Extremely Low Frequencies (ELF)
Areas of scientific consensus

Biological effects, basic mechanisms, interaction mechanisms

Clemens Dasenbrock
Definition(s)

Consensus: “…scientific evidence is the clearest and … little controversy“

Low frequency magnetic fields
- In vivo
- In vitro
- Dose response?

Static magnetic fields
- In vivo, in vitro

Low frequency electric fields

Summary
Some medical peer-reviewed journal articles refer to ELF in the context of "extremely low frequency (ELF) magnetic fields (MF)" with frequencies of 50 Hz and 50–80 Hz.

United States Government agencies, such as NASA, describe ELF as non-ionizing radiation with frequencies between 0 and 300 Hz.

The WHO have used ELF to refer to the concept of "extremely low frequency (ELF) electric and magnetic fields (EMF)" and have also referred to "ELF electric and magnetic fields in the frequency range >0 to 100,000 Hz (100 kHz)." The WHO also stated that at frequencies between 0 and 300 Hz, "the wavelengths in air are very long (6000 km at 50 Hz and 5000 km at 60 Hz), and, in practical situations, the electric and magnetic fields act independently of one another and are measured separately."

Wikipedia, 2011-11-03
http://en.wikipedia.org/wiki/Extremely_low_frequency
ELF - Literature (on biological effects, limits, etc.)

- Power-frequencies (50 or 60 Hz)
  - Magnetic fields: majority of studies
  - Electric fields: few studies

- Very low frequency (VLF, 3-30 kHz) fields
  - Switched gradient magnetic fields used in MRI
  - Weaker VLF fields emitted by visual display and TV

- Overview(s)
  - BEMS 2011 presentations of Lagroye, Fedrowitz, …
Low frequency magnetic fields (LF-MF)

Biological effects in vivo (1)

- Rodent genotoxicity & gene expression analysis
  - DNA strand breaks in brain tissue
    - No DNA strand breaks (negative comet assay) after 0.1, 1, 2 mT, 60 Hz, 2h exposure to rat and mouse brain cell homogenates (McNamee 2005); no confirmation of Lai&Sinh results
  - MN increase after 21d in utero exposure of mice to 0.65 MT, 50 Hz; but not in adult mice (Udroiu 2006)
  - CA and MN ↑ in BM (of 4 rats/gr) at 1 mT, 50 Hz, 4h (but not for 45 d) (Erdal 2007)
  - genes for proliferation & tumor-associated proteins not affected in rat mammary cells at 0.1 mT (Fedrowitz 2009)
Low frequency magnetic fields (LF-MF)
Biological effects *in vivo* (2)

- Neurobehaviour & neuroendocrine system
  - Memory and anxiety-related behaviour affected
    - at 1.1 -2.0 mT, 50 Hz in rodents (SCENIHR 2009) &
    - at 2 mT, 60 Hz in 1-day old chicks (Sun 2010)
  - Neurotransmitters of the opioid and cholinergic systems affected (?)
  - Changes in antioxidant defense system in brain cortices of rats
    at 0.1 mT, 50 Hz (Falone 2008)
  - Melatonin & stress-related hormones (pituitary-adrenal axis): inconsistent results
Low frequency magnetic fields (LF-MF)
Biological effects *in vivo* (3)

- Blood and immune system
  - Inconsistent data, e.g.
    - at 10 µT - 2 mT in humans: NK cell counts: ↑ , WBC counts: ≈ or ↓
    - at 10 µT - 30 mT in mice or rats: NK cells: ≈ or ↓ , WBC counts: ≈ or ↓
    - at 0.97 mT in rats: no alterations in haematology (Cakir 2009)

- Oxidative stress increased in
  - female Wistar rats, 1 mT, 50 Hz (Erdal 2008),
  - female 19 mo. (!) Sprague Dawley rats, 0.1 mT, 50 Hz (Falone 2008)

- Reproductive effects → *J. Juutilainen’s presentation*
Low frequency magnetic fields (LF-MF) 
Biological effects *in vivo* (4)

- Cancer (animal)
  - no adequate animal model for lymphoblastic leukemia available
  - no effect on spontaneous mammary tumours in rats
  - study in CD-1 mice ongoing *(Lewin 2012 ?)*

- Co-carcinogenic / tumor promoting effects in rodents
  - 7, 70, 100, 350 µT
  - on induced lymphomas/leukemia in CD-1 mice: No *(Negish 2008)*
  - on pre-neoplastic liver lesions, on induced skin & brain tumors: mostly negative *(WHO 2007)*

  - on induced mammary cancer: (?) - Yes at 0.1 mT, 50 Hz *(Fedrowitz 2009)*
Low frequency magnetic fields (LF-MF)  
Biological effects *in vitro* (1)

- Increased ROS production
  - $\geq 1$ mT, 50 Hz (Ayse 2010, Frahm 2010, Henrykowska 2009, Eleuteri 2009)
  - $>0.025 – 0.1$ mT (Farina 2010, Morabito 2011, Mannerling 2010)
  - Human leukaemia cells; PC12, glioblastoma & muscle cells

- Genotoxic effects
  - No induction of genotoxicity below 50 mT (WHO 2007)

  - DNA fragmentation (depending on cell proliferation !) in human fibroblasts at 1 mT, 50 Hz (Focke 2010)
  - Chromosomal instability, after co-exposure ($1 – 5$ mT + Bleomycin, MMS, $H_2O_2$) in different cells (SCENIHR 2009)
Low frequency magnetic fields (LF-MF)
Biological effects *in vitro* (2)

**Genotoxicity (cont’d)**

**DNA strand breaks**

- Human fibroblasts, melanocytes, rat granulosa cells at 1 mT, 50 Hz, 5’ on/10’ off, 24 h; but **not** in human lymphocytes, monocytes and muscle cells (Ivancsits 2005)
- Human lymphocytes
  - at 0.001 – 0.1 mT, 50 Hz, 18 h (Luceri 2005), ...
  - Co-exposure 3 mT, 50Hz + MNNG or 4-NQO, but not LF-MF alone (Villarini 2006)
- Co-exposure of human neuroblastoma cells at 1 mT, 50 Hz + H$_2$O$_2$, but **not** LF-MF alone (Falone 2007)
Gene expression altered

- >0.012 mT
  - Human (glioma, leukaemia, breast cancer) cells: Yes
  - But
    - p53, BRCA-1, p21WAF, c-myc: No or ‘melatonin-effect’ in MCF-7 and/or MCF-7 Mel1a cells (Girgert 2009)

Protein expression affected?

- 0.025 – 0.1 mT
  - hsp 70, human leukaemia cells (Mannerling 2010)
  - BAG-3, human M14 melanoma cells (Basile 2011)
- 0.0012 mT: humane glioma cells (Kanitz 2007)
Low frequency magnetic fields (LF-MF)
Dose response, genotoxicity, neurobehaviour, cancer

- No dose response
  - Most relevant physical parameter (for a dose response)
    - Magnetic flux density or
    - Induced electric field strength
    - Frequency
    - Time/duration?
    - Intermittent vs. continuous exposure
- Limited evidence for genotoxicity, tumor promotion & effects on neurobehaviour
- No evidence for carcinogenicity
- No causal mechanism
Static magnetic fields (SMF)
Biological effects …

- Orientation of forces applied on biological molecules with magnetic properties (Hb, rhodopsin, free radicals, NO)
  - Effects detectable at ~1 T, no health consequences (SCENIHR 2009)

- Hypothetic mechanisms
  - Enzyme activities altered
  - Prolonged lifetime of free radicals
  - Apoptosis
  - and their consequences on cancer
Static magnetic fields (SMF)
Biological effects \textit{in vivo}

- Neurophysiological effects
  - In humans during exposure in a \(\geq 1.5\) T MRI scanner
  - Pain reduction in mice at \(\geq 0.4\) mT (SCENIHR 2009)
  - Avoidance behaviour in rats at \(\geq 2\) T (Houpt 2007)
  - Cognition & emotional behaviour in mice impaired, but no anxiety effect at 128 mT (Ammari 2008)
Static magnetic fields (SMF)
Biological effects in vitro (1)

- Genotoxic effects
  - Transient MN induction in human lymphocytes after MRI scanning
  - Time-dependent increase in single-strand DNA break, in frequency of both CAs and MN in cells exposed to 3 T for 0, 22, 45, 67, and 89 min (Lee 2011)
  - DNA damage and altered gene expression using cultured cell lines
    - Inconsistent results (SCENHIR 2009)
    - Transient in HUVECs at 300 mT (Potenza 2010)
Static magnetic fields (SMF)
Biological effects *in vitro* (2)

- Cell viability affected
  - $>> 6 \text{ mT}$
  - much dependent on cell-type

- Induction of ROS
  - in HUVECs at 300 mT (Potenza 2010),
  - in $A_i$ (hamster-human) cells exposed to 8.5 T (not 1, 4 T !) (Zhao 2001), or
  - in human fetal lung (WI-39) fibroblasts after 18 h (not after 5 d !) exposed to 230-250 mT (21-120 mT in the culture flask)
Static magnetic fields (SMF)

Conclusion

- Neurobehaviour
  - affected

- Transient effects on
  - Genotoxicity
  - ROS formation
  - to be further elucidated

- Cell viability
  - always to be verified
Low frequency electric fields (LF-EF)
Bio...mechanisms

  - Impairment of cell membranes at
    - ~100 V/m for longitudinal cells (fibroblasts, nerve & muscle cells)
    - ~1 V/m for small round cells (lymphocytes)
  - under “semi-static” conditions
- No confirmation by *in vivo* and *in vitro* studies

- Most relevant physical parameter (for a dose EF-MF dose model)
  - Induced electric fields and flux in the body
    - very heterogenous (dependent on tissue)
Low frequency electric fields (LF-EF)
Biological effects

- Direct stimulation of myelinated nerve fibers
  - above 4-6 V/m (internal field strength) (ICNIRP 2010)
- Induction of magnetic phosphenes
  - Perception of faint flickering light in the periphery of the visual field
  - Threshold for induction 50 – 100 mV/m at 20 Hz
- EMF hypersensitivity: No
- Transient arousal & “stress” at 3-13 kV/m in animals (WHO 2007)
  - aversive to >50 kV/m (rat)
- Responses, ranging from perception to annoyance, through surface-electric charge effects (painful microshocks)
  - >> 2 kV/m at 50-60 Hz
Low frequency electric fields (LF-EF)

Biological effects ...

- **In vivo**
  - Micro-discharging / -shocks
  - No hints for accumulative effects
  - No causal relationship to cancer

- **In vitro & in vivo**
  - No genotoxic and
  - No non-genotoxic effects
    (signalling, alteration(s) in immune system & endocrine function)
Summary

ELF – (E)MF ...

- Do not cause cancer in animals
- Influence the nervous system and neurobehaviour at >>1 mT
- May cause (transient) genotoxicity, changes in the redox and differentiation status of cells at flux densities of \( \geq 0.1 \) mT
- No dose response
- No mechanism(s) for interaction(s) on cellular level known / confirmed up to now
- Consideration: Epi-studies direct to an association between (low) MF and childhood leukaemia
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