# Design and Development of Extremely Low-Frequency Pulsed Electromagnetic Field Chamber for Biomedical Applications

**Thesis submitted in partial fulfillment**
**for the Award of Degree**

## Doctor of Philosophy

**by**

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*Dedicated*
*To*
*My Beloved Parents*

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It is certified that the work contained in the thesis titled **"Design and Development of Extremely Low-Frequency Pulsed Electromagnetic Field Chamber for Biomedical Applications"** by **"Chandra Kant Singh Tekam"** has been carried out under my supervision and that this work has not been submitted elsewhere for a degree.

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I, **Chandra Kant Singh Tekam**, certify that the work embodied in this Ph.D. thesis is my own bonafide work carried out by me under the supervision of **Dr. Sanjeev Kumar Mahto** for a period from **July 2016** to **June 2023** at the **SCHOOL OF BIOMEDICAL ENGINEERING**, Indian Institute of Technology (Banaras Hindu University), Varanasi, India. The matter embodied in this Ph.D. thesis has not been submitted for the award of any other degree/diploma. I declare that I have faithfully acknowledged and given credits to the research workers wherever their works have been cited in my work in this thesis. I further declare that I have not willfully copied any other's work, paragraphs, text, data, results, *etc.*, reported in journals, books, magazines, reports dissertations, thesis, *etc.*, or available at websites and have not included them in this thesis and have not cited as my own work.

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Sanjeev Kumar Mahto 28.06.23

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**(Chandra Kant Singh Tekam)**

**Date:**

**Place: Varanasi**

# LIST OF FIGURES

| | |
|---|---|
| EM | Electromagnetic |
| ELF | Extremely low-frequency |
| ELF-PEMF | Extremely low frequency pulsed electromagnetic field |
| Hz | Hertz |
| kHz | Kilohertz |
| GHz | Gigahertz |
| AC | Alternating current |
| DC | Direct current |
| λ | Wavelength |
| c | Speed of light in vacuum |
| E | Energy |
| h | Plank's constant |
| υ | Frequency |
| VLF | Very low frequency |
| RF | Radiofrequency |
| MF | Magnetic field |
| EF | Electric field |
| E | Electric field strength |
| B | Magnetic flux density |
| T | Tesla |
| $\mu_0$ | Permeability of free space |
| $\mu_r$ | Permeability of magnetic material |
| dl | Vector line segment |
| I | Current flow in conductor |
| G | Gauss |
| mG | Milligauss |
| kV | Kilovolt |
| H | Magnetic field strength |
| $F_c$ | Faraday's constant |
| A | Crossectional area |
| F | Force |
| q | Charge |

| | |
|---|---|
| μT | Microtesla |
| nT | Nanotesla |
| χ | Magnetic susceptibility |
| M | Magnetization |
| ODC | Ornithine decarboxylase |
| TBIL | Total bilirubin |
| WBC | White blood cell |
| SMF | Static magnetic field |
| ND | Neurodegenerative |
| PHB | Primary human brain |
| REMF | Repeated electromagnetic field stimulation |
| BAP | Amyloid-β protein |
| PC | Protein carbonyl |
| MDA | Malondialdehyde |
| PEF | Pulsed electric field |
| nsPEF | Nanosecond pulsed electric field |
| TRIMprob | Tissue resonance interaction method |
| LEET | Low energy emission therapy |
| TTF | Tumour treatment fields |
| SD | Sprague-Dawley |
| BSA | Bovine serum albumin |
| DAPI | 4′,6-diamidino-2-phenylindole |
| CAEC | Central animal ethical committee |
| ANOVA | Analysis of variance |
| PAS | Periodic acid-schiff |
| CNS | Central nervous system |
| PNS | Peripheral nervous system |
| ICNIRP | International commission on non-ionizing radiation protection |
| MRI | Magnetic resonance imaging |
| miRNA | Micro ribonucleic acid |
| DNA | Deoxyribonucleic acid |
| $\frac{dB}{dt}$ | Rate of change of magnetic field |

| | |
|---|---|
| A549 | Lung adenocarcinoma cell line |
| GIST-T1 | Human gastrointestinal stromal cancer cell line |
| HCT116 | Human colon cancer cell line |
| PC9 | Human lung cancer cell line |
| LFRSMF | Low frequency rotating static magnetic field |
| MCF7 | Breast cancer cell line |
| MCF10 | Non-tumorigenic cell line |
| NIH3T3 | Fibroblast cell line |
| HL60 | Human leukemia cell line |
| K562 | Lymphoblast cell line |
| A375 | Human malignant melanoma cell line |
| H4 | Human neuroglioma cell line |
| SaOS-2 | Human osteosarcoma cell line |
| HepG2 | Hepatocellular carcinoma cell line |
| ALP | Alkaline phosphate |
| MNPs | Magnetic nanoparticles |
| ROS | Reactive oxygen species |
| MDA-MB231 | Breast cancer cell line |
| SW480 | Colon cancer cell line |
| HL7702 | Normal human liver cells |
| Bel7402 | Human liver carcinoma cell line |
| U251 | Glioblastoma cancer cell line |
| AFP | Alpha fetoprotein |
| UP-TTD | Ultrasound powered device |
| AST | Aspartate aminotransferases |
| ALT | Alanine aminotransferases |
| CK-MB | Creatine phosphokinase mb |
| MTT | 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide |
| $R_c$ | Radius of coil |
| N | Number of wires turns |
| D | Coil separation distance |
| $d_w$ | Wire diameter |

| | |
|---|---|
| R | Resistance of wire |
| ρ | Resistivity of wire |
| SWG | Standard wire gauge |
| PTSD | Post traumatic stress disorder |
| ATP | Adenosine triphosphate |
| C6 | Glial cell line |
| NCCS | National centre for cell sciences |
| DMEM | Dulbecco's modified eagle's medium |
| PBS | Phosphate buffer saline |
| FBS | Fetal bovine serum |
| EDTA | Ethylenediaminetetraacetic acid |
| EPM | Elevated plus maze |
| DG | Dentate gyrus |
| CA | Cornu ammonis |
| SD | Standard deviation |
| APP | Amyloid precursor protein |
| TMZ | Temozolomide |
| GBM | Glioblastoma multiforme cell line |
| IAEC | Institute animal ethical committee |
| RBC | Red blood cells |
| RFP-L929 | Red fluorescent protein mouse fibroblast cell line |
| H&E | Haematoxylin and eosin |
| ULF-PEMF | Ultralow frequency pulsed electromagnetic field |
| PC12 | Pheochromocytoma |
| F-actin | Filamentous actin |
| 293T | Human embryonic kidney cell line |

# PREFACE

Extremely low-frequency pulsed electromagnetic fields (ELF-PEMF) are omnipresent in our environment due to the rise in industrial activity, transmission lines, and household applications of electrical and electronic devices. A wider range of electrical and electronic device-generated magnetic fields are considered safe. Numerous studies have been done to look into the potential health impacts of long-term ELF-PEMF exposure (≥ 1 h/day). However, the scientific evidence is mixed, and more research is needed to establish conclusive findings for exposure duration (≤ 1 h/day). The biological effects of magnetic fields primarily depend on magnetic flux density, frequency, and duration. Moreover, biological effects can be divided into thermal and non-thermal, which cause membrane depolarization, excitation, and electrostimulation. The World health organization (WHO) also considers the rising electromagnetic fields in the environment a potential health concern worldwide. However, some studies have also reported the applications of extremely low frequency (ELF) fields for treating neurological, muscle, and cancer disorders. ELF-PEMF is a non-invasive, cost-effective therapeutic technique that uses low-intensity, low frequency magnetic fields for treatment of various diseases.

We have designed, fabricated, characterized, and applied uniform magnetic flux densities for bioelectromagnetic studies under *in vivo* and *in vitro* conditions. The computational simulation was performed on ANSYS electromagnetic suite (18.0) to determine the magnetic flux densities and behaviors of magnetic flux lines. The effects of ELF-PEMF on cell lines (C6, RFP-L929, A549, MCF-7, and HepG2) as well as on behavioral (spontaneous alternation, anxiety, motor coordination, and locomotor activity) and biochemical parameters (AST, ALT, bilirubin, serum creatinine, and CK-MB) of rats were studied under *in vitro* and *in vivo* conditions, respectively, using the custom-made

monoaxial Helmholtz coil. The ELF-PEMF effects on various behavioral, biochemical, and histological parameters were performed to determine the onset of harmful effects at early stages; however, no harmful effects were incidentally observed under the present experimental conditions. Additionally, we have devised a novel therapeutic approach to kill cancer cells. Results have also shown that the magnetic field noticeably induced cell death in lung adenocarcinoma (A549) cells under *in vitro* conditions.

The magnetic field may provide a novel non-invasive approach to cancer treatment and thus offers advantages over other methods to increase patient safety. The magnetic field treatment can also be supplemented by metal nanoparticles for drug delivery, magnetically modified scaffold for wound healing, and peripheral nerve injury. Further studies must determine the exact molecular mechanism for such therapeutic purposes.

***Keywords:***

*ELF-PEMF, Spontaneous alternation, Anxiety, A549, MCF7, C6, RFP-L929, AST, ALT, Ck-MB.*