

## Selectivity of Adaptation in Single Units: Implications for fMRI Experiments

Understanding the neural basis of adaptation (repetition suppression) is critical for interpreting fMRI-adaptation experiments. Sawamura and colleagues provide a critical stepping-stone by elucidating the relation between neural adaptation and response selectivity. They find some cross-adaptation by two different stimuli that activate the same neuron.

Adaptation (also referred to as repetition-suppression) reflects the phenomenon of reduced responses to repeated presentation of a specific stimulus. Adaptation effects are robust and can be measured with single-unit recordings, fMRI, and EEG and in many cortical regions, including visual areas, auditory cortex, and prefrontal cortex. Despite the robustness of adaptation effects and the increased interest in the field, the underlying neural mechanisms are not well understood. Adaptation may reflect a proportional reduction in firing rate to repetitions of a specific stimulus, change in the tuning of neural responses for repeated stimuli, or shortening of the processing time for repeated stimuli (for a recent review see (Grill-Spector et al., 2006). In the current issue of *Neuron*, Sawamura and colleagues (Sawamura et al., 2006) present a novel study that provides an important stepping-stone for elucidating neural mechanisms underlying adaptation.

Understanding the neural mechanisms of adaptation effects is important for two main reasons: (1) adaptation has become a popular tool for characterizing functional properties of neural populations in humans with fMRI (especially given claims that it tags specific neural populations within fMRI voxels [Grill-Spector and Malach, 2001]); (2) there is a potential relation between adaptation effects and behavioral priming (Schacter and Buckner, 1998; Wiggs and Martin, 1998). Priming refers to improved performance in accuracy and response time for repeated items and occurs under the same conditions as adaptation. However, recent results show that adaptation in object-selective cortex can occur without priming (Sayres and Grill-Spector, 2005) and priming can occur without adaptation in object-selective cortex (Dobbins et al., 2004), somewhat weakening previous claims that adaptation in object-selective cortex reflects behavioral priming (Schacter and Buckner, 1998; Wiggs and Martin, 1998).

In a typical fMRI-adaptation experiment, researchers measure the reduction of the BOLD response to identical repeated stimuli, the reduction of BOLD response by different, albeit related stimuli (e.g., the same object in different views) compared to nonrepeated stimuli. The finding that adaptation levels for different-related stimuli were similar to those of adaptation by identical stimuli suggests that neural populations are insensitive to the difference between the related stimuli because

there was cross-adaptation. In contrast, recovery from adaptation by different-related stimuli (i.e., no cross-adaptation) suggests that neural populations are sensitive to the differences between related stimuli. However, inferring neural tuning from fMRI-adaptation depends both on the relation between fMRI (BOLD signals) and action potentials (Logothetis et al., 2001; Mukamel et al., 2005) and the relation between neural adaptation and stimulus selectivity. The underlying assumption based on previous single-unit studies (Lueschow et al., 1994) is that adaptation and stimulus sensitivity are related. The goal of the present study by Sawamura and colleagues was to directly examine the relation between selectivity and adaptation level of single neurons in monkey inferotemporal (IT) cortex.

The current study follows a previous study from the same group (Sawamura et al., 2005), in which they showed that adaptation effects measured with fMRI in monkey IT are similar to adaptation effects measured with fMRI in human lateral occipital complex (LOC) (Grill-Spector et al., 1999). Measuring adaptation effects in the same cortical region and similar experimental designs with different methods (single-cell physiology and fMRI) provides a bridge between adaptation effects in neurons and fMRI within the same species. Given the similarities between fMRI-adaptation effects in human LOC and fMRI-adaptation in monkey IT, these results have implications for interpreting human fMRI-adaptation studies.

In the study presented in the current issue of *Neuron*, Sawamura and colleagues measured responses in monkey IT cells when they presented monkeys repeated items of object stimuli. They tested the effects of repetition on IT cell responses when repeating identical images that activated a cell (A-A or B-B), presenting alternating sequences of two images that activated the cell (i.e., repeats of A-B), and presenting alternating sequences of images in which the first image did not produce a significant response in the neuron (i.e., repeats of C-A). These stimuli were presented in two experiments: in the first they presented stimuli repeated up to 30 times, and in the second they presented stimuli embedded within a sequence of other nonrepeated images. The motivation for using two designs was to examine adaptation effects in two designs commonly used in fMRI: block designs (Grill-Spector et al., 1999) in which stimuli are repeated many times, and event-related designs (Kourtzi and Kanwisher, 2001) in which there is only one repetition of an image embedded within a long sequence of stimuli.

Sawamura and colleagues found that repeating the same image (AA or BB) produced maximal adaptation. Across neurons, they did not find a relation between the strength of adaptation and the level of initial signal. Instead, they found that the level of adaptation was constant for a neuron. This is consistent with a model suggesting that adaptation produces a proportional reduction of the neural responses (see fatigue model, Grill-Spector et al., 2006). Showing an image that the neuron was unresponsive to did not affect the response

to a subsequent image that the neuron responded to (i.e., there was no adaptation). However, showing two images that the neuron responded to produced adaptation, but lesser than repeated presentation of an identical image. These data suggest that neural adaptation effects show higher sensitivity than the initial responses to the same stimulus.

What are the implications of the present study for the interpretation of fMRI-adaptation studies? (1) This study shows that there is cross-adaptation. Thus, two different stimuli that activate the same neuron will elicit some cross-adaptation. Conversely, if one finds fMRI-adaptation for a pair of stimuli it is likely that these two stimuli activate the same neurons. (2) Cross-adaptation in neurons was always smaller than adaptation by identical repeats. This is commonly found in fMRI-adaptation experiments, but see [Kourtzi and Kanwisher \(2001\)](#). (3) The effects of cross-adaptation in neural responses are more consistent with block fMRI-adaptation than short-lagged adaptation with a single repeat. This could be because of two reasons: (1) the mismatch between response-selectivity of neurons and neural adaptation decreases with repetition and (2) there are differential levels of neural adaptation and fMRI-adaptation for one stimulus repetition, but the level of neural adaptation and fMRI-adaptation are more similar following many repetitions (compare present study to [Henson et al., 2004](#); [Sayres and Grill-Spector, 2005](#)).

Several questions remain open. Answering these questions will be crucial for understanding the neural mechanisms underlying adaptation ([Grill-Spector et al., 2006](#)). (1) Which neural population adapts most? Neurons that are optimally tuned to a stimulus, or neurons that are responsive, but not optimal? The current study shows that the initial level of response does not predict the level of adaptation, but [Sawamura et al.](#) did not examine whether the best stimulus from their set was also the optimal one. (2) What is the effect of adaptation when adapting a cell with its optimal stimulus compared to adaptation by a nonoptimal stimulus? For example, if the initial response to A is greater than that to B, will the adaptation level of B-A and A-B be similar or different? (3) Does adaptation affect the tuning width of neural receptive fields? For example, does adaptation make the tuning width narrower (see [Wiggs and Martin, 1998](#))? (4) Is the relation between neural adaptation and selectivity similar for immediate (short-lag) adaptation and long-lag adaptation with many intervening stimuli between repeats? It is unknown whether the same neural mechanisms underlie immediate and long-lagged adaptation. However, fMRI researchers use both types of adaptation paradigms for inferring the functional properties of neural populations (e.g., [Grill-Spector et al., 1999](#); [Vuilleumier et al., 2002](#)).

Future research that will link between monkey physiology, monkey fMRI, and human fMRI will provide the ultimate link in understanding effects across species (monkey and humans) and methods (single-unit recordings and fMRI). [Sawamura and colleagues](#) provide a critical stepping-stone.

## Kalanit Grill-Spector<sup>1</sup>

<sup>1</sup>Department of Psychology and  
Neuroscience Program  
Stanford University  
Stanford, California 94305

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