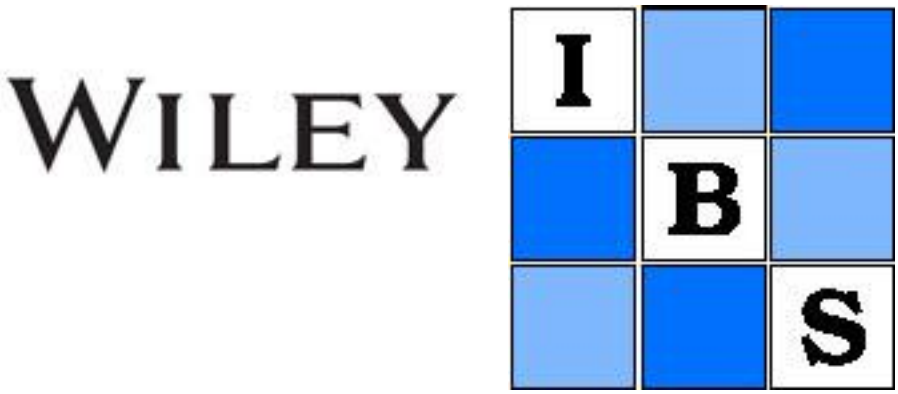

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THE USE OF A SEMI-MARKOV MODEL FOR DESCRIBING SLEEP PATTERNS

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SUMMARY

The Markov chain model proposed by Zung *et al.* [1965] for sleep patterns was tested with more data, and found inadequate for describing sleep stage sequences because the data do not fit the geometric distribution required by the model.

Instead, a semi-Markov process was shown to adequately represent the data. Predictive ability was illustrated. The parameters generated by a semi-Markov model correctly distinguished 11 out of 12 insomniacs from 11 out of 12 normal subjects.

The transition probability for the progression from stage 1 to stage 2 is consistent over the night for subjects age 3 to 69. The transition probability for progression from stage 2 to stage 3, however, changes each hour during the night for the ages tested (20 to 69). The curve of these changes has the same general form except for ages 40–49 years. This age is well known for a high incidence of insomnia.

1. INTRODUCTION

Despite the unquestioned utility of increasingly microscopic descriptions of electronencephalographic (EEG) sleep patterns in terms of changes in specific variables at specific times during the night, some efforts are presently being directed toward summary descriptions of a night's sleep. However, unlike pre-EEG descriptions of sleep, these summaries must take into account significant changes in at least the major variables, and must also furnish a quantifiable means for distinguishing between normal and disturbed sleep.

At this point in the state of the art, such a summary will, of necessity, be based upon a mathematical model. The task then is to apply an appropriate model to a set of sleep variables which is dynamic enough to furnish a useful descriptor of a night's sleep.

Zung *et al.* [1965] selected a Markov chain as the model, and the succession of sleep stage changes throughout the night as the EEG variable to which this model was applied.

Both of these choices are attractive: the general area of Markov processes may well contain a likely model for the description of sleep patterns because it provides computable conditional probabilities; the sequence of sleep stage shifts over the night is not only easy to ascertain, but it is emerging as one

of the most promising variables in the study of insomnia (Karacan *et al.* [1971]; Williams *et al.* in press).

However, the Zung *et al.* [1965] model should now be reevaluated—which reevaluation should not fail to note the ingenuity and vision of their work.

The present paper (1) will show the inadequacy of the Markov chain model used by Zung *et al.* [1965; 1967], (2) will present as an alternative, a semi-Markov model, (3) will exhibit some results obtained by use of the semi-Markov model, and (4) will discuss the utility of this approach.

For the benefit of readers not familiar with designations currently applied to the variations in amplitude and frequency obtained in continuous all-night EEG recordings on human subjects, a brief set of definitions is contained in Table 1. For a more exhaustive treatment of the subject, the reader is referred to the *Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects* (Rechtschaffen and Kales [1968]). For a nontechnical account see *Current Research on Sleep and Dreams* (U.S. Department of Health, Education and Welfare [1965]).

2. INADEQUACY OF A MARKOV CHAIN MODEL

Zung *et al.* [1965; 1967] used a Markov chain model to describe the sequence of sleep stage changes over the night pattern. They used three minutes as a time unit, assigning a stage to each three minute period. (We use one minute for a stage throughout this paper. It is more detailed and more often used than the three minute stages). They let $t = 1, 2, \cdots$ be the time units; $t = 1$, for the first three minutes, $t = 2$, for the second three minutes, etc.

TABLE 1
DEFINITIONS OF EEG SLEEP STAGES

Subjective State	Sleep Stage	Requirements (during one minute)
Awake	0	more than 30 seconds of alpha activity
Light sleep	1	less than 30 seconds of alpha activity no more than 1 spindle or K-complex less than 13 seconds of delta activity
	2	more than 1 spindle or K-complex less than 13 seconds of delta activity
	3	more than 13 seconds of delta activity but less than 30 seconds of delta
Deep sleep	4	more than 30 seconds of delta activity

Then, if J_t is the stage assigned to the time unit, J_t may take the sleep stages 0, 1, 2, 3, or 4, as its value. Zung *et al.* [1965] considered J_t to be a nonhomogeneous Markov chain, such that:

$$P_r\{J_{t+1} = j \mid J_0 = i_0, J_1 = i_1, \cdots, J_t = i\} = P_r\{J_{t+1} = j \mid J_t = i\} = P_{ij}(t).$$

They used two undisturbed sleep nights for 14 normal female subjects between the ages of 20 to 39, for estimating transition probabilities $P_{ij}(t)$. For 8 hours of sleep, there are 16 half hour phases. Since in each half hour phase they assume $P_{ij}(t)$ to be constant, they estimated a 5×5 transition probability matrix for each phase from the 28 nights of sleep data.

We found that a Markov chain model is inadequate for the following reasons: suppose that J_t is a Markov chain. Let X_t be the consecutive units of time that J_t remains in a certain stage (say stage i). According to the assumption of a Markov chain model, X_t should satisfy a geometric distribution, i.e.

$$P_r[X_t = k \mid J_t = i] = p_{ii}^{k-1}(t)(1 - p_{ii}(t)) \quad k = 1, 2, \cdots \tag{2.1}$$

provided $p_{ii}(t)$ remains unchanged during the half hour phase. Strictly speaking, (2.1) should be a truncated geometric distribution since k is limited by the half hour phase. But we neglect this small tail probability.

Table 2 gives the distribution of X_t from a sample of 34 nights of sleep for 20–39 year old normal females. A chi-square test of goodness-of-fit showed a significant difference ($p = 0.01$) between the sample distribution and the geometric distribution. Hence, the Markov chain model is inadequate. Besides the young female group which Zung *et al.* [1965] used, normal males (aged 20–39, 40–50, 60–69), pregnant women, and insomnia patient data were tested. None of these data fits the geometric distribution required by a Markov chain model.

3. FITTING DATA BY A SEMI-MARKOV MODEL

Assume instead, that the whole night's sleep pattern is a nonhomogeneous semi-Markov process. The definition and basic properties of a semi-Markov process can be found in Pyke [1961a, b]. The nonhomogeneity is due to the fact that the minute by minute distribution of stages is not the same during different parts of the night. It is well known (U.S. Department of Health, Education, and Welfare [1965]) that a person has more stage 4 sleep in the first two hours than in the last two hours, and more stage 1 REM in the later part of the night than in the early part.

Let $n = 0, 1, 2, \cdots$ be the nth stage change, J_n be the stage that a person is in after the nth stage change, and X_n be a random length of time (sojourn time) at stage J_{n-1}. The relationship is given as follows:

$$X_0 \text{ is defined as } 0,\ J_0 = 0,$$

$$P_r\{J_n = j, X_n \leq x \mid J_0, J_1, \cdots, J_{n-1} = i, X_0, X_1, \cdots, X_{n-1}\} = P_{ij}(t)Q_i'(x) \tag{3.1}$$

TABLE 2

SLEEP DURATION OF NORMAL FEMALES (AGE 20–39)

	One-minute segments														
Frequency \ minute	1	2	3	4	5	6	7	8	9	10	11–15	16–20	21–25	26–30	≥31
F0	2	1	2	2	1	2	3	3	1	2	6	4	1	3	1
F1	3	1	2	1	0	1	1	3	2	1	1	3	1	0	0
F2	9	9	8	1	4	2	1	1	4	3	9	6	5	5	10
F3	22	10	7	6	5	5	5	4	1	1	1	0	0	0	0
F4	2	1	1	2	0	3	0	2	1	0	6	1	1	5	7

F0 is the frequency of stage 0 in the first hour of sleep. (There are few occurrences of stage 0 in the later hours). F1,F2,F3, and F4 are the frequencies of stages 1,2,3, and 4 respectively in the third hour of sleep. None of them shows the shape of a geometric distribution except F3. F0, F1, F2, and F4 are significantly different from a geometric distribution by chi-square test at 0.99 confidence.

where $t = \sum_{i=0}^{n-1} X_i$, the total time slept so far, $P_{ij}(t)$ is the transition probability from stage i to stage j at the time t, $Q_i^t(x)$ is the distribution function of the sleep duration at stage j at time t. For example, one may in the beginning, spend 5 minutes in stage 0, 6 minutes in stage 1, 3 minutes in stage 2, 4 minutes in stage 3, then we have $J_0 = 0$, $X_1 = 5$, $J_1 = 1$, $X_2 = 6$, $J_2 = 2$, $X_3 = 3$, $J_3 = 3$, $X_4 = 4$ respectively.

Our model is a special case of Pyke's [1961a] model where he assumed the distribution function $Q_i^t(x)$ in (3.1) to be $Q_{ij}^t(x)$, i.e. the duration distribution function depends not only on where one is (the present stage i), but also where he goes (the next stage j). Our data do not show any necessity for his assumption. Hence we use $Q_{ij}^t(x) = Q_i^t(x)$ independent of j.

Since the probability of skipping a stage (e.g. going from 2 to 4 without entering 3) is relatively small in comparison to that of not skipping one, we assume $p_{ij}(t) \neq 0$ only when $j = i \pm 1$. If there is a jump, say from stage 2 to 3 and from 3 to 4, then the duration at stage 3 is 0. Hence the only transition probabilities to be estimated are p_{12}, p_{10}, p_{21}, p_{23}, p_{32}, p_{34}. Since $p_{10} = 1 - p_{12}$, $p_{21} = 1 - p_{23}$, and $p_{32} = 1 - p_{34}$, we reduce the total of 25 transition probabilities of Zung's model (p_{ij} $i, j = 0, 1, \cdots, 4$) to a total of 3.

4. RESULTS

In order to estimate $p_{ii}(t)$ and $Q_i{}^t(x)$, we assume that in each hour the changes of $p_{ii}{}^t$ and $Q_i{}^t$ are small and can be considered as constants. Using the estimation technique of Pyke and Moore [1969], we obtained the transition probabilities $\hat{p}_{ii}{}^t$ and distribution functions $\hat{Q}_i{}^t$ from the following data: normal females of age 20–39; normal males of age 3–5, 6–12, 20–29, 30–39, 40–49, 50–59, and 60–69. All these data are obtained from the Sleep Laboratory, Department of Psychiatry, University of Florida. Each group contains 10 to 12 people and each person slept 6 to 10 nights in the Sleep Laboratory. The first 2 or 3 nights are not counted since the subject might not be accustomed to the sleep condition in the laboratory. The following results are obtained.

A. For each person, the transition probability from stage 1 to stage 2 is constant during the sleep, i.e. $p_{12}(t)$ is independent of t. This has been tested by two-way analysis of variance. Let $\hat{p}_{12}(t, s)$ denote the estimated transition probability of the sth person at tth hours. Considering t and s as factors, we ran a two way analysis of variance in each group. It has been shown that $\hat{p}_{12}(t, s)$ is independent of t (tested at 0.05 significance level). Table 3 shows the mean $\hat{p}_{12}$ (average over subjects within an age group) for each male group.

B. Figure 1 and Figure 2 show the estimated mean transition probabilities $\hat{p}_{23}(t)$ and $\hat{p}_{34}(t)$ (average over subjects within the group at the given hour t). $\hat{p}_{34}(t)$ is not reliable because of the small amount of stage 3 sleep. Age effects are obvious. A general pattern in $\hat{p}_{23}(t)$ is also obvious.

C. The distribution functions $\hat{Q}_i{}^t(x)$ are not constant from hour to hour within each age group. We used the chi-square test to test whether the distribution functions $Q_i{}^t(x)$ are the same from hour to hour. We rejected this hypothesis at 0.05 significance level for most tests. The remaining small number of nonsignificant chi-square values are apparently due to chance.

D. The parameters of the semi-Markov model have been used for discriminant analysis. The data of 12 insomnia and 12 control subjects have been collected in the Sleep Laboratory, University of Florida. Each of them has slept 6 to 8 nights. Each one's transition probabilities and distribution functions are estimated. Since we know that an isomnia is hard to get into deep sleep and has a long awaking period in the beginning, we used $\hat{p}_{12}$, $\hat{p}_{23}(t)(t$ = 1st, 2nd, and 3rd hour), and $\hat{\mu}_1 = EX_1$ as a 5-variate random variable for discrimination. The "stepwise discriminant analysis (BMDO 7M)" of BMD computer program (Ed. by Dixon [1968]) is used.

TABLE 3

THE TRANSITION PROBABILITIES p_{12} OF MALES AT DIFFERENT AGES

Age	3-5	6-12	20-29	30-39	40-49	50-59	60-69
p_{12}	0.867	0.850	0.811	0.853	0.685	0.779	0.657

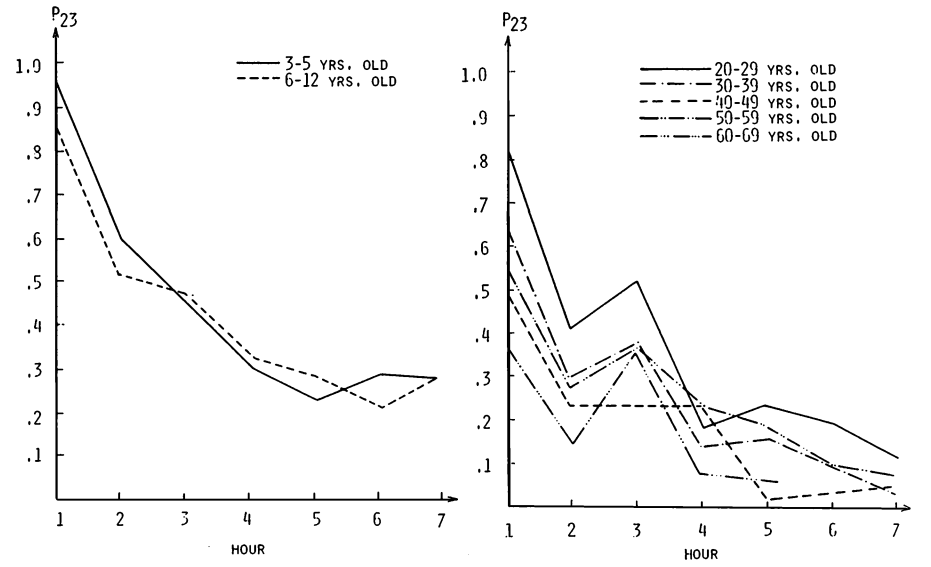

FIGURE 1
TRANSITION PROBABILITIES FROM STAGE 2 TO STAGE 3

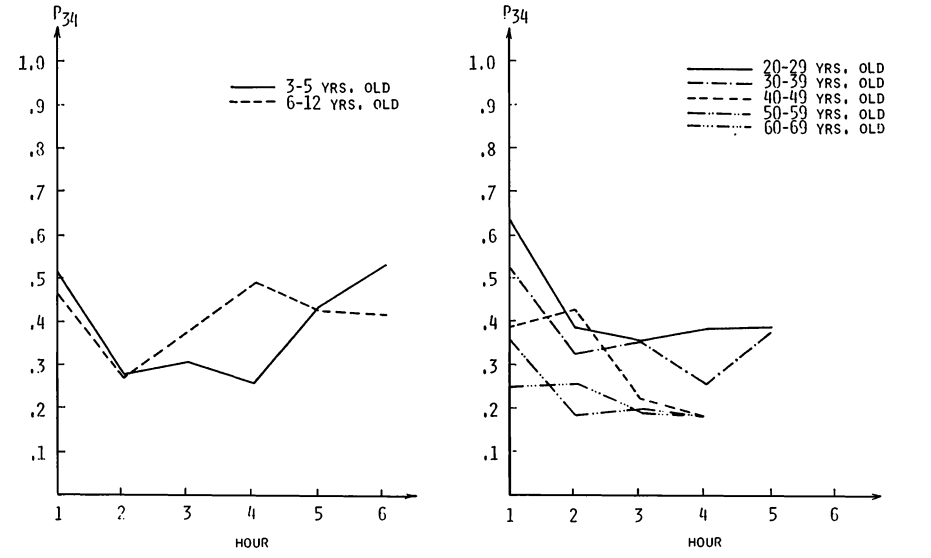

FIGURE 2
TRANSITION PROBABILITIES FROM STAGE 3 TO STAGE 4

If the 5-variable is used for discrimination, the probabilities of misclassification of both groups is 0.083. Since the program uses the original data to estimate the error, the real probabilities of misclassifications by this discrimination function might be higher than 0.083 (see e.g. Lachenbruch and Mickey [1968]).

E. The adequacy of a semi-Markov model has been checked by using the estimated transition probabilities and sojourn time distributions to predict the percentage of each stage in total sleep. The method is given in the Appendix. The data of the male group of age 60–69 are used. Figure 3 shows the closeness between the predicted and actual values.

5. DISCUSSION

Section 1 above shows that the Markov chain model suggested by Zung *et al.* [1965] does not fit the data because the sequence of sleep stage changes over the night does not form the geometric distribution required by the model.

However, the data do fit the requirements of a semi-Markov process, as is shown in section 3, which has the advantage of reducing the number of transition probabilities from 25 to a total of 3. In section 4 the resulting probabilities are used to discriminate between different kinds of subjects.

It is interesting to note that p_{12} , the probability of moving from stage 1 to stage 2, is constant throughout the night for all subjects in a given age group, whereas p_{23} , the probability of moving from stage 2 to stage 3, changes as the night progresses. However, this change in p_{23} is very much the same for all of the age groups tested from 20 to 69 years, with the exception of the 40–49 year old group. While it is difficult to infer very much from the

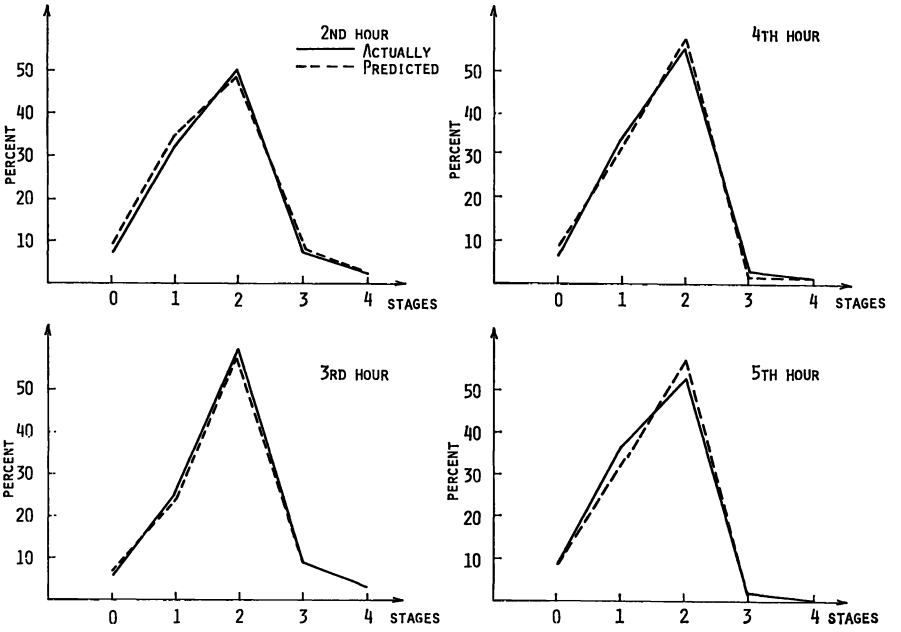

FIGURE 3
PREDICTED PERCENTAGE

p_{34} curve (Figure 2) because of the relatively small amount of data, it may be noted that it follows the general pattern of the curve for p_{23} .

Although the immediate objective of this study was to use a large body of data in order to test the adequacies of the Markov chain model and the semi-Markov model, these new insights into sleep pattern which emerged are also of considerable interest.

Since sleep patterns are known to change with age, we did not expect to find the degree of orderliness in stage change probabilities as we progressed through the age groups. The one group which does not conform is the 40–49 year old group. This is also the age group where insomnia is most prevalent, and where there is a great deal of variability even among normal subjects (Karacan *et al.* [1971]).

The model therefore is of use, not only as a tool for distinguishing between types of sleep patterns (e.g., normal vs abnormal), but may also show promise of shedding new light on the sleep process even in this first application.

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L'UTILISATION D'UN MODELE SEMI-MARKOVIEN POUR DECRIRE LE SOMMEIL

RESUME

La chaine de Markov proposée par Zung et al [1965] comme modèle de sommeil a été testée avec davantage de données et trouvée inadéquate pour décrire la suite des états de sommeil du fait que les données ne suivent pas la distribution hypergéométrique requise.

En remplacement, on a montré qu'un processus semi-markovien est plus adéquat relativement aux données. Sa valeur prédictrice a été illustrée. Les paramètres engendrés par le modèle semi-markovien ont permis de distinguer 11 insomniaques sur 12 de 11 sujets normaux sur 12.

La probabilité de transition pour la progression de l'état 1 à l'état 2 est stable au cours de la nuit pour des sujets d'âge variant de 3 à 69 ans. Cependant, la probabilité de transition pour la progression de l'état 2 à l'état 3 change chaque heure au cours de la nuit pour les âges testés (20 à 69 ans). La courbe de ces changements a une forme constante sauf pour les âges compris entre 40 et 49 ans. Cet âge est bien connu pour sa grande incidence d'insomnie.

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APPENDIX

Using the transition probabilities $\hat{p}_{ii}{}^t$ and the estimated means $\hat{\mu}_i(t)$ of the sojourn time distribution $Q_i{}^t(x)$, we can predict the percentage of each stage in each hour. We assume that within each hour $p_{ii}{}^t$ and $\mu_i(t)$ are constants. For any given hour, let

T_i = the total time that one spent at stage i, and

N_i = the number of times he enters stage i.

If we assume that one hour is long enough for the process to reach its stationary state, then ET_i is approximately equal to $\mu_i EN_i$. Whether the process will reach its stationary state in one hour depends on the initial probability distribution and the distribution $Q_i{}^t$ which is not easy to estimate. Since the variation of $p_{ii}{}^t$ from hour to hour is not large, the initial distribution should be close to the stationary distribution of the Markov chain J_n defined in section 3. Hence the assumption of stationarity should be close to the reality.

The estimated value of EN_i can be found by a Laplace inverse transformation method (Kshirsagar and Gupta [1967]). Since the distribution functions $Q_i(x)$ are hard to estimate, their Laplace transformations are unknown. But the mean of Q_i can be estimated with high accuracy. Since the transition of stages forms a Markov chain, we use the stationary distribution of the Markov chain as an approximation to the ratio $EN_0 : EN_1 : EN_2 : EN_3 : EN_4$. The transition matrix is

$$\begin{bmatrix} 0 & 1 & 0 & 0 & 0 \\ p_{10} & 0 & p_{12} & 0 & 0 \\ 0 & p_{21} & 0 & p_{23} & 0 \\ 0 & 0 & p_{32} & 0 & p_{34} \\ 0 & 0 & 0 & 1 & 0 \end{bmatrix}.$$

It is well known (Karlin [1966] p. 66) that stationary probabilities
$\pi_0 : \pi_1 : \pi_2 : \pi_3 : \pi_4$

$$= 1 : 1/p_{10} : p_{12}/p_{10}p_{21} : p_{12}p_{23}/p_{10}p_{21}p_{32} : p_{12}p_{23}p_{34}/p_{10}p_{21}p_{32} . \quad \text{(A-1)}$$

Substituting all the estimated values of p_{ij} and μ_i into (A-1) and $ET_i = \mu_i EN_i$, we obtain the percentage of each stage in the total sleep.

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