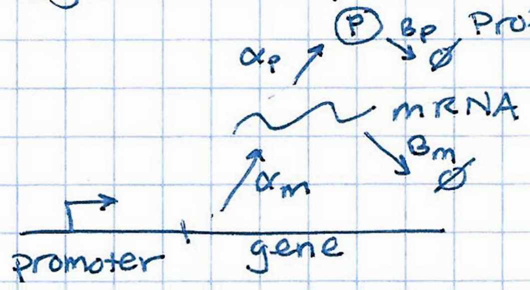
MODELING GENE EXPRESSION WITH DIFFERENTIAL EQNS

CONSTITUTIVE GENE EXPRESSION

(eg. CONSTANT, NO REGULATION)



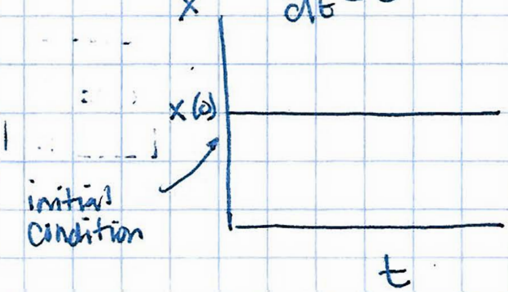
let $m = $ mRNA, $p = $ protein

ORDINARY DIFFERENTIAL EQUATIONS (ODEs)

$\frac{dx}{dt}$ = rate of change of x over time

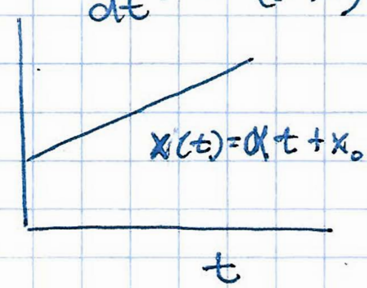
STATIC

$\frac{dx}{dt} = 0$



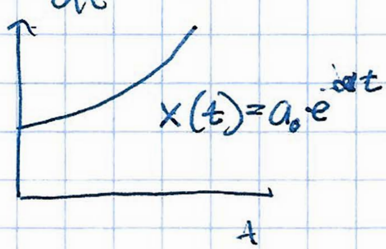
ZEROTH ORDER

$\frac{dx}{dt} = \alpha \quad (\alpha > 0)$



FIRST ORDER

$\frac{dx}{dt} = \alpha x \quad (\alpha > 0)$



X CAN BE A BIOCHEMICAL SPECIES (mRNA, protein).

LAW OF MASS ACTION

$$X + Y \underset{k_2}{\overset{k_1}{\rightleftharpoons}} Z$$

THE RATE OF A REACTION IS PROPORTIONAL TO THE PRODUCT OF THE CONCENTRATION OF THE REACTANTS

$$\frac{dX}{dt} = -k_1 X \cdot Y + k_2 Z$$

$$\frac{dY}{dt} = -k_1 X Y + k_2 Z$$

$$\frac{dZ}{dt} = k_1 X Y - k_2 Z$$

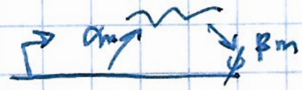
FOR DIMERS,

$$X + X \xrightarrow{k} Y$$

$$\frac{dX}{dt} = -2kX^2 \qquad \frac{dY}{dt} = kX^2$$

IN GENERAL, THE EXPONENT CORRESPONDS TO THE # OF MOLECULES ($n = 2$).

OK SO LET'S APPLY THIS TO mRNA & PROTEIN



mRNA

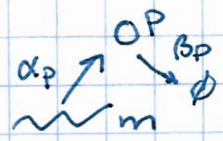
$$\frac{dm}{dt} = \alpha_m - \beta_m m$$

- USE LAW OF MASS ACTION
- ASSUME DNA CONSTANT

α_m: synthesis constant

β_m: degradation constant

protein



$$\frac{dp}{dt} = \alpha_p m - \beta_p p$$

FINAL MODEL

$$\frac{dm}{dt} = \alpha_m - \beta_m m$$

$$\frac{dp}{dt} = \alpha_p m - \beta_p p$$

NOW WE NEED:
- PARAMETER VALUES
- INITIAL CONDITIONS

BUT EVEN BEFORE WE SOLVE $m(t)$, $p(t)$ WE CAN FIND STEADY-STATE RELATIONSHIP

$$\frac{dm}{dt} = 0 = \alpha_m - \beta_m m_{ss} \qquad m_{ss} = \alpha_m / \beta_m$$

$$\frac{dp}{dt} = 0 = \alpha_p m_{ss} - \beta_p p_{ss} \qquad p_{ss} = \frac{\alpha_p m_{ss}}{\beta_p} = \frac{\alpha_p \alpha_m}{\beta_p \beta_m}$$

EVEN WITHOUT SOLVING WE CAN SEE HOW PARAMETERS WILL IMPACT THE STEADY STATE BEHAVIOR OF THE SYSTEM.

CONVERTING ODES TO MATLAB CODE

WE WILL REPRESENT OUR VARIABLES (mRNA (m) AND PROTEIN AS A **STATE** VECTOR, WHERE ALL SPECIES STACKED (ONE COLUMN).

$$x = \begin{bmatrix} m \\ p \end{bmatrix} \qquad \begin{array}{l} x(1) = m \\ x(2) = p \end{array} \Rightarrow \frac{dx}{dt} = \begin{bmatrix} \frac{dm}{dt} \\ \frac{dp}{dt} \end{bmatrix}$$

OK SO NOW WE'RE GOING TO BUILD A FUNCTION TO REPRESENT OUR CONSTITUTIVE SYSTEM IN MATLAB. IF YOU ARE NOT FAMILIAR WITH MATLAB, THERE IS A HANDOUT AND ONLINE TUTORIALS AVAILABLE.

WE NEED ~~1~~ SCRIPT TO SOLVE THE SYSTEM.

PARAMETERS CAN BE DEFINED IN THE FUNCTION OR IN THE SCRIPT AND FED TO THE FUNCTION.

(SEE MATLAB SCRIPTS AND PLOTS)

OUTPUT OF THE MATLAB SCRIPTS WILL BE A MATRIX

OUTPUT = [t, x]

column vector $t = \begin{bmatrix} 1 \\ \vdots \\ t_f \end{bmatrix}$ $\qquad x = \begin{bmatrix} x(1), x(2) \ldots x(n) \\ \\ \\ \end{bmatrix}$ ← @ t = 1 ⋮ @ t_f

SO FOR EACH SPECIES IN X THE COLUMN WILL GIVE THE VALUES AT THE TIME CORRESPONDING TO THE ROW @ THAT TIME.

TO GET THE VALUES CORRESPONDING TO mRNA AT ALL TIME POINTS, WE WRITE

x(:,1)

ALL TIME * (:) — * POSITION 1 WHICH IS ALL mRNA. (1)