The Optoretinogram at 38

Jeffrey B. Mulligan

NASA Ames Research Center

OSA Fall Vision Meeting, September 2018
Symposium honoring Donald I. A. MacLeod

A new grad student arrives at UCSD in 1980

- Where is Don?
- Senior grad students give me my homework, and a warning

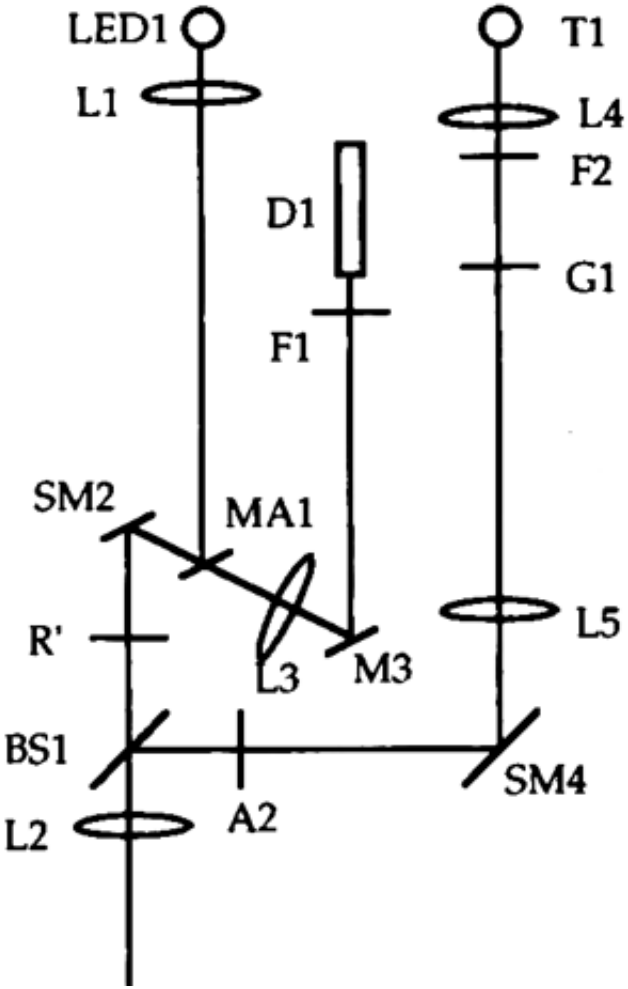
Don's interest is piqued by a paper in Science

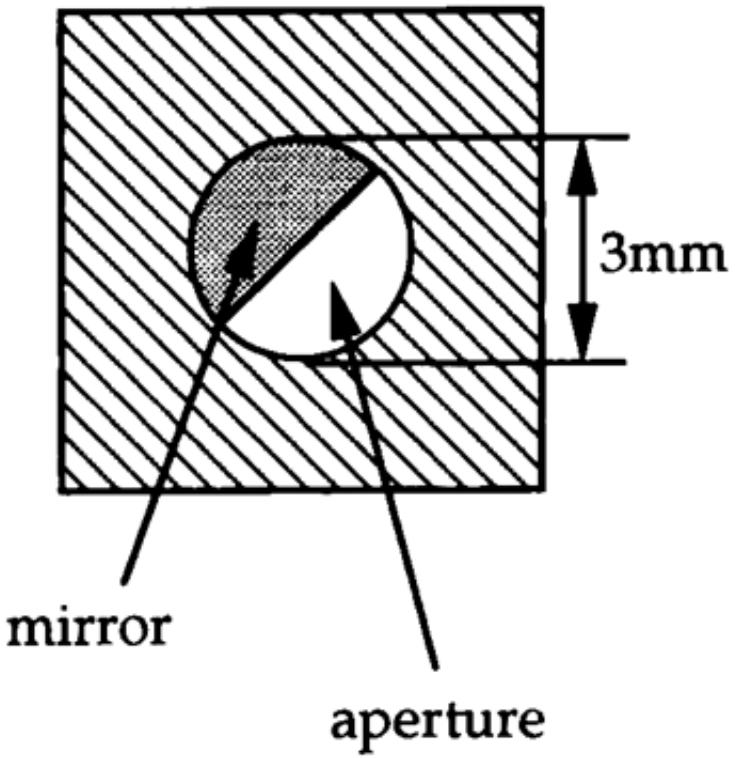
Rapid Light-Induced Changes in Near Infrared Transmission of Rods in *Bufo marinus*

Abstract. *Rapid transient changes in axial transmission of near infrared light through the outer segments of retinal rods of* Bufo marinus *are induced by illumination. The reasons for these changes are not clear. The changes in optical transmission may be useful in the study of photoreceptor function. However, the study of photoreceptor functions through the use of indicator dyes may be confounded by the intrinsic light-induced changes of optical properties of the photoreceptor cells.*

from Harary, H. H., Brown, J. E., and Pinto, L. H. (1978). Science, v. 202, pp. 1083-5.

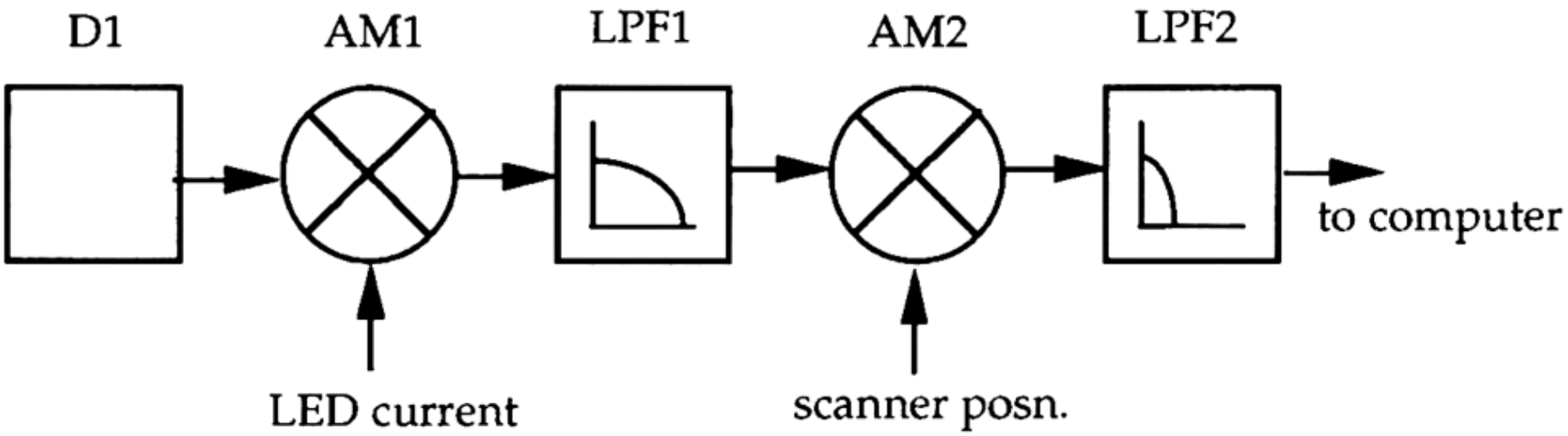
Jeff is turned loose on a collection of parts





MA1

Jeff is turned loose on a collection of parts



10 years later, a negative result appears

Vision Science and Its Applications

Summaries of papers presented at the Vision Science and Its Applications Topical Meeting

February 11–15, 1994
Santa Fe, New Mexico

SATURDAY, FEBRUARY 12, 1994—*Continued*

SaE8 In search of an optoretinogram, Jeffrey B. Mulligan, *NASA Ames Research Center;* Donald I. A. MacLeod, *UC–San Diego.* The infrared reflectance of the retina was measured as a function of visual stimulation. Unlike results *in vitro* studies, no visually evoked changes were observed. **(p. 167)**

Discussant: Francois C. Delori, *Schepens Eye Research Institute*

A positive result in 2000

Slow Optical Changes in Human Photoreceptors Induced by Light

Peter J. DeLint, Tos T. J. M. Berendschot, Jan van de Kraats, and Dirk van Norren

IOVS, v. 41, pp. 282-289.

Fast and slow reflectance changes

DISCUSSION

We found slow reflectance changes (i.e., factor 2 in Figs. 2B and 3) in the fovea during light and dark periods that cannot be explained by variations in the absorption of cone pigments. This observation in human subjects is, to our knowledge, the first of its kind in 40 years of fundus reflectometry. The results of our experiments provide firm evidence that the source of the newly found reflectance changes lies in or near the cone photoreceptors. First, the factor analysis indicated that there

from DeLint et al., IOVS, v. 41, pp. 282-289.

Fast and slow reflectance changes

Conclusions. The characteristics of the slow reflectance changes all point to the cone photoreceptors as the origin. Most likely, alterations in the index of refraction between the interphotoreceptor matrix and photoreceptors lie at the base of this hitherto unknown phenomenon. (*Invest Ophthalmol Vis Sci.* 2000;41:282–289)

from DeLint et al., IOVS, v. 41, pp. 282-289.

Another result in 2006

Visual Stimulus–Induced Changes in Human Near-Infrared Fundus Reflectance

Michael D. Abràmoff,[1,2] *Young H. Kwon,*[1] *Dan Ts'o,*[3] *Peter Soliz,*[4] *Bridget Zimmerman,*[5] *Joel Pokorny,*[6] *and Randy Kardon*[1,2]

IOVS 47(2), 715-721.

And another result in 2007

In vivo functional imaging of human cone photoreceptors

Ravi S. Jonnal, Jungtae Rha,* Yan Zhang, Barry Cense, Weihua Gao, and Donald T. Miller**

School of Optometry, Indiana University, Bloomington, Indiana 47405
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***Current affiliation: Alcon Laboratories, Inc., Ft. Worth, Texas 76134*
rjonnal@indiana.edu

Optics Express, 15(24), 16141-16160.

And another result in 2008

Intrinsic Signals from Human Cone Photoreceptors

Kate Grieve and Austin Roorda

IOVS 49(2), 713-719.

And another result in 2008

Conclusion

Unambiguous intrinsic signals were recorded in five of 15 of our subjects. The scattering changes detected were caused by the visible stimulus, as proved by the presence of the stimulus form in the difference images. The response magnitude averaged over the stimulated area increased between 0% and 5% increase, with a time course of seconds. The signal at the cone photoreceptor layer came from the photoreceptors themselves and not the spaces between them. Increased scattering responses from individual cones reached approximately 20%. In our experiments, the most robust responses were measured at a 3° peripheral location with a bright stimulus.

from Grieve & Roorda (2008), IOVS 49(2), 713-719.

And another result in 2009

In Vivo Functional Imaging of Intrinsic Scattering Changes in the Human Retina with High-speed Ultrahigh Resolution OCT

V. J. Srinivasan[1], Y. Chen[1, 2], J. S. Duker[2], and J. G. Fujimoto[1*]

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[2]New England Eye Center, Tufts Medical Center, Boston, Massachusetts 02116
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Optics Express, 17(5), 3861-3877.

And just last year...

Research Article | Vol. 8, No. 11 | 1 Nov 2017 | BIOMEDICAL OPTICS EXPRESS 5098

Biomedical Optics EXPRESS

Non-invasive assessment of human cone photoreceptor function

ROBERT F. COOPER,[1,2] WILLIAM S. TUTEN,[1,2] ALFREDO DUBRA,[3] DAVID H. BRAINARD,[2] AND JESSICA I. W. MORGAN[1,4,*]

[1]*Ophthalmology, Scheie Eye Institute, University of Pennsylvania, Philadelphia, PA, USA*
[2]*Psychology, University of Pennsylvania, Philadelphia, PA, USA*
[3]*Ophthalmology, Stanford University, Stanford, CA, USA*
[4]*Center for Advanced Retinal and Ocular Therapeutics, University of Pennsylvania, Philadelphia, PA, USA*
[*]*jwmorgan@pennmedicine.upenn.edu*

Back to amphibians...

Rapid optical coherence tomography and recording functional scattering changes from activated frog retina

Xin-Cheng Yao, Angela Yamauchi, Beth Perry, and John S. George

Applied Optics (2005), 44(11), 2019-2023.

Back to amphibians...

Retina

In Vivo Confocal Intrinsic Optical Signal Identification of Localized Retinal Dysfunction

Qiu-Xiang Zhang,[1] *Rong-Wen Lu,*[1] *Christine A. Curcio,*[2] *and Xin-Cheng Yao*[1,3]

IOVS (2012), 55(13), 8139-8145.

Back to amphibians...

OPEN

SUBJECT AREAS:
DIAGNOSTIC MARKERS
RETINA
IMAGING AND SENSING

Received
3 September 2014

Accepted
5 March 2015

Published
22 April 2015

Functional Optical Coherence Tomography Enables *In Vivo* Physiological Assessment of Retinal Rod and Cone Photoreceptors

Qiuxiang Zhang[1], Rongwen Lu[1], Benquan Wang[1], Jeffrey D. Messinger[2], Christine A. Curcio[2] & Xincheng Yao[1,2,3]

[1]Department of Biomedical Engineering, University of Alabama at Birmingham, Birmingham, AL 35294, [2]Department of Ophthalmology, University of Alabama at Birmingham, Birmingham, AL 35294, [3]Department of Bioengineering, University of Illinois at Chicago, Chicago, IL 60607.

Scientific Reports (2015), 5:9595, 1-10.

This is complicated!?

- Effects at many layers?
- Consistent across sites - or not?

Should there be an "optoretinogram" (ORG) ?

- Rolls off the tongue - shorter than "intrinsic optical signals"
- Analogy to electroretinogram (ERG)
- Unlike ERG, relatively easy to measure multiple, independent signals
- Time will tell...
- THANK YOU!
- - and THANK YOU Donald!!!