Investigating structural features which control the dissolution of bioactive phosphate glasses: Beyond the network connectivity

Jamieson K. Christie *, Richard I. Ainsworth, Nora H. de Leeuw

Department of Chemistry, University College London, 20 Gordon Street, London WC1H 0AJ, UK

ABSTRACT

We have used classical molecular dynamics simulations to characterise the structure of three compositions of silver-containing phosphate glasses with 45 mol% P_2O_5, 30 mol% CaO, and varying amounts of Na_2O and Ag_2O. These compositions all have the same network connectivity, allowing us to highlight two other structural features which will affect the glass dissolution. Firstly, the number of different phosphate chains bonded to each modifier atom was computed and it was observed that silver and sodium bind to roughly the same number of phosphate chains, despite the differences in their local environments. Secondly, the clustering of modifier cations was characterised and shown to be enhanced at low concentrations of sodium and silver, but not to exist for calcium.

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1. Introduction

Very many different types of glasses are implanted into the body for medical reasons. Because of its amorphous structure, glass is not restricted to specific stoichiometries, as crystalline materials are. This means that glass has a wider range of possible compositions, and the properties of an amorphous implant can be tuned to optimise the efficacy of the therapy by varying the glass composition.

Glasses implanted into the body will react chemically with their local environment [1,2], and many will degrade [3,4]. Understanding the degradation is crucial [5]: the dissolution products of 45S5 bioglass are useful and promote the creation of new bone [6], by contrast, aluminosilicate glass compositions used for radiotherapy must be as durable as possible [7]. If a glass is to deliver a drug or nutrient at a specific rate, then its dissolution needs to be precisely controlled [8,9]. Much recent research work has sought to improve our understanding of glass dissolution processes and the structural and compositional features that affect them.

In principle, the factors which control glass dissolution are wide-ranging and could include the glass structure at various length scales, the diffusion of ions through the glass and their exchange between the surface and environment, changes in the glass surface structure, the solution chemistry and pH, among others. However, despite these possibilities, a good understanding of the glass dissolution can often be obtained from its bulk atomic structure alone, which is useful because the bulk structure is accessible from experiment and computer simulation.

The most important structural parameter which affects the dissolution of a glass is the *network connectivity* [10,11]. The network connectivity (NC) is defined as the average number of bridging oxygen (BO) atoms bound to a network-forming cation, where a BO atom is defined as an oxygen atom which is chemically bound to two network polyhedra. Oxygen atoms which do not connect two network polyhedra are called non-bridging oxygen (NBO) atoms. The NC depends critically on composition because the inclusion of network-modifying cations such as sodium or calcium typically breaks T–O–T bonds (where T is a network former, phosphorus in these glasses) causing the formation of NBO and decreasing the network connectivity [12].

High values of NC typically indicate a well-connected glass network which is not prone to dissolution and is not bioactive. Lower values indicate a fragmented, disconnected network which has many reactive sites and is both prone to dissolution and bioactive. 45S5 bioglass, which is highly bioactive and bonds to both bone and soft tissue, has a NC of 1.9; likewise, bioactive phosphate glasses which have 45 mol% P_2O_5 [3] have NCs of 1.8. Whilst bioactivity is difficult to define and is certainly not a precise function of NC, Hill [11] identified that compositions with NC as high as 2.6 can still be bioactive, but Tilocca identified that compositions with NC greater than 3.0 are bioinactive and very durable [12,13].

It was clear from its first uses [10,11] to describe glass structure, that the NC cannot capture all of the structural features which affect the dissolution. Recently, we and others have shown through computer simulation other features of the glass structure, particularly present at length

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* Corresponding author.
E-mail address: jamieson.christie@ucl.ac.uk (J.K. Christie).

Table 1
The simulated compositions (mol%) and their densities.

Composition	P_2O_5	Na_2O	Ag_2O	CaO	Density (g cm^{-3})
A5	45.0	20.0	5.0	30.0	2.707
A10	45.0	15.0	10.0	30.0	2.854
A15	45.0	10.0	15.0	30.0	3.001

scales beyond the first neighbour shell, which are also pertinent. We briefly outline some here:

 i. Clustering of network-modifying cations, such as Na, Ca, Ag, Sr, Y. These cations are not necessarily distributed evenly throughout the glass [13–16], and cluster together, which decreases bioactivity [12].
 ii. Mesoscale segregation of network. The NC can vary spatially throughout the material: for example, fluorinated 45S5 bioglass separates into silicate-rich and silicate-poor regions due to fluorine's preferential bonding to the network modifiers in the glass [17,18], which does not happen for fluorinated phosphate-based glass [19].
 iii. Modifier-chain bonding. For phosphate-based bioactive glasses with <50 mol% P_2O_5, the dissolution is controlled by the bonding of the phosphate chains to the modifier atoms [20], such that small changes in the Na/Ca ratio, which do not alter the NC, lead to order-of-magnitude changes in the dissolution rate [3,21].

In this work, we use an example multicomponent system, i.e., a silver-containing phosphate-based bioactive glass, with 45 mol% P_2O_5 and varying amounts of Na_2O, Ag_2O and CaO. In addition to the interest from the glass structure perspective, silver-containing glasses are known to be antibiotic [8,22]. Substituting Ag_2O for Na_2O leads to a decrease in glass dissolution rate [22] for glasses with 50 mol% P_2O_5. There is no evidence for mesoscale segregation of this system, and so we will concentrate on the other two factors, namely: clustering of modifier cations, and the nature of network-modifier-chain bonding and its changes with composition. These properties are accessible through the use of molecular dynamics (MD) simulation techniques, which have been used not just to study glass properties, but also to connect the atomic structure of glass to its use as biomedical implants [12,13,15,16,20, 23–25]. In this work, we use classical MD, in which the interatomic forces are approximated by an empirical expression. Although this approximation can introduce errors, it also reduces the computational expense sufficiently to allow us to model systems containing thousands of atoms, which are large enough to look at modifier-chain bonding and clustering. Smaller, more accurate, models created with first-principles MD, in which the forces are computed from a quantum-mechanical

representation of the electronic structure, are not large enough to allow this.

2. Methods

Classical molecular dynamics simulations were performed using the DLPOLY code [26] using a formal-charge, polarizable interatomic force field previously used by us to describe silver-containing [27] and other [20,28] phosphate-based bioactive glasses, in simulations which have given glass structures in agreement with experiment.

The simulation methodology used is identical to that in Ref. [27], which we outline briefly here. Models containing about 2000 atoms were prepared by randomly and independently placing atoms into a cubic periodic box of the appropriate density, subject to the constraint that no atom be closer to another than within ~85–90% of the expected interatomic separation. The densities of these compositions were extrapolated from the experimentally measured density of the Ag-free composition [29], using our knowledge of how Ag_2O substitution for Na_2O affects the density of very similar glass compositions [27]. After a short zero-temperature relaxation, the simulation was run in an NVT ensemble for 50 ps at 2500 K to equilibrate the liquid. The temperature was then reduced in units of 100 K, and at each temperature, the simulation was run for 50 ps, corresponding to a cooling rate of ~2 K/ps. At 300 K, the simulation was run for 250 ps, the last two-thirds of which forms the production run. All data stated are averaged over snapshots taken from this run. Simulated compositions and densities are given in Table 1.

Although this cooling rate is substantially faster than that used to prepare glasses experimentally, simulated cooling rates of this order of magnitude have been used to prepare accurate structural models of glasses in agreement with experimental results using classical molecular dynamics simulations [28,30].

3. Results

Pictures of the models at 300 K are given in Fig. 1.

Because the local silver environment in phosphate-based glasses has been studied before [27], as has the structure of Ag-free phosphate glasses [20,28], we mention them only in the context of those structural features which most profoundly affect the dissolution, which have not yet been characterised for these glasses.

The modifier–oxygen bond lengths and coordination numbers are given in Table 2. The coordination numbers are broken down into bonding to bridging and non-bridging oxygen atoms. Although all modifier atoms prefer to bond to NBO, when more than one are present, they "compete" to satisfy their preferred bonding environment [31]. This
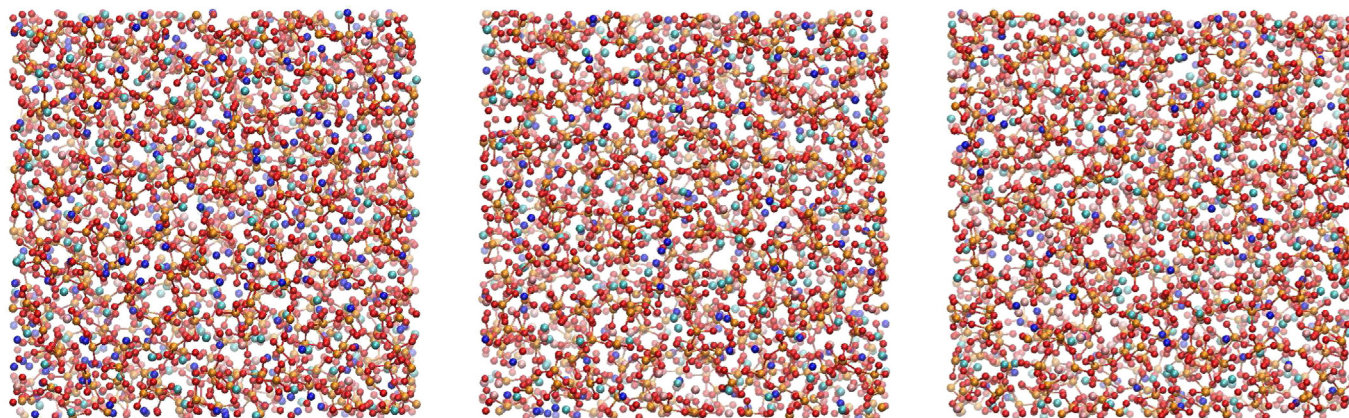

Fig. 1. Views of the A5 (left), A10 (middle) and A15 (right) compositions. The colours are red (oxygen), tan (phosphorus), dark blue (sodium), light blue (calcium) and pink (silver). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)