



# Cognitive Science Online

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## Column: Interview with Robert Galambos



Dr. Robert Galambos is one of the pioneers of neuro-electrophysiology whose distinguished and varied research career has made many significant contributions to our understanding of the mammalian auditory system. Dr. Galambos received his Ph.D. in Biology from Harvard University in 1941 and his M.D. from Rochester University in 1945. He worked at a number of research and academic institutions before finally settling, in 1968, at the University of California, San Diego as a founding member with R. B. Livingston and T. H. Bullock of the world's first neuroscience department. Dr. Galambos is currently professor of neurosciences emeritus at UCSD and continues to do research on animal and human visual systems at Gabor Juhasz's lab in Budapest.

The following interview was conducted by **David Groppe**.

**CSO: In your 2002 keynote lecture to the International Organization of Psychophysiology, you named four of your experiments as your favorites. Could you briefly summarize them here?**

**Dr. Galambos:** I'll try. Here they are:

1. **Bat echolocation:** The year is 1939 and Don Griffin and I are graduate students. His professor (G. W. Pierce) has just invented a device that makes ultrasonic sounds audible, and they have just used it to show that bats make sounds we cannot hear. My professor (Hallowell Davis) has just devised a laboratory method for estimating the range of sound frequencies animals can hear, and I have just used it to show an anesthetized bat ear responds to sounds at least an octave above our upper limit. At this point Don and I hang wires from the ceiling of a room and use the ultrasonic detector to show flying bats utter characteristic trains of ultrasonic cries when avoiding the wires, but blunder helplessly into them when their ears are plugged or the mouth is tied shut. Conclusion: Flying bats emit high-pitched cries and locate obstacles by perceiving the echoes (my thesis experiments).

Every aspirant neuroscientist should live through at least one experience like

ours. We did all the experiments during one year, 1939-40. Everything we predicted would happen did happen. Nothing ever went wrong. We never disagreed. We did the library work after we knew the answer and found that for 150 years, dozens of fine brains had worked hard to find it and failed; needless to say, this enhanced our self-esteem. Also, our solution was so simple, complete, and easy to understand that even school-children told the story correctly after hearing it once. Finally, after we left our joint problem, certain we had made no mistakes, we both lived long lives during which no error has ever been found, so far as I am aware.

2. **Auditory microelectrode experiments:** I was a typical busy graduate student during that 1939-40 year, dividing it into days spent with bats and days developing and using a microelectrode rig for isolating single auditory neurons in the anesthetized cat brain. In 1940, Birdsey Renshaw published from the Davis lab the first use of the microelectrode to record single mammalian brain cells in situ (they were cat hippocampus cells, his thesis problem). I overlapped him for a few months and while he was still around, and with his help, I modified his set-up, began pushing micros into the cochlear nucleus, and was promptly rewarded with auditory tuning curves and enough ancillary information to fill several publications. These data ended some century-old theoretical arguments about the hearing mechanism, and I have always been happy to have introduced, with Renshaw, this powerful physiological method still used world-wide.
3. **An infant hearing test:** Neuroscientists sometimes recognize and seize the opportunity to convert their laboratory data into a useful clinical tool. This happened to me in the 1970s. I had a lab at the San Diego Speech, Hearing, and Neurosensory Center at the time, and was searching for an objective method to estimate the hearing of babies and children. (Some doctors still dropped a bedpan on the floor to find out whether a baby was deaf.) A former post-doc, Don Jewett, sent me from San Francisco a preprint of his first report of the Auditory Brainstem Response (ABR), a computer-averaged click-evoked waveshape he and J. S. Williston extracted from the adult EEG; it visualizes the auditory nerve activity moving into and through the brainstem nuclei. During the next several years my group (mainly Kurt Hecox, Paul Despland, and Carol Schulman) described the normal and pathological infant ABR, developed it into a practical hearing and neurological test, and convinced the hospital administration to let us use it to identify the newborns with hearing loss before they leave for home. That program, initiated in 1977, was still in operation in 2002, when I last asked, and the method has become widely used in both neurology and hearing clinics for evaluating the status of patients unable or unwilling to cooperate in the conventional testing procedures.
4. **Visual experiments:** Someone once asked Clint Eastwood which of his movies he liked best. His answer was, "My last one." That's the way I feel too. Some years ago at a scientific meeting in Budapest I met Gabor Juhasz, the director of a physiology lab there, who suggested we plan some experiments together. Thanks to daily email exchanges and frequent airplane rides (one year I made three round trips), this collaboration has generated three rat visual experiments now available for downloading at the [PNAS website](#). Our most important new finding is that the retina outputs a complete neuronal analysis of the scene about three times every second; we call these volleys Retinal Functional Units, RFU, because each one contains all the what, where, and when information the retina collected during the previous fixation. We believe the human visual perceptual experience is the joint product of these approximately 300 ms RFUs, which leave the retina in an endless stream, and the cortical processing of the information those RFUs deliver.

**CSO:I've been told you have interesting views on the glia and the sources of**

## **the EEG. Can you tell us about them?**

**Dr. Galambos:** Soon after electron microscope images became available in the mid-1950s, people realized brains have three major compartments, by volume about 40% glia, 40% neurons, and 20% extra-cellular fluid. Brains store memories and mediate sensory and motor phenomena because each compartment makes its unique contribution within the bony box they share. It seems to me unreasonable to believe we will understand the mechanism of such events as the electrogenesis of the EEG, and the cognitive potentials extracted from it, by studying the 40% neuronal compartment alone. So let's have the 3-compartment model in mind as we design and perform our experiments.

That said, how well have I followed my advice? During the 1960s I made three attempts to make some headway, and failed every time. The first experiment produced antibodies to cells, including glia cells, from a particular brain region (caudate nucleus, for example), followed by injection of that antibody product into the cerebrospinal fluid of a recipient animal (cat), and the search thereafter for possible EEG and behavioral changes. Animals treated for many weeks finally showed impressive EEG and anatomical changes, but only a few behavioral ones. Our naive experiment produced nothing specific or reportable, and we gave up after six years. The experiment might be worth redoing today using the specific glia antigens modern technology might be able to produce.

My second was a glia experiment based on the finding by Newman and others that the big cell of the retina, the Muller cell, is a glial cell that generates electric currents as it maintains potassium ion homeostasis in the extracellular space. The empirical questions to be tested were: Do brain astrocytes similarly regulate extracellular K<sup>+</sup> concentration and, secondarily, produce the EEG current flow? In Budapest we enticed some chemists to make the necessary potassium electrodes and actually used a few to test for spontaneous, experimental, and stimulus-dependent K<sup>+</sup> changes on and in cat cortex. Unfortunately, it proved impossible to keep the group together long enough to collect the data needed to complete the project.

My third attempt was spawned by Charles Pomerat's time-lapse pictures showing cultured glial cells in constant motion—elongating, contracting, and migrating. My need to find out whether this goes on continuously in the normal brain was irresistible. With two engineers, I undertook to obtain time-lapse pictures of normal cat neurons and glia a few mm below the pial surface using an implanted microscope objective lens. We encountered what turned out to be insoluble optical and mechanical problems, and terminated our effort with two small published notes showing cells a few mm below the surface of dead brain and spinal cord. So far as I know, and despite the enormous technical advances of the past 40 years, time-lapse pictures of normal brain cells in situ still exist only in the imagination. I will probably never know whether my astrocytes elongate and contract when I am awake, and stop doing this when I fall asleep.

## **CSO: Do you have any advice for young researchers beginning their careers?**

**Dr. Galambos:** I do. The greatest breakthroughs in our field during the next 10-20 years are likely to come from human and behaving animal experiments designed with the 3-compartment brain model in mind. Get in line with your plan early. However, be prudent and spend at least half your time getting publishable results from experiments highly likely to yield them. I saved my three exciting but unsuccessful glia brainstorms until I was a full professor with tenure, and even then my lab kept very busy with ordinary human and animal evoked potential experiments.

## **CSO: How did you come to find the 40 Hz response here at UCSD?**

**Dr. Galambos:** When we began the infant ABR testing at Children's hospital in the 1970s we used ordinary laboratory equipment - a calibrated stimulator, a standard EEG amplifier connected to one of the big, early commercial averaging computers,

and so on. There was no single box designed to produce, process, and write out those newborn ABRs, and I thought there ought to be. My graduate students spread the word that I was looking for someone who could create it and one morning Kurt Hecox introduced me to Peter Talmachoff, a joint MD-PhD student looking for a thesis problem. Peter's undergraduate major had been physics, and before long UCSD bioengineering Professor Intaglietta and I had him designing and fabricating the instrument I had in mind. Two years later, when it was ready for testing on student volunteers, Peter asked what stimulus frequency to use. I said, "Try 40 Hz, that's what we use in the clinic." Next day he appeared with unusually large 40 Hz sinusoids in his records, which we promptly dismissed as stimulus artifact. However, more extensive measurements showed the bandpass of Peter's amplifier included more low frequencies than the clinical devices, and the 40 Hz waveshapes were real. Scott Makeig, my last graduate student, took up the problem when Peter left for his internship a few months later, and the three of us coauthored the 40 Hz paper.

At the time Peter left two commercial ABR recording instruments had been introduced. Peter's version was never brought to market, but in its time it was as accurate and useful as the best of them.

**CSO: Can you give to us more details about your current work on the visual system?**

**Dr. Galambos:** Our current visual experiments are direct descendents of the failed cortical astrocyte experiments described above. We implanted two electrodes in that chronic rat preparation, one on the cornea (which records the electroretinogram, ERG, thought by some to represent Muller cell activity), the other on the visual cortex (to record the evoked potential, VEP). In the new rats we added an optic chiasm electrode, which visualizes optic nerve volleys en route to the lateral geniculate nucleus. Visual stimuli were always delivered through LEDs glued permanently to the skull. For these latest rats our two goals, conceptually, are to study the stimulus-locked responses at the beginning, middle, and end of the anatomical visual system, and to trace the temporal succession of those events as the visual information flows from retina to cortex.

I had become disenchanted with the conventional assumption that the best way to understand the visual system is to examine it one cell at a time. Our new rat preparation makes available a normal mammalian visual system prepared to respond to stimuli under our complete control at any time of day or night, awake or asleep. During the last several years it has delivered a rich harvest of new information, the most important of which is the RFU: rat and human retinas deliver these unique, complete, detailed analyses of the scene every 300 ms or so. Another finding, a complete surprise, is that sleep reversibly modulates RFU amplitude: the mammalian retina appears to be continuously under brain control, presumably by way of the serotonin efferent fibers known to reach it from the midbrain. Still another new finding is the demonstration that the cortical VEP waveshape is the mirror image of the RFU waveshape, which means the lateral geniculate nucleus transfers its retinal input monosynaptically; we are still trying to define situations in which this is not true. Space limitations prevent listing six more unpublished findings microelectrode physiologists have failed to uncover.

These visual experiments reinforced two lessons I learned long ago. First, the key to reporting biological information not already known is to use a new animal model, new recording technique, or a new measuring instrument. Our implanted rat model that carries its own stimulators is new. The bat experiments with Griffin could not be performed until each of our professors had developed his new measurement method. And it was only because of innovations in microelectrode amplification that I was able to record from single cochlear nucleus neurons and resolved the long-standing debates.

The second old lesson is that people tend to become strongly negative if you present them with facts that challenge what they already know to be true. The RFU is such a

fact, and most people think RFUs cannot exist because current dogma has no place for them. For the first time in my life referees are rejecting my papers, and so far I have not found arguments that change their minds about our RFUs. Truth to tell, better men than I have similarly endured rejection of their scientific claims, and suffered more. Galileo was sentenced to prison for life because he insisted the earth moved around the sun, and Semmelweis, the Hungarian physician, was driven mad by the opposition to his claim that doctors with dirty hands somehow kill women they attend at childbirth. Perhaps I should be happy to find myself in such good company, and take heart from J.T. Bonner's recent remark: "If one has a finding that goes against accepted wisdom and is accordingly attacked, that often means it is an important discovery that needs time for the scientific community to get used to." So, as I wait impatiently for our colleagues to get used to RFUs, here is my final thought: May each reader of these words find himself or herself in my fix some day.

**For those interested in learning more about Dr. Galambos' research, views on neuroscience, and personal history, he has published two autobiographies.**

Galambos, R. (1992) A career retrospective. In *The Neurosciences: Paths of Discovery, II*. Samson, F. & Adelman, G. (eds.) pp. 260-280.

Galambos, R. (1996) Robert Galambos. In *The History of Neuroscience in Autobiography, Volume 1*:178-220. Society for Neuroscience.

**And the keynote address mentioned in the interview is published as well:**

Galambos, R. (2003) Four favorite experiments and why I like them. *International Journal of Psychophysiology*, 48, pp. 133-140.

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In this section of *Cognitive Science Online*, we will feature interviews with cognitive scientists. If you have suggestions for future issues please **contact the editors** . Please also feel free to interview your favorite scientists and help out with this section of the journal!