aligned (see electron micrograph).

Crystals of nanocrystals are not new. Indeed, it has been known for some time that, under appropriate conditions, narrow size distributions of particles will self-assemble into ordered structures. What is new about this work is the level of control demonstrated, and the implications are many. For example, if the particles are in sufficient proximity that their electronic wave functions overlap, then the array will develop a unique electronic structure. In solid-state terminology, controlling this interaction is analogous to manipulating the width and shape of the energy bands of the extended solid. Such control is relatively commonplace for one-dimensional superlattices but is unheard of for the three-dimensional case.

The authors point out that their techniques should be applicable to nearly any particle system, provided that techniques for producing sufficiently narrow size distributions can be found. For the special case of metal nanocrystals, recent work indicates that narrow size distributions may not even be necessary (*10*). The dispersional attractions between metal particles are relatively strong and scale geometrically with particle size. This leads directly to size-dependent phase separations followed by superlattice formation, all within a single step.

The superlattice structures discussed in this issue represent only a first step toward putting quantum crystals into complex environments. Many applications envisioned for quantum dots are device-oriented, single-particle tasks that have various wiring, geometry, and insulation requirements. The development of techniques for the parallel construction of such devices remains a major challenge.

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Ensemble Activity and Behavior: What's the Code?

Sam A. Deadwyler and Robert E. Hampson

The brain processes enormous streams of temporally and spatially varying information within anatomically precise networks, by reading a poorly defined spatiotemporal code (*1*). Single-electrode recordings can determine both the firing rate of individual neurons and the correlation of this rate with sensory and behavioral events, but such perievent histograms reveal only small bits of the activity in the brain. This approach to understanding the neural basis of cognition and behavior is like trying to decipher a video image one pixel at a time while the video image constantly changes: Only as one views many pixels does the image become apparent. For this reason, large-scale neuronal recordings are necessary to examine activity in ensembles of neurons (*2*) and to understand how the brain processes behaviorally relevant information.

Much of our thinking about networks and ensembles in the mammalian brain has come from studies of single-electrode recordings of neurons obtained serially, in moderate to large numbers, within the same experimental context. The recordings are then combined and analyzed, post hoc (*3*). Such reconstructed ensembles reveal recurring temporal firing patterns associated with specific sensory stimuli. This approach is analogous to restarting the video (one hopes at exactly the same place) over and over again and observing a different pixel each time, eventually reconstructing the video image after a sufficient number of pixels have been serially processed. Such studies show that ensembles of 50 to 100 neurons can uniquely encode a finite number of input features (*3*). Because such analyses are by necessity reconstructed, they provide only indirect evidence that the neural activity driving behavior is distributed among coherent neurons (*4*). Nevertheless, most models of decision-making by neural networks assume such a distribution (*5*).

Although problematic, this approach has been productive. Georgopoulos (*6*) provided the initial evidence that populations of neurons in the motor cortex of the monkey encode information better than single neurons. In ensembles that code the direction of limb movement, a derived intention vector predicted limb movements more accurately than individual neurons. Studies by Schultz *et al.* (*7*) showed temporally distinct firing of different types of neurons in the monkey striatum during a task, such that the combined ensemble suggested that the triggering of one cell by another could temporally link the different phases of the task.

Technical developments now allow direct recording of ensemble activity in behaving animals: These include (i) multielectrode fabrication techniques (*8*), (ii) multichannel (10 or more) recording of extracellular neural spike data in awake behaving animals (*9*), and (iii) appropriate statistical analysis (*10*). Although implementation of this new technology is in its infancy, several new findings have emerged. Wilson and McNaughton (*11*) recorded from 100 neurons in rats that were exploring a novel environment. They observed a tight correspondence between place-field firing and movement trajectories (*6*), although the pattern of firing in these neurons could have reflected the animal's presence in, rather than a movement toward, a particular location (*12*).

It is essential to use appropriate statistical analyses to identify what kind of information is actually encoded by ensembles during behavioral events (*13*). Nicolelis *et al.* (*14*), recording from large ensembles of neurons, demonstrated that interaction between sensory receptive fields for whisker movement is widespread and is likely to involve most of the whisker-projection area of the cortex and thalamus. Using principal components and factor analysis of ensemble firing, they found that sensory receptive fields consisted of both temporally and spatially distributed firing patterns and that particular subsets of neurons functionally combined to provide parallel, distributed encoding of tactile stimuli within ensembles. In addition, they demonstrated a 7- to 12-Hz rhythm initiated in the cortex that eventually synchronized neurons in the thalamus and trigeminal nucleus and modulated tactile encoding as a function of exploratory movements. Thus, there is an association among sensory input, ensemble encoding, and processing of that information during behavior.

Correct computation and appropriate

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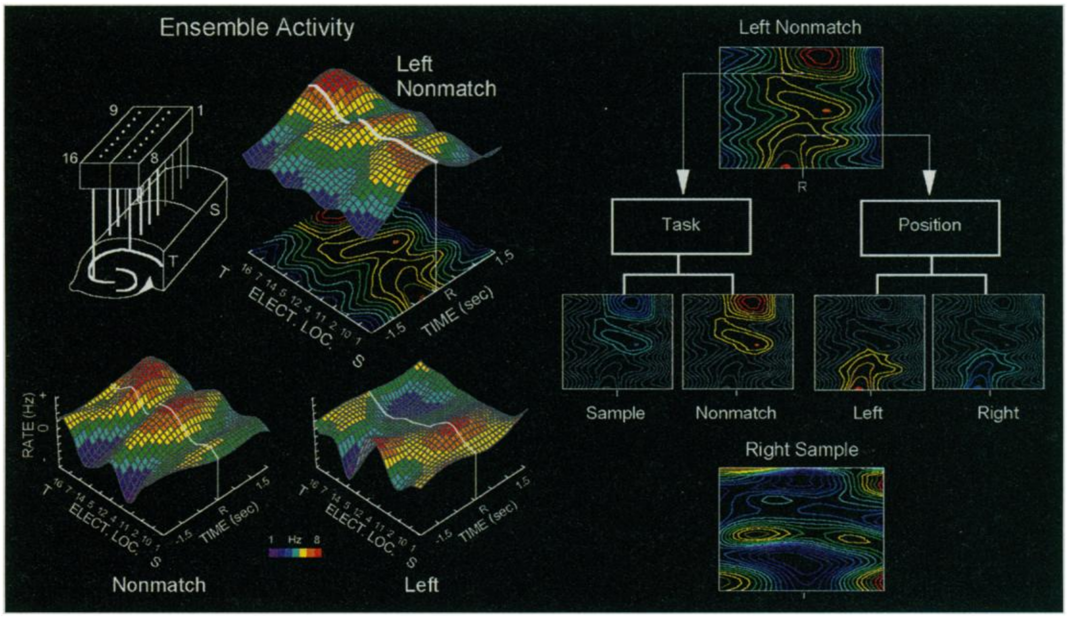
interpretation of the information content within ensembles is critical to deciphering the nature of the ensemble code. Because these calculations depend on both the information content and its distribution within the population (*15*), ensemble representations of behavioral or cognitive processes are likely to be at least as complex as the input patterns they must resolve (*16*). Moderate numbers (10) of hippocampal neurons (see figure, upper left) were simultaneously recorded from rats performing a two-lever version of a spatial delayed nonmatch to sample (DNMS) task (*17*). Task-relevant information was encoded in overlapping patches of distinct spatiotemporal firing within anatomically precise regions of the hippocampus (see figure, Ensemble Activity). The spatiotemporal firing maps in the hippocampus contain both unique as well as complementary patterns of activity related to the execution of responses within a DNMS trial.



Ensemble codes. (Left) Example of an ensemble firing pattern for 10 hippocampal neurons. Left nonmatch response of a DNMS trial displayed as a three-dimensional firing surface constructed from multiple perievent histograms (250-ms time bins) recorded ±1.5 s before and after execution of the behavioral response (R and white stripe). The CA1 (1-8) and CA3 (9-16) septotemporal recording sites, shown on the electrode array at the left, alternate along the electrode location axis (S and T) of the surface to preserve anatomic representation within the ensemble. The color contour beneath the firing surface represents the two-dimensional spatiotemporal projection of the surface activity with firing rate represented by the indicated color bar (1 to 8 Hz). The two, three-dimensional surface patterns at the bottom depict the same ensemble firing rate adjusted by the normalized variances (range of ±1.0) extracted separately by the analysis for task phase (Nonmatch) and lever position (Left). **(Right)** The contour surface has been demarcated by the representational features designated by the two extracted surface firing patterns (Nonmatch, Left) at lower left. The complementary features within the same dimensions (Sample, Right) are illustrated by the same contour but with a different color (blue). Spatial and temporal aspects of each dimension can overlap or interleave within neurons from the same ensemble as long as there remains a spatiotemporal distribution unique to a particular behavioral response. An example of a different spatiotemporal distribution of firing within the same ensemble is shown for a Right Sample response in which both of the above regions do not show distinct firing. [Data taken from (*5*).]

Information relevant to task performance was encoded by separate variance sources extracted by population (multivariate) analysis techniques (*18*) from the overall ensemble firing pattern (see figure, lower two surfaces). Contextual (see right side of figure, Sample versus Nonmatch phase) and operational (Left versus Right lever presses) dimensions of the behavioral events in the DNMS trial were represented by precise patterns, which differed with respect to spatial distribution within the hippocampus (see figure, Task versus Position contours). Features within a dimension were encoded by complementary patterns (that is, reciprocal firing rates) in the same set of spatially distinct neurons (see figure, Sample versus Nonmatch, Left versus Right contours). Different behavioral events, even within the same trial (see figure, Right Sample), were associated with different spatiotemporal firing across the same ensemble of neurons. The ensemble patterns were present only during the execution of task-relevant responses and not during the delays (*17*). The functional significance of the encoded patterns was illustrated by analyses of behavioral errors; 87% of trials resulting in errors were associated with inappropriate ensemble codes. Encoding within hippocampal ensembles was therefore expressed as conjunctions (*19*) of discrete firing patterns, each associated with a separate dimension, category, or feature of a task. The patterns appeared instantaneously and completely at the time of execution of the behavioral response (see left side of figure, R and white stripe on surfaces).

Hopfield (*20*), describing the virtues of "temporally distinct patterns of action potentials" from different neurons as a means of encoding and decoding stimulus representations, noted that for encoding new stimuli "the simplest scheme is to have a multiplicity of time delays" across the same sets of neurons. Such a mechanism could provide the basis for short-term memory (*21*). The figure illustrates this principle by the separation of distinct spatiotemporal patterns within the overall ensemble, which vary independently as a function of different behavioral dimensions. In studies of sequences of cued (context-related) arm movements (*22*), appropriate ensemble firing patterns in the motor cortex could be switched to the intended direction of movement within milliseconds. The appropriate ensemble firing pattern was anticipated and immediately selected from the overall set of possible movement patterns when the cue for a particular movement was presented.

Is there anything to be gained by having firsthand knowledge of ensemble firing patterns? Our findings (*17*), and those of others (*6, 11, 13, 14, 22*), point to the superiority of ensemble recordings. The ensemble code itself likely represents multiple dimensions of a single behavioral event (*17*). Hence, the full significance of the code cannot be extracted by examining the activity of single neurons whose instantaneous activity can only vary along one dimension (changes in firing rate). With multiple neuron recording, detection of the dynamic properties of ensemble representations is possible. Indeed, co-existent spatiotemporal patterns of activity with variance properties that reflect not only different behavioral components, but also the contexts in which those behaviors occur, have already been identified (see figure).

A Perspective in *Science* (*23*) suggested a high degree of convergence of sensory information onto individual hippocampal neurons. That concept can now be taken one step further to explore representations within hippocampal ensembles. We may have stumbled onto this representational scheme within hippocampal ensembles in our systematic investigations with multiple neuron recording in well-defined behavioral circumstances. Even so, the existence of such precise segregation of spatiotemporal firing along both contextual and behavioral dimensions makes it likely that this principle of information representation may be present in other brain regions.

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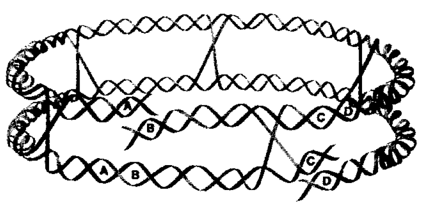
25. Sponsored by National Institute on Drug Abuse grants DA03502, DA07625, and DA00119 (to S.A.D.) and DA08549 (to R.E.H.). We thank D. Woodward, G. Carelli, and L. Porrino for comments.

Resistance to Radiation

Michael J. Daly and Kenneth W. Minton

A human exposed to less than 5 Gy (1 Gy = 100 rad) of ionizing radiation would suffer almost certain death. Measured against this degree of radiation resistance, the bacterium *Deinococcus radiodurans* is truly remarkable, capable of surviving 5000 to 30,000 Gy of ionizing radiation (*1*). Such a dose will shatter the organism's chromosomes into hundreds of fragments, yet *D. radiodurans* possesses an extraordinary ability to recover, owing to its supremely efficient DNA repair machinery. The cell's powerful repair system can assemble intact chromosomes from the hundreds of fragments remaining after a 10,000-Gy dose. In as little as 12 to 24 hours, a *recA*-dependent recombinational pathway restores the chromosomes without lethality or mutagenesis (*2*).



Hypothetical double chromosome structure showing double-strand DNA breaks (at loci A-B and C-D) held in alignment by virtue of persistent Holliday junctions.

How is this possible? It might be because a chromosomal fragment can always find an intact homologous neighbor to serve as a repair template. In *D. radiodurans*, chromosomes may exist in pairs that are aligned relative to one another by Holliday junctions (*3*). Thus, a radiation-induced chromosome double-strand break would not be lethal, because an identical undamaged DNA duplex is available nearby (see figure).

Why does this extreme radiation resistance exist? Such high radiation fluxes have never occurred in the natural world, even in the early days of Earth's formation. But another stress—dehydration—afflicts *D. radiodurans* and also causes massive DNA fragmentation in this nonsporulating organism. The radiation resistance of *D. radiodurans* may be a serendipitous result of its ability to repair its DNA after severe dehydration (*4*). Thus, the efficient repair system might be best thought of as a mechanism to heal DNA fragmentation, whatever its cause.

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