

several tens of pixels in the image (typically 64) and by the high signal-to-noise ratio in the spectra. The authors extensively describe the sources of errors, both of a statistical nature at different stages of the data processing (signal, plasmon energy, temperature) and of an intrinsic nature due to the specimen itself (nonhomogeneity of the specimen, role of gain boundaries, influence of thickness variations). They also justify the noninvasive character of their thermometer, noting that the current in the electron probe should not provoke an appreciable temperature rise in a thermal conductor about 100 nm thick. The technique paves the way for a more thorough investigation of the factors governing the spatial resolution, as it distinguishes those contributions related to the measurement technique (delocalization arising from the use of a high-energy electron beam) from those associated with the quantity (temperature) under measurement depending on the local transport of heat via electrons or phonons.

Another emerging application of STEM-EELS, made accessible by the implementation of monochromators, is that of vibrational spectroscopy (7). In the case of high-angle impact scattering of incident electrons on the nuclei of the specimen, the same type of data processing as that used by Mecklenburg *et al.* could provide a way to the mapping of masses and isotopes with atomic resolution (8). To distinguish  $^{12}\text{C}$  from  $^{13}\text{C}$ , for instance, it would be necessary to measure shifts of a few milli-electron volts on the center of characteristic peaks situated in the tens of milli-electron volts loss range.

The work of Mecklenburg *et al.* opens new routes for pushing the limits in the micro (nano)-electronics domain. In particular, the combination of fabrication techniques for devices of smaller sizes and STEM instruments with aberration correctors for the probe (more current in a probe of given size) and with monochromators (with typical 10-meV energy resolution giving access to the natural width of the involved excitations) could enable fundamental studies of the quantum aspects of heat conduction. ■

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10.1126/science.aaa5311

## NEUROSCIENCE

# Our skewed sense of space

The distribution of neuron activity reveals an organization that supports the brain's spatial mapping capacity

By György Buzsáki

**T**he hippocampus is the brain region where spatial maps of our surroundings are encoded. A specific location will activate a set of neurons called place cells to represent the particular place. What happens as the number of environments encountered increases? Does the hippocampus continually create and store distinct independent “maps” for each locale, or can place cells be recruited for more than one map to generalize across locales? It appears that both mechanisms contribute in unique ways.

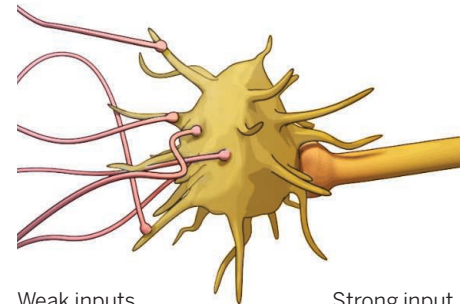
At any given position of space, a subset of hippocampal pyramidal cells is active (hence they are called “place cells”), and the firing fields of single neurons (“place fields”) can be regarded as units of spatial representation ( $T$ ). Collectively, the active sets of place cells track the position of the animal in the environment, and thus they are hypothesized to provide a “code” for space. But the exact nature of this code is unknown.

Several overlapping stories emerged recently about the statistical structure of hippocampal neuronal activity (firing patterns) and its relationship to “coding” for the environment (2–5). The activity of place cells when an animal (rat) experiences a small, large, new, or familiar environment demonstrates that although the majority of these neurons have single place representation, a small minority can have many (see the second figure). Analyses of the observed skewed distribution of place fields and other log-like features of the firing patterns of hippocampal neurons offer a link between physiological organization and the long-known Weber-Fechner law of psychophysics, which describes our subjective perceptions on a logarithmic scale. Accordingly, when the stimulus strength is multiplied, the strength of our perception is only additive.

To examine the relationship between neuronal firing patterns in the hippocampus and the nature of representation of the environment, rats were tested in a familiar open field, a linear maze, and a radial arm maze. Although the majority of CA1 and CA3 pyramidal neurons had single place fields, a small fraction fired at multiple locations (2).

Thus, both the majority and the minority of hippocampal neurons tiled the environments and the distribution of space coverage by individual place cells was strongly skewed (see the second figure). The within-place field firing rates of individual neurons were also skewed and followed a lognormal form (i.e., a bell-shaped distribution on a log scale). In turn, firing rates correlated with both the number and size of place fields (5).

In a given environment, only a fraction of pyramidal neurons are active. Will every



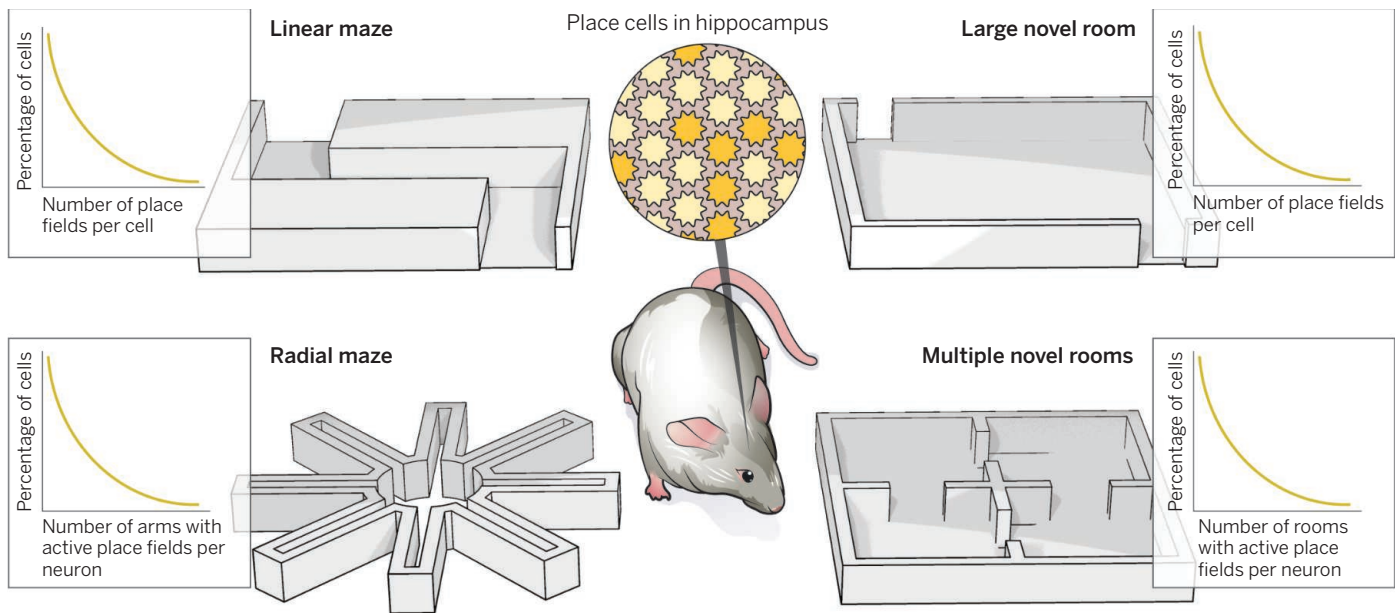
Weak inputs

Strong input

**Mixed messages.** Neurons with multiple place fields have higher firing rates than the majority of neurons with single place fields. Thus, neurons downstream of the hippocampus receive a mixed message—the majority of weakly active neurons convey information about the distinctness of the environment, whereas the strongly firing minority suggests similarity.

neuron eventually become a place cell if the animal explores a large environment? Another recent study explored this question by training rats to run an expandable maze track with lengths of 3, 10, 22, and 48 m in the same large room (3). Place cells active on the short tracks could form additional place fields for larger tracks, as new place cells were recruited from the pool of silent hippocampal cells. The number of fields formed by the CA1 pyramidal neurons was strongly skewed: A few neurons had many fields, whereas many neurons had only one or none. By increasing the maze length, the place fields showed a log-like recruitment, and extrapolation from the observed distributions suggested that nearly all hippocam-

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**Skewed distribution.** The number of place fields per neuron (place cell) in the hippocampus shows a skewed distribution with most place cells having none or one place field, whereas a minority have several place fields. This distribution is present in an open environment (shown as a linear maze), radial arm maze, large room [presented as linear tracks of increasing size in a single room (3)], or in multiple rooms [new or familiar (4)].

pal pyramidal cells would be active in an environment with a diameter of ~1 km.

In another study, investigators asked whether independent place cell codes are present in multiple environments (4). Rats were placed in one familiar box as well as in 10 new boxes, each placed in a different room. Most CA3 pyramidal neurons fired only in a single box, but a small minority fired in all or multiple boxes, showing a lognormal distribution of the overlap of neuronal activity in the different rooms. Thus, although the hypothesis of completely independent (or “orthogonal”) representation is supported by the majority of place cells with single-room activity, the “heavy tail” of distributions containing ~15% of the neurons active in multiple rooms suggests a more complex picture.

Overall, these studies (2–5) demonstrate that the skewed distribution of place fields is a general rule, irrespective of the nature or size of the testing environment. What could be the advantages of the skewed distributions for coding for space? From the perspective of independent coding (6), the minority of neurons with multiple place fields are regarded as “noise” or imperfection of the system. But when other physiological features of the heavy “tail-forming” minority are also considered, a different picture emerges. The small subset of place cells is not only more active in multiple environments, but their firing rates are higher, they emit more spike bursts (i.e., a higher proportion of spikes with interspike intervals less than 6 ms), and their place fields

are larger than those of the majority neurons (4, 5).

The higher mean firing rates of the active minority within their place fields correlate with their firing rates during sleep in the animal’s home cage (5). Furthermore, the diligent minority fires synchronously with other neurons more frequently in all brain states during both sleep and waking than the slower-firing majority and critically, it exerts a relatively stronger and more effective excitation on its targets. The distribution of the magnitude of collective population firing pattern is also lognormal (5). The consequence of this population organization is that in the physiological time frames of theta oscillations and sharp wave ripples of neuronal activity (4, 5), approximately half of the spikes emitted by the hippocampal neurons are contributed by the active minority; the remaining half are contributed by the great majority of neurons with single place fields. This mixed output is what the downstream observer-classifier neurons of the hippocampal output must use to generate action (see the first figure).

This emerging picture of hippocampal dynamics suggests that neurons at the opposite ends of the distributions may convey different but complementary types of information. The ever-active minority of place cells may be responsible for generalizing across environments and affords the brain the capacity to regard no situation as completely unknown because every alley, mountain, river, or room has elements of previously experienced similar situations. In many situations,

this minority provides the “best guess” of the hippocampus and offers “good enough” solutions to get by. On the other hand, the majority of less active neurons constitute a large reservoir that can be mobilized (7) to precisely distinguish one situation from another and incorporate novel ones as distinct.

The distribution of synaptic strengths, neuron firing rates, population synchrony, axon conduction velocity, and macroscopic connectivity of neuronal networks throughout the brain displays a skewed, typically lognormal form (8, 9). The relationships among these multilevel skewed distributions need to be explored to better understand network operations that underlie brain function. An important practical implication of these recent studies is that analyzing physiological data by parametric statistics is a violation because most variables are skewed. The theoretical implication is that brain dynamics supported by lognormal statistics may be the neuronal mechanism responsible for Weber-Fechner (log) perceptions, including our sense of space. ■

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10.1126/science.aaa6505

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