Glucose-sensing photonic crystals are promising for the significant advance of continuous glucose monitoring systems due to the naked-eye colorimetric readouts and noninvasive detection of diabetes, but the long response time hampers their practical applications. Here, for the first time probes of photonic nanochains (PNCs) are demonstrated that are capable of continuously and reversibly sensing glucose concentration ($[\text{glucose}]$) variation within seconds by color change without power consumption, much faster by 2–3 orders of magnitude than previous ones. They are comprised of 1D equidistant arrays of magnetic nanoparticles enveloped by tens-of-nanometer-thick phenylboronic acid-functionalized hydrogels, and fabricated by developing selective concentration polymerization of monomers in binary microheterogeneous solvents of dimethyl sulfoxide (DMSO) and H$_2$O. In this process, both 3-acrylamido phenylboronic acid (AAPBA) and N-2-hydroxyethyl acrylamide (HEAAm) are preferentially dissolved in the small volume of free DMSO concentrated in the vicinity of poly vinylpyrrolidone coated Fe$_3$O$_4$ colloidal nanoparticles (Fe$_3$O$_4$@PVP), yielding Fe$_3$O$_4$@PVP@poly(AAPBA-co-HEAAm) PNCs after UV irradiation under magnetic field. The PNCs in phosphate buffered solution have a wavelength-shift range up to 130 nm when $[\text{glucose}]$ changes from 0 to 20 × 10$^{-3}$ m. The results can facilitate real-time glucose monitoring and provide an alternative to produce functional organic–inorganic nanostructures.

1. Introduction

Glucose concentration in body fluids is the most important biochemical indicator to diagnose diabetes,[1] loss of consciousness, vascular disease or neurocognitive changes.[2] A variety of glucose probes and sensing technologies have been developed including electrochemical sensors,[3] fluorescent dyes,[4] and surface plasmon resonance nanoparticles or nanoantenna.[5] Some of them are in practical uses and commercialized. Compared to them, glucose-sensing photonic crystals (PCs) could vary the colors in a wide range of visible spectra following Bragg diffraction due to the volumetric changes with glucose concentration ($[\text{glucose}]$).[5] This colorimetric assay ensures the simplicity and practicality to be read by naked eye as well as the potential application for noninvasive glucose monitoring via urine or tear fluid.[6] Moreover, it is label-free, without external power consumption, not susceptible to electromagnetic fields, and suitable for sterile remote sensing and making wearable devices. These remarkable advantages are expected to enable it to advance continuous glucose monitoring (CGM) systems, which are currently based on subcutaneously inserted electrochemical sensors. These devices generally suffered from signal drift due to electrochemical reaction instability, and thus needed calibration using frequent fingerstick blood tests, causing obvious pains and inconvenience to the patients on multiple-dose insulin injection or insulin pump therapy.
Up to now, several kinds of glucose-sensing PCs have been developed. For example, with time-consuming dialysis and post-treatment for attaching phenylboronic acid (PBA) moieties, crystalline colloidal arrays (CCAs) of highly charged monodispersed polystyrene nanospheres were implanted in the PBA-modified hydrogel matrix for glucose monitoring.\(^\text{[7]}\) After a tedious stringent process containing template fabrication, monomer infiltration, and the etching process with hazardous hydrofluoric acid or organic solvent, inverse opal PCs are also available for sensing glucose with the assistance of mechanical robust polymers to maintain their structure stability.\(^\text{[8]}\) Hologram-based sensors for detecting glucose have also been fabricated by laser recording techniques, which are costly, sophisticated and hard for mass production.\(^\text{[9]}\) Nevertheless, the so far developed sensing motifs all suffered from long response time, and none of them show real-time continuous glucose monitoring ability, which, however, is necessary for CGM systems to make optimal therapeutic decisions, such as timely insulin delivery.\(^\text{[10]}\) For instance, CCA and holographic sensors normally consume tens of minutes or even hours to reach the equilibrium response due to the relative long diffusion distance of glucose molecules in thick hydrogel (usually at least tens of microns).\(^\text{[7b,9b]}\) Inverse opal PCs have interconnected voids to facilitate the diffusion of analytes, but still demonstrate slow kinetics and hysteresis as the voids are occupied when the gel is swollen.\(^\text{[11]}\)

Herein, we have for the first time reported probes of glucose-sensing photonic nanochains (PNCs) with response time in seconds by developing selective concentration polymerization of monomers in dimethyl sulfoxide (DMSO)-water microheterogeneous binary solvents. The so-reported PNCs are individual nanochains of 1D periodically arrayed magnetic nanoparticles fixed by tens-of-nm-thick hydrogel shells of poly(3-acrylamido phenylboronic acid-co-N-2-hydroxyethyl acrylamide) (poly(AAPBA-co-HEAAm)). They are able to continuously and reversibly change the structural color with [glucose] within seconds, much faster by 2–3 orders of magnitude than other counterparts due to the significantly reduced diffusion length toward analyte glucose. With less than 40 mol% DMSO in solvent, AAPBA and HEAAm prefer to locate in the vicinity of poly vinylpyrroldione coated Fe\(_3\)O\(_4\)@PVP colloidal nanoparticles (Fe\(_3\)O\(_4\)@PVP), yielding glucose-sensing PNCs after polymerization under magnetic field. The as-obtained PNCs exhibit a structural color frequency-shift range up to 130 nm when [glucose] changes between 0 and 20 × 10\(^{-3}\) M, achieving the visual detection of [glucose] in a continuous mode. The PNCs could achieve real-time continuous glucose monitoring and the miniaturization of visual glucose sensors, while the developed polymerization technology may provide an effective route to fabricate functional polymer-based hybrid nanostructures.

### 2. Results and Discussions

#### 2.1. Characterization and Glucose-Sensing Performances of Fe\(_3\)O\(_4\)@PVP@poly(AAPBA-co-HEAAm) Photonic Nanochains

Figure 1 illustrates the characterization of the typical Fe\(_3\)O\(_4\)@PVP@poly(AAPBA-co-HEAAm) PNCs. Almost all of the nanochains presented curved states without magnetic field (Figure 1a), while they gradually became straight parallel to the magnetic field direction with an average length of 10–15 \(\mu\)m (Figure 1b). This indicates their magnetism and flexibility. Figure 1c shows that the nanochains display bright green dots in the dark-field mode when they are aligned parallel to the magnetic field direction. This suggests the structural colors of photonic crystals (PCs). The scanning electron microscopy (SEM) and transmission electron microscopy (TEM) images in Figure 1d,e reveal that the nanochain is a 1D ordered particle chain with the same interparticle distance. As reported in previous literature, \(^\text{[12]}\) 1D PNCs diffract light of a specific wavelength as determined by Bragg’s law confirming that the bright green colors in Figure 1c stem from the periodical structure of 1D PNCs. In the nanochain, all the magnetic nanoparticles are covered and connected by an organic layer of only about 10–20 nm. The EDS in Figure S1 (Supporting Information) also suggests that the inner cores of the nanoparticles are mainly composed of Fe and O elements, and the shell layers mainly contain C, N, O, B elements, which constitute PVP, HEAAm, and AAPBA. FT-IR spectrum in Figure 1f shows that the absorption peaks at 3428 and 1660 cm\(^{-1}\) are attributed to the N–H group of the acrylamide group (–CONH–) and the stretching vibration of the C=O group of HEAAm, respectively.\(^\text{[13]}\) The peaks at 1437 and 1313 cm\(^{-1}\) are assigned to the stretching vibration peaks of the benzene ring skeleton and the B–O bond of AAPBA.\(^\text{[14]}\) The absorption peak at 583 cm\(^{-1}\) was ascribed to Fe–O in Fe\(_3\)O\(_4\),\(^\text{[15]}\) From Figure 1g, the percentage of Fe\(_3\)O\(_4\) and organic substances (PVP and poly(AAPBA-co-HEAAm)) can be calculated to be 59.6 and 40.4 w%, respectively. As the percentage of PVP in the Fe\(_3\)O\(_4\)@PVP magnetic nanoparticles has already known to be 8.8 w% from previous research,\(^\text{[16]}\) the rest poly(AAPBA-co-HEAAm) can be obtained to be 31.6 w% in the PNCs. Furthermore, as the content of B and Fe was measured by the ICP analysis to be 0.30 and 28.65 w%, respectively, the weight ratio between Fe and B was 95. Thus, the molar ratio of HEAAm to PAAmBBA in the shell layer poly(AAPBA-co-HEAAm) of the PNCs could also be figured out to be 4.8. The above data prove that the prepared 1D PNCs are comprised of poly(AAPBA-co-HEAAm) hydrogel as the shell layer and the Fe\(_3\)O\(_4\)@PVP nanoparticles as the cores.

Figure 1h depicts that the prepared PNCs have good dispersibility in the phosphate buffered solution (PBS). With the increment of [glucose] from 0 to 20 × 10\(^{-3}\) M, their dispersed solution shows the color from green to red. Notably, the color demonstrates a conspicuous transition at around 7 × 10\(^{-3}\) M, corresponding to the diagnosis indicator of diabetes.\(^\text{[17]}\) Namely, when the solution containing PNCs displays red, [glucose] is above this point, representing the possibility of illness. In contrast, when it turns yellow or green, [glucose] is in the normal fasting blood glucose concentration.\(^\text{[18]}\) Figure 1i shows the shifting of the diffraction wavelength (\(\lambda\)) of the PNCs during a cyclic sweep of [glucose] between 0 and 20 × 10\(^{-3}\) M. The \(\lambda\) shifts red with increasing [glucose]. The shifting range of \(\lambda\) surpasses 80 nm when [glucose] increases from 0 to 20 × 10\(^{-3}\) M. The \(\lambda\) at each [glucose] both in the increasing and decreasing sweep basically overlapped, proving the good reversibility of the PNCs. Figure 1j shows that the optical fiber spectrometer almost synchronously records the equilibrated wavelength of the PNCs when [glucose] changes, suggesting that the response time is within a few seconds. This response time is at least two to three orders of magnitude shorter than that of the other glucose-sensing PCs, which often take min-
utes or even hours to reach the equilibrium. For example, a 10 μm thick polyacrylamide hydrogel film functionalized with AAPBA needed 1.5 h to reach ~90% equilibrium. The apparent diffusivity of glucose in the hydrogel follows 1D diffusion equation \( \tau = P/2D \), where \( \tau \), \( l \), and \( D \) are the time for glucose molecules to reach a steady state, film thickness, and the diffusion constant of glucose molecules, respectively. As \( D \) in hydrogels is much lower than that in water (5.2 × 10⁻⁶ cm² s⁻¹) and was calculated to be about 9.2 × 10⁻¹¹ cm² s⁻¹, the \( \tau \) for the Fe₃O₄@PVP@poly(AAPBA-co-HEAAm) PNCs is theoretically estimated to be around 20 ms owing to the ultrathin thickness of the hydrogel shell (≈20 nm), consistent with our observation. Similar swift responsiveness has also been observed in the responsive hydrogel-based PNCs recently constructed exclusively by hydrophilic monomers.

Previous PNCs are all based on hydrophilic monomers and fabricated by hydrogen bond-guided template polymerization method, where the monomers (or in the assistance of carboxylic acidic polymers) form strong hydrogen bonds with the building blocks of PCs, such as, uniform superparamagnetic Fe₃O₄@PVP nanoparticles. In contrast, the probes of glucose-sensing photonic crystals reported herein are based on relatively hydrophobic 3-acrylamido phenylboronic acid, impossible to obtain following the hydrogen bond-guided template polymerization. In order to decipher the formation mechanism of the glucose-sensing PNCs, the influences of polymerization parameters such as solvent composition, monomer concentration and their ratio etc. on the morphologies and dispersity of the products were respectively studied in Figure 2. For the homopolymerization of AAPBA with Fe₃O₄@PVP nanoparticles in DMSO-H₂O mixed solvents under magnetic field, there appear three zones with changing the AAPBA concentration (cAAPBA) and \( \chi_D \), as shown in Figure 2a. In zone I, the whole prepolymer solution will be transformed into a bulk solid hydrogel without any fluidity after UV irradiation due to the high cAAPBA. With decreasing cAAPBA below a critical value at different \( \chi_D \) (upper black line in Figure 2a), zone II emerges where the obtained products are nanochains. In this zone, the prepolymer solution after UV polymerization will generate a liquid containing randomly distributed nanochains. The length of these nanochains becomes short with the reduction of cAAPBA or the growth of \( \chi_D \) until zone (III+IV) appears, in which only short nanochains of 2–3 μm in length or nanoparticles are produced. Interestingly, the length of nanochains drastically decreases when \( \chi_D \) is more than 40%. This unique phenomenon might be correlated with the microheterogeneity of DMSO aqueous solution. For a DMSO aqueous solution, most
DMSO molecules form stable DMSO-water clusters with water molecules via strong hydrogen bonding at a lower \( \chi_D \), and fraction of free DMSO molecules increase abruptly when \( \chi_D \) is above the eutectic point, corresponding to \( \chi_D \) of \( \approx 30\% \) [18]. AAPBA is relatively hydrophobic when compared to the other components, and it together with Fe\(_3\)O\(_4\)@PVP nanoparticles prefers to be dissolved in free DMSO rather than in DMSO-water clusters or free water. Consequently, when \( \chi_D \) is lower than the eutectic point, the small volume of free DMSO bearing with AAPBA prefer to stay in the vicinity of Fe\(_3\)O\(_4\)@PVP nanoparticles, while most of free water and DMSO-water clusters are located away from the Fe\(_3\)O\(_4\)@PVP nanoparticles. In this scenario, monomer molecules AAPBA concentrated in the vicinity of Fe\(_3\)O\(_4\)@PVP nanoparticles are polymerized under magnetic field and UV irradiation into Fe\(_3\)O\(_4\)@PVP@AAPBA nanochains. As evidence, when \( \chi_D = 30\% \) and \( c_{AAPBA} \) is 10 times larger than the eutectic point.
lower than its corresponding gel point, Fe$_3$O$_4$@PVP@PAAPBA nanochains with an average length around 5–10 μm were still fabricated. This postulation is also supported by the fact that when $\chi_D$ is above the eutectic point, there are more volume of free DMSO, in which AAPBA are allowed to be distribute uniformly. This causes to lower the $c_{\text{AAPBA}}$ around the Fe$_3$O$_4$@PVP nanoparticles. As a result, nanochains diminish.

2.2. Formation Mechanisms of Fe$_3$O$_4$@PVP@poly(AAPBA-co-HEAAm) Photonic Nanochains

Another noteworthy phenomenon is that when $\chi_D<15\%$, with the increment of $c_{\text{AAPBA}}$, the obtained nanochains first become long, and then get short following a maximum, as depicted in Figure 3. Upon increasing $c_{\text{AAPBA}}$ in zone II, the possibility to form long nanochains is greatly enhanced, in consistence with the growing nanochains when $\chi_D>15\%$. However, further increasing $c_{\text{AAPBA}}$ will significantly shorten the chain length. The solubility of excessive PAAPBA in the mixed solvent drops rapidly when $\chi_D<15\%$, and they will quickly precipitate out of the mixed solvent making a whitish solution shown in the digital picture in the lower left corner of Figure S2 (Supporting Information). Therefore, when the PAAPBA layer on nanochains has not become sufficiently thick and robust to maintain the integrity of nanochains, they will precipitate out together in a form of short nanochains or nanoparticles due to their incompatibility with the solvent.

Since the Fe$_3$O$_4$@PVP@PAAPBA nanochains are relatively hydrophobic, they cannot be dispersed in aqueous solution. This impedes their further application for glucose detection. Accordingly, hydrophilic comonomer HEAAm is incorporated to increase the hydrophilicity of the nanochains, prompting their utilization near physiological environment. The influences of HEAAm concentration ($c_{\text{HEAAm}}$) and $\chi_D$ on the fabrication of Fe$_3$O$_4$@PVP@PHEAAm nanochains are shown in Figure 2b. The gelation line for HEAAm is relatively flat compared with that of AAPBA depicted in Figure 2a. Meanwhile, there are only short nanochains with an average length around 2–3 μm appearing in the area encircled by two black lines (zone III) and there is even no appearance of zone II. In contrast, the nanochains obtained by AAPBA are much longer in zone II. Below the black line displays a U-shaped feature, which also rises if $\chi_D$ surpasses the eutectic point. However, when $\chi_D$ is lower than 15%, higher $c_{\text{HEAAm}}$ is also needed to form short nanochains, which make the black line below climb up again. All of the above characteristics might be associated with the hydrophilicity of HEAAm. Specifically, as comonomers HEAAm are miscible with both DMSO and water, they are inclined to be uniformly distributed in the whole prepolymer solution when $\chi_D<15\%$ (corresponding to water rich region) or $\chi_D>40\%$ (corresponding to DMSO rich region). Then, higher $c_{\text{HEAAm}}$ is needed to form nanochains in these two areas, in accordance with the uprising black line in the lower part of Figure 2b. If 15%<$\chi_D<$40%, most DMSO and water form DMSO-H$_2$O clusters. Thus, relatively low $c_{\text{HEAAm}}$ is required to form nanochains in this region. However, the Fe$_3$O$_4$@PVP@PHEAAm nanochains are obviously shorter than those acquired by AAPBA. Because even if 15%<$\chi_D<$40%, there still exists free water diluting $c_{\text{HEAAm}}$ around the Fe$_3$O$_4$@PVP nanoparticles surrounded by DMSO molecules.

Figure 2c demonstrates the phase diagram and dispersibility of the products obtained by the copolymerization of AAPBA and HEAAm with Fe$_3$O$_4$@PVP nanoparticles in DMSO-H$_2$O mixed solvents under magnetic field. The regions in the phase diagram are also divided into those belonging to gels, nanochains, short-nanochains, and nanoparticles. The whole gelation line is
shown in Figure S2 (Supporting Information). It is very similar to that of the pure HEAAm shown in Figure 2b. This was because only \(c_{\text{HEAAm}}\) was altered, whereas \(c_{\text{AAPBA}}\) was fixed at a relatively low level \((0.025 \times 10^{-3} \text{ M})\). Thus, it is \(c_{\text{HEAAm}}\) that determines the formation of gel in Figure 2c. As the ratio of HEAAm to AAPBA \((c_{\text{HEAAm}}/c_{\text{AAPBA}})\) increases, the nanochains gradually become short, as shown in images \(\odot, \odot, \) and \(\odot\) of Figure 3c. The hydrophilic transition of the copolymer poly(AAPBA-co-HEAAm) may account for the above results given that the increasing hydrophilicity makes the copolymer more like PHEAAm rather than PAAPBA. As seen in Figure 2a,b, the nanochains obtained by relatively hydrophobic PAAPBA are much longer than those based on hydrophilic HEAAm, provided that PAAPBA does not precipitate out of the solution. This is because monomer AAPBA is mainly dissolved in DMSO preferentially surrounding the Fe\(_3\)O\(_4@PVP\) nanoparticles, whereas the solvation of AAPBA by water is relatively suppressed. The blue line in Figure 2c is associated with the dispersibility of the prepared products in the PBS 8.0 buffer. Increasing \(c_{\text{HEAAm}}\) facilitates the dispersion of the obtained nanochains in the buffer solution. Accordingly, only the PNCs fabricated in zone II (dispersed) in the phase diagram may possess excellent glucose responsiveness.

Based on the above phase diagrams of the products obtained by the polymerization of responsive monomer AAPBA and comonomer HEAAm with monodispersed Fe\(_3\)O\(_4@PVP\) nanoparticles in DMSO-H\(_2\)O mixed solvents under magnetic field, we have proposed the preparation principle of the glucose-sensing PNCs in Scheme 1, which is called selective concentration polymerization of monomers in microheterogeneous solvents. First, the monomers, crosslinking agent, initiator and uniform colloidal Fe\(_3\)O\(_4@PVP\) nanoparticles are evenly dispersed in DMSO solvent. After adding water, there is strong hydrogen-bonding interactions between DMSO and water to form DMSO-H\(_2\)O clusters, meanwhile there was a small amount of free DMSO as well as free water in the solution. According to the analysis in Figure 2, the small volume of free DMSO molecules with relatively hydrophobic AAPBA (the n-octanol/water partition coefficient \(\log \text{Pow} = -0.73\), SDS from Sigma-Aldrich) are more likely to stay around Fe\(_3\)O\(_4@PVP\) nanoparticles. HEAAm (the n-octanol/water partition coefficient \(\log \text{Pow} = 1.787\), SDS from Sigma-Aldrich) is added as a comonomer to improve the hydrophilicity of the final products. Consequently, the Fe\(_3\)O\(_4@PVP@\)poly(AAPBA-co-HEAAm) PNCs are obtained by in-situ polymerization initiated with ultraviolet radiation under a magnetic field.

Scheme 1. Formation mechanism of the glucose-sensing PNCs. In the mixed solvent of DMSO and H\(_2\)O, most DMSO molecules form DMSO-H\(_2\)O clusters via strong hydrogen-bonding interactions besides a small volume of free DMSO. The small volume of free DMSO prefers to stay around Fe\(_3\)O\(_4@PVP\) nanoparticles and have much better solubility to AAPBA and comonomers than the DMSO-H\(_2\)O clusters and free H\(_2\)O. Consequently, Fe\(_3\)O\(_4@PVP@\)poly(AAPBA-co-HEAAm) PNCs are obtained by in-situ polymerization initiated with ultraviolet radiation under a magnetic field.

### 2.3. Effects of Microstructures of Fe\(_3\)O\(_4@PVP@\)poly(AAPBA-co-HEAAm) Photonic Nanochains on Glucose-sensing Capabilities

In order to elucidate the relationship between the glucose-sensing capabilities of the PNCs and the microstructures, and consequently get the maximum glucose response range of the PNCs, we have fabricated a series of PNCs by varying the feeding ratio of AAPBA and HEAAm \((c_{\text{HEAAm}}/c_{\text{AAPBA}})\), as well as \(X_D\). Figure 4 shows the diffraction wavelength shift range \(\Delta \lambda_D\) of the PNCs in PBS buffer when the [glucose] changes between 0 and \(20 \times 10^{-3}\) M at room temperature under magnetic field. With increasing \(c_{\text{HEAAm}}/c_{\text{AAPBA}}\) at each fixed \(X_D\), \(\Delta \lambda_D\) of the PNCs first rises, and then drops following a maximum value \(\Delta \lambda_{\text{max}}\); in accordance with those of the glucose responsive PC films. Typically, the higher the concentration of boronic groups, the greater a response presents. However, excessive AAPBA content will make the hydrogel more hydrophobic, causing it to swell less in PBS buffer solutions. This accounts for the trend of the curves in Figure 3. The comparison of the \(\Delta \lambda_{\text{max}}\) of samples at each \(X_D\) indicates that when \(X_D>5\%\), all the \(\Delta \lambda_{\text{max}}\) at each \(X_D\) occur when the \(c_{\text{HEAAm}}/c_{\text{AAPBA}} = 3.4\). Meanwhile, as \(X_D\) decreases, the \(\Delta \lambda_{\text{max}}\) at each \(X_D\) gradually increases. The corresponding dark-field microscopic images shown in Figure 3b–f indicate that the chain lengths of those products become longer and longer. This is related to the increase in the thickness of the polymer gel layer around the nanochains, as proved by the change of TG in Figure S3 (Supporting Information). Therefore, it is reasonable to presume that the PNCs contain more glucose responsive hydrogel between neighboring nanoparticles. This hypothesis can also be verified by the initial peak position of those products in PBS buffers without glucose under magnetic field in Figure S4 (Sup-
Figure 4. Glucose-sensing capability and morphologies of the Fe₃O₄@PVP@poly(AAPBA-co-HEAAm) PNCs. a) The diffraction wavelength shift range (Δλ) when [glucose] changes between 0 to 20 × 10⁻³ M versus c_{HEAAm}/c_{AAPBA} for the PNCs obtained at different χ_D. b–f) Dark-field microscope images of the products corresponding to the Δλ_{max} at each χ_D in (a). c_{AAPBA} = 0.025 × 10⁻³ M.

Figure 5. The dark-field microscope images of the nanochains prepared at χ_D = 2.7% and different c_{HEAAm}/c_{AAPBA}. The lower left insets show the optical images of the reacted solution taken after UV polymerization.

Because the interparticle distance is proportional to the peak position according to Bragg’s law, and the initial peak position of the nanochains in the same dispersion medium represents more poly(AAPBA-co-HEAAm) hydrogel occupying the interparticle distances. Furthermore, the hydrogels acquired at χ_D>5% and c_{HEAAm}/c_{AAPBA} = 3.4 almost have an identical composition, indicating an almost equivalent expansion ratio responding to [glucose]. In these circumstances, thicker hydrogel between nanoparticles in the PNCs will induce larger glucose response range. For example, if the interparticle area containing 30 nm thick hydrogel, and the expansion ratio is 1.5, the actual swelling distance is greater than 20 nm thick hydrogel (Δ d_{np} = 30 × 0.5 > Δ d_{np} = 20 × 0.5). When χ_D<5%, the c_{HEAAm}/c_{AAPBA} corresponding to Δλ_{max} are no longer at 3.4 but shift to 5.3. This is caused by the transition of dispersity of the polymer in the mixed solvent. As it can be seen in Figure 2c, if χ_D is lower than 5%, the products prepared at c_{HEAAm}/c_{AAPBA} = 3.4 are out of zone II (dispersed) in the phase diagram resulting in the agglomeration of nanochains as well as the aforementioned whitening phenomenon during the polymerization (polymer together with short nanochains or nanoparticles quickly precipitate out of the solution). Consequently, the content of HEAAm is increased to avoid whitening of the solution during polymerization and obtain longer nanochains to achieve large glucose responsiveness (Figure 5). Among all the samples, the PNCs obtained at χ_D = 2.7% and c_{HEAAm}/c_{AAPBA} = 5.3 have the longest chain length, and their glucose-responsive range is up to 130 nm.

Figure 6 shows the relationship between the diffraction wavelength of the Fe₃O₄@PVP@poly(AAPBA-co-HEAAm) PNCs at different [glucose] and the preparation conditions including the amount of the crosslinking agent (δ) and polymerization magnetic field (H). The rising δ brings the increase in the crosslinking degree and thus the rigidity of PNCs. Consequently, the swelling or shrinking capability of their hydrogel coatings is limited along with the glucose-response ranges (Figure 4a). This is confirmed by the consecutively descending peak positions of the PNCs at [glucose] of 20 × 10⁻³ M with increasing δ. The above tendency is similar to that of our previous pH responsive PNCs, but the two systems show great differences in the extent of the peak position variation induced by adding the same δ. For example,
when $\delta$ changed from 2% to 4%, the pH responsive PNCs maintained less than 60% of its original response range at 2%. In contrast, the glucose responsive PNCs hold 75% of the response range at the same condition. This is because the pH responsive PNCs adopted more hydrophobic ethylene glycol dimethacrylate (EGDMA) as the crosslinking agent, while the glucose responsive PNCs utilized hydrophilic BIS. According to the mechanism in this paper, hydrophilic BIS may distribute more evenly in DMSO-$H_2O$ mixtures making them less efficient to concentrate around Fe$_3$O$_4$@PVP nanoparticles. In fact, if BIS was substituted by EGDMA in the preparation procedure of glucose responsive PNCs, much less crosslinker is needed to produce the same effects of contraction. However, EGDMA also raises the hydrophobicity of the PNCs deteriorating their dispersity in aqueous buffer solutions.

The influence of the $H$ used in the polymerization process on the diffraction wavelength of the PNCs has further been examined. As $H$ increases, the obtained PNCs show blue shifted $\lambda$ in the PBS buffer solution without glucose (Figure 4b). It is easy to understand that strong $H$ will compress the spacing of nanoparticles during the polymerization causing shorter wavelengths to be selected for reflection. Thus, the visually perceptible response ranges of the PNCs to [glucose] could be readily modulated by adjusting both $\lambda$ and $H$.

3. Conclusion

In conclusion, we have demonstrated a new category of optical responsive probes capable of rapidly, continuously and reversibly sensing glucose concentration based on structural color variation, Fe$_3$O$_4$@PVP@poly(AAPBA-co-HEAAm) PNCs. The PNCs are wrapped by only tens of nanometer thick hydrogel shell, prompting the fast diffusion of glucose molecules and significantly reduced response time to a few seconds, at least two orders of magnitude better than their previous counterparts. They are obtained by selective concentration polymerization of monomers in DMSO-$H_2O$ microheterogeneous binary solvents. The morphology evolution and the formation mechanism of the products were systematically interrogated depending on the $\chi_D$ of the binary solvents as well as the concentration of monomers. When $\chi_D<40\%$, most DMSO will form hydrogen-bonding clusters with water, and the populations of free DMSO drop greatly. Relatively hydrophobic AAPBA along with little free DMSO molecules have a tendency to reside in the periphery of the Fe$_3$O$_4$@PVP nanoparticles, which amplified the microheterogeneity of the monomer distribution. Thus, PNCs are obtained after polymerization under magnetic field. The incorporation of HEAAm into the hydrogel increases the dispersibility of the PNCs in PBS buffer solution. The maximum diffraction peak-shift range ($\Delta \lambda_{\text{max}}$) of the PNCs is closely related to the content of poly(AAPBA-co-HEAAm) hydrogel in the PNCs, which is inversely proportional to $\chi_D$ used in polymerization. The PNCs show an optical spectra wavelength-shift range up to 130 nm when [glucose] changed from 0 to $2 \times 10^{-3}$ m, benefiting for naked-eye detection. It is expected that the as-developed glucose sensing PNCs enable the real-time continuous glucose monitoring as well as the miniaturization of glucose diagnosis devices. The developed selective concentration polymerization of monomers in microheterogeneous solvents may pave a way to construct functional polymer-inorganic hybrid nanostructures.

4. Experimental Section

Materials: 3-Acrylamido phenylboronic acid (AAPBA) was purchased from Sigma-Aldrich, N-(2-Hydroxyethyl) acrylamide (HEAAm), $N,N'$-methylenebisacrylamide (BIS), 2-Hydroxy-2-methylpropionophenone (HMPP) were obtained from Aladdin Co. Ltd. Dimethyl sulfoxide (DMSO), D(+)-glucose were purchased from Sinopharm Chemical Reagent Co. Ltd, China. All of the above reagents were used as received without further purification. Deionized water (Aquapro) was used for the experiment. Superparamagnetic Fe$_3$O$_4$@PVP colloidal nanoparticles with an average particle size of 150 nm were synthesized by a one-pot solvothermal polyol process according to our previous report, and stored in ethanol for further use ($10 \text{ mg mL}^{-1}$).[13]

Preparation of Prepolymerization Solution: The stock solution of Fe$_3$O$_4$@PVP colloidal nanoparticles was obtained by centrifuging their ethanol solution (1 mL) and then dispersing it into DMSO (0.455 mL) under sonication. The stock solutions of monomers or photoinitiators were produced by dissolving AAPBA (0.5 $\times 10^{-3}$ m), HEAAm (4.25 $\times 10^{-3}$ m), BIS (0.1 $\times 10^{-3}$ m), and HMPP (0.2 $\times 10^{-3}$ m) in 545, 181, 500, and 500 m $\mu$L DMSO, respectively.

Preparation of Fe$_3$O$_4$@PVP@AAPBA Photonic Nanochains: The Fe$_3$O$_4$@PVP colloidal nanoparticles stock solution (12 $\mu$L), AAPBA stock solution (27.5 $\mu$L), HMPP stock solution (2 $\mu$L), DMSO (58.6 $\mu$L), and deionized water (900 $\mu$L) were first mixed in a 10 mL glass beaker to form a prepolymer solution by sonication. Then, the beaker was placed above the center of a 10 $\times$ 10 $\times$ 2 cm NdFeB square magnet with a distance of...
2.0 cm (500 Gs) for 120 s. Subsequently, the UV light was turned on for curing (5 min). Afterward, 3 mL DMSO was added into the beaker to dilute the solution. Finally, the products of Fe₃O₄@PVP@PAAPBA PNCs were magnetically separated from the solution and re-dispersed in DMSO for storing. A variety of products were obtained by changing the concentration of AAPBA or D in the prepolymer solution.

Preparation of Fe₃O₄@PVP@ poly(AAAPBA-co-HEAam) photonic nanochains: The Fe₃O₄@PVP colloidal nanoparticles stock solution (12 μL), HEAam stock solution (18.5 μL), BIS stock solution (13 μL), HMPP stock solution (10 μL), DMSO (60 μL), and deionized water (900 μL) were first mixed in a 10 mL glass beaker to form a prepolymer solution by sonication. Then, the beaker was placed above the center of a 10 × 2 cm NdFeB square magnet with a distance of 2.0 cm (500 Gs) for 120 s, and subsequently illuminated by the UV light for 5 min. Afterward, 3 mL DMSO was added into the beaker to dilute the solution. Finally, the products of Fe₃O₄@PVP@ poly(AAAPBA-co-HEAam) PNCs were magnetically separated from the solution and re-dispersed in DMSO for storing. Various products were obtained by changing the concentration of HEAam or D in the prepolymer solution.

Characterization: All digital photos were taken by using iPhone mobile phone. A JEOL JSM-2100F transmission electron microscope (TEM) instrument (JEOL, Japan) was used to capture TEM images with an acceleration voltage of 200 kV. The field-emission scanning electron microscopy (FE-SEM) images were collected by using a Hitachi S-4800 scanning electron microscope. A 60-SXB FTIR spectrometer was used to collect Fourier transform infrared (FTIR) spectra in the range of 400–4000 cm⁻¹ with a resolution of 4 cm⁻¹. A NETZSCH-STA449C/G instrument was used to conduct thermal analysis. All the dark-field microscope images were captured by a field-emissionscanning electron microscope (FE-SEM) microscope (Zeiss Axio Observer5M, Germany).

Glucose Detection: First, a PBS buffer with pH = 8.0 and physiological ionic strength (150 × 10⁻³ M) was prepared according to a previous study.[6] During the test, the PNCs were dispersed in the above PBS buffer, then, adding a small amount of high-concentrated glucose solution (12 m) to adjust its concentration. After shaking for 5 s, it was placed on a 200 Gs magnetic field, and the diffraction spectrum was detected along the magnetic field direction by a fiber optic spectrometer. All the tests were performed at room temperature.

Supporting Information
Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest
The authors declare no conflict of interest.

Data Availability Statement
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords
colorimetric sensing, glucose monitor, photonic crystal nanochains, preparation mechanism, response time

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