JOHN E. DOWLING Gordon and Llura Gund Research Professor of Neurosciences Professor of Ophthalmology (Neuroscience) Harvard University

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PERSONAL

Born: August 31, 1935; Pawtucket, Rhode Island, USA

EDUCATION

Harvard College, A.B., 1957 (Biology) Harvard Medical School, 1957-1959 Harvard University, Ph.D., 1961 (Biology)

Positions and Employment

1961	Instructor, Department of Biology, Harvard University, Cambridge, MA
1961-1964	Assistant Professor of Biology, Harvard University, Cambridge, MA
1964-1971	Assistant and Associate Professor of Ophthalmology and Biophysics, Johns
	Hopkins University, Baltimore, MD
1970-1974	Founding Co-director, Neurobiology Course, Marine Biological
	Laboratory, Woods Hole, MA
1971-1987	Professor of Biology, Harvard University, Cambridge, MA
1975-1978	Chairman of the Biology Department, Harvard University, Cambridge, MA
1980-1984	Associate Dean of the Faculty of Arts and Sciences, Harvard University,
	Cambridge, MA
1981-1998	Master of Leverett House, Harvard University
1986-	Professor of Ophthalmology (Neuroscience), Harvard Medical School,
	Boston, MA
1987-2001	Maria Moors Cabot Professor of Natural Science, Harvard University,
	Cambridge, MA
1998-2001	Founding Co-director, Neural Development and Genetics of Zebrafish
	Course, Marine Biological Laboratory, Woods Hole, MA
1999-2004	Harvard College Professor, Harvard University, Cambridge, MA
Dowling CV 2/12/2016	1

2001-2015	Gordon and Llura Gund Professor of Neurosciences, Harvard University,
	Cambridge, MA
2015-	Gordon and Llura Gund Research Professor of Neurosciences, Harvard
	University, Cambridge, MA

Honors and Awards

1970	Friedenwald Medal, Association for Research in Vision and
	Ophthalmology
1971	Edridge-Green Lecturer, Royal College of Surgeons of England
1972	Fellow, American Academy of Arts and Sciences
1975-1985	Associate, Neuroscience Research Program
1976	Member, National Academy of Sciences
1978-1979	Guggenheim Fellow
1979	Annual Award, New England Ophthalmological Society
1981	Fellow, American Association for the Advancement of Science
1981	Retina Research Foundation Award of Merit
1982	M.D. (Hon.) University of Lund, Sweden
1986	Alcon Research Institute Recognition Award
1987	National Eye Institute MERIT Award
1991	Prentice Medal, American Academy of Optometry
1992	Member, American Philosophical Society
1992	Von Sallman Prize, International Society for Eye Research
1993	Taylor Smith Orator, New England Ophthalmological Society
2000	The Helen Keller Prize for Vision Research
2001	Llura Ligget Gund Award for Lifetime Achievement and Recognition of
	Contribution to Foundation Fighting Blindness
2008	Paul Kayser International Award in Retina Research
2009	Glenn A. Fry Medal in Physiological Optics
2012	Doctor of Laws degree (Hon.), Dalhousie University, Canada
2015	D. Sci. (Hon.), State University of New York
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MAJOR BOARDS, COUNCILS, AND COMMITTEES

Current

Board of Scientific Governors Meeting, Lowy Medical Research Institute 2012-National Eye Institute Audacious Goals Steering Committee, 2012-Lasker/International Retinal Research Foundation, Initiative for Innovation in vision science, Project Chair, 2008-.
Scientific Advisory Board, Institut de la vision, Paris, Chair 2008-.
Board of Directors, Harvard University Press, 1997-.
Scientific Advisory Board, Center for Neural Science, New York University, 1992-.
Trustee, Massachusetts Eye and Ear Infirmary, 1986-.
Scientific Advisory Board, Foundation Fighting Blindness, 1971-.

Past, 1980-

International Advisory Committee, King Abdullah University of Science and Technology, Saudi Arabia, 2009-2011 Trustee, Marine Biological Laboratory, 2007-2011 Chair, Faculty Standing Committee on Degrees in Neurobiology, Harvard University, 2006-2011 Head Tutor, Neurobiology Concentration, Harvard University, 2005-2010 Board of Directors, American Association for the Advancement of Science, 2004-2008 Chairman of the Board of Governors, Association for Research in Ophthalmology and Vision Foundation, 2001-2007 Co-chair, Ad hoc Faculty of Arts and Sciences Committee on Women in Science, Harvard University, 2000-2002 Advisory Board, Bunting Institute, Radcliffe College, 1999-2003 Board, Office for the Public Understanding of Science, National Research Council, 1999-2004 Scientific Advisory Board, Doreen Grace Fund and The Brain Center, 1999-2011 Co-Chair, Faculty Standing Committee on Mind, Brain and Behavior, Harvard University, 1998-2008 President of the Corporation, Marine Biological Laboratory, 1998-2007 President, Association for Research in Vision and Ophthalmology, 1996-1997 Board of Directors, Alliance for Eye and Vision Research, 1995-2004 Editorial Board, Physiological Reviews, 1994-2000 Scientific Advisory Board, Central Institute for the Deaf, 1994-2002 Council, National Academy of Sciences, 1993-1996 Council, Faculty of Arts and Sciences, Harvard University, 1980-1984; 1993-1995 Chairman, FASEB Summer Conference on Biology, Chemistry and Modeling of Vision, 1992 Scientific Advisory Board, Knights Templar Eye Foundation, 1991-2006; Chair, 2003-2006 Scientific Advisory Board, Research to Prevent Blindness, 1991-1999 Trustee, Association for Research in Vision and Ophthalmology, 1991-1998 Educational Advisory Board, John S. Guggenheim Memorial Foundation, 1991-2007 Medical Advisory Board, Howard Hughes Medical Institute, 1989-1992 Associate Editor for Cellular Neurobiology, Journal of Neuroscience, 1989-1994 Trustee Executive Committee, Marine Biological Laboratory, 1988-1990 Council, National Eye Institute, 1986-1990 Scientific Advisory Board, Whitney Marine Laboratory, 1986-1991 Chairman, Commission on Life Sciences, National Research Council, 1985-1988 Governing Board, National Research Council, 1985-1988; 1994-1997 Council, Society of Neuroscience, 1980-1984 PUBLICATIONS AND CONTRIBUTIONS TO SCIENCE

Contributions to Science

a. My earliest publications focused on the ocular effects of vitamin A deficiency in rats. I mapped out the biochemical, anatomical and physiological changes that

occur in the retina as a function of time. A major discovery was that vitamin A acid (now retinoic acid) would substitute for all somatic functions of vitamin A, but not those involved in its role as chromophore of the visual pigments. Thus, I could isolate the effects of the deficiency to the eye. Much later our laboratory examined the effects of retinoic acid on early eye development, showing that retinoic acid was required for ventral retinal formation but not the dorsal retina.

- i. Dowling, J. E. and Wald, G. Vitamin A deficiency and night blindness. Proc. Natl. Acad. Sci., 44, 648-661, 1958.
- ii. Dowling, J. E. and Wald, G. The biological function of vitamin A acid. Proc. Natl. Acad. Sci., 46, 587-608, 1960.
- iii. Hyatt, G. A., Schmitt, E. A., Marsh-Armstrong, N. R. and Dowling, J. E. Retinoic acid- induced duplication of the zebrafish retina, Proc. Natl. Acad. Sci., 89, 8293-8297, 1992.
- iv. Marsh-Armstrong, N., McCaffery, P., Gilbert, W., Dowling, J. E. and Dräger, U. C. Retinoic acid is necessary for development of the ventral retina in zebrafish. Proc. Natl. Acad. Sci., 91, 7286-7290, 1994.
- b. Another early observation I made and that I and my colleagues continued to explore is the relation of visual sensitivity to visual pigment levels in the photoreceptors. In both vitamin A deficiency and after bright light adaptation. I discovered there is an approximate log-linear relationship between visual sensitivity and visual pigment level in the photoreceptors. We have studied light and dark adaptation in the intact eye, isolated retina, and under various conditions, identifying and analyzing both neural and photochemical mechanisms of visual adaptation.
 - i. Dowling, J. E. Chemistry of visual adaptation in the rat. Nature, 188, 114-118, 1960.
 - ii. Dowling, J. E. Neural and photochemical mechanisms of visual adaptation in the rat. J. Gen. Physiol., 46, 1287-1301, 1963.
 - iii. Weinstein, G. W., Hobson, R. R. and Dowling, J. E. Light and dark adaptation in the isolated rat retina. Nature, 215, 134-138, 1967.
 - iv. Dowling, J. E. and Ripps, H. Visual adaptation in the retina of the skate. J. Gen. Physiol., 56, 491-520, 1970.
 - v. Dowling, J. E. and Ripps, H. Adaptation in skate photoreceptors. J. Gen. Physiol., 60, 698-719, 1972.
 - vi. Kleinschmidt, J. and Dowling, J. E. Intracellular recordings from Gecko photoreceptors during light and dark adaptation. J. Gen. Physiol., 66, 617-648, 1975.
 - vii. Green, D. G., Dowling, J. E., Siegel, I. M. and Ripps, H. Retinal mechanisms of visual adaptation in the skate. J. Gen. Physiol., 65, 483-502, 1975.
 - viii. Pepperberg, D., Lurie, M., Brown, P. K. and Dowling, J. E. Visual adaptation: effects of externally applied retinal on the light-adapted, isolated skate retina. Science, 191, 394-396, 1976.
 - ix. Dowling, J. E. and Ripps, H. The proximal negative response and visual adaptation in the skate retina. J. Gen. Physiol., 69, 57-74, 1977.

- c. Much of my career has been spent studying the functional organization of the vertebrate retina, first in primates, then in amphibians and fish. The anatomical studies were at both light and electron microscopial level and identified the synapses, both chemical and electrical, found in the retina. We have provided crude wiring diagrams of various retinas that have been useful in suggesting synaptic pathways through the retina and how the receptive fields of retinal cells are formed synaptically. Another, related focus of my group has been to record intracellulary from retinal cells. This work was pioneered by Frank Werblin, a graduate student who recorded and stained rods, horizontal, bipolar, amacrine and ganglion cells in the mudpuppy retina: the first time this was accomplished in any retina. Subsequent recordings by other lab members were made from Müller cells, rods and cones, horizontal cells subtypes, amacrine cells, and ganglion cells in a variety of species. Finally, we have explored the pharmacology of the retina identifying neurotransmitters used by various retinal cells including the photoreceptor and bipolar cells.
 - i. Dowling, J. E. and Boycott, B. B. Organization of the primate retina: electron microscopy. Proc. Roy. Soc. B, 166, 80-111, 1966.
 - Dowling, J. E. Synaptic organization of the frog retina: an electron microscopic analysis comparing the retinas of frogs and primates. Proc. Roy. Soc. B, 170, 205-228, 1968.
 - iii. Boycott, B. B. and Dowling, J. E. Organization of the primate retina: light microscopy. Phil.Trans. B, 255, 109-184, 1969.
 - iv. Dowling, J. E. and Werblin, F. S. Organization of retina of the mudpuppy, Necturus maculosus: I. Synaptic structure. J. Neurophysiol. 32, 315-338, 1969.
 - v. Werblin, F. S. and Dowling, J. E. Organization of the retina of the mudpuppy, Necturus maculosus. II. Intracellular recording. J. Neurophysiol., 32, 339-355, 1969.
 - vi. Miller, R. F. and Dowling, J. E. Intracellular responses of the Müller (glial) cells of mudpuppy retina: their relation to the b-wave of the electroretinogram. J. Neurophysiol., 33, 323-341, 1970.
 - vii. Fain, G. L. and Dowling, J. E. Intracellular recordings from single rods and cones in the mudpuppy retina. Science, 180, 1178-1181, 1973.
 - viii. Dowling, J. E. and Ripps, H. Effect of magnesium on horizontal cell activity in the skate retina. Nature, 242, 101-103, 1973.
 - ix. Lasater, E. M. and Dowling J.E. Carp horizontal cells in culture respond selectively to L-glutamate and its agonists. Proc. Natl. Acad. Sci., 79, 936-940, 1982.
 - x. Qian, H. and Dowling, J.E. Novel GABA responses from rod-driven retinal horizontal cells. Nature, 361, 162-164, 1993.
- d. An interest of my laboratory for many years has been the role of dopamine as a neuromodulator in the retina. This has included anatomical, biochemical and physiological studies, especially on the effects of dopamine on the fish horizontal cells.

- i. Dowling, J. E. and Ehinger, B. Synaptic organization of the aminecontaining interplexiform cells of the goldfish and Cebus monkey retinas. Science, 188, 270-273, 1975.
- Dowling, J. E. and Ehinger, B. The interplexiform cell system. I. Synapses of the dopaminergic neurons of the goldfish retina. Proc. Roy. Soc. B 201, 7-26, 1978.
- iii. Hedden, W. L. and Dowling, J. E. The interplexiform cell system. II. Effects of dopamine on goldfish retinal neurons. Proc. Roy Soc. B 201, 27-55, 1978.
- Watling, K. J. and Dowling, J. E. Dopaminergic mechanisms in the teleost retina. I. Dopamine-sensitive adenylate cyclase in the homogenates of carp retina: effects of agonists, antagonists and ergots. J. Neurochem 36(2), 559-569, 1981.
- v. Van Buskirk, R. and Dowling, J. E. Isolated horizontal cells from carp retina demonstrate dopamine-dependent accumulation of cyclic AMP. Proc. Natl. Acad. Sci. 78, 7825-7829, 1981.
- Vi. Lasater, E. M. and Dowling, J. E. Dopamine decreases the conductance of the electrical junctions between cultured retina horizontal cells. Proc. Natl. Acad. Sci 82, 3025-3029, 1985.
- vii. Knapp, A. G. and Dowling, J. E. Dopamine enhances excitatory amino acid-gated conductances in cultured retinal horizontal cells. Nature, 325, 437-439, 1987.
- viii. McMahon, D. G., Knapp, A. G. and Dowling, J. E. Horizontal cell gap junctions: Single-channel conductance and modulation by dopamine. Proc. Natl. Acad. Sci. 86, 7639-7643, 1989.
- e. Another major interest of mine going back to early days is that of inherited retinal degenerations. Sidman and I were the first to analyze in depth the RCS rat retinal degeneration and beginning in the 1990's we undertook a large forward-genetics program with zebrafish generating and analyzing mutants that affect retinal structure function and development. A number of these mutants have turned out to be valuable in understanding photoreceptor, developmental visual mechanisms
 - i. Dowling, J. E. and Sidman, R. L. Inherited retinal dystrophy in the rat. J. Cell Biol., 14, 73-109, 1962.
 - Brockerhoff, S. E., Hurley, J. B., Janssen-Bienhold, U., Neuhauss, S. C., Driever, W. and Dowling, J. E. A behavioral screen for isolating zebrafish mutants with visual system defects. Proc. Natl. Acad. Sci., 92, 10545-10549, 1995.
 - Brockerhoff, S. E., Hurley, J. B., Niemi, G. A. and Dowling, J. E. A new form of inherited red-blindness in zebrafish. J. Neurosci., 17, 4236-4242, 1997.
 - iv. Link, B. A., Fadool, J. M., Malicki, J. and Dowling, J. E. The zebrafish young mutation acts non-cell autonomously to uncouple differentiation from specifications for all retinal cells. Development, 127, 2177-2188, 2000.

- v. Allwardt, B., Lall, A. B., Brockerhoff, S. E. and Dowling, J. E. Synapse formation is arrested in retinal photoreceptors of the zebrafish nrc mutant. J. Neurosci., 21, 2330-2342, 2001.
- vi. Gross, J. M., Perkins, B. D., Amsterdam, A., Egana, A., Darland, T., Matsui, J. I., Sciascia, S., Hopkins, N. and Dowling, J. E. Identification of zebrafish insertional mutants with defects in visual system development and function, 170, 245-261, Genetics, 2005.
- vii. Emran, F. Rihel, J., Adolph, A., Wong, K. Y., Kraves, S. and Dowling, J. E. OFF- ganglion cells cannot drive the optokinetic reflex in zebrafish. Proc. Natl. Acad. Sci., 104, 19126-19131, 2007.
- viii. Leung, Y. F. P. Ma, Link, B. A. and Dowling, J. E. Factorial microarray analysis of zebrafish retinal development, Proc. Natl. Acad. Sci., 105, 12909-12914, 2008.
 - ix. Li, Y, Matsui, J. I. and Dowling, J. E. Specificity of the horizontal cellphotoreceptor connections in the zebrafish (Danio rerio) retina, J. Comp. Neurol. 516, 442-453, 2009.
 - x. Le, H.G., Dowling, J.E., and D.J. Cameron. Early retinoic acid deprivation in zebrafish results in micropthalmia. Vis. Neurosci. 29, 219-228, 2012.
- f. Finally, over the years, our laboratory has studied aspects of vision in invertebrates, especially in the horseshoe crab and dragonfly, as well as the photoreceptors and neuronal organization in the lamprey and zebrafish pineal gland.
 - i. Dowling, J. E. Discrete potentials in the dark-adapted eye of Limulus. Nature, 217, 28-31, 1968.
 - Chappell, R. L. and Dowling, J. E. Neural organization of the ocellus of the dragonfly. I. Intracellular electrical activity. J. Gen. Physiol., 60, 121-147, 1972.
 - iii. Dowling J. E. and Chappell, R. L. Neural organization of the dragonfly ocellus. II. Synaptic structure. J. Gen. Physiol. 60, 148-165, 1972.
 - iv. Armett-Kibel, C., Meinertzhagen, I. A. and Dowling, J. E. Cellular and synaptic organization in the lamina of the dragonfly Sympetrum rubicundulum. Proc. Roy. Soc. Lond. B, 196, 385-413, 1977.
 - v. Pu, G. A. and Dowling, J. E. Anatomical and physiological characteristics of the pineal photoreceptor cell in the larval lamprey, Petromycon marina. J. Neurophysiol. 46, 1018-1038, 1981.
 - vi. Allwardt, B.A. and Dowling, J. E. The pineal gland in wild-type and two mutant zebrafish with retinal defects. J. Neurocytol., 130, 493-501, 2001.

Books

- Dowling, J. E. and J.L. Dowling, Jr. *Vision: How it Works and What Can Go Wrong*. (April 2016) MIT Press, Cambridge, MA.
- Dowling, J. E. *The Retina: An Approachable Part of the Brain* Revised Edition (2012) Belknap, Harvard University Press, Cambridge, MA.

Dowling CV 2/12/2016

- Dowling, J. E. *The Great Brain Debate: Nature or Nurture?* (2004) Joseph Henry Press, Washington, D. C.
- Dowling, J. E. *Neurons and Networks: An Introduction to Behavioral Neuroscience*, 2nd edition, (2001) Harvard University Press, Cambridge, MA.
- Dowling, J. E. *Creating Mind: How the Brain Works* (1998) W. W. Norton & Co., New York, NY.
- Dowling, J. E. *Neurons and Networks: An Introduction to Neuroscience* (1992) Harvard University Press, Cambridge, MA.
- Dowling, J. E. *The Retina: An Approachable Part of the Brain* (1987) Belknap, Harvard University Press, Cambridge, MA.

Volumes Edited

- Dowling, J.E., and Wright, K (eds). Restoring Vision to the Blind (2014): A Report by the Lasker/IRRF Initiative for Innovation in Vision Science. Lasker Foundation, New York.
- Dowling, J.E., and Wright, K (eds). Diabetic Retinopathy: Where we are and A Path to Progress (2012): A Report by the Lasker/IRRF Initiative for Innovation in Vision Science. Lasker Foundation, New York.
- Dowling, J.E., and Wright, K. (eds) Astrocytes and Glaucomatous Neurodegenteration (2010): A Report by the Lasker/IRRF Initiative for Innovation in Vision Science. Lasker Foundation, New York.
- Dowling, J., Stryer, L., and Wiesel, T. (eds). *A Colloquium on Vision: From Photon to Perception* (1996) PNAS 93, 557-639.
- Barlow, R., Dowling, J. E. and Weissmann, G. (eds.) *The Biological Century: Friday Evening Talks at the Marine Biological Laboratory*. (1992) Harvard University Press, Cambridge, MA.
- Dowling, J.E., Kolb, H. and Wässle, H. (eds.) *Proceedings of the Brian Boycott Festschrift* (1991) Visual Neuroscience, Vol. 7 No. 1/2, Cambridge University Press, Cambridge, England
- Dowling, J. E., Kolb, H., Miller, R. and Tomita, T. (eds). *Retinal Neurocircuitry, with Special Reference to Synaptic Transmission*, (1983) Proceedings of the 4th Taniguchi International Symposium on Visual Science, Vision Res., Vol. 23, Pergamon Press, Oxford.
- Dowling, J. E., Proenza, L. M. and Atwell, C. W. (eds.) <u>Nutrition, Pharmacology and Vision</u>, Proceedings of a Symposium Sponsored by the Committee on Vision of the National Research Council (1982) Retina, Vol. 2, pp. 231-380.

- Cone, R. A. and Dowling, J. E.(eds.) *Membrane Transduction Mechanisms* (1979) Society of General Physiologists, Raven Press, New York.
- Poppel, E., Held, R. and Dowling, J. E. (eds.) *Neuronal Mechanisms in Visual Perceptions* (1977) Neuroscience Res. Prog. Bull., Vol. 15, M.I.T. Press, Cambridge, MA.
- Landers, M.B., Wolbarsht, J. L., Dowling, J. E. and Laties, A. M. (eds.) *Retinitis Pigmentos: Clinical Implications of Current Research* (1977) Plenum Press, New York.
- Shipley, T. and Dowling, J.E. (eds.), *Visual Processes in Vertebrates* (1971) Vision Res. Suppl., Vol. 11, Pergamon Press, Oxford.
- Wald, G., Hopkins III, J., Albersheim, P., Dowling, J. E., and Denhardt, D. (eds), *Twenty-six Afternoons of Biology*, (1962), Addison-Wesley, Reading, MA.
- 272 Research laboratory publications to date