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| Complete List of Authors: | Scott, Holli; James Madison University, Chemistry<br>Davis, Ani; James Madison University, Chemistry<br>Peters, Gretchen Marie; James Madison University, Chemistry and Biochemistry |
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ARTICLE

# Cooperative crosslinking in polyvinyl alcohol organogels

Holli R. Scott, Ani N. Davis, and Gretchen Marie Peters*

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Manipulating and optimizing the properties of gels is important for practical applications but can be both synthetically difficult and expensive. In this work, we report an easily tunable polyvinyl alcohol (**PVA**) organogel formed with boric acid (**BA**) and 1,4-benzenediboronic acid (**1,4-BDBA**) as crosslinkers. While **PVA** and **BA** alone form weak aggregations in DMSO, adding small amounts of **1,4-BDBA** dramatically improves the material properties and gelation. **PVA** organogels made with mixtures of **BA** and **1,4-BDBA** have improved thermal properties, lower CGCs, and higher G′ than those with either crosslinker alone. We propose that these enhanced material properties are the result of cooperative **PVA** crosslinking between **1,4-BDBA** and **BA**. As the properties of this system can be improved by simply varying the ratio of crosslinkers, these organogels are highly adjustable and are a practical alternative to PVA hydrogels.

## Introduction

Gels are useful for a variety of applications, including drug delivery,[1,2] separations and environmental remediation,[3,4] and tissue engineering.[5] Because these uses require different material properties, there is interest in developing straightforward methodologies for manipulating and controlling the properties of gels. From a practical sense, altering the properties of a gel can be both labour-intensive and costly, requiring extensive synthesis and fabrication. Thus, the use of commercially available materials to form tunable gels is quite attractive. Polyvinyl alcohol (**PVA**) is a commercially available and biocompatible polymer with a high propensity to form gels and films.[6] **PVA** gels are formed by covalently crosslinking the alcohol-rich backbone of the polymer yielding a fibrous gel network that impedes the flow of the bulk solution. While a number of different crosslinkers can be used to gel **PVA**,[7–12] some of the most common are boron-based compounds, such as boric acid ($B(OH)_3$, **BA**). **BA** reversibly binds to diols via tetravalent borate ester motifs and can readily function as a crosslinker and gelating agent for diol-containing small molecules[13,14] and polymers.[15–17] Gelation of **PVA** with **BA** has been well-established under aqueous conditions, but typically requires the presence of a strong base.[18–21] Because of this, **PVA**-**BA** gels are often impractical for real-world applications, particularly with biological and medical purposes.

**PVA** organogels (i.e., gels made in non-aqueous media) provide a unique alternative to these highly basic **PVA**-**BA** hydrogels. The use of organic solvents rather than water in this system avoids the necessity of caustic conditions and expands the variety of boron-based crosslinker that can be used. In particular, diboronic acids (such as **1,4-BDBA**) have been shown to be highly effective **PVA** crosslinkers but are typically not water-soluble. Because they can be readily functionalized using traditional synthetic methods, diboronic acids offer a unique platform for introducing new properties and function into the gel. Thus, it is of interest to explore **PVA** organogels and utilize diboronic crosslinkers for crosslinking and gelling **PVA**.

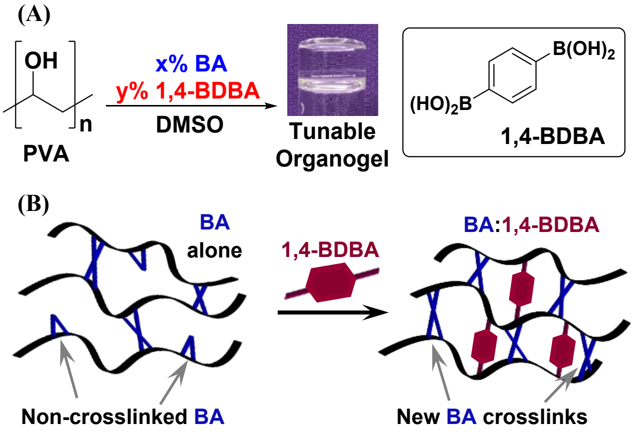

**Figure 1.** (A) **PVA** organogels formed with mixtures of **BA** and **1,4-BDBA** in DMSO are highly tunable and have improved properties compared to those made with **BA** alone. (B) We propose the enhanced material properties are due to the formation of new **PVA-BA** crosslinks promoted by **1,4-BDBA**.

To date, **PVA** organogels have been shown to be self-healing and adhesive[22] and have been used to extract dyes from water,[23] as a gel electrolyte for capacitors and batteries,[24] and as a medium for cleaning and conserving art.[25–27] In recent years it has been shown that **BA** can crosslink partially hydrolysed polyvinyl acetate (the partially acetylated precursor to **PVA**) to form gel-like dispersions in organic media, such as DMSO.[26,28] That being said, extensive studies into materials

*Department of Chemistry and Biochemistry, James Madison University, Harrisonburg, VA 22807*

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formed with **BA** and **PVA** in organic solvents remain largely unexplored.[29–31]

Herein, we report a novel, tunable **PVA** organogel formed in DMSO with mixtures of **BA** and 1,4-benzenediboronic acid (**1,4-BDBA**) (Fig. 1). The tunability of this system is unique in that it arises from a cooperative event in which additional **PVA** crosslinks are formed by both **BA** and **1,4-BDBA** when **1,4-BDBA** is introduced into the gel. While **PVA** with **BA** alone yields weak, viscous dispersions, exchanging as little as 10% of the **BA** crosslinker for **1,4-BDBA** results in a dramatic improvement in the material and rheological properties. Specifically, with added **1,4-BDBA**, we observe both a decrease in critical gelation concentration (CGC) and an increase in storage modulus (G′). Additionally, gels formed with both **1,4-BDBA** and **BA** show improved thermal and self-healing properties compared to those with **BA** alone. We attribute these enhancements to the efficiency of **1,4-BDBA** as a **PVA** crosslinker and the formation of additional **BA** crosslinks through a cooperative effect. This mechanism and the formation of more densely crosslinked **PVA** network with **BA**:**1,4-BDBA** mixtures is supported by evidence from infrared (IR) spectroscopy and scanning electron microscopy (SEM). These gels require no synthesis and can be formed by simply mixing at room temperature. Furthermore, we can easily alter the crosslinking density and properties of the gel by varying the ratio of **BA** to **1,4-BDBA**. We propose that these systems provide a valuable alternative to **PVA-BA** hydrogels, and that this cooperative crosslinking mechanism is useful for manipulating and tuning the properties of gels.

## Experimental

**Materials and general experimental.** Polyvinyl alcohol (**PVA**) (100% hydrolysed, average MW = 14,000), 1,4-benzenediboronic acid (**1,4-BDBA**) (≥95.0%), 1,3-propanediol (**1,3-PD**) (98%) and DMSO (99.9+%) were purchased from Sigma-Aldrich. Boric acid (**BA**) (99+%) was purchased from Alfa Aesar, and deuterated DMSO (99.9%) was purchased from Cambridge Isotope Labs. **PVA** was stored in a desiccator and monitored periodically for water absorption using thermal gravimetric analysis. Rheological data were collected on an Anton Paar MCR 302 series rheometer. Differential scanning calorimetry (DSC) measurements were performed using a TA Instruments Discovery DSC-250. SEM images were obtained using a Zeiss instrument at 10.0 kV. UV-Vis spectra were recorded on an Agilent 8453 UV-Visible spectrophotometer. FT-IR spectra were recorded on a Thermo Scientific Nicolet iS10 spectrometer, equipped with a SMART iTX attenuated total-reflection (ATR) accessory. NMR spectra were recorded on a Bruker AVIII-400 operating at 400.13 MHz. Chemical shifts are reported in ppm relative to the residual solvent peak.

**Procedure for gel preparation.** Stock solutions of polyvinyl alcohol (**PVA**), boric acid (**BA**) and 1,4-benzenediboronic acid (**1,4-BDBA**) were prepared in DMSO at 10 wt% and 200 mM, respectively. All solutions were heated and stirred until the solute was fully dissolved and stored at room temperature. Gels were prepared in vials by adding the appropriate amount of each stock solution. The **PVA** stock solution was warmed slightly prior to adding to the vial to allow for easy transfer and accurate measurements. After all reagents were added, the solution was stirred with a spatula until combined and a gel formed. Gels were allowed to equilibrate at room temperature before analysis. All analyses were performed in triplicate and at different time points to ensure the gels had reached equilibrium.

**Procedure for IR studies.** Gels were prepared as described in the general gel preparation and washed with water to exchange the DMSO solvent. Samples were then flash frozen in liquid nitrogen and lyophilized and IR spectra were recorded.

**Procedure for rheology studies.** Gels were prepared as described in the general gel preparation procedure. Rheological measurements were performed at 25 °C using a 25 mm parallel plate. Gel samples were loaded onto the Peltier plate and allowed to equilibrate for 10 min. Strain sweeps were performed at 10 rad/s by varying strain from 0.1 to 100%. Frequency sweeps were performed at 1% strain from 0.1 to 100 rad/s. Strain sweeps were performed both before and after each frequency sweep to ensure no changes in the sample occurred. Hysteresis loops were performed by alternating from low strain (5 %) to high strain (500 %) at a constant angular frequency of 10 rad/s. Each measurement was done in triplicate with new gel samples for each trial.

**Procedure for DSC studies.** Gels were prepared as described in the general gel preparation. Samples were hermetically sealed in an aluminium pan, and measurements were carried out under nitrogen gas flow. The samples were first equilibrated to -40°C, then heated to 40°C at a rate of 5°C/min. After heating, the sample was cooled to -40°C at the same rate. Each measurement was done in triplicate with new gel samples for each trial.

**Procedure for transmittance studies.** Gels were prepared in plastic cuvettes at 100mM total crosslinker concentration and 5% **PVA** using the general gel preparation described. Transmittance (%T) at 600 nm was measured using UV-visible spectroscopy, and each measurement was done in triplicate.

**Procedure for SEM studies.** Gels were prepared as described in the general gel preparation and washed with water to exchange the DMSO solvent. Samples were then flash frozen in liquid nitrogen and lyophilized and SEM images were obtained.

**Procedure for NMR soak studies.** Gels were prepared at 15 mM total crosslinker concentration, 5% **PVA**, and 0.25 mL total volume, according to the general gel preparation procedure. These gels were stirred into a ball to maximize surface area and subsequently soaked in 0.6 mL of d6-DMSO for 15 minutes. The soak time was optimized prior to measurements. The soak solution was transferred to an NMR tube. A 50:50 mixture by volume of $CH_2Cl_2$: DMSO was prepared in a capillary tube and calibrated using known concentrations of **BA**. This capillary tube containing the internal standard was added to the NMR tubes, and $^1$H NMR spectra were recorded at room temperature and 1024 scans. Concentrations of **BA** were quantified by integrating the **BA** signal relative to the calibrated internal standard.

## Results and discussion

As little is known about **PVA-BA** organogelation, we first examined the efficiency of **BA** as a **PVA** crosslinker and gelator in organic media. Using inversion tests, we observed a notable increase in the viscosity of 5% **PVA** in DMSO between 7 and 8 mM **BA** (Fig. 2). Below 7 mM **BA**, all 5% **PVA** samples were non-viscous, free-flowing solutions. At concentrations of **BA** greater than 10 mM, 5% **PVA** forms self-supporting DMSO materials that can hold their weight when inverted. These results are mirrored in viscometry measurements. We observed a sharp increase in the kinematic viscosity of **PVA** solutions between 6 and 8 mM **BA**, suggesting the CGC is within this range (Fig. S1). Notably, **PVA**-**BA** did not gel in any of the other organic solvents tested, even at high concentration (Fig. S2).

Though these **PVA-BA** materials formed in DMSO appear to be gels on a macroscopic scale, rheologically, these systems do not possess the characteristics of a "true" gel. Typically, the formation of a continuous gel network results in the material exhibiting solid-like rheology.[32] When examined as a function of frequency, the storage modulus (G') of the gel will remain larger than its loss modulus (G''), and the G' will be independent of frequency, indicating that the fibrous network does not relax even over long timescales. As shown in Fig. 3, the **PVA-BA** material made with 5% **PVA** and 50 mM **BA** in DMSO (blue circles) does not fit this definition. Namely, while there are regions in which the G′ is greater than the G′′ (plateauing at a maximum of ~2010 Pa), both moduli vary significantly as a function of frequency. At low angular frequency (i.e., long timescales), the G′′ of the **PVA-BA** material is larger than G′, meaning this material displays viscous, liquid-like behavior. However, as the angular frequency is increased (i.e., shorter timescales), G′ increases while G′′ decreases, and the material displays gel-like properties. These rheological data suggest that the **PVA**-**BA** materials are highly viscous and weakly aggregated dispersions of **PVA** polymers, a finding consistent with **BA** materials reported by Weiss, et. al. formed with partially hydrolysed poly(vinyl acetate).[28,32–34]

These results also imply that **BA** is not a particularly effective **PVA** crosslinker under these conditions. Thus, we turned our attention to improving **BA**'s crosslinking ability and establishing more uniform material properties. We theorized that introducing a more efficient **PVA** crosslinker, such as **1,4-BDBA**, could enhance the material properties, as has been seen with dual-crosslinked gels.[35–44] Notably, when 25% of the **BA** crosslinker is exchanged for **1,4-BDBA**, we indeed observe a marked improvement in the rheological properties of **PVA**-**BA** materials (Fig. 3, red squares). Specifically, the **PVA** material made with 25% **1,4-BDBA** has a higher G′ value (~5200 Pa at 10 rad/s) and moduli that are less dependent on frequency. This suggests that crosslinking **PVA** in DMSO with a mixture of **BA** and **1,4-BDBA** yields a "true" organogel. Furthermore, the presence **1,4-BDBA** in the **PVA-BA** system results in a significantly stiffer material.

Having seen these enhancements with only 25% **1,4-BDBA**, we next systematically varied the ratio of **1,4-BDBA** to **BA**. For these studies, we held the overall crosslinker concentration constant (50 mM total) and made **PVA** gels with varying ratios of **BA** to **1,4-BDBA**. The properties of these systems were assessed by oscillatory rheology and compared to **PVA** materials made with **BA** alone. As anticipated, addition of **1,4-BDBA** as a crosslinker resulted in improved rheological

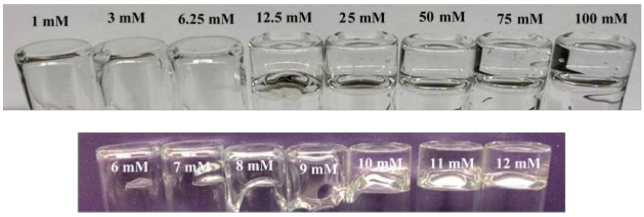


**Figure 2.** Inverted vials of 5% **PVA** in DMSO with increasing amounts of **BA** (top = 1-100 mM; middle = 6-12 mM). These materials become vicious between 7 and 8 mM **BA** and are self-supporting by 10 mM **BA**.

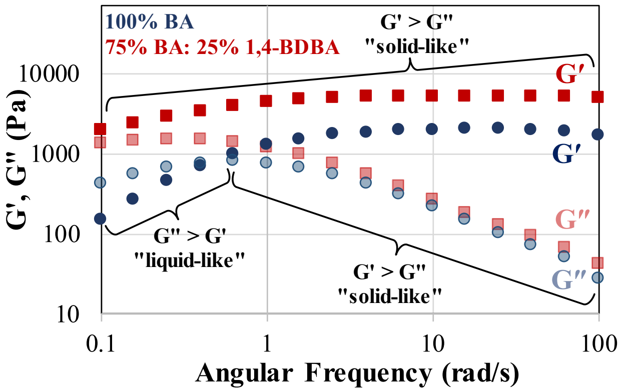


**Figure 3**. Oscillatory frequency sweep of 100% **BA** (5% **PVA** and 50 mM **BA** in DMSO; blue circles) and 75% **BA** and 25% **1,4-BDBA** (5% **PVA**, 37.5 mM **BA** and 12.5 mM **1,4-BDBA** in DMSO; red squares) at 1% strain. **PVA** materials crosslinked with **BA** alone have moduli that vary with frequency, crossing over from liquid-like to solid-like at higher frequencies. Conversely, with 25% **1,4-BDBA**, there is an increase in G′ and the material no longer has a crossover point.

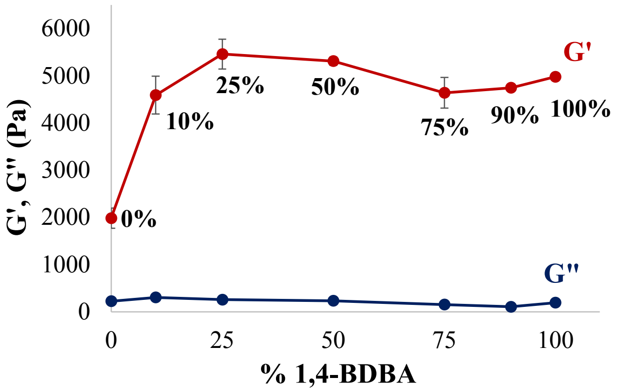
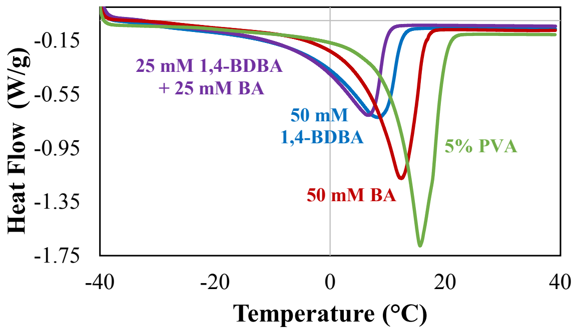


**Figure 4.** Storage and loss moduli obtained from strain sweeps at 1% strain with varying ratios of **BA:1,4-BDBA** (50 mM total, 5% PVA in DMSO). With 10% **1,4-BDBA**, the G′ increases from ~2000 Pa to ~4600 Pa. The G′ continues to increase with increasing %**1,4-BDBA** and levels off at ~5000 Pa.

properties, even at low concentrations of **1,4-BDBA** (Fig. S3-4). As shown in Fig. 4, exchanging just 10% **BA** for **1,4-BDBA** more than doubles the G′ value relative to a **PVA-BA** material with no **1,4-BDBA** (from ~2000 Pa to ~4600 Pa). At 25% and 50% **1,4-BDBA**, G′ values increase further, reaching the peak G′ of ~5300-5500 Pa. Beyond the 50:50 mixture of crosslinkers, we observe a small decrease in the storage modulus, and the material stiffness levels out at G′ value of ~5000 Pa. Because there is little to no change in moduli beyond this point, we decided to use 50:50 ratios for subsequent studies.

As the composition of the gel matrix will influence the thermodynamic stability of the material, we also characterized the impact the addition of **1,4-BDBA** has on the thermal properties of **PVA-BA** system. Onset temperatures, peak temperatures, and enthalpies for **PVA** materials with **BA**, **1,4-BDBA**, and 50:50 **BA**:**1,4-BDBA**, as well as 5% **PVA** alone, were determined via differential scanning calorimetry (DSC). Each material was equilibrated at -40°C and subsequently heated to 40°C. The transition observed in this region corresponds to the melting of the DMSO solvent. In the absence of crosslinker, the melting temperature of DMSO in 5% **PVA** is 15.23 ± 0.44°C, with an onset of 10.01 ± 0.79°C (Fig. 5). The addition of 50 mM **BA** shifts the peak temperature of this transition to 11.78 ± 0.67°C with an onset temperature of 2.54 ± 1.87°C. The decrease in both peak and onset temperatures suggest **BA** is forming crosslinks with **PVA**. Previous studies have shown that crosslinking within a polymeric system can impede the bulk solvent's ability to form intermolecular interactions and freeze.[45] Thus, the observed decrease in the melting temperature of DMSO is consistent with the presence of new **PVA**-**BA** crosslinks.

The transition temperatures for gels formed with **1,4-BDBA** are lower than those recorded for **PVA** with **BA**. The peak and onset temperatures of a 50 mM **1,4-BDBA** gel are 7.55 ± 1.65°C and -7.68 ± 5.12°C, respectively (Fig. 5). This decrease in transition temperature relative to the **PVA-BA** gels indicates **1,4-BDBA** forms more crosslinks with **PVA** than **BA**. Interestingly, the thermal properties of gels formed with 50:50 **BA**:**1,4-BDBA** (50 mM total crosslinker) are analogous to those of **1,4-BDBA** alone. Specifically, for the 50:50 **BA**:**1,4-BDBA** gel, we observe a peak temperature at 7.71 ± 0.78°C and onset temperature at -7.27 ± 0.91°C. Because these transition temperatures are nearly identical to those obtained for the **1,4-BDBA** gel, we can infer that the disruption of solvent interactions is occurring to a similar extent in both gels and that the crosslinking densities are essentially the same. These data are consistent with the trends observed rheologically and suggest the addition of **1,4-BDBA** not only improves the material stiffness of **PVA**-**BA** gels, but also the thermal properties materials.



| Sample | Onset T (°C) | Peak T (°C) | Enthalpy (J/g) |
|---|---|---|---|
| 5% PVA | 10.01 ± 0.79 | 15.23 ± 0.44 | 163.15 ± 1.76 |
| 50 mM BA | 2.54 ± 1.87 | 11.78 ± 0.67 | 151.66 ± 1.90 |
| 1,4-BDBA 50 mM | -7.68 ± 5.12 | 7.55 ± 1.65 | 141.20 ± 4.35 |
| 25 mM BA + 25 mM 1,4-BDBA | -7.27 ± 0.91 | 7.71 ± 0.78 | 140.34 ± 4.17 |

**Figure 5.** Top: Representative DSC curves for 5% **PVA** in DMSO (green) and 5% **PVA** with 50 mM **BA** (red), 50 mM **1,4-BDBA** (blue), and 25 mM **1,4-BDBA** + 25 mM **BA** (purple), respectively. Bottom: Onset temperatures, peak temperatures, and enthalpies obtained from DSC curves. As crosslinking increases within the sample, the onset and peak temperatures for DMSO melting decrease. The similarities between the **1,4-BDBA** and **BA**:**1,4-BDBA** gels indicate that **PVA** is crosslinked to a similar degree.

This increase in crosslinking with added **1,4-BDBA** is also reflected in transmittance (%T) and scanning-electron microscopy (SEM) studies. As shown in Fig. 6A & B, the opacity of the **PVA-BA** gels visibly increases when **1,4-BDBA** is added. Spectroscopically, **PVA**-**BA** gels with **1,4-BDBA** have lower %T (%T = ~47.7% at 600nm with 50% **1,4-BDBA**, Fig. S5) than those crosslinked with **BA** alone (%T = ~87.4% at 600nm with 0% **1,4-BDBA**, Fig. S5). SEM images of lyophilized **PVA-BA** gels (Fig. 6C) show a loss of morphological uniformity and the appearance of fiber-like networks when **1,4-BDBA** is introduced (Fig. 6D). Again, these results are consistent with **1,4-BDBA** yielding a more densely crosslinked **PVA-BA** gel network.

The gelation point, CGC, and self-healing properties were similarly impacted with the addition of **1,4-BDBA**. For CGC measurements, we maintained a crosslinker ratio of 50:50 **1,4-BDBA**:**BA** and varied the total concentration of crosslinker. Visually, we found that self-supporting **PVA** gels form in DMSO at concentrations greater than 5 mM total crosslinker (i.e., 2.5 mM **BA** + 2.5 mM **1,4-BDBA**) (Fig. S6). Notably, **PVA** materials crosslinked with **BA** or **1,4-BDBA** alone cannot hold their weight at this concentration (Fig. 2 & S7). Similarly, the kinematic viscosity of **PVA** solutions with 50:50 **1,4-BDBA**:**BA** sharply increased between 4 and 5 mM total crosslinker, significantly lower than the CGC obtained with **BA** alone. Likewise, self-healing properties varied significantly when **1,4-BDBA** was introduced. We found that when **PVA** materials are subjected to high oscillatory strain (γ = 500%; ω = 10.0 rads $s^{-1}$), they undergo to transition to a liquid-like state (G′′ > G′) (Fig. S8). When the amount of strain is decreased (γ = 5%; ω = 10.0 rads $s^{-1}$), systems crosslinked with **BA** alone does not return to a solid-like state (G′ > G′′) and the integrity of the material is lost (Fig. S8A). In contrast, **PVA** gels formed with 50:50 **1,4-BDBA**:**BA**

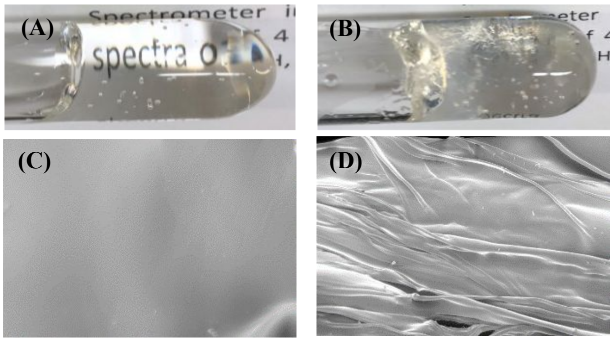


**Figure 6.** Top: visual representation of the opacity of **PVA** gels (5% in DMSO) with 50 mM **BA** (A) and 25 mM **1,4-BDBA** + 25 mM **BA** (B). Bottom: cross-sectional SEM images of lyophilized **PVA** gels with **BA** (C) and 50:50 **1,4-BDBA**:**BA** (D).

gels readily reform when the strain is lowered, and the resulting material has a G′ similar to that of the initial gel (Fig. S8B). This healability with **1,4-BDBA**:**BA** mixtures is also apparent visually with fractures repairing and gels becoming self-supporting within minutes (Fig S9). Based on these results, we can conclude that the addition of **1,4-BDBA** improves **PVA** gelation with **BA** and yields a more continuous, self-healing **PVA** network.

Importantly, while **1,4-BDBA** is a more effective **PVA** crosslinker than **BA** (evidenced by the high G′ in 100% **1,4-BDBA**), the improvement in material properties observed with **BA**:**1,4-BDBA** mixtures cannot be attributed to the addition of **1,4-BDBA**-**PVA** crosslinks alone. That is, the formation of new crosslinks between **PVA** and **1,4-BDBA** does not fully account for the increase in G′ observed in the **BA**:**1,4-BDBA** gels. This is most apparent when comparing the rheological properties of **PVA** gels formed with **BA** and **1,4-BDBA** alone at 25 mM crosslinker. The G′ values for these systems, as well as the G′ for the 50:50 **BA**:**1,4-BDBA** gel, are shown in Fig. 7. These storage moduli were obtained from strain sweeps at 10 rad/s and 1% strain (Fig. S3-4 & S10-11). The **PVA** material formed with 25 mM **BA** has a G′ of ~1000 Pa, while the **PVA** gel formed with 25 mM **1,4-BDBA** has a G′ ~1880 Pa. In combining these two crosslinkers, we would anticipate the resulting **PVA** material would have a G′ value equal to the combination of the individual crosslinkers at 25 mM (i.e., G′ of ~2880 Pa). However, we consistently record G′ values for the **BA**:**1,4-BDBA** gels of ~5300 Pa, which is slightly higher than 50 mM **1,4-BDBA** alone.

This suggests that **1,4-BDBA** is not only introducing new crosslinks between **PVA** and itself but is also improving the ability of **BA** to function as a crosslinker (Fig. 1). Thus, we propose that there is crosslinking cooperativity in **PVA** gels with combinations of **BA** and **1,4-BDBA**. To probe this proposed mechanism, we first evaluated the formation of covalent borate ester crosslinks using Fourier transform infrared spectroscopy (FTIR) (Fig. S12-S13). FTIR spectra of lyophilized **PVA**-**BA** with and without **1,4-BDBA** show absorption bands between 1298-1302 cm$^{-1}$ and 1012-1017 cm$^{-1}$, which we attribute to the B-O-C bending.[46,47] We also see evidence for O-B-O stretching frequencies between 660-710 cm$^{-1}$ in all boron-containing spectra (Fig S13).[48] These findings indicate that **PVA** forms covalent borate esters linkages with the boron crosslinkers. Additionally, these IR data are consistent with B-O bond formation inducing gelation.

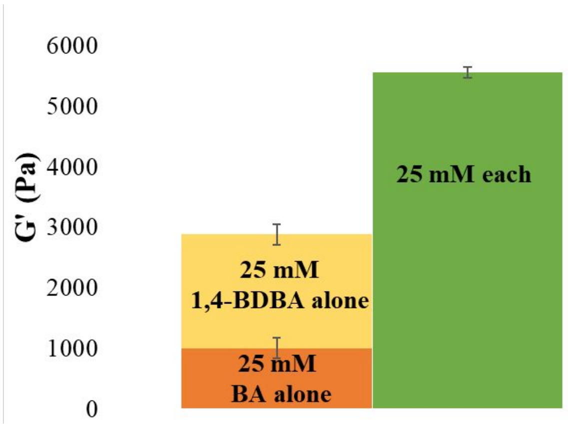


**Figure 7.** Storage moduli obtained from strain sweeps of **PVA** gels (5% in DMSO) made with 25 mM **BA** alone (orange), 25 mM **1,4-BDBA** alone (yellow), and 50 mM **BA**:**1,4-BDBA** (25 mM each, green). The **BA**:**1,4-BDBA** gel has a significantly higher G' than the combination of **BA** and **1,4-BDBA** at 25 mM.

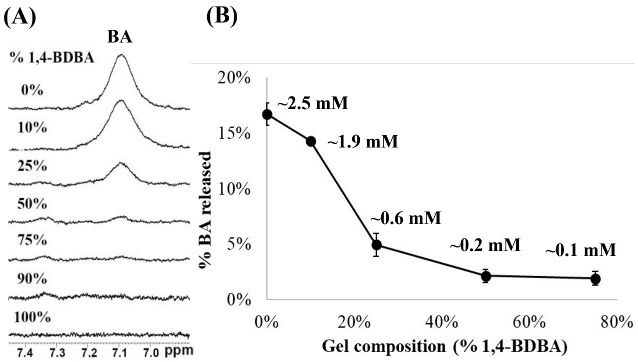


**Figure 8**. (A) $^1$H NMR of d6-DMSO wash solutions. The **BA** signal at 7.1 ppm decreases as the %**1,4-BDBA** in **PVA**-**BA** gel increases. (B) The percentage and concentration of **BA** released from **PVA**-**BA** gels as a function of %**1,4-BDBA** added. Again, the percentage of the initial concentration of **BA** that is released upon washing decreases with increasing %**1,4-BDBA**.

Though IR studies provide useful insights into the types of crosslinks formed within **PVA**-**BA** materials, little can be gleaned about the proposed cooperative crosslinking mechanism when **1,4-BDBA** is introduced. Thus, to test this theory, we designed a series of soak tests with the **BA**:**1,4-BDBA** gels. We rationalized that the porous nature of a gel would allow us to rinse the materials and wash out any non-crosslinked **BA** that remained in the pores. Thus, if **1,4-BDBA** is cooperatively crosslinking **PVA** and stabilizing the B-O bonds between **BA** and **PVA**, we would expect to see a decrease in the amount of **BA** released into the bulk solution upon washing. By analyzing the wash solutions, we can indirectly probe the impacts of **1,4-BDBA** on **BA**’s crosslinking within the gel network.

For these experiments, we formed a series of **PVA** gels (5% **PVA**) at 15 mM total crosslinker concentrations and various ratios of **1,4-BDBA** to **BA**. We then soaked these materials in d6-DMSO. After 15 min of soaking, we removed aliquots of the wash solution and recorded $^1$H NMR spectra. The $^1$H NMR spectra of these washes show a distinct signal for **BA** at ~7.1 ppm (Fig. 8A). As we increase the %**1,4-BDBA** in the **PVA**-**BA** gels, this signal decreases and ultimately disappears by ~90% **1,4-BDBA**. This suggests that the amount of **BA** released from the gels indeed decreases with higher percentages of **1,4-BDBA**.

By integrating this **BA** signal relative to a calibrated $CH_2Cl_2$ internal standard (Fig. S14), we can determine the concentration of **BA** in solution and calculate the %**BA** released from the gel (Fig. 8B). Importantly, the %**BA** released was calculated relative to the initial concentration of **BA** in the gel. That is, for a 10% **1,4-BDBA** gel, the total initial concentration of **BA** was 13.5 mM. Thus, with ~1.9 mM **BA** released into the bulk solution, the %**BA** released is ~14%. In comparing the %**BA** released from these gels, we observe an immediate decrease in **BA** concentration with added **1,4-BDBA**. Specifically, from 0% to

10% **1,4-BDBA**, there is a decrease in the **BA** released from ~17% to ~14%. This trend continues with increasing amounts of **1,4-BDBA**, and by 25% **1,4-BDBA**, only ~5% of the initial **BA** is released. With gels containing >25% **1,4-BDBA**, we observe less than ~1% **BA** in the wash solution. These data are consistent with the proposed cooperative crosslinking mechanism. As we increase the %**1,4-BDBA** in the **PVA**-**BA** gels, **BA** is better able to form crosslinks with **PVA**, and thus less **BA** is expelled upon washing. This mechanism not only accounts for decrease in %**BA** released, but also the improved material properties.

## Conclusions

Here, we have demonstrated that the addition of even substoichiometric amounts of **1,4-BDBA** dramatically enhances **BA** crosslinking in **PVA** organogels. These materials are stiffer and have improved rheological and thermal properties as compared to those with **BA** alone. We propose that this is due to a cooperative crosslinking mechanism in which **1,4-BDBA** promotes the formation of new **BA**-**PVA** crosslinks. To the best of our knowledge, this is the first example of such a mechanism in **PVA**-**BA** gels. Because these materials are easily synthesized and adjusted, they are both a viable and tunable alternative to **PVA** hydrogels. We are currently exploring the impacts of altering the structure of the diboronic acid crosslinker as a means of both altering the material properties and developing a better mechanistic understanding of cooperative crosslinking in **PVA**-**BA** gels. As numerous diboronic acids are commercially available, these systems have the potential to yield a wide range of cooperatively crosslinked **PVA** organogels. Additionally, we are investigating the applicability of cooperative crosslinked **PVA** gels as stimuli-responsive media for environmental remediation and separations.

## Conflicts of interest

There are no conflicts to declare.

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## References

1 T. R. Hoare and D. S. Kohane, *Polymer (Guildf).*, 2008, **49**, 1993–2007.
2 C. L. Esposito, P. Kirilov and V. G. Roullin, *J. Control. Release*, 2018, 271, 1–20.
3 J. Y. C. Lim, S. S. Goh, S. S. Liow, K. Xue and X. J. Loh, *J. Mater. Chem. A*, 2019, 7, 18759–18791.
4 B. O. Okesola and D. K. Smith, *Chem. Soc. Rev.*, 2016, **45**, 4226–4251.
5 R. Jin and P. J. Dijkstra, *Chem. Rev.*, 2010, **101**, 1869–1879.
6 M. Aslam, M. A. Kalyar and Z. A. Raza, *Polym. Eng. Sci.*, 2018, 58, 2119–2132.
7 K. C. S. Figueiredo, T. L. M. Alves and C. P. Borges, *J. Appl. Polym. Sci.*, 2009, **111**, 3074–3080.
8 J. M. Gohil, A. Bhattacharya and P. Ray, *J. Polym. Res.*, 2006, **13**, 161–169.
9 R. Y. M. Huang and J. W. Rhim, *Polym. Int.*, 1993, **30**, 129–135.
10 N. Işiklan and O. Şanli, *Chem. Eng. Process. Process Intensif.*, 2005, **44**, 1019–1027.
11 M. Krumova, D. López, R. Benavente, C. Mijangos and J. M. Pereña, *Polymer (Guildf).*, 2000, **41**, 9265–9272.
12 G. M. Peters, X. Chi, C. Brockman and J. L. Sessler, *Chem. Commun.*, 2018, **54**, 5407–5409.
13 G. M. Peters, L. P. Skala, T. N. Plank, B. J. Hyman, G. N. M. Reddy, A. Marsh, S. P. Brown and J. T. Davis, *J. Am. Chem. Soc.*, 2014, **136**, 12596–12599.
14 G. M. Peters, L. P. Skala, T. N. Plank, H. Oh, G. N. M. Reddy, A. Marsh, S. P. Brown, S. R. Raghavan and J. T. Davis, *J. Am. Chem. Soc.*, 2015, **137**, 5819–5827.
15 G. Bocchinfuso, C. Mazzuca, C. Sandolo, S. Margheritelli, F. Alhaique, T. Coviello and A. Palleschi, *J. Phys. Chem. B*, 2010, **114**, 13059–13068.
16 M. Grassi, R. Lapasin, T. Coviello, P. Matricardi, C. Di Meo and F. Alhaique, *Carbohydr. Polym.*, 2009, **78**, 377–383.
17 B. Balakrishnan and A. Jayakrishnan, *Biomaterials*, 2005, **26**, 3941–3951.
18 E. Z. Casassa, A. M. Sarquis and C. H. Van Dyke, *J. Chem. Educ.*, 1986, **63**, 57–60.
19 R. K. Schultz and R. R. Myers, *Macromolecules*, 1969, **2**, 281–285.
20 K. W. Mclaughlin, N. K. Wyffels, A. B. Jentz and M. V Keenan, *J. Chem. Educ.*, 1997, **74**, 97–99.
21 M. Van Duin, J. A. Peters, A. P. G. Kieboom and H. Van Bekkum, *Tetrahedron*, 1984, **40**, 2901–2911.
22 X. Su, H. Wang, Z. Tian, X. Duan, Z. Chai, Y. Feng, Y. Wang, Y. Fan and J. Huang, *ACS Appl. Mater. Interfaces*, 2020, **12**, 29757–29766.
23 S. Ren, P. Sun, A. Wu, N. Sun, L. Sun, B. Dong and L. Zheng, *New J. Chem.*, 2019, **43**, 7701–7707.
24 J. Chatterjee, T. Liu, B. Wang and J. P. Zheng, *Solid State Ionics*, 2010, **181**, 531–535.
25 E. Carretti, L. Dei and R. G. Weiss, *Soft Matter*, 2005, 1, 17–22.
26 T. T. Duncan, B. H. Berrie and R. G. Weiss, *ACS Appl. Mater. Interfaces*, 2017, **9**, 28069–28078.
27 E. Carretti, M. Bonini, L. Dei, B. H. Berrie, L. V. Angelova, P. Baglioni and R. G. Weiss, *Acc. Chem. Res.*, 2010, **43**, 751–760.
28 L. V. Angelova, M. Leskes, B. H. Berrie and R. G. Weiss, *Soft Matter*, 2015, **11**, 5060–5066.
29 E. J. Lee and B. C. Kim, *Fibers Polym.*, 2013, **14**, 2097–2102.
30 H.-H. Wang, T.-W. Shyr and M.-S. Hu, *J. Appl. Polym. Sci.*, 1999, **74**, 3046–3052.

31 H.-H. Wang, T.-W. Shyr and M.-S. Hu, *J. Appl. Polym. Sci.*, 1999, **73**, 2219–2226.

32 C. W. Macosko, *Rheology : principles, measurements, and applications*, VCH, 1994.

33 J. Mewis and A. J. B. Spaull, *Adv. Colloid Interface Sci.*, 1976, **6**, 173–200.

34 W. B. Russel, D. A. Saville and W. R. Schowalter, *Colloidal Dispersions*, Cambridge University Press, Cambridge, 1989.

35 X. Liu, J. Zhang, M. Fadeev, Z. Li, V. Wulf, H. Tian and I. Willner, *Chem. Sci.*, 2019, **10**, 1008–1016.

36 P. Lin, S. Ma, X. Wang and F. Zhou, *Adv. Mater.*, 2015, **27**, 2054–2059.

37 J. Zhang, S. Hou, Y. Chen, J. Zhou, H. Chen and Y. Tan, *Soft Matter*, 2019, **15**, 9797–9804.

38 K. Mayumi, A. Marcellan, G. Ducouret, C. Creton and T. Narita, *ACS Macro Lett.*, 2013, **2**, 1065–1068.

39 T. Kimura and K. Urayama, *ACS Macro Lett.*, 2020, **9**, 1–6.

40 J. Guo, Y. Li, Y. Zhang, J. Ren, X. Yu and X. Cao, *ACS Appl. Mater. Interfaces*, 2021, **13**, 40079–40087.

41 T. Nakajima, T. Chida, K. Mito, T. Kurokawa and J. P. Gong, *Soft Matter*, 2020, **16**, 5487–5496.

42 T. Nakajima, T. Kurokawa, H. Furukawa and J. P. Gong, *Soft Matter*, 2020, **16**, 8618–8627.

43 C. Imaoka, T. Nakajima, T. Indei, M. Iwata, W. Hong, A. Marcellan and J. P. Gong, *Sci. Adv.*, 2023, **9**, eabp8351.

44 G. Chen, S. Tang, H. Yan, X. Zhu, H. Wang, L. Ma, K. Mao, C. Yang and J. Ran, *Polymers (Basel).*, 2023, **15**, 724–738.

45 T. Nakaoki and H. Yamashita, *Open J. Org. Polym. Mater.*, 2016, **06**, 86–97.

46 N. Shawgi, S. Xi Li, S. Wang, Z. Wang and Y. Nan Nie, *J. Sol-Gel Sci. Technol.*, 2017, **82**, 450–457.

47 R. V. Gadhave, S. K. Vineeth, P. A. Mahanwar and P. T. Gadekar, *J. Adhes. Sci. Technol.*, 2021, **35**, 1072–1086.

48 B. M. Rambo and J. J. Lavigne, *Chem. Mater.*, 2007, **19**, 3732–3739.