

# Assault by Lightning

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*“To stand against the deep dread-bolted thunder?  
In the most terrible and nimble stroke  
Of quick cross lightning?”*

[William Shakespeare, *King Lear*, Act 4, Scene 7]

**The article highlights the mechanism of nerve injury due to lightning strike, a process in which tiny holes are created in the cells when the human body is struck by lightning. These holes (called electropores) collapse the ionic gradient across the cell and impair its functions, causing slow death of the cell.**

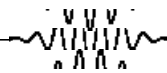
Lightning strike is one of the most awe-inspiring of natural phenomena. It involves an electrical discharge between the atmosphere and the earth and can generate electrical currents and temperatures of very high magnitude. The potential difference between the earth and the atmosphere can reach over 100 million volts and the peak current 30,000 amperes. This can generate peak power of the order of  $10^9$  kilowatts reaching temperatures of the order of 50,000 degrees C. Any conducting object that is in the path of the discharge will also bear the brunt of the assault, including human beings.

Lightning strike results in about 20% immediate fatality. In many instances, individuals survive because lightning passes through the outer surface of the body. But this can have severe long-term consequences. Survivors of lightning may not have external injuries, but are left with deep neurological injuries that can affect both physical and behavioural functions.

Lightning can injure the body in two ways. Once struck by lightning, the electricity follows the path of least resistance, which comprises the nervous system, arteries and veins leading

## Keywords

Electroporation, transmembrane voltage, ion channels, action potential.

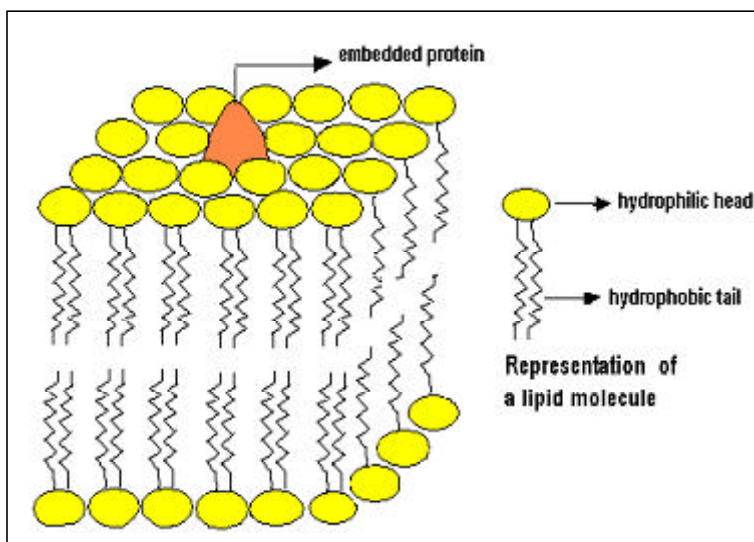


to the heart, the brain and the spinal cord. In this process some cells are killed immediately leading to acute problems. There exists, however, another mechanism whereby some nerve cells are not killed directly; rather, the electricity causes tiny holes in the plasma membrane, a process called *electroporation*. The cell loses its ionic balance, which disables the conduction of nerve impulses, and also is not able to keep the nutrients in or wastes out, leading to the eventual death of the cell. When enough cells are killed, the patient begins to notice various neurological difficulties. Injury due to electroporation remains a very difficult part of diagnosis. The silent process shows its impact only later.

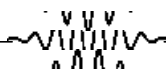
### The Plasma Membrane

Like all cellular membranes, the plasma membrane consists of both lipids and proteins. The fundamental structure of the membrane is the phospholipid bilayer (See *Figure 1*).

The plasma membrane forms a stable barrier between the inside and outside of the cell, particularly for charged molecules. Proteins embedded within the phospholipid bilayer carry out the specific functions of plasma membrane, including selective transport of the molecules. The embedded proteins mediate the



**Figure 1. The lipid bilayer.** The most abundant membrane lipids are the phospholipids. They consist of a polar hydrophilic head and two non-polar hydrophobic tails. In an aqueous environment, the polar heads form electrostatic and hydrogen bonds with the polar water molecules while the non-polar tails repel water molecules. To minimize chemical energy of the system, the two lipid layers cluster together with the inner space between the two layers away from the water molecules. The polar heads are faced outward from both sides, chemically interacting with water molecules, effectively shielding the hydrocarbon tails from the water molecules. This structure is hence called a lipid bilayer.

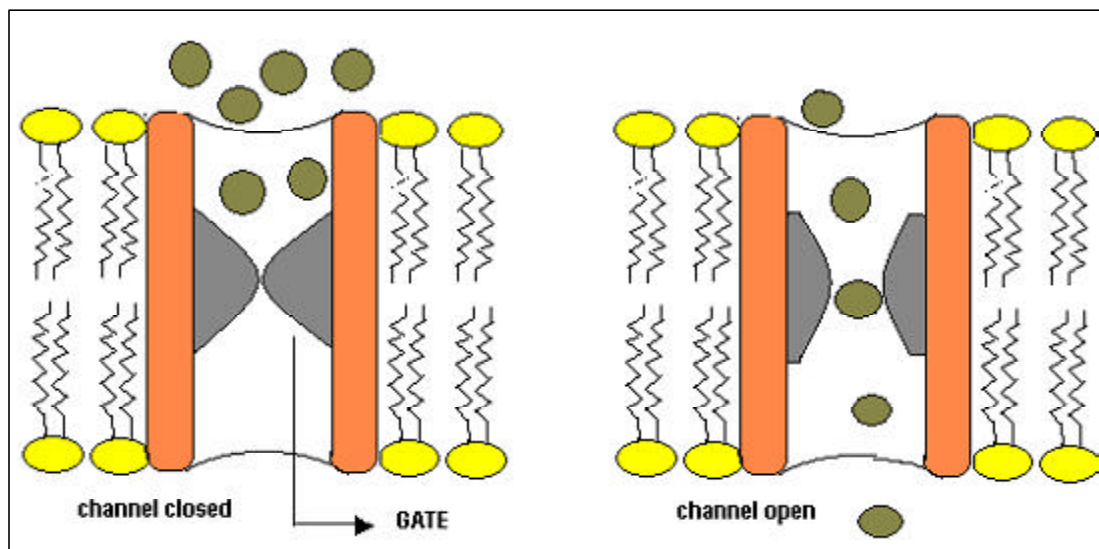


movement of molecules and ions across the plasma membrane. Small molecules of appropriate size and charge can freely pass across the lipid bilayer through specific channels formed by membrane proteins. The best characterized channel proteins are the ion channels that mediate the passage of ions across the plasma membrane. These channels are characterized by a special property: They are not permanently open; instead, the opening of ion channels is regulated by 'gates' that transiently open in response to a specific stimulus. Some channels, known as ligand-gated channels, open in response to the binding of neurotransmitters and similar signal molecules whereas others known as voltage-gated channels open in response to changes in electric potential across plasma membrane. (See Figure 2)

**Figure 2. Model of an ion channel. In closed conformation, the flow of ions is blocked by gate. Opening of the gate allows ions to flow rapidly through the channel. The channel contains a narrow pore that restricts passage to ions of appropriate size and charge only.**

### Establishment of the Transmembrane Voltage (TMV)

The flow of ions through ion channels is dependent on the establishment of ion gradients across the plasma membrane. All cells including nerve cells, contain ion pumps that transport ions through channels actively (i.e. against the concentration gradient). Energy required for traveling against the concentration gradient is derived from ATP hydrolysis. As a result, the ionic composition of the cytoplasm is different from that of the

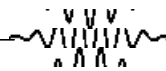


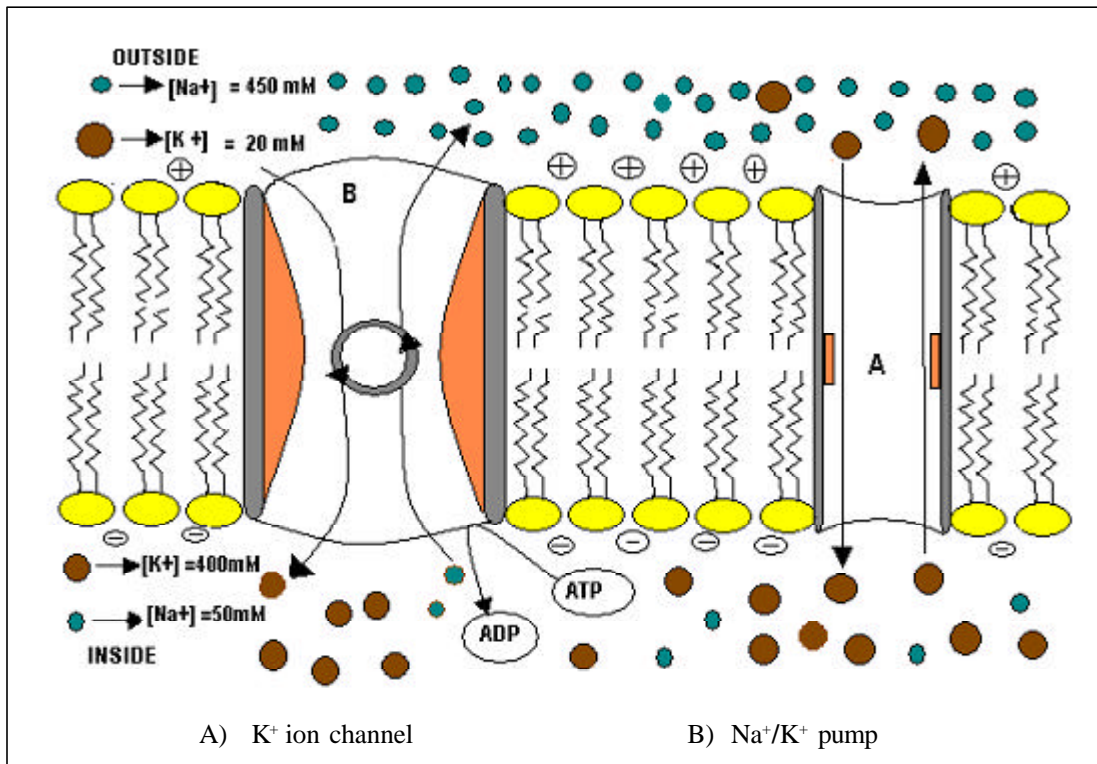
extracellular fluids. For example  $\text{Na}^+$  is actively pumped out of the cell while  $\text{K}^+$  is pumped in. Therefore, the concentration of  $\text{Na}^+$  is about ten times higher in the extracellular fluid than inside of the cell whereas the concentration of  $\text{K}^+$  is twenty times higher in the cytosol than in the surrounding medium.

Because ions are charged, their transport results in the establishment of an electric gradient across the plasma membrane. The permeability of the membrane to  $\text{K}^+$  ions is higher and the 20-fold higher concentration of  $\text{K}^+$  inside as compared to the extracellular fluid drives the flow of  $\text{K}^+$  out of the cell through the channels. However, since  $\text{K}^+$  is positively charged, this efflux of  $\text{K}^+$  from the cell generates an electric potential across the membrane, with the inside of the membrane becoming negative with respect to outside. This membrane potential opposes the continuing flow of  $\text{K}^+$  out of the cell, and the system approaches a dynamic equilibrium state in which the membrane potential balances the  $\text{K}^+$  concentration gradient being maintained by the ion pumps. Thus, in resting state, a potential is established across the plasma membrane. This potential is called Transmembrane Voltage (TMV). (See *Figure 3*).

### **Action Potential: The Nerve Impulse**

The stimulus and response signals travel via nerves in the form of 'action potentials'. The arrival of a signal causes depolarization of the membrane as a result of the opening of a few ion channels that cause a flow of  $\text{Na}^+$  ions along the gradient. The membrane potential changes from  $-70$  mV to approx  $+30$  mV in less than a millisecond. This process is positively co-operative. Depolarization of adjacent regions of the plasma membrane opens the *voltage-gated* protein channels that are permeable to  $\text{Na}^+$  causing the rapid influx of  $\text{Na}^+$  that swiftly depolarizes the cell membrane. This allows the depolarization 'wave' to travel along the axon. The signal is transmitted from one cell to another either directly through synaptic connections known as gap junctions or via neurotransmitters such as acetylcholine across synapses that activate the ligand-gated channel proteins.





**Figure 3. Ion gradients and resting TMV of nerve cells. Only the concentration of Na<sup>+</sup> and K<sup>+</sup> is shown, because these are the ions that function in the transmission of impulses. Na<sup>+</sup> is pumped out of the cell while K<sup>+</sup> is pumped in, so the concentration of Na<sup>+</sup> is higher outside than inside of the nerve cell, whereas the concentration of K<sup>+</sup> is higher inside than outside. The ion pumps, using energy derived from ATP hydrolysis, actively transport the ions across the plasma membrane.**

Thus rapid transmission of nerve impulses takes place over long distances. The depolarized membrane is repolarized rapidly by virtue of the ion pumps that pump out the excess Na<sup>+</sup> ions. Thus, the transmembrane voltage is of central importance in transmission of nerve impulses and the functioning of the nervous system.

### Electroporation

The magnitude of transmembrane voltage is usually -70 mV. This value does not seem much until we realize that the plasma membrane is only 3.5nm thick. Thus, voltage gradient across plasma membrane is 0.07 V per  $3.5 \times 10^{-7}$  cm or 200,000 V/cm. (To appreciate this consider that high voltage transmission lines for electricity utilize a gradient of about 200,000 V/km.)

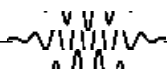
When a lightning strikes a person, it randomly enters and exits through the path of least resistance. The nervous system, upon

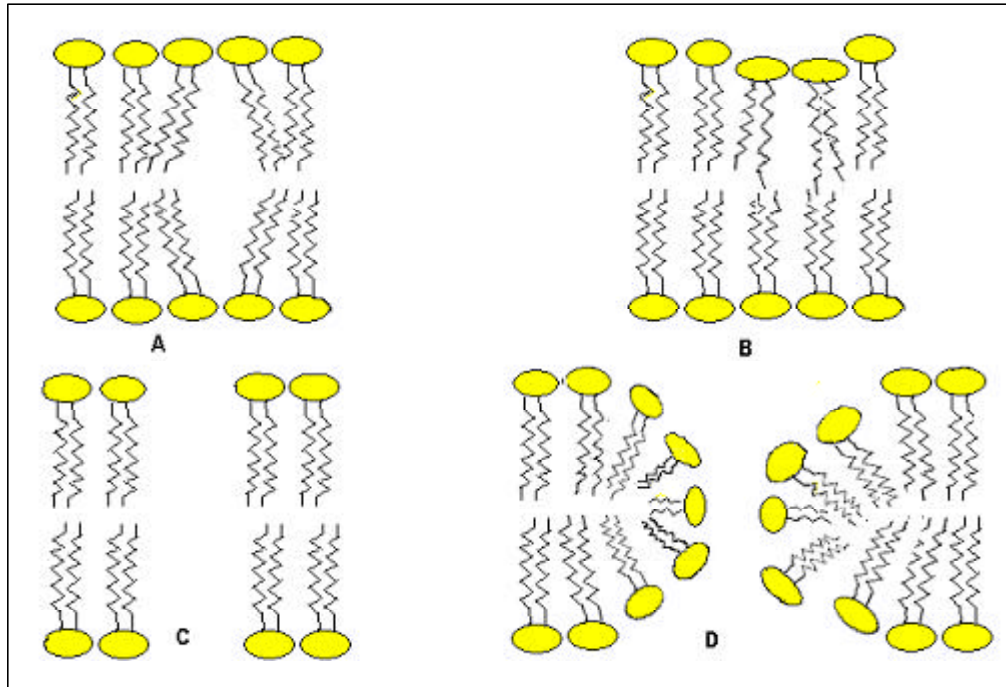
such an assault, is impressed with a very high potential. This potential elevates the TMV, further intensifying the electric field. A high electric field such as this can disrupt the lipid matrix and can create breaks in the bilayer. The plasma membrane acts like a capacitor, the nonconducting hydrophobic interior functioning as a dielectric, sandwiched by the electrically conducting polar heads and ions surrounding the medium. When the voltage across the dielectric (hydrophobic interior) changes due to elevation of TMV, there is an increase in its free energy. In other words the stress on the dielectric increases. Since all systems change in such a way that free energy is minimized, a pore evolves on the plasma membrane allowing the ion gradient to collapse (similar to electric breakdown of a capacitor). It does so by pushing the hydrophilic heads (forming a 'dimple') and then creating an open edge that exposes the hydrophobic region to the water molecules resulting in an unfavorable energy state of the system. The energy required to maintain the circumference of a large hydrophilic pore is significantly lower than that required to maintain a large hydrophobic pore. Hence the hydrophilic polar heads skew in and the pore is now made of hydrophilic heads. (See *Figure 4*)

The free energy change  $\Delta E$  is quantified by the transient aqueous pore model [1], in which electrical pulses of very short duration are impressed on living cells. The relationship between free energy and pore radius is given by the following equation:

$$\Delta E(r, U) = 2\pi r g - \pi r^2 \Gamma - (C_{LW}/2) (\pi r^2) U^2.$$

$\Delta E(r, U)$  is the change in free energy,  $r$  is the radius of pore and  $U$  the transmembrane voltage. In the first term ( $2\pi r g$ ),  $g$  is the linear energy density at the circumference of the pore. The term represents the energy gain due to edge formation of pore. In the second term ( $\pi r^2 \Gamma$ ),  $\Gamma$  is surface energy density of the lipid bilayer membrane; the term represents the energy of a lipid area the size of the pore. Subtracting this from the first term is to account for the energy lost due to cutting of such a lipid area.  $C_{LW}$  in the third term is the difference in specific capacitance





**Figure 4.** Drawings of hypothetical structures for transient and metastable membrane. Configurations believed to be relevant to electroporation. A) lipid layer disruption B) aqueous protrusion or 'dimple' C, D) Hydrophobic pores which are called 'primary pores' and they transform to hydrophilic pores on crossing the critical radius. The transient aqueous pore model assumes that transitions from A®B®C or D occur as  $U$  (TMV) is increased. They form, when transmembrane voltage is significantly elevated, and persist after  $U$  has decayed to a small value through pore conduction.[5].

when water replaces the lipid at the pores. When the pore is formed, water fills the cylindrical region formerly occupied by lipid. Exchanging the dielectric constant of the membrane for that of water effectively changes the capacitance in the pore region and yields the change in electrical energy as indicated by the third term.

From the expression, it is apparent that the pore radius depends on the free energy of pore formation. The transition from hydrophobic pore to hydrophilic pore is of critical importance. Initially all pores appear in hydrophobic version and the transition takes place when their radius, surpasses a critical value. If the pore grows beyond a critical radius, the pore opening re-

mains irreversible. When lightning strikes there is an extraordinary high voltage associated with it and there is a substantial elevation in TMV. This causes a large increase in free energy of the bilayer. The evolving pore grows beyond the critical radius (18nm) and all the hydrophobic pores are converted to hydrophilic pores. These pores are stable and thus the cell experiences irreversible electrical breakdown.

It would be intuitive to ask, would the cell be spared if the radius does not cross the critical value? The answer is both yes and no. If the radius does not cross the critical value, then electroporation is a reversible phenomenon, i.e. the pores seal back. This aspect of electroporation has been successfully harnessed in genetic engineering where the cells are *transiently* opened under the influence of applied electric field and drugs and genes are injected into it via the pores. However, in lightning injury, the voltage and free energy change are of such high magnitude that electroporation remains irreversible.

## Conclusions

The TMV is of extreme physiological importance to the cell; needless to say, its collapse completely impairs the cell function. Maintenance of ionic gradient requires metabolic energy and as the guarding barrier is rendered inoperative, there is a continuous loss of energy. Also the cell is unable to keep the nutrients in or wastes out. Thus the cell eventually dies out. When enough cells are killed by this slow death, the victim notices an onset of various neurological difficulties. The autonomic nervous system, the master control system of the body that regulates the body's involuntary activities such as heartbeat, digestion and temperature control, is particularly vulnerable to electroporation. When this well-coordinated system gets impaired, unpredictable neurological problems start occurring, diagnosis and treatment of which remains a challenge.

## Suggested Reading

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