Life and Death Theory

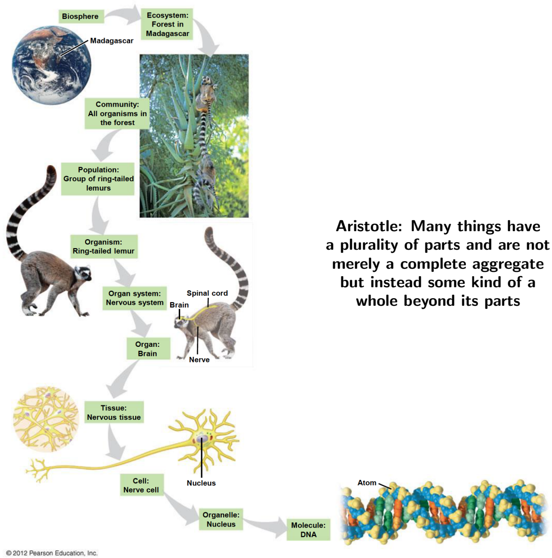
Part 1

Ali Fathi

September 4, 2021

Emergence Properties

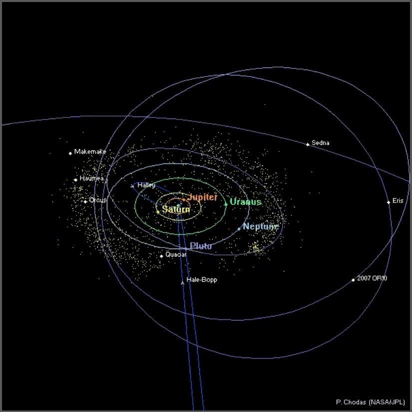
-or phenotypes

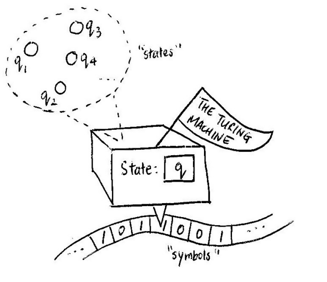


Aristotle: Many things have a plurality of parts and are not merely a complete aggregate but instead some kind of a whole beyond its parts

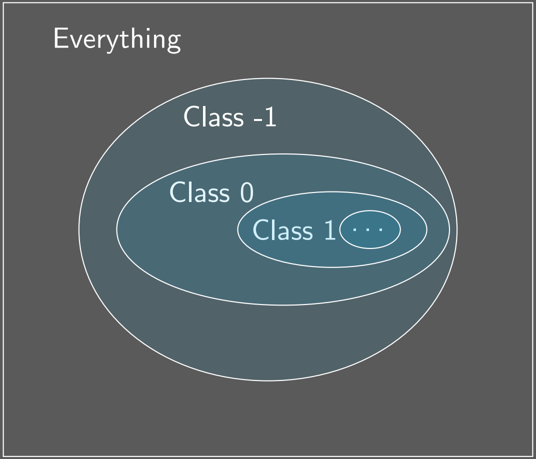
Biology Abstraction

-Math, Physics and Biology



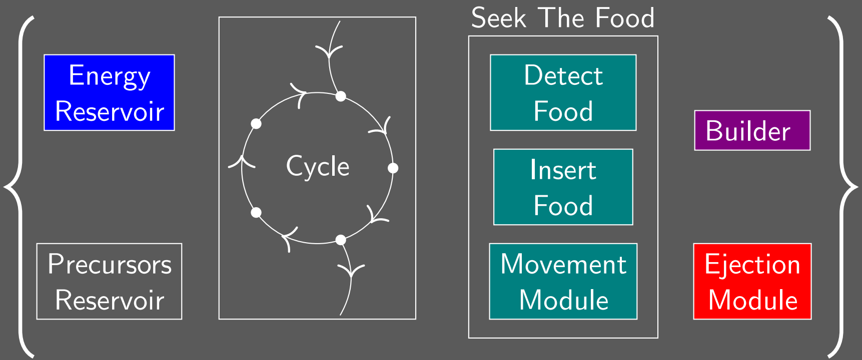


Life Classes
-modeling



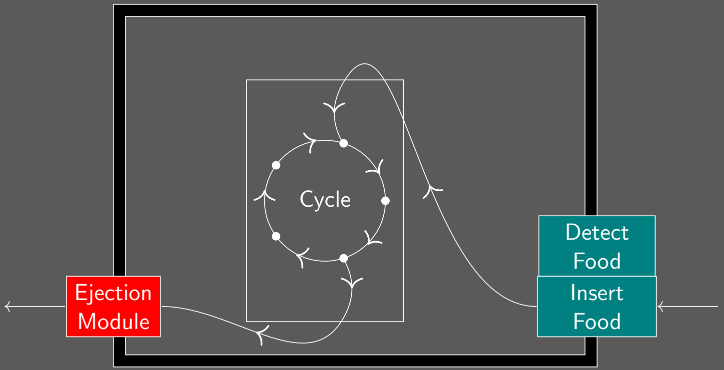
Agent and Modules

-intuitional



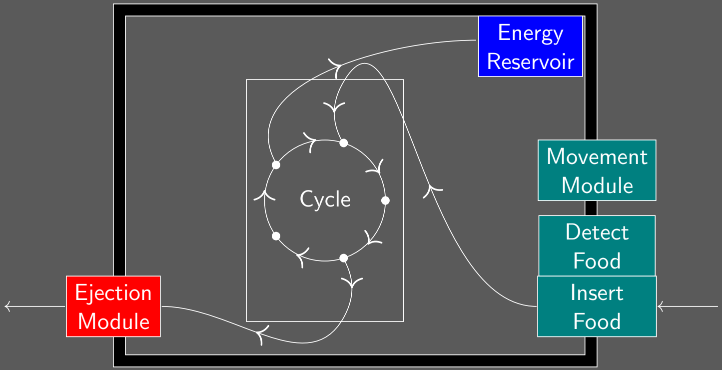
Class -1

-A tuple of 5 modules



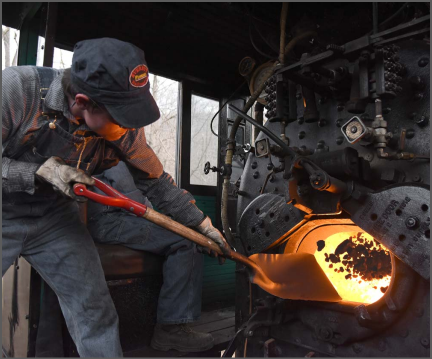
Class 0

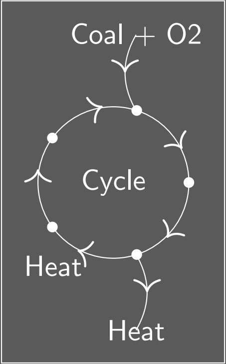
-A tuple of 6 modules



Cycle

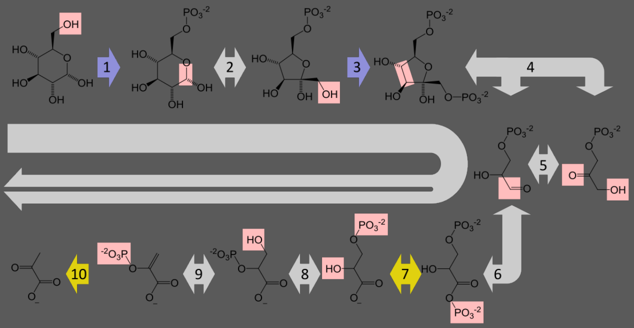
-living is repetitive





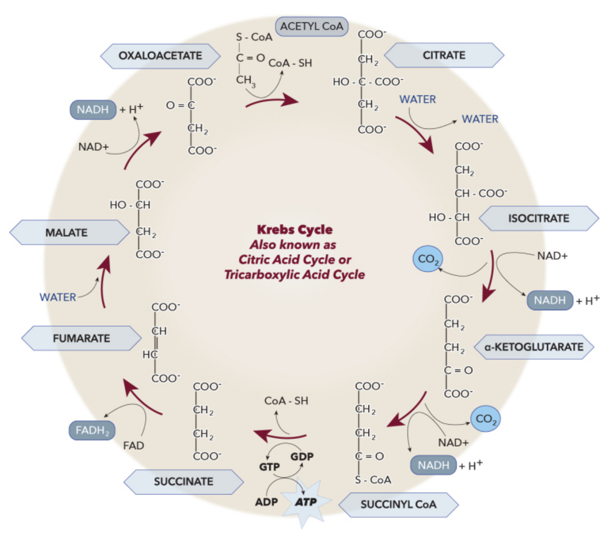
Glycolysis

-an example



Krebs Cycle

-an example



Mikaeelis Formula

-two-way reaction

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} P + E$$

Mikaeelis Formula

-simple enzyme (not cooperative, etc)

$$\mathrm{S} + \mathrm{E} \underset{\mathrm{k}_{-1}}{\overset{\mathrm{k}_1}{\rightleftharpoons}} \mathrm{C} \underset{\mathrm{k}_{-2}}{\overset{\mathrm{k}_2}{\rightleftharpoons}} \mathrm{P} + \mathrm{E}$$

$$\frac{d[S]}{dt} = -k_1[S][E] + k_{-1}[C]$$
$$\frac{d[C]}{dt} = k_1[S][E] + k_{-2}[P][E] - (k_{-1} + k_2)[C]$$
$$\frac{d[E]}{dt} = -k_1[S][E] - k_{-2}[P][E] + (k_{-1} + k_2)[C]$$
$$\frac{d[P]}{dt} = k_2[C] - k_{-2}[P][E]$$

Mikaeelis Formula

-some assumptions

$$\frac{d[C]}{dt} + \frac{d[E]}{dt} = 0 \Rightarrow [C] + [E] = \text{const.} := ec$$

Quasi-steady-state:

$$\frac{d[C]}{dt} = 0 \Rightarrow [C] = \frac{k_1[S] + k_{-2}[P]}{k_{-1} + k_2 + k_1[S] + k_{-2}[P]}.ec$$

$$\frac{d[P]}{dt} = -\frac{d[S]}{dt} := v(t) = \frac{k_1 k_2[S] - k_{-1} k_{-2}[P]}{k_{-1} + k_2 + k_1[S] + k_{-2}[P]}.ec$$

Mikaeelis Constants Finding

-lab works

For $[S] \gg [P]$, $\frac{k_{-1}+k_2}{k_1}$:

$$v(t) \approx k_2.ec \Rightarrow k_2 \checkmark$$

For $[P] \gg [S]$, $\frac{k_{-1}+k_2}{k_{-2}}$:

$$v(t) \approx -k_{-1}.ec \Rightarrow k_{-1} \checkmark$$

Equilibrium (no need for enzyme!):

$$\frac{[P]}{[S]}\Big|_{v=0} = \frac{k_1 k_2}{k_{-1} k_{-2}} := k_{eq} \qquad \text{(Haldane equation)}$$

Reaction Block

-Steady-State

$$\cdots \rightleftharpoons \mathrm{X}_i \xrightleftharpoons[k_{-1}]{\mathrm{E}_i \;\; k_1} \mathrm{C}_i \xrightleftharpoons[k_{-2}]{k_2 \;\; \mathrm{E}_i} \mathrm{X}_{i+1} \rightleftharpoons \cdots$$

$$k_1[X_i][E_i] - k_{-1}[C_i] = v \tag{1}$$

$$k_2[C_i] - k_{-2}[X_{i+1}][E_i] = v \tag{2}$$

$$[E_i] + [C_i] = \text{const.} := ec_i \tag{3}$$

Reaction Block
-Steady-State

$$
\begin{aligned}
k_1[X_i][E_i] - k_{-1}[C_i] &= v \\
k_2[C_i] - k_{-2}[X_{i+1}][E_i] &= v \\
[E_i] + [C_i] &= \text{const.} := ec_i
\end{aligned}
$$

$$
\begin{aligned}
[C_i] &= \frac{k_1 ec_i[X_i] - v}{k_{-1} + k_1[X_i]} \\
[E_i] &= \frac{k_{-1} ec_i + v}{k_{-1} + k_1[X_i]} \\
[X_{i+1}] &= \frac{k_1(k_2 ec_i - v)[X_i] - (k_2 + k_{-1})v}{k_{-1}k_{-2}ec_i + k_{-2}v}
\end{aligned}
$$

Reaction Block

-Steady-State

$$[X_{i+1}] = \frac{k_1(k_2 ec_i - v)[X_i] - (k_2 + k_{-1})v}{k_{-1}k_{-2}ec_i + k_{-2}v}$$

$$[X_{i+1}] = A_i[X_i] - B_i$$

$$A_i = \frac{k_1(k_2 ec_i - v)}{k_{-2}(k_{-1}ec_i + v)}$$

$$B_i = \frac{(k_2 + k_{-1})v}{k_{-2}(k_{-1}ec_i + v)}$$

Reaction Block

-Steady-State

$$\alpha_i := \frac{ec_i}{v}$$

$$K_M := \frac{k_{-1} + k_2}{k_1}$$

$$[X_{i+1}] = A_i[X_i] - B_i$$

$$A_i = \frac{k_1}{k_{-2}} . \frac{k_2\alpha_i - 1}{k_{-1}\alpha_i + 1}$$

$$B_i = K_M . \frac{k_1}{k_{-2}} . \frac{1}{k_{-1}\alpha_i + 1}$$

(note: $[X_{n+1}]$ shouldn't become negative)

Reaction Block
-Excess of Enzyme

$$\alpha_i >> \frac{1}{k_{-1}}, \frac{1}{k_2}$$

$$A_i \approx \frac{k_1 k_2}{k_{-1} k_{-2}}$$
$$B_i \approx 0$$

(Haldane equation)

Reaction Block

-Simplification

$$\cdots \rightleftharpoons \mathrm{X}_i \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{X}_{i+1} \rightleftharpoons \cdots$$

$$v = k_1[X_i] - k_{-1}[X_{i+1}] \tag{4}$$

Reaction Block
-Simplification

$$v = k_1[X_i] - k_{-1}[X_{i+1}]$$

$$[X_{i+1}] = \frac{k_1[X_i]}{k_{-1}} - \frac{v}{k_{-1}} = A_i[X_i] - B_i$$

$$A_i = \frac{k_1}{k_{-1}} := k_{eq}, \quad B_i = \frac{v}{k_{-1}}$$

(Compare with

$$A_i = \frac{k_1}{k_{-2}}.\frac{k_2\alpha_i - 1}{k_{-1}\alpha_i + 1}, \quad B_i = K_M.\frac{k_1}{k_{-2}}.\frac{1}{k_{-1}\alpha_i + 1})$$

Reaction Block

-many-to-many

$$\cdots \rightleftharpoons \mathrm{X}_i \underset{k_{-1}}{\overset{U_{1:l} \quad V_{1:m}}{\overset{k_1}{\rightleftharpoons}}} \mathrm{X}_{i+1} \rightleftharpoons \cdots$$

$$v = k_1[X_i][U_1]\cdots[U_l] - k_{-1}[X_{i+1}][V_1]\cdots[V_m] \tag{5}$$

Reaction Block

-many-to-many

$$v = k_1[X_i][U_1]\cdots[U_l] - k_{-1}[X_{i+1}][V_1]\cdots[V_m]$$

$$[X_{i+1}] = \frac{k_1}{k_{-1}}.\frac{[U_1]\cdots[U_l]}{[V_1]\cdots[V_m]}.[X_i] - \frac{v}{k_{-1}}.\frac{1}{[V_1]\cdots[V_m]} = A_i[X_i] - B_i$$

$$A_i = \frac{k_1}{k_{-1}}.\frac{[U_1]\cdots[U_l]}{[V_1]\cdots[V_m]}, \quad B_i = \frac{v}{k_{-1}}.\frac{1}{[V_1]\cdots[V_m]}$$

$$k_{eq} := \frac{k_1}{k_{-1}} = Q_{eq} := \frac{[V_1]\cdots[V_m][X_{i+1}]}{[U_1]\cdots[U_l][X_i]}\Big|_{v=0}$$

Reactions Chain

-one-to-one reactions

$$\xrightarrow{v} \mathrm{X}_0 \rightleftharpoons \cdots \rightleftharpoons \mathrm{X}_n \xrightarrow{v}$$

$$[X_n] = (A_{n-1} \cdots A_1 A_0)[X_0] - \sum_{i=0}^{n-1} (A_{n-1} \cdots A_{i+1}) B_i \qquad (6)$$

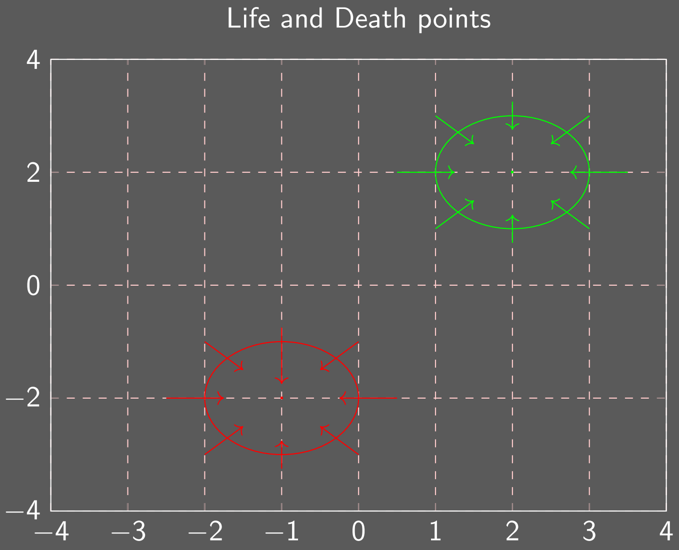
In simplified one-to-one case:

$$[X_n] = (\prod_{j=0}^{n-1} k_{eq}^{(j)})[X_0] - v.\sum_{i=0}^{n-1}(\prod_{j=i+1}^{n-1} k_{eq}^{(j)}).\frac{1}{k_{-1}^{(i)}} \qquad (7)$$

$$\coloneqq C_n.[X_0] - D_n.v \qquad (8)$$

Life and Death

-equilibriums



Death Condition

-Equilibrium

$$v = 0$$

$$[X_{i+1}] = \frac{k_1 k_2}{k_{-1} k_{-2}}.[X_i]$$

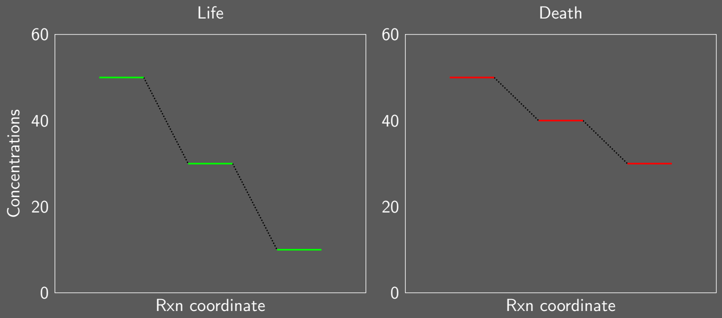
$$\Rightarrow [X_n] = (\prod_{i=0}^{n-1} \frac{k_1^{(i)} k_2^{(i)}}{k_{-1}^{(i)} k_{-2}^{(i)}}).[X_0] \,\text{(first model)}$$

$$[X_{i+1}] = \frac{k_1}{k_{-1}}.[X_i]$$

$$\Rightarrow [X_n] = (\prod_{i=0}^{n-1} k_{eq}^{(i)}).[X_0] = C_n.[X_0] \,\text{(simplified model)}$$

Concentrations Comparison

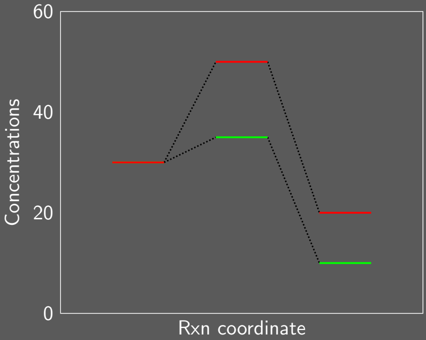
-Life and Death



(note: concentrations are not necessarily decreasing)

Concentrations Comparison

-More Accurate



(assumed $[X_0]$s are equal)

Next Session
-part 2

- Numerical analysis for an example (glucose to lactate fermentation)