INTRODUCTION

Based on the increasing number of diseases, injuries and trauma and the limitations associated with current standard therapies, research is progressing in the field of tissue engineering (TE) to develop alternative ways to repair and regenerate damaged tissue.1-5 Bone TE typically involves a porous scaffold, used as temporary support for cell attachment, possibly combined with growth factors and other biomolecules to improve cellular functions during the regeneration process.6-8

Bioactive glasses (BGs) are attractive candidates for filling bone defects due to their bioactive properties, characterized by the ability to support the proliferation and differentiation of bone cells and to form a strong bond to bone.9-12 Moreover, the possibility to fabricate scaffolds or fibers from BGs makes them interesting for bone TE.13 The first BG composition, invented by Hench and co-workers, consists of 45 Si2O-24.5 CaO-24.5 Na2O-6 P2O5 (in wt%) and is well-known as the 45S5 composition.13 Compared to other BG compositions, 45S5 BG has been the most used BG in biomedical applications and in
research so far. However, when sintering 45S5 BG particles into porous scaffolds, the crystallization at temperatures of 600–700°C prevents maximum densification and thus makes difficult the manufacture of (amorphous) scaffolds with adequate mechanical properties. One explored approach to reduce the tendency of glasses to crystallize has been through exploiting the so-called mixed-alkali effect by introducing several alkaline earth oxides and alkali oxides simultaneously in the glass. This approach was successfully utilized in the development of the 13-93 BG composition, composed of 53% SiO\textsubscript{2}-6 Na\textsubscript{2}O-12 K\textsubscript{2}O-5 MgO-20 CaO-4 P\textsubscript{2}O\textsubscript{5} (in wt%).

A key property of the 13-93 and 45S5 BG compositions (as well as other BG compositions) is their ability to form an amorphous calcium phosphate or hydroxyapatite surface layer during degradation. Since the content of the network forming oxides in BGs is lower than in conventional (e.g., soda-lime) glasses, BGs exhibit an open network structure, which allows water molecules to easily interact with the BG network. The dissolution process, as described by Hench et al., starts with an ion exchange of Ca\textsuperscript{2+}/Na\textsuperscript{+} with H\textsuperscript{+} from the solution at the interface of the dissolution medium and the BG. This leads to an increase in the local alkalinity, resulting in the formation of a silica-rich layer on the BG surface and a pH increase of the medium. Due to the high local pH, more silanols get incorporated in the silica-rich layer, which is further repolymerized. Calcium and phosphate ions then migrate from the BG through the silica-rich layer and form, together with calcium and phosphate ions from the solution, an amorphous calcium phosphate layer on top of the silica-rich layer. This layer crystallizes subsequently to hydroxyapatite. However, due to the initial formation of the silica-rich layer, 13-93 and 45S5 BGs can (depending on the used form, e.g. particles, disks, etc.) convert slowly (and incompletely) to HA.

To overcome the relatively reduced HA conversion, particularly in the 13-93 silicate composition, borate BGs have been developed. In the case of borate BGs, the glass network is formed by boron trioxide instead of silica. Borate BGs are promising alternatives to silicate BGs due to their faster degradation rate (based on their lower chemical durability) and their complete conversion to hydroxyapatite. The formation of hydroxyapatite and therefore the resulting (complete) conversion of borate BGs to hydroxyapatite are similar to the described steps of hydroxyapatite formation of silicate BGs. The main difference is that no initial formation of a silica-rich layer occurs. Moreover by partially replacing SiO\textsubscript{2} by boron-trioxide, different borosilicate BGs based on the 13-93 composition have been developed showing that the dissolution rate as well as the hydroxyapatite formation can be tailored by varying the relative content of B\textsubscript{2}O\textsubscript{3}. Since the (partial) replacement of silica by boron-trioxide has great influence on the thermal, structural and mechanical properties of BGs and therefore also on the properties of scaffolds fabricated out of these BGs, the structural changes occurring in silicate, borosilicate and borate BGs need to be examined. However, especially in the case of borosilicate BGs containing three different network formers (silica, phosphorus pentoxide, and boron trioxide), the structure is quite complex and challenging to analyze. In general, boron in BGs is either four- or three-fold coordinated. In a previous research, it was found that low amounts of B\textsubscript{2}O\textsubscript{3} are present in the form of [BO\textsubscript{4}] structural units, which leads to a rigid and more cross-linked structure. If higher amounts of boron are introduced in the glass structure, metaborates transform into pentaborate in the form of [BO\textsubscript{3}] units, leading to a more distorted and fragile glass structure. Moreover a lower resistance to hydrolysis with increasing boron trioxide content could be found (resistance against hydrolysis: Si-O-Si>Si-O-B>B-O-B). Besides the new short-range order species ([BO\textsubscript{4}] or [BO\textsubscript{3}] structural units), the intermediate-range associations (e.g., Si-O-B, P-O-B linkages) additionally increase the complexity of the glass structure.

The objective of this study was to characterize the glass structure of silicate, borosilicate and borate BGs based on a composition close to 13-93 BG and to investigate the effect of the changed glass structure on the properties of silicate, borosilicate, and borate glass scaffolds. Since the morphology and mechanical properties are crucial for the success of a scaffold in bone TE, in this study these properties were examined and related to the glass composition. Moreover by dissolution tests using simulated body fluid, the scaffolds' degradation rate and their ability to form hydroxyapatite on their surfaces were investigated. The results should provide an informed approach to design suitable B-containing BGs for scaffold fabrication and can be used as a guidance to develop tuned BG compositions for applications in both bone and soft TE.

## 2 MATERIALS AND METHODS

### 2.1 Glass fabrication

Silicate (13-93-based), borosilicate (13-93-BS), and borate (13-93-B) BGs based on a composition close to 13-93 BG were fabricated using the melt-quenching method. In case of 13-93-B BG, 56.6 wt% of SiO\textsubscript{2} was replaced by 56.6 wt% of B\textsubscript{2}O\textsubscript{3} and in case of 13-93-BS BG, 36.6 wt% of B\textsubscript{2}O\textsubscript{3} and 20 wt% of SiO\textsubscript{2} were used. It should be noted that the silicate BG is based on the 13-93 BG composition (mentioned in the Introduction), with slight modification in order for the respective borate composition to be the well-known 13-93B3 BG reported in literature. Analytical grade reagents, including H\textsubscript{3}BO\textsubscript{3}, Na\textsubscript{2}CO\textsubscript{3}, K\textsubscript{2}CO\textsubscript{3}, MgO, CaCO\textsubscript{3}, (CaHPO\textsubscript{4}) (2(H\textsubscript{2}O) (all from Sigma-Aldrich), and Belgian quartz sand were used. Melting was performed in a platinum crucible at 1360°C for 3 h (13-93-based BG), at 1050°C for 2 h (13-93-B) and at 1100°C for 3 h (13-93-BS). Subsequently, all BGs were casted and annealed (at 520°C). Melting was performed twice to ensure homogeneity.
obtained BGs were then milled using a zirconia planetary mill (Retsch GmbH, Germany) to a fine powder with an average particle size of 5–20 μm. The final compositions of the fabricated BGs in wt.% and mol.% are shown in Table 1.

### 2.2 Glass characterization

The obtained BG powders were characterized using X-ray diffraction (XRD) analysis (Miniflex 600 HR, Rigaku, Japan) to ensure that amorphous materials were obtained. The powders were analyzed directly after milling (particle size 5–20 μm), no further preparation was done. Data were collected over a 20° range from 20° to 60° with a step size of 0.02°.

Measurements in the middle infrared (MIR) were carried out using a Bruker Vertex 70v vacuum spectrometer. Samples were prepared using the standard KBr pellet method. 128 scans were accumulated with a resolution of 4 cm⁻¹.

Raman studies were executed using Witec Alpha 300 M+ spectrometer. 1800 grating and 100x ZEISS objective were employed for the measurements. Each sample was measured for approx. 15 minutes (two accumulations for 7 minutes each). Spectra were normalized and de-spikes filter was applied using Witec Project FIVE PLUS software. Raman spectra deconvolution was carried out using Bruker OPUS 7.2 software. Levenberg marquardt iteration algorithm with a starting ratio of 0.5 set of Gaussian-Lorentzian peaks was used. The highest value of local residue RMS error was recorded at approx. 2.

High-resolution, solid-state magic angle spinning nuclear magnetic resonance spectroscopy (MAS-NMR) spectra were measured using the APOLLO console (Tecmag) and the 7 T/89 mm superconducting magnet (Magnex). A Bruker HP-WB high speed MAS probe equipped with the 4 mm zirconia rotor and the KEL-F cap was used to spin the sample.

The ³¹P MAS-NMR spectra were measured at the 121.264 MHz resonance frequency, spinning the sample at 8 kHz. A single 2 μs rf pulse, corresponding to π/2 flipping angle was applied. The acquisition delay in accumulation was 20 s, and 256 scans were acquired. The ppm frequency scale was referenced to the ³¹P resonance of TMS (Tetra-Methylo-Silane). The peak fitting of the ³¹P MAS-NMR spectra was performed by an automatic procedure, without introducing any a priori assumptions about the line positions or their widths. The minimum number of components that produces satisfactory residuals was chosen.

The ¹¹B MAS-NMR spectra were measured at the 96.11 MHz resonance frequency, spinning the sample at 10 kHz. A single 2 μs rf pulse, corresponding to π/4 flipping angle in the liquid was applied. The acquisition delay in accumulation was 1 s, and 256 scans were acquired. The Boron-11 nucleus is quadrupolar, therefore the NMR line positions depend both on the chemical shift and the second order quadrupolar shift, which is magnetic field dependent. The lines assignment was based on their shapes, which are sensitive to the symmetry of the electric field present in the lattice. The symmetry of the tetragonal BO₄ site is higher, leading to smaller quadrupolar interaction and narrower line. The ¹¹B line positions for BO₄ and BO₃ sites are typical for the ¹¹B spectra of inorganic glasses taken at the magnetic field of 7 T. The ppm frequency scale was referenced to the ¹¹B resonance of 1 mol H₃BO₃.

### 2.3 Scaffold fabrication

Borate, borosilicate and silicate BG scaffolds were produced by the foam replica technique using cylindrical polyurethane (PU) foams (45 ppi, Eurofoam Deutschland GmbH Schaumstoffe) with a height and diameter of 6 mm (for compression tests, foams of 12 mm height and diameter were used). The slurry used to produce silicate scaffolds was prepared by dissolving 0.6 wt.% polyvinyl alcohol (PVA) in distilled water at 80°C. After cooling down the PVA solution, glass powder was added in a ratio 1:1 (weight ratio) to the solution and stirred for 1 hour before further use. In case of borate (13-93-B) and borosilicate (13-93-BS) scaffolds, instead of PVA, 0.6 wt.% of ethyl cellulose was used as binder and dissolved in ethanol instead of water (due to the poor resistance of boron containing BG to dissolution in water). Then, 13-93-BS or 13-93-B BG powder was added to the ethyl cellulose-ethanol solution in a ratio 1:1 (weight ratio) and stirred for another hour. For all scaffolds, PU foams were dipped for 1 min in the respective slurry. Then, the foams were taken out, the extra slurry was manually squeezed out and the foams were dried at 60°C for 1 h. Afterwards, the dip coating procedure was repeated once
and the foams were dried overnight at 60°C. After drying, the obtained green bodies (coated foams) were heat treated to burn out the PU foam (400°C for 1 h) and to sinter the different scaffolds (1 h at 700°C [silicate 13-93-based], 600°C [13-93-BS], and 560°C [13-93-B]), with a heating rate of 2°C per min.

### 2.4 Scaffold characterization

Scanning electron microscopy (SEM) analysis (Auriga 0750, Zeiss, Oberkochen, Germany) was performed in order to investigate the morphology of the different scaffolds. BG scaffolds were fixed on a sample holder by carbon tape. The SEM was operated at 1 kV and working distance of 2 mm. The porosity of the different foams was calculated based on the measured density of the solid glass ($\rho_{\text{solidBG}}$) according to the Archimedean principle:

$$\rho_{\text{solidBG}} = \frac{m_{\text{mass air}}}{m_{\text{mass air}} - m_{\text{mass water}}} \times \rho_{\text{water}}$$

and using the following formula:

$$\text{porosity} = (1 - \frac{m}{\rho_{\text{solidBG}} \times \text{volume}}) \times 100$$

The mean scaffold porosity was calculated based on 10 different samples. Additionally, XRD and Fourier Transform Infrared Spectroscopy (FTIR, Nicolet 6700, Thermo Scientific, Germany) measurements were done. Prior to FTIR and XRD measurements, scaffolds were crushed and milled using a mortar to obtain a fine powder. XRD analysis was carried out using a diffractometer (MiniFlex 600 HR, Rigaku, Japan) over a 2θ range from 20° to 60° with a step size of 0.02°. FTIR spectra were collected with a resolution of 4 cm$^{-1}$ and in the range of 4000 to 550 cm$^{-1}$. The mechanical properties of the different scaffolds were tested using a universal testing machine (Instron 5960, Germany). 10 cylindrical samples of each scaffold type were tested using a speed of 5 mm/min and a load cell of 1 kN. In order to assess the dissolution profile and the acellular bioactivity of the fabricated BG scaffolds, samples were immersed in simulated body fluid (SBF) according to the protocol of Kokubo et al.$^{56}$ for 3, 7 and 14 days. After the different immersion times, the pH of the SBF was recorded and the concentration of released ions was determined using optical emission spectroscopy with inductively coupled plasma (ICP-OES, Plasma 40, Perkin Elmer, USA) following the standards PN-EN ISO 11885:2009. In order to stabilize the collected SBF solutions after immersion tests, the solutions were acidified using 1 mL of 1 M nitric acid to a pH of 2. The collected scaffolds after immersion in SBF were weighed and further characterized using FTIR, SEM and XRD.

### 3 RESULTS

#### 3.1 Characterization of BGs

In order to confirm the amorphous structure of the studied materials, XRD analyses were carried out. As shown in Figure 1, the silicate 13-93-based BG shows a hump centered at ~30° 2θ and the boron-containing 13-93-B and 13-93-BS BGs show two humps centered at ~30° and ~45° 2θ, which are typical for amorphous silicate, borosilicate, and borate BGs, as reported elsewhere.$^{32,33,57}$ None of the fabricated BGs showed any significant crystallization peaks, proving their amorphous nature (although it should be mentioned that the XRD pattern is quite noisy and small peaks might be not visible). The short range order of the different glass structures was investigated. Best suited for this task are spectroscopic methods, especially mid-infrared (MIR), Raman and MAS NMR spectroscopy. The lack of long-range ordering in spectroscopic methods is manifested by a significant broadening of the signals, which results in an overlapping of individual bands and therefore hinders or even prevents precise interpretation. Thus, it was necessary to decompose individual spectra into component bands. In this context, the purpose of the study was to determine the effect of boron cations on the structure of a silicate 13-93-based glass. Figures 2-5 depict the decomposed MIR and Raman spectra as well as $^{29}$Si MAS NMR and $^{31}$P MAS NMR spectra of the 13-93-based silicate BG.

![Figure 1: XRD patterns of the produced silicate (13-93-based), borate (13-93-B), and borosilicate (13-93-BS) BGs proving their amorphous nature.](wileyonlinelibrary.com)
visible: Si=O (structural defects), P=O; silico-oxygen (Si-O(Si)), and phosphosilico-oxygen bridges (Si-O(P)), as well as broken oxygen (Si-O− and P-O−) bridges. Based on previous research and available literature data, individual bands are assigned as follows: 1288 cm\(^{-1}\): asymmetrical stretching vibrations of Si=O and P = O, 1151 and 1019 cm\(^{-1}\): asymmetrical stretching modes of Si-O(P) and Si-O (Si) linkages and 915 cm\(^{-1}\): asymmetrical stretching vibrations of Si-O− and P-O− units. The next two bands at 787 and 760 cm\(^{-1}\) are responsible for symmetrical stretching vibrations of the phosphosilico- Si-O(P) and silico-oxygen Si-O(Si) bridges. Moreover two low-intensity bands at 706 and 604 cm\(^{-1}\) come from the so-called pseudo-lattice vibrations related to the presence of 3- and 6- membered silico-oxygen rings. The other two bands (500 and 467 cm\(^{-1}\)) are attributed to bending vibrations of O-P-O and O-Si-O units, respectively. The parameters of individual bands and their assignment are summarized in Table 2.

Figure 3 shows the decomposition of the Raman spectrum of 13-93-based glass. As far as Raman spectra of silicate glasses are concerned, bands associated with Q\(^4\)Si-Q\(^0\)Si units (where Q is the number of bridging oxygens BO) are usually located within the following Raman shift ranges: 1150–1100 cm\(^{-1}\)-Q\(^4\)Si, 1090–1050 cm\(^{-1}\)-Q\(^3\)Si, 1000–950 cm\(^{-1}\), Q\(^2\)Si, 880 cm\(^{-1}\)-Q\(^1\)Si.
and 850 cm$^{-1}$-$Q_0$Si. As it can be observed in Figure 3, the bands associated with $Q_3$Si (1088 and 1009 cm$^{-1}$) and $Q_2$Si (949 cm$^{-1}$) are seen to dominate. Furthermore, the band with relatively small full width at half maximum (FWHM) at 598 cm$^{-1}$ is associated with the so-called $D_2$ defect resulting from the presence of the 3-membered
silico-oxygen rings \(^{67,68}\). In addition, the presence of the bands in the 460–420 cm\(^{-1}\) range is due to bending vibrations of O-Si-O units along with the O-P-O ones. The parameters of individual bands and their assignment are summarized in Table 3.

As can be seen, the substitution of SiO\(_2\) by B\(_2\)O\(_3\) leads to changes in the Raman spectrum (Figure 4). Bands typical for B-O units are present at approx. 1400, 990, 767, and 509 cm\(^{-1}\). They can be assigned to vibrations of penta-, tetra-, and diborate groups as well as ring breathing vibrations of both BO\(_3\) and BO\(_4\) groups (Table 4).\(^{76,77}\) Bands typical for Q\(^1\)P and Q\(^0\)P units are also visible.\(^{59,78,79}\)

The 13-93-BS glass has a borate-silico-phosphate matrix and therefore its spectrum is very complex (Figure 5). Bands typical for borosilicate and borophosphate glasses are visible and summarized in Table 5.

### Table 5: Raman band assignment for 13-93-BS BG

| Band position [cm\(^{-1}\)] | Band assignment | FWHM | Integral intensity [%] | Integral intensity |
|-----------------------------|-----------------|------|------------------------|-------------------|
| 423                         | \(\delta\) O-P-O Q\(^1\)P\(^{69,78}\) | 38   | 1.1                    | 2.6               |
| 461                         | \(\delta\) O-Si-O | 61   | 2.6                    | 6.0               |
| 514                         | Pentaborate, tetraborate, and diborate groups\(^{76}\) | 69   | 4.1                    | 9.5               |
| 568                         | D\(_2\) 3-membered Si-O rings \(^{70,71}\) / Q\(^1\)P\(^{78,79}\) | 53   | 4.7                    | 11.0              |
| 624                         | Danburite-like rings\(^{80}\) | 56   | 4.4                    | 10.3              |
| 702                         | \(v_1\) Q\(^1\)P | 93   | 14.8                   | 34.4              |
| 764                         | 6-membered ring breathing vibrations of both BO\(_3\) triangles and BO\(_4\) tetrahedra\(^{76}\) | 51   | 8.0                    | 18.6              |
| 905                         | \(v_1\) Q\(^1\)Si | 54   | 2.2                    | 5.0               |
| 949                         | \(v_2\) Q\(^2\)Si / Q\(^2\)P\(^{67,68}\) | 41   | 16.2                   | 37.6              |
| 992                         | \(v_3\) Q\(^3\)Si / Pentaborate and tetraborate groups\(^{76}\) | 60   | 10.8                   | 25.0              |
| 1062                        | \(v_1\) Q\(^3\)Si | 95   | 17.3                   | 40.1              |
| 1417                        | \(v\) BO\(_3\) bonding BO\(_4\)\(^{77}\) | 122  | 8.5                    | 19.7              |
| 1476                        | \(v\) BO\(_3\) bonding BO\(_3\)\(^{77}\) | 91   | 8.9                    | 20.7              |

**Figure 6** \(^{31}\)P MAS NMR of the (A) 13-93-based BG, (B) 13-93-BS, and (C) 13-93 B after deconvolution process. The black lines show the original spectrum, whereas the red line is the result of the deconvolution process. [Color figure can be viewed at wileyonlinelibrary.com]
The $^{31}$P MAS NMR spectra of 13-93-based, 13-93-BS, and 13-93-B glasses are shown in Figure 6A–B, respectively, and the results of their deconvolutions are presented in Table 6. Within the experimental accuracy, the spectra are practically identical. All three samples exhibit two components at about +3 and −4 ppm, with relative intensities of about 85% and 15%. They can be assigned to $Q^0P$ and $Q^1P$, respectively.45,73,74,81

The $^{29}$Si MAS NMR spectra of 13-93-based and 13-93-BS BGs are presented in Figure 7A,B, respectively, and the results of their deconvolutions are presented in Table 7. In spite of rather poor signal to noise ratio, the fitting to two components in the case of the 13-93-based BG and to three components in the case of the 13-93-BS BG is satisfactory, as can be seen on the residual plots. The peaks located at about −100 and −90 ppm can be assigned to $Q^3Si$ and $Q^2Si$, respectively. An additional, strong peak at −82 ppm that appears in the $^{29}$Si MAS NMR spectrum of the 13-93-BS bioactive glass can be tentatively assigned to the $Q^1Si$ units.81

The $^{11}$B MAS NMR spectra of 13-93-BS and 13-93-B BGs are presented in Figure 8A,B, respectively, and the results of their deconvolutions are presented in Table 8. Boron ions can be present in the tested glasses in tetragonal or trigonal coordination. Since $^{11}$B is a quadrupolar nucleus, it is sensitive to the local symmetry of the electric field, exhibiting relatively narrow spectrum for the tetragonal site, and a typical, broad second order quadrupolar shape for the trigonal site. Both samples show practically identical $^{11}$B MAS NMR spectra, which consist of the trigonal and tetragonal components with about 3 to 2 ratio.

Detailed analysis of the obtained MAS NMR and Raman spectra reveal the complex nature of the studied glasses. Substitution of silicon with boron in 13-93-based BG leads to the appearance of bands typical for boron compounds, e.g. penta-, tetra- and diborate groups as well as ring breathing vibrations of both BO$_3$ and BO$_4$ units (Figure 4). This is confirmed by MAS NMR studies, which indicate that boron is in both 3 and 4 coordination, of which the former is dominant (Figure 8A,B; Table 8). The introduction of boron has little effect on the phosphate units, whose coordination according to $^{31}$P NMR studies almost does not change (the integral intensity [%] changes by 1%). This result is not entirely in line with the Raman analysis of the tested glasses, where bands typical for the vibrations of $Q^1P$ and $Q^0P$ units are visible, and their integral intensities are greater than for the 13-93-based BG spectrum. This result may be due to the nature of the measurement method (the diameter of the 488 nm laser spot is approx. 700 nm), as well as the low content of phosphorus itself (below 2 mol%), which in turn may lead to local fluctuations in the density of phosphorus ions. It is also important to note the role of the relative strength of the Raman cross section of both vitreous B$_2$O$_3$ and P$_2$O$_5$, which are almost 5 times higher than that from v-SiO$_2$.82 Introducing boron into the 13-93-based BG matrix (13-93 BS glass) leads to breaking the silicon-oxygen bonds. This is confirmed by the $^{29}$Si MAS

![TABLE 6 Deconvolution of $^{31}$P MAS-NMR spectra for the three investigated BGs.](image)

| Sample      | Peak position [ppm] | FWHM [ppm] | Relative intensity [%] |
|-------------|---------------------|------------|------------------------|
| 13-93-based | 3.9                 | 7.7        | 88                     |
|             | −4.4                | 8.0        | 12                     |
| 13-93-B     | 2.8                 | 8.5        | 87                     |
|             | −4.5                | 7.6        | 13                     |
| 13-93-BS    | 3.3                 | 7.9        | 84                     |
|             | −4.1                | 7.7        | 16                     |

![FIGURE 7 $^{29}$Si MAS NMR spectrum of the (A) 13-93-based and (B) 13-93-BS BGs after the deconvolution process. The black line shows the original spectrum, whereas the red line is the result of the deconvolution process. [Color figure can be viewed at wileyonlinelibrary.com]](image)
NMR studies (Figure 7B; Table 7). The appearance of $Q^1\text{Si}$ units is observed, the share of which is 54%. At the same time a decrease in the quantity of $Q^2\text{Si}$ and $Q^3\text{Si}$ groups is observed. The analysis of $^{31}\text{P}$ NMR data shows that the number of $Q^1\text{P}$ groups slightly increases at the expense of $Q^0\text{P}$ units (Table 6). Comparing the $^{11}\text{B}$ NMR spectra of 13-93 B (Figure 8B) and 13-93 BS glasses (Figure 8A), we also observe a slight decrease in the amount of $BO_3$ units at the expense of $BO_4$ groups. The above observations are also confirmed by Raman studies: a decrease in the intensity of the integral $Q^3\text{Si}$ band (Tables 4 and 5) as well as changes in the intensity of the integral bands around 1400 cm$^{-1}$ ($BO_3$ bonding to $BO_3$ and $BO_4$ units) are seen. At the same time, it is difficult to clearly and directly confirm the changes of $BO_4$ groups due to the overlap of the bands with $Q^3\text{Si}$ units in the range of approx. 990 cm$^{-1}$.

3.2 | Characterization of BG scaffolds

3.2.1 | Morphology and mechanical properties

The 13-93-based, 13-93-BS and 13-93-B BG powders were used to fabricate scaffolds (Figure 9) by using the foam replica method and sintered according to their thermal properties, as investigated in a previous study.\textsuperscript{28} The pinkish color observed in the 13-93-based BG scaffold observed in Figure 9 might be due to impurities introduced during the melting procedure at high a temperature (1360°C) in a platinum crucible. The morphology of the resulting three types of BG scaffolds was examined using SEM. According to Figure 9, scaffolds of all glasses showed an interconnected pore network and a pore size range of 200–400 µm. However, the surface of the 13-93-based and 13-93-BS BG scaffold struts is seen to be smooth (according to higher magnification images), whereas the struts of 13-93-B BG scaffolds appear rougher. This is a sign that the BG particles in the case of silicate\textsuperscript{13-88} and borosilicate (13-93-BS) BGs are sintered together (via a viscous flow mechanism\textsuperscript{54}), which results in suitable densification. In contrast, the 13-93-B BG particles appear to be not (completely) fused together, resulting in a greater porosity of around 95%. In contrast, lower porosities could be observed by the borosilicate 13-93-BS BG (around 57%) and silicate 13-93-based BG scaffolds (around 78%).

While high porosities are favorable for cell ingrowth and migration, they also lead in general to a reduction of the scaffold mechanical properties.\textsuperscript{83,84} This could be also observed in this study. While borosilicate 13-93-BS BG scaffolds exhibited the lowest porosity, they also showed the highest compressive strength (4 ± 2 MPa). In contrast, silicate 13-93-based BG and borate 13-93-B BG scaffolds exhibit compressive strengths of 0.6 ± 0.3 MPa and 0.2 ± 0.1 MPa, respectively. Due to the high variability and typical jagged stress-strain curve (Figure 10), the compressive strength values are only indicative.\textsuperscript{54,55} In terms of porosity and pore size range, scaffolds of all three glasses lie in the range of trabecular bone (50–90%, 100–500 µm), but only borosilicate BG scaffolds provide suitable mechanical properties in comparison to trabecular bone (2-12 MPa).\textsuperscript{27}

### TABLE 7 Deconvolution of $^{29}\text{Si}$ MAS-NMR spectra

| Sample      | Peak position [ppm] | FWHM [ppm] | Relative intensity [%] |
|-------------|---------------------|------------|------------------------|
| 13-93-based | –88.5               | 15.7       | 80                     |
|             | –98.4               | 12.0       | 20                     |
| 13-93-BS    | –82.3               | 10.2       | 54                     |
|             | –90.7               | 10.0       | 37                     |
|             | –100.5              | 7.3        | 9                      |

**FIGURE 8** $^{11}\text{B}$ MAS NMR spectrum of (A) 13-93-BS and (B) 13-93-B BGS after the deconvolution process. The black line shows the original spectrum, whereas the red line is the result of the deconvolution process. [Color figure can be viewed at wileyonlinelibrary.com]
3.2.2 | Chemical and physical characterization

To confirm that no crystalline phases were created during sintering, XRD analyses were carried out. As shown in Figure 10A, no crystalline peaks were detected confirming the amorphous character of all scaffolds. Additionally, the fabricated scaffolds were examined using FTIR (Figure 10B). In case of silicate 13-93-based BG scaffolds, the typical characteristic peaks could be detected at 470 cm$^{-1}$ and in the range of 900–1100 cm$^{-1}$, corresponding to the bending and stretching vibrations of Si-O-Si bonds, respectively.\textsuperscript{38,55,85,86} In case of borate 13-93-B BG scaffolds, typical characteristic peaks are seen in the range of 900–1100 cm$^{-1}$, corresponding to the B-O stretching of BO$_4$ units. In addition, peaks in the range of 1300–1500 cm$^{-1}$ correspond to the B-O stretching of BO$_3$ units.\textsuperscript{55,87} Moreover, the peak at 700 cm$^{-1}$ is also an indicator of the B-O stretching of BO$_4$ units.\textsuperscript{88,89} This is in accordance to the results obtained by NMR (Figure 5), where the presence of BO$_3$ and BO$_4$ units was detected. In case of borosilicate 13-93-BS BG scaffolds, all mentioned characteristic peaks of borate and silicate scaffolds were detected, proving the presence of silica and boron trioxide in the glass structure.

| Sample   | Peak position [ppm] | FWHM [ppm] | Relative intensity [%] |
|----------|---------------------|------------|------------------------|
| 13-93-B  | -19.8               | 3.9        | 40                     |
|          | trigonal            |            |                        |
| 13-93-BS | -19.5               | 4.1        | 36                     |
|          | trigonal            |            |                        |

3.2.3 | In vitro dissolution in SBF

To investigate the apatite-forming ability of the scaffolds, a series of samples of all three BGs was immersed in SBF for up to 14 days. During immersion, the weight loss of the scaffolds and the pH change of the medium were recorded. As shown in Figure 11A, 13-93-B and 13-93-BS BG scaffolds showed almost the same weight loss rate in SBF. In contrast, 13-93-based BG scaffolds showed a remarkable

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**Figure 9** Photographs and SEM images of silicate (13-93-based), borate (13-93-B), and borosilicate (13-93-BS) bioactive glass scaffolds fabricated by the foam replica method. The inserts show the surface of the scaffold struts in high magnification indicating a fairly smooth surface in case of 13-93-based and 13-93-BS BG scaffolds and a rough surface for 13-93-B BG scaffolds. [Color figure can be viewed at wileyonlinelibrary.com]
slower weight loss rate, which seems to be retarded after 3 days in SBF. In contrast, all scaffolds led to a similar increase of pH. After 14 days, the increase of pH was found to be the highest for borosilicate glass scaffolds (pH of 8.07 ± 0.09), followed by borate (pH of 7.95 ± 0.02) and silicate (pH of 7.86 ± 0.05) BG scaffolds. The findings fit well with results reported in literature for similar glass compositions\(^{35,90}\) and can be explained by the more acidic nature of B(OH)\(_3\) compared to Si(OH)\(_4\), leading to a better compensation of the strongly basic NaOH responsible for the pH increase.

In addition to weight loss and pH measurements, the collected SBF after immersion tests was examined using ICP-OES. Based on the measurements and by subtracting the amount of ions in the pure SBF, the released or consumed amount of ions by the different BG scaffolds could be determined (measurements of sodium release are not shown). According to Figure 12, in case of silicate 13-93-based and borate 13-93-B BG scaffolds, no boron and silicon release could be detected, respectively. Interestingly, although the BG compositions contained different amounts of silica, no significant difference between the total amount of silicon released from 13-93-based and 13-93-BS BG scaffolds (around 68 mg/L) could be found. In contrast, a clearly higher release of boron could be found from 13-93-B BG scaffolds (121 ± 15 mg/L) compared to 13-93-BS BG scaffolds (85 ± 22 mg/L). Similar results were obtained in a previous study examining the release profile of the used BG particles (before scaffold fabrication).\(^{38}\) The consumption of P and minor release/consumption of Ca indicate the formation of a CaP-rich apatite layer on the scaffold surfaces formed during immersion in SBF. Especially in the case of phosphorus, the faster consumption of P during immersion of 13-93-B and 13-93-BS BG scaffolds compared to 13-93-based BG scaffolds proves the higher reactivity of the borate and borosilicate BG scaffolds. In addition, the release rates of Mg and K indicating that slightly (not significant) higher released amounts could be detected for borosilicate and borate BG scaffolds compared to silicate 13-93-based scaffolds.
To analyze the formation of an apatite layer on the surface of the different fabricated BG scaffolds, the collected scaffolds after 14 days of immersion in SBF were examined using SEM (Figure 13). As expected, scaffolds based on each of the three glasses exhibited apatite formation in form of cauliflower-like structures, which is a typical finding in this type of studies on BGs. However, less amount of apatite formation was qualitatively observed on silicate 13-93-based BG scaffolds (as determined by simple inspection of the SEM images).

In order to quantify these observations, FTIR and XRD analyses were performed. As shown in Figure 14A-C, after 14 days of immersion in SBF, in case of all fabricated BG scaffolds, the functional groups related to CaP-rich species were found. The double peak present in the range of 560–600 cm$^{-1}$ can be attributed to bending vibrations of PO$_4^{3-}$ groups. Moreover, the peak at around 870 cm$^{-1}$, mainly found for 13-93-BS and 13-93-B BG scaffolds, corresponds to the vibration mode of CO$_3^{2-}$ groups. In addition, the peak at 1000–1100 cm$^{-1}$ is further characteristic for stretching vibrations of PO$_4^{3-}$ groups, therefore proving the presence of CaP-rich species on the surface of the different BG scaffolds.

4 | DISCUSSION

The structure of glasses can be in general described by three components, the network formers, the network modifiers and intermediate oxides. In case of BGs, the glass network structure can be formed by silica, boron trioxide, or/and phosphorus pentoxide. Here, silica or/and boron trioxide were used to fabricate a set of BGs. All produced BGs, based on the 13-93 composition, showed a high amount of network modifiers (Na$_2$O, K$_2$O, MgO, and CaO). Network modifiers change the atomic glass structure by turning bridging oxygens into non-bridging oxygens (from dominantly covalent to ionic bonding). Based on the introduction of network modifiers, a glass network (its polymerization degree) can be described by the number of bridging oxygens (n) per network forming atom (Q), mostly referred as Q$^n$ units. Since in this study the amount of network modifiers was not changed, all changed structural and mechanical properties can be attributed to the different network formers.

By MIR, NMR, and Raman studies, it was shown that the silicate composition is composed mainly (around 80%) of Q$^2$Si units and (around 20%) of Q$^3$Si units. Moreover, the network is also composed of P$_2$O$_5$ in form of Q$^1$P units (around 12%). However, the main part of P$_2$O$_5$ (around 88%) is present in the form of orthophosphates. In case of silicate glasses, previous studies showed the great (favorable) impact of low amounts of P$_2$O$_5$, present in the form of loosely bound orthophosphate units (Q$^0$P), whose fast release rate favors the bone-bonding ability of such silicate glasses.

These results are in accordance to previous studies, where the network structure of the silicate 45S5 BG was found to be mainly composed of Q$^2$Si, Q$^3$Si, and Q$^1$P units. In contrast to silicate (and phosphate) BGs, the initial addition of network modifiers to borate glasses does not turn bridging...
FIGURE 13 Relative release of ions during the immersion of the different BG scaffolds in SBF as a function of time. The concentrations of ions found in the reference (pure SBF) were subtracted from the measured amounts of ions released in medium containing the dissolution products of the scaffolds in order to quantify the relative release of ions. [Color figure can be viewed at wileyonlinelibrary.com]
oxygens into non-bridging oxygens. Vitreous borate BGs are formed by BO₃ units (in the form of trihedrons or triangles). An initial increase of modifier content leads to the formation of BO₄⁻ units, which turn back to BO₃ groups with increasing modifier content (the so-called boron anomaly). 100-103 Here, the pure borate BG was found to be composed of [BO₄] units (around 40%) and [BO₃] units (around 60%). Moreover, in accordance with the silicate 13-93-based BG, phosphorus pentoxide is mainly present in the form of orthophosphates (around 87%). The results are in agreement with a previous study, where, based on a silicate BG (composed of SiO₂-Na₂O-CaO-P₂O₅-K₂O), a series of borosilicate BGs was developed and investigated using Raman and NMR measurements. 73 Interestingly, the partially replacement of silica by boron trioxide changed the coordination of QⁿSi units. It could be observed that with increasing boron content, the polymerization degree of the silico-oxygen network decreased, as expected. In contrast, the ratio of [BO₃] to [BO₄] did not significantly change. This result is in agreement with the literature, where it is reported that non-bridging oxygens are preferentially formed at silicate groups compared to borate groups. 46,73,104 In summary, in case of borosilicate 13-93-BS BG, silica is composed of Q¹Si (≈54%), Q²Si (≈37%) and Q³Si (≈9%) units, boron trioxide is composed of [BO₃] (≈64%) and [BO₄] (≈36%) and phosphorus pentoxide is composed of Q⁰P (≈84%) and Q¹P (≈16%) units (Figure 15).

To evaluate the effect of the change of network former on the final properties of BG scaffolds, silicate, borosilicate, and borate scaffolds were fabricated (Figure 16). For all BGs, it was possible to obtain amorphous scaffolds exhibiting suitable pore size ranges. 105 The obtained pore sizes and porosities have been also observed in previous studies using similar BG compositions. 27,33,35,55 Amorphous scaffolds offer two advantages compared to crystallized scaffolds. First, crystallized scaffolds exhibit in general a large number of defects and cracks (for example due to limited sintering densification), which can result in decreased compressive strengths 54 and, second, amorphous phases are less stable during dissolution resulting in better bioactivity and adjustable (controllable) degradation kinetics. 55 Therefore, in this study, higher mechanical strengths compared to the reported compressive strengths for crystallized 45S5 BG scaffolds were obtained. 106 However, clear differences between the measured porosities and mechanical properties of the scaffolds based on the three BGs considered in this study were found. In accordance to SEM images (Figure 9), viscous flow sintering has taken place for borosilicate 13-93-BS and
silicate scaffolds, whereas the SEM images of borate 13-93-B scaffolds indicate that the particles did not fuse completely together. By achieving viscous flow sintering, higher densified struts can be obtained, which in general results in higher compressive strengths. This could be observed here, whereas the measured porosities and mechanical properties of the scaffolds correlate well (the lower the porosity, the higher the compressive strength). Therefore, depending on the final application, scaffold properties can be tuned to match for instance different parts of the trabecular bone (porosity of 50–90%, compressive strength of 0.2–12 MPa).  

As indicated, replacing silica by boron trioxide in the BG structure has also a great influence on the resulting properties of the silicate, borosilicate, and borate scaffolds, which could be especially assessed by the dissolution test in SBF. Based on rough calculations, it can be determined how much of the total introduced amount of B and Si (the main network former) could be released within 14 days of immersion in SBF. In case of silicate 13-93-based BG scaffolds, around 7% of the total Si content was released and in case of the borate 13-93-B BG scaffolds, around 15% of the total amount of B was released within 14 days. This result proves the greater degradability of the borate BG scaffolds, as already reported in the literature. Moreover, around 24% of Si and 15% of B were released from the 13-93 BS BG scaffolds. Although the dissolution behavior of this kind of BGs has been investigated in the past, here the ion-release and degradation behavior of the obtained scaffolds are (for the first time) correlated with the results obtained by the structural analysis of the three kinds of BGs. As mentioned above, no significant change of the coordination of boron ions in the borate and borosilicate BGs was found. Accordingly, no significant change of the (relative) release rate of B ions was measured. Additionally, NMR results indicated that a depolymerization of the silico-oxygen network occurs in case of borosilicate BG, which in turn leads to a higher (relative) release rate of Si ions from 13-93-BS scaffolds compared to the silicate BG scaffolds. Therefore, it can be concluded that

FIGURE 15 FTIR spectra of (A) silicate (13-93-based), (B) borate (13-93-B), and (C) borosilicate (13-93-BS) BG scaffolds immersed for 3, 7, and 14 days in SBF; (D) XRD patterns of the different BG scaffolds after immersion in SBF for 14 days. Relevant peaks are discussed in the text. [Color figure can be viewed at wileyonlinelibrary.com]
based on the BG structure the ion release rate (dissolution products) of BGs can be estimated. Future studies should examine which ion-release and degradation rates are needed in different applications of BGs in contact with soft or hard tissues in order to determine the optimum BG composition for the intended applications.

5 CONCLUSIONS

The structure of silicate, borosilicate and borate BGs based on the 13-93 composition was successfully analysed using NMR, MIR, and Raman spectroscopy. It was found that the replacement of silica by boron trioxide leads to a depolymerization of the silico-oxygen network. Moreover no significant difference in the coordination of P and B ions inside the glass network was found for borosilicate and borate BGs. In accordance with the results obtained by the structural analyses, the degradation and resulting ion release profile of scaffolds fabricated from the silicate, borosilicate and borate BGs changed. The possibility to design BG compositions for the fabrication of optimal scaffolds, providing specific degradation and biological properties, is possible by modifications of the structure/composition of 13-93-based BGs.

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CONFLICTS OF INTEREST

There are no conflicts to declare.
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