All four causes of indeterminacy, individually and combined, reduce the precision of prediction.

One may raise the question at this point whether predictability in classical mechanics and unpredictability in biology are due to a difference of degree or of kind. There is much to suggest that the difference is, in considerable part, merely a matter of degree. Classical mechanics is, so to speak, at one end of a continuous spectrum, and biology is at the other. Let us take the classical example of the gas laws. Essentially they are only statistically true, but the population of molecules in a gas obeying the gas laws is so enormous that the actions of individual molecules become integrated into a predictable—one might say "absolute"—result. Samples of five or 20 molecules would show definite individuality. The difference in the size of the studied "populations" certainly contributes to the difference between the physical sciences and biology.

Conclusions

Let us now return to our initial question and try to summarize some of our conclusions on the nature of the cause-and-effect relations in biology.

1) Causality in biology is a far cry from causality in classical mechanics.

2) Explanations of all but the simplest biological phenomena usually consist of sets of causes. This is particularly true for those biological phenomena that can be understood only if their evolutionary history is also considered. Each set is like a pair of brackets which contains much that is unanalyzed and much that can presumably never be analyzed completely.

3) In view of the high number of multiple pathways possible for most biological processes (except for the purely physicochemical ones) and in view of the randomness of many of the biological processes, particularly on the molecular level (as well as for other reasons), causality in biological systems is not predictive, or at best is only statistically predictive.

4) The existence of complex codes of information in the DNA of the germ plasm permits teleonomic purposiveness. On the other hand, evolutionary research has found no evidence whatsoever for a "goal-seeking" of evolutionary lines, as postulated in that kind of teleology which sees "plan and design" in nature. The harmony of the living universe, so far as it exists, is an a posteriori product of natural selection.

Finally, causality in biology is not in real conflict with the causality of classical mechanics. As modern physics has also demonstrated, the causality of classical mechanics is only a very simple, special case of causality. Predictability, for instance, is not a necessary component of causality. The complexities of biological causality do not justify embracing nonscientific ideologies, such as vitalism or finalism, but should encourage all those who have been trying to give a broader basis to the concept of causality.

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Physiological Implications of Laser Beams

The very high radiation flux densities of optical masers point to important biomedical applications.

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Development of molecular amplifiers in the visible and near-visible region (*1*) of the electromagnetic spectrum has been in progress at several laboratories. Such amplifiers go under the designation of "laser" or optical maser, the former term being an acronym for *l*ight *a*mplification by *s*timulated *e*mission of *r*adiation. Such devices have been successfully demonstrated at several places (*2*), and several industrial organizations have made them available commercially. It is almost certain that lasers will be incorporated into communications and other technologies at a rapid rate. This article presents some preliminary calculations which are of physiological interest in terms of the hazard associated with laser beams and their potential employment as biological and clinical tools.

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Properties

From the point of view of physiological interest there are two important properties of laser beams, the extremely collimated character of the light and its high degree of monochromaticity. The collimation property implies the possibility of obtaining large energy densities in narrow beams. The optimum divergence angle of a laser beam, ϕ_{min}, is limited only by the wavelength of the light emitted and the diameter of the laser source in accord with the Fraunhofer diffraction relationship:

$$\phi_{min} = 2.44\,\lambda/D_L \qquad (1)$$

Here λ is the wavelength of the emitted laser light and D_L is the diameter of the beam emerging from the laser source or from a subsequent lens system, if one is used.

The spectral line of laser light is potentially much narrower than the spectral lines achievable by ordinary excitation processes in gas discharge tubes or arcs, which are limited by the Doppler widths of spontaneous radiative transitions of individual atoms. Laser light, comprised as it is of coherent superposed wave trains emitted during induced transitions, is not so limited. Spectral lines narrow as the power of the laser source increases; lines as narrow as 10^{-6} of a Doppler width have been observed (*3*), as predicted by theory (*1*).

Retinal Energy Density from Laser Beams

In subsequent paragraphs we give approximate formulas for retinal spot size and light intensity under various conditions. Consider a laser source that gives an energy release of S joules per burst for a pulsed laser or of S watts for a continuously operated laser. The energy flux density or intensity is $I = S/A_B$ where A_B is the cross-sectional area of the beam. At a distance r centimeters from the laser source (sufficiently great so that the laser can be regarded as a point source), I is also given by:

$$I = \frac{S}{A_B} \rightarrow \frac{S}{\Omega r^2} \qquad (2)$$

where Ω is the solid angle into which the laser light is delivered. For a small far-field angular beam width ϕ,

$$\Omega = \pi \phi^2/4 \qquad (3)$$

The diameter of any beam of light may be decreased (increased), with corresponding angular magnification (minification), by an appropriate pair of lenses or mirrors (see Fig. 1). For such an afocal lens pair the relation $D\phi = D'\phi'$ holds approximately, where D and D' are, respectively, diameters of the incident and exit beams and ϕ and ϕ' are angles between rays within the beams. That is, the angular distribution of light rays within the beam is magnified (minified) by such a lens pair.

When a beam is incident upon a pupillary area C (in square centimeters), an amount of light IC will actually enter the eye. Depending on the wavelength, more or less of this energy will be absorbed by the cornea, lens, aqueous, and vitreous structures before the light reaches the retina. According to Ludvigh and McCarthy (*4*), about 70 percent of the red light (7000 A) incident on the eye reaches the retina (Table 1).

Table 1. Light transmission through the human eye (*4*).

Color	Wavelength (A)	Transmission (%)
Red	7000	70
Orange	6000	61
Yellow	5800	59
Green	5000	49
Blue	4700	43
Violet	4100	10

When the fraction of incident light transmitted to the retina is designated by p, the intensity R at the retina is the total energy reaching the retina divided by A, the area of the retinal image, or:

$$R = ICp/A \qquad (4)$$

R is in joules per square-centimeter burst or in watts per square centimeter, depending upon whether the laser oscillator is pulsed or continuously radiating light. There are a number of special cases of interest which may be deduced from Eq. 4. Their discussion requires several parameters in addition to those previously defined.

The smallest angular displacement, $\xi_{\min}$, that can be resolved by the eye cannot be less than ξ_F, the angular resolution determined by the Fraunhofer diffraction pattern produced by the pupil, regarded as a circular aperture upon which plane wave radiation is incident. Using the Rayleigh criterion, one has

$$\xi_{\min} \geqq \xi_F = 2.44\ \lambda/D_E \qquad (5)$$

where λ is the wavelength of the incident radiation and D_E is the aperture of the pupil. In a real eye, the retinal spot is larger than the Fraunhofer spot. It follows that, if f is the focal length of the eye, the minimum diameter $h_{\min}$ of any retinal image spot is simply:

$$h_{\min} = f\xi_{\min} \qquad (6)$$

In the subsequent discussion we also make use of the retinal spot angle η, which is the angular displacement subtended by the retinal spot at the eye lens. By this definition, the diameter of the image on the retina h is given by:

$$h = f \tan \eta \simeq f\eta \qquad (7)$$

Angle η may or may not be the same as the object angle subtended by the geometrical diameter of the laser source, depending upon considerations which will be made evident below. Specifying the object angle θ, one finds from elementary optics that:

$$\tan \theta = D_L/r$$

For small θ,

$$\theta \simeq D_L/r \qquad (8)$$

Now for sufficiently small distances the eye may not be able to encompass the entire laser source because of the small angular divergence, ϕ, of rays within the laser beam. Rays from the edge of the laser may not enter the eye. This would be true when

$$\theta = D_L/r > \phi \qquad (9)$$

However, the minimum effective image spot angle can never be less than $\xi_{\min}$.

If the object angle θ is less than the laser beam angle ϕ but greater than the minimum retinal spot angle $\xi_{\min}$, ($\xi_{\min} < \theta < \phi$), then the image angle and object angle are equal:

$$\eta = \theta \text{ and } h = f\theta \qquad (10)$$

If the object angle is greater than the laser beam angle but the latter is greater than $\xi_{\min}$—that is, $\xi_{\min} < \phi < \theta$—the retinal spot angle is equal to the laser beam angle, or:

$$\eta = \phi \text{ and } h = f\phi \qquad (11)$$

If either θ or ϕ is smaller than $\xi_{\min}$, then $h = f\xi_{\min}$, as already mentioned.

In the ensuing paragraphs we shall consider the observer moving nearer to the laser source from a distant point under which the conditions of case A prevail.

Case A. This is the far-field case in

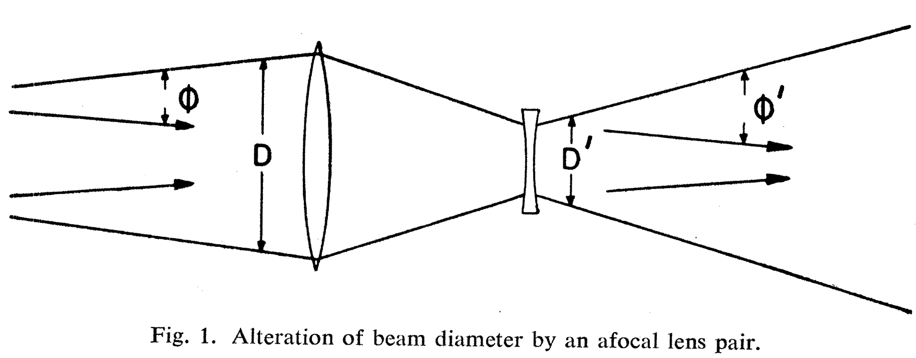

Fig. 1. Alteration of beam diameter by an afocal lens pair.

which the eye can see light from all parts of the laser but the retinal-image spot size is limited by the Fraunhofer diffraction pattern formed by the eye—that is, $\theta < \phi$, $\theta < \xi_{\min}$. For the retinal energy density one has:

$$R = \frac{ICp}{A} = \frac{S}{\Omega r^2} \cdot \frac{4\,Cp}{\pi h_{\min}{}^2} = \frac{16SCp}{\pi^2 \phi^2 f^2 \xi_{\min}{}^2 r^2} \qquad (12)$$

Making use of Eq. 5 and of $C = \pi D_E{}^2/4$, one has alternatively:

$$R = \frac{4SD_E{}^4 p}{(2.44)^2 \pi \phi^2 f^2 \lambda^2 r^2} \qquad (12a)$$

Case B. This is the near-field case in which the laser beam can no longer be considered as coming from a point source. The retinal spot size will be larger than the minimum due to eye diffraction if both the object angle and the angle between rays in the beam are larger than the Fraunhofer angle of the pupil ($\xi_{\min} < \theta, \phi$). Then the spot size is given by Eq. 10 or Eq. 11.

A more general formula for the retinal energy density or intensity, valid for case *B* as well as all other cases, is given by Eq. 13:

$$R = \frac{16SCp}{\pi^2 r^2 f^2 \phi^2 \theta^2 \xi^2_{\min}} [\min(\phi,\theta,\xi_{\min})]^2 \qquad (13)$$

or

$$R = \frac{4S\,D_E{}^2 p}{\pi r^2 f^2 \phi^2 \theta^2 \xi^2_{\min}} [\min(\phi,\theta,\xi_{\min})]^2 \qquad (13a)$$

Here, min $(\phi,\theta,\xi_{\min})$ is equal to the smallest of the three angles: ϕ, θ, and $\xi_{\min}$. Note that R is inversely proportional to r^2 in the far-field case, when $\theta < \phi, \xi_{\min}$, and is independent of r otherwise.

Case C. The beam may be smaller than the pupil as it enters the eye. This situation might obtain either because the laser diameter is smaller than the diameter of the pupil or because the beam diameter has been made smaller by a lens train (Fig. 1). In either case the spot size will be enlarged. The energy density or intensity in the spot focused on the retina will again be given by Eq. 13a if D_E is taken to be the diameter of the beam passing through the pupil and r is the distance from the eye to the laser, or, if a lens system is employed, to the last lens.

The TRG Vireo I laser light, a pulsed ruby laser used in the animal experiments reported by Zaret *et al.* in this issue (*5*), has the following approximate values for the parameters previously discussed: $S = 0.1$ joule per burst; $\phi = 0.005$ radian; $\lambda = 7 \times 10^{-5}$ cm (6943 A); $D_L = 1$ cm; and pulse duration $= 0.5$ msec. The range of D_E in the normal eye depends principally upon accommodation to the level of illumination and varies from about 0.15 to 0.6 cm (*6*). From Eq. 5 we find, for a wavelength of about 7×10^{-5} cm, that $0.00014 < \xi_F < 0.00057$ radian for 0.6 cm $> D_E >$ 0.15 cm; $\xi_{\min}$ is somewhat larger than ξ_F, but in any case, $\xi_{\min} < \phi$ for the Vireo I. Taking D_E as 0.5 cm for purposes of calculation, one immediately infers that the critical distance r_c which separates the near-field case from the far-field case is given by

$$r_c = \frac{D_L}{\xi_{\min}} \qquad (14)$$

The critical distance r_c is then somewhat less than

$$\frac{D_L}{\xi_F} = \frac{D_E D_L}{2.44\lambda} = 2.9 \times 10^3 \text{ cm} \qquad (15)$$

when $D_E = 0.5$ cm is taken for purposes of calculation. Taking $p = 0.7$ and $f = 1.67$ cm (*7*), one calculates for the near-field case ($r < r_c$) from Eq. 13 or 13a that $R = 326$ joules per square-centimeter per burst.

This is roughly the retinal energy density that would be delivered by direct viewing of the sun for about ½ minute (*8*) and about 6 times the energy density required to produce a retinal burn in the experiments of Eccles and Flynn (*9*). In these experiments the eyes of rabbits were exposed to telescopically concentrated sunlight. Different intensity rates were used for various elapsed times. Eccles and Flynn made exposures at 6, 40, 50, and 70 calories per square centimeter per minute within the focused retinal spot. An exposure of 40 cal/cm^2 min for 30 seconds appeared to be innocuous, while 50 cal/cm^2 min for the same period was likely to produce a retinal lesion. The latter exposure corresponds to an integrated intensity of about 100 joule/cm^2. On the other hand, the higher intensity for only 10 seconds, corresponding to an integrated intensity of 50 joule/cm^2 was sufficient to produce a lesion. At 6 cal/cm^2 min an exposure of 12 minutes was required to produce retinal damage—an integrated intensity of about 300 joule/cm^2.

The existence of an intensity or energy density rate-dependence is clearly evident. It is probable that there is a short integration time within which damage is proportional to the integrated intensity, irrespective of the rate. If this time is very much shorter than 10 seconds, then the integrated intensity obtained with the 0.5-millisecond duration of the Vireo I laser pulse may be considerably more than 6 times that required to produce a retinal lesion.

We conclude that the laser, being an emitter of high-intensity light, is a new energy source to be explored with regard to its effects on ocular and other tissues with a view toward biomedical application. Furthermore, persons working with laser light sources should be alerted to the potential occupational hazard.

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