Electronic Supporting Information (ESI)

Complexation of short ds RNA/DNA oligonucleotides with Gemini micelles: a time resolved SAXS and computational study.

Sara Falsini,[a] Emanuela Di Cola,[b] Martin In,[c] Maria Giordani[e], Stefano Borocci,[d,e] and Sandra Ristori[f]

a. Department of Chemistry "Ugo Shiff" & CSGI, University of Florence, via della Lastruccia 3, 50019 Sesto Fiorentino, FI, Italy;

b. European Synchrotron Radiation Facility (ESRF), 71 avenue des martyrs 38000, Grenoble, France;

c. Laboratoire Charles Coloumb, UMR, 5221 CNRS-UM2, Place Eugène Bataillon, F-34095 Montpellier Cedex 05, France;

d. Dipartimento per la Innovazione nei Sistemi Biologici, Agroalimentari e Forestali (DIBAF), Università degli Studi della Tuscia, Largo dell'Università, snc 01100, Viterbo, Italy;

e. CNR-Istituto di Metodologie Chimiche, Area della Ricerca di Roma 1, Via Salaria km 29,300, 00015, Monterotondo RM, Italy;

f. Dipartimento di Scienze della Terra, Università di Firenze, Via La Pira 4, 50121, Firenze, Italy.

corresponding author: sandra.ristori@unifi.it

a) Experimental

Figure S1: SAXS intensity profiles of 12-6-12 micelles, siRNA and complexes at two different charge ratios (CR=0.75 and CR=1.25) recorded 20 ms after mixing. In the complex solution, the total surfactant concentration (1.25 x 10^{-3} M) is ~ 1.5 times the CMC of 12-6-12. In the reference systems siRNA is 4.5 x10^{-5} M and 12-6-12 is 1.25 x10^{-3} M.

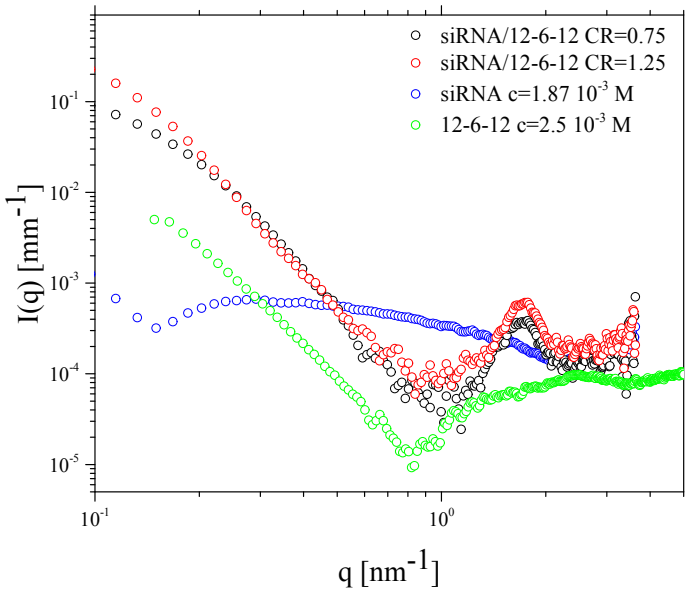
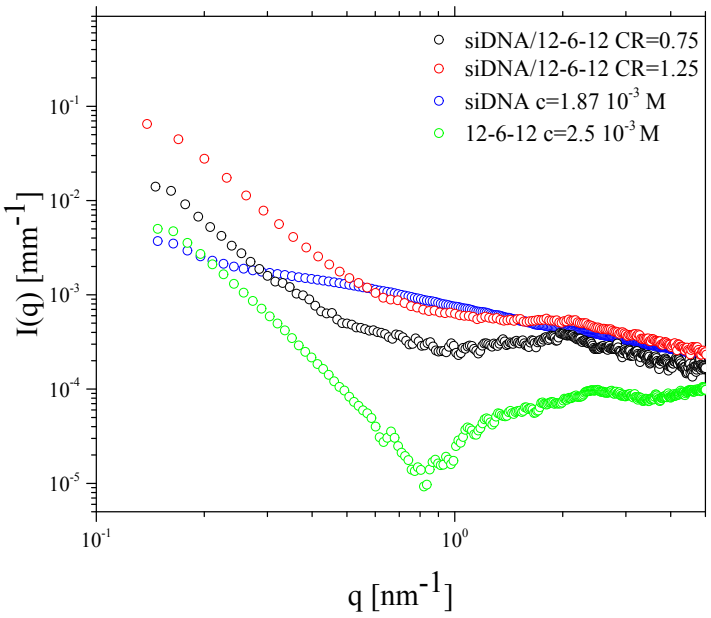


Figure S2: SAXS intensity profiles of 12-6-12 micelles, siDNA and complexes at two different charge ratios (CR=0.75 and CR=1.25) recorded 20ms after mixing. In the complex solution, the total surfactant concentration (1.25 x 10^{-3} M) is ~ 1.5 times the CMC of 12-6-12. In the reference systems siDNA is 4.5 x10^{-5} M and 12-6-12 is 1.25 x10^{-3} M.



b) MD simulation

Table S1: Details of Simulated Systems.

Complex	Micelle Charges	ODN Charges	Charge Ratio (-/+)	Number of Na^+ and Br^- ions	Water molecules
Monomeric Complex					
DNA/12-3-12	+54	-40	0.74	40 + 54	24675
SiRNA/12-3-12	+54	-40	0.74	40 + 54	24661
DNA/12-6-12	+54	-40	0.74	40 + 54	24596
SiRNA/12-6-12	+54	-40	0.74	40 + 54	24596
Dimeric Complex					
DNA/12-3-12	(+54)×2	(-40)×2	0.74	80 + 108	36979
SiRNA/12-3-12	(+54)×2	(-40)×2	0.74	80 + 108	37063
DNA/12-6-12	(+54)×2	(-40)×2	0.74	80 + 108	36979
SiRNA/12-6-12	(+54)×2	(-40)×2	0.74	80 + 108	36976

Table S2: Properties of the micelle of 12-3-12 and 12-6-12 averaged over the last 20 ns of MD simulations. Aggregation number (N), radius of gyration (Rg), principal moment of inertia (I_1, I_2, I_3) and eccentricity of the micellar aggregates.

	12-3-12 micelle	**12-6-12 micelle**
N	27	27
R_g (nm)	1.47±0.01	1.53±0.01
I_1 (10^4 u nm^2)	1.210±0.043	1.458±0.023
I_2 (10^4 u nm^2)	1.680±0.066	1.997±0.044
I_3 (10^4 u nm^2)	1.838±0.060	2.216±0.041
Eccentricity	0.196±0.05	0.225±0.06

The radius of gyration for a molecular aggregate of N atoms is given by:

$$R_g = \frac{1}{M}\sqrt{\sum_{i=1}^{N}\left[m_i (d_i)^2\right]} \qquad \text{(eq. S1)}$$

where m_i is the mass of atom i, d_i is the distance of atom i from the centre of mass of the aggregate and M is the total mass of the aggregate.

The eccentricity, e, is defined as[1]:

$$e = 1 - \frac{I_{min}}{I_{ave}} \qquad \text{(eq. S2)}$$

where I_{min} is the principal moment of inertia with the smallest magnitude and I_{ave} is the average of I_1, I_2 and I_3. For a sphere e=0.

Figure S3: Radial density distribution from the centre of mass of the 12-3-12 (a) and 12-6-12 (b) micelle.

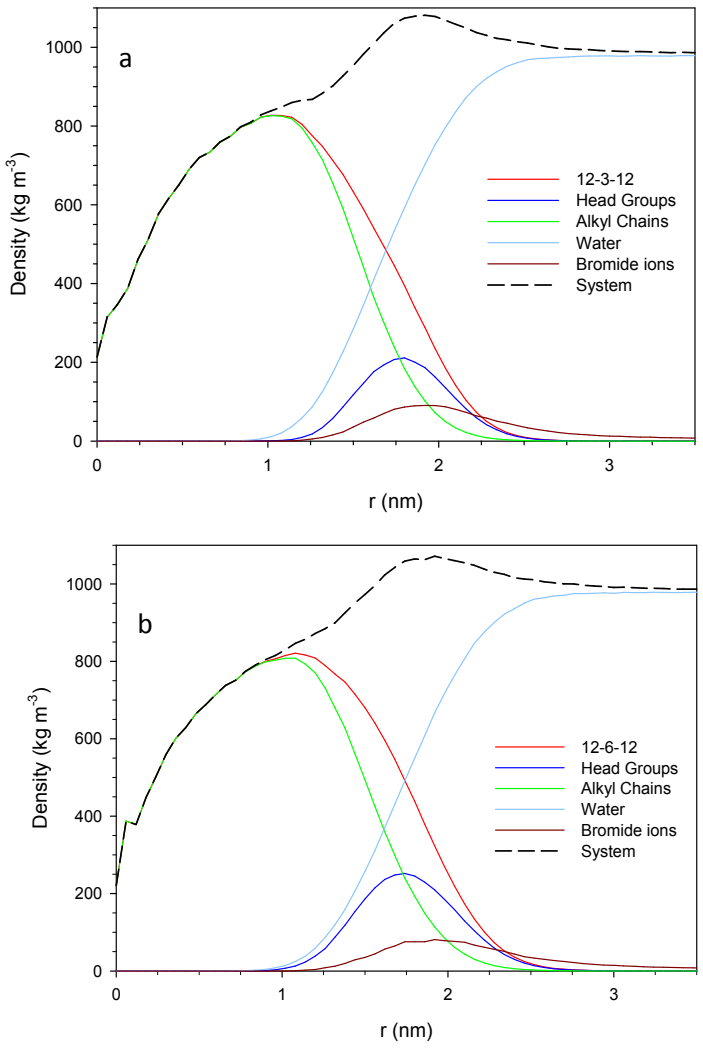


Figure S4: Structure of the simulated systems during various step of complexation: a) siRNA and micelle of 12-6-12, b) siDNA and micelle of 12-6-12.

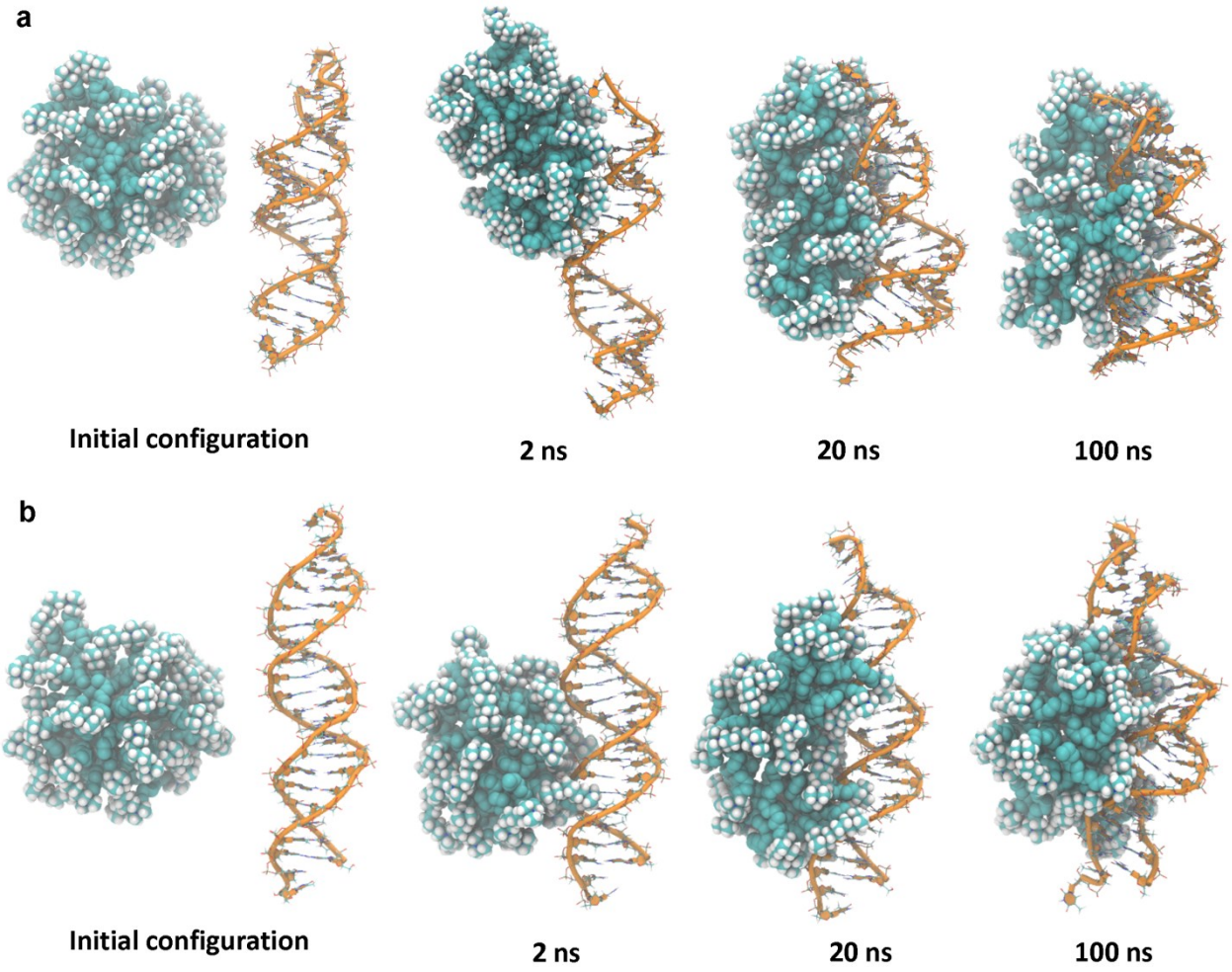


Figure S5: Probability distribution of the averaged intramolecular distance between nitrogen atoms of 12-3-12 (a) and 12-6-12 (b) surfactants in isolated micelle and in the contact region with ODN (within 0.3 nm of atoms of ODN). Gemini in isolated micelle (black line), Gemini surfactants close to siDNA (blue line) and Gemini surfactants close to siRNA.

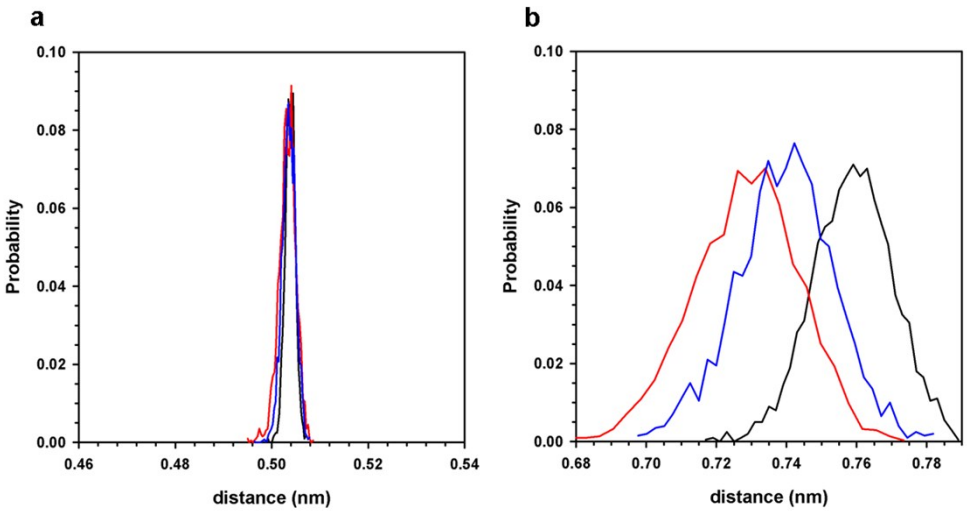


Figure S6: Radial distribution function of phosphate groups for siDNA (blue line) and siRNA (red line)

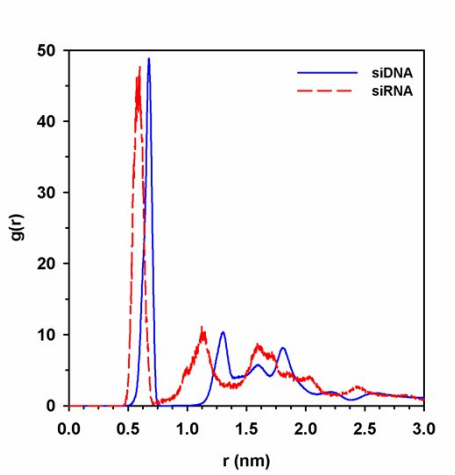
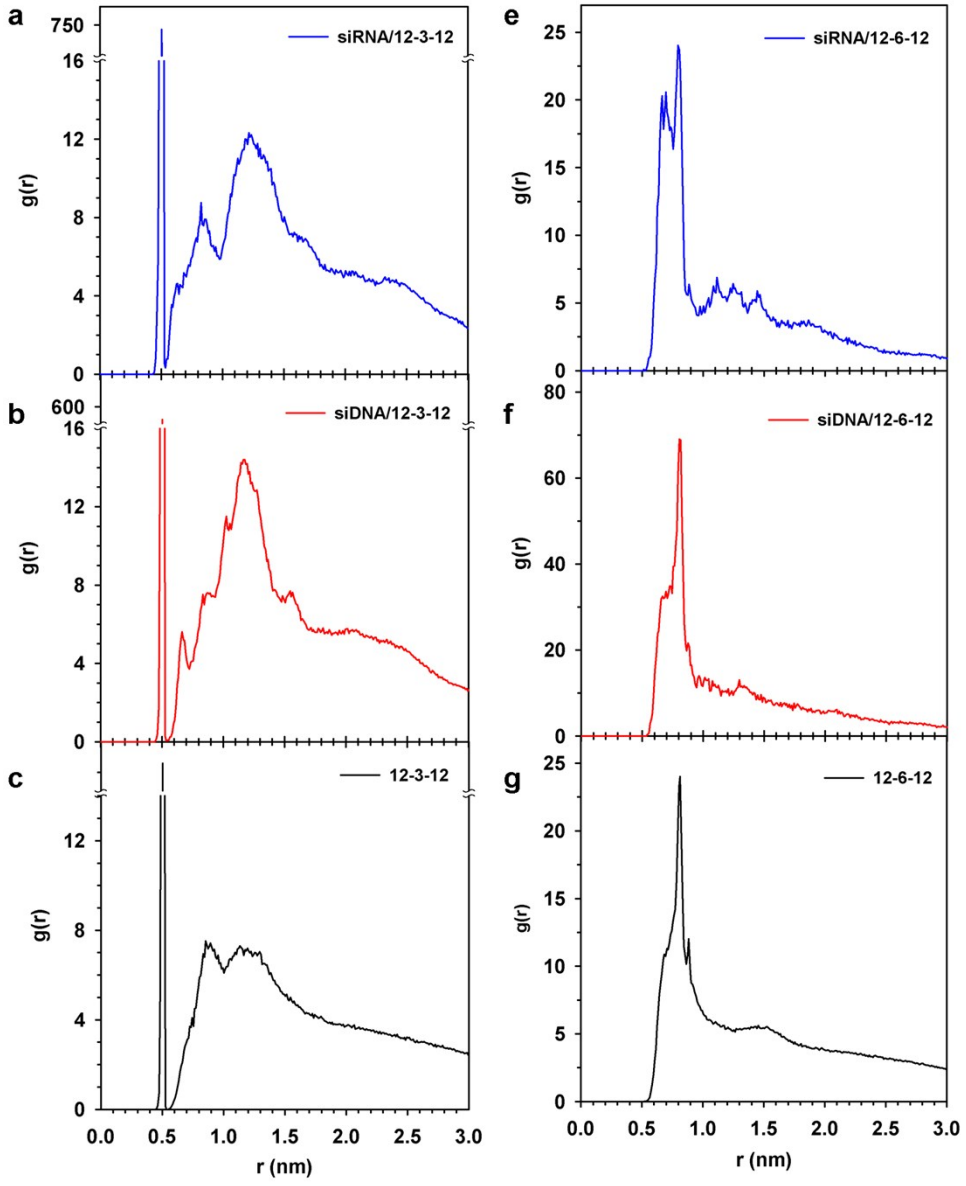


Figure S7: Radial distribution function of nitrogen atoms for12-3-12 (a-b) and 12-6-12 (e-f) within 0.3 nm of from any atom of siRNA (blue line) and siDNA (red line) considering the intramolecular and intermolecular interaction. c) RDF of nitrogen atoms in 12-3-12 isolated micelle, d) RDF of nitrogen atoms in 12-6-12 isolated micelle.



References

1 Salaniwal, S.; Cui, S. T.; Cochran, H. D.; Cummings, P. T. *Langmuir* **2001**, *17*, 1773-1783.