Integrative Molecular Medicine

Review Article ISSN: 2056-6360

Hypothesis on a signalling system based on molecular vibrations of structure forming macromolecules in cells and tissues

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Abstract

Cells and tissues are tree-dimensional systems. The scaffolds are established by macromolecules such as proteins, polar lipids, glucosaminoglycans, glycoproteins, cholesterol forming networks and membranes. These structures are permanently changed, remodelled, restored. The chemical signalling is insufficient to inform on spatial aspects where changes are needed and it should be supplemented by physical signals. All molecules show molecular vibrations at the temperature of living systems. This oscillation of macromolecules creates infrared radiation. As the molecules carry functioning groups the infrared radiation is characterised by defined peaks. Frequencies of mid- infrared spectrum below 1300 cm-1 can penetrate without being weakened by water absorption. The peaks are modified by the specific environment of the molecule and change in the course of chemical reactions. If the cells responsible for supply of restoring or remodelling enzymes are capable to realize these signals the spatial aspects can be verified. The hypothesis presented is that these cells develop receptors at the cell membrane, and at the nuclear envelope for intracellular actions, based on resonance principle to record and process these signals. The cell membrane is a barrier for intracellular signals to avoid disturbance of adjacent cell. The interaction between tissue cells and their extracellular matrix in developing organism are very intensive. Signalling based on molecular vibration could be important in the memory process as well. If the information unit is stored as a modified macromolecule the specific changed vibration signal could be retrieved by the dendrite spine of the neurone after depolarisation. The retrieval process would not change the stored information unit and would be very energy efficient. The neurone represents the active part of storage and retrieval. If the hypothesis is experimentally proved a high amount of new research activities are induced up to new applications in stem cell research, cancer research, therapeutic possibilities, plant research.

Introduction

Although information on the environment of living organisms is based on chemical and physical signals, in cells and tissues of creatures the signal systems are almost exclusively based on chemical principles. That is surprising because such systems are not sufficient to report on spatial aspects, however living systems, tissues and cells are three- dimensional systems in which the structures are of outstanding importance. These structures consist of macromolecular networks differently composed and mutely connected via hydrogen bondings and van deer Waal's bonds. Many small molecules frequently with signal function are attached to these structures or are generated from them. The network is permeated by a solution of many inorganic and organic substances in water that amounts to more than 95 percent. These systems can exist in all phases between solid and fluid. Changes of the phase structure of parts of the systems could be a functional feature. The structure –relevant networks have to be permanently maintained and interferences could result in severe disturbances. The systems are subjects of regeneration and restoring processes throughout life time. Specific enzymes and specific constituents have to be provided at defined locus in appropriate time. Most requirements arise during cell deviation and development of required tissues from first cell up to complete organism. The structures of the cell, cell membrane, membranes of endoplasmic reticulum, Golgi, nuclear envelope, mitochondria organelles consist of micellar bilayers which are as extremely dynamic as the ECM. A universal information system permanently reporting on spatial aspects available intra- and extracellular seems to be necessary adding to the well elucidated chemical based signalling systems. This should be energy sufficient and continuously available. Electromagnetic signals coming directly from the structures could best fulfil the requirements. As all molecules show oscillation behaviour above zero generating an electromagnetic radiation, this molecular vibration of the structure forming macromolecules is to be taken in account.

Molecular vibration

The molecular vibration has been comprehensively investigated. The different spectroscopic methods are based on these features of the molecules and these analytical methods are described in detail in the chemical and technical literature [1-3]. Only a few aspects having importance for our contemplation are depicted and described in the following.

All molecules show constant translational and rotational motion with a frequency less than 10^{12} to approximately 12^{14} above zero. The number of different vibrations in a molecule with n atoms is 3n-5 for

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Key words: *signalling, molecular vibration, infrared radiation, nuclear envelope, cell membrane, extracellular matrix, memory,*

Received: August 18, 2015; **Accepted:** September 11, 2015; **Published:** September 14, 2015

nonlinear molecules. Oscillations sharing a common atom influence each other. If the frequencies are similar a new oscillator is formed by means of coupling. If the frequencies are very much apart, each oscillator remains fairly independent and have about the same frequencies of vibration in any molecule [2]. However, the environment of the molecules especially adjacent molecules with appropriate interaction with the molecule changes the vibration state [2]. Absorption and emission of electromagnetic radiation of specific frequencies are based on molecular vibrations.

Molecular vibration creating infrared radiation

All materials including biological macromolecules emit continuously radiation when they are in thermal equilibrium with the environment caused by the molecular vibration. Energy from the environment is absorbed by the molecule in question which leads to a higher state of energy of the molecule. This usually relaxes back to the lower energy state by releasing heat and or quanted radiation with characteristic frequencies in accordance with the chemical structure. Functional groups in the molecule, especially those increasing the dipole characteristics of the molecule result in pronounced peaks whereas the mass of carbon –hydrogen bonds yield in broad incomprehensive bands [2,3]. The frequencies of the emitted radiation are generally between 30-30000 cm^{-1}. The frequencies being emitted by macromolecules of structure components at the temperature of living systems are between 4000-400 cm^{-1} [3]. These frequencies due to molecular vibration by modulation of the dipole moment of the molecule are in the mid-infrared spectral range. As the main component of the environment of the intra- and extracellular structure components is water, only frequencies not being absorbed by water are able to penetrate a defined distance. The water-absorption reaches its maximum in the range of 1300-1900 cm^{-1} and above 3200 cm^{-1} [2,4]. That`s why only frequencies outside this range are able to penetrate distances of interest in tissues and cells of some μm. Changes in the networks of macromolecules are mainly caused by chemical reactions leading to an activated state of the molecules in question. This is accompanied by a strong change of the emitted radiation in respect to energy amount and frequency. This shift could be valuable to realize the area where actions are needed.

Due to these data it can be concluded that all structure components in living systems continuously emit an infrared radiation in the mid-infrared spectral range. The functional groups in the molecules cause sharp peaks in the spectrum. The frequencies are entirely characteristic for every component in the specific environment including adjacent molecules and phase structure. Photons with frequencies below 1300 cm^{-1} and above 1900 cm^{-1} are able to penetrate distances of interest in cells and tissues for reason of signalling. Chemical changes in a locus of a structure element result in liberation of different signal molecules as well as in remarkable change of the infrared radiation emitted. Both, the chemical and the physical signals together give the entire information. They are complementary to each other, however, it is unknown whether cells or intracellular structures are able to pick up and process the physical images. The receptor function could be based on resonance principle.

Hypothesis of intracellular afferent signalling based on molecular vibrations

The structure elements in the cell are diverse membranes such as the cell membrane, the endoplasmic reticulum, the Golgi apparatus, the diverse organelles, the mitochondria membrane, the nuclear envelope. All of them consist of plenty of specific proteins closely connected with a variety of polar lipids as phospholipids, sphingolipids, glycolipids, and cholesterol. More than 1000 lipid individuals have been identified. The lipids form the ground structure of a bilayer, in which the proteins are specifically integrated. These structures are very dynamic [5-8]. Multiple receptor functions and diverse transport tasks have to be accomplished. Signal molecules are generated from the structure lipids. Parts of Golgi or endoplasmic reticulum are used to generate transport containers [6,9]. The structures have to be permanently restored and regenerated. These complicated procedures require very effective signalling concerning chemical as well as spatial aspects. In a former article it was postulated that the molecular vibration via the infrared radiation is the signalling base for the spatial aspects [10]. The polar lipids are reasonable candidates for their high dipole moment. The receptor function based on resonance principle could be implemented by constituents of the outer layer of the nuclear envelop [11-15]. This signal along with the chemical signals coming from the cleavage products could be transferred into the nucleus for further processing. A precondition of this working hypothesis is that the postulated IR-signal can not leave the cell, not penetrated and disturbed adjacent cells. The construction of the outer cell membrane acts as an effective barrier for the postulated IR-frequencies.

Information system of extracellular matrix based on molecular vibration

Tissues consist of cells and extracellular matrix (ECM) mostly in sophisticated variation concerning substructures and the variety of cell populations. Between all components there is a close cooperation in a given tissue. The cells create the specific ECM forming their direct environment. This environment permanently undergoes remodelling processes where components are degraded, substituted, restored and modified. That is the situation in the adult organism. However, it occurs in broad measure in the complex processes of cell differentiation including establishment and maintenance of stem cell niches [16,17] epithelial branching, morphogenesis, angiogenesis and all steps of development [18-23]. As scaffold for the cells in the tissue but also as reservoir for growth factors and chemical signal substances ECM influences very intensively many cell functions [13,24-26]. Disturbed ECM metabolism results in deregulated cell proliferation, loss of cell differentiation, uncontrolled invasion and other failures; congenital defects, cancer, disturbed physical and neurological development could be the result. Maintenance and realisation of specific requirements in three-dimensional networks are necessary [18,27-30]. Main classes of macromolecules are proteins, glycogroteins, glycosaminoglycans, lipoproteins, phospholipids, sphingolipids. Every class has got many subgroups and an enormous variety of specific individuals [31,32]. These compounds of very different compositions form specific networks in several phase structures. The various cells are tissue-dependently integrated in these scaffolds. The enzymes responsible for the permanent process of renovation and modification are secreted by these cells. Some enzymes are stored in specific containers in the cells so that they can be released very quickly. Synthesis and liberation are controlled on transcriptional and translational level. The splitting products as a result of the degradation of ECM and the locally released growth factors have signal function for respective cells such as integrines, adhesion molecules, eicosanoids, lysophospholipids, lysosphingolipids and others [22,23,33,34]. This chemical signalling system is very sensitive but it is insufficient to inform on the spatial aspect where an enzymatic action is necessary. If the cells are capable to recognize and process the infrared photons coming from the structures in question, the cells would obtain the complete information on what as

well as where an action is needed and the cell next to the area of interest could be activated. The signalling frequencies of interest would be very different in the different tissues in accordance with the composition of specific ECM. However, all macromolecules contain functioning groups often polarising the molecule remarkably. These groups emit IR-radiation with sharp peaks.

Specific receptors at the outer cell membrane possibly acting on resonance principle would be a critical precondition. Only changes of specific molecular vibration patterns have to be recognized by the receptors and might lead to specific cell reactions. It is important that the IR-signals reach the specific cells and are not exclusively absorbed by water as discussed above. The signals in combination with the specific chemical signals have to be processed simultaneously. A tissue rather comprehensively investigated concerning the interaction between ECM and cells is the central nervous system.

The ECM of the brain amounts to a remarkable portion of the brain mass. It consists of a meshwork of diverse glycoproteins like lamilines and proteoglycans as chondritin –and heparansulfat proteoglycans with a high amount of attached signal molecules. The intensive cooperation of the different cells of the nervous system and the ECM during the development was investigated in detail showing strong affects on all aspects of development of the central nervous system [35,36]. Dendritic spines are the receptive contacts of the neurons with the ECM. It could be shown that ECM is a critical regulator of spine and synapse stability and plasticity. The spine head wearing adhesion receptors can bind the ECM ligands for further processing in downstream signalling proteins. This might be the signalling way for requirements of restoring processes in those cells responsible. However the spatial aspect can not be reported in this way. We assume the signal is completed by IR-signals. If these signalling works in this way, those signals could have importance also in the complicated process of memory,

Possible importance of molecular vibration in the process of memory

The memory processes are mainly hypothetical [37]. The enormous variety of information continuously arriving at the brain is stored in very different areas using variable systems which result in short-term, medium- or long-term storage. These are influenced by numerous aspects like emotions, metabolic and endocrine variables. The great deal of storage and retrieval tasks are running constantly and simultaneously. 20% of the total energy consumed are needed for brain performance [36,38,39]. However, compared with a supercomputer, the brain is incredible more energy efficient. The input of information units includes a plurality of energy consuming steps for ion transports across membranes for the purpose of polarization-depolarisation of the axoms and dendrites, transformation into signal molecules at the synapses and finally for storing by means of chemical reactions [38,36,40]. These are different depending on the intended "storage time". For long-term storage a relatively stable change of the storage medium is required. Theoretically red-ox –reactions, formation of chelating complexes of metal-ions with macromolecules like GAG, changes of the chemical conformation of macromolecules or changes of the charge of those molecules could be the basis. There are hypotheses for all, nevertheless, they need energy. For the retrieval of stored information three basic requirements have to be fulfilled:

1. The molecule structure must not be changed because the retrieval procedure has to be repeatable.

2. The energy consumption must be minimal, since the retrieval processes occur more frequently than storage.

3. The signal provided has to be unique for the information stored.

These requirements can be fulfilled by physical but not by chemical processes. A hitherto not discussed possibility is based on the principle of molecular vibrations. The storing would change the structure of the molecule or the group of molecules and thereby the specific frequency of the vibration and the characteristics of the IR-signal as well. If the information unit is of interest, specific receptors in the spines of the dendrites of the specific neurons would be activated by depolarisation and the information unit could be retrieved and processed without change of the corresponding structure and without additional energy. The molecular substrates of the storing procedure are intensively discussed in the literature. It has been proved that the spines are of central importance indicating change of shape and charge [41,42]. The molecular storage medium is not clear. The changed charge of a specific spine of a dendrite might be the active procedure in the retrieval process [42], which enables the neuron to receive a signal provided by the stored information unit. The macromolecules of spines themselves are in question to constitute the store medium, the ECM consisting of specific proteins, gangliosides, cholesterol, phospholipids, sphingolipids, possibly by forming of chelating complexes together with metal ions are in discussion [43-45], also the posttranslational modification of proteins as storage medium for long-lasting memory and epigenetic processes influencing the transcription and protein synthesis are discussed [46]. All these hypotheses are in line with the hypothesis that the retrieval of stored information units is primarily based on molecular vibrations and the permanently existing signals are retrieved when the specific dendrite spine is activated by depolarisation as a result of the centrally triggered demand

Conclusions

The hypothesis has to be experimentally proved using different cell cultures, isolated cell organelles, synthetic tissues. The first task is to identify some specific infrared frequencies capable to induce specific cell reactions possibly combined with chemical signals. The greatest challenge would be to reveal specific receptors at the cell membrane as well as at the nuclear envelope. The speculative considerations in respect to the importance for neuronal functions could be investigated in animals with highly developed and primitive neural systems using IR-radiation with frequencies in question. If the hypothesis is proved, a multitute of different challenges would arise from microbiology, plant biology up to new therapeutically applications. Physical influences on intima of arteries, articular cartilage, ECM of brain and on stem cell research could be discussed. Technical application in informatics could be discussed too because of the high energy efficiency of the generation of IR-signals by biochemical macromolecules. An entirely new direction of research would be created.

Competing interest

The author declares that he has no competing interest.

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