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Hypothesis on interactions of macromolecules based on molecular vibration patterns in cells and tissues

Werner Jaross[1]

[1]*Institute of Clinical Chemistry and Laboratory Medicine, University Hospital Carl Gustav Carus, Technische Universitaet Dresden, Fetscherstrasse 74, 01307, Dresden, Germany*

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1. ABSTRACT

The molecular vibration patterns of structure-forming macromolecules in the living cell create very specific electromagnetic frequency patterns which might be used for information on spatial position in the three-dimensional structure as well as the chemical characteristics. Chemical change of a molecule results in a change of the vibration pattern and thus in a change of the emitted electromagnetic frequency pattern. These patterns have to be received by proteins responsible for the necessary interactions and functions. Proteins can function as resonators for frequencies in the range of 10^{13}–10^{15} Hz. The individual frequency pattern is defined by the amino acid sequence and the polarity of every amino acid caused by their functional groups. If the arriving electromagnetic signal pattern and the emitted pattern of the absorbing protein are matched in relevant parts and in opposite phase, photon energy in the characteristic frequencies can be transferred resulting in a conformational change of that molecule and respectively in an increase of its specific activity. The electromagnetic radiation is very weak. The possibilities to overcome intracellular distances are shown. The motor-driven directed transport of macromolecules starts in the Golgi apparatus. The relevance of molecular interactions based on this signaling for the induction and navigation in the intracellular transport is discussed.

2. INTRODUCTION

Numerous processes in cells and tissues are associated with manifold electric and electromagnetic phenomena, whose importance gradually gains appreciation in the scientific community (1–11). Polarized molecules and macromolecular structures generate electrical fields, which are important as driving forces for charged molecules and aggregates. The movement of charged particles produces magnetic fields and the oscillation of polar structures generates electromagnetic radiation with very different frequencies, most of them of very low intensity, hence this effect is called ultra- weak photon emission (11–13). Frequencies in a wide range of 10^{9}–10^{15} Hz can be measured (with corresponding photon energies 10^{-23}–10^{-19}J). That means the range from infrared (IR) up to ultraviolet (UV) radiation (6). The modern chemical analysis uses extensively spectroscopic methods for qualitative and quantitative analysis of chemical compounds based on absorption or emission of defined frequencies or frequency patterns. It is probably that nature exploits those energy-efficient possibilities of encoding and processing information on biochemical changes. There is also a need for such signaling because the well-elucidated chemical signaling does only inform insufficiently on spatial aspects in the three-dimensional systems of cells and tissues (8, 9).

In previous articles (14, 15) it was hypothesized that changes of structure elements in the cell membranes, as well as in MT, ER, mitochondria and others, are associated with changes of their molecular vibration patterns resulting in the possibility of signaling regarding the area and the specific of

the structural changes in addition to the chemical signaling. That system could also extracellularly play a role in the interaction of cells with the extracellular matrix (15). Furthermore, it was hypothesized that this characteristic of the molecules holds importance in storing and retrieval of memory units in the complicated process of memory formation. In this article some aspects of the resonance recognition of vibration patterns by proteins as precondition for molecular interactions and possible relevance of that kind of interaction in motor-driven intracellular transport will be discussed.

3. THE VIBRATIONAL HYPOTHESIS

All molecules show oscillatory behaviour above absolute zero of temperature (16, 17). The intensity of these molecular vibrations depends on temperature and is remarkably high at the temperature of living systems. The energy is provided by the enthalpy of the metabolic processes. All atoms of a molecule participate in the vibration pattern. The number of different vibrational modes in a molecule of n atoms is 3n-6 for non-linear molecules. The frequency of every vibration depends on the type of the bond, in particular on their polarity, which is caused by the de-localisation of the binding electrons and non-covalent interactions of surrounding atoms of the same or of other molecules. The phase structures have additional influence. The functional groups in a macromolecule dominate the vibration pattern, while the mass of carbon hydrogen bonds exhibits only uncharacteristic vibration. The characteristics of the molecular vibration are in detail described in excellent articles and books dealing with spectroscopic theory (16, 17). Molecular vibrations continuously create electromagnetic radiation consisting of uncharacteristic heat radiation and a specific pattern with characteristic peaks caused by the vibration of the functional groups of the molecule. The frequency pattern is characteristic for a specific macromolecule in the defined conditions. E g. Uncomplicated structured proteins like Collagen or Elastin show 4–6 strong beside many weak bands in the Raman or in the IR spectrum (18, 19). The emitted energy is in the range 1meV-3 eV; the frequencies are between 4000–400 cm^{-1} (10^{13}–10^{15} Hz) Most of the bands of the functional groups can be found in the range of 2000–900cm^{-1} (18, 19). Water absorbs radiation in the range of 1300–1900 cm^{-1}.Only frequencies, which are not absorbed by water, can penetrate a certain distance. Many of the vibrational peaks of polar lipids as well as proteins are in the IR-range of 1000–1200cm^{-1} and therefore they are able to cover distances in nano-scale. The charge and specific structure of the membrane make the electromagnetic signals unable to penetrate uncontrolled the cell membrane, which is important to avoid perturbing adjacent cells. The EM radiation patterns are exact images of their sources with respect to chemical structure and spatial position, and therefore they are candidates for signaling. The change of a molecular structure by chemical reaction results often in splitting products which are immediately further processed. The newly synthesised small molecule besides the changed macromolecules might participate in the formation of the fingerprint vibrational EM-signal (e. g. synthesis of prostaglandins from phospholipids of the cell membrane).

4. RESONANCE RECOGNITION BY PROTEINS

A requirement of successful signaling is that the system responsible for restoration or further development of the changed structure is able to harvest and process those signals. Such molecules are proteins like enzymes, transportation-proteins, structure components, components of signaling transduction-network and of the genetic machineries. Cosic and their co-workers (20–23) have intensively investigated the interaction between proteins and proteins with other macromolecules as DNA. They showed that proteins can function as resonators for frequencies in range of 10^{13}–10^{15} Hz in accordance with the length of the amino acid chain. By means of Fourier Transformation every amino acid in the chain was assigned with a certain value correlating with the energy of de-localized electrons of this amino acid (respectively with the polarity of the molecule group caused by the specific functional groups) (21). The distance between the amino acids is about 3.8 Ä. The velocity of the electric charge on the backbone of the protein-chain amounts to 7.87x105 m/s. The calculated resonance frequency range follows. Cosic and their group developed the Resonant Recognition Model using these data (22). The identification and calculation of relevant frequencies of proteins and other molecules is possible by its application.

The resonance frequencies of proteins are in accordance with the molecular vibration frequencies respectively the electromagnetic radiation of diverse macromolecules of various structure elements of the cell such as complex lipids, proteins, glycoproteins and others. If an EM-signal reached a protein target and the specific frequency pattern of both molecules are matching and are in opposite phase the photon energy will be transferred resulting in an activation of the recipient. The result might be a change of the conformation of the molecule which could lead to an induction of a likely specific chemical enzymatic reaction s. footnote (or transfer of the signal to another reactant because the frequency pattern of the recipient is also changed). Principally, the hypothesis has similarity with the Lock-and-Key-theory of chemical reactions. The vibration patterns are detailed images of the chemical structures. However, the frequency pattern hypothesis does not only directed to the reaction centre of the

molecule. The significant pattern of a molecule is characterized by frequencies of various parts of the molecule. The reaction centre plays an important but not the only role. If the coincidence of a certain number of specific peaks is very high the interaction could be successful resulting in transfer of energy. Probably there are dominant frequencies rich in energy which explain that function of molecules can be induced by the application of isolated frequencies as shown experimentally by Cosic *et al* (23). They reported that groups of proteins sharing the same biological function have one frequency component in common. The authors could demonstrate that by means of that one frequency specific target proteins could be activated. From these findings conclusions could be drawn that the complete pattern does not need to be matched for activation. The degree of accordance of frequency pattern that is necessary for successful energy transfer might be very different in various bio-molecule pairs.

5. SIGNAL STRENGTH AND SIGNAL TRANSMISSION

The electromagnetic energy emitted by a single structure-forming molecule is extremely low (17, 24). It was postulated that specific frequencies generated by molecular vibrations on a cellular level can hardly be perceived by other structural elements because of the strong background noise (24), especially when the signal has to cover a distance up to several micrometers. Short distances those comparable to molecular dimensions might be bridged. This is probably the way of direct interaction of molecules e. g. the DNA-repair-machinery or in signal transduction networks (24, 25). However, a signal may come from the cell membrane and has to reach the nuclear envelope or the Golgi apparatus situated close to the nucleus that means a distance of several µm. For these purposes the signals should be stronger. Theoretically, there are some possibilities to achieve it. The signal may not only come from one molecule, but also from many identical molecules situated at the locus in question. This is typical of enzymatic reactions. A catalytic reaction of an enzyme is continuing until the inhibitory effect stops them (e. g. by product inhibition). If the frequencies are coherent they could overcome larger distances. Funk discussed in this issue that coherence of frequency patters emitted by biomolecules could be strongly promoted by the surrounding quasi-crystalline water molecules. The turnover frequencies of the activated enzymes could be of additional relevance for coherence if that frequencies are matched with parts of the molecular vibration frequency pattern of the changed molecule. Moreover electromagnetic waves with higher energy and lower frequency can be used as carrier waves, frequency- or amplitude-modulated with the signal frequencies emitted from the changed molecules as used in radio and television broadcasting (25). Such a system requires a transmitter that sends out the carrier as well as the signal waves and a receiver that can resonate at the correct carrier frequency. The oscillation of polarized structural elements such as cell membrane rafts or microtubules (12, 25–27) might be able to produce appropriate carrier frequencies able to overcome intracellular distances. The frequencies of MT oscillations have been found to be in the range from THz down to KHz (10, 11). The MT structure itself could also be the base for forwarding the IR-photons with a minimal loss of energy if they are used as waveguides. The quasi- crystalline ordered water molecules inside and outside of the charged tubular structur of the MT could promote that (see Funk, this issue).

6. EM-INTERACTIONS OF MACROMOLECULES AND THE INTRACELLULAR ACTIVE DIRECTED TRANSPORT

To maintain the cells alive a great deal of different intracellular transportation tasks are necessary. From small to large objects, molecules to organelles, have to be carried from the place of synthesis to specific areas in the three-dimensional space of the cell. These processes are mainly driven by actively directed transport. Main components in this very complicated procedure are the macromolecules of the cytoskeleton which function as network of roadways, the motor proteins which move on the roads and carry the cargo with the required objects. Important components of cytoskeleton are the MT, the actin filaments and the intermediate filaments consisting of heteropolymers with high polarity. Most of these components are highly dynamic showing permanent polymerization and depolarization transformation. The motor proteins move by means of chemical energy provided by energy-rich phosphates. The cargoes consist of the target substances wrapped with several molecules, especially specific proteins, glycoproteins, complex lipids, etc. These transport vehicles are established and composed in the Golgi apparatus. There are excellent reviews on the intracellular transport and their components (28–33). Only very few aspects of these processes will be briefly delineated below:

The Golgi apparatus is located near the nucleus, close to the centrosome. It consists of an endomembrane system made up of a series of compartments connected by microtubule elements. The cis-Golgi network near to the nucleus is connected with ER. The trans-Golgi network is connected with the MT system. The basic elements are membrane- enclosed disks known as cisternae. The chemical composition is similar to that of the ER consisting of different polar lipids and proteins. Proteins and most of the macromolecules scheduled for the transport are synthesized in the ER and transported to the Golgi apparatus (31, 32). At

this location these molecules have to be post-translationally modified by phosphorylation, removal of manose molecules, addition of N-acetylglucosamin, sulfatation, glycosylation. Glycosaminoglycsans are synthesized in the Golgi. These procedures are performed by a cluster of enzymes during the way of the molecules from the cis- face to the trans-face. The matured proteins and other molecules are sorted, completed with a coat and prepared for direct transport as vesicles. The vesicles carry proteins with signal sequences which determine the finale destination. Specific coat- proteins, COPII and COPI [31] play a key role during the complicated procedure of post-translational modification of proteins and final formation of the cargo on the way from cis – to the trans network. Coat- proteins control the attachment of motors, their activity and moving direction (32, 34–37).The cargoes are transported by means of multiple motors often with opposite preferred directions. Some of those motors are attached to the cargo at the same time. This kind of motion is described as “tug of war” because the moving is discontinuous with interruptions and has often to change the direction due to obstacles.

The Golgi is most likely the area where the electromagnetic signals are accepted coming from any specific area in the three- dimensional space of the cell where substitution or restoring of macromolecules is needed. Such signals together with the chemical signals could induce the maturation of the bio-molecules and all procedures up to the formation of the cargo- motor complex as well as the whole active transport process of navigation until the destination is reached. This assumption includes a direct interaction of molecules bridging larger distances. The energy for the motor-driven transport is provided by energy-rich phosphates, and the driving direction is generally defined by the electric fields of the very polar MTs and actin filaments.However, it seems additionally necessary to navigate the transport-units caused by the obstacles on the way. This could be performed by the coat proteins of the carrier using EM-.frequencies coming from the destination area.

7. DISCUSSION

There are a few preliminary observations supporting the hypothesis that the interactions of macromolecules in cells and tissues are based in part on emission and recognition of electromagnetic radiation patterns. These findings concern mostly the interaction of cells. Cultured cells could influence each other, even if they are specifically separated so that only EM- signals could be exchanged (24). In plant biology the influence of light on growth and proliferation and the active movement of some flowers (e. g. sunflowers) in the direction of the source of light can be interpreted in this way. Cells in culture were successfully influenced and tumour-cells and normal cells can be successfully differentiated (33, 38) using EM- frequencies calculated by means of the Resonance Recognition Model of Cosic. It was demonstrated comparing various characteristics that the specific molecular vibrational patters have highest potential to differentiate between agonists and antagonists of adenosine receptor ligands. The adenosine receptor is a very important target of modern pharmaceuticals (39). The authors identified highly informative features of molecular vibrations of the ligands and the receptor which “are indispensable for ligand recognition” (40). The findings that “The activation of proteins involves energies of the same order and nature as the electric radiation of light” (23) is also in accordance with the hypothesis. Cosic found that for the common function of some proteins (e. g. the oncogene property) only one frequency is typical. This resonance frequency could not be found in other proteins lacking these characteristics (23). The hypothesis presented here is a generalization of that one regarding the precondition of interaction: The interaction and energy-transfer is determined by the matching of the frequency pattern in analogy with the Lock-and- Key theory. This involves a whole frequency pattern and not only on one frequency. Similar to that theory, inhibition - and disturbance mechanisms could be discussed. The vibration and resonance-recognition mechanism might have high intracellular importance as well play roles in genetic mechanisms in the nucleus as in signal transduction networks between cell membrane and nucleus. It might have high relevance extracellularly especially in the interaction between the cells and the extracellular matrix important in all processes of development and regeneration of the various tissues and as well as in information processes in the nervous systemsuch as storage and retrieval of memory units (15). It was also discussed elsewhere that biophotons could serve as signals between neurons and that the myelinated axons could serve as photonic waveguides (41). Although sizes and composition of MTs are very different, we discussed briefly here that MT structures could be important in intracellular signal transduction. The function of this information system in complex cell programs like mitosis, meiosis and apoptosis is a vast area of emerging research.

8. CONCLUSIONS

The hypothesis presented here has to be proven experimentally in many respects. If it succeeds and specific patterns can be recognized, numerous biological processes might be influenced by man using electromagnetic-based technologies and possibly replacing or augmenting pharmacological interventions.

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Footnote: A change of the conformation of a molecule means that a number of dipol-dipol-forces (Van der Waals forces) and hydrogen bonds have to be disbanded and re-formed. The bond energy of a dipol-dipol bond is about 2 kJ/mol or respectively 6x 10^{-19} J. The bond energy of a hydrogen bond amounts to tenfold of that. The energy of one photon in IR- range is about 0,1–4x10^{-19} The energy of certain number of coherent IR photons are sufficient to cause a conformational change of a molecule.

Key words: Signaling; Signal Transduction; Molecular Vibration; Resonance Recognition; Infrared Radiation; Direct Intracellular Transport; Navigation, Review

Send correspondence to: Werner Jaross, Institute of Clinical Chemistry and Laboratory Medicine, University Hospital Carl Gustav Carus, Technische Universitat Dresden, Fetscherstrasse 74, 01307, Dresden, Germany, Tel. +49 351 6441388, Fax 0351 458 4332, E-mail: werner.jaross@gmx.de