1PAC: A one-detector gamma-gamma perturbed correlation technique for the determination of the physical-chemical status of ^{111}In labelled compounds

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Introduction: Analysing perturbed angular correlations (PAC) of cascade γ-emissions is a sensitive tool in condensed matter science, with applications to tasks involving nuclear hyperfine interactions (HFI). The time-integrated angular correlation of cascade (TIAC) γ-rays is given by $\overline{W(\theta, \infty)} = 1 + A_{22}\overline{G_2(\infty)}Q_2P_2(\cos(\theta)) + \dots$, A_{ii}-angular correlation coefficients depending on spins and multipolarities of transitions; $P_i(\cos\theta)$-Legendre polynomials; Q_i-solid angle correction factors; $G_i(\infty)$-TIAC perturbation factor [1,2]. A new 1PAC method (perturbed angular correlation measured with one detector) was developed recently [3]. For quantification the perturbation factor the summing peak composed of two cascade γ-rays (the perturbation-affected parameter) was related to the summing peak composed of one γ-ray and one X-ray (the perturbation non-affected parameter). The resulting parameter is the *relative probability of recording of cascade γ-rays $R_{\gamma1+\gamma2}$*, which is equal to a TIAC. The approach was demonstrated for [111]In [3,4].

Experimental: Using commercially available ^{111}In, ^{111}In-DTPA and ^{111}In-DTPA-octreotide were synthesised using a carrier amount of 10^{-6} M In.. The binding of ^{111}In-DTPA-octreotide to somatostatin receptors was simulated by its absorption on C-18 resin. 1PAC measurements in 0.1 M NaCl solution have been carried out for samples with volumes of 0.5 ml and activities of about 60 kBq, with a co-axial HPGe detector of volume 250 cm^2 at the room temperature. The sample-detector distance was 38 mm.

The pH of Na(H)Cl electrolytes was varied for these compounds in the range of about 3 to 8, while for solutions without the ligands, the hydrolysis of ^{111}In was studied in the range of pH 1 to 13, Figure 1.
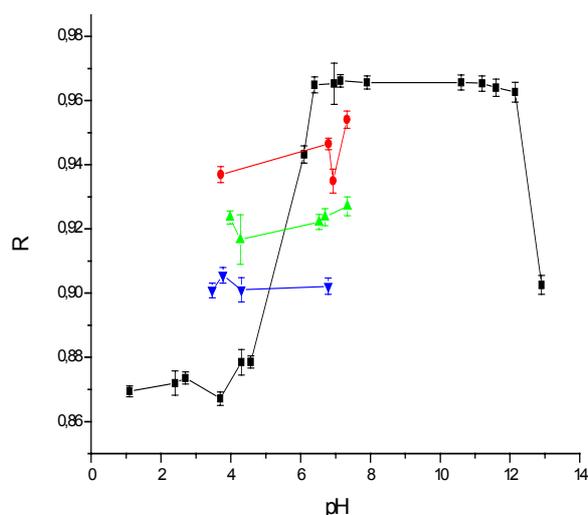
In the latter case, the value of $R_{\gamma1+\gamma2}$ strongly increases in the region of pH = 5-7, what is due to the transition of the radionuclide from $[In(H_2O)_6]^{3+}$ into insoluble $In(OH)_3$. The difference of $R_{\gamma1+\gamma2}$ in acidic and alkaline media is explained by the difference of the perturbation factors $G_2(\infty)$ for In^{3+} in the case of $[In(H_2O)_6]^{3+}$ ("liquid", $G_2(\infty)=1$) and $In(OH)_3$ ("solid", $G_2(\infty)=0,2$).

In the case of the ^{111}In labelled compounds, the value of $R_{\gamma1+\gamma2}$ mainly depends on the size of the molecules, which increases from ^{111}In-DTPA to ^{111}In-DTPA-octreotide and ^{111}In-DTPA-octreotid bound to C18. With increasing of molecular size $G_2(\infty)$ decreases ($R_{\gamma1+\gamma2}$ increases). The characteristic parameters of $R_{\gamma1+\gamma2}$ of the compounds in the range of pH of about 4 – 7 are summarised in Table 1.

Table 1: mean $R_{\gamma1+\gamma2}$ values for different ^{111}In compounds in physiological solutions

Compounds	$R_{\gamma1+\gamma2}$	Statistical error
[111]In(OH)$_3$	0,965	0,001
^{111}In-DTPA	0,903	0,002
^{111}In-DTPA-octreotide	0,923	0,004
^{111}In-DTPA-octreotide+C18	0,943	0,009

Conclusion: It is a paradigm that non-invasive detection of γ-radiation can be performed quantitatively regarding the absolute activity of a radionuclide, while the chemical form of the radionuclide is „non-visible". However, the proposed method for the measurement of the γ-γ perturbed angular correlation for cascade γ-emissions using one detector only indeed allows to analyse the chemical status of ^{111}In in different compounds. As the local chemical environment of ^{111}In is responsible for the nuclear hyperfine interactions and the related time-integrated angular correlation of the cascade γ-rays, every ^{111}In compound shows a characteristic value of the parameter $R_{\gamma1+\gamma2}$. Concerning nuclear medicine, the approach might be applied to characterise non-invasively the kinetics and yield of labelling reactions starting from acidic $^{111}In[In(H_2O)_6]^{3+}$ solutions, the formation of side-products such as ^{111}In hydroxide or colloids, but also the occurrence of metabolites, i.e. the "fate of the label": The somatstatin analogue octreotide, labelled with ^{111}In is widely adopted as radioactive tracer in oncology due to the high expression of somatostatin receptors in the neuroendocrine tumours. Octreotide is attached to the receptor and possibly internalised, thereby changing its chemical status. Thus this process of attaching the receptor could be visualised *in vivo*.

Figure 1:
pH dependence of $R_{\gamma1+\gamma2}$ values for different ^{111}In compounds
black: In; red: In-DTPA-octreotide+C18; green: In-DTPA-octreotid (10^{-5} M DTPA-octreotide); blue: In-DTPA (10^{-5} M DTPA)

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