

Evaluation of Specific Absorption Rate as a Dosimetric Quantity for Electromagnetic Fields Bioeffects

Dimitris J. Panagopoulos^{1,2*}, Olle Johansson³, George L. Carlo⁴

1 Department of Biology, University of Athens, Athens, Greece, **2** Radiation and Environmental Biophysics Research Centre, Athens, Greece, **3** Experimental Dermatology Unit, Department of Neuroscience, Karolinska Institute, Stockholm, Sweden, **4** The Science and Public Policy Institute, Institute for Healthful Adaptation, Washington, D.C., United States of America

Abstract

Purpose: To evaluate SAR as a dosimetric quantity for EMF bioeffects, and identify ways for increasing the precision in EMF dosimetry and bioactivity assessment.

Methods: We discuss the interaction of man-made electromagnetic waves with biological matter and calculate the energy transferred to a single free ion within a cell. We analyze the physics and biology of SAR and evaluate the methods of its estimation. We discuss the experimentally observed non-linearity between electromagnetic exposure and biological effect.

Results: We find that: a) The energy absorbed by living matter during exposure to environmentally accounted EMFs is normally well below the thermal level. b) All existing methods for SAR estimation, especially those based upon tissue conductivity and internal electric field, have serious deficiencies. c) The only method to estimate SAR without large error is by measuring temperature increases within biological tissue, which normally are negligible for environmental EMF intensities, and thus cannot be measured.

Conclusions: SAR actually refers to thermal effects, while the vast majority of the recorded biological effects from man-made non-ionizing environmental radiation are non-thermal. Even if SAR could be accurately estimated for a whole tissue, organ, or body, the biological/health effect is determined by tiny amounts of energy/power absorbed by specific biomolecules, which cannot be calculated. Moreover, it depends upon field parameters not taken into account in SAR calculation. Thus, SAR should not be used as the primary dosimetric quantity, but used only as a complementary measure, always reporting the estimating method and the corresponding error. Radiation/field intensity along with additional physical parameters (such as frequency, modulation etc) which can be directly and in any case more accurately measured on the surface of biological tissues, should constitute the primary measure for EMF exposures, in spite of similar uncertainty to predict the biological effect due to non-linearity.

Citation: Panagopoulos DJ, Johansson O, Carlo GL (2013) Evaluation of Specific Absorption Rate as a Dosimetric Quantity for Electromagnetic Fields Bioeffects. PLoS ONE 8(6): e62663. doi:10.1371/journal.pone.0062663

Editor: Nils Cordes, Dresden University of Technology, Germany

Received: November 21, 2012; **Accepted:** March 22, 2013; **Published:** June 4, 2013

Copyright: © 2013 Panagopoulos et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: The authors have no support or funding to report.

Competing Interests: The authors have declared that no competing interests exist.

* E-mail: dpanagop@biol.uoa.gr

Introduction

Specific Absorption Rate (SAR) is defined as the amount of absorbed non-ionizing radiation power (or rate of absorbed energy) by unit mass of biological tissue.

The reason for the introduction of SAR as a non-ionizing radiation – Radio Frequency (RF) Electromagnetic Field (EMF) dosimetric quantity, was – as with the rate of absorbed dose in the ionizing case – to describe the amount of absorbed energy and the rate by which it is absorbed within an exposed tissue and not just the radiation/field intensity on its surface. This derives from the fact that when radiation exposes matter, most usually, it does not interact completely with it and in such a case only a part of its energy gets absorbed. The remainder just passes through without affecting the medium.

The amount of absorbed energy by a certain amount of matter (within a certain time interval) will determine the degree of interaction. But in the case of biological matter this is not as

simple. Biological tissue is a much more complicated and organized form of matter compared to inanimate. The degree of interaction does not necessarily determine the biological effect because that depends on which specific bio-molecule – or set of bio-molecules – from a whole tissue or organ will interact with the radiation. Some bio-molecules may get damaged while others may not by the same amount of radiation energy absorbed within the same time-interval.

Interaction between man-made electromagnetic radiation and living matter

Man-made electromagnetic waves are produced by electromagnetic oscillation circuits (“Thomson” circuits), not by atomic events (as in the case of natural electromagnetic radiation – infrared, visible, ultraviolet, x-rays, γ), and for this they are polarized in contrast to natural electromagnetic radiation that is not. The plane of polarization is determined by the geometry of

the circuit. Polarized electromagnetic waves (in contrast to non-polarized) can produce interference effects and induce coherent forced-vibrations on charged/polar molecules within a medium.

When a polarized, non-ionizing electromagnetic oscillation – wave – passes through a mass of polar and charged molecules, such as those composing biological tissue induces a forced-oscillation on each of these particles that it meets and transfers to each of them a tiny part of its energy. This induced oscillation will be most intense on the free particles which carry a net electric charge such as the free (mobile) ions that exist in large concentrations in all types of cells or extracellular biological tissue determining practically all cellular/biological functions [1,2]. The induced oscillation will be much weaker or even totally negligible on the polar biological macromolecules and the water molecules that do not have a net charge and additionally are usually bound chemically to other molecules.

After each such event of interaction between the wave and a charged or polar particle, the remaining wave continues on its way through the tissue possibly scattered by a tiny angle and reduced by a tiny amount in its amplitude/intensity. After large numbers of such events, depending on the tissue's mass, density, and the number of polar/charged molecules, the remaining wave, if any, leaves the tissue as a scattered wave of reduced amplitude/intensity.

When the amplitude/intensity E of the oscillating field or wave is decreasing after interaction with the charged/polar molecules of a medium, its energy density decreases as well, according to the equation for the energy density of a plane, harmonic electromagnetic wave (as those usually produced by “Thomson” circuits):

$$W_{em} = \epsilon \epsilon_0 E^2 \quad (1)$$

W_{em} is the total energy per unit volume of the electromagnetic wave, and E the intensity of the electric component of the wave within a medium with relative permittivity ϵ . $\epsilon_0 = 8.854 \times 10^{-12} \text{ C}^2/\text{N}\cdot\text{m}^2$ is the vacuum permittivity.

That means that a part of its energy per unit volume is transferred to the charged/polar molecules of the medium.

The amount of energy absorbed by a single free ion within biological tissue will manifest itself as kinetic energy of the forced-oscillation induced on that particle. The maximum kinetic energy of the forced-oscillation is given by:

$$\epsilon_i = \frac{1}{2} m_i u_o^2 \quad (2)$$

where, m_i is the ion mass which in the case of a Na^+ ion, is $m_i \cong 3.8 \times 10^{-26} \text{ kg}$. u_o is the particle's maximum velocity of the forced-oscillation assumed to be equal to $\cong 0.25 \text{ m/s}$, which is the drift velocity of Na^+ ions along an open trans-membrane sodium channel, as calculated by patch-clamp ionic current measurements through open channels [3–5]. This maximum velocity (and kinetic energy) of the free ion is independent of the frequency of the external field [5,6].

From Eq. (2) we get that the energy absorbed by a single ion due to the interaction with the electromagnetic wave, is: $\epsilon_i \cong 1.2 \times 10^{-27} \text{ J}$.

Considering that the concentration of free ions within cells is on the order of 1 ion per nm^3 [1] and a typical cell volume up to $10^3 \mu\text{m}^3$, a single cell contains about 10^{12} free ions and thus it will absorb about $10^{12} \times 10^{-27} \text{ J} = 10^{-15} \text{ J}$. A human body of average size consisting of $\sim 10^{14}$ cells, will absorb about $10^{14} \times 10^{-15} = 10^{-1} \text{ J}$. For waves emitted by a supposed

unidirectional antenna operating with 1 W (= 1 J/sec) output power, (thereby transmitting energy 1 J per sec) it takes about 10 human bodies in sequence in order to be totally absorbed, according to the above mechanism, which seems a reasonable result.

But as mentioned already, except of the energy absorbed by mobile ions within biological tissue there will be additional energy absorption by the water dipoles and the charged or polar macromolecules like proteins, lipids, or nucleic acids, which will also be forced to oscillate by the applied field. While we can have an estimation as shown above for the energy absorbed by mobile ions, we are unable to estimate much smaller amounts of energy absorbed by charged or polar biological molecules. These smaller amounts of energy may be of decisive importance for the biological effect.

Even if we could accurately estimate macroscopically the amount of absorbed energy by a whole organ (e.g. by measuring an increase in temperature if any), again the biological effect depends basically on which specific bio-molecule(s) will absorb a certain amount of energy during a certain time-interval and this is impossible to discern. For example, when radiation is absorbed by lipids the damage will most likely be less than when the same amount of energy is absorbed within the same time-interval by enzymes and potentially even smaller than when absorbed by nucleic acids – especially DNA. Moreover, the situation becomes even more complicated in case that the biological effects are indirect. For example, a damage in the DNA may be due not to the energy absorbed directly by the DNA molecule but due to a conformational change in a membrane protein leading to irregular alteration of intracellular ionic concentrations [5,6] and this in turn giving a signal for a cascade of intracellular events causing irregular release of free radicals or DNases which finally damage DNA (indirect effect).

Thus, even if we were able to determine the total amount of energy absorbed by an organ, tissue, or even a single cell during a certain time-interval, we still are not able to know the biological effect because this depends on the amounts absorbed by a variety of different biomolecules presenting widely varying interactive sensitivities to the radiation. In regard to ionizing radiation, this is well established. More specifically, it is well known that the biological effects of ionizing radiation depend a) on the type of ionizing radiation; it is known that equal doses (absorbed energy per unit mass of biological tissue, in $\text{Gy} = \text{J/kg}$) of different radiation types (e.g. alpha, beta, gamma, x, etc) absorbed during the same time-interval, result to different biological effects on the same type of biomolecule/tissue, b) on the type of biomolecule/tissue that absorbs a certain dose at a certain rate; a certain dose of a specific type of radiation – absorbed within a certain time-interval – will induce different effects on different biomolecules/tissue-types depending on their sensitivity and size [7,8,9]. We may then reasonably speculate that respectively, different types of non-ionizing radiation of the same SAR (differing between them in modulation, frequency, polarization, wave shape, etc) will induce different effects on a given type of biomolecule/tissue and moreover, that sensitivity of different biological molecules plays a crucial role in regard to the possibility of damage by a specific type of non-ionizing radiation at a certain SAR as well. These important issues are not addressed by SAR dosimetry.

Thereby, it follows that in the case of biological matter, the amount of absorbed energy as well as the rate of its absorption (SAR) does not determine the biological effect.

The absorbed energy is normally well below the thermal level

While we are unable, as explained, to calculate accurately (microscopically) the absorbed energy at cellular level, we can estimate macroscopically with some satisfactory accuracy the energy absorbed by a whole body, or organ or tissue. But as we shall show (in the next section of the present study), only when the absorbed energy is large enough to cause measurable temperature increases. This naturally occurs when the absorbed radiation has a frequency above the lower limit of infrared which is about 3×10^{11} Hz [2]. Man-made microwave radiation used in modern telecommunications and other applications with frequencies 10^8 – 10^{10} Hz cannot directly cause temperature increases in biological tissue unless it is of large enough power density (well above 1 mW/cm^2). Radiation of even lower frequency would need to be of even larger power/intensity to produce thermal effects. Usual microwave intensities in modern human environment (mainly due to mobile telephony handsets and base station antennas, Wi-Fi, and radio-television station antennas) range between $0.01 \text{ }\mu\text{W/cm}^2$ and $100 \text{ }\mu\text{W/cm}^2$. Man-made radiation that has neither the frequency nor the intensity to cause thermal effects, it can still be absorbed – as explained above – in much smaller quantities by inducing forced-oscillations on polar molecules and free charges such as the free ions within all living cells. These forced-oscillations are superimposed on the thermal vibration of the same particles, increasing their thermal energy. But as we shall demonstrate, the energy of the oscillations induced by external EMFs at environmental exposure levels (intensities) is normally millions of times smaller than the average thermal energy kT of the molecules within a biological tissue, and thus does not produce measurable temperature increases. Although these induced oscillations (with kinetic energy usually millions of times lower than the average thermal energy) normally do not add to tissue temperature, they can still cause severe biological alterations (such as DNA damage) without heating the tissue [10]. These are called “non-thermal effects” and if not properly equilibrated by the organism’s immune and other compensatory systems, they may very well result in health effects [11–14].

The maximum velocity of the ion’s induced vibration is assumed to be, $u_o \cong 0.25 \text{ m/s}$ as explained, and the corresponding maximum kinetic energy calculated by Eq (2), is: $\epsilon_i \approx 10^{-27} \text{ J}$.

This ion possesses also an additional average velocity u_{kT} , due to its thermal energy. The average kinetic energy of a single-atom molecule/free ion due to thermal motion [15], is:

$$\epsilon_{kT} = \frac{1}{2} m_i u_{kT}^2 = \frac{3}{2} kT \tag{3}$$

which gives:

$$u_{kT} = \sqrt{\frac{3kT}{m_i}} \tag{4}$$

where $T = 310 \text{ }^\circ\text{K}$ (the temperature of the human body 37°C), $k = 1.381 \times 10^{-23} \text{ J}\cdot\text{K}^{-1}$ the Boltzmann’s constant, and m_i the ion’s mass ($m_i \cong 3.8 \times 10^{-26} \text{ kg}$ for Na^+ ions) [5,6].

From Eq (3), (4) we get: $\epsilon_{kT} \cong 6.4 \times 10^{-21} \text{ J}$, and $u_{kT} \cong 0.58 \times 10^3 \text{ m/s}$.

Comparing the values of the above two different velocities/energies we find that, the maximum velocity acquired by a free ion within a cell due to an environmental EMF is normally about

$2.3 \times 10^3 (\cong \frac{u_{kT}}{u_o})$ times smaller than its average thermal velocity

and its corresponding maximum kinetic energy $\epsilon_i = \frac{1}{2} m_i u_o^2$ induced by the environmental EMF is about 5.3×10^9 times smaller than the average thermal energy $\frac{3}{2} kT$ of such a particle.

The average values of the environmental EMF-induced velocity and kinetic energy are even smaller than the above average thermal values.

Thereby, we have shown that oscillations induced on biological molecules by environmental EMFs do not usually contribute to the tissue temperature, except if these fields were millions of times more powerful, like for example the fields within a microwave oven operating at about 1000 W and focusing all of its radiating power within its cavity, in contrast to e.g. a GSM (Global System for Mobile telecommunications) mobile phone (~ 0.1 – 1 W) or even a mobile telephony base station antenna (~ 10 – 100 W) radiating (and distributing their energy) in all directions within wide angles.

Except of the tissue heating by high-power microwave radiation, the induction of small temperature increases on the order of 0.15 – 0.3°C has been reported after exposure of biological samples (*C. elegans*) to continuous wave 1 W , 1 GHz microwave radiation within a Transverse Electro-Magnetic (TEM) cell [16]. Nevertheless, in real exposure conditions as e.g. in the case of a GSM mobile phone during normal “talk” operation the average power density even in contact with the antenna hardly exceeds 0.2 – 0.3 mW/cm^2 and does not induce temperature increases at a 0.05°C level as shown by use of a sensitive Hg thermometer with 0.05°C accuracy [17,18]. Similar findings are also presented by other experimenters [19,20]. Human exposure from base station antennas at a distance of a few meters is normally of even lower power densities.

Thus, environmental man-made EMFs are indeed unlikely to induce temperature increases in biological tissue, not even at the level of 0.05°C . Even the well-established thermal effect of “microwave hearing” attributed to thermo-elastic waves induced within the human/animal head by pulsed microwave radiation is calculated to correspond to temperature increases at a threshold of only $5 \times 10^{-6}^\circ\text{C}$ [21]. Moreover, in the present paper it is shown theoretically that the energy absorbed by moving particles (free ions) within biological tissue due to environmental EMFs is millions of times smaller than the average thermal energy of such particles. Therefore if any temperature increases occur within biological tissue during exposure to environmentally accounted EMFs, they will normally be several orders of magnitude below 1°C and thus are not detectable.

The fact that the energy absorbed by living organisms due to the action of environmentally accounted man-made EMFs is indeed millions of times smaller than the average bio-molecular thermal energy, is the main reason why initially it was believed by scientists and authorities that environmental EMFs could not induce any biological effect [22]. That was based on the arbitrary hypothesis that an external EMF can only affect a living organism by increasing its temperature. Therefore, any non-thermal biological effect due to environmental man-made EMFs should be either not real, or attributed to hypothetical mechanisms such as the “stochastic resonance” by which biological matter can allegedly amplify small bits of information in a “sea” of white (thermal) noise by using the energy of the noise [23]. Such speculations – although they cannot be excluded – are not anymore necessary, since it is now known that due to forced-oscillation, the coherent motion (in the same direction) of several charged particles (free

ions) within a cell in phase with a polarized external field can exert a larger resultant force on certain sensors (such as e.g. the voltage-sensors of electro-sensitive ion channels on cell membranes) than the mutually extinguishing forces on the same sensors due to their random thermal motions in all possible different directions [5,6].

Even though some scientists still express skepticism regarding the existence of non-thermal effects [24], there is already a large and constantly increasing number of studies indicating that environmental man-made EMFs can produce severe biological alterations such as DNA damage without heating the biological tissue [10,11,17–20,25–32]. This can take place through non-thermal mechanisms that involve direct changes in intracellular ionic concentrations or changes in enzymatic activity [5,6,33–35]. DNA damage may lead to cancer, neurodegenerative diseases, reproductive declines, or even heritable mutations. Brain tumors, decrease in reproductive capacity, or symptoms reported as “microwave syndrome” (headaches, memory loss, fatigue, etc), are observed among people exposed to mobile telephony radiation during recent years [30,36–45]. Recently the International Agency for Research on Cancer (IARC) has classified RF/microwave EMFs as “possibly carcinogenic to humans” [46].

The physics and biology of SAR

Usually, SAR values are reported in papers regarding exposure of biological material to RF EMFs, without any information about their calculation and without reporting the corresponding error.

As already mentioned, SAR is defined as the ratio of the absorbed power P , per unit mass of tissue, (in W/kg). To be more accurate, since electric power is not equally absorbed by different parts of biological matter, SAR is defined as the incremental power dP absorbed by an incremental mass of the tissue dm contained in a volume element dV of a given density ρ [47]:

$$SAR = \frac{dP}{dm} \tag{5}$$

where $dm = \rho dV$, (ρ in kg/m^3).

Using Ohm’s law:

$$j = \sigma \tag{6}$$

where j is the electric current density (in A/m^2) within the tissue due to the internal electric field E generated within the tissue, and σ the specific conductivity of the tissue (in S/m), relation (5) after operations (see Appendix S1), becomes:

$$SAR = \frac{\sigma \cdot E^2}{\rho} \tag{7}$$

From the derivation of the last relation for SAR (Appendix S1) it is obvious that the quantities: j (generated current density), E (generated internal electric field), ρ (tissue density), σ (tissue conductivity) are assumed to be constant within an organ (e.g. eye) or a group of organs (e.g. head) of a living body where we want to calculate SAR. This, of course, is an oversimplification since every organ or group of organs consists of many different types of biological tissue and all the above quantities vary significantly between different biological tissues and even within a single type of tissue and within a single cell.

More specifically, conductivity varies for different tissues and different field frequencies. For example at a frequency of 1 GHz, conductivity in different tissues of the human body can vary from

about 0.04 S/m (bone marrow) to about 2.45 (cerebro-spinal fluid). Moreover the conductivity of a given tissue type increases considerably and non-linearly with frequency (up to a hundred times for a frequency range between 10^5 – 10^{10} Hz) [48]. Even within a single cell, conductivity can have large variations from 10^{-7} S/m (cell membrane) to 0.5–1 S/m (cytoplasm, extracellular aqueous solution) [49,50].

In addition, the available data on tissue conductivity are collected from measurements on dead animals and include large variations in relation to both tissue type and frequency range [48,51]. These variations become even larger at *in vivo* conditions in alive animals. Higher conductivity values up to ~300% than those previously reported, were recently measured in porcine organs of just sacrificed animals. The differences were attributed to the fact that the organs were still alive and filled with blood during the measurements in contrast to the previous studies which were performed on dead organs [52]. Moreover, the electrical properties of tissues – especially of the head – in all animals change with age. The relative permittivity of an adult human brain is calculated to be around 40 while the corresponding value for a young child’s brain is between 60 and 80 resulting in almost double the radiation absorption and SAR [53,54].

Moreover, human tissue density varies from about 900 kg/m^3 (fat) to about 1200 kg/m^3 (tumor) between different soft tissue types and reaches a value of about 1800 kg/m^3 for bones [51].

From this analysis it follows that Eq. (7) provides a poor definition of SAR due to the large variations of the related quantities, regardless of the estimating method. Thus, any estimating method for SAR based on Eq. (7) (see next section) includes a very large uncertainty.

For an homogeneous medium (thus neglecting again the local density variations) with specific heat c , [in $\text{J}/(\text{kg}\cdot\text{K})$] (thus neglecting also the local variations in the specific heat) and by use of a form of the calorimetry law:

$$\frac{dQ}{dt} = m \cdot c \cdot \frac{dT}{dt} \tag{8}$$

equation (5), becomes:

$$SAR = c \cdot \frac{dT}{dt} \tag{9}$$

where: $\frac{dQ}{dt}$ is the wave power, transformed into an incremental amount of heat dQ , within the tissue of mass m , producing an incremental temperature increase dT during the incremental time interval dt .

For a measurable time interval δt and a corresponding measurable temperature increase δT , Eq. (9) can be written as:

$$SAR = c \cdot \frac{\delta T}{\delta t} \tag{10}$$

Since variations in specific heat within biological matter are usually much smaller than corresponding variations in conductivity [48,51,55] resulting in a much more uniform temperature than electric field distribution, Eqs. (9), (10) provide a better way for SAR estimation and, consequently, definition.

In addition, while differences in internal electric field intensity are retained during the whole exposure period since they depend

on tissue permittivity which has large variations even within a single cell, differences in temperature between different locations of a tissue or organ are extinguished short time after the beginning of a constant exposure and temperature gets evenly distributed within a whole organ or even body. Moreover, while tissue conductivity and permittivity/internal electric field change significantly with different frequencies of the external field/radiation, specific heat is independent from the external field and depends only on tissue properties. In case of exposure to microwave radiation which includes more than one different frequencies (carrier, pulse, modulation frequencies), conductivity and internal field intensity depend on different simultaneous frequencies and their accurate estimation becomes, in any case, extremely complicated.

Even if we consider only one frequency and additionally neglect internal electric field intensity and density differences, conductivity variations alone result in a considerably larger variability of *SAR* as calculated by Eq (7) than by Eq. (10). For example, most organs/parts of the human/animal body contain both muscle and fat tissues. While at 1 GHz muscle conductivity (~ 1.006 S/m) is about 1760% higher than fat conductivity (~ 0.054 S/m), muscle specific heat (~ 3.5 kJ/kg·K) is only 56% higher than fat specific heat (~ 2.3 kJ/kg·K). This would result to a $\sim 1700\%$ larger variability in the *SAR* of this specific organ or part of the animal body when estimated by Eq (7) than when estimated by Eq. (10). At smaller frequencies conductivity variations increase considerably resulting in an even larger variability in the *SAR* calculation while specific heat has the same value. For example, at 10 MHz the above difference in *SAR* variability ($\sim 1700\%$) between Eqs (7) and (10) becomes $\sim 2125\%$ (or 21.25 times larger variability in *SAR* value according to Eq (7) than according to Eq (10)) [56,57]. If we add variations in internal electric field intensity and tissue density we may have hundreds of times larger variability in *SAR* values according to Eq (7) than according to Eq (10). Thus, while variation in *SAR* calculation according to Eq (10) is restricted to measurement errors and the assumption that ϵ has the same value throughout the tissue, which somehow can be tolerated, corresponding variation in *SAR* according to Eq (7) includes similar errors plus tenths or even hundreds of times larger variability. This shows exactly that the only way to estimate *SAR* with some satisfactory accuracy is by measuring macroscopically the corresponding temperature increases – if any – within biological matter.

Therefore, it follows that *SAR* actually applies only to thermal effects and it actually expresses the rate by which electromagnetic energy from an external electromagnetic wave/field is converted into heat within biological matter. But as we have shown already, man-made electromagnetic fields at environmental levels do not normally cause thermal effects (measurable temperature increases within exposed biological matter) and this is in agreement both with experimental studies [10,11,17–20,28,31,32,58] and plausible proposed mechanisms for the action of EMFs on cells [5,6,33–35]. Thereby, it follows that, *SAR* is not a proper measure to describe the biological activity of man-made electromagnetic fields at environmental levels.

The estimation of *SAR*

SAR is estimated by one of the following ways, [59]: 1) Insertion of micro-antennas or probes into the tissue, which detect the internal electric field. If the conductivity and the density of the tissue are known (assuming they have constant values) and neglecting local variations in internal field value, the *SAR* can be computed from Eq. (7). 2) Insertion of miniature thermal probes into the tissue. If a change δT in the temperature of the tissue is recorded, caused by the radiation/field during a time interval δt ,

and the tissue is supposedly homogeneous with known specific heat, then *SAR* can be computed by Eq. (10). 3) Numerical modeling, like the Finite Difference Time Domain, (FDTD) method, simulating the spatial distribution of the radiation energy within an object with the dimensions of the human body and computing *SAR* by Eq. (7). All the above ways/methods include significant error.

The first way does not take into account the local variations of conductivity, density and internal electric field within the tissue as explained already. Therefore this approach to *SAR* assessment is highly simplified compared to the complexity of real biological matter.

The second way provides a better approximation since temperature is much more evenly distributed within biological tissue than conductivity or electric field. But this assumes that there are detectable temperature increases (δT) – thus assuming solely thermal effects – while usually there are not as already shown, and additionally, the insertion of needles (thermal probes) disturbs any living tissue/organ and distorts its physical properties in unpredictable ways.

The third way, like the FDTD method, considered the best, simulates numerically the tissue by use of computers, dividing its volume into little pieces (voxels). Each voxel is assigned to certain values of conductivity, permittivity and density. Then *SAR* is again computed according to Eq. (7). Since within each voxel conductivity, permittivity, and density are assumed to be constant, this way also (alike the first way) represents an approximation and simplification. This is why earlier *SAR* estimations, defining the current criteria for whole body average *SAR* [60], are questioned by more recent and more accurate FDTD calculations [61–63]. In any case, all methods of simulation, no matter how much improved, are and will always be, highly simplified compared to living tissue, since they can never take into account the countless variations in the physical parameters of living matter especially at cellular level.

It follows that all the existing methods for *SAR* estimation, and especially those based on Eq (7), have serious deficiencies.

In addition, it becomes evident that all methods for *SAR* estimation are highly sophisticated, complicated, and time-consuming, so that *SAR* cannot be readily measured/calculated by use of the equipment of an ordinary radiation/biological laboratory.

The non-linearity between electromagnetic exposure and biological effect

Dosimetry in science is necessary in order to find a quantitative relationship between cause and effect. The more well defined this relationship, the more useful the dosimetry. By knowing the relationship between cause and effect, we can predict the effect for different values of the magnitude of the cause for which we might have no experimental data. The most accurate prediction is when the cause-effect diagram is a straight line, e.g., where doubling the cause doubles the effect. In such a case we say that the cause-effect relationship is linear.

The biological/health effects from man-made EMFs/non-ionizing radiation, do not follow a linear dose-response (or cause-effect) relationship according to the experimental evidence. Experiments have shown that, the absorption of a larger amount of energy by the same mass of a given tissue and within the same time-interval, does not necessarily induce a larger biological effect. In other words, a more intense field or larger *SAR* does not necessarily relate to a larger biological response or consequent health effect.

The non-linearity of biological effects of man-made EMFs, and especially RF/microwave fields modulated by Extremely Low Frequency (ELF) signals (0–300 Hz), where the largest effects do not correspond to the largest *SAR* or intensity values, has been reported in several experiments since the mid-seventies [64–67]. Since then, it has been repeatedly verified by numerous studies [18,31,68]. For example, in one of the studies regarding effect of GSM radiation on the permeability of the blood-brain barrier in rats, and although other studies found no effect on the blood-brain barrier [69], it was reported that the strongest effect was produced by the lowest *SAR* values which corresponded to the weakest radiation intensity [68].

Moreover, in several studies, regions of increased bioactivity called “windows” were recorded, where the biological effects reach a maximum compared to the effects at smaller or larger values of a physical parameter like the intensity (and thus *SAR*) or frequency of the radiation. The “windows” represent an as yet unexplained phenomenon of the biological effects of EMFs, where increased bioactivity appears within certain values of a physical parameter of the field/radiation, but not for lower or higher values of this parameter [18,31,67,70,71]. Recently an intensity window on the biological effects of mobile telephony radiation was discovered where the effect on DNA damage was more intense around the value of $10 \mu\text{W}/\text{cm}^2$ in terms of the microwave – carrier – radiation intensity, than for intensities larger than $250 \mu\text{W}/\text{cm}^2$. More specifically, the borders of this “window” were found to be located between 8 and $28 \mu\text{W}/\text{cm}^2$ [18,72].

In such a case of non-linearity, the inaccuracy between cause and predicted effect can be large. We should not make it even larger by using a dosimetric quantity that is further inaccurately estimated such as the *SAR*. Instead, we should at least use a measure that can be known more precisely.

Such a more precise quantity is the radiation/field intensity on the surface of the biological object as measured by any qualified and calibrated radiation/field meter (plus the additional physical parameters of the field/radiation which can also be accurately known, such as pulse and/or carrier frequency, waveform, modulation etc).

Any inaccuracy in the intensity measurement, as for example it may occur within an antenna’s reactive near field, would be further increased in a corresponding *SAR* estimation. More specifically, if the electric field intensity E varies significantly within an antenna’s near field, the corresponding *SAR* value depending on E^2 (according to Eq. 9) will include this variation plus the variation in the conductivity and density of the biological matter.

The reason for the non-linearity between electromagnetic exposure and biological effect may well be exactly the fact that the amount of absorbed energy or the rate of its absorption (*SAR*, field intensity) does not determine the biological effect as we explained. Indeed, the amount of absorbed energy during a certain time-interval (in other words the rate of energy absorption) increases with increasing intensity or *SAR*. If the corresponding biological effect increased proportionally, there would be no “windows” or other non-linear effects in regards to intensity or *SAR*. Nevertheless such effects exist and they are repeatedly recorded since the mid-seventies.

Finally, the non-linearity of several types of biological effects has been reported regardless of exposure to EMFs, and in response to a variety of external factors such as ionizing radiation, physiological, pharmacological, or chemical agents, environmental contaminants, etc [73–78], indicating that a non-linear response to environmental factors is intimately associated with living matter.

Discussion and Conclusions

As explained, the only way that *SAR* can be calculated more accurately is through Eq. (10) by measuring temperature increases within the exposed biological tissues. But as shown in the present study, man-made EMFs at environmental levels do not normally cause measurable temperature increases except if they were millions of times more powerful. Thus, *SAR* – although not formally introduced specifically as a thermal term – actually refers only to thermal effects while the vast majority of the reported effects from environmental EMFs are non-thermal.

Moreover, as we explained, even if *SAR* for a whole body, organ, tissue, or even a single cell could be accurately estimated for exposures to environmentally accounted man-made EMFs, the biological effect depends on which specific biomolecule(s) absorb certain amount of energy within a certain time-interval, and this is impossible to discern.

Further, *SAR* offers no information at all with respect to frequency, waveform, or modulation of the EMF/radiation although these parameters are directly related in the literature to biological (and consequent health) effects. More specifically, it is repeatedly reported that amplitude-modulated or pulsed fields are more bioactive than non-modulated or continuous fields of the same carrier frequency, and the same average intensity (and thus the same *SAR*) [31,64–67,79–87]. Moreover, it is reported that signals of the same *SAR* but with different modulation types produce different effects in the same biological sample [79,81,84]. Real voice-modulated electromagnetic waves are considered to be more bioactive than simulated/periodically-modulated waves of similar other parameters and of the same *SAR* [10,28,31,58]. In some cases it is also reported that microwave radiation modulated in amplitude by an ELF field, produced similar effects with the specific ELF field alone [84].

A plausible explanation for the reported increased bioactivity of the ELF components of a microwave field can be given by the “ion forced-oscillation theory” [5,6], according to which the bioactivity of oscillating EMFs is inversely proportional to the frequency of the field and directly proportional to the amplitude of the forced-oscillation induced on free ions in the vicinity of cell membrane electro-sensitive channels within the exposed biological tissue. Moreover, according to the same theory, pulsed fields are twice as much bioactive than the corresponding continuous wave (CW) fields with identical other parameters [5,6] and this explains the results of several studies reporting that pulsed fields are more bioactive than the corresponding CW ones [80,82,85,86].

A significant effect of carrier and modulation/pulse repetition frequency in microwave radiation is also indicated by several studies which have reported that fields of the same *SAR* but of different carrier or modulation frequencies produced different biological effects on the same biological sample [71,88–90].

The above evidence regarding the importance of modulation and frequency of EMFs in regard to their biological activity is in total contradiction with any *SAR* approach, since it becomes evident that *SAR* alone – even if accurately estimated – is inadequate for predicting the biological effect, and the type of modulation as well as the frequency (modulation/pulse, carrier) have to be considered.

Thus, not only the biological effect depends upon undetermined tiny amounts of energy/power absorption by specific biomolecules exhibiting different sensitivities to the specific external field/radiation, but, moreover, it depends upon characteristics of the field/radiation, not taken into account in *SAR* calculation, such as modulation and frequency. Moreover, as explained, *SAR* estima-

tion encounters significant error, especially in the case of environmentally accounted man-made EMFs.

In contrast to *SAR*, the characteristics of the external field, (intensity, frequency, etc.), can at the very least be measured much more accurately in any case. In case that the biological object is exposed within the reactive near field of an antenna where large variations of the intensity occur, *SAR* would be even more inaccurately estimated.

For taking into account possible field distortion by the exposed biological object due to possible resonance phenomena and localized regions of enhanced radiation absorption, although such phenomena are not expected to alter significantly the field, radiation/field intensity measurements must be carried out both in the presence and in absence of the biological object and in different locations corresponding to different parts of its surface. In case that the measured values in presence and in absence of the object are significantly different between them, both sets of measured values must be reported.

Certainly, because of the usually accounted non-linearity in the response of living matter to different external/environmental agents and especially to EMFs, neither *SAR*, neither radiation/field intensity are expected to be precise predictors of the induced biological effects. But at the very least, radiation/field intensity can be readily and more accurately measured than *SAR* can ever be estimated, especially for environmentally accounted man-made EMFs.

We conclude that *SAR* should not be considered as a proper dosimetric quantity to describe non-thermal effects which constitute the vast majority of the effects produced by man-made EMFs in our everyday environment. *SAR* should only be used complementarily to intensity measurements and the methods of its calculation along with the corresponding error should always be reported so that the reader can have information about the variability of the stated *SAR* values. For the same reason the

radiation/field meter type and model used to measure the exposing field should always be reported in papers plus the variability (e.g. standard deviation) of the measured intensity values.

As increasing evidence is being accumulated for intense biological activity of man-made EMFs with consequent adverse effects on the human health and the natural environment, the need for fast and reliable measurement/dosimetry of such fields is becoming demanding. Thus, the measurement/dosimetry of EMFs should be easily performed by biological/radiation laboratories around the world by proper use of accurate field/radiation meters which are readily available in the market and easy to be used by qualified scientists/technicians, and not be based on complicated, time-consuming, and largely inaccurate methods of *SAR* estimation that cannot be readily performed.

Supporting Information

Appendix S1

(DOC)

Acknowledgments

This study was supported by the University of Athens, Greece, the Swedish Allergy, Cancer and Diabetes Foundation, and the Karolinska Institute, Stockholm, Sweden. The contribution of Prof. A. R. Liboff with remarks and suggestions on the manuscript is gratefully acknowledged. The Irish Doctors Environmental Association, the Alliance for Irish Radiation Protection, Daryl Vernon, and Brian Stein, are gratefully acknowledged for their general support.

Author Contributions

Analyzed the data: DJP OJ GLC. Wrote the paper: DJP OJ GLC. Conceived and designed the study: DJP. Performed calculations: DJP.

References

- Alberts B, Bray D, Lewis J, Raff M, Roberts K, et al. (1994) *Molecular Biology of the Cell*. Garland Publishing, Inc, NY, USA.
- Panagopoulos DJ, Margaritis LH (2003) Theoretical Considerations for the Biological Effects of Electromagnetic Fields, In: Stavroulakis P, ed. "Biological Effects of Electromagnetic Fields", Springer: 5–33.
- Neher E, Sakmann B (1992) The patch clamp technique. *Scientific American* 266: 28–35.
- Stryer L (1996) *Biochemistry*, 4th ed., WH Freeman and Co, NY, U S A.
- Panagopoulos DJ, Messini N, Karabarounis A, Philippetis AL, Margaritis LH (2000) A mechanism for action of oscillating electric fields on cells. *Biochem Biophys Res Commun* 272: 634–640.
- Panagopoulos DJ, Karabarounis A, Margaritis LH (2002) Mechanism for action of electromagnetic fields on cells. *Biochem Biophys Res Commun*, 298(1): 95–102.
- Dertinger H, Jung H (1970) *Molecular Radiation Biology*. Springer, Berlin.
- Coggle J (1983) *Biological Effects of Radiation*. Taylor & Francis.
- Hall EJ, Giaccia AJ (2006) *Radiobiology for the Radiologist*. Lippincott Williams & Wilkins, Philadelphia.
- Panagopoulos DJ (2011a) Analyzing the Health Impacts of Modern Telecommunications Microwaves. In: Berhardt LV, ed. *Advances in Medicine and Biology*, Vol. 17. Nova Science Publishers, Inc, New York, USA.
- Johansson O (2009) Disturbance of the immune system by electromagnetic fields—A potentially underlying cause for cellular damage and tissue repair reduction which could lead to disease and impairment. *Pathophysiology* 16(2–3): 157–77.
- Carlo GL (1998) *Wireless Phones and Health: Scientific Progress*. Kluwer Academic Publishers, Boston MA, xiii, 413 pages.
- Carlo GL, Jenrow RS (2000) Scientific progress – wireless phones and brain cancer: current state of the science. *Med Gen Med* 2(3): E40. Wireless Technology Research, Washington, DC, USA.
- Carlo GL, Thibodeaux PG (2001) *Wireless Phones and Health: State of the Science*. Kluwer Academic Publishers, Boston MA, xii, 287 pages.
- Mandl F (1988) *Statistical Physics*. Wiley, 2nd edition.
- Dawe, Smith B, Thomas DW, Greedy S, Vasic N, et al. (2006) A small temperature rise may contribute towards the apparent induction by microwaves of heat-shock gene expression in the nematode *Caenorhabditis Elegans*. *Bioelectromagnetics* 27(2): 88–97.
- Panagopoulos DJ, Chavdoula ED, Nezis IP, Margaritis LH (2007) Cell Death induced by GSM 900MHz and DCS 1800MHz Mobile Telephony Radiation. *Mutation Research* 626: 69–78.
- Panagopoulos DJ, Chavdoula ED, Margaritis LH (2010) Bioeffects of Mobile Telephony Radiation in relation to its Intensity or Distance from the Antenna. *International Journal of Radiation Biology* 86(5): 345–357.
- Kwee S, Raskmark P (1998) Changes in cell proliferation due to environmental non-ionizing radiation 2. Microwave radiation. *Bioelectrochemistry and Bioenergetics* 44: 251–255.
- Velizarov S, Raskmark P, Kwee S (1999) The effects of radiofrequency fields on cell proliferation are non-thermal. *Bioelectrochemistry and Bioenergetics* 48: 177–180.
- Elder JA, Chou CK (2003): Auditory response to pulsed radiofrequency energy. *Bioelectromagnetics*. 6: S162–73.
- Adair RK (1991) Biological Effects on the Cellular Level of Electric Field Pulses. *Health Physics* 61(3).
- Kruglikov Dertinger (1994) Stochastic resonance as a possible mechanism of amplification of weak electric signals in living cells. *Bioelectromagnetics*. (6): 539–47.
- Verschaeve L, Juutilainen J, Lagroye I, Miyakoshi J, Saunders R, et al. (2010) In vitro and in vivo genotoxicity of radiofrequency fields. *Mutat Res*. 705(3): 252–68.
- Lai H, Singh NP (1995) Acute low-intensity microwave exposure increases DNA single-strand breaks in rat brain cells. *Bioelectromagnetics* 16(3): 207–10.
- Lai H, Singh NP (1997) Melatonin and a spin-trap compound block radiofrequency electromagnetic radiation-induced DNA strand breaks in rat brain cells. *Bioelectromagnetics*, 18(6): 446–54.
- Lai H, Singh NP (1996) Single- and double-strand DNA breaks in rat brain cells after acute exposure to radiofrequency electromagnetic radiation. *Int J Radiat Biol*. 69(4): 513–21.
- Panagopoulos DJ, Margaritis LH (2008) Mobile Telephony Radiation Effects on Living Organisms. In Harper A.C. and Bures R.V. eds, "Mobile Telephones: Networks, Applications and Performance", Nova Science Publishers, New York, 107–149.

29. Panagopoulos DJ (2012) Effect of Microwave Exposure on the Ovarian Development of *Drosophila melanogaster*. *Cell Biochemistry and Biophysics* 63: 121–132.
30. Phillips JL, Singh NP, Lai H (2009) Electromagnetic fields and DNA damage. *Pathophysiology*. 16(2–3): 79–88.
31. Goodman EM, Greenbaum B, Marron MT (1995) Effects of Electro-magnetic Fields on Molecules and Cells. *International Rev. Cytol.* 158: 279–338.
32. Carpenter RL, EM (1968) Evidence For Nonthermal Effects of Microwave Radiation: Abnormal Development of Irradiated Insect Pupae. *IEEE Transactions on Microwave Theory and Techniques*, 19(2): 173–178.
33. Liboff AR (1985) Cyclotron resonance in membrane transport. In Chiabrera A, Nicolini C, Schwan HP, eds. "Interactions between Electromagnetic Fields and Cells", Plenum Press, London.
34. Liboff AR, McLeod BR (1988) Kinetics of channelized membrane ions in magnetic fields. *Bioelectromagnetics* 9: 39.
35. Lednev VV (1991) Possible mechanism for the influence of weak magnetic fields on biological systems. *Bioelectromagnetics* 12: 71–75.
36. Khurana VG, Teo C, Kundi M, Hardell L, Carlberg M (2009) Cell phones and brain tumors: a review including the long-term epidemiologic data. *Surgical Neurology* 72(3): 205–14.
37. Hardell L, Carlberg M, Söderqvist F, Mild KH, Morgan LL (2007) Long-term use of cellular phones and brain tumours: increased risk associated with use for > or = 10 years. *Occup Environ Med.* 64(9): 626–32. Review.
38. Hardell L, Carlberg M, Hansson Mild K (2009) Epidemiological evidence for an association between use of wireless phones and tumor diseases. *Pathophysiology*. 16(2–3): 113–22.
39. Vignera SL, Condorelli RA, Vicardi E, D'Agata R, Calogero AE (2012): Effects of the Exposure to Mobile Phones on Male Reproduction: A Review of the Literature. *Journal of Andrology*, 33: 350–356.
40. Agarwal A, Deepinder F, Sharma RK, Ranga G, Li J (2008) Effect of cell phone usage on semen analysis in men attending infertility clinic: an observational study. *Fertil Steril.* 89(1): 124–8
41. Agarwal A, Desai NR, Makker K, Varghese A, Mouradi R, et al. (2009) Effects of radiofrequency electromagnetic waves (RF-EMW) from cellular phones on human ejaculated semen: an in vitro pilot study. *Fertil Steril.* 92(4): 1318–25.
42. De Iuliis GN, Newey RJ, King BV, Aitken RJ (2009) Mobile phone radiation induces reactive oxygen species production and DNA damage in human spermatozoa in vitro. *PLoS One* 4(7): e6446.
43. Levitt BB, Lai H (2010) Biological effects from exposure to electromagnetic radiation emitted by cell tower base stations and other antenna arrays. *Environ. Rev* 18: 369–395.
44. Navarro AE, Segura J, Portolés M, Gómez- Perretta de Mateo C (2003) The Microwave Syndrome: A Preliminary Study in Spain. *Electromagnetic Biology and Medicine*, 22 (2–3): 161–169.
45. Johansson O (2006) Biohypersensitivity: State-of-the-art of a functional impairment. *Electromag Biol Med.* 25: 245–258.
46. IARC (2011) IARC Classifies radiofrequency electromagnetic fields as possibly carcinogenic to humans. Press Release, 31 May 2011. Available: http://www.iarc.fr/en/media-centre/pr/2011/pdfs/pr208_E.pdf.
47. NCRP (1981) Radiofrequency electromagnetic fields. Properties, quantities and units, biophysical interaction and measurements. National Council on Radiation Protection and Measurements, Report No 67, Washington, DC.
48. Gabriel S, Lau RW, Gabriel C (1996a): The dielectric properties of biological tissues: II. Measurements in the frequency range 10 Hz to 20 GHz. *Phys. Med. Biol.* 41: 2251–2269.
49. Foster KR, Schwan HP (1989) Dielectric properties of tissues and biological materials: a critical review. *Critical reviews in Biomedical Engineering*, 17(1): 25–103.
50. Fear EC, Stuchly MA (1998) A novel equivalent circuit model for gap connected cells. *Phys. Med. Biol.* 43: 1439–1448.
51. Gabriel S, Lau RW, Gabriel C (1996b) The dielectric properties of biological tissues: III. Parametric models for the dielectric spectrum of tissues. *Phys. Med. Biol.* 41: 2271–93.
52. Spottorno J, Multigner M, Rivero G, Alvarez L, de la Venta J, et al. (2012) In Vivo Measurements of Electrical Conductivity of Porcine Organs at Low Frequency: New Method of Measurement. *Bioelectromagnetics*, 33(7): 612–9.
53. Peyman A, Rezaadeh AA, Gabriel C (2001) Changes in the dielectric properties of rat tissue as a function of age at microwave frequencies. *Phys. Med. Biol.* 46(6): 1617–1629.
54. Christ A, Gosselin M-C, Christopoulou M, et al. (2010b) Age-dependent tissue-specific exposure of cell phone users. *Phys. Med. Biol.* 55: 1767–1783.
55. Haemmerich D, Schutt DJ, dos Santos I, Webster JG, Mahvi DM (2005) Measurement of temperature-dependent specific heat of biological tissues. *Physiol. Meas.* 26(1): 59–67.
56. Leonard J, Foster K, Athey T W (1984) Thermal properties of tissue equivalent phantom materials. *IEEE Transactions on Biomedical Engineering*, 31: 533–536.
57. IEEE (2002) IEEE Recommended Practice for Measurements and Computations of Radio Frequency Electromagnetic Fields With Respect to Human Exposure to Such Fields, 100 kHz–300 GHz. *IEEE Std C95.3TM–2002 (R2008)*.
58. Panagopoulos DJ (2011b) Biological Impacts, Action Mechanisms, Dosimetry and Protection issues of Mobile Telephony Radiation. In Barnes MC, Meyers NP eds, "Mobile Phones: Technology, Networks and User Issues", Nova Science Publishers, Inc., New York, USA.
59. Moulder JE, Erdreich LS, Malyapa RS, Merritt J, Pickard WF, et al. (1999) Cell Phones and Cancer. What is the Evidence for a Connection? *Radiation Research*, 151: 513–531.
60. ICNIRP (1998) Guidelines for limiting exposure to time-varying electric, magnetic and electromagnetic fields (up to 300 GHz). *Health Phys.* 74: 494–522.
61. Wang J, Fujiwara O, Kodera S, Watanabe S (2006) FDTD calculation of whole-body average SAR in adult and child models for frequencies from 30 Phys Med Biol 51(17): 4119–27.
62. Flyckt VM, Raaymakers BW, Kroeze H, Legendijk JJ (2007) Calculation of SAR and temperature rise in a high-resolution vascularized model of the human eye and orbit when exposed to a dipole antenna at 900, 1500 and 1800 Phys Med Biol. 52(10): 2691–701.
63. Gandhi Om P, Morgan LL, de Salles AA, Han Y-Y, Herberman RB, et al. (2012) Exposure Limits: The underestimation of absorbed cell phone radiation, especially in children. *Electromagnetic Biology and Medicine* 31(1): 34–51.
64. Bawin SM, Kaczmarek LK, Adey WR (1975) Effects of modulated VMF fields, on the central nervous system. *Annals of the N.Y. Academy of Sciences* 247: 74–81.
65. Bawin SM, Adey WR (1976) Sensitivity of calcium binding in cerebral tissue to weak environmental electric fields oscillating at low frequency. *Proceedings of the National Academy of Sciences of the USA* 73: 1999–2003.
66. Bawin SM, Adey WR, Sabbot IM (1978) Ionic factors in release of ⁴⁵Ca²⁺ from chick cerebral tissue by electromagnetic fields. *Proceedings of the National Academy of Sciences of the USA.* 75: 6314–6318.
67. Blackman CF, Benane SG, Elder JA, House DE, Lampe JA, et al. (1980) Induction of calcium – ion efflux from brain tissue by radiofrequency radiation: Effect of sample number and modulation frequency on the power – density window. *Bioelectromagnetics*, (NY) 1: 35 – 43.
68. Eberhardt JL, Persson BRR, Brun AE, Salford LG, Malmgren LOG (2008) - brain barrier permeability and nerve cell damage in rat brain 14 and 28 days after exposure to microwaves from GSM mobile phones. *Electromagnetic Biology and Medicine* 27: 215–229.
69. Stam R (2010) Electromagnetic fields and the blood-brain barrier. *Brain Res Rev.* 65(1): 80–97.
70. Blackman CF, Kinney LS, House DE, Joines WT (1989) Multiple power-density windows and their possible origin. *Bioelectromagnetics* 10(2): 115–128.
71. Liboff AR (2003) Ion cyclotron resonance in biological systems: experimental evidence. In: Stavroulakis P. ed. "Biological Effects of Electromagnetic Fields", Springer, 76–113.
72. Panagopoulos DJ, Margaritis LH (2010) The Identification of an Intensity "Window" on the Bioeffects of Mobile Telephony Radiation. *International Journal of Radiation Biology* 86(5): 358–366.
73. Calabrese EJ, Baldwin LA (2003) HORMESIS: The Dose-Response Revolution. *Annual Review of Pharmacology and Toxicology* 43: 175–197.
74. Samoilov MO, Lazarevich EV, Semenov DG, Mokrushin AA, Tyul'kova EI, et al. (2003) The Adaptive Effects of Hypoxic Preconditioning of Brain Neurons. *Neuroscience and Behavioral Physiology* 33(1): 1–11.
75. Mitchel RE (2006) Low doses of radiation are protective in vitro and in vivo: evolutionary origins. *Dose Response.* (2): 75–90.
76. Lenic S, Cortvrindt R, Eichenlaub-Ritter U, Smitz J (2008) Continuous exposure to bisphenol A during in vitro follicular development induces meiotic abnormalities. *Mutat Res.* (1–2): 71–81.
77. Averbek D (2010) Non-targeted a paradigm breaking evidence. *Mutat Res.* (1–2): 7–12.
78. Kundrát P, Friedland W (2012) Non-linear response of cells to signals leads to revised characteristics of bystander effects inferred from their modelling. *Int J Radiat Biol.* (10): 743–50.
79. Lin-Liu S, Adey WR (1982) Low frequency amplitude modulated microwave fields change calcium efflux rates from synaptosomes. *Bioelectromagnetics.* (3): 309–22.
80. Somosy Z, Thuroczy G, Kubasova T, Kovacs J, Szabo LD (1991) Effects of modulated and continuous microwave irradiation on the morphology and cell surface negative charge of 3T3 fibroblasts. *Scanning Microsc* 5(4): 1145–1155.
81. Veyret B, Bouthet C, Deschaux P, de Seze R, Geffard M, et al. (1991) Antibody responses of mice exposed to low-power microwaves under combined, pulse-and-amplitude modulation. *Bioelectromagnetics* 12(1): 47–56.
82. Bolshakov MA, Alekseev SI (1992) Bursting responses of Lymnea neurons to microwave radiation. *Bioelectromagnetics* 13(2): 119–129.
83. Thuroczy G, Kubinyi G, Bodo M, Bakos J, Szabo LD (1994) Simultaneous response of brain electrical activity (EEG) and cerebral circulation (REG) to microwave exposure in rats. *Rev Environ Health*, 10(2): 135–148.
84. Penafiel LM, Litovitz T, Krause D, Desta A, Mullins MJ (1997) Role of modulation on the effect of microwaves on ornithine decarboxylase activity in L929 cells. *Bioelectromagnetics* 18(2): 132–41.
85. Höytö A, Luukkainen J, Juutilainen J, Naarala J (2008) Proliferation, oxidative stress and cell death in cells exposed to 872 MHz radiofrequency radiation and oxidants. *Radiat. Res.* 170(2): 235–243.
86. Franzellitti S, Valbonesi P, Ciancaglini N, Biondi C, Contin A, et al. (2010) Transient DNA damage induced by high-frequency electromagnetic fields (GSM 1.8 GHz) in the human trophoblast HTR-8/SVneo cell line evaluated with the alkaline comet assay. *Mutat Res.* 683(1–2): 35–42.

87. Campisi A, Gulino M, Acquaviva R, Bellia P, Raciti G, et al. (2010) Reactive oxygen species levels and DNA fragmentation on astrocytes in primary culture after acute exposure to low intensity microwave electromagnetic field. *Neurosci Lett.* 31 473(1): 52–55.
88. Detlavs I, Dombrovska L, Turauska A, Shkirmante B, Sluskii L (1996) Experimental study of the effects of radiofrequency electromagnetic fields on animals with soft tissue wounds. *Sci Total Environ* 180(1): 35–42.
89. Marková E, Hillert L, Malmgren L, Persson BR, Belyaev (2005) Microwaves from GSM mobile telephones affect 53BP1 and gamma-H2AX foci in human lymphocytes from hypersensitive and healthy persons. *Environ Health Perspect.* (9): 1172–7.
90. Hinrikus H, Bachmann M, Lass J, Tomson R, Tuulik V (2008) Effect of 7, 14 and 21 Hz modulated 450 MHz microwave radiation on human electroencephalographic rhythms. *Int J Radiat Biol.* 84(1): 69–79.