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Deciphering elapsed time and predicting action timing from neuronal population signals

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INTRODUCTION
The neural basis of temporal processing has gathered increasing interest in the field of neuroscience (CoulI et al., 2004; Mauk and Buonomano, 2004; Buhusi and Meck, 2005; Buonomano and LaJe, 2010). Recent studies have discovered brain regions that exhibit activity correlated to the elapsed time while animals were kept waiting for several seconds for a variety of actions; for instance, the basal ganglia and the cerebellum are activated during time perception tasks (Rao et al., 2001; Matell et al., 2003; Meck et al., 2008; Jin et al., 2009), the prefrontal and parietal cortices exhibit neuronal climbing activity in delay response tasks or motor planning (Niki and Watanabe, 1979; Brody et al., 2003; Durstewitz, 2003, 2004; Leon and Shadlen, 2003; Reutimann et al., 2004), and the pre-supplementary motor area (pre-SMA), as well as premotor and primary motor areas exhibit both ascending and descending neuronal activities in an interval timing task (Lebedev et al., 2008; Mita et al., 2009; Rickert et al., 2009; Kilavik et al., 2010).

Rather than detecting neuronal involvement in timing behavior, we attempt here to decode the lapse of time from neuronal population signals throughout the time period during which subjects were required to estimate the passage of time. We reason that it should be possible to assess the passage of time, by deciphering temporal information hidden in the noisy firing of a population of neurons, enabling the monitoring of time as if watching an hourglass. Accordingly, we apply a theoretical approach to determine the lapse of time in the range of seconds from time-dependent tendencies in the overall properties of the firing of individual neurons. Such inverse inference is thought to be given shape by conforming to the Bayesian principle that allots the probability to the possible causes that may have led to the given results (Rieke et al., 1997; MacKay, 2003; Beck et al., 2008; Quiroga and Panzeri, 2009; Jazayeri and Shadlen, 2010; Pillow et al., 2011).

For this study, we design a basic Bayesian algorithm that estimates the lapse of time from neuronal population signals averaged over a short interval, and apply it to neuronal spike trains recorded from the pre-SMA, previously found to exhibit salient modulation in firing activity over several seconds during which monkeys were kept waiting for action (Mita et al., 2009). In the experiment, monkeys were requested to recall a pre-assigned interval of time selected from several alternatives. We attempt to estimate not only the current lapse of time, but also the scheduled total waiting time-interval, both of which are needed for the agent in the brain that determines the timing of action. In the population analysis, we determine whether or not the neuronal representation of the elapsed time is influenced by a scheduled total time-interval in each waiting trial; we examine whether the elapsed time is represented as actual passage of time or relative to the entire scheduled interval.

RESULTS
In a previous study (Mita et al., 2009), we reported that neurons in the pre-SMA exhibited systematic temporal variation in their firing rates while monkeys were estimating time-interval. In this experiment, the monkeys were trained to hold down a key for longer than a pre-assigned time-interval that was selected from several
alternatives, including 4 and 8 s. Each trial began when the monkey pressed a hold key. Instruction light designating the waiting-interval was illuminated 1–2 s later for 2 s. The monkeys were rewarded with juice 0.5 s after releasing the key if they held it longer than the pre-assigned time-interval, and became skilled at these tasks with a success rate of over 80%. Neuronal firing data were obtained using a conventional single-unit recording method. The presumed single-neurons to which spikes were sorted out are called units. In the present analysis, we used 25 units that were selected as being significantly task-related (the Wilcoxon signed rank test, p < 0.01; Materials and Methods). While the previous study explored single-neuronal activities correlated to the passage of time, here we attempted to decode time from activity of neuronal populations.

**DECODING THE ELAPSED TIME FROM NEURONAL POPULATION SIGNALS**

First, we devised an algorithm for decoding the lapse of time (Figure 1; Materials and Methods) and applied it to an ensemble of 25 units that exhibited salient modulation in firing activity over several seconds. Simple average of their population activities was not an adequate measure to estimate the time, because the average activity indicated no prominent dependency on the time (Figure 2). By contrast, the Bayesian “TIME DECODER 1” developed here allowed us to draw an inference about the elapsed time by combining information of specific temporal variation in individual unit activity. Here, the passage of time was estimated only from N = 25 spike trains that were obtained by joining the recordings of different units across different trials. After selecting a single set of spike trains as a test set, the Bayesian decoder was adjusted to the rest of spike trains that were not used for the test set. The decoding capability was evaluated by repeating this validation test 100 times (Materials and Methods).

TIME DECODER 1 estimates the conditional probability of the elapsed time t given the population activities \( \mathbf{a}_t \equiv (a_{t_1}, a_{t_2}, \ldots, a_{t_N}) \) at actual time \( T \), which are given by the numbers of spikes that \( N = 25 \) units have generated in a 1-s interval of \( [T-1, T] \). Here, the time decoding algorithm was independently applied to an individual waiting task of \( S = 4 \) or 8 s. For each test set of population signals derived from the actual elapsed time \( T \), we selected the conjectured time \( t = \tau^* \) that rendered the highest confidence level in the decoder. The conjectured times \( t^* \) obtained for 100 test sets of the population signals were distributed narrowly around the actual time \( T \) and typically deviated on the order of 1 s (Figures 3A,B). The first and last time boxes gave higher confidence than others. This is presumably because a time box at each end has only one neighboring box, and accordingly the probability to leak out is smaller.

In addition, we examined the manner in which the accuracy in estimating time depends on the number of units (Figure 3C). Namely, we measured the error of the conjectured time \( t^* \) from the actual time \( T \) by changing the number of units. For the case of \( N < 25 \), we randomly selected smaller subset of units. In these cases, the prediction accuracy fluctuated according to the selection of ensembles but it did not depend on particular units; this indicates that time is not represented at the single-unit level but is distributed over many units. The cases for \( N > 25 \) were tested by employing multiple spike trains from every unit and virtually regarding them as independent neuronal data. The prediction accuracy increased with the number of neurons.

**ANALYZING NEURONAL CODING OF THE ELAPSED TIME AND SCHEDULED TIME-INTERVAL**

Next, we attempted to simultaneously estimate the scheduled waiting time-interval \( S \) as well as the elapsed time \( t \) by devising “TIME DECODER 2” (Figure 4; Materials and Methods). This algorithm allows us to estimate the elapsed time \( t = \tau^* \) using only signals that have rendered the correct conjecture of the scheduled interval, \( s^* = S \) (Figure 5A). The distribution of \( \tau^* \) was very close to that of \( \tau \) obtained with TIME DECODER 1 for each scheduled time-interval \( S = 4 \) or 8 s (Figure 3). Exclusive information that TIME DECODER 2 provides is the inference of the scheduled waiting time-interval, which is obtained by marginalizing the conditional probability distribution (Figure 4C). The percentage of correctly hitting the actual waiting time-interval, \( s^* = S \), turned out to be significantly high (\( p \approx 0.7 \)), showing that the scheduled waiting time-interval \( S \) can be decoded from the activities of only \( N = 25 \) units even in the middle of the waiting period (Figure 5B).

In addition, TIME DECODER 2 provided us more intriguing information of the manner in which the time is encoded in neuronal populations. This information was revealed by estimating the elapsed time \( t \) under the presumption that the scheduled waiting time-interval \( S \) is different from the actual \( S \): if the conjectured time \( t \) indicates the original lapse of time \( T \) independently of the presumption of the entire waiting time-interval \( S \), we should conclude that the neuronal populations encode the raw physical time. However, it turned out that the conjectured time \( t \) was scaled with an assumption about the entire scheduled interval \( s \): the elements of the confusion matrix representing rescaled time schema, \( t/s = T/S \), indicated the higher probability than the elements representing the raw physical time schema, \( t = T \) (Figure 5C). This fact implies that the neuronal ensemble is gauging the passage of time relatively to the entire scheduled interval (Renoult et al., 2006).

To visualize the neuronal encoding of the lapse of time, we mapped the temporal variation of the population activities in \( N \)-dimensional state-space onto a plane of the first two principal components (Nicolelis et al., 1995; Serruya et al., 2002): the neuronal trajectories of two waiting tasks ran almost in parallel, with the passage of time in the 4-s task moving at double the speed of the 8-s task (Figures 6A,B). This indicates that the neuronal populations represent the passage of time in a manner relative to the entire scheduled waiting-interval, \( T/S \), rather than the raw physical time, \( T \) (Figure 6C). For 100 sets of sample trajectories for 4- and 8-s tasks, we compared the preference to either the raw physical timescale or the relative timescale, which is determined by the shorter average distance in the two-dimensional plane connecting either \( T = 1, 2, 3, \) and 4, or \( T/S = 1/4, 1/2, 3/4, \) and 1. The majority of the sample datasets exhibited the preference for relative time coding (77/100 samples), indicating again that timing is gauged in the relative timescale (Chi-squared test, \( p < 0.01 \)).

**ANALYZING NEURONAL DATA BY ALIGNING AT THE ONSET OF MOVEMENT**

In the above, we have shown the results of analysis performed on population signals aligned at the onset of the cue signal. We also performed the same analyses on the data aligned at the time of key
release movement, in which case the time is measured retrogressively (Figure 7A). Here, we summarize quantitative results obtained by the data alignment at movement onset.

Average activity of neuronal population activities neither indicated prominent dependency on the time (Figure 7B). It is noteworthy that their variance decreased in time until approximately 1 s prior to the initiation of motor action (Figure 7C).

The accuracy of decoding time using the two kinds of time decoders did not exhibit any notable difference between the cue onset and the motion onset analyses. In the state-space analysis measuring the orbit distance in the plane of two principal components, we observed subtle differences: in the analyses of cue onset and the motion onset analyses. In the state-space analysis (Figure 6), the points connected by green arrows schematically represent trajectory of one trial. The colored ellipses represent their distributions, the N-dimensional state-space. A vector \( \hat{a} \), moves differently from trial to trial. The probability \( P(t | a_n) \) allotted to every elapsed time \( t \) given the population signals recorded at the actual time \( T \) (Eq. 1). (C) The decoding analysis provided two compelling conclusions with respect to the participation of the pre-SMA in interval timing. First, activity of the neuronal ensemble represents not only the lapse of time but also the scheduled waiting time-interval in each trial. These two pieces of information are necessary for an agent that determines the timing of action without receiving any information from external clocks. Second, the lapse of time is gaged in a manner scaled relative to the entire waiting time-interval, rather than in the raw physical timescale. Such representation of time is close to our naive sense of timing (Allan, 1979; Renoult et al., 2006; Brown et al., 2007).

In conventional neurophysiological analyses, neuronal correlates to the animal’s behavior are detected by superposing neuronal spike trains obtained from typically tens of repeated trials. The trial average is a standard method for removing high single-trial variability of the neuronal activity (Churchland et al., 2010). Here we adopted a method of population decoding in analyzing the neuronal activity in waiting time task. The knowledge that is added to the averaging

**FIGURE 1** | A device for decoding the elapsed time from neuronal signals. (A) Lapse of time in the waiting-interval and neuronal population activities. Neuronal spikes were recorded while monkeys held down a key longer than the pre-assigned waiting time-interval \( S = 4 \) s or \( 8 \) s. Population signals \( \hat{a}_n = [a_1, a_2, \ldots, a_N] \) are referred to as a set of firing rates or the numbers of spikes elicited from \( N \) neurons in a 1-s interval just before the elapsed time \( T \). (B) Schematic representation of neuronal population-activity trajectory in the N-dimensional state-space. A vector \( \hat{a} \), moves differently from trial to trial. The points connected by green arrows schematically represent trajectory of one trial. The colored ellipses represent their distributions, \( P(t | a_n) \) (Eq. 3). (C) The probability \( P(t | a) \) allotted to every elapsed time \( t \) given the population signals recorded at the actual time \( T \) (Eq. 1). For a given set of signals, the elapsed time \( t \) is conjectured as the time that rendered the highest confidence (Eq. 4).

**DISCUSSION**

In the present study, we developed a method for decoding time and applied it to neuronal population signals recorded in the pre-SMA. The decoding analysis provided two compelling conclusions with respect to the participation of the pre-SMA in interval timing. First, activity of the neuronal ensemble represents not only the lapse of time but also the scheduled waiting time-interval in each trial. These two pieces of information are necessary for an agent that determines the timing of action without receiving any information from external clocks. Second, the lapse of time is gaged in a manner scaled relative to the entire waiting time-interval, rather than in the raw physical timescale. Such representation of time is close to our naive sense of timing (Allan, 1979; Renoult et al., 2006; Brown et al., 2007).

In conventional neurophysiological analyses, neuronal correlates to the animal’s behavior are detected by superposing neuronal spike trains obtained from typically tens of repeated trials. The trial average is a standard method for removing high single-trial variability of the neuronal activity (Churchland et al., 2010). Here we adopted a method of population decoding in analyzing the neuronal activity in waiting time task. The knowledge that is added to the averaging
The present study has attempted to determine the timing of action from neuronal signals, under the assumption that the waiting task has already started. In considering real applications, it is equally important to know the task state itself, namely to determine whether or not the waiting task is currently running, as has been investigated by Achtman et al. (2007). It is worthwhile to examine the possibility of extending the present analysis into this direction.

The algorithms we implemented in this analysis are basic, and thus decoding efficiency can be improved by more complicated analyses. For the purpose of simply enhancing the capability in estimating time, we may consider introducing the Bayesian updating method that refers to the history of the neuronal states. As we were concerned with the neuronal time codes here, we attempted to determine time solely from neuronal population signals averaged over a short interval, without referring to its history. Even under this condition that limits the information to the activity in 1 s, it is still possible to overcome fluctuation by smoothing sequential states and selecting the essential signals as suggested for improving the current BCI/BMI technology (Nicolelis et al., 1995; Carmena et al., 2003; Lebedev and Nicolelis, 2006; Santhanan et al., 2006; Cunningham et al., 2009; Jacobs et al., 2009; Rickert et al., 2009; Bansal et al., 2011; Pillow et al., 2011). In the present analysis, we were rather free from such potential fluctuation as we used a small number of units that were already selected as being significantly task-related. In an actual situation in which signals are recorded from randomly sampled units that are not entirely correlated to the task, it would be worthwhile to consider introducing more elaborate techniques.

There has been a great deal of debate on the neuronal mechanisms of interval timing (Pillow et al., 2008; MacEw and Epstein, 2009). Although we have assumed here that timing is represented in the temporal modulation of the neuronal firing rate, there are other possible means that may account for determining a time-interval, such as assembling multiple oscillators (Miall, 1989, 1993; Matell and Meck, 2004), using delay lines (Fiala et al., 1996; Ivry, 1996) or observing complex neuronal states (Karmarkar and Buonomano, 2007; Számary and Izhikevich, 2009).

Rather than proposing a specific model, we propose here a hypothesis that will allow consistent comprehension of the experimental facts revealed in the present analysis: we focus on a fact that there are units that display both ascending and descending activities, and the firing frequencies of those different neurons are approaching similar values, as evidenced by the decrease in the deviation of firing rates among various units (Figure 2B). By aligning data at the time of movement onset, we observed that the frequency condensation is occurring approximately 1 s prior to the initiation of motor action (Figure 7A).

We wish to argue here a theoretical possibility of such frequency condensation for being related to movement initiation signal. It is noteworthy that frequency condensation of regular spike trains may induce coincidental occurrence of spike (Hopfield and Brody, 2001). Although interesting, this issue is based on firing regularity, which we found to be absent by using the metric of local variation (Shinomoto et al., 2003, 2009). If the units with ascending and descending activities consist of different types of neurons, such as excitatory and inhibitory neurons (Leon and Shadlen, 2003; Mongillo et al., 2008; Gavornik and Shouval, 2011), their frequency condensation must induce large modulation in outgoing signals. It has been argued that frequency condensation of excitatory and inhibitory neurons would be necessary for understanding the neural coding of movement initiation signals.
inhibitory neurons may facilitate rhythmic activity even in the presence of noise (Shimokawa and Shinomoto, 2006). Although we are not in the stage to narrow down to a single model to explain the present phenomena, there is room that the frequency condensation is related to an initiation of an action.

The present study demonstrated that an attempt to determine the timing from neuronal signals may provide insight for the neuronal mechanisms of gaging time, determining a given passage of time, and preparing and executing action. The estimation of the passage of time was possible even from dozens of neurons if they are selected from an appropriate brain region. In addition to providing a hypothesis for the neuronal coding of time, the present results also point to the possibility for developing devices that are capable of predicting the time for subjects to initiate voluntary action. Such devices may assist in the development of the BCI that provides signals for motor planning.

**MATERIALS AND METHODS**

**WAITING TASK AND RECORDING PROCEDURE**

Two Japanese monkeys (Macaca fuscata) were cared and trained to perform the “interval-generation task” designed in a former study (Mita et al., 2009). All procedures for animal care and experimentation were in accordance with the guidelines of the National Institutes of Health.

The monkeys were trained to hold down a key for longer than a pre-assigned time-interval that was selected from 2, 4, and 8 s. The required waiting-interval is instructed by the color of LED that was lit for the initial 2 s of the interval. In the present study, we analyze 4 and 8-s tasks that genuinely require estimating the time-lapse.

Neuronal firing data were obtained using a conventional single-unit recording method. Extracellular recordings of single-neuron discharges were made using a standard technique of transdural recording (Evarts, 1968). Glass-insulated Elgiloy-alloy microelectrodes, with impedances of 1.5–3 MΩ (measured at 1 KHz) were used. Up to two neuronal discharges were collected from a single recording using a window discriminator that produced a pulse for each valid spike that met both amplitude and time constraints (Bak and Schmidt, 1977). Extreme care was taken to sort out spikes belonging to each single-neuron, avoiding spurious contamination of spikes from other neurons. This was confirmed by real-time, high-speed monitoring of spikes on a computer display, which were triggered by each sorted pulses. The spiking signals were recorded while the waiting tasks were repeated dozens of times (ranges from 12 to 91 times, average 44). For the present analysis, we selected 25 units that were significantly task-related, exhibiting a significant modulation of the firing rate following the cue signals (the Wilcoxon signed rank test, \( p < 0.01 \)) from among 200 units in the pre-SMA examined in the former study under a less significant criterion (\( p < 0.05 \)).

**PROCEDURES FOR TIME DECODING AND ITS VARIATION**

We implement algorithms for decoding the lapse of time and applied them to the population signals. As neuronal signals are available here only from single-unit recordings, we construct virtual population signals by collecting single spike trains from individual neurons.
(3) Validate the capability of the time decoder by applying it to the test set of signals.

(4) Repeat (1) through (3) 100 times by randomly selecting test spike trains.

We attempt to estimate the lapse of time with an accuracy of 0.5 or 1 s, respectively, for a task involving waiting 4 or 8 s. It may appear difficult to achieve this accuracy using signals whose waiting times deviated on the same order. Nevertheless, an inference is drawn if decisions are made based on the majority of the population data. Here, we units \((N = 25)\) for each task of 4 and 8 s. The population signals are used for adjusting the decoder and validating the decoding capability in the following procedure.

(1) Extract single spike trains from individual units to construct a test set of population signals (one spike train from each neuron).

(2) Construct the time decoder by using the information of the mean and variance of the firing rates of the remaining spike trains, which were not used for the test set.

(3) Validate the capability of the time decoder by applying it to the test set of signals.

(4) Repeat (1) through (3) 100 times by randomly selecting test spike trains.

We attempt to estimate the lapse of time with an accuracy of 0.5 or 1 s, respectively, for a task involving waiting 4 or 8 s. It may appear difficult to achieve this accuracy using signals whose waiting times deviated on the same order. Nevertheless, an inference is drawn if decisions are made based on the majority of the population data. Here, we
First, we attempt to decode the lapse of time from unit signals recorded in each task having a scheduled waiting-time interval of 4 or 8 s; we implement an algorithm that allocates the probability to conjecture the elapsed times \( t \) given population signals (Figure 1C) using the Bayes theorem (Rieke et al., 1997; MacKay, 2003; Quiroga and Panzeri, 2009),

\[
p(t | a_r) = \frac{p(a_r | t) p(t)}{p(a_r)},
\]

show the method of analysis performed on virtual population signals constructed by aligning recorded spike trains according to the onset of the cue signal that informs the initiation of the waiting-interval. We have also tested the case of aligning data at the time of movement onset (Figure 7A), but the essential features remained the same.

Here, we refer to the “population signals” or “population activities” as a set of firing rates of \( N \) units measured in 1 s (equivalently, the numbers of spikes elicited in a 1-s interval) prior to the “elapsed time” \( T \) (Figure 1A). Accordingly, a vector representing the population activities moves in time \( T \) in the \( N \)-dimensional state-space (Figure 1B).

FIGURE 5 | Estimation of the elapsed time and the scheduled time-interval. (A) Distribution of the elapsed time \( t^* \) conjectured from samples that rendered the correct conjecture for the scheduled interval \( s = S \). (B) Percentage of hitting the correct scheduled time-interval, \( s = S \), given 100 test sample sets of population signals at every time \( T \). (C) The elapsed time was conjectured under the postulate that the scheduled waiting-interval \( s \) is different from the actual interval \( S \) (cases for incorrect postulate). Dashed lines represent the linear relationship between the conjectured \( t^* \) and actual \( T \) elapsed time, representing two different sets of relative timescales; \( t^* = 2T \) for \( s = 2S = 8 \) (left), or \( t^* = T/2 \) for \( s = S/2 = 4 \) (right). The average probability of hitting the relative timescale was 0.33, while that of hitting the physical timescale is 0.22.

DECODING THE ELAPSED TIME: TIME DECODER 1
First, we attempt to decode the lapse of time from unit signals recorded in each task having a scheduled waiting-time interval of 4 or 8 s; we implement an algorithm that allocates the probability to conjecture the elapsed times given population signals (Figure 1C) using the Bayes theorem (Rieke et al., 1997; MacKay, 2003; Quiroga and Panzeri, 2009),
where \( \tilde{a}_T \equiv (a_1^T, a_2^T, \ldots, a_N^T) \) represents the population activities of \( N = 25 \) units observed at the real elapsed time \( T \). Here, we divide the scheduled waiting time-interval of 4 or 8 s into 8 pieces, namely \( t = 0.5, 1, 1.5, \ldots, 4 \), or \( t = 1, 2, 3, \ldots, 8 \), and chose equal prior probabilities \( p(t) = 1/8 \). The denominator on the right-hand side is obtained by marginalizing joint probability,

\[
\rho(\tilde{a}_T) = \sum_T p(\tilde{a}_T | t) p(t).
\]  

The unit activities are mostly mutually independent at every \( T \), because the data are the collection of unit recordings obtained from independent trials, in each of which only one or two units were sorted out. Thus the probability of population activity is factorized into the probabilities of individual unit firing rates as

\[
p(\tilde{a}_T | t) = \prod_{i=1}^{N} p(a_i^t | t).
\]  

We further assume that the firing activity \( a_i^t \) for each unit had a Gaussian distribution with given average and variance computed from the training signals at each given time \( T \). Though the Gaussian distribution gives finite probability for the negative rate as an artifact, it gave the better prediction results than the Poisson distribution.
distribution, presumably because the data do not obey the Poisson distribution due to large across-trial variability. We fitted the Gauss and Poisson distribution functions to the distributions of the firing rates \(a_i\) recorded every second in 4-s task (\(T = 1, 2, 3, 4\)), for 5 units that were recorded most frequently (\(i = 1, 2, 3, 4, 5\)). It is plainly observed that the Gauss distribution is superior to the Poisson distribution in fitting the actual distribution (Figure 8).

The procedure to estimate the probability of conjecturing the elapsed times \(t\) is summarized as follows.

1. Construct the conditional probability distribution function \(p(a_t | t)\) according to Eq. 2, as a product of the Gaussian functions given by the information of the mean and variance of the firing rates.

2. Compute the marginal distribution \(p(a_t)\) according to Eq. 2, with \(p(t) = 1/8\).

3. Construct the function \(p(t | a_t)\) according to Eq. 1.

In presuming the elapsed time \(t\) at which population signals would have been recorded, we employ the maximum a posteriori (MAP) criterion, that is to choose a conjecture \(t = t'\) that rendered the highest confidence or \(p(t | a_t)\), or

\[ t' = \arg \max_t p(t | a_t). \quad (4) \]

**DECODING THE SCHEDULED TIME-INTERVAL AND THE ELAPSED TIME: TIME DECODER 2**

Second, we augment the algorithm so that it may decode not only the current elapsed time but also the scheduled waiting time-interval assigned in each trial solely from population signals (Figure 4A). This inference is obtained by allotting the probability to the combination of the conjectured elapsed time \(t\) and the scheduled waiting-interval \(s\). To allot equal prior probabilities to two tasks of different waiting-intervals, we evenly divide each total...
time-interval, \( s = 4 \) or \( 8 \) s, into the same number of pieces, namely, \( 8 \) pieces consisting of \( t = 0.5, 1, 1.5, \ldots, 4 \) for \( s = 4 \), and \( t = 1, 2, 3, \ldots, 8 \) for \( s = 8 \) (Figure 4B). In constructing the conditional probability,

\[
p(t|s, \tilde{a}_{t,s}) = \frac{p(t|s) p(s)}{p(\tilde{a}_{t,s})},
\]

we choose equal prior \( p(t, s) = \text{constant} = 1/16 \) for every combination of \( (t, s) \). Here in particular, we denote the population activities as \( \tilde{a}_{t,s} \) by specifying the real scheduled interval \( S = 4 \) or \( 8 \) in addition to the real elapsed time \( T \). The degree in which the firing signals contain information of the scheduled waiting-interval \( s \) is estimated by marginalizing the joint probability distribution (Figure 4C),

\[
p(s|\tilde{a}_{t,s}) = \sum_t p(t|s, \tilde{a}_{t,s}).
\]

In presuming the scheduled waiting-time interval \( s \) to which population signals would have belonged, we employed the MAP criterion again, that is to choose a conjecture \( s = s' \) that rendered the highest confidence \( p(s|\tilde{a}_{t,s}) \), or

\[
s' = \arg\max_s p(s|\tilde{a}_{t,s}).
\]

The conditional probability of the elapsed time \( t \) given the conjecture scheduled time-interval \( s \) can be obtained using Bayes' relation again as

\[
p(t|s, \tilde{a}_{t,s}) = \frac{p(t|s, \tilde{a}_{t,s})}{p(s|\tilde{a}_{t,s})}.
\]

In presuming the elapsed time \( t \) under an assumption that the scheduled time-interval is \( s' \), we employ the MAP criterion again, that is to choose a conjecture \( t = t' \) that rendered the highest confidence \( p(t|s', \tilde{a}_{t,s}) \), or

\[
t' = \arg\max_{t'} p(t|s', \tilde{a}_{t,s}).
\]

**VISUALIZATION OF NEURONAL TRAJECTORIES IN THE STATE-SPACE**

To analyze the dynamics of the population signals, we map the \( N \)-dimensional vector representing the population activities \( \tilde{a}_{t,s} \equiv (a_{1,t,s}, a_{2,t,s}, \ldots, a_{N,t,s}) \) into a lower-dimensional space using a dimensionality-reduction method based on principal component analysis (PCA; Nicolelis et al., 1995; Serruya et al., 2002). The process of performing the PCA analysis is summarized as follows.

1. Segment 4-s trials into \( 40 \times 0.1 \) s intervals, and 8-s trials into \( 40 \times 0.2 \) s
2. Compute mean firing rate \( \langle a_{i,t,s} \rangle \) averaged over all trials for each \( (i, t, s) \) unit in 1 s prior to the elapsed time \( T \).
3. Construct a set of vectors representing average population activities \( \langle \tilde{a}_{t,s} \rangle = \{(a_{1,t,s}, a_{2,t,s}, \ldots, a_{N,t,s})\} \).
4. For those 80 population vectors, we determine their most significant covariance using PCA.

Then, the population neuronal trajectory is mapped to each principal component axis by weight-summing the activities of individual units with the coefficients of unit eigenvector that corresponds to each principal component axis. Here we analyzed the neuronal trajectories in a plane of the first two principal components.

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