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Q1 # Electromagnetic waves and living cells: A kinetic thermodynamic approach

Q2 Umberto Lucia

Dipartimento Energia, Politecnico di Torino, Corso Duca degli Abruzzi 24, 10129 Torino, Italy

HIGHLIGHTS

- Cells transports phenomena can occur across the cells membranes.
- Cells can also actively modify their behaviours in relation to any change of their environment.
- Their wasted heat represents also a sort of information.
- Effects of electromagnetic fields modify the cell membrane behaviour.
- Cells change their energy management.

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ABSTRACT

Cells are complex thermodynamic systems. Their energy transfer, thermo-electro-chemical processes and transports phenomena can occur across the cells membranes, the border of the complex system. Moreover, cells can also actively modify their behaviours in relation to any change of their environment. All the living systems waste heat, which is no more than the result of their internal irreversibility. This heat is dissipated into their environment. But, this wasted heat represents also a sort of information, which outflows from the cell towards its environment, completely accessible to any observer. The analysis of irreversibility related to this wasted heat can represent a new useful approach to the study of the cells behaviour. This approach allows us to consider the living systems as black boxes and analyse only the inflows and outflows and their changes in relation to any environmental change. This analysis allows also the explanation of the effects of electromagnetic fields on the cell behaviour.

1. Introduction

During the last decades, a great number of experiments have been developed on the interactions between low frequency and low amplitude electromagnetic fields and the living systems. They highlighted some biophysical and biochemical consequences on the cells behaviour. Some of these experimental evidences can be summarized as follows: Q3

1. *in vitro* studies:
   - HeLa (human cervical cancer) and PC-12 (rat pheochromocytoma) cells [1], continuously exposed for 72 h, to ELF–EMF of (1.2 ± 0.1) mT, at 60 Hz, decrease in proliferation 18.4% (HeLa) and 12.9% (PC-12);
   - HeLa cells exposed to PEMF [2] of 0.18 T, at 0.8 Hz, for 16 h: they decrease 15% in proliferation, as observed 24 h later;
   - PC-12 cells exposed to ELF–EMF [3] at 50 Hz of different intensities and durations: transient decrease of the proliferation rate and morphological differentiation has been observed;

E-mail address: umberto.lucia@polito.it.

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- Human colon adenocarcinoma cells exposed to ELF–EMF of 1.5 mT peak and 1 Hz, for 360 min: they decrease in cell growth [4];
- HCA-2/1cch (human colon adenocarcinoma) cells exposed to 25 Hz, 1.5 mT, for 2 h and 45 min in presence of dexamethasone: they decrease $(55.84 \pm 7.35)\%$ in the relative cells number [5];
- HTB 63 (melanoma), HTB 77 IP3 (ovarian carcinoma), and CCL 86 (lymphoma; Raji cells) cell lines: 64 h exposure [6] under a 7 T uniform static magnetic field leads to reduction of viable cell number by $(19.04 \pm 7.32)\%$ for HTB 63, $(22.06 \pm 6.19)\%$ for HTB 77 IP3, and $(40.68 \pm 8.31)\%$ for CCL 86;
- WiDr (human colon adenocarcinoma), MCF-7 (human breast adenocarcinoma), and MRC-5 (embryonal lung fibroblast) have been exposed to 3 mT static MF, modulated in amplitude with 3 mT ELF-MF, at 50 Hz, with a superimposition of ELF magnetic field, for 20 min. Both WiDr and MCF-7 cells showed morphological evidence of increased apoptosis. MRC-5 cells remained intact and did not show any increase in apoptosis [7]; Q4
- HL-60 and ML-1 (Human Myeloblastic Leukaemia) cells undergo apoptosis (detected through ladder type-DNA fragmentation) after exposure [8] at 50 Hz, 45 mT ELF–EMF for time periods of 1 and 2.5 h;
- SCL II (human squamous cell carcinoma) cells and AFC (human amniotic fluid) continuously exposed at 50 Hz, 0.8–1.0 mT EMF, for 48 h and 72 h: they increase in the frequency of micronucleus (MN) formation and the induction of apoptosis has been observed [9];
- SH-SY5Y (human neuroblastoma) cells continuously exposed to a 900 MHz radiofrequency radiation (SAR: 1 W kg^{-1}), for 24 h: reduction in the viability of neuroblastoma cells [10];

2. *in vivo* studies:
   - Antitumour and immunomodulatory effects of pulsed magnetic fields have been observed when the pulse width is 238 μs, the peak magnetic field is 0.25 T, the frequency 25 Hz, 1000 Hz and the magnetically induced eddy currents in B16-BL6 melanoma model mice is 0.79–1.54 A m^{-2}. Exposure of mice in pulsed magnetic fields lasted in 16 days. Anticancer and immunomodulatory properties of pulsed magnetic stimulation and decrease of tumour growth and elevated production of tumour necrosis factor (TNF-a) have been observed in mouse spleens [11];
   - Extremely low-frequency pulsed-gradient magnetic field with the maximum intensity of 0.6–2.0 T, gradient of 10–100 T m^{-1}, pulse width of 20–200 ms and frequency of 0.16–1.34 Hz, presented antitumour and antiangiogenic properties, in exposed Kunming mice bearing murine tumour [12–14];
   - Male Fischer-344 rats, subjected to the modified resistant hepatocyte model, were exposed to 4.5 mT–120 Hz ELF–EMF. The results showed a decrease of more than 50% of the number and the area of γ-glutamyl transpeptidase-positive preneoplastic lesions, glutathione S-transferase placental expression, a decrease of proliferating cell nuclear antigen, Ki-67, and cyclin D1 expression. These results showed inhibition of preneoplastic lesions, through antiproliferative activity of ELF–EMF [15];
   - Nude mice, bearing a subcutaneous human breast tumour (MDA-MB-435), were exposed for 70 min daily, for six consecutive weeks, to modulated MF (static with a superimposition of extremely low frequency fields at 50 Hz), of total intensity of 5.5 mT. The anticancer activity of MF was compared to that of cyclophosphamide. The inhibition on spread and growth of lung metastases caused by MF was greater than that caused by cyclophosphamide [16];
3. clinic studies:
   - A combination of tumour-specific frequencies may have a therapeutic effect. A total of 1524 frequencies, ranging from 0.1 to 114 kHz, were identified from 163 cancer patients, while a compassionate treatment was offered to 28 patients with advanced cancer (breast, ovarian pancreas, colon, prostate, sarcoma and other types of cancer). The patients received a total of 278.4 months of experimental treatment and the median treatment duration was 4.1 months per patient. None of the patients, who received experimental therapy, reported any side effects of significance. Two of the patients presented a complete and partial response to the treatment and four patients presented stable disease. A woman, with breast cancer, showed a complete disappearance of some lesions, according to PET-CT (Positron emission tomography-computed tomography), and significant improvement of the overall condition. Thus, the tumour-specific frequencies provide an effective and well tolerated treatment which may present antitumour properties in end-stage patients [17];
   - Eleven patients with mean age of 60 years and with stage IV, locally advanced or metastatic disease (adenocarcinoma, duct carcinoma, squamous cell carcinoma and other types), were enrolled in a human pilot study conducted. Patients were exposed for 5 days/week, over 4 weeks, according to two different static magnetic fields schedules: 20 min daily (4 patients) and 70 min daily (7 patients). Results showed that MF-exposed patients present mild or no side effects. Moreover, this pilot study supports the evidence that human exposure to MF with specific physical characteristics is associated with a favourable safety profile and good tolerability [18];
   - Ten patients with recurrent glioblastoma were treated by using a 100–300 kHz magnetic fields. No serious adverse events were observed in all patients, after >70 months of cumulative treatment. The median time of disease progression and median overall survival were more than double the reported medians of historical control patients. This type of fields can be used as a safe and effective treatment for cancer patients [19];
   - In 2008, a pilot study was developed to investigate the safety and efficacy of low-intensity, intermediate-frequency electric fields in 6 patients (heavily pretreated with several lines of therapy) with metastatic solid tumours, while no additional standard treatment option was available to them. A device was used to emit the frequencies 100–200 kHz, at a field intensity of 0.7 V/cm. A patient presented 51% reduction in tumour size, after 4 weeks of fields' treatment.