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Review

Static magnetic fields as a factor in modification of tissue and cell structure: a review**

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A b s t r a c t. This review is intended to contribute to the evidence of the effects of static magnetic field on cells and tissue, as well as to present research results that will elucidate the complex matters involved in the formation and remodeling of cells. The cell characteristics studied in the papers that are reviewed include cell viability and proliferation, aggregation and their differentiation, structure and membrane potential. A moderate static magnetic field in the most commonly used range of 2-80 mT has potential application in the formation and remodeling of plant and human cells. However, in the case of cancer cells, the range of fields commonly used was 0.2-9 T. Magnetism promotes changes in plant cell growth, which prompts the cell to proliferate, thereby ensuring an increased rate of biomass production. Some researches presented the enhancement of the differentiation of plant cells and skeletal muscle tissue by over 30% at 80 mT static magnetic field. Changes in the cell cycle and growth reflect directly on the cell number and viability and provide useful information to detect modifications in the cell machinery. Static magnetic field, depending on its intensity, enhances cell proliferation and thus may improve, among other processes, tissue regeneration, wound healing and the inhibition of cancer cell proliferation. Researchers showed, among other things, that cells under the influence of static magnetic field changed their shape, had a larger chloroplast, stiffer cell wall, density of the cytoskeleton and cytoplasm contained several mitochondria. Numerous studies also discussed the behavior of the cell membrane of plant and animal organisms, including humans, under the influence of an static magnetic field. The effects of static magnetic field on the cell membrane of plant and human cells were similar. The research results indicate that static magnetic fields can significantly change membrane depolarization and its potential that regulates ion movement and thus can have a significant impact on the properties and biological functionality of the cell. Studies have shown that continuous application of static magnetic field caused deformation and damage of cell membrane. Based on the theoretical analyses presented also in this review, it can be concluded that static magnetic field affects cells and tissue, giving them changes in properties and behaviors and modulates, *e.g.* in the activity of ion channels. Thus it may produce effects leading to changes in the functioning of the cell. It is possible to formulate directions for further research aimed at using static magnetic fields for the non-invasive remodeling and formation of plant and human cells.

K e y w o r d s: magnetic fields, viability, proliferation, structure, cells

1. INTRODUCTION

Static magnetic field (SMF) as a constant field is classified as a weak, moderate and strong fields (Marycz *et al.*, 2018). External magnetic fields, due to their nature, penetrate into biological tissue, thanks to which they can cause changes at the cellular level such as: magnetic induction,

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magneto-mechanical interaction, and electron spin interactions. The cell can be considered as a system of components susceptible to the SMF, with electrical charges (ions, free electrons) and molecules with magnetic moments (Barbic, 2019; Binhi and Prato, 2017; Binhi, 2016; Lemessa *et al.*, 2022; Teng, 2005).The cell can be considered as a system of components susceptible to the SMF, with electrical charges (ions, free electrons) and molecules with magnetic moments.

Various studies have been carried out on the influence of magnetic fields on plants and animals, including human tissues and cells, as well as environmental shaping (Binhi and Rubin, 2022; Darvishi *et al.*, 2023). SMFs are widely used in therapy and effectively affect the growth, development and qualitative features of the structures of cells in living organisms, which has been proven by numerous studies, although the mechanism of action is not fully understood (Albuquerque *et al.*, 2016; Bodewein *et al.*, 2019; Chen *et al.*, 2017; Sarraf *et al.*, 2020). Static magnetic fields have been proven to cause a large variety of biological effects at the cellular and whole organism levels. However, such effects on living cells are quite different depending on the parameters of the SMF, such as homogeneity, intensity, and exposure time. Studies investigated the effects of SMF exposure (0.1 μT to over 20 T) on various type of plants, human and animals cells depending on exposure time (1 h to days). It was shown that an SMF of approximately 0.2-7 T has potential applications in biological systems, the main purpose of which is to explain the formation and dynamic remodeling of living structures (Levin, 2020; Zhang *et al.*, 2016). Weak, moderate and strong magnetic fields with magnetic induction between 180 mT, 1 T and 10 T and a spatial gradient of up to 100 T m^{-1} (Tesla per meter) have been successfully used in medicine for diagnostics and therapy. SMFs are also non-invasive and have great potential for side effects (Lei *et al.*, 2020; Lew *et al.*, 2018; Lv *et al.*, 2021; Pooam *et al.*, 2019; Shang *et al.*, 2019).

Magnetic fields (MF) with intensities ranging from 5 to 200 mT can also be used to enhance the growth of plant cells and cellular components, affecting, among other impacts, the softening of the structure, color change, sugar accumulation, production of organic acids, as well as the accumulation of secondary metabolites for agricultural, industrial and biotechnological purposes (Blümler, 2021; Descamps *et al.*, 2021; Li *et al.*, 2022; Rekena *et al.*, 2019; Saletnik *et al*., 2022ab). The influence of magnetic fields on living organisms, their tissues, cells and intracellular processes shows significant variation. Researchers have reported that SMF enhances cell viability, proliferation (Costa *et al.*, 2020; Escobar *et al.*, 2020; Feng *et al.*, 2022; Huo *et al.*, 2020; Luo *et al.*, 2021), cell diffusion (Zablotskii, 2022; Waskaas, 2021), cell division (Coletti *et al.*, 2007; Darwish and Darwish, 2022; Jin *et al.*, 2019; Prina-Mello *et al.*, 2005; Wong *et al.*, 2015), and changes cell morphology and membrane potential. However, some biological effects of SMFs reported in the literature are not consistent or are even controversial which may be caused by differences in the magnetic field used and the types of biological samples. These results clearly indicate the complexity and diversity of the biological effects of SMFs, which should be subjected to a synthetic approach, taking into account various aspects of research and the effects obtained (Jin *et al.*, 2019; Babaei-Ghazvini *et al.*, 2020; Ercan, 2022; Fatima *et al.*, 2021; Hassanpour and Niknam, 2020). Many studies have also shown that an SMF inhibits cancer cell viability and proliferation (Tian *et al.*, 2018; Zhang *et al.*, 2016; Zhang *et al.*, 2017b). Therefore, it can be considered an additional tool that can be used with SMF-based medical devices to modulate individual cells and improve regenerative processes in the organism. It should be noted that this effect of the magnetic field on the structural differentiation of cells depends on the magnetic susceptibility of the target. The SMF may modify the electromagnetic properties of biomolecules, membrane permeability, and enzyme activity in biochemical pathways (Hassanpour and Niknam, 2020).

SMF has been shown to have a positive effect on cell dynamics by increasing the proliferation rate, cell differentiation, division and stimulating protein synthesis caused by an increase in the cell membrane potential that can lead to the formation and remodeling of a cell (Carvalho, 2022; Levin, 2012; Sundelacruz *et al.*, 2009; Zablotskii *et al.*, 2016b). Research conducted in recent years has shown that intracellular molecular motors and biochemical processes are controlled by electrical charges, although so far no model explaining the functioning of the body has been developed. To explain biomagnetic effects, it is necessary to understand the mechanism by which the magnetic field affects cells. The biological effects of static magnetic fields have been reviewed by many authors. However, the current study focuses on the simultaneous presentation of the effect of an SMF on the cells of living organisms (plant, animal and human) based on the results of experimental studies and theoretical analyses.

This review is intended to contribute to recent evidence of the effects of SMF on cells and tissue, as well as to present research results that will elucidate the complex matters involved in the formation and remodeling of cells as an act of changing or altering their structure. This study focuses on presenting the effect of SMF on cells in terms of their viability, proliferation, aggregation and differentiation, structure, and membrane properties.

2. CELLS AND TISSUE

2.1. Viability and growth

Multiple studies have been conducted on the effect of an SMF on the viability of plant and animal cells, including human cells. This effect varied depending on the type of cells and exposure conditions (field gradient, field strength, direction of the field vector and exposure time) (Deanici *et*

al., 2022; Feng *et al.*, 2023; Gurhan *et al.*, 2021; Luo *et al.*, 2021; Tian *et al.*, 2018). Static magnetic fields (SMFs) have different effects on the activities of different cell types. This effect on biological systems can be classified as stimulating, inhibitory or null (Zhang *et al.*, 2017c; Santos *et al.*, 2022). Many studies have been taken to determine the effect of static magnetic field with different intensities on the growth rate of biomass. The application of SMF intensity had a positive effect on the growth of plant tissue of *C. fusca* microalgae grown under controlled conditions compared to a control (Deamici *et al.*, 2018, 2021). The growth rate (biomass concentration) was more than 85% greater when a 25 mT SMF was applied for 24 h d^{-1} for 15 days. The same trend has been shown in other studies. Deamici *et al.* (2016) and Bauer *et al.* (2017) showed that an SMF of 60 mT for 24 and 1 h d^{-1} for 15 days increased the biomass concentration for *Chlorella fusca* by 20.5% while for *Chlorella kessleri* for 1 h d^{-1} for 10 days, it was 83.2% higher than for a control sample. The algal density of algae treated with 150 mT range of static magnetic field was 56.01% higher than in the control group after 4 days (Luo *et al.*, 2021). However, algal density was lower than for the control group at 40 mT for the first three days. This was similar to the results of Costa *et al.* (2020) for the biomass of *Chlorella homosphaera* treated with 30 mT MF. Many publications have been presented regarding cell growth rate and increase in biomass for different microalga species exposed to SMFs with different strengths and exposure times (Deamici *et al.*, 2022). MFs with an intensity of 10 to 500 mT have been used to biostimulate microalga growth. SMF in the intensity range from 10 to 500 mT was used to biostimulate the growth of microalgae, but the most common values were up to 100 mT. The highest rate of biomass increase, compared to the control group, was recorded at 60 and 10 mT for *Spirulina* sp. (by 95%) and *Dunaliella salina* (by 84%), respectively. There are some studies of cell growth rate and biomass increase for different plant species exposed to SMFs with different strengths and exposure times (Kagami and Urabe, 2001; Luo *et al.*, 2021; Small *et al.*, 2012). Generally, it was found that the growth rates of plant of studied species decrease with increasing cell size. SMF exposure also induced progression of the cell cycle of plant cells (Belyavskaya, 2004; Kagami and Urabe, 2001; Luo *et al.*, 2021; Santos *et al.*, 2017; Small *et al.*, 2012). Mohammadi *et al.* (2018) reported that tobacco cells treated with 0.2 mT SMF remained in G1 for a longer period compared to control cells. After 6 h exposure to SMF, only 24% of the SMF-treated cells entered the S-phase, while a maximum of S-phase cells of the SMF-treated group was detected after 10 h of treatment. They exposed tobacco cells to SMF by placing them on a shaker (120 rpm min^{-1}) and reported that samples treated with 0.2 mT SMF remained in the G1 phase for a longer period compared to control cells. Exposure of tobacco cells to SMF reduced the cell growth and their dry weight were 20% lower to compare to the controls at 24 h (Mohammadi *et al.*, 2018).

Numerous studies reported that an SMF has affected the growth rate and viability of human and animal cells for both cancerous and healthy tissues. Gurhan *et al.* (2021) using two sets of Helmholtz coils showed that the growth rate of HT-1080 fibrosarcoma cells was significantly greater with SMFs in the range of 200-400 μT compared to the control sample when the SMF was oriented perpendicularly to the bottom of the flask. For SMF 400 μT, this parameter reached the value of 28%. However, the growth rate of cells significantly decreased at 600 μT. A horizontal orientation of the SMF contributed to the reduction of the value of the study parameter. Wang *et al.* (2014) reported that cell viability and cell number of human breast adenocarcinoma (MCF-7) cells significantly decreased after 72 h of exposure to a 0.26 to 0.33 T SMF induced by a cylindrical superconducting magnet compared to the control group. Yang *et al.* (2021) using superconducting stated that the tumor weight was reduced by 44.7% at the end of 21 days under an upward 9.4 T SMF while, in contrast, the downward orientation of the SMF did not inhibit tumor growth. However, Tian *et al.* (2018) tested 5 human solid tumor cell lines cells with the neodymium permanent magnets and found that the cell numbers of lung cancer cells were reduced after a 2 day treatment in an upward direction SMF (South pole was on the top of cells) of 0.26-0.5 T, but not by downward direction magnetic fields (North pole was on the top of cells). Zhang *et al.* (2016) found that epidermal growth factor receptor (EGFR), a protein that is over-expressed and highly activated in multiple cancers, can be directly inhibited by SMFs (induced by magnet material) of 0.05 and 1 T, reducing the cell number. Tenuzzo *et al.* (2006) using neodymium magnetic disks showed that the viability of HepG2 cells significantly decreased by 30% within the first 4 h of exposure to 6 mT SMF. Valiron *et al.* (2005) demonstrated results indicating a significant loss of epithelial cells (HeLa) at 13 T. They used a superconducting magnet and stabilized the sample temperature at 37°C. Other studies confirm that cancer cell growth could be inhibited by 1 T SMF (Zhang *et al.,* 2017b; Luo *et al.*, 2016).

Many studies demonstrate the positive and negative impact of an SMF on the cell viability of healthy tissues depending on the intensity and duration of exposure. Rekena *et al.* (2021) showed that suspension-type CHO (Chinese hamster ovary) cell viability under a 0.66 T SMF treatment increased to 96.2% on day 9 compared to 92.1% in the control group. However, static MF exposure had no significant long-term effect on cell viability. NK92-MI cells (human NK-natural killer cell line) after application of a 0.4-T SMF, increased viability 1.21-fold compared to the sham group (Lin *et al.*, 2019). The viability of osteocytes in a 16 T SMF cultured for 48 h was also significantly higher than those of the control (Yang *et al.*, 2021). Many studies have shown the inverse effect of SMF on cell viability. Wang *et al.* (2016) showed that exposure to 0.5 T SMF

for 7 days decreased the viability of adipose-derived stem cells from male Lewis rats by about 8%. Javani Jouni *et al.* (2013) demonstrated that increasing intensity and time of exposure to an SMF significantly decreased the viability of bone marrow stem cells. The most significant decrease in viability was 100% at 15 mT for 72 and 96 h caused by the SMF. Another study by Kaku *et al.* (2010) indicated that a 0.01 mT SMF for 15 min hold-time, and a temperature plunging by 30°C, resulted in the greatest survival rate of human periodontal ligament (PDL) cells. Chiu *et al.* (2007) showed that increasing the intensity of SMF from 0.1 to 0.4 T significantly decreased the cell number of osteoblast-like MG63 (ATCC CRL-1427) after 24 h exposure time. Many researchers (Guoping *et al.*, 2010; Romeo *et al.*, 2016; Zhang *et al.*, 2017a, b) conducted studies on healthy and cancer cells, but they did not show a significant effect of SMF on their viability. Zhang *et al.* (2017a, b) showed that a 1 T SMF did not affect the cell viability of 15 different cell lines, including non-cancerous cell line 293 T as well as CHO cells and human cancer cell lines CNE-2Z, A431 and A54. However, with higher cell density, SMF reduced the number of cells in solid human tumor cell lines in most of the cases studied. So far, most studies found that the cell cycle of humans, animals and plants was not affected by SMFs (Babaei-Ghazvini *et al.*, 2020; Hassanpour and Niknam, 2020; Zhang *et al.*, 2017a, b).

2.2. Proliferation

Many researchers have evaluated the effects of SMF on proliferation, and the results have been varied depending on the intensity of SMF, application time and type of cells, their age and health. Treatment with a suitable SMF strength in the range of 10-150 mT could promote cell proliferation and biomass formation (Costa *et al.*, 2020; Deamici *et al.*, 2018, 2021; Kataria *et al.*, 2019; Rekana *et al.*, 2021). In contrast, Mohammadi *et al.* (2018) found that the exposure of synchronized tobacco cells to a weak SMF of 2 mT at 24 h produced a remarkable reduction in cell growth and their dry weight was 20% lower than that of the control sample. This effect of weak magnetic field (WMF) was also summarized in Belyavskaya's *et al.* (2004).

Many studies have been conducted on the interaction between SMFs and living cells of humans and animals. The results obtained varied depending on the type of cells and the field parameters applied. Multiple pieces of evidence showed that SMFs may enhance cell proliferation. Wu *et al.* (2022) showed that 140 mT SMF with 72 h exposure time can increase the human mesenchymal stem cell (MSC) proliferation rate by 23%. Zheng *et al.* (2018) showed that 1 mT of SMF can promote the proliferation of dental pulp stem cells (DPSCs). Marędziak *et al.* (2016) found that a 0.5 T SMF increased the proliferation rate of human adipose-derived mesenchymal stem cells (HASCs) and enhanced both viability and osteogenic properties. Kim *et al.* (2015) showed that 15 mT SMF treatment on human bone marrow-derived mesenchymal stem cells (MSCs) enhanced cell proliferation and could improve bone regeneration around dental implants and abutment teeth. Feng *et al.* (2022) found that a 0.5 T SMF treatment of fibroblasts significantly increased cell proliferation and the wound area closure rate in diabetic mice. In addition, they stated that a downward directed SMF was more effective in promoting the proliferation, migration, and survival of cells than an upward. Escobar *et al.* (2020) found that a 2 mT SMF applied for 3 h increased the cell proliferation of chondrocytes, however, it tended to cause an inhibition lasting for 1 h after 5 and 8 days. Martino *et al.* (2010) found that 60 and 120 μT SMFs increased the cell proliferation of human umbilical vein endothelial cells by 40% over a period of 2 days. There are also some studies showing that SMFs could inhibit the proliferation of some cell types. For example, Sadri *et al.* (2017) examined the effect of SMF in human cord-derived mesenchymal stem cells and found a significantly reduced proliferation rate, that exposure to 18 mT SMF caused a longer proliferation doubling time compared to the control samples. Feng *et al.* (2010) showed that exposure of osteoblastic cells to a 0.4 mT SMF significantly decreased the proliferation rate relative to unexposed cells, with a maximum 1.2-fold difference after a 24 h exposure time. Chiu *et al.* (2007) found that the proliferation of osteoblast-like cells was significantly decreased at 0.4 T SMF after 24 h exposure time compared to a non-treated group.

Many researchers have evaluated the effects of SMF on tumors, and the results have proven its ability to inhibit cancer cell proliferation under certain conditions. Yang *et al.* (2020) investigated the effect of 1 T SMF on HCT116 and LoVo cancer cells of humans and found that in the upward direction cell proliferation was significantly reduced ($p < 0.05$) in exposed samples after 8 h. Tian *et al.* (2018) found that the GIST-T1 tumor weight in an upward direction 0.2-1 T SMF was reduced by 19.3%. Zhang *et al.* (2017b) showed a significant effect of 1 T SMF on cell proliferation depending on their density. They found that exposure to an SMF for 2 days reduced the cell number in 6 solid cancer cell lines at higher cell density by 15%, while in the 6 non-cancer cell lines, there was no reduction. Luo *et al.* (2016) studied four different human cancer cell lines, HeLa (human cervical carcinoma cell line), HCT116 (human colorectal carcinoma cell line), CNE-2Z (human nasopharyngeal cancer cell line) and MCF7 (human breast cancer cell line) and found that 1 T SMFs increased antitumor efficacy and induced combinational effects with chemo drugs that are drug-specific.

However, there are also some studies showing that cell proliferation was not affected by SMFs. For example, Molo and Ordu (2021) exposed bone marrow mesenchymal stem cells to 328 mT SMF for 6 days and found no significant changes in cell proliferation and growth. Zablotskii *et al.* (2014a) exposed MSC cultures to 1.2 T SMF for 2 or 7

days and found that cell proliferation did not significantly differ when compared to the control group. Zhang *et al.* (2017c) presented a summary of some reported studies on SMF-induced cell prolifertion/growth changes. They found that the effect of SMF on cell proliferation depends not only on the cell type, but also on the magnetic field intensity as well as cell density, and in this respect further research is necessary to discover the mechanisms and specific effects of a given SMF on a specific cell type.

2.3. Cell aggregation and differentiation

Cell aggregation plays an important role in tissue formation. A few studies show that cell aggregation could be affected by SMFs. For example, Luo *et al.* (2021) studied the effect of SMF on the aggregation of *Chlorella vulgaris* cells. The aggregation percentage on the second day for 0, 40 and 80 mT SMFs increased by 6.7, 7.5, and 6.6%, respectively, compared to the first day. However, the aggregation percentage at 150 mT increased by only 1.9%. On the fourth day, the effect of 80 mT SMF on aggregation percentage was the highest compared to other applications of MF. By contrast, Luo *et al.* (2020) found that the aggregation percentage of *Chlorella vulgaris* cells treated with 80 and 150 mT SMFs was significantly lower than the control samples; the greater difference was 29.74% with 80 mT. They stated that an SMF can cause extracellular polysaccharides (EPS) to adhere more closely to the surface of algal cells. Aggregation plays an important role in cell division and development (Fassler *et al.*, 2021). However, Jin *et al.* (2019) then examined the 600 mT SMF effect on cell division of *Arabidopsis* root meristem cells using the transgenic line expressing β-glucuronidase (GUS) and found that SMF promotes root growth through enhancement of cell division.

Darwish and Darwish (2022) also showed a significant effect of SMF on human cell aggregation. They found that the magnetic forces induced by 0.24-2.2 mT SMF may cause aggregation of tau protein and affect the microtubule structure of the tau protein, leading to protein tangles. Other studies have shown the effect of SMF on human cell differentiation. Zablotskii *et al.* (2014a, 2016a), stated that an MF can affect the differentiation of stem cells into specific cell types by magneto-mechanical stress induced in mesenchymal stem cells. Dini *et al.* (2009) studied the effect of a 6 mT SMF on the differentiation of U937 cells induced by TPA (12-O-tetradecanoyl-13-phorbol acetate) and found that exposure to an SMF alone for up to 72 h increased the differentiation of cells, while exposure to both treatments resulted in a negative effect. Kim *et al.* (2015) demonstrated that a 15 mT SMF may have a use as a modulator of cell differentiation of MSC and this treatment may also improve bone regeneration. Chiu *et al.* (2007) showed that MG63 cells exposed to a 0.4 T SMF exhibited a more differentiated cell morphology. Another study by Coletti *et al.* (2007) which applied an 80 mT SMF documented the enhancement of the differentiation of skeletal muscle tissue by over 40% and also an increase in the accumulation of actin and myosin and the formation of large multinucleated myotubes.

2.4. Cell structure

Numerous studies have been performed on the effect of an SMF on the cell structure of plant and animal organisms, including humans. The studies have shown a significant impact of SMFs on changes in the size and shape of plant cells depending on the intensity and direction of the MF and taking into account different cell types and exposure conditions. For example, Hassanpour and Niknam (2020) found that different intensities of SMF changed the cell fresh weight and morphology of *M. chamomilla*. Cell fresh weight increased at 4 mT, however, decreased at 2 and 6 mT SMF and cells with a more round shape appeared at 6 mT on day 10, as compared to the control sample. Belyavskaya (2001) also reported significant changes in the structure of pea root meristem cells exposed to a 0.5-2 mT SMF and showed that mitochondria changed their shape from elongated to roundish and were 1.5-2 times bigger in diameter than those in control cells. Fatima *et al.* (2021) reported that after exposure of soybean plants to a 200 mT SMF they showed visible changes in their morphology and documented an increase in the average width of the midrib and minor veins of the third trifoliate leaves. Jin *et al.* (2019) observed the effect of a 600 mT SMF on the size of root meristem cells in *Arabidopsis*. They stated that the meristem size of treated seedlings was 9.66% longer than in untreated samples. The best results were achieved when the magnetic direction is adjusted to be in parallel to the gravity vector. Shokrollahi *et al.* (2018) showed that a 5 h day^{-1} exposure of soybean tissue to a 30 mT SMF decreased the size of the protein. Small *et al.* (2012) reported that an exposure to a 10 mT SMF for 12 days produced a similar decrease in cell size in *Chlorella kessleri* and changes in organelle organization, which is controlled by the cytoskeleton. They stated that the cells exposed to an SMF had a larger chloroplast with many more starch granules compared to the control cells. Selim and El-Nady (2011) found significant changes in the internal leaf and stem structure parameters of a tomato plant which was subjected to a 50 mT SMF pretreatment to seeds and water. They documented an increase in the thickness of the cortex and xylem of the stem and the thickness of the lamina, palisade and spongy tissues and vascular bundles compared to untreated plants. Another study reported that exposure of tobacco cells to 10 and 30 mT SMFs produced visible changes in their morphology. Abdolmaleki *et al.* (2007) reported that the average size of the treated cells significantly decreased and cleavage of the nucleus and its vacuolization appeared in cell morphologies when they were compared to those of the control cells. Bitonti *et al.* (2006) confirmed the trends of changes in the cell size and morphology of maize cells

with a 7 T MF. They found a reduction in the number and size of the quiescent centre in the root apical meristem, however, the cells of the root cap in seedlings of maize showed an increase in their length and mean area compared to the control group. In addition, metaxylem cells in the MF treatment exhibited nuclei with very condensed chromatin. Babaei-Ghazvini *et al.* (2020) also found that the exposure of cellulose nanocrystals (CNC) of corn starch to a 1.4 T SMF affected their structure. A significant impact was observed on the alignment of the CNC particles in the starch polymer matrix. Thus, the tensile strength and Young's modulus of nanocomposites were improved. On the other hand, Haneda *et al.* (2006) suggested that the exposure of cultures of cell suspension of *Catharanthus roseus* to a 302 mT SMF strengthened the cell wall.

Multiple studies present the exposure of different types of human and animal cells to SMFs in the range of 0.5 μT to 17 T, which may induce changes in cell morphology (Albuquerque, 2016; Dong *et al.*, 2019; Gurhan *et al.*, 2021; Kagami and Urabe, 2001; Zhang *et al.*, 2017c). For example, Darwish and Darwish (2022) found a significant effect of 0.24-2.2 mT SMF on the microtubule structure of tau protein and stated that an SMF has the potential to be used in a therapeutic procedure inducing changes in the molecular environment of the proteins. Yang *et al.* (2021) evaluated the cytoskeleton in an osteocyte-like cell line (MLO-Y4) after exposure to a 16 T SMF for 48 h and found that the fractal dimension of the microfilament and microtubule of osteocytes significantly increased. They also stated that an SMF promoted the rearrangement of microfilaments and microtubules in osteocytes. The exposure of cells to an MF affects cytoskeletal components such as actin filaments, microtubules and intermediate filaments, which are responsible for maintaining their shape and internal structures (Vergallo and Dini, 2018). Zheng *et al.* (2018) confirmed the rearrangement in the cytoskeleton of mesenchymal stem cells (dental pulp stem cells) with a 1-4 mT SMF. They demonstrated that the cytoskeleton density became much higher with a multi-angled cell shape compared with the control group and that a 4 mT SMF was more efficient. Marędziak *et al.* (2016) studied the morphology of mesenchymal stem cells from human adipose tissue under a 0.5 T SMF for 14 and 21 days. They found that the cell cultures exposed to the SMF had nuclei located asymmetrically towards one of the cell poles and the cytoplasm of the cells contained several mitochondria.

Studies have also shown that SMF affects cancer cells in relation to their morphology. For example, Zhang *et al.* (2017a) found that the spindle width increased in both CNE-2Z and RPE1 exposed to a normal field direction of a 27 T SMF. They stated that the combined alignment effects of both microtubules and chromosomes in the magnetic field affected the morphological changes. Wang *et al.* (2014) showed different responses to exposure of human breast adenocarcinoma cells (MCF-7) and cervical carcinoma cells (HeLa) to a 0.26-0.33 T SMF. The cell Young's modulus for HeLa cells was not significantly altered, however for MCF-7 it decreased compared to the control group, indicating a different actin distribution. Other studies showed changes in the morphology of cancer cells affected by a 6 mT SMF. Dini *et al.* (2009) found a significant modification to the shape of human U937 myeloid leukaemia cells which appeared to have a higher shape index than that of the control probe. They also observed de-arranged F-actin microfilaments and F-actin concentrated in differentiated U937 cells exposed to a 6 mT SMF for up to 72 h. Chionna *et al.* (2005) confirmed the shape and cytoskeletal modification in other cells. They demonstrated the formation of lamellar and bubble-like microvilli under an SMF in Hep G2 cells.

In the literature, some studies tried to link the effect of an SMF on the modification of the morphology of animal cells. For example, Chanana *et al.* (2022) observed redistribution of mitochondria in mouse peritoneal macrophages exposed to a 1.24 T SMF for 48 h and found that the changes in the mitochondria distribution were statistically highly significant. In addition exposure to the magnetic field gradient caused redistribution of the organelles away from the nucleus and cell elongation (Bz 1.2 T at the distance of 5 and 10 cm). Iwasaka (2019) studied the structure of a bone-forming osteoblast cell line exposed to a 5 T SMF. He showed that there was a deformation of the cell shape with a reduction of cellular width and changed structures with a round appearance under the SMF. Van Huizen (2019) found that exposure of animal tissue to a 200 μT WMF during planarian regeneration produced blastema sizes that were significantly reduced as compared to the control group. He observed significant reductions of blastema size under a 100-400 μT SMF but in contrast there was a significant increase under 500 μT. Wosik *et al.* (2018) showed that the exposure of macrophages to a 1.24 SMF caused an elongation in length of over 150 μm producing a thin tail and disruption of the Golgi complex.

2.5. Cell membrane structure

Numerous studies have examined the behavior of the cell membrane of plant and animal organisms, including humans as a result of the action of an SMF (Albuquerque *et al.*, 2016; Binhi *et al.*, 2001; Lin *et al.*, 2019; Wu *et al.*, 2022; Zablotskii *et al.*, 2018). The study results show that SMF may significantly change cell membrane potential and thus it may have a significant impact on the properties and biological functionality of cells. For example, Ercan *et al.* (2022) observed the plant root tip cells of barley exposed to different strengths of SMF and 250 mT and showed that continuous application of an SMF caused deformation and damage of the cell membrane and staining of the nuclei (Bahadir *et al.*, 2018; Hossain *et al.*, 2021). This was observed in all samples treated with an MF. However, Selim and Selim (2019) showed a 43% percentage increase

in membrane integrity (permeability) for plants treated with magnetized grains and magnetized water irrigated in a 30 mT SMF. These results are inconsistent with those reported by Selim and El-Nady (2011) on tomatoes. Payez *et al.* (2013) demonstrated the effect of a 30 mT SMF on the structures of wheat cell membranes and found an increase in membrane integrity compared to the control sample. Poinapen *et al.* (2013) also confirmed the enhancement of tomato membrane integrity exposed to 126 and 208 mT SMFs. They observed an increase in the gel lipid component and a decrease in the fluid component. The opposite relationship was found by Afzal *et al.* (2015) in early planted maize and Selim *et al.* (2019) in wheat tissue with magnetic water irrigated affecting membrane permeability reduction, however the osmotic pressure increased. Other studies also showed the changes in the integrity of human cell membranes. For example, Wu *et al.* (2022) investigated the effect of a 140 mT SMF on human mesenchymal stem cells. They showed that exposure to an SMF caused membrane depolarization induced by various ion channels which regulate the transmembrane flow of ions. A change in membrane potential was observed when the cells were exposed to an SMF for 30 min. Lew *et al.* (2018) found changes in the plasma membrane of dental pulp stem cells to a fluid to gel-like form after exposure to a 0.4 mT SMF for 30 min. These changes were not persistent or damaging to the cell membrane. Hsieh *et al.* (2015) confirmed that a 0.4 mT SMF increased the cell membrane rigidity of dental pulp cells, which is directly related to higher fluorescent anisotropy. Lin *et al.* (2013) demonstrated the effect of 0.4-0.8 T SMFs on human erythrocytes during the slow cooling procedure and found a decrease in membrane fluidity resulting in a reduction in basal membrane permeability. Lew *et al.* (2021) summarized the effect of an SMF on the membrane-cytoskeleton which induces the magnetic gradient forces causing changes to the cell membrane, ion channels and cytoskeleton. The change in membrane permeability induced in this way allows an influx of ions and a remodeling of the cytoskeleton.

Other studies conducted on cancer cells show similar effects of an SMF on the cell membrane. For example, Gurhan *et al.* (2021) investigated the effects of 0.5 to 600 μT (SMFs) for 4 days on HT-1080 human fibrosarcoma cells and found increasing concentrations of mitochondrial calcium and a membrane potential with increased MF intensities over 200 μT. Wang *et al.* (2018) confirmed the significant effect of an SMF on increasing the membrane potential of PC12 cells only when using a 1 T SMF with a 1-6 h exposure time. However, Calabro *et al.* (2013) showed an inverse relationship with exposure to a 2.2 mT SMF for 24 h on the SH–SY5Y cell and found a decrease of membrane mitochondrial potential of up to 30%. On the other hand, Lin *et al.* (2019) showed a strengthening of the membrane structure and a reduced membrane fluidity of NK92-MI cells exposed to a 0.4 T SMF. Wang *et al.* (2014), however, found that the membrane of MCF-7 treated by a 0.26 to 0.33 T SMF was visually rougher than the control sample, which affects the substrate-adhesion capability of cells.

A summary of the impact of the magnetic field on plants and animals, including human cells, described in the individual sections of this chapter, is presented in Tables 1-4.

Table 1. Effect of SMF on plant cell viability (V), proliferation (P), differentiation (D), structure (S), membrane (M) with value of effect (S-significant, N-non significant)

Cell type	Method	Cell or tissue response	Value of effect	Main topic	Reference
Root meristem cells of *Arabidopsis*	600 mT for 7 days	Depending on field direction, increase in cell division, cell number, root meristem length, and meristematic cortex cells. No significant changes in length of mature epidermis cells	S N	V S D	Jin *et al*., 2019
Arthrospira platensis cells	30 mT for 1 and 24 h per day for 10 days	Increase in cellular growth reaching higher biomass concentration after 4 days at 1 h per day	S	V	Deamici *et al*., 2019a
Root tip cells of barley (*Hordeum vulgare*)	20, 42, 125, and 250 mT for 2 weeks	Increase in deformation of and damage to the cell membranes altering their potential, ion transfer	S	M	Ercan *et al*., 2022
Bean (*Phaseolus vulgaris* L.)	130 mT for 14 days	Increase in number of cells in the metaphase and telophase stages	S	V	Mroczek-Zdyrska *et al*., 2016

Table 1. Continuation

Cell type	Method	Cell or tissue response	Value of effect	Main topic	Reference
Cell suspension cultures of *Catharanthus roseus*	302 mT for 0-250 min	Improved regeneration of protoplasts with increasing value of force applied and strengthening the cell wall structure by increasing the Young's modulus of the regenerated cell wall	S	V S	Haneda *et al*., 2006
Cellulose nanocrystals of corn (*communis frumentum*) starch	1.4 T for 72 h	Improved tensile strength and Young's modulus, elongation of nanocomposites and alignment of nanocrystals. Decreased permeability of water vapor	S N	S	Babaei-Ghazvini *et al*., 2020
Chlorella fusca LEB 111 (C. fusca)	25 mT for 1 and 24 h per day for 15 days	Increase in concentration of biomass in controlled conditions, and also uncontrolled for 24 h per day after 4 days of treatment. Changed protein profile with degradation of the protein bands	S	V	Deamici *et al*., 2021
Chlorella fusca LEB 111	30 and 60 mT for 1 and 24 h per day for 15 days	Increase in biomass concentration: higher after 1 h per day after 1 day of cultivation	S	V	Deamici *et al*., 2019b
Chlorella fusca LEB 111	30 and 60 mT for 1 and 24 h per day for 10 days	Increase in biomass concentration after 1 h per day at 30 mT for 8-10 days and at 60 mT for 1 and 24 h per day for 8-15 days	S	V	Deamici *et al*., 2016
Chlorella homosphaera	15, 30, 60 mT for 1 and 24 h per day for 15 days	Increase in growth parameters, biomass concentration at 30 and 60 mT (1 h d^{-1}) and productivity at 30 and 60 mT	S	V	Cota *et al*., 2020
Chlorella kessleri LEB 113	30 and 60 mT for 1 and 24 h per day for 10 days	Increase in biomass concentration after 8 h at 30 mT and 4 h at 60 mT, higher value at 60 mT for 1 h per day	S	V	Bauer *et al*., 2017
Chlorella kessleri	10 mT for 12 days	Change in cell ultrastructure with increasing chloroplast area and starch granule area, chloroplast starch granule area, starch granule number, decreasing pyrenoid starch area and max. thylakoid stacking	S	S	Small *et al*., 2012
Chlorella vulgaris cells	40, 80 and 150 mT for 2 h per day for 4 days	Increase in density (cell numbers mL^{-1}) at 80 and 150 mT after 2 days. Decreased aggregation percentage at 150 mT in first day	S	D	Luo *et al*., 2021
Chlorella vulgaris cells	20-150 mT for 2 h per day for 16 days	Increase in cell number, highest at 80 mT after 16 days, extracellular polysaccharides adhered to cell membrane at 150 mT. Decrease in aggregation percentage of cells and extracellular polysaccharides dissolved in the cell at 0.08 m T	S	V D	Luo *et al*., 2020
Chlorella vulgaris	10-50 mT for 12 h	Increase in specific growth rate at 10-35 mT and lipid peroxidation at 35-50 mT	S	V	Wang *et al*., 2008

Table 1. Continuation

Cell type	Method	Cell or tissue response	Value of effect	Main topic	Reference
Matricaria chamomilla cells	2, 4 and 6 mT for 1 h within 3 days	Increase in cell fresh weight at 4 mT on day 13 of subculture. Cell leaching appeared with rounder shape at 6 mT. No significant effect on cell viability	S	V S	Hassanpour and Niknam, 2020
Spring maize (*Zea mays*)	150 mT for 3 min. to seeds	Decrease in cell membrane permeability in early planted maize with enhanced phenolic and chlorophyll contents	S	M	Afzal *et al*., 2015
Maize cells (*Zea mays* L., Pioneer HI-Bred)	7 T for 10 and 30 h	Increase in cell area of root cap and cell length of metaxylem. For 30 h decrease in cell size in both height and width and cell number in center of roots. Change in structure profile of root cap cells with small statocytes indicating structural disorder and metaxylem cells with nuclei having highly condensed chromatin	S	S	Haneda *et al*., 2006
Pea (*Pisum sativum* L.)	0.5-2 mT	Increase in number of lipid bodies along plasmalemma, density and diameter of mitochondria and relative volume in cells. Change in cell structure with granules of various sizes of mitochondria and hyaloplasm of meristem cells. Decrease in volume of granular nucleolus component and nucleolus vacuoles.	S	S	Belyavskaya, 2001
Soybean (*Glycine max* (L.) variety JS-9560)	200 mT for 1 h of seed pretreatment	Increase in width of midrib and width of minor veins of third trifoliate leaves	S	S	Fatima *et al*., 2021
Soybean (*Glycine max* L. Merrill)	200 mT for 1 h to seeds	Increase in biomass accumulation expressed as a mass of atoms, molecules	S	V	Kataria, 2019
Soybean (*Glycine max* L. Merrill)	20 and 30 mT for 5 h per day for 5 days	Change in numbers in size distribution of catalase (BLC), ferritin (HSF), and apoferritin (HAS) increasing size of HSF and HAS and decreasing size of BLC at 30 mT	S	V S	Shokrollahi, 2018
Spirulina sp. LEB 18	25 mT for 1 and 24 h per day for 15 days	Increase in concentration of biomass and altered protein profile for 24 h per day in uncontrolled conditions	S	V P	Deamici *et al*., 2018
Spirulina platensis	0.1-0.55 T for 1-9 days	Increase in cell dry weight at fields below 0.4 T after 2 days. Decreased cell dry weight at fields greater than 0.4 T after 5 and 7 days	S	V	Li *et al*., 2007
Nicotiana tabacum cv. Barley 21 cells	0.2 m T for 0-24 h	Decrease in dry weight of cells for 3-12 and 24 h. Change in cell cycle progression	S	V	Mohammadi *et al*., 2018
Taxus chinensis var. mairei Y cells	3.5 mT for 8 days	Increase in cell viability within the first 4 days, extracellular conductivity at 6 days and cell biomass density	S	V	Shang *et al*., 2004

Table 1. Continuation

Cell type	Method	Cell or tissue response	Value of effect	Main topic	Reference
Tobacco cells (*Nicotiana tabacum* L. cv. Burley 21)	10 mT and 30 mT for 5 days, and for 5 h per day, for 5 days	Decrease in cell size in length and width at 30 mT. Increased percentage of dead cells. Change in morphological features of cells with cleavage of nucleus and its vacuolization. Increase in level of peroxidation of membrane lipids of suspension cultured tobacco cells	S	S M	Abdolmaleki *et al*., 2007; Sahebjamei *et al*., 2007
Tomato (*Solanum lycopersicum*) plasma membrane	126 and 208 mT	Change in structure of plasma membrane with increase in gel components, protein component (at 208 mT) and decrease in fluid component of the lipids. Increased intensities of plasma membrane at 208 mT and decreased intensities of buffer. Change in molecular structure to rigid and aligned	S	M	Afzal *et al*., 2013
Tomato (*Lycopersicum esculentum* L. cv StrainB)	50 mT pretreatment to seeds and water in real time	Change in internal structure of stem with increasing thickness of cortex and xylem tissues and leaf structure parameters with increasing thickness of lamina, palisade, spongy tissues and vascular bundles	S	S M	Selim and El-Nady, 2011
Microalgae *Tribonema* sp. cells	30 mT for 25 days	Increase in biomass concentration in semi-continuous cultures after 22 days and in batch cultures after 5 days at temperature below 30°C	S	V	Huo *et al*., 2020
Wheat (*Triticum aestivum* L.) cultivars Sakha 93 and Sids 9	50 mT used to magnetize water for irrigation	Increase in thickness of the midvein and lamina by 29% and 12% respectively, diameter of metaxylem vessel by 20%, length of midvein bundle by 6%. Decrease in membrane permeability	S	S M	Selim and Selim, 2019
Young fresh leaf cells of wheat (*Triticum*)	50 mT used for seeds and irrigating water in real time	Increase in membrane integrity percentage (membrane permeability) with magnetized grains and water	S	M	Zadeh-Haghighi and Simon, 2019
Wheat (*Triticum aestivum* L. cv. Kavir)	30 mT for 5 h per day for 4 days	Decrease in rate of membrane lipid peroxidation and electrolyte leakage, reinforcement of membranes	S	M	Payez *et al*., 2013
Wheat (*Triticum*) pollen mother cells	1, 3, 5 and 7 T for 1, 3 and 5 h to seeds	Increase in micronucleus, chromosomal bridge, lagging chromosome, and abnormal segregation at 5 or 7 T	S	S D	Pingping *et al.*, 2007

Table 2. Effect of SMF on human cell viability (V), proliferation (P), differentiation (D), structure (S), and membranes (M) with value of effect (S-significant, N-non significant)

Cell type	Method	Cell or tissue response	Value of effect	Main topic	Reference
		Healthy cells			
Chondrocytes cells	1-2 mT for 3 h, every 6 h for 8 days	Increase in cell proliferation at 2 mT for 3 h at 8 days and Glycosaminoglycan synthesis at 2 mT	S	P	Escobar *et al*., 2020
Chondrocytes cells	0.6 T for 72 h	Increase in metabolic activity	S	V	Stolfa *et al*., 2007
Human embryonic kidney (HEK) 293 cell	0.5 T for 48 h	No significant changes in cell surface morphology, however a parallel increase in the number of microvilli was observed with time	N	S	El-Gaddar *et al.,* 2013
Human erythrocytes	slowly frozen with 0.4 T or 0.8 T for 24 h	Decrease in membrane fluidity and enhanced erythrocyte membrane stability	S	M	Lin *et al*., 2013
MRC-5 human foetal lung fibroblasts	370 mT for 1 h per day and continuous exposure for 24 h	No significant changes in the viability and comet parameters (tail moment, tail length, number of hedgehogs)	N	V S	Lin *et al*., 2016
Human primary skin fibroblast and Chinese hamster ovary	13 T for 3 h	No significant effect on cell viability, cycle distribution and plating efficiencies	N	V	Guoping *et al.*, 2010
Skin fibroblasts	0.2 T for 1 h	Decrease in reactivity with lectins at plasma membrane, diameter of cell, cell proliferation, changed cell morphology with spindle-like shape with long, straight and stiff protrusions surrounded by numerous very thin and sharp cytoplasmic expansions and with irregular appearance of plasmalemma and cells forming deep globular masses	S	V S	Pacini *et al*., 2003
Lymphocytes	3-20 mT for 72 h	Decrease in cell viability, lysosomal activity. Increase in reactive oxygen species (ROS) production and percentages of modified cells (elongation, nucleus and cytoplasm blebbing, ruffled surface)	S	V S	Vergallo *et al*., 2013
Lymphocytes	6 mT for 1-7 days	Decrease in percentage of cell death. Increase in calcium concentration. Changed morphology with lamellar microvilli and hollows	S	V S	Tenuzzo *et al.*, 2009

Table 2. Continuation

Cell type	Method	Cell or tissue response	Value of effect	Main topic	Reference
Mesenchymal stem cells	140 mT for 24, 48, 72, 96, 120, and 144 h	Increase in cell proliferation rate by 23% for 72 h. Membrane depolarization transduced by T-type voltage-gated calcium channels into second-messenger cascades (*e.g.*, ERK, JNK) that regulate downstream gene expression (*e.g.*, FOS, EGR1)	S	P M	Wu *et al.*, 2022
Mesenchymal stem cells	328 mT for 6 days	Decrease in alkaline phosphatase activity and mineralization in the cells. No significant changes in proliferation and growth	S	V P	Molo and Ordu, 2021
Mesenchymal stromal cells	0.08 T over 24 h	Increase in cell elongation (cell length) and production of vascular endothelial growth factor-A promoting vascular permeability and cell migration. No significant effect on proliferation, viability and phenotypic identity	S N	V P S	Manjua *et al.*, 2021
Mesenchymal stem cells (dental pulp stem cells)	1, 2 and 4 mT for 12 and 24 h	Increase in cytoskeleton density at 2 and 4 mT, proliferation, cell migration, gene expression and osteo/odontogenesis and mineralization in cells at 1 mT	S	P S	Zheng *et al.*, 2018
Dental pulp stem cells	0.4 T for 3 days	Increase in proliferation and changed molecular structure of membrane and cytoskeleton architecture	S	P M	Lew *et al.*, 2018
Mesenchymal stem cells	2, 18 and 24 mT for 24 h and 21 days	Decrease in viability after 36 h post exposure, proliferation rate and cell population in G1 phase at 18 mT	S	V P	Sadri *et al.*, 2017
Mesenchymal stem cells from human adipose tissue	0.5 T for 14 and 21 days	Increase in proliferation factor, colony forming efficiency, concentration of collagen type I, osteopontin, bone morphogenetic protein 2, number of osteogenic nodules and calcium content of osteoblast. Decrease in alkaline phosphatase and phosphorus content of osteoblast	S	V P S	Marędziak *et al.*, 2016
Mesenchymal stem cells	3, 15, and 50 mT for 1-21 days	Increase in cell proliferation and alkaline phosphatase activity highest at 15 mT after 14 or 21 days of exposure, amount of calcium in mineral deposits at 15 and 50 mT	S	V P	Kim *et al.*, 2015
Mesenchymal stem cell	1.2 T for 2, 3 and 7 days	No significant changes in cell proliferation and DNA damage	N	P	Zablotskii *et al.*, 2014a
Monoblastic cells (pro-monocyte)	6 mT for 1, 2 and 3 days	Decrease in degree of cell differentiation, adhesion rate of cells	S	V D	Pagliara *et al.*, 2005

Table 2. Continuation

Cell type	Method	Cell or tissue response	Value of effect	Main topic	Reference
Myoblast cells	80 mT for 1, 3 and 5 days	Increase in orientation (anisotropy) of cells with more aligned bundles forming larger myotube, differentiation efficiency of cell, actin accumulation resulting in the formation of thicker and longer actin stress-fiber. No changes in cell proliferation	S N	P D	Ciletti *et al*., 2007
Oligonucleotides-duplex DNA	300 mT in real time	Increase in electronic conductivity of duplex DNA which may cause exaggerated radical-induced DNA damage	S	D	Soumyanarayanan *et al*., 2016
Osteoblasts, cementoblasts, and periodontal ligament cells	3, 15 and 50 mT for 3, 7 and 14 days	Increase in alkaline phosphatase activity, density of osteocalcin, osteopontin and osteoblast-specific-transcription, factor mRNA, calcium content in osteoblasts and the formation of mineralized nodules	S	V	Kim *et al*., 2017
Osteoblastic cells MG-63 cells	0.4 T for 1– 5 days	Decrease in proliferation rate of cells for 3 days. Increased alkaline phosphatase activity for 1 day	S	P V	Feng *et al*., 2010
Osteoblast-like cells	0.1, 025 and 0.4 T for 24, 48 and 72 h	Increase in membrane rigidity, alkaline phosphatase activity and extracellular matrix. Decrease in proliferation effects of growth factors for 24 h	S	V P M	Chiu *et al*., 2007
MG63 osteoblast-like cells	0.1, 0.25 and 0.4 T for 12-48 h	Decrease in number of cells, growth rates and membrane fluidity. Increase in alkaline phosphatase activity for 48 h	S	V M	Chiu *et al*., 2007
Osteoblast-like cells	0.4 T for 12, 24, 48, and 72 h	Increase in cell numbers for 24 h and differentiated morphologic features with extracellular matrix from the plasma membrane after 24 h and abundant matrix vesicles after 48 h	S	V S	Huang *et al*., 2006
Osteocyte-like cell line, MLO-Y4,	16 T for 8-48 h	Increase in cellular viability, fractal dimension of the cytoskeleton, iron levels in osteocytes, connexin 43 protein expression. Decrease in sclerostin protein expression, apoptosis and changed secretion of cytokines	S	V S	Yang *et al.*, 2021
Periodontal ligament (PDL) cells	0.01 and 0.15 mT for 15 min	Increase in cell viability depending on temperature	S	V	Kaku *et al*., 2010
Periodontal ligament cells	10 mT and 120 mT for 12, 36 and 60 h	Change in structure of cytoskeleton F-actin with shortening to oval forms and disordering depending on field conditions. Decrease in area Ac of cell cross section for 60 h	S	S	Xu *et al*., 2008

Table 2. Continuation

Cell type	Method	Cell or tissue response	Value of effect	Main topic	Reference
Tau protein	0.24-2.2 mT for 2 min	Increase in vibrating molecules in the amplitude of and intensity of yield. Tau protein's microtubule structure affected (leading to protein aggregation)	S	D S	Darwish and Darwish, 2022
Umbilical vein endothelial cells	60 and 120 mT for 1 h and 24 h per day for 2, 3 and 4 days	Increase in cell proliferation for 24 h per day	S	P	Martino *et al.*, 2010
		Cancer cells			
HCT116 and LoVo cells	1 T for 8 h	Induction of disregulation of DNA replication resulting in different numbers of cells surviving in up- and down-MF. Decreased cell proliferation	S	V P	Yang *et al*., 2020
CNE-2Z and RPE1 human cells	27 T for 4 h	The magnetic torque affected microtubules and chromosomes and spindle morphology	S	S	Zhang *et al*., 2017a
Human cervical carcinoma, breast cancer, colorectal carcinoma and nasopharyngeal cancer cells	1 mT for 2–12 h and 3, 7 days	Increase in abnormal mitotic spindles and mitotic index of HeLa cells for 7 days. Decrease in cell number in synchronized HeLa cells by mitotic arrest at 10-12 h	S	V P	Luo *et al.,* 2016
SH-SY5Y neuronal-like cells	2.2 mT for 4- 24 h	Decrease in membrane mitochondrial potential at 24 h. Changed cell homeostasis and structure of cellular proteins and lipid components	S	S M	Calabrò *et al*., 2013
U937 myeloid leukemia cells	6 mT for 24, 48 and 72 h	Increase in degree of differentiation of cells and shape index for 48 and 72 h and calcium concentration for 24-48 h. Change in cell morphology with inhibition of cell attachment and appearance of membrane roughness and large blebs	S	S M D	Dini *et al*., 2009
Glioblastoma cells	8, 30 and 300 mT for 3 h	Increase in cell modification from elongated to rounded cells with micronuclei and vacuolized cytoplasm, mean cellular height, density of actin distribution and filament contraction. Change in membrane organization with increasing standard deviation of roughness	S	S M	Teodori *et al*., 2006
Promyelocytic leukemic HL-60 cells	6 mT	Decrease in frequency of cells in the early apoptotic compartment. Induced cells to enter the necrotic phase of apoptosis more rapidly indicating that the plasma membrane is becoming more permeable	S	M	Teodori *et al.*, 2002

Table 2. Continuation

Cell type	Method	Cell or tissue response	Value of effect	Main topic	Reference
Human lung cancer A459 cell growth in mice	9.4 T for 0-88 h	Decrease in cell number depending on field direction for 24 h	S	V	Yang *et al*., 2021
Human breast adenocarcinoma (MCF-7) and cervical carcinoma cells (HeLa).	0.26 to 0.33 T for 72 h	Decrease in viability and proliferation after 48 h, number of attached cells and Young's modulus after 72 h of MCF-7 cells. Increase in roughness of cell membrane of MCF-7 cells	S	V P S M	Wang *et al*., 2014
Hep G2 cells	6 mT for 24 h	Decrease in cell viability and growth rate. Increased apoptosis, calcium concentration, percentage of cells with altered morphology (*i.e*., rounder and more fibroblast-like shape) with cytoskeletal modifications	S	V P S	Chionna *et al*., 2005
Human fibrosarcoma HT-1080 cells	0.5 and 600 µT for 48 and 72 h and 4 days	Increase in cell growth rate at 200-500 µT for 72 h and 200-400 µT depending on field direction, membrane potential and mitochondrial calcium concentrations at 200-500 µT. Decrease in cell growth rate at 600-µT for 4 days	S	V M	Gurhan *et al.*, 2021
NK92 mI and K562 cell lines	0.4 T for 48 h (NK cells) and 4 h coculturing with K562 cell lines	Increase in viability and killing activity of NK92-MI cells when pre-exposed to SMF for 48 h. Decreased fluidity of cell membrane	S	V M	Lin *et al*., 2019
		Healthy and cancer cells			
NK cell line (NK92-MI) and erythroleukemic cell line (K562)	0.4 T for 72 h and 4 h	Increase in cell viability, greater membrane structural order (by DPH), ability to kill cells (for 48 h) for NK cells	S	V M	Lin *et al*., 2019
5 Human solid tumor, 2 leukemia and 4 non-cancer cell lines (epithelial cells of retinal pigment, small airway and trachea). Chinese hamster ovary cells	0.2-1 T for 2 days	Decrease in number of all human solid tumor cell lines and leukemia cells in suspension depending on direction and value of magnetic field. No significant changes in the cell numbers of non-cancer cells	S	V P	Tian *et al*., 2018
Different types of human cancer cells (HCT116, A431, A549, PC3, MCF7 and EJ1 cells) and non-cancer (293T, RPE1, HSAEC-2KT, HSAEC-30KT and HBEC-30KT cells)	1 T for 2 days	Decrease in number of cancer cells at higher cell densities. No significant effect on cell cycle or cell death	S	V P	Zhang *et al*., 2017b

Table 2. Continuation

Cell type	Method	Cell or tissue respons	Value of effect	Main topic	Reference
Melanoma, adult adipose stem cell line, adult skin fibroblasts	35–120 mT for 18 h and 4, 7, 11, 14 days	Decrease in cell number. No significant changes for adult adipose stem cell line. Decrease in growth of melanoma cells by 20% on day 7	S	V	Sullivan *et al.*, 2011
Neuroblastoma (NG108-15), fibroblastoma (NIH/3T3), and osteoblastoma (MC3T3-E1) cells(human)	30 and 120 mT for 4 h	Increase in cell diffusion constant for neuroblastoma and fibroblastoma Change in cell diffusion constant for osteoblastoma depending on field strength and exposure direction	S	V	Hashimoto *et al*., 2007
Human lymphocytes, mice thymocytes, 3DO, U937, HeLa, HepG2 and FRTL-5 cells	6 mT for 24 and 48 h	Decrease in cell viability of Hep G2 and FRTL-5. Increase in intracellular levels of calcium, apoptosis of 3DO, Hep G2 and FRTL-5 cells, mitosis (except of lymphocytes and FRTL-5) and cell viability of thymocytes and HeLa.	S	V P S	Tenuzzo *et al.*, 2006
Human epithelial, rat fibroblast and mouse fibroblast cells	7, 13 and 17 T for 30 and 60 min	Decrease in cell adhesion, number of cells, cell area of fibroblastic cells and number of neurons. Increased modifications of the cell adhesive structure, cytoskeletal disorders.	S	V P S	Valiron *et al.*, 2005
Lymphocytes and U937 cells	6 mT for 5 days	Decrease in apoptotic rate Increase in calcium content Changed cell surface modifications with cell shape distortion and presence of lamellar microvilli	S	P S	Chionna *et al*., 2003
8 human cancer cell lines, 3 rat cancer cell lines and 2 non-cancer cell lines	0.26, 0.50, 1 and 9 T for 1–9 h	Increase in cellular ATP (adenosine-5'-triphosphate) levels and mitochondrial membrane potential at 1 T for 1 and 6 h and decrease at 9 T for 3 h	S	M	Wang *et al*., 2018
HCT116, CNE-2Z and CHO cells	0.05, 1 and 9 T for 3 days	Decrease in number of cancer cells at 1 and 9 T, reduced proliferation of CHO-EGFR cells (Chinese Hamster Ovary cells with EGFR overexpression) and EGFR-expressing cancer cell lines by 35%	S	V P	Zhang *et al*., 2016
HeLa cell line and normal skin fibroblast (Hu02)	10 mT for 24 and 48 h	Increased cell death of HeLa cell line for both times and Hu02 for 24 h post treatment	S	V	Kamalipooya *et al*., 2016

Table 3. Effect of SMF on animal cells regarding viability (V), proliferation (P), differentiation (D), structure (S), membrane (M) with value of effect (S-significant, N-non significant)

Cell type	Method	Cell or tissue respons	Value of effect	Main topic	Reference
Chinese hamster ovary	0.66 T for 0-14 days	Increase in number (with Nuclear Buds) and viability of cells (for 9 days). None affected by cell chromosomal damage.	S	V	Rekena *et al.*, 2021
Equine adipose-derived stem cells	0.5 T for 7 days	Increase in number of microvesicles per cell, number of colonies formed from 100 cells, proliferation of the cells, concentration of bone morphogenetic protein 2 and vascular endothelial growth factor, colony-forming efficiency. Decrease in calcium concentration and tumor necrosis factor	S	V	Maredziak *et al*., 2015
Mouse embryonic fibroblasts (NIH3T3) and fibroblast cells (L929)	0.5 T for 12-48 h	Increased vitality, proliferation and migration of cells	S	V P	Galland and Pazur, 2022
Mouse macrophages	1.24 T for 48 h	Clustering of cation channel receptors TRPM2, which are the Ca2+-permeable cation channels from the ion transport protein family. Change in macrophage concentration at the corners of the central magnet and the dispersion of Golgi complex	S	S	Chanana *et al*., 2022
Macrophages from C57BL/6 mice	1.24 T for 48 h	Increase in number of cells with nuclear vinculin, number of elongated cells and average length from 50 to over 150-um. Disrupts actin-dependent molecules and structures such as the Golgi complex, vinculin (focal adhesions), and receptors	S	V S	Wosik *et al*., 2018
Mice (*M. musculus*) myoblast cells	0.2 T for 48 h	Decrease in number and growth of cells	S	V	Kim and Im, 2010
Mouse bone-forming cell line (osteoblast, MC-3T3-E1	5 T in real time	Change in intracellular components, texture pattern and coloring of intracellular macromolecule structures	S	S	Iwasaka *et al.,* 2019
Murine osteosarcoma cell line K7M2 and human osteosarcoma cell line MG63	0.2-0.7 T for 3, 5 and 7 days	Increase in proliferation and diameter of tumorspheres	S	P	Zhao *et al*., 2021

Table 3. Continuation

Cell type	Method	Cell or tissue respons	Value of effect	Main topic	Reference
Mice pre-osteoclast RAW 264.7 cells	16 T for 2 and 4 days	Decrease in iron absorption and iron storage-related protein expression, total protein in mitochondria mitochondrial concentration, activity of tartrate-resistant acid phosphatase (TRAP), osteoclastic differentiation and resorption activity. Increase in cellular adenosine triphosphate (ATP)	S	V	Dong *et al*., 2019
Stem cell of planaria	0.1-0.6 mT for 1-72 h	Stem cell activity affected increasing blastema size at 0.5 m T and decreasing at 0.2 m T after 24 h	S	P S	Van Huizen *et al*., 2019
Adipose-derived stem cells from male Lewis rats	0.5 T for 7 days	Decrease in viability, proliferation, cytokine secretion, expression of surface antigens and stem cell specific markers, and adipogenic and osteogenic differentiation	S	V P S	Wang *et al*., 2016
Mesenchymal stem cells from rats	1.2-1.5 T generated by patterned micro-magnets for 2-3 days	Decrease in number of cell clusters. Increase in ion concentration and cell migration	S	V	Zablotskii *et al*., 2013
Rat cortical neuron cells	0.1, 0.5, 0.75, 1, 2, 5 T for 1 h	Increase in activation of the extra cellular-regulated kinase associated with cell differentiation and resting calcium concentration at 0.75 T	S	D	Prina-Mello *et al*., 2005

Table 4. Effect of MF on the cell from theoretical analyses (viability - V, proliferation - P, differentiation - D, structure - S, membrane - M)

Cell types	Method	Cell or tissue response	Main topic	Reference
Paramagnetic and diamagnetic molecules	20.8-110 T MF	Increase in diffusion of diamagnetic molecules and decrease in diffusion of paramagnetic molecules in cell cytoplasm. Diffusion model developed from the mechanism of the MF's effect on diffusion. Cell-to-cell communication can also be directly affected by MFs	D	Zablotskii *et al*., 2016a
Biological cells	Bioelectric parameters of cells	Computational model of organism development produced on the basis of the bioelectric properties of cells. The development of the organism can, potentially, be controlled by the progress of the membrane electric potential from depolarization to polarization, the resulting effect on cell proliferation capability, the determination of the cell and tissue bioelectric state (in particular the transmembrane potential) during organ or organism development and through the contribution of bioelectric potentials and currents in the different activity conditions of cells	M	Carvalho, 2022

Table 4. Continuation

Cell types	Method	Cell or tissue response	Main topic	Reference
Cell membrane	100 T SMF	Changed cell membrane potential and magnetically assisted intracellular diffusiophoresis of large proteins	M	Zablotskii *et al*., 2021
Ferritin protein	0.1-2 T SMF	Mechanisms of ion channel activation based on the magneto-caloric effect, mechanical cell membrane deformation by the diamagnetic force, and the mechano-thermal Einstein-de-Haas effect. Effect of the magnetic particle in ferritin on the ion channels in cell membranes	M	Barbic *et al*., 2019
Biological cells	Weak magnetic fields	Induced effect of particle transitions by spin-orbit interaction giving coupling of the spin magnetic moment with the spatial motion of the particle. This may arise in ordered biophysical structures such as biomembranes, tubulin microtubules, nerve synapses, and DNA. Particle transfer between wells under dissipation conditions depends on the magnitude and direction of MF	M S	Binhi, 2019
Biological cells	SMF	Decreased precession of the magnetic moments of rotating molecules relative to the biophysical structures in some conditions, which results in the mixing of the quantum levels of magnetic moments. Information on the molecular rotations can be obtained from the shift of the spectral peaks	S	Binhi and Prato, 2018
Biological cells	High-gradient magnetic field up to 10 mT m^{-1}	Affected the intracellular biomechanical forces. Increased cell responses arise at timescales varying from a fraction of a second to days depending on cell type, magnitude of magnetic gradient and time of exposure. Changed redistribution of F-actin filaments and microtubules in the direction of quasi-equilibrium of the cell body. Predicted threshold of gradient fields for producing a change in ion diffusion through the magnetic gradient stress. Change in opening/closing voltage-gated ion channels. Induction of cell death through mechanical rupture of a cell by magnetic gradient forces with different directions. Prevented cancer cells from dividing and arrested tumor growth. Induced a variety of time scales and thresholds of cell responses to magnetic gradient forces	V S M	Zablotskii *et al*., 2018
Biological cells	Weak magnetic fields	Increase in rate of intracellular enzymatic reaction accompanied by electron transfer. Induced production of biologically important molecules for cell growth	V	Letuta *et al.,* 2017
Biological cells	High-gradient magnetic fields (approximately 1T)	Induced cytoskeleton remodeling (elongating the cells), cell division and cell reprogramming, mechanical stress in the membrane, membrane bending, migrating membrane receptor proteins. Change in probability of ion channel on/off switching events and ion flux balance and membrane potential. Decrease in cell growth	V S M	Zablotskii *et al*., 2016b

3. POSSIBLE MECHANISMS AND FUTURE PROSPECTIVES

Electric and magnetic potentials play a significant role in the functioning of living organisms because all cells are systems charged by components such as electrons, paramagnetic ions, protons, magnetic nuclei *etc*.). Therefore, they exhibit a drastic reaction to the magnetic field (SMF) applied, which may stimulate and control cellular functions such as viability, proliferation, migration, differentiation, morphology, and molecular synthesis (Harb *et al.*, 2021; Islam *et al.*, 2020; Selim *et al.*, 2019; Wu *et al.*, 2022; Zablotskii *et al.*, 2018). Figure 1 presents the cellular effects of using the magnetic field on the example of high gradient magnetic field (HGMF) for cell remodeling from the point of view of biomedical applications. Intracellular effectors of HGMF include: cytoskeletal remodeling, change in ion channel probability, membrane mechanical stress and deformation, ion flux balance and membrane potential. Similar effectors have been grouped into viability, differentiation, and cell structure, and membrane potential can be distinguished in the case of applying moderate static magnetic field (MSMF) to plant and animal cells, which are presented in Fig. 2.

In this context, numerous factors need to be taken into account with the application of the appropriate intensity of MF to enhance the cell dynamics and avoid cell damage (Binhi and Rubin, 2022; Dziergowska *et al.*, 2021; Ercan *et al.*, 2022). Many factors must be taken into account when applying the appropriate MF intensity to increase cell dynamics and avoid cell damage, and at the same time to obtain a tool (Binhi and Rubin, 2022; Dziergowska *et al.*, 2021; Ercan *et al.*, 2022). As a consequence, these activities lead to the development of tools for the formation and remodeling of plant, human and animal cells. In this topic, it is important to understand the mechanism of the magnetic field impact on living organisms.

Magnetic fields have been proven to cause biological effects on the cellular impacting on their properties and biological functionality. The basic mechanism regulating cell properties is bioelectric signals that control their cell behavior (Carvalho, 2022). The electrostatic energy stored in the membrane of a spherical cell with a radius of 10 μm and voltage of 70 mV is many times greater than the energy of thermal fluctuations, chemical bonds and bending of the membrane (Hsieh *et al.*, 2015; Zablotskii *et al.*, 2016b). They influence processes such as shaping, stiffness, endocytosis, adhesion, creeping, division and apoptosis. Cell membrane stiffness is proportional to membrane voltage (Chiu *et al.*, 2007; Levin, 2012). Hence undifferentiated cells (capable of rapid proliferation) with low membrane potential values are highly plastic and tend to depolarize (Carvalho, 2022; Levin, 2012,2020; Zablotskii *et al.*, 2018). In contrast, mature cells tend to hyperpolarize. In this way, the stiffness of the cells can be influenced by changing the membrane voltage. For example, cancer cells have low membrane potentials and so they are more plastic and highly invasive. Analyses show that a magnetic field with an intensity of 1 T with a gradient of up to 1 GT m^{-1} can significantly change the membrane potential of a cell, and thus have a significant impact on the properties and biological functionality of cells (Levin, 2012; Yang and Brackenbury, 2013; Zablotskii *et al.*, 2016b). The magnetic gradient forces create an ion flux through the cell membrane, thus the presence of an SMF alters the ion flux balance across the cell membrane, this in itself changing the membrane potential (Sear *et al.*, 2019; Zablotskii *et al.*, 2016ab). The MF affects the cell membrane allowing the

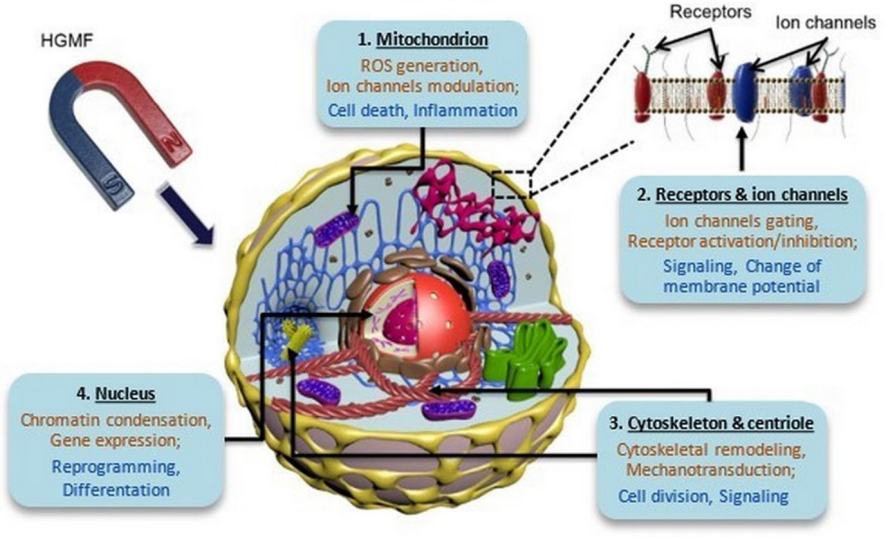

Fig. 1. Schematic illustration of the possible cellular effects of HGMFs and intracellular effectors (Zablotskii *et al.*, 2016b).

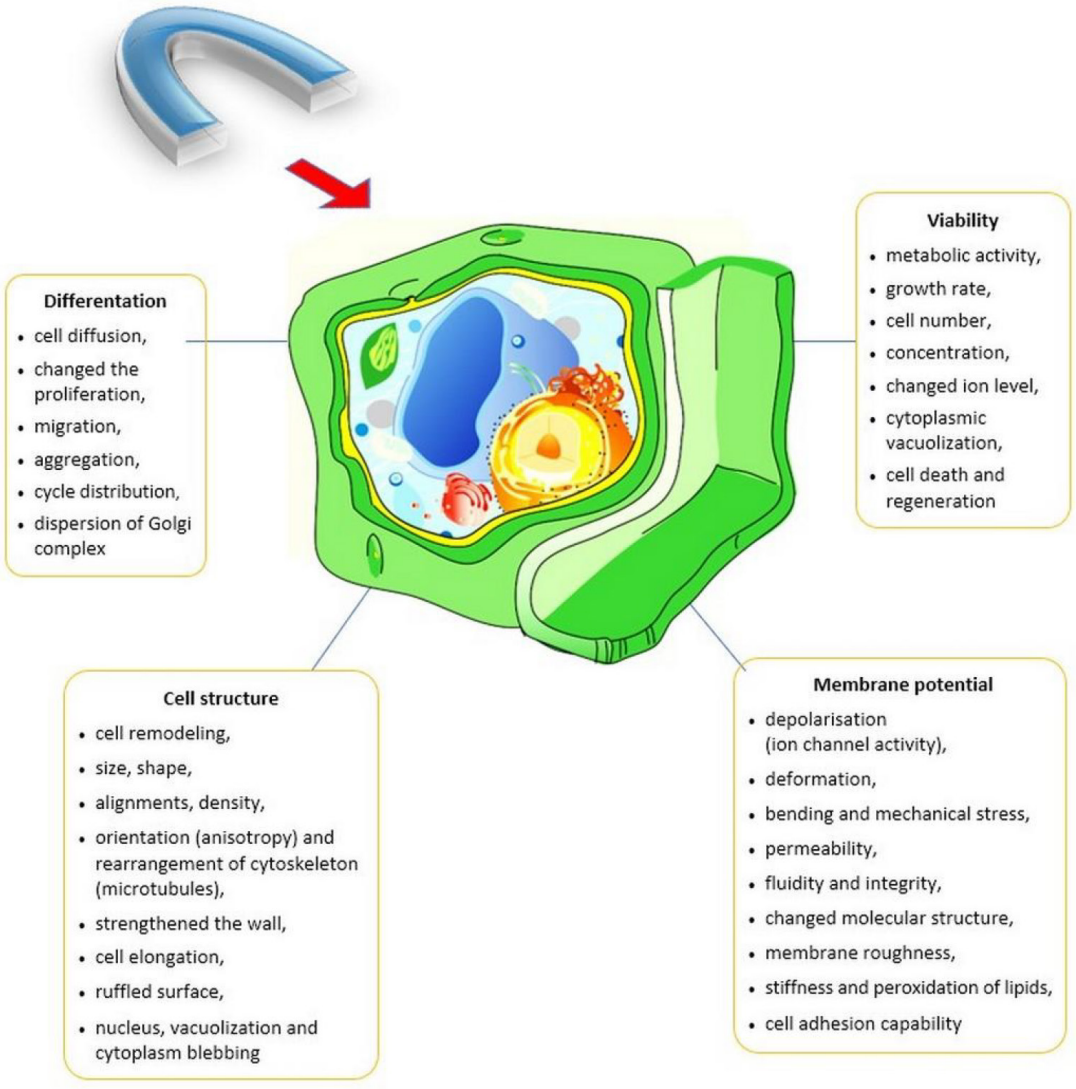

Fig. 2. Presentation of possible cellular effects of MSMF for cell remodeling of plant and human cells and its effectors (own analysis).

active transport of ions by opening the ion channel and by the stimulation of pumps and thus may affect the properties, growth and viability of cells.

Magnetic fields can also influence the differentiation of stem cells into specific cell types and their behavior by coordinating the magneto-mechanical stresses generated in the cells (Sundelacruz *et al.*, 2009; Zablotskii *et al.*, 2014a, 2021, 2022). Cell division can be induced or assisted by a spatial magnetic field gradient (Lew *et al.*, 2021; Wong *et al.*, 2015; Zablotskii *et al.*, 2021, 2022; Zhang *et al.*, 2017c). An example of the configuration of the magnetic field and the force distribution of the magnetic gradient generated in the gap between two uniformly magnetized magnets, developed on the basis of a theoretical model, is presented in the study (Zablotskii *et al.*, 2016ab). The magnetic gradient acting on a cell can create pressure inducting inner stress that promote in cell wall rupture. On the other hand, compression of tissue by magnetic gradient can split cells form tissue. Similar mechanism of seed cover damage was observed for pea seed compressed between two objects. Other analyses show that magnetic pressure can limit tumor growth of Fe-enriched cancer cells due to the attractive force of the magnetic gradient in this case. This mechanism is confirmed by studies in which an applied mechanical stress greater than 500 Pa slowed down the rate of tumor growth, preventing cell division (Dobrzański and Szot, 1997; Jin *et al.*, 2012; Zablotskii *et al.*, 2016). Zhang *et al.* (2023c) showed that SMF of 320 mT can enhance the proliferation and differentiation of mesenchymal stem cells (MSCs).

Other studies show the importance of membrane potential values, especially concerning the activity of ion channels, in the regulation of cell function (Albuquerque *et al.*, 2016; Gurhan *et al.*, 2021; Wang *et al.*, 2018; Wu *et al.*,

2022; Zablotskii *et al.*, 2018, 2022). Ion channel activity can be activated through various mechanisms. However, the activity of stretch-activated ion channels can be changed by deforming the cell membrane, which can occur in a magnetic field with a gradient greater than 1 kT m^{-1}. Another way of driving the gating of ion channels (opening/closing) is related to the change of cell membrane potential in a field with a gradient of 1GT m^{-1} (Zablotskii *et al.*, 2016b). In neuronal cells, the opening/closing of voltage-gated ion channels occurs at a membrane potential value of 7-12 mV. For example, cancer cells usually have a low membrane potential, which is associated with the overexpression of certain ion channels (Accardi, 2015). Membrane potential controls the differentiation of stem cells, thus potentially directing the differentiation pathway, and also plays an important role in the organization of cytoskeleton and cell division proteins (Levin *et al.*, 2012; Strahl and Hamoen, 2010). The impact of magnetic fields with a gradient value of 106 T m^{-1} can be manifested by a change in the probability of opening/closing mechanosensitive ion channels, which are gated by mechanical stresses occurring in the cell membrane (Accardi, 2015; Bialecka-Fornal *et al.*, 2012; Law *et al.*, 2016; Zablotskii *et al.*, 2014b) to the activity of ion channels. In the cell membrane, mechanosensitive ion channels are responsible for transducing mechanical into electrical signals.

Studies show the impact of external SMFs on the cell's cytoskeleton, which is responsible for its shape and function (Zablotskii *et al.*, 2013, 2014a, 2016a). The cell consists of structural micro- and nanoparticles with different magnetic susceptibilities that can respond to magnetic forces induced by an MF. Model analyses show that basic cell components such as F-actin, intermediate filaments and microtubules are responsible for maintaining mechanical balance in response to external factors. Therefore, depending on the balance between the strength of the magnetic gradient and the forces generated by the cytoskeleton filaments, various biological effects may arise, *e.g.* cytoskeleton remodeling, changes in cell shape and size, mechanical stresses in the membrane, deformation and bending of the membrane, ion channels on/off switching, changing the balance of ion flux and membrane potential, Golgi complex rearrangement (Wosik *et al.*, 2018; Zablotskii *et al.*, 2016b; Zhang *et al.*, 2017c). The effect of an SMF depends on the type of cell, its stage of development and health, its intensity and the conditions of application of the MF.

Recently, the potential biomedical application of SMF has been widely studied in the context of its beneficial effects on health as well as its use to support the growth of plant cells and cellular components and their structural changes. A static magnetic field is an increasingly recognizable tool in complementary medicine, biotechnology and the processing industry, which, by modulating the metabolism of individual cells, can improve the body's regenerative processes, formation and dynamic remodeling of living structures (Alam *et al.*, 20023, Chansoria *et al.*, 20023, Lei *et al.*, 2020; Lew *et al.*, 2018; Lv *et al.*, 2021, Blümler, 2021; Descamps *et al.*, 2021; Hafeez *et al.*, 20023, Li *et al.*, 2022; Rekena *et al.*, 2019; Saletnik *et al*., 2022, Zhang *et al.*, 2023b, c). Electromagnetic stimulation has been used in medicine as a tool to increase wound healing, bone regeneration, on dental implant osseointegration, cancer treatment and as a component of magnetic resonance technique (Cecoro *et al.*, 2022; Hollenberg *et al.*, 2021; Marycz *et al.*, 2018). MF can also be used on an industrial scale for the production of biomolecules (carbohydrates, proteins, lipids, pigments) in photoreactors, plant cultivation, extending the shelf life and quality of the product, freezing preservation of fruits and vegetables (Dhiman *et al.*, 2023; Font *et al.*, 20023; Hassanpour *et al.*, 2023; Pawełek *et al.*, 20022; Qiao *et al.*, 2023).

The key to understanding the action of an MF in biological systems is the mechanism of radical pairs; which act as magnetosensitive agents. Electron transfer is a source of radical pairs and accompanies many biochemical processes (Buchachenko and Kuznetsov, 2021; Lahiri *et al.*, 2001). The energy involved in the recombination of radical pairs results from the interaction between the spins of unpaired electrons and the spin of adjacent nuclei; between the spins of the radical pair; and the interaction of the isolated spin and magnetic field (the Zeeman interaction) that causes the direction of the electron's magnetic moment of the electron to oscillate (Albuquerque *et al.*, 2016). Spin interactions with external magnetic fields will cause the state of the radical pair to oscillate between the S (singlet) and T (triplet) states and may lead to various biochemical reactions (Hore *et al.*, 2020; Rodgers, 2009).

Free radicals are highly oxidizing and can damage nucleic acids, proteins, and lipids and at the same time can damage DNA. They can be activated by magnetic fields (Yang *et al.*, 2021; Yuan *et al.*, 2020). An important problem to be investigated is the identification of magnetic field-sensitive radical pairs, as well as the appropriate chemical reactions and the corresponding kinetic rates (Hogben *et al.*, 2009; Rishabh *et al.*, 2022). Many chemical reactions that take place in the cell involve the transfer of electrons that can be affected by the MF (Scandalios, 2002). Consequently, they are crucial for many important biological functions, including energy production, oxidation, DNA repair, RNA methylation, apoptosis, protein folding, cytoskeletal dynamics, detoxification, and neuronal development (Hamdane *et al.*, 2016; Vitali *et al.*, 2016; Zwang *et al.*, 2018). However, these processes must be carefully regulated because the free electrons generated by such redox reactions can attack and damage cellular macromolecules (Espinosa-Diez *et al.*, 2015; Sies *et al.*, 2017).

There are also other highly magnetic materials in biological systems that can be affected by an MF, such as ferrimagnetic minerals (including iron and nickel oxides), iron-binding proteins, and iron-sulfur cluster proteins. Iron

and sulfur cluster proteins play a key role in many cellular functions, especially in electron transport. Cryptochrome is the main protein that plays a significant role in magnetoreception (Qin *et al.*, 2016).

An SMF can change the following membrane properties: hyperpolarization, redox potential, and fluidity. In this way, there is a change in the accumulation of ions within and outside the cell, which can affect its overall charge and the diffusion of molecules. As a result, changes in calcium ion content occur in cells exposed to an SMF, increasing their content in the cytoplasm (De Nicola *et al.*, 2006; Morris and Skalak, 2007; Nuccitelli *et al.*, 2006; Rosen, 2003; Tenuzzo *et al.*, 2009). Calcium ions act as a second messenger in signaling pathways (Lei *et al.*, 2020) and are capable of switching on the RPM by electron transfer. Magnesium ions, on the other hand, serve as an electron acceptor. Magnetic ions are more effective in relation to nonmagnetic ions; they increase the inhibition of DNA synthesis by a factor of several times (Buchachenko, 2016; Zhang *et al.*, 2017c, 2023a). This means that nuclear magnetic ions inhibit the synthesis of DNA, m-RNA and t-RNA, controlling the processes in the cell, *e.g.*, replication, transcription and translation, thus these ions can affect cell viability. In summary, MF can control the following processes: DNA synthesis, which extends DNA strands to form genes; cleavage, the cutting of DNA chains causing DNA damage and destroying genes; and DNA repair (Buchachenko and Kuznetsov, 2021).

An SMF can also affect DNA rotation by speeding up or slowing it down which process is assisted or opposed by Lorentz forces (Yang *et al.*, 2020). Slowing down DNA rotation causes a time delay in DNA replication, while speeding it up does not necessarily lead to faster DNA replication and transcription. This effect is more pronounced in the specific case of the vertical direction of the SMF. It can be assumed that an SMF may also affect the alignment of individual DNA molecules and their tightness (Zablotskii *et al.*, 2018). Most probably, the preference for a vertical DNA orientation may arise during DNA replication, which presumably may affect its dynamics. Thus, an SMF destabilizes the DNA replication machinery and can cause cell death, and can lead to different expression and functions of cell growth regulators, which potentially regulate the number of cells. With the rapid accumulation of DNA replication errors, cells die (Karanam *et al.*, 2020).

Effect of MF on the cell from theoretical analyses have been presented by many researchers. Binhi (2023) developed a mathematical model that combines the radical pair mechanism and the statistical amplification mechanism, so it can explain the biological effects of weak MFs. Zhang *et al.* (2023b) presented a model for the effect of SMFs on radical pair recombination. Analysis of the mechanism of action of SMF on biological systems showed that this field influences the speed and efficiency of biochemical reactions by influencing the electron spin. Carvalho (2022) developed a computational model of body development created on the basis of the bioelectric properties of cells. Thanks to this, through the participation of bioelectric potentials and currents in various conditions of cell activity, the development of the organism can potentially be controlled. Barbic *et al.* (2019) presented the mechanisms of activation of ion channels based on the magneto-caloric effect, which results in mechanical deformation of the cell membrane under the influence of diamagnetic and mechanothermal forces. Other researchers (Binhi and Prato, 2018; Binhi, 2019) described the effect of particle transitions through spin-orbit interaction, giving coupling of the spin magnetic moment with spatial movement of the particle. This can occur in biophysical structures such as biomembranes, tubulin, microtubules, neural synapses, and DNA. Altered precession of spin magnetic moments molecules in relation to biophysical structures in certain conditions, resulting in mixing quantum levels of magnetic moments. Zablotskii *et al.* (2016b, 2018) used for analyses high-gradient magnetic field and presented the mechanism of cell response to a magnetic field gradient, which causes a change in ion diffusion, opening/closing voltage-gated ion channels. Moreover, it induces cancer cell death by mechanical disruption, cytoskeletal reconstruction (cell elongation) and cell reprogramming. The impact of this field under certain conditions can prevent the division and growth of cancer cells.

Based on the results obtained, it is possible to formulate directions for further research aimed at using an SMF to stimulate the growth, viability and non-invasive remodeling and formation of plant and human cells. In this respect, there is a need to conduct both experimental research and modeling based on theoretical analyses. The main goal is to understand the mechanism of initiation and development of processes occurring in the cell under the influence of SMF, which, among other things, modulates the potential of the cell membrane, especially in terms of the activity of ion channels. As a consequence, this may lead to reprogramming of cells, changing their properties and achieving qualitative and regenerative effects in plant and human tissues.

4. CONCLUSIONS

The static magnetic field (SMF) is an indispensable factor in the natural environment and plays an important role in plant and animal organisms, including humans. Based on a wide review of the literature, it can be concluded that an SMF affects cells and tissue, giving them new properties and behaviors. This effect depends on the intensity and direction of the SMF, the length of time of its application, the type of and conditions for cell growth, development and health.

In general, the studies presented in this article use different experimental setups and therefore are difficult to compare in terms of the effects obtained. A literature review covering the period 2002-2023 was performed regarding the impact of SMF on cell formation and remodeling. The range of intensity of the fields used and application time was: 0.2 mT – 7 T and 0-16 days for plants; 0.01 mT – 16 T and 0-21 days for healthy human cells; 0.5 μT – 27 T and 0-7 days for cancer cells; 0.1 mT – 16 T and 14 days. Moderate SMF in the most commonly used range of 2-80 mT has potential applications in the formation and remodeling of plants and animals, including human cells, depending on the cell type and exposure time. In the case of cancer cells, the range of fields used was 0.2-9 T. To induce SMF, the researchers used: two sets of Helmholtz coils for weak SMF, neodymium permanent magnets for moderate SMF and superconducting magnet for high SMF. To ensure the proper cell culturing conditions, magnets were placed in the 37°C CO_2 cell incubator. However, during high MF exposure temperature control of the cell samples was achieved using water-heated copper supports on which culture dishes were fixed. Many studies have suggested that upward-direction SMFs may be more beneficial than downward direction SMFs. It was possible to define a lot of the most often exposed objects: cells isolated from organisms of plants (root meristem, cell suspension cultures, cellulose nanocrystals of corn, plasma membrane, fresh leaf and cells of bean, maize, pea, soybean, tobacco, tomato, microalgae, wheat) and human (chondrocytes, erythrocytes, skin fibroblasts, lymphocytes, mesenchymal stem, dental pulp stem, myoblast, osteoblastic, osteocyte, periodontal ligament, tau protein). Cancer cells such as were also exposed to SMF: breast cancer, cervical carcinoma, colorectal carcinoma, and nasopharyngeal, tumors of the central nervous system. From an application perspective, the results presented demonstrate how important it is to investigate the biological effects of an SMF, which could be utilized to determine new approaches in cell remodeling.

The cell characteristics studied in the papers that are reviewed include cell viability and proliferation, aggregation and their differentiation, structure and membrane potential. Numerous scientific studies have also shown that SMFs affect the growth rate and viability of plant, human and animal cells, regardless of whether they are cancer or healthy ones. This influence can be stimulating, inhibiting or null. The use of an SMF intensity in the range of 10-600 mT on plant cells had a significant effect on their growth and cell division causing an increase in biomass concentration from 10% to approximately 90%. However, the most common values of SMF were up to 100 mT. It was shown also that the growth rates of plant species decrease with increasing cell size. SMF exposure also induced progression of the cell cycle of plant cells. Changes in the cell cycle and growth reflect directly on the cell number and viability and provide useful information to detect modifications in the cell machinery. A significant increase in the viability of healthy cells most often exposed to an SMF was observed in the range of 0.4-0.6 T. In the case of cancer cells exposed to the field, a significant decrease in their viability was found, depending on the intensity of the SMF, exposure time and cell type. However, most of the studies presented have shown that SMFs do not affect the cell cycle of living organisms.

Many scientists have also shown a significant effect of SMF on the inhibition of cancer cell proliferation under certain conditions of exposure to this field. A moderate SMF (1 mT – 1 T) increased antitumor effectiveness up to 30% depending on its intensity and exposure time. In some cases, a reduction in tumor weight to about 45% was observed under 9 T SMF depending on the direction of the field. This also shows how important SMF can be as a tool for modulating individual cells and improving regenerative processes in the body within a framework that must be selectively specified for a specific cell type.

The research results presented in this review also showed a significant effect of SMF on changes in the size and shape of plant cells depending on the intensity and direction of the MF action and taking into account different types of cells and exposure conditions. The studies showed, among other things, that the cells changed their shape from elongated to round and in terms of size, they had a larger chloroplast with a much larger number of starch granules compared to the control cells. Moreover, processes of cleavage of the nucleus and vacuolization in the cell structure were observed. In addition, cells treated with an MF showed nuclei with highly condensed chromatin, which significantly improved the strength and stiffness of the cell wall.

The exposure of different types of plant, human and animal cells to an SMF can induce changes in cell morphology. Exposure of cells to an SMF affected cytoskeleton elements such as actin filaments, microtubules and intermediate filaments, which are responsible for maintaining the shape and internal structure of the cell. Cell elongation (cell length) was observed, which was related to the rearrangement of the cytoskeleton. Studies showed that the density of the cytoskeleton was significantly higher and the cells had nuclei located asymmetrically to one of the cell poles, and the cytoplasm of the cells contained several mitochondria, compared to the control group. In addition, studies have also indicated that SMF affects cancer cells by modifying their shape, the occurrence of de-arranged F-actin microfilaments and concentrated F-actin, and the formation of lamellar and vesicle-like microvilli. Other studies have shown that under SMF there was a deformation of the cell shape, a reduction of cellular and changed structures with a round appearance.

Numerous studies also discussed the behavior of the cell membrane of plant and animal organisms, including humans, under the influence of an SMF. The effects of

SMF on the cell membrane of plant and human cells were similar. The research results indicate that SMFs can significantly change the potential of the cell membrane, and thus can have a significant impact on the properties and biological functionality of the cell. Exposure to SMF caused membrane depolarization, a change in membrane potential that regulates ion flow. Studies have shown that continuous application of SMF caused deformation and damage to the cell membrane, including nuclear staining. It was observed that in SMF-treated samples, there was an increase in the lipid component of the gel, an increase in membrane integrity, and a decrease in the fluid component. Some studies showed a 43% percentage increase in membrane integrity (permeability) for plants treated with 30 mT SMF. Other studies have shown that the cell membrane under the influence of an SMF became visually rougher than the control sample, affecting the ability of the cells to adhere to the substrate.

The appropriate combination of magnetic field strength and irradiation time affects seed germination, increased plant productivity, and crop development. Magnetic fields affect root and shoot length, water and CO_2 absorption, and photosynthetic pigment content, resulting in increased agricultural production. In unfavorable abiotic stress conditions such as drought, salinity, soil contamination with heavy metals, magnetic fields alleviates the effects of stress by increasing the level of antioxidants and decreasing oxidative stress. The stunted growth of plants under adverse light and temperature conditions can be can be limited through magnetic fields. MF application may influence to reduces plant disease index by modulating calcium signaling, proline and polyamine pathways. Emphasizing, literature review suggest that the effects of magnetic fileds on plant growth and development are species and genotype specific. In general, despite all the efforts and research on MF, there are still gaps in human knowledge and further experimentation is needed.

In conclusion, both experimental studies and theoretical modeling are needed to understand the effects of the MF on cells. Based on theoretical analyses and experimental observations, it can be concluded that the SMF may affect *e.g.* biomagnetic effects, leading to cell reprogramming. The properties and biological functions of cells can be influenced in this way. The cell is a complex system consisting of many components sensitive to magnetic fields, *e.g.* ions or free electrons. However, it should be emphasized that interactions dependent on magnetism can occur from a combination of many ideal conditions.

Interest in the clinical application of magnetic and electromagnetic stimulation is increasing worldwide. Numerous articles have discussed the possibility of initiating the influence of magnetic and electromagnetic fields on various biological processes that are crucial for the treatment of various injuries and diseases. Further studies are needed to obtain a more complete understanding of the cellular effects of SMFs and thus this knowledge could be used to design application systems for the production of healthy food and non-invasive medical procedures.

Conflicts of Interest: The authors declare no conflict of interest.

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