

Supplementary Material

Energy Landscapes of Dynamic Ensembles of Rolling Triplet Repeat Bulge Loops: Implications for DNA Expansion Associated with Disease States

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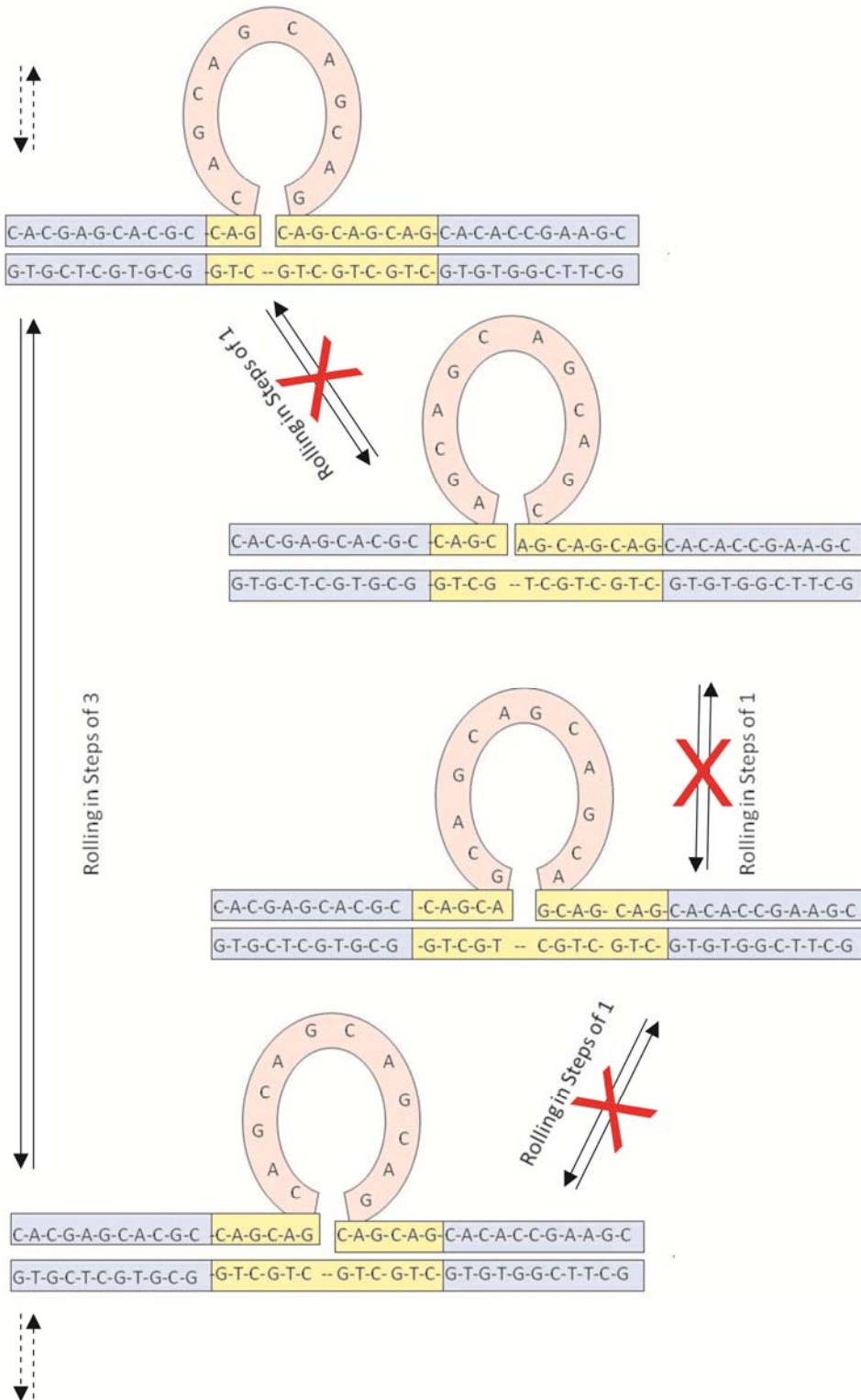
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Supplementary Figure S1



Supplementary Figure S1: A schematic representation for different loop arrangements in steps of 3 bases (on left side), in comparison to loop migration in single base steps (right side). The figure illustrates why a given CAG repeat is located either entirely within the loop or entirely within the duplex domain. Loop migration in steps of 3 bases maintains the alignment of CAG repeats within the bulge loop and maintains stable CG/GC base pairs closing the loop domain. By contrast, loop migration via single base steps would result in altered alignments of bases within the loop domain, which would disrupt those intra loop interactions that make CNG repeats unusually stable. Single base steps also would cause less stable base pairs to close the loop domain (CG/AT, in the case of 1 step, AT/GC in case of 2 base steps). Foot printing studies¹⁻⁴ on free CNG repeat DNA's and on static CNG bulge loops consistently show alignment of the bases in a CNG register only, with no evidence for base arrangements corresponding to single base steps. Such chemical probing results are in agreement with conclusions based on other biophysical techniques.⁵⁻⁷ In this work, we observe quantized changes in enthalpy that scale with the number of CAG repeats in the duplex domain (not shown). Such quantized enthalpy changes can only be accounted for by loop positions that differ in steps of 3 bases. Collectively, these observations support loop migration in steps of 3 bases, as presented in the manuscript.

References

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