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Study of the effect of filling thermoplastic medical polyurethane with PVA, PLA or diatomite on the relaxation times distributions of ^{1}H NMR

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Abstract

In this work, to characterize the mobility of different sections of the macromolecules of polyurethane (PUR), polyvinyl alcohol (PVA), and polylactic acid (PLA), as well as the density of crosslinks of the polymer chains when using fillers, we used the distributions of spin-lattice and spin-spin relaxation times for the protons. It is shown that the rigidity of the thermoplastic polymers depends on the sizes of the granules of the diatomite filler, which can embed in the polymer matrix. Consequently, relaxation times are reduced. If PLA is the filler of PUR, the dynamics of the molecules in the chains and the spin-spin interaction of the protons are affected by the crosslinking of PUR by PLA. An increase in crosslinks density reduces the rate of polymer degradation.
Keywords: PUR; PVA; PLA; filaments; FDM 3D printing; scaffolds; NMR relaxometry.

1. Introduction

Polyurethanes (PURs) are one of the most widely developed synthetic polymers for biomedical applications. The main advantage of PURs is the ease of modification of their physicochemical and mechanical properties, which can be changed by proper selection of the raw materials used for their synthesis. This is especially important in the field of materials used in regenerative medicine for tissue regeneration with the ability of these materials to subsequent biodegradation. These polymers represent a very wide variety of materials with individual properties, confirmed by the increasing number of publications devoted to PURs research. PVA-crosslinked polyurethanes [1] show slow degradation, hydrophilic properties, hemocompatibility and cytocompatibility in the human body. Under physiological conditions, the degradation of urethane bonds is unlikely, and defragmentation of the chains occurs mainly due to the hydrolytic degradation of flexible PUR blocks. The presence of crosslinking changes the properties of polymer materials and creates the conditions for their use in the biomedical field.

The most important degradation mechanism of most implanted polymers is chemical hydrolysis. Intensive degradation begins when water molecules enter the polymer network, causing chains hydrolysis. Different intensities of degradation of polyurethanes can be achieved by mixing them with other polymers. PLA are a biocompatible polyester that decomposes in the environment into non-toxic products. The mixing of polyurethanes with PLA affects their degradation [2]. PUR-PLA mixture can be useful as a long-term degrading material for tissue engineering. Polymers intended for use as biomedical scaffolding materials should degrade in contact with the biological fluids of the human body. In this regard, it is important to study the hydrophilicity of polymers intended for use in medicine. In [3], the method of optical polarimetry was used to study the hydrophilicity of polyurethane. It was shown that the swelling of this elastomer increases its initial optical anisotropy and decreases the photoelasticity

coefficient. The effect of polyurethane swelling on the dynamics of this elastomer macromolecules was also studied. The study [4] of the degradation of polymer films by photocolorimetry showed that the mechanisms of crosslinking, crystallization and destruction of macromolecules under the influence of various factors can also cause a change in their optical properties.

The properties of PUR, PVA, and PLA with different fillers have been studied by many authors. For example, diatomite, as a natural inorganic nanoporous filler, was used to evaluate the improvement of the mechanical and thermal insulation properties of rigid polyurethanes in [5]. A new method for producing polyurethane foam composite material containing diatomaceous earth and characterizing by special physicochemical characteristics was proposed in [6]. The study of PLA/DE composites [7] with the aim of opening up new possibilities for these materials, demonstrated the clear incompatibility of PLA and DE in the composite. To improve the mechanical strength of polyurethane foams obtained using PEG polyol, a mixture with PLA was used in [8]. It was shown that the content of PLA in the mixture of polyols significantly affects the structure of polyurethane foams. In work [9], innovative composites were developed using polyetherimide and as a natural filler of two different types of diatomaceous earth. Mechanical tests and microstructural studies of these composites were carried out to assess the effect of the filler and its content. The results showed an increase in Young's modulus with an increase in the content of diatomite.

The use of three-dimensional printing technologies is promising for the manufacturing of scaffolds in medicine. Medical grade thermoplastic polyurethanes (PUR) and PVA are well suited for the manufacture of filaments for FDM (Fused Deposition Modeling) 3D printers. The main requirement for these materials is their biocompatibility and the ability to degrade at a given speed when in contact with living body tissue. In [10], various properties of PCL and thermoplastic PUR were studied to optimize filaments formation during melt extrusion. A study of the degradation of polyurethanes showed that it is accompanied by ruptures of urethane bonds. This means that thermoplastic polyurethanes (TPU), consisting of alternating rigid (solid) and flexible (soft) blocks, are subjected to the separation of these blocks. Flexible TPUs were synthesized using materials suitable for creating biomedical polyurethanes and manufacturing filaments by melt extrusion [11]. The influence of the formation process of filaments on the physico-mechanical, chemical, rheological properties, as well as on the biocompatibility and hemocompatibility of filaments is investigated. A number of modifiers for medical polymer systems used for 3D FDM printing are presented in the review article [12]. Polymer systems designed as filaments for 3D printing can be easily modified with many inorganic and organic compounds by hot melt extrusion. Fillers and plasticizers are used to improve the mechanical, thermal, rheological and viscoelastic properties of filaments. Pharmaceutical ingredients of drug delivery systems, scaffolds for bone regeneration, etc., may be added as modifiers. The modifiers listed in [12] are promising compositions for the production of filaments with increased biocompatibility.

In general, mechanical methods, FE-SEM, FT-IR spectroscopy, ^{1}H NMR spectroscopy, Differential Scanning Calorimetry, etc. are used to study medical polymer systems. In a few works, the NMR relaxometry method with the inversion of the Laplace transform was used for the study of polymers. For example, in [13] the Laplace transform inversion method was used to study the distribution of T_2 relaxation times in polyurethane. FID signals of solid polymers were represented using a mixture of Gaussian and exponential functions. The integration interval of the full range of T_2 distribution was divided here into two regions: a Gaussian relaxation area with shorter T_2 relaxation times and an exponential relaxation area with longer relaxation times. In [14], ^{1}H NMR relaxometry was used to study the effect of water on crosslinked polyurethane coatings. An attempt was made to correlate the molecular mobility and the interaction with water for polymers with the microstructures of a highly crosslinked polyurethane system. Free induction NMR (FID) signals of solid polymers contain a lot of information about molecular dynamics. The NMR method is widely used to study the movements of macromolecules, their

parts, and the state of crosslinks in polymer meshes. Aliphatic polyurethanes were studied in [15] using the low-field ^{1}H NMR relaxometry method with the inversion of integral transform. In this work, the distribution of spin – lattice and spin – spin relaxation times was used to characterize the mobility of various sections of aliphatic polyurethane macromolecules and the density of crosslinks of polymer chains. The effect of poly (ethylene glycol) and calcium glycerol phosphate modifiers on the dynamics of PUR molecules was studied. The degradation of polymers using NMR relaxometry was studied in [16]. The change in the distribution of relaxation times was used here to detect changes in the quality of polymers caused by various external factors.

For 3D printing of scaffolds, it is possible to use filaments from polyurethane (PUR), polyvinyl alcohol (PVA), a mixture of PUR and PVA (in different ratios), and filaments from the above polymers filled with diatomaceous earth (diatomite). The aim of this work was to study the effect of the ratio of PUR, PVA, and PLA components and the filling of these polymers with diatomaceous earth on the distribution of proton NMR relaxation times. In this work, the NMR relaxometry method with the inversion of integral transform is used for the first time to study the molecular dynamics of thermoplastic polymers with fillers for 3D printing.

2. Experimental

Relaxation NMR measurements were done at 300 MHz proton frequency with a 7 Tesla superconducting magnet and a helium bath cryostat. The investigated filaments for 3D - printing were studied in a post-extrusion state. MAS method was not used in the work. Solid polymers can be prepared for MAS NMR measurements in two ways: either precisely machining the suitable sample insert for the MAS rotor from the bulk polymer or grinding the sample into the fine powder. The first way was not applicable in our case, because the polymerization of the samples occurs during the extrusion process, and the samples have the form of filaments. Grinding the samples into a fine powder was not desirable, because this would lead to a size effect influence on the relaxation times and to the mechanical destruction of polymer crosslinks. In this regard, the measurements were performed statically, CSA and dipole interactions were not compensated. To measure the T_1 spin-lattice relaxation time, we used inversion-recovery pulse sequence 180° – τ – 90°. To measure the T_2 spin-spin relaxation time, we used the Carr - Purcell - Meiboom - Gill (CPMG) pulse sequence. These well-tried methods provide necessary reliability of measurements for determining spin-lattice and spin-spin relaxation times. Typical parameters of the used pulse sequences are: 90-degree pulse duration t_w^{90} = 5 μs, Relaxation delay = 0.5-1 s, ADC discretization period = 1 μs, Number of scans = 256. The experimental data are represented as following functions:

$$S(\tau) = \int_0^\infty f(T_1)\left[1 - kexp\left(-\frac{\tau}{T_1}\right)\right]dT_1 + err, \quad (1)$$

$$S(t) = \int_0^\infty f(T_2)exp\left(-\frac{t}{T_2}\right)dT_2 + err, \quad (2)$$

where $f(T_1)$ and $f(T_2)$ are the distribution functions of the spin-lattice and spin-spin relaxation times, *err* is the noise contribution. The sought-after array of the distribution of relaxation times is the inverse Laplace transform of the set of exponentially decaying signals, which is the array of experimental data, and is calculated using the regularization and least squares method using the CONTIN algorithm [17]. The program is implemented in the MATLAB environment, and based on minimizing the standard deviation using "fminsearch" optimization function. For an acceptable processing time, the number of points in the input data array was chosen equal to 128-256, and the distribution functions were calculated for 50-100 points. In the calculation process, from 50 to 200 iterations were used. As a result of the implementation of the algorithm, functions are calculated and graphs of the distribution of relaxation times are built.

For research we used samples of thermoplastic polymers prepared in the laboratory of the Department of Polymer Technology of the Gdansk Polytechnic University. The polymers were heated to their melting point and mixed in a twin-screw extruder. The filament formed at the exit

of the extruder hardens and cools to room temperature. Solid filament pieces with a diameter of 2 mm and a length of 8-10 mm were placed in the tube for NMR measurements. All measurements were performed at 295K temperature.

3. Results and discussion

The studied polymers have different structures, molecular weights and dynamics of molecules and their parts, which determines the relaxation rates and the complexity of relaxation times distributions. The different mobility of the molecules also determines the multimodality of the distribution of spin-lattice relaxation times. The positions of the peaks in the distributions depend not only on the composition of the macromolecules, but also on the presence and types of fillers that improve those or other properties of the polymers.

The distributions of proton NMR relaxation times in the "pure" PUR, PVA, PLA, and Diatomite materials (Fig. 1), as one would expect, differ significantly. Aliphatic polyurethane (PUR) is a thermoplastic polymer consisting of rigid and elastic organic units containing hydrogen [18]. A chain of high and low molecular weight polymer blocks is linked by urethane groups. Oligomeric α, ω-dihydroxy (ethylene-butylene adipate) (dHEBA) and poly (ethylene glycol) (PEG) are high-molecular-weight polymers. 1,6-hexamethylene diisocyanate (HDI) is a low-molecular-weight polymer. 4-butanediol (BDO) is used as a chain extender. The soft segments provide the elastomeric nature of the polyurethane, and the hard segments provide good mechanical strength due to the hydrogen bonds formed between the urethane groups. Soft and hard blocks have different mobility, which determines different relaxation times of the NMR protons of these segments. In addition, the amplitude of vibrations of the tails and mid blocks of macromolecules also differs. The modality of the distributions is also different due to the presence of molecular fragments with different relaxation rates.

Polyvinyl alcohol (PVA) - is a water - soluble synthetic polymer. It is not suitable for 3D printing and can only be used as support for printing with other materials. Hydrogen in this polymer is a part of CH -, CH_2 - and OH - groups of macromolecules, i.e. PVA has 3 nonequivalent proton positions. The mobility of these groups is different, which leads to multimodal distributions of the T_1 and T_2 relaxation times. Polylactic acid (PLA) is a biodegradable, biocompatible polymer that is an alternative to traditional chemically resistant polymers. Hydrogen here is a part of CH_3 - groups and CH - groups inside the polymer chains of macromolecules. These groups have different dynamics, which is reflected in the relaxation times distributions. Diatomite or diatomaceous earth (D.E.) is 80–90% SiO_2 silica. The NMR signal, which is observed in "pure" D.E., can be a signal from a small number of protons of water filling the pores of diatomite. The multimodality of the relaxation times distributions is caused by different pore sizes and reflects the pore size distribution.

The peaks in the multimodal distributions of T_1 and T_2 relaxation times (Fig. 1) can be supposedly assigned to the protons of the corresponding functional groups in the polymers. More mobile groups correspond to longer relaxation times.

The spin-spin relaxation time is largely determined by the same factors as the spin-lattice relaxation time. But for spin-spin relaxation, there are two additional factors. The first is the decay of coherence caused by the inhomogeneity of the magnetic field, the second is a change in the resonant frequency of the nucleus due to some dynamic process leading to a change in its chemical environment (exchange, inhibited rotation, conformational transitions, etc.). Therefore, the number of peaks in the distributions T_1 and T_2 are not necessarily the same. The number of peaks in the T_1 distribution is determined by the different mobility of the rigid and elastic blocks, the middle and tail parts of the polymer macromolecules. The number of peaks in the T_2 distribution is also determined by different spin-spin intramolecular and intermolecular interactions. Peaks in both distributions show only dominant relaxation times in the sample.

The distributions of relaxation times for PUR with the addition of diatomite in different proportions are shown in Fig. 2. It shows that the addition of diatomite does not affect the

relaxation times distribution in PUR. The inversion of the Laplace transform allows resolving peaks whose positions on the time axis differ from each other by at least 2 times. The accuracy in determining the position of the peak depends on the number of points in the considered interval and on the signal-to-noise ratio. In our measurements, this error is approximately 10%. Given this fact the distribution shown in Fig. 2 can be considered almost the same. Diatomite is simply a light inert filler here. It does not enter into connection with polymer chains and does not affect the dynamics of PUR macromolecules. The signal from water in the pores of diatomite (curve 4 in Fig. 1) in the distributions of Fig. 2 does not occur due to absent of water after preparation of the composite. If the diatomaceous powder is sufficiently fine, then it can act as a polymer-reinforcing filler, since it causes an increase in stiffness due to the inclusion of filler in the polymer matrix. In this case, the relaxation times of the PUR protons would decrease.

A different picture is observed in the distributions of the PVA relaxation times with the addition of diatomite (Fig. 3). Here, the distributions of T_1 and T_2 change. As can be seen from fig. 3a, the addition of diatomite substantially changes the shape of the T_1 distribution curve. With increasing diatomite concentration, 3 well-resolved lines form from a very wide line of pure PVA. The distributions of T_2 times are bimodal and contain big short-time and small long-time peaks. The T_2 time value of the main peak increases for PVA + 2.5% diatomite, and then decreases for PVA + 5% diatomite (Fig. 3b), but this does not happen with a small peak in T_2 distributions. The change in the position of the main T_2 peak with increasing concentration of diatomite can be presumably explained as follows. With the addition of a neutral filler, on the one hand, at the locations of the granules of filler, the distance between the macromolecules increases, the spin-spin interaction decreases, and T_2 increases. On the other hand, small granules of diatomite powder fall into the cells of the polymer network, while increasing its rigidity and decreasing T_2. At a concentration of 2.5% of filler, the influence of the first mechanism prevails, and the T_2 time of the main peak increases. At a concentration of 5%, the increasing stiffening mechanism has a greater effect and T_2 decreases.

The addition of diatomite to PLA (2.5%, 5%) does not affect the distribution of proton relaxation times in the polymer. The inorganic filler of silicon dioxide is a neutral substance that does not have bonds with PLA chains. The mobility of fragments of polymer chains could decrease with a sufficiently fine diatomaceous powder, since it can cause an increase in stiffness due to the ingress of filler into the polymer matrix. Large particles of diatomite cannot penetrate into the polymer network and increase its rigidity.

The addition of PVA to polyurethane (2.5%, 5%, 7.5%, 10%) practically does not affect the distribution of relaxation times. The composite material obtained from the melt using a twin-screw extruder is a simple mixture of two polymers and there are no crosslinks of PUR chains by PVA. And since the percentage of PUR mass content prevails, the distribution of relaxation times remains close to curves 1 in Fig. 1 a and 1b. Thus, the composite studied in this work differs from the polymer obtained in [1], where PUR crosslinked with PVA was synthesized by two-stage polymerization in a solvent.

Fig. 4 shows the distributions of relaxation times for PUR supplemented with PLA in different ratios. Unlike PVA, the addition of PLA to PUR significantly changes the nature of T_1 and T_2 distributions (Fig. 4). PLA protons, like PUR protons, contribute to the relaxation times distribution curves. The magnitude of this contribution depends on the percentage of PLA in the polymer mixture. When heated, PLA bioplastic is more fluid than PVA. When a filament is fabricated from a PUR and PLA melt in a twin-screw extruder, a partial crosslinking of the PUR by PVA is likely to occur, which affects the dynamics of the molecules in the chains and the spin-spin interaction of protons. The structure of polyurethanes for PLA-containing mixtures is violated, and the distance between the polymer frameworks becomes larger in comparison to the reference sample. The density of the PUR - PLA mixture and the order of the chains in the polymer network are lower than in pure polyurethane, which causes the migration of molecules of any external medium into their structure. As shown in [2], the mixing of polyurethane with PLA causes an increase in the sorption of oil and water.

The change of the shapes of T_1 and T_2 times distributions with increasing filler concentration (Fig. 4) is not monotonic. This indicates the complexity of the object of study. In the presence of filler, heterogeneity of the polymer structure occurs. Due to the joint crosslinking of the polymers, a polymer composition of several phases is created. Nuclei with different mobility have different relaxation times. The heterogeneity of proton mobility is determined by a different degree of microphase crosslinking, depending on the concentration of PLA. The short components of relaxation times correspond to protons of strongly cross-linked domains with a more complete network structure, and long relaxation times correspond to protons of sparsely cross-linked domains with a defective network structure. Partial crosslinking gives rise to domains of strongly crosslinked polymers, the order of the chains in the polymer network decreases and in a complex way depends on the concentration of the filler. This apparently explains the non-monotonic nature of the changes in the multimodal T_1 and T_2 distributions.

4. Conclusion

Thus, to study the effect of filler on the mobility of fragments of polymer macromolecules, on the density of chain crosslinks, and on the modification of polymer properties for 3D printing, we used the distribution of NMR relaxation times of hydrogen nuclei. It is assumed that the influence of the diatomite filler on the rigidity of thermoplastic polymers for the FDM 3D printing of scaffolds depends on the size of the filler granules that can embed in the polymer matrix. This leads to a reduction of relaxation times. When for PUR is used as a PLA filler, the dynamics of molecules in chains and the spin-spin interaction of protons are affected by crosslinking of PUR via PLA. An increase in crosslinks density reduces the rate of polymer degradation. The addition of PVA to polyurethane has practically no effect on the relaxation times distribution, since the composite material obtained from the melt using a twin-screw extruder is a simple mixture of two polymers and there is no crosslinking of PUR by PVA.

This study can help to expand the range of methods for controlling the properties of medical polymers suitable for the manufacture of filaments for FDM 3D - printers. The use of the above polymers allows to obtain biocompatible structures with different properties for use in various fields of medicine.

Conflicts of Interest: The authors declare no conflict of interest.

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Figure captions:

Fig. 1. Distribution of relaxation times in "pure" materials: ***1*** –PUR, ***2*** – PVA, ***3*** – PLA, ***4*** – Diatomite.

Fig. 2. Distributions of relaxation times for PUR with diatomite: ***1*** – 0%, ***2*** –1.5%, ***3*** –2.5%, ***4*** – 3.5%, ***5*** – 5%.

Fig. 3. Distributions of relaxation times for PVA with diatomite additive: ***1*** – 0%, ***2*** –2.5%, ***3*** – 5%.

Fig. 4. Distribution of relaxation times for PUR with the addition of PLA: ***1*** – 0%, ***2*** – 2.5%, ***3*** – 5%, ***4*** –7.5%, ***5*** –10%, ***6*** –12.5%, ***7*** –15%.

Figure

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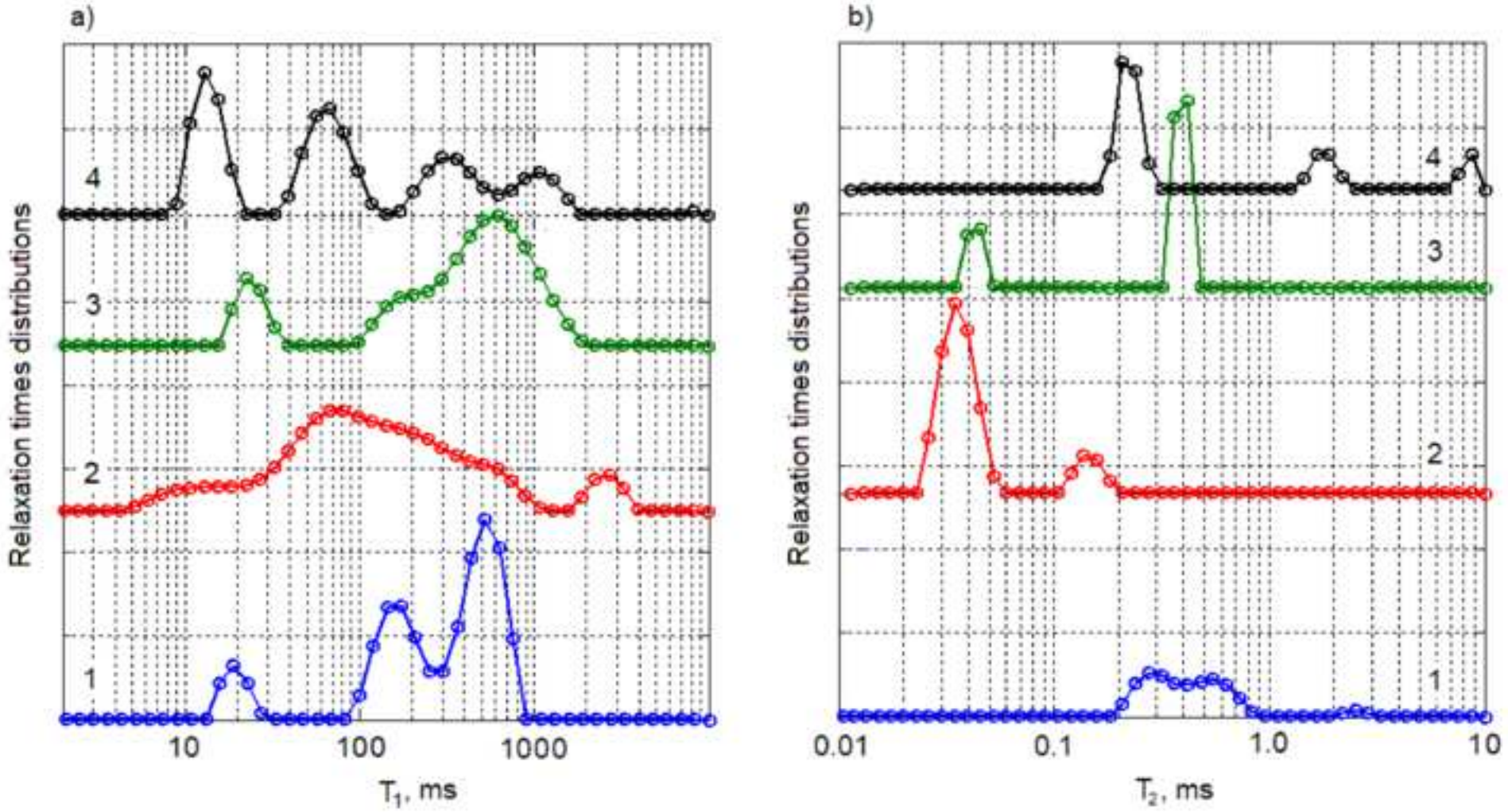

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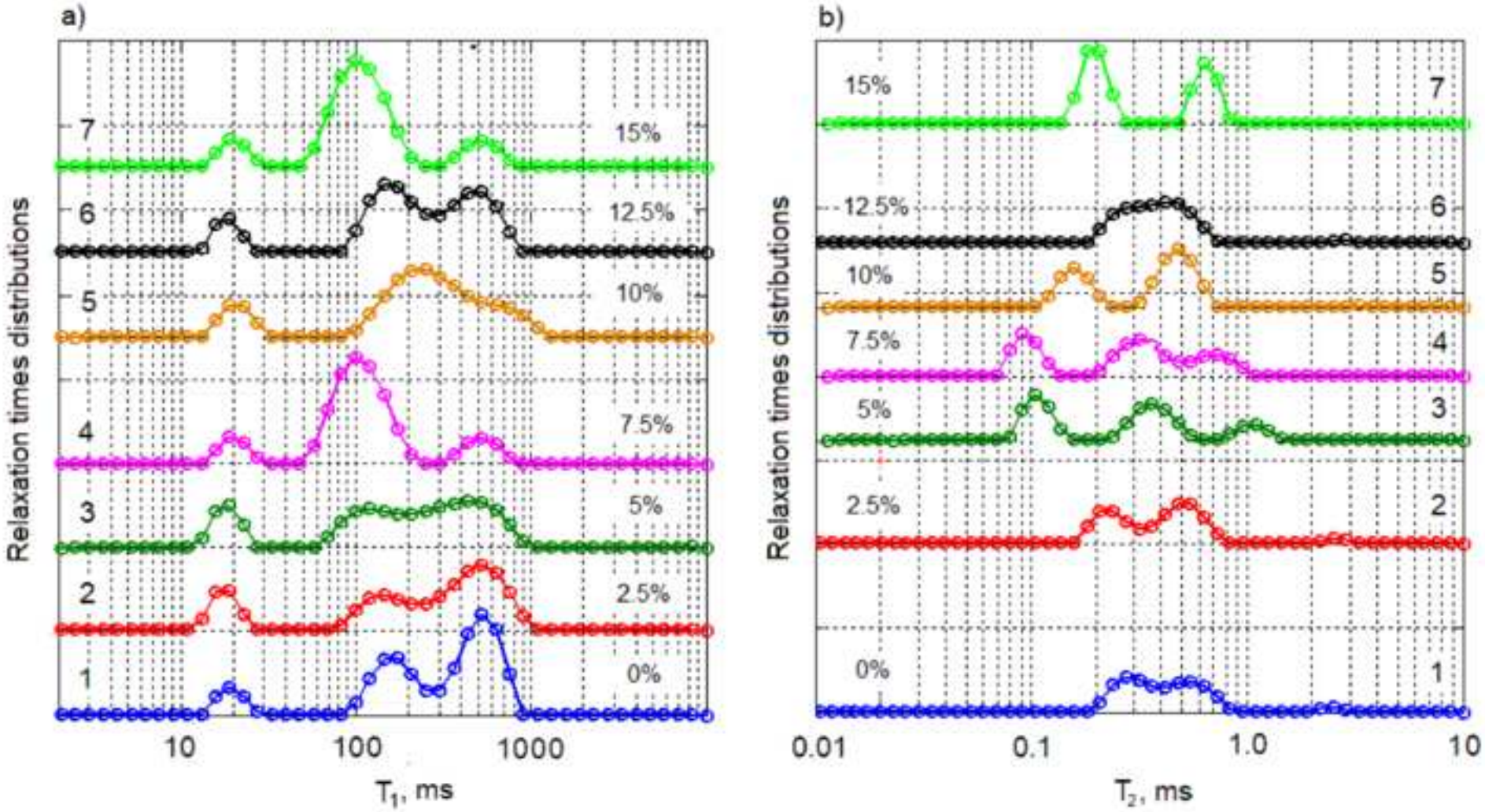

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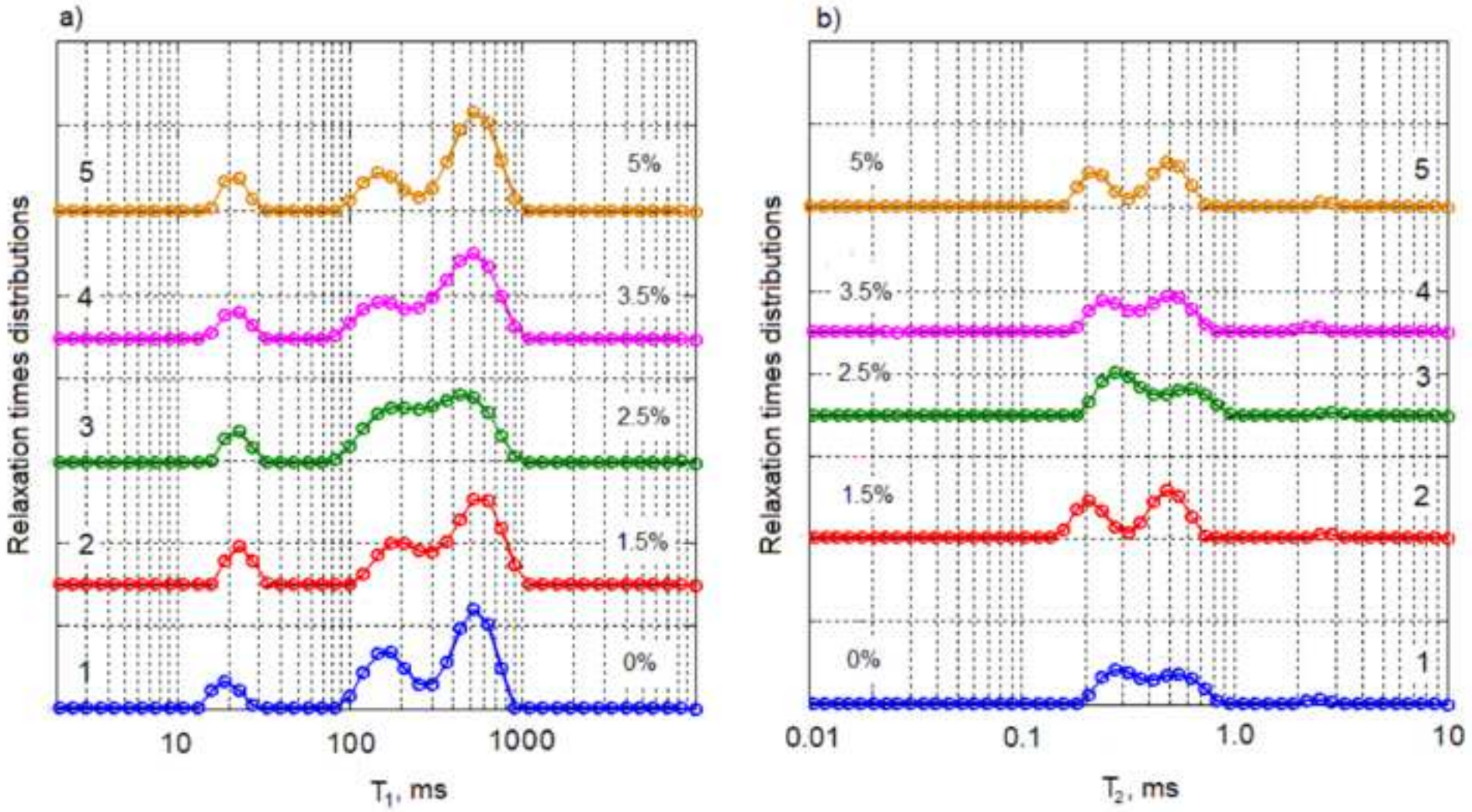

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