Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

The Molecular Mechanism of Structural Changes in the Antimicrobial Peptide CM15 Upon Complex Formation with Drug Molecule Suramin: a Computational Analysis

Gergely Kohut[a,b], *Adam Sieradzan*[c], *Ferenc Zsila*[a], , *Tünde Juhász*[a], *Szilvia Bősze*[b], *Adam Liwo*[c], *Sergey A. Samsonov*[c*], *Tamás Beke-Somfai*[a,d*]

[a]Institute of Materials and Environmental Chemistry, Research Centre for Natural Sciences, Hungarian Academy of Sciences H-1117 Budapest, Magyar tudósok körútja 2, Hungary

[b]MTA-ELTE Research Group of Peptide Chemistry, Hungarian Academy of Sciences, Eötvös Loránd University, Budapest 112, P.O. Box 32, H-1518 Budapest, Hungary

[c]Faculty of Chemistry, University of Gdańsk, ul. Wita Stwosza 63, 80-308 Gdańsk, Poland

[d]Department of Chemical and Biological Engineering, Physical Chemistry, Chalmers University of Technology, SE-412 96 Göteborg, Sweden

Supplementary Materials

Figure S1. Per residue decomposition of total binding free energy of CM15 residues (left) and suramin fragments (right). Top panel: AD3 data, bottom panel: DMD data.

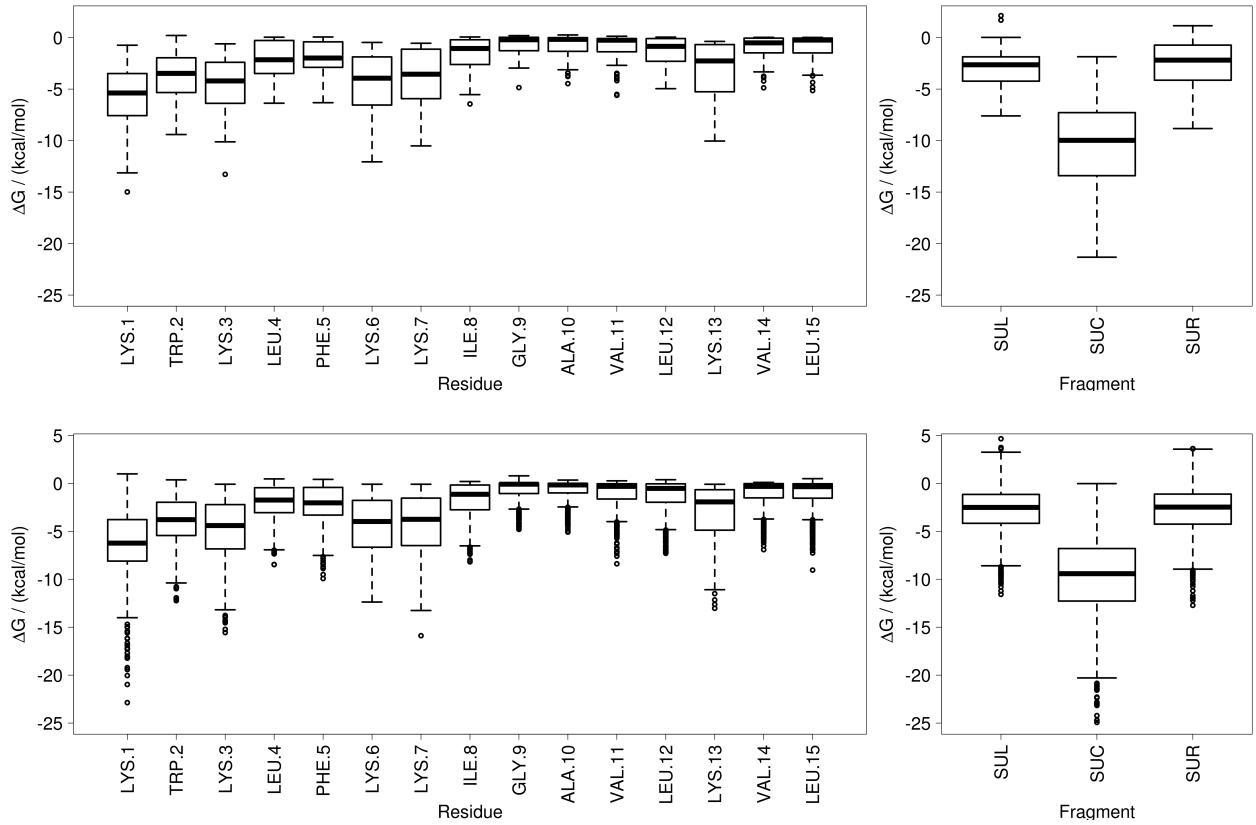


Figure S2. Per residue decomposition of Van der Waals energies of CM15 residues (left) and suramin fragments (right). Top panel: AD3 data, bottom panel: DMD data.

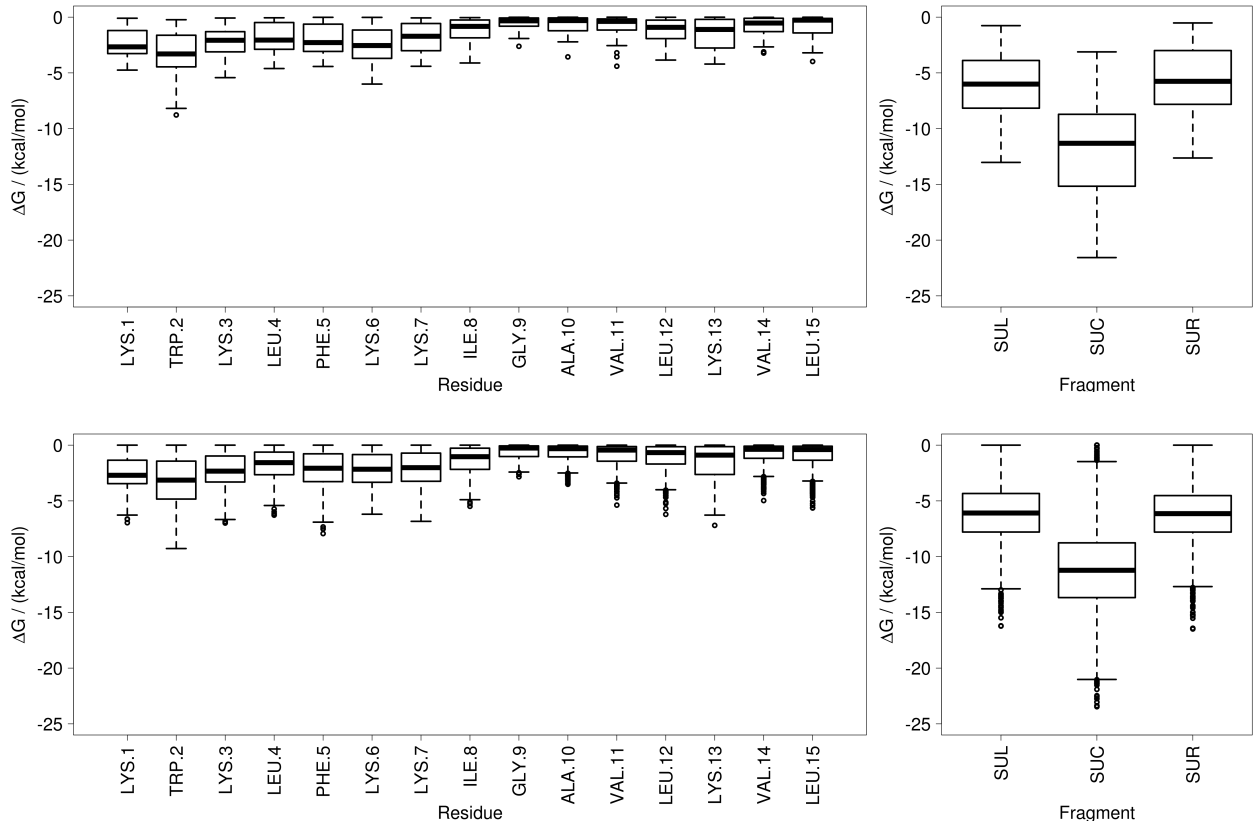


Figure S3. Per residue decomposition of electrostatic energies of CM15 residues (left) and suramin fragments (right). Top panel: AD3 data, bottom panel: DMD data.

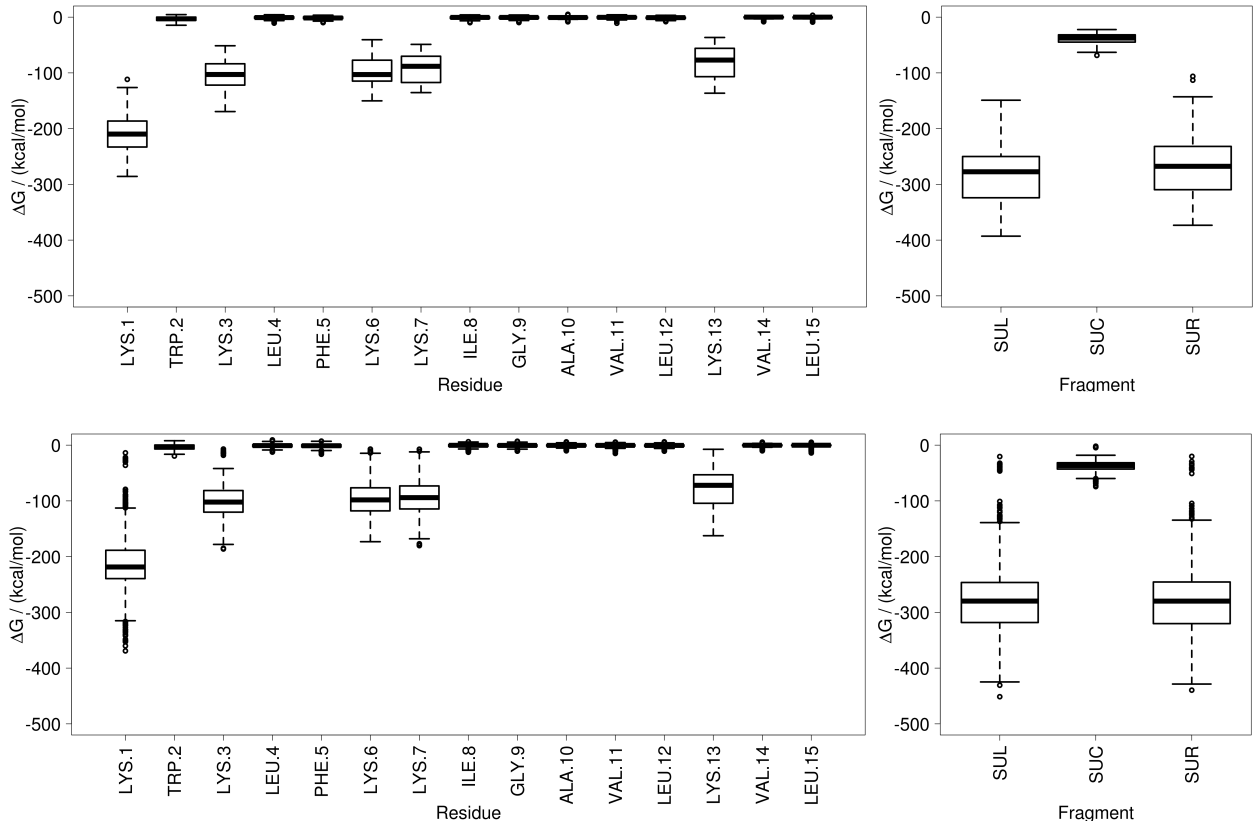


Figure S4. Per residue decomposition of polar solvation energies of CM15 residues (left) and suramin fragments (right). Top panel: AD3 data, bottom panel: DMD data.

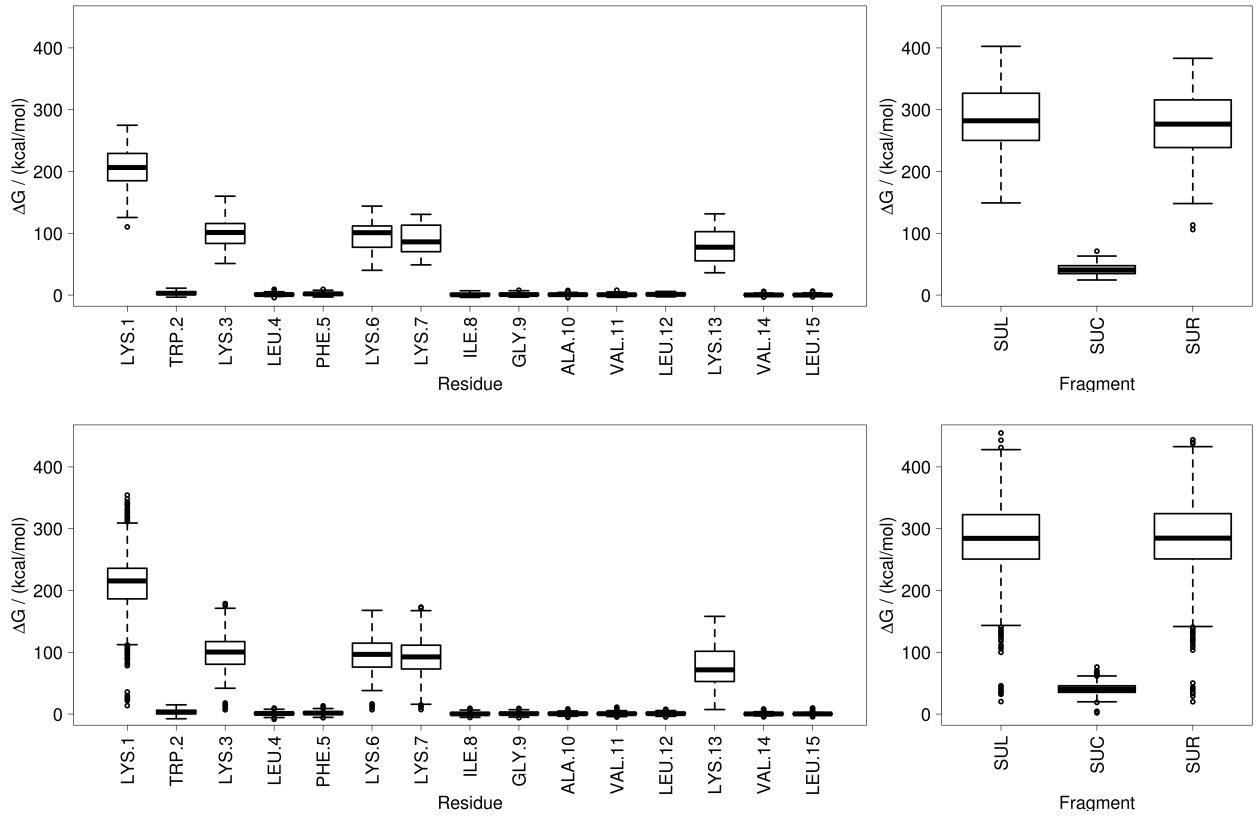


Figure S5. Per residue decomposition of non-polar solvation energies of CM15 residues (left) and suramin fragments (right). Top panel: AD3 data, bottom panel: DMD data.

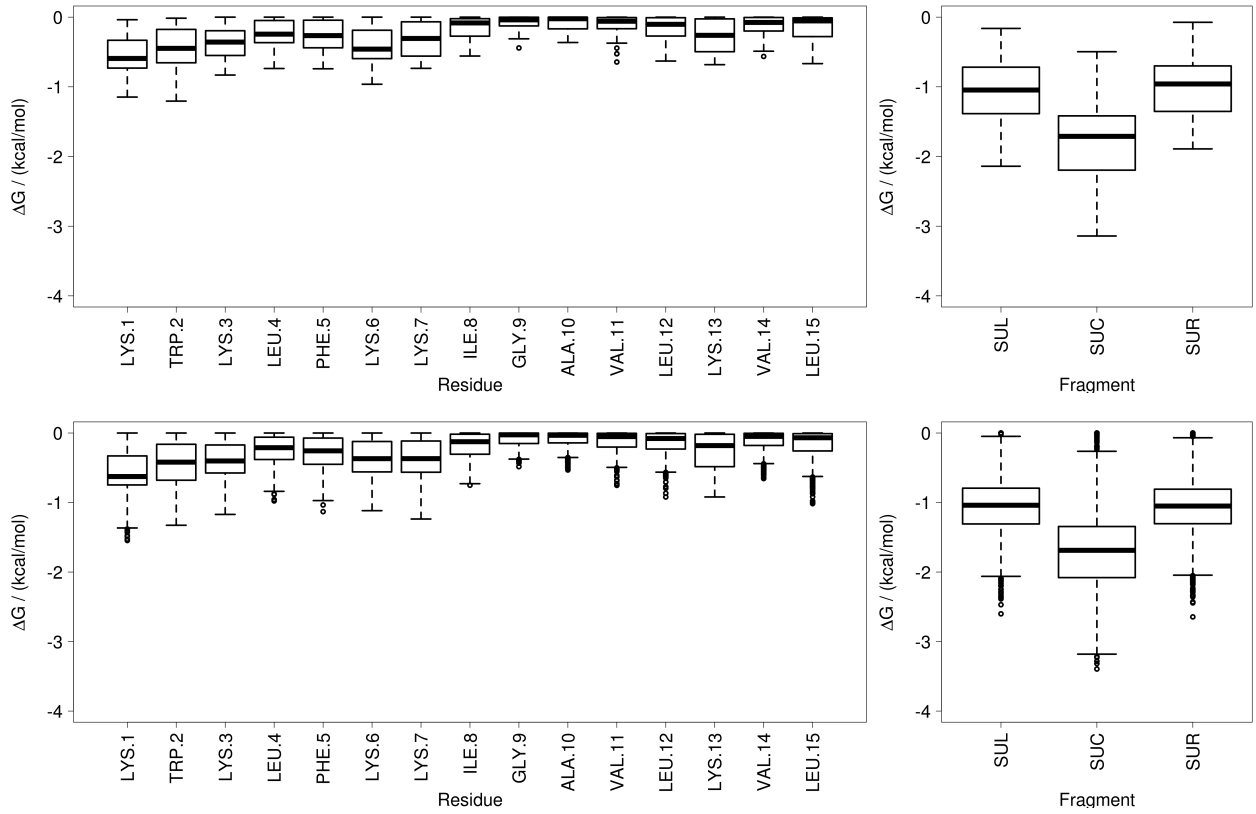


Figure S6. Example of CM15-suramin complex structure based on its MM-GBSA binding free energy. Black dashed lines show the salt bridges and H-bonds between the suramin and CM15 atoms. Only H atoms attached to N atoms are explicitly shown. Structure 2 of 10 according to the MM-GBSA ranking.

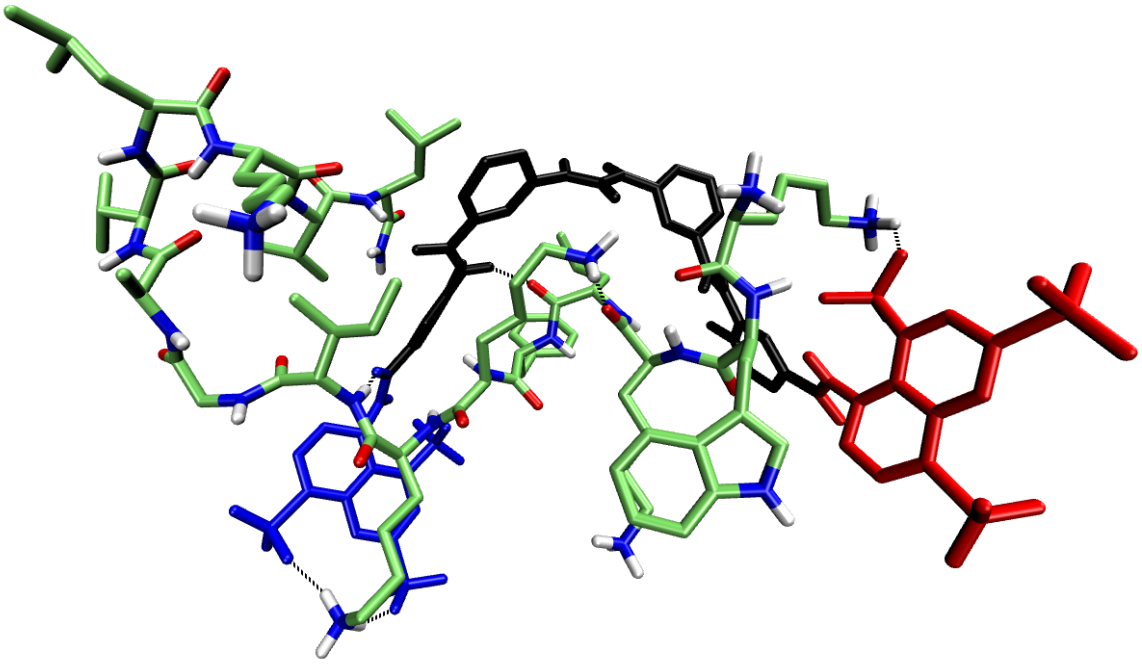


Figure S7. Example of CM15-suramin complex structure based on its MM-GBSA binding free energy. Black dashed lines show the salt bridges and H-bonds between the suramin and CM15 atoms. Only H atoms attached to N atoms are explicitly shown. Structure 3 of 10 according to the MM-GBSA ranking.

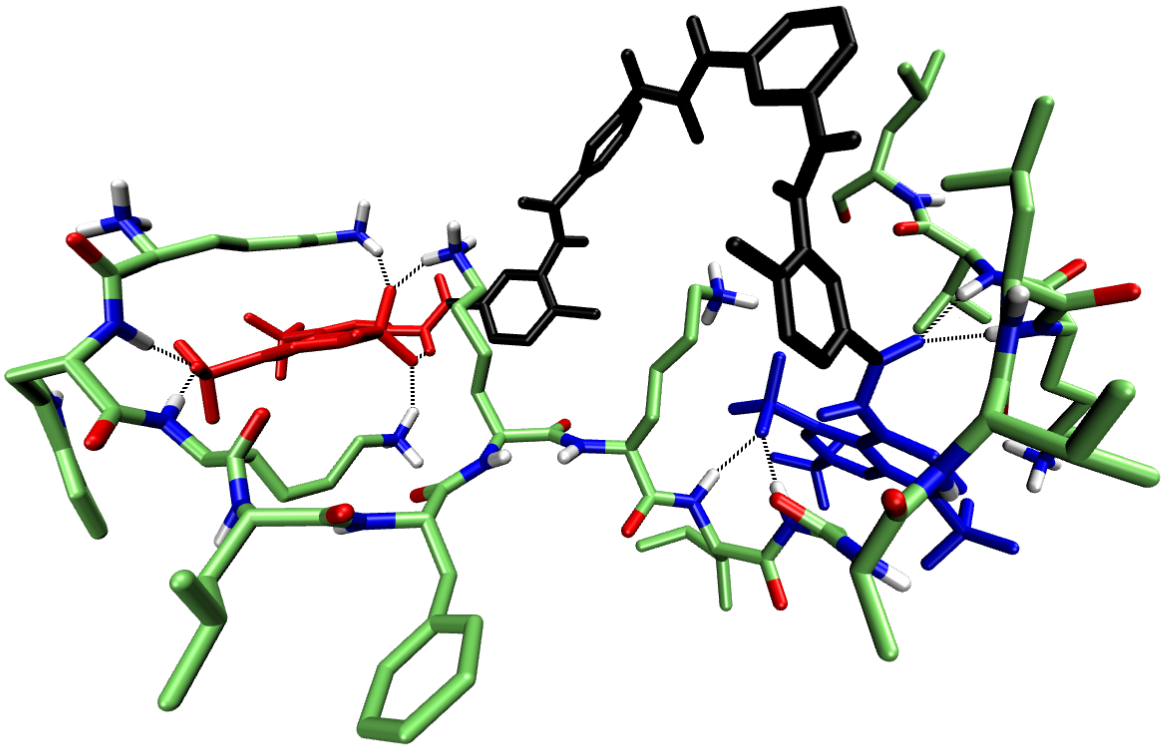


Figure S8. Example of CM15-suramin complex structure based on its MM-GBSA binding free energy. Black dashed lines show the salt bridges and H-bonds between the suramin and CM15 atoms. Only H atoms attached to N atoms are explicitly shown. Structure 4 of 10 according to the MM-GBSA ranking.

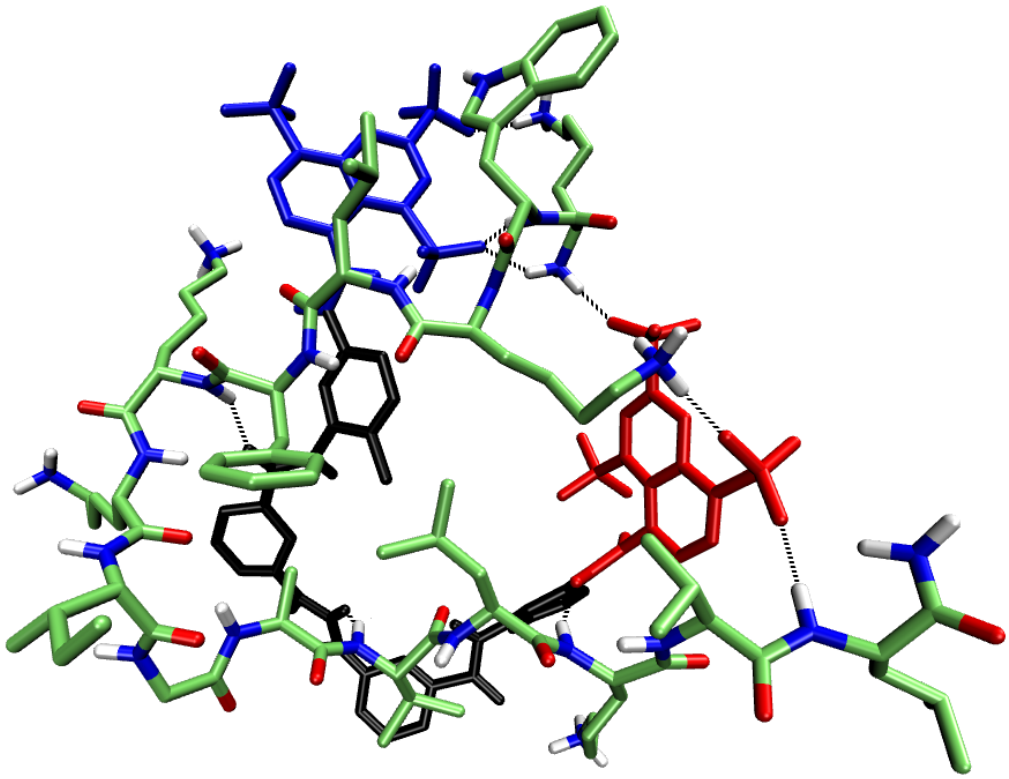


Figure S9. Example of CM15-suramin complex structure based on its MM-GBSA binding free energy. Black dashed lines show the salt bridges and H-bonds between the suramin and CM15 atoms. Only H atoms attached to N atoms are explicitly shown. Structure 5 of 10 according to the MM-GBSA ranking.

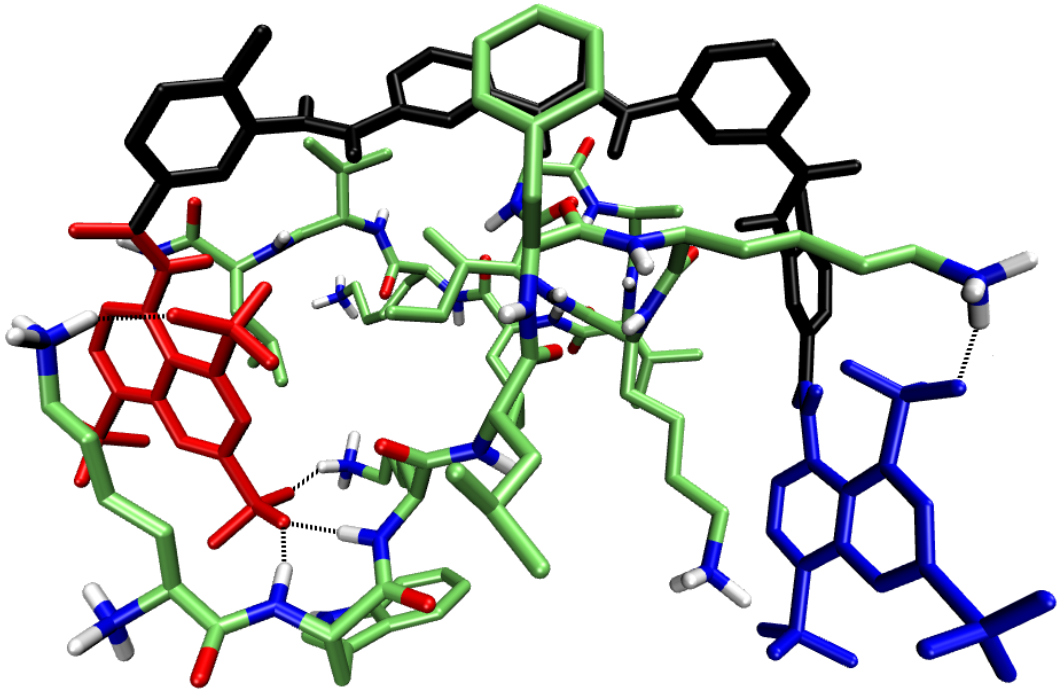


Figure S10. Example of CM15-suramin complex structure based on its MM-GBSA binding free energy. Black dashed lines show the salt bridges and H-bonds between the suramin and CM15 atoms. Only H atoms attached to N atoms are explicitly shown. Structure 6 of 10 according to the MM-GBSA ranking.

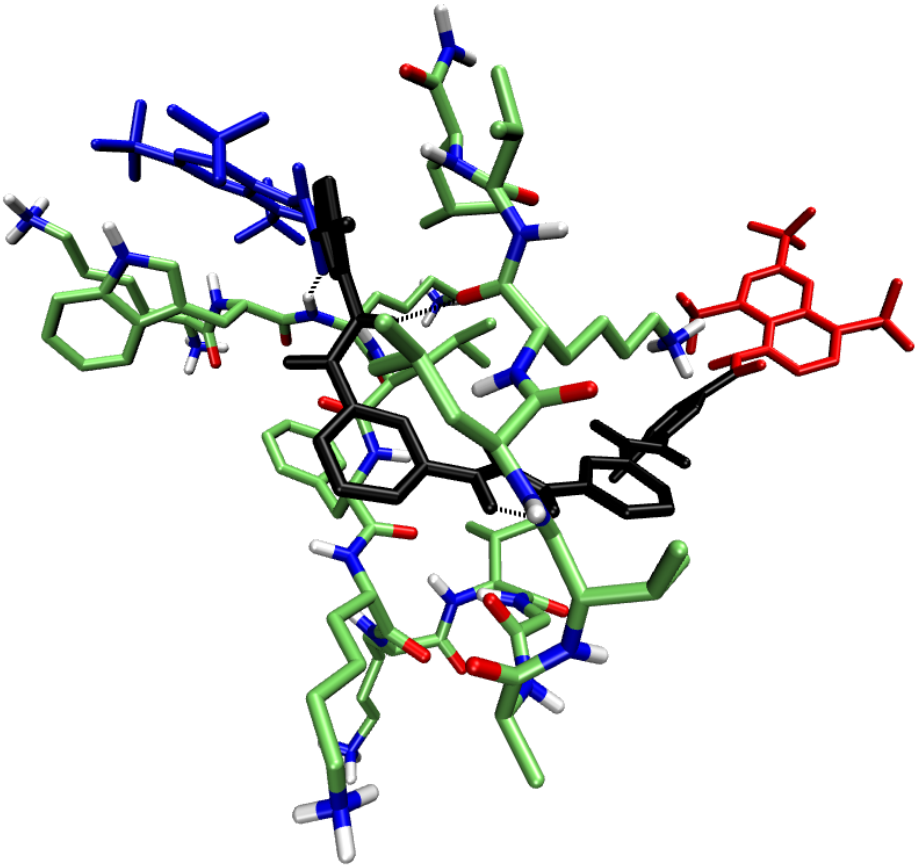


Figure S11. Example of CM15-suramin complex structure based on its MM-GBSA binding free energy. Black dashed lines show the salt bridges and H-bonds between the suramin and CM15 atoms. Only H atoms attached to N atoms are explicitly shown. Structure 7 of 10 according to the MM-GBSA ranking.

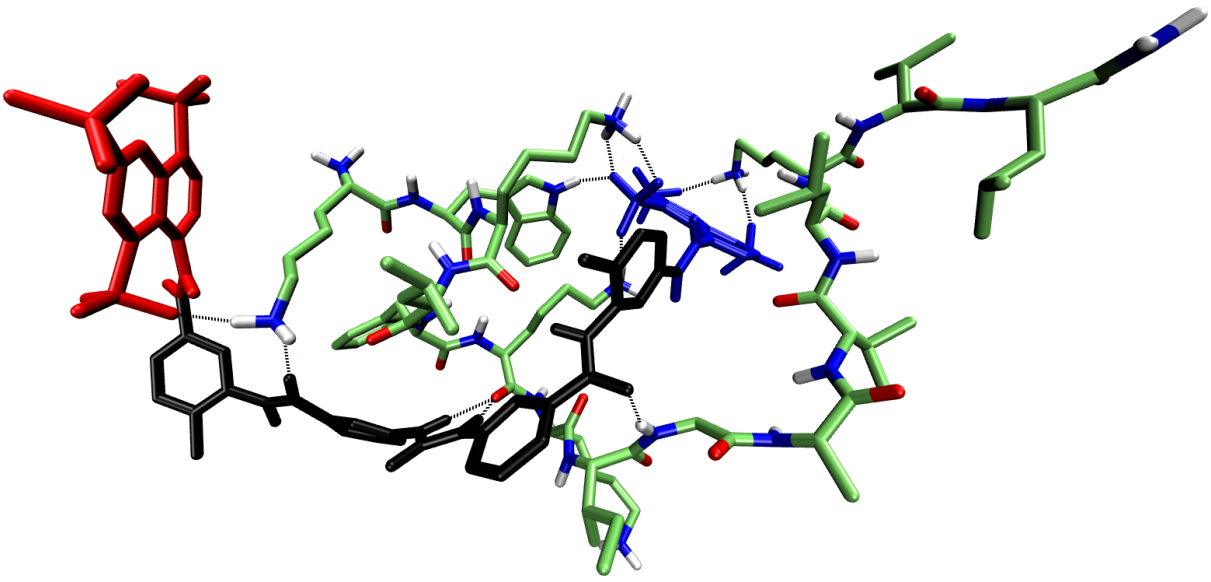


Figure S12. Example of CM15-suramin complex structure based on its MM-GBSA binding free energy. Black dashed lines show the salt bridges and H-bonds between the suramin and CM15 atoms. Only H atoms attached to N atoms are explicitly shown. Structure 8 of 10 according to the MM-GBSA ranking.

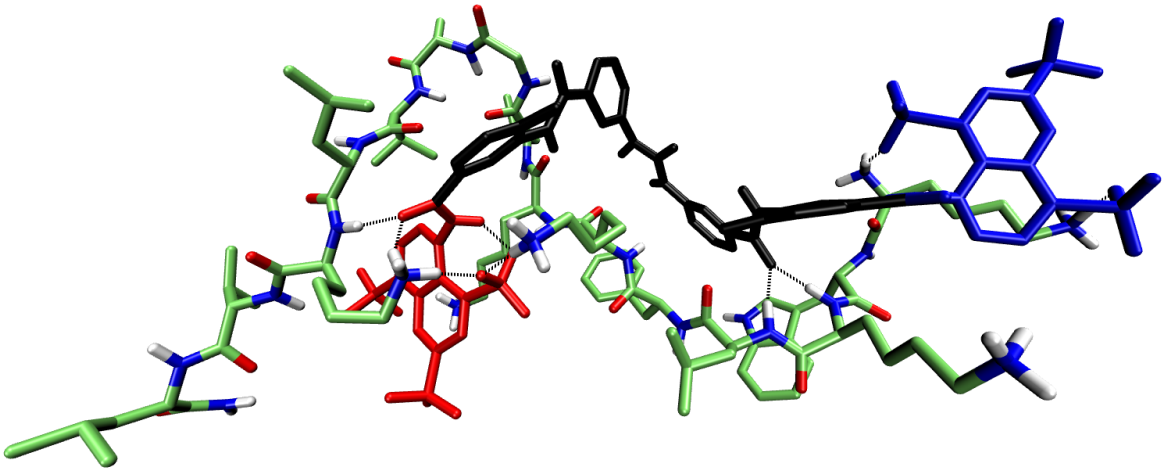


Figure S13. Example of CM15-suramin complex structure based on its MM-GBSA binding free energy. Black dashed lines show the salt bridges and H-bonds between the suramin and CM15 atoms. Only H atoms attached to N atoms are explicitly shown. Structure 9 according to the MM-GBSA ranking.

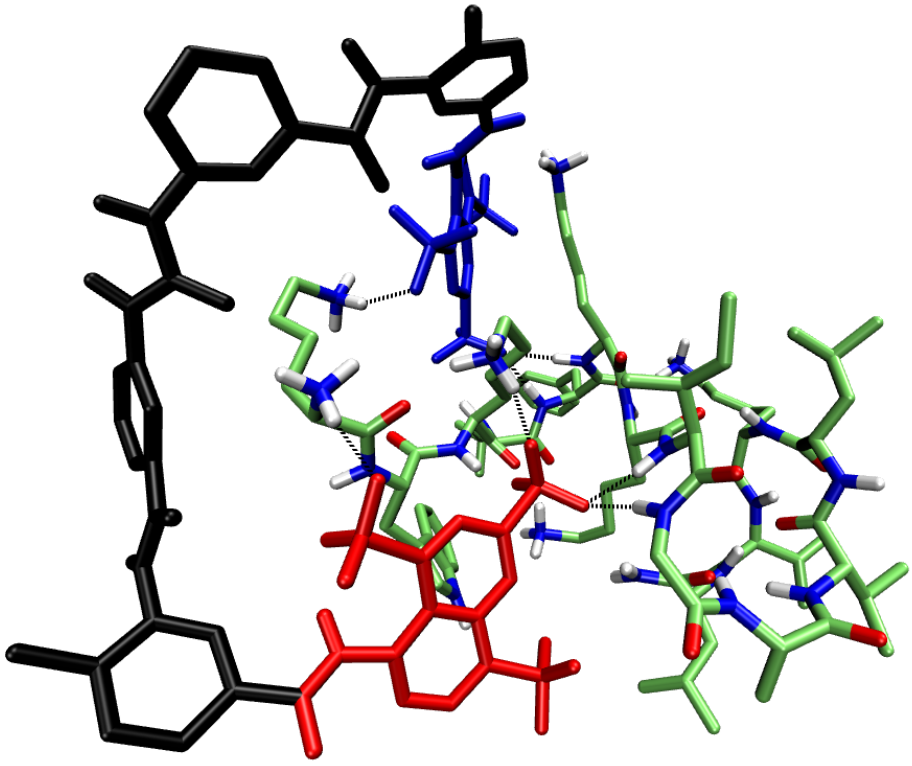


Figure S14. Example of CM15-suramin complex structure based on its MM-GBSA binding free energy. Black dashed lines show the salt bridges and H-bonds between the suramin and CM15 atoms. Only H atoms attached to N atoms are explicitly shown. Structure 10 of 10 according to the MM-GBSA ranking.

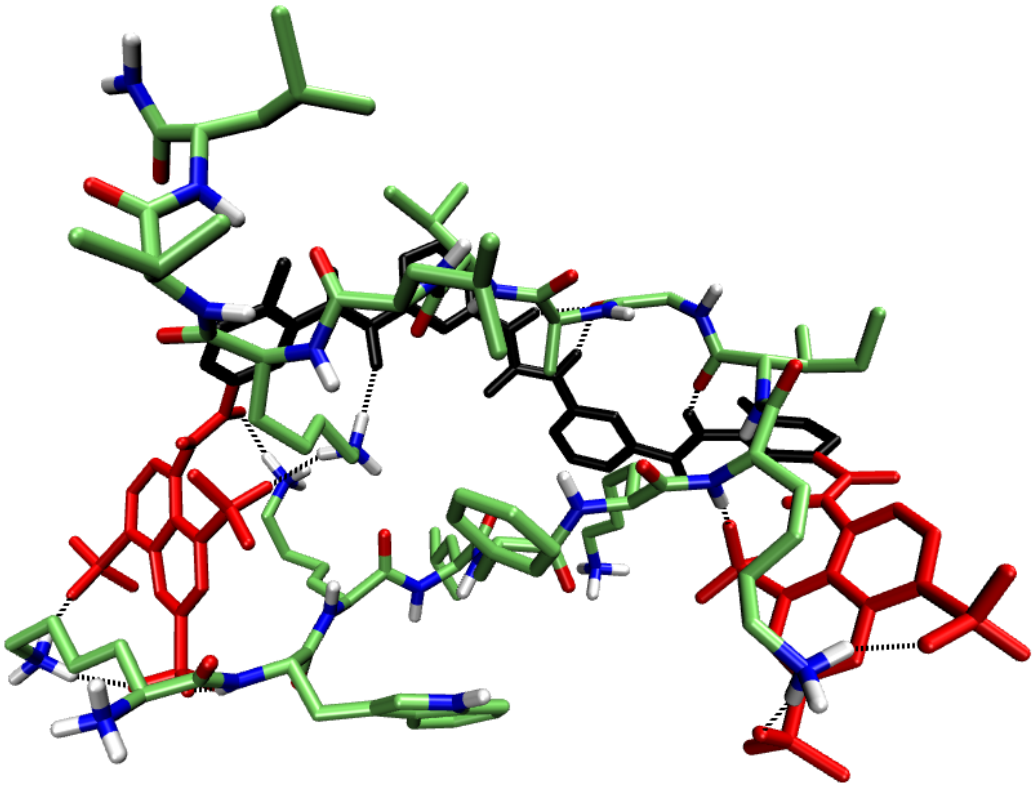


Figure S15. Percentage of 3_{10}-helix secondary structure element content as a function of time.

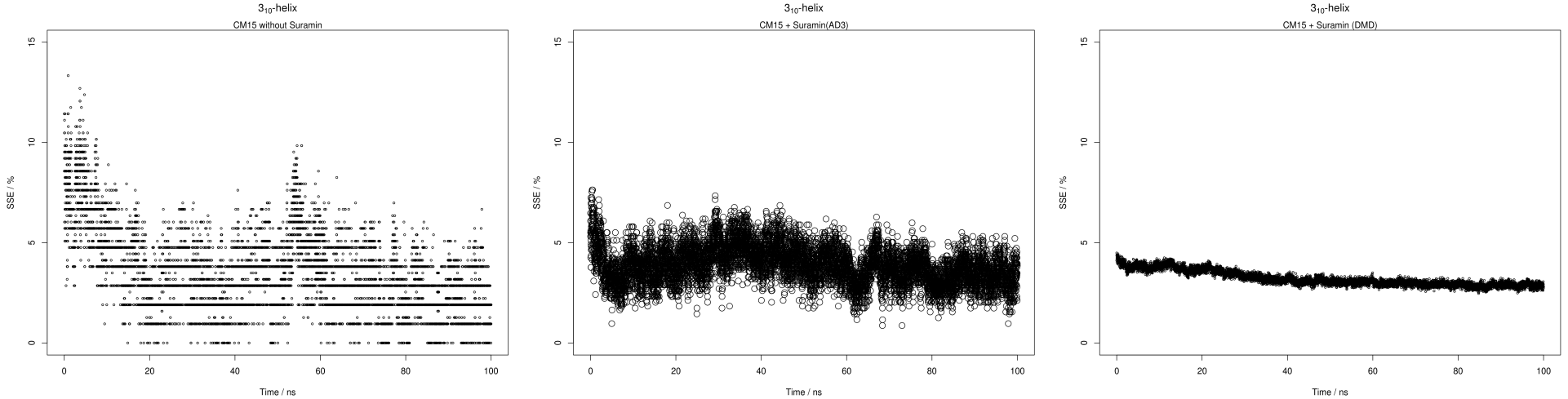


Figure S16. Percentage of π-helix secondary structure element content as a function of time.

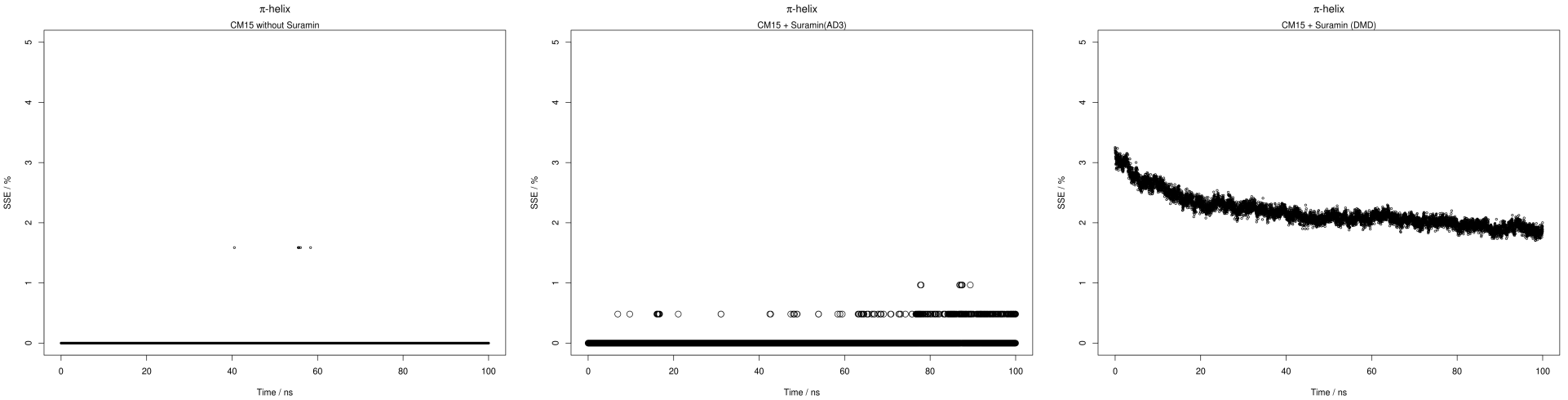


Figure S17. Percentage of antiparallel β-sheet secondary structure element content as a function of time.

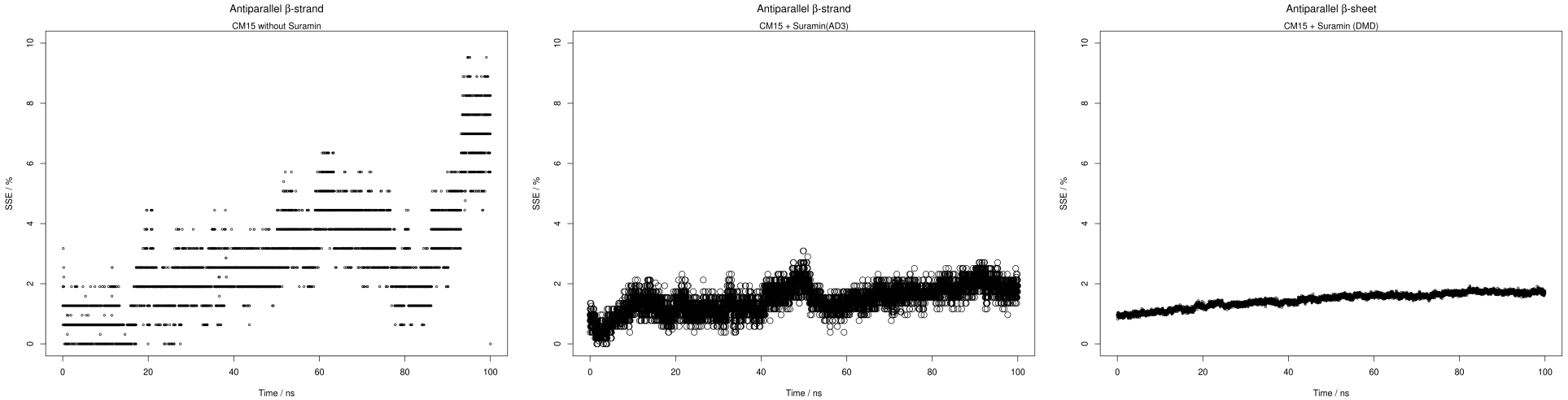


Figure S18. Percentage of parallel β-sheet secondary structure element content as a function of time.

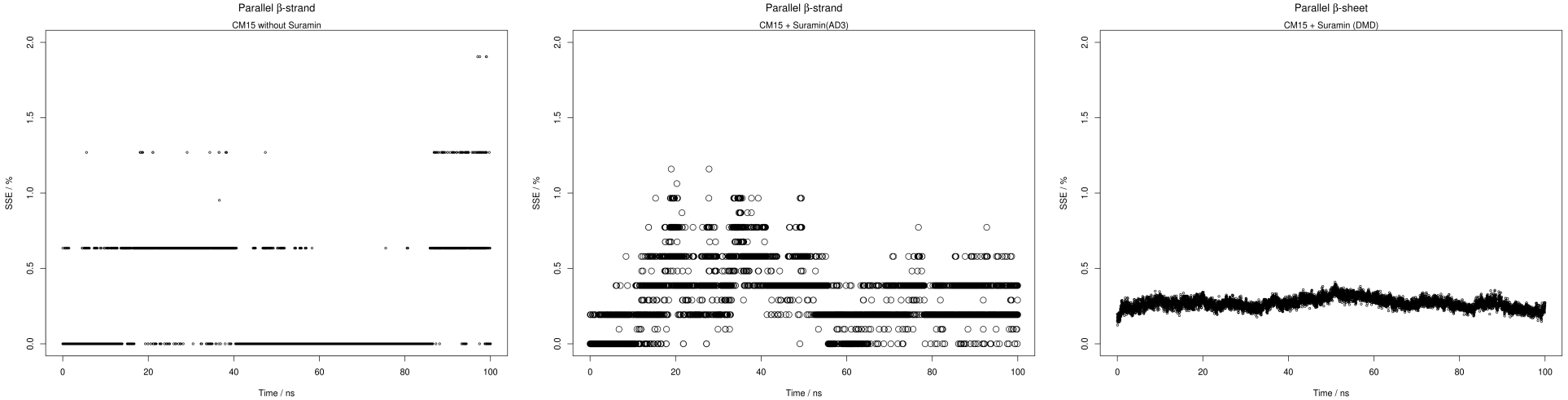


Figure S19. Percentage of turn secondary structure element content as a function of time.

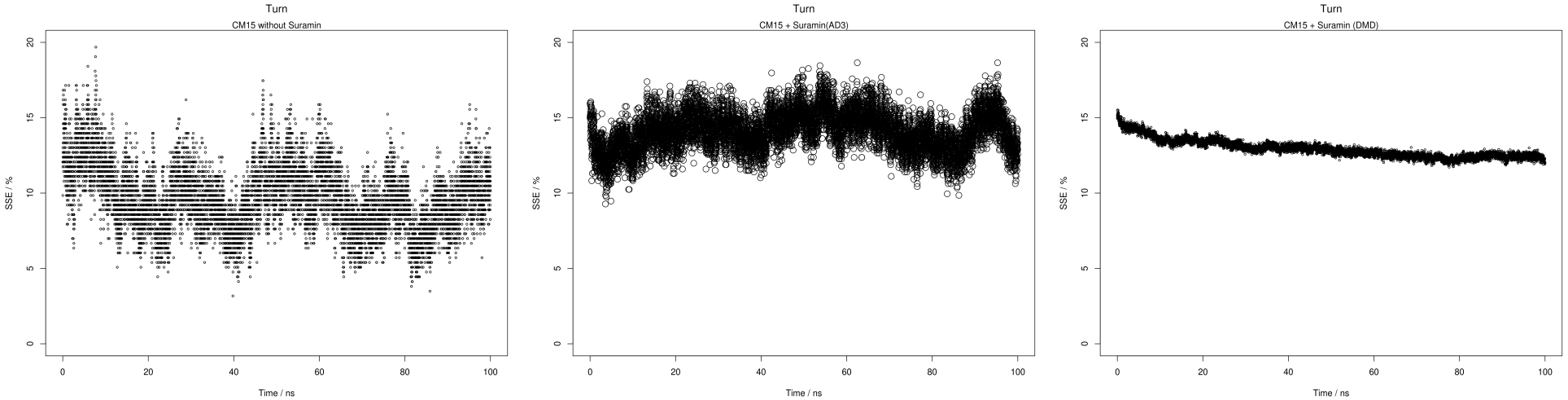
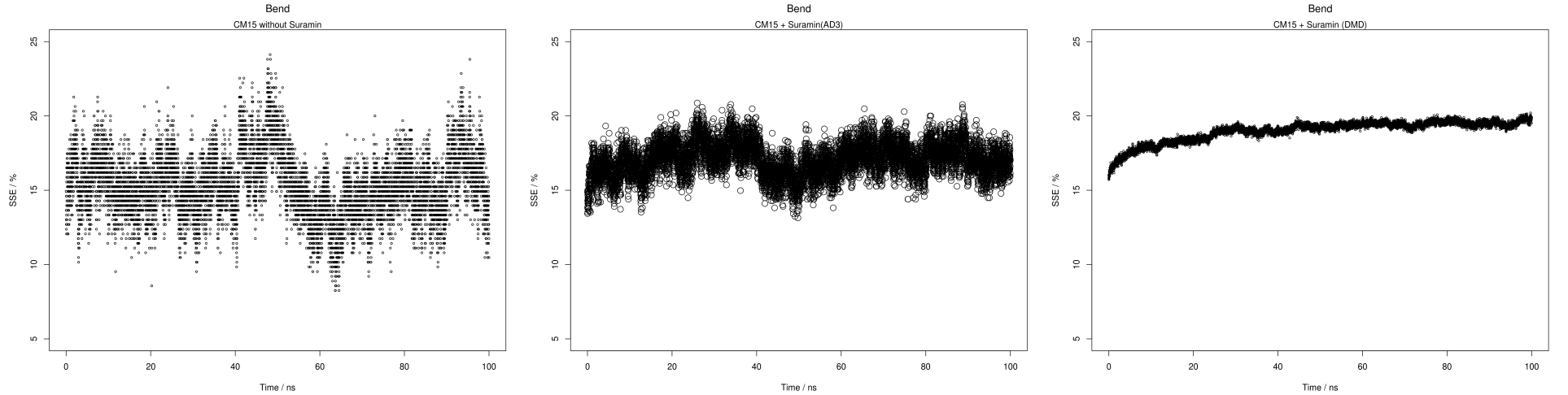
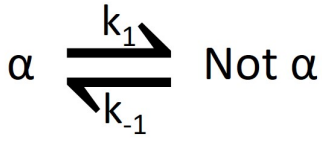


Figure S20. Percentage of bend secondary structure element content as a function of time.



Kinetics



Let x be the mole fraction of the residues in α-helical conformation. Then the mole fraction of all the other residues is 1 -x. Then the kinetic differential equation can be solved as:

$$\frac{-dx}{dt} = k_1 x - k_{-1}(1-x)$$

$$\frac{dx}{dt} = -(k_1 + k_{-1})x + k_{-1}$$

$$\frac{dx}{dt} = -(k_1 + k_{-1})\left(x - \frac{k_{-1}}{k_1 + k_{-1}}\right)$$

$$\int \frac{dx}{\left(x - \frac{k_{-1}}{k_1 + k_{-1}}\right)} = \int -(k_1 + k_{-1})\,dt$$

$$\ln\left(x - \frac{k_{-1}}{k_1 + k_{-1}}\right) = -(k_1 + k_{-1})t + C$$

$$x = \frac{k_{-1}}{k_1 + k_{-1}} + Ae^{-(k_1 + k_{-1})t}$$

Figure S21. Time evolution of CV1 in the first replica. Left side: CM15 in the absence of suramin, Right side: CM15 in the presence of suramin.

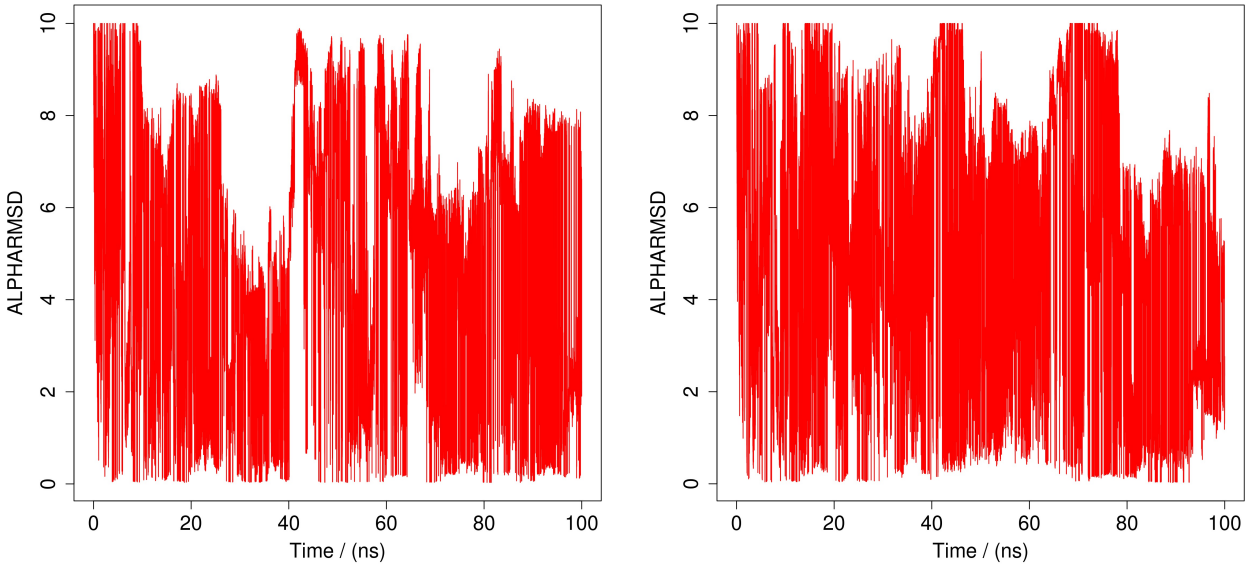


Figure S22. Time evolution of CV2 in the second replica. Left side: CM15 in the absence of suramin, Right side: CM15 in the presence of suramin.

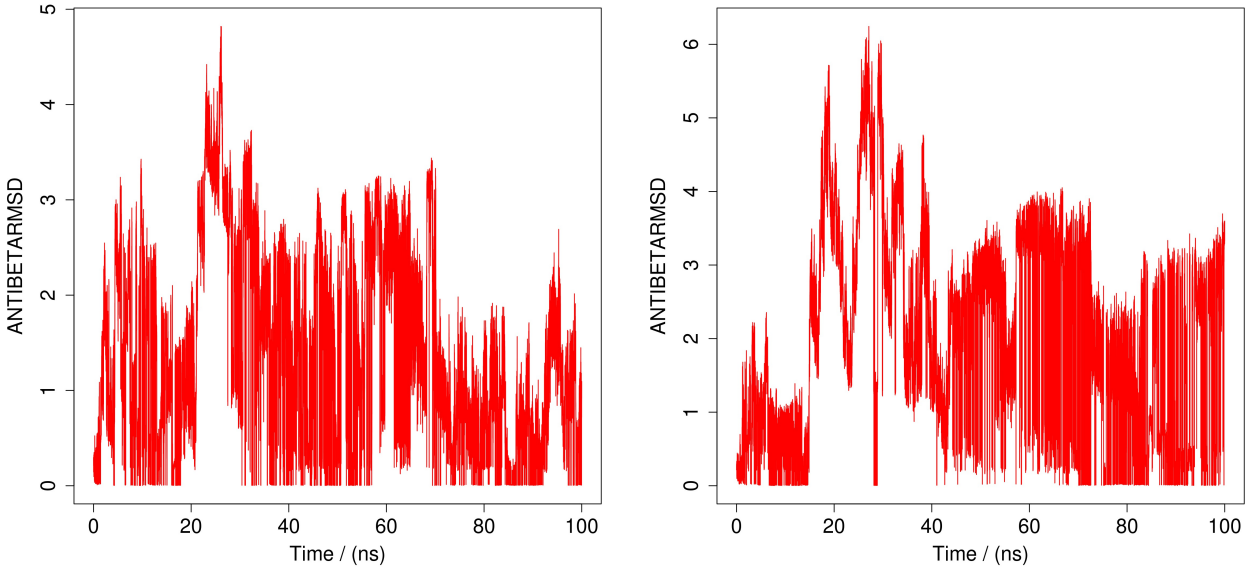


Figure S23. Time evolution of CV3 in the third replica. Left side: CM15 in the absence of suramin, Right side: CM15 in the presence of suramin.

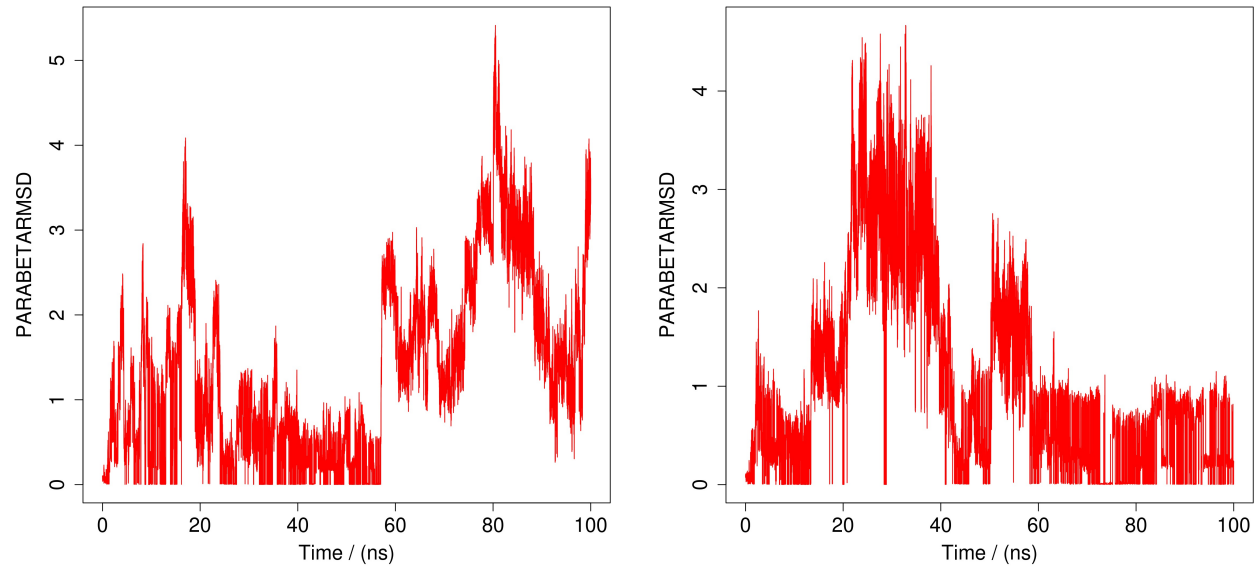


Figure S24. Time evolution of CV4 in the fourth replica. Left side: CM15 in the absence of suramin, Right side: CM15 in the presence of suramin.

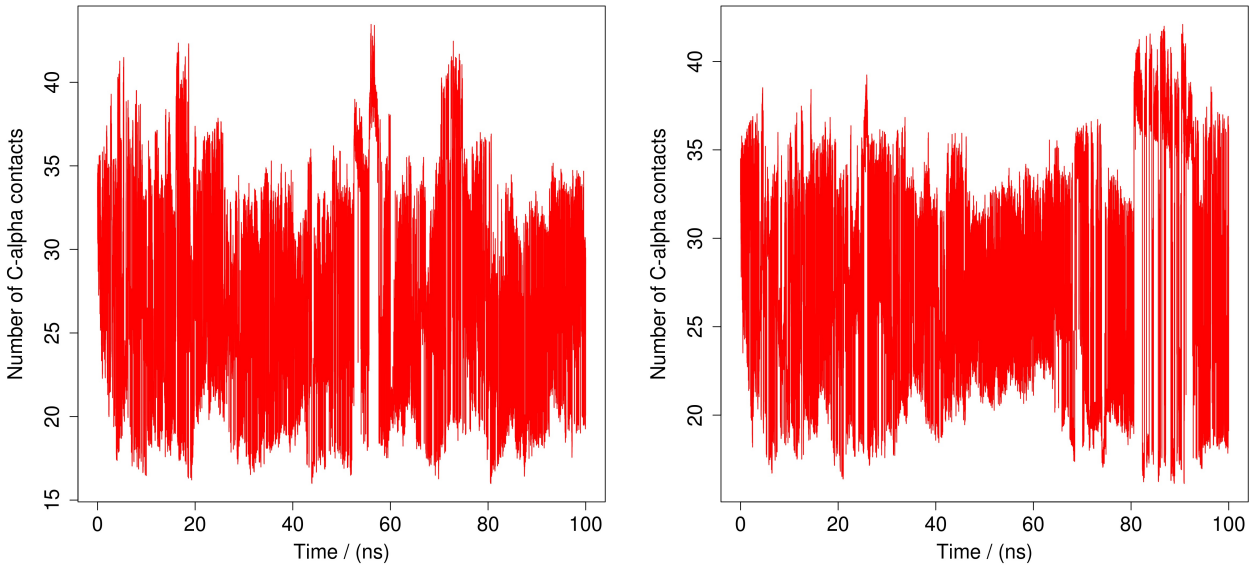


Figure S25. Time evolution of CV5 in the fifth replica. Left side: CM15 in the absence of suramin, Right side: CM15 in the presence of suramin.

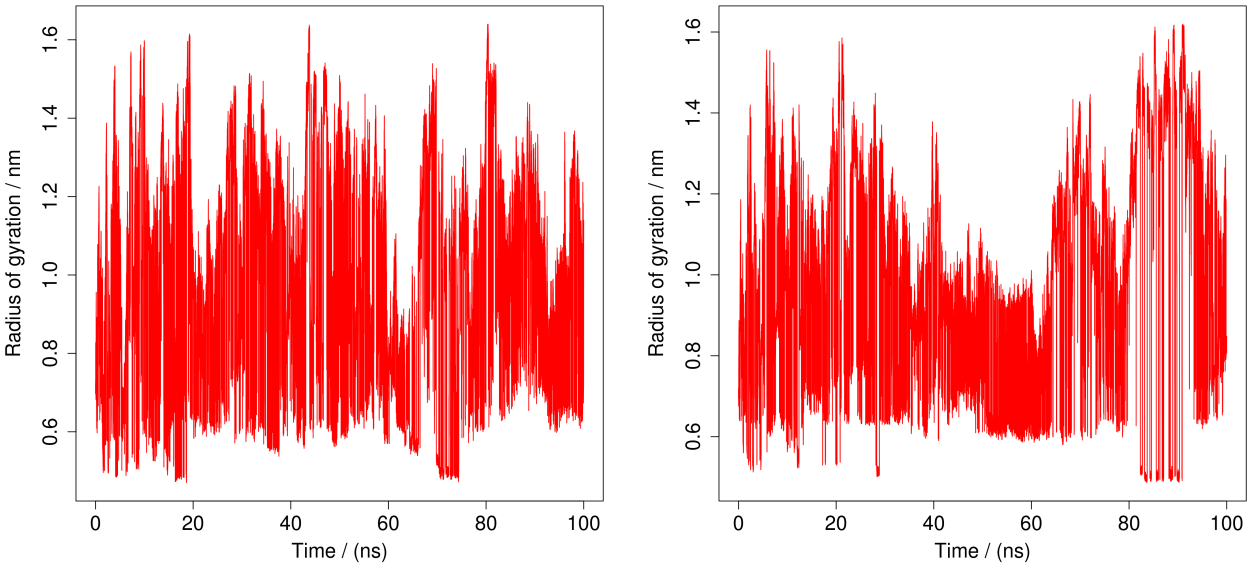


Figure S26. Time evolution of the deposited hills in the first replica. Left side: CM15 in the absence of suramin, Right side: CM15 in the presence of suramin.

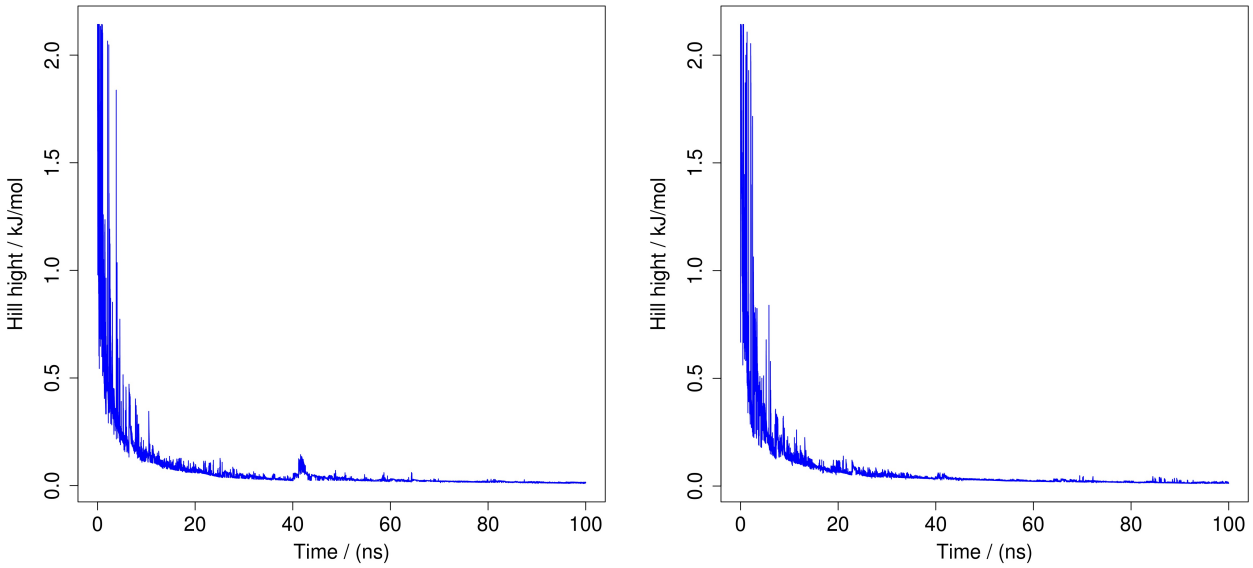


Figure S27. Time evolution of the deposited hills in the second replica. Left side: CM15 in the absence of suramin, Right side: CM15 in the presence of suramin.

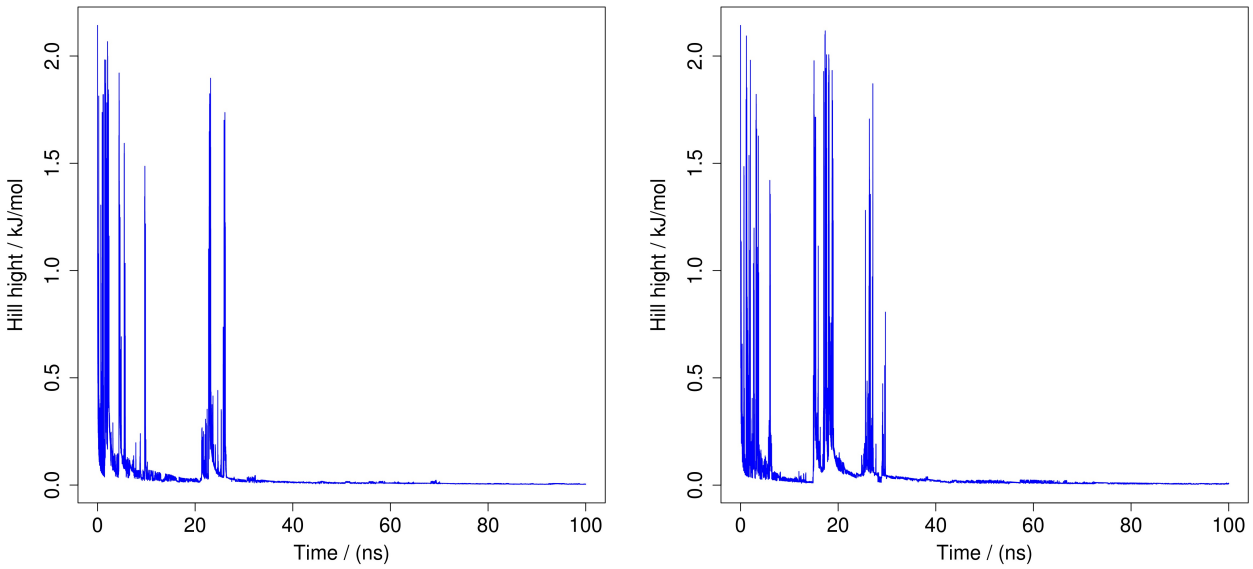


Figure S28. Time evolution of the deposited hills in the third replica. Left side: CM15 in the absence of suramin, Right side: CM15 in the presence of suramin.

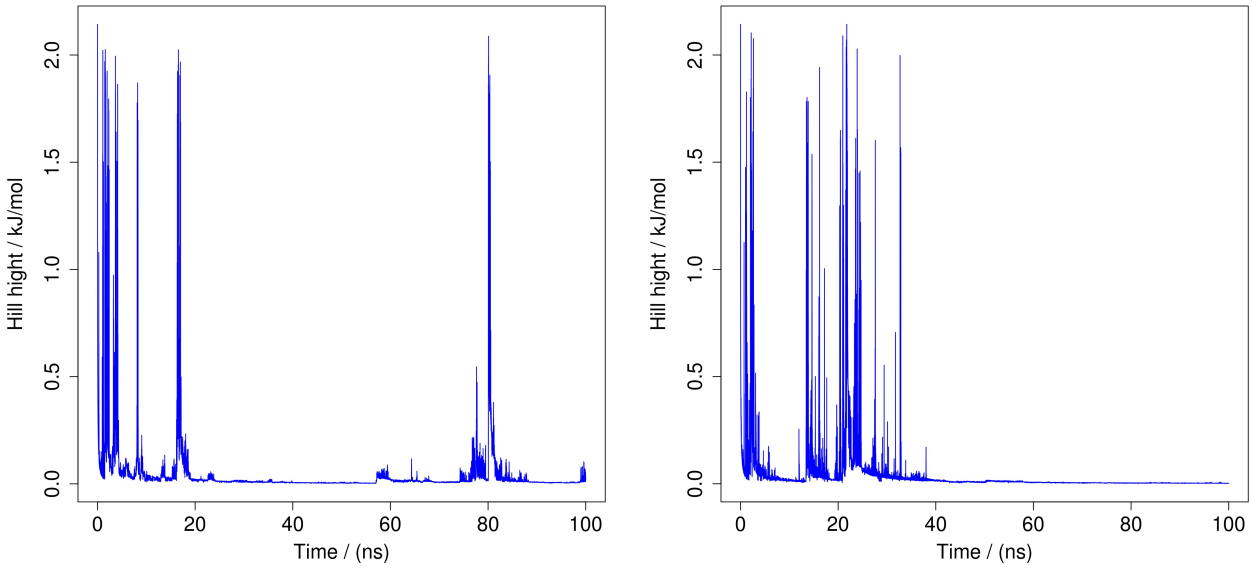


Figure S29. Time evolution of the deposited hills in the fourth replica. Left side: CM15 in the absence of suramin, Right side: CM15 in the presence of suramin.

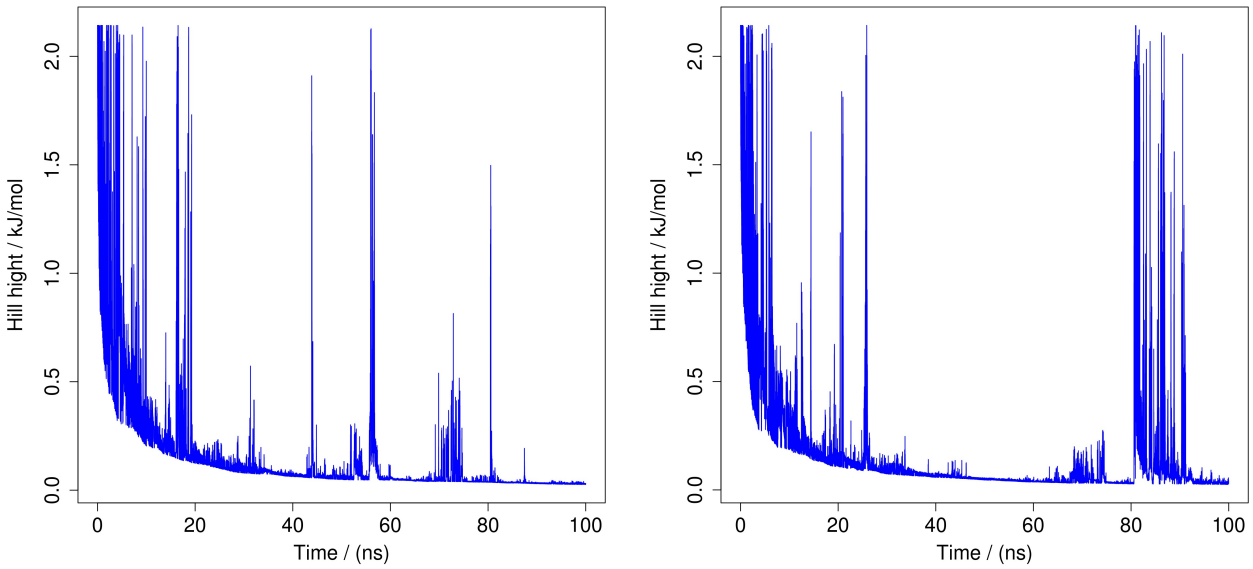


Figure S30. Time evolution of the deposited hills in the fifth replica. Left side: CM15 in the absence of suramin, Right side: CM15 in the presence of suramin.

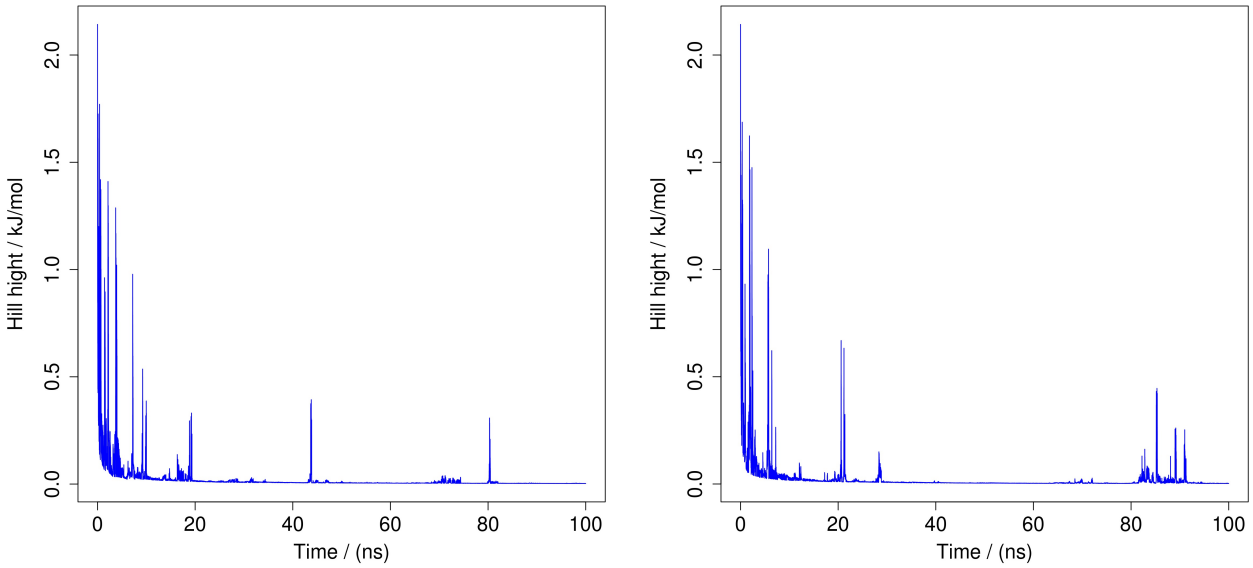


Figure S31. Time evolution of the secondary structure of CM15 calculated by DSSP. Top panel: CM15 alone. Bottom panel: CM15 in the presence of suramin.