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Dynamics of Sleep-Wake Transitions During Sleep

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Abstract. – We study the dynamics of the awakening during the night for healthy subjects
and find that the wake and the sleep periods exhibit completely different behavior: the durations
of wake periods are characterized by a scale-free power-law distribution, while the durations of
sleep periods have an exponential distribution with a characteristic time scale. We find that
the characteristic time scale of sleep periods changes throughout the night. In contrast, there
is no measurable variation in the power-law behavior for the durations of wake periods. We
develop a stochastic model which agrees with the data and suggests that the difference in the
dynamics of sleep and wake states arises from the constraints on the number of microstates in
the sleep-wake system.

In clinical sleep centers, the "total sleep time" and the "total wake time" during the night are
used to evaluate sleep efficacy and to diagnose sleep disorders. However, the total wake time
during a long period of nocturnal sleep is actually comprised of many short wake intervals
(Fig. 1). This fact suggests that the "total wake time" during sleep is not sufficient to
characterize the complex sleep-wake transitions and that it is important to ask how periods of
the wake state distribute during the course of the night. Although recent studies have focused
on sleep control at the neuronal level [1, 2, 3, 4], very little is known about the dynamical
mechanisms responsible for the time structure or even the statistics of the abrupt sleep-wake
transitions during the night. Furthermore, different scaling behavior between sleep and wake
activity and between different sleep stages has been observed [5, 6]. Hence, investigating the
statistical properties of the wake and sleep states throughout the night may provide not only
a more informative measure but also insight into the mechanisms of the sleep-wake transition.

We analyze 39 full-night sleep records collected from 20 healthy subjects (11 females and
9 males, ages 23–57, with average sleep duration 7.0 hours). We first study the distribution
of durations of the sleep and of the wake states during the night (Fig. 1). We calculate the
cumulative distribution of durations, defined as

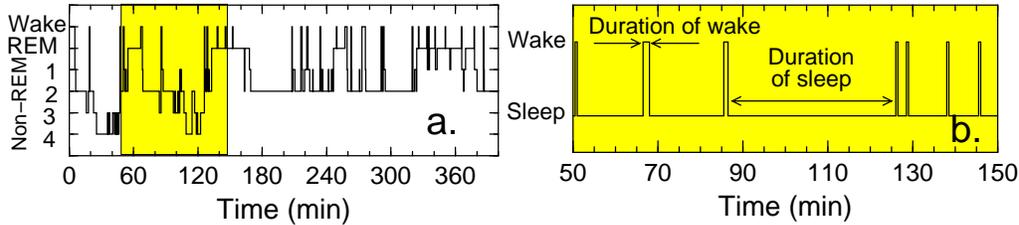$$P(t) \equiv \int_t^\infty p(r)dr \,, \tag{1}$$

Fig. 1. – Sleep-wake transitions during nocturnal sleep. (a) Representative example of sleep-stage transitions from a healthy subject. Data were recorded in a sleep laboratory according to the Rechtschaffen and Kales criteria [16]: two channels of electroencephalography (EEG), two channels of electrooculography (EOG) and one channel of submental electromyography (EMG) were recorded. Signals were digitized at 100 Hz and 12 bit resolution, and visually "scored" by sleep experts in segments of 30 seconds for sleep stages: wakefulness, rapid-eye-movement (REM) sleep and non-REM sleep stages 1, 2, 3 and 4. (b) Magnification of the shaded region in (a). In order to study sleep-wake transitions, we reduce the five sleep stages into a single sleep state by grouping rapid-eye-movement (REM) sleep and sleep stages 1 to 4 into a single sleep state.

where $p(r)$ is the probability density function of durations between r and $r + dr$. We analyze $P(t)$ of the wake state, and we find that the data follow a power-law distribution,

$$P(t) \sim t^{-\alpha} . \tag{2}$$

We calculate the exponent α for each of the 20 subjects, and find an average exponent $\alpha = 1.3$ with a standard deviation $\sigma = 0.4$.

It is important to verify that the data from individual records correspond to the same probability distribution. To this end, we apply the Kolmogorov-Smirnov test to the data from individual records. We find that we cannot reject the null hypothesis that $p(t)$ of the wake state of each subject is drawn from the same distribution, suggesting that one can pool all data together to improve statistics without changing the distribution (Fig. 2a). Pooling the data from all 39 records, we find that $P(t)$ of the wake state is consistent with a power-law distribution with an exponent $\alpha = 1.3 \pm 0.1$ (Fig. 3a).

In order to verify that the distribution of durations of wake state is better described by a power law rather than an exponential or a stretched exponential functional forms, we fit these curves to the distributions from pooled data. Using Levenberg-Marquardt method, we find that both exponential and stretched exponential forms lead to worse fits. The χ^2 errors of power-law fit, exponential fit and stretched exponential fit are 3×10^{-5}, 1.6×10^{-3} and 3.5×10^{-3}, respectively. We also check the results by plotting (i) $\log P(t)$ versus t and (ii) $\log(|\log P(t)|)$ versus $\log t$ [1] and find in both cases that the data are clearly more curved than when we plot $\log P(t)$ versus $\log t$, indicating that a power law provides the best description of the data [2].

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[1] For the stretched exponential $y = a \exp(-bx^c)$, where a, b and c are constants, the $\log(|\log y|)$ versus $\log x$ plot is not a straight line unless $a = 1$. Since we don't know what the corresponding value of a is in our data, we can not rescale y so that $a = 1$. The solution is to shift x for a certain value to make $y = 1$ when $x = 0$, in which case $a = 1$. In our data, $P(t) = 1$ when $t = 0.5$, so we shift t by -0.5 before plotting $\log(|\log P(t)|)$ versus $\log t$.

[2] According Eq. 1, if $P(t)$ is a power-law function, so is $p(t)$. We also separately check the functional form of $p(t)$ for the data with same procedure and find that the power law provides the best description of the data.
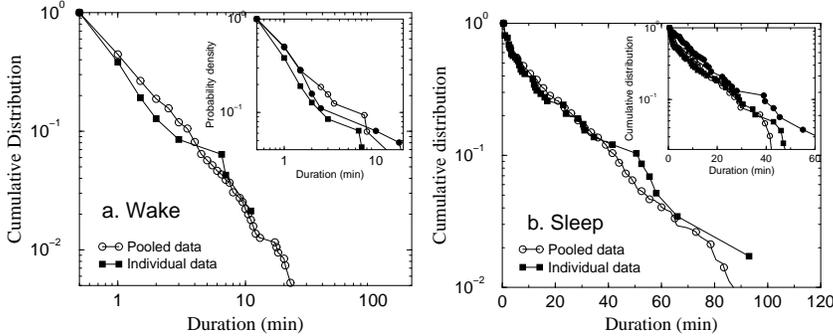
Fig. 2. – Cumulative probability distribution $P(t)$ of sleep and wake durations of individual and pooled data. Double-logarithmic plot of $P(t)$ of wake durations (a) and semi-logarithmic plot of $P(t)$ of sleep durations (b) for pooled data and for data from one typical subject. $P(t)$ for three typical subjects is shown in the insets. Note that due to limited number of sleep-wake periods for each subject, it is difficult to determine the functional form for individual subjects. We perform K-S test and compare the probability density $p(t)$ for all individual data sets and pooled data for both wake and sleep periods. For both sleep and wake, less than 10% of the individual data fall below the 0.05 significant level of disproof of the null hypothesis, that $p(t)$ for each individual subject is very likely drawn from the same distribution. The K-S statistics significantly improves if we use recordings only from the second night. Therefore, pooling all data improves the statistics by preserving the form of $p(t)$.

We perform a similar analysis for the sleep state and find, in contrast to the result for the wake state, that the data in large time region ($t > 5$ min) exhibit exponential behavior

$$P(t) \sim e^{-t/\tau}. \tag{3}$$

We calculate the time constants τ for the 20 subjects, and find an average $\tau = 20$ min with $\sigma = 5$. Using the Kolmogorov-Smirnov test, we find that we cannot reject the null hypothesis that $p(t)$ of the sleep state of each subject of our 39 data sets is drawn from the same distribution (Fig. 2b). We further find that $P(t)$ of the sleep state for the pooled data is consistent with an exponential distribution with a characteristic time $\tau = 22 \pm 1$ min (Fig. 3b).

In order to verify that $P(t)$ of sleep state is better described by an exponential functional form rather than by a stretched exponential functional form, we fit these curves to the $P(t)$ from pooled data. Using Levenberg-Marquardt method, we find that the stretched exponential form lead to worse fit. The χ^2 errors of exponential fit and stretched exponential fit are 8×10^{-5} and 2.7×10^{-2}, respectively. We also check the results by plotting $\log(|\log P(t)|)$ versus $\log t$ [1] and find that the data are clearly more curved than when we plot $\log P(t)$ versus t, indicating that an exponential form provides the best description of the data.

Sleep is not a "homogeneous process" throughout the course of the night [7, 8], so we ask if there is any change of α and τ during the night. We study sleep and wake durations for the first two hours, middle two hours, and the last two hours of nocturnal sleep using the pooled data from all 39 records (Fig. 4). Our results suggest that α does not change for these three portions of the night, while τ decreases from 27 ± 1 min in the first two hours to 22 ± 1 min in the middle two hours, and then to 18 ± 1 min in the last two hours. The decrease in τ implies that the number of wake periods increases as the night proceeds, and we indeed find that the average number of wake periods for the last two hours is 1.4 times larger than for the first two hours.

We next investigate mechanisms that may be able to generate the different behavior ob-
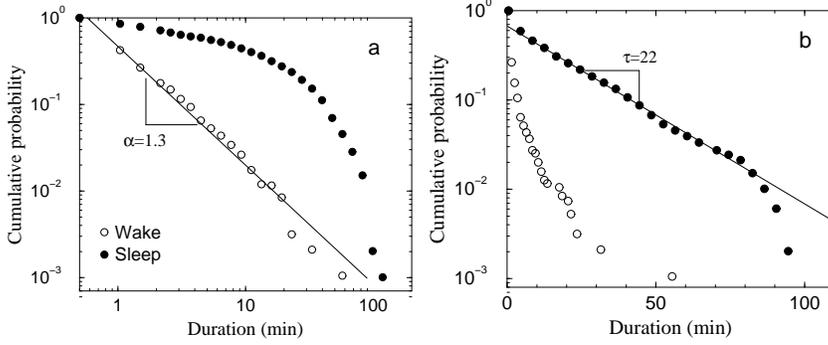
Fig. 3. – Cumulative distribution of durations $P(t)$ of sleep and wake states from data. (a) Double-logarithmic plot of $P(t)$ from the pooled data. For the wake state, the distribution closely follows a straight line with a slope $\alpha = 1.3 \pm 0.1$, indicating power-law behavior of the form of Eq. (2). (b) Semi-logarithmic plot of $P(t)$. For the sleep state, the distribution follows a straight line with a slope $1/\tau$ where $\tau = 22 \pm 1$, indicating an exponential behavior of the form of Eq. (3). It has been reported that the individual sleep stages have exponential distributions of durations [17, 18, 19]. Hence we expect an exponential distribution of durations for the sleep state.
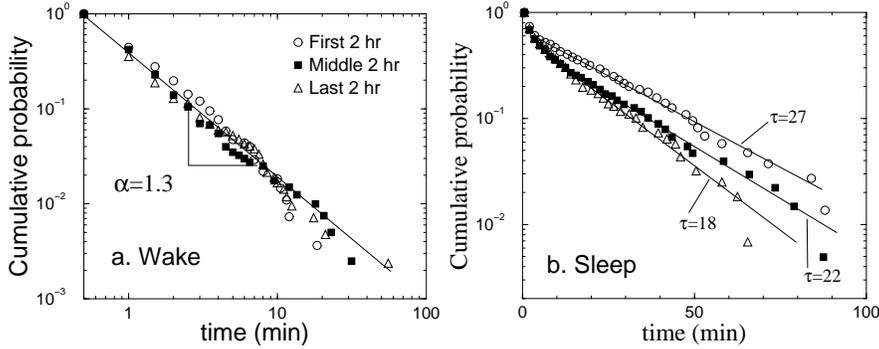

Fig. 4. – $P(t)$ of sleep and wake states in the first two hours, middle two hours and last two hours of sleep. (a) $P(t)$ of wake states; the power-law exponent α does not change in a measurable way. (b) $P(t)$ of sleep states; the characteristic time τ decreases in the course of the night.

served for sleep and wake. Although several quantitative models, such as the two-process model [9] and the thermoregulatory model [10], have been developed to describe human sleep regulation, detailed modeling of frequent short awakening during nocturnal sleep has not been addressed [11]. To model the sleep-wake transitions, we make three assumptions (Fig. 5):

Assumption 1 defines the key variable $x(t)$ for sleep-wake dynamics. Although we consider a two-state system, the brain as a neural system is unlikely to have only two discrete states. Hence, we assume that both wake and sleep "macro" states comprise large number of "microstates" which we map onto a continuous variable $x(t)$ defined in such a way that positive values correspond to the wake state while negative values correspond to the sleep state. We further assume that there is a finite region $-\Delta \le x \le 0$ for the sleep state.

Assumption 2 concerns the dynamics of the variable $x(t)$. Recent studies [2, 4] suggest that a small population of sleep-active neurons in a localized region of the brain distributes inhibitory inputs to wake-promoting neuronal populations, which in turn interact through a
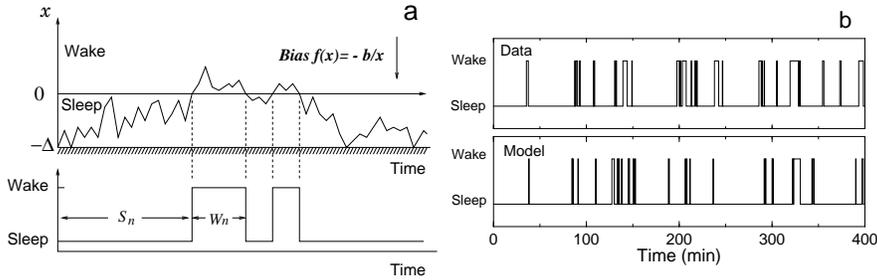
Fig. 5. – (a) The upper panel illustrates the dynamics of the model. The state $x(t)$ of the sleep-wake system evolves as a random walk with the convention that $x > 0$ corresponds to wake state and $-\Delta \leq x \leq 0$ corresponds to the sleep state. In the wake state there is a "restoring force," $f(x) = -b/x$, "pulling" the system towards the sleep state. The lower panel illustrates sleep-wake transitions from the model, where S_n and W_n indicate the durations of the n-th sleep and wake states, respectively. (b) Comparison of typical data and of a typical output of the model. The visual similarity between the two records is confirmed by quantitative analysis (Fig. 6).

feedback on the sleep-active neurons. Because of these complex interactions, the global state of the system may present a "noisy" behavior. Accordingly, we assume that $x(t)$ evolves by a random-walk type of dynamics due to the competition between the sleep-active and wake-promoting neurons.

Assumption 3 concerns a bias towards sleep. We assume that if $x(t)$ moves into the wake state, then there will be a "restoring force" pulling it towards the sleep state. This assumption corresponds to the common experience that in wake periods during nocturnal sleep, one usually has a strong tendency to quickly fall asleep again. Moreover, the longer one stays awake, the more difficult it may be to fall back asleep, so we assume that the restoring force becomes weaker as one moves away from the transition point $x = 0$. We model these observations by assuming that the random walker moves in a logarithmic potential $V(x) = b \ln x$, yielding a force $f(x) \equiv -dV(x)/dx = -b/x$, where the bias b quantifies the strength of the force.

Assumptions 1-3 can be written compactly as:

$$\delta x(t) \equiv x(t+1) - x(t) = \begin{cases} \epsilon(t), & \text{if } -\Delta \leq x(t) \leq 0 \quad \text{(sleep)}, \\ -\frac{b}{x} + \epsilon(t), & \text{if } x(t) > 0 \quad \text{(wake)}, \end{cases} \tag{4}$$

where $\epsilon(t)$ is an uncorrelated Gaussian-distributed random variable with zero mean and unit standard deviation. In our model, the bias b and the threshold Δ may change during the course of the night due to physiological variations such as circadian cycle [9, 11].

In our model, the distribution of durations of the wake state is identical to the distribution of return times of a random walk in a logarithmic potential. For large times, this distribution is of a power law form [12, 13, 14, 15]. Hence, for large times, the cumulative distribution of return times is also a power law, Eq. (2), and the exponent is predicted to be

$$\alpha = \frac{1}{2} + b. \tag{5}$$

From Eq. (5) it follows that the cumulative distribution of return times for a random walk without bias ($b = 0$) decreases as a power law with an exponent $\alpha = 1/2$. Note that introducing a restoring force of the form $f(x) = -b/x^\gamma$ with $\gamma \neq 1$, yields stretched exponential distributions [15], so $\gamma = 1$ is the only case yielding a power-law distribution.
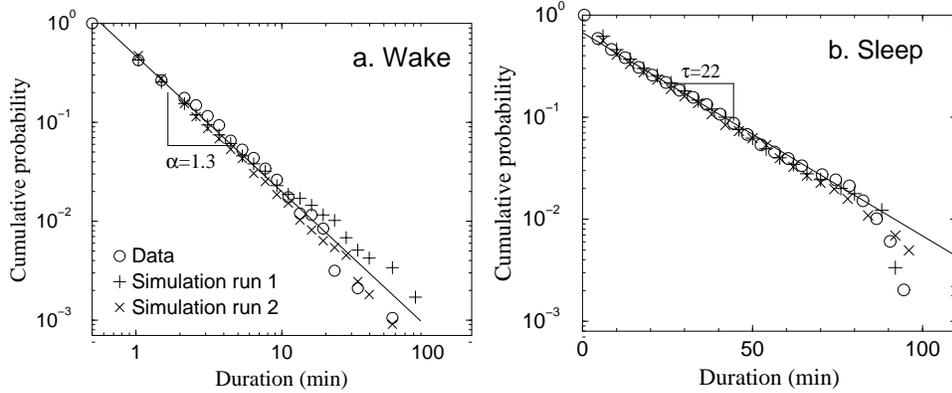
Fig. 6. – Comparison of $P(t)$ for data and model (two runs with same parameters). (a) $P(t)$ of the wake state. (b) $P(t)$ of the sleep state. Note that the choice of Δ depends on the choice of the time unit of the step in the model. We choose the time unit to be 30 seconds, which corresponds to the time resolution of the data. To avoid big jumps in $x(t)$ due to the singularity of the force when $x(t)$ approaches $x = 0$, we introduce a small constant λ in the definition of the restoring force $f(x) = -b/(x + \lambda)$. We find that the value of λ does not change α or τ.

Similarly, the distribution of durations of the sleep state is identical to the distribution of return times of a random walk in a space with a reflecting boundary. Hence $P(t)$ has an exponential distribution, Eq. (3), in the large time region, with the characteristic time τ predicted to be

$$\tau \sim \Delta^2. \tag{6}$$

Equations (5) and (6) indicate that the values of α and τ in the data can be reproduced in our model by "tuning" the threshold Δ and the bias b (Fig. 6). The decrease of the characteristic duration of the sleep state as the night proceeds is consistent with the possibility that Δ decreases. Our calculations suggest that Δ decreases from 7.9 ± 0.2 in the first hours of sleep, to 6.6 ± 0.2 in the middle hours, and then to 5.5 ± 0.2 for the final hours of sleep. Accordingly, the number of wake periods of the model increases by a factor of 1.3 from the first two hours to the last two hours, consistent with the data. However, the apparent consistency of the power-law exponent for the wake state suggests that the bias b may remain approximately constant during the night. Our best estimate is $b = 0.8 \pm 0.1$.

To further test the validity of our assumptions, we examine the correlation between the durations of consecutive states. Consider the sequence of sleep and wake durations $\{ S_1 \ W_1 \ S_2 \ W_2....S_n \ W_n \}$, where S_n indicates the duration of n-th sleep period and W_n indicates the duration of n-th wake period (Fig. 5a). Our model predicts that there are no autocorrelations in the series S_n and W_n, as well as no cross-correlations between series S_n and W_n, the reason being that the uncorrelated random walk carries no information about previous steps. The experimental data confirms these predictions, within statistical uncertainties.

Our findings of a power-law distribution for wake periods and an exponential distribution for sleep periods are intriguing because the same sleep-control mechanisms give rise to two completely different types of dynamics—one without a characteristic scale and the other with. Our model suggests that the difference in the dynamics of the sleep and wake states (e.g. power law versus exponential) arises from the distinct number of microstates that can be explored by the sleep-wake system for these two states. During the sleep state, the system

is confined in the region $-\Delta \leq x \leq 0$. The parameter Δ imposes a scale which causes an exponential distribution of durations. In contrast, for the wake state the system can explore the entire half-plane $x > 0$. The lack of constraints leads to a scale-free power-law distribution of durations. In addition, the $1/x$ restoring force in the wake state does not change the functional form of the distribution, but its magnitude determines the power-law exponent of the distribution using Eq. (5).

Although in our model the sleep-wake system can explore the entire half-plan $x > 0$ during wake periods, the "real" biological system is unlikely to generate very large value (i.e., extreme long wake durations). There must be a constraint or boundary in the wake state at a certain value of x. If such a constraint or boundary exists, we will find a cut-off with exponential tail in the distribution of durations of the wake state. More data are needed to test this hypothesis.

Our additional finding of a stable power-law behavior for wake periods for all portions of the night implies that the mechanism generating the restoring force in the wake state is not affected in a measurable way by the mechanism controlling the changes in the durations of the sleep state. We hypothesize that even though the power-law behavior does not change in the course of the night for healthy individuals, it may change under pharmacological influences or under different conditions, such as stress or depression. Thus, our results may also be useful for testing these effects on the statistical properties of the wake state and the sleep state.

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