

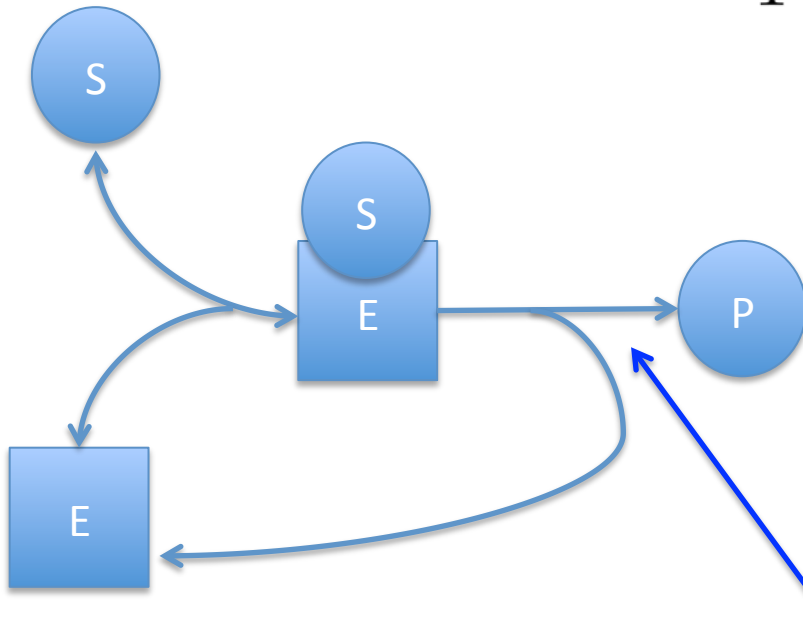
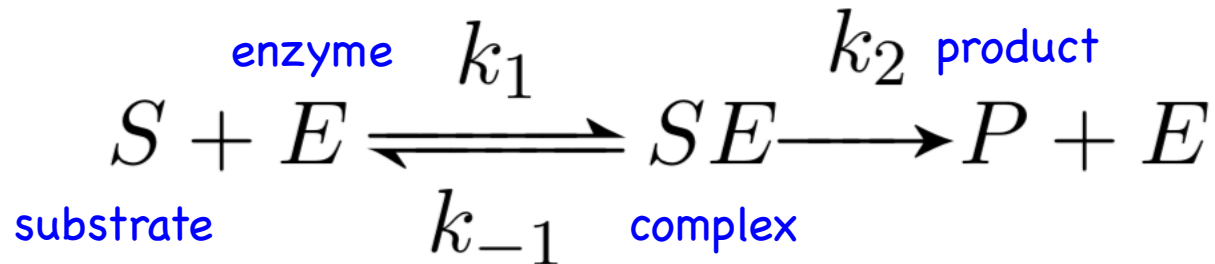
CS341 Systems Biology I

Lecture 5

Administrative Stuff

- Project 1 due tonight
- Don't forget to fill out the partnership-effectiveness google form.
- HW5 posted (due by lecture 6)
- Project 2 will be posted soon

The complete model includes the enzyme as a reactant (a variable that is part of a reaction)



$$\begin{aligned}
 \frac{dS}{dt} &= -k_1 \cdot S \cdot E + k_{-1} \cdot SE \\
 \frac{dE}{dt} &= -k_1 S \cdot E + k_{-1} SE + k_2 \cdot SE \\
 \frac{dP}{dt} &= k_2 \cdot SE \\
 \frac{dSE}{dt} &= k_1 \cdot S \cdot E - k_{-1} \cdot SE - k_2 \cdot SE
 \end{aligned}$$

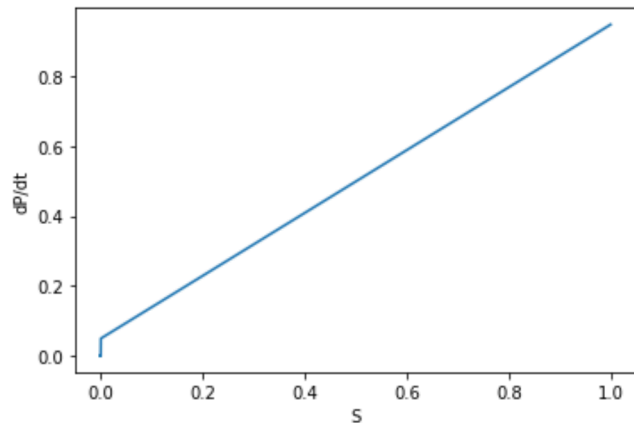
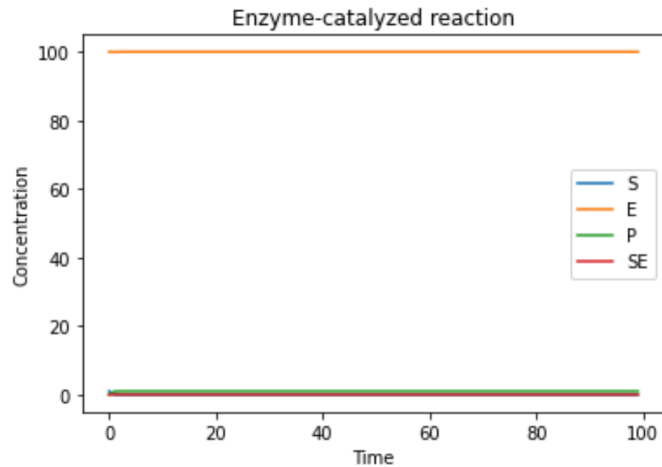
the process we are most interested in simulating

Goal: understand dynamics of full system

But then make smaller model that does not need ODEs for E or SE

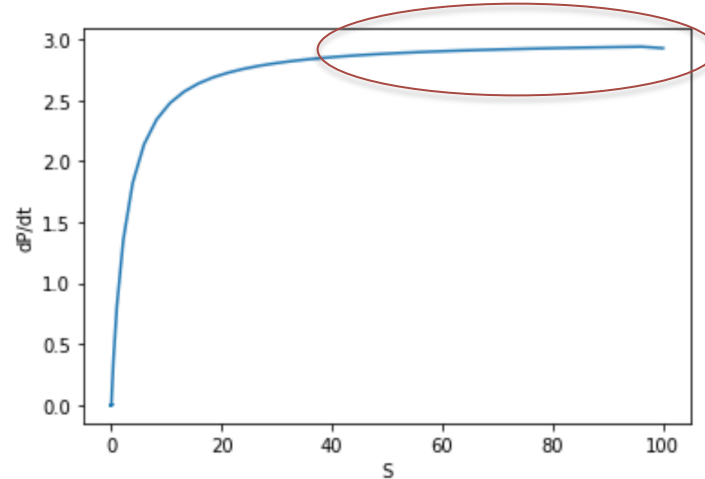
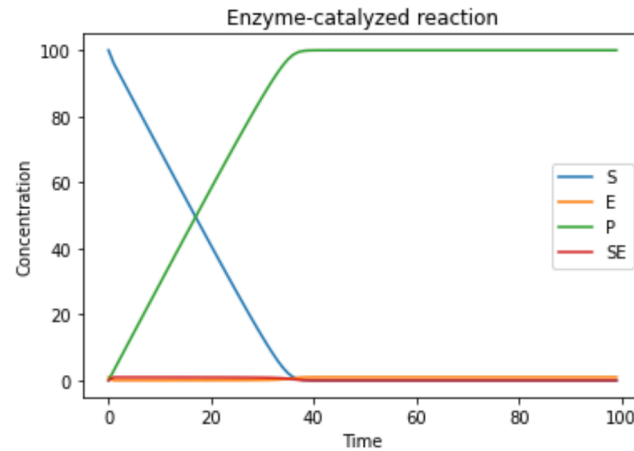
i.e. find expression for dP/dt that depends on S instead of on SE.

Much less substrate than enzymes
(rarely seen in biology)



$dP/dt = kS$
except when $S \sim E$

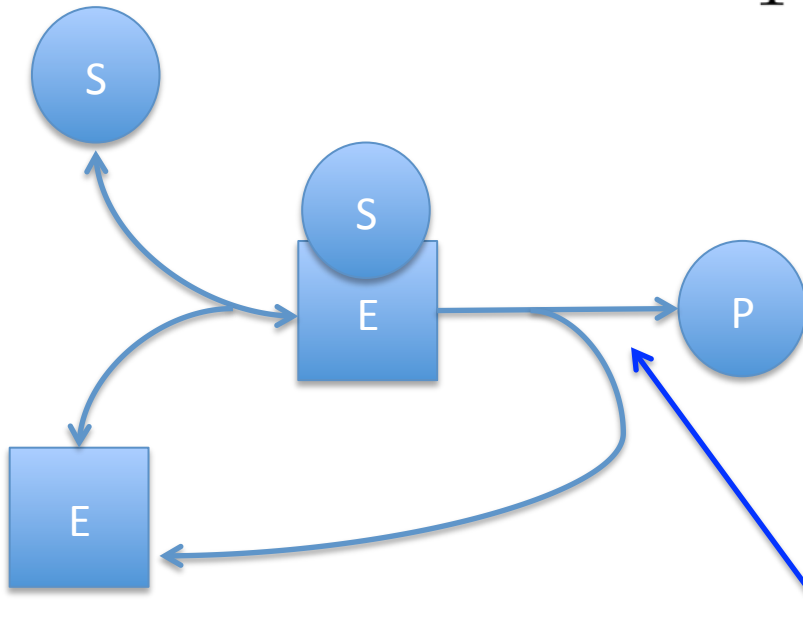
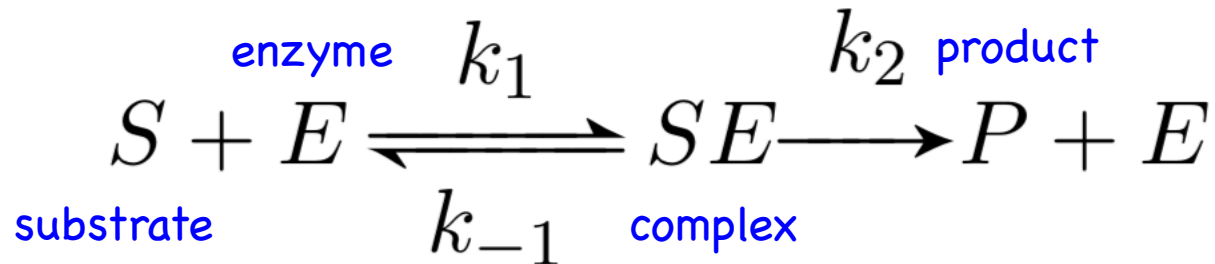
Not very many enzymes
(common in biology)



$dP/dt = c$
would be
appropriate

To capture entire curve, we either need full model
or Michaelis-Menton kinetics
 $dP/dt = v_{max} * S/(S+K)$

The Michaelis-Menton Model needs variables for S and P only. E is captured in the parameter v_{max}



$$\begin{aligned}
 \frac{dS(t)}{dt} &= -v_{max} \frac{S}{K_m + S} \\
 \frac{dP(t)}{dt} &= v_{max} \frac{S}{K_m + S}
 \end{aligned}$$

the process we are most interested in simulating

Goal: understand dynamics of full system

But then make smaller model that does not need ODEs for E or SE

i.e. find expression for dP/dt that depends on S instead of on SE.

Neuropeptides, electrophysiology, and pathways added to capture known differences between VIP and AVP

[illegible]
$$f_1(P_n, B_a, Creb, Erk) = v_{1b} \frac{B_a}{k_{1b}(1 + (P_n/k_{1b})^p) + B_a} + p_e \frac{Erk^p}{Erk^p + K_e^p} + p_c \frac{Creb^p}{Creb^p + K_c^p}$$
$$f_2(P_n, B_a, Creb) = v_{4b} \frac{P_n^r}{k_{4b}^r + P_n^r}$$
$$F = 8 \frac{P_m^n}{P_m^n + K_F^n} + F_v \gamma + F_a \xi$$
$$f_3(P_n, B_a) = v_{ab} \frac{B_a}{k_{lb}(1 + (P_n/k_{li})^p) + B_a}$$
$$C = c_F F + c_v \gamma + c_a \xi + c_P P_m$$
$$\xi = \frac{A_m \text{ AVP (Mean field)}}{A_m + K_{AVP}}$$
$$\begin{aligned}
\frac{dP_m}{dt} &= f_1(P_n, B_a, Creb, Erk) - k_{1d}P_m \\
\frac{dP_c}{dt} &= k_{2b}P_m^q - k_{2d}P_c - k_{2t}P_c + k_{3t}P_n \\
\frac{dP_n}{dt} &= k_{2t}P_c - k_{3t}P_n - k_{3d}P_n \\
\frac{dB_m}{dt} &= f_2(P_n, B_a, Creb) - k_{4d}B_m \\
\frac{dB_c}{dt} &= k_{5b}B_m - k_{5d}B_c - k_{5t}B_c + k_{6t}B_n \\
\frac{dB_n}{dt} &= k_{5t}B_c - k_{6t}B_n - k_{6d}B_n + k_{7a}B_a - k_{6a}B_n \\
\frac{dB_a}{dt} &= k_{6a}B_n - k_{7a}B_a - k_{7d}B_a \\
\frac{dV_o}{dt} &= v_gF - v_gV_o \quad \text{VIP released from cell} \\
\frac{dA_m}{dt} &= f_3(P_n, B_a) - a_dA_m \quad \text{AVP transcribed} \\
\frac{dA_o}{dt} &= A_mF - a_oA_o \quad \text{AVP released from cell} \\
\frac{dCreb}{dt} &= v_c\gamma + a_c\xi + c_cCa - c_dCreb \quad \text{CREB} \\
\frac{dErk}{dt} &= v_e\gamma + e_cCa - e_dErk \quad \text{ERK}
\end{aligned}$$

Kinetics we have learned so far and the processes that can be modeled by them

Mass-Action Kinetics

- zeroeth order
 - basal rate of transcription
 - $dP/dt = k$
- first order
 - transport into and out of nucleus
 - degradation
 - undimerization
 - $dP/dt = k \cdot P$
- second order
 - dimerization
 - $dP_{12}/dt = k \cdot P_1 \cdot P_2$

Michaelis-Menton Kinetics

- enzyme-aided reactions
- any process whose rate reaches a maximum (the effects saturate)
- $dP/dt = v_{\max} \cdot S / (S + K)$

What is missing? How to capture transcriptional regulation