# Mega Macromolecules as Single Molecule Lubricants for Hard and Soft Surfaces

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## Supplementary Information

**Supplementary Discussion:**

**Stribeck curve plots COF vs Hersey number**

A Stribeck curve plots COF vs Hersey number, the key variable in a Stribeck curve. The Hersey number, a dimensionless number, is derived from multiplying velocity (m/s) with viscosity (Pa.s = N.s/m2), and dividing by load per unit length (N/m). The lubrication in the presence of a fluid of incompressible materials has been well characterized with respect to specific modes, classically displayed on Stribeck curves, which defines the lubrication modes and is fundamental in understanding lubrication. In order to elucidate the relative contributions of the mega HPGs and other control lubricants to the different modes of lubrication, we determined the Stribeck curves for the metal on metal surface. Given the experimental constraints for the cartilage on cartilage surface experiments, we performed a more limited experiment.

**Supplementary Table 1**. Hydrodynamic diameters, degree of branching, and hydration of the mega HPGs and comparison with low molecular weight analogues.

| Entry | $M_w$ (Đ) | Degree of Branching[a] | Hydrodynamic diameter (nm)[b] | Hydration (number of water molecules per polymer)[c] |
|---|---|---|---|---|
| HPG-1 | 120 kDa (1.15) | 0.56 | 9.20[3] | - |
| HPG-2 | 491 kDa (1.40) | 0.57 | 12.60[4] | - |
| HPG-3 | 840 kDa (1.20) | 0.56 | 20.4 ± 0.5 | - |
| mega HPG-1 | 1300 kDa (1.20) | 0.57 | 21.2 ± 0.4 | 68600 |
| mega HPG-2 | 2900 kDa (1.20) | 0.54 | 30.6 ± 0.6 | 125500 |
| mega HPG-3 | 9300 kDa (1.40) | 0.53 | 43.0 ± 0.4 | 389300 |

[a]Determined by quasi-elastic light scattering (QELS) analysis. [b]Measured by $^{13}C$ inverse gated NMR spectroscopy. [c]Determined by DSC.

**Supplementary Table 2**. Comparison of solubility of mega HPGs with other linear synthetic polymers

| Entry | Sample ($M_n$) | Solubility (mg/mL) |
|---|---|---|
| 1 | mega HPG-2 (2.5 MDa) | 380 |
| 2 | PEO (8 MDa) | 20 |
| 3 | PEO (4 MDa) | 25 |
| 4 | PVA (0.205 MDa) | 200 |

**Supplementary Table 3**. Statistics derived for Fig. 3a (Error bars represent standard deviation, N = 3 replicates; one-way ANOVA used to compare groups, statistical differences are defined as $p<0.05$ =*, $p<0.01$=**, $p<0.0001$ =****)

| Tukey's multiple comparisons test | Mean Diff. | 95.00% CI of diff. | Significant ? | Summary | Adjusted P Value |
|---|---|---|---|---|---|
| 7% mega-HPG-1 vs. 7% mega-HPG-2 | -6.06E-05 | -0.002929 to 0.002808 | No | Ns | >0.9999 |
| 7% mega-HPG-1 vs. 7% mega-HPG-3 | -4.66E-05 | -0.002915 to 0.002822 | No | Ns | >0.9999 |
| 7% mega-HPG-1 vs. BSF | -0.000474 | -0.003343 to 0.002394 | No | Ns | 0.9994 |
| 7% mega-HPG-1 vs. 23% mega-HPG-1 | -0.004145 | -0.007014 to -0.001276 | Yes | ** | 0.0024 |
| 7% mega-HPG-1 vs. 23% mega-HPG-2 | -0.003445 | -0.006314 to -0.0005762 | Yes | * | 0.0128 |
| 7% mega-HPG-1 vs. 23% mega-HPG-3 | -0.02821 | -0.03108 to -0.02534 | Yes | **** | <0.0001 |
| 7% mega-HPG-1 vs. Synvisc | -0.000948 | -0.003816 to 0.001921 | No | Ns | 0.9509 |
| 7% mega-HPG-1 vs. Pennzoil | -0.000109 | -0.004166 to 0.003948 | No | Ns | >0.9999 |
| 7% mega-HPG-2 vs. 7% mega-HPG-3 | 0.000014 | -0.002855 to 0.002883 | No | Ns | >0.9999 |
| 7% mega-HPG-2 vs. BSF | -0.000414 | -0.003282 to 0.002455 | No | Ns | 0.9998 |
| 7% mega-HPG-2 vs. 23% mega-HPG-1 | -0.004084 | -0.006953 to -0.001216 | Yes | ** | 0.0028 |
| 7% mega-HPG-2 vs. 23% mega-HPG-2 | -0.003384 | -0.006253 to -0.0005156 | Yes | * | 0.0148 |
| 7% mega-HPG-2 vs. 23% mega-HPG-3 | -0.02815 | -0.03102 to -0.02528 | Yes | **** | <0.0001 |
| 7% mega-HPG-2 vs. Synvisc | -0.000887 | -0.003756 to 0.001982 | No | Ns | 0.9659 |
| 7% mega-HPG-2 vs. Pennzoil | -4.83E-05 | -0.004105 to 0.004009 | No | Ns | >0.9999 |
| 7% mega-HPG-3 vs. BSF | -0.000428 | -0.003296 to 0.002441 | No | Ns | 0.9997 |
| 7% mega-HPG-3 vs. 23% mega-HPG-1 | -0.004098 | -0.006967 to -0.001230 | Yes | ** | 0.0027 |
| 7% mega-HPG-3 vs. 23% mega-HPG-2 | -0.003398 | -0.006267 to -0.0005296 | Yes | * | 0.0143 |
| 7% mega-HPG-3 vs. 23% mega-HPG-3 | -0.02817 | -0.03103 to -0.02530 | Yes | **** | <0.0001 |
| 7% mega-HPG-3 vs. Synvisc | -0.000901 | -0.003770 to 0.001968 | No | Ns | 0.9628 |
| 7% mega-HPG-3 vs. Pennzoil | -6.23E-05 | -0.004119 to 0.003995 | No | Ns | >0.9999 |
| BSF vs. 23% mega-HPG-1 | -0.003671 | -0.006539 to -0.0008020 | Yes | ** | 0.0074 |
| BSF vs. 23% mega-HPG-2 | -0.002971 | -0.005839 to -0.0001020 | Yes | * | 0.0395 |
| BSF vs. 23% mega-HPG-3 | -0.02774 | -0.03061 to -0.02487 | Yes | **** | <0.0001 |
| BSF vs. Synvisc | -0.000473 | -0.003342 to 0.002395 | No | Ns | 0.9994 |
| BSF vs. Pennzoil | 0.000365 | -0.003692 to 0.004422 | No | Ns | >0.9999 |
| 23% mega-HPG-1 vs. 23% mega-HPG-2 | 0.0007 | -0.002169 to 0.003569 | No | Ns | 0.9918 |
| 23% mega-HPG-1 vs. 23% mega-HPG-3 | -0.02407 | -0.02694 to -0.02120 | Yes | **** | <0.0001 |
| 23% mega-HPG-1 vs. Synvisc | 0.003197 | 0.0003286 to 0.006066 | Yes | * | 0.0231 |

| | | | | | |
|---|---|---|---|---|---|
| 23% mega-HPG-1 vs. Pennzoil | 0.004036 | -2.097e-005 to 0.008093 | No | Ns | 0.0517 |
| 23% mega-HPG-2 vs. 23% mega-HPG-3 | -0.02477 | -0.02764 to -0.02190 | Yes | **** | <0.0001 |
| 23% mega-HPG-2 vs. Synvisc | 0.002497 | -0.0003714 to 0.005366 | No | Ns | 0.1149 |
| 23% mega-HPG-2 vs. Pennzoil | 0.003336 | -0.0007210 to 0.007393 | No | Ns | 0.1541 |
| 23% mega-HPG-3 vs. Synvisc | 0.02726 | 0.02440 to 0.03013 | Yes | **** | <0.0001 |
| 23% mega-HPG-3 vs. Pennzoil | 0.0281 | 0.02405 to 0.03216 | Yes | **** | <0.0001 |
| Synvisc vs. Pennzoil | 0.000839 | -0.003218 to 0.004896 | No | Ns | 0.9973 |

**Supplementary Table 4**. Statistics derived for Fig. 4. (Error bars represent standard deviation, N = 3 or greater replicates; one-way ANOVA used to compare groups, statistical differences indicated by asterisk where $p<0.05$ =*, $p<0.01$=**, $p<0.0001$ =****)

| Tukey's multiple comparisons test | Mean Diff. | 95.00% CI of diff. | Significant ? | Summary | Adjusted P Value | |
|---|---|---|---|---|---|---|
| Synvisc vs. OA SF (mild) | 0.01787 | -0.04312 to 0.07887 | No | ns | 0.9954 | A-B |
| Synvisc vs. OA SF (severe) | -0.07995 | -0.1282 to -0.03172 | Yes | **** | <0.0001 | A-C |
| Synvisc vs. BSF | 0.0378 | -0.003765 to 0.07936 | No | ns | 0.1058 | A-D |
| Synvisc vs. PBS | 0.02111 | -0.01624 to 0.05847 | No | ns | 0.714 | A-E |
| Synvisc vs. mega HPG-1 7% | 0.01298 | -0.03015 to 0.05611 | No | ns | 0.9944 | A-F |
| Synvisc vs. mega HPG-1 23% | 0.02934 | -0.01379 to 0.07248 | No | ns | 0.4569 | A-G |
| Synvisc vs. mega HPG-2 7% | 0.01254 | -0.03270 to 0.05778 | No | ns | 0.9971 | A-H |
| Synvisc vs. mega HPG-2 23% | 0.0133 | -0.03194 to 0.05854 | No | ns | 0.9953 | A-I |
| Synvisc vs. mega HPG-3 7% | 0.03907 | -0.004066 to 0.08220 | No | ns | 0.1089 | A-J |
| Synvisc vs. mega HPG-3 23% | 0.03842 | -0.006813 to 0.08366 | No | ns | 0.1657 | A-K |
| OA SF (mild) vs. OA SF (severe) | -0.09782 | -0.1625 to -0.03312 | Yes | *** | 0.0002 | B-C |
| OA SF (mild) vs. BSF | 0.01993 | -0.03997 to 0.07982 | No | ns | 0.9879 | B-D |
| OA SF (mild) vs. PBS | 0.003239 | -0.05382 to 0.06030 | No | ns | >0.9999 | B-E |
| OA SF (mild) vs. mega HPG-1 7% | -0.004894 | -0.06589 to 0.05610 | No | ns | >0.9999 | B-F |
| OA SF (mild) vs. mega HPG-1 23% | 0.01147 | -0.04953 to 0.07247 | No | ns | 0.9999 | B-G |
| OA SF (mild) vs. mega HPG-2 7% | -0.005332 | -0.06784 to 0.05717 | No | ns | >0.9999 | B-H |
| OA SF (mild) vs. mega HPG-2 23% | -0.004572 | -0.06708 to 0.05793 | No | ns | >0.9999 | B-I |
| OA SF (mild) vs. mega HPG-3 7% | 0.02119 | -0.03981 to 0.08219 | No | ns | 0.9833 | B-J |
| OA SF (mild) vs. mega HPG-3 23% | 0.02055 | -0.04195 to 0.08306 | No | ns | 0.9889 | B-K |
| OA SF (severe) vs. BSF | 0.1177 | 0.07092 to 0.1646 | Yes | **** | <0.0001 | C-D |
| OA SF (severe) vs. PBS | 0.1011 | 0.05793 to 0.1442 | Yes | **** | <0.0001 | C-E |
| OA SF (severe) vs. mega HPG-1 7% | 0.09293 | 0.04470 to 0.1411 | Yes | **** | <0.0001 | C-F |
| OA SF (severe) vs. mega HPG-1 23% | 0.1093 | 0.06107 to 0.1575 | Yes | **** | <0.0001 | C-G |
| OA SF (severe) vs. mega HPG-2 7% | 0.09249 | 0.04237 to 0.1426 | Yes | **** | <0.0001 | C-H |
| OA SF (severe) vs. mega HPG-2 23% | 0.09325 | 0.04313 to 0.1434 | Yes | **** | <0.0001 | C-I |
| OA SF (severe) vs. mega HPG-3 7% | 0.119 | 0.07079 to 0.1672 | Yes | **** | <0.0001 | C-J |
| OA SF (severe) vs. mega HPG-3 23% | 0.1184 | 0.06825 to 0.1685 | Yes | **** | <0.0001 | C-K |

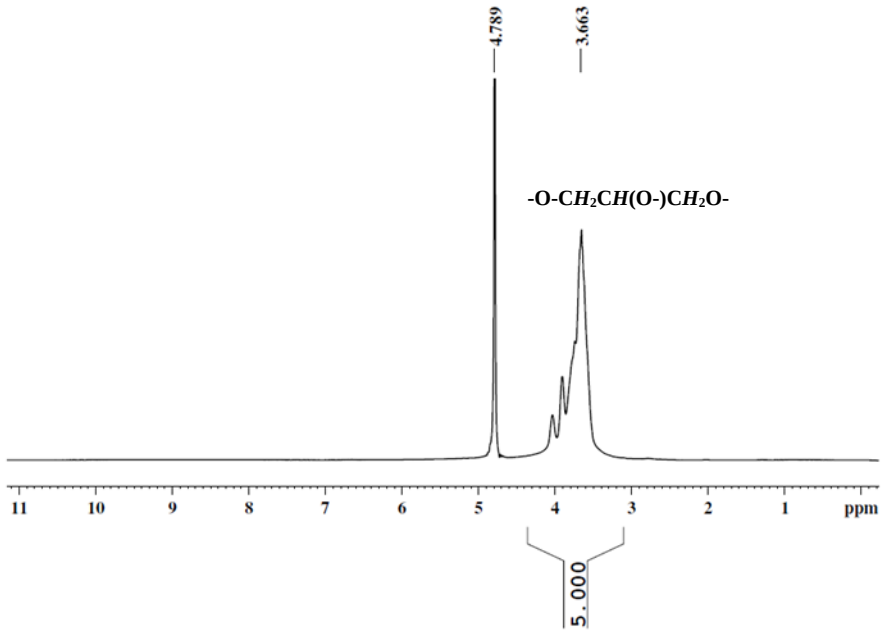
| | | | | | | |
|---|---|---|---|---|---|---|
| BSF vs. PBS | -0.01669 | -0.05222 to 0.01884 | No | ns | 0.8838 | D-E |
| BSF vs. mega HPG-1 7% | -0.02482 | -0.06638 to 0.01674 | No | ns | 0.6443 | D-F |
| BSF vs. mega HPG-1 23% | -0.008455 | -0.05002 to 0.03311 | No | ns | 0.9998 | D-G |
| BSF vs. mega HPG-2 7% | -0.02526 | -0.06900 to 0.01849 | No | ns | 0.6879 | D-H |
| BSF vs. mega HPG-2 23% | -0.0245 | -0.06824 to 0.01925 | No | ns | 0.7249 | D-I |
| BSF vs. mega HPG-3 7% | 0.001267 | -0.04030 to 0.04283 | No | ns | >0.9999 | D-J |
| BSF vs. mega HPG-3 23% | 0.000626 | -0.04312 to 0.04437 | No | ns | >0.9999 | D-K |
| PBS vs. mega HPG-1 7% | -0.008133 | -0.04549 to 0.02922 | No | ns | 0.9996 | E-F |
| PBS vs. mega HPG-1 23% | 0.008231 | -0.02912 to 0.04559 | No | ns | 0.9996 | E-G |
| PBS vs. mega HPG-2 7% | -0.008571 | -0.04834 to 0.03120 | No | ns | 0.9997 | E-H |
| PBS vs. mega HPG-2 23% | -0.00781 | -0.04758 to 0.03196 | No | ns | 0.9999 | E-I |
| PBS vs. mega HPG-3 7% | 0.01795 | -0.01940 to 0.05531 | No | ns | 0.8682 | E-J |
| PBS vs. mega HPG-3 23% | 0.01731 | -0.02245 to 0.05708 | No | ns | 0.925 | E-K |
| *mega* HPG-1 7% vs. mega HPG-1 23% | 0.01636 | -0.02677 to 0.05950 | No | ns | 0.969 | F-G |
| mega HPG-1 7% vs. mega HPG-2 7% | -0.000438 | -0.04568 to 0.04480 | No | ns | >0.9999 | F-H |
| mega HPG-1 7% vs. mega HPG-2 23% | 0.000322 | -0.04492 to 0.04556 | No | ns | >0.9999 | F-I |
| mega HPG-1 7% vs. mega HPG-3 7% | 0.02609 | -0.01705 to 0.06922 | No | ns | 0.6271 | F-J |
| mega HPG-1 7% vs. mega HPG-3 23% | 0.02544 | -0.01979 to 0.07068 | No | ns | 0.7197 | F-K |
| mega HPG-1 23% vs. mega HPG-2 7% | -0.0168 | -0.06204 to 0.02844 | No | ns | 0.9732 | G-H |
| mega HPG-1 23% vs. mega HPG-2 23% | -0.01604 | -0.06128 to 0.02920 | No | ns | 0.9807 | G-I |
| mega HPG-1 23% vs. mega HPG-3 7% | 0.009722 | -0.03341 to 0.05285 | No | ns | 0.9995 | G-J |
| mega HPG-1 23% vs. mega HPG-3 23% | 0.009081 | -0.03616 to 0.05432 | No | ns | 0.9998 | G-K |
| mega HPG-2 7% vs. mega HPG-2 23% | 0.000761 | -0.04649 to 0.04801 | No | ns | >0.9999 | H-I |
| mega HPG-2 7% vs. mega HPG-3 7% | 0.02652 | -0.01871 to 0.07176 | No | ns | 0.6683 | H-J |
| mega HPG-2 7% vs. mega HPG-3 23% | 0.02588 | -0.02137 to 0.07313 | No | ns | 0.75 | H-K |
| mega HPG-2 23% vs. mega HPG-3 7% | 0.02576 | -0.01947 to 0.07100 | No | ns | 0.7048 | I-J |
| mega HPG-2 23% vs. mega HPG-3 23% | 0.02512 | -0.02213 to 0.07237 | No | ns | 0.7816 | I-K |
| mega HPG-3 7% vs. mega HPG-3 23% | -0.000642 | -0.04588 to 0.04460 | No | ns | >0.9999 | J-K |

**Supplementary Table 5.** COF for other lubricants

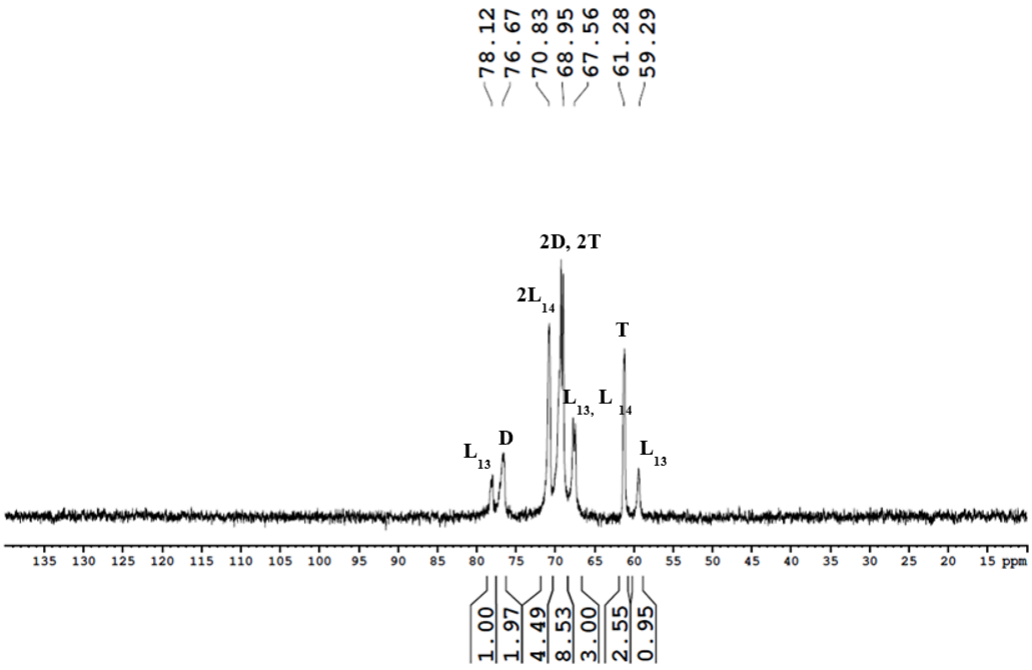
| Lubricant | System specifics | COF | References |
|---|---|---|---|
| Lubricin | Bovine cartilage on glass; 40% compressive strain imposed on each plug to ensure boundary mode, and 60min allowed for hydrostatic pressure to equilibrate | 0.093 | https://doi.org/10.1002/jor.23370 |
| Inflammed SF 24 $^{o}$C | Human cartilage on cartilage; 30N load, 1 mm/s speed | 0.109 (static)/ 0.089 (dynamic) | 10.1007/s11249-006-9069-11 |
| Inflammed SF 37 $^{o}$C | Human cartilage on cartilage; 30N load, 1 mm/s speed | 0.06 (static)/ 0.055 (dynamic) | 10.1007/s11249-006-9069-12 |
| Water | Human cartilage on cartilage; 30N load, 1 mm/s speed | 0.059 (static)/ 0.05 (dynamic) | 10.1007/s11249-006-9069-13 |
| NaCl 15mM | Human cartilage on cartilage; 30N load, 1 mm/s speed | 0.07 (static)/ 0.06 (dynamic) | 10.1007/s11249-006-9069-14 |
| NaCl 150mM | Human cartilage on cartilage; 30N load, 1 mm/s speed | 0.089 (static)/ 0.067 (dynamic) | 10.1007/s11249-006-9069-15 |
| PBS | Early OA human cartilag on cartilage, 6.27 N load, 1 mm/s sliding speed, 900s test duration | 0.134 +/- 0.034 | doi: 10.1016/j.joca.2009.03.020 |
| PBS | Late OA human cartilag on cartilage, 6.27 N load, 1 mm/s sliding speed, 900s test duration | 0.106 +/- 0.053 | doi: 10.1016/j.joca.2009.03.021 |
| Human SF | Early OA human cartilag on cartilage, 6.27 N load, 1 mm/s sliding speed, 900s test duration | 0.04 +/- 0.018 | doi: 10.1016/j.joca.2009.03.022 |
| Human SF | Late OA human cartilag on cartilage, 6.27 N load, 1 mm/s sliding speed, 900s test duration | 0.042 +/- 0.015 | doi: 10.1016/j.joca.2009.03.023 |
| PBS | Early OA human cartilag on glass, 6.27 N load, 1 mm/s sliding speed, 3600s test duration | 0.026 +/- 0.009 | doi: 10.1016/j.joca.2009.03.024 |
| PBS | Late OA human cartilag on glass, 6.27 N load, 1 mm/s sliding speed, 3600s test duration | 0.024 +/- 0.009 | doi: 10.1016/j.joca.2009.03.025 |
| Human SF | Early OA human cartilag on glass, 6.27 N load, 1 mm/s sliding speed, 3600s test duration | 0.02 +/- 0.07 | doi: 10.1016/j.joca.2009.03.026 |

| | | | |
|---|---|---|---|
| Human SF | Late OA human cartilag on glass, 6.27 N load, 1 mm/s sliding speed, 3600s test duration | 0.19 +/- 0.001 | doi: 10.1016/j.joca.2009.03.027 |
| Poly-oxanorbornane carboxylate | Bovine cartilage on cartilage; torsional friction for 10,080 rotations at 22 mm/s, 0.78 MPa compressive strain | 0.015 ± 0.01 | https://doi.org/10.1016/j.biomaterials.2018.08.009 |
| Poly-oxanorbornane carboxylate containing pendent triethylene glycol chains | Bovine cartilage on cartilage; torsional friction for 10,080 rotations at 22 mm/s, 0.78 MPa compressive strain | 0.0316 ± 0.0005 | https://doi.org/10.1021/acsbiomaterials.9b00085 |
| High-molecular-weight lubricious polymer with poly(2-methyl-2-oxazoline) side chains | Immature bovine cartilage mounted on a ball-on-disc microtribometer; 5 mm/s speed; 0.5, 0.7 and 0.9 MPa pressure for 10 minutes each | 0.02 - 0.1 | DOI: 10.1002/anie.201712534 |
| Lubricin mimetic - chondroitin sulfate backbone with type II collagen and HA binding peptides | Trypsin treated cartilage on glass with lubricin mimetic AND purified, commercially availabl HA; 0.0873 rad/sec sliding speed; 2 min test duration | 0.1 - 0.3 | DOI: 10.1016/j.biomaterials.2015.09.012 |
| pAA:PEG lubricant library with varying backbone lengths and ratios of the two polymers | Bovine cartilage on XX; 40% compressive strain impossed on each plug to ensure boundary mode, and 60min allowed for hydrostatic pressure to equilibrate | 0.14 - 0.248 | https://doi.org/10.1002/jor.23370 |
| sodium poly(7-oxanorbornene-2-carboxylate) | Cartilage on cartilage equilibrated for 60 min and then subjected to a relative rotation of +2 revolutions (720°) at 5 deg/s (an effective velocity of 0.3 mm/ s) | 0.06+-0.02 | https://pubs.acs.org/doi/abs/10.1021/ja400695h |

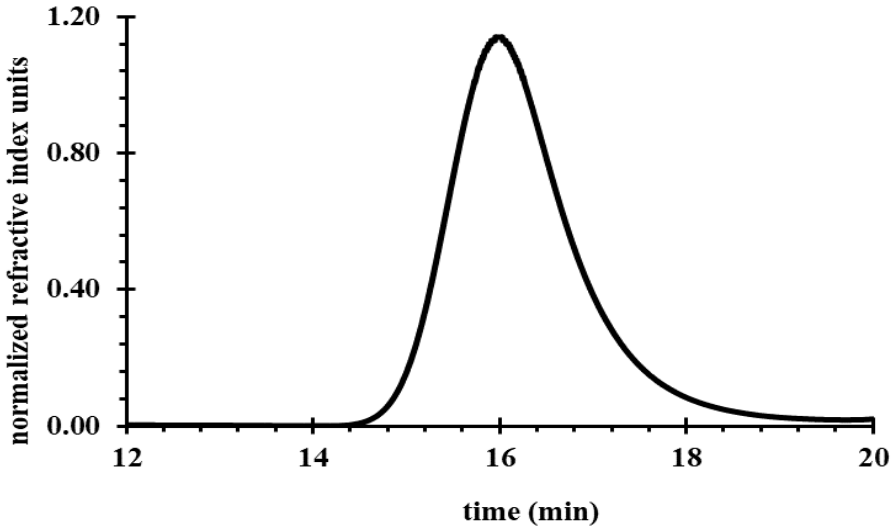
**Supplementary Figures:**



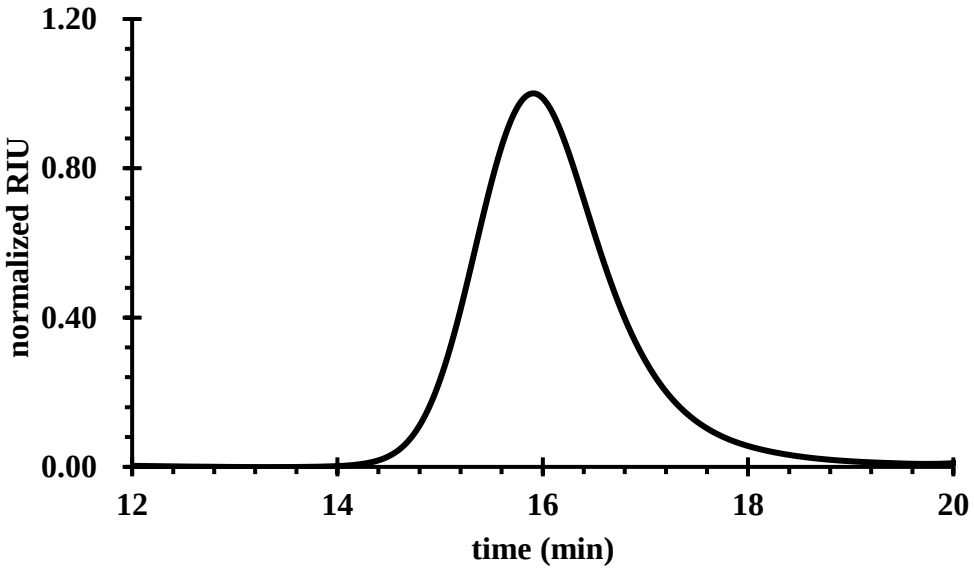

**Supplementary Figure 1.** $^{1}$H NMR spectrum ($D_2O$, 400 MHz) of the HPG macroinitiator.



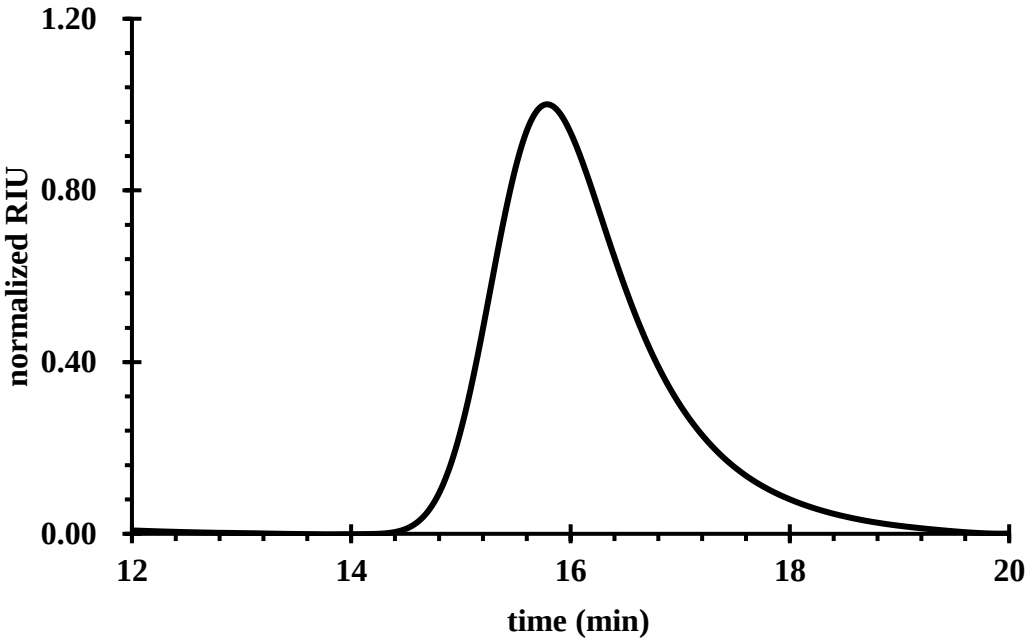

**Supplementary Figure 2.** $^{13}$C NMR spectrum ($D_2O$, 100 MHz) of the HPG macroinitiator.



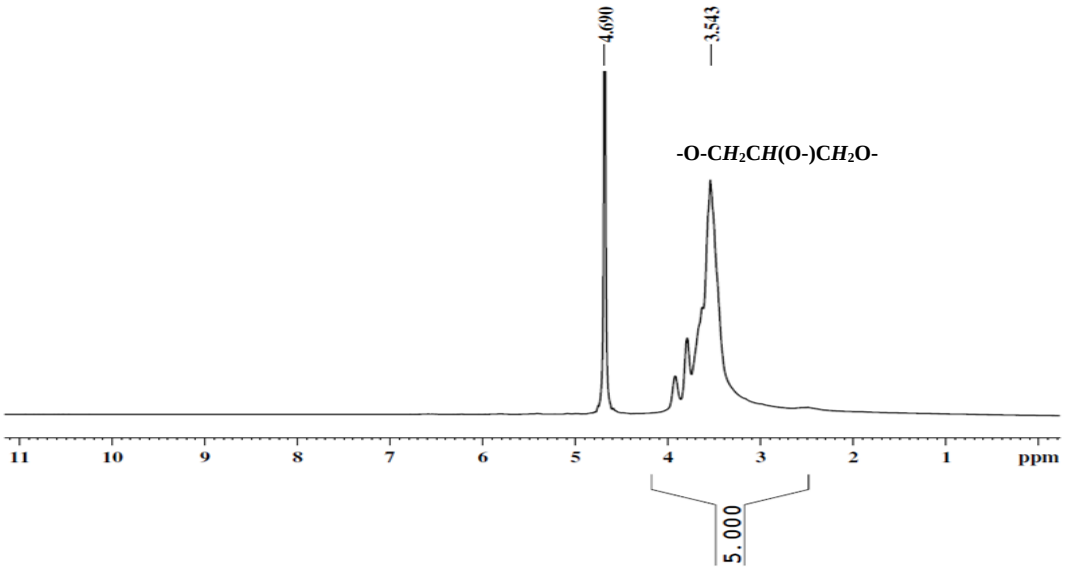

**Supplementary Figure 3**. GPC-MALS chromatogram (0.1 M $NaNO_3$ buffer, pH 7.4) of the HPG macroinitiator.



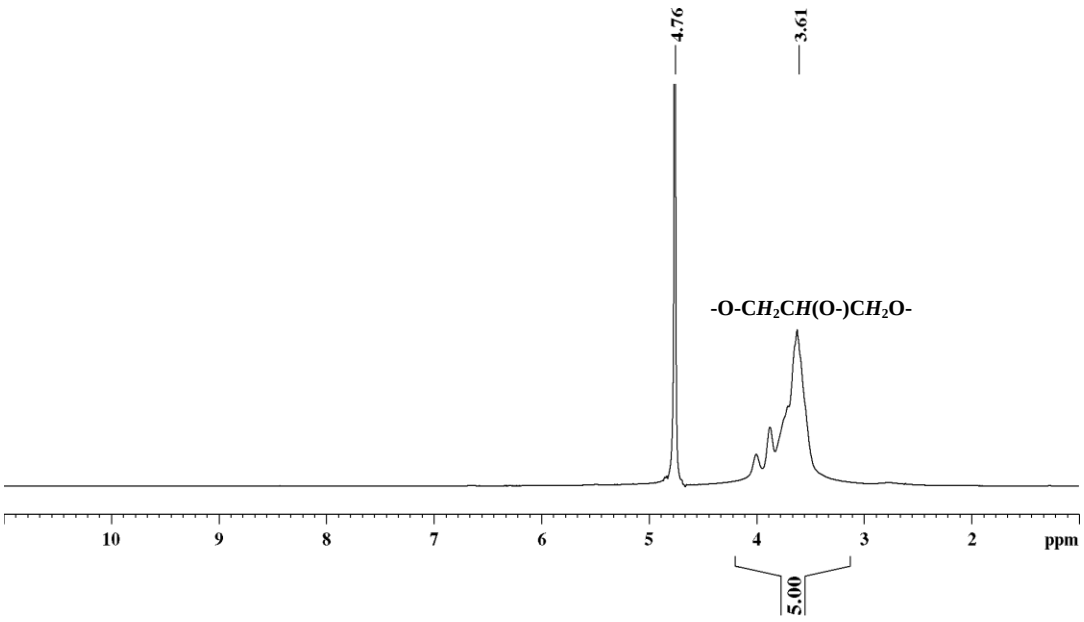

**Supplementary Figure 4**. GPC-MALS chromatogram (0.1 M $NaNO_3$ buffer, pH 7.4) of the mega HPG-1 ($M_w$-1.3 MDa).



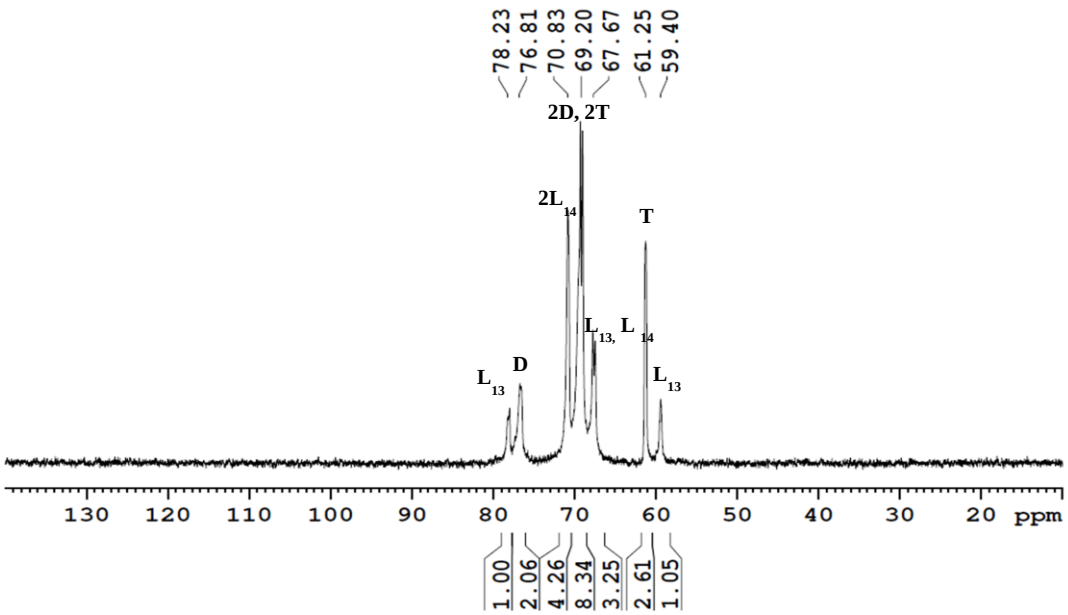

**Supplementary Figure 5.** GPC-MALS chromatogram (0.1 M $NaNO_3$ buffer, pH 7.4) of the mega HPG-2 ($M_w$-2.9 MDa).



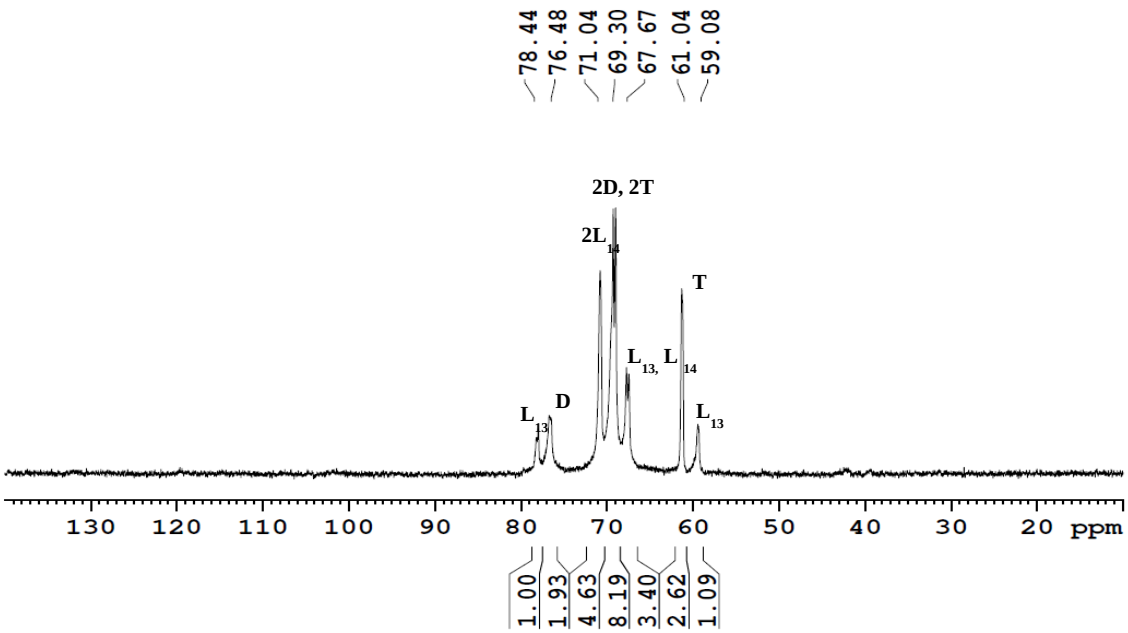

**Supplementary Figure 6.** $^1H$ NMR spectrum ($D_2O$, 400 MHz) of the mega HPG-1 ($M_w$-1.3 MDa).



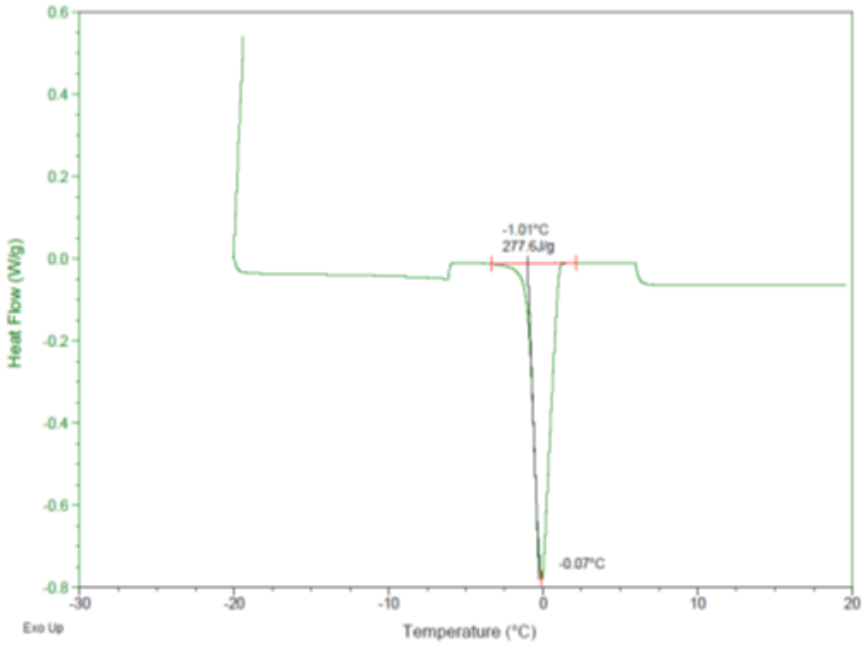

**Supplementary Figure 7**. $^{1}$H NMR spectrum ($D_2O$, 400 MHz) of the mega HPG-2 ($M_w$-2.9 MDa).



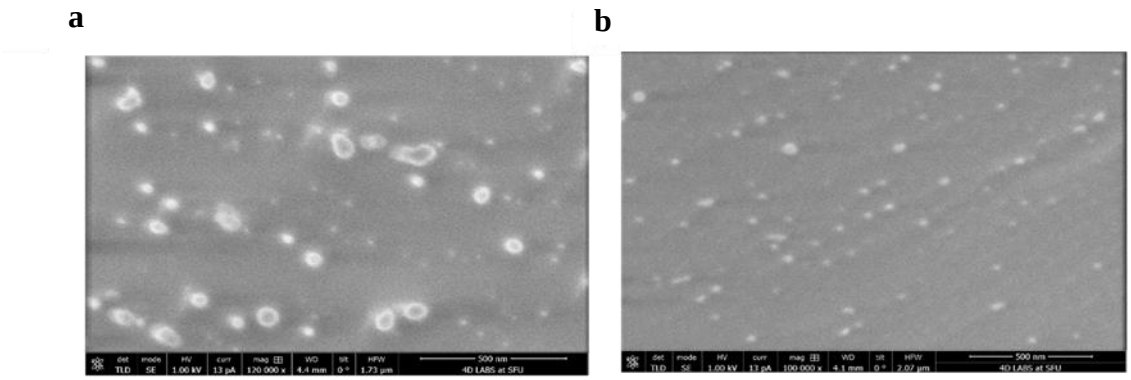

**Supplementary Figure 8**. $^{13}$C NMR spectrum ($D_2O$, 100 MHz) of the mega HPG-1 ($M_w$-1.3 MDa).



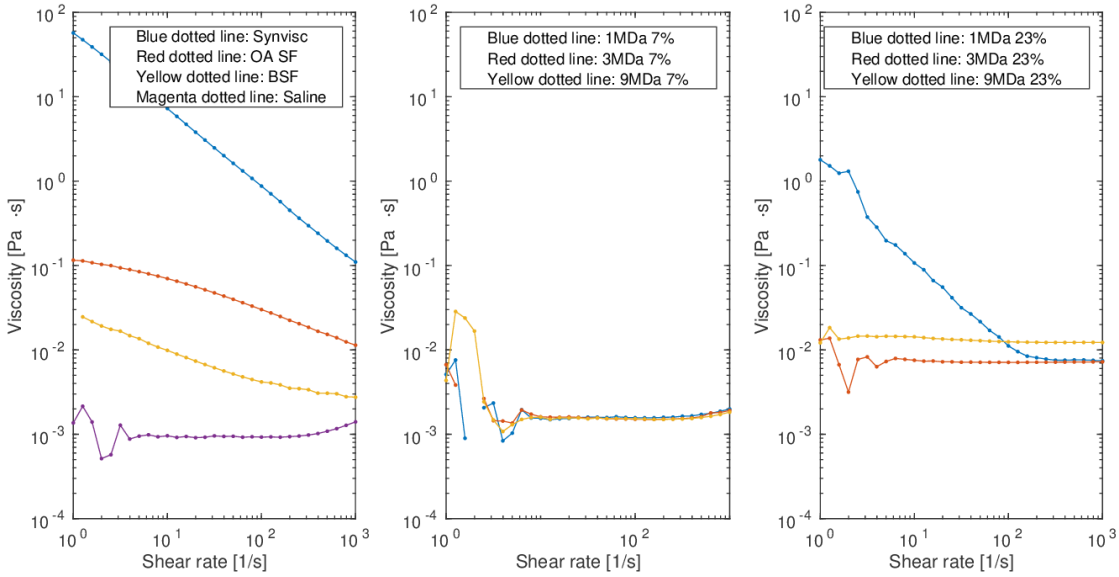

**Supplementary Figure 9**. $^{13}C$ NMR spectrum ($D_2O$, 100 MHz) of the mega HPG-2 ($M_w$-2.9 MDa).



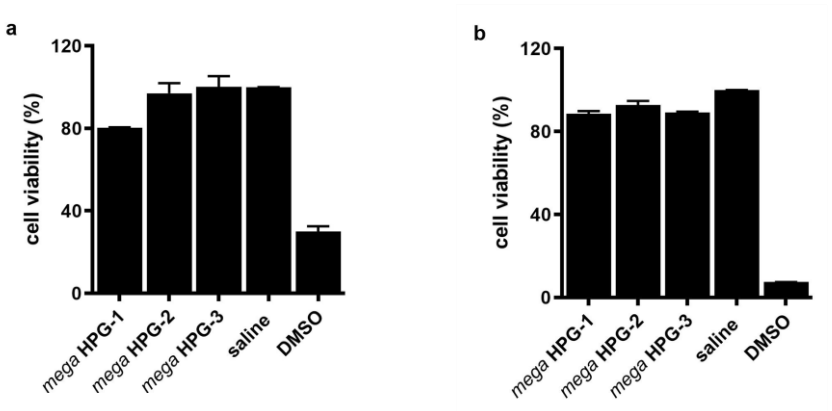

**Supplementary Figure 10.** Differential scanning calorimetry (DSC) thermogram of the mega HPG-3.



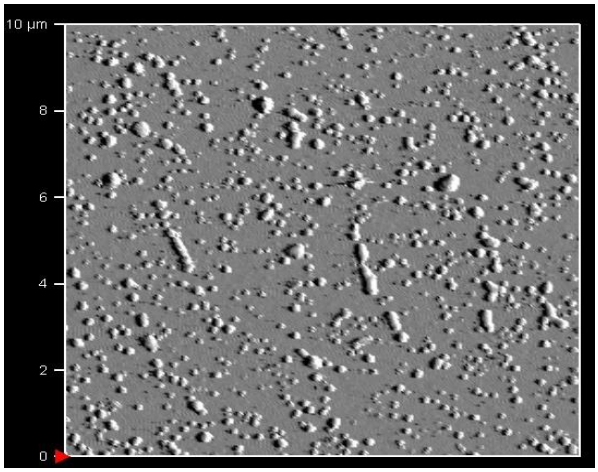

**Supplementary Figure 11**. Cryo SEM images of mega HPG-1 (**a**) and mega HPG-2 (**b**)




**Supplementary Figure 12**. The viscosity-shear rate behavior of mega HPGs at two different concentrations (7 and 23 wt%) and compared with Synvisc One (Synvisc), osteoarthritic synovial fluid (OA SF), bovine synovial fluid (BSF), and saline.




**Supplementary Figure 13.** Cell viability of mega HPGs-1, 2, and 3 (1.25 mg/ml) towards Tc28a2 juvenile human chondrocytes (**a**) and 3T3 murine fibroblast cells (**b**). Cells were incubated with either mega HPGs, saline, or DMSO for 48 h at 37 °C. After washings, the metabolic activity of the cells was assessed by MTT assay. Six replicates were performed and each study was repeated in quadruplicates. Average values and standard deviation are reported. Cell viability of mega HPGs (≥80%) irrespective of the cell line confirmed the high cell compatibility of the mega HPGs.




**Supplementary Figure 14.** AFM image of mega HPG-3 chemically adhered to the surface of an epoxide functionalized glass slide in 2D.