



# Advanced Research on Interaction Mechanisms of electroMagnetic exposures with Organisms for Risk Assessment

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#### 1 Historical Context

The residential use of electricity began in the late 1800s, initially mainly to power indoor lighting. The advent of electrical lighting changed human society irrevocably, allowing people to control their working and leisure lives as never before [1]. The replacement of gas lighting with electric lighting in factories led to improved conditions for workers: lower temperature for more comfort at work, better lighting for fewer accidents, less exposure to pollution, and reduced hazard of fire.

Electrification was arguably the most important engineering achievement of the time, playing an integral role in the second industrial revolution, a period of unprecedented increase in economic growth with significant improvement in living standards and increased productivity. As the use of electricity broadened, changes in society accelerated. The development of electrically driven elevators, for example, enabled the design of skyscrapers, and electrified street railways became the basis for public transportation networks, both of which were drivers of urbanisation.

The development of the infrastructure for transmission lines and electrical grids, initially for industry and rail, was a critical driver of rapid industrialisation and economic growth during the 20<sup>th</sup> century. Transmission of electric power at high voltage reduces the amount of energy lost due to the resistance of the wires [2], enabling the long-distance transmission required to make widespread residential electrification feasible. Household electrification became common in industrialised cities in the early 1900s and later spread to rural areas; by mid 20<sup>th</sup> century, most industrialised nations were fully electrified.

#### 2 Electricity in Society

It is difficult to imagine life in western society today without readily available electrical power. Electricity delivered through power lines is used for lighting, food storage and preparation, cleaning tasks, communication, entertainment, to operate computers and innumerable household appliances. The importance of readily available electricity in today's society is immeasurable. Developing countries need access to a steady supply of electricity to help drive the transition to industrialised status, access that depends on major infrastructure investment to create sustainable sources and distribution grids. Energy precariousness and access are global societal issues, and lack of access to electricity is a reliable indicator of a nation's level of energy poverty [3]. One of the challenges of electrification programmes in developing countries is for progress to keep pace with population growth [4]. In both industrial and developing nations, densely populated areas are generally those locations that also have the highest density of high voltage power lines [5].

Most industrial machines and household appliances are powered by the 50 Hz (Europe and rest of the world) or 60 Hz (North America and most of South America, south Japan, Korea) electric grid systems. Currently, mega grids, based on high voltage DC (HVDC) lines to transport energy efficiently over large distances, are being planned. In single conductors of AC and DC current, the density of the magnetic field at a given distance is directly proportional to the magnitude of the electric current flowing; the intensity of magnetic fields is expressed in tesla (T), milliTesla (mT), or microTesla ( $\mu$ T), or in gauss (G): 10,000 G = 1 T [6]. The field density decreases with the distance from the lines, and for optimised multiline configurations, the fields of the different lines cancel each other at larger distances and the decrease in field density with distance is even steeper. The magnetic field density underneath a power line is about 20  $\mu$ T; levels of ELF-MF in

residential settings are much lower, about 0.07  $\mu$ T in Europe and 0.11  $\mu$ T in North America. The electric fields under power lines can be thousands of volts per metre, while average values in the home are two orders of magnitude lower [7]. Close to certain appliances, the magnetic field density can be on the order of a few hundred  $\mu$ T but decreases even more steeply than from a line source.

### 3 ELF-MF in Society

All life forms, including humans, have lived and evolved in the presence of the Earth's natural electromagnetic radiation [8]. The human body, like all living tissues, is electromagnetic in nature, and an organism's internal electromagnetic fields interact with the environmental electromagnetic fields [9]. In recent decades, though, the growing use of electricity in everyday life has led to increased environmental exposure to man-made electromagnetic fields from the generation of electricity, its transmission over high voltage lines, and its use in domestic appliances, industrial machinery, broadcasting, and telecommunications [10]. All people living in industrialised nations are exposed all day, every day to varying levels of electric and magnetic fields, and new artificial sources of electromagnetic fields are continually being created with the advances in technology and sea changes in social behaviour. Exposure to manmade electromagnetic fields can disrupt the precise electromagnetically driven mechanical processes in living cells. Depending on the strength and frequency of the fields and the length of time exposed, exposure of living tissues to electromagnetic fields can generate heat [11], affect how genes are expressed [12], alter cell membrane function [13], and generally interfere with normal cell function. Disruption of the intrinsic electromagnetic interactions of cells can upset normal cellular defence mechanisms and impair metabolism [14], consequences that can impact health and, in turn, society.

The question of whether exposure to very low-level ELF-MF is injurious to health has been a topic since the 1970s. In 2001, the International Agency for Research on Cancer rated exposure to ELF-MF related to power transmission and the use of electrical appliances as a "Group 2 B carcinogen", i.e., possibly cancer causing, based on limited scientific evidence for an association with childhood leukaemia [15]. The association has been consistently observed in more than 20 population studies since the 2001 classification, but never with data clear enough to warrant a change in classification.

Childhood leukaemia is a rare disease with an annual incidence of about 50 - 55 leukaemia cases per million children [16–18]; the total number of new cases per year in the early 2000's worldwide can estimated at ca. 50,000. Residential magnetic field exposures are generally under 0.3  $\mu$ T, with only 1 – 4% of children living under conditions where exposure levels higher than 0.3  $\mu$ T [7]. If exposure to magnetic fields causes childhood leukaemia, then the number of cases attributable to magnetic field exposure in the European Union would be on the order of 50 – 60, corresponding to 1.5 – 2.0% of the total incidence, and the impact on public health of ELF-MF exposure at the global level can be considered quite small [19]. When considered at the personal level, however, for a sick child and the child's loved ones, the impact is devastating.

The scientific evidence for an association between ELF-MF exposure and other health effects, including other childhood and adult cancers, neurodegenerative diseases, diseases of the immune

system, neurobehavioural problems like depression and suicide, reproductive and developmental disorders, and cardiovascular disease, is much weaker than for childhood leukaemia [20]. The international exposure guidelines established by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) for exposure to ELF-MF are designed to keep exposures low enough to avoid hazardous acute nerve excitation. In general, human exposure levels in western society are far below the thresholds that would produce such changes.

## 4 Impact on Health of Artificial Lighting

All life forms, including humans, have evolved in the presence of 24 h daily light/dark cycles, and have endogenous biochemical and physiological mechanisms intrinsically linked to alternating periods of natural daytime sunlight and nighttime darkness. Until quite recently in evolutionary history, humans spent daytime hours exposed to sunlight and nighttime hours in the dark. The advent of electrification in modern society has upended the natural circadian rhythm of human exposure to light — the working habits of modern human society keep people indoors away from the sun during the day, and access to artificial light allows them to pursue light-requiring activities throughout the night [21]. Such disruption of circadian rhythms can have effects on a host of normal bodily functions, including sleep, core temperature maintenance, hormone secretion, gene expression, etc., with consequences for health. Circadian disruption is suspected to be linked to a range of disease states, including diabetes, obesity, depression, and certain cancers. Thus, the societal benefits associated with modernisation, electrification, and artificial lighting, are both beneficial and costly to health.

# 5 Societal Benefits of ARIMMORA

The ARIMMORA consortium was formed and funded to address the science underlying the possible link between ELF-MF exposure and cancer risk. The consortium brought together environmental scientists, biologists, electrical engineers, and computer scientists who developed a multipronged interdisciplinary approach that combined human, animal, and cell exposure studies to seek answers to the question of how exposure to ELF-MF might be associated with childhood leukaemia.

Laboratory studies that address the association of childhood leukaemia with exposure to ELF-MF have generally suffered from a lack of an appropriate test animal — one that can faithfully mimic a child's response to exposure — and a dearth of mechanistic data. The continuing situation of uncertainty regarding the potential for ELF-MF to cause childhood leukaemia is dissatisfactory for primary prevention, public health, and, in particular, for public health policy planning. The perception that exposure to ELF-MF is a potential health hazard is discomforting, and the failure of the scientific world to clarify the level of risk even in view of the large number of studies conducted and the bulk of scientific data collected compromises public faith in the scientific method.

The ARIMMORA research plan included strategies to specifically target the development of a laboratory animal strain, one that expresses a gene known to predispose children to leukaemia, for testing environmental exposure to ELF-MF and to explore the biophysical mechanisms underlying the development of malignant disease.

The new genetically modified *TEL-AML1* + laboratory mouse developed by ARIMMORA researchers is a major step forward for the scientific community. The number of animals that could be tested within the time and budget constraints of the project were sufficient to generate an estimate of the disease frequency in the animals but insufficient to definitively support disease causality. Future research efforts will have to be carried out with larger numbers of animals to secure the statistical power required to settle the question of causality in this animal model. One of the signature achievements of ARIMMORA is that now an appropriate animal model is available for those future studies.

The ARIMMORA research results also contributed to a better understanding of the biophysical mechanisms underlying the interactions of ELF-MF with cells and tissues. The findings from studies on the exposure of cell cultures point to the involvement of epigenetic responses and cell signalling pathways, although at a level too small to be important for cancer progression. Furthermore, indications were found that very low intensity magnetic fields of less than a  $\mu$ T are capable of evoking the cell signalling responses, and that ELF-MF effects on cell signalling pathways are modulated by exposure to blue light, indicating a role for cryptochrome. Both findings are important as these levels are below what is considered to be a high exposure in residential settings and much smaller than the current safety limits.

ARIMMORA achieved major contributions to the practice of dosimetry and could definitely bring clarification to the best exposure matrix. One important finding is that the induced E-fields as well as the induced H-fields need to be characterized and reported as neither can be excluded as to interact with the biological system.

It was also confirmed that the mean personal exposure is well correlated with bedroom exposure in children despite the many near-field ELF-MF sources that dominate the maximum personal exposure. Before the ARIMMORA results, it could not be excluded that near-field sources might increase the population of highly exposed children (> $0.4 \mu$ T).

The mean exposure of the children measured is below 0.1  $\mu$ T, which corresponds approximately to a peak spatially averaged induced E-field over 2 × 2 × 2 mm of 20  $\mu$ V/m. Only a small proportion, ca. 1 – 4% of children, are exposed to magnetic field levels >0.3  $\mu$ T.

Analysis of household near-field sources shows that fields decay steeply with distance from the device or appliance; hence the incident magnetic field exposure is relatively local. Furthermore, very few sources produce induced E-fields of significant intensity; those that do would normally either be relatively far from children or would be used only for a very short periods of time, i.e., fans, hair dryers, or vacuum cleaners. For example, it is very uncommon behaviour to stand close to the motor at the rear of a fan or to lie on top of a vacuum cleaner, corresponding to the locations of the highest radiated fields; further, the decay of the fields from domestic appliances is steep, thus, the fields tend to act only very locally on the body. Because these local sources act over relatively small cross sectional areas, induced E-field exposure for a given peak field strength is relatively much lower than that for fields of similar magnitude from more homogeneous sources such as power lines. Therefore in general, it is probable that localised very short-term exposures are of lower importance than long-term more uniform exposures from both incident and induced field perspectives.

The knowledge about the induced field in exposed children has also been brought to a new level through application of the latest most powerful solvers, anatomical models children, and morphing and poser functions. The induced field increases roughly as a function of the cube root of the weight of the child, which increases as the child ages. The relative values of the E-fields in different tissues change as the children develop and grow, however the distribution of field values maintains the same characteristics. The tissues that are consistently more highly exposed in terms of induced E-fields are skin, subcutaneous adipose tissues (SAT), vertebrae, skull, and large intestine. The least exposed tissues include pineal body, hypothalamus, mid brain, adrenal gland, and pharynx and oesophagus.

Harmonic components of the magnetic field add some contributions to the overall level of the Efields induced in children and foetuses. Although these contributions increase with frequency and cannot be neglected, the amplitudes are low, even in the worst-case scenarios.

The consortium did not identify any urgent need to characterize the exposure of near-field sources beyond what has been achieved within ARIMMORA as today's near-field sources only expose children for a very short time and only very local for both the induced H-field and E-field. Furthermore, there are no indications today for an association from epidemiological studies between leukaemia and exposures by near-field sources.

For the ARIMMORA research initiative, a number of innovative research tools were developed and used. 1) In addition to the above-mentioned *TEL-AML1* + laboratory mouse, 2) an improved device for measuring the properties of ambient electromagnetic fields was designed and constructed, and the prototype was validated and used to collect data. 3) Exposure systems for cell cultures and for humane housing of rodents were developed, manufactured, and installed. 4) In the course of the project, one of the cell culture exposure systems was adapted for exposures and sham exposures at sub- $\mu$ T levels of ELF-MF and for co-exposure to light, to test for the involvement of the light-sensitive protein cryptochrome in the cell signalling response. These commercially available tools will benefit future investigations.

Altogether, the ARIMMORA research results were not sufficient to reach the highly ambitious objective, namely, to close the question of whether or not exposure to ELF-MF contributes to the incidence of childhood leukaemia. However, the major contributions achieved and summarised above point to future research that could provide a step-change in future assessments. The consortium recommends that future investigations be addressed with one or two 3-year research programs of similar size.

#### 6 Implications for Safety Policy

The findings of ARIMMORA are insufficient to impact decisions on safety policy at present but mandate that the research effort be accelerated and that the current concept of 'prudent avoidance' should be encouraged and reinforced. The concept of 'prudent avoidance' dictates that reasonable measures to prevent or minimise exposure be continued until research data emerges to support a more or less extreme approach. Those responsible for making public policy should proceed cautiously when considering action towards minimising exposure.

The policy of prudent avoidance in view of the current state of knowledge regarding the risk of childhood leukaemia from ELF-MF exposure might include deciding to locate newly built child care centres, kindergartens, and schools at sufficient distance from high voltage power lines, or, conversely new lines far from existing schools. However, there is as yet insufficient scientific evidence to justify the relocation of existing institutions and power lines.

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