Response of muonium to oxygen impurities in hemoglobin and other biological aqueous solutions for application to studies on hypoxia

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Hypoxia, or low oxygenation, is known as an important factor in tumor biology; in cancer patients, an accurate measurement of O_2 concentration in specific regions may prove important in the management of treatment and outcome of the disease[1)]. For this purpose, improved O_2 detection methods are required. Several trials that employ PET, MRI and EPR have been conducted[1)].

In this article, we propose the use of μ^+ as a new sensitive method to probe the existence of paramagnetic O_2 in cancerous tumors in the human body. The μ^+ in water is known to take the states of diamagnetic μ^+ such as μ^+OH (60%), paramagnetic muonium (Mu, $\mu^+ + e^-$) (20%), and a missing fraction (20%). In Mu, a half becomes an ortho state with spin 1, providing a spin rotation signal with a precession pattern (1.39 MHz/G) that is 100 times faster than that of diamagnetic μ^+. There have been experimental studies on the oxygen-dissolving effects of the spin relaxation rate (λ_{Mu}) of paramagnetic Mu in pure water due to electron spin exchange interactions with paramagnetic O_2 in water; the rate change of λ_{Mu} against O_2 concentration is $(1.8 \pm 0.1) \times 10^{10}$ (litr/mol) s^{-1}[2)]. The sensitivity for $PO_2(\mu)$ in pulsed μSR becomes $0.5 \times 10^{-6} \sim 0.5 \times 10^{-3}$ (mol/litr). The $PO_2(\mu)/PO_2$(s.l.) becomes $0.4 \times 10^{-3} \sim 0.4$, which perfectly corresponds to the condition in hypoxia. The unsolved problem regarding the muon method is the background effect of other magnetic molecules, which provides the motivation for the present study.

The experiment was conducted at Port 2 of RIKEN-RAL using 60 MeV/c decay positive muons. Spin rotation and its relaxation were detected under 2.2 G transverse fields and at room temperature. In pure water, the Mu spin precession was found to achieve faster relaxation against increase in O_2, and this result is consistent with the existing data[2)].

The biological samples are as follows. 1) **Albumin:** Bovin serum (plasma) albumin is a single polypeptide chain consisting of about 583 amino acid residues and no carbohydrates. 2) **Serum:** Donor horse serum is sterile filtered serum that has been screened for mycoplasma and adventitous viruses. 3) **Hemoglobin** (Hb): Polymerized hemoglobin of bovine origin in a lactated Ringer's solution at 13 % concentration. It is violet-colored taken and is as deoxy-Hb.

Before measuring the O_2 dependence of λ_{Mu}, its dependence on the concentration of each biological molecule was systematically measured. The decreasing rate of λ_{Mu} was obtained as 25 MHz/(g/litr) for albumin, 1 MHz/(vol. %) for serum and 3.1 MHz/(g/litr) for Hb

Then, by determining the relevant concentration for each molecule, the O_2 dependence of λ_{Mu} was measured. The results for these three aqueous solutions are summarized in Fig. 1. The λ_{Mu} in these biological aqueous solutions was found to experience an almost similar change in relaxation against increasing O_2 concentration as that for pure water. For Hb, λ_{Mu} was expected to exhbit a different behavior since the increase in O_2 makes decrease of magnetic Deoxy-Hb and increase of non-magnetic Oxy-Hb causing the decrease in λ_{Mu}. By solving Hill's equation[3)], such an effect can be predicted. The obtained result is very encouraging for application to hypoxia; there is one-to-one correspondence between λ_{Mu} and O_2 concentration, which allows the unique determination of PO_2

Before carrying out the clinical application of the proposed method to studies on hypoxia, it is important to conduct systematic studies on the behavior of O_2 impurities in various other biological aqueous systems, especially with high-concentration Hb. On the other hand, by using the concept of the advanced μ^+ beam, which is an accelerated beam of ultra-slow muon, one can expect the stopping region confinement to be 10 μm^3 at cm-region depth of the human body. Thus, we are approaching a realization of the advanced cancer inspection by using muons appears possible.

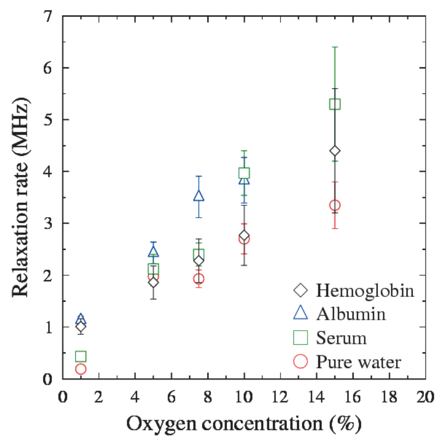

Fig. 1 Summary of dependence on O_2 concentration of muonium relaxation rates in pure water and water solution of 0.04 wt. % albumin, 0.5 vol. % serum and 0.07 wt. % hemoglobin.

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