The eukaryotic mechanism directed by bioelectricity: creation and enlightenment (I)

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Abstract

i. The electricity and electromagnetic field are the intrinsic property of the nature and universe, and the life created by the nature. The eukaryotic cells, rather than prokaryotic cells, perform the complicated and highly developed function of the organisms. On eukaryotic mechanism, two vital issues are urgent to update: (i) whether or not the bioelectric excitation operates in the interior of eukaryotic cells and how it operates the activity of eukaryotic cells; and (ii) how the organelles are managed into the coordinated and united work, and from where the potent dynamic energy that support the activity of organelles generates.

The eukaryotic cells are prior to prokaryotic cells with highly developed membrane-bound organelles. What this work focuses on is not only the complicated membrane system of eukaryotic cells, but with the bran-new insight: as an engineer, given the materials and the layout of eukaryotic membrane system, what does it imply? — This work discovers the intrinsic principle and mechanism on eukaryotic working directed by bioelectricity and bioelectromagnetic field, from materials and layout, to flowchart, presenting the perfect and ingenious design art of the nature on the creation of bioorganic electricity and eukaryotic working, which endows human being the precious enlightenment on the generation and utilization of bioorganic electricity.

ii. Based on the highly developed molecular cell biology researches, this work brings the in-depth insight into the static layout and dynamic relationship of eukaryotic compositions, combined with the knowledge on medical electrophysiology of action potential. The indeed eukaryotic mechanism is

grounded on the biomolecular network and operated by the electrophysiologic resonant system, by which the eukaryotes performs the complicated function with energetic vitality. The cell is the combination of the strictly organized biomolecules and bioelectricity, which contains the novel subject of molecular biology-founded cell electrophysiology: as an bioengineer, given the resonance which is optimal for generating the coordinated and united work among components, and given the electric oscillation which is optimal for generating energy, what biomaterials and how layout are designed to operate electric oscillation and resonance? — In the way of molecular biology-founded cell electrophysiology, the nature creates the eukaryotes that perform the marvelous functions of lives, and highlight the ingenious principle on bioorganic energy generation with the property of ecological, sustainable, convenient and portable, and digitally perpetual operation.

iii. The modern information technology and modern energy development and utilization have achieved the unprecedented height. Can a bran-new leap come up in the future, not on quantity, but on quality? — To compare, the source and channel on the existing principle are monistic, while it is stereo (interacted)-dualistic in the relationship of inter-variation that the generation of information and the generation, transmission and utilization of electromagnetic energy of eukaryotes ground in ingenious relativity, from where the variation and creation in unity generate.

This work highlights as follows:

I. The principle and operation mechanism of bioorganic electromagnetic field and bioorganic electricity generation of eukaryotic cells.

i. The interaction between cell matrix and mobile charged ions: the formation of bioorganic electromagnetic field

ii. The sandwich structure and the compartmentalized functional zone of organelle membranes: the generation of maneuverable bioorganic electricity

iii. The configuration and layout of organelle membrane systems: the bioorganic electric resonant components and resonant coupling

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II. The creation of eukaryotic bioorganic energy and enlightenment: from principle to design

i. Bioorganic electricity: bioorganic energy resource and power system

ii. Bioorganic information: bioorganic smart (informationized) power system

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iv. The essential principle in the creation of bioorganic electricity generation: the ingenuous relativity

Keywords

eukaryotic mechanism, eukaryotic bioelectric excitation, eukaryotic bioelectromagnetic field, bioorganic electricity generation, bioorganic information, bioorganic energy resource; cell electrophysiology, biomembrane, plasma membrane, endoplasmic reticulum, sarcoplasmic reticulum, mitochondrion, nucleus, Golgi apparatus; action potential, neuronal excitation, skeletal muscle excitation, muscle contraction

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The eukaryotic mechanism directed by bioelectricity: creation and enlightenment

Part I The materials and layout for generating bioorganic electricity

I The bioorganic electricity generated by action potential: process, prerequisite and rules

The bioelectricity created by action potential which generates the regular electric currents is the property of the living organisms to perform the function. The course of action potential is formed with the transmembrane motions of mobile ions (mainly positively charged ions), which is composed of two processes: the double-diffusion process in which the ions move down concentration gradients forms the coupled depolarization and repolarization phase in the form of convection, and the course of convection (depolarization and repolarization) causes the displacements of ions into their counter sides; and the double-exchange process in which the ions move against concentration gradients forms

the resting phase in the form of double-exchange, which causes the double-displacement of ions into their counter sides, returning back into their original regions. The course of action potential is composed of the double-diffusion (convection) which forms the extrinsic visible “real part” of action potential with the depolarization and repolarization phase, and the double-exchange which forms the intrinsic invisible “imaginary part” of action potential with the resting phase.

The diffusion motion is that the ions move from the region of higher chemical potential to the region of lower chemical potential following the chemical potential gradient, which is driven by thermodynamics to get individual chemical potential equilibrium (diffusion equilibrium). The prerequisite for the diffusion motions of depolarization and repolarization in the counter directions is the asymmetric transmembrane distribution of ions on the counterpart sides of membrane, which forms the significant thermodynamic chemical potential difference of ions in the counter directions. This prerequisite is achieved by the double-exchange motion between ions.

The double-exchange (double-displacement) is the ions are simultaneously exchanged from the original regions into the counter sides against concentration gradients in face-to-face counter directions. The course of double-exchange results from electromagnetic dynamics to get systemic electromagnetic equilibrium between exchangers and metal ions. It forms the significant concentration difference of ions with the selective asymmetric distribution on the counterpart sides. Gibbs-Donnan equilibrium is used to describe the behavior of charged particles against diffusion equilibrium, which fails to distribute evenly but causes a difference of chemical potential arising between two parts. Via the process of double-exchange, the result of ion distributions after double-diffusion is inversed to restore into the original state.

The double-exchange of ions, which is applied in the industrial processes of purification, separation, and decontamination to move out and purify ions, are performed by the exchangers (beds) of the ion-exchange resins made of charged polymers. The negatively charged polymers, which contain net negative charged groups to offer high affinity for counterions (cations) with the electrostatic attraction, take effect as the exchangers that support the sorption and exchange of positively charged ions (metal ions and proton) onto the surface of negatively charged polymers via the electrostatic attraction in order to gain electric neutrality [1 Crini]. (*The polymers may act as the amphoteric exchangers for exchange both cations and anion, because the component of positive charges is also contained by the polymers; the anion, e.g., chloride ion, may participate in some type of action potential either*)

The process of ion exchange has properties as follows: it is a reversible process that allows ions to freely move back and forth by adding or removing the ions; the polymer exchangers have binding

preferences for certain ions compared to others, dependent on their chemical structures; the double-exchange is predominated by the cation higher in reactivity; and the double beds which are different in electrostatic intensity instead of the single bed are more efficient for double-exchange.

The reactivity series (or activity series) of metal ions on the application of double displacement reactions and the extraction of metals refers to that the competition of metal ions in which the one higher in reactivity predominates the exchange that it can displace those lower in the reactivity series. The reactivity series of metal ions present analogous to their series in electropositivity, Cs > Rb > K > Na > Li > Ra > Ba > Sr > Ca > Mg > Al > Ti > Mn > Zn > Cr> Fe > Cd > Co > Ni > Sn > Pb > (H2) > Sb > Bi > Cu > W > Hg > Ag> Pt > Au. The counterion attribute of positively charged metal ions (and proton) and the electropositive series in reactivity imply that the double-exchange of electrically charged ions is under the dominance of electromagnetic dynamics.

To form the selective asymmetric redistribution of cations on the counterpart sides of membrane with the significant transmembrane concentration difference that enables the ion diffusion motions of depolarization and repolarization in the counter directions, the double exchangers for cations (metal ions and proton) on the either side of membrane that are constructed by the negatively charged polymers different in electrostatic intensity which electromagnetically interact with the counterions competitive in the reactivity are required.

Summary. The action potential is performed by the motion of mobile ions what is composed of the extrinsic part of the double-diffusion (depolarization and repolarization) in the form of convection and the intrinsic part of double-exchange between mobile ions, in which the result of double-exchange plays the role prerequisite for depolarization and repolarization diffusions of action potential. The system of materials for generating action potential consists as follows:

(i) The water to provide aqueous solution for mobile ion motions; (ii) the mobile couterions (metal ions and proton) with the different (competitive) reactivity; (iii) the ground substances (negatively charged polymers) with the different electrostatic intensity in response to counterions; and (iv) the lipid bilayer membrane which function as the “potential barrier” that separate the metal ions.

Note that (i) both ion motions of diffusion and exchange are essentially of physical processes driven by the thermodynamics and electromagnetodynamics, which can “naturally” operate lack of the participant of chemical catalyzers; and (ii) the chemical action of guest molecules, typically the ester guest molecules (e.g., acetylcholine and ATP) and aromatic guest molecules (e.g., norepinephrine), can vary the size and shape of the lattices of polymers via chemophysical action to

take effect on ion motions.

II The dose-dependent elastic lattices constructed by negatively charged polymers interact with counterions: attractive action vs. hydrophilic action

Like charges repel and unlike charges attract, described as Coulomb law of electrostatics. The counterions (metal ions and proton), due to the electropositive property, are attracted non-covalently and reversibly with electronegative polymers through electrostatic interaction in the way of sorption. The counterions so act as the crystal nodes of lattices to connect the negatively charged groups between polymers.

i. Attractive action and the compressible space

Because the electron has the smaller mass and thus larger space-filling property, the spatial distance between the negatively charged carriers are much expanded due to the electrostatic repulsion between their electron clouds, and the spatial size (spatial extension) of negatively charged polymers are thus much larger than that of parent molecules. Because the electrostatic attraction between positive- and negative charges resists the electrostatic repulsion, the size of lattice constructed by counterions and polymers can be compressible in significant degree by the positive charges, and the negative charges can be pulled pretty approach to each other by their attraction to positive charges.

This character is termed “like-charge attraction induced by counterions” and discovered by various techniques (using x-ray diffraction or others) that like-charge attraction between polyelectrolytes is induced by counterion charge density waves, and typically that metal ion arrangement in the “zipper-like” mode enables the closed bounding of polymers together, in which the size of polymer lattice turns to be compressed in response to the existence of metal ions [2 Angelini, 3 Nagornyak]. And the more metal ions attracted to the negative charges, which locate surround negative charges in the more dimensions, causes the greater compressed space between the adjacent negatively charged carriers.

ii. Hydrophilic action and the extensible space

In aqueous solution, the electronegative oxygen atom of water molecule would be attracted electrostatically to the positive charge of metal ions. Under the action of electromagnetic field, the metal ion acts as the coordination center, and the water molecules surround metal ion in the array of first (primary) and second coordination sphere, known also as hydration shell or hydration sphere [4 Dudev]. The shell can be several molecules thick, dependent on the charge of metal ions, and their

distribution and spatial dimensionality [5 Ball].

As the positively charged counterions are captured by the weak negatively charged polymers, because of the hydrophilic action that the layers of water molecules are attracted surrounding the metal ion, the size of lattice constructed by counterions and polymers can be significantly expand, especially alkali metals and alkaline earth metals that have the intensive metal character and electropositivity. It is described as “egg-box” mode of metal ion arrangement that enables the expanded space between polymers [6 de Kerchove]. And the more metal ions attracted to the negatively charged polymers causes the greater expanded space between the adjacent negatively charged carriers.

iii. The screening action: attractive action vs. hydrophilic action

The screening action refers to the electromagnetic field of charged particles is counterbalanced and shielded by the additional charges, that when the unequal oppositely charged particles meet and attract each other, the electromagnetic field action of the weakly charged one is counterbalanced and screened by the electromagnetic field of strong one, and which electromagnetic field of positive- or negative charge predominates is dependent on the electrostatic intensity of charges.

As the positively charged counterions (metal ions and proton) are captured by the negatively charged polymers, the size of lattices constructed by negatively charged polymers and metal ions results from the competition of the charge intensity between metal ions and polymers: the strong negatively charged groups carried by polymers counteract and shield the positive charges carried by metal ions so that the attractive action predominates, in which metal ions play the role that pull the counterpart negative charged polymers closer with the compressed lattices; in contrast, the weak negatively charged groups carried by polymers are counteracted and shielded by the positive charges carried by metal ions so that the hydrophilic action predominates, in which metal ions play the role that extends the lattices with the additional water molecule layers.

iv. Summary I. The property of interaction: sensitivity and reversibility

The interaction (attractive action and hydrophilic action) between negatively charged polymers and positively charged counterions (metal ions and proton) are dependent on the electrostatic intensity of negative charges carried by the polymers, which determines the lattice space being compressed or expended in response to the counterions; and the amplitude of alternation (compressed or expended) is elastic in the dose-dependent sensitivity and reversibility in response to adding or removing ions, in which the greater concentration causes the greater amplitude of alternation and vice versa.

v. Summary II. The connotation of the counter interactions (attractive action vs. hydrophilic action) for double-exchange motion

The negative charged polymers interact with counterions in the opposite actions (attractive action and hydrophilic action) imply that the conflicting different electrostatic intensity of the negative charges carried by polymers.

It has the sharp significance on the setting of exchangers for double-exchange. Due to the electromagnetic attribute of double-exchange, the greater difference in electrostatic intensity of exchangers causes the greater asymmetric distribution (spontaneous symmetry breaking) of ions (different in reactivity) with the greater chemical potential gradient on the counterpart sides of membrane. As aforementioned, the selective asymmetric distribution of ions onto the counterpart sides of membrane is prerequisite for double-exchange of action potential which enables the diffusion (down concentration gradient) of depolarization and repolarization.

As the double exchangers separated by the membrane are set with the attractive action predominated-polymers and the hydrophilic action predominated-polymers on the either side of membrane, it results in the maximized asymmetric redistribution on the counterpart sides and so the maximized transmembrane concentration gradient of ions, which is the optimal prerequisite for the depolarization and repolarization diffusion of action potential.

III The ground substances for generating action potential: the connotation of cell matrix

The matrix proteins (ground substances) form the networks of matrixes that surround cell, extend throughout cell, and fill in the organelles. The cell matrix is composed of the extracellular matrix proteins that surround cell, the cytoskeletal proteins (cytoplasmic matrix) which extend throughout the cytoplasm from nucleus to plasma membrane, and the organelle matrixes inside organelles. The extracellular matrix proteins are made of the ground substance of polysaccharides. The cytoskeletal proteins (cytoplasmic matrix) are made of the ground substances of microfilaments (actin filaments), intermediate filaments, and microtubules. All the ground substances are made of negatively charged polymers that have large net negative charge densities distributed over their surfaces [7 Janmey, 8 Janmey PA].

i. Polysaccharides

Glycosaminoglycans (GAGs) are the ground substance extending and filling in extracellular matrix.

They are long unbranched polysaccharides consisting of a repeating disaccharide unit, which contain carboxyl or sulfate groups that carry negative charges [9 Seyrek]. The presence of both carboxyl and sulfate groups gives a high density of negative charges along the chains so that polysaccharides are highly negatively charged. Due to the electrostatic attractions, the negative charges noncovalently attract a condensed counterion cloud of positively charged metal ions (K+, Na+, and Ca2+) [10 Salehizadeh].

Because the metal ions (K+, Na+, and Ca2+) are osmotically active, the polysaccharides are strongly hydrophilic, and form the highly hydrated porous gels. The pores are formed in "egg (metal ion)-box model", and the size of pores are evidently enlarged by the increased concentration of counterions [6 de Kerchove]. Due to the highly hydrated space, the polymers adopt highly extended conformations so that occupy a huge volume relative to their mass. It creates a swelling pressure which enables the matrix to withstand compressive forces, and provides mechanical support primarily.

Location. Polysaccharides act as ground substances filling in the extracellular matrix (the exterior of cell), and also filling in the organelles such as endoplasmic reticulum to provide swell pressure and mechanical support for organelles.

ii. Cytoskeletal proteins: microfilaments, intermediate filaments and microtubules

The cytoskeletal proteins of microfilaments, intermediate filaments, and microtubules all contain the highly negatively charged groups. Opposite to extracellular matrix protein polysaccharides, the cytoskeletal proteins are hydrophobic instead of hydrophilic, and they are not extended but the aggregated rod-like polymers that bundle together as in the cell [7 Janmey, 11 Edelstei, 12 Nancy], which seems to violate the Coulomb law of electrostatics in which like charges repel.

It is because these protein filaments are not in the circumstances of vacuum, but in the solution of intracellular environment where they are surrounded by the positively charged counterions which condense upon their charged surface (due to the opposite charges attract), leading to their rod-like bundling by overcoming the repulsive forces [12 Nancy]. Its underlying mechanism is described as “like-charge attraction between polyelectrolytes induced by counterions” [2 Angelini], in which counterions are found that play a central role for generating attractions. This effect contributes to ionic conductance along the longitudinal axes of cytoskeletal proteins (microfilaments, intermediate filaments, and microtubules) [12 Angelini, 9 Nancy J, 11 Nancy J].

(i) Microfilaments (actin filaments)

Microfilaments are composed of two helical, interlaced strands of actin [13 Grimard]. Actin carries around 11 net negative charges at neutral pH [7 Janmey]. Through nonspecific electrostatic effects, a condensation of positively charged counterions is attracted by the negatively charged groups along the actin strands with the "zipper-like" arrangement on the surface and along the longitudinal axes of actin filaments; which is critical to actin filaments sustaining ionic conductances [2 Angelini, 14 Lin EC, 15 Priel]. The zipper-like charge alignment enables the close bundling of actin filaments together, pulling them "attracted" closely [2 Angelini, 16 Shikinaka].

Cations binding on actin along its length drive actin to incorporate into polymerization, and determine the filament flexural rigidity, depending upon the type and concentration of cations [17 Kang, 18 Kang]. A threshold concentration of polycations is required to the assembly of actin filaments, which counteracts the repulsion between negative charges and forms lateral aggregation (attraction) of filaments [16 Shikinaka, 19 Tang]. In the presence of high concentrations, multivalent linear waves of counterions condense [2 Angelini]. Increasing the concentration of positively charged counterions causes a significant increase in the intercalation (attraction) of actin within the microfilament molecules, indicating that the intercalation of actin is generated and intensified by electrostatic interactions with counterions [13 Grimard, 20 Hase].

Location. The actin filament network is arranged with the barbed-end of each filament attached to the cell's peripheral membrane (the interior of cell); the actin filament is also found in cell nucleus.

(ii) Intermediate filaments

Intermediate filaments are composed of a family of proteins sharing common structural features that include an N-terminal 'head' domain, a C-terminal 'tail' domain, and a central α-helical 'rod' domain, in which the amino acid sequences of "head" and "tail" domains are variable, whereas the rod domains are highly conserved. The interaction of the rod domain which generates a coiled coil forms the basic building-block of intermediate filaments [21 Stromer, 22 Snider, 23 Block].

The intermediate filaments, like microfilaments and microtubules, are the polyelectrolyte natures that highly negatively charged, and therefore electrostatically interact strongly with cations, have the strong affinity with cations, with the similar mechanism of condensed counterions as that of other cytoskeletal proteins of microfilaments and microtubules [8 Janmey PA, 23 Block J]. A condensed counterions of cations, involving mono- (metal ions, proton), di- (metal ions) and/or multivalent ions, act as the reason for the attractive interaction between the negatively charged side arms of intermediate filament for the assembly of polymerization with the electrostatic interaction [8 Janmey

PA, 24 Lin YC, 25 Dammann Köster 2014, 26 Brennich].

Filament assembly was basically done in the presence of physiological metal ions (K+, Na+, Ca2+, and Mg2+) and polycations, with the threshold concentration required [25 Dammann Köster 2014, 27 Stromer, 28 Dammann Nöding 2012]. Increasing the concentration develops the degree of polymerization of the filament networks in a quantitative way, playing the role described as "compaction" [28 Dammann Nöding 2012], "zipping" [27 Stromer], and "thicken" [26 Brennich], and as the "crosslinkers" [24 Lin YC Yao NY, 29 Köster, 30 Lin YC Broedersz], giving the elastic property of these networks.

As increasing Mg2+ concentration in the drops, the compaction of the networks becomes more aggregated [28 Dammann], and the further assembled filaments show a lateral compaction step after the filament formation [27 Stromer]. Changes the concentration of monovalent K+ and divalent Mg2+ affect the internal organization of the resulting filaments, in which the higher concentrations of Mg2 + lead to thicker vimentin filaments [27 Stromer, 26 Brennich]. Upon addition of divalent ions (Mg2+ and Ca2+), the stiffness of network increases considerably, suggesting that cations act as effective cross-linkers to the elastic properties of networks [29 Köster, 30 Lin YC Broedersz]. Depending on the level of cation concentrations, the aggregation process manifests itself in a "zipping together" of the intermediate filaments [25 Dammann Köster 2014]. Cations mediate attractive interactions between the negatively charged side arms of the intermediate filaments thereby forming cross-links [24 Lin YC Yao NY]. The presence of monovalent and divalent cations induces identical cross-linking of the networks as indicated by rheology studies [24 Lin YC Yao NY, 29 Köster], and the cross-linking interactions would be mediated by a collection of divalent ions interwoven, intercalated into the entangled side arm structure [24 Lin YC Yao NY]. The mesh size of vimentin (type III intermediate filament) networks decreases upon addition of MgCl2, and the mesh size is reduced in response to the addition of cation concentration, and the cations act as effective cross-linkers, further stiffening the network by reducing the mesh size [29 Köster].

Location. Intermediate filaments organize the internal tridimensional structure of the cell to anchor organelles; Intermediate filaments also serve as structural components of the nuclear lamina on the interior of the nuclear envelope.

(iii) Microtubules

Microtubules are made from the polymerization of tubulin monomers into hollow cylinders. The walls of the microtubule are composed of linear protofilaments (a number between 10 and 16)

arranged in parallel, and tubulin dimers carry about 30 net negative charges at neutral pH [7 Janmey]. The surface charges for the tubulin monomer are mostly electronegative, especially the C-terminal region where is rich in negatively charged glutamate residues so that contain high density of the surface electronegative charges [31 Nogales, 32 Wehenkel, 33 Roll-Mecak]. The negative charges are particularly concentrated on the ridges of protofilaments, giving the longitudinal arrangement of charges which establishes a sizable linear charge density [34 Baker, 35 Minoura]. Due to the hollow cylindrical configuration of microtubules, at the longitudinal section, the electrostatic distribution of positively charged counterions play the attraction (compaction) role as that of "zipper"; and at the cross section, they take the attraction effect as that of "hoop" compacted the wall between the tubulin monomers of hollow cylinder [15 Priel A Tuszynski JA].

The high density of the surface electronegative charge, are most critical to the electrostatic distribution of the condensed positive counterion cloud on the surface and along the length of the microtubule. The condensed counterions (mobile metal ions) bound to highly negatively charged microtubules can move along the long axis, which is consistent with the high conductivity (metal ionic-based conductivity) of microtubules [35 Minoura, 12 Woolf, 36 Priel A Ramos].

The assembly of a microtubule depends on the availability of the positive counterions that are electrostatically attracted to the negative charged surface of microtubule, which counteracts the self-repulsion between negative charges, and the polymerization is enhanced by cations (especially metal ions) selectively results from shielding of the negatively charged groups of glutamate-rich C termini of the tubulin monomers [37 Diaz, 38 Wolff, 39 Mechulam]. The metal ions, involving the monovalent alkali metal ions (K+, Na+) and alkaline earth metal divalent cations (Mg2+, Ca2+) generate the reversible aggregation of tubulin, depending upon the concentration of metal ions [38 Wolff, 40 Weisenberg].

Location. Microtubules, as part of a structural network within cytoplasm, offer mechanical support and organize organelles and other cellular components, including the endoplasmic reticulum and the Golgi apparatus.

iii. Summary. Comparison between polysaccharides and cytoskeletal proteins in response to counterions: opposite and commonness

(i) Opposite: attractive action vs. hydrophilic action

All the ground substance proteins (polymers) of cell matrix, involving polysaccharides and cytoskeletal proteins (microfilaments, intermediate filaments and microtubules) are highly negatively

charged to capture counterions with electrostatic attraction. The polymers take opposite effects in response to cations: the polysaccharides take the strong hydrophilic action; the cytoskeletal proteins (microfilaments, intermediate filaments and microtubules) take the intense attractive effects. It implies the electrostatic intensities of negative charges carried by polysaccharides and cytoskeletal proteins are in conflicting difference.

As described, the conflicting difference in electrostatic intensity of negatively charged polymers leads to the extraordinary significance on double-exchange for counterions (metal ions and proton): the negatively charged property of polymers captures counterions with electrostatic attraction, and the sharp difference in electrostatic intensity of polymers leads to the maximized asymmetric redistribution, which is the optimal prerequisite for the depolarization and repolarization diffusion of action potential.

(ii) Commonness: sensitivity (dose-dependence) and reversibility

The negatively charged polymers have the commonness in response to counterions. Both the amplitudes of alteration (the hydrophilic action of polysaccharides and the attractive action of cytoskeletal proteins) are highly sensitive to the quantity of cations in the dose-dependent and reversible manner. The hydrophilic action and attractive action are both intensified by adding dose and weakened by removal [7 Janmey, 38 Wolff, 40 Weisenberg].

The sensitivity and reversibility in dose-dependence lead to the evident elastic property of lattice spaces in response to cation diffusion flux (inflow and outflow).

IV The connotation of cell layout on the ground substances: the relativity in “sandwich” structure

i. “Sandwich” structure (sandwich matrix-membrane system)

“Sandwich” here refers to the structure that the lipid bilayer membrane sandwiches between the two negatively charged polymer exchangers (polymer/membrane/polymer').

(i) Plasma membrane sandwich. The plasma membrane locates between the polysaccharides on the exterior side (extracellular matrix) and the microfilaments on the interior side (cell peripheral matrix).

(ii) Endoplasmic reticulum (ER) membrane sandwich. The ER membrane locates between the intermediate filaments together with microtubules on the exterior side (cytoplasmic matrix) and the polysaccharides on the interior side (ER matrix).

(iii) Inner nuclear membrane sandwich. The inner nuclear membrane locates between the polysaccharides on the exterior side (nuclear envelope matrix) and the intermediate filaments on the interior side (nuclear lamina, and nuclear matrix together with microfilaments).

The membrane of the rough endoplasmic reticulum (RER) is continuous with the outer nuclear membrane, and the lumen of nuclear envelope (perinuclear space) is continuous with the lumen of RER where the polysaccharides fill in. The inner nuclear membrane which encloses the nucleoplasm is covered by the nuclear lamina, a mesh of intermediate filaments.

(iv) Inner mitochondrial membrane (involving cristae) sandwich. The inner mitochondrial membrane locates between the intermediate filaments on the exterior side (cytoplasmic intermembrane space matrix) and the polysaccharides on the interior side (mitochondrial matrix).

The studies report cytoplasmic intermembrane space has a water content of 3.8 μl/mg protein, while the mitochondrial matrix 0.8 μl/mg protein [41 Soboll]. It indicates the ground substance of mitochondrial matrix is in the hydrophilic action of polysaccharides, in contrast to the attractive action of cytoplasmic matrix (mainly intermediate filaments).

ii. Summary. The property of sandwich structure in strict relativity: attractive action vs. hydrophilic action

The plasma membrane, ER membrane, inner nuclear membrane, and inner mitochondrial membrane that enclose cell matrix and organelle matrixes are in the identical property that the membranes are all located between the coupled negatively charged polymers which are in the conflicting electrostatic intensity that oppositely respond with cations with attractive action vs. hydrophilic action.

Is the predominant character of eukaryotes the membrane systems that enclose organelles? Definitely, the predominant character of eukaryotes is the strict sandwich matrix-membrane systems that enclose organelles, which are composed of the sandwich structure (polymer/membrane/polymer') that the membrane is sandwiched between the coupled negative charged ground substances in the conflicting electrostatic intensity that oppositely respond with cations with attractive action vs. hydrophilic action.

As known previously, the layout of eukaryote with the strict sandwich matrix-membrane structure has the extraordinary significance which is irreplaceable on the function as the optimal double-exchangers for counterions (metal ions and proton), with the maximized asymmetric distribution and transmembrane concentration gradient of cations on the counterpart sides of membrane, which is optimally prerequisite for the depolarization and repolarization diffusion of action potential; and with the high sensitivity and reversibility in the dose-dependent manner in response to cation diffusion motions (inflow and outflow).

So, the system of materials enabling electric excitation of action potential is composed as follows: (i) the water to provide aqueous solution for mobile ion motions; (ii) the mobile counterions (metal ions and proton) with the different (competitive) reactivity; and (iii) the sandwich matrix-membrane structure in which the lipid bilayer membrane is sandwiched between the coupled negative charged polymers in conflicting electrostatic intensity that oppositely interact with counterions with attractive action vs. hydrophilic action.

V The coupled asymmetric distribution of counterions in sandwich structure for generating bioelectricity: the connotation in strict relativity

i. The asymmetric distribution on the exterior/interior of membrane and the reactivity of metal ion (proton)

The sandwich matrix-membrane structure, in which the lipid bilayer membrane is sandwiched between the coupled negative charged polymers in the opposite interactions with counterions, leads to the maximized asymmetric redistribution of counterions in different (competitive) reactivity on the counterpart sides (exterior/interior) of membrane, shown as follows.

(i) **The Na+ (Na+ and Ca2+)/K+ distribution on the exterior/interior of plasma membrane**. Na+ (Na+ and Ca2+) has the stronghold (higher in concentration) in the exterior and K+ interior. K+ (interior) is the one higher in reactivity comparted to that of Na+ and Ca2+ (exterior), in accordance with the reactivity series of metal ions (Cs > Rb > K > Na > Li > Ra > Ba > Sr > Ca > Mg > Al > Ti > Mn > Zn > Cr> Fe > Cd > Co > Ni > Sn > Pb > (H2) > Sb > Bi > Cu > W > Hg > Ag> Pt > Au).

(ii) **The Mg2+/Ca2+ distribution on the exterior/interior of ER membrane**. Mg2+ has the stronghold in the exterior and Ca2+ interior. The Ca2+ (interior) is the one higher in reactivity comparted to that of Mg2+ (exterior).

ER acts as the significant Ca2+ pool. The free Ca2+ concentration is 250-600 μM (0.25-0.6 mM) in the ER but 10-100 nM in cytoplasm [42 Demaurex]. Mg2+ acts as the important cation in intracellular fluid, the free Mg2+ concentration in cytosol is usually close to 0.5 mM, which is significantly higher than that outside of cell and in ER.

(iii) **The H+/Ca2+ distribution on the exterior/interior of inner mitochondrial membrane (cristae)**. H+ has the stronghold in the exterior and Ca2+ interior. The Ca2+ (interior) is the one higher in reactivity comparted to that of H+ (exterior).

Mitochondrion, like ER, forms another free Ca2+ pool of the cell [43 Rizzuto]. The free Ca2+ concentration in mitochondrial matrix is about tens of micromolar levels [44 Ivannikov]. The electron transport chains that locate at cristal membrane comprise a series of dehydrogenases (e.g., NADH dehydrogenase, succinate dehydrogenase) that undertakes the incremental release of energy and proton (H+), and pumps H+ into the cristal lumen (intracristal space). It causes proton accumulation in cristal lumen, and the lumen of cristae acts as the proton pool [45 Mannella]. In contrast, it is about pH 7.8 of mitochondrial matrix [46 Poburko]. Note that it is the cristae of inner membrane where the electron transport chains locate, which are the invaginations of the inner membrane rather than the boundary zones of inner membrane (inner boundary zones) juxtaposed to the out membrane.

The counter concentration gradients of H+ and Ca2+ across the inner membrane generate the resting membrane potential ($\Delta\Psi m$), which is measured highly negative inside (usually negative 170-200 mV) by using permanent cationic fluorescent probes in living cells [47 Johnson, 48 Lemasters]. This highly negative inside resting membrane potential is caused by the net preferential outward motion of Ca2+ (higher in reactivity compared to H+), like the resting potential of plasma membrane (-70 mv in neurons) which is caused by the net preferential outward motion of K+ (higher in reactivity compared to Na+).

ii. Summary. The connotations of the coupled asymmetric distribution of counterions in sandwich structure: the foundation of ion diffusions in convection, resting membrane potential, endogenous action potential mechanism and leakage potential

The maximized asymmetric redistribution of counterions (metal ions and proton) on the counterpart sides (exterior/interior) of membrane, with the strict characteristic that the ion higher in reactivity has stronghold in the interior, contains the connotations as follows.

(i) The foundation of depolarization and repolarization

The maximized asymmetric redistribution of cations on the counterpart sides of membrane (Na+ (Na+ and Ca2+)/K+, Mg2+/Ca2+, H+/Ca2+) optimally generates the significant transmembrane thermodynamic chemical potential gradient of ions to support the ion diffusions of depolarization and repolarization in the counter directions in the form of convection.

(ii) The foundation of resting membrane potential

The metal ion higher in reactivity, rather than those lower ones, dominates the exchange and presents the net preferential transmembrane motion that overwhelms other ions.

Because it is the ions higher in reactivity and higher in concentration that has stronghold on the interior of membrane, the resting membrane potential predominantly arises from the equilibrium potential of K+ (plasma membrane), and Ca2+ (ER membrane and mitochondrial membrane), which results from their net preferential transmembrane motion down chemical potential gradient so that the resting membrane potentials are in the polarized states (positive outside but negative inside) at the value of their equilibrium potentials (the membrane potential at which there is no net flow transmembrane, refer to Nernst equation and Goldman equation).

(iii) The foundation of endogenous action potential mechanism

The resting membrane potential (positive outside but negative inside) caused by the equilibrium potential of the ion higher in reactivity and higher in concentration inside forms the "potential barrier" that obstructs the inward flow of the ions lower in reactivity and higher in concentration outside.

The potential barrier plays the role that (i) it raises the potential energy gradient of the inward diffused ions to enhance inward diffusion down potential gradient, taking the effect like the dams in hydroelectricity that it provides the dynamic energy that converts from potential energy for inward diffusion to motivate convection; and (ii) it obstructs the inward ion diffusion with the resistance of resting potential, acting as the sluice that tune off and on the process of action potential, so that the inward depolarization diffusion of ions down chemical potential gradient is under the control of the height of potential barrier formed by the equilibrium potential of higher reactive ion, by which varying the equilibrium potential by varying the ratio on the exterior/interior ion concentrations (refer to Nernst equation and Goldman equation), especially in the way of local leakage due to the higher concentration inside, acts as the endogenous sluice to turn off and on the inward depolarization diffusion of action potential.

(iv) The foundation of leakage potential

The higher reactivity permits the preferential transmembrane motion of the ion, and the higher inside concentration is competent to the outward leakage of the ion which causes the hyperpolarized membrane potential. The reduced interior ion concentration caused by leakage leads to the endogenous and spontaneous depolarized resting potential (reentry potential) and the consequential action potential discharge.

The amplitude of leakage determines the amplitude of depolarized resting potential to control the activation and inactivation of action potential excitation, in which the depolarized resting potential up to threshold activates action potential, and the greater leakage the greater depolarized resting potential, while the excessive leakage that causes the dissipation of transmembrane gradient abolishes the diffusion to induce the inactivate state.

Part II The differentiation of membrane zones and the endogenous mechanism for generating bioelectric excitation

VI The differentiation of junctional zones and working zones of plasma membrane: the endogenous mechanism in relation

VII The differentiation of junctional zones and working zones of ER membrane: the endogenous mechanism in relation

VIII The differentiation of junctional zones and working zones of inner mitochondrial membrane: the endogenous mechanism in relation

IX Summary. The endogenous mechanism and property of electric excitation of organelles

Part III On informationization of bioelectromagnetic signals

X The connotation of action potential in information: complex-signals, encoding and transmission, spread spectrum, Shannon entropy and energy level

Part IV On bioelectromagnetic AC oscillations

XI Organelle excitations and the functional morphology of membrane systems: the utilization and conversion of AC oscillations

XII The layout of organelles and energy transmission of eukaryote: resonance structure and resonance-coupling

Part V Summary. The principle and operation mechanism of bioorganic electromagnetic field and bioorganic electricity generation of eukaryotic cells

XIII Summary I. The eukaryotic mechanism of bioelectromagnetic field and bioelectricity: bioorganic electromagnetic field and bioorganic electric power system

XIV Summary II. The creation of eukaryotic bioorganic energy and enlightenment: from principle to design

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