Modeling and Optimization of Neural Activation during Spinal Cord Stimulation

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Abstract

Spinal Cord Stimulation (SCS) is a neurostimulation technique used to alleviate several kinds of chronic pain. Computer modeling of SCS is a powerful tool in predicting the effects of an electrical stimulus on nerve fiber activation. The UT-SCS, developed at the University of Twente, Enschede, The Netherlands, has provided useful insights on the mechanisms of SCS. Nevertheless, this software presents several limitations. This work aimed at building a first approach to a novel SCS model in an attempt to overcome the UT-SCS software limitations. A state-of-the-art Finite Element software, COMSOL Multiphysics®, was used in combination with MATLAB. Several fiber activation parameters were determined and compared with those yielded by the UT-SCS model. The simulations were performed for two different three-lead configurations and the current was gradually steered across the contacts. In general, the results given by the two SCS models were in agreement. The differences were hypothesized to be due to geometrical differences between the two models. Moreover, the potential field distributions were more robust in the COMSOL model than in the UT-SCS. The performance of the two contact configurations in the new SCS model was then compared. The configuration consisting of two anodes on each side of a cathode gave overall better results at the cost of a lower current amplitude.

Keywords: Spinal Cord Stimulation, Computer Modeling, COMSOL Multiphysics, Volume conductor model, McNeal's fiber model, Current steering

1 Introduction

1.1 Background

The Spinal Cord (SC) is the most caudal part of the central nervous system. It receives sensory information from the skin, joints and muscles of the trunk and limbs and contains the motor neurons responsible for both voluntary and reflex movements.

There are 31 pairs of spinal nerves linking the SC with muscles and sensory receptors in the skin. Each of these nerves has a sensory division that emerges from the dorsal region of the cord (dorsal roots, DRs) and a motor division that emerges from the ventral aspect (the ventral roots). The DRs carry sensory information, such as pain, temperature, touch and proprioceptive sensations, from muscles and skin. The area of skin innervated by a single DR is known as a *dermatome*.

The DR fibers, upon entering the SC, branch into an ascending and a descending segment. The ascending fibers can travel uninterruptedly in the longitudinal Dorsal Columns (DCs), in the white matter of the SC, towards the brain.

The DCs are arranged somatotopically at each spinal level, meaning that there is a correspondence between the organization of the fibers and the body areas they innervate [5]. The distribution of the dermatomes at a low-thoracic level (T11) is depicted in Figure 1.

Spinal Cord Stimulation (SCS) is an electrical neurostimulation technique aimed at alleviating several kinds of chronic pain.

It is based on the "gate-control" theory developed in 1965 by Melzack and Wall, which states that the activation of large afferent fibers blocks certain pain pathways [8]. The technique was first introduced in 1967 [10] and consists of applying an electric current to contacts mounted on leads which are surgically implanted in the patient's spinal cord. The generated electric potential field is capable of activating large sensory fibers, thereby blocking the transmission of noxious stimuli to the brain, while eliciting a

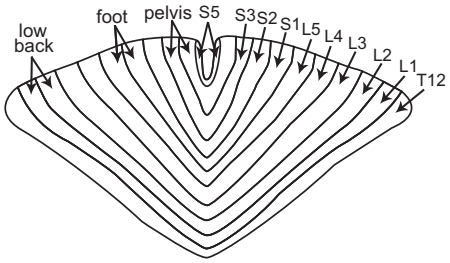

Figure 1: Topographical representation of dermatomes in the dorsal columns of the T11 segment [7]. Fibers originating from caudal (sacral) regions are at dorsomedial positions, while fibers from more rostral levels enter more laterally in the DCs.

"tingling" sensation (*paresthesia*) in the affected body regions. The aim of SCS is to completely cover the painful regions with this sensation. It is thought that, in order to accomplish that, the DC fibers should be activated, rather than the DR fibers. Due to the somatotopic organization of the DCs, when these fibers are activated an extense region of the body feels the effect of the stimulus. In contrast, the activation of DRs is felt only at a single dermatome [1]. Moreover, the DR fibers carry various types of afferent fibers, which, once activated, are likely to produce uncomfortably sharp paresthesiae, pain and even motor responses [9].

Despite being a widely used technique, the SCS mechanisms are still not fully understood. This limits its applicability and hinders an accurate determination of the most effective combination of stimulation parameters to be used in each patient [3].

With the aim of better understanding the effect of electrical stimulation on nerve fiber activation, several computer models mimicking SCS have been developed in the past few decades. The UT-SCS model was created in the 90's in the University of Twente, Enschede, The Netherlands [11–16]. It comprises a volume conductor model and a fiber model. The former consist of a 3D representation of the SC in which electrical stimuli can be applied. The resulting distribution of the electric potentials can be determined by Poisson's equation, $-\nabla \cdot (\sigma \nabla V) = Q_j$, and depends on the geometry and the physical properties of the several compartments in the volume conductor. Secondly, this induced-field leads to the flow of current across nerve fiber membranes. The response of the membranes to the potential field determined in the volume conductor model can then be determined using a fiber model. In 1976, McNeal developed a mathematical model of a myelinated nerve fiber, in which he compared a nerve fiber to an electrical cable [6]. McNeal predicted, in his calculations, that a fiber is depolarized when it is placed in the vicinity of a cathode and hyperpolarized when it is close to an anode.

One of the many modeling studies performed in the UT-SCS software was the Transverse Tripolar Stimulation (TTS) [17]. The TTS electrode comprises a central cathode and two long lateral anodes, which are placed transversely with respect to the cathode. This contact configuration allows for the transversal steering of the applied electric field and therefore enables the control of DC activation regions, as depicted in Figure 2. The steering of the activated DC region implies that, clinically, paresthesia is also steered, as can be concluded from the somatotopic organization of the DCs.

Besides this steering possibility, the TTS configuration also allows anodal shielding in the lateral regions, namely in the DR fibers. As such, it was proposed that transversely steering the electric field could improve the control of paresthesia, both by increasing the range of stimulation possibilities, and thus enhancing the flexibility and adjustability of SCS systems, and by increasing the DR thresholds. These predictions were proved in a clinical study by Wesselink *et al* [17].

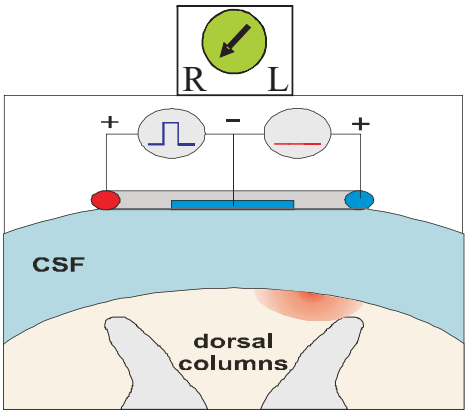

Figure 2: Example of how a TTS electrode with a dual-channel voltage stimulator can be used to control paresthesia steering by controlling the area of activation of DCs. R: Right; L: Left; Red shaded region: activated DCs. A pulse is applied in the right channel, thereby displacing the activated area to the left [4].

1.2 Motivation and Goals

It has been acknowledged that the UT-SCS software presents several limitations to researchers. In particular, it is not flexible in what concerns the development of the model geometry. Moreover, the finite difference method implemented to determine the potential field distribution resulting from the application of a stimulus uses a cubic discretization grid. Hence, all supposedly curved components of the spinal cord must be approximated by straight line segments.

Another drawback, or a limitation when compared to recent softwares, concerns the fact that more sophisticated finite element algorithms already exist, meaning that the computational power and accuracy of the SCS model can indeed be improved. COMSOL Multiphysics® is an example of a state-of-the-art platform for computer modeling using powerful finite element algorithms, providing, at the same time, a user-friendly and flexible interface for building complex physical models.

The primary aim of the present work is to build a first approach to a new SCS model in a COMSOL/MATLAB environment. It should serve as a starting point for the development, in the long term, of a more complex SCS simulation software with improved and more flexible features with respect to the UT-SCS.

An additional goal is to analyze the performance of two different triple-lead configurations involving the transversal steering of current across laterally placed anodes. This is intended to mimic TTS in cylindrical percutaneous leads, which are easier to be implanted surgically.

2 Methods

2.1 Volume conductor model

The first step in building the volume conductor model in COMSOL is to create its geometry. First, a 2D cross-section of the SC model is drawn in an xy-plane (Figure 3, left). Afterwards, the 2D geometry is extruded into the third dimension in the z-axis (rostro-caudal) direction. The resulting model (Figure 3, right) represents the T11-T12 segment of the spinal cord and its surrounding anatomical structures.

After building the geometry representing the SC structures, the lead(s) can be inserted in the 3D model at any desired location. Two contact configurations were modeled in this work, as depicted in Figure 4.

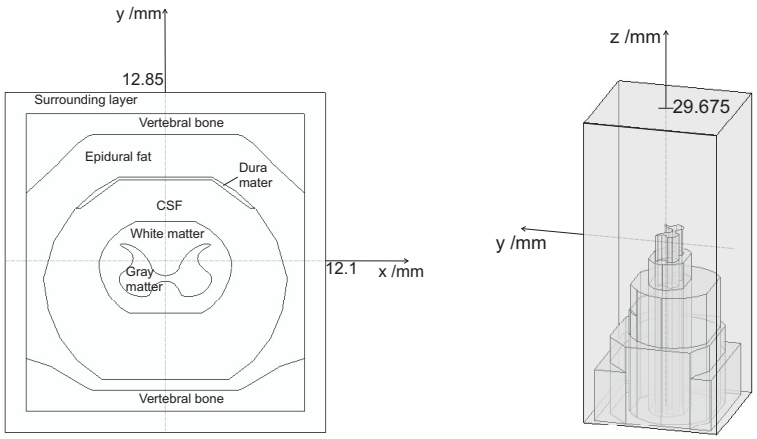

Figure 3: Transversal and lateral views of the volume conductor model. The 3D structure on the right was manipulated in a manner that the shapes of its compartments could all be visible. In reality, they all have the same rostro-caudal length.

These configurations belong to the Modeling Plan that is currently being followed at the University of Twente and which is being funded by Advanced Bionics, a neurotechnology company dedicated to the development of SCS equipment.

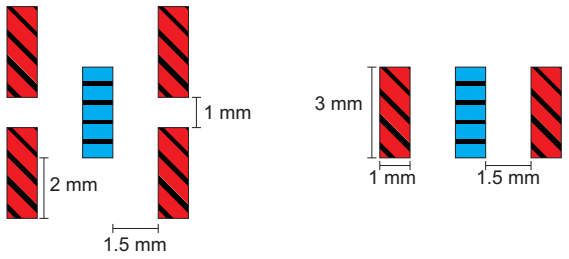

Figure 4: Frontal view of Models E (left) and F (right) contact configurations. Blue with horizontal lines: cathodes; light red with oblique lines: anodes.

A significant difference between the geometry of the two SCS models is the curvature of the dura mater (Figure 5). The implications of such disparities will be addressed later.

The following step consists of assigning each compartment of the model with the respective electrical conductivity. Then, the boundary conditions of the FE model need to be set. In particular, the surfaces that compose each of the modeled contacts are defined as current sources. The density of the injected current at these surfaces, J_n, is calculated accordingly with each current steering situation that is being modeled. In all simulations, the cathode is given a current density such that a total current of -1 mA is being applied.

The transversal electric field steering is modeled by varying the anodal current ratio in several steps: 100|0, 95|5, 90|10, 80|20, 70|30, 60|40, 50|50, 40|60, 30|70, 20|80, 10|90, 5|95 and 0|100. These numbers represent the percentage of anodal current applied to the right lead anodes and to the left lead anodes, respectively. For the two anodes in the same lead (in the case of a Model E configuration), the current is distributed equally. The total anodal current must sum +1 mA in order to equilibrate the cathodal

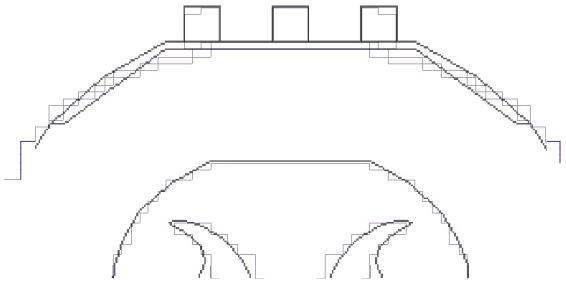

Figure 5: Detail of the superposition of the transversal geometries showing the curvatures of the dura mater, the white and the gray matter. The placement of the three leads on the dorsal border of the dura is also shown.

current.

The final steps comprise the discretization of the model (*meshing*) and the definition of the Solver Parameters in COMSOL.

2.2 Fiber model

Two fiber configurations were modeled in MATLAB. The first was a longitudinal fiber, representing a DC fiber, which was used to determine the DC threshold and the area of recruited DC fibers. The second type consisted of a lateral longitudinal fiber to which six collateral fibers and one curved fiber were attached. This fiber "system" represents a DR fiber coming from the periphery and is used to determine the threshold of activation of DR fibers. The geometric parameters of the modeled fibers were calculated as indicated in [6]. The placement of the fibers was the same as that which has been used in recent UT-SCS modeling studies.

McNeal's model was then used to determine the time variation of the membrane potential at each fiber node. Whenever this value was above 50 mV, the fiber was said to be activated.

2.3 Output parameters

The implementation of the fiber model and its connection with the solution of the volume conductor model enabled the analysis of several clinically relevant SCS parameters:

- $\mathbf{I_{DC}}$ [mA]: Dorsal Column fibers' activation threshold;
- $\mathbf{I_{DR}}$ [mA]: Dorsal Root fibers' activation threshold;
- $\mathbf{I_{PT}}$ [mA]: Paresthesia Threshold, corresponding to the lowest value between I_{DC} and I_{DR};
- $\mathbf{I_{DT}}$ [mA]: Discomfort Threshold, defined as: $I_{DT} = 1.4 \times I_{DR}$ [2];
- **TR** [-]: Therapeutic Range, defined as: $TR = I_{DT}/I_{PT}$.
- $\mathbf{S_{RA}}$ [mm^2]: Maximum DC recruited area, which is the region in the spinal cord comprising the DC fibers that become activated at I_{DT};

3 Results and Discussion

3.1 Comparison between the two SCS models

3.1.1 Volume conductor models

The potential field distributions in the two SCS models, for a transverse bipole placed on the dura mater are depicted in Figure 6. These results concern a z-slice taken about 1 cm below the center of the model.

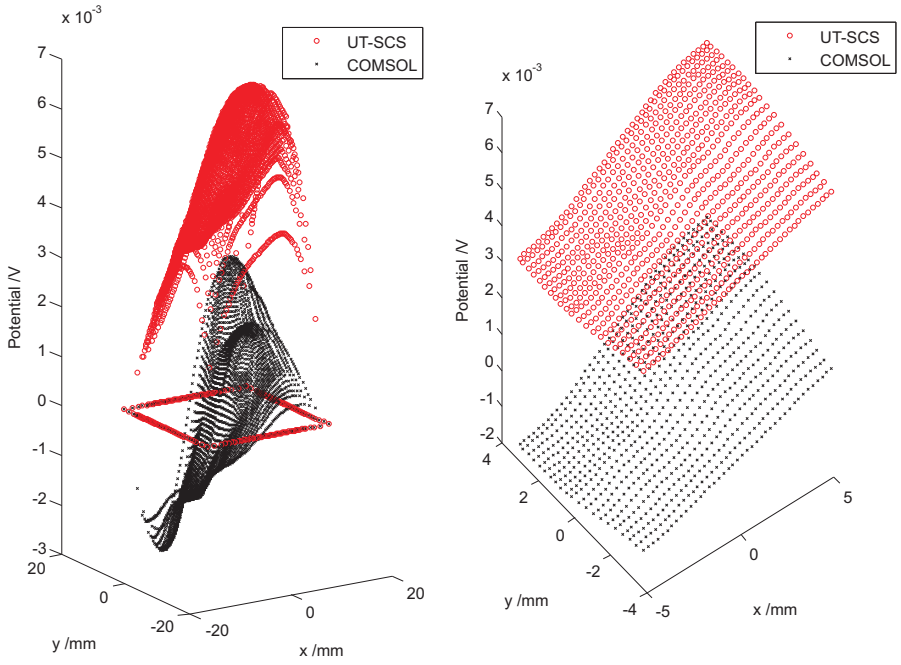

Figure 6: Transverse bipole (-1 mA/1 mA) on the dura: Potential distributions in the two models at z = -11.115 mm over the entire z-slice (left) and in the SC region (right).

In the case of a transverse bipole, the UT-SCS software gives a potential field distribution that is clearly asymmetric. Considering the symmetry of the contact configuration, one would expect the potential field distribution to be also symmetric. More precisely, a variation from negative values on the right side of the model to positive values on the left should be obtained in such contact configuration (cathode on the right and anode on the left), being zero in the dorso-ventral midline. This result is observed in the plot concerning the COMSOL model, whereas the UT-SCS result consists mostly of positive values of the electric potential. Thus, COMSOL gives clearly more robust results than the UT-SCS software.

3.1.2 Fiber activation parameters

Since in McNeal's model it is only the second derivative of the potentials that plays a role in fiber activation, the innacuracies of the electrical potentials in the UT-SCS model were not further investigated. The fiber parameters were thus computed and compared in both SCS models. This was done for the two contact configurations E and F, although only the main results for Model E will be presented here (Figure 7), since the observations were similar for Model F.

The DC fiber activation thresholds seem to be in agreement. In fact, the difference between the two values is in most cases less than 5%.

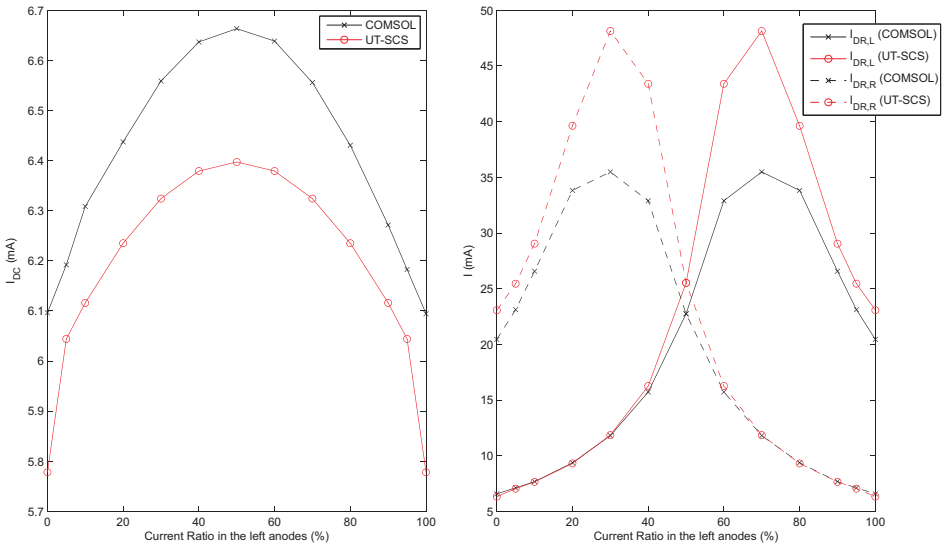

Figure 7: DC (left) and DR thresholds for Model E at all steering ratios. I_{DR} is the minimum between the thresholds of a left and a right fiber system

Considering the left DR fiber, the differences are most prominent at the ratios 40|60, 30|70 and 20|80. A possible explanation for the dissimilarities of the DR thresholds in the two models might lie in the shape of the dura mater of the UT-SCS, particularly in the way the lateral contacts are attached to it.

The slightly different placement of the contacts in the two models (Figure 5) necessarily creates differences in the current distributions. The fact that the thresholds are significantly different only at a very particular range of current ratios indicates that the sensitivity of the fiber to the current density distributions varies with the steering ratio.

In fact, at the ratios ranging from 100|0 until 50|50, the current density distribution is shifted more to the right side of the SC. Therefore, the left fiber does not "notice" the differences which most certainly exist between the current distributions in the two models. When the current ratio approaches 40|60, and until the ratio of 20|80, i.e., when the current is distributed more towards the left side of the SC, those differences seem to have an effect on the fiber activation. The difference in the position of the first activated nodes in the two SCS models supports this observation, since it is precisely at these steering ratios that the z-coordinates of the nodes differ the most.

The increased proximity of the thresholds in the last steering ratios can be explained by the fact that the fiber gets activated at a region far from the dorsal border (at approximately z = -5 mm in both models). Thus, and similarly to what has been explained for the rightmost steering ratios, the fiber is not influenced by small differences in the current density distributions.

After the observation of these differences, a test was performed in the UT-SCS model. The dura mater was extended such that the contacts could be placed the way they were modeled in COMSOL. It was observed that the resulting DR thresholds decreased significantly (over 20%) and became closer to those that had been determined in the new SCS model.

The area of DC fibers recruited at I_{DT} were also calculated. The results were in good agreement. The slight differences that were found were possibly due to the already mentioned disparities in the geometries. Another explanation lies in the fact that, since the values of I_{DR} are not the same, the I_{DT} are different as well. Consequently, the recruited areas should also differ.

3.2 Comparison between configurations E and F

The paresthesia threshold, the discomfort threshold and the therapeutic range obtained with the two contact configurations in the new SCS model are compared in Figure 8. The maximum recruited DC areas are shown in Figure 9.

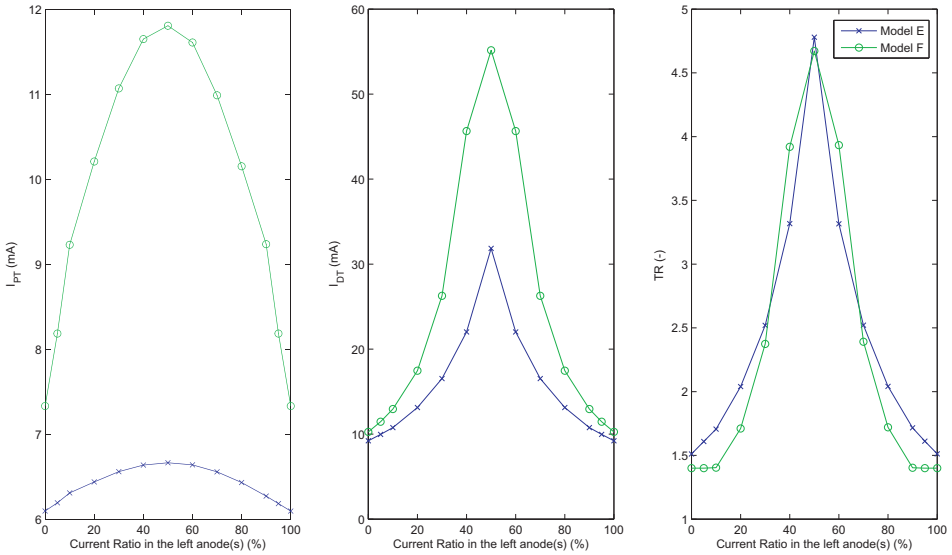

Figure 8: Paresthesia and Discomfort thresholds and TR for Models E and F at all steering ratios.

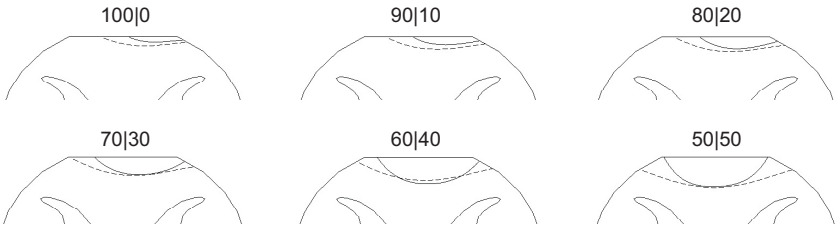

Figure 9: Maximum recruited DC areas for Models E and F, at several steering ratios. Dashed line: Model E; Full line: Model F.

Model E shows significantly lower I_{PT} and I_{DT} values. The first result can be explained by the presence of a longitudinal component of the current density axis, which is not there in Model F (the contacts are at a totally transverse position). This component is essential to activate the longitudinal DC fibers, which are, at most current ratios, responsible for the paresthesia threshold. The I_{DT} is higher in Model F, meaning that the DR fibers are being more effectively shielded. This is because the anodal current is not being divided over two contacts (this is the case in Model E). Thus, each lateral anode receives a higher current than in Model E, thereby shielding the DR fibers better.

Considering the other results presented above, several clinical outcomes can be predicted by this modeling study. Model E presents (in general) a larger TR. Therefore, it seems to be a better candidate for a clinically applicable contact configuration. Moreover, it is shown in Figure 9 that Model E is capable of activating a larger area of DC fibers. Thus, and knowing the somatotopic organization of DC fibers

(Figure 1), it can be predicted that the area covered by paresthesia will be more extense when a Model E configuration is used. Remarkably, this can be achieved using a lower current amplitude.

Furthermore, not only is the maximum recruited area larger in Model E at all steering ratios, but also it is more lateral. In contrast, Model F activates mostly medial fibers, thereby reaching only more caudal dermatomes. This reinforces the idea that Model E enables a broader coverage of dermatomes with paresthesia.

Additionally, at all steering ratios with the exception of 60|40 and 40|60, the maximum area of DC activation is deeper in Model E. This means that a larger number of fibers per dermatome will be activated. The paresthesia felt by the patient will thus be more intense when such configuration is used.

Evidently, a Model F configuration might be preferable over Model E in the case that the particular condition of a patient requires stimulating only medial fibers, i.e., when paresthesia is to be elicited only at more sacral dermatomes. This configuration is, nevertheless, highly energy consuming, meaning that other alternatives should probably be considered.

4 General Remarks

This work consisted of creating a new SCS model in a COMSOL/MATLAB environment. In order to validate the new model, the results given by the simulations performed on it were compared with those given by the UT-SCS software.

The main conclusion that can be drawn from the first part of this work is that the new model has successfully been validated with the UT-SCS software. Moreover, it has been shown that the numerical algorithms used by COMSOL yield more consistent results than those utilized in the UT-SCS software. This new SCS model seems to be, thus, a proper starting point for the development of a more sophisticated, flexible and accurate SCS software.

A further analysis was then performed in the new SCS model using two different triple-lead configurations. Model E, which consisted of two anodes on each side of a central cathode, yielded overall better results (larger recruited areas at the cost of a much lower current amplitude) than Model F, which used only one anode on each lateral lead.

5 Future Work

Having in mind the long-term goal of creating a new SCS model capable of improving and overcoming the limitations of the UT-SCS software, the most evident suggestions for future work consist of further developing the model described here.

In particular, the interface between COMSOL and MATLAB can be more deeply explored. For instance, it would be useful if some parameters of the FE model, such as the position of the contacts and the current boundary conditions, could be set in MATLAB, without the need of redefining previously built configurations in the COMSOL GUI.

Additionally, the approximations that have so far been made in the UT-SCS software no longer need to be assumed in new modeling studies. The dura mater, which is currently being modeled as a dorsal layer, can be extended to its real shape (completely surrounding the CSF). Moreover, the percutaneous leads can be modeled as full-length cylinders rather than disjunct parallelepipeds.

A more extensive study on the mesh parameters should also be done. In particular, finer meshes should be considered as long as the computational power required for solving the problem does not become compromised.

Another important issue that has been raised in this work is the high sensitivity of the UT-SCS results (particularly the DR thresholds) to minor changes in the model geometry. A more flexible software will enable further and more thorough sensitivity studies regarding geometric parameters of the SCS model. Such analyses can be of high relevance, especially when considering the large anatomical variability of the SC within human subjects.

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