A dogged pursuit of coincidence
Philip X. Joris

You might find this additional info useful...

This article cites 10 articles, 6 of which can be accessed free at:
http://jn.physiology.org/content/96/3/969.full.html#ref-list-1

This article has been cited by 1 other HighWire hosted articles
Axonal Branching Patterns as Sources of Delay in the Mammalian Auditory Brainstem: A Re-Examination
Shotaro Karino, Philip H. Smith, Tom C. T. Yin and Philip X. Joris
[Abstract] [Full Text] [PDF]

Updated information and services including high resolution figures, can be found at:
http://jn.physiology.org/content/96/3/969.full.html

Additional material and information about Journal of Neurophysiology can be found at:
http://www.the-aps.org/publications/jn

This information is current as of March 2, 2012.
ESSAYS ON APS CLASSIC PAPERS

A dogged pursuit of coincidence

Philip X. Joris
Laboratory of Auditory Neurophysiology, Medical School, Campus Gasthuisberg, K.U.Leuven, B-3000 Leuven, Belgium

This essay looks at the historical significance or two APS papers that are freely available online:


THE MEDIAL SUPERIOR OLIVE (MSO) is a rather small binaural nucleus in the superior olivary complex of the mammalian auditory brain stem. Why is a 1969 study of this nucleus consistently listed among the most cited papers of the Journal of Neurophysiology?

In 1948, psychophysiologist Loyd Jeffress published a short proposal for the representation of interaural time differences (ITDs) by a place code in the nervous system (Jeffress 1948). ITDs arise from differences in pathlength between a sound source and the two ears and change smoothly with azimuth. They range from zero directly in front to maximal values of approximately 700 μs at the sides of the head, and can be discriminated at submillisecond values (10–20 μs). Jeffress proposed that monaural afferent neurons from both ears, which phase-lock to low-frequency sounds, converge on binaural coincidence detectors but with different neural pathlength, so that the binaural neuron experiences an “internal delay”. If the internal delay exactly compensates for the “external delay” (the ITD), the coincidence neuron receives synchronous inputs and is maximally excited. By a systematic arrangement of the difference in pathlength of the inputs from the two ears, binaural neurons systematically differ in their internal delay along one dimension of the nucleus, and thereby code for different azimuthal sound positions (Fig. 1). Thus temporal information from the monaural inputs is converted into a rate and place code. This idea was later put into a more general formal framework of crosscorrelation (Licklider 1959) and forms the basis for virtually all computational models of binaural hearing.

At the time this model was formulated, the first single-unit data of the auditory brain stem were becoming available. The MSO was a frequent target of binaural studies because it was known to be bilaterally innervated by the cochlear nucleus. Binaural sensitivity was indeed found (e.g., Moushegian et al. 1964) but a coherent view of MSO physiology had not emerged, perhaps because these studies mostly relied on transient stimuli (clicks). The first convincing demonstration of sensitivity to ITDs in sustained sounds was for single neurons in the inferior colliculus (Rose et al. 1966), which receives output from the MSO. This report was followed a couple of years later by the studies of Goldberg and Brown.

The 1969 paper by Goldberg and Brown forms a class by itself. The first reason for its longevity has little to do with binaural physiology per se. The increased use of computerized data acquisition enabled new ways of graphing and measuring spike timing (Gerstein and Kiang 1960). Of great interest in auditory physiology was the quantification of phase-locking, and a satisfactory metric had not yet been found (Rose et al. 1967). Goldberg and Brown introduced “vector strength”, which has been the standard since. Each spike is represented by a vector with unit length and phase equal to the stimulus phase at the spike’s time of occurrence (Fig. 2A). Vectorial addition of all spikes and normalization of the resultant vector by the total number of spikes yields the vector strength. It is mathematically equivalent to the normalized Fourier component at the stimulus frequency. The Goldberg and Brown paper is strikingly innovative in introducing many other new metrics and analyses. With the benefit of hindsight, vector strength seems almost obvious, but it was clearly the result of careful thought on how to best summarize response dimensions with a single number.

Another reason why this paper is so influential is its sizable number of ITD-sensitive neurons recorded in the superior olivary complex. Previous investigators had experienced difficulty in obtaining MSO recordings in the cat – a difficulty that has been confirmed in many studies since and which may be tied to cellular function (Scott et al. 2005). Recorded extracellularly, MSO action potentials are small and difficult to discriminate from the very strong field potentials generated by the phase-locked inputs. Goldberg and Brown turned to the dog, which has a larger MSO than the cat. In a combined anatom-
ical/physiological study (Goldberg and Brown 1968), they first described the basic connectivity, binaural response types, and field potentials of the dog MSO. The subsequent 1969 paper built on this knowledge to study binaural sensitivity of this region in detail.

What makes the 1969 study a landmark paper, more than the number of neurons, is the simplicity and elegance of the binaural tests and the coherent picture that emerged. MSO neurons showed clear modulation in average discharge rate to tones played through earphones at different ITDs. The “most favorable ITD”, i.e., the ITD at which the maximal response was obtained, did not seem to depend on stimulus intensity. Moreover, by comparing ITD functions with monaural responses, Goldberg and Brown provided the first evidence of MSO neurons functioning as coincidence detectors. The test they devised is illustrated in Fig. 2. This MSO neuron shows clear sensitivity to ITDs of a binaural 1000 Hz tone (Fig. 2B). The response is maximal for a small (approximately 100 μs) lead of the stimulus to the contralateral ear. At this “most favorable ITD” the response far exceeds the responses to monaural stimulation, obtained by presenting the same stimulus only at the ipsilateral or contralateral ear. Examination of the phase of these monaural responses (Fig. 2A) shows that the response to ipsilateral stimulation leads the response to contralateral stimulation by about 0.15 cycles of the 1000 Hz stimulus, or 150 μs. This predicts that maximal coincidence of the inputs will be obtained when the stimulus to the ipsilateral is delayed by approximately 150 μs, which is indeed close to the actual “most favorable ITD” observed (Fig. 2B).

The vector strength, ITD-sensitivity, and coincidence analysis constitute only about a third of Goldberg and Brown’s paper, which contains many other gems. Reading the paper today, one is struck not only by the amount of data and elegance of the analysis, but also by the breadth and completeness of the study, the careful phrasing and reasoning, and overall the “modern feel” of the paper. Subsequent to this work, both authors left the auditory field and pursued very productive careers studying the vestibular and somatosensory system, respectively. Jay Goldberg’s seminal studies of the vestibular system, with César Fernández, are featured in another essay (Angelaki 2005). Over the subsequent years scattered reports on MSO physiology appeared but it took more than 20 yr before completion of a study that went beyond the groundwork laid by Goldberg and Brown.

Remarkably, the other most cited auditory study of the Journal is another study of the MSO (Yin and Chan 1990). These authors recorded from 39 histologically confirmed neurons in the MSO of the cat, and made several observations which constituted a conceptual advance to the paper of Goldberg and Brown. First, by widening the stimulus arsenal, they did not only test for coincidence detection but also for its more general formulation of crosscorrelation (Licklider 1959). Pure tones are deterministic stimuli that are rare in natural environments. If a pure tone is

![Figure 1](jn.physiology.org)  
*Fig. 1.* Goldberg and Brown’s illustration of Jeffress’ place theory. The axonal length of the inputs differs for MSO neurons (numbered 1 through 7) at different positions in the nucleus. Interestingly, this schematic deviates from Jeffress’ original proposal, which posited delay lines in branches of individual axons, rather than across axons.

![Figure 2](jn.physiology.org)  
*Fig. 2.* Goldberg and Brown’s (1969) test of coincidence detection, illustrated for an MSO neuron from the study by Yin and Chan (1990). A: monaural responses to a 1000 Hz ipsi- and contralateral tone. Instantaneous discharge rate is graphed as a function of stimulus phase. Circles indicate 60 spikes/s and phase in degrees. Average phases are 0.02 cycle (ipsi) and 0.87 cycle (contra). B: sensitivity to ITDs of the same tones. Waveforms schematically indicate ITDs at which the stimuli are in-phase (vertical dashed lines) and out-of-phase. Average response rates to monaural stimuli are shown with horizontal lines and were very similar for the two ears.
broadcast through a free-field speaker, the waveforms at the two ears can only differ in their amplitude and phase. Natural stimuli however can also differ at the two ears in their waveform statistics, to which humans are exceedingly sensitive. Thus the sensitivity to temporal differences between the ears not only subserves locating sound sources in space, but also detection of signals in acoustically cluttered environments. There are many similarities here to the visual system, where sensitivity to binocular disparities not only subserves depth perception but also the breaking of camouflage. Yin and Chan showed that MSO neurons exhibit ITD-sensitivity to broadband noise; that major features of this sensitivity can be predicted from a linear summation of the responses to tones and that it is absent for uncorrelated stimuli; and that a count (by computer) of coincidences in spiketrains to monaural stimulation captures the essential features of the actual binaural response. They also showed that the ITD-sensitivity of MSO extends to high-frequency amplitude-modulated stimuli. Finally, they were the first (and the only ones, to this day) to test the core prediction of the Jeffress model in the mammal: the presence of a place map. Goldberg and Brown provided solid evidence for the transformation of a temporal code (phase-locking in the monaural afferents) into a rate code (firing rate of MSO neurons), but they did not examine whether there is a systematic organization, in neural space, of the tuning to ITDs. This requires sampling of MSO activity at different spatial locations in the nucleus, a tedious task because of the recording difficulties already mentioned. Yin and Chan pooled data from several animals in which MSO recordings were obtained at different antero-posterior MSO positions, and observed indeed a correlation between the placement of the peaks in the ITD curves and the cell’s anatomical location. Moreover, the spatial gradient they observed was consistent with anatomical evidence for delay lines, subsequently described by Yin and colleagues.

We return to the question why these two MSO studies are the most highly cited studies of the auditory system among the many published in the *Journal of Neurophysiology*. The nature of ITD coding in mammals is currently a subject of much controversy, fueled by an abundance of recordings in the inferior colliculus and a paucity of MSO recordings (Palmer and Kuwada 2005). The studies by Goldberg and Brown, and Yin and Chan, stand out as full-length, quantitative, innovative studies of a structure from which it is difficult to obtain electrophysiological data. In addition, examination of the studies that cite these manuscripts shows that these classic papers have a wider relevance than to binaural physiology. Binaural time sensitivity is the premier illustration of submillisecond temporal processing in mammals, including humans. Such processing may be important for other perceptual attributes, e.g., pitch, and provides one example how a neural assembly may perform an operation as intricate as a crosscorrelation. The studies of Goldberg and Brown, and Yin and Chan, provided seminal tools, data, and concepts, (plus also some discrepancies!), not only for the field of binaural hearing, but for the study of neural temporal processing in general.
REFERENCES


