scene with the viewers on there was a little, but not much, more color; (iv) when the head was tilted through a 45 degree arc the colors became much more saturated [A typical remark at this stage was: "The colors have come back again".]; (v) all observers, when looking at the "red" image in one eye and the "white" image in the other, chose to have a neutral density filter, varying from 0.7 to 1.1, put over the short record projector in addition to the 0.4 neutral density filter which was already there. The 0.4 neutral density filter was the one which produced the best variety of color without the viewers; (vi) this additional neutral density filter reduced the range of color seen without the viewers. In spite of this the colors were still much more evident with the head held at a 45 degree angle than with the head held horizontal.

In the second experiment four transparencies were used, two identical transparencies being placed side by side in each projector (see Fig. 1). Both transparencies in the long record "red" projector were polarized vertically, while those in the short record "white" projector were polarized horizontally. Both pairs of records were registered on the nondepolarizing screen, but where the right-hand picture appeared the screen was covered with a white card to depolarize the light. The observer's viewer contained two polarizers, one oriented vertically before one eye and the other oriented horizontally before the other eye. As long as the observer held his head horizontal both eyes saw both records in the picture on the white card; and each eye saw only one record in the light which was registered on the nondepolarizing screen.

Six observers were asked to look at the two doubly lighted screen areas and compare them, being careful to keep their heads horizontal. The observers were placed so that the two pictures appeared to be the same in brightness to the naked eye. To start with, the neutral density filter over the "white" projector was 0.4, the one most commonly used to give the best variety of color. All six observers found the left-hand picture to be colorless compared with the right-hand picture. Objects which were green, pink, yellow, and blue on the right were gray on the left; objects which were red on the right were black or reddish on the left. In fact, the left-hand picture was almost completely red and gray, whereas the right-hand picture had quite a variety of color in it.

The neutral density filter over the "white" projector was then varied, and the observer was asked to pick the one that made the two images look most nearly alike. Three of the observers chose a density of 1.0; one, 0.7; one, 1.1; and one, 1.3. At this stage the two images still looked different. Some of the cool objects looked green in the left-hand picture, but the green was unsaturated compared with that in the right-hand picture. Some pink objects looked the same in both pictures. Two objects which looked respectively orange and red in the right-hand picture could not be distinguished from each other in the left-hand picture.

Throughout the experiment there was lustre in the left-hand picture; it was never seen in the right-hand picture. Accompanying the lustre in three objects which had different densities in the two component light patterns was an alternation of color which was a form of binocular rivalry. For example, an object in the left-hand picture which was light and red for one eye, and black for the other, would appear red at one moment and black the next. The colors in these objects on the left half of the screen obviously could not match the colors on the right side permanently, since two separate colors were seen at different times in the left-hand picture of the objects, and only one color was seen in the right-hand counterpart. The most impressive part of the demonstration was that the colors in the left-hand picture which did not show rivalry (that is, those colors which did "fuse") were not a very close match either. It is well known that one does not obtain identical colors from a binocular combination of monocular stimuli and from physical mixture of the same two stimuli on one retina when uniform fields of the two stimuli are used.

From the results reported here, we are forced to disagree with Geschwind and Segal, and with Pastore, and to say that the results obtained when a "red" image is presented to one eye and a "white" image is presented to the other are not the same as those obtained when both images are combined on the same retina, either in one eye or in both (*6*). We have not performed enough experiments to know whether a "red" image presented to one eye and a "white" image presented to the other, at one particular relative brightness value, can be made to look like both images presented to both eyes at another particular relative brightness value. Even if this should occur, we could not agree with Pastore's statement that "Land's major results can be obtained stereoscopically" (*7*). Our experience suggests that one would have to have a remarkably colorless subject in the case where both wavelength components are presented to both eyes, if this were to match the case where one wavelength component is presented to one eye and the other wavelength component to the other eye. Nor can we agree that these experiments provide any support for the claim that the colors are formed after cerebral fusion of information from the two eyes. It is entirely possible that they are formed instead in the retina or in the lateral geniculate body.

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References and Notes

1. E. H. Land, *Proc. Nat. Acad. Sci. U.S.* **45**, 115, 636 (1959).
2. Color names can be used in two senses—to describe a sensation or to describe a correlate of bands of wavelengths. In this paper, to avoid confusion, quotation marks have been used whenever a color name is used in the latter sense.
3. N. Geschwind and J. R. Segal, *Science* **131**, 608 (1960).
4. N. Pastore, *ibid.* **131**, 1400 (1960).
5. E. H. Land and W. A. Hunt, *ibid.* **83**, 309 (1936).
6. In a recent letter, Hayward appears to have come to the same conclusion as Geschwind, Segal, and Pastore: see R. Hayward *J. Opt. Soc. Amer.* **52**, 226 (1962).
7. When these experiments are performed with "red" light and "green" light, and with other light combinations, the results seem to be slightly different.

30 August 1962

A Theory of Middle Ear Muscle Function at Moderate Sound Levels

Abstract. The minor amplitude modulations of auditory input, which are introduced by the middle ear muscle acoustic reflex at moderate and low sound intensities in the cat, may contribute significantly to signal analysis or attention mechanisms of the auditory system.

To anyone who has pursed his lips and emitted a high-pitched squeak in the vicinity of a cat, whether somnolescent or ambling along in cat-like pursuits, the participation of the peripheral auditory system in the animal's orientating response is immediately evident—the outward twitch of the pinna, the abrupt halt in ongoing activity . . . the pause . . . then relaxation and resumption of whatever came before, unless the stimulus be repeated. In addition to the reaction of the pinna, the muscles

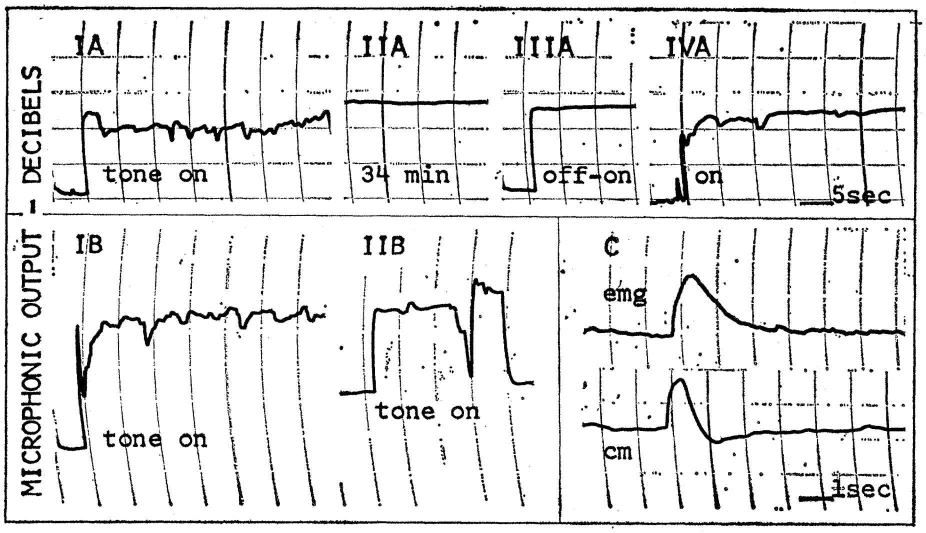

Fig. 1. Middle-ear-muscle-altered cochlear microphonic (CM) amplitudes for a 1-kcy/-sec tone (*A, B*). *A* and I*B* were closed field, restrained environments; II*B* was open field, unrestrained; *C* was open field, restrained. The top trace in *C* is a rectified, integrated electromyogram (EMG) from the contralateral stapedius. For CM's, a horizontal chart division equals 7.5 db (relative to about 1 μv).

of the middle ear participate in the response, greeting the onset of the sound with an initial twitch contraction, and then reduction of auditory input occurs. This attenuation of sound transmission presents somewhat of an enigma to those who feel that orienting responses are an organism's attempt to bring its nervous system into focus on the initial stimulus. For this case, in the auditory system one might predict that this is best accomplished by allowing more sound, not less, to enter for processing, unless, of course, more information can be obtained, or processed, by amplitude modulation of the ensuing signal than would be lost in sensitivity. It is our purpose to advance this conjecture.

It is well known that contractions and relaxations of the middle ear muscles do amplitude-modulate sound transmission through the middle ear. As sound intensity increases, muscle contractions become stronger, thus increasing attenuation. In the past, the nature of the response occurring with rather loud sound has emphasized the reflex's role in protection of the cochlea from sound damage (*1*). In addition, however, at less intense stimulus levels which produce orienting responses, such as we have considered, muscle contractions still occur. Sound attenuation still results, but the critical parameters are altered to emphasize stimulus novelty and habituation. As a result, an alert or an experimentally naive animal, or one accustomed either to the test sound or the environment, but not to both, will often show marked initial reflex activity while their counterparts may show little or none.

Such alterations in muscle responses were observed in 30 alert cats. Measurements were obtained through chronically implanted electrodes within the reflex loop (muscles, round window, cochlear nuclei), and the effects mentioned were noted on serial testing over periods up to 4 months in several environments; sound presented free-field, restrained and unrestrained, and through ear inserts designed to maintain a constant sound level regardless of animal movements (*2*).

Figure 1 shows some typical round-window-reflected changes in the cochlear microphonic amplitude resulting solely from contractions and relaxations of the middle ear muscles. Part *A* demonstrates the decrement in reflex activity (initial "on" or orienting response) occurring over a 2-hour period of almost constant tone presentation. As the tone is initially introduced (I), response is relatively brisk. It is virtually absent (II) after continuing for 34 minutes, and no longer demonstrates an "on" response at 75 minutes (III) when the tone is, for the first time, turned off, then on again. Some return of initial activity (IV) can be seen later (78 minutes), after the brief introduction of a novel tonal stimulus activated prior to the resumption of the continuous tone. Part *B* shows the change in the level of reflex activity of an animal that can be obtained (same day) to the same stimulus tone in different environments [I*B*, nonhabituated; II*B*, fully habituated (*3*)]. Part *C* shows a free-field measurement before, during, and after the novel stimulus of a lip-pursing squeak, as suggested in the opening paragraph. Note that the ambient noise level (baseline) is also decreased by the muscle contraction.

Measurements from the muscle-implanted electrodes confirm these round-window observations. Responses of a similar nature (using low frequency tones) have been obtained through bipolar electrodes implanted in the vicinity of the cochlear nuclei in the three cats with satisfactory electrode placements (tested only in a closed-field sound environment, Fig. 1*A*).

To summarize, a high degree of individual variability was noted; some cats habituated more easily and without regard, per se, to their auditory thresholds. In most subjects, variation in the contraction of the muscles—and subsequent sound attenuation—could be divided, albeit semiartificially, into two components: (i) a gradual slow overall relaxation as the stimulus continued (part *A*I–II) and, (ii) a smaller, more rapid amplitude modulation (>1/3 sec) occurring within the "type 1" relaxation (parts I*A* and I*B*). The former seems primarily related to habituation to the sound itself; the latter seems related to habituation in the environment (*4*). These minor and more rapid amplitude modulations were correlatable to the apparent degree of an animal's alertness and were also seen, in alert cats, in diminished form in the absence of a specific auditory input, and in situations where the animal's threshold was close to or at the intensity of the sound stimulus.

Within a consideration of the previously expressed notion of an orienting response, these observations by no means obviate the accepted protection theory of the muscle for loud sound. They do, however, suggest a second function at less intense sound levels. We suggest that such amplitude modulations—particularly the more rapid ones—observed in our animal provide a mechanism for constantly changing the auditory input, in a manner perhaps analogus to that observed in the eye and in the fine movements of its muscles (*5*). Such an "auditory vibrato" may indeed be sufficient compensation for a slight loss in stimulus intensity, and may aid in either auditory analysis or maintenance of attention (*6*).

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References and Notes

1. E. G. Wever and M. Lawrence, *Physiological Acoustics* (Princeton Univ. Press, Princeton, 1954). Chapter 10 is an excellent summary of the protection theory as well as several other theories.

→ R. Galambos and A. Rupert, *J. Acoust. Soc. Am.* **31**, 349 (1959); F. B. Simmons, *Ann. Otol. Rhinol. Laryngol.* **68**, 1126 (1959); *ibid.* **69**, 1063 (1960); *ibid.*, in press.

3. The environment was a conditioned-avoidance shuttle box, in which the cat had been trained almost daily for 2 months, at threshold. For the figured test, suprathreshold sounds were used, to which it was obvious that the cat paid no attention.
4. More gross fluctuations have been described by Starr (personal communication), attributable to contractions associated with body movement. These, of course, also occurred in our cats but were usually recognizable. See, for example, II*B* here, at about 12 seconds after "tone on."
5. R. M. Pritchard, *Sci. Am.* **204**, 72 (1961).
6. This work was supported by National Institutes of Health grants B-2167 and B-3407.

27 August 1962

Chemical Indexing: An "Atom Total" Based on Cyclic Features of Structure

Abstract. The atom-total of a compound may be obtained from an equation which substitutes cyclic features of structure for hydrogen atoms. This method is useful for checking a compound's molecular formula against its structural formula or systematic name. While it applies to all chemical compounds, it is of most value for compounds with complex ring structures.

Writers as well as editors and indexers of technical papers generally make an atom count of an organic structure and check this total against the total of the previously determined molecular formula.

This method may work well enough with simple structures. However, when applied to complex structures, it is tedious, time-consuming, and often inaccurate. This results from the difficulty of including all the hydrogen atoms around the structure.

If the atom-total could be obtained by exclusion of hydrogen atoms from the count, the checking might possibly be simplified. Since it might be assumed that the other univalent atoms have replaced hydrogen in the molecule, all univalent atoms would be excluded from the count.

Soffer has shown how to generalize molecular formulas in terms of the number of cyclic features of structure (*1*). He has expressed this relationship in the following equation:

$$\rho = 1 + \tfrac{1}{2} \sum n_v(v-2)$$

where ρ is the number of cyclic features (rings and multiple bonds) and n is the number of atoms of covalence v. Soffer's equation can be solved for number of univalent atoms n_{I} as follows:

$$\rho = 1 + \tfrac{1}{2}\,[-n_{\mathrm{I}} + n_{\mathrm{III}} + 2n_{\mathrm{IV}} + 3n_{\mathrm{V}} + 4n_{\mathrm{VI}} \ldots]$$

or

$$2\rho = 2 - n_{\mathrm{I}} + n_{\mathrm{III}} + 2n_{\mathrm{IV}} + 3n_{\mathrm{V}} + 4n_{\mathrm{VI}} \ldots$$

Then

$$n_{\mathrm{I}} = 2 + n_{\mathrm{III}} + 2n_{\mathrm{IV}} + 3n_{\mathrm{V}} + 4n_{\mathrm{VI}} \ldots - 2\rho$$

In its general form, the equation is

$$n_{\mathrm{I}} = 2 + \sum_{v=2}^{8} n_v(v-2) - 2\rho.$$

Since cyclic features can be noted separately as rings and multiple bonds, the term ρ is expressed as the sum of rings R and double bonds Δ, or $\rho = R + \Delta$. (For this purpose, double bonds exist as two-membered rings.) Each triple bond contributes two cyclic features to the structure. Therefore triple bonds are expressed as 2Δ. However, for most cases the equation is

$$n_{\mathrm{I}} = 2 + \sum_{v=2}^{8} n_v(v-2) - 2(R+\Delta). \quad (1)$$

Feldman (*2*) has used an equation similar to this to solve for number of hydrogen atoms for another purpose.

Derivation of an equation which eliminates consideration of univalent atoms from the atom-total is possible by substitution of Eq. 1 in an equation which expresses the total number of atoms in a molecule. The atom-total is, logically, the summation of all atoms, n, of covalence v.

$$T = \sum n_v$$

or

$$T = n_{\mathrm{I}} + n_{\mathrm{II}} + n_{\mathrm{III}} + n_{\mathrm{IV}} + n_{\mathrm{V}} + n_{\mathrm{VI}} + n_{\mathrm{VII}} + n_{\mathrm{VIII}} \quad (2)$$

where Roman numerals refer to the covalances of the respective atoms.

Substitution of Eq. 1 for n_{I} in Eq. 2 gives

$$T = 2 + n_{\mathrm{II}} + 2n_{\mathrm{III}} + 3n_{\mathrm{IV}} + 4n_{\mathrm{V}} + 5n_{\mathrm{VI}} + 6n_{\mathrm{VII}} + 7n_{\mathrm{VIII}} - 2(R+\Delta)$$

or, in its general form,

$$T = 2 + \sum_{v=2}^{8} n_v(v-1) - 2(R+\Delta). \quad (3)$$

For most compounds, the equation can be reduced to

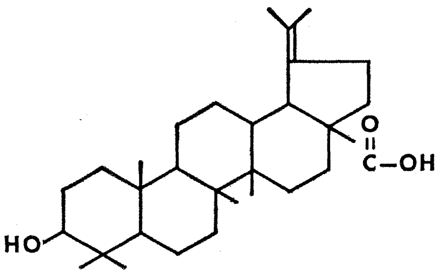
$$T = 2 + n_{\mathrm{II}} + 2n_{\mathrm{III}} + 3n_{\mathrm{IV}} + 4n_{\mathrm{V}} - 2(R+\Delta)$$

or, more specifically,

$$T = 2 + 3n_{\mathrm{C}} + 2n_{\mathrm{N,P^{III}}} + n_{\mathrm{O,S^{II}}} + 4n_{\mathrm{P^{V}}} - 2(R+\Delta)$$

where n_{C} is the number of carbon atoms; $n_{\mathrm{N,P^{III}}}$ is the number of nitrogen or phosphorus(III) atoms; $n_{\mathrm{O,S^{II}}}$ is the number of oxygen or sulfur(II) atoms; and $n_{\mathrm{P^{V}}}$ is number of phosphorus (V) atoms. Examples are as follows:

1) For betulinic acid, $C_{30}H_{48}O_3$ (81), the structure is



The structure shows that the equation must be

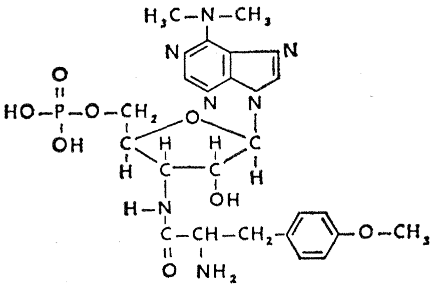
$$T = 2 + 3n_{\mathrm{C}} + n_{\mathrm{O}} - 2(R+\Delta)$$

and $n_{\mathrm{C}} = 30$, $n_{\mathrm{O}} = 3$, $R = 5$, and $\Delta = 2$.

$$T = 2 + 3(30) + 3 - 2(5+2) = 81.$$

From the molecular formula, $30 + 48 + 3 = 81$, the total number of atoms in betulinic acid.

2) The molecular formula of puromycin 5′-phosphate is $C_{22}H_{30}N_7O_8P$ (68).



The equation is

$$T = 2 + 3n_{\mathrm{C}} + 2n_{\mathrm{N}} + n_{\mathrm{O}} + 4n_{\mathrm{P}} - 2(R+\Delta)$$

and $n_{\mathrm{C}} = 22$, $n_{\mathrm{N}} = 7$, $n_{\mathrm{O}} = 8$, $n_{\mathrm{P}} = 1$, $R = 4$, and $\Delta = 9$.

$$T = 2 + 3(22) + 2(7) + 8 + 4(1) - 2(4+9) = 68.$$

If the components of a given systematic name are familiar, the values for the n's, R, and Δ might be determined from the fundamental ring system plus increments, thus eliminating entirely the structural formula. For example:

1) The acetate of 17-hydroxy-6-methylprogesterone has a molecular formula of $C_{24}H_{34}O_4$ (62). From the name, n_{C} must be 21 (from progesterone) plus 2 (from acetate) plus 1