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Study of thermal scattering for organic tissues through molecular dynamics

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Abstract. Boron Neutron Capture Therapy (BNCT) is an experimental therapy for tumors which is based on the nuclear reaction that occurs when ^{10}B is irradiated with thermal neutrons. Calculations for BNCT with Monte Carlo N-Particle (MCNP) take into account the thermal scattering treatment for hydrogen bound in bulk water for any organic tissue. However, in these tissues, hydrogen is also present in macromolecules (protein, lipids, etc.) and in confined water.

Thermal scattering cross section for hydrogen in an organic tissue can be determined by calculating the scattering law S(α,β). This function can be obtained with the nuclear data processing system NJOY from the vibrational frequency spectrum of an atom in a molecular system. We performed calculations of the frequency spectrum from molecular dynamics simulations using the program GROMACS. Systems composed of a peptide in a water box were considered, with different proportions of water molecules. All-atom potentials for modeling this molecules were used in order to represent the internal vibrational normal modes for the atoms of hydrogen. The results showed several internal normal modes that in the case of hydrogen bound in bulk water do not appear.

1. Introduction

Boron Neutron Capture Therapy (BNCT) is a treatment for tumors which are based on the nuclear reaction that occurs when ^{10}B is irradiated with thermal neutrons [1]. It has been applied to the tumors which have had a poor response to traditional therapies such as surgery, gamma radiotherapy and chemotherapy. Nowadays, feasibility studies and clinical trials are being carried out all over the world. In order to obtain appropriate outcomes, delivering high enough doses to the tumor and low enough doses to normal tissues is essential. BNCT is applied to a number of other tumors, using neutrons in wide energy ranges. In order to prepare the treatment plan, numerical dosimetry calculations must be performed.

The results in BNCT numerical dosimetry depend on the nuclear data used in the particle transport calculations. Concerning neutron transport, the parameter that describes the interaction between neutrons and nuclei is called neutron cross section and it is related to the probability that a neutron interacts with a nucleus. In particular, the scattering cross section (σ_s) is related to the reaction in which the neutron remains free after the collision [2]. At neutron energies below several electron-volts, thermal motion of atoms and chemical binding states alter the neutron scattering cross section. Under this condition, the scattering cross section is called thermal scattering cross section [3]. Thermal scattering libraries contain the information of the double differential thermal scattering cross section. This parameter for neutrons with incident energy E, secondary energy E' and scattering angle Ω on a material with bound scattering cross section σ_b and mass number A at temperature T can be written as:

$$\frac{d^2\sigma}{dEd\Omega} = S(\alpha, \beta)\frac{\sigma_b}{4\pi kT}\sqrt{\frac{E'}{E}} \tag{1}$$

where S(α,β), the scattering law, is a function of the dimensionless change in momentum α, and the dimensionless change in energy β:

$$\alpha = \frac{E' + E - 2\sqrt{E'E}\mu}{AkT} \quad \beta = \frac{E' - E}{kT} \tag{2}$$

where μ is the cosine of the angle between the paths of the incident and scattered neutrons. The default treatment for thermal neutron scattering in many transport codes is the "free gas treatment", which neglects the chemical binding between the target nuclei. Existing thermal libraries normally correspond to standard materials at some temperatures. In calculations for BNCT numerical dosimetry, hydrogen bounded in bulk water has been typically taken into account to describe thermal scattering. Nevertheless, tissues are composed of other substances that also contain hydrogen and even the water content cannot be considered in bulk state for a large fraction of its distributions in tissues. We have determined that the differences in thermal neutron flux calculations using libraries for hydrogen in polyethylene or hydrogen in water, in phantoms of adipose tissue, can reach values of 9%, depending on the type of source and irradiated geometry. These results, have showed the importance of

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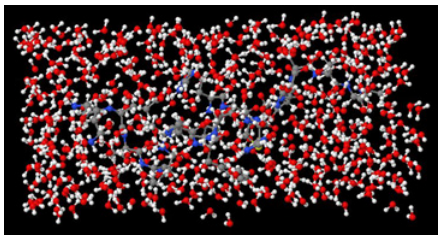

Figure 1. S-peptide molecule in a water box.

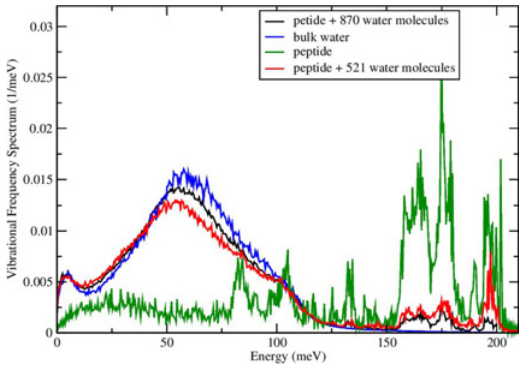

Figure 2. Vibrational spectrum for Hydrogen in a peptide and in a water box.

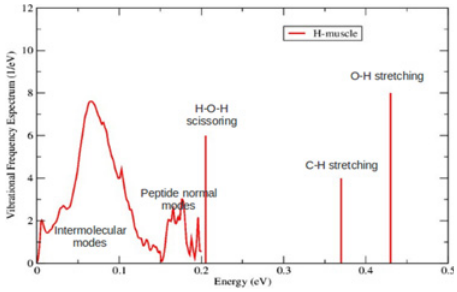

Figure 3. Simplified spectrum for hydrogen in hydrated S-peptide.

utilizing the appropriate thermal scattering treatment for each organic tissues in dosimetry calculations [4].

2. Methods

We performed calculations of the frequency spectrum through molecular dynamics using the program GROMACS [5]. This technique was selected because it allows to obtain the velocity autocorrelation function (VAC) and then, applying the Furier Transform, the frequency spectrum can be calculated. A system composed of a peptide in a water box was considered (see Fig. 1). We started the study with pepetides because proteins are compound by these molecules, and organic tissues are compound by macromolecules like proteins, lipids, ADN, etc.. All-atom potencials for modeling this molecules were used in order to represent the internal vibrational normal modes for the atoms of hydrogen.

Using the information of the normal modes present in a peptide, in bulk water and considering that a muscle tissue is compound by 79% of water, 17% of protein, 2.2% of lipids and 1.8% of other macromolecules [6], we calculated the vibrational spectrum for hydrogen

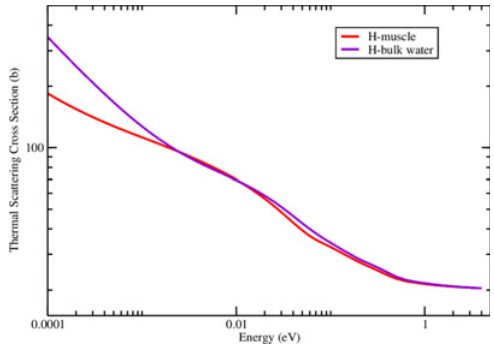

Figure 4. Total scattering cross section for hydrogen in hydrated S-peptide, per hydrogen atom, compared with the total cross section for hydrogen in bulk water.

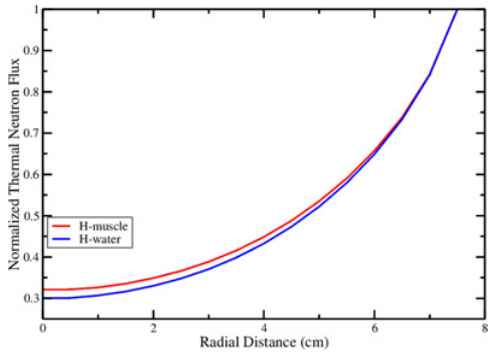

Figure 5. Thermal flux profile for a spherical phantom with a surface source.

in a muscle tissue. With this spectrum and the code NJOY [7], we calculated the thermal scattering libraries for hydrogen bounded in a muscle tissue. Finally we performed calculations of the thermal neutron flux profile with MCNP6 [8] in a spheric phantom with muscle tissue and a superficial neutron source. For these calculations we considered different libraries for hydrogen, in order to calculate how these molecular differences in the frequency spectra impact the thermal neutron flux, which is intimately related to BNCT neutron dosimetry.

3. Results

Figure 2 shows the results of the GROMACS simulations considering the following cases: S-peptide, S-peptide in a water box with 521 water molecules and S-peptide in a water box with 870 water molecules. In the case of the S-peptide Fig. 2 shows, in the region of 150–200 meV, vibrational modes related to the groups CH_2, CH_3 y NH_2 (represented by the resonance-like structure). In the cases of the S-peptide in the water box, the figure shows these normal modes, but, at lower energies, it shows the normal modes due to the bulk water.

Using this information, we calculated an approximate spectrum for hydrogen in a muscle tissue. Figure 3 show these results.

With the code NJOY we generated a library for hydrogen bounded in a muscle tissue. Figure 4 shows the total scattering cross section for hydrogen in muscle and for hydrogen in bulk water.

With MCNP we performed a calculation of the thermal neutron flux profile in a spheric phantom. Figure 5 shows

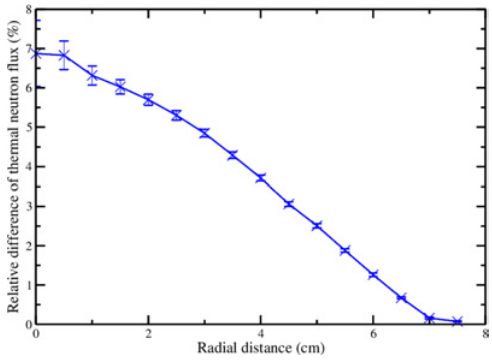

Figure 6. Relative percentage difference in the thermal flux for a spherical phantom, calculated with two different thermal scattering libraries: bulk water and muscle.

this results using different libraries: hydrogen in muscle and hydrogen in bulk water.

Finally, Fig. 6 shows the relative percentage difference between the calculations of the Fig. 5.

4. Conclusions

The results obtained with GROMACS showed that in the frequency spectrum for hydrogen bound in a protein there are several internal normal modes that in the case of hydrogen binding in bulk water do not appear. For example, the stretching between the hydrogen and carbon atoms is not considered in the case of hydrogen in bulk water. The results obtained with MCNP showed that the relative differences between the flux calculated with different libraries reached values up to 7% at very low energies. This study highlights the fact that a systematic non-negligible error might be involved when the appropriate tissue thermal treatment is not considered.

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