Supporting Information

DLS measurements

We show here the DLS measurements of our LNPs which show that the particles are 100 nm in diameter.

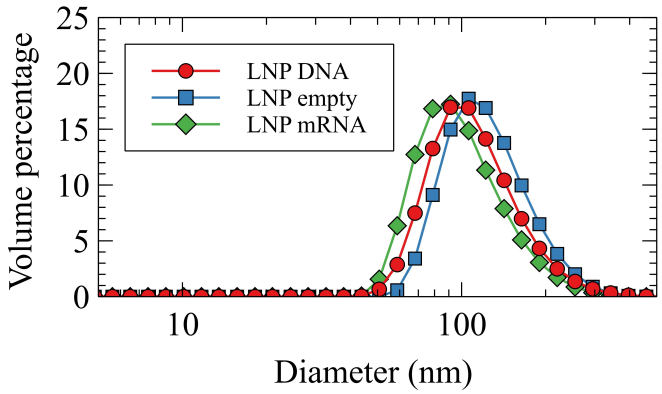

Figure 1: *Size distribution of particles used in this study, LNP DNA, LNP mRNA, and empty LNPs*

Properties of isolated pDNA LNPs

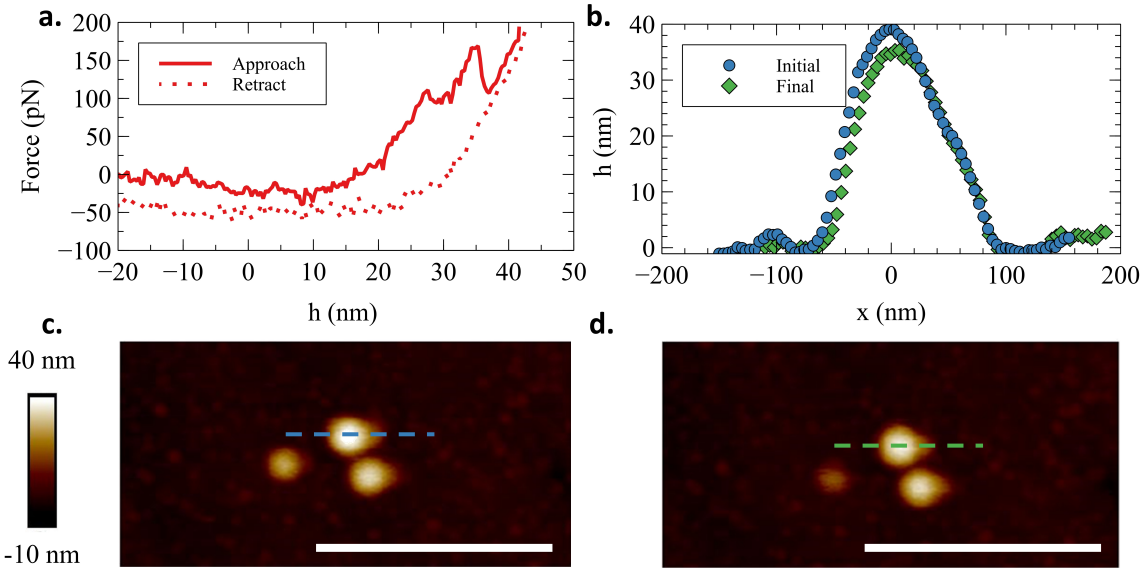

Figure 2: *Mechanical analysis of a pDNA LNP isolated. (a) Force curve, (b) Section of the particle before and after the force curve, (c) and (d) images of the particle respectively before and after the force curve. Dots represent the location of the cut and the white bar represents a scale of 200nm.*

Figure 2 shows a representative example of the results obtained with pDNA LNPs in zones of the drops where they are isolated. We use a 40 nm tip. In Figure 2a, the approach curve on the particle after contact ($h = 0$) presents several jumps which shows that it rearranges. These rearrangements induce a change in the area of the tip/particle contact, and thus in the apparent stiffness of the particles. The particle is crushed by the tip over of the order of its height and yet sections of the particle before and after the experiment show

almost no change in the topology of the particle (Fig.2b, c, d). Therefore the particle returns to its initial shape after having been completely deformed. This behaviour contrasts strongly with what we observed when the pDNA particles are packed in a dense layer. When they are isolated the pDNA particles can deform reversibly because they have the possibility of rearranging on the surface. In contrast, when they are packed the particles cannot rearrange which induces a stronger forcing of the particle causing its rupture. As a summary we find that observing particles when they are densely packed enables to obtain a more reliable measurement and to differentiate particles with different biopolymer loadings. This is the reason why we decided to perform all our measurements on densely packed layers