Component project #1: **Gene Recognition and Signal Detection**

Bor-Sen Chen, Tsai-Yun Lin and C. S. Tseng  
Department of Electrical Engineering, National Tsing Hua University  
Department of Life Science, National Tsing Hua University

In this period, we pay more attention to the following topics: (a) Regulation Signal detection, (b) modeling of development, (c) construction of genetic expression network, and (d) stability and robustness of traits. They are described by the following subsections.

(a) Regulation Signal Detection:  
In this study, the regulation signal of transcription is detected from gene expression during Dectyostelium development. The gene expressions during development is given as the following

![Figure 1: Experimental expression profile of genes](image)

The dynamic of the *ith* gene is described by the following equation

\[
\frac{dx_i(t)}{dt} = \lambda_i x_i(t) + g_i(t) \tag{1}
\]

where \( \lambda_i \) denotes the characteristic of gene \( x_i(t) \), which is related to half life, and the regulation signal \( g_i(t) \) is expressed by the following function

\[
g_i(t) = \sum_{j=1}^{n} a_{ij} u(t - \tau_j) \tag{2}
\]
where \( u(t) \) is the block signal, \( \lambda_i \) and \( a_j \) needs to be estimated from the expression profiles in Fig. 1.

After \( \lambda_i \) and \( a_j \) are estimated, then the regulation signal \( \hat{g}_i(t) \) of the \( ith \) gene is obtained as

\[
\hat{g}_i(t) = \sum_{j=1}^{\infty} \hat{a}_j u(t - \tau_j)
\]

which is described in Fig. 2. It is seen to match the onset and ceasing of experiment results.

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Fig. 2. The regulation signals during the Dictyostelium development

(b) Modeling of Development in Orchid Flowers

The model for mitosis and endoreduplication is given by

\[
\frac{dN(t)}{dt} = kN(t)(1 - \frac{N(t)}{N_{\text{max}}})
\]

\[
\frac{dN_{2c}(t)}{dt} = 2kN(t)(1 - \frac{N(t)}{N_{\text{max}}}) - r_1(t)N_{2c}(t)
\]

\[
\frac{dN_{4c}(t)}{dt} = -r_2(t)N_{4c}(t) + r_1(t)N_{2c}(t) - kN(t)(1 - \frac{N(t)}{N_{\text{max}}})
\]

\[
\frac{dN_{8c}(t)}{dt} = -r_3(t)N_{8c}(t) + r_2(t)N_{4c}(t)
\]

\[
\frac{dN_{16c}(t)}{dt} = r_3(t)N_{8c}(t)
\]
Where \( N(t) = N_{2c}(t) + N_{4c}(t) + N_{8c}(t) + N_{16c}(t) \) = total number of nuclei and \( r_1(t), r_2(t), r_3(t) \) are the transition rates.

Our modeling problem lies in how to estimate the transition rates \( k(t), r_1(t), r_2(t) \) and \( r_3(t) \) from experimental data, which is shown in Fig. 4. The solution of \( N(t), N_{2c}(t), N_{4c}(t), N_{8c}(t) \) and \( N_{16c}(t) \) are given in Fig. 3.

![Fig. 3. The experimental data and the models](image)

![Fig. 4. The transition rates](image)
(c) Genetic Regulation Network from Microarrays

\[ \frac{dx_i(t)}{dt} = \sum_{j=1}^{N_i} a_{ij} x_j(t) + n_i(t) \quad i = 1,2,...,M \quad t = t_1,...,t_M \]  

(5)

Where \( x_i(t) \) denotes the expression level of the \( ith \) gene, see Fig. 5.

Since \( N>>M \), it is very difficult to estimate the regulation function \( a_{ij}(t) \) from (5). A suboptimal technique is developed to estimate \( a_{ij}(t) \).

\[ \mathcal{F} = a_1 x_1 a_2 x_2 + a_3 x_3 + ... + a_n x_n \]

Fig. 5 Genetic Regulation Network

(d) Identifiability, Stability and Robustness of Pathways or Traits

(i) Consider the following pathway in gene regulation (see Fig. 6)

\[ \frac{dm(t)}{dt} = f(p(t)) - Vm(t) + \nu(t) \]

\[ \frac{dp(t)}{dt} = Lm(t) - Up(t) + n(t) \]  

(6)
The eq. (6) can be linearized as

\[
\frac{dm(t)}{dt} = Cp(t) - Vm(t) + v(t) \\
\frac{dp(t)}{dt} = L m(t) - Up(t) + n(t)
\]

Our problem is how to estimate $C, V, L, U$, and $v(t), n(t)$ from the data $m(t)$ and $p(t)$. After the parameters $C, V, L, U$ have been estimated, we will discuss some biological phenomena based on (7) from the system perspective, for example, stability, robustness.

(ii) Consider the following trait in Fig. 6
Consider the system description of traits in Fig. 6, which can be described by the following dynamic equation

$$\begin{align*}
\frac{dx_1}{dt} &= \begin{bmatrix} a_{11} & a_{12} & a_{13} & a_{14} \\ a_{21} & a_{22} & a_{23} & a_{24} \\ a_{31} & a_{32} & a_{33} & a_{34} \\ a_{41} & a_{42} & a_{43} & a_{44} \end{bmatrix} \begin{bmatrix} x_1(t) \\ x_2(t) \\ x_3(t) \\ x_4(t) \end{bmatrix} + \begin{bmatrix} d_1 \\ d_2 \\ d_3 \\ d_4 \end{bmatrix} \\
y &= \begin{bmatrix} c_1 & c_2 & c_3 & c_4 \end{bmatrix} \begin{bmatrix} x_1(t) \\ x_2(t) \\ x_3(t) \\ x_4(t) \end{bmatrix} + e
\end{align*}$$

Fig. 7 The system description of traits

In this study, we will identify $a_{ij}, d_i(t), c_i, e(t)$ in (7) from the experimental data. After the parameters are identified, we will discuss the properties of traits from the properties of the system, for example, stability, robustness (sensibility).
If the system is perturbed, for example, \( a_y \rightarrow a_y + \Delta a_y \), by some mutations \( \Delta a_y \). How large can the trait system tolerate the perturbations (mutation). From the system theory, we will discuss the tolerance (robustness) of the perturbation. Some interactions \( a_y \) may tolerate large perturbation; some interactions may not. It will be discussed from system point of view. Furthermore, we will discuss the stability of the trait while other genes are augmented to these traits.