



## Critical role of model organism selection in assessing weak urban electromagnetic field effects: Implications for human health

Miroslava Sincak<sup>a</sup>, Petra Adamkova<sup>b</sup>, Vlasta Demeckova<sup>b</sup>, Miroslav Smelko<sup>c</sup>, Pavol Lipovsky<sup>c</sup>, Milan Oravec<sup>d</sup>, Alena Luptakova<sup>e</sup>, Jana Sedlakova-Kadukova<sup>a,f,\*</sup>

<sup>a</sup> Institute of Chemistry and Environmental Sciences, Faculty of Natural Sciences, Ss. Cyril and Methodius University in Trnava, Nám. J. Herdu 2, Trnava, 917 01, Slovakia

<sup>b</sup> Faculty of Natural Science, Pavol Jozef Safarik University in Kosice, Srobarova 2, 041 54, Kosice, Slovakia

<sup>c</sup> Faculty of Aeronautics, Technical University of Kosice, Letna 9, Kosice. 042 00, Slovakia

<sup>d</sup> Faculty of Mechanical Engineering, Technical University of Kosice, Letna 9, Kosice. 042 00, Slovakia

<sup>e</sup> Slovak Academy of Sciences, Institute of Geotechnics, Watsonova 45, 04001 Kosice, Slovakia

<sup>f</sup> ALGAJAS s.r.o., Pražská 16, 04011 Kosice, Slovakia

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### ABSTRACT

The impact of electromagnetic fields on human health has been investigated in recent years using various model organisms, yet the findings remain unclear. In our work, we examined the effect of less-explored, weak electromagnetic fields commonly found in the urban environments we inhabit. We studied different impacts of electromagnetic fields with a frequency of 50 Hz and a combination of 50 Hz and 150 Hz, on both yeasts (*Saccharomyces cerevisiae*) and human macrophages. We determined growth, survival, and protein composition (SDS-PAGE) (*Saccharomyces cerevisiae*) and morphology of macrophages (human monocytic cell line). In yeast, the sole observed change after 24 h of exposure was the extension of the exponential growth phase by 17 h. Conversely, macrophages exhibited morphological transformations from the anti-inflammatory to the pro-inflammatory type within just 2 h of exposure to the electromagnetic field.

Our results suggest that effects of electromagnetic field largely depend on the model organism. The selection of an appropriate model organism proves essential for the study of the specific impacts of electromagnetic fields. The potential risk associated with the presence of pro-inflammatory M1 macrophages in everyday urban environments primarily arises from the continual promotion of inflammatory reactions within a healthy organism and deserves further investigation.

### 1. Introduction

In today's society, electric and electronic devices have become an integral part of our daily lives, rendering it nearly impossible to imagine functioning without them. Every year, a plethora of new devices reached the market, embraced by a vast population. However, amidst this technological revolution, the question of electromagnetic field (EMF) safety and its impact on our well-being remains unclear. In studies exploring the impact of electromagnetic fields (EMFs), inconsistent and contradictory findings are often reported, a phenomenon attributable to variations in the parameters of the studied fields and the selection of model organisms.

Bakery yeast (*Saccharomyces cerevisiae*) stands as a widely employed

model organism in numerous biological disciplines. Research on yeast is indispensable for unravelling the fundamental principles of human health and disease [1]. Previous studies have examined the effects of magnetic fields on yeast, highlighting that exposure to static magnetic fields can induce metabolic changes that impact key subcellular functions [2,3], influence DNA integrity and cause genetic alterations [4]. While most studies report positive EMF-induced changes in growth and viability [5], a few authors have documented negative effects [6,7], and some have found no discernible effects [8]. Changes in growth, proliferation, and cellular respiration were observed when testing strong static fields (100–300 mT). These changes are usually attributed to oxidative stress [5] (Fig. 1).

Assessing the parameters of blood and immune cells appear as a more

\* Corresponding author at: University of Ss. Cyril and Methodius in Trnava, Faculty of Natural Science, Nam. J. Herdu 2, 917 01 Trnava, Slovakia.

E-mail address: [jana.sedlakova.fpv@ucm.sk](mailto:jana.sedlakova.fpv@ucm.sk) (J. Sedlakova-Kadukova).

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comprehensive approach to study and understand the effects of magnetic fields on human health. Macrophages are classified into two categories: classically activated spindle-shaped pro-inflammatory M1 and spherical-shaped anti-inflammatory M2 [9,10]. Macrophages are responsible for phagocytosing foreign antigens, maintaining tissue homeostasis, and participating in wound healing, as well as the development of non-functional angiogenesis in various types of cancer and chronic inflammatory conditions [11]. The magnetic field (60 mT) exhibited the capability to either decrease or increase the production of reactive oxygen species, depending on the duration of exposure [12]. Studies have demonstrated that a magnetic field with a frequency of 50 Hz and intensity of 0.5 mT is able to polarize macrophages towards the pro-inflammatory M1 phenotype, characterized by the production of inflammatory cytokines such as IL-1 $\beta$ , IL-6, and TNF $\alpha$  [13,14]. In contrast to phenotypic changes, a low-frequency electromagnetic field alone did not lead to an increased incidence of necrosis, apoptosis, or damage to DNA integrity in macrophage cell cultures [15,16].

The studies mentioned earlier predominantly investigated high-intensity magnetic fields, which are seldom encountered in standard anthropogenic settings. This stands in contrast to weak magnetic fields (<0.5 mT) with sinusoidal waveforms and frequencies of 50 or 150 Hz, as posited by Gajšek et al. [17], which are believed to be generated by commonplace electrical appliances. To date, no review or experimental study has identified weak urban electromagnetic fields as posing a threat to human health or to the components of the vascular and immune systems. Urban electromagnetic field refers to the electromagnetic radiation present in urban environments, arising from various sources such as power lines, electronic devices, communication systems, and wireless networks [18].

The real electromagnetic field present in urban environments often includes not only the industrial frequency of 50 Hz but also its dominant harmonics, such as the 150 Hz frequency. Based on some measurements, the ratio between them can be as high as 4:1 or even higher, although higher ratios are less common [19]. In addition to that, exposure to a multitude of anthropogenic electromagnetic fields spanning a wide range of frequencies, including low frequencies (0 to 50 Hz) and high-frequency GHz (e.g., wireless LAN networks), poses an additional and significant factor warranting consideration. The pervasive presence of electromagnetic radiation, combined with our limited knowledge about its impact on human health, gives rise to concerns among the general public. Even when not actively using electronic devices, individuals experience continuous exposure to electromagnetic radiation emanating from power distribution networks, household appliances, and mobile

phones [18], further accentuating these apprehensions.

The objective of our study was to assess the appropriateness of two frequently employed model organisms, yeasts and macrophages, in elucidating the impacts of ubiquitous weak electromagnetic fields prevalent in urban environments. Simulating real urban conditions, we investigated their effects on yeasts (*Saccharomyces cerevisiae*) and human macrophages M1 to compare their suitability in predicting the risks of weak urban electromagnetic fields to human health. The yeast *S. cerevisiae* is one of the most studied organisms in terms of magnetoreception, and the results are widely extrapolated to animals and humans at the cellular level. Investigating macrophages, as integral components of multicellular organisms, can help us understand not only the potential effects of urban magnetic fields on organisms but also the specific effects of magnetic fields on macrophages, which are integral to the human immune system. The geomagnetic field ( $B_g \approx 50 \mu\text{T}$ ), a constant natural abiotic factor served as a reference point [20].

## 2. Material and methods

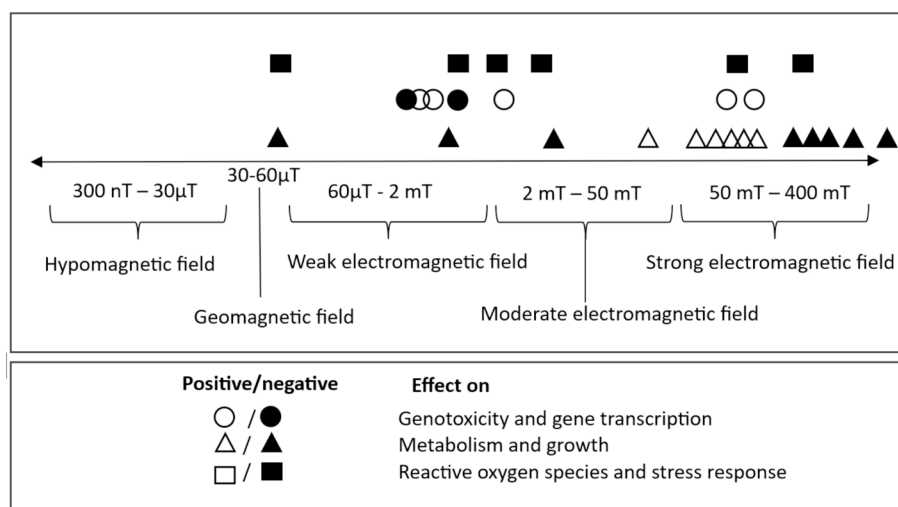
### 2.1. Model organisms

#### *Saccharomyces cerevisiae*

The bakery yeast (*Saccharomyces cerevisiae*) (CCY 21-4-13, distillery culture) was obtained from the collection of the Chemical Institute of SAV in Bratislava (Slovakia). The yeast culture was maintained on MD agar (61 g / 1000 ml of distilled H<sub>2</sub>O, composition: 20 g/l malt extract, 20 g/l dextrose, 15 g/l agar) (Sigma-Aldrich). For liquid cultures we used YPD Broth (composed of: 1 % (w/v) yeast extract, 2 % (w/v) peptone, and 2 % (w/v) glucose (all from Sigma-Aldrich) in distilled water.

#### THP -1 cell line

The M2 subtype macrophages (human monocytic cell line THP-1) were the ATCC-American Type Culture Collection (USA). Monocytes were obtained from the European Collection of Authenticated Cell Cultures. THP-1 cells were then cultured in R10 culture medium (RPMI-1640 with L-glutamine, 10 % (v/v) fetal bovine serum (FBS)) and incubated at 37 °C in a 95 % humidity atmosphere with 5 % (v/v) CO<sub>2</sub> content. THP-1 monocytes were differentiated and polarized into M1 (classically activated) and M2 (alternatively activated) macrophages according to protocol by [21].



**Fig. 1.** The range of electromagnetic and magnetic fields studied and their effect on *S. cerevisiae* (results published in the years 1950–2023). Indicated are positive (empty labels) and negative effects (filled labels) on genotoxicity and gene transcription (circles), metabolism and growth (triangles) and oxidative stress and stress response (squares).

## 2.2. Magnetic field induction

The magnetic field (simulation of the urban magnetic field) was induced by feeding electrical current into the designed circular coil system from Tektronix AFG 1022 2-channel generator and own designed current source through digital multimeter HAMEG HMC 8012 operating as control amperemeter. The fields generated in the coil system were verified by the VEMA 04 fluxgate magnetometer with a sensitivity of 2 nT/LSB and a sampling frequency of 1000 Hz. Prior to measurements, the magnetometer was calibrated with a method utilizing the neural network. This involved training the network with a dataset of raw sensor data and corresponding accurate measurements. Through iterative learning, the neural network fine-tuned its parameters to accurately map raw data to calibrated measurements. This calibrated magnetometer ensured precise data collection for various applications. The electric current used to induce the magnetic field was measured by the electric current generator, and the magnetic field in the coil was measured using a magnetometer (VEMA 04 fluxgate) throughout the experiment at frequent time intervals.

A specially designed copper circular coil (Supplementary Fig. 1) was constructed specifically for this experiment. The coil comprised two windings, with six tube holes for sample placement evenly distributed around the perimeter, ensuring a homogenous test field. In this study the theoretical urban electromagnetic field (50 Hz) and the real electromagnetic field with combination of 50 and 150 Hz in ratio 4:1 measured in previous study by the authors have been tested. The characteristics of the tested fields are shown in Table 1.

## 2.3. Experimental design: Yeast

A yeast stock culture was inoculated into a YPD medium and pre-cultivated for 18 h. The culture was then divided into experimental cultures (exposed to electromagnetic fields) and control cultures (maintained at background levels). Two sets of experiments were conducted, each involving different electromagnetic field conditions (M50 or M50/150), along with corresponding control groups (Table 1). The experimental cultures were exposed to electromagnetic fields for 24 h and subsequently kept under laboratory conditions for an additional 24 h (recovery phase). Meanwhile, the control cultures remained under laboratory conditions for the entire 48-hour duration of the experiment.

Measurements of pH, redox potential, cell counting, and viability assessment were conducted at both 24 and 48 h, as indicated by the star in Fig. 2. To construct the growth curve, 50  $\mu$ l of the yeast culture was sampled every two hours throughout the entire cultivation period, excluding the nighttime hours.

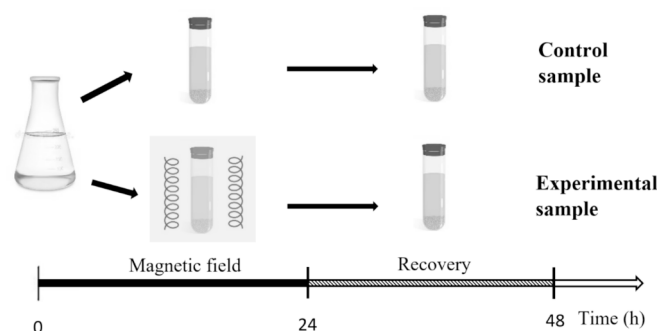
pH and redox potential were measured using a teslameter (Xylem Analytics Germany GmbH, DE). Before measuring the pH and redox potential, the culture was filtered through a cell filter (0.22  $\mu$ m) (Techno Plastic Products AG, CH), to increase the stability of the signal when measuring the redox potential.

The viability of yeast was determined by counting the number of colony-forming units (CFU). We evaluated the growth using a growth curve constructed by counting cells in the Bürker chamber. The number

**Table 1**

Description of electromagnetic fields tested and used in this study for experiments.

Abbreviation	Description
M50	Electromagnetic (sinusoidal course, $f = 50$ Hz, amplitude = 20 $\mu$ T)
M50/150	Electromagnetic (sinusoidal course, $f = 50$ Hz and 150 Hz, ratio between harmonic components 4:1, amplitude = 20 $\mu$ T)
control	geomagnetic; field of the Earth in Košice, Slovakia (laboratory conditions) (50 $\mu$ T $\pm$ 0,1 $\mu$ T, VEMA 04 fluxgate magnetometer) – background level
M1	pro-inflammatory phenotype of macrophages
M2	anti-inflammatory phenotype of macrophages



**Fig. 2.** Experiment design and parameter measurement intervals during the experiment.

of non-budding and budding cells (containing at least one bud) was also evaluated. All measurement of pH, redox potential, growth and survival were performed in triplicates.

Yeast cell proteins from a single colony were extracted using cell beads according to Dunn et al. [22]. To determine the concentration of soluble proteins [22], we used a kit (Modified Lowry Protein Assay Kit, Pierce, Rockford IL) (Thermo Fisher Scientific, USA). Using denaturing polyacrylamide gel electrophoresis (SDS-PAGE) we monitored changes in the protein profile of exposed *S. cerevisiae* cultures. The cell extract was prepared by sonication of 10 ml of yeast culture with a sonicator (Sonopuls, Bandelin, Germany) for 35 min on ice [23]. Electrophoretic separation was used to display the protein profile (Power Supply Adapter Set, Fisherbrand™, United Kingdom).

## 2.4. Experimental design: Macrophages

The human monocytic cell line THP-1 culture was cultivated in R10 medium composed of RPMI-1640 medium supplemented with 10 % (v/v) bovine serum (Gibco, Massachusetts, Grand Island, USA) and 2 mM L-glutamine. No antibiotics were applied. Pro-inflammatory (M1) macrophages and anti-inflammatory (M2) macrophages were generated by differentiation of THP-1 monocytes in the presence of 25 ng/mL phorbol 12-myristate 13-acetate (PMA) for three days or 10 nM 1,25-(OH)<sub>2</sub>-Vitamin D3 (Sigma-Aldrich, St. Louis, USA), for seven days according to Daigneault [9]. M1 macrophages were then washed with distilled water and allowed to rest in fresh R10 medium without PMA for an additional 24 h.

Afterward, differentiated M2 macrophages were exposed to magnetic fields with a frequency of 50 Hz or 50 and 150 Hz with an amplitude 20  $\mu$ T for 2 h. The macrophages were plated to a final density of  $1 \times 10^4$  cells/well in R10 medium in 96 flat-bottomed well tissue culture plates (Sarstedt, Nümbrecht, Germany). For the purposes of morphological analysis, polarized macrophage subsets were visualized using the IncuCyte® ZOOM reader (Essen Bioscience, Ann Arbor, USA). Cells were imaged every 30 min during the period of 24 h with 10 x objective using the brightfield channel. We use the IncuCyte® Zoom software for analyzing the images (Essen Bioscience, Ann Arbor, USA). M1 macrophages typically display a more elongated, spindle-shaped morphology, often accompanied by the presence of prominent pseudopodia, reflecting their pro-inflammatory phenotype. In contrast, M2 macrophages typically adopt a rounder, amoeboid-like shape, indicative of their anti-inflammatory and tissue repair functions.

## 3. Results and discussion

### 3.1. EMF impact on yeasts

During cultivation in the magnetic field, we observed no significant alterations in pH (5.5  $\pm$  0.2) and redox potential (153  $\pm$  9 mV) when compared to the control conditions (Table 2).

**Table 2**

pH and redox potential of experimental culture and control culture of *S. cerevisiae* before (initial) and after 24-hour magnetic field exposure.

Parameter	control		M50		M50/150	
	initial	after exposure	initial	after exposure	initial	after exposure
pH	6	5.4	6	5.6	6	5.4
Redox potential (mV)	133.7	153.5	133.7	156.3	133.7	144.8

The slight increase in redox potential observed under all conditions (both experimental and control) can be attributed to nutrient consumption during the logarithmic phase of yeast growth, as documented by [24]. In studies involving stronger static electromagnetic fields (10–35 mT), some researchers noted changes in pH alongside an increased nutrient uptake or biomass production [25]. Similar to our findings, authors who reported no change in pH [8] also did not observe alterations in growth or metabolic changes in biomass.

Throughout the exposure to the magnetic field (M50 or M50/150), we noted only small and statistically insignificant alterations in growth rate, biomass production, and the count of budding cells. In the course of the experiment, we compared two methodologies for yeast growth determination: CFU/ml and cell counting in chamber. Notably, the methodology employed for yeast cell counting exhibited greater accuracy, with standard deviations ranging from 2 to 7 times lower compared to those obtained through CFU counting. In the Fig. 3, the growth curve is illustrated with corresponding number of cell and number of budding cell for each culture after 24 and 48 h of cultivation (Fig. 3).

In our study, we compared the methodology of colony-forming units per milliliter (CFU/ml) with cell counting in a Burkler chamber by analyzing the standard deviation for each method across all tested samples. Our findings revealed that the SD values obtained through CFU/ml were consistently 2 to 7 times higher than those obtained through cell counting. Consequently, in accordance with existing literature, we concluded that cell counting in a Burkler chamber represents a more accurate methodology for quantifying cell numbers.

The only noticeable changes occurred in the delayed onset of the stationary growth phase following exposure to a magnetic field (M50/150) (Fig. 3). After the magnetic field exposure, there was a delay of 17 h in the initiation of the stationary growth phase, corresponding with the peak presence of budding cells. Most likely, the yeast cells detected the alternation in the external magnetic field, leading to a slower progression through the growth phases as they acclimated to this new field.

Similar results were only reported in two research papers [5,26]. The authors proposed that the delay is attributable to the magnetic field

causing the demise of a certain portion of the yeast population, while the remaining cells adapted to the altered magnetic conditions. This adaptation could explain the delayed onset of the growth phases (ref). In our study, we find these explanations less plausible, as we did not observe a significant decrease in the number of viable cells during the initial hours of cultivation. Most likely, the observation of Markkanen et al. [27] can better explain recorded changes. Their findings revealed that exposure to an electromagnetic field (120  $\mu$ T, 50 Hz) affected cell cycle kinetics, suggesting that the observed growth retardation might be connected to cell cycle arrest associated with DNA repair.

Several studies have reported the inhibitory effects of magnetic fields; however, these studies used much stronger magnetic fields [5,28] or focused on yeast strains with DNA repair deficiencies [7]. To date, only a single study has investigated the effects of a similarly weak magnetic field (1 mT) Ivancsits et al. [29], which also reported a positive effect of the static magnetic field on the formation of double-stranded DNA breaks. As of now, no other published studies have explored the effects of such low-intensity fields on yeast.

Based on our results, measurements of media pH and redox potential did not indicate changes in the metabolic activity of the yeast cells after exposure to the magnetic field; they only revealed a delayed onset of the stationary phase of growth.

We hypothesize that weak, low-frequency fields are not strong enough to cause a substantial stimulation or inhibition of growth. However, these fields may be perceived by the yeast culture, influencing the transition through different growth phases.

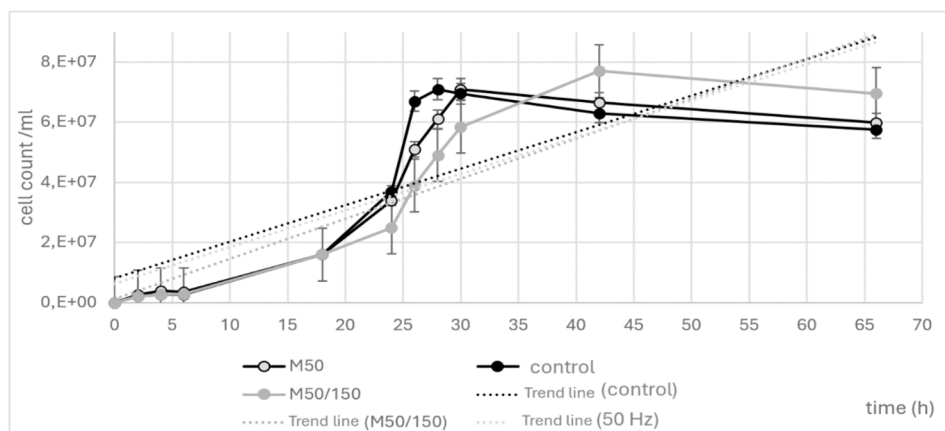
### 3.1.1. SDS-PAGE protein profile

Using denaturing electrophoresis, we monitored the protein profile of the experimental and control cultures of *S. cerevisiae*. In general, we can say that we did not observe changes in the protein composition captured on the polyacrylamide gel compared to the control since the number of bands and the color intensity were similar in all columns. We observed distinct bands in the region of 48–50 kDa and in the region of approximately 38 kDa (Fig. 4).

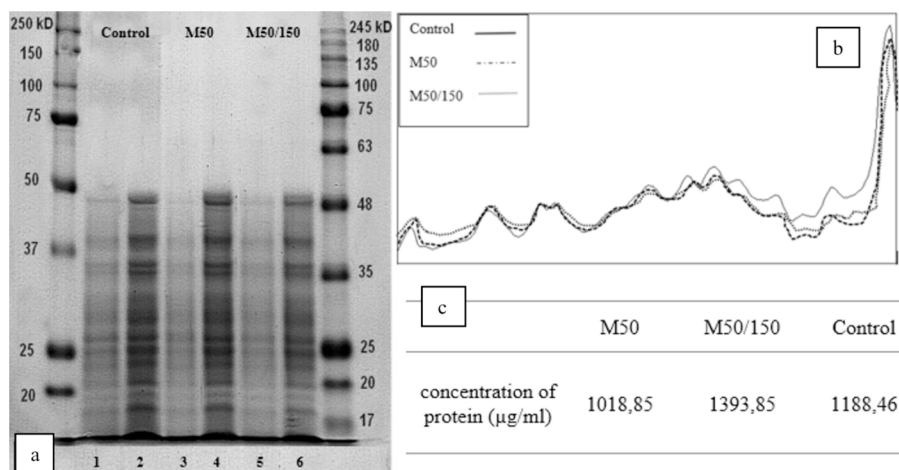
Although we performed whole-proteome extraction from yeast cultures, we did not capture proteins with a molecular mass larger than 50 kDa. We did not observe any changes in protein profile that can be captured by SDS-PAGE. Changes in the protein composition were not observed also by the authors Anton-Leberre et al. [30] studying the effect of static and pulsed fields on *S. cerevisiae*.

### 3.2. Macrophages

After exposure of macrophages to the magnetic fields for 2 h, we noted a change in macrophage phenotype from globular type M2



**Fig. 3.** Growth curve, cell counts, and CFU/ml of *S. cerevisiae* after 24 h of exposure to magnetic/hypomagnetic fields, followed by an additional 24 h (48 h total) in geomagnetic field exposure and control (continuously in geomagnetic field), along with corresponding trend lines.



**Fig. 4.** (a) SDS-PAGE gel depicting proteins extracted from control (geomagnetic field) and samples of *S. cerevisiae*. Lane 1 and 2: control, Lane 3 and 4, M50; Lane 5 and 6, M50/150. (b) Intensity of protein bands estimated by JImage software fluorescence. (c) Protein concentration from control (geomagnetic field) and samples (magnetic and hypomagnetic field) determined by the Lowry protein extraction method.

(Fig. 5A) to spindle M1 type (Supplementary Fig. 2). This change was observed immediately after 2 h of exposure (Fig. 5B, C) and persisted for the next 12 h (Fig. 5D, E). The phenotypic change back to M2 macrophages occurred 24 h after exposure in both tested magnetic fields (Fig. 5 F, G).

Only studies by Wosik et al. [13,14] have focused on the changes in macrophage morphology following exposure to electromagnetic fields. Interestingly, while these authors employed an extremely strong magnetic field (104 T/m, similar to that used in MRI scans) induced by a neodymium magnet, they we observed similar phenomenon using weak electromagnetic fields of urban origin. Wosik et al. [13,14] demonstrated that a magnetic field can induce a spindle-shaped phenotype in macrophages, likely by disrupting the actin cytoskeleton. This phenotypic change was found to be preceded by alterations in the organization of the Golgi complex, membrane receptors, plasma membrane permeability, and the flow of  $Ca^{2+}$  ions into the cell. The elongation of macrophages induced by the magnetic field, as described by Wosik et al. [13,14], closely resembled the phenotype achieved through pharmacological means (inhibitor Y27632) or genetic manipulation of the RhoA pathway deletion [31,32,33]. Unlike genetic or pharmacological manipulation, the shape of the cell recorded after exposure to a magnetic field may or may not necessarily mean a functional change. Therefore, it is necessary to experimentally investigate the functional state of macrophages, for example, by analysing surface markers and transcriptomic changes.

All aforementioned authors did not assess whether the observed effect of the magnetic field is temporal or permanent. The modulation of macrophage plasticity, shifting from M2 macrophages to pro-inflammatory M1 macrophages through the influence of electromagnetic fields, holds therapeutic promise in treating tumors by sustaining an active immune response in the organism. The concern regarding the emergence of pro-inflammatory M1 macrophages in everyday urban life primarily centres around the constant promotion of inflammatory reactions in an otherwise healthy organism, potentially leading to chronic autoimmune diseases. The real urban electromagnetic field (M50/150) present a potential risk that the urban electromagnetic infrastructure may pose even within a short period.

#### 4. Conclusion

Based on our observations, macrophages appear to be more responsive to the presence of an electromagnetic field, making them a more proper model organism for describing the influence of the urban electromagnetic environment on humans compared to yeasts. Our

results demonstrate that while yeasts did not exhibit changes in growth, pH, and redox potential within 24 h under low-intensity fields (20 μT and 50 or 50/150 Hz), immune system cells detected a magnetic field alteration within just 2 h, manifested in a shift in their phenotype.

Though these changes were temporary, the transformation of macrophages into pro-inflammatory M1 macrophages raises concerns about the potential risks associated with prolonged exposure to the weak urban electromagnetic fields that surround us daily. Continuous exposure to electromagnetic fields in our daily lives may have adverse effects on our health, as demonstrated through the use of macrophages as model organisms.

#### Declarations

#### Ethical Approval

This is an observational study. The Slovak Research Ethics Committee has confirmed that no ethical approval is required.

#### 6. Consent to Participate

In this study, no human tissues, patients, or animals were involved. Therefore, no Consent to Participate was required.

#### 7. Consent to Publish

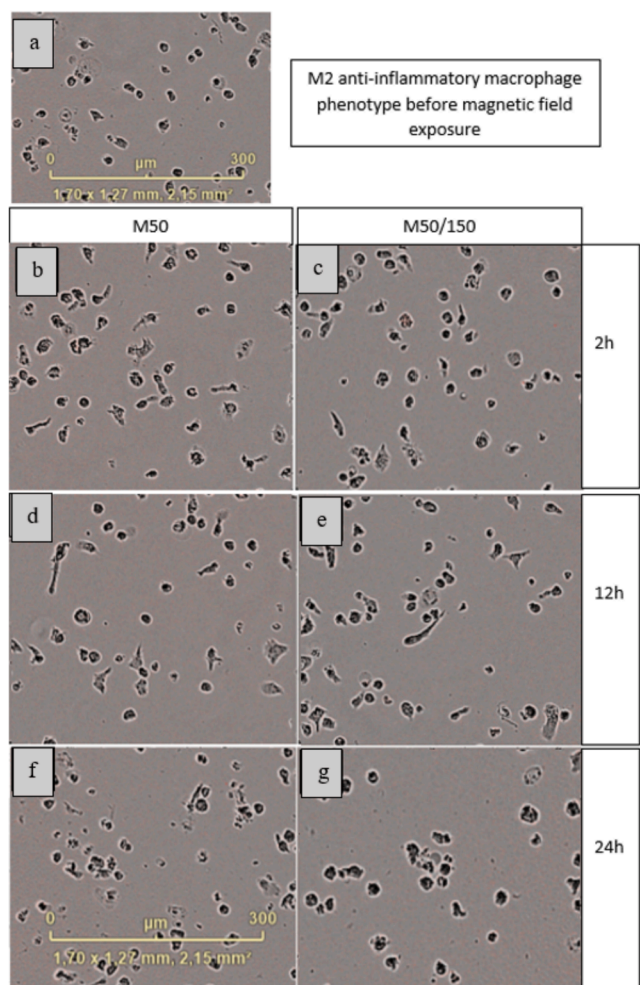
In this study, no human tissues, patients, or animals were involved. Therefore, no Consent to Publish was required.

#### Authors Contributions

Author M.Si. wrote the paper. Author J.S-K and V.D conceived formal analyses. Authors M.Sm., P.L. and M.O. provided methodology. Authors M.Si and J.S-K performed Data curation. Author M.Si performed the experimental cultivation of yeast. Authors V.D and P.A performed the macrophage cultivation and analysed the results. Authors J.S-K. M. Si., A.L., V.D, and P.A edited and reviewing the manuscript.

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**Fig. 5.** M1 and M2 macrophages exhibit distinct morphological characteristics. M1 macrophages typically display a more elongated, spindle-shaped morphology, often accompanied by the presence of prominent pseudopodia, reflecting their pro-inflammatory phenotype. In contrast, M2 macrophages typically adopt a rounder, indicative of their anti-inflammatory and tissue repair functions. In the normal Geomagnetic field, anti-inflammatory M2 macrophages exhibited a roundish phenotype (Figure a). Following exposure to magnetic fields (M50 and M50/150) for 2 h (Figures b and c), we observed a notable transformation in M2 macrophages, with a shift towards an elongated morphology, accompanied by the emergence of thin, tail-like extensions reminiscent of the characteristic phenotype of M1 macrophages. This spindle-shaped morphology persisted unchanged for 12 h (Figures d, e). However, after 24 h, macrophages reverted to their M2-like rounded phenotype in both magnetic field conditions (Figures f, g).

#### CRediT authorship contribution statement

**Miroslava Sincak:** Writing – review & editing, Writing – original draft, Data curation. **Petra Adamkova:** Writing – review & editing. **Vlasta Demeckova:** Writing – review & editing, Formal analysis. **Miroslav Smelko:** Methodology. **Pavol Lipovsky:** Methodology. **Milan Oravec:** Methodology. **Alena Luptakova:** Writing – review & editing. **Jana Sedlakova-Kadukova:** Writing – review & editing, Formal analysis, Data curation.

#### Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: [Jana Sedlakova-Kadukova reports financial support was provided by

Scientific grant agency of the Ministry of Education, Research, Development and Youth of the Slovak Republic. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper].

#### Data availability

Data will be made available on request.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bioelechem.2024.108756>.

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