Electronic Supplementary Information (ESI)

Environmentally sensitive nanohydrogels decorated with three-strand oligonucleotide helix for controlled loading and prolonged release of intercalators

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Formulas used in Electrochemical Impedance Spectroscopy (EIS) analysis

The impedance of the CPE parameter in the Ershler – Randles model applied in fitting calculated data to experimental EIS points is described by Eq.(1):

$$Z_{CPE} = T^{-1}(j\omega)^{-\phi} \qquad (1)$$

where, ω is angular frequency, j = $(-1)^{1/2}$, *T* is capacitive coefficient, and ϕ is the exponent value.

The average double layer capacitance, C_{dl} is combined with the capacitive coefficient *T* and can be calculated according to Eq. (2):

$$T = C_{dl}^{\phi}(R_s^{-1}R_{CT}^{-1})^{1-\phi} \qquad (2)$$

where R_s and R_{CT} are the values of solution resistance and the resistance of the charge transfer.

As the semi-infinitive diffusion of 1-electron simple redox species ($[Fe(CN)_6]^{3-/4-}$) takes place, the mass transfer resistance (Warburg impedance, W), visible in EIS plots as a linear part (see Fig.5 of ms.), can be estimated from Eq.(3):

$$W = \sigma\omega^{1/2}(1 - j) \tag{3}$$

where the Wartburg parameter, σ, is described as (Eq.(4)):

$$\sigma = \frac{RT}{n^2F^2\sqrt{2}}[\frac{1}{\sqrt{D_o}}\frac{1}{C_o} + \frac{1}{\sqrt{D_R}}\frac{1}{C_R}] \tag{4}$$

and D_o and C_o are diffusion coefficient and concentration of oxidized form, respectively, and D_R and C_R are diffusion coefficient and concentration of the reduced form of the redox species.

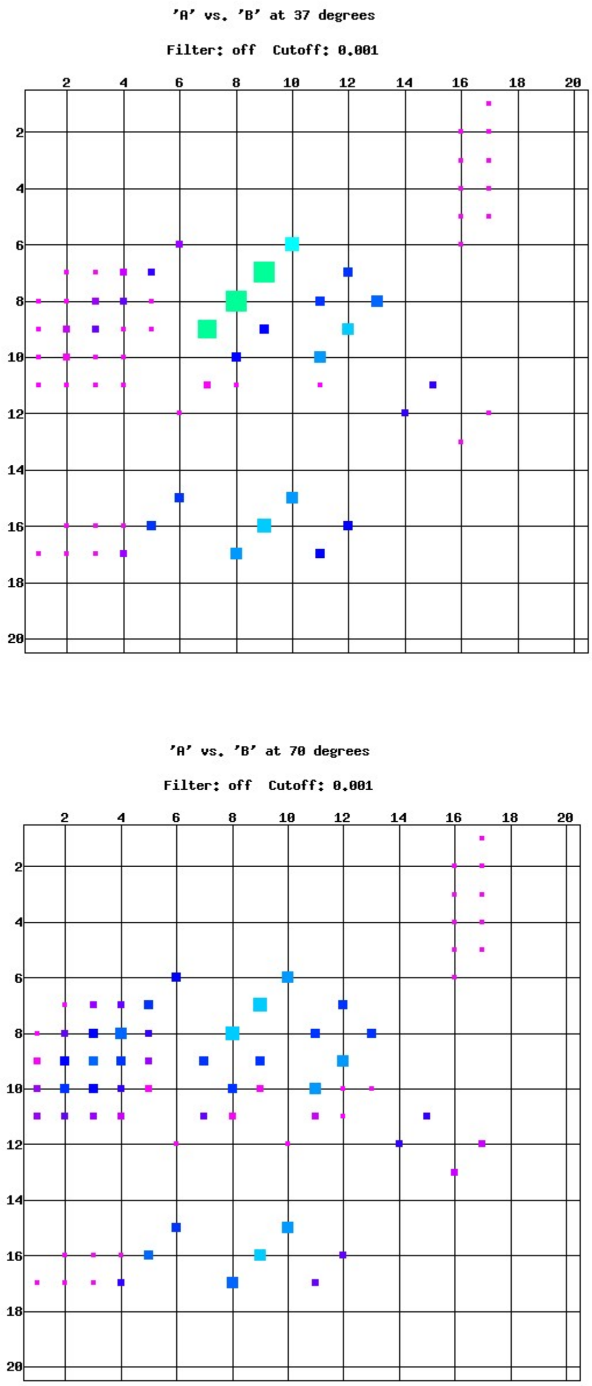
The electron transfer-rate constant, k_0, can be determined using Eq. (5):

$$k_0 = (\frac{\sigma}{R_{CT}})/\frac{2\xi^{\alpha}}{2D_{ox}} \tag{5}$$

where k_o is electron-transfer rate constant, $\xi = (\sqrt{D_{Ox}/D_{Red}})$ (for 1-electron, fast and reversible electrode process of $[Fe(CN)_6]^{3-/4-} \approx 1$), α is transfer coefficient and is assumed to be equal to 0.5, D_{ox} is the diffusion coefficient of $[Fe(CN)_6]^{3-/4-}$ that was taken from [1] as 0.896 x 10^{-5} cm^2s^{-1} and corrected to the value of 0.726 x 10^{-5} cm^2s^{-1}, as the diffusion coefficient of $[Fe(CN)_6]^{3-/4-}$ has 19% lower values in the PNIPA gel environment compared to aqueous conditions [2].

1. Figures

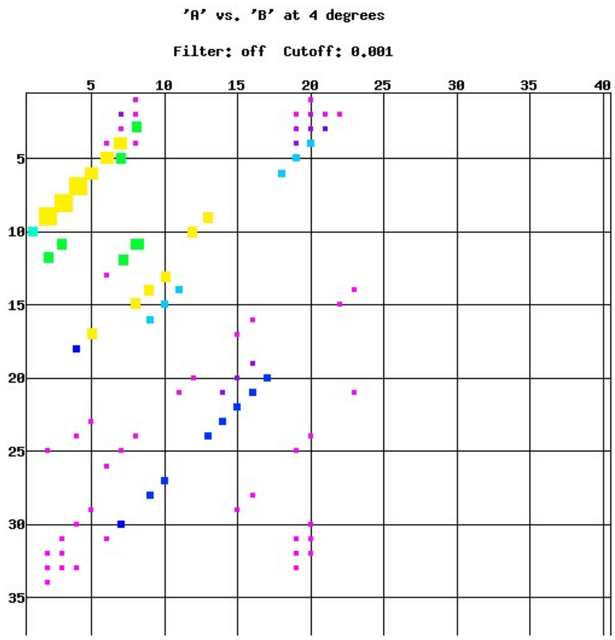
- **Oligo 1 5’ Acryd-GGGGG-GCTCTTGGAACT 3’**
- **Oligo 2 5’ Acryd GGGGG-TGAGTAGACACT 3’**



Range	Color
0.000 ≤ P ≤ 0.010	#FF00FF
0.010 < P < 0.012	#CC00FF
0.012 ≤ P < 0.017	#9900FF
0.017 ≤ P < 0.023	#6600FF
0.023 ≤ P < 0.033	#3300FF
0.033 ≤ P < 0.046	#0000FF
0.046 ≤ P < 0.065	#0033FF
0.065 ≤ P < 0.091	#0066FF
0.091 ≤ P < 0.128	#0099FF
0.128 ≤ P < 0.180	#00CCFF
0.180 ≤ P < 0.253	#00FFFF
0.253 ≤ P < 0.356	#00FFCC
0.356 ≤ P < 0.5	#00FF99
0.500 ≤ P < 0.644	#00FF66
0.644 ≤ P < 0.747	#00FF33
0.747 ≤ P < 0.820	#00FF00
0.820 ≤ P < 0.872	#33FF00
0.872 ≤ P < 0.909	#66FF00
0.909 ≤ P < 0.935	#99FF00
0.935 ≤ P < 0.954	#CCFF00
0.954 ≤ P < 0.967	#FFFF00
0.967 ≤ P < 0.977	#FFCC00
0.977 ≤ P < 0.983	#FF9900
0.983 ≤ P < 0.988	#FF6600
0.988 ≤ P < 0.990	#FF3300
0.990 ≤ P ≤ 1.000	#FF0000

Fig. 1S Simulation of the ability of oligo1 and oligo2 strands for additional selfhybridization.

- **Oligo 1-2** 5’ Acryd GGGGG-TGAGTAGACACTGCTCTTGGAACT-GGGGG Acryd-3’
- **Oligo 3** 3’ ACTCATCTGTGACGAGAACCTTGA 5’



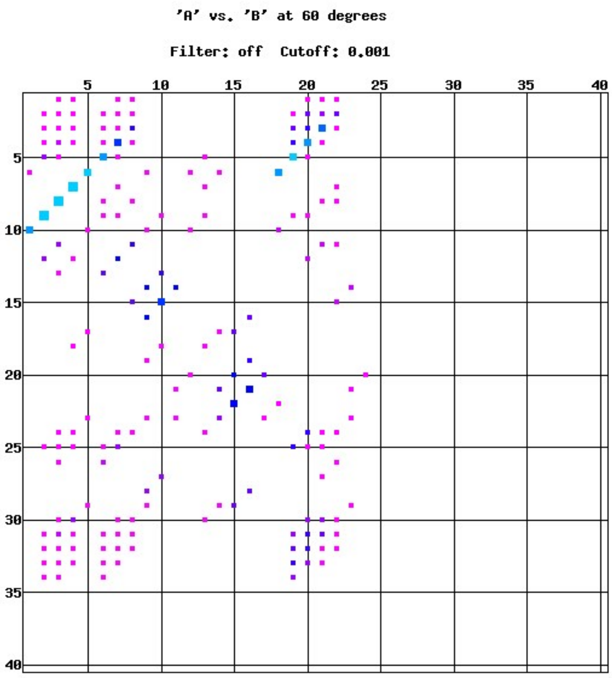


Fig. 2S Simulation of the ability of oligo1-2 and oligo3 strands for selfhybridization.

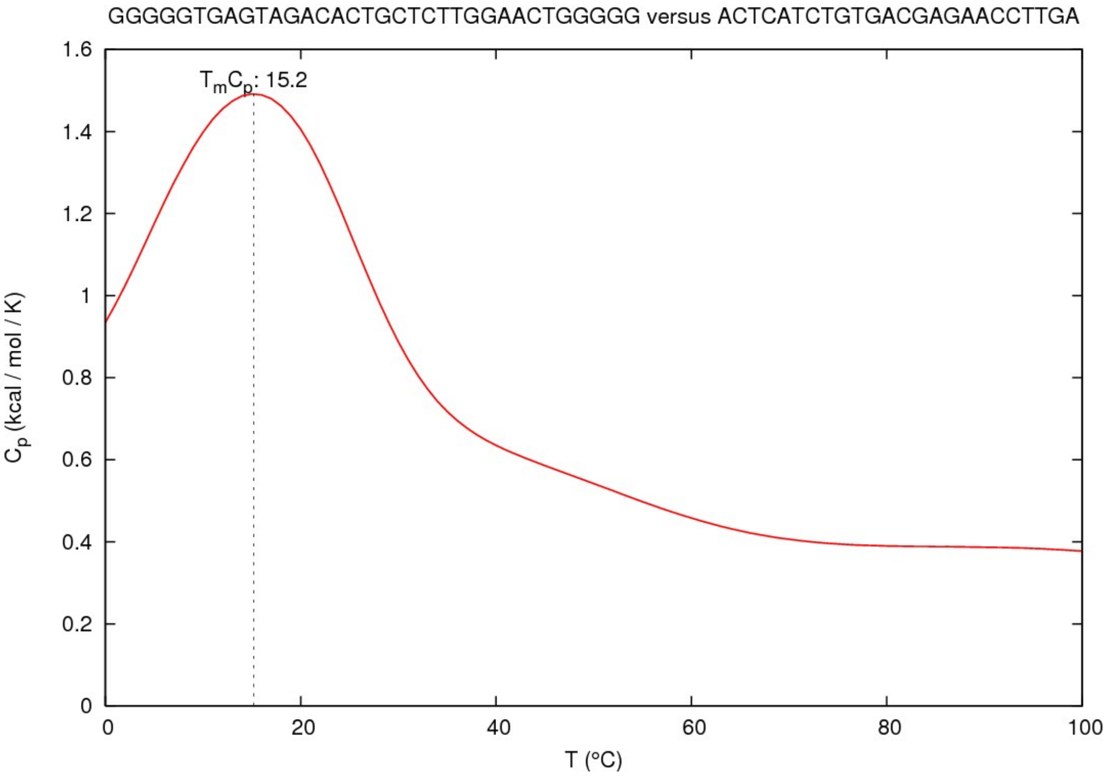
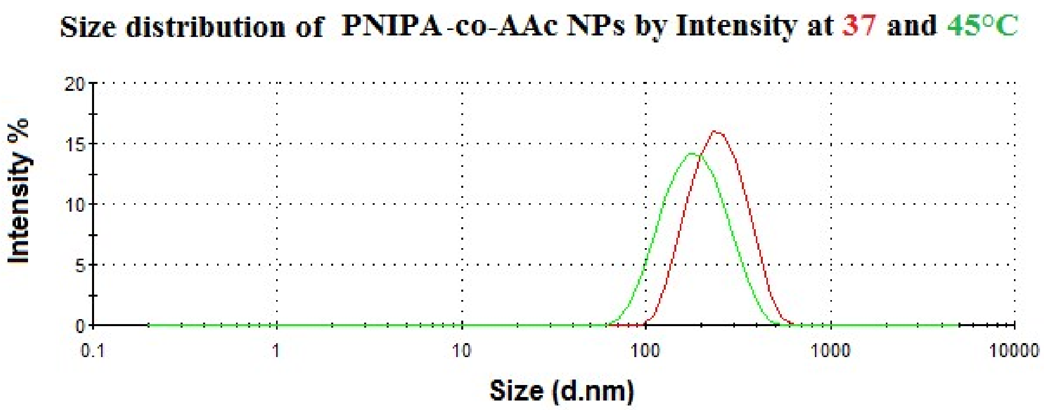
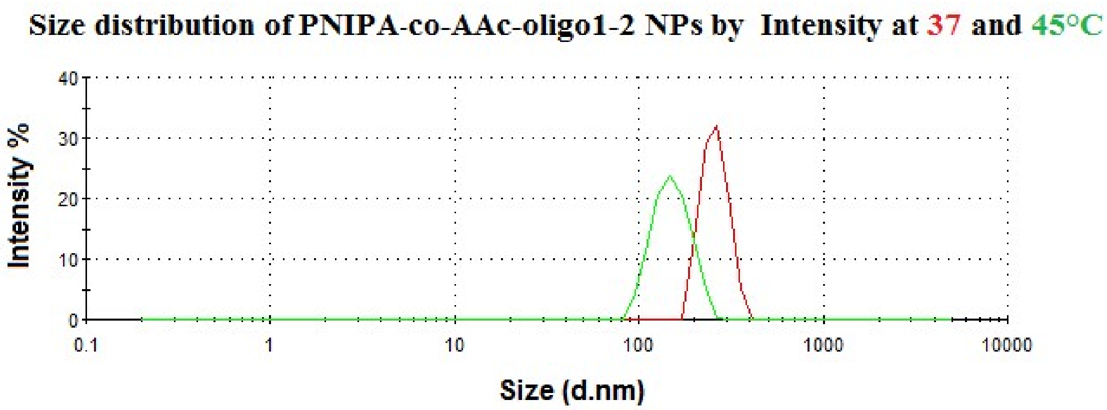


Fig. 3S Simulation of the T_m and C_p of oligo1-2-3 tri-segment hybrid.

A)



B)



C)

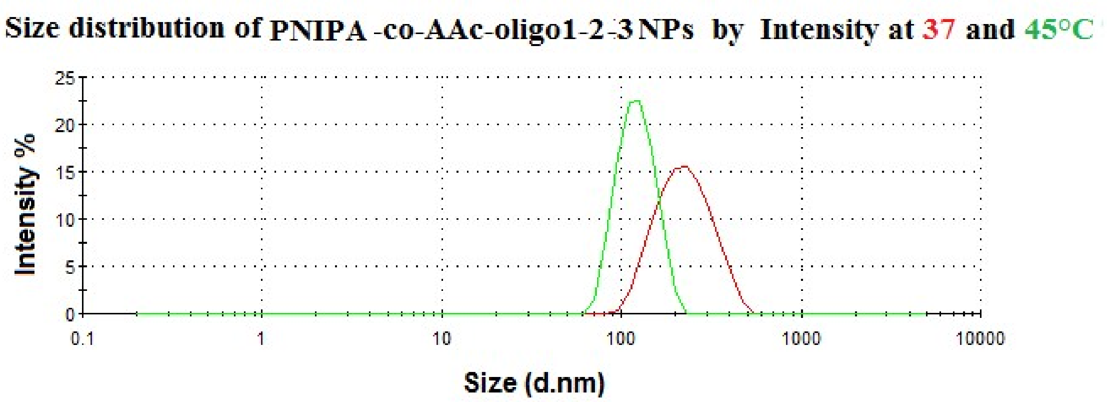
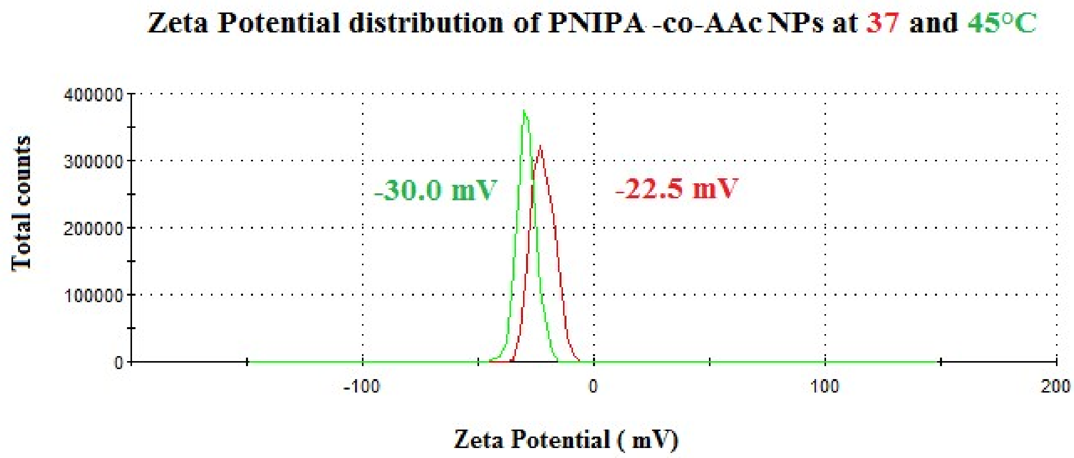
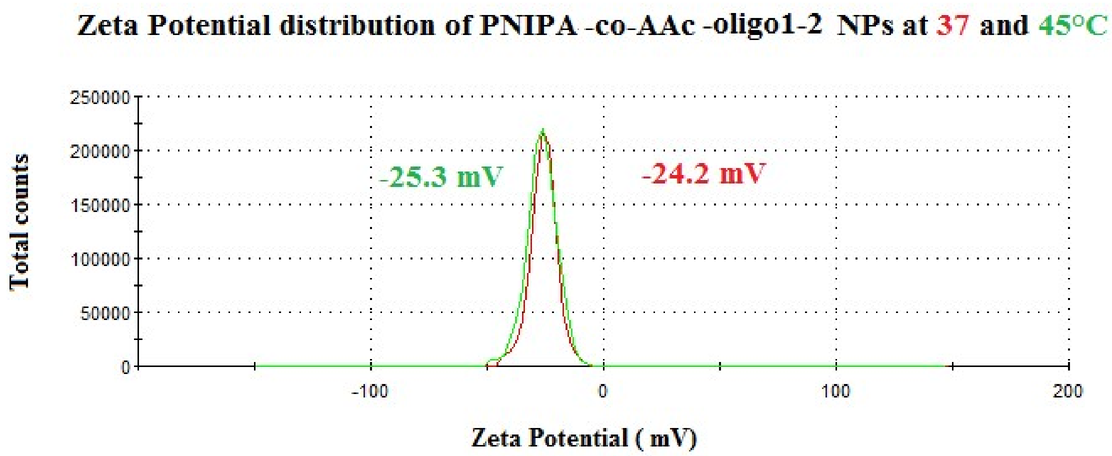


Fig. 4S Sizes of PNIPA-co-AAc- (A), PNIPA-co-AAc-oligo1-2- (B) and PNIPA-AAc-oligo1-2-3 nanogels (C) obtained by DLS at 37 and 45 °C, respectively.

A)



B)



C)

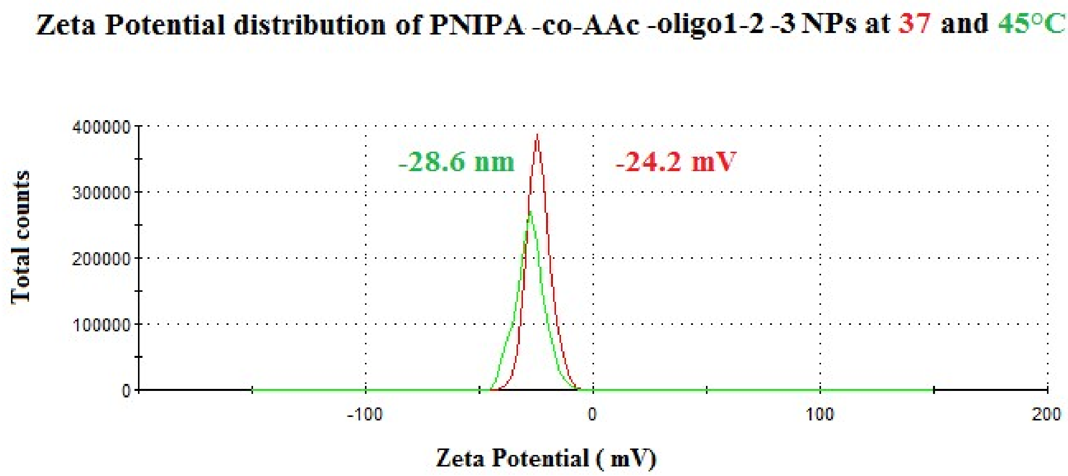
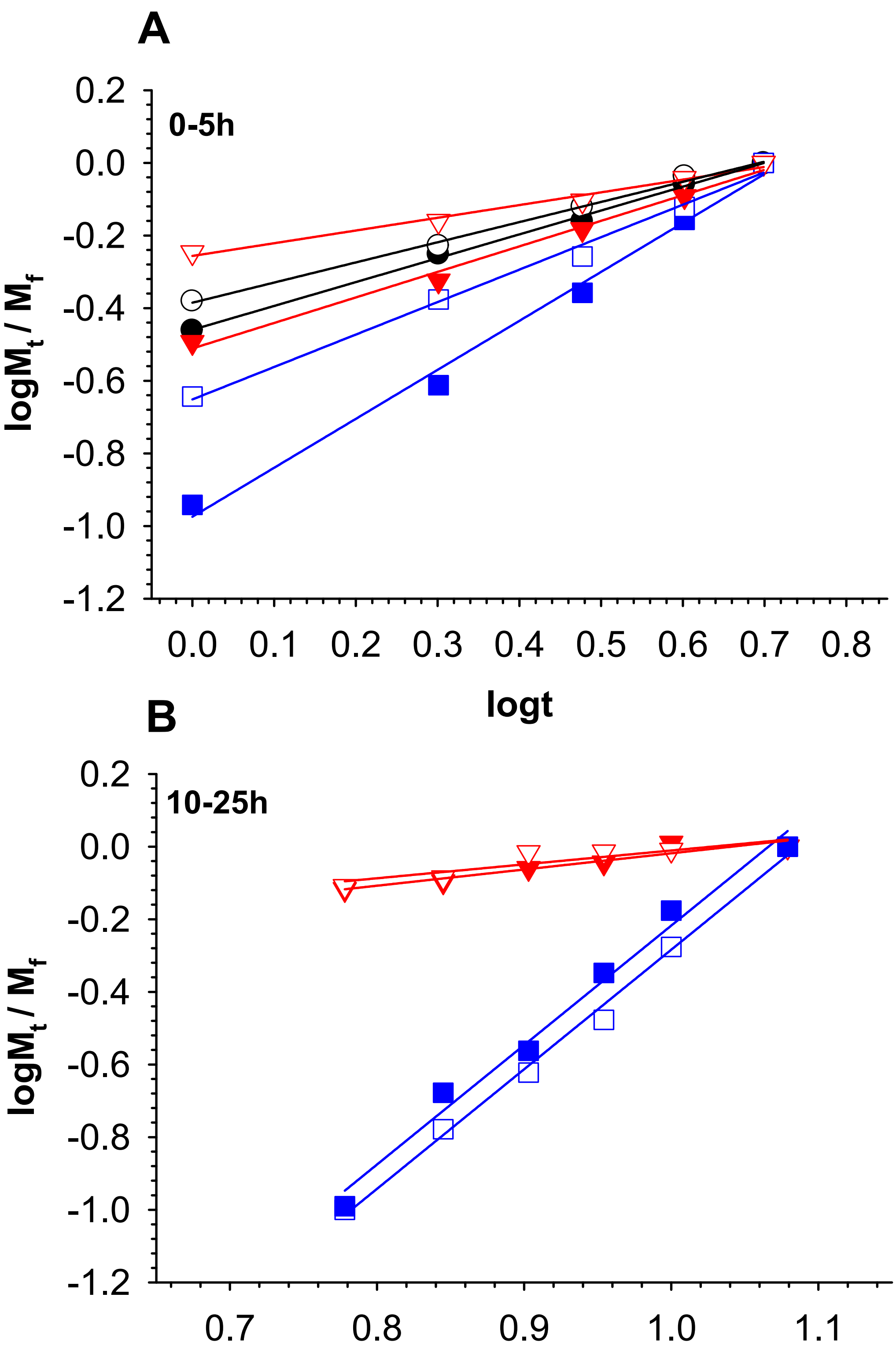


Fig. 5S Zeta potentials of PNIPA-co-AAc- (A), PNIPA-co-AAc-oligo1-2- (B) and PNIPA-AAc-oligo1-2-3 nanogels (C) recorded by DLS at 37 and 45°C, respectively.



A
0-5h
logMt / Mf
logt
0.2
0.0
-0.2
-0.4
-0.6
-0.8
-1.0
-1.2
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
B
10-25h
logMt / Mf
logt
0.7
0.8
0.9
1.0
1.1

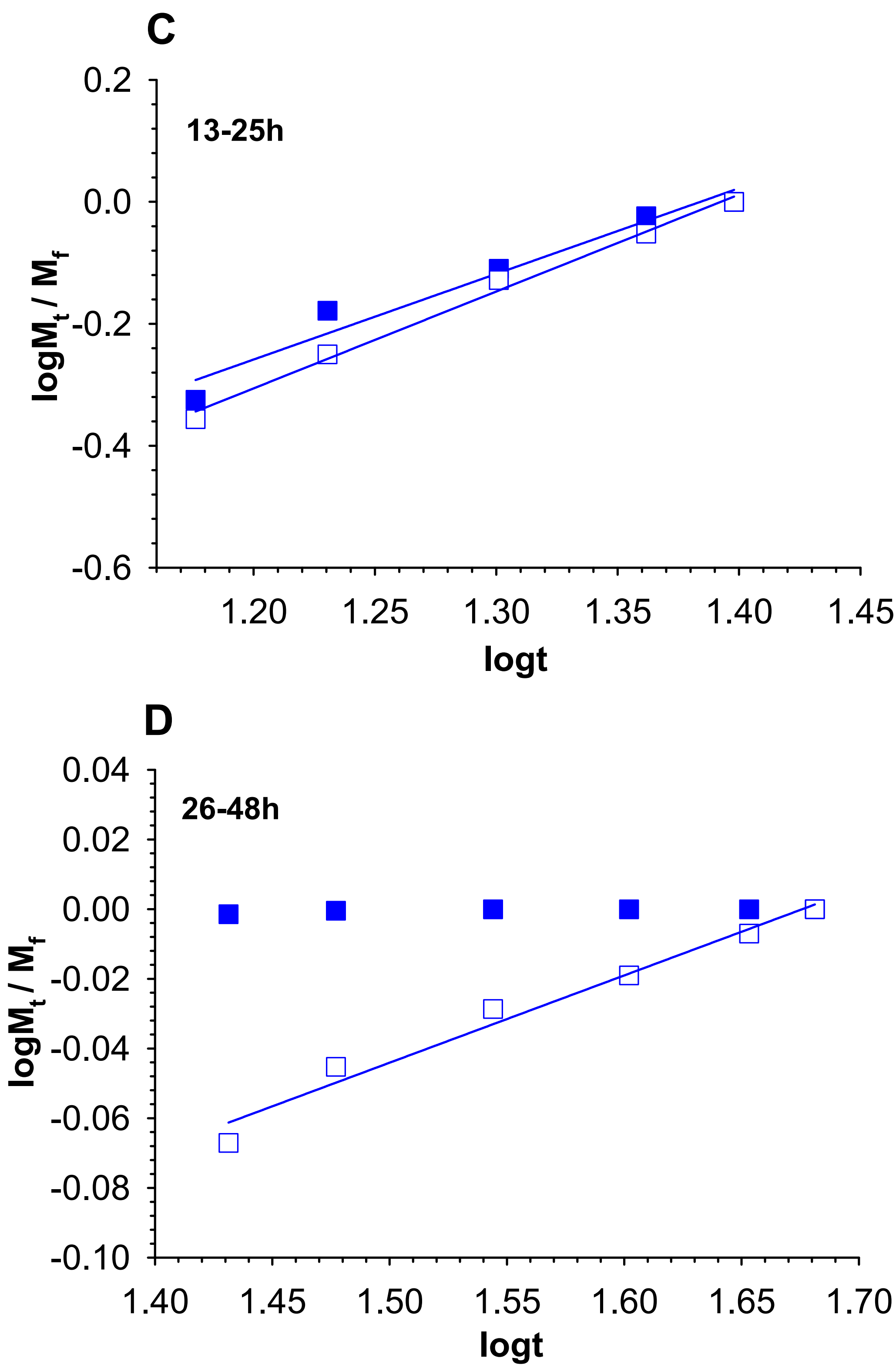


Fig. 6S Plots of log (Mf/Mt) vs. log t constructed according to Peppas model in selected ranges of time (A-D) for the release of doxorubicin from: PNIPA-co-AAc- (black circles), PNIPA-co-AAc-oligo1-2- (red triangles) and PNIPA-AAc-oligo1-2-3 nanogels (blue squares). Temperature: 37 °C (filled symbols), 45°C (empty symbols).

[1] D. Lide, H. Frederikse, Handbook of Chemistry and Physics, CRC Press, New York, 2007.

[2] M. Karbarz, M. Gniadek, Z. Stojek, One dimensional volume-phase transition of N-isopropylacrylamide gels on the surface of gold electrodes, *Electroanal*., 2005, **17**, 1396-1400.