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# EVOLUTIONARY INTRIGUE OF TRANS-MEMBRANE MOBILITY

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## ABSTRACT

*The multi-dimensional methodology of gaining multiple processes of evolution for proceedings associated with trans-membrane has been contemplated upon. The study looks at the evolution of the trans-membrane, the line of processes associated with the trans-membrane mobility, where there is a clear line of policy drawn by the evolution, starting from the simplest ones to the complex, to the highly complex. There is an emphasis of what these processes are, that begin humbly and then turn to evolve higher; where the trans-membrane processes that did not require energy molecules, and those that required energy for the processes. There is a focus on the highly evolved ion channels such as Ca2+, Na+, K+ and Cl- across the trans-membrane, their nature and more emphasis is thrown on their evolution, with critical commentary on the kind of tactic evolution tries to draw over their evolvement. The study tries to trace out evolution's strategy for the trans-membrane mobility.*
Key words: Evolution, trans-membrane, cell membrane, ion channels:*Ca2+, Na+, K+ and Cl-*

## INTRODUCTION

The transport of molecules across cell membranes has been an acute phenomenon and its understanding has been remarkable, since the development of modern technology. The cell

membrane acts as a barrier to the two totally different environments-the inside and the outside of the cell. The environment surrounding the cell is so much significant to the cell in so much the mechanism to the inside of cell, on the contrary the cell depends on the environment for its nutrients, chemical, and the physical parameters for its own endurance and procreation, directly the cell depends on its environment for almost everything without which its existence would cease by design and in this context it is understood that the environment influences the cell to synthesize molecules that are necessary for the design of its cellular integrity (Barnabas and Lamb, 2011). The subtleness of the development of the membrane barrier between two totally different environments is a dynamic strategy of evolution, since nature has chosen the environment outside to be cautiously supportive to the cell, therefore the environment itself acts as a life support system to the cell. To understand the complexity of the transmembrane it ought to be rather understood on the grounds of its evolvement as well as its functioning, since evolution of the transmembrane has been a long drawn contest for the type of molecules environment synthesizes and the membrane-kind nature modifies to facilitate transmembrane mobility. The cell membrane stands as a remarkable multifunctional design; The modern cell membrane or the cell wall (prokaryotes) has been thoroughly designed in the evolution to combat intense stress conditions where in the membrane acts an haemostatic barrier for the cell, further it acts as a shield to various precursors from outside, takes part in cell multiplication and also acts as a defense mechanism as in prokaryotes. To bring about all these functions on the same platform as in a single layered structure is nature's sensation, perhaps even evolution's best gamble, in all the permutation and combination, if it was never meant to be otherwise. Dualism has been nature's chosen strategy on many fronts in the evolution of organisms and in this context it is 'the molecule and the membrane' 'assimilation and ejection' of the trans-membrane, lower evolved metabolic processes and the higher evolved metabolic processes. Evolution portrays or deals in lower evolved processes in as much as its higher evolved processes, thus it is fitting to understand that evolution seldom presents or underlines only the higher evolved processes in any system. This is immensely evident in the transmembrane potentials in terms of simple diffusion mechanisms across membrane as well as complex and highly specialized ion channels. To decode this particular behavior of nature's duality, evolution never underestimates its own processes at any given levels, should the highly evolved processes

fault point blank, the lower ones are made to do up and visa-versa, more over the situations and the environmental circumstance might have a probability of knocking out either one out of function, in such case the other is made to carry out, but the whole point of evolution is arrive at a process of higher significance, to give birth to structural and metabolic diversity, which is discussed here in terms of transmembrane and its functions. Thus nature seldom leaves its properties to chance.

## EVOLUTION OF THE TRANS-MEMBRANE

The evolution of the membrane is fascinating in terms of speculations, perhaps if it is done in the most logical sense, it could be rather justified or even if it got close to it. It has been noted that the first biologically vital membranes would have been composed of mixtures of amphiphiles with moderately short chain lengths so that such membranes might detain and concentrate macromolecules, but still offer access to ionic nutrient solutes in the exterior aqueous phase(Deamer *et al*.2002).. It has been thought that at some instance in the early evolution, a primitive transport system would have to be evolved, a polymeric compound that could break in the bilayer structure and offer a channel. Certain RNA molecules have been verified to network with lipid bilayers and thus produce ion-conducting channels (Vlassov *et al.,* 2001). It is highly likely that basic amphiphilic molecules could have take part in the formation of primitive membranes rather than complex molecules, (Deamer *et al*.2002) consequently amphiphiles on the support of isoprene derivatives were found to be components of primitive cell membranes, this has been found to be consistent with molecular fossil evidence from evolutionarily deep branching of Archaean microbial populations(Ourrison and Nakatani, 1994). Further, the prebiotic membranes would have contained long-chain acids and alcohols that supply the amphiphilic property of current membrane lipids and these compounds happened to be observed in the carbonaceous meteorites (Lawless and Yuen, 1979; Naraoka *et al.,*1999) and they could have been formed under simulated geo-chemical conditions perhaps similar to hydrothermal systems at high pressures and temperatures.(McCollom *et al.,* 1999; Rushdi and Simoneit, 2001).Thus such amphiphiles could also structure vesicles,(Hargreaves and Deamer, 1978; Apel *et al.,* 2002)the chain length, concentration, amphiphile composition, temperature, pH and head group characteristics, could contribute to the stability of these vesicles. These vesicles tend to

contribute to a selective permeability barrier, as shown by osmotic activity and ionic capture and hence it is also noted that as chain length enlarges, firmness also increases, and vesicles form at lower concentrations.(Deamer *et al*.2002) It is significant that at least one biological membrane is composed entirely of single-chain amphiphiles in a mixture of chlorosulfolipids, fatty acids, and cholesterol (Chen *et al.,* 1976), suggesting that single chain amphiphiles could serve as boundary structures in the membranes of contemporary cells. As we go further we tend to encounter a paradox in that a boundary membrane potentially isolates a primitive catalytic replicating system from the nutrients required for growth. The solution to this is that primitive membranes composed of simple amphiphiles were significantly permeable to ionic solutes. Such that the size would be sufficient to allow molecules as phospholipids of biomembranes since they usually have one or more *cis*-unsaturated bonds in their hydrocarbon chains to guarantee that bilayers stay put fluidity at physiological temperatures.(Deamer *et al*.2002) Therefore, it may seems rational to propose that the earliest biologically important membranes might have been composed of mixtures of amphiphiles with short chain lengths, so that such membranes may capture and concentrate macromolecules, at the same time still provide access to ionic nutrient solutes in the external aqueous phase. Perhaps, at some point evolution, a primitive transport system might have to evolve, may be in the form of a polymeric compound that can penetrate the bilayer structure and therefore present a channel.(Deamer *et al*.2002). Finally, It has been noted that selected RNA species have been observed to network with lipid bilayers and produce ion-conducting channels (Vlassov *et al.,* 2001). Further different levels of functions of the transmembrane are discussed here to understand their levels of functioning in terms of evolutionary processes and significance. We look at the processes which are at the base, as they move towards the higher end developments.

## The Earliest Evolutionary Trans-membrane Processes: The Non-Energy Requiring Ones

**Osmosis** is thought to be one of the earliest processes of the evolutionary transmembrane processes perhaps even the most simplest of all such processes where in water diffuses down the gradient across a semi-permeable membrane and direction of movement of molecules is dependent on the concentration of solutes on either sides of the membrane hence depending

upon the concentration of the solutes, the solution may be hypotonic, hypertonic or isotonic (Soodak and .Iberall, 1978). The further modification of such simple processes include **diffusion** which involves the movement of solute molecules from their higher concentration to their lower concentration along the concentration gradient until an equilibrium is achieved and in case of charged species, movement across the membrane depends on electrochemical potential and also the ability of molecules to diffuse across the membrane depends on it's size and type and the chemical nature of membrane (Cussler, 1986). The rate at which diffusion occurs depends on temperature, permeability coefficient, size of the molecules and the steepness of the concentration gradient (Wijmans and Baker, 1995). The further modification of such processes is the **facillated diffusion** which is diffusion with the help of transport proteins, a mechanism of passive transport for molecules that are unable to diffuse across membrane despite the presence of a concentration gradient. This is mostly due to the large size of the molecule, insolubility of the molecule in lipids and involves the binding of the molecule to be transported to a selective membrane spanning protein called facilitative transporter consequently binding of the molecule on one side triggers the conformational change in the protein, exposing solute to the other surface of the membrane from where it diffuses down the concentration gradient eg., Erythrocyte Glucose transporter which has different conformations, each requiring different steric requirements this mechanism happens to take place much faster than simple diffusion (Yasuda and Petterlin,1973). Usually, hydrophilic molecules that cannot pass freely through the lipid bilayer do so passively through this mechanism. From the above observations it is evident that evolutionary derivative of the biochemical processes begin in the simplest form and consolidate on each of the processes to evolve higher. Simple diffusion barrier that was impermeable to small molecules would not have been useful, since it would have prevented both access to needed substances and elimination of waste products . The evolution of size-selective membrane pores that retained macromolecules but passed small molecules would have partly solved the problem, but more-selective exchange pathways and transport mechanisms for both ions and nutrients would probably have been selectively advantageous

**The Later Derived Evolutionary Trans-membrane processes: The Energy Requiring Ones**

The complex the biological matrix processes, the more energy requiring it becomes, It is henceforth observed that the processes that developed later are the ones that require energy (Sundaresan and Leo, 2007). Some of these include the **Protein pumps**; which involve the transport of molecules against a concentration gradient and involve the expenditure of energy (ATP), absorbance of light, transport of electrons or the flow of other substances down the concentration gradient. Primary active transport involves ATP dependent ion pumps and secondary active transport utilizes the ion gradients generated by the primary transporters. Secondary active/ coupled transport includes Symporters, Antiporters and Uniporter systems (Marger and Saier, 1993). It is observed that a whole lot of protein complex gets associated with transmembrane processes during evolvement. Another such processes is e**xocytosis** which involves the movement of proteins out of the cell across the cell membrane into the extracellular space and it involves the fusion of the secretary vesicle or secretary granule with the plasma membrane and the subsequent discharge of it's contents. The process is also involved in membrane remodeling when compounds synthesized in the golgi are carried in vesicles to the plasma membrane. Further such types of evolutionary development is the e**ndocytosis** which refers to a process by which the cell takes up extracellular macromolecules across the plasma membrane usually they are divided into two categories- Bulk phase endocytosis and receptor mediated endocytosis (Battey *et al* 1999). Bulk phase endocytosis involves uptake of extracellular fluids and thus is also referred to as pinocytosis or cellular drinking. **Pinocytosis** is two types the fluid phase pinocytosis which is a non selective process in which, the uptake of solute is proportionate to its concentration in the surrounding extracellular fluid and the absorptive pinocytosis which is a receptor mediated selective process primarily responsible for uptake of macromolecules for which there are a finite number of binding sites on the plasma membrane (Steinman *et al*.1976). **Phagocytosis** is an another type of such processes which involves the uptake of large particles by the cell via large endocytic vesicles called phagosomes (Sbarra and Karnovsky. 1959) and the **Receptor mediated endocytosis** involves the uptake of specific extracellular macromolecules following their binding to receptors on the external surface of the plasma membrane (Wileman *et al* 1985 ; Stahl and Schwartz,1986). This provides a means to for the

selective and efficient uptake of macromolecules that may be present at relatively low concentrations in the extracellular fluids. Having observed the gradual movement of natural biological technology from the most simple to more assisted forms of processes, evolution tends to move its processes to higher complex development as it follows.

**The Highly Advanced Evolutionary Derived Trans-membrane Mobility: The Ion Channels** The formation of complex processes in evolution is attributed to execute highly defined processes. Formation of ion channels is a developmental process that gave them great degree of freedom as an energy-fueled transport mechanism that moved metabolites bidirectional, in the face of their electrochemical gradient. Ionic fluxes across cellular membranes intercede an incredible variety of biological processes that are vital for the viability of most life-forms. These fluxes are important for cell volume regulation and swimming behavior in unicellular organisms, actions of stomatal pores in plants, and muscle contraction, exocrine cell secretion, and the generation of neuronal excitability in higher animals(Hille,1992). In many cases, these biological processes are eventually dependent on fluxes of specific ions which are firmly regulated by intracellular and extracellular signals. The permeation pathway responsible for moving ions across the hydrophobic environment of cellular membranes is provided by a diverse family of integral membrane proteins called ion channels, whose structural and functional properties have been the focus of long study. Eukaryotic organisms most likely advanced the structure of the membrane by making it less permeable. This principle organization of the cell might have worked well enough to promise both survival of the organisms and the attainment of their primary functions, such as nutrition and osmoregulation. A further prerequisite concerned with is the communication from the external world to the inside of the cell. This mandatory needed a appropriate messenger that, from the outside, would, on certain stimuli, enter the cell and evoke specific biological responses. These processes engage channel forming molecules whose water filled interiors form electrical shunts that essentially offer barrier-less pathways for transport of charged and polar species. A dielectric barrier can be termed for the impermeability of membrane to ion flow on either side. Thus, precise types of integral proteins known as ion channels or ionophores have been formed to transport ions across the membrane. Ion channels display certain important properties; They conduct ions swiftly, highly permeable, many ion channels

are highly selective that is merely certain ion species flow while others are barred and their function is regulated (conduction of ions is turned on or off) in response to specific environmental stimuli. The important ion channels include Sodium-potassium ion channels, calcium channels and chloride channels (Hille 1992; Byrne and Schultz, 1994). Ion channels tend to open and close by gating mechanisms, depending on the channel type, gating stimulus may be binding of a ligand, membrane electric field or both. Thus ion channels are can be termed as 'water filled biological sub-nanotubes' formed by large protein molecules which serve as conduits for rapid, regulated ion movement across the cell membrane. These ion channels play vital roles in electrical signaling, regulation of hormone and neurotransmitter release, control of cell and body electrolyte and volume homeostasis, transduction of external stimuli to sensory signal and many more physiological functions, thus for the cell or organism a smooth functioning of ion channels has become obligate constraint . Members of this integral membrane protein family have evolved unique and stunning properties of ionic selectivity, activation gating which is regulated channel opening, and inactivation gating by regulated channel closure, which make them ideally suitable for a specific biological task. Expression studies have recommended that these proteins are present in essentially all eukaryotes from protists and fungi to plants and animals. In evolution were the functional diversity rich and the appearance of primordial channels is thought about in speculations. Of late studies have provided compelling models for the generation of ion channel diversity, and it has been assumed that these proteins arose very early in eukaryotes possibly through the modification of prokaryotic porins, colicins, or ABC (ATP-binding cassette) transporters (Hille B 1992). A significant additional step in understanding this evolutionary process comes with the account in the issue of the sequence analysis of a prokaryotic gene whose predicted protein product shares extensive topological and structural similarity with eukaryotic K+ channels. This protein most likely represents the most primitive homolog in the spectrum of modern ion channels and may therefore provide the closest look yet at the ancestral ion channel protein. Evolutionary studies are in general complicated retrospective studies attempting to infer the structural origins of modern proteins with information only from the successful survivors of the evolutionary process. Although it would be useful, knowledge of the structure of proteins from extinct organisms is lacking(Hille B 1992).. Traditional biophysical methods have provided detailed functional analyses of ion channel

properties, including the conformational changes underlying activation and inactivation, the mechanisms of ionic selectivity and permeation, and the specific interactions with pharmacological agents. In addition, modern molecular genetic techniques have facilitated the isolation, cloning, and expression of genes encoding ion channels in a range of organisms hence these examinations have exposed that ion channels can be divided into distinct families and subfamilies, with increasingly conserved functional and structural similarity (Hille B 1992).

## EVOLUTION OF THE CALCIUM CHANNELS

The diversity of Ca2+ channels was evident from some of the earliest recordings of Ca2+ currents (Nowycky *et al*., 1985).Basically active Ca2+ transport is similar to most active transports which is a sluggish procedure that compose signals relying on transmembrane transport of the messenger Ca2+ ions predominantly slow. Yet, a presence of concentration gradient for Ca2+ ions which is due to the active Ca2+speed, much quicker signals could be sent from outside the cell to the inside by Ca2+ fluxes through passive-transport structures such as ionic channels(Anderson and. Greenberg, 2001). In the most circumstance the first channel with dual functions such as selectivity toward Ca2+ions and the gating function, with the potential to open and close would prove valuable. Structures such as these passive, and the reason that the Ca2+ gradient across the membrane be present, would have produced an equally precise and so much faster signal than would the active Ca2+transport. Other hypotheses that regard as other types of channels as the primeval channel seem less probable due to the above count. For instance Na+ channels is thought to have appeared relatively late, as they were rarely found in lower animals such as Protozoa, Porifera, and Coelenterata. On the contrary, K+ channels, considered very mature though, would have seldom served a purpose if a K+ gradient across the membrane was not established, as also in Na+ channels. At about this occasion, the internal of the cell had probably accumulated previously a certain quantity of membrane-impermeable macromolecules for cellular metabolism, each carrying several negative charges and may have slowly drifted the resting membrane potential away from neutrality and established salt gradients. It has been noted that in eukaryotes, resting membrane potential ranges between -20 and -90 mV. (Anderson and. Greenberg, 2001) Voltage-gated channels can actually be

operated only by a small change of membrane potential which is a far too slow process in these primitive organisms, relying as it does on translocation of charges (ions) across the membrane through active-transport mechanisms (Catterall *et al,* 2003), although a potential difference across the membrane was probably achieved by this time, the first Ca2+selective channels could have been gated by stimuli other than membrane voltage, it is highly likely that these primitive Ca2+ channels were directly activated by mechanical or chemical stimuli from outside(Anderson and. Greenberg, 2001). The pore-forming unit of all known Na+ and Ca2+ channels, is a single protein composed of four linked domains, each of which is highly homologous to a single 6-TM K+ channel protein. Like K+ channels, Na+ channels, and, to a greater extent, Ca2+ channels, demonstrate certain structural and functional variation. The diversity of Ca2+ channels was apparent from a number of earliest evidence of Ca2+ currents which exposed three broad classes L-type currents, T-type currents, and N-type currents, many of which co-exist in the same animal if noting the same cell. Because L and N type currents both require large depolarization's for activation, they were classified as high voltage-activated currents, whereas T-currents, which require only small depolarization's were classified as low voltage-activated LVA (Anderson and. Greenberg, 2001).

## EVOLUTION OF THE SODIUM CHANNELS

Sodium channels are integral membrane proteins that form ion channels, conducting Na+ ions through cell membrane. (Hille, 1992; Littleton and Ganetzky,2000). They are classified according to the trigger that opens the channel for such ions, i.e. either a voltage-change by voltage-gated sodium channels or binding of a substance such as a ligand to the channel by ligand-gated sodium channels. In certain excitable cells such as neurons, myocytes, and certain types of glia, sodium channels are responsible for the rising phase of action potentials. It is thought that Na+ channels were derived from Ca2+ channels at the origin of the nervous system (Hille. B, 1992) Voltage-gated sodium channels usually consist of an alpha subunit that forms the ion conduction pore and one to two beta subunits that exhibit several functions including modulation of channel gating (Catterall WA et al 2003). Expression of the alpha subunit singly is sufficient to produce a functional channel. The family of sodium channels has known to have nine known members, with amino acid identity less than 50% in the transmembrane and extracellular loop regions. The proteins of these

channels are named Nav1.1 through Nav1.9. The gene names are referred to as SCN1A through SCN11A, where the SCN6/7A gene is part of the Nax sub-family and has uncertain function. The likely evolutionary relationship between these channels, based on the similarity of their amino acid sequences, and most sodium channels are distinguished not only by differences in their sequence but also by their kinetics and expression profiles. Voltage dependent Sodium channels were thought to be evolved from Calcium channels at the origin of nervous system development thereby bestowing the facility to carry out action potentials exclusive of interfering with intracellular calcium this was armored by noticeable deficiency of sodium current in sponges (Anderson and. Greenberg, 2001). Before the application of molecular cloning techniques to Na+ channels, the basic idea was that there would have been many different K+ and Ca2+ channels to detail the variety of currents that had been recorded from diverse tissues, where there were probably only one or a few Na+ channels. Na+ currents from organisms as diverse as mammals and jellyfish were remarkably similar to all were fast, transient currents that served to rapidly depolarize the cell's membrane in order to propagate the signal down the length of an axon, or to trigger other events e.g. con- traction, secretion(Anderson and. Greenberg, 2001). Few noticeable variation between various Na+ currents were a certain pharmacological peculiarities TTX-resistance in some instances and the result that certain Na+ channels could be blocked by rare channel blockers including certain cone shell toxins. When sequence data became available, it became evident that there are a variety of different Na+ channels, and it is now recognized that mammals have 11 different Na+ channel subunit genes for review, more over, almost all mammalian Na+ channels were noted to be remarkably similar. Whereas several mammalian HVA Ca2+ channels L vs non-L share as little as 30-35% identity. Most dissimilar mammalian Na+ channels demonstrate over 75% identity to each other. Multiple Na+ channels are also found in invertebrates, but to a more limited extent (Anderson and. Greenberg, 2001).

Voltage-gated Na+ channels play certain important functional roles in the generation of electrical excitability in most vertebrate and invertebrate species. These channels are members of a superfamily that includes voltage-gated K+, voltage-gated Ca2+ and cyclic-nucleotide-gated channels. There seems to be around nine genes encoding voltage-gated Na+ channels in mammals, with a tenth homologous gene that has not been shown to encode a functional channel. Other vertebrate and invertebrate species have a smaller number of Na+

channel genes. The mammalian genes have been classified into five branches in a phylogenetic tree, and they are localized on four chromosomes. Four of the branches representing the four chromosomal locations probably resulted from the chromosomal duplications that led to the four Hox gene clusters. These duplications occurred close to the emergence of the first vertebrates. The fifth branch probably evolved from a separate ancestral Na+ channel gene (Anderson and Greenberg, 2001). There are two branches in the invertebrate tree, although members of only one of those branches have been demonstrated to encode functional voltage-gated Na+ channels. It is possible that the other branch may have diverged, so that its members do not represent true voltage-gated Na+ channels. Vertebrate and invertebrate Na+ channels appear to be derived from a single primordial channel that subsequently evolved independently in two lineages. **Evolution of the Potassium Channels** The evolution of K+ channels is a subject of much conjecture, but the manifestation of this family right through the biological world indicates that they were ancient proteins, not the highly advanced cells that were considered when they were described at earlier times (Jan and Jan, 1997). In eukaryotes, eubacteria, and archaeabacteria the genomes which are sequenced contain at least one K+ channel (Anderson and Greenberg, 2001). The principal subunits of K+ channel are found to be the major and highly varied of the ion channels, this thought to be due to the large number of genes coding for K+ channel principal subunits, not only this but the other processes such as alternative splicing, causing multiple mRNA transcripts from a single gene, heteromeric assembly of diverse principal subunits, RNA editing and finally posttranslational modifications. (Coetzee *et al,* 1998**).** The most diverse, structurally and functionally are the voltage-gated K+ channels, the literature on these channels is already abundant (Gary Yellen, 2002). The 6-TM building block constitutes the basic pore-forming unit of most eukaryotic voltage gated K+ channels, with the functional channel being formed by the assembly of four of these subunits in the membrane. Earlist studies also identified four original members of the voltage gated K+ channel family Kv1, Kv2, Kv3, Kv4 which, respectively, correspond to the *shaker* (Papazian *et al* .1987) *shab*, *shaw* and *shal* channels originally identified in *Drosophila* (Gutman GA *et al.*2005), more recent work with mammals has identified other varieties Kv5,6,8,9. Furthermore, many Kv families contain several members i.e. Kv1.1..Kv1.6; Kv2.1..Kv2.2; Kv3.1..Kv3.3; Kv4.1..Kv4.3; Kv9.1..Kv9.2., (Gary Yellen, 2002). each with slightly different functional

properties that in many cases can be linked to structural differences (Anderson and Greenberg, 2001). Because the functional tetrameric channel is formed by the assembly of four subunits, which need not be identical but can be closely related subunits or splice variants thereof, the number of potential structural combinations is enormous (Gary Yellen, 2002).

## EVOLUTION OF THE CHLORIDE CHANNELS

Chloride channels are a superfamily of not so well understood ion channels consisting of approximately 13 members. Chloride channels demonstrate a diversity of important physiological and cellular roles that include regulation of pH, volume, homeostasis, organic solute transport, cell migration, cell proliferation and differentiation hence the CLC family operates its membrane proteins in diverse physiological contexts in functioning of its transmembrane movements (Jentsch, 2008). Two distinct mechanistic subtypes of these proteins have been grouped: Cl−-specific channels and proton-coupled Cl− (or, in plants, NO3−) exchangers (Zifarelli and Pusch, 2007). And also on the basis of certain sequence homology the chloride channels can be subdivided into a number of groups, these channels have been constructed as homodimers where every subunit function as a full-fledged exchanger (Nguitragool and Miller, 2007; Zdebik et al., 2008), these proteins trade ions athwart the membrane in opposite directions of two Cl− ions per H+ in the proton-coupled Cl− exchangers (Accardi and Miller, 2004; DeAngeli et al., 2006; Nguitragool and Miller, 2006; Graves et al., 2008; Miller and Nguitragool, 2009). This family of these ion channels contains 10 or 12 transmembrane helices, each protein forms a single pore in their structures further, it has been shown that some members of this family form homodimers, in terms of primary structure, they are unrelated to known cation channels or other types of anion channels. Three CLC subfamilies have been found in animals. CLC-1 (P35523) is involved in setting and restoring the resting membrane potential of skeletal muscle, while other channels play important parts in solute concentration mechanisms in the kidney. Chloride channels tend to keep up secure ion quantities contained with-in plant cells (Zifarelli and Pusch, 2007). The hypothesized modification through evolution from primeval ABC transporter molecules to CFTR Cl− channels (Childers.M *et al*. 2007) engross considerable structural modification of the protein molecule to eliminate one of the two gates. Yet, for CLC family constituent,

the evolution from CLC antiporter to CLC Cl– channels could engage additional delicate modifications if the hypothesized CLC antiport mechanism mentioned over is accurate. In order to eliminate one gate, uncoupling the Cl– and H+ transport could convene the rationale that jamming the H+ transport, as it has been observed in the mutational studies of Gluex and Gluin, has altered the bacterial antiporter into a Cl– uniporter (or Cl– channel) that is replacing any of the residues with nonprotonatable side chains removes H+ but keeps the Cl– movement (Picollo and Pusch, 2005; Scheel *et al*., 2005; Accardi and Miller, 2004; Jayaram *et al*., 2008; *Zdebik et al*., 2008; Accardi *et al*., 2005). For CLC members, the remainders that match up to Glu-203 of CLC-ec1 (the Gluin) is therefore no more a residue among the channel members, on the other hand a glutamate residue is conserved in the members which was understood as transporters. It is rather hard to envisage that evolution change a transporter into an ion channel by a single amino acid mutation, though such a relative among the sequence analysis and functional classification is exceptional. Conceivably further wide structural changes are implicated, and supplementary academic and investigational work is desirable to intensify the knowing of the structural/functional association among ion channels and transporters in the family. Future work could undo the speculations thus made and also throw new light of our understanding of the above said.

## CONCLUSIONS

The evolutionary processes are steady from the simple to the compound to the highly complex, this reflects literally on the transcending developments of transmembrane potentials of the cell. On the contrary the very evolution of the cell membrane is a multi-dimensional colloquial strategy without a stringent policy. It has been noticed that, in the case of the non-energy dependent (passive), energy dependent (active) and the highly complex trans-membrane mobility processes are generally understood to play a pivotal role in the subsistence of the cell and subsequently on the organism throughout the evolution. They can be considered as one of the many indicators of the patterns of adaptability shown by different biological systems for different environmental parameters and circumstances. It seems that evolutionary systems do not mind the expenditure of energy molecules for the developing complex processes, consequently progressive forms of different processes were observed from non energy requiring to energy requiring, perhaps after all in the interest of the cell's

energy bank, use of energy molecules to propel transmembrane processes is not at all a taxing affair to the cell because the cell had already developed its energy dynamo efficiently and therefore probably ready to take on progressive leap. When the higher processes are observed in the evolutionary interest of the ion channels there are hypothesizes, that mostly speculate but with closest logical debate. Each of the ion channel has evolved in its pattern but having a common theme such as specificity, protein subunits, voltage gating, pore size etc.Ca2+ channels have been thought to be the earliest evolved channels due to the earliest recordings of Ca2+ currents according to one hypothesis, their fluent ability to communicate to the inside of the cell. Na+ channels have been associated with complexity of developing the voltage gating, though they have been known to evolve relatively late, they were thought to be evolved from calcium channels at the origin of nervous system development thereby conferring the facility to carry out action potentials exclusive of interfering with intracellular calcium. The K+ channels have evolved like no other channels and diversified far higher than other channels, they are found far and wide in organisms in all most all the three domains, their expression in the genomes make them even more complex, work on the K+ channels is more intense and highly explored and vast literature being available on them. Finally, the chloride channels have been thought be evolved from a transporter molecule and they have been known to maintain the homeostasis of the organism. It has been observed that the mathematics of the formation of the diversity, the subunits and every single process has been highly stringent and clearly accurate so as to deliver the requirements for the cell. Evolution has always dealt its processes in a mixture of simple and complex, accommodating both without discrimination. The mode in which evolution plots it own biochemical processes, forming a laid out map over a colossal period of time, a critically designed, is conceptualized as an evolutionary intrigue for processes such as trans-membrane mobility. Evolution tends to uphold several of its policy processes at any given time, for evolution is the final strategist.

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