1. Call to Order
   Chairman Hirata called the meeting to order at 0910 h.

2. Introduction of those Present
   Each of the attendees introduced her/himself. (See Attachment 1.)

3. Approval of Agenda
   Following a motion by Reilly that was seconded by Ziskin, the agenda was approved. (See Attachment 1a.)

4. SC6 Chairman’s Reports (See Attachment 2.)
   Hirata mentioned the mission of SC6: 1) The goal of SC 6 is the eventual resolution of uncertainties, and recommendation of analysis tools/data applicable to human exposure standards, in addition to follow and assess the recent literature on EMF dosimetry modeling both for nerve stimulation effects caused by EMF at frequencies below ~100 kHz and for heating effects caused by RF energy absorption at frequencies above ~100 kHz, and 2) the target is to discuss the established effect (electrostimulation and thermal effect); Chronic exposure is out of the scope.
   Hirata provided update information about IEEE/ICES Workshop on Current Status on Low-Frequency Dosimetry. Nine speakers were selected for the topics on electromagnetic modeling, nerve activation modeling, and their combined modeling.
   ICES AdCom Member Reilly provided information of suggested topics on low-frequency dosimetry. Priority survey of suggested topics was summarized. The general guidance of working group was presented.

5. Technical Presentations
   1) COST-EMF MED and Single axon measurement setup based on Lumbricus Terrestris. (See Attachments 3 and 4.)
      Antonio Sarolic made a presentation on European COST EMF-MED initiative. The purpose of the initiative is to support the research on beneficial effects of EMF and their biomedical applications.
In his second presentation, Sarolic presented a single-axon measurement setup based on earthworm as an animal model. Preliminary results were in good agreement with theoretical neuron models. He discussed that the model is useful for studying waveform effects on nerve excitation.

2) *Compliance issues for LF pulsed exposures.* (See Attachment 5)

Valerio De Santis made a presentation on the compliance assessment procedures for LF pulsed exposures. Firstly, he summarized current issues with existing compliance issues specified by safety standards and guidelines (ICNIRP-1998/2010, IEEE C95.1/C95.6, HBVG). Then, he proposed a compliance assessment procedure based on the Inverse Fourier Transform (IFT) of the signal under-test showing better reproducibility and robustness against time- and frequency-domain biases. Finally, he provided some general ideas for future works and improvements in compliance assessment techniques for pulsed exposures.

3) *Target tissues for electrostimulation.* (See Attachment 6.)

Ilkka Laakso made a presentation on medical applications using low-frequency EMF. He reviewed techniques using DC, AC and pulsed stimuli. Common effects and side effects of stimulation were retinal phosphenes, skin pain sensation, and activation of PNS or CNS. He discussed that magnetically induced electric fields may stimulate CNS neurons or motor nerves at lower intensities before there is a painful sensation in the skin.

6. **New Business**

Hirata mentioned possible working group formation on threshold assessment by comparing with measurement and computation. Following a motion by Meltz that was seconded by Graf, the establishment of working group has been approved. Legros and Laakso have been appointed as co-chairs. General statement of the working group will be circulated to SC6 members.

Hirata reviewed the research trend for radio-frequency exposure, especially for frequencies above 6 GHz. In addition to call for proposal by MMF, a Japanese project has been reviewed. Computational results by Hirata for thermal time constants and the relationship between SAR and temperature elevation were also presented.

7. **Date and Place of Next Meeting**

The next meeting will be held at the Motorola Solutions, Inc. facility, Plantation, FL, 12 January 2016

8. **Adjourn**

There being no further business the meeting was adjourned at noon.
# Attendance List

## TC95 SC6 Meeting, 12 June 2015

<table>
<thead>
<tr>
<th>#</th>
<th>Name (last)</th>
<th>Name (first)</th>
<th>Affiliation</th>
<th>SC6 Member?</th>
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<tbody>
<tr>
<td>1</td>
<td>Bailey</td>
<td>Bill</td>
<td>Exponent</td>
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<td>2</td>
<td>Bodemann</td>
<td>Ralf</td>
<td>Siemens</td>
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<tr>
<td>3</td>
<td>Bowman</td>
<td>Joe</td>
<td>NIOSH</td>
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<tr>
<td>4</td>
<td>Chen</td>
<td>Xi Lin (Vick)</td>
<td>St. Jude Medical Inc</td>
<td>Y</td>
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<tr>
<td>5</td>
<td>Chou</td>
<td>C-K</td>
<td>Independent Consultant</td>
<td>N</td>
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<td>6</td>
<td>Cleveland</td>
<td>Robert</td>
<td>EMF Consulting</td>
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<td>7</td>
<td>Colville</td>
<td>Frank</td>
<td>US Army PHC</td>
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<td>8</td>
<td>Doczkat</td>
<td>Martin</td>
<td>FCC</td>
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<td>9</td>
<td>Graf</td>
<td>Kevin</td>
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<td>10</td>
<td>Haes</td>
<td>Donald</td>
<td>BAE Systems</td>
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<td>11</td>
<td>Hirata</td>
<td>Akimasa</td>
<td>Nagoya Institute of Technology</td>
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<td>12</td>
<td>Kavet</td>
<td>Robert</td>
<td>EPRI</td>
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<td>13</td>
<td>Kauenberg</td>
<td>B Jon</td>
<td>USAF</td>
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<td>14</td>
<td>Laakso</td>
<td>Ilkka</td>
<td>Nagoya Institute of Technology</td>
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<td>15</td>
<td>Legros</td>
<td>Alexandre</td>
<td>Lawson Health Research Institute</td>
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<tr>
<td>16</td>
<td>Mathur</td>
<td>Rajat</td>
<td>Hammett &amp; Edison</td>
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<tr>
<td>17</td>
<td>Mletz</td>
<td>Marty</td>
<td>Retired</td>
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<td>18</td>
<td>Miyagi</td>
<td>Hiroaki</td>
<td>JANUS</td>
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<td>19</td>
<td>Ohkubo</td>
<td>Chiyoji</td>
<td>Japan EMF Information Center</td>
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<td>20</td>
<td>Petersen</td>
<td>Ron</td>
<td>R C Petersen Associates. LLC</td>
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<td>21</td>
<td>Reilly</td>
<td>J Patrick</td>
<td>Metatec Associates</td>
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<td>22</td>
<td>Sarolic</td>
<td>Antonio</td>
<td>University of Split</td>
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<td>23</td>
<td>Sindia</td>
<td>Suraj</td>
<td>Intel</td>
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<td>Wessel</td>
<td>Marvin</td>
<td>Global RF Solutions</td>
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<td>25</td>
<td>Ziskin</td>
<td>Marvin</td>
<td>Temple University</td>
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<td>26</td>
<td>De Santis</td>
<td>Valerio</td>
<td>University of L’Aquila</td>
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<td>27</td>
<td>Schmid</td>
<td>Gernot</td>
<td>Seibersdorf Laboratories</td>
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<td>28</td>
<td>Alon</td>
<td>Leeor</td>
<td>New York University</td>
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<td>Truong</td>
<td>Dennis</td>
<td>City College of New York</td>
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<td>30.</td>
<td>Visser</td>
<td>Auke</td>
<td>Royal Netherlands Navy</td>
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</table>
1. Call to Order
   Hirata
2. Introduction of those Present
   All
3. Approval of Agenda
   Hirata
4. Chairman’s Reports
   Hirata
   a) Mission of SC6
   Hirata
   b) Workshop
   Hirata
   c) LF Topics
   Reilly
5. Technical Presentations
   EU project COST EMF-MED
   Sarolic
   Single axon measurement setup based on lumbricus terrestris
   Sarolic
   Compliance issues for LF pulsed exposures
   De Santis
   Target tissue for electrostimulation
   Laakso
6. New Business
   Hirata
   a) Working Groups
   Hirata
   b) RF Topics
   Hirata
7. Date and Place of Next Meeting
   Hirata
Agenda

1. Call to Order       Hirata
2. Introduction of those Present       All
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   a) Mission of SC6       Hirata
   b) Workshop       Hirata
   c) LF Topics       Reilly
5. Technical Presentations
   Saloric, De Santis, Laakso
6. New Business       Hirata
   a) Guidance of Working Groups Formation       Hirata
   b) RF Topics       Hirata
7. Date and Place of Next Meeting       Hirata
Chairman’s report

a) Mission of SC6 (1)

- The goal of SC 6 will be the eventual resolution of uncertainties, and recommendation of analysis tools/data applicable to human exposure standards, in addition to follow and assess the recent literature on EMF dosimetry modeling both for nerve stimulation effects caused by EMF at frequencies below ~100 kHz and for heating effects caused by RF energy absorption at frequencies above ~100 kHz.

- Our target is to discuss the established effect (electrostimulation and thermal effect); Chronic exposure is out of the scope.
Chairman’s report

a) Mission of SC6 (2)

- SC-6 will coordinate closely with the other subcommittees, especially with SC 3 and SC 4, who are currently working on the update and merger of IEEE Std C95.1&C95.6 into a single standard.
- SC-6 may collaborate with other standardization body, when promoting IEEE Std C95 standards from technical aspects.
Chairman’s report
b) LF Workshop (1)

0830 – 1640 h        Sunday, 14 June 2015
Chapel Hall, Asilomar Conference Center
Pacific Grove, California, USA

● Opening Remark
● “Rationale behind EMF Compliance Assessment Protocols,”
  Andreas Christ (Research Consultant, Cabo Frio (RJ), Brazil ) and Jafar Keshvari
  (Microsoft Corporation, EMF Research and Standards, Espoo, Finland )
● “Measurement of dielectric characteristics of biological tissues from ELF to
  MMW frequencies,” Kanako Wake, Kensuke Sasaki, and Soichi Watanabe
  (National Institute of Information and Communications Technology, Tokyo, Japan )
● “The role of skin modelling in ELF/LF magnetic field exposure assessment based
  on IEEE C95.6 and ICNIRP 2010,” Schmid Gernot (Seibersdorf Laboratories,
  Austria )
● “Review of ELF/LF dosimetry for magnetic field exposure in Japan,” Kenichi
  Yamazaki (CRIEPI, Yokosuka, Japan )
Chairman’s report

b) LF Workshop (2)

- “Modeling of transcranial Electrical Stimulation (tES): Implications for Safety and Efficacy,” Dennis Truong and Marom Bikson (City College New York, USA)
- “Survey of Electrostimulation models,” J Patrick Reilly (Metatec Associates, USA)
- “Magnetophosphene perception threshold in humans exposed to ELF MF up to 50 mT – experimental data and a modelling approach,” Alexandre Legros (Lawson Health Research Institute, Canada)
- “Insights on human response to EMF exposure obtained by combining detailed anatomical induction models and modern neuronal dynamics models,” (IT’IS Foundation, Switzerland)
- “Multi-scale induction and electrostimulation model with experimental validation,” Ilkka Laakso and Akimasa Hirata (Nagoya Institute of Technology, Japan)

Discussion on Future Research Topics
SC6 Suggested Topics

Survey of priority results
A. Modeling of \textit{in-situ} fields from externally applied EMF or electric current

- A.1: Measure tissue conductivity
- A.2: Model tissue conductivity
- A.3: Numerical artefacts
- A.4: Spatial Averaging
- A.5: Diverse induct. models
- A.6: Synaptic effects
- A.7: Validation

The chart indicates the priority levels:
- High priority
- Medium priority
- Low priority
B. Electrostimulation modeling

- B.1: PNS target tissue
- B.2: $\frac{dE}{dx}$ vs E(x)
- B.3: Model consistency
- B.4: Waveform sensitivity
- B.5: Modeled neuron
- B.6: Type of neuron
- B.7: Synapse model (CNS)
- B.8: Model availability
- B.9: Computational artefacts
- B.10: Validation

Legend:
- high priority
- medium priority
- low priority
C. Issues related to exposure limits

- C.1: PNS target tissue
- C.2: Consistency of models
- C.3: Model specificity
- C.4: RL reduction factors
- C.5: dE/dx vs E(x)
- C.6: Compliance test: non sinusoid
- C.7: Structure
- C.8: Statistical models

Legend:
- high priority
- medium priority
- low priority
SC6 Objectives

- Formation of Working Groups around “Topics”
- Develop Papers
  - Research papers
    - Original theoretical or experimental data
  - Review Papers
    - Assess state of science
    - Recommended future research topics
  - SC6 review and consensus.
SC6 Papers Content

- General statement of topic.
- Summary of developments in the field.
- Discrepancies, controversies, missing info.
- Importance of unresolved issues
  - Relevance to human exposure limits
- New theoretical or experiments data.
- Recommendations for new studies.
SC6 Publications

- Format suitable for publication
  - Seek journal having interest

- Authorship
  - Acknowledge WG leader & Members
  - Need to conform to requirements
    - IEEE
    - Journal
    - SC6 Members.
EMF-MED
A paradigm shift in biomedical EMF research: from EMF research to innovative biomedical technology

Action Chair:
Prof Dr Antonio Šarolić
FESB, University of Split, CROATIA
antonio.sarolic@fesb.hr

IEEE ICES TC95 Workshop, SC6 meeting
Pacific Grove, 12 June 2015
Presentation outline:

- Background on COST EMF-MED
- About COST Actions in general
- Scientific topics
- Challenges
- COST EMF-MED objectives
- COST EMF-MED Action implementation and ongoing activities
- Other developments in the topic of EMF-MED
Background

• Human body: an electrical object

• Numerous possibilities of interactions

• Why not use them for the benefit of health...?

• ...systematically?
Background

• Previous research initiatives: harmful short-term effects of high-level EMFs

• **Beneficial** biological effects → **health-promoting** uses and applications

• Based on both high-level and low-level EMFs (above and below thermal and stimulation thresholds)
Exciting possibilities

• Novel modalities for EMF-based cancer treatment

• Applications and procedures based on EMF exposure/stimulation of excitable and nonexcitable tissues

• Interaction mechanisms, in many cases, still not understood (!)
Existing needs

- Existing applications → improvement and optimisation

  
  *This Directive does not cover suggested long-term effects.*

  *The Commission shall keep under review the latest scientific developments.*

  *If well-established scientific evidence on suggested long-term effects becomes available, the Commission shall consider a suitable policy response, including, if appropriate, the submission of a legislative proposal to address such effects.*
Initiative

• All pre-conditions seemed ready for systematic approach → proposal for COST Action EMF-MED

• This paradigm shift was proposed by the Action proposer, to a multidisciplinary group of EMF researchers at the last MC meeting of the now-completed COST Action BM0704 in April 2012.
Initiative (2)

- After a preparatory workshop and the consensus on the Action aims, objectives, research topics, keywords and title, the proposal was applied to COST.

- In the 2nd try, after passing the 3-stage evaluation (preliminary proposal, full proposal, and presentation in front of the DC pool of biomedical experts), the proposal was approved as COST Action BM1309 (final success ratio in that call was 4%).
COST framework explained

• From www.cost.eu: COST is an intergovernmental framework for European Cooperation in Science and Technology, allowing the coordination of nationally-funded research on a European level.

• COST funds pan-European networks of scientists and researchers across all science and technology fields. These networks, called 'COST Actions', promote international coordination of nationally-funded research.
COST framework explained (2)

• COST does not fund research itself, but provides support for networking activities carried out within COST Actions.

• COST Actions are bottom-up science and technology networks completely open to all researchers and stakeholders, with a four-year duration and a minimum participation of five COST Countries.
COST framework explained (3)

- COST Actions are active through a limited range of (well defined) networking tools, such as meetings, workshops, conferences, training schools, short-term scientific missions (STSMs) and dissemination activities.

- COST Actions are open to researchers from universities, public and private research institutions, as well as to NGOs, industry and SMEs.
COST is an intergovernmental framework that includes 36 Member Countries and one Cooperating State. This allows researchers from these countries to embark upon networking opportunities by participating in science and technology networks called 'COST Actions'.

However, COST Actions do not limit participation to scientists from COST Member Countries only...
COST framework explained (5)

- COST's 36 Member Countries are: Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Montenegro, The Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, United Kingdom and Former Yugoslav Republic of Macedonia. Israel is a Cooperating State.
COST framework explained (6)

• In order to support science and technology networking across borders, COST is also working on enhancing international cooperation by involving researchers (subject to approval on a case-by-case basis) from:
  – Near Neighbour Countries: Albania, Algeria, Armenia, Azerbaijan, Belarus, Egypt, Georgia, Jordan, Lebanon, Libya, Moldova, Morocco, the Palestinian Authority, Russia, Syria, Tunisia and Ukraine
COST framework explained (7)

– International Partner Countries: Argentina, Australia, Bangladesh, Brazil, Canada, Chile, China, Colombia, Costa Rica, Honk Kong, India, Indonesia, Iraq, Japan, Republic of Korea, Mauritius, Mexico, Namibia, New Zealand, Pakistan, Peru, Saudi Arabia, Singapore, South Africa, Sudan, Thailand, United Arab Emirates, United States of America and Uruguay
COST EMF-MED Scientific focus - Topic 1: EMF-based cancer interactions, treatment and related applications

High-level EMF cancer treatment:

- Using high-level EM energy to overheat the tumour
- Difficult to target the tumour tissue without damaging the surrounding tissue
High-level EMF cancer treatment:

- Could be improved and optimized by:
  - personalised treatment planning
  - novel types of antennas and applicators
  - using magnetic nanoparticles
Computation of a patient-specific plan for hyperthermia treatment (neck area)
Low-level (below thermal level) EMF cancer treatment:

- Local or whole-body treatment with low-level EMFs having accurate and precise characteristics
- Interactions at non-thermal level
- Emerging methodology
- Breakthrough potential
- Explanation still lacking (!)
EMF-based cancer diagnosis:

- "tumour-specific frequency signature"
- impedance tomography and radar-like applications
- use of functionalized nanoparticles (e.g. magnetic)
- complementing current methods, improve diagnosis accuracy.
COST EMF-MED Scientific focus - Topic 2: EMF-based non-cancer interactions and applications

EMF stimulation/exposure of excitable and non-excitabile tissues

• surface, subcutaneous, implanted electrodes (electric field)

• contactless application (magnetic field)
Topic 2: EMF-based non-cancer interactions and applications (2)

- Excitable tissues:
  - inducing, suppressing, or synchronizing spiking and signal propagation across neurons
  - treating neurological, neurodegenerative and psychiatric disorders and conditions
• Non-excitable tissues:
  – affecting cell differentiation and proliferation
  – e.g. tissue healing, growth, or regeneration; fractures and non-union consolidation
• Excitable and non-excit able tissues:
  – need for better understanding of mechanisms between stimuli, target tissues, and targeted diseases or effects
  – need to improve targeting and optimize the stimulus
• Topic 2 also includes other biomedical procedures, applications, and technologies, that are:

  – essentially and functionally based on EMFs

  – benefiting from sharing or reusing the same research methods and tools
COST EMF-MED Scientific focus - Topic 3: EMF dosimetry – in silico tools and measurements

• Understanding and control of physical, technical, and tissue parameters

• Achieving and maintaining repeatability of experiments and procedures (needed in Topics 1 and 2)

• Relying on computational simulations ("in silico" tools) and measurements
Topic 3: EMF dosimetry - *in silico* tools and measurements (2)

- The tools to be developed or improved include:

  - simulation tools (multi-physics, multi-scale)
Topic 3: EMF dosimetry - *in silico* tools and measurements (3)

– anatomical models (functionalized, integrated, multi-level)
Topic 3: EMF dosimetry - *in silico* tools and measurements (4)

– dosimetric measurement equipment and methods
Topic 3: EMF dosimetry - *in silico* tools and measurements (5)

– exposure/application equipment and methods (for tight control over relevant parameters)
Challenges

Interactions:

- They are in many cases still in "black box".
- Many possible mechanisms, hard to pinpoint the relevant ones.
- Need to clarify the interaction mechanisms in order to understand and optimize the effects.
Challenges (2)

Low-Frequency Electromagnetic Field Exposure Enhances Extracellular Trap Formation by Human Neutrophils through the NADPH Pathway

Lieke A. Golbach\textsuperscript{a} Marleen H. Scheer\textsuperscript{a} Jan J.M. Cuppen\textsuperscript{b} Huub Savelkoul\textsuperscript{a} B.M. Lidy Verburg-van Kemenade\textsuperscript{a}
Challenges (3)

Uncertainties in measurement setups → also in the associated results:

• Poor exposure control

• Exposure setup not consistent across experiments → difficult to replicate experiments.

• Need to establish clear guidelines for experimentation
Challenges (4)

In vitro exposure: Linear and non-linear thermodynamic events in Petri dishes

Alessandra Paffi¹, Micaela Liberti¹, Francesca Apollonio¹, Asher Sheppard² and Quirino Balzano³,*

Article first published online: 20 MAY 2015
DOI: 10.1002/bem.21923

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Fig. 5. Power loss density (PLD) (a) and current density J (b) in a horizontal plane of a Petri dish filled with 4 ml of liquid with meniscus, exposed to a plane wave propagating from the left with H- polarization (H along the z-axis) at 1.8 GHz, 100 V/m E-field amplitude.
Challenges (5)

Translation from bench to bedside (from interactions to applications):

- Wide range of different studies on different levels
- Hard to find a relevant starting point
- Need to focus to a specific application
Challenges (6)

Lot of noise in market and in the perception of EMF modalities:

• Need to clarify and verify the (non)efficiency of marketed devices

• Need to improve regulations on EMF-based medical devices

• Health risk or health promoting?
Challenges (6)

• It is becoming increasingly easy for individuals to buy brain-modulating devices.
• But when purchased outside clinical settings, they are unregulated, with no system to ensure their safety (sold as Cognitive Enhancement Devices).
COST EMF-MED Objectives

1) Build the capacity for scientific networking and research on the topic of innovative and beneficial uses of EMFs in biomedical applications within Europe:

• increasing the number of highly trained and qualified researchers,
• pooling the relevant knowledge and research facilities,
• establishing collaborations that will result in new research initiatives.
COST EMF-MED Objectives (2)

2) Achieve a better understanding of EMF interactions with the human body at the molecular, cellular, tissue and system level, and the resulting health impacts.

3) Provide a sound scientific basis for better understanding of the existing and the introduction and development of innovative applications of EMFs in medicine.
COST EMF-MED Objectives (3)

4) Develop appropriate computational and measurement tools for EMF dosimetry as well as optimal exposure and application setups.

5) Enable Early-Stage Researchers (ESRs) to gain knowledge and training in this promising field, and maintain the gender balance.
COST EMF-MED Objectives (4)

6) Promote and/or establish new links with industrial partners:
   • by converging academic and industrial research,
   • resulting in possible new commercial applications,
   • increasing the number of academic partners collaborating with industrial partners.
COST EMF-MED Objectives (5)

7) Provide inputs and recommendations for Health Technology Assessment (HTA) for commercial applications and for adequate policies, evaluation, monitoring and vigilance systems.

8) Strengthen the position of EU in this field with respect to the rest of the world.
Action facts

• 31 COST countries + researchers from USA

MC meetings

• 1st MCM (Kick-off): Brussels, April 2014
• 2nd MCM: Split, October 2014
• 3rd MCM: Madrid, March 2015
• 4th MCM: Prague, November 2015
Working groups

WG1: Cancer EMF interactions and applications
(WG1 Leader: Gerard van Rhoon, Netherlands)
• High-level EMF cancer treatment
• Low-level EMF cancer treatment
• EMF-based cancer diagnostics

WG2: Non-cancer EMF interactions and applications
(WG2 Leader: Paolo Ravazzani, Italy)
• EMF stimulation/exposure of non/excitable tissues
• Other miscellaneous biomedical procedures, applications, and technologies that are essentially and functionally based on EMFs
Working groups (2):

**WG3: EMF dosimetry - in silico tools & measurements**

(WG3 Leader: Niels Kuster, Switzerland)

- Multi-physics, multi-scale simulation tools
- Functionalized, integrated, multi-level anatomical models
- Dosimetric measurement equipment and methods
- Exposure/application equipment and methods
Workshops:

• **EMF Interaction with Excitable Tissues**, Madrid, 6 March 2015
  - Transcranial brain stimulation - interactions, technology, clinical applications
  - Nerve models and their integration into functional anatomical models
  - Functional Electrical Stimulation
  - Various EMF-neural interactions, phenomena and medical applications

• **Designing Focused Deep Hyperthermia by EMF**, Zurich, 23 June 2015

• next workshop: Prague, 18 November 2015, topic *tbd*
Training Schools:

- **European Training School on Clinical Trials**, Galway, May 2015, (co-organization with COST Action TD1301)
- **Training School on Health Technology Assessment**, Warwick, September 2015
- **Diagnostic and Therapeutic Applications of Electromagnetics**, Torino, September 2015, (co-organization with European School of Antennas)
- **EBEA Erice International School of Bioelectromagnetics: EMFs and Nervous System: Biological effects, Methodological Aspects and Medical Applications**, Erice, April 2016, (co-organization with European Bioelectromagnetics Association)
STSMs:

9 approved in the 1st Grant Period (June 2014 – May 2015):
• Theoretical and experimental studies on EM field-induced electrophysiological effects (41 days)
• Novel approach to bio-electromagnetic effects measurements and quantification of metabolic activity (100 days)
• Experimental evaluation of a microwave sensor performance on pneumothorax diagnosis (25 days)
• Pre-market assessment of EMF interactions and applications: a case study on electroporation (7 days)
STSMs (2):

- Evaluation of pulsed EMF anti-inflammatory effect on in vitro model of tendinopathy (90 days)
- Nanosecond pulsed electric fields on liposomes for potential drug delivery applications (20 days)
- Analysis of EEG and MEG signals using Empirical Mode Decomposition Phase Locking method (23 days)
- Mechanistic Modeling, Optimization and Risk Assessment of Electro-Muscular Incapacitation Devices (EMD) (15 days)
- Neuroprotective and neuroregenerative effects of the electrical stimulation of long term amputees (7 days)
Working module proposals:

- EMF-based neural repair and regeneration
- Effect of stimulus waveform to nerve excitability
- Vagus nerve stimulation
- EMF modulation of acetylcholine-mediated plasticity in the mammalian cortex
- Cerebellar and spinal neuromodulation by transcutaneous current stimulation - from basic science to technical progress and clinical applications
- Transcranial magnetic resonance guided focused ultrasound for noninvasive treatment of brain diseases
- Non-Invasive Brain Stimulation (NIBS) - application of EMFs in neuroscience
Working module proposals (2):

- Focused EMF hyperthermia with online guidance and improved dose models
- Microwave thermal ablation for cancer therapy
- Diagnosis and treatment of cancer with very low levels EMFs modulated at tumor-specific frequencies (non-thermal interactions)
- Pulsed EMFs as an innovative approach for functional tissue engineering of connective tissues
- The Role of Pulsed EMFs in the Regenerative Medicine of the Musculoskeletal System
Working module proposals (3):

- Drug delivery activated by EMFs
- Applications of low-intensity millimetre waves radiation for drug delivery purpose and mechanistic studies
- ELF magnetic fields and immune response modulation
- Genes and cellular mechanisms involved after ELF stimulation
- Induction of adaptive response by non ionizing radiation
- EMFs and molecular structures
- Sensors and sensing strategies in biomedical applications
Working module proposals (4):

- Neural tissue models
- EMF Microdosimetry
- Dielectric properties at low frequencies
- Electromagnetic-thermal dosimetry of the human brain
- The zebrafish embryo as an animal model
Other developments:

- COST Action TD1104: European network for development of electroporation-based technologies and treatments
- COST Action TD1301: Development of a European-based Collaborative Network to Accelerate Technological, Clinical and Commercialisation Progress in the Area of Medical Microwave Imaging
- COST Action TD1402: Multifunctional Nanoparticles for Magnetic Hyperthermia and Indirect Radiation Therapy
Electroceuticals spark interest

Industry and academia invest in treating diseases by delivering electrical charges to nerves.

Sara Reardon

02 July 2014
GlaxoSmithKline’s big bet on electroceuticals

Meg Tirrell | @megtirrell
Wednesday, 11 Mar 2015 | 5:33 PM ET

A few years ago, Moncef Slaoui, then GlaxoSmithKline’s head of research, challenged his team to come up with a new pillar of medicine.

The British drugmaker already makes traditional small-molecule pills and biologic therapies made with living cells, and it sells vaccines and consumer products. One area not yet tapped by medicine? The electrical signals that govern many of the functions in our bodies.

Read More ➤ What!?! Specialty drug spending jumps 31%

By better understanding our bodies’ electrical systems, GSK hopes to design technology small and smart enough to manipulate them and possibly conquer diseases from rheumatoid arthritis to asthma to diabetes.
Electroceuticals: swapping drugs for devices

SCIENCE / 28 May 13 / by OLIVIA SOLON

Bioelectronics is the field of developing medicines that use electrical impulses to modulate the body’s neural circuits as an alternative to drug-based interventions. How far away are we from having these very targeted “electroceuticals”?

Twenty years ago, neurosurgeon and researcher Kevin Tracey was studying whether an experimental molecule called CNI-1493 could limit damage to the brain after a stroke. His team was injecting the molecule into the brains of rats during a stroke to see how successfully it prevented swelling -- an immune system response -- of the brain.

To Tracey’s surprise the drug not only prevented swelling locally, but it shut down the immune response in the whole body. The drug was having an effect that went far beyond its target organ.

---

ATTACHMENT 3
An Electrode in the Brain Turns Off Depression

Electrical stimulation deep within the brain may alleviate devastating mood disorders

By Andres M. Lozano and Helen S. Mayberg

“I suddenly feel calm.” Our patient, a middle-aged woman who suffered from severe depression, uttered these beautiful words in the operating room just a few seconds after one of us (Lozano) applied electrical stimulation to a selected area deep in her brain. The operation, which took place in 2003 at Toronto Western Hospital, relied on only local anesthesia so that the woman could remain conscious and talk to us.

SEE ALSO:

Prospect of Home-Brew Drugs Demonstrates the Wonders of the Bat Brain
Electronic Medicine Fights Disease

Stimulation of the nervous system could replace drugs for inflammatory and autoimmune conditions

By Kevin J. Tracey

I am a brain surgeon who is fascinated by inflammation. Along with my laboratory colleagues, I examine molecules that cause inflammation so that we can discover methods for alleviating the pain, swelling and tissue damage that is a consequence of many diseases.
GlaxoSmithKline R&D chief touts the future of 'electroceuticals'

February 11, 2014 | By Damian Garde

Looking beyond the small-molecule drugs and biologic treatments that have dominated therapeutic development over the past generation, GlaxoSmithKline's (GSK) all-encompassing R&D department is trying to get a jump on the future of medicine, and research chief Moncef Slaoui is betting that there's a great deal of promise in drug-mimicking electronics.

In an interview with The China Post, Slaoui said GSK, like every major drug developer, will eventually face a diminishing returns curve in drug R&D. In the long term, how many more therapies can the industry possibly discover using only traditional biochemistry?

"We asked ourselves this question about 2 1/2 years ago," Slaoui told the newspaper, "challenging ourselves to see if there are other modalities that would open up new horizons ... and when we thought about it, we realized that when we use chemical structure or recombinant protein as a medicine, what we use in fact are the structures of these medicines to interact with the structure of a receptor or protein in our body ... So we asked the question: 'Can we use electrical impulses to modify the way organs function?'"
Mapping The Body’s Wiring For Medical Breakthroughs

BY ROGER HIGHFIELD / AUGUST 7, 2014 9:28 AM EDT
Thank you for your attention!

More data and contact info:

www.COST-EMF-MED.eu

E-mail:
COST-EMF-MED@fesb.hr
or
antonio.sarolic@fesb.hr
Single axon measurement setup based on *Lumbricus Terrestris*

Prof Dr Antonio Šarolić, Dr Zlatko Živković
FESB, University of Split, CROATIA
antonio.sarolic@fesb.hr

IEEE ICES TC95 Workshop, June 2015, Pacific Grove
SC6 meeting
Presentation outline:

- Introduction
- Lumbricus terrestris
- Measurement setup
- Results overview and comparison with SENN model
- Conclusion
Introduction

- **Single axon studies → controllable measurements**
  - effects of stimulus parameters
  - verifying the computational stimulation models (IEEE ICES SC6 activities)

- **Biomedical studies on nerve stimulation**
  - mostly: ELF rectangular pulses
  - new applications → different waveforms?

- **EMF safety**
  - standards: continuous sine wave, vs.
  - complex waveform in the IF range?
Introduction (2)

Measurements on humans (mammalians)?

- Arbitrary waveform?
- Sufficiently high currents?

Spatial and temporal integration:
- in the nerve bundle
- in the muscle

- AP recording
Measurements on humans (ulnar nerve excitation)?

- Evoked potential data for different delays ($t_D$) and current ($I_{in}$) as a function of time ($t$).
Lumbricus terrestris (Earthworm)

- easy to obtain
- easy to keep alive
- easy preparation for experiment
- survive the experiment intact
Earthworm anatomy
Measurement setup
Measurement setup (2)
Measurement setup (3)

- temperature observed and noted during the experiment
# SENN model parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fiber diameter ($D$)</td>
<td>$20 , \mu m$</td>
</tr>
<tr>
<td>Axon diameter at node ($d$)</td>
<td>$0.7 \cdot D$</td>
</tr>
<tr>
<td>Nodal gap ($w$)</td>
<td>$2.5 , \mu m$</td>
</tr>
<tr>
<td>Axoplasmic resistivity ($\rho_i$)</td>
<td>$100 , \Omega \cdot cm$</td>
</tr>
<tr>
<td>External medium resistivity ($\rho_e$)</td>
<td>$300 , \Omega \cdot cm$</td>
</tr>
<tr>
<td>Membrane capacitance ($c_m$)</td>
<td>$2 , \mu F/cm^2$</td>
</tr>
<tr>
<td>Membrane conductivity ($g_m$)</td>
<td>$30.4 , mS/cm^2$</td>
</tr>
<tr>
<td>Internodal distance ($L_i$)</td>
<td>$100 \cdot D$</td>
</tr>
</tbody>
</table>

*McNeal, 1976; Reilly, 2011*

![Diagram of SENN model parameters](image)

- $y_A = 5 \, \text{mm}$
- $L = 20 \cdot y_A = 10 \, \text{cm}$
- $N_R = 51 \, \text{nodes}$
- $\tau = 110 \, \mu \text{s}$
- $I_{rb} = 2.03 \, \text{mA}$

**Stimulation waveforms:**
- a single monophasic rectangular pulse, phase duration $0.01 - 5 \, \text{ms}$
- sine CW, frequency $0.1 - 20 \, \text{kHz}$
Results comparison – SD curves

• cannot compare absolute values → relative comparison
• x axis normalized to appropriate time constant
• y axis normalized to rheobase

Reilly, 2011
Results comparison – SD curves (2)

• **rheobase current difficult to measure** (large uncertainty for both very short and very long pulses)

• **therefore, rheobase current found from the fitting exponential function**

\[
I_{TH}(t_D) = \frac{I_{rb}}{1 - e^{-t_D/\tau}}
\]

• fitted to ca. 10 measured points of SD curve (least squares method in *Wolfram Mathematica*)
Results comparison – SD curves (3)
Results comparison – SD curves (4)

<table>
<thead>
<tr>
<th></th>
<th>Chronaxie</th>
<th>$\tau$</th>
<th>$I_{rb}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worm 1</td>
<td>0.19</td>
<td>0.28</td>
<td>0.38</td>
</tr>
<tr>
<td>Worm 2</td>
<td>0.14</td>
<td>0.20</td>
<td>0.30</td>
</tr>
<tr>
<td>Worm 3</td>
<td>0.22</td>
<td>0.32</td>
<td>0.39</td>
</tr>
<tr>
<td>Worm 4</td>
<td>0.26</td>
<td>0.37</td>
<td>0.29</td>
</tr>
<tr>
<td>Worm 5</td>
<td>0.12</td>
<td>0.17</td>
<td>0.27</td>
</tr>
</tbody>
</table>
Results comparison – frequency response
Conclusions

• The developed single-axon measurement setup is convenient and precise

• Allows to generate arbitrary stimulus in a wide amplitude and frequency range
  (to be expanded in the next version, to larger amplitudes and higher frequency → shorter pulses)

• Due to custom-made constant-current stimulator, waveform is preserved regardless of the load impedance
Conclusions (2)

• Experimental results agree very well with SENN
• Good basis for stimulation model validation and excitability studies

Acknowledgement

This study was performed within the research project 023-0000000-3273 "Measurements in EMC and EM health effects research" supported by the Ministry of Science, Education and Sports of the Republic of Croatia.
Compliance Assessment with LF Pulsed Exposures: Current Issues and Future Works

Valerio De Santis
University of L’Aquila, Italy
Outline

• introduction

• in-force compliance assessments
  ✓ ICNIRP 1998/2003/2010
  ✓ IEEE C95.6-2002/C95.1-2005
  ✓ HVBG 2001

• proposed compliance assessment
  ✓ IFT approach

• conclusions

• future works
  ✓ IFT + waveform factor approach
Introduction

Sinusoidal-type waveform

Time-Domain

Frequency-Domain

\[ A_p \rightarrow t \rightarrow FFT \rightarrow A_{rms} \rightarrow f_i \rightarrow f \]

- Straightforward compliance assessment
  - Compare the dosimetric quantity \( A_{rms} \) with the respective exposure limit (EL) at the frequency \( f_i \)
Introduction

Pulsed-like waveform

- how to assess compliance with LF pulsed exposures?
  - time-domain vs. frequency-domain approach?
  - linear vs. non-linear summation rule?
Introduction

key-points for a good compliance assessments are

• simplicity\(^1\)
  ✓ “the simpler the better”

• accuracy\(^1\)
  ✓ not overly conservative nor lenient

• reproducibility\(^2\)
  ✓ different approaches should provide the same results

\(^1\) J.P. Reilly, and A.M. Diamant, “Neuroelectric mechanisms applied to low frequency electric and magnetic field exposure guidelines – Part II: Non sinusoidal waveforms,” *Health Phys.*, 83 356-365, 2002

### ICNIRP 1998

**Table 4: Basic restrictions for time varying electric and magnetic fields for frequencies up to 10 GHz**

<table>
<thead>
<tr>
<th>Exposure characteristics</th>
<th>Frequency range</th>
<th>Current density for head and trunk (mA m⁻² (rms))</th>
<th>Whole-body average SAR (W kg⁻¹)</th>
<th>Localized SAR (head and trunk) (W kg⁻¹)</th>
<th>Localized SAR (limbs) (W kg⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occupational exposure</td>
<td>up to 1 Hz</td>
<td>40</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>1–4 Hz</td>
<td>40 f</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>4 Hz–1 kHz</td>
<td>10 f</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>1–10 kHz</td>
<td>β100 f</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>100 kHz–10 MHz</td>
<td>β100 f</td>
<td>0.4</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>10 MHz–10 GHz</td>
<td>—</td>
<td>0.4</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>General public exposure</td>
<td>up to 1 Hz</td>
<td>8 f</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>1–4 Hz</td>
<td>8 f</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>4 Hz–1 kHz</td>
<td>2 f</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>1–100 kHz</td>
<td>β500 f</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>100 kHz–10 MHz</td>
<td>β500 f</td>
<td>0.08</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>10 MHz–10 GHz</td>
<td>—</td>
<td>0.08</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

**Summation rule adopted by ICNIRP 1998**

\[
CF_i = \sum_{i=1 \text{ Hz}}^{10 \text{ MHz}} \frac{A_i}{EL_i} \leq 1
\]

- \(A_i = B_{rms}(f_i), J_{rms}(f_i), \ldots\)
- \(EL_i = RL_B(f_i), BR_J(f_i), \ldots\)

- no phase information is taken into account \(\rightarrow\) overly conservative
- non-linearity of nerve not taken into account \(\rightarrow\) conservative
ICNIRP 2003/2010

### Basic Restrictions

<table>
<thead>
<tr>
<th>Exposure Characteristic</th>
<th>Frequency Range</th>
<th>Internal Electric Field (V m⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occupational exposure</td>
<td>1–10 Hz</td>
<td>0.5f</td>
</tr>
<tr>
<td></td>
<td>10 Hz–25 Hz</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>25 Hz–400 Hz</td>
<td>2 × 10⁻³f</td>
</tr>
<tr>
<td></td>
<td>400 Hz–3 kHz</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>3 kHz–10 MHz</td>
<td>2.7 × 10⁻⁴f</td>
</tr>
<tr>
<td>All tissues of head and body</td>
<td>3 kHz–10 MHz</td>
<td>2.7 × 10⁻⁴f</td>
</tr>
<tr>
<td>General public exposure</td>
<td>1–10 Hz</td>
<td>0.1f</td>
</tr>
<tr>
<td></td>
<td>10 Hz–25 Hz</td>
<td>0.01f</td>
</tr>
<tr>
<td></td>
<td>25 Hz–1000 Hz</td>
<td>4 × 10⁻⁴f</td>
</tr>
<tr>
<td></td>
<td>1000 Hz–3 kHz</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>3 kHz–10 MHz</td>
<td>1.35 × 10⁻⁴f</td>
</tr>
<tr>
<td>All tissues of head and body</td>
<td>3 kHz–10 MHz</td>
<td>1.35 × 10⁻⁴f</td>
</tr>
</tbody>
</table>

### Reference Levels

<table>
<thead>
<tr>
<th>Frequency Range</th>
<th>E-field Strength (kV/m)</th>
<th>H-field Strength (A/m)</th>
<th>Magnetic Flux Density (T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–10 Hz</td>
<td>5</td>
<td>3.2 × 10⁻⁴f</td>
<td>4 × 10⁻⁸f²</td>
</tr>
<tr>
<td>8–25 Hz</td>
<td>5</td>
<td>4 × 10⁻⁵f</td>
<td>5 × 10⁻⁷f</td>
</tr>
<tr>
<td>25–50 Hz</td>
<td>5</td>
<td>1 × 10⁻²</td>
<td>2 × 10⁻⁴</td>
</tr>
<tr>
<td>50–400 Hz</td>
<td>2.5 × 10⁻⁵f</td>
<td>1 × 10⁻²</td>
<td>2 × 10⁻⁴</td>
</tr>
<tr>
<td>400 Hz–3 kHz</td>
<td>2.5 × 10⁻⁵f</td>
<td>4 × 10⁻⁵f</td>
<td>8 × 10⁻⁵</td>
</tr>
<tr>
<td>3 kHz–10 MHz</td>
<td>8.35 × 10⁻²</td>
<td>21</td>
<td>2.7 × 10⁻⁵</td>
</tr>
</tbody>
</table>

Note: In the frequency range above 100 kHz, RF-specific basic restrictions need to be considered additionally.

- **Summation Rule Adopted by ICNIRP 2003/2010**

\[
CF_2 = \left| \sum_{i=1}^{10 \text{ MHz}} \frac{A_i}{EL_i} \cos \left( 2\pi f_i t + \phi_i + \phi \right) \right| \leq 1
\]

\[
\phi_i = \begin{cases} 
\pi & \text{for } EL_i \propto f^{-2} \\
\pi / 2 & \text{for } EL_i \propto f^{-1} \\
0 & \text{for } EL_i \propto f^0 \\
-\pi / 2 & \text{for } EL_i \propto f^1 
\end{cases}
\]

- no sound-based biological rationale for the filter phase \( \phi \)
- non-linearity of nerve not taken into account \( \Rightarrow \) conservative
IEEE C95.6-2002/C95.1-2005

**maximum permissible exposure**

<table>
<thead>
<tr>
<th>Frequency range (Hz)</th>
<th>General public</th>
<th>Controlled environment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$B - \text{ms}$ (mT)</td>
<td>$H - \text{rms}$ (A/m)</td>
</tr>
<tr>
<td>$&lt;0.153$</td>
<td>118</td>
<td>9.39x10^4</td>
</tr>
<tr>
<td>$0.153 - 20$</td>
<td>$18.1f$</td>
<td>$1.44x10^4f$</td>
</tr>
<tr>
<td>$20 - 759$</td>
<td>$0.904$</td>
<td>719</td>
</tr>
<tr>
<td>$759 - 3000^6$</td>
<td>$687f$</td>
<td>$5.47x10^5f$</td>
</tr>
</tbody>
</table>

*Within this frequency range the term "action level" is equivalent to the term "general public" in IEEE Std C95.6-2002.

**basic restrictions**

<table>
<thead>
<tr>
<th>Exposed tissue</th>
<th>$f_0$ (Hz)</th>
<th>$E_0$ (rms) (V/m)</th>
<th>$E_0$ (rms) (V/m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain</td>
<td>20</td>
<td>5.89 x 10^{-3}</td>
<td>1.77 x 10^{-2}</td>
</tr>
<tr>
<td>Heart</td>
<td>167</td>
<td>0.043</td>
<td>0.043</td>
</tr>
<tr>
<td>Extremities</td>
<td>3350</td>
<td>2.10</td>
<td>2.10</td>
</tr>
<tr>
<td>Other tissues</td>
<td>3350</td>
<td>0.701</td>
<td>2.10</td>
</tr>
</tbody>
</table>

**approach 1: time-domain approach**

$$A_p = \dot{B}_p(t), E_p(t), \cdots$$

$$EL(f^*) = MPE_B(f^*) \omega^*, BR_E(f^*), \cdots$$

$$CF_3 = \frac{A_p}{\sqrt{2} \cdot EL(f^*)} \leq 1$$

$$f^* = 1/2t_p$$

$t_p$ = time between waveform zero-crossing or $1/e \cdot A_p$ for exponential signals

- $t_p$ and $A_p$ sensitive to measurement noise or time-domain biases
- $t_p$ not uniquely defined for signals never crossing the zero nor exponential
### Maximum Permissible Exposure

<table>
<thead>
<tr>
<th>Frequency range (Hz)</th>
<th>General public</th>
<th>Controlled environment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$B_{\text{rms}}$ (mT)</td>
<td>$H_{\text{rms}}$ (A/m)</td>
</tr>
<tr>
<td>$&lt; 0.153$</td>
<td>118</td>
<td>9.39 x 10^4</td>
</tr>
<tr>
<td>$0.153 - 20$</td>
<td>18.1/f</td>
<td>1.44 x 10^4/f</td>
</tr>
<tr>
<td>$20 - 759$</td>
<td>0.904</td>
<td>719</td>
</tr>
<tr>
<td>$759 - 3000(f)$</td>
<td>687/f</td>
<td>5.47 x 10^5/f</td>
</tr>
</tbody>
</table>

\[ CF_4 = \sum_{i=1}^{5 \text{MHz}} \frac{A_i}{EL_i} \leq 1 \]

\[ A_i = B_{\text{rms}}(f_i), \ E_{\text{rms}}(f_i), \cdots \]

\[ EL_i = MPE_B(f_i), \ BR_E(f_i), \cdots \]

- no phase information is taken into account → overly conservative
- non-linearity of nerve not taken into account → conservative
HVBG 2001 (Heinrich)

time-domain approach

\[ CF_5 = \frac{A_p}{\sqrt{2 \cdot EL(f') \cdot V}} \leq 1 \]

\[ A_p = B_p(t) \quad \text{for} \quad f' = 1/4 \tau_{\text{min}} \]

\[ EL(f') = RL_B(f') - MPE_B(f') \]

\[ V = \begin{cases} V_{\text{max}} = 8 & \text{for} \quad \sqrt{T/\tau_D} \geq 8 \\ \sqrt{T/\tau_D} & \text{for} \quad \sqrt{T/\tau_D} < 8 \end{cases} \]

\[ \tau_D = \sum \tau_{pi} \]

\[ T = \begin{cases} T_{\text{max}} = 1 \text{ s} & \text{for long pulses} \\ T & \text{for normal pulses} \end{cases} \]

\( V = \) weighting factor taking into account the effective pulse stimulation compared to sine

- \( \tau_{\text{min}} \) strongly sensitive to measurement noise or time-domain biases
- no sound-based biological rationale for the maximum value of \( V = 8 \)

H. Heinrich, “Assessment of non-sinusoidal, pulsed, or intermittent exposure to low frequency electric and magnetic fields,” Health Phys. 92 541–547, 2007

De Santis et al., “Human exposure from pulsed magnetic field therapy mats: a case study with 3 commercial products,” Bioelectromagnetics, 36 149-161, 2015

Compliance Assessment in Practice


De Santis et al., “Human exposure from pulsed magnetic field therapy mats: a case study with 3 commercial products,” Bioelectromagnetics, 36 149-161, 2015

Effect of DC-Offset on CF₃

unbiased signal

dc-biased signal
Effect of DC-Offset on CF$_3$

unbiased signal

dc-biased signal

<table>
<thead>
<tr>
<th>Compliance assessment</th>
<th>DC offset ($\mu$T)</th>
<th>$A_p$ (mT)</th>
<th>$t_p$ (ms)</th>
<th>$f^*$ (kHz)</th>
<th>$EL(f^*)$ ($\mu$T)</th>
<th>$CF_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICNIRP 1998</td>
<td>0</td>
<td>0.04</td>
<td>0.30</td>
<td>1.7</td>
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<tr>
<td>(B-field RL)</td>
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<tr>
<td></td>
<td>-10</td>
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<td>0.03</td>
<td>17</td>
<td>6.25</td>
<td>3.39</td>
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<td>ICNIRP 2010</td>
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<td>0.04</td>
<td>0.30</td>
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<td>48</td>
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<td>(B-field RL)</td>
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<tr>
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<tr>
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<td>-10</td>
<td>0.03</td>
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</table>
Effect of Signal Noise on CF$_3$
Effect of Signal Noise on $\text{CF}_5$

noisy signal

noise-free signal
Effect of Signal Noise on $CF_5$

**Table:**

<table>
<thead>
<tr>
<th>Compliance assessment</th>
<th>Noise removal</th>
<th>$A_p$ (mT)</th>
<th>$\tau_{min}$ (ms)</th>
<th>$f'$ (kHz)</th>
<th>$EL(f')$ (µT)</th>
<th>$CF_5$ (V)</th>
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</thead>
<tbody>
<tr>
<td>ICNIRP 1998 (B-field RL)</td>
<td>no</td>
<td>0.21</td>
<td>0.01</td>
<td>25</td>
<td>6.25</td>
<td>23.8 (1.0)</td>
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<td></td>
<td>yes</td>
<td>0.20</td>
<td>1.0</td>
<td>0.25</td>
<td>20</td>
<td>4.42 (1.6)</td>
</tr>
<tr>
<td>ICNIRP 2010 (B-field RL)</td>
<td>no</td>
<td>0.21</td>
<td>0.01</td>
<td>25</td>
<td>27</td>
<td>5.50 (1.0)</td>
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<tr>
<td></td>
<td>yes</td>
<td>0.20</td>
<td>1.0</td>
<td>0.25</td>
<td>200</td>
<td>0.44 (1.6)</td>
</tr>
<tr>
<td>IEEE 2002/2005 (B-field MPE)</td>
<td>no</td>
<td>0.21</td>
<td>0.01</td>
<td>25</td>
<td>205</td>
<td>0.72 (1.0)</td>
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<td>0.20</td>
<td>1.0</td>
<td>0.25</td>
<td>904</td>
<td>0.10 (1.6)</td>
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</table>
Effect of Sampling/Windowing on $\text{CF}_{1,2,4}$

- Original signal
- 3\textsuperscript{rd}-replica
- 5\textsuperscript{th}-replica
Effect of Sampling/Windowing on $CF_{1,2,4}$

original signal

3$^{\text{rd}}$-replica

5$^{\text{th}}$-replica

<table>
<thead>
<tr>
<th>Signal truncation</th>
<th>ICNIRP 2010 ($E_{\text{CNS BR}}$)</th>
<th>IEEE 2005 ($E_{\text{brain BR}}$)</th>
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</thead>
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<tr>
<td></td>
<td>$CF_{1,4}$</td>
<td>$CF_{2}$</td>
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<tr>
<td>original</td>
<td>3.07</td>
<td>1.13</td>
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<td>1 3rd-replica</td>
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<td>1.18</td>
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<tr>
<td>original</td>
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<td>1.21</td>
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<td>1.25</td>
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<tr>
<td>original</td>
<td>3.16</td>
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<td>5 3rd-replica</td>
<td>4.56</td>
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<td>5.21</td>
<td>1.20</td>
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</table>
Proposed Solution

Inverse Fourier Transform (IFT) approach

\[ CF_6 = \max \left| \text{IFT} \left( \frac{A(f)}{\sqrt{2} \cdot EL(f)} \right) \right| \leq 1 \]

- effective against time-domain biases (measurement noise and DC offset)
- effective against frequency-domain biases (sampling time and windowing)
- over-conservatism due to non-linearity of nerve stimulation not addressed
- over-conservatism due to PW instead of CW stimulation not addressed

Summary of Compliance Assessment

IH cooker

PMFT mats

MRI operator

<table>
<thead>
<tr>
<th>DC offset (μT)</th>
<th>Noise remove</th>
<th>Signal truncation</th>
<th>CF1,4</th>
<th>CF2</th>
<th>CF3</th>
<th>CF5</th>
<th>CF6</th>
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<tbody>
<tr>
<td>0</td>
<td>no</td>
<td>1 original</td>
<td>3.45</td>
<td>0.97</td>
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<td>0.72</td>
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<td>1.02</td>
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<td>0.25</td>
<td>0.82</td>
<td>1.33</td>
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</tbody>
</table>
Conclusions

• CF_{1,4} are overly conservative (add in-phase assumption)
• CF_2 accounts for the signal phase but introduces an ‘artificial’ phase
• time-domain approaches CF_{3,5} are strongly sensitive to bias on measurement setup (DC-offset and moreover noise level)
• existing solutions can lead to notably different results
  ➢ one product can be IEEE compliant (CF_3) or not (CF_4) depending on the adopted approach
• proposed approach CF_6 is the most robust and ‘fairly-conservative’ but does not address non-linearity and stimulus effectiveness
Future Works

IFT approach + waveform coefficient $F_w$

$$CF_7 = \max \left| IFT \left( \frac{A(f)}{\sqrt{2} \cdot EL(f)} \right) \frac{1}{F_w} \right| \leq 1$$

$A(f)$ = complex-valued FT of the signal under-test

$EL(f)$ = exposure limit at frequency $f$ (rms)

$F_w$ = weighting factor taking into account the effective pulse stimulation compared to continuous sinewave (derived using the SENN model)

$$F_w = \frac{I_{th,pulse}}{I_{th,sin}(f^*)}$$

$I_{th,pulse}$ = threshold derived for the PW-signal

$I_{th,sin} = \text{threshold of CW-sinewave at } f^* = 1/(2t_p)$

- Inspired to the V coefficient proposed by Heinrich
Multiple Frequency Compliance

Non-linear Biology-Based Spectral Assessment (NBBA)

\[ B_{50,\text{equ}} = \sum_{f=1\ \text{Hz}}^{150\ \text{Hz}} \frac{f \cdot B_f}{f_{50}} + \sum_{f>150\ \text{Hz}}^{2\ \text{kHz}} \frac{f_{450} \cdot B_f}{f} \]

Future Works

IFT approach + waveform coefficient $F_w$

\[ CF_\gamma = \max \left| \text{IFT} \left( \frac{A(f)}{\sqrt{2} \cdot EL(f)} \cdot \frac{1}{F_w(f)} \right) \right| \leq 1 \]

$A(f) =$ complex-valued FT of the signal under-test

$EL(f) =$ exposure limit at frequency $f$ (rms)

$F_w =$ weighting factor taking into account the non-linearity of fiber nerves

$F_w(f) = \alpha(f)$

- Inspired to the NBBA summation rule proposed by Leitgeb
- An extension to pulsed rather than multiple-frequency signals must be found
Open Issues

- does not distinguish between several biological mechanisms as a function of frequency (i.e., phosphenes below 1 kHz and PNS nerve stimulation above 1 kHz)
- SENN model applicable only for PNS nerve stimulation
- phosphenes numerical model needed to close the gap
Future Works

IFT approach + waveform coefficient $F_w$

$$CF_7 = \max \left| \text{IFT} \left( \frac{A(f)}{\sqrt{2 \cdot EL(f) F_w(f)}} \right) \right| \leq 1$$

$A(f) = $ complex-valued FT of the signal under-test
$EL(f) = $ exposure limit at frequency $f$ (rms)

$F_w = $ weighting factor taking into account the non-linearity of fiber nerves and the effective pulse stimulation compared to continuous sinewave

$$F_w(f) = \begin{cases} 
1 & \text{for } f < 1 \text{ kHz (due to phosphenes)} \\
\frac{I_{th, pulse}}{I_{th, sin}(f^*)} \cdot \alpha(f) & \text{for } f \geq 1 \text{ kHz (SENN+NBBA derived)}
\end{cases}$$

- Inspired to both Heinrich and Leitgeb approaches to account for both non-linearity and effective pulse stimulation
Final Recommendations

\[
CF_2 = \sum_{i=1}^{10 \text{ MHz}} \frac{A_i}{EL_i} \cos \left( 2\pi f_i t + \phi_i + \phi \right) \leq 1
\]

\[
CF_6 = \max \left| IFT \left( \frac{A(f)}{\sqrt{2 \cdot EL(f)}} \right) \right| \leq 1
\]

• CF₆ in practice is **more immune** to frequency-domain biases

• time-domain approaches CF₃,₅ are more representative of electro-stimulation but strongly sensitive to **bias** on measurement setup
  - product safety standards (IEC, IEEE/ICES TC34,...) should provide technical guidelines to specify how to minimize measurement errors/biases

• experimental setups on magneto-phosphenes are **needed** to close the gap in the low-frequency range (below 1 kHz)
  - general-purpose PW signals rather than CW-sinus should be investigated to derive phosphene thresholds
Target tissues for electrostimulation

Ilkka Laakso

Nagoya Institute of Technology, Japan
(=> Aalto University, Finland)
DC & AC stimulation
AC(&DC) stimulation: Phosphenes

"Electrical stimulation of the visual cortex" does not work:

- significant current flows through the eyes


Electrostimulation devices

Time scale: 100 us pulses
When magnetically stimulating peripheral nerves, a local cocontraction of muscle under the coil is observed. We assessed whether this contraction results from: (1) magnetic stimulation of motor nerves, or (2) direct depolarization of the muscle membrane. Wrist extensor muscles of normal subjects were magnetically stimulated with the coil placed directly above the muscle. Neurorogical transmission was then blocked by atracurium using a technique of local curarization. As a reference, the radial nerve was stimulated electrically. Magnetic and electrical stimuli were applied alternatingly every 10 s. Twitch force of wrist extension was measured isometrically over a period of about 70 min including the phase of complete neuromuscular block. Twitch amplitudes elicited by magnetic and electrical stimuli were equivalent during the whole experiment. These results suggest that muscle cocontraction following magnetic stimulation results from depolarization of terminal motor nerve branches. © 1994 John Wiley & Sons, Inc.

Key words: magnetic stimulation • motor evoked potentials • atracurium • local curarization • ischemia

MUSCLE & NERVE 17:1170–1175 1994

MAGNETICALLY INDUCED MUSCLE CONTRACTION IS CAUSED BY MOTOR NERVE STIMULATION AND NOT BY DIRECT MUSCLE ACTIVATION

JOCHEN MACHE TANZ, MD, CHRISTIAN BISCHOFF, MD, REINER PICHLM EIER, MD, HERMANN RIESCHER, BERND-U LLRICH MEYER, MD, ASTRID SADER, MD, and BASTIAN CONRAD, MD

In recent studies using magnetic devices for the stimulation of peripheral nerves an artifact was observed that resulted from an undesired contraction of muscle in the vicinity of the stimulation coil. The muscular contraction was much stronger than the muscle response elicited by electrical pulses that depolarized the peripheral nerve trunk to a comparable extent. Magnetic stimulation above the muscle has a potential clinical importance, since Zhu and Starr were able to evoke cerebral potentials by such magnetic muscle stimulation. It is not self-evident whether this stimulation is due to stimulation of nerve terminals or due to muscle activation. The muscle contraction induced by magnetic stimulation was compared with that induced by voluntary muscle activity, and the possibility to stimulate muscle directly using electrical stimulation via surface electrodes has been shown by Hill et al. Lotz and coworkers described that no muscle twitches could be magnetically elicited in patients undergoing routine anesthesia including curarization for standard surgical procedures. If this effect was due to the curarization it could be inferred that the muscular contraction following magnetic stimulation was based on neuromuscular transmission and that it resulted from stimulation of nerve branches. However, Lotz et al. did not explicitly exclude interactions.
Motor nerves, not muscles

=> No more muscle contractions

⇒ Motor nerve (1) was stimulated, not muscle fibres (4)
### Summary

<table>
<thead>
<tr>
<th>Desired effects</th>
<th>Electrical stimulation</th>
<th>Magnetic stimulation</th>
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<tbody>
<tr>
<td>Plasticity induction</td>
<td>DC &amp; AC Pulsed (~100 us)</td>
<td>Pulsed (~100 us)</td>
</tr>
<tr>
<td>PNS stimulation (also CNS, but very painful)</td>
<td>CNS stimulation</td>
<td>PNS stimulation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Undesired effects</th>
<th>Electrical stimulation</th>
<th>Magnetic stimulation</th>
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<tr>
<td>Skin tingling</td>
<td>Painful skin stimulation</td>
<td>Non-target motor nerve stimulation</td>
</tr>
<tr>
<td>Retinal phosphenes (when switched on and off)</td>
<td></td>
<td>(Skin stimulation??)</td>
</tr>
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AC magnetic fields: **retinal phosphenes** [no applications (yet)]