This project was initiated in September 2001 to investigate the availability of new cross section data, to upgrade the physics database used in Monte Carlo (MC) based charged particle track structure simulation models, and to test the sensitivity of these upgrades against measured electron transport spectra that have only recently become available. This was scheduled as a three year project, and received an additional year of no-cost extension.

Track structure simulation codes can provide a detailed event-by-event description of charged particle interactions with tissue that is needed to quantitatively assess the initial molecular-level damage caused by the absorption of ionizing radiation in a cellular environment. As modern techniques in molecular radiation biology yield more detailed information on the local yields and biological consequences of radiation induced clusters of damage, there is increasing concern that the physics used in the development of Monte Carlo charged particle track simulation codes might not be adequate to provide the quantitative information needed to enable mechanistic interpretation of biological effects at the molecular level.

Owing to the importance of mathematical modeling in this project we were exceeding pleased to obtain supplemental funding for this project in order to successfully recruit Dr. M. Dingfelder to the project and to the faculty of East Carolina University during the second year of this project. Dr. Dingfelder is an expert on Monte Carlo modeling and of the physics of charged particle interactions with matter. Following his university training in theoretical physics, Dr. Dingfelder has served on the staff of both the Institute for Radiation Protection, GSF, Germany, where PARTRAC was developed, and on the staff of the University of Barcelona, where he worked on the theory of inelastic electron scattering cross sections. In addition to maintaining strong associations with these institutions, he also maintains collaboration with a number of theorists active in radiation transport theory, such as Drs. James Turner and Rufus Ritchie retired ORNL, Mitio Inokuti, Retired ANL, and elsewhere, resulting in continued advances in our understanding of electron interactions in condensed phase material.
Throughout the four years during which this project received funding it helped support graduate training so that students might gain a better understanding of the fundamental processes of radiation transport in biologic tissue, and they in turn contributed greatly to our progress. Two doctoral students have been supported by this project; Craig Conticchio, working with Dr. Lapicki, made extensive progress in the calculation of differential cross sections for tissue constituents, and Irakli Jorjishvili has been studying the theory of ion and electron scattering under the direction of Dr. Dingfelder. Mr. Conticchio was also supported by DOE to attend the Nobel Scholars meeting in Germany in the summer of 2003. Both Naim Öztürk (now a medical physicist in Cooperstown, NY) and Jacob Gersh (currently a doctoral student in our Biomedical physics program at ECU) have worked on this project while studying for their Master’s degree in Medical Physics. Naim helped us get the PARTRAC code in operation and scoring routines written for use on the East Carolina University computer and Jacob has been investigating algorithms for the numerical description of radiation induced damage clusters and methods to incorporate target geometry into the event-by-event Monte Carlo energy transport analysis. In addition, Nick Evans has worked as an undergraduate student during summers with Dr. Shinpaugh in the evaluation and measurement of some important cross sections for Monte Carlo track simulation, completed research for his Master’s degree in Applied Physics; and is now a doctoral student at the University of Georgia; his research at ECU focused on measurement of ionization cross sections for intermediate-energy ions in atomic and molecular targets. These students have all contributed extensively to the goals of this project, and in the process have gained a greater appreciation for the questions involved in quantitative dosimetry and its application in modern radiation biology.

The common understanding that clusters of damage created in critical sub-cellular sites by the absorption of ionizing radiation are formed most efficiently at electron track ends has focused our attention to the ability of Monte Carlo track simulation to accurately describe low-energy electron transport. This focus is also justified because the cross sections used for low-energy electron interactions, energies below 500 eV, are derived from theoretical techniques more appropriate to high-energy electrons and prone to uncertainties when used for lower incident energies. As a metric for investigation of the ability of Monte Carlo simulation to reliably describe electron transport we chose to compare simulations with the measured spectra of electrons ejected from thin foils following proton impact. These spectra involve electron interactions in condensed phase and the comparison is a test of MC codes that does not require information on any chemical reactions.

Unfortunately, when this project began, there was no experimental information available for electron transport in water, and no cross sections were available for electron transport in anything other than carbon foils. Thus our first comparisons were between the Monte Carlo calculations based on transport in water and measurements for carbon foils. This comparison showed divergence between calculation and measurement below about 100 eV, with the discrepancy rapidly increasing as the electron energy decreased to 10 eV. Unfortunately most charged particle track simulation codes in current use, including the code PARTRAC developed at GSF-Neuherberg we were using, did not follow electron
transport below the ionization threshold in liquid water, about 10 eV. To focus on low-energy electron interactions where we anticipated the largest uncertainties we first needed to extend the Monte Carlo code, PARTRAC in this case, to describe electron transport to lower energy. This was done by incorporating data from Leon Sanche’s laboratory that were published in 2003 (Michaud et al., 2003). Incorporation of these data for inelastic cross sections for electron energies from 1 to 100 eV provided a new code capable of covering electron transport in water for the broad energy region from 1 eV to 10 keV. The results still diverged at low energy from the measured yields of electrons from carbon as well as from recent measurements for electron emission from amorphous solid water (water-ice) (Christou 2004). The largest discrepancies in spectral shape are in the electron energy range from a few eV to about 50 eV where the largest discrepancy was found to be as much as a factor of five. This was a major finding made possible by the recent data for electron transport in amorphous solid water of Christou (2004) and had lead to a re-evaluation of the cross sections for liquid water used in the PARTRAC code.

As noted, the discrepancy between calculated and measured electron yields raised questions as to the appropriateness of the elastic and inelastic cross sections being used to describe electron transport in water. First, can one expect amorphous solid water to be a reasonable substitute for liquid water? Generally it is expected that this is an appropriate test media. So we first looked at the available elastic scattering cross sections for the condensed phase. The elastic scattering cross sections of Michaud et al. were nearly a factor of 50 smaller than the model-potential scattering cross sections used in PARTRAC. Incorporating Michaud’s cross sections in PARTRAC, in place of the computed cross sections normally used, actually increased the discrepancy. This comparison suggests that the observed discrepancy between experiment and calculation must be with other cross sections, or with the comparison between the water calculations (PARTRAC) and ice measurements (although the low-energy data of Michaud et al. were also obtained for ice). We continue to search for better methods to calculate electron cross sections in the 10 to 500 eV range. For example, a recent paper (Fernández-Varea et al., 2005) explores new methods to derive liquid phase electron interaction cross sections. These new data have not yet been incorporated into PARTRAC to determine whether they will be better predictors of measured yields, although plans are underway to do so.

The comparison of calculated yields for electron transport in liquid water to experimental results in amorphous solid water is complicated somewhat by a measured decrease in the yield of very low-energy electrons as the thickness of ice is increased (Christou, 2004). The decrease in yield can be attributed to trapping of electrons by the polar nature of the ice, and/or by positive charge build-up as electrons are ejected from the surface of the insulating ice layer, thus producing a defocusing effect of the detection of the electrons. Using the PARTRAC code, extended to a low electron transport limit of 1 eV, we have explored the effect of electron trapping. By introducing a potential trap with variable potential energy depth and variable width we were able to show that indeed electrons would be removed from the spectra as the foil thickness increased if the trapping energy were a function of ice thickness. Unfortunately, to our knowledge a theory does not currently exist that will allow a clear estimate of the dependence of a trapping potential
on ice thickness. In addition, if a residual charge is produced on the ice surface as electron are emitted, a similar effect might be produced, and this latter effect seems more appropriate based on measurements of Christou (Christou 2004). This remains an open question that will require continued investigation.

Our studies involving comparison of MC computed emission spectra with measurements for electrons ejected following proton impact with thin layers of amorphous solid water frozen was a good means to explore effects of electron transport, but additional information is needed to better understand effects of changes in electron scattering cross sections on the probability of producing clusters in nanometer sized cellular volumes. To this end we have been developing algorithms to screen charged particle tracks for the frequency of clusters of different size and composition. Our first results clearly showed the added track complexity produced when vibrational excitation, as incorporated in the Michaud et al. data, was included in the PARTRAC code. These detailed simulations including molecular vibration have potential to aid in the estimation of DNA strand breaks that might accompany slow electron transport leading to dissociative-attachment to vibrationally excited targets, i.e., assessment of the probability of a slow electron being in the vicinity of a vibrationally excited DNA molecule. Currently the code only describes water, but with the inclusion of a database of other constituents being derived from this project, as well as work at GSF on DNA bases, one could simulate electron transport in water and its association with other important molecules of the cellular milieu.

One of our goals of this project was to extend the database of interaction cross sections to target materials beyond water. For example, if inelastic cross sections calculated for charged particle interactions in carbon were incorporated into the Monte Carlo code, comparisons of calculated electron spectra could be made to results measured for carbon foils where the build up of static charge from electron emission or from trapping of low-energy electrons are not expected, thus providing a more direct test of the electron transport portion of the Monte Carlo simulation. The theoretical technique employed for deriving these cross sections involves first finding analytic solutions describing differential ionization cross-sections (d\(\sigma/dE\)) for atomic targets within the first Born approximation. We have now developed analytic solutions for proton interactions with atoms having atomic numbers one to eighteen. These can be used as the basis set to describe interactions of ions and electrons with molecules and condensed phase material by incorporation of appropriate electronic bonding properties. We have recently tested these calculations by using additivity to produce molecular cross sections for molecular water and methane and have obtained excellent agreement with published measurements for proton impact. These calculations are currently being extended to electron impact.

Another area where we have made some progress within the last year of the grant has been the study of effects of target structure on the energy deposition process. Not only is the structure of the charged particle track important in the determination of local spatial patterns of energy deposition, but the structure of the target, interfaces between regions of different atomic constituents or densities, can also influence the local properties of energy deposition. One of our students (Gersh) has been investigating the variations is the
absorbed fraction of energy deposited at interfaces and in microscopic tissue volumes with dimensions derived from trabecular bone. We think this is an important of research to couple charged particle track structure with the unique structures in biologic tissue.

In summary, we have made considerable progress in accomplishing our program goals. The first goal was to evaluate the physical interaction cross sections used in Monte Carlo track simulation codes to reflect the differences in the components of the stopping medium. We have incorporated the measured cross sections for low-energy electron impact in ice and calculated cross sections for ion impact on elements from hydrogen to argon; similar cross sections for electron impact are underway. Finally, a goal was to test the sensitivity of codes to these changes in target parameters. We have made a number of tests of the code using different elastic and inelastic cross section for electron transport yields in amorphous solid water and will soon be able to test results for carbon. The PARTRAC code now includes updated cross sections for electron impact in water, will soon be available with other target constituents, and is available for further applications to better understand the production of damage clusters by protons and electrons. In addition, software has been developed to screen the Monte Carlo produced tracks for the production of clusters of different sizes, types, and frequencies providing tools to explore the relative spatial differences in cluster damage produced by protons and electrons over a wide range of energies.

Where does this work lead? The extension of the PARTRAC code to lower energies, and continuing efforts to improve the low-energy database (electron collisions for energies <500 eV) will provide a reliable tool for the quantitative assessment of damage cluster formation in critical cellular components. For example, one can explore whether specified cluster types might lead to miss-repair and subsequent genomic instability and assess the relative frequencies of subsets of cluster types. With the availability of the new cross sections for elemental constituents of tissue one could develop a track structure simulation code that can truly describe the cell morphology, not simply describe the track in water and overlay the cell/DNA structure as is currently done. We believe good progress has been made and that we are on the threshold of a new level of quantitative spatial dosimetry for use in the study of mechanistic radiobiology.

Publications and Presentations:

Publications:


Presentations with Published Abstracts


Papers presented, not listed in Published Abstracts above:


M. Dingfelder. Biophysical charged particle track structure simulations: Models and Basic Data. Invited talk (Colloquium) given at the Department of Physics, East Carolina University, February 11, 2005

M. Dingfelder. Simulation of DNA damage induced by ionizing radiation. Invited talk given at the Department of Biology, East Carolina University, February 17, 2005.


S. Segui, M. Dingfelder, and J.M. Fernández-Varea, Fully relativistic inelastic cross sections in the plane-wave Born approximation. Abstract accepted for poster presentation at the XXIV International Conference on Photonic, Electronic and Atomic Collisions (ICPEAC), to be held in Rosario, Argentina, July 20-26, 2005.


Literature Cited

