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Paradigmatic Working Memory (Attractor) Cell in IT Cortex

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We discuss paradigmatic properties of the activity of single cells comprising an attractor—a developed stable delay activity distribution. To demonstrate these properties and a methodology for measuring their values, we present a detailed account of the spike activity recorded from a single cell in the inferotemporal cortex of a monkey performing a delayed match-to-sample (DMS) task of visual images. In particular, we discuss and exemplify (1) the relation between spontaneous activity and activity immediately preceding the first stimulus in each trial during a series of DMS trials, (2) the effect on the visual response (i.e., activity during stimulation) of stimulus degradation (moving in the space of IT afferents), (3) the behavior of the delay activity (i.e., activity following visual stimulation) under stimulus degradation (attractor dynamics and the basin of attraction), and (4) the propagation of information between trials—the vehicle for the formation of (contextual) correlations by learning a fixed stimulus sequence (Miyashita, 1988). In the process of the discussion and demonstration, we expose effective tools for the identification and characterization of attractor dynamics.[1]

1 Introduction

1.1 Delay Activity in Experiment. A number of cortical areas, such as the inferotemporal cortex (IT) and prefrontal cortex, have been suggested as part of the working memory system (Fuster, 1995; Miyashita & Chang, 1988; Nakamura & Kubota, 1995; Wilson, Scalaidhe, & Goldman-Rakic, 1993). The phenomenon is detected in primates trained to perform a delay match-to-sample (DMS) task, or a delay eye-movement (DEM) task, using, in each case, a relatively large set of stimuli. It is observed in single-unit extracellular recordings of spikes following, rather than during, the presentation of a

[1] A color version of this article is found on the Web at:
http://www.fiz.huji.ac.il/staff/acc/faculty/damita

sensory stimulus. In these tasks, the behaving monkey must remember the identity or location of an initial eliciting stimulus in order to decide on its behavioral response following a second stimulus. This latter test stimulus is, with equal likelihood, identical to or different from the first stimulus in the DMS task and is simply a "go" signal in the DEM task. In these areas of the cortex, neurons are observed, in rather compact regions of the same area (called *modules* or *columns*), to have reproducible elevated spike rates during the delay period, after the first, eliciting stimulus has been removed.[2] Such elevated rate distributions have been observed to persist for long times (compared to neural time constants)—as long as 30 seconds. The rates observed are in the range of about 10–20 spikes per second (s^{-1}), against a background of spontaneous activity of a few s^{-1}. The subset of neurons that sustain elevated rates, in the absence of any stimulus, is selective of the preceding, first, or sample stimulus. Thus, the distribution of delay activity could act as a neural representation or memory of the identity of the eliciting stimulus, transmitted for later processing in the absence of the stimulus.

Moreover, in one experiment in which training was carried out with eliciting stimuli presented in a fixed order, it was observed that though the stimuli were originally generated to be uncorrelated, the resulting learned delay activity distributions (DADs), corresponding to the uncorrelated stimuli, were themselves correlated (Miyashita & Chang, 1988). That is, there was an elevated probability that the same neuron would respond with an elevated delay activity for two stimuli that were close in the sequence. In fact, the magnitude of the correlations expressed the temporal separation of the stimuli in the training sequence: the closer two stimuli were in the training sequence, the higher the correlation of the corresponding two DADs. (For a detailed discussion, see Amit, 1994, 1995; and Amit, Brunel, Tsodyks, 1994.)

1.2 The Attractor Picture. These experimental findings have been interpreted as an expression of local attractor dynamics in the cortical module: A comprehensive picture has been suggested (Amit 1994, 1995; Amit et al., 1994) that connects the DAD to the recall of a memory into a working status and views the DAD as a collective phenomenon sustained by a synaptic matrix formed in the process of learning. The collective aspect is expressed in the mechanism by which a stimulus that had been learned previously has left a synaptic engram of potentiated excitatory synapses connecting the cells driven by the stimulus. When this subset of cells is reactivated, they cooperate to maintain elevated firing rates in the selective set of neurons, via the same set of potentiated synapses, after the stimulus is removed. In this way, these cells can provide each other, that is, each one of the group, with an afferent signal that clearly differentiates the members of the group from

[2] A similar phenomenon has been observed in the motor cortex by Georgopoulos (private communication).

other cells in the same cortical module. Theoretical and simulation studies have demonstrated that this signal may be clear enough to overcome the noise generated by the spontaneous activity of all other cells, provided that not too many stimuli have been encoded into the synaptic system of the module. A large number of "correct" neurons must collaborate to sustain the pattern. A rough estimate is that about 1000–2000 cells would collaborate in a given DAD (Brunel 1994), out of some 100,000 cells in a column of 1 mm^2. There would be considerable overlap between DADs.

The collective nature of the DAD is related to its attractor property. Since so many cells collaborate, the DAD is robust to stimulus "errors." That is, even if a few of the cells belonging to the self-maintaining group are absent from the group initially driven by a particular test stimulus, or if some of them are driven at the "wrong" firing rates, once the stimulus is removed, the synaptic structure will reconstruct the "nearest" distribution of elevated activities of those it had learned to sustain. The reconstruction (the attraction) will succeed provided the deviation from the learned template is not too large. All stimuli leading to the same DAD drive activities in the basin of attraction of that attractor. Each of the stimuli presented repeatedly during training creates an attractor with its own basin of attraction (see Amit & Brunel, 1995). In addition, the same module can have all neurons at spontaneous activity levels, if the stimulus has driven too few of the neurons belonging to any of the stimuli previously learned.

1.3 Attractors and Learning Correlations. According to the attractor picture, attractors are established through the learning process. In experiments in which monkeys performed a DMS task using as many as 100 stochastically generated visual stimuli, selective delay activities were formed for all images repeatedly used in the training phase. This finding supports a dynamic interpretation for the delay activity and confirms the presence of a learning process, since it is rather unlikely that synaptic structures related to these stimuli had been generated prior to training. In fact, no associated delay activities were found for new images—not used during training—but introduced subsequently in the testing stage (Miyashita & Chang, 1988). Moreover, the correlations between DADs for sequentially appearing stimuli in the fixed training order, corresponding to uncorrelated images, are even more directly related to learning, inasmuch as these correlations are dependent on the particular fixed order in which the stimuli appeared in the particular training protocol. Learning these correlations presents a puzzle that is naturally resolved in the attractor picture: How does the information contained in one image (used as the first, eliciting, stimulus in one trial) propagate, in the absence of the image, until the next image in the sequence is presented, several seconds later, as the first stimulus in the next trial?

Attractors provide a natural vehicle for the propagation of this information (Griniasty, Tsodyks, & Amit, 1993; Amit et al., 1994; Amit, 1995), as follows: During training, there are initially no delay activity attractors. If

the stimuli in the training set are uncorrelated, as DADs are first formed they are necessarily uncorrelated because there is no way to communicate information between successive stimuli. Once the uncorrelated DADs have been formed, however, these DADs themselves may be used to propagate information between trials. Recall that in half of the trials, the second stimulus is identical to the first (so as to maintain an unbiased probability of same and different trials). This second stimulus may also leave behind a delay activity distribution, during the intertrial interval, identical to the DAD excited by the first stimulus, during the interstimulus interval of the trial. If this delay activity is not disturbed by the motor response of the animal (and other unmonitored visual or nonvisual events in the intertrial interval), then it may persist through the intertrial interval and will be present in the network when the next image in the sequence is presented as the first stimulus in the successive trial. This delay activity will be present in the sense that there will be a time window in which the cells of the delay activity are still at elevated rates, while the cells corresponding to the new stimulus begin to be driven. Information is then available for learning the correlation of the two (Brunel, 1996).

1.4 Experimental Questions. In this study, we outline an experimental program. We show recordings, and results of their analysis, from a paradigmatic cell—an IT neuron with a clear delay activity, which we were successful in holding for a long, stable recording session, sufficient for a detailed series of tests. Given the very detailed recordings of selective delay activities reported by Miyashita and Chang (1988); Miyashita (1988); Sakai and Miyashita (1991); Wilson et al. (1993); and Nakamura and Kubota (1995), on the one hand, and the detailed picture of attractor networks (Amit, 1994, 1995; Amit et al., 1994) on the other, one naturally asks what would be expected of a cell that participates in an attractor net. We ask the question in this article, and describe in detail the expected answer by demonstrating the results from this particularly rich paradigmatic neuron.

Our goal is not to present data that give a definitive answer to this question of whether IT delay activity reflects an attractor network serving stimulus image memory. For that we would have to record and analyze many cells from more than one monkey. We wish instead to raise the issues quantitatively and point out, by considering in detail data from a single example, what experiments need to be carried out and what behavior one must expect from neurons participating in an attractor neural net.

The central issue with which we deal is neuronal behavior following presentation of a degraded stimulus. This is because the attractor picture naturally implies basins of attraction for every attractor. That is, it predicts that although the input to IT will be different for stimuli of different degrees of degradation, the attractor, that is, the delay activity distribution within IT, will always be the same, as long as the degraded stimulus is not too far from

the original. Thus, the attractor theory predicts very different characteristics for the response of IT neurons during stimulation (reflecting the response driven by the input to IT) and the response following stimulation (reflecting the attractor state).

Testing empirically the attractor picture raises a set of issues:

1. IT observability. Are the stimuli used in these experiments identifiable at the level of the relevant cortical region, namely, IT? Do these stimuli induce neuronal responses in the recorded area that are clearly higher than spontaneous, as well higher than the delay activities? Are these responses different for the different stimuli?

2. Significance of prestimulus activity. Interstimulus interval (ISI) activity is identified in relation to activity immediately preceding the first stimulus of a trial. Is the latter merely spontaneous activity, or could it be delay activity following the second stimulus in the preceding trial? The question is particularly pertinent when trials are organized in series.

3. Moving in the space of IT-observable stimuli. What is the effect of stimulus degradation, for example, using degraded or noisy stimuli? What is the effect on visual responses (during the stimulus) and on attractor dynamics, as expressed in a given cell?

4. Basin of attraction. Does motion in IT-observable space bring about an abrupt change in delay activity?

5. Information transport between consecutive trials. Can delay activity act as the agent for the generation of correlations between sequentially appearing stimuli, as in Griniasty et al. (1993) and Amit et al. (1994)?

2 Methods

2.1 Preparation, Stimuli, and Task. A rhesus monkey (*Macaca mulatta*) was trained to perform a DMS task on 30 stochastically generated images, 15 fractals, and 15 Fourier descriptors; much as in Miyashita (1988) and Miyashita, Higuchi, Sakai, and Masui (1991), the two types were randomly intermixed. Three examples of the stimuli are shown in Figure 1: from left to right, two fractals and a Fourier descriptor. The left two images, the fractals, are the ones we used in recording most of the data reported here.

The behavioral paradigm was as follows. Following the appearance of a flickering fixation point on the monitor screen in front of the monkey, the monkey was to lower a lever and keep it in the down position for the duration of the trial (see Figure 2). After the lever was lowered and following

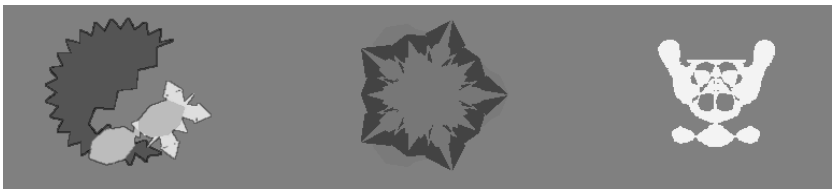


Figure 1: Three of the 30 color images used in the DMS experiments. (Left) Fractal stimulus, which induced the clearest delay activity for the neuron of Figure 3 (number 5 in the figure) and therefore called the best stimulus for this neuron. (Center) Fractal stimulus that induced delay activity indistinguishable from the average prestimulus activity, as demonstrated in Figure 3 (number 17 in the figure), and is therefore called the worst stimulus for this neuron. (Right) A Fourier descriptor type stimulus, which induced response 14 in Figure 3.

a 1000 ms delay, the first (eliciting, or sample) stimulus was presented on the screen for 500 ms. The ISI was 5 seconds. Following this delay, the second (test) stimulus was shown, also for 500 ms. This second test stimulus was the same as the first sample stimulus in half of the trials and different in the other half (chosen randomly from the other 14 stimuli of its type, fractal or Fourier descriptors). After the second stimulus was turned off, the monkey had to shift the bar left or right depending on whether the second stimulus was the same as the first or different, respectively, and then, when the fixation point stopped flickering, to release the bar. Correct responses were rewarded by a squirt of fruit juice (see Figure 2). The monkey had been trained to a performance level not less than 80 percent correct responses when the reported experiment took place.

2.2 Recording. We recorded extracellularly spike activity from single neurons of the inferotemporal cortex. The experiment is still in progress so we cannot give the histological verification of the recorded cell. However, the coordinates of the position of the guide tube were A14 L15 during vertical penetration into the ventral cortex. The experimental procedures and care of the monkey conformed to guidelines established by the National Institutes of Health for the care and use of laboratory animals.

After a cell was isolated by a six-channel spike sorter (Multi-Spike Detector; ALPHA OMEGA Engineering, Nazareth, Israel), the experiment proceeded in two stages. During the first stage, all 30 stimuli were presented one to three times. Average PST (peri-stimulus) response histograms were produced online, as demonstrated in Figure 3. From these, the best and worst stimuli were determined by eye. The best stimulus was that which evoked the clearest excess of the average rate in the ISI over the average rate in the period immediately preceding the first stimulus (the prestimu-

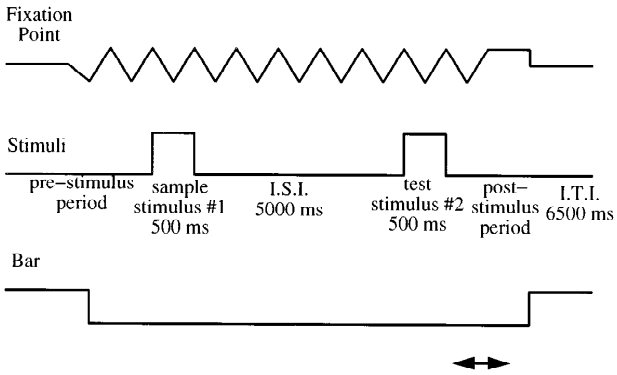


Figure 2: Schematic sequence of events in each phase of DMS task.

lus rate: stimulus 5 in Figure 3, corresponding to Figure 1, left). The worst stimulus was selected as one that produced an overall weak response and an indistinct difference between prestimulus and delay period firing rate (stimulus 17 in Figure 3, corresponding to Figure 1, center). At this stage, the prestimulus firing rate was interpreted naively as the average activity in a 1.0 second interval prior to the presentation of the trial's first stimulus.

For the second stage of the experiment, a new image set was created from the chosen best and worst stimuli. The red-green-blue (RGB) pixel map of each image was degraded by superimposing uniform noise at one of four levels. That is, we generated from each of these two images a set of five images: the pure, original one (referred to as degradation 0) and four degraded images, each at an increasing level of degradation (levels 1–4). The DMS task was then resumed, using as the first (sample) stimulus in the DMS task a randomly selected image from the new set of 10 (original and degraded) images. The second stimulus, the test image, was randomly selected as an undegraded version of either the best or the worst stimulus. In Figure 4 we reproduce the best stimulus and degraded versions of this image at each of the four degradation levels used in this second stage of the experiment.

2.3 Mean Rate Correlation Coefficient. In order to test various hypotheses concerning the structure and origin of persistent activities, we introduce a coefficient measuring the correlation of the trial-by-trial fluctuations of the mean firing rates—or spike counts—in two different intervals. The mean rate correlation (MRC) is defined as follows: x_n and y_n ($n = 1, \ldots, N_{st}$—the total number of selected trials) are, respectively, the spike counts in two

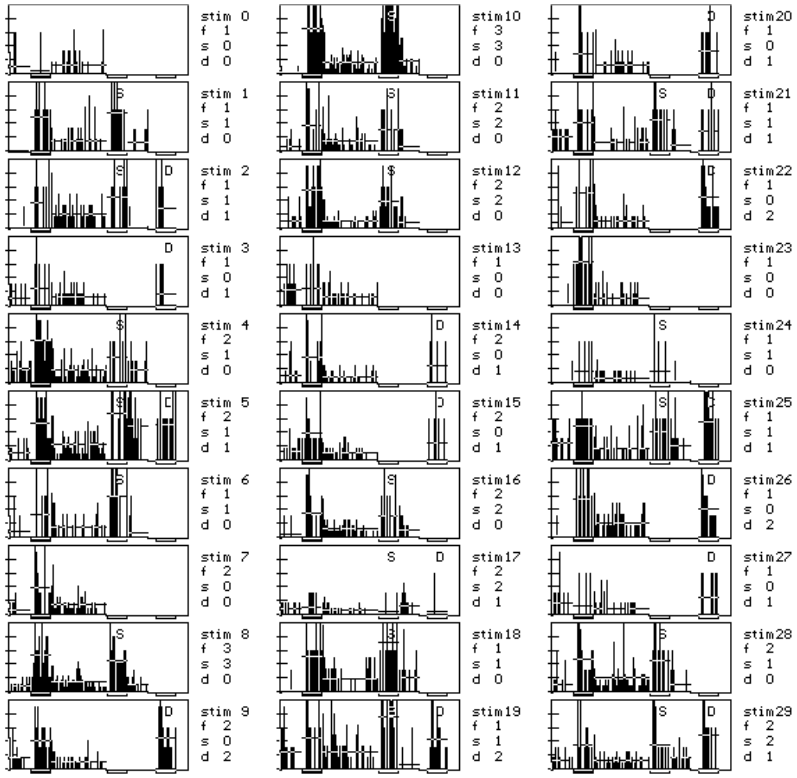


Figure 3: Spike rate histograms (full scale = 50 s^{-1}) for a small number of trials of the entire set of 30 color stimuli, used online for the selection of best and worst stimuli. Each window is divided into six temporal intervals; the neuron's activity is binned and averaged for the different trials with the same stimulus. From left: Prestimulus interval (66 ms per bin for the 1000 ms just prior to the first stimulus of the trial); first, or sample, stimulus period (33 ms per bin for 500 ms); delay (ISI) interval (125 ms per bin for 5 sec); second, or test, stimulus period (showing the response for the one-half of the trials when the stimulus was the same as the first; 33 ms per bin for 500 ms); post–second stimulus interval (showing the activity when the second stimulus was the same as the first; 66 ms per bin for 1000 ms). Finally we show the response to the second stimulus of other trials (when the first stimulus was not that of this window, but the second stimulus was that of this window (so that the trial was a nonmatch trial; 33 ms per bin for 500 ms). The horizontal line over each interval is the average rate in the interval. On the right of every window are stimulus number, number of trials with this image as first stimulus (f); number of trials with the same stimulus as second stimulus in the cases of same (s) and different (d) trials. Best is stimulus 5, the one evoking the highest excess of the average rate in the ISI over the average prestimulus rate; worst is stimulus 17, the one having an overall weak response. Vertical ticks are 10 spikes / sec.

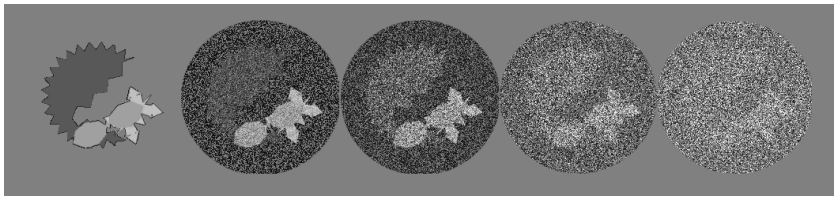


Figure 4: Image degradation (in color) as gradual motion in stimulus space for testing the attractor dynamics of delay activity. From left to right: pure best image (0 noise), then four levels of noise on RGB map.

intervals in the nth trial. Then:

$$MRC = \frac{\langle (x - \langle x \rangle)(y - \langle y \rangle) \rangle}{\sqrt{(\langle x^2 \rangle - \langle x \rangle^2)(\langle y^2 \rangle - \langle y \rangle^2)}} \tag{2.1}$$

where $\langle \cdots \rangle$ denotes the estimate of the expectation of a random variable performed over all the selected trials, that is,

$$\langle x \rangle = \frac{1}{N_{st}} \sum_{i=1}^{N_{st}} x_i.$$

This coefficient measures the extent of the correlation between the deviations from the mean over the selected set of trials, of the spike counts in each of the two intervals. With this tool, we monitor whether high rates during visual stimulus presentation imply high rates in the delay period and low imply low, whether high (low) counts at the beginning of a delay period imply high (low) counts in later intervals in the delay, and whether high (low) counts following a given second stimulus are related to high (low) counts in the period immediately preceding the first stimulus of the succeeding trial, its prestimulus interval.

The value of the MRC is in the interval $[-1, 1]$. The standard of comparison for the magnitude of this coefficient will be established by considering subclasses of trials in which the average rates in both intervals are both high or both low. For instance, the MRC of the subset of responses to the worst stimulus is calculated by performing the expectation of equation 2.1 over the trials in which the worst stimulus was presented as a sample. In this case, if the fluctuations about the mean spike count are random and hence uncorrelated, the MRC coefficients will set the scale for lack of correlation. As we shall see, large values of MRC can capture two different phenomena: (1) trial-by-trial correlation of the fluctuation of the individual counts about their mean and (2) the existence of subsets of trials with very different mean counts in each, while within each subset, fluctuations about the mean may even be uncorrelated.

3 Experimental Testing and the Special Cell

The issues raised in section 1.4 will now be discussed in the same order in terms of the responses of a single IT cell. The intention is not to claim that the data presented here give a definite answer to these questions. That would require the recording and analysis of many cells and, traditionally, in more than one monkey. The objective, rather, is to raise the questions, the problems, and the potential answers by considering in detail the record of a particularly rich cell that exhibits behavior in relation to which we may pose most of the problems and demonstrate the form answers may take. Following continued recording from numerous neurons in this and another monkey, we will be able to report whether this area of IT may in fact serve this memory function for DMS tasks. Alternatively, we may report that too few IT neurons have the expected significant DAD activity to be able to serve this function under the conditions used in our experiment, and it would be best to look for such DADs elsewhere. Finally, we may find that delay activity is present in IT but does not generally have the properties we expect (and which are reported here for this single cell), so that our understanding of cortical dynamics should best be revised.

3.1 Identification of the Stimulus. Delay activity distributions are likely to be sustained by the synaptic structure, learned or preexisting. The fact that the delay activities are selective to the preceding stimulus implies that the synaptic structure can sustain a variety of distributions in the absence of a stimulus. Which of the stable delay activities is actually propagating depends on which was the last effective stimulus. But different stimuli presented on the monitor screen may not actually lead to different neuronal responses in deep structures (higher cortical areas) such as the IT cortex, since the differences may well be filtered out at afferent levels. It is the representation of the stimulus as it affects the cells of IT that is relevant for which of the DADs is excited or learned. Thus, for example, it may be that differences of scale or color in the external image may result in very similar distributions of afferents when arriving at the IT cortex. In that case, they cannot elicit different DADs. In other words, stimuli and stimulus differences must be IT observable. (For some recent work on observability of stimulus variation in IT, see Kovacs, Vogels, & Orban, 1995.)

What can give rise to different DADs are significantly different distributions of synaptic inputs that arrive from previous cortical areas to IT. These distributions, in turn, can be observed by recording the neuronal activity in the attractor network during presentation of the stimulus. In fact, the IT cortex is particularly propitious in this respect because rates observed during the presence of the stimulus in visually responsive cells that participate in a DAD are much higher than those observed for the same cells during interstimulus intervals of the trial. (See, e.g., Miyashita & Chang, (1988), and responses in the underlined intervals in the histograms for best stimu-

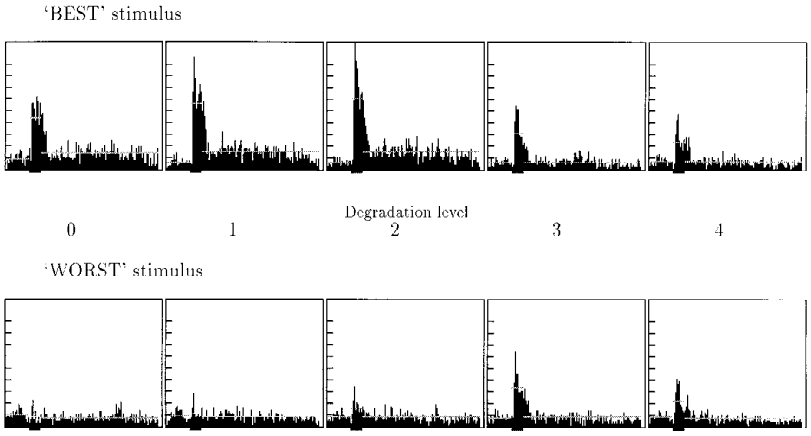
lus in Figure 5.) This allows a very clear identification of the stimulus, for comparison with the attractor. In other cortical areas, such as the prefrontal cortex, this may not be as clear (see, e.g., Wilson et al., 1993; and Williams & Goldman-Rakic, 1995).

The range of responses during the stimulus and during the ISI, as in Figures 3 and 5, exhibits IT observability of the stimuli as well as of their differences. Thus, the stimuli used for this experiment, the 30 fractals and Fourier descriptors, are IT observable in that the responses to some of them are much higher than the background spontaneous rates, as well the rates during the delay period ISI. This difference from background will be measured quantitatively below. In addition, it is clear that our neuron also differentiates between stimuli (e.g., between the best and the worst stimuli) during and following the stimulation.

3.2 Delay Activity and Spontaneous Activity. It is quite common to consider the ongoing activity before the first stimulus (the prestimulus activity) in a given cell as spontaneous activity. Delay activity is considered significant if its rate is significantly higher than the prestimulus rate. In this way, one observes in Figure 5, in the first three windows on the left of the best stimulus row, that the average rate (the horizontal line) during the delay (the last, wide interval) is higher than in the prestimulus interval of the current trial (see the numbers in the table below the histograms). They become equal in the two windows on the right (see section 4). In the leftmost window of the best row of histograms, corresponding to the undegraded best stimulus, the ratio ISI / pre-stim rates is 13 / 8, which may not be considered very convincing as a signal-to-noise ratio.

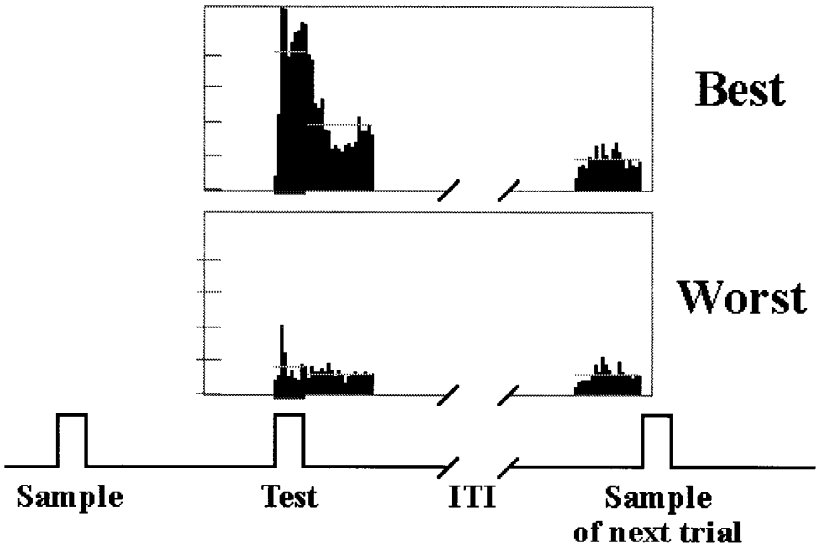
But in a context in which delay activities exist, prestimulus rates are not necessarily spontaneous. For example, if the second stimulus in a trial evokes a DAD when presented as a first stimulus and if the neuron being observed has an elevated rate in this DAD, then one would expect that following the second stimulus, this neuron would have an elevated rate. In fact, this is observed in Figure 6, where we plot histograms of spike rates that follow presentation and removal of the best (top) and the worst (bottom) stimuli as second stimulus. These histograms are averages over all trials at all levels of the first stimulus degradation, since the second stimulus is always undegraded. What one observes is that following the best second stimulus, the level of post–second-stimulus persistent rate is as high as the delay activity for the first three levels (0–2) of degradation in Figure 5 (no degradation and the next two levels of degradation). This is true even when the first stimulus, due to its degradation, does not provoke significant delay activity. It is consistent with the fact that this persistent activity is provoked by the second stimulus that is never degraded.

Another expression of the same fact is presented in Figure 7. These are the trial-by-trial distributions of the post–second stimulus average rate for best



Stim	Trial no	Prestim	Stim1	ISI1	ISI2	ISI3	ISI4	ISI5	total ISI
B0	12	8.6+ 1.0	46.3+ 3.0	17.3+ 1.9	12.3± 1.3	13.8± 0.7	12.3± 1.6	9.6± 1.9	13.1 ± 0.8
B1	12	5.7± 0.9	60.8± 5.4	20.9+ 2.3	15.8+ 1.1	14.4+ 1.3	12.6± 1.6	8.7± 1.3	14.5 ± 0.9
B2	12	5.3± 1.2	67.8⊥ 4.8	21.6⊥ 1.6	15.6⊥ 1.3	13.3± 1.9	12.0± 1.0	9.3± 1.3	14.3 + 0.8
B3	12	5.5± 0.5	33.2± 2.7	8.8± 1.4	5.5⊥ 0.7	8.5⊥ 2.0	4.2⊥ 0.6	3.0± 0.8	6.0 ± 0.6
B4	13	6.7± 0.9	25.0± 1.6	9.9± 0.8	6.5± 0.8	5.8± 0.9	4.2± 0.6	4.6± 0.7	6.2 ⊥ 0.3
W0	13	9.6+ 1.1	8.0± 1.2	6.7± 0.8	5.5± 0.7	6.5± 0.8	8.9± 1.4	4.3± 0.6	6.4 ± 0.4
W1	13	8.1+ 1.1	10.6+ 1.3	8.0± 0.8	9.1± 1.0	7.4± 0.5	6.2± 1.1	4.7± 1.1	7.1 ± 0.5
W2	12	7.5+ 1.0	17.2+ 1.9	9.2+ 1.0	8.8+ 1.0	6.2+ 0.9	6.1± 1.0	5.7± 0.6	7.2 ± 0.5
W3	12	7.0⊥ 1.2	34.8± 2.6	11.8± 1.3	7.3+ 1.3	6.3+ 1.0	4.8+ 0.9	4.9± 0.8	7.0 ± 0.5
W4	12	7.4± 0.9	23.7⊥ 2.9	10.7⊥ 0.9	5.5⊥ 0.8	5.5± 0.7	4.4± 1.0	4.3+ 0.9	6.1 + 0.5

Figure 5: Testing attractor dynamics: spike rate histograms (rate scale 10 s^{-1}, bins 50 ms) for best (top row) and worst (second row) first stimulus, each original, and four levels of degradation. Each histogram is divided into three intervals. From left: prestimulus of the current trial, first stimulus, delay interval. The horizontal line over each interval is average rate in the interval. The value of the average rates for each interval is reported in the table below the histograms with the mean rates and the standard errors (in s^{-1}). The delay interval (ISI) has been divided in five parts of 1 s each. The mean rate of the activity during the entire ISI is in the last column on the right. For both best and worst first stimulus, one observes a variation of the rate during stimulation (the visual response) as a function of the level of degradation. For the first three windows in the "best" row, there is significant invariant delay activity. In the last two levels of degradation, the delay activity drops and becomes indistinguishable from the delay rate for the "worst" stimuli. The rate in the first second of the ISI, following a strong visual response, is significantly higher than the mean rate of the delay interval. This is due to the latency of the external stimulus. (See section 3.5.)



Stim	Trial no	Stim2	Post-stim	Pre-stim (Next trial)
B0	62	44.7± 1.3	18.5± 0.8	8.6± 0.5
W0	61	8.2± 0.5	5.7± 0.4	5.7± 0.4

Figure 6: Testing information transmission across trials: spike rate histograms for best and worst second stimulus and the corresponding table of mean rates (as in Figure 5). The histogram windows are divided in four intervals: second stimulus (underlined), postsecond stimulus, central part of intertrial interval (invisible), and the prestimulus of the successive trial. Note that the prestimulus activity of the trial following best second stimulus is significantly higher than that following the worst second stimulus. It carries the information about the second stimulus of the previous trial (see the text and Figure 7).

and worst stimuli (plotted above and below the axis, respectively, though both are positive valued, of course).[3]

The distributions differ significantly according to the T-test: $P(\text{Tst}) < 10^{-5}$. If this elevated rate were to continue beyond the monkey's behavioral response, it would arrive at the following trial as an elevated rate and appear

[3] In calculating the average poststimulus rate, we take an interval starting 250 ms after the second stimulus is turned off, to exclude latency of response to the stimulus. (See section 3.5.)

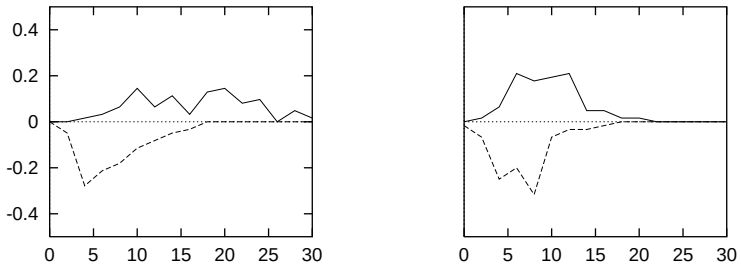


Figure 7: Trial-by-trial rate distributions of post–second stimulus (left) in s^{-1} and pre–first stimulus of the next trial (right) for best (continuous line) and worst (dashed line, for clarity in negative values). The two distributions differ significantly in the second case, carrying the information about the second stimulus of the trial. The poststimulus interval is on average 710 ms, starting 250 ms after the stimulus, to avoid latency effects.

as an elevated prestimulus activity before the next trial. There are previously reported indications that delay activity does in fact survive motor reaction events (Nakamura & Kubota, 1995), though here there is a novelty in that the postreaction activity is not motivated by the behavioral paradigm. As a test of this possibility we separated the average prestimulus rates over the entire set of trials ($N = 123$ trials) into two sets, according to the preceding second stimulus (see Figure 6). It turns out that the average prestimulus rate in the group of trials following trials in which the second stimulus was the best stimulus ($N = 62$) is 8.6 s^{-1} while for those following trials where the second stimulus was the worst stimulus ($N = 61$), the average prestimulus rate is 5.7 s^{-1}. (This difference is significant according to the T-test: $P(\text{Tst}) < 10^{-5}$.) Yet another test of this effect will be discussed in section 3.6.

A simple tool suggests itself for improved online monitoring of the relevant prestimulus activity: to reduce (though not fully eliminate) the effect of persistent post–second stimulus high rate, one should consider the average prestimulus activity over all trials, including all stimuli. This will help, provided the number of DADs in which the cell under observation participates is relatively low. That would be the typical case.[4] (See also Miyashita & Chang, 1988.)

3.3 Attractor Dynamics. Attractor dynamics (associative memory) as a description of persistent DADs implies that each DAD is excited by a whole class of stimuli. Each of these stimuli raises the rates of a sufficient number of cells belonging to the DAD so that via the learned collateral synaptic ma-

[4] We are indebted to Nicolas Brunel for this observation.

trix, they can excite the entire subset of neurons characterizing the attractor and maintain them with elevated rates when the stimulus is removed. The class of stimuli leading to the same persistent distribution is the basin of attraction of that particular attractor. As one moves in the space of stimuli, at some point the boundary of the basin of attraction of the attractor is reached. Moving even slightly beyond this boundary, the network will relax either into another learned attractor or to the grand attractor of spontaneous activity. (See Amit & Brunel, 1997; and Amit, 1995.)

To test the validity of the attractor picture one has to be able to do the following:

1. Move in the space of stimuli by steps that are not too big, so that there is a choice between staying inside the basin and moving out. Recall that moving in this space does not mean only changing the stimuli, but changing them in a way that is IT observable.
2. Find IT-observable changes in stimuli and have the delay activity unchanged.
3. Arrive at IT-observable changes in stimuli that will go over the edge (i.e., will not evoke the same DAD).

A convincing demonstration of these phenomena would require recording a large number of cells, especially since most cells with high rates in the same DAD (corresponding to the same stimulus) are predicted to lose their rates together. The prototypical behavior of such cells expresses itself on our single cell. First, Figure 5 demonstrates the required motion in stimulus space at the level of the IT cortex. In the five windows for the best stimulus as well as in those for the worst, going from left to right, corresponding to increasing the degradation level as presented in Figure 4, there is a clear variation in the visual response: the neuron's spike rate during stimulation. This implies that the choice of the degradation mode is an IT-observable motion in stimulus space, as required in point 1 above.

Second, in the top three windows in the best stimulus row, the delay activity is essentially invariant, as would have been expected if the stimulus were moving within the basin of attraction of that DAD. This corresponds to point 2 above.

Third, as the level of degradation increases to reach the right-most two windows for the best stimulus, the delay activity disappears (see Figure 5). The average rate in the delay period becomes that of the reduced prestimulus activity discussed above, in accordance with the expectation in point 3 (see the table in Figure 5). This rate is also the same as that during the delay in all five windows corresponding to the worst stimulus.

The discussion of point 1 calls for a comment concerning the fact that as the best image is initially degraded, the visual response increases. Only in the fourth and fifth levels of degradation (3, 4) does the visual response decrease. This may seem contradictory, in that one might naively expect

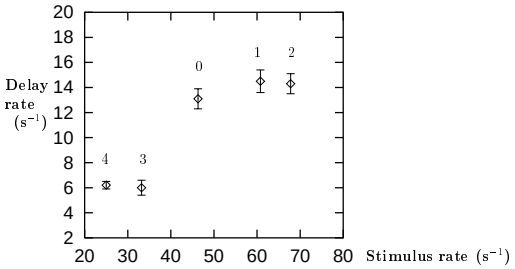


Figure 8: Average delay activity rate (in s^{-1}, *y*-axis) versus average stimulus response (in s^{-1}, *x*-axis) for five levels of degradation of best stimulus. The degradation level is indicated above each data point (0 for pure image). Error bars are standard errors. Note that the stimulus response difference between 1 and 0, where delay activity is essentially constant, is larger than between 0 and 3, where delay activity collapses. Recall that 0 implies pure stimulus.

that the visual response should be maximal for the pure image and decrease monotonically with degradation. But on second thought, it should be clear that there is no reason that a particular cell should be maximally tuned to the image rather than to a degraded version of it. In fact, looking at other cells, we find that although there is not a strong systematic trend for the visual response as a function of the degradation level, on the average the visual response decreases with degradation. Nor is there any argument why there should be (Yakovlev, Fusi, Amit, Hochstein, & Zohary, 1995). What is essential is that there be a set of neurons that have a strong visual response and a corresponding significant elevated delay rate, and when the images change moderately, the delay activity remain invariant and when they change enough, the delay activity change abruptly. Our paradigmatic cell would have belonged to such a class had it existed.

This cell gives yet two more strong signals of the attractor property. Looking at the visual response to the degraded best stimulus in decreasing order of rates suggested above (2–1–0–3–4), one observes in the table in Figure 5 and in Figure 8 that the rate difference from 1–0 is 14.5 $s^{-1}$and there is no noticeable change in delay activity. Yet going from 0–3 the visual response changes by 13.1 s^{-1}, and the delay activity collapses. In other words, the decrease in the delay activity seems precipitous, as a function of the visual response, as would befit a watershed at the edge of the basin of attraction.

The second signal is related to the fact that in the images used for testing the attractor property (see Figure 4), as the degradation noise is introduced, a circle appears around the figure (for technical reasons). This might have been perceived by the monkey as a different stimulus. That is, as the figure gets increasingly blurred, it is the circle that is most visible. Yet the delay ac-

Table 1: Correlations of Delay Activity in Subintervals of ISI

First Stimulus Selection	Degradation Levels	Time Intervals	Number of Trials	MRC
B+W	0-1-2	ISI1-ISI5	74	0.399
B	0-1-2-3-4	ISI1-ISI5	61	0.382
B	0-1-2	ISI1-ISI5	36	0.080
B	3-4	ISI1-ISI5	25	−0.123
W	0-1-2	ISI1-ISI5	38	0.089

Note: The intervals are the first 1 second following the removal of the stimulus and the last 1 second of the delay interval.

tivity for the first three degradation levels (0–2) of the best stimulus remains unchanged with the appearance of the circle. The delay activity disappears when the degradation level crosses the critical level, despite the continued presence of the circle. Moreover, the circle produces no effect for the worst stimulus, despite the fact that it is visible there as well. This may be interpreted as due to the fact that the degradation circle appears only during testing and is not seen often enough to have been learned.

3.4 Delay Interval MRC. To test the attractor interpretation more closely, we calculated the MRC (see section 2.3) between the average rates in the 1 second immediately following the first stimulus and the 1 second immediately preceding the second stimulus. The results are summarized in Table 1. In a subset of trials with best and worst first stimuli and the first three degradation levels (0–2) we find MRC $= 0.399$. Note that in this subset of 74 trials, there are 36 trials with elevated delay activity and 38 with low delay activity. In other words, the high MRC may be attributed to the presence of two underlying subpopulations with different means. Similarly, in the subset of trials with best first stimuli and all degradation levels (second row in the table), there are 61 trials, of which 36 have elevated delay activity and 25 do not, and MRC $= 0.382$.

The 61 trials with best first stimulus are then divided into two subsets: one for the first three degradation levels ($N_{st} = 36$) and one for the last two ($N_{st} = 25$). In the first subset there is elevated delay activity; there is none in the second. For these two subsets we find MRC $= 0.080$ and -0.123, respectively. We conclude that the average delay rates in the first subset of trials remain high throughout the ISI and low in the second set. The deviations from the mean in each subset, at the beginning and the end of the ISI, are uncorrelated. This constitutes an example of the first option described at the end of section 2.3 and provides scales for high and low correlations.

Table 2: Single Neurons versus Attractor Dynamics: Correlations Between Visual Response and Several 1-Second Intervals of the ISI

First Stimulus Selection	Degradation Levels	Time Intervals	Number of Trials	MRC
B	0-1-2	ST1-ISI1	36	0.407
B+W	0-1-2-3-4	ST1-ISI1	123	0.784
B	0-1-2	ST1-ISI4	36	0.085
B	0-1-2	ST1-ISI5	36	−0.098

Note: First two rows have high MRCs due to latency of visual response. No correlation in later intervals.

3.5 Single Neurons versus Attractors Dynamics. An alternative scenario to the attractor picture may attribute the enhanced delay activity to some change in the internal state of single cells. Such a scenario would imply that the change in the internal state of the cell is triggered by the level of the visual response. This would be required to make the persistent delay activity stimulus selective. It would further imply a correlation between the rate during the ISI and the rate during the visual response. Table 2 summarizes the MRCs between the visual response to the first stimulus and various 1 second intervals of the ISI. We find that the rate during the visual response to the first stimulus is correlated with the rate in the first 1 second interval of the ISI (MRC $= 0.407$), even in a subset of trials with stimuli all leading to elevated delay activity, that is, the 36 trials corresponding to the best stimulus at degradation levels 0–2. This high MRC in a trial set with a narrow distribution of rates indicates that the trial-by-trial fluctuations of the rate in the first 1 second of the ISI are correlated with the fluctuations in the rate during the visual response. In fact, if the effect of splitting the means is added, by computing the MRC of the visual response rates with the rates in the first 1 second of the ISI for all trials ($N_{st} = 123$), we find MRC $= 0.784$. These high correlations we associate with the latency of the visual response. In fact, it appears from Figure 5 that the visual response penetrates about 250 ms into the ISI.

Next we take the same set of 36 trials (best with degradation 0–2), which gave MRC $= 0.407$ between the rate in the visual response and the rate of the first 1 second of the ISI. The MRCs between the rate of the visual response and the rate in the fourth and fifth 1 seconds of the ISI are 0.085 and –0.098, respectively (third and fourth rows in the table). We conclude that beyond the first second of the ISI, the fluctuations of the visual response are not correlated with the fluctuations of the delay activity. This makes the single-cell scenario rather implausible.

3.6 Information Transmission Across Trials. The discussion in section 3.2 of the meaning of prestimulus activity provides a partial confirmation of the scenario of information transport between first stimuli in consecutive trials, essential for the formation of the Miyashita correlations (Miyashita, 1988). That scenario requires that information about the coding of one stimulus be able to traverse the time interval between consecutive trials. The scenario proposed (Griniasty et al., 1993; Amit et al., 1994; Amit, 1995) is that DADs, when they first become stable, are uncorrelated. When they are stable, they would be provoked as much by a (same) second stimulus in a trial as by the first one. Since the second stimulus in half of the trials is the same as the first (to prevent bias in the DMS paradigm), in half of the training trials the activity in the intertrial interval will be the same as the delay activity elicited by the first stimulus of the preceding trial. If training is done by a fixed sequence of first stimuli, then upon half of the presentations of a given first stimulus, the activity distribution in the IT module, in the intertrial interval, would be the same as the delay activity corresponding to the immediately preceding first stimulus. The joint presence of the delay activity of the previous stimulus and the activity stimulated by the current first stimulus is hypothesized to be the information source for the learning, into the synaptic structure, of the correlations between the delay activities corresponding to consecutive images.

We calculated the MRCs between the average rate in the 1 second immediately following the second stimulus and the average rate in an interval of 1 second immediately preceding the successive first stimulus (see Table 3). The idea is that since (for technical reasons) we do not have recordings during the entire interval separating two trials, if the activity between trials were to be undisturbed by the monkey's response, to arrive at the next first stimulus, the MRC of the activities in the two extreme subintervals between trials should be similar to that between the two extreme subintervals in the undisturbed ISI. In fact, MRC $= 0.320$ for the intertrial interval performed over all the available trials ($N_{st} = 123$). The entire set of trials is composed of two well-balanced subsets with two different intertrial mean rates. This is so because the second stimulus is never degraded, so for $N_{st} = 62$ the second stimulus is a pure best image, leading to high intertrial persistent activity, and for $N_{st} = 61$ of the trials, the preceding second stimulus is the pure worst image, leading to low intertrial activity.

This value is compared with the MRCs of extreme ISI intervals in trial subsets of similar statistics, with balanced subsets of low and high averages. Those would correspond to the first and second row in Table 1. In fact, the numbers are close. If the 123 trials are separated into two subsets—one with preceding best and one with preceding worst—we find MRC $= 0.038$ and MRC $= 0.120$, respectively (rows 2 and 3 in Table 3). These would be naturally compared with MRCs of subintervals of trials with best and worst first stimulus, with degradation levels (0–2) (third and fifth rows in Table 1) that are, respectively, 0.080 ($N_{st} = 36$) and 0.089 ($N_{st} = 38$).

Table 3: Information Transmission Across Trials: MRCs of 1 Second Post–Second Stimulus and 1-Second Pre–Next First Stimulus

Second Stimulus of Previous Trials	Time Intervals	Number of Trials	MRC
B+W	POST and PRE	123	0.320
B	POST and PRE	62	0.038
W	POST and PRE	61	0.120

Note: For a few trials, the time interval after the second stimulus is less than 1 second; for those trials, the mean rate is calculated over the available time interval. First row: the high MRC is due to presence of two different means. Last two rows: absence of correlation in unimodal subsets of trials.

4 Discussion

The cell we have discussed presents a rich phenomenology, naturally interpreted in the learning-attractor paradigm. To establish the various characteristics of attractor dynamics and their internal structure, many more good recorded cells are required. Our underlying intention has been to exploit this cell merely as an example of the kind of features that a cell participating in a presumed attractor scenario may have. Looking back at the wealth of data drawn from this cell, we feel we can say more. This collection of data can hardly be accounted for in other paradigms suggested to date.

Most prominent of these is the propagation of the persistent elevated rates following the test stimulus, after this matching stimulus is turned off, and even after the behavioral reaction is completed. The amount of data collected for this cell and the tools we have sharpened to analyze them leave no doubt that this propagation can indeed take place. In fact, we have found that this persistent activity is as robust when it crosses the intertrial interval (including the behavioral response) as it is crossing the ISI delay interval between sample and match. What is surprising is that following the second stimulus and the reaction, there is no apparent need for maintaining the active memory. One might have expected that the persistent activity distribution would die down at this point. It does not. This has been observed also by Nakamura and Kubota (1995), but the novelty here is that the delay activity continues to persist even when there seems to be no functional role for it. What seriously modifies the delay activity is a new visual stimulus—either the second stimulus following the ISI or the first in another trial, much as in Miller, Li, and Desimone (1993).

The fact that a DAD can get across the intertrial interval is an essential pillar in the construction of the dynamic learning scenario for the generation of the Miyashita (1998) correlations in the internal representations (working

memory) of stimuli often experienced in contiguity. Our single-cell result suggests that such correlations may find their origin in the arrival of selective persistent activity related to one stimulus at the presentation of the consecutive stimulus in the next trial.

The collective attractor picture would have been fuller had we had a case in which there is no visual response and yet elevated delay activity. In Sakai and Miyashita (1991) such cases are shown. Yet the mean rate correlation analysis on this cell shows that neural activity during the delay period is correlated with the visual response only in the immediate interval following the stimulus—strong evidence that what determines the actual spike rate later into the ISI is beyond the single cell. It is most likely the result of the interaction of this cell with other cells that participate in the same DAD, via potentiated synapses.

Finally, there is an additional, behavioral correlate to the activity of this cell. When the performance level (percentage correct responses) of the monkey is considered versus the level of stimulus degradation, averaged across experiments, it is found that the performance is similar for the first three levels of degradation. Then, for the fourth and fifth levels, performance drops abruptly to chance level, just as our cell indicates that the stimuli are not now in the basin of attraction of the DAD (Yakovlev et al., 1995). This effect calls for much further study, and it opens new vistas toward identification of a potential functional role of the delay activity. Sakai and Miyashita (1988) turned to the pair associate paradigm because the monkeys perform the DMS task well even for stimuli that do not generate delay activity ("new stimuli"). Here we see that in the absence of delay activity, the DMS task was not performed successfully if the sample stimulus was very degraded.

Our paradigmatic cell suggests that the mechanism that allows matching to an identical new sample may not work when the monkey has to match to a very degraded image. Yet as long as the DAD (the attractor) is effective, it corrects for the degradation, by attracting to the prototype delay activity, and the task can be performed.

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Without the experimental and intellectual contribution of Shaul Hochstein and Ehud Zohari, this article would not have been possible. Had we had it our way, both would have figured among the authors. We have benefited from the contribution of Gil Rabinovici to the experiment. This cell was found during his stay in our lab as a summer project in his course of premedical studies at Stanford University. We are also indebted to J. Maunsel and R. Shapley for help in the early stages of this experiment and the detailed comments of Misha Tsodyks. This work was partly supported by grants from the Israel Ministry of Science and the Arts and the Israel National Institute of Psychobiology and by Human Capital and Mobility grant ERB-CHRX-CT93-0245 of the EEC.

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