TOOLBOX

Complex mathematics simplifies brain imaging

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Cracked code: A mathematical algorithm makes it possible for researchers to see how one image changes the brain response to another one that follows it.

A complex mathematical technique can improve the sensitivity of experiments that rely on brain imaging, allowing researchers to study how the brain responds to sequences of stimuli, according to a study published in the June issue of *NeuroImage*[1].

Studies have suggested that the brain's reaction to a visual stimulus, such as a photograph of a face, is influenced by the image that precedes it[2]. For example, the response to a face seen after the image of a house might be different than after the image of a mailbox.

This phenomenon is particularly relevant in autism. For example, typical controls perceive a neutral expression as happy when it follows an image of an angry face. By contrast, people with autism tend to see both images as negative[3].

Functional magnetic resonance imaging, or fMRI, is limited in its ability to detect this carry-over effect, making it challenging to study the brain regions involved in certain aspects of autism.

This is in part because fMRI measures changes in blood flow within the brain, and is not fine-tuned enough to separate a carry-over effect from delayed blood flow in response to the previous image.

In the new study, researchers used a de Bruijn cycle — an ordered mathematical arrangement that efficiently generates every possible combination of a number of variables — to direct the order of black and white images shown to individuals during an fMRI scan. This is the same principle safecrackers use to break locks.

Researchers doing imaging studies can apply this cycle to present the house, face and mailbox images in every possible order, says lead investigator **Geoffrey Aguirre**, assistant professor of neurology at the University of Pennsylvania.

The order may appear to be random, but an algorithm used to construct the cycle sets the sequence to alternate between images likely to elicit strong and weak brain responses, as measured by fMRI.

The cycling generates periods of downtime that allow the blood flow changes to catch up. "It creates a slow wave of changes in neuronal activity, which fMRI is particularly good at measuring," says Aguirre. The technique is also applicable to other forms of brain imaging, such as electroencephalography and magnetoencephalography, both of which are used extensively in autism research.

Aguirre and his colleagues are using the technique to study how the brains of people with autism respond to sequences of stimuli differently than controls do. The goal is to identify a sequence that has one pattern for controls and a different pattern for those with autism.

References:

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3. Rutherford M.D. *et al. J. Autism Dev. Disord.* Epub ahead of print (2011) **PubMed**