# 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

Mosby
Year Book
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

A Year Book Medical Publishers imprint of Mosby-Year Book, Inc.

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

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 91-13378
617.7 1547—dc20 CIP
DNLM/DLC
for Library of Congress

# 47

# Magnetically Evoked Retinal Responses

## Sven Erik G. Nilsson

Light sensations evoked by stimuli other than incident photons are called phosphenes. In general, such sensations appear as a faint, flickering light in the periphery of the visual field. Phosphenes may be elicited by different stimuli, such as pressure upon the eye, mechanical shock, certain chemical agents, electric currents (electrophosphenes), and magnetic fields (magnetophosphenes).[24] Magnetophosphenes were first documented by D'Arsonval.[6] Early studies mainly concerned the location in the visual field and the appearance of the light sensation.[3, 8, 29]

A number of biological effects induced by static fields and high magnetic flux densities (e.g., survey by Kholodov[11]) or by alternating fields, generally concerning microwaves and radio frequency radiation (e.g., review by Glaser et al.[10]), have been described or proposed. Magnetophosphenes, however, show a reproducibility that is better than that of most other magnetobiological phenomena, which makes the retina a valuable model for studying the biological effects of magnetic fields on nervous tissue. Magnetophosphenes are elicited by the influence of magnetic flux densities from about 10 mT milliteslas (mT) and at frequencies of 10 to 100 Hz.

## THRESHOLDS AND SENSITIVITY MAXIMA OF MAGNETOPHOSPHENES

Magnusson and Stevens[22] found that magnetophosphenes depend upon the intensity and frequency of the magnetic field. We have studied the threshold relations systematically.[19, 21] Magnetophosphenes were induced by applying time-variable (10 to 50 Hz) electromagnetic fields with flux densities of 0 to 40 mT over the temples of volunteers. Phosphenes were elicited from about 10 mT with a sensitivity maximum at 30 Hz in darkness (Fig 47–1). With higher luminance levels (0.1 and 1.2 cd/m$^2$, respectively) the sensitivity maximum moved toward lower frequencies (25 and 20 Hz, respectively). During dark adaptation, after preadaptation to a luminance of 130 cd/m$^2$, there was a small but significant ($P < .05$) decrease in sensitivity from about 10 to 16 mT that approximately followed the time course of dark adaptation (Fig 47–2).

It seems that the sensitivity maxima may be explained on the basis of the law of induction, from which it follows that current density is proportional to the magnetic flux density multiplied by the frequency. Going from low to higher frequencies, the threshold value should decrease, assuming that a constant current density is necessary for phosphene generation. If one further assumes that a certain summation time is required for synaptic processing, it becomes clear that the threshold will increase again when, with increasing frequency, the summation time becomes very short. The small decrease in sensitivity during dark adaptation may be due to an increase in the retinal noise level.

When volunteers with normal color vision were tested against three discrete background colors (443,

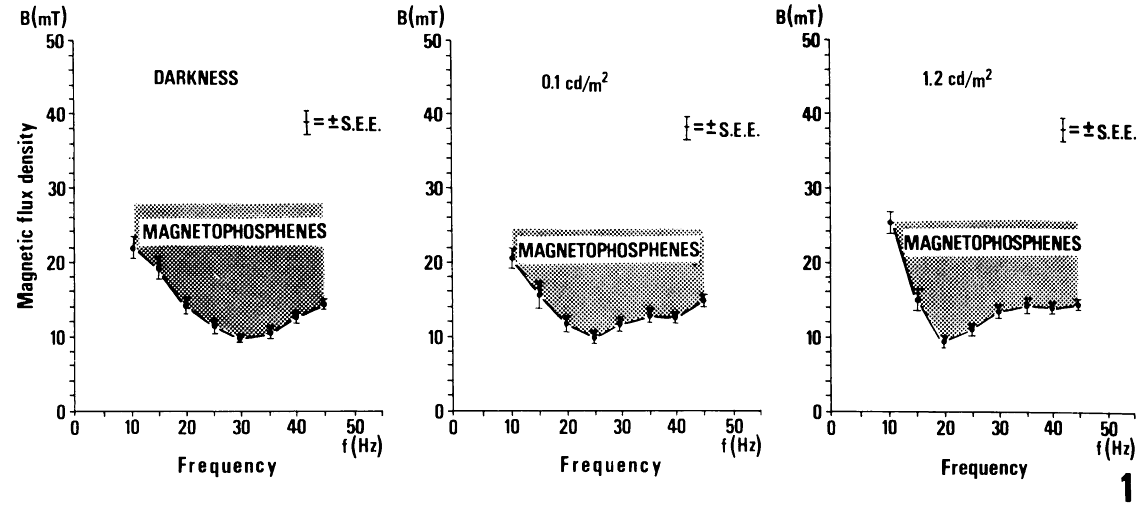

**FIG 47–1.**
Magnetophosphene threshold values for a group of 11 volunteers were determined in darkness or with a broad-spectrum background light at luminance levels of 0.1 or 1.2 cd/m$^2$, respectively. (Adapted from Lövsund P, Öberg PÅ, Nilsson SEG, et al: *Med Biol Eng Comput* 1980; 18:326–334.)

531, and 572 nm) at a luminance of 3 cd/m$^2$ regarding thresholds for magnetophosphenes, they were found to have two sensitivity maxima, one at 20 to 25 Hz and a second one above 40 Hz (Fig 47–3).[19, 21] On the contrary, color-defective volunteers of the deutan type showed only one maximum (at 20 to 25 Hz) when looking at the 531- or 572-nm backgrounds, whereas both maxima were present when they were tested against the 443-nm background.

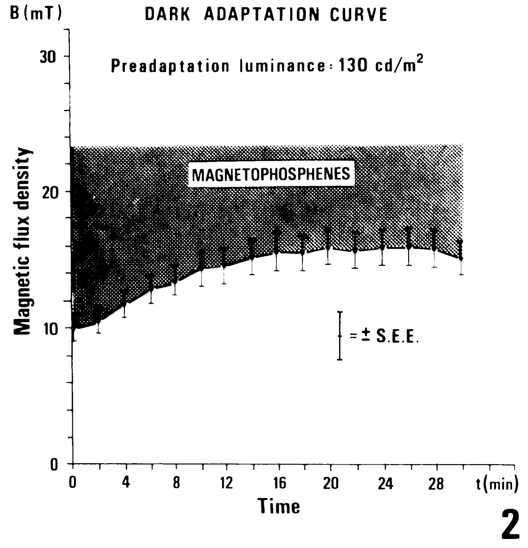

**FIG 47–2.**
Magnetophosphene threshold values determined during dark adaptation. Values are averages of results with frequencies of 20, 30, and 35 Hz; mean values for 8 volunteers are presented. (From Lövsund P, Öberg PÅ, Nilsson SEG: *Acta Ophthalmol* 1979; 57:812–821. Used by permission.)

The two-humped curves in normals may possibly be interpreted as a combination of two curves with different thresholds to current density. These two curves could represent two different "channels" in the retina, one sensitive and slow and the other one less sensitive but faster, thus able to follow higher frequencies. This hypothesis receives some support from the fact that deutans do not show the second hump, which may indicate that in deutans the function of the second channel differs from that in normals.

## PHOSPHENE-RELATED MAGNETIC FIELDS IN THE ENVIRONMENT

Are there magnetic fields in the environment with flux densities above the threshold (about 10 mT) for phosphenes and with frequencies from 10 to 100 Hz? Welding machines (0 or 50 Hz) generally have magnetic flux densities up to 10 mT, but in certain cases the density may be as high as 130 mT[1, 18, 19] (Hansson Mild, personal communication). A volunteer with his head covered so as to exclude all light experienced magnetophosphenes close to a welding machine with a flux density of about 10 mT. Electrosteel furnaces (1 to 600 Hz) generate flux densities up to 10 mT, except for induction heaters (50 to 10,000 Hz), which may have densities up to

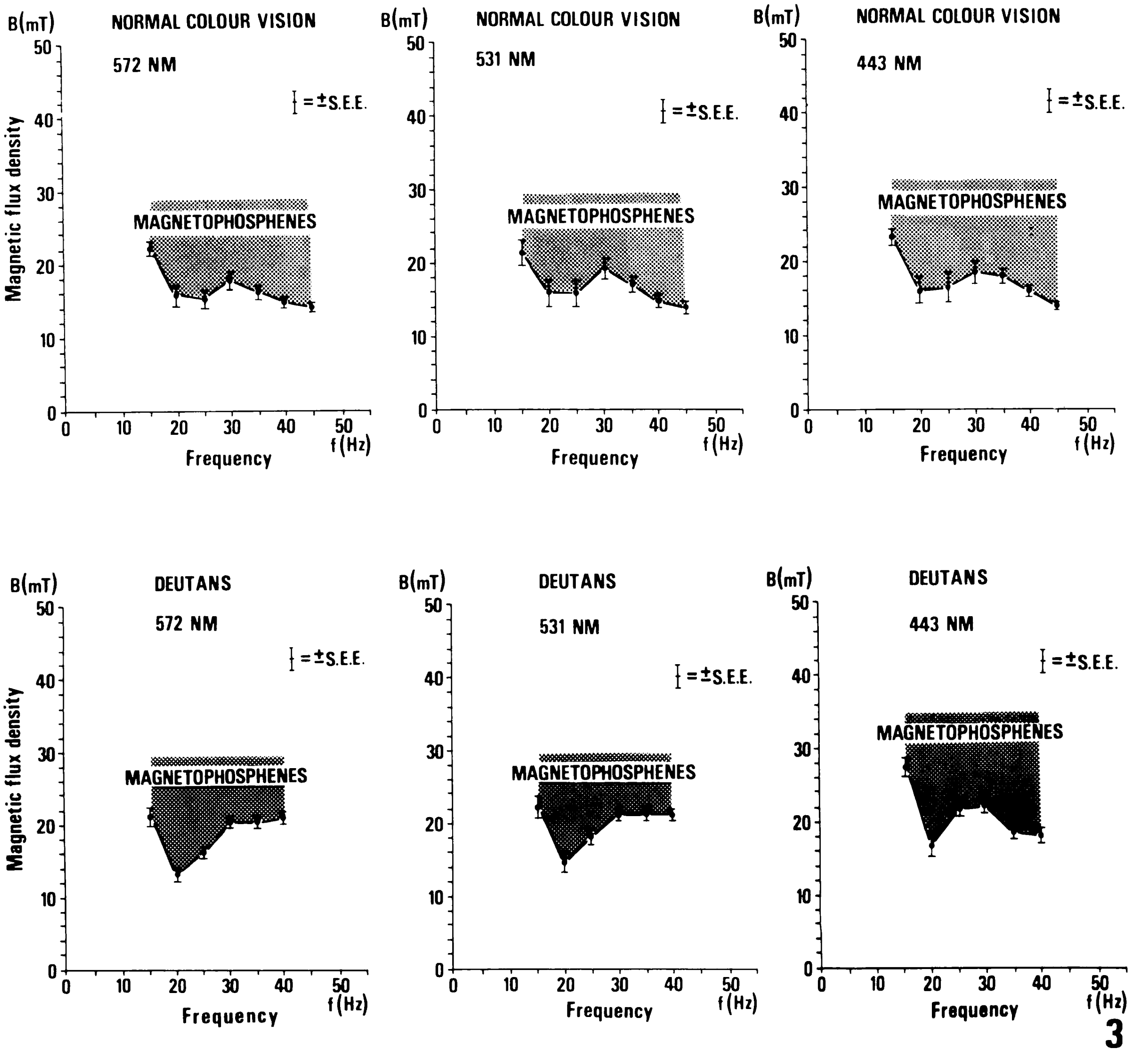

**FIG 47-3.**

Magnetophosphene threshold values for a group of six volunteers with normal color vision *(top row)* and for a group of nine color-defective (deutans) volunteers *(bottom row)*. Background light was at wavelengths of 572, 531, or 443 nm, with a luminance level of 3 cd/$m^2$. (Adapted from Lövsund P, Öberg PÅ, Nilsson SEG, et al: *Med Biol Eng Comput* 1980; 18:326–334.)

70 mT.[18, 19] Flux densities around industrial demagnetizers (50 Hz) and in electric locomotives (16.7 Hz) may be as high as 50 mT.[17, 23] The earth's magnetic field (static) has a flux density (<0.1 mT) far below the threshold of phosphenes.[18, 19]

## COMPARISON OF MAGNETOPHOSPHENES AND ELECTROPHOSPHENES

The sensitivity curves for electrophosphenes (electrode position, temple-temple; current frequency, from 10 to 45 Hz; current strength, 0 to 0.3 mA) and for magnetophosphenes (magnet poles, temple-temple; frequency, 10 to 45 Hz; magnetic flux density, 0 to 40 mT) tested with a broad-spectrum background light at a luminance of 3 cd/$m^2$ are shown in Figure 47–4,A.[20] In both cases the sensitivity maximum is located at 20 Hz. There are small but significant ($P < .05$) differences between the curves from 10 to 17 Hz and from 25 to 30 Hz, but a very pronounced difference from 35 to 45 Hz.

According to the law of induction, the induced current density is directly proportional to the magnetic field and the frequency. Thus it is possible to calculate the magnetic flux density required to induce the necessary current density by dividing threshold values (current density) for electrophosphenes by frequency. In this way, a theoretical

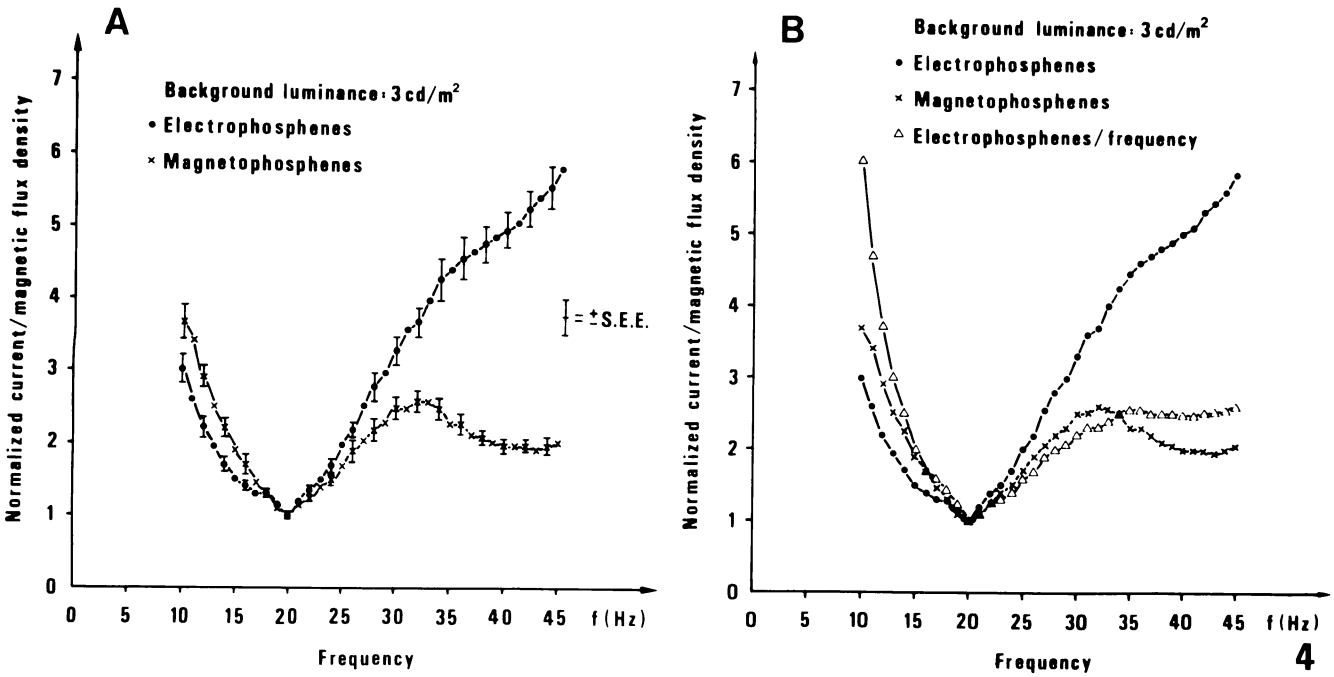

**FIG 47–4.**

**A**, threshold values for magnetophosphenes and electrophosphenes for a group of 11 volunteers under broad-spectrum background light at a luminance level of 3 cd/m$^2$. **B**, same as **A**, but with an additional curve, where the threshold values for electrophosphenes have been divided by the frequency values. (From Lövsund P, Öberg PÅ, Nilsson SEG: *Med Biol Eng Comput* 1980; 18:758–764. Used by permission.)

threshold value curve for magnetophosphenes is obtained. The theoretical and recorded magnetophosphene curves show a fairly good conformity (Fig 47–4,B).

## THE POSSIBLE SITE OF GENERATION OF MAGNETOPHOSPHENES

The possible anatomical site of generation of magnetophosphenes has been a subject of speculation. Dunlap[8] and Fleischmann[9] suggested the optic nerve and the visual cortex, whereas Barlow et al.[2] considered the retina as the likely site of action. Valentinuzzi[30] developed mathematical models to aid further analysis of phosphenes on the assumption that they are generated in the retina.

Electrophosphenes were studied in detail earlier than magnetophosphenes (e.g., review by Knighton[14]). Both phosphenes show several similarities. On this basis, Barlow et al.[2] proposed that they are generated in the same retinal structures. It is likely that the alternating magnetic field induces intracellular and extracellular currents in the retina that change membrane potentials and synaptic activity in the same way as light or electric stimulation. It might be suspected that elongated and regularly oriented cells such as the photoreceptors, bipolar cells, and perhaps horizontal cells would be more sensitive to induced currents than other cells. Regarding the generation of electrophosphenes, photoreceptors and bipolar cells are favored by Brindley,[4] photoreceptors and horizontal cells by Knighton,[12–15] bipolar and horizontal cells by Potts and Inoue,[25] and glial cells by Carpenter.[5]

We studied two totally blind subjects.[21] One of them suffered from retinitis pigmentosa at a stage when all photoreceptors seemed to have degenerated. There are reasons to believe that in such patients the bipolar and ganglion cells survive, at least partially.[28] This patient experienced magnetophosphenes, faint but definite and with pronounced afterimages. It appears that these phosphenes could not have been generated in photoreceptors, more probably in bipolar cells. This experiment does not exclude photoreceptors as a site of generation of magnetophosphenes, but it seems to indicate that magnetophosphenes may originate in other cells besides photoreceptors. Similar results were found by Potts and Inoue,[25] who demonstrated in rats with

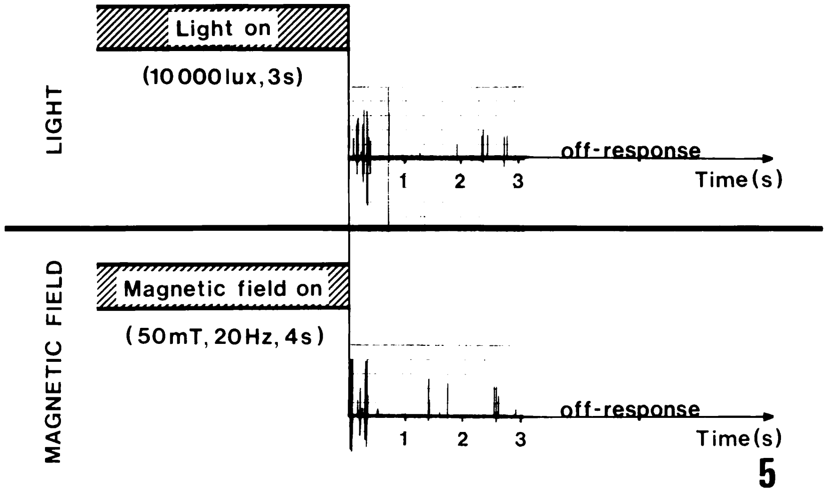

**FIG 47–5.**
Action potentials from an on/off ganglion cell after cessation of stimulation with light or a magnetic field, respectively. (From Lövsund P, Öberg PÅ, Nilsson SEG: *Med Biol Eng Comput* 1981; 19:679–685. Used by permission.)

photoreceptor dystrophy that a normal electrically evoked response could be obtained in spite of the fact that there was no visually evoked response. The second blind subject we studied had both eyes removed long ago because of absolute glaucoma. This patient did not experience magnetophosphenes.[21] The result favors the notion that magnetophosphenes are generated in the retina and not in the brain.

We performed extracellular recordings from ganglion cells in a frog eyecup preparation in connection with light and magnetic stimulation (flux densities up to 80 mT; frequencies, 20, 25, and 30 Hz).[16] Stimulation with 20 Hz gave rise to a larger number of action potentials than the other frequencies used. The latency from light stimulus to response to light was significantly ($P < .05$) increased by a mean of 4 ms when the preparation was simultaneously exposed to the magnetic field. The ganglion cells responded to magnetic stimulation only upon "on," "off," or "on/off." There was an important difference between magnetic and light stimulation, however, in that the cells that were on-cells in response to light stimulation became off-cells in response to magnetic stimulation and vice versa. Furthermore, the interval between light stimulus and response in on/off-cells was 85 ms on average, whereas the interval was about 5 ms only when magnetic field stimulation was used. Figure 47–5 demonstrates the similarity between off-responses from an on/off-cell upon light and magnetic field stimulation, respectively. Taken together, the results show definite similarities between the responses to both types of stimuli but also clear-cut differences. It seems that the same retinal channels are used, but in somewhat different ways.

When Na-aspartate, 0.1 mL of a 10mM solution, or $CoCl_2$, 0.1 mL of a 2mM solution, was added to the frog preparation, the responses to light as well as to magnetic field stimulation disappeared. If the responses reappeared later, they did so simultaneously for both stimuli. The abolishment of the responses seems to favor an action of the magnetic field stimulation on the photoreceptors since aspartate is considered to break the connection between the photoreceptors and the following neurons,[7, 26, 27] and since $CoCl_2$ blocks most of the activity proximal to the photoreceptors (Tomita T, personal communication). However, the effects of aspartate and $CoCl_2$ are still not quite clear. In summary, it seems likely that magnetophosphenes are generated mainly in the photoreceptors but that other cells, e.g., bipolar cells, may be excitable to a certain extent as well.

## Acknowledgment

This study was supported by the Swedish Medical Research Council (Project No. 12X-734) and by the Swedish Work Environment Fund.

## REFERENCES

1. Abramovich-Poliakov DK, Kleiner AI, Kolodub FA, et al: Clinical features of the effect of electromagnetic

fields in contact electric welding (in Russian). *Vrach Delo* 1979; 4:106–110.

2. Barlow HB, Kohn HI, Walsh EG: Visual sensations aroused by magnetic fields. *Am J Physiol* 1947; 148:372–375.
3. Beer B: Über das Auftreten einer subjectiven Lichtempfindung im magnetischen Felde. *Wien Klin Wochenschr* 1902; 15:108–109.
4. Brindley GS: The site of electrical excitation of the human eye. *J Physiol* 1955; 127:189–200.
5. Carpenter RHS: Electrical stimulation of the human eye in different adaptational states. *J Physiol (Lond)* 1972; 221:137–148.
6. D'Arsonval MA: Dispositifs pour la mesure des courants alternatifs de toutes fréquences. *Compt Rend Soc Biol* 1896; 3:450–451.
7. Dowling JE, Ripps H: Aspartate isolation of receptor potentials in the skate retina. *Biol Bull* 1971; 141:384–385.
8. Dunlap K: Visual sensations from the alternating magnetic field. *Science* 1911; 33:68–71.
9. Fleischmann L: Gesundheitsschädlichkeit der Magnet-Wechselfelder. *Naturwissenschaften* 1922; 10:434.
10. Glaser ZR, Brown PF, Allamong JM, et al: *Bibliography of Reported Biological Phenomena ('Effects') and Clinical Manifestations Attributed to Microwave and Radio-Frequency Radiation.* Ninth Supplement to Bibliography of Microwave and R F Biologic Effects. U.S. Department of Health, Education and Welfare. National Institute of Occupational Safety and Health, Cincinnati, Ohio, 1977.
11. Kholodov YuA (ed): *Influence of Magnetic Fields on Biological Objects.* Springfield, Va, Joint Publication Research Service, National Technical Information Service, 1974.
12. Knighton RW: An electrically evoked slow potential of the frog's retina. I. Properties of response. *J Neurophysiol* 1975; 38:185–197.
13. Knighton RW: An electrically evoked slow potential of the frog's retina. II. Identification with PII component of electroretinogram. *J Neurophysiol* 1975; 38:198–209.
14. Knighton RW: *Electrical Stimulation of the Frog's Retina* (doctorial dissertation). University of Michigan, Ann Arbor, 1973.
15. Knighton RW: Modification of the frog's electroretinogram by transretinal direct current. *J Neurophysiol* 1975; 38:210–216.
16. Lövsund P, Nilsson SEG, Öberg PÅ: The influence on frog retina of alternating magnetic fields with special reference to ganglion cell activity. *Med Biol Eng Comput* 1981; 19:679–685.
17. Lövsund P, Öberg PÅ, Nilsson SEG: Elektromagnetiska fält i svensk svets- och stålindustri. V. En undersökning av magnetfält kring avmagnetiseringsanläggning vid Fagersta AB, Österbyverken, Österby bruk (in Swedish). LiU-IMT-R-0014. Department of Biomedical Engineering, Linköping University, Sweden, 1976.
18. Lövsund P, Öberg PÅ, Nilsson SEG: ELF magnetic fields in electrosteel and welding industries. *Radio Sci* 1982; 17(suppl):35–38.
19. Lövsund P, Öberg PÅ, Nilsson SEG: Influence on vision of extremely low frequency electromagnetic fields. Industrial measurements, magnetophosphene studies in volunteers and intraretinal studies in animals. *Acta Ophthalmol* 1979; 57:812–821.
20. Lövsund P, Öberg PÅ, Nilsson SEG: Magneto- and electrophosphenes. A comparative study. *Med Biol Eng Comput* 1980; 18:758–764.
21. Lövsund P, Öberg PÅ, Nilsson SEG, et al: Magnetophosphenes. A quantitative analysis of thresholds. *Med Biol Eng Comput* 1980; 18:326–334.
22. Magnusson CE, Stevens HC: Visual sensations caused by changes in the strength of a magnetic field. *Am J Physiol* 1911; 29:124–136.
23. Östberg O, Svensson G: Occupational health aspects of magnetic fields in electric locomotives: Survey measurements and literature review (in Swedish). *Reports of the University of Luleå*, Sweden, 1976: 34T.
24. Oster G: Phosphenes. *Sci Am* 1970; 222:82–87.
25. Potts AM, Inoue J: The electrically evoked response of the visual system (EER). III. Further contribution to the origin of the EER. *Invest Ophthalmol* 1970; 9:814–819.
26. Sillman AJ, Ito H, Tomita T: Studies on the mass receptor potential of the isolated frog retina. I. General properties of the response. *Vision Res* 1969; 9:1435–1442.
27. Sillman AJ, Ito H, Tomita T: Studies on the mass receptor potential of the isolated frog retina. II. On the basis of the ionic mechanism. *Vision Res* 1969; 9:1443–1451.
28. Szamier RB, Berson EL, Klein R, et al: Sex-linked retinitis pigmentosa: Ultrastructure of photoreceptors and pigment epithelium. *Invest Ophthalmol Vis Sci* 1979; 18:145–160.
29. Thompson SP: A physiological effect of an alternating magnetic field. *Proc R Soc* 1910; 82:396–398.
30. Valentinuzzi M: Theory of magnetophosphenes. *Am J Med Electr* 1962; 1:112–121.