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Short Note

On the Non-linear Model of a Fundamental Biological Process: An Extension of the Masuyama Model

Masafumi AKAHIRA*

Abstract

Second order approximation of the fundamental biological process (FBP) is given as a non-linear model of the process. This is an extension of the linear model of the FBP by Masuyama (1989). An application of the non-linear model to practical data is also presented.

1. Introduction

It is useful to consider the FBP in investigating biological phenomena like height growth, eruption of tooth and so on. In the monograph (1989) Masuyama introduced a linear model of the FBP as follows. For each i=1, ..., n, let $X_i = X(t|\theta_i)$ be a FBP for the i-th person with a parameter θ_i representing the characteristic at time t, and $X_0 = X(t|\theta_0)$ that for the reference person. Assume that $\theta_i - \theta_0$ is sufficiently small, since the fundamental system is very conservative. Then

$$X_i = X_0 + D_0(\theta_i - \theta_0) \quad \text{with} \quad D_0 = \partial X/\partial\theta\,|_{\theta_0}$$

holds approximately. Hence

$$X_i = E_0 + D_0\theta_i, \quad E_0 = X_0 - D_0\theta_0\,,$$

and

$$X. = E_0 + D_0\theta.\,,$$

where the mean with respect to i is denoted by a dot in place of i. If $\theta. \neq 0$, then, eliminating D_0, we have

$$X_i = a_i + b_i X. \quad \text{with } b_i = \theta_i/\theta. \text{ and } a_i = E_0(1 - b_i). \tag{1.1}$$

If E_0 is positive and independent of t, then the correlation coefficient between a_i and b_i is exactly equal to -1. For the existence of independent solution for X, it is necessary and sufficient that $[X(t|\theta) - \{\partial X(t|\theta)/\partial\theta\}\theta]/\theta^2$ is Lebesgue integrable in the neighborhood of θ_0 and X is of the following form

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* Institute of Mathematics, University of Tsukuba, Tsukuba, Ibaraki 305, Japan

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$$X = \theta P(t) + q(\theta), \tag{1.2}$$

where p (•) is independent of θ and q (•) is independent of t. The quite good fitness of the linear model (1.1) is confirmed in the monograph (1989) by Masuyama using many examples on biological data, e.g. those on the height growth and the eruption of tooth of normal persons, etc.

In the paper (1979) of Masuyama, it is mentioned that the height of a girl with chromosomal aberration shows a slightly convex curve on the graph (see also Masuyama, 1980, page 140). This seems to suggest a possibility on an extension of the linear model. In this paper we shall extend the above model to a non-linear model, more precisely, second order approximation of the FBP. An application of the model to the practical data is presented.

2. Second order approximation of the FBP

For each i=1, ..., n, let θ_i be a parameter representing the characteristic of the i-th person of the FBP $X = X(t|\theta)$, where t and θ belong to a time domain T and an open set of R^1, respectively. Assume that $X(t|\theta)$ satisfies such smoothness condition as twice differentiability on θ for each $t \in T$. We also assume that, for each i=1, ..., n, the parameter θ_i is very close to the parameter θ_0 of the FBP $X_0(t) = X(t|\theta_0)$ of the reference person, that is, for sufficiently small $|\Delta_\theta|$ independent of i, $\theta_i - \theta_0 = O(|\Delta_\theta|)$ (i= 1, ..., n). By the Taylor expansion, we have for each i = 1, ..., .n,

$$\begin{aligned} X_i(t) = X(t|\theta_i) &= X(t|\theta_0) + \{\partial X(t|\theta_0)/\partial\theta\}(\theta_i - \theta_0) + (1/2)\{\partial^2 X(t|\theta_0)/\partial\theta^2\} \\ &\quad \cdot (\theta_i - \theta_0)^2 + o(\Delta_\theta^2) \\ &= X(t|\theta_0) + D_0(t)(\theta_i - \theta_0) + (1/2) D_1(t)(\theta_i - \theta_0)^2 + o(\Delta_\theta^2) \quad \text{(say)}, \end{aligned}$$

hence, for each i = 1, ..., n,

$$\begin{aligned} X_i(t) &= X_0(t) + D_0(t)(\theta_i - \theta_0) + (1/2) D_1(t)(\theta_i - \theta_0)^2 + o(\Delta_\theta^2) \\ &= C_0(t) + C_1(t)\theta_i + (1/2) D_1(t)\theta_i^2 + o(\Delta_\theta^2), \end{aligned} \tag{2.1}$$

where $C_0(t) = X_0(t) - D_0(t)\theta_0 + (1/2)D_1(t)\theta_0^2$ and $C_1(t) = D_0(t) - D_1(t)\theta_0$.

Denoting the mean with respect to i by a dot in place of i, we obtain

$$X_\cdot(t) = (1/n)\sum_{i=1}^{n} X_i(t) = C_0(t) + C_1(t)\theta_\cdot + (1/2)D_1(t)(s_\theta^2 + \theta_\cdot^2) + o(\Delta_\theta^2), \tag{2.2}$$

where $\theta_\cdot = (1/n)\sum_{i=1}^{n}\theta_i$ and $s_\theta^2 = (1/n)\sum_{i=1}^{n}(\theta_i - \theta_\cdot)^2 = (1/n)\sum_{i=1}^{n}\theta_i^2 - \theta_\cdot^2$.

Since $s_\theta^2 = O(\Delta_\theta^2)$, it follows from (2.2) that

$$X_\cdot(t) = C_0(t) + C_1(t)\theta_\cdot + (1/2)D_1(t)\theta_\cdot^2 + O(\Delta_\theta^2). \tag{2.3}$$

Since, from (2.3),

$$C_1(t)\theta_{\cdot} = X_{\cdot}(t) - C_0(t) - (1/2)D_1(t)\theta_{\cdot}^2 + O(\Delta_\theta^2).$$

assuming that $\theta_{\cdot} \neq 0$ and putting $b_i = \theta_i/\theta_{\cdot} (i=1, \ldots, n)$, we have from (2.1)

$$\begin{aligned} X_i(t) &= C_0(t)(1 - b_i) - (b_i/2)D_1(t)\theta_{\cdot}^2 \\ &\quad + (b_i^2/2)\{D_1(t)/C_1^2(t)\}\{C_0(t) + (1/2)D_1(t)\theta_{\cdot}^2\}^2 \\ &\quad + b_i[1 - b_i\{D_1(t)/C_1^2(t)\}\{C_0(t) + (1/2)D_1(t)\theta_{\cdot}^2\}]X_{\cdot} \\ &\quad + (b_i^2/2)\{D_1(t)/C_1^2(t)\}X_{\cdot}^2(t) + O(\Delta_\theta^2) \\ &= \alpha_i(t) + \beta_i(t)X_{\cdot}(t) + \gamma_i(t)X_{\cdot}^2(t) + O(\Delta_\theta^2) \quad \text{(say)} \quad (i = 1, \ldots, n) \end{aligned} \tag{2.4}$$

Then it is easily seen that (2.4) is a non-linear model as an extension of the linear model (1.1). From the above we may also consider a second order approximation of the FBP $X(t|\theta)$ as a non-linear model as follows:

$$\begin{cases} X(t|\theta) = \hat{X}(t|\theta) + O(\Delta^2), \\ \hat{X}(t|\theta) = C_0(t) + C_1(t)\theta + (1/2)D_1(t)\theta^2, \end{cases} \tag{2.5}$$

where $\Delta = |\theta - \theta_0|$ (see Fig. 1). Here we assume that the term $O(\Delta^2)$ is independent of t.

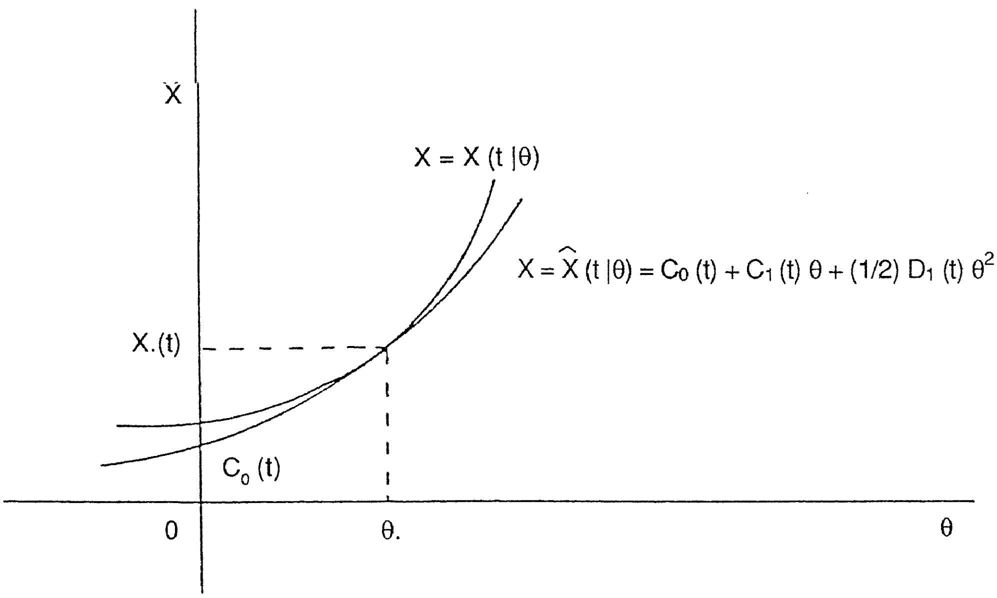

Fig. 1: Second order approximation of the FBP $X(t|\theta)$

Then a type of the non-linear model (2.4) can be derived from (2.5) through (2.1) and (2.3).

Next we consider the relationship to (1.2). From (2.5) we have

$$\partial X(t \mid \theta)/\partial\theta = C_1(t) + D_1(t)\,\theta + O(\Delta), \tag{2.6}$$

$$\partial^2 X(t \mid \theta)/\partial\theta^2 = D_1(t) + O(1). \tag{2.7}$$

Substituting (2.7) into (2.6) we obtain

$$C_1(t) = \partial X(t \mid \theta)/\partial\theta - \left\{\partial^2 X(t \mid \theta)/\partial\theta^2\right\}\theta + K\theta + O(\Delta), \tag{2.8}$$

where K is a constant. From (2.5), (2.7), (2.8) we have

$$\begin{aligned} X(t|\theta) &= C_0(t) + [\{\partial X(t|\theta)/\partial\theta\} - \{\partial^2 X(t|\theta)/\partial\theta^2\}\,\theta + K\theta]\theta \\ &\quad + (1/2)\,[\{\partial^2 X(t|\theta)/\partial\theta^2\} - K]\theta^2 + O(\Delta), \\ &= C_0(t) + \{\partial X(t|\theta)/\partial\theta\}\,\theta - (1/2)\,[\{\partial^2 X(t|\theta)/\partial\theta^2\} - K]\,\theta^2 + O(\Delta). \end{aligned} \tag{2.9}$$

If

$$X(t \mid \theta) - \{\partial X(t \mid \theta)/\partial\theta\}\,\theta + (1/2)\,[\{\partial^2 X(t \mid \theta)/\partial\theta^2\} - K]\,\theta^2 \tag{2.10}$$

is a function $q_0(\theta)$ of only θ, then $X(t|\theta)$ can be expressed as the form

$$X(t \mid \theta) = P_1(t)\,\theta + P_2(t)\,\theta^2 + Q(\theta), \tag{2.11}$$

where $P_1(t)$ and $P_2(t)$ are independent of θ and $Q(\theta)$ is independent of t, provided that $1/\theta$, $q_0(\theta)/\theta^2$ and $q_0(\theta)/\theta^3$ are Lebesgue integrable in the neighborhood of θ_0. Conversely, if $X(t|\theta)$ is of the form (2.11), then (2.10) is function of only θ. Hence, in order that $C_0(t) + O(\Delta)$ is independent of t, it is necessary and sufficient that $1/\theta$, $q_0(\theta)/\theta^2$ and $q_0(\theta)/\theta^3$ are Lebesgue integrable in the neighborhood of θ_0 and $X(t|\theta)$ is of the form (2.11). This shows that (2.11) is an extension of (1.2).

3. An application of the non-linear model to practical data

It is known from the monograph (1989) of Masuyama that the data on the heights of normal persons is well fitted to the linear model given in the introduction. An application of the non-linear model (2.4) to data on the height of a girl with chromosomal aberration is given by Masuyama (1990), and, in this section, the application is presented. From a graph of the height given in Masuyama (1980, page 140; 1989, page 6) the data is obtained as follows:

age t (years)	0	6	7	8	9	10	11
h_i (t) (cm)	0.0	103	108	112	117	121	124
h. (t) (cm)	0.000	114.7	120.4	126.0	131.7	138.1	145.0

Here $h_i(t)$ and $h.(t)$ denote a height of the girl and the mean height at the age t as of April 1, 1979, the sample size being of the order of 10^4 for each age class given by the Ministry of Education of Japan. It is noted that $h_i(t)$ and $h.(t)$ are taken as $X_i(t) = X(t|\theta_i)$ and $X.(t)$ in section 2, respectively. Here θ_i may be interpreted as a parameter on the chromosome of the girl. Then it follows by a regression method that the second order approximation $\hat{h}_i(t)$ of $h_i(t)$ is given by

$$\hat{h}_i(t) = -0.02065 + 1.0658h.(t) - 0.001405h_{.}^{2}(t),$$

which is regarded as a correspondence to the right-hand side of (2.4) without the remainder term. Then the correlation coefficient of h_i (t) and $\hat{h}_i(t)$ is approximately equal to 0.9999. Hence the data seems to be well fitted to the non-linear model. Indeed, it is remarked by Masuyama (1979, 1980) that, in this example, the data is not fitted to the linear model.

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