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Comparing the SENN and the MRG Electrostimulation Models in the Context of Occupational Exposure Limit Values

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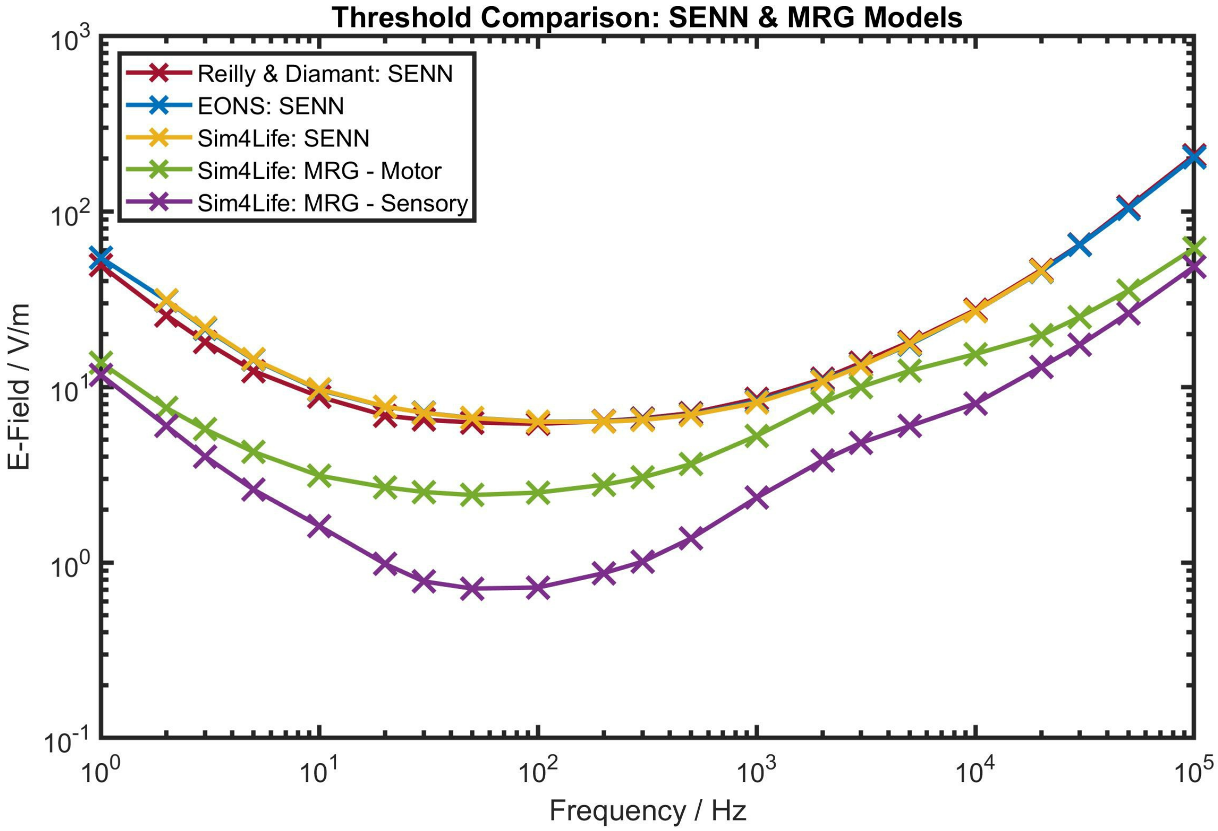

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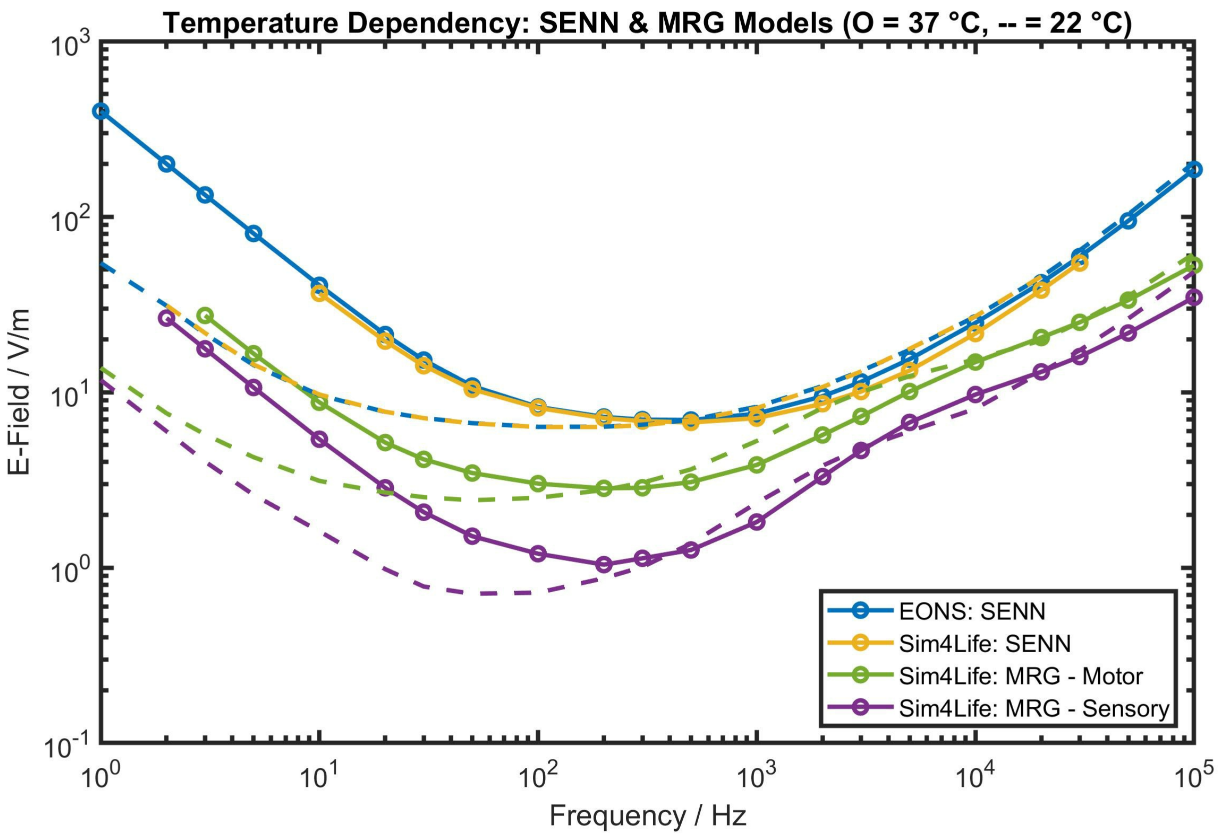

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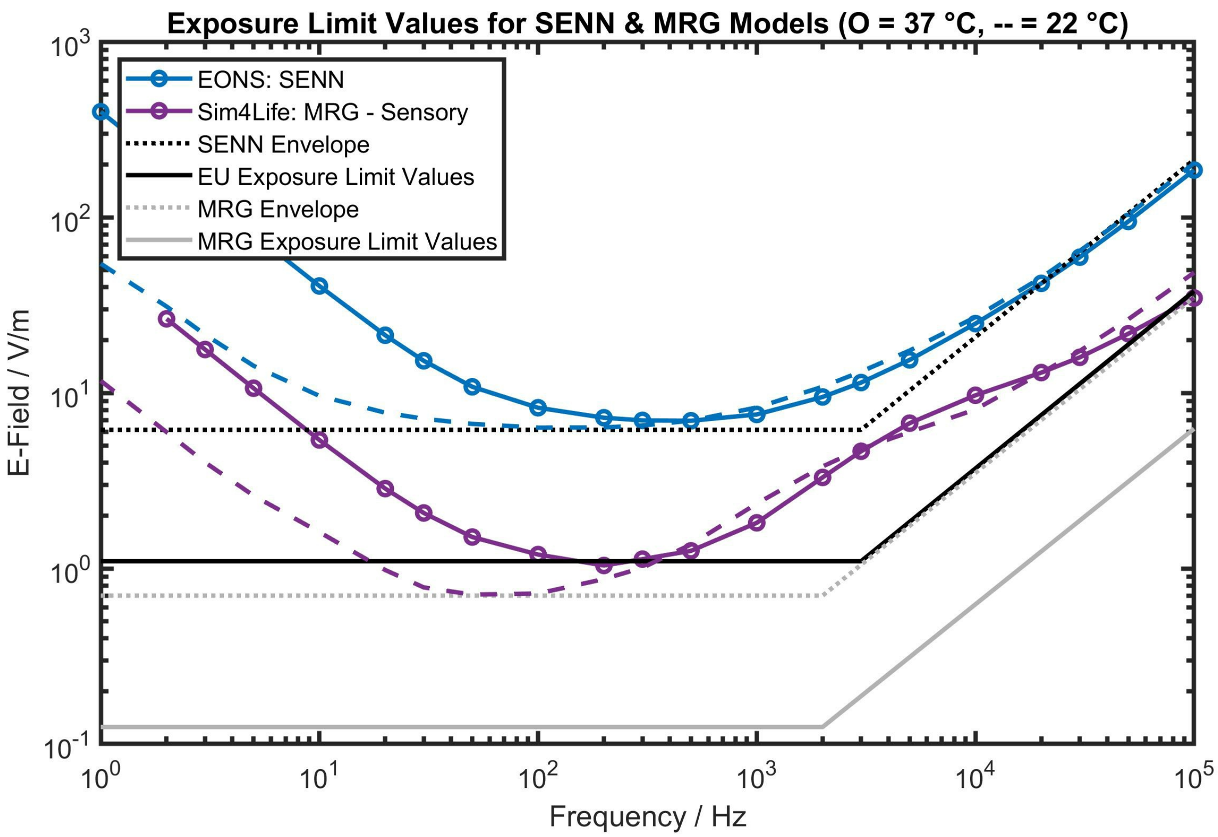

SUMMARY

Occupational exposure limit values (ELVs) for electric fields inside the body can be derived from thresholds for action potential generation. These thresholds are calculated based on electrostimulation models. The spatially extended nonlinear node model (SENN) is often used to determine such thresholds. The more detailed model by McIntyre, Richardson and Grill (MRG) is seen as more realistic. This work compares thresholds calculated with the SENN and the MRG models for frequencies between 1 Hz and 100 kHz and temperatures between 22 °C and 37 °C. Results show that MRG thresholds are lower than SENN thresholds. In the context of occupational ELVs, using the MRG model would lead to approximately ten times lower limit values.

INTRODUCTION

The EU directive 2013/35/EU [1] specifies occupational exposure limit values (ELVs) for adverse health effects of body internal electric fields. These ELVs are based on recommendations given by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) for occupational exposure in 2010 [2]. ICNIRP states that their recommendations are based on experimental findings as well as theoretical calculations using an electrostimulation model (please note that additional limit values for sensory effects are based on thresholds for phosphene perception). The spatially extended nonlinear node electrostimulation model (SENN) has been used by Reilly and Diamant [3] to derive exposure guidelines which are partially comparable to the ICNIRP guidelines and are being applied by the IEEE standard C95.1-2019 [4]. For further information on the derivation of ELVs from SENN thresholds see Soyka et al. [5].

Another, potentially more realistic electrostimulation model was introduced by McIntyre et al. [6] and is called the MRG model. The MRG model differs from the SENN model by including paranodal sections, a double-cable structure, finite myelin impedance and altered membrane channel dynamics. For example, the MRG model was successfully used to describe experimentally determined perceptual thresholds for human arms and legs exposed to magnetic fields [7]. The MRG model was further refined by Gaines et al. [8] resulting in two models: “MRG - Sensory” and “MRG - Motor” which are more specific to the type of nerve under investigation.

These two models and the SENN model are implemented in the Sim4Life[1] simulation environment and were used to determine thresholds for this study. Furthermore, the SENN model implementation by Reilly & Diamant [3] and another freely available SENN model implementation (called EONS) by Tarnaud et al. [9] were used. Therefore, there were five simulation setups in total: SENN by Reilly & Diamant, SENN in EONS, SENN in Sim4Life, and MRG - Sensory and MRG - Motor in Sim4Life as well.

The goal of this study was to compare thresholds and the potential ELVs resulting from these thresholds for different electrostimulation models. Furthermore, the influence of temperature on thresholds was investigated as well.

In accordance with a worst-case approach, which is usually applied for defining safety relevant limits, the lowest calculated thresholds were used to derive hypothetical ELVs. These are compared to the current ELVs and the potential impact on safety guidelines is discussed.

METHODS

The SENN model implementation by Reilly & Diamant represents the standard to which the other models can be compared, because its results form the basis for the current ELVs. Reilly & Diamant

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[1] Sim4Life V7.0, ZMT, https://zmt.swiss/sim4life/

chose a temperature of 22 °C for their studies. This temperature cannot be adjusted in their software, without modifying and recompiling the FORTRAN source code which we did not do in this study. In the Sim4Life and EONS simulation tools temperature settings can easily be adjusted. The body core temperature of 37 °C was chosen as a comparison value to investigate the influence of temperature on the thresholds. The Sim4Life simulation environment allows calculating thresholds for all three models and both temperatures. However, in some cases no valid thresholds could be obtained with the Sim4Life models for very low or very high frequencies. Therefore, the EONS SENN model implementation was used in addition which allowed the calculation of SENN model thresholds for both temperatures across the full frequency range. Furthermore, having three different simulation tools allows for a cross comparison between the tools for the SENN model at 22 °C.

All simulations used the same setup (matching the original setup by Reilly and Diamant): an axon (20 µm diameter) within and parallel to a homogenous electric field with a sinusoidally varying amplitude (1 Hz to 100 kHz). The simulation tools adjust the amplitudes via a titration procedure until the smallest amplitude (the threshold) is found for which an action potential (at least 80 mV depolarization) is elicited [3].

After calculating all five simulation setups at 22 °C and verifying that they give similar results, all but Reilly & Diamant's SENN model implementation (for which the temperature was not easily adjustable) were additionally run at 37 °C.

ELVs are derived from the thresholds by placing an envelope around the thresholds and applying a safety factor [5]. The envelope consists of two lines. The first line has a constant value E_0 which is defined by the lowest threshold. The second line is proportional to the frequency. It is starting from the corner frequency f_C which is chosen such that all thresholds are just enclosed by the envelope. The safety factor between the ELVs from the EU directive and the SENN thresholds' envelope is $6.15\,V/m \,/\, 1.1\,V/m \approx 5.6$.

In accordance with a worst-case approach, this procedure was applied for the lowest thresholds found from the previous calculations. The resulting ELVs are compared to the current ELVs from the EU directive.

The time course of the membrane voltage at the first and last node of Ranvier was visually checked at threshold level intensity to verify the action potential. For some frequencies the time course followed the sinusoidal shape of the stimulus and did not show the typical action potential shape in the Sim4Life simulation environment. These cases were excluded from the results. Looking further into the issue revealed that there might a problem with the titration procedure for high E-field values. Running simulations without the titration procedure and manually setting the E-field amplitude to the thresholds calculated with the EONS SENN implementation results in the typical action potential shape in Sim4Life as well. Further investigations are necessary to better understand the issue but are beyond the scope of this work. Please note that the excluded cases are not essential for answering our research questions.

RESULTS

Figure 1 shows the thresholds for all five simulation setups at 22 °C. The SENN thresholds are very similar for all simulation tools and only show negligible differences in the low frequency range. As described in the Methods section, the Sim4Life simulation environment had difficulties finding the thresholds for some frequencies and therefore these values were excluded (missing yellow markers).

Figure 2 shows the same thresholds in addition with the calculations at 37 °C for all but Reilly & Diamant's model.

Figure 3 shows the thresholds for the EONS SENN model and the MRG - Sensory model for both temperatures, together with the corresponding envelopes and the resulting ELVs. The MRG - Sensory model was chosen because it has the lowest thresholds and can be seen as a worst-case scenario from an occupational safety perspective. The EONS SENN model is comparable to Reilly & Diamant's original model and additionally allows investigating the influence of temperature on thresholds. It represents the currently implemented ELVs in the EU directive.

The envelope for the EONS SENN model has the following parameters: lowest threshold $E_0 = 6.3\ V/m$ and corner frequency $f_C = 3\ kHz$. And the envelope for the MRG - Sensory model has the following parameters: lowest threshold $E_0 = 0.7\ V/m$ and corner frequency $f_C = 2\ kHz$.

DISCUSSIONS

Comparing the SENN model thresholds at 22 °C (Figure 1) shows that all three simulation tools give very similar results. The same holds true at 37 °C for the Sim4Life and the EONS simulations (Figure 2). This cross-check between simulation tools provides a good indicator for the validity of the simulations.

One of the goals of this study was to investigate the influence of temperature on the action potential thresholds. Figure 2 shows that for frequencies above approximately 300 Hz the thresholds for 22 °C and 37 °C are rather similar. Below 300 Hz the thresholds for 37 °C are significantly higher than those for 22 °C. An increase of the thresholds with temperature is expected at low frequencies, because the ion channels' time constants become smaller at higher temperatures. At low frequencies, the effect of fast sodium activation can be neglected, compared to the relatively slow inactivation and activation of sodium and potassium currents, respectively. As a result, sodium current inactivation and potassium current activation will increasingly counteract neuronal excitation at higher temperatures, eventually resulting in heat block [10, 11]. In contrast, at high frequencies the sensitivity of the threshold to the temperature is small, because all the gate parameters will need several periods to reach their steady state values. Because thresholds at 22 °C are lower than at 37 °C, they provide a conservative estimate for potentially adverse health effects. Note that current ELVs are based on SENN thresholds at 22 °C (Figure 3). For future guidelines, it might be helpful to take temperature effects into account when giving recommendations for very hot or very cold working environments. Furthermore, it might be helpful to consider the temperature differences between body parts e.g., the limbs in comparison to the chest or the brain.

In general, it was found that the MRG models give up to ten times lower thresholds than the SENN model calculations. This is of course very important from a safety point of view since it raises the question if the current ELVs are too high. For example, Figure 3 shows that the MRG – Sensory thresholds around 50 Hz are below the current ELVs.

Note that the thresholds for the MRG models have inflection points around 3 kHz which are not present for the SENN model thresholds. Therefore, an envelope rising linearly with increasing frequency might not be the best option for deriving ELVs from these thresholds. Since both MRG models show these inflection points for both temperatures, it seems likely that this is a real effect and not some kind of artifact. Indeed, the sensory and motor MRG models include active membrane dynamics in the paranodal and internodal sections. Inflection points are expected when different frequencies result in initiation of action potentials at different locations along the axon, similar to observed deviations from classical strength-duration curves [12].

Previous work [5] also showed how changes in electrostimulation modelling can lead to different ELVs. It is very important to get good experimental data to be able to verify and choose between the different models. Davids et al. [7] describe a good fit for perceptual thresholds in arms and legs for magnetic field stimulation between approximately 0.5 and 10 kHz with the original MRG model. Fresnel et al. [13] are planning on running similar studies at 50 Hz and 60 Hz for magnetic field stimulation of the leg. Future work could pool such data and try to differentiate between different models. However, such an approach needs to model the induction of the electric field in the body as well. Properly calculating the induced electric field is important because the electrostimulation depends on the orientation of the nerve fibre with respect to the field.

CONCLUSIONS

This work showed that action potential thresholds based on MRG electrostimulation models are lower than thresholds calculated by the SENN model. Furthermore, it showed that for calculating thresholds, temperature settings of either 22 °C or 37 °C only made a difference for frequencies smaller 300 Hz. Deriving exposure limit values from MRG thresholds in the same way as they are derived from SENN thresholds, results in approximately 10 times smaller values than those currently given in the EU directive for occupational exposure. Further experimental data is needed to understand which model is better suited to derive exposure guidelines. Nevertheless, future guidelines should take MRG model results into account.

REFERENCES

[1] The European Parliament and the Council of the European Union (2013) Directive 2013/35/EU on the Minimum Health and Safety Requirements Regarding the Exposure of Workers to the Risks Arising from Physical Agents (Electromagnetic Fields)

[2] International Commission on Non-Ionizing Radiation Protection (2010) Guidelines for Limiting Exposure to Time-Varying Electric and Magnetic Fields (1 Hz to 100 kHz). Health Phys, 99(6)

[3] J. P. Reilly & A. M. Diamant (2011) Electrostimulation: Theory, Applications, and Computational Models: Artech House Publishers. SENN Model Implementation: https://us.artechhouse.com/Assets/reslib/reilly/reilly.html

[4] Institute of Electrical and Electronics Engineers (2019) IEEE Standard for Safety Levels with Respect to Human Exposure to Electric, Magnetic, and Electromagnetic Fields, 0 Hz to 300 GHz. C95.1-2019. https://standards.ieee.org/standard/C95_1-2019.html

[5] F. Soyka et al. (2022). The Influence of Membrane Channel Dynamics on Occupational Exposure Limit Values. BioEM 2022, Nagoya, Japan.

[6] C. C. McIntyre et al. (2002) Modeling the Excitability of Mammalian Nerve Fibers: Influence of Afterpotentials on the Recovery Cycle. J. Neurophysiol., 87(2), 995-1006

[7] M. Davids et al. (2017) Predicting Magnetostimulation Thresholds in the Peripheral Nervous System using Realistic Body Models. Sci. Rep., 7(1)

[8] J. L. Gaines et al. (2018) A Model of Motor and Sensory Axon Activation in the Median Nerve Using Surface Electrical Stimulation. J. Comput. Neurosci., 45(1), 29-43

[9] T. Tarnaud et al. (2022). EONS: Evaluation of Non-Sinusoidal Magnetic Fields for Electromagnetic Safety to Intermediate Frequencies. BioEM 2022, Nagoya, Japan.

[10] F. Rattay & M. Aberham (1993). Modeling Axon Membranes for Functional Electrical Stimulation . IEEE Trans. Biomed. Eng., 40(12), 1201-1209

[11] Z. Mou et al. (2012). A Simulation Study of the Combined Thermoelectric Extracellular Stimulation of the Sciatic Nerve of the Xenopus Laevis: The Localized Transient Heat Block. IEEE Trans. Biomed. Eng., 59(6), 1758-1769

[12] F. Rattay et al. (2012). Strength–Duration Relationship for Intra- Versus Extracellular Stimulation with Microelectrodes. Neuroscience 214, 1-13

[13] E. Fresnel et al. (2022). Peripheral Nerve Stimulation Thresholds in Human Subjects Exposed to the Extremely Low-Frequency Magnetic Fields. BioEM 2022, Nagoya, Japan.

Figure 1: Thresholds for action potential generation based on five simulation setups for a temperature of 22 °C. The SENN model thresholds are very similar for the three different simulation tools. The MRG – Sensory model produces the lowest thresholds.

Figure 2: Thresholds are shown for two temperatures: 22 °C (dashed lines, same as in Figure 1) and 37 °C (solid line and circular markers). The EONS and the Sim4Life simulation tools give very similar results for the SENN model. For frequencies below 300 Hz temperature has a significant influence, resulting in higher thresholds for higher temperatures.

Figure 3: Thresholds for the SENN and the MRG – Sensory models at 22 °C and 37 °C. The corresponding envelopes (dotted lines) are used to derive the ELVs which include an additional safety factor of 5.6. The ELVs based on the MRG model would be up to 10 times lower than the ELVs given in the current EU directive. Note that thresholds at 22 °C provide the most conservative values for defining the envelopes.

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