

# Dynamic Neuronal Representation in the Prefrontal Cortex

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**Abstract** The present paper investigated the neural mechanisms underlying dynamic neural representation in the prefrontal cortex (PFC), which is thought to play a crucial role in flexible cognitive behavior. Neural representation is discrete or continuous according to the information to be encoded. The multistable attractor model is a plausible theory of flexible control of representation. Attractor states are dependent on functional connectivity in which neuronal subpopulations actively communicate with one another at any particular moment in time. We discussed new optogenetics tools to manipulate the state of local circuits to investigate dynamical neural function.

**Keywords** Prefrontal cortex • Attractor • Dynamics

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## 1 Introduction

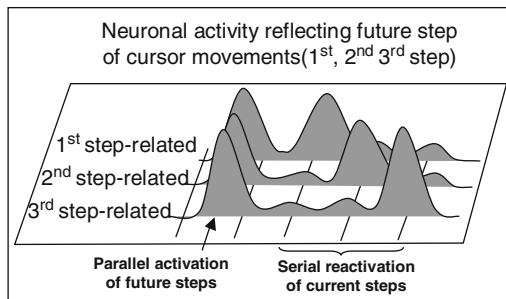
The brain interacts with the world through the body and creates representations of the internal state of the body and external state of the environment to cope with the ever-changing world in a flexible manner. Recent studies have revealed that the prefrontal cortex (PFC) plays a crucial role in flexible cognitive behavior by adaptively encoding various aspects of goal-directed behavior through cross-modal and cross-temporal integration according to a given behavioral context [1–4]. Adaptive representation depends on functional connectivity in which neuronal subpopulations constantly communicate with one another. Thus, it is important to understand the mechanisms underlying the dynamic processing of neural activity in local PFC circuits.

We investigated the neural mechanisms underlying flexible performance during cognitive tasks in non-human primates by analyzing the neuronal dataset using a representation-level approach to determine the information encoded by each neuron and a dynamic-system approach to describe the neural system as a state defined by a set of variables mapped in the state space over time [5–7]. The physiological variables measured included field potential, spiking activity, membrane potentials, and other quantitative physiological parameters. The representation-level and dynamic-system approaches are not mutually exclusive and represent two sides of the coin. We examined the neural mechanisms underlying flexible cognitive control by reviewing recent findings on representational and dynamic approaches. Moreover, we discuss the need for innovative research tools to study dynamic neural states in vivo. Optogenetics, a promising new tool, allowed us to manipulate the state of local circuits with high space–time resolution.

## 2 Dynamic Representation of Information

Neurons in the PFC are thought to be involved in an executive function by dynamically processing neural representations to cope with future demands in a prospective manner. Accumulating evidence indicates that prefrontal neurons not only hold external and internal information in a working memory but also transform online information from one type of behaviorally relevant information to another in a flexible manner [8–14]. These studies have suggested the existence of two types of representation: discrete and continuous. Our previous studies investigating PFC involvement in flexible mapping between goals and actions provide an example of dynamic representational changes in discrete information. Monkeys were trained to perform a path-planning task that required the use of two manipulanda to move the cursor from an initial position in a maze displayed on the computer screen to reach a given goal [10, 11, 14]. The goal was one of four peripheral positions in the maze that could be reached by various combinations of cursor movements. Several PFC neurons exhibited initial selectivity for the final goal and subsequent

**Fig. 1** Examples of discrete representation



selectivity for the immediate goal of the first action during the preparatory period [10, 11]. We also observed neuronal activity representing the first, second, and third steps of future actions during the late preparation period [14]. Three examples of PFC neuronal activity associated with the first, second, and third steps of the path-planning task are shown in Fig. 1. Each neuron exhibited a distinct response only for the preferred future action. Furthermore, many of these neurons were reactivated during the execution period of each step. Therefore planned future actions were represented in a parallel manner in advance and serially executed with stepwise re-activation of the PFC neurons.

Behavioral tasks requiring an association between different types of discrete representations often involve a transition between different classes of representation. For example, stimulus–response association task involves the transition between representations of sensory domain and motor domain.

In a recent paper [15], we described continuous representation with a graded magnitude of neural activity. Interval timing of an action is a continuous variable, but a particular interval is often specified in a discrete manner. The pre-supplementary motor area (pre-SMA) is located in the medial frontal cortex and is closely connected with the prefrontal areas. To investigate pre-SMA-encoded interval timing, we trained animals to perform a time-production task that required them to determine a hold time of three different intervals before initiating a key-release movement in response to three color cues on the computer screen. We found two types of responses in the pre-SMA: a ‘time-specific’ response that reflected the retrieval of a specific interval of time in response to a visual cue and a ‘time-graded’ response that exhibited decay or build-up changes in activity depending on the length of the interval (Fig. 2).

The time-specific discrete responses and time-graded continuous parametric responses contributed equally to the generation of interval timing. Continuous and discrete representations also appear to play a crucial role in decision-making. Gold and Shadlen [16] claimed that the neural process underlying decision making requires a continuous process of evidence accumulation and a binary decision by filtering continuous magnitude data with adjustable thresholds in their work using perceptual decision-making tasks. Furthermore, a study that compared two vibration frequencies in the frontal cortex during a decision-making task reported integration of discrete and parametric neural presentations [9].

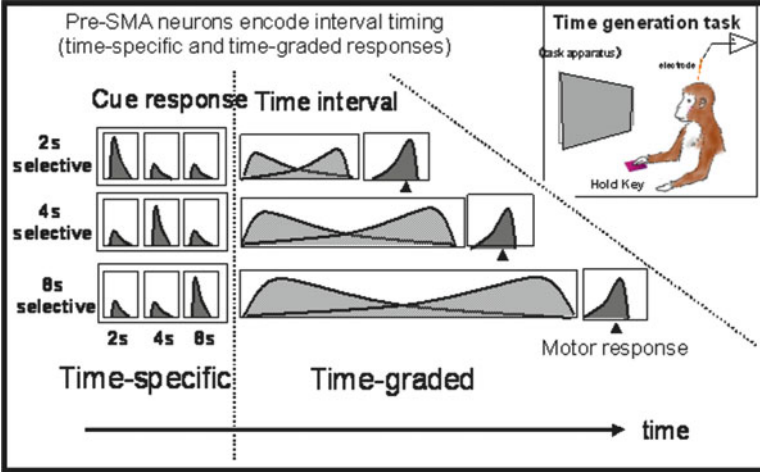


Fig. 2 Examples of parametric representation

### 3 Representations as Attractor States

Theoretically, the working memory-related persistent neuronal activity commonly observed in the PFC is thought to be an attractor state in that relatively small amounts of variation in this state lead it back to the same state [6, 17, 18]. Multiple attractors consist of ensembles of neurons with resting and active states such that a memory state can be represented by one state of attractors. This formulation is plausible insofar as a state of local circuits is dynamically stable in time. However, in real-time situations in the face of various behavioral demands, neural representations in one dimension at one epoch must be dynamically linked with different-dimensional representations at the next epoch to cope with various internal and external changes. Representations can be switched by reorganizing attractor states according to short-term changes in synaptic efficacy such as synaptic facilitation or depression. In this way, attractor states allow a neural system to work within different characteristic frames of reference corresponding to different types of representations. In our preliminary studies, we observed neural model-based dynamic multiple-attractor states that reproduce representational changes from goals to actions in the PFC. In this model, information in one modality is encoded by multiple attractor states of a neural population. When the attractor state is transformed into another state by short-term changes in synaptic efficacy, an overlapping but different cluster of neurons encodes information in that modality. Thus, the multi-dimensional information is represented as a different configuration of neurons, and short-term synaptic changes in local circuits contribute to maintain or shift attractor states in local circuits (i.e., synapse ensembles [19]). We believe dynamically reorganizable multi-attractor model can be applicable to flexible representational changes across multi-dimensional information observed in the PFC.

## 4 Local Circuits Underlying Dynamic Representation

Attractor states are maintained and modulated at different hierarchical levels in local neural circuits [17, 20]. (1) The intrinsic regenerative dynamics of single neurons involves positive feedback between membrane depolarization/spike discharges and active inward currents that can produce persistent activity outlasting a transient input current pulse. (2) Excitatory and inhibitory balance within inputs to dendrites of a single neuron and/or within a local circuit play an important role in the maintenance or switching of attractor states working within excitatory recurrent collaterals. (3) Cortico–cortical interactions contribute to the coordination of attractors by biasing weights of information flows within interconnected target areas. (4) Neurons in the various cortical areas are interlinked through multiple semi-open loops such as the thalamo–cortical loop, cortico–basal ganglia, and cortico–cerebellar loop. These loops may contribute to the selection, maintenance, and suppression of attractor states. Furthermore, changes in one hierarchical level may influence neural states in other levels. Contingent phenomena caused by an ensemble of neurons, such as oscillation of local field potentials, synchronous activities, and fluctuations in neuronal activities within local circuits, may influence the maintenance or reorganization of neural states. Until recently, the study of dynamic attractor states within cortical circuits has been difficult because an appropriate method to manipulate the state of local circuits with high resolution of space and time was not available.

## 5 Optogenetics as a New Tool to Manipulate Local Circuits

Optogenetics, a promising new tool for the assessment of neural states, uses a combination of genetic and optical methods to control targeted neurons by inducing inward or outward currents across stimulated membranes [21]. Recently, channelrhodopsin-2 (ChR2)-mediated photo stimulation of neurons has been used to investigate the state of neural networks in vivo. Preliminary results using transgenic rats expressing ChR2 in neurons demonstrated that optogenetic injection of the patterned oscillatory currents (opto-current clamp) caused state changes in local circuits [22]. Optically induced perturbation of local circuits are a useful method to study the mechanisms underlying attractor-state reorganization at the mesoscopic level.

## 6 Discussion and Conclusions

Transiently active ensembles of neurons dynamically represent relevant information in the cortical association areas including the prefrontal cortex. We classified representations into two types according to whether the information to be encoded

was a discrete (binary) or continuous (parametric) representation. Dynamic changes in representation are thought to reflect a multiple-attractor state, which is dependent on rapidly changing functional connectivity in the cell assembly. According to this idea, it is very important to intervene and evaluate the state of local circuits in vivo experiments of animals with high time and space resolution. Recent progress in bio-opto engineering including optogenetics has allowed us to optically manipulate the state of local circuits in the cortex while simultaneously electrically monitoring their activity. Innovative bio-optical methods for neuroscience will open new avenues for understanding neural dynamics.

## References

1. Fuster, J. M. "The Prefrontal Cortex, Fourth Edition" Academic Press. (2008).
2. Miller EK, Cohen JD. An integrative theory of prefrontal cortex function. *Annu Rev Neurosci.* 24(2001):167–202.
3. Duncan, J. An adaptive coding model of neural function in prefrontal cortex. *Nat. Rev. Neurosci.* 2(2001): 820–829.
4. Tanji, J., and Hoshi, E. Role of the lateral prefrontal cortex in executive behavioral control. *Physiol. Rev.* 88(2008), 37–57.
5. Haken, H. Principles of brain functioning: Berlin, Heidelberg, New York, Springer. (1996).
6. Amit DJ. Modeling Brain Function: The World of Attractor Neural Networks. Cambridge University Press. (1992)
7. Izhikevich EM. Dynamical Systems in Neuroscience The MIT Press (2010)
8. Rainer G, Rao SC, Miller EK. Prospective coding for objects in primate prefrontal cortex. *J Neurosci.* 19(13)(1999):5493–505.
9. Romo R, Brody CD, Hernández A, Lemus L. Neuronal correlates of parametric working memory in the prefrontal cortex. *Nature.* 399(1999):470–3.
10. Saito N, Mushiake H, Sakamoto K, Itoyama Y, Tanji J. Representation of immediate and final behavioral goals in the monkey prefrontal cortex during an instructed delay period. *Cereb Cortex.* 15( 2005):1535–46.
11. Sakamoto K, Mushiake H, Saito N, Aihara K, Yano M, Tanji J. Discharge synchrony during the transition of behavioral goal representations encoded by discharge rates of prefrontal neurons. *Cereb Cortex.* 18( 2008):2036–45.
12. Genovesio A, Tsujimoto S, Wise SP Feature- and order-based timing representations in the frontal cortex. *Neuron.* 63 (2009):254–66.
13. Tanji J, Mushiake H. Which object appeared longer? *Neuron.* 63 (2009):148–9.
14. Mushiake H, Saito N, Sakamoto K, Itoyama Y, Tanji J. Activity in the lateral prefrontal cortex reflects multiple steps of future events in action plans. *Neuron.* 50(2006):631–41.
15. Mita A, Mushiake H, Shima K, Matsuzaka Y, Tanji J. Interval time coding by neurons in the presupplementary and supplementary motor areas. *Nat Neurosci.* 12(2009):502–7.
16. Gold JJ, Shadlen MN. The neural basis of decision making. *Annu Rev Neurosci.* (2007) 30:535–74.
17. Wang XJ. Synaptic reverberation underlying mnemonic persistent activity. *Trends Neurosci.* 24(2001):455–63.
18. Rolls, E. T., Loh, M., Deco, G., and Winterer, G. (2008). Computational models of schizophrenia and dopamine modulation in the prefrontal cortex. *Nat. Rev. Neurosci.* 9, 696–709.
19. Buzsaki G. Neural syntax: cell assemblies, synapsembles, and readers. *Neuron.* 68 (2010):362–85.

20. Haider B, McCormick DA Rapid neocortical dynamics: cellular and network mechanisms. *Neuron*. 62(2009):171–89.
21. Zhang F, Aravanis AM, Adamantidis A, de Lecea L, Deisseroth K. Circuit-breakers: optical technologies for probing neural signals and systems. *Nat Rev Neurosci*. 8(2007):577–81.
22. Wen L, Wang H, Tanimoto S, Egawa R, Matsuzaka Y, Mushiaki H, Ishizuka T, Yawo H. Opto-current-clamp actuation of cortical neurons using a strategically designed channelrhodopsin. *PLoS One*.5(9) (2010) :e12893.

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