Supporting Material: The role of histone tails in the nucleosome: A computational study

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Methods

REMD configurations

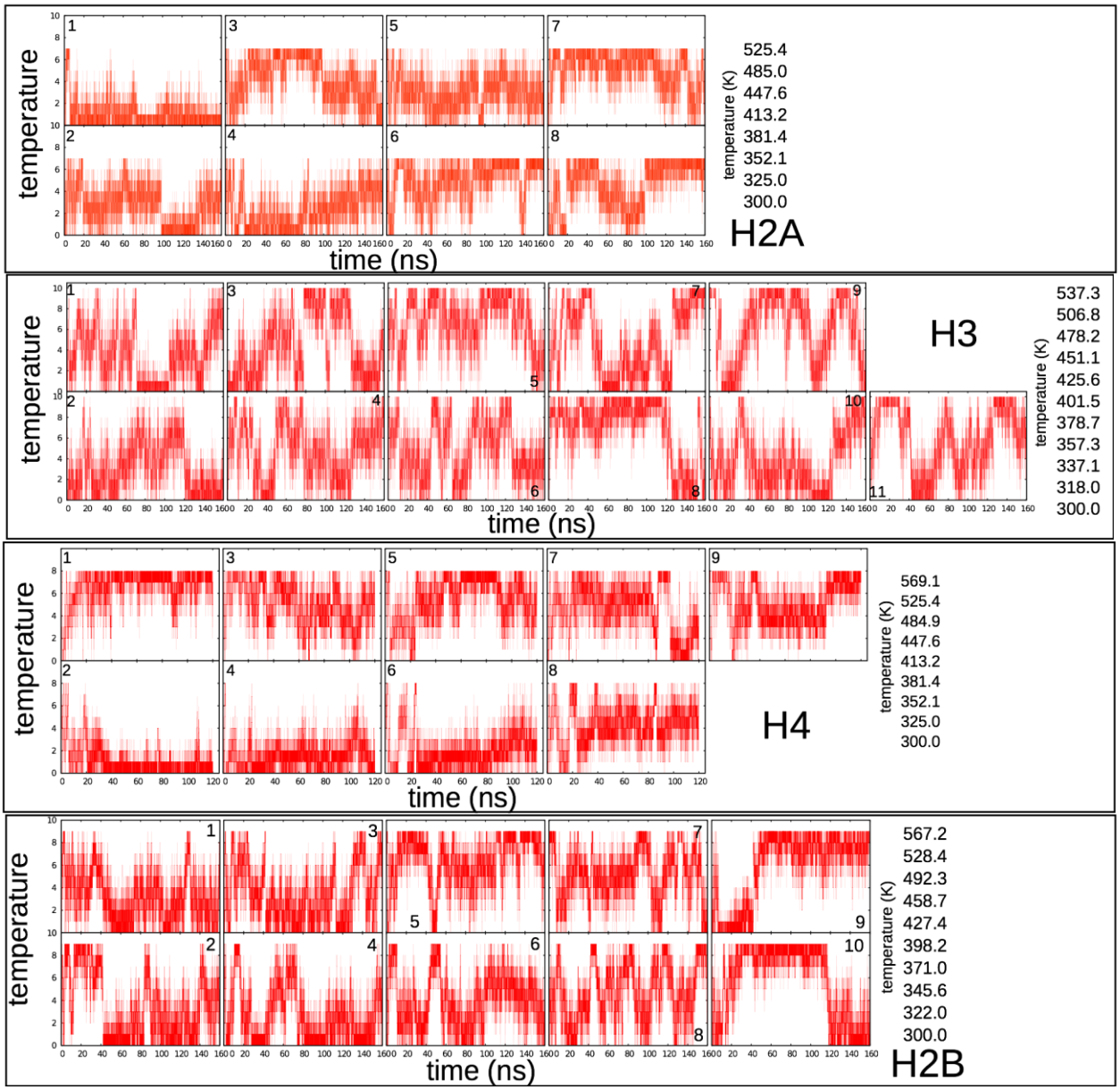

Figure S1. **Temperature space of the REMD simulations**. Results for trajectories of histone tails H3 (160 ns), H2B (160 ns), H4 (120 ns) and H2A (160 ns). Panels show the different replicas starting from the chosen temperature levels.

Test 1: Robustness of results against REMD conditions

To investigate a possible dependence of the results on the exchange rate (number of replicas) we performed a further simulation of the histone tail H2A on the nucleosome using 10 instead of 8 replicas in the same temperature range. The result is an exchange probability of 0.22. At the same time we reduced the frequency for exchange attempts from an attempt every 100 steps (0.2 ps) to an attempt every 400 steps (0.8 ps). Figure S2 shows the temperature space and exchange probabilities for both runs.

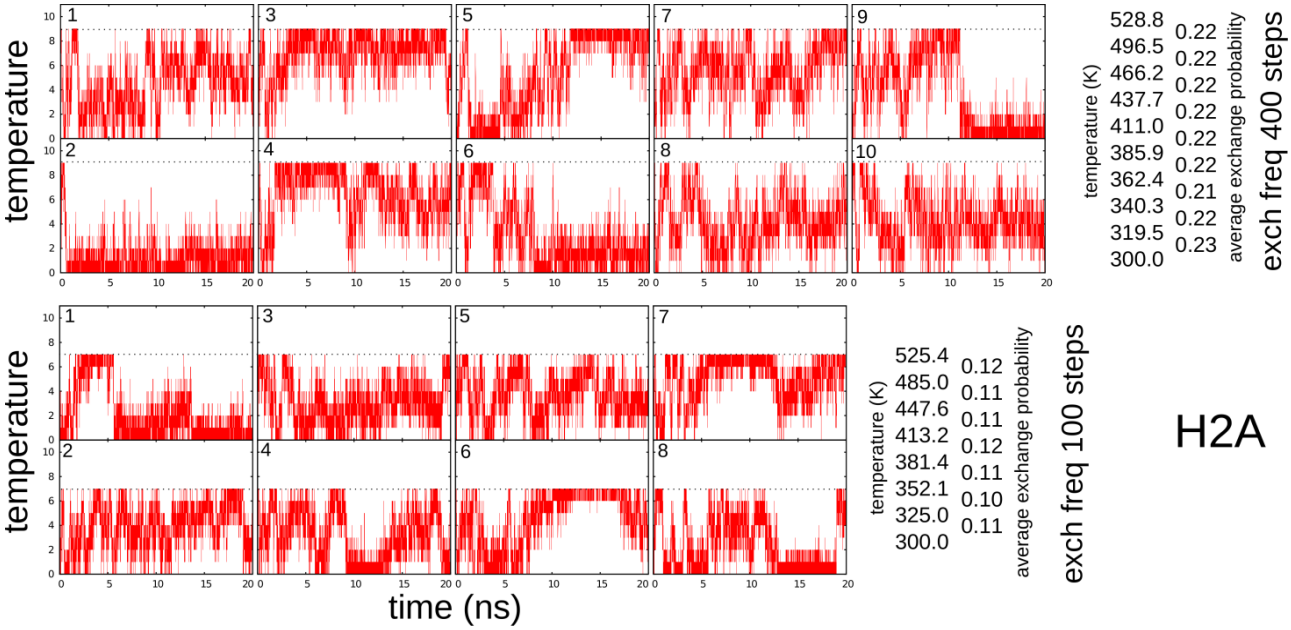

Figure S2**. Temperature space of REMD simulations of H2A tail**. Results of a REMD simulations with 10 replicas, a resulting exchange probability of about 0.22 and exchange attempts every 0.8 ps (400 steps) and the simulation of H2A with 8 replicas, an exchange probability of 0.1 and exchange attempts every 0.2 ps (100 steps). Panels show the different replicas starting from the chosen temperature levels.

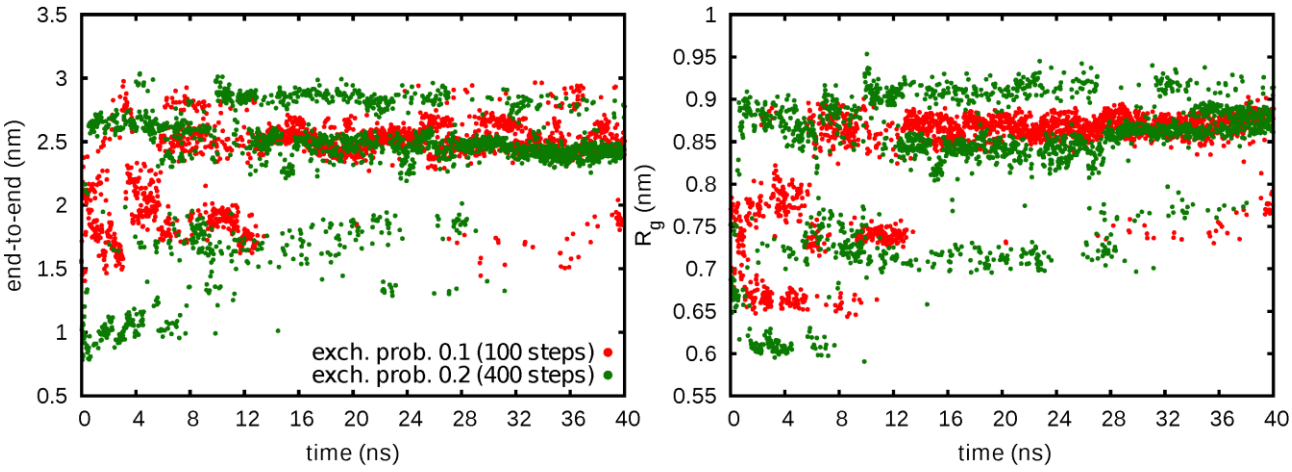

Figure S3. **End-to-end distance and radius of gyration**. Comparison of results of the two trajectories shown in Fig. S2.

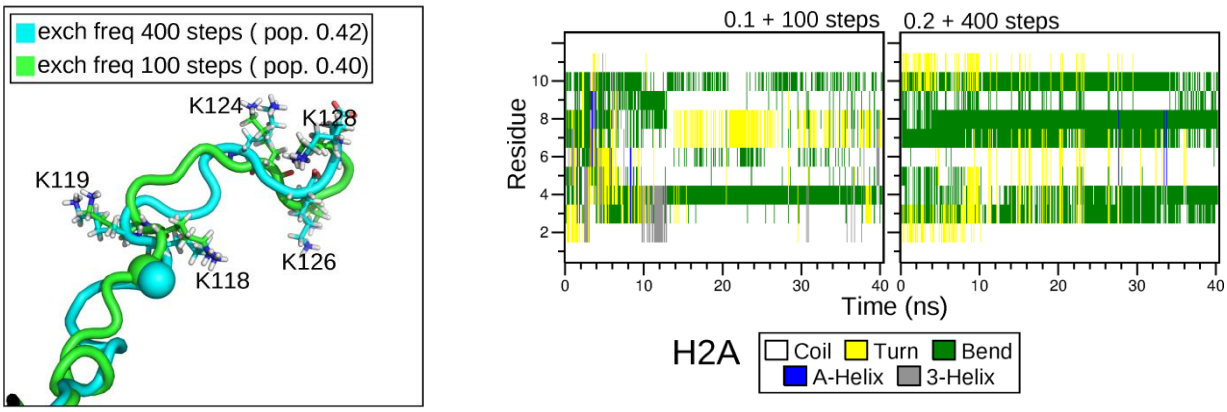

Figure S4**. Conformation and secondary structure of the H2A tail**. Comparison of results of the two trajectories shown in Fig. S2.

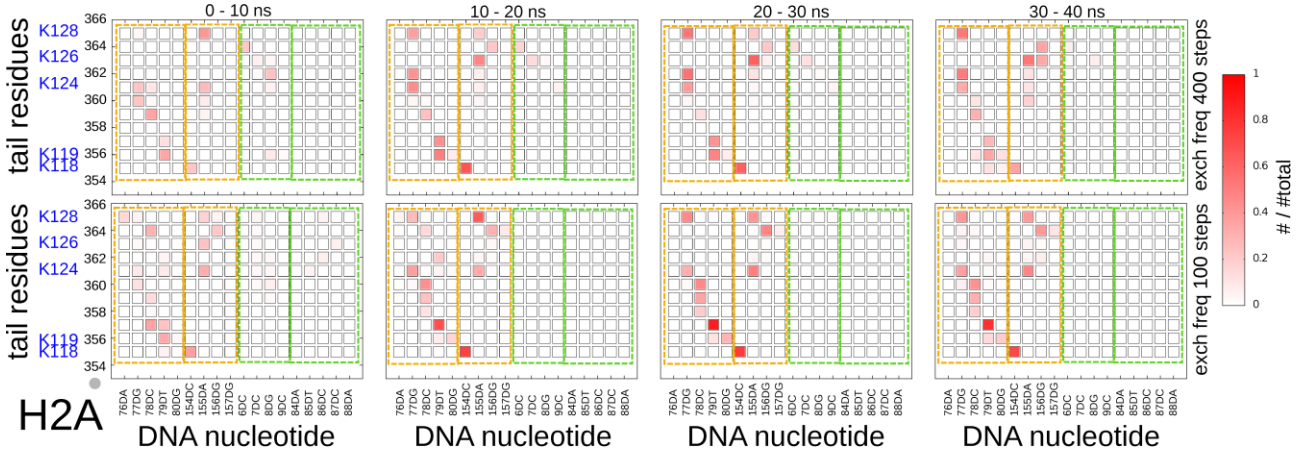

Figure S5. **Probability of contacts between histone tail residues and DNA phosphate for H2A tail.** Comparison of results of the two trajectories shown in Fig. S2.

The exchange is in both runs sufficient. For a comparison of the dynamics of both REMD runs we study the end-to-end distance and the radius of gyration (Fig. S3), results of a cluster analysis, the secondary structure (Fig. S4) and DNA:tail contacts (Fig. S5).

Both simulations converge to the same end-to-end distance and radius of gyration, whereas the 0.1 (100 steps) REMD seemed to converge faster. Results for secondary structure are also similar. In both cases we find bends around residue 4 and 10 and coil around the same residues.

Figure S4 shows also the highest populated clusters of both REMD runs. The probabilities are 0.42 and 0.40 for the 400 steps and 100 steps exchange frequency. Charged lysine residues, except the K126, make contacts with the same DNA phosphat groups for both runs.

For a comparison of DNA:tail contacts we devided the 40 ns trajectory into four parts and calculated the population of each contact (Fig. S5). Both results show the same DNA:tail contacts, but the run with 10 replicas and attempts every 400 steps seems to converge more slowly. We expect the results to converge to the same DNA:tail contacts for the whole tail when we would extend the simulation.

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Test 2: Test of an longer cutoff in the GB simulation

A too short cutoff can have dramatic influences on the dynamics of the histone tails (see Ref. (1)). Compared to the example shown in (1) our simulations contains 10 bp of linker DNA. For this reason we do not expect such an drastic effect, since the H3 tail is close to the linker DNA.
To investigate a possible dependence on the chosen cutoff we performed further REMD simulations of H3 and H2A using a cutoff of 2.5 nm instead of 1.5 nm. This results in a longer simulation time (0.6 ns/day instead of 3 ns/day). Fig. S6 shows results for the number of DNA:tail contacts for H2A and H3. The number of contacts for the REMD simulation with a 2.5 nm cutoff agree well for both tails with results using a 1.5 nm and we do not expect any influence on the dynamics of the histone tails in the REMD simulations.

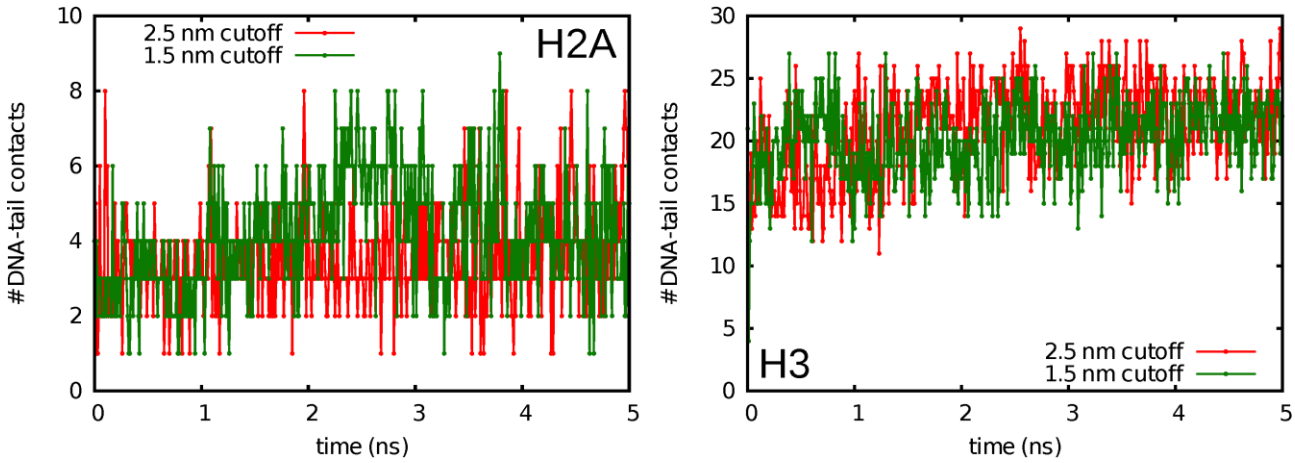

Figure S6. **Number of contacts between DNA and histone tail H2A and H3.** Comparison of results using a cutoff of 1.5 and 2.5 nm in the GB simulation.

Test 3: Dependence of results on the definition of the freeze group

To justify the approximation of freezing the whole nucleosome except the tail under investigation, we performed a further simulation of the H4 tail keeping 16 residues less fixed. The new system contains 42 free residues instead of 26 as in the tail definition in Fig. 1.
We have chosen H4 for the test, since we extended already H2A in the present REMD simulation. For H3 and H2B we do not expect any influence since both N-terminal tails protrude between two DNA strands and are thus fixed by binding to the phosphate groups (compare Fig. S31 and S32).
Fig. S7 shows results for end-to-end distance and the radius of gyration. Both runs converge to the same values, whereas the convergence for the shorter tail is faster.
The conformation of the cluster with the highest population and the secondary structure agree well for both system from residue 1 till 19 (see Fig. S8). The reason for this can be seen in Fig. S9 showing the probability of the DNA:tail contacts. Residues R3, K5, K8, K12, K16 and R17 make the same contacts for both systems (after 30 ns).

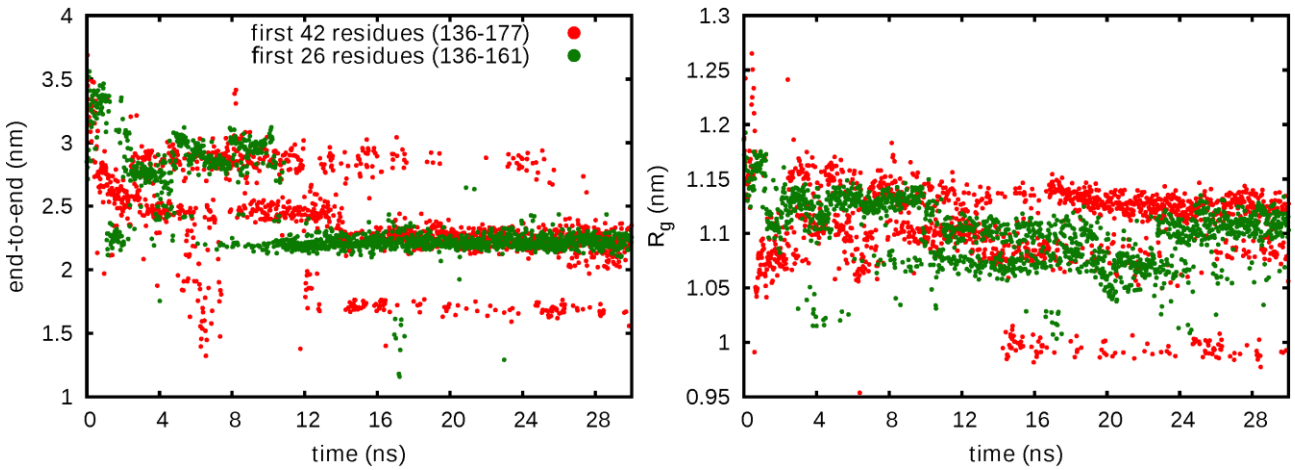

Figure S7. **End-to-end distance and radius of gyration**. Comparison of results of the two REMD simulation with a different number of free residues of the histone H4.

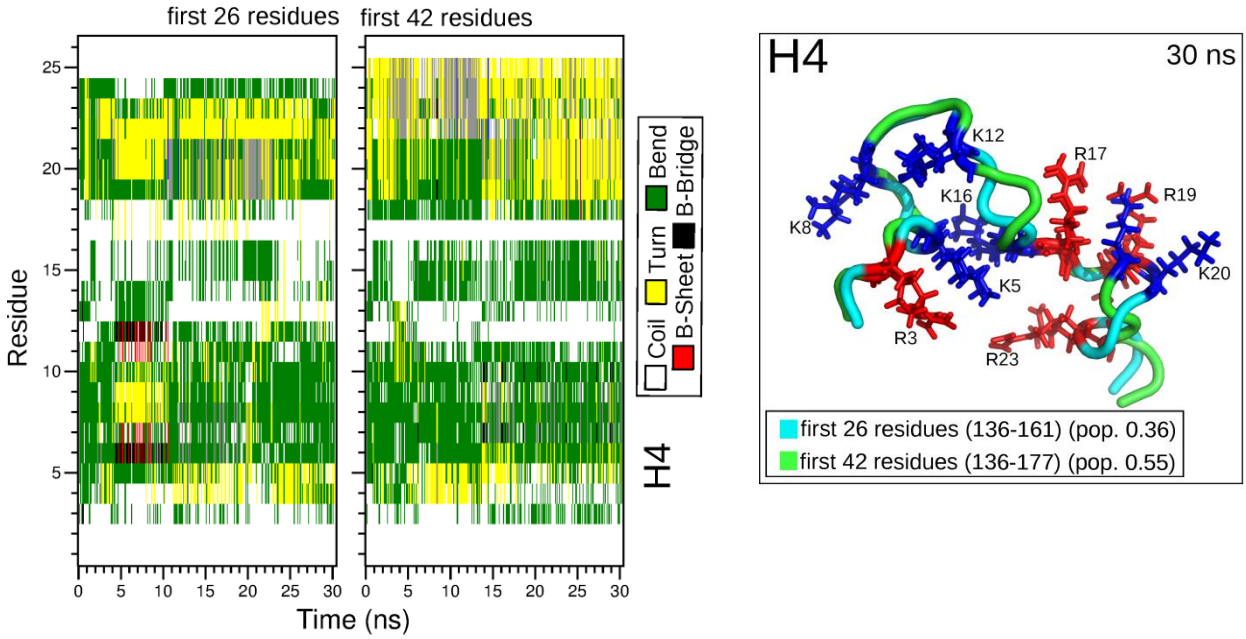

Figure S8. **Secondary structure and conformation of the H4 tail**. Comparison of results of the two REMD simulation with a different number of free residues of the histone H4.

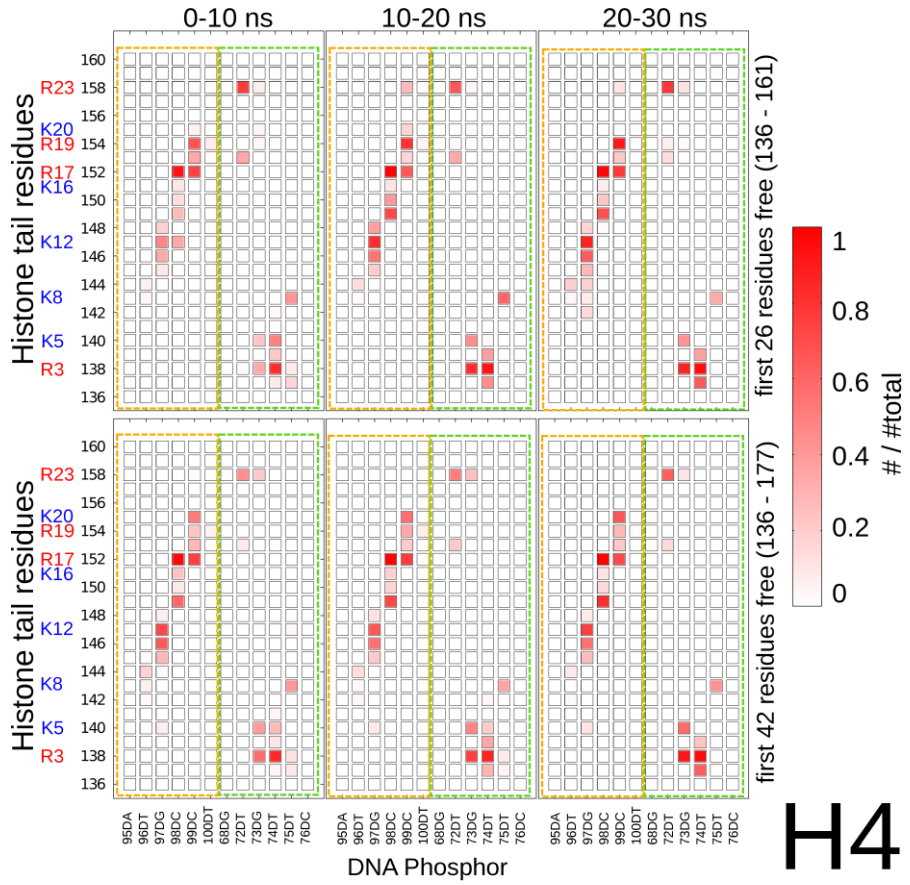

Figure S9. **Probability of contacts between histone tail residues and DNA phosphate for H4 tail.** Comparison of results of the two REMD simulation with a different number of free residues of the histone H4.

Convergence

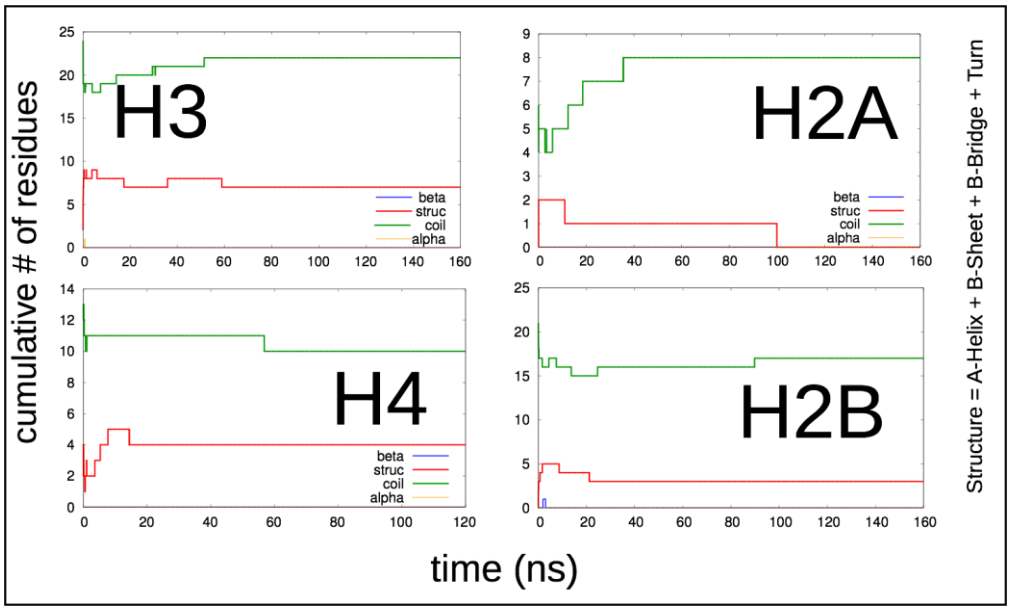

Figure S10. **Accumulated number of residues in a structure for all histone tails.**

Results of implicit REMD simulations

Isolated histone tails

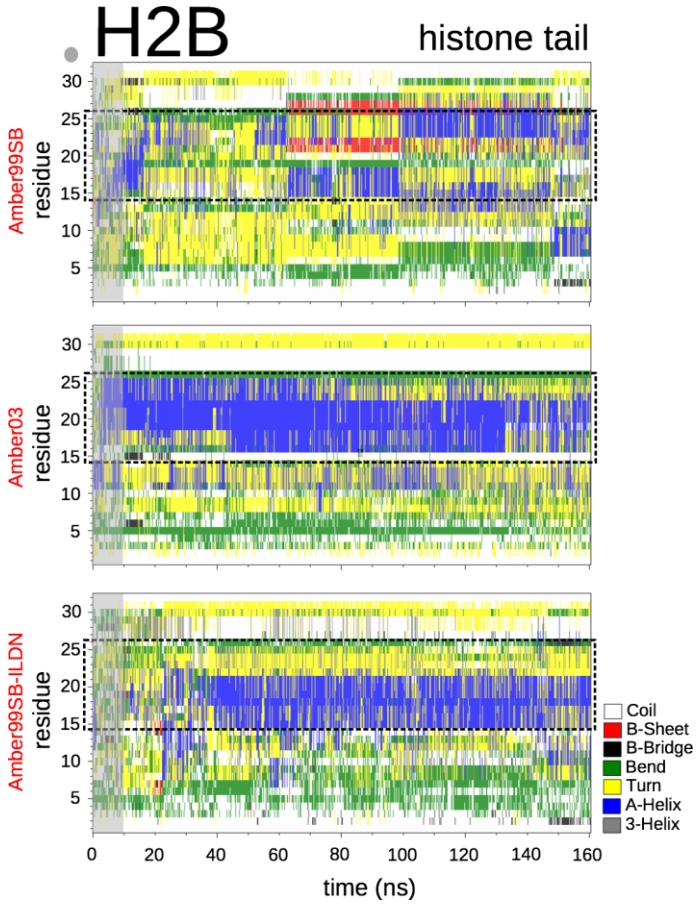

Figure S11. **Secondary structure of the isolated H2B histone tail**. Shown are results for the lowest temperature level 300 K of the REMD calculation. Used were the three force fields Amber99SB, Amber03, Amber99SB-ILDN . Black boxes are added to make a comparison between different force fields easier

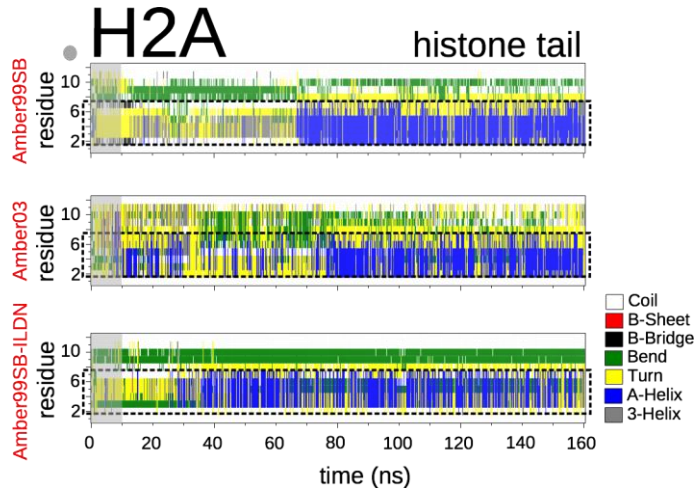

Figure S12. **Secondary structure of the isolated H2A histone tail**. Shown are results for the lowest temperature level 300 K of the REMD calculation. Used were the three force fields Amber99SB, Amber03, Amber99SB-ILDN . Black boxes are added to make a comparison between different force fields easier

Results for the nucleosome

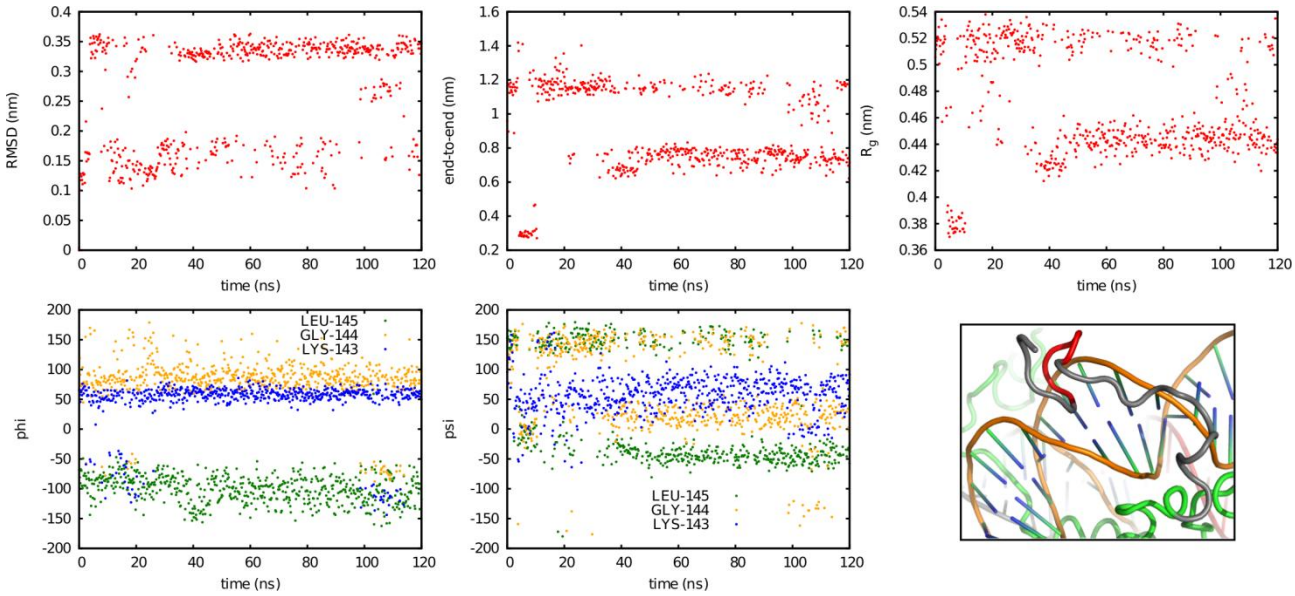

Figure S13. **RMSD, end-to-end distance, radius of gyration, and the dihedral angles *φ* and ψ for a part of the H4 tail** (residue 7 to 11; GKGLG, red in right lower panel).

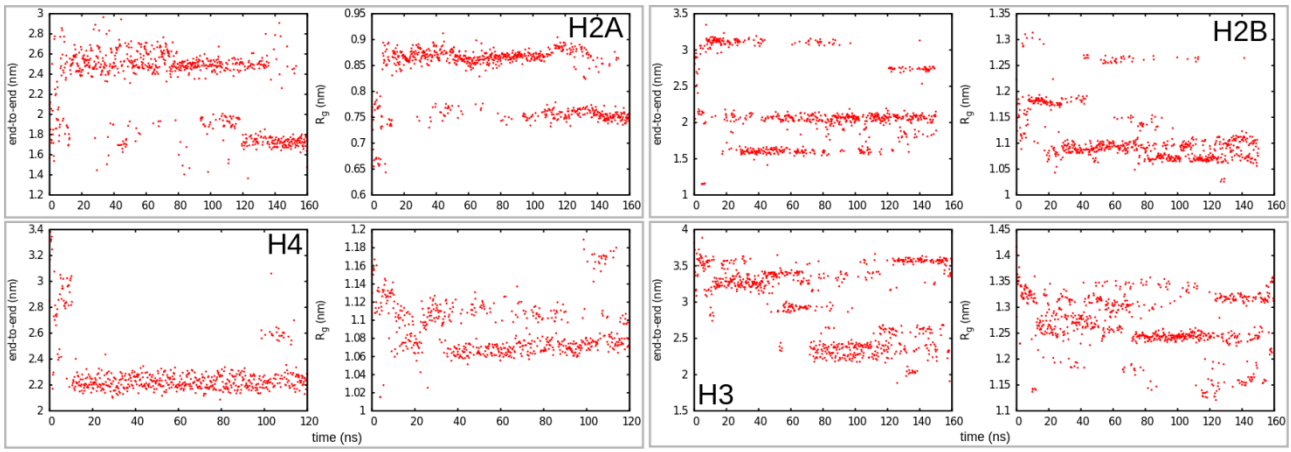

Figure S14**. End-to-end distance and radius of gyration for H4, H3, H2B and H2A tail**.

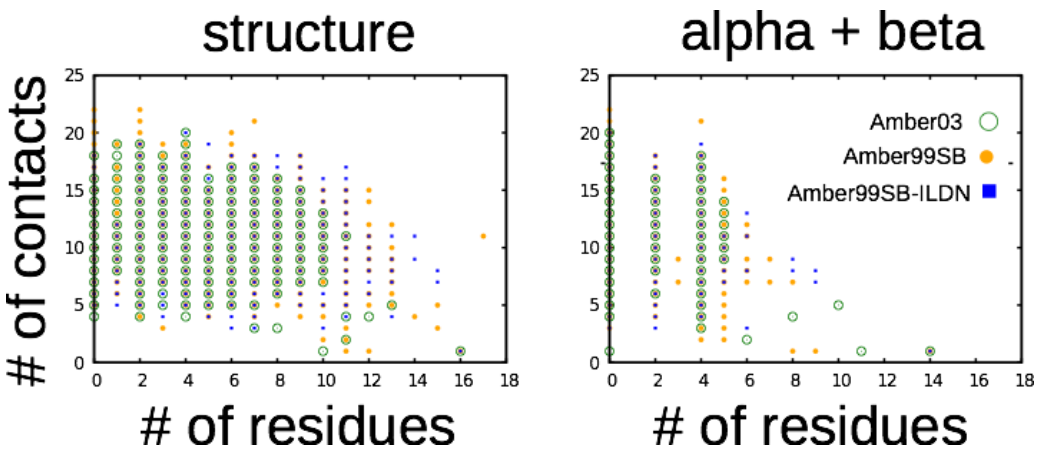

Figure S15. **Number of contacts versus number of residues in a secondary structure**. Results for force fields Amber99SB, Amber03 and Amber99SB-ILDN are shown.

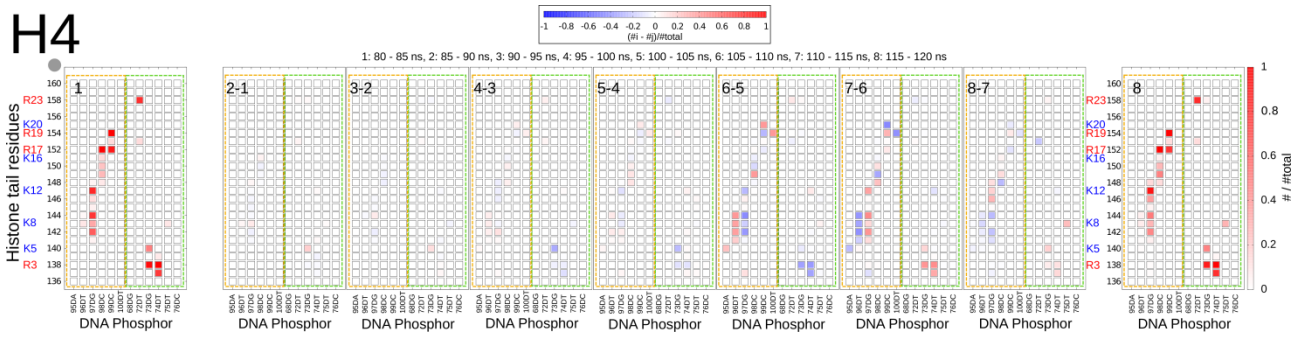

Figure S16. **Probability of contacts between histone tail residues and DNA phosphate for H4 tail**. The last part of the trajectory (80 to 120 ns) is divided in eight smaller intervals to see how the contacts evolve. The panels left and right show the total probabilities, the panels in-between the increase or decrease.

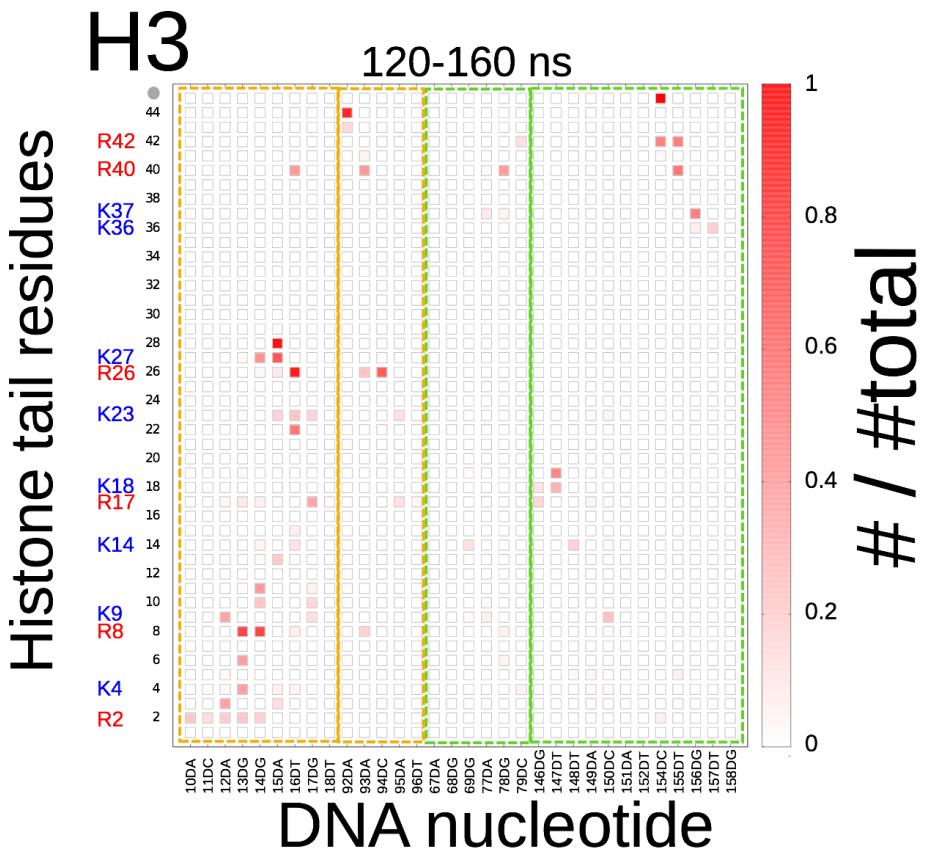

Figure S17. **Probability of contacts between histone tail residues and DNA phosphate for H3 tail**. The last part of the trajectory (120 to 160 ns) was studied and the threshold for a contact was 0.3 nm. Coloured boxes indicate different DNA strands.

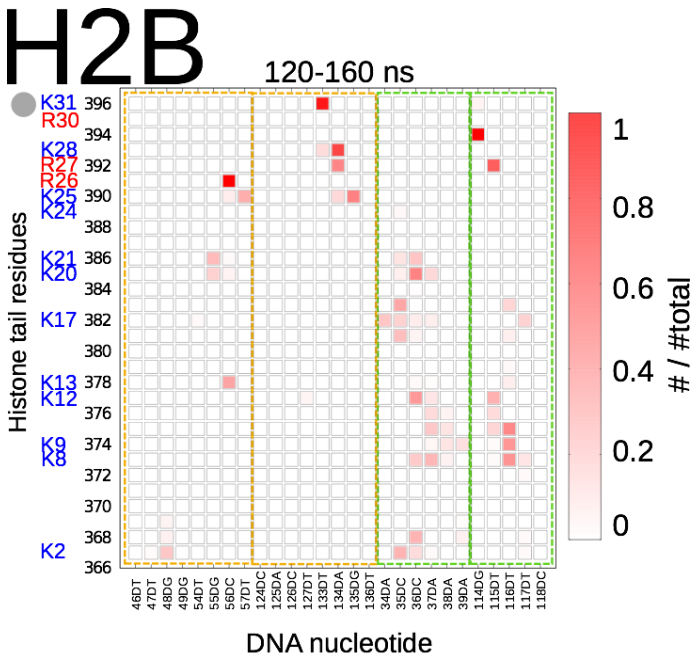

Figure S18. **Probability of contacts between histone tail residues and DNA phosphate for H2B tail**. The last part of the trajectory (120 to 160 ns) was studied and the threshold for a contact was 0.3 nm. Colored boxes indicate different DNA strands.

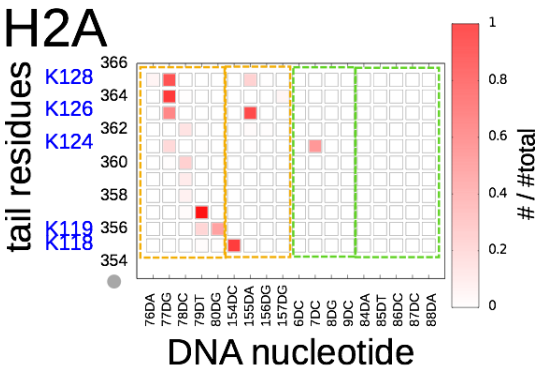

Figure S19. **Probability of contacts between histone tail residues and DNA phosphate for H2A tail**. The last part of the trajectory (120 to 160 ns) was studied and the threshold for a contact was 0.3 nm. Colored boxes indicate different DNA strands.

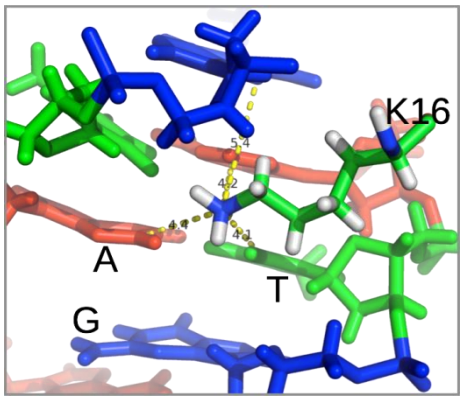

Figure S20. **Cations-π interaction of K16 of H4 tail**. Residue K16 and the surrounding base pairs adenine (red), guanine (blue) and thymine (green). Distances were calculated between the cationic group of K16 and the centroid of the base ring. Angles are defined as the angle formed between the cationic group, the base centroid, and a point positioned normal to the plane. Distances and angles are 0.42 nm, 54° or 0.44 nm, 48° between adenine and K16, 0.54 nm, 22° between guanine and K16 and 0.41 nm, 72° between thymine and K16.

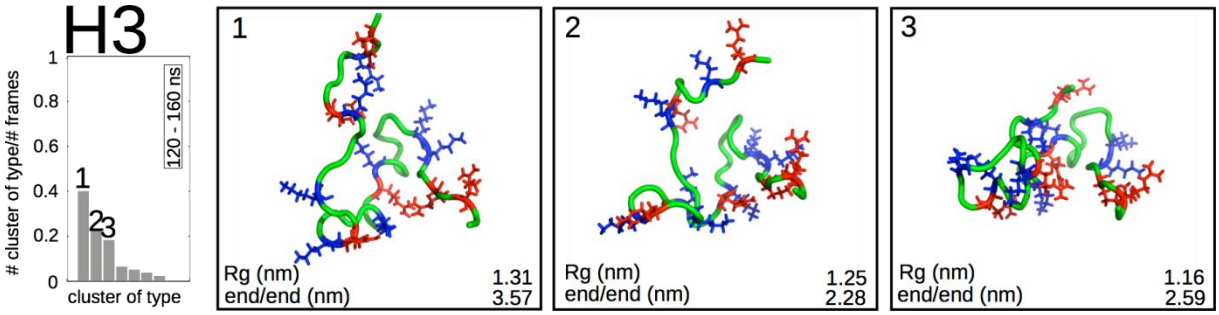

Figure S21. **Results of a cluster analysis of H3 tail**. The cutoff was 0.2 nm and the last part of the trajectory (120 to 160 ns) was used. The probability and the conformations of the cluster representative of the three most populated clusters are shown.

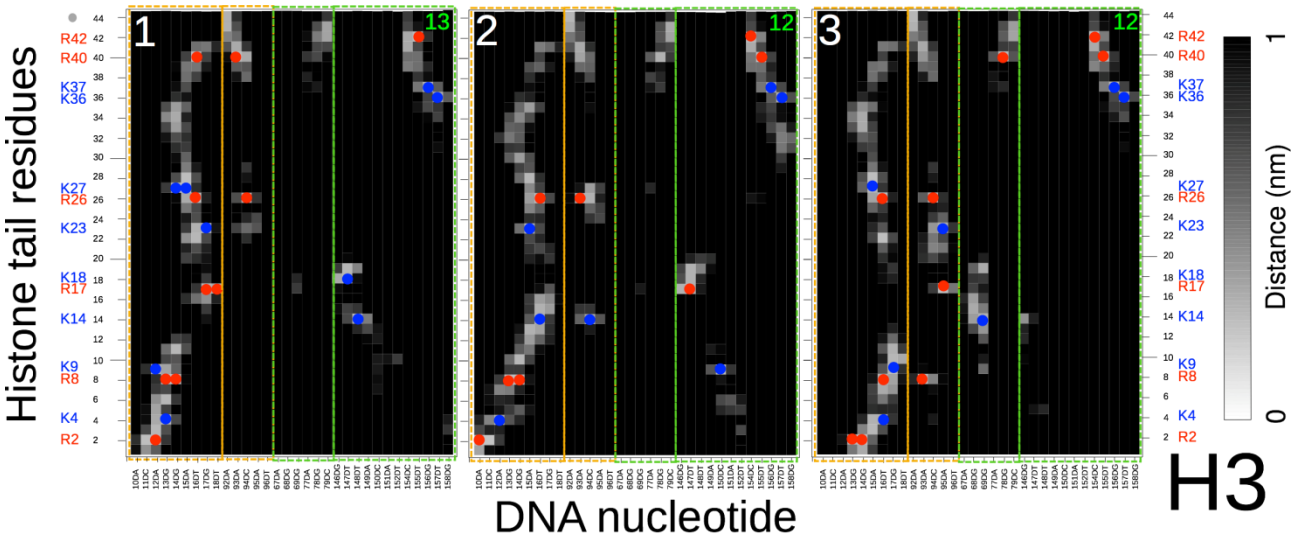

Figure S22. **Distance maps for the three most populated clusters of H3 tail**. Distances were measured between histone tail residues and the phosphate group of each nucleotide. Blue circles and red circles indicate contacts of lysines and arginines with DNA phosphate groups (cutoff 0.3 nm). Green numbers indicate the number of neutralized charges.

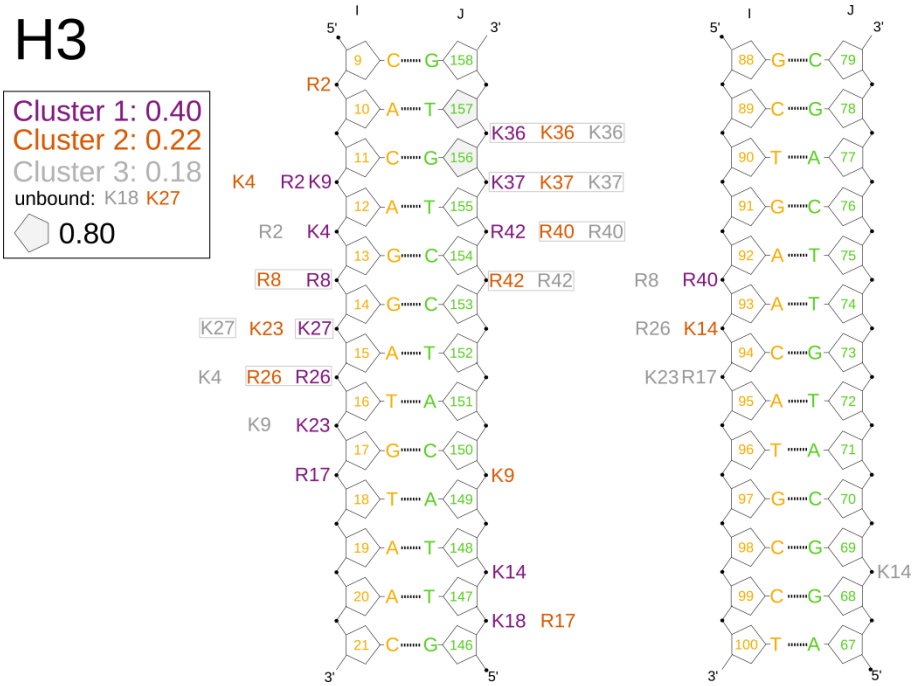

Figure S23. **Tail:DNA interactions of the H3 tail**. Interactions between histone tail and DNA for the clusters found in Fig. S8. Grey boxes indicate interactions found in all three clusters.

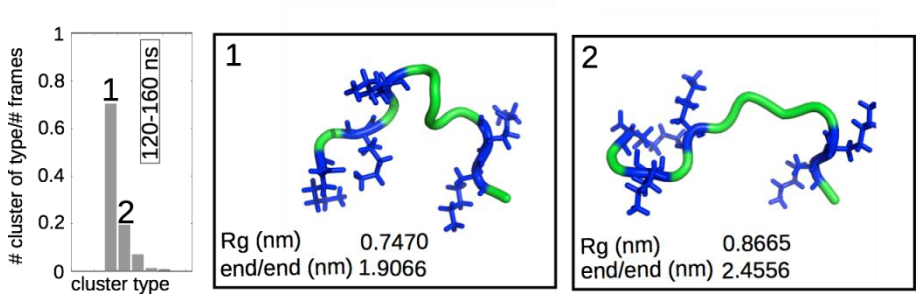

Figure S24. **Results of a cluster analysis of H2A tail**. The cutoff was 0.2 nm and the last part of the trajectory (120 to 160 ns) was used. The probability and the conformations of the cluster representative of the three most populated clusters are shown.

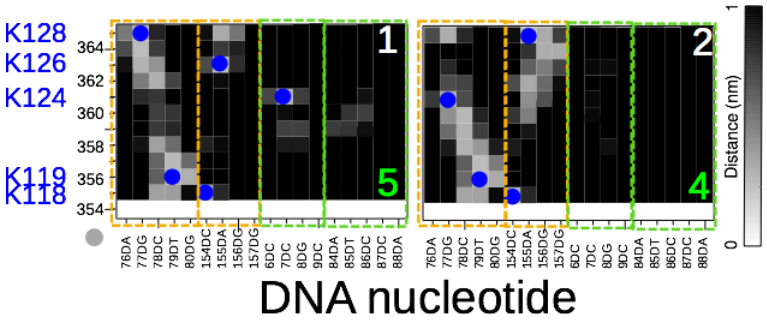

Figure S25. **Distance maps for the three most populated clusters of H2A tail**. Distances were measured between histone tail residues and the phosphate group of each nucleotide. Blue circles and red circles indicate contacts of lysines and arginines with DNA phosphate groups (cutoff 0.3 nm). Green numbers indicate the number of neutralized charges.

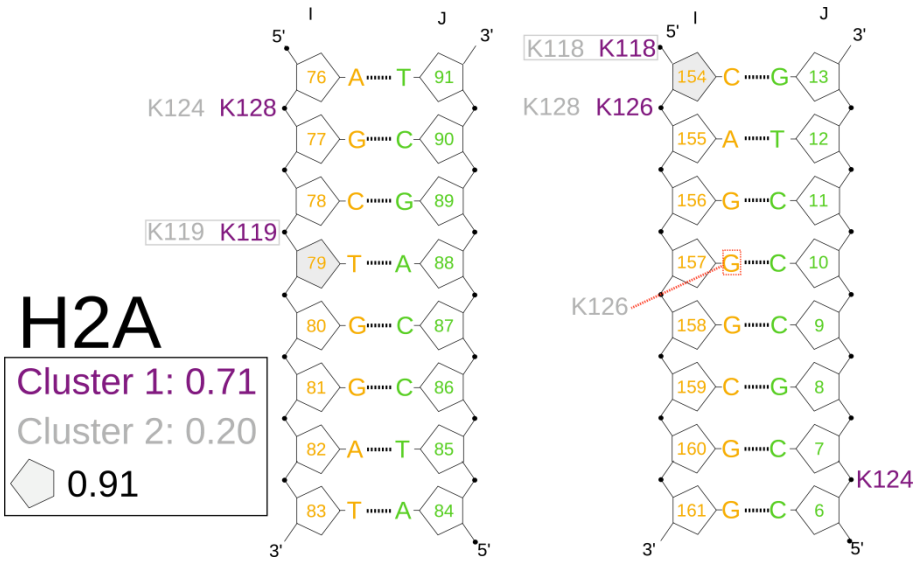

Figure S26. **Tail:DNA interactions of the H2A tail**. Interactions between histone tail and DNA for the clusters found in Fig. S11. Grey boxes indicate interactions found in both clusters. The red dashed line illustrate cation-π interactions.

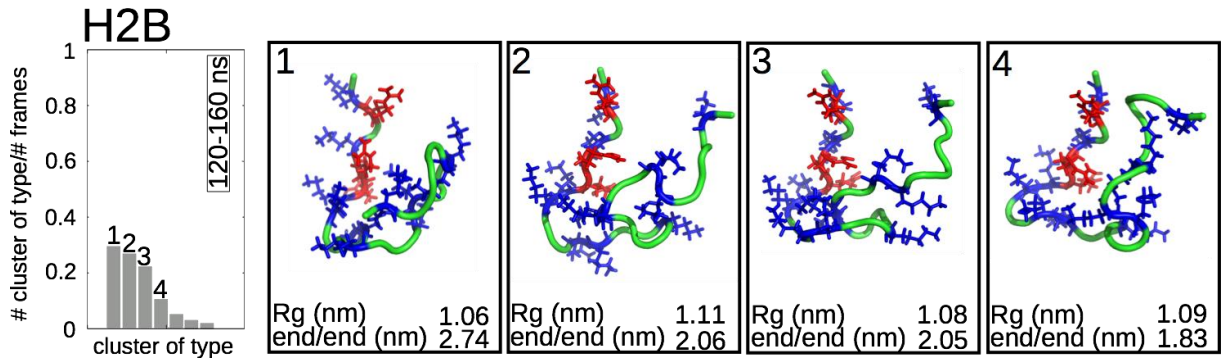

Figure S27**. Results of a cluster analysis of H2B tail**. The cutoff was 0.2 nm and the last part of the trajectory (120 to 160 ns) was used. The probability and the conformations of the cluster representative of the three most populated clusters are shown.

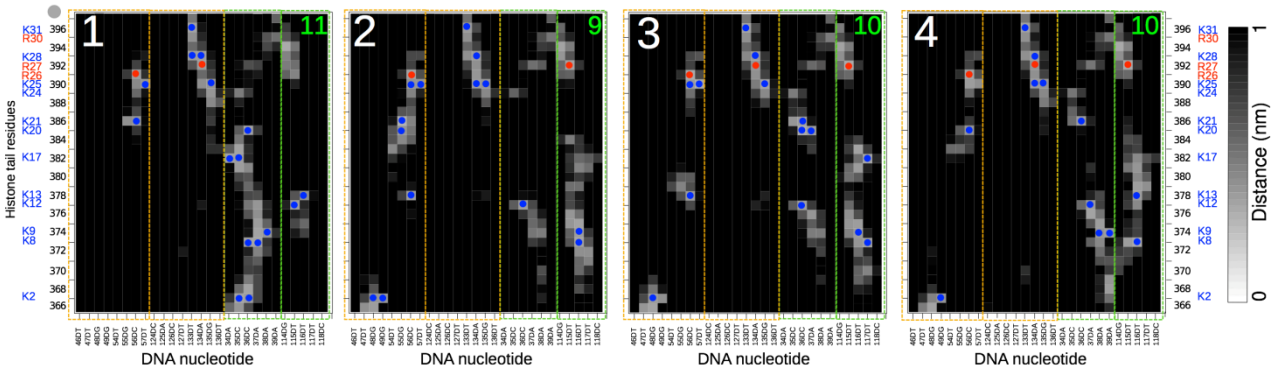

Figure S28. **Distance maps for the three most populated clusters of H2B tail**. Distances were measured between histone tail residues and the phosphate group of each nucleotide. Blue circles and red circles indicate contacts of lysines and arginines with DNA phosphate groups (cutoff 0.3 nm). Green numbers indicate the number of neutralized charges.

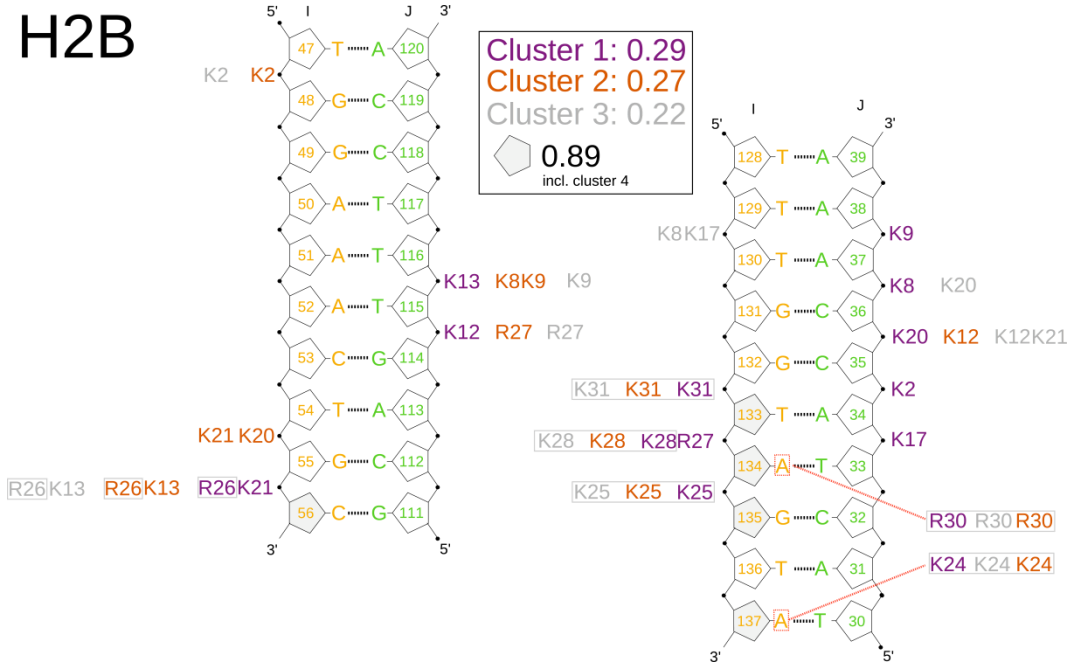

Figure S29. **Tail:DNA interactions of the H2B tail**. Interactions between histone tail and DNA for the clusters found in Fig. S14. Grey boxes indicate interactions found in all four clusters. The red dashed line illustrate cation-π interactions.

Explicit solvent MD results

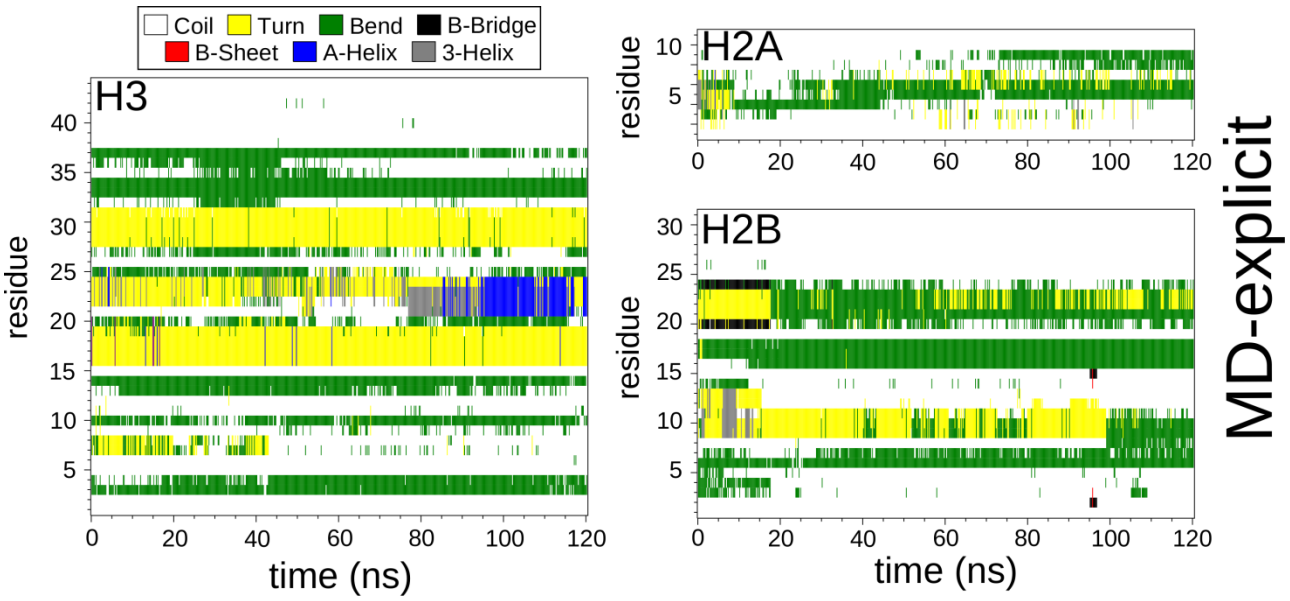

Figure S30. **Secondary structure of the H3, H2A and H2B histone tail of the MD simulation with explicit solvent**. Force field AMBER99SB was used. Different types of structure as indicated. The simulation was initialized with the most probable configuration identified by results of the REMD simulations.

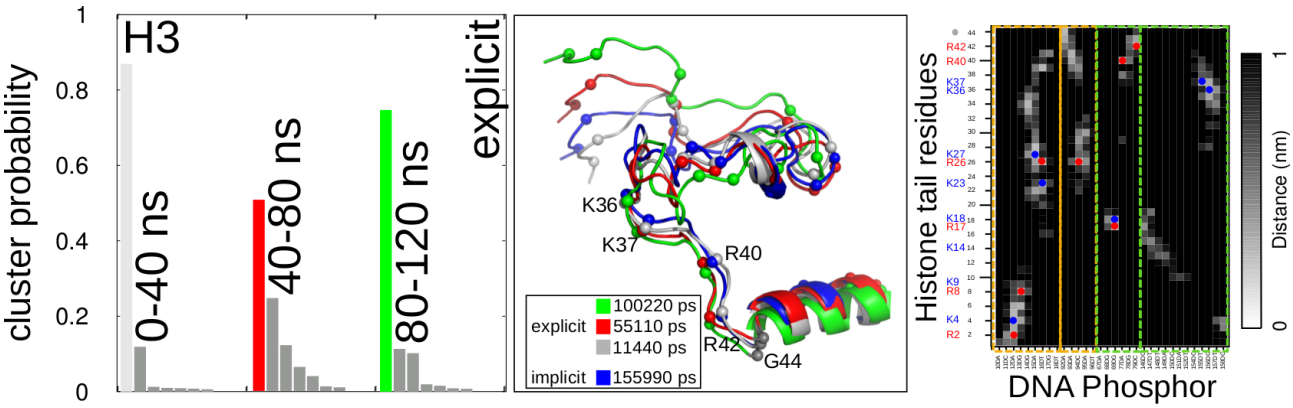

Figure S31. **Results of a cluster analysis of the MD simulations with an explicit solvent**. Shown are results for the H3 tail. The cutoff was 0.2 nm and the trajectory was divided into 3 intervals. Evolution of cluster populations, conformation of the dominant cluster of each interval (including starting configuration from the implicit REMD) and distance map of the dominant configuration in the last interval (80-120ns). Lysines, arginines and the end of the tail (grey) are indicated as beads.

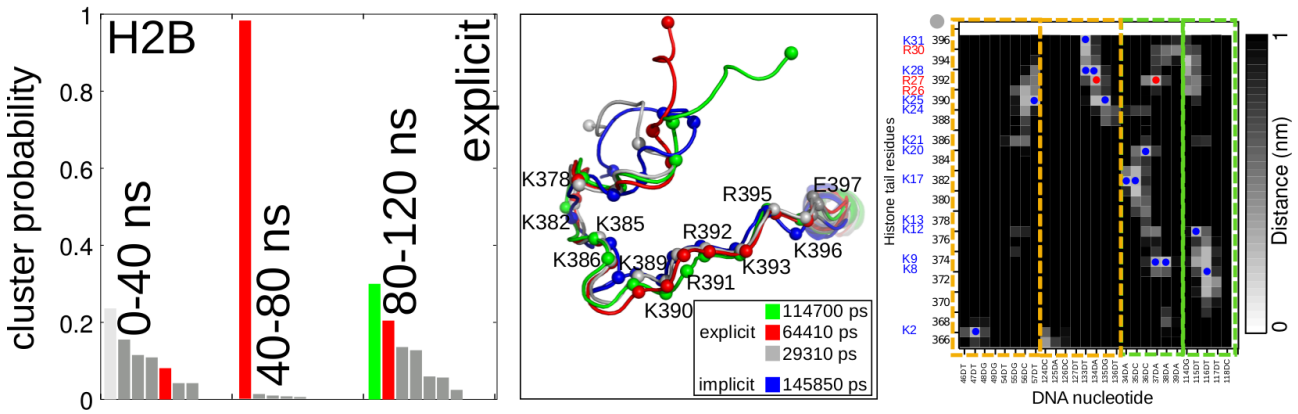

Figure S32. **Results of a cluster analysis of the MD simulations with an explicit solvent**. Shown are results for the H2B tail. The cutoff was 0.2 nm and the trajectory was divided into 3 intervals. Evolution of cluster populations, conformation of the dominant cluster of each interval (including starting configuration from the implicit REMD) and distance map of the dominant configuration in the last interval (80-120ns). Lysines, arginines and the end of the tail (grey) are indicated as beads.

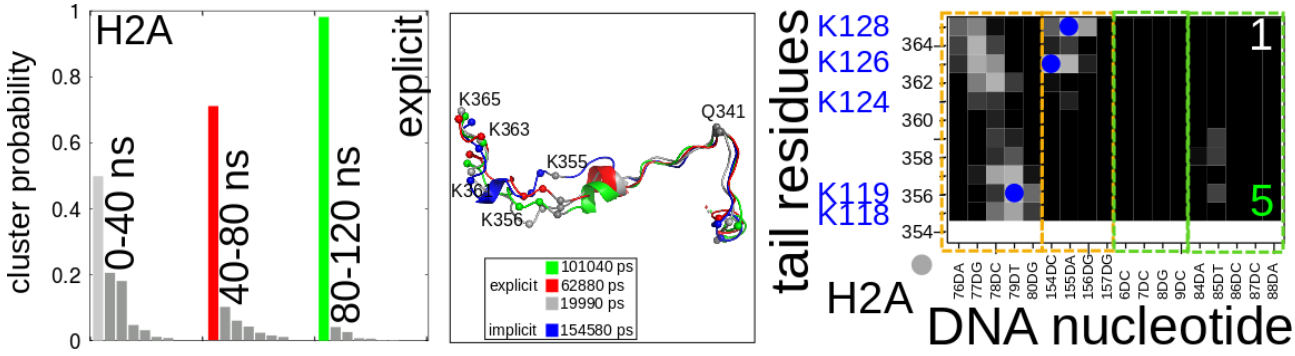

Figure S33. **Results of a cluster analysis of the MD simulations with an explicit solvent**. Shown are results for the H2A tail. The cutoff was 0.2 nm and the trajectory was divided into 3 intervals. Evolution of cluster populations, conformation of the dominant cluster of each interval (including starting configuration from the implicit REMD) and distance map of the dominant configuration in the last interval (80-120ns). Lysines, arginines and the end of the tail (grey) are indicated as beads.

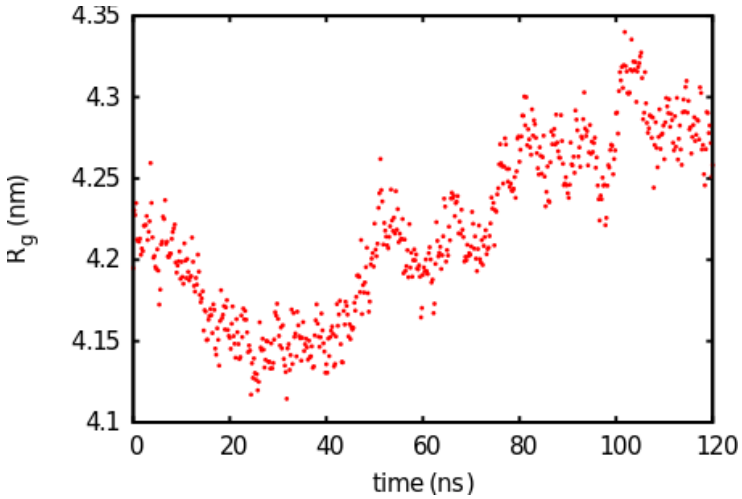

Figure S34. **Radius of gyration of the whole nucleosome**. Shown are results from the explicit solvent MD simulation.

Supporting References

1. Anandakrishnan, R., Daga, M., Onufriev, A.V. (2011). An n log n generalized born approximation. J. Chem. Theory. Comput. 7, 544-559.