Fractal network of DNA/polycation bundles bring long-term colloidal stability to polyplexes

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Transfection, the delivery of genetic material into cells, is foreseen as the ultimate step in diseases treatment, with the possibility to induce the manufacture of customized proteins as curating agent. The need for favorable interactions between negatively charged DNA or RNA and globally negatively charged liposomes-based cells’ membranes is generally answered to by using polycations complexing DNA. Such complexes can be obtained using densely branched, small polyethyleneimines (PEI), known for their good biocompatibility.

We describe the physico-chemical analyses of such aqueous complexes obtained with long DNA (ca. 300 bp, 100 nm) and commercially available polycations, at high concentration (ca. 1%), exhibiting long-term (over 6 months) colloidal stability, by means of scattering techniques and direct imaging. The behavior reported is understood as a “colloidal stability”, where a fractal structure across the whole sample helps to prevent the macroscopic phase separation. This depiction is supported by cryo-TEM images (see figure), showing a dense network made of beams of DNA-rods, the short-scale spacing and long-scale ordering of which is best seen by SAXS (see figure). The whole picture of these complexes is obtained by combining cryo-TEM, SANS and SAXS.

Left: Cryo-TEM image of DNA/polyethyleneimine mixture in buffer; the full length of the picture is 775 nm; dark spots correspond to DNA rods in the focusing plane; gray stripes are DNA-bundles.
Right: SAXS spectra of DNA/PEI at various molar ratios amine / phosphate: 0 is pure DNA, 1 is pure polymer; spectra are incrementally shifted vertically by an order of magnitude for readability. The Bragg peaks at high q indicate the high ordering of the DNA rods inside the bundles; the intensity increase at low q indicate the presence of a fractal network with an overall size of ca. 100 nm, the length of the DNA used here.