Identification of a Violet Receptor in Human Color Vision

Edgar Auerbach* and George Wald

Biological Laboratories, Harvard University, Cambridge

ONE of the most pressing tasks of visual physiology, still largely unfulfilled, is to identify the various types of cone concerned with human color vision and to learn their properties. Probably the closest approach to accomplishing this is found in the work of Stiles (*1*). Stiles measured the visibility of a small test stimulus of one color viewed foveally against an adapting field of another color. His measurements display characteristic inflections, like those that ordinarily mark transitions between cone and rod vision, although they involve the responses of cones alone. By analyzing these functions, Stiles has derived a trio of curves that appear to represent the spectral sensitivities of three classes of cone. De Vries (*2*) later reported similar measurements, leading to much the same result.

The present experiments (*3*) involve measurements of dark adaptation, which reveal the presence in the human retina of a species of cone selectivity sensitive to violet light, the excitation of which induces a violet sensation. The crux of the procedure is to adapt the eye very strongly with red, orange, or yellow light, which spares the violet receptor, and then to measure its dark adaptation with test lights of low wavelengths. In this way one finds that the first 2 to 3 min of dark adaptation are occupied with a receptor with maximal sensitivity in the neighborhood of 436 mμ.

Procedure. All our measurements of visual threshold were performed with the spectral adaptometer described earlier (*4*). In this instrument, 10 wavelengths are isolated with color filters from the radiation of a high-pressure mercury arc lamp. The test field was circular and subtended an angle of 1° with the eye. It was exposed for flashes of 1/5 sec. Its brightness was regulated with a pair of annular neutral wedges, rotating in opposite directions so as to compensate each other. A variable fixation point permitted the location of the image of the test field on any desired portion of the retina within a radius of 12° of the fixation point. The relative energies of the test illuminations were measured with a barrier layer photocell, calibrated at our laboratory and by the National Bureau of Standards.

For light adaptation, a 1000-w concentrated filament lamp was used, at a distance of 65 cm from a large lens (diameter 11.5 cm; focal length, 18 cm). The eye was placed at the lens focus, so as to be in the position of Maxwellian view, in which most of the lens surface appeared to be evenly illuminated. The wavelength composition of the adapting field was regulated with color filters, its brightness with neutral filters.

The brightnesses of both white and colored adapting lights were measured with a Macbeth illuminometer. That is, all brightnesses were evaluated in terms of the standard white of this instrument. The adapting lights used in our experiments were very bright indeed—of the order of 10^4 to 10^6 millilamberts.

Observations. Figure 1 shows the dark adaptation of a normal observer, following 5 min exposure to white light (5.0×10^5 millilamberts). Thresholds were measured at 621 mμ in the orange and at 436 mμ in the violet. Each dark-adaptation curve consists principally of two sections: a first rapid fall of threshold to a plateau, the adaptation of the cones; followed by a second fall of threshold to a final plateau, the adaptation of the rods. The cone section, measured at 436 mμ, persists for about 13 min and displays minor inflections; measured at 621 mμ, it is simple in form and persists for about 30 min. This is because the cones are much more sensitive to orange than to violet light, whereas in the rods this relationship is reversed (the Purkinje phenomenon). As a result, the transition from cone to rod thresholds is marked by a crossing of the dark-adaptation curves, a direct expression of the Purkinje shift.

Figure 2 shows a series of similar measurements following adaptation to lights of various wavelengths. The curves following white-light adaptation are similar to those of Fig. 1. Following adaptation to yellow light, containing all visible wavelengths longer than 490 mμ, much the same result is obtained.

Adaptation to orange light (> 520 mμ), however, produces a very different result. Dark adaptation measured at 621 mμ is much as before, but at 436 mμ it has changed markedly. For the first 2 min of dark adaptation, the threshold for violet light lies *below* that for orange, the reverse of the familiar cone relationship. After about 2 min, the curves cross in what may be called a reverse Purkinje shift. Then after about 15 min of dark adaptation, the curves cross again in the true Purkinje shift, marking the change from cone to rod thresholds. Adaptation to orange-red light (> 590 mμ) yields a similar result, somewhat accentuated.

Following such adaptations to orange-to-red light, the measurements at 436 mμ display two distinct cone plateaus, separated by a break; and frequently also—as in Fig. 2 at the lower right and in Fig. 3—associated with the shift to the second plateau, the color sensa-

tion at the threshold is reported to change. All these effects are evidences of the essential heterogeneity of cone dark adaptation.

The most significant feature of this result is the special sensitivity to violet light displayed by the cones in the first 2 to 3 min of dark adaptation. How is this achieved? Inspection of the curves in Fig. 2 shows that dark adaptation measured at 621 mμ is only slightly affected by the quality of light adaptation. The special effect of orange- or red-light adaptation is, not so much to raise further the threshold to orange light, as to fail to raise it to violet light. That is, the effect of orange or red light adaptation is not so much to increase the adaptation of red-sensitive receptors, as to spare a violet-sensitive receptor.

The spectral sensitivity of this receptor can be measured by a procedure illustrated in Fig. 3. Normal subjects were adapted repeatedly to intense orange-to-red light, and their dark adaptation was measured at 8 wavelengths available in our spectral adaptometer. Figure 3 shows a small sample of such data, selected from a long series of measurements with seven subjects. Between 5 and 12 min of dark adaptation, these curves exhibit the familiar relative sensitivities ordinarily associated with human cone vision; but during the first 2 min, the measurements made at 405, 436, and 492 mμ display the special properties of the violet receptor.

From such families of curves as shown in Fig. 3, extended to include the other wavelengths, one can read off values of the threshold at each wavelength, at 1 and 10 min of dark adaptation. In this way one obtains the spectral sensitivity curves shown in Fig. 4. They are plotted in terms of $-\log$ threshold, that is, log 1/threshold, or log sensitivity.

Figure 4 shows that at 1 min of dark adaptation following orange-to-red light adaptation, the spectral sensitivity of cone vision is dominated by a high, narrow peak, maximal in the neighborhood of 436 mμ. This is the sensitivity curve of the violet receptor. Beside it is the broad, subsidiary maximum at about 555 mμ ordinarily characteristic of cone vision. After 10 min of dark adaptation, the latter maximum has become dominant. Nothing remains of the violet maximum but a shallow inflection.

Such an inflection in the spectral sensitivity curve of human cone vision has been noted before. It is much accentuated in the region of the macula lutea, and has been ascribed there to the presence of the macular pigment, xanthophyll (*5*). The fact that peripheral areas of the retina also display a shallow inflection suggested that they too contain small amounts of macular pigment. It seems from the present observations, however, that in the peripheral retina this inflection is caused mainly by the violet receptor. The same effect must exist also in the central retina, where, however, an added inflection is superimposed on it, owing to the macular pigment.

We have as yet made measurements at too few wavelengths to define accurately the shape and position of the sensitivity curve of the violet receptor. The available data, however, are in good agreement with previous estimates of this function. In Fig. 4 we show for comparison Stiles's curve of what he calls the "blue mechanism" (*6*), here plotted to an arbitrary height (*1b*). Our curve agrees about as well also with the short-wavelength "Grundempfindung" of König and Dieterici, maximal at about 450 mμ (*7*).

We speak of this as the violet receptor because its maximum sensitivity is in the violet, and because when it alone is stimulated under the conditions we have described, normal observers ordinarily report the threshold sensation as violet. There is no opportunity here to go in detail into the vexatious question whether

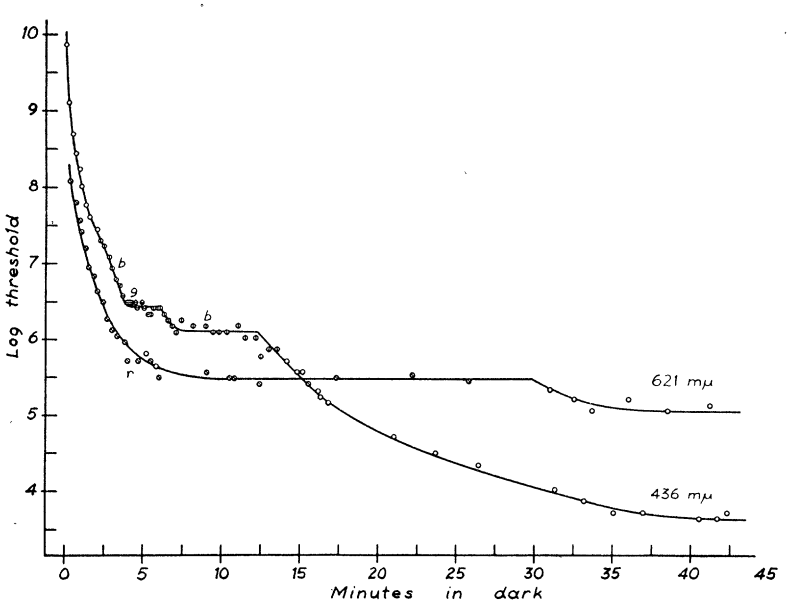

Fig. 1. Dark adaptation measured in the orange (621 mμ) and in the violet (436 mμ), following exposure of the eye to white light (5.0×10^5 millilamberts) for 5 min. A 1° test field was used, fixated 6° from the fovea, and exposed for flashes of 1/5 sec. All observations are monocular. Log threshold is expressed in relative energy units. Thresholds seen as colorless are plotted as open circles; others are marked with a small letter: *b*, blue; *g*, green; *r*, red. Each dark-adaptation curve consists of two main sections, separated by a break: a first portion, owing to the dark adaptation of the cones, followed by a second section, owing to the rods. Even the cone section as measured at 436 mμ displays inflections and changes of hue, caused presumably by the participation of various types of cone in the measurement.

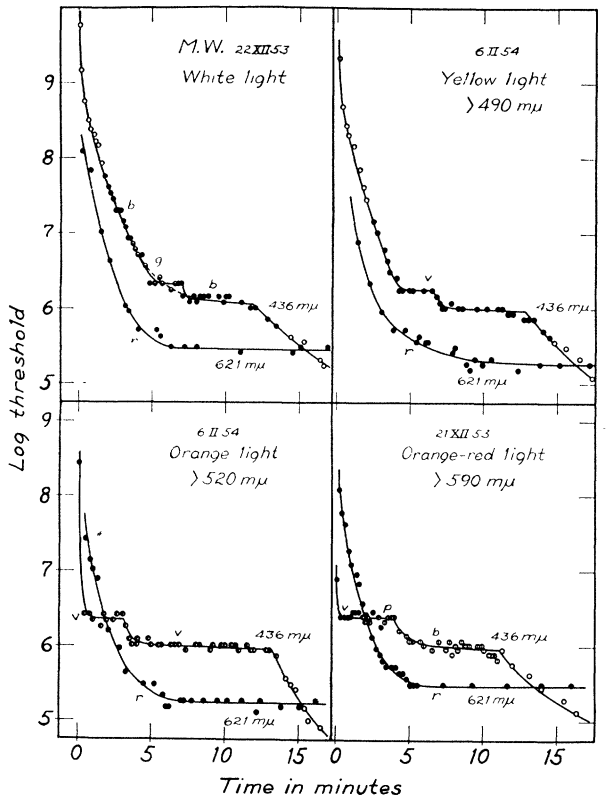

Fig. 2. Dark adaptation measured at 436 and 621 mμ following adaptation to lights of various wavelength composition. Otherwise as in Fig. 1. The colored lights used in light adaptation included all visible wavelengths above those stated in the heading of each figure. The adapting log brightnesses in millilamberts are as follows: white, 5.70; yellow, 6.34; orange, 6.15; orange-red, 5.87. As in Fig. 1, open circles represent thresholds seen as colorless; those seen as colored are accompanied by small letters: *v*, violet; *p*, purple; and so on. After exposure to the white or yellow light, the dark adaptation of the cones follows a relatively conventional course; but after exposure to light of longer wavelengths, the measurements at 436 mμ for the first 2 to 3 min exhibit the special characteristics of the violet receptor.

the primary sensation associated with this receptor is violet or blue (see *8*). It seems to us probably to be violet; and in certain ways to behave as a true primary. So, for example, when dark adaptation is measured with violet light following light adaptation in the orange-to-red, the threshold, when initially the violet receptor seems to be functioning alone, is usually reported as violet; but with the fall of threshold to the second cone plateau, marking the entrance of other types of cone, the threshold sensation commonly changes to blue. Examples are seen in the lower right-hand part of Fig. 2 and in the measurements at 405 and 436 mμ in Fig. 3.

Up to this point we have discussed the effects of adaptation with orange-to-red light. It is interesting to contrast these with the effects of blue-light adaptation. This is done in Fig. 5, which shows spectral sensitivity curves measured at 1 and 10 min of dark adaptation following light adaptation in the orange-to-red and blue. The curves for orange-to-red light adaptation are as in Fig. 4. After 1 min in the dark following blue-light adaptation, the sensitivity curve displays only the conventional cone maximum at about 555 mμ. The inflection in the violet region has been erased, which is added evidence that in the peripheral retina this is associated with the violet receptor rather than with the presence of an absorbing pigment. Just as the major effect of red-light adaptation is to spare the violet receptor, the major effect of blue-light adaptation is to depress its sensitivity. Yet significant differential effects are evident also at longer wavelengths. The spectral sensitivity curves measured at 1 min of dark adaptation cross at about 510 mμ; to the right of this point, the sensitivity is consistently higher following adaptation to blue light than following adaptation to red.

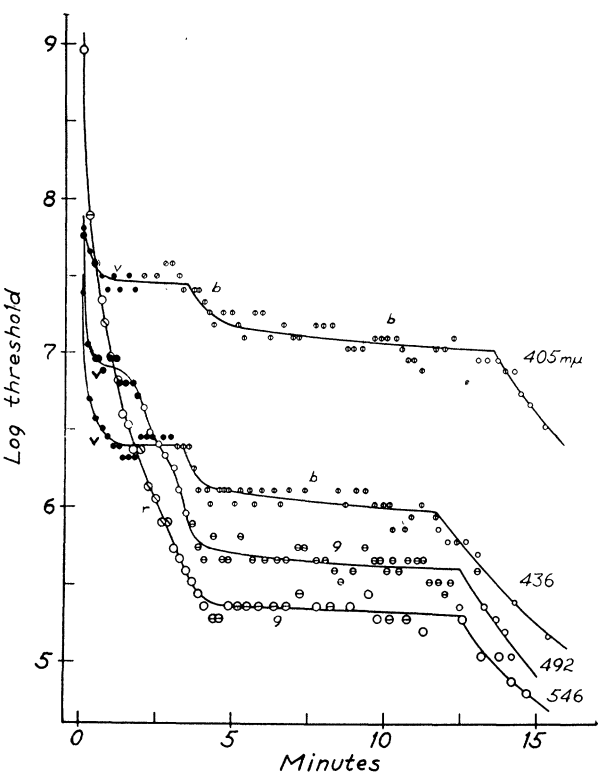

Fig. 3. Dark adaptation measured at four wavelengths following light adaptation in the orange or orange-red (log brightness, 5.87 or 6.14 millilamberts). Dark adaptation measured at 546 mμ is relatively simple in form; but the curves measured at 405, 436, and 492 mμ begin with the thresholds of the violet receptor and display special discontinuities for this reason. From such a family of curves, one may read off the thresholds at each wavelength at 1 and 10 min of dark adaptation. It is in this way that the curves shown in Figs. 4 and 5 were obtained.

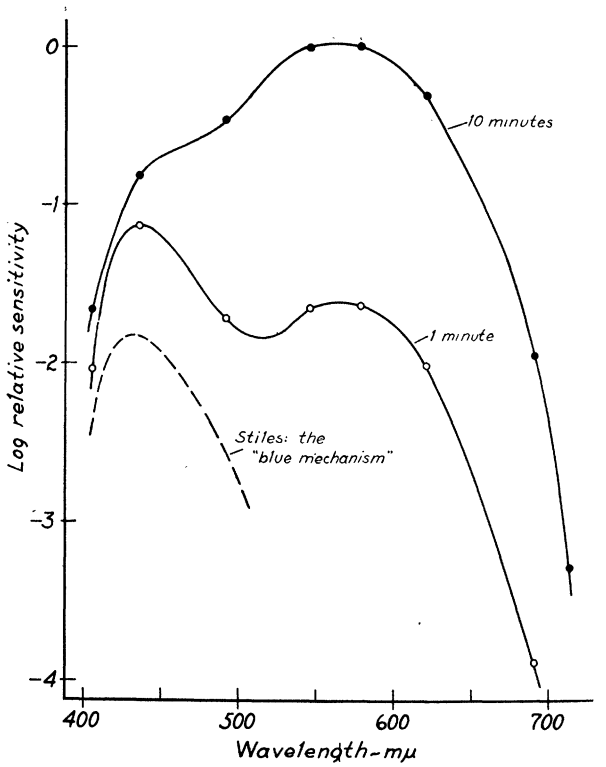

Fig. 4. Spectral sensitivity of cone vision measured at 1 and 10 min of dark adaptation following exposure to orange-to-red lights. Averaged data from seven normal observers, involving a 1° test field, centered 6° below the fixation point. Ordinates are log relative sensitivity (−log threshold). The curve obtained at 10 min of dark adaptation resembles the conventional photopic luminosity function, maximal at about 555 mμ. At 1 min of dark adaptation, however, the curve is bimodal; the primary maximum at about 436 mμ is that of the violet receptor. For comparison, the curve of Stiles's "blue mechanism" is shown also.

Even after 10 min of dark adaptation something remains of these distinctions. In the violet the sensitivity tends to be a little higher following adaptation to red light, whereas in the orange and red it is higher following adaptation to blue.

Experiments similar to those described have been performed also with protanopes and deuteranopes. Following exposure to intense orange or red light, the dark adaptation of both types of color-blind, measured at 621 mμ, is normal in shape, although the protanope thresholds are abnormally high, an expression of the subject's red-blindness. After exposure to orange or red light, dark adaptation measured at 436 mμ in both types of color-blind is simple in form and seems to involve the violet receptor alone. No such inflections and changes in color sensation appear as those that accompany cone dark adaptation in normal observers. Indeed, all our observations with protanopes and deuteranopes are consistent with the view that each of these possesses only two types of cone—the violet receptor and one other.

We have not yet had the opportunity to examine a tritanope. We have, however, made measurements in the central fovea of a normal observer, a region of the retina that has been characterized at times as "blue-blind" (*9*). Although genuine phenomena of great interest lie behind this characterization, they are not to be explained by the absence of the violet receptor, for this structure appears prominently in a 0.5° area of the central fovea as elsewhere in the retina.

References and Notes

* Hadassah research fellow in ophthalmology, from Hadassah University Hospital, Jerusalem.

1. W. S. Stiles, *Proc. Roy. Soc.* (*London*) B, **127**, 64 (1939); *Ned. Tijdschr. Natuurk.* **15**, 125 (1949); *Rev. opt.* **28**, 215 (1949).
2. H. de Vries, *J. Opt. Soc. Amer.* **36**, 121 (1946); also W. S. Stiles, *ibid.* **36**, 491 (1946).

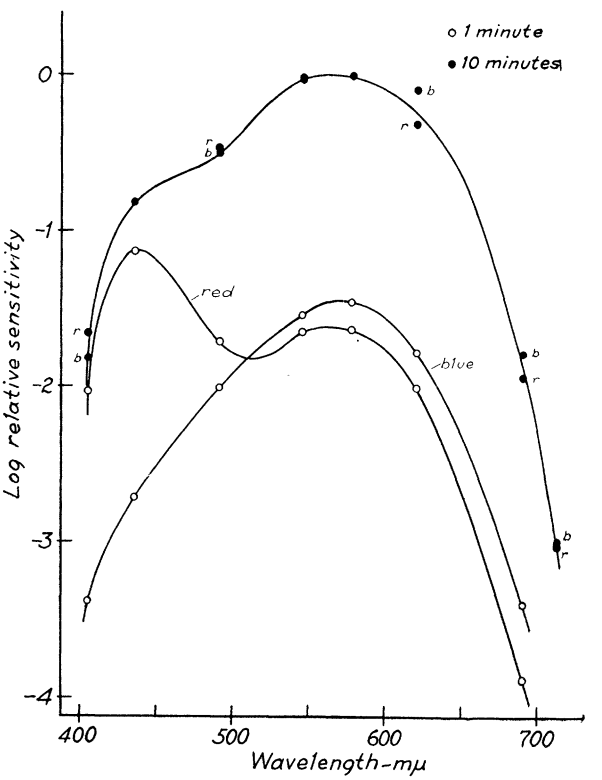

Fig. 5. Spectral sensitivity of cone vision measured at 1 and 10 min of dark adaptation, following exposure to orange-to-red or to blue lights. The curve at 1 min of dark adaptation after red-light adaptation displays the high peak at 436 mμ of the violet receptor, in addition to the lower, conventional photopic maximum. The corresponding curve after blue-light adaptation has the latter maximum alone; all evidence of the violet receptor has been erased. After 10 min of dark adaptation, both sets of data display the ordinary photopic maximum and also a shoulder at low wavelengths, a residue from the violet receptor. The 10-min curve also still exhibits signs of the differential effects of red- and blue-light adaptation: the sensitivity following red adaptation (*r*) tends to be higher at short wavelengths and lower at long wavelengths than following blue-light adaptation (*b*).

3. This investigation was supported in part by funds from the Rockefeller Foundation and the Office of Naval Research. We should like also to express our appreciation to the Institute for Advanced Study, Princeton, where this paper was written.
4. G. Wald, *J. Opt. Soc. Amer.* **35**, 187 (1945).
5. ———, *Science* **101**, 653 (1945); *Documenta Ophthal.* **3**, 94 (1949).
6. Stiles refers to a second "blue mechanism" which, in addition to the peak at about 435 mμ, is relatively sensitive throughout the remainder of the spectrum. This may represent the composite effect of the violet receptor and other types of cone discharging through the same optic nerve fiber.
7. A. König and C. Dieterici, *Z. Psych. und Physiol. Sinnesorgane* **4**, 241 (1892); reprinted in A. König, *Physiologischen Optik* (Barth, Leipzig, 1903), p. 214.
8. G. F. Göthlin, *J. Opt. Soc. Amer.* **34**, 147 (1944).
9. A. König, *Sitzber. deut. Akad. Wiss. Berlin* (1894), p. 577; reprinted in A. König, *Physiologischen Optik*, chap. 24; E. N. Willmer, *Nature* **153**, 774 (1944); E. N. Willmer and W. D. Wright, *ibid.* **156**, 119 (1945).

Social Implications of the Genetics of Man*

A. H. Sturtevant

California Institute of Technology, Pasadena

MAN is one of the most unsatisfactory of all organisms for genetic study. The time interval between successive generations is long, at best individual families are too small to establish ratios within them, and the test-matings that a geneticist might want cannot be made. Obviously no geneticist would study such a refractory object, were it not for the importance that a knowledge of the subject has in other fields.

One consequence of the difficulty of the material is that the exact mode of inheritance is known for very few of the differences among individuals. It is important that suspected cases be recorded, in order that other workers may check them; but there is an unfortunate tendency to accept such records as demonstrations rather than as suggestions. After examining some of the available published evidence, I am convinced that, even for some of the standard textbook examples, the evidence for the accepted mode of inheritance is far from conclusive—and that it would be recognized as at best suggestive, if any organism other than man were concerned.

There are enough unambiguous examples known to make it clear that the same principles are at work in man as in all other higher animals and plants—and even without such evidence, enough is known about the cytology of human tissues to give us confidence that no peculiar kind of inheritance is to be expected in man. In fact, much of the argument concerning the practical aspects of the genetics of man is best based on experimental evidence from other organisms rather than on what is known directly from study of human populations.

The position is especially unsatisfactory with respect to the heritability of the most important of all human differences—namely, mental ones. It would be possible to quote recent authorities for rather extreme positions on each side of this question. To some there appears to be no clear evidence for genetic differences in mental capacities among most individuals or among races, the observed mental diversity being attributed to environmental effects; to others the position is reversed—the environment accounts for little, genetic differences for nearly all the observed diversity. In these circumstances it is necessary to examine what direct evidence we have.

At the sensory level there is good evidence for inherited differences. There can be no question that such things as color-blindness, night-blindness, or sensitivity to the bitter taste of phenylthiourea are simply inherited; and one may confidently suppose that other such inherited sensory differences remain to be discovered. As has been pointed out by Blakeslee, we all live in different worlds by virtue of inherited differences in our sensory reactions to external stimuli. It should further be pointed out that these differences have effects at the highest mental levels. About 8 percent of white males are at least partially red-green blind; and when such a man looks at a painting he does not see what the artist put there or what other people see. It is clear that this simple and rather frequent genetic property has inevitable effects on the esthetic life of the individual.

These remain rather trivial sorts of differences; but there is another large class of inherited mental differences that is far from trivial. Certain types of severe mental derangement, such as Huntington's chorea or phenylketonuria, clearly have at least a large inherited element in their causation, although for most of them the exact method of inheritance may be regarded as somewhat uncertain.

However, what we are really most interested in is the vast array of differences lying between these extremes; and it is just here that the difficulty of the human material becomes most serious. When one is dealing with complex characters that vary more or less continuously in diverse respects, a genetic analysis is difficult in any material; in the case of man, a direct attack on the problem looks even more difficult.

One thing we want to know is: What portion of

* Presidential address at the Pacific Division of AAAS, Pullman, Wash., 22 June 1954.