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Previews

Listening for the Right Sounds

Onyekachi Odoemene[1,2] and Anne K. Churchland[2,*]
[1]The Watson School of Biological Sciences, Cold Spring Harbor, NY 11724, USA
[2]Cold Spring Harbor Laboratory, Cold Spring Harbor, NY 11724, USA
*Correspondence: churchland@cshl.edu
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In this issue of *Neuron*, Rodgers and DeWeese (2014) developed a new paradigm in which rats had to select or ignore an auditory stimulus, depending on its context. The authors recorded neurons in primary auditory and medial prefrontal cortex. Surprisingly, they found that stimulus context had the largest effect in the moments before the stimulus was presented.

Neural systems must interpret the barrage of inputs that arrive from the various senses. This problem is evident even within a single sense: the brain must select relevant stimuli while ignoring irrelevant ones. For example, in the auditory system, humans often face the challenge of selecting the voice of one speaker amid the din of many; this has been dubbed the "cocktail party problem." Animals must similarly be able to select relevant sounds while ignoring irrelevant ones—even rodents must contend with a complex auditory world. Developing the equivalent of a "cocktail party" for animal models, however, has proved challenging. As a result, many questions persist about the mechanisms for stimulus selection in the auditory system.

In contrast, this problem has been well studied in the visual system: a number of behavioral paradigms exist in which animals are trained to select relevant stimuli and ignore distractors. Two mechanisms have been identified as supporting this ability. In the first, selected stimuli drive a stronger response in sensory neurons, by virtue of top-down modulation from frontal structures (Desimone and Duncan 1995; Maunsell and Treue 2006). This is referred to as the "Gating Model," on the idea that only selected stimuli pass through a "gate," giving them a privileged ability to influence behavior. The Gating Model makes two predictions for neural responses. First, selected sensory stimuli should drive stronger responses than ignored stimuli. Second, responses should differ in sensory areas that reflect the gating versus prefrontal areas that drive the gating.

An alternative to the Gating Model is that there are network-level changes from one context to the other. For instance, selected and ignored stimuli could engage a single neural structure but engage that structure in different ways. For example, the same stimulus might activate one pool of neurons in a context where it is selected, and a different pool of neurons in a context where it is ignored. The predictions are the opposite of the Gating Model: first, selected and ignored stimuli could have a similar effect on firing rates; second, responses might be similar in sensory versus prefrontal areas.

A paper in the current issue of *Neuron* addresses head-on the issue of stimulus selection mechanisms in the auditory system. Rodgers and DeWeese (2014) started off by developing an auditory stimulus selection task for rats. On each trial, rats were presented with two salient sensory stimuli: a warble and a white noise burst (Figures 1A and 1B). Those cues told the animal whether to go to a peripheral port, or just stay put. The tricky part is that in each block, rats had to select only one of the two cues and ignore the other. In the "pitch" block, the pitch of the warble indicated what to do, and in the "spatial" block, the spatial location of the burst indicated what to do. Training animals to appreciate that there are two contexts is no small feat. After all, the same pair of stimuli, say, a left noise burst + low warble, instructed the animal to go left in the spatial context (Figure 1A) but right in the pitch context (Figure 1B). To make any headway on the task, the animals needed a clear understanding of the context. For the most part, their behavior indicates that they had such an understanding: performance was accurate, and rats could readily tolerate multiple context shifts within a session, usually adjusting to the new context after only a few trials.

Rodgers and DeWeese (2014) then recorded spikes from two areas while the animals were engaged in the task: primary auditory cortex (A1) and medial prefrontal cortex (mPFC). First, they examined the stimulus-driven responses: the short-latency changes in firing rate following the warble and white noise burst. Surprisingly, these stimulus-driven responses were very similar for selected versus ignored stimuli in both A1 and mPFC. In fact, a linear decoder was able to estimate the stimulus from the neural response similarly for selected and ignored stimuli. This is evidence against the Gating Model: sensory-driven responses appear to pass through the "gate" regardless of whether they are selected.

Although context did not affect the stimulus-driven response, a clear signature of context was evident in the firing rates in the moments preceding the stimulus. During that time, many neurons had a strong preference for one context versus the other. Some fired more in the pitch context; others fired more in the spatial context. Even more surprising is that Rodgers and DeWeese (2014) observed this effect not only in mPFC, but also in A1, a primary sensory area. In fact, this context dependence was similarly strong in both areas.

How might this prestimulus activity support the animals' ability to select the right cue? The observations of Rodgers and DeWeese (2014) refute a Gating Model and instead point to a network-level change. One possibility is that neurons participate in an all-or-none fashion in a given context. Neurons

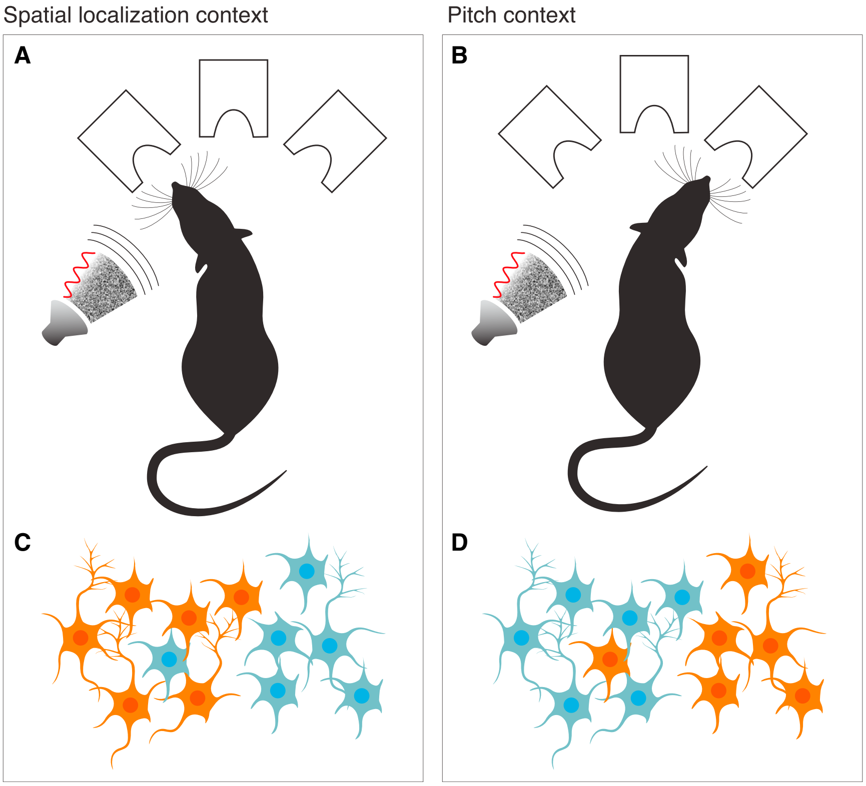

Figure 1. Schematic of Stimulus Selection Task and Hypothetical Population Response
(A) Rat in behavioral apparatus on a trial in which a white noise stimulus and a low-pitch warble are played from the left speaker. Because this is a "spatial" context, the correct response is to go to the left reward port.
(B) Same as (A) except that the trial is presented in the "pitch" context, so the low-pitch warble indicates that the correct response is the right reward port.
(C) Hypothetical population responses to the stimuli in (A) presented in the "spatial" context. A subset of neurons (colored red) has elevated firing rates.
(D) Hypothetical population response to the same stimuli, this time presented in the "pitch" context. A different subset of neurons is active compared with the "spatial" context, shown in (C).

elevated during the pitch context (Figure 1B, left), for example, could drive the animal's decision during that context, perhaps by targeting a particular set of downstream neurons in premotor areas. Neurons elevated during the spatial context (Figure 1B, right), by contrast, might target a different set of downstream neurons. Rodgers and DeWeese (2014) trained a network according to this scheme and found that it performed well on the task, getting the response correct about 80% of the time. Interestingly, the effect of context in the model, as in the brain, was only on firing rates during the prestimulus period and not on the stimulus-driven response.

A closely related possibility is that a single population of neurons participates in both contexts, in a graded, rather than all-or-none, fashion. In other words, stimulus selection might be accomplished by changing the weights that define how downstream areas decode a single pool of neurons. This idea, that stimulus selection is accomplished at the network level, has support in the visual system (Mante et al., 2013) and could be at play here as well.

The ability to distinguish such candidate mechanisms is bolstered by the opportunity to identify and manipulate specific neural pathways. The rodent model developed by Rodgers and DeWeese (2014) will enable future experiments that identify A1 or mPFC neurons that project to premotor areas and selectively activate the population during behavior (Znamenskiy and Zador 2013). These tools, taken together with rodent behavioral paradigms of increasing sophistication, pave the way for a circuit level understanding of how animals use complex sensory stimuli to guide decisions.

REFERENCES

Desimone, R., and Duncan, J. (1995). Annu. Rev. Neurosci. *18*, 193–222.

Mante, V., Sussillo, D., Shenoy, K.V., and Newsome, W.T. (2013). Nature *503*, 78–84.

Maunsell, J.H.R., and Treue, S. (2006). Trends Neurosci. *29*, 317–322.

Rodgers, C.C., and DeWeese, M.R. (2014). Neuron *82*, this issue, 1157–1170.

Znamenskiy, P., and Zador, A.M. (2013). Nature *497*, 482–485.