

# Influence of electron capture after-effects on the stability of $^{111}\text{In}(^{111}\text{Cd})$ -complexes with organic ligands

L.G. Shpinkova<sup>a,\*</sup>, A.W. Carbonari<sup>b</sup>, S.M. Nikitin<sup>a</sup>, J. Mestnik-Filho<sup>b</sup>

<sup>a</sup> Department of Nuclear Spectroscopy Methods, Institute of Nuclear Physics, Lomonosov Moscow State University, Moscow 119899, Russian Federation

<sup>b</sup> Instituto de Pesquisas Energéticas e Nucleares, IPEN–CNEN/SP, P.O. Box 11049, 05422-970 São Paulo – SP, Brazil

Received 9 March 2001; in final form 27 March 2002

## Abstract

The TDPAC technique was applied to verify a hypothesis about the influence of electron capture after-effects on the integrity of radiometal complexes with organic ligands in aqueous solutions. The neutral aqueous solutions of DTPA-complexes with two parent isotopes,  $^{111}\text{In}(\text{EC})^{111}\text{Cd}$  and  $^{111\text{m}}\text{Cd}$ , were used for direct comparison of dynamic interaction parameters. Data for the parent  $^{111}\text{In}$ –DTPA complexes revealed three fractions with essentially different relaxation constants, including an “unperturbed” fraction, which, according to the hypothesis, is due to small fragments of the initial complexes disintegrated as a result of Auger-process and the following Coulomb fragmentation. Only one fraction with a relaxation constant of  $3(1) \times 10^6 \text{ s}^{-1}$  was observed for the  $^{111\text{m}}\text{Cd}$ –DTPA solution confirming the proposal about the influence of electron capture after-effects. Measurements with the frozen solutions allowed determining the electric field gradient (EFG) at Cd-sites in complexes with DTPA,  $V_{zz} = 6.7(2) \times 10^{21} \text{ V/m}^2$  with an asymmetry parameter  $\eta = 0.75(5)$ . © 2002 Published by Elsevier Science B.V.

## 1. Introduction

$^{111}\text{In}$  is one of the most commonly used isotopes in time differential perturbed angular  $\gamma\gamma$ -correlation (TDPAC) experiments. This isotope has a convenient half-life, 2.7 days, and can easily be produced in cyclotron.  $^{111}\text{In}$  transforms into  $^{111}\text{Cd}$  by electron capture (EC) decay (Fig. 1), and angular correlations of the well known 172–245 keV

$\gamma$ -ray cascade in  $^{111}\text{Cd}$  (proceeding via the 245 keV state characterised by spin  $I = 5/2$ , half-life  $T_{1/2} = 84 \text{ ns}$ , and quadrupole moment  $Q = 0.8 \text{ b}$ ) are being measured. From TDPAC data, an information on electric quadrupole hyperfine interaction (EQI) of the probe nucleus with its local environment can be extracted. The method is characterised by the applicability to systems with extremely low concentration of probe atoms (about  $10^{12}$  radioactive atoms per sample) and the sensitivity to the charge density distribution around the probe atom. The theory and the method of perturbed angular correlations of nuclear radiations are described in detail in [1].

\* Corresponding author. Tel.: +7-095-939-51-54; fax: +7-095-939-08-96.

E-mail addresses: lgs@opts.phys.msu.ru, lgs@srd.sinp.msu.ru (L.G. Shpinkova).

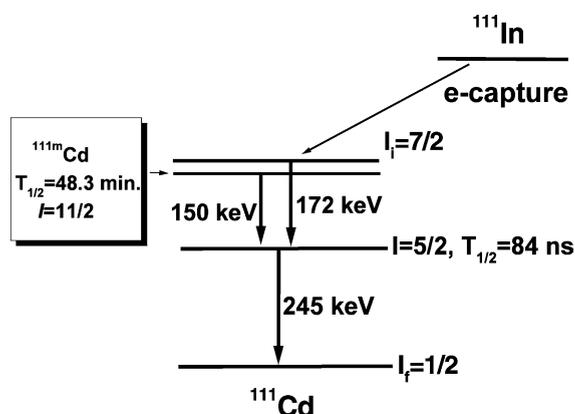


Fig. 1. The decay scheme of  $^{111}\text{In}$  and  $^{111m}\text{Cd}$ .

$^{111}\text{In}$  is also used in the modern nuclear medical practice. Low-weight organic molecular complexes with  $^{111}\text{In}$  are used in medical chemistry for preparing diagnostic radiopharmaceuticals (RPH). One of the most important characteristics of such complexes is their stability in vivo, i.e. at a certain temperature and physiological values of pH, in a presence of other positive ions, transferrin and other components of blood. In vitro stability is usually a good indication that the complex is to be stable in vivo and it can be regarded as a candidate for designing new RPH [2].

As RPH have a low concentration of radioactive probes and conventional methods cannot always be used, it seems reasonable to use TDPAC technique for studying the molecular characteristics of  $^{111}\text{In}$ -complexes with organic ligands. A possibility of applying TDPAC for studying organic objects has been demonstrated earlier in a number of works (see, for example, reviews [3,4] or [5]). In particular, the method can be applied to express assessing the stability of In-complexes with newly synthesised ligands [6].

Using the  $^{111}\text{In}$  probe in TDPAC experiments, one actually deals not with  $^{111}\text{In}$  itself, but with its daughter  $^{111}\text{Cd}$ , i.e., with a different chemical element. Thus, a process of chemical rearrangement of the molecule under study should be considered while interpreting experimental data. Also, the radioactive decay leads to so-called after-effects, which can cause a severe disturbance of the nearest environment of the daughter cadmium ion.

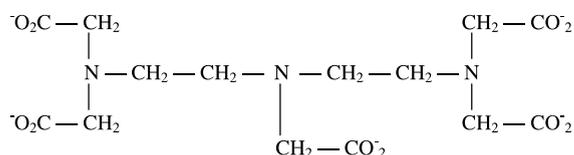
Numerous experimental studies of after-effects caused by EC,  $\beta$ - and  $\alpha$ -decays have been performed for last few decades. A summary of the works done by 1970 is given in [7]. There has been achieved an understanding that the after-effects are not important in TDPAC studies of metallic systems because of a considerable lag caused by a finite lifetime of the initial state of the  $\gamma\gamma$ -cascade and the fast relaxation due to conduction electrons [8]. In insulators [9] and oxides (see, for example [10]), the after-effects should be considered while interpreting experimental data. A problem of molecular dynamics studies in liquids obscured by after-effects was discussed in [4].

A possibility of molecule disintegration caused by EC after-effects, initiated by the Auger-process, was discussed in [11] for interpretation of two fractions with considerably different parameters of dynamic EQI observed for aqueous solutions of  $^{111}\text{In}$ -complexes with organic ligands. The fraction characterised by a low, nearly zero, relaxation constant was assigned to the fragments of the initial complexes, which had not survived the Auger-process and the following Coulomb fragmentation ("light fraction"). The abundance of the "survival" fraction was proposed to reflect the complex stability [12]. A comparison of the survival fractions for In-complexes with diethylenetriaminepentaacetic acid (DTPA) and nitrilotriacetic acid in aqueous solutions for different concentrations of carrier (stable In) was done in [13]. The results of the work confirmed, though indirectly, the hypothesis that the EC after-effects could cause the metal–ligand complex disintegration.

The present work has been undertaken in order to verify directly the validity of the proposal about the influence of the EC after-effects on disintegration of the In(Cd)-complexes with organic ligands in aqueous solutions. Perturbed angular correlation was measured for the solutions of complexes with two parent isotopes,  $^{111}\text{In}$  and  $^{111m}\text{Cd}$  (see Fig. 1). The latter is an isomeric state of  $^{111}\text{Cd}$  with the half-life 48 min, so all problems with after-effects and a chemical rearrangement of the complexes are excluded. The suitable for TDPAC measurements  $\gamma\gamma$ -cascade 150–245 keV, discharging the  $^{111m}\text{Cd}$ , proceeds via the same

intermediate excited state 245 keV as the  $\gamma\gamma$ -cascade used with the parent  $^{111}\text{In}$  isotope. According to the hypothesis made, in case of  $^{111\text{m}}\text{Cd}$ , only one fraction with non-zero relaxation constant is to be expected.

In this work, DTPA, a commonly used ligand in RPH designing, was chosen as an organic ligand, of which complexes with In and Cd are known to be stable in neutral aqueous solutions [14]. DTPA has 3 nitrogen atoms and 5 carboxyl groups, which can potentially form an 8-coordination complex with a metallic ion:



It is commonly adopted, that In [2] and Cd [15] form a 6-coordination complex with DTPA.

## 2. Theory

### 2.1. EQI studied by TDPAC

EQI represents an interaction of a nuclear quadrupole moment  $Q$  of a probe atom with an EFG characterised by the main component,  $V_{zz}$ , and the asymmetry parameter,  $\eta = |(V_{xx} - V_{yy})/V_{zz}|$ . The EQI parameters are sensitive to the local charge distribution, and, in particular, to the symmetry of the probe atom site. In case of the static quadrupole interaction (when the distribution of electric charges around the probe atom does not change with time), the perturbation coefficient of the angular correlation can be written in the form

$$G_2(t) = \sum_l a_l(\eta) \cos\{\omega_l(\eta)t\} \exp\{-\Lambda\omega_l(\eta)t\}, \quad (1)$$

where  $a_l$  are the amplitude coefficients depending on  $\eta$ ,  $\omega_l$  are the functions of  $\eta$  and the quadrupole frequency  $\nu_Q = (eQV_{zz})/h$ ,  $\Lambda$  is a full width at half-maximum of the quadrupole frequency distribution around the mean value assuming its Lorentzian shape.

In case of solutions, the probe nucleus experiences a dynamic interaction, since the local environment of the molecule containing the radioactive probe is randomly changing due to the Brownian motion. The spin orientation of the nucleus is changing with a typical time constant that is known as the re-orientational correlation time  $\tau_c$  [16], which describes the molecule mobility in the solution. The larger  $\tau_c$  the slower the molecular motion. A typical value of  $\tau_c$  for small molecules or ions in dilute solutions is  $10^{-11}$  s or less [1].

The Abragam and Pound theory [17] can be applied to dilute solutions with low viscosity giving the following perturbation coefficient

$$G_2(t) = \sum_i f_i e^{-\lambda_{2i}t}, \quad (2)$$

where  $f_i$  describes abundance of the given sort of molecules in the solution with a typical relaxation constant  $\lambda_{2i}$ .

The relaxation constant  $\lambda_2$  is proportional to the square of the quadrupole frequency  $\nu_Q$  and the re-orientational correlation time  $\tau_c$ . For the spin of the intermediate level of the  $\gamma$ -ray cascade  $I = 5/2$

$$\lambda_2 \approx 2.53\nu_Q^2\tau_c. \quad (3)$$

In the rotational diffusion theory,  $\tau_c$  for a spherical molecule is described by the following equation [18]

$$\tau_c = \frac{4}{3}\pi\eta r^3/kT, \quad (4)$$

where  $r$  is the molecular radius,  $\eta$  and  $T$  – the solution viscosity and temperature. Thus, if the parameters of dynamic ( $\lambda_2$ ) and static ( $\nu_Q$ ) EQI can be measured for the same molecules (for example, for the aqueous solutions at room and liquid nitrogen temperatures), the radius of the molecule can be assessed.

### 2.2. Electron capture after-effects

Electron capture decay leaves a hole in the K- or L-shell, initiating an emission of Auger-electrons. The process of filling the holes in the electron shells of the daughter ion develops as a cascade of vacancies moving to the outer shells of

the ion and resulting in its shock ionisation. When the vacancy cascade reaches the outer shells of the daughter ion, the neighbouring atoms start to be involved in the Auger-process and also gain a positive charge. The Auger process is very fast,  $\approx 10^{-13}$  s, and it results in the excessively charged electronic environment of the highly charged positive ion formed after EC decay. The nearest neighbours supply the central ion with electrons in order to neutralise its high charge. This process is being followed by the Coulomb repulsion between positive ions.

For example, after  $^{111}\text{In}$  EC, the average charge acquired by molecules  $^{111}\text{CdI}$  in the Auger process was shown to be +9 [19]. The energy of the Coulomb repulsion between Cd and I ions in CdI molecule was estimated to reach 120 eV. In more complicated molecules the repulsion energy is shared between larger number of atoms, though, its value could be still high enough to cause a break of chemical bonds and a partial or full disintegration of the molecule.

Being statistical, the Auger process could cause a disintegration of some molecules, while other stay intact being more or less disturbed. The relaxation to the equilibrium conditions depends on time and the degree of disturbance. If a molecule stayed intact after the EC decay, one should consider only the process of the chemical rearrangement of the molecule around the new chemical element. If a molecule disintegrated, the radioactive ion can stay as a free ion in the solution or can be re-chelated provided that free ligands are available to form a new complex. While analysing the experimental results, the typical times for all processes mentioned above are to be compared with the time window available in the TDPAC experiments. Thus, for the  $\gamma\gamma$ -cascade, used in the TDPAC experiments with  $^{111}\text{In}$ , the time window is determined by the half-lives of the initial ( $1.2 \times 10^{-10}$  s) and intermediate ( $8.4 \times 10^{-8}$  s) states.

### 3. Experimental

$^{111\text{m}}\text{Cd}$  was produced by neutron irradiation of 1 mg piece of natural metallic cadmium in the 5MW-swimming pool type reactor at IPEN–

CNEN/SP in a neutron flux of  $2 \times 10^{13}$  neutron/ $(\text{cm}^2 \text{ s})$  for 2 h. The abundance ratio of  $^{110}\text{Cd}$  in natural cadmium is about 12% and the other radioactive isotopes are also produced during the irradiation. The energy spectrum measured with a Ge-detector 50 min after the irradiation is shown in Fig. 2. The lines of the used  $\gamma\gamma$ -cascade 150–245 keV in  $^{111}\text{Cd}$  are the most intense in the spectrum and the data could be accumulated for 4–5 h after irradiation. There are several additional lines in the spectrum, of which the most intense are the lines 158.5 and 273 keV. The line at 273 keV originates from the decay of excited  $^{117}\text{In}$ , which is a product of  $^{117}\text{Cd}$  and  $^{117\text{m}}\text{Cd}$  decays (half-lives are 2.4 and 3.4 h, respectively).  $^{117}\text{Cd}$  and  $^{117\text{m}}\text{Cd}$  are produced by neutron irradiation of  $^{116}\text{Cd}$  (abundance ratio is 7.5%) with activation cross sections of 0.05 and 0.025 b, respectively. The line at 158.5 keV is from the  $^{117}\text{Sn}$  decay, which is, in turn, a product of  $^{117}\text{In}$  (half-life is 42 min). In TDPAC experiment, the lines 158.5 and 273 keV could not be cut off by the energy windows selecting the first and the second cascade  $\gamma$ -rays. Those lines contributed to the prompt and random coincidences, which were taken into account in the data analysis procedure, and did not interfere into the “true” coincidences of  $\gamma_1$ – $\gamma_2$  in  $^{111}\text{Cd}$ .

After the irradiation, 1 mg of Cd was initially dissolved in 0.3 ml of 1M nitric acid, which was completely evaporated, then – dissolved in 0.3 ml

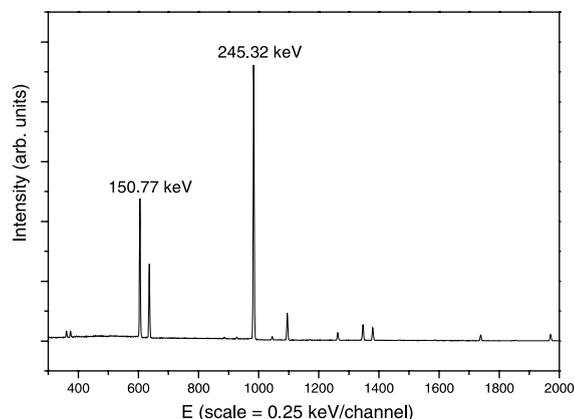


Fig. 2. Energy spectrum measured 50 min after neutron irradiation of natural Cd.

of 1 M hydrochloric acid, which was also evaporated. Finally, 0.5 ml of hydrochloric acid was added to the entire activity resulting in the 0.018 M-concentration of Cd in the solution. 0.1–0.2 ml of this stock solution (depending on the radioactivity) was added to the tenfold volume of the 2 mM DTPA solution in 0.5M-concentrated HCl. Thus, the ratio of Cd:ligand concentration was close to 1:1 (with a slight DTPA excess). The pH value was adjusted using sodium hydroxide solution. The TDPAC measurements were performed with liquid samples (1.5–2 ml of a solution in a plastic tube) at 293 K and with solid samples (frozen solutions kept in liquid nitrogen, 77 K).

Check experiments were done with neutral solutions (pH = 7.0) of  $^{111}\text{In}$ -DTPA complexes at 293 K. The samples were prepared using a commercially available (Nordion, Canada) carrier free solution of  $^{111}\text{InCl}_3$  and 2 mM solution of DTPA in 0.5M HCl. The In:ligand concentration ratio was 1:infinity (1: $\infty$ ).

It is necessary to point out, that the concentration of DTPA, relative to In and Cd, was different for the samples with two parent isotopes. Nevertheless, the results for two isotopes can be compared. We are interested in a presence or absence of the fraction with the low relaxation constant for the solution of  $^{111\text{m}}\text{Cd}$ -DTPA complexes. Such fraction was observed [13] for the sample with  $^{111}\text{In}$ -DTPA complexes at different concentration ratios [In]:[DTPA]. If this fraction is due to the complex fragmentation after EC decay, then adding carrier (In or Cd) to the In-DTPA solution could only lead to its increase. This is related to the fact that in carrier-free conditions, due to a high excess of ligand molecules, the cadmium ion, liberated from the complex, could be re-chelated producing new Cd-DTPA complex, which would not contribute to the “light fraction”. In solutions with added carrier, the concentration of free ligand molecules is much smaller, and the re-chelating process is suppressed. So, the minimal light fraction abundance is to be expected in the carrier-free solution, and the EQI parameters for another fraction could be determined with higher accuracy and compared to those determined for  $^{111\text{m}}\text{Cd}$ -DTPA complexes.

The angular correlations of the 172–245 and 150–245 keV  $\gamma$ -ray cascades in  $^{111}\text{Cd}$  were mea-

sured using a conventional slow-fast TDPAC spectrometer at IPEN-CNEN/SP equipped with 4  $\text{BaF}_2$  scintillators and XP2020Q PMT. The resolution time was 0.8 ns.

12 Coincidence spectra  $N_i(\theta, t)$  were accumulated simultaneously at the angles  $\theta = 90^\circ$  and  $180^\circ$  between the detectors. The anisotropy spectra of angular correlations were obtained by the standard formula

$$R(t) = 2 \frac{N(180, t) - N(90, t)}{N(180, t) + 2N(90, t)} \cong A_{22} Q_2 G_2(t), \quad (5)$$

where

$$N(180, t) = \sqrt[4]{\prod_{i=1}^4 N_i(180, t)},$$

$$N(90, t) = \sqrt[8]{\prod_{i=1}^8 N_i(90, t)},$$

$A_{22}$  is the correlation coefficient (theoretical values are  $-0.18$  for the 172–245 keV cascade and  $+0.16$  for the 150–245 keV  $\gamma$ -ray cascade in  $^{111}\text{Cd}$ );  $Q_2$  is the solid angle and sample size correction and  $G_2(t)$  is a perturbation coefficient containing information about EQI.

The anisotropy spectra were obtained taking into consideration the finite time resolution, a random coincidence background and a prompt curve. Spectra  $R(t)$  were fitted using the least square method in accordance with the models (1) or (2). First few channels disturbed by the prompt curve and a spectrometer malfunction were not used in the data analysis.

To determine the values of  $A_{22} Q_2$  in the experimental geometry for the used cascades in  $^{111}\text{Cd}$ , initial solutions of  $^{111\text{m}}\text{Cd}$  and  $^{111}\text{In}$  used for the sample preparations were measured at room temperature. For the solution of  $^{111\text{m}}\text{Cd}$  in 0.5 M HCl an unperturbed angular correlation was observed, while a slight damping of anisotropy function was detected for the aqueous solution of carrier-free  $^{111}\text{InCl}_3$  due to a dynamic interaction characterised by a relaxation constant of  $1.0 \times 10^6 \text{ s}^{-1}$ . This value is in agreement with  $\lambda_2$  given in [20] for indium hydroxycomplexes at pH = 3.0 and 3.7 ( $1.1 \times 10^6 \text{ s}^{-1}$ ). Values of  $A_{22} Q_2$  are 0.094(1)

and  $-0.122(1)$  for solutions of  $^{111m}\text{Cd}$  and  $^{111}\text{In}$ , respectively. The smaller value of the geometrical correction coefficient for the parent  $^{111m}\text{Cd}$  in comparison with  $^{111}\text{In}$  is due to the much larger volume of the used  $^{111m}\text{Cd}$  sample (0.3 and 1.5 ml for  $^{111}\text{In}$  and  $^{111m}\text{Cd}$ , respectively).

#### 4. Results and discussion

The TDPAC measurements for the aqueous solutions of  $^{111m}\text{Cd}$ –DTPA complexes at  $\text{pH} = 7.0$  were repeated five times at  $T = 293$  K. The results were reproducible and the spectra were added up forming the spectrum given in Fig. 3(a). This is a typical case of dynamic interaction and the spectrum could be well fitted by Eq. (2) assuming only one exponential function. An attempt to fit the data using the equation

$$R(t) = a_0 + a_1 e^{-\lambda_2 t}$$

resulted in the zero value for the  $a_0$  parameter. Thus, no “unperturbed fraction” due to unbound probe atoms or some light molecules containing the probe atoms was observed in the case of  $^{111m}\text{Cd}$ –DTPA complexes in contrast to  $^{111}\text{In}$ –DTPA [12,13]. Such result was expected from the hypothesis made for the explanation of two fractions observed for the  $^{111}\text{In}$ –DTPA solutions.

The relaxation constant  $\lambda_2$  for the complexes  $^{111m}\text{Cd}$ –DTPA was found to be  $3(1) \times 10^6 \text{ s}^{-1}$ . This value is comparable with  $2.5 \times 10^6 \text{ s}^{-1}$  obtained in [21] for the sample with parent  $^{111}\text{In}$ –DTPA complexes, but is much smaller than the values obtained in [13],  $11 \times 10^6$  to  $19 \times 10^6 \text{ s}^{-1}$ .

The spectrum for the sample of  $^{111}\text{In}$ –DTPA measured in the present work (Fig. 3(b)) could be satisfactorily fitted by Eq. (2) only assuming two exponential functions and a constant term,  $a_0$

$$R(t) = a_0 + a_1 e^{-\lambda_2^{(1)} t} + a_2 e^{-\lambda_2^{(2)} t}.$$

The obtained value of  $a_0$  is close to that one presented in [13], but both damping constants (see Table 1) differ from  $\lambda_2$  given in [13]. The possibility to resolve two exponents in the present work might be due to the better resolution of the spectrometer, better accumulated statistics and the finer time scale than used both in [13,21]. In [13] the time scale was rather rough, about 6 ns/channel, and in [21] the spectra were shown for the time interval starting only from  $\approx 55$  ns. So, it is not surprising that the fast exponent was not observed in both cited works. Additional experiments with  $^{111}\text{In}$ –DTPA solutions using the same spectrometer as in [13], but with rather finer time scale (about 1 ns/chan) also revealed a three-component spectrum [22].

Within the experimental errors, the relaxation constant  $4.2(5) \times 10^6 \text{ s}^{-1}$  is equal to  $\lambda_2$  for the  $^{111m}\text{Cd}$ –DTPA complex. Thus, the fraction characterised by this relaxation constant can be assigned to Cd–DTPA complexes, which survived the Auger-process after  $^{111}\text{In}$  decay or formed as a result of cadmium re-chelating after a full disintegration of the initial complex.

The fraction with higher  $\lambda_2$  (the abundance is about 20%) might represent the complexes in transient state after In decay into Cd, when EFG

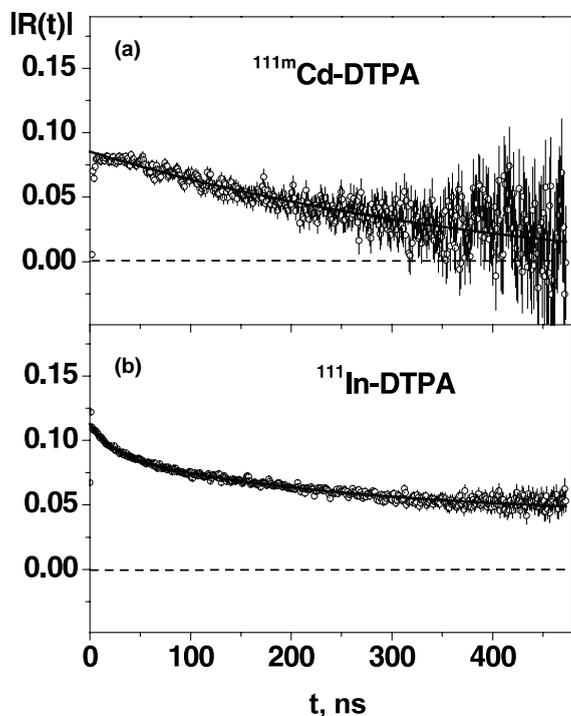


Fig. 3. TDPAC spectra of the 150–245 keV (a) and 172–247 keV (b)  $\gamma$ -ray cascade in  $^{111}\text{Cd}$  obtained at 293 K for neutral solutions of DTPA-complexes with  $^{111m}\text{Cd}$  and  $^{111}\text{In}$ , respectively. The fitting functions are shown by solid curves.

Table 1

Fitting parameters of dynamic EQI for aqueous solutions of DTPA complexes with  $^{111m}\text{Cd}$  and  $^{111}\text{In}$ 

Sample	$a_0$	$a_1$	$\lambda_2^{(1)}$ ( $10^6 \text{ s}^{-1}$ )	$a_2$	$\lambda_2^{(2)}$ ( $10^6 \text{ s}^{-1}$ )
$^{111m}\text{Cd}$ -DTPA, pH=7	0.0	0.090(6)	3(1)	–	–
$^{111}\text{In}$ -DTPA, pH=7	0.041(2)	0.049(2)	4.2(5)	0.022(1)	44(3)

rapidly changes due to the chemical rearrangement of the complex. If so, one can estimate that such processes have a typical time of 20 ns. The formation of some clusters, which can also explain the existence of the second fraction, as well as  $\text{In}_2$  DTPA complexes found in [23] for a solution with  $\text{In}:\text{DTPA}$  concentration ratio 1:1 seems to be not realistic in the carrier-free solution with a high excess of the ligand.

Using Eq. (3), the re-orientational correlation time  $\tau_c$  can be estimated for the  $\text{Cd}$ -DTPA complexes, if the quadrupole frequency  $\nu_Q$  is known. Its value could be measured in case of a static EQI, i.e. with complexes immobilised, for example, by shock freezing of the solution.

The frozen solutions of  $^{111m}\text{Cd}$ -DTPA at pH = 1.5; 4.0; 7.0 and 10.0 were measured at  $T = 77 \text{ K}$  as well as a frozen neutral solution of  $^{111m}\text{Cd}$  with adding no ligand. The spectra are shown in Fig. 4 and the fitting parameters in accord with Eq. (1) are listed in Table 2. A distribution of the quadrupole frequencies around the average value, characterised by the full width at half-maximum  $\Delta$ , was taken into account. Such distributions arise due to random configurations of water and ligand molecules around the probe atoms and are typical for frozen solutions.

At pH = 1.5, the spectrum for  $\text{Cd}$ -DTPA does not differ from the spectrum for the neutral  $\text{Cd}$  solution with no DTPA, which might indicate that no complex is being formed at low pH values. At pH = 4.0, the EQI parameters become close to the values typical for the  $\text{Cd}$ -DTPA complex at higher pH. There was observed no difference for the TDPAC spectra for pH = 7 and 10.

The observed tendency of the  $\text{Cd}$ -DTPA complex formation at pH > 4 is in a good agreement with data [15], where  $\text{Cd}$ -DTPA solutions were studied by the proton magnetic resonance technique at different pH. It was shown there that at pH < 3, all four terminal carboxyl groups are

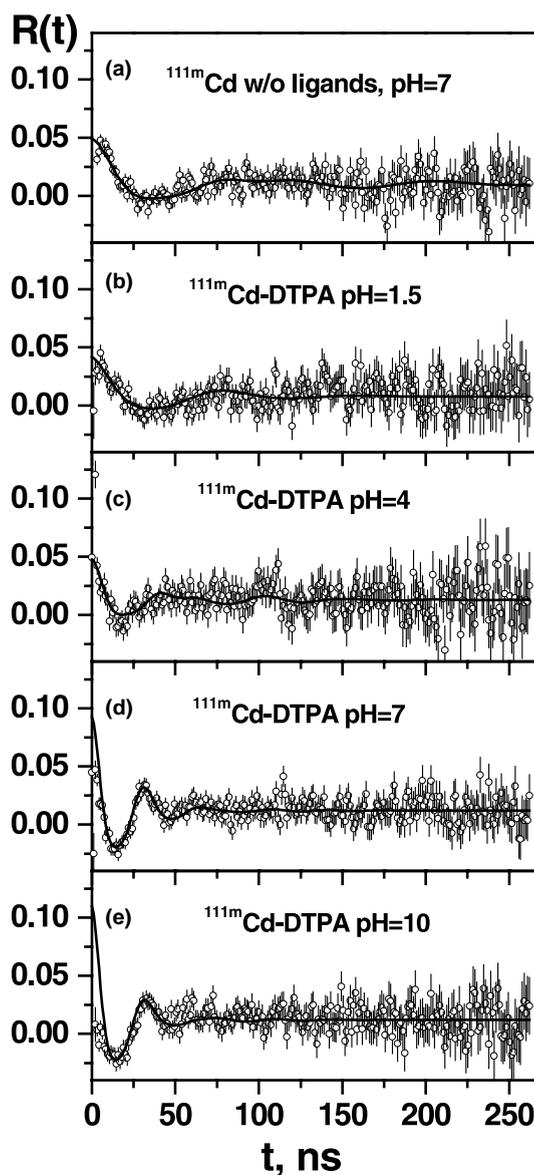


Fig. 4. TDPAC spectra measured at 77 K for the neutral solution of  $^{111m}\text{Cd}$  (a) and solutions of  $^{111m}\text{Cd}$ -DTPA complexes with pH = 1.5 (b); 4.0 (c); 7.0 (d) and 10.0 (e). The approximation functions are shown by solid curves.

Table 2

Fitting parameters of static EQI for frozen aqueous solutions of  $^{111m}\text{Cd}$  without and with DTPA at different pH and  $^{111}\text{In}$ -DTPA complexes at pH = 7.0

Solution	$\nu_Q$ (MHz)	$\eta$	$A$ (%)
$^{111m}\text{Cd}$ , pH = 7.0	51(2)	0.5(1)	18(4)
$^{111m}\text{Cd}$ -DTPA, pH = 1.5	49(9)	0.9(6)	30(10)
$^{111m}\text{Cd}$ -DTPA, pH = 4.0	99(4)	0.6(1)	14(5)
$^{111m}\text{Cd}$ -DTPA, pH = 7.0	125(2)	0.77(4)	17(3)
$^{111m}\text{Cd}$ -DTPA, pH = 10.0	125(3)	0.72(5)	21(4)
$^{111}\text{In}$ -DTPA, pH = 7.0	170(30)	0.4(2)	50(10)

equivalent, then, most possibly, are not bound to Cd ion, and the complex is not formed yet. At  $\text{pH} \leq 4.5$ , the complex is protonated and highly labile. With pH increasing, the complex lability is decreased, and its structure stays practically unchanged up to  $\text{pH} = 10$ . According to [15], Cd-coordination in the complex with DTPA is octahedron with three terminal carboxyl groups and three nitrogen atoms.

Thus, one can assume that at  $\text{pH} = 7.0$ , Cd-DTPA is a fully deprotonated complex, which is characterised by the parameters obtained in the present work, namely: re-orientational correlation time  $\tau_c = 7.7 \times 10^{-11}$  s, the main EFG component  $V_{zz} = 6.7(2) \times 10^{21}$  V/m<sup>2</sup> and the asymmetry parameter  $\eta = 0.75(5)$ . The large value of  $\eta$  gives an evidence of a high asymmetry of the local Cd environment in the complex. Then, the octahedral Cd-coordination proposed for such aminopoly-carboxylate complexes is a very rough simplification and, in practice, the octahedron is substantially deformed.

Using the values of  $\nu_Q = 125$  MHz and  $\lambda_2 = 3 \times 10^6$  s<sup>-1</sup>, from (3) and (4), the radius of the Cd-DTPA complex formed in the neutral aqueous solution can be assessed as 4.2 Å. Considering the number of atoms in the complex, this value seems to be realistic unlike the value of 12.4 Å found in [21] for the  $\text{InCl}_3$  solution at  $\text{pH} = 1.4$ .

A very broad distribution ( $A \approx 50\%$ ) of the quadrupole frequency with the average value of  $\nu_Q = 170(30)$  MHz was observed for the neutral

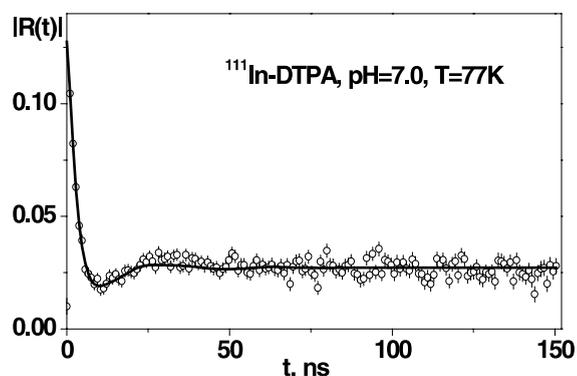


Fig. 5. TDPAC spectrum measured at 77 K for the neutral solution of  $^{111}\text{In}$ -DTPA complexes. The approximation function is shown by the solid curve.

frozen solution of parent  $^{111}\text{In}$ -DTPA complexes (Fig. 5). The observed difference in  $A$  parameters for parent complexes  $^{111m}\text{Cd}$ -DTPA and  $^{111}\text{In}$ -DTPA should be attributed to the influence of after-effects and an excitation of the molecule due to the chemical rearrangement of the complex after  $^{111}\text{In}$  decay. Though, one can note that the difference in the average frequencies is not dramatic indicating the similarity of the local environment of the probe  $^{111}\text{Cd}$  atoms in both complexes. The shift of the average  $\nu_Q$  to the higher value is in agreement with the observation of the fast component in the dynamic spectrum for the  $^{111}\text{In}$ -DTPA solution.

## 5. Conclusion

The results of this work confirmed that the hypothesis about the EC after-effects influence on the integrity of  $^{111}\text{In}(\text{Cd})$ -complexes with organic ligands is correct. The direct comparison of the data obtained with  $^{111}\text{In}$ -DTPA and  $^{111m}\text{Cd}$ -DTPA parent complexes showed that a part of Cd-DTPA complexes disintegrate after  $^{111}\text{In}$  EC, which causes Auger process in daughter Cd, the following Coulomb repulsion and, as a consequence, break of chemical bonds.

The EC after-effects and a chemical rearrangement of the molecule should be taken into consideration while using  $^{111}\text{In}$  as the parent isotope in

studies of low weight organic molecular complexes, though the averaged values obtained with  $^{111}\text{In}$  could be used as a rough estimations for Cd-complex parameters. The fast component found in the dynamic spectrum of  $^{111}\text{In}(\text{Cd})\text{-DTPA}$  can indicate a presence of high transient EFG due to the complex rearrangement after In decay into Cd. This can give a possibility of studying such fast processes and assessing their typical times.

The following parameters of static and dynamic electric quadrupole interactions of  $^{111}\text{Cd}$  in complexes with DTPA in neutral aqueous solutions were obtained using  $^{111\text{m}}\text{Cd}$  as the parent isotope: the re-orientational correlation time  $\tau_c = 7.7 \times 10^{-11}$  s, the main component of EFG  $V_{zz} = 6.7(2) \times 10^{21}$  V/m<sup>2</sup>, and the asymmetry parameter  $\eta = 0.75(5)$ . The high value of the latter parameter indicates that Cd coordination in the complex is not a regular octahedron. The radius of the Cd–DTPA complex was assessed to be  $r = 4.2 \text{ \AA}$ .

It was confirmed that at low pH values (pH < 4), there was no Cd–DTPA complex formed, while in neutral and alkaline solutions the complex is stable and its structure remains unchanged in a wide pH range (up to 10).

### Acknowledgements

It is a pleasure to thank the IPEN/CNEN reactor crew for their efficient work allowing research with the short-living  $^{111\text{m}}\text{Cd}$ , Dr. R.N. Saxena for valuable discussions and helpful suggestions and M. Saiki for technical support. The work was supported by the FAPESP grant No. 1999/12994-1 and the RFBR grants, No. 01-02-16625 and 02-02-17506.

### References

[1] R.M. Steffen, G. Fraunfelder, in: E. Karlsson, E. Matthias, K. Siegbahn (Eds.), *Perturbed Angular Correlations*,

- North-Holland Publishing Company, Amsterdam, 1964 (Chapter 1).
- [2] D.E. Reichart, J.S. Lewis, C.J. Anderson, *Coord. Chem. Rev.* 184 (1999) 3.
- [3] R. Bauer, *Q. Rev. Biophys.* 18 (1985) 1.
- [4] A. Lerf, T. Butz, *Angew. Chem. Int. Ed. Engl.* 26 (1987) 110.
- [5] K.J. Hwang, in: G. Gregoriadis (Ed.), *Liposome Technology*, vol. III, CRC Press, Inc., USA, 1984 (Chapter 16).
- [6] Z.Z. Akselrod, B.A. Komissarova, G. Kryasny, E.N. Shirani, L.G. Shpinkova, A.A. Sorokin, V.N. Kulakov, S.M. Nikitin, A.N. Shirokov, S.G. Ermolenko, *J. Radioanal. Nucl. Chem. Lett.* 199 (5) (1995) 357.
- [7] J.E. Thun, in: H. van Krugten, B. van Nooijen (Eds.), *Angular Correlation in Nuclear Disintegration*, Rotterdam University Press, Groningen, 1971.
- [8] S.G. Cohen, in: A.J. Freeman, R.B. Frankel (Eds.), *Hyperfine Interactions*, Academic Press, New York, 1967.
- [9] H. Haas, D.A. Shirley, *J. Chem. Phys.* 58 (1973) 3339.
- [10] S. Habenicht, D. Lupascu, M. Uhrmacher, L. Ziegeler, K.P. Lieb, *Z. Phys. B* 101 (1996) 187.
- [11] V.N. Kulakov, S.M. Nikitin, T.N. Babushkina, A.N. Shirokov, A.A. Sorokin, B.A. Komissarova, L.G. Shpinkova, G.K. Ryasny, *Koordinatsionnaya Khimiya* 23 (1997) 883.
- [12] V.N. Kulakov, A.A. Sorokin, Z.Z. Akselrod, A.N. Shirokov, L.G. Shpinkova, *Vestnik MGU, seriya Khimiya* 39 (1998) 305.
- [13] L.G. Shpinkova, V.N. Kulakov, A.A. Sorokin, G.K. Ryasny, B.A. Komissarova, S.M. Nikitin, *Z. Naturforsch.* 53a (1998) 630.
- [14] A.L. Martell, R.M. Smith, *Critical Stability Constants*, Plenum Press, New York, 1974.
- [15] P. Letkeman, J.B. Westmore, *Can. J. Chem.* 49 (1971) 2073.
- [16] A.G. Marshall, *Biophysical Chemistry*, New York, 1978.
- [17] A. Abragam, R.V. Pound, *Phys. Rev.* 84 (1953) 369.
- [18] P. Debye, *Polar Molecules*, Dover Publ., New York, 1945.
- [19] M. Schumacher, I. Borshert, H. Langhoff, *Z. Physik* 246 (1971) 396.
- [20] G.R. Demille, D.L. Livesey, K. Mailer, S.R. Turner, *Chem. Phys. Lett.* 44 (1976) 164.
- [21] P.C. Hargrave, F.A. Smith, K. Bown, R. Carr, *Chem. Phys. Lett.* 246 (1995) 626.
- [22] A.S. Golubeva, S.M. Nikitin, G.K. Ryasny, L.G. Shpinkova, A.A. Sorokin, A.S. Uzbyakova, to be published.
- [23] T.A. Babushkina, A.B. Sokolov, G.E. Kodina, *Teoreticheskaya i Eksperimentalnaya Khimiya* 12 (1976) 558.