starting point in mapping the network-level changes in other brain regions implicated in depression. High-speed, circuit-level optical methods are better suited than single-cell physiology to detect and quantitatively describe spatiotemporal dynamics (such as areal spread of activity) that may be altered in psychiatric disease. These circuit dynamics measures relate to how information propagates rather than to a specific neural code. We propose that depression may depend on changes in the ability of information representations to organize and percolate through sparsely active networks.

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Characterizing the Limits of Human Visual Awareness

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Momentary awareness of a visual scene is very limited; however, this limitation has not been formally characterized. We test the hypothesis that awareness reflects a surprisingly impoverished data structure called a labeled Boolean map, defined as a linkage of just one feature value per dimension (for example, the color is green and the motion is rightward) with a spatial pattern. Features compete with each other, whereas multiple locations form a spatial pattern and thus do not compete. Perception of the colors of two objects was significantly improved by successive compared with simultaneous presentation, whereas perception of their locations was not. Moreover, advance information about which objects are relevant aided perception of colors much more than perception of locations. Both results support the Boolean map hypothesis.

Many experiments have explored the process of attentional selection in vision, chiefly through visual search tasks in which observers try to find a single specified target, which may or may not be present in a display (*1*–*4*). Selection sometimes involves sequential checking of different elements, whereas in other search tasks a parallel selection process can exclude all but a single target (*3*, *5*). What has been scarcely investigated at all, however, is an even more fundamental question about human vision: What is the informational content of any single momentary act of conscious perception?

Consider, for example, the array of four colored disks shown in Fig. 1A. Can a human observer attend to all four disks and simultaneously be aware of the presence of two blue, one red, and one green disk? A recently proposed theory of attention contends that we cannot (*6*). According to this account, momentary conscious access, although flexibly controlled through voluntary attending, is nonetheless constrained to have the representational content of a data structure termed a labeled Boolean map. There is evidence that visual perception analyzes the scene along a number of different basic dimensions, such as color, motion, spatial frequency, and orientation (*3*, *5*, *7*). The data structure of a labeled Boolean map may thus associate at most one value at a time for each of these independent visual dimensions (for example, color is green and motion is rightward) as labels with a spatial pattern (i.e., the set of location values composing the Boolean map) (*6*). Here, we deal only with the case of within-dimension competition, so the claim can be abbreviated for present purposes as awareness of only a single feature value. A choice of three potential Boolean maps could represent either the red, the green, or the blue disk(s) in Fig. 1A. These would afford the observer conscious access to both the location(s) and the color of the attended disk(s). On the other hand, the map could instead encompass disks of more than one color simultaneously, and in that case there would be explicit awareness of all locations but not of the colors. Figure 1B illustrates the representational content of a few (but not all) of the possible percepts that might be elicited by these stimuli according to the present hypothesis.

The claim that conscious access is limited to a "one-feature-multiple-locations" format generates numerous predictions (*6*). Here, we focus on one especially critical and counterintuitive prediction, namely the proposed asymmetry between conscious access to multiple features and to multiple locations. The Boolean map theory predicts that multiple features can only be consciously accessed one by one, whereas multiple locations can be accessed at the same time.

In the first experiment, we presented two objects either at the same time (simultaneous condition) or one by one (successive condition), followed by a single probe (either a color patch or a location marker, to be judged as having been present in the display or not). For any type of visual information (feature or location), if two such values cannot be accessed at the same time, then observers should perform worse in the simultaneous condition. If, however, two such values can be simultaneously accessed without attentional limitation, then observers should perform equally in

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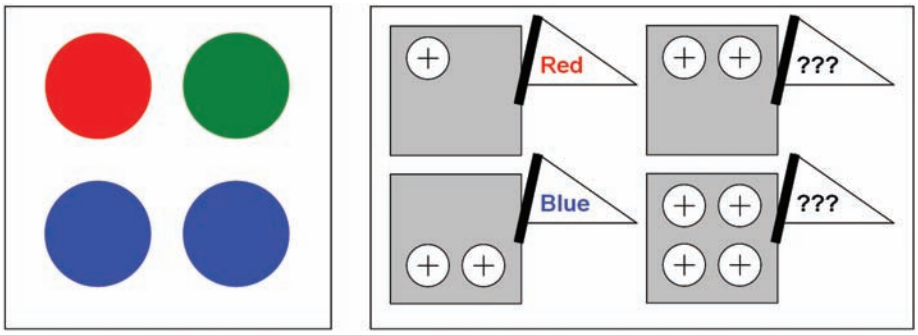
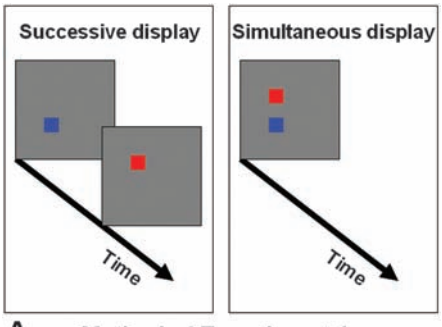


Fig. 1. (**A**) A sample display. (**B**) Some possible states of awareness (possible percepts) when viewing the sample display of (A) in a single brief exposure. When only disks of one color are selected (left two examples), both the locations of the disks and that color value can be consciously accessed. When more than one color is present in the selected disks (right two examples), only the locations of the disks, but not their colors, can be consciously represented. In (B), the regions marked with plus signs stand for the selected regions of the Boolean map, and the flags stand for the color information that is associated with the selected region as a label. The selected region in the map and the color label constitute the only visual information that is consciously accessible at one time.



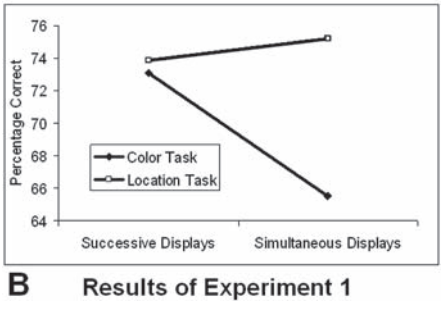
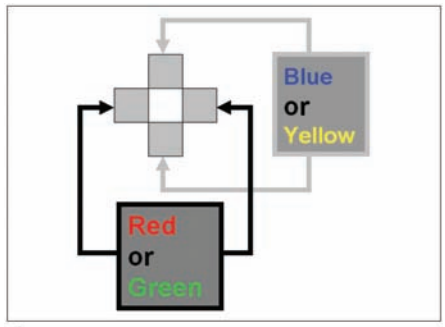


Fig. 2. The method (**A**) and results (**B**) of experiment 1. We presented two objects either at the same time or one by one. Each frame was followed by a visual mask to limit processing to a brief exposure. In each trial, the observer had to report whether a probe target color or location, presented at the end of the trial, was present or absent. The performance (as measured by the mean of accuracy over observers) was significantly better for successive than for simultaneous displays in the color task ($P < 0.005$) but not in the location task (interaction significant, $P < 0.02$).

the simultaneous and in the successive conditions (*8*, *9*). Thus, the Boolean map account implies that, for judgments of color, the observers should perform significantly better in the successive than in the simultaneous condition, whereas for judgments of location, the observers should perform equally in both conditions. We compared observers' performance in the successive and in the simultaneous conditions for both colors and locations with stimuli like those in Fig. 2A. To ensure a sensitive comparison between accuracies of different conditions in this experiment (and the one below), we always presented the objects very briefly and then masked them. The results are given in Fig. 2B, and they confirm the predictions. Moreover, simple quantitative modeling shows that the difference between successive and simultaneous conditions closely fits the prediction from a strictly sequential model [Supporting Online Material (SOM text)], suggesting that perceiving one color not only causes a moderate decrement in the perception of the second color, but may well prevent the perception of the second color altogether.

In the second experiment, two squares were always presented simultaneously. Square 1 appeared in the top or bottom location and was blue or yellow. Square 2 appeared in the left or right location and was red or green (Fig. 3) (*10*). Some observers were tested on the color and others on the location of one square (the target). The two possible colors (or locations) of the target were shown along with the associated response keys (e.g., "left j right k" would be shown for a location test on square 2, shown in Fig. 3B). In prior-information blocks, the target was either always square 1 or always square 2 across the whole block. Thus as soon as the display appeared, observers knew which square was the target. In no-information blocks, the choice of target varied randomly from trial to trial, although the association between colors and locations remained the same. For any type of visual information (feature or location), if there are attentional limitations on access, then



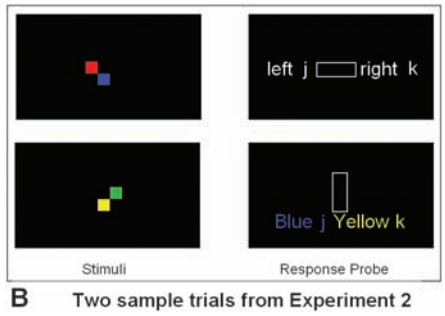


Fig. 3. The method of experiment 2. (**A**) How the two objects were presented in each display. Square 1 (indicated by gray lines) was presented in the top or bottom location, and this object could be blue or yellow. Square 2 (indicated by black lines) was presented on the left or right, and this object could be red or green. (**B**) Two examples of the displays. In this experiment, one group of observers was tested on the color and another on the location of one of the squares. The two possible colors (or locations) of the target were shown along with the associated response keys (e.g., "left j right k"). In the prior-information condition, the tested square was in the prespecified pair (e.g., left-right and red-green) that remained constant across the entire block, so the observers needed only to perceive the relevant object. In the no-information condition, the tested square randomly varied from trial to trial, so the observers had to try to catch both objects to do the tasks.

knowing in advance which object will be tested should allow the observer to focus on that object and perceive it significantly better. On the other hand, if two presented values (locations or colors) can be simultaneously accessed without attentional limitation, then advance information would not produce any advantage. Again, the theory claims that access to visual awareness is restricted to one feature at one time, whereas no such restriction should exist for multiple locations. Therefore, for a task on feature values, the observers should perform substantially better with the prior information than without; but no such benefit should be present for a task based on location values.

For the color task, the accuracies were 72.6% for the no-information condition and 80.3% for the prior-information condition (a benefit of 7.7%, $P < 0.00001$). For the location task, the

accuracies were 73.2% for the no-information condition and 75.4% for the prior-information condition (a benefit of 2.2%, significantly smaller than the benefit of 7.7% in color task, $P < 0.001$). The substantial asymmetry of effect of prior information in encoding feature values and location values provides distinctive support for the Boolean map analysis.

Taken together, the experiments reported here [along with other evidence recently presented (*6*)] are consistent with the claim that observers have conscious access to only one feature value at one time but have conscious access to more than one location simultaneously. Does the present conclusion—that only one feature can be consciously accessed at any one time—conflict with the well-known evidence for parallel feature processing in the visual search literature (*3*, *5*)? The parallel feature processing demonstrated in that research generally involves the spatially parallel rejection of homogeneous distractors in search of a feature target, a claim that is consistent with the Boolean map hypothesis.

The present results can also be seen as showing that multiple location values can be represented as a holistic pattern or surface (i.e., observers can encode them together as a unit), thus avoiding competition. Feature values, on the contrary, evidently cannot constitute a comparable sort of pattern in feature space (e.g., color space), and thus each needs its own separate visual representation.

The Boolean map format is supported not only by the results of the very austere perceptual tasks investigated here but also by a range of results assessing observers' ability to apprehend complex patterns in relatively rich displays, such as matching, mentally rotating, or judging the symmetry of arrangements of colors or orientations in large grids of elements (*6*, *11*, *12*). In each of these situations, it seems clear that, although people can abstract the spatial distribution of one feature value at a time, even in complex patterns, they are unable to become aware of the distribution of more than one feature value at a time.

This conclusion may seem at odds with ordinary introspection, which may suggest that we can become aware of a heterogeneous world with many feature values at the same time, not the mere spatial distribution of a single feature value. What is to be made of this paradox? The sense that human observers have of being simultaneously aware of varied colors, shapes, directions of motion, and so forth may reflect experiences that are not occurring at any single instant but rather at different times. As some philosophers have noted, our assessment of the content of our awareness may reflect not what we have in mind at one instant, but rather what we can readily fetch with a quick act of will (*13*). Recent studies on change blindness (*14*–*16*) also suggest that visual awareness is starkly limited and that our apparently rich visual experience is likely to be a substantial overestimation of what is actually consciously available.

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Supporting Online Material

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SOM Text
Fig. S1

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Immunization by Avian H5 Influenza Hemagglutinin Mutants with Altered Receptor Binding Specificity

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Influenza virus entry is mediated by the receptor binding domain (RBD) of its spike, the hemagglutinin (HA). Adaptation of avian viruses to humans is associated with HA specificity for α2,6- rather than α2,3-linked sialic acid (SA) receptors. Here, we define mutations in influenza A subtype H5N1 (avian) HA that alter its specificity for SA either by decreasing α2,3- or increasing α2,6-SA recognition. RBD mutants were used to develop vaccines and monoclonal antibodies that neutralized new variants. Structure-based modification of HA specificity can guide the development of preemptive vaccines and therapeutic monoclonal antibodies that can be evaluated before the emergence of human-adapted H5N1 strains.

The ability of influenza viruses to adapt from animals to humans is determined by several viral gene products [reviewed in (*1*)]. Among them, the viral hemagglutinin (HA) is of particular interest; it binds to specific sialic acid (SA) receptors in the respiratory tract that affect transmission (*1*–*3*). At the same time, it affects sensitivity to neutralizing antibodies, the primary determinant of immune protection (*4*, *5*). The receptor binding domain (RBD) within HA is composed of less than 300 amino acids, situated at the outer surface on top of the viral spike (*6*–*10*). SA binding is mediated by a cavity bordered by two ridges (Fig. 1A), formed by loop 220 (amino acids 221 to 228), loop 130 (amino acids 135 to 138), and a helical domain at amino acids 190 to 197 (numbering based on H3 A/Aichi/2/68) (*10*). The structures of the H1, H5, and H3 HAs have been previously described (*6*–*10*), and the H1 and H5 RBD show greater structural and genetic similarity to one another than to H3 (Fig. 1A).

To define mutations that change receptor recognition, we focused initially on differences between H5 and H1 (A/South Carolina/1/18), which recognizes α2,6-SA linkages, particularly amino acids 190, 193, and 225 (Fig. 1B). Individual or combination mutations to create pseudoviruses were made in which amino acids were replaced at certain positions, described by the single-letter code for the amino acid (*11*), as for example, aspartic acid substituted for glutamic acid at position 190 (E190D). We also used a mutant suggested previously to increase α2,6 recognition, Q226L,G228S (*9*). Surface expression of these HAs was confirmed by flow cytometry (fig. S1A), and pseudotyped lentiviral vectors were produced after cotransfection of neuraminidase (NA). Entry into 293A renal epithelial cells, which ex-

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