

# Synaptic dynamics and decision making

Gustavo Deco<sup>a</sup>, Edmund T. Rolls<sup>b</sup>, and Ranulfo Romo<sup>c,1</sup>

<sup>a</sup>Institució Catalana de Recerca i Estudis Avançats, Department of Technology, Computational Neuroscience, Universitat Pompeu Fabra, 08018 Barcelona, Spain; <sup>b</sup>Oxford Centre for Computational Neuroscience, Oxford, United Kingdom; and <sup>c</sup>Instituto de Fisiología Celular-Neurociencias, Universidad Nacional Autónoma de México, 04510 México D.F., Mexico

Contributed by Ranulfo Romo, March 1, 2010 (sent for review December 16, 2009)

**During decision making between sequential stimuli, the first stimulus must be held in memory and then compared with the second. Here, we show that in systems that encode the stimuli by their firing rate, neurons can use synaptic facilitation not only to remember the first stimulus during the delay but during the presentation of the second stimulus so that they respond to a combination of the first and second stimuli, as has been found for “partial differential” neurons recorded in the ventral premotor cortex during vibrotactile flutter frequency decision making. Moreover, we show that such partial differential neurons provide important input to a subsequent attractor decision-making network that can then compare this combination of the first and second stimuli with inputs from other neurons that respond only to the second stimulus. Thus, both synaptic facilitation and neuronal attractor dynamics can account for sequential decision making in such systems in the brain.**

ventral premotor cortex | attractor network | short-term memory | synaptic facilitation | vibrotactile

**D**uring decision making, we may need to compare stimuli that occur at slightly different times. A question therefore arises of how the first stimulus is remembered and is then compared with the second stimulus. One well-known paradigm for studying such decision making is the comparison of two vibrotactile stimuli applied sequentially (1–5). It is found in the ventral premotor cortex (VPC) that some neurons reflect the decision making itself, responding, for example, if the first vibrotactile stimulus ( $f_1$ ) applied to the hand is higher in flutter frequency than the second ( $f_2$ ), whereas other neurons respond to the decision  $f_2 > f_1$  [figure 2g–i in the article by Romo et al. (5)]. In addition to these neurons, others reflect the memory of  $f_1$ , as shown by the “partial differential neurons,” one of which recorded in the ventral prefrontal cortex (5) is illustrated in Fig. 1. These neurons respond to  $f_1$  during the presentation of  $f_1$ , do not respond in the first part of the delay period, and gradually ramp up toward the end of the delay period to a firing frequency that reflects  $f_1$  and then are influenced by  $f_2$  during the decision period when  $f_2$  is presented (5). The responses of these neurons may be related to the decision making (5), because, as shown in Fig. 1, if  $f_1 > f_2$ , the firing during  $f_2$  is higher than when  $f_1 < f_2$  for a given  $f_2$ . In this paper, we propose a synaptic mechanism that contributes to their response properties and introduce a theory of how they could be important in the decision-making process.

## Model

The main neurobiologically realistic approach to decision making is to use an attractor network, in which input 1, the evidence for decision 1, would be applied as a bias  $\lambda_1$  to population 1 of interconnected neurons encoding by their firing decision 1, and input 2, the evidence for decision 2, would be applied as a bias  $\lambda_2$  to population 2 of interconnected neurons encoding decision 2 (6–12) (Fig. 2B). These neurons compete via inhibitory interneurons, and one population wins the competition, which is enhanced nonlinearly by the positive feedback implemented by the recurrent collateral excitatory connections within each population. A problem arises in sequential decision making if inputs  $\lambda_1$  and  $\lambda_2$  are encoded by the same neurons, as is the case for the encoding of vibrotactile stimuli in the VPC. The neurons have firing rates that are linearly related to

the flutter frequency, and thus use a rate code to encode the flutter frequency. The problem arises that the neurons that respond to  $f_1$  (the first vibrotactile stimulus) and remember  $f_1$  after the delay period will also respond to  $f_2$ , such that their encoding of  $f_1$  is contaminated by  $f_2$ . This makes straightforward application of the standard attractor network model of decision making problematical, because  $f_1$  is not separately available from  $f_2$ . We propose here that the solution is to provide as inputs to the decision-making attractor network the combination input just described that reflects in the comparison period the combination  $f_1$  and  $f_2$  as in the partial differential neurons (5) and neurons that reflect  $f_2$  [which are present in the VPC during the comparison period (5)] and show how this can be achieved. We argue that it is inevitable, given the rate encoding with broad tuning of the neurons in the VPC to the vibrotactile stimuli, that  $f_1$  will be contaminated by  $f_2$  and that a solution of the type we propose is needed. Indeed, we argue that the partial differential neurons are fundamental to the solution of the decision-making problem by this brain region, and we analyze next how the responses of the partial differential neurons could be produced. We know of no previous theory of the mechanisms by which the partial differential neurons are produced, of the exact utility of these neurons in decision making, or of exactly how sequential decision making could be implemented when the same neurons code for the first and second stimuli.

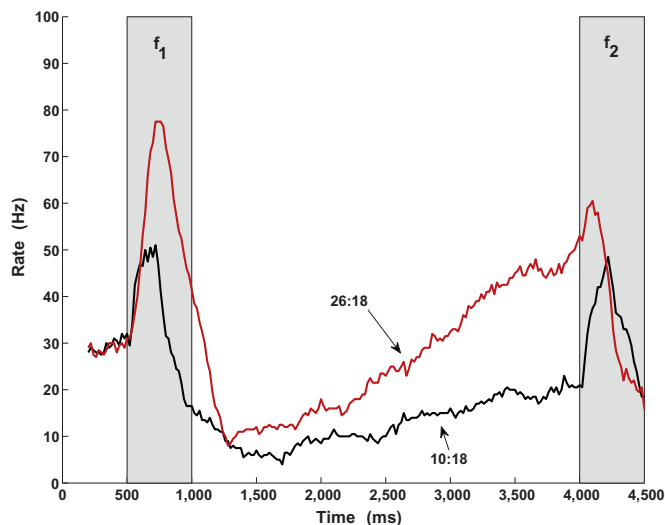
We model the partial differential neurons with the network shown in Fig. 2A using integrate-and-fire neurons as described in *SI Text*. There is a single population of neurons receiving inputs from the vibrotactile stimuli (the excitatory selective population in Fig. 2A) with excitatory interconnections that use short-term synaptic facilitation to implement the short-term memory of  $f_1$  during the delay period and continue to influence the firing during the comparison (decision) period. Short-term synaptic facilitation is used in the model, because the partial differential neurons do not continue their firing during the early part of the delay period (5) (Fig. 1). Thus, we suggest that a synaptic mechanism rather than neuronal recurrent connections to maintain the firing must be used in the brain, and the synaptic facilitation mechanism allows a graded effect that reflects the firing rate of  $f_1$  to be processed. Short-term synaptic facilitation is implemented using a phenomenological model of calcium-mediated transmission (13). We note that synaptic facilitation is caused by the increased accumulation of residual calcium at the presynaptic terminals, which increases the probability of neurotransmitter release (14). This type of synaptic facilitation is common in higher cortical areas, such as the prefrontal cortex (14–16), in contrast to early sensory areas in which depression is more usual (14). The synaptic efficacy of the recurrent connections between excitatory neurons is modulated by the utilization parameter  $u$  (the fraction of resources used), reflecting the calcium level. When a spike reaches the presynaptic terminal, calcium influx in the presynaptic terminal causes an in-

Author contributions: G.D., E.T.R., and R.R. designed research; performed research; analyzed data; and wrote the paper.

The authors declare no conflict of interest.

<sup>1</sup>To whom correspondence should be addressed. E-mail: rromo@ifc.unam.mx.

This article contains supporting information online at [www.pnas.org/cgi/content/full/1002333107/DCSupplemental](http://www.pnas.org/cgi/content/full/1002333107/DCSupplemental).



**Fig. 1.** Activity of a single neuron of the “partially differential” type recorded in the VPC during the vibrotactile decision-making task, after Romo et al. (5), as illustrated in figure 2 J–L of that paper. The  $f_1$  period was from 500 to 1,000 ms, there was then a delay period, and the  $f_2$  period when  $f_2$  was applied and this decision was made was from 4,000 to 4,500 ms.  $f_2$  was 18 Hz in both cases. When  $f_1$  was 26 Hz (red plot), the firing rate during  $f_1$ , at the end of the delay period, and during the comparison period when  $f_2$  was being applied was higher than when  $f_1$  was 10 Hz (black plot). Thus, the firing of this type of neuron during  $f_2$  helps in the decision that  $f_1 > f_2$  when  $f_1$  is 26 Hz and that  $f_1 < f_2$  when  $f_1$  is 10 Hz. Approximately 30 trials were used to generate these peristimulus time histograms for each pair for this single neuron.

crease of  $u$ , which increases the release probability of transmitter, and thus the strength of that synapse, as described in *SI Text*. The time constant of the decay of the synaptic facilitation is regulated by parameter  $\tau_F$ , which is experimentally around 1–2 s (16) [i.e., large enough to be able to sustain memory and allow comparison for short delays (3 s in our case)]. In addition, there is an excitatory nonselective population that enables us to show later that short-term memory recall toward the end of the delay period is selective for the neurons that were activated by  $f_1$  and that showed synaptic facilitation because of this activation.

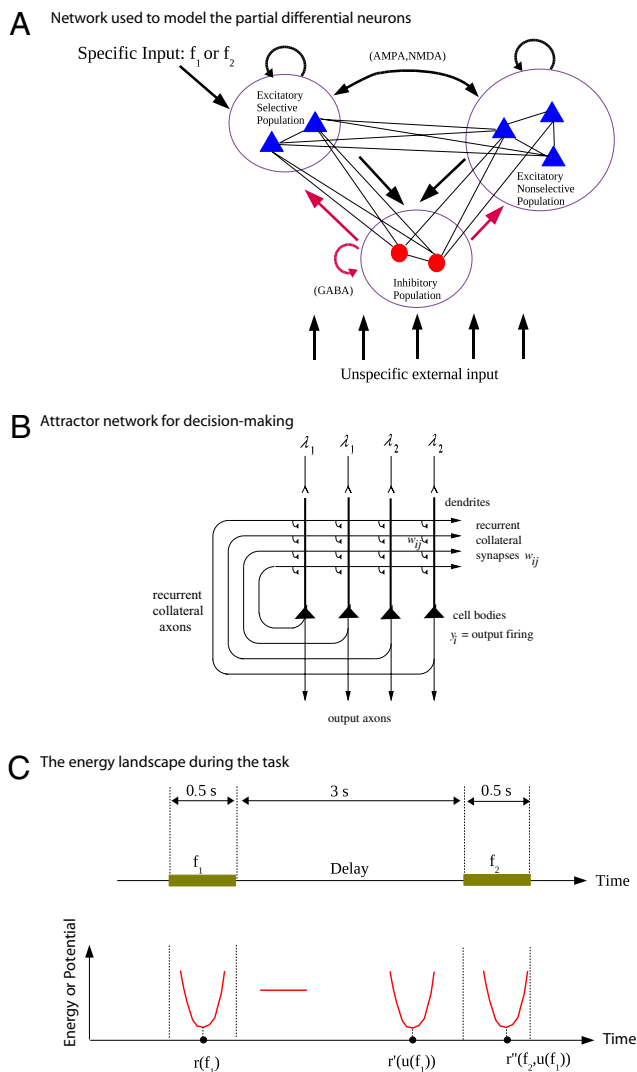
## Results

Fig. 2C shows the operation of this system. When a population of selective neurons is externally stimulated ( $f_1$  for 500 ms applied as  $\lambda_{stim}$ ), the network has an attractor evident as high firing activity of the selective population,  $r(f_1)$ , and low activity of the nonselective population. The firing rate of the selective population reflects the vibrotactile stimulation frequency being applied, as described previously. When the external stimulation  $f_1$  is removed, the attractor disappears, because the connectivity was designed such that only the spontaneous level of activity is stable. Nevertheless, during the presentation of the first stimulus,  $f_1$ , the synapses between neurons in the selective population were increased by synaptic facilitation. If an external nonspecific stimulation is then applied to all neurons in the network, the level of competition increases and the underlying differences in the facilitated synapses can be read out by the dynamics and result in the emergence of an attractor in the delay period corresponding to high firing activity,  $r'[u(f_1)]$  (Fig. 2C) of the selective population and low activity for the rest. (This nonspecific external input is obtained by linearly incrementing the external rate during the delay period from 2.4 kHz (per neuron, the sum of the number of spikes received over all synapses by the neuron) to reach 2.544 kHz after 3 s, and its time course is set to produce the time course of the effects found neurophysiologically in the VPC, as shown in Fig. 1. One way in which

such ramping activity, common in the prefrontal cortex during delay periods, can be produced is by the transition between different weakly coupled attractor states (17). The firing rate at the end of the delay period will reflect the vibrotactile frequency that was applied as  $f_1$ , as a result of the graded synaptic facilitation effect. After that, the second stimulus,  $f_2$ , is presented for 500 ms, and, again, an attractor corresponding to high firing activity,  $r'[f_2, u(f_1)]$ , of the selective population and low activity for the rest emerges (Fig. 2C). The resulting attractor shows a firing rate response that is a function of  $f_1$  and  $f_2$ , because the facilitated synapses in the selective population have a memory of  $f_1$  and the external input introduces a dependency on  $f_2$ . In this way, the neurons in the selective population show time-varying encoding, first of the external stimulus  $f_1$ , which reflects its memory (in a continuously graded form), and at the end of the delay period, during the presentation of the second stimulus,  $f_2$ , which reflects both  $f_2$  and the memory of  $f_1$ . The dynamics, as demonstrated by large-scale simulations, are explicitly shown in Figs. 3 and 4.

Fig. 3 shows for two cases (Left:  $f_1 = 10 < f_2 = 18$  Hz; Right:  $f_1 = 26 > f_2 = 18$  Hz) the temporal evolution of the firing rate (Fig. 3A) and the synaptic utilization,  $u$ , variable (Fig. 3B) in the selective population. The underlying spiking activity of 24 randomly chosen neurons of the selective population is also shown in the rastergrams for these two cases (Fig. 3C and D). When the first stimulus,  $f_1$ , is applied, an attractor showing high activity in the selective neurons builds up. Even more, the firing rate of the selective neurons encodes the different  $f_1$  stimuli, with higher firing rates for the higher vibrotactile frequencies (Fig. 3A). The synapses between the neurons in the selective population are also differently facilitated for the different vibrotactile frequencies  $f_1$  (Fig. 3B). This is very important because it establishes the basis of the encoding of a continuously graded memory that reflects by the firing rate the frequency of the vibrotactile stimuli. In fact, after applying a nonspecific linearly increasing external input (a learned attention signal) during the delay, the system is able to extract the underlying synaptic information and generate an attractor of high firing rate activity in the selective population, which encodes at the end of the delay the previously applied stimulus  $f_1$ . During the application of the second stimulus,  $f_2$ , the level of activity of the selective neurons (attractor) will depend on the synaptic history (i.e.,  $u(f_1)$ ) and on  $f_2$ . This can be seen explicitly in Fig. 3A and B, where the temporal evolution of the firing rate and synaptic utilization variable,  $u$ , for the 26:18 case is contrasted with the values obtained for the 10:18 case.

To characterize the encoding role of the selective neurons during the whole task, we performed simulations for different pairs of stimulus combinations  $f_1$  and  $f_2$ . In this set of pairs, trials can be divided into two types: those in which  $f_2 > f_1$  ( $f_2 = f_1 + 8$  Hz; black dots and regression lines in Fig. 4A–C) and those in which  $f_2 < f_1$  ( $f_2 = f_1 - 8$  Hz; red dots and regression lines in Fig. 4A–C). The difference of 8 Hz yields a level of performance of over 90% correct (both in the simulations and in the experiments). The simulations were run with 30 trials per stimulus pair. The stimulus pairs used were as follows: 10:18, 14:22, 18:26, 18:10, 22:30, 22:14, 26:34, 26:18, 30:38, 30:22, 34:42, and 34:26. The neuronal responses across trials are analyzed as functions of  $f_1$  and  $f_2$ . Each trial started with 500 ms without external stimulation (the spontaneous state), followed by stimulation with  $f_1$  for 500 ms, a delay period without stimulation from 1,000 ms until 4,000 ms, and then a comparison period of 500 ms during which the stimulus  $f_2$  was applied. We calculated the population firing rate of the selective neurons in time windows of 20 ms. Fig. 4 shows the results for the simulated data. Fig. 4A refers to the first stimulation period (from 500 ms until 1000 ms). Fig. 4B refers to the last 500 ms of the delay period (3,500–4,000 ms). Fig. 4C refers to the comparison period (4,000–4,500 ms). Data for Fig. 4A and B are displayed as a function of  $f_1$ ; data for Fig. 4C are displayed as a function of  $f_2$ . The selective neurons of the model show a strong  $f_1$ -dependent



**Fig. 2.** (A) Network of spiking integrate-and-fire neurons with synaptic facilitation between excitatory pyramidal neurons to model the “partially differential” neurons recorded in the VPC. The model implements a dynamic competition between different neurons that reads out the history of activation of the network through the underlying facilitated synaptic dynamics using a nonspecific external input applied to all neurons. The network contains excitatory pyramidal cells and inhibitory interneurons. The neurons are fully connected (with synaptic strengths as specified in *SI Text*). There are two different types of neuron population or pool: excitatory and inhibitory. There are two subtypes of excitatory pool, namely, selective and nonselective. The selective pool encodes the vibrotactile stimulation by its firing rate and corresponds to the partially differential neurons. The recurrent arrows indicate recurrent connections between the different neurons in a pool. The gray lines show the connections in the fully connected network. (B) Attractor or autoassociation single-network architecture for decision making. The evidence for decision 1 is applied via the  $\lambda_1$  inputs and that for decision 2 is applied via the  $\lambda_2$  inputs. The synaptic weights,  $w_{ij}$ , have been associatively modified during training in the presence of  $\lambda_1$  and at a different time of  $\lambda_2$ . When  $\lambda_1$  and  $\lambda_2$  are applied, each attractor competes through the inhibitory interneurons until one wins the competition, and the network falls into one of the high firing rate attractors that represent the decision. (C) Evolution of the energy landscape during the different phases of the experimental setup corresponding to a sequential vibrotactile discrimination task. The synaptic efficacy of the recurrent connections between excitatory neurons is modulated by the utilization parameter,  $u$  (the fraction of resources used), reflecting the calcium level, and  $u$  increases when a spike reaches the presynaptic terminal (*SI Text*). The red U-shaped symbols indicate that attractor-related firing is present, with a firing rate indicated below [e.g.,  $r(f_1)$ ]. When the population of selective neurons is externally stimulated by an external vibrotactile stimulus  $f_1$  for 500

response during the first stimulation period, which is lost when the stimulus is removed (as shown in the first part of the delay period). During the delay period, the selective neurons start to encode the memory of the first stimulus,  $f_1$ , because of the facilitated synaptic buffer that is read out by the competitive dynamics of the network driven by the slow increase of the nonspecific external signal. During the comparison period, the response is selective for the condition  $f_2 < f_1$ . (The error bars reflect the SD over the trials, and the lines demonstrate a linear fit).

The dependence of the firing rate response can be quantified by an arbitrary linear function of both  $f_1$  and  $f_2$  [i.e., assuming that the population rate  $r(t) = a_1(t)f_1 + a_2(t)f_2 + a_3(t)$ , the coefficients  $a_1(t)$  and  $a_2(t)$  serve as direct measurements of the firing rate dependence on  $f_1$  and  $f_2$ , respectively] (5). Fig. 4D shows the temporal evolution of these coefficients. This again reflects that selective neurons first encode the sensory stimulus  $f_1$ ; then, after suppression of this stimulus, during the delay period, they retain the memory of the previously presented stimulus  $f_1$  in the synaptic facilitation rather than in the firing rates; and, finally, during the presentation of the second stimulus,  $f_2$ , they encode the comparison. The simulations we describe capture accurately the responses of the neurons actually recorded in the VPC, an example of which is shown in Fig. 5.

The reason why the neuronal response is greater for the condition  $f_1 > f_2$  than for the condition  $f_1 < f_2$  for a given  $f_2$  during the comparison period (Fig. 4C) can be understood as follows. After the presentation of the second stimulus,  $f_2$ , the activity of the attractor network is clearly dependent on the value of  $f_2$ . However, because the synapses of the population receiving the external vibrotactile input for  $f_1$  are still in their facilitated state (and there is additional nonspecific activation being applied), the firing rate of the attractor also reflects the memory of  $f_1$ . That is, the attractor shows a high firing rate that depends on both  $f_1$  and  $f_2$  [i.e.,  $r'(f_2, u(f_1))$ ]. Having an attractor in which the selective neurons sensitive to the external vibrotactile stimulation show a high activity rate depending on  $f_1$  and  $f_2$  can be thought of as an attractor that is sensitive to the difference between  $f_1$  and  $f_2$  for a given frequency  $f_2$ . This can be understood using the linear correlation method utilized for the analysis of the neurophysiological experiments and the simulations (i.e., if the rate  $r = a_1f_1 + a_2f_2 + c$ , we can rewrite this as  $r = a'(f_1 - f_2) + b'f_2 + c'$ ) (Fig. 4D). Thus, the firing rate when  $f_2$  is presented reflects both the value of  $f_2$  and the difference between  $f_1$  and  $f_2$ . This explains the emergence of partial differential neurons (Fig. 4C). To be explicit, in the comparison period, the firing rate reflects the sum of  $f_2$  and the memory of  $f_1$ , and this sum is lower if  $f_1 < f_2$  than if  $f_1 > f_2$  for a given  $f_2$ .

The separate lines in Fig. 4C for the cases  $f_1 > f_2$  (red set of points) and  $f_1 < f_2$  (black set of points) show that these neurons convey information about the relative magnitudes of  $f_1$  and  $f_2$ . However, this information can only be read off from this population of neurons by taking into account the value of  $f_2$ . In

ms, the network has an attractor evident as high firing activity of the selective population,  $r(f_1)$ , and low activity for the nonselective population. When the external stimulation  $f_1$  is removed, the attractor disappears, because only the spontaneous state is stable in the absence of stimulation. At the end of the delay period, by applying an external nonspecific stimulation to all neurons in the network, the firing rate of the selective population,  $r'[u(f_1)]$ , will reflect the memory of the vibrotactile frequency that was applied as  $f_1$  as a result of the graded synaptic facilitation effect. After the delay period, the second stimulus,  $f_2$ , is presented for 500 ms, and, again, an attractor corresponding to high firing activity  $r'(f_2, u(f_1))$  of the selective population and low activity for the rest emerges. The resulting attractor shows a firing rate response that is a function of  $f_1$  and  $f_2$ , because the facilitated synapses in the selective population have a memory of  $f_1$  and the external input introduces a dependency on  $f_2$ .





with the firing of the  $f_2$  neurons, the decision taken will be in one direction if  $f_1$  is high in frequency relative to  $f_2$  and in the other direction if  $f_1$  is low in frequency relative to  $f_2$ . In effect, the partial differential neurons allow the value of  $f_2$  to be taken into account in making the decision, such that the attractor network can subtract the exact value of  $f_2$  from the decision reached and reflect just the difference between  $f_1$  and  $f_2$ . It is this functionality that effectively allows a decision plane between the parallel lines shown in Fig. 4C, and thus decisions that  $f_1 < f_2$  or  $f_1 > f_2$  be reached independent of the particular value of  $f_2$ .

## Discussion

If the partial differential neurons analyzed in this paper and the neurons in the VPC that respond only to  $f_2$  (5) are used as the two inputs to a conventional attractor decision-making network, that decision-making network will make the correct decision of whether  $f_1 > f_2$  or  $f_2 > f_1$ . The operation of this type of decision-making network for vibrotactile decision making has been analyzed by Deco and Rolls (7, 12), and neurons that reflect the operation of this decision-making network have been recorded in the VPC (5). The presence of these three types of neurons in the VPC (5) is consistent with the theory described in this paper of how they are all essential to decision making. Indeed, when the neurons in the decision-making system respond to both the stimuli to be compared but with a different firing rate to the two stimuli, the system described here is an efficient solution to how the decision-making process occurs.

We note that some neurons in the VPC respond with decreasing firing rates as a function of the vibrotactile flutter frequency (5), and according to our theory, these could produce partial differential neurons with lower activity when  $f_1 > f_2$ . We also suggest that the same mechanism described here could contribute to the auditory flutter decision making that is reflected in the firing rates of neurons in the VPC (18).

In any brain system in which the stimuli are encoded by the firing rates of the neurons (including flutter frequency and many

intensity/weight discriminations), sequential decision making is difficult, because the representation of the first stimulus is contaminated with the second stimulus, with which it must be compared. We have shown that if a population of neurons (e.g., partial differential neurons in the VPC) responds to a linear combination of the first and second stimuli, comparison by a decision-making network of this signal with a signal from other neurons that encode just the second stimulus (i.e., from neurons that do not have short-term memory) enables the correct decision to be reached about the relative values of the two stimuli. The relative values of the stimuli can be compared by the decision-making network independent of the magnitude of the second stimulus by attractor decision-making networks that account for many of the properties of the decision neurons in the VPC (7, 11). In the context of the two-stage process, we note that the simple use of an attractor decision-making network approach would need an input that reflects just  $f_1$  and another that reflects just  $f_2$ , and the former is not present in the VPC or in any rate-encoding system. In this scenario, the presence of the partial differential neurons described here, which provide a combined representation of  $f_2$  and  $f_1$ , provides an important, perhaps essential, way for this sequential decision making to be performed. Moreover, we have shown that synaptic facilitation provides a mechanism for remembering the first stimulus not only during the delay period but in the decision period. If different neurons code for the stimuli in a decision-making system, they can then be applied directly to the decision-making attractor network, as described by Rolls and Deco (12) in *The Noisy Brain: Stochastic Dynamics as a Principle of Brain Function*.

**ACKNOWLEDGMENTS.** We acknowledge funding from the Spanish Research Project BFU2007-61710, CONSOLIDER CSD2007-00012, and the Oxford McDonnell Centre for Cognitive Neuroscience. R.R. was supported by an International Research Scholars Award from the Howard Hughes Medical Institute and grants from the Dirección del Personal Académico, Universidad Nacional Autónoma de México, and Consejo Nacional de Ciencia y Tecnología, Mexico.

- Hernández A, Salinas E, García R, Romo R (1997) Discrimination in the sense of flutter: New psychophysical measurements in monkeys. *J Neurosci* 17:6391–6400.
- Romo R, Brody CD, Hernández A, Lemus L (1999) Neuronal correlates of parametric working memory in the prefrontal cortex. *Nature* 399:470–473.
- Romo R, Hernández A, Zainos A, Lemus L, Brody CD (2002) Neuronal correlates of decision-making in secondary somatosensory cortex. *Nat Neurosci* 5:1217–1225.
- Hernández A, Zainos A, Romo R (2002) Temporal evolution of a decision-making process in medial premotor cortex. *Neuron* 33:959–972.
- Romo R, Hernández A, Zainos A (2004) Neuronal correlates of a perceptual decision in ventral premotor cortex. *Neuron* 41:165–173.
- Wang XJ (2002) Probabilistic decision making by slow reverberation in cortical circuits. *Neuron* 36:955–968.
- Deco G, Rolls ET (2006) Decision-making and Weber's law: A neurophysiological model. *Eur J Neurosci* 24:901–916.
- Wong KF, Wang XJ (2006) A recurrent network mechanism of time integration in perceptual decisions. *J Neurosci* 26:1314–1328.
- Wong KF, Huk AC, Shadlen MN, Wang XJ (2007) Neural circuit dynamics underlying accumulation of time-varying evidence during perceptual decision making. *Front Comput Neurosci* 1:6.
- Wang XJ (2008) Decision making in recurrent neuronal circuits. *Neuron* 60:215–234.
- Deco G, Rolls ET, Romo R (2009) Stochastic dynamics as a principle of brain function. *Prog Neurobiol* 88:1–16.
- Rolls ET, Deco G (2010) *The Noisy Brain: Stochastic Dynamics as a Principle of Brain Function* (Oxford Univ Press, Oxford).
- Mongillo G, Barak O, Tsodyks M (2008) Synaptic theory of working memory. *Science* 319:1543–1546.
- Zucker RS, Regehr WG (2002) Short-term synaptic plasticity. *Annu Rev Physiol* 64:355–405.
- Hempel CM, Hartman KH, Wang XJ, Turrigiano GG, Nelson SB (2000) Multiple forms of short-term plasticity at excitatory synapses in rat medial prefrontal cortex. *J Neurophysiol* 83:3031–3041.
- Wang Y, et al. (2006) Heterogeneity in the pyramidal network of the medial prefrontal cortex. *Nat Neurosci* 9:534–542.
- Deco G, Ledberg A, Almeida R, Fuster J (2005) Neural dynamics of cross-modal and cross-temporal associations. *Exp Brain Res* 166:325–336.
- Lemus L, Hernández A, Romo R (2009) Neural encoding of auditory discrimination in ventral premotor cortex. *Proc Natl Acad Sci USA* 106:14640–14645.