Key Lessons From Multi-Scale Modeling Of Body, Tissue, Cell, And Sub-Cellular Structures

K. Carlson[1], J. Arle[1], T. Dreeben[2], N. Paudel[3], S. Dokos[4], J. A. Tuszynski[5], E. Federov[6], Z. Bomzon[6]

[1]Harvard Medical School/Beth Israel Deaconess Medical Center, Boston, MA, USA
[2]Osram Opto Semiconductors, Exeter, NH, USA
[3]IEEE, Greenville, NC, USA
[4]University of New South Wales, Sydney, NSW, Australia
[5]University of Alberta, Edmonton, AB, Canada
[6]Novocure Ltd., Haifa, Israel

Abstract

Modeling the effects of electromagnetic fields on biological structures on the order of the body and tissues to the micro (1e-6)-and nano (1e-9) level of cells and sub-cellular structures presents formidable challenges. We share the major lessons we have learned using COMSOL Multiphysics® AC/DC module in these models.

Lesson One. The finite element physical and time scales must approximate the smallest physical component, or the shortest time constant, or the physical or time component that is most sensitive to scaling. Examples: a microtubule dimer (8e-9 m), the opening or closing of an ion channel gate (1e-6 s), the edge of an electrode (100 nodes distributed on the 1e-3 m edge).

Lesson Two. Interweave analytic and finite element modeling approaches. Simplistically, when it is cheaper (faster and easier) to take an analytic approach, do so, when it is cheaper to take a FEM approach, do so, but there are additional considerations. Always intermix analytic approaches into your FEM.

Lesson Three. Like Freddie Hansen, build many small, specialized models and few large, complex models. Small, specialized models are built and validated in hours or days and are designed to answer a specific circumscribed question. Large, complicated models take months or years to build, can be difficult to validate and understand, and should only be built when the coupled interaction of their parts must be studied.

As the mathematician John von Neumann said decades before biology adopted a systems approach, a result in a small-scale model can be used as a black box axiom in a larger-scale model.

Lesson Four. To attack the microcosm or to bridge multiple scales, use dimensionless modeling, which is a powerful tool that can circumvent the vexing problems run into when modeling the microscosm.

Figures used in the abstract

Figure 1 : Using 0.1 ms sampling rate to validate a charge-balanced rectangular waveform emitted by an electrode array on the human spinal cord to treat neuropathic pain.

Figure 2 : Using 0.001 ms to examine nerve fiber membrane potential building over 5 wave periods until an action potential is generated.