

$$\dot{m}_i = r_{x,i} u_i - (\mu + \theta_{m,i}) m_i + \lambda_i, \quad i = 1, 2, \dots, N \quad (\text{mRNA})$$

$$\dot{p}_i = r_{L,i} w_i - (\mu + \theta_{p,i}) p_i \quad (\text{protein})$$

—  $r_{x,i} u_i$ : production rate of mRNA  $i$ ;  $r_{L,i} w_i$ : production rate of protein

—  $\lambda_i$ : leak of gene  $g_i$ ;  $0 \leq u(\dots) \leq 1$ ;  $0 \leq w(\dots) \leq 1$

—  $\mu + \theta_{m,i}$  or  $\mu + \theta_{p,i}$ : dilution and degradation term

Suppose we defined intracellular conc. as nmol (or  $\mu\text{mol}$ ) per unit basis  $B$ , where  $B$  is an abstract volume basis. To derive the material balance governing the specific intracellular conc. of the  $j^{\text{th}}$  species  $x_j$  [ $\text{mol}/B$ ] we start from the general mole balance and the standard four terms (accumulation, in/out and generation):

$$\dot{n}_{x,\text{acc},j} = \dot{n}_{x,\text{in},j} - \dot{n}_{x,\text{out},j} + \dot{n}_{x,\text{gen},j} \quad j = 1, 2, \dots, \mu$$

—  $\mu$ : # of intracellular species;  $x$ : specific single cell from ppl of cell.

No connective transport into or from the cellular phase

$$\dot{n}_{x,\text{in},j} = \dot{n}_{x,\text{out},j} = 0$$

$$\Rightarrow \dot{n}_{x,\text{acc},j} = \dot{n}_{x,\text{gen},j}, \quad j = 1, 2, \dots, \mu.$$

Assuming some abstract volume  $B$ , then:

$$\frac{d}{dt} \int_B x_j dB = \int_B (\dots) dB, \quad j = 1, 2, \dots, \mu.$$

first term is accumulation term, RHS is generation term.

After making the WMA, the integral balance eqn. reduce to a more recognizable form:

$$\frac{d}{dt} (x_j B) = (\dots) B, \quad j = 1, 2, \dots, \mu.$$

Expanding the derivative and simplifying gives:

$$\dot{x}_j = (\dots) - x_j B^{-1} \dot{B}, \quad j = 1, 2, \dots, \mu.$$

—  $B^{-1} \dot{B}$ : intracellular dilution term

In unit system:  $B = X V_R$ ,  $\dot{B} = \dot{X} V_R + X \dot{V}_R$

$B^{-1} \dot{B} = X^{-1} \dot{X} + V_R^{-1} \dot{V}_R$ , in a batch culture,  $V_R$  is constant, so  $\dot{V}_R = 0$

$$B^{-1} \dot{B} = X^{-1} \dot{X}, \quad \text{where } \dot{X} = \mu X, \quad \text{so } B^{-1} \dot{B} = X^{-1} \mu X = \mu = \frac{\dot{X} V_R}{X V_R} + \frac{X \dot{V}_R}{X V_R} = \frac{\dot{X}}{X} + \frac{\dot{V}_R}{V_R} \Rightarrow \boxed{\mu = 0}$$

Since no dilution in cell free:  $\dot{m}_i = r_{x,i} u_i - \theta_{m,i} m_i + \lambda_i$

$$\dot{p}_i = r_{L,i} w_i - \theta_{p,i} p_i$$