WORLD SCIENCE AND TECHNOLOGY
MODERNIZATION OF TRADITIONAL CHINESE MEDICINE AND MATERIA MEDICA
Volume 11, Issue 5, October 2009
Online English edition of the Chinese language journal

Cite this article as: Mode Tradit Chin Med Mater Med, 2009, 11(5): 670–678

REVIEW

Interpretation of the Biological Essence of Meridians with Plant Neurobiology and Animal Nerval Evolution

Yin Dazhong[1, 2]*, Zhao Linli[2]
[1] Guangdong Provincial Academy of Chinese Medical Science, Guangdong Provincial Hospital of TCM, Dade Road 111, Guangzhou 510120, China
[2] Key Laboratory of Protein Chemistry and Developmental Biology of Ministry of Education, College of Life Sciences, Hunan Normal University, Changsha, Hunan 410081, China

Abstract: In the absence of a clear and independent anatomical structure, the biological nature of meridians (Jingluo) and the mechanism of acupuncture and moxibustion and so on to prevent and cure diseases in the traditional Chinese medicine remain mysterious. Through summary and analysis of the evolution of animal nervous system and comparison with the information transmission systems of plants (the so-called "plant neurobiology"), the common biological structure and the basic law of information transmission of biological system were open-mindedly reviewed and described in this paper. For the first time, the biological information transmission systems were classified into three major levels as follows: (1) the brain-related central nervous system (the neural level), (2) the vessel-dependent information transmission system without the typical nerval structure (the vessel level), and (3) the intercellular and the cell-environmental signal communication systems (the cellular level). Electronic and biochemical signal transmissions were pinpointed as two major means of information dissemination pattern in the life system. In summary, the complicated information transmission functions and traits of the meridians are suggested as an interplay of the performances of the three major systems applying electronic and physicochemical materials, namely the "321-Integration Theory" of meridians.

Key words: Acupuncture and moxibustion (AM), animal nerval evolution, meridians (Jingluo), biological information transmission (BIT), plant neurobiology

1 Meridian essence and its research status

Researches and hypotheses on essence and mechanisms of meridian have been extraordinarily complex as well as fruitful. Through decades of acupuncture and moxibustion (AM) meridian research, four major branches of interpretation on meridian have been formed by scholars both at home and abroad. The four major branches are neurophysiology, physio-biochemistry, biological field, and connective tissues. Scholars of neurophysiology branch believe that the meridian phenomenon is the functional representation of nervous system, and its research is focused mainly on cerebral cortex, hippocampus, hypothalamus, brain stem reticular structure, spinal cord, peripheral nerves, autonomic nerve, and so on. However, it is quite obvious that it cannot interpret the phenomena of slow signal transmission, bilateral transmission, lower electric resistance (ER), and high oxygen partial pressure along meridians. Scholars of physio-biochemistry branch discovered that the meridian is related to the transmission of multiple physicochemical compounds and biochemical substances, including a variety of neurotransmitters and ions, such as neurokinin, substance P, serotonin, histamine and calcitonin gene-related peptide. This interpretation of meridian is similar to the "nervism," with a wider coverage, but it cannot interpret the meridian phenomena independently. Scholars of biological field branch have proposed many field theories related to sound, light, electricity, heat, and magnet, but they are short of definite determination of three-dimensional structure to the meridian. Scholars of connective tissue branch believe that the fascia in the connective tissue is the material base of the meridian: the meridian channel is attached to the fascia tissue, and it is a strip structure essential for adjusting the human function by relying on the nerve, blood and lymph vessels; collateral is a network of small blood vessels that relies on the nerve, blood and lymph vessels to adjust the responses and activities of human [1]. Because the interpretation and understanding of these research findings and phenomena are complex and fail to come to any agreement, these issues remain mysterious in traditional Chinese medicine (TCM).

1.1 Material structures and features of the meridian

Does the meridian have a substantive morphology in biological organisms? In 1963, Bong Han Kim from North

Received date: 19 October 2009
*** Corresponding author.** Tel: +86-731-88872786; Fax: +86-731-88872786; E-mail: dazhongyin@hotmail.com
Foundation item: Supported by the National High-tech Research Development Project (2008AA02Z411), and the Key Project of Hunan Science and Technology Agency (06FJ3001)

Korea reported, to the great surprise of the world, that he found the entity of the meridian and acupuncture points, namely the so-called structure of “Bong Han Corpuscle and Bong Han Vessel” [2], but he was defamed by this boast. Some scholars in China have put forward that the meridian is a tissue based on morphology, whose width is about 1.0 mm [3], but there is no further confirmation report till date.

Although the anatomic structure of the meridian cannot be determined, several findings have been made in the research of meridian characteristics in accordance with the traditional meridian chart. For over half a century, there are many scholars both at home and abroad to constantly research the low ER characteristic of the meridian. In 1950s, Japanese scholars Nakatani Yoshio, et al. [4, 5] measured the low-resistance point of human body surface and identified 26 (24 + 2) low-resistance lines in human body, which are called “Ryodoraku”, although it is different from the 12 + 2 meridian lines identified by Chinese scholars. Since then, many researches were reported in this aspect, for example, some studies have reported the low-resistance nature of meridian acupuncture points, whose ER is generally 80-100 KΩ and the ER of surrounding place is over 600 KΩ. As reported, the low ER points are basically lined along the meridian, of which 90% low ER points are distributed in the meridian channels. This data are different from the current research findings of this lab (unpublished data). Lee [6] discovered that the conductivity from Hegu to Quchi along the meridian is significantly higher than that from Hegu to non-acupoint segment and the electric conductivity along the meridian line is higher than that of nonmeridian line. Nonetheless, a preferable electric conduction was observed between two acupoints along meridian line. Chen Daoliang et al. [7] claimed that there is junctional intercellular communication along the meridian in the deep tissue of rabbits and mouse, and consequently they proposed the existence of continuous and unblocked junctional intercellular communication along the meridian in the deep epidermis. By studying the low ER characteristic of the meridian, Li Gang proposed that “the meridian is a kind of signal conductive tissue with specially electric characteristic cells,” and he believes that this could be a breakthrough for the substantial study of the meridian.

In 1973, Zhu Zongxiang [8] further identified the universal existence of the meridian phenomenon; then, a number of scholars also reported the meridian’s positioning in the skin surface and corresponding physio-biochemical manifestations, for example, covert transmission of sensation, bilateral transmission, trans-metamere conduction, low ER and high conductivity, high oxygen partial pressure, high sound transmission, transmission of tracing substances, preference for lightening and heating, enhanced level of Ca^{2+} concentration, Acupoint-Viscera correlativity, advantage for conduction of high-frequency vibration and low-frequency vibration after stimulation, and so on. Furthermore, based on certain biophysical concepts, a number of researches advanced different “field theories” of the meridian, including electric field, magnetic field, and field of infrared ray, superposition of electromagnetic resonance, soliton wave, and so on.

However, no clear anatomical structure of the meridians has been discovered by the biomedical researches in human body or animals till date, so there still exists vigorous debate concerning the existence of the meridian in human body or even among other organisms.

1.2 Mechanism study of “Collateral Disease Theory” on Qi and blood regulation

Recently, professor Wu Yiling has proposed a “Frame of Collateral Disease Theory” – so-called the “3-Dimentional Net System” of diseases based on the traditional theory of meridian. This theory postulated that “the horizontal collateral system is a network originated from the vertical meridian channels, segmented by layers, arranged in a crisscross pattern in the whole body, and distributed widely among the visceral tissues. Although it is enormous and complicated, which presents evident-segmented stratification and spatial distribution, it conveys or distributes, scatters, and penetrates the Qi and blood for the transmission of meridian signal to the visceral tissues of the whole body at certain speed and state.” He believes that the speed and state of Qi and blood distributed in the collateral network is also obviously different from the transmission of Qi and blood in meridian channels, and it is characterized by “slow flow, facial dispersion, end-end connection, interchange of fluid and blood, two-direction fluid, and functional regulation, and so on.”

This theory divided the collateral branches into collateral of “Qi” and collateral of “Xue” in a narrow sense: Qi collateral runs or controls the fluid, and the Xue collateral runs or controls the blood. In this theory, the fluid in the Qi has covered the nerves, internal secretion, and immunity regulation function in the western medicine. Furthermore, the “operation or running of the Qi and Xue” is the basic function of the collateral net, the unblocked running of the Qi and Xue in the channel is the foundation for the collateral system to maintain the normal life motion and the internal stability of human body. Meanwhile, it believes that “the collateral is a channel for the distribution and circulation of blood and fluid, with small complex net-system widely distributed in the whole body. Hence pathogen invasion may easily affect the running and the distribution of blood and fluid in the system and result in some pathologic changes such as collateral block or collateral disorder, stagnancy of Qi collateral, obstruction of collateral, jerky collateral system, accumulation of collateral metabolites, stagnation of heat toxicity, and so on.” Wu has put forward that the stagnation of Qi collateral caused from the asthenia is the early phase of the collateral pathologic syndrome leading functional changes to structural changes [9].

1.3 Carriers for the information transmission of the meridian

Various hypotheses about the carrier for information transmission of the meridian have been proposed:

Yang Weisheng [10] hypothesized that the meridians ought to be passages with low resistance for diffusion of the meridian-signal carriers. The meridian-signal carriers ought to be histamine, and the meridian biological signal amplifier must be mast cells. Furthermore, according to these, a hypothesis for the function of the meridians is proposed, which suggests that in addition to the loose connective tissue network, the circulation of blood and nervous systems are also integrated and functioning together.

Xie Haoran [11] believed that the meridian-collateral system of TCM refers to the regulating system and are composed of the known loose connective tissue, liquid-Qi of tissue, energy substances, nerves, blood vessels, lymphatic system, and so on. This network exists in the fascia space among skin, muscle, and bone structure; some may associate with unknown synthetic functions. These tissues and structures participate in the regulation and control of unknown comprehensive functional system.

In general, in the field of the traditional medicine, "nothingness is used to replace the concreteness," and imagination prevails over substance, and the presumption that the meridian is the pathway of "Qi" have been published in various forms, which have been extremely confusion in modern science. According to the author of this study, the meridian is actually the biological information transmission (BIT) system, which is not insubstantial, instead it exists in the form of well-known structures of anatomic tissues. By reviewing current knowledge of modern neurobiology, there are two kinds of basic manners of BIT in organisms, namely electric signals and physicochemical signals, including neurotransmitters, hormones, cellular factors, secondary messengers, and metabolic products. For example, the BIT of nervous system is the combination of the transfer of "electric signal" and the transfer of "neurotransmitter signal" (more details are well elaborated in vast literature of the modern neurobiology).

1.4 Generality of animal and plant signal conductivity (meridian phenomenon)

A large number of facts have indicated that the "meridian phenomenon" exists not only in the animal but also in the plant. From the Darwin's Theory of Evolution, it can be presumed that the BIT of the animals and plants may have the common anatomical and physio-biochemical mechanisms [12]. By studying Hami melon and banana, Zhu Zongxiang proved that the "meridian phenomenon" also exists in plants and fruits [13].

To better understand the above-mentioned meridian phenomena and their characteristics in humans or in high animals without the disturbance or complication of nervous system, we may tentatively move our attention onto the information transmission mechanism of the plant tissues and cells.

2 "plant neurobiology" and related research

The signal transmission system of higher plant refers to the phenomenon that the plant sends out signals and transmits it to the target for making corresponding reaction due to external stimulation [14]. Though the rigid structure of the plant cells restricts its elasticity, most electrochemical functions of the cell membrane of plants are basically identical to that of the animals' [12]. Substantial physical disturbances (electric current, shock, temperature cataclysm, and so on) or organic solvents all can interfere with the physical status of the plasma membrane and change the membrane potential similar to the electric signal transmission of neurons in animals. Alteration of membrane potential can burst out the electric wave impulse and release physiologic active substances, for example, wound hormone, and acetylcholine (a kind of animal neurotransmitter) when the stimulation strength is beyond the critical value (usually called threshold). This impulse may transmit over a long distance. The fluctuation of membrane potential can further regulate the gate of ion channels and then continuously promote the transmission of the signals within the cells or among different cells [14].

Although there is no nervous system as yet in plants similar to that in animals for the transmission of electric signal, related studies have shown that there exists potential transmission in plants similar to that in the tissue of animals. For example, Bose, an Indian scholar, proved in his study that the *Mimosa pudica* can send out the transmission of action wave upon the harmless stimulation or excitation and the transmission of action potential in the plants basically complies with the law of "all or none, refractory period, regulative, cathode close while anode open" [15]. This explains that the excitable tissues of the animals and plants have the common BIT mechanisms. The giant internodal cell of *Chara* is usually used as an ideal experimental model of the nervous fiber studies of the animals. Furthermore, such studies confirm that the transmission of electrochemical waves of the higher plants caused from the harmful stimulation is mainly via two information transmission manners of (1) local electric current and (2) wound hormone release, which are identical to the information transmission mechanism of the animal tissue [16].

2.1 Transmission manner of plant electric signal

In the electric information transmission research of plants, two basic waveforms can be observed: the action wave and the variation wave (Fig.1).

2.1.1 Transmission of action potential (electron-related BIT)

2.1.1.1 Transmission of local electric current

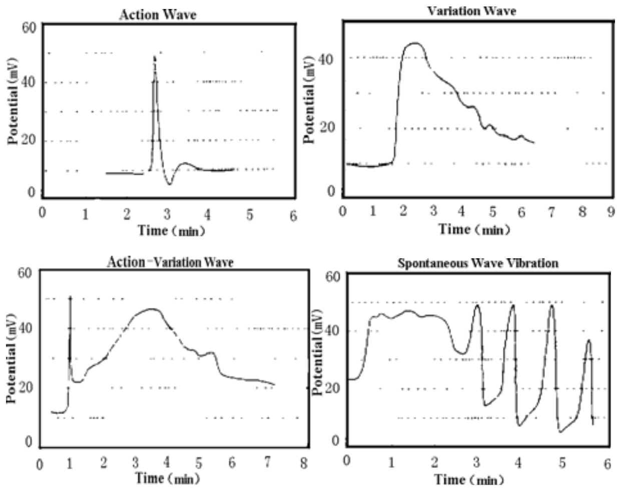

Fig. 1 Main Waveforms Observed in the Experiments of Signal Transmission of Higher Plants [12]

(information transmission related to depolarization of cellular membrane)

In 1930, Osterhout et al. [17] reported that the action potential can be blocked by chloroform when it is transmitted on the internodal cell membranes of *Nitella flexilis*, but the action potential can make a detour from the blocked area, which can be transmitted when a salt bridge connects the two ends of the blocked area. This finding indicates that the transmission of the action potential is carried via circulation of local electric current. Then, Auger [18] and Sibaoka [19] showed that the transmission velocity of the action wave can be speeded up when the external media resistance reduces, which has further proven the existence of local electric current. Replacing the salt bridge using electric connection in the internodal cells of *Chara braunii*. Tabata et al. [20] also confirmed the theory of electric transmission of Osterhout, et al.

2.1.1.2 Electric coupling transmission (electric signal transmission of plasmodesmata)

In 1995, Lou Chenghou et al. [21] used plasmodesmata for measuring the ER and showed that plasmodesmata can greatly reduce the resistance between cells and provide effective channel for electric current from one cell to another cell, thus proving the fact of intercell electric coupling of the plant tissues.

The electric coupling transmission of action potential has also been demonstrated in higher plants. The immersion of the leaf stalk of the *M. pudica* into 0.0l M KCl may enhance the speed of the action potential by 10%, and immersion into 0.1M NaC1 may increase its speed by 60%. This confirms the theory of electric coupling [22]. If surgery is used to cut off the vascular bundle, the action potential can still be quickly transmitted into nonexciting cells [23]. This phenomenon cannot be interpreted by the dispersion of chemical transfer. Furthermore, Zawadzki, et al. [24] showed that the action potential is transmitted from one exciting end to other end via the electric coupling over the blocked stems of *Lupin*.

2.1.2 Transmission of variation potential (chemical- or transmitter-related BIT)

In 1916, Ricca [25] showed that certain substance may be released or emitted from the wound (it is later called the wound hormone or Ricca factor) in case of any transfer of variation potential due to the harmful stimulation, the substance may pass through the nonliving tissue and cause potential change in the neighboring living tissue. Later, Van Sambeek, et al. [26] showed that the transfer of various potential can be generated by disposing the separated leaf stalk base by coarse extract containing the "wound hormone" factor. Recently, Schildknecht, a German organic chemist, and his co-workers separated the compound similar to Ricca factor from *Mimosa pudica* and *Acacia farnesiana*. By analysis of its structure, he indicated that the compound is 4-O-[3, 5-Dihydroxybenzoic acid] β-D-glucosid-6'-sulfate (a PLMF, periodic leaf movement factor) containing the β-glucoside, which can be transferred to the leaf cushion with the transpirational flow that result in the closing of small leaf blades. It is activated when the solution reaches the concentration of 10^{-5}-10^{-7}M [27]. To conclude, the transfer of variation potential has involved different chemical substances.

After discovering the existence of the wound hormone in 1916, Ricca proposed the tentative idea that the wound hormone will be transmitted with the transpirational flow. Then, Snow [28] and Van Sambeek [26], et al. supported this idea and developed the hypothesis of transpirational flow. The later research indicates that the variation potential will not be transmitted only for one direction just like the transpiration flow, and its transmission speed is also higher than the speed of transpirational flow. For example, using *M. pudica*, the speed of variation potential is 10 times the maximum speed of transpirational flow, which are 3 mm/s and 0.3 mm/s, respectively [15]. For this reason, the transmission of variation potential is related to the transpirational flow, but not decided by the transpirational flow.

Furthermore, Ren Haiyun, et al. [29] studied the transmission manner of variation potential in the *Tradescantia albiflora* by using the extracellular or intracellular micro electrode and microscope injection. The leaf blade of *T. albiflora* can be divided into different patterns, namely stem-associated symplast structure (comparable to the vertical meridian, with vessel pattern information transmission, hereinafter indicated as "VPIT") or nonsymplast structure (comparable to the collateral net system, with cellular pattern information transmission, hereinafter indicated as "CPIT"). The variation potential can be transmitted quickly in symplast structure (VPIT), which is much faster than the free dispersing speed of chemicals in the liquid phase; but among the nonsymplast structure (CPIT), the transmission of variation wave is rather slow, and it is 1/10 the speed of the variation wave in the symplast structure.

As to the transmission of variation potential involved with the chemical substance, Lou Chenghou, et al. [30] suggested that it is performed via the following ways: the wound hormone released from the tissue due to the harmful stimulation will cause potential fluctuation of the surrounding tissues and the emergent fluctuation of the potential will again cause the release of the wound hormone from this tissue, and the newly produced wound signal will arouse or stimulate the potential change of its adjacent tissues in the same manner. The variation potential is transmitted in the pattern of electrochemical wave.

2.2 Transmission pathway of electric signal in plants

2.2.1 Transmission pathway of action potential

Several studies have suggested that the phloem in the stem of plants and majority of cortex have participated in the transmission of action potential, and the action potential can be transmitted in different tissues. First, Bose [15] discovered that the phloem and xylem can transmit the action potential by inserting electrodes into different depths of leaf stalk. With microelectrode and fluorescent dye injection, Sibaoka [31] showed that the parenchymal cells at primary xylem and the slender parenchymal cells at phloem of *M. pudica* leaf stalk are the transmitting cells of the action potential. The membrane potential of these cells is higher (−150mV~−160mV), and the membrane potential of surrounding cells is lower (about −50mV). Further studies have shown that, in the plant stem, the action potential is transmitted via the slender parenchymal cells (VPIT) with a higher membrane potential in the vascular bundle, and the action potential across different vascular bundles is transmitted via the parenchymal cells among the bundles (CPIT). What is different is that, the action potential in the leaves of *M. pudica* is transmitted to different directions via the excited cells (CPI-T). In addition, it is shown that, by using the microelectrode technology, the action potential can be transmitted either along the phloems or on opposite direction (VPIT) in the plants with double-phloem vascular bundles such as pumpkin.

In summary, the BIT of action potential in plants has been studied in more detail than that among animal cells, which has already provided a number of useful information for research of BIT with animal cells.

2.2.2 Transmission pathway of variation potential in plant

As early as 1935, Houwink [32] observed that the variation potential will occur after the peak value of action potential in the *M. pudica* when he distinguished the transfer of action potential and variation potential. Then, Lou Chenghou [16] used the *Tropaeolum majus* to carry out the cutting experiment of leaf vein and discovered that the variation potential caused from the burnt leaf blades of *T. majus* can be transferred along the vascular bundle (leaf vein, VPIT) and can also be transmitted over the parenchymal tissues (CPIT). The transmission speed of the former is faster, and both two transmission speeds are too high to be interpreted by the free dispersion or flow of wound chemicals. The same circumstance [29, 30] is also observed in a variety of higher plants. In the stems of *Vicia faba* and watercress, it is observed that the variation potential is transmitted *via* the parenchymal cells among the vascular bundles. Roblin, et al. [33] discovered that the transmission speed of variation potential along the transpirational flow was faster than that of opposing the flow when burning the leaves of *Vicia faba*. When reversing the transpirational flow, the said phenomenon was also reversed. Furthermore, the variation potential can be transmitted from one vascular bundle in the stem to another vascular bundle. This indicates that the action potential can be transmitted in cross-bundle directions (CPIT). Studies have demonstrated that the transmission of variation potential can be performed either due to the electric coupling effect or due to the chemical stimulation among different cells. In addition, it has been known that the leaf sequence of watercress is 2/5, namely the vascular bundle of the first leaf is connected with the sixth leaf in the same vascular bundle of the stem, and the vascular bundle of the second leaf is connected with the seventh leaf in the same vascular bundle, and so on. By a cutting experiment of vascular bundles, the transfer law of variation potential at various side branches of the watercress was studied, and it is discovered that the variation potential resulting from burning is transmitted by separated vascular bundles (VPIT) and there is other detectable signal among the vascular bundles (CPIT). During the transmission of potential signals, relevant signals have been observed in the parenchymal cells of both cortex and marrow, respectively.

Moreover, some experiments demonstrated that the variation potential can be transmitted from one end of the vascular bundle to another end of the vascular bundle. This means that the variation potential can be transmitted along the vascular bundle (VPIT). It is also discovered that the variation potential can still be transmitted if different broken vascular bundles is bridged by a water-filled plastic tube, which proves that the variation potential can be transmitted over apoplasts (CPIT) [25]. To summarize, the variation potential can be transmitted either along the symplast or along the apoplasts.

2.3 Physiologic functions of the electric signal transmission in the plants

The transmission pathway of the electric signal in the plants is closely related to the physiologic functions of plants such as plant's organ movement, extension and growth, stomatal movement, substance metabolism, and so on. Davies

[35] postulated that the action potential of plant electric signal is characterized by rapidity, ubiquity, transient in a physiologic need, and this signals can bring the information from one part of the plant to another part to stimulate the plant to generate the physiologic changes such as the movement, growth, physiologic metabolism, and substance transportation to communicate among plant's parts and with the surroundings [36]. Wildon [37] discovered that a local damage in tomato plant can quickly activate long-distance protease inhibitors via the electric signal, and such electric signal is exactly the action potential. Several recent studies have found that the electric signal of the plant plays an important role in physiologic functions, for instance, transcription, translation [38], cytoplasmic calcium levels, peroxidation [39], respiration [40], and photosynthesis [41]. In addition, some studies reported that the action potential is closely related to blue light-induced phototropism [42,43], flower induction [44], pollination [45,46], phloem transport [47-49], and the rapid, systemic use of plant defenses [50-55].

3 Implication of meridian-like BIT from evolution of animal's nerve system

Numerous data have shown that various manifestations observed through the meridian-related information transmission are related not only to plant BIT but also to the BIT in the primary animals.

3.1 Nervous evolution of animals

Unicellular protozoa and single-cell animals have no nervous system, such as euglena and paramecium, but they can feel the external stimulation and make different corresponding reactions. Multicellular animals, such as sponge, have a primary nervous system. There is no synaptic contact among their neurons, but they have the function of perception and movement.

Coelenterata has the nervous network composed of bipolar neuron or multipolar neuron and sensory cell fiber, which enables the excitation to undergo diffusive transmission via the synaptic contact, such as *Hydra*, *Medusa*, and so on. Brain ganglion and nerve cord connecting the transverse nerve appear in the *Platyhelminth*. Ganglion and central nerve chain dominating the contraction of muscles appears in *Annelida*. Such a nerve chain is more concentrated in the animals of *Arthropoda*.

Mollusca animal has brain ganglion, side ganglion, internal ganglion, and foot ganglion, and the nervous system connected from the four ganglions, and especially their brain are composed of integrated ganglions. The evolution of vertebrate animals is the further perfection of the brain structure and function. The animal nervous system is evolved from diffuse structure to network structure, to trapezoid structure, to chain structure, and to tubular structure, until the frontal lobe is divided into five parts and cerebral cortex [56].

3.2 Inspiration from the Nervous Evolution of Animals

Cell is the basic unit of life. Regardless of the unicellular or multicellular creatures, the cellular activities will be carried out in certain environment and the life activity of cells is sociable. The complicated information transmission among the cells and with environment is referred to as cell communication [57]. During cellular communication, the cell will identify signals form the surrounding cells or the environment and convert them to molecular and functional changes. Consequently, they may exert influence on the environment and other cells [58].

At the beginning of animal evolution and when the cell differentiation is not yet established in lower animals, far from being have a nervous system, there is no real brain, neuron, and synapse, but it can still deal with the information from the outside and it responds by direct reaction to the external stimulation [59]. The unicellular organism has no nervous system, for example, from the amoeba, we can see that the whole process of the amoeba, including aspiration, digestion, excretion, and movement, is carried out by its own single cell, and meanwhile, the amoeba can complete the simplest analysis of the external stimulation via the reaction against the substance signal, for example, depart from the harmful stimulation and approach to the food [60]. The information response ability represented by the primary animals is similar to the "Brain of Tree" proposed by Darwin [61], which looks like the root tip of the plants that is extended to the place with rich nutrition. The perception competence of multicellular primary animals shall also be realized via the transfers of cell gap substance and electric signal. The secondary signal transmission system in such primary animals has undoubtedly provided the substance foundation of the tissue structure and cell biology for many phenomena related to the meridian information transfer, such as recessive transmission of sensation, bilateral transmission, trans-metamere conduction, low impedance and high conductivity, high oxygen partial pressure, high response to sound, transmission of tracing substance, in favor of lightening and heating.

It is noteworthy that British scientist discovered that there is an enteric nervous system (ENS) in the human body that does not depend on the central nervous system and the peristalsis reflection can independently control and carry forward the food in the digestive tract. In fact, in the middle period of 1900s, German psychiatrist Auerbach was surprised when he observed the internal organs under the microscope. He discovered that the quantity of neurons on the bowel walls is astonishing, and he did not know that what he discovered is the general headquarters of the digestive organs of human body. The related studies have shown that the pressure is given to the small intestine of the anesthetized dog, it can result in the contraction of mouth and the looseness of anus and a high-strength electric wave signal is monitored, which was called "Law of Small Intestine Signal." Several studies have shown that responses of motor neurons will disappear after the contact from the central nervous system to bladder and skeletal muscle is cut off, and the physiological functions are kept on after the contact between the central nervous system and the intestines has been cut off. Unfortunately, this independent ENS concept has once been erroneously believed as the relay-neurons of the parasympathetic nerve and the nervous pathway between the central nervous system and the intestine effector (e.g. smooth muscle, blood vessel, and gland). This concept has become the teaching material of medical education for a long time [62]. Recently, Gershon [63], a professor of Columbia University, restudied and proposed the concept of gut brain or abdominal brain, which is called "the second brain" in human body. This has undoubtedly provided the extreme interpretation for the odd life phenomenon of "meridian-viscera correlativity" in current studies and discoveries of AM.

4 Proposal of "Integration Theory for BIT System" (the 321 Integration Theory)

The prevention and cure mechanism of the meridian and AM are the eternal enigma in the field of Chinese and western medicines and also an extremely difficult problem in the research of biology medicine for centuries. Numerous studies have shown that, with regard to the response of the external environment, organisms in the nature have not only different BIT patterns among different species but also different BIT systems in the same body.

From the above review, we are astonishing to discover that the research on the information transmission of plant cells/tissues is more mature and profound than that of the animal cells/tissues. This has provided important inspiration to the understanding of meridian essence. Darwin proposed [61] that the root of plant is similar to the diffuse brain of lower animals in his book "The Power of Movement in Plant" 100 years ago. Bose in 1924 formally proposed the concept of plant neurobiology [64]. American electronic expert Backster applied his liar-testing instrument to study plants and found "Evidence of a primary perception in plant life" and published this paper in the *Journal of International Parapsychology*. In 1968, Backster stated that plants have memory and perception capability similar to animals [65].

In recent years, the "plant neurobiology" rose again, Volkov (2000) made comparative research of the plant phloem and the animal axon, which showed that the plant phloem is the conductor of biochemical impulse and showed that plant vessel is full of the electrolytes like the animal axon [66]. Baluška, et al. (2004) addressed that the apical area of the plant is the plant control center and plays the role just like the brain. They believed that the plant has the ability of acquisitioning information, study, and memory. The plant can exchange information via the action potential in a long distance. Also, the skeleton of plant F-actin and Myosin VIII passing through the plasmodesmata pathway is the nervous synapses of plants. They also believed that growth hormone of plants serves as the nervous signal molecule of plants, and high-speed nervous activities and information transfer between ground growth point and the apical area of the plant are carried out via vascular tissues [67]. Stahlberg (2006) assumed that the plant nerve not only owns the action potentials like animal nerves but also the unique slow-wave potentials [68]. Brenner (2006), et al. elaborated plant neurobiology as the mechanism [69] of signal transmission in the plant body dealing with information obtained from the external environment. Recently, the concept of "plant neurobiology" has been criticized by 33 experts, who commented that this concept does not increase our understanding of plant biology, plant cell biology, and signal transmission. There is no sufficient evidence showing that neither neuron, nor synapse, nor brain exists in plants [70].

Through vigorous debate, academic society is still unable to accept the view that plants own nervous systems like animals, but it seems that the functions of "quasi-nerve system" of plants can be verified mutually to some meridian-signal phenomena of animals. Not only their morphologies are similar but also their biology regulation mechanisms – that is, the "electric signals" and "physicochemical signals" are the fundamental transmission manners of both plants and animals. From the "wave-particle duality" of the BIT, the material foundation and the physicochemical nature of human body regulated or carried out in the meridian and its related systems can be established. For this reason, we believe that a novel "unified theory of BIT system" may be raised to interpret the meridian phenomena and then integrate the BIT regulation system of plants and animals. This unified theory may not only interpret the parallel evolution of the BIT of the plants and animals but also elaborate the importance of information processing of the plants.

Through the macroscopic comparison and analysis of the above-mentioned transmission system of the plants and animals, the BIT regulation system can be classified as follows: (1) nervous system (nerve level), (2) fluid information transmission system (vessel level), and (3) cell information transmission system (cellular level).

First, "nervous system" refers to various high-speed information transfer systems owning the neurons, axons, synapses, and neurotransmitters, including the higher nervous structure and the autonomous nerves not controlled by the brain, and even the relatively independent lower nervous structure (the so-called "intestine-brain"). Second, "fluid information transfer system" refers to the BIT realized through various biologic conduits in organisms without classic nervous system, for example, transmission of nutrients and hormones in the plant vessels and sieve cells, transmission of hormones and various information factors in the blood vessels and lymphoid systems of the animals. Third, "cellular information transfer system" refers to the cellular information communication that is relatively primary in evolution, mainly including the electric signal transfer between cells and cross cells with environment, may be at a relatively lower speed. (Tab. 1)

Tab. 1 Classification of BIT Systems and Their Similarities and Differences

	Biological Structures	Transmission Manners	Transmission pathways	Species
Nervous system	Nerve structure	Electric signals; Chemical signals	Nerve	Animals
Fluid/Vessel information transmission system	No nerve structure; Relying on vessel structure	Electric signals; Chemical signals	Vessel	Animals/Plants
Cellular information transmission system	No nerve structure; Not relying on vessel structure	Electric signals; Chemical signals	Cell	Animals/Plants

The biological information and its transfer can be divided into two manners, namely electric signals and chemical signals as shown in Table 1. The two BIT manners are interconnected, regardless of animals or plants, high organisms or low organisms. The BIT systems/mechanisms are classified into three levels, any level possesses both BIT manners, and only their biological structure, pathway, speed, and substance of the information transfer are different from each other. Information transmission of different levels and categories can overlap, impose, and also complement and transform from each other.

It should be admitted that the effort of scholars to look for the anatomical structure of the meridian has been basically failed, but a large number of related studies have indicated the objective existence of the electric physiological and biochemical phenomena besides the action of nervous conduction. After the gradation of BIT system, the material base of TCM therapeutic measure such as AM, which plays the stimulation role in the BIT systems at various levels in the animals and plants, can be observed. Any action or phenolmenon out of the higher nervous activities or related to the "meridian" shall undoubtedly belong to the "sub-levels of infor- mation transmission", or the so-called "plant neurobiology."

Under the guidance of the "Theory of BIT System Integration" and in the presence of "two manners and three levels" BIT structure in the organisms, the meridian is no longer a vague and insubstantial imagination that cannot be seen and touched, instead it is a macroscopic integration of anatomical entity structure. It is now clearly specified media and targets that can be found for the therapeutic principle and practice, and they conform to the basic biophysical and biochemical laws. This theory has embodied the philosophy from the macroscopic view to microscopic view of "one gives birth to two, two gives birth to three, and three gives birth to everything" proposed by the ancient Chinese philosopher Lao Zi. Looking back from the microscopic world to macroscopic world, this theory can be called as "321 Integration Theory" representing the BIT integration of "three levels with two manners" in the organisms. This "321 Integration Theory" has finally established a unified interpretation of meridian in preventing and treating health problems of humans.

By combining the "electric–chemical" concepts of the BIT with the difference and complexity of the organism, the biomedical integrative effects on the "meridian channel," such as low impedance, linearity, stagnation, self-consistency, uncertainty, tendon character, tissue exclusive property, individual difference, variability, and so on, can be understood. With "electric–chemical" concepts of BIT, the theoretical problems in the field, such as "unsteady character of TCM therapies" related to meridian, "self-consistent principle," "applying therapy to any place where effective," and "rather missing the acupoint than missing the channel," and so on, can be interpreted. This can help explain various healthcare techniques used by TCM in clinic practices, including pressing, wiping, pricking, scratching, scraping, twisting, vibrating, plucking, AM, and so forth.

We hereof state that the time to scientifically explain the meridian-related biological phenomena has arrived. In the framework of "321 Integration Theory," we believe that the mechanisms of AM in resisting and preventing diseases is to send different regulation signals to various tissues of the organism to result in certain influence on three BIT systems (also see review [71]) through electric and chemical substances, enabling the associated tissue cells to make fast or slow reactions and enabling organisms to change the endocrine situation, so as to recover the balance of organismic metabolisms, to enhance the defense response, to resist various etiologies or various damages resulting from different stresses and finally recovering organisms' health.

Abbreviations:

Acupuncture and moxibustion (AM)

Biological information transmission (BIT)

Electric resistance (ER)

Traditional Chinese medicine (TCM)

Vessel pattern information transmission (VPIT), comparable to the vertical meridian

Cellular pattern information transmission (CPIT), comparable to the collateral net system

References

[1] Hua P, Lv H, Yuan L *et al*. Four main schools of thought and analysis in studies of channels and collaterals. *China Acupuncture & Moxibustion* 2006; 26(6): 407-413.

[2] Zhang WB, Guo Y, Lin YY *et al*. 50 Years' Retrospection of Meridian Study and Future Research Trend. *World Science Technology-Modernization of Traditional Chinese Medicine* 2005; 7(5): 99-104.

[3] Zhu ZX. Modern Biology and Physics Demonstration of Classic Meridian School. *Bulletin of Biology* 1988; (6): 1-4.

[4] Nagahama H, Maruyama M. *Research of Meridians*. Chiba University Medical School Kyorin Shaoin [in Japanese], Tokyo. 1950.

[5] Nakatani, Yoshio. An aspect of the study of Ryodoraku. *Clinic of Chinese Medicine* 1956, 3(7): 54.

[6] Lee MS, Jeong SY, Lee YH *et al*. Differences in electrical conduction properties between meridians and non-meridians. *Am J Chin Med* 2005; 33 (5): 723-728.

[7] Chen DL, Wan L, Xie JZ. Establishment of Continuity of Epidermal Gap Junctional Intercellular Communicatin Along Meridians during Human Embryonic Development. *Journal of Fujian College of Traditional Chinese Medicine* 2000; 10(1): 33-35.

[8] Zhu ZX, Xu RM. Modern Study of Chinese Meridian Science. *World Science Technology-Modernization of Traditional Chinese Medicine* 2000; 2(5): 23-26.

[9] Wu YL. Systemic Construction and Subject Value of Luobing Theory. *Frontier Science* 2007; (2): 40-46.

[10] Yang WS. Investigation of the Lower Resistance Meridian Ⅳ.Speculation on the Physiological Functions of Acupuncture Meridians. *Acta Scientiarum Naturalium Universitatis Pekinesis* 2008; 44(2): 281-288.

[11] Xie HR, Li FC, Ma XS. Discussion on the Essence of Meridian-Collateral System. *Acupuncture Research* 2007; 32 (3): 210-213.

[12] Lou CH. Electrochemical wave transmission in higher plants. *Acta Biophysica Sinica* 1996; l2 (4): 739-744.

[13] Zhu ZX, Xu RM, Hao JK *et al*. Is there any meridian in Plant? – Discovery of Low Resistance along the Meridian and High-Sound Lines in the Hami Melon and Banana. *Chinese Journal of Nature* 1988; 11(11): 880.

[14] Lou CH, Hua BG. Plant Signal System – its Role in Functional Integration and Applicable Environment. *Chinese Bulietin of Life Sciences* 2000; 12(2): 49-51.

[15] Bose C. The nerve mechanism in plants. *Green Co, London Longman*, 1926.

[16] Lou CH, Shao LM, Zhu ZL. Electric Wave Transmission of Stimulation in Plants. *Journal of China Agricultural University* 1959; (5): 1-12.

[17] Osterhout WJV, Hill SE. Negative variations in *Nitella* produced by chloroform and by potassium chloride. *J. Gen. Physiol* 1930; 13(4): 459-467.

[18] Auger D. Contribution a l''etude de la propagation de la variation dectrique chez les Charace'es. *Compt rend Soc Biol* 1933; 113: 1437-1440.

[19] Sibaoka T. Conduction of action potential in the plant cell. *Trans.Bose Res. Inst* 1958; 22 (115): 43-56.

[20] Tabata T, Sibaoka T. An Analysis of Osterhout and Hill's Salt Bridge Experiments in *Characeae Internode*. *Plant and Cell Physiology* 1986; 27(4): 711-716.

[21] Lou CH. Protoplasm Continuity in Plants. *Journal of Integrative Plant Biology* 1955; 4(3): 183-222.

[22] Sibaoka T. Acceleration of the exitatory conduction in the submerged petiole of *Mimosa pudica*. *Sci. Rep. Tohoku Univ. (Biol.)* 1960; 26: 199-204

[23] Sibaoka T. Action potentials in plant organs. *Symp Soc Exp Biol* 1966; 20: 49-73.

[24] Brant-Zawadzki MN, Minagi H, Federle MP *et al*. High resolution CT with image reformation in maxillofacial pathology. *American Journal of Roentgenology* 1982; 138(3): 477-483.

[25] Ricca U. Solution d'un problemc dc physiologic:la propagation de stimulus dans la sensitive. *Atchivcs Italiennes de Biologie* 1916; 65: 219-232.

[26] Van Sambeek JW, Picard BG. Mediation of rapid electrical, metabolic, transpirational, and photosynthetic changes by factors released from wounds. II. Mediation of the variation potential by Ricca's factor. *Can Bot* 1976; 54: 2651-2661.

[27] Snow R. Conduction of Excitation in Stem and Leaf of *Mimosa pudica*. *Proc R Soc Lond B* 1924; 96: 349-374.

[28] Ren HY, Lou CH. Electric Wave Transmission within and between Symplastic Regions in Higher Plants. *Acta Phytophysiolgica Sinica* 1993; 19(3): 265-273.

[29] Lou CH. Riddle of the Vascular System—the Life Vein of Higher Plants**.** *Plant Physiology Communications* 1992; 28 (1): 1-10.

[30] Sibaoka T. Excitable cells in *Mimosa*. *Science* 1962; 137 (3525): 226-227.

[31] Houwink AL. The conduction of excitation in *Mimosa pudica*. *Rec Trav Bot Necl* 1935; 32: 51-91.

[32] Roblin G, Bonnemain JL. Propagation in *Vicia faba* Stem of a Potential Variation Induced by Wounding. *Plant Cell Physiol* 1985; 26(7): 1273-1283.

[33] Guo JY, Yang XL. Electrical Signals in Higher Plants. *Chinese Agricultural Science Bulletin* 2005; 21(10): 188-191.

[34] Davies E. New functions for electricalsignals in plants. *New Phytologist* 2004; 161: 607-610.

[35] Lu SF. Transmission Pathway and Manner of Electric Signals in Plants. *Chinese Bulletin of Botany* 1996; 13(4): 23-27.

[36] Wildon DC, Thain JF, Minchin PEH *et al*. Electrical signaling and systemic proteinase inhibitor induction in the wounded plant. *Nature* 1992; 360: 62-65.

[37] Stankovic B, Davies E. Wounding evokes rapid changes in tissue deformation, electrical potential, transcription, and translation in tomato. *Plant and Cell Physiology* 1997; 39(3): 268-274.

[38] Trebacz K, Dziubinska H, Krol E. Electrical signals in long-distance communication in plants. *In Communications in Plants. Neuronal Aspects of Plant Life* (Balusˇka, F. *et al*., eds). Springer Verlag, Amsterdam, 2006: 277-290.

[39] Filek M, Koscielniak J. The effect of wounding the roots by high temperature on the respiration rate of the shoot and propagation of electric signal in horse bean seedlings (*Vicia fabal. minor*). *Plant Science* 1997; 123(1-2): 39-46.

[40] Koziolek C, Grams TEE, Schreiber U *et al*. Transient knockout of photosynthesis mediated by electrical signals. *New Phytol* 2004; 161: 715-722.

[41] Volkov AG. Electrophysiology and phototropism. *In Communication in Plants: Neuronal Aspects of Plant Life* (Balusˇka, F. *et al*., eds), Springer Verlag, Amsterdam. 2006: 351-368.

[42] Volkov AG. Green plants: electrochemical interfaces. *J Electroanal Chem* 2000; 483: 150-156.

[43] Wagner E *et al*. Hydro-electrochemical integration of the higher plant–basis for electrogenic flower initiation. *In Communication in Plants: Neuronal Aspects of Plant Life* (Balusˇka, F. *et al.*, eds), Springer Verlag, Amsterdam. 2006: 369-389.

[44] Sinyukhin AM, Britikov EA. Action potentials in the reproductive system of plants. *Nature* 1967; 215: 1278-1280.

[45] Spanjers AW. Biolelectric potential changes in the style of *Lilium longiflorum Thunb*. After self- and cross-pollination of the stigma. *Planta* 1981; 153: 1-5.

[46] Fromm J, Eschrich W. Transport processes instimulated and non-stimulated leaves of *Mimosa pudica*. *Trees-Structure and Function* 1988; 2(1): 7-17.

[47] Fromm J, Bauer T. Action potentials in maize sieve tubes change phloem translocation. *J Exp Bot* 1994; 45(4): 463-469.

[48] Fisahn J, Herde O, Willmitzer L *et al*. Analysis of the transient increase in cytosolic Ca^{2+} during the action potential of higher plants with high temporal resolution: requirement of Ca2+ transients for induction of jasmonic acid biosynthesis and PINII gene expression. *Plant Cell Physiol* 2004; 45(4): 456-459.

[49] Wildon DC, Thain JF, Minchin PEH *et al*. Electrical signaling and systemic proteinase inhibitor induction in the wounded plant. *Nature* 1992; 360: 62-65.

[50] Malone M, Palumbo L, Boari F *et al*. The relationship between wound-induced proteinase inhibitors and hydraulic signals in tomato seedlings. *Plant Cell Environ* 1994; 17(1): 81-87.

[51] Herde O, Fuss H, Peña-Cortés H *et al*. Proteinase inhibitor II gene expression induced by electrical stimulation and control of photosynthetic activity in tomato plants. *Plant Cell Physiol* 1995; 36(4): 737-742.

[52] Herde O, Atzorn R, Fisahn J *et al*. Localized wounding by heat initiates the accumulation of proteinase inhibitor II in abscisic acid deficient tomato plants by triggering jasmonic acid biosynthesis. *Plant Physiol* 1996; 112(2): 853-860.

[53] Stankovic B, Davies E. Both action potentials and variation potentials induce proteinase inhibitor gene expression in tomato. *FEBS Lett* 1996; 390(3): 275-279.

[54] Stankovic B, Davies E. The wound response in tomato involves rapid growth and electric responses, systemically upregulated transcription of proteinase inhibitor and calmodulin. *Plant Cell Physiol* 1998; 39(3): 268-274.

[55] Han FR. Evolution of Animal Nervous System. *Journal of Normal Colleges* 1998; 3(3): 62-64.

[56] Wu KF. *Cell Communications and Diseases*. Science Press, Beijing. 2006: 1-3.

[57] Xu XX, Dai Y, Liu QY. Cell Communication and Its Pharmacology of on Traditional Chinese Medicine. *World Science Technology-Modernization of Traditional Chinese Medicine* 2008; 10(1): 98-102.

[58] Ye LM. Development of Nervous System. *Chinese Journal of Medicine* 1954; (3): 26-29.

[59] Л.A. Fan GY *et al*. Evolution of Nervous System. *Bulletin of Biology* 1957; (2): 39-43.

[60] Tian ZS, Wu XZ, Chen C. On "Abdominal Brain (The Second Brain)". *Chinese Journal of Surgery of Integrated Traditional and Western Medicine* 2005; 11(5): 454-457.

[61] Gershon MD. *The second Brain*. Harper Collins, New York. 1999

[62] Darwin C. *The power of movement in plants*. John Murray, London, UK. 1881.

[63] Bose JC. *The physiology of photosynthesis*. Longmans, Green and Co., London, UK. 1924.

[64] Backster C. Evidence of a primary perception in plant life. *International Journal of Parapsychology* 1968; 10(4): 329-348.

[65] Volkov AG. Green plants: electrochemical interfaces. *J Electroanal Chem* 2000; 483(1-2): 150-156.

[66] Baluška F, Mancuso S, Volkmann D *et al*. Root apices as plant command centres: the unique ‘brain-like’ status of the root apex transition zone. *Biologia (Bratisl.)* 2004; 59 (Suppl. 13): 1-13.

[67] Stahlberg R. Historical overview on plant neurobiology. *Plant Signal Behav* 2006; 1(1): 6-8.

[68] Brenner E, Stahlberg R, Mancuso S *et al*. Plant neurobiology: An integrated view of plant signaling. *Trends Plant Sci* 2006; 11(8): 413-419.

[69] Alpi A, Amrhein N, Bertl A *et al*. Plant neurobiology: no brain, no gain? *Trends in Plant Science* 2007; 12(4): 135-136.

[70] Yin DZ. An Explanation for the “Causal Treatment” of TCM Based on Modern Science. *Chinese Journal of Integrative Medicine* 2007; 27(7): 581-583.