Jour. Ind. Soc. Ag. Statistics
51(2&3), 1998 : 173-186

Intra-Individual Variation—A Manifestation of Homeostasis

Shobha Rao
Agharkar Research Institute, Pune

SUMMARY

Intra-individual variation contributes significantly to the total variation in intake as observed in an experiment conducted on school children. It is shown that malnourished children not only have lower attained weights or heights as compared to their normal counterparts but also have lower variability in increments. Man can maintain body weight and carry out assigned tasks on a wide range of intakes due to existence of a substantial intra-individual variation in daily intake. It is suggested that estimation of undernutrition or poverty should use a cut-off point and not the average requirement. The paper discusses the metabolic experiment undertaken for studying the nature of within variation. The statistical analysis of long term metabolic data from animal and human experiment showed that magnitude of auto correlation reflects the power with which regulation at any given level of intake is controlled. The value decreases as intake falls below normal levels.

Keywords: Protein gap, Intra-individual variation, Serial correlation, Autoregresive model, Homeostasis, Auto correlation.

1. Introduction

Human variations encountered in the field of nutrition research are amazing. Almost each measured variable exhibits a wide range of variation which calls for proper understanding. For example, whether it is energy intake or body measurements such as weight, height or work capacity or even clinical manifestation of a disease, the range of variation observed among individuals of same age or sex groups is simply astonishing.

Between individual variations are perhaps trivial and don't require an elaborate proof. Indeed, variations within the same individual over time are biologically important, but are often ignored in nutrition research. While between individual variations can be attributed to exogenous factors, the within individual variations often highlight intrinsic factors associated with the interaction of a individual with environmental stimuli. Within individual variation i.e. intra-individual variation is, therefore, a reflection of biological individuality. Dismissing it as arising from errors of measurement, without understanding the underlying mechanism that gives rise to the observed variation, is to deny the role of Biometry. Prof. Sukhatme's efforts in last two decades at Agharkar Research Institute, Pune has made pioneering contributions in establishing the importance of intra-individual variability in explaining homeostatic phenomena, which is fundamental in biology. This write-up provides me an opportunity to bring out some of his important contributions and their far reaching implications which are useful not only for advancing science of Nutrition but for betterment of mankind.

2. *Protein-Gap — A Myth Exploded*

In the 1960's one of the most widely discussed nutritional problems was that of the so-called 'protein-gap'. The significant differences observed between the protein intake of people from developing countries and those from developed countries, together with the evidence of associated clinical malnutrition in the former, led nutritionists to conclude that the major nutritional problem facing the world in general, and the developing countries in particular was the shortage of protein.

It was, however, Prof. Sukhatme [9], who first pointed out that, this was in clear contradiction with the fact that the protein supplies per person per day even in India were more than adequate to meet the average requirement of a person as determined by FAO standards. Being the Director of Statistics Division at FAO, Prof. Sukhatme was, on one hand in a fortunate situation to have the access to the data from various developing countries. On the other hand, the situation was unfortunate, in the sense that being amidst of Westerners his thoughts and interpretations of data were almost on the opposite side. It was not an easy job, but his persistent efforts on all fronts including the collection and analysis of new data from NSS and diet surveys, he was able to show that almost all protein deficient diets were also energy deficient. There was almost no diet which was deficient in protein but adequate in energy. This important break-through proved that inadequate energy intake was a major factor and that protein deficiency was an associated result. His work showed that the inter-relationship between protein and energy must receive due consideration in assessing protein malnutrition. This major finding was subsequently supported by data from many developing countries and thus myth of protein-gap was exploded. It was, however, not a pleasant situation to many Westerners as it would be hampered the proposed dumping of milk powder packets to many developing countries.

3. Safe Level of Protein Intake

The implications of this major finding were directly reflected in the new definition of protein requirement adopted in FAO/WHO report [3]. The discontent among nutritionists resulted in drastically increasing the protein requirements in FAO/WHO Report on Energy & Protein Research. The report shows a fundamental difference in the approaches to and meaning of energy and protein requirements. Unlike energy, protein needs are defined at an individual level and as such are set well above the average level. The estimates of safe protein intake levels are thus set at the upper range of individual requirements, i.e. m+2s were m is the average requirement and s is the standard deviation for inter-individual variation in requirement. It was further assumed that individuals eating below the safe level, while not necessarily malnourished, run the risk of developing protein deficiency and that the risk increases as the intake falls below safe level. Clearly, the implication is that requirements are fixed for each individual and variation in requirement over time within the same individual i.e. intra-individual variation is considered negligible.

4. Evidence of Intra-individual Variation

Assuming intra-individual variation to be negligible is denying the biological individuality of a man. It was, therefore, of crucial importance to prove the existence of intra-individual variation and characterise its nature for understanding the biological individuality. The systematic research on animals and humans was planned to study these issues and following are some examples offering the evidence for existence of intra-individual variation.

We report data from diet surveys conducted on school children. Diet survey was carried out (Rao [7]) for a week once in every 3 months on school children aged 13-18 yrs. staying in hostel. Intake was assessed by 'weigh as you eat' method. The hierarchical model of analysis of variance was used to obtain estimates of variance between subjects, variance between periods (weeks) within subjects and variance between days within subjects (Table 1).

Since the four diet surveys covered a period of one year, changes in body weight were taken into consideration by doing ANOVA for intakes expressed per kg body weight and is given in the same table.

It can be observed that although the standard deviation (σ_w) obtained from ANOVA of weekly mean (i.e. 179) is lower than that obtained from ANOVA of daily intakes (339), it is much larger than would be expected on the assumption of randomness of daily intakes (i.e. 128). Secondly, mean square between weeks is also significant and persists even after intake is expressed

Table 1. Analysis of variance for daily and weekly mean intake (Pooled for all rounds)

Source	d.f.	Daily intake (Kcal)		Weekly mean intake (Kcal)		Weekly mean intake (Kcal) per kg body weight	
		M.S.	Est. of var.	M.S.	Est. of var.	M.S.	Est. of var.
Between subjects	42	1718132	53102 (32*)	251343	54822(63)	185.9	40.8(65)
Between weeks within subjects	129	231259	19391 (12)	32054	32054(37)	22.6	22.6 (35)
Between days within weeks within subjects	1032	95518	95518 (56)	–	–	–	–
σ_w	–	–	339	–	179	–	475
Mean	–	–	2018	–	2018	–	55.13
C.V.%	–	–	17	–	9	–	8.6

* Figures in parentheses represent percentage of total variation

as per kg body weight. Thus adjustments of changes in body weight only marginally affect the within variability suggesting that within the wide range of intra-individual variation, intakes are poorly correlated with weights. Intra-individual variation thus, contributes significantly (12%) to the total variation in intake.

In order to study nature of variation for the short term period, data on dietary intakes was collected for 49 consecutive days on a subsample of five students who volunteered themselves (Rao [6]). All the 7 weeks belonged to the same season. The daily intakes were observed to vary with coefficient of variation of the order of 15-20% (Fig. 1). The ANOVA for daily as well as weekly mean intake given in Table 2 shows that mean square between weeks is significantly greater than the mean square between days. It can be observed that variability in weekly mean intake/kg is 8% and is of the same order as that observed from long term data (Table 1). Thus, it was observed from long term as well as short term data that far from being random, intra-individual variation contributes significantly to total variation in intake. Further, variation in weekly mean intakes appeared to be a stable component of intra-individual variation.

Measurements of intake are different in character from those of weight or height. If weight or height of an individual is measured on two or more successive days, the coefficient of variation would be only of the order of 2% or even less, and in this case a major part of the variation would be due to measurement errors. But in case of dietary intake, besides the measurement error; social, cultural and economical factors are responsible for variation in intake. Hence a part of the observed variation in daily intake of an individual will arise as a result of his response to these environmental stimuli. Although, such a response would vary from day to day (and hence daily intake) as time advances, the stability of variation in weekly mean intakes, suggests that the process underlying the observed daily variation is of stationary type.

5. Within Variability in Growth

What is true of intake, appears to be true for growth velocities. The analysis of serial measurements is even more crucial in growth studies. Growth is essentially a time related process, and within variability in growth is of vital interest, although often ignored in nutrition research. It is commonly seen that studies attempting evaluation of feeding programmes often use only initial and final measurements without utilising the important intermitant observations even when available. Within variations in growth too, are important for understanding

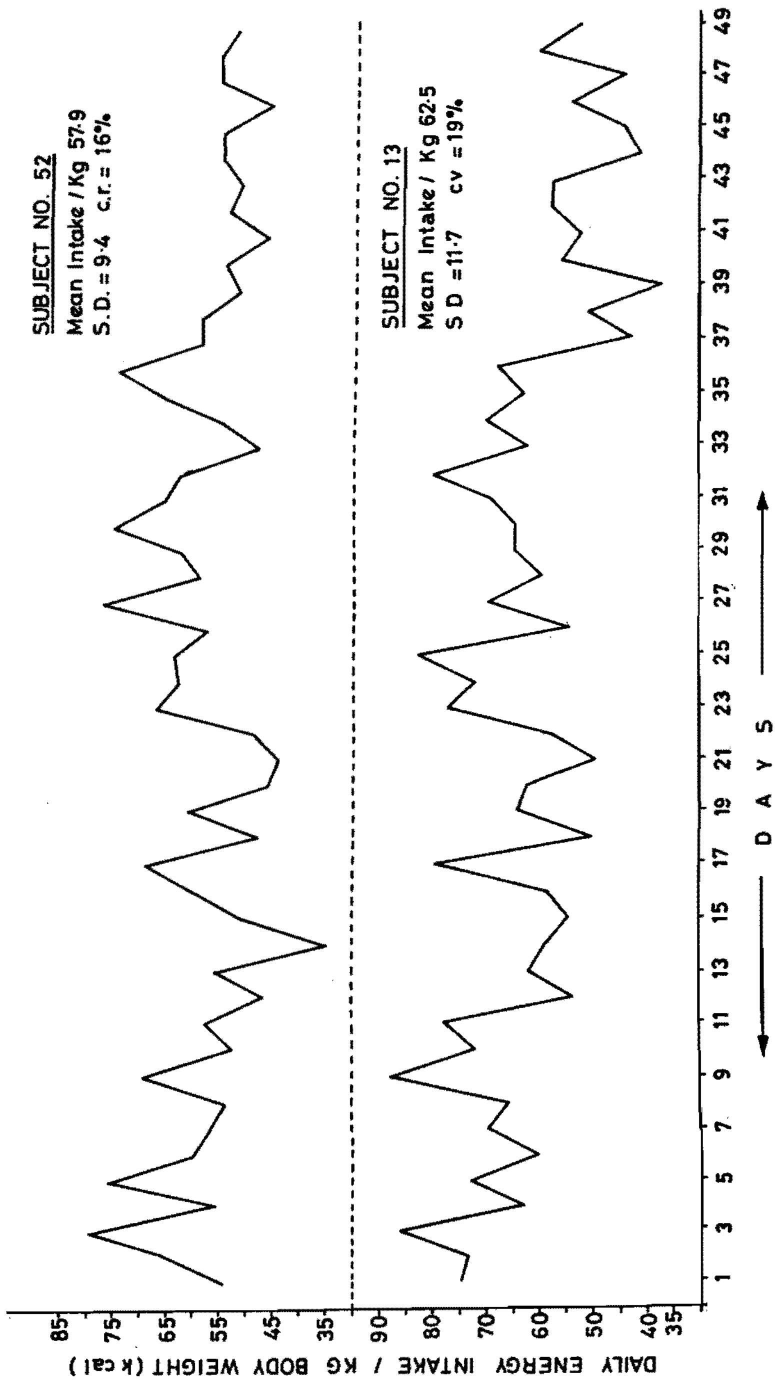

Fig. 1 : Daily energy intake/kg body weight of two subjects

Table 2. Analysis of variance for daily and weekly mean intakes/kg body weight of 5 students observed over 49 d

Source	d.f.	Daily intake/kg body weight		Weekly mean intake/kg body weight	
		Mean square	Estimate of variance	Mean square	Estimate of variance
Between subjects	4	248.39	1.6(2)	35.48	1.62(6)
Between weeks within subjects	30	168.69	12.36(13)	24.11	24.11(94)
Between days within weeks within subjects	210	82.13	82.13(85)	–	–
Standard devision (σ_w)	–	–	9.72	–	4.9
Mean intake (kcal/kg/d)	–	–	59.2	–	59.2
C.V.%	–	–	16	–	8.3

* Figures in brackets represent percentage with total variance

growth process and has far reaching implications for assessment of malnutrition as well as for evaluating feeding programmes.

We refer to a data on rural pre-school children (n=277) who were measured for weight and height every 3 months over the period of two years (Nayak [5], Joshi [4]). The ANOVA for increments shows (Table 3) that within individual variation for weight increment are much higher compared to between individual variation in case of normal as well as malnourished children. In fact, within variability forms a dominant source of variation. It thus shows that even normal children don't grow with uniform rates as often assumed. Further, within variation (σ_w) was observed to be higher for normal children as compared to malnourished children. The analysis thus indicates that malnourished children not only have attained lower weights or heights as compared to their normal counterparts but also have lower variability in increments. Malnutrition thus hampers the capacity of the individual to interact with the environment.

This observation has obvious implications for evaluating feeding programmes. For example, periodic evaluation of feeding programmes would be much more meaningful than having it based on only initial and final measurements. Secondly, many intervention programmes have entry and exit criteria defined in terms of fixed weight gain estimated from data on normal children. Therefore, the decision should be based on the range of weight gain instead of a fixed weight gain or else it could go wrong in view of the large within variations in weight gain observed among normal children.

6. *Implication for Estimating Undernutrition*

Measurement of poverty and undernutrition have been a subject of intensive debate (Dandekar [1], [2]). Conventionally, average energy requirements are used for this purpose. The implication of this logic for comparing intake with requirement to assess incidence of undernutrition is important. If we take average requirement as reference standard, we will almost certainly find half of the people even in healthy population will have intakes below their requirement at any given point of time, giving incidence of undernutrition as 50%. The fallacy is, therefore, obvious. To use average energy requirement for calculating incidence of poverty, is to suggest, by implication, that intra-individual variation in energy balance in man maintaining body weights and doing assigned tasks is zero, which we know it is not and cannot be.

The fact that there exists a substantial intra-individual variation in daily intake, implies that man can maintain body weight and carry out assigned tasks on a wide range of intakes. Estimation of undernutrition or poverty, therefore,

Table 3. ANOVA for 3 monthly weight increment for normal & malnourished children

Source of variation	(1 –3) yr						(3–5) yr					
	Normal			Malnourished			Normal			Malnourished		
	d.f.	M.S.S.	F	d.f.	M.S.S.	F	d.f.	M.S.S.	F	d.f.	M.S.S.	F
Between individual	30	0.0647	0.26	125	0.0980	0.42	30	0.0686	0.29	59	0.0869	0.50
Within individual	217	0.2454		882	0.2356		217	0.2367		420	0.1735	
σ_w	–	0.4954 (n.s.)			0.4854			0.4865*			0.4165	
Mean	–	0.4234			0.3905			0.3519			0.3416	
C.V.% (within)	–	117.0			124.3			138.3			121.9	

* Within variation is higher for normal children as compared to malnourished children

should use a cut-off point of not the average requirement (m) but the m-3sd where sd represents standard deviation of the within variation in intake of individuals of reference type. Or else, by exaggerating poverty we merely help the non-poor to capture the benefits of the official programmes for poor, leaving the poor where they are or to worse off.

Critical appraisal of the problem of estimating incidence of undernutrition was presented by Prof. Sukhatme at the Joint Meeting of the Royal Statistical and Nutrition Societies of London, in his paper on World's Hunger as early as 1961 and his work was greatly appreciated by offering him a prestigious GUY MEDAL.

7. *Nature of Intra-individual Variation*

The need for developing statistical models to describe the phenomenon according to a biological interpretation of the underlying mechanism has been emphasized in literature. With phenomena in life sciences in particular being dynamic and time-dependent, time series models have great scope in the fields of biology, medicine and health.

The fact that variance of weekly mean intakes was persistent and stable, suggests that stationary stochastic models could be most appropriate, for describing the within variability. As there were no long term data reported in literature, several metabolic experiments were undertaken for studying the nature of within variation. One of the relevant example is described below.

The data pertains to long term N-balance experiments on adult rats fed at varying protein levels (Rao *et al* [8]). Data from two experiments conducted on adult male albino rats (i) fed at maintenance and (ii) below maintenance level, in order to study the failure of the model during physiological stress, is considered. Serial correlations for the nitrogen output of individual rats under different experimental conditions are shown in Table 4. It was observed that the daily nitrogen output could suitably be explained by autoregressive model of order one AR1 for the rats fed on milk powder diet (experiment 1A). In experiment 1B, however, as the protein source was of lower quality, the weight maintenance was difficult initially but could be restored when additional calorie supplementation in the form of starch (1-3 g) was given as and when required.

The first part in experiment 1B before the supplementation revealed nonsignificant serial correlation and no pattern could be identified while in second part after supplementation significant serial correlations confirmed AR1 model as seen in case of rats in experiment 1A. It means that pattern of fluctuation revealed by serial correlations changes when either calories or

Table 4. Serial correlation of nitrogen of rats in different experiments

Lag	Experiment 1A+		Experiment 1B*				Experiment 2**		
	Rat C3	Rat C4	Rat 3		Rat 4		Rat 2	Rat 3	Rat 4
			a	b	a	b			
1.	0.4338	0.3657	–0.1260	0.2679	0.0535	0.5046	0.0748	–0.0396	0.0741
2.	0.1669	0.0487	0.1509	0.1250	–0.0081	0.2737	–0.1496	–0.1107	–0.0103
3.	0.0969	–0.0317	–0.1232	0.0410	–0.0169	0.1193	0.0206	–0.1892	–0.0108
4.	0.1146	–0.0283	–	0.0648	–	0.0543	0.1397	0.1319	0.1131
5.	0.0585	0.0111	–	0.0691	–	–0.0115	–	–	–
6.	–0.1463	0.0037	–	–0.1880	–	0.0311	–	–	–
7.	–0.0332	–0.0042	–	–	–	–	–	–	–
Nature of series	Stationary	Stationary	Random	Stationary	Random	Stationary	Random	Random	Random

a. Before supplementation
b. After supplementation
+ Duration 78 days; protein level 7 per cent. Protein source; Cereal + pulse + milk powder. Calories/100 g food = 398; ad-lib food intake.
* Duration 100 days; protein level 7 per cent. Protein source; Cereal+pulse, Calorie3s /100g food = 390; food intake kept constant.
** Duration 42 days, first 7 days all the rats fed on maintenance protein level (7%) next 16 days on 1% protein level followed by 19 days on '0' protein level calories/100 g food = 402.
As decreasing trend in body weight as well as N-output was significant, serial correlations in this case were computed only after removing this trend.

proteins are at a marginal level. Further, all the rats in experiment 1B fed at very low levels of protein showed all the serial correlations to be non-significant indicating random series and did not show any pattern as was observed on maintenance protein level. Thus, during condition of stress when the underlying mechanism breaks down then output series were random. We have illustrated elsewhere (Tilve [13]) that similar results are obtained when rate are fed at excessively high protein levels.

The above illustration points out how time series model would be useful to study physiological processes and in particular the application to N output data has been discussed. We have demonstrated earlier (Rao *et al* [8]) that AR1 model is the manifestation of the fact that the series under consideration exhibits regulated phenomenon and thus above interpretation is biologically sound.

Subsequently, the finding that daily nitrogen balance series can be best represented by an autoregressive model of order one was also tested on data from metabolic experiments on human adults. In fact, both protein and energy balance in adult humans are shown to be autoregulated (Sukhatme and Margon [11], [12]). Sukhatme and Margon have thus shown that autoregressive model implies that the daily requirements for man in health will be distributed around a constant mean with stationary variance. They have therefore, concluded that protein deficiency must be defined as failure of the process to be in statistical control and cannot be defined in the manner that assumes requirements to be fixed. As daily energy balance too, revealed stationary stochastic nature of variation, it is concluded that "requirement" is a dynamic concept, and energy balance will vary as a matter of course about zero.

8. *Significance of Intra-individual Variation*

In living biological systems, we must expect a time lag in balancing intake with expenditure. Periods of stress of strain may modify the time lag, but there is always movement towards balance through built-in autoregulatory mechanisms. The fact that the distribution of energy balance is stochastic, suggests that the expected energy balance value is zero and the standard deviation is independent of time. The fact that energy balance is regulated also follows from the evidence that balance is regulated also follows from the evidence that humans possess a physiological regulatory mechanism for controlling appetite and energy expenditure. The statistical analysis of long term metabolic data from animal and human experiment further showed that magnitude of autocorrelation ρ reflects the power with which regulation at any given level of intake is controlled. The values of ρ decreases as intake falls below normal levels. In fact outside the range of intra-individual variation ρ is zero and indicates that individual is under stress.

This range of within variation within which autoregulatory mechanism operates to maintain energy balance infact represents limits of homeostasis. Intra-individual variation would thus, appear to reflect the capacity to adapt (or regulate intake and expenditure) in such a way that the expected value of daily energy balance is zero while the variance is constant over time.

These findings have generated worldwide debate and Sukhatme-Margon model is being tested by many researchers. It has given new basis for defining requirements and have evolved newer concepts in nutrition. Detailed discussions of various newer concepts postulated by Prof. Sukhatme [10] are published in a book 'Newer Concepts in Nutrition and their Implications for Policy' and has served a useful book for researchers. His ideas were always well ahead of time and many nutritionists are yet to understand these. There is hardly any doubt that his work in the field of nutrition has made fundamental contributions and will be valued for ever in future.

REFERENCES

[1] Dandekar, V.M., 1981. On measurement of poverty. *Econ. Pol. Week.*, **16(30)**, 1241-1250.

[2] Dandekar, V.M., 1982. On measurement of undernutrition. *Econ. Pol. Week.*, **17(6)**, 203-212.

[3] Joint FAO/WHO Ad-hoc Expert Committee, 1973. Report on Energy and Protein Requirements. WHO Tec. Rep. Ser. No. 522.

[4] Joshi, S., 1996. Studies of variations in growth patterns of rural pre-school (1-5 yrs) children. A Ph. D. Thesis submitted to University of Poona.

[5] Nayak, S., 1990. Variations in increments of weights and heights of pre-school children from two socio-economic classes. A M. Phil. dissertation submitted to University of Poona.

[6] Rao, S., 1987. Variations in dietary intake of adolescents. *Hum. Nutr. Clin. Nutr.*, **41C**, 71-79.

[7] Rao, S., 1988. Intra-indiviual variation in energy intake of adolescents. *Nutr.*, **4(4)**, 297-300.

[8] Rao, S., Kanade, A.N., Joshi, S. and Paranjape, S., 1991. Application of time-series models to detect regulatory patterns in nitrogen output of adult rats. *J. Apply. Stat.*, **18(2)**, 215-232.

[9] Sukhatme, P.V., 1961. The world's hunger and future needs in food supplies. *J. Roy. Statist. Soc.*, **A**, **124**, 463-525.

[10] Sukhatme, P.V., 1982. Newer concepts in nutrition and their implications for policy. Ed.: Sukhatme P.V., Maharashtra Association for the Cultivation of Science, Pune.

[11] Sukhatme, P.V. and Margon, S. 1978. Models for protein deficiency. *Amer. J. Clin. Nutr.*, **31**, 1237-1256.

[12] Sukhatme, P.V. and Margon, S., 1982. Autoregulatory homeostatic nature of energy balance. *Amer. J. Clin. Nutr.*, **35**, 355-365.

[13] Tilve, S., 1982. Variation in daily urinary N of adult rats fed on varying protein levels. *J. Nutr.*, **112** (3), 453-460.