Supplementary Information

"Solvent selection causes remarkable shifts of the "Ouzo region" for poly(lactide-*co*-glycolide) nanoparticles prepared by nanoprecipitation"

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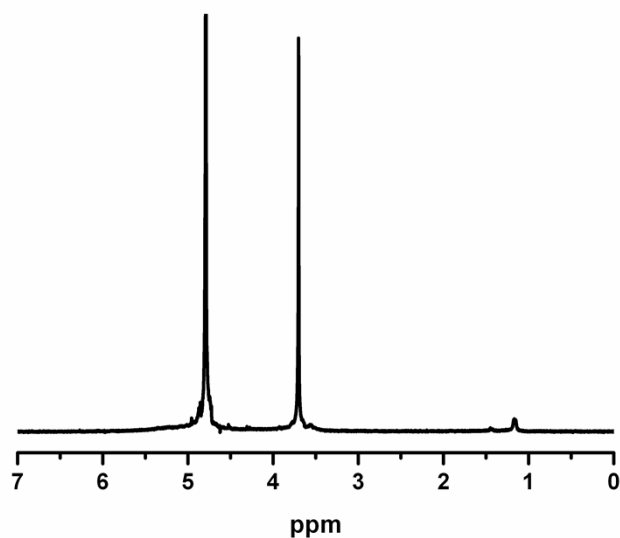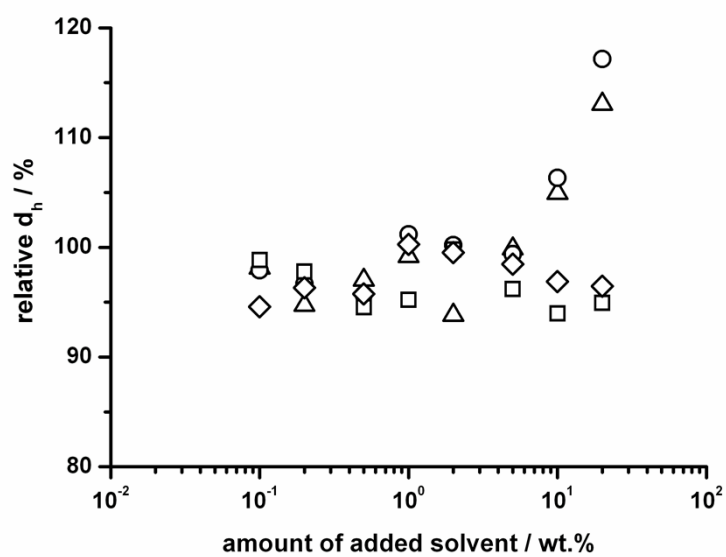
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1. TABLES

Table S1. Slopes and Correlation Coefficients from Linear Regression Analysis of the Experimental Data Presented in Figure S9.

Solvent	slope	R^2
THF	1.09	0.992
1,4-doixane	1.29	0.993
acetone	0.91	0.987
DMSO	1.17	0.994

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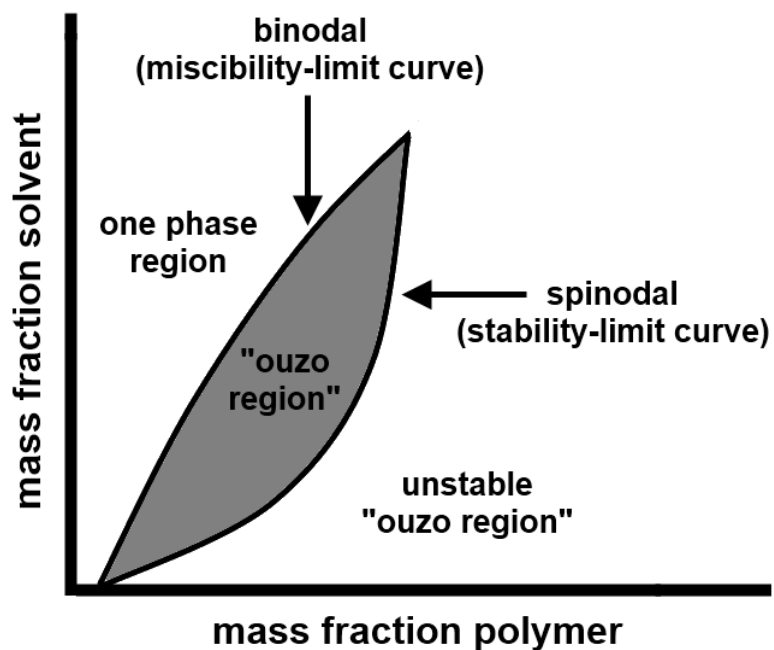
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2. FIGURES
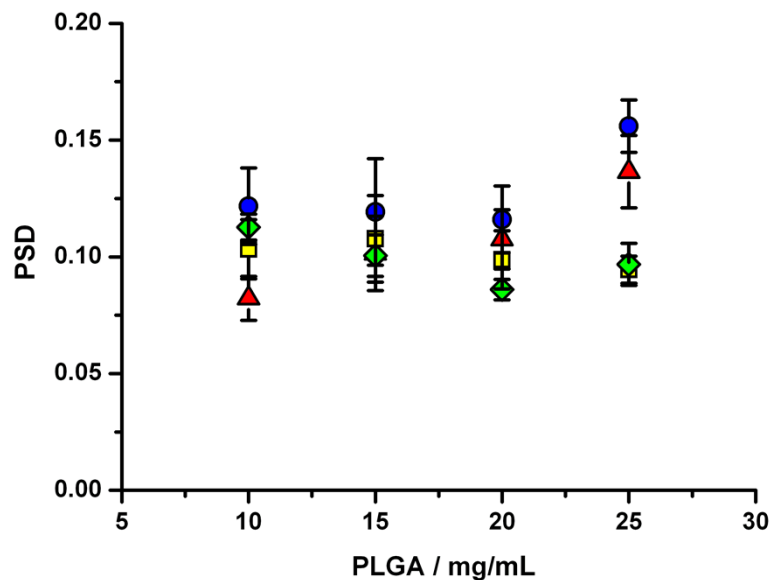

Figure S1. Representative ^{1}H-NMR spectrum of a polymer nanosuspension. PLGA-NPs were prepared as described in the *Materials & Methods* section using acetone as solvent and D_2O containing 0.1 wt.% of poloxamer 188 as non-solvent phase. The dominant signals at ~1.2, ~3.7 and ~4.8 ppm correspond to protons found in poloxamer 188, PLGA and H_2O.

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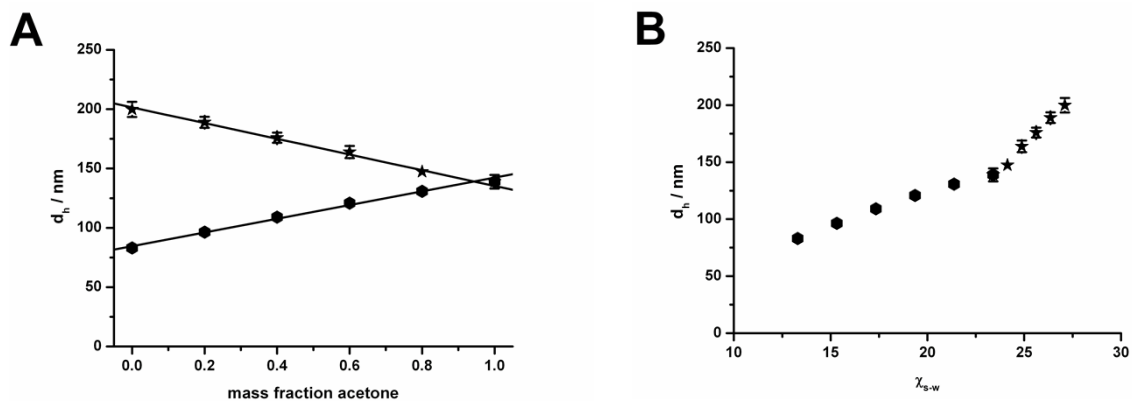
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Figure S2. Swelling of PLGA-NPs in aqueous suspension as a function of the amount of added organic solvent (triangles: THF, circles: 1,4-dioxane, squares: acetone, diamonds: DMSO).
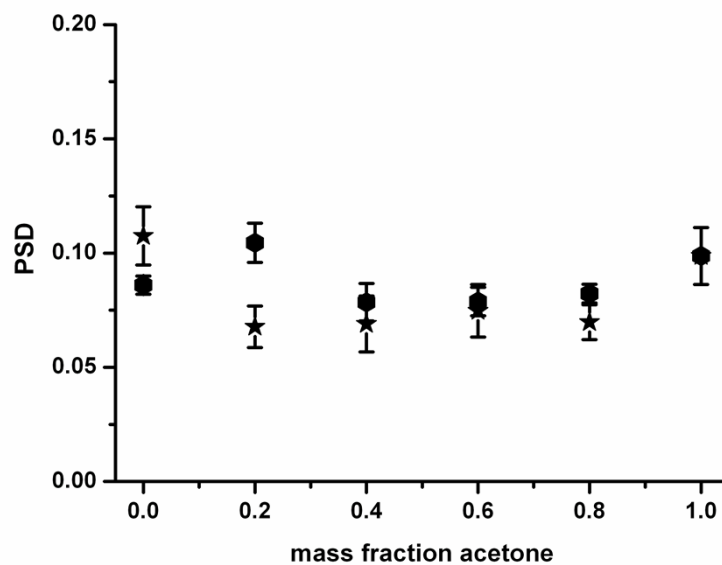
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Figure S3. Schematic of a right triangle, three-component (polymer/solvent/non-solvent) phase diagram. The "Ouzo effect" (formation of stable nanosuspensions) occurs for polymer solutions brought into the metastable region ("Ouzo region") between the miscibility-limit (binodal boundary) and stability-limit curve (spinodal boundary) by polymer precipitation in a non-solvent.

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Figure S4. Size distribution characteristics of PLGA-NPs as a function of the initial polymer mass concentration in the organic phase. 1 ml of organic phase (triangles: THF, circles: 1,4-dioxane, squares: acetone, diamonds: DMSO) containing increasing amounts of PLGA was injected into 5 ml of water containing 0.1 wt.% of poloxamer 188. Values are presented as the mean ± SD ($n = 4$).
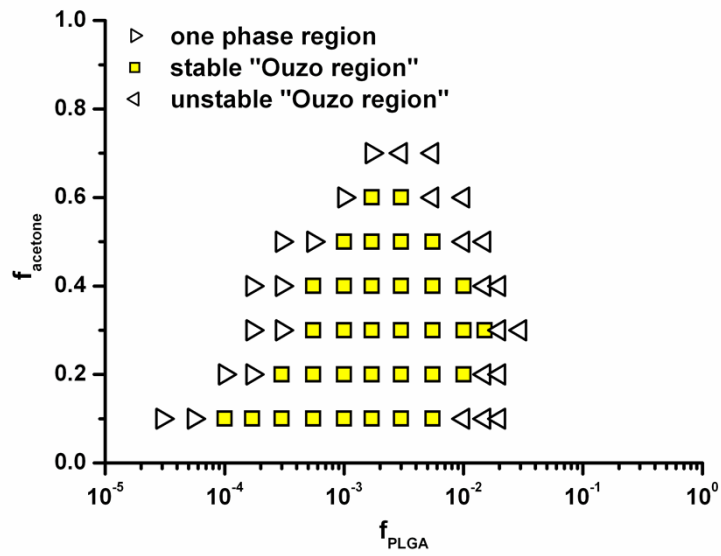
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Figure S5. Size of PLGA-NPs as a function of the applied solvent mixture (A) and $\chi_{s\text{-}w}$ (B). 1 ml of organic phase containing 20 mg of PLGA were injected into 5 ml of water containing 0.1 wt.% of poloxamer 188 (stars: THF/acetone, hexagons: DMSO/acetone). Values are presented as the mean ± SD ($n = 4$). No SD bars are shown if SD fell into the symbol. The straight lines in (A) represent linear fits of the experimental data ($R^2 > 0.99$).

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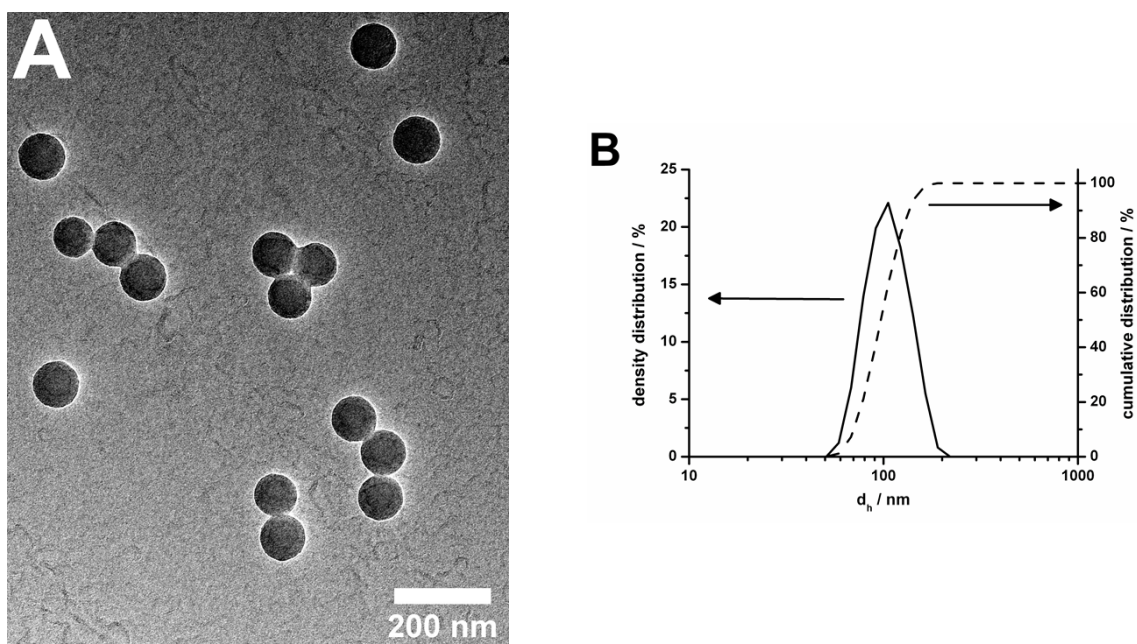
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Figure S6. Size distribution characteristics of PLGA-NPs as a function of the applied solvent mixture. 1 ml of organic phase containing 20 mg of PLGA were injected into 5 ml of water containing 0.1 wt.% of poloxamer 188 (stars: THF/acetone, hexagons: DMSO/acetone). Values are presented as the mean ± SD ($n = 4$).

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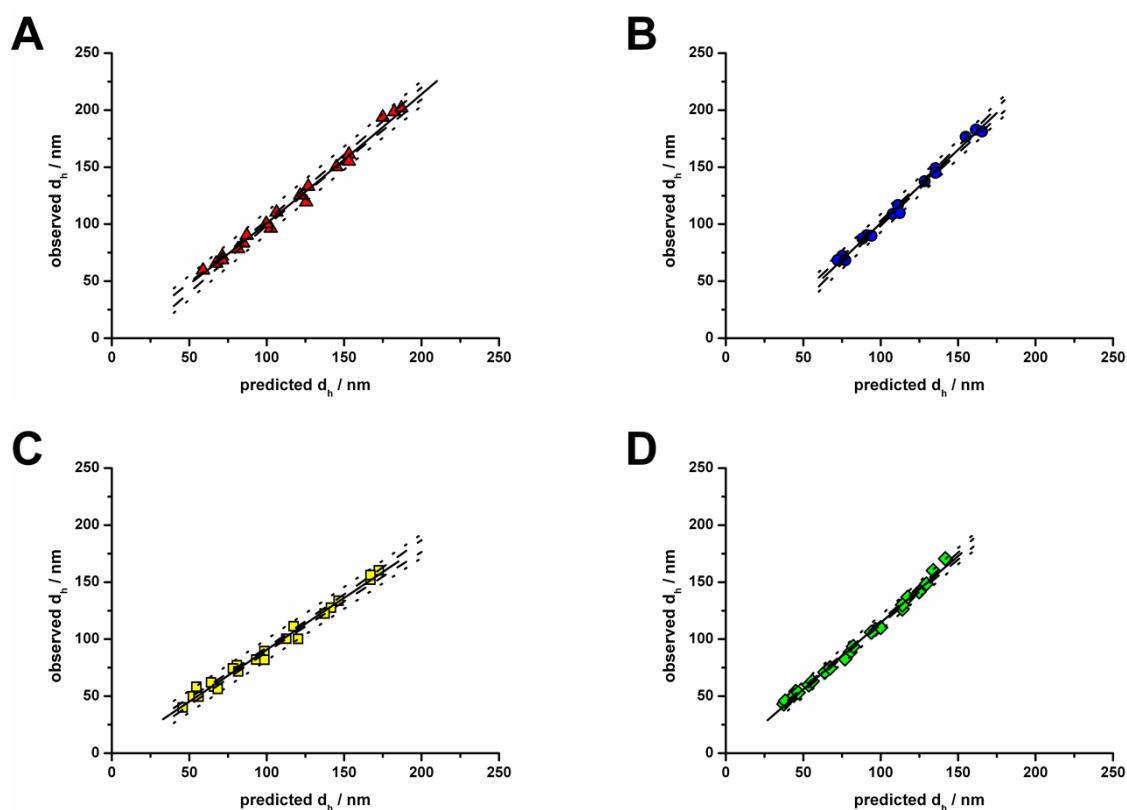
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Figure S7. Experimental "Ouzo diagram" for the ternary system composed of PLGA, acetone and water (containing 0.1 wt.% of poloxamer 188) at 25 °C.

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Figure S8. Representative TEM image (A) and particle size distribution curve from DLS (B) for PLGA-NPs found within the "Ouzo region". The solid line in (B) represents the particle size density distribution, the dashed line the cumulative particle size distribution.

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Figure S9. Correlation of observed and predicted sizes of PLGA-NPs (d_h) found within the "Ouzo region" ((A) THF, (B) 1,4-dioxane, (C) acetone, (D) DMSO). Calculations were performed with the results presented in Figure 3B and Equation 2. The straight lines represent linear fits of the experimental data. Information on the respective slopes and regression coefficients can be found in Table S1. The dashed and dotted lines represent the 95 % prediction (for new observations) and confidence (for the mean of many observations) intervals of the experimental data, respectively.

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