LETTER TO THE EDITOR

Acetylcholine in Synaptic Transmission

Dear Sir:

It was my great delight to see the paper published in the *Biophysical Journal* by Maurel and Galzigna (1971) that bears direct relevance to my dipole theory of chemical synaptic transmission (1968). During the formation of that theory, I was uncertain about the actual value of the dipole moment of acetylcholine (AcCh) in a synaptic cleft and I could only make a guess at that time. I have been hoping that some biochemists might be interested in doing the measurements, thus bringing out a value close to reality after the publication of my paper. The effort of Maurel and Galzigna to make their result available at this time is indeed a worthwhile contribution.

On the surface, their measured value of $p = 2.6 \pm 0.2$ D for $AcCh^+$ in *chloroform* differs appreciably from the assumed value of $p = 48$ D in *water* given in my paper. When the solvents are quite different such as chloroform ($\epsilon = 4.84$) and water ($\epsilon = 80$), the value of p is bound to be different, and it is not as important as p/ϵ as far as the electric field or potential is concerned (Frohlich, 1958). In fact, the electric field produced by a disc of dipoles as given in my paper (1968) is

$$F = \frac{n}{2R}\left(\frac{p}{\epsilon}\right),$$

where n is the dipole density and R is the disc radius. The values of p/ϵ used by me and obtained by Maurel and Galzigna are:

$$p/\epsilon \text{ (in water)} = 48/80 = 0.6 \text{ (Wei)},$$

$$p/\epsilon \text{ (in chloroform)} = 2.6/4.84 = 0.54 \text{ (Maurel and Galzigna)}.$$

The two values of p/ϵ given above differ only by 10% which would affect my calculation rather slightly even if the liquid structure in a synaptic cleft were more like chloroform than water. The value of R (1 μ) which I used was taken from Eccles' book (1957) and it could not be wrong in the order of magnitude if the synaptic structures were taken into consideration. The dipole density n was determined by assuming a dipole spacing of 3 A which cannot be far off the mark. Even though the actual values of R and n were somewhat less than what I used, the ratio of $n:R$ may not be affected as much and my previous calculations would still not be out of order. Thus, quantitatively, the data presented by Maurel and Galzigna has not discounted my theory as their paper seems to indicate. On the contrary, it tends to reinforce my conviction because of the close agreement of the assumed (0.6) and the measured (0.54) p/ϵ for $AcCh^+$.

In essence, my theory was founded on first principles, Newton's law and Coulomb's law. It only requires the transmitter molecules to *behave* like electric dipoles. The exact structure

and geometrical configuration of the dipoles, whether they be $AcCh^+$, $AcCh^+Cl^-$, or even other strange forms, is not essential for the theory. In principle, the theory should be valid for other kinds of transmitter molecules than AcCh as long as they behave like dipoles. This is a feature and a virtue of a *physical* theory in contrast to a *chemical* theory.

Additional note: The existence of ion pairs such as $(AcCh)^+(Cl)^-$ in water is rather unlikely for the very same reason as nonpairing of Na^+Cl^- in water. In chloroform, even if $AcCh^+$ and $(AcCh)^+(Cl)^-$ coexist, the difference in their dipole moments would arise from dipole lengths rather than from pole charges. According to my theory (Wei, 1968, p. 402), the critical size of the dipole array is independent of the dipole length (layer thickness) and hence all my previous calculations would be affected minimally.

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