

Alkyl triphenyl phosphonium surfactants as nucleic acid carriers: complexation efficacy toward DNA decamer, interaction with lipid bilayer and cytotoxicity study

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Lipophilicity of compounds could be characterized in terms of $\log P$ (*n*-octanol/water distribution coefficient). Compound is considered as hydrophobic (lipophilic), if $\log P > 5$ [S1, S2]. One of the fundamental properties of surfactants, their surface tension, was used to evaluate their partition between *n*-octanol/water phases, using calibration surface tension isotherms for CTAB and TPPB-16. Values of $\log P$ calculating with the use of eq.S1 are equal to 1.96 and 2.24 for CTAB and TPPB-16 respectively, indicating the somewhat higher lipophilicity of the latter (Table S1). Though these characteristics are only for the sake of comparison, and both surfactants cannot be considered as hydrophobic species.

1. Determination of distribution coefficient between n-octanol and water

10 mL of CTAB or TPPB-16 aqueous solutions (1 g/L) was mixed with 10 mL of *n*-octanol. The mixture was vigorously stirred during 4 hours at room temperature. After that aqueous and organic phases were divided from each other using separation funnel. Aqueous part was

evaporated at 100-200 °C for full removal of the solvent. Obtained residue was dissolved in fresh portion of water (10 mL). Surface tension of prepared aqueous solution of amphiphile was measured using Kruss K6 tensiometer (ring detachment method). Concentration of surfactant in solution was determined using calibration surface tension isotherms for amphiphiles initially reported in [S3]. The logarithm of distribution coefficient (log P) was calculated using following equation:

$$\log P = \left(\frac{C_{init} - C_{fin}}{C_{fin}} \right) \cdot \frac{V_{AP}}{V_{OP}} \quad (S1),$$

where C_{init} and C_{fin} are concentration of the surfactant in aqueous phase before and after experiment, respectively; V_{AP} – the volume of aqueous phase; V_{OP} – the volume of organic phase.

Table S1. Values of the logarithm of distribution coefficient between *n*-octanol and water for CTAB and TPPB-16.

Amphiphile	Surface tension, mN/m	Concentration, mM	log P
CTAB	66.8	0.03	1.96
TPPB-16	64.1	0.01	2.24

S1. R.Mannhold , G.I. Poda, C.Ostermann, I.V. Tetko, Calculation of molecular lipophilicity: state-of-the-art and comparison of log p methods on more than 96000 compounds, J. Pharm. Sci. 98 (2009) 861–893.

S2. D. Miller. Measuring and testing liquid analysis or analysis of the suspension of solids in a liquid surface tension, 2007, US Patent 20090019923.

S3. G.A. Gainanova, G.I. Vagapova, V.V. Syakaev, A.R. Ibragimova, F.G. Valeeva, E.V. Tudriy, I.V. Galkina, O.N. Kataeva, L.Y. Zakharova, S.K. Latypov, A.I. Konovalov, Self-assembling systems based on amphiphilic alkyltriphenylphosphonium bromides: elucidation of the role of head group, J. Colloid Interface Sci. 367 (1) (2012) 327–336.

2. Solution behaviour of phosphonium surfactants with admixture added

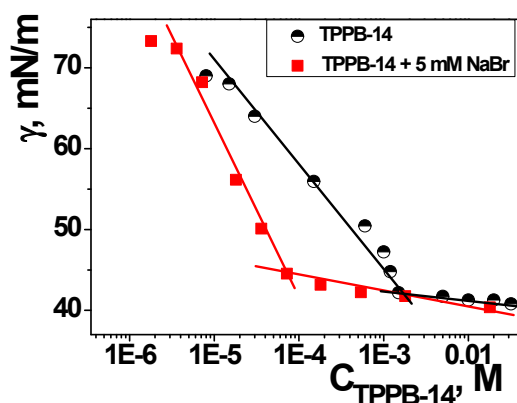


Fig. S1. Surface tension isotherms of TPPB-14 aqueous solutions in single system and in the presence of 5 mM NaBr; 25 °C.

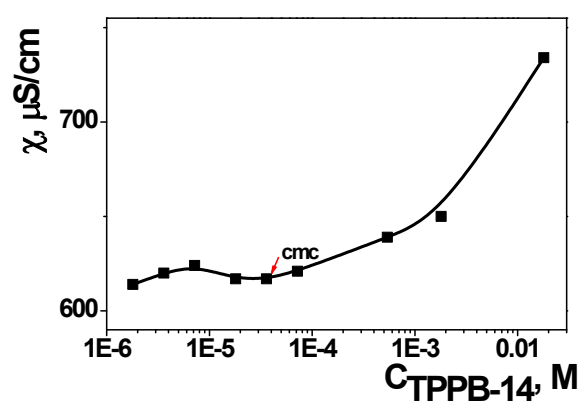


Fig. S2. Specific conductivity versus surfactant concentration plots of TPPB-14 aqueous solutions in the presence of 5 mM NaBr; 25 °C.

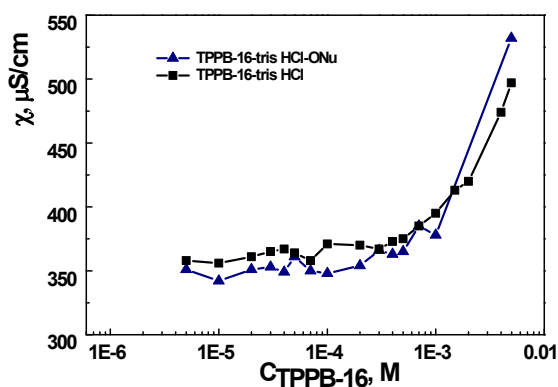


Fig. S3. Specific conductivity versus surfactant concentration plot for TPPB-16-ONu; 4 mM tris-buffer, 2 mM ONu (per a nucleotide unit); pH 8.2, 25 °C.

3. TPPB-n/ONu complexation

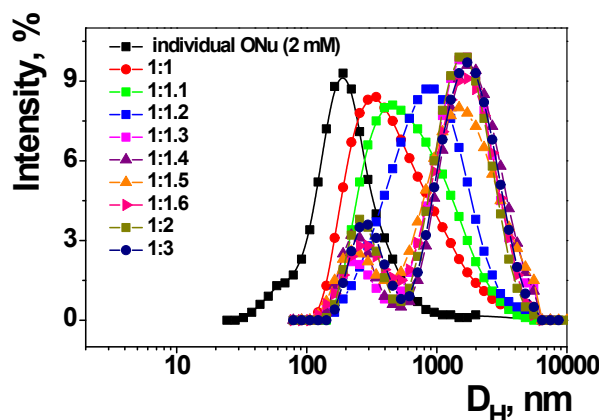


Fig. S4. Intensity averaged size distribution for ONu/TPPB-14 binary system at various ONu/TPPB-14 molar ratios; 25 °C.

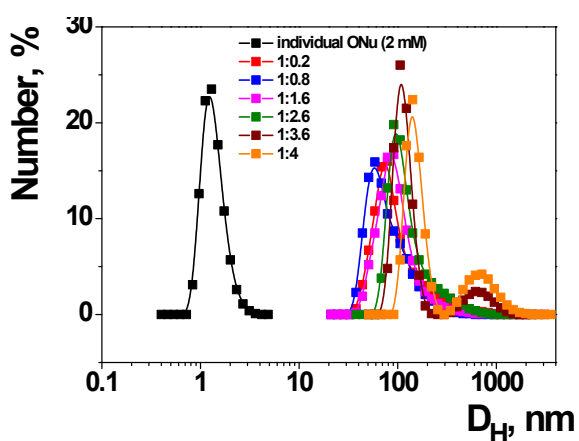


Fig. S5. Number averaged size distribution for ONu/TPPB-14 binary system at various ONu/TPPB-14 molar ratios; 25 °C.

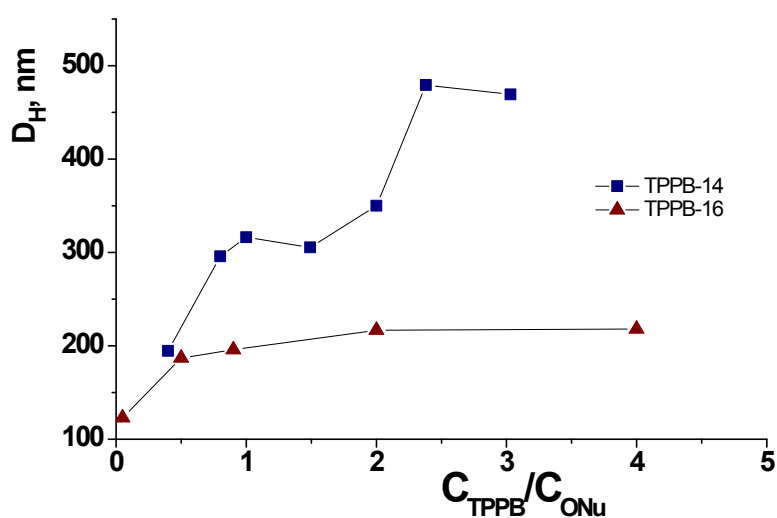


Fig. S6. Hydrodynamic diameter (z-average) versus TPPB-n molar ratio plots for TPPB-14/ONu and TPPB-16/ONu binary systems; 25 °C.

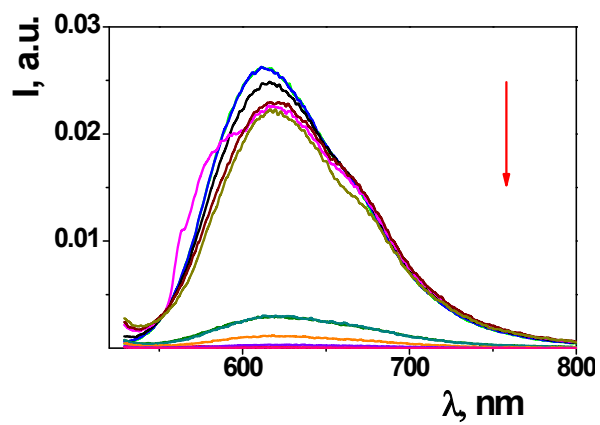


Fig. S7. EB fluorescence spectra for ONu/TPPB-16 binary system. The arrow direction indicates surfactant concentration increase from 0.2 to 2 mM.

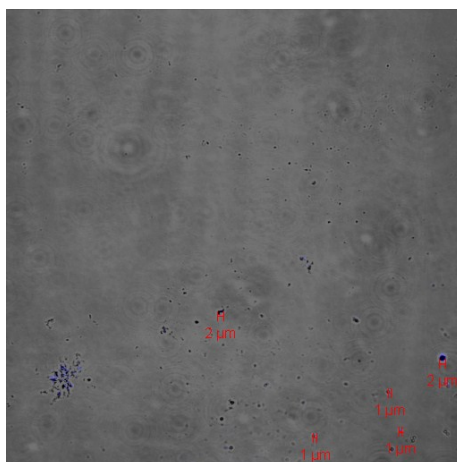


Fig.S8. The confocal microscope images of lipoplexes formed in ONu-TPPB-16 system prior to the cmc point; $C_{\text{TPPB-16}} = 0.05 \text{ mM}$; $C_{\text{ONu}} = 0.996 \text{ mM}$.

4. Integration with lipid bilayer

	Mean (mV)	Area (%)	St Dev (mV)
Zeta Potential (mV): -0.949	Peak 1: -0.949	100.0	2.95
Zeta Deviation (mV): 2.95	Peak 2: 0.00	0.0	0.00
Conductivity (mS/cm): 0.0826	Peak 3: 0.00	0.0	0.00

Result quality : Good

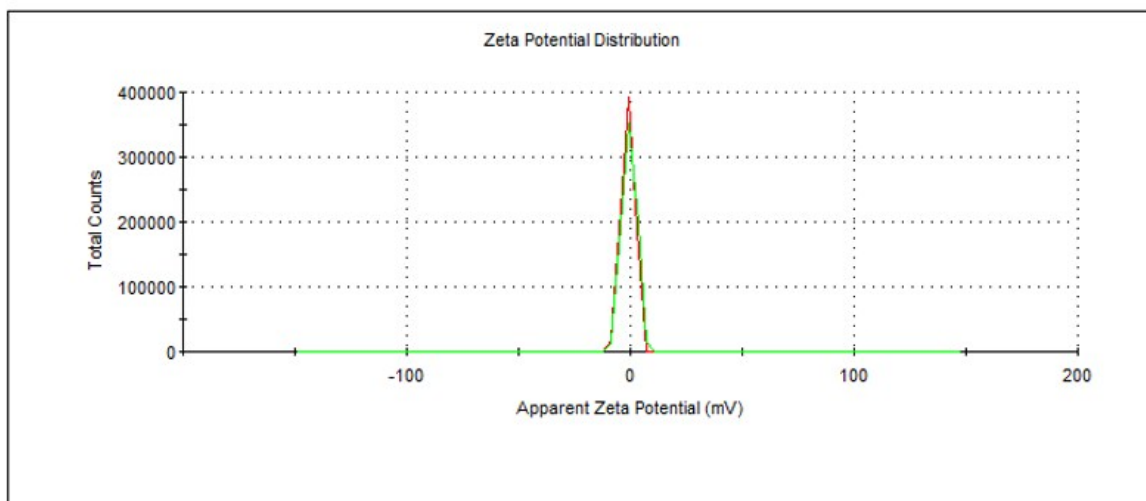
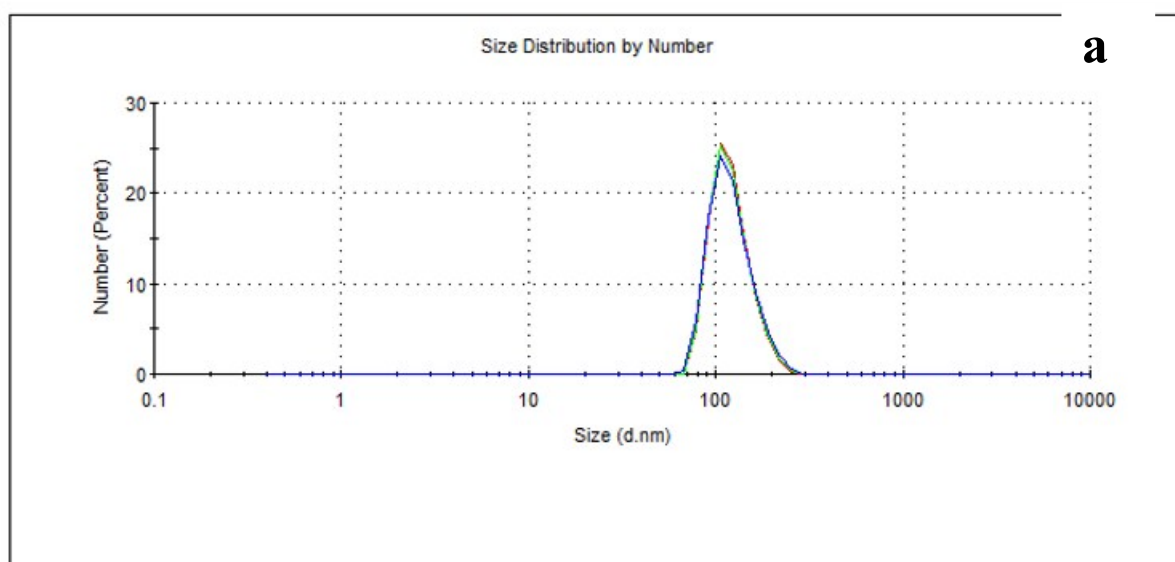


Fig. S9. Zeta potential of DPPC individual liposomes; C = 0.7 mM; 25 °C.

	Size (d.nm):	% Number:	St Dev (d.nm):
Z-Average (d.nm): 145.2	Peak 1: 121.7	100.0	29.95
Pdi: 0.101	Peak 2: 0.000	0.0	0.000
Intercept: 0.932	Peak 3: 0.000	0.0	0.000

Result quality : Good



	Size (d.nm):	% Intensity:	St Dev (d.nm):
Z-Average (d.nm): 145.2	Peak 1: 148.8	100.0	34.04
Pdl: 0.101	Peak 2: 0.000	0.0	0.000
Intercept: 0.932	Peak 3: 0.000	0.0	0.000
Result quality : Good			

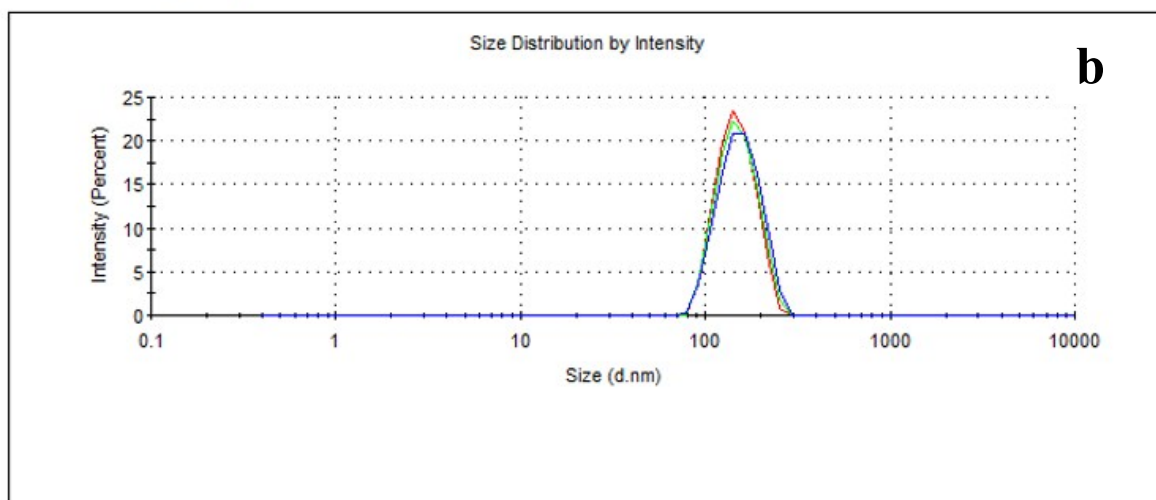


Fig. S10. Number- (a) and intensity-averaged (b) size distribution for DPPC individual liposomes; $C = 0.7$ mM; 25 °C.

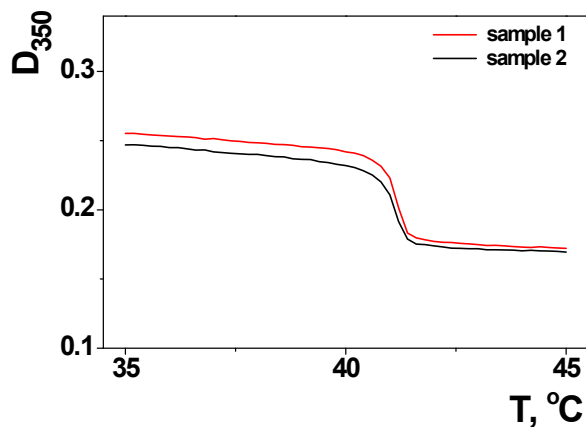


Fig. S11. Typical turbidimetric plots for different samples of DPPC individual liposomes; $C_{\text{DPPC}} = 0.7$ mM.

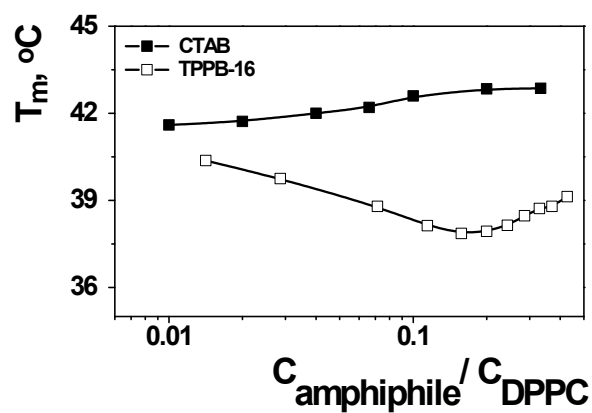


Fig. S12. DPPC main phase transition temperature versus amphiphile/DPPC molar ratio plot for CTAB/DPPC [S4] and TPPB-16/DPPC binary systems.

S4. Gabdrakhmanov D.R., Valeeva F.G., Samarkina D.A., Lukashenko S.S., Mirgorodskaya A.B., Zakharova L.Y., The first representative of cationic amphiphiles bearing three unsaturated moieties: self-assembly and interaction with polypeptide / *Colloids Surf., A.*, 2018, т.558, с.463-469.

5. *Effect of surfactants on DNA transformation*

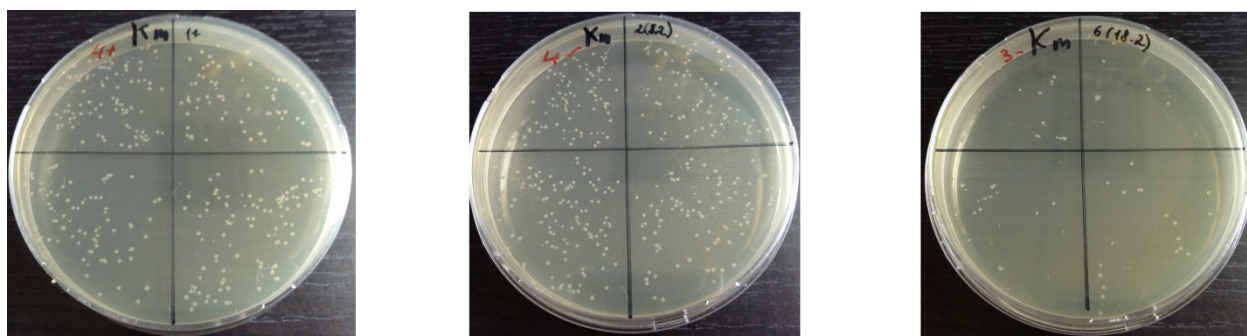


Fig.S13. Cups with transformed bacteria: A) pEGFP-N1 plasmid DNA; B) pEGFP-N1 plasmid DNA with TPPB-8 ($P_+/P_- = 2$); C) pEGFP-N1 plasmid DNA with TPPB-18 ($P_+/P_- = 2$)