ODE Examples

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Some figures are from Wikipedia.

ODEs in Biology

- Most biological reactions are modeled with the following reaction kinetics:
  - Law of mass action
    - Irreversible Reaction
    - Reversible Reaction
  - Michaelis-menten enzyme kinetics

Ir-reversible Reactions

- *Reaction Rate:*

- *In many reactions, the powers in may not be a, b.*

Ir-reversible Reactions

- *Example: Combustion*
  - *e.g,. burning sugar (sucrose)*
  - *See ode_examples.mlx*

U.S. CHEMICAL SAFETY AND HAZARD INVESTIGATION BOARD

Aftermath of the February 2008 dust explosion and fire at Imperial Sugar refinery in Port Wentworth, Ga.

https://www.acs.org/content/dam/acsorg/education/resources/highschool/chemmatters/archive/chemmatters-december-2010-sugar-an-unusual-explosive.pdf

Reversible Reactions

- Two reactions, occurring simultaneously:

- Example:

- See ode_examples.mlx

Intermediate Reactions

- *There may be several intermediate reactions making up the overall reaction*
- *Example: Reaction of hydrogen and nitric oxide:*

- *The observed rate equation:*

Intermediate Reactions

- *The elementary steps are:*
  - *fast equilibrium:* with equilibrium constant
  - *slow:* with rate constant
  - *fast:*
- <u>*The slowest elementary step controls the reaction rate:*</u>
  - *Rewrite:*

Binding Kinetics

- *Reversible Receptor-Ligand binding to form Complex:*
- *At equilibrium:*
- *Binding, association constant:*
- *Dissociation constant:*
- *The kinetics can be determined analytically.*
  - *See: https://en.wikipedia.org/wiki/Receptor-ligand_kinetics*

Binding Kinetics

- Find the steady-state concentration of the bound receptor

- See ode_examples.mlx

Enzyme Kinetics

- Overall reaction:

- But reaction does not follow
- Enzymatic reactions are composed of two steps: association and catalysis:

- *Overall reaction rate:*
  - *We need to replace C with measurables.*
- *Assumptions:*
  - *P<<S, E<<S*
  - *Then:*
- *At steady state, rate of formation & consumption of C equal:*

- *Define :*

- *Replace with ():*

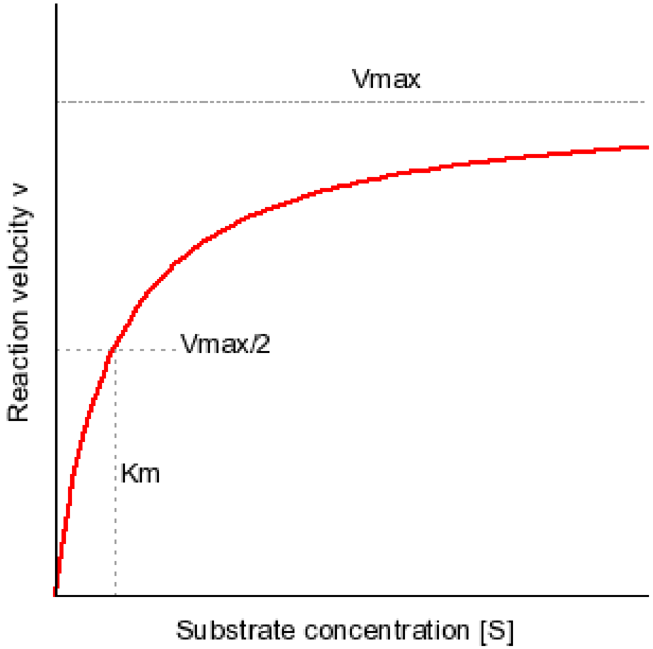
- *Plug back in rate equation:*

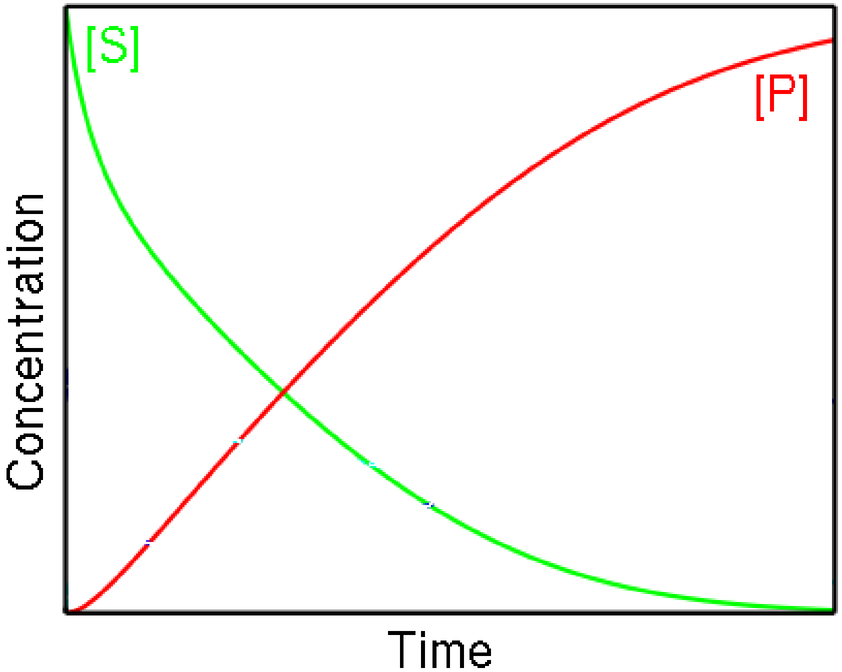
- *Maximum velocity occurs when enzyme is saturated (all enzyme is tied up with)*

- *rate now becomes:*

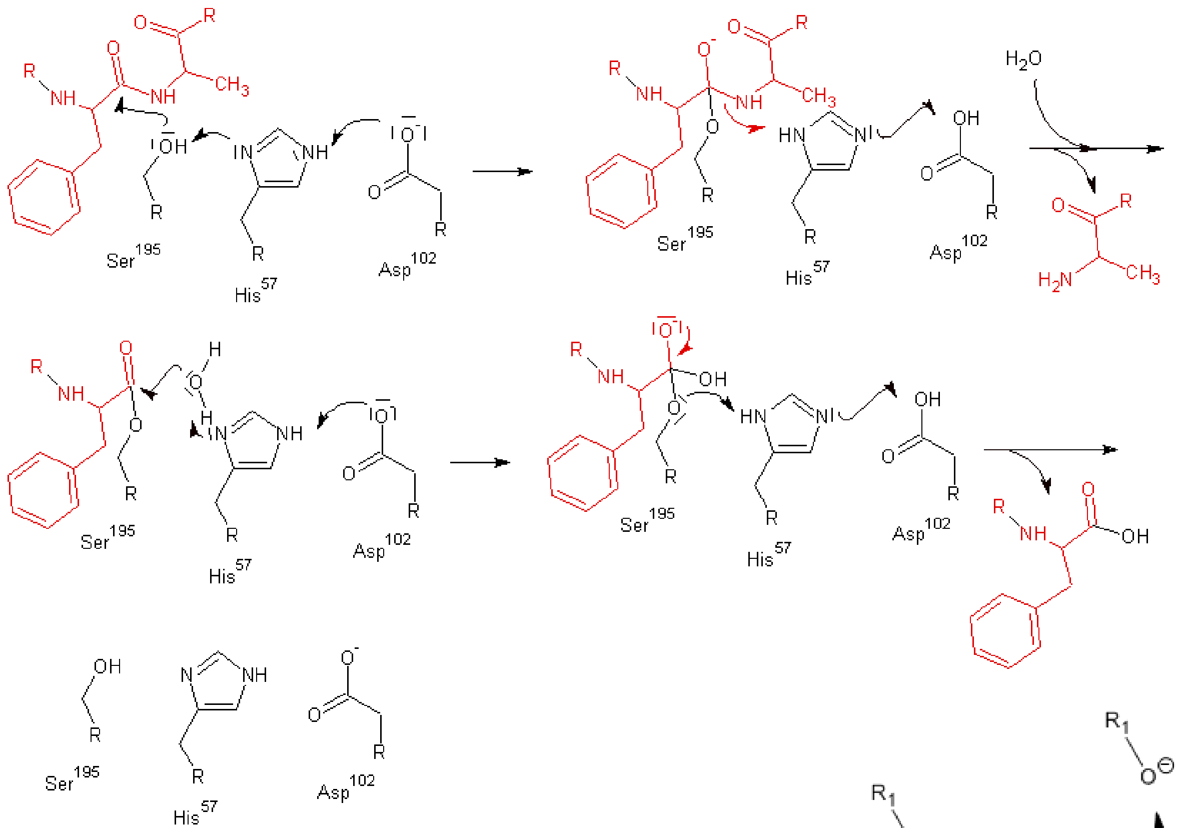
Michaelis-Menten Enzyme Kinetics

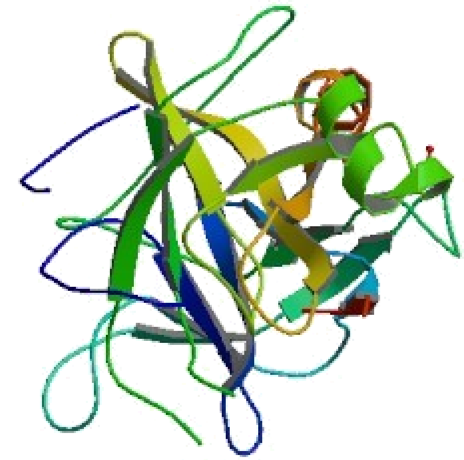
- *There is a closed form solution.*

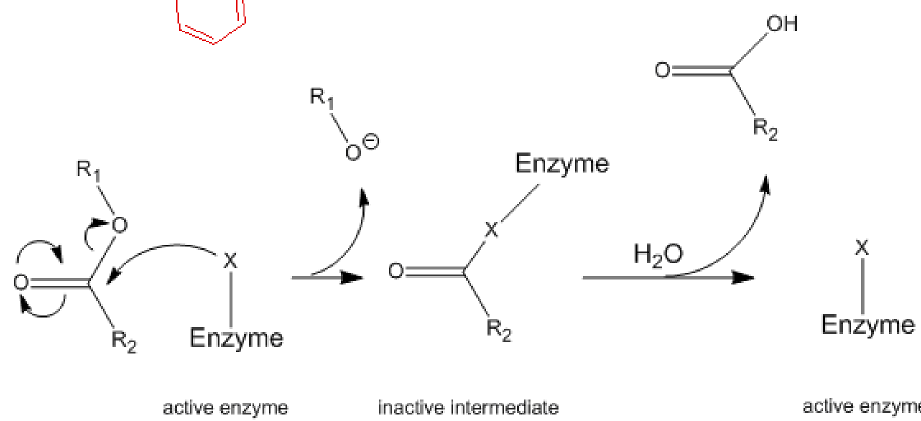




Example: Chymotrypsin







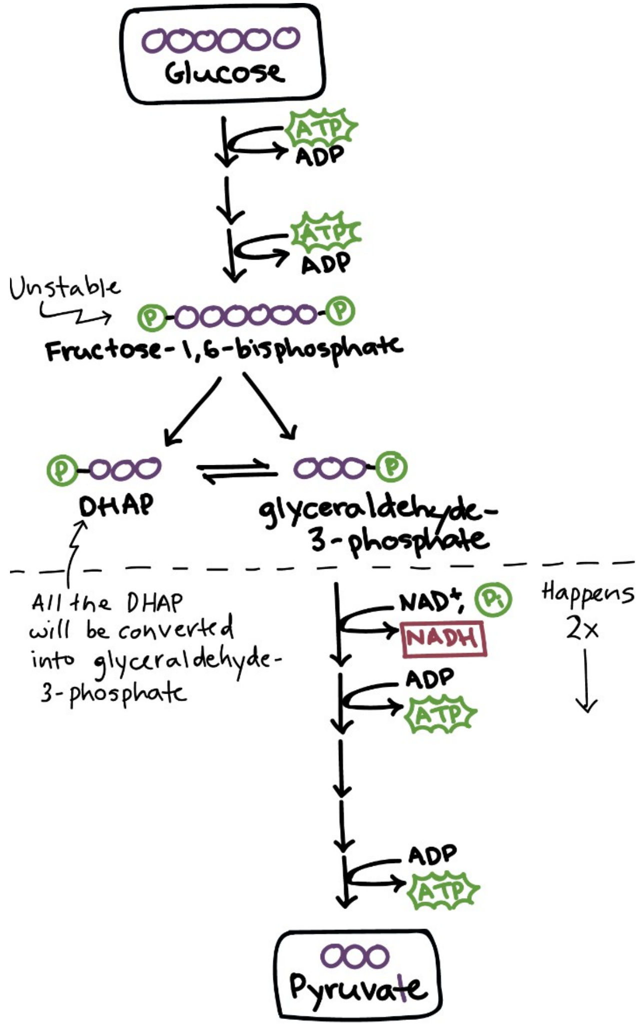
https://chem.libretexts.org/Core/Physical_and_Theoretical_Chemistry/Kinetics/Case_Studies%3A_Kinetics/Chymotrypsin_II
https://en.wikipedia.org/wiki/Chymotrypsin

Example: Chymotrypsin

- Assume cleavage of substrate by chymotrypsin follows Michaelis-Menten kinetics:

- See ode_examples.mlx

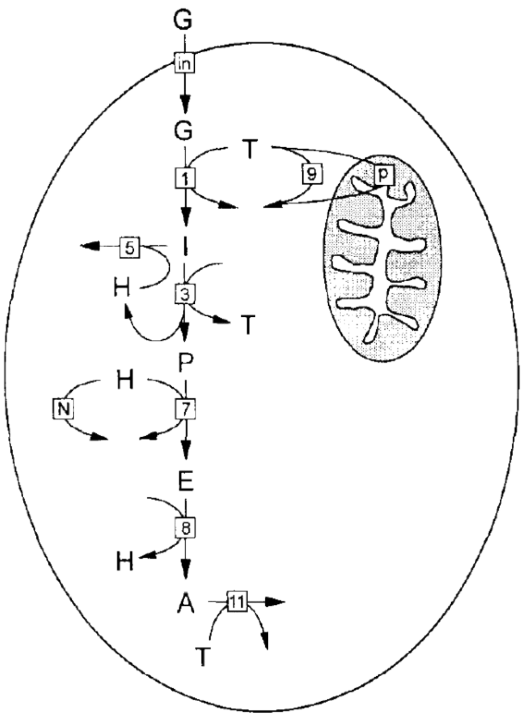
Network of Reactions: Glycolysis



https://www.khanacademy.org/science/biology/cellular-respiration-and-fermentation/glycolysis/a/glycolysis

Glycolytic Oscillations

- *Repetitive fluctuations in concentrations of metabolites (classical experiments in yeast and muscle)*
- ***G***:*intracellular glucose/hexose,* ***T***:*ATP,* ***I***:*triose phosphates,* ***H***:*NADH,* ***P***:*pyruvate,* ***E***:*ethanol,* ***A***:*acetate*



$$
\begin{aligned}
v_1(T,G) &= k_1 TG \\
v_3(T,I,H) &= k_3(C_{AD} - T)I(P_{tot} - I - T)(C_N^{tot} - H) \\
v_5(I,H) &= k_5 IH/(K_H + H) \\
v_7(P,H) &= k_7 PH/(H + K_{HP}) \\
v_8(E,H) &= k_8 E(C_N^{tot} - H) \\
v_9(T) &= k_9 T \\
v_{11}(A,T) &= k_{11} AT \\
v_p(T) &= k_p T/(K_M + T) \\
v_N(H) &= k_N H/(H + K_{HO})
\end{aligned}
$$

http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.158.5518&rep=rep1&type=pdf

Glycolytic Oscillations

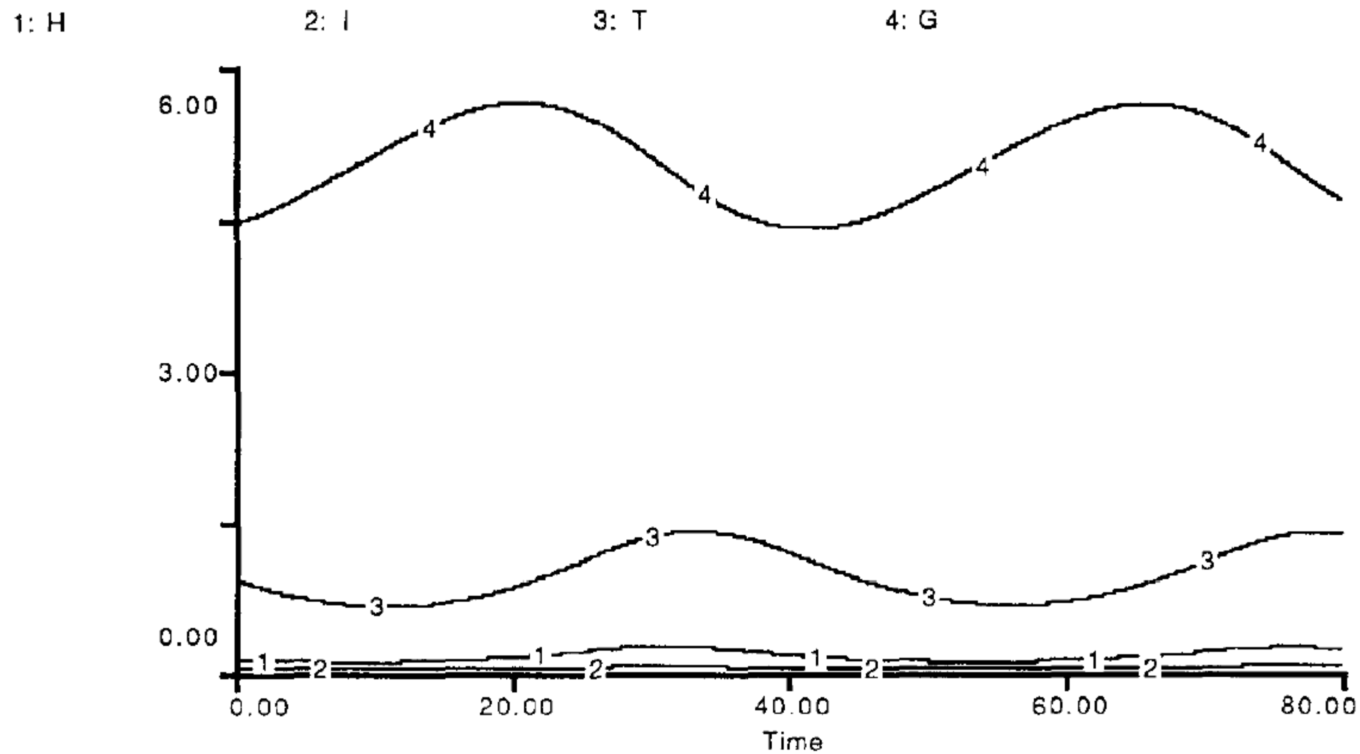
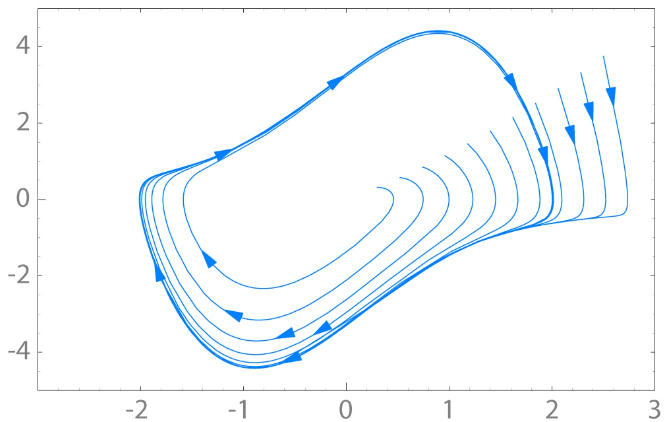


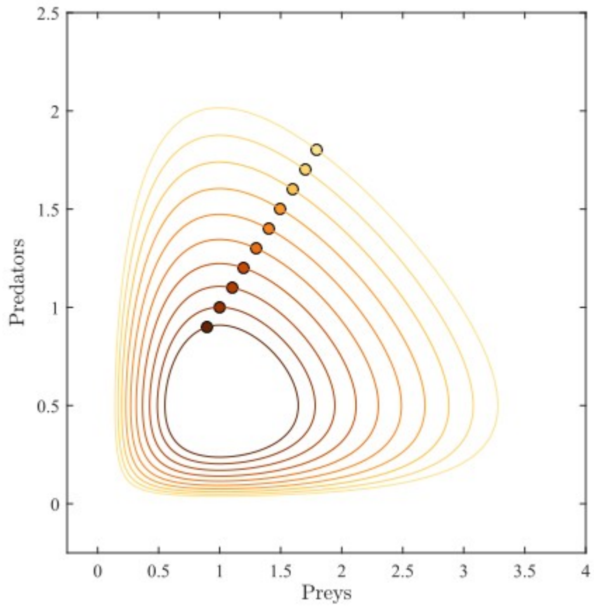
Fig. 3. A simulation of the full model of Fig. 1 with $V_{in} = 0.24$, $k_1 = 0.05$, $k_3 = 0.05$, $k_5 = 0.4$, $k_7 = 0.1$, $k_8 = 0.001$, $k_9 = 0.3$, $k_{11} = 0.02$, $K_H = 0.02$, $K_{HP} = 0.2$, $K_m = 2$, $k_{HO} = 0.2$, $k_p = 0.5$, $k_N = 0.08$, $C_{AD} = 8$, $P_{tot} = 10$, $C_N^{tot} = 8$, $E = 2$. Shown are the oscillating concentrations of NADH (1), triose phosphates (2), ATP (3) and hexose (4) after the system had relaxed to its limit cycle.

Glycolytic Oscillations

- *Limit Cycle in Glycolytic Oscillations is different than oscillations in Lotka-Volterra*



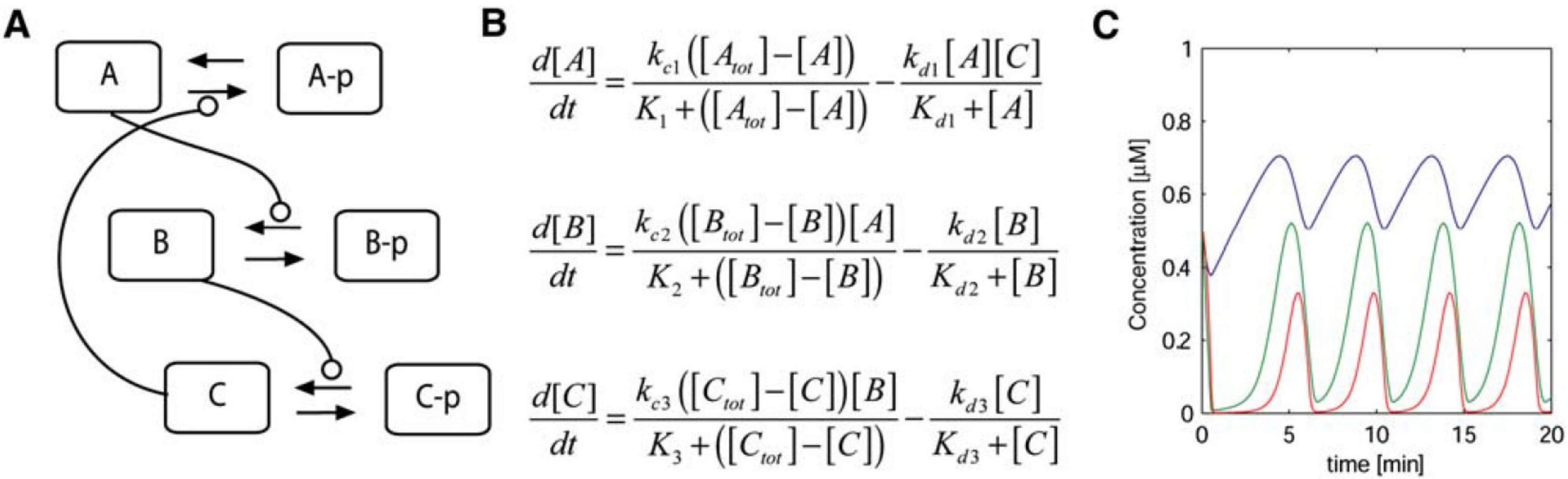
Stable Limit Cycle:
https://en.wikipedia.org/wiki/Limit_cycle



Lotka-Volterra
https://en.wikipedia.org/wiki/Lotka%E2%80%93Volterra_equations

Example

- *A generic three-component repressive network:*



Mogilner et al., Developmental Cell 11:279–287, 2006.