More is Better Than One: The Strength of Interdisciplinarity

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Abstract Bioelectromagnetism, a scientific niche sector that studies the interaction of ElectroMagnetic Fields (EMF) with biological systems, is an interdisciplinary field of research. The following are just a few examples of current unanswered questions that still foster my interest. Could the exposure to Extremely Low Frequency (ELF) electric and magnetic fields generated by power lines, and Radio Frequency (RF) electromagnetic fields emitted by radio antennas and wireless networks cause possible adverse health effects? Could RF field exposures at realistic power densities cause systemic body warming in humans? Is warming the main cause of any observed RF fields effects? How can we explain RF field subtle effects or non-thermal effects at absorbed power level well below the existing safe exposure limits? Do we know RF field long-term effects? Do we know the biophysical interaction mechanisms between RF fields and biological systems that are caused other than a change in temperature? The rather complex structure of the human body and dosimetry—evaluation of the dose of RF fields when the human tissue is exposed- makes difficult the studies and the reported effects to be described by classical dose–response relationships. Furthermore, the intensity and frequency and/or modulation—the physical parameters of the electromagnetic field itself-dependence is not consistent with classical physicochemical responses of living systems to physical or chemical agents. Does this mean that we have to stop searching for answers? No, I don't think so. These are the intriguing issues that encourage the creativity of scientist across disciplines, who look for answers that will enhance humanity's knowledge as well as how we relate as humans to electromagnetism.

1 Motivations: How I Developed an Interest in Science

I enrolled in the Faculty of Pharmacy for family motives (my favourite aunt was a pharmacist), not because it was my preferred subject matter. However, later on I was to appreciate this choice, given the number of hours spent in the laboratory.

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I have always been fascinated by hands on research that made me feel active and elated, then, I became captivated by biochemistry; the study of matter made up of atoms that combined together form biomolecules; the study of complex chemical reactions and metabolism. What beauty existed within the understanding of all this knowledge! Every day, on leaving the university grounds, I found myself in front of the “Istituto Superiore di Sanita” (ISS), the National Institute of Health of Italy. I was curious and knew that inside that building, important medical research studies took place and that some Nobel Prize winners had carried out their researches there: biochemists such as, Ernst Boris Chain, who was the co-discoverer of penicillin, or Daniel Bovet, who discovered antihistamines. It is important to know the reputation of the place that will influence the choices of where to invest one’s future, therefore, I did everything to get into ISS. In the Laboratory of Toxicological Biochemistry directed by Prof. Vittorio Silano, a pure biochemist, I found what looked like an “artisan’s workshop”; a Master of great professional experience, who knew how to command even through his humanity; he was surrounded by talented biologists and chemists full of **enthusiasm**, who were assisted by highly qualified technicians, one of whom had worked directly with Daniel Bovet. There was passion; time spent in the laboratory seemed to fly and with total commitment I performed the tasks given to me. I was educated in the precision of measurements, **honesty** in recognizing a negative result, as well as critically interpreting every sort of scientific evidence, and always questioning my (and their) own ideas. I acquired experience on a great number of techniques that would later permit me to deal with the complex problems of biochemical research. In 1982, I was chosen among various research fellows to follow the studies started by a researcher (who was leaving for an internship), on the purification of a new α-amylase—an enzyme that hydrolyzes starch and glycogen-different from other α-amylase, which is well characterized and produced by *Bacillus subtilis*. The positive results were the subject of my first-first authored publication. This period of time in the laboratory at ISS proved fundamental for my scientific maturation, because it allowed me to acquire more awareness and familiarity with experimental work.

At the laboratory, there was a strong interest in ecotoxicology—a multidisciplinary field that integrates the concepts of toxicology and ecology—thus we began to study the enzymatic cytochrome dependent monooxygenases P-450. This system represents the main path of metabolism and drug detoxification in the human body. It was known that this metabolic system could also play a role in the transformation of some chemical substances (present in the environment) into carcinogenic substances. However, it was not known whether this metabolic system was present in some organisms situated on various levels of the biological scale, that were used in the laboratory as bioindicators since they were particularly sensitive to the changes made to the ecosystem that they inhabit. Thus, quails, trout and water fleas (*Daphnia magna*) appeared on our laboratory benches from which we had to extract the liver in order to characterize the said drug metabolism system. It was a very time consuming and meticulous job; imagine how much time and patience it takes to excise a sample of the liver from a water flea, a crustacean, measuring only a few centimetres. But, it turned out to be worthwhile as well, not only regarding the results of the experiments—we had discovered that even the water fleas have this metabolic system- but also because we received international and national funding that allowed us to buy laboratory equipment, never imagined possible before, such as a very expensive CARY double wavelength and beam spectrophotometer with which one attains superb differential spectra of the cytochrome P-450. Invitations began to arrive requesting us to present our results to the most important congresses; and, in my case, be chosen to participate in prestigious courses of study, such as the one promoted by UNESCO at the Stockholm Arrhenius Laboratory. There I was able to converse with scientists who represented all my bibliographic references like Joseph W. De Pierre, who was the first to characterize the P-450 metabolic system in a rat liver. However, it was my participation in a Summer School on the multidisciplinary evaluation of environmental risks on human health—held at the University of Siena in 1988—that was to consolidate my interest in interdisciplinary science. I felt at ease with other participants coming from various disciplines and other parts of the world (some of whom I am still in contact with today), as well as with professors, who ranged from entomologist to “disastrologo”, from biochemist to philosopher.

In 1990, prestigious scientists such as Nobel Laureate Rita Levi Montalcini, Enzo Bonmassar, and others decided to open a scientific “research area” at CNR in Rome, focused on interdisciplinary studies. I joined as a tenured researcher one of their Institutes to follow my interests in the development of biomimetic systems that imitate the function and the structure of a more complex biological system. Their applications can be diverse from the biological (proto cell, bioreactors) to the therapeutic sector (drug and vaccine delivery).

Later, my encounter with a group of electronic engineers collaborating with Prof. Guglielmo D’Inzeo, initiated my studies of Bioelectromagnetism. An area of study that was then developing, the purpose of which was to understand how living organisms interact with EMF, that is to say, that portion of the spectrum whose electromagnetic waves, these days, come exclusively from artificial and technological sources produced by man for electrification and radio communications. Gugliemo asked me to give lectures in his course, at “La Sapienza” University in Rome, on plasma membrane and its artificial models (i.e., liposome). He was always present at my lectures and, at the end of each one, he would continue to ask for more clarifications and insights, experiences that sometimes lasted as long as the lecture itself. I found the approach required by these studies intriguing (interdisciplinary, by its own nature); although it did call for a considerable effort to make engineers, biophysicists, pharmacists and biologists to break away their specialized language and find a common ground of communication. The results were such that dozens of students from electronic engineering applied for Master or Doctorate’s theses in my laboratory. At that time, there was no Faculty of Bioengineering! My expectations were high; it was well-known that the cell membrane was the primary target of the interaction between EMF and living organisms, however, by applying a simplification to this very complex cellular system, we would have been able to give a substantial contribution, at a molecular level, to the understanding of the biophysical mechanisms at the base of this interaction.

2 Work Done: My Personal Scientific Approach

I would never initiate a discussion with “We, the biochemists”, since I find it a bit annoying when those from other specializations do. I never felt like being a member of a corporation or association no matter how authoritative or respected. I consider the researcher’s skills at the same level as craftsman or creative artist with a practical understanding of the problems at hand, as well as the knowledge of the most appropriate ways to deal with them. I have always worked with dedication, constancy, and intelligence on my practices trying to improve and, therefore, innovate them. I have never been driven by the urgency to increase the number of my publications or to think that publication metrics are the primary means of being evaluated; and, I never stopped questioning my self, my colleagues, and the world around me regarding what I was doing. There are an infinite number of questions going on in the heads of people involved in science.

In the case of Bioelectromagnetism the questions that emerge can affect different fields of research: (*i*) biological ones: can we use the EMF, to which probably living organisms are not adapted, as probes to study the functions of living organisms? (*ii*) medical ones: overlapping external EMF with consequent modification of a physiological process can alter electromagnetically active processes of cells? and (*iii*) health: can the growing and continued exposure to EMF, virtually ubiquitous in the environment, have long-term consequences on human’s health? Under no circumstances, today, are there any definite answers.

With respect to health—my specific interest in the ELF electric and magnetic field—notwithstanding the initial scepticism of the scientific community with respect to the American epidemiological studies that, in 1979, had indicated a three-fold increase in the incidence of leukaemia in children residing near power lines; more than 2500 articles were published on the biological effects of EMF in the next thirty years. Clearly, though, the ELF-EMF generated for electrification have *very low* field frequencies and, therefore, carry much less energy than those involved in different chemical or physical phenomena that normally occur in biosystems and, based on the limits set by law, they are also at low intensity. Consequently, they do not directly interfere with the cellular electrical activities (for example nerve endings, muscles or heart). Despite the above, numerous studies in vitro (on cells) and in vivo (on animals) had indicated biological effects on cellular proliferation, on biomolecules (DNA, RNA, proteins), increase of cancer, and some functions of the cell membrane, such as the transport of calcium ions and ligand-receptor bonds. Due to its electrical properties and its function as a barrier to the outside, the cell membrane was indicated as the primary target of interaction with EMF and, most of all, the calcium ion (Ca^{2+}), whose physiological role as second messenger is to allow an external signal to propagate within the cell thus modulating several biochemical processes. Based on this ion, several mechanistic models have been identified, highlighting a crucial point for bioelectromagnetism regarding the interaction between ELF-EMF and membrane components, e.g. cyclotron ion resonance, a phenomenon related to the movements of ions in a magnetic field. However, these mechanisms were not able to explain all of the biological effects observed up until then, suggesting the possibility that there were multiple mechanisms or that there others primary targets should be considered. The latter was exactly what we explored together. With electronic engineers, with whom I collaborated, we focused our attention on the very components of the membrane (i.e., phospholipids) rather than free ions (i.e., calcium). To be able to do this, we needed a simpler model system than whole cell. The simplification of the complex world has always fascinated mankind, however, in the process of simplification, a scientific approach must always be adopted.

At that time, I was studying bioreactors in which an enzyme capable of catalyzing the study reaction was enclosed within a liposome. The liposome made up of phospholipids, mimics the structure and the function of the cell membrane, but compared to the latter, it has a decreased level of complexity in its molecular composition, thus allowing studies of the interaction of EMF with cell membrane at molecular level. The first series of experiments were disappointing because the effects of the ELF-EMF were at the limit of statistical variation and not reproducible, most likely, due to the fact that the detection of the effect on the membrane permeability was indirect: the sample was exposed to ELF-EMF and later the enzymatic activity was measured.

Was it possible to reveal the possible effect in real time during the exposure of the sample itself to reduce artefacts or a possible reversibility of the action? I pondered about this question day and night, even dreamt about it. Yes! The effect could be revealed in real time! It was the time of celebration when the new ELF-EMF exposure device, nicknamed "chick", due to its yellow colour, arrived at the lab. Inside this device it was possible to co-locate both the sample and the optical probe used to measure the enzymatic activity during the ELF-EMF exposure. Thus, the detection of the effect on the permeability function was direct in this case. We were the first to have a rigorous 'real time' experimental set-up, which was later adopted by the entire scientific community of bioelectromagnetics for in vitro studies. The experimental results were excellent and, above all, due to a brilliant piece of thinking by two of our young engineers, a clear correlation was found between experimental data and theoretical analysis and, consequently, a mechanism of interaction was hypothesized and proposed. They demonstrated with mathematical calculations that the energy (even if low) transferred by the ELF-EMF to a dipole, a component of the polar head of the phospholipids, was sufficient to give a small tap to the dipole and consequently make it rotate—like a balloon attached to a rod—thus modifying the very position of the phospholipids in the liposome. That was just enough to create a small free space, which, in turn, could alter the permeability function. The proposed biophysical mechanism, based on Larmor precession theory, made it possible to predict more specific biological effects as a function of well-established parameters of exposure to ELF-EMF. If our theory was right, then it had to also work on alternative membrane models ('theory testing is comparative'): that is what I verified developing several new artificial membrane models over the years. In one case, I was able to obtain, due to a *weak* serendipity (we had left the sample in the fridge for one night without processing it immediately), the first reconstitution of a functional gap junction in pairs of closely apposed lipid bilayers, as experienced in cells. Intercellular communications mediated by gap junction channels plays an important role in many cellular processes. Recently, we have built a bioelectrical model of a neural axon to study the effects of microwaves on the propagation of the electrical signal, with possible future medical applications.

Even though we obtained important results, regularly published in respected scientific journals, the topic was not considered to be sufficiently trendy for scientific journals with a very high impact factor. The difficulty of defining a dose for EMF exposure, due to the characteristics of frequency, intensity, modulation and exposure time, does not allow for the evaluation of the biological effects with a classic dose–effect relationship, and this creates perplexity about the possible sensitivity of biological organisms to EMF.

Besides that, thanks to the previously mentioned new experimental models, more targeted, rigorous and screening in vitro studies are being conducted today regarding the characteristics of EMF, laying the basis for future discoveries in the field of Bioelectromagnetism.

To conclude this section, I would like to emphasize the importance I have placed on the combination of research (producing knowledge) and teaching (transmitting knowledge), which, in my opinion, must remain indissoluble. In this regard, with considerable organizational and financial efforts, I founded an International Summer School at the CNR Research Area of Tor Vergata-Rome for the promotion and development of studies and research in the pharmaceutical, biomaterials, and tissue engineering and molecular simulation. The characteristic of this school is its interdisciplinarity. Postdoc students from all over the world and from different academic fields (physics, engineering, chemistry, biology, medicine, mathematics) follow highly specialized lecturers on cell model systems, given by internationally recognized professors, along with practical exercises on high level techniques and technological instruments (e.g. advanced sensors, precise analytical methods, enhanced imaging capabilities as well as sophisticated computational tools) conducted by physicists, engineers and mathematicians in the laboratories of the CNR Area.

3 Science Today and Tomorrow

The phrase that best summarizes my view of science was said back in 1986 by Rita Levi Montalcini, Nobel Laureate in Medicine: “Science is the only thing that distinguishes Homo Sapiens from the rest of living creatures. It must be **cultivated**, certainly not blocked.” Science must be cultivated because science proceeds in steps, and with the help of those who come first to those who come later, and mutual collaboration among scientists, it adds new discoveries to earlier discoveries in a continuum. It needs time “Tempore patet occulta veritas”—“The passing of time unveils the hidden truth” [was the motto on emblem of some of Sir Francis Bacon’s texts]. Therefore, typical of those who do scientific research is a sort of continuous and confident dedication driven by a desire *to unveil* something, proceeding by the sound method of trial and error in order to offer objective and reproducible answers, but not *absolute unchangeable truths.* Science therefore needs to be not only today but **always**. Yet society today has managed to upset this cornerstone, and on a par with everything else around us, it has become a here-today-gone-tomorrow fad.

Let us examine one case. As I mentioned in the previous section, numerous studies performed in the 1990's had indicated a possible correlation between exposure to EMF and the occurrence of harmful effects on human health. The term EMF, incomprehensible to most people, made its way from electrical engineering textbooks to newspaper articles. Even though the term remained largely misunderstood, it became familiar/common. The perception of the risk from exposure to EMF at an industrial and radio frequency (RF) spread and grew in the public mind to such an extent that decision makers were prompted to promote targeted research programs-selecting the type of questions in advance and narrowing their depth as much as possible, hoping to obtain *certain* acceptable answers and enabling the issuing of recommendations and regulations. Since science cannot be asked for answers it is incapable of giving, the results of these studies were not the absolute truth the bureaucrats hoped to receive. The results were devoid of cause-and-effect correlations with refutable epidemiological data and with contradictory in vivo and in vitro studies, meaning that no risk could be determined with sufficient certainty. The only well-established thing was that the power (measured in Watt/m^2) of RF fields had to be kept very low to avoid thermal effects. Therefore, exposure levels were set in the main EU countries, mainly based on the EU Council's 2001 precautionary principle, which had to be complied with-in order to protect the health of the population. Subsequently, the public's attention to these issues declined—it has been shown that humans are not rational at all when it comes to risk assessment—and as a consequence that of the decision-makers who are so very sensitive to public opinion. Over the last few decades very limited economic resources have been devoted, particularly in Italy, to *progressive* research programs—worthwhile ones according to Imre Lakatos's classification—because they delve deeper into topics. In those cases, curiosity-driven research, i.e., useless science, is welcome, much to the chagrin of EU agencies who favour projects with timescale prediction of the milestones (in year 1 discover this, in year 2 discover this) and fund on a publication basis (total number of publications in journals preferably with a high impact factor that strongly depends on the number of their readers, who in turn privilege hot topics and abstracts that attract attention). Meanwhile, industry and technological progress—though indirectly still a product of science—has moved on with all its social consequences. And here we are today with the advent of 5G—the fifth generation technology for mobile broadband networks that surpasses the 4G LTE commonly used today—that promises connectivity beyond all predictions and unprecedented integration with the virtual world -from driverless vehicles to the Internet industry, from smart cities to machine-to-machine communication (Internet of Things = IoT). To be able to live with such heavy data traffic we have to accept: (1) a change in currently used frequency channels to higher RF fields, and (2) an explosion of traffic between base transceiver stations (BTS). We are not prepared for this, and do not know if there may be risks for the health of the population. In Italy, to allow the 'applicability' of 5G and in the future of 6G now under development, exposure limits will have to be raised at least tenfold, in terms of electric field strength from 6 to 61 V/m, at the expense of the precautionary principle. It is desirable for future research to delve into the issue of the impact on the humans of the frequencies to be used in 5G and 6G. For example, we do not know what are the non-thermal effects even regardless of their power, nor do we know their long-term effects. Above all, however, we need to identify a relevant biophysical mechanism for the action of RF fields that is fundamental for interpreting non-linear results that do not fit into the usual cause-and-effect patterns. Thus, efforts should no longer be directed solely toward innovation and potential economic gains; they must also be directed toward avoiding undesirable consequences. Are citizens sufficiently informed about this? Scientific outreach (i.e., explaining the subject to the uninitiated) is needed more than ever and will need to be done with fairness, timeliness, and in comprehensible terms.

The great revolution nowadays is to develop and heighten people's numerical/scientific literacy because science must become part of our lives to build a better world.

4 Advice to the Next Generation of Scientists

I believe that participating in scientific research to learn and acquire new and greater knowledge of nature is a fascinating 'craft'. You may object, with cause, as I have been a scientist my whole life, but I am truly convinced of this. I deeply love my field of work and I truly believe that it can be extremely useful and helpful to humanity, though science may not always have an answer to every issue we have in today's society. For example science does not tell us who we are, or what values may benefit us all, it does not tell us how to live in peace or in a more equitable and fair world. It would be fair to acknowledge the value and relevance it simply has. If you have indeed chosen to pursue a profession in the sciences, but you are still unsure or undecided on about which field to enter, then challenge yourself by exploring other subjects, by asking questions, read materials and study. You could possibly explore these other fields in science other than those of your thesis or doctorate. Familiarity with scientific literature, while participating in lectures and conferences, is very useful in providing you with a deeper understanding of the opportunities, and finally with the laboratory you wish to join to expand your learning and your overall exploration of your selected field. In my opinion, a good environment, for a young researcher to grow and learn is a sort of 'renaissance artisan workshop', a smaller laboratory where to truly learn the craft, with a team of creative artists. In a creative laboratory the young researcher would be part of a smaller team, where the tendency to compete and envy, are curbed by teamwork and common goals. Teamwork will provide the young researcher with the tools, camaraderie, support that are necessary to explore her/his own individual creativity, (one must not forget that freedom in research and creativity are complementary and without the first the second cannot thrive).

Be mindful and use care when choosing a mentor and teacher, one with great professional experience (so that you will have the opportunity to learn from real-life experience, often not found in books that you have read during your academic career). Your mentor should be recognized among peers, and must be able to support your growth by sharing their experiences with kindness and empathy. The relationship should evolve and become familiar where as a young researcher you have the opportunity to learn daily, working, perhaps imitating at first and then creating your own way to investigate. A mentor should transmit technical knowledge to young researchers as well as allow them to experience the social and cultural environment of the scientist profession as well as expose them to the inter- and trans-disciplinary nature of science. In the twenty-first century it is essential that scientific work becomes trans-disciplinary, where work transcends the confines and boundaries of traditional scientific fields, where creativity allows for new research and knowledge. It is relevant to fully comprehend the interconnections that are formed by the multidimensional nature of our world. Once you have decided on the field you wish to pursue, put in your best effort to realize your goals, don't give up and never surrender to mediocrity, always aim to be the best you can be. The road will be uphill (saying this from personal experience), and does not always get easier as you progress in your career.

In the past we used to go to the library to research a topic, today when we are interested in a new subject or research we type a few words on a search engine and we access information. In the best case you might find 'just' a few hundred articles that you should study. You may choose to spend a few years reading all that has already been written or you may select just a few, (but what is the criteria you use to select them?). The risk is to rediscover what has already been found and written about or in a subject leading to a dead-ended. I do realize that today, at least in Italy, a young researcher, with inadequate pay, in order to advance their career must "publish or perish", the latter option being more likely. Though the 'push' to publish as much as possible might impact the quality of your publications, find the courage if you can, to rebel against that pressure to publish in excess. Writing a scientific research article, should require an in-depth understanding and knowledge of the preceding publications, and should be original, essential, simple, clear, rigorous, honest and complete. By explaining your discoveries, synthetically, even if they represent years of work, and carefully using words with the goal to harmonize the overall context to make it approachable by others, will allow you to gain humility and perspective. Remember research is an instrument of knowledge, not a tool to gain power or fuel competition.

In the laboratory you should work with rigor, method and patience (anything observed once needs to be repeated or replicated for it to have relevance), with total dedication and closing your eyes (i.e., ignoring) when facing difficulty (in that way you can face challenges that others, more critical and acute, would not confront). These factors are essential to your success and personal satisfaction. In scientific research you are absorbed by progressive revelations, even if they may be a small contribution to the general advancement of knowledge, it gives the researcher great satisfaction in the moment of discovery, however small, only you could have placed that tile in the mosaic. That tile in the future will allow you, or someone else; to take that starting point and continue from they're towards new discoveries. The essence of scientific research is sharing discoveries and collaboration. Take your time when elaborating experimental results: learn to understand the significance of revealing anomalies (serendipity); have doubts (they are the root of knowledge) welcome them without fear but as a possibility; tolerate a few errors as they may be necessary, at times beautiful (the tower of Pisa), or at times fertile (Fermi and the slow neutrons); be open to challenge your own ideas and those of others, science gives us objective answers and not absolute truths (Einstein *vs.* Galileo).

Try to share your knowledge—teaching and propagating science- education and science are important for society, and vice versa. If we can divulge scientific knowledge, sharing the derived advantages for humanity, so that public opinion may view science in a much more favourable light and influence the decisions of politicians in regard to the importance of funding scientific research. This will also lead a larger number of young people, hopefully an increasing percentage of women, to pursue a degree in science.

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