Appearance of pulsed infrared light: second harmonic generation in the eye

Qasim Zaidi and Joel Pokorny

In certain conditions, when the human eye is irradiated by pulsed IR laser light, the observer sees the light as yellow or green. This could be due to second harmonic generation by the cornea, the lens, the retina, or two-photon absorption by the photopigments. It is shown that the most likely cause of this phenomenon is second harmonic generation at the cornea.

I. Introduction

Infrared lasers are becoming increasingly available and are being used for a variety of clinical purposes. Knowledge about the interaction of high energy IR light with ocular structures is important for these applications. In this paper the visual effects of irradiating the human eye by pulsed IR laser light are examined.

In 1965 Vasilenko *et al.*[1] reported that IR light from pulsed lasers was visually matched to yellow-green or orange light. Since then a number of investigators have replicated this observation using a variety of pulsed lasers. Sliney *et al.*[2] measured the power of a 1064-nm IR light required for threshold observation of the second harmonic with and without a high rejection filter (< 0.01% transmission outside 1065 ± 5 nm) between the laser and eye. The measured thresholds were the same in both cases, indicating that the second harmonic was generated in the eye and was not an artifact of the light source. In Table I, published reports concerning the color appearance of pulsed IR laser light are summarized. The table shows that pulsed IR laser lights with wavelength >928 nm are matched to light of about half of the wavelength, i.e., the second harmonic of the laser light. In Table I, there are three main exceptions to the wavelength-halving rule. First, Vasilenko *et al.*[1] report that for 5×10^{-6}-s pulses of 948.6-nm light only the IR was detected at threshold, and Sliney *et al.*[2] report matching two different wavelengths to a 1060-nm incident light, 530 nm for 20×10^{-9}-s pulses, and 536 nm for 0.2×10^{-3}-s pulses. Third, the measurements of Dmitriev *et al.*[3] (taken from Fig. 2 of their paper) indicate that the matched wavelength was slightly less than half of the wavelength for laser wavelengths between 925 and 1000 nm and slightly more than half of the wavelength for laser wavelengths longer than 1000 nm.

Another observation for which no adequate explanation has been presented concerns energy integration of laser pulses by the visual system. Detection of IR laser light conforms to Bloch's law ($L.t$ = constant) when the first harmonic is detected.[2] However, violations of the law for second harmonic detection have been reported for pulses of 1060-nm wavelength. Savin *et al.*[4] found that threshold energy was an order of magnitude lower for a 50×10^{-9}-s pulse than for a 5×10^{-3}-s pulse. Sliney *et al.*[2] confirmed this violation for a 20×10^{-9}-s vs a 0.2×10^{-3}-s pulse as did Savin and Kolchin[5] for a 15×10^{-9}-s vs a 0.5×10^{-3}-s pulse. In contrast, for incoherent white light Bloch's law has been shown to be valid[6,7] for durations as short as 4.11×10^{-7} and 8×10^{-9} s.

There is no agreement about the underlying nonlinear mechanism or its anatomical location in the eye. Two different mechanisms have been tentatively postulated: (1) second harmonic generation by the outer segments of the photoreceptors[5]; and (2) two-photon capture by the photopigments in the retina.[3] No direct evidence supporting either of these hypotheses exists.

Dmitriev *et al.*[3] report an experiment aimed at locating the ocular structure responsible for frequency doubling. They measured the threshold for detecting the second harmonic through a 3-mm artificial pupil when a diffuser for a point source 0.1 mm in diameter was placed at various distances between 30 and 90 cm away

Qasim Zaidi is at Columbia University, Department of Psychology, New York, New York 10027, and J. Pokorny is at University of Chicago, Eye Research Laboratories, Chicago, Illinois 60637.

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Table I. Summary of Published Work on Color Appearance of Pulsed Infrared Light

Laser wavelength (nm)	Matched wavelength (nm)	Second harmonic (nm)	Pulse length (s)	References
928.0	447.0	464.0	10×10^{-9}	Dmitriev *et al.* (1979)
948.6	948.6	474.3	5×10^{-6}	Vasilenko *et al.* (1965)
951.0	464.0	475.5	10×10^{-9}	Dmitriev *et al.* (1979)
987.0	493.5	480.0	10×10^{-9}	Dmitriev *et al.* (1979)
1002.0	501.0 ± 3	501.0	$10\text{–}20 \times 10^{-9}$	Prokopyev (1980)
1002.0	500.0	501.0	10×10^{-9}	Dmitriev *et al.* (1979)
1010.0	509.0	505.0	10×10^{-9}	Dmitriev *et al.* (1979)
1032.0	516.1 ± 3	516.1	$10\text{–}20 \times 10^{-9}$	Prokopyev (1980)
1060.0	531.0 ± 14	530.0	50×10^{-9}	Savin *et al.* (1975)
1060.0	530.0	530.0	20×10^{-9}	Sliney *et al.* (1976)
1060.0	536.0	530.0	0.2×10^{-3}	Sliney *et al.* (1976)
1064.0	532.0	532.0	20×10^{-9}	Sliney *et al.* (1976)
1064.0	1064.0	532.0	1–10	Sliney *et al.* (1976)
1082.0	548.0	541.0	10×10^{-9}	Dmitriev *et al.* (1979)
1111.0	566.0	555.5	10×10^{-9}	Dmitriev *et al.* (1979)
1114.3	560.0 ± 4	557.1	5×10^{-6}	Vasilenko *et al.* (1965)
1117.7	560.0 ± 4	558.85	5×10^{-6}	Vasilenko *et al.* (1965)
1130.3	565.1 ± 3	565.15	$10\text{–}20 \times 10^{-9}$	Prokopyev (1980)
1132.0	576.0	566.0	10×10^{-9}	Dmitriev *et al.* (1979)
1146.0	582.0	573.0	10×10^{-9}	Dmitriev *et al.* (1979)
1152.5	576.0 ± 7	576.25	5×10^{-6}	Vasilenko *et al.* (1965)
1162.0	590.0	581.0	10×10^{-9}	Dmitriev *et al.* (1979)
1176.0	592.0	588.0	10×10^{-9}	Dmitriev *et al.* (1979)
1179.0	584.0 ± 13	589.5	5×10^{-6}	Vasilenko *et al.* (1965)
1202.0	600.0	601.0	10×10^{-9}	Dmitriev *et al.* (1979)
1271.4	635.7 ± 3	635.7	$10\text{–}20 \times 10^{-9}$	Prokopyev (1980)

Note: For each reported observation, the table shows the wavelength of the incident pulsed laser light, the wavelength the light is matched to, the calculated second harmonic wavelength, the pulse length of the incident light, and the reference. For convenience the pulse lengths are shown in terms of milliseconds, microseconds, or nanoseconds.

from the aperture. They made two assumptions: first, that the power of the second harmonic would be proportional to the square of the power of the incident IR divided by the area of the incident surface; and, second, that the size of the image on the retina would be proportional to the magnification factor. From these assumptions and the inverse square law, they deduced that the threshold would be proportional to the square of the distance if frequency doubling occurred at the cornea or the lens but only linearly proportional to the distance if frequency doubling occurred at the retina. They reported that their results support localization at the retina. Two additional observations have been presented as evidence that supports locating the mechanism for frequency doubling in the retina: Savin and Kolchin[5] report that test objects illuminated by IR laser light were perceived as green visual shapes conforming to the test objects; and Prokopyev[8] found that when laser light was focused on the blind spot, no detection occurred.

One further aspect of the appearance of the field is of interest. Dmitriev *et al.* (800–900 nm)[3] and Prokopyev (1002 nm)[9] report that the second harmonic appears as a point inside a larger IR field.

II. Nonlinear Optical Processes

There are two possible physical processes which could account for the observed nonlinearity: (a) second harmonic generation by one of the anatomical structures of the eye and (b) two-photon absorption by the visual photopigments.

To describe the interaction of light with matter, Maxwell's equations have to be supplemented with material laws. These laws usually connect variables like electron polarization to the induced field strength by a linear relationship. However, when the field strength is very high, such as is produced by a laser, the relationship can only be described by a polynomial involving square, cube, and higher integer powers of the field strength. Using such nonlinear relations in Maxwell's equations leads to new types of solution. When a light wave of one frequency impinges on a nonlinear substance, new waves are created in its interior associated with twice, thrice, or higher integral multiples of the incident frequency. A nonlinear substance is any medium possessing an electric susceptibility that is a nonlinear function of the intensity of the radiation. In principle, almost any solid substance without inversion symmetry can produce second harmonic radiation providing the peak power of the incident electromagnetic field is sufficiently large. (The existence of random molecular orientations in a substance necessarily implies the presence of bulk inversion symmetry.) The polarization wave produced by the interaction of the input radiation with the nonlinear material propagates through the medium and radiates an electromagnetic wave with a frequency that is different from that of the input fundamental wave. The generated power of the second harmonic is proportional to the square of the local field strength. Since normal dispersive effects are present in the medium, the propagation velocity of the second harmonic wave differs from that of the polarization that produced it. As a result, destructive interference between frequency components severely limits the second harmonic generation efficiency. To the extent that the structure of the material is conducive to phase-matching, i.e., matching the propagation velocities, the contribution of dispersive effects to second harmonic generation inefficiency is reduced.

The molecular organization of various ocular structures can be used to evaluate their potential for second harmonic generation. The intraocular fluids can be ruled out, because second harmonic generation in fluids is caused only by dynamic fluctuations in the molecular orientations and so is highly inefficient. The cornea, lens, and retina all possess a molecular structure that could generate the second harmonic. Electron micrographs and light scattering measurements show that a major portion of the cornea contains long cylindrical fibrils arranged in one or two preferred directions with local order extending over distances comparable to the wavelength of light.[10,11] An x-ray scattering study has shown that the lens has a short-range spatial order of crystallin proteins.[12] The molecular architecture of the outer segment membrane of photoreceptors is thought to consist of a bimolecular leaflet of lipid sandwiched between layers of protein. The lipid molecules lie parallel to the long axis of the outer segments, while the proteins are oriented with their molecules at right angles to them.[13]

Just like the nonlinear dispersion effect above, there are also nonlinear absorption effects. In the traditional picture of absorption, the transition rate of an atomic system going from a ground state 1 to an excited state 2 is proportional to the photon number n. But at high enough photon numbers available from the laser, the transition rate can be proportional to n^2 or n^3, and in such situations individual atoms absorb more than one photon at a time. Two-photon absorption is accompanied by fluorescence, as the transition is through an intermediate state at a higher energy level than the excited state,[14] and the photoproducts of two-photon absorption can be different from the photoproducts of single-photon absorption.[15,16]

Two-photon absorption can be ruled out as a factor on the following grounds. Visual pigments would fluoresce as a result of two-photon absorption.[16,17] This fluorescence would be at a longer wavelength than the second harmonic. The mixture of these two lights would always be matched to a wavelength longer than the second harmonic, which is inconsistent with the measurements presented in Table I.

III. Explanation of Observations

In light of the above considerations, the most probable mechanism underlying the above observations is second harmonic generation. The efficiency of second harmonic generation in the eyes, i.e., the ratio of the power of the second harmonic to the power of the incident light, is very low. The second harmonic will be detected at threshold instead of the IR only when the product of the efficiency of second harmonic generation with the ratio of the sensitivity for half of the wavelength to the sensitivity for the incident wavelength is greater than one. In Fig. 1 the log of this ratio of sensitivities for wavelengths from 760 to 1100 nm is plotted. The visual sensitivity for wavelengths shorter than 700 nm is taken from Judd's corrected version of the CIE V_λ as interpolated and tabulated by Vos.[18] The sensitivity for wavelengths longer than 700 nm is taken from Walraven and Leebeck.[19] Their curve is based on Goodeve's[20] measurements of spectral sensitivity up to 900 nm and is extrapolated to 1100 nm along the line suggested by Griffin *et al.*[21] and corrected for the transmittance of the eye media. For an approximate efficiency[22] of 10^{-10}, Fig. 1 predicts that second harmonic detection should occur at threshold for laser wavelengths longer than 1000 nm; this agrees with Vasilenko's results (Table 1). However, second harmonic generation is a nonlinear process: the efficiency is a function of peak power and is not constant for any wavelength. The cutoff wavelength for second harmonic detection, therefore, depends on the peak power of the incident laser. By using shorter pulses, Dmitriev *et al.* found second harmonic detection for wavelengths shorter than 948.6 nm for which Vasilenko *et al.* reported detection of the first harmonic only. Only Sliney *et al.*[2] have presented data detailed enough for us to derive the efficiency of the second harmonic generation. For their observers, the estimated efficiency at 1064 nm for a 20×10^{-9}-s pulse is 2.78×10^{-8}.

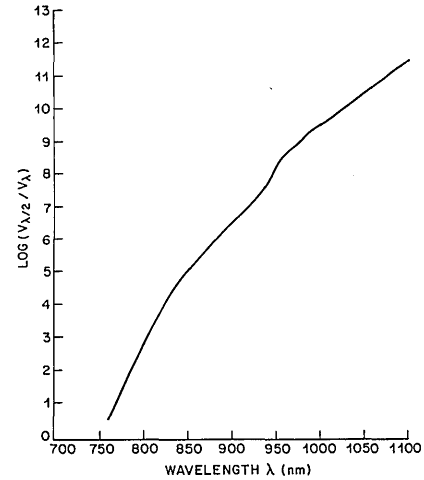

Fig. 1. For each wavelength λ, the curve shows the log of the ratio of the spectral sensitivity to light of half of the wavelength [$V_{(\lambda/2)}$] to the spectral sensitivity to light of that wavelength V_λ. Whenever the product of the efficiency of second harmonic generation with this ratio is greater than one, the second harmonic is detected at threshold.

We suggest that the systematic deviations from the second harmonic reported in Dmitriev *et al.*[3] (Table I) are a result of color mixture between the perceived IR and the second harmonic. From standardized color matching functions,[23] it can be shown that the dominant wavelength of the mixture of a small percent of an

IR (taken as the same chromaticity as 700 nm) and a large percent of the second harmonic is shorter than the second harmonic when the wavelength of the second harmonic is shorter than 494 nm and longer than the second harmonic when the second harmonic is longer than 494 nm. This parallels the color matching behavior of Dmitriev *et al.*'s subjects.

All the threshold measurements that show violations of Bloch's law are in terms of total power. However, the harmonic conversion efficiency is a monotonically increasing function of laser peak power. Peak power is higher for a shorter pulse of the same shape, wavelength, and total power as a longer pulse; consequently, the intensity of the second harmonic generated will be greater for shorter pulses. This phenomenon has two implications; first, for broad pulses, e.g., 1–10 s, the total power needed to generate sufficient second harmonic for detection may be greater than the threshold for the detection of the IR, in which case the second harmonic will not be detected at the threshold.[2] This also explains the discrepancy between the first two lines of Table I. Vasilenko *et al.*[1] were unable to detect the second harmonic for light of 948 nm with a pulse length of 5×10^{-6} s, but Dmitriev *et al.*[3] were able to detect the second harmonic for a shorter incident wavelength of 928 nm by using shorter pulses of 10×10^{-9} s. Second, the intensity of the second harmonic incident on the retina will be greater for shorter pulses, and Bloch's law will seem to be violated. The conversion efficiency for pulses of 1060 nm that are matched to 530 nm can be calculated from the measurements made by Sliney *et al.* The efficiency is estimated by dividing the interpolated total power at threshold for 530 nm by the measured total power at threshold for 1060-nm pulses. For a 0.2×10^{-3}-s pulse, the estimated efficiency is $\sim 1.8 \times 10^{-9}$, while for a 20×10^{-9}-s pulse it is $\sim 3.35 \times 10^{-8}$. Therefore, there will be more IR light mixed with the second harmonic for a 0.2×10^{-3}-s pulse than for a 20×10^{-9}-s pulse. This is consistent with the observation made by Sliney *et al.* that a stimulus of 1060 nm was visually matched to a 530-nm source for 20×10^{-9}-s pulses and to 536 nm for 0.2×10^{-3}-s pulses.

IV. Anatomical Location of Second Harmonic Generation

Direct measurements of the efficiency of second harmonic generation by the different structures of a living mammalian eye have not been made. In this section we show that published evidence either points to the cornea as the generator of the second harmonic or is equivocal.

Relevant experimental work was done by Fine and Hansen[22] who irradiated a variety of excised rabbit and dog ocular structures by pulsed ruby laser (694 nm). Cornea and sclera emitted measurable radiation at 347 ± 0.2 nm, but lens and retinal–choroidal tissue did not. Fine and Hansen estimated the power of the generated second harmonic to be $\sim 10^{-10}$ of the incident laser light. The efficiency of second harmonic generation increased as the fundamental irradiance was increased, and the second harmonic pulse was temporally narrower than the incident pulse. Both of these properties are consequences of the nonlinearity of the process. Hochheimer[24] also reports second harmonic conversion in physiologically maintained excised rabbit corneas. Although caution is necessary in generalizing from excised samples, these are the only data which directly implicate the specific ocular structures of cornea and sclera as the site of frequency doubling.

The Dmitriev *et al.*[3] experiment described in the first section would be conclusive only if the size of the image on the retina varied significantly as the diffuser was moved from 30 to 90 cm from the eye. A 0.1-mm source subtends a visual angle of ~1 min of arc from a distance of 30 cm and smaller angles for distances >30 cm. Based on measurements of the point spread function of the eye[25] the retinal image formed by this source is within the point diffraction image for all distances between 30 and 90 cm. Therefore, the threshold for detecting the second harmonic should be proportional to the square of the distance from the diffuser irrespective of the ocular structure generating the second harmonic. The Dmitriev *et al.* experiment is, therefore, inconclusive.

The experiments of Savin *et al.*[5] and Prokopyev[9] on shape perception do not necessarily imply localization of frequency doubling at the retina. No measurements of the scatter of the second harmonic by ocular structures have been made. Roth and Freund[26] found that the second harmonic light generated in wet rat-tail tendon was strongly forward-scattered, i.e., within a few milliradians. The cornea is much more organized than a rat-tail tendon, so the liklihood is that forward-scattering would be good enough to preserve image shape from cornea to retina. The cornea and the succeeding ocular structures are virtually transparent to wavelengths in the visible part of the spectrum. Therefore, there is little scatter of the second harmonic after it is generated at the cornea. Therefore, shapes illuminated by pulsed laser light will be perceived veridically, and laser light focused on the blind spot will not be detected.

The appearance of the second harmonic as a small spot inside a larger red field reported by Prokopyev[9] and Dmitriev *et al.*[3] is a consequence of the axial chromatic aberration of the human eye. The eye accommodates so as to focus the midregion of the spectrum on the retina and is simultaneously 0.75-diopter hypermetropic for the red[27,28] and even more hypermetropic for the IR. The green second harmonic generated at the cornea will be focused as a point on the retina, whereas IR light will appear as a larger diffuse field.

V. Summary

In summary, a hypothesis is presented that the cornea generates an attenuated second harmonic of pulsed IR laser light, which is detected by the photoreceptors. The published evidence is consistent with this hypothesis, and the hypothesis explains the published details of color appearance, visual thresholds, appearance of the field, shape perception, and violations of Bloch's law.

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tes book complete, he is dipping back into journalism. He has started writing a column periodically for *The Nation*, the magazine that first brought him to Washington in 1940.

A long-time student of the Supreme Court, he was fascinated by the hearings last October on Judge Robert H. Bork's nomination to the Supreme Court. On balance, he said, he is glad the nomination was defeated because he could not abide Judge Bork's views on privacy and civil rights. "But I couldn't help but feel sorry for him," he remarked. "In a way, I sort of wish he'd gone on the Court. He's a brilliant man, and I think he might well have changed." After reflection, he continued: "Responsibility, you know, often makes people rise to the occasion."

Mr. Stone is also embarking on another scholarly project. "It seems so fanciful at 80 to be thinking of something new that I hesitate to talk about it," he said. Pressed, he let on what he is thinking about: a series of biographical essays on the seminal figures involved in freedom of thought in human society. He expects it will take years of research and study and writing.