Week Six

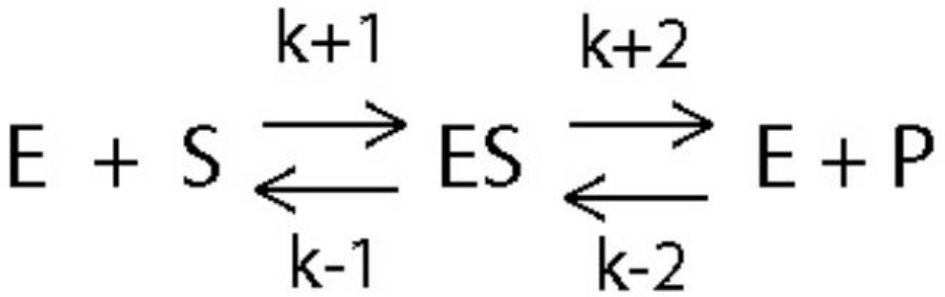
- Enzymatic reaction and its kinetics
- Binding reaction
- Logic gates and system design with the binding and enzymatic reactions
- The ordinary differential equation (ODE)

Enzyme kinetics

- Enzyme kinetics is the study of the chemical reactions that are catalyzed by enzymes.
- In enzyme kinetics, the reaction rate is measured, and the effects of varying conditions are investigated. How to control the reactions?
- The most important chemical reactions for living things

wikipedia

Enzyme kinetics (engineer's perspective)



E=[E];S=[S];ES=[ES];P=[P]

$E_0 = E_{t=0}$ initial enzyme concentration; ES_0; S_0; P_0

Engineer's perspective:

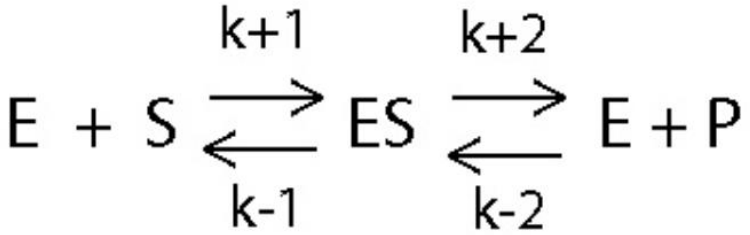
$dS/dt=-k_1*E*S+k_{-1}*ES$

$dE/dt=-k_1*E*S+ k_{-1}*ES+ k_2*ES$

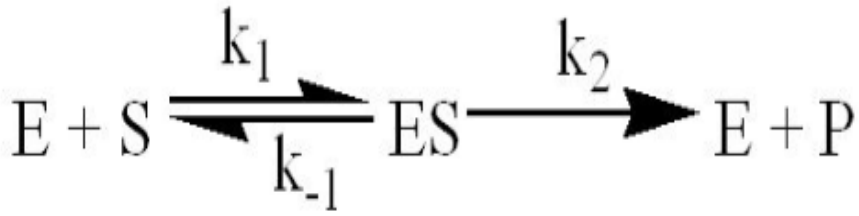
$dES/dt=k_{1*}E*S- k_{-1}*ES +k_2*ES$

$dP/dt=k_2*ES-k_{-2}*ES$

Steady State Assumption #1



K_{-2} is so small that it can be ignored



$$dS/dt=-k_{1*}E*S+k_{-1}*ES$$

$$dE/dt=-k_1*E*S+ k_{-1}*ES+ k_2*ES$$

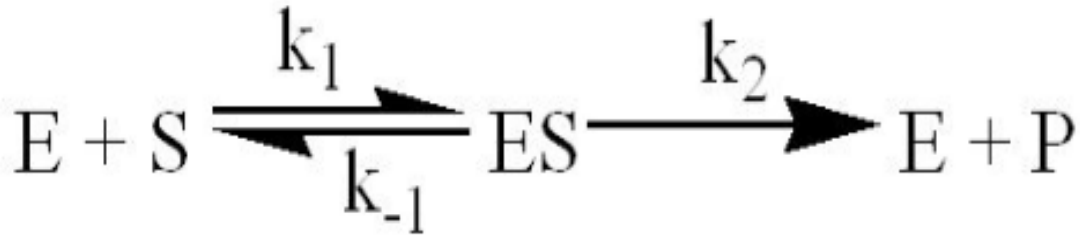
$$dES/dt=k_{1*}E*S- k_{-1}*ES + k_2*ES$$

$$dP/dt=k_2*ES$$

Steady State Assumptions #2

ES is constant. Formation of ES is the same as the loss of ES:

$dES/dt=k_1 * E * S - (k_{-1}+k_2)*(E_0 - E)=0$



E=[E];S=[S];ES=[ES];P=[P]
initial conditions
(enzyme concentration)
$E_0 = E_{t=0}$ $E_0 = E+ES$
$ES_0=0$; S_0; $P_0=0$

$dS/dt=-k_{1*} E * S+k_{-1}*(E_0 - E)$

$dP/dt=k_2*(E_0 - E)$

$dE/dt=-k_1*E*S+ k_{-1}* (E_0 - E)+ k_2*(E_0 - E)$

Michaelis-Menten Equation at steady state

$$d[P]/dt = v = \frac{k_2 E_0 [S]}{(k_{-1}+k_2)/ k_1+[S]} = \frac{V_{max}[S]}{K_m +[S]}$$

$$\mathbf{V_{max} = k_2 E_0}$$

$$\mathbf{K_m=(k_{-1}+k_2)/ k_1}$$

Leads to the traditional Michaelis-Menten equation to characterize the reaction efficiency With V_0 initial rate.

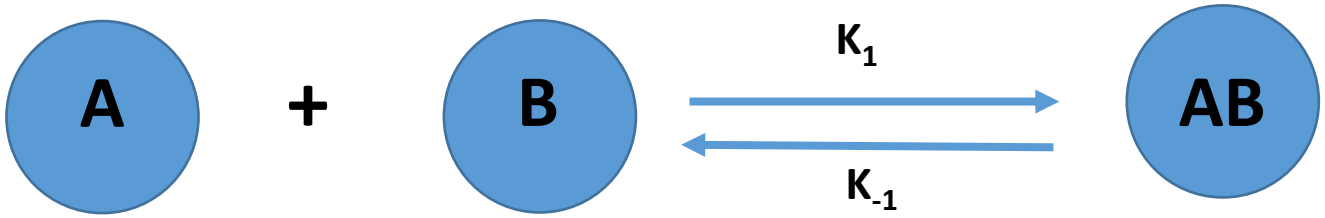
$$V_0 = \frac{V_{max}[S]_0}{K_m +[S]_0}$$

Enzyme kinetics (biologist's perspective)

- **V_{max}** is the reaction rate when the enzyme is fully saturated by substrate, indicating that all the binding sites are being constantly reoccupied. The higher **V_{max}**, the faster the enzyme converts the substrate to product.
- **K_m** measures the enzyme affinity or capacity. Lower **K_m** means less [S] needed to reach **V_{max}**, the higher enzyme capacity.
- **K_{cat}**= V_{max}/[E], turnover number: the maximum number of chemical conversions of substrate molecules per second for a single catalytic site. For example, the carbonic anhydrase has a turnover number of 400,000 s−1
- Catalytic Efficiency= **K_{cat}/ K_m** (combine the enzyme capacity and enzyme turnover number)

$$V_0 = \frac{V_{max}}{1 + K_m/[S]_0}$$

Binding reaction

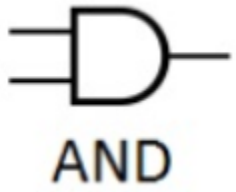


$$d[AB]/dt = k_1*[A][B]-k_{-1}*[AB]$$

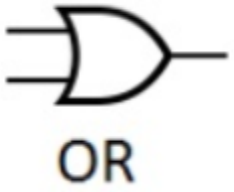
$$d[B]/dt = -k_1*[A][B]+k_{-1}*[AB] = - d[AB]/dt$$

Systems of chemical reactions as logic gates

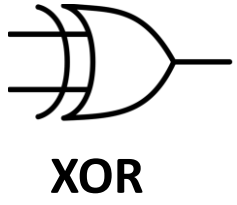
A logic gate is a mathematical and electronic term. We are going to design systems of chemical and enzymatic reactions to perform the same functions as logic gates, at the same time we can optimize the system for better performance.



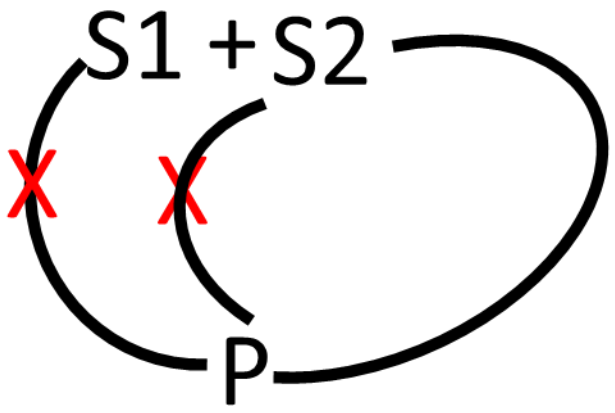
S1	S2	P
0	0	0
1	0	0
0	1	0
1	1	1

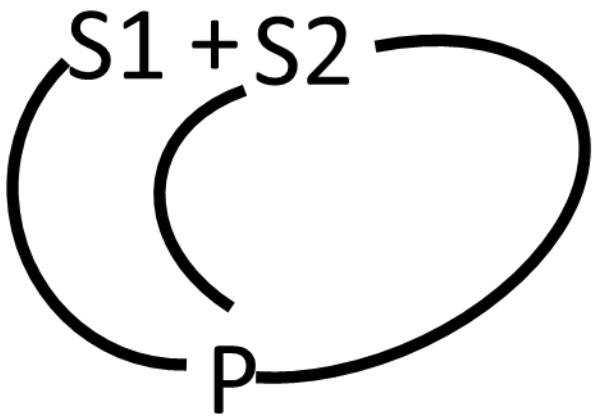


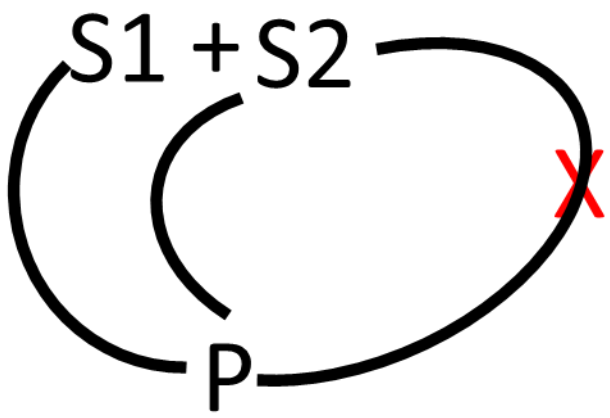
S1	S2	P
0	0	0
1	0	1
0	1	1
1	1	1



S1	S2	P
0	0	0
1	0	1
0	1	1
1	1	0

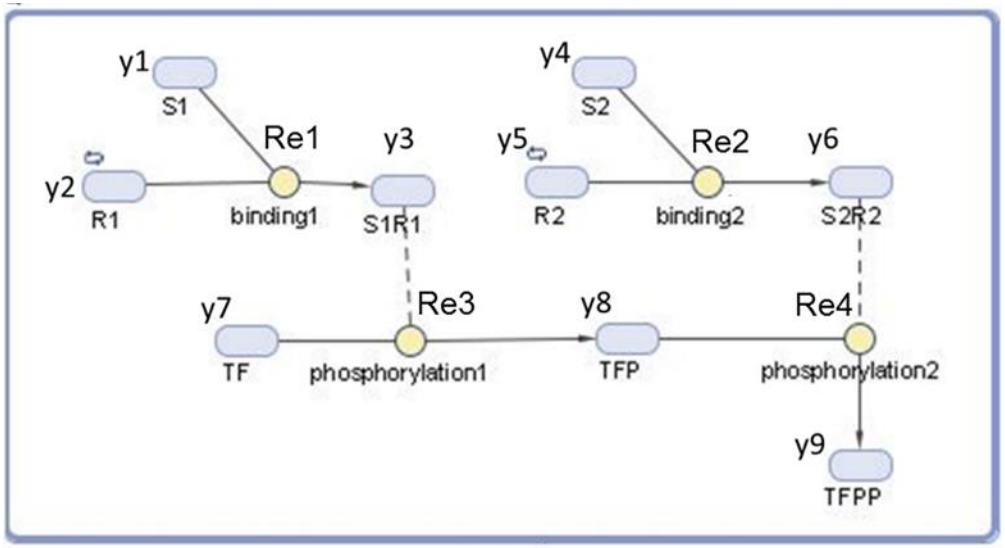




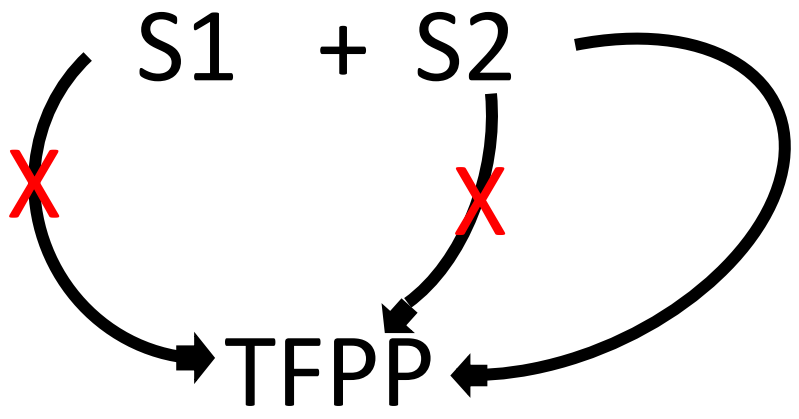


Systems of chemical reactions as an AND gate

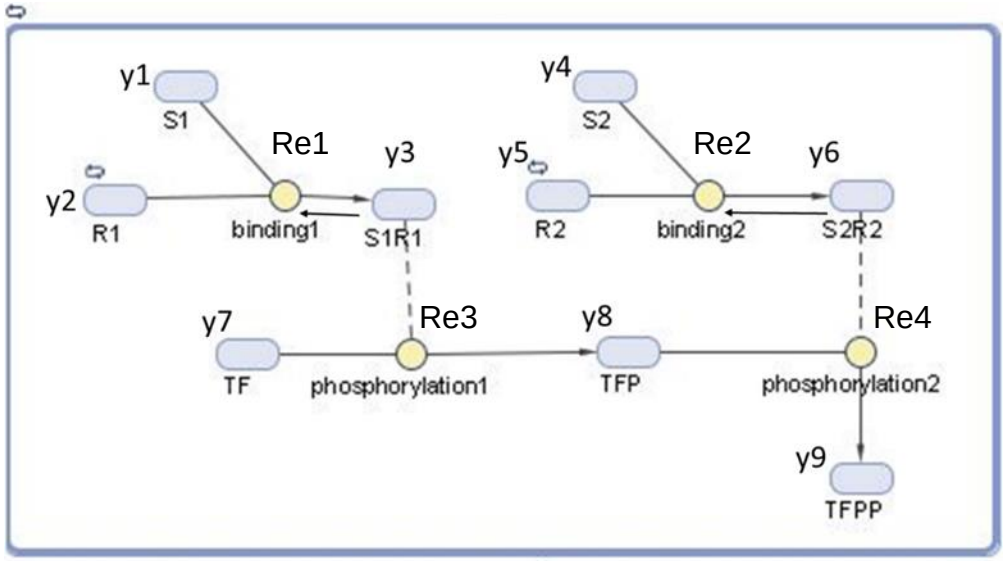
We are designing a system with four reactions to mimic an AND gate: two binding reactions and two enzymatic reactions (yellow circles)



S1	S2	TFPP
0	0	0
1	0	0
0	1	0
1	1	1



Establish the ODEs to describe the reactions



How will S1(y1) and S2(y2) affect the system?

- $R_{binding1} : k_{forward}[S1][R1] - k_{reverse}[S1R1]$
- $R_{binding2} : k_{forward}[S2][R2] - k_{reverse}[S2R2]$
- $R_{phosphorylation1} : \frac{Vmax[S1R1][TF]}{km + [TF]}$
- $R_{phosphorylation2} : \frac{Vmax[S2R2][TFP]}{km + [TFP]}$

y(1):S1
y(2):R1
y(3):S1R1
y(4):S2
y(5):R2
y(6):S2R2
y(7):TF
y(8):TFP
y(9):TFPP

Re1:(d(S1R1)/dt): re1 = kf*y(1)*y(2) - kr*y(3)

Re1:(d(R1)/dt): -re1 = -kf*y(1)*y(2) + kr*y(3)

Re2:(d(S2R2)/dt): re2= kf*y(4)*y(5) - kr*y(6)

Re3:(d(TFP)/dt): re3= Vmax*y(7)*y(3)/(km + y(7))

Re4:(d(TFPP)/dt): re4=Vmax*y(8)*y(6)/(km + y(8))

Establish the ODE

In andpathwaysimple.m

```
dy = zeros(9,1);
dy(2) = -re1;
dy(3) = +re1;
dy(5) = -re2;
dy(6) = +re2;
dy(7) = -re3;
dy(8) = +re3-re4;
dy(9) = +re4;
```