References and Notes

- 1. E. K. Gallin and J. I. Gallin, J. Cell Biol. 75, 277
- (1977)2. E. K. Gallin and D. R. Livingood, *ibid.* 85, 160 (1980).
- (1980).
 3. E. K. Gallin, Science 214, 458 (1981); J. J. Cole, F. V. McCann, P. M. Guyre, Fed. Proc. Fed. Am. Soc. Exp. Biol. 41, 1616 (1982).
 4. J. H. Passwell, J-M. Dayer, E. Merler, J. Immu-123, 115 (1970).
- H. Fassweit, J.-M. Dayer, E. Merler, J. Iminu-nol. 123, 115 (1979).
 L. T. Yam, C. Y. Li, W. H. Crosby, Am. J. Clin. Pathol. 55, 283 (1971).
 G. Valet, H. L. Jenssen, M. Krefft, G. Ruhen-stroth-Bauer, Blut 42, 397 (1981).
 J. Koester and J. H. Byren, Cold Spring Harbor D. Koester and J. H. Byren, Cold Spring Harbor
- Reports in the Neurosciences (Cold Spring Harbor Laboratories, Cold Spring Harbor, N.Y., 1980), vol. 1.
- 8. E. K. Gallin, M. L. Wiederhold, P. E. Lipsky,

A. S. Rosenthal, J. Cell. Physiol. 86, 653 (1975).
S. L. Newman, R. A. Musson, P. M. Henson, J.

- S. L. Newman, K. A. Musson, P. M. Henson, J. Immunol. 125, 2236 (1980).
 D. Wuest, R. Crane, J. J. Rinehart, J. Reticu-loendothel. Soc. 30, 147 (1981).
 P. M. Guyre, G. Crabtree, J. Bodwell, A. Munck, J. Immunol. 126, 666 (1981).
 G. Meuret, J. Bammert, G. Hoffman, Blood 44, 801 (1974); D. M. Whitelaw, Cell Tissue Kinet. 5 311 (1972)
- 5, 311 (1972). 13. We thank W. Parker, Dartmouth-Hitchcock
- Medical Center, for providing human alveolar cells. Supported by NIH grants BRSG05392 (to F.V.M.), CA17323, and AM0535, P.M.G. received partial support from the Kroc Foundation.
- Present address: Medical Department, Brookhaven National Laboratories, Upton, N.Y. 11973.
- 13 May 1982; revised 5 October 1982

Two-Component Hearing Sensations Produced by Two-Electrode Stimulation in the Cochlea of a Deaf Patient

Abstract. Dissimilarities in perception elicited by stimulation with two electrodes were estimated. A two-dimensional spatial configuration was found to be suitable to represent the dissimilarity data, and the two dimensions could be interpreted as corresponding to the position of the apical and basal electrode of the two-electrode combination. A speech-processing strategy that converts acoustic, first and second formants to two-electrode stimulation is proposed.

Previous speech studies in a number of research centers have shown that useful speech information could be presented to deaf patients by electrical stimulation of the residual auditory nerve fibers with the use of single- or multiple-electrode prostheses implanted in the cochlea (1-4). In our laboratory, electrical stimulation was produced by electrodes implanted in the scala tympani of the human cochlea, and a speech-processing strategy was formulated on the basis of psychophysical information obtained from our patients (5, 6). In the speechprocessing strategy currently used by our patients with multiple-electrode cochlear implants, fundamental frequency of voicing is converted to the repetition rate of electric pulses delivered to the electrodes, and the second formant frequency of speech is converted to electrode position. Only one electrode is activated during a stimulus period (inverse of repetition rate).

There are four major psychophysical observations (5, 6) that support this speech-processing strategy: (i) individual electrodes produced pitch sensations in accordance with the tonotopic organization of the cochlea, (ii) pitch increased with repetition rate, (iii) the pitch sensations produced by repetition rate and the electrode position are perceived separately in the same way as Plomp (7) described for acoustic fundamental rate and single formant frequency, and (iv) the auditory system was able to discriminate short duration electrode transitions but not short transitions of electric repetition rate. Electrode transitions are therefore suitable for encoding the rapidly changing segmental speech information contained in the second formant frequency, and transitions of electric repetition rate are more suitable for encoding the slowly time-varying suprasegmental information contained in the fundamental frequency.

We investigated the possibility that, in addition to the fundamental and second formant frequencies, activation of an additional electrode during a stimulus period would present further speech information such as the first formant frequen-



Fig. 1. Two-dimensional configuration representing the dissimilarities among the ten twoelectrode stimuli: spatial configuration obtained by multidimensional scaling on the left half, and the stimulus matrix showing correspondence between the alphabetical symbols and the electrode pairs on the right.

cy (8, 9). The subject (MC1), a 50-yearold male who suffered from total hearing loss after a car accident, was our first cochlear implant patient. Pure-tone and speech audiometry, both under headphones and in a monitored sound field, had elicited no hearing responses in either of his ears for acoustic stimuli at the maximum output levels of the audiometers, and evaluation showed that this patient received no benefit from a conventional hearing aid (4).

In the implant operation (4), an array of ten electrodes was inserted through an opening in the round window membrane for a distance of 15 mm around the scala tympani. The electrodes were numbered from 0 to 9 in the apical to basal direction. These electrodes, spaced 1.5 mm apart, were driven by an implanted receiver stimulator. Residual auditory nerve fibers were activated by biphasic current pulses with each phase fixed at 180 µsec.

For this study, pulse trains 300 msec in duration with 50 msec rise-decay times were used. The current levels for a twoelectrode stimulus were chosen so that the loudness produced by each electrode in isolation was approximately the same. The pulse trains delivered to the electrode pair were at the same repetition rate, with the pulses on the more apical electrode leading by 0.5 msec. There was, therefore, no temporal overlap between pulses on the two electrodes. This is necessary because it is difficult to balance the loudness contributions of the two electrodes from overlapping pulses due to current summation in the cochlea.

The perceptual dissimilarities among ten two-electrode stimuli were estimated by triadic comparisons (7). The ten electrode pairs were: 1-2, 1-4, 1-6, 1-8, 2-4, 2-6, 2-8, 4-6, 4-8, and 6-8. The repetition rate was 166 repetitions per second, and loudness was balanced across the ten stimuli. Three stimuli chosen in random order were presented to the patient, and he was asked to judge which two stimuli from the triad were the most similar and which two were the least similar. A dissimilarity value of 2 was assigned to the least similar, 0 to the most similar, and 1 to the remaining combination of two stimuli. A matrix of dissimilarity values was constructed for the ten stimuli after the presentation of all possible triads. Three matrices obtained in separate sessions were combined, and the resulting matrix was analyzed by a nonmetric multidimensional scaling (MDS) procedure (10) for distance functions specified by Minkowski coefficients

ranging from 0.3 to 2. In the analysis dissimilarity values in the matrix are transformed to distances between stimuli in a spatial configuration because the relationship between dissimilarity and distance is assumed to be monotonicthat is, similar stimuli are close together and very different ones are far apart. MDS searches for the spatial configuration and the monotonic relationship that minimize a criterion function known as "stress."

The two-dimensional configuration for the ten stimuli with Minkowski coefficient 0.5 and the correspondence between the alphabetical symbols and the electrode pairs are shown in Fig. 1. The Minkowski coefficient 0.5 in the range 0.3 to 2 corresponds to minimum stress among the two-dimensional configurations. A two-dimensional configuration was considered suitable because the stress (8.4 percent) was much smaller than that for one dimension (27 percent). The two-dimensional configurations with other Minkowski coefficients followed closely the configuration as depicted in Fig. 1, and the difference in stress values between one and two dimensions was also similar.

The close resemblance between the two configurations of the alphabets in the left and right panels in Fig. 1 indicates that the axes of the two-dimensional configuration can be interpreted as corresponding to the position of the more apical electrode and the more basal electrode of the two-electrode combination. A Minkowski coefficient of 0.5 implies that the dissimilarities between two electrode pairs differing in both apical and basal electrodes is even greater than the sum of the two component dissimilarities. These results suggest that twoelectrode stimulation was perceived as a sensation with two components and may therefore be used to present speech information with two components, such as the first and second formants. The two axes for electrical stimulation in Fig. 1 parallel those corresponding to the first and second formant frequencies in the analysis of acoustic vowel confusion by MDS (11). If a one-dimensional configuration had been acceptable, this would have indicated that the sensation produced by two-electrode stimulation would not be able to convey information with two components.

The results indicate that, in addition to the presentation of the second formant by activation of only one electrode during a stimulus period in a speech processor, as described by Tong et al. (5), speech information such as the first formant may be presented to implant patients by two-electrode stimulation. The speech information related to the fundamental frequency of speech, on the other hand, can be encoded in electric repetition rate as in the speech processor. This was shown to be feasible (9) because the discriminability of repetition rate for two-electrode stimulation was as good as or better than that for single-electrode stimulation. Finally, we should note that the electric pulse trains used in this study, although adequate in generating two-component sensations, may not be the optimal stimulus configuration for use in a speech processor with two-electrode stimulation. Differences in the perceptual characteristics produced by electric stimulus configurations that differ both in the order of occurrence and the amount of delay between the two apical and basal electrodes are not yet known. Y. C. TONG

R. C. DOWELL P. J. BLAMEY G. M. CLARK

Department of Otolaryngology, University of Melbourne, Parkville, Victoria 3052, Australia

References and Notes

- 1. For summary of results from various centers see the abstracts and papers in *Proceedings of the International Cochlear Implant Conference*, (New York Academy of Sciences, New York, April 1982).
- F. B. Simmons, J. M. Epley, R. C. Lummis, N. 2 Guttman, L. S. Frishkopf, L. D Zwicker, *Science* **148**, 104 (1965). D. Harmon, E.
- Zwicker, Science 148, 104 (1965).
 Y. C. Tong, G. M. Clark, R. C. Dowell, L. F. A. Martin, P. M. Seligman, J. F. Patrick, Acta Oto-Laryngol. 92, 193 (1981).
 G. M. Clark, Y. C. Tong, L. F. A. Martin, Laryngoscope 91, 628 (1981).
 Y. C. Tong, G. M. Clark, P. J. Blamey, P. A. Busby, R. C. Dowell, J. Acoust. Soc. Am. 71, 152 (1982).
 Y. C. Tong, P. I. Blamey, R. C. Dowell, G. M.

- Y. C. Tong, P. J. Blamey, R. C. Dowell, G. M. Clark, paper presented at the 102nd meeting of the Acoustical Society of America, December 1981.
- 7.
- R. Plomp, Aspects of Tone Sensation (Academic Press, London, 1976), p. 109.
 R. C. Dowell, Y. C. Tong, P. J. Blamey, G. M. Clark, paper presented at the 102nd meeting of 8. the Acoustical Society of America, December
- Y. C. Tong and G. M. Clark, in *Proceedings of* the International Cochlear Implant Conference 9. the International Cochlear Implant Conference (New York Academy of Sciences, New York, April 1982).
 10. J. B. Kruskal, Psychometrika 29, 1 (1964).
 11. R. N. Shepherd, in Human Communication: A Unified View, E. E. David and P. B. Denes, Eds. (McGraw-Hill, New York, 1972).
 12. Supported by the National Health and Medical Research Council of Australia the Department
- Research Council of Australia, the Department of Science and Technology of Australia, the Channel 10 Deafness Appeal, the Deafness Foundation of Victoria, and the Lions Interna-

13 May 1982; revised 9 August 1982

Virus Infection of Culturable Chlorella-Like Algae and **Development of a Plaque Assay**

Abstract. Four distinct viruses with double-stranded DNA are known to replicate in Chlorella-like algae symbiotic with hydras and paramecia. An attempt was made to infect a number of cultured Chlorella strains derived from invertebrate hosts with these viruses. One of the viruses, PBCV-1, replicated in two of the algal strains. Restriction endonuclease analysis of the viral DNA showed that the infectious progeny virus was identical to the input virus; thus, Koch's postulates were fulfilled. Viral infection of the two Chlorella strains has allowed the large-scale production of a eukaryotic algal virus and the development of a plaque assay for the virus.

Although viruses that infect cyanobacteria (blue-green algae) have been studied extensively (1), little is known about viruses of eukaryotic algae (1, 2). Most viruses or virus-like particles in eukaryotic algae have been detected by ultrastructural studies, and only a few attempts (3) have been made to characterize these particles because the viruses are difficult to obtain in sufficient quantity. Several factors contribute to this lack of material: (i) usually only a few algal cells contain particles, (ii) usually the cells contain particles in only one stage of the life cycle, (iii) the cells that have particles may not lyse, and (iv) the particles may not be infectious. Consequently, finding a culturable eukaryotic alga that can be synchronously and efficiently infected with a virus would provide an opportunity to study a new type of virushost relationship.

We recently identified and partially characterized four distinct viruses with double-stranded DNA that replicate in Chlorella-like green algae symbiotic with hydras or paramecia (4, 5). These virusdesignated HVCV-1, HVCV-2, es. HVCV-3 (from Hydra viridis Chlorella), and PBCV-1 (from Paramecium bursaria *Chlorella*), first appear in the algae a few hours after the algae are isolated from their hosts. Within 24 hours most of the algae are lysed. The source of the viruses is unknown, but we have found them in all symbiotic algae from hydras and paramecia that we have examined. The viruses may be latent in some or all of the algae as long as the latter remain in a symbiotic relationship with their host (4, 5). Removing the algae from their host may induce the viruses to enter a lytic phase. Regardless of the source of the viruses, their appearance usually pre-