Difference equations

• The first order is trivial

I) Linear :

I. a) 1 equation

$$\boxed{x_{n+2} - \beta x_{n+1} + \gamma x_n = 0}$$ (Second or higher order).

↳ Pol. Char. $\lambda^2 - \beta\lambda + \gamma = 0$

$$\hookrightarrow \lambda_{1,2} = \frac{\beta \pm \sqrt{\overbrace{\beta^2 - 4\gamma}^{\delta}}}{2}$$

Sol : $\boxed{x_n = A_1 \lambda_1^n + A_2 \lambda_2^n}$

A_1 et A_2 définit par les cond initiales
↳ x_0, x_1

• If $\delta > 0$: $\lambda_{1,2}$ are real.

- if $|\lambda_{1,2}| < 1 \Rightarrow$ converge to 0
- if ~~of~~ one of the $|\lambda_i| > 1 \Rightarrow$ diverge
- $\lambda_i < 0$ oscillation in sign.

• If $\delta < 0$: $\lambda_1 = a + bi \quad \lambda_2 = a - bi$

↳ $r := (a^2 + b^2)^{1/2}$

$\phi := \arctan(b/a)$

So $x_n = A_1 (a+bi)^n + A_2 (a-bi)^n$

$= A_1 r^n (\cos(n\phi) + i \sin(n\phi)) + A_2 r^n (\cos(n\phi) - i \sin(n\phi))$

$= B_1 r^2 \cos(n\phi) + i B_2 r^2 \sin(n\phi)$ $\quad B_1 = A_1 + A_2, \; B_2 = A_1 - A_2$

by linearity of solutions:

$$\boxed{x_n = C_1 r^n \cos(n\phi) + C_2 r^n \sin(n\phi)}$$

ϕ : oscillating part

• $r < 1$: converge to zero. $r > 1$: amplification

• $r = 1$ constant amplitude oscillation.

I.b) System of equations : (for 2 eq, but can be generalized)

$$\boxed{\begin{aligned} x_{n+1} &= a_{11} x_n + a_{12} y_n \\ y_{n+1} &= a_{21} x_n + a_{22} y_n \end{aligned}} \qquad A = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix}$$

↳ can be converted in a simple equation.

$$\boxed{x_{n+2} - \underbrace{(a_{11} + a_{22})}_{\beta} x_{n+1} + \underbrace{(a_{11} a_{22} - a_{21} a_{12})}_{\gamma} x_n = 0}$$

(!) $\beta = a_{11} + a_{22} = \mathrm{Tr}(A)$ $\qquad \gamma = (a_{11} a_{22} - a_{21} a_{12}) = \det(A)$

↳ find $\lambda_{1,2}$ as in part a)

Rem : $\lambda_{1,2}$ are the eigenvalues of A $\rightarrow$ $\boxed{\det(A - \lambda \mathrm{Id}) = 0}$

II) Non-linear :

$$\boxed{x_{n+1} = f(x_n, x_{n-1}, \dots)} \quad \text{no general solution}$$

II.a) basics

- Steady state : X_s such that $\boxed{X_s = f(X_s)}$ (fixed point)

- Stability of steady state : 1) little perturbation : $X_n = X_s + x_n$ (x small)

so $X_{n+1} = \cancel{X_s} + x_{n+1} = f(X_n) = f(X_s + x_n) \overset{\text{Taylor}}{\simeq} \cancel{f(X_s)} + \left.\dfrac{df(x)}{dX}\right|_{X_s} \cdot x_n$

so $\boxed{x_{n+1} = \left(\left.\dfrac{df}{dX}\right|_{X_s} \right) x_n}$

condition of stability : $\boxed{\left| \left.\dfrac{df}{dX}\right|_{X_s} \right| < 1}$ (!) have to be recalculated for each steady state $X_{S_1}, \dots, X_{S_n}$

- Case of oscillation between 2 points : Stable oscillation of period 2 : 2 points : $\bar{X}_1, \bar{X}_2$

$$\boxed{x_{n+2} = f(f(x_n)) = x_n} \quad \text{we pose} \quad \boxed{g(x) = f(f(x))} \quad g = f \circ f$$

$\boxed{k = n/2 \text{, } n \text{ even}}$

↳ $\boxed{x_{k+1} = g(x_k)}$

↳ we search for Steady state of g (as in the simple case).

Stability condition : $\left| \left.\dfrac{dg}{dX}\right|_{\bar{X}_i} \right| < 1 \iff \boxed{\left| \left.\dfrac{df}{dX}\right|_{\bar{X}_1} \cdot \left.\dfrac{df}{dX}\right|_{\bar{X}_2} \right| < 1}$

The last condition may be more difficult to compute, but remember that steady state x_s of f is also steady state of g.

So we can factorize g by f and simplify the computations.

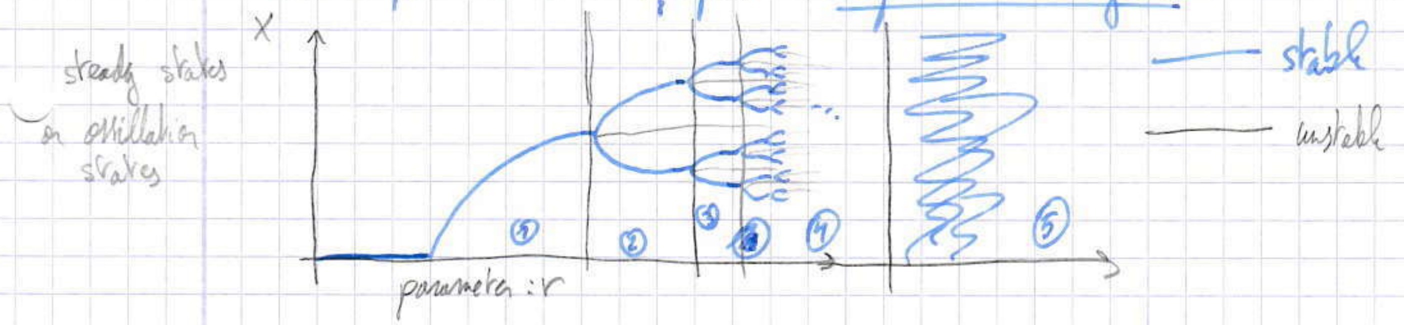
- Oscillation between multiple points

For some equations (Ex: logistic equation), we will have a parameter (Ex: r)

- By increasing progressively r we will have:

1) 1 stable s.s → 2) stable oscillation between 2 points → 3) stable oscillation between 4 points. → 4) st oscil. 2^n points → 5) Chaos.

We can represent it in a diagram : Bifurcation diagram



The cases ① and ② are clearly explained

The cases ③, ④ are similar to ② but with $\boxed{g := f^{\circ n}}$ $n = 4, 8, 16, \dots$

II.b) System of difference equations ($n = 2$)

$$\boxed{\begin{cases} x_{n+1} = f(x_n, y_n) \\ y_{n+1} = g(x_n, y_n) \end{cases}}$$

Steady states : $\boxed{\begin{matrix} \bar{x} = f(\bar{x}, \bar{y}) \\ \bar{y} = g(\bar{x}, \bar{y}) \end{matrix}}$

Stability : $X = \bar{X} + x'$
$Y = \bar{Y} + y'$

$$f(\bar{X} + x', \bar{Y} + y') \simeq f(\bar{X}, \bar{Y}) + \overbrace{\frac{\partial f}{\partial x}\Big|_{\bar{X},\bar{Y}}}^{a_{11}} x' + \overbrace{\frac{\partial f}{\partial y}\Big|_{\bar{X},\bar{Y}}}^{a_{12}} y'$$

$g(\bar{X} + x', \bar{Y} + y') \simeq$ "

$a_{21} = \frac{\partial g}{\partial x}\Big|_{\bar{X},\bar{Y}}$ $a_{22} = \frac{\partial g}{\partial y}\Big|_{\bar{X},\bar{Y}}$

so : $\left.\begin{matrix} x'_{n+1} = a_{11} x'_n + a_{12} y'_n \\ y'_{n+1} = a_{21} x'_n + a_{22} y'_n \end{matrix}\right\}$ (syst of lin diff eq)

$A = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix}$

$\beta = Tr(A)$ $\gamma = Det(A)$

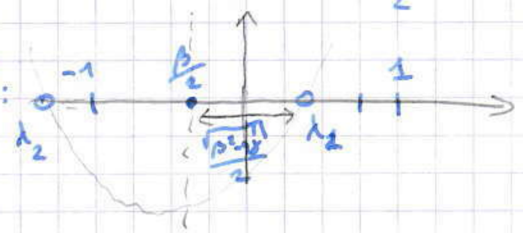
↳ $\lambda_{1,2}$: sol of $\det(A - \lambda I_d) = 0 \to \lambda^2 - \beta\lambda + \gamma = 0$

stability condition: $\boxed{|\lambda_{1,2}| < 1}$

- **Remark about the polynomial** $\boxed{\lambda^2 - \beta\lambda + \gamma = 0}$

We want that $\lambda_{1,2} = \dfrac{+\beta \pm \sqrt{\beta^2 - 4\gamma}}{2}$ such that $\lambda_{1,2} \in [-1, 1]$

recall:



- First condition: $\frac{\beta}{2} \in [-1,1] \Rightarrow \boxed{|\beta| < 2}$
- Second condition: supp $\beta > 0$

we have to verify: $\dfrac{\beta + \sqrt{\beta^2 - 4\gamma}}{2} < 1$

$\Rightarrow \sqrt{\beta^2 - 4\gamma} < 2 - \beta$

$\Rightarrow \cancel{\beta^2} - 4\gamma < \cancel{\beta^2} - 4\beta + 4$ the $\beta < 0$ is a similar case

? $\Rightarrow \boxed{\gamma + 1 > \beta}$

conclusion: $\boxed{|\beta| < 1 + \gamma < 2}$ condition such that $|\lambda_{1,2}| < 1$ complex case?

II.c) Logistic equation (discrete version) $f(x) = rx(1-x)$

$$\boxed{X_{n+1} = r X_n (1 - X_n)}$$

Steady states: $\boxed{X_{s_1} = 0 ;\ X_{s_2} = 1 - 1/r = \frac{r-1}{r}}$ $\boxed{\left(\frac{df}{dx}\right) = r - 2rx}$

Stability: for X_{s_1}: $\left(\frac{df}{dx}\right)_{X_{s_1}=0} = r \rightarrow$ stable for $\boxed{r \in [0, 1]}$

stab cond: $\left|\frac{df}{dx}\Big|_{x_s}\right| < 1$

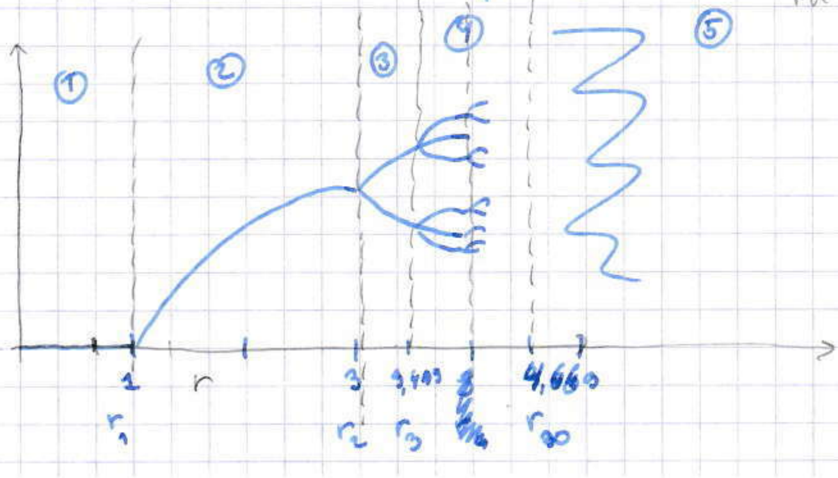
for X_{s_2}: $\left(\frac{df}{dx}\right)_{X_{s_2} = \frac{r-1}{r}} = 2 - r \rightarrow$ stable for $\boxed{r \in [1, 3]}$

So: for $r \in [0,1]$: $X_n \rightarrow 0$, for $r \in [1,3]$ $x_n \rightarrow \frac{r-1}{r}$

After $r=3$: periodic oscillation of 2^n points.

For ③ we use $\boxed{g = f(f(x))}$

bifurcation diagram



III) Application to population dynamics

$\lambda \in [0,1]$
$\alpha, b > 0$

Model 1 : $\boxed{N_{t+1} = \underbrace{\left(\frac{1}{\alpha} N_t^{-b}\right)}_{f(N)} (\lambda N_t)}$

→ rate of pregnancy

→ fraction of survival to generation $(t+1)$

Steady state $\boxed{N_s = \left(\frac{\lambda}{\alpha}\right)^{1/b}}$ $\quad \left.\frac{d f(N)}{d N}\right|_{N_s} = 1-b$

stability condition : $\boxed{0 < b < 2}$

Model 2 $\boxed{N_{t+1} = N_t \exp\left(r\left(1 - N_t/K\right)\right)}$ Steady state : $\boxed{N_s = K}$

stability : $\boxed{0 < r < 2}$

Model 3 : $\boxed{N_{t+1} = \lambda N_t \left(1 + a N_t\right)^{-b}}$

Host-parasit model : N_t : density of host $\quad \lambda$: host reproduction rate

P_t : density of parasite $\quad c$: # of egg in a para-host.

$f(N_t, P_t)$: fraction of host non-para

$$\boxed{\begin{cases} N_{t+1} = \lambda N_t f(N_t, P_t) \\ P_{t+1} = c N_t (1 - f(N_t, P_t)) \end{cases}}$$

find $f(N_t, P_t)$ → poisson distribution.

$P(X=k) = \frac{\mu^k}{k!} e^{-\mu}$, μ : mean

mean $\mu = \frac{a P_t N_t}{N_t} = \frac{\text{\# of encounter}}{\text{per } N_t \text{ individual}} \Rightarrow \boxed{\mu = a P_t}$

so $\boxed{f(N_t, P_t) = P_\mu(X=0) = e^{-a P_t}}$

steady states : $\boxed{P_s = \frac{\ln \lambda}{a} \qquad N_s = \frac{\lambda \ln(\lambda)}{(\lambda - 1) a c}}$

Differential equations

I) Simple cases

- First order, homogène : $\boxed{\frac{dx}{dt} = f(t)\, x}$

$$\Rightarrow \frac{1}{x}\, dx = f(t)\, dt \Rightarrow \int_0^t \frac{1}{x}\, dx = \int_0^t f(t)\, dt$$

primitive

$$\Rightarrow \ln(x(t)) - \ln(x_0) = \int_0^t f(t)\, dt = F(t)$$

$$\Rightarrow \boxed{x(t) = x_0\, e^{F(t)}}$$

Sometimes also work with separated variables : $\boxed{\frac{dx}{dt} = f(t) \cdot g(x)}$

- First order, non-homogen : $\boxed{\frac{dx}{dt} = f(t)\, x + g(t)}$ ①

1) Solve the homogen equation : $x_h(t) = K_0\, \phi(t)$
2) Variation des constantes : suppose $K_0 = K(t)$
   inject in ① and find $K(t) \rightarrow x_p(t) = K(t)\, \phi(t)$
3) $\boxed{x(t) = x_p(t) + x_h(t)}$

- Second order, constant coeff, homogen:

$$\boxed{\frac{d^2x}{dt^2} - \beta \frac{dx}{dt} + \gamma x = 0} \rightarrow \text{Pol. char : } \lambda^2 - \beta\lambda + \gamma = 0$$

$$\hookrightarrow \lambda_{1,2} = \frac{\beta \pm \sqrt{\beta^2 - 4\gamma}}{2}$$

- $\beta^2 - 4\gamma > 0$: real case $\boxed{x(t) = A_1\, e^{\lambda_1 t} + A_2\, e^{\lambda_2 t}}$

- $\beta^2 - 4\gamma < 0$: complex conjugate

$\lambda_1 = a + bi$

$\lambda_2 = a - bi$

$$\boxed{x(t) = A_1\, e^{at} \cos(bt) + A_2\, e^{at} \sin(bt)}$$

- A linear system : $\left.\begin{aligned} \frac{dx}{dt} &= a_{11} x + a_{12} y \\ \frac{dy}{dt} &= a_{21} x + a_{22} y \end{aligned}\right\}$ can be converted into the previous case.

• Logistic growth $\boxed{\dfrac{dN}{dt} = rN\left(1-N/K\right)} = rN\cdot g(N)$

Pose $Z = \frac{1}{N} \to \dfrac{d\left(\frac{1}{Z}\right)}{dt} = -\frac{1}{Z^2}Z' = r\left(\frac{1}{Z}\right)\left(1-\frac{1}{KZ}\right)$

$$\Rightarrow Z' = -r\left(Z-\frac{1}{K}\right) = \int \frac{1}{\left(Z-\frac{1}{K}\right)}dZ = -r\int dt$$

$$\Rightarrow Z - \frac{1}{K} = e^{-rt}k_0 \quad \text{with } k_0 = \frac{B-N_0}{N_0 B} \qquad N_0 = N(0)$$

$$\Rightarrow \boxed{N(t) = \frac{\cancel{B}K N_0}{N_0 + (B-N_0)e^{-rt}}} \qquad \text{Steady state}: \boxed{N = K}$$

II) When the eq is too complex to be resolved.

~~Preliminary definition~~

II. a) 1-variable system $\boxed{\dfrac{dX}{dt} = f(X)}$

Steady state : $\boxed{\left.\dfrac{dX}{dt}\right|_{X_S} = f(X_S) = 0}$

Stability : Perturbation : $X = X_S + x$

$$\frac{dX}{dt} = \frac{dX_S}{dt} + \frac{dx}{dt} = f(X) = f(X_S + x) \overset{\text{Taylor}}{\simeq} f(X_S) + \left.\frac{df}{dX}\right|_{X_S} x + \dots$$

$$\Rightarrow \boxed{\frac{dx}{dt} = \left.\frac{df}{dX}\right|_{X_S} x}$$ ~~stability condition~~: posons : $\boxed{\lambda := \left.\dfrac{df}{dX}\right|_{X_S}}$

$$\frac{dx}{dt} = \lambda x \Rightarrow \int \frac{1}{x}dx = \lambda\int dt \Rightarrow \boxed{x(t) = x_0 e^{\lambda t}}$$

stability condition : $\boxed{\left.\dfrac{df}{dX}\right|_{X_S} = \lambda < 0}$

• Logistic growth $\boxed{\frac{dN}{dt} = rN\left(1 - N/K\right)} = rN \cdot g(N)$

Pose $Z = \frac{1}{N} \rightarrow \frac{d\left(\frac{1}{Z}\right)}{dt} = -\frac{1}{Z^2} Z' = r\left(\frac{1}{Z}\right)\left(1 - \frac{1}{KZ}\right)$

$\Rightarrow Z' = -r\left(Z - \frac{1}{K}\right) = \int \frac{1}{\left(Z - \frac{1}{K}\right)} dZ = -r \int dt$

$\Rightarrow Z - \frac{1}{K} = e^{-rt} k_0$ with $k_0 = \frac{B - N_0}{N_0 B}$ $N_0 = N(0)$

$\Rightarrow \boxed{N(t) = \frac{B N_0}{N_0 + (B - N_0) e^{-rt}}}$ Steady state : $\boxed{N = K}$

II) When the eq is too complex to be resolved.

~~Preliminary definition~~

II. a) 1-variable system $\boxed{\frac{dX}{dt} = f(X)}$

Steady state : $\boxed{\left.\frac{dX}{dt}\right|_{X_S} = f(X_S) = 0}$

Stability : Perturbation : $X = X_S + x$

$\frac{dX}{dt} = \frac{dX_S}{dt} + \frac{dx}{dt} = f(X) = f(X_S + x) \overset{\text{Taylor}}{\simeq} f(X_S) + \left.\frac{df}{dX}\right|_{X_S} x + \dots$

$\Rightarrow \boxed{\frac{dx}{dt} = \left.\frac{df}{dX}\right|_{X_S} x}$ ~~stability condition~~: posons : $\boxed{\lambda := \left.\frac{df}{dX}\right|_{X_S}}$

$\frac{dx}{dt} = \lambda x \Rightarrow \int \frac{1}{x} dx = \lambda \int dt \Rightarrow \boxed{x(t) = x_0 e^{\lambda t}}$

Stability condition : $\boxed{\left.\frac{df}{dX}\right|_{X_S} = \lambda < 0}$

II.b) 2-variable system

$$\boxed{\left.\begin{aligned}\frac{dX}{dt} &= f(X,Y)\\ \frac{dY}{dt} &= g(X,Y)\end{aligned}\right\}}$$

Steady state : (X_s, Y_s) such that $\boxed{\begin{aligned}f(X_s,Y_s)&=0\\ g(X_s,Y_s)&=0\end{aligned}}$

stability : perturbation : $\left.\begin{aligned}X &= X_s + x\\ Y &= Y_s + y\end{aligned}\right\}$

Jacobienne

$$\Rightarrow \left.\begin{aligned} f(X,Y) &\simeq f(X_s,Y_s) + \overset{a_{11}}{\left(\frac{df}{dX}\right)_{X_s,Y_s}} x + \overset{a_{12}}{\left(\frac{df}{dY}\right)_{X_s,Y_s}} y \\ g(X,Y) &\simeq g(X_s,Y_s) + \quad '' \; a_{21} \qquad\qquad '' \; a_{22}\end{aligned}\right\} \qquad J = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22}\end{pmatrix}$$

p. char.

$\hookrightarrow$ solve : $\det(J - \lambda\, Id) = 0 \rightarrow \lambda^2 - \beta\lambda + \gamma = 0 \qquad \lambda_{1,2} = \frac{\beta \pm \sqrt{\beta^2 - 4\gamma}}{2}$

So $\left.\begin{aligned} x(t) &= A_1 e^{\lambda_1 t} + A_2 e^{\lambda_2 t} \\ y(t) &= B_1 e^{\lambda_1 t} + B_2 e^{\lambda_2 t}\end{aligned}\right\}$ (real case)

Complex case : $\lambda_1 = a+bi$, $\lambda_2 = a-bi$ $\quad \left.\begin{aligned} x(t) &= A_1 e^{at}\left(\cos(bt+\phi_1)\right) \\ y(t) &= A_2 e^{at}\left(\cos(bt+\phi_2)\right)\end{aligned}\right\}$

- $\beta^2 - 4\gamma > 0$: real case stability condition: $\boxed{\lambda_{1,2} < 0}$
  - $\lambda_1, \lambda_2 < 0$: stable node
  - $\lambda_1 < 0,\ \lambda_2 > 0$: unstable saddle
  - $\lambda_1, \lambda_2 > 0$: unstable node

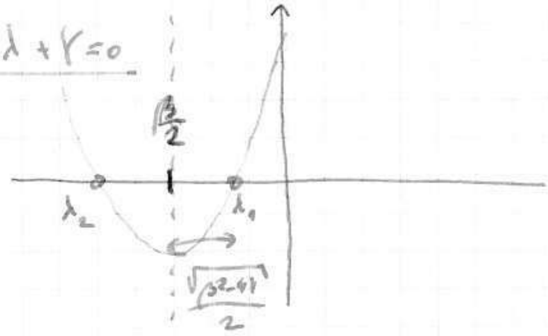
- $\beta^2 - 4\gamma < 0$: complex conjugated : $\lambda_1 = a + bi \quad \lambda_2 = a - bi$

  where $a = \frac{\beta}{2} \qquad b = \frac{\sqrt{4\gamma - \beta^2}}{2}$

  stability condition: $\boxed{a = \frac{\beta}{2} < 0}$ real part of the roots
  - $a = 0$: cycle
  - $a < 0$: stable focus
  - $a > 0$: unstable focus

Rem: case of N-variables : stability condition : $\boxed{\lambda_i < 0 \quad \forall i}$

- Observation on the polynomial $\lambda^2 - \beta\lambda + \gamma = 0$



- If $\beta^2 - 4\gamma > 0$: real case :

We want stability $\rightarrow$ $\boxed{\lambda_1, \lambda_2 < 0}$

Cond 1 : $\boxed{\beta < 0}$

Cond 2 : if $\beta < 0$: $\frac{\beta + \sqrt{\beta^2 - 4\gamma}}{2} < 0 \Rightarrow \sqrt{\beta^2 - 4\gamma} < -\beta$

$\Rightarrow \beta^2 - 4\gamma < \beta^2$

$\Rightarrow \boxed{\gamma > 0}$

So : stability if: $\boxed{\beta < 0 \;;\; \gamma > 0}$

Enzyme reactions

Dans le cadre des réactions enzymatiques, il est parfois difficile de tout résoudre explicitement.

On peut faire 2 hypothèses simplificatrices. (1 à la fois)

$S_1 + \cdots + S_n \xrightarrow{\text{Enzymes}} P_1 + \cdots + P_n$

$S_1 + \cdots + S_n + E \rightleftarrows [\;] \longrightarrow P_1 + \cdots + P_n + E$

E ressort inchangé !

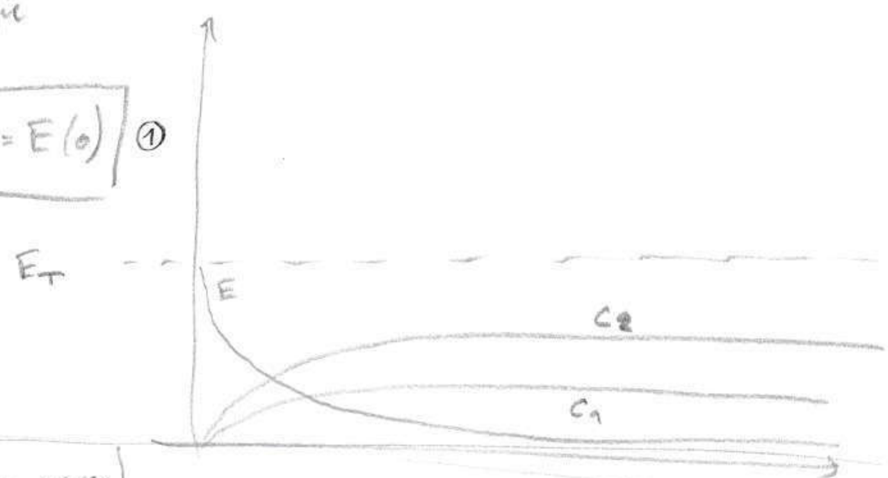
Avant de faire les hypothèses, remarquons :

l'Enzyme (E) peut être seule ou liée à des complexes

et peuvent prendre la forme de complexes enzymatiques. (C_i)

Mais leur quantité totale reste inchangée

$$\boxed{E_T = E + C_1 + \cdots + C_k = \text{constante} = E(0)} \quad ①$$



1°) Hyp 1 : Instantaneous equilibrium (moins précise)

- On suppose que les réactions d'équilibre sont bcp plus rapides que celle générant les produits.

$$k_1, k_2, \ldots, k_n, k_{-1}, k_{-2}, \ldots, k_{-n} >> k_{p_1}, k_{p_2}, \ldots, k_{p_k}$$

- On suppose que toutes (complexe) enzym(atique) est constant dans le temps.

$$\frac{dE}{dt} = 0, \frac{dC_1}{dt} = 0, \ldots, \frac{dC_n}{dt} = 0 \quad \text{en niant les termes en } k_{p_i} !$$

Ex : $S + C_1 \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} C_2 \xrightarrow{k_2} E + P$

$$\boxed{\frac{dC_2}{dt} = 0 = k_1 S C_1 - k_{-1} C_2 - \cancel{k_2 C_2} = 0} \quad ②$$

2°) Hyp 2 : Quasi-steady-state-assumption (QSSA) (plus précis)

- On suppose que tous (complexe) enzym(atiques) est constant dans le temps.

$$\boxed{\frac{dE}{dt} = 0, \frac{dC_1}{dt} = 0, \ldots, \frac{dC_n}{dt} = 0} \quad ②$$

Dans les 2 cas : On prend tout $C_{i_1}, \dots, C_{i_m}$ qui produisent P.

$$\left.\begin{array}{ll} C_{i_1} & \xrightarrow{k_{i_1}} P + (\dots) \\ \vdots & \\ C_{i_m} & \xrightarrow{k_{i_m}} P + (\dots) \end{array}\right\}$$

Ainsi : $$\boxed{v = \frac{dP}{dt} = k_{i_1} C_{i_1} + \dots + \dots + k_{i_m} C_{i_m}} \quad (3)$$

En injectant (2) dans (1), nous arrivons à exprimer les C_i en fonction de E_T, S, k_j

Ex : $$\boxed{C_{i_1} = E_T \left(\frac{S}{K_{i_1} + S}\right)} \quad (4)$$

où on pose : si 1°) $K_{i_1} = \frac{k_{-j_1}}{k_{j_1}}$ (forme proportionnelle)

(ce sont des exemples)

2°) $K_{i_1} = \frac{k_{-j_1} + k_i}{k_{j_1}}$ (affine)

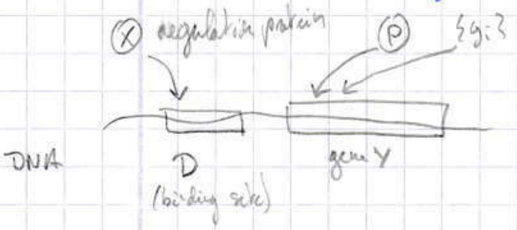
En injectant (4) dans (3), nous pouvons conclure.

$$v = \frac{dP}{dt} = \underbrace{k_{i_1} E_T}_{:= V_1} \left(\frac{S}{\cancel{K}_{i_1} + S}\right) + \dots + \underbrace{k_{i_m} E_T}_{:= V_m} \left(\frac{S}{K_{i_m} + S}\right)$$

"notion de vitesse maximale"

$$\boxed{v = V_1 \left(\frac{S}{K_{i_1} + S}\right) + \dots + V_m \left(\frac{S}{K_{i_m} + S}\right)}$$

Transcriptional activity



X : regulation protein

D_0 : unbinded binding site

D_1 : binded binding site

P : RNA polymerase

$\{g_i\}$: set of single nucleotides

Y : Y mRNA or Y protein (assumed the same)

Model 1

- We will alwas have that : $\boxed{D_T := D_0 + D_1}$ ① constant
- We will suppose that QSSA : $\boxed{\frac{dD_0}{dt} = \frac{dD_1}{dt} = 0}$ ② $\frac{dY}{dt} = k_t P Q \cdot D_1$

↳ we have to find D_1 with ①.②

1) Simple activation

- X active Y production

$$\xrightarrow{k_s} X \xrightarrow{k_d}$$
$$X + D_0 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} D_1$$
$$D_1 + P + \{g_i\} \xrightarrow{k_t} D_1 + P + Y$$

$$\Rightarrow \boxed{\frac{dY}{dt} = \underbrace{k_t P Q D_T}_{V_s \text{ const}} \frac{X}{K_1 + X} \quad K_1 = \frac{k_{-1}}{k_1}}$$

$\boxed{K_1 = \frac{k_{-1}}{k_1}}$ $\boxed{V_s = k_t P Q D_T}$

2) Auto-regulation

- X regulate itself
- D_0 and D_1 can product X

$$X \xrightarrow{k_d}$$
$$X + D_0 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} D_1$$
$$D_0 + P + \{g_i\} \xrightarrow{k_t} D_0 + P + X$$
$$D_1 + P + \{g_i\} \xrightarrow{\alpha k_t} D_1 + P + X$$

$$\boxed{\frac{dX}{dt} = V_s \left(\frac{K_1 + \alpha X}{K_1 + X} \right) - k_d X}$$

$\alpha = 1$ constant synthetisation

$\alpha > 1$ auto-activation

$\alpha < 1$ auto-inhibition

3) Activation with multiple binding sites (2 sites)

- X have to bind to 2 site to activate.
- α factor of cooperation between the 2 sites
- AND function

$$\xrightarrow{k_s} X \xrightarrow{k_d}$$
$$X + D_0 \underset{k_1}{\overset{k_1}{\rightleftharpoons}} D_1$$
$$X + D_1 \underset{k_{-1}}{\overset{\alpha k_1}{\rightleftharpoons}} D_2$$
$$D_2 + P + \{g_i\} \xrightarrow{k_t} D_2 + P + Y$$

$$\boxed{\frac{dY}{dt} = V_s \frac{\alpha X^2/K_1^2}{1 + 2X/K_1 + \alpha X^2/K_1^2}}$$

3. a) independence $\alpha = 1$

$$\boxed{\frac{dY}{dt} = V_s \left(\frac{X/K_1}{1 + X/K_1} \right)^2}$$

3. b) strong cooperation $\alpha >> 1$

$$\boxed{\frac{dY}{dt} \simeq V_s \frac{\alpha (X/K_1)^2}{1 + \alpha (X/K_1)^2}}$$

3. c) Multiple binding sites + strong cooperation (n sites)

$$\boxed{\frac{dY}{dt} = V_s \frac{\alpha (X/K_1)^n}{1+\alpha(X/K_1)^n} = V_s \frac{X^n}{K^n + X^n}}$$ avec $\boxed{K = \frac{K_1}{\sqrt[n]{\alpha}}}$

4) Activation by dimeric complex

- X have to fusion in order to activate
- We suppose the fusion fast
↳ $\boxed{\frac{dX_2}{dt} = 0}$ (1)

$$\left.\begin{array}{l} \xrightarrow{k_s} X \xrightarrow{k_d} \\ X + X \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X_2 \\ X_2 + D_0 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} D_1 \\ D_1 + P + \{y_i\} \xrightarrow{k_t} D_1 + P + Y \end{array}\right\}$$

$$\boxed{\frac{dY}{dt} = V_s \frac{X^2}{K_1 K_2 + X^2}}$$

5) Simple inhibition

- X inhibits the production of Y

$$\left.\begin{array}{l} \xrightarrow{k_s} X \xrightarrow{k_d} \\ X + D_0 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} D_1 \\ D_0 + P + \{y_i\} \xrightarrow{k_t} D_0 + P + Y \end{array}\right\}$$

$$\boxed{\frac{dY}{dt} = V_s \frac{K_1}{K_1 + X}}$$

6) Inhibition and activation : - X activate, - Y inhibits } D_0, DY, DXY : do not produce Z; DX : produce Z

Remark : $P(X \text{ bound}) = \frac{X}{K_1 + X} = \frac{(X/K_1)}{1+(X/K_1)}$, $P(Y \text{ not bound}) = 1 - \frac{Y}{K_2 + Y} = \frac{1}{1+(Y/K_2)}$

then : $P(X \text{ bound}, Y \text{ not bound}) = \frac{(X/K_1)}{1 + (X/K_1) + (Y/K_2) + (XY/K_1K_2)}$

So : $$\boxed{\frac{dZ}{dt} = V_s \frac{(X/K_1)}{1+(X/K_1)+(Y/K_2)+(XY/K_1K_2)}}$$

$\rightarrow X \rightarrow \qquad \rightarrow Y \rightarrow$

$D_0 + X \rightleftharpoons DX \qquad D_0 + Y \rightleftharpoons DY$

$DX + Y \rightleftharpoons DXY \qquad DY + X \rightleftharpoons DXY$

$DX + P + \{y_i\} \xrightarrow{k_t} DX + P + Z$

Network and motifs.

- We represent biological interactions as (oriented) graph. Ex: Transcriptional regulation.
- We notice that some motifs are overrepresented in biological networks comparing to a random graph! ↳ 

We notice : $\boxed{\text{overrepresented motif} \Leftrightarrow \text{biological function}}$

0) Not regulated molecule (S)

$$\xrightarrow{k_s} X \xrightarrow{k_d}$$

$$\boxed{\begin{aligned} \frac{dX}{dt} &= a - bX \\ X(t) &= \frac{a}{b} - \frac{a}{b} e^{-bt} \end{aligned}}$$

1) Negative auto regulation (NAR)

$$\xrightarrow{k_s} X \xrightarrow{k_d}$$

$$\boxed{\frac{dX}{dt} = a \frac{K^n}{K^n + X^n} - bX}$$

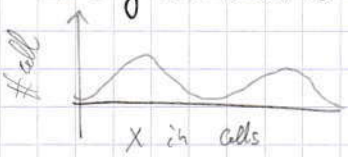
n = number of binding sites, AND function

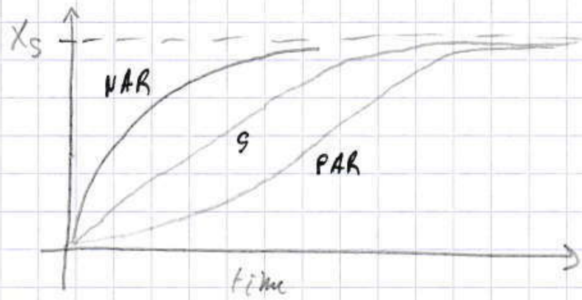
- Speed up the response time
- Reduce the cell-cell variation in proteins

2) Positive autoregulation (PAR) $\xrightarrow{k_s} X \xrightarrow{k_d}$

$$\boxed{\frac{dX}{dt} = a \frac{X^n}{K^n + X^n} - bX}$$

- Slow the response time
- Increase the cell-cell variant in protein
  ↳ is strong can creat a bistability.

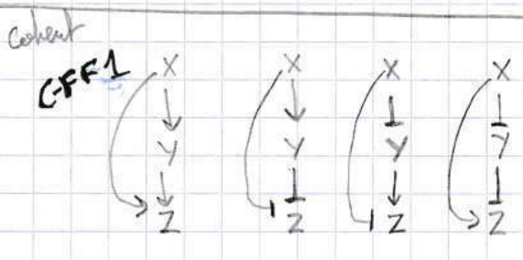


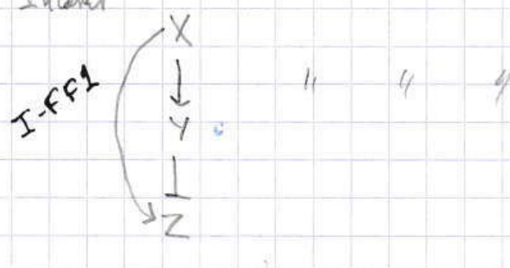


Feedforward loop (FFL)

a) Coherent
↳ the action of 2 factor are coherent

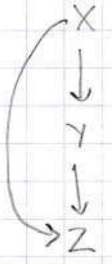
b) Incoherent
↳ action of 2 factor are incoherent





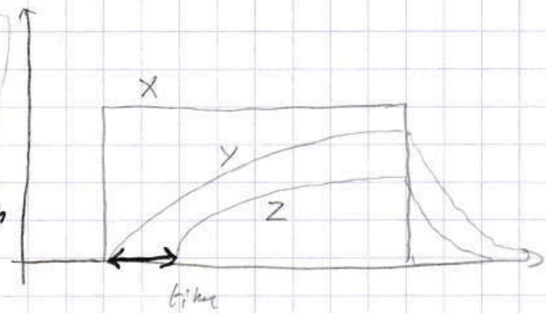
• C-FF1 : Can have function AND : ~~to~~ Z need X and Y activation to be produced

OR : need X or Y activation to be produced



AND :

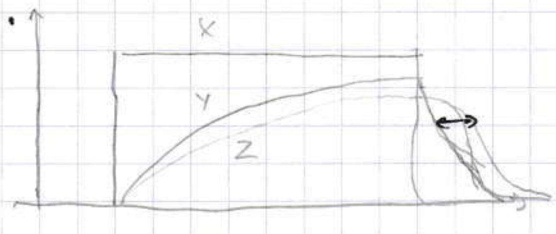
$$\boxed{\frac{dZ}{dt} = a_1\left(\frac{X^n}{K^n+X^n}\right) a_2 \left(\frac{Y^n}{K^n+Y^n}\right) - k_d Z}$$



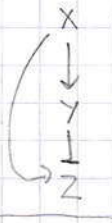
• create a delay in activation

OR

$$\boxed{\frac{dZ}{dt} = a_1\left(\frac{X^n}{K^n+X^n}\right) + b_1 \left(\frac{Y^n}{K^n+Y^n}\right) - k_d Z}$$



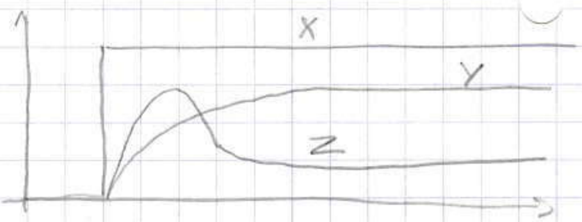
• create a delay in "stop"



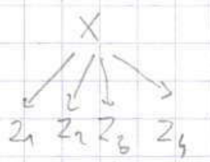
• I-FF1 : • accelerate the response

• create a pulse.

• Fold change detection (?)

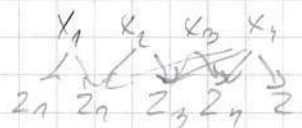


• Multi output



• Can create temporal order of Z_i apparition

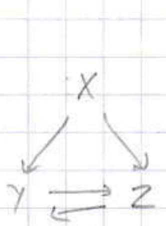
• Dense overlapping regulons



• Multiples out/in puts.

• functions (AND/OR or others) have to be specified.

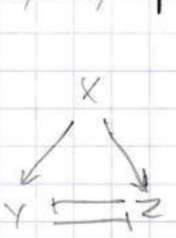
• Double FFL.



positive

S.S : 1) ~~Y~~ OFF
Z OFF

2) ~~Y~~ ON
Z ON



negative

1) Y ON
Z OFF

2) Y OFF
Z ON