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A New Light in Nerve Theory

The most recent discoveries of negative fixed surface charge, infra-red emission and birefringence change in nerves strongly suggest the important role of surface dipoles on axon membrane in nerve mechanisms.

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The study of nerve excitation and conduction has a queer start and a slow following. It all started from Galvani's accidental discovery of frog's leg twitching when touched with copper and iron in 1786. He proposed perhaps the hisotrical first of nerve theories, the "animal electricity" which soon excited the then scientific community. This flare did not last long for it was quickly quenched by Volta's famous experiment--the "Voltaic pile." Such an unpleasant affair kept nerve theorists in silence for more than a hundred years and unfairly suppressed one of the most brilliant ideas in science, devastating effect on nerve studies which we still feel to this day.

It was not until the turn of the 20th Century that there was a resurgence of serious attempt to interpret nerve phenomena. In 1902, Bernstein boldly postulated an "Ionic Hypothesis" which contains two essential points: (1) in the resting state, the membrane is permeable only to potassium ions but completely impermeable to ions of all other kinds and (2) upon excitation, the membrane suffers breakdown and suddenly becomes permeable to all ion species. It was amazing that a hypothesis as simple as this for a rather complex system won immediate acception and had been most popular for forty years. Its influence on neurophysiology is still hanging over to this date. The key to the success of Bernstein's hypothesis lies in its simplicity and in its ready explanations for the resting potential and the "all-or-none" response. In

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conception, Bernstein introduced the important roles of membrane potential and membrane permmeability in nerve excitation as:(1) the selective membrane permeability to ions, (2) the change of membrane permeability with membrane potential to ions, and(3) the dependance of the resting membrane potential on the ion concentrations by the Nernst relation. Thus in fact,Bernstein was the founder of the more general "membrane theory". Though some facts were found later not quite in agreement with the original form of his hypothesis, the main spirit of the membrane theory has been going strong for over 60 years. Needless to say, it is a monument in neuro-science.

Around 1940, there came two crucial facts disturbing the Bernstein's hypothesis. Hodgkin and Huxley observed that the action potential (the Membrane potential during stimulation) reversed its polarity at its peak. Boyle and Conway then found that the resting membrane of muscle fibres was permeable to chloride ions as well as potassium. In the following ten years, Hodgkin and Huxley made extensive studies on squid giant axon with a new tool (microelectrode) and improved techniques, and obtained results not only in enormous amount but also in fine details never seen before. Their work has been elegantly described by B. Katz in two articles published in Scientific American (November, 1952 and September, 1961). Out of their experimental work, Hodgkin and Huxley postulated the now well-known "Sodium Theory".The sodium theory rests on three things: the sodium ion in the external solution, the sodium pump within the membrane and the sodium conductance of the membrane. The first (Na ions) is real while the other two are conceptual. In nerve excitation, the three things work as follows. The presence and the high concentration of sodium ions in the external solution are essential to begin with. In the resting state, the sodium pump constantly pumps Na ions out thus maintaining high Na concentration in the external solution and apparently low membrane permeability to Na. Upon excitation, the sodium pump relaxes and hence the sodium conductance of the membrane momentarily increases. As a result, there is a sudden inward rush of Na ions which give rise to the action potential. The series of events were beautifully illustrated in Katz's two articles aforementioned. As Katz has described, the success of the sodium theory is really outstanding. For their great contribution, Hodgkin and Huxley were awarded Nobel prize in physiology and medicine for 1963.

Katz and others have well pointed out that there are still some fundamental questions which remain unanswered. The question

most often raised is, why does the sodium conductance of the membrane mementarily increase upon excitation? Since the sodium theory inherits the very spirit of Bernstein's membrane theory, many difficulties are deep-rooted. Among others, the concepts of membrane potential and membrane permeability are at the heart of the problem. It is fair to say that most of the experimental work on nerve and muscle menbranes were to measure and to understand these two things. Unfortunately, these two things are not as simple as they appear, and the more they are studied, the more untenable they become. This paradox was made particlarly manifest after the perfused studies of squid giant axon done since 1961. Part of the results was described by P. F. Baker in Scientific American, March, 1966.

In the perfusion experiments, the jelly-like axoplasma in the axon is flushed out and an artificial solution is forced in and perfusing through. The external solution may be sea water or an artificial one. In this way, one can use any recipe at his disposal for the compositions of the inner and outer solutions. One of the most surprising results from perfusion experiments performed on the both sides of Atlantic (Plymouth in England and and Woods Hole in the U.S.A.), is that the squid nerve axon maintains its excitability over a wide range of resting potentials. This raises a very fundamental question, is the membrane permeability closely related to the membrane potential? If the answer is no, then the very spirit of the membrane theory is at stake. If the answer is yes, the above result would imply that the squid axon maintains its excitability over a wide range of membrane permeabilities, which is again contrary to the basic belief of the membrane theory and the sodium theory. A way to resolve this puzzle was suggested by Baker, Hodgkin and Meves. They conceived that excitability changes are likely to depend on the potential difference (E_M) across the membrane rather than on the total potential difference (E_R) between internal and external solutions. To understand this, let us look at the potential profile in Fig. 1. The meanings of E_R and E_M are now obvious. In all experiments only E_R can be observed and it is the so called membrane potential as known to the neurophysiologist. The recognition of the importance of the unobserved E_M over the observed E_R is indeed a giant step forward in conception. But besides E_M and E_R, there are inner and outer barrier potentials E_i and E_o (see Fig. 1.). What is the relative importance of E_o and E_i to E_M? The answer to this question is very crucial and could be the key to the understanding of nerve excitation and

conduction. Before we try to answer this question, let us learn more from the perfusion experiments.

Another very interesting finding from perfused squid axon is that the nerve can be excitable in a great variety of ionic environments. Tasaki and his group had made extensive studies in this respect and their results were really astonishing. The two particular cases they tried are worth mentioning here: (1) both the inner and outer solutions devoid of Na and (2) Na in the inner and Ca in the outer solutions. In both cases, nerve excitability were observed. For the first case, the sodium theory can hardly offer an adequate explanation because Na is totally absent. In the second case, the sodium theory would predict an early outward Na current and an action potential retaining the same polarity as the resting potential. The reason is that if the sodium conductance of the membrane were to increase momentarily upon stimulation as postulated in the sodium theory, then the inner Na ions should go out and thus bring the inner potential even more negative. Contrary to this prediction, Tasaki and his co-workers obtained results similar to that found in the normal case, i.e. Na sitting outside. The findings from these two cases indicate that the presence of Na ions in the external solution is not indispensable for nerve excitation and that a specific increase of sodium conductance of the membrane upon stimulation may not be the mechanism responsible for the production of action potential in an otherwise normal situation. Thus great care and caution must be exercised if one tends to extend the validity of the sodium theory to beyond the limit of the well established classical cases (say normal squid axon).

Most of the difficulties encoutered in nerve physiology center around the time-honoured concept--the membrane permeability for which there is no unique definition and no standard method of measurement. As an illustration, we cite a most recent example. Garner and Grundfest (1968) have obtained many "anomalus" observations in their study of permeability of alkali metal cations in lobster muscle. They asserted, "Assuming that osmometric data are the more direct measure of permeability, it is obvious that conclusions as to permeability that are based on electrophysical data can be far off the mark". Thus to seek understanding based on the permeability concept and measurements is open to question, skepticism and controversy. What is really needed is some physical concepts which one can grasp easily and some physical facts which one can observe and interpret without ambiguity. The time has just arrived. The three exciting developments which came in succession in

April, May and June of 1968, suddenly opened a new era of physical approach to nerve studies and hence dawned the hope of revealing the mystery of neutral events. We shall tell this grand story step by step.

Elementary physics shows us that at the bottom (hidden or unhidden) of every electrical phenomenon, there is electric charge. A current is flow of charges and a potential arises from charge distribution. Curiously enough, the question of whether there is any electric charge on an axon membrane was seldom raised in the past, to say nothing of its location and how much. Now, this question is answered in the affirmative by Segal. Using a simple set-up, Segal found that a suspended giant axon of squid or lobster was moving in a direction opposite to the applied electric field. This means that there is negative fixed charge on the outer surface of the axon. The minimum values of surface charges on the axons of squid and lobster as determined by Segal were 1.9×10^{-8} and 4.2×10^{-8} coul/cm^2 respectively. The significance of this finding is so profound that it needs some exploration.

We have now two things definite about the electrical properties of an axon: there is negative fixed charge on the outer surface, and the polarity of the resting membrane potential is positive outside and negative inside. Electrostatics tells us that a negative charge is the location of minimum potential and a positive charge, that of maximum potential. This simple principle dictates that there would be also negative fixed charge on the inner surface of the axon. If the inner surface were neutral or positively charged, then the inside potential would be higher than outside (negatively charged), contrary to the observed polarity of the resting potential. An immediate question is, how can the negative charges on the two surfaces of 70A apart be held fixed against the strong Coulomb repulsion? The question is answered by the charge neutrality condition. That is, there must be positive charges between the two negative charge sheets so that the whole membrane is neutral. By Coulomb attraction, it is very likely that a positive charge sheet is formed right close to but behind each negative charge sheet. In other words, there could be two dipole layers, one on each side of the membrane with the negative end facing the aqueous phase. This electrical structure is depicted in Fig. 2. From the simple principle in electrostatics aforementioned, the potential should go down from positive charge to negative charge. Thus the potential profile for the structure in Fig. 2 should look like that shown in Fig. 1. This not only justifies the potential profile in Fig. 1 but also suggests a

possible origin for the barrier potentials E_i and E_o. Now we come to the heart of the problem, that is, the role of surface dipoles on an axon membrane. Before we go on, we need to know a little about dipole physics.

A simple dipole is a one-dimensional structure of fixed length d with charges q and -q at the two ends. The product qd is called the dipole moment (p). This dipole is also called a permanent dipole because its dipole moment is fixed and does not change with the external electric field. Another kind of dipole is the induced dipole. This is illustrated in Fig. 3. At no field, the center positively charged core and the surrounding negative charge cloud are concentric spheres and the whole structure has no dipole moment. Suppose now an electric field is applied in the direction from left to right. Then the negative charge cloud will be pulled to the left and the positive core pushed to the right. As a result, the centers of gravity of positive and negative charges no longer coincide but are displaced by a distance d, and thus a dipole moment qd is induced by the field. Many kinds of atoms and molecules have this property. In the following, we shall deal only with permanent dipoles.

A dipole will not move in an uniform electric field because the force on the negative pole is exactly balanced by that on the positive pole. However, the equal and opposite forces on the two poles will exert tension or compression on the bond between the poles. If the bond is not entirely rigid, the dipole will be stretched or compressed to some extent in the microscopic scale under the field. Once the bond is slightly deformed, the inertia will tend to restore it to the undeformed state. As a result, a dipole molecule could vibrate in an electric field (see Fig. 4). Besides vibration, there is rotation to consider. Unless the dipole orientation is exactly in line with the field direction, the equal and opposite forces on the two poles will impart a torque and hence tend to rotate the dipole. It is easy to see that by Coulomb interaction, the field is to rotate the dipole into an orientation opposite to the field direction(Fig.5). We can say that for a free dipole, there are two stable orientations, one parallel and the other antiparallel with the field.

Let us consider a two-dimensional dipole layer, consisting of simple dipoles of density N (i.e. N dipoles per unit area). The side view of this dipole layer is shown in Fig. 6. If all the dipoles are parallel, i.e. the positive poles in one plane the negative poles in another, then the dipole potential will be proportional to the density N and it goes down from the positive side to the negative side.

Suppose there are a few number of dipoles of density N_2 oriented in the opposite direction (Fig. 7). These few dipoles will tend to annul the effect of the majority of dipoles (density N_1). The dipole potential will be then proportional to $(N_1 - N_2)$. From this simple reasoning, one can gather that the dipole potential may be either increased or decreased by repopulating the dipoles in the two orientations (or two states). The simplest way to flip dipoles is by applying an electric field of proper magnitude and right direction. The dipoles in the two states will have different energies (see Fig. 8), say E_1 (the lower) and E_2 (the upper). Suppose the applied field (F) is parallel with the majority dipoles of population N_1 and energy E_1. If the dipole energy gained from the field, pF where p is the dipole moment, is equal to or greater than the energy difference $(E_2 - E_1)$ between the two states, then a number of dipoles in the lower state will flip to the upper state (opposite orientation), thus reducing the dipole potential. The decrease of both the dipole population N_1 and the dipole potential may be called "depolarization". (Fig. 9). If the applied field is parallel with the minority dipoles of population N_2 and energy E_2, then N_2 tends to decrease or N_1 tends to increase, resulting in an increase of the dipole potential. This situation is called "hyperpolarization" (Fig. 10).

Now we are in a position to explain nerve excitation from the dipole point of view. Consider a Na ion just outside the outer dipole barrier (Fig. 2). This Na ion is under two driving forces. The first is exerted by the outer dipole field (or potential gradient) which is in the outward direction. The second is the diffusional force which arises from the Na concentration gradient that is in the inward direction. In the resting state, the outer barrier is so high that the outward electric force overpowers the inward diffusional force, thus keeping Na ions out. If one applies a negative potential to the negative poles of the outer dipole layer, the dipole layer will be depolarized and the dipole potential lowered. This in turn will reduce the dipole field and so the electric force on the Na ion. When the reduction of the electric foece is large enough so that it is overpowered by the diffusional force, the Na ions will be driven inward and bring the positive charge with them. The sudden inward flow of positive charges will raise the inner potential and can make it positive relative to outside. This transient change of membrane potential is called the action potential whose appearance signifies the occurrance of nerve excitation.

To summarize, the dipole theory would suggest the following sequence of events: stimulation--dipole flipping--lowering of outer

dipole barrier potential--in-flow of Na ions--apearance of action potential. It is clear from this sequence that nothing is specially geared to Na ions. This implies that the Na ions are not indispensable, and the sodium pump and the sodium gate are not necessary for nerve excitation. But if the dipole theory just does this, it would not be considered as anything better than the Sodium theory but a different point of view. When we come to thermal and optical events in nerve, we shall find definitely the advantage of one over the other.

As discussed before, a polar molecule can have vibration and rotation. Each vibro-rotational state is associated with a definite energy. For a large molecule, the V-R energy is in the range of several kT, where k is the Boltzmann constant and T, the absolute temperature. kT is usually taken to be the thermal energy of a particle at temperature T. At room temperature (T is about $300^{o}K$), kT is equal to 25 milli-electron-volts. Suppose some dipoles have been excited to the upper state by stimulation. When the stimulation is removed, the excited dipoles will relax to the lower state. In this downward transition process, an amount of energy $E_2 - E_1$ will be released. Since $E_2 - E_1$ is in the order of kT, this released energy could be detected as "heat". From quantum mechanical point of view, the released energy has the units called "quanta", each quantum being $h\nu = E_2 - E_1$, where h is the Planck's constant and ν, the frequency of the emitted wave. If say $E2 - E_1$ is equal to 4kT or 100 milli-electron-volts, the emission frequency will be 2.5×10^{13} hertz or the corresponding wavelength is about 12 microns which is in the infrared range. Indeed both heat production and infrared emission from stimulated nerves have been observed. Since every dipole has many neighbors and all of them have the same energy states, then the energy quanta $h\nu(=E_2 - E_1)$ released as a result of a dipole flop could be "reabsorbed" by the neighboring dipoles. This follows the same principle as you are to receive the desired TV channel by tuning the Channel dial (for selecting frequency). In quantum theory, this phenomenon is known as "resonance absorption" which is illustrated in Fig. 11. It is quite possible that a large portion of heat production could be reabsorbed in this way and the rest be emitted as infrared radiation. Abbott, Howarth and Ritchie did find that 80% of the heat produced after nerve stimulation was reabsorbed. Fraser and Frey have most recently detected infrared emission from active live crab nerves with an intensity of $6uW/cm^2$. This emission exceeded the black-body radiation and the stimulus artifact heating by two

orders of magnitude and must be located at the surface of the nerve. They estimated that the infrared radiation energy accounted for about 15% of the heat production as measured by Abbott et al.

Besides heat production and infra-red emission, there is another amazing development which was made known in May, 1968. Cohen, Keynes, and Hille have found conclusively that there was a bona fide birefringence change which coincided with the action potential in a squid axon. (Fig. 12). Their experiments showed that the birefringence change was not associated with the bulk of the axoplasm in the squid axon but rather has a radial optic axis and arises from sources disposed in a cylindrical region at the outer edge of the axon or in the sheath. The records also indicated that a large part of the birefringence change was directly dependent on the potential difference across the membrane. They suggested that the Kerr effect (change of refractice index with electric field) in molecules larger and more polar than water could be so large that even a small amount of reorientable protein at the outer or inner surface of the membrane would be sufficient to account for their observations. It is most gratisfying that the observation and the suggestion by Cohen et al agree so well with the electrical structure shown in Fig. 2 which is derived from Segal's result. That the dipole theory can adquately interpret the thermal, electrical and optical events in nerves is a no small feat. With this encouragement, we shall proceed to a more complex problem, the mechanism of nerve conduction.

The first question is, how a nerve impulse (action potential) moves from one point to the next? This can be easily answered by dipole flip-flop. Suppose point A (Fig. 13) in a nerve is stimulated. Some dipoles in region A will flip up and the barrier potential will be lowered, thus resulting in an action potential at that point. As the excited dipoles flop down at A, some neighboring dipoles will flip up because of resonance absorption. So the barrier potential at the neighboring point is lowered and an action potential appears there. This process will go on and on and one sees impulse propagation along the axon.

The most subtle question on nerve conduction is, how is "amplification" provided in the nerve to make nerve transmission apparently unattenuated? The answer to this question requires more physics than what we have so far discussed. Let us go back to the potential profire shown in Fig. 1. The higher potential in the membrane region will trap negative ions coming from both sides. If we

use N to stand for "excess negative", the membrane region may be called an N-region. The excess negative ions have many functions to perform. The obvious one is to buffer the interaction between the two dipole layers at the opposite interfaces of the membrane. On the other hand, the negative charges on the inner and outer surfaces will attract positive ions to the immediate vicinity. If p stands for "excess positive", then there will be two P-layers, one close to each side of the membrane and in the aqueous phase. Thus the electrical structure of an exon membrane and its immediate vicinity is P ← N → P where the arrows indicate interface dipole layers and their orientations. This is shown in Fig. 14. What does this P ← N → P structure mean to us? Well, we shall have to know a little about the favourite son in electronics--the transistor. The most popular type of transistors is called the junction type. A junction transistor has a sandwich structure in the form of either pnp or npn, where n stands for "excess negative" particles (electrons) and p for "excess positive" particles (holes) in a certain semiconductor material, say germanium or silicon. At the junction between n-type and p-type materials, there is a dipole layer. The dipole layer, however, is not composed of individual simple dipoles, but rather made of accumulated electrons on one side and accumulated holes on the other (see Fig. 15). If the transistor is bare, i.e. not connected to any external potentials, the potential profile in the three regions will be the one shown in the lower part of Fig. 15. Under this condition, very few holes (positively charged particles) will be able to overcome the junction barrier and to move from one side to the other. The electrons in the center N-region are kept in by the higher potential. So nothing is expected to happen in a "bare" transistor. Now, if a forward bias (positive potential to p-side and negative potential to n-side) is applied to the emitter junction J_e and a reverse bias (positive potential to n-side and negative potential to p-side) applied to the collector junction J_c of the transistor, the potential profile will be modified to that shown in Fig. 16. You see that the emitter barrier is lowered while the collector barrier is heightened. This is because the forward bias pulls mobile electrons and holes away from the junction but the reverse bias pushes more of them toward the junction. When the accumulated charges on the two sides of a dipole layer are reduced or increased, so will the dipole potential. The lowering of the emitter barrier enables the holes from the emitter region to diffuse across the center region. As they arrive at the far side of the collector junction, their positive charges will tem-

porarily modify the collector barrier potential. At that instant, the so-called "transistor action" takes place, thus producing amplification. The techincal details may be found from an electronics textbook and will not be described here. The above description, though oversimplified, does indicate that there is a close similarity in electrical structure and potential profile of an axon and a pnp transistor. Furtheremre, the physical laws and principles governing the dynamical behaviour of charged particles, be they electrons, holes or ions, are all the same. Thus if the outer barrier of an axon membrane can be lowered, there is no reason why an axon would not take a "transistor action". Indeed, a detailed transistor theory has been applied to nerve axon and it was able to offer adequate interpretations for a large class of important phenomena, including the most recent ones. To some readers, the marriage of nerve actions and transistor theory is rather strange and perhaps surprising. It is not so if one realizes the fact that electrons and ions in similar physical environments should behave the same in many ways. Here is the case in point to demonstrate the bonus of interdisciplines.

So far we have only been concerned with nerve axon, the simplest element in the nerve system. When we come to the central nervous system (CNS), the complexity goes up by many orders of magnitude. For example, in a human brain, there are 10^{10} neurons. Between neurons, there are small gaps (usually not wider than 200A) called synapses. How does a nerve impulse jump across a synapse? This has been a hot debate over 90 years and it is yet to be settled. Now, we shall show how mobile dipoles may play an important role in synaptic transmission.

It has been observed over the years that when a nerve impulse reaches a nerve ending, it triggers the release of certain molecules called acetylcholine (ACh) from the vesicles situated inside the presynaptic membrane (Fig. 17). An ACh molecule is made of choline and acetic acid and is thus not symmetrical in structure. An unsymmetrical molecular structure implies that the centers of gravity of the positive and the negative charges do not coincide and hence the molecule is very likely a dipole. On this basis, we may regard ACh molecules as dipoles. When ACh molecules are released into the synaptic cleft, their dipole orientations will be initially in random directions. (Fig. 17). However, as they approach in close proximity to the postsynaptic membrane, the ACh on the foremost front will become oriented one after another under the influence of the near field of the dipole layer at the membrane

surface. The first layer of ACh dipoles when fully oriented will extend the field backwards and hence the later-coming ACh will follow suit. The process will go on and on and finally a multi-layer-ACh dipole array is formed in the cleft space. This is shown in Fig. 18. As described before, there are excess Na ions right close to the membrane dipole barrier. Each Na ion in this region is acted upon by three forces f_1, f_2, and f_3. f_1 is the electric force exerted by the membrane dipole layer, f_2, the diffusional force or the chemical force arising from the concentration gradient of Na ions and f_3, the electric force produced by the ACh dipole array. The Na ion will be driven into the postsynaptic membrane if the resultant force (the sum of f_1, f_2 and f_3) is in the inward direction. Since f_1 and f_2 can be estimated, then the minimum value of f_3 can be calculated from the zero-resultant-force condition. In order to produce f_3 of this minimum value, the ACh dipole array must reach a critical size. This makes us understand why the cleft space is important for chemical synaptic transmission. Calculation shows that a minimum space of 130 A would be required. This is in good agreement with the observation (150-200A) of synapse. Since it takes time for the ACh dipoles proceeding from the initial random orientations (Fig. 17) to the final formation of dipole array (Fig. 18), there must be a delay between the arrival of a nerve impulse at the presynaptic membrane and the appearance of action potential in the postsynaptic membrane, a well-known fact in chemical synaptic transmission. Here again there is a good agreement between calculation (0.5-50 msec) and observation (0.3-300 msec) of synaptic delay. It can be further shown that the dipole theory is able to account for many other important phenomena which have never been understood before in chemical synaptic transmission.

In summary, we have dealt with three essential physical entities for nerve actions: ions, dipoles and fields. The interactions and interplays between the three can be studied by application of physical laws and principles. We have shown in the above that this approach gives us a fresh understanding in thermal, electrical and optical events taking place in the nervous system. That this approach is advisable and useful has been suggested by the two Nobelists. E. Schrodinger, the founder of quantum mechanics, stated in his book, "What is life? the following motto, "The working of an organism requires exact physical laws". F. Crick, famous for the Watson-Crick double-helix model of DNA went even further by saying, "The ultimate aim of modern movement in biology is in fact to explain <u>all</u> biology in terms of physics and chmistry"

(from his book, "of molecules and man".) This we believe is the right direction to pursue if we are to achieve an ultimate understanding of nerve mechanisms.

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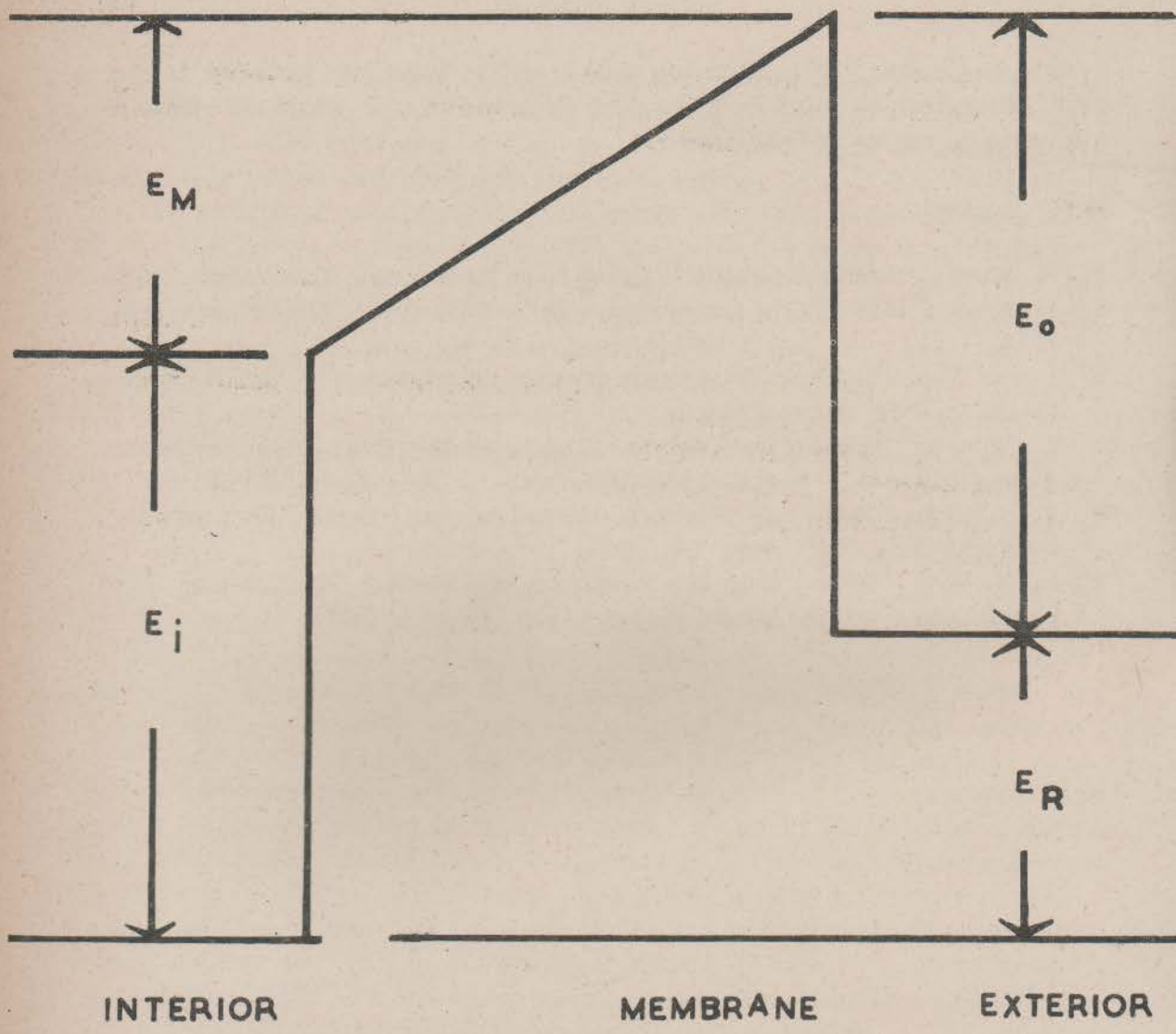


Fig. 1. Potential profile across an axon membrane. E_R is the observed membrane potential between internal and external solution; E_M, the potential across the two boundaries of the membrane; E_i and E_o, the inner and outer barrier potentials at the membrane interfaces.

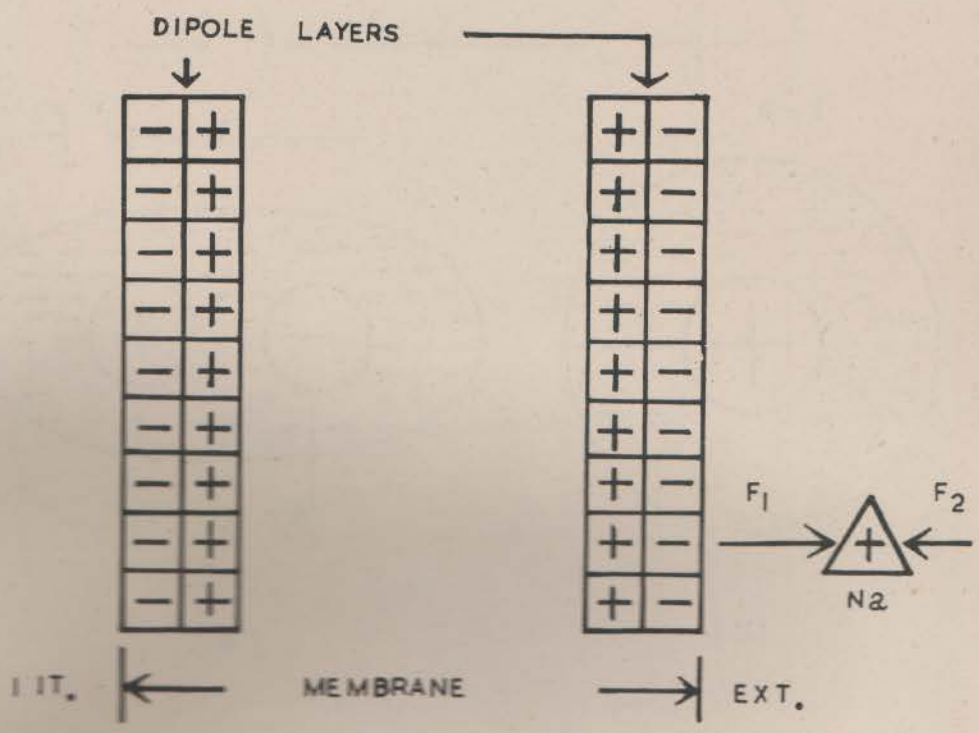


Fig. 2. An electrical structure of axon membrane as derived from Segal's experimental evidence for fixed negative surface charge, the polarity of resting membrane potential and the Coulomb interaction between charges. A Na ion near the outer dipole layer is subject to two driving forces: f_1, the electric force from the dipole layer and the diffusional (Chemical) force arising from the Na concentration gradient.

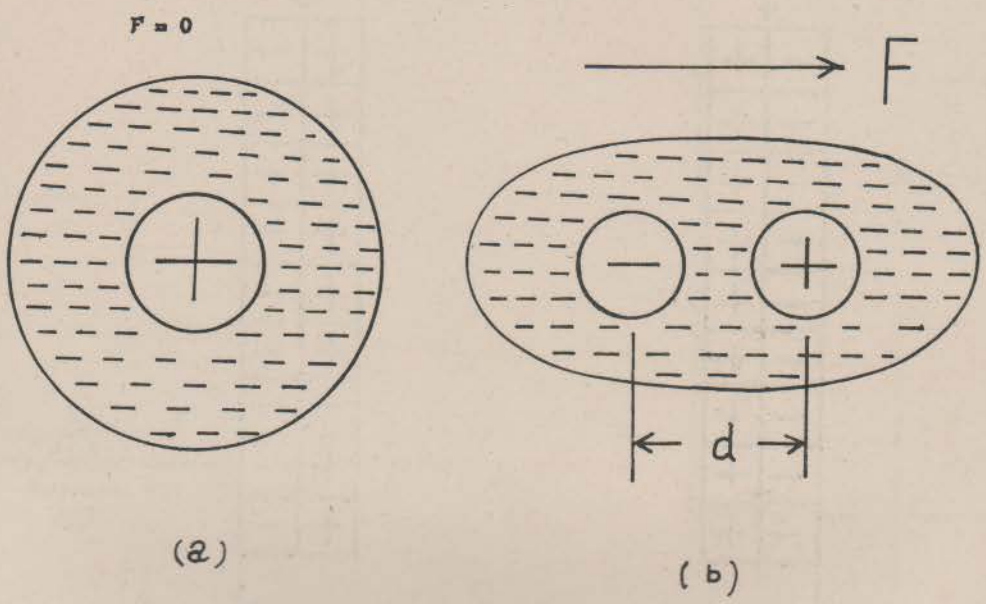


Fig. 3. The charge distributions of a neutral molecule under two conditions: (a) non-polar under zero electric field because the centres of gravity of positive and negative charges coincide with each other and (b) induced polarization under an external electric field for the field displaces positive and negative charges in opposite directions. The molecule is said to be an induced dipole.

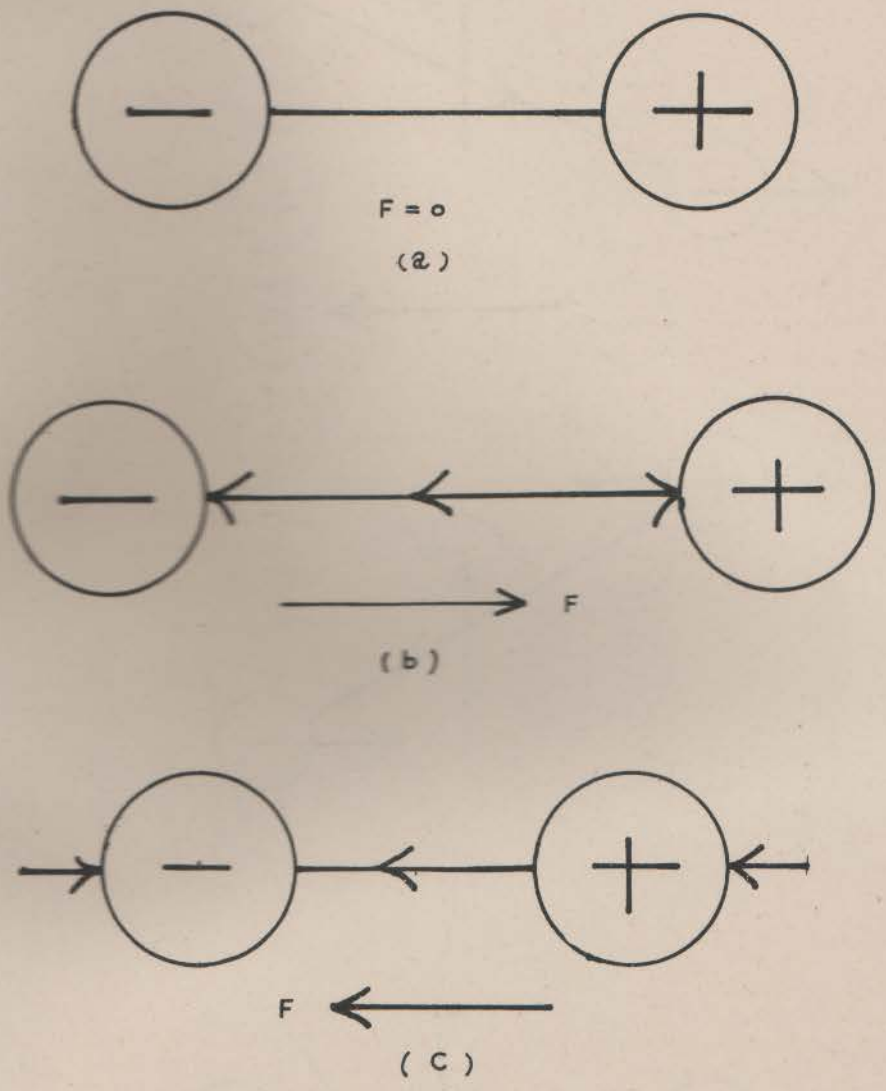


Fig. 4. Dipole vibration: (a) Under zero electric field, the dipole may have thermal vibrations but little strain, (b) When a field is applied in a direction opposite the dipole orientation, the dipole will be subject to stretching and (c) When a field is applied in the same direction as the dipole orientation, the dipole will be under compression. The stressing forces by the field and the restoring force in the bond between poles tend to set the dipole into vibration other than normal thermal vibrations.

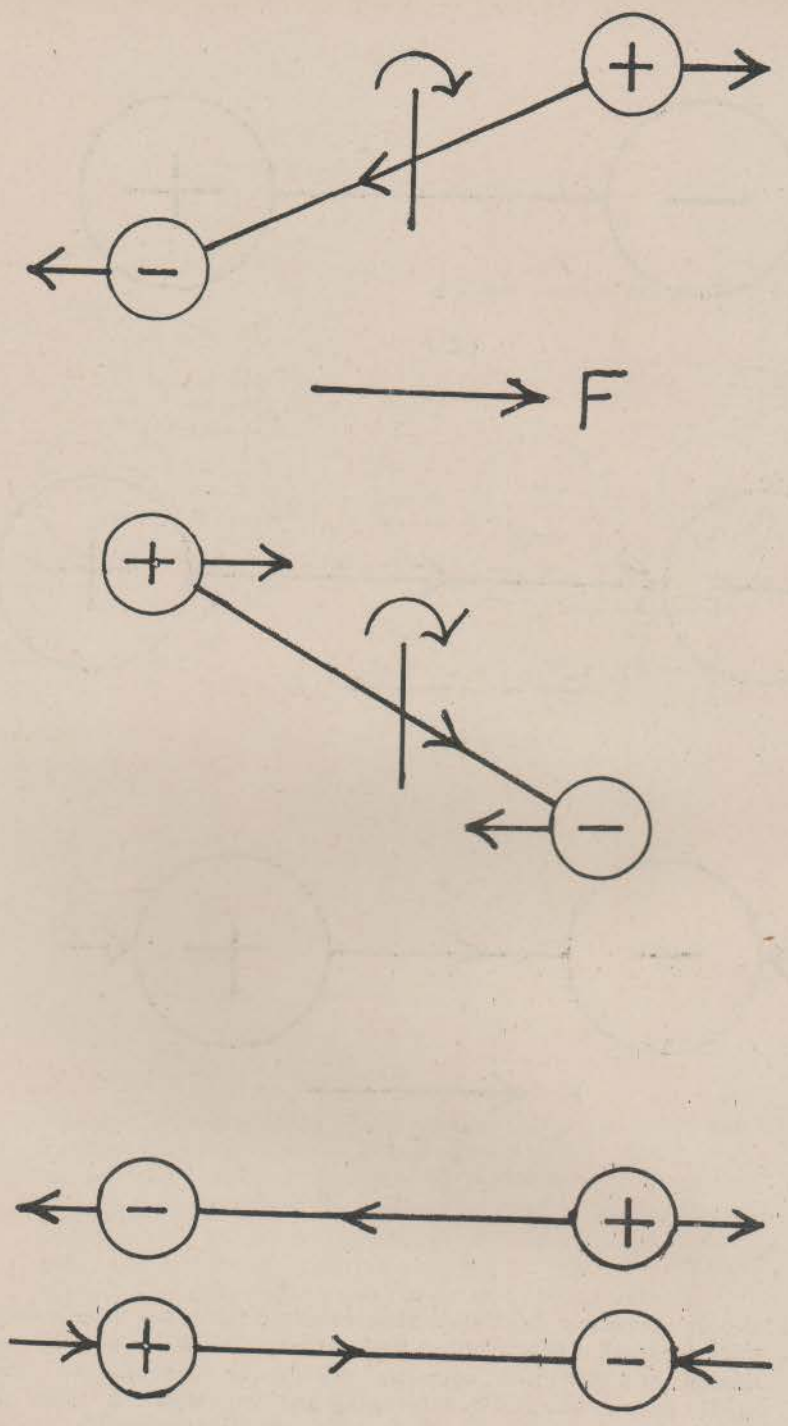


Fig. 5. Dipole rotation. Dipoles whose orientations are not in line with the field are imparted a torque and hence tend to rotate to the orientation opposite to the direction of the field. The two dipoles on the lower part whose orientations are opposite to each other but are in line with the field will have the least tendency to rotate. These two orientations represent two equilibrium states of the dipole.

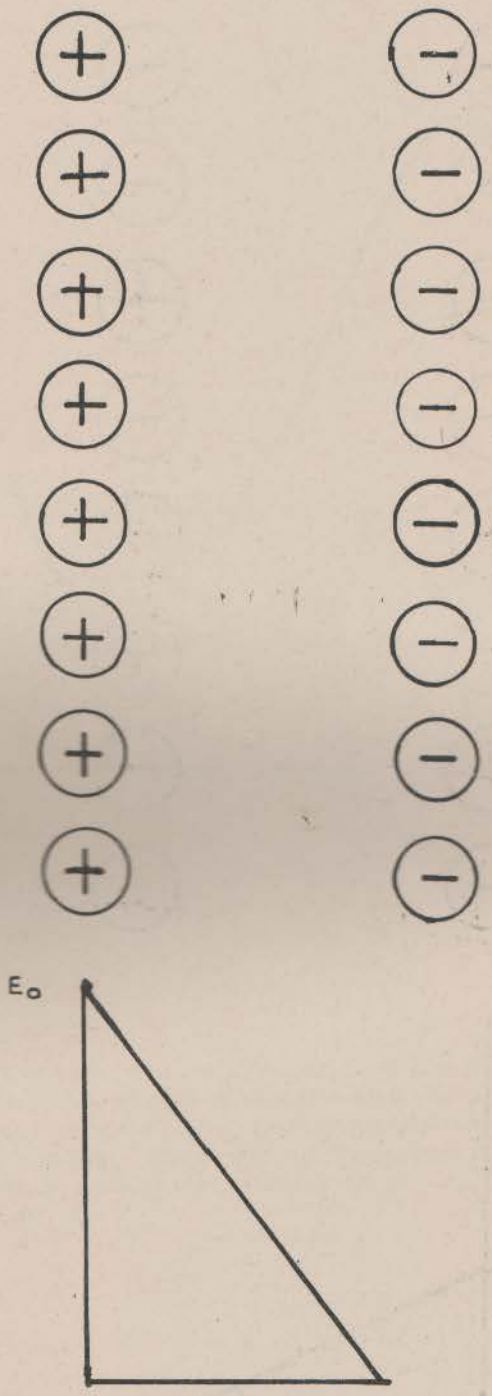
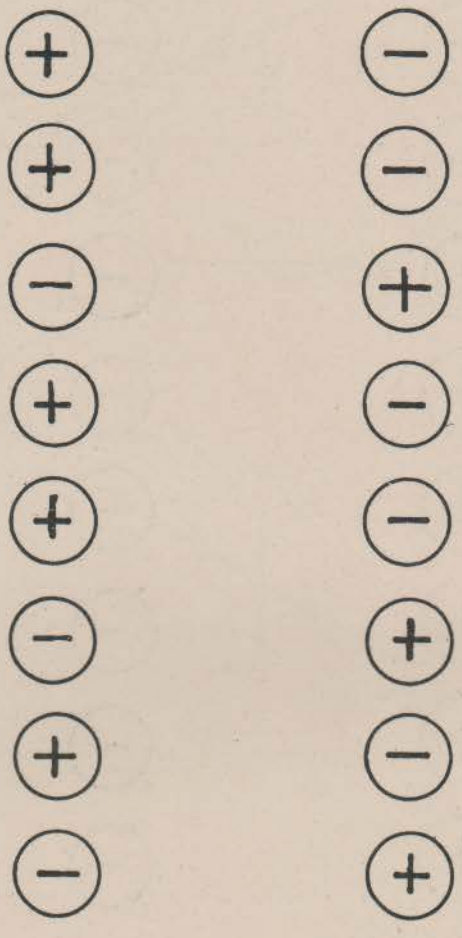


Fig. 6. The upper part shows dipoles of density N, all with parallel orientations (i.e., in the same direction). The lower part shows the potential profile from the positive - pole plane to the negative - pole plane. The barrier potential E_0 is proportional to the dipole density N.



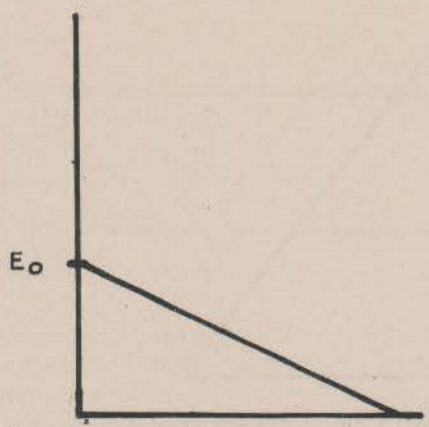


Fig. 7. The upper part shows dipoles of density N_1 in one orientation and dipoles of density N_2 in the opposite orientation. The lower part shows the potential profile from the positive-pole plane to the negative-pole plane. The barrier potential E_o is now proportional to (N_1-N_2) and is thus much lower than that shown in Fig. 6, Assuming $N=N_1+N_2$.

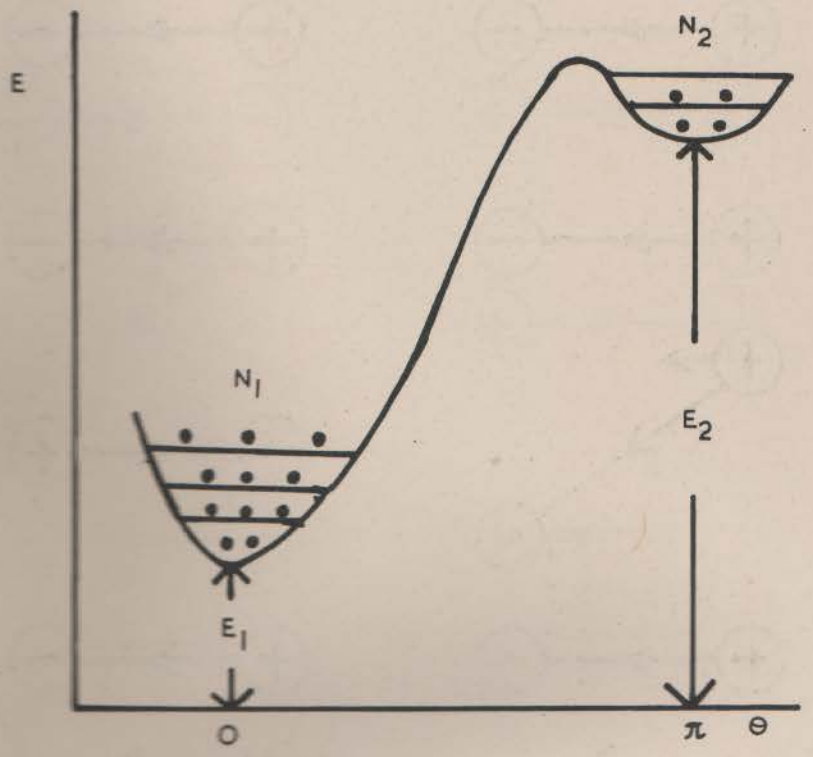


Fig. 8. Dipole energy versus the angle of rotation. The graph shows two groups of dipole states, one around the zero angle of rotation and another around the π (180°) angle of rotation. The two groups have densities of population N_1 and N_2 and energies around E_1 and E_2 respectively.

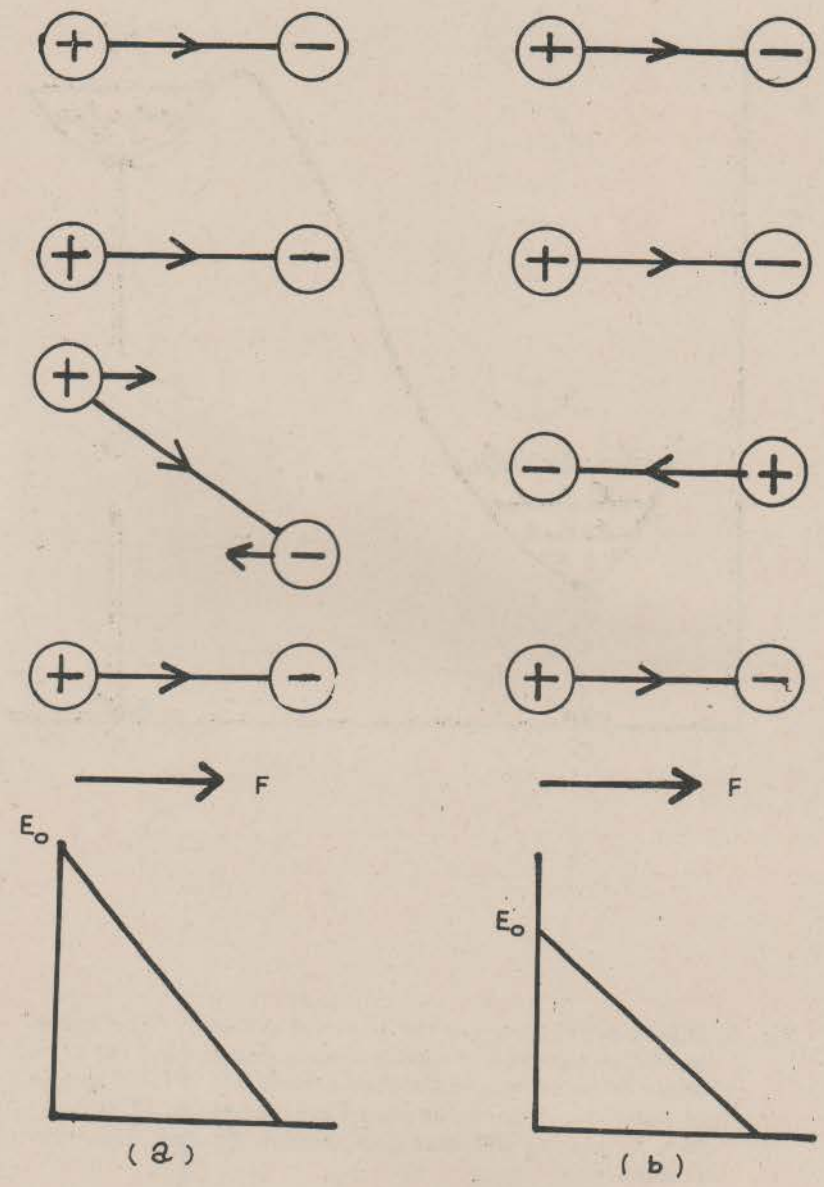


Fig. 9. Depolarization of a dipole barrier by the field, (a) When a field is applied in a direction "parallel" with the orientation of the majority dipoles, dipoles whose orientations are not in line with the field are driven toward the orientation opposite to the field. The lower part shows the potential profile and the barrier potential just before the field application. (b) After the field perturbation, there are two sets of dipoles: the majority of density N_1 oriented parallel with the field and the minority of density N_2 oriented antiparallel with the field. The lower part shows the potential profile and the reduced barrier potential E_o' which is proportional to $N_1 - N_2$.

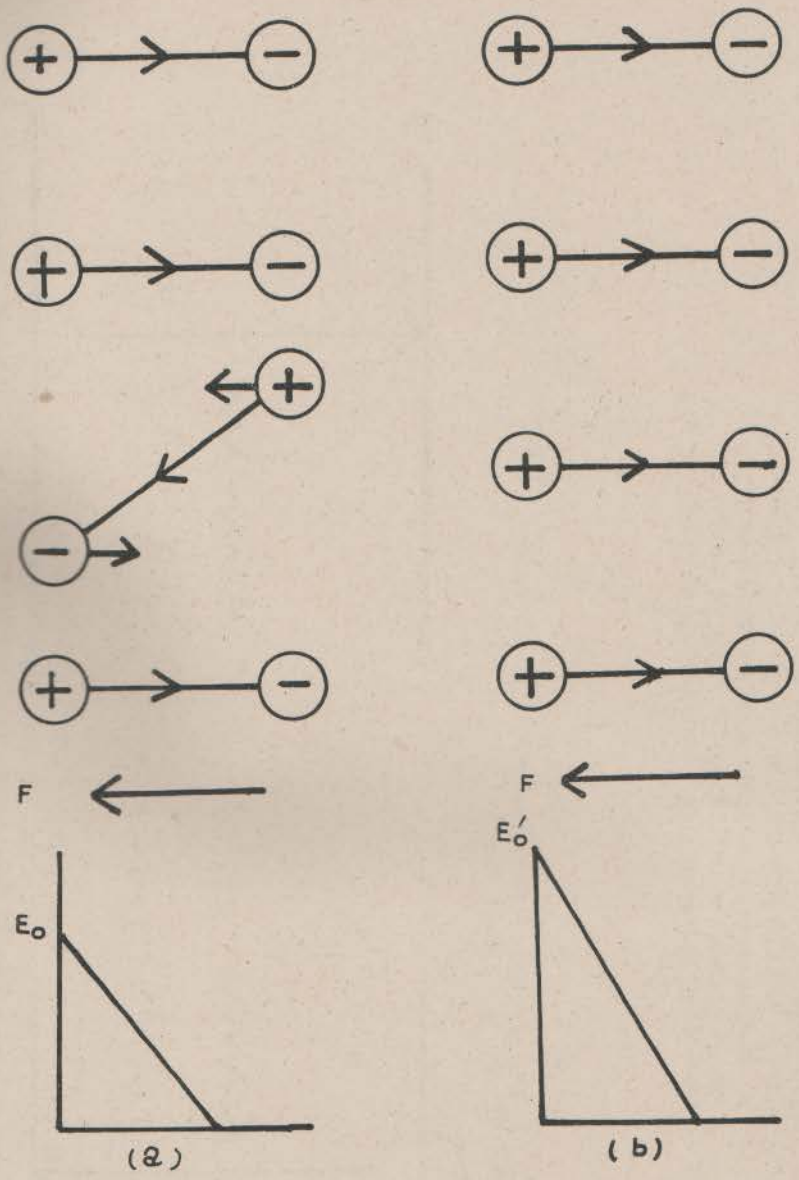


Fig. 10. Hyperpolarization of a dipole barrier by the field. (a) When a field is applied in a direction "antiparallel" with the orientation of majority dipoles, dipoles of other orientations will be driven towards the orientation also opposite to the field. The lower part shows the potential profile and the barrier potential just before the field is applied. (b) After the field perturbation, the number of dipoles with orientation "antiparallel" with the field direction is increased. The lower part shows the potential profile and the barrier potential as a result of repopulation of dipoles. Note that the barrier potential E'_o is increased and hence "hyperpolarization"

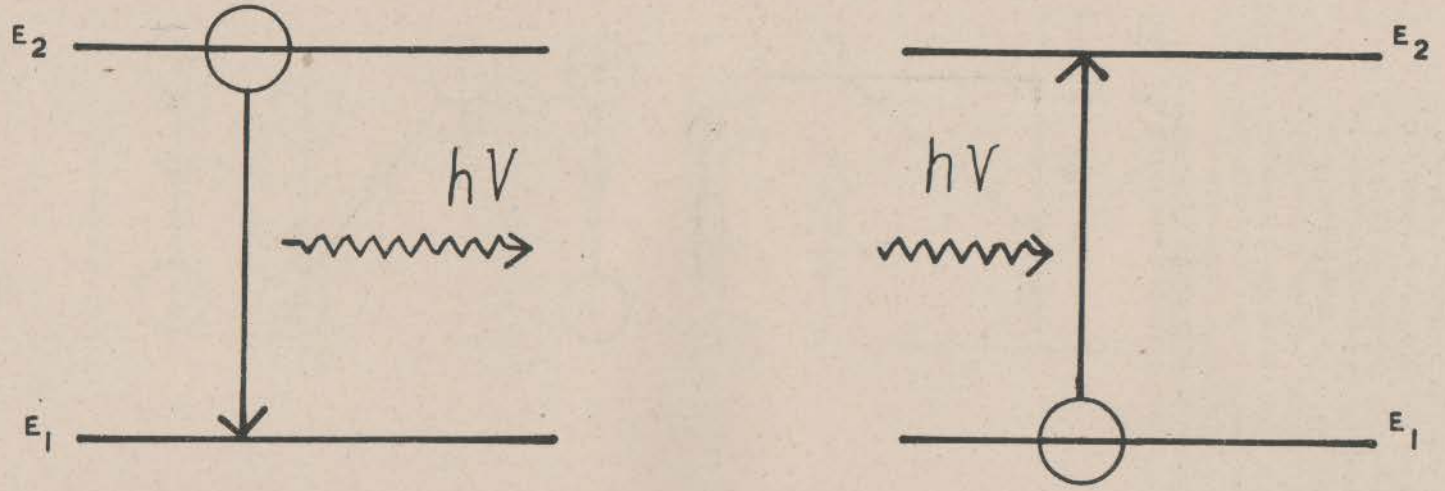


Fig. 11. Resonance absorption. As a molecule flops down (shown on the left), energy quanta $h\nu$ are emitted. These energy quanta could be reabsorbed by a neighboring dipole (on the right) which would then flip up. The phenomenon may be likened to a broadcast station and a receiver turned to the station-emitting frequency.

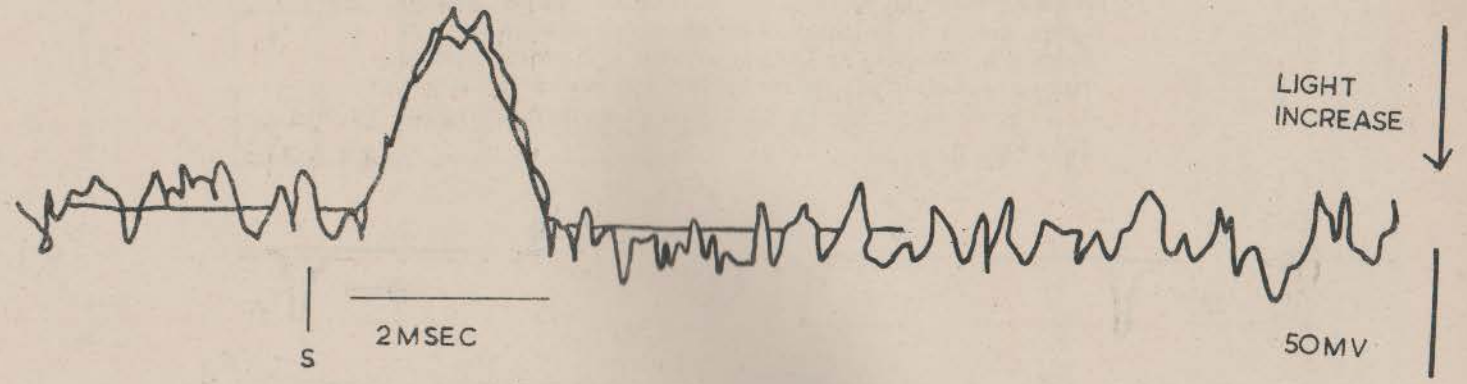


Fig. 12. Birefringence and the action potential in a squid giant axon. The thick noise trace is the light passing through crossed polars with the axon at 45° to the plane of polarization; the central part of the axon and the recording electrode were stopped out. The arrow represents a light increase of 5×10^{-6}/impulse. The thin smooth trace is the action potential recorded. Temperature 7°C. (After Cohen, Keynes and Hille, Nature 218, 438, May 4, 1968).

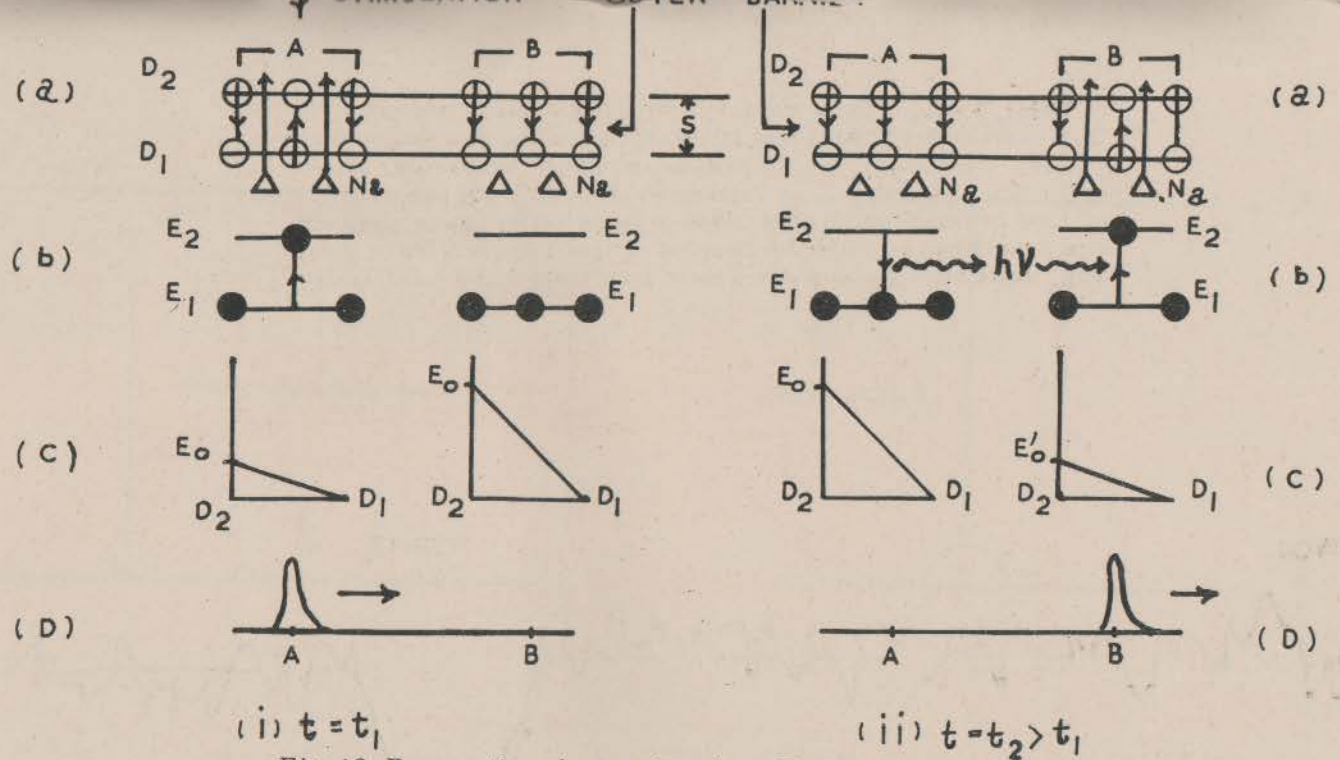
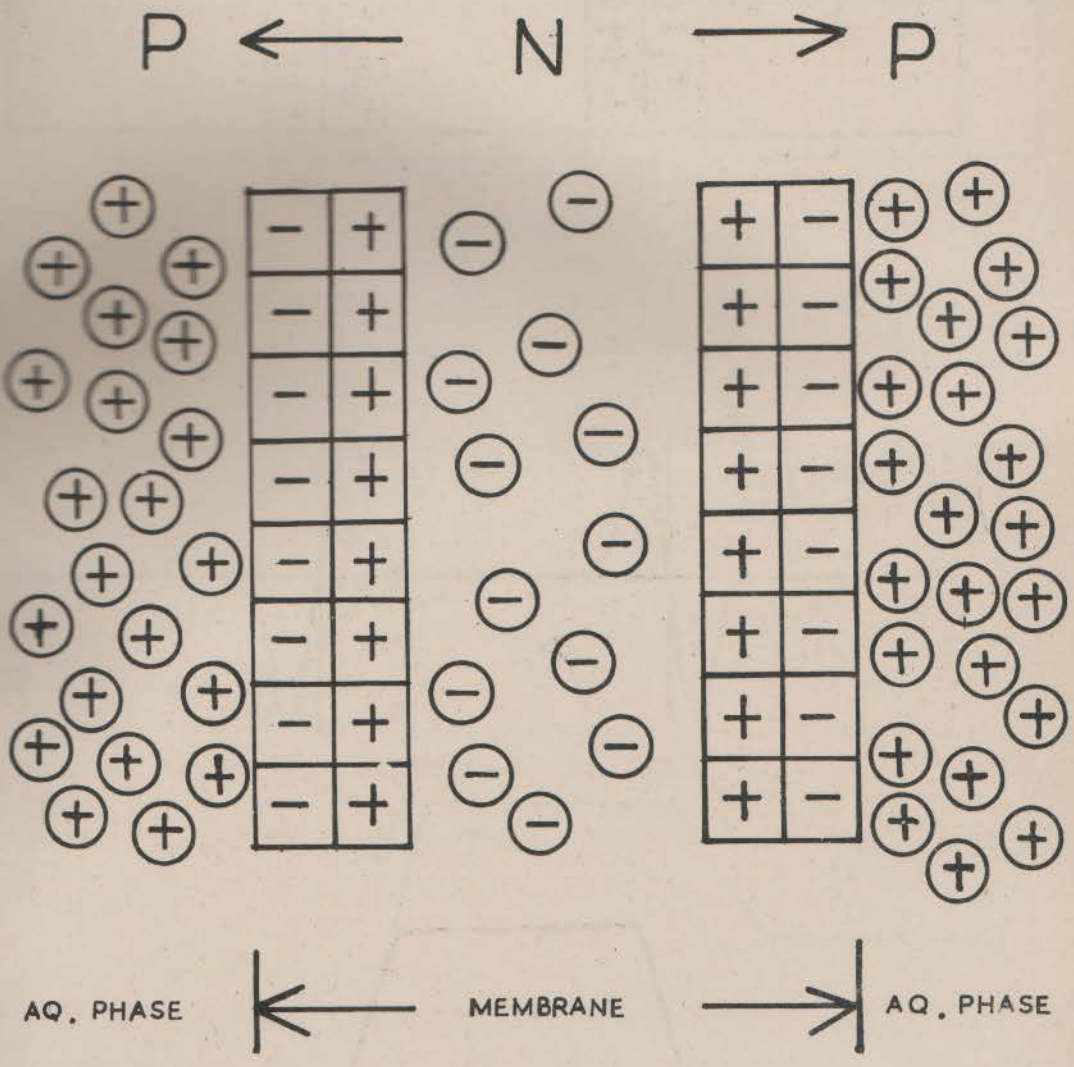


Fig. 13. Propagation of nerve impulse. Events occuring at $t = t_1$ are shown on the left, (a) Stimulation is impressed at A, causing flipping of dipoles (shown as red) and a sudden in-flow (blue lines) of Na ions. Dipoles at B are unaffected. (b) excitation of a dipole at A but none at B. (c) the barrier potential is reduced at A but not at B. (d) a nerve impulse or action potential appears at A. Events occurring at $t = t_2 > t_1$ are shown on the right. (a) a dipole flipping at B and hence in-flow of Na ions (b) Dipole flop at A gives energy quanta $h\nu$ which are reabsorbed by a dipole at B, causing the latter flipping up. (c) The barrier potential at A restores to the resting value while that at B is reduced. (d) a nerve impulse is advanced to B.



ig. 14. Electrical structure of an axon membrane and its immediate vicinity. At the membrane interfaces, there are dipole layers, one on each side with negative poles facing the aqueous phase. Within the membrane, there are excess negative (N-type) mobile ions. In the immediate vicinity of each dipole in the aqueous phase, there is an excess layer of mobile positive (P-type) ions whose concentration is greater than that in the bulk solution. Thus the electrical structure may be represented by P ← N → P where the arrows indicate the dipole layers and their orientations.

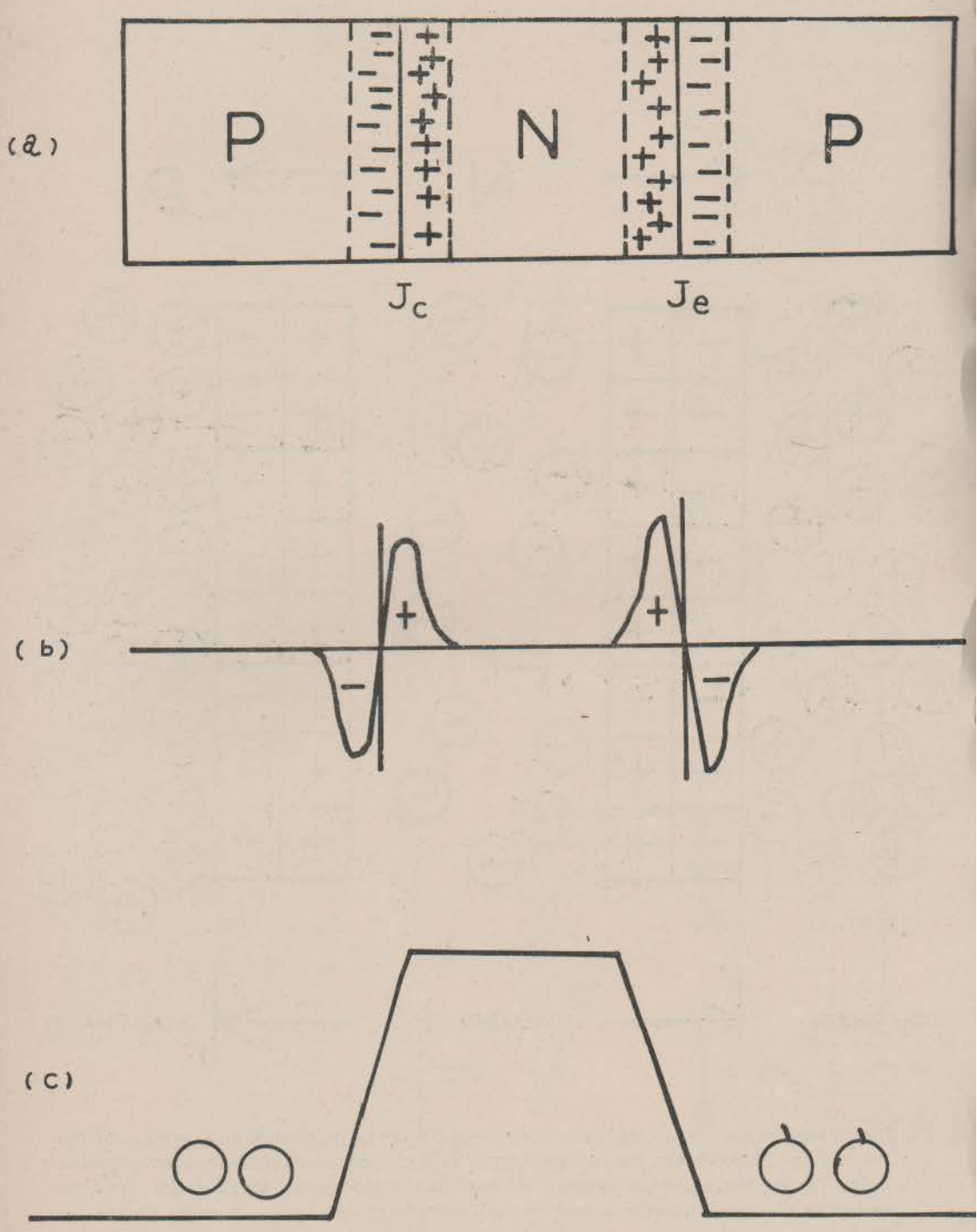


Fig. 15. A bare transistor. (a) A bare transistor consists of three semiconducting sections separated by two junction regions. The P-section has excess positive holes and the N-section, excess negative electrons. The two junction regions are dipole layers with accumulated electrons and holes on the P- and N-sides respectively. (b) the charge distributions in the two junction regions (c) the potential profile in a bare transistor. Because of the high barriers at the junctions, the positive holes on either side are barred from going to the other side. Hence no "transistor action" takes place.

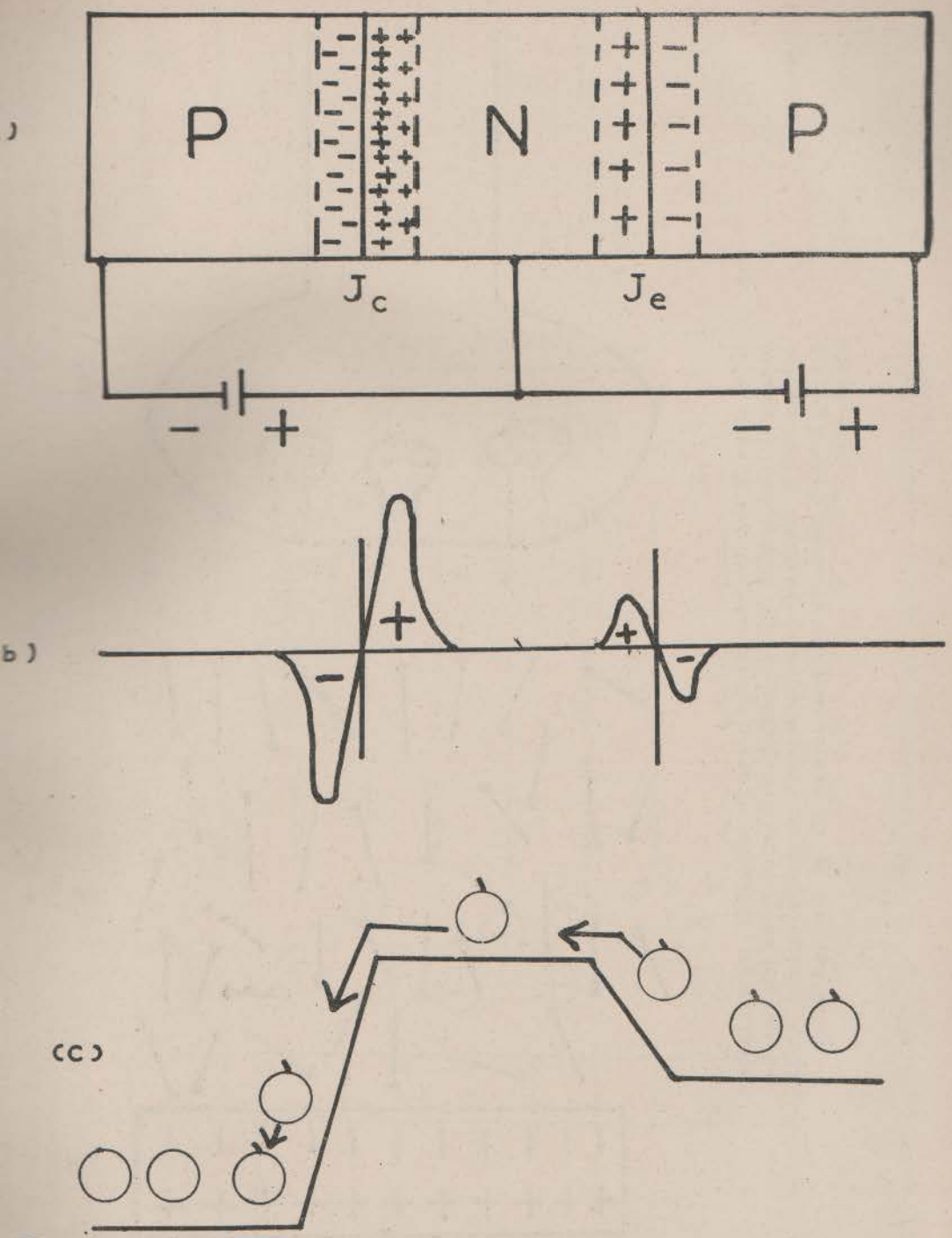


Fig. 16. A biased transistor. (a) The emitter junction J_e is biased in the forward direction (positive to P, negative to N). The forward bias pulls electrons and holes away from the junction and hence reduce the charge density of the dipole layer. The collector junction J_c is biased in the reverse direction (positive to N, negative to P). This bias pushes neighboring electrons and holes toward the junction and hence increases the charge density. (b) charge redistribution under a forward bias at J_e and a reverse bias at J_c. Compare this with that shown in Fig. 15 (b) in a bare transistor and notice the change. (c) the modified potential profile under the biased condition. The emitte barrier is lowered and the collector barrier is heightened. The lowering of the emitter barrier enables the positive holes (shown as apples with green stems) on the right side to overcome the reduced barrier and hence flow to the other side.

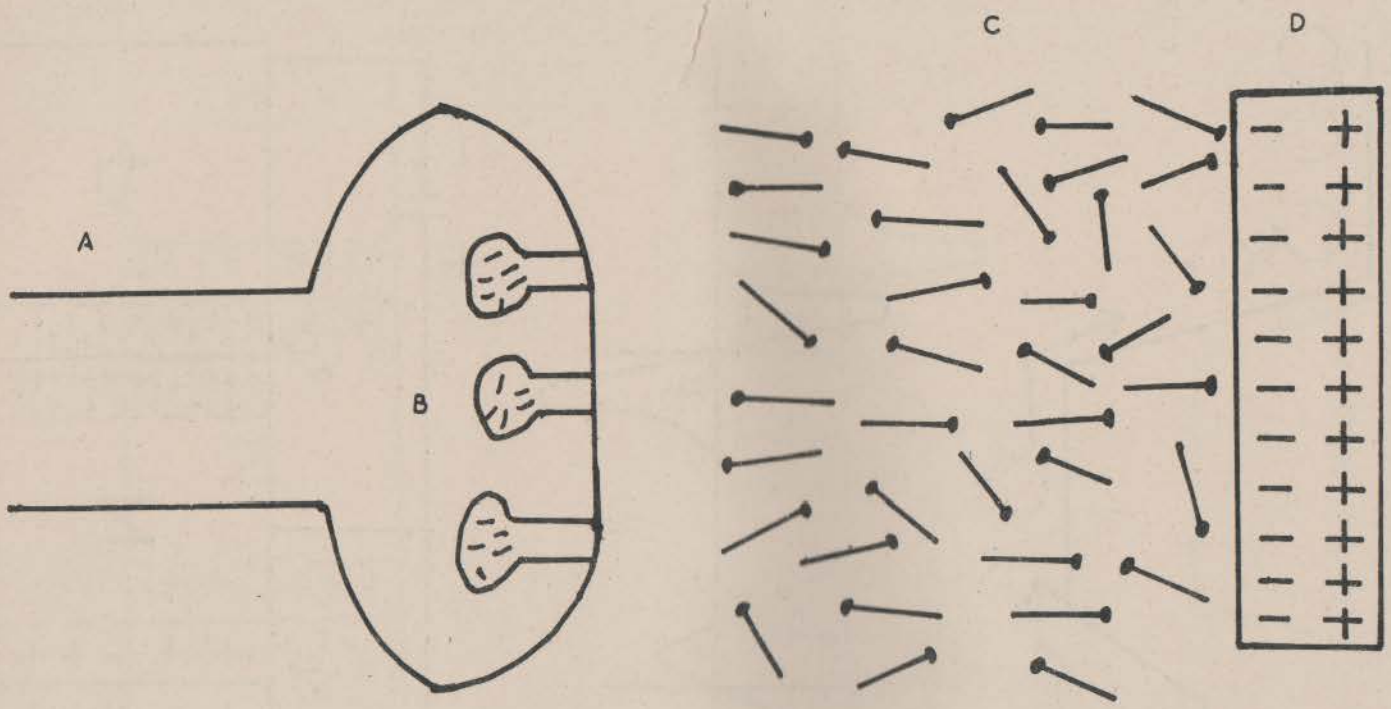


Fig. 17. When a nerve impulse reaches the nerve terminal (A), the enclosed viscles (B) are opened thus releasing ACh molecules (C) to the synaptic cleft. They are initially in random orientations while moving toward the surface (dipole barrier D) of the postsynaptic membrane.

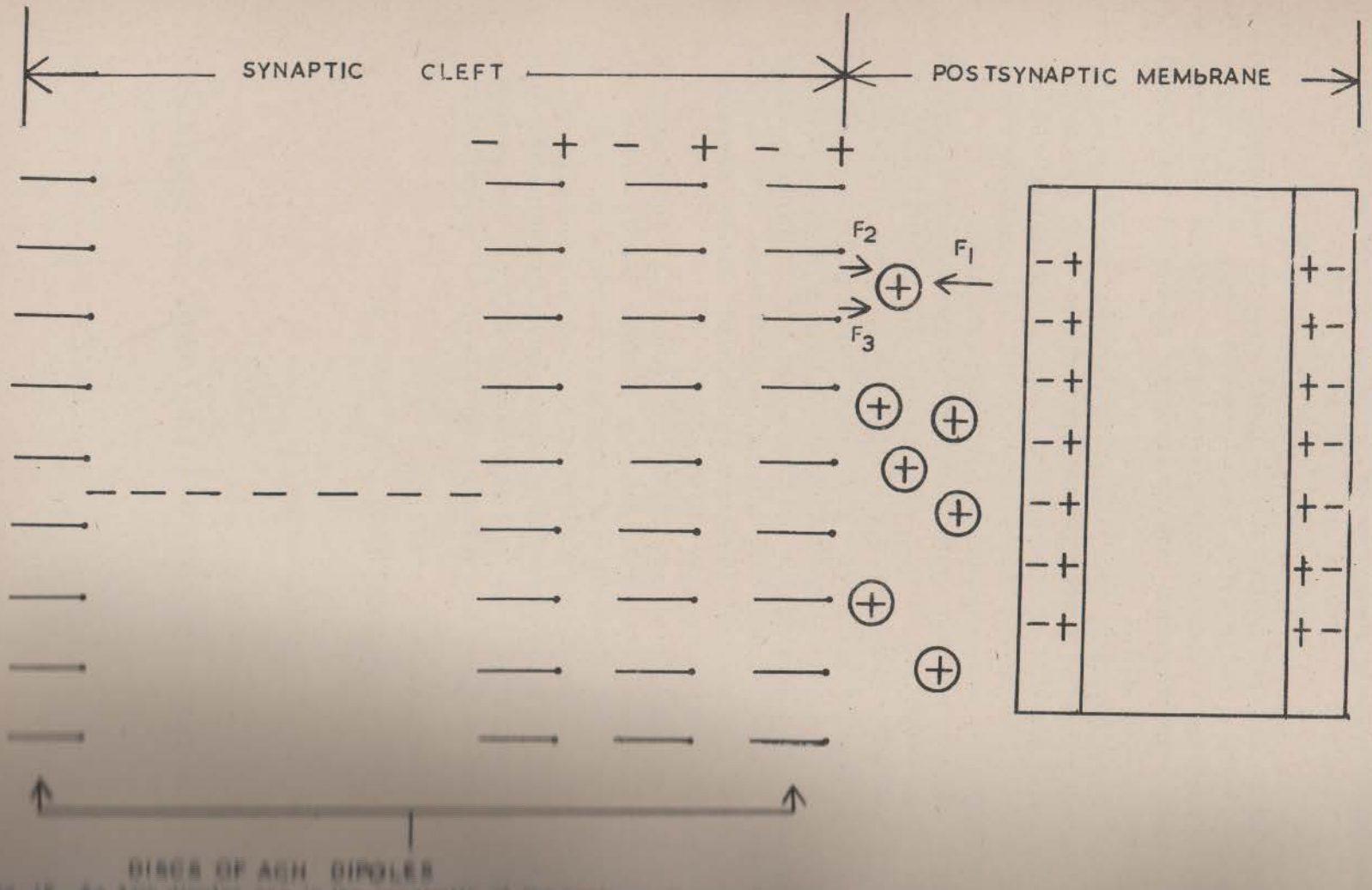


Fig. 18. As ACh dipoles are in the proximity of the postsynaptic membrane, those on the foremost front will become oriented under the near field of the membrane dipole layer. The field will extend backward so as to form ACh dipoles into an array. A positive ion on the cleft side of the membrane dipole barrier is now subject to three driving forces: f_1 from the membrane dipole layer, f_2 arising from concentration gradient and f_3 from the ACh dipole array. The positive ion will be driven into the postsynapse if the resultant force is in the inward direction.