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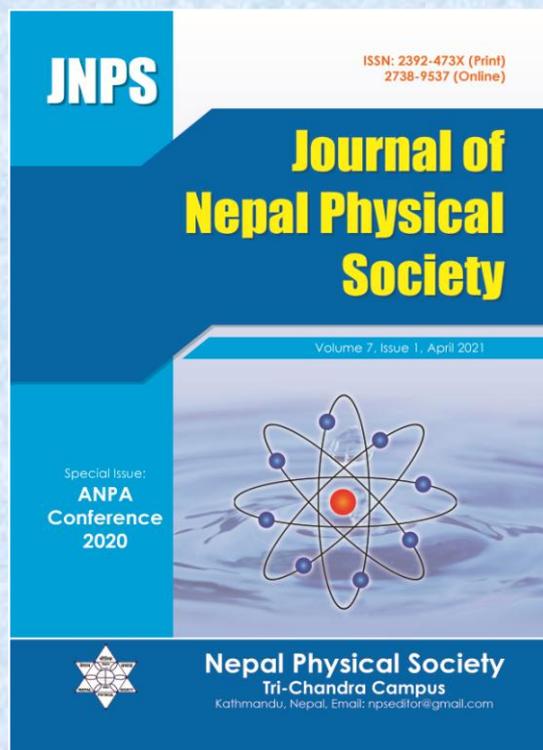
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A Review of Life Science Studies with Muons

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ABSTRACT

Positive muon is a spin half elementary particle lies in the second generation leptons in standard model of particles. It has been used as a sensitive magnetic (spin) probe for study of life and materials. Due to its special characteristics – 100% polarization and asymmetric decay to positron, it provides information about local electronic and spin states of material in which it stops. The asymmetry, relaxation of muon and its charge states in materials provide information about the interested phenomena. For life sciences study, muon can probe the dynamics of electron, proton, ions, H, O₂, reaction dynamics, catalytic processes, concentration of molecules, magnetic behaviors, etc. in the biosamples. Here, the applications of positive muon to understand the life related phenomena are reviewed.

Keywords: Muon spin rotation, Biomolecules, Life science.

1. INTRODUCTION

Materials and life phenomena have been studying with the application of positive muon available in accelerator facilities in the world. Among life and materials study, there are various studies in materials than life (biology) using the muon technique. After discovery of muon in 1936 by Anderson and Neddermann [1], the first muon spin rotation and relaxation experiment was reported by Garwin in 1957 [2]. The muonium (the bound state of muon and an electron, $\text{Mu} = \mu^+e^-$) was discovered in 1960 by Hughes [3]. Then after 2 decades, a muon experiment in dilute aqueous solution of DNA were reported [4]. Initially, reaction dynamics of chemical reaction were studied [5]. In 2000, Nagamine *et al.* [6] reported the electron transfer in cytochrome c protein in which the phenomena was explained based on electron labeled muon method [7] and the muon data were analyzed by Risch-Kehr function [8] initially developed for polyacetylene. In recent years, many trials to understand the electron transfer in proteins [9, 10] and DNA [11, 12], measurement of concentration of molecules in biosamples [13], real biosample from patient [14], etc. can be found in the literatures. Here, a brief review of life science studies with muons is presented.

2. WHY MUON?

Muon is a spin half elementary particle lies in the lepton family of second generation of standard model of particles. It is available in cosmic ray (naturally) and in accelerator facilities through the decay of pion. The mass of muon is about 207 times of electron mass and 1/9 times of proton mass. The gyromagnetic ratio of muon is around three times higher than that of proton which makes it more sensitive in materials. Two special characteristics of muon – spin polarized and asymmetric decay (due to violation of parity in weak interaction) (life time 2.2 μs) to positron make the muon as exotic tool. It works as sensitive magnetic (spin) probe in which it stops. Using muon spin rotation and relaxation (μSR) method, it provides the information the local electronic and spin states of materials.

Muon acts as spin polarized probe so it behaves as magnetic needle in materials. It can apply at any temperature and without perturbation of system. Its time window ($10^{-11} - 10^{-5}$ s) is wider than the other techniques (NMR, neutron and Mossbauer). Unlike electron and proton, when high energy muon incident into materials there are no braking radiation, pair production and nuclear reactions happened. It can approach to higher depth in the materials. It stops

interstitial sites near the high electron density. Its bound state with an electron known as muonium which is like a light isotope of hydrogen. It is an exotic atom made up of two lepton particles. The Mu can predict/mimic the behavior of H in the materials. For life sciences study, muon can probe the dynamics of spin, electron, proton, ions and H. It also probes the dynamics of reaction, catalytic processes, concentration of molecules, magnetic behaviors, etc. and phenomena based on these processes (like electron transfer in respiratory system, photosynthesis process, diagnosis of disease, clinical and medical areas).

3. MUON SPIN ROTATION AND RELAXATION (μ SR) METHOD

μ SR stands for muon spin rotation, relaxation, and

resonance. The intention of the mnemonic acronym is to draw attention to the analogy with NMR and ESR. When muons are incident on material, decayed positrons are collected by detectors (forward and backward) around the sample [Fig. 1]. Time evolution of those positrons provide the information about the material. Suppose, F is positron events collected by forward counter and B is that by backward counter, then asymmetry = $(F - \alpha B) / (F + \alpha B) = A_0 G(t)$, where α is alpha factor depends on efficiency of detectors and sample positions, A_0 is initial asymmetry, and $G(t)$ is polarization function. Based on our need, we can apply external magnetic field along (longitudinal field or zero field measurement) or perpendicular (transverse field measurement) to direction of momentum of incident beam [7, 15].

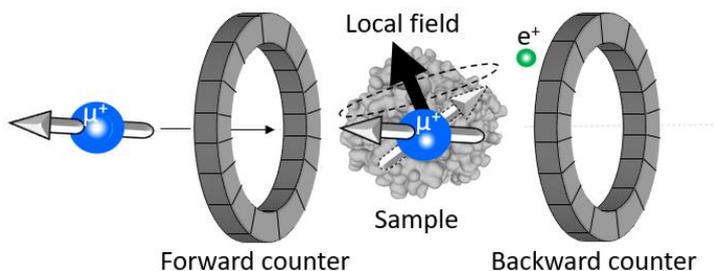


Fig. 1: Schematic diagram of μ SR set up. Initially, spin of incident muon is opposite to its momentum. In sample, it precesses according to Larmor's precession in the local/external field and finally decays to positron along the direction of muon at the time of decay.

4. μ SR IN BIOMOLECULES

4.1 Experiment

Initial studies were reported on the reaction of Mu (Chemical dynamics) of Mu in solutions [4, 5]. To my best knowledge, the first muon experiment in biosamples (dilute aqueous solution of DNA) was reported by Bucci *et al.* [4]. There are around 60%

diamagnetic muon, 20% Mu and remaining 20% as missing fraction estimated in water [16]. Among the 20% Mu, the half of them (ortho state of Mu) were observed as the long lived Mu rotational signal in water [17]. The fraction of charge states of muon in materials depends on the materials and environment [schematic in Fig. 2].

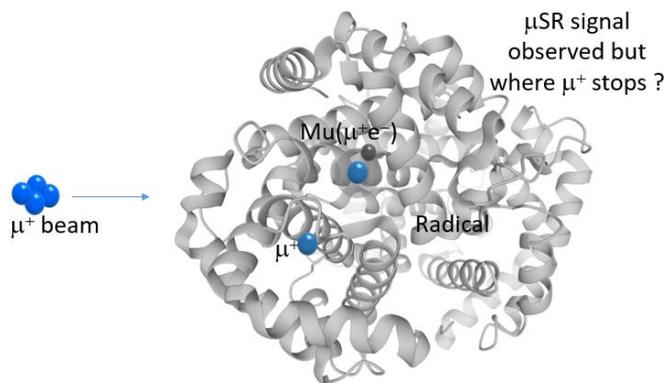


Fig. 2: Schematic diagram of muon in biomolecules. From μ SR signal, we can distinguish muon and muonium formation in the sample but the stopping sites of those charge states are not clearly understood yet.

The μ SR in dried horse spleen ferritin was reported by Cristofolini *et al.* [18] in which they mentioned the two muon fraction originated from organic shell and one from muons stopped in the mineral core. But it is hard to compare with hydrated real sample due to existence of water. Later, Telling [19] studied in ferritin and apoferritin and Bossoni *et al.* studied the biosample from Alzheimer patient [14]. In the study of spin dynamics of ferritin proteins isolated from the brain of an Alzheimer's disease patient, the authors mentioned that, in their preliminary study, the ferritins from the healthy control are filled with a mineral while ferritins from the patient contain a crystalline phase with a larger magnetocrystalline anisotropy, possibly compatible with magnetite or maghemite [14]. In fact, so far we do not know the stopping site of muon or Mu in such macromolecules.

Nagamine *et al.* established the electron labeled muon method to understand the muon in biological macromolecules [7]. The dimensionality of electron transfer in cytochrome c was explained based on Risch-Kehr (RK) parameter. Later, hydration dependent and temperature dependent studies were also explained by using the RK function. His team also reported the measurement of magnetism in hemoglobin (human blood) [20] and the further extension in aqueous solution of biosamples (hemoglobin, serum, albumin, TBS) were also reported [13]. It is found that the detection of concentration of oxygen molecule in biological aqueous solution indicates the future applications of muon as a noninvasive probe for detection and distribution of oxygen in cancerous/tumorous tissues to diagnosis the early-stage cancer. Torikai *et al.* [11] and Hubbard *et al.* [21] reported the electron transfer in DNA [11]. There are other trials on amino acids and peptide bonds to understand the stopping site of muon and electron transfer mechanism [22]. Kiyotani *et al.* [23] also reported some trials to understand the electron and proton transfer in enzyme reactions.

4.2 Theoretical study

The μ SR data of polyacetylene [24] was explained by RK stochastic theory [8]. Based on that, μ SR data in protein [6, 10] were explained but there is no theory to explain muon behavior in such complex bio-systems. The theoretical interpretation to understand the muon behavior in biomolecules is not established so far. The major challenge is stopping site of muon in the sample. In order to estimate the stopping site of muon and support the measurement, the theoretical study is quite

necessary. The first-principles calculations to estimate muon sites in the protein [25], DNA [26] and their constituents [27] were reported. Because of complexity of system and computational cost, the H-passivated or isolated system were used in the calculations but to interpret the real biosamples, one has to consider the computational model well. For the systematic study to know the stopping site of muon and establish the muon for life sciences, Pant *et al.* [28] initiated theoretical work assuming different possibilities by extending the main chain of amino acid as peptide bonds in real proteins. It is found that the significant effect of termination of main chain on muon stopping in the amino acids [29]. Quantum theory and first-principles calculations (or simulations) are necessary to interpret the muon behavior in biomolecules.

5. CONCLUSIONS AND FUTURE PROSPECTS

Due to complexity in geometry and dynamic system, the application of muon to life sciences is slow with respect its use in material science. Systematic experimental and theoretical studies (starting from peptide bond, amino acids, to big samples) are quite necessary to understand the life phenomena through the eye of muon and future applications towards clinical/medical fields.

Since there are no quantum mechanical theoretical interpretation of μ SR data in biological macromolecules, it is still challenging to have smooth progress in this field. The first-principles calculation of muon in real system will help to understand the stopping site of muon and muonium in the biosample. As a systematic study, we need to know the behavior in muon in water, buffer and individual constituents of the sample to understand the signal from macromolecules. It is challenging to separate the water and buffer signals from the observed muon signal from the biosamples. Furthermore, with the ongoing development of ultra-slow muon microscopy in Japan Proton Accelerator Complex (J-PARC), it is expected that even the intact small biosample will be studied but the preparation of experimental environmental for such study is another challenge.

EDITOR'S NOTE

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