Supporting Information

The anomaly in bioactive sol-gel borate glasses

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Results and Discussion

Sol-gel processing



Figure S1. Sol-gel processing overview of SGBGs. Overview from drying (after 2d at 120 °C), calcination (400 °C) and grinding, to resultant glass surfaces shown via SEM imaging.

X-ray Diffraction



Figure S2. X-ray diffractograms of the calcined SGBGs. All glasses were amorphous after calcination at 400 $^{\circ}$ C.

Quantifying fraction of N₄ units using ATR-FTIR

In addition to MAS-NMR, ATR-FTIR spectra can also be used to quantify integrated intensities at the two different bonding regions, $880-1150 \text{ cm}^{-1}$ and $1200-1550 \text{ cm}^{-1}$, which correspond to the 3- and 4-coordinated boron units termed A₃ and A₄, respectively. The relative integrated intensity A_r, is given by Equation 1:

$$A_r = \frac{A_4}{A_3}$$
 Equation 1

It is possible to estimate the fraction of 4-coordinated boron ions (N₄) from Equation 2:

$$N_4 = \frac{A_r}{\alpha + A_r}$$
 Equation 2

where α is the relative integrated absorption coefficient of boron tetrahedra versus boron triangles.¹⁻³ The α value was previously generated by comparing SrO-B₂O₃ NMR data (MO = 0.4, 0.44, N₄ = 0.44, 0.39)⁴ with FTIR data⁵ to obtain a value of α = 1.3. However, this α value was also used for BaO- and CaO-borate glass estimations because of the lack of NMR data for binary compositions.¹ MgO-B₂O₃ glasses had distinctly lower A_r values and therefore another α value of 1.9 was used for their calculations.⁵ For alkali-borates, previous studies examining Li₂O-B₂O₃ glasses have used an α value of 1.5. Therefore, in the current study, an α value of 1.3 may not be ideal for CaO-B₂O₃ glasses, especially since previous IR spectroscopy data have shown that the maximum N₄ value shifts to higher values with increasing alkaline-earth field strength⁵ which is the opposite trend for alkaline-earth borates.^{6, 7} Table S1 gives α values in this study which were generated using A_r values from ATR-FTIR and N₄ values from ¹¹B MAS NMR data and Equation 2.

Table S1: A_r (from ATR-FTIR data), N₄ (from MAS-NMR data), and calculated α values for the range of glasses investigated in this study

	Ca20	Ca30	Ca40	Ca50	Ca60	Ca70
Ar	0.79	1.14	1.66	1.90	1.06	0.47
N ₄	0.35	0.45	0.54	0.54	0.52	0.41
α	1.46	1.39	1.42	1.62	0.98	0.67

The average α across the compositional range is 1.26±0.32 which is close to what Yiannapolous et al proposed.⁵ However, the α calculation in that study only used MO values of 0.4 and 0.47 where it was approaching the maxima A_r content (*i.e.*, x = 0.5 MO). By using this approach, α is averaged until the relative maxima (*i.e.*, MO = 0.519) of A_r and N₄ over the range of Ca20–50 gives $\alpha = 1.47\pm0.09$, which we approximate to $\alpha = 1.5$ and used to plot Fig. 2c. This value falls between the MgO-B₂O₃ ($\alpha = 1.9$) and SrO-B₂O₃ ($\alpha = 1.3$) values. Since Ca field strength is between that of Mg and Sr, we would expect our new α to be within this range. However, since there is still very limited information on binary CaO-B₂O₃ glasses, more studies are needed to further refine this value.

The fraction of 4-coordinated borate units in Fig. 1c are also plotted using R values in Table S2 and Fig. S3b&c. It can be observed that the melt-quench derived glasses of the same composition using ¹¹B MAS-NMR reach a relative maxima similar to the SGBGs used in this study. We are unaware of any other NMR data relating of binary CaO-B₂O₃ glasses above 50 mol% CaO (*e.g.*, R>1).

Mol%	Ca20	Ca30	Ca40	Ca50	Ca60	Ca70
CaO	20 (26.1)	30 (33.1)	40 (42.1)	50 (51.9)	60 (62.6)	70 (73.3)
B_2O_3	80 (73.9)	70 (66.9)	60 (57.9)	50 (48.1)	40 (37.4)	30 (26.7)
R	0.25 (0.35)	0.43 (0.50)	0.67 (0.73)	1 (1.08)	1.5 (1.67)	2.33 (2.75)

Table S2: Calculated. (Measured), and R (CaO/B₂O₃) Values of SGBG Compositions (mol%)



Figure S3. Structural properties of calcined SGBGs. (a) ATR-FTIR spectra and ¹¹B MAS-NMR line spectra of calcined SGBGs show the typical peaks relating to 3- and 4-coordinated boron with linear fits over the range of modifier additions. The same structural properties are plotted in terms of "R" (CaO/B₂O₃) using both quadratic (b) and linear (c) lines to demonstrate the trend using least square fit. Melt-quench derived CaO-B₂O₃ glasses from Wu and Stebbins⁸ (hollow gold triangles) and Jin et al.⁹ (hollow blue spheres) are also shown for comparison in b & c as well as the gray dashed line which represents N₄=R.

Comparison of textural and physical properties

The textural properties of the glasses are given in Table S3. To visualize the unique property trends of these SGBGs, a series of graphs comparing the property trends of SSA, PV, and density are shown in Figures S5-7. Linear regression or quadratic equations using the least square fit are shown to help demonstrate the trends.

Table S3: Glass particle textural properties: Average Median (D_{50}) and Mean (D_{AVG}) Diameter, Specific Surface Area (SSA), Average Pore Volume (PV), Average Pore Width, and Density. (n=3).

ID	Particle Size (µm)		SSA (m²/a)	Pore Volume	Pore Width	Density
	D ₅₀	D _{AVG}	(m-/g)	(cm²g)	(nm)	(g/cm²)
Ca20	51.0	54.9	1 ± 0	0.07 ± 0.01	84.0 ± 0.9	1.78
Ca30	21.1	28.4	91 ± 4	0.63 ± 0.04	20.9 ± 0.4	2.18
Ca40	22.0	29.7	158 ± 17	1.22 ± 0.13	20.3 ± 0.9	2.28
Ca50	26.4	34.5	107 ± 5	0.87 ± 0.09	23.6 ± 0.5	2.42
Ca60	30.8	39.2	77 ± 2	0.44 ± 0.02	16.3 ± 0.5	2.49
Ca70	30.5	37.8	66 ± 1	0.37 ± 0.01	16.0 ± 0.5	2.64



Figure S4. Textural and physical properties of SGBGs versus M_F plotted in terms of "R". (a) Specific surface area (SSA) and (b) pore volume (PV) change with CaO content according to the borate anomaly, by indicating relative maxima values. In contrast, (c) density increases linearly with CaO content. Simple linear (solid line) and quadratic (dashed line) equations using a least squares fit are shown to help demonstrate the trend.



Figure S5. Comparison of specific surface area (SSA) trends with increasing CaO. Increasing CaO content led to an initial increase in SSA up to approximately 40 mol% followed by a decrease with a further increase in CaO content ("•"). In contrast, a linear decrease in SSA has been reported in binary sol-gel CaO-SiO₂ glasses with the addition of CaO (hollow blue triangles and hollow green squares)¹⁰. *SSA for the pure silica gel-glass monolith was 679.87±8.67 m²/g.¹¹



Figure S6. Comparison of pore volume (PV) trends with increasing CaO. Increasing CaO content led to an initial increase in PV up to approximately 40 mol% followed by a decrease with a further increase in CaO content ("•"). In contrast, a linear increase in PV has been reported in binary sol-gel CaO-SiO₂ glasses (*Pore volume for the pure silica gel-glass monolith was $0.433\pm0.009 \text{ cm}^3/\text{g}$).¹¹



Figure S7. Comparison of density trends with increasing (a) M_F CaO and (b) R values (CaO/B₂O₃). Increasing CaO content led to a linear increase in density ("•") which was also observed for other binary melt-quench derived borate glasses measured with He pyncometery¹² (purple squares) and bulk density¹³ (pink triangles). Binary sol-gel CaO-SiO₂ glasses in (a) (hollow blue triangles) demonstrate the opposite trend as density decreases with increasing CaO content (*density for the pure silica gel-glass monolith was estimated to be 1.335 g/cm³).¹¹

Bioactivity in SBF

pH change and ionic release in SBF

The pH change and the release of boron and calcium ions, through glass dissolution in SBF at a 1.5 mg/mL ratio were measured to investigate their reactivity (Fig. S8). The pH change of the SBF solution due to glass dissolution was measured at 0.5, 2, 6, 24, and 168 h (n=3) with an Accumet XL20 pH meter. Furthermore, the release of boron and calcium ions from glass particles (n=3) in SBF was quantified using an inductively coupled plasma–optical emission spectrophotometer (ICP-OES; Thermo Scientific iCAP 6500, USA). Collected aliquots were filtered through a 0.2 μ m nylon filter then stored in a 15 mL falcon tube followed by dilution with 4% (w/v) nitric acid (Fisher Scientific, Canada). Serially diluted solutions of boron (0.5, 5, 50 ppm) and calcium (0.2, 2, 20 ppm), were used as standards.

Glasses with higher calcium content exhibited greater increases in the pH of the SBF solution (Fig. S8a). These results corresponded with our previously investigated 4- and 3-component SGBGs where the highest number of modifiers led to greater increases in pH.^{14, 15} After the initial increase in pH, all compositions exhibited a slightly decreasing pH trend, which might be attributed to the consumption of calcium to form HCA or calcite.

Similarly, ICP-OES (Figs. S8b and c) indicated that all compositions, except for Ca20, released the majority of their boron or calcium ions by 0.5h, which has been previously observed with other SGBG compositions in DIW^{14, 15} and SBF.¹⁶ These release rates were dependent on composition and remained relatively stable up to 168h. Ca20 showed a slower rate of release of boron and calcium ions overtime until 168h (Fig. S8b and c). This may be due to the high borate content or significantly reduced surface area (Table S3) limiting contact with SBF and the release of ions. It also suggests that a certain amount of boron ion release is required to initiate HCA

conversion (Fig. 4). Furthermore, high borate containing glasses (70 mol%) have previously demonstrated linear dissolution profiles.¹⁷ We previously hypothesized that one of the reasons SGBGs were highly bioactive was their ability to rapidly release phosphorus ions,¹⁴ however, along with our previous work,¹⁵ this study has demonstrated that phosphate is not a necessary component for rapid HCA conversion in SBF. This is distinct from silicate glasses which ultimately depend on phosphate content for bioactivity.¹⁸



Figure S8. pH and release of boron and calcium ions in SBF. (a) pH versus immersion time (log scale). There was a rapid initial increase in pH within the first 0.5h, followed by a decrease with longer immersion time. ICP-OES of (b) boron and (c) calcium ion release from SGBGs in SBF versus time (log scale) demonstrated rapid ion release dependent on composition while Ca20 demonstrated a slower release profile, which may be due to lower SSA and PV values. Dashed line in (c) represents calcium ion content in SBF.

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