

Supplemental Figures

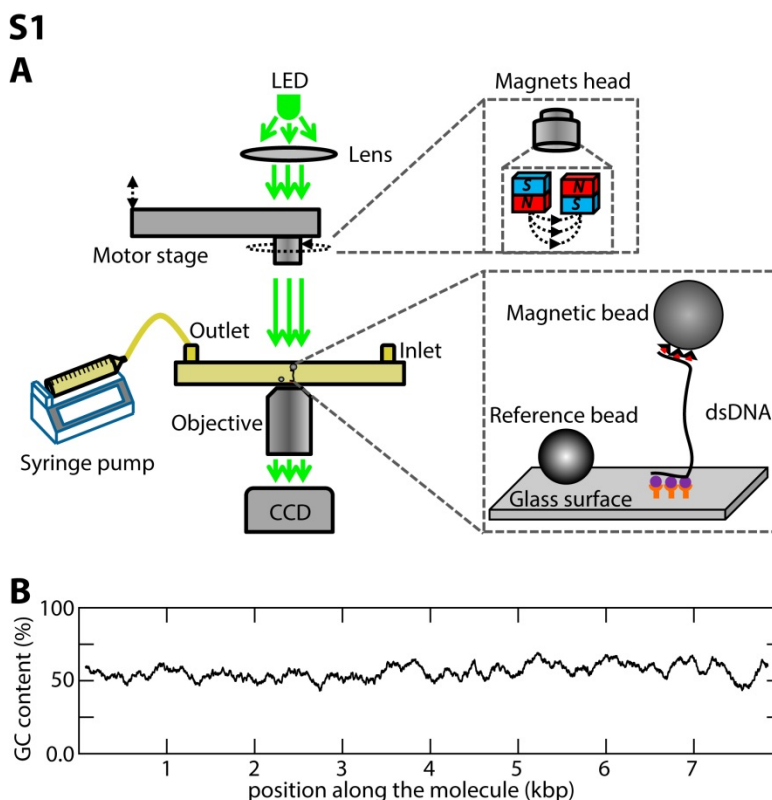


Figure S1: Magnetic tweezers experiment. A) In the magnetic tweezers, a single dsDNA molecule within a flow cell is attached at one end to a glass surface through multiple DIG/anti-DIG bonds, and at the other end to a super-paramagnetic bead through multiple biotin/streptavidin bonds. This tethering method results in a rotationally constrained DNA molecule. By placing a pair of external magnets above the bead, a well-defined stretching force can be applied to the DNA, which can be varied by changing the distance between the magnets and the bead. Rotating the pair of magnets will make the super-paramagnetic bead rotate, resulting in a changed supercoiling density of the DNA. The bead is imaged by a CCD camera using a home-build inverted microscope. Beads, DNA, proteins and buffers are flushed in by pipetting into the inlet and removing the waste by a syringe pump. To correct for drift, a polystyrene non-magnetic reference bead that is attached to the bottom of the flow cell is tracked simultaneously with the magnetic bead. B) GC content along the 7.9 kB molecule using a 150bp moving average.

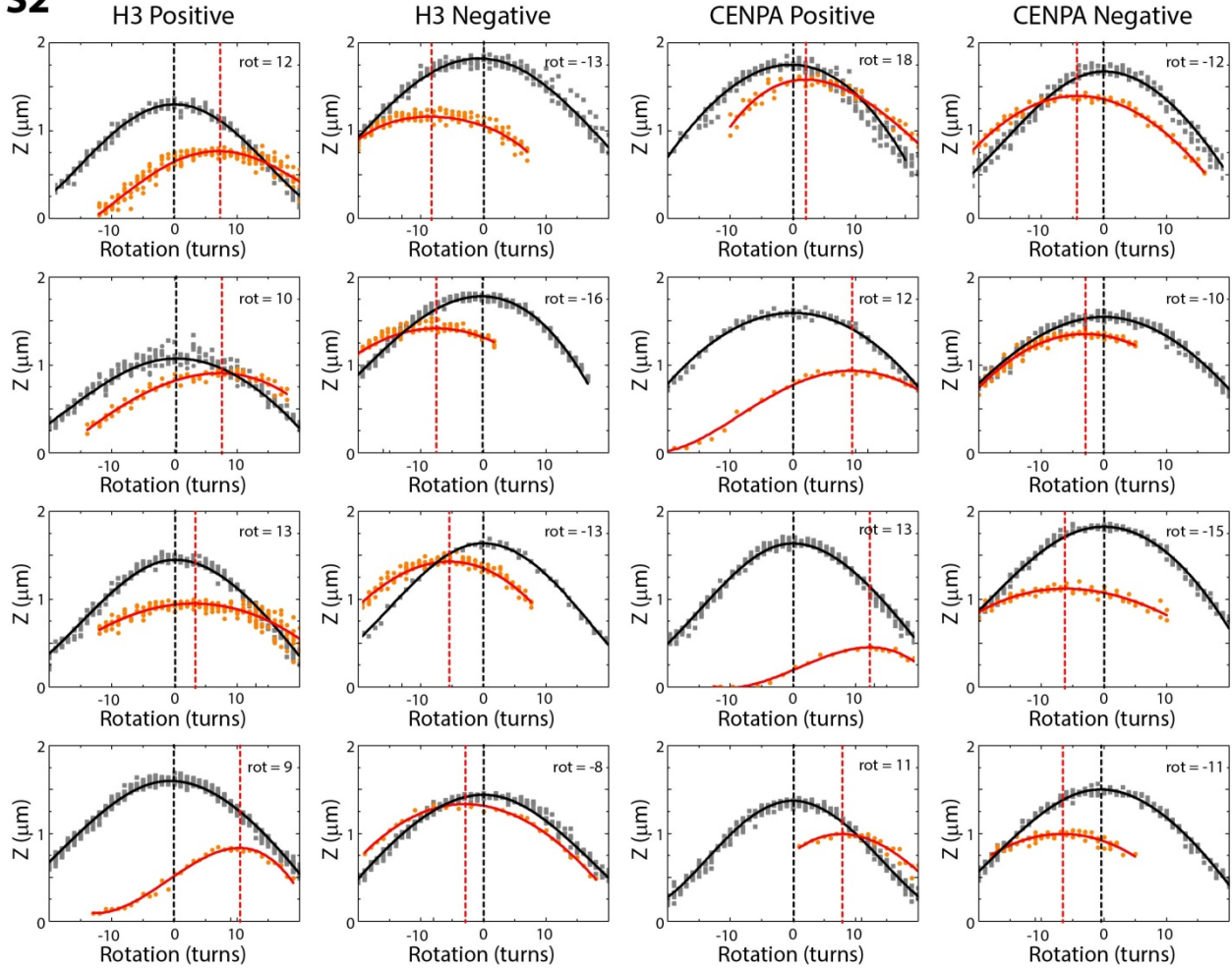
S2

Figure S2: Rotation curves. A larger set of example rotation curves similar to those of main Figure 2. Each panel represents a different molecule and measurement condition. Rotation curves of bare DNA (grey squares) before the experiment are compared to rotation curves of DNA with nucleosomes (orange circles) after nucleosome assembly. The dotted lines indicate the center of each rotation curve (black before, and red after nucleosome assembly). The applied rotations before assembly are noted down in the upper right corner. It is seen that the maximum of the orange rotation curves is always moved towards the right when positive supercoiling was applied, and to the left when negative supercoiling was applied before assembly, which indicates that it is the applied supercoiling that determines the handedness of the assembled nucleosomes. First column: H3 nucleosomes assembled onto positively supercoiled DNA. Second column: H3 nucleosomes assembled onto negatively supercoiled DNA. Third column: CENP-A nucleosomes assembled onto positively supercoiled DNA. Fourth column: CENP-A nucleosomes assembled onto negatively supercoiled DNA.

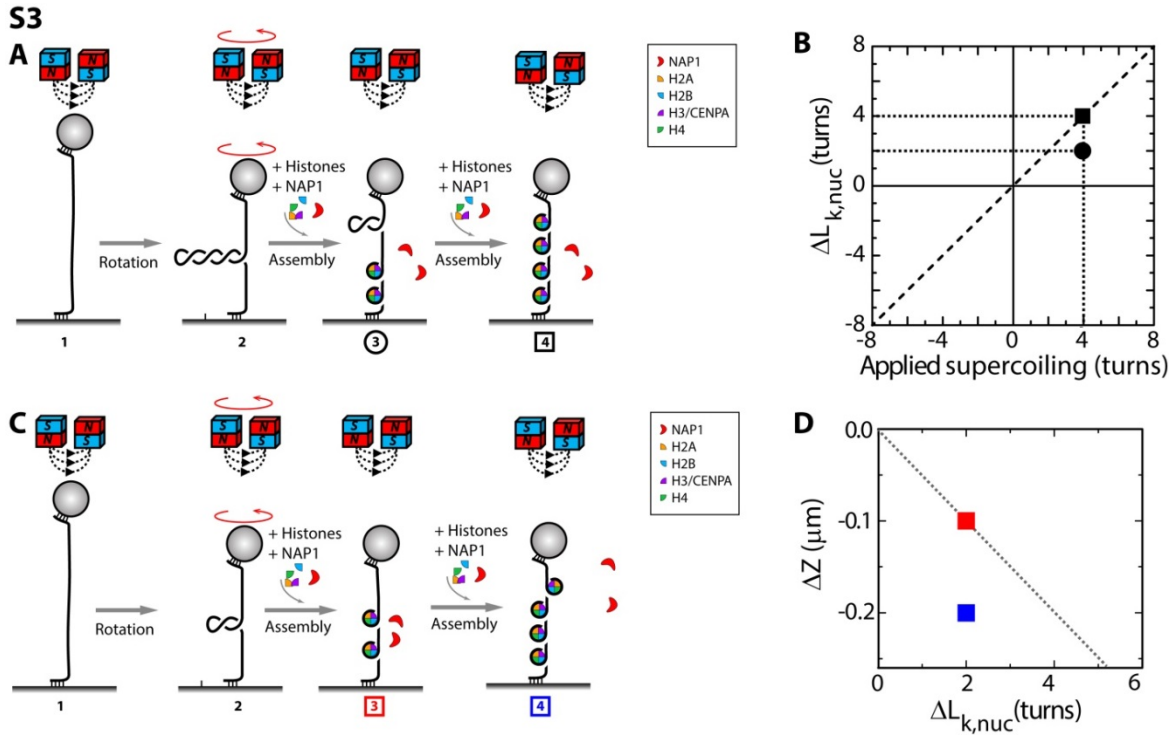


Figure S3: Illustration of partial, full and over- assembly of nucleosomes. A) Cartoon showing partial (3) and complete (4) assembly of nucleosomes with respect to the applied supercoiling. At step 1 the DNA molecule is relaxed. Consecutively at step 2, four positive supercoils are applied. At step 3, NAP1 and histones are flushed in and two positive nucleosomes are assembled, removing only two of the four positive supercoils. When two more nucleosomes are assembled in step 4, the remaining two positive supercoils are also removed. (B) Assuming that positive nucleosomes have a linking number of +1, steps 3 and 4 from cartoon A) would appear as the black circle and square in main Figure 3A, respectively: Depending on the completeness of the consecutive assembly, the total change in linking number due to nucleosome assembly is +2 (step 3) or +4 (step 4). (C) Cartoon showing complete assembly and over-assembly with respect to the applied supercoiling. At step 1 the DNA molecule is relaxed. Two positive supercoils are applied before NAP1 and histones are flushed in (step 2). These two positive supercoils are removed when two positive nucleosomes are assembled (step 3). When more nucleosomes are assembled in step 4 (over-assembly), no driving torque exists to determine the nucleosome handedness and both positive and negative nucleosomes can be assembled. (D) Assuming a compaction of 50nm per nucleosome, and that positive (negative) nucleosomes have a linking number of +1 (-1), steps 3 and 4 from cartoon C) would appear as the red and blue squares in main Figure 3B. The dotted line shows the slope of 50nm compaction per unit change in linking number. Over-assembly leads to data points that lie below this dotted line.

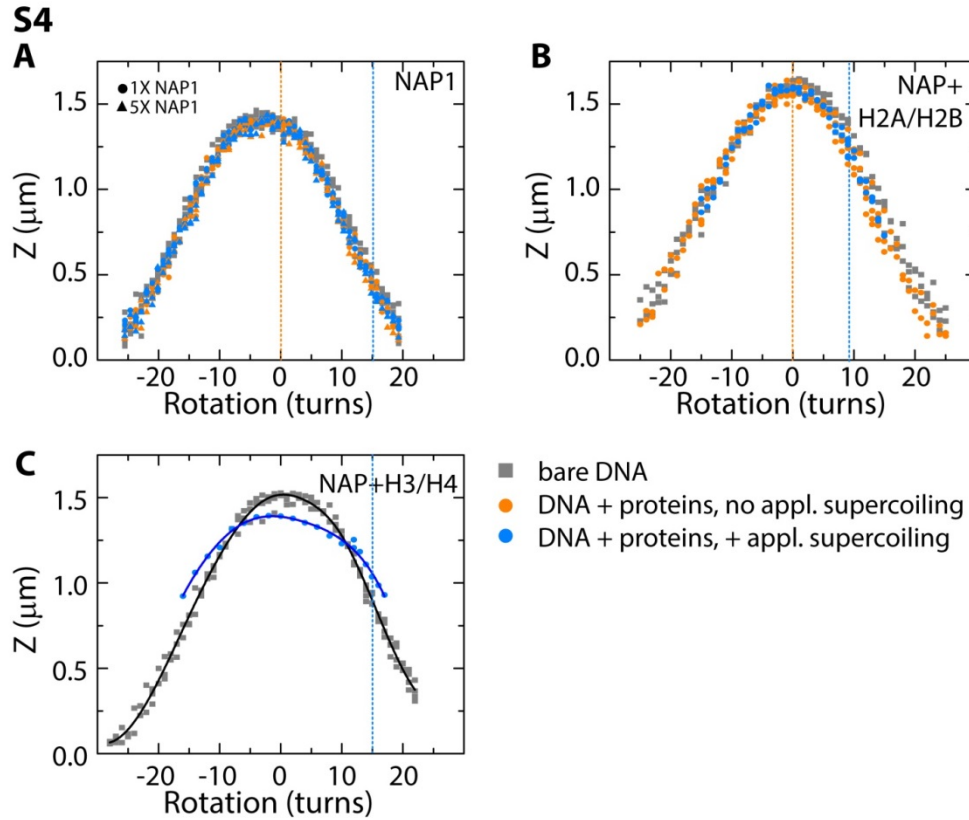


Figure S4: Control Experiments. A) *NAP1* addition: To study the effect of *NAP1* on DNA, first the bare DNA is measured (grey squares) and consecutively *NAP1* is flushed in at a concentration of 0.3nM (same amount as in the results of the main figures), while the applied rotation is 0 turns, and subsequently a rotation curve is measured (orange circles). As *NAP1* does not change the rotation curve, another 0.3nM of *NAP1* is flushed in while the applied rotation is +15 turns (blue circles). While still no change in the rotation curve occurs, the amount of flushed in *NAP1* is increased up to 1.5nM, 5 times the standard value. Again at an applied rotation of 0 (orange triangle) and +15 turns (blue triangle), no change in the rotation curve occurs. *NAP1* thus clearly has no effect on the rotation curve, and therefore no effect on the compaction or the linking number of the DNA molecule. B) *NAP1*, *H2A*, *H2B* addition: Rotation curves before (grey squares) and after (orange and blue circles) a flush of 0.4nM *NAP1* preincubated with 0.4nM *H2A* and 0.4nM *H2B*. Independent of the applied supercoiling during the protein flush (0 on orange, +15 in blue), the rotation curve of DNA in the presence of *NAP1* and *H2A/H2B* remains unaltered. C) *NAP1*, *H3*, *H4* addition: Rotation curves before (grey squares) and after (blue circles) a flush of *NAP1* (0.2nM) preincubated with *H3* (0.7nM) and *H4* (0.7nM). The applied supercoiling is +15 supercoils. In agreement with previous magnetic tweezers experiments on *NAP1* and *H3* and *H4*, the rotation curves broadens and decreases its maximum¹⁻³.

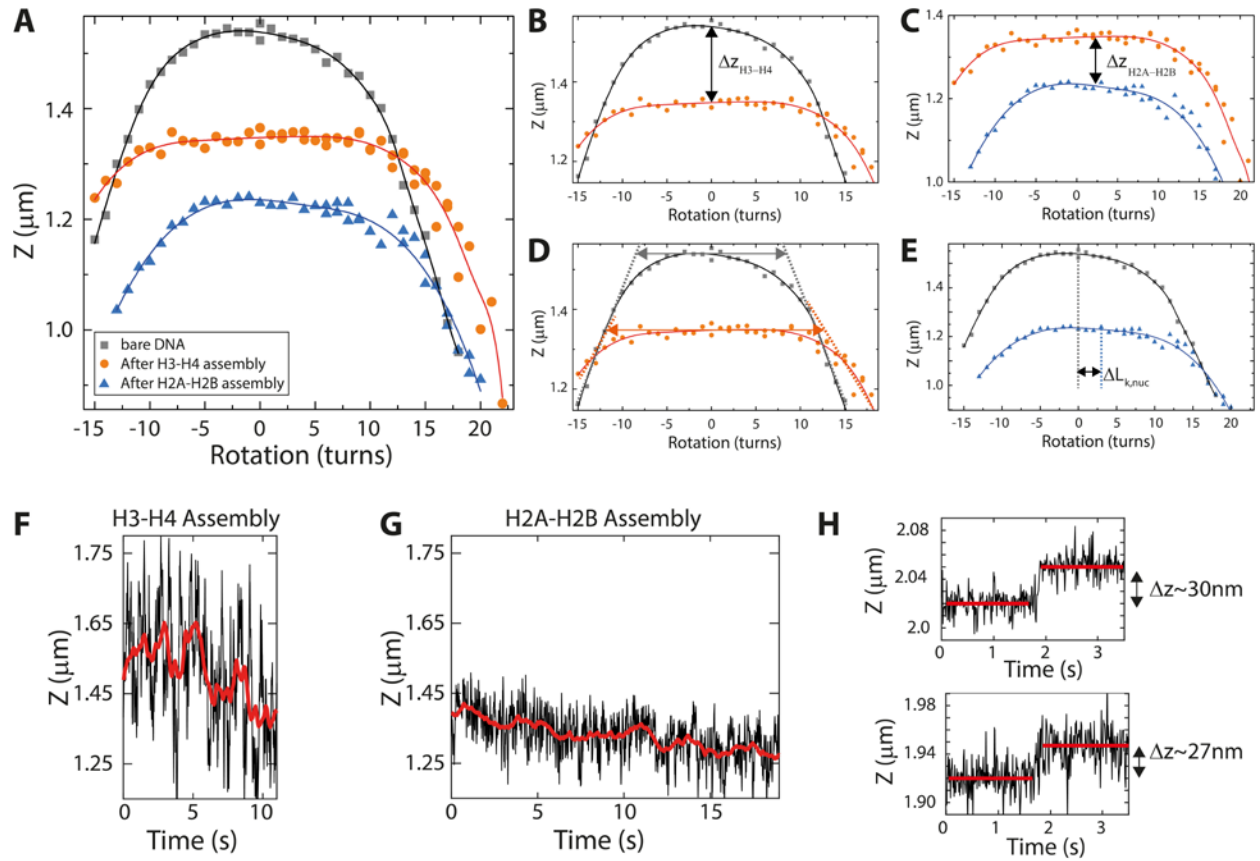


Figure S5: Two-step nucleosome assembly. A) Rotation curves of two-step nucleosome assembly. To verify that the shift in rotation curve occurs after *complete* assembly of an octameric nucleosome, we assembled nucleosomes in a two-step manner on positively supercoiled DNA – similarly as previously done in the absence of supercoiling¹. Prior to assembly, the rotation curve of bare DNA at 0.3pN applied stretching force was measured (grey squares, black line is data interpolation). Next, at zero applied rotations, *Drosophila* NAP1 preincubated with *Drosophila* core histones at a ratio NAP1:H3:H4 of 1:0.93:0.93 was flushed in and tetramers were assembled onto the DNA (orange circles, red line is data interpolation). Finally, unbound NAP1 and H3-H4 histones were flushed out, +12 turns were applied to the DNA with tetramers, and NAP1 preincubated with histones at a ratio NAP1:H2A:H2B of 1:0.93:0.93 was flushed in to form complete nucleosomes onto the DNA (blue triangles, blue line is data interpolation). B-E) show parts of the data shown in A). B) The compaction after the tetramer assembly, Δz_{H3-H4} , is the difference in height of the rotation curves before and after assembly of H3-H3 tetramers. In this experiment $\Delta z_{H3-H4} = 200 \pm 25$ nm. C) The compaction due to the assembly of H2A and H2B onto the previously assembled H4-H4 tetramers is $\Delta z_{H2A-H2B} = 113 \pm 25$ nm. D) As previously shown in Ref.1-3, the assembly of H3-H4 tetramers broadens the rotation curve as tetramers can change their handedness when supercoiling is applied, resulting in a broadening of the rotation curve by 1.7 turns per assembled tetramer¹. Based on the broadening of 6 ± 2 turns, we conclude that 3 to 4 tetramers were assembled onto the DNA. E) The linking-number shift due to complete nucleosome assembly in this experiment was 3 ± 1 turns. Note that the width of the rotation curve of DNA with nucleosomes is less wide than that of the H3-H4 tetrasomes and now again comparable to the width of the bare DNA rotation curve. F) Length

decrease of the DNA molecule versus time when the H3-H4 tetrasomes were assembling onto the DNA. G) Length decrease of the DNA molecule versus time when subsequent addition of H2A and H2B finalized the assembly of the nucleosomes onto the DNA. H) Two examples of the increase in the length of the molecule after a high force ($>15\text{pN}$) was applied to disassemble the inner turn of the nucleosome. The disassembly steps are 27 and 30nm, in agreement with the results in Fig. 4B and previously reported values³⁻⁷.

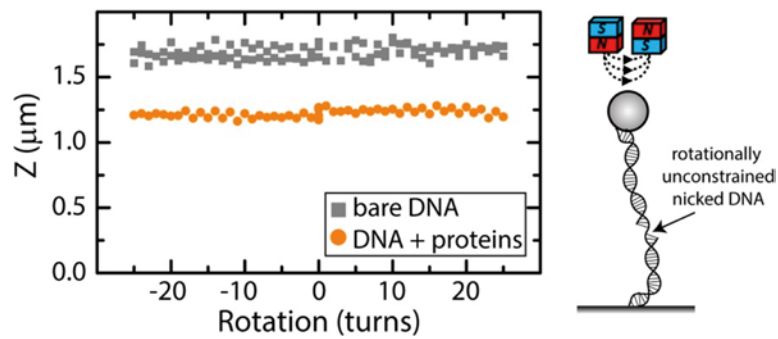
S6

Figure S6: Rotation curve on a nicked DNA molecule. The left panel shows the rotation curves of a nicked DNA molecule before (grey squares) and after (orange circles) nucleosome assembly. When a single nick occurs in a double stranded DNA molecule, the single DNA backbone that remains intact is free to rotate about its axis (see cartoon on the right). Therefore, rotating the magnets will not induce any supercoiling to the DNA and the end-to-end length is independent of the applied number of magnet rotations. Nucleosomes can still assemble and will decrease the DNA end-to-end length Z .

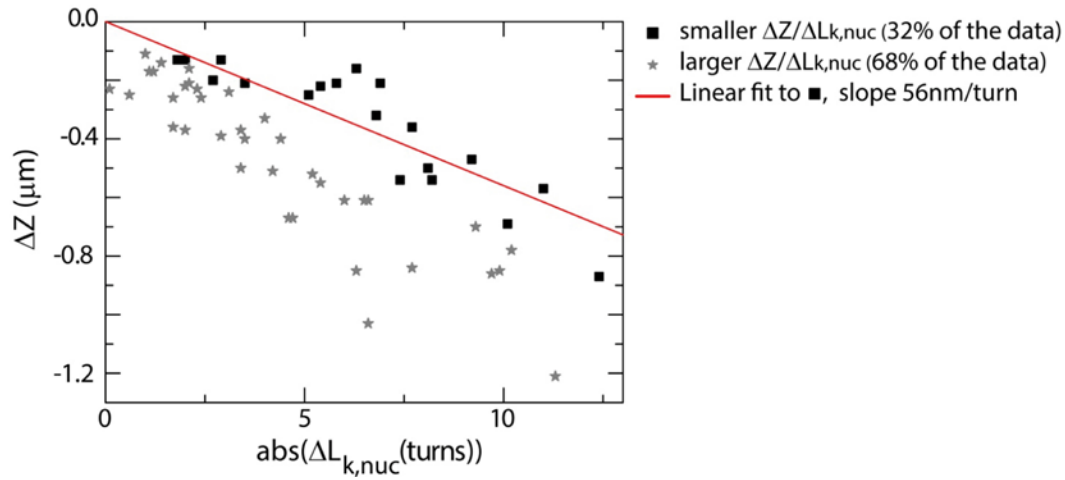
S7

Figure S7: Linking number change and compaction upon nucleosome assembly. Similar to main Figure 3, the DNA end-to-end length Z is given as function of the absolute value of the total linking number of the assembled nucleosomes. The measured $\text{abs}(\Delta Z/\Delta L_{k,nuc})$ is an upper limit, due to multiple reasons (cf. discussion in Figure S3). For example, when more nucleosomes assemble than the supercoiling that is applied, there is no driving force that determines the handedness of the assembled nucleosomes (cf. Figures S3C and D), allowing nucleosomes of both handednesses to form. To estimate of the minimal compaction per linking number, a linear fit is made through the origin to one third of the data with the smallest $\text{abs}(\Delta Z/\Delta L_{k,nuc})$. The slope of this fit gives a compaction of 56nm per unit turn.

Supplemental References

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Supplemental Information

Sequence of the magnetic tweezers construct, without handles, ordered from magnetic bead to glass surface.

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