MedCrave
Step into the World of Research
Journal of Otolaryngology-ENT Research

Mini Review

Open Access
CrossMark

The work of the olfactory cell

Abstract

Work is the basic physical quantity that determines the amount of energy needed to perform a given task. In the case of smell, it is a complex process of receiving odor signals from the outside world, transforming them in the olfactory cell into the form of chemical bonding energy, which is converted into electrical energy of the action potential at the synapse between the I and II neurons of the olfactory pathway. Regardless of the many transformations of energy along the way, the signal reaching the brain must be recognizable in quality and intensity. The olfactory organ works around the clock, although olfactory sensations do not reach the brain at night. Very strong odors like ammonia can wake you from sleep. The entire system uses external energy to perform work. Similar to the nerve cell and the auditory cell, the olfactory cell is an excitable cell, meaning that the action of an external stimulus leads to a response in the form of depolarization of the cell. A bidirectional action of the cell is created. In addition to the normal work related to the life of the cell - like with any other cell, for that matter, there is work related to the transformation of the olfactory signal in the cell and the transmission of this signal to the synapse. These two levels of olfactory cell activity are closely related, dependent on each other, using the same substrates and frequently the same transmission pathways. The level related to cell life is the constitutive level, while the second level, related to signal transmission, is the regulated level. This latter level begins with taking over the energy of odor substance - an odorant, which, regardless of its size, has kinetic energy, potential energy and electron energy. By binding with the GPCR receptor and acceptor, the odorant causes the transfer of some of its own energy, that associated with the odor. The electron cloud of the odorant, after combining with the electron cloud of the receptor, loses a certain amount of electrons or protons. After transmitting information to the acceptor, such a molecule is detached from the receptor and enzymatically destroyed. OBP is just an intermediary for these reactions. Further transformations of the energy of the olfactory signal take place in the cell and synapse.

Keywords: receptor, olfactory cell, electron, synapse

Volume 15 Issue 3 - 2023

Jan Myjkowski
Retired physician, Poland

Correspondence: Jan Myjkowski, Retired physician, a specialist in otolaryngology – pensioner, Poland, Tel +48782449179, Email janmyjkowsk@poczta.onet.pl

Received: December 14, 2023 | **Published:** December 28, 2023

Abbreviations: GPCR, G protein-related receptor; OBP, odorant binding protein; PIP2, phosphatidylinositol diphosphate; GDP, guanosine diphosphate; CAMP, cyclic adenosine monophosphate; PKA-protein kinase A; CA, adenylyl cyclase; CREB, camp response element binding protein; DAG, diacylglycerol; IP3, inositol triphosphate; COP, coating protein; MT, microtubules; ER, endoplasmic reticulum; NSF, N-ethylmaleimide sensitive fusion protein, cytosolic fusion factor; SNAP, protein binding NSF to the Golgi apparatus; t-SNARE, membrane receptors for SNAP proteins; v-SNARE, vesicular SNAP protein receptors; TGN, Trans Golgi Network – a compartment of the Golgi apparatus

Energy transformations of the olfactory signal

The combination of the odorant molecule with the receptor results in the summation of the energies of both molecules. The increasing internal energy of the receptor causes conformational changes in the receptor protein and the transfer of energy to the G protein, which accompanies the receptor. Odor molecules (donors) have a positive or negative electrical charge or are neutral. Neutral molecules transfer energy by contact between the electron clouds of the molecules and by collisions between the molecules. Each atom has electrons that form an electron cloud 0.1 to 0.4 nm in diameter around the atom's nucleus. For example, a carbon atom has a diameter of 0.2 nm and the diameter of the nucleus of this atom is 2 x 10^{-5} nm. The size of this cloud depends on the number of orbitals in which the electrons are distributed. Electrons in the outer orbital - the valence orbital - readily enter into bonds with other atoms to form atomic and covalent bonds. There are an incomplete number of electrons in the valence orbital, these electrons are easily donated to form atomic bonds, or electrons are accepted to complete the orbital. The closer to the nucleus, the more energy the electron has. For a hydrogen atom - very often involved in reactions - the energy of the electron, located in the first orbital, is minus 13.6 eV. Such energy is necessary to remove the electron from the first orbital. Successive electron shells 1,2,3,4, etc. are the principal quantum numbers the further away the shell, the lower the electron energy. Energy decreases proportionally to the square of the principal quantum number. The energy of electrons decreases, while the distances from the nucleus of successive electron orbitals increase proportionally to the square of the principal quantum number.

An electron can change its orbital, but in order to move to an orbital closer to the nucleus, it must receive additional energy Changing 1 orbital from 2 to 1 requires 3.4 eV. Such transitions are quantized, which means that there is a jump or isn't - there is no middle ground. If an atom in a molecule receives a quantum of energy from another atom or molecule, the electron jumps to an orbital closer to the nucleus - its internal energy increases - in a quantized step. The so-called excited state of the atom is formed, which, unlike the ground state, is unstable. Such state is unstable and there is an immediate attempt to return to the ground state by emitting 1 photon of energy - when it's about the transition of 1 atom by 1 orbital. If in molecule-odorant binding we have such transitions innumerable, or transitions by 2 orbitals or more, or ionization of an atom, i.e. sending an electron beyond orbitals, then there are 10^{20} possibilities to transmit different types of quantized energy. This gives an innumerable amount and variety of transmitted information about odors.[1]

The odorant transfers to the acceptor only energy and not chemical composition. The energy received by the acceptor, is subsequently passed on to the receptor, and amplified, but cannot be changed. The acceptor is part of the receptor. The odorant binding with the acceptor is unstable. If the odorant was not unbound from the acceptor, the receptor would be permanently blocked. The tendency of an atom or molecule in an excited state to return to the lowest-energy ground state, in accordance with the principle of entropy, results in the transfer of energy further and, at the same time, the loss of transmitted energy causes unbinding of odorant molecule. In the case of very small molecules, such a reaction takes place in 10^{-14} s. large molecules unbind up to 1,000 times slower, but the time is still 10^{-11} s. The mechanism of unbinding of the odor particle from the acceptor is related to the concept of dissociation energy. The molecule detached from the acceptor does not excite it again, because it is in the ground state, the excitation energy has been transferred to the GPCR acceptor.[2]

The receptor received a packet of quantized energy from the odorant, which caused conformational changes in the receptor. The number of possibilities for the formation of new conformers is proportional to the square of a sum of the odorant and receptor atoms - it is gigantic. This gives 10^{20} possibilities for transmitting different scents and their intensity.

The energy of the resulting GPCR conformer acts on the G protein - it transfers energy. Increased GPCR energy stimulates the G protein by phosphorylation of GDP to GTP bound to the alpha unit of the G protein.[3] The phosphorylation reaction of GDP to GTP is an endothermic reaction and the energy comes from the energy of the olfactory signal. The attachment of one phosphate to the terminal ADP group requires 46-54 kJ/mol of external energy. The alpha subunit bound to GTP dissociates from the beta and gamma units, having ATPase properties, detaches 1 phosphate from GTP, and the energy obtained stimulates adenylyl cyclase, an enzyme that converts cytosolic ATP into cAMP. The amount of cAMP molecules produced is proportional to the intensity of the olfactory signal. GDP formed from GTP, binds to beta/gamma units and forms a new G protein, which binds with the inner surface of the cell membrane with the GPCR receptor, ready to receive new information. Beta/gamma units stimulate Phospholipase C. The speed of these individual reactions is estimated at 10^{-12} s. G protein-related reactions are much slower. The increased level of cAMP acts on cAMP-dependent calcium channels and starts depolarization of the olfactory cell.

Sequentially, voltage-dependent sodium channels open, and the permeability of the cell membrane to sodium is increased by over 100 times. When the potential inside the cell becomes positive, sodium channels close and potassium channels open. Potassium moves out of the cell. Sodium-potassium pumps move sodium ions out of the cell. Calcium ions are transferred outside the cell and into the endoplasmic reticulum, mitochondria and nucleus.

The complete cycle of depolarization and repolarization takes approximately 4ms. During depolarization, the level of calcium in the cell rises sharply, which is important in further intracellular transformations related to the transmission of olfactory information.[4] Information is transmitted to the nucleus, there is activation of genes responsible for the production of all proteins related to the transmission of information, and proteins related to normal cell life. One of these proteins are olfactory receptors encoded in the nucleus, produced in ribosomes, folded, provided with an address and sent to hairs - the ends of dendrites. Every 2 months, the receptors are replaced with new ones.

There is some ambiguity associated with G protein-related receptors. Sources say that 800 types of different receptors belonging to the G Protein Coupled Receptor (GPCR) group have been found in the human genome, accounting for about 3% of the entire genome. The problem is that the entire group of GPCR receptors includes: Adrenergic, adenosine, dopamine, histamine, cannabinoid, melatonin, opioid, serotonin receptors and olfactory ones. It is true that the Nobel Prize winners reported that they had identified 339 "complete genes" in humans, belonging to 172 subfamilies of odorant receptors.

Energy absorbed by odor molecules is transferred via G proteins to target and intermediate effectors subject to precise regulation based on the interaction of dynamic, structural and genetic systems. Regulation through dynamic system affects the reaction rate of the main enzymatic pathways. Regulation through the structural system involves the interaction of cell organelles and the influence on the membranes separating them, regulating the availability of substrates and cofactors. Genetic regulation is the influence on the production of proteins and their half-life.[5] The olfactory cell exhibits outstanding polarity, which means that proteins produced in the ER, passing through the TGN, have different address markers. They must be precisely sorted and directed to the apical, lateral or basal part of the cell, to the dendrite, e.g. receptor proteins, or to the axon - enzymes and transmitter.

It is extremely interesting at what stage the amount of produced proteins of the basic product of the hair cell is regulated, i.e. proteins necessary for the functioning of the cell, such as structural proteins and enzymes of lysosomes and mitochondria. It is likely that this takes place at the stage of transcription triggered by second messengers. The energy of odorant molecules acting through G proteins stimulates CA to produce cAMP, and this activates PKA affecting metabolic processes in the cell, and affects gene transcription, after PKA is transported to the cell nucleus.[6,7] Active PKA phosphorylates the residues of the 133rd amino acid, serine, in the CREB protein. Some CA isoforms can also be regulated by Ca++ ion-activated calmodulin. Also, calmodulin-dependent kinases activated by increasing Ca levels can phosphorylate serine 133 CREB.[8,9]

The second enzymatic pathway simultaneously activated by G proteins is the phosphoinositol metabolism cycle. The level of Ca++ depends, among other things, on IP3, the breakdown product of PIP2. The second PIP2-derived active factor is DAG, which together with Ca++ activates PKC. This one, in turn, is inactivated when the level of DAG, or the level of Ca++ in the cell, decreases. These processes outlined briefly, vividly demonstrate the importance of connections between energy metabolism pathways and the pathways for processing and transmitting olfactory information in the cell. If we add genetic mechanisms, regulatory mechanisms of ion and proton pumps, the action of chaperones responsible for protein folding, and mechanisms of quality control of protein production in the ER (*calnexin*) to the intracellular processes described here, it will be easier to understand the functioning of the olfactory organ at the level of the olfactory cell. The primary energy obtained from the odorant processed in the cell maintains the proportions of the original signal intensity. The production of enzymes, sodium, potassium and chlorine ion pumps, involved in depolarization and repolarization of the cell, is increased.

The production of the transmitter, its packaging into vesicles, and its transport from the endoplasmic reticulum and the Golgi apparatus are activated. Molecular motors dynein and kinesin are required for transport. There is an increased demand for ATP, the universal provider of energy. Transmitter secretion is dependent on the intensity of the olfactory signal. The contents of synaptic vesicles, the vesicle

membrane and molecular motors are encoded in the nucleus, produced in the cell's organelles and transported along the axon to the synaptic spine. The cell's calcium level, which depends on the olfactory signal, is the signal to transfer the contents of the vesicles to the synapse. The number of vesicles emptied, that is, the amount of transmitter, is proportional to the transmitted signal.[10]

A very important step in the transmission of olfactory information is the production, transport and storage of the transmitter in the presynaptic area of the axon. Peptide transmitters are encoded in the nucleus and produced in the ER. This is where the portioning and packaging in transport vesicles takes place. These vesicles pass through the dictyosomes of the Golgi apparatus[11] and on the trans side are released into the cytoplasm as synaptic vesicles. Coating proteins are responsible for packaging the transmitter into vesicles. The coating complex - coatomer - includes 13 COP proteins (coating proteins). They are divided into COP I and COP II. COP II proteins (5 proteins) are responsible for progressive transport. In contrast, COP I (8 proteins) are responsible for retrograde transport, the recycling of cell membranes. Budding vesicles are formed in the donor compartment and migrate to the acceptor compartment. Thanks to the mechanism of homeostasis and membrane recycling, the balance in the size of donor and acceptor compartments is maintained. Movement of synaptic vesicles takes place due to the released energy from ATP, or GTP. 2 proteins that are molecular motors have ATPase properties. They have the ability to move along the MT surface. Kinesin is responsible for the movement of vesicles forward, to the periphery. Dynein is responsible for the retrograde movement. The head domain of these proteins is the motor that moves along the MT, while the tail domain binds to synaptic vesicles pulling them along. MT-associated proteins interact with MTs and molecular motors. They are responsible for the organization of MTs and for binding MTs with cell organelles and synaptic vesicles. In formed vesicle, the protein density is 5 times higher than in the ER. In contrast, in a mature vesicle in the presynaptic area, the protein concentration increases approximately 200 times compared to the ER. The coatomer-coated vesicle cannot bind to the acceptor membrane, and must be released from the protein coat. This release is related to the action of specific ATPases.

In order for the synaptic vesicle released from the envelope to fuse with the synaptic membrane, the presence of a cytosolic fusion factor, soluble SNAP proteins, and SNARE receptors on the acceptor membrane is necessary. The address code of the vesicle receptor molecule v-SNARE allows in locating the binding proteins - t-SNARE. The process involving the release of substances contained inside membranous vesicles from the synaptic spine is called exocytosis. Facilitating direct contact between the synaptic vesicle membrane and the inner surface of the synapse requires prior liquefaction of the cytoplasm located in this area. The transition of the cytoplasm from the gel to the sol state is carried out with the participation of gelsolin activated by calcium ions. In the presence of Ca^{++}, gelsolin breaks actin filament bonds in the cortical part of the cytoplasm and inhibits actin polymerization. When calcium level rises more than 10-fold then other related proteins, which act similarly to gelsolin, are activated. At most, calcium levels can increase up to 100 times, but for a very short time and in a limited space. The olfactory cell is a cell with a regulated method of secreting vesicles in the synaptic spine. Synthesis and secretion of the product are separated from each other. It is possible to accumulate vesicles and release them as needed in significant quantities.[11-13]

The chemical bond energy carried by the transmitter is proportional to the energy obtained from the odorant, and can be amplified. An increase in calcium levels in the presynaptic area is a signal to release a portion of the transmitter into the synapse. The amount of transmitter is proportional to the energy of the signal. These vesicles are moved by anterograde transport from the site of generation to the presynaptic zone. The molecular motor that moves vesicles toward the presynaptic membrane is kinesin.

The membrane surrounding the vesicle has the same structure as all cell membranes, it becomes embedded in the presynaptic membrane. In this way, the mass of the presynaptic membrane increases, but only for a short time, after which the embedded part of the vesicle membrane is separated and sent back by retrograde transport to the Golgi apparatus. The enzymatic protein - molecular motor - dynein is responsible for retrograde transport. These membranes migrate back and are used to create new synaptic vesicles. This is known as cell membrane recycling.

The secretion of the transmitter into the synapse is related to the transmission of information received by the receptor. The synaptic gap, approx. 50 nm wide, is filled with fluid, in which the transmitter moves from the presynaptic to postsynaptic membrane in 0.5 ms. Upon reaching the postsynaptic membrane, the transmitter binds to specific ion channels causing them to open. The transmitter is active only for a period of approx. 1ms, after which it is dissociated from the ion channel due to dissociation energy and is degraded by enzymes present in the synaptic gap. Thanks to this, there is no blockade of postsynaptic membrane receptors. Part of the transmitter can be moved outside the synapse. The level of transmitter drops rapidly, after which the ion channels become sensitive to its new influx.

Typically, transmitters cause the opening of sodium channels, the influx of Na^{+} ions into the postsynaptic area, which is the initial section of the afferent nerve of the next neuron. A depolarization potential is formed on the postsynaptic membrane, the so-called excitatory postsynaptic potential–action potential. If a certain depolarization threshold is exceeded-approximately 15 mV-this depolarization travels along the afferent nerve to the next synapse. Many regulatory mechanisms are associated with synaptic transmission, such as presynaptic and postsynaptic inhibition and summation, spatial and temporal summation, enzymatic degradation and transmitter reabsorption. Frequently, in addition to the primary transmitter, there is a co-transmitter, which plays a regulatory role-it supports or inhibits the transmitter.

Conclusion

At the synapse, the energy of the chemical bonds of the transmitter is converted into electrical energy of the postsynaptic potential transmitted to the central nervous system. At the synapse, the process of encoding the transmitted information takes place.[8,13] Coding involves ordering the number and size of impulses in a nerve fiber or fiber bundle, depending on the information contained in the signal. In each subsequent synapse, information is decoded, the electrical signal is converted into the chemical energy of the transmitter, the basic information reaching the synapse is integrated with additional information from the interneurons, the chemical energy is converted into electrical energy of postsynaptic excitatory potential with simultaneous encoding. After crossing several synapses and inter-synaptic sections, information in the form of pulses of energy reaches the central nervous system, as an action potential. In the brain, the information is decoded, subjected to an analysis similar to Fourier analysis and compared with the information stored in permanent memory. An olfactory image is formed. It takes about 100 milliseconds to process information in an olfactory cell and transmit it to the synapse. Thousands of proteins are involved in the transmission

of information. Each of them has its own genetic code and half-life, which ranges from a few minutes to several dozen minutes. Protein production is subject to the laws of transcription, translation, splicing, post-translational processing, labeling, folding, transport and degradation in proteosomes or other cellular organelles.

Acknowledgments

None.

Conflicts of interest

Author declares that there is no Conflicts of interest.

References

1. Piela L. Idee chemii kwantowej. *Wydawnictwo Naukowe PWN Warszawa*; 2022. 1300 p.
2. Malinic B, Hirono J, Sato T, et al. Combinatorial receptor codes for odors. 1999;96(5):713–723.
3. Skangiel-Kramska J, Rogozińska K. Zmysł węchu–Kodowanie zapachów–Nagroda Nobla z fizjologii lub medycyny w 2004 roku. *Kosmos – Problemy Nauk Biologicznych*. 2005;2-3(267–268):149–154.
4. Obrębowski A. Zarys klinicznej olfaktologii i gustometrii; 2022.112 p.
5. Mathews H, Freedland R, Miesfeld R. Biochemia i Biologia Molekularna. *Pruszyński i Spółka*; 2000. 536 p.
6. Mydlikowska-Śmigorska A, Krzysztof Śmigórski. Podstawy neuroanatomiczne i neurofizjologiczne ludzkiego układu węchowego. *Neuropsychiatria i Neuropsychologia*. 2016;11(4):125–134.
7. Breer H. Olfactory receptors: molecular basis for recognition and discrimination of odors. *Annal Biomed Chem*. 2003;377(3):427–433.
8. Myjkowski J. Narząd węchu. *Magazyn Otorhinolaryngologiczny*. Tom XXII; 2023. 92–97 p.
9. Turin L. A method for the calculation of odor character from molecular structur. *J Theor Bio*. 2002;216(3)367–385.
10. Myjkowski J. Submolecular theory of hearing. *HSOA J Otolaryngology Head Neck Surgery*. 2022;8:069.
11. Kordowiak A. Aparat golgiego, rola tej organelli w komórkach. *Wydawnistwo Uniwersytetu Jagiellońskiego*; 2001.105 p.
12. Fuller GM, Shields D. *Podstawy molekularne biologii komórki*. PZWL: Warszawa; 2000. 300 p.
13. Sharma A, Kumor R. Zmysł węchu. *Neuropharmacology*. 2019;17(9):891–911.