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Atomic structure and dissolution properties of yttrium-containing phosphate glasses

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ABSTRACT

We have conducted classical molecular dynamics simulations of three compositions of yttrium-containing phosphate glasses, to study the atomic structure around yttrium, and understand how yttrium incorporation will affect the glass dissolution rate. The Y-O bond length is about 2.2 Å and the coordination number is 6.3. To avoid effects due to different network connectivities, our compositions were chosen to keep the Q^n distribution and network connectivity roughly constant, which was confirmed through direct calculation. For these compositions, the structure of the phosphate network is comprised of finite-length chains of PO_4 tetrahedra bound to the network modifiers. We showed that yttrium bonds to 4.2-4.3 of these chains, compared to 3.8 for calcium, and 3.1-3.2 for sodium. This implies that yttrium will bond more parts of the glass to the same place, and therefore, that yttrium incorporation will strengthen phosphate glass against dissolution, making it potentially suitable for radiotherapy applications where a durable glass is required.

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INTRODUCTION

Glassy (amorphous) materials have a wide range of use in modern medicine[1]. The most familiar is probably the silicate-glass composition known as Bioglass which bonds directly to bone and soft tissue[2,3], and is therefore used in bone repair and dentistry applications. Another clinical application is the use of aluminosilicate glass microspheres as a carrier of radioactive yttrium. The spheres are injected into a tumour to irradiate it or the blood vessels surrounding it directly, in a technique known as *in situ* radiotherapy[4]. In this application, control of the degradation of the microspheres is vital. It is imperative that as little ^{90}Y as possible dissolve from the glass into the bloodstream whilst it is still radioactive, otherwise the radioactive yttrium will travel throughout the body, irradiating the patient, possibly fatally. Since ^{90}Y has a half-life of 64 hours, the glass should be stable for at least a few weeks.

It is, therefore, of great interest to understand what factors drive the glass dissolution and how they can be controlled. The dissolution of silicate glasses in the body environment occurs *via* a complicated multi-step process[5,6] and, despite considerable study[7-10], is not completely understood. Silicate glass has a highly connected three-dimensional network structure in which SiO_4 tetrahedra are chemically bonded through bridging oxygen (BO) atoms at their vertices to build up the glass structure. The series of reactions by which the glass dissolves is not straightforward. At the moment, therefore, the aluminosilicate glass composition used in *in situ* radiotherapy (17.1 mol% Y_2O_3, 18.9 mol% Al_2O_3, 64.0 mol% SiO_2) was chosen[4] because it had the slowest dissolution of eight compositions measured. This is satisfactory for the radiotherapy treatment alone, but it means that the glass spheres themselves can linger in the body after the treatment, potentially for years, with unknown long-term effects. A potentially superior option would be to incorporate yttrium into a material whose dissolution behaviour was better understood and which could be controlled.

We turn, therefore, to the use of phosphate glasses. Phosphate glasses have a dissolution rate which depends sensitively on glass composition and which can vary over several orders of magnitude[11]. Phosphate glasses are also built up from tetrahedra, PO_4 in this case, but the connectivity of the network is rather lower, and biomedically relevant compositions typically have about 1.8 BO atoms per phosphate tetrahedron[12]. This means that the structure of the glass is formed of finite-length chains of PO_4 tetrahedra (Q^2 phosphorus atoms in the centre of the chain, Q^1 at the ends) surrounded by network-modifying cations, usually sodium and calcium. This structure, rather simpler than the 3D silicate glass network structure, means that it is possible to elucidate what controls the dissolution of these glasses, at least for certain compositions: computational[13] work has shown, that for glasses with less than 50 mol% P_2O_5, the dissolution rate is controlled by the different amount of these chains chemically bonded to the different modifiers; this is consistent with experiment[14]. Our previous work has shown that the field strength (Z/a^2, where Z is the ionic charge, and a is the ionic radius) drives much of the local bonding around the cations. We have previously considered cations with a range of field strengths: singly charged cations including sodium[13] and silver[15,16], doubly charged cations including calcium[13] and strontium[17], and the fluoride anion[18], but this is the first time we have considered a triply charged cation. We emphasise, as shown in previous work[16,18], that this implies that the network connectivity (NC, the average number of BO atoms per PO_4 tetrahedron) alone is not a complete description of the relationship between the glass structure and its dissolution.

In this paper, we conduct classical molecular dynamics simulations of different compositions of yttrium-containing phosphate glass and characterise the structure of the glass at both short and medium length scales. We show the extent of the bonding of the yttrium atoms to the phosphate chains, how this differs from the bonding of the other modifiers to the

phosphate chains, and the consequences for the dissolution rate. We outline the implications for the use of yttrium-doped phosphate glass as a material for *in situ* radiotherapy.

METHODOLOGY

Classical molecular dynamics simulations were performed using the DLPOLY Classic code[19]. Three compositions of yttrium-containing phosphate glasses were modelled (Table I). Their densities were estimated from how yttrium incorporation affects the density of related glasses[20,21], and the experimentally measured density of the equivalent yttrium-free glass composition[22]. These compositions were chosen so that they all had the same network connectivity, to remove any effect of changing the network connectivity on their structure.

For each composition, about 2000 atoms were randomly and independently placed in a cubic periodic box, subject to the constraint that no two atoms were closer than about 80-90% of their expected interatomic distances. Four independent models were generated for each composition; all data shown are averaged over these models. The size of the box was initially chosen to give a density of 95% of the estimated experimental density to mimic thermal expansion at high temperature. Each model was then run in the NVT ensemble at 2500 K for 40 ps to equilibrate the liquid, before being run for 40 ps at each of the following temperatures: 2000 K, 1500 K, 1000 K, 500 K and 300 K. After the 2000 K run, the model was resized to give the estimated experimental density. Unless otherwise stated, all data given here are averaged over snapshots taken from the final two-thirds of the 300 K run.

The interatomic forces are represented by a formal-charge, polarisable force field[12,20], given in Table II. A polarisable potential was used because these are known to give Q^n distributions closer to experiment than non-polarisable potentials[23], and a correct description

of the medium-range structure described by the Q^n distribution is very important to understand the bioactivity of the glass. The short-range cutoff is 8Å, and the Ewald summation with a cutoff of 12Å is used to evaluate the interatomic Coulomb forces. Polarisability is incorporated through an adiabatic shell model (with a shell mass of 0.2 amu) on the oxygen atoms, requiring a small MD timestep of 0.2 fs. At low values of r, the O_s-O_s potential is modified to remove unphysical behaviour, as in ref.[25]

Although the cooling rate used to prepare these glasses is several orders of magnitude faster than that used experimentally, this methodology with similar cooling rates has been used for classical MD simulations of bioactive phosphate[12,13,16] and silicate[20,21,26,27] glasses, providing structures which are in agreement with experimental data.

RESULTS

The structure of the Y-free glass has been extensively characterised before[12,13]; here we present our results to show the novelty in this work, which is the effect of yttrium incorporation on the structure at short and medium length scales.

Figure 1 shows the Y-O partial pair-correlation function for all three compositions studied. There is a sharp peak at 2.21Å corresponding to the Y-O bond length. This bond length, and the pair-correlation function as a whole, show very little dependence on composition. Figure 2 shows the Y-O partial pair-correlation function compared to that for Na-O and Ca-O, for Y6-PBG as a representative composition. The Y-O bond length is shorter than the Ca-O or Na-O bond lengths, and the distribution of distances is narrower, as seen in the sharper first peak of $g_{YO}(r)$ compared to that of $g_{NaO}(r)$ or $g_{CaO}(r)$ (Figure 2), as also found for yttrium-containing silicate glass[21].

The first minimum in $g_{YO}(r)$ occurs at $r \approx 3.0$Å, which we use as a cut-off to compute the Y-O coordination number for the three compositions as 6.3. This is comparable to the Na-O and Ca-O coordination numbers which were found to be 6.4-6.5. All modifier-oxygen coordination numbers are given in Table III.

The structure of these particular compositions has not been examined experimentally, but our results are consistent with previous experiments on related compositions. Neutron diffraction data on yttrium alumino-phosphate glasses gave a Y-O bond length of 2.25Å and a coordination number of 5.75-6.0[28]. Although this coordination number is smaller than ours, the effect of the network-intermediate aluminium ion might be partially responsible for the difference. When yttrium is incorporated into bioactive silicate glass, also containing Na_2O and CaO like our compositions, computer simulation found a Y-O bond length of 2.17Å and a coordination number of 5.6[20]. First-principles and classical computer simulation of yttrium aluminosilicate glasses has shown a larger Y-O bond length of 2.27-2.29Å with a coordination number between 6.2 and 6.8, strongly dependent on composition[26,29]. A Y-O bond length of 2.31Å and a composition-dependent coordination number between 6.4 and 7.0, was found from classical molecular dynamics simulations on yttrium aluminosilicate glasses with high alumina and low silica content[30].

Bridging oxygen (BO) atoms are those oxygen atoms which are chemically bonded to two phosphorus atoms, bridging two PO_4 tetrahedra. Modifier cations prefer to bond to non-bridging oxygen (NBO) atoms, which are oxygen atoms which do not bridge two tetrahedra. Where there is more than one modifier atom present, they "compete" for their preferred bonding environments, which leads to different amounts of NBOs and BOs in the first coordination shell of these atoms[13,15-17,21,31]. In Table IV, we show the percentage of non-bridging oxygen atoms in the first coordination shell of the modifier cations. For all of our

compositions, sodium has the smallest percentage of NBOs, and yttrium the most, with yttrium bonding almost completely exclusively to NBOs.

The network connectivity (NC) is often used to describe the bioactivity of glasses[5,6]. The NC depends on the ratio of number of oxygen atoms to the number of phosphorus atoms, a ratio which we kept constant in these compositions. To check that the NC was indeed constant, we computed the Q^n distribution for all compositions and found that they were all almost identical, with 23-27% Q^1, 65-72% Q^2, and 4-8% Q^3, for a network connectivity of 1.78-1.81.

With others, we have shown[13] that the dissolution of phosphate glasses with less than 50 mol% P_2O_5 is controlled by the extent to which the network-modifying cations bond to the surrounding phosphate chains, with different modifiers bonding to different numbers of chains, strengthening or weakening the network as more or fewer chains are anchored to the same cation. We have computed the number of phosphate chains bound to each cation; this is not equal to the number of PO_4 phosphate tetrahedra, as some tetrahedra are part of the same chain. For the first time, in this work, we look at the number of phosphate chains bound to a cation with a charge of 3+. The number of chains bonded to each network-modifying cation is given in Table V. There is a clear increase in the number of chains bonded to yttrium, compared to the number of chains bonded to calcium, which is in turn larger than the number of chains bonded to sodium.

DISCUSSION

We have studied, through computer simulation, the effect of incorporating yttrium on the structure and properties of phosphate glasses, particularly as they relate to biomedical applications. Yttrium is already incorporated into silicate glass for use in *in situ* radiotherapy, and the success of that application relies on the glass being durable whilst the yttrium is still

radioactive, so it is important to understand how the yttrium affects the phosphate glass dissolution.

We found that yttrium acts as a network modifier in these glasses, with a Y-O bond length of about 2.2Å and a coordination number of 6.3. The bond length and coordination number are slightly lower than those for sodium and calcium, the other modifiers used in biomedically relevant compositions of phosphate glass. As expected, all three modifiers bond to substantial amounts of NBOs in their first coordination shell, but the proportions differ, with yttrium most able to satisfy its preference for NBOs, with 99% of its neighbours being NBOs. Previous work[13,17,31] has linked this bonding to the field strength of the cations, with atoms with higher field strength, such as Y (field strength ≈ 0.6 e Å^{-2}, where e is the charge of an electron) more able to satisfy its bonding preferences at the expense of cations with lower field strength, e.g. Ca (field strength ≈ 0.33 e Å^{-2}) or Na (field strength ≈ 0.19 e Å^{-2}). This explanation is consistent with our results here.

We have deliberately chosen our compositions to keep the Q^n distribution and network connectivity constant, and confirmed this was the case through direct calculation. The NC depends on the ratio of the numbers of oxygen to phosphorus atoms, so swapping Y_2O_3 groups for Na_2O or CaO will change this ratio and alter the network connectivity. To keep the network connectivity constant, we were therefore obliged to increase the phosphate content as Y_2O_3 content increased.

The most crucial parameter for the use of phosphate glasses in radiotherapy is the dissolution rate, and this will also be important for other applications. We follow on from our previous work and show that, because yttrium binds to more phosphate chains (4.2-4.3) than sodium (3.1-3.2) or calcium (3.8) does, the glass compositions containing more yttrium will be stronger and more resistant to dissolution, at least for compositions at constant network

connectivity. Since the effect of substituting Ca for Na on the dissolution is known to be very large[11], and the difference in number of chains bonded to Y compared to the number bonded to Ca, is only slightly smaller than the difference between those bonded to Ca and Na, it seems likely that yttrium incorporation into these glasses could allow their dissolution rate to be tuned over a very wide range indeed.

CONCLUSION

We have conducted classical molecular dynamics simulations of three yttrium-containing phosphate glass compositions and characterised the structure of the glasses. Yttrium acts as a network modifier with a bond length of 2.2Å and a coordination number of 6.3. Compared to the other modifiers present in the glass, sodium and calcium, yttrium has a higher atomic charge and field strength, and this means that its first coordination shell has a greater proportion of non-bridging oxygen atoms than in the shells of sodium or calcium. Crucially, it also bonds to more phosphate chains than either calcium or sodium, which strengthens the glass and makes it less prone to dissolution. Yttrium is used as a source of radiation for *in situ* radiotherapy, and the implication of our work is that the inclusion of yttrium into phosphate glass compositions would lead to a lower dissolution rate and low release rate of yttrium, and hence yttrium-containing phosphate glass could be potentially suitable for use in radiotherapy.

ACKNOWLEDGMENTS

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FIGURE CAPTIONS

Figure 1. The yttrium-oxygen partial pair-correlation function $g_{YO}(r)$, for the yttrium-containing glass compositions.

Figure 2. The partial pair-correlation functions $g_{NaO}(r)$, $g_{CaO}(r)$ and $g_{YO}(r)$, for Y6-PBG as a representative composition.

TABLES

Composition	P_2O_5 (mol%)	Na_2O(mol%)	CaO (mol%)	Y_2O_3 (mol%)	Density (g/cm^3)
Y-free	45.0	25.0	30.0	0.0	2.560
Y2-PBG	46.8	23.1	28.1	2.0	2.590
Y4-PBG	48.6	21.2	26.2	4.0	2.621
Y6-PBG	50.4	19.3	24.3	6.0	2.651

Table I. Compositions and densities of the glasses studied.

Table II. The interatomic potential used, consisting of a Buckingham term V_{ij}, three-body terms V_{ijk}, and a core-shell interaction V_{cs}.

	$V_{ij} = A \exp(-r/\rho) - C/r^6$		
	A (eV)	ρ (Å)	C (eV Å^6)
P-O$_s$	1020.0	0.34322	0.03
O$_s$-O$_s$	22764.3	0.149	27.88
Na-O$_s$	56465.3453	0.193931	0.0
Ca-O$_s$	2152.3566	0.309227	0.09944
Y-O$_s$	1444.836	0.347	0.1
	$V_{ijk} = \frac{1}{2} k_{3b} (\theta - \theta_0)^2$		
	k_{3b} (eV rad^{-2})	θ_0 (deg)	
O$_s$ -P-O$_s$	3.3588	109.47	
P-O$_s$ -P	7.6346	141.179333	
	$V_{cs} = \frac{1}{2} k_{cs} r_{cs}^2$		
	k_{cs} (eV Å^{-2})	O$_c$ (e)	O$_s$ (e)
O$_c$-O$_s$	74.92	+0.8482	-2.8482

Table III. Coordination numbers of the yttrium-containing glass compositions. Errors are standard deviations over the four independent models of each composition.

Composition	Na-O	Ca-O	Y-O
Y2-PBG	6.4 ± 0.0	6.5 ± 0.1	6.3 ± 0.2
Y4-PBG	6.5 ± 0.0	6.4 ± 0.1	6.3 ± 0.1
Y6-PBG	6.5 ± 0.1	6.4 ± 0.1	6.3 ± 0.1

Table IV. Proportion of non-bridging oxygen atoms in the first coordination shell of the modifier cations of the yttrium-containing compositions studied. Errors are standard deviations over the four independent models of each composition.

Composition	Na-O	Ca-O	Y-O
Y2-PBG	(76 ± 1)%	(94 ± 1)%	(100 ± 0)%
Y4-PBG	(76 ± 0)%	(93 ± 1)%	(99 ± 0)%
Y6-PBG	(75 ± 1)%	(93 ± 1)%	(99 ± 1)%

Table V. The average number of phosphate chains bound to each modifier atom, for the yttrium-containing compositions studied. Errors are standard deviations over the four independent models of each composition.

Composition	Na-O	Ca-O	Y-O
Y2-PBG	(3.2 ± 0.1)	(3.8 ± 0.1)	(4.3 ± 0.3)
Y4-PBG	(3.2 ± 0.1)	(3.8 ± 0.1)	(4.3 ± 0.1)
Y6-PBG	(3.1 ± 0.2)	(3.8 ± 0.1)	(4.2 ± 0.1)

Y6-PBG