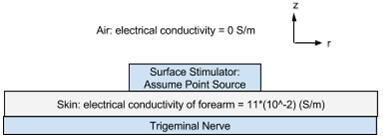
Computational Modelling

To test the feasibility of the NeuroSigma’s Monarch eTNS System, computational modelling was used to determine if surface stimulation on the face could stimulate sensory fibers of the trigeminal nerve using the parameters employed by the NeuroSigma device (120 Hz, 250 μs, asymmetric biphasic square pulse ranging from 0-100 mA) [4].

The system see below in *Figure 1,* was modeled using NEURON and consisted of a current point source on the surface of the skin, a layer of skin of a given depth, and a trigeminal nerve sensory fiber of a given fiber diameter at a distance of 1.03mm[3].



*Figure 1. Simplified Model of TNS Surface Stimulation*

The parameters used in the system were at default set as the axon parameter values used in Homework 2. The rest were found from literatureand are as follows:

|  |  |
| --- | --- |
| Parameter | Value |
| Conductivity[1] |  |
| Fiber Diameters[2] | Average: 14.5 um  A-Beta (12-14um) and C fibers (~1um) |

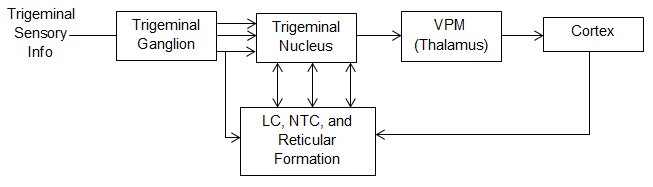
The threshold stimulus currents required to evoke action potentials in fiber diameters of 14.5um and 0.5um was found to be -0.05625 mA and -0.4207 mA respectively. Therefore, given the calculated threshold currents, it is feasible that the NeuroSigma surface stimulation could stimulate both the small C-fibers and larger A-Beta fibers of the trigeminal nerve. However, it is important to note that this model is grossly simplified and makes several assumptions. The next step is to incorporate more biophysically accurate features into the simplified model and then re-run the simulation to see how the threshold currents change. The most significant change would be to model the electric potential field of a disk electrode as opposed to a point source.

Trigeminal Nerve Pathway

To determine if the proposed mechanism of action for TNS is in fact feasible, the pathways and connections made by the Trigeminal Nerve were studied, in order to elucidate the possible effects of TNS in the various brain regions to which it projects.

A diagram of the Trigeminal Nerve connections is shown below, but will be explained briefly here. The terminal ends of the nerve fiber converge at the level of the Trigeminal Ganglion [10]. These neurons project into several segments of the Spinal Nucleus V within the Pons [7]. The Spinal Nucleus V contains reciprocal projections to the NTS, LC, and reticular formation [5]. The cell bodies within these spinal nuclei then project axons upwards, ascending the spinothalamic tract, and ultimately relay to the VPM of the thalamus, where they will project to regions of the cerebral cortex, most prominently the somatosensory cortex [6] [8].

In summary, the Trigeminal Nerve projects to many diffuse regions within the central nervous system, which, in a manner similar to VNS, may inhibit epileptic foci by causing transient increases in firing rate. This keeps the neurons from achieving synchronous activity.



*Figure 2. Simplified Model of Trigeminal Nerve Projections*

Works Cited

**Computational Model**

[1] Sunaga, Takahiro et al. “Measurement of the Electrical Properties of Human Skin and the Variation among Subjects with Certain Skin Conditions.” *Physics in Medicine and Biology* 47.1 (2002): N11. Web. 6 Nov. 2014.

[2] Pennisi, E. et al. “Histometric Study of Myelinated Fibers in the Human Trigeminal Nerve.” *Journal of the Neurological Sciences* 105.1 (1991): 22–28. Web. 5 Nov. 2014.

[3] Ha, Richard Y. et al. “Analysis of Facial Skin Thickness: Defining the Relative Thickness Index. [Miscellaneous Article].” *Plastic & Reconstructive Surgery May 2005* 115.6 (2005): 1769–1773. Web. 5 Nov. 2014.

[4] DeGiorgio, Christopher M. et al. “Pilot Study of Trigeminal Nerve Stimulation (TNS) for Epilepsy: A Proof-of-Concept Trial.”*Epilepsia* 47.7 (2006): 1213–1215. Web. 6 Nov. 2014.

**Trigeminal Nerve Pathway**

[5] DeGiorgio, Christopher M., Erika E. Fanselow, Lara M. Schrader, and Ian A. Cook. “Trigeminal Nerve Stimulation: Seminal Animal and Human Studies for Epilepsy and Depression.” *Neurosurgery Clinics of North America*, Epilepsy Surgery: The Emerging Field of Neuromodulation, 22, no. 4 (October 2011): 449–56. doi:10.1016/j.nec.2011.07.001.

[6] King, Michael S. “Anatomy of the Rostral Nucleus of the Solitary Tract.” In *The Role of the Nucleus of the Solitary Tract in Gustatory Processing*, edited by Robert M. Bradley. Frontiers in Neuroscience. Boca Raton (FL): CRC Press, 2007. <http://www.ncbi.nlm.nih.gov/books/NBK2541/>.

[7] "Medical Neurosciences." Medical Neurosciences. UW Madison, n.d. Web. 06 Nov. 2014.

<http://www.neuroanatomy.wisc.edu/virtualbrain/BrainStem/03CNV.html>.

[8] Patestas, Maria A., and Leslie P. Gartner. "Cranial Nerves." *A Textbook of Neuroanatomy* (2005): 992. *A Textbook of Neuroanatomy*. Blackwell Publishing. Web. 4 Nov. 2014. <http://www.blackwellpublishing.com/patestas/chapters/15.pdf>.

[9] “The Trigeminal Nerve (CN V) - TeachMeAnatomy.” Accessed November 6, 2014. http://teachmeanatomy.info/head/cranial-nerves/trigeminal-nerve/.

[10] “Trigeminal Nerve Anatomy,” June 19, 2013. http://emedicine.medscape.com/article/1873373-overview.