pected on several simple hypotheses. We interpret the results through the use of a model (*8*) that includes a source of variability intrinsic to the observer and a sampling efficiency, ϕ, that is independent of image noise. This sampling efficiency characterizes the performance of the method used by the visual system to sample the image, weight the coefficients appropriately, integrate the result, and utilize a priori information.

One can use the equations of the model (*8*), the definition of d_I', and a threshold signal energy, E_T, defined for an observer d' of unity to obtain the equation $E_T = (N_o + N_e)/\phi$. This equation describes the straight lines plotted in Fig. 2. The ideal detector has $\phi = 1$ and $N_e = 0$, so its performance falls on a line of slope 1. A detector that had $\phi = 1$ and nonzero intrinsic noise would give the dotted line of slope 1 and nonzero intercept. Finally, a detector with intrinsic noise and suboptimal sampling efficiency would give a line of higher slope as is indicated for the observer results. We used the above equation and weighted linear regression of the experimental data to estimate the intrinsic noise spectral density and observer sampling efficiency for each type of target signal.

Our experimental statistical efficiencies were in the range from 0.2 to 0.7 (with standard errors between 0.05 and 0.1) and are model-free estimates. The model-dependent calculations of sampling efficiencies and intrinsic variabilities were highest for a pulse burst of 4.6 cycle/deg. This target was the largest in spatial extent and was located near the peak of contrast sensitivity of the visual system. The other targets had smaller spatial extents, lower intrinsic variance, and lower sampling efficiencies. The sampling efficiencies ranged from 0.54 ± 0.07 to 0.83 ± 0.15.

It is possible that intrinsic observer noise is a function of image noise. For example, $N_e = A + BN_o + CN_o^2 \ldots$. If the coefficients B and C are positive, our estimates of intrinsic noise and sampling efficiency are both too low.

What do these measurements mean? There is not much scope for improvement of the sampling efficiencies we have obtained. It is possible that this very high efficiency occurs because these targets are well matched to processing mechanisms at early levels in the visual pathways. Several models (*2*) hypothesize local Fourier analysis of small regions of image, and this would involve cross-correlation with a few cycles of a spatial sinusoid. Furthermore, "simple" cells in the primary visual cortex of cats and monkeys possess properties that would enable the cells to act as cross-correlators for our "simple" signals (*9*).

There have been models based on sensory cross-correlation of received signals with expected signals. Such a model has been proposed for motion detection and pattern vision (*10*), and for echo location by bats (*11*). Measured human auditory efficiencies up to 0.4 have also been reported for discrimination of damped sinusoidal tones (*12*).

We have presented a method for investigating the absolute performance of the visual system that allows one to separate efficiency loss due to intrinsic observer variability and noise from residual inefficiencies. The results show that the residual inefficiency is very low under certain conditions, suggesting that very efficient processing methods must be used.

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4. The signals and noise can be described by the ratio, $E/N_o = \int_{-\infty}^{\infty}\int s^2(x,y)dxdy/N_o$, where $s(x,y)$ is the difference between the two displayed signals (differing only in amplitude), E is the signal energy, and N_o is the two-sided spectral density of the noise. For two-alternative forced-choice experiments and complete a priori information, the ideal observer's d_I' is equal to $\sqrt{E/N_o}$. We determined the observer's index, d', from the percentage of correct responses, P, using $d' = 2erfi(2P - 1)$, where *erfi* is the inverse error function.
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6. The Gaussian pulse burst of amplitude, A, and frequency, f, is given by $g(x,y) = A\cos(2\pi fx)\exp[-(x^2 + y^2)/2\sigma^2]$, where σ is the standard deviation of the Gaussian envelope (and always equals $1/f$). All signals had height equal to width.
7. The images were generated by computer. The image noise had a Gaussian probability distribution and flat power spectrum.
8. One model will be outlined here. The difference signal $s(x,y)$ has a Fourier transform $S(u,v)$, where u and v are spatial frequencies. An example of a nonideal receiver is one that receives the signal through a predetection filter with frequency response $F(u,v)$, detects the signal through an adaptive filter whose response is $M(u,v)$, and adds intrinsic noise with spectral density $N_iG^2(u,v)$. The detectability index in this case is
$$[d'_G]^2 = I_2^2/(I_3N_o + I_4N_i)$$
with
$$I_2 = \int_{-\infty}^{\infty}\int S(u,v)F(u,v)M(u,v)dudv,$$
$$I_3 = \int_{-\infty}^{\infty}\int F^2(u,v)M^2(u,v)dudv, \text{ and}$$
$$I_4 = \int_{-\infty}^{\infty}\int G^2(u,v)dudv$$
Sampling efficiency, ϕ, is defined as the ratio I_2^2/EI_3, and the effective receiver noise spectral density, N_e, is defined by the ratio N_iI_4/I_3. The statistical efficiency of this suboptimal receiver is
$$F = \left(\frac{d'_G}{d'_I}\right)^2 = \phi\left(\frac{N_o}{N_o + N_e}\right)$$
An energy-detector model is also consistent with our results [D. B. Green and J. A. Swets, *Signal Detection Theory and Psychophysics* (Wiley, New York, 1966), pp. 209–232].
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13. We thank J. Sandrik for his assistance in display calibration, D. Pelli for useful discussion and comments, B. Fowler for assistance in preparing this manuscript, and A. B. Watson for suggesting that we use σ equal to the reciprocal of f. This work was done while A.B. held an FDA visiting scientist award at the Bureau of Radiological Health.

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Hydralazine Reactions

The observations by Dubroff and Reid (*1*) on reactions of hydralazine with ^{3}H-labeled thymidine and ^{3}H-labeled deoxycytidine in aqueous solutions, both in the dark and in the presence of light, need to be criticized. (i) Hydralazine is extensively (85 percent) bound to human plasma proteins (*2*). At the usual dose, the highest free concentration is $10^{-7}M$ to $10^{-6}M$; Dubroff and Reid used $10^{-5}M$ to $10^{-1}M$. (ii) The half-life of hydralazine in man is short (about 1 hour), and thus average plasma levels are even lower (*3, 4*). (iii) Dubroff and Reid did not consider that the major portion of apparent hydralazine in human plasma is present as labile conjugates (with pyruvic and α-ketoglutaric acids and acetone) (*5*). (iv) Hydralazine is unstable at *p*H 7.4 and 37°C (*6*). Between 0.5 and 28 days (*1*),

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most of the drug would decompose. Thus decomposition products may be the reactive species in the system described by Dubroff and Reid. This criticism regarding stability has been made about other studies (*7*). (v) Hydralazine is known to concentrate (400:1, vessel concentration to plasma concentration) in blood vessels of animals after a dose of ^{14}C-labeled hydralazine (*7*). Immunogenic reactions may be initiated in vessels, or their collagen (*7*). Collagen is known to have carbonyl groups capable of reacting with amino groups (*8*). (vi) Several reviews deal with hydralazine (*4, 7, 9, 10*), and two cover physicochemical properties and assay methods in detail (*7, 9*). Thus Dubroff and Reid should consider the measurement of hydralazine in their experiments.

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The major criticism of Dayton and Israili is that the actual concentrations of free hydralazine in plasma are lower than the $1.0 \times 10^{-5} M$ we reported. First, it is likely that highly negatively charged nucleic acids can compete more effectively than albumin and other plasma proteins for binding to hydralazine. Second, in patients susceptible to hydralazine-induced lupus erythematosus, plasma concentrations of $1.0 \times 10^{-6} M$ hydralazine can be achieved (*1, 2*). The latter concentration is corrected for and excludes labile conjugates with pyruvic and α-ketoglutaric acids and acetone. Third, we have shown reactions of hydralazine at $1.0 \times 10^{-7} M$ with [methyl-^{3}H]thymidine. At $1.0 \times 10^{-7} M$ hydralazine, 3.8 percent of [methyl-^{3}H]thymidine is converted to product, and at $1.0 \times 1.0^{-5} M$ hydralazine, 9.5 percent of [methyl-^{3}H]thymidine is converted to product under the conditions described in (*3*). Fourth, the short half-life is unimportant in that when hydralazine-associated systemic lupus erythematosus is at risk, hydralazine is usually administered every 6 hours. Fifth, it is not known how much alteration of thymidine or DNA may be required to induce hydralazine-associated systemic lupus erythematosus.

Divalent cations and *p*H are critical in the decomposition of hydralazine to phthalazine (*4*). The *p*H of our buffer (7.4) and the presence of potent cation complexing agents, citrate ions, in our buffer served to inhibit hydralazine decomposition (*5*). Hydralazine showed very little decomposition in our incubation medium even after 5 days at 37°C (0.3 percent by high-performance liquid chromatography analysis).

The concentration of hydralazine in vessels (400:1, vessel:plasma ratio) results in hydralazine concentrations of $4 \times 10^{-4} M$ to $4 \times 10^{-5} M$. Such hydralazine is available to react with thymidine and DNA. Further, this reaction would be markedly enhanced by ultraviolet light reaching vessels in the papillary dermis.

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