BIOELECTRODYNAMICS AND BIOCOMMUNICATION

Editors
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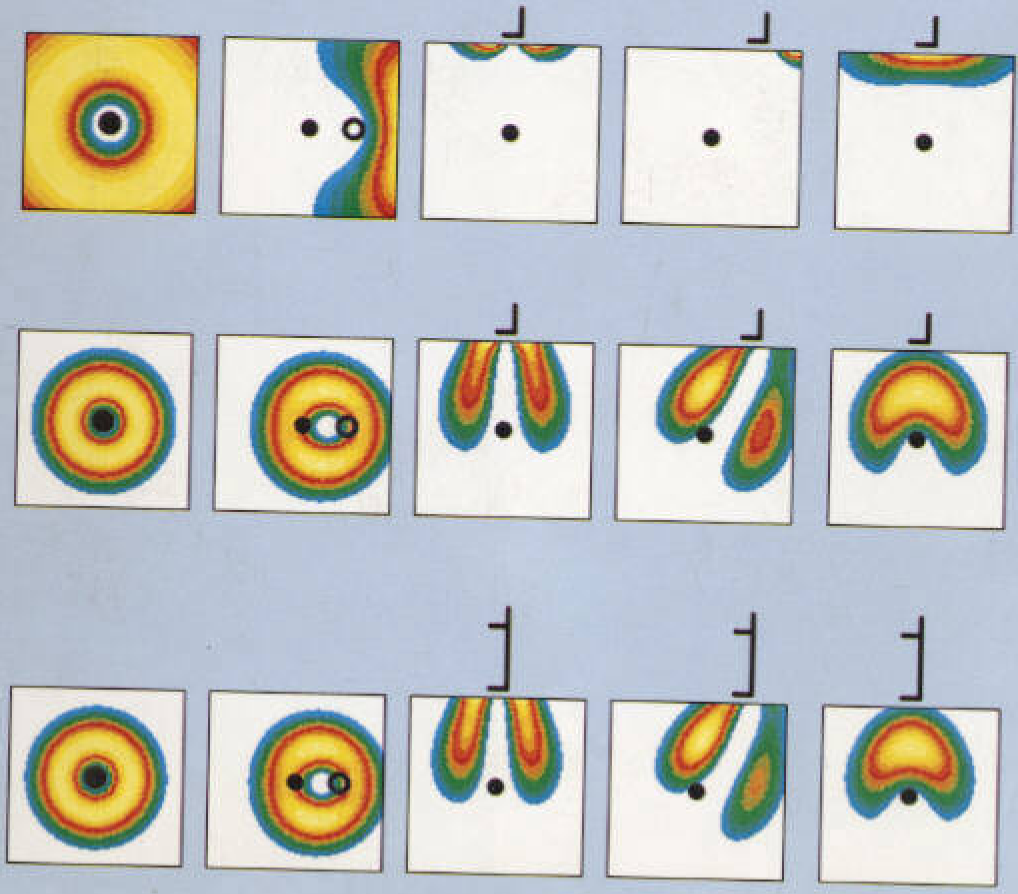

World Scientific

Chapter 3

Biological Effects of Weak Electromagnetic Fields

Cyril W. Smith

3.1 Introduction

Textbooks of electrophysiology[1] make the explicit or implicit assumption that no frequencies greater than the highest components of the cellular action-potential waveform (10 kHz) are of biological significance. If this were indeed the case, this Chapter would finish here. Twenty years ago, Frey and Bowers[2] realised that electromagnetic spectrum allocations and health hazards were matters of public concern as the availability of inexpensive solid-state power sources engendered new microwave applications. Relatively large numbers of microwave systems might then come under the unsupervised control of private individuals or organizations. Safety standards established when microwave systems were uncommon and when the average citizen was unlikely to be irradiated by a microwave beam could become inadequate if microwave beams were to be emitted from cars, as well as traffic signals, telecommunications towers and airport radars.

As a measure of the magnitude of the problem, they considered the case of radar-equipped cars emitting 50 mW within a beam of 2° producing a power density of 100 μ W/cm^2 at a distance of 5 m. Although the beam might be scanned and the car in motion, thereby reducing greatly the radiation incident on any given individual, that same person could be subject to simultaneous irradiation from many cars similarly equipped. Such power levels would be inconsequential according to the current U.S. safety standards but, would be significant relative to standards in Eastern Europe.

The microwave region of the electromagnetic spectrum formally begins at 300 MHz (free-space wavelength 1 m), but in general, electromagnetic radiation begins to be appreciably absorbed by humans at frequencies greater than about 15 MHz. The eye lens and the testes in particular have limited ability to dissipate heat and hence are especially vulnerable to microwave irradiation. The threshold power densities required to produce thermal effects in animals and humans are well-known. Non-thermal effects were not included in the considerations when the U.S. radiation safety level was set at an average of 10 mW/cm² (100 W/m²) for long term exposures. However, non-thermal effects were apparently influential in the establishment of the maximum standard of 10 μW/cm² (100 mW/m²) in the former Soviet Union[3].

The U.S. radiation safety standard was confirmed by their Tri-Service Program of research on biomedical aspects of microwave radiation[4], although some workers felt this research was "largely irrelevant"[5] to the subject of non-thermal non-ionizing radiation because it rejected the East European data and did not adequately consider the possibility of low-power radiation hazards.

"Incomplete understanding of the effects of microwave radiation on biological systems, combined perhaps with personal and institutional prejudice, has led to the current anomalous situation in which different countries have adopted safety standards that differ by several orders of magnitude"[2].

When in 1989, Simon Best and I wrote *Electromagnetic Man*[6], the situation was much the same. We noted that,

"The general public - particularly in America - got their first real idea of the potential military applications of electromagnetic fields in 1976, when the United States claimed that their Embassy in Moscow was being irradiated with microwave beams by the Russians...However, what was perhaps equally if not more disturbing was the eventual disclosure that the irradiation had been happening since 1953 and that the State Department and five previous governments had known about it since it started......several diplomats developed leukaemia; two of the U.S. Ambassadors serving during the period (1953-77) died of cancer and the third died in 1986 of leukaemia which was first discovered in 1975."

Recently, it was suggested to me while I was on a visit to the Commonwealth of Independent States (C.I.S.), that this episode represented no great malevolent plot against the U.S.A. but, rather, was the result of incompetence in the use of microwaves to recharge the batteries of Soviet listening devices planted within the U.S. Moscow Embassy.

By the mid-1970's it was already apparent to many that microwave radiation could be biologically harmful. Dr. Milton Zaret, of Scarsdale, New York, had identified a particular form of posterior subcapsular cataract in the eye as being the signature of radiofrequency and microwave exposure; this became apparent while he was carrying out a health study of radar maintenance men for the U.S. Air Force in 1964[7].

In our Conclusion to *Electromagnetic Man*[6], we posed the question, "What level of electromagnetic radiation is safe?" and continued:

"The present U.S. and U.K. guideline of 100 W/m² (10 mW/cm²) as the upper limiting exposure to microwave radiation represents a fraction of the power density

of tropical sunlight. But it is only reasonable from the point of view of avoiding widespread thermal injury, and represents enforceable legislation. The level of non-ionising radiation which will produce no effects of any kind in any person could not be lived with from an engineering stand-point in view of the expectations society has from modern electronics. It is even below the level of non-ionising radiation which people themselves emit and which can affect other hypersensitive persons in their vicinity."

3.2 Review of Literature

In his introduction to *Interactions between Electromagnetic Fields and Cells*[8], Schwan pointed out that in connection with microwave radiation:

"The medically oriented work before the second world war led almost immediately to a split between two different schools of thought. One had it that whatever therapeutic or other effect was observed was caused by a noticiable temperature increase and that, therefore, the results observed were due to heat and not caused by electrical fields per se. The other school of thought believed that direct field interactions termed nonthermal or athermal are important. This controversy led to some hundred publications of variable quality. The debate was never settled and these papers are largely forgotten."

The radar developments during the second world war were rapidly applied to therapeutic techniques from which the interest in the dielectric properties of biological materials had its resurgence, this because even by the late 1920's, Fricke, at the Cleveland Clinic, U.S.A., had investigated the dielectric properties of cells and found that the capacitance of tumour tissue differed from that of normal tissue, a fact which has yet to penetrate conventional medical awareness.

Dielectric properties of materials relate to their interaction with electric fields (steady and alternating), as for example when they are placed between the plates of a capacitor. The dielectric properties arise from the patterns and motions of electric charges associated with atoms and their chemical bonds. At very high frequencies, the dielectric properties merge with those of optical refraction.

The dielectric properties of biological materials, fluids and water have been thoroughly measured over a wide frequency range[9,10,11]. They do not show indications of sharp resonance phenomena. The classical Debye resonance is broad and extends over several decades in frequency[9], not characteristic of the observed non-thermal biological responses to microwaves and millimeter waves which will be discussed later.

Until recently, it was very necessary to look at the 'Acknowledgments' section of publications on the effects of non-ionizing radiation to see who had funded the work, in order to be able to assess its significance. Increased openess with regard to the electrical environment came partly as the result of the judicially instituted 'New York Power Lines Project'[12] and partly as a result of the recession whereby laboratories which had ceased to be funded by vested interests chiefly concerned with minimizing the risk of legal action being taken against them, were no longer inhibited regarding the publication of "inconvenient" results. Becker[13] and Brodeur[14] discuss the background to this manipulation of information and research projects.

The best sources to scan for updating information on the biomedical effects of non-ionizing radiation are to be found in the three newsletters: *Bioelectromagnetics Society Newsletter*[15], past issues of which contain many articles relevant to microwave effects in biological systems[16]; *Electromagnetics News*[17] and *Microwave News*[18] both of which have published various articles on the effects of non-ionizing radiation as well as reports, updates and correspondence relating to the electromagnetic environment, current research studies and safety standards in different countries.

The specialist journals for this area include: *Bioelectromagnetics*, and *Electro- and Magnetobiology* (formerly *Journal of Bioelectricity*).

The Office of Naval Research, U.S.A., has, for many years, published a quarterly digest of current literature on the "Biological Effects of Nonionizing Electromagnetic Radiation". This has now resumed publication as a scientific abstracting journal under the name, *BENER Digest Update*[19] There is also an electronically searchable extended set of abstracts *EMF Database* available. Many of the leading scientific and engineering journals carry the occasional article of relevance.

There are also a whole series of conferences whose proceedings represent valuable sources of information. These include: The Annual Conferences of the Institute of Electrical and Electronics Engineers (IEEE) Engineering in Medicine and Biology Society (EMBS)[20] ; the various meetings of The Bioelectromagnetics Society (BEMS)[15], the European Bioelectromagnetics Association (EBEA)[21] and the Bioelectrical Repair and Growth Society (BRAGS)[22].

For those who want an introduction to the biological effects of microwaves and millimeter waves rather than to be updated in the subject, I offer the following summary.

At a lecture given in the 1990 General Assembly of the International Union of Radio Science (URSI) held in Prague[23], Ross Adey concluded that,

"It is no longer a matter of speculation that biomolecular systems are responsive to low level, low frequency electromagnetic fields. Not only is tissue heating not the basis of these interactions, but the many instances of responses windowed with respect to field, frequency and intensity set a rubric for their consideration in physical mechanisms involving long range ordering at the atomic level".

"From theoretical consideration of the collisional basis of molecular interactions with microwave and far-infrared fields, there is no compelling evidence for resonant absorption in ordinary molecular fluids below 3,000 GHz. This model is supported

by the virtual absence of experimental evidence for interaction with CW fields at frequencies below the GHz range other than by heating. On the other hand, RF fields that are sinusoidally amplitude-modulated at ELF frequencies produce a wide range of biological interactions...."

Among the interactions listed were, the entrainment of brain rhythms and the conditioning of brain responses to imposed fields, and the modulation of brain states and behavioral states[24]; strong effects on cell membrane functions including the modulation of intercellular communication through gap-junction mechanisms[25]; the reduction of cell mediated cytolytic immune responses[26]; and the modulation of intracellular enzymes that are markers of signals arising at cell membranes which are then coupled intracellularly.

For more than two decades, Adey and his co-workers have been studying the effects of ELF electric fields and amplitude modulated RF and microwave fields on cerebral tissue Ca^{2+} efflux[23]. They found that the maximum effect occurred for the ELF or modulation frequency of 16 Hz, but the effects exhibited narrow windows in frequency and amplitude and were biphasic in respect of applied electric field gradients, differing by a factor of 10^6. Adey discussed these effects in terms of dissipative processes and cooperative phenomena in cell membranes containing receptor proteins.

With the discovery of intracellular enzymes that respond to signals initiated at cell membranes as a response to electromagnetic field exposure, Adey and his co-workers[23] also found intramembranous particles inserted into the lipid bilayer membrane. Their outer tips are negatively charged glycoprotein strands which attract calcium and hydrogen ions and form receptor sites for chemical stimulation of the molecules. These form a calcium-mediated direct path for inwardly directed biosignals between the cell surface and intracellular enzymes and organelles. Again there are windows in frequency and amplitude as well as differing sensitivities for various cell functions (see Tsong and Gross, this volume). The presence of Ca^{2+} ions is essential for microwave effects on the binding of a ligand to β-adrenergic receptors of rat erythrocyte membranes.

The effects of low frequency modulation on the microwave carrier represent a further complication to the assessment of microwave and millimeter wave effects on living systems. It is now possible to buy microwave oscillators at frequencies going above 100 GHz, well into the millimeter wave region, which are coherent to a fraction of a Hertz. However, oscillators with this coherence were not in general used for most of the experiments reported in the literature. One must presume that in the majority of experiments, frequency components which included the power supply frequency and its harmonics were present as amplitude or frequency modulation of the microwaves. Such frequencies are within that band of frequencies extending from below 1 Hz to a few hundred Hz that are known to be particularly effective biologically and which include the all permeating Schumann Bands of ionospheric radiation within which all evolution has taken place.

Blackman[27] has reviewed the highly reproducible biological influences of low frequency sinusoidal electromagnetic signals, both alone and superimposed on RF carrier waves. The association of calcium ions with brain tissue was selected as the biochemical marker because calcium-ion efflux from chick brain tissue *in vitro* occurs at non-thermal levels. Combined with the results of studies of brain biochemistry and EEG in animals, synaptosomes and human neuroblastoma cells in culture, this provides evidence that CNS tissue from several species, including humans, are affected by low intensity RF-fields modulated by specific low frequencies. The biological systems which have so far been investigated are quite diverse, nevertheless, the consistent features are the specificity of the ELF and the involvement of the geomagnetic field.

In 1968, Webb first reported the frequency dependent inhibition of bacterial growth by 136 GHz millimeter radiation[28] and, in 1974, Devyatkov and co-workers[29] reported the existence of frequency-dependent low-intensity microwave effects in biological systems over the frequency range 39 GHz to 60 GHz.

Devyatkov's report contained results of experiments by Sevastyanova and Villenskaya showing that millimeter waves at certain frequencies around 42 GHz and at intensities above a certain threshold, exerted a protective effect on mouse bone marrow cells pre-exposed to X-radiation (see Wu, this volume). Subsequently this work was repeated with better frequency resolution and showed indications of a 60 MHz periodicity within the band of millimeter wave frequencies that were effective. Another study, this time investigating the decrease in synthesis of β-lactamase in penicillin-resistant strains of *E. coli* and *Staphylococcus aureus*, showed frequency selective effects in *S. aureus* at frequencies which did not have any effect on the *E. coli*.

Grundler *et al*[30,31,32] have described experiments which showed a resonant response in the growth rate of yeast cells irradiated with millimeter waves, they used the region of 42 GHz as suggested by the work reported by Devyatkov[29] on *Rhodotorula ruba*. They found an exponential growth rate reproducible within $\pm 4\%$ and that this could be influenced by continuous millimeter wave fields corresponding to a power flux density of a few mW/cm^2. There was a fine frequency structure which had a periodicity of 8 MHz. Initially, the cell concentrations were measured by photometry, which only gave the results of the average reaction to millimeter radiation of 10^6 cells in a stirred suspension.

To overcome the disadvantages inherent in photometry, Grundler and co-workers[31] developed a method for studying the kinetics of single cell growth during microwave irradiation. With this, they clearly demonstrated a direct microwave influence. In comparison with the controls, there were significant radiation induced asymmetries and double peaks in the cell cycle time distributions for both the first and second cell division cycles indicating the presence of subgroups of cells. In the case of the double peaked distributions, one peak remained close to the control value while the other showed a displacement due to the irradiation. Even though all the cells were contained in a monolayer within an area of only 0.2 mm^2, the effect of the microwaves was to produce a sub-culture of cells. These microwave frequencies were stabilised to ± 1 MHz of the 42 GHz used. The results again showed a similar resonant frequency dependence with the same resonance width of 8 MHz to that observed in the photometric measurements.

Experiments at 84 GHz — double the previous frequency — also gave significant radiation effects, although these were mainly during the second cell division cycle. By means of a computer controlled cell counter, tests could be made over one complete cell cycle, a lower temperature (25°C) was used to extend the cell cycle to 5 hours. These results showed that the microwave influence is restricted to the G_1-phase of the cell cycle at the frequency used.

Cycles of cell division are divided into four phases.The first phase (G_1)and the third phase (G_2) are periods of cell nuclear activity during which most of the significant metabolic activities occur. The DNA replication takes place during the second phase (the so-called S-phase, or synthesis period). By the time that the brief fourth mitotic (or M-phase) begins, the chromosomes will have completed replication. The first signs of mitosis are condensations of chromosomes (prophase), which then move apart towards the cell equatorial plane with a microtubule spindle between them (prometaphase), they align at opposite ends of the cell (metaphase), the chromatids separate to become independent chromasomes (anaphase), after which nuclear reorganization takes place and nuclear membranes form (telophase). If cell division (cytokinesis) is to occur this may or may not synchronise with mitosis.

Webb[33] has investigated the effects of millimeter waves for over 25 years. In experiments from 59 GHz - 143 GHz using cell cultures of the bacterium *E. coli*, he found effects on the growth rate, and on DNA and RNA and protein synthesis, which had sharp frequency windows and as well as windows within the cell division cycle. Two sets of sub-frequencies were effective, one set went in integer multiples of 7 GHz, the other in integer multiples of 5 GHz. Raman spectroscopy revealed no resonant activity in the nutrients or in resting cells, but sharp peaks were observed when the cells were activated by a nutrient containing an oxidizable carbon energy source (see Wu, this volume).

Resonant microwave absorption in solutions of *E. coli* DNA was first observed by Edwards, Swicord and co-workers[23,34]. The DNA was randomly nicked by low concentrations of the endonuclease DNase. It was supposed that this produced a dynamic length distribution whose mean length decreased with time. Enhanced microwave absorption occurred as the sample length distribution changed to correspond to the region giving significant absorption in the experimental frequency range, which extended from 0.4 to 12 GHz. The frequency f of the observed resonances and the DNA length l as determined by the number of base pairs, were related to the acoustic velocity v by

$$v_{circular} = (n+1)fl$$

or

$$v_{linear} = \left(n + \frac{1}{2}\right) fl$$

where the subscript distinguishes linear and circular DNA molecules, and $n = 0, 1, 2 \ldots$

These resonances appear to be sharper than the frequency stability of the experiments since the standard deviations at the peaks are seen to be generally worse than at the skirts of the resonances[34].

With these as with many other bioelectromagnetics experiments, replication in other laboratories did not come easily, sometimes it did not come at all. It must be realised that in such work, one is dealing with a multi-variable experimental system involving a living system. Pickard[16] has listed criteria for the reproducibility of bioelectromagnetics experiments[36]. Marino[35] has made some pertinent remarks on, "Negative studies and common sense" in an editorial of this title. He points out that, "The careful student of bioelectricity quickly learns to separate poison-pill experiments and sophistry from facts and rational analysis, and to determine which individuals and groups are truly interested in building bioelectricity into a useful and important science, and which are interested in burying the subject under a mountain of innuendo, doubt and disdain. The bad news is that judges and other generalist laymen, unfamiliar with the concept of the null hypothesis, may be susceptible to the Siren call of the negative study."

The scanning-tunnelling-microscope (STM) has been applied to the visualization of biological materials[37]. Recently, Michel *et al* at I.B.M., Zurich, have devised a scanning surface harmonic microscope which is capable of operation at microwave frequencies[38,39]. It essentially consists of a conventional STM inside a tuneable microwave resonator positioned so that the microwave electric field at the tip is maximized and normal to the sample surface. The resonant cavity is tuned to a harmonic of the applied fundamental frequency. Non-linearities in the electron movement on the surface generate harmonics in the resonator which are detected by a spectrum analyser and fed-back to the tip-to-surface spacing control servo. The resulting surface images contain contrast related to local changes in the non-linearity of electron movement in the sample.

The operation of the scanning tunnelling microscope at microwave frequencies permits the study of surface processes at frequencies up to about 10 GHz. The use of third-harmonic imaging, which is possible due to the non-linearity induced in the surface electrons, avoids the ubiquitous problem of tip contact when there are thin insulating layers on the sample surface. Promising areas of application include the identification and properties of molecular absorbates with resolutions of 0.3nm, self-assembled monolayers, single organic molecules, biological macromolecules and biological membranes.

3.3 Characteristic Response to Microwaves and Millimeter Waves

The response to microwave irradiation which is common to all biological systems, alive and dead, and to biomaterials and water, is the microwave heating effect. The initial bioengineering work on this came largely from Schwan's laboratory[8] at the University of Pennsylvania. One result of which was the invention of the microwave cooker for preparing food in submarines. The penetration depth of microwaves into tissues, the reflection effects at interfaces, and the specific absorption rate (SAR) in skin, fat and muscle were all evaluated for a range of frequencies. When the organism, organ or biostructure is a half-wavelength in size (for humans that is in the range 30-300 MHz or just below the microwave region), there is resonance absorption and the absorbed energy is a maximum. From 300 MHz to 3 GHz, there can be focussing of the microwaves by curved surfaces such as the bone of the skull; this can lead to local hot-spots. Beyond 3 GHz, the penetration depth of the radiation decreases and surface heating effects predominate and resemble those of infrared or sunlight. In the frequency range 500 MHz - 2 GHz, an incident energy flux density of 10 mW/cm^2 (100 W/m^2) will produce an average temperature rise of about 0.5°C in the human body.

There is a fundamental relation between the incident power density of electromagnetic radiation and the electric and magnetic field components of the radiation. There is a generalised form of Ohm's Law relating the electric field $E(V/m)$ to the magnetic field $H(A/m)$ through the characteristic impedance Z (ohms) of the medium within which the radiation propagates. This is valid so long as measurements are made far enough away (usually the order of a wavelength) from the antenna or radiation source, thus:

$$E = H.Z$$

or, in terms of power density W (Watts/m^2)

$$W = E^2/Z = H^2.Z$$

In free space, the characteristic impedance has a fundamental value which is approximately Z = 377 ohms. The various microwave exposure limit tables cited by Grandolfo[40] have been rounded off and implicitly assume values for Z in the range 372 - 400 ohms.

Hence, an incident power density of 100 W/m^2 corresponds to an electric field $E =$ 194 V/m or a magnetic field $H = 0.5$ A/m in free-space.

The magnetic flux density B is related to H by

$$B = \mu_o H$$

where μ_o is the permittivity of free space and has the value 1.26 x 10^{-6} H/m. Hence 100W/m^2 corresponds to a $B = 0.65\mu$T. This would be superimposed on a static geomagnetic field of about 50μT.

Within water or a biological fluid, the effective values of permittivity must be taken into account and the calculations become more complicated. The magnetic permeability in bio-materials is effectively that for free-space. Hasted[9] gives the dielectric parameters for water up to optical frequencies. For biological materials, data can be found in books by Hasted[9], Pethig[10] and Grant *et al*[11]. However, if one is dealing with a coherent system, as is very likely the case, then the interaction of the incoming radiation will not be with individual molecules, but with domains of coherence as considered by Del Guidice *et al*[41]. The result is that the velocity of propagation in the coherent medium may fall from the 300 Mm/s of free-space value to as little as 1-10 m/s.

Other possible mechanisms of interactions between microwaves and biological systems include[42] the effect of electric fields on chemical equilibrium, chemical rate constants and conformational transformations; interaction-forces between microscopic particles in an external electric field leading to the formation of pearl-chains; torque forces inducing cell rotation; effects on ligand-binding in the cell membrane.

The absorbed microwave energy also gives induced conduction currents and their associated magnetic fields in irradiated tissues. These can affect ion motion and membrane potentials. Non-linearities of cells and tissues may rectify alternating currents to give D.C. which has ion-transport properties and can lead to electrolysis.

However, all these phenomena are within the realms of classical physics. The real issue is whether living systems are completely described by classical physics, or whether quantum physics is needed in addition. This boundary is crossed as soon as energy gap phenomena become involved. Pethig observed many years ago[43] that since the energy gap of a protein is of the order of 5 eV, and all the redox reactions going on in the human body represent an electric current of 200A, this corresponds to a power of 1 kW, of the correct order for the metabolic rate.

People have repeatedly reported being able to 'hear' the presence of a microwave beam[81,82], such as from a radar transmitter. This was finally tracked down to a thermal effect mediated by electromechanical interaction distal to the cochlea[44]. The threshold for a response from single auditory neurons in the cat to pulsed microwave radiation is as low as 4 μJ/g per pulse. Although this is regarded as a thermal effect, it corresponds to about 3 phonons per pulse of microwaves, emphasising that the sensitivity of the ear is as close to the phonon threshold as the eye is to the photon threshold.

One biological effect which does involve energy levels is magnetic resonance (NMR). The nuclear magnetic moment, even in a strong magnetic field, does not give a resonance up into the microwave region (e.g. proton-NMR = 42.6 MHz/Tesla), but the electron has its resonance at 28 GHz/Tesla and this is applied to electron spin resonance (ESR) techniques which are important for the detection of free radicals[45].

In my laboratory, we have shown that microwaves and radiofrequencies modulated at the particular frequency which satisfies the proton-NMR condition in the geomagnetic field (approx. 2 kHz) are particularly efficient in the production of cataracts in bovine eye lenses *in vitro*[46].

These hazardous conditions could arise in a subject moving routinely about in the non-uniform steady magnetic field of a typical laboratory in the presence of suitably modulated microwaves. These NMR-resonances are so sharp (ppm) that it is not practicable to set the frequency of an ordinary oscillator to obtain NMR conditions given the nominal value of the magnetic field. The resonance condition is realised by sweeping slowly through the appropriate frequency or magnetic field holding the other parameter constant. The relaxation time for NMR in biological tissues is in the range 0.5-3 seconds.

In the early literature on biological effects of microwaves, there are cases where reported effects increased as the incident microwave power densities were reduced, although there was usually an associated increase in the scatter of the results, so they were dismissed as unreliable. No one seems to have asked the questions, "Do the effects extrapolate to infinity as the power is reduced to zero? If not, at what incident power density does the turn-down occur?"

In experiments involving low level microwave radiation, the biological effects were initially characterised by being small and difficult to reproduce by other workers in other laboratories, or even failing to reproduce at all. Grundler[31], while noting the theoretical conjectures of Kaiser[47] on reproducibility, considers several criteria in respect of low power microwave experiments.

A stressed biological system is more sensitive to microwaves (synergism), as for example microwaves combined with X-rays[29,48]. The latter would increase the free radical concentration, the former might prolong their lifetimes. Incubation in an alternating magnetic field has been reported to enhance the effects of ionizing radiation[49]. Chemical or other known environmental stressors might also act synergistically with microwaves.

Frequency specific biological reactions may depend on the biological cell system used. When the same specific enzymatic reaction was tested in different cell systems, microwave irradiation did have an effect on *Staphylococcus aureus*, but had no effect on *E. coli*[50].

The biological parameters to be tested should not be of too specific a nature. Cell growth, which is dependent on many factors, is affected by microwaves in a frequency specific manner but, microwaves produced no lethal mutagenic or chromosomal effects in micro-organisms.

Microwave effects may only occur in certain phases of the cell cycle. A yeast was only sensitive to microwave irradiation in the G_1-phase at the frequency used[31].

The temperature of cells in pre-experiment storage may affect subsequent microwave interactions[31]. Many experimental techniques rely on synchronised cell cultures which are notoriously difficult to achieve[51]. These techniques may involve pre-experiment storage of the culture at a low temperature while in the resting phase to bring all cells to the same condition. Growth is then promoted by raising the temperature to that for incubation, possibly accompanied by an osmotic shock. Grundler[31] reports preliminary results whereby cells stored at 4°C gave no microwave effects, whereas cells stored at 30°C did give microwave effects.

The existence of microwave modulation effects, particularly modulations within the ELF range, which covers the most biologically active frequencies, has not been considered or controlled in many experiments. Grundler was stabilising frequency to only ±1MHz (in 42 GHz) so the spectral composition of the microwaves used would not have been known or controlled from 0.1 Hz to 100 Hz. Mechanical vibration is used by insect systems to generate highly coherent sub-millimeter wave effects[52]. Vibration is difficult to eliminate particularly in urban buildings, and experiments are unlikely to have been made in vibration-free laboratories.

Finally, I could add to this list the possibility that the experimenters themselves may affect the outcome of their experiments. This could happen if the experimenter were radiating biologically active frequencies as has been observed with electrically hypersensitive persons[53] and healers[54]. Robert Jahn, of Princeton University[55], has carried out many experiments with a wide range of mechanical and electrical systems and found that ordinary subjects can, by intention, influence a system in some way and consistently at highly significant levels of probability.

As evidence for operator effects, I have demonstrated in cooperation with Wekroma at Brione, Switzerland[6], that a beaker of water held in the hand for one minute showed changes in its optical spectrum, particularly at wavelengths below 420 nm. It is necessary to use 10 cm optical path length cuvettes in a differential spectrometer, suggesting the possibility of some resonance interaction between the water and the cuvette. Similar results have been independently obtained by Kurick, Institute of Physics, Kiev, Ukraine, and reported at the 1st. International Conference on "Water Systems and Information", Kiev, May 12-17, 1992.

3.4 Threshold Effects

The interesting things in physics happen at thresholds, yet it is characteristic of research into biological effects of microwaves that workers have been more concerned

with accurately reproducing power levels, measuring SAR's and building anaechoic chambers than in looking for thresholds. The reason is tied to concepts of ionizing radiation dosimetry and the power levels permitted by regulatory bodies on the basis of thermal effects.

Rea and co-workers have developed an effective protocol for demonstrating electromagnetic field sensitivity in human subjects[56]. The study was carried out in four phases. The first phase devloped criteria for controlled testing using an environment low in chemical, particulate, and EMF pollution. The second phase involved a single blind challenge of 100 patients who complained of EMF sensitivity. The 25 of these who were found to be EMF sensitive were compared to 25 healthy naive volunteer controls, none of whom reacted to any challenge on test. Of the 25 EMF sensitive patients, 16 had positive signs and symptoms plus objectively determined autonomic nervous system changes. In the fourth phase, the 16 EMF-sensitive patients were re-challenged double-blind only to frequencies to which they were found to be most sensitive. These were inserted randomly into 5 placebo challenges. The active challenges were 100% positive and all placebo tests were negative. The frequency range of these tests was from 0.1 Hz to 5 MHz. I have found[53] that some patients show a continuum of sensitivities extending well into the microwave region as seen in Figure 3.1, so this protocol would be applicable to tests at microwave and millimeter wave frequencies.

The approach to the detection of microwave effects used in the former Soviet Union and certain East European countries was based on changes shown by functional states such as reversible changes in nervous and cardiovascular systems and behavioral or psychological changes. Boris Savin of the Institute of Industrial Hygiene and Occupational Diseases, Moscow, has discussed the importance of experimental data on the effect of radio and microwaves on the higher nervous activity for the determination of safety standards[57]. Yuri Kholodov heads the Group of Electromagnetic Neurophysiology at the Institute of Higher Nervous Studies, Moscow, which has studied the reactions of the human nervous system to electromagnetic fields from steady fields to microwaves using the EEG as an indicator[58].

The consequence of these different approaches has been that for many years, safety standards were a thousand times higher in the West than in the East. Hasted wrote in 1973,

"Although it is very difficult to understand in physical terms just how non-thermal effects can arise, it is worth mentioning that there are many responsible scientists in the U.S.A. who do not discount the Soviet reports, and make use of the lower permissible levels in their own laboratories."[9].

Lack of adequate microwave technique has been the basis of much of the Western criticism of work from the former Soviet Union, where workers have on the other hand considered other aspects to be of greater importance. Increasing the incident power density above a threshold does not produce a proportional increase in the

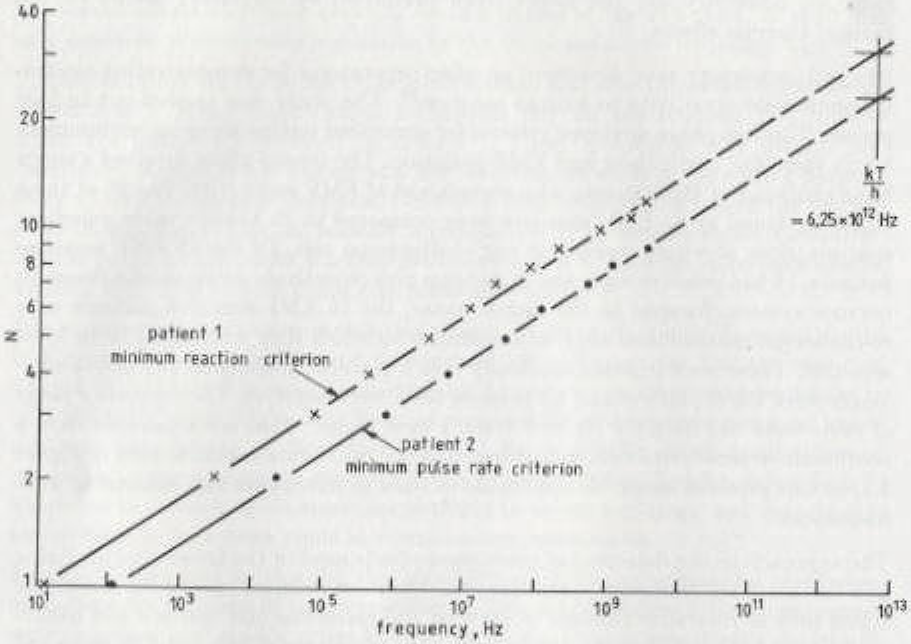

Figure 3.1: *Diagram showing the range of continuous electromagnetic hypersensitivities for two patients. The sections of solid lines represent frequencies which provoked patient specific reactions. Patient 1 had symptoms consistent with non-specific disturbances to the autonomic nervous system. Patient 2 had increased heart rate (tachycardia). The points indicate frequencies which provided neutralization of the respective symptoms. The measurements in the case of Patient 2 were done 'blind' to the patient. The dotted lines are extrapolations to the frequency corresponding to the mean thermal energy (kT). The ordinates are integer numbers representing the order of successive harmonics. The mathematical relationship is characteristic of a fractal equation.*

biological effect so, knowing the power density at the threshold is more important than elsewhere.

To investigate long term irradiation effects, the Institute of Clinical and Experimental Medicine, Novosibirsk, has had single cell lines in culture for 25 years, a feat of which any brewery could be proud. The Institute has found that live and dying cells can communicate very precise information using only optical (ultra-violet) means, and that a laser beam can take the imprint of bio-information and transmit it to other cell cultures.

Workers at the environmental research A. N. Marzeev Institute, Kiev[59], have stimulated autoimmune reactions in rats by microwave irradiation (2375 MHz) getting a destabilization of functional activity of the immune system humoral factors at 500 $\mu W/cm^2$. Cytochrome was affected at these levels. Autoimmunity could be stimulated by immunization of intact animals with brain tissue of rats exposed at 50 and 500 $\mu W/cm^2$, the process was dependent on the microwave intensity[60].

Chronic exposure of domestic fowl to very low intensity microwave radiation was reported by Tanner and Romero-Sierra[61] to give increased mortality rate and profound deterioration in health of the survivors.

A report from The People's Republic of China by Chiang *et al*[62] of investigations into the effects of the environmental microwave exposure of humans, concluded that in the highest exposed groups the visual reaction time and short term memory were worse and that there may have been effects on the CNS and immune systems.

Lester and Moore[63,64] found that cancer tended to occur on leading terrain crests relative to radar transmissions and was less frequent in the valleys, and also that counties in the U.S.A. with an Air Force Base had significantly higher incidences of cancer mortality.

Szmigielski *et al*[65] have carried out a retrospective study from 1971-1980 of immunologic and cancer related aspects of exposure to low-level microwave and radiofrequency fields. It showed a clear increase in the risk of cancer among subjects occupationally exposed to microwaves and radiofrequencies.

Some years ago, Andreyev and co-workers[66] published their first results of indications of special characteristic frequencies in humans, and subsequently a comprehensive report of research into the physical mechanisms of low-intensity radiation on biological systems[67]. The experiments showed that a human organism with functional disorders can distinguish insignificant frequency changes of external electromagnetic radiation in the millimeter frequency band, with a resonance half-width of 20 MHz. Low intensity radiation at specific frequencies in the range 50-70 GHz and at power flux densities from mW/cm^2 to $\mu W/cm^2$ incident on acupuncture zones connected with 'malfunctioning' organs, produces a sensory response accompanied by a strongly pronounced therapeutic effect. The method was tested on more than 4000 patients for some pathologies. When visiting Kiev, I enquired how the choice of millimeter wave frequency was made, and was referred to the microwave oxygen lines in this region all of which have therapeutic applications. Millimeter wave applicators have been designed for various clinical applications. These authors conjecture that,

"An informational connection with an external field and energy transport along limit cycle space trajectories may be conditioned by protein spin states..... Electromagnetic waves in the range 45-65 GHz arising in the organism due to transitions between sub-levels of a triplet spin-spin splitting, provide a universal long-acting coherence which is not limited by nonuniformities of real living structures. The role of short-acting activators may be played by enzyme complexes, as their activity is known to depend on spin orientation of the external electrons in active centres in a trigger way... Thus we consider the living organism to be a quantum system and a dissipative structure formed as a result of a non-equilibrium phase transition which constantly reproduces itself due to self-organization processes."

Devyatkov and co-workers have published a study of millimetric wave interactions with biological objects and water[68].

From the point of view of physics, Fröhlich[51] characterised thresholds and active biological systems by three properties. First, they are relatively stable but far from equilibrium, which require that the various excitations are stabilized, pointing to the existence of metastable states. Second, they exhibit a non-trivial order, which requires a motional order as is found in the existence of macro-wavefunctions in superconductors and superfluids, but which also exists in non-equilibrium systems such as lasers or in maintained particular excitations such as sound waves; its generalisation leads to coherence. Third, they have extraordinary dielectric properties, which arise from the high electric fields maintained in membranes in conjunction with the sensitivity to very weak electromagnetic fields with sharp frequency response.

The coherent excitation of a single polar mode depends in a step-like manner on the rate of energy supply but with a time-lag while coherence becomes established. This type of excitation requires a strong non-linear interaction with the "heat bath" which attempts to impose its temperature on the particle distributions. While in a Bose gas the number of particles is fixed so that Einstein condensation and superconductivity arise only when the temperature is sufficiently lowered, in the biological situation the temperature is fixed and the number of quanta is increased by the rate of energy supply until the threshold is reached.

The ultimate threshold for magnetic effects is the linkage of a single quantum of magnetic flux with the cross-sectional area of a coherent cell or organism. The integral of the magnetic field over a cross-section perpendicular to it is defined as the magnetic flux, Φ, which is shown by Fröhlich to be an integer multiple of the flux quantum, $\Phi_o = h/2e = 2.07 \times 10^{-15}$ Wb. Although this originated in superconductivity, it is not restricted to it but is a completely general phenomenon. The possibility and experimental evidence that living systems are sensitive to, and use magnetic flux quanta, has been presented by Del Giudice *et al*[69]. If a system is able

to respond to the magnetic flux quantum, then it has the Josephson effect available.

The Josephson effect is a macroscopic quantum phenomenon of superconductivity in which the current flow between two regions of superconducting long-range order, separated by a barrier which is a non-superconductor, is dependent , not on the voltage between the regions, but on the phase difference, Ψ, of order parameters, which have properties similar to those of wave functions in elementary quantum mechanics. The phenomena are divided into stationary (DC) and non-stationary (AC) effects depending upon whether the variables change with time. The most important of the ac effects are Josephson oscillations which take place if the voltage has a dc component, V, at a frequency, f related to the voltage by (approximately) 500MHz/μV, or exactly:

$$2\pi f = d\Psi/dt = \frac{2e}{\hbar} \cdot V$$

where e is the electron charge and $\hbar$ is Planck's constant divided by 2π.

3.5 Cellular Basis

The cellular basis for bioelectromagnetic effects in the microwave and millimeter wave region requires a physical model for the biological cell[70]. The frequencies for non-linearly excited coherent oscillations may be based on any of the possible modes of resonance as shown in Figure 3.2, but they may also be much lower as in the case of limit cycles. They may also not be determined by structures but, by hyperfine energy levels.

Any structure, whether a biological system or a musical instrument, will have some natural resonance frequencies determined by its dimensions and the velocity with which waves travel within it. The fact that a cell is visible against its surroundings means that it has a different refractive index and hence waves will be, at least, partially reflected at its boundaries. These waves may acquire energy as they travel and build up to become sustained oscillations.

There are of the order of 3000 enzymes controlling the chemistry of a biological cell. The high catalytic power of an enzyme requires a reduction of the activation energy. A metastable state with a high internal electric field may be nature's way of activating an enzyme catalysed reaction. Frequency selective long-range interactions may arise from the excitation of coherent vibrations and give the selective attraction of enzymatic substrates[71].

The importance of the frequency 100 GHz assumed by Fröhlich for fundamental biological activities was strongly supported by the publication of research from the former Soviet Union[29]. Physically, this frequency corresponds to a an acoustic mode

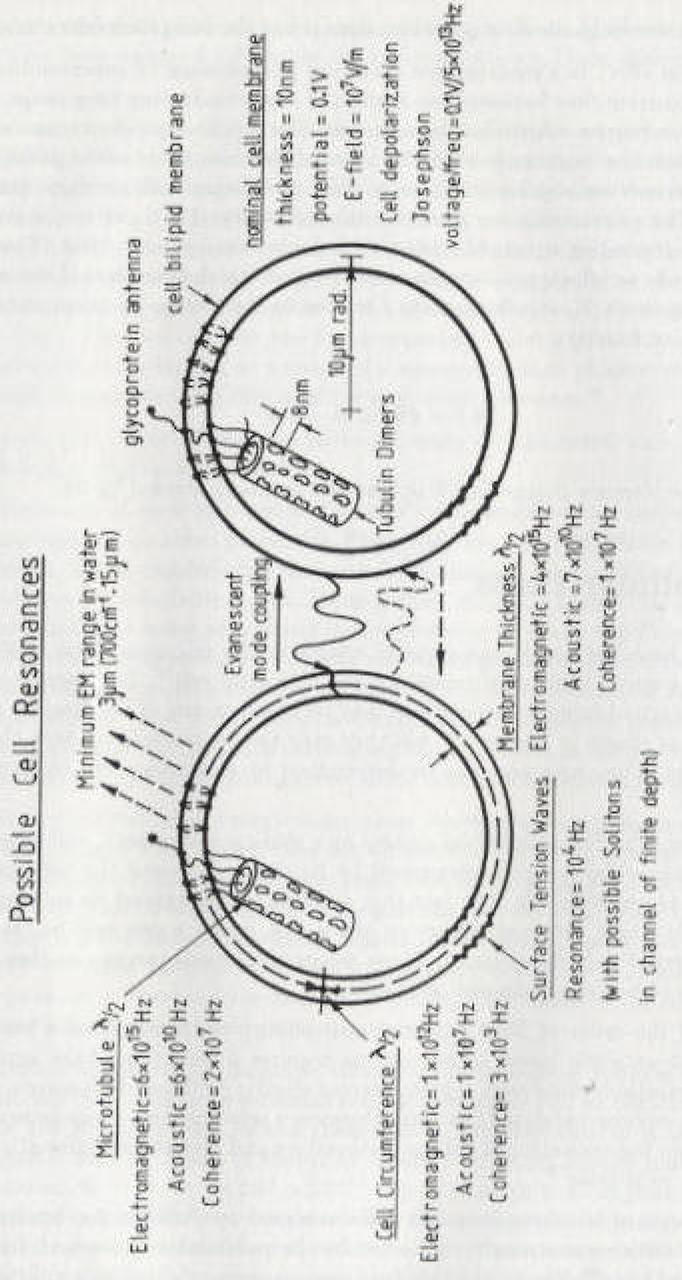

Figure 3.2: *Diagram showing possible resonances relating to the sizes of features of an idealized biological cell. There will also be resonances corresponding to hyperfine energy levels not related to the cell geometry.*

resonance in the thickness of the cell membrane for which its dimension is a half-wavelength (Fig. 3.2).

The stimulated Raman effect has been used to investigate the possibility of far-infrared sub-millimeter coherent oscillations in biological molecules and cells. The effect depends on the coherent pumping of molecules into excited vibrational or rotational states by the electric field of a laser beam which is above some critical intensity threshold. The molecules relax and emit isotropically the inelastic scattered radiation. This relaxation may be coherently stimulated. The intensity of the Raman scattered radiation is three orders of magnitude below the Rayleigh elastically scattered radiation which is at the laser frequency. In the inelastic collisions, the laser photons may lose or gain energy. If they lose energy to the molecules, the Raman scattering appears at a lower frequency giving a Stokes line, if they gain energy from the molecules, the Raman scattering appears at a higher frequency giving an anti-Stokes line. The freqency shift is given by the energy change divided by Planck's constant. The ratio of the anti-Stokes to Stokes intensities compares the number of molecules donating and accepting energy. In 1977, Webb *et al* published a series of Stokes and anti-Stokes laser-Raman spectra of synchronized active cells of *E. coli* bacteria[72]. The average cell size of an *E. coli* cell ranges from 1.1 μm - 1.5 μm wide by 2 μm - 6 μm long over the growth cycle. For the circumferential half-wavelength mode in the lipid bilayer shown in Figure 3.2, the resonances should come within the band of wave numbers 320 cm^{-1} to 100 cm^{-1} according to the above range of cell sizes. The spectra taken by Webb 40 minutes after incubation showed Raman lines at 150 cm^{-1}, at 50 minutes they were at 120 cm^{-1}, and at 60 minutes they were close to 100 cm^{-1}. The corresponding frequencies are from 4.5 THz to 3 THz (1 THz = 10^{12} Hz).

The mean frequency corresponding to thermal energy (kT_{300}) at biological temperatures is 6.25 THz, so that these highly coherent frequencies could be thermally pumped resonances in which a Bose condensation had occurred.

My laboratory was probably the first to demonstrate coherent oscillations in the radiofrequency region of around 8 MHz from yeast cells at the time of cytokinesis[73]. This frequency is the same as the periodicity found in the millimeter wave experiments by Grundler *et al*[31,32]. Webb has pointed out that this is also the frequency that one would expect from the rate constant for the hydrolysis of ATP.

It was only possible to find these coherent 8 MHz oscillations experimentally because a series of steps had been found in voltage-current characteristics of thin films of yeast cells[69]. On previous occasions, cell systems had been found to react to magnetic fields at levels corresponding to a single magnetic flux quantum linking the measured cell cross- section. One of the consequences of magnetic flux quantization is the Josephson effect which gives a frequency to voltage interconversion of 500 MHz/μV. It was possible to adjust the experimental conditions while observing the voltage steps until the expected frequency came within the range of a radio-frequency spectrum analyser. The coherent oscillations were then sought and found. They lasted for only for a few minutes one mean generation time (4 hours) after starting the synchronous cell incubation[73]. Under other experimental conditions, voltage steps corresponding to frequencies up to about 2 GHz were observed[69].

In earlier experiments in my laboratory[74], the enzyme, lysozyme was used as the dielectric in a point-plane electrode configuration within a section of X-band to wave-guide. It was found that on irradiation with 9 GHz, steps appeared in the voltage-current characteristic. Applying the Josephson effect conversion gave the corresponding frequencies of 20 MHz and 40 MHz. The coupling-in of weak signals at either of these frequencies gave a 15-fold increase in the DC conductivity and the steps increased so that they then corresponded to 300 MHz.

All chemical reactions involve energy change and involve quantum physics; there is no chemistry in classical physics. The energy of a chemical reaction is of the order of electron-volts (1 eV = a chemical energy of approx. 100 kJ/mole = a photon wavelength of 1.24 μm). Biochemical reactions catalysed by enzymes require an activation energy to switch on their remarkable effectiveness. That living systems use coherent optical frequencies for biocommunication has been demonstrated by Popp[75] (see also Popp et al, this volume). There are biophotons available in living systems at frequencies high enough for single quantum photochemistry to occur.

Ordinary organic (non-bio-) chemical reactions are affected by an external magnetic fields, static and alternating, from the low audio up to microwave frequencies. McLauchlan[76] has described how weak magnetic fields can affect chemical reactions involving free radicals, which also includes much of essential bioenergetics[17]. The major effect of the magnetic field is to remove degeneracies of the sub-levels of triplet radical pairs whose energies are equal in zero field, but differ progressively and linearly as an applied field is increased, according to the Zeeman effect. The Zeeman separation of the states exceeds the magnitude of the hyperfine interaction at a few milliTesla. Vanag and Kuznetsov[77] have considered how the radical reactions of lipid peroxidation, the enzyme reactions involving paramagnetic molecules, and photochemical reactions could be influenced by magnetic fields through the mechanism of spin exclusion.

Evidence that living systems are making use of the Josephson effect has already been referred to[69]. This offers a postulate for a procedure whereby the power density threshold for the interaction of microwaves with living systems might be determined.

Grundler *et al*[31] arranged their microwave exposure system so that the cells were exposed to the electric field component. If a microwave electric field across a biological structure (e.g. cell, synapse, membrane) is considered as a Josephson weak link experiment and, if the applied microwave radiation is sufficient to give a field related voltage across the weak-link equal to, or greater than the Josephson voltage corresponding to its frequency, then this combination will try simultaneously to force the phase difference of the order parameter and the potential across the weak-link junction, leaving no degrees of freedom to the biological system.

The result might be the paralysis of bio-signals trying to use that resonance to trigger a chemical reaction at the site of the weak-link junction. The range of frequencies over which this could happen will depend on the extent of available resonances or hyperfine energy level structure.

The 42 GHz experiments on yeast cells by Grundler *et al*[31,32] were reported at power flux densities of the order of 1 mW/cm^2 (10 W/m^2). This must have exceeded all the thresholds since highly resonant effects were observed. The corresponding fields over the diameter of the yeast cells cells of mean volume 30 μm^3 would not have been greater than 30 V/m, assuming that the effective dielectric constant was that of water (approximately 16 at 42 GHz). This would give about 900 μV across the cell diameter, the largest likely weak-link, or less, if the weak-link is a sub-cellular structure and is more than 10-times the Josephson voltage of 84 μV corresponding to the frequency 42 GHz. This suggests that the ultimate power density threshold at this frequency might be 100 times less, as little as 10 μW/cm^2 (0.1 W/m^2). This is nearer to the safety levels adopted by the East European countries[40] and suggested effects at still lower power densities[78].

At the 1st. International Conference on "Water Systems and Information" held in Kiev, Ukraine, May 12-17, 1992, I presented evidence that living systems can make use of a low frequency alternating magnetic vector potential. The magnetic flux density B (Tesla) is of mathematical necessity related to a vector **A** such that **B**=curl**A**.

It was long thought that **A** was merely a mathematical convenience, but it was eventually shown experimentally by a number of workers that **A**, the magnetic vector potential, has a physical reality. The most thorough demonstration[79] came from the Hitachi Research Laboratories, near Tokyo. A toroid contains the magnetic field within its volume but the magnetic vector potential spreads into the surrounding space and can influence a beam of electrons in a diffraction experiment by interacting with their wavefunction. This is the Aharanov-Bohm effect, the production of a relative phase shift between two electron beams enclosing a magnetic flux even if they do not experience the magnetic flux[80].

The magnetic vector potential is a vector directed in the same direction as the current giving rise to the magnetic field. A changing magnetic vector potential gives rise to an electric field E thus,

$$\mathbf{E} = -d\mathbf{A}/dt$$

E is not affected by magnetic screening materials so there is the possibility of magnetic effects at near zero values of the magnetic flux density **B** if the magnetic flux to which they are subjected is attenuated by magnetic shielding rather than distance from the current source.

From these experiments, it appears that bio-information might be carried on the magnetic vector potential while the magnetic field formats the medium. If magnetic vector potential effects in living systems extend to the microwave and millimeter wave region, this would provide a possible mechanism for interaction with the long-range order of the postulated Josephson weak-link junctions in living systems through their interaction with the order parameter, which has properties analogous to the wave function in elementary quantum mechanics.

What is now urgently needed is to be able to read the language of electromagnetic bio-communication to complement our understanding of the genetic code.

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