Polyurethane-based thiomers: A new multifunctional copolymer platform for biomedical applications

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Attenuated Total Reflectance Fourier Transform Infrared (ATR-FTIR) spectroscopy

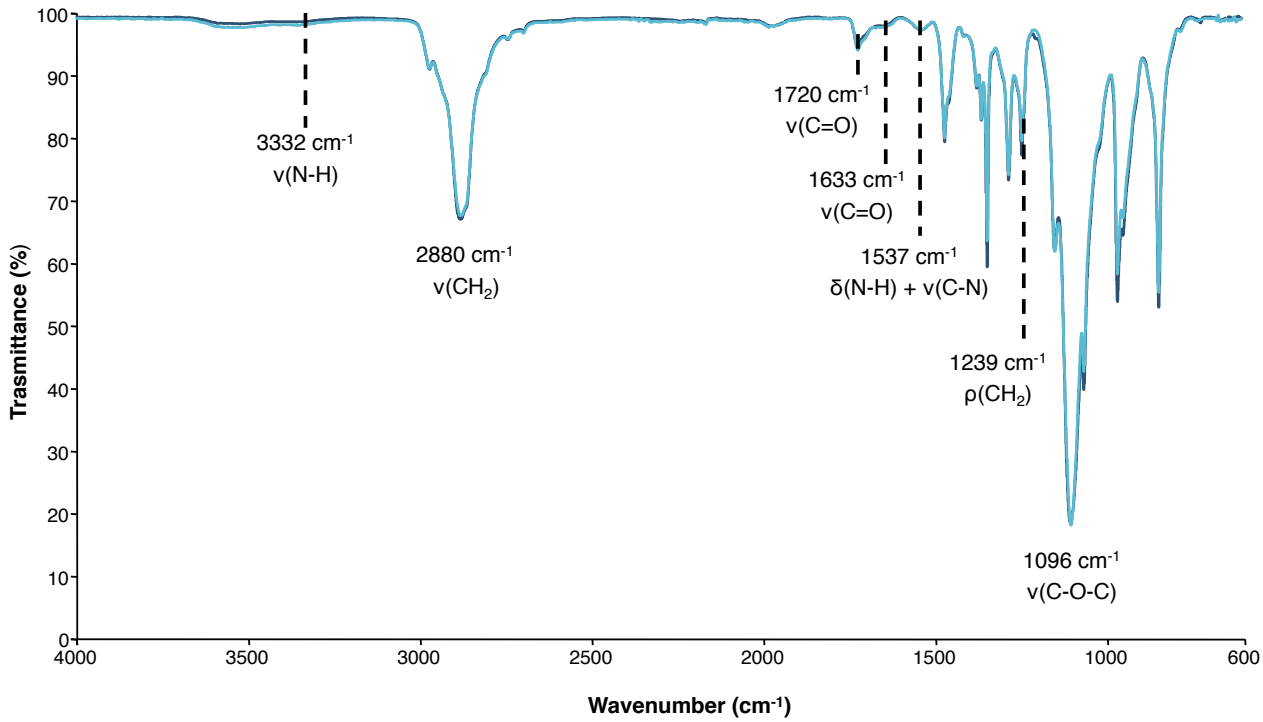


Fig. S1. ATR-FTIR spectra of DHP407 (light blue) and D-DHP407 (dark blue).

Size Exclusion chromatography

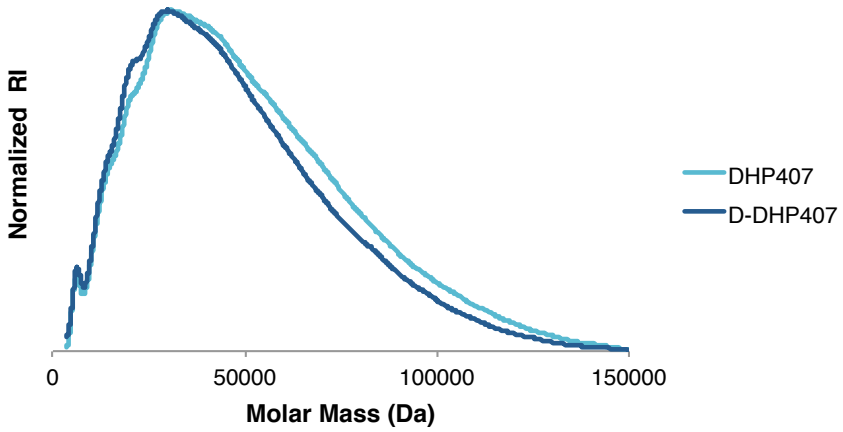


Fig. S2. Molecular weight distribution profiles (normalized Refractive Index (RI) *vs* molar mass) of the synthesised polyurethane before (DHP407 – light blue) and after (D-DHP407 – dark blue) acid treatment to remove Boc protecting groups.

Orange II Sodium Salt colorimetric assay

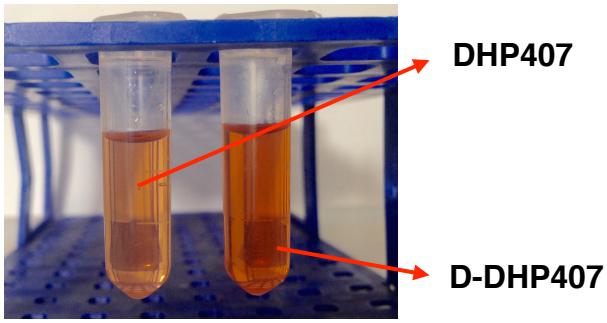


Fig. S3. Orange II Sodium Salt colorimetric assay performed on DHP407 (light orange – Orange molecules absorbed) and on D-DHP407 (dark orange – Orange molecules absorbed and grafted to –NH groups) samples.

Dynamic Light Scattering measurements

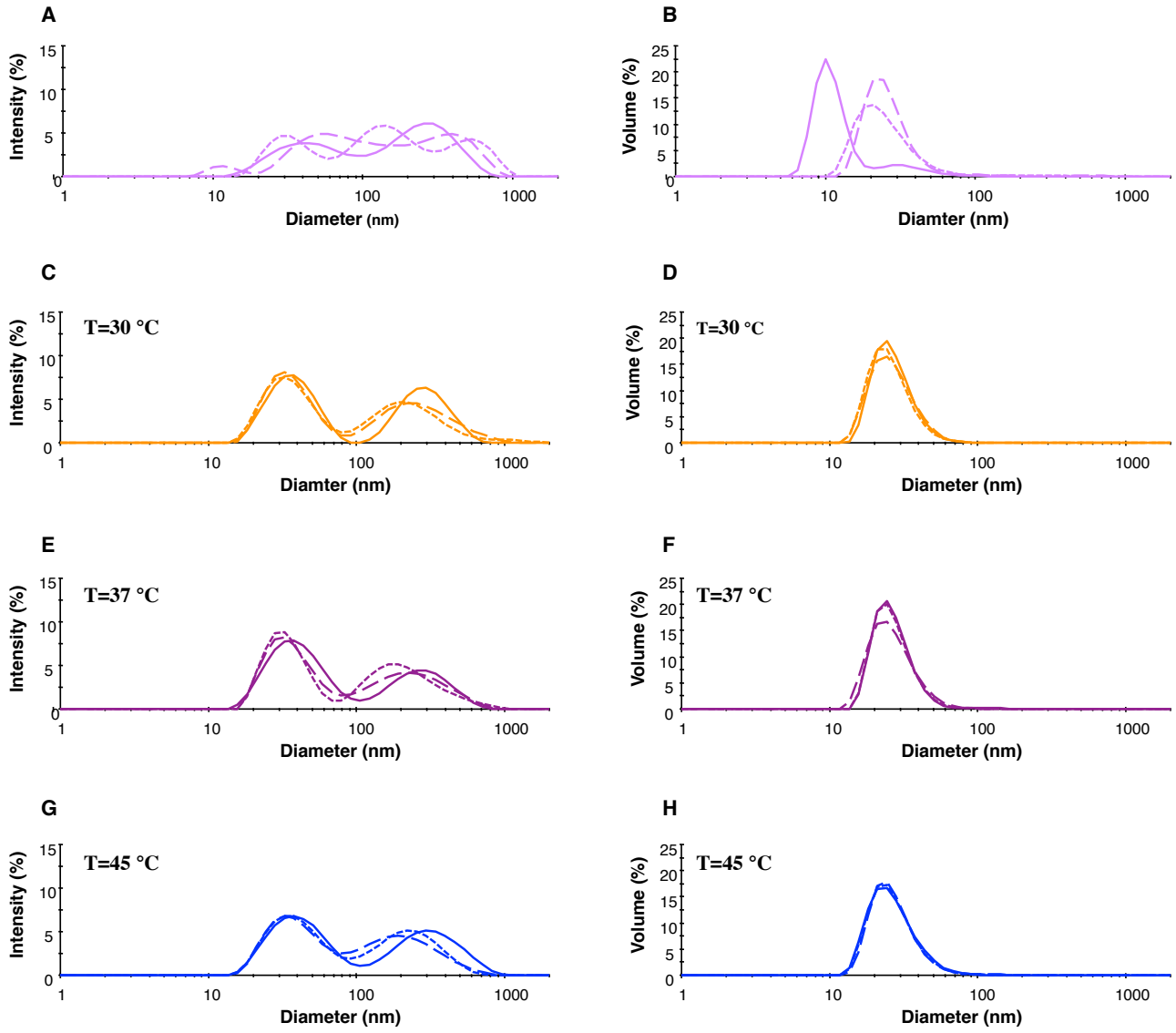


Fig. S4. Distribution by intensity (A, C, E, G) and by volume (B, D, F and H) of the hydrodynamic diameter of the polymeric micelles and aggregates in D-DHP407 solutions with 1% *w/V* concentration measured at different temperatures (25 °C – 30 °C – 37 °C and 45 °C). Continuous, dash and dot lines represent measurements conducted on three different samples prepared in the same conditions.

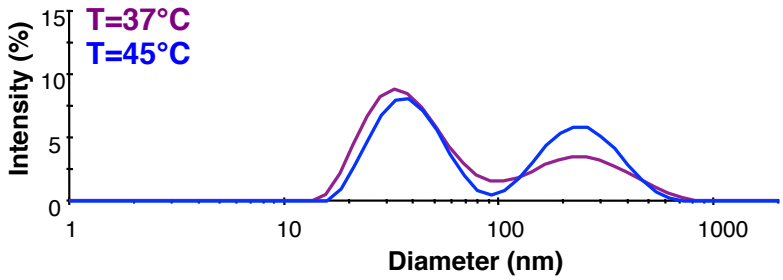


Fig. S5. Hydrodynamic average diameter profiles (intensity patterns) of D-DHP407 at 0.5% *w/V* concentration measured at 37 °C (purple) and 45 °C (blue).

Attenuated Total Reflectance Fourier Transform Infrared (ATR_FTIR) spectroscopy

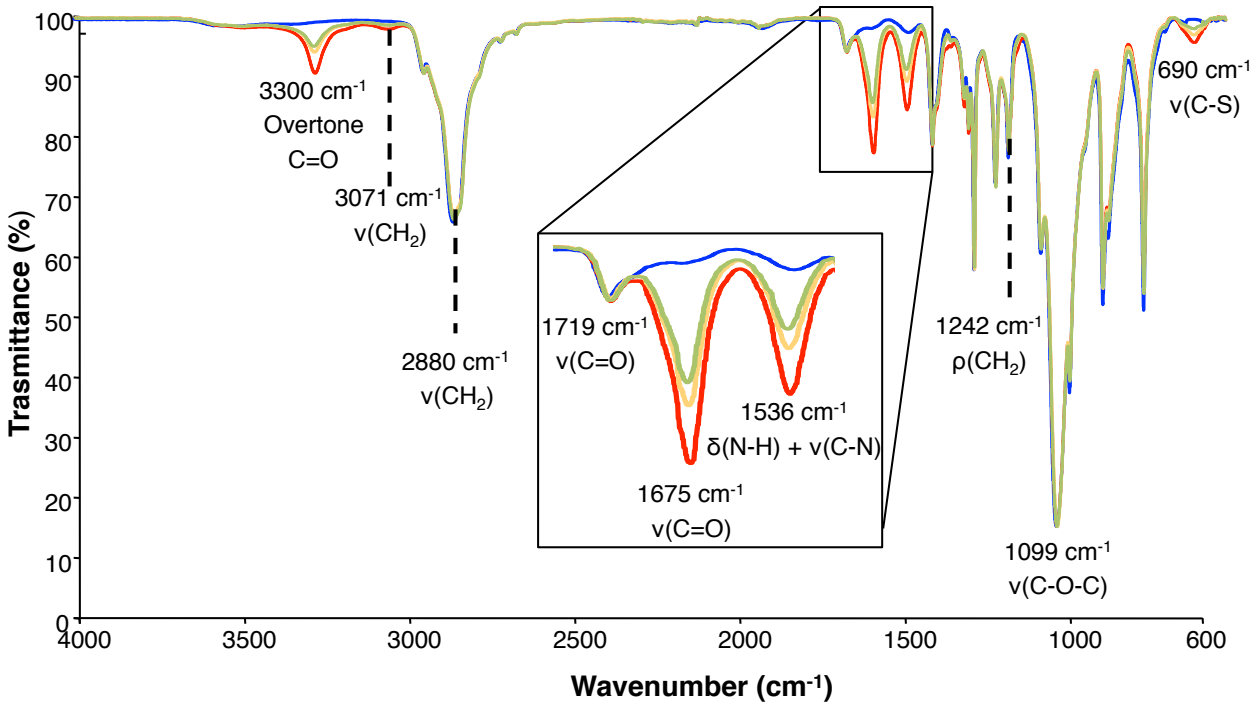
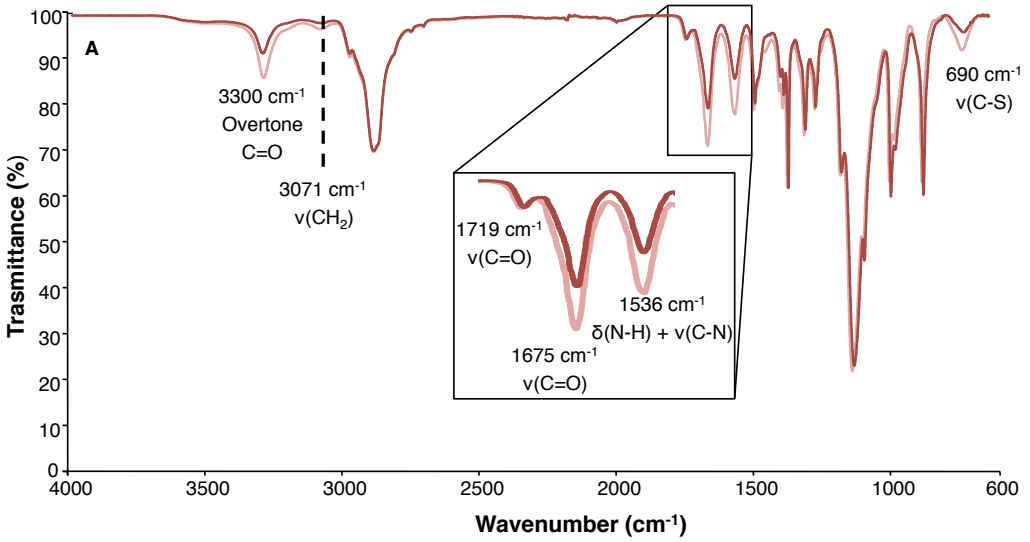
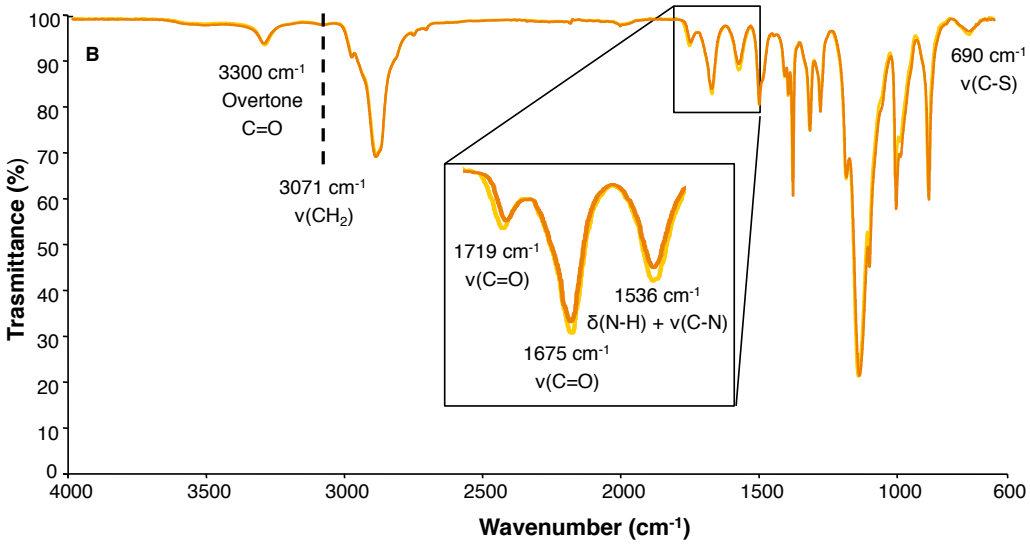


Fig. S6. Averaged ATR-FTIR spectra of D-DHP407 (blue) and S-DHP407 after TGA grafting at pH 4 (red), 5 (yellow) and 7 (green) and 24 h reaction time. Differences between spectra are reported as magnifications.


A
3300 cm-1
Overtone
C=O
3071 cm-1
v(CH2)
1719 cm-1
v(C=O)
1536 cm-1
δ(N-H) + v(C-N)
1675 cm-1
v(C=O)
690 cm-1
v(C-S)
Trasmittance (%)
Wavenumber (cm-1)


B
3300 cm-1
Overtone
C=O
3071 cm-1
v(CH2)
1719 cm-1
v(C=O)
1536 cm-1
δ(N-H) + v(C-N)
1675 cm-1
v(C=O)
690 cm-1
v(C-S)
Trasmittance (%)
Wavenumber (cm-1)

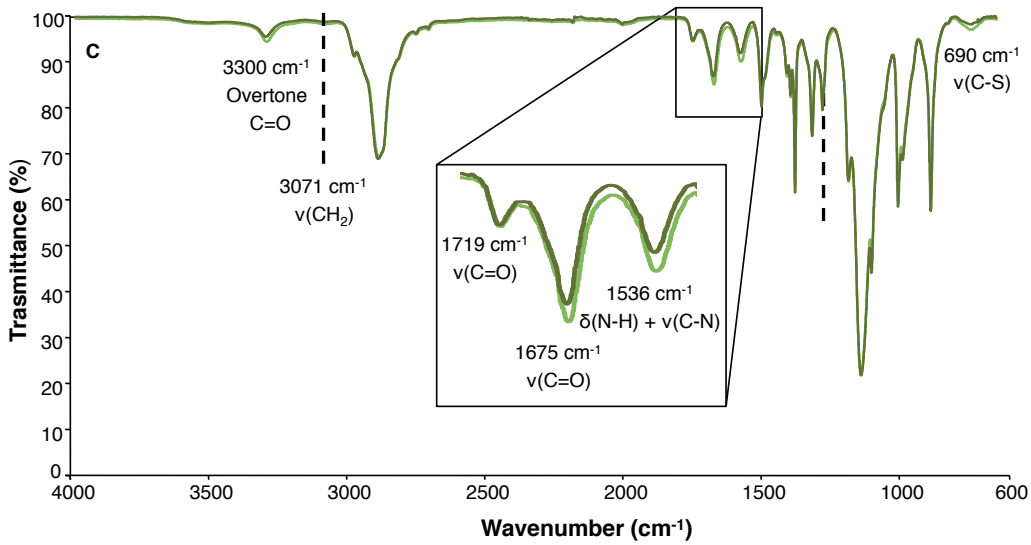

C
3300 cm-1
Overtone
C=O
3071 cm-1
v(CH2)
1719 cm-1
v(C=O)
1536 cm-1
δ(N-H) + v(C-N)
1675 cm-1
v(C=O)
690 cm-1
v(C-S)
Trasmittance (%)
Wavenumber (cm-1)

Fig. S7. Averaged ATR-FTIR spectra of S-DHP407 samples obtained by adjusting the grafting reaction pH at 4 (A), 5 (B) and 7 (C) for 6 h (light line) and 24 h (dark line). Main differences between spectra are reported as magnifications.

Dynamic Light Scattering measurements on S-DHP407_pH4_6h

To investigate whether TGA grafting could influence polyurethane thermo-sensitivity, DLS measurements were also performed on thiomer-based solution at 0.5% *w/V* concentration at 25 °C, 37 °C and 45 °C, according to the protocol adopted for D-DHP407 characterisation (Fig. S8). Specifically, the polymer exposing the highest amount of thiol groups/g of polymer (i.e., S-DHP407_pH4_6h) was considered for this analysis.

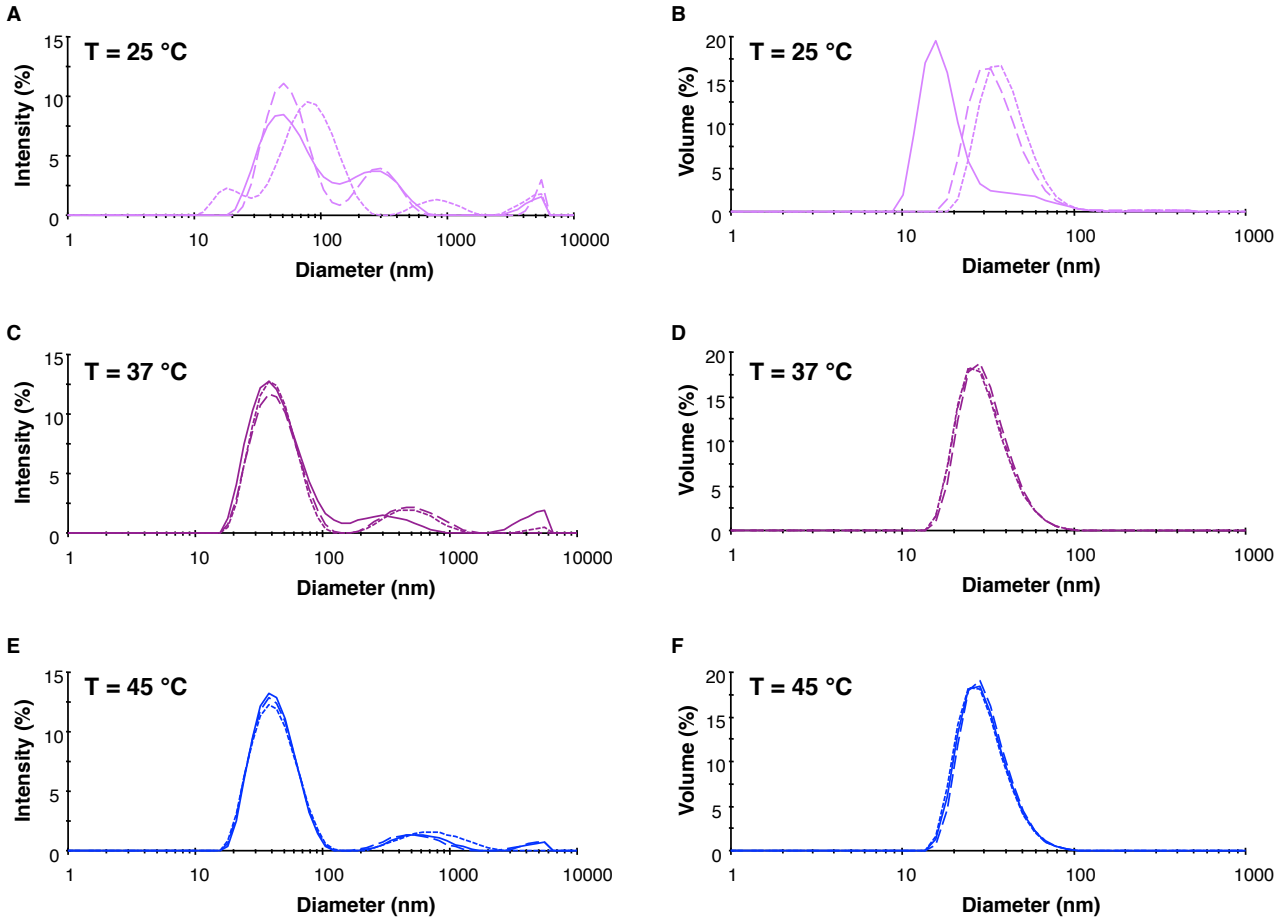


Fig. S8. Distribution by intensity (A, C, E) and by volume (B, D, F) of the hydrodynamic diameter of the polymeric micelles and aggregates in S-DHP407_pH4_6h solutions with 0.5% *w/V* concentration measured at different temperatures (25 °C –37 °C and 45 °C). Continuous, dash and dot lines represent measurements conducted on three different samples prepared in the same conditions.

According to data reported for D-DHP407 samples at 25 °C (Fig. 4), no clear chain organisation was detected also for thiomer-based solutions at the lowest tested temperature (Fig. S8_A and B), due to the high system instability. Upon temperature increase up to 37 °C (Fig. S8_C) a well-defined double peak appeared, ascribed to single micelles (46.24±1.9 nm) and aggregates (451.38±25.08 nm), respectively. This bimodal chain organisation was further confirmed at 45 °C (Fig. S8_E) with micelles and aggregates showing a mean hydrodynamic diameter of 46.01±0.9 nm and 622.91±54.89 nm, respectively, thus proving that micelle nucleation proceeded upon temperature increase. Hence, TGA grafting did not affect polymer thermo-responsiveness. On the contrary, both S-DHP407-based micelles and clusters showed higher hydrodynamic diameters compared to D-DHP407-based ones, suggesting that the exposure of thiol groups induced the formation of a thicker hydrated shell around them which accounts for the observed increased in their dimension. However, only one peak at about 30 nm was identified from the volume patterns (Fig. S8_D and F), according to D-DHP407 results. Thus, also for thiomer-based solutions the amount of aggregates present in the sample was negligible (< 1% at each analysed temperature).