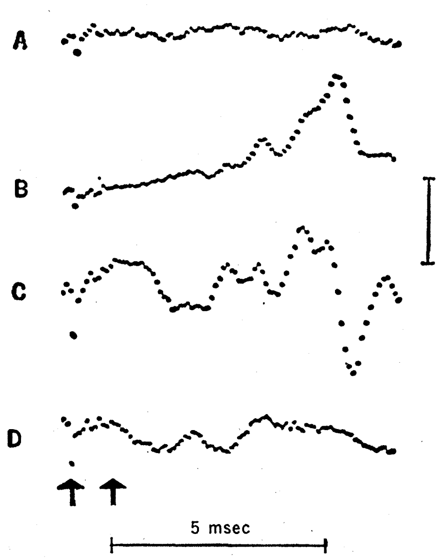

Fig. 2. Recordings from same subject as in Fig. 1D, at 75-db sensation level. (A) Vertex-neck with ears plugged. (B) Vertex-neck recorded at bandpass at 10 hz to 2 khz. (C) Vertex-wrist. (D) Neck-wrist. Vertical calibrations: A, C, D, 0.5 μv; B, 1.1 μv.

and D), and was usually a negative wave with a peak latency of about 2.4 msec from the arrival of the stimulus at the ear. When allowance is made for intensity and air conduction time, this wave has about the same peak latency as the second wave of Yoshie *et al.* (*1*) recorded from the external ear canal. This latency is so short as to strongly suggest that the potential is generated in the brain stem. In anesthetized cats, Jewett (*4*) has shown that a volume-conducted positive potential recorded at the scalp, but synchronous in time with N_2 recorded at the round window, is generated in the vicinity of the cochlear nucleus. If this is analogous to the first negative wave in the human record, then subsequent waves may indicate sequential contributions from successive neurons, as they do in the cat (*4*). While it may thus be possible to associate a given wave with activity in a distinct portion of the auditory system, it seems unlikely that any but the earliest of the waves will represent exclusively the activity of specific nuclei or tracts; potentials from both ascending and descending fibers can occur simultaneously, and postsynaptic slow waves can have durations extending over the time of several waves (*4*). We wish to defer the labeling of the waves until a nomenclature based upon some clearly defined reference point (such as N_1) can be developed.

The evoked potentials of Fig. 1 were obtained by means of a bandpass filter which effectively reduced the EEG "noise" at the input to the TDH-9. This filtering makes direct interpretation of the potential difficult, owing to the differentiating property of the filter and the phase-lead introduced. Recordings made without the filter (bandpass 10 hz to 2 khz) showed that all of the waves, except possibly the first, were positive at the vertex with respect to the neck (Fig. 2B). The positivity is consistent with the interpretation that these waves are generated, at least in part, by action potentials traveling toward the vertex (*4*).

The contribution of the neck reference to the waveform was studied by recording vertex-wrist and neck-wrist (Fig. 2, C and D). Neck-wrist recordings showed none of the later waves, but may have shown the first wave (Fig. 2D); however, the electrocardiographic artifact caused variability in the waveform of a similar magnitude. Simultaneous recordings will be necessary to determine the potential distribution of this initial wave. Some workers (*7*) have offered evidence that, under certain conditions, evoked responses to very intense auditory stimulation may be generated by the musculature of the head, particularly the neck. Three lines of evidence argue against such an origin for the potentials described in this report: (i) neck-wrist recordings do not show the waves as would be expected if the generators were in the neck; (ii) the potentials were recorded with sensation levels of 65 db (Fig. 1E), much lower than the reported threshold for the muscular response (*4*); (iii) the latency of the earliest wave is so short that, given conduction velocities and lengths comparable to that of the auditory nerve plus synaptic delay, there is insufficient time for impulses to leave the skull. Electromyogenic potentials in the middle ear muscles have a latency of about 10 msec with intense stimulation (*8*), so they are unlikely to be the generator of any of the waves reported here.

When the click intensity was reduced, the response showed an increased latency (Fig. 1E), as has been reported for the auditory nerve response N_1 (*1*). Since the latency of the later waves was increased only by the same amount as the early waves, it would appear that this effect on latency is less prominent in later synapses. It is also evident (Fig. 1E) that a decrease in stimulus intensity changes the waveshape and lowers the size of the early waves while the later biphasic wave remains at about the same magnitude.

DON L. JEWETT
MICHAEL N. ROMANO
JOHN S. WILLISTON
Departments of Physiology and Neurosurgery, University of California Medical Center, San Francisco 94122

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Denver Earthquakes

Simon (*1*) states in her abstract that "it appears unnecessary to explain the Denver earthquakes in terms of pressure induced by the introduction of waste fluid." In the light of the data that she presents, such a statement is unwarranted and extremely misleading. As she has concluded, her data do indicate that present-day broad patterns of seismicity in Colorado agree with those deduced from historical records, and that there was therefore some degree of tectonic strain in basement rocks of the Denver area prior to the injection of waste fluids at the Rocky Mountain Arsenal well. But her data also indicate that very numerous (1698 of magnitude $\gtrsim 1$ over the period from 1962 to 1968) earthquakes in the Denver area *began* at the time waste fluid was first injected at the Arsenal well. This frequency of seismic events and the resultant concentration of energy release are not in accord with historical records. In addition, Simon cites pumping tests conducted by Army Engineers in 1968 in which an attempt to withdraw fluids from the well resulted in numerous small shocks. Simon's data in effect substantiate the work of Evans (*2*) and

Healy *et al.* (*3*), who attempted to show that the Denver earthquakes are the result of waste fluid pressures acting in conjunction with a preexisting system of tectonic stress in the basement rocks. In other words, waste fluid pressures appear to have been a *necessary* element in the initiation of the Denver earthquakes.

EDWIN KARP
Department of Geology, New York University, New York 10003

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Three points to be emphasized in answer to the remarks of Karp are:

1) No seismograph stations with sensitive, matched, short-period instruments existed near Denver to record very small earthquakes there from the time of the largest felt shock in 1882 (*1*) until the Colorado School of Mines opened its observatory (GOL) in January 1962. The first Denver earthquake was recorded only 4 months after that.

2) The smallest earthquakes (magnitude $\gtrsim 1.0$) have always occurred quite near the wellhead on the Rocky Mountain Arsenal grounds. The larger earthquakes extend from slightly south of the well along a line 10 km to the northwest. The southern line of epicenters is sharply delineated whereas the northern boundary is diffuse (*2*).

3) There were three shocks of magnitude $\gtrsim 5.0$ in 1967, more than a year *after* termination of fluid injection. These larger shocks continue to date, 3 years after closing the well. In 1969 there have been two shocks of magnitude 3.5, with 14 more, greater than magnitude 2.5, felt by residents of the area.

The tectonic strains under northeast Denver are more apt to be the cause of the earthquakes now, as in the past, than fluid pressure which has not increased, but which has actually been decreasing, over the last 3 years (*3*).

RUTH B. SIMON
Department of Geophysics, Colorado School of Mines, Golden 80401

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19 December 1969

Allelic Form of Enzymes

Those of us who work on allelic form of enzymes in natural populations are often faced with the problem of distinguishing various hypotheses about the genetics of these enzymes. It is sometimes rather difficult to distinguish multiple protein forms produced by one locus from the results of two or more loci especially when these loci may be evolutionary duplications of each other and closely linked. An interesting case that has arisen concerns alcohol dehydrogenase in maize. Here on electrophoretic gels there are two separate systems of bands with a fast and slow form for each system. In addition, the second system shows in crosses between the fast and slow form an intermediate or hybrid band as well as the two parental bands. Two alternative explanations have been offered for these observations; one by Schwartz (*1*) proposes the two sets are the products of one genetic locus but that there is a second locus that codes for an enzymetically inactive polypeptide that interacts with the products of the first locus to produce the two different sets. An alternative explanation is given by Scandalios (*2*) who suggests that there are two loci, one responsible for the first set of bands and the second for the other. These two hypotheses both need to explain one overriding fact and that is that, in virtually every individual looked at, the fast band of the first set is accompanied by the fast band of the second set, and the slow band of the first set by the slow band of the second set with individuals heterozygous for the first set also being heterozygous for the second set. This virtually perfect association between the two systems leads Schwartz to his hypothesis and is met by Scandalios' extra assumption that the two loci that he postulates are very closely linked and out of random association with each other.

In order to test this hypothesis, Scandalios has looked for crossovers whose occurrence would tend to support his view, and in the paper just cited he presents three recombinant kernels out of a total of 20,124 kernels resulting from the selfing of F_1 plants between the fast and the slow varieties. The occurrence of these recombinants is then offered as proof of Scandalios' two closely linked genes hypothesis. Whereas I cannot distinguish the two hypotheses on the basis of the evidence so far presented, it is the purpose of this note to point out that the evidence presented by Scandalios does not in fact support the two closely linked genes hypothesis. Since there are only three so-called recombinants out of 20,000, the genes are indeed very closely linked. But two of the three exceptions are, under his hypothesis, homozygous for a recombinant chromosome. Since these are F_2 plants, it must mean that an identical rare recombinant occurred both in the sperm nucleus of the pollen and the egg nucleus that formed these kernels. Moreover, this rare double event must have occurred twice, once for each case. The chance of either one of these kernels appearing is quite small, and the chance that two of the three kernels would be of this form is vanishingly small. Alternative hypotheses might be a crossover in either pollen or ovule and a deletion or a mutation in the other nucleus involved in the union. But, again, there are impossibly rare occurrences. Whatever the source of the exceptional kernels that Scandalios reports, recombination between two closely linked genes is terribly unlikely.

R. C. LEWONTIN
Department of Biology, University of Chicago, Chicago, Illinois 60637

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Whereas I appreciate Lewontin's comments, he does not say more than that alternative explanations may be possible for the alcohol dehydrogenase (ADH) recombinants in maize, which I have recovered (*1*). The main point of my note was that the electrophoretically fast and slow variants of the two zones of ADH activities in maize are not associated without exception. The explanation Lewontin thinks I have proposed may be "terribly unlikely" and the association may be "virtually perfect" but it is not perfect. That is the fact. The occurrence of such recombinant types is compatible with my hypothesis.

In addition, I would like to point out that I did not speak of the "frequency of occurrence," but rather of the "frequency of recovery of the aberrant types." This distinction was made to allow for other, more physiological, explanations for the small number of aberrants we see and may not reflect the true frequency of the recombinational events. We are dealing with biologically active molecules that are close