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Positron Lifetime Spectroscopy of Silicon Nanocontainers for Cancer Theranostic Applications

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Abstract

Biocompatibility and biodegradability of porous silicon (por-Si) nanoparticles (NPs), as well as the fact that they can selectively accumulate in tumor tissues, allow using them as containers for delivery of diagnostic markers or drugs for therapy of cancer tumors. Advantages of por-Si NPs as carriers of drugs are also favorable due to the high surface area and large pore volume. To apply por-Si NPs as nanocontainers it is necessary to have the comprehensive information about their porosity. In our work we use the positron annihilation lifetime (PAL) spectroscopy for porosity investigation. Samples of por-Si were prepared by electrochemical etching of heavily boron doped crystalline Si wafers in a hydrofluoric acid solution. The prepared por-Si films were dried and mechanically milled to obtain powder of NPs, which was pressed into tablets for PAL investigation. Ortho-positronium components of the measured positron lifetime spectra allowed us to evaluate the pore size distribution in por-Si NPs as continuous bimodal one with two peaks near 1 nm and 3 nm.

Keywords: positron annihilation lifetime spectroscopy, positronium, porous silicon nanoparticles, nanocontainers, porosimetry, theranostics.

1. Introduction

In recent years, porous silicon (por-Si) nanoparticles (NPs) have been extensively studied for diagnostics and therapy of cancer tumors [1]. The great attention to por-Si NPs for applications in biomedicine is caused because of its important properties as (i) biocompatibility, i.e. an ability to be incorporated into the body without side effects, and (ii) biodegradability, i.e. an ability to be dissolved and to be excreted from the body. Advantages of por-Si NPs as carriers of drugs are also favorable due to the high surface area and large pore volume. Besides it is possible to control the parameters of the

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porous structure (porosity, pore diameter, surface area, hydrophobicity/hydrophilicity) in a wide range. Biocompatibility and biodegradability of por-Si NPs, as well as the fact that they can selectively accumulate in tumor tissues, allow using them as containers for delivery of diagnostic markers or therapeutic drugs to the tumor [1]. To use por- Si NPs as nanocontainers it is necessary to have the comprehensive information about their porosity. One of the most informative and accurate methods for studying pores structure in Si is positron porosimetry. This technique based on positron annihilation lifetime (PAL) spectroscopy is a highly suitable method for thorough investigation of nanopores and mesopores. The PAL spectroscopy is a non-destructive technique, which uses the positronium (electron–positron bound state) as a probe for porosity investigation [2]. The lifetime of positronium allows us to evaluate the pore size and the positronium yield can be used to monitor changes in pore concentration.

2. Positron annihilation lifetime spectroscopy

A study of pore structure by positrons is based on measurements of the positron lifetime spectrum. It is known that fast positrons emitted by isotope source are slowing down to thermal energies in a time less than 1 picosecond. Then they diffuse in the bulk and either annihilate in free collisions with the bulk electrons or localize at trapping centers as vacancies, vacancy complexes and pores. Positron lifetime is very sensitive to the electron density of the material. Open volume defects have a lower electron density than the bulk. The larger the defect size, the longer the positron can live in it. In addition, the presence of large pores leads to the formation of positronium (Ps), which is a bound state of electron and positron (Fig. 1). There are two possible Ps states depending on the relative spin orientation of electron and positron. The configuration with antiparallel spins, which is called para-positronium (p-Ps), decays preferentially into two gamma (γ) quanta with energy of 511 keV and mean lifetime τ_S = 0.125 ns. The configuration with parallel spins is known as ortho-positronium (o-Ps), which preferentially decays via 3 γ-quanta emission. Since the probability of 3γ-annihilation is much less than that for the 2γ-process the former lifetime is larger and it accounts τ_T = 142 ns.

In the bulk of material the ortho-positronium lifetime is shortened because of pick-off annihilation with bulk electrons. The annihilation rate in this case can be expressed as

$$\lambda_A = \frac{\lambda_S + 3\lambda_T}{4} \approx 2\ ns^{-1}, \tag{1}$$

where $\lambda_S = \frac{1}{\tau_S}$. $\lambda_T = \frac{1}{\tau_T}$ - annihilation rates of p-Ps and o-Ps, respectively.

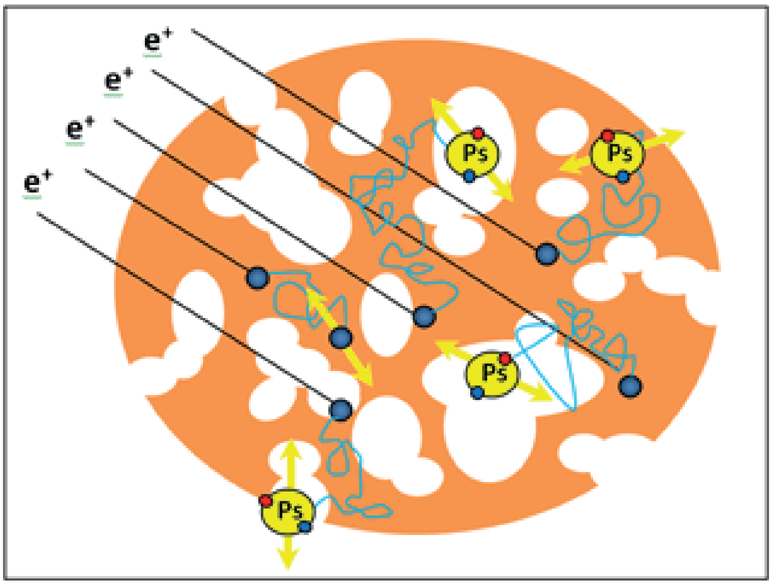

Figure 1: Schematic view of positron interactions in a porous nanoparticle.

For an o-Ps localized in a pore the annihilation rate is the weighted sum of vacuum rate and bulk rate:

$$\lambda_{pore} = \frac{\lambda_S + 3\lambda_T}{4} \cdot P + \lambda_T (1 - P), \tag{2}$$

where *P* is the probability of superposition of ortho-positronium wave function with the bulk one. This probability strongly depends on the pore size. In order to estimate the size dependence of *P* one can consider a quantum well for o-Ps as shown in Fig.2.

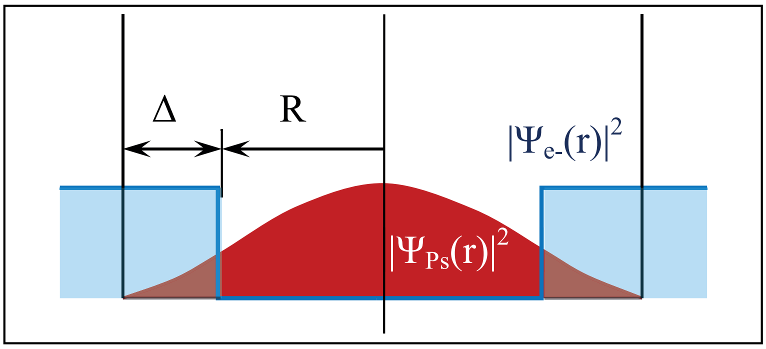

Figure 2: Tao-Eldrup model of positronium in a spherical infinite potential well.

For pore sizes smaller than 1 nm the pick-off probability is calculated by the Tao-Eldrup model (TE) [3], where the pores are modelled as spherical, infinite potential wells of radius R+Δ (see Fig. 2). Here R represents the radius of the electron-free volume and Δ is the thickness of region, where the o-Ps wavefunction $\varphi(r)$ overlaps with the bulk. The superimposition probability in the TE model is given by the following equation:

$$P = \int_{R}^{R+\Delta} \psi(r) r^2 dr = 1 - \frac{R}{R+\Delta} + \frac{1}{2\pi} \sin\left(\frac{2\pi R}{R+\Delta}\right) \tag{3}$$

For most materials the value of Δ changes from 0.166 to 0.19 nm.

In larger pore sizes (>1 nm) the positronium can occupy different energetic levels with different superimposition probability. To calculate it at a given temperature, it is necessary to take the Boltzmann distribution into account. For this case the RTE (Rectangular Tao-Eldrup) model was developed [4]. The annihilation rate for 3D cubic pores according RTE model can be evaluated by Eq.4.

$$\lambda_{RTE}(D,T) = \lambda_A - \frac{\lambda_S - \lambda_T}{4}\left[1 - \frac{2\delta}{D} + \frac{\sum_{i=1}^{\infty} \frac{1}{i\pi} \sin\left(\frac{2i\pi\delta}{D}\right) e^{\left(-\frac{\beta \cdot i^2}{D^2 kT}\right)}}{\sum_{i=1}^{\infty} e^{\left(-\frac{\beta \cdot i^2}{D^2 kT}\right)}}\right]^3, \tag{4}$$

where D is the pore size, T is temperature, $\delta = 0.18$ nm, $\beta = 0.188$ eV · nm^2.

Measuring the annihilation rate $\lambda_{Ps} = 1/\tau_{Ps}$ allows the determination of the pore size using Eq.4. The positron lifetime τ_{Ps} is measured using the positron annihilation lifetime spectroscopy (PALS). In our research the measurements were performed at room temperature by means of a conventional isotope spectrometer. We employed a ^{22}Na positron source with activity of 2 MBq and collected about 10 million annihilation events. The width of resolution function of the spectrometer is 235 ps. Fig. 3 shows the conventional PALS measuring geometry for solid-state samples.

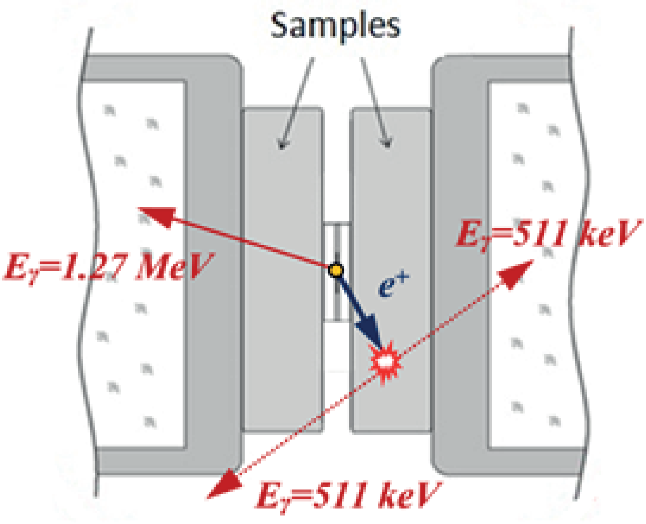

Figure 3: Geometry of PALS measurement for solid-state samples.

The positron lifetime is measured as a time interval between the signal from the nuclear gamma quantum (1.27 MeV) accompanying positron production in the beta decay of ^{22}Na, and the signal from the annihilation gamma quantum (511 keV).

The measured positron lifetime spectrum consists of several exponential components. Short-lived components are associated with the positron annihilation in bulk and point defects. Long-lived components (>1 ns) related to the positronium annihilation in pores.

To analyze the short lifetimes of the positron the detectors are usually located not on a straight line with the sample, but at an angle to exclude the imposition of the pulses produced by nuclear and annihilation gamma quanta. For long-lived components, the distortion is not so significant, and the detectors can be arranged in the "face to face" geometry.

3. Samples preparation

Samples of por-Si were prepared by standard electrochemical etching of heavily boron-doped c-Si wafers (Fig.4 a) with surface orientation (100) and specific resistivity of 10-20 mΩ·cm in a solution of HF and ethanol (HF(50%):C_2H_5OH = 1:1) at etching current density of 60 mA/cm^2 for 1 h (see, for example Ref.[1]). The prepared films with thickness about 100 μm were separated from c-Si substrates by a short increase of the current density up to 600 mA/cm^2. Aqueous suspensions of por-Si NPs were obtained by mechanical grinding of por-Si films. The morphology of por-Si films and mean sizes of the NPs were studied by using a scanning electron microscope (SEM) and a transmission electron microscope (TEM). According to the TEM data the size of por-Si NPs (Fig.4 b) is distributed in a wide range from 50 nm to 500 nm. The NPs have porous structure and exhibit a tendency to agglomerate. For the PAL investigation the por-Si NPs were dried and pressed into tablets with lateral size of 5 mm and thickness of about 1 mm (Fig.4 c).

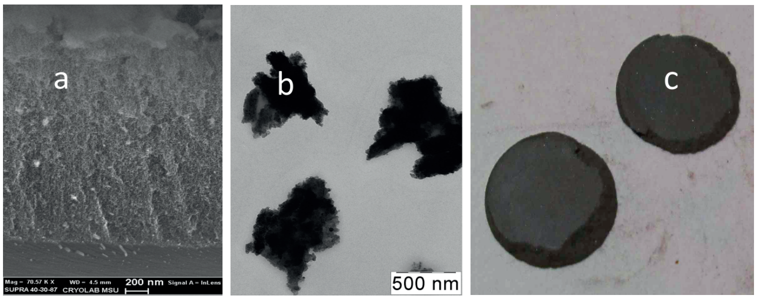

Figure 4: a) cross-sectional SEM image of por-Si film on c-Si wafer; b) TEM image of por-Si NPs; c) digital optical image of pressed tablets of por-Si Nps for PALS investigation.

4. Results and discussion

Measurements of the o-Ps lifetime require a special configuration of the PAL spectrometer. A significant distortion of long-lived component is caused by random coincidences. High rate of random coincidences reduce the measured positron lifetime. For weak isotope sources (~1 MBq) the distortion of short lifetime components (<1 ns) is negligible. But for o-Ps lifetimes it is necessary to analyze the influence of random coincidences on measured positronium lifetimes. Simulation of high count rates for stop detector of the PAL spectrometer shows that detectable distortion of o-Ps lifetimes is observed for count rates more than 10^6 s^{-1}. (Fig.5-a). A stronger limitation of the counting rate is due to the high variance of the measured lifetimes of o-Ps because of statistical uncertainty caused by random coincidences. This effect was investigated in [5]. Fig.5b shows the count rates, when the statistical uncertainty reaches the value of 1%. These restrictions make it possible to choose spectrometer parameters such that distortions in the o-Ps lifetime spectrum are acceptable. For the measurements with por-Si nanoparticles the counting rate does not exceed $4 \cdot 10^4$ s^{-1}.

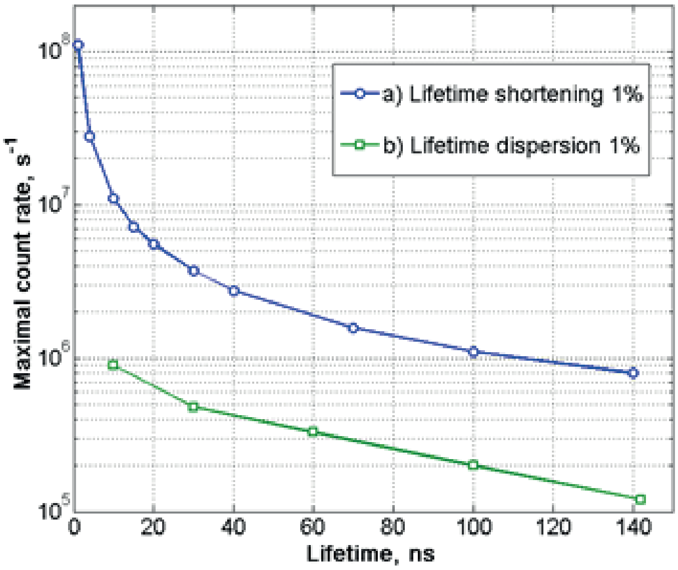

Figure 5: Restriction of counting rate due to the distortion of o-Ps lifetime by random coincidences: a) shortening the o-Ps lifetime component by 1%; b) increase of statistical uncertainty up to 1%.

The measured lifetime spectra *N(t)* were analyzed by means of the decomposition on four exponential components in the following way:

$$N(t) = \int_{-\infty}^{+\infty} R(t - t') \cdot \sum_{i=1}^{4} I_i \cdot e^{-\frac{t'}{\tau_i}} dt', \qquad (5)$$

where $R(\Delta t)$ is the resolution function of the spectrometer.

The mean lifetime of the first component τ_1 = 280 ps is associated with the positron annihilation in bulk and point defects, τ_2 = 450 ps – with the positron annihilation in pores and from surface states. The components τ_3 = 2 ns and τ_4 = 37 ns are associated with the Ps annihilation in pores. The experimental spectrum and the exponential components are shown in Fig. 6.

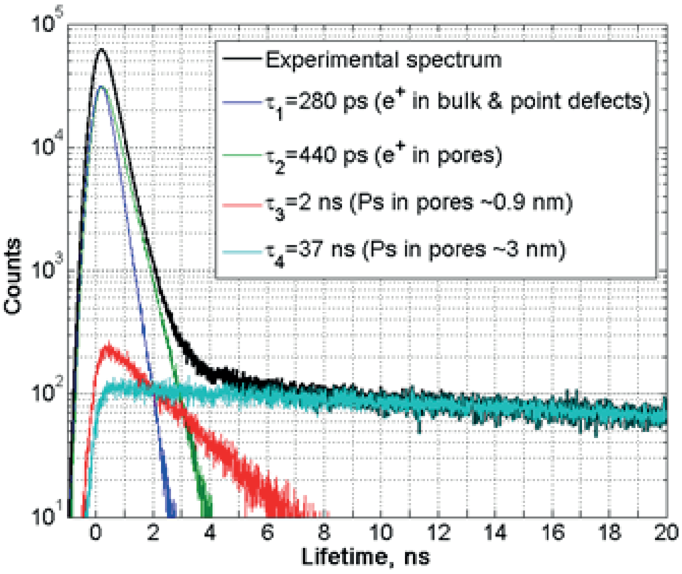

Figure 6: Decomposition of the measured lifetime spectra.

Table 1 shows the lifetimes and intensities of the exponential components. The intensities of the components show that 58% of annihilation events occur in the pores, 8% from witch related to o-Ps annihilation.

Table 1: Results of decomposition of the measured lifetime spectra.

τ, ns	0.28	0.44	2	37
I, %	42	50	1	7

Fig.7 shows the calculated dependence of the o-Ps lifetime on pore size (Eq.4). Green and red lines on the graph correspond to the obtained o-Ps lifetimes and point on the pore sizes in the investigated sample. The uncertainty characterizing the obtained lifetimes is sufficiently large, which indicates the continuity of the pore size distribution. But the prevailing pore sizes in the investigated por-Si nanoparticles are sizes about 1 and 3 nm.

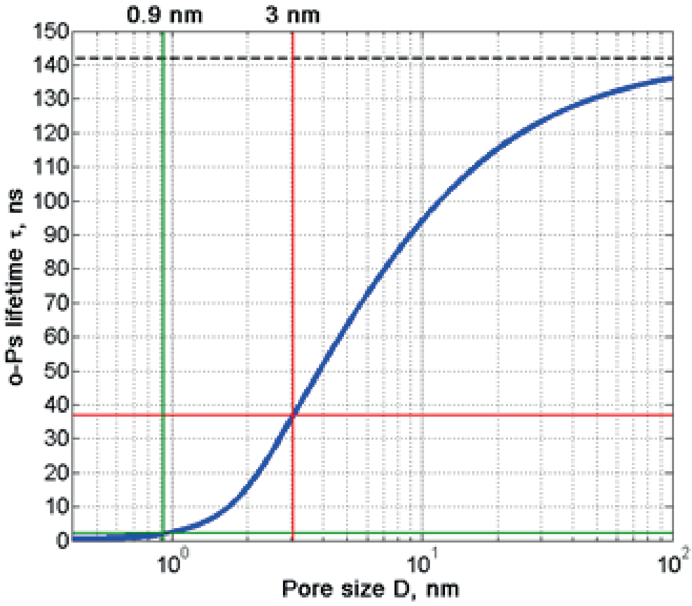

Figure 7: Determination of the pore sizes using the measured o-Ps lifetime.

5. Conclusion

The obtained results indicate that the pore size distribution in por-Si NPs is continuous. It is apparently bimodal with two local peaks near 1 nm and 3 nm. Such pore sizes seem to be favorable for loading of anticancer drug and allow applications of porous silicon nanoparticles in cancer theranostics.

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