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The Possible Role of Molecular Vibration in Intracellular Signalling

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Abstract

The exchange of information within the cell is extremely complex. Besides the well-studied chemical signalling, physical signalling is required to fulfil spatial and temporal aspects. The Golgi apparatus and the microtubule skeleton system are the decisive structures for numerous intracellular transport tasks . Close communication between the Golgi apparatus and the cell periphery is an absolute prerequisite for the well-directed positioning of structural elements. The majority of the substances that influence the cell from the membrane transmit the information to the intracellular destination via signal transduction pathways. It is discussed in detail that the transmission of information in both systems is based on emission and resonance of electromagnetic patterns in the infrared frequency range generated by the vibrations of the respective molecules. This radiation with fingerprint patterns must be coherent to activate enzymes. Coherence could be achieved by the chemical reactions of the molecules to be replaced or in the signal transduction pathways, by the phosphorylation of the transduction proteins. The quasicrystalline structure of water is essential for that coherence.

Keywords: Signal transduction, Molecular vibration, Resonance recognition, Infrared radiation, Molecular interaction

Introduction

Life is bound to manifold interactions of cells, cell systems and cell elements with each other and with the environment under specific chemical and physical conditions.

Whereas most of the chemical signalling processes are excellently investigated in detail, some signalling processes remain unclear and could be physical. Examples are most of the information processes in the brain, many control mechanisms in cell division and development of organisms, some information processes in the cell, between the cells and between cells and extracellular matrix.

Endogenous electric and electromagnetic phenomena are increasingly becoming a focus of research in these areas [1-11]. The vibrations of molecules, molecule parts, molecular aggregates, and cell organelles generate electromagnetic radiation with frequencies in the infrared range at the temperature of life. Although the energy of this radiation is very low, this radiation appears principally suitable for intracellular as well as extracellular signalling processes.

The intracellular signalling processes are extremely complex, with numerous metabolic, developmental and regenerative processes running in parallel, which requires very intensive temporal and spatial coordination [6]. The base for that is sufficient signalling in which all structural components and organelles of the cell can be involved. The correct communication between different organelles such as ER, mitochondria, endosomes, lysosomes, cell membrane, nucleus and MT system is essential and selective disturbances are crucial in the pathogenesis of various diseases.

The hypothesis that the molecular vibration of the structure-forming macromolecules plays an essential role besides the chemical signalling in this intracellular signalling is discussed below concerning two important processes, the communication between the Golgi apparatus and the cell periphery for the replacement of structural elements and the signal transduction from

the cell membrane to the nucleus after binding on a cell membrane receptor.

Intensive communication between the Golgi and all structural elements of the cell is the precondition for the development and regeneration of the cell and its elements. Specific molecules and molecular groups must be delivered to defined spatial places, which requires close communication between the respective location of the need in the cell and the Golgi apparatus. The Golgi apparatus is the room in which the needed proteins are stored after synthesis in the rough endoplasmic reticulum (Rough ER). There the proteins are finalized after ordering and than motor-driven transported via the skeleton routes to the area of need. This communication between the Golgi apparatus and the cell periphery based on electromagnetic radiation pattern created by the molecular vibration was considered in detail in a former article. That work will be received here [12-14]. The elements of directed transport play a central role in this process. It is assumed that a coherent stream of photons is directed from the location of the need to the Golgi apparatus via the cytoskeleton and that the called molecules are motor-driven navigated to the location of the need using this signal via the skeleton.

The coherence must be preserved, and this is possibly promoted by the specific structure of the cytoskeleton together with the quasicrystalline order of water [12].

Another group of intracellular signalling processes is based on the fact that extracellular endogenous or foreign substances that carry information dock onto specific receptors of the cell membrane to transmit the information to the cell nucleus. In this signal transduction pathways, many specific molecules are involved as reaction chains or networks [15-17]. These chains and networks are well investigated. However, the question is not answered clearly, how is the information passed from one molecule to another and finally to the cell nucleus. This topic will be discussed in this article.

Molecular Vibrational Hypothesis

All molecule vibrate above the temperature of the absolute zero [18,19]. With an increase of the temperature the intensity of vibration increases. Every atom of a molecule shows their oscillation, which frequency depends on the type of atom, the type of bond, the configuration of the molecule-group, and the adjacent molecular groups. Every molecule forms an individual pattern. Nonlinear molecules with n atoms show 3n-6 different vibrations. That means a macromolecule in the cell shows a pattern with plenty of different frequencies. These oscillations create electromagnetic radiation in IR range with a typical frequency pattern. While the carbon-carbon and carbon-hydrogen bonds produce only uncharacteristic heat- bands, the oscillations of the heteroatoms create characteristic peaks. The theory is described in detail in books of spectroscopy [18,19]. The frequencies of this radiation are mostly in the infrared range. Molecular vibrations of proteins and complex lipids are in the range of 10^{13}-10^{15} Hz. Most of the functional groups with heteroatoms show bands in the range of 2000-900 cm^{-1}. Proteins and complex lipids display mostly peaks in the IR range of 1000-1200 cm^{-1}, while the absorption by water is in the range 1300-1900 cm^{-1}. The emitted energy is very low (1 meV-3 eV) [20-22], however the radiation can become coherent under specific conditions with much higher energy output.

Resonance Recognition

For signalling, the receiver has been able to process the signal emitted by the specific structure. Cosic and co-workers [23] have investigated the interaction of protein-protein and protein- DNA. They could show that proteins resonate the frequencies in the range of 10^{13}-10^{15} Hz [21-24]. That means the vibration pattern of macromolecules of different kinds could be recognized by proteins and the energy could be transferred under specific conditions. The frequency patterns of two interacting molecules have to match in some important frequencies and these must be in opposite phase [25]. If the photon energy is high enough the transfer can result in changes in the conformation of parts of the molecule or chemical reactions. As shown experimentally by Cosic et al. [24], specific isolated frequencies can induce the function of a protein under certain circumstances. The authors showed that proteins with the same or similar biological functions have some common frequencies, needing for activation of that specific target protein [25,26]. That means there are dominant frequencies in a pattern and a complete match is not needed.

The Coherence of Emitted Photons

The frequencies created by the molecular vibration are hardly able to result in structural changes in other molecules because of the low energy and the high background noise especially if the signal has to overcome a distance of some micrometres [27-29}. That is the case during the communication of the Golgi apparatus with the cell periphery. In the Golgi, the received signal should be able to activate at least one particular enzyme. That means the received energy must be sufficient to change the conformation of parts of that molecule [12,30]. This change might be different in every molecule. It depends on many factors such as adjacent molecular groups, isomeric structure, hydrogen bonds, and several dipole-dipole forces. The binding energy of the very weak dipole-dipole bond is 6×10^{-19} J. The binding energy of the hydrogen bond is tenfold higher and energy differences between several

conformations of a molecular group depend very strongly on that characteristic. The stereoisomers of the structurally very simple cyclohexane show energy differences of more than 5 x 10^{-19} J. The energy of a photon in IR range amounts to 1-4 x 10^{-19} J. That means some coherent photons are principally necessary to induce a change of the resulting molecule e. g. activation of an enzyme.

The conditions supporting coherence of photon emission of macromolecules in the cell have been reviewed by Funk [6]. For their generation, the particular molecule must be transferred in an excited state in course of a chemical reaction. Such reactions could be oxidation, hydrolysis, substitutions, phosphorylations or other reactions. If the neighbouring molecules of the reacting molecule have a crystalline-like order the emitted photon stream could be coherent and the coherence should persist for a certain time. Some researchers have investigated the importance of quasicrystalline-structured water in the cell [31-33]. Most of the water in the cell has such a structure induced by the charge of the membranes as well as the charge of proteins.

The Golgi Apparatus

The Golgi apparatus is the central location in the cell where the molecules produced in the ER are stored and prepared for intracellular transport. The basic structure of these organelles is similar in all cells despite their great diversity. The Golgi apparatus is located close to the cell nucleus and directly connected to the microtubule (MT) system (Trans- Golgi), while the Cis-Golgi is connected to the ER [34-36]. The basal elements are the cisternae, which consist of membrane-enclosed disks. Several cisternae form respectively stacks. The chemical structure of the elements are the same as the ER: proteins and complex lipids. The proteins and other macromolecules produced in the ER are transported to the Golgi on MT and stored there. Upon request, they are finished there and prepared for transport. Various molecules are posttranslationally modified by glycosylation, phosphorylation, sulfation, and the addition of n-acetylglucosamine. Glycosaminoglycans are directly synthesized in the Golgi. During transport from cis-face to trans-face of the Golgi, many enzymes are working on the molecules delivered from the ER. The finished molecules are provided with different signal proteins as a coat. Finally, the transport-vesicles are completed by signal molecules to determine the final destination and motor proteins for the directed transport on the road system [34-37]. It consists of MT, actin and intermediate filaments and forms the cytoskeleton which is highly dynamic by permanent polymerization and depolymerization [38-40]. The moving of the cargo-vesicles on the roads is discontinuous, sometimes on opposite directions. The chemical energy is provided by energy-rich phosphates.

A large number of cells are secretory cells; macromolecules intended for secretion are packed in transport vesicles, transported via the MT-skeleton system to the cell membrane and, after fusion with the membrane, released into the extracellular space. The corresponding signalling processes are comprehensively described including the signal molecules involved [40]. In the three-dimensional cell system, structural components must constantly be replaced because they have been altered by various chemical processes: synthesis (e.g. prostanoids), oxidation, hydrolysis, substitution, etc. Specific signals from that area should be sent out and transferred to the Golgi to start the substitution process. Since the signal has to inform about the chemical characteristics of the molecule to be replaced as well as about its spatial position, the signal must be a physical one.

Communication between Golgi and Cell Periphery

If a molecule in the cell periphery is changed by a chemical reaction the vibration signal and its corresponding EM fingerprint pattern is changed. The emitted photon stream is coherent during the chemical reaction. The quasicrystalline structure of water supports the coherence [31-33]. It is supposed that the signal is conducted to the Golgi apparatus employing the cytoskeleton -MT system. The diameter of the MT s is too small for the wavelengths of the IR radiation to be directly used as waveguides [12], however, the structure of the MT- system with their charge results in quasicrystalline water around the MT s. This structure can extend without interruption from the cell periphery up to the Golgi and principally it can be used as a waveguide. In the Golgi apparatus, the frequency pattern is recognised by a specific enzyme through resonance and the energy can be transferred. This can lead to conformational changes in the molecule resulting in activation. In subsequent reactions, further enzymes are activated and the requested macromolecule is completed and provided with the necessary signal and motor proteins for transport via the skeleton-MT system. The motor-driven transport unit is navigated to the site of request using the IR-frequency pattern signal coming from that location [12,13].

The Intracellular Signal Transduction Pathways

The signalling in the cell for substances that dock onto the cell membrane and send the information to the nucleus is well investigated. The MT transport system does not play a decisive role, however, plenty of cytoplasmic proteins take part in the transduction process. The signal transduction pathways are manyfold and molecules with specific signals for cells are extremely diverse. Signal molecules can include

proteohormones, growth factors, cytokines, chemokines, transmitters, various antigens, pharmaceutical drugs and a wide variety of chemical substances. Such molecules called ligands to dock onto specific receptors on the cell membrane are introduced into the cell as a complex product, or they pass the information onto specific molecules in the cell, which transmit the signal to the cell nucleus via a molecular biological cascade. Links between the various cascades form networks [40-42].

This signal transduction consists of a combination of signalling events characterised by phosphorylation of the specific proteins involved and the information transfer. Several phosphokinases catalyse these phosphorylations. The first step is the binding of the ligand to the receptor. The membrane receptors consist of an extracellular and an intracellular part. The binding of the signal molecule results in changes of conformation of the receptor. This change induces a chain of biochemical events intracellularly known as a signalling pathway. Many proteins take part in that biochemical cascade. Several cascades interact with one another forming networks. These complicated molecular networks are necessary for coordination of signals, and to pass the very different information correctly to the nucleus [40]. During this transduction, the signal can be amplified involving hundreds of molecules. When the signal is transduced till the nucleus envelop some so-called LINK-proteins are involved in the transfer process through the membrane working like the transduction proteins of the cytoplasm. After crossing the envelope the signal is transduced to the specific DNA to induce the particular transcription-translation reactions.

The majority of the signal transduction steps are based on protein phosphorylation catalyzed by protein kinases. Each transduction step thus involves the transfer of the specific information and the activation of the corresponding phosphokinase. The path from the membrane receptor to the cell nucleus is usually a few micrometres. The average diameter of an involved macromolecule is only a few nm. The links in a transduction chain are usually several layers of water through which the signal is passed on. Because of the charge of the membranes and the polarity of the proteins, this water has a quasi-crystalline structure.

Corresponding to our hypothesis that intracellular signalling processes are mainly carried out by photons, it can be assumed that the communication between these chain links takes place using electromagnetic fields which transfer the particular information and leads to the specific enzyme activation. The signals that pass through the intracellular transduction pathway are extremely diverse leading to different effects. Because a large variety of different receptor proteins exists in the cell membrane the primary messengers can find suitable receptors. In contrast to the large variety of receptors, the variety of proteins in the transduction cascades is limited. Different signals have been conducted through the same cascades. In principle, a protein can resonate different frequency patterns resulting in different conformational changes. The emitted vibration pattern would mirror that. A protein of the transduction cascade can, therefore, receive and transmit different signals. It can only be speculated that modern information theory and quantum computer technology will make these processes better understandable (Possibly, a peak is composed of photons that differ by quantum energy and this quantum spectrum is preserved during signal transmission. This could be another way to transport different information). When the signal reaches the nucleus the charge of this membrane acts as a barrier for the photons [6], however, the Link proteins enable the transfer through the membrane.

Discussion

The basic idea of the hypothesis discussed here is the assumption that molecules can communicate with each other based on electromagnetic radiation generated by molecular vibrations.

This ultra-weak radiation can be coherent under specific conditions. This is the prerequisite that the photon energy is sufficient to activate enzymes by energy transfer resulting in conformational changes.

With the help of specific EM radiation und sufficient radiation energy, numerous chemical reactions can be triggered or carried out, which is used in technical processes [43,44]. In the hypothesis presented here, however, the central aspect is not the transfer of energy but the recognition and transmission of information employing EM frequency patterns. Some references can be found in the literature on the significance of endogenous electromagnetic radiation for signalling in tissues and cells:

Using molecular vibratory patterns, agonists and antagonists of the adenosine receptor ligands can be successfully differentiated, an important goal in pharmacological research [45-47].

Tumour cells and healthy cells could be differentiated experimentally with the help of emitted EM frequencies, which were calculated using Cosic's Resonant Recognition Model [47].

It is discussed that the biochemical mechanism of smell is not based on the chemical bonding of odorant molecules to molecules of the sense of smell, but pattern recognition of molecular vibrations. Among many other indications, the following experimental result may strongly support this hypothesis: Drosophila fly can differentiate between

certain molecules and their deuterated form although both have the same chemical structure and therefore the same affinity to the receptor, however, differences in the molecular vibration patterns [48].

Cells in culture interact with each other, even if they are separated from each other in a way that direct mass transfer is not possible [28]. This means that communication is physical. In dying melanoma cells it has been shown that there is a direct correlation between chemical changes in the cells and specific photon emission. Different wavelengths are important in cell-to-cell communication [49].

Proteins with the same function e.g. oncogenes also have certain identical characteristic frequencies in their vibration patterns. The differentiation of stem cells into osteoblasts is triggered by light of specific wavelengths as Cosic et al. has shown [24].

The electrical charge of the membrane prevents the passage of coherent photons. Hence intracellular signalling is not sufficient to disturb neighbouring cells. Although the mitochondria and the nucleus have intensive intra-organellar signalling possibly based on molecular vibrations the communication with other organelles is mainly chemical reasoned by their membrane sheathing. The interaction of extracellular proteins and microbial proteins with cells is based on their binding to membrane receptors [50,51]. The molecular vibration, IR-patterns could be important to find the receptors.

The life processes of the cell mitosis and apoptosis run according to fixed programs. However, all steps must be strictly controlled and comprehensively coordinated. This requires constant feedback [6]. These manifold co-ordinations are only possible by physical means and the molecular vibration might be of relevance.

Conclusions

According to this hypothesis, molecules can react with each other even if they are not in contact. This explains many biological processes. The vibrational hypothesis can also explain the communication between the extracellular matrix and different cells, as well as between them in organs. The generalization of the hypothesis and comprehensive evidence may enable new therapeutic applications. Man is constantly learning from biology and the principles of plenty of technical processes can be found in biology. The technical application of that hypothesis would open many new possibilities. However, several biological phenomena will probably only become completely explainable with the comprehensive application of modern quantum physics and there, we are at the beginning phase.

Conflict of Interest Statement

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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