How does temperature affect the conformation of single DNA molecules below melting temperature?

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The double stranded DNA molecule undergoes drastic structural changes during biological processes such as transcription during which it opens locally under the action of RNA polymerases. Local spontaneous denaturation could contribute to this mechanism by promoting it. Supporting this idea, different biophysical [1-3] studies have found an unexpected increase in the flexibility of DNA molecules with various sequences as a function of the temperature, which would be consistent with the formation of a growing number of locally denatured sequences. Here, we take advantage of our capacity to detect subtle changes occurring on DNA by using high throughput tethered particle motion to question the existence of bubbles in double stranded DNA under physiological salt conditions through their conformational impact on DNA molecules ranging from several hundreds to thousands base pairs [4]. Our results strikingly differ from previously published ones, as we measure a bending modulus that remains stable with temperature as expected for intact double stranded DNA.

[1] Forties,R.A., Bundschuh,R. and Poirier,M.G. The flexibility of locally melted DNA. *Nucleic Acids Res.*, **37**, 4580–4586 (2009)

. [2] Geggier,S., Kotlyar,A. and Vologodskii,A. Temperature dependence of DNA persistence length. *Nucleic Acids Research*, **39**, 1419–1426 (2011).

[3] Driessen,R.P.C., Sitters,G., Laurens,N., Moolenaar,G.F., Wuite,G.J.L., Goosen,N. and Dame,R.T. Effect of Temperature on the Intrinsic Flexibility of DNA and Its Interaction with Architectural Proteins. *Biochemistry*, **53**, 6430–6438 (2014).

[4] Brunet,A., Salomé,L., Rousseau,P., Destainville,N., Manghi,M. and Tardin,C. How does temperature impact the conformation of single DNA molecules below melting temperature? *Nucleic Acids Res.*, 10.1093/nar/gkx1285 (2017).