

Towards Bone Regeneration: Hybrid Sol-Gel and Spray-Drying Production of Bioactive Glass for Additive Manufacturing

Guillaume Marchal¹, Damien Coibion¹, Frederic Boschini¹, Rudi Cloots¹, Nicolas Somers¹

¹ GREEnMat, University of Liège, Belgium

Abstract

Scaling up the production of bioactive glasses for bone tissue engineering while preventing crystallisation remains a critical challenge. Achieving a strictly amorphous state is essential for optimal bioactivity, yet conventional large-scale thermal treatments often trigger phase separation or crystallisation. To address this issue, this work develops a novel, scalable, and fully aqueous sol-gel synthesis combined with a spray-drying process, capable of producing a quasi-amorphous 68S-like silicate bioactive glass powder (69.33 SiO₂, 24.39 CaO, 4.87 P₂O₅, 1.41 Na₂O, in wt.%) at a 0.5 kg per day scale. By using low-cost water glass as both the silica and sodium precursor, rapid and eco-friendly gelation is achieved. Beyond the mere scale-up of the process, a key technological advance of this route lies in the optimization of a washing protocol. This step systematically removes nitrate by-products and stabilizes the low-sodium amorphous network, effectively suppressing crystallisation pathways during subsequent calcination at 500°C. This stable amorphous product exhibits exceptional bioactivity, triggering accelerated biomimetic hydroxyapatite growth within one day of incubation in Simulated Body Fluid (SBF). Furthermore, the spray-dried powder possesses optimised particle morphology and physicochemical properties specifically tailored for vat photopolymerisation. Complex, high-resolution 3D bone scaffolds were successfully printed by stereolithography (SLA) to demonstrate the usefulness of the synthesised powder. This sustainable manufacturing route effectively bridges the gap between fundamental glass science and advanced additive manufacturing, offering an economically viable pathway towards highly bioactive, patient-specific clinical grafts.

1.

The demand for bone grafts is increasing owing to population ageing and higher life expectancy. Bone repair, especially for large defects caused by trauma, tumours, or degenerative diseases, remains a significant clinical challenge [1]. Although autografts are considered as the gold standard, they are limited by supply and donor-site morbidity, whereas allografts carry risks of rejection and disease transmission. Synthetic biomaterials are therefore crucial for meeting these clinical needs. Among the available options (metals, ceramics and polymers), each class of material has its own advantages but also inherent limitations in terms of bioactivity, degradation, and integration with host tissue [2,3].

Bioactive glass (BG), discovered by Hench in the 1970s, is a highly promising candidate for bone regeneration. BG can directly bond to bone through the rapid formation of a carbonated hydroxyapatite (HCA) layer. Its composition can be tailored, enabling control over dissolution kinetics, ion release, and biological stimulation [4]. When combined with Additive Manufacturing (AM) techniques, BG enables the fabrication of patient-specific scaffolds with precise architecture, controlled porosity and customized mechanical properties [5].

Despite its potential, industrial production remains limited. The traditional melt-quenching method requires very high temperatures (typically around 1400°C), producing a monolithic glass that must then be milled into powder, a step that is energy-intensive and difficult to control. Classical sol-gel synthesis offers high purity and superior bioactivity owing to low-temperature processing but relies on expensive and hazardous alcohol-based precursors (e.g., TEOS, TEP). Furthermore, this method provides low yields (often only a few grams), and the long gelation, ageing, and solvent-evaporation steps hinder industrial scale-up [6].

Recent research in bioactive glass synthesis has increasingly focused on more sustainable, water-based sol-gel methods coupled with innovative drying techniques such as spray-drying [7,8]. Spray-drying, in particular, is a versatile approach for producing uniform powders with a controlled particle size distribution, making it highly suitable for AM applications. Nebulisation of the liquid formulation allows drying within a fraction of a second at temperatures below 200°C, in contrast to time-consuming conventional drying in an oven. By optimising the spray-drying process, it becomes possible to reduce the overall production costs, enhance throughput, and improve the scalability of bioactive glass production. [9].

A critical requirement for high bioactivity is the maintenance of a fully amorphous state. Unlike crystalline structures, an amorphous network is inherently more unstable and disordered, creating a more reactive surface that facilitates the ionic exchange required for bone bonding. However, achieving a strictly non-crystalline network remains challenging, and few studies have successfully demonstrated a fully amorphous bioactive glass [10].

In this work, we develop a fully aqueous sol-gel process coupled with spray-drying to produce bioactive glass powder at a 500 g per day scale. The target composition is a 68S-like bioactive glass (67.49 wt.% SiO₂, 23.40 wt.% CaO, 9.11 wt.% P₂O₅) [11]. The selection of the 68S composition aims to optimise the structural stability of the glass network. Increasing the silica content increases the glass transition temperature and effectively shifts the crystallisation window, which is crucial for maintaining a purely amorphous state during thermal processing. This strategy highly reduces synthesis time and cost while producing amorphous, printable particles. The resulting powder is then shaped by a stereolithography-based AM process (SLA) to demonstrate its suitability for the large-scale production of personalised bone implants.

2. Experimental procedure

2.1. Operating mode

First, an aqueous solution was prepared by dissolving calcium nitrate (Ca(NO₃)₂·4H₂O, Carl Roth) and phosphoric acid (85%, Merck) in deionized water. As illustrated in Figure 1, the silica and sodium sources were introduced dropwise into this solution using a water glass reagent. Water glass (Carl Roth) consists of an aqueous solution of sodium oxide (Na₂O - 8 wt%) and silica (SiO₂ - 27 wt%), serving as a cost-effective, inorganic precursor in this sol-gel synthesis. During the addition of water glass at a controlled flow rate of 4 mL/min, a disperser (IKA T 18 Digital ULTRA-TURRAX®) was operated to ensure optimal dispersion and homogeneity of the suspension (Figure 1). This continuous homogenisation step also prevented clogging of the spray-dryer injection nozzle during subsequent processing. Owing to the high-energy shearing applied by the disperser, the temperature of the medium reached 60°C, while the resulting solution exhibited a strongly alkaline pH.

Once the addition of water glass was complete, the suspension was directly processed using a spray-dryer operated in fountain mode (with an injection flow rate of 25 mL/min and an outlet temperature of 120°C) to dry the particles and obtain a powder with a narrow particle size distribution. Each individual batch consisted of 1 L of precursor solution, corresponding to a theoretical yield of 100 g of material, from which a collection efficiency of 85% was experimentally achieved. The obtained powder was then washed with Milli-Q water followed by technical-grade ethanol (99% purity) to remove residual by-products. This washing step induced a mass reduction of approximately 45% owing to the removal of soluble nitrate salts. Finally, the powder was heat-treated in a furnace at 500°C for 2h to yield the final bioactive glass powder.

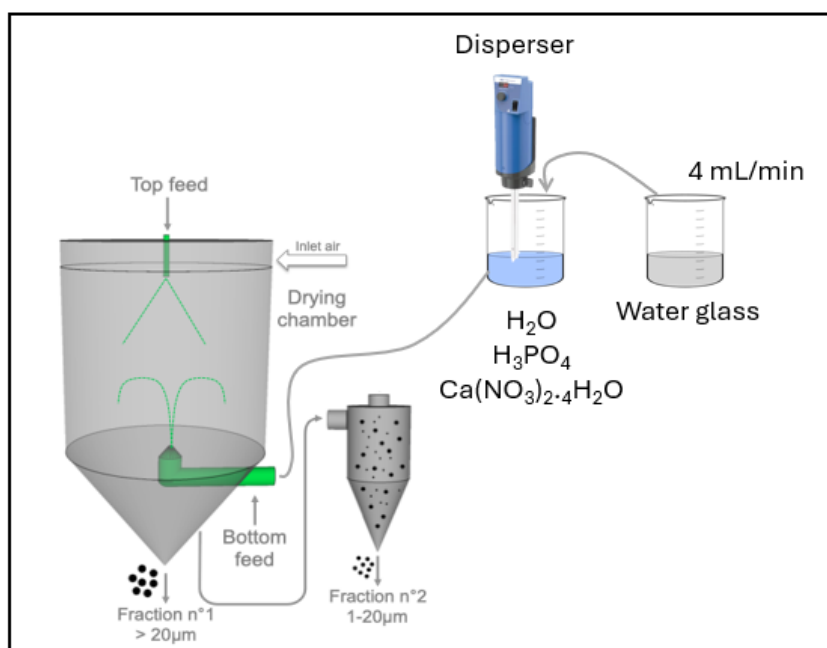


Figure 1: Schematic representation of the synthesis procedure

2.2.3D printing: stereolithography

Stereolithography (C900, 3DCeram printer) is used to produce the 3D-printed parts. According to the literature, gyroid structures were selected because of their unique interconnected porous architecture, which mimics the structure of natural trabecular bone [12]. A 3D-printing paste is developed by mixing 39.4 wt.% bioactive glass powder, 12.8 wt.% phosphoester-type dispersing agent, 15.4 wt.% polyethylene glycol plasticiser and 32.4 wt.% acrylate resin. To obtain a homogeneous paste, a dual asymmetric centrifugator (SMART DAC 600, Hauschild SpeedMixer) is used to disperse the powder in the resin. A tricylinder miller (EXACT 50i) is used to break down residual agglomerates.

As the paste layer thickness spread by the scraper during printing is set to 100 µm, a cure depth of 150 µm is required. The 50 µm overcure ensures cohesion between the printed layers and prevents delamination.

The scanning speed (10,000 mm/s) and laser power (50 mW) are determined by photopolymerisation tests. During these tests, thin sheets are printed using different laser powers and scanning speeds [13]. The thickness of the sheets is then measured, and the printing parameters are selected accordingly.

2.3. Post-printing process

Following the 3D-printing process, the organic binder was removed to obtain purely inorganic bioactive glass parts, this thermal step is referred to as debinding. To optimise this thermal cycle while preventing the crystallisation of the bioactive glass matrix, thermogravimetric and differential scanning calorimetry analyses (TGA-DSC, Setaram Labsys, Evo instrument, heating rate of 10°C/min) were performed. Once the organic phase had been fully pyrolysed, the 3D parts were subjected to a subsequent sintering stage to promote densification, reduce residual porosity and enhance the final mechanical properties. Different sintering temperatures were evaluated, and their effects are thoroughly discussed in detail in the Results section.

2.4. Characterisation techniques

2.4.1. Physicochemical characterisations of powders

X-ray diffraction (XRD) is carried out at different stages of the synthesis to identify the amorphous bioactive glass phase and any possible crystalline by-products. XRD analyses are performed in Bragg-Brentano geometry using a Bruker D8 Twin-Twin diffractometer equipped with a Lynxeye-XET 1D detector, Bruker (Cu-K α radiation, $2\theta = 5-70^\circ$, step size of 0.02° , step time of 0.2 s/channel and rotation speed of 15 rpm).

Fourier-transform infrared spectroscopy (FTIR) analyses were performed by attenuated total reflectance (ATR) on a few milligrams of powder using a Nicolet IS5 spectrometer with an ID7 ATR accessory (Thermo Scientific) equipped with a diamond crystal. The spectra are obtained by averaging 32 scans.

The particle size distribution of the powders after spray-drying and calcination is measured using a laser particle size analyser (Malvern Mastersizer 3000). Each measurement is repeated three times immediately after dispersion of the suspension with an ultrasound probe for 30 seconds. The volume-based median diameter, $D_v(50)$, is obtained for each powder. The particles are assumed to be non-spherical, and the refractive index of the bioactive glass was set to 1.52.

To complement the particle size analyses, the specific surface area of powders is determined using the BET method (Brunauer, Emmett and Teller) with a Micromeritics ASAP 2020 Plus instrument. Degassing was performed for 6 h at 150°C with a heating ramp of 10°C/min. Adsorption measurements are performed under N₂ from 0 to 0.3 P/P₀ with a step of 0.03. The Rouquerol method was used to determine the specific surface area [14].

Scanning Electron Microscopy (SEM, TESCAN Clara) is used to study the morphology of the powders. X-ray Fluorescence (XRF, S8 Tiger, Bruker) is then used to obtain a semi-quantitative elemental analysis of the bioactive glass.

2.4.2. Bioactivity characterisation

Bioactivity is evaluated using Simulated Body Fluid (SBF) test according to ISO 23317 [15]. Pressed bioactive glass pellets (1.2g of powder pressed under 2-tonne load, 20 mm in diameter) are incubated in SBF at a concentration of 2 mg/mL for 7 days at 37°C. During

incubation, stirring is applied to ensure good homogeneity of the solution without significant pH changes, thereby avoiding unwanted precipitation. The solution is refreshed every 2 days. After 1, 2, 3, 5 and 7 days, samples are washed with Milli-Q water, dried in a desiccator and analysed by XRD and SEM.

If the powder material is bioactive, a crystalline phase of carbonated hydroxyapatite (HCA) should be visible by SEM and in the XRD pattern. HCA formation is explained by a classical dissolution-precipitation mechanism. Upon immersion, the rapid exchange of H^+ ions from the solution with Na^+ and Ca^{2+} ions from the glass matrix leads to the formation of a silica-rich layer, followed by the migration of Ca^{2+} and PO_4^{3-} ions to the surface, resulting in the crystallisation of the biomimetic HCA layer [16].

In vitro cytotoxicity was evaluated using an indirect extraction method. Three replicates of pellets were first incubated in culture medium (Dulbecco's Modified Eagle Medium, DMEM) for 24 h to obtain the corresponding extract solution. This extract was then used either undiluted (100% extract) or diluted with fresh culture medium to concentrations of 50% and 25%. L929 fibroblasts were subsequently brought into contact with these extracts and incubated under standard culture conditions for 72 h. Following incubation, cell viability was assessed using an MTT assay, where the tetrazolium salt contained in the culture medium is reduced by cellular dehydrogenases into a formazan derivative. The amount of produced formazan, which is directly proportional to the number of metabolically active cells, was then quantified by colorimetric spectrophotometry at a wavelength of 490 nm.

3. Results and analysis

3.1. Synthesis of bioactive glass

Erreur ! Source du renvoi introuvable. shows the XRD patterns of BG powder at different stages. The XRD pattern of the powder collected after spray-drying (A) shows a weak amorphous halo characteristic of bioactive glass, together with a dominant crystalline phase of sodium nitrate. Sodium nitrate forms as a by-product of the synthesis owing to the large release of Na^+ and NO_3^- ions, originating from water glass and calcium nitrate respectively, during sol-gel reactions. A washing step with water and ethanol is required to remove sodium nitrate efficiently, taking advantage of its high solubility in water (~900 g/L). The ethanol washing step helps to limit changes in pore structure and prevents excessive deformation during drying [17]. Thermal decomposition of sodium nitrate occurs near 600°C, a temperature at which the glass begins to crystallise, making thermal removal incompatible with the maintenance of optimal bioactivity [18]. Moreover, because of the strong glass network, it is difficult to remove all nitrates solely by thermal decomposition. Pattern B confirms the complete removal of sodium nitrate after washing. After calcination at 500°C (C), a small peak attributable to hydroxyapatite appears, together with a broad amorphous halo at around $25^\circ 2\theta$, typical of silica-based bioactive glass [19,20].

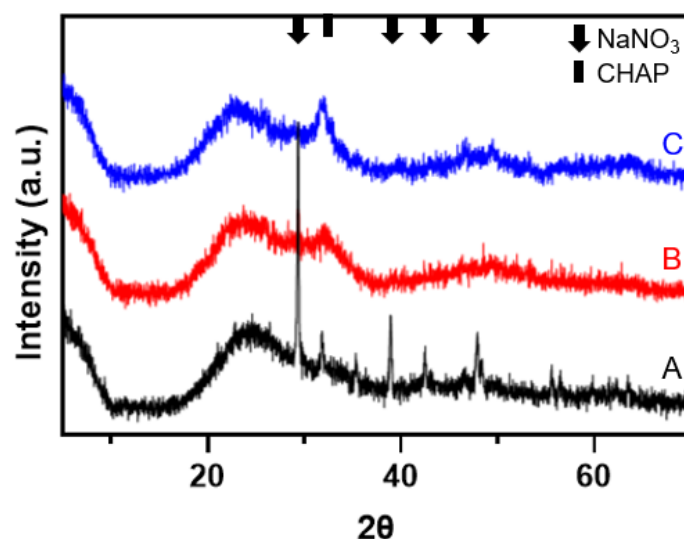


Figure 2: XRD patterns of A) BG after spray-drying B) BG after washing and C) BG after calcination at 500°C.

The synthesis was independently repeated 8 times to ensure process reproducibility and to accumulate sufficient material for additive manufacturing. Based on the mass balance reported in Table 1 of the Supporting Information, the average powder recovery yield was 85 ± 2 wt.% after spray-drying and 42 ± 5 wt.% after washing. No additional mass loss was observed during the subsequent calcination step. The washing step therefore represents the main yield-limiting stage of the process, primarily because of the removal of sodium nitrate and associated powder losses.

Starting from a theoretical glass-equivalent mass of 100 g per batch, 42 ± 5 g of calcined glass powder was obtained after washing and thermal treatment. After removal of the particle fraction larger than $20 \mu\text{m}$, the final mass of usable glass particles below $20 \mu\text{m}$ was 37.8 ± 5 g per batch, corresponding to an overall process yield of 37.8 ± 5 wt.%.

The washing step removes sodium nitrate while also increasing the porosity, resulting in a substantial increase in the specific surface area from 39 to $272 \text{ m}^2/\text{g}$. Therefore, a calcination step at 500°C for 2h is required to decrease the specific surface area ($65 \text{ m}^2/\text{g}$) and improve dispersion of the bioactive glass powder during paste preparation [21].

Figure 3 presents the TGA-DSC curves obtained before and after washing of the bioactive glass. The 10 wt% weight loss (black curve) observed between 440 and 640°C, together with the simultaneous endothermic peak (green curve) in figure 3A corresponds to NaNO₃ decomposition. After the washing step (figure 3B), this peak disappears, confirming the elimination of NaNO₃. The first weight loss in both curves corresponds to the loss of adsorbed water.

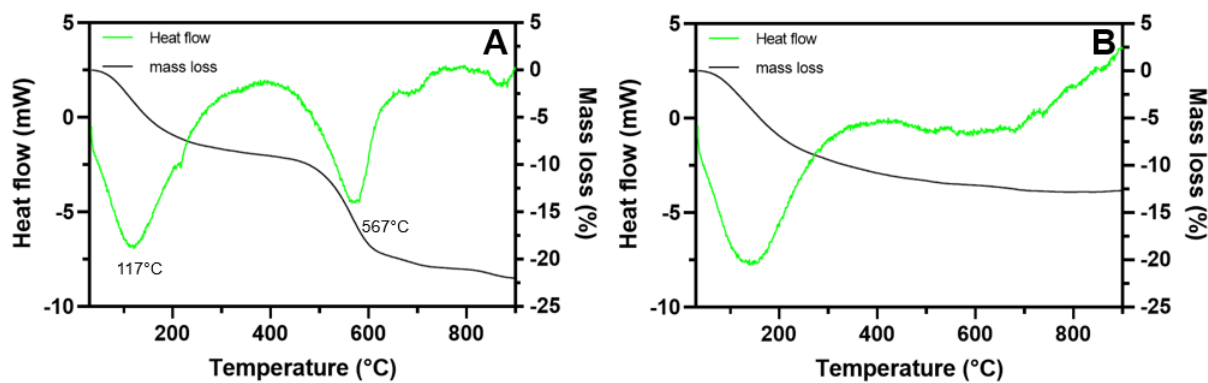


Figure 3: TGA-DSC curves of BG powder before (A) and after (B) washing.

The mean diameter of the particles collected by gravity at the bottom of the spray-dryer is $84.5 \pm 0.8 \mu\text{m}$, whereas the smaller particles collected by the cyclone have a mean diameter of $23.4 \pm 0.6 \mu\text{m}$. The corresponding weight fractions are 10 wt% and 90 wt%, respectively. For stereolithography process, particles with a granulometry below $20 \mu\text{m}$ are preferred [22]. Only the smaller fraction is used for further experiments. As shown in figure 4B, washing ($D50 = 21.6 \pm 0.2 \mu\text{m}$) and calcination ($D50 = 21.5 \pm 0.3 \mu\text{m}$) do not significantly modify the particle size.

Although the powder has a $D50$ exceeding $20 \mu\text{m}$, this is not problematic because, during paste preparation, the tricylinder miller breaks down the agglomerates owing to the narrow gap between cylinders ($10 \mu\text{m}$). This shifts the particle size distribution towards smaller particles, giving a final $D50$ of $12.2 \pm 0.2 \mu\text{m}$ (red curve in figure 4B).

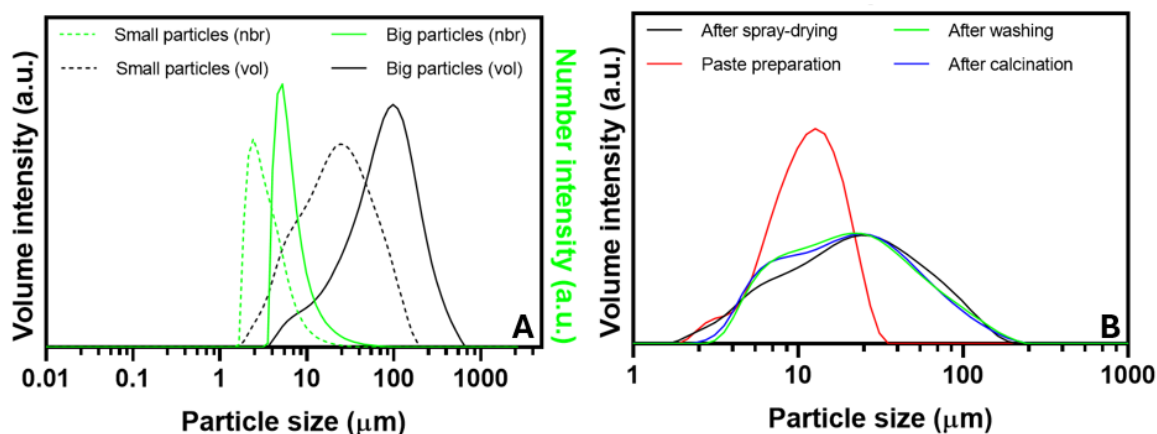


Figure 4: A) Particle size distribution of BG powders after spray-drying (small and large particles) B) Particle size distribution of the small BG powder at each step: after spray-drying, after washing, after calcination at 500°C (ready for printing) and after paste preparation (after tricylinder).

Figure 5 illustrates the morphology of the powder. The particles display an irregular morphology. Before washing (Figure 5A), sodium nitrate crystals are clearly identifiable

(highlighted in red); they appear smoother and have a well-defined spherical shape. After washing, SEM micrographs confirm their removal (Figure 5B).

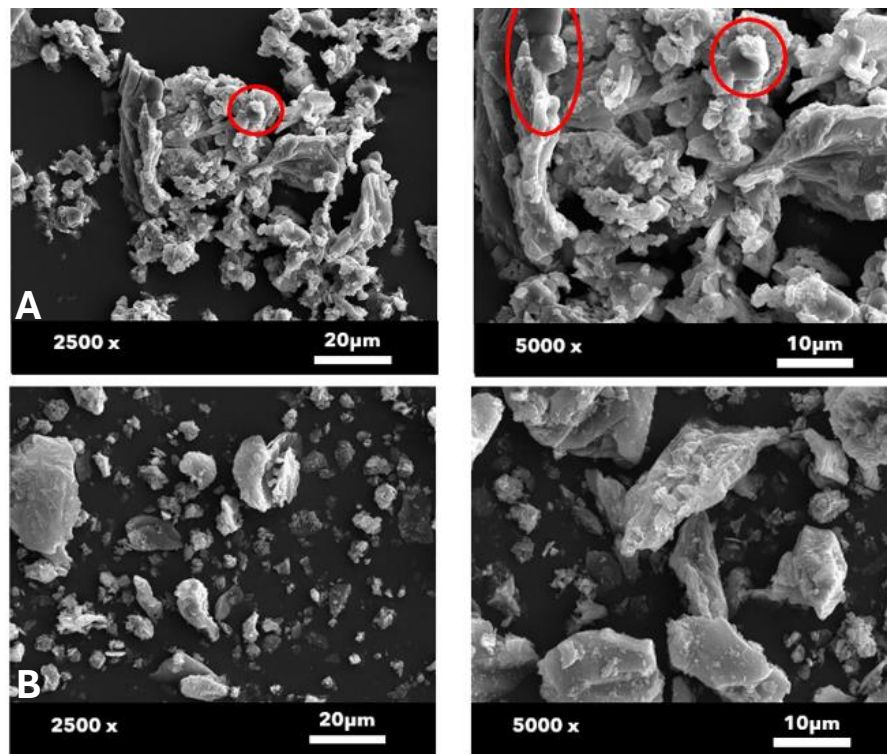


Figure 5: SEM micrographs before (A) and after (B) the washing step (~20 µm).

The final chemical composition of the synthesised bioactive glass powder, determined by XRF is 69.33 SiO₂, 24.39 CaO, 4.87 P₂O₅, 1.41 Na₂O, in wt.%. The resulting formulation matches a standard 68S bioactive glass network, with only a minor residual percentage of Na₂O remaining incorporated in the structure. This residual sodium originates from the water glass precursor used to enable the scalable aqueous sol-gel process. Although water glass serves primarily as the silica source, it inherently introduces sodium into the medium as a fluxing agent. Most of these sodium ions are systematically removed during the washing step through dissolution and removal of soluble NaNO₃ by-products, leaving only a minor fraction within the final stabilised glass network.

The synthesis approach presented here combines the structural control of sol-gel chemistry with the scalable particle engineering offered by spray-drying, providing distinct parameters with which to tune the properties of the bioactive glass.

Composition is governed explicitly by the initial precursor stoichiometry in the alkaline sol. Because spray-drying involves the rapid drying of individual aerosolised droplets, it limits macroscopic phase separation and helps to lock the targeted multicomponent chemical composition uniformly across all particles.

Reactivity (*in vitro* bioactivity) is tuned by both textural and chemical factors: higher calcium content disrupts the rigid siloxane (Si-O-Si) network and accelerates ion exchange, while the rapid solvent-evaporation rate during spray-drying preserves a highly amorphous matrix with

enhanced specific surface area, providing numerous reaction sites for rapid hydroxyapatite nucleation.

3.2. Bioactivity of the glass

After complete characterisation of the powder, bioactivity is evaluated by immersion in SBF. Before immersion, the XRD pattern already exhibited very weak diffraction feature that could be attributed to carbonated hydroxyapatite. However, the sample remained predominantly amorphous, and no HCA-like crystallites were observed by SEM. After only 24h, the XRD pattern retained the amorphous glass halo, while HCA diffraction peaks became clearly distinguishable (ICDD: PDF 01-073-7334) at 26° , 32° , 47° , 50° and 53° 2θ , confirming both bioactivity and surface reactivity. The XRD patterns collected after 2, 3, 5, and 7 days show a gradual increase in HCA crystallisation, as presented in Figure 6.

Figure 7A shows the SEM image of the reference sample before incubation (0h), with no evidence of HCA formation, whereas Figure 7B illustrates the initial appearance of hydroxyapatite crystallites after 1 day of incubation. Figures 7C and 7D highlight the progressive increase in hydroxyapatite crystallinity between day 1 and day 7. After 7 days, the crystallites appear more defined and exhibit greater height and organisation.

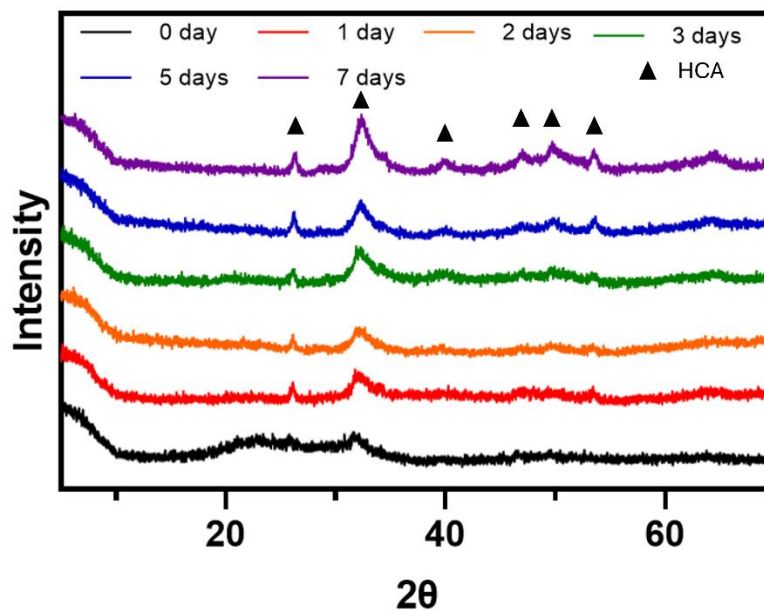


Figure 6: XRD patterns after SBF testing.

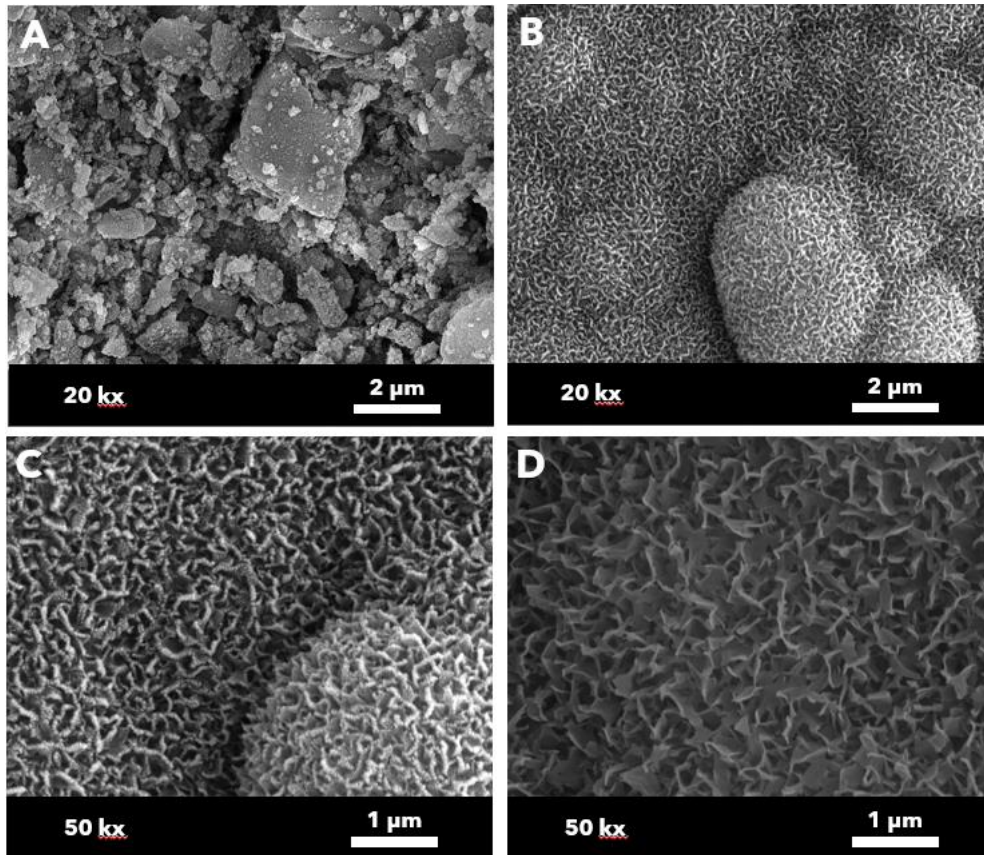


Figure 7: SEM micrographs of bioactive glass pellets A) before testing B) and C) after 24h and D) after 7 days of SBF incubation.

Longer immersion times would provide a more comprehensive understanding of the bioactivity mechanism. However, long-term degradation and steady-state ion-release investigations will be conducted as part of upcoming *in vivo* studies to more closely mimic physiological environments.

The *in vitro* cytotoxicity of the scaled-up bioactive glass was evaluated on L929 fibroblasts using varying concentrations of the glass extract (100%, 50%, and 25%), as shown in Figure 8. The results indicate a clear dose-dependent effect on cell viability. The undiluted extract (100%) exhibited a cytotoxic effect, reducing cell viability to approximately 31%. This behaviour is frequently reported *in vitro* for highly reactive bioactive glasses. Under static extraction conditions, the rapid dissolution of the glass network leads to a burst release of alkaline ions, causing a sharp, localized increase in pH that is detrimental to cell survival.

However, when the extract was diluted with fresh culture medium to better simulate the dynamic fluid turnover found *in vivo*, cell viability improved significantly. At a 50% extract concentration, cell viability reached approximately 77%, and it further increased to 97% for the 25% extract concentration. According to the ISO 10993-5 standard, a material is considered non-cytotoxic if the cell viability remains above the 70% threshold. Therefore, the results obtained at 50% and 25% concentrations confirm the adequate biocompatibility of the synthesized glass. These findings demonstrate that the scale-up process does not adversely affect the biological properties of the material, supporting its safe use for bone regeneration applications.

While these preliminary results confirm the fundamental biocompatibility of the synthesized powder, a more comprehensive biological evaluation will be conducted in future studies. Specifically, further tests will investigate the influence of densification and temperature profiles on the cytotoxicity of the final 3D-printed bioactive glass parts.

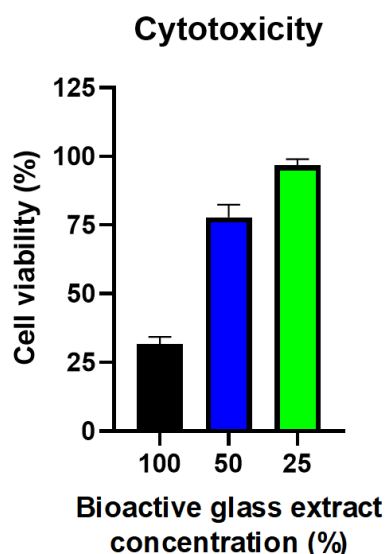


Figure 8: in vitro cytotoxicity testing

3.3.3D printing: stereolithography

The main challenge in the AM of bioactive glass by stereolithography is the removal of all organic components and the densification of the 3D-printed parts while avoiding crystallisation of the glass. To the authors' knowledge, only very few studies have reported amorphous, densified 3D-printed bioactive glass parts produced by the SLA process [10,23]. The flexibility of our synthesis process enables the tunability of bioactive glass properties (composition, reactivity, particle size, etc.) to achieve this objective. Finally, the selection of resins and additives for the 3D paste was carefully considered to provide efficient debinding at lower temperature. To determine an appropriate thermal treatment for the 3D-printed parts, TGA–DSC analysis was performed. As shown in Figure 9, a pronounced exothermic peak is observed between 300 and 550°C, corresponding to thermal decomposition of the resin and other organic components. In addition, the thermogravimetric curve reveals several distinct mass-loss steps, which provide valuable information for defining an optimised thermal debinding cycle.

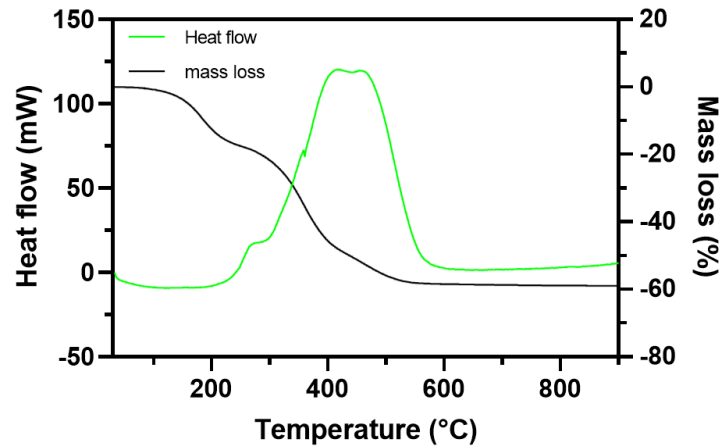


Figure 9: TGA-DSC curve of the green gyroid.

After debinding at 550°C for 30 min, quasi-amorphous 3D structures were obtained, only one crystalline peak remained at $32^\circ 2\theta$ corresponding to hydroxyapatite (Figure 13). This debinding step is required to remove all organic components and obtain parts composed exclusively of bioactive glass. The effective removal of organic species was confirmed by FTIR analysis. As shown in Figure 10, the characteristic absorption bands associated with organic compounds disappeared ($\text{C}=\text{O}$ bond at 1700 cm^{-1} and $\text{C}-\text{H}$ bond at 2800 cm^{-1}), while only the vibrations of the inorganic glass network remained, namely the $\text{Si}-\text{O}-\text{Si}$ stretching vibration band around 1000 cm^{-1} and the $\text{P}-\text{O}$ vibration near 600 cm^{-1} [24].

Figure 11 presents a photograph of the 3D-printed parts in the green state (right), after debinding (centre), and after sintering (left).

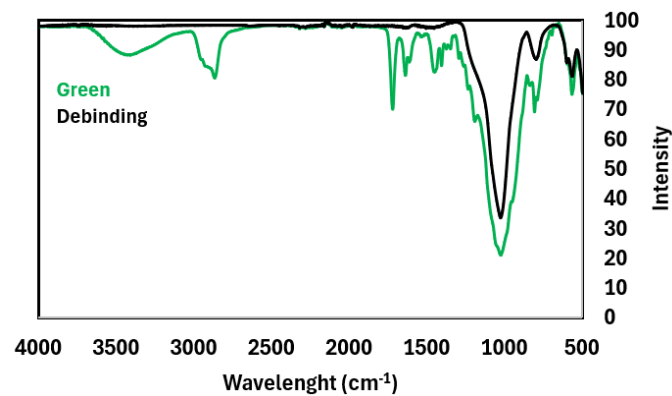


Figure 10: FTIR spectra of the green and debound parts.

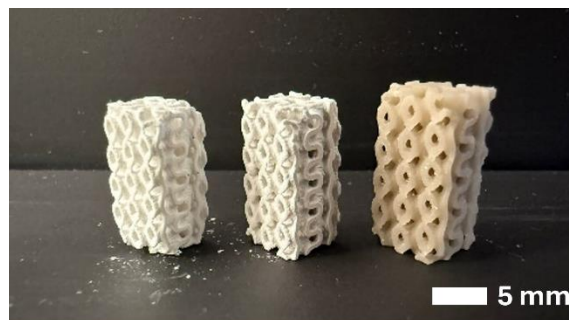


Figure 11: From left to right: sintered, debound and green 3D bioactive glass gyroids.

The most challenging step after printing is the sintering process. High temperatures are required to maximise the densification of the printed parts. However, the material imposes an upper temperature limit owing to its natural tendency to crystallise [25]. To optimise the sintering treatment of the 3D parts, *in situ* high-temperature X-ray diffraction (HTXRD) measurements have been performed. In this setup, a heating furnace is integrated into the XRD instrument, allowing diffraction patterns to be recorded continuously during heating. The analysis focused on the main HCA diffraction peaks located at 32° and 33° 2θ , shown in figure 12. Based on these HTXRD measurements, the onset of crystallisation was detected at around 650°C , which defines an upper temperature limit for sintering while retaining the amorphous character.

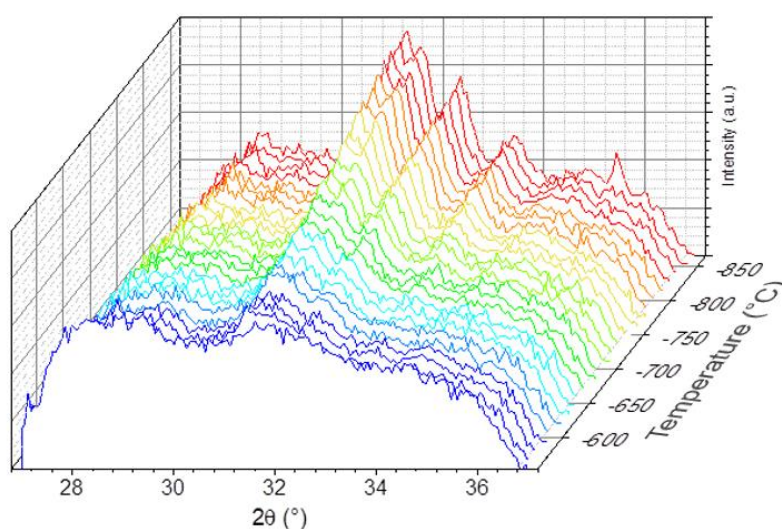


Figure 12: HTXRD analysis on bioactive glass powder.

Based on these data, three thermal cycles were tested, at 650°C , 700°C and 750°C for 2h to evaluate the crystallisation of the 3D parts during sintering. Figure 13 shows the XRD patterns obtained after these treatments. A small amount of crystalline HCA was detected in all patterns. However, no significant variation in the HCA peak intensity was observed between the different conditions. This suggests that HCA is present only at the nucleation stage, and that higher temperatures would be required to promote further crystallisation. Nevertheless, the presence of carbonated hydroxyapatite is not detrimental since it is a bioactive material. We also observed that this crystalline phase is similar to the HCA formed during SBF testing. These observations suggest that a small amount of HCA within the implant does not hinder bioactivity and may even enhance it.

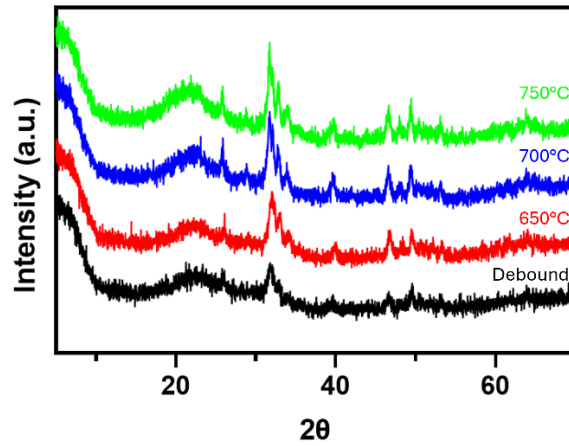


Figure 13: XRD patterns of debound and sintered parts.

Finally, SEM observations were performed on the green parts and on the parts sintered at 700°C. Figure 14A shows an SEM image of the green part. Minor surface cracks can be observed, together with limited light-scattering effects (Figure 14A), indicating good printing resolution. Figure 14B highlights the intimate mixing between the resin and the bioactive glass powder in the green state.

Figures 14C and 14D present SEM images of the sintered parts. Overall shrinkage of the structure is observed after sintering, together with a decrease in pore size from approximately 600 μm to 400 μm . Figure 14D further demonstrates the limited degree of sintering, which explains the challenge encountered in achieving high densification while avoiding crystallisation of the bioactive glass. The thermal treatment at 700°C for 2h allowed the printed

parts to reach a relative density of 75% (determined by the Archimedes method) while keeping crystallisation at a minimum.

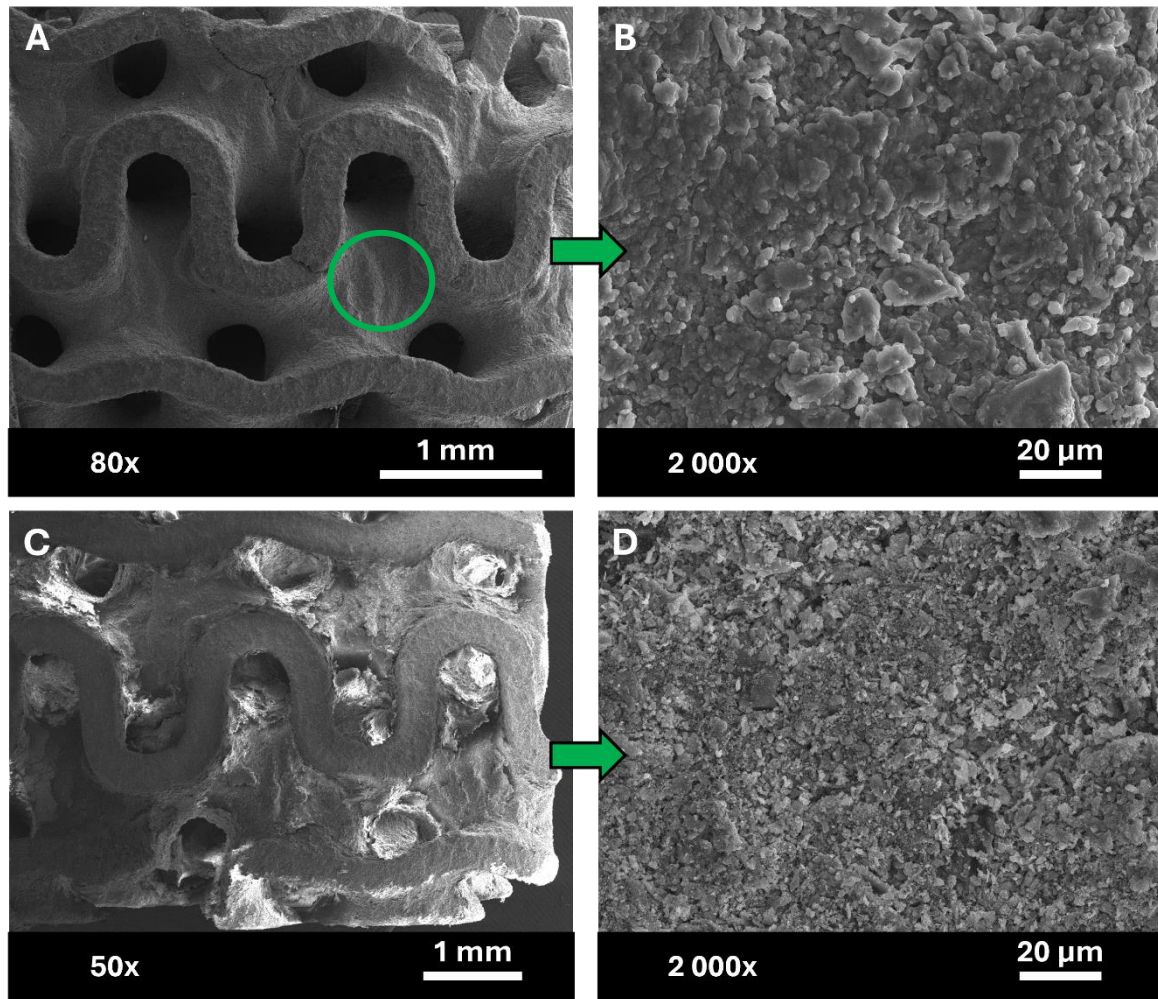


Figure 14: SEM images of 3D parts: A) green part at low magnification B) green part at higher magnification C) sintered part at low magnification and D) sintered part at higher magnification.

4. Discussion

To evaluate the significance of the developed manufacturing route, the results obtained in this work were compared with the current literature focusing on the additive manufacturing of bioactive glasses by vat photopolymerisation (SLA/DLP). To date, most research has targeted the traditional 45S5 composition. A critical challenge frequently reported in these studies is the inevitable high-temperature crystallisation that occurs during the debinding and sintering stages. This premature phase transformation into crystalline phases significantly decreases the bioactivity of the material by altering its dissolution rate [16,26–28].

In contrast, the processing window established in this study for the spray-dried, sodium-modified 68S powder overcomes this technological bottleneck by enabling structural densification while preventing extensive crystallisation.

This study primarily focuses on the scalable synthesis of a novel bioactive glass powder and demonstrates its suitability for additive manufacturing by vat photopolymerisation for bone tissue engineering. Nevertheless, certain technical limitations remain to be addressed in

future work. At present, achieving full densification of the printed scaffolds while preserving their amorphous structure represents the main challenge. The 3D-printed parts in this work reached a relative density of 75%, which consequently limits their immediate mechanical performance for load-bearing applications. Ongoing research is therefore dedicated to optimising the sintering window to maximise density without triggering crystallisation. Among the methods under investigation, ultrafast sintering techniques appear highly promising. By using extremely high heating rates, fast sintering can bypass critical crystallisation temperature ranges, potentially allowing access to higher densification temperatures while maintaining the highly bioactive amorphous state of the glass network.

5. Conclusion

A simple and scalable aqueous sol-gel synthesis combined with spray-drying was successfully developed to produce large quantities of quasi-amorphous bioactive glass powder. Thanks to this combination, production can reach up to 0.5 kg per day. The use of low-cost precursors and water-based sol-gel chemistry significantly reduces the cost and complexity of the process while maintaining suitable particle size distribution for AM. After washing and calcination at 500°C, the powders remain quasi-amorphous, with only slight nucleation of carbonated hydroxyapatite. The produced material demonstrates rapid HCA formation in SBF and can be processed into 75% dense 3D-printed parts with limited crystallisation.

6. Acknowledgements

The authors warmly thank Virginie Bertrand and the MS Lab who helped us with the bioactivity and cytotoxicity test. In addition, the authors also thank Fanny Lambert and Sébastien Blasutig from the GeMMe laboratory (Georesources, Mineral Engineering & Extractive Metallurgy) at ULiège for the XRF analyses.

7. Bibliography

- [1] Y. Gao, M.A. Seles, M. Rajan, Role of bioglass derivatives in tissue regeneration and repair: A review, *Reviews on Advanced Materials Science* 62 (2023). <https://doi.org/10.1515/rams-2022-0318>.
- [2] J. Colat-Parros, F. Jordana, Les substituts osseux, Lecture notes, Société Francophone de biomatériaux Dentaires, 2009.
- [3] T. Albrektsson, A. Wennerberg, On osseointegration in relation to implant surfaces, *Clin. Implant Dent. Relat. Res.* 21 (2019) 4–7. <https://doi.org/10.1111/cid.12742>.
- [4] L.L. Hench, The story of Bioglass®, *J. Mater. Sci. Mater. Med.* 17 (2006) 967–978. <https://doi.org/10.1007/s10856-006-0432-z>.
- [5] Y. Chen, W. Li, C. Zhang, Z. Wu, J. Liu, Recent Developments of Biomaterials for Additive Manufacturing of Bone Scaffolds, *Adv. Healthc. Mater.* 9 (2020). <https://doi.org/10.1002/adhm.202000724>.

- [6] G. Kaur, G. Pickrell, N. Sriranganathan, V. Kumar, D. Homa, Review and the state of the art: Sol–gel and melt quenched bioactive glasses for tissue engineering, *J. Biomed. Mater. Res. B Appl. Biomater.* 104 (2016) 1248–1275. <https://doi.org/10.1002/jbm.b.33443>.
- [7] Y.J. Chou, C.W. Hsiao, N.T. Tsou, M.H. Wu, S.J. Shih, Preparation and in vitro bioactivity of micron-sized bioactive glass particles using spray drying method, *Applied Sciences (Switzerland)* 9 (2019) 19. <https://doi.org/10.3390/app9010019>.
- [8] G. Molino, A. Bari, F. Baino, S. Fiorilli, C. Vitale-Brovarone, Electrophoretic deposition of spray-dried Sr-containing mesoporous bioactive glass spheres on glass–ceramic scaffolds for bone tissue regeneration, *J. Mater. Sci.* 52 (2017) 9103–9114. <https://doi.org/10.1007/s10853-017-1026-5>.
- [9] A. Saberi, A. Behnamghader, B. Aghabarari, A. Yousefi, D. Majda, M.V.M. Huerta, M. Mozafari, 3D direct printing of composite bone scaffolds containing polylactic acid and spray dried mesoporous bioactive glass-ceramic microparticles, *Int. J. Biol. Macromol.* 207 (2022) 9–22. <https://doi.org/10.1016/j.ijbiomac.2022.02.067>.
- [10] A.R. Boccaccini, Q. Chen, L. Lefebvre, L. Gremillard, J. Chevalier, Sintering, crystallisation and biodegradation behaviour of Bioglass®-derived glass-ceramics, *Faraday Discuss.* 136 (2007) 27–44. <https://doi.org/10.1039/b616539g>.
- [11] R. Li, A.E. Clark, L.L. Hench, An investigation of bioactive glass powders by sol-gel processing., *J. Appl. Biomater.* 2 (1991) 231–239. <https://doi.org/10.1002/jab.770020403>.
- [12] K. Hayashi, R. Kishida, A. Tsuchiya, K. Ishikawa, Superiority of Triply Periodic Minimal Surface Gyroid Structure to Strut-Based Grid Structure in Both Strength and Bone Regeneration, *ACS Appl. Mater. Interfaces* 15 (2023) 34570–34577. <https://doi.org/10.1021/acsami.3c06263>.
- [13] I. Gibson, D. Rosen, B. Stucker, M. Khorasani, Additive manufacturing technologies, Springer International Publishing, 2020. <https://doi.org/10.1007/978-3-030-56127-7>.
- [14] P. Kowalczyk, A. V. Neimark, S. Furmaniak, A.P. Terzyk, K. Kaneko, Graphene-domain theory for high-surface-area nanoporous carbons: Beyond the BET method, *Carbon N. Y.* 245 (2025). <https://doi.org/10.1016/j.carbon.2025.120737>.
- [15] F. Baino, S. Yamaguchi, The use of simulated body fluid (SBF) for assessing materials bioactivity in the context of tissue engineering: Review and challenges, *Biomimetics* 5 (2020) 57. <https://doi.org/10.3390/biomimetics5040057>.
- [16] M. Plewinski, K. Schickle, M. Lindner, A. Kirsten, M. Weber, H. Fischer, The effect of crystallization of bioactive bioglass 45S5 on apatite formation and degradation, *Dental Materials* 29 (2013) 1256–1264. <https://doi.org/10.1016/j.dental.2013.09.016>.
- [17] L.M. Mukundan, R. Nirmal, D. Vaikkath, P.D. Nair, A new synthesis route to high surface area sol gel bioactive glass through alcohol washing: a preliminary study, *Biomater* 3 (2013). <https://doi.org/10.4161/biom.24288>.
- [18] E.S. Freeman, The Kinetics of the Thermal Decomposition of Sodium Nitrate and of the Reaction between Sodium Nitrite and Oxygen, *Journal of Physical Chemistry.* 60 (1956) 1487–1493. <https://doi.org/10.1021/j150545a005>.

- [19] G. Goller, H. Demirkiran, F.N. Oktar, E. Demirkesen, Processing and characterization of bioglass reinforced hydroxyapatite composites, *Ceram. Int.* 29 (2003) 721–724.
[https://doi.org/10.1016/S0272-8842\(02\)00223-7](https://doi.org/10.1016/S0272-8842(02)00223-7).
- [20] K. Emre Oksuz, Effect of Composition and Sintering Temperature on the Structure and Properties of Porous Bioactive Glass Scaffolds, *Chiang Mai J. Sci* 46 (2019) 568–578.
<http://epg.science.cmu.ac.th/ejournal/>.
- [21] L. Xing-Bang, H. Zhong, J.-X. Zhang, Y.-S. Duan, D.-L. Jiang, Powder Characteristics on the Rheological Performance of Resin-based Zirconia Suspension for Stereolithography, *Journal of Inorganic Materials* 35 (2020) 231–235. <https://doi.org/10.15541/jim20190091>.
- [22] T.P. Herd, C.L. Cramer, S.R. Schmid, Resin chemistry and particle size influence on stereolithography with silicon carbide, 2025. www.sciencedirect.com.
- [23] L. Hambitzer, Z. Hosneolfat, K. Griebenow, R. Prediger, S. Kluck, I. Ketterer, S.B. Zaidi, D.S. Brauer, F. Kotz-Helmer, High-Resolution Stereolithography of Amorphous, Dense and Mechanically Stable Bioactive Glass, *Adv. Mater. Technol.* 10 (2025).
<https://doi.org/10.1002/admt.202500925>.
- [24] A. Saberi, A. Behnamghader, B. Aghabarari, A. Yousefi, D. Majda, M.V.M. Huerta, M. Mozafari, 3D direct printing of composite bone scaffolds containing polylactic acid and spray dried mesoporous bioactive glass-ceramic microparticles, *Int. J. Biol. Macromol.* 207 (2022) 9–22.
<https://doi.org/10.1016/j.ijbiomac.2022.02.067>.
- [25] A.R. Boccaccini, Q. Chen, L. Lefebvre, L. Gremillard, J. Chevalier, Sintering, crystallisation and biodegradation behaviour of Bioglass®-derived glass-ceramics, *Faraday Discuss.* 136 (2007) 27–44. <https://doi.org/10.1039/b616539g>.
- [26] O. Bretcanu, X. Chatzistavrou, K. Paraskevopoulos, R. Conradt, I. Thompson, A.R. Boccaccini, Sintering and crystallisation of 45S5 Bioglass® powder, *J. Eur. Ceram. Soc.* 29 (2009) 3299–3306. <https://doi.org/10.1016/j.jeurceramsoc.2009.06.035>.
- [27] Z. Dong, J. Gong, H. Zhang, Y. Ni, L. Cheng, Q. Song, L. Tang, F. Xing, M. Liu, C. Zhou, Preparation and Characterization of 3D Printed Porous 45S5 Bioglass Bioceramic for Bone Tissue Engineering Application, *Int. J. Bioprint.* 8 (2022) 207–216.
<https://doi.org/10.18063/ijb.v8i4.613>.
- [28] Z. Ma, J. Xie, X.Z. Shan, J. Zhang, Q. Wang, High solid content 45S5 Bioglass®-based scaffolds using stereolithographic ceramic manufacturing: process, structural and mechanical properties, *Journal of Mechanical Science and Technology* 35 (2021) 823–832.
<https://doi.org/10.1007/s12206-021-0144-9>.