = protein
# T = transcription factor
# Km = rate of mRNA production
# Kp = rate of protein production
# dm = rate of mRNA degradation
# dp = rate of protein degradation
# a = promoter leaking

# P + D -Km-> M + D, D is not consumed and nor DNA
# M -Kp-> P + M, not being consumed
# M -dm-> 0
# P -dp-> 0
# 0 -a-> M

# Da + nT <-K1/K2->  Di
# implies Da/Di = K**d/(T**n + K**n)
```

```python

n = 2
K = 1

def hill(T, K, n):
    return T**n/(K**n + T**n)

def modelP(y, t, Km, Kp, dm, dp, a, D_0, K, n):
    [M, P] = y
    dMdt = Km*hill(P, K, n)*D_0 - dm*M + a
    dPdt = Kp*M - dp*P

    dydt = [dMdt, dPdt]
    return dydt

K = 0.5
def plot_modelP(y, t, Km, Kp, dm, dp, a, D_0, K, n, plot_M=True, plot_P=True):
    # initial condition
    y0 = [M_0, P_0]

    # time points
    t = np.arange(0, total_time, dt)

    # solve ODE
    y = odeint(modelP, y0, t, args=(Km, Kp, dm, dp, a, D_0, K, n))


    # plot results
    if plot_M: plt.plot(t, y[:,0], label = "M(n= " + str(n) + ")")
    if plot_P: plt.plot(t, y[:,1], label = "P(n= " + str(n) + ")")

    plt.xlabel("Time[s]")
    plt.ylabel("Concentration[M]")
    plt.legend(loc = "best")

plt.figure(figsize=(15,11))
for n in range(1,10):
    plot_modelP(y, t, Km, Kp, dm, dp, a, D_0, K, n, plot_P=False)

plt.show()

plt.figure(figsize=(15,11))
for n in range(1,10):
    plot_modelP(y, t, Km, Kp, dm, dp, a, D_0, K, n, plot_M=False)

plt.show()
```



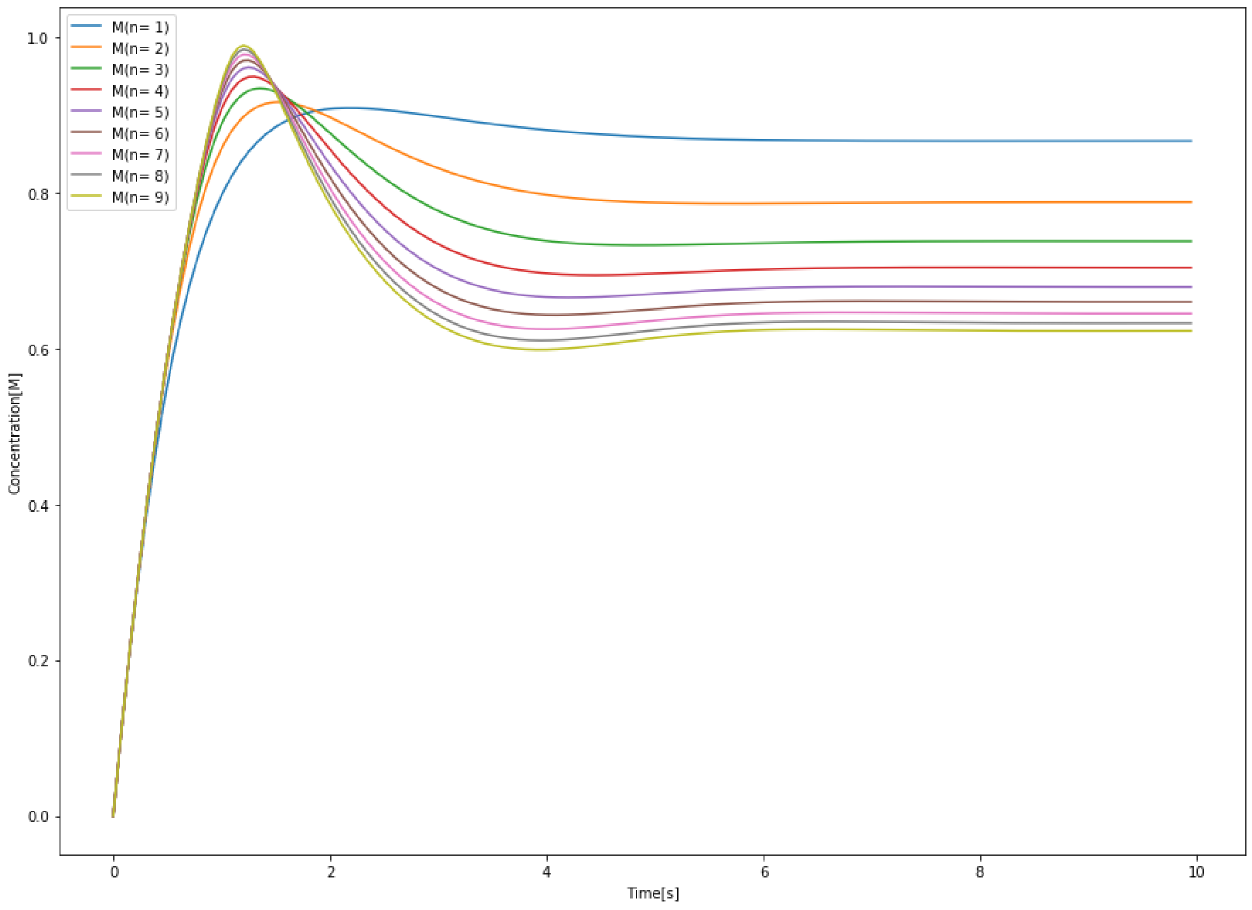
M(n= 1)
M(n= 2)
M(n= 3)
M(n= 4)
M(n= 5)
M(n= 6)
M(n= 7)
M(n= 8)
M(n= 9)
Concentration[M]
Time[s]
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
0
2
4
6
8
10

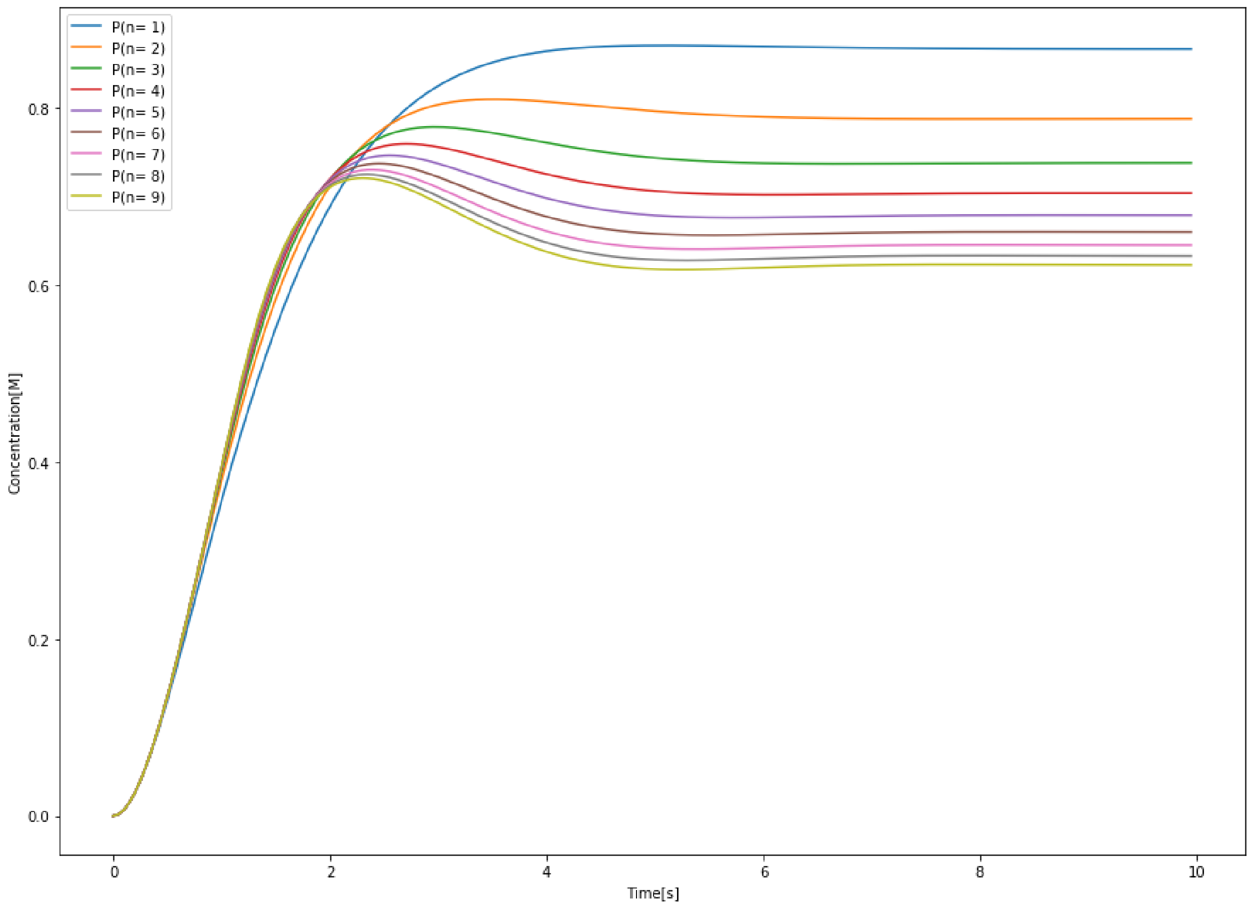


1.6 Negative feedback

Script 1.6.1 (python)

```python
# M = mRNA
# D = DNA
# P = protein
# T = transcription factor
# Km = rate of mRNA production
# Kp = rate of protein production
# dm = rate of mRNA degradation
# dp = rate of protein degradation
# a = promoter leaking

# P + D -Km-> M + D, D is not consumed and nor DNA
# M -Kp-> P + M, not being consumed
# M -dm-> 0
# P -dp-> 0
# 0 -a-> M

# Da + nT <-K1/K2->  Di
# implies Da/Di = K**d/(T**n + K**n)

n = 2
K = 1

def hill_repress(T, K, n):
    return K**n/(K**n + T**n)

def modelN(y, t, Km, Kp, dm, dp, a, D_0, K, n):
    [M, P] = y
    dMdt = Km*hill_repress(P, K, n)*D_0 - dm*M + a
    dPdt = Kp*M - dp*P

    dydt = [dMdt, dPdt]
    return dydt

K = 0.5
def plot_modelN(y, t, Km, Kp, dm, dp, a, D_0, K, n, plot_M=True, plot_P=True):
    # initial condition
    y0 = [M_0, P_0]

    # time points
    t = np.arange(0, total_time, dt)

    # solve ODE
    y = odeint(modelN, y0, t, args=(Km, Kp, dm, dp, a, D_0, K, n))


    # plot results
    if plot_M: plt.plot(t, y[:,0], label = "M(n= " + str(n) + ")")
    if plot_P: plt.plot(t, y[:,1], label = "P(n= " + str(n) + ")")

    plt.xlabel("Time[s]")
    plt.ylabel("Concentration[M]")
    plt.legend(loc = "best")

plt.figure(figsize=(15,11))
for n in range(1,10):
    plot_modelN(y, t, Km, Kp, dm, dp, a, D_0, K, n, plot_P=False)

plt.show()

plt.figure(figsize=(15,11))
for n in range(1,10):
    plot_modelN(y, t, Km, Kp, dm, dp, a, D_0, K, n, plot_M=False)

plt.show()
```


M(n= 1)
M(n= 2)
M(n= 3)
M(n= 4)
M(n= 5)
M(n= 6)
M(n= 7)
M(n= 8)
M(n= 9)
Concentration[M]
Time[s]
0.0
0.2
0.4
0.6
0.8
1.0
0
2
4
6
8
10


P(n= 1)
P(n= 2)
P(n= 3)
P(n= 4)
P(n= 5)
P(n= 6)
P(n= 7)
P(n= 8)
P(n= 9)
0.0
0.2
0.4
0.6
0.8
Concentration[M]
0
2
4
6
8
10
Time[s]