The Mammalian Brain in the Electromagnetic Fields Designed by Man with Special Reference to Blood-Brain Barrier Function, Neuronal Damage and Possible Physical Mechanisms

Leif G. Salford,[1,*] Henrietta Nittby,[1] Arne Brun,[2] Gustav Grafström,[3] Lars Malmgren,[4] Marianne Sommarin,[5] Jacob Eberhardt,[3] Bengt Widegren[6] and Bertil R. R. Persson[3]

[1] *Department of Neurosurgery, Lund University, Sweden*
[2] *Neuropathology, Lund University, Sweden*
[3] *Medical Radiation Physics, Lund University, Sweden*
[4] *Applied Electronics, Lund University, Sweden*
[5] *Department of Plant Biochemistry, Lund University, Sweden*
[6] *Tumour Immunology, Lund University, Sweden*

Life on earth was formed during billions of years, exposed to, and shaped by the original physical forces such as gravitation, cosmic irradiation, atmospheric electric fields and the terrestrial magnetism. The Schumann resonances at 7.4 Hz are an example of oscillations possibly important for life.[1]

The existing organisms are created to function in harmony with these forces. However, in the late 19th century mankind introduced the use of electricity, in the early 20th century long-wave radio and in the 1940-ies short-wave radio. High frequency RF was introduced in the 50-ies as FM and television and during the very last decades, microwaves of the modern communication society spread around the world. Today, however, one third of the world's population is owner of the microwave-producing mobile phones and an even larger number is exposed to the cordless RF emitting systems. To what extent are all living organisms affected by these, almost everywhere present radio frequency fields? And what will be the effects of many years of continuing exposure?

Since 1988 our group has studied the effects upon the mammalian blood-brain barrier (BBB) in rats by non-thermal radio frequency electromagnetic fields (RF-EMF). These have been shown to cause significantly increased leakage of the rats' own blood albumin through the BBB of exposed rats, at energy levels of 1W/kg and below, as compared to non-exposed animals in a total series of about two thousand animals.[2)–6)] One remarkable observation is the fact that the lowest energy levels, with whole-body average power densities below 10mW/kg, give rise to the most pronounced albumin leakage. If mobile communication, even at extremely low energy levels, causes the users' own albumin to leak out through the BBB, also other unwanted and toxic molecules in the blood, may leak into the brain tissue and concentrate in and damage the neurons and glial cells of the brain.

In later studies we have shown that a 2-h exposure to GSM 915 MHz, at non-thermal SAR-values of 0.2, 2 and 200 mW/kg, gives rise to significant neuronal damage, seen not only 50 days after the exposure[7] but also after 28 days but not after 14 days. Albumin extravasations and uptake into neurons was enhanced after 14 days, but not after 28.[8]

In our continued research, also the non-thermal effects on tissue structure and memory function of long-term exposure for 13 months are studied.[9] We have also performed micro-array analysis of brains from rats exposed to short term GSM both at 1,800 MHz and at 900MHz and have found significant effects upon gene expression of membrane associated genes as compared to control animals.[10),11)]

Most of our findings support that living organisms are affected by the non-thermal radio frequency fields. Some other studies agree while others find no effects.

*) Corresponding author. E-mail: Leif.Salford@med.lu.se

The mechanisms by which the EMFs may alter BBB permeability are not well understood. At low field strengths, the effects on body temperature are negligible and thus heating effects are not involved. A change in the physicochemical characteristics of membranes has been suggested as a cause.[12)]

We have performed experiments to verify a quantum mechanical model for interaction with protein-bound ions. Our results show that controlled frequency and amplitude of ELF EM fields upon spinach plasma vesicles can steer transport over the membrane.[13)] This may be a first proof of a resonance phenomenon where appropriate levels of frequency and amplitude in the right combination have the potency to communicate with the biology of membranes and transport systems. Our study has prompted us to elaborate on magnetic resonance models; the Ion Cyclotron Resonance (ICR) model and the Ion Parametric Resonance (IPR) Model in an attempt to explain the occurrence of resonance frequencies. This is extensively described here under the heading: Mechanisms behind the effects of electromagnetical fields upon biology.

We also bring forward the concept of solitons being active in membranes and DNA/RNA-transcription as a possible mean to understand and prove the biological effects of EMF.

The Nishinomiya-Yukawa International and Interdisciplinary Symposium 2007 raised the question: What is Life? An obvious and simple answer could be: It is DNA!

The DNA strand can be looked upon as an antenna resonating in the microwave band 6GHz with its harmonics and subharmonics.[14)−18)] If this holds true, the dramatic situation might exist, that all living organisms have a receptor for the newly constructed and world-wide man-made microwaves, leading to a direct effect upon the function of DNA - in concordance with our experimental findings!

Our generation invented the microwave emitters. We now have an imperative obligation to further investigate the links between EMF and biology in order to prevent possible detrimental effects of the microwaves.

§1. Introduction

Our Universe was born in the "Big Bang" approximately 15 billion years ago, our sun and most of the stars were formed 10 billion years later.

Four and a half billion years ago our Earth was formed and already 1.5 billion years after this, the earliest unicellular life/bacteria/cyanobacteria started life on Earth.

Two and a half billion years ago the first photosynthesis by blue-green algae took place and 1 billion years ago the first nucleated cells with organelles emerged. This was followed 500 million years ago by the creation of the first vertebrates and they finally lead to the development of mammals and then, 2 million years ago, the emergence of our own species, Homo.

Since its origin, life on Earth has been exposed to, and shaped by, the original physical forces such as gravitation, cosmic irradiation, atmospheric electric fields and the terrestrial magnetism.

Life has also developed in a multitude of cyclic events occurring with different intervals: Earth's own rotation (1 day), Earth's revolution around the sun (1 year), the sun's rotation around its own axis (27 days), the synodic period of the moon (29.5 days) and further, the magnetic storms generated by the solar flare generating solar winds with plasma flows which appear 10 times in a month and vary with an eleven year periodicity. These magnetic storms produce alterations of the Earth's geomagnetic field (GMF) lasting from hours to days all around the Earth. The GMF forms an extremely important shield around the Earth, the magnetosphere with its magnetosheath, preventing the solar wind to reach Earth's surface at a harmful level.

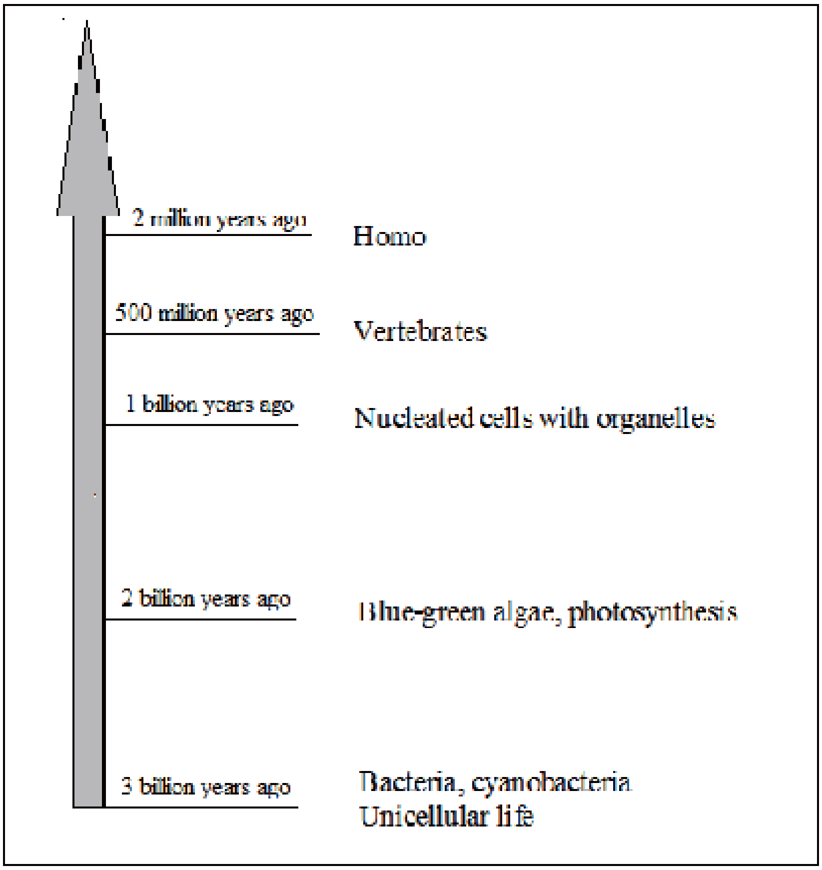


Fig. 1. Time-line for the origin of life (for a more detailed time tree, see Williams 2007).

The protective effect of the magnetosheath can be seen as the solar wind approaches the magnetosphere, where it drops abruptly. A shock wave, known as a bow shock, develops, reminding of the waves in front of a ship travelling through the water, and thus the solar wind deflects around the magnetosphere.

Earth is surrounded by its thin atmosphere reaching only about 180 km above its surface. In parallel with this exists the 3-layered ionosphere (Fig. 2), with its innermost D-region surrounding Earth 80-90 km above its surface. Between 100 and 150 km is the E-region and between 150 and 180 km the F-region. The existence of the ionosphere is an absolute prerequisite for the development and persistence of life.

The enhanced X-rays from solar flares, extreme ultraviolet and all other forms of ultraviolet light are prevented from reaching Earth by the ionosphere whilst visible light and infrared rays pass it.

Ionized particles (mainly protons and electrons) and the enhanced X-rays from solar flares are prevented from reaching Earth by the ionosphere. Short wave ultraviolet radiation is absorbed by the ozone-layer in the stratosphere, whilst longer wave UV-radiation, visible light and infrared rays pass it.

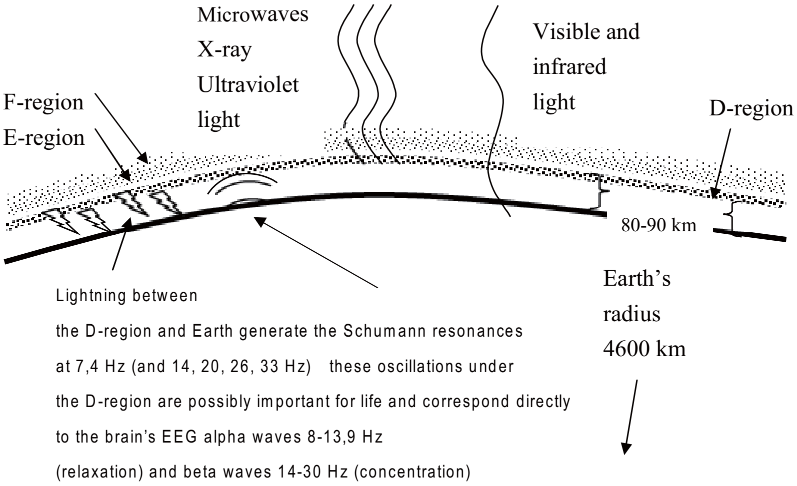


Fig. 2. Ionosphere and Schumann resonances.

The level of naturally occurring microwaves at the Earth's surface is extremely low. High frequency microwaves are stopped by the ionosphere, especially its D-region. This function is of importance for the conclusions drawn in this presentation.

Natural extremely low frequency electromagnetic fields are formed by electrical discharges in the atmosphere due to the resonance cavity formed by the surface of the Earth and the charged ionosphere resonances occur. These resonance frequencies are named after W. O. Schumann who already 1952 predicted their existence, and were recorded in 1960 by Balser and Wagner.[20)]

The Schumann resonances at 7.8, 14, 20, 26, 33, 39, and 45 Hz[21)–23)] are examples of natural oscillating electromagnetic fields of importance. It is possible that these resonances with their frequency predominantly at 7.8 Hz but also at 14-45 Hz, have played — and play — a role in the tuning of the spontaneous frequencies of the mammalian brain, where the frequency during relaxation is around 8 to 14 Hz, and during concentration 14-30 Hz.

Natural extremely low frequency ELF magnetic fields are also generated by the currents in the electrical discharges between clouds and the surface of the Earth.[24)] The daily variation of these ELF magnetic fields is strongly correlated to variations in the atmospheric magnetic field.[25)]

The always present geomagnetic field (GMF) of the Earth is a prerequisite for life. It not only shields us from the solar wind, but also has direct functions for life such as orientation of pigeons,[26)] plant branching, orientation of root branches and shielding of the geomagnetic field causes biological alterations such as decrease of the vital functions in bacteria and effects upon meristem (cf. stemcells in animals) of seedling roots of pea, flax and lentil and electron microscopy reveals changes in the mitochondrial structure.[27)]

Evidence has also been brought forward that we have endogenous internal rhythms in blood pressure and heart rate, which are close to, however not identical to, the period length of the rhythms in the solar wind. So, it has been proposed, that these were installed genetically by natural selection at some time in the distant geological past.[28)] It has also been shown that magnetic storms cause additional biological dysfunctions. Thus, bacterial bioluminescent intensity varies according to the amplitude and duration of the MSs. Further, medical studies correlate MSs with anxiety and irritability and lower attention and accuracy, with an increment of the probability of road accidents[29)] and aviation accidents.[30)] Also, acute attacks of cardiovascular diseases, such as myocardial infarction and stroke, become more frequent.[31)]

We have to conclude that the existing organisms are created to function in harmony with the abovementioned fields and forces which existed when life was born 3 billion years ago. And so was the situation until the generation of our grandparents. They invented the wonders of our modern life. Thus, in the late 19th century mankind introduced the use of electricity. Until then the ELFs, extremely low frequency electromagnetic fields, were represented on Earth principally only by the Schumann resonances. But now Tesla constructed the induction motor, Morse introduced the long-range telegraph, Bell the telephone, Edison developed the commercial electrical networks and electricity spread around the globe. Marconi introduced the wireless receiver 1896 and in the early 20th century long-wave radio and in the 1940-ies short-wave radio appeared.

Compared to the estimated natural background level of natural ELF magnetic fields below 1 pT/Hz (10^{-12} T/Hz) for which the previous generations of human beings had been exposed, the average exposure in the modern world is about 100 000 times higher!

§2. Microwaves

In 1964 Penzias and Wilson discovered the cosmic microwave background (CMB) which fills the whole universe and which originates from the Big Bang. Also ongoing cosmic processes in for example intergalactic gas clouds with temperatures of about 30°K contribute to some cosmic microwaves. But microwaves are heavily attenuated by the ionosphere and the atmosphere. *Thus the natural electromagnetic background radiation in radiofrequency and the microwave band is extremely low at the Earth's surface.*

The integrated spectral distribution of the microwave background in space results in a power density of about 0.4 μW m^{-2}. A great deal of this radiation is thus reflected by the Earth's magneto- and ionosphere or is absorbed by water and other molecules in the atmosphere. A rough estimate of the power density of CMB at the Earth's surface varies from 10^{-21} to 10^{-14} Wm^{-2} equivalent to 10^{-15}–10^{-8c} μWm^{-2}. This level of radiation is extremely low and extremely sensitive measuring equipment is required for its recording.

Thus microwaves had so far been extremely low on Earth's surface, but in the 1950-ies high frequency RF was introduced as FM and television and during the very last decades, *microwaves of the modern communication society spread around the world for the first time and now exceed the natural levels by many orders of magnitude* (Table I).

Table I. Incident energy from a spectrum of sources of electromagnetic energy. These are not actually measured values. They are guideline values set by authorities. (For microwave ovens U.S. Food and Drug Administration since 1971). The actual standard 5 mW/cm^2= 50 W/m^2 at 5 cm from oven surface, 0.5 mW/m^2 at 50 cm at 2.45 GHz corresponds to 10 W/m^2 = 2W/kg, and 50 W/m^2 = 10 W/kg.

Source	Energy flux density (W/m2)
Natural Background	$< 10^{-14}$
Microwave oven, RF leakage standard	
5 cm for surface	50
50 cm from surface	0.5
Cell telephone (2 GHz) public guideline	10
Cell telephone (850 MHz) public guideline	4.3
RF levels near cellular base antenna (calculated)*)	0.05

*) Typical E-field levels in proximity to cellular telephone base stations (< 200 m).[32]

Today one third of the world's population owns the microwave-producing mobile phones and an even larger number is exposed to the cordless RF emitting systems ("passive mobile phoning"[5]). To what extent are all living organisms affected by these new, almost everywhere present radio frequency fields? And what will be the effects of many years of continuing exposure?

These questions are extremely important to answer. Our generation and our children are the first to be exposed during a lifetime to the microwaves, which are exponentially increasing underneath the ionosphere which was intended to prevent their access to Earth, at least partially.

Scientists have studied the effects of ELF and MW since the 60-ies, and an abundance of reports have emerged, especially during recent years, many of them demonstrating significant effects upon biology and health, while others have failed to show effects. In this communication we will summarize the results of some of our work in the field since 1988 and also comment to a lesser extent upon the work of other research groups. During recent years, several scientific reports in respected journals have shown significant, but often weak, effects upon cells *in vitro*, experimental animals and also humans (for reference see 33)-35)).

Recent epidemiological studies indicate that long term exposure might increase the risk for some tumour forms (for review see 36)). In a Swedish case-control study it was reported that the use of analogue and digital cellular telephones and cordless phones was correlated to an increased risk for malignant brain tumours. Regarding the use of digital cellular telephones, an odds ratio of 1.9 was observed and with a > 10-year latency period this odds ratio was increased to 3.6.[37]

It has also been shown that mobile phone emission modulates (with increase in some cases, and decrease in others) inter hemispheric functional coupling of EEG alpha rhythms.[38]

The mechanisms through which the electromagnetic fields exert their effect upon cells and organisms are not well understood. This may be part of the reason why the results of different laboratories diverge and it should be pointed out that it is as important to reveal the mechanisms as it is to demonstrate their effects upon biology. In this publication we also dwell at some length at the theoretical models trying to explain the biological effects of EMF in relation to our own experiments on EMF steering of calcium passage over spinach plasma vesicle membranes.

§3. The Blood Brain Barrier (BBB) of the mammalian brain

Since 1988 our group has studied the effects of RF electromagnetic fields upon the blood-brain barrier (BBB) and we have collected an extensive experimental experience in this field. RF electromagnetic fields have been revealed to cause significantly increased leakage of albumin through the BBB of exposed rats as compared to non-exposed animals — in a total series of about two thousand animals. We have exposed rats to various magnetic and electromagnetic fields, as well 915 MHz continuous wave (CW) as pulse-modulated at various repetition rates (50-200 pulses per s), and we have confirmed these findings in our laboratory in follow-up studies with real GSM-900 and GSM-1800 exposures.[2),3),5)−7),39)]

The mammalian brain is protected from exposure to potentially harmful compounds in the blood by the blood-brain barrier (Fig. 3). Being formed by the vascular endothelial cells of the capillaries in the brain, this hydrophobic barrier maintains and regulates the very sensitively tuned environment within the mammalian brain.

The blood-brain barrier is a highly complex system, in which several kinds of cells exert a wide range of functions. Some of the main characteristics are described below.

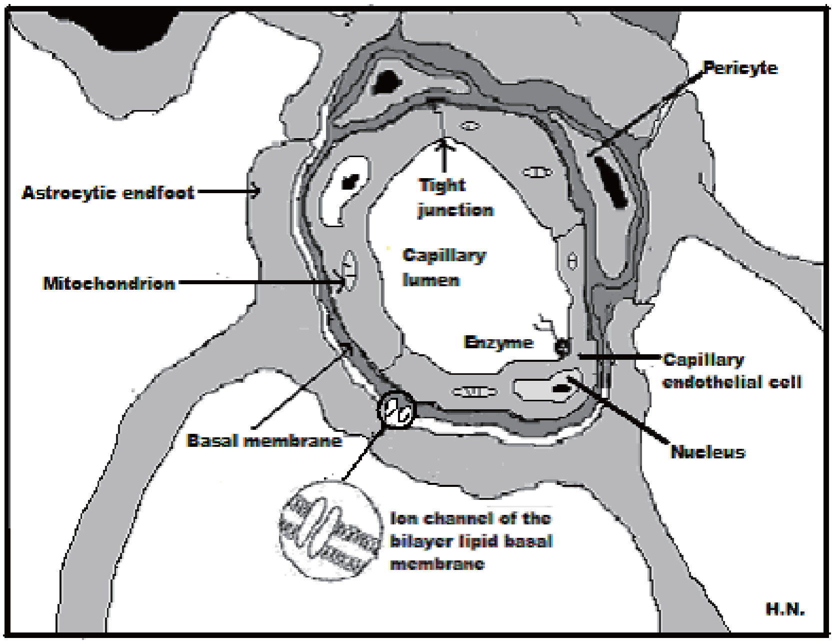


Fig. 3. The blood-brain barrier.

- The cell-to-cell contacts between the capillary endothelial cells are sealed with tight junctions, forming a permeability barrier, which is much more selective as compared to the fenestrated sealing of other capillaries.

- The outer surface of the endothelial cells is surrounded by protrusions (end feet) from astrocytes. Thereby, the endothelial cells and the neurons are connected and also, a second hydrophilic barrier is formed. Also, the astrocytes are implicated in the maintenance, functional regulation and repair of the blood-brain barrier.

- A bilayer basal membrane supports the ablumenal surface of the endothelial cells. This membrane might also further restrict the passage of macromolecules into the brain parenchyma.

- Pericytes are other periendothelial accessory structures of the blood-brain barrier. These have capacity for phagocytosis as well as antigen presentation and in fact, they seem to contribute significantly to the immune mechanisms of the central nervous system.[40]

In addition to these structural properties of the blood-brain barrier, there are also several physiological characteristics of major importance, e.g. the high number of mitochondria within the endothelial cells (five-fold higher as compared to muscular endothelial cells of rats)[41] and also, the low number of pinocytotic vesicles for nutrient transport through the endothelial cytoplasm. These are properties, which speak in favour for an energy-dependent transcapillary transport system. Of importance in the context of the blood-brain barrier permeability restriction, is also the enzymatic barrier of the cerebral endothelium, which metabolizes drugs and nutrients and thereby prevent their passage into the brain parenchyma.[42]

Taken together, all these characteristics of the blood-brain barrier guarantee that only those molecules, which are either hydrophobic (such as oxygen, nitric oxygen and steroid hormones), or bind to specific receptors (such as certain amino acids and sugars), can pass freely from the blood circulation out into the brain parenchyma. Additionally, there is also a weight-selectivity, where particles of a larger molecular weight are more effectively excluded from passage over the blood-brain barrier. Also, active transport out from the brain parenchyma and metabolization of certain drugs, made possible by an intact blood-brain barrier, stabilises and optimises the environment surrounding the neurons of the mammalian brain.

In a number of pathological conditions, such as epileptic seizures, sepsis and severe hypertension, the integrity of the blood-brain barrier is disturbed. The sensitively tuned balance within the brain parenchyma is thereby disrupted. This might lead to cerebral oedema, increased intracranial pressure and in the worst case, irreversible brain damage. Also, potentially carcinogenic molecules can gain free access to otherwise protected areas of the mammalian brain. Of importance to remember, is also, that transient openings might be harmful enough to result in permanent tissue damage.[43]

In conclusion, an intact and fully functioning blood-brain barrier is essential for the proper function of the mammalian brain.

Rectangular pulsed RF were generated by switching the MW generator (900 MHz) on and off with a rectangular pulse train of various repetition frequencies (4-217 Hz). We started our studies on albumin passage over the BBB a repetition frequency of 16 Hz and then with its harmonies of 4, 8 and also 50 Hz, which was felt relevant, as it is the standard voltage of the European power supply, with a carrier wave of 915 MHz. At an early stage also 217 Hz modulation was added as this was the frequency of the then planned GSM system. In all experiments endogenous substances such as albumin and fibrinogen, which occur naturally in the blood circulation, were used for the detection of BBB leakage, which is identified by anti-rat albumin rabbit antibodies and rabbit anti-human fibrinogen.

This work was published in 1994[3] and 1997[6] and comprised sham or 915 MHz exposure for in most cases 2 hours (both CWs and pulsed modulated waves). These results, based on 246 rats 1994 and more than 1,000 rats 1997 (the majority EMF exposed and about 1/3 sham-exposed) concluded that there was a significant difference between the albumin extravasation from brain capillaries into the brain tissue between the differently exposed groups and the controls. It is important to point out that though all animals in the 1997 series (and basically all of our experiments) are inbred Fischer 344 rats, only at the most 50% of the identically exposed animals display albumin extravasation (in CW animals and somewhat less in the other exposed animals). Even the sham exposed animals had some albumin leakage though only in seventeen per cent as a mean of all controls and at a lesser extent. The detection of leakage in unexposed animals presumably is due to our very sensitive immune histological methods.

The most remarkable observation was that exposure with whole-body average power densities below 10mW/kg gave rise to a more pronounced albumin leakage than higher power densities, all at non-thermal levels. If the reversed situation were at hand, we feel that the risk of cellular telephones, base-stations and other RF emitting sources could be managed by reduction of their emitted energy. The SAR

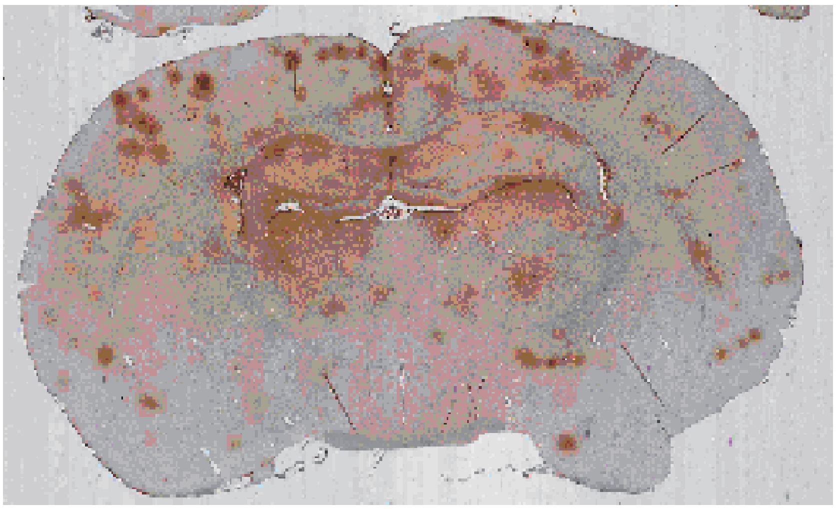


Fig. 4. Pathological leakage around brain capillaries demonstrated by immuno assaying against blood albumin. Fischer 344 male rat (# 3987, weighing 292 g) exposed to 1899 MHz CW microwaves in an anechoic chamber for 2 hours at SAR ≈ 2mW/kg. Ten minutes after this exposure, the animal was anaesthetised and sacrificed.

value of around 1 mW/kg exists at a distance of more than one meter away from the mobile phone antenna and at a distance of 150-200 metres from a base station. This has led us to coin the concept passive mobile phoning for all non-users who are exposed.[5)]

The maximally allowed SAR-value for occupational exposure is 10 W/kg, and 2 W/kg is the maximally allowed SAR-value for public exposure. At a frequency of 900 MHz, these values are reached at power densities of 22.5 W/m^2 for maximally allowed occupational exposure, and 4.5 W/m^2 for maximally allowed public exposure. That is, 1 W/kg corresponds to 2.25 W/m^2 at a frequency of 900 MHz.

In many studies of pharmacological effects in connection with RF exposure, response is only seen at a certain dose range, and not at higher or at lower dosages. This is named “the inverted U-function”. A similar RF response characteristic has been observed by us, seen as a more pronounced albumin leakage at lower than at higher power densities. According to Adey, this kind of dose response might constitute the basis for window effects observed in connection to RF exposure.[44)]

In the majority of our studies, EMF exposure of the animals has been performed in transverse electromagnetic transmission line chambers (TEM-cells)(for reference see 2),3),5)-7),39),45),46).) These TEM-cells are known to generate uniform electromagnetic fields for standard measurements. In each TEM-cell, two animals can be placed, one in an upper compartment and one in a lower compartment. The experimental model allows the animals, which are un-anaesthetized during the whole exposure, to move and turn around in the exposure chamber, thus minimising the effects of immobilization induced stress, described by Stagg et al.[47)]

It is important to point out that the position of the animals in upper or lower compartments does not affect the magnitude of observed albumin leakage. Also, we have concluded, with our total series of more than two thousand exposed animals, that there is no difference in the sensitivity to EMF exposure between male and female animals as far as albumin leakage is concerned.

Our initial findings of albumin leakage have been repeated by others,[48)] with 900 MHz exposure of rats for 4 hours at brain power densities ranging from 0.3 to 7.5

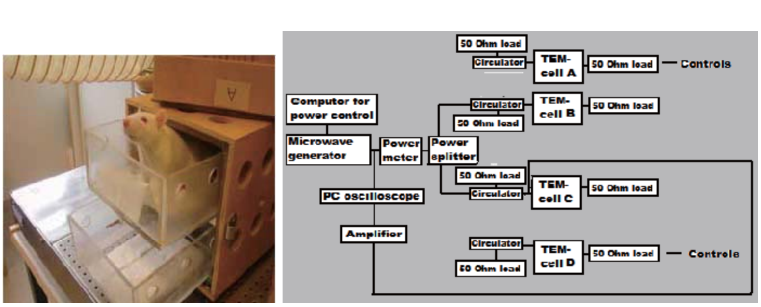


Fig. 5. Left: A rat in the upper exposure tray of a TEM-cell for 915 MHz microwaves. Right: Block diagram of the 4 TEM-cell arrangement used in the experiments in Lund. A microwave power generator is used for feeding the TEM-cells. A power splitter divides the power form the RF generator into equal parts that are fed to each TEM-cell. The output from the cells is terminated in a 50 Ohm dummy load.

W/kg. Another group, working in Bordeaux, and led by Prof Pierre Aubineau, has also demonstrated evidence of albumin leakage in rats exposed for 2 hours to GSM-900 MHz at non-thermal SAR-values of 0.12, 0.5 and 2.0 W/kg, using fluorescein-labelled proteins. The results were presented at two meetings[49] and are very similar to ours, described above.

Support for our findings that low intensity GSM 900 MHz electromagnetic fields influence the BBB is also found in the *in vitro* proteomic studies on a human endothelial cell line by the group of Leszczynski.[50],[51]

§4. Neuronal damage

Our consistent findings of albumin passage over the BBB and spread in the surrounding brain tissue with albumin uptake in the cytoplasm of neurons and glial cells brought up the question whether this might lead to neuronal damage.

In a series of experimental situations, neuronal degeneration has been observed in areas with BBB disruption and it has been suggested that BBB leakage is the major reason for nerve cell injury such as that seen in dark neurons.[52]

It has also been observed after intracarotid infusion of hyperosmolar solutions in rats;[53] in the stroke-prone hypertensive rat;[52] and after acute hypertension by aortic compression in rats.[55] Further, epileptic seizures cause extravasation of plasma into brain parenchyma.[54] The cerebellar Purkinje cells are heavily exposed to plasma constituents and degenerate in epileptic patients.[55] This effect may, however, as well be attributed to hypoxia. It has been postulated that albumin is the most likely neurotoxin in serum.[56]

In order to seek for neuronal damage in our experimental model, we exposed Fischer 344 rats for 2 hours with non-thermal GSM at SAR values 120, 12 and 1.2 mW/kg.[7] We made the remarkable observation that a significant ($p<0.002$) neuronal damage is seen in rat brains 50 days after such an exposure.

It is notable, that we see areas in hippocampus and cortex of exposed animals where the cytoplasm of neurons are filled with autologous albumin while neighbouring neurons display the shrunken and dark state of a “dark neuron” which is a very sick or dying neuron. It may be so that the leakage of albumin out in the neuropil starts a deleterious process whereby more albumin leaks through the endothelium and finally becomes too heavy a burden for the affected neurons. Hassel et al.[57] have demonstrated that injection of albumin into the brain parenchyma of rats gives rise to neuronal damage. When 25 micro litres of rat albumin is infused into rat neostriatum, 10 and 30, but not 3 mg/ml albumin causes neuronal cell death and severe axonal damage. It also causes leakage of endogenous albumin in and around the area of neuronal damage.

Findings similar to ours in the animals sacrificed late after exposure have been reported in Wistar rats.[58] Twenty-two female rats were exposed to a 900 MHz electromagnetic GSM near-field signal for one hour a day for seven days. The peak specific absorption rate (SAR) of the brain was 2 W/kg. This resulted in scattered and grouped dark neurons in the cortex, hippocampus and basal ganglia, mixed in among normal neurons with distributions of scores significantly different between the control and the GSM exposure group ($p < 0.01$).

In continued work we have proven our own finding from 2003 — in a study of 96 non-anaesthetized rats which were exposed or sham exposed for a duration of 2 hours at specific absorption rates (SAR) of 120, 12, 1.2 and now also 0.12mW/kg. The extravasation of albumin, uptake into neurons and occurrence of damaged neurons were assessed 14 or 28 days later. Albumin extravasation and uptake into neurons was significantly enhanced after 14 days, but not after 28. The occurrence of dark neurons, on the other hand, was significantly enhanced only after 28 days. After 28 days, neuronal albumin uptake was significantly correlated to occurrence of damaged neurons.[8)]

In ongoing and recently completed experimental work, we have studied lifelong exposure to GSM 900 as well as the effects of short term exposure to GSM 900 and 1800 in living rats. Lifelong exposure to microwaves seems to be the future of the young generation. Therefore, we have studied male and female Fischer 344 rats, exposed for 2 hours to GSM 900, and sham exposed in our TEM-cells once a week for 13 months. After this they were studied for cognitive functions and compared to cage controls. Significant effects of exposure upon episodic memory function have been demonstrated and published.[9)] In short, the cognitive functions were evaluated in the episodic-like memory test. The GSM-exposed rats had significantly impaired memory for objects and their temporal order of presentation ($p=0.02$). The detection of a place in which an object was presented, that is the spatial memory function, was not affected by the GSM exposure. In rats, hippocampus is involved in aspects comparable to human declarative memory, and is seems possible that the reduced memory functions that we observed are correlated to hippocampal alterations induced by the mobile phone exposure. Also, temporal order memory, depending on cortical areas such as the perirhinal cortex in the medial temporal lobe, the prefrontal cortex and the interaction between these areas, might explain the reduced temporal order memory of the GSM exposed rats. Finally, after the memory tests had been performed, all animals were sacrificed and the brains are now under examination for albumin leakage, neuronal and glial damage and other signs of pathology.

The possibility that microwaves may affect our DNA has received increased attention since recent epidemiological studies indicate that long term exposure (10 years mobile phone use) increases the risk for developing tumours in the exposed brain hemisphere, both the benign vestibular schwannoma arising from the balance nerve and the highly malignant glioblastoma multiforme.[36),37),59)] Regarding the development of vestibular schwannoma, the relative risk seen ten years after the start of mobile phone use, was 1.9 (with confidence interval 0.9-4.1).[59)] When only tumours occurring at the same side of the head as the mobile phone had been normally used, the relative risk increased to 3.9 (with confidence interval 1.6-9.5). In a pooled analysis of case-controlled studies on malignant brain tumours, cumulative life use of $>$ 2, 000 hours of mobile phoning revealed an odds ratio of 3.7 (confidence interval of 1.7-7.7).[60)]

Studies of gene expression patterns in the living animal may elucidate also other aspects such as effects on genes involved in membrane transport and other basal functions of the living cell *in situ*.

In collaboration with Belyaev and his group we have exposed rats for 6 hours to GSM-900 RFs at SARs of 0.4mW/kg and investigated the genetic expression from cerebellar tissue. Alterations of genes encoding proteins for BBB functions were observed.[10)]

We have now studied whether 6 hours of exposure to the radiation from a GSM mobile phone at 30mW/kg has an effect upon the gene expression pattern in rat brain cortex and hippocampus — areas where we have observed albumin leakage from capillaries into neurons and neuronal damage. Microarray analysis of 31 099 rat genes, including splice variants, was performed in cortex and hippocampus of 8 Fischer 344 rats, 4 animals exposed to GSM for mobile communications electromagnetic fields for 6 hours in an anechoic chamber and 4 controls kept for the same length of time in the same anechoic chamber without exposure. Gene ontology analysis of the differentially expressed genes of the exposed animals versus the control group revealed interesting differences between exposed animals and controls. Genes of interest for membrane transport show highly significant differences.[11)] This may be of importance in conjunction with our earlier findings of albumin leakage into neurons around capillaries in exposed animals and has also lead us to look into the mechanisms behind these effects — see below under **DNA Transcription process, Solitons and Microwaves.**

§5. Mechanisms behind the effects of electromagnetic fields upon biology

5.1. *Interaction of ELF with calcium metabolism*

Beyond what is described above, we have also performed experiments where an increase of the Ca^{2+}-efflux over plasma membranes has been observed in plasma vesicles from spinach exposed to ELF.[13)]

We could show that suitable combinations of static and time varying magnetic fields directly interact with the Ca^{2+}-channel protein in the cell membrane, and we could quantitatively confirm the model proposed by Blanchard.[61)]

Calcium has many important roles in all living organisms. Apart from its structural role in, for example, bone matrix, plant cell walls, and in stabilizing membranes, it plays an essential role in cellular homeostasis, most notably as an intracellular messenger.[62)] The free Ca^{2+} concentration in the cytosol is strictly kept at 0.1-0.2 μM, which is much lower than that found in the intracellular Ca^{2+}-stores or the extra-cellular space. The cytosolic free Ca^{2+} ion concentration has influence upon growth and development of the organism and its daily functions as well as death in apoptosis.[62)]

It has been suggested that the mechanism underlying alterations of Ca^{2+}-fluxes involves inducible changes of both static and time varying magnetic fields.[63] The studies of the effects on Ca^{2+}-influx over cell membranes are of importance in the perspective of human health, considering the crucial role of Ca^{2+}-flux played in cellular communications.

The mechanism, by which magnetic fields might interact with biological systems, has been called magnetoreception. Different models try to provide the theoretical framework explaining how this is made possible, and these models are also important for future model-guided investigations of the magnetoreception.

In order to explore the mechanism for possible biological effects of the enhanced ELF radiation environment, we investigated how the transport of Ca^{2+} ions over the membrane of spinach plasma vesicles varies with frequency and amplitude of ELF magnetic field exposure. Bauréus-Koch et al.[13)] studied the calcium flux through calcium channels in highly purified plasma membranes of spinach (Spinacia oleracea L.).[13)]

A bio-resonance phenomenon was found where appropriate combinations of frequency and amplitude have the potency to affect bio-membranes and their Ca^{2+} -ion transport systems at various degrees and directions. With a static magnetic field $B_{DC} = 37.0 \pm 0.5\ \mu T$ we found resonances of $B_{AC} = 25.9 \pm 0.3\ \mu T$ (peak), at the frequencies of 7, 21, 24, and 31 Hz. The Ca2+ -ion efflux ratio at those exposure conditions appears to deviate significantly compared to that of sham exposures.[13)]

Three Gaussian peaks with the same width of 2.5±0.4 Hz could be fitted through the data points with peaks at the frequencies 20.9±0.3, 25.4±0.4, and 30.2±0.5 Hz with a χ^2 value of 6.0. These frequencies correspond well to the resonance frequencies 20.7 Hz (Mn_{ion}, $n = 1$) 25.2 Hz ($^{45}Ca_{ion}$, $n = 1$), and 31.1 Hz (Mn_{ion}, $n = 1$), respectively.[13)]

With our Ca^{2+}-efflux studies over plasma membranes as a basis, our research was further extended into the field of magnetic resonance models; mainly the Ion Parametric Resonance (IPR) Model as proposed by Lednev;[64),65)] in an attempt to explain the occurrence of resonance frequencies. In short, Lednev's model considers the polarization of the oscillation of an ion bound to a protein in a combination of static and time-varying magnetic fields.

In our studies of spinach vesicles, the calcium flux was modified at frequencies that corresponded to resonance frequencies for non-hydrated ions of $^{40}Ca^{2+}$, Mn^{2+} and Mn^{3+}. The resonance frequencies were linearly related to the strength of the static magnetic field applied. The resonance frequency of 24 Hz could be attributed to $^{45}Ca^{2+}$ ($n = 1$) or $^{24}Mg^{++}$ ($n = 2$). Lednev[64)] predicts an amplitude dependence that follows the Bessel functions.

In our experiments, we concluded that the resonance could be attributed to $^{45}Ca^{2+}$. However, as in the experiments performed by Blackman,[66)] a factor of two had to be included in the argument of the Bessel function.

In 1996, Lednev[65)] modified his model, in order to avoid some of the problems identified in the original theory.[67)] In this modified version the amplitude window is described by the square of the Bessel functions. A fit to our data[13)] demonstrates that the factor of two is not required as previously to fit the experimental data to the theory.

Taken together, our experimental results of the interaction of ELF magnetic fields with Calcium bound to proteins in the cell membrane fit extremely well with quantum mechanical interaction models.[61),63),68)] Thus, we have shown that ELF magnetic fields interact with Calcium and Manganese ions in plasma membranes at specific frequencies in accordance to a quantum mechanical interaction model.[13)]

The search for the mechanisms behind the effect of electromagnetic interactions with biological systems has continued. Another way to address the issue, as compared to our model with the purified membrane system, with theoretical, physical models as a basis, is the biological examination of signalling pathways possibly affected by magnetic fields. As has been shown by Sun et al.,[68] a possible mechanism for the bioeffects produced by ELF-EMF exposure could be protein tyrosine phosphorylation. 50 Hz power-frequency magnetic fields could activate the stress-activated protein kinase (SAPK),[70] however, not through the phosphorylation of the upstream kinase of SAPK (SEK1/MKK4).[71] Noise MF with certain intensity could inhibit the biological effect induced by 50 Hz MF, as seen by the reduced activation of SAPK when noise and 50 Hz exposures were applied simultaneously.[72] With continued research of this kind, a mosaic of EMF target proteins might crystallize.

§6. Transmembral transportation — Solitons and microwaves

A major portion of this paper dwells on the passage of albumin from the brain capillaries out into the surrounding brain and the cytoplasm of neurons and astrocytes, and the remarkable observation that it is the lowest energy levels that give rise to the most pronounced albumin leakage.

The mechanisms by which the EMFs may alter BBB permeability are not well understood. At low field strengths, the effects on body temperature are negligible and thus heating effects are not involved. It has been suggested that physicochemical characteristics of membranes are changed.[12] One of the great pioneers in the field, Ross Adey discussed the mechanisms behind a possible direct, non-thermal effect of RF radiation upon the central nervous system. He studied amplitude-modulated radiofrequency fields and suggested in 1988 that co-operative processes in the cell membrane might be reactive to the low energy of an electromagnetic field. This oscillating field might result in changes of the membrane potential.[74]

The question might find an answer within a theory which we hereby bring forward

– the possible soliton function in membranes.

The word soliton emanates from John Scott Russell's observation of the solitary wave

In 1834, while conducting experiments to determine the most efficient design for canal boats, this young Scottish engineer made a remarkable scientific discovery, which he described in his "Report on Waves" after his first sighting of a soliton or solitary wave, by Russell called a "Wave of Translation" on the Union Canal near Edinburgh.[73]

The migration of soliton energy in molecular systems was first considered by Davydov and Kisluka[75] by the use of a quantum coherent wave theory. Solitons were considered important for energy transfer and storage in biological structures, as described by Davydov[76] and then by Fröhlich,[77] as coherent dipolar propagating waves. These applications of quantum field theory to biological systems inspired many theoretical physicists to study biological systems with a special interest focused upon tubulin. This filamentous protein is a fundamental building block of the cytoskeleton matter.[78),79)] Microtubules are important components of the cytoskeleton, responsible for cellular organization and information processing.[80)] Microtubules of the neurons in the brain might be active components of brain functioning and information processing. Endogenous electromagnetic waves are considered to be moving in the cavity of the microtubules, transporting and carrying information. The relevant mechanism of electromagnetic wave interaction has been suggested to be spontaneous breakdown of symmetry in the biological, well ordered structures. Such interaction occurs with the dipole moments of the molecules in the brain microtubules.[79)]

Abdalla et al.[81)] studied the problem of information propagation in the brain microtubules, considering propagation of electromagnetic waves in a fluid of permanent electric dipoles. The problem reduces to sine-Gordon wave equation in one space and one time dimension. The energy balance of the voltage along with the neuronal projection and the microtubule z-axis, results in generation of solitons and propagation of kinks or anti-kinks along the microtubule proto-filaments. The tubulin tails are coupled to the dipoles of nearby water molecules at the microtubule surface and the change of their conformational status at the place of the soliton twist. The standing breather swinging at certain tubulin tail (or breather formed by 2-3 coupled swinging tubulin tails) could catalyze microtubule attachment proteins (MAP) and promote or inhibit the action of kinesin-proteins involved in the microtubule dynamics.[82)]

Another interesting result of the work of Abdalla et al.[81)] is the fact that the frequency parameters, which showed up in the model, are compatible with the size of microtubules of brain structures and with the transition period observed for the so called conformational changes of the tubulin dimer protein (namely 1-100 GHz).

The applications of exogenous, electromagnetic waves in this frequency interval, that coincide with that we use for wireless communication, interact with the endogenous electromagnetic wave that might result in biological actions. This may be the mechanism behind our observation of memory impairment in rats exposed to 0.9 GHz microwaves as described above.

Solitons as actors in biology thus have been discussed since the 1970-ies. The effects in biological membranes have recently been brought to the fore by two researchers at the Niels Bohr Institute in Copenhagen, T. Heimburg and AD Jackson in their publication: "On soliton propagation in biomembranes and nerves".[83)] They write:"The lipids of biological membranes and intact biomembranes display chain melting transitions close to temperatures of physiological interest. During this transition the heat capacity, volume and area compressibilities, and relaxation times all reach maxima. Compressibilities are thus nonlinear functions of temperature and pressure in the vicinity of the melting transition, and we show that this feature leads to the possibility of soliton propagation in such membranes. In particular, if the membrane state is above the melting transition, solitons will involve changes in lipid state". The authors discuss solitons in the context of several properties of nerve membranes under the influence of the action potential, including mechanical dislocations and temperature changes.

In a recent paper, the same authors support their hypothesis by pointing out that the Hodgkin-Huxley model for nerve signal transduction never explained the function of anesthesia. The soliton model on the other hand might give an answer. They conclude that anesthetics lower the temperature at which lipids become solid, making it difficult for the soliton waves to form. This should prevent nerves from sending pain signals.

It is known that the action of general anaesthetics is proportional to their partition coefficient in lipid membranes (Meyer-Overton rule). This solubility is, however, directly related to the depression of the temperature of the melting transition found close to body temperature in biomembranes. Heimburg and Jackson proposed a thermodynamic extension of the Meyer-Overton rule, which is based on free energy changes in the system and thus automatically

incorporates the effects of melting point depression. This model accounts for the pressure reversal of anaesthesia in a quantitative manner. Further, it explains why inflammation and the addition of divalent cat-ions reduce the effectiveness of anesthetics.[84)] (Charles Overton was professor of pharmacology at Lund University 1907-1930.)

The statement by Heimburg and Jackson is extremely interesting in reference to an extensive and thorough work on pain perception and electromagnetic fields performed by a research group in London Ontario since the early 1980-ies. (Their work stimulated our group to visit London Ontario and to join in the field in 1988.) In a recent review by the group, "Pain perception and electromagnetic fields", it is concluded that the effects on pain, nociception (pain sensitivity) and opiate-mediated analgesia (pain inhibition) constitute one of the most reproducible and reliable effects of EMFs with observed decrease in pain threshold (Del Seppia et al. 2007). In early studies on the nociception of rodents, the animals were placed on a metal surface at a standard temperature (50°C for mice) and the time taken to respond to the heat stimulus with a stereotypic averse withdrawal was recorded. The exposure to a heterogenous time-varying magnetic field resulted in an enhanced basal nocturnal sensitivity and reduced levels of morphine induced analgesia in mice. Also in connection with geomagnetic storms, mice were similarly less responsive to the analgesic effect of morphine. Further studies, with the land snail Cepaea nemoralis, showed that continuous EMF exposure induced hyperalgesia in a duration-dependent manner (at exposure times ranging from 2 hours to 120 hours). It is also pointed out that the increased pain perception by EMF may be a reason for the increasing prevalence of pain problems in the modern society. (For further discussion of these results, see 84).)

With the solid evidence collected from more than 50 publications, most of them based on studies on the land snail, Cepaea nemoralis but also mice and rats, it is tempting to give the solitons a chance in the search for, and definition of, the physiological mechanisms involved.

Exposure to pulsed magnetic fields (MF) has been shown to have a therapeutic benefit by increasing pain thresholds not only in animals, but also in humans. In a recent study it was concluded that MF exposure does not affect basic human perception, but can increase pain thresholds in a manner indicative of an analgesic response.[85)]

We suggest that soliton models will be considered in studies on the relation between pain, anaesthesia and electromagnetic field exposure. Further those models could be applied to study the effect of EMF field on membrane permeability for various molecules such as calcium and albumin.

It is striking that the soliton theory also may be instrumental in the explanation of how the DNA transcription process is possibly influenced by the Microwaves:

§7. DNA Transcription process, solitons and microwaves

The Nishinomiya-Yukawa International & Interdisciplinary Symposium 2007 raised the question: What is Life? An obvious and simple answer could be: It is DNA!

The DNA strand can be looked upon as an antenna resonating in the microwave band 6GHz with its harmonics and subharmonics.[14)–18)] If this holds true, the dramatic situation might exist, that all living organisms have a receptor for the newly constructed and world-wide man-made microwaves, leading to a direct effect upon the function of DNA — in concordance with our experimental findings!

Screening of gene expression by microarray technology provides new powerful means for the search for molecular pathways and to elucidate possible molecular markers of response of brain cells to MWs. However, to our knowledge, only two studies have been published on the effects of GSM microwaves upon the gene expression in the CNS after exposure of the whole organism.[10),11)] This material was first presented at the 4th International Workshop, 16-20 October 2006, Crete Greece.[87)]

Those studies are described above and have shown that 6 hours of exposure to GSM 900 MW (at the very low SAR value of 0.4 mW/kg) and 1800 MW (at SAR value 30 mW/kg), to brain cells *in vivo* gives rise to highly significant alterations of gene expressions in cerebellar, cortical and hippocampal cells.

These findings are supported by a series of recent publications where the influence of RF of the type emitted in GSM has been studied in vitro in different cell cultures, proving effects upon gene expression in cultured human cells[88)–90)] and rat neurons[91)] through non-thermal mechanisms.

In the search for a possible mechanism behind these effects of the man-made microwaves upon living organisms, we have explored the effects of microwaves on the DNA/RNA transcription process. In the following we bring forward the possibility of a soliton mechanism in the interaction between microwaves and the DNA/RNA transcription process.

§8. The DNA transcription process

The first step in genome expression is DNA transcription from the original DNA template contained in the cell, is to make a copy — the RNA messenger — which will then be used as a 'master copy' in determining protein sequences in accordance with the genetic information. The evolutionary advantage of such a messenger is obvious: in this way, the original DNA is opened — and thus less protected — for as small a time as possible.[92)]

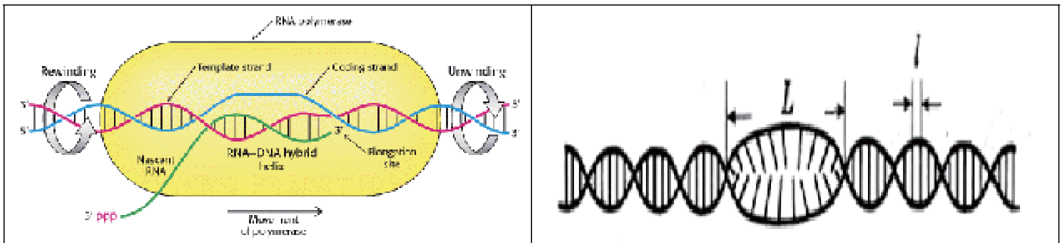
In the DNA transcription process, a specialized enzyme (RNA-Polymerase or

RNAP) binds to a specific site of the DNA double helix and unwinds it in a local region of 15-20 bases, thus creating a "transcription bubble"; the RNAP and the bubble travel then along the DNA, copying its sequence and producing a RNA-Messenger to be later used to express genes or replicate the local sequence. This process requires a very finely tuned coordination of the motion of RNAP — and production of the RNA-Messenger — with the dynamics of the DNA double chain. In the active phase of the process, the RNAP proceeds along the DNA chain at a speed of several tens or hundreds of base pairs per second. Since each base pair is linked by two or three hydrogen bonds, the energy involved in such a process, even considering only the one to open (and close) the DNA chain, is of the order of at least hundred, if not thousand, H bonds per second. This corresponds to about to a power 300 fW (1 fW = 1 femto-W = 10^{-15} W).

§9. Solitons hiding in DNA and their role in RNA transcription

In a pioneering paper which appeared in 1980, Englander, Kallenbach, Heeger, Krumhansl and Litwin suggested that nonlinear excitations in the DNA double chain could be instrumental in this process and allow the motion of the transcription bubble to occur at near-zero energy cost. In particular, as the fundamental motion undergone by DNA nucleotides in this process is a roto/torsional one, they suggested modelling the DNA molecule as a double chain of coupled pendulums; the relevant nonlinear excitations would then be (topological) solitons pretty much like those, well known in the sine-Gordon equation[93] (Fig. 6).

Englander et al.[93] concluded that precedent for a frequency w, of MHz in double helices implies extended open segments with $(L/l) = 10$, compatible with the mobile defect model hypothesized (Fig. 7). Experimental indications for processes as fast as



Transcription Bubble. A schematic representation of a transcription bubble in the elongation of an RNA transcript. Duplex DNA is unwound at the forward end of RNA polymerase and rewound at its rear end. The RNA-DNA hybrid rotates during elongation.

FIG. 1. Diagram of a mobile defect within DNA. The base-pair spacing l is 3.4 Å for the normal B helix, shown to the left and right of an open state. The open state involves loss of one half turn of helix, spread over a length L of 10 base pairs, and corresponds to a $-\pi$ soliton. The defect travels to the right or left by opening base pairs in the direction of motion and reclosing behind. The bases within the soliton are shown as tilted to suggest their altered winding with retention of stacking but loss of base-pair hydrogen bonds.

(Englander et al., 1980)

Fig. 6. Solitons in transcription.

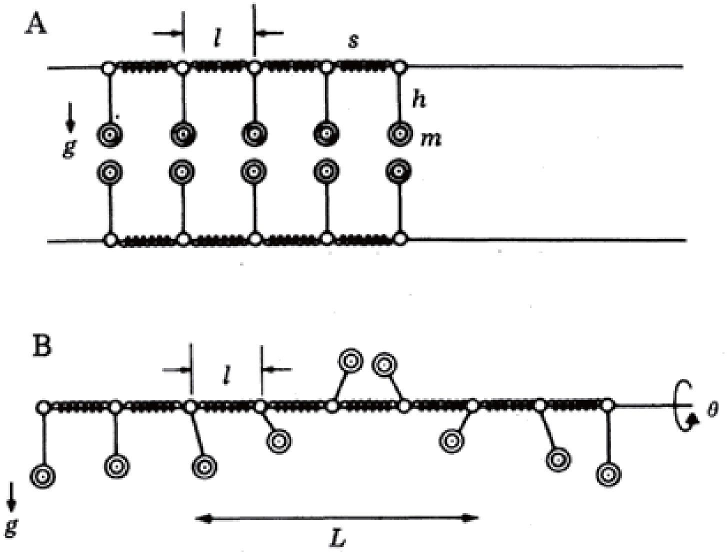


Fig. 7. A mechanical analogue of the DNA double chain, as presented by Englander et al.[92] Linear chains of the bases (here modelled as pendulums, each with a mass m and length h, with a space in between corresponding to l≈ 3.4Å) are connected by sugar-phosphate backbones (modelled as springs). One strand of the DNA double helix is able to undergo torsional oscillations (angle θ) about the sugar-phosphate backbone in the presence of the restoring gravitational force $= m * g$.
A) The DNA double helix in its ground state.
B) Soliton excitation mode, with large-amplitude excursion of one of the pendulum. The excitation is spread to the group of pendulums within the range of L.

GHz exist, but imply very large open structures with $(L/1) = 1000$. Characteristic attempt frequencies of MHz, on the other hand, seem to be more reasonable in terms of hydrodynamic, melting, and NMR data. The overall activation energy for forming solitons was estimated to 6 kcal/mol which corresponds to $(L/l) = 100$.[93] The binding energy of individual hydrogen bonds is in the same order of magnitude.

Nonlinear-waves in DNA was suggested by Polozov and Yakushevich[94] to be involved in the regulation of transcription.[94] Prohofsky[95] proposed that the hydrogen-bond-stretch (HBS) bands of the double helix appear to be nonlinear enough to support solitary-wave energy concentration. Coupling this fact to predictions of a self-consistent theory of helix melting gives rise to speculations of a mechanism for base pair melting in RNA transcription which is consistent with the known energy needs of that process.[95]

Guided by the idea of the order parameter of Landau, Zhou and Zhang[96] analysed the structure and various nonlinear motions in DNA. They argued for the use of four significant variables, i.e., the conformational, rotational, longitudinal and transverse motions. Several sets of nonlinear discrete equations with more reasonable Hamiltonian were established, and their solution of small amplitude (phonons) and large amplitude (soliton or solitary waves) have been given. They speculated in the possible significant implications in duplication, transcription and drug intercalation in DNA.[96)]

Gaeta[97)] suggested that nonlinear excitations could play a role in the process of DNA transcription, i.e. that the transcription bubble could correspond to a solitary wave travelling along the chain, which the RNAP could then 'surf' in order to access the base sequence with no energy to provide for opening the double helix. He discussed the general idea of providing a simple model for a specific DNA process, and argued that despite the tremendous complexity of the DNA model, this approach is not bound to fail. Recalling the main features of the model proposed by Yakushevich, he mentioned some encouraging achievements and several limitations.[97)]

These limitations, however, more than being inherent to the model, are limitations of the studies conducted so far. It is clear that the model is too simple to be valid as it is. What is needed is to go 'one step further' in the Yakushevich classification of DNA models, but only a more thorough analysis can focus on the detailed refinements which are needed.[98)] In particular, Gaeta[97)] pointed out several directions in which he suggested that it is necessary to generalize the model and to investigate its behaviour, such as considering real nucleic acid base sequences and microwave thermal effects.

9.1. *Dissociation phase transition in DNA*

Bishop, Dauxois, and Peyrard proved the existence of a 'dissociation' phase transition in DNA, considered as a one dimensional system.[99)–103)] Indeed it models DNA as a one-dimensional chain, and by singling out *one* degree of freedom per base — corresponding to 'radial' displacements along the axis joining the two bases of a pair — that is, the degree of freedom thought to be the most relevant for the process under study.

Their theory for DNA melting compares successfully to experimental data on the detailed (spatiotemporal) dynamics of DNA melting. It can predict not only average quantities, as should anyway be the case with a statistical mechanics approach, but a spatiotemporal pattern.[104)]

9.2. *DNA and microwave absorption*

A nontrivial theory for dsDNA phonons and its associated nonlinear modes is provided by the Peyrard-Bishop model[104)] whose Hamiltonian is given by:

$$H_{PB} = \sum_{i=0}^{N} \left(\frac{P_i^2}{2m} + \frac{k}{2}(x_{i+1} - x_i)^2 + V_{H(x_i)} \right),$$

$$V_{H(y)} = U_0(\exp(-y/\lambda) - 1)^2,$$

where $p_i = mv_i$ is the momentum of the ith base pair,

x_i is the relative coordinate of displacement at each base pair,

v_i its velocity,

k is the harmonic coupling along each of the chains, and

V_H refers to the Morse potential representing hydrogen bonds between each base pair.

Fits to experimental data reveal that the well-depth is about normal room temperature (O(10-2 eV)). In a more realistic Peyrard-Bishop-Dauxois model the spring constant k is allowed to vary along the double chain to reflect the requisite stacking energy dependence.[105]

In the presence of an electric field oscillating in time but spatially homogeneous on the length scale of the dsDNA, we make the following replacement, which follows from standard classical electrodynamics:

$$p_i \to p_i - q_i A(t)/c,$$
$$A(t) = -\frac{E_O c}{\omega_0} \sin(\omega_0 t),$$

where

q_i is the charge at the ith bond,

A is a component of the vector potential that exhibits solely a time-dependence,

c is the speed of light,

E_0 is the amplitude of the incident EM radiation, and

ω_0 is its frequency.

The charge could be electronic, or it could be a counter-ion adsorbed from the aqueous, ionic solvent. We are primarily interested in small perturbations, with a view to estimating at what level they become sinister.

Chivantis describes a dsDNA system, with the following Hamiltonian density, which is the continuum version of the Peyrard-Bishop-Dauxois model.[14),105)]

$$H_{dsDNA} = \frac{1}{2}\left[(1 - \Lambda(t))(\partial_t \phi(x,t))^2 + c_D^2(\phi(x,t)(\partial_x \phi(x,t))^2\right] + V_H(\phi(x,t))$$
$$c_D^2(\phi(x,t)) = c_0^2(1 + \rho \exp(-2\alpha\phi(x,t)))$$

where

$\Lambda(t) = \alpha^2 \sin(\omega_0 t)^2$

$\alpha = \sqrt{\frac{2\beta Q^2 \sigma^2}{m\omega_0^2}} < 1$

$cD(\phi)$ refers to the extension proposed by Dauxois.[100)]

It causes a stiffening of the backbone as the hydrogen bonds fluctuate. This stiffening reflects the stacking energy dependence of dsDNA. This extension was found to be crucial in understanding the thermal denaturation of dsDNA

It is important to note that the solvent serves to siphon off energy from the disturbance in a very sensitive way. Small changes in the coupling to the solvent bath of phonons affect dramatically the breather modes excited by the EM fields. Experiments where the coupling between the solvent and a DNA molecule is varied will be extremely useful in directing the future development of the understanding of EM effects on the dynamics of DNA.[14)]

The free energy needed to melt a GC base pair is generally accepted to be 3.5 kcal/mole and that for an AT base pair 1 kcal/mole. If inflow of this amount of energy occurred, the net energy requirements of transcription would easily be met. The reason to consider this form of energy transfer to the transcription complex is that we believe it would involve the nonlinear hydrogen-bond stretch (HBS) modes. The regime in which the bands of the torsional acoustic (TA) and hydrogen-bondstretch (HBS) modes of DNA interpenetrate each other has been considered by Golo.[16] He proposes a simple model accommodating the helix structure of DNA and, within its framework, to find a three-wave interaction between the TA and HBS modes. This phenomenon is useful for studying the action of microwave radiation on a DNA molecule. Thus, using Zhang's mechanism of the interaction between the system of electric dipoles of a DNA molecule and microwave radiation, he showed that the latter could bring about torsional vibrations that maintain HBS vibrations.

Microwave radiation would maintain the HBS modes and there is no need for long exposures of the sample to radiation. Golo[16] estimated for the pure experimental system, the critical power density, 100 mW/cm^2, which is by orders of magnitude larger than that officially prescribed, i.e., at 900 MHz 2W/kg corresponds to 4500 mW/m^2 or 0.45 mW/cm^2, and at > 2 GHz 10 W/kg corresponds to 10000 mW/m^2 or 1 mW/cm^2.[16] The question is, however, if the theoretically derived limit of 100 mW/cm^2 is valid for in vivo exposure conditions. Thus there is still much more research to be done before we might answer that question.

§10. Conclusion

The first living organisms arose on Earth when it had existed for 1.5 billion years. During the following 3 billion years, life on Earth was formed by, and existed in harmony, with the original physical forces such as gravitation, cosmic irradiation, atmospheric electric fields and the terrestrial magnetism and the cyclic celestial events. This was the world where evolution resulted in Homo sapiens, "the wise man". It took him 200 000 years to reach the level of knowledge where he could dramatically alter the physical forces on Earth. During the last century the levels of ELFs and MWs have been hugely increased in our habitat under the ionosphere.

Even if many studies have seen no effects of the EMFs upon biology, an abundance of scientific reports in respected journals have shown significant, though often weak, effects upon cells *in vitro*, in experimental animals and also in humans.

If the man made EMFs, such as those utilized in mobile communication, even at extremely low SAR values, causes the users' own albumin to leak out through the BBB, which is meant to protect the brain, also other unwanted and toxic molecules in the blood, may leak into the brain tissue. There they concentrate in, and damage, the neurones and glial cells of the brain according to our studies. It cannot be excluded that this, (especially after many years intense use) may promote the development of autoimmune and neuro-degenerative diseases!

It is our generation who invented the microwave emitters. We now have an imperative obligation to further investigate the links between EMF and biology in order to prevent the possible detrimental effects of the microwaves. The concept of solitons as active in membranes and RNA-transcription may be one key to open new paths in the search — a search which must be an imperative not only for researchers but also for states and organisations world-wide.

References

1) N. Cherry, Natural Hazards **26** (2002), 279.
2) L. G. Salford, A. Brun, J. Eberhardt, L. Malmgren and B. Persson, in *Interaction Mechanism of Low-Level Electromagnetic Fields in Living Systems*, ed. B. Nordén and C. Ramel (Oxford University Press, Oxford, 1992), p. 251.
3) L. G. Salford, A. Brun, K. Sturesson, J. Eberhardt and B. Persson, Microscopy Research and Technique **27** (1994), 535.
4) L. G. Salford, B. Persson and A. Brun, in *Non-Thermal effects of RF Electromagnetic Fields*, ed. J. H. Bernhardt, R. Matthes and M. H. Repacholi (International Commission on Non-Ionizing Radiation Protection, Munich, 1997), p. 131.
5) L. G. Salford, B. Persson, L. Malmgren and A. Brun, in *Téléphonie Mobile - Effets Potentiels sur la Santé des Ondes Électromagnétiques de Haute Fréquence*, ed. M. Pietteur (Embourg, Belgium, 2001), p. 141.
6) M. Peyrard and A. R. Bishop, Phys. Rev. Lett. **62** (1997), 2755.
7) L. G. Salford, A. E. Brun, J. L. Eberhardt, L. Malmgren and B. R. R. Persson, Environmental Health Perspectives **111** (2003), 881.
8) J. Eberhardt, B. R. R. Persson, L. Malmgren, A. Brun and L. G. Salford, "Blood-brain barrier permeability and nerve cell damage in the rat brain 14 and 28 days after exposure to microwaves from GSM mobile phones", (submitted manuscript).
9) H. Nittby, G. Grafström, D. P. Tian, L. Malmgren, A. Brun, B. R. R. Persson, L. G. Salford and J. Eberhardt, Bioelectromagnetics (2008a), published on line Dec. 2007.
10) I. Y. Belyaev, C. B. Koch, O. Terenius, K. Roxstrom-Lindquist, L. O. Malmgren, W. H. Sommer, L. G. Salford and B. R. Persson, Bioelectromagnetics **27** (2006), 295.
11) H. Nittby, M. Krogh, G. Grafström, H. Berlin, G. Rehn, J. Eberhardt, L. Malmgren, B. R. R. Persson, B. Widegren and L. G. Salford, "Exposure to global system for mobile communications at 1800 MHz significantly changes gene expression in rat hippocampus and cortex", (submitted manuscript).
12) R. Shivers, M. Kavaliers, G. Teskey, F. Prato and R. Pelletier, Neuroscience Lett. **76** (1987), 25.
13) C. L. M. Bauréus-Koch, M. Sommarin, B. R. R. Persson, L. G. Salford and J. L. Eberhardt, Bioelectromagnetics **24** (2003), 395.
14) S. M. Chitanvis, J. Polymer Science Part B-Polymer Physics **44** (2006), 2740.
15) G. S. Edwards, C. C. Davis, J. D. Saffer and M. Swicord, Phys. Rev. Lett. **53** (1984), 1284.
16) V. L. Golo, J. Exp. Theor. Phys. **101** (2005), 372.
17) E. W. Prohofsky, Bioelectromagnetics **25** (2004), 441.
18) C. T. Zhang, Phys. Rev. A **35** (1987), 886; Phys. Rev. A **40** (1989), 2148.
19) R. J. P. Williams, J. R. Soc. Interface **4** (2007), 1049.
20) M. Balser and C. Wagner, Nature **188** (1960), 638.
21) W. O. Schumann, Z. Naturforsch. **7a** (1952), 149.
22) P. V. Bliokh, A. P. Nicholaenko and Yu. Fillipov, in *IEE Electromagnetic Waves Series 8* (P. Peregrinus Ltd., Stevenage, 1980).
23) D. D. Sentman, Radio Science **22** (1987), 595.
24) D. D. Sentman, in *Handbook of Atmospheric Electrodynamics*, vol. I, ed. H. Volland (CRC Press, Boca Raton, 1995).
25) R. E. Holzer and D. E. Deal, Nature **177** (1956), 536.
26) T. E. Dennis, M. J. Rayner and M. M. Walker, Proc. Biol. Sci. **274** (2007), 1153.
27) P. Galland and A. Pazur, J. Plant Res. **118** (2005), 371.
28) F. Halberg, G. Cornélissen, P. Regal, K. Otsuka, Z. Wang, G. S. Katinas, J. Siegelova, P. Homolka, P. Prikryl, S. M. Chibisov, D. C. Holley, H. W. Wendt, C. Bingham, S. L. Palm, R. P. Sonkowsky, R. B. Sothern, E. Pales, M. Mikulecky, R. Tarquini, F. Perfetto, R. Salti, C. Maggioni, R. Jozsa, A. A. Konradov, E. V. Kharlitskaya, M. Revillam, C. Wan, M. Herold, E. V. Syutkina, A. V. Masalov, P. Faraone, R. B. Singh, R. K. Singh, A. Kumar, R. Singhs, S. Sundaram, T. Sarabandi, G. Pantaleoni, Y. Watanabe, Y. Kumagai, D. Gubin, K. Uezono, A. Olah, K. Borer, E. A. Kanabrockia, S. Bathina, E. Haus, D. Hillman, O. Schwartzkopff, E. E. Bakken and M. Zeman, Biomed Pharmacother. **58** (2004), Suppl 1, S150.

29) P. Volpe, Photochem. Photobiol. Sci. **2** (2003), 637.
30) F. I. Komarov, V. N. Oraevski ĭ, Iu. P. Sizov, L. B. Tsirul'nik, Kh. D. Kanonidi, I. B. Ushakov, P. M. Shalimov, M. V. Kimlyk and D. V. Glukhov, Heliogeophysical Factors and Aviation Accidents **43** (1998), 742.
31) G. Villoresi, T. K. Breus, L. I. Dorman, N. Iuchi and S. I. Rapoport, Biofizika **40** (1995), 983, (Article in Russian).
32) R. Coray, P. Krähenbühl, M. Reiderer, D. Stoll and G. Neubauer, *Immissionen in Salzburg. Bundesamt für Metrologie und Akkreditierung* (Lindenweg 50, CH-3003 Bern-Wabern, 2002).
33) G. Hyland, Lancet **356** (2000), 1833.
34) L. G. Salford, H. Nittby, A. Brun, G. Grafström, J. L. Eberhardt, L. Malmgren and B. R. R. Persson, The Environmentalist **27** (2007), 493.
35) H. Nittby, G. Grafström, J. L. Eberhardt, L. Malmgren, A. Brun, B. R. R. Persson and L. G. Salford, Electromagnetic Biology and Medicine (2008b). Article accepted for publication.
36) M. Kundi, K. Mild, L. Hardell and M. O. Mattsson, J. Toxicol. Environ. Health B: Crit. Rev. **7** (2004), 351.
37) L. Hardell, M. Carlberg and K. H. Mild, Environmental Research **100** (2006a), 232.
38) F. Vecchio, C. Babiloni, F. Ferreri, G. Curcio, R. Fini, C. Del Percio and P. M. Rossini, Eur. J. Neuroscience **25** (2007), 1908.
39) L. G. Salford, A. Brun, J. L. Eberhardt and B. R. R. Persson, Bioelectrochem. Bioenerg. **30** (1993), 293.
40) W. E. Thomas, Brain Res. Rev. **31** (1999), 42.
41) W. H. Oldendorf, M. E. Cornford and W. J. Brown, Ann. Neurol. **1** (1977), 409.
42) J. F. Ghersi-Egea, A. Minn and G. Siest, Life Sciences **42** (1988), 2515.
43) T. E. O. Sokrab, B. B. Johansson, H. Kalimo and Y. Olsson, Acta Neuropathology **75** (1988), 557.
44) W. R. Adey, in *Interaction Mechanism of Low-Level Electromagnetic Fields in Living Systems*, ed. B. Nordén and C. Ramel (Oxford University Press, Oxford, 1992), p. 47.
45) J. Van Hese, L. Martens, D. De Zutter, C. De Wagter, L. Malmgren, B. R. R. Persson and L. G. Salford, IEEE Transactions on Electromagnetic Compatibility **34** (1991), 292.
46) L. Martens, J. Van Hese, D. De Sutter, C. De Wagter, L. O. G. Malmgren, B. R. R. Persson and L. G. Salford, Bioelectrochem. Bioenerg. **30** (1993), 73.
47) R. B. Stagg, L. H. Havel3rd, K. Pastorian, C. Cain, W. R. Adey and C. V. Byus, Radiat. Res. **155** (2001), 584.
48) K. Fritze, C. Sommer, B. Schmitz, G. Mies, K.-A. Hossmann, M. Kiessling and C. Wiessner, Acta Neuropathologica **94** (1997), 465.
49) F. Töre, P. E. Dulou, E. Haro, B. Veyret and P. Aubineau, *Proc. the 5th International congress of the EBEA, Helsinki, Finland* (2001), p. 43; *Proc. the 24th annual meeting of the BEMS* (2002), p. 61.
50) D. Leszczynski, S. Joenväärä, J. Reivinen and R. Kuokka, Differentiation **70** (2002), 120.
51) R. Nylund and D. Leszcynski, Proteomics **4** (2004), 1359.
52) K. Fredriksson, H. Kalimo, C. Nordborg, B. B. Johansson and Y. Olsson, Acta Neuropathologica (Berl) **76** (1988), 227.
53) T. S. Salahuddin, H. Kalimo, B. B. Johansson and Y. Olsson, Acta Neuropathologica (Berl) **76** (1988), 1.
54) A. Mihày and B. Bozo'ky, Acta Neuropathology **127** (1984a), 251; Acta Neuropathology **65** (1984b), 471.
55) T. E. Sokrab, H. Kalimo and B. B. Johansson, Epilepsia **31** (1990), 1.
56) S. Eimerl and M. Schramm, Neuroscience Lett. **130** (1991), 125.
57) B. Hassel, E. G. Iversen and F. Fonnum, Neuroscience Lett. **167** (1994), 29.
58) A. Ilhan, A. Gurel, F. Armuten, S. Kamisifi, M. Iraz, O. Akyol and S. Ozen, Clinica Chimica Acta **340** (2004), 153.
59) S. Lőnn, A. Ahlbom, P. Hall and M. Feychting, Epidemiology **15** (2004), 653.
60) L. Hardell, M. Carlberg and K. H. Mild, Int. Arch. Occup. Environ. Health **79** (2006b), 630.
61) J. P. Blanchard and C. F. Blackman, Bioelectromagnetics **15** (1994), 217.
62) G. E. Kass and S. Orrenius, Environ. Health Perspect **107** (1999) (Suppl. 1), 25.

63) C. Fanelli, S. Coppola, R. Barone, C. Colussi, G. Gualandi, P. Volpe and L. Ghibelli, FASEB J. **1** (1999), 95.
64) V. V. Lednev, Bioelectromagnetics **12** (1991), 71.
65) V. V. Lednev, Biophysics **41** (1996), 224.
66) C. F. Blackman, J. P. Blanchard, S. G. Benane and D. E. House, Bioelectromagnetics **15** (1994), 239.
67) R. K. Adair, Bioelectromagnetics **13** (1992), 231.
68) V. V. Lednev, *Electricity and Magnetism in Biology and Medicine* (1993), p. 550.
69) W. J. Sun, Y. N. Yu, H. Chiang, Y. D. Fu and D. Q. Lu, Electro- and Magnetobiology **20** (2001a), 207.
70) W. J. Sun, H. Chiang, Y. D. Fu, Y. N. Yu, H. Y. Xie and D. Q. Lu, Electro- and Magnetobiology **20** (2001b), 415.
71) W. J. Sun, Y. N. Yu, H. Chiang, Y. D. Fu, H. Y. Xie and D. Q. Lu, Electro- and Magnetobiology **21** (2002a), 97.
72) W. J. Sun, H. Chiang, Y. Fu, D. Lu and Z. Xu, Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi **20** (2002b), 246, (Article in Chinese).
73) W. R. Adey, Prog. Clin. Biol. Res. **257** (1988), 81.
74) J. S. Russell, *Report on Waves, 14th meeting of the British Association for the Advancement of Science* (BAAS, 1844).
75) A. S. Davydov and N. I. Kislukha, Phys. Status Solidi B **59** (1973), 465; Phys. Status Solidi B **75** (1976), 735.
76) A. S. Davydov, Studia Biophysica **62** (1977), 1.
77) H. Fröhlich, Int. J. Quantum Chem. **23** (1983), 1589.
78) S. R. Hameroff and R. C. Watt, J. Theor. Biology **98** (1982), 549.
79) E. Del Guidice, S. Doglia, M. Milani and G. Vitiello, Nucl. Phys. B **275** (1986), 185.
80) L. A. Amos and A. Klug, J. Cell Science **14** (1974), 523.
81) E. Abdalla, B. Maroufi, B. C. Melgar and M. B. Sedra, Physica A **301** (2001), 169.
82) L. A. Amos and D. Schlieper, *Microtubules and maps. Fibrous Proteins: Muscle and Molecular Motors* (Elsevier Academic Press Inc., San Diego, 2005).
83) T. Heimburg and A. D. Jackson, Proc. Natl. Acad. Sci. USA **102** (2005), 9750.
84) T. Heimburg and A. D. Jackson, Biophysical J. **92** (2007), 3159.
85) C. Del Seppiaa, S. Ghionea, P. Luschib, K. P. Ossenkopp, E. Choleris and M. Kavaliers, Neuroscience and Biobehavioral Reviews **31** (2007), 619.
86) N. M. Shupak, F. S. Prato and A. W. Thomas, Neuroscience Lett. **363** (2004), 157.
87) L. G. Salford, M. Krogh, G. Grafstöm, H. Nittby, G. Rehn, H. Berlin, J. L. Eberhardt, L. Malmgren, R. B. R. Persson and B. Widegren, *Abstract for the 4th International Workshop: "Biological Effects of Electromagnetic Fields", 16–20 Oct. 2006, Crete, Greece.*
88) S. Lee, D. Johnson, K. Dunban, H. Dong, X. Ge, Y. C. Kim, C. Wing, N. Jayathilaka, N. Emmanuela, C. Q. Zhou, H. L. Gerber, C. C. Tseng and S. M. Wang, FEBS Lett. **579** (2005), 4829.
89) S. Pacini, M. Ruggiero, I. Sardi, S. Aterini, F. Gulisano and M. Fulisano, Oncol. Res. **13** (2002), 19.
90) D. Remondini, R. Nylund, J. Reivinen, F. Poulletier de Gannes, B. Veyret, I. Lagroye, E. Haro, M. A. Trillo, M. Capri, C. Franceschi, K. Schlatterer, R. Gminski, R. Fitzner, R. Tauber, J. Schuderer, N. Kuster, D. Leszczynski, F. Bersani and C. Maercker, Proteomics **6** (2006), 4745.
91) R. Zhao, S. Z. Zhang, G. D. Yao, D. Q. Lu, J. Huai and Z. P. Xu, Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi **24** (2006), 222, (Article in Chinese).
92) W. Saenger, *Principles of nucleid acid structure* (Springer, Berlin, 1988).
93) S. W. Englander, N. R. Kallenbach, A. J. Heeger, J. A. Krumhansl and S. Litwin, Proc. Natl. Acad. Sci. USA **77** (1980), 7222.
94) R. V. Polozov and L. V. Yakushevich, J. Theor. Biology **130** (1988), 423.
95) E. W. Prohofsky, Phys. Rev. A **38** (1988), 1538.
96) G. F. Zhou and C. T. Zhang, Physica Scripta **43** (1991), 347.
97) G. Gaeta, J. Biol. Phys. **24** (1999), 81.
98) L. V. Yakushevich, Quarterly Reviews of Biophysics **26** (1993), 201; Physica D **79** (1994), 77.
99) T. Dauxois and M. Peyrad, Phys. Rev. Lett. **70** (1993), 3935.

100) T. Dauxois, M. Peyrad and A. R. Bishop, Phys. Rev. E **47** (1993a), 684.
101) T. Dauxois, M. Peyrad and P. A. Bishop, Phys. Rev. E **47** (1993b), R44.
102) T. Dauxois, M. Peyrad and C. R. Willis, Physica D **57** (1992), 267.
103) M. Peyrard, T. Dauxois, H. Hoyet and C. R. Willis, Physica D **68** (1993), 104.
104) M. Peyrard and A. P. Bishop, Phys. Rev. Lett. **62** (1989), 2755.
105) N. Theodorakopoulos, T. Dauxois and M. Peyrard, Phys. Rev. Lett. **85** (2000), 6.