COMPUTATIONS IN BIOLOGICAL SYSTEMS

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Purpose

The purpose of this synopsis is to summarize the methods used to calculate electric fields and current densities induced by exposure to Extreme-Low-Frequency (ELF) electric and magnetic fields. The application of these methods to issues of biological dosimetry have been discussed in NIEHS Science Review Symposiums on *In Vitro* Research Findings (March 1997) and Clinical and *In Vivo* Research Findings (April 1998).

Field-induction Effects

It is well known that alternating electric (E) and magnetic fields (B) outside the body are capable of inducing electric fields within the body. While this induced E-field is the exposure metric most closely related to tissue stimulation, the density of current flowing in tissues (J) expressed in mA/m^2 is also sometimes used. This parameter is proportional to the induced E-field by Ohm's Law, $J = \sigma E$, where σ is the tissue conductivity.

A variety of biological responses ranging from weak sensory effects to cardiac fibrillation has been observed at induced current densities greater than 10 mA/m^2, with the severity of the effects directly related to the magnitude of the field. Of all the mechanisms proposed to "explain" biological responses to electric and magnetic fields, only field-induction mechanisms are supported by a coherent body of theoretical and biological evidence.

Need to Compute Induced Fields and Currents

Mathematical models to estimate currents and electric fields induced in the body have been used to characterize work environments and exposures of animals in laboratory studies. In addition, guidelines designed to prevent potential adverse effects of induced fields in the work environment have used simple dosimetric models to derive acceptable short-term and workday field-exposure limits (Bailey et al., 1997).

Computational Methods

The early bioelectromagnetic computational methods represented the body by a variety of simple objects such as cylinders, conducting loops or spheres, and ellipsoids (Hart, 1988). In most cases the conductivities of these models were assumed to be homogeneous. Solutions to these models were obtained by simple analytical methods for average and maximum E and J. The accuracy of these simple models to predict effects of environmental electric field exposures on internal electric fields and current densities has been extensively studied in animals and humans, e.g., Kaune and Phillips, 1980; Kaune and Forsythe, 1985.

More recently, the development of efficient computational algorithms and high-speed computers has led to the application of numerical methods to solve Maxwell's equations for the body in terms of individual cubes or voxels that are electrically distinct, with assigned conductivities. The advantages of these methods lie in the ability to model the complex shape and anatomy of the body, account for regional variations in conductivity, and estimate electric field or current densities in small cubes of tissue (Paulson, 1997).

A variety of numerical computation methods is used in bioelectromagnetics computing. The numerical methods most commonly used to compute induced E and J at ELF frequencies are as follows:

- the Finite-Difference-Time-Domain (FDTD) method,
- the Scalar-Potential-Finite-Difference (SPFD) method,
- the three-dimensional Impedance Method (IM), and
- the Finite-Element Method (FEM).

While the computational strategies of the methods differ, the results, as will be discussed below, are similar. The choice of the method depends upon the simulated field exposure, the size and shape of the object to be modeled, the resolution as reflected by the size of modeling element (voxel), computational efficiency, and memory requirements. Recently, a hybrid of the finite difference methods (FDTD/SPFD) has been employed for computing solutions to E-field exposures. This method first uses the FDTD method to develop a low-resolution solution to the computation of interior and surface potentials; then, the SPFD method is used to compute a more refined solution for interior potentials, using smaller-sized voxels (De Moerloose et al., 1997). As employed in the modeling of the body the resolution of these methods is between 1 mm and 1.31 cm. At the cellular level, the Finite-Element-Method has also been used for computations of E at a higher 1-µm resolution.

Validation of Methods

The accuracy of the computational models has been tested in several ways. The first compares the results of the numerical method with those obtained by analytical solutions for simple models (Gandhi and Chen, 1992; Dawson et al., 1996; Furse and Chen, 1998) and simple models with heterogeneous conductivities (Dawson, 1998; Dawson and Stuchly, 1996; De Moerloose et al., 1997; Dawson et al., 1997a; 1998). The second way compares solutions for simple models obtained by two different methods (Dawson et al., 1996). The third method compares the results of numerical methods to values measured in saline-filled models and animals (Gandhi and Chen, 1992; Xi et al., 1994; Dawson et al., 1998). In these validation tests, the numerical methods are reported to be quite accurate. The overall error of the methods used in one laboratory is estimated to be 3% (average values); < 20% (maximum values) (Stuchly, 1998). The agreement between laboratories for computations of human models exposed to uniform fields also appears to be good.

The accuracy estimates above, however, pertain to the computational method, not the data that are put into computations. In particular, these estimates do not reflect the effect of biological

factors that are not included in the model (model uncertainty) such as membranes, nerves, gap junctions, and so on. Two factors—shape complexity and uncertainty in conductivity values assigned to voxels—degrade the potential accuracy when more realistic, anatomically correct representations of the human body are modeled.

The difficulty in representing complex anatomical shapes can partially be overcome by representing tissues by very small voxels. However, the computational and memory requirements define practical limits on the size of the voxel for large tissue volumes.

The second factor refers to uncertainties in the conductivity values assigned to each voxel. The conductivity of each voxel must be assigned by reference to an anatomical atlas or magnetic resonance imaging (MRI) scan. This is difficult to do accurately at the borders of tissues and tissues with small volumes. Moreover, the experimentally determined values of σ that one assigns to the voxels for some tissues are subject to considerable uncertainty and error. The effect of assigning different published values of σ to a few tissues was demonstrated by Dawson and Stuchly (1998a).

Three laboratories have been active in using the numerical methods listed above to obtain values for induced E and J in anatomically correct representations of humans or animals. Table 1 shows, for each study, the numerical method that was used, the object modeled, the resolution of the model (voxel size), the field exposure, and comments on the purpose of the study.

Table 1: Numerical Modeling of Induced Electric Field and Current Density in Whole and Partial Body Anatomical Models

Investigator	Method	Object	Voxel Size	Field	Purpose
Gandhi & Chen, 1992	FDTD IM scaled to 10 MHZ	body	1.31 cm	E, B	spatial distribution in body cross-sections; grounded vs. ungrounded
Stuchly & Xi, 1994	IM	cells	120 µm	B	gap junction effects
Xi et al., 1994	IM	rat, mouse body	1.5 mm 1.0 mm 1.31 cm	B	species comparisons; field orientation
Baraton & Hutzler, 1995	FEM	body	varies	B	workers near power lines
Cheng et al., 1995	IM	head	0.5 cm	E+B	appliance exposures (hair dryers, shavers)
Stuchly & Zhao, 1996	IM	head body	0.665 cm 1.3 cm	B	workers near power lines
De Moerloose et al., 1997	FDTD quasi-static	body	7.2 mm	E, B	vertical currents through body

Investigator	Method	Object	Voxel Size	Field	Purpose
Fear & Stuchly, 1998	FEM	cells	1µm	E	gap junctions effects; dispersed & clustered cells
Dawson et al., 1997b	SPFD FDTD/SPFD	body	3.6 mm	E, B	comparison of E & B fields
Dawson et al., 1997a	SPFD	body	3.6 mm 7.2 mm	B	tissue variations; voxel size
Dawson et al., 1998	FDTD/SPFD	body	3.6 mm 7.2 mm	E	comparisons between "free space," grounded, and "wearing shoes"
Dawson and Stuchly, 1998a	SPFD	body	3.6 mm	B	effect of field orientation, assumed conductivity
Dawson & Stuchly, 1998b	SPFD	body	3.6 mm	B	anisotropic effects
Note: abbreviations identified in text.					

The table shows that various numerical methods have been used to model the whole human body exposed to uniform E- and B-fields. The effects of magnetic fields from point sources such as appliances have also been studied. Rats and mice have been modeled, but only for whole-body averages and current flow. Computing the induced E-field in animals by tissue type or anatomical location has not yet been reported (because of the effort and difficulty in assigning tissue and conductivity values to voxels in small animals). Two papers used numerical methods to model the electrical environment of cells under *in vitro* conditions.

Overall, most of the variables examined by these methods are shown to have effects consistent with theory and prior research. However, many scientists have been surprised that these methods reveal that there are a number of organs with high induced E-fields and current densities. For example, the data from one study shows that a 1-mT magnetic-field exposure would cause the average current density induced in 12 organs and fluids of the body to exceed the 10 mA/m^2 (Dawson and Stuchly, 1998a). This is the current density level recommended by all ELF guidelines as a internal exposure not to be exceeded in occupational or other environments (Bailey et al., 1997).

Implications for Risk Assessment

1. Numerical methods now allow effects of electric and magnetic fields to be estimated at the tissue level, rather than at the level of body organs. The methods also reflect more accurate values because anatomically correct shape values have been incorporated. These data could be used to revise estimates for maximum recommended electric- and magnetic-field exposures in occupational environments.

2. As yet, no rationale has been provided for using these methods to estimate risks from induced internal fields and currents at environmental and occupational field levels.

3. The descriptions of exposures in all laboratory experiments should be provided in sufficient detail that post-hoc calculations of induced fields can be performed.

4. Until more is known about the potential errors resulting from the inability of present models to reflect possibly relevant biological structures, e.g., tissue membranes, and the capability of the methods to predict biological responses, the interpretation of variations in predicted values within small organs or subtissues should be made with caution.

5. The use of numerical methods to calculate tissue specific induced E-fields in laboratory rats should be encouraged for standard exposure conditions.

6. Because no research has confirmed adverse effects of environmental ELF fields on critical target organs, the potential value of this method for risk assessment has yet to be determined. In certain occupational environments, however, this method could be expected to have a significant impact on research, including exposure assessment and dose-response activities that relate to acute hazards of tissue stimulation.

Remaining Questions

1. What further testing of the methods should be done to enhance our confidence in the predictions for small tissue volumes?

2. Are the data obtained by numerical methods to date sufficient to warrant a petition to guideline organizations to urge that these data be considered in updating occupational exposure recommendations?

3. What scenarios involving contact currents would be meaningful to model by numerical methods?

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