
Principles and Practice of Clinical Electrophysiology of Vision

Editors

JOHN R. HECKENLIVELY, M.D.
Professor of Ophthalmology
Jules Stein Eye Institute
Los Angeles, California

GEOFFREY B. ARDEN, M.D., PH.D.
Professor of Ophthalmology and
Neurophysiology
Institute of Ophthalmology
Moorfields Eye Hospital
London, England

Associate Editors

EMIKO ADACHI-USAMI, M.D.
Professor of Ophthalmology
Chiba University School of Medicine
Chiba, Japan

G.F.A. HARDING, PH.D.
Professor of Neurosciences
Department of Vision Sciences
Aston University
Birmingham, England

SVEN ERIK NILSSON, M.D., PH.D.
Professor of Ophthalmology
University of Linköping
Linköping, Sweden

RICHARD G. WELEBER, M.D.
Professor of Ophthalmology
University of Oregon Health Science Center
Portland, Oregon

 **Mosby
Year Book**

St. Louis Baltimore Boston Chicago London Philadelphia Sydney Toronto



Dedicated to Publishing Excellence

Sponsoring Editor: David K. Marshall
Assistant Director, Manuscript Services: Frances M. Perveiler
Production Project Coordinator: Karen E. Halm
Proofroom Manager: Barbara Kelly

Copyright © 1991 by Mosby-Year Book, Inc.
A Year Book Medical Publishers imprint of Mosby-Year Book, Inc.

Mosby-Year Book, Inc.
11830 Westline Industrial Drive
St. Louis, MO 63146

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without prior written permission from the publisher. Printed in the United States of America.

Permission to photocopy or reproduce solely for internal or personal use is permitted for libraries or other users registered with the Copyright Clearance Center, provided that the base fee of \$4.00 per chapter plus \$.10 per page is paid directly to the Copyright Clearance Center, 21 Congress Street, Salem, MA 01970. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collected works, or for resale.

1 2 3 4 5 6 7 8 9 0 CL CL MV 95 94 93 92 91

Library of Congress Cataloging-in-Publication Data

Principles and practice of visual electrophysiology / [edited by]

John R. Heckenlively, Geoffrey B. Arden.

p. cm.

Includes bibliographical references.

Includes index.

ISBN 0-8151-4290-0

1. Electroretinography. 2. Electrooculography. 3. Visual evoked response. I. Heckenlively, John R. II. Arden, Geoffrey B. (Geoffrey Bernard)

[DNLM: 1. Electrooculography. 2. Electrophysiology.

3. Electroretinography. 4. Evoked Potentials, Visual. 5. Vision

Disorders—physiopathology. WW 270 P957]

RE79.E4P75 1991

617.7 1547—dc20

DNLM/DLC

for Library of Congress

91-13378

CIP

The Use of Light-Emitting Diodes in Electrophysiology and Psychophysics

Chris Hogg

Light-emitting diodes (LEDs) are nearly ideal sources for many purposes. They are small, require low voltages and currents to drive them, and can be controlled by simple electronic means to give either continuous light outputs or extremely brief flashes (or both together) over a large range of intensities. Their light output changes by less than 10% in intensity or relative spectral emission over 50,000 hours of use.¹³ These properties not only simplify calibration but also reduce the frequency with which it is needed. Many different colors of light are available in a variety of different packages with differing optical properties. The majority of the available devices are inexpensive. The chief difficulties users are likely to experience are due to the low intrinsic source brightness, which is considerably less than for some arc or incandescent sources. Nevertheless, even where considerable quantities of light are required (for example, in electroretinography (ERG), LEDs can be used to advantage.

LEDs are members of the family of epitaxial semiconductor junction diodes. A junction is formed by growing a very thin crystal of a semiconductor directly onto another, slightly different semiconductor surface. The two layers of semiconductor material (frequently gallium aluminium arsenide) each contain different impurities (dopants). As a result of these impurities, one layer contains an excess of free electrons and the other an excess of holes (positive charge). The energy required to move a charge across the junction against the concentration gradient of free electrons or holes is considerable and larger than in other types of diode (approximately

3:1). This energy "band gap" must be exceeded if current is to be passed through the junction. When the device is forward biased, electrons move from the negative material to the positive, and a corresponding movement of positive charge or "holes" occurs in the reverse direction. When an electron and hole pair recombine, energy is emitted as a photon. The characteristic wavelength of the photon is given by the energy band gap. Thus, it is more difficult to produce short-wavelength LEDs since the higher energy gap must be maintained with the controlled flow of charges. The construction of the epitaxial layer determines the direction of light emitted, and the absence of a resonating (reflective) cavity prevents the stimulated emission of radiation by the photons, so the light is not coherent and contains a number of differing wavelengths. However, light is emitted over a relatively narrow bandwidth. For a typical red LED (for illustrative purposes, a Stanley HBR5566X) the peak is at 660 nm, and the half-power bandwidth is ± 30 nm. The construction of a "typical" LED is shown in Figure 28-1.

The semiconductor is mounted on a "lead frame" and encapsulated in a plastic (epoxy) housing with an internal spherical lens. The combination of junction structure, epoxy, and lens type determines the spatial output characteristics of the device, and for many LEDs, including all the "brightest," the light is concentrated in a cone, which can be represented in a polar diagram (Fig 28-2) with a half-power spatial/polar distribution of ± 7.5 degrees.

A typical device requires 50 mA at around 2 V to produce its maximum output, so it is both easy to

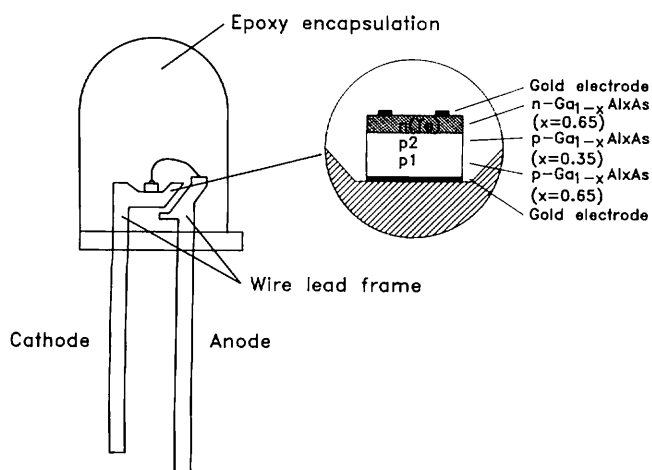


FIG 28-1.
Construction of a typical LED.

control and intrinsically safe to use in a clinical environment. The junction of most modern devices thus exhibits low electrical impedance but is nevertheless fairly robust, being able to tolerate significant overloads for short periods. Various types of LEDs are available. Some are devised for special purposes, for example, alphanumeric display components or indicators. There is a great range of shape, size, and intensity. A number of devices are packaged with additional circuitry that provides a constant current flow or flashes the device on and off. Other devices contain more than one junction and can produce two or even three colors, but these are so specialized that their value for purposes other than those for which they were designed, that is, for instrument displays, is limited. However, some square-packaged arrays may be useful for producing checkerboards or similar displays.

The colors quoted by manufacturers vary from in-

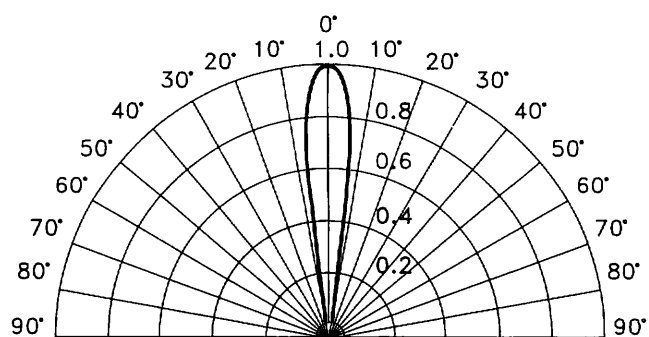


FIG 28-2.
Polar diagram showing the concentration of light in an LED.

frared to blue, but this may be misleading. In general, red LEDs are by far the brightest and have peak emission at 660 nm. Yellow LEDs are also efficient light emitters and peak at about 580 nm, so a variety of oranges can be obtained. Green LEDs are now available with a considerable light output. However, all have peak emission at about 560 nm, which, it should be remembered, is the peak of the **photopic** relative spectral sensitivity curve. This characteristic is unfortunate since "green" light is often thought to stimulate rods selectively. Various filters are also incorporated in the plastic capsules of green LEDs to remove the longer wavelengths, but none provides a filter effective enough to modify the output in any significant manner. If additional external filters are employed, it will be found that the proportion of light emitted below 510 nm is so low (<5%) that it is difficult to obtain a blue-green light of adequate intensity for most electrophysiology. Blue LEDs are currently available from only one manufacturer and are significantly different from all others. They have considerably less light output, and the voltage required at the junction is significantly higher, as is the junction capacitance. The peak of the light output is at 480 nm, but the bandwidth is wider than that of many other devices and asymmetrical, being broader toward the longer wavelengths. The relative spectral emission varies somewhat with the drive current. The devices are also much more costly and "fragile." A single red LED may cost a few pennies, while a blue LED with $\frac{1}{100}$ the output costs \$50. Nevertheless, blue LEDs are very useful to the physiologist and clinician and, with suitable filtering, can provide wavelength stimuli as low as 450 nm or extending to as high as 520 nm; thus, LEDs can be used for many purposes previously requiring incandescent sources and monochromators or interference filters.

The relationship between applied current (or voltage) and light output of a typical device is shown in Figure 28-3 and, for a region of about $1\frac{1}{2}$ decades, can be seen to be approximately linear. Above or below this region, marked nonlinearities occur. Since in general users wish to control the intensity in a simple ergonomic way over a much larger range, a variety of drive circuits have been devised.

For a simple flash stimulator a voltage drive circuit may be used quite effectively (Fig 28-4) and the relationship between light output and applied voltage determined by calibration. Better performance can be obtained by replacing the voltage drive with a current source or ideally by placing the LEDs in the

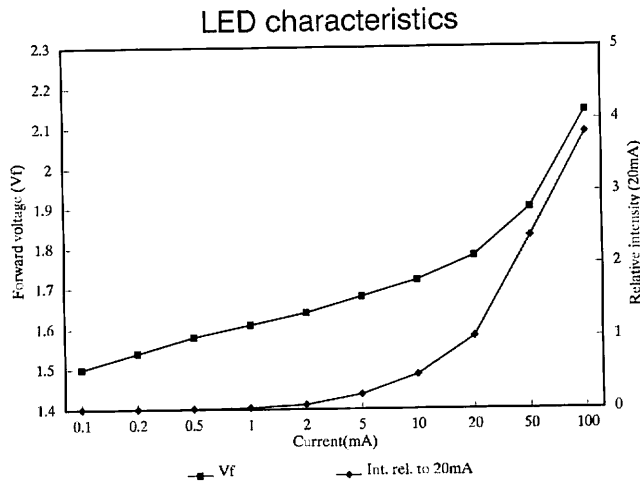


FIG 28-3. Relationship between applied current and light output of a typical LED.

feedback loop of a current drive (Fig 28-5). This technique, while a significant improvement over the simple circuit in Figure 28-4 still limits the range of linearity available to around $2\frac{1}{2}$ decades. Thus if a true sinusoidal output is required, the depth of modulation can never be 100%.

Two alternative techniques may be used to obtain linear control over intensity. The first consists of pulse density modulation.^{5,9} The LEDs are driven by pulses of about 100-ns duration, each of fixed power content. Light intensity is altered by changing the repetition rate of the pulses. An upper pulse frequency limit of 5 MHz is readily attained. For low intensities, a rate of 50 Hz is well above the critical fusion frequency of the human eye, and thus a wide range of intensity of an apparently continuous source can be achieved. If these pulses are derived from a linear voltage-controlled oscillator (VCO), a

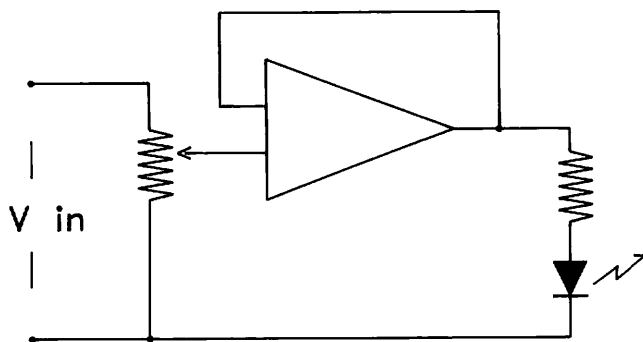


FIG 28-4. Voltage drive circuit of a simple flash stimulator.

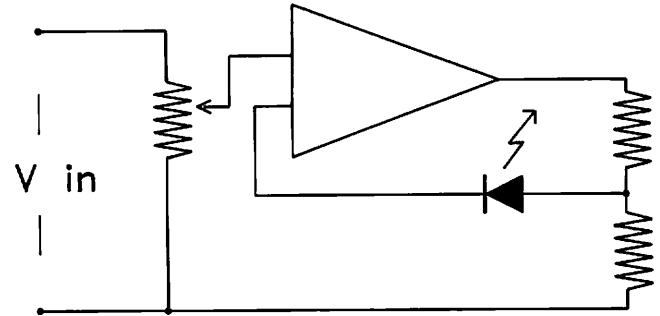


FIG 28-5. Feedback loop of a current drive to enhance the performance of an LED.

device in which the frequency of the output is related to the applied voltage, the output pulses are shaped and used to drive the LEDs through a fast switching circuit. Although good VCOs with the required range are difficult to produce, several are available as either integrated or hybrid circuits and can be driven from any waveform source so that very complex temporal changes can easily be produced. The light intensity may also be simply controlled without changing the waveform by passing the output of the VCO through frequency divider circuits. These may be readily produced by using standard logic components. Thus, a visual stimulator with a dynamic range of six orders of magnitude, consistent modulation capability, high stability, and fine control of intensity may be easily produced.

One major drawback to the pulse density modulation system derives from the high-speed switching of LEDs, especially if an array dissipating large amounts of energy is required. Each pulse contains frequency components much greater than the pulse repetition rate (5 MHz) that are caused by damping inadequacies of the power switching circuits. Thus the LED array acts as a very high frequency (VHF) radio transmitter and may radiate tens of watts. Because the source is usually very close to both the patient and preamplifier and since modern clinical amplifiers use high-input impedance field effect transistor input stages, which in practice make very effective FM radio receivers (the common-mode rejection ratio [CMMR] is relatively low at a very high frequency for the technically minded), large stimulus artifacts are generated. Therefore the pulse modulation technique is primarily of use for psychophysical experiments.

An alternative approach is to use a low-frequency current source to drive the LEDs and continuously measure their output with a photodiode or similar

device. The output from the detector circuit is compared with the waveform input signal and any difference used to modify the LED drive current and thus the light output. This "constant current modulation" approach will only operate effectively over a range of three to four orders of magnitude; to go beyond this would require an unduly complex set of drive circuitry.

ARRAYS

The low power requirements and general ease of use make LEDs an ideal choice for many types of stimulator; however, because of both the size of the radiating area and the relatively low radiant energy of many types of LED it is generally necessary to use a number of devices to construct an effective stimulus. Here again the low drive requirements make it a simple matter, providing some care is taken in the design to interconnect a number of the diodes in an array. By using either the pulse or constant current modulation approach an array of several hundred LEDs can be assembled to provide the required stimulus. They can be connected in series, parallel, or a combination of both. Thus if nine devices are required for the stimulus and the power unit has an output of 9 V (three LEDs, each with a forward voltage drop of 2 V at 50 mA, could be connected in series [Fig 28-6, A]), then three identical chains connected in parallel (Fig 28-6, B) will give a stimulus with maximum light output at 150 mA. Care should be taken to ensure that the forward voltages of the diodes are similar or, alter-

natively, select a resistor to balance the current through the three chains.

APPLICATIONS

Since Drasdo and Woodall⁷ first employed LEDs for scotometry a wide range of equipment has been described, mostly for psychophysical testing. Thus, LEDs have been used for determining de Lange curves in clinical circumstances, for analyzing rod-cone interactions, for measuring dark adaptation and spectral sensitivity, for field screening, and for many other psychophysical and electrophysiological applications.

STIMULATORS FOR ELECTROPHYSIOLOGY

Visual Evoked Response

Commercially available stimulators include LEDs mounted in goggles similar to those used by swimmers (Nicolet instruments). A small array of red LEDs is used. They are designed for monitoring the visual evoked response (VER) in special conditions, such as in operating theaters where the small size and low voltages used are advantageous. Arrays of square red LEDs used to produce small high-contrast checkerboard displays ideally suited to transportable recording systems are available from most manufacturers. In another application, LEDs were used to produce a stimulator that could be used inside an oxygen incubator for premature infants.¹⁴

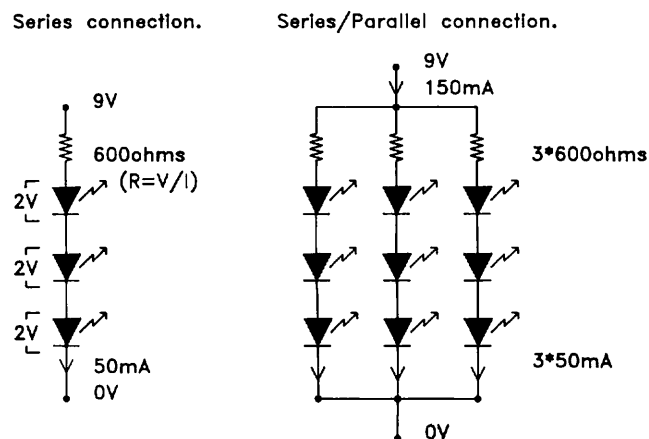


FIG 28-6.
Series and parallel connections of LEDs.

Electroretinography

Alfieri and Sole¹ described the use of yellow LEDs to produce mixed rod and cone responses. Kooijman and Damhof¹² mounted red, green, and blue LEDs on a contact lens to obtain a greater range of stimuli. However, such systems do not generate light of intensity equivalent to common discharge lamps. The recent development of high-efficiency LEDs²³ has modified this position. Figure 28-7 shows the ERGs obtainable with an array of 250 LEDs used to form a "Ganzfeld" stimulator. It can be seen that these are comparable to those obtained when using a Grass PS22 stroboscope.³ Light intensity is usefully varied over a range of 3×10^6 by altering both the intensity and the duration of the flashes. The maximum flash duration for which Bloch's law holds is 30 ms; in our

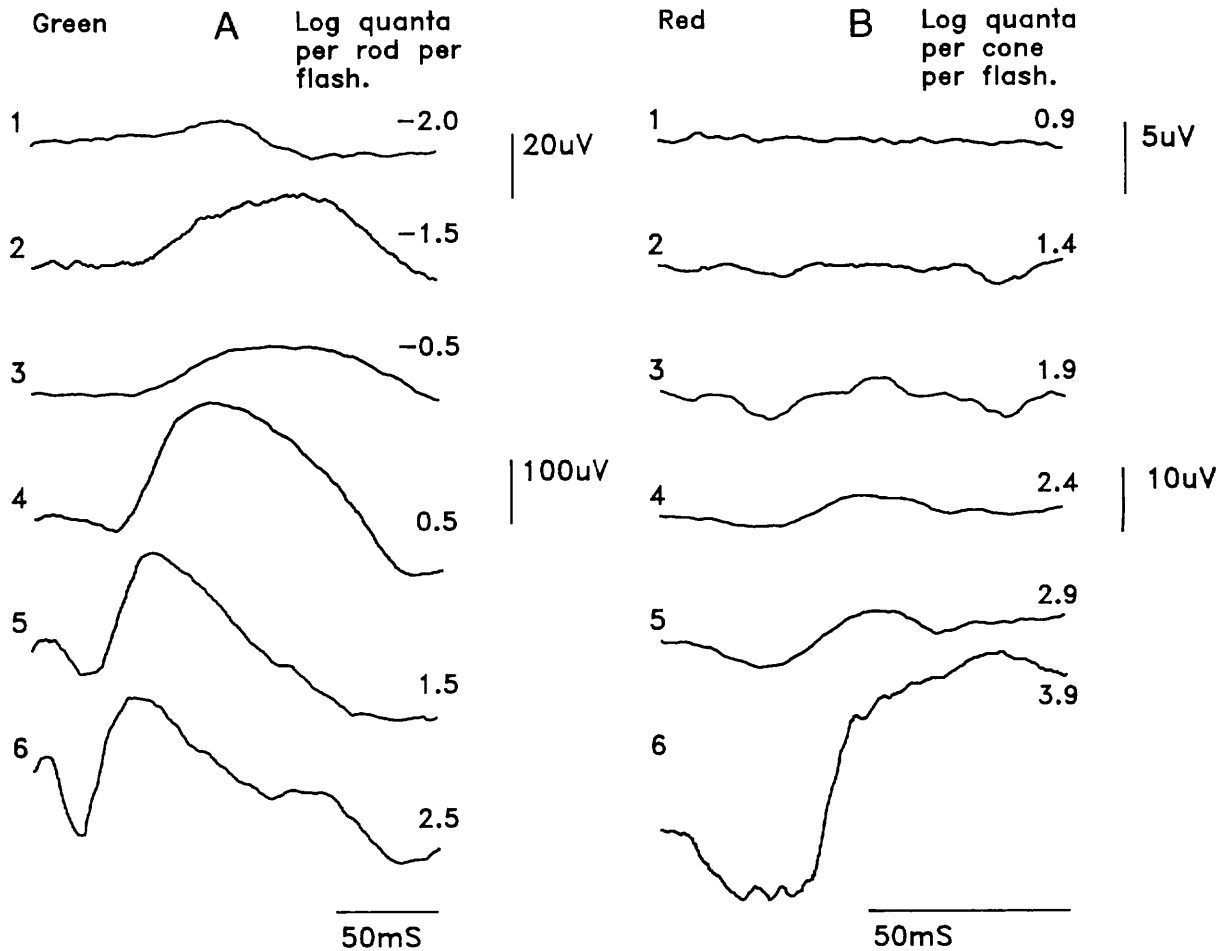


FIG 28-7.

A, responses 1 to 6 show the ERG, recorded from green LEDs over a range of 4.5 log units: the weakest stimuli evoke a "threshold negative response," the intermediate stimuli smooth rod b-waves of increasing amplitude and decreasing latency, and the more intense flashes produce large a-waves and oscillatory potentials. **B**, the red light responses 1 to 6 show a triphasic threshold negative response from the long-wavelength cones. The cone responses show prominent a-waves, and those to more intense flashes peak slightly later than do those evoked by weaker flashes, this being due in part to rod contamination.

system light intensity may be altered by changing flash duration from 0.01 to 30 ms and intensity from maximum to 1/1,000 in fixed steps. Additionally, a ten-turn potentiometer allows continuous variation of light intensity.

The minimal green stimulus evokes the scotopic threshold negative response (Fig 28-7, A—response 1). The entire voltage amplitude/light intensity relationship can be explored and "saturated" scotopic responses obtained (Fig 28-7, A—responses 1 to 6). These have an even more marked a-wave than those obtained with a Grass PS22 (the most commonly employed stroboscope). With red or red plus green flashes (Fig 28-7, B—responses 1 to 6), large flicker and oscillatory potentials are obtained under photo-

pic conditions. Since 50% duty cycle flicker is available, the temporal frequency of flicker can be changed without altering the level of light adaptation, and if desired, sinusoidal stimulation can be used. In addition, flashes may be superimposed on a separate background so that increment thresholds can be determined and rod-cone interactions demonstrated. Off-responses are produced to more prolonged flashes. The amplitude shows no further increase when the flash duration exceeds 100 ms. Finally, transitions from red to green can be achieved to isolate long- and medium-wavelength color mechanisms. In Figure 28-8, note that there is little stimulus artifact because the display produces relatively little radiated interference.

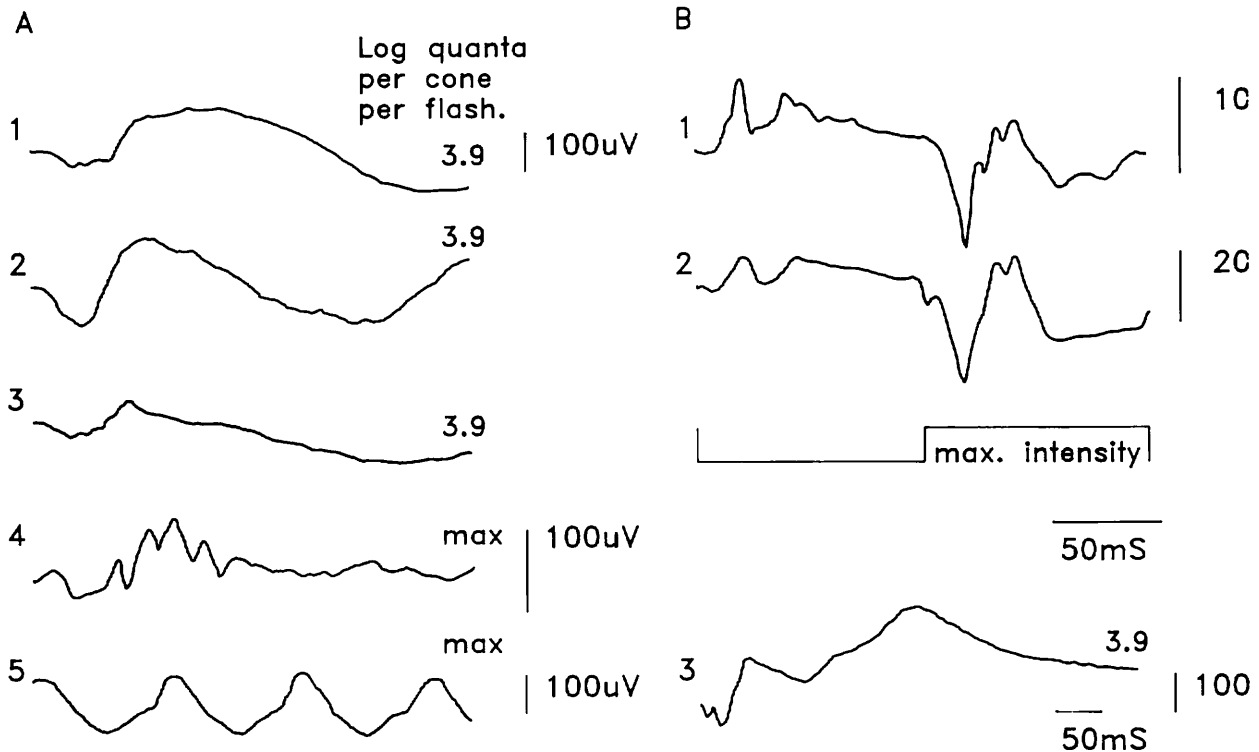


FIG 28-8.

A, response 1 shows the ERG evoked in the dark-adapted state by intense red flashes (see Fig 28-7, B—response 6). Note the photopic and scotopic components. Response 2 shows that the addition of a dim green background increases the photopic and decreases the scotopic components (evidence of release from suppressive rod-cone interaction). In response 3, a more intense green background decreases all responses. Response 4 shows the filtered oscillatory potentials. Note the high amplitude. Response 5 shows the large responses to a 33-Hz flicker with a 50% duty cycle. Note that both cornea-positive and -negative components can be seen. **B**, response 1 shows at about 10 ms that the complex “off”-response from a 100-ms green flash is repeated every 200 ms. Note the “on”-response in the second part of the trace. Response 2 has conditions as in response 1, but the flash is red. Response 3 has an intense red plus green flash recorded on a slower time base to show the c-wave.

REFERENCES

1. Alfieri R, Sole P: Electrophysiological examination and cine-angiofluorographic study of vasculopathies in man, in Schmoger E, Kelsey JH (eds): *Visual Electrodagnosis in Systemic Diseases*. Proceedings Series, Vol 23, ISCEV, *Documenta Ophthalmologica*, 1979.
2. Arden GB: Rod-cone interactions in night-blinding disease. *Jpn J Ophthalmol* 1987; 31:6-19.
3. Arden GB, Carter RM, Hogg CR, Powell DJ, Ernst WJ, Clover GM, Lyness AL, Quinlan MP: A modified ERG technique and the results obtained in X-linked retinitis pigmentosa. *Br J Ophthalmol* 1983; 67:419-430.
4. Arden GB, Frumkes TE: Stimulation of rods can increase cone flicker ERGs in man. *Vision Res* 1986; 26:711-721.
5. Arden GB, Hogg CR: Rod-cone interactions and analysis of retinal disease. *Br J Ophthalmol* 1985; 69:404-415.
6. Construction and performance of high efficiency red, yellow and green LED materials. Hewlett Packard application bulletin, 1975.
7. Drasdo N, Woodall A: Flicker fusion scotometry with solid state light sources. *Optician* 1971, pp 10-13.
8. Epstein CM: True checkerboard pattern reversal with light emitting diodes. *Electroencephalogr Clin Neurophysiol* 1979; 47:611-613.
9. Ernst W, Faulkner DJ, Hogg CR, Powell DJ, Arden GB, Vaegan: An automated static perimeter/adaptometer using light emitting diodes. *Br J Ophthalmol* 1983; 67:431-442.
10. Frumkes TE, Naarendorp F, Goldberg SH: The influence of cone adaptation on rod mediated flicker. *Vision Res* 1986; 26:1167-1176.
11. Goldberg SH, Frumkes TE, Nygaard RW: Inhibitory influence of unstimulated rods in the human retina. *Science* 1980; 221:180-181.
12. Kooijman AC, Damhof A: ERG measurements with red and yellow-green LEDs as light source for stimulation and adaptation. *Doc Ophthalmol* 1982; 31:31-38.
13. LED solid state reliability. Hewlett-Packard application note 1017.
14. Mushin J, Hogg CR, Dubowitz LMS, Skouteli H, Arden GB: Visual evoked responses to light emitting

- diode (LED) photostimulation in newborn infants. *Electroencephalogr Clin Neurophysiol* 1984; 58:317–320.
15. Nygaard RE, Frumkes TE: LEDs: Convenient, inexpensive sources for visual experimentation. *Vision Res* 1982; 23:435–440.
16. *Opto Electronic Components Data Book*. Stanley Electric Co, Ltd, 1988.
17. *Opto Electronic Designers Catalogue*. Hewlett-Packard, 1988.
18. Pratt H, Schacham S, Barak S: A pattern reversal stimulator using optical fibres. *Electroencephalogr Clin Neurophysiol* 1984; 59:172–174.
19. Seiple WH, Seigel IM, Carr RE, Mayron C: Objective assessment of deLange functions using the focal ERG. *J Optom Physiol Opt* 1986; 63(1):1–6.
20. Spydell JD: A low cost light emitting diode photic stimulator. *Electroencephalogr Clin Neurophysiol* 1983; 55:485–486.
21. Takahashi K: Brighter output lights the way for broad new uses for LEDs. Stanley Electric Co, Ltd.
22. Tyler CW, Ernst W, Lyness AL: Photopic flicker sensitivity losses in simplex and multiplex retinitis pigmentosa. *Invest Ophthalmol Vis Sci* 1984; 25:39–46.
23. Watanabe M: Technical development of LEDs composed of searching for high brightness devices. *J Electr Electron Engin* 1988; 86–88.
24. Weyrich C: Blue-light emitting silicon-carbide diodes. Siemens technical publication.