

CURRICULUM VITAE

RICHARD P. BOBBIN

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Education:

Northeastern University, College of Pharmacy, Boston, Massachusetts. B.S. awarded in 1964.

Tulane University, New Orleans, Louisiana. M.S. awarded 1967 (Pharmacology).

Tulane University, New Orleans, Louisiana. Ph.D. awarded 1969 (Pharmacology).

University of Florida, Gainesville, Florida. Postdoctoral Fellowship 1969-1971 (Neuroscience).

M.S. Thesis:

An experimental study of the effect of bradykinin on the marginal ear vein of the rabbit (Paul S. Guth, Preceptor).

Doctoral Dissertation:

An investigation of the hypothesis that gamma-aminobutyric acid or an analogue is the inhibitory transmitter at the olivo-cochlear nerve hair-cell junction (Paul S. Guth, Preceptor).

Highlights of Research Activities:

A large number of my laboratory's research publications demonstrated that acetylcholine, glutamate and ATP met various criteria for the identification of neurotransmitters in the cochlea. The following summarizes some of that research.

My laboratory was the first to demonstrate that intracochlear application of acetylcholine mimicked the effects of the neurotransmitter of the medial olivocochlear bundle on cochlear microphonics, the

compound action potential of the auditory nerve (Publication #4) and on the sound evoked mechanical responses of the cochlea as monitored by DPOAEs (Publication # 44). We were the first to demonstrate the unique pharmacology of the acetylcholine receptor of the medial olivocochlear bundle, both to acetylcholine agonists and antagonists, at the level of the slow change in the EP evoked by medial olivocochlear bundle stimulation (Publication #6), at the level of the mechanical change in the cochlear partition as monitored by DPOAEs (Publication # 51) and at the level of the single isolated outer hair cell (Publication # 52).

My laboratory was the first to suggest glutamate as a candidate for the afferent neurotransmitter released by the inner hair cells (Publication #12; Abstracts #9 & #10). We were the first to demonstrate that glutamate mimicked the hair cell afferent transmitter by increasing the rate of firing of the auditory nerve (Publication #13). We were the first to demonstrate that glutamate was released from a hair cell system (lateral line) by natural stimulation (Publication #15) and we were the first to demonstrate that depolarization of cells in the cochlea with potassium also released glutamate (Publication #24). Both studies showed that glutamate met the release criterion for the identification of the afferent hair cells transmitter. We were the first to demonstrate the blockade criterion for glutamate as the hair cell transmitter by demonstrating the reduction in the compound action potential of the auditory nerve and sound-evoked firing of the auditory nerve by glutamate antagonists (Publications #20, # 27, #31, # 33, #81). We were the first to suggest that the glutamate receptor, NMDA, had no detectable role (Publication # 25) in generating action potentials in the auditory nerve fibers synapsing on the inner hair cells and that the glutamate receptor, AMPA, played a dominant role (Publication # 77, #81).

My laboratory was the first to suggest that ATP may be a neurotransmitter in the cochlea (Publications #12, #53, # 54). We were the first to demonstrate that the quadratic DPOAE may reflect the action of ATP on Deiters= cells through the use of ATP antagonists (Publications #70, #73) and to demonstrate that ATP can be both cytotoxic and mitogenic to cells in the cochlea (Publication # 71).

My laboratory was the first to demonstrate that nitric oxide (NO) reduced the endocochlear potential and to suggest that this was the mechanism for the observed suppression of the cochlear microphonics and the compound action potential of the auditory nerve (Publication #60). We were the first to demonstrate that intense sound and potassium depolarization induced the release of glutathione from cochlear tissue (Publications #46, # 61).

Research Activities:

My major research activities are concerned with neurotransmitter pharmacology, biochemistry and molecular biology using the peripheral auditory organ as a model system. In addition, I have minor interests in ototoxic drugs and noise induced deafness. Current investigations are being carried out to discover:

1. The identity, mechanisms of action and pharmacology of chemical transmitters and modulators in the cochlea with current emphasis being placed on the function of extracellular ATP on supporting cells.
2. The physiology, pharmacology and biochemistry of the efferent nerve fibers in the cochlea.
3. The mechanisms of action of ototoxic drugs such as aspirin.
4. The mechanism by which sound induces a hearing loss.

Publications:

- 1) Bobbin, R.P. and Guth, P.S. Venoconstrictive action of Bradykinin. **J. Pharmacol. Exp. Therap.**, **160** (1):4-20, 1968.
- 2) Bobbin, R.P., Gonzalez, G., and Guth, P.S. Effects of aminooxyacetic acid on cochlear potentials and the Preyer reflex. **Nature**, **223**:70-71, 1969.
- 3) Bobbin, R.P. and Guth, P.S. Evidence that gamma-aminobutyric acid is not the inhibitory transmitter at the crossed olivocochlear nerve-hair cell junction. **Neuropharmacology**, **9**:567-574, 1970.
- 4) Bobbin, R.P. and Konishi, T. Acetylcholine mimics crossed olivocochlear bundle stimulation. **Nat. New Biol.**, **231**:222-223, 1971.
- 5) Bobbin, R.P. and Gondra, Maria I. Effect of intravenous aminooxyacetic acid on the guinea pig cochlear potentials. **Neuropharmacology**, **12**:1005-1007, 1973.
- 6) Bobbin, R.P. and Konishi, T. Action of cholinergic and anticholinergic drugs at the crossed olivocochlear bundle-hair cell junction. **Acta Otolaryngol.**, **77**:56-65, 1974.
- 7) Bobbin, R.P. and Gondra, M.I. Effect of intracochlear aminooxyacetic acid on cochlear potentials and endolymph composition. **Ann. Otol. Rhinol. Laryngol.**, **84**(2):192-197, 1975.
- 8) Bobbin, R.P. and Gondra, M.I. Effects of intense low frequency sound (sonic boom) on the cochlea. **Environ. Res.**, **9**:48-54, 1975.
- 9) Bobbin, R.P. Recording site in the organ of Corti determined by an electrode-marking technique. **Arch. Otolaryngol.**, **102**:45-48, 1976.
- 10) Bobbin, R.P. and Gondra, M.I. Effect of nicotine on cochlear function and noise-induced hair cell loss. **Ann. Otol. Rhinol. Laryngol.**, **85**(2):247-254, 1976.

- 11) Bobbin, R.P., Guth, Mary S., and Mines, A.B. An examination of an electro-chemical mechanism for noise-induced hair cell loss: Noise with aminooxyacetic acid (AOAA). **Trans. Am. Acad. Ophthalmol. Otolaryngol.**, **82**:299-304, 1976.
- 12) Bobbin, R.P. and Thompson, M.H. Effects of putative transmitters on afferent cochlear transmission. **Ann. Otol. Rhinol. Laryngol.**, **87**:185-190, 1978.
- 13) Bobbin, R.P. Glutamate and aspartate mimic the afferent transmitter in the cochlea. **Exp. Brain Res.**, **24**:389-393, 1979.
- 14) Bobbin, R.P., May, J.G., and Lemoine, R.L. Effects of pentobarbital and ketamine on brain stem auditory potentials: Latency and amplitude intensity functions after intraperitoneal administration. **Arch. Otolaryngol.**, **105**:467-470, 1979.
- 15) Bledsoe, S.C., Jr., Bobbin, R.P., Thalmann, R., and Thalmann, I. Stimulus-induced release of endogenous amino acids from the Xenopus laevis lateral-line organ. **Exp. Brain Res.**, **40**:97-101, 1980.
- 16) Bledsoe, S.C., Jr., Bobbin, R.P., and Chihal, D.M. Kainic acid: An evaluation of its action on cochlear potentials. **Hear. Res.**, **4**:109-120, 1981.
- 17) Bobbin, R.P., Bledsoe, S.C., Jr., and Chihal, D.M. Effect of asphyxia and aminooxyacetic acid on the slow potential evoked by crossed olivocochlear bundle stimulation. **Hear. Res.**, **5**:265-269, 1981.
- 18) Bobbin, R.P., Bledsoe, S.C., Jr., Chihal, D.M., and Morgan, D.N. Comparative actions of glutamate and related substances on the Xenopus laevis lateral line. **Comp. Biochem. and Physiol.**, **69C**:145-147, 1981.
- 19) Kisiel, D. and Bobbin, R.P. Interaction of aminooxyacetic acid and ethacrynic acid with intense sound at the level of the cochlea. **Hear. Res.**, **6**:129-140, 1981.
- 20) Bledsoe, S.C., Jr. and Bobbin, R.P. Effects of D- α -aminoadipate on excitation of afferent fibers in the lateral line of Xenopus laevis. **Neurosci. Lett.**, **32**:315-320, 1982.
- 21) Bledsoe, S.C., Jr., Chihal, D.M., Bobbin, R.P., and Morgan, D.N. Comparative actions of glutamate and related substances on the lateral line of Xenopus laevis. **Comp. Biochem. and Physiol.**, **75C**:119-206, 1983.
- 22) Bobbin, R.P., Bledsoe, S.C., Jr., Winbery, S., Ceasar, G., and Jenison, G.L. Comparative actions of GABA and acetylcholine on the Xenopus laevis lateral line. **Comp. Biochem. and Physiol.**, **80C**:313-318, 1985.

- 23) Jenison, G.L. and Bobbin, R.P. Quisqualate excites spiral ganglion neurons of the guinea pig. **Hear. Res.**, **20**:261-265, 1985.
- 24) Jenison, G.L., Bobbin, R.P., and Thalmann, R. Potassium-induced release of endogenous amino acids in the guinea pig cochlea. **J. Neurochem.**, **44**:1845-1853, 1985.
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- 28) Puel, J.-L., Bobbin, R.P., and Fallon, M. An ipsilateral cochlear efferent loop protects the cochlea during intense sound exposure. **Hear. Res.** **37**, 65-70, 1988.
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- 33) Puel, J.-L., Bobbin, R.P., and Fallon, M. Suppression of auditory nerve activity in the guinea pig cochlea by 1-(p-bromobenzyl)-piperazine -2,3-dicarboxylic acid. **Brain Research**, **487**:9-15, 1989.
- 34) Puel, J.-L., Bledsoe, S.C., Jr., Bobbin, R.P., Ceasar, G., and Fallon, M. Comparative actions of salicylate on the amphibian lateral line and the guinea pig cochlea. **Comp. Biochem. and Physiol.**, **93C**:73-80, 1989.
- 35) Bobbin, R.P., Ceasar, G., and Fallon, M. Potassium induced release of GABA and other substances from the guinea pig cochlea. **Hear. Res.** **46**, 83-94, 1990.

- 36) Bobbin, R.P., Jastreboff, P.J., Fallon, M., and Littman, T. Nimodipine, an L-channel Ca^{+2} antagonist, reverses the negative summing potential recorded from the guinea pig cochlea. **Hear. Res. 46**, 277-288, 1990.
- 37) Bobbin, R.P., Fallon, M., Puel, J.-L., Bryant, G., Bledsoe, S.C., Jr., Zajic, G., and Schacht, J. Acetylcholine, carbachol, and GABA induce no detectable change in the length of isolated outer hair cells. **Hear. Res. 47**, 39-52, 1990.
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- 39) Pou, A.M., Fallon, M., Winbery, S., and Bobbin, R.P. Lowering extracellular calcium decreases the length of isolated outer hair cells. **Hear. Res. 52**: 305-311, 1991.
- 40) Bobbin, R.P., Ceasar, G., and Fallon, M. Changing cation levels (Mg^{2+} , Ca^{2+} , Na^{+}) alters the release of glutamate, GABA and other substances from the guinea pig cochlea. **Hear. Res. 54**: 135-144, 1991.
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- 46) Bobbin, R.P. and Fallon, M. Intense sound increases the level of an unidentified amine found in perilymph. **Hear. Res. 63**: 157-162, 1992.
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- 52) Erostequi, C., Norris, C.H., and Bobbin, R.P. In vitro pharmacologic characterization of a cholinergic receptor on outer hair cells. **Hear. Res. 74:** 135-147, 1994.
- 53) Kujawa, S.G., Erostequi, C., Fallon, M., Crist, J., and Bobbin, R.P. Effects of ATP and related agonists on cochlear function. **Hear. Res. 76:** 87-100, 1994.
- 54) Kujawa, S.G., Fallon, M., and Bobbin, R.P. ATP antagonists cibacron blue, basilen blue and suramin alter sound-evoked responses of the cochlea and auditory nerve. **Hear. Res. 78:** 181-188, 1994.
- 55) Erostequi, C., Nenov, A.P., Norris, C.H., and Bobbin, R.P. Acetylcholine activates a K^+ conductance permeable to Cs^+ in guinea pig outer hair cells. **Hear. Res. 81:** 119-129, 1994.
- 56) Kujawa, S.G., Fallon, M., and Bobbin, R.P. Time-varying alterations in the f_2 - f_1 DPOAE response to continuous primary stimulation. I. Response characterization and contribution of the olivocochlear efferents. **Hear. Res. 85:** 142-154, 1995.
- 57) Skellett, R.A., Crist, J.R., Fallon, M., and Bobbin, R.P. Caffeine-induced shortening of isolated outer hair cells: An osmotic mechanism of action. **Hear. Res. 87:** 41-48, 1995.
- 58) Chen, C., Nenov, A., Norris, C.H., and Bobbin, R.P. ATP modulation of L-type calcium channel currents in guinea pig outer hair cells. **Hear. Res. 86:** 25-33, 1995.
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- 60) Chen, C., Nenov, A. P., Skellett, R., Fallon, M., Bright, L., Norris, C.H. and Bobbin, R.P. Nitroprusside suppresses cochlear potentials and outer hair cell responses. **Hear. Res. 87:** 1-8, 1995.
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Reviews, Books, Book Chapters and Published Proceedings:

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116) Bobbin, R.P. Caffeine and ryanodine demonstrate a role for the ryanodine receptor in the organ of Corti. **Abstracts of the 26th Midwinter Research Meeting, Association for Research in Otolaryngology**, Daytona Beach, Florida, abstract 623, pg. 156, February 22-27, 2003.

117) Bobbin, R.P., Parker, M., and Wall, L. Thapsigargin suppresses cochlear potentials and DPOAEs and is toxic to hair cells. **Abstracts of the 27th Midwinter Research Meeting, Association for Research in Otolaryngology**, Daytona Beach, Florida, abstract 973, pg. 130, February 21-26, 2004.

118) Parker, M.A., Gray, B., Bakhtiarova, A., Snyder, E.Y., Wall, L., Bobbin, R.P., and Cotanche, D.A. Detection of stem cells transplanted into the cochlea by fluorescent in situ hybridization. **Abstracts of the 27th Midwinter Research Meeting, Association for Research in Otolaryngology**, Daytona Beach, Florida, abstract 1033, pg. 138, February 21-26, 2004

Special Lectures (select):

Aminooxyacetic acid protects against noise-induced cochlear hair cell loss. Lecture - Coleman Memorial Laboratory, Departments of Physiology and Otolaryngology, University of California at San Francisco, San Francisco, California, November, 1975.

A drug that prevents noise-induced hearing loss? Lecture - Memphis Speech and Hearing Center, Memphis State University, Memphis, Tennessee, December 3, 1976.

Recordings from inside the hair cells. 11th Colorado Medical Audiologic Workshop, Vail, Colorado, March 5-12, 1977.

Auditory physiology. Lecture and videotape presentation, 12th Colorado Otology-Audiology Workshop, Vail, Colorado, March 4-11, 1978.

Classifications and mechanisms of action in ototoxic drugs. 12th Colorado Otology-Audiology Workshop, Vail, Colorado, March 4-11, 1978.

Interaction of drugs with intense sound at the level of the cochlea. Research Discussion, National Aerospace Medical Research Laboratory, Naval Air Station, Pensacola, Florida, August 17, 1978.

Effects of damaging levels of intense sound on the cochlea - A review of effects and mechanisms. 13th Colorado Otology-Audiology Workshop, Vail, Colorado, March 3-10, 1979.

Measurement and treatment of hearing problems in children. Continuing Education Program, Pediatric Pharmacy, presented by Xavier University of Louisiana, December 8, 1985.

Hair cell function and transmitters. Tutorial session at the Second Annual Meeting of the American Academy of Audiology, New Orleans, April 28, 1990.

Excitatory amino acids in the cochlea: physiology and pharmacology. Departement Biologie-Santé, Université Montpellier II, France, Mardi 5 Juin 1990.

Outer hair cells: motors in the inner ear with a novel acetylcholine receptor. The University of Michigan, Kresge Hearing Research Institute, April 15, 1993.

Transmitters in the cochlea: ATP as a neuromodulator in the organ of Corti. The University of Michigan, Kresge Hearing Research Institute, October 28, 1998.

A review of the electrophysiological evidence that nitric oxide has a role in the inner ear. Presidential Symposium, Advances in Nitric Oxide Research, Association for Research in Otolaryngology, St. Petersburg Beach Florida, February 20, 2000.