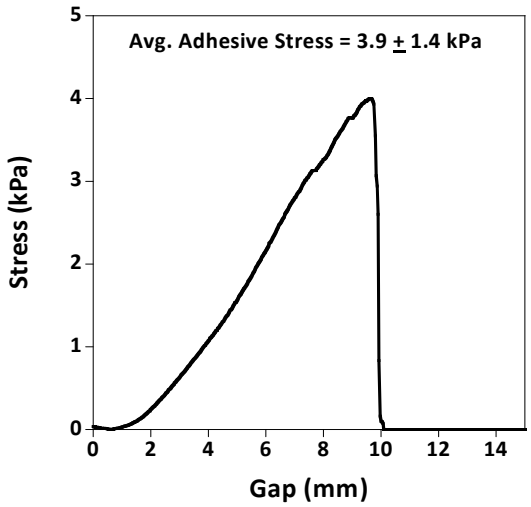
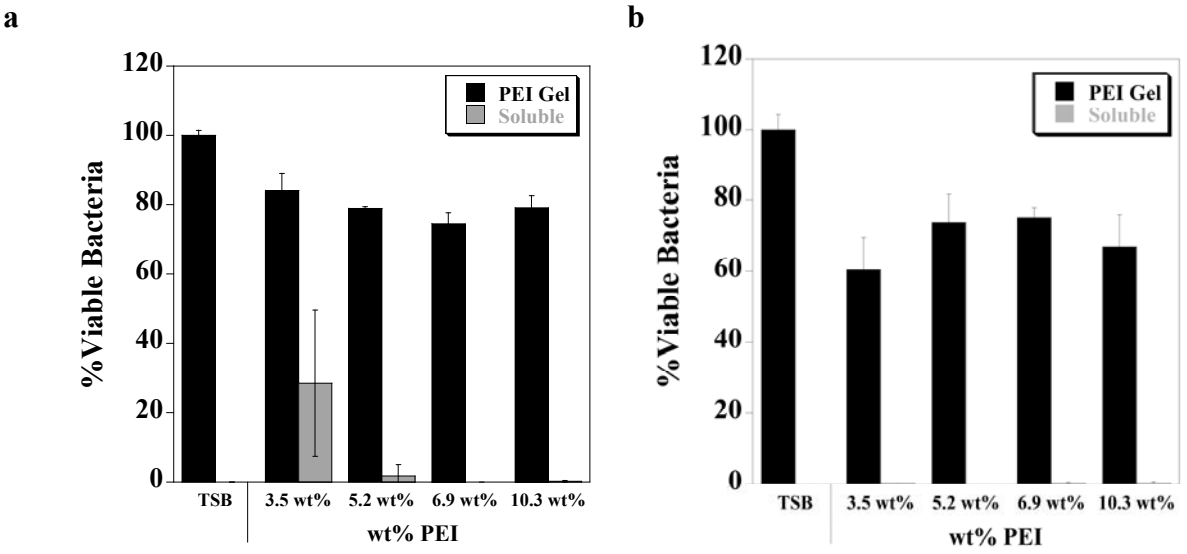
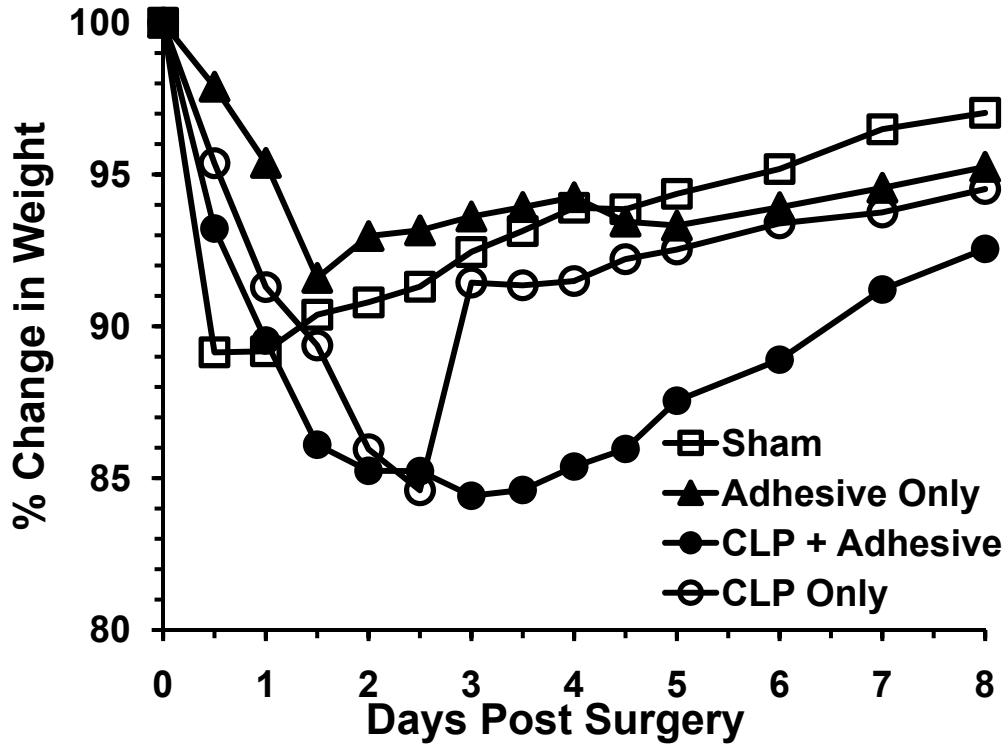


Supplementary Figure 1 | Bioadhesive stress measurements of fibrin glue (Tisseel). Porcine tissue was assessed by uniaxial lap-shear measurements to determine adhesive stress of fibrin glue.

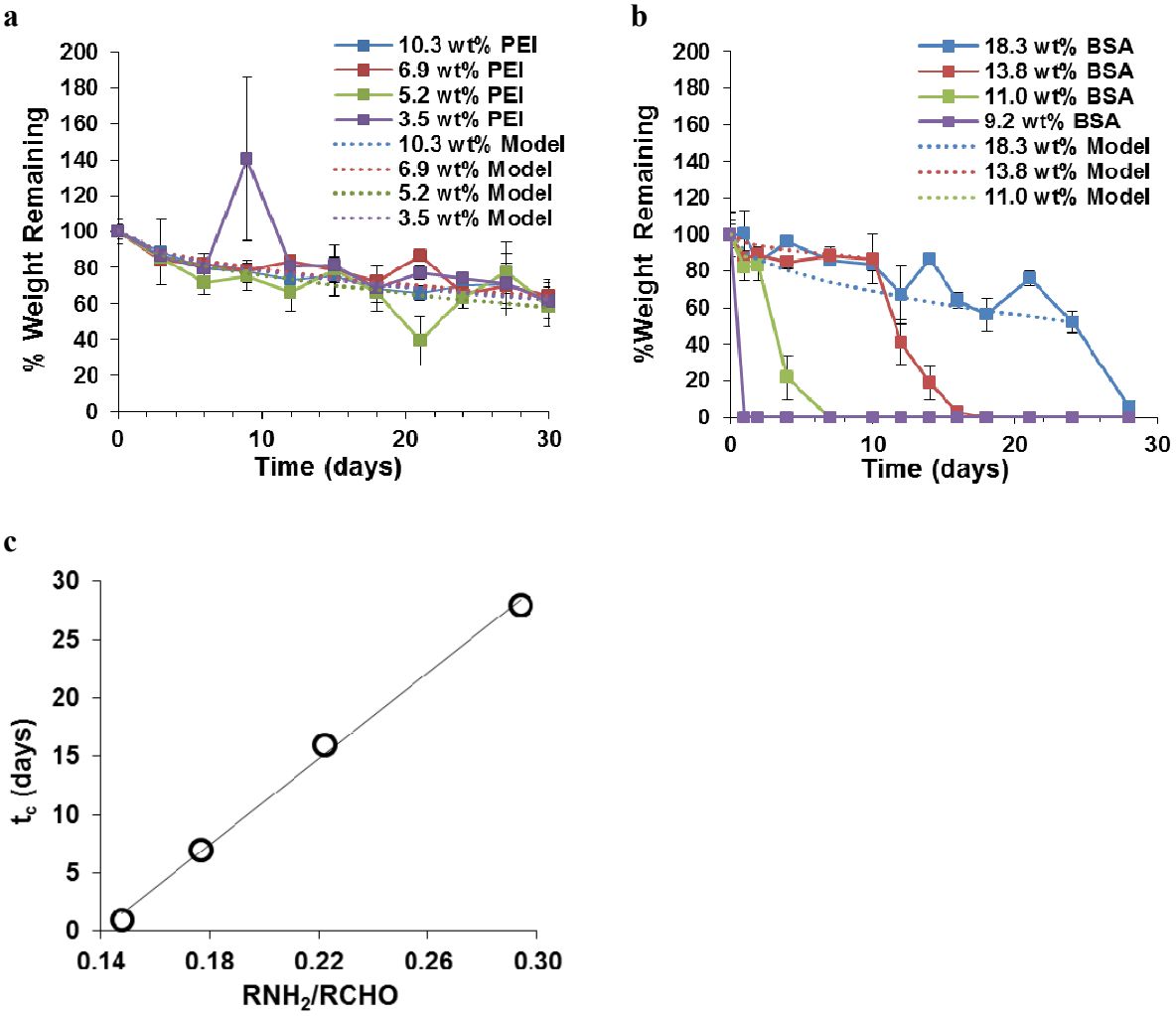


Supplementary Figure 2 | PEI is not leeched from bioadhesive gels. 10^4 CFU mL^{-1} (**a**) *E. coli* and (**b**) *S. aureus* exposed to cell culture inserts containing adhesive gels (■) or soluble PEI (■) at the same concentrations utilized to form the hydrogels. Data taken at 24 hours (n = 3; error bars, s.d.).

Supplementary Figure 3 | Gross anatomical images of bacterial infection control mice. Animals were injected with 2.5 wt% PDA crosslinked with 6.9 wt% PEI bioadhesive followed by an injection of 10^8 CFU mL^{-1} *S. pyogenes* at a separate location.

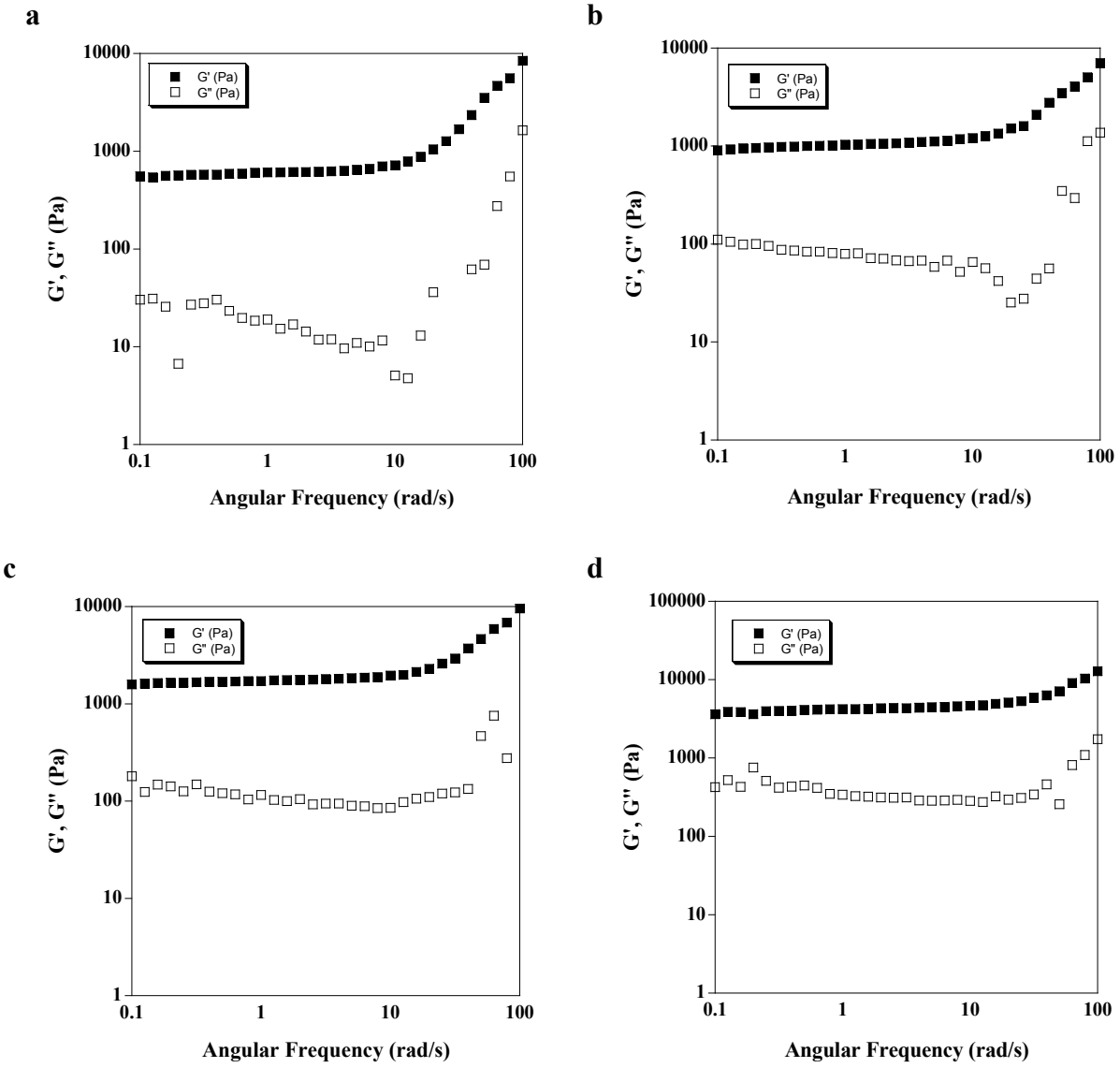


Supplementary Figure 4 | Percent weight change of mice for the CLP model. Weight change in mice receiving sham, adhesive only, CLP with application of adhesive (2.5 wt% PDA crosslinked with 6.9 wt% PEI), and CLP only (n = 8).

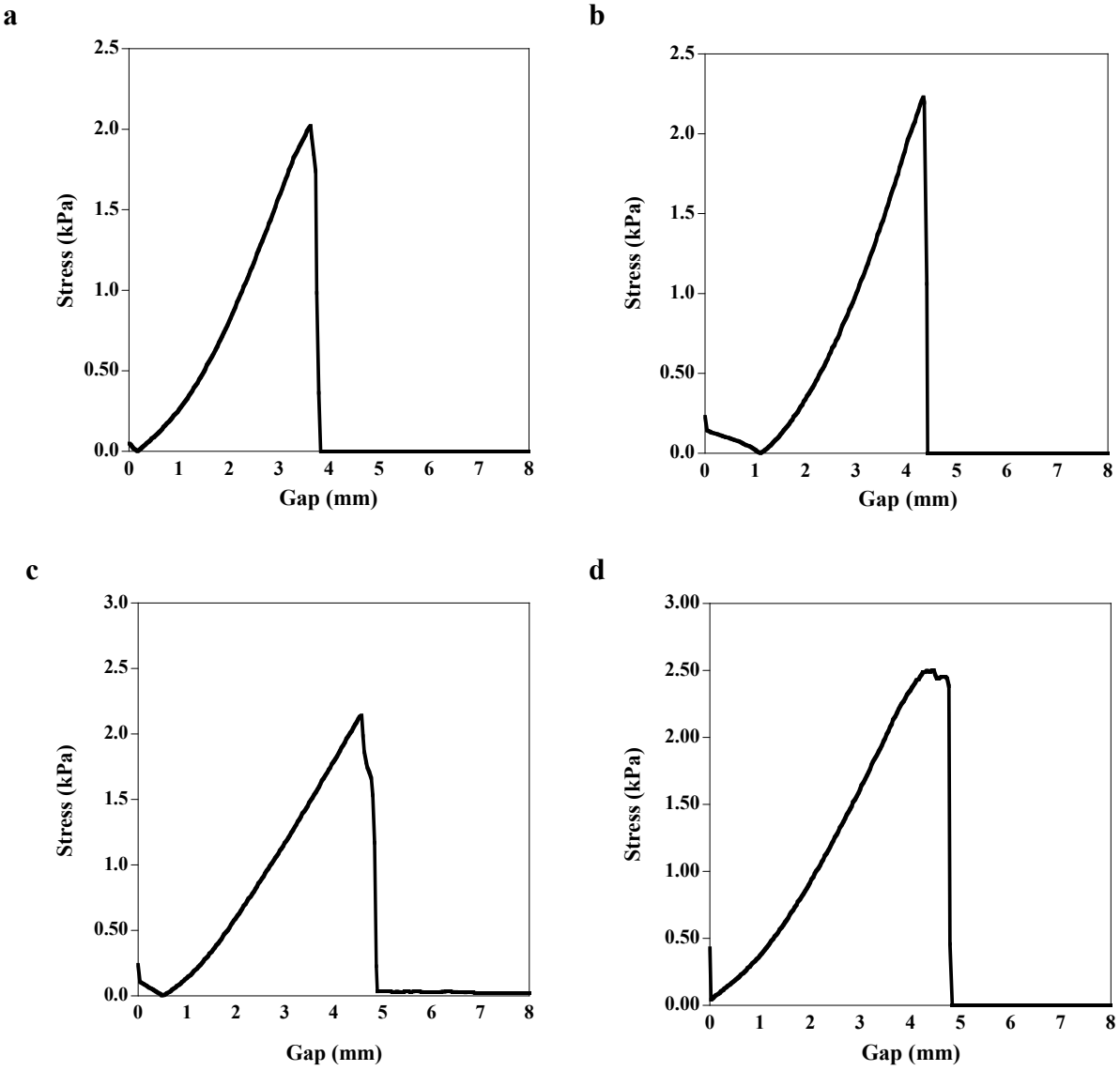


Amine Component	$RNH_2/RCHO$	k_{deg} [$days^{-1}$]	t_c [days]
10.3 wt% PEI	5.4	0.068	978
6.9 wt% PEI	3.6	0.066	646
5.2 wt% PEI	2.7	0.077	480
3.5 wt% PEI	1.9	0.069	315
18.3 wt% BSA	0.3	0.098	28
13.8 wt% BSA	0.2	0.041	16
11.0 wt% BSA	0.15	0.120	7
9.2 wt% BSA	0.1	-	1

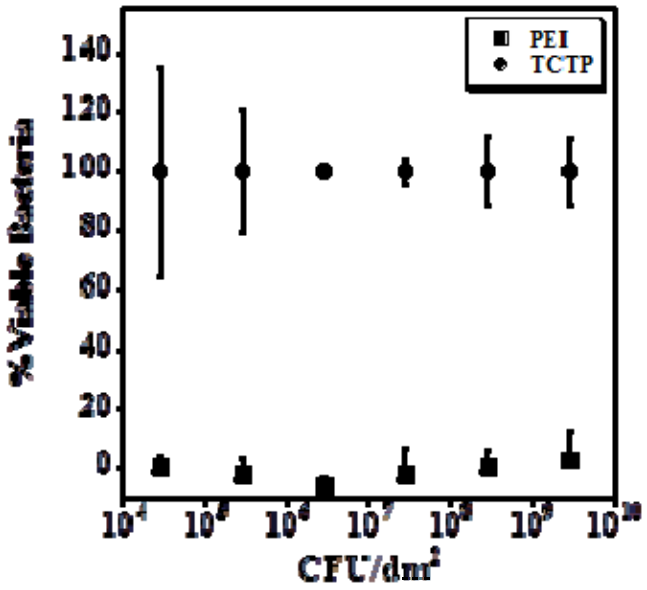
Supplementary Figure 5 | Degradation of bioadhesive gels. (**a**) *Ex vivo* degradation of 2.5 wt% PDA crosslinked with 3.5 wt% PEI (purple), 5.2 wt% PEI (green), 6.9 wt% PEI (red) and 10.3 wt% PEI (blue) (n = 3, error bars, s.d.); the slow degradation phase for each formulation was fit to $M_t/M_o = k_{deg}t^n$ and are shown as dashed lines. (**b**) Degradation of 7.5 wt% PDA crosslinked with 9.2 wt% BSA (purple), 11.0 wt% BSA (green), 13.8 wt% BSA (red) and 18.3 wt% BSA (blue) (n = 3, error bars, s.d.); the slow degradation phase fits shown as dashed lines. (**c**) Linear dependence of time to reverse gelation (t_c) values on $RNH_2/RCHO$ ratios; y = 184.46X – 25.78, $R^2 = 0.997$. The $RNH_2/RCHO$ values are based on 52% PDA functionalization.



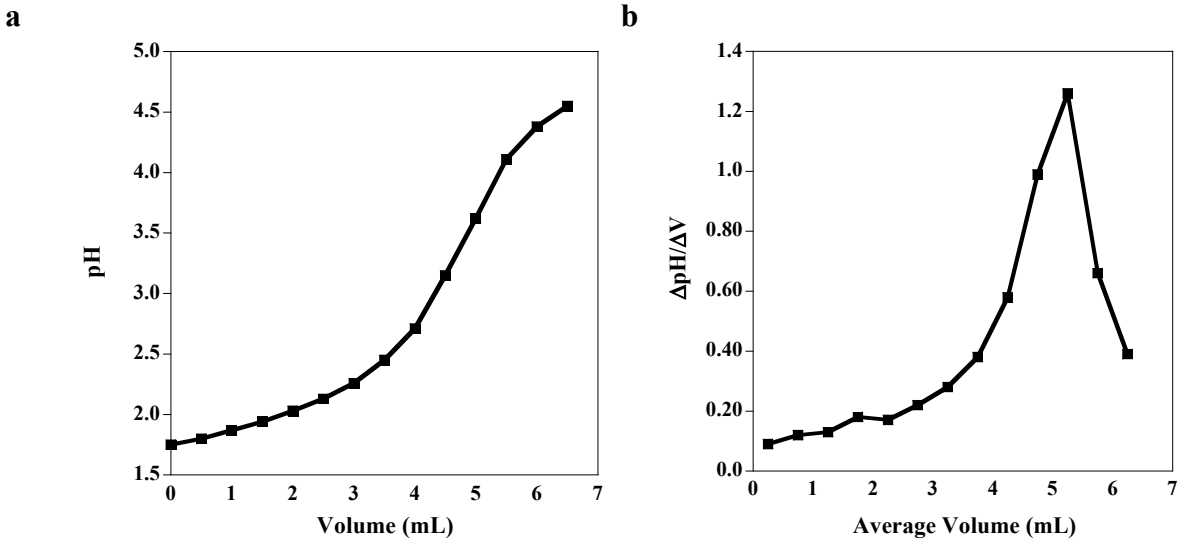
Supplementary Figure 6 | Oscillatory rheology of preformed adhesive gels. Dynamic frequency sweeps were performed for 2.5 wt% PDA crosslinked with (**a**) 3.5 wt% PEI, (**b**) 5.2 wt% PEI, (**c**) 6.9 wt% PEI and (**d**) 10.3 wt% PEI are shown (n = 4).



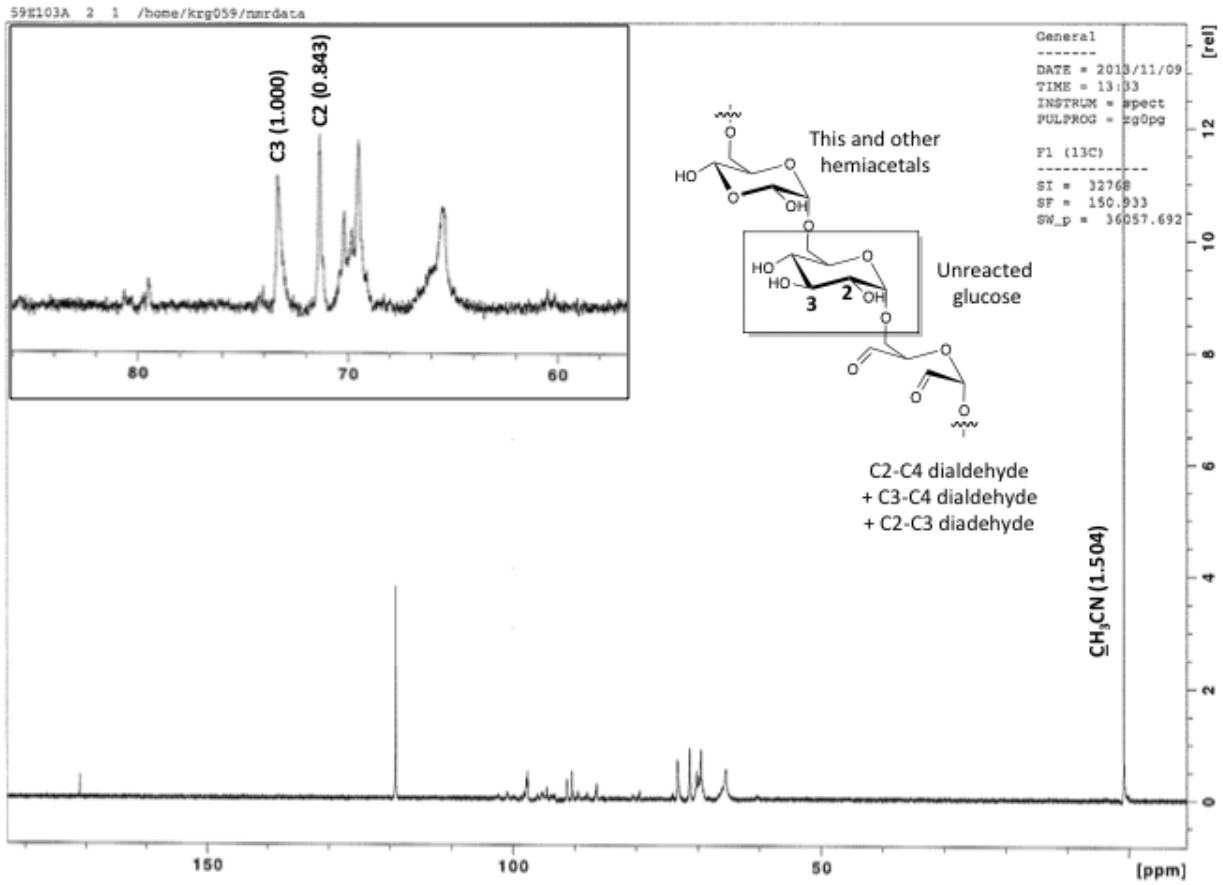
Supplementary Figure 7 | Adhesive failure of bioadhesives. Stress measurements of 2.5 wt% PDA crosslinked with (**a**) 3.5 wt% PEI, (**b**) 5.2 wt% PEI, (**c**) 6.9 wt% PEI and (**d**) 10.3 wt% PEI as assessed by uniaxial lap-shear measurements employing porcine tissue.



Supplementary Figure 8 | Antibacterial activity of adhesive towards S. pyogenes. TCTP (□) and 2.5 wt% PDA crosslinked with 6.9 wt% PEI (■) surfaces challenged with increasing concentrations of *S. pyogenes* (n = 3, error bars, s.d.).



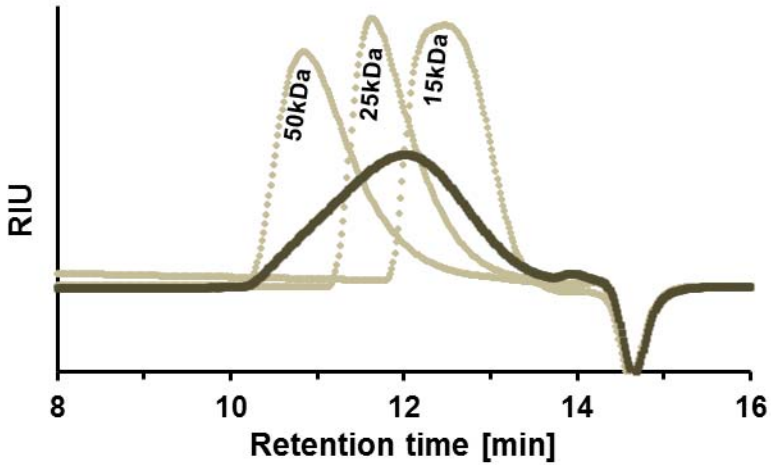
Supplementary Figure 9 | Calorimetric analysis of polydextran aldehyde oxidation. (**a**) Polydextran aldehyde (PDA) titration with hydroxyl-amine. (**b**) The first derivative of the titration was utilized to determine the equivalence point



Supplementary Figure 10 | ^{13}C NMR analysis of polydextran aldehyde oxidation ^{13}CNMR of polydextran aldehyde (PDA) in D_2O buffer (10 mM NaD_2PO_4, pD 7.5) with acetonitrile internal standard. Oxidation of dextran leads to the formation of multiple aldehyde species as well as various hemiacetals that are in equilibrium in aqueous solution. In addition, incomplete oxidation leaves unreacted glucose units intact within the PDA. The integration values for C2 and C3 were averaged (0.9) and this value represents one carbon in the calculation of percent functionality for the dextran oxidation reaction.

SAMPLE	M_p	STDEV	M_n	STDEV	M_w	STDEV	M_w/M_n	STDEV
52% PDA	20.3	0.8	15.5	0.4	21.5	0.2	1.4	0.1

M_p = peak molecular weight (kDa)
M_n = number average molecular weight (kDa)
M_w = weight average molecular weight (kDa)
M_w/M_n = polydispersity index



Supplementary Figure 11 | Size exclusion chromatography of oxidized dextran. Molecular weight standards (15, 25 and 50 kDa) are shown in a tan color with size exclusion results of 52 % functionalized PDA overlaid in dark green (n = 3; representative chromatograms shown).

Supplementary Methods

Materials

T-25 dextran was purchased from Pharmacosmos. Sodium periodate, hydroxyl amine, methyl orange, branched PEI, LB and agar was purchased from Sigma. Tryptic soy broth and Trypticase^{TM} soy agar plate containing 5% sheep blood were purchased from BD. Dulbecco's phosphate buffered saline was purchased from Corning.

Dextran Oxidation and Functionalization Quantification

Dextran (25 kDa, 10 g, 0.0616 mol glucose monomer) was dissolved in 400 mL of milli-Q water[1]. Then 9.91 g of sodium periodate (0.04631 mol) dissolved in 100 mL of milli-Q water was added to the dextran solution and stirred for 24 hours at room temperature, in the dark. The reaction was quenched with diethylene glycol and stirred for 2 hours. After which, the reaction mixture was extensively dialyzed (MW cutoff – 12.3 kDa) against milli-Q water over 3 days with frequent water changes. The oxidized dextran solution was removed from the dialysis tube, shell frozen in a round-bottomed flask with N_2 (l) and lyophilized, affording a white fluffy powder.

Oxidation of dextran leads to the formation of multiple aldehyde species as well as the formation of various hemiacetals within the polymer. All of these species are in equilibrium when PDA is dissolved in aqueous solution[2]. The relative oxidation, or percent functionalization[3], was determined by both colorimetric analysis and ^{13}CNMR. The colorimetric analysis (Supplementary Figure 9) was performed by dissolving 100 mg of oxidized dextran in 25 mL of 0.25 N hydroxylamine hydrochloride ($H_2NOH{\cdot}HCl$) containing ~0.007 w v^{-1}% methyl orange (pH adjusted to 4). Reaction of hydroxylamine with aldehyde depletes both aldehyde and

hemiacetal since these species are in equilibrium. At any rate, the mixture was allowed to stir for 2 hours, after which the reaction was titrated with 0.1 N NaOH. The volume of the NaOH solution and the respective pH after each addition was recorded. The percent functionality was calculated by:

$$\%\ \text{Functionality} = 100\ \times \frac{\text{mol dialdehyde}}{\text{mol of gluc}} = 100\ \times \frac{V_{\text{NaOH}}\ \times\ N_{\text{NaOH}}\ \times 0.5}{m_{\text{dextran}}\ \div\ \left(MW_{\text{gluc}} - 18\right)} \qquad (1)$$

Where the moles of dialdehyde were experimentally determined from the volume of 0.1 N NaOH needed to titrate the polydextran aldehyde sample (divided by 2; 2 aldehydes produced per oxidation reaction). The moles of glucose were determined from the mass of the starting dextran (m_{dextran}). The percent functionality determined by colorimetric analysis is 52%. ^{13}CNMR was also employed to determine percent functionality according to:

$$\%\ Functionality = 100\ \times \frac{\text{mol}\ GU_{\text{i}} - \text{mol}\ GU_{\text{F}}}{\text{mol}\ GU_{\text{i}}} \qquad (2)$$

Here the difference with respect to the number of moles of glucose units before (mol GU_{i}) and after oxidation (mol GU_{F}) is used to determine percent functionality. The initial number of moles of glucose units is known and represents the moles of glucose units available before oxidation. The moles of glucose units remaining after oxidation in the PDA was determined by NMR by integrating carbons 2 and 3 of the glucose ring (see Supplementary Figure 10), which had well-resolved chemical shifts. A delay time (D1 = 2 min) employed during spectral acquisition over 3 days allowed integration of the C2 and C3 carbon chemical shifts relative to

the internal standard ($\underline{C}H_3CN$). Data was collected on a Bruker Avance AV-III spectrometer equipped with a 3 mm TXI cryogenic probe, and operating at 150 MHz for ^{13}C. The NMR sample was prepared by dissolving 30.16 mg of PDA in 0.8 mL of D_2O buffer (10 mM NaD_2PO_4, pD 7.5). This amount of PDA theoretically represents 1.86×10^{-4} moles of glucose units before oxidation. Dissolution of PDA took overnight. After which time, 8 μL (1.53×10^{-4} mole) spectroscopy grade acetonitrile was added as an internal standard. The percent functionality determined by NMR analysis is 51%.

Size exclusion chromatography of PDA samples (at 1mg mL^{-1}) was performed on an HP 1100 series LC system equipped with an Agilent ZORBAX PSM300 column and Wyatt OptiLab Refractive Index detector. 100mM sodium acetate buffer (pH 6.4) was used as the mobile phase at a flow rate of 0.4 mL min^{-1}. The molecular weight of PDA was determined by comparing the retention volume to linear dextran 15 kDa – 50 kDa standards (Sigma Aldrich) ran under the same conditions (Supplementary Figure 11).

Polyethylenimine Preparation

Purchased branched polyethylenimine (PEI, 25 kDa, 2.06 g) was dissolved in 10 mL of milli-Q water by sonication. The resulting 20.6 wt% PEI stock solution was adjusted to pH 7.6 with HCl. All of the PEI formulations were prepared from this stock solution, by diluting with milli-Q water.

Gelation time determination

Due to rapid hydrogel formation it was impossible to directly measure the gelation time rheologically. Therefore, a pipette method was employed as described by Elisseef et al[4].

Briefly, 50 μL of 5 wt% PDA dissolved in buffer (23.5 mM NaH_2PO_4, 80.6 mM Na_2HPO_4, pH 7.3) was added to an eppendorf tube. To this, an equal volume of any one of the formulations of PEI in water (pH 7.6) was added and repeatedly pipetted up and down until it was impossible to pipette anymore. The time at which the solutions could not be pipetted was defined as the gelation time. The average time was calculated from five independent measurements for all gel formulations.

Supplementary References

1. Maia, J., Ferreira, L., Carvalho, R., Ramos, M.A. & Gil, M.H. Synthesis and characterization of new injectable and degradable dextran-based hydrogels. *Polymer* **46**, 9604-9614 (2005).
2. Maia, J., Carvalho, R.A., Coelho, J.F.J., Simoes, P.N. & Gil, M.H. Insight on the periodate oxidation of dextran and its structural vicissitudes. *Polymer* **52**, 258-265 (2011).
3. Zhao, H. & Heindel, N.D. Determination of degree of substitution of formyl groups in polyaldehyde dextran by hydroxylamine hydrochloride method. *Pharm. Res.* **8**, 400-402 (1991).
4. Strehin, I., Nahas, Z., Arora, K., Nguyen, T. & Elisseeff, J. A versatile pH sensitive chondroitin sulfate-PEG tissue adhesive and hydrogel. *Biomaterials* **31**, 2788-2797 (2010).