PROPER AGE AND AGE AT MENARCHE (ADDENDA)

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SUMMARY

A mathematical model of the almost-one parameter (ALONPA) hypothesis [5, 13] was proposed in the previous paper [15] in Japanese. This is its English version with some additional results.

The fundamental biological process, such as the height growth, or the eruption of deciduous tooth, is characterized by the fact that the individual variability of its systemic parameter is very small, so that the process can be linearized. Then there exists a fixed point on this linearized curve (or linearized sequence of points), which suggests that this aimed-at value would be memorized by gene(s) in hypophyseal cells. The catch-up phenomena support this surmise.

0. Introduction

The idea was suggested by the following facts found during the study of the biochemical individual variability [3].

Let C_i be the concentration of a blood constituent for the i -th person. Then the among-person variability is represented by the standard deviation (SD) of $X_i = \log C_i$, say SD_x , but not by the SD of C_i itself, say SD_c , since SD_x , but not SD_c , is in general independent of the race, the sex, the age etc. [1, 5, 9].

Furthermore, the first and the second quasi-constancy hold for SD_x , but not for SD_c , and a multiplicative model with respect to two factors, i.e. the species and the substance in blood, holds for SD_x , but not for SD_c [2, 5, 9], so that the human SD_x of a substance is estimable by animal SD_x 's as a "missing value".

SD_x is smaller for fundamental substances in life, e.g. Na, Cl, Ca, total protein, and glucose in blood [3] and enzymes in cell in particular [6]. This means that the creation of the life was an extremely rare chance phenomenon and the life continues, if and only if this favorable fundamental system is maintained and the personal deviation of its systemic parameter from its standard is sufficiently small. In other words, the inter-person homeostatis holds with respect to these fundamental substances for the life. The well-known (intra-person) homeostatis is a necessary, but not sufficient, condition for this inter-person one.

1. Mathematical Model

Let $X(T|w_i) = X_i$ be a fundamental biological process with a positive parameter w_i for the i -th person. The 0-th person may be called a reference person and assume that the difference $(w_i - w_0)$ is sufficiently small, so that the following approximation holds among the means of X_i , say m_i :

$$(1.1) \quad m_i = m_0 + D_0(w_i - w_0) = E_0 + D_0 w_i, \quad D_0 = \partial m / \partial w|_0, \quad E_0 = m_0 - D_0 w_0.$$

Taking the sample mean with respect to i , we get

$$(1.2) \quad m. = E_0 + D_0 w. .$$

Eliminating D_0 , we have

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$$(1.3) \quad m_i = a_i + b_i m. , \quad b_i = w_i / w. , \quad \text{and} \quad a_i = E_o (1 - b_i).$$

Hence $a. = 0$ and $b. = 1$. b_i may be called rate constant of growth.

The mean in the c -th group is given by

$$(1.4) \quad m_c = a_c + b_c m. .$$

Then the mean in the d -th group ($d \neq c$) is given by

$$(1.5) \quad m_d = A_d + B_d m_c , \quad B_d = b_d / b_c \quad \text{and} \quad A_d = a_d (1 - B_d),$$

which is useful in practice to reduce error to meet our model (see [11]).

When $m.$ is fixed, the population variance of m_i is given by

$$(1.6) \quad V_m = (s_a - s_b m.)^2 = V_b (m. - E_o)^2, \quad V_b = s_b^2,$$

where s_a and s_b denote the SD's of a_i and b_i respectively (see Fig. 5₂ in [15]).

In general, E_o is dependent on t_i . If E is independent of t and E/w_o is integrable with respect to w in the neighborhood of w_o , then m_i takes the following form;

$$(1.7) \quad m_i(t) = w_i Y(t) + Z(w_i),$$

where $Y(t)$ is independent of w_i and $Z(w_i)$ is independent of t respectively.

By (1.3) we get

$$(1.8) \quad m_i = E_o + b_i (m. - E_o),$$

which means that the point (E_o, E_o) is a fixed point on the line (1.3).

Let $t = t_f$ at this fixed point. Then we have

$$(1.9) \quad m_i = E_o + w_i [Y(t) - Y(t_f)].$$

This formula suggests that there must exist a gene or genes which memorize the aimed-at value $Y(t_f)$.

We may assume without loss of generality that the population mean of w_i is equal to one, then we have

$$(1.10) \quad m_i = E_o + w_i (m - E_o) \\ = E_o (1 - w_i) + w_i m ,$$

and

$$(1.11) \quad V_m = V_w (m - E_o)^2 = V_w D_o^2, \quad \text{or} \quad SD_m = |D_o| SD_w .$$

We have assumed the continuity of m with respect to w , but m may be discrete with respect to t . In fact, in case of the age at eruption of the α -th deciduous tooth D_α , (1.3) holds for $\alpha = 1 \sim 40$ [12, 14], where $X = \log t_\alpha$.

2. Height Growth in the Second Phase

We have assumed empirically the following formula

$$(2.1) \quad h_i(t) = a_i + b_i h.(t),$$

where $h_i(t)$ denotes the height of the i -th person at his (or her) chronological age t in the second phase, which is the common part of individual adolescence periods [8, 9] (see e.g. Fig. 1, 2, 3, 4, 6 and 7 in [15]). In other words, we neglect minor errors, such as errors in measurement, rounding error in age and seasonal variation, and we set $m_i = h_i$. Then, higher correlation coefficients (CC), namely $-0.99 \sim -0.99999$, between a_i and b_i were obtained. Thus we have said "almost-one parameter (ALONPA)". This is justified by the third relation in (1.3) [9, 10] (see e.g. Fig. 8 in [15]). Higher CC's are shown, when (1.5) is applied to the group mean height. It would be needless to notice that the variance of a mean is not greater than that of a single observation.

The proper age $s_i = b_i t$ was introduced in the previous paper to derive the following relation

$$(2.2) \quad dh_i/ds_i = dh./dt ,$$

which says that the velocity is independent of the individuality, if the

individualized age, i.e. the proper age, is used instead of the chronological age t . The mechanism of growth is identical with that of the reference person except a slight difference in its systemic parameter.

The second fundamental relation, E_0 being a positive constant,

$$(2.3) \quad s_h(t) = \pm[s_a - s_b m(t)] = \pm s_b [E_0 - m(t)],$$

where $m(t)$, s_h , s_a and s_b denote the mean of $h_i(t)$ and SD's of $h_i(t)$, a_i and b_i in the population^a respectively, holds, where a_i and b_i are redefined using m instead of m_i in (1.3). [7, 9].

3. Multivariate Case

Identifying $X(t|w_i)$ with the j -th component of a k -dimensional (column) vector $X(t|w_i)$, for $j = 1, 2, \dots, k$, we can have the following relations:

$$(3.1) \quad m_i = E_0 + D_0 w_{0i}, \quad D_0 = \partial m / \partial w|_0, \quad E_0 = m_0 - D_0 w_0,$$

$$(3.2) \quad m_i = E_0 + D_0 w_i, \quad \text{and}$$

$$(3.3) \quad m_i = (1 - b_i)E_0 + b_i m_i, \quad b_i = w_i / w_i, \\ = E_0 + b_i(m_i - E_0).$$

If E_0 is independent of t and E/w^2 is integrable with respect to w in the neighborhood of w_0 , we have

$$(3.4) \quad m_i(t) = w_i Y(t) + Z(t),$$

where $Y(t)$ is independent of w_i and $Z(w_i)$ is independent of t .

The formula (2.3) corresponds to the following variance-covariance matrix in the population; V_w being the population variance of w_i , we get

$$(3.5) \quad V_m(t) = V_w(m - E_0)(m - E_0)' = V_w D_0 D_0',$$

where we assume as before that the population mean of w_i is equal to 1.

4. Age at Menarche

At the end of the previous paper, we gave an empirical formula between the age at menarche t_{mi} and the rate constant b_i in the second phase, viz.

$$(4.1) \quad E[t_{mi}] = 12.792 b_i^{0.1342} \quad (\text{see Fig. 10 in [15]}),$$

where the CC between $\log b_i$ and $\log t_{mi}$ is 0.92 for 0.990-normal white girls of sample size $n = 28$ [15, 16] (these selected girls are denoted by new moons in Fig. 10 in [15]). Here we say Q-normal, when the individual CC between $h_i(t)$ and $h_i(t)$ is at least equal to Q .

We note that b_i in the second phase can be estimated utilizing E , whose value is fairly stable with respect to the generation [10]. However, it is under-(or over-)estimated for the late (or early) maturing girl. Hence we propose another empirical formula from a different viewpoint.

Let t_v be the age at her maximal velocity of growth. (Don't mistake this natural maximum for the exceptional one due to the catch-up.) Then,

(i) t_v and t_v are positively correlated,

(ii) t_v^m and the increment $\Delta h(t_v)$ are negatively correlated, and

(iii) t_v^m and $|\Delta^2 h(t_v)|$ are negatively correlated,

so that we may assume the following empirical formula;

$$(4.2) \quad E[t_{mi}] = A_{0i} + A_{1i} t_{vi} + A_{2i} h_i(t_{vi}) + A_{3i} h_i(t_{vi} + d) + A_{4i} h_i(t_{vi} + 2d) \\ + A_{5i} h_i(t_{vi} + 3d).$$

where $d = 1/2^{yr}$. The CC between the estimated and the observed t_v is 0.92 for 0.990-normal white girls of sample size $n = 50$ (see Fig. 1). We note that so far as we have surveyed,

(iv) $t_v < t_v^m$ holds for 70 white girls [13], and

(v) $t_v < t_v^m < t_v + d$ holds for ca. 30% of 0.990-normal girls.

Two cases^m denoted by full moons in Fig. 1 seem to be exceptional, but its reason is not clear, since their clinical histories were not available. We note

Fig. 1

that the Q-normality does not necessarily guarantee the physiological normality of growth, even if $Q = 0.990$ (see Fig. 3 and Fig. 4 in [15]). The existence of the catch-up in these figures supports our surmise that the aimed-at value is memorized somewhere-- most probably in hypophysis-- in body. Other examples of the catch-up are seen in Fig. A1 (male Tibia) in [8] and in Fig. 1b in [12].

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