EM-WAVE CHARACTERIZATION OF TUMOR MORPHOLOGY

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Introduction

With the standard use of the Magnetic Resonance Imaging, the non-invasive visualization of human soft tissue became possible. The technology was so successful, that it has dominated the medical imaging field. Solutions for various geometries and configurations relevant to clinical settings have been computed [1]. Of interest to this contribution, is the use of MRI in cancer detection [2]. In recent years other methods have been proposed that are based on electromagnetic wave scattering, most notably in the microwave region [3],[4]. The majority of these methods rely on finite-difference methods to solve the differential equations for points in space. Other authors have been able to measure bacterial diameters using the Discrete Dipole Approximation [5] [6] but not an object as large and un-symmetric as a tumor.

In this paper we present results on the characterization of an irregular object. We show how to extract several parameters useful in creating a global description of the object.

A now standard algorithm for solving electromagnetic problems is based on work done by Purcell and Pennipacker [7] to explain absorption of light by interstellar matter. The object under study is made of dipoles, whose strengths depend on the total field at that site. Once the problem is solved, the total field is the sum of the source (distant astronomical object) field, and the fields form the elementary dipoles.

The standard formulation of Purcell and Pennypacker has some intrinsic limitations in its applicability to biomedical materials. Particularly, this numerical method was unable to reproduce analytical results for cases of large dielectric constants and resulted in undesirable oscillations near the boundary of the object under study. In modern implementations [8] the original assumption of a "compound'' object interacting with electromagnetic radiation is retained but the dipoles are replaced by a collection of small dielectric spheres. The internal and external fields for each one of the spheres are calculated from Mie scattering. Considering the interactions between each one of the spheres in the "compound'' object and using some of the considerations of the Effective Medium Theory the internal and external electric fields are calculated.

Method

To simulate the growth of a tumor, we implemented a stochastic model of tumor growth [9]. The model simulates the proliferation of cells based on the probability of reproduction or differentiation. Cell differentiation always leads to the death of the cell and the probability of extinction tends to one with the passing of time. The model correctly reproduces Gompertz law, a statement based on the empirical understanding of tumor dynamics. Pseudocode follows:
Define probability parameters a, b - Create an N*N*N cubic lattice - Place a cancerous cell in middle of the lattice - Loop for a given time frame - Loop for every cancerous cell - Define a parameter p based on the number of neighboring healthy cells - Generate a random number q<1 - If q >a then - Generate a random number q2 - Else If q2 < b - Kill neighbouring cell - End If - generate a random number q3 - If q3 >p Then - Turn neighboring cell into malignant cell - End If - End loop - End Loop.

More accurate models for the propagation of brain tumors have been proposed by Kansal and Torquato[10] but the current model is sufficient for the purposes of this paper.

We begin the simulation with a single cell placed in the center of the N^3 cubic lattice. The probabilities for each cell of dividing or differentiating are defined through the constant parameters a or b. These parameters, being probabilities, must be smaller than unity. However, it has been observed that not all possible combinations of parameters lead to a growing tumor and some may even lead to the tumor's death. To avoid this problem it was found (by trial and error) that values of a=0.49 and b=0.06 produce adequate results. The algorithm cycles through the lattice and for any cancerous cell determines whether that given cell will spread to its neighbors or will die off depending on the value of the randomly generated numbers. By repeating this process, we were able to simulate the continuous growth of the tumor.

Due to the complexity of its structure, the calculation of the scattered field off a tumor is intractable analytically. Fortunately, it has been shown [7] that it is possible to evaluate the field using

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computational techniques with arbitrary accuracy [8]. The program (DDSCAT) uses the Discrete Dipole Approximation in conjunction with various optimization techniques that allow it to maximize the accuracy and speed of the results. DDSCAT allows the computation of the scattered field for arbitrary geometries and the processing of the results using various algorithms. In this study, the results were calculated using the "Preconditioned BiConjugate Gradient with Stabilization" (PBCGST) solution method as well as the "GPFA Fast Fourier Transform". To determine the dipole polarizabilities the "Lattice Dispersion Relation" (LATTDR) [11] was used, with a scattering tumor, a highly irregular object due to its stochastic nature, whose shape was fed into DDSCAT, in the presence of a 3GHz plane wave. We further assumed that the scattering was to be done in a dielectric medium of healthy cells and hence requiring only 2 dielectric constants. Those were taken to be of 50 for both the dead and the malignant cells and of 9 for the healthy cells. We defined an effective radius as that of a sphere of volume equal to that of the scatterer: aeff = 0.62V**(1/3). The scatterer was assumed a cubic lattice of side length 16cm. The incident polarization state was set to $\hat{y}$ whereas the target rotation was limited to one. Thus, the scattering was evaluated for one orientation of the target rather than averaging over several orientations. Due to the stochastic nature of the tumor, this does not affect the results in any significant way. Finally, readings were taken at points in space specified by two angle parameters: T and F, where T was varied from 0 to 180 degrees in intervals of 30 degrees while F was varied from 0 to 90 degrees using the same intervals.

Geometrical characterization of the complex object

In order to characterize the tumor we define several parameters, which were continuously calculated as the tumor grew. First, the volume was computed as the sum of dead and cancerous cells. The center of mass of the tumor was also computed and so was the mass dipole. Finally, the eccentricity of the tumor was calculated for every frame. These parameters, taken together, allow to uniquely characterizing the irregular shape of the tumor via minimization techniques. Here, we only consider the volume, for demonstration, but the same technique can be extended to the other parameters as well.

Results

Since the intensities of the scattered field were calculated for every frame, we were able to superimpose that data on top of the parameters that we calculated for every frame. This allowed us to see how the intensity varied with respect to a given parameter- eccentricity, for instance.

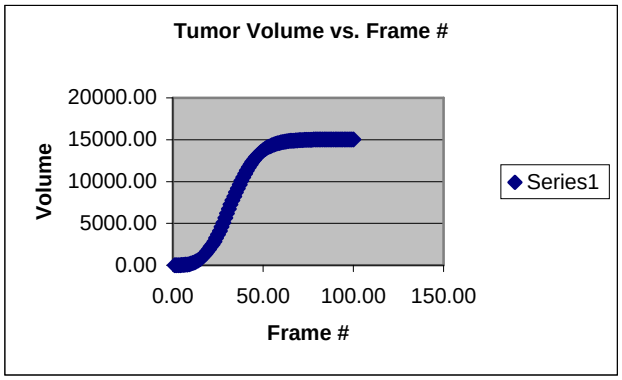


Fig. 1: Volume is defined as the number of dead and cancerous cells

To test the code, we show in figure 1, that the volume of the tumor obeys Gompertz' law and asymptotically approaches a constant value. Scattering information was obtained at several different points in space.

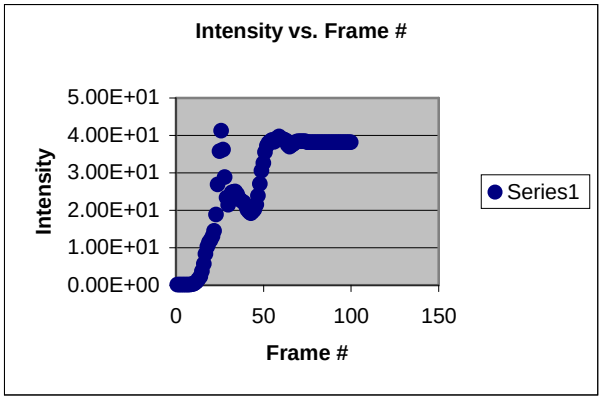
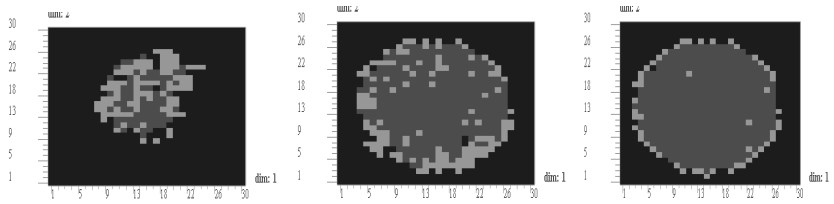


Fig. 2: T=0 ,F=0



t=20, Volume: 2756 t=40, Volume: 12960 t= 60, Volume: 14944

Fig. 3: Cross sections were generated for the given parameters a, b at the plane dividing the cubic lattice in half for several frames (denoted by t).

Shown in figure 2 is the variation of the intensity with respect to the frame number (the equivalent of the time). This information was then overlaid with the data obtained for the variation of the volume with respect to the frame number (fig. 3) to obtain the parametric plots shown below.

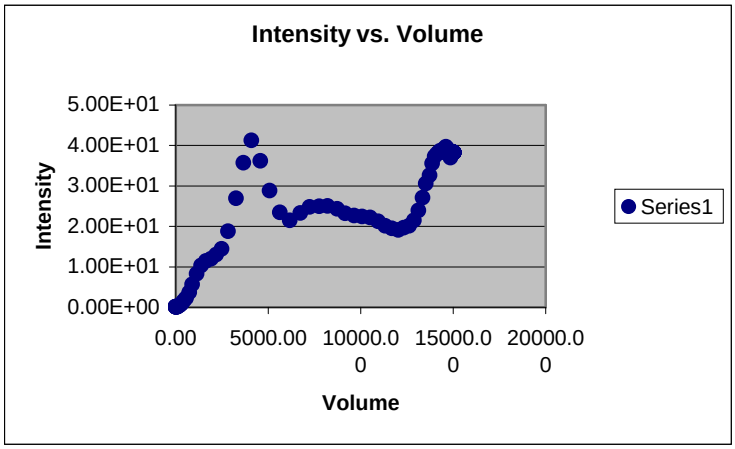


Fig. 4: T=0 ,F=0

For a given orientation, it is not possible to uniquely determine the volume of the tumor for all intensity regions. However, by considering the data from different positions of the detectors we can eliminate spurious solutions and obtain a unique volume.

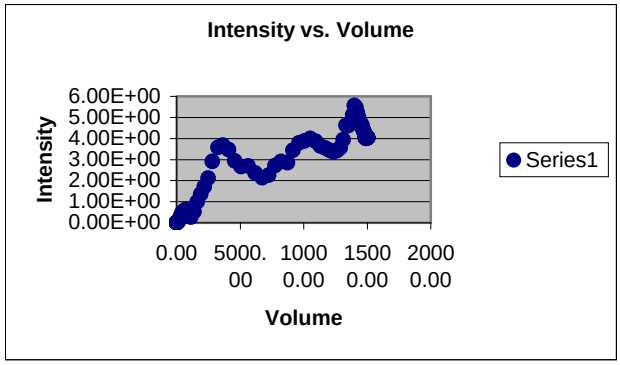


Fig. 5: T=120 ,F=90

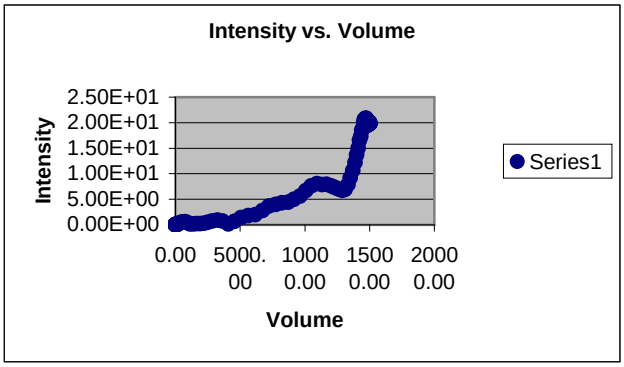


Fig. 6: T=180 ,F=90

Conclusion

This work presents the first application of the Dipole approximation to electromagnetic scattering, to characterize the irregular shape of a tumor. Our results show that by placing detectors at a variety of orientations around the scattering center, the problem can be inverted in the sense that size, eccentricity and orientation can be obtained from scattering cross sections.

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