

'Mechani of high-frequency

Report from a journey to biophysics of living cells at exposure to mobile radio high-frequency electromagnetic fields (HF-EMF)

On May 22nd and 23rd 2001 the 'Seminar on Mechanisms for Interactions of RF Energy with Biological Systems' took place at Radisson Barcelo Hotel in Washington D.C. Besides a number of high-ranking biophysicists from the area of high-frequency research also biologists from the FGF were invited to the workshop as observers and discussion participants.

tion of the Repacholi study on mobile radio and transgenic mice being conducted in Australia and Italy. This did not happen. The 'Germany study' of the workgroup from Mainz around J. Michaelis is already well-known, and we all vividly remember the controversial discussion.

Worth remembering are a few valuable contributions being fundamental for the understanding of interaction mechanisms of electromagnetic fields.

As already mentioned at the beginning of this report, this year's meeting - compared to the annual meetings having taken place since Copenhagen 1994 - so far was the smallest event concerning the number of presentations. Surely, this is not only due to the drastic cuts in the submitted contributions, but also to the difficulties caused by the very high dollar exchange rate.

Though table 1 shows the contributions as listed by the program; however, it gives a wrong impression. Whereas only few lectures were cancelled (N=6), in poster presentations 31 out of 139 were missing, that is over 20%. A somewhat depressing trend that will hopefully not continue next year.

In the end, none of the presented studies gives irrefutable proof of an acute health risk caused by field exposure below recommended thresholds, neither in the ELF range nor concerning higher frequencies, especially of mobile radio.

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Conclusions

Whereas previous BEMS meetings could be characterised by a catchword or slogan, this year's meeting is not so easily described. As at previous events both good and less convincing contributions were presented. We could neither report on spectacular new studies nor on newly gained generally accepted insight on the current risk discussion. Secretly, participants reckoned on the publishing of the test replica-

sms for interaction

energy with biological systems' in Washington

The following scientists participated in the event sponsored and planned by the MMF (Mobile Manufacturers Forum):

- Dean Astumian (Department of Physics, University of Maine, USA)
- Quirino Balzano (consultant, formerly Florida Research Laboratories, Motorola, Inc., USA)
- Frank Barnes (Department of Electrical Engineering and Computer Science, University of Colorado, USA)
- Howard Bassen (Electrophysics Branch, US Food and Drug Administration [FDA], USA)
- Ferdinando Bersani (Dipartimento di Fisica, Università di Bologna, Italy)
- Chris Davis (Department of Electrical Engineering, University of Maryland, USA)
- Larry Dworsky (Florida Research Laboratories, Motorola, Inc., USA)
- Roland Glaser (Institute of Biology and Experimental Biophysics, Humboldt University Berlin, Germany)
- Frank Gollnick (Research Association for Radio Applications - Forschungsgemeinschaft Funk e.V., FGF -, Germany)
- Sakari Lang (Nokia Research Center, Finland)
- William F. Pickard (Department of Electrical Engineering, Washington University, USA)
- Earl Prohofsky (Physics Department, Purdue University, USA)
- Asher Sheppard (Asher Sheppard Consulting, USA)
- Mays Swicord (Florida Research Laboratories, Motorola, Inc., USA)
- James Weaver (Harvard-MIT Division of Health Sciences and Technology, Massachusetts Institute of Technology, USA).

As the event did without the usual lectures prepared in advance, the participants could concentrate on in-detail discussions on the meeting's topics. This approach led to an extraordinarily tight and highly effective debate with corresponding concrete results. The following topic catalogue was meant as a guide for discussion:

1. Temperature gradients caused by HF EMF
2. HF EMF interaction at the cellular level
3. HF EMF interaction at the molecular/chemical level



4. Interaction between many particles (cooperativity, coherence, non-linear dynamical processes, stochastic resonance)
5. Magnetic dipole interaction

At the end of the conference, all questions still unresolved were gathered and combined in a task list. Research tasks from this list presently are commissioned to experienced scientists. The aim is to find answers to the most important unresolved questions within a relatively short time period (around a year), either by mathematical calculations or by experimental studies. The seminar was part of a series of scientific discussion panels to the greatest part organised (or to be organised within this year) by the FGF such as the workshop 'Biological and Biophysical Research at Extremely Low- and Radio-Frequencies' having taken place in Bad Münstereifel in December 2000 (see FGF Newsletter 1/01), and a follow-up workshop under the title 'Physical Effects of Pulsed RF Fields at Microscopic and Molecular Dimensions (Microdosimetry)' which will be held by the FGF from December 17th to 19th 2001 in Dresden. In Dresden, first results of the now commissioned research projects will be presented and discussed. Further workshops are planned. Thus, a central question consistently is dealt with being of increasing importance in the context of possible disadvantageous effects of mobile radio fields on biological systems and humans: Are there at all concrete physical mechanisms unequivocally pointing to a (possibly detritous) impact on biological substance? Surely – as is done now – one must rather look at the anatomy of cell bindings and cells (down to the molecular level) than at the anatomy of whole organisms searching for possible sites of interaction between high-frequency pulsed fields with biological material (see also FGF

Newsletter 1/01). Fundamental for this new approach is that the fields in question in the physical sense are extremely weak and that registered energy peaks only have an extremely short-time impact (in the nano-up to the microsecond range).

Mays Swicord marked the beginning of the seminar in Washington by comparing the currently used approach to the research activity of the recent past. Whereas until now detectable biological reactions caused by electromagnetic fields have been searched for, at present rather the other end of an assumed interaction chain is of interest: Should there be found concrete evidence for effects of mobile phone fields in the above mentioned physical interaction (i.e., target objects at the molecular level that can be affected), then also explicable effects on measurable biological parameters would be conceivable via the subsequently altered biochemical reactions within the cells. Until now the dilemma of research is that, though time and again there is indication (if only to a smaller part) of biological effects – also caused by weak fields –, they never can be explained based upon a conclusive interaction model at the molecular level. But as long as there is no conclusive explanation, it remains doubtful whether the found effects actually were caused by fields applied during experiment or rather by a possibly unnoticed side effect.

No effect without chemical reaction

In his contribution to the discussion, James Weaver confirmed that biological effects on cells and molecules caused by field exposure only can be expected where there has been a 'beforehand' alteration of a basic chemical reaction. 'No effect without chemical reaction' – the well-known papers of Litovitz (f.e. 1993) stood against

this opinion. According to Litovitz, direct field effects on crucial target molecules are possible via resonance with the irradiated waves (without the detour via chemical reactions). This aspect again was discussed in depth later on (see below).

Further, Weaver emphasized the fact that though the irradiated energy during transfer to biological material distributes evenly within cell microstructures, it may deposit quite inhomogeneously depending on individual material properties of the structures.

The problem of temperature in the microrange

The intervention of Weaver ignited a debate on the question how big temperature alterations in the tissue and especially within the cell and/or its microstructures caused irradiation of mobile radio fields can be and over which time period these alterations can affect biomolecules.

Frank Barnes presented calculations simulating the impact of a picosecond-pulse of a high-frequency signal on hair cells (hair cells in the inner ear converting sound signals into electrical signals for the brain). In eight steps calculations for pulses of an inhomogeneous wave with a duration of 12 to 64 ps were conducted. From this excitation resulted (mathematically) a stimulus conduction to the brain - theoretical evidence for a possible neural processing of the extremely short pulse signals. Further existing basic data on this issue were presented and discussed:

- According to Barnes, a temperature alteration of around 0.5° C leads to a reliably identifiable protein denaturation ('coagulation').
- In experiment, Barnes determined effects on the firing rate (i.e. sequence rate) of pacemaker neurons (nerves determining or conducting the sequence of certain

body functions) at a relatively high energy input (around 1° C/s).

- Two generally renowned publications from the year 2000 identified the strongest 'hot spot' (calculated spatially limited spot of increased temperature and/or accumulated energy in the tissue caused by high-frequency radiation) in human head models at an energy input like that of mobile phoning at 0.06° C.

In this context, William Pickard objected that in truth velocity is the crucial factor concerning temperature: a certain up and down of temperature within a healthy body in the range of 1° C is quite normal. However, if temperature at a microscopic structure f.e. increases and decreases 100 times per second caused by externally irradiated energy, that would be an abnormal effect the body is not used to. Consequently, in this case the body could have difficulties to cope with such effects. Thus, in Pickard's view biological effects caused by temperature increase can not per se be excluded: 'Effects caused by temperature increase are possible; whether it leads to effects depends on the size of the increase and the duration of its impact.'

Dean Astumian found that the passage of a calcium ion through a membrane channel takes around 10⁻⁷ seconds (a ten millionth second). Calculations established that high-frequency fields of above 10 MHz are highly improbable to have a greater impact on this process.

Following discussion, the requirements of a thorough and exact research on following still unresolved questions were formulated:

- an exact theoretical determination of temporal and spatial temperature and energy radiants at the microscopic (nanometer range, molecules) and the macroscopic level (up to mm range, cells and tissue). Question: How does a temperature altera-

tion in time intervals below 1 millisecond (at pulsed signals) down to 1 nanosecond (more or less equivalent to a sine oscillation at a signal around 1 GHz) occur?

- to determine whether such gradients are strong enough to stimulate and/or change biochemical processes
- observations on temperature alterations at time intervals below 1 millisecond and under complex geometric conditions (biological cells of different shape and size).

Interaction at the cellular level

During this part of discussion introduced by Ferdinando Bersani hypotheses on interaction models concerning HF field exposure of two important publications were critically examined. One of the articles (Apollonio et al. 1998) identifies a transmembrane potential caused by a HF field of 1 microvolt as physical cause of an altered ion flux through cell membrane ion channels. However, present experts were not able to comprehend how this so-called 'induced membrane potential' physically is supposed to happen. The explanations given by the mentioned paper do not suffice. The theories of Chiabrera et al. (2000) on the cause of effects of HF fields on ligand (binding partners) bindings to cell receptor molecules (f.e. binding of Ca²⁺ ions to calcium receptors) met with serious doubt, too. The dynamics of ligand binding altered by HF field exposure and supposedly being responsible for the effect are not sufficiently explained. Part of the participants even claimed that some numbers given in the publication were not correct. As an urgent subject of further research in this area concrete experimental methods for tests on the above mentioned dynamic alterations at ligand binding at HF field exposure were addressed. Concerning membrane potential alterations depicted by Apollonio et al. (1998) it was



concluded that new calculations are required to learn more about exact thresholds of field strengths and frequencies at which the described effects at all can occur.

According to Pickard & Rosenbaum (1978), the known direct electrical rectifier effect of cell membranes on HF fields is based on non-linearities affecting ion movements across the cell membrane. This would explain certain biological effects. However, according to Pickard, this type of rectifying is not possible anymore above a carrier frequency of around 10 MHz, since the length of time needed by ions to cover a relevant distance is inconsistent with a noticeable impact of HF waves in this area. So ions are unaffected by the increasingly fast oscillating HF field above 10 MHz because of their relative inertia.

In this context, further research requirements with following foci was identified:

- refined calculations of threshold values concerning field strengths, carrier frequencies and pulsation parameters up to which a direct effect on cell membrane potentials is possible
- calculations meant to determine whether multi-cell structures compared to single cells (on which existing knowledge is based) possibly strengthen or weaken the rectifying effect
- electrical non-linearities of cells in the lower GHz frequency range should be examined by means of physical measurement methods.

In their publications, Kotnik & Miklavcic (2000) add to known calculations after Schwan on the effects on the membrane potential of a round cell exposed to an electric field. The observations include field strengthening at dielectric cross-layers (f.e. the cross-section of cell membrane and cell plasma within the cell or external medium) in their observations.

- Theoretical papers should clarify whether the accordingly possible temperature increases in the small dimensions of a cell membrane (around 1/100000 mm) are relevant for biological systems based upon the extremely short exposure intervals of pulses and upon frequencies as applied by mobile radio.

Living cell membranes on the inside and on the outside are covered by layers of oppositely charged ions. By external fields these 'anti-ions' can be polarised ('alpha dispersion' known from low-frequency field exposure). As there is no well-defined limit frequency concerning the development of this phenomenon, participants also discussed a theoretically possible occurrence in the lower GHz frequency range of mobile radio. Here, particularly those biological processes could be of relevance that so to speak are permanently 'balanced precariously' concerning their energy balance. Such processes occurring within cells and at cell plasma membranes f.e. are:

- the alternation of certain protein molecules between two nearly identical energy states
- cell and protein molecule accumulation (aggregation)
- the stringing of colloid particles into strands or
- the complicated processes of biochemical 'proof reading' during multiplication (at cell division) and reading (for protein synthesis) of our genotype (DNA).

All these processes show an extremely low energy turnover, nevertheless being highly effective, since the systems concerning energy content are located at an unstable 'saddle point'. Therefore, already a slight external influence on the concerning system - above all often repeated processes as the mentioned 'proof reading'-, could lead to a noticeably increased error rate.

- The scientists recommended the commissioning of exact calculations on the mentioned mechanisms of ion polarisation and 'proof reading'. Here, one should determine the quantitative limits up to which external interferences, f.e. of mobile radio fields, still can be of biological relevance. If possible, in this respect - as well as concerning other aspects - one should always consider multi-cellular systems compared to single cells, added to by the possible impact of the above mentioned inhomogeneous dielectric cross-layers.

Real biological structures always are three-dimensional structures with own field distribution. James Weaver made clear that laboratory research in single cells or single cell layers always is limited by the fact that field distribution within the tissue can never be completely replicated. In spite of that, such tests are sensible and necessary as a component of overall research. As Weaver explained, additional state-of-the-art calculations can hugely improve portability of single cell measurements to conditions within body tissue.

Interaction at the molecular and the chemical level

Concerning this topic, a number of the theoretically possible mechanisms was discussed being responsible for 'capturing' energy input of mobile radio fields in biological system, i.e. for effective biological or chemical depositing. Only if such mechanisms can be proved, biological effects caused by fields are conceivable at all. Here, during discussion the mechanisms found for partially very high energy input had to be recalculated for consideration of low-energy values occurring in the mobile radio range (i.e. affecting humans within the set limit value range). The central question in this respect is: Can under

conditions of a normally strong mobile radio frequencies in the range of 1-2 GHz at all develop an effective signal penetrating cell membrane and reaching the inner cell?

As the first conceivable mechanism the resonance of GHz fields with biological molecules was addressed. At body temperature, biomolecules are permanently in a state of a vibrational movement caused by the existing heat ('thermal noise'). After discussing the available scientific literature on this topic, the conclusion was that especially the strong dampening of molecular movement by the surrounding water molecules diminish probability that biomolecules show resonance with weak fields in the frequency range of 1-2 GHz being subsequently altered concerning their functioning. Only at a 'ballistic' setup where centrifugal powers dominate, sharp resonances can develop (as is f.e. the case in electrons being conducted through metal - here, elastic collisions dominate; the dampening loses importance).

- It was suggested to examine by means of calculations whether a 'ballistic' transfer of ions through proteins forming membrane channels can occur (channel proteins within cell membrane). This would be a theoretical approach to understand biological effects caused by resonance phenomena. In this case, there would have to be something like a porous protein with an internal vacuum, a notion, however, the assembly thought of as highly improbable.

Some other mechanisms at closer inspection neither did seem to be an adequate approach to explain energy transfer to biomolecular components. The addressed phenomena

- phase transfers of biological molecules (f.e. at β -lactose),

- Kapitza resistance and
- abnormally weak dampening

are thoroughly explained by the corresponding scientific literature. Phase transfers at β -lactose were found only at very high energy input of 400 W/kg; the impact of the Kapitza resistance probably can not surmount a factor of 2, and the phenomenon of abnormally weak dampening was seen as scarcely conceivable in the context of biomolecules.

Other mechanisms were at least seen as a conceivable explanation for biological effects requiring further research. This concerns ions (f.e. calcium ions) bound or held by certain molecules (f.e. calmodulin) or membrane channels like in a cage ('caged ions') without surrounding water molecules. It would be important to know whether for ions in this particular state - despite still existing strong dampening - resonance phenomena ('capture' of energy) worth mentioning can occur. In the view of the experts, the question whether fields of mobile radio are capable to interfere with ongoing enzymatic processes (material turnover at regulating or response mediating protein molecules, the 'enzymes') as well requires further research. Here, the energy of HF fields would have to be stored together with higher short-term energy states enzymes are in. However, some of the present experts doubted that artificially altered energy states stay on long enough to lead to biological and biochemical effects.

An estimate William Pickard presented illustrated what size f.e. a biological structure must have for 'capturing' (absorbing) the energy of a mobile radio field of 10 W/kg chosen as an example under average conditions within a time period of 1 second. The values given as an example were chosen deliberately large. The result of the calculation was that the respective struc-



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ture must have a size of around 7 nanometer being approximately equivalent to the thickness of a cell membrane. As in such large structures (at molecular dimensions) the input energy exists in many physical energy states (modi), it was thought highly improbable that the overall energy could 'flow together' into a state which would then cause an effective chemical alteration. In this context, resonance phenomena as well were thought impossible, since the duration of EMF impact would have to be increased up to an unrealistic range. Thus, the above mentioned results of Litovitz can neither be explained by resonance nor by other theories.

Dean Astumian presented a theory based upon aggregation (conglomeration) phenomena known from colloid chemistry (chemistry of suspended, bloated, undispersed particles) suggesting that induced dipole components in non-spherical objects can add up to a netto dipole component. Such a bigger dipole component in the area of a molecule theoretically could interact with an externally input high-frequency field. In this context, phenomena like for example the wandering of protein molecules in a certain direction at so-called

'capping processes' (concentration of certain proteins in special areas of the cell membrane) at cell surfaces (f.e. lymphocytes, white blood plasma) were addressed. There could be as well an impact on the powers active between certain proteins in blood serum triggering erythrocyte chaining (red blood plasma aggregation). However, other participants found that these examples do not necessarily are true for possible far-reaching effects of biologically relevant power impact.

In the end, concerning the topic of molecular/chemical interactions all possible mechanisms were questioned because of temporal aspects at collisions, binding events and transfer between molecules. The time period between these events always is much longer than the duration of events themselves. Thus, (simplifyingly) the timespan for an effect caused by an artificial HF field theoretically would be much too short for energy to produce a biologically relevant effect, i.e. because of the short time theoretically there can not be taken enough energy off the HF signal to produce an effect. Generally speaking: For biological effects to occur at all (at molecular dimensions) a biological structure has to 'capture' an energy input from the artificially built field being at least equivalent to the energy of the existing 'thermal noise' (see above). In this context, it must be examined whether the recent results of Kotnik & Miklavcic (2000) are correct. In this case, alterations of cell membrane potentials (in contrast to the older currently accepted models of Schwan, see above) as well would be possible caused by mobile radio frequencies in the GHz range. According to Dean Astumian, the theoretical findings of Kotnik and Miklavcic suggest that under mobile radio conditions biologically relevant membrane potential alterations up to 500 μV are possible. How-

ever, the physical interaction described in the corresponding publications is difficult to understand even for experts.

Interaction between many particles

Concerning this topic range, Chris Davis at first addressed the well-known model of Fröhlich claiming a far-reaching coherence between electric dipoles at the surface of cell membranes. Physically, coherence means that several linked oscillating waves have the same frequency and constant phase difference (known from light waves of laser light). Coherence at cell membranes could be a theoretical angle for explaining an impact of HF fields on living cells. However, the participants of the workshop concluded that the theory of Fröhlich is not convincing, since it is based on several unrealistic assumptions and was not confirmed by experiment:

- The dampening by the existing water molecules is not considered.
- According to Fröhlich's formulas an unrealistic thickness of the cell membrane would be necessary to obtain a functioning model.
- Fröhlich's formulas do not present numerical data which could help to confirm the theory.

In a study soon to be published, Adair (2001) dealt with the problem drawing the conclusion that far-reaching cooperative mechanisms like coherence at cell membranes are not possible because of the mentioned dampening by water.

On the other side, synchronisation of coupled oscillating systems certainly is possible without strong dampening. The existence of such synchronised systems in living tissue should be further explored. Moreover, we should calculate field strengths at which such systems despite existing dampening coherently oscillate.

Non-linear dynamics generally is seen as a useful approach to explain sensitive reactions of complex systems towards external stimuli. But according to participants, in the context of the direct impact of mobile radio fields on biological systems this approach can be ignored because of the physical nature of the possibly to be expected impact.

As well the so-called 'stochastic resonance' (stochastic: including random quantities and random events in statistical evaluation) that can be used as an explanation for a heightened sensitivity of other reaction systems, had to be classified as practically of no relevance concerning the impact of HF fields. Here, 'stochastic resonance' can not alter the effective signal-to-noise ratio by a factor worth mentioning. According to James Weaver, many studies conducted on this aspect did not consider regular physiological temperature variation in biological systems. Thus, this explanatory approach in search of a possible target point for mobile radio fields in biological systems either was dismissed.

Magnetic dipole interactions

In his introduction to this topic, James Weaver explained that so-called 'magnetosomes' (magnetic particles, i.e. ferromagnetic material surrounded by a double membrane) among others are found within the cells of the human brain. Their structure is similar to that of magnetic bacteria as well bearing magnetic particles. Until today it is not clear whether magnetosomes in the brain have a particular function, and if so, what function that is. Kirschvink (1996) thought about the possibility that small amounts of the 'biologic magnetite' could absorb ('capture') sufficient energy from external fields via the mechanism of 'ferromagnetic resonance' resulting in a local heating of the magne-

tosomes' environment. However, Kirschvink himself estimated the temperature rise as being so small that one can not speak of a biological relevance ($=10^{-4}$ ° C, i.e. less than $1/10000$ ° C at a cell exposed to mobile radio frequencies with a strength of 10 mW/cm²). Moreover, the magnetosomes within the cells are surrounded by an electrically isolating layer, the double membrane (consisting of phospholipid molecules). This isolation effect diminishes induced currents (eddy currents) in the environment of magnetosomes further inhibiting an effective heating - a factor that was partially overlooked in recent studies (Dobson et al. 2000). The possibility of local heating caused by magnetosomes was dismissed by the participants of the workshop.

However, in William Pickard's view it is conceivable that a phonon separated by a HF field from the magnetite ('sound quantum', 'lattice vibration quantum'; hypothetical elementary particle that can act as an energy conductor at electromagnetic radiation similarly to the photon) can alter f.e. a protein within the cell membrane (here a 'transmembrane protein') in such a way that it reacts chemically altered at its end at the cell outer wall. To completely exclude effects caused by magnetites, according to Pickard one would still have to show that the material can not pass on the possibly absorbed energy to further use (i.e. altering something).

The 'radical pair mechanism' (RPM) leading to the development of the (in living cells chemically aggressive reacting) 'free radicals' was among others described for the impact of strong (Steiner & Ulrich 1989), but also for relatively weak (Grisson 1995) static magnetic fields. The present scientists did not discuss this topic in detail, since no corresponding effects of HF fields are known.



- However it was pointed to the requirement of theoretical calculations to determine the limits of applicability of the RPM for the area of mobile radio high-frequency fields.

Results

On the whole, the Washington workshop identified artificial heating of biological material as the only logical and seemingly physically possible mechanism scientifically proved for an effective interaction with high-frequency fields of mobile radio. However, a number of other mechanisms are conceivable and/or already proved as effective in other areas. Future theoretical analyses and possibly their experimental exploration are necessary to examine certain other or newly proposed mechanisms to see for which frequency, intensity and biological target areas they are true at all, i.e. where they have an effective impact. The initially mentioned follow-up workshop on this topic the FGF will organise in December 2001 in Dresden is meant to make a contribution to the scientific exchange of special knowledge and the views of the respective experts required to this end.

Dr. Frank Gollnick as a biologist for a long time was staff member at the Physiological Institute of the University Bonn and is now scientific consultant of the FGF.

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