

Structure-property relationships in borophosphate glasses for soft-tissue regeneration: Insights from NMR spectroscopy and dissolution behaviour

By

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A thesis submitted to the Faculty of Graduate and Postdoctoral Studies of the University of Manitoba in partial fulfillment of the requirements of the degree of

Doctor of Philosophy

Department of Chemistry

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Winnipeg

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Abstract

Bioactive glasses have emerged as promising biomaterials for hard- and soft-tissue regeneration due to their ability to bond with biological tissues and stimulate healing. Originally introduced in 1969, silicate-based bioactive glasses such as 45S5 Bioglass, have paved the way for various glass compositions, including borate and phosphate glasses. While silicate and phosphosilicate bioglasses are primarily employed in orthopedic and dental applications, borate glasses have shown significant potential in soft-tissue engineering due to their higher degradation rates and ability to deliver therapeutic ions.

This research focuses on the structural and dissolution properties of borophosphate glasses designed for soft-tissue regeneration, aiming to establish an understanding of the composition-structure-property relationship to fine-tune the degradation rate of borophosphate glasses for optimal wound healing applications. A primary objective is the structural analysis of borophosphate glasses to detail their short- and medium-range order using magic angle spinning (MAS) nuclear magnetic resonance (NMR) spectroscopy, defining how borate and phosphate species form the glass network and how these structural units correlate with dissolution behaviour. While glass-ceramics have been widely studied in silicate-based bioactive glasses, little is known about phase separation in borophosphate glasses. This thesis examines the dissolution behaviour of phase-separated borophosphate glasses and its implications for bioactivity, particularly for applications such as tendon-to-bone repair. To enhance antimicrobial properties and promote wound healing, borophosphate bioactive glasses are doped with silver as a therapeutic ion. The degradation rates of these glasses will be optimized to ensure a controlled release of bioactive ions at the wound site, providing an alternative to antibiotic treatments. By correlating glass structure with dissolution behaviour and investigating the effects of phase separation and therapeutic ion incorporation, this research will contribute to the development of advanced biomaterials for soft-tissue engineering. The findings will aid in designing tunable bioactive glasses for wound healing applications, ultimately improving patient outcomes and advancing regenerative medicine.

Acknowledgements

My journey in the pursuit of knowledge has been successful thanks to the unwavering support and encouragement I have received from many individuals over the years. First and foremost, I express my deepest gratitude to my supervisor, Prof. Scott Kroeker, for his invaluable guidance and support. His encouragement and mentorship have been instrumental in shaping my understanding of the subject and broadening my academic perspective. I am forever indebted to him for his confidence in me, fostering new ideas, and providing numerous opportunities to present my work at prestigious conferences worldwide.

I extend my sincere appreciation to my Ph.D. committee members, Prof. John Sorensen, Prof. Douglas Thomson, and Prof. Christian Kuss, for their continuous guidance, insightful discussions, and invaluable contributions that have helped me achieve my research goals. My gratitude also goes to Dr. Arun Krishnamurthy for his mentorship during my early days, his friendship, and our cherished coffee-break discussions that enriched my experience.

I am thankful to the past and present members of the Kroeker research group, including, Lucas Segato, Angela Lu, Clara Zwanziger, Katrina Bergmann, Aiden Farrant, Surani Weerasundarage, Deep Hasnukhbhai Patel, James Zwaagstra, James Simmons, Kai Penner, Daniel Caceres, Kiera Palmer, Mykhailo Brytskyi and Thulasi Elumalai, for their friendship, scientific discussions, and for making my time in the lab truly enjoyable.

I extend my appreciation to Dr. Dave Davidson for his assistance with the NMR facility and their help in conducting experiments. I am also grateful to Ms. Emy Komatsu, Mr. Michael Opyr, Dr. Tom Ward and Dr. Ravinder Sidhu for granting me unrestricted access to analytical instruments, which was instrumental in the timely completion of my projects.

I am thankful to the Department of Chemistry and the Faculty of Graduate Studies at the University of Manitoba for providing me with the opportunity to study in Canada and for the financial support I have received over the years. My gratitude extends to the Chemistry Graduate Student Association and the Faculty of Science, U of M, for their travel grants, which enabled me to share my research at various scientific gatherings.

Finally, I wish to express my heartfelt gratitude to my wife for her unwavering support and encouragement. Her belief in me has been a cornerstone of my success, and I could not have reached this milestone without her.

Dedication

To my wife

For her love and support

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List of abbreviations and units

T_g	Glass-transition temperature
TTT	Time Temperature Transformation diagram
BO	Bridging oxygen
CN	Coordination number
NBO	Non-bridging oxygen
S/V	Surface-area-to-volume ratio
μm	Micrometer/microns
$\text{\AA}$	Angstrom
g/cm^3	Gram per cubic centimeter
K_B	Boltzmann constant
K	Kelvin
J	Joule
T_c	Critical temperature
CFS	Cation field-strength
$\hat{H}$	Hamiltonian
T_1	Spin-lattice relaxation or Longitudinal relaxation
T_2	Spin-spin relaxation or Transverse relaxation
RD	Recycle delay
NMR	Nuclear Magnetic Resonance
CT	Central transition
ST	Satellite transition
EFG	Electric field gradient
MAS	Magic angle spinning
PSD	Pre-scan delay
FID	Free induction decay
CPMAS	Cross-polarization magic angle spinning
G/L	Gaussian/Lorentzian
C_Q	Quadrupolar coupling constant
PXRD	Powder x-ray diffraction
XRD	x-ray diffraction
SEM	Secondary electron microscopy

SE	Secondary electron
BSE	Back-scattered electron
EDS	Energy-dispersive x-ray spectroscopy
ICP-OES	Inductively-coupled plasma optical-emission spectroscopy
NIR	Normalized ion release
SV	Surface-area-to-volume ratio
HA	Hydroxyapatite
OAp	Oxyapatite
T _m	Melting temperature
PBS	Pauling bond strength
BV	Bond valence
REDOR	Rotational echo double resonance
REAPDOR	Rotational echo adiabatic passage double resonance
MQMAS	Multiple quantum magic angle spinning
TQMAS	Triple quantum magic angle spinning
R-INADEQUATE	Refocused Incredible Natural Abundance Double QUAntum Transfer Experiment

1- Introduction

1-1- Oxide glasses

1-1-1- What is a glass?

Glass has been around for a long time, with natural types like obsidian predating life on earth. Synthetic oxide glasses, discovered around 6,000 years ago, are now widely used in various everyday and high-tech applications.¹ Some argue that we are currently in the "Glass Age" due to its crucial role in modern civilization.²

Traditionally, glass refers to inorganic materials formed by melting and cooling without crystallizing. This definition is used in standards like DIN, ISO, and ASTM.³ Over the years, many traditional and new types of glasses, including chalcogenide, fluoride, bromide, oxyfluoride, and oxynitride, have been developed, with around 400,000 compositions recorded in the SciGlass database.⁴ Recently, even hybrid metal-organic framework materials have been used to make glasses.⁵

The various definitions of glass have evolved over time in glass science. Gustav Heinrich Johan Apollon Tammann in 1933 called glass "undercooled solidified melts."³ Doremus in 1973 defined it as a material cooling from a liquid state, becoming rigid progressively.⁶ Wong and Angell in 1976 associated glass with x-ray amorphous material showing the glass transition.³ In 1976, Mari described glasses as amorphous solids obtained by fast cooling a molten mass.³ Zarzycki in 1982 characterized glass as a non-crystalline solid undergoing the glass transition.³ Rao in 2002 defined glass as a solid obtained by supercooling a liquid and is x-ray amorphous.⁷ In 2013, Gutzow and Schmelzer described glasses as thermodynamically non-equilibrium, kinetically stabilized amorphous solids.⁸ Varshneya's recent definition is that glass is a solid with a non-crystalline structure continuously converting to a liquid upon heating.⁹

A different and more detailed explanation was recently presented by Zanotto, highlighting the fundamental characteristics of glasses is as follows: "Glass is a nonequilibrium, non-crystalline condensed state of matter that exhibits a glass transition. The structure of glasses is similar to that of their parent supercooled liquids (SCL), and they spontaneously relax toward the SCL state. Their ultimate fate, in the limit of infinite time, is to crystallize." This definition is intended for those familiar with the concept of the glass transition.³

1-1-2- Types of glasses

Oxide glasses are a diverse family of materials used in both everyday items and advanced technological applications. They are composed of networks like borate, silicate, phosphate, borosilicate, and borophosphate, along with network modifiers including alkali metals, alkaline earth metals, and transition metals. In this thesis all experimental activities, discussion and properties are limited to oxide glasses. While the work in this thesis focuses exclusively on oxide glasses, a brief description of other types of glasses is provided to illustrate the versatility of glasses.

Chalcogenide glasses consist of S, Se, Te and possibly nearby elements in the periodic table including Ge and As. These elements have similar electronegativity and form covalent bonds which is contrary to more common glasses like silicates with more ionic nature. One of the primary applications of the chalcogenides is their utilization for optical purposes in the mid-infrared.¹⁰

Halide glasses, composed of fluorine, chlorine, bromine, or iodine, are interesting glasses due to their broad transparency spectrum, extending from ultraviolet to infrared wavelengths. However, synthesizing halide glasses is challenging. They require thorough experimental handling to ensure complete amorphous structure. Moreover, their predominantly ionic bonding makes them highly susceptible to moisture compared to conventional glasses oxide. These types of glasses are mainly used in optical applications and as hosts for ionic conduction.¹¹

1-1-3- Glass transition temperature

Upon cooling a glass from a melt, if crystallization is bypassed, the substance formed below the melting point is called a supercooled liquid. The change in the enthalpy of the melt as a function of temperature is shown schematically in Figure 1-1.

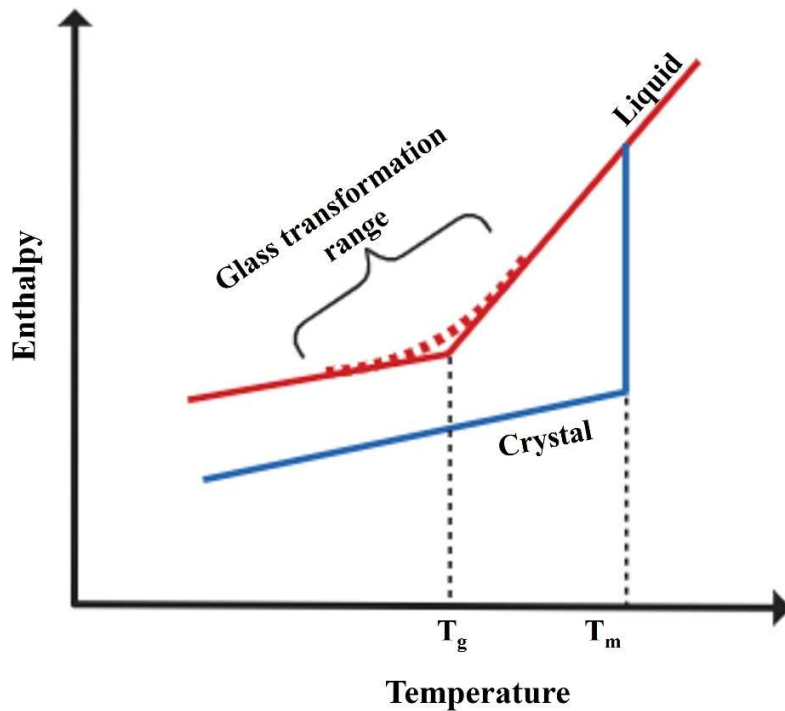


Figure 1-1) Effect of temperature on the enthalpy of a glass-forming melt. T_m and T_g denote the melting and glass transition temperatures, respectively.

For a glass-former composition there is no abrupt decrease in enthalpy, which contrasts with the behaviour of a crystalline material. In the case of the glass, further decrease in temperature results in an increase in the viscosity. This means that atoms cannot completely rearrange to the equilibrium crystalline structure. At this point the enthalpy starts deviating from the equilibrium line and a gradually decreasing slope is followed until it eventually becomes a frozen liquid. The viscosity of the frozen liquid, *i.e.*, glass, is too high and the structure of the liquid becomes fixed. The region between the limits where the enthalpy is that of the equilibrium liquid and that of the frozen liquid is called the glass transformation region.¹²

The glass transformation occurs within a range of temperatures; however, it is convenient to specify a single temperature to represent the onset of the glass transition range for a given glass composition. This temperature is known as the glass transition temperature, T_g , which is measured by a change in either thermal analysis curves or thermal expansion curves.¹² Angell suggested an alternative method for measuring the T_g , namely, the temperature at which the viscosity of the supercooled liquid is equal to 10^{12} Pa·s. Glass transition temperatures vary from below 50 K to above 1500 K depending on the glass composition.¹³

1-1-4- Why is a glass formed?

Although glass science has been studied for hundreds of years and it was first produced thousands of years ago, the answer to this question is not straightforward. In principle, any liquid vitrifies if the melt is cooled sufficiently quickly to bypass crystallization. This condition is widely applicable to many commercially available oxide glasses. SiO₂, GeO₂, B₂O₃ and P₂O₅ are among the oxides that easily form glass networks by themselves or in combination with other oxides. However, it is not easy to predict which composition under which conditions turn into a glass after cooling it from a melt. In fact, there are several factors contributing to understanding the glass forming ability of a melt, including the kinetics of vitrification, configurational complexity of the system, and structural factors.¹⁴

The following section, kinetic theory, briefly reviews the fundamental principles underlying the glass-forming ability of melts from a kinetic perspective. Although this section is not directly used to discuss the data presented in the various projects of this thesis, its importance in glass science and its relevance the concept of devitrification (see chapter 4), makes it worthwhile to include in this thesis.

Kinetic theory:¹⁵ The above discussion can be better explained by understanding the nucleation and growth kinetics in a melt: how fast must a melt be cooled to form a glass?

The free energy changes when a spherical nucleus is formed in a melt with the solid-liquid interfacial energy between the growing nucleus and the melt, γ_{sl} , and radius, r , is calculated as follow:

$$\text{Volume free energy} = -\frac{4}{3}\pi r^3 \frac{\Delta G_v}{V_m} = -\frac{4}{3}\pi r^3 \frac{\Delta H_f}{V_m} \left[\frac{\Delta T}{T_m} \right] \quad \text{Eq.1-1}$$

$$\text{Surface energy} = 4\pi r^2 \gamma_{sl} \quad \text{Eq.1-2}$$

where ΔG_v is Gibbs free energy, ΔH_f is enthalpy of fusion per unit mole and V_m is the molar volume of the crystal phase. By summing up eq. 1-1 and 1-2 the excess free energy change, ΔG_{exc} , is calculated as:

$$\Delta G_{exc} = 4\pi r^2 \gamma_{sl} - \frac{4}{3}\pi r^3 \frac{\Delta H_f}{V_m} \left[\frac{\Delta T}{T_m} \right] \quad \text{Eq.1-3}$$

The change in ΔG_{exc} as a function of r is plotted in Figure 1-2. ΔG_{exc} shows a maximum since the required energy for creation of a new surface scales with r^2 while the term of volume energy scales with r^3 . The required energy for overcoming the highest energy barrier for nucleation is called critical free energy, ΔG_c :

$$\Delta G_c = \frac{16\pi\gamma_{SL}^3 V_m^2}{3\Delta H_f^2 (1-T/T_m)^2} \quad \text{Eq. 1-4}$$

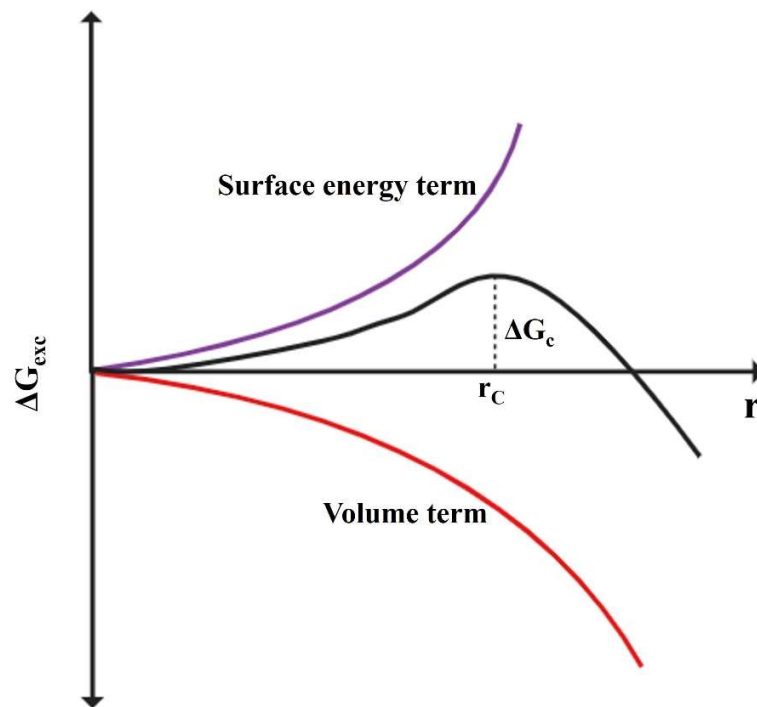


Figure 1-2) Free energy versus a nucleus radius for a given temperature lower than melting temperature, $T < T_m$

The rate of nucleation per unit volume (number of nuclei per cubic meter per second) is denoted by

$$I_v = vN_n^{\text{eq}} \quad \text{Eq. 1-5}$$

where v is the frequency of successful atom jumps across the nucleus liquid interface and N_n^{eq} denotes the metastable equilibrium concentration (per unit volume) of the nuclei. Then one can calculate I_v for homogenous nucleation as follows:

$$I_v = v_0 N_v \left[\exp \left(-\frac{\Delta G_m^*}{KT} \right) \right] \left[\exp \left(-\frac{\Delta G_c}{KT} \right) \right] \quad \text{Eq.1-6}$$

in which k is Boltzmann constant and ΔG_m^* is the free energy of activation that an atom needs to cross the nucleus-liquid interface. The first term and second exponential terms are called kinetic and thermodynamic barriers to nucleation, respectively.

The above discussion is valid for homogenous nucleation, however, in most cases crystals are nucleated on impurity particles, container walls and interfaces. These sites are preferred mainly because they have higher free energies: they reduce γ , and they decrease the strain energy that may suppress the nucleation and growth process.

In terms of heterogenous nucleation, the steady-state rate of nucleation of a supercooled liquid on a flat surface is calculated as below:

$$I_v = v_0 N_s \left[\exp \left(-\frac{\Delta G_m^*}{KT} \right) \right] \left[\exp \left(-\frac{\Delta G_{het}}{KT} \right) \right] \quad \text{Eq.1-7}$$

where N_s denotes the number of atoms or formula units of the liquid in contact with the substrate per unit area. ΔG_{het} is measured as

$$\Delta G_{het} = \Delta G_c (2-3\cos\theta+3\cos^3\theta)/4 \quad \text{Eq.1-8}$$

where θ is the contact angle between the γ_{lv} and γ_{sl} as shown in Figure 1-3.

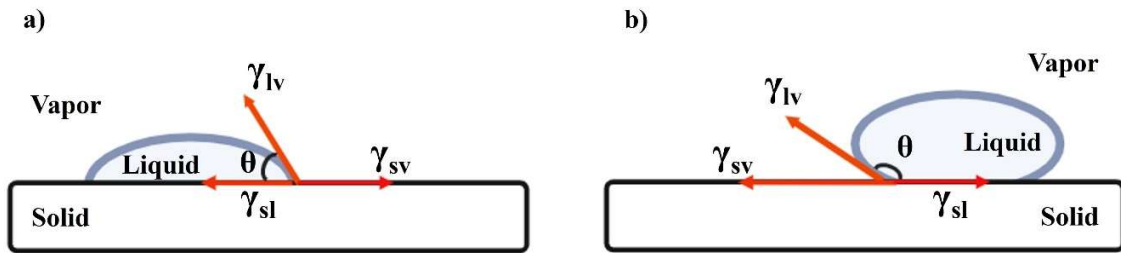


Figure 1-3) Wetting system showing forces acting on the liquid drop. A) wetting system and b) non-wetting system with $\theta > 90^\circ$ adopted from Reference [15]

After the formation of nuclei, a growth process will be followed which depends on the nature of the growing interface. It has been shown that this phenomenon is related to the entropy of fusion, ΔS_f . The growth rate u can be expressed by:

$$u = \frac{10KT}{3\pi\eta\lambda^2} \left[1 - \exp\left(-\frac{\Delta S_f \Delta T}{RT}\right) \right] \quad \text{Eq.1-9}$$

In this equation λ and η represent the jump distance and viscosity, respectively. ΔS_f is the entropy of fusion per unit mole and R is the ideal gas constant.

By determining the nucleation and growth rate of the crystalline phase, we can address the question of the critical cooling rate (CCR) of a melt necessary to prevent the detectable formation of a crystalline phase. The first step is plotting a time-temperature-transition (TTT) curve for a given composition (Figure 1-4). Using this plot one can determine the amount of time required for a specific volume fraction to crystallize at any temperature. This can be obtained by Johnson-Mehl-Avrami equation:

$$\frac{V_t}{V} = 1 - \exp\left(-\frac{\pi}{3} I_v u^3 t^4\right) \quad \text{Eq.1-10}$$

where V_t is the total volume transformed after time t .

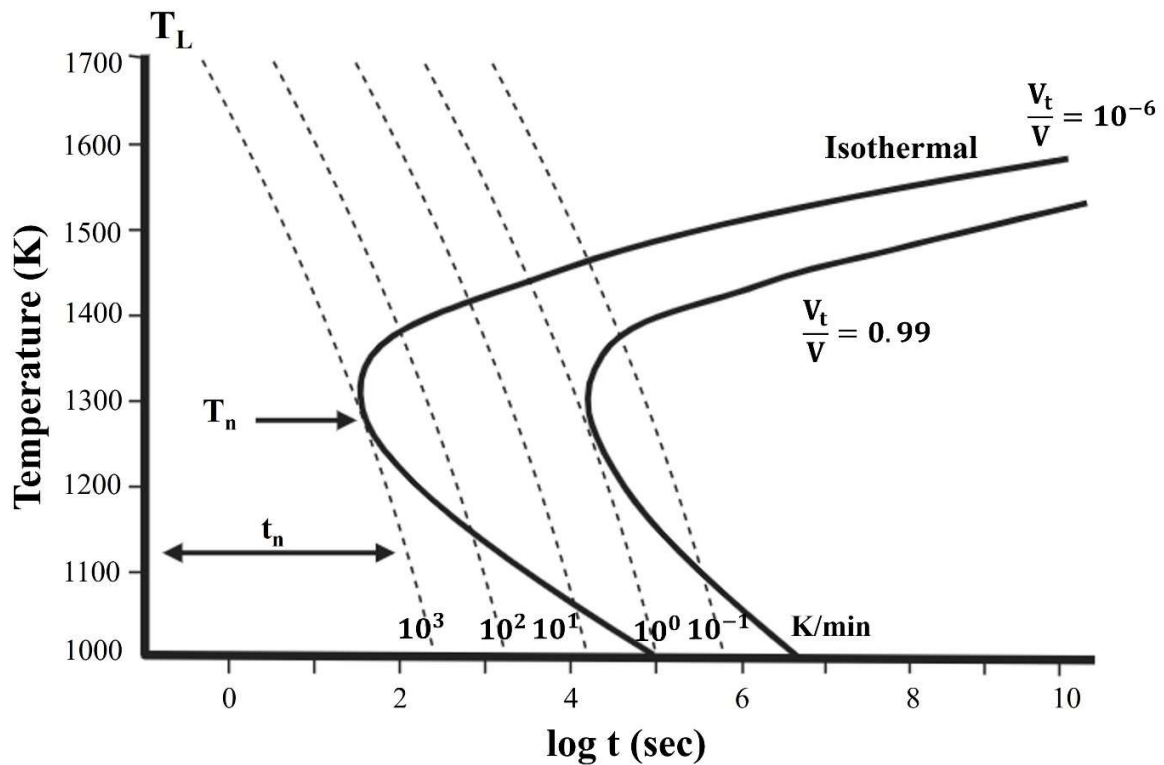


Figure 1-4) Isothermal Time-Temperature-Transition diagram. Adapted from Reference [15] T_n , and t_n are the temperature and time corresponding to the nose of the TTT curve, respectively.

Once the TTT diagram is constructed, the CCR can be calculated by the estimate below:

$$CCR \approx \frac{T_L - T_n}{t_n} \quad \text{Eq.1-11}$$

where T_L , T_n , and t_n are the temperature of the melt, and the temperature and time corresponding to the nose of the TTT curve, respectively.¹⁵

1-1-5- Structure of oxide glasses

The structure of oxide glasses is commonly explained by the Zachariasen–Warren random network model, which was proposed by Zachariasen in 1932¹⁶ and supported by early XRD studies conducted by Warren and colleagues.¹⁷ The structure of oxide glasses generally follows specific rules outlined by Zachariasen, including:¹⁸

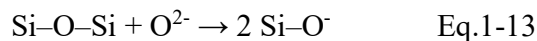
- 1- An oxygen atom (O) is not linked to more than two network-forming cations (A).
- 2- The coordination number (CN) of oxygen around the network-former cations must be small, i.e., 3 or 4 (CN of an atom is defined as the number of other atoms that are bonded to it).
- 3- The oxygen polyhedra should share corners with each other, not edges or faces.
- 4- For a three-dimensional network, at least three corners of each polyhedron must be shared.¹⁸

Based on Zachariasen's rules a commonly accepted model known as the *continuous random network* model has been developed. This model attributes the disordered structure of the glass network to the distribution of the M–O–M bond angle. For example, in a silicate-based glass the O–Si–O bond angles and Si–O bond lengths in an SiO₄ polyhedron are almost the same as those in a crystalline quartz. However, there is a distribution of the Si–O–Si bond angle which enables SiO₄ tetrahedra to connect together continuously and randomly to form a 3D network.¹⁸

The first coordination sphere of a cation is considered its *short-range order* which involves the cation and the surrounding oxygens. The *medium-range order* is defined as the connectivity between the structural units (polyhedra) that form the short-range order; in other words, the next-nearest neighbour of a given cation is the intermediate range order in oxides. In glasses, because of the distribution of the bond lengths and bond angles no periodic atomic arrangement is

observed. The structure of glass is primarily composed of network formers (e.g., SiO₂, B₂O₃) and network modifiers (e.g., Na₂O, K₂O, SrO).

Network formers are defined as the high field strength cations that can form a bond with oxygen with ionicity less than 50%. Si, B and P cations have high charges, relatively high electronegativities and form three and four-coordinated structural units. Since they form strong bonds and interconnected structures, their melts show high viscosity, slow diffusion and crystal growth rate, all of which are conducive to favourable glass-forming ability.¹⁹ When oxygen connects two network formers it is called a *bridging oxygen* (BO). Oxides with larger size and lower charges (e.g., alkaline earth and alkalis) are categorized as *network modifiers*. In the glass structure, these cations have a predominantly ionic interactions with oxygen. Another important characteristic of network modifiers is that they can not form an extended three-dimensional network backbone by their own. When a network modifier is introduced to the pure network former melt, *non-bridging oxygens* (NBO) are formed. According to the following reaction, the O²⁻ anion from the network modifier oxide, for example Na₂O, interacts with the bridging oxygen connecting SiO₄ tetrahedra which results in the formation of an NBO¹⁹



The accompanying cations, i.e., Na⁺, act as charge compensators and interact electrostatically with the newly formed anionic species, Si-O⁻, to preserve the neutrality of the whole composition.¹⁹

Alkali and alkaline earth cations can function differently in borate glasses. In these glasses in addition to their network modifying role, they charge-compensate the anionic species. In such cases, the following reaction occurs:¹⁹



This mechanism dominates up to 20-30 mol% modifier oxide, beyond which the formation of NBOs begins to become important.²⁰

Some oxides, such as Al₂O₃ and TiO₂, can function as either network formers or modifiers depending on the overall glass composition. These are referred to as intermediate oxides. Intermediate oxides do not easily form glass on their own, but they can do so when combined

with a modifier, as has been observed for Al_2O_3 in $\text{CaO-Al}_2\text{O}_3$ melts. Apart from Al_2O_3 , other significant conditional glass formers include Ga_2O_3 , Sb_2O_3 , TiO_2 , TeO_2 , V_2O_5 , Nb_2O_3 , and Bi_2O_3 . For example, the networks in binary aluminate and gallate glasses are based on $\text{AlO}_{4/2}$ and $\text{GaO}_{4/2}$ tetrahedra, respectively. $\text{O}_{4/2}$ means that all four oxygens in an Al- or Ga-tetrahedron are shared with another network former, i.e., are bridging oxygens. However, in more complex systems involving a glass former, aluminum can exhibit mixed four-, five-, and six-coordination.¹⁸ In Figure 1-5 a schematic of a glass structure with its components is depicted.

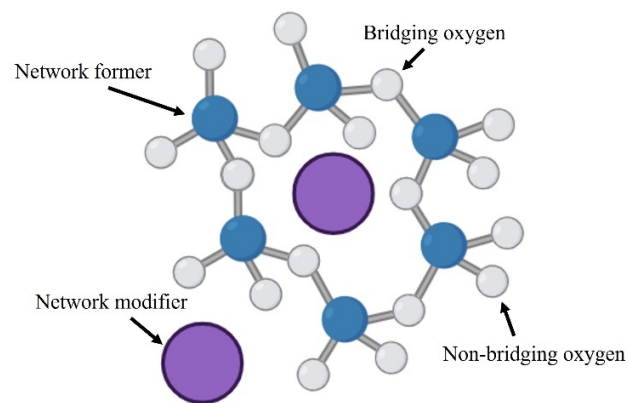


Figure 1-5) Schematic of the structure of a glass

Zachariasen's model can be used to predict the presence of major oxide glass formers such as SiO_2 , GeO_2 , B_2O_3 , P_2O_5 . However, there are a few limitations associated with the model including lack of consideration for modified oxides, multicomponent systems, and non-oxide glasses. Moreover, exceptions to its principles are evident, as seen in alumina-lime glasses and chain-like glass structures, such as metaphosphate glasses.¹⁴

An alternative criterion for glass formation, proposed by Stanworth, stipulates that the electronegativity of cations in oxide glasses should range between 1.90 and 2.20.²¹ In some glass-forming systems, electronegativity alone is not sufficient to determine whether a glass will form. This happens when bond strength (which depends on factors like ionic size, charge, and coordination number) plays a crucial role in stabilizing the glassy structure. In such cases, just knowing the electronegativity range is not enough, and additional factors like bond strength must also be considered to accurately predict glass formation.¹⁴

Dietzel²² assessed the incorporation of cations into the network structure based on their field strength, defined as

$$\text{CFS} = \frac{z}{r^2} \quad \text{Eq.1-12}$$

where z represents cationic charge and r indicates the mean cation-oxygen bond length (in Å). Lower field-strength cations (e.g., alkalis) are considered as network modifiers, while those with higher field strengths (e.g., Si, P, or B) are network formers (Table 1-1).²³ However, while this theory aids in categorizing the glass-forming propensity of conventional systems, it does not apply universally.²⁴

Table 1-1) Cation field-strengths of some cations for the specified coordination numbers (Reference 23)

Cations	Mean bond length(Å)	Coordination number	Field-strength ($z/\text{Å}^2$)
Si⁴⁺	1.625	4	1.51
B³⁺	1.475	4	1.38
P⁵⁺	1.537	4	2.13
Al³⁺	1.746	4	0.99
Na⁺	2.441	6	0.16
Ag⁺	2.537	6	0.15
Ca²⁺	2.398	6	0.36

1-1-6- Phosphate glasses

Historically phosphate glasses have been used in various applications including water-stable compositions in the 1940s,²⁵ development of solid-state lasers in the 1960s, and utilization in nuclear waste immobilization by the 1970s. Recent innovations have resulted in manufacturing absorbable medical devices and controlled delivery of trace elements. Additionally, their intriguing electrical properties have prompted research into their applications in dielectrics, semiconductors, and fast-ion conductors.²⁶

In crystalline compounds containing PO₄ units, despite being flexible, the P–O bond length has a range centered at about 1.54 Å, with the largest 1.555 Å for Li₃PO₄ and the smallest 1.516 Å for AlPO₄. Internal and intra-tetrahedral angles of the PO₄ units are, 110-120° and 125-153°,

respectively.²⁷ Since the short-range order in crystalline compounds and glasses is comparable, this information is used for characterizing the phosphate glasses. Condensed phosphates form chains and networks with corner-sharing tetrahedral PO₄ groups.^{28,29} Chains of 5–10 tetrahedra are typically straight due to charge repulsion, while longer chains increase in flexibility.²⁶

Phosphate groups are categorized by Pⁿ species based on the number of bridging oxygens in a tetrahedron. Compared to silicates, due to the 5+ nominal charge of phosphorus, PO₄ units have a double bond.²⁶ Therefore, the maximum number of BO for a given stable Pⁿ species is n=3, P³, which is called ultraphosphate. In the case of n=0, an isolated orthophosphate is formed.

The short-range structures of binary phosphate glasses can be described by the type and concentration of phosphate tetrahedra present. Van Wazer³⁰ established relationships to show how the distribution of tetrahedral sites in binary alkali phosphate glasses depends on composition. When a network modifier oxide, R₂O, is added to a phosphate glass, the degree of network connectivity is reduced by substituting highly inter-connected tetrahedra with ones containing more non-bridging oxygens to preserve charge balance:



Figure 1-6 shows the molecular diagram of these phosphate units. In cases where multiple phosphorus atoms are shown, the phosphorus shaded in grey represents the designated cation for charge calculations. It should be noted that P³ is a neutral species, while P², P¹, and P⁰ are anionic species carrying 1, 2, and 3 negative charges, respectively.

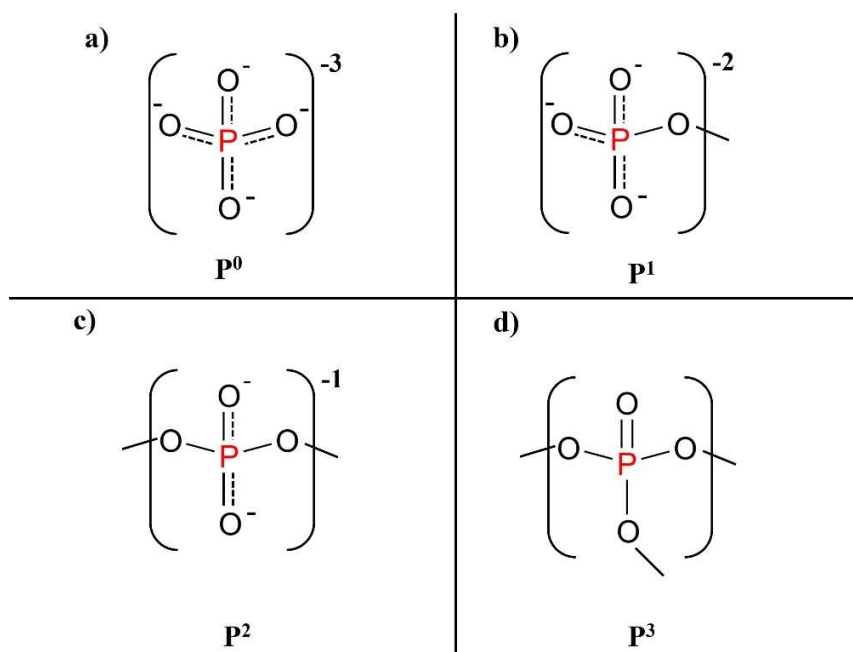


Figure 1-6) Schematic of phosphate species in phosphate glasses. a) P⁰, b) P¹, c) P² and d) P³.

³¹P magic angle spinning (MAS) NMR is effective in validating these compositional predictions as it can distinguish peaks corresponding to phosphorus in tetrahedra with varying degrees of polymerization. The isotropic chemical shifts are typically around 20 ppm apart, while the peak widths are relatively narrow (see Figure 1-7).^{31,32}

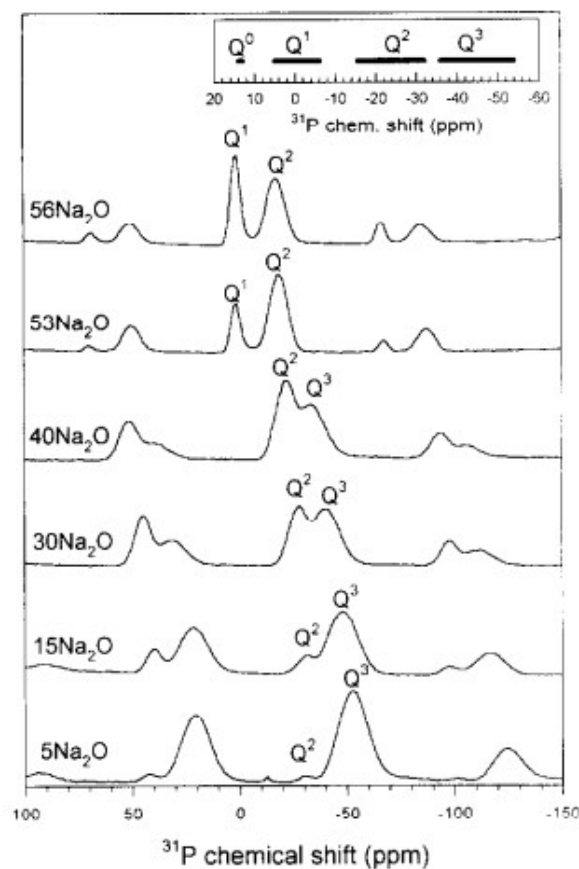


Figure 1-7) ^{31}P MAS NMR in a $\text{Na}_2\text{O}-\text{P}_2\text{O}_5$ glass series from reference [32] (in this figure Q^n denotes P^n species), which shows the change in phosphate species with changing Na_2O content.

1-1-7- Borate glasses

Borate glasses have been widely used in industry and have attracted significant attention from the scientific community due to their versatile properties. Boron oxide is commonly added to commercial glasses, offering benefits such as lowering the working temperature of the glass in a controlled way. Borate-based glass systems are particularly suitable for biomedical applications^{33–35} lithium batteries,³⁶ and optical and optoelectronic application.³⁷ Reference [37] reviews the application of borate glasses in industry.

The density of boron oxide glass varies depending on its preparation and annealing conditions, typically falling within the range of 1.80 to 1.90 g/cm³. This density differs considerably from that of crystalline boron oxide, which has a 2.46 g/cm³ density at room temperature. Therefore, borate glasses are notably less dense than crystals, with only about 75%

of their density because of boroxol rings (see below).³⁸ The crystalline form of boron oxide melts at 450 °C, with a boiling point of 1860 °C. However, the glass transition temperatures (T_g) of borate glasses are influenced by factors like water content, measurement techniques, and quenching rate, making it a complex property to define. Reported T_g values in the SciGlass database range from 200 to 300 °C, with the majority falling between 250 and 280 °C.³⁹

When boron (B^{3+}) reacts with oxygen (O^{2-}), it forms a boron ion coordinated with three oxygen atoms, while each oxygen atom is coordinated with two boron atoms. This arrangement can be described as sp^2 hybridization, resulting in triangular boron-oxygen structures observed in both crystalline and glassy forms of boron oxide (Figure 1-8a).³⁹ The significant difference in density between the crystal and glass indicates that the structure of borate glasses differs substantially from its crystalline polymorph at room temperature. Spectroscopic analysis suggests that in boron oxide glass, approximately 65-80% of boron atoms are arranged in boroxol rings, as depicted in Figure 1-8c. However, such rings are not present in the B_2O_3 crystal structure.⁴⁰

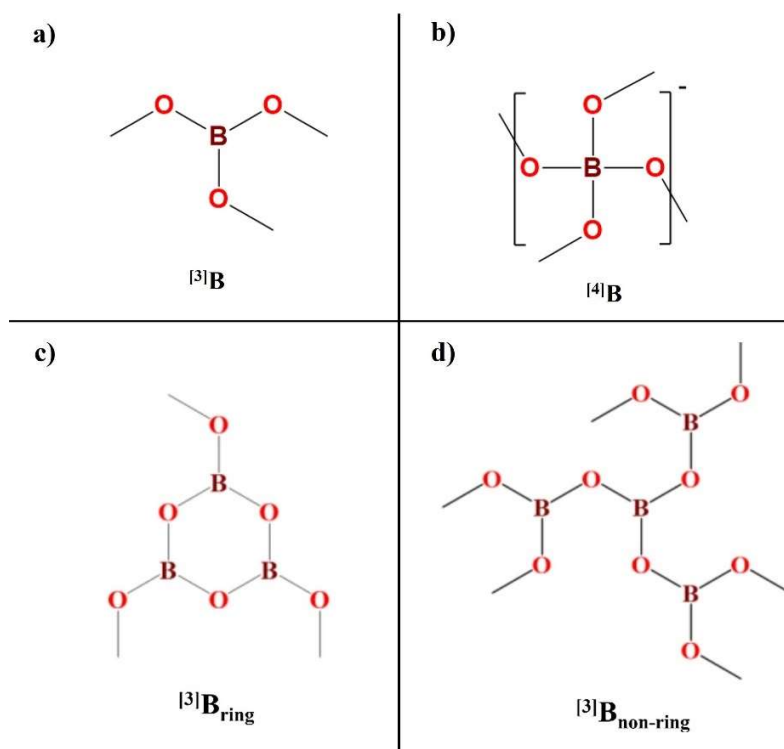


Figure 1-8) Molecular diagram of a) $[3]B$ (three-coordinated boron), b) $[4]B$ (four-coordinated boron) c) three-coordinated boron with ring and d) non-ring configuration in a borate glass

In 1958, Silver and Bray used nuclear magnetic resonance (NMR) for investigating the structure of borate glasses.⁴¹ They reported that boron exists in borate glasses with two coordination numbers, 3 and 4. The fraction of four-coordinated boron, denoted N_4 , is determined by²⁰

$$N_4 = \frac{I(^{[4]}\text{B})}{I(^{[4]}\text{B}) + I(^{[3]}\text{B})} \quad \text{Eq.1-19}$$

where $I(x)$ is the integrated intensity obtained from fitting ^{11}B MAS NMR spectra. Because oxygen is more electronegative than boron, the negative charge on the BO_4^- tetrahedron is spread out across the entire structural unit. Consequently, it is energetically unfavorable for BO_4^- tetrahedra to be immediate bonded neighbours. This structural explanation was proposed by Abe for the first time in 1952.⁴² It is worth noting that the heteropolar B–O bonds of the BO_3 structural units in vitreous B_2O_3 are already polarized, resulting in a slight negative charge (δ^-) on the oxygen atoms and a corresponding positive charge ($3/2\delta^+$) on the boron atoms.

In binary $\text{Na}_2\text{O}-\text{B}_2\text{O}_3$ glasses, N_4 reaches a maximum at 30 mol% of Na_2O , or $R = 0.43$ (Figure 1-9). However, it should be noted that the R value at which N_4 reaches a maximum depends on the types of the network modifier.⁴³ In principle, boron coordination in melts and glasses is strongly governed by the composition, temperature, and pressure.⁴⁴

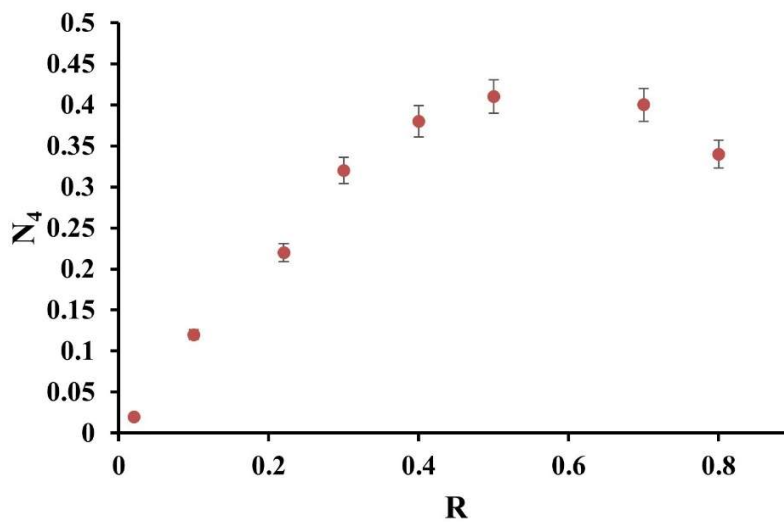


Figure 1-9) The fraction of four-coordinated boron, $^{[4]}\text{B}$, as a function of $R=\text{Na}_2\text{O}/\text{B}_2\text{O}_3$ from reference [20]

In addition to these parameters, the cation field strength of the network modifier plays an important role in N_4 value. For instance, a review of several investigations into the binary alkali borate system indicates that modifier oxides with stronger cation field strength might encourage the formation of four coordinated boron in certain compositions.⁴⁵ Recent findings from advanced, high-resolution ^{11}B MAS NMR studies on lithium borate glasses show higher N_4 values compared to sodium borate glasses when R exceeds 0.5. A general trend is observed among Na-, Rb-, and Cs-borate glasses.^{20,43}

1-1-8- Dissolution mechanism in oxide glasses

When oxide glasses interact with water, several phenomena can take place. Hydration involves water molecules penetrating the glass structure, potentially disrupting interactions between network elements. Hydrolysis occurs when water molecules directly react with the covalent M–O bonds in the glass network, in which some reversibility is possible. Ion exchange happens when ions from the solution replace modifier cations in the glass, with selective leaching occurring if a proton replaces the modifier. Selective leaching reactions are typically irreversible due to the formation of hydroxyl groups, which can lead to condensation reactions or network hydrolysis, removing ion exchange sites. Selective dissolution refers to the removal of incorporated species from the glass network, often through irreversible hydrolysis and condensation reactions. If the most reactive sites are network-forming elements, the entire glass structure can dissolve uniformly. These reactions can occur sequentially or simultaneously, making glass dissolution a complex process with parallel reactions. Specific examples illustrating the interplay between these reactions depend on the structure and chemistry of the glass compositions.⁴⁶

1-1-8-1- Dissolution stages for oxide glasses

The process of oxides dissolving in water solutions is crucial for various applications. It plays a critical role in determining the chemical resistance of industrial ceramics, the effectiveness of nuclear waste immobilization, degradation of the biomaterials in the body, and the natural breakdown of minerals. Understanding the thermodynamic equilibria and kinetics of these dissolution reactions is essential for predicting the rate at which oxides dissolve.⁴⁷

The dissolution behaviour of silicate glasses is well established and the involved mechanisms have been studied meticulously.⁴⁶ Therefore, in this section the fundamental aspects of glass dissolution are discussed based on the interactions of silicate-based glasses with water which is generally applicable to other types of oxide glasses.

The resistance of glass to water corrosion, known as chemical durability, is not solely about the glass itself but also depends on various factors including the chemistry of the dissolving medium. Reactions between a glass and water involve ion exchange, hydrolysis of network forming species, and dissolution of hydrolysed species into the solution. These reactions release glass components into the solution or incorporate them into alteration products on the glass surface. Factors like temperature, solution pH, and concentration of dissolved species control the reaction rates. Ion exchange, hydrolysis, dissolution, and alteration product formation processes are interconnected, primarily by the solution chemistry and properties of the amorphous layer on the glass surface. This combination leads to three characteristic stages of reaction progress (Figure 1-10).⁴⁶

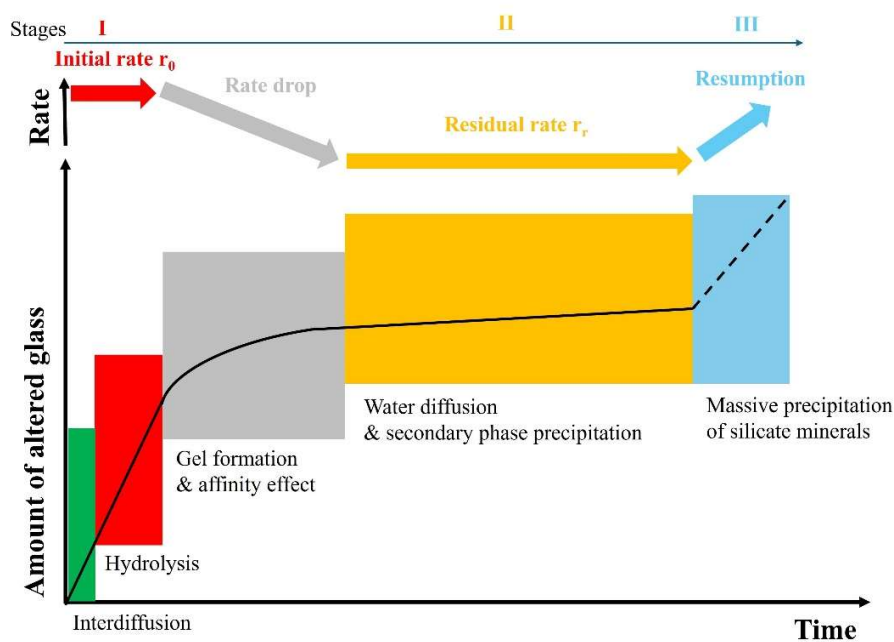


Figure 1-10) Stages of glass corrosion in silicate and borosilicate glasses, adapted from reference [46]

Stage I involves the initial corrosion of the glass surface without solution feedback. This stage is called *the forward rate* and is denoted by r_0 . For a given temperature and pH, stage I has the maximum dissolution rate which is governed by the hydrolysis of the network former units. As time goes by and the solution is filled more with the ions leached from the glass, the driving force for dissolution is diminished. Eventually, as the solution becomes saturated with Si a solution layer boundary forms; a passivation layer precipitates on the surface, signalling the onset of stage II. This phase, also termed the *residual rate regime*, sees a decline in the reactions observed in stage I, halting glass dissolution and restoring its durability. Factors such as pH, temperature, glass composition, and solution composition greatly influence the kinetics and duration of stage II. In stage III, zeolites and other silicate phases crystallize from the amorphous Si layer, depleting it of Si and eventually leading to the loss of this protective layer. This stage marks the recurrence of glass dissolution, as the protective barrier is compromised.⁴⁶

The time spent in each stage depends on environmental parameters like temperature, pH, solution composition, flow, and glass composition. In fast-flowing environments, Stage I dominates, while in slow or static conditions, Stage II is quickly reached. Stage III may occur in some systems with the precipitation of secondary phases, but not always, with some systems exhibiting slow alteration rates akin to Stage II behaviour for extended periods.⁴⁶

1-1-9- Phase separation

Phase separation has frequently posed challenges in glass production. It alters the uniformity and the physical and chemical properties of the molten glass, making it difficult to shape, and reducing the quality of the finished glass.⁴⁸ There are two types of phase separation in glasses, liquid-liquid phase separation and crystalline phase separation in an amorphous matrix. Liquid-liquid phase separation is not the interest of this work. Specific compositions of borophosphate glasses are prone to crystalline phase separation if it exists. This phenomenon is better understood by considering the cation field strength, CFS, of various cations. In borophosphate glasses containing network modifiers with high CFS such as Ca^{2+} and Mg^{2+} , the formation of crystalline compounds is more likely than a borophosphate glass with Na^+ and Cs^+ as the network modifier. This is because P^{5+} cations with high CFS can induce strong ordering of the oxygen anions about the cations, leading to clustering, and ultimately to nucleation and crystallization of phases that separate from the glass. It should be emphasized that crystalline

phase separation is a complex phenomenon which is governed by the composition of the glass. The ratio of B to P, the type, amount and number of the network modifiers and cooling rate can vary the homogenous vitrification of the melts significantly.

1-2- Biologically active glasses

Biomaterials play a vital role in numerous applications, including cardiovascular devices, wound healing, implants, dental treatments, orthopedics, and tissue engineering.⁴⁹⁻⁵³ Scientists in both industry and academia have dedicated significant research and development efforts to biomaterials over the past decades. These materials possess distinct properties like bioactivity, mechanical similarity to tissues, and compatibility with biological systems, making them essential components in various medical applications.⁵⁴

In the 1960s, the first generation of biomaterials aimed to closely match the chemical and physical properties of host tissues to minimize cytotoxic responses.^{34,55} This generation focused on achieving "inertness" to prevent foreign body reactions or biological rejection. Molecular biology, emerging in the 1970s, greatly contributed to the fields of biomaterials and biomedical engineering, especially when integrated with advancements in genomics and proteomics. In the following decades, research shifted towards developing bioactive materials capable of eliciting appropriate biological responses, particularly at the interface between biomaterials and host tissues.⁵⁴

Over the past decade, there has been significant innovation in biomaterial development, fueled by advancements in molecular biology. This progress has provided a solid framework for comprehending concepts like degradation kinetics, biocompatibility, and synthesis techniques. As a result, there is now an unparalleled understanding of biomimetic and smart biomaterials, capable of mimicking nature's hierarchical structures.⁵⁴

Bioactive glasses and ceramics hold great promise for clinical use because of their excellent biocompatibility, bioactivity, and versatile compositions and properties. In 1969, Hench developed the first bioactive glass, Bioglass 45S5, which has been FDA-approved and utilized in clinical settings since the 1980s.⁵⁶ Hench conducted his research on developing a material capable of bonding with bone after a discussion with a US Army colonel during a bus ride. The colonel, recently returned from the Vietnam War, inquired about the possibility of creating

materials durable enough to survive the harsh conditions inside the human body. Available implant materials at the time, such as metals and polymers designed to be biologically inert, tended to cause fibrous encapsulation instead of establishing a stable connection with tissues after implantation.⁵⁷ He came up with degradable glass within the $\text{Na}_2\text{O}-\text{CaO}-\text{SiO}_2-\text{P}_2\text{O}_5$ system, featuring a high calcium content. This composition was chosen because when it is immersed in the simulated body fluid it forms hydroxyapatite (HA), which is the composition of the bone mineral. The significant finding came with the discovery that a glass with the composition 46.1 SiO_2 , 24.4 Na_2O , 26.9 CaO , and 2.6 P_2O_5 (mol%), later named 45S5, formed an exceptionally strong bond with bone, which could not be removed without fracturing the bone.^{58–61}

Afterward, a new era was established in the field of materials science, bioactive ceramics leading to the development of numerous new materials and products derived from variations of bioactive glasses including glass-ceramics, and ceramics like synthetic hydroxyapatite and other calcium phosphates.⁵⁰ In this context, a *bioactive material* refers to a substance that elicits a favourable response from the body, typically by forming a bond with host tissue, most commonly bone.⁶² It should be noted that bioactivity is no longer limited to the formation of a HA layer on the bioactive glass, and the emergence of borate and borophosphate glasses as potential medications for soft-tissue regeneration requires a more general definition: a bioactive glass is a material that elicits a response within the biological system. This could be either the formation of a new bond between the tissue and the biomaterial or inducing healing mechanisms involved in wound treatment.

With further research and development, the applications of bioactive glasses have expanded to a wider range of clinical uses. These include the use of 45S5 bioactive glass in middle ear prostheses for patients with conductive hearing loss, as well as its incorporation into certain toothpaste formulations like NovaMin, where it serves as a desensitizing agent to alleviate dentin hypersensitivity.

Yan et al. developed a new type of bioactive glasses known as mesoporous bioactive glasses in 2004.⁶³ The development of these nanostructured bioactive glasses increased the interest in their potential as delivery systems for therapeutic compounds such as drugs, proteins, and phytochemicals. Researchers aim to use these materials to trigger biological processes that facilitate tissue regeneration in organs with defects.⁶⁴ More recently, bioactive glasses have been

explored for their potential in healing epithelial tissues and promoting soft tissue regeneration, particularly in certain aspects of wound healing applications.⁶⁵

In contrast to hard tissue regeneration in which a relatively durable glass is required to be able to form a new layer on its surface, researchers seek fast-dissolving compositions for soft tissue engineering. In this case, the idea has been shaped based on the fact that tissue attachment is not considered necessary; however, delivering ions to the injury site to stimulate a biological response in order to accelerate healing becomes paramount. In addition, providing fast treatment for injuries like burns and skin wounds becomes vital when bacterial infections are likely to occur. By taking into account these criteria, boron-based glasses are considered the most promising candidates in this field since their degradation rate is higher than silicate glasses; their relevance to wound healing has already begun to be exploited.⁶⁶

Bioactive glasses have gained attention for wound treatment applications due to their capacity to incorporate biologically active elements like Ag, Mg, Sr, and Zn into their networks. These glasses release ions when exposed to a fluid environment, which can stimulate various cell functions such as epithelial cell migration and fibroblast proliferation. Additionally, they can induce angiogenesis, promote hemostasis, and exhibit antibacterial properties. As a result, these materials can influence different stages of the wound healing process.⁶⁵

1-2-1- Borophosphate glasses for wound healing

Borophosphate glasses have captured the attention of glass scientists due to their versatility in various applications such as ionic lithium batteries⁶⁷, biomaterials⁶⁸, catalysts⁶⁹, and optical uses.⁷⁰ Borophosphate glasses contain two network formers, namely P^{5+} and B^{3+} . The presence of multiple network formers in the structure of the glass results in interesting characteristics, thanks to structural units like P_{mB}^n (where n ranges from 1 to 3 and m from 0 to 3) and $[4]B_{nP}$ where n is the number of phosphorus in the next nearest neighbour of a given boron tetrahedron. For example, P_{1B}^3 is a phosphate species in which a PO_4 is linked to two PO_4 and one BO_4 unit, as shown in Figure 1-11. In glasses there is a relationship between the composition, structure and properties. Since borophosphates boast versatile structural units, their properties can be tuned more widely than borates and phosphates, in which only one network former constructs the glass network. In the case of soft tissue regeneration, particularly wound healing, the flexibility in the

dissolution rate, pH of the solution, and therapeutic ions offers additional benefits to these glasses.

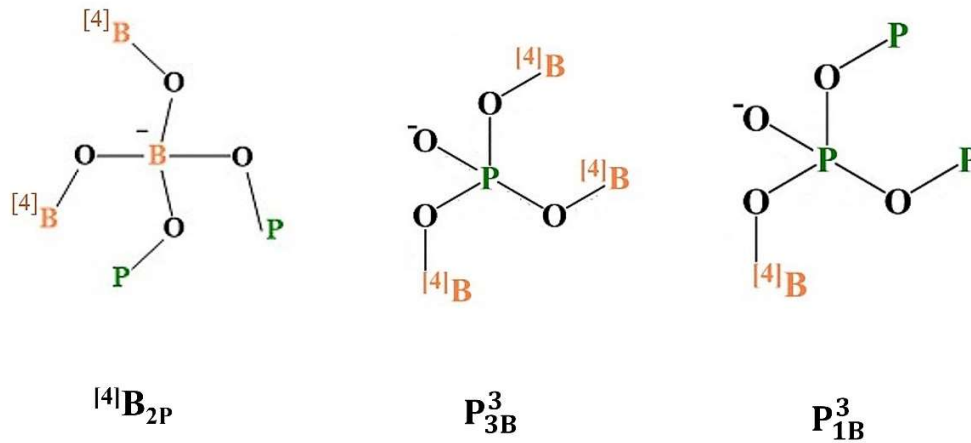


Figure 1-11) Schematic of phosphate and borate units in a borophosphate glass

This study aims to investigate the atomic-level structure of potential borophosphate glasses and correlate these insights with their dissolution characteristics. Such understanding will empower scientists and engineers in product design, leveraging insights into the behaviour of bioactive glasses within the human body. Key attributes of the envisioned product include a controllable degradation rate and a straightforward fabrication

1-3- Nuclear Magnetic Resonance Spectroscopy

1-3-1- Angular momentum and nuclear magnetism

A magnetic nucleus has an intrinsic angular momentum, which is called spin, with the quantized magnitude of $\sqrt{I(I+1)}\hbar$, where the spin quantum number I for a given nucleus may have one of the following values:

$$I = 0, \frac{1}{2}, 1, \frac{3}{2}, 2, \dots$$

Isotopes of the same element may have different quantum numbers. For example, the spin quantum numbers for ^{13}C and ^{12}C are $\frac{1}{2}$ and 0, respectively, meaning that ^{13}C is an active NMR nucleus while ^{12}C with $I = 0$ has no angular momentum, no magnetic moment and consequently no NMR response. It should be noted in the following section “spins” will be used as a synonym for magnetic nuclei as is common practice in NMR.^{71,72}

Angular momentum can be conceptualized as a vector, denoted by $\vec{I}$, with quantized direction and magnitude. In this vector representation, it has $2I + 1$ allowed projections onto an arbitrarily chosen axis, typically labeled as the z-axis. Thus, the projection of $\vec{I}$ onto the z-axis is $I_z = m\hbar$ where m is the magnetic quantum number, taking on $2I + 1$ values ranging from $-I$ to $+I$.

$$m = I, I-1, I-2, \dots, -I$$

For example, in the case of a spin- $\frac{1}{2}$ nucleus, the angular momentum has two permitted z-components, $+\frac{1}{2}\hbar$ and $-\frac{1}{2}\hbar$. The I_z for a nucleus with $I = 1$ is as follows: $I_z = -\hbar, 0$, and $+\hbar$. The space quantization of the above examples is shown in Figure 1-12.

1-3-2- Nuclear magnetic moments

The magnetic moment of a nucleus is proportional to its spin. The magnetic moment, which is a vector quantity, is linked to the angular momentum $\vec{I}$ by the equation

$$\vec{\mu} = \gamma\hbar\vec{I} \quad \text{Eq. 1-20}$$

where γ is the gyromagnetic ratio of the nucleus and $\hbar$ is called reduced Planck constant ($=h/2\pi$).

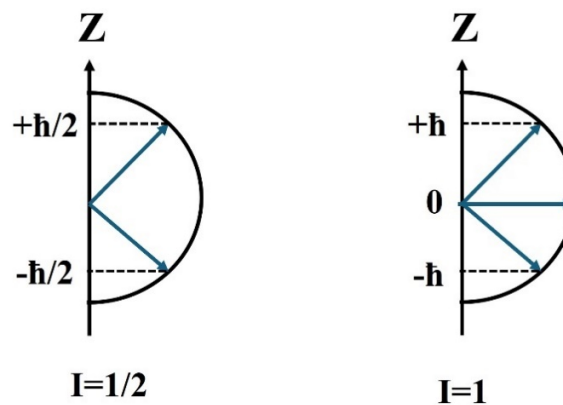


Figure 1-12) Space quantization of the angular momentum of spin- $\frac{1}{2}$ and spin-1 nuclei

1-3-3- Energy levels

In the absence of a magnetic field the energy levels of a spin-I nucleus are degenerate. When an external magnetic field is applied this degeneracy is removed. In classical physics the energy of a magnetic moment $\vec{\mu}$ in a magnetic field $\vec{B}$ is calculated as below:

$$E = - \vec{\mu} \cdot \vec{B} \quad \text{Eq.1-21}$$

The direction of the spin quantization axis in a strong external magnetic field is in the same direction as $\vec{B}$, hence

$$E = - \vec{\mu} \cdot \vec{B} = - \mu_z B \quad \text{Eq.1-22}$$

where μ_z is the z component of the magnetic moment and B is the strength of the field. E can be rewritten as

$$E = - m\hbar\gamma B \quad \text{Eq.1-23}$$

This results in equally spaced energy levels, shifted in proportion to the magnetic field strength, the gyromagnetic ratio, and the z-component of angular momentum.

The selection rule for NMR spectroscopy ($\Delta m = \pm 1$) dictates that transitions occur between adjacent energy levels. This means that the resonance condition depends on the product of the gyromagnetic ratio and the magnetic field strength.

$$\Delta E = \hbar |\gamma| B \quad \text{Eq.1-24}$$

and the resonance frequency is calculated as

$$\nu = \frac{|\gamma|B}{2\pi} \quad \text{Eq.1-25}$$

1-3-4- Bulk magnetization and relaxation:

In an NMR experiment, the sample typically contains a large number of nuclei, each undergoing precession around the direction of the magnetic field, denoted as $\vec{B}_0$. However, due to variations in the precession phase of individual spins (known as the random phase approximation), the total nuclear magnetization, $\vec{M}$, within a unit volume is obtained by summing these individual contributions. The components of the magnetic moment perpendicular to $\vec{B}_0$ cancel each other

out, resulting in $\vec{M}$ aligning parallel to the applied magnetic field. $\vec{M}$ reaches a non-zero equilibrium value, M_0 , along this longitudinal direction because the applied field, $\vec{B}_0$, tends to align magnetic moments predominantly in the $\vec{B}_0$ direction.

The populations of the energy levels of spins in a magnetic field are given by Boltzmann distributions in which it is assumed that spins are identical and non-interacting. In a spin- $\frac{1}{2}$ nucleus like ^1H with two energy levels α , lower $m = +\frac{1}{2}$ and β , upper $m = -\frac{1}{2}$ at a temperature T the ratio of the populations is

$$\frac{N_\beta}{N_\alpha} = \exp(-\Delta E/k_B T) \quad \text{Eq.1-26}$$

where $\Delta E = \hbar\gamma_H B$ and k_B is the Boltzmann constant. For example, at 9.4 T and 300 K, one finds $\Delta E = 2.65 \times 10^{-25}$ J, $k_B T = 4.14 \times 10^{-21}$ J and $\Delta E/2k_B T = 6.4 \times 10^{-5}$. Based on this calculation the energy needed to change the spin orientation is significantly smaller compared to the thermal energy, meaning that the fraction of spins in the lower level is slightly different from those in the upper level. For such small $\Delta E/k_B T$ values Eq. 1-26 is simplified to the following equation.

$$p = \frac{n_\alpha - n_\beta}{n_\alpha + n_\beta} \approx \frac{\Delta E}{2k_B T} \quad \text{Eq.1-27}$$

This relative polarization difference which is called polarization, p , shows that NMR has inherently low sensitivity. Using the given data, Eq. 1-27 yields a value of $p = 3.200 \times 10^{-5}$. In fact, for every 15,624 spins in the upper level, there are 15,625 in the lower level. This means the polarization will be even lower for ^1H nuclei in a weaker field, or for spins with smaller gyromagnetic ratio.

In any spectroscopic method, whether it involves electromagnetic fields exciting molecules, atoms, electrons, or nuclei, the transition from a lower energy level to an upper one occurs with the same likelihood as the reverse transition from the excited state to the ground state. The overall absorption of energy, and consequently, the intensity of the spectroscopic transition, depends on the disparity in populations between the two levels. In NMR spectroscopy, where the upward transitions outnumber the downward transitions by only one part in 10^4 - 10^6 , it is akin to detecting only one nucleus in every 10^4 - 10^6 . Hence, optimizing signal strengths is crucial, such

as by utilizing strong magnetic fields to maximize ΔE and therefore the polarization. Additionally, nuclei with large gyromagnetic ratios and high natural abundance are preferred.

We can consider the magnetization more generally. The net magnetization, $\vec{M}$, of the sample is the vector sum of all of the individual moments $\vec{\mu}$. Imagine that the magnetization vector has been tilted away from the z-axis, forming an angle with it. After this tilt, the vector no longer remains stationary; instead, it begins to rotate around the direction of the external magnetic field, tracing out the surface of a cone with a fixed opening angle (see Figure 1-13). This rotational motion of the magnetization vector around the field is known as Larmor precession and is calculated by Eq. 1-25.

The key question becomes how the magnetization can be tilted away from its equilibrium along the z-axis. This is achieved by applying a small magnetic field in the x-axis, but one that oscillates at or very close to the Larmor frequency. When this oscillating field is on resonance with the Larmor frequency, it can effectively tip the magnetization away from the z-axis, despite the presence of the much stronger static field B_0 . In practice, the same coil used to detect the NMR signal is also used to generate this oscillating magnetic field. By supplying radiofrequency (RF) power to the coil, an alternating current is produced, which in turn generates an oscillating magnetic field along the x-direction. This field is known as the radiofrequency field.

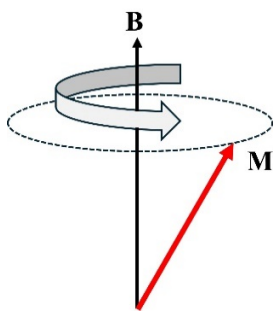


Figure 1-13) Larmor precession of the magnetization vector $\vec{M}$ of nuclear spins with $\gamma < 0$ in a magnetic field $\vec{B}_0$

The equilibrium nonzero $\vec{M}_z$ exists because the moments aligned parallel to $\vec{B}_0$ are energetically favoured over those aligned antiparallel. To return to equilibrium after absorption from the $\vec{B}_1(t)$ field, a radiofrequency field oscillating at or near the Larmor frequency which is

perpendicular to $\vec{B}_0$, the moments must transfer energy to their surroundings, commonly referred to as the "lattice," even when dealing with liquid or gaseous materials. The process of M_z relaxing to its equilibrium value is termed "*longitudinal*" or "*spin-lattice*" relaxation and is characterized by a time constant known as T_1 . In liquids, T_1 tends to be short, whereas in solids, it can be considerably longer. For instance, T_1 lasts a few milliseconds in water but extends to thousands of seconds in ice.⁷²

In spin-spin relaxation, also known as transverse relaxation, spins lose coherence and begin to precess asynchronously in the xy-plane, reducing the vector component of bulk magnetization and thereby decreasing signal intensity. The Bloch equation describing the transverse magnetization for an ensemble of spins in an external magnetic field is given by:

$$\vec{M}_{xy}(t) = \vec{M}_0 e^{-\frac{t}{T_2}} \quad \text{Eq.1-28}$$

where $\vec{M}_{xy}(t)$ represents the time-dependent magnetization in the transverse plane, and $\frac{1}{T_2}$ is the transverse relaxation rate. Spin-spin relaxation primarily results from inhomogeneities in the external magnetic field $\vec{B}_0$ and interactions between spins, which cause fluctuations in their nuclear magnetic moments. These fluctuations lead to variations in resonance frequencies and ultimately result in the loss of coherence. A transition between nuclear spin states influences the local magnetic fields of neighbouring nuclei, inducing an opposing transition, often referred to as a flip-flop transition. While these transitions conserve the system's total energy, they alter the angular momentum of the nuclei, leading to changes in their Larmor frequencies and further disrupting coherence. The effective transverse relaxation rate, accounting for both static field inhomogeneities and spin-spin interactions, is represented as $\frac{1}{T_2^*}$ and is given by:

$$\frac{1}{T_2^*} = \frac{1}{T_2} + \frac{1}{T_2'} \quad \text{Eq.1-29}$$

where $\frac{1}{T_2}$ represents the decay of magnetization due to spin-spin interactions, and $\frac{1}{T_2'}$ accounts for the decay caused by field inhomogeneity.

1-3-5- NMR interactions

In NMR spectroscopy, a spin is manipulated by applying an external magnetic field $\vec{B}_1$.

Information regarding the atomic-scale environment of a nucleus resides in the interactions between the nucleus and its surroundings. The total interaction energy of a nucleus is the sum of all the individual Hamiltonians to which it is subject. These interactions are consolidated in the internal Hamiltonian, denoted as $\hat{H}_{\text{int}}$, which includes components such as $\hat{H}_D$ (magnetic dipolar interaction), $\hat{H}_{\text{cs}}$ (chemical shielding), $\hat{H}_k$ (modification of the magnetic field due to conduction electrons), $\hat{H}_J$ (indirect spin-spin coupling), $\hat{H}_p$ (interaction with unpaired electron spins), and $\hat{H}_Q$ (electric quadrupole interaction).

In diamagnetic insulating solids, spin- $\frac{1}{2}$ nuclei undergo various interactions, including $\hat{H}_D$, $\hat{H}_{\text{cs}}$, and $\hat{H}_J$. Materials containing paramagnetic centers exhibit strong interactions between unpaired electrons and nuclei, potentially leading to significant shifts and broadening of the NMR signal. Fluctuating magnetic fields from electron spins can induce efficient relaxation, particularly in solids where nuclei relax slowly or in materials with paramagnetic ions, where small amounts (typically ~ 0.1 mol%) may be added to facilitate relaxation.

Nuclei with spin $I > \frac{1}{2}$ are additionally affected by the electric quadrupole interaction ($\hat{H}_Q$), arising from the interaction between the nuclear electric quadrupole moment (eQ) and the gradient in the electric field at the nucleus. Despite being an electrical interaction, $\hat{H}_Q$ impacts the NMR spectrum due to its dependence on the magnetic quantum number. Approximately three-quarters of NMR-active nuclei have $I \geq 1$, and the quadrupole interaction can induce significant splitting relative to the Zeeman effect.

All these internal interactions impacting NMR spectra can be described using a comprehensive expression involving tensors:

$$\hat{H}_m = k_m I_i T_{ij}^m A_j^m \quad \text{Eq.1-30}$$

Here, $\hat{H}_m$ represents one of the component Hamiltonians. For each interaction, there exists a constant k , a 3x3 second-rank tensor T , and another vector quantity, which could be either a field

or a spin interacting with a given nucleus with spin- I . These interactions are outlined in Table 1-2, alongside interactions with external magnetic fields.

Table 1-2) Summary of NMR interactions from reference [72]

H_m	Interaction	T_{ij}	A_i	Typical size (Hz)	Comments
H_z	Zeeman	Unitary	B_0	10^7 - 10^9	Interaction with main magnetic field
H_{RF}	RF	Unitary	B_1	10^3 - 10^5	Interaction with rf field
H_D	Dipolar	D	I	10^3 - 10^4	Through space spin-spin interaction, axially symmetric traceless tensor
H_{CS}	Chemical shielding	Σ	B_0	10^2 - 10^5	Alteration of the magnetic field by the electrons
H_J	Indirect spin	J	I	1 - 10^3	Spin-spin interaction mediated via the bonding electrons through the contact interaction
H_P	Paramagnetic	P	S	10^2 - 10^5	Interaction with isolated unpaired electrons
H_K	Knight shielding	K	S	10^2 - 10^5	Interaction with conduction electrons via the contact interaction
H_Q	Quadrupolar	V	I	10^3 - 10^7	Interaction of nuclear quadrupolar moment with the electric field gradient

1-3-5-1- Chemical shielding

The pivotal advancement that elevated NMR from an intriguing physical phenomenon of nuclear magnetic moments to a widely applicable technique in analytical sciences was the realization that the precise resonance frequency is contingent upon the chemical environment of the nucleus.^{73,74} This discovery, named chemical shielding, showed that the exact resonance frequency serves as an extremely sensitive probe of the chemical surroundings, as it depends on electron density and thereby reflects chemical bonding. Chemical shielding stems from alterations in the actual magnetic field experienced by the nucleus, induced by changes in the electron distribution surrounding it. As a first-order approximation, chemical shielding exhibits a linear relationship with the strength of the applied magnetic field. This effect can either augment

or diminish the primary applied magnetic field, termed paramagnetic or diamagnetic, respectively.

The three-dimensional distribution of electron density in a material implies that chemical shielding is described by a second-rank tensor ($\vec{\sigma}$), and the corresponding Hamiltonian is denoted as

$$\hat{H}_{cs} = \gamma h \vec{I} \cdot \vec{\sigma} \cdot \vec{B}_0 \quad \text{Eq.1-31}$$

The orientational dependency is evident in the chemical shielding tensor, which, in its principal axis system (PAS), is diagonal with principal components σ_{XX} , σ_{YY} and σ_{ZZ} . In a crystalline powder sample, all orientations of the PAS system of the shielding tensor are present, and for most orientations, the PAS does not align with the laboratory (LAB) frame, where the z-axis aligns with the direction of the applied magnetic field, $\vec{B}_0$. Hence the tensor representation gives in the PAS

$$\sigma^{PAS} = \begin{bmatrix} \sigma_{XX} & 0 & 0 \\ 0 & \sigma_{YY} & 0 \\ 0 & 0 & \sigma_{ZZ} \end{bmatrix} \quad \text{Eq.1-32}$$

which when transformed into the laboratory frame becomes

$$\sigma^{LAB} = \begin{bmatrix} \sigma_{xx} & \sigma_{xy} & \sigma_{xz} \\ \sigma_{yx} & \sigma_{yy} & \sigma_{yz} \\ \sigma_{zx} & \sigma_{zy} & \sigma_{zz} \end{bmatrix} \quad \text{Eq.1-33}$$

The tensor components are denoted by uppercase subscripts in the PAS and lowercase subscripts in the laboratory frame. The connection between these frames involves rotating the axes via matrices incorporating Euler angles, which define the rotation, resulting in

$$\sigma^{LAB} = R(\alpha\beta\gamma) \sigma^{PAS} R^{-1}(\alpha\beta\gamma) \quad \text{Eq.1-34}$$

Then the field at the nucleus is calculated as follows, which includes both the main field and the shielding:

$$B = (1 - \sigma)B_0 = \begin{bmatrix} 1 - \sigma_{xx} & -\sigma_{xy} & -\sigma_{xz} \\ -\sigma_{yx} & 1 - \sigma_{yy} & -\sigma_{yz} \\ -\sigma_{zx} & -\sigma_{zy} & 1 - \sigma_{zz} \end{bmatrix} \begin{bmatrix} 0 \\ 0 \\ B_0 \end{bmatrix} = \begin{bmatrix} -\sigma_{xz}B_0 \\ -\sigma_{yz}B_0 \\ (1 - \sigma_{zz})B_0 \end{bmatrix} \quad \text{Eq.1-35}$$

After transformation, only the zz-component is considered since it is aligned with the external magnetic field $\vec{B}_0$. The xz and yz terms make only second-order contributions. Therefore, the Hamiltonian governing the chemical shielding is given by

$$\hat{H}_{cs} = \gamma h I_z \sigma_{zz} \vec{B}_0 \quad \text{Eq.1-36}$$

With an appropriate set of rotation from the PAS to LAB frame one can calculate the σ_{zz} tensor element as

$$\sigma_{zz} = \sigma_{iso} + \frac{\Delta\sigma}{2} [(3\cos^2\theta - 1) + \eta(\sin^2\theta\cos 2\phi)] \quad \text{Eq.1-37}$$

where $\Delta\sigma = \sigma_{zz} - \sigma_{iso}$ and $\eta = \frac{\sigma_{xx} - \sigma_{yy}}{\Delta\sigma}$ are called shielding anisotropy and asymmetry, respectively.

The angles θ and Φ represent the polar angles of the LAB frame within the PAS of the tensor. Changes in various components of the shielding tensor correspond to the local symmetry around the nucleus, defined by three parameters. Instead of specifying the three principal components individually, combinations of them are reported, i.e., the isotropic value, the anisotropy, and the asymmetry.

In NMR experiments, the frequency of the sample (ν_{sample}) is referenced to the resonance frequency of a standard (ν_{ref}).

$$\delta_{sample} = \frac{\nu_{sample} - \nu_{ref}}{\nu_{ref}} \times 10^6 \quad \text{Eq.1-38}$$

The tensor elements of the chemical shift also need to be defined. Mason⁷⁵ proposed to standardize the definitions by labeling the three elements in the PAS as δ_{11} , δ_{22} , and δ_{33} , with δ_{11} and δ_{33} are the highest and lowest frequency, correspondingly. Using this convention, isotropic chemical shift, δ_{iso} , span, Ω , and skew, κ , are defined as follows:

$$\delta_{iso} = \frac{\delta_{11} + \delta_{22} + \delta_{33}}{3} \quad \text{Eq.1-39}$$

$$\Omega = \delta_{11} - \delta_{33} \quad \text{Eq.1-40}$$

$$\kappa = \frac{3(\delta_{22} - \delta_{iso})}{\delta_{11} - \delta_{33}} \quad \text{Eq.1-41}$$

1-3-5-2- Dipolar interaction

To calculate the contribution of dipolar interaction to the total internal Hamiltonian, one must first determine the energy of two interacting dipoles $\vec{\mu}_1$ and $\vec{\mu}_2$ which are separated by distance r . This energy is classically given by the following equation:

$$E_D = \frac{\mu_0}{4\pi} \left[\frac{\mu_1 \mu_2}{r^3} - \frac{3(\mu_1 r)(\mu_2 r)}{r^5} \right] \quad \text{Eq.1-42}$$

By substituting $\vec{\mu}_1 = \gamma \hbar I_1$ and $\vec{\mu}_2 = \gamma \hbar I_2$ into the eq. 1-42 the quantum mechanical Hamiltonian can be derived which is

$$\hat{H}_D = \frac{\mu_0 \gamma_1 \gamma_2 \hbar^2}{4\pi r^3} \left[I_1 I_2 - \frac{3(I_1 r)(I_2 r)}{r^2} \right] \quad \text{Eq.1-43}$$

This equation can be rewritten in Cartesian coordinates by taking into account that $I_1 \cdot r = I_{1x}x + I_{1y}y + I_{1z}z$. In polar coordinates we have

$$x = r \sin \theta \cos \Phi \quad \text{Eq.1-44}$$

$$-y = r \sin \theta \sin \Phi \quad \text{Eq.1-45}$$

$$z = r \cos \theta \quad \text{Eq.1-46}$$

which converts the equation 1-43 into the following alphabet expression:

$$\hat{H}_D = \frac{\mu_0 \gamma_1 \gamma_2 \hbar^2}{4\pi r^3} (A + B + C + D + E + F) \quad \text{Eq.1-47}$$

The A-F terms in the $\hat{H}_D$ are

$$A = I_{1z} I_{2z} (3 \cos^2 \theta - 1) \quad \text{Eq.1-48}$$

$$B = -\frac{1}{4} [I_{1+} I_{2-} + I_{1-} I_{2+}] (3 \cos^2 \theta - 1) \quad \text{Eq.1-49}$$

$$C = -\frac{3}{2} [I_{1+} I_{2z} + I_{1z} I_{2+}] (\sin \theta \cos \theta) \exp(-i\varphi) \quad \text{Eq.1-50}$$

$$D = -\frac{3}{2} [I_{1-} I_{2z} + I_{1z} I_{2-}] (\sin \theta \cos \theta) \exp(+i\varphi) \quad \text{Eq.1-51}$$

$$E = -\frac{3}{4} [I_{1+} I_{2+}] (\sin^2 \theta) \exp(-2i\varphi) \quad \text{Eq.1-52}$$

$$F = -\frac{3}{4} [I_{1-} I_{2-}] (\sin^2 \theta) \exp(+2i\varphi) \quad \text{Eq.1-53}$$

These terms are categorized into two groups, secular and non-secular. Terms A and B commute with I_z and are called the secular part, $\hat{H}_D^{\text{sec}}$ while term C-F denoted as the non-secular part of the Hamiltonian, $\hat{H}_D^{\text{non sec}}$. The secular part of the $\hat{H}_D$ is independent of the time; however, the C-F equations are time-dependent at frequencies ω_0 and $2\omega_0$.

$$\hat{H}_D^{\text{sec}} = \frac{\mu_0 \gamma_1 \gamma_2 \hbar^2}{4\pi r^3} (A + B) = \frac{\mu_0 \gamma_1 \gamma_2 \hbar^2}{8\pi r^3} \left[2I_{1z}I_{2z} - \frac{1}{2} [I_{1-}I_{2+} + I_{1+}I_{2-}] \right] (3\cos^2\theta - 1) \text{ Eq. 1-54}$$

In this equation θ is the angle between the internuclear vector and the magnetic field $\vec{B}_0$ which is along the z axis.

Given that the frequency of the time dependence of $\hat{H}_D^{\text{non sec}}$ is significantly higher than the frequency or energy of $\hat{H}_D^{\text{sec}}$, the time-average of the non-secular portion of the dipolar Hamiltonian effectively approaches zero. Consequently, the non-secular component can be disregarded for all spectroscopic intents and purposes.

The $\hat{H}_D^{\text{sec}}$ for a homonuclear dipolar Hamiltonian is different from the heteronuclear one. However, both of them depend on the orientation of the inter-nuclear vector and the inverse cube of the distance.

1-3-5-3- Quadrupolar interactions

For nuclei with $I > \frac{1}{2}$, the distribution of the electrical charge in the nucleus is not spherical which leads to an electric quadrupole moment. By expanding the Taylor series of the energy of a charge distribution in an electrostatic potential $\rho(r)$, one can find the electric field gradient which gives an orientational dependence to the effect of this interaction on the NMR spectrum.

For an electric field gradient tensor

$$\sum_i V_i = 0 \quad \text{Eq.1-55}$$

This property means that only two of its three components need to be known for defining V. It is more convenient to define these as the largest component:

$$V_{ZZ} = eq_{zz} \quad \text{Eq.1-56}$$

and the asymmetry parameter is given by

$$\eta_Q = \frac{V_{xx} - V_{yy}}{V_{zz}} \quad \text{Eq.1-57}$$

In order to derive the quadrupole Hamiltonian of a spin in a magnetic field, the Hamiltonian must undergo a transformation from the PAS to the LAB frame, while retaining only the terms that commute with I_z . Then one can find the orientation dependence and perturbation of the Zeeman energy to first-order as follows:

$$E^{(1)} = \frac{C_Q h}{8I(2I-1)} [3\cos^2\theta - 1 + \eta\sin^2\theta\cos 2\phi] (3m^2 - I(I+1)) \quad \text{Eq.1-58}$$

where $C_Q = \frac{e^2 q Q}{h}$ is the quadrupolar coupling constant. The Zeeman splitting results in a series of evenly spaced energy levels, illustrated for a spin- $\frac{5}{2}$ system in Figure 1-14. To first order, the quadrupole splitting generates symmetric transitions, with the magnitude of the effect influenced by C_Q and its shape determined by η . This first-order term divides the spectrum into $2I$ components, with single quantum intensity being detected.

For the central transition of non-integer quadrupolar nuclei the primary perturbation is of second order. After the rotation of the tensor elements in the second-order equation, the second-order line can then be calculated for any transition. To determine the lineshape of the central transition, one must calculate the second-order perturbation of the quadrupolar interaction on the $(\frac{1}{2}, -\frac{1}{2})$ transition. This calculation yields distinctive lineshapes for the central band, offering insights into the local symmetry of the electric charge surrounding the nuclear site. In the case of axially symmetry (i.e., $\eta=0$)

$$v_{1/2, -1/2}^{(2)} = -\frac{1}{16\nu_0} \left[\frac{3C_Q}{2I(2I-1)} \right]^2 \left[I(I+1) - \frac{3}{4} \right] (1 - \cos^2\beta)(9\cos^2\beta - 1) \quad \text{Eq.1-59}$$

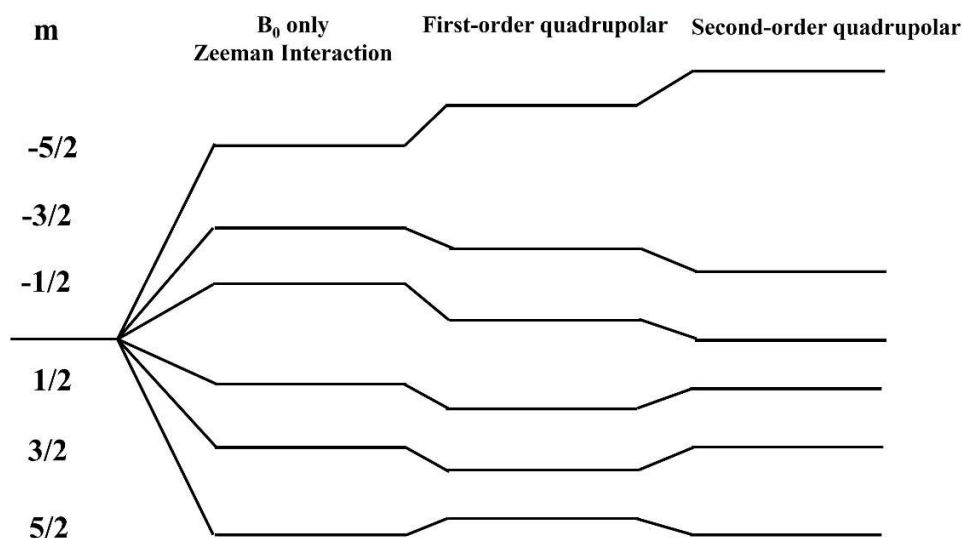


Figure 1-14) Energy level diagram of a spin- $\frac{5}{2}$ system showing the Zeeman interaction and the first- and second-order quadrupole perturbation of the energy levels

1-3-6- Solid state NMR spectroscopy

The NMR spectra of solids are broadened due to various interactions, including those between nuclear dipole moments, between quadrupole moments of quadrupolar nuclei and the electric field gradient (EFG) at the nucleus, and by the anisotropy of electronic shielding at different structural sites. In liquids, the rapid and random tumbling motion of molecules averages the dipolar interaction and shielding anisotropy. This rapid motion causes all nuclei in a given atomic environment to experience the same average magnetic field, resulting in narrow NMR spectra. In solids, many interactions causing line broadening can be minimized or eliminated by spinning the sample very rapidly (typically 10-60 kHz,) at an angle of 54.74° to the axis of the applied magnetic field, known as the magic angle (Figure 1-15).

Magic angle spinning (MAS) is arguably the most widely used technique to enhance spectral resolution in solid-state NMR spectroscopy. In this method, the solid sample, typically a powder, is placed into a container called a rotor. This rotor is inclined at a fixed angle to the magnetic field and rapidly spun about its symmetry axis.

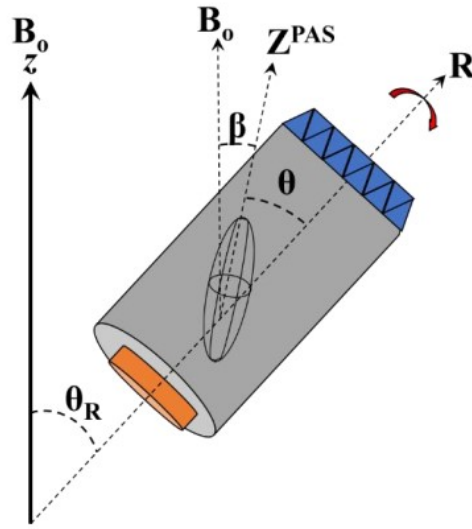


Figure 1-15) Schematic of magic angle setting where the cylinder is oriented at the angle of 54.74° with respect to the external field $\vec{B}_0$

Each crystallite orientation now includes a modulation factor of $\frac{1}{2}(3\cos^2\theta-1)$ which is equal to $P_2(\cos\theta)$, the second-order Legendre polynomial. When θ is set to $54^\circ 44' 8''$, the value of $P_2(\cos\theta)$ becomes zero, causing the anisotropic part to disappear and leaving only the isotropic part, as seen in solution. It is important to note that this cancellation is strictly valid if only first-order broadening effects are present.

In order to examine the effect of MAS on dipolar interactions one needs to consider the spatially dependent dipolar Hamiltonian. The magnitude of this interaction is determined by the orientation of a fixed internuclear vector. When the sample is rotated about an axis, the "average" orientation of any given internuclear vector aligns with the rotation axis. This axis can be set such that the interaction is modulated in a way that

$$\langle 3\cos^2\theta - 1 \rangle = \frac{1}{2}(3\cos^2\theta_m - 1)(3\cos^2\beta - 1) = 0 \quad \text{Eq.1-60}$$

In many cases, considering only the first-order broadening terms is insufficient. As noted, second-order quadrupole effects often dominate the lineshape of the static spectra of the central transition of non-integer quadrupolar nuclei. Due to the more complex angular variation of this interaction, MAS is unlikely to achieve complete averaging of this term. Quadrupole effects often result in more complex spectra compared to those from first-order effects alone.

Additionally, in systems experiencing multiple interactions, there is coupling between these interactions, leading to cross terms (e.g., the second-order quadrupole interaction can be seen as the cross term of the quadrupole interaction with itself). These terms can produce both additional isotropic effects and residual anisotropic effects under MAS.

The second-order quadrupolar interaction dominates the line shape of the central transition in a static spectrum. This interaction involves both second-order and fourth-order Legendre polynomial terms, which represent the anisotropic parts of the second-order quadrupolar broadening. These polynomials are given by:

$$P_2(\cos\theta) = \frac{1}{2}(3\cos^2\theta - 1) \quad \text{Eq.1-61}$$

$$P_4(\cos\theta) = \frac{1}{8}(35\cos^4\theta - 30\cos^2\theta + 3) \quad \text{Eq.1-62}$$

By spinning the sample at the magic angle, the anisotropic component of the second-order broadening can be eliminated, but the anisotropic component can only be partially averaged out. As a result, the second-order quadrupolar broadening of the central transition is only partially reduced, producing a peak with a distinctive second-order lineshape. Spinning the sample at the magic angle reduces the width of the central transition compared to the powder pattern, but the incomplete averaging of the second-order quadrupolar interaction still causes residual broadening with a second-order lineshape.

An important effect of residual second-order quadrupolar broadening is that the isotropic shift of the peak does not align with its center of gravity (Figure 1-16). The isotropic second-order quadrupolar shift is represented by

$$\nu_{\text{Qiso}}^{(2)}(I, m) = -\frac{3C_Q^2}{40\nu_0 I^2 (2I+1)^2} [I(I+1) - 9m(m-1) - 3] \left(1 + \frac{\eta^2}{3}\right) \quad \text{Eq.1-63}$$

The relation between the isotropic chemical shift (δ_{iso}) and the center-of-gravity shift (δ_{CG}) is given by

$$\delta_{\text{CG}} = \delta_{\text{iso}} - \frac{3}{40} F(I) \frac{C_Q^2}{\nu_0^2} \left(1 + \frac{\eta^2}{3}\right) \quad \text{Eq.1-64}$$

where $F(I)$ is a spin-dependent factor and is given by $[I, F(I)]: \left(\frac{3}{2}, \frac{1}{3}\right); \left(\frac{5}{2}, \frac{2}{25}\right); \left(\frac{7}{2}, \frac{5}{147}\right); \left(\frac{9}{2}, \frac{1}{54}\right)$.

The line-width of the central transition produced by the second-order quadrupolar effect is,

$$\Delta\nu_Q^{(2)} = F(I) \frac{C_Q^2(6+\eta)^2}{224\nu_0} \quad \text{Eq.1-65}$$

This defines the threshold spinning speed required for MAS to begin partially averaging the second-order quadrupolar interaction. While the central transition is typically observed in quadrupolar NMR, satellite transitions (corresponding to different magnetic quantum numbers, m) may also be visible. In such cases, MAS effectively averages out the $P_2(\cos\theta)$ term but only partially averages the $P_4(\cos\theta)$ term. Notably the coefficient of this residual interaction depends on the nuclear spin quantum number (I) and the transition (m). As a result, the residual second-order quadrupolar effects under MAS will vary between transitions and for different nuclear spins.

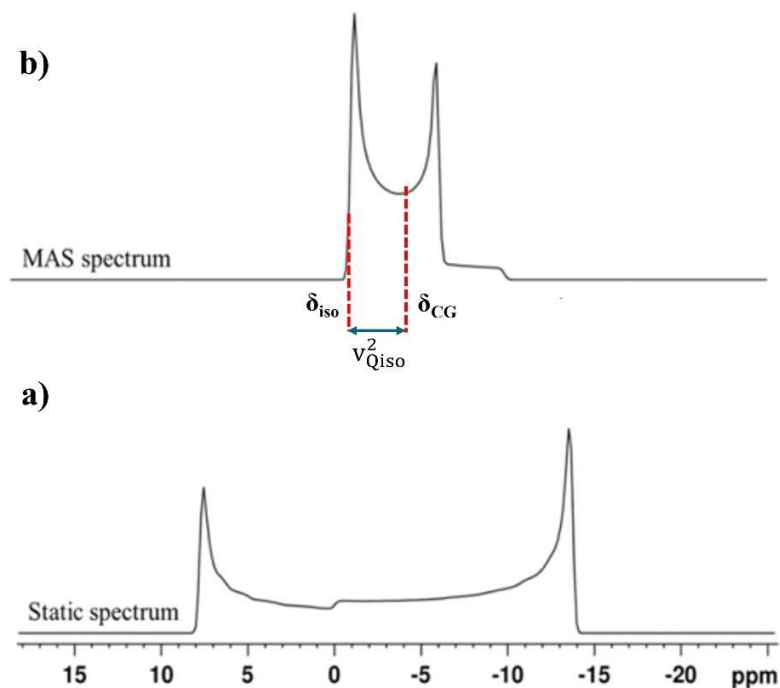


Figure 1-16) a) Static spectrum of a quadrupolar nucleus. b) The effect of magic-angle spinning on the breadth of the central transition. The second-order quadrupole broadened centreband showing the isotropic chemical shift (δ_{iso}) and the center-of-gravity shift (δ_{CG}).

1-4- Materials and Methods

1-4-1- Synthesis of glasses

Although there are various methods to synthesize glasses, the majority are still made by melting batch components at high temperatures. This process involves selecting raw materials, calculating their relative proportions for the batch, and accurately weighing and mixing these materials to create a homogeneous starting mixture. During the initial heating, these raw materials undergo a series of chemical and physical transformations to form the melt. Achieving a homogeneous liquid melt may demand additional processing steps, such as removing unmelted batch residues, impurities, and bubbles. For commercial production, the melt must be formed into specific shapes, followed by heat treatments to relieve stresses generated during cooling or to strengthen the glass through thermal tempering. However, on the laboratory scale, most of the steps could be skipped since the batch size is substantially smaller than production-line scale.

Glasses were synthesized in 3 g batches by mixing the appropriate oxides and carbonates in stoichiometric ratios and melting the mixture at temperatures ranging from 1000 to 1450°C, depending on the glass composition. A Thermolyne® box furnace was used to melt glasses under 1100°C while the compositions with a melting point between 1100°C and 1450°C required a stage-operated Deltech® vertical-tube furnace. The oxides and carbonates were accurately weighed and mixed in 95/5 Pt/Au crucibles. The melt was rapidly quenched by dipping the bottom of the crucible in water.

The obtained homogenous glass pieces were crushed and sieved using stainless steel sieves and stored in a desiccator before dissolution analysis. The powders below 100 µm were utilized for NMR and powder x-ray diffraction analysis, while 100-180 µm were used for dissolution studies. Boron oxide (B₂O₃) was synthesized in the lab by heating boric acid (H₃BO₃) gradually to 850°C and quenching the base of the crucible in water, while the other oxides and carbonates were used as received.

1-4-2- NMR instrumentation and methodology

1-4-2-1- NMR instrumentation

Solid-state NMR experiments including single pulse Bloch-Decay and Multiple Quantum Magic Angle Spinning (MQMAS) were performed using 600 MHz and 500 MHz spectrometers

operating at a magnetic field of 14.1 T and 11.7 T located at the Prairie Regional NMR Facility, University of Manitoba. Meanwhile, J-resolved ^{31}P Incredible Natural Abundance Double QUAntum Transfer Experiment (INADEQUATE) NMR and double-resonance NMR including Rotational Echo Double-Resonance (REDOR) and Rotational Echo Adiabatic Passage Double-Resonance (REAPDOR) were performed in the IFSC department, University of Sao Paulo, Brazil using a 600 MHz spectrometer operating at a magnetic field of 14.1 T. Further information on the probe hardware and the experimental parameters is given in each chapter.

1-4-2-2- Single Pulse

The single-pulse experiment, also known as the Bloch-decay sequence, involves a single radiofrequency pulse followed by an acquisition period during which the free-induction decay (FID) is recorded (Figure 1-17). There is a brief pre-scan delay between the pulse and the acquisition period to switch the transmitting coil to receive mode. The RF pulse tips the magnetization into the x-y plane, and the degree of this perturbation, known as the flip angle or tip-angle, is controlled by adjusting the pulse duration. A cycle of one pulse, pre-scan delay, and acquisition time constitutes one scan. When multiple scans are conducted, a recycle delay is included to allow the magnetization to return to its equilibrium position, maximizing the perturbation and optimizing the signal-to-noise ratio.

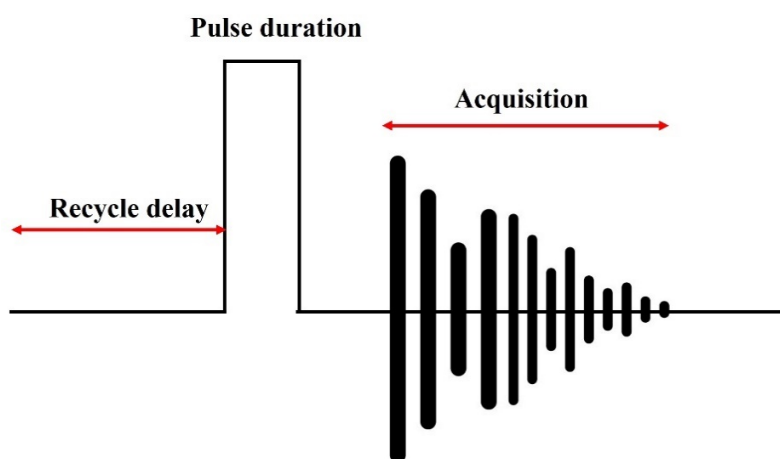


Figure 1-17) An illustration of the single-pulse experiment pulse sequence

In cases with long spin-lattice relaxation times (T_1), shorter pulse durations are used to slightly tip the magnetization, allowing shorter relaxation delays to suffice between scans. The

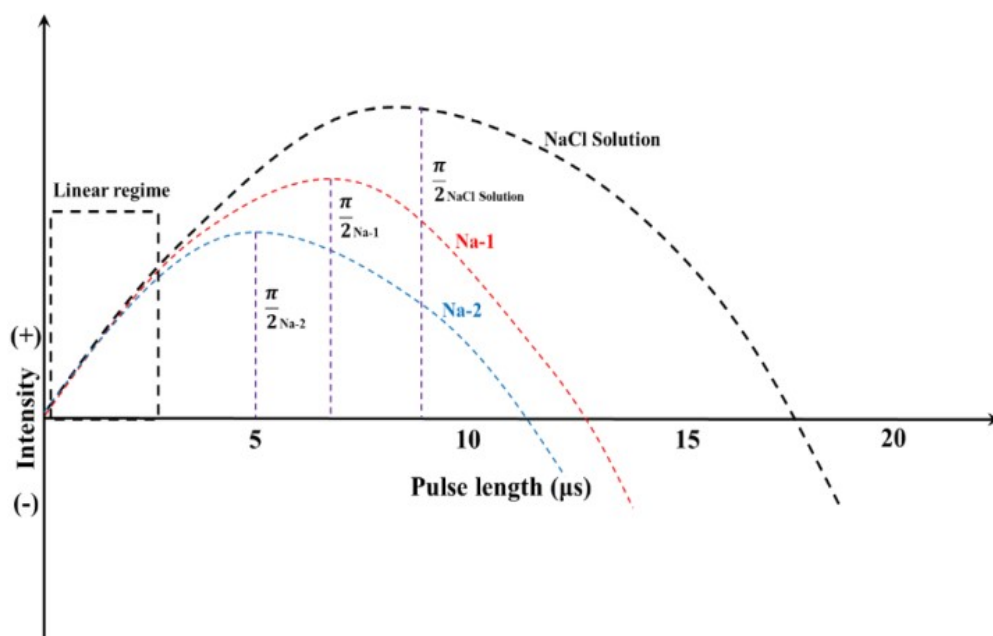


Figure 1-18) ^{23}Na nutation curves of a NaCl solution and Na^+ subject to different quadrupolar interactions. The linear regime where the pulse responses are similar is highlighted.

flip angle and the minimum required recycle delay have an exponential relationship. For a spin with a relaxation time of T_1 , 50% of the maximum signal can be achieved by setting the flip-angle to 30° , with a recycle delay that is 1/5th of the time required for full relaxation.

In samples with quadrupolar nuclei present in multiple chemically distinct sites, the response of the nuclei to an applied RF pulse can vary (Figure 1-18). Consequently, it is important to take measures to ensure that spectral intensities are quantitative. Similar pulse responses are observed within the linear regime of these nutation curves, corresponding to short flip angles. In solid-state NMR experiments involving quadrupolar nuclei, a 15° flip-angle is typically used. This flip angle is calculated from the 90° ($\pi/2$) pulse length (Eq. 1-66) optimized for a reference solution [$\pi/2$ (solution)] of the quadrupolar nucleus being studied.

$$\frac{\pi}{2}(\text{solid}) = \frac{\frac{\pi}{2}(\text{solution})}{1+1/2} \quad \text{Eq.1-66}$$

1-4-2-3- Rotational Echo Double Resonance (REDOR)

REDOR is a powerful technique to investigate the proximity and spatial arrangement in a system through heteronuclear dipolar interaction. In this pulse sequence the dipolar coupling interaction between two nuclear spins I and S are manipulated in a way that the averaged out dipolar

interaction under MAS is reintroduced.⁷⁶ Figure 1-19a shows the cancellation of dipolar coupling in a complete rotor cycle T_R for the observed nucleus S since this interaction oscillates during one rotor period. However, by applying a π -pulse to the non-observed Spin-I, one can re-couple the interaction by inverting the sign of the dipolar Hamiltonian. The pulse sequence for this experiment is shown in Figure 1-19b. The signal for the observed nuclei is typically acquired using a rotor-synchronized Hahn echo sequence, while dipolar recoupling is achieved by applying 180° pulses to the spin-I during each rotor cycle. Synchronized MAS condition means that the time τ is an integer multiple of the MAS rotation period. This condition ensures that the I nuclei remain within the same local magnetic field and continue interacting with the same S spins as they follow the same spatial path until refocusing occurs.⁷⁷

The total signal loss due to re-introducing heteronuclear dipolar coupling is determined by the normalized difference signal $\Delta S/S_0 = (S_0 - S)/S_0$, comparing signal intensities obtained without recoupling pulses (intensity S_0) to those with recoupling pulses applied (intensity S). By plotting $\Delta S/S_0$ as a function of the dipolar evolution time (N_{TR}), which is the rotor period multiplied by the number of rotor cycles, the magnitude of the dipolar coupling can be assessed quantitatively using van-Vleck second moments, $M_{2(S-I)}$, specifying the average mean square dipolar coupling strength of a multiple system as defined in Eq. 1-67.

$$M_{2(S-I)} = \frac{4}{15} \left(\frac{\mu_0}{4\pi} \right)^2 S(S+1) \gamma_I^2 \gamma_S^2 \sum_s r_{IS}^{-6} \quad \text{Eq. 1-67}$$

This is obtained by fitting the initial parabolic segment (from $0 \leq \Delta S/S_0 \leq 0.20$) of the REDOR dephasing curve using the following expression:⁷⁸

$$\frac{\Delta S}{S_0} = \frac{4}{3\pi^2} (N_{TR})^2 M_{2(S-I)} \quad \text{Eq. 1-68}$$

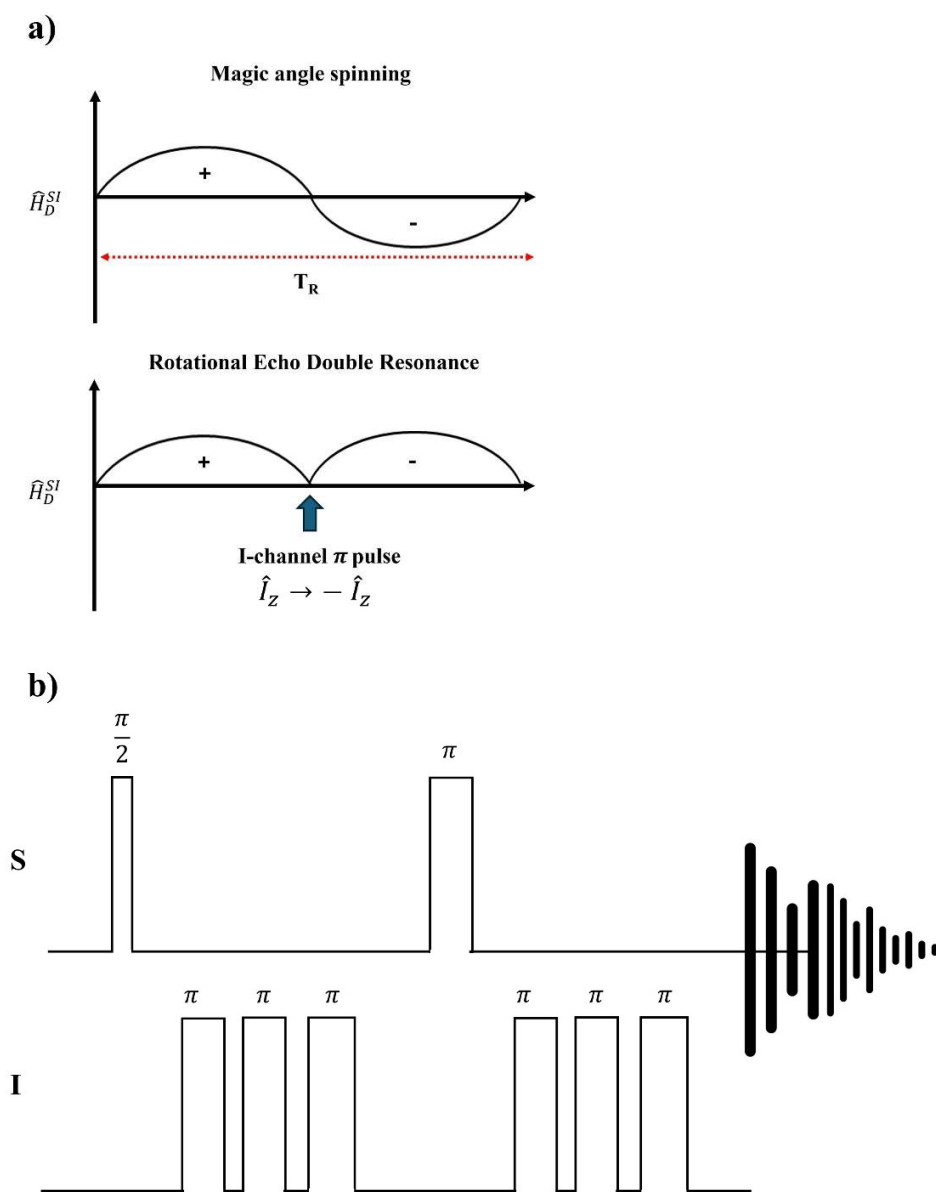


Figure 1-19) Principle of the Rotational Echo Double Resonance (REDOR) experiment. a) the heteronuclear dipolar Hamiltonian under Magic Angle Spinning (MAS) and REDOR conditions. b) Pulse sequence elements of REDOR experiment. T_R denotes the time for one complete rotation of the rotor

1-4-2-4- Rotational Echo Adiabatic Passage Double Resonance (REAPDOR)

Similar to REDOR, REAPDOR is also a double resonance technique that helps to investigate the heteronuclear dipolar coupling between spins S and I by manipulating the states of both spins. In

this case cases, where the non-observed I nuclei have spin $> \frac{1}{2}$ the S{I} REDOR experiment becomes less efficient due to the anisotropy of the quadrupolar interaction, which causes significant off-resonance shifts for the non-central Zeeman transitions of the I nuclei.⁷⁹ In such cases, these transitions may not be affected by the π pulses applied for dipolar recoupling, and a variation of the method known as rotational echo adiabatic passage double resonance (REAPDOR) technique is applied, employing continuous-wave irradiation of the quadrupolar nuclei for a duration of $T_R/3$. As MAS modulates the energies of the nuclei in their non-central Zeeman states, they can transiently resonate while the radiofrequency field is active for the quadrupolar nucleus.⁷⁹ This temporary resonance allows for population transfers between these levels during irradiation, effectively recoupling dipolar interactions of the observed nuclei with quadrupolar nuclei in non-central Zeeman states. This enhances the overall dipolar dephasing effect in a calculable manner.⁷⁸ Figure 1-20 shows the pulse sequence for this NMR experiment.

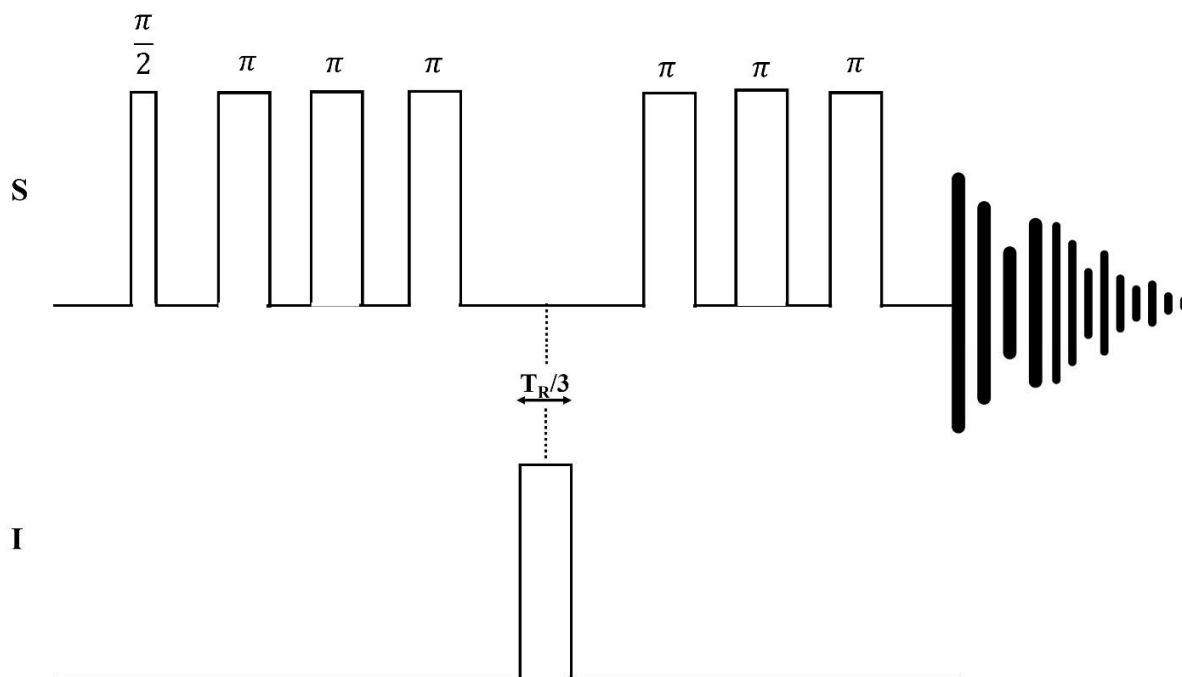


Figure 1-20) Pulse sequence scheme for Rotational Echo Adiabatic Passage Double Resonance (REAPDOR) experiment. T_R denotes the time for one complete rotation of the rotor

1-4-2-5- 1D Refocused Incredible Natural Abundance Double QUAntum Transfer Experiment (R-INADEQUATE)

The Refocused-INADEQUATE pulse sequence was designed to generate double-quantum coherences through J-coupling interactions. Originally it was developed to detect natural-abundance ^{13}C – ^{13}C linkages. This technique is now widely applied in various applications. In the current work, this pulse sequence is employed to detect P–O–P linkages in borophosphate systems.⁸⁰

Figure 1-21 illustrates the pulse sequence. Essentially, this sequence measures how the amplitude of double-quantum coherence evolves through a series of pulses selected by suitable phase cycling as the time interval (t_1) increases. Signals captured during the detection interval (t_2) yield a two-dimensional dataset. After applying a double Fourier transform, a correlation plot linking two frequency domains is produced.

In a modified, one-dimensional form of this experiment (R-INADEQUATE), the interval t_1 is fixed at short durations. Consequently, double-quantum coherences are converted into detectable single-quantum signals, but their modulation is not recorded. This adaptation allows selective detection of species coupled through $^2J(^{31}\text{P}$ – $^{31}\text{P})$, as double-quantum coherences arise specifically from J-couplings between the two nuclei involved. The primary benefit of this one-dimensional version is the ability to acquire structural information more rapidly; however, it does not enable the identification of multiple couplings.⁸⁰

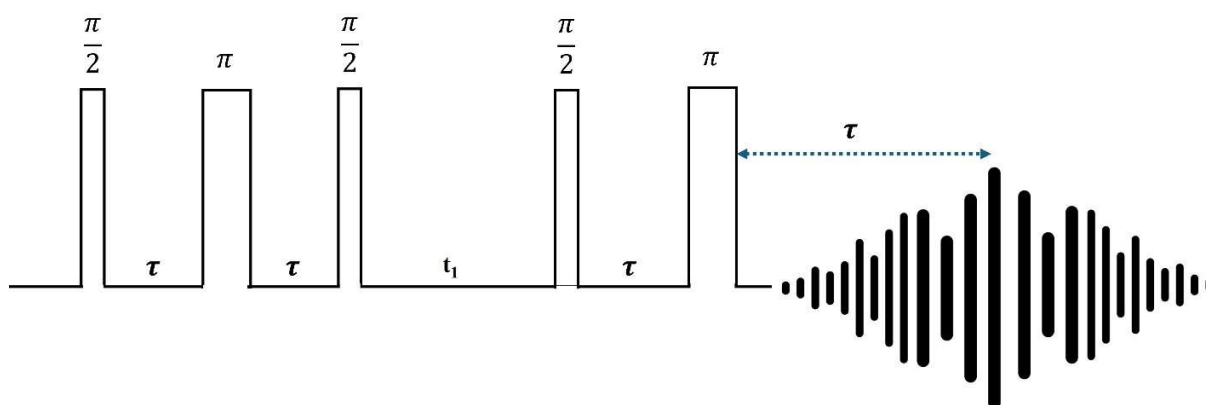


Figure 1-21) Pulse sequence scheme of 1D Refocused Incredible Natural Abundance Double QUAntum Transfer Experiment (R-INADEQUATE). t_1 and τ are fixed time constants

1-4-2-6- Multiple Quantum Magic Angle Spinning (MQMAS)

Multiple Quantum Magic Angle Spinning (MQMAS) is a two-dimensional technique developed to improve the resolution in spectra of quadrupolar nuclei, whose Zeeman energy levels are influenced by quadrupolar interactions.^{81,82} These interactions are sufficiently strong to require second-order perturbation theory for accurate interpretation, as outlined in section 1-3-5-3.

Figure 1-22 shows the z-filtered Triple-Quantum Magic Angle Spinning (TQMAS) pulse sequence at the, along with its coherence pathway. The first pulse (P_1) is a hard pulse that converts magnetization into TQ coherence, with stronger pulses leading to more efficient conversion. During the evolution time t_1 , the TQ coherence evolves until the second pulse (P_2) transforms it back into zero-quantum coherence. Any unwanted coherences are removed through appropriate phase cycling. A soft P_3 pulse then selectively excites only the central transition to observable magnetization. During the detection period (t_2), the signal is collected while the magnetization echo is refocused. Correlating single- and triple-quantum coherences effectively removes anisotropies caused by both first- and second-order quadrupolar perturbations in a 2D MQMAS spectrum.⁸³

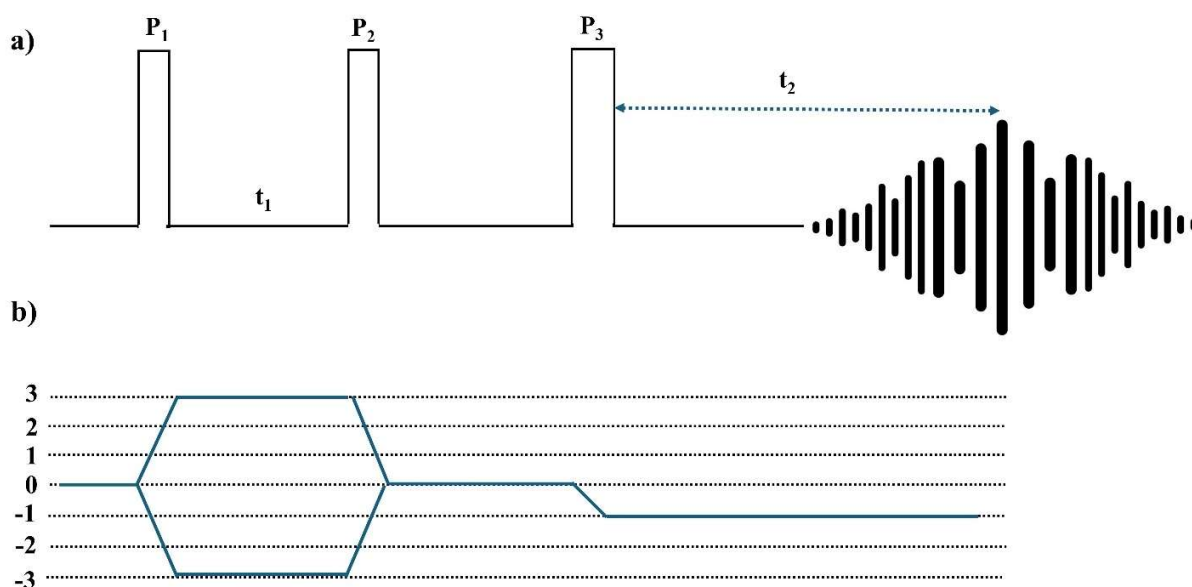


Figure 1-22) a) Schematic of the z-filter Triple Quantum Magic Angle Spinning (TQMAS) technique with the corresponding b) coherence path diagram. P_1 : excitation pulse, P_2 : conversion pulse and P_3 : soft pulse to convert the magnetization to the observable coherence.

1-4-2-7- Fitting NMR spectra

The DMFit software⁸⁴ was used for fitting NMR spectra. This program is used for analyzing NMR spectra of a wide range of materials including crystalline phases, amorphous materials and solutions. Several modules are available for deconvolution of NMR spectra obtained under MAS or static conditions for both spin-1/2 and quadrupolar nuclei.

The NMR spectra of ^{31}P and tetrahedral ^{11}B were deconvolved using a Gaussian-Lorentzian (G/L) mixture to achieve the best fit. When boron resides in trigonal planar (^{11}B) coordination environments, it was fit using the Quasar module,⁸⁵ which simulates second-order quadrupolar line shapes of the central transition. The relatively small C_Q of ^{11}B results in a symmetric resonance with predominantly Gaussian character, whereas the larger C_Q of ^{31}P leads to a broader signal exhibiting a second-order quadrupolar line shape.⁸⁶

In disordered materials such as glasses, the local environments experienced by ^{23}Na and ^{27}Al are not unique but instead form a statistical geometric distribution. As a result, the observed NMR spectrum represents a superposition of signals from nuclei experiencing a range of quadrupolar interactions, reflecting the underlying distribution of EFGs arising from structural disorder. In such cases, conventional single-site quadrupolar models are insufficient, and a statistical description of the quadrupolar interaction parameters is required. The Czjzek model provides a probability density function to describe the distributions of both the magnitude and asymmetry of the quadrupolar interaction tensor, thereby linking spectral broadening directly to structural disorder.⁸⁷

All fittings were performed manually. The input parameters including peak position, peak width, mixture of G and L, asymmetry parameter, quadrupolar coupling constant and intensity were fixed by the user and the resultant integrated intensity is reported. These parameters were chosen based on relevant documented parameters and experience from binary borate and phosphate systems with a narrow uncertainty, and carefully optimized to ensure fitting with meaningful NMR parameters.

1-4-3- Powder x-ray diffraction

Powder x-ray diffraction (PXRD) is a standard technique used to determine crystal structures and perform phase identification of crystalline minerals.^{88,89} XRD works by directing an x-ray beam at a crystalline solid at a known wavelength (λ) and angle (θ) and then measuring the intensity of the diffracted x-ray. When the x-ray beam encounters the crystal, part of it passes through the atomic planes while another part is diffracted back into the diffractometer, which measures the intensity of diffracted beam. The angles at which the x-rays are irradiated range from 0 to 90°. The x-ray beam is rotated with respect to the sample to irradiate different atomic planes; for example, at 20° might allow the beam to pass through without hitting an atomic plane, while at 65° might result in the beam hitting the lattice and being diffracted towards the diffractometer.^{89,90}

Crystalline phases produce diffractograms characterized by sharp Bragg peaks, which result from the diffraction of x-rays by different lattice planes within their ordered structures. In contrast, amorphous materials lack long-range periodic atomic arrangements and oriented lattice planes, leading to the absence of such distinct peaks. Instead, glasses exhibit a broad, featureless signal known as the amorphous halo. However, in phase-separated glasses, the diffractogram displays both the amorphous halo and sharp Bragg peaks, indicating the presence of crystalline phases. These peaks can be analyzed to identify the crystallites present.⁸⁹

As a result, PXRD was primarily employed to verify the amorphous nature of the synthesized glasses and to determine the chemical composition of crystalline phases in phase-separated samples. Phase identification was conducted by matching the observed Bragg peaks with a database of diffraction patterns corresponding to various known crystalline structures.

1-4-4- Electron microscopy

When an incident electron beam with energy E_i strikes a sample, the electrons may be reflected, absorbed, transmitted, or emitted. Additionally, x-rays and other forms of radiation can be emitted due to electronic transitions. These emitted electrons and photons are subsequently detected, offering insights into the sample's topography, crystallography, chemical composition, and other physical structural details.

When electrons interact with a material, they lose energy through inelastic and elastic scattering. This energy loss is measured in electron volts, which is the energy change of an electron moving across an electric potential difference of 1 V. Elastic scattering, caused by interactions with atomic nuclei, changes the direction of the electrons with minimal energy loss. In contrast, inelastic scattering, which occurs due to interactions with valence and core electrons, leads to energy loss with little change in direction.

Electron microscopy⁹¹ is a widely utilized technique for analysing the surface properties of organic and inorganic materials, providing valuable insights into external morphology, chemical composition, and mesoporous structures. An electron source can emit electrons either through a thermionic emission filament (such as tungsten or lanthanum hexaboride, LaB₆) or via a field emission atomically sharp tip (either hot or cold). The electron beam is defocused and focused using a series of magnetic lenses within a vacuum. This focused electron beam is then scanned over the surface of the sample, interacting with it to produce images or composition data. The detection of reflected or scattered electrons generates secondary electron images (SEI), backscattered electron images (BEI), or elemental x-ray maps. The resolution of SEM is close to a few nanometers, with magnifications reaching several hundred thousand times.

Secondary electron imaging (SEI) involves detecting electrons with energies below 50 eV. These secondary electrons, having lost their original energy through inelastic scattering with atomic electrons, are emitted from the first few nanometers of the surface. Image contrast in SEI is achieved because the secondary electron yield is highest when the electron beam is perpendicular to the sample surface. Thus, features on the sample at different angles relative to the beam produce varying yields of secondary electrons, creating areas of different brightness.

In contrast, backscattered electron imaging (BEI) detects higher-energy electrons that retain much of their original energy due to elastic scattering with atomic nuclei, exiting the sample with energies greater than 50 eV. These electrons originate from deeper within the sample, resulting in lower lateral resolution compared to SEI. The contrast in BEI depends on the chemical composition of the sample, known as Z-contrast: regions with higher atomic numbers (Z) emit more backscattered electrons and appear brighter than regions with lower atomic numbers.⁹²

1-4-5- Inductively-coupled plasma optical emission spectroscopy

Inductively-Coupled Plasma Optical Emission Spectrometry (ICP-OES) is a powerful and widely used technique for determining trace elements in various sample types. ICP-OES works by emitting photons from excited atoms and ions in a radio-frequency discharge. Liquid and gas samples can be directly injected, while solid samples usually need to be dissolved into a solution. The solution is turned into an aerosol and directed into the plasma's central channel, where temperatures reach around 10,000 K. The aerosol vaporizes, releasing the analyte elements as free atoms in a gaseous state. These atoms are further excited and can become ions, which emit photons as they return to their ground state. The wavelength of these photons identifies the elements, and their quantity correlates with the concentration of element in the sample.

The instrumentation for ICP-OES is straightforward: photons emitted by the plasma are collected using lenses or mirrors and directed into a monochromator, which selects specific wavelengths. These wavelengths are then converted into electrical signals by a photodetector, amplified, processed, and displayed on a computer.⁹³ To calibrate an ICP-OES, solutions with known concentrations of each element are measured. These data are used to create a calibration curve, which establishes the relationship between the light intensity at specific wavelengths and the element concentration in the solution.

The concentration in the upper calibration solution should be high enough to ensure good reproducibility, ideally at least 100 times above the limit of detection. It should also match the upper limit of the expected sample concentration range, as extrapolation increases error risk. Practical experience indicates that samples slightly more concentrated than the upper calibration solution can still yield good results, depending on the reproducibility of the upper calibration solution's measurement. The upper standard should not exceed the linear range of the calibration function, and its concentration should be low enough to prevent carryover, particularly for elements prone to memory effects, the presence of residual analyte residues from previous samples, such as boron. Typically, the lower end of the working range does not match the lower calibration solution concentration, which is usually the blank solution. Instead, it is set at the limit of quantification.⁹⁴

1-5- Scope of the thesis

The central premise of this thesis is that glass composition, structure, and properties are fundamentally interconnected. For bioactive glasses intended for soft-tissue regeneration, one of the most critical properties is their dissolution behaviour in physiological conditions.

Understanding and predicting the dissolution rate of a given glass composition, particularly within borophosphate systems, is therefore essential for designing materials with targeted degradation profiles. A key objective of this work is to develop a mechanistic understanding of dissolution in borophosphate glasses so that both prediction and controlled tuning of degradation rates become achievable.

Achieving this goal requires a detailed examination of the glass structure. Borophosphate systems present a particular challenge because they contain numerous borate and phosphate species. One of the hypotheses guiding this thesis is that the medium-range order of the glass network plays a significant role in determining durability. By investigating how structural units connect across compositions, this work aims to elucidate the relationship between medium-range structure and dissolution behaviour, thereby contributing to a more predictive understanding of bioactive borophosphate glasses.

Pure water was selected as the aqueous environment in order to establish a fundamental understanding of how the glass interacts with water alone, given that the human body is predominantly composed of water. This approach intentionally avoids the additional complexities introduced by simulated body fluid (SBF) or Tris-based buffers, where interactions among multiple ions, the reprecipitation of crystalline phases, and complex chemical equilibria can obscure the intrinsic dissolution behaviour of the glass. By adopting this simplified medium, the present work lays the groundwork for future studies to clearly distinguish whether changes in dissolution behaviour arise from the glass composition and structure themselves or from modifications in the chemistry of the surrounding solution.

1-6- Thesis outline

This thesis is organized into six chapters. Chapter 1 provides a comprehensive review of the foundational concepts relevant to this work. It covers essential topics in glass science, including the structural principles of amorphous materials, the dissolution behaviour of glasses in aqueous environments, and the fundamentals of solid-state NMR spectroscopy. These concepts are

discussed in sufficient depth to ensure that readers are well-prepared for the results and discussions presented in subsequent chapters. The second part of Chapter 1 offers an overview of the experimental methods and characterization techniques employed throughout this thesis. This includes descriptions of the procedures used to synthesize the glass samples, as well as the analytical tools applied to investigate their structure, microstructure, and dissolution behaviour.

Chapter 2 explores how the structural complexity of sodium borophosphate glasses governs their dissolution behaviour by examining the interplay between composition, properties and structure. The chapter outlines a systematic methodology used to map the structural units within the glass network, integrating experimental tools such as double-resonance NMR with theoretical approaches including Pauling bond-strength analysis and charge-compensation modelling. Particular attention is given to the role of sodium as a network modifier, whose concentration strongly influences how negative charge is distributed among borate and phosphate units. These variations in connectivity, both heteropolar and homopolar, provide the structural basis for understanding how different species dissolve at different rates, establishing the broader framework through which the relationship between glass structure and dissolution behaviour is investigated in this thesis.

Chapter 3 is dedicated to advanced solid-state NMR techniques and their application in resolving the structural features of the glasses investigated in this thesis. Understanding glass structure at the medium-range order is essential for interpreting and predicting physical behaviours. In chapter 2, several complementary structural analysis tools are introduced, including single-pulse solid-state NMR, charge-compensation calculations, and Pauling bond strength theory. To enhance the reliability of the structural interpretations obtained from these methods, dipolar-based double-resonance NMR experiments are necessary.

Chapter 4 focuses on understanding how devitrification affects the dissolution behaviour of borophosphate glasses intended for soft-tissue regeneration. While silicate-based bioactive glasses have historically been transformed into glass-ceramics to improve mechanical properties, such modifications often reduced their bioactivity. In contrast, borophosphate systems have not been extensively studied in terms of how phase-separation or partial crystallization influences their biological performance.

Chapter 5 examines the role of therapeutic ion incorporation in tailoring the structure and dissolution behaviour of borophosphate glasses for biomedical applications, particularly in the context of chronic or infected wounds. This chapter is motivated by the need to understand how adding therapeutic cations modifies the glass network and how these structural changes influence the dissolution process.

Chapter 6 summarizes the major findings of this thesis and reflects on the broader implications for the design of borophosphate glasses for soft-tissue regeneration. The chapter also identifies promising directions for future research, including long-term degradation studies under physiologically relevant conditions, further research on glass forming ability of borophosphate glasses, computational chemistry, and the development of new compositions tailored for specific clinical applications.

2- Investigating dissolution behaviour of $\text{Na}_2\text{O-B}_2\text{O}_3\text{-P}_2\text{O}_5$ glasses from properties-structure-composition perspective

2-1- Introduction

Bioactive glasses are a class of biomaterials that have shown great promise in tissue regeneration. When a bioglass is in contact with a tissue it can form a new bond between the tissue and the material or it is capable of inducing a response within the biological system.⁵⁸ Soft-tissue regeneration has become the most recent application for bioactive glasses.⁴⁹ In this field, inducing biological response is prominent rather than formation a new bond like hydroxyapatite (HA) in bone implants. Borate, phosphate and borophosphate-based glasses are mainly used for soft tissue regeneration because they dissolve rapidly in the body medium.^{46,47,95,96} In these applications, ion release to the injury site matters. In other words, dissolution properties are the main concern.

Borophosphate glasses, interesting inorganic compounds containing two network formers, have intrigued glass scientists increasingly because of their ability to serve in diverse applications including ionic lithium batteries, bone grafts/implants, catalysts⁶⁸ and optical applications.^{70,97} Various structural units such as $^{[4]}\text{B}$, $^{[3]}\text{B}$, and $\text{P}_{\text{mB}}^{\text{n}}$ ($\text{n}=1\text{-}3$, $\text{m}=0\text{-}3$) confer interesting features upon borophosphate glasses. In fact, the combination of network formers in the structure of the glasses primarily accounts for properties in borophosphates such as improved mechanical properties⁹⁸ and enhanced ionic conductivities.⁹⁹ Although features like fast dissolution rate and the ability to shape them into fibers enabled borate glasses to be employed as a biomaterial for wound healing, the significant increase in pH caused by the dissolution of borate glasses in an aqueous medium is considered a limitation for soft-tissue regeneration applications like wound healing. The effect of the pH on wound healing is complex, with apparently conflicting results in the published literature. For example, it is argued that most of the bacteria that cause infection in a wound grow at alkaline pH.¹⁰⁰ On the other hand, another report asserts that the antibacterial properties of bioactive glasses are due to their creation of alkaline conditions.¹⁰¹ The pH of chronic wounds has been reported to be 7.2 to 8.9, while the range of an open wound ranges from 6.5 to 8.5. Therefore, borate glasses with dissolution products that raise the pH of an aqueous medium would be considered as less desirable candidates. This issue is not faced in a phosphate glass since upon dissociation of phosphate

units in the solution the pH is decreased. This effect is driven by hydrolysis reactions, where P–OH groups formed from the cleavage of P–O–P bonds by water undergo deprotonation, leading to an increase in free H^+ ions in the solution and, consequently, a decrease in pH.¹⁰² However, their higher kinetic fragility leads to a narrow temperature range unsuitable for fiber drawing, limiting their potential use as fibers¹⁰³—the most popular format for wound dressings. Additionally, their hygroscopic behaviour¹⁰⁴ poses practical challenges for handling and storage. Overcoming these restrictions has motivated glass scientists to develop bioactive borophosphate glasses as candidates for soft-tissue regeneration. The combination of network-forming cations has increased the structural complexity of the glasses and demanded greater understanding of how the properties relate to the structure.

Boron is a small element placed in the group 13 of the periodic table. It has been discussed that in comparison with other elements, boron boasts more diversity and complexity in inorganic chemistry.¹⁰⁵ Its small size and high ionization energy are considered as the main factors that govern the chemical nature of boron. In addition, B has a high affinity for oxygen which is a dominant characteristic that accounts for the extensive chemistry of borates.¹⁰⁵ Among glass network formers phosphorus has the highest cation field strength, the ratio of the cation's charge to the square of mean cation–oxygen bond length, $2.13 \text{ \AA}^{-2}$. This value is $1.51 \text{ \AA}^{-2}$ and $1.38 \text{ \AA}^{-2}$ for Si^{4+} and B^{3+} , respectively. In glasses, phosphate tetrahedral units are generally thought to include a double P=O bond, which allows them to have a maximum of three bridging oxygen.¹⁰⁶

The correlation between structure and properties of a given composition is considered a chief concern among glass scientists. In the case of borophosphate glasses, however, this connection is difficult to establish since the characterization of intermediate range order in these glasses is a demanding task. This challenge comes from various reasons, among them assigning phosphorus speciation properly. Although 1D NMR spectroscopy provides valuable information with regard to short range order in glasses, fitting ^{31}P MAS NMR lineshape is challenging due to significant peak overlap from phosphate tetrahedra with different connectivity. This uncertainty can be alleviated to a large extent by taking into account constraints including the B/P ratio, ^{11}B MAS NMR results, and Pauling Bond Strength theory (PBS).

Within the past few decades, researchers tried to reveal the connectivity in borophosphate glasses and depict the extent of P–O–B linkages. Recently Liu et al correlated the mechanical

properties of a series of lithium borophosphate glasses to the structural features.⁹⁸ They concluded that adding boron to the phosphate system reduced the number of non-bridging oxygens (NBOs) associated with phosphate species and increased the formation of P–O–B linkages. The alteration in the network and also substitution of the phosphate units for ^[4]B accounted for augmentation in the average network rigidity, density, Vickers hardness, T_g and Young's modulus. In another study Munoz-Senovilla et al¹⁰⁷ worked on the relationship between kinetic fragility (m) – which refers to how quickly a liquid's viscosity increases as it cools towards its glass transition temperature – and the structure of borophosphate glasses. Their study shows that m decreases with increasing the boron content of the glasses up to 10 mol% B₂O₃. Beyond this point the kinetic fragility demonstrates a linear increase with boron. They related this behaviour to the number of the P–O–P and P–O–B linkages in the glass series. Below 10 mol% B₂O₃ the glass structure is dominated by the homopolar P–O–P bonds while it is populated by B–O–P bonds in boron-rich glasses.

Considering the composition-structure-property relationship in bioactive glasses designed for soft-tissue healing, the dissolution behaviour of the samples in the body medium is an essential characteristic of these biomaterials. In this study a series of Na₂O–B₂O₃–P₂O₅ glasses was designed to examine the influence of the glass structure on the dissolution properties. In this work we address the question of how the medium range-order affects the dissolution rate. In other words, what is the relationship between the number of the P–O–B linkages and the dissolution behaviour? Pure water was chosen as the aqueous medium to establish fundamental knowledge about the interaction between the glass and an aqueous environment (as the human body primarily consists of water). This choice avoids the additional complexities introduced by simulated body fluid (SBF) or Tris-based buffer solutions, where interactions between multiple ions, potential reprecipitation of crystalline phases and complex formation can obscure the intrinsic dissolution of the glass. By adopting this simplifies medium, the present work allows future studies to clearly distinguish whether observed changes in glass dissolution behaviour arise primarily from the glass composition and structure, or from alterations in the chemistry of the dissolving medium.

2-2- Experimental details

2-2-1- Glass synthesis

A series of melt-quenched sodium borophosphate glasses (Table 2-1, Figure 2-1) with the nominal composition $(\text{Na}_2\text{O})_{0.2}[(\text{B}_2\text{O}_3)_x(\text{P}_2\text{O}_5)_{1-x}]_{0.8}$ where $0.25 \leq x \leq 0.75$ was prepared by using boric acid, $(\text{NaPO}_3)_6$ (Fisher Scientific, analytical grade) and phosphoric acid 85% (Fisher Scientific) as raw materials. First, boric acid was heated gradually to 850 °C and quenched to obtain B_2O_3 . For each glass composition, a 3-gram batch was weighted in a 95/5 Pt/Au crucibles and left in a box furnace overnight at 200 °C. Melting for P20 and P30 was performed at 1100°C, and for P40-P60, at 1325°C with 15-30 min dwell time. ICP-OES analysis was performed to determine the composition of the prepared glasses. For this purpose, 12 mg of the pulverized glasses were dissolved in milliQ water 2%v/v HNO_3 . After glasses were pulverized, thin plates were made and heated at 50° intervals to determine the melting temperatures which is called re-melting here.

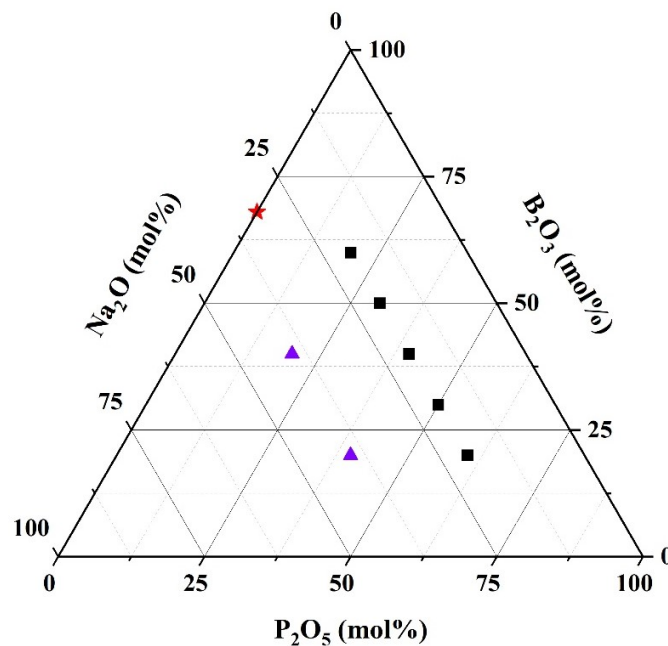


Figure 2-1) Composition of the glasses in a ternary diagram

Table 2-1) Nominal and analyzed compositions of the samples (mol%)

	Nominal			Analyzed ($\pm 2\%$)				
	P ₂ O ₅	B ₂ O ₃	Na ₂ O	P ₂ O ₅	B ₂ O ₃	Na ₂ O	K [‡]	L*
P20	20	60	20	18	61.2	20.8	0.29	0.26
P30	30	50	20	27.4	51.5	21.1	0.53	0.27
P40	40	40	20	38.3	39.1	22.6	0.98	0.29
P50	50	30	20	47.6	30.4	22.0	1.56	0.28
P60	60	20	20	56.8	22.2	21.0	2.56	0.26
B40	20	40	40	18.2	39.3	42.5	0.46	0.74
B20	40	20	40	38.5	21.0	40.5	1.83	0.68
B68	-	68	32	-	67.2	32.8	-	0.49
[‡] P ₂ O ₅ /B ₂ O ₃								
*Na ₂ O/(B ₂ O ₃ +P ₂ O ₅)								

To examine the effect of the Na₂O content on the glass structure and subsequently the dissolution behaviour, two more glasses with 40 mol% Na₂O and different nominal B:P ratios of 2:1 and 1:2 were prepared. In addition, a P₂O₅-free glass was synthesized as a reference point to probe the influence of phosphorus on the dissolution behaviour. The composition with highest fraction of four-coordinated boron reported in the literature was selected, 68B₂O₃-32Na₂O (mol%).²⁰ Since visual inspection suggested no phase separation in the whole series, samples were ground using a pestle and mortar and sieved into two particle sizes: below 100 μm and 100-125 μm . The former was used for NMR, XRD and determining the composition using ICP, and the latter was used for dissolution study.

2-2-2- Dissolution experiments

Dissolution studies were performed in milliQ water at room temperature with an initial pH of 7.3 $\pm$ 0.1 to exclude the effects of the common buffer solutions used for dissolution behaviour of the bioactive glasses. The glass powder (with particle sizes between 105 and 125 μm) to water ratio was set to 13:1 (mg/ml). This ratio was chosen since preliminary results of dissolving glasses

with lower powder-to-water ratio showed that P20-P30 dissolves completely in less than 15 minutes. In order to keep uniformity of dissolution conditions for all samples the ratio was kept the same for all samples. Dissolution tests were run in two replicates in PET centrifuge tubes. For mass-loss experiments the dissolution was terminated at each time point reported in Table 2-3. The undissolved solids of each series were washed with 150 ml of anhydrous ethanol and stored in Parafilm-covered vials for subsequent characterization. The insolubility of glasses in anhydrous ethanol was confirmed before rinsing them. pH values were recorded at the same time of day on days reported in Table 2-3.

Due to the high dissolution rate in these samples an experiment was done to determine the amount of required sample for dissolution study. Four separate tests were run in which the glass powder:water ratio was kept the same, 13:1, but the mass of the powder was changed from 100.0, 200.0, 400.0 and 800.0 mg. After 15 minutes the glass was retrieved and the mass losses were as follows: 73, 61, 56 and 54%. Because beyond 200 mg glass powder the results were within $\pm 3\%$ error, this sample size was chosen as the optimum value for the dissolution studies.

2-2-3- X-Ray Diffraction (XRD)

X-ray diffractograms were collected by a D4 Endeavor X-Ray diffractometer (Bruker, Billerica, MA, USA). Finely ground samples (particle sizes $< 100 \mu\text{m}$) were mounted on polymer diffraction plates and subjected to Cu K α radiation generated at a voltage and current of 40 kV and 40 mA, respectively. Scanning was done within the range 10-60° (2 θ) with a step size of 0.02 and acquisition time of 20 s, corresponding to 2000 steps. To ensure homogenous sampling, scanning was performed while the sample was spinning at 15 rpm.

2-2-4- Inductively Coupled Plasma- Optical Emission spectroscopy (ICP-OES)

ICP-OES analysis of aliquots after dilution by nitric acid 2% (w/v) in Falcon tubes was carried out using a Varian 725-ES Spectrometer equipped with an autosampler Varian SPS3 to quantify the amount of boron, phosphorus and sodium. The standards for these elements were as follows: boron, Fluka Analytical (1000 ± 3 ppm), phosphorus, Sigma-Aldrich (1000 ± 3 ppm) and sodium, PlasmaCAL (1000 ± 5 ppm).

2-2-5- Solid-State NMR spectroscopy (SSNMR)

All NMR spectra were acquired on a Varian ^{UNITY}Inova 600 ($B_0 = 14.1\text{T}$) spectrometer using a 3.2 double resonance Varian-Chemmagetics H(F)-X MAS probe. One-dimensional ^{11}B , ^{23}Na and ^{31}P magic angle spinning (MAS) NMR spectra were acquired using a Bloch-decay pulse sequence with optimized experimental parameters represented in Table 2-2. All samples were spun at 54.74° with a spinning rate of 25 kHz. For quadrupolar nuclei ^{11}B and ^{23}Na , a 15° tip angle was applied to excite sites with various quadrupolar coupling constants while a 20° tip angle was used for ^{31}P to account for what is expected to be a long spin-lattice relaxation time. In the ^{11}B MAS NMR spectra, the $^{[4]}\text{B}$ peak intensity was corrected for the underlying satellite transition by subtracting its spinning sideband from the original spectrum.

Table 2-2) Parameters used to collect NMR data, and shift references

	Pulse width (degree)	Recycle Delay (s)	#Scans	Shift reference
^{11}B	15	1	1024	0.1 M H_3BO_3 (+19.6 ppm relative to $\text{BF}_3\text{Et}_2\text{O}$)
^{23}Na	15	1	1024	0.1 M NaCl
^{31}P	20	60	128	85% H_3PO_4

1D refocused-INADEQUATE method¹⁰⁸ was employed to acquire ^{31}P double-quantum filtered spectra. In this process, double-quantum coherence is generated through indirect ^{31}P - ^{31}P spin-spin coupling and then converted to single-quantum coherence for observation. The experimental conditions included a spinning speed of 15.0 kHz, a 90-degree pulse length of 2.3 μs , and a relaxation delay of 120 s (preceded by a pre-saturation train before each scan). The mixing time for creating double-quantum coherence was 16.6 ms, corresponding to an indirect spin-spin coupling constant $^2J(^{31}\text{P}\text{-}^{31}\text{P})$ of 30 Hz.

The measurement parameters employed for $^{11}\text{B}\{^{31}\text{P}\}$ REDOR NMR experiments are: rotor frequency 15.0 kHz, length of the refocusing pulse on the observe channel 4.6 μs , nutation frequency on the recouple channel 109 0 kHz, length of the recoupling pulse 2.78 μs and relaxation delay 2 s. In all the REDOR experiments XY-4 phase cycling was utilized for the recoupling π -pulses.¹⁰⁹

2-2-6- Solution ^{31}P NMR spectroscopy

^{31}P NMR spectra were collected on a Bruker Avance III 500 MHz spectrometer ($B_0 = 11.7\text{ T}$) equipped with a 5 mm probe. 85% H_3PO_4 and D_2O (filled in a capillary tube) were used as the reference and internal lock signal, respectively. To acquire the spectra, an NMR tube was filled with 10 mg of the samples along with 0.6 ml distilled water. Spectra were collected every three minutes using a 15 s delay, 30° pulse width and 34 scans.

2-3- Results

2-3-1- Synthesis

Table 2-1 lists the results of the ICP-OES for examining the composition of the glasses. The analyzed compositions consistently show a reduction in P_2O_5 content compared to the nominal values, indicating phosphorus loss during the melting process. The discrepancy between the nominal and analyzed compositions is between 2 to 10 %.

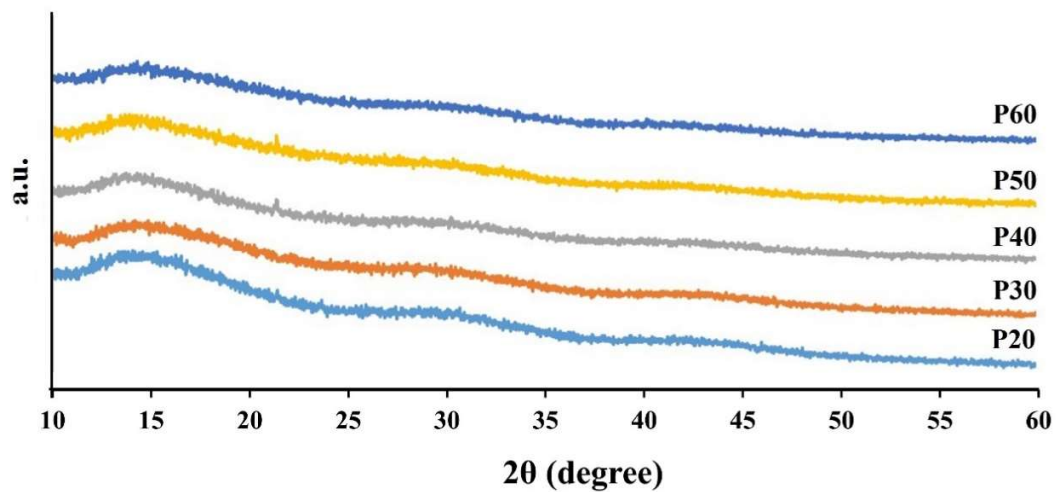


Figure 2-2) XRD diffractograms of as-made glasses

Figure 2-2 shows the x-ray diffractograms of the as-made glasses. Except for P40 and P50, diffraction patterns show a background with no sharp peaks, indicating that samples are amorphous. By careful inspection a very small peak at c.a. $2\theta = 21^\circ$ is detected in sample containing 40 mol% P_2O_5 . By considering the main peak of the BPO_4 phase appears at $2\theta = 25^\circ$ and ^{31}P NMR results, most probably this phase is attributed to BPO_4 . The slight shift observed in

the XRD diffractogram can be attributed primarily to the incorporation of Na⁺ cations into the crystalline structure of BPO₄. This incorporation likely occurred due to the quenching of P40 from a high temperature (1325°C). Furthermore, the presence of a broad peak with low intensity indicates poor crystallinity, further supporting the observed deviation in peak positions. Because the amount of phase separation is too low (see further details in NMR section) all samples were treated as pure glasses.

2-3-2- Dissolution behaviour: Elemental release and pH

The elemental dissolution profile of glasses is shown in Figure 2-3. These graphs show the normalized ion release (NIR)¹¹⁰ of the glasses as a function of the immersion time in the aqueous medium.

$$\text{NIR} = \frac{C_i \times V}{f_i \times m} \quad \text{Eq. 2-1}$$

NIR is related to the concentration of the element in the leachate as determined from ICP-OES analysis (C_i , ppm), the sample volume (v , L), the mass fraction of the element present in the bulk glass (f_i), and the original mass of the powdered sample (m , mg). Although all elements have similar behaviour within a given glass through the dissolution, comparing glasses with each other reveals different dissolution rates. P20 reaches the maximum loss faster than P40 however, their initial dissolution rate is comparable. On the other hand, P60 continues dissolving over the entire seven-day experimental time of this test. In Figure 2-4 the dissolution profiles of all glasses are grouped according to their constituent elements (Na, B, and P). All elements exhibit a similar dissolution trend. Based on these dissolution profiles, P20, P30, and P40 can be grouped into one category, while P50 and P60 fall into another distinct category. In Figures 2-3 and 2-4, NIR values greater than 1 are likely related to the propagation of errors associated with glass composition, pipetting technique, mass balance and glassware used for the dissolution study.

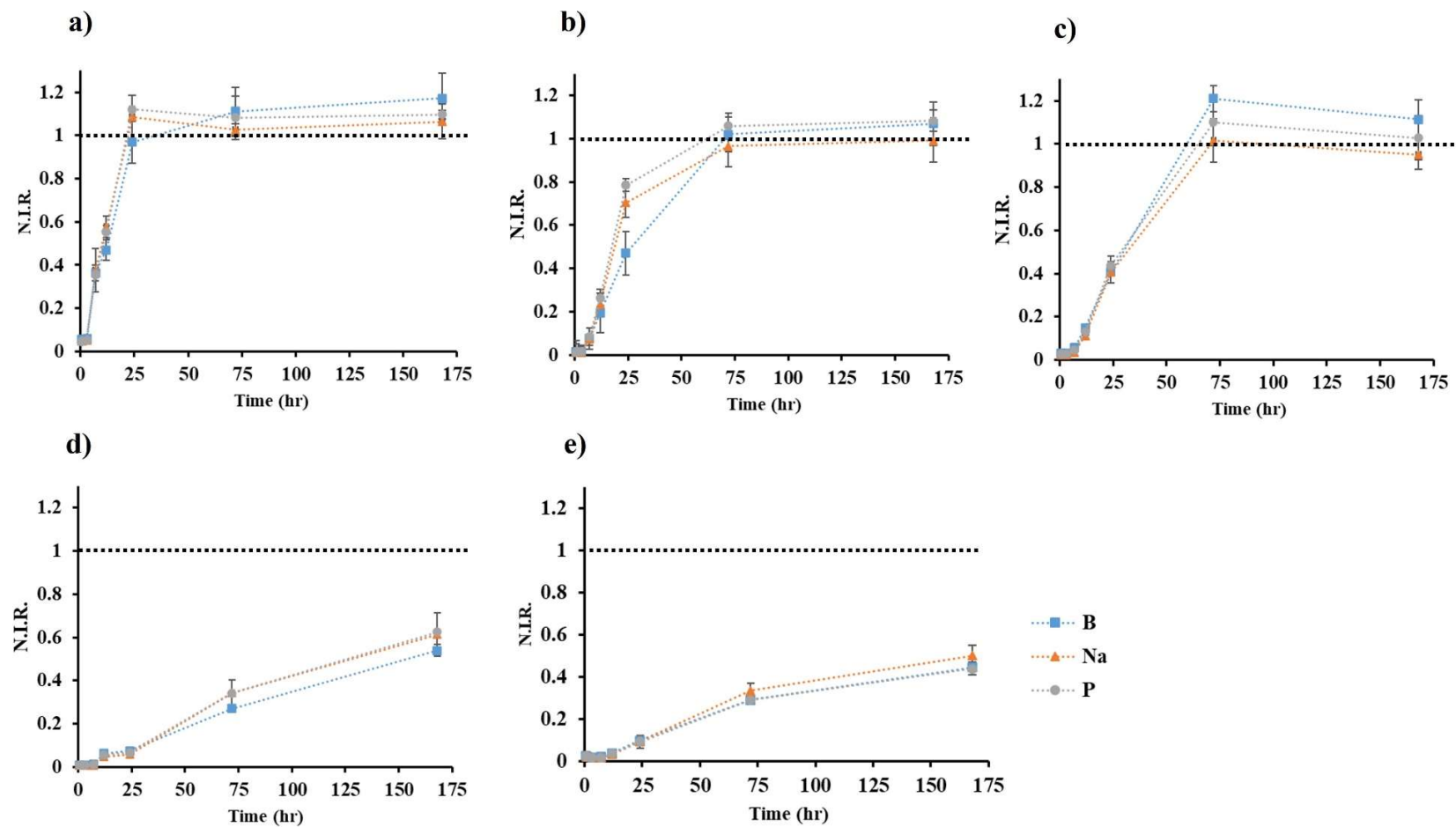


Figure 2-3) Elemental dissolution profile obtained by Inductively Coupled Plasma ICP – OES, grouped by glasses. a) P20, b) P30, c) P40, d) P50, e) P60. The horizontal dashed line indicates full dissolution.

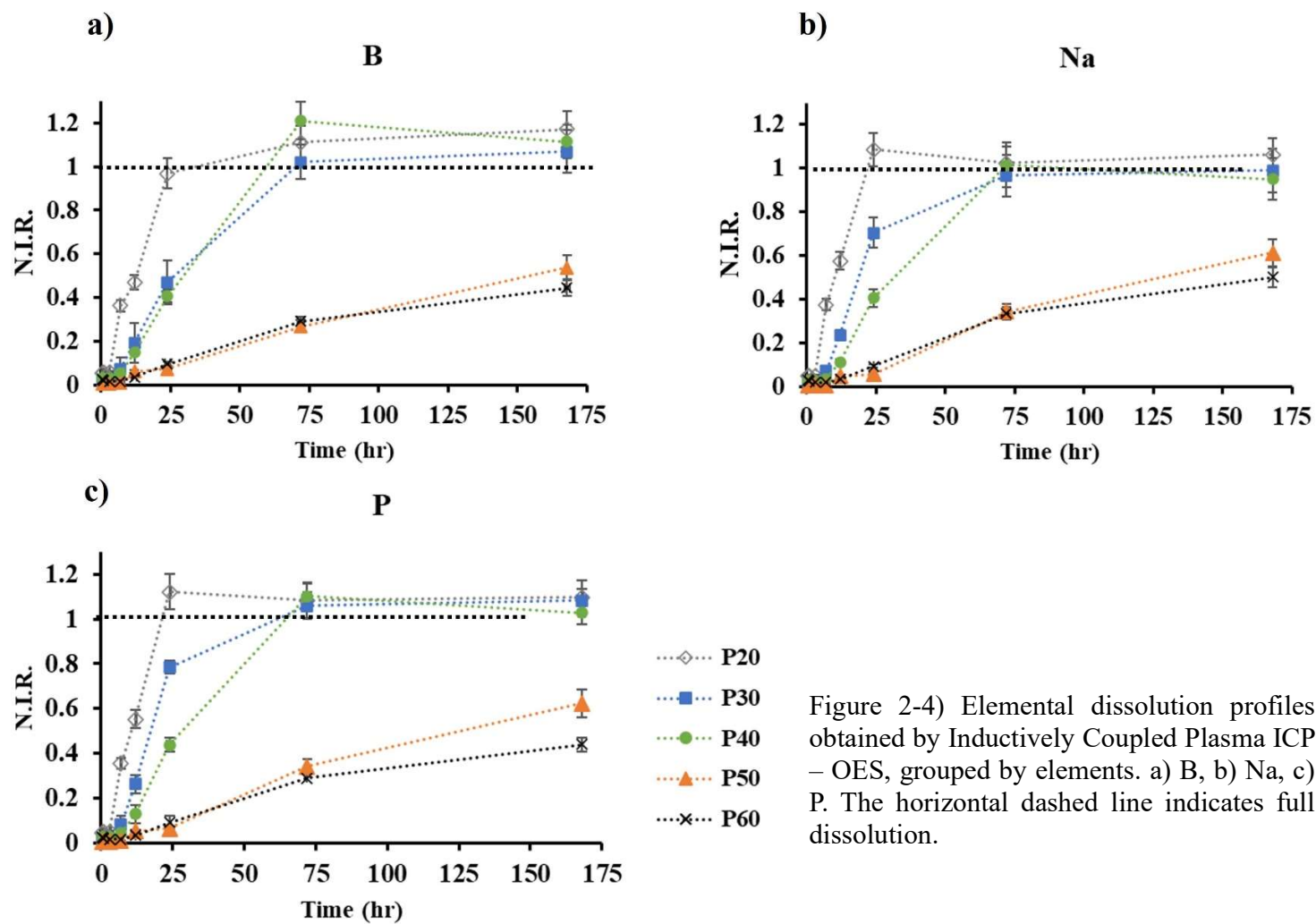


Figure 2-4) Elemental dissolution profiles obtained by Inductively Coupled Plasma ICP – OES, grouped by elements. a) B, b) Na, c) P. The horizontal dashed line indicates full dissolution.

The pH measurement and mass loss results for glasses are reported in Table 2-3. Glasses containing 60 and 50 mol% B₂O₃ show a high dissolution rate in which more than half of the sample is dissolved within 15 minutes.

Table 2-3) pH and mass loss (%) measurements of the dissolved samples in the water

	15 min		24 hr		7 days	
	Mass loss%	pH (± 0.1)	Mass loss%	pH (± 0.1)	Mass loss%	pH (± 0.1)
P20	58.5 $\pm$ 3	6.5	100	5.6	100	5.6
P30	55.5 $\pm$ 3	3.2	100	2.6	100	2.6
P40	8 $\pm$ 1	3.0	82.8 $\pm$ 1	2.4	100	2.0
P50	3.5 $\pm$ 0.5	3.6	11 $\pm$ 0.5	2.6	50.4 $\pm$ 1	1.8
P60	6 $\pm$ 0.5	3.0	8 $\pm$ 0.5	2.6	37.6 $\pm$ 1	1.8
B40	83.6	8.2	100	6.1	100	6.0
B20	14	5.3	100	5.0	100	5.0

The pH of the glasses (Figure 2-5) was monitored during the dissolution test, concurrent with the aliquots collected for elemental analysis. P20 exhibits a gradual 1-unit decrease in pH, reaching approximately 6 after 7 hours, followed by a slight further decrease to 5.6 after 7 days. In contrast, the pH of the remaining samples rapidly drops to 3 within 30 minutes. P30 and P40 stabilize at pH values of 2.6 and 2.0, respectively, after 7 days, while P50 and P60 reach lower end values of 1.80.

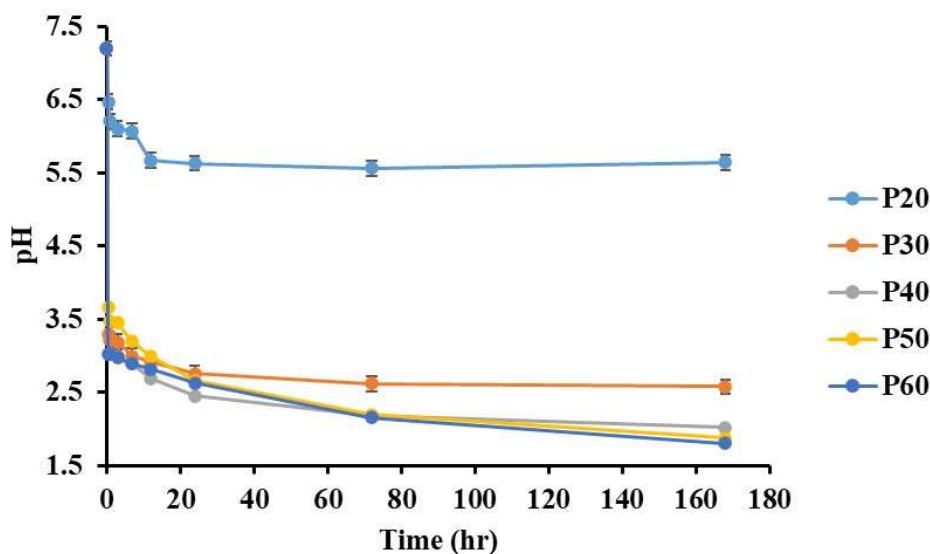


Figure 2-5) Solution pH of the dissolving water as a function of time

2-3-3- Structural analysis before dissolution

2-3-3-1- ^{11}B MAS NMR

The ^{11}B MAS NMR spectra of the glasses are presented in Figure 2-6. Two boron species, three-coordinated boron ($^{[3]}\text{B}$) with quadrupolar coupling constant (C_Q) ≈ 2.5 MHz and four-coordinated boron ($^{[4]}\text{B}$) with $C_Q \approx 0.5$ MHz,⁸⁶ are well resolved in the boron-rich glass, P20. The difference between the lineshapes of three and four-coordinated boron comes from the symmetry around the boron atom. Those boron atoms occupying trigonal sites have second-order quadrupolar interactions that cannot be averaged out with MAS NMR, leading to broadening. It has been shown that in borate glasses three-coordinate boron comprise two species, ring and non-ring boron.^{111,112} In the current glass series two components are needed to fit the $^{[3]}\text{B}$ signal and they were assigned to ring and non-ring boron.⁸⁶ In the case of $^{[4]}\text{B}$, B atoms experience a weak quadrupolar interactions because of the high symmetry in the tetrahedral sites, so a narrow lineshape is observed. By replacing boron by phosphorus, the intensity of the $^{[3]}\text{B}$ signal decreases gradually and vanishes eventually in the samples containing 50 mol% P_2O_5 and higher. The fraction of $^{[4]}\text{B}$ ($N_4 = [^{[4]}\text{B}] / ([^{[4]}\text{B}] + [^{[3]}\text{B}])$), increases from 0.43 to 1 (see Table 2-4 for fitted parameters) when B_2O_3 is replaced by P_2O_5 . It should be noted that the central transition of the $^{[4]}\text{B}$ peak overlaps with the centerband of the satellite transition. Therefore, its intensity needs to

be adjusted. This correction is made by subtracting the intensity of the first sideband from the $^{[4]}\text{B}$ peak.

In the majority of samples $^{[4]}\text{B}$ is composed of more than one species. It has been well established that these species are characterized as $^{[4]}\text{B-O-P}$ linkages¹¹³ that usually are denoted as $^{[4]}\text{B}_{\text{mP}}$ where $m = 0-4$ is the number of phosphorus linked to boron. In P20, the glass with 60 mol % B_2O_3 , this peak consists of three species. The first species is $^{[4]}\text{B}_{2\text{P}}$, which means a boron is surrounded by two phosphorus and two boron atoms, resonates at -0.20 ppm, and the second component, $^{[4]}\text{B}_{3\text{P}}$ occurs at -2.20 ppm. By incorporating more phosphorus, while the overall $^{[4]}\text{B}$ signal moves to lower frequencies, the fraction of each species changes monotonically. The $^{[4]}\text{B}$ in P30 was fit to three components at -0.20, -1.55 and -3.50 ppm attributed to $^{[4]}\text{B}_{2\text{P}}$, $^{[4]}\text{B}_{3\text{P}}$ and $^{[4]}\text{B}_{4\text{P}}$ moieties. In the case of B40 the glass is composed of $^{[4]}\text{B}_{3\text{P}}$ and $^{[4]}\text{B}_{4\text{P}}$ structural units with the integral intensity of 34 and 52%, correspondingly. Deconvolution of the phosphorus-rich samples, P50 and P60, indicates that the boron tetrahedra are mainly bonded to four phosphorus. The full width at half maximum for $^{[4]}\text{B}_{\text{nP}}$ was set to 0.4 ± 0.1 kHz except for P30, because this sample contains three borate species. The fractions of each component are summarized in Table 2-4.

By increasing the amount of network modifier, Na, the structure of the glasses undergoes substantial changes. The ^{11}B MAS NMR spectrum of B40 (Figure 2-7) shows that the peak maximum of the $^{[4]}\text{B}$ appears at 0.00 ppm, which means that phosphorus is not abundant in the next-nearest-neighbour shell of a given $^{[4]}\text{B}$. Fitting this signal reveals that $^{[4]}\text{B}$ comprise only one species: $^{[4]}\text{B}_{1\text{P}}$. In the case of B20 the fitting shows that $^{[4]}\text{B}_{3\text{P}}$ and $^{[4]}\text{B}_{4\text{P}}$ with isotropic chemical shifts of -1.0 and -3.0 ppm, respectively, are the major four-coordinated constituents. The N_4 value in the boron-rich sample B40 is 0.57 while the phosphorus-rich sample B20 has 95 percent $^{[4]}\text{B}$ (Table 2-4).

A binary borate glass, $\text{Na}_2\text{O-B}_2\text{O}_3$, was also made to see the change in the $^{[4]}\text{B}$ signal with the presence of the B-O-P linkages in the borophosphate glasses. $^{[4]}\text{B}$ was fitted with one component which is resonated at +1.0 ppm. The ^{11}B MAS NMR spectrum for this glass is shown in Figure 2-7.

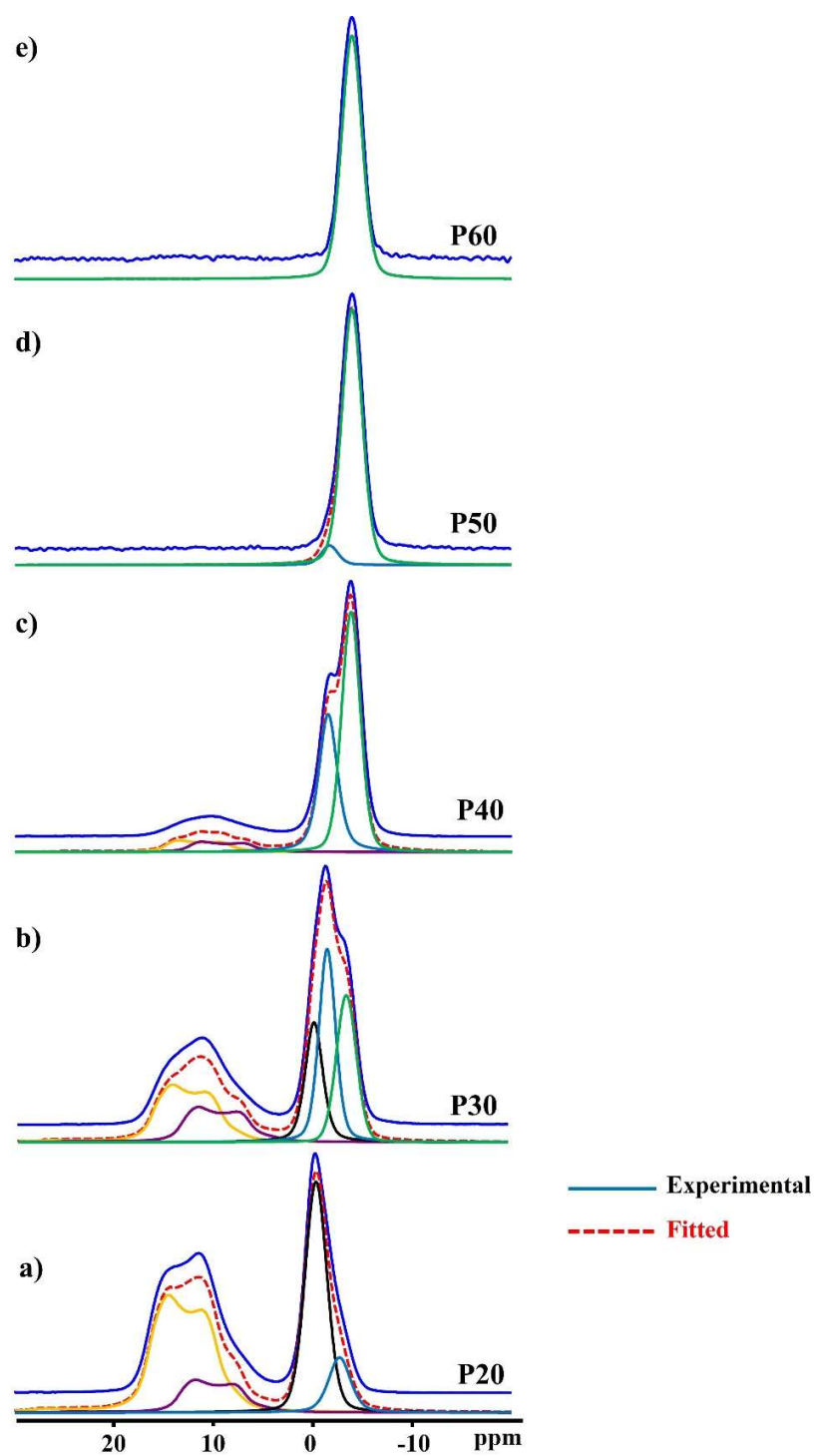


Figure 2-6) ^{11}B MAS NMR spectra of a) P20, b) P30, c) P40, d) P50, e) P60 before dissolution. $^{[3]}\text{B}_{\text{ring}}$, $^{[3]}\text{B}_{\text{non-ring}}$, $^{[4]}\text{B}_{2\text{P}}$, $^{[4]}\text{B}_{3\text{P}}$, and $^{[4]}\text{B}_{4\text{P}}$

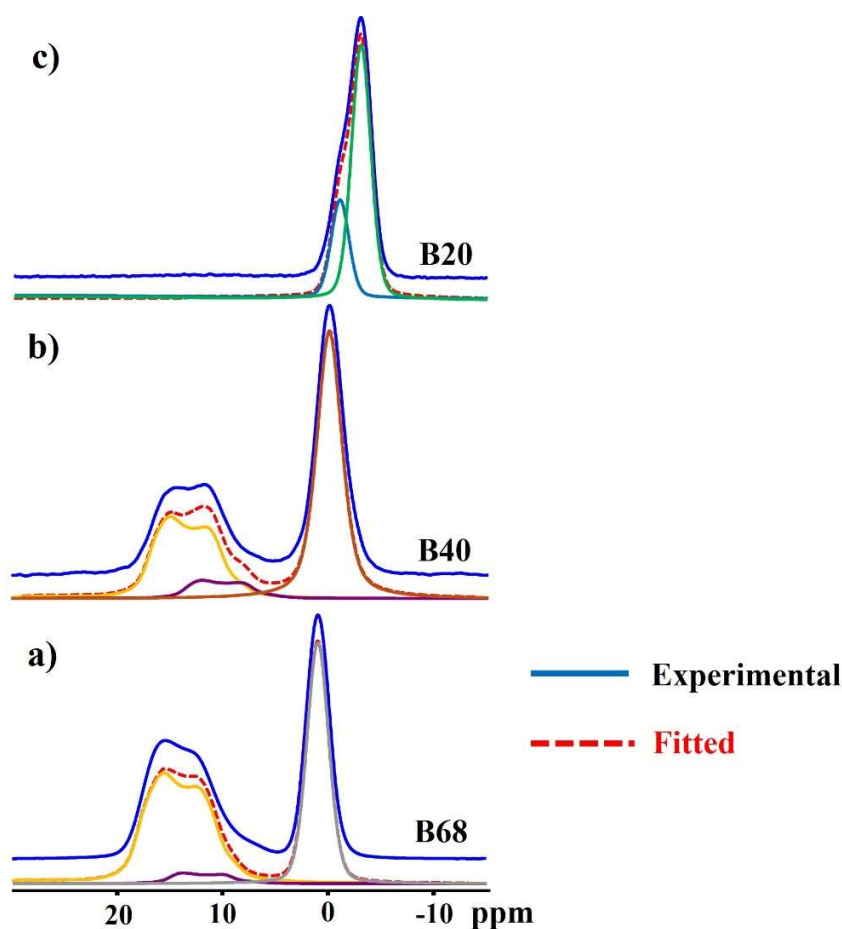


Figure 2-7) ^{11}B MAS NMR of a) B68, b) B40, c) B20 before dissolution. $^{[3]}\text{B}_{\text{ring}}$, $^{[3]}\text{B}_{\text{non-ring}}$, $^{[4]}\text{B}_{0\text{P}}$, $^{[4]}\text{B}_{1\text{P}}$, $^{[4]}\text{B}_{3\text{P}}$, and $^{[4]}\text{B}_{4\text{P}}$

All curve fittings for 1D NMR spectra were done manually. In the case of four-coordinate boron signals, for example, a Gaussian/Lorentzian (G/L) model was used to fit the curve. The input parameters are peak position, peak width, mixture of G and L, and amplitude. In manual fitting, all these parameters are fixed by the user and the resultant integrated intensity is reported. Since the parameters are fixed, the change in the integrated intensity of a species is low, ca. 1%, when that parameter is changed within the narrow uncertainty limit reported in the tables. For example, in Table 2-4, the isotropic chemical shift of $^{[4]}\text{B}_{4\text{P}}$ species in P30 fixed to -3.50 ppm with ± 0.1 ppm uncertainty. Therefore, the integrated intensity obtained with fixed peak widths will have an uncertainty of ± 2 .

Table 2-4) Parameters used for fitting ^{11}B magic angle spinning (MAS) NMR spectra.

	^{13}B				^{14}B									
	$^{13}\text{B}_{\text{ring}}$		$^{13}\text{B}_{\text{non-ring}}$		$^{14}\text{B}_{2\text{P}}$		$^{14}\text{B}_{3\text{P}}$			$^{14}\text{B}_{4\text{P}}$				N_4
	δ_{iso} (ppm)	Int. (%) ± 2	δ_{iso} (ppm)	Int. (%) ± 2	δ_{iso} (ppm)	W (kHz)	Int. (%) ± 2	δ_{iso}	W (kHz)	Int. (%) ± 2	δ_{iso}	W (kHz)	Int. (%) ± 2	
P20	+17.1	45	+14.2	12	-0.2	0.40	30	-2.2	0.50	13	-	-	-	0.43
P30	+16.8	26	+14.0	14	-0.2	0.40	16	-1.5	0.24	22	-3.5	0.46	20	0.60
P40	+16.2	7	+14.0	6	-	-	-	-1.5	0.42	34	-3.8	0.42	52	0.86
P50	-	-	-	-	-	-	-	-1.7	0.32	7	-3.9	0.38	93	1
P60	-	-	-	-	-	-	-	-	-	-	-3.9	0.40	100	1
$^{14}\text{B}_{1\text{P}}$														
B40	+17.6	37	+14.3	7	0.0	0.52	56	-	-	-	-	-	-	0.56
$^{14}\text{B}_{3\text{P}}$ $^{14}\text{B}_{4\text{P}}$														
B20	+16.5	5	-	-	-	-	-	-1.0	0.38	28	-3.0	0.41	67	0.95
$^{14}\text{B}_{0\text{P}}$														
B68	+18.5	44	-	-	+1.0	0.45	56	-	-	-	-	-	-	0.56

C_Q fixed to 2.5 MHz with a tolerance of ± 0.1 MHz, W: Full Width at Half Maximum (peak width) and δ_{iso} fixed to values reported in the table, Int: Integrated

intensities were fitted and then N_4 values were calculated, η fixed to 0.2 with a tolerance of ± 0.1

2-3-3-2- $^{11}\text{B}\{^{31}\text{P}\}$ REDOR NMR

Figure 2-8 shows the $^{11}\text{B}\{^{31}\text{P}\}$ REDOR dephasing curve as a function of dephasing time for the P20-P50 glass series. The dephasing curve of P20 shows that there are three types of four-coordinated boron including $^{[4]}\text{B}_{1\text{P}}$, $^{[4]}\text{B}_{2\text{P}}$ and $^{[4]}\text{B}_{3\text{P}}$. Each point, normalized difference signal intensities $\frac{\Delta S}{S_0}$, in the dephasing curves was calculated by fitting the S (with recoupling pulsing) and S_0 (without recoupling pulsing) spectra obtained at various dipolar evolution time, NT_R .¹¹⁴ Figure 2-9a shows representative S spectra for P30 at $\text{NT}_\text{R} = 0.13, 0.40, 0.66, 0.93,$ and 1.20 ms, respectively. In the four-coordinated region there are three species which dephases differently under REDOR experiments. The intensity of the dephased spectra is governed by the rotor evolution time and strength of the heteronuclear dipolar interaction.⁷⁹ In fact, for a given B, changing the number of linked P alters the M_2 value, since M_2 is inversely proportional to r^6 (Eq. 1-67). Figure 2-9b shows different attenuation of the intensity of subspectra in the four-coordinated boron region. In Figure 2-8 the dephasing curve of crystalline BPO_4 is also included as the model compound to validate the REDOR pulse sequence. In addition, the crystal structure of this compound is very well known, consisting of alternating boron and phosphorus tetrahedra, which means for any given B cation there are four B–O–P linkages.¹¹⁵ Therefore, the dephasing curve of crystalline BPO_4 is strong and serves as a reference for assigning the species found in borophosphate glasses.

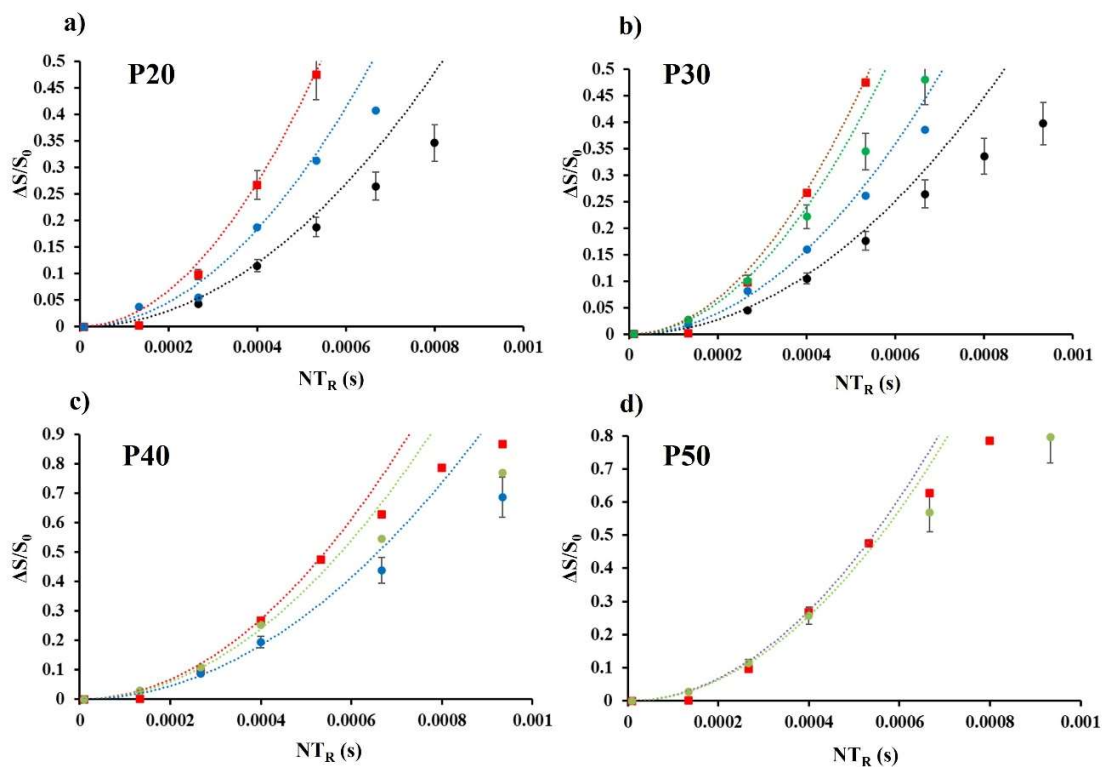


Figure 2-8) $^{11}\text{B}\{^{31}\text{P}\}$ REDOR dephasing curve as a function of the rotor period evolution time a) P20, b) P30, c) P40, d) P50; BPO_4 , $^{[4]}\text{B}_{2\text{P}}$, $^{[4]}\text{B}_{3\text{P}}$, and $^{[4]}\text{B}_{4\text{P}}$

Table 2-5) Second moments, $M_{2(\text{B-P})}$, obtained from fitting the $^{11}\text{B}\{^{31}\text{P}\}$ REDOR dephasing curves ($\times 10^6 \text{ rad}^2\text{s}^{-2} \pm 10\%$)

	$^{[4]}\text{B}_{2\text{P}}$	$^{[4]}\text{B}_{3\text{P}}$	$^{[4]}\text{B}_{4\text{P}}$
P20	7.9	12.1	-
P30	7.9	11.6	15.8
P40	-	12.1	15.8
P50	-	-	16.9
BPO₄	-	-	18.0

Second moments, $M_{2(\text{B-P})}$, are calculated using Eq. 1-68 and Table 2-5 summarizes the results for the glass series P20–P60. Each B–O–P linkage typically contributes approximately $4\text{--}5 \times 10^6$

$\text{rad}^2\text{s}^{-2}$ to the overall second moment. To enable quantification of the dephasing curves for glasses, crystalline BPO_4 was measured by $^{11}\text{B}\{^{31}\text{P}\}$ REDOR NMR as a model compound. The experimentally obtained M_2 value for this compound is $12.5 \times 10^6 \text{ rad}^2\text{s}^{-2}$. Given that the calculated M_2 value for BPO_4 is $18 \times 10^6 \text{ rad}^2\text{s}^{-2}$, a correction factor of 0.67 is applied to the glasses to account for the lower M_2 values obtained experimentally. This discrepancy comes from instrumental factors including missed pulse and finite pulse length in relation to the rotor period. For example, P30 is fitted with three distinct borate species, $^{[4]}\text{B}_{2\text{P}}$, $^{[4]}\text{B}_{3\text{P}}$ and $^{[4]}\text{B}_{4\text{P}}$ yielding M_2 values 7.9 , 11.6 and $15.8 \times 10^6 \text{ rad}^2\text{s}^{-2}$, respectively. These second moment values support the borate assignments for P30, and a similar reasoning applies to the other glasses.

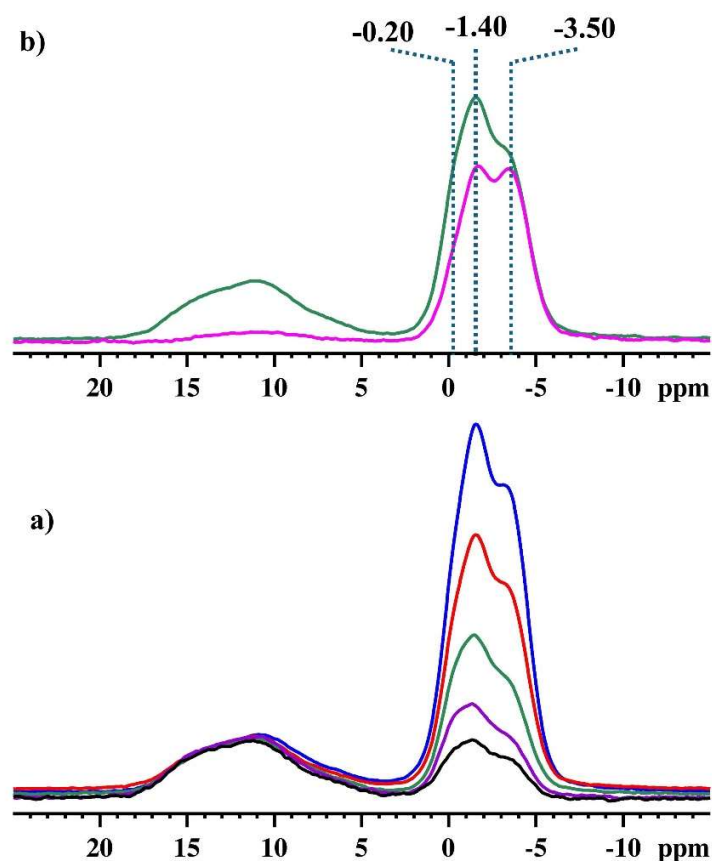


Figure 2-9) a) Representative S spectra for P30 at $\text{NT}_R = 0.133, 0.4, 0.66, 0.93$, and 1.2 ms. b) S and ΔS spectra for P30 at $\text{NT}_R = 0.66$. S and S_0 denotes intensity of the signal with and without dipolar interaction, respectively. $\Delta S = S - S_0$. NT_R refers to the dipolar evolution time.

2-3-3-3- ^{31}P MAS NMR & ^{31}P R-INADEQUATE MAS NMR

Figure 2-10 shows the ^{31}P MAS NMR spectra of the as-made samples. All spectra have a symmetrical broad lineshape which is the characteristic of borophosphate glasses because they contain various types of $\text{P}_{\text{mB}}^{\text{n}}$ species with strongly overlapping peak positions. The chemical shift ranges of various phosphate units, as reported in the literature, are compiled and presented in Figure 2-11. Table 2-6 summarizes the ^{31}P MAS NMR spectra curve fitting based on a minimum number of the fitting components. In the current glass series, ^{31}P MAS NMR reveals that P20 is dominated by $\text{P}_{2\text{B}}^2$, $\text{P}_{3\text{B}}^3$, while in P30 the fraction of $\text{P}_{2\text{B}}^2$ decreases at the expense of $\text{P}_{3\text{B}}^3$. The fraction of $\text{P}_{3\text{B}}^3$ reaches a maximum of 80% in P30 and remains as high as 75% in P40. With the decrease of B_2O_3 content in this glass series $\text{P}_{3\text{B}}^3$ starts to be replaced by structural units containing a smaller number of B–O–P units, i.e. $\text{P}_{2\text{B}}^3$ and $\text{P}_{1\text{B}}^3$. P50 and P60 are mainly constructed by 40 and 50% $\text{P}_{2\text{B}}^3$, respectively. High-P samples P50 and P60 also contain a small fraction of $\text{P}_{0\text{B}}^3$. In the NMR spectrum of P50, a small narrow peak at -29.9 ppm is superimposed on the broad peak, which is an indication of the presence of crystalline BPO_4 (-29.3 ppm). Since its integrated intensity is less than 2%, this component was neglected in the structural analysis.

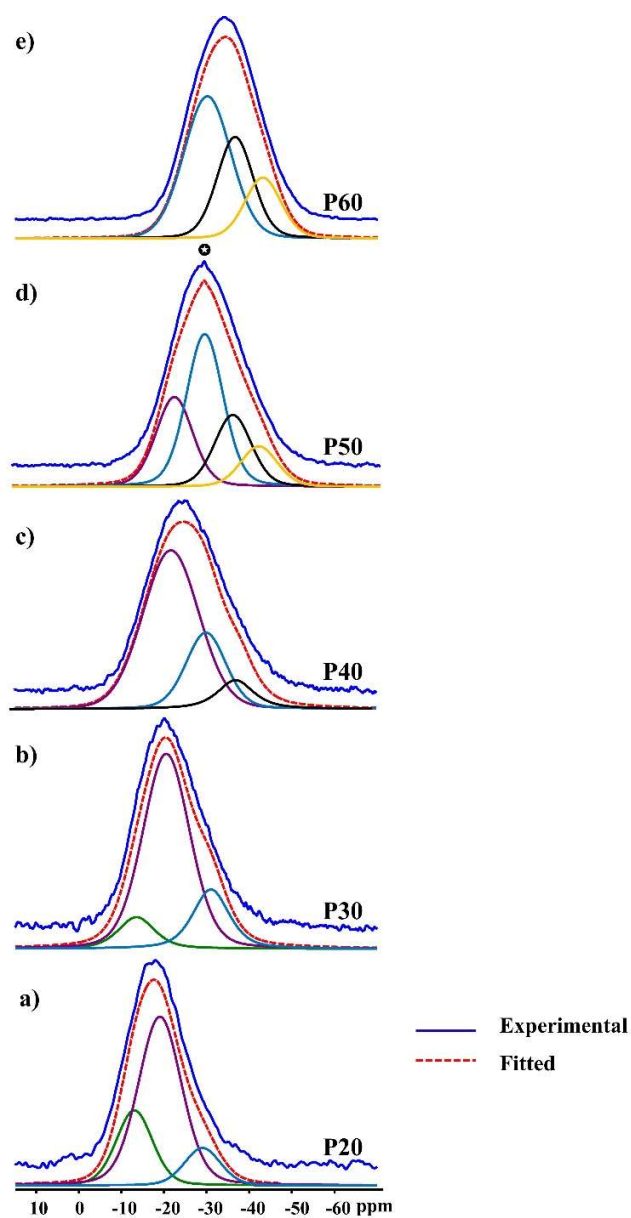


Figure 2-10) ^{31}P MAS NMR spectra of a) P20, b) P30, c) P40, d) P50, e) P60. The asterisk shows a peak assigned to crystalline BPO_4 . $\text{P}_{2\text{B}}^2$, $\text{P}_{3\text{B}}^3$, $\text{P}_{2\text{B}}^3$, $\text{P}_{1\text{B}}^3$, and $\text{P}_{0\text{B}}^3$

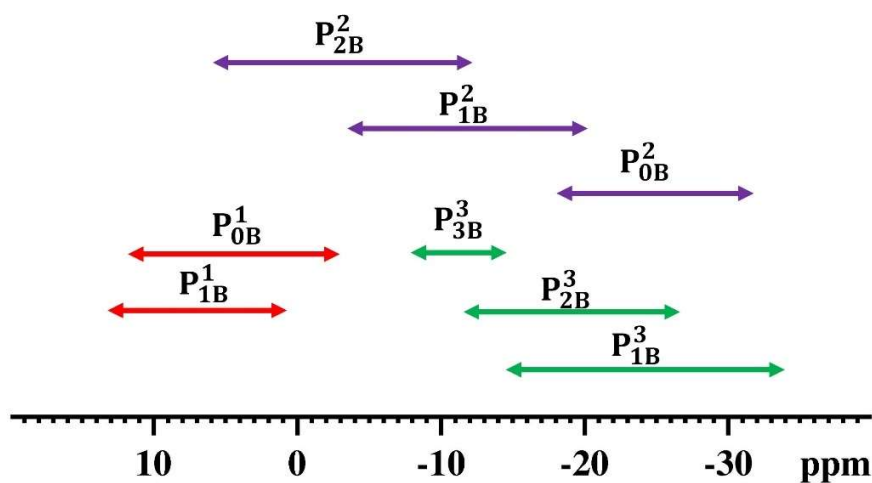


Figure 2-11) Chemical shift ranges of different phosphate units reported in the literature.
References [104, 116, 117, 119, 120, 129]

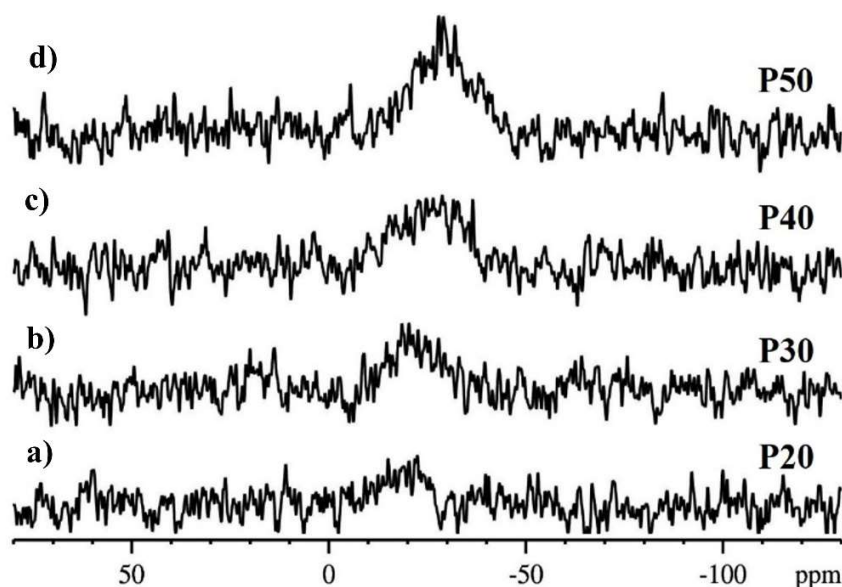


Figure 2-12) ^{31}P R-INADEQUATE MAS NMR of a) P20, b) P30, c) P40 and d) P50

Figure 2-12 shows the ^{31}P R-INADEQUATE MAS NMR of the glass series. Glass containing 20 mol % P_2O_5 shows a weak signal centered at -20 ppm. The peak maximum for the remaining glasses follows the trend observed in ^{31}P MAS NMR spectra. With an increase in the P_2O_5 content from 20 mol% to 50 mol % the intensity of the signal improves; however, the signal-to-noise ratio for the entire glass series is low because of the small concentration of P–O–P linkages (see below).

Figure 2-13 shows the ^{31}P MAS NMR spectra for B40 and B20, glasses containing 40 mol% Na_2O . Following the same assignment strategy to deconvolve the spectra fittings yields 14% $\text{P}_{0\text{B}}^1$, 65% $\text{P}_{1\text{B}}^2$ and 21% $\text{P}_{2\text{B}}^2$ for B40, whereas B20 was found to possess $\text{P}_{1\text{B}}^2$, $\text{P}_{2\text{B}}^2$ and $\text{P}_{2\text{B}}^3$ with fractions of 7, 50 and 43%, respectively (Table 2-6)

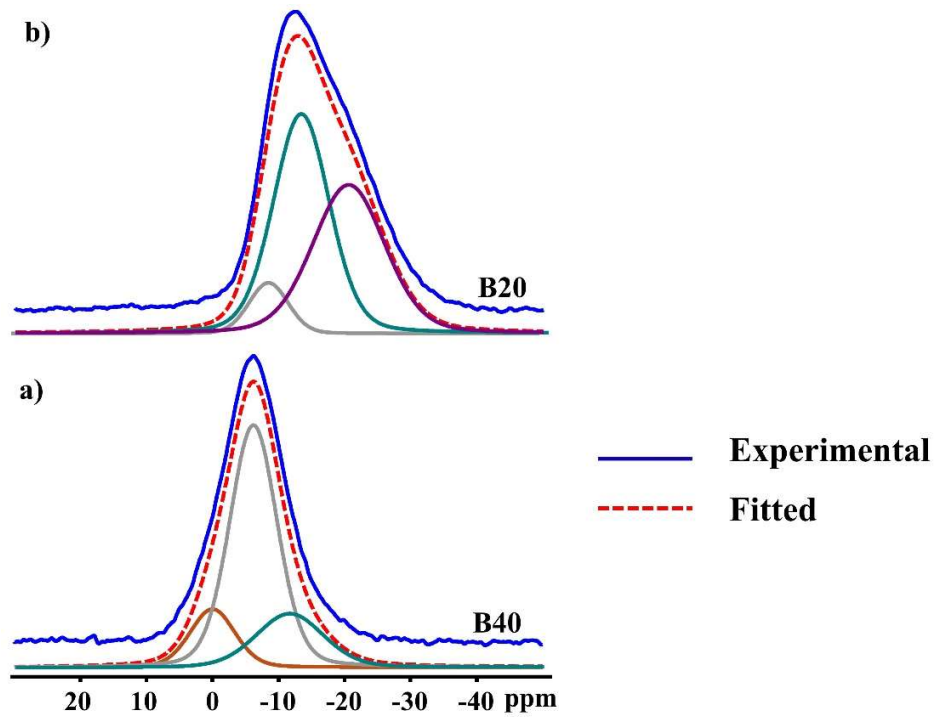


Figure 2-13) ^{31}P magic angle spinning (MAS) NMR spectra of a) B40 and b) B20.
 $\text{P}_{0\text{B}}^1$, $\text{P}_{1\text{B}}^2$, $\text{P}_{2\text{B}}^2$ and $\text{P}_{2\text{B}}^3$

Table 2-6) Parameters used for fitting ^{31}P magic angle spinning (MAS) NMR spectra

	$\text{P}_{2\text{B}}^2$			$\text{P}_{3\text{B}}^3$			$\text{P}_{2\text{B}}^3$			$\text{P}_{1\text{B}}^3$			$\text{P}_{0\text{B}}^3$		
	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)
P20	-13.5	2.00	42	-20.0	2.20	50	-29.0	2.00	8	-	-	-	-	-	-
P30	-13.5	2.00	10	-20.5	2.60	80	-31.0	2.00	10	-	-	-	-	-	-
P40	-	-	-	-21.5	3.00	75	-30.0	2.20	20	-37.0	2.00	5	-	-	-
P50	-	-	-	-22.5	2.00	30	-29.5	2.00	40	-36.0	2.00	20	-42.0	2.00	10
P60	-	-	-	-	-	-	-30.0	2.60	50	-36.5	2.00	35	-43.0	2.00	15
Na40 series															
	$\text{P}_{0\text{B}}^1$			$\text{P}_{1\text{B}}^2$			$\text{P}_{2\text{B}}^2$			$\text{P}_{2\text{B}}^3$					
B40	0.0	1.90	14	-6.0	2.00	65	-12.0	2.90	21	-	-	-			
B20	-	-	-	-8.0	1.70	7	-13.0	2.50	50	-20.5	3.10	43			
Isotropic chemical shift fixed with a tolerance of ± 0.5 ppm, W: Full Width at Half Maximum (Peak width) fixed with a tolerance of ± 0.05 kHz, Int: Integrated intensity $\pm 2\%$ (fitted)															

2-3-4- During dissolution

^{31}P NMR was done to determine the phosphate species found in solution as a function of dissolution time, which provides insight into the relative solubility of the phosphate species released from the glass. Figure 2-14 shows the solution ^{31}P NMR for P20. At the outset of the dissolution experiment a single peak is observed at +0.35 ppm for P20. As time goes by another peak appears at around +0.25 ppm the intensity of which increases during the dissolution experiment. These two peaks are assigned as HPO_4^{2-} and H_2PO_4^- with the isotropic chemical shifts +0.35 and +0.25 ppm, respectively.¹¹⁶ Figure 2-15 shows the change in the fraction of these two peaks as a function of time. It should be noted that error bars are not included in the plots of integrated species intensities versus time. Although such estimates are important, accurately estimating and combining the uncertainties arising from instrumental error, compositional variations, and integration of NMR signals proved difficult in this work.

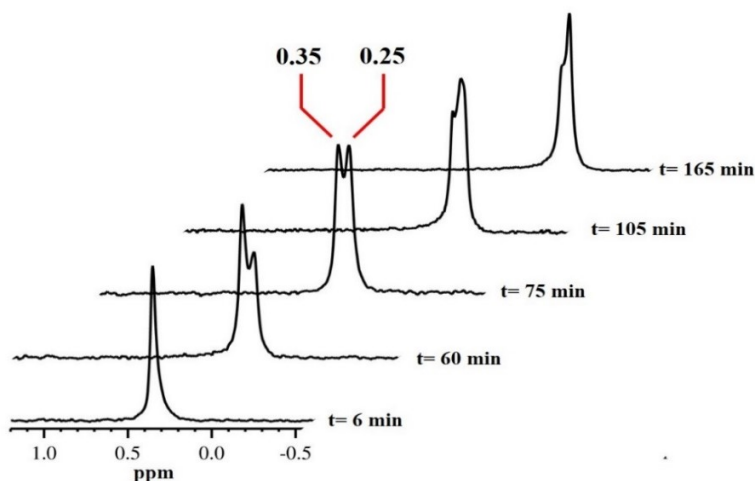


Figure 2-14) Time evolution solution ^{31}P NMR spectra of P20

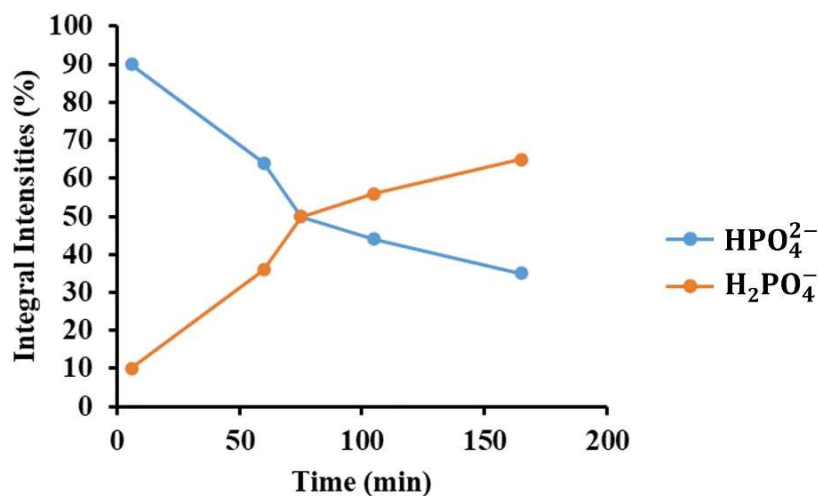


Figure 2-15) Change in the integral intensities of HPO_4^{2-} and H_2PO_4^- as a function of time for P20 obtained from Figure 2-14

Figure 2-16 shows the solution ^{31}P NMR for P30, which exhibits only one peak at +0.15 ppm with the intensity increasing during the *in situ* dissolution experiment. This signal is attributed to H_3PO_4 .^{116,117} In the cases of P40 and P50 (Figure 2-17 and Figure 2-19), a sharp peak at 0 ppm in the initial stages of the dissolution appears while the second peak at -10 ppm comes into the picture after 145 and 90 minutes for P40 and P50, respectively. The signals at 0 and -10 ppm are attributed to orthophosphates, P^0 , and pyrophosphates, P^1 ^{116,117}, respectively.

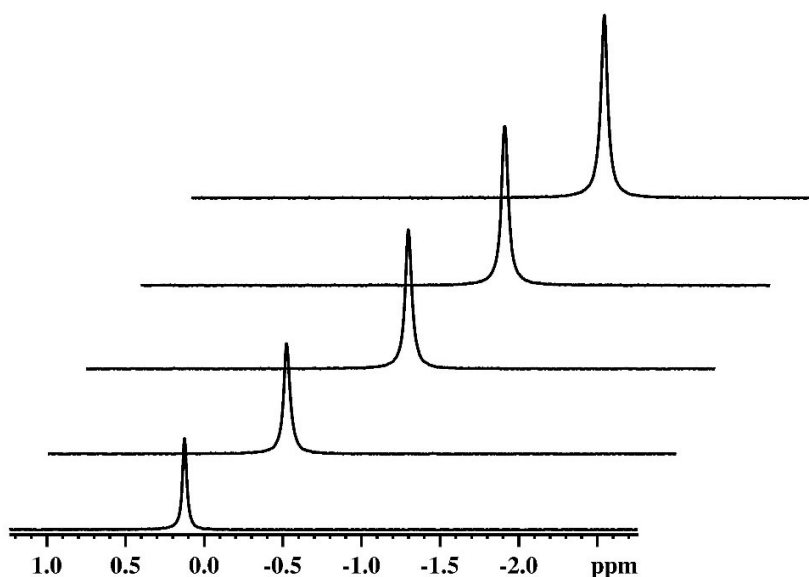


Figure 2-16) Time evolution solution ^{31}P NMR spectra of P30

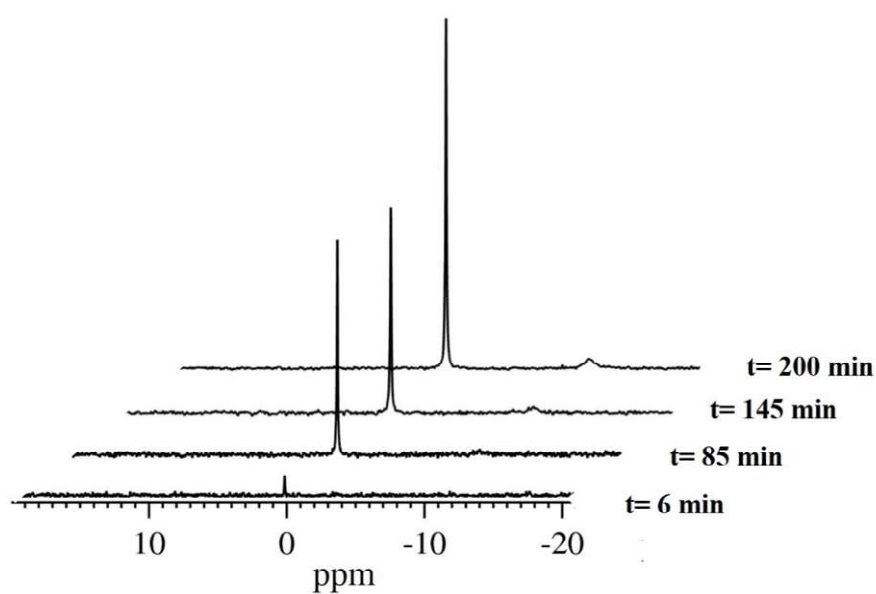


Figure 2-17) Time evolution solution ^{31}P NMR spectra of P40

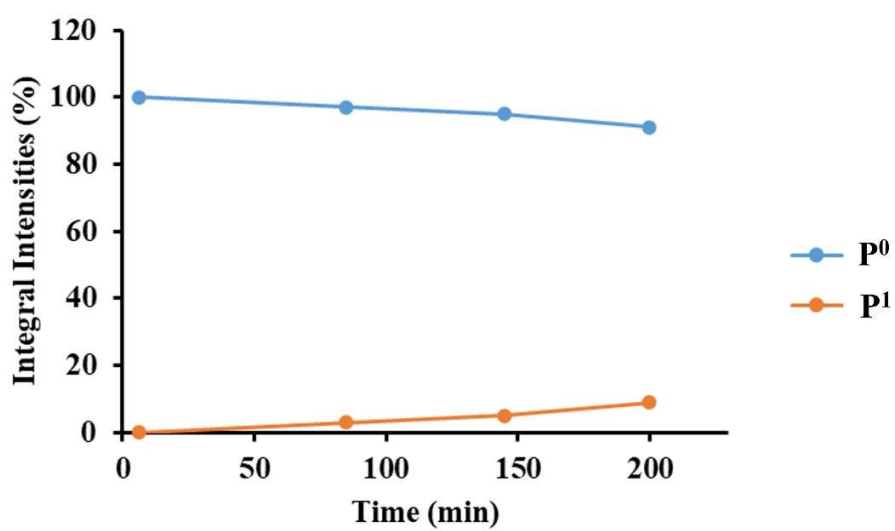


Figure 2-18) Change in the relative integral intensities of P⁰ and P¹ species as a function of time for P40 obtained from Figure 2-17

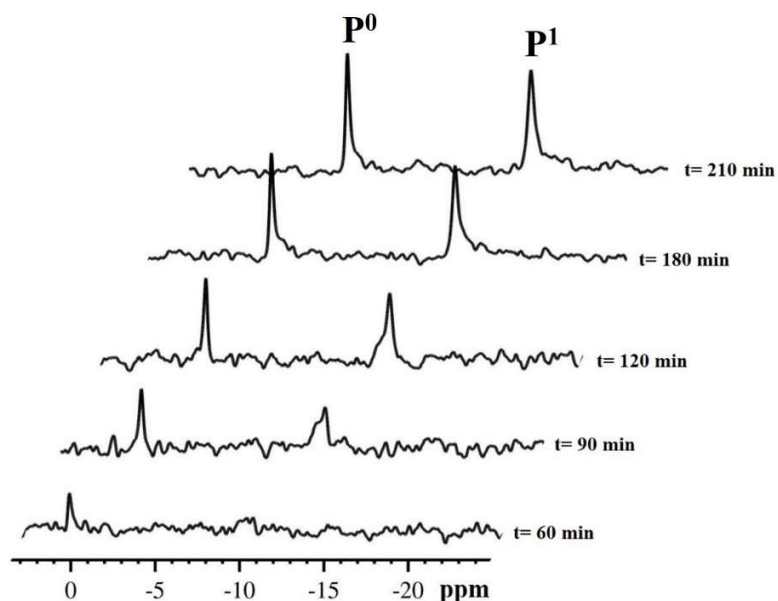


Figure 2-19) Time evolution solution ^{31}P NMR spectra of P50

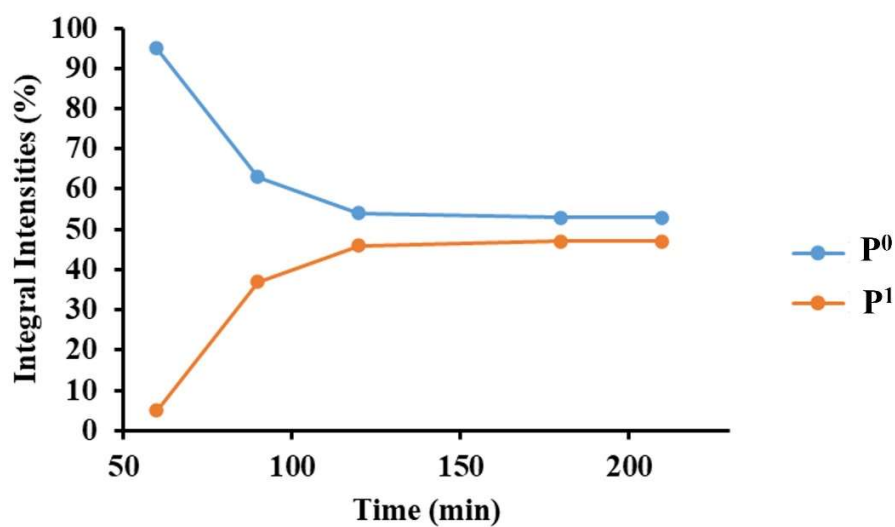


Figure 2-20) Change in the relative integral intensities of P^0 and P^1 as a function of time for P50 obtained from Figure 2-19

In the case of P60 (Figure 2-21), in addition to 0 and -11.0 ppm, two more peaks can be seen at longer dissolution times, after 190 minutes. The third peak resonates at -21.5 ppm and the fourth one is located at -23.6 ppm. These peaks are assigned to P^2 .^{116,117} The relative integrated

intensities of the phosphate species as a function of time are depicted in Figure 2-22. As it can be seen the intensity of P^0 decreases as time goes by, while P^1 and P^2 show a slight increase then reach a plateau after 150 minutes.

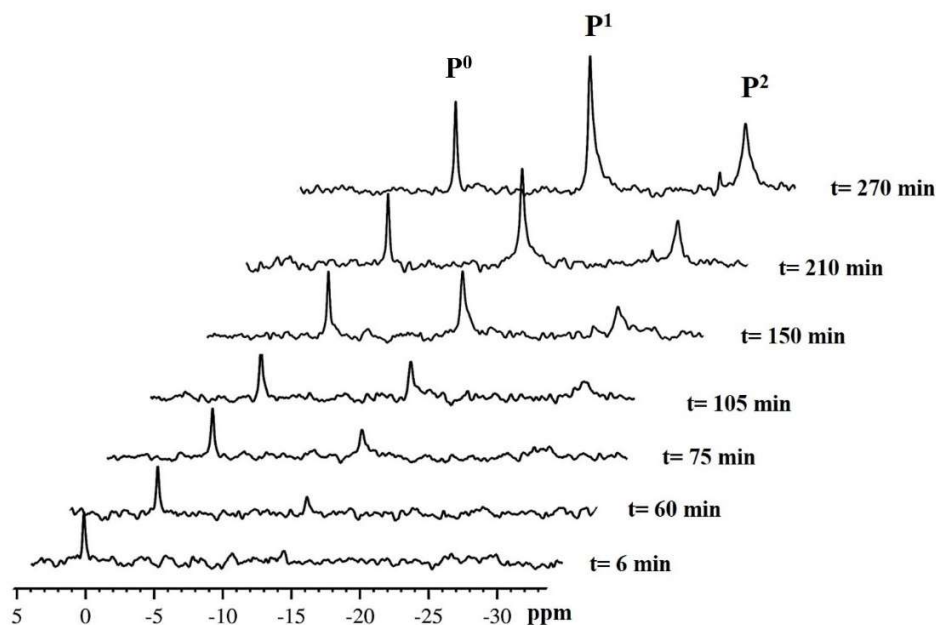


Figure 2-21) Time evolution solution ^{31}P NMR spectra of P60

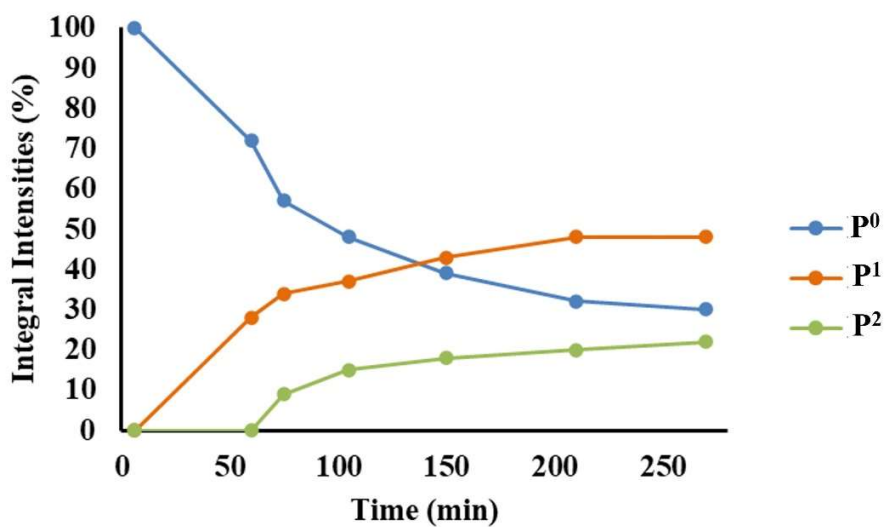


Figure 2-22) Relative integral intensities of P^0 , P^1 and P^2 as a function of time for P60 obtained from Figure 2-21

2-3-5- Structural analysis after dissolution

Analysing the glasses after immersion by NMR and XRD provides information that helps understand the effect of the glass structure on the dissolution behaviour. For example, by comparing the ^{31}P MAS NMR spectra before and after dissolution one can find in a given glass which phosphate species undergoes substantial changes. Therefore, the relative solubility of different structural units can be discussed. In addition, lineshape changes may provide insight into the congruency of dissolution.

Figure 2-23 shows the XRD diffractograms of the glasses after dissolution in water. The undissolved portions of P20, P30, and P40 were collected after 15 minutes for XRD analysis. For glass P50, the undissolved portion was collected after one week, while for P60, samples were collected after 24 hours and again after one week.

The XRD diffractograms of P20-P40 (15 minutes) and P50 (7 days) show no distinct peaks, indicating the absence of crystalline phases. In contrast, the diffractogram of P60 after 24 hours shows Bragg peaks at $2\theta = 25^\circ$ and 40° . After 7 days, the same peaks appear with increased intensity. These peaks correspond to crystalline BPO_4 (ICSD collection code 55082).

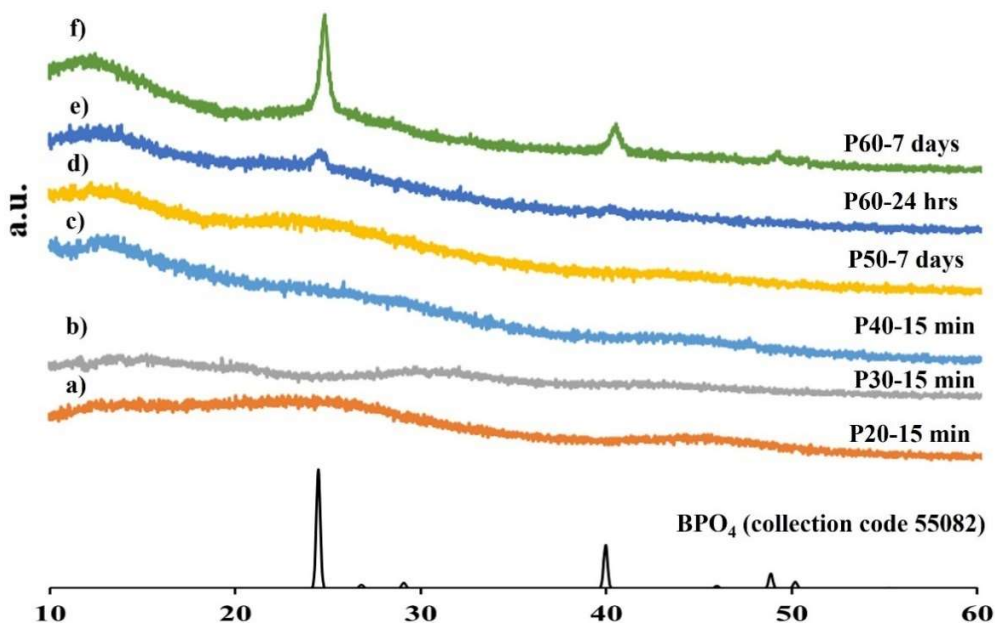


Figure 2-23) XRD diffractograms of a) P20, b) P30, c) P40 after 15 min dissolution d) P50 after 7 days dissolution e) P60 after 24 hrs and f) P60 after 7 days dissolution alongside BPO_4 from ICSD with collection code 55082

Generally, the lineshapes of the ^{11}B MAS NMR spectra of the solid remaining after the dissolution experiments are the same as the spectra before dissolution. However, in P20, the three-coordinated boron signal is displaced to higher frequency. The corresponding ^{11}B MAS NMR spectra are shown in Figure 2-24 in which before- and after-dissolution results are overlaid for comparison. The ^{11}B MAS NMR spectra were fitted by DMFit and the results are summarized in Table 2-7. By comparing N_4 values before and after dissolution tests, it can be seen that except for P20, for which the fraction of four-coordinated boron shows a ca. 13% reduction, all glasses have the same N_4 . The effect of H^+ on the structure of glass surface in a boron-rich borophosphate glass is discussed in detail in section 2-4-5.

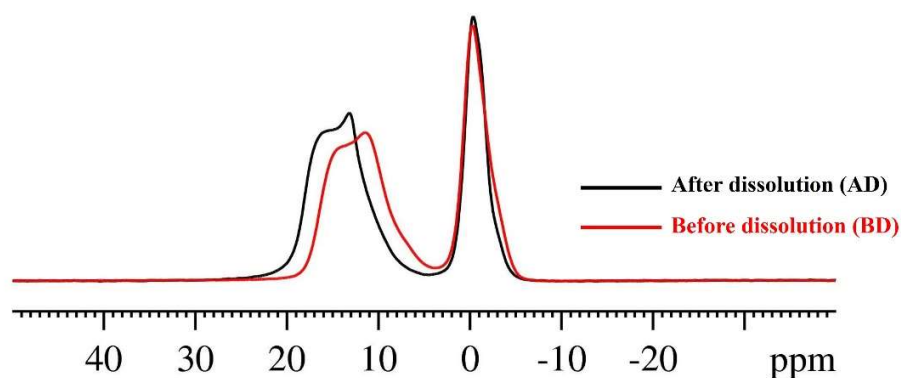


Figure 2-24) ^{11}B magic angle spinning (MAS) NMR of P20 before and after 15 min dissolution

Fitting the ^{11}B MAS NMR spectrum of the water-treated sample containing 20 mol% P_2O_5 reveals that there are three four-coordination boron components with isotropic chemical shifts at 0, -1.2 and -2.85 ppm. Dissolving the rest of the samples in the aqueous medium did not induce considerable changes in their ^{11}B MAS NMR, neither chemical shifts nor the percentages.

The ^{31}P MAS NMR spectra before and after dissolution appear identical, with two exceptions. In P20 the peak shifts to higher frequency Figure 2-25, indicating that the structure of this glass was altered significantly after being immersed in the water. By comparing the two spectra, the fitted post-dissolution spectrum reveals that $\text{P}_{1\text{B}}^3$ no longer exists.

Figure 2-25b shows the ^{31}P MAS NMR spectra of P60 after 1 and 7 days of immersion in water. After 24 hrs of immersion, the lineshape of the broad peak is the same as the lineshape of the pristine glass. However, two small relatively narrow peaks are observed at 0 and -8 ppm.

After 7 days the center-of-gravity of the broad peak remains the same as the previous spectra, but the peaks at higher frequencies are intensified and become narrower. These peaks are characteristic of a crystalline phase. In addition, another sharp peak forms at -30 ppm which is an indication of crystalline BPO₄.¹¹³

Table 2-7) Parameters used for fitting ^{11}B MAS NMR spectra after dissolution experiments

	^{13}B					^{14}B								
	δ_{iso} (ppm)	Int. (%) ± 2	δ_{iso} (ppm)	Int. (%) ± 2	δ_{iso} (ppm)	W (kHz)	Int. (%) ± 2	δ_{iso} (ppm)	W (kHz) ± 0.03	Int. (%) ± 2	δ_{iso} (ppm)	W (kHz) ± 0.03	Int. (%) ± 2	N ₄
	$^{13}\text{B}_{\text{ring}}$		$^{13}\text{B}_{\text{non-ring}}$			$^{14}\text{B}_{2\text{P}}$			$^{14}\text{B}_{3\text{P}}$			$^{14}\text{B}_{4\text{P}}$		
P20-15min	+18.8	45	+16.0	17	-0.4	0.42	31	-2.4	0.38	6	-	-	-	0.37
P30-15min	+16.1	22	+14.0	15	-0.2	0.40	15	-1.5	0.38	23	-3.5	0.46	22	0.63
P40-24hrs	+15.7	7	+13.4	6	-	-	-	-1.6	0.34	35	-3.9	0.44	51	0.87
P50-24hrs	-	-	-	-	-	-	-	-1.7	0.40	5	-4.0	0.45	95	1.0
P50-7days	-	-	-	-	-	-	-	-1.5	0.40	5	-3.9	0.48	95	1.0
P60-24hrs	-	-	-	-	-	-	-	-	-	-	-4.0	0.44	100	1.0
P60-7days	-	-	-	-	-	-	-	-3.4	0.11	4	-3.9	0.44	96	1.0
	$^{13}\text{B}_{\text{ring}}$		$^{13}\text{B}_{\text{non-ring}}$			$^{14}\text{B}_{1\text{P}}$			$^{14}\text{B}_{3\text{P}}$			$^{14}\text{B}_{4\text{P}}$		
B40	+18.5	22	+17.0	21	+0.2	0.50	57	-	-	-	-	-	-	0.57
B20	-	-	-	-	-	-	-	-1.3	0.44	43	-3.0	0.40	57	1.0
B68	+18.6	47	+15.7	7	+1.0	0.40	34	-1.1	0.37	7	-3.2	0.33	5	0.46
C _Q (quadrupolar coupling constant) fixed at 2.50 MHz with a tolerance of ± 0.15 MHz. δ_{iso} (isotropic chemical shift) fixed with a tolerance of ± 0.5 in ^{13}B and ± 0.1 in ^{14}B species. W: Full Width at Half Maximum (peak width) fixed with a tolerance of ± 0.03 kHz, η (asymmetry parameter fixed at 0.2 with a tolerance of ± 0.1 , Int (Integrated intensity) fitted to obtain N ₄														

Table 2-8) Parameters used for fitting ³¹P MAS NMR spectra after dissolution experiments

	P_{0B}¹			P_{2B}²			P_{3B}³			P_{2B}³			P_{1B}³			P_{0B}³		
	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)
P20-15min	-3.5	2.20	32	-10.3	2.30	54	-17.0	2.40	14	-	-	-	-	-	-	-	-	-
P30-15min	-3.5	2.90	13	-12.0	2.40	23	-19.5	2.50	40	-27.5	2.70	24	-	-	-	-	-	-
P40-24hrs	-	-	-	-	-	-	-21.5	3.00	65	-30.0	2.20	25	-37.0	2.00	10	-	-	-
P50-24hrs	-	-	-	-	-	-	-22.5	2.00	25	-29.5	2.00	45	-36.0	2.00	22	-42.0	2.00	8
P50-7days	-	-	-	-	-	-	-22.5	2.00	24	-29.5	2.00	44	-36.0	2.00	22	-42.0	2.00	10
P60-24hrs	-	-	-	-	-	-	-	-	-	-30.0	2.60	50	-36.5	2.00	30	-43.0	2.00	18
P60-7days	-	-	-	-	-	-	-	-	-	-30.0	2.60	51	-36.5	2.00	24	-43.0	2.00	16
Na40 series																		
	P_{0B}¹			P_{1B}²			P_{2B}²			P_{2B}³								
B40	-1.3	1.90	54	-6.0	1.90	36	-12.0	1.90	10	-	-	-						
B20	-	-	-	-8.0	1.70	8	-12.5	2.40	50	-20.5	3.10	42						
δ_{iso} isotropic chemical shift fixed with a tolerance of ± 0.5 ppm, W: Full Width at Half Maximum (Peak width) fixed with a tolerance of ± 0.05 kHz, Int: Integrated intensity $\pm 2\%$ (fitted)																		

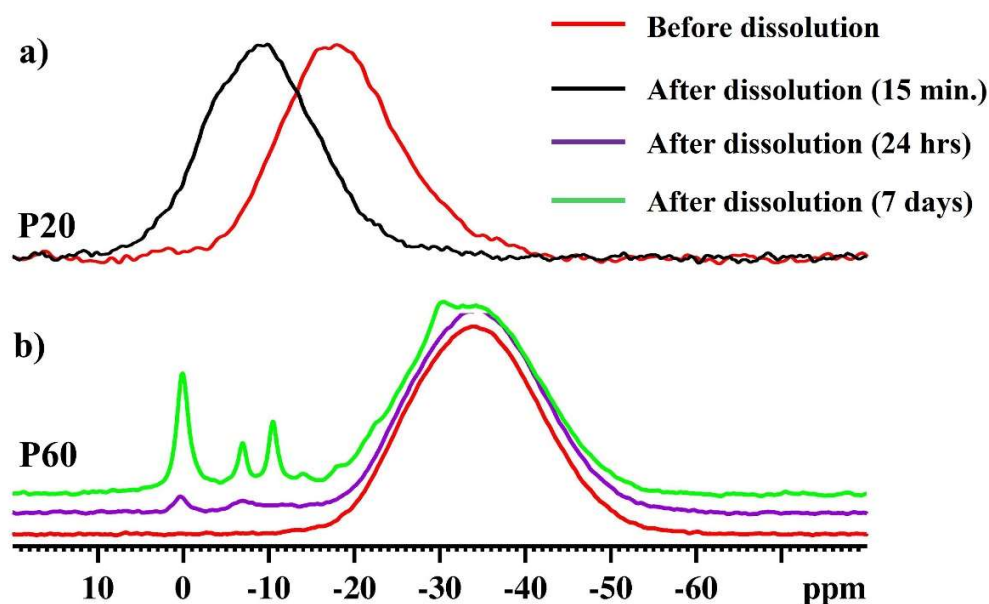


Figure 2-25) ^{31}P magic angle spinning (MAS) NMR spectra of a) P20, b) P60 before and after dissolution.

2-4- Discussion

2-4-1- Glass structural analysis: short-range order

In a binary $\text{A}_{2/z}\text{O}-\text{B}_2\text{O}_3$ glass where $\text{A}_{2/z}\text{O}$ is either an alkali ($z = 1$) or alkaline earth oxide ($z = 2$), the structure of the glass is populated by $^{[3]}\text{B}$ and $^{[4]}\text{B}$ units. Generally, the fraction of four-coordinate boron increases linearly with R , where R is $\text{A}_{2/z}\text{O}/\text{B}_2\text{O}_3$. This alteration of the coordination number happens because the oxygen provided by $\text{A}_{2/z}\text{O}$ converts $^{[3]}\text{B}$ to $^{[4]}\text{B}$ and the extra negative charge on four-coordinated boron is compensated by the accompanying cation. This conversion reaches a maximum value of ca. 0.43,⁴³ which depends on the type of the cation,⁴⁵ and eventually decreases because of $^{[4]}\text{B}-^{[4]}\text{B}$ avoidance. This means that the formation of $^{[4]}\text{B}-\text{O}-^{[4]}\text{B}$ linkages is significantly limited due to the negative charge carried by each BO_4 unit. However, in $\text{A}_{2/z}\text{O}-\text{P}_2\text{O}_5-\text{B}_2\text{O}_3$ the presence of phosphorus as the second network former changes the N_4 trend by providing phosphate groups to separate BO_4 groups, removing the need to change coordination. Figure 2-26 illustrates the fraction of four-coordinated boron in the current ternary $\text{Na}_2\text{O}-\text{P}_2\text{O}_5-\text{B}_2\text{O}_3$ system as a function of Na_2O content. For comparison, the result of the binary sodium borate glasses from Reference [20] is also plotted.

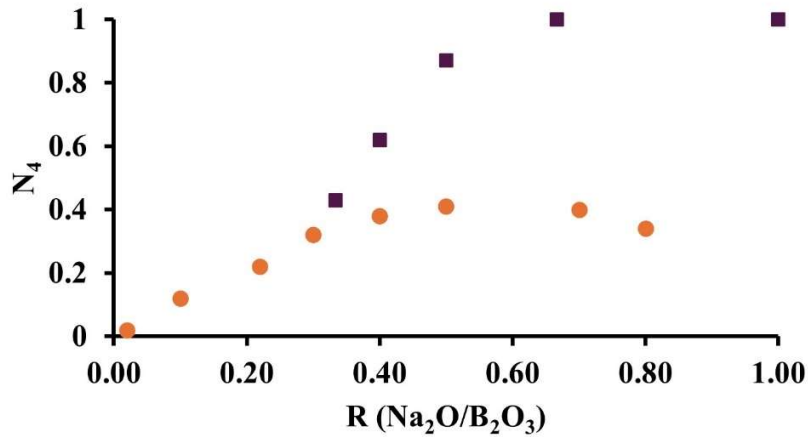


Figure 2-26) The relationship between N_4 and R in borate ● (Reference [20]) and borophosphate glasses ■ (current work)

In contrast to binary borates, the N_4 value in borophosphate glasses climbs as the amount of Na_2O is increased. In other words, if $\frac{\text{P}_2\text{O}_5}{\text{B}_2\text{O}_3} \geq 1.5$, boron is only formed with a coordination number of four. This behaviour is quite different from $\text{Na}_2\text{O-SiO}_2\text{-B}_2\text{O}_3$ glasses with similar Si/B atomic ratios. For example, Inoue et al¹¹⁸ showed that in a sodium borosilicate glass with $K = \text{SiO}_2/\text{B}_2\text{O}_3 = 0.5$ (Si/B = 1) and $R = 0.5$, the fraction of four-coordinated boron is 0.35, while in the current work, P40 with $K=1$ (P/B = 1) and $R = 0.5$ gives rise to $N_4 = 0.87$. Considering that the Na_2O content is only 20 mol%, which is lower than typically reported for sodium borophosphate glasses in the literature, the question arises whether Na_2O is directly responsible for changing the boron coordination number from three to four, thus facilitating the formation of P–O–B bonds. Alternatively, does P_2O_5 itself create conditions enabling boron atoms to form tetrahedral units, subsequently resulting in the formation of P–O–B linkages? Based on results presented, we find that phosphorus converts $^{[3]}\text{B}$ to $^{[4]}\text{B}$ in the current borophosphate glasses, unlike what is concluded in binary borate or borosilicate glasses where addition of sodium cations charge compensates the charge deficit on $^{[4]}\text{B}$.

2-4-2- Glass structural analysis: medium-range order

Glass scientists seek to establish relationships between the structure of a glass and its properties. As glasses lack periodic long-range order, discussion on the structure of a glass is held

predominantly on the short-range order. However, it is doable to determine the next nearest neighbour of a given polyhedron and build toward medium-range order.

The structure of the $A_2O-B_2O_3-P_2O_5$ glasses (A = alkali metal cations) has been extensively explored using ^{31}P MAS NMR spectroscopy and advanced double-resonance NMR techniques including $^{11}B\{^{31}P\}$ REDOR, $^{23}Na\{^{31}P\}$ REDOR¹¹⁹ and ^{31}P refocused INADEQUATE.⁹⁹ Although these techniques provide valuable information about the medium-range order of borophosphate glasses, assignment of phosphate species is very demanding. For instance, the chemical shift of P_{3B}^3 has been documented to appear between -9.5 and -15.1 ppm which is almost fully overlapped with P_{1B}^2 , the chemical shift of which is reported to be between -9.5 to -14 ppm (Figure 2-11). Their structural network is particularly complex due to the strong preference for heteroatomic B–O–P connections over homonuclear B–O–B or P–O–P linkages,¹²⁰ resulting in significant interconnectivity between borate and phosphate structural groups. Borate units in a tetrahedral environment, $[4]B$, promote the formation of multiple phosphate species with distinct configurations. When the chemical shift ranges of the reported phosphate species are plotted (Figure 2-11), it suggests the potential existence of nine distinct phosphate units. However, these units show significant overlap in their isotropic chemical shift ranges, complicating spectral interpretation and preventing definitive structural conclusions. In order to determine the most likely borate and phosphate species a few constraints were considered to minimize the ambiguity of the assignments.

- 1- Charge compensation calculations
- 2- The number of P–O–B linkages
- 3- Total number of oxygens

For the abovementioned calculations, error propagation is not rigorously applied to estimate the measurement uncertainty. This is because there are multiple sources of error at different stages of the calculation, some of which are known, while others are not easily quantifiable. For the analyzed composition which forms the base of all calculations, sources of error arise from factors including the ICP calibration curve, burette, mass balance, and purity of raw materials. These uncertainties would then need to be propagated through sequence calculations in which the composition is multiplied by the integrated intensities obtained from NMR spectroscopy,

leading to a highly complex error estimation. Accordingly, this type of error analysis is rarely presented in the literature.

2-4-2-1- Charge compensation calculations

Charge-compensation calculations are one of the constraints used to determine the likely connectivity of phosphate units to surrounding network formers. The idea is that one of the roles of the alkali cations in the glass structure is balancing the negative charge on the anionic species in the structure. There are two scenarios for charge compensation calculations. In the following both will be described in detail, and it will be shown that the second scenario is valid.

Scenario 1:

In a glass the sum of positive and negative charge should be equal. In this scenario it is assumed that the distribution of the negative charges in the anionic species in a borophosphate glass is the same as binary borate and phosphate glasses. The anionic species in phosphate glasses are P^0 , P^1 and P^2 , while in a borate glass it is BO_4^- with -3, -2, -1 and -1 charge attributed to them, respectively. In this nomenclature for example P^0 means a phosphate unit without BO and P^2 denotes a phosphate structural unit with two BOs. P^3 units are considered neutral since it is assumed to be a tetrahedral phosphate unit with three BOs and a double bond. Figure 1-6 and Figure 1-8 shows the schematic of this anionic species.

The amount of negative charge on BO_4^- units is calculated as follows:

$$\text{Negative charge of the } BO_4^- = 2 \times B_2O_3 \text{ (mol \%)} \times N_4 \quad (\text{per unit formula}) \quad \text{Eq.2-3}$$

It should be noted that in the current glass series it is assumed that there are no NBOs on $[^3]B$. In this glass series Na^+ cations play the charge-compensation role. The amount of the available sodium cations for charge balancing is calculated as $2 \times Na_2O$ mol % since each mol of Na_2O carries two mol of Na^+ . Calculations in Table 2-9 show the negative and positive charges for each glass.

Table 2-9) Negative charge associated with BO_4^- , and positive charges from Na^+ based on scenario 1

	Negative charge from BO_4^-	Positive charge from Na^+
P20	$2 \times 61.2 \times 0.43 = 52.6$	$2 \times 20.8 = 41.6$
P30	$2 \times 51.5 \times 0.62 = 63.9$	$2 \times 21.1 = 42.2$
P40	$2 \times 39.1 \times 0.87 = 68$	$2 \times 22.6 = 45.2$
P50	$2 \times 30.5 \times 1.0 = 61$	$2 \times 22.0 = 44$
P60	$2 \times 22.2 \times 1.0 = 44.4$	$2 \times 21 = 41.6$

By comparing the total negative and positive charges in each glass, it becomes evident that this scenario does not accurately describe the populations of the various structural units within this glass series, as the calculated negative charges exceed the available positive charges. Furthermore, including the negative charges associated with the anionic phosphate species alongside those from the borate species only amplifies this discrepancy.

Scenario 2:

Charge-compensation calculations in scenario 1 revealed that attributing the negative charges to phosphate anionic units, based on what is common in phosphate glasses, are not appropriate in borophosphate glasses. In fact, the amount of the negative charges on the NBOs in a phosphate unit in the borophosphate glasses are different from phosphate glasses. In order to understand it better, concepts from *Bond-Valence Theory* and *Pauling Bond Strength* may be used.

Bond-valence theory¹²¹ is one approach to find out how the glass connectivity is distributed in the glasses. This model relies on the correlation between bond length and bond valence to validate the atomic arrangements in minerals, and has also been applied to glasses including zinc phosphate,¹²² aluminoborate,¹²³ aluminoborophosphate¹²⁴ and aluminophosphate.¹²⁵ The empirical relationship between bond length and bond valence is calculated using

$$S_{ij} = \exp \left[\frac{R_{ij} - d_{ij}}{B} \right] \quad \text{Eq.2-4}$$

where S_{ij} is the experimental bond valence for the atom pair i and j , R_{ij} , obtained from analysing a large number of crystal structures containing i and j atom pairs, is the bond-valence parameter, d_{ij} is their bond length and B is a constant usually considered to be $0.37 \text{ \AA}$.¹²⁶ By taking into

account that the B–O bond length for three- and four-coordinated boron is 1.372 and 1.475 Å, S_{ij} is calculated as 1.0 and 0.745 v.u., respectively. These are valency contributions of cations to a neighbouring anion, O^{2-} . These values are similar to PBS, which is calculated by dividing the charge of the cation by its coordination number, making PBS suitable for deducing glass network connectivity.

In the case of P^{5+} , multiple maxima in the bond-length distribution of P–O are observed because various numbers of BO per phosphorus tetrahedron exist. This is concluded from the analysis of thousands of crystal structures of phosphate compounds.¹²⁷ Therefore, bond valences for P–O are calculated as 1.25, 1.33, 1.5 and 2 v.u. for phosphate tetrahedra containing zero, one, two and three BO, respectively. In other words, the P–O bond valence depends on the number of BOs and the type of cation to which they are bonded.

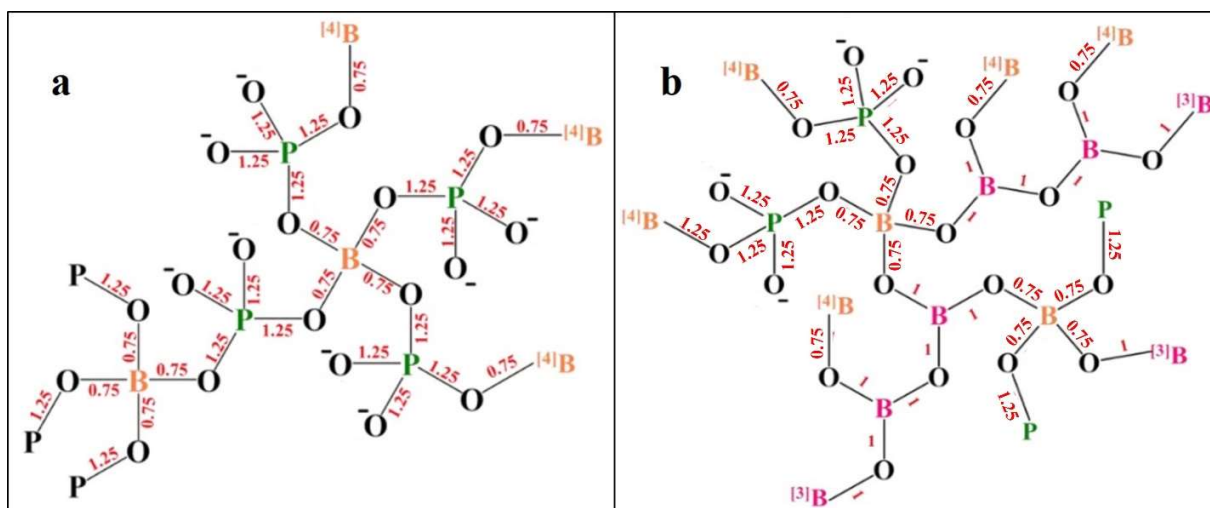


Figure 2-27) Pauling bond strength map of crystalline a) $CsZnBP_2O_8$ and b) $Li_2B_3PO_8$

Analyzing the network connectivity using PBS in crystalline borophosphates with known crystal structures is a good starting point. Afterward, this rationale can be applied to validate the proposed network connectivity in the borophosphate glasses in conjunction with NMR results. The current glass series can be divided to two groups; P20-P40 containing three- and four coordinated boron, and P50-P60 constructed by only $[^4B]$. Figure 2-27 depicts the Pauling bond strength map of crystalline $CsZnBP_2O_8$ (ICSD collection code 410871). PBS is calculated by dividing the charge of the cation by its coordination number. This compound and P50-P60 have compositions with comparable P/B ratios, 2, 1.5 and 2.5 respectively, but different alkali content.

The fraction of network modifier oxides for CsZnBP₂O₈, P50 and P60 is 55.7, 20 and 20 mol%, respectively. In these compositions the P/B ratio is ≥ 1.5 in which boron is found only in four coordination. Based on the bond valence theory calculation, the bond strength contribution of B³⁺ in the P–O–B linkages with B–O bond length 1.47 Å is 0.76. This value in P–O–B bonds for P–O is calculated as 1.23 since the bond length between phosphorus and oxygen is 1.54 Å. These calculations are in line with the Pauling bond strength model in which B³⁺ and P⁵⁺ contributes 0.75 and 1.25 v.u. to the P–O–B linkages, respectively.

In order to analyse the P–O–B connectivity for P20, P30 and P40, one can look into the Li₂B₃PO₈ structure (ICSD collection code 192496) (Figure 2-27b). The ^[3]B–O bond length in ^[4]B–O–^[3]B linkages are 1.34 and 1.38 Å, which gives rise to bond strengths of 1.09 and 0.98 v.u., respectively. Bond strength calculation using Eq. 2-4 for ^[4]B–O shows that four-coordinated boron contributes 0.78 v.u. in ^[4]B–O–P linkage because its bond length is 1.46 Å. The length of the P–O bond in ^[4]B–O–P is 1.50 Å, which means its calculated bond strength contribution is 1.36 v.u. While these calculations are in good agreement with the PBS calculations for P–O–B linkages, there is a charge deficiency, -0.25 v.u., in the ^[4]B–O–^[3]B linkages. These negative charge deficiencies are balanced by Na⁺ cations.

Based on the charge distribution of the model crystalline compounds with various P/B ratio it is assumed that when the glass is populated mainly by P³ and P² units the charge deficit present on ^[4]B is balanced by the phosphate units, and sodium cations serve as charge compensators to balance the negative charge on phosphate NBOs. This scenario is more likely when the amount of charge compensator in the system is low (failure of charge compensation calculations in scenario 1). This argument is supported by ²³Na{³¹P} and ²³Na{¹¹B} REDOR NMR where Eckert¹¹⁹ showed that the dephasing curve of the former is much stronger than that of the latter, which is interpreted as the presence of Na cations being in closer proximity to P than B cations.

In the case of P20-P60 glass series, based on the chemical shifts (Figure 2-11) the following phosphate species were chosen as the dominant phosphate units with fixed δ_{iso} in curve fitting: P_{2B}², P_{3B}³, P_{2B}³, P_{1B}³ and P_{0B}³ (see section 1-2-1 for the representative molecular diagram of these species). By taking into account the Pauling bond strength model the possible negative charge on NBOs on phosphate species is shown in Figure 2-28. For examples P_{2B}³ carries -0.5 negative

charge because the distribution of the charges in BO results in a valency contribution of 1.5 v.u. to the NBO.

$$\text{Negative charge} = 2 \times \text{P}_2\text{O}_5 \text{ (mol\%)} [\{I(\text{P}_{2\text{B}}^2) \times 1.5\} + \{I(\text{P}_{3\text{B}}^3) \times 0.75\} + \{I(\text{P}_{2\text{B}}^3) \times 0.5\} + \{I(\text{P}_{1\text{B}}^3) \times 0.25\}] \text{ (per unit formula)} \quad \text{Eq. 2-5}$$

where I(x) represents the integrated intensity of the x units reported in Table 2-6. Based on PBS, $\text{P}_{0\text{B}}^3$ is a neutral species.

$$\text{P20: } 2 \times 18 \text{ mol P}_2\text{O}_5 \times \{ (0.35 \text{ P}_{2\text{B}}^2 \times 1.5) + (0.60 \text{ P}_{3\text{B}}^3 \times 0.75) + (0.05 \text{ P}_{2\text{B}}^3 \times 0.5) \} = 35.5$$

$$\text{P30: } 2 \times 27.4 \text{ mol P}_2\text{O}_5 \times \{ (0.1 \text{ P}_{2\text{B}}^2 \times 1.5) + (0.80 \text{ P}_{3\text{B}}^3 \times 0.75) + (0.1 \text{ P}_{2\text{B}}^3 \times 0.5) \} = 43.8$$

$$\text{P40: } 2 \times 38.3 \text{ mol P}_2\text{O}_5 \times \{ (0.75 \text{ P}_{3\text{B}}^3 \times 0.75) + (0.20 \times \text{P}_{2\text{B}}^3 \times 0.5) + (0.05 \text{ P}_{1\text{B}}^3 \times 0.25) \} = 51.7$$

$$\text{P50: } 2 \times 47.6 \text{ mol P}_2\text{O}_5 \times \{ (0.3 \text{ P}_{3\text{B}}^3 \times 0.75) + (0.40 \times \text{P}_{2\text{B}}^3 \times 0.5) + (0.2 \text{ P}_{1\text{B}}^3 \times 0.25) \} = 45.2$$

$$\text{P60: } 2 \times 56.8 \text{ mol P}_2\text{O}_5 \times \{ (0.50 \times \text{P}_{2\text{B}}^3 \times 0.5) + (0.35 \text{ P}_{1\text{B}}^3 \times 0.25) \} = 38.3$$

The relatively small differences (3 - 14%) between the calculated negative charges and the available positive charges in the glasses support the glass network analysis provided in Table 2-6.

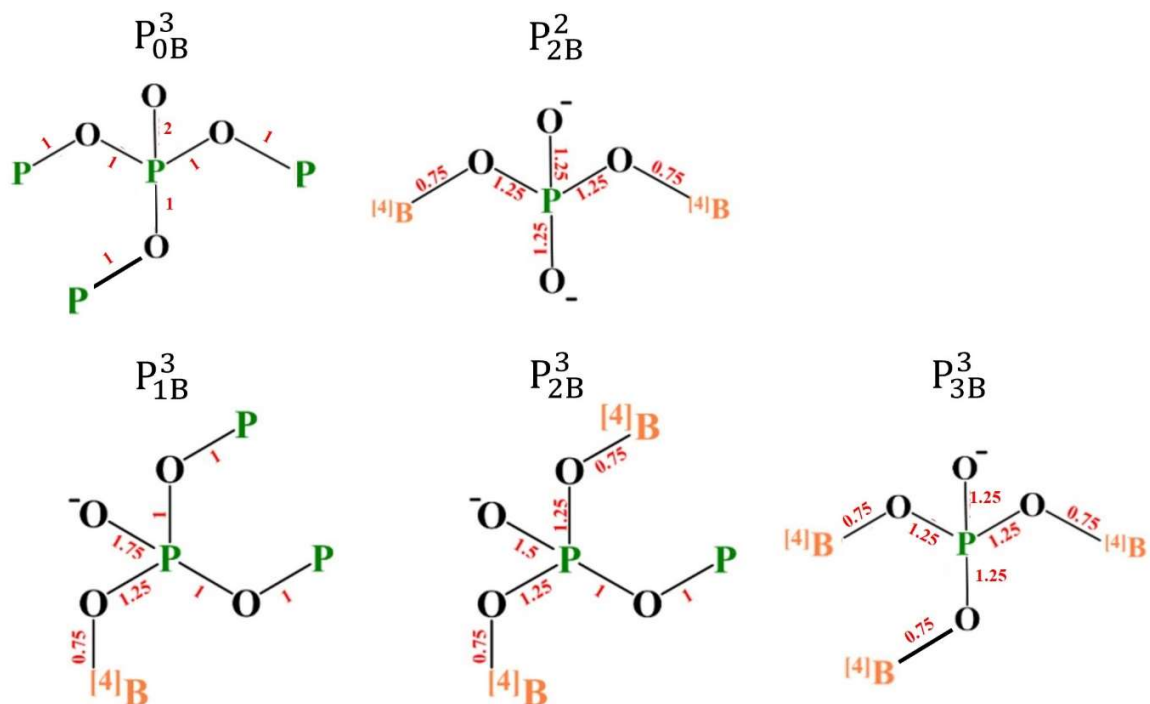


Figure 2-28) Phosphate species in the glasses with the next nearest neighbour. Numbers on bonds calculated based on PBS model.

2-4-2-2- The number of P–O–B linkages

After finding the most plausible phosphate and borate species, an additional check on the reliability of the assignment is calculating the number of the B–O–P linkages from ^{11}B and ^{31}P MAS NMR independently. In the following, B–O–P and P–O–B represent the results of calculations based on the ^{11}B and ^{31}P MAS NMR, respectively.

$$\text{P–O–B} = 2 \times \text{P}_2\text{O}_5 (\text{mol}\%) \times [\{I(\text{P}_{1\text{B}}^3) \times 1\} + \{I(\text{P}_{2\text{B}}^3) \times 2\} + \{I(\text{P}_{3\text{B}}^3) \times 3\} + \{I(\text{P}_{1\text{B}}^2) \times 1\} + \{I(\text{P}_{2\text{B}}^2) \times 2\}] \quad \text{Eq. 2-6}$$

$$\text{B–O–P} = 2 \times \text{B}_2\text{O}_3 (\text{mol } \%) \times [\{I(^{[4]}\text{B}_{1\text{P}}) \times 1\} + \{I(^{[4]}\text{B}_{2\text{P}}) \times 2\} + \{I(^{[4]}\text{B}_{3\text{P}}) \times 3\} + \{I(^{[4]}\text{B}_{4\text{P}}) \times 4\}] \quad \text{Eq. 2-7}$$

Table 2-10) The number of P–O–B linkages calculated from ^{31}P MAS NMR and ^{11}B MAS NMR (per unit formula)

	P–O–B	B–O–P
P20	94	116
P30	153	189
P40	212	244
P50	191	237
P60	153	177

The borate species are assigned with relatively low ambiguity for two primary reasons: first, the number of borate species with overlapping chemical shifts is fewer compared to phosphate species; and second, double-resonance NMR is used to find the number of phosphorus atoms in the next-nearest-neighbor coordination to boron. Thus, the number of B–O–P linkages derived from ^{11}B MAS NMR serves as a reference point for evaluating the number of P–O–B linkages from ^{31}P MAS NMR data. Indeed, phosphate species assignments were chosen to fulfill several key requirements simultaneously: charge compensation calculations, the number of P–O–B linkages matching closely with B–O–P linkages, and consistency with the total number of oxygens (see section 2-4-2-3). Although some discrepancies remain in each pair reported in Table 2-10, these assignments represent the best possible solutions considering the constraints mentioned above.

2-4-2-3- Total number of oxygens

Another check on the borate and phosphate species assignments is calculating the total number of oxygens in a given glass and comparing it with the available oxygens from the composition. If these values are close to each other, it may be concluded that the determined species are plausible. The total number of oxygens from the compositions, $[\text{O}]_{\text{comp}}$, calculated as follows (per unit formula):

$$[\text{O}]_{\text{comp}} = 3 \times \text{B}_2\text{O}_3 (\text{mol } \%) + 5 \times \text{P}_2\text{O}_5 (\text{mol } \%) + \text{Na}_2\text{O} (\text{mol } \%) \quad \text{Eq. 2-8}$$

$$\text{Oxygens from NMR} = [\text{B–O–B}] + [\text{B–O–P}] + [\text{P–O–P}] + [\text{NBO}] \quad \text{Eq. 2-9}$$

$$\text{P–O–P} = 2 \times \text{P}_2\text{O}_5 (\text{mol}\%) \times \left[\{I(\text{P}_{0\text{B}}^3) \times \frac{3}{2}\} + \{I(\text{P}_{1\text{B}}^3) \times \frac{2}{2}\} + \{I(\text{P}_{2\text{B}}^3) \times \frac{1}{2}\} \right] \quad \text{Eq. 2-10}$$

$$\text{B-O-B} = 2 \times \text{B}_2\text{O}_3 (\text{mol}\%) \times \left[\{I(^{[4]}\text{B}_{3\text{P}}) \times \frac{1}{2}\} + \{I(^{[4]}\text{B}_{2\text{P}}) \times \frac{2}{2}\} + I(^{[4]}\text{B}_{1\text{P}}) \times \frac{3}{2}\} + \{I(^{[3]}\text{B}) \times \frac{3}{2}\} \right]$$

Eq. 2-11

$$\text{NBO} = 2 \times \text{P}_2\text{O}_5 (\text{mol}\%) \times \{(1 \times \text{P}^3) + (2 \times \text{P}^2)\} \quad \text{Eq. 2-12}$$

Table 2-11) Comparison between the total number of oxygens (per unit formula) from composition, $[\text{O}]_{\text{comp}}$, ^{11}B and ^{31}P MAS NMR

	$[\text{O}]_{\text{comp}}$	^{11}B MAS NMR	^{31}P MAS NMR
P20	294	318	295
P30	313	343	307
P40	331	362	324
P50	349	389	331
P60	372	385	361

By comparing the results from ^{11}B and ^{31}P MAS NMR with the theoretical number of the oxygens, one can conclude that the determined borate and phosphate species result in the total number of oxygens close to the theoretical values. This constraint further supports the assignments provided in this glass series.

2-4-3- Structural units as a function of the composition: X–O–Y linkages, BO & NBO, phosphate & borate fractions

Figure 2-29 shows the fraction of various phosphate and borate species in the glass series. P60 (containing 20 mol% B_2O_3) is populated with P^3 , which is the sum of P_{nB}^3 species, and $^{[4]}\text{B}$ units. When P_2O_5 is replaced by B_2O_3 the amount of P^3 units decreases monotonically while $^{[4]}\text{B}$ reaches a maximum of 43.5%, then gradually dropped to 32%. Beyond 40 mol% B_2O_3 , the fraction of $^{[3]}\text{B}$ steadily grows and in P20 becomes the most abundant species in the glass.

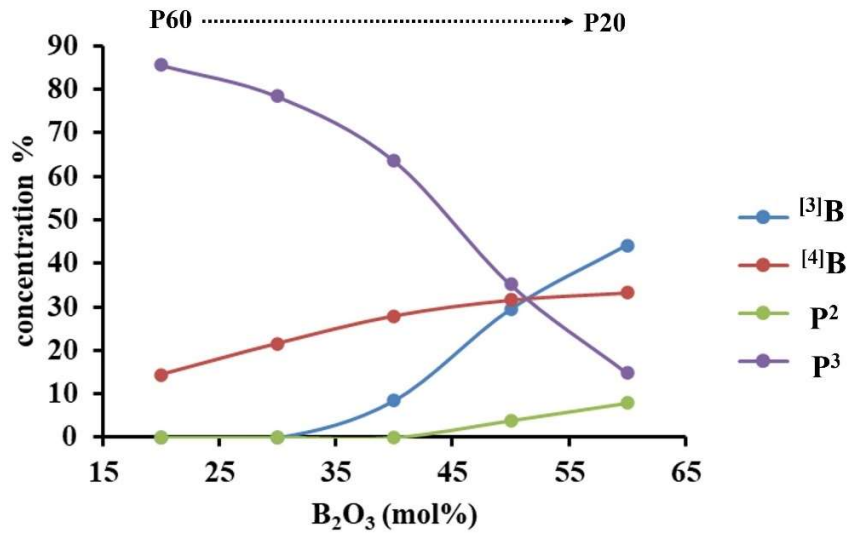


Figure 2-29 Distribution of borate and phosphate units in the P20-P60 glass series

The fraction of BOs and NBOs can be calculated using the following equations.

$$\text{BO (\%)} = \frac{\sum \text{X-O-Y}}{\text{Total O}} \quad \text{Eq. 2-13}$$

$$\text{NBO (\%)} = \frac{\text{NBO}}{\text{Total O}} \quad \text{Eq. 2-14}$$

where $\sum \text{X-O-Y}$ is the sum of the B-O-B, P-O-B and P-O-P linkages for a given glass. Total O and NBO are calculated using Eq. 2-8 and 2-12, respectively.

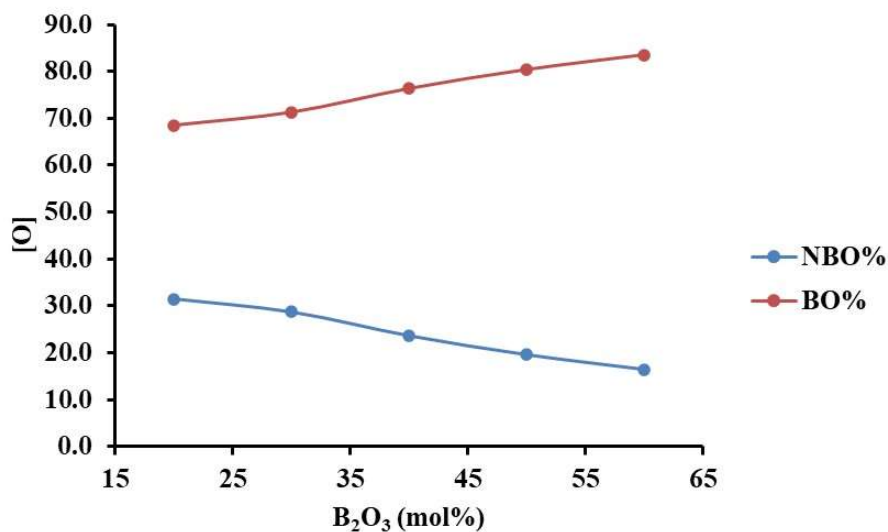


Figure 2-30) The fraction of bridging oxygens (BOs) and non-bridging oxygens (NBOs) in the P20-P60 glass series

Figure 2-30 illustrates that with increasing B₂O₃, the number of BOs throughout this glass series increases while NBO fraction declines. The fraction of BOs in P60 is 70%. As more B₂O₃ is introduced in the glass, the amount of NBO drops since P³ units are replaced by ^[3]B units. Figure 2-29 reveals that beyond 40 mol% B₂O₃, ^[4]B begins to level off, however P³ and ^[3]B undergo a decrease and increase trend, respectively. Therefore, the number of NBOs is governed by P³. Each P³ unit introduces one NBO per tetrahedron to the glass structure. It should be noted again that in these glass series we assume that no NBO is formed in ^[3]B units.

The relationship between the re-melting temperature and ^[4]B_{4P} was graphed in Figure 2-31a. It is evident from the plot that there is a significant correlation between the fraction of the ^[4]B_{4P} and the re-melting temperature. As the fraction of ^[4]B_{4P} increases the re-melting point also increases. This finding is inline with the required temperature to melt the glass when initially raw materials were mixed. P60 was melted at 1100 °C and with the decrease of B₂O₃ the temperature reached 1350 °C for P60.

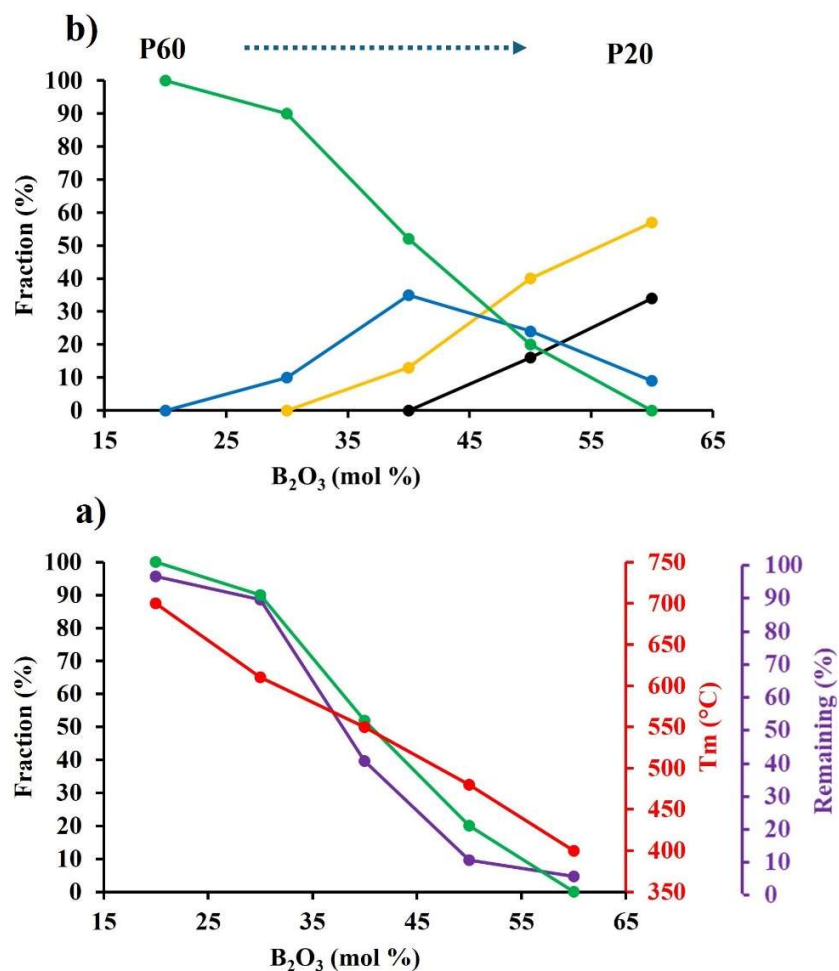


Figure 2-31) a) Relationship between re-melting temperature (T_m), fraction of $[^4]B_{4P}$ and remaining of the glass in water after 1 hour b) distribution of borate units in the glass series $[^3]B$, $[^4]B_{2P}$, $[^4]B_{3P}$ and $[^4]B_{4P}$

In Figure 2-31a, the right-hand y-axis shows the remaining of the glass (%) after 1 hour of dissolution, as a measure of durability, for direct correlation between the fraction of $[^4]B_{4P}$ and durability in the glass series. As it can be seen the durability is governed by the fraction of the $[^4]B_{4P}$ species. P60 with 100% $[^4]B_{4P}$ has the highest durability. In P20 and P30, where the glasses are populated by 0 and 20 % $[^4]B_{4P}$, the amount remaining drops to 6 and 10 %, respectively. It should be noted that with increasing B_2O_3 the number of NBO decrease (Figure 2-30), however the durability is not improved. By introducing more P_2O_5 in the glass and correspondingly more $[^4]B_{4P}$, the glass durability improves. Figure 2-31a also shows that the remelting temperature and

the durability have the same trend, both of which are a measure of the increased connectivity in the glass structure.

Figure 2-32 represents the fraction of X–O–Y linkages in the glasses as a function of the B₂O₃ content. The number of the linkages was calculated using equations 2.6, 2.9 and 2.10. Then, to report the percentage of the X–O–Y, each linkage was divided by the sum of all bonds. For example, for P–O–P

$$\text{Percentage of P-O-P} = \frac{\text{the number of P-O-P}}{(\text{P-O-P}) + (\text{P-O-B}) + (\text{B-O-B})} \quad \text{Eq. 2.15}$$

The number of B–O–B linkages continuously grows with introducing boron into the glass while the fraction of P–O–P drops from 38% to less than 1% in P60 and P20, respectively. P–O–B shows a parabolic trend with a maximum at 84%. ³¹P R-INADEQUATE NMR (Figure 2-12) supports these calculations. This NMR measurement qualitatively confirms that the number of the P–O–P linkages in P20 is low, which was calculated 0.5%. As the P₂O₅ content increases the number of homonuclear P–O–P bonds rises. These trends are in agreement with the previous works reported in the literature.^{99,128}

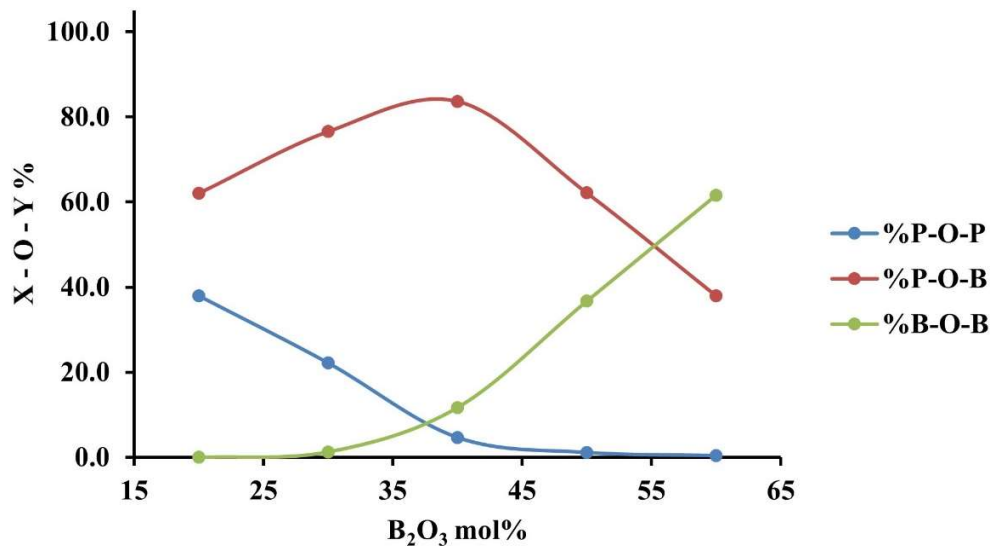


Figure 2-32) The fraction of X–O–Y linkages for P20-P60 glass series. X = P and/or B

2-4-4- Structure of glasses containing 40 mol% Na₂O

By comparing the structural units in the glass series containing 20 mol% Na₂O and the equivalent glasses containing 40 mol% sodium oxide, the effect of sodium content on the topology is revealed. In the phosphorus-rich samples P60 and B20, ³¹P MAS NMR indicates that P_{2B}³ and P_{2B}², respectively, are the major constituents (Figure 2-10 and Figure 2-13). Based on the ¹¹B MAS NMR, a given B cation in B20 is surrounded by three and four P cations (Figure 2-7). This means that when the amount of network modifier, Na₂O, is doubled in the borophosphate glasses the phosphate network is depolymerized and more NBOs are formed on phosphate units. This causes fewer BOs to be available on phosphate units to bond to [⁴]B. Hence a small fraction of [⁴]B–O–[³]B linkages is detected in B20 (Table 2-4). This finding is in line with the lack of [³]B–O–P linkages reported in the literature.¹²⁹

The charge-compensation calculations for B20 were done using scenario 2 because it is populated mainly with P² and P³:

B20: $2 \times 38.5 \text{ mol P}_2\text{O}_5 \times \{(0.50\text{P}_{2\text{B}}^2 \times 1.5) + (0.07\text{P}_{1\text{B}}^2 \times 0.75) + (0.43\text{P}_{2\text{B}}^3 \times 0.5)\} = 78.3 \text{ per unit formula}$

revealing that there is 3% difference between the experimental (40.5 mol % Na₂O $\times$ 2 = 81 per unit formula) and calculated amount of network modifier in these glasses, which suggests the phosphate and borate assignments are most likely valid.

In the case of B40, the charge compensation calculation could be done based on scenario 1 because the main phosphate structural units are P¹ and P², which means there are fewer B–O–P linkages and subsequently less change in the phosphate charge distribution. Hence the distribution of the negative charges on the NBOs in phosphate units is considered the same as the phosphate glasses, i.e. -2 and -1, for P¹ and P², respectively. In this case each [⁴]B unit carries a negative charge which is balanced by Na⁺ cations.

[⁴]B negative charge: $2 \times \text{B}_2\text{O}_3 \text{ (mol \%)} \times \text{N}_4 = 2 \times 39.3 \times 0.56 = 44 \text{ mol \%}$

Phosphate units negative charge: $2 \times 18.2 \text{ P}_2\text{O}_5 \times \{(0.14 \text{ P}^1 \times 2) + (0.86 \text{ P}^2 \times 1)\} = 41 \text{ mol \%}$

Na⁺ positive charge: $2 \times 42.5 \text{ Na}_2\text{O} = 85 \text{ mol } \%$

The sum of the negative and positive charges in this glass is in good agreement, supporting the assignments provided in Table 2-4 and Table 2-6.

2-4-5- Dissolution behaviour of glasses

It is well known that the isotropic chemical shift of orthophosphates in solution ³¹P NMR is sensitive to pH, particularly in the pH range between 5 to 8.¹¹⁶ Therefore, in order to interpret the ³¹P solution NMR spectra the concentration of the phosphate species versus pH should be considered (Figure 5a in Reference [116]). The two peaks observed in Figure 2-14 is related to the formation of HPO₄²⁻ and H₂PO₄⁻ during dissolution of the P20 with the isotropic chemical shifts +0.35 and +0.25, respectively. The pH measurement indicates that the solution containing P20 undergoes a ca. 1-unit change in the pH after 15 minutes being immersed in water, from initial pH = 7.3 to 6.5. The pH after complete dissolution is 5.6, suggesting that the reaction $\text{H}_2\text{PO}_4^- \leftrightarrow \text{HPO}_4^{2-} + \text{H}^+$ is taking place under these dissolution conditions. The pH behaviour of P30 shows a huge difference in comparison with P20. Within 15 minutes the pH drops to 3.2 from the initial 7.3, and eventually reaches 2.6 when it is dissolved completely. P20 contains 18 mol% P₂O₅, while P30 contains 27.4 mol% P₂O₅. Conversely, the B₂O₃ content decreases from 61.2 mol% in P20 to 51.5 mol% in P30. This means that P30 has a higher proportion of P₂O₅ and a lower proportion of B₂O₃. Since P₂O₅ lowers the pH and B₂O₃ raises it, P30 exhibits a lower pH compared to P20. The single sharp peak at 0 ppm and figure 5a in Reference [116] confirms that H₃PO₄ is the dominant species in the solution containing P30 sample. Another example of the effect of pH on the δ_{iso} is observed in the P¹ chemical shift where in the neutral medium P₂O₇⁴⁻ resonates at ca. -7.0.¹¹⁶ However, this value changes to -10.0 at pH = 2, which is the case for P40-P60 samples.

The exchange of Na⁺ with H⁺ during dissolution likely causes a rearrangement of the glass surface structure. Given the abundance of protons in aqueous environments, structural changes in the residual glass are expected. In B20, which contains approximately 60% [³]B, interactions between water and both [³]B and [⁴]B units could lead to variations in the N₄ value after dissolution. It should also be noted that the ¹¹B MAS NMR spectrum shown in Figure 2-24 reflects contributions from both the unaltered glass core and the potentially modified glass surface. Thus, the observed decrease in N₄ is most probably attributed to surface interactions

with water during dissolution. Although B30 contains about 40% ^{10}B , the identical N_4 values observed before and after dissolution can likely be explained by the difference in solution pH: for B20 the pH drops to ~ 6.5 after 15 minutes, whereas for B30 it decreases further to ~ 3 after the same duration.

The influence of pH on glass dissolution has two dimensions: glasses can alter the pH of the surrounding solution as they dissolve, and at the same time, the dissolution mechanism is itself dependent on the pH of the solution. Dissolution rates are strongly pH-dependent; for instance, borate glasses tend to dissolve more slowly in neutral or slightly basic solutions compared to acidic environments.¹³⁰ In the case of phosphate glasses, hydrolysis of P–O–P bonds is proton-catalyzed, meaning that a decrease in pH can further accelerate hydrolysis reactions.¹³¹ Most likely, in the case of borophosphate glasses, the acidic environment enhances the dissolution rate by promoting proton-catalyzed bond breaking, similar to phosphate systems. However, because both composition and medium-range structural features also influence dissolution, further experiments are needed in which the solution chemistry is systematically varied for a fixed glass composition. Such controlled studies would help separate the direct effect of pH from structural and compositional factors, providing a clearer understanding of the dissolution mechanism in these glasses.

When boron-rich samples, P20 and P30, are immersed in water, only P^0 is observed in the solution. No P^1 is detected by solution ^{31}P NMR, although the main constituents of P20, for example, are $\text{P}_{2\text{B}}^2$ and $\text{P}_{3\text{B}}^3$. However, the ^{31}P MAS NMR shows that $\text{P}_{0\text{B}}^1$ and $\text{P}_{2\text{B}}^2$ are the major components of this glass after dissolution (Table 2-8). In $\text{M}_2\text{O-P}_2\text{O}_5$ glasses one explanation for the absence of P^1 species in the solution is that phosphate hydrolysis is catalysed under acidic and alkaline conditions.¹³² However, in the current borophosphate glasses other parameters should also be considered provide explanation for this observation since all glasses show acidic medium upon dissolving in water. Even in the case of P50 and P60, $\text{pH}_{24 \text{ hrs}} \approx 1.8$, and the acidity is much higher than P20 and P30. Figure 2-29 shows that P20 are formed by 35% ^{10}B and 26% ^{11}B , meaning that the remaining 39% phosphate units are surrounded by borate units with B–O–B linkages. Therefore, only orthophosphates enter the solution. In P40 the ^{10}B concentration decreases to 5% at the expense of P^3 with the fraction 38%. Further augmentation of P^3 units in

the P50 and P60 glasses is reflected in the presence of P^1 and P^2 units in the solution ^{31}P NMR spectra.

These observations raise the question of whether P^3 is hydrolysed into P^2 and P^1 in phosphate-rich glasses. In a study on the $\text{CaO-Na}_2\text{O-P}_2\text{O}_5$ glass series the ^{31}P solution NMR spectra collected after one to 14 days indicate that when glasses are immersed in the dissolving media, P^3 is detected first followed by the appearance of P^1 and P^0 , depending on whether the medium is deionized water or buffer solution.¹¹⁶ However, in the current borophosphate series P^0 is consistently identified in the solution followed by the appearance of P^1 and P^2 depending on the composition. Comparison between the dissolution behaviour of phosphate and borophosphate glasses indicates that P-O-B bonds in $\text{P}_{2\text{B}}^3$ and $\text{P}_{3\text{B}}^3$ units are hydrolysed once they enter water.¹¹⁰ Using chromatography, Freudenberg et. al. showed that the measured anions released into solution agreed with those predicted by these calculations for several series of Na-Ca/Sr borophosphate glasses.¹¹⁰ However, this prediction results in a discrepancy between chromatography and ^{31}P solution NMR. This may be partly because chromatography is performed under slightly alkaline conditions to prevent hydrolysis of phosphate chains. In contrast, during ^{31}P solution NMR after a few hours the solution becomes highly acidic and most of the bonds undergo hydrolysis, which causes deviation from what is predicted by chromatography. This disagreement was also noted by Brauer.¹¹⁶ Another reason could be the partial hydration of the phosphate-rich glasses before the dissolution experiment started, as they are hygroscopic.

Interpretation of Figure 2-22 should be done carefully because the trend may be misleading. One might conclude that P^0 is converting to P^1 and P^2 as time passes. However, this reaction is almost impossible, as it has been shown in sol-gel chemistry that the formation of P-O-P bonds does not take place under simple conditions.¹³³ Instead, if we assume that once we put P60 in water, 20% of the sample dissolved, initially all P_2O_5 enters the water as P^0 with 100% intensity. After a while another 20% is dissolved, for example, which is in the form of P^1 and P^2 only. Therefore, the fraction of P^0 decreases because its amount is constant in the aqueous medium.

By comparing the phosphate units before and after dissolution (Figure 2-24), one notices that B-O-B linkages are more susceptible to hydrolysis than P-O-B linkages since the remaining material from the P20 dissolution comprises $\text{P}_{1\text{B}}^2/\text{P}_{2\text{B}}^2$ and $\text{P}_{0\text{B}}^1$, with at least one P-O-B

bond. P40, P50 and P60 contain branch phosphates, P^3 . However, this species is absent in their solution ^{31}P NMR spectra since only rings and chains can exist in an aqueous medium.¹³⁴ It is argued that in P^0 , P^1 and P^2 species the doubly bonded oxygen is more stable than P^3 since they have a delocalized electron. The lack of resonance between different structures in P^3 results in a higher energetic state and subsequently more easily dissolvable in an aqueous medium.¹³⁴

B40 and B20 samples may be considered analogues of P20 and P60, respectively, since these samples are boron- and phosphorus-rich glasses with 40 mol% Na_2O . B20 is mainly populated by B–O–P linkages, 84%, which is comparable to P60, in which B–O–P is the dominant bond, 65%. Although B20 and P60 respond similarly to water treatment in their early stages, their long-term behaviour in the aqueous medium is quite different (Table 2-3). This behaviour highlights the impact of network modifier content on the borophosphate glass structure and thereafter on the dissolution properties.

Table 2-1 reveals that the mass loss of the binary borate glass B68 is lower than P20 and P30 within the first 15 minutes. Although all are dissolved after two hours, there is a considerable distinction in the initial stage of degradation. This response to the aqueous medium can be explained by comparing the number of NBOs in these glasses. B68 consumes all Na_2O to form the maximum amount of $^{[4]}\text{B}$, which means no oxygen is available to form NBO in $^{[3]}\text{B}$. Therefore, the highest degree of network connectivity occurs in this glass. In the case of P30, for example, 20 mol % NBO forms in the glass.

The results of this study demonstrate that the dissolution behavior of borophosphate glasses is governed by their medium-range order, with the concentration of $^{[4]}\text{B}_{4\text{P}}$ playing a central role. Using NMR, it was shown that variations in the population of this species directly influence the connectivity of the glass network and, consequently, its durability in aqueous environments. This insight highlights the importance of medium-range structural features, beyond simple compositional factors, in controlling dissolution properties. By identifying $^{[4]}\text{B}_{4\text{P}}$ as a key structural parameter, these findings provide a pathway for the rational design of borophosphate glasses with tunable dissolution rates, opening new possibilities for developing tailored biomaterials for soft tissue healing.

3- Short- and medium-range order of sodium aluminoborophosphate glasses studied by dipolar NMR spectroscopy

3-1- Introduction

Aluminoborophosphate (AlBP) glasses are a class of oxide glasses containing several network formers, B_2O_3 , P_2O_5 and under certain circumstances, Al_2O_3 . The presence of multiple network formers in a glass gives rise to complexity in the network connectivity, imparting mechanical properties to the glass that are of interest for various applications. AlBP glasses are used as durable hosts for encapsulating $(Ca_3(PO_4))_2$, β -tricalcium phosphate (β -TCP), which has important potential for nuclear waste immobilization because it can accommodate various radioactive cations in its structure depending on the type and their preferred substitution site.¹³⁵ Sodium aluminoborophosphate glasses can also be used as enamel coatings on a soda-lime silicate glass in order to increase their corrosion resistance and mechanical strength.¹³⁶

Phosphate glasses are used in a wide range of applications including energy storage and conversion systems¹³⁷, lasers,¹³⁸ ionic conductors,¹³⁹ biomaterials¹⁴⁰ and high-level nuclear waste immobilization matrices.^{141,142} While their chemical durability is low in comparison with silicate glasses¹⁴³ it can be significantly enhanced by the addition of boron or aluminum oxides, which increase the overall network connectivity, producing both, enhanced thermal stability and ionic conductivity.^{104,144,145} However, this structural modification results in a complexity in the network of the mixed-former glasses, producing a variety of local environments, and potentially a wide variety of connectivities. Early NMR studies of Al_2O_3 - B_2O_3 - P_2O_5 glasses were focused on short-range order, using ^{11}B , ^{27}Al and ^{31}P magic-angle spinning (MAS) NMR.^{146,147} While that work was able to quantify the distribution of the coordination numbers of the various species detected, no information was available regarding their connectivities (medium-range order).

As well documented in the literature, advanced solid state NMR techniques can provide a suitable toolbox for studying short- and medium-range order in such multi-component glasses in a quantitative fashion. The results obtained can be rationalized on the basis of Pauling bond strength (PBS)^{18,121,124,148} and bond valence (BV)^{121,127,149–151} models. These concepts are widely used in crystallography to explore bonding arrangements in crystalline systems. Pauling's contributions, particularly his ionic model and principle of local charge neutrality¹³⁶, have been

influential. He introduced the concept of bond strength, the ratio of atomic valency to coordination number, explaining crystal network topology. The correlation between PBS and bond length in crystals^{152–154} led to the bond valence concept.^{151,155} While empirically derived bond valence is more accurate, PBS offers insights into electron density in ion-pair bonds.¹⁴⁸ In cases with small bond length distributions and no site distortions, PBS can be applied alongside experimental techniques to analyze bonding in complex systems like aluminoborophosphate glasses. To date, few studies have discussed network connectivity using Pauling bond strengths in connection with experimental results.¹²⁴

Alternatively, a direct experimental approach to the connectivity distribution is aimed at a quantitative measurement of magnetic dipole-dipole interactions. In the realm of high-resolution conditions provided by magic-angle spinning, the pivotal method for measuring heteronuclear dipolar interactions is the rotational echo double resonance (REDOR) experiment.^{77,109} While MAS alone cancels the magnetic dipole-dipole coupling throughout the rotor period (T_R), the application of π -pulses to the non-observed I-spins during the rotor cycle leads to periodic sign inversions of the dipolar Hamiltonian, causing the interaction to be re-coupled.

In a previous publication¹²⁴ we have used PBS and BV principles to narrow down the range of interconnections which are likely to be present in the glass and interpret/fit the 1D NMR spectra accordingly. This indirect approach yielded the conclusion that these glasses consist predominantly of $P_{3(Al/B)}^3$ and $P_{2(Al/B)}^3$ units in sodium aluminoborophosphate glasses and probably contain few if any of $^{[5]}Al-O-P$ bonds. In the present contribution we have used dipolar-based double-resonance NMR methods to put these predictions to a quantitative test. Here we report the results of a comprehensive multinuclear double resonance NMR study of sodium aluminoborophosphate glasses along the composition line $40 Na_2O-40 P_2O_5-(20-x)-Al_2O_3-x B_2O_3$, providing detailed quantitative insights into the network connectivity distribution in this glass system.

3-2- Experimental

3-2-1- Sample preparation and characterization

Glasses within the compositional series $40 Na_2O-40 P_2O_5-(20-x) Al_2O_3-x B_2O_3$ were prepared using the melt-quench technique. The variable x ranged from 0 to 20 mol% in 5 mol%

increments. Glassy B_2O_3 was synthesized by heating H_3BO_3 gradually up to $850\text{ }^{\circ}\text{C}$ and quenched to obtain B_2O_3 . Analytical grade sodium hexametaphosphate $(NaPO_3)_6$, alumina (Al_2O_3), and freshly made glassy boron oxide (B_2O_3) were combined in three-gram batches based on target compositions (Table 3-1). The mixture was melted at $1100\text{ }^{\circ}\text{C}$ for 15 minutes in 95/5 Pt/Au crucibles. Quenching was achieved by immersing the crucible bases in water, and the resulting glasses were collected, ground, and stored in tightly capped glass vials within a desiccator. All glasses exhibited optical clarity, and x-ray diffraction showed no signs of crystallization.

While no compositional analysis was done on the final glasses, the mass losses were only 2-4%, thought to be due to P_2O_5 volatilization during melting. Glasses reported in the literature with the same analyzed compositions as B0 and B20, made by Brow¹⁵⁶ and Jiang,¹⁵⁷ respectively, showed $T_g = 405$ and 384°C . Comparing these values with those reported in Table 3-1 (407 and 390°C) provides evidence that the compositions are close to nominal.

Thermal analyses were carried out with a Netzsch DSC Phönix differential scanning calorimeter (IFSC, University of Sao Paulo, Brazil) using a heating rate of 10 K min^{-1} . Using the Proteus Thermal Analysis software, the glass transition temperatures were determined from the onset region of the observed thermal event by the tangent intersection method.

Table 3-1) Nominal compositions (mol%) and glass transition temperatures, T_g

x	B_2O_3	Al_2O_3	Na_2O	P_2O_5	$T_g[^{\circ}\text{C}]$
0	0	20	40	40	407
5	5	15	40	40	426
10	10	10	40	40	437
15	15	5	40	40	422
20	20	0	40	40	390

3-2-2- NMR experiments

All double-resonance NMR experiments were conducted on a Bruker Avance Neo spectrometer, operating at 14.1 T (600 MHz), with a Bruker HXY 2.5 mm probe (IFSC, University of Sao Paulo, Brazil). Table 3-2 summarizes the NMR measurement parameters used to acquire one-dimensional single pulse spectra. In the ^{11}B MAS NMR spectra, the ^{14}B peak intensity was corrected for the underlying satellite transition by subtracting its spinning sideband from the original spectrum. In addition, the unidimensional refocused-INADEQUATE method¹⁰⁸ was employed to acquire ^{31}P double-quantum filtered spectra. The experimental conditions included a spinning speed of 15.0 kHz, a 90-degree pulse length of 2.3 μs , and a relaxation delay of 120 s (preceded by a pre-saturation train before each scan). The mixing time for creating double-quantum coherence was 16.6 ms, corresponding to an indirect spin-spin coupling constant $^2J(^{31}\text{P}-^{31}\text{P})$ of 30 Hz. The measurement parameters employed for the various double-resonance NMR experiments are summarized in Table 3-3. In all the REDOR experiments XY-4 phase cycling was utilized for the recoupling π -pulses.¹⁰⁹ ^{31}P -observed REAPDOR experiments were done by applying a pre-saturation train of 15 $\pi/2$ pulses separated by 5 ms.

Table 3-2) NMR measurement conditions for the multinuclear single-pulse experiments

	^{11}B	^{27}Al	^{23}Na	^{31}P
Rotor frequency n_r[kHz]	20.0	20.0	20.0	20.0
Nutation frequency n_1 [kHz]	108.7	62.5	166.7	108.7
Pulse length t_p[μs]	0.6	1	0.4	0.7
Relaxation delay D_1 [s]	2	2	2	200
Shift reference	0.1 M H_3BO_3 (+19.6 ppm relative to $\text{BF}_3\text{Et}_2\text{O}$)	1 M $\text{Al}(\text{NO}_3)_3$	0.1 M NaCl	85% H_3PO_4

Table 3-3) NMR measurement conditions for the double resonance experiments: rotor frequency n_r , length of the refocusing pulse on the observe channel $t_p(\text{obs})$, nutation frequency on the recouple channel n_1 , length of the recoupling pulse $t_d(\text{rec.})$, relaxation delay $D_1(\text{s})$

	$n_r[\text{kHz}]$	$t_p(\text{obs})[\mu\text{s}]$	$n_1[\text{kHz}]$	$t_d(\text{rec.})[\mu\text{s}]$	$D_1[\text{s}]$
$^{11}\text{B}\{^{31}\text{P}\}$ REDOR	15.0	4.6	109	2.78	2
$^{11}\text{B}\{^{23}\text{Na}\}$ REDOR	15.0	3.3	150	3.25	2
$^{11}\text{B}\{^{27}\text{Al}\}$ REDOR	15.0	3.3	150	2.70	2
$^{27}\text{Al}\{^{31}\text{P}\}$ REDOR	15.0	3.6	139	3.05	0.5
$^{23}\text{Na}\{^{31}\text{P}\}$ REDOR	15.0	4.8	109	3.00	0.5
$^{31}\text{P}\{^{11}\text{B}\}$ REAPDOR	15.0	2.78	110	22.2	50
$^{31}\text{P}\{^{23}\text{Na}\}$ REAPDOR	15.0	3.0	167	22.2	50
$^{31}\text{P}\{^{27}\text{Al}\}$ REAPDOR	15.0	3.0	164	22.2	50

In all of the dipolar recoupling experiments each normalized difference signal intensity $\frac{\Delta S}{S_0}$ data point at a given dipolar mixing time, NT_R , was obtained by fitting the signal S (with dipolar recoupling) and the signal S_0 (without dipolar recoupling) spectra to a Gauss/Lorentz lineshape function.¹¹⁴ In the case of the REDOR experiments, dipolar second moments $M_{2(X-Y)}$ (X being the observe, and Y being the recoupled- nucleus) were determined by applying a parabolic fit to the REDOR data within the range $\Delta S/S_0 \leq 0.25$, according to Eq. 1-68. Crystalline BPO_4 , AlPO_4 and NaPO_3 were employed as a model compound for dipolar calibration. Their theoretically expected (van Vleck) $M_{2(X-P)}$ values are $M_{2(B-P)} = 18.4 \times 10^6 \text{ rad}^2\text{s}^{-2}$, $M_{2(Al-P)} = 5.64 \times 10^6 \text{ rad}^2\text{s}^{-2}$, and $M_{2(Na-P)} = 3.7 \times 10^6 \text{ rad}^2\text{s}^{-2}$, respectively.

3-3- Results

3-3-1- T_g measurements

Figure 3-1 shows the glass transition temperature (T_g) as a function of the B_2O_3 content in the glass series. illustrates a compositional dependence that is rather strikingly non-linear. The T_g of the boron-free glass is 407 °C. This temperature increases to 437 °C as the B_2O_3 increased to 10 mol%. Further increase in boron content causes a reduction of the transition temperature to 422

and 390 °C for B15 and B20 glasses. The uncertainty reported in Figure 3-1 is due to variability intrinsic to the tangent intersection method of finding the onset region of the glass transition temperature. Since in this method the T_g is estimated by intersecting two lines, a range of T_g can be found depending on the lines chosen.

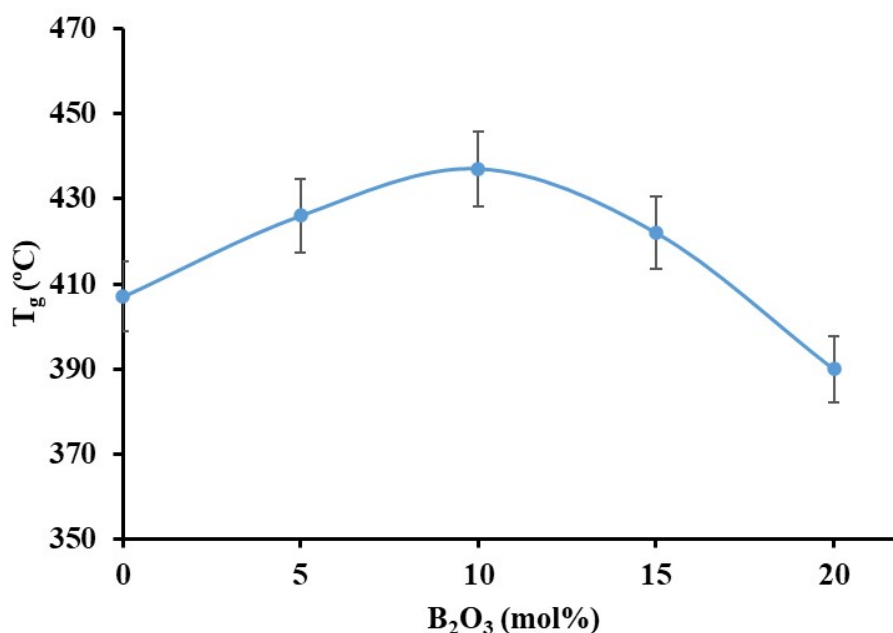


Figure 3-1) The relationship between glass transition temperature (T_g) and glass compositions

3-3-2- ^{11}B MAS NMR and $^{11}\text{B}\{^{31}\text{P}\}$ REDOR

Figure 3-2 shows the ^{11}B MAS NMR spectra of the glasses. They consist of a relatively broad signal near 16 ppm with rather low area fraction ($\sim 10\%$), attributed to three-coordinated boron, $^{[3]}\text{B}$, and two dominant intense sharp signals near zero ppm (90%) which are assigned to four-coordinate boron, $^{[4]}\text{B}$, species. Results obtained for the borophosphate glass B20 agree with the data published on a very similar ternary glass by Zielniok et al.¹²⁰ Table 3-4 summarizes all the ^{11}B lineshape parameters obtained from simulations. The lineshape attributed to the $^{[3]}\text{B}$ species is strongly affected by the anisotropy of the nuclear electric quadrupolar interactions as described by second order perturbation theory (section 1-3-5-3). The C_Q value of ~ 2.5 MHz corresponds to a typical value of trigonal-planar environments with three bridging oxygen species, $^{[3]}\text{B}$.⁸⁶ The asymmetry parameter η cannot be precisely determined from the lineshape, owing to the effect

of superimposed isotropic chemical shift distribution, which significantly influences ^{11}B MAS NMR lineshapes of ^{13}B units at magnetic field strengths exceeding 9.4 T.

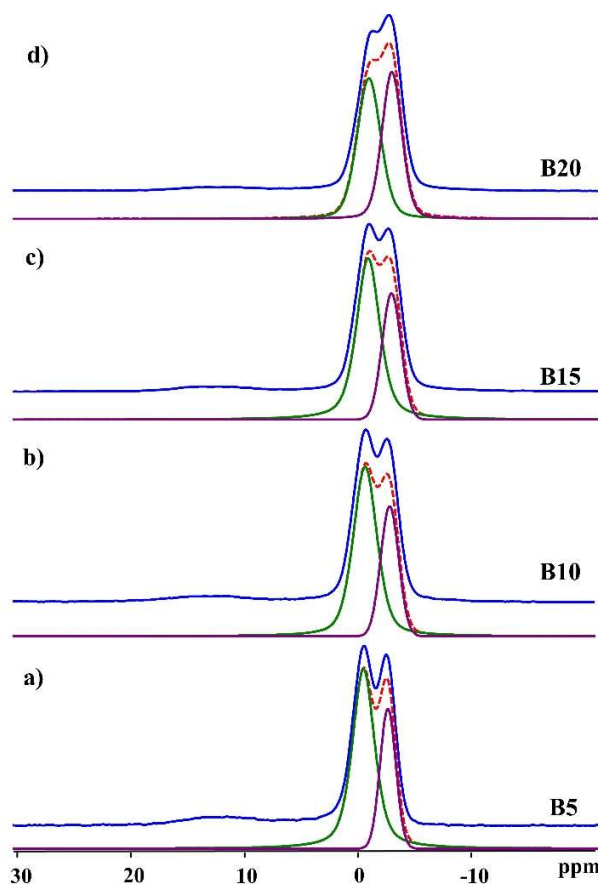


Figure 3-2) ^{11}B MAS NMR spectra of a) B5, b) B10, c) B15 and d) B20. Solid blue line: experimental and dotted red line: fitted spectra. $^{14}\text{B}_{3\text{P}}$ and $^{14}\text{B}_{4\text{P}}$

The close-to-tetrahedral electronic environment of the ^{14}B units produces rather weak quadrupolar interactions ($C_Q \approx 0.5$ MHz) and hence relatively sharp signals.⁸⁶ Evidently, multiple ^{14}B units are present, whose lineshapes are overlapping. It has been shown that the chemical shift of the boron species which is denoted by $^{14}\text{B}_{n\text{P}}$ is affected by the number n of the bonded P species, and δ_{iso} decreases with increasing n (from 0.0 ppm for $n = 0$ to -3.5 ppm for $n = 4$).¹¹³ Based on this information we attribute the peak maxima observed near ca. -1.0 and -3.0 ppm dominantly to $^{14}\text{B}_{3\text{P}}$ and $^{14}\text{B}_{4\text{P}}$ species, respectively. However, $^{14}\text{B}_{2\text{P}}$ units may also be present as well and contribute signal intensity at the low-frequency wing of the lineshape. As shown below,

this attribution is consistent with the REDOR data and also confirmed by chemical shift calculations, which indicate about a 2 ppm difference between $^{[4]}\text{B}_{3\text{P}}$ and $^{[4]}\text{B}_{4\text{P}}$ species.¹¹³ Upon gradual substitution of B_2O_3 by Al_2O_3 , we note a slight decrease of $\langle n \rangle$ suggesting a small reduction in the degree of B–O–P linking, although the latter remains the dominant mode of connectivity on this composition line.

Table 3-4) $^4\ ^{11}\text{B}$ isotropic chemical shifts δ_{iso} and dipolar second moments $M_{2(\text{B-P})}$ of the glasses under study. $M_{2(\text{B-P})}$ values corrected based on the theoretical $M_{2(\text{B-P})}$ obtained from crystalline $\text{BPO}_4 = 18.4 \times 10^6 \text{ rad}^2 \text{ s}^{-2}$, based on a measured raw value of $M_{2(\text{B-P})} = 12.5 \times 10^6 \text{ rad}^2 \text{ s}^{-2}$

	$^{14}\text{B}_{4\text{P}}$			$^{14}\text{B}_{3\text{P}}$			δ_{iso} (ppm) ± 0.1
	δ_{iso} (ppm) ± 0.1	Int. (%) ± 1	$M_{2(\text{B-P})} \times 10^6 \text{ rad}^2 \text{ s}^{-2}$	δ_{iso} (ppm) ± 0.1	Int. (%) ± 1	$M_{2(\text{B-P})} \times 10^6 \text{ rad}^2 \text{ s}^{-2}$	
B5	-2.7	32	11.1	-0.5	59	8.1	1
B10	-2.9	36	11.1	-0.8	57	8.1	1
B15	-2.7	39	11.1	-0.7	56	8.1	1
B20	-2.8	39	11.4	-0.9	57	9.8	1

C_Q (quadrupolar coupling constant) fixed at 2.50 MHz with a tolerance of ± 0.15 MHz. δ_{iso} (isotropic chemical shift) fixed in ^{13}B and ± 0.1 in ^{14}B species. W: Full Width at Half Maximum (peak width) fixed with a tolerance of ± 0.03 kHz, η (asymmetry) fixed at 0.2 with a tolerance of ± 0.1 , Int (Integrated intensity) fitted to obtain N_4

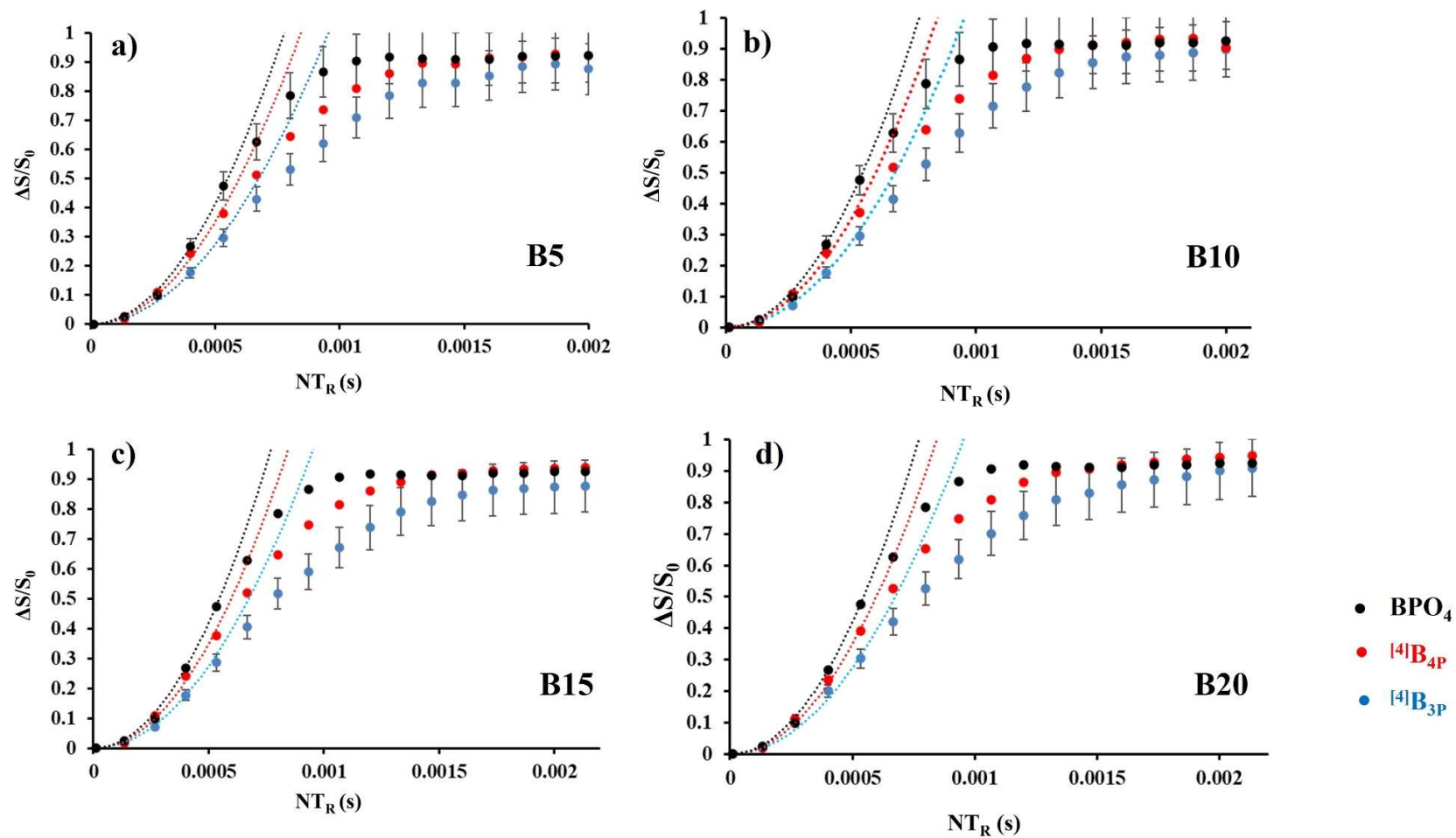


Figure 3-3) $^{11}\text{B}\{^{31}\text{P}\}$ REDOR dephasing curves for the two $^{[4]}\text{B}$ species observed in a) B5, b) B10, c) B15, d) B20 and for the model compound BPO_4 . Parabolic approximations to the initial regimes are included. S and S_0 denotes intensity of the signal with and without dipolar interaction, respectively. $\Delta S = S - S_0$. NT_R refers to the dipolar evolution time.

Figure 3-3 shows the $^{11}\text{B}\{^{31}\text{P}\}$ dephasing curve of B5-B20. As two ^{41}B signals are resolved, two distinct REDOR curves can be obtained. Also included is the dephasing curve measured for the crystalline model compound BPO_4 , which is constructed from $^{41}\text{B}_{4\text{P}}$ units with four B–O–P linkages at a distance of 2.77 Å and serves as an important calibration compound in the present case. Table 3-4 summarizes the second moments $M_{2(\text{B-P})}$, which are extracted from Eq. 1-68 via parabolic analysis, following calibration according to the results of the $^{11}\text{B}\{^{31}\text{P}\}$ REDOR measurement on BPO_4 . Previous REDOR work has shown that $M_{2(\text{B-P})}$ values in borophosphate glasses depend linearly on the average number of B–O–P linkages with an increment of $4\text{--}5 \times 10^6 \text{ rad}^2\text{s}^{-2}$.^{129,158} Thus, the results obtained on the present glasses confirm the attribution of $\langle n \rangle$ values of 3 and 4, respectively, for these two $^{41}\text{B}_{\text{nP}}$ species, consistent with their chemical shifts. For the Al-free glass B20, the somewhat larger values of $M_{2(\text{B-P})}$ suggest a slightly stronger degree of B–O–P connectivity (or shorter distances) compared to the mixed AlBP glasses, consistent with the information given above. Finally, the $^{11}\text{B}\{^{31}\text{P}\}$ REDOR data show no evidence for ^{31}B –O–P connectivities. Qualitative $^{11}\text{B}\{^{23}\text{Na}\}$ REDOR studies show further, that the dipolar interaction strengths that both ^{41}B units with ^{23}Na are similar (Figure 3-4) and $^{11}\text{B}\{^{27}\text{Al}\}$ REDOR experiments show no experimental evidence for ^{11}B – ^{27}Al dipole-dipole interactions. Thus, we conclude that the fraction of B–O–Al linkages in these glasses can be neglected.

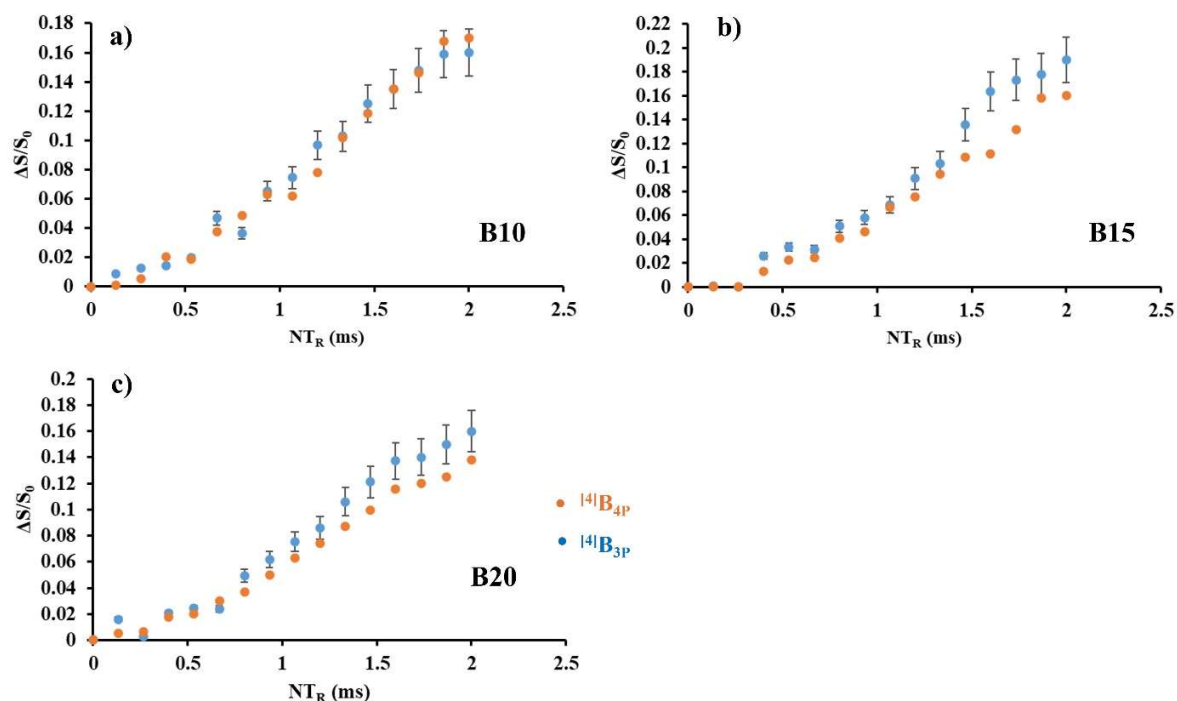


Figure 3-4) $^{11}\text{B}\{^{23}\text{Na}\}$ REDOR dephasing curves for a) B10, b) B15, and c) B20. S and S_0 denotes intensity of the signal with and without dipolar interaction, respectively. $\Delta S = S - S_0$. NT_R refers to the dipolar evolution time.

3-3-3- ^{27}Al MAS NMR and $^{27}\text{Al}\{^{31}\text{P}\}$ REDOR

Figure 3-5 shows the ^{27}Al MAS NMR spectra. All the glasses contain aluminum with coordination numbers 4, 5 and 6 with isotropic chemical shifts near 50, 20 and -10 ppm, respectively. The data were fitted with the Czjzek model assuming a wide distribution of electric field gradients.⁸⁷ The results are summarized in Table 3-5. For the pure aluminophosphate glass, the spectra are in excellent agreement with the spectra published by Zhang and Eckert on melt-cooled and sol-gel glasses having the same composition (40% Na_2O -20% Al_2O_3 -40% P_2O_5).¹⁵⁹ In the mixed aluminoborophosphate glasses subject to the present study, the Al coordination distribution is greatly affected by the boron content. Figure 3-5 shows that the integrated intensity of $^{[6]}\text{Al}$ increases at the expense of $^{[4]}\text{Al}$ with increasing B_2O_3 content in the glass series, while the fraction of the $^{[5]}\text{Al}$ units changes slightly as a function of glass composition.

Consequently, the average coordination number of the Al species increases with increasing boron content in the glasses (see Table 3-5).

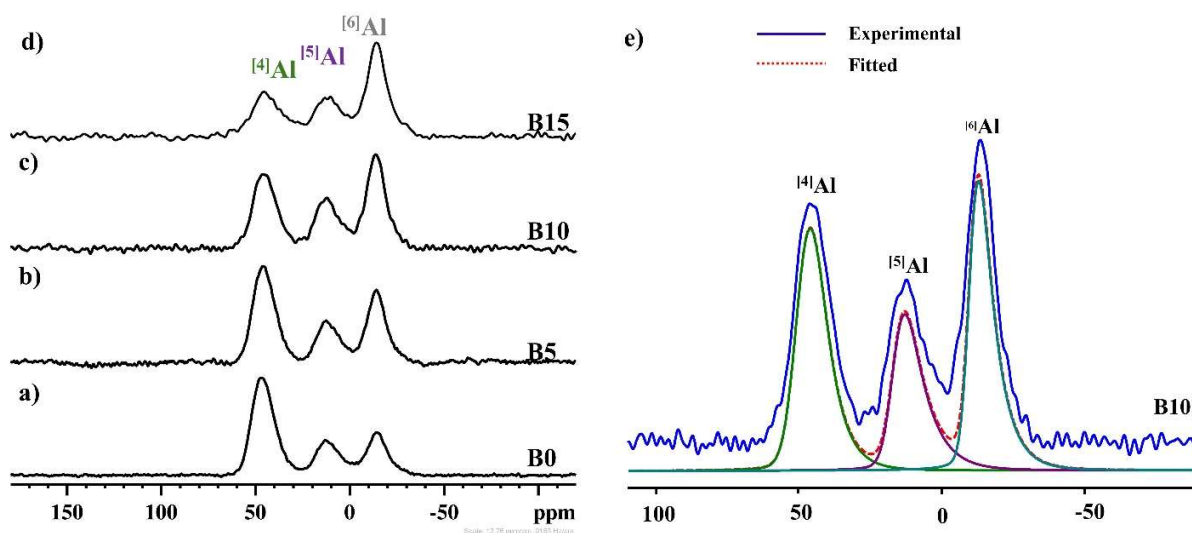


Figure 3-5) ^{27}Al MAS NMR spectra of a) B0, b) B5, c) B10, d) B15 and f) lineshape analysis for sample B10 using the CzSimple¹⁶⁰ module of DMfit. In $^{[n]}\text{Al}$, "n" denotes the Al coordination number

Table 3-5) Lineshape parameters used for fitting ^{27}Al MAS NMR spectra, isotropic chemical shift δ_{iso} , modulus of the average quadrupolar coupling constant $\langle|C_Q|\rangle$, and average Al coordination numbers in the glasses under study.

	$^{[4]}\text{Al}$			$^{[5]}\text{Al}$			$^{[6]}\text{Al}$			
	δ_{iso}	$\langle C_Q \rangle$	Int.	δ_{iso}	$\langle C_Q \rangle$	Int.	δ_{iso}	$\langle C_Q \rangle$	Int.	$\langle\text{CN}\rangle$
B15	50.7	2.40	28	16.9	2.50	27	-9.6	2.50	45	5.17
B10	50.7	2.30	37	16.9	2.40	25	-9.6	2.40	38	5.01
B5	51.0	2.40	50	16.6	2.40	20	-9.4	2.40	30	4.81
B0	52.0	2.40	58	16.7	2.40	20	-9.5	2.40	22	4.64

Fixed parameters: C_Q with a tolerance of ± 0.05 MHz, δ_{iso} with a tolerance of ± 0.5 ppm
Fitted parameter: Int: Integrated intensity $\pm 2\%$

Figure 3-6 shows the $^{27}\text{Al}\{^{31}\text{P}\}$ REDOR curves. The dephasing curves of the ^{27}Al nuclei in all their three coordination states are essentially identical and similar to that observed in within experimental error for crystalline AlPO_4 (4 Al–O–P linkages at a distance of 3.0 Å) These results

agree with those observed previously for a wide range of sodium aluminophosphate glasses¹⁵⁹ and indicate that the second coordination sphere of all the aluminum species is dominated by phosphorus. Also, the isotropic chemical shifts observed point towards the exclusive formation of Al–O–P linkages. We note that the $M_{2(\text{Al-P})}$ values of four- and six-coordinated Al are about the same within experimental error, because the effect of the larger coordination number of $^{[6]}\text{Al}$ is offset by the effect of the longer Al–O–P distance when compared to four-coordinated aluminum. This has been previously evidenced for sodium aluminophosphate glasses mirroring the REDOR curve.⁴⁰ This observed trend is consistent with the chemical shift information and holds true for all the glasses examined. Finally, we note that qualitative $^{27}\text{Al}\{^{11}\text{B}\}$ REDOR experiments were also conducted but showed no evidence of dipolar dephasing, once again providing no evidence of Al–O–B linking.

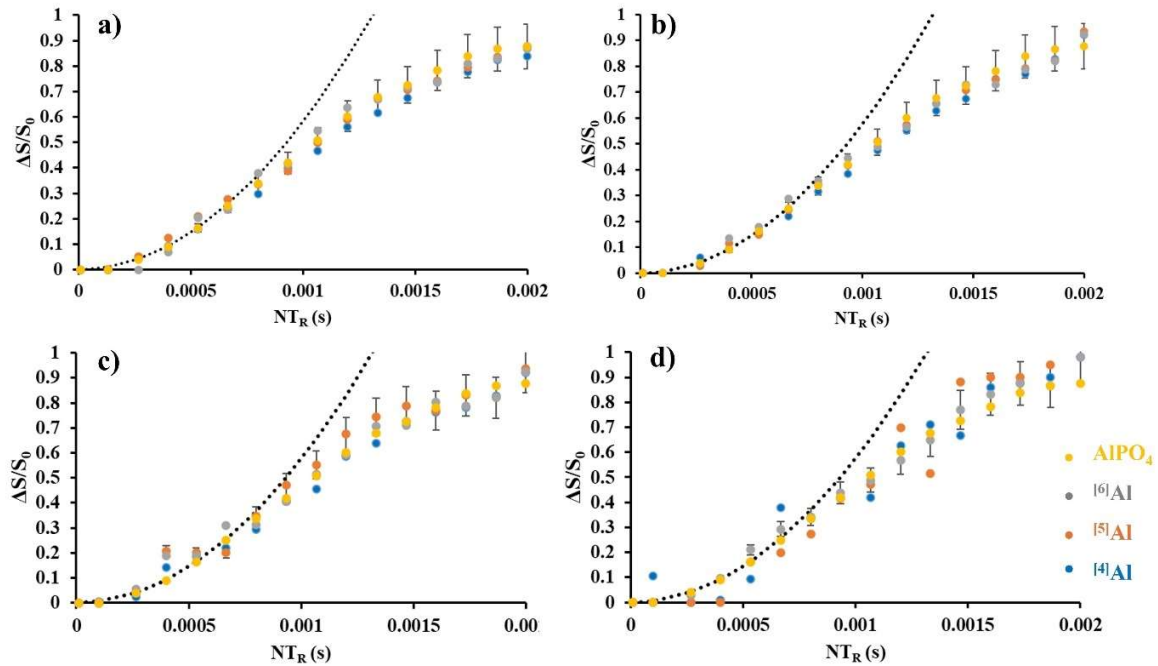


Figure 3-6) $^{27}\text{Al}\{^{31}\text{P}\}$ REDOR dephasing curves, a) B0, b) B5, c) B10, d) B15. Parabolic approximations to the initial regimes are included. S and S_0 denotes intensity of the signal with and without dipolar interaction, respectively. $\Delta S = S - S_0$. NT_R refers to the dipolar evolution time.

3-3-4- ^{31}P MAS, Refocused INADEQUATE, $^{31}\text{P}\{^{27}\text{Al}\}$, and $^{31}\text{P}\{^{11}\text{B}\}$ REAPDOR NMR

Figure 3-7a-e show the ^{31}P MAS NMR spectra of the glasses under study. They are poorly resolved, presumably due to the presence of multiple overlapping components from different $\text{P}_{\text{mY}}^{\text{n}}$ species where Y can be B, Al or P. While the deconvolution shown in Figure 3-7 might be considered tentative, it is actually constrained by additional experimentations. These constraints are based on double quantum filtering experiments by 1D-refocused INADEQUATE spectra. This sequence utilizes the homonuclear indirect ^{31}P - ^{31}P spin-spin coupling as a mechanism of double quantum filtration, leading (after appropriate phase cycling) to the selective detection of species with P–O–P linkages. An example is given in Figure 3-7f, for the sample B0, where a single resonance at -12 ppm can be observed, which can be attributed to the superimposed signals of $\text{P}_{2\text{Al}}^3$ and $\text{P}_{1\text{Al}}^2$. On the other hand, the ^{31}P resonances of those species lacking P–O–P linkages are missing in the double-quantum filtered spectra (Figure 3-7e), allowing also a straightforward identification of the peak near -3.0 ppm to $\text{P}_{2\text{Al}}^2$ and $\text{P}_{3\text{Al}}^3$ sites via difference spectroscopy.

For B20 the situation is more complicated: the R-INADEQUATE spectrum can be fitted assuming two spectral components: a dominant one near -15 ppm arising from structural units such as $\text{P}_{2\text{B}}^3$, and $\text{P}_{1\text{B}}^2$ units, and a broad shoulder that may be attributable to $\text{P}_{1\text{B}}^3$ units. Comparison with the single-pulse spectrum indicates that the signal contribution lacking P–O–P linkages can be simulated by a single Gaussian comprising the $\text{P}_{2\text{B}}^2$ and $\text{P}_{3\text{B}}^3$ units. We note that for the samples B5, B10, and B15, the spectral editing approach used via double-quantum filtering was not successful, due to the overlap of potentially 15 resonances from species with P–O–P connectivity and without P–O–P connectivity. Owing to this complexity, it was also not possible to resolve responses from these species at distinct chemical shifts using $^{31}\text{P}\{^{27}\text{Al}\}$ and $^{31}\text{P}\{^{11}\text{B}\}$ REAPDOR difference spectra. Although these latter techniques were found to be unsuitable for spectral editing purposes, Figure 3-8 illustrates that the magnitude of the REAPDOR difference signal $\Delta\text{S}/\text{S}_0$ measured at a fixed dipolar mixing time of 1.5ms, shows the expected dependence on the chemical composition of the samples.

Table 3-6 summarizes the information extracted from the simplified deconvolution model outlined above, guided by the R-INADEQUATE results obtained on the B0 and B20 glasses. We note that the chemical shifts of the two components show a systematic dependence on the

x-value. This may reflect a systematic dependence of the chemical shift of a given P_{mAlB}^3 species on the specific structural environment considered, i.e., a P_{mB}^n structural unit may have a different chemical shift than a P_{mAl}^n or a mixed species. On the other hand, the chemical shift trend may also reflect a systematic change in the average phosphate connectivity $\langle n \rangle$. As discussed further below, the number of B–O–P linkages from ^{11}B MAS NMR is significantly lower than the number of Al–O–P linkages from ^{27}Al MAS NMR, and hence, we must conclude that either the P^2 / P^3 ratio or the extent of P–O–P linking increases with increasing boron content of these glasses.

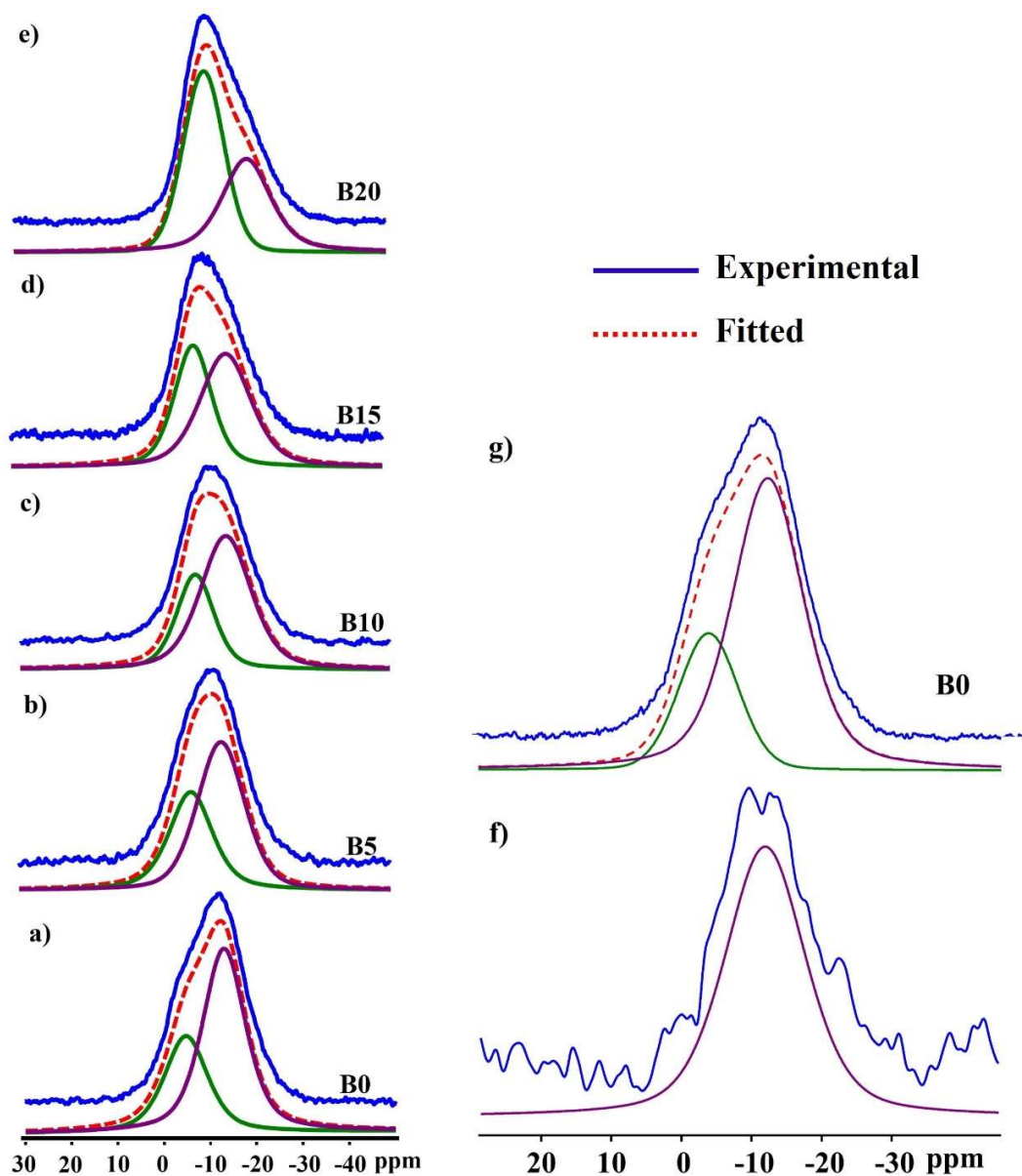


Figure 3-7) ^{31}P MAS NMR spectra of a) B0, b) B5, c) B10, d) B15, e) B20 fitted with two Gaussian components. Comparison of the f) R-INADEQUATE and g) the single-pulse spectra measured for sample B0.

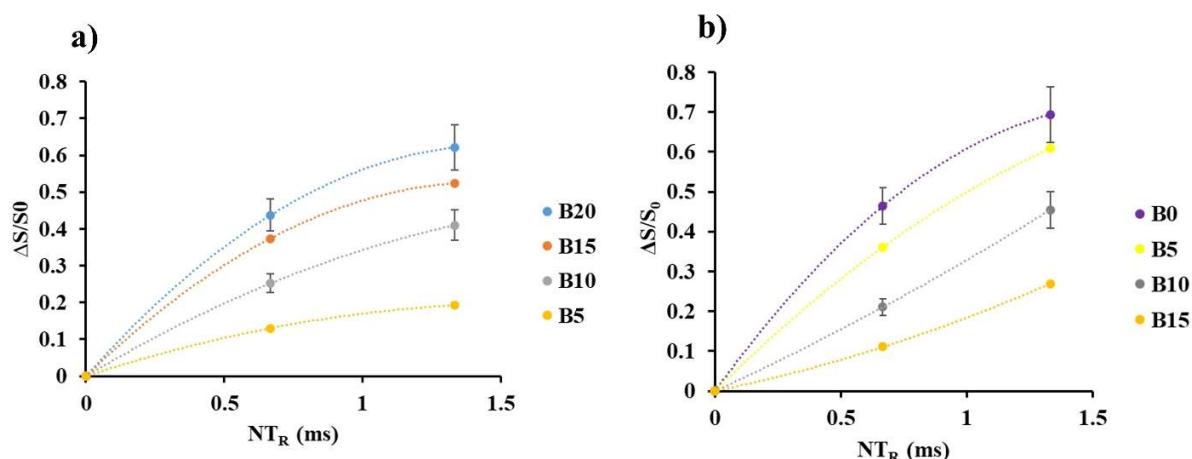


Figure 3-8) a) $^{31}\text{P}\{^{11}\text{B}\}$ REAPDOR, b) $^{31}\text{P}\{^{27}\text{Al}\}$ REAPDOR normalized difference signal intensities measured at two dipolar mixing times for the glasses under study. S and S_0 denotes intensity of the signal with and without dipolar interaction, respectively. $\Delta S = S - S_0$. NT_R refers to the dipolar evolution time. Dotted lines serve as a guide for eye.

Table 3-6) Parameters used for fitting ^{31}P magic angle spinning (MAS) NMR spectra.

	$P_{3(B,Al)}^3$			$P_{2(B,Al)}^3$		
	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)
B0	-4.5	2.50	24	-12.9	3.40	76
B5	-6.5	2.50	27	-13.9	3.40	73
B10	-8.2	2.50	37	-15.2	3.40	63
B15	-9.7	2.50	45	-17.1	3.40	55
	P_{1B+}^2 / P_{2B}^2			P_{2B}^3		
B20	-11.2	2.50	57	-20.1	3.40	43

δ_{iso} isotropic chemical shift fixed with a tolerance of ± 0.5 ppm, W: Full Width at Half Maximum (Peak width) fixed with a tolerance of ± 0.05 kHz, Int: Integrated intensity $\pm 2\%$ (fitted)

3-3-5- ^{23}Na MAS NMR and $^{23}\text{Na}\{^{31}\text{P}\}$ REDOR

Figure 3-9 shows the ^{23}Na MAS NMR spectra. The data show the typical asymmetric lineshapes generally observed for sodium ions in an amorphous environment. They can be fitted by the Czjzek model assuming a wide distribution of quadrupolar coupling constants affecting the lineshape in the regime described by second-order perturbation theory.⁸⁷ Czjzek model describes the distribution function of the electric field gradient (V_{zz}) and the asymmetry parameter (η), taking into account structural randomness arising from variations in the angular positions of ions within coordination shells, as well as the absence of correlations among ionic charges distributed across different coordination shells. It should be noted that the δ_{iso} values of sodium with

different coordination numbers are very similar, and the distribution is too narrow at the magnetic field strength used in this study (14.1 T) to allow any distinction to be observed. The fitted curves reveal that there is essentially no change of isotropic chemical shift (see Table 3-7), indicating a constant local environment of Na in these glasses.

Table 3-7) ^{23}Na MAS NMR lineshape parameters, isotropic chemical shift δ_{iso} , modulus of the average quadrupolar coupling constant $\langle|C_Q|\rangle$, and dipolar second moments $M_{2(\text{Na-P})}$

	δ_{iso} (ppm)	$\langle C_Q \rangle$ [MHz]	$M_{2(\text{Na-P})}$ [$10^6 \text{ rad}^2\text{s}^{-2}$] $\pm 10\%$
B0	-10.3	2.50	3.7
B5	-11.2	2.50	3.5
B10	-11.2	2.50	2.9
B15	-11.4	2.50	3.4
B20	-11.5	2.50	3.4

Fixed parameters: C_Q with a tolerance of ± 0.05 MHz, δ_{iso} with a tolerance of ± 0.1 ppm;
Fitted parameter: Intensity $\pm 1\%$

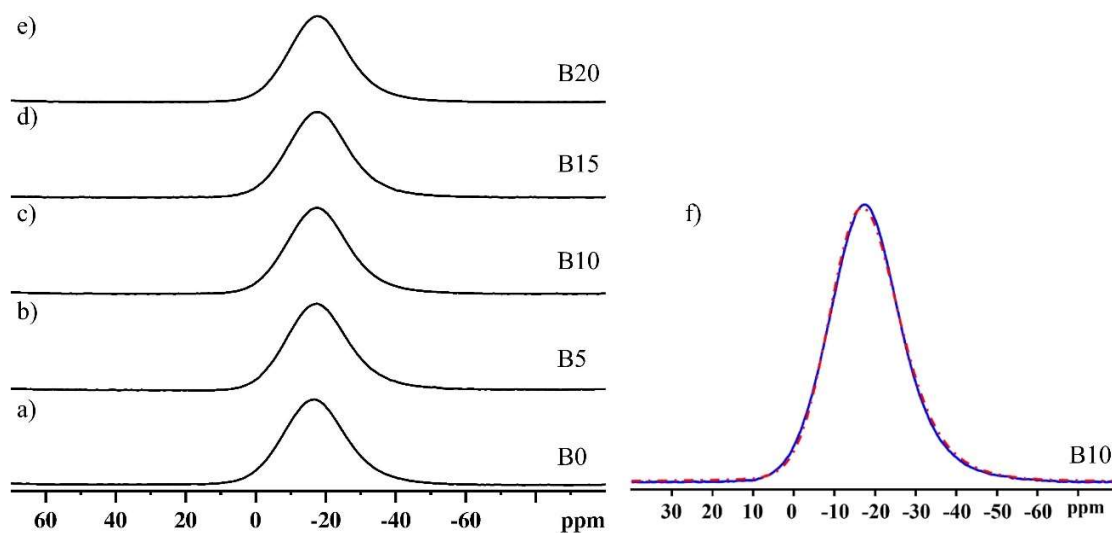


Figure 3-9) ^{23}Na magic angle spinning (MAS) NMR spectra of a) B0, b) B5, c) B10, d) B15, e) B20 and f) lineshape fit of the ^{23}Na MAS NMR spectra to the Cjzek model.

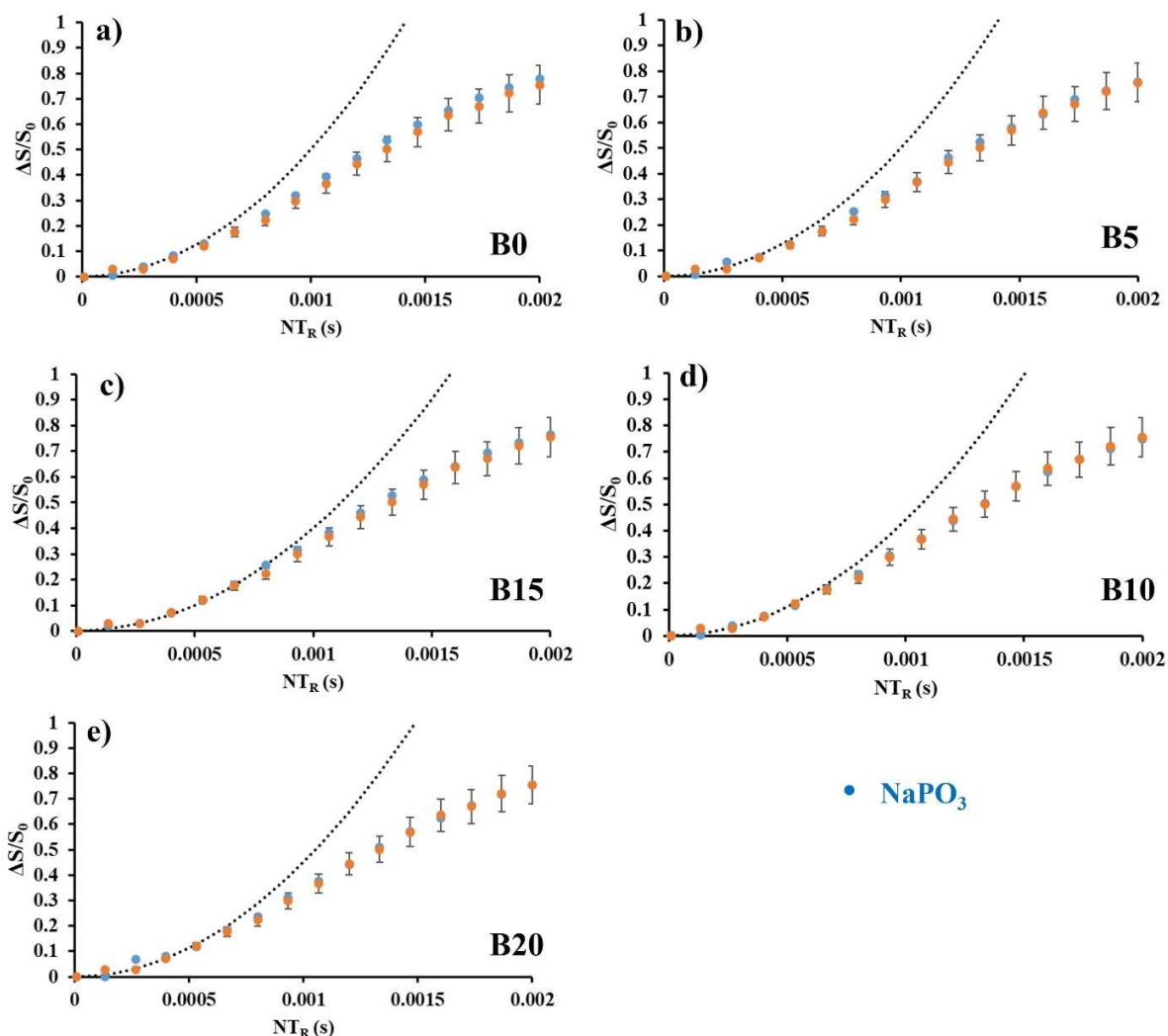


Figure 3-10) $^{23}\text{Na}\{^{31}\text{P}\}$ REDOR dephasing curves for glass B10 and the model compound NaPO_3 . a) B0, b) B5, c) B10, d) B15, e) B20. Parabolic approximations to the initial regimes are included. S and S_0 denotes intensity of the signal with and without dipolar interaction, respectively. $\Delta S = S - S_0$. NT_R refers to the dipolar evolution time.

The $^{23}\text{Na}\{^{31}\text{P}\}$ REDOR data shown in Figure 3-10, reveal no dependence on composition within experimental error. The second moment values $M_{2(\text{Na-P})}$ extracted from the data via Eq. 1-68 are close to the value measured for glassy NaPO_3 .¹⁶¹ These results indicate that the second coordination sphere of the sodium ions is dominated by the phosphate anions as in pure sodium aluminophosphate glasses¹⁵⁹ and in crystalline NaPO_3 . As previously discussed for sodium

borophosphate glasses,⁹⁹ the ^{11}B nuclei make essentially no contribution to the second coordination sphere of the sodium ions, as the local formal negative charge of the $^{[4]}\text{B}$ species is delocalized onto the P^3 and P^2 phosphate species to which they are linked through the corresponding bond valence gradient. As a consequence of this situation the oxygen atoms involving B–O–P linkages are essentially uncharged and do not attract Na^+ ions for charge compensation. Rather, the charge is dispersed on the non-bridging oxygen atoms of the neighbouring P^3 and P^2 units present in these glasses. For these reasons borophosphate glasses with these compositions do not feature Na/B proximity.⁹⁹ In other words, the borate species do not compete with the phosphate species for network modification. This conclusion is also reinforced by the very slow dephasing of the ^{11}B nuclei in the dipolar field of the ^{23}Na spins.

3-4- Discussion

Figure 3-2 shows that in all glasses, the boron atoms are dominantly forming $^{[4]}\text{B}$ and only a small fraction (4-9%) are three coordinated. In a borophosphate glass, the $^{[4]}\text{B}$ units are connected to various phosphate species and based on the number of the P cations around a given B, the chemical shift changes.¹²⁰ While in the current aluminoborophosphate glasses various $^{[4]}\text{B}_{\text{nP}}$ units are present, the dominant species are of the $^{[4]}\text{B}_{3\text{P}}$ and $^{[4]}\text{B}_{4\text{P}}$ types. These findings are in agreement with the $M_{2(\text{B-P})}$ values extracted from the REDOR NMR data. Overall, the results of the present study are consistent with previous work on alkali and silver borophosphate glasses, indicating a strong preference of $^{[4]}\text{B}$ –O–P connectivity, while $^{[3]}\text{B}$ –O–P connectivity is discriminated against.^{99,120,158} Thus, the results of the present study indicates that this observation holds true in aluminoborophosphate glasses as well. This finding is supported by the bond–valence theory previously applied to describe the glass connectivity in aluminoborophosphate glasses.¹²⁴

The NMR data enable a quantitative assessment of the connectivity distribution in this glass system. In the pure borophosphate glass B20, for which we can see from Table 3-4, the number of B–O–P linkages per formula unit is calculated as seen in section 2-4-2-3:

$$\text{B–O–P} = 2 \times \text{B}_2\text{O}_3 \text{ (mol \%)} \times [\{I(^{[4]}\text{B}_{1\text{P}}) \times 1\} + \{I(^{[4]}\text{B}_{2\text{P}}) \times 2\} + \{I(^{[4]}\text{B}_{3\text{P}}) \times 3\} + \{I(^{[4]}\text{B}_{4\text{P}}) \times 4\}]$$

Eq. 3-2

$$= 2 \times 20 \times [\{0.57 \times 3\} + \{0.39 \times 4\}] = 130.8 \text{ per unit formula}$$

This means there are $130.8 \div 40 = 3.27$ linkages per boron atom. As the REDOR experiments indicate that the ^{11}B - ^{31}P dipolar coupling strengths involving the ^{13}B units are extremely weak, we will make the simplifying assumption that ^{13}B -O-P linkages are non-existent in our glasses, consistent with previous results on other borophosphate glasses with similar compositions. The number of B-O-B linkages is given by:

$$\begin{aligned} \text{B-O-B} &= 2 \times \text{B}_2\text{O}_3 \text{ (mol\%)} \times \left[\{I(^{14}\text{B}_{3\text{P}}) \times \frac{1}{2}\} + \{I(^{13}\text{B}) \times \frac{3}{2}\} \right] \quad \text{Eq. 3-3} \\ &= 2 \times 20 \times \left[\{0.57 \times \frac{1}{2}\} + \{0.04 \times \frac{3}{2}\} \right] = 13.8 \text{ per unit formula} \end{aligned}$$

The number of P-O-P in this glass is calculated as:

$$\begin{aligned} \text{P-O-P} &= 2 \times \text{P}_2\text{O}_5 \text{ (mol\%)} \times \left[\{I(\text{P}_{2\text{B}}^3) \times \frac{1}{2}\} + \{I(\text{P}_{1\text{B}}^2) \times \frac{2}{2}\} \right] \quad \text{Eq. 3-4} \\ &= 2 \times 40 \times \left[\{0.43 \times \frac{1}{2}\} + \{0.28 \times 1\} \right] = 39.6 \text{ per unit formula} \end{aligned}$$

A similar analysis can be done, in principle, for the aluminophosphate glass B0, with the added complexity that higher-coordinated aluminum species $^{[5]}\text{Al}$ and $^{[6]}\text{Al}$ are observed to be present. The $^{27}\text{Al}\{^{31}\text{P}\}$ REDOR experiments suggest that all the Al species are fully connected to phosphate species, leading to an overall higher degree of connectivity compared to the situation in the borophosphate glasses. Lacking evidence to the contrary, Al-O-Al linkages are not considered. To discuss appropriate connectivity scenarios, an inspection of the structures of some crystalline model compounds in the phase diagram $\text{NaPO}_3\text{-Al}_2\text{O}_3$ ^{162,16399} can provide some guidance. The structures available in the ICSD are $\text{Na}_7\text{Al}_4\text{P}_9\text{O}_{32}$ with the collection code 261924 (formal composition 35 Na_2O -20 Al_2O_3 -45 P_2O_5) and $\text{Na}_6\text{Al}_3\text{P}_5\text{O}_{20}$ with the collection code 143045 (formal composition 42.9 Na_2O -21.4 Al_2O_3 -35.7 P_2O_5). The structure of $\text{Na}_7\text{Al}_4\text{P}_9\text{O}_{32}$, which can also be written as $\text{Na}_7\text{Al}_4[\text{P}_2\text{O}_7]_4\text{PO}_4$, is constructed from all six-coordinated Al species making six Al-O-P linkages. Eight out of nine P atoms contain one P-O-P linkage.¹⁶³ Wyckoff position P1(8e) is a $\text{P}_{3\text{Al}}^4$ unit, Wyckoff position P2(8e) is a $\text{P}_{2\text{Al}}^3$ species with one NBO, while Wyckoff position P3 (2a) is a $\text{P}_{4\text{Al}}^4$ unit. The structure of $\text{Na}_6\text{Al}_3\text{P}_5\text{O}_{20}$ contains $^{[4]}\text{Al}$ and $^{[6]}\text{Al}$ species in the ratio 1:2. 70% of the P atoms sitting on eleven crystallographically distinct positions are of the $\text{P}_{3\text{Al}}^3$ type. They have mixed coordinations, being linked to one $^{[4]}\text{Al}$ and two $^{[6]}\text{Al}$ units each, whereas 30% of the P inventory are of the $\text{P}_{4\text{Al}}^4$ type, being mostly connected to $^{[6]}\text{Al}$ species. Again, the $^{27}\text{Al}\{^{31}\text{P}\}$ REDOR data can be used to extract the number of Al-O-P linkages. Using the information given in Table 3-5 we obtain a value of 185.6 for glass B0:

$$\text{Al-O-P} = 2 \times \text{Al}_2\text{O}_3 (\text{mol}\%) \times \langle \text{CN} \rangle \quad \text{Eq. 3-5}$$

For B0 it is calculated as $\text{Al-O-P} = 2 \times 20 (\text{mol}\%) \times 4.64 = 185.6$ per unit formula. This number can be checked again for consistency with the ^{31}P MAS-NMR peak deconvolution, guided by the R-INADEQUATE experiment. Table 3-6 suggests a decomposition into 24% $\text{P}_{3\text{Al}}^3$ and 76% $\text{P}_{2\text{Al}}^3$ units in this case. Thus, number of P-O-Al linkages per unit formula deduced from this peak deconvolution (179.6) stands in agreement with the number of Al-O-P linkages obtained from ^{27}Al MAS NMR.

In order to find P-O-P linkages for the mixed Aluminoborophosphate glasses, first the number of NBOs per formula unit should be determined using Eq. 3-6:

$$\text{NBO} = 2 \times \text{P}_2\text{O}_5 (\text{mol}\%) \times [\{1 \times \text{I}(\text{P}^3)\} + \{2 \times \text{I}(\text{P}^2)\}] \quad \text{Eq. 3-6}$$

Then one can find the number of the P-O-P linkages by subtracting the total number of oxygens from the compositions, $[\text{O}]_{\text{comp.}}$, from sum of B-O-B, B-O-P and Al-O-P linkages as follows:

$$\text{P-O-P} = [\text{O}]_{\text{comp.}} - (\text{B-O-B} + \text{B-O-P} + \text{Al-O-P} + \text{NBO}) \quad \text{Eq. 3-7}$$

The percentage of X-O-Y (and X-O-X) is calculated by dividing it by the total number of linkages. For example, for P-O-P

$$\text{Percentage of P-O-P} = \frac{\text{the number of P-O-P}}{(\text{P-O-P}) + (\text{P-O-B}) + (\text{B-O-B}) + (\text{Al-O-P})} \quad \text{Eq. 3-8}$$

Table 3-8) Percentage of X-O-Y and X-O-X linkages obtained from ^{27}Al and ^{11}B NMR experiments

	B-O-B	B-O-P	Al-O-P	P-O-P
B0	0	0	84.4	15.6
B5	3.9	13.9	65.6	16.6
B10	7.1	28.6	45.5	18.7
B15	9.7	44.2	23.5	22.6
B20	15.8	75	0	9.2

Table 3-8 summarizes the connectivity information for all the samples, including the mixed aluminoborophosphate glasses, as obtained from the ^{11}B and ^{27}Al MAS NMR analysis. We note that in this case the ^{31}P MAS NMR spectra are too complex to be analysed in detail, due to the large number of possible connectivities and permutations of linkages to P, Al and B

connectivities. In these mixed systems, unfortunately, the poor resolution obtained in the spectra makes it impossible to identify any preferences with regard to either connectivity (P^3 vs. P^2) or linking with $[^4]Al$, $[^5]Al$, $[^6]Al$ units versus linking with $[^4]B$ units. In principle, the mixed systems might comprise up to 14 species. In addition, Al–O–B linkages could also be imagined in the mixed system. Even though our $^{27}Al/^{11}B$ double resonance experiments suggested that the concentrations of such linkages are not high, such interactions cannot be excluded completely.

Using Eq. 3-9 and 3-10 it is possible to compare the connectivity information of Table 3-9 with that predicted based on a statistical linkage model of bridging oxygen atoms. These probabilities are given by

$$W_{X-O-X} = \frac{1}{2} \times \langle n_X \rangle^2 [X_2O_z]^2 \quad \text{Eq. 3-9}$$

for homo-atomic connectivities X–O–X (X = B, Al, or P), and

$$W_{X-O-Y} = \langle n_X \rangle \langle n_Y \rangle [X_2O_z][Y_2O_n] \quad \text{Eq. 3-10}$$

for heteroatomic connectivity, X–O–Y. Here $\langle n_X \rangle$ and $\langle n_Y \rangle$ are the average connectivities of the elements B, Al, and P in the glass considered (Table 3-9). Normalized probabilities can then be obtained by dividing the individual W_i values by their total sum of all the possible combinations.

Table 3-9) The average connectivity of the network formers.

Glass	$\langle n_B \rangle$	$\langle n_{Al} \rangle$	$\langle n_P \rangle$
B0	0	4.64	3.00
B5	3.91	4.81	3.00
B10	3.93	5.01	3.00
B15	3.95	5.17	3.00
B20	3.96	0	2.45

Since both B and Al can adopt multiple coordination numbers, their average coordination numbers are calculated from the integrated intensities corresponding to each coordination environment, as reported in Tables 3-4, 3-5 and 3-6 using the following equations.:

$$\langle n_B \rangle = \{I(^{[4]}B) \times 4\} + \{I(^{[3]}B) \times 3\} \quad \text{Eq. 3-11}$$

$$\langle n_{Al} \rangle = \{I(^{[4]}Al) \times 4\} + \{I(^{[5]}Al) \times 5\} + \{I(^{[6]}Al) \times 6\} \quad \text{Eq. 3-11}$$

$$\langle n_P \rangle = \{I(P^3) \times 3\} + \{I(P^2) \times 2\} \quad \text{Eq. 3-12}$$

Figure 3-11 compares the result of this random linkage simulation with the experimental data on homoatomic (P–O–P, B–O–B, Al–O–Al) and heteroatomic (Al–O–P, P–O–B, B–O–Al) connectivity. The results illustrate a strong chemical preference for P–O–B and Al–O–P connectivity. The concentration of P–O–P linkages is sub-statistical, and neither Al–O–Al nor Al–O–B connectivities can be detected. The experimentally detected level of B–O–B is comparable to that predicted by a statistical scenario.

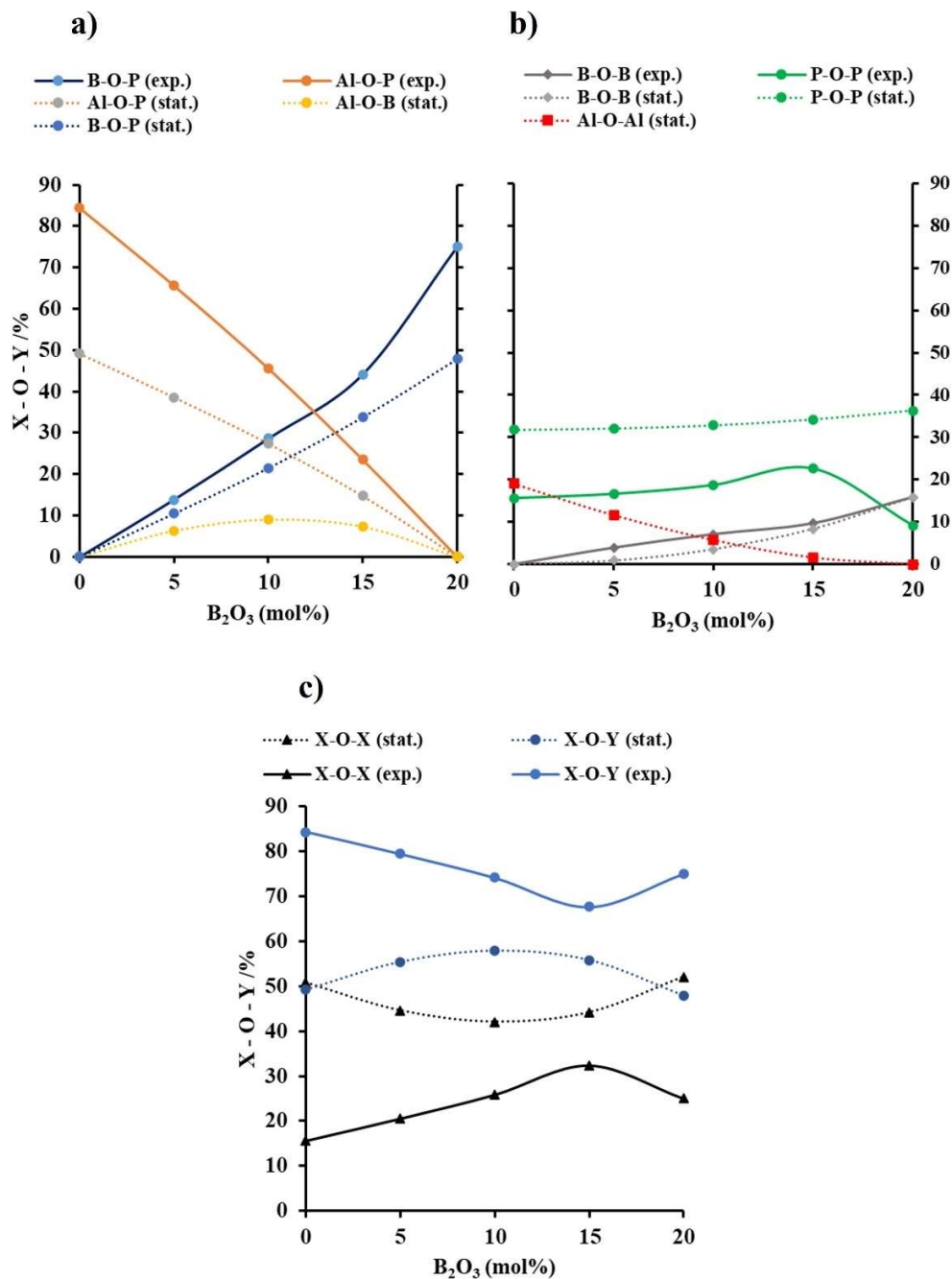


Figure 3-11) Comparison of experimental a) hetero- and b) homoatomic connectivities (solid symbols and curves) with those predicted by a statistical random linkage model (solid symbols dashed curves). c) Comparison regarding the summed homo- and heteroatomic bonds

Finally, we note that none of the connectivity parameters listed in Table 3-9 shows a non-linear composition dependence with a maximum at $x = 10$, as displayed by the trend of the glass

transition temperatures (Figure 3-1). Possible origins of that maximum may lie within some contribution due to Al–O–B linking which was not detected in our experimentation. Finally, we point out the possibility that the thermal stability is rather driven not so much by the total number of linkages, as by the number of linkages per unit volume.

This chapter demonstrates the effectiveness of double-resonance NMR in probing the medium-range order of mixed aluminoborophosphate glasses. The findings broadly support earlier results obtained using the Pauling bond strength approach, reinforcing the reliability of that model while offering direct experimental validation. Nonetheless, some discrepancies remain, particularly in the borate assignments, underscoring the complexity of these systems. Overall, the work highlights the critical role of double-resonance NMR as a powerful tool for elucidating the structural intricacies of borophosphate glasses.

4- NMR study of devitrified borophosphate glasses for tissue-regeneration

4-1- Introduction

Bioactive glasses are considered to be some of the most promising biomaterials that have enriched health science by introducing various compositions with different applications. This novel class of biomaterials emerged about 55 years ago when Professor Larry Hench responded to the need for a composition similar to bone mineral to be implanted in the body.⁵⁷ “45S5”, a phosphosilicate bioglass, is the most famous composition in the realm of bioactive glasses and has been exploited widely within the past few decades. When this type of bioactive glass is used as an implant, a hydroxyapatite (HA) layer forms on its surface, facilitating the bone repair process.

Since the early days of bioactive glasses and glass-ceramics, bioactivity has traditionally been defined and assessed by the ability of the material to form a hydroxyapatite layer upon immersion in bodily fluids or simulated body fluid. However, over the past few decades, this definition has evolved, particularly with the development of bioactive glasses for soft tissue engineering applications such as wound and burn healing. In these contexts, HA formation is no longer considered a necessary indicator of bioactivity. Instead, the ability of a material to elicit specific biological responses is now regarded as the defining feature of bioactivity for a given composition.

Applications range from treating dental hypersensitivity by adding glass particles to toothpaste¹⁶⁴ to hyperthermia cancer treatment of bone.¹⁶⁵ Recently, boron-containing glasses, including borates, borosilicates and borophosphates, have drawn researchers' attention to soft-tissue regeneration^{53,166} since these compositions show higher degradation rates in simulated body fluid (SBF) solution compared with silicate-based glasses.^{167,168} In fact, the low durability of borate-based glasses is the key factor suiting them for applications like wound healing^{35,169} or nerve repair.^{170,171} Although some scars and burns can be healed nicely by natural regenerative properties of skin, on other occasions it takes a long time for full restoration, and this delay is attached to a serious health risk for the patient, because they might be infected by bacteria.¹⁷² Hence, developing techniques and treatments through which therapeutics may be delivered

rapidly to injury sites have been scientists' concern. However, it should be noted that B and P can be toxic if released into the body too quickly.¹⁷³ This problem underlines the importance of predicting and tuning the degradation rate of the borate-based bioactive glasses for tissue engineering.

Boron was used for the first time in 1987 in the treatment of *Pseudomonas* wound infection in the form of boric acid, and was successful at the dose of 3% within 6 days without any toxic side-effects.¹⁷⁴ Later, it was shown that boron can accelerate wound healing by activating angiogenesis.¹⁷⁵ In addition, it promotes the proliferation, migration and production of vital growth factors of dermal cells.¹⁷⁶ Phosphorus also plays a pivotal role in the bioactivity of glasses and glass-ceramics. By scrutinizing the $\text{SiO}_2\text{-CaO-Na}_2\text{O-P}_2\text{O}_5$ glass series structure using solid-state NMR technique, Eden concluded that increasing the P content to 6 mol% compensates for the lack of bioactivity of the glasses with a high level of network connectivity.¹⁷⁷

Developing phase-separated bioactive glasses in form of glass-ceramics primarily has been an attempt to address the shortcomings of bioglasses, especially those of silicates, including poor thermal properties,^{178,179} high coefficient of thermal expansion,¹⁸⁰ as well as low mechanical strength.⁶⁰ A bioactive glass with these shortcomings is hard to synthesize and shape into implants for hard-tissue regeneration. Although these challenges have consumed a great deal of cost and effort, studying the correlation between the degree of crystallinity and dissolution behaviour in phase-separated borophosphate bioactive glasses has been largely neglected. In this work, “phase-separation” refers to the melt devitrification, i.e., formation of a crystalline phase that separates from the original melt during the quenching process.

In 2011, Liang et al. prepared a glass-ceramic scaffold with the composition, $25\text{Na}_2\text{O-}25\text{CaO-}5\text{P}_2\text{O}_5\text{-}45\text{B}_2\text{O}_3$ (mol%), to investigate the effect of crystalline rhenanite, NaCaPO_4 , on the in vitro bioactivity.⁶⁰ They concluded that the bioactive residual glass phase promotes rapid hydroxyapatite formation due to its high solubility in 0.25 M K_2HPO_4 solution (pH 9.0) at 37 °C, whereas the rhenanite crystalline phase, known for its osteoconductive properties, results in a slower apatite formation observed after 7 days. In another study¹⁸¹ the bioactivity and antibacterial properties of glass-ceramics in the $59.5\text{B}_2\text{O}_3\text{-}2\text{P}_2\text{O}_5\text{-}9.5\text{CaO-}19.5\text{Na}_2\text{O-}9\text{CaF}_2\text{-}$

0.5Ag₂O (mol%) system was evaluated. It was concluded that all samples exhibited strong antibacterial activity, regardless of crystallization time.

The properties of glasses are determined by their compositions and structures so that by changing the composition, the structure will be changed and, consequently, the properties will be tuned. Hence, determining the relationship between structure/composition and a specific property is of paramount importance in glass science. To the best of our knowledge, the dissolution behaviour of phase-separated borophosphate glasses has not been studied from the structural point of view using NMR spectroscopy, a powerful tool to depict the short-range order of glasses. This work aims to investigate the role of phosphorus in the dissolution behavior of CaO-Na₂O-B₂O₃-P₂O₅ glasses and phase-separated glasses in SBF solution. In this study, the effect of phase-separation on ion release and HA formation will be examined. This research may contribute to the design of biomaterials for tendon-to-bone injuries, where both soft and hard tissues are damaged.

4-2- Experimental

4-2-1- Glass synthesis

Table 4-1 shows the compositions of the samples that were synthesized by the melt-quenching technique using (NaPO₃)₆ (Fisher Scientific, analytical grade), Na₂CO₃ (Fisher Scientific, ≥ 99.8%), CaCO₃ (Baker Chemical Co., ≥ 99.9%) and boric acid as starting materials. The proper amounts of starting reagents were mixed and added to Pt/Au crucibles (3-gram batch) and were decarbonated overnight at 980 °C. Boric acid was first converted to B₂O₃ at 850°C to avoid splattering during melting. Each batch was melted at 1100°C for 30 minutes to ensure homogeneity and subsequently the bottom of the crucible was quenched in water. A 3-5% mass loss was observed after quenching, which has been attributed to volatilization of phosphorus during the melting process. Therefore, data analysis will be done based on the nominal composition with ±5% deviation. Since some samples showed phase-separation compositional analysis were not done. The resultant glass pieces were crushed using an agate mortar and pestle and sieved into two particle sizes: below 100 μm and 105-125 μm.

Table 4-1) Nominal compositions of the samples (mol%)

	P0	P1	P2	P3	P4	P5	P10
B₂O₃	55.0	54.0	53.0	52.0	51.0	50.0	45.0
P₂O₅	0.0	1.0	2.0	3.0	4.0	5.0	10.0
Na₂O	15.0	15.0	15.0	15.0	15.0	15.0	15.0
CaO	30.0	30.0	30.0	30.0	30.0	30.0	30.0

4-2-2- Dissolution experiments

SBF was prepared according to Kokubo¹⁸² as the medium for immersing the particles to determine their degradation behaviour (Table 4-2). The dissolution experiments were performed over 5 days, during which time aliquots were collected every 2 hours in the first day and every 24 hours for the remaining days. The glass particles (105-125 µm) to solution ratio was kept at 1.5 mg/mL¹⁸³ and conducted at 37 °C for five days in PET containers. The initial volume of SBF was 100 ml, and at each time point a 0.25 ml aliquot was collected. For pH measurement and aliquot collection, the bottles were removed from the oven one-by-one and processed quickly to avoid cooling them to room temperature.

Table 4-2) Ionic concentrations of SBF solution from reference [182]

Ion	Ion concentrations (mM)
Na⁺	142.0
K⁺	5.0
Mg²⁺	1.5
Ca²⁺	2.5
Cl⁻	147.8
HCO₃⁻	4.2
HPO₄²⁻	1.0
SO₄²⁻	0.5
pH	7.4

4-2-3- Solid-state NMR

NMR spectroscopy was done on a Varian ^{Unity}INOVA 600 MHz spectrometer equipped with a Chemagnetics 1.6 mm triple-resonance solid-state probe for ²³Na and ¹¹B. All samples were spun at 54.74°, with a spinning rate of 25 kHz. Bloch-decay acquisition with a pulse length of 0.4 μs was used to collect the signal. To excite sites with various quadrupolar coupling constants (C_Q) equally, a tip angle of ca. 15° was applied. The number of scans for ¹¹B and ²³Na was 1024 and 2048, respectively, while the relaxation delay (D_1) for these nuclei was set to 1 and 2 s. In order to acquire ³¹P spectra, a Bruker Avance III 500 MHz spectrometer ($B_0 = 11.7$ T) with a double-resonance 2.5 mm solid-state NMR probe was used. Acquisition parameters were as follows: 30° tip angle, 2.5 μs pulse length, 64 scans and 200 s relaxation delay. $D_1 = 5 \times T_1$, where T_1 is the relaxation time which was measured by the inversion recovery method. Chemical shift references for ²³Na, ¹¹B and ³¹P were 0.1 M NaCl (0 ppm), 0.1 M H₃BO₃ (+19.6 ppm relative to BF₃·OEt₂ (0 ppm)) and 85% H₃PO₄ (0 ppm), respectively.

The magic angle spinning (MAS) NMR spectra were deconvoluted using DMFit.⁸⁴ For spin-1/2 nuclei (i.e., ³¹P) mixed Gaussian/Lorentzian peaks were used, whereas for quadrupolar nuclei (i.e., ¹¹B and ²³Na) the Czjzek model was used in Quasar⁸⁵ and CzSimple,¹⁶⁰ respectively. In the ¹¹B MAS NMR spectra, the [⁴]B peak intensity was corrected for the underlying satellite transition by subtracting its spinning sideband from the original spectrum.

4-2-4- Scanning Electron Microscopy (SEM)

SEM images were acquired using a Quanta FEG 650 microscope (FEI, ThermoFisher, Oregon, USA) equipped with an energy-dispersive x-ray spectroscopy (EDS) system. Glass particles were mounted on the substrate and coated by carbon. Images were captured in a low-vacuum mode 120 Pa with 10 kV accelerating voltage for both secondary and backscattered electron images. A large-field detector and a concentric higher-energy electron detector was used for SE and BSE images, respectively.

4-2-5- X-ray Diffraction (XRD)

X-ray diffraction analysis was carried out using a D4 Endeavor X-ray diffractometer (Bruker, Billerica, MA, USA). Glass particles with sizes less than 100 μm were mounted on polymer diffraction plates and diffraction data were collected using Cu K_α radiation generated at a voltage

and current of 40 kV and 40 mA, respectively. Experiments were done under the following conditions: 2θ range was between 10 and 60° , step size 0.02° , acquisition time 20 s and number of scans 2000. To determine the identities of crystalline phases, the Inorganic Crystal Structure Database (ICSD) was used.

4-2-6- Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES)

ICP-OES analysis of leachates after immersing glasses in the SBF was done utilizing an Agilent 8900 triple-quad mass spectrometer equipped with a seaFAST sample introduction system. The calibration curve (1000 ppm individual standards from Inorganic Ventures) was validated with NIST1640a trace elements in natural water and TM-27 natural water from Environment and Climate Change Canada Reference Material. Aliquots were diluted by a factor of 12 by 2% HNO_3 for ICP analysis.

4-3- Results

4-3-1- Before dissolution

4-3-1-1- XRD diffractograms

Figure 4-1 shows the XRD patterns of the as-synthesized samples. Samples containing up to 2 mol% P_2O_5 are amorphous. However, P3 contains a tiny fraction of a crystalline phase, as peaks at 32° and 33° are observed. With increasing P these peaks become more intense, and another peak at 26° evolves, which are attributed to an apatite-like structure.

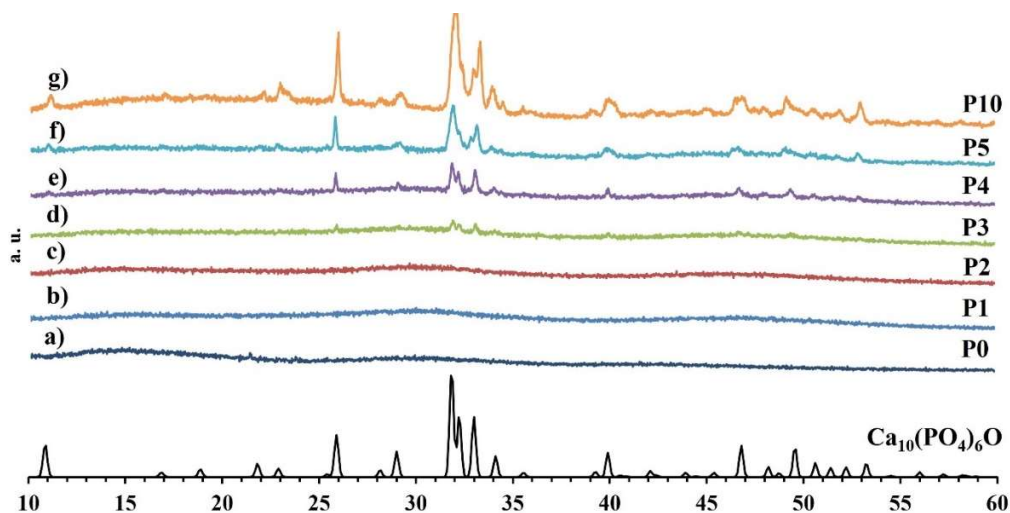


Figure 4-1) X-ray diffractograms of the as-made a) P0, b) P1, c) P2, d) P3, e) P4, f) P5, g) P10 alongside $\text{Ca}_{10}(\text{PO}_4)_6\text{O}$ from ICSD with collection code 252289

By comparing the P10 and P5 XRD spectra with ICDS database, it is most likely an oxyapatite $\text{Ca}_{10}(\text{PO}_4)_6\text{O}$ phase (collection code: 252289).

4-3-1-2- ^{11}B MAS NMR spectroscopy

^{11}B MAS NMR spectra are presented in Figure 4-2 for the as-made samples, along with extracted parameters from curve-fitting, summarized in Table 4-3. ^{11}B MAS NMR spectra of all glasses show a broad characteristic peak of three-coordinated boron, $^{[3]}\text{B}$, as well as a relatively narrow peak assigned to four-coordinated boron, $^{[4]}\text{B}$. In this series, $^{[3]}\text{B}$ were fitted using two species and are labeled 1- BO_3 and 2- BO_3 . The broader NMR lineshape for $^{[3]}\text{B}$ arises due to significant quadrupolar interactions caused by its trigonal planar sites. Conversely, $^{[4]}\text{B}$ exhibits a narrow lineshape due to weaker quadrupolar interactions from the tetrahedral sites. For P0 to P5, δ_{iso} for $^{[3]}\text{B}$ units are at ca. +18 and +15 ppm, while the $^{[4]}\text{B}$ signal resonates at ca. +1.0 ppm. Replacing boron by phosphorus induces a subtle change in δ_{iso} in glasses P0 to P5; however, its shift to lower frequency is more pronounced in P10. Similar behaviour is observed for three-coordinated boron species. The fraction of boron presents as $^{[4]}\text{B}$, labeled N_4 in Table 4-3, in these series shows a constant value, 41 ± 1 , for P0 to P5. However, incorporating 10 mol % P_2O_5 results in a ca. 24% decrease in the $^{[4]}\text{B}$ fraction. It should be noted that two species were used to fit $^{[3]}\text{B}$ to obtain the N_4 value. Because the isotropic chemical shifts of $^{[3]}\text{B}$ units are overlapped the precision of their integrated intensities is low. Hence the overall integral intensities are used for calculating N_4 values.

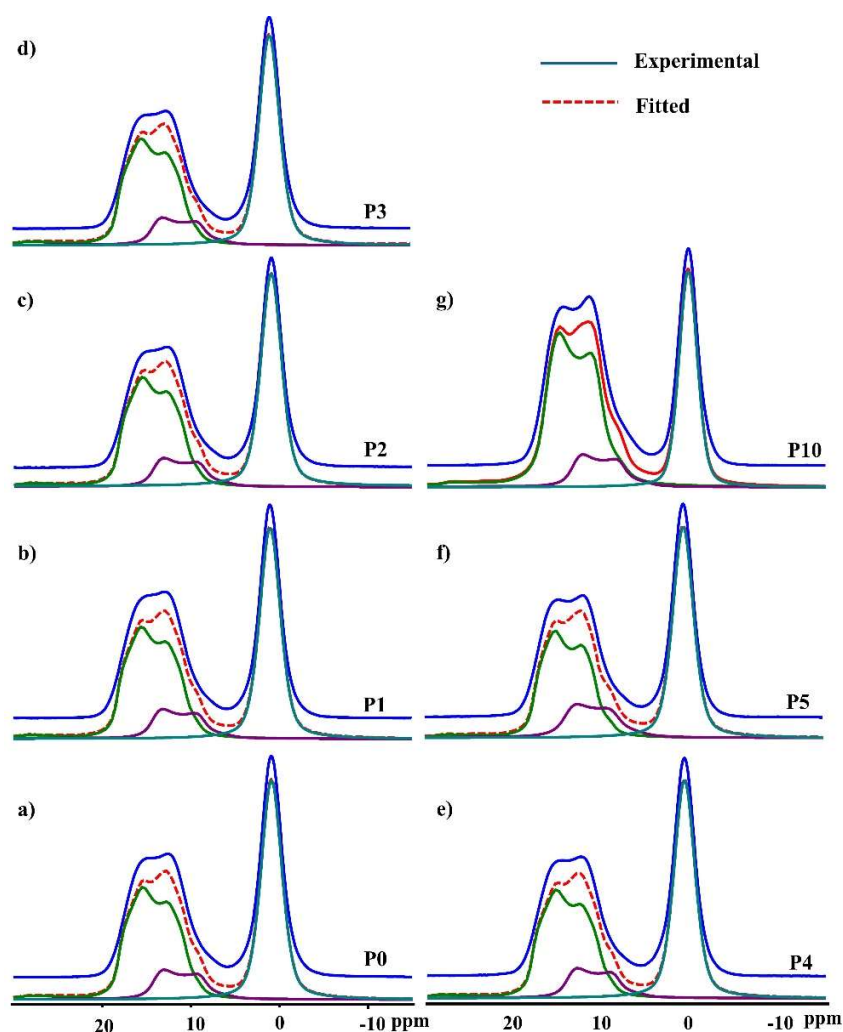


Figure 4-2) ^{11}B magic angle spinning (MAS) NMR spectra of as-made a) P0, b) P1, c) P2, d) P3, e) P4, f) P5 and g) P10. 1-BO_3 , 2-BO_3 , $^{[4]}\text{B}_{\text{OP}}$ (in P0-P5), $^{[4]}\text{B}_{\text{IP}}$ (in P10)

4-3-1-3- ^{31}P MAS NMR spectroscopy

Figure 4-3 shows the ^{31}P MAS NMR spectra of as-synthesized samples. The fitting parameters including isotropic chemical shift, peak width and integrated intensity are summarized in Table 4-4. P1 and P2 shows a weak broad signal resonating at ca. +3.8 ppm. This signal is assigned to P_{OB}^1 , i.e., a phosphate unit with one P–O–P linkage and three NBOs.^{99,129,184} P3 shows a slightly narrower peak at +3.0 ppm superimposed on a hump; the former represents a crystalline phase, and the latter is characteristic of phosphorus in a glassy phase. The intensity of the sharp peak at +3.0 ppm becomes dominant as the phosphorus content increases. By incorporating 10 mol % P_2O_5 in the sample, a new peak at -11.5 ppm emerges which is assigned to P_{IB}^2 , a phosphate unit containing one B–O–P, one P–O–P and two NBOs.^{129,184} The integral intensity of the crystalline

phase in P3 is 21 % and reaches a maximum of 62 % in P4. By incorporating more P_2O_5 into the samples this value slightly drops to 57 ± 3 % and remains the same up to 10 mol % P_2O_5 .

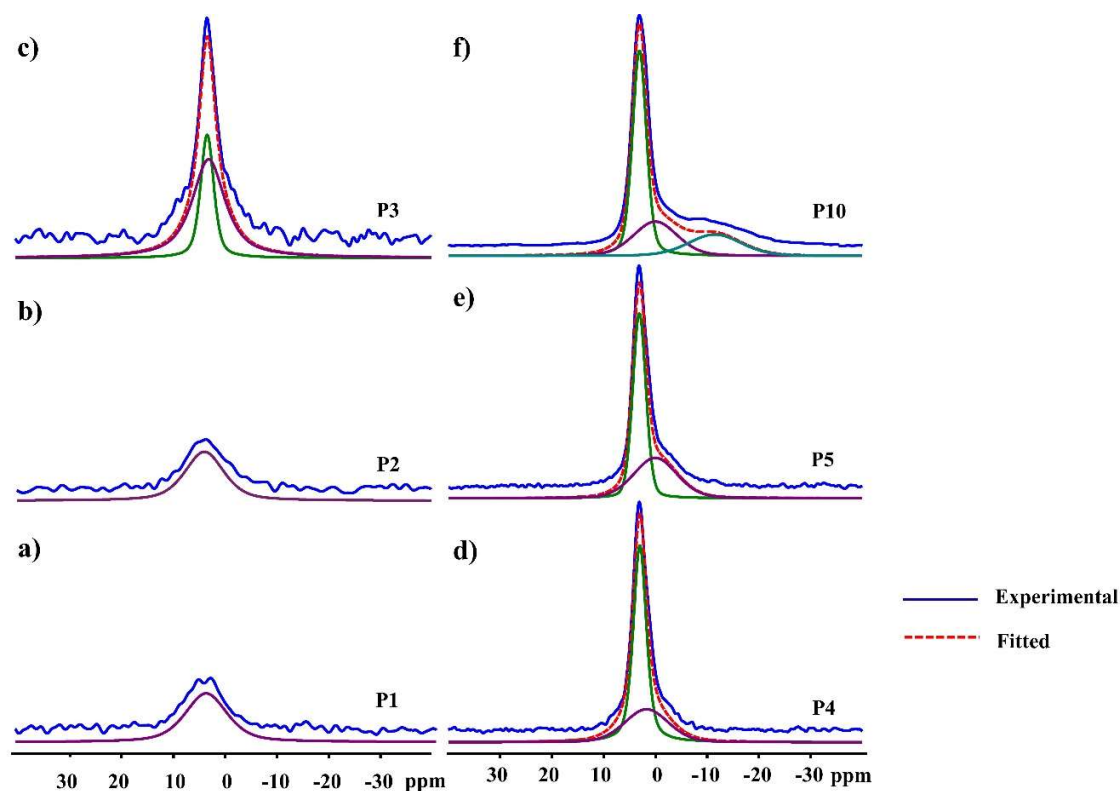


Figure 4-3) ^{31}P magic angle spinning (MAS) NMR spectra of as-made a) P1, b) P2, c) P3, d) P4, e) P5, and f) P10. P_C^0 , P_{OB}^1 , P_{1B}^2

4-3-1-4- ^{23}Na MAS and TQMAS NMR spectroscopy

Figure 4-5 depicts ^{23}Na MAS NMR spectra of the samples. All spectra show a broad signal with a peak maximum at ca. -9.0 ppm. All broad spectra suggest a wide distribution of the quadrupolar interactions in the glass. The average C_Q for all samples is ca. 2.8 MHz. Compared with other samples, P10 shows an unusual broadening at the top part of the spectrum which implies that the spectrum is composed of more than one component. The presence of two signals may be interpreted as sodium in distinctly different chemical environments, possibly crystalline and glassy environments.

Table 4-3) Parameters used for fitting ^{11}B magic angle spinning (MAS) NMR spectra.

	^{13}B								^{14}B						
	1-BO_3				2-BO_3				$^{14}\text{B}_{0\text{P}}$			$^{14}\text{B}_{1\text{P}}$			
	δ_{iso} (ppm)	C_Q (MHz)	η ± 0.1	Int. (%) ± 2	δ_{iso} (ppm)	C_Q (MHz)	H	Int. (%) ± 2	δ_{iso} (ppm)	W (kHz)	Int. (%) ± 2	δ_{iso} (ppm)	W (kHz)	Int. (%) ± 2	N_4
P0	+18.3	2.40	0.6	45	+15.1	2.40	0.2	13	+0.9	0.50	42	-	-	-	0.42
P1	+18.4	2.40	0.6	45	+15.2	2.40	0.2	14	+1.0	0.50	41	-	-	-	0.41
P2	+18.3	2.40	0.6	45	+15.1	2.40	0.2	13	+0.9	0.50	42	-	-	-	0.42
P3	+18.3	2.40	0.6	45	+15.1	2.40	0.2	13	+0.9	0.50	42	-	-	-	0.42
P4	+18.3	2.40	0.6	44	+15.1	2.40	0.2	14	+0.9	0.50	42	-	-	-	0.42
P5	+17.9	2.40	0.5	41	+15.0	2.40	0.2	18	+0.8	0.50	41	-	-	-	0.41
P10	+17.4	2.40	0.3	58	+14.5	2.40	0.2	12	-	-	-	+0.5	0.47	32	0.32

Fixed parameters: δ_{iso} : isotropic chemical shift with a tolerance of ± 0.5 and ± 0.1 ppm for BO_3 and ^{14}B species, respectively. C_Q : quadrupolar coupling constant with a tolerance of ± 0.15 MHz, η : asymmetry parameter with a tolerance of ± 0.1 , W: Full Width at Half Maximum (peak width) with a tolerance of ± 0.03 kHz

Fitted parameter: Int: Integrated intensity

Table 4-4) Parameters used for fitting ^{31}P magic angle spinning (MAS) NMR spectra.

	P_C^0			$\text{P}_{0\text{B}}^1$			$\text{P}_{1\text{B}}^2$		
	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)
P1	-	-	-	+3.9	1.80	100	-	-	-
P2	-	-	-	+3.8	1.80	100	-	-	-
P3	+3.0	0.60	32	+2.8	1.50	68	-	-	-
P4	+3.0	0.60	62	+1.7	2.00	38	-	-	-
P5	+3.1	0.60	57	0.0	2.00	43	-	-	-
P10	+3.1	0.60	54	0.0	2.00	27	-11.5	2.40	19

Fixed parameters: δ_{iso} : Isotropic chemical shift with a tolerance of ± 0.2 ppm, W: Full Width at Half Maximum (Peak width) with a tolerance of ± 0.05 kHz

Fitted parameter: Int: Integrated intensity $\pm 2\%$

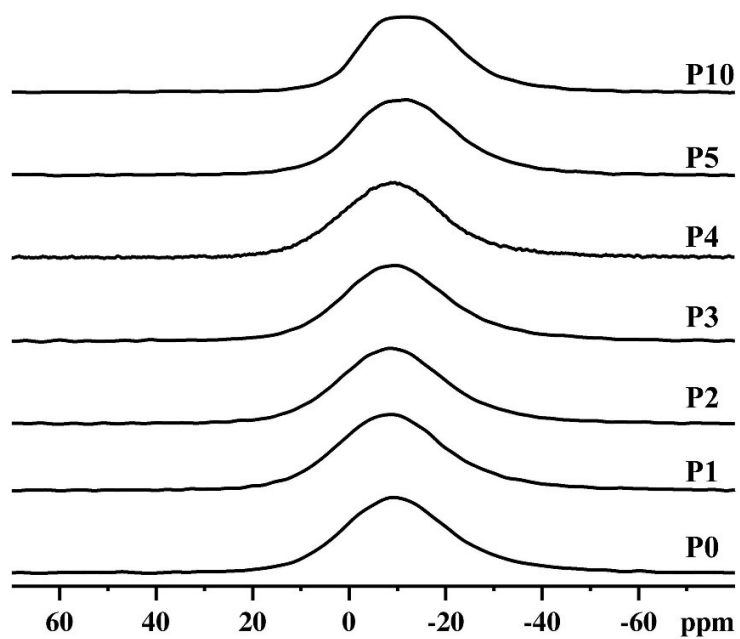


Figure 4-4) ^{23}Na magic angle spinning (MAS) NMR spectra of the as-made samples

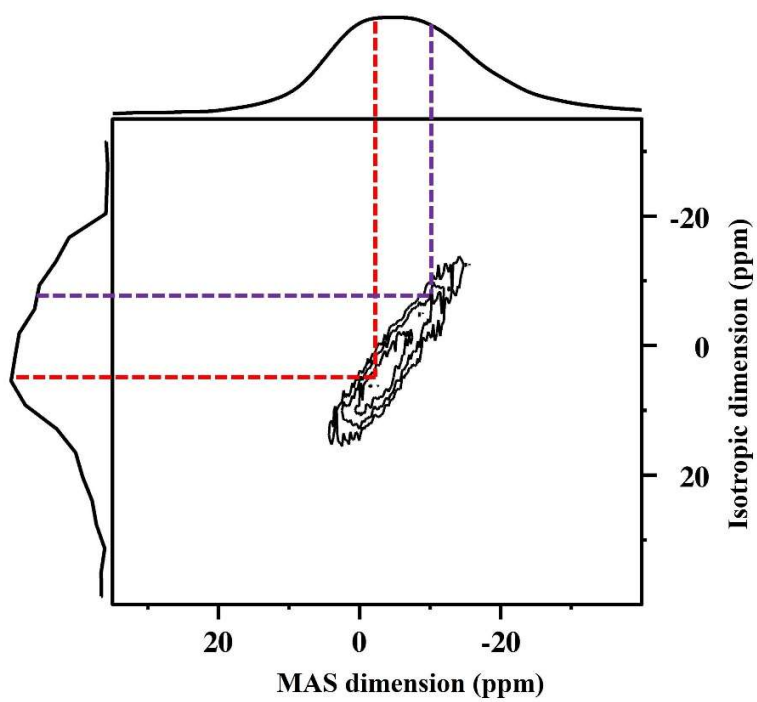


Figure 4-5) ^{23}Na triple quantum magic angle spinning (TQMAS) NMR spectrum for P10

Figure 4-5 shows the ^{23}Na TQMAS NMR for P10. The isotropic dimension indicates that sodium occupies two distinct chemical environments. In an TQMAS experiment, the excitation efficiency depends on the quadrupolar parameter, $P_Q (=C_Q\sqrt{1 + \frac{\eta^2}{3}})$. Consequently, comparing integrated signal intensities of species with different P_Q values may not yield reliable results.

Table 4-5) ^{23}Na magic angle spinning (MAS) NMR parameters for samples before and after dissolution experiments

	Before dissolution		After dissolution	
	δ_{iso} (ppm)	$\langle C_Q \rangle$ (MHz)	δ_{iso} (ppm)	$\langle C_Q \rangle$ (MHz)
P0	-2.0	2.80	+0.5	3.10
P1	-1.5	2.70	+0.5	3.00
P2	-1.5	2.70	+0.5	2.90
P3	-1.5	2.80	-0.5	2.00
P4	-2.0	2.80	-1.0	2.00
P5	-4.0	2.80	-1.5	1.90
P10	See Figure 4-5		-1.2	1.80
Fixed parameters: C_Q with a tolerance of ± 0.05 MHz, δ_{iso} with a tolerance of ± 0.1 ppm, Fitted parameter: Intensity $\pm 1\%$				

4-3-1-5- SEM & EDS

Backscattered-electron (BSE) mode images of P2, P5 and P10 along with EDS analysis are shown in Figure 4-6. P2 lacks crystalline phases since no bright area can be detected using SEM, whereas the P5 and P10 images confirm phase separation in samples with higher amount of phosphate, which are consistent with XRD results. By comparing the EDS spectra for P2 and P5, spot 1 indicates a phase rich in Na-Ca-P, with a similar intensity, but spot 2 is mainly a calcium phosphate phase with a minor amount of sodium. In P10, spot 2 shows the same EDS spectra as P5 however there is a significant difference between spot 1 in P10 and other samples. The Al signal observed in the EDS spectra is attributed to background from the aluminum sample holder. It should be noted that boron is not easily detected by EDS and does not appear in this dataset.

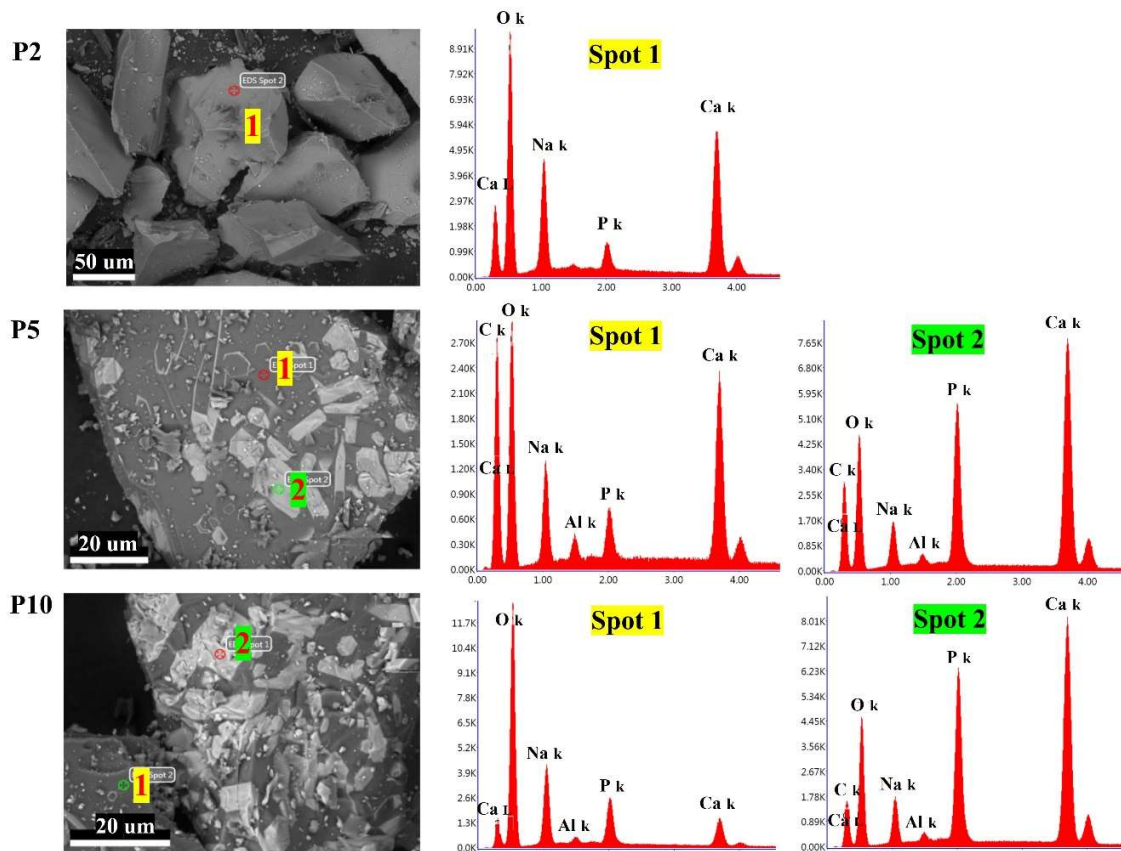


Figure 4-6) Scanning electron Microscope (SEM) images of the as-made samples along with energy dispersive X-ray spectroscopy (EDS) analysis

4-3-2- After dissolution

4-3-2-1- XRD diffractograms

After immersing samples in SBF for five days, the washed and dried leftover material was collected to be examined using XRD. As it can be seen in Figure 4-7, all samples except for P0 show the presence of crystalline phases which are well-crystallized in P3-P10 and poorly crystallized in P1 and P2. Direct comparison between XRD profiles of the samples before and after dissolution shows that samples with a higher amount of phosphorus show more crystallinity, as the peaks become more intense. Determining the exact composition for the newly formed crystalline phase is challenging; however, the peak positions of the diffractograms suggest that a hydroxyapatite phase, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ (collection code: 97849), has formed after immersing samples in SBF solution.

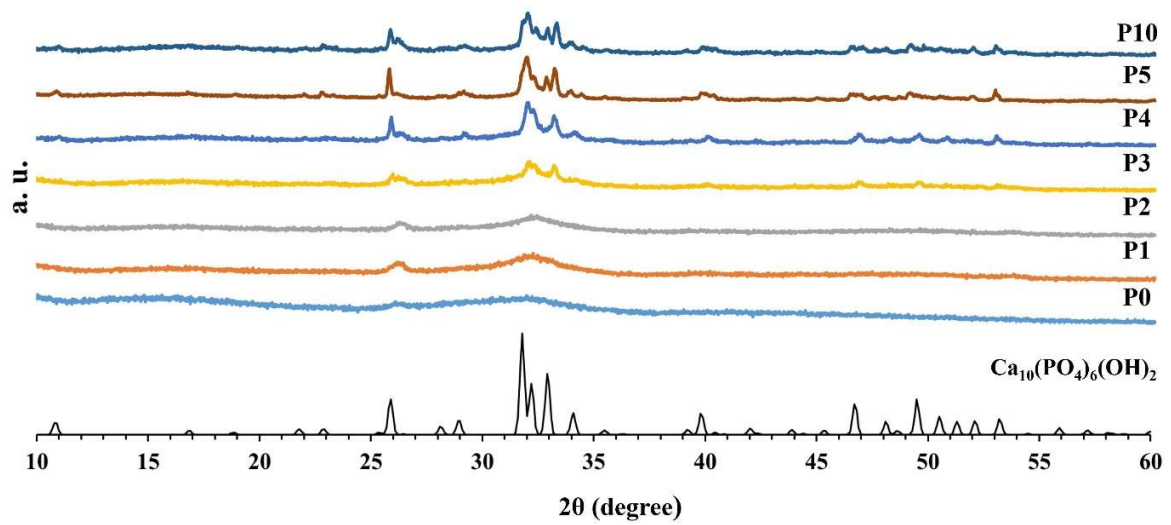


Figure 4-7) X-ray diffractograms of the simulated body fluid (SBF)-treated samples

4-3-2-2- ^{11}B MAS NMR spectroscopy

^{11}B MAS NMR of the glasses after dissolution (Figure 4-8) shows that all glasses are constructed by $^{[4]}\text{B}$ and $^{[3]}\text{B}$ species, however the intensity of P5 and P10 is very low compared with the rest of the glasses (Figure 4-9), which implies a higher degradation rate. After dissolving samples in SBF, δ_{iso} for $^{[4]}\text{B}$ is at +1.0 ppm which is the same as pre-dissolution results. N_4 values are reported in Figure 4-8.

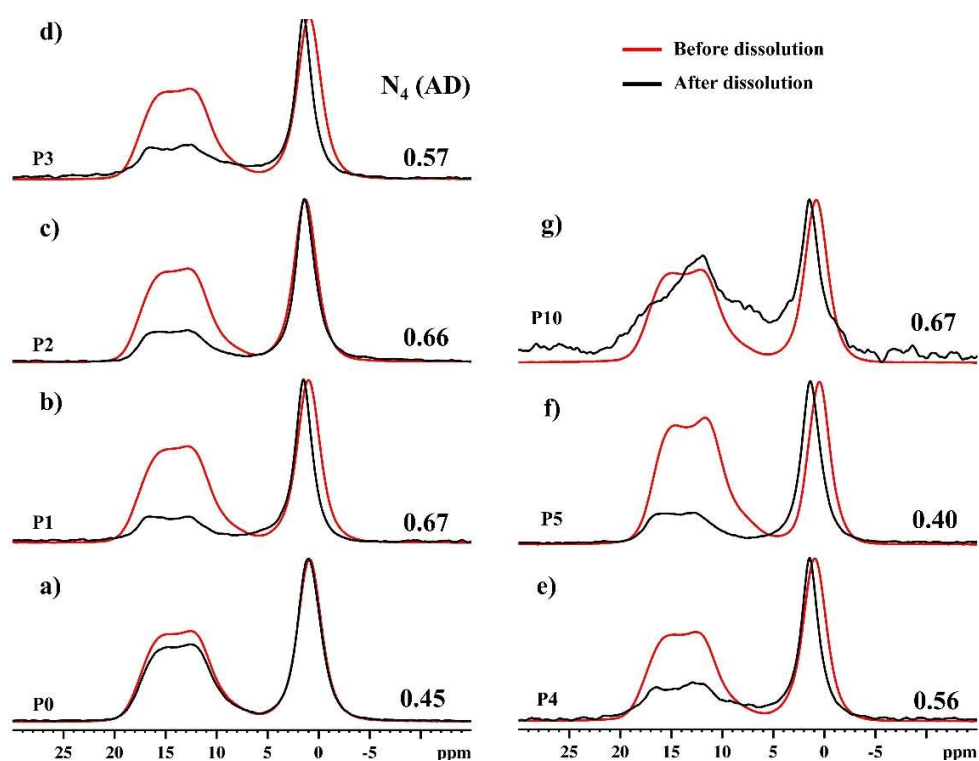


Figure 4-8) ^{11}B magic angle spinning (MAS) NMR spectra of a) P0, b) P1, c) P2, d) P3, e) P4, f) P5 and P10 before and after dissolution. The fraction of four-coordinated boron, N_4 values, for post dissolution experiments are reported

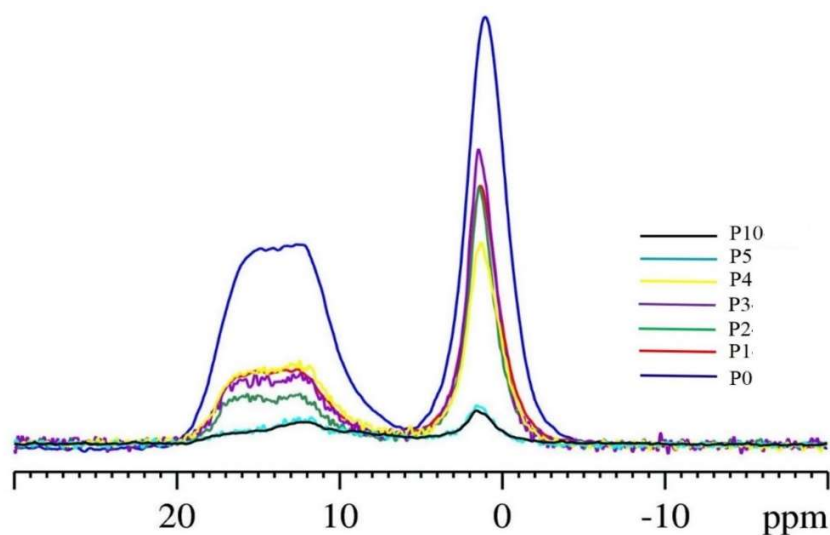


Figure 4-9) ^{11}B magic angle spinning (MAS) NMR spectra of the simulated body fluid (SBF)-treated samples (scaled based on the weight of the samples)

4-3-2-3- ^{31}P MAS NMR spectroscopy

Figure 4-10 shows the ^{31}P MAS NMR spectra of all samples after immersion in SBF solution. P0 is composed of two signals: a narrow peak at +3.1 ppm superimposed on a broad peak centered at +2.7 ppm. The latter is attributed to an amorphous calcium phosphate phase, ACP, and the former is assigned to reprecipitated hydroxyapatite.^{185,186} P1-P10 also have a broad and a narrow peak which are attributed to a glassy and crystalline HA/OAp/ACP phase, respectively. The intensity of the narrow peak in these samples is $71 \pm 4\%$. Due to significant overlap in their isotropic chemical shifts, the HA/OAp/ACP phases in these samples are not quantitatively analyzed. By comparing the ^{31}P MAS NMR spectra of P10 before and after dissolution (Figure 4-11) one may notice that the $\text{P}_{1\text{B}}^2$ signal observed in the before dissolution (BD) spectrum is not observed in the after dissolution (AD) spectrum.

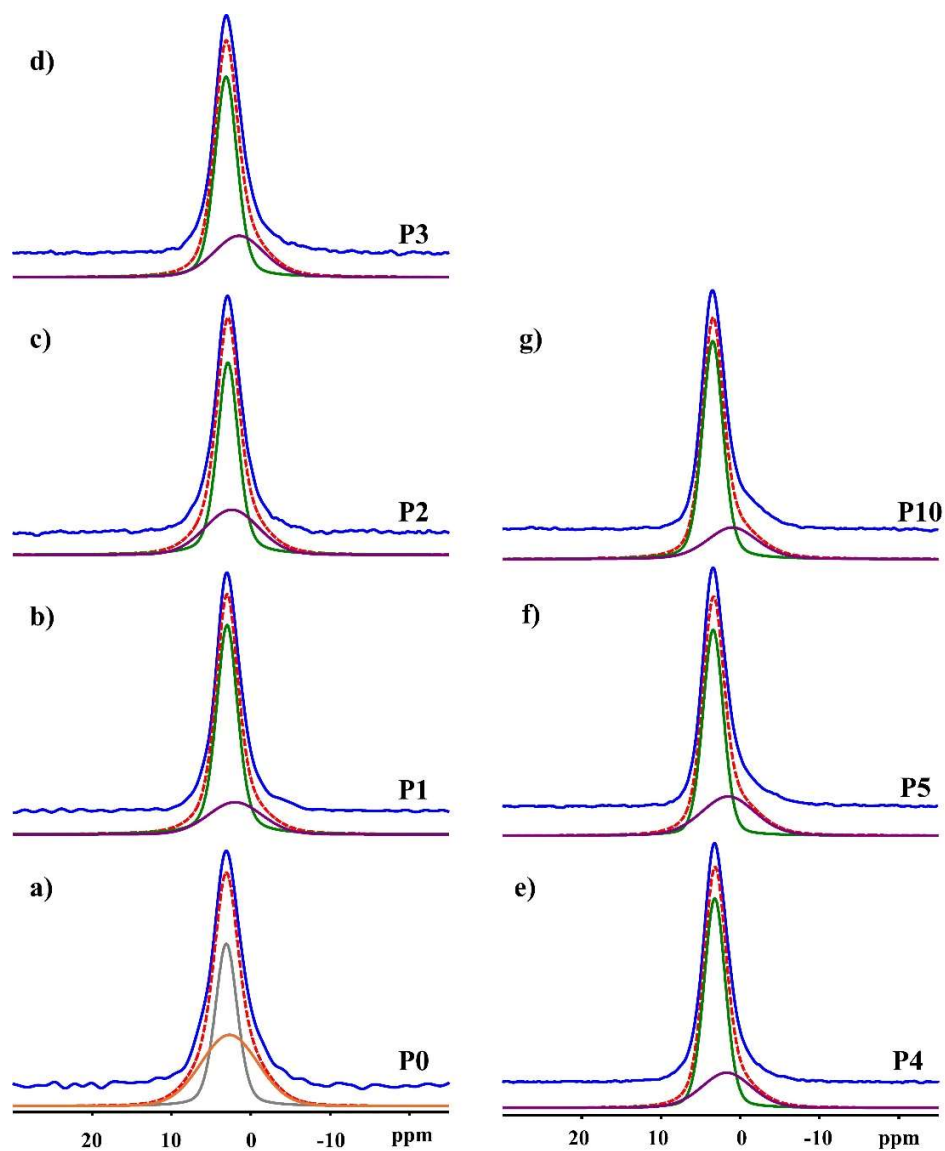


Figure 4-10) ^{31}P magic angle spinning (MAS) NMR spectra of a) P0, b) P1, c) P2, d) P3, e) P4, f) P5 and g) P10 after 5 days dissolution experiments. In P0: ACP=amorphous calcium phosphate, HA=hydroxyapatite, in P1-P10: HA/ ACP/OAp =oxyapatite, P_{OB}^1

Table 4-6) ^{31}P magic angle spinning (MAS) NMR parameters used for fitting spectra after dissolution experiments

ACP				HA		
	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)
P0	+2.7	1.72	50	+3.1	0.66	50
P_{0B}¹				HA/OAp/ACP		
P1	+2.0	1.60	27	+3.0	0.64	73
P2	+2.2	1.60	34	+2.9	0.64	66
P3	+1.5	1.50	30	+3.1	0.65	70
P4	+1.7	1.50	28	+3.2	0.64	72
P5	+1.5	1.60	33	+3.4	0.61	67
P10	+1.0	1.50	25	+3.4	0.62	75

Fixed parameters: δ_{iso} : Isotropic chemical shift with a tolerance of ± 0.2 ppm, W: Full Width at Half Maximum (Peak width) with a tolerance of ± 0.05 kHz

Fitted parameter: Int: Integrated intensity $\pm 2\%$

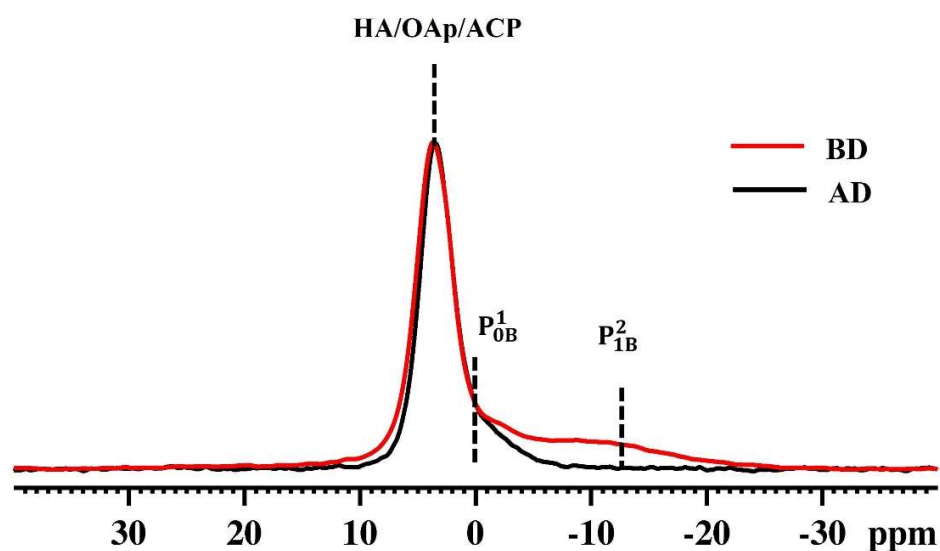


Figure 4-11) Comparison between ^{31}P magic angle spinning (MAS) NMR spectra before (BD) and after (AD) dissolution experiment for P10. HA=hydroxyapatite, OAp =oxyapatite, ACP=amorphous calcium phosphate

4-3-2-4- ^{23}Na MAS NMR spectroscopy

Post-dissolution ^{23}Na MAS NMR spectra are shown in Figure 4-12. Crystalline phase-free samples, P0-P2, show a broad peak with average chemical shifts at +0.5 ppm. The average C_Q values 2.9 ± 0.1 suggest the distribution of the sodium in a glassy phase for these samples. P3-P10 resonate at lower frequencies and have significantly lower C_Q than those of P0-P2.

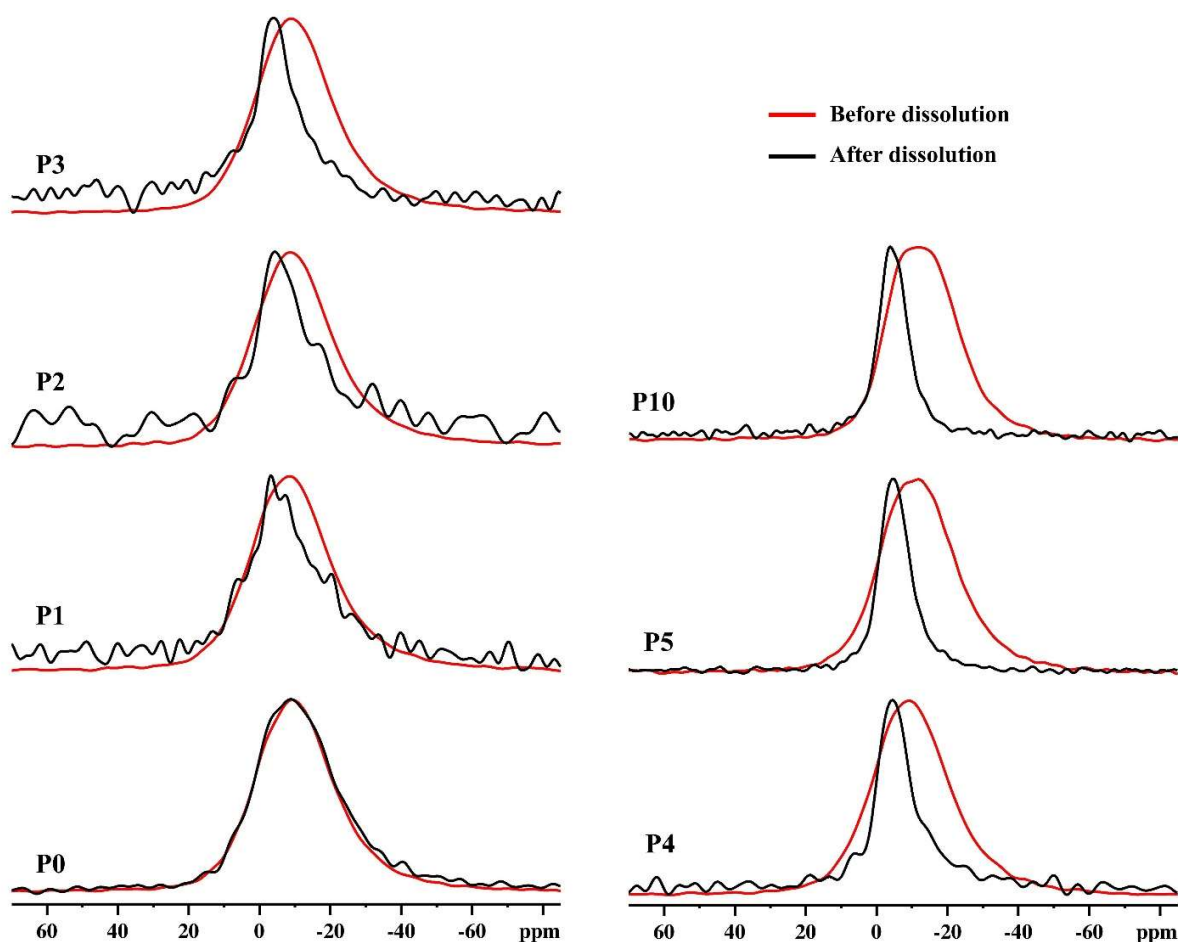


Figure 4-12) ^{23}Na magic angle spinning (MAS) NMR spectra (absolute intensities) before (red) and after (black) dissolution experiments.

4-3-2-5- ^1H MAS NMR spectroscopy

Figure 4-13 shows the ^1H MAS NMR spectra of P10 before and after dissolution. Figure 4-13a shows that the sample does not contain hydrogen in its as-made form. It should be noted that

since the rotor and stator contain hydrogen and show up as background signals, the ^1H MAS NMR for empty rotors with the same conditions as the filled rotors was measured for both before and after dissolution samples. In the SBF-treated sample, Figure 4-13b, signals at +1.1 and +0.6 ppm come from the background and +3.1 ppm is attributed to ethanol which comes from washing the leftover solids at the end of dissolution experiment. After dissolution the remaining P10 solids have signals at -0.2 and +5 ppm which are attributed to hydroxyapatite and adsorbed surface water.¹⁸⁵

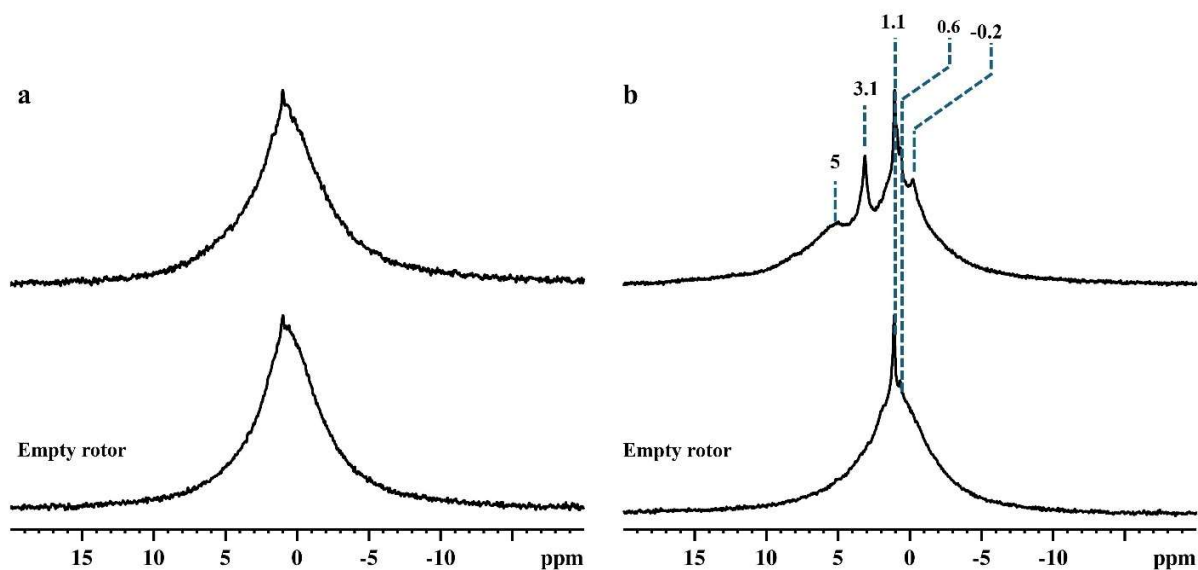


Figure 4-13) ^1H magic angle spinning (MAS) NMR spectra of P10, a) before and b) after dissolution.

4-3-2-6- SEM and EDS

SEM images of the solids remaining after a dissolution trial in SBF at two magnifications for P0, P5 and P10 are shown in Figure 4-14. By comparing the semi-spherical shapes observed before dissolution (Figure 4-6) with the irregularly shaped solids collected after dissolution (500 μm), it is readily observed that glass particles are almost all dissolved after five days. In the SEM image of P2 with higher magnifications a new morphology is observed. Reprecipitation with a spherical shape is attributed to the formation of HA. In P10, the formation of well-formed crystallites is seen in the image with higher magnification. The EDS analysis for all samples confirms that the newly formed crystals consist of calcium and phosphate, which is in line with XRD results.

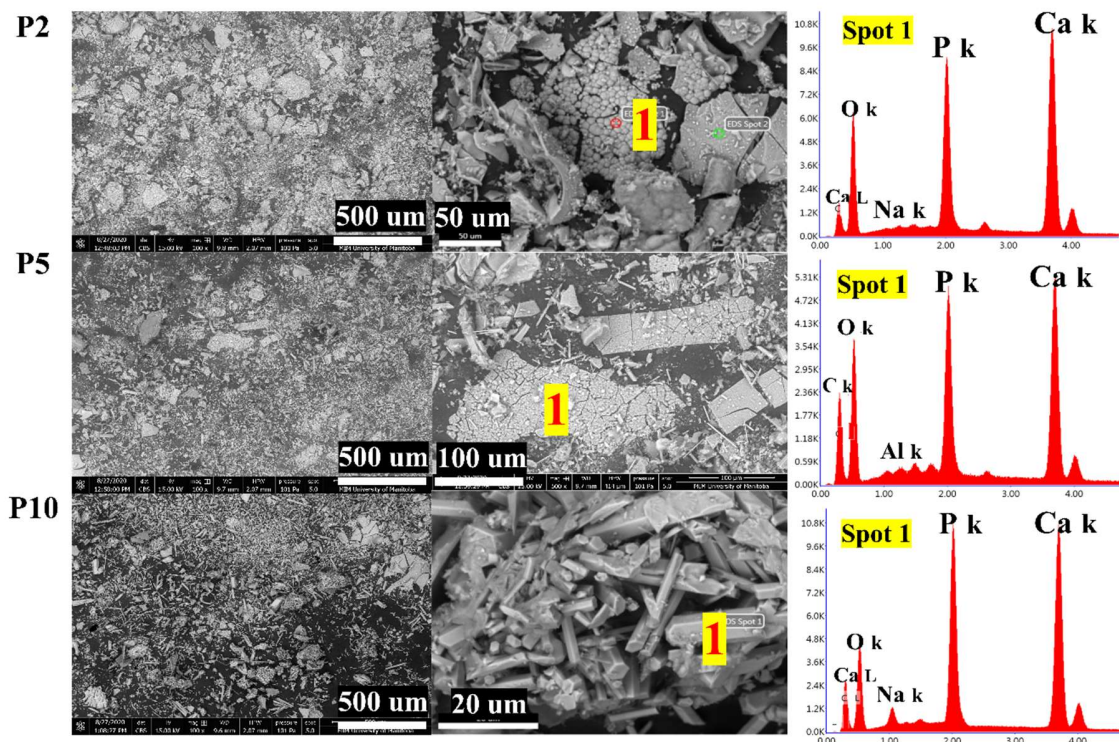


Figure 4-14) Scanning electron microscope (SEM) images of the samples after immersing in simulated body fluid (SBF) for 120 hr alongside energy dispersive x-ray spectroscopy (EDS). For each sample two magnifications are shown.

4-3-2-7- ICP-OES and pH measurements

The pH changes of the SBF solution as a function of time are plotted in Figure 4-15. The behaviour of P0 to P4 is very similar: the pH increases rapidly to 7.3-7.5 within 10 hours, afterward steadily rising to 7.8-8.1 by the end of the dissolution study. P5 and P10 exhibit different behaviour. The pH of the P5 does not change considerably after 10 hours, however, after 35 hours, it reaches 7.4 and plateaus, while P10 shows changes within the error (0.1) during the dissolution study.

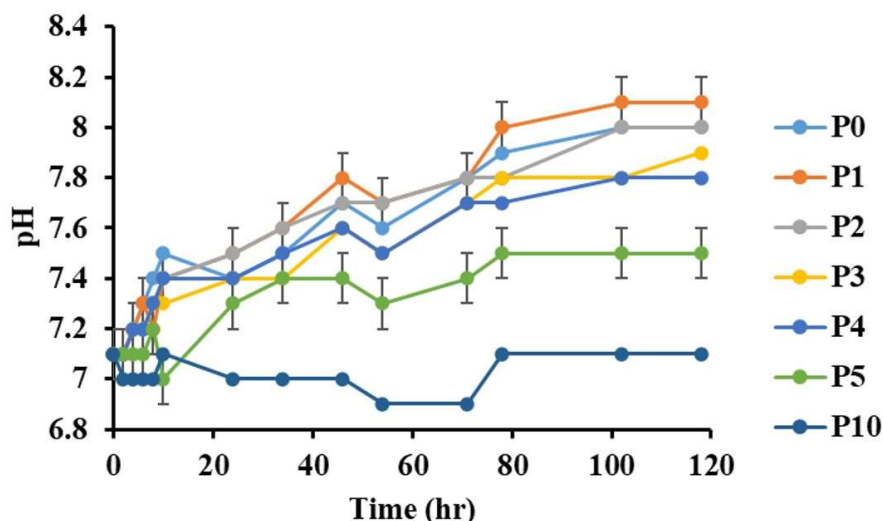


Figure 4-15) Changes in the pH of the simulated body fluid (SBF) solution during dissolution study

The phosphorus, boron and calcium elemental release into solution of P0, P5 and P10 are plotted in Figure 4-16, with P0 representing P0-P4, which displayed similar behaviour. The boron dissolution profile reveals that all glasses dissolve steadily over the experiment duration. P0 and P5 reach a plateau only after 58 and 34 hours, respectively. The ICP profile of P10 clearly indicates that this sample dissolves rapidly after only two hours, after which it levels off.

P0-P4 release calcium continuously during the dissolution period. P5 exhibits a steady increase within the first 60 hours; after that a plateau reaches up to the end of the experiment. P10 shows no considerable changes within 35 hours, while after that, it starts to take up Ca from the solution as time zero shows the content of the element *i* in the pristine SBF solution.

The P release data show that P0-P5 absorb phosphorus from the solution. P10 follows a different behaviour; it releases phosphorus abruptly into the solution followed by absorbing P from the medium after 35 hours.

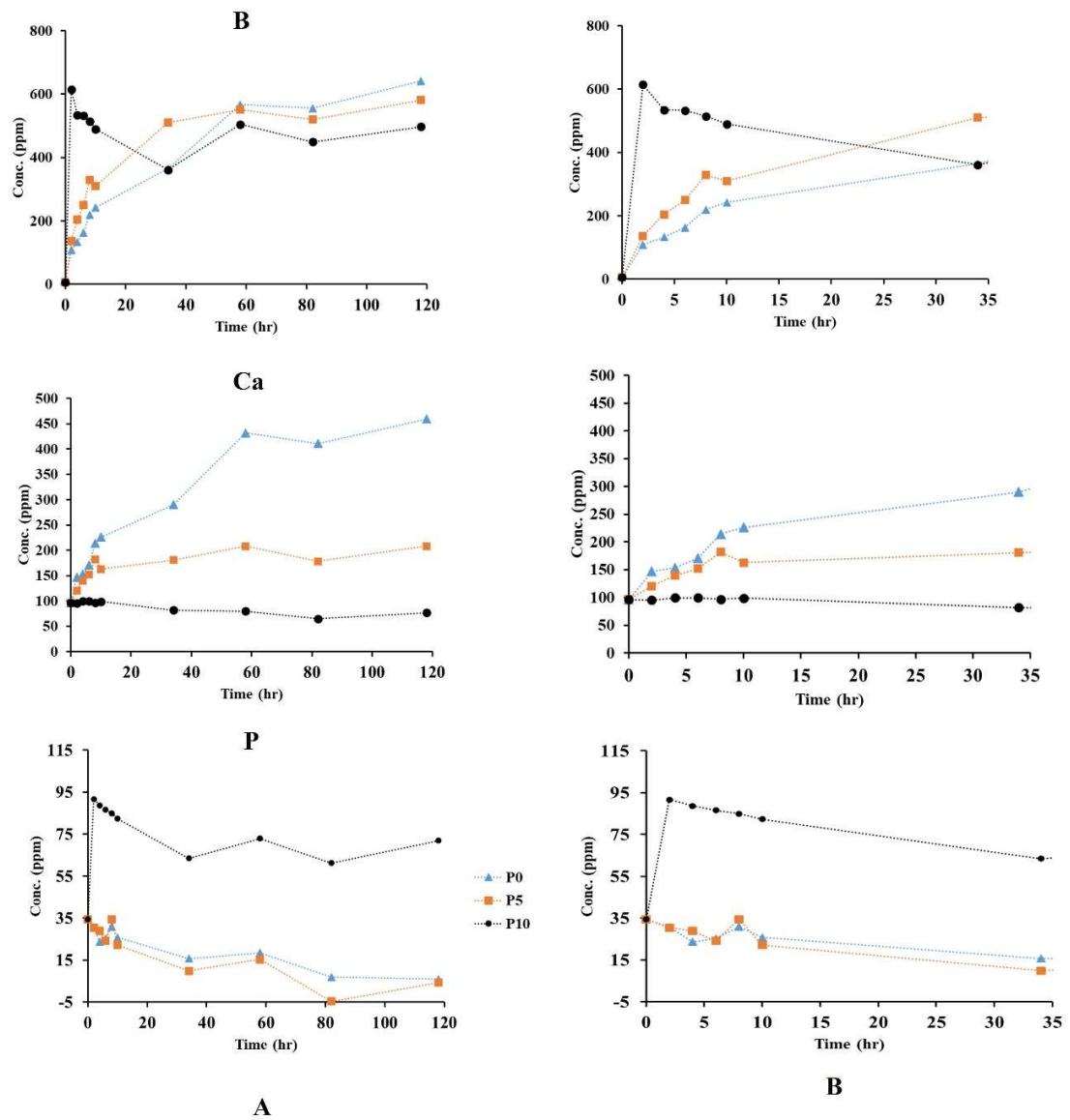


Figure 4-16) Column A) Inductively coupled plasma (ICP-OES) elemental profile of the boron, calcium and phosphorus (time 0 shows the simulated body fluid SBF signal) for the entire experiment. Column B) shows the first 35 hours of the experiments.

4-4- Discussion

4-4-1- Calculating the composition of the glassy and crystalline phases

The current work deals with pure (P0-P2) and phase-separated glasses (P3-P10). The formation of Ca- and P-rich crystallites embedded in a glassy matrix was observed SEM images and EDS spectra (Figure 4-14). X-ray diffractograms confirm that this compound is an apatite-like phase, oxyapatite, a calcium-phosphate phase which has the similar composition to bones and teeth minerals. The structure of the oxyapatite is a controversial topic in the literature. Elliott¹⁸⁷ showed that OAp retains the structure of HA, with a hexagonal crystal structure and the $P6_3/m$ space group. However, several publications have reported the structure of OAp as hexagonal with $P\bar{6}$ space group.^{188–190} ^{31}P MAS NMR spectra of P3 to P10 show a narrow peak resonating at +3.0 ppm, which most likely originates from OAp with a crystal structure similar to that of HA. The ^1H MAS NMR spectrum of P10 before dissolution does not show any signal, which indicates that there is no H in this crystalline phase. In an amorphous phase, the broadening observed in the ^{23}Na NMR spectrum arises from second-order quadrupolar interactions—evident as a tail on the right-hand side of the spectrum—as well as from distributions in δ_{iso} .¹⁹¹ The ^{23}Na MAS NMR spectra of P3 to P5 samples lack sharp peaks, as a sign of sodium in a crystalline phase, which means the apatite-like compound contains only Ca and P cations. Considering the results from SEM, XRD and NMR it is concluded that the crystalline compound formed in the phase-separated samples is oxyapatite, $\text{Ca}_{10}(\text{PO}_4)_6\text{O}$ (collection code: 252289). Although this compound is reported as an unstable phase it is likely to be formed at high temperature during melting samples and stabilized by quenching the crucible in the water. It should be noted that unambiguous attribution of this phase to one specific apatite composition may not be possible because the structure of apatite allows for a broad range of compositional variations that can accommodate various atoms in its structure.¹⁹²

In order to discuss the relationship between the structure of glasses and their compositions, it is necessary to estimate the composition of the residual glassy phase in P3–P10, where crystallization occurs in the as-made materials. This calculation can be done by considering the integral intensity of the crystalline signal observed in ^{31}P MAS NMR spectra and taking into account that the composition of the crystalline phase is $\text{Ca}_{10}(\text{PO}_4)_6\text{O}$. For example, the integral intensity of the crystalline phase in ^{31}P MAS NMR in P3 is 32% (Figure 4-3). From the

composition of the sample, it has 3 mol% P₂O₅ (6 mol % P). Therefore $0.32 \times 6 \approx 2$ P belongs to the crystalline phase. From the composition, Ca₁₀(PO₄)₆O, the P:Ca ratio is 6:10 which means that ca. 3 mol % Ca (= CaO) goes to the crystalline phase. By subtracting these amounts from the nominal composition of P3, the composition of the glassy phase may be estimated. ²³Na TQMAS NMR shows that some sodium in P10 enters oxyapatite phase. Using the isotropic chemical shifts of the glassy and crystalline components from the isotropic dimension in Figure 4-5, the MAS spectrum of P10 was fitted under the assumption of identical C_Q values. Based on this fitting, 2.25 mol% of Na₂O is incorporated into the crystalline phase (15% int. intensity $\times$ 15 mol% Na₂O in P10 = 2.25 mol%). Table 4-7 summarizes the calculation for P3 to P10. The number in parentheses shows the composition of the glassy phase scaled to 100%. These values will be used to discuss the relationship between the composition and the structure of the glass, including N₄, dissolution behaviour and network connectivity.

Table 4-7) Composition of oxyapatite (OAp) and residual glassy phase (G) in phase-separated samples (mol%)

	P3		P4		P5		P10	
Integrated intensity from ³¹ P MAS NMR	OAp 32%	G 68%	OAp 62%	G 38%	OAp 57%	G 43%	OAp 54%	G 46%
B ₂ O ₃	-	52 (54) ^a	-	51 (57)	-	50 (57)	-	45 (61)
P ₂ O ₅	1	2 (2)	2	2 (2)	3	2 (2)	5	5 (6)
CaO	3	27 (28)	8	22 (24)	10	20 (23)	18.0	12 (16)
Na ₂ O	-	15 (16)	-	15 (17)	-	15 (17)	-	13 (17)

^a values in parentheses show the percentage of the glassy phase scaled to 100%

4-4-2- Structure of the as-made samples

In silicate glasses the introduction of alkali and alkaline-earth cations into the glass structure results in breaking Si–O–Si linkages and generating NBOs.^{193,194} However, incorporating alkali and alkaline-earth cations into borate glasses changes the glass structure in a different way. It is well established that the addition of network modifiers to a borate glass initially results in the conversion of [³]B to [⁴]B units and an increased degree of connectivity of the glass structure.¹⁹⁵ With further addition of these cations to a borate glass, the BO in [³]B is replaced by NBO. The

degree of $^{[3]}\text{B}$ to $^{[4]}\text{B}$ conversion is governed by the type and the amount of network modifier.^{43,196} For instance, $N_4 = R$ (where $R = \text{M}_2\text{O}/\text{B}_2\text{O}_3$) is valid for a binary $\text{Na}_2\text{O}-\text{B}_2\text{O}_3$ glass up to 35 mol% sodium oxide ($R = 0.55$),²⁰ while in the $\text{CaO}-\text{B}_2\text{O}_3$ system, beyond $R = 0.5$ the network begins to depolymerize, with NBO formation on $^{[3]}\text{B}$ units.¹⁹⁷

Figure 4-17 shows the relationship between the structure, N_4 , and the calculated residual glassy phase composition (values reported in parentheses in Table 4-7) for the current work, as well as literature values for binary $\text{Na}_2\text{O}-\text{B}_2\text{O}_3$ and $\text{CaO}-\text{B}_2\text{O}_3$ glasses. Stebbins⁴⁴ showed that incorporating Na_2O and CaO in a borate glass affect the glass structure, particularly N_4 , differently. When sodium is the network modifier, for $R < 0.43$, N_4 is equal to R which is very well established in the literature.^{20,112,198} The negative deviation from this equation at higher alkali loadings indicates that NBOs start to form. In the case of CaO , they show that NBO formation begins at lower R values. However, at $R = 0.67$, calcium borate glasses exhibit higher N_4 values. This unexpected increase likely results from the greater energetic stabilization of adjacent tetrahedral boron units ($^{[4]}\text{B}-\text{O}-^{[4]}\text{B}$) when charge compensation is provided by cations with higher charges. The influence of cation charge becomes particularly evident when comparing Na^+ and Ca^{2+} , as they possess nearly identical ionic radii.⁴⁴

The glassy phases of P0-P5 contain between 0 and 2.5 mol P_2O_5 which is low enough to be treated as a binary $\text{Ca} - \text{Na} - \text{borate}$ glass. N_4 for P0-P5 with the R value ranges between 0.6 and 0.8 equals to ca. 0.41 which is comparable with the results of Stebbins. In addition, Yiannopoulos *et al.* reported $N_4 \approx 0.40$ for 45 mol% CaO ($R = 0.82$) in a binary $\text{CaO}-\text{B}_2\text{O}_3$ glass system,¹⁹⁶ which is close to the result of the current work. In other words, this N_4 analysis is another check on the composition of the residual glass. P10 is a borophosphate glass containing 6 mol% P_2O_5 . This sample is composed of anionic phosphate species, $\text{P}_{0\text{B}}^1$ and $\text{P}_{1\text{B}}^2$, which should be charge-compensated by Na^+ and Ca^{2+} . Therefore, fewer network modifiers are available to convert $^{[3]}\text{B}$ to $^{[4]}\text{B}$, hence N_4 is lower (0.32). As Figure 4-2 demonstrates, by introducing phosphorus to the borate-based glass from 0 to 5 mol%, a slight shift toward lower frequencies is detected in $^{[4]}\text{B}$ species. This displacement of the isotropic chemical shift is pronounced in the P10 sample because a considerable number of $\text{B}-\text{O}-\text{P}$ linkages have formed in the glass structure.^{113,120}

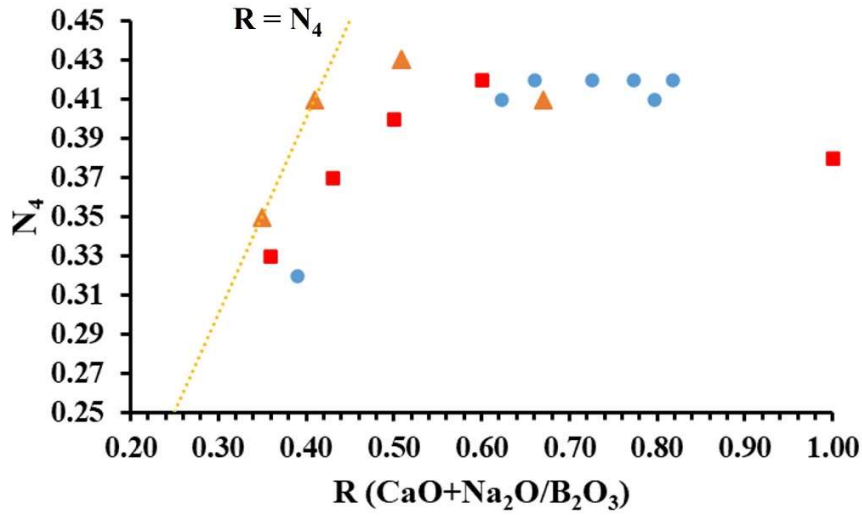


Figure 4-17) Fraction of four-coordinated boron, N_4 , as a function of R value. Orange and red from reference [44]. The yellow dashed line is $R = N_4$

4-4-2-1- Charge-compensation calculations

The estimated composition of the residual glassy phase as well as the ^{11}B and ^{31}P NMR assignments can be checked by doing charge-compensation calculations. As discussed in chapter 2, the total negative charge from anionic species in a glass must be balanced by the positive charge provided by Ca^{2+} and Na^+ . In the residual glassy phase, $^{[4]}\text{B}$ is an anionic species that carries one negative charge, so:

$$\text{Negative charge associated with } ^{[4]}\text{B} = 2 \times \text{B}_2\text{O}_3 (\text{mol } \%) \times N_4 \quad \text{Eq. 4-1}$$

P1-P5 contain $\text{P}_{0\text{B}}^1$, an anionic species carrying two negative charges. in addition to $\text{P}_{0\text{B}}^1$, P10 contains $\text{P}_{1\text{B}}^2$ carrying one negative charge, So:

$$\text{Negative charge associated with phosphate units} = 2 \times \text{P}_2\text{O}_5 (\text{mol } \%) \times \{2 \times f(\text{P}_{0\text{B}}^1) + 1 \times I(\text{P}_{1\text{B}}^2)\} \quad \text{Eq. 4-2}$$

where $I(x)$ is the fraction of x species in the residual glassy phase. The integrated intensity of phosphate species in the residual glassy phase reported in Table 1-1 should be scaled to 100%. Therefore, the integrated intensity of $f(\text{P}_{0\text{B}}^1)$ in P1-P5 is 1 while in P10 the fraction of $\text{P}_{0\text{B}}^1$ and $\text{P}_{1\text{B}}^2$ is 59 and 41 %, respectively.

$$\text{Total negative charge} = \Sigma \text{ negative charge (B)} + \Sigma \text{ negative charge (P)} \quad \text{Eq. 4-3}$$

$$\text{Total positive charge} = 2 \times (\text{CaO} + \text{Na}_2\text{O}) \text{ mol \%} \quad \text{Eq. 4-4}$$

Table 4-8 shows the results of the calculations for sum of negative and positive charges in the samples.

Table 4-8) Calculated total positive and negative charges in the glassy phase of P0–P10 (Eq. 4-1)

	B₂O₃ (mol %)	N₄	Negative charge (B)	P₂O₅ (mol %)	Negative charge (P)	Total negative charge	CaO (mol %)	Na₂O (mol %)
P0	55.0	0.42	46	0	0	46 + 0 = 46	30.0	25.0
P1	54.0	0.41	44	1.0	4	44 + 4 = 48	30.0	16.0
P2	53.0	0.42	45	2.0	8	45 + 48 = 53	30.0	17.0
P3	54.0	0.42	46	2.0	9	46 + 9 = 54	28.0	18.0
P4	57.0	0.42	48	2.0	7	48 + 7 = 55	24.0	19.0
P5	57.0	0.41	47	2.0	10	47 + 10 = 57	23.0	20.0
P10	61.0	0.32	39	6.0	20	38 + 20 = 58	16.0	26.0

By comparing the total negative and total positive charge, it is observed that all samples exhibit a surplus positive charge. This suggests the presence of additional negatively charged anionic species, i.e. $^{[3]}B$ with one NBO which is denoted by OBO_2 .

Negative charge required to balance extra positive charge = $2 \times B_2O_3 \text{ (mol \%)} \times I(OBO_2)$ Eq.4-5

where $I(OBO_2)$ is the fraction of $^{[3]}B$ with one NBO required to balance the surplus positive charge. For P0:

$$44 \text{ mol \% required negative charge} = 2 \times 55 \text{ mol \% } B_2O_3 \times I(OBO_2) \rightarrow I(OBO_2) = 0.40$$

Table 4-9 shows the result of this calculation for the glassy phase of P0-P10.

In a glass $^{[3]}B = OBO_2 + BO_3$ where BO_3 denotes three coordinated boron with three BOs.

The following equations can be used to check the consistency of estimated NBO concentrations as percent of total oxygen, N_{NBO} .

$$N_{NBO} = 2 \times (R - N_4) / (3 + R) \quad \text{Eq. 4-6}$$

$$N_{NBO} = 2 \times OBO_2 / (3 + R) \quad \text{Eq. 4-7}$$

where $R = (CaO + Na_2O) / B_2O_3$

The result of this calculation for the glassy phase of P0-P10 is shown in Table 4-9. There is good agreement between the results obtained from Eqs. 4-6 and 4-7 for P0–P5, which supports the estimated concentration of OBO_2 species in these glasses. However, this agreement does not hold for P10. It is therefore concluded that remaining glassy phase of P10, containing 6 mol% P_2O_5 , there are enough P species to carry some of the additional negative charge. This conclusion is further supported by the observation that the discrepancy between the total negative and positive charges is only 9% when OBO_2 species are excluded from the charge balance. In addition, as shown in Table 4-3, the η value used for fitting two $^{[3]}B$ components is 0.2, which is the typical value for three-coordinated boron without NBOs.

Table 4-9) Calculated amount of surplus positive charge and fraction of OBO₂ species in the remaining glassy phase of P0-P10.

	Surplus positive charge	f (OBO ₂)	f(BO ₃)	N _{NBO} Eq. 4-6	N _{NBO} Eq. 4-7
P0	90 – 46 = 44	0.40	0.18	21	21
P1	90 – 48 = 42	0.39	0.20	20	20
P2	90 – 53 = 37	0.35	0.23	19	19
P3	87 – 54 = 33	0.31	0.27	16	16
P4	82 – 55 = 28	0.24	0.34	13	13
P5	81 – 57 = 24	0.21	0.38	12	12
P10	67 – 58 = 9	0.07	0.68	4	4

4-4-3- Dissolution behaviour

Since as-made P0 does not have P₂O₅, there is no ³¹P MAS NMR spectrum recorded. However, after dissolution the ³¹P MAS NMR spectrum shows ACP and crystalline HA phases. This observation aligns with the findings of Eden,¹⁸⁶ who showed that in bioactive phosphosilicate glasses ACP initially forms and subsequently crystallizes into HA. P1-P10 show the same behaviour. Comparison of the ³¹P MAS NMR spectra before and after dissolution indicates that the residual glassy phase has dissolved - either partially or completely - and that new phases, namely ACP and HA, have reprecipitated. It should be noted that the broad peak observed in the post-dissolution ³¹P MAS NMR spectra originates from both ACP and the remaining glassy phase, making unambiguous quantification of these components challenging.

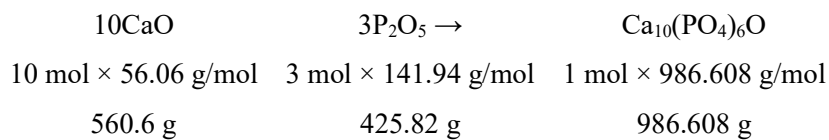
In silicate glasses, the dissolution behaviour and degradation rate, as well as the formation of an HA layer is discussed with reference to the silicate network connectivity (Q_{Si}^n).¹⁹⁹ The connectivity is reduced as network modifiers are introduced into its structure and consequently, it dissolves faster in the aqueous medium. Brow showed that in borate glasses the dissolution

properties are governed by the N_4 ratio and the types of the modifier in the glass.²⁰⁰ In fact, it has been shown that the required energy for hydrolysis of the trigonal species is less than four-coordinated boron; hence borate glasses rich in $^{[3]}\text{B}$ will dissolve faster than those containing a higher amount of $^{[4]}\text{B}$.²⁰⁰ Another factor that may influence the dissolution behaviour is the concentration of NBOs within the glass structure. Glasses with higher NBO content are generally expected to exhibit faster dissolution rates compared to those with fewer NBOs, despite being associated the trigonal boron. In addition, phase separation accelerates the dissolution rate because larger phase boundary at the interface of remaining glassy phase and crystalline OAp is accessible to the solution. This interfacial area between the glass and crystalline phase has excess free energy that is expected to enhance the dissolution rate.⁴⁷ Therefore, by comparing the N_4 values of the pristine samples tabulated in Table 4-3 and the ICP-OES elemental profiles of boron in SBF, the sharp increase in the dissolution rate of P10 can be attributed to its low N_4 value (0.32) and a high degree of phase separation. In P5, two factors are competing: the high amount of $^{[4]}\text{B}$ favours a lower degradation rate but high interfacial energy from phase separation tends to dissolve the glass faster. The ^{11}B MAS NMR spectrum shows that in this competition, interfacial energy factor takes over the dissolution behaviour and the sample dissolves faster than P0-P4 with comparable $^{[4]}\text{B}$ contents. By comparing P0-P5, one can assess the influence of NBO and $^{[4]}\text{B}$ species on the dissolution rate of the glasses. (Since P3 marks the onset of phase-separation and contains only a small fraction of crystalline phase, it can be grouped with P0-P2 for this analysis.) Although all these samples share similar N_4 values, they differ in their NBO content. However, their boron dissolution profiles are comparable, suggesting that the dominant factor governing dissolution in this composition range is the concentration of $^{[4]}\text{B}$ species.

During the dissolution of glasses in SBF solution, two competing processes occur: formation of phosphorus-bearing ions related to phosphoric acid, a strong acid with $\text{pK}_a = 2.1$, which lower the pH, and formation of basic species like NaOH which raise the pH.^{201,202} In addition, the dissolution of borate species in water raise pH. In P10, the residual glassy phase contains 6 mol % P_2O_5 . Upon dissolution, this relatively high phosphate content contributes to a greater release of acidic species, effectively outweighing the influence of basic components and maintaining a low pH of 7.1 ± 0.1 throughout the five-day experiment. In contrast, the pH of samples P0-P5 gradually increases over time. This is because the glassy phases of these samples contain only

around 2 mol% P₂O₅, which is not enough to counteract the pH-raising effect of the basic species.²⁰²

After the dissolution experiments, a portion of each sample remained and was collected for further analysis by NMR. To understand the nature of these residues and explore the relationship between sample durability and composition, it is important to remember that a fraction of the remaining material is phase-separated, consisting of crystalline OAp with low solubility, i.e., ~0.087 g/L at 25 °C in water.²⁰³ Therefore, it is necessary to calculate the mass fractions of both the glassy and crystalline OAp phases in these samples. To do so, first the glass composition should be converted from mol % to wt. %. For example, P3 contains 6 wt. % P₂O₅. Based on ³¹P MAS NMR this sample has 32 % crystalline phase, indicating that 2 wt. % of the P₂O₅ is associated with Ca₁₀(PO₄)₆O.



The CaO : P₂O₅ mass ratio is 5.60 : 4.25 in oxyapatite. Therefore, 2 g P₂O₅ needs 3 g CaO to form the crystalline phase. In this example, mass fraction of the crystalline phase in the pristine sample is ca. 5 wt. %. Table 4-10 summarizes the results for the phase-separated samples. The last row in this table shows the remaining mass of the sample after dissolution study. By comparing this data with the calculated wt. % of OAp in P3 to P10 samples it is possible to compare the remaining mass of samples after dissolution more accurately. After 5 days immersion of P3 in SBF, 19 wt. % was collected while 32 wt. % of P10 remained undissolved. Since the crystalline fraction of as-made P3 is 5.0 wt. %, and it is a barely dissolvable phase, it is concluded that about 14 wt. % of the remaining mass after dissolution experiment is the sum of the ACP, hydrated OAp and pristine glassy phases.

In the case of P10, ca. 25 wt. % of the as-made samples is crystalline. Hence much of the remaining mass after dissolution consists of ACP, hydrated OAp and crystalline phases, with only about 7 % attributed to the undissolved glassy phase. This aligns with the ICP-OES results, which indicate that the amorphous phase of P10 dissolves rapidly while the residual HA crystalline phase with low solubility (~0.0003g/L at 25 °C in water for Ca₁₀(PO₄)₆(OH)₂²⁰³) acts as a nucleation site for apatite layer formation. The morphology of HA in this sample is needle-

like with a hexagonal cross section and is dissimilar from the rest of the glasses (Figure 4-14). Given that the crystalline phase resists dissolution, the smaller amount of remaining glassy phase in P10 (7 %) compared to P3 (14 %) confirms its higher dissolution rate, consistent with the ICP-OES data.

Table 4-10) Composition of oxyapatite (OAp) and residual glassy phase (G) in phase-separated samples before dissolution (wt. %) and fraction of remaining glasses after dissolution experiments.

	P3		P4		P5		P10	
Integrated intensity from ³¹ P MAS NMR	OAp 32 %	G 68%	OAp 62%	G 38%	OAp 57%	G 43%	OAp 54%	G 27 %
B ₂ O ₃	-	54	-	53	-	51	-	44
P ₂ O ₅	2	4	5	3	6	4	11	8
CaO	3	23	7	18	8	17	14	9
Na ₂ O	-	14	-	14	-	14	-	13
Calculated OAp (wt%)	5		12.0		14		25	
Remaining after dissolution (wt%)	19		25		27		32	

After dissolution, XRD reveals that the HA formed on samples containing 3 mol % P₂O₅ and more are crystalline because of the relatively sharp Bragg peaks assigned to the HA structure. P0, P1 and P2 also show bioactivity but the degree of the crystallinity of the HA-like structure is low, which can be deduced by a hump around $2\theta = 28^\circ$ and 32° in XRD patterns and their broad ²³Na MAS NMR spectra. Eden et. al. showed by ²³Na MAS NMR spectroscopy that sodium enters ACP or HA phases after exposure of bioactive silicate base glasses in SBF. They showed a narrow peak resonating at -7.5 ppm (peak maximum) collected from the SBF-treated glasses, and attributed it to sodium in the newly formed layer.²⁰⁴ Therefore, the ²³Na MAS NMR isotropic chemical shift at ca. -2.0 ppm in P4, P5 and P10 is assigned to a crystalline HA containing sodium. In addition, intense Ca and P peaks in EDS spectra reveal that all samples show HA formation after 5 days immersion in SBF. Considering these data, in P0, P1 and P2 glasses the calcium phosphate phase is amorphous but samples with more than 3 mol % P₂O₅ (P3 is considered as the onset of the phase separation, see Figure 4-3) calcium phosphate forms as a crystalline apatite phase.

In this chapter, it is demonstrated that ^{31}P MAS NMR spectroscopy is a suitable technique for estimating the composition of the residual glassy phase in a series of phase-separated Na–Ca–B–P samples. Charge compensation calculations are employed to evaluate the distribution of borate and phosphate species within the estimated remaining glassy matrix. The dissolution behaviour of both homogeneous and phase-separated samples is found to be governed by a combination of factors, including the concentration of $^{[4]}\text{B}$ species, the amount of NBOs, and the extent of phase boundaries in the system. In homogeneous glasses (P0-P2), the dissolution rate is primarily controlled by the $^{[4]}\text{B}$ content. In contrast, for phase-separated samples, higher degrees of phase separation—reflected by greater amounts of OAp crystalline phase—correlate with increased degradation rates in SBF. Furthermore, in homogeneous samples, it is concluded that HA formation in the SBF occurs only after the initial formation of amorphous calcium phosphate ACP within the glass structure. In the case of phase-separated glasses, the mechanism is more complex, as pre-existing OAp phases may act as nucleation sites for HA formation. However, the potential formation of ACP in these samples cannot be ruled out without direct experimental evidence.

Borate-based glasses are used as biomaterials for mainly soft tissue regeneration as they boast higher degradation rates which are favourable and prerequisite in the relevant disease/issues while silicate bioglasses are better candidates for bone- and teeth-related needs because a high rate of dissolution (and subsequently HA layer formation) is not required. "This glass series shows that borate-based biomaterials may exhibit a range of dissolution behaviours compatible with both soft-tissue ion release and apatite-formation for bone and teeth reinforcement.

5- Silver-doped borophosphate glasses for wound-healing applications

5-1- Introduction

The most common soft-tissue wounds are surgeries, injuries, diabetes, burns and vascular disease.²⁰⁵ These can be classified based on the depth, tissue layer involved, and duration of treatment to better describing wounds and their management.⁶⁵ Regardless of their cause, wounds may be categorized as acute or chronic.²⁰⁵ The former is defined as a wound that is healed through an organized and appropriate repair process, and after a specific amount of time the tissue is substantially restored.²⁰⁵ In the latter case, the optimal anatomical and functional integrity cannot be achieved.²⁰⁵ This is one of the reasons that external interference is crucial. By taking into account the severity, size and damage depth, an acute wound is expected to heal within 8 to 12 weeks, while the chronic wound may not show signs of healing after 6 weeks.⁶⁵ Statistics regarding death associated with wounds and the required funding for medication show how important this area is for governing authorities and health care systems. In 2016, diabetes mellitus claimed 1.6 million lives globally and was the seventh leading cause of death. The World Health Organization (WHO) predicts that 5.1 million people will die due to diabetes by 2060.⁶⁵ Between 2008 and 2016, 3275 people died in the United States because of the severity of burn injuries.⁵³ Medical care expenses for all wounds types in the United States was evaluated to be between \$28.1 and \$96.8 (USD) in 2014.²⁰⁶

When it comes to wound care practice, “TIME” is an acronym referring to negative interference in the healing process: tissue (T), infection (I) moisture (M) and epithelial (E).²⁰⁵ Among these factors, infection is the main focus of the current work. However, in patients with underlying health conditions, various factors hinder the healing process, often leading to chronic wounds—such as ulcers in individuals with diabetes—who face a persistent risk of inflammation and potentially life-threatening infections.⁵¹ Therefore, it is vital to protect wounds from infections to prevent further fatal threats.

The most widespread approach to managing bacterial infection is the prescription of antibiotics and antiseptic products. However, these therapies have resulted in bacterial resistance.²⁰⁷ Hence, alternative methods are required for protecting wounds from infections, and accelerating the healing process.

Bioactive glasses have been shown to be effective candidates for hard and soft tissue regeneration.^{34,49,50,64} Silicate- and phosphate-based glasses have been commercialized for bone and dental applications, with several products—such as implants and scaffolds—already patented.²⁰⁸ However, in 1987, researchers discovered biofilms developing on the surface of implanted bioglasses, which increased the risk of bacterial infection.²⁰⁹ Hence, novel approaches aimed at minimizing bacterial adhesion and inhibiting biofilm formation are currently being investigated in both in vitro and in vivo.²¹⁰

One approach to improve the antibacterial properties of bioactive glass is loading it with silver because of its bactericidal properties.²¹¹ One of the inherent characteristics of silver is that it does not develop bacterial resistance, which makes it superior to antibiotics.²¹² Although Ag has been utilized and commercialized as protection against bacterial infections, its mechanism for killing and stopping growing bacteria still is controversial. Mechanisms including binding to microbial DNA and sulfhydryl groups of bacterial enzymes, inhibiting cell metabolism and damaging integrity of the cell membrane have been proposed.^{213,214}

Table 5-1 summarizes the relevant research on silver-loaded bioactive glasses in hard- and soft-tissue regeneration. The literature survey reveals that the structural effects of adding silver to borophosphate glasses have not been well studied. Considering the fundamental relationship between the composition, structure and properties of glasses, investigating the structure of borophosphate glasses containing Ag₂O will contribute to understanding the dissolution of these glasses in an aqueous environment. In this research the structure of a series of melt-quenched Na₂O- Ag₂O-B₂O₃-P₂O₅ glasses will be characterized by solid-state NMR spectroscopy and compared with their dissolution behaviour to infer structural controls on properties due to network bonding and topology.

Table 5-1) Literature survey on silver-loaded bioactive glasses for tissue regeneration

Composition	Silver content (mol%)	Synthesis route	Comments	Year	Citation
SiO ₂ - P ₂ O ₅ - CaO - Ag ₂ O	3wt.%	SG	bacteriostatic effect on E.coli MG1655	2000	²¹¹
SiO ₂ - P ₂ O ₅ - CaO - Ag ₂ O	3wt.%	SG	E.coli, P. aeruginosa, S. Aureus	2002	²¹⁵
P ₂ O ₅ - CaO - Na ₂ O - Ag ₂ O	0-15	MQ		2006	²¹⁶
SiO ₂ - CaO - Ag ₂ O	1	SG	Several foam scaffolds with various ions release rates prepared.	2006	⁶¹
SiO ₂ - CaO - P ₂ O ₅ - Ag ₂ O	5	SG	E.coli MG1655	2008	²¹⁷
B ₂ O ₃ - P ₂ O ₅ - CaO - MgO - Na ₂ O - K ₂ O	0.75 -2 wt.%	MQ	Glass containing 2%wt. silver are toxic while 0.75-1%wt. didn't show toxicity.	2010	²¹⁸
SiO ₂ - P ₂ O ₅ - CaO - Ag ₂ O	1-10	SG	E.coli, S. aureus	2012	²¹⁹
P ₂ O ₅ - CaO - Na ₂ O - Ag ₂ O	0-20		Computational chemistry using first-principle and classical technique.	2014	²²⁰
B ₂ O ₃ -SiO ₂ -CaO-Ag ₂ O	0.3-3	MQ		2014	²²¹
SiO ₂ - P ₂ O ₅ -MgO - CaO - Ag ₂ O	1-2	MQ	E.coli Non-toxic	2017	²²²
SiO ₂ - P ₂ O ₅ - CaO - Na ₂ O - Ag ₂ O	2 wt.%	BI	E.coli, S. aureus	2018	²²³
B ₂ O ₃ - P ₂ O ₅ - CaO - Na ₂ O - Ag ₂ O	0.15-1	SG	E.coli, S. aureus	2019	²²⁴
P ₂ O ₅ - CaO - Na ₂ O - Ag ₂ O	1-14	C	S. aureus	2019	²²⁵

MQ: melt-quenching, SG: sol-gel, BI: bio-inspired, C: Coacervate

5-2- Experimental

5-2-1- Synthesis:

Glasses were synthesized by the melt-quench technique in 3-gram batches. Calculated amounts of (NaPO₃)₆ (Fisher Scientific, analytical grade), Na₂CO₃ (Fisher Scientific, ≥ 99.8%), Ag₂O, and H₃BO₃ were mixed in 95:5 Pt: Au crucibles and placed in a box furnace at 850°C for 6 hours for dehydration and decarbonation. The temperature was raised to 1100 °C and the samples were

heated for 5-10 minutes before being quenched in water. The silver-loaded glasses exhibited a pale yellow colouration. The nominal and experimental compositions of $(\text{Ag}_2\text{O})_x(\text{Na}_2\text{O})_{0.35-x}(\text{P}_2\text{O}_5)_{0.25}(\text{B}_2\text{O}_3)_{0.40}$ glasses, where $0 \leq x \leq 0.03$, are given in Table 5-2. To determine the actual compositions, 10 mg of glass powder was fully dissolved in a 2%v/v nitric acid and the concentration of constituents were measured using ICP-OES. For all glasses the mass loss was 2-4 wt. %, which reflects the loss of P and Ag. The glass discs were ground and separated according to size using two sieves, 180 and 105 μm . Glass particles collected between two sieves with particle sizes of 105-180 μm and $< 105 \mu\text{m}$ were stored separately in a sealed glass vials and kept in a desiccator until further analysis.

Table 5-2) Nominal and analysed composition of the silver-loaded borophosphate glasses

	Nominal (mol%)				Experimental (mol%) $\pm 2\%$			
	Ag ₂ O	Na ₂ O	B ₂ O ₃	P ₂ O ₅	Ag ₂ O	Na ₂ O	B ₂ O ₃	P ₂ O ₅
Ag0	0	35	40	25	0	34.7	41.3	24.0
Ag0.5	0.5	34.5	40	25	0.2	35.3	40.4	24.1
Ag1	1	34	40	25	0.8	33.8	41.2	24.2
Ag1.5	1.5	33.5	40	25	1.4	34.0	40.9	23.7
Ag2	2	33	40	25	1.9	32.6	41.2	24.3
Ag3	3	32	40	25	2.9	30.4	42.3	24.4

5-2-2- Dissolution experiments

Sieved glass particles (105-180 μm) were massed to 200.0 mg and added to 15mL of milliQ water in polyethylene terephthalate (PET) beakers. Prior to adding the glasses, and for the duration of the study, the pH was monitored using a Fisher Scientific Accumet AB150 pH probe. The dissolution study was performed in two replicates at room temperature with no temperature control. After each glass powder was added to the water, aliquots of 0.25mL of the leachate were collected at 0.5, 1, 2, 4, 6, 10, and 30 hours and stored in plastic test tubes for ICP-OES analysis, while the pH readings were also recorded at these time intervals. After 30 hours, any remaining undissolved glass was filtered out of each solution, washed with anhydrous ethanol, and dried in an oven for 2 hours at 110 °C. Once dry, the glass samples were transferred into vials, sealed and stored in a desiccator.

5-2-3- Inductively coupled plasma optical emission spectroscopy (ICP-OES)

The ICP-OES measurements were done using a Varian 725-ES ICP Optical Emission Spectrometer with a radial-view plasma system and a vortex mixer. Each leachate aliquot was diluted from 0.25 mL to 5 mL with analytical grade 2% HNO₃ solution before the ICP-OES measurements. The instrument was calibrated using trace metal grade primary standards of sodium ($999 \pm 5 \mu\text{g/mL}$), phosphorus ($10058 \pm 4 \mu\text{g/mL}$), silver ($1002 \pm 6 \mu\text{g/mL}$) from BDH, and boron ($1000 \pm 4 \mu\text{g/mL}$) from Accurate.

5-2-4- Nuclear magnetic resonance (NMR) spectroscopy

NMR analysis was carried out on a Varian 600 MHz spectrometer equipped with a Chemagnetics 1.6 mm double-resonance solid-state NMR probe. All samples were spun at the magic angle with a spinning speed of 20 kHz (± 5 Hz). At a magnetic field of 14.08 T, the resonance frequencies of ¹¹B, ²³Na and ³¹P are 192.54, 158.74 and 242.86 MHz, respectively. One-dimensional Bloch-decay experiments were carried out with pulse lengths and relaxation delays, respectively, of 0.33 μs and 4 s for ¹¹B; 0.37 μs and 2 s for ²³Na; 1 μs and 200 s for ³¹P. The pulse lengths in ¹¹B and ²³Na measurements corresponded to a tip angle of 22.5° which equally excites all the sites, irrespective of quadrupolar coupling constants (C_Q). For ³¹P, a tip angle of 30° was used due to long T_1 values, which were measured by inversion recovery method. MAS NMR signals were averaged over 1024, 1024 and 32 transients for ¹¹B, ²³Na and ³¹P, respectively. Deconvolution of ¹¹B MAS NMR spectra was carried out using the DMfit software developed by Massiot *et al.*²²⁶ The Quasar model was used to fit [³]B peaks which were broad and structured due to significant second-order quadrupolar interactions as compared to [⁴]B peaks which were fit with gaussian/lorentzian-shaped peaks. The CzSimple model¹⁶⁰ was used to determine the isotropic chemical shift and C_Q of ²³Na MAS NMR spectra.

5-2-5- X-ray diffraction analysis

X-ray diffraction analysis was carried out using D4 Endeavor Bruker X-ray diffractometer. The samples were finely ground and mounted on polymer diffraction plates and subjected to x-rays. Cu-K α radiation was generated at a voltage and current of 40 kV and 40 mA. The 2 θ was scanned between 10° and 50° with a step size of 0.020 and an acquisition time of 20 seconds

corresponding to 2000 steps. The sample was spun at 15 rpm during data acquisition to ensure homogeneous sampling.

5-3- Results

5-3-1- Before dissolution

5-3-1-1- X-ray diffraction

Figure 5-1 shows the x-ray diffractograms of the samples before dissolution. The XRD patterns of all samples lack Bragg peaks, showing only a background “halo” indicative of an amorphous phase.

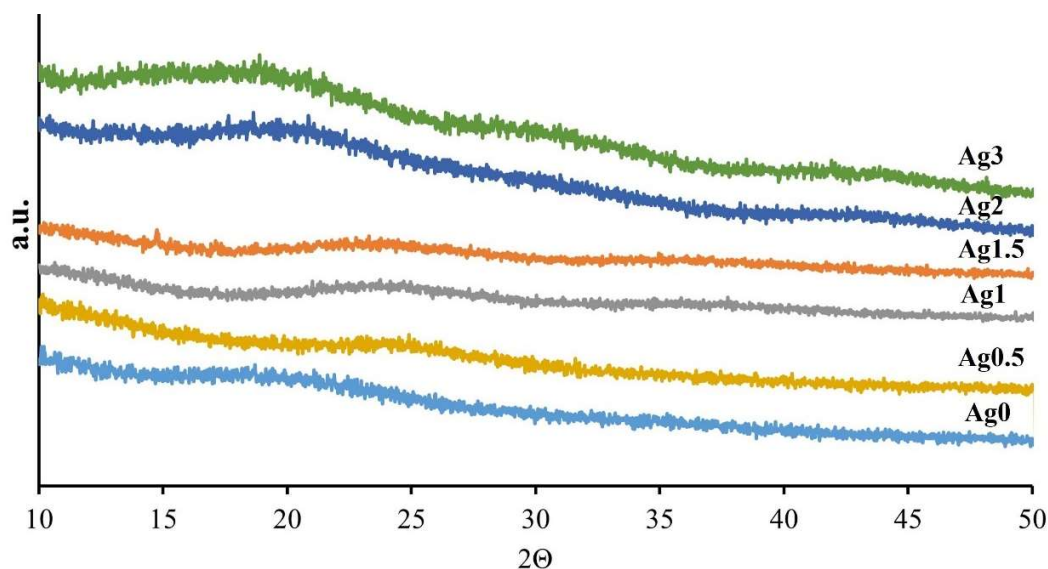


Figure 5-1) X-ray diffractograms of samples before dissolution

5-3-1-2- ^{11}B MAS NMR spectroscopy

Figure 5-2 shows ^{11}B MAS NMR spectra for all glasses before dissolution. All spectra have two distinct regions which denotes the presence of $^{[3]}\text{B}$ and $^{[4]}\text{B}$.²²⁷ Each $^{[3]}\text{B}$ region is fitted by two components interpreted as ring and non-ring boron (see Figure 1-8). Table 5-3 shows that in these glasses the $^{[4]}\text{B}$ signal consists of two four-coordinate species, differing by the number of phosphate polyhedra in the next-nearest neighbouring positions. In Ag0, this region is assigned to $^{[4]}\text{B}_{2\text{P}}$ and $^{[4]}\text{B}_{3\text{P}}$ (see Figure 1-11) with chemical shifts of -0.17 and -2.5 ppm. $^{[4]}\text{B}_{2\text{P}}$ is a four-coordinated boron with two bridging oxygens connected to boron cations and two bridging oxygens bonded to phosphorus, and $^{[4]}\text{B}_{3\text{P}}$ is a boron tetrahedron with one B–O–B linkages and

three B–O–P linkages. These designations are considered to imply the medium-range order in the glass, as they specify connectivity beyond the first coordination sphere. With the addition of up to 3 mol% Ag_2O to this glass the chemical shifts of these components are slightly shifted to lower frequency, ca. -0.42 and -2.85 respectively.

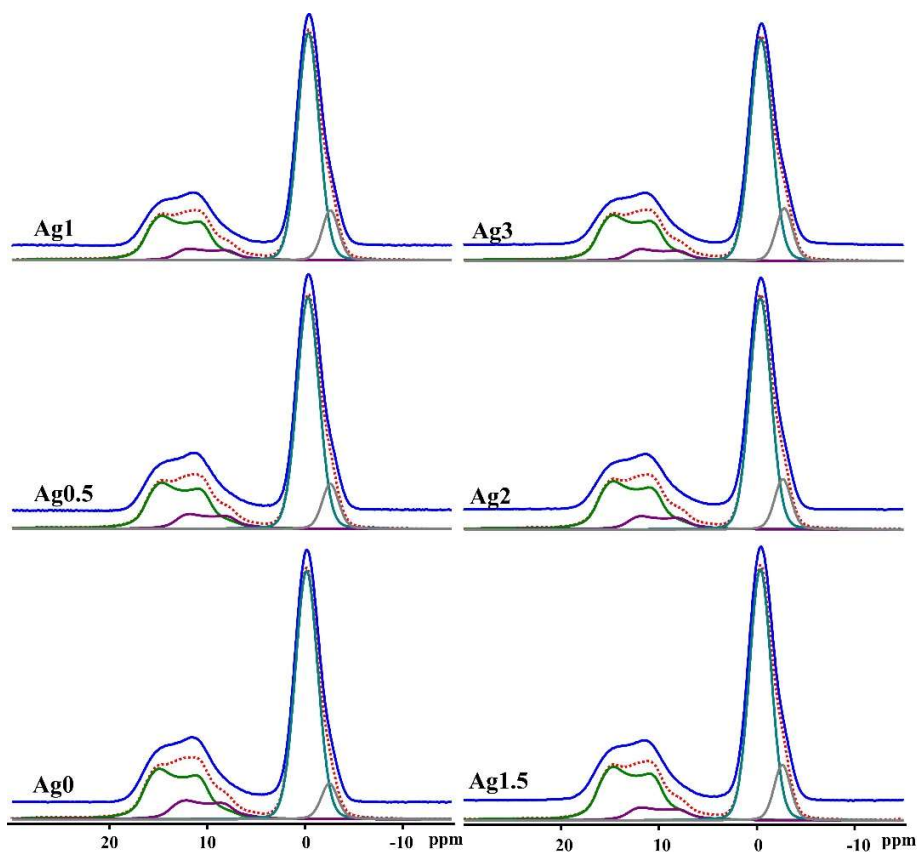


Figure 5-2) ^{11}B magic angle spinning (MAS) NMR spectra of as-made glasses. solid blue: experimental. Dotted red: fitted $^{[3]}\text{B}_{\text{ring}}$, $^{[3]}\text{B}_{\text{non-ring}}$, $^{[4]}\text{B}_{2\text{P}}$ and $^{[4]}\text{B}_{3\text{P}}$

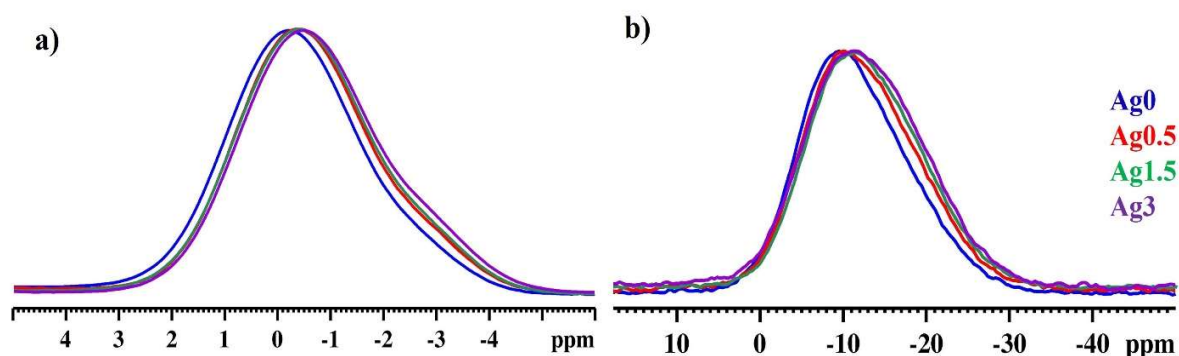


Figure 5-3) Comparison between a) ^{11}B lineshape of ^{11}B magic angle spinning (MAS) NMR spectra and b) ^{31}P MAS NMR spectra for Ag0, Ag0.5, Ag1.5 and Ag3

The change in the fraction of $^{[4]}\text{B}$ in this glass series upon doping with Ag_2O is negligible. However, a slight change in the ratio of $^{[4]}\text{B}_{2\text{P}}$ and $^{[4]}\text{B}_{3\text{P}}$ with increasing Ag_2O can be observed. Comparing each pair of glasses does not show a significant reduction in the integral intensity of $^{[4]}\text{B}_{2\text{P}}$ at the expense of $^{[4]}\text{B}_{3\text{P}}$. However, the whole glass series shows a general trend in which the fraction of $^{[4]}\text{B}_{3\text{P}}$ in Ag3 is marginally higher than it is in Ag0 (Figure 5-3).

5-3-1-3- ^{31}P MAS NMR spectroscopy

^{31}P MAS NMR spectra of all glasses before dissolving in the aqueous medium are shown in Figure 5-4, and Table 5-4 summarizes the fitting parameters obtained. All glasses were fitted with two components, $\text{P}_{2\text{B}}^2$ and $\text{P}_{2\text{B}}^3$ with isotropic chemical shifts -9.8 ± 0.4 and -19.1 ± 0.1 , respectively (Figure 2-11). Much of the glass is populated by $\text{P}_{2\text{B}}^2$ which has two B–O–P linkages per P cation. With the addition of Ag_2O to the base borophosphate glass, the integral intensity of $\text{P}_{2\text{B}}^2$ species decreases slightly at the expense of $\text{P}_{2\text{B}}^3$. The fraction of $\text{P}_{2\text{B}}^2$ is 75% in Ag0 while it slightly decreases to 69 and 68% in glasses containing 0.5 to 1.5 mol% Ag_2O , respectively. A significant change is detected in the integral intensity of the phosphate structural units with the addition of more than 2 mol% Ag_2O to the base glass. Ag3 has 35% $\text{P}_{2\text{B}}^3$ and 65% $\text{P}_{2\text{B}}^2$, showing an increasing trend in the population of species with higher number of BOs with the addition of Ag_2O to the glass.

Figure 5-16 and Figure 5-17 in the Appendix show the comparison between the ^{11}B and ^{31}P MAS NMR spectra of two borophosphate glasses made at different times. The parameters used

for fitting these spectra are summarized in Table 5-9 and Table 5-10. This comparison shows that the integrated intensity of different borate and phosphate species for a given glass composition, when synthesized and characterized independently, differ by no more than $\pm 2\%$. These results may be extended to the Ag_2O -doped glasses discussed in this chapter, indicating that the fits may be considered acceptably reproducible.

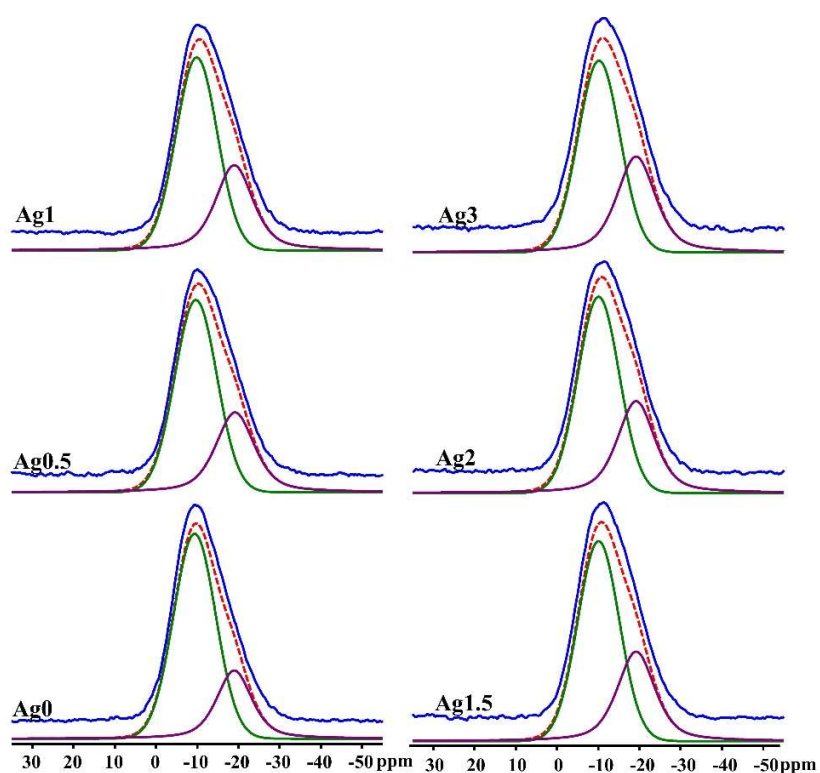


Figure 5-4) ^{31}P magic angle spinning (MAS) NMR spectra of the as-made glasses.
solid blue: experimental. Dotted red: fitted. $\text{P}_{2\text{B}}^2$ and $\text{P}_{2\text{B}}^3$

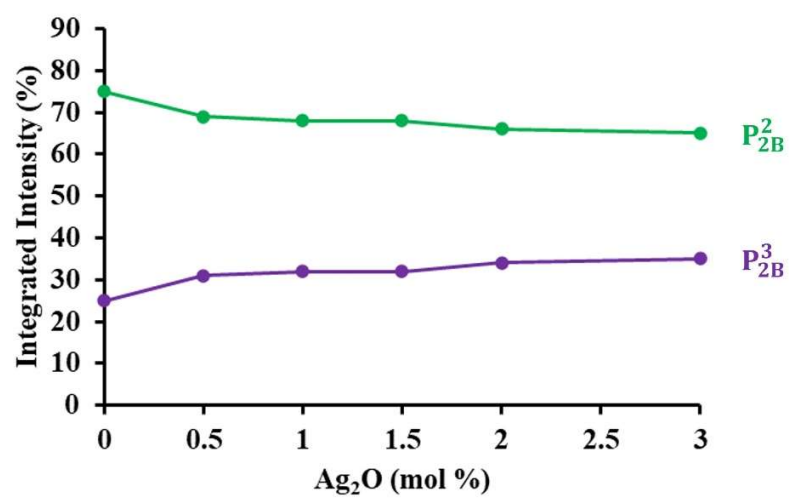


Figure 5-5) Integrated intensity of phosphate species as a function of Ag_2O content obtained from Figure 5-4

Table 5-3) Parameters used for fitting ^{11}B magic angle spinning (MAS) NMR spectra of silver-bearing borophosphate glasses

	$^{13}\text{B}_{\text{ring}}$		$^{13}\text{B}_{\text{non-ring}}$		$^{14}\text{B}_{2\text{P}}$			$^{14}\text{B}_{3\text{P}}$		N_4	
	δ_{iso} (ppm)	Int. (%)	δ_{iso} (ppm)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso}	W (kHz)	Int. (%)	
Ag0	+17.3	29	+14.5	11	-0.2	0.51	54	-2.5	0.38	6	0.60
Ag0.5	+17.0	28	+14.0	9	-0.3	0.51	55	-2.6	0.38	8	0.63
Ag1	+17.0	28	+14.0	7	-0.3	0.50	55	-2.6	0.38	10	0.65
Ag1.5	+17.1	30	+14.0	7	-0.3	0.50	54	-2.6	0.38	9	0.63
Ag2	+17.1	29	+14.0	8	-0.3	0.50	54	-2.6	0.38	9	0.63
Ag3	+17.1	29	+14.0	7	-0.4	0.50	54	-2.8	0.38	10	0.64

Fixed parameters: δ_{iso} : isotropic chemical shift with a tolerance of ± 0.5 and ± 0.1 ppm for BO_3 and ^{14}B species, respectively. C_Q : quadrupolar coupling constant with a tolerance of ± 0.15 MHz, η : asymmetry parameter with a tolerance of ± 0.1 , W: Full Width at Half Maximum (peak width) with a tolerance of ± 0.03 kHz

Fitted parameter: Int: Integrated intensity $\pm 2\%$

Table 5-4) Parameters used for fitting ^{31}P magic angle spinning (MAS) NMR spectra of silver-bearing borophosphate glasses

	$\text{P}_{2\text{B}}^2$			$\text{P}_{2\text{B}}^3$		
	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)
Ag0	-9.4	2.90	75	-19.0	2.40	25
Ag0.5	-9.7	2.90	69	-19.2	2.60	31
Ag1	-9.9	2.80	68	-19.0	2.50	32
Ag1.5	-10.1	2.80	68	-19.2	2.50	32
Ag2	-10.1	2.80	66	-19.2	2.50	34
Ag3	-10.2	2.90	65	-19.2	2.60	35

Fixed parameters: δ_{iso} : Isotropic chemical shift with a tolerance of ± 0.2 ppm, W: Full Width at Half Maximum (Peak width) with a tolerance of ± 0.05 kHz

Fitted parameter: Int: Integrated intensity $\pm 2\%$

5-3-1-4- ^{23}Na MAS NMR spectroscopy

Figure 5-6 shows ^{23}Na MAS NMR spectra of the glasses. The isotropic chemical shifts (Table 5-5) in this glass series show a subtle change when Ag_2O is substitute for Na_2O (The dashed line represents the change in the center of gravity, serving as a visual guide.). δ_{iso} for Ag0 is -5.5 ppm and it does not change significantly for the glasses containing up to 2 mol % Ag_2O . Further incorporation of silver into the glasses decreases the isotropic chemical shift to -6.2 ppm for Ag3. The C_Q of all spectra is in the range of 2.5-2.6 MHz which is typical for sodium in glasses.^{114,228} It is important to note that the δ_{iso} values for sodium across different coordination environments are very close, and the narrow distribution at the 600 MHz magnetic field used in this study prevents clear differentiation.

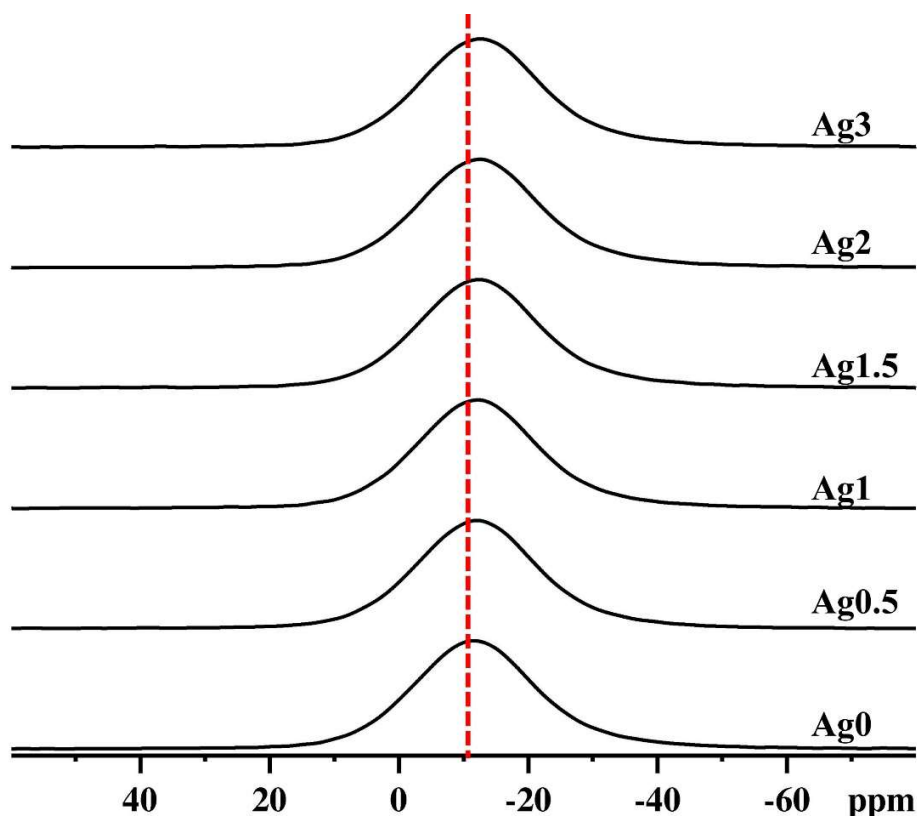


Figure 5-6) ^{23}Na magic angle spinning (MAS) NMR spectra of as-synthesized samples

Table 5-5) ^{23}Na magic angle spinning (MAS) NMR parameters used for fitting spectra of glasses before and after dissolution

	Before Dissolution		After Dissolution	
	δ_{iso} (ppm)	$\langle C_Q \rangle$ (MHz)	δ_{iso} (ppm)	$\langle C_Q \rangle$ (MHz)
Ag0	-5.5	2.60	-2.0	2.60
Ag0.5	-5.5	2.60	-4.5	2.70
Ag1	-5.5	2.60	-4.1	2.60
Ag1.5	-5.7	2.50	-3.8	2.70
Ag2	-5.8	2.50	-3.7	2.70
Ag3	-6.2	2.50	-3.8	2.60

Fixed parameters: quadrupolar coupling constant C_Q with a tolerance of ± 0.05 MHz, isotropic chemical shift δ_{iso} with a tolerance of ± 0.1 ppm
Fitted parameter: Intensity $\pm 1\%$

5-3-2- After dissolution

5-3-2-1- ^{11}B MAS NMR spectroscopy

Figure 5-7 shows ^{11}B MAS NMR spectra of the glasses after dissolving in water for 30 minutes and Table 5-6 tabulates the fitting parameters. Similar to spectra of glasses before water-treatment, four components were used to fit ^{11}B MAS NMR spectra after dissolution. Two components for ^{13}B denote ring and non-ring boron as well as two components for ^{14}B , which are attributed to $^{14}\text{B}_{2\text{P}}$ and $^{14}\text{B}_{3\text{P}}$ based on the chemical shifts. Comparison between ^{11}B MAS NMR spectra before and after dissolution in the aqueous medium (Figure 5-8a) reveals that neither peak positions nor ratio between integral intensities of two three-coordinated boron have changed considerably. Ring and non-ring boron show δ_{iso} values of $+16.9 \pm 0.2$ and $+14.1 \pm 1$ ppm, respectively. The N_4 values for the samples after dissolution study are comparable to the N_4 values for glasses before dissolution. This value across the whole glass series is 0.65 ± 0.1 . Although the ^{14}B species did not alter after dissolution, the ratio between them slightly changes; the integrated intensity of $^{14}\text{B}_{3\text{P}}$ increases at the expense of $^{14}\text{B}_{2\text{P}}$.

Figure 5-7 shows the ^{11}B MAS NMR spectrum of the remaining Ag3 after 3 days in water, where it can be seen that the ^{14}B signals constitute 95% of the boron. Since the ^{13}B signal in this

sample is so low, a single Gaussian peak was used to fit it and calculate the N_4 value. This sample also consists of 84% $^{[4]}\text{B}_{3\text{P}}$ and 11% $^{[4]}\text{B}_{4\text{P}}$.

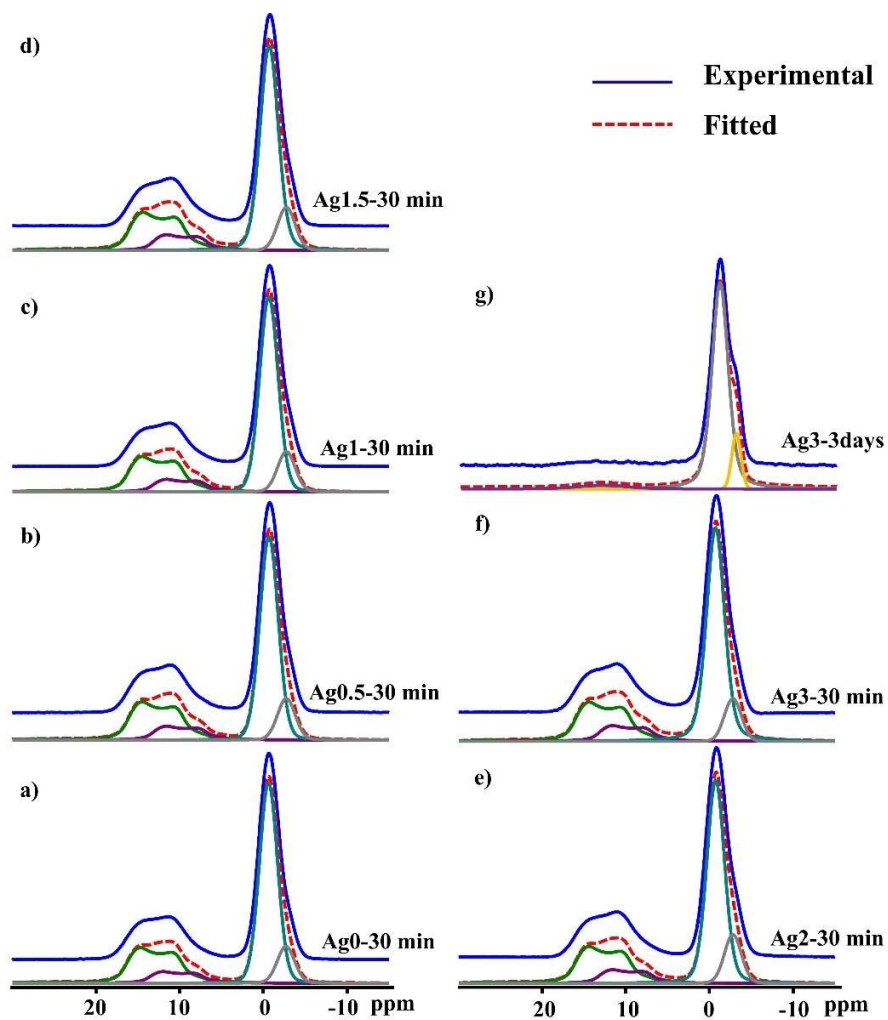


Figure 5-7) ^{11}B magic angle spinning (MAS) NMR spectra of a) Ag0, b) Ag0.5, c) Ag1, d) Ag1.5, e) Ag2, f) Ag3 after 30 minutes and g) Ag3 after 3 days dissolving in water. $^{[3]}\text{B}_{\text{ring}}$, $^{[3]}\text{B}_{\text{non-ring}}$, $^{[4]}\text{B}_{2\text{P}}$, $^{[4]}\text{B}_{3\text{P}}$ and $^{[4]}\text{B}_{4\text{P}}$

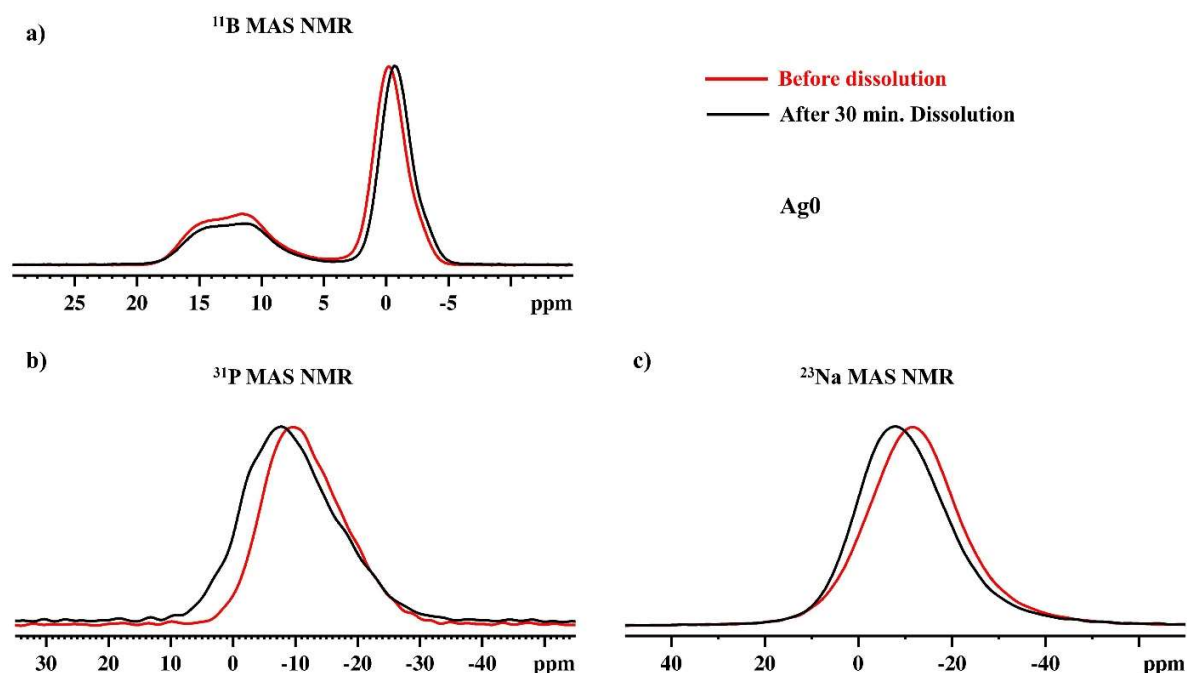


Figure 5-8) Ag0 before and after 30 min dissolving in water. a) ^{11}B magic angle spinning (MAS) NMR, b) ^{31}P MAS NMR, c) ^{23}Na MAS NMR.

5-3-2-2- ^{31}P MAS NMR spectroscopy

Figure 5-9 represents the ^{31}P MAS NMR spectra of glasses after dissolution experiments. Table 5-7 summarizes the isotropic chemical shifts, peak widths and integral intensities of the silver-doped sodium borophosphate glasses after immersion in water for 30 minutes. All glasses are populated by $\text{P}_{0\text{B}}^1$, $\text{P}_{2\text{B}}^2$, $\text{P}_{2\text{B}}^3$ with isotropic chemical shifts -3.0 , -9.9 ± 0.5 and -19.2 ± 0.2 , respectively. In comparison with the results before dissolution, $\text{P}_{0\text{B}}^1$ is a structural unit which is observed in all glasses after dissolving in water (Figure 5-8b). While these species do not show any specific trend across the glass series, the ratio between $\text{P}_{2\text{B}}^2$ and $\text{P}_{2\text{B}}^3$ before and after dissolution remains the same (Figure 5-10). In Ag0 the ratio between the fraction of $\text{P}_{2\text{B}}^2$ and $\text{P}_{2\text{B}}^3$ before and after dissolution is ca. 3. In the case of silver-doped glasses this ratio is ca. 2 before and after dissolution (Figure 5-11). In Ag2 and Ag3 a small peak is observed at $+28.5$ ppm which is assigned to Ag_3PO_4 .²²⁹ After 3 days, Ag3 shows a substantial change in ^{31}P MAS NMR. This spectrum features a narrow peak at $+28.5$ ppm, which is a crystalline reprecipitate of Ag_3PO_4 . The broad peak is the remaining glass with three structural units, $\text{P}_{1\text{B}}^1$, $\text{P}_{0\text{B}}^1$, and $\text{P}_{2\text{B}}^2$ with chemical shift $+2.3$, -3.0 and -7.9 ppm, respectively.

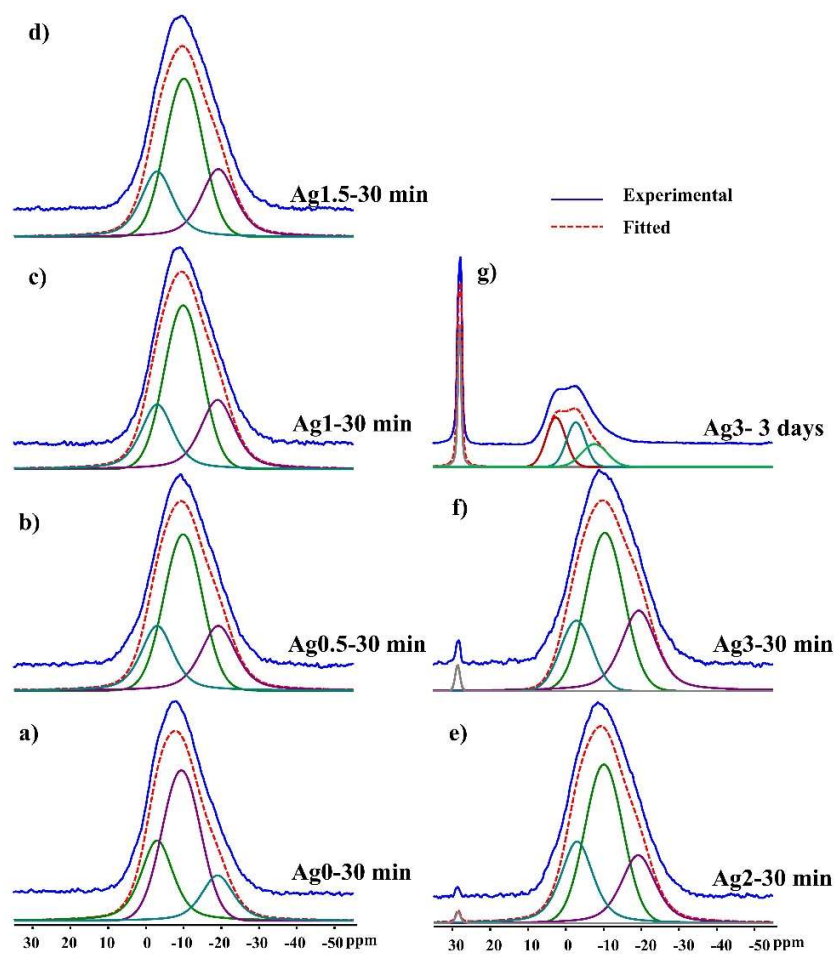


Figure 5-9) ^{31}P magic angle spinning (MAS) NMR spectra of a) Ag0, b) Ag0.5, c) Ag1, d) Ag1.5, e) Ag2, f) Ag3 after 30 minutes and g) Ag3 after 3 days dissolving in water. $\text{P}_{0\text{B}}^1$, $\text{P}_{2\text{B}}^2$, $\text{P}_{2\text{B}}^3$, and Ag_3PO_4

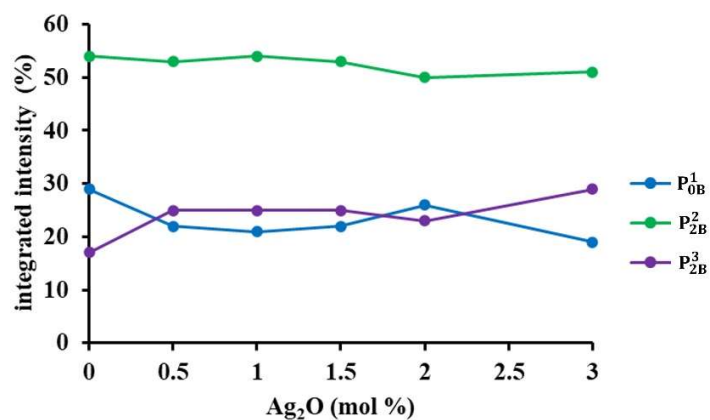


Figure 5-10) Integrated intensity of phosphate species after 30 min dissolving in water

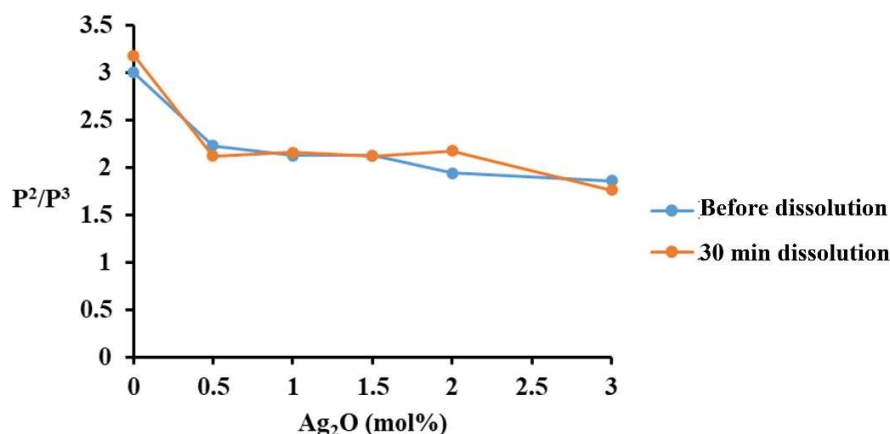


Figure 5-11) The P^2/P^3 ratio before and after 30 min dissolving in water

5-3-2-3- ^{23}Na MAS NMR spectroscopy

Immersing the glasses in water induces a measurable change in the ^{23}Na isotropic chemical shift. δ_{iso} for Ag0 is -2.0 ppm, while this value for the rest of the glasses is ca. -4.1 ± 0.4 ppm. It should be noted that the comparison between before and after dissolving samples in water for 15 minutes reveals δ_{iso} of -5.5 and -5.8 ± 0.4 ppm for Ag0 and 1.5-3% silver-bearing glasses, respectively. In Figure 5-8, Ag0 is presented as a representative example to illustrate the changes in the ^{23}Na MAS NMR spectra before and after 30 minutes dissolving in water.

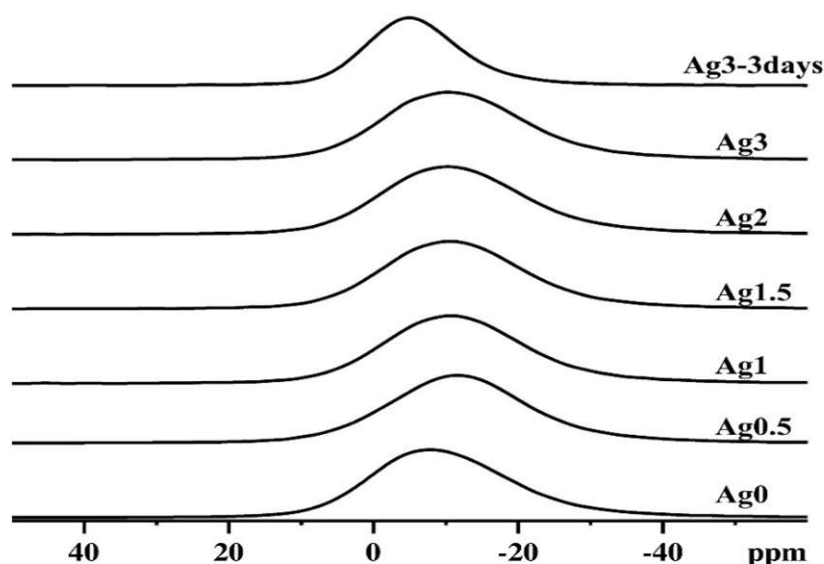


Figure 5-12) ^{23}Na magic angle spinning MAS NMR spectra after dissolution study

Table 5-6) Parameters used for fitting ^{11}B magic angle spinning MAS NMR spectra after 30 minutes and 3 days of dissolution in water

	^[3] B _{ring}		^[3] B _{non-ring}		^[4] B _{2P}			^[4] B _{3P}			N ₄
	δ _{iso} (ppm)	Int. (%)	δ _{iso} (ppm)	Int. (%)	δ _{iso} (ppm)	W (kHz)	Int. (%)	δ _{iso}	W (kHz)	Int. (%)	
Ag0	+17.1	26	+14.3	8	-0.6	0.49	56	-2.7	0.47	10	0.65
Ag0.5	+16.9	27	+13.9	9	-0.7	0.50	53	-2.7	0.48	11	0.64
Ag1	+16.9	25	+13.9	9	-0.7	0.50	55	-2.7	0.48	11	0.66
Ag1.5	+16.8	26	+13.9	10	-0.7	0.50	53	-2.7	0.48	11	0.64
Ag2	+16.8	26	+13.9	9	-0.7	0.48	53	-2.8	0.46	12	0.66
Ag3	+16.8	26	+13.9	10	-0.7	0.49	55	-2.8	0.46	9	0.65
Ag3-3days	-	-	-	5	-1.0	0.44	84	-3.0	0.25	11	0.95
Fixed parameters: δ _{iso} : isotropic chemical shift with a tolerance of ±0.5 and ±0.0 ppm for ^[3] B and ^[4] B species, respectively. C _Q : quadrupolar coupling constant with a tolerance of ±0.15 MHz, η: asymmetry parameter with a tolerance of ±0.1, W: Full Width at Half Maximum (peak width) with a tolerance of ±0.03 kHz Fitted parameter: Int: Integrated intensity ±2 %											

Table 5-7) Parameters used for fitting ^{31}P magic angle spinning (MAS) NMR spectra after 30 minutes and 3 days of dissolution in water

	Ag₃PO₄			P_{0B}¹			P_{2B}²			P_{2B}³		
	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)
Ag0	-	-	-	-3.0	2.40	29	-9.4	2.90	54	-19.0	2.40	17
Ag0.5	-	-	-	-3.0	2.40	22	-9.9	2.90	53	-19.2	2.60	25
Ag1	-	-	-	-3.0	2.40	21	-9.9	2.80	54	-19.0	2.50	25
Ag1.5	-	-	-	-3.0	2.40	22	-10.1	2.80	53	19.2	2.50	25
Ag2	+28.5	0.36	< 1	-3.0	2.400	26	-10.1	2.80	50	-19.2	2.50	23
Ag3	+28.5	0.36	< 1	-3.0	2.4	19	-10.5	2.90	51	-19.5	2.60	29
	Ag₃PO₄			P_{1B}¹			P_{0B}¹			P_{2B}²		
	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)
Ag3-3days	+28.5	0.24	27	+2.3	1.400	29	-3.0	1.40	26	-7.9	1.90	18
Fixed parameters: δ_{iso} : Isotropic chemical shift with a tolerance of ± 0.2 ppm, W: Full Width at Half Maximum (Peak width) with a tolerance of ± 0.05 kHz												
Fitted parameter: Int: Integrated intensity $\pm 2\%$												

5-3-3- ICP-OES

The elemental profiles of the glass constituents, boron, phosphorus, sodium and silver, dissolved in milliQ water are plotted in Figure 5-13. In this figure, normalized ion release (NIR) of the glasses as a function of the immersion time in water (see Eq. 2-1). Generally, all elemental concentrations reach a plateau around 10 hours, indicating that they are fully dissolved. Closer inspection of the diagrams shows different dissolution rates.

Figure 5-13a shows the concentration of silver in the dissolving medium for Ag0.5- Ag3. The majority of the glasses is dissolved within 10 hours; however, Ag3 dissolves slower than Ag1. After 4 hours, Ag1 reaches 40% of its total ion release while for Ag3 it is only 8 %. After 10 hours the detected amount of silver in water is ca. 97 and 85 % of their total amount for Ag1 and Ag3, respectively. The dissolution behaviour of these glasses over the full 30-hour experiment is similar in terms of the trend of the silver release.

ICP-OES analysis for boron reveals that in the initial stage of the dissolution, 0.5 to 2 hours, the glass without silver, Ag0, shows a burst in boron concentration. The release of B in water after 2 hours for Ag0 is a magnitude of order higher than that of Ag3. The boron elemental profile of Ag3 is quite different from those of Ag0 and Ag1 in which it is leached into the water with a lower rate. After four hours 13 % of the total boron is detected followed by a linear trend with steeper slopes, indicating a higher dissolution rate from 4 to 10 hours.

Figure 5-14 illustrates that the normalized loss profiles for boron, sodium and phosphorus are similar, with comparable release elemental rates corresponding to dissolution rates. By overlaying the elemental profiles, it is shown that the dissolution behaviour of these three elements is the same in each glass, indicating that the glass dissolution is congruent. NIR values greater than 1 in Figure 5-13 and Figure 5-14 are thought to be related to uncertainties in the preparation and measurements.

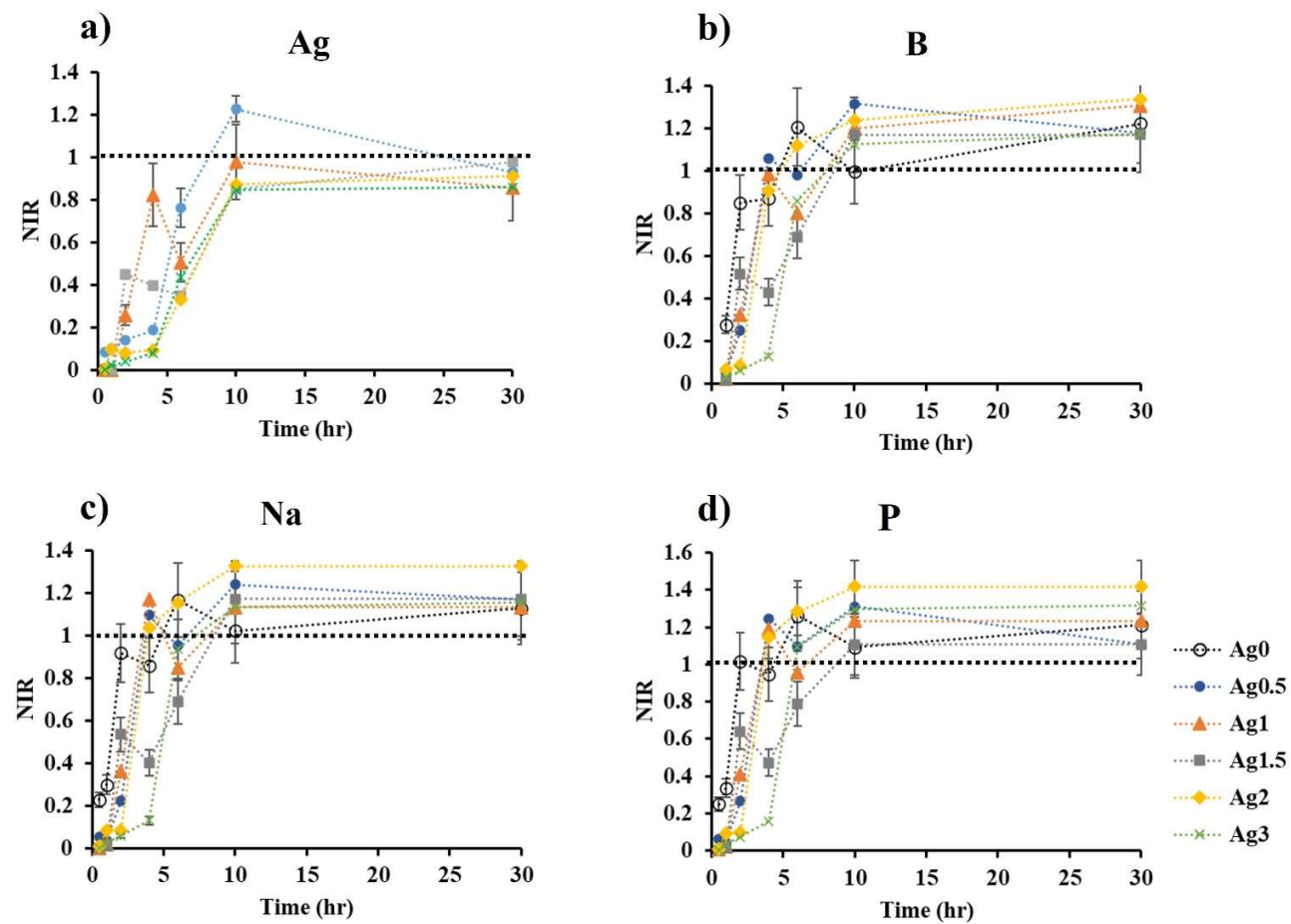


Figure 5-13) Dissolution profiles obtained by inductively coupled plasma ICP-OES: a) Ag, b) B, c) Na and d) P. The horizontal dashed line indicates full dissolution. NIR = normalized ion release

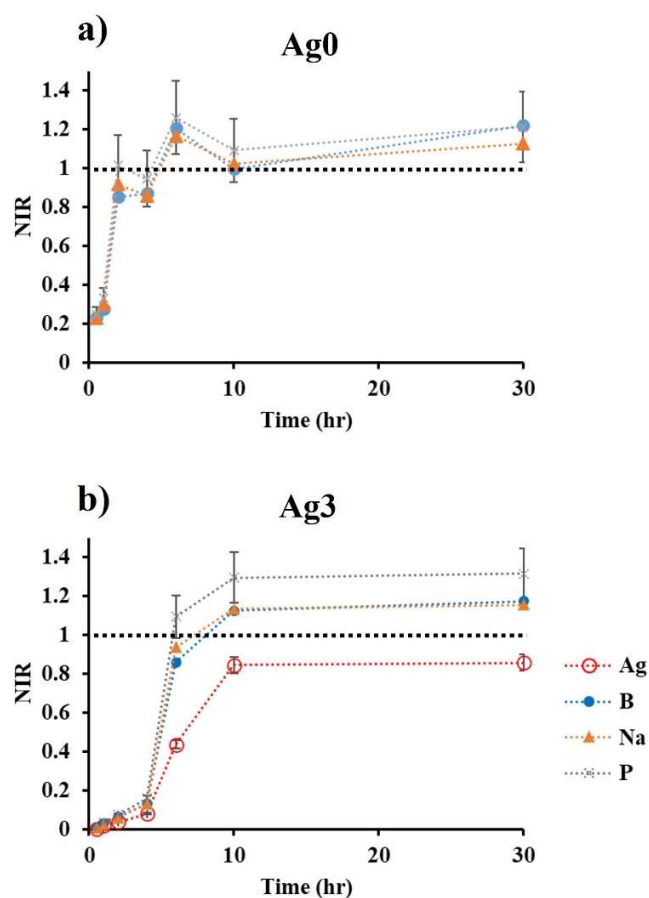


Figure 5-14) Elemental dissolution profiles of a) Ag0 and b) Ag3. The horizontal dashed line indicates full dissolution. NIR = normalized ion release

5-3-4- Mass loss and pH measurements

The change in the pH of the dissolving medium is shown in Figure 5-15. The initial pH of the milliQ water is 7.2, but drops to 6.4 ± 0.1 after an hour. After 2 hours of dissolution Ag1 and Ag3 reach a pH of 6.0, while Ag0 decreases to 6.2 in this time interval. Ag0 shows a slight increase in pH between 2 and 6 hours of the test: the pH changes from 6.2 to 6.4, after which time the pH levels off for the duration of the experiment. The glass containing 3 mol% Ag₂O shows a constant decrease in pH over the first 6 hours of the experiment, after which a marginal rise from 5.9 to 6.1 is observed.

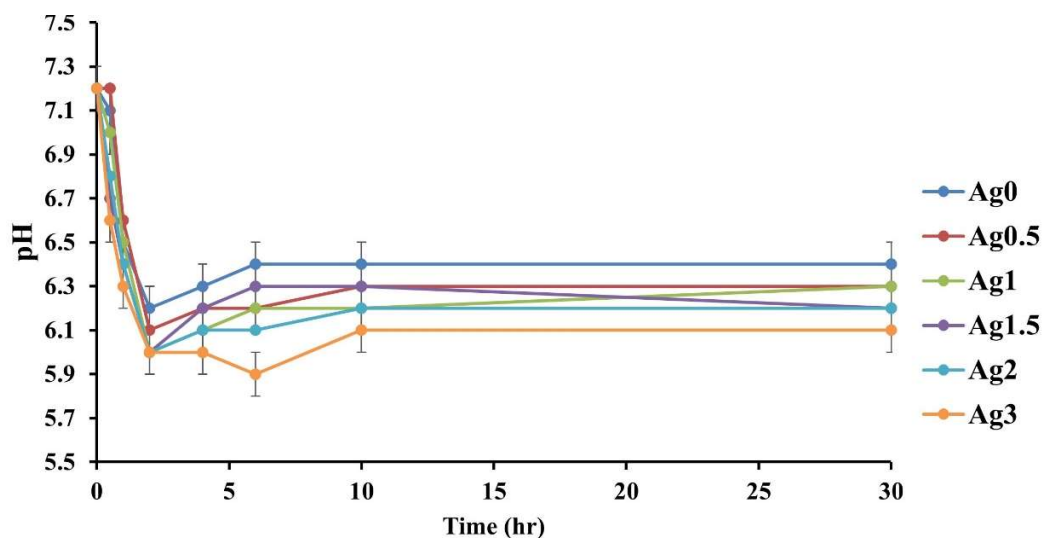


Figure 5-15) pH of the dissolving medium during dissolution study

The mass loss data after 30 minutes and 3 days of dissolution in water are tabulated in Table 5-8. After 30 minutes almost half of the Ag0 glass is dissolved, while this amount is slightly lower for Ag0.5, Ag1 and Ag1.5. However, the mass losses of Ag2 and Ag3 are considerably lower than the glass without silver after 30 minutes: 35 wt% of these samples dissolve into water in half an hour. Whereas Ag0 dissolved completely after three days, a few milligrams of the silver-bearing glasses were retrieved.

Table 5-8) Mass loss of the samples after 30 minutes and 3 days immersing in water

	30 minutes	3 days
Ag0	49.0±2.1	100
Ag0.5	37.5±2.0	99.2±0.5
Ag1	40.5±1.8	98.7±0.5
Ag1.5	40.5±1.5	97.6±1.0
Ag2	35.0±2.4	94.7±2.5
Ag3	35.0±2.0	94.8±1.0

5-4- Discussion

5-4-1- Ag-Doped borophosphate glasses: evidence for amorphous nature

Borophosphate glasses may be considered “mixed-network former” systems in which various connectivities between borate and phosphate structural units exist. The topology in borophosphate glasses depends on the B:P ratio,^{129,184} the type and amount of network modifiers,⁹⁹ as well as the synthesis conditions. In the current glass series, the nominal B:P ratio was kept constant at 1.6 and silver oxide was substituted for sodium oxide up to 3 mol%. The reason for choosing 3 mol% as the upper loading limit is because higher Ag level can be toxic to living tissue in the body, and it has been shown that glasses containing less than 3 mol% Ag₂O pass cell viability tests under various conditions.²³⁰

The lineshapes of the ²³Na MAS NMR spectra are broad and featureless signals characteristic of sodium cations in a disordered environment. Although in this glass series the change in the δ_{iso} is not significant and it is difficult to attribute it to a major change in the structural function of the sodium in the glass, a trend is observed which suggests that a structural alteration is happening. These data confirm that there is no sodium-bearing crystalline phase separation in these glass series. In addition to XRD measurement, this information along with the lack of sharp peaks in ³¹P MAS NMR spectra, which is associated with crystalline phosphate phases, confirms that glasses can be synthesized without crystalline phase separation, which is crucial for therapeutic purposes because the presence of different phases with varying dissolution rates can complicate the dissolution behaviour of the whole system. One of the advantages of the glasses is their ability to accommodate various cations in their composition non-stoichiometrically. This ability enables glasses to be promising candidates for wound healing applications since various therapeutic ions can be doped in them. In this study Ag was doped in the glass up to 3 mol% without phase separation occurs.

5-4-2- Structure of glasses

³¹P NMR spectra of all glasses consist of a broad peak suggesting a disordered chemical environment around the phosphorus atoms. This broadening is characteristic of ³¹P MAS NMR spectra in borophosphate glasses since several overlapping signals assigned to various species exist in the spectrum.

5-4-2-1- Structure of Ag0

Mapping out the network structure of borophosphate glasses requires several constraints to narrow down the number of possible borate and phosphate structural units with overlapping isotropic chemical shifts. Since these constraints are discussed in detail in section 2-4-2, here they will be applied with a brief explanation.

Based on the results of $^{11}\text{B}\{^{31}\text{P}\}$ NMR obtained in chapters 2 and 3, it was concluded that $^{[4]}\text{B}_{2\text{P}}$ and $^{[4]}\text{B}_{3\text{P}}$ have chemical shifts ca. -0.17 and -2.50 ppm, respectively. Therefore, the tetrahedral boron peaks in Ag0 are assigned to these two species. With these assignments the number of B–O–P linkages may be calculated:

$$\begin{aligned}\text{B–O–P} &= 2 \times \text{B}_2\text{O}_3 (\text{mol } \%) \times [\{I(^{[4]}\text{B}_{2\text{P}}) \times 2\} + \{I(^{[4]}\text{B}_{3\text{P}}) \times 3\}] & \text{Eq. 5-1} \\ &= 2 \times 41.3 \times [\{0.54 \times 2\} + \{0.06 \times 3\}] = 104 \text{ per formula unit}\end{aligned}$$

Based on the isotropic chemical shifts of different phosphate species reported in chapter 2, $\text{P}_{2\text{B}}^2$ and $\text{P}_{2\text{B}}^3$ are the most probable phosphate species. The number of P–O–B linkages from ^{31}P MAS NMR calculated based on these species and their corresponding integral intensity should match the number of B–O–P linkages obtained from ^{11}B MAS NMR which is 104.

$$\begin{aligned}\text{P–O–B} &= 2 \times \text{P}_2\text{O}_5 (\text{mol } \%) \times [\{I(\text{P}_{2\text{B}}^2) \times 2\} + \{I(\text{P}_{2\text{B}}^3) \times 2\}] & \text{Eq. 5-2} \\ &= 2 \times 24 \times [\{0.75 \times 2\} + \{0.25 \times 2\}] = 96 \text{ per formula unit}\end{aligned}$$

The above calculations show that there is a good agreement between ^{31}P MAS and ^{11}B MAS NMR results when the number of P–O–B is calculated.

Another constraint is the charge compensation calculations which provide further support for the phosphate assignments. As discussed in chapter 2, in a given glass the amount of negative charge of the anionic species should be balanced by the amount of positive charge provided by Na^+ in Ag0:

$$\begin{aligned}\text{Negative charge} &= 2 \times \text{P}_2\text{O}_5 (\text{mol } \%) [\{I(\text{P}_{2\text{B}}^2) \times 1.5\} + \{I(\text{P}_{2\text{B}}^3) \times 0.5\}] & \text{Eq. 5-3} \\ &= 2 \times 24 \times [\{0.75 \times 1.5\} + \{0.25 \times 0.5\}] = 60\end{aligned}$$

$$\text{Positive charge} = 2 \times \text{Na}_2\text{O} (\text{mol } \%) = 2 \times 34.7 = 69.4 \quad \text{Eq. 5-4}$$

These calculations show that the phosphate assignments are the most probable species in the Ag0 glass which is in line with findings in chapter 2.

5-4-2-2- Structure of Ag_{0.5}-Ag₃

The role of Ag in the glasses can be predicted by noting that its cation field strength (CFS, charge = +1, coordination number = 6) is comparable to that of Na⁺, 0.15 and 0.18 Z/Å², respectively. CFS is a suitable tool employed to predict the roles of various cations as network former, network modifiers and intermediates in oxide glasses. Therefore, the CFS value for Ag⁺ suggests that silver is a network modifier in the oxide glasses.^{231,232} By replacing Na₂O with Ag₂O no changes are observed in the lineshape of [³B] signals of the spectra. By taking into account that NBOs do not exist in the BO₃ units and also Na⁺ does not interact strongly with BO₄⁻ in borophosphate glasses, this observation is expected because silver acts as a network modifier in these glasses.

Alkali and alkaline earth cations show a range of CFS because of their wide range of radii and various charges, i.e., +1 and +2. Therefore, their coordination numbers and subsequently their ability to compensate the negative charges of NBOs in phosphate, borate and silicate glasses differ. This concept is extended to the mixed-network former glasses with a degree of complexity. In silicate glasses, the cations with smaller radii and higher valence, like Mg²⁺, depolymerize the SiO₂ network structure, forming anionic species. The tendency to form more NBOs is ranked in terms of the CFS of the network modifiers as Mg²⁺ > Ca²⁺ > Sr²⁺ > Ba²⁺ > Li⁺ > Na⁺ > K⁺.²³³

In boron-bearing glasses the number of oxygen anions surrounding B is three or four. In fact, in these glasses alkali and alkaline earth cations have another function which is compensating the charge deficit on anionic species like BO₄⁻. Eq. 1 shows the change in the boron coordination number in a binary M₂O-B₂O₃ glass in the presence of the charge compensator:



where BO_{2/2}O⁻ denotes a three-coordinated boron species with one NBO. At high R value, i.e., 0.7, heavier alkali cations stabilize NBOs whereas lighter ones stabilize four-coordinated boron.²⁰ Stebbins et. al.⁴⁴ showed that at low modifier content R<0.45 borate glasses containing sodium calcium and barium have higher N₄ in the order Na⁺ > Ba²⁺ > Ca²⁺ suggesting the enhanced NBO stabilization for the divalent alkaline earth cations.

Binary phosphate glasses have been studied very well in the past few decades. In these types of glasses alkali and alkaline earth cations have been added to the P₂O₅ glass network and the

structural changes inspected by Raman, EXAFS and NMR spectroscopy. Brow et al²³⁴ showed that in metaphosphate glasses, $A_{2/z}O-P_2O_5$ where $A = Na, Li, Ba, Ca, Zn, Mg$ and z is the charge of the cation, phosphorus shielding increases systematically with the CFS of the network modifier. The chain stiffness reported for metaphosphate glasses with higher modifier CFS was attributed to the greater bond ionicity caused by these cations. The statistical analysis of $RO-P_2O_5$ glasses where $R =$ alkaline earth cations, reveals that for compositions in which $RO < P_2O_5$ the averaged phosphate structures of P^2 and P^3 created by network modifiers are independent of the type of RO . However, the CFS of the alkaline earth network modifiers noticeably alters the average bond strength which is reflected in the ^{31}P isotropic chemical shift of the P^n species.²³⁵

Borosilicate glasses are mixed-network-formers systems for studying the effect of network modifiers on the structural changes in the glass. In a recent publication,²³⁶ alkali cations were used to make 16 A_2O -10 B_2O_3 -74 SiO_2 glasses in order to investigate the effect of modifiers with varying CFS on the network connectivity. The T_g measurement in this glass series indicated that glass transition temperature linearly increases with the size of the A_2O cations which is in contrast to borate or phosphate glasses where the higher the CFS the higher the T_g . The fraction of ^{41}B , N_4 , was determined using ^{11}B MAS NMR and it was decreased in the order $Cs > Rb > K > Na > Li$. In addition, ^{11}B NMR showed that the δ_{iso} of four-coordinated boron shifts toward lower frequencies as the size of the alkali cation increases. This observation was attributed to the effect of the network modifiers CFS on the mixing of silicate and borate polyhedral, $Si-O-B$ linkages.²³⁶

It has been shown that the fraction of ^{41}B in a ternary borate glass containing two types of network modifiers is altered by the mixed network modifiers effect.¹⁹⁸ Bray in 1989 showed that the N_4 value in a mixed alkali borate glass is less than either of the N_4 values for the relevant single alkali glasses.¹⁹⁸ Since then, the structure and properties of various ternary borate or ternary silicate glasses have been studied to demonstrate the mixed alkali effect (MAE) in these glasses. However, when the glass contains two network formers, the structure of the glass does not always undergo such changes. In a series of borosilicate glasses containing pairs of Na_2O-K_2O and Na_2O-Rb_2O as the network modifiers with $R (A_2O/B_2O_3) = 4$ and $K (Si_2O/B_2O_3) = 0.75$, ^{11}B MAS NMR results are the same as a ternary $Na_2O-B_2O_3-SiO_2$ glass.²³⁷ However, by changing the R and K to 2 and 2.1, respectively, ^{11}B MAS NMR spectra of the ternary and

quaternary glasses are substantially different.²³⁷ In other work on aluminoborate glasses no change in the network former fraction was observed in BaO-Al₂O₃-B₂O₃ with or without Li₂O, whereas in MgO-Al₂O₃-B₂O₃ glasses containing Li₂O as the second network modifier the fraction of the aluminate and borate unit changed.²³⁸ Although in Reference [234] the absence or presence of the mixed modifier effect (MME) was referred to further study, in the latter example the lack of MME was attributed to the same CFS of Li and Ba cations.

There is no systematic research work on borophosphate glasses to show the effect of network modifier on N₄ values. In the current borophosphate series the addition of Ag to the glasses slightly increases the fraction of the ^[4]B_{3P} and P_{2B}³ which means that the glass containing 3 mol% Ag₂O is marginally more polymerized than the base Ag0 glass. Ag⁺ and Na⁺ (both with CN = 6) also have the same CFS values however a change in the glass structure is observed in the borophosphate glasses containing Ag and Na as the network modifiers. This indicates that CFS alone does not govern the structural role of modifiers. Differences in electronegativity, polarizability, and electronic configuration between Ag and Na also influence the glass structure.²³⁹

Changes in the structure of silver-doped glasses may potentially be attributed to compositional differences rather than the effect of silver on the glass structure. However, the evidence suggests otherwise. First, the changes observed in the ³¹P and ¹¹B MAS NMR spectra with the addition of Ag₂O to the base glass are systematic (Figure 5-3), whereas the variations in the analysed compositions appear to be random (Table 5-2). Second, the initial response of the glass to an aqueous medium differs between Ag0 and Ag3, as reflected in their ICP ion-release data (Figure 5-13). For example, B in Ag3 is released slower than in Ag0 within the first 5 hours.

5-4-3- Structure of the glass after dissolution

Table 5-6 shows the isotropic chemical shifts and quadrupolar coupling constants of the glass series before and after dissolution. By comparing the δ_{iso} and C_Q from the spectra fitted using the CzSimple module,¹⁶⁰ one learns that sodium in the retrieved glasses after 30 minutes dissolution has a different chemical environment in the Ag0 and Ag-bearing glasses. The chemical shift of the sodium, or other network modifiers, in disordered oxide environments is attributed to the coordination size it resides in.²⁴⁰ The lower the chemical shift, the bigger the size of the coordination site (i.e., higher CN). In this glass series generally the δ_{iso} of the samples after dissolution is higher than as-synthesized glasses, which means that the number of the

electrostatic interactions between Na and NBO is lower. This observation is better understood by considering the effect of H^+ in the water-treated glasses. H^+ (or H_3O^+) through hydration of the glass can replace by Na^+ and interact with the NBO. Therefore, the number of the $Na^+ \cdots O^-$ interactions decreases, which means the coordination number of the sodium cations decreases. This is reflected in the higher isotropic chemical shift in ^{23}Na MAS NMR spectra.

The dissolution of B_2O_3 and P_2O_5 in water affects the pH differently. The former increases the pH while the latter decreases it. It should be noted that the first acid dissociation constant K_a for phosphoric acid is 7.1×10^{-3} which makes it a fairly strong acid.²³⁹ Therefore when a borophosphate glass is dissolved in water the pH of the aqueous solution depends on the amount of the phosphate and borate species released into the solution. In addition, the network modifiers play a role in the pH of the solution. Alkali and alkaline earth cations raise the pH because the solvated cations increase the acid dissociation constant of their bound water molecules.²⁴¹ All glasses in the current borophosphate series show a drop in pH which is attributed to H_3PO_4 formation from PO_4^- species released into the aqueous medium. The end point pH in Ag-loaded glasses is slightly lower than in the Ag-free glass. This is because of the lower acid dissociation constant of Na in comparison with Ag.²⁴¹ In other words, the solvated sodium cations in water increase the pH more than silver cations. Therefore, the solution containing Ag3 glass which is loaded with 3 mol% Ag_2O , is more acidic than the silver free glass, Ag0.

Ag2 and Ag3 glasses are less soluble than Ag0 in 30 minutes and after a 3-day dissolution period: Ag0 was dissolved completely while ca. 10 mg (4%) Ag2 and Ag3 was collected. Although discussing the presence of mixed modifier effect in the current glass series is challenging based on the discussion in section 5-4-1-2, the relatively higher durability of these glasses can be linked to the MME in these glasses. It has been shown that the chemical durability of glasses containing different types of cations is enhanced.²⁴² On the other hand, doping sodium borophosphate glasses with Ag_2O shows a trend of increasing connectivity in the glasses based on the NMR results. Whether the change in the structure of the glasses with silver loading is related to the MME or not, the increased chemical durability reflects higher network connectivity.

Glasses dissolve congruently or incongruently based on their compositions. The degradation of the silicates and borosilicates is incongruent because the ion leaching into the aqueous medium is preferential.²⁴³ In other words, the dissolution profiles of the constituents is not

identical. However, borate and borophosphate shows congruent dissolution behaviour. The current glass series does not show any preferential leaching as it can be seen in the ICP-OES profiles. This behaviour is crucially important for bioglasses applicable in soft tissue regeneration particularly in wound healing. In this type of degradation, the glass is homogeneously dissolved into the wound site and all therapeutic ions are delivered to the desired place.

This glass series has the same N_4 values before and after 30 minutes of dissolution. By comparing the before and after dissolution ^{31}P MAS NMR spectra, homogeneous degradation of the glass is observed since the glass structure does not undergo substantial alteration. However, the Na^+ and H^+ exchange during dissolution causes a rearrangement in the glass structure. H^+ has a CFS substantially different from alkali and alkaline earth cations. Additionally, when the glass is in contact with water the amount of H^+ is abundant, hence the change in the structure of the remaining glass is expected. The different physical properties of the X–O–Y linkages in a borophosphate also are a factor which affects the dissolution behaviour. As shown in chapter two the glasses containing $^{[4]}\text{B}_{4\text{P}}$ show higher durability. In other work it has been shown that glasses containing a greater number of P–O–B linkages are mechanically superior to glasses with a smaller number of these bonds.⁹⁸ Analogously, it is expected that these bonds are less susceptible to hydrolysis.

^{31}P MAS NMR of the remaining Ag3 after 3 days dissolution shows that it is a combination of crystalline Ag_3PO_4 and residual glass. The sharp peak at +28.5 ppm is attributed to Ag_3PO_4 which is most probably the reprecipitation product.²²⁹ The broad peak centred at 0 ppm indicates the amorphous nature of the leftover. ^{23}Na MAS NMR of this sample is a broad signal with no sharp signal superimposed on it. This means that sodium did not incorporate into the reprecipitated phosphate compound remains in the glassy portion of the collected sample.

In this chapter in a borophosphate glass series, replacing Na_2O with Ag_2O does not alter the lineshape of the $^{[3]}\text{B}$ signal, which is consistent with expectations since BO_3 units do not contain NBOs and Na^+ has only a limited interaction with BO_4^- . This supports the conclusion that Ag_2O acts as a network modifier in these systems. The unaltered ^{23}Na MAS NMR chemical shift observed for silver-free and silver-containing samples further supports this point.

In the silver-free glass, the boron environments are primarily $^{[4]}\text{B}_{2\text{P}}$ and $^{[4]}\text{B}_{3\text{P}}$. ^{31}P MAS NMR analysis shows that $\text{P}_{2\text{B}}^2$ and $\text{P}_{2\text{B}}^3$ are the main phosphate species. Upon doping with Ag_2O ,

the integrated intensity of $^{[4]}\text{B}_{3\text{P}}$ increases at the expense of $^{[4]}\text{B}_{2\text{P}}$. Phosphate environments are also slightly modified, with change in the integrated intensity of $\text{P}_{2\text{B}}^3$ from 25% in Ag0 to 35% in Ag3. Together, these changes suggest that silver incorporation enhances the degree of network connectivity.

This structural conclusion is consistent with the dissolution behavior of the glasses in water. The Ag2 and Ag3 glasses show slightly lower dissolution rates compared to Ag0: while Ag0 dissolves completely within 3 days, 2-3% of Ag2 and Ag3 remain undissolved. This enhanced durability is likely linked to the increased network connectivity in the Ag-doped glasses. Another possible explanation is the mixed modifier effect, which, although challenging to confirm experimentally, may also contribute to the improved chemical durability observed.

Patients with chronic and infected wounds may require external support for weakened immune systems. While traditional treatments like collagen dressings and vacuum therapy exist, bioactive glasses offer a simpler and controllable alternative. Conventional treatments struggle to fully restore native skin anatomy, whereas advancements in bioactive glasses show promise for complete tissue regeneration.⁶⁵ Additionally, with growing antibiotic resistance, alternative antimicrobial solutions are needed. Therefore, silver-doped borophosphate glass emerges as a promising candidate for biomedical applications, offering lack of antibiotic resistance. Although the impact of possible reprecipitation of crystalline phases during dissolution in aqueous media on wound healing remains controversial, it is recommended to avoid glasses with a P:B ratio greater than 1.5. Additionally, fibrous glasses may demonstrate higher efficacy in clinical settings due to their high surface area

5-5- Appendix

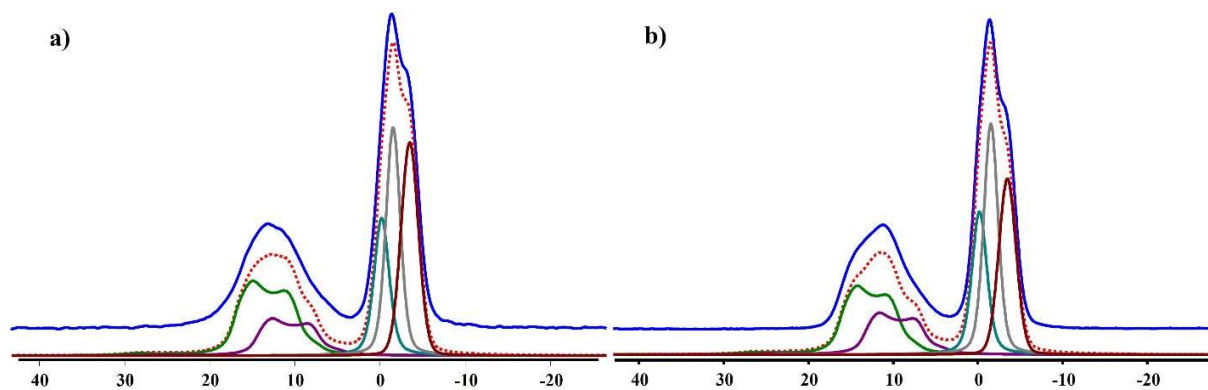


Figure 5-16) ^{11}B magic angle spinning (MAS) NMR spectrum of P30 (20 Na₂O – 30 P₂O₅ – 50 B₂O₃ (mol%)) made on a) September 2022 and b) April 2020.

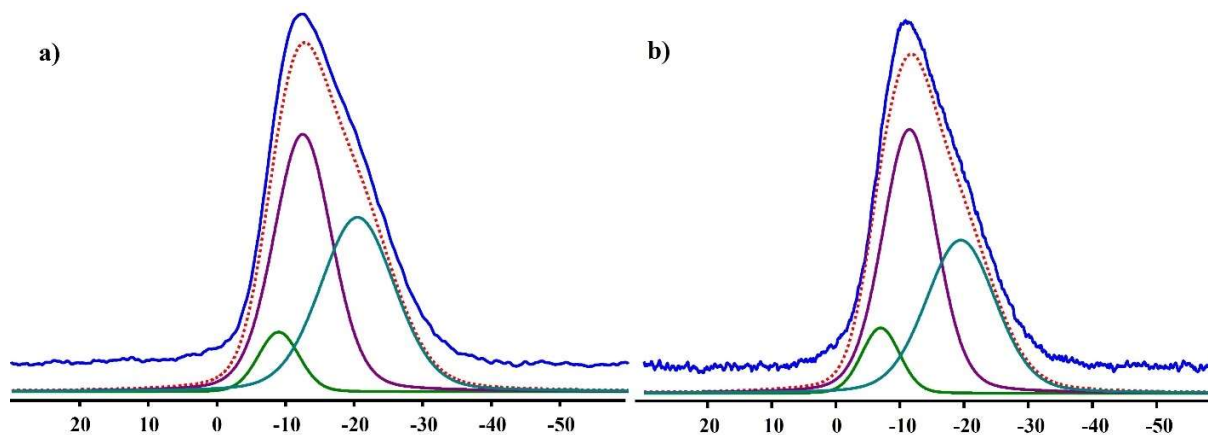


Figure 5-17) ^{31}P magic angle spinning (MAS) NMR spectrum of B20 (40 Na₂O – 40 P₂O₅ – 20 B₂O₃ (mol%)) made on a) February 2022 and b) September 2016.

Table 5-9) Parameters used for fitting ^{11}B magic angle spinning (MAS) NMR spectra

	^{13}B						^{14}B								N_4
	$^{13}\text{B}_{\text{ring}}$		$^{13}\text{B}_{\text{non-ring}}$		$^{14}\text{B}_{2\text{P}}$		$^{14}\text{B}_{3\text{P}}$			$^{14}\text{B}_{4\text{P}}$					
	δ_{iso} (ppm)	Int. (%)	δ_{iso} (ppm)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso}	W (kHz)	Int. (%)	δ_{iso}	W (kHz)	Int. (%)		
P30- a	17.5	28	15.2	12	-0.2	0.40	15	-1.5	0.24	23	-3.5	0.46	22	0.60	
P30- b	16.8	26	14.0	14	-0.2	0.40	16	-1.5	0.24	22	-3.5	0.46	20	0.60	

Table 5-10) Parameters used for fitting ^{31}P magic angle spinning (MAS) NMR spectra

	$\text{P}_{1\text{B}}^2$			$\text{P}_{2\text{B}}^2$			$\text{P}_{2\text{B}}^3$		
	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)	δ_{iso} (ppm)	W (kHz)	Int. (%)
B20-2016	-7.0	1.70	9	-12.0	2.50	52	-19.5	3.10	39
B20-2022	-8.0	1.70	7	-13.0	2.50	50	-20.5	3.10	43

6- Conclusions and future directions

6-1- Conclusions

The focus of this thesis research was to investigate the relationship between the structure of borophosphate glasses and their dissolution behaviour in aqueous media. Various borophosphate glasses with different B/P ratio were synthesized by melt-quenching techniques. Multinuclear solid-state NMR was the primary tool to disclose the structure of the borophosphate glasses. Other complementary techniques such as XRD, SEM and ICP were used to understand the chemistry of glasses before and after exposure to aqueous solution. Taken together, the individual projects presented in this thesis lead to several general conclusions.

In a series of sodium borophosphate glasses, the fraction of four-coordinated boron increases linearly with boron content, which contrasts with the well-known boron anomaly observed in binary borate glasses. This trend suggests that the formation of $^{[4]}\text{B}-\text{O}-\text{P}$ linkages plays a significant role in facilitating the coordination change of boron from trigonal to tetrahedral. In this mechanism, the additional negative charge associated with the anionic $^{[4]}\text{B}$ species is likely delocalized across the $\text{B}-\text{O}-\text{P}$ bonds, thereby stabilizing the tetrahedral environment.

The formation of multiple borate and phosphate species in borophosphate glasses gives rise to a wide range of connectivity among the network-forming polyhedra. In this thesis, a systematic approach combining experimental techniques—such as double-resonance NMR—with theoretical tools—including Pauling bond strength analysis and charge compensation calculations—is employed to identify the most probable structural units present in the glass network. Although borophosphate glasses have been previously studied, a comprehensive methodology for structural mapping under multiple constraints remains largely absent from the literature.

This thesis demonstrates that the concentration of network modifiers plays a critical role in determining the medium-range order of borophosphate glasses. In binary borate and phosphate glasses, it is well established that Na^+ compensates for the negative charges associated with anionic species such as $^{[4]}\text{B}$ and P^2 units. However, in borophosphate systems, the interaction between sodium ions and these anionic species is strongly influenced by the sodium content. The charge distribution within $\text{B}-\text{O}-\text{P}$ linkages varies significantly between glasses with low sodium

content ($\text{Na}_2\text{O} < 20 \text{ mol}\%$) and those with high sodium content ($\text{Na}_2\text{O} > 40 \text{ mol}\%$). In sodium-deficient compositions, the negative charge of $^{[4]}\text{B}$ units is delocalized across the $\text{B}-\text{O}-\text{P}$ linkages, indicating a more complex mechanism of charge compensation.

One of the key implications of the diverse $\text{X}-\text{O}-\text{Y}$ connectivity in borophosphate glasses is its influence on dissolution behavior. In a $\text{CaO}-\text{Na}_2\text{O}-\text{P}_2\text{O}_5$ glass system,¹¹⁷ for example, ^{31}P solution NMR has shown that P^3 units are released first, followed by P^1 and P^0 , depending on the dissolution medium. In contrast, the borophosphate glass series studied in this thesis consistently shows that P^0 is released first, followed by P^1 and P^2 , with the sequence depending on composition. This difference arises from the influence of heteropolar ($\text{B}-\text{O}-\text{P}$) and homopolar ($\text{P}-\text{O}-\text{P}$) linkages on the dissolution mechanism.

Additionally, the medium-range structural diversity of borophosphate glasses contributes to a wide range of dissolution rates, which differ significantly from those of binary borate glasses. We show that in borophosphate systems, the concentration of $^{[4]}\text{B}_{4\text{P}}$ species plays a key role in determining glass durability, the resistance of glass to water corrosion, in aqueous environments. For instance, sodium borophosphate glasses with the particle size of $100\text{-}180 \mu\text{m}$ lacking $^{[4]}\text{B}_{4\text{P}}$ can dissolve in as little as 15 minutes, while glasses with a high concentration of $^{[4]}\text{B}_{4\text{P}}$ may take up to a week to dissolve completely. This tunable dissolution behaviour is highly advantageous in biomedical applications. It allows for the design of materials with tailored ion release profiles, enabling therapeutic delivery to wound sites at different healing stages. Moreover, the congruent dissolution observed – evidenced by elemental profiles from ICP-OES and post-dissolution NMR analysis – further supports the potential of these glasses as promising candidates for wound healing applications.

In borate glasses, dissolution is primarily governed by the N_4 ratio, as $^{[3]}\text{B}$ species require less energy for hydrolysis than $^{[4]}\text{B}$ species,²⁰⁰ leading to faster dissolution in $^{[3]}\text{B}$ -rich glasses. In a series of phase-separated glasses, we show that phase separation further accelerates dissolution by increasing phase boundaries and interfacial energy. The rapid dissolution rate of P10, containing 10 mol% P_2O_5 , is explained by its N_4 value and ICP-OES elemental profiles. In P5, containing 5 mol% P_2O_5 , competing factors—higher $^{[4]}\text{B}$ content (slowing dissolution) and increased phase boundaries from phase separation (accelerating dissolution)—determine degradation behaviour. ^{11}B MAS NMR confirms that phase boundaries dominate, making P5

dissolve faster than P0–P4, despite similar ^{41}B content. This study may help developing glass-ceramics for new applications where both soft- and hard-tissue regeneration is required, e.g., tendon to bone fracture. In addition, in this project the composition of the glassy and crystalline phases of the samples is estimated by ^{31}P MAS NMR. Since NMR is a quantitative technique, the fraction of the crystalline phase was calculated by considering the integral intensity of the fitted ^{31}P MAS NMR spectra.

Silver as a therapeutic cation is successfully doped into a borophosphate glass system to develop a potential bioactive glass with enhanced antibacterial properties for wound healing applications. Up to 3 mol% Ag_2O is incorporated without inducing phase separation, maintaining a homogeneous glass structure. The slight increased in glass durability observed may be attributed to an increased network connectivity. However, the mixed-modifier effect is another possible explanation for this observation. Although confirming the presence of MME is challenging, the enhanced durability of these glasses suggests its influence. Both silver-free and Ag-loaded glasses demonstrate congruent dissolution behavior, with over 98% of the material (particle size of 100-180 μm) dissolving within three days, indicating high solubility. These findings suggest that Ag-doped borophosphate glasses serve as promising candidates for wound healing applications, offering sustained antibacterial activity without the risk of antibiotic resistance commonly associated with conventional treatments.

In this thesis research, various tools are utilized to investigate the structure of the glasses including solid state NMR, charge compensation calculation and Pauling Bond Strength theory. In other to further validate our conclusions drawn by the above-mentioned tools, dipolar-based double-resonance NMR methods were employed to portray the glass structure. To study complex sodium aluminoborophosphate glasses, REDOR, REAPDOR and R-INADEQUATE were used in elucidating connectivity in glasses. $^{11}\text{B}\{^{31}\text{P}\}$ REDOR confirmed that $^{41}\text{B}_{3\text{P}}$ and $^{41}\text{B}_{4\text{P}}$ forms the dominant borate species. $^{27}\text{Al}\{^{31}\text{P}\}$ REDOR, $^{31}\text{P}\{^{27}\text{Al}\}$ REAPDOR and ^{31}P R-INADEQUATE suggest the phosphate network in alumiophosphate glass primarily consists of $\text{P}_{3\text{Al}}^3$ and $\text{P}_{2\text{Al}}^3$ units in a 1:3 ratio, corresponding to $\text{Na}_3\text{Al}_2(\text{PO}_4)_3$ and $\text{Na}_6\text{Al}_2(\text{P}_2\text{O}_7)_3$ compositions. The glass transition temperatures vary with B_2O_3 content.

6-2- Future directions

Throughout this research, significant insights have been gained into the structure, dissolution behaviour, and properties of borophosphate glasses. However, several questions remain unanswered, highlighting opportunities for further investigation.

6-2-1- Stability of silver-containing glasses in biological environments

The stability of silver-containing glasses in biological environments warrants further investigation. While this study has demonstrated the promising potential of silver doping for soft-tissue regeneration, its behaviour over extended periods in simulated body fluids (SBF) or in actual biological conditions has not been tested. Future research should focus on examining the leaching kinetics, biocompatibility, and potential antimicrobial effects of silver ions over prolonged exposure, ensuring that these glasses maintain their desired properties without unwanted side effects. In this thesis, a series of borophosphate glasses with B/P ratio of 1.6 and a modifier content of 35% was studied. It is suggested that further work also examine borophosphate glasses with $B/P < 1$ and varying modifier contents.

6-2-2- Glass forming ability of borophosphate glasses

There is a lack of comprehensive work on the glass forming ability of borophosphate glasses, and the reasons behind phase separation in these glasses remain unclear. While phase separation has been well-investigated in silicate and borosilicate glasses, its role in borophosphate glasses has not been fully explored. Understanding why phase separation occurs in these materials and how it affects their properties is crucial. NMR could play a key role in answering these questions, as it is highly sensitive to the local environment of different atomic species. By analyzing the local coordination and connectivity of boron, phosphorus, and other cations, NMR can provide insights into the structural differences between the phases and their influence on the overall behaviour of glass.

6-2-3- Alternative dopants and therapeutic cations including Sr and Zn loaded glasses for biomedical applications

Strontium promotes soft tissue regeneration and wound healing by enhancing fibroblast proliferation,⁶⁵ stimulating growth factors and reducing inflammation. These properties make strontium a promising agent for improving chronic wound healing. Zinc plays a crucial role in wound healing by supporting keratinocyte and melanocyte proliferation, stabilizing immune cell

function, and enhancing the activity of key enzymes involved in tissue remodeling.⁶⁵ Its anti-inflammatory and antibacterial properties further aid in promoting faster recovery of chronic wounds. From the structural role of these cations in the glasses, this study could provide more insight into the role of the Zn in borophosphate glasses since it can adopt either role of the network modifier or network former based on the composition of the glass. On the other hand, Sr remains as a network modifier in the entire range of the composition of the glass. Understanding how these two potential therapeutic glass dopants influence the structure, and properties would provide valuable information on designing bioactive glasses with tailored degradation rates and ion release profiles to optimize their performance in soft-tissue regeneration and wound healing applications.

6-2-4- Computation and simulation

Computational methods such as Density Functional Theory (DFT) can be valuable tools for investigating medium-range order in borophosphate glasses. The complexity of these glasses, with their diverse structural units, makes it challenging to fully determine the medium-range order using NMR alone. DFT calculations can provide insights into the local environments and bonding interactions, helping to complement NMR data and refine our understanding of the glass structure by predicting chemical shifts of different components. Therefore, phosphate and borate assignments can be done less ambiguously. This combination of computational and experimental techniques could enhance the characterization of borophosphate glasses, enabling more precise design for specific applications.

These suggested studies aim to address several key open questions, including the roles of network modifiers and the long-term stability of specific dopants on the properties of borophosphate glasses. By investigating these factors, we can gain deeper insights into the structural and chemical behaviour of these glasses, allowing us to optimize their performance for soft tissue regeneration applications. This enhanced understanding will ultimately contribute to the development of more effective and tailored materials for wound healing, tissue repair, and other biomedical uses.

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