

Chromatin looping and the probability of transcription

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According to the worm-like chain model of polymers, the end-to-end distance (r) of a polymer chain follows the probability distribution [1,2] :

$$P_{wc}(r; L, \ell_p) 4\pi r^2 dr = \frac{3\sqrt{3}r^2 dr}{2\sqrt{\pi}(L\ell_p)^{3/2}} e^{-3r^2/4L\ell_p} (1 - w(r, L, \ell_p))$$

where

$$w(r, L, \ell_p) = \frac{5\ell_p}{4L} - \frac{2r^2}{L^2} + \frac{33r^4}{80L^3\ell_p} + \frac{79\ell_p^2}{160L^2} + \dots$$

in which L is the contour length of the polymer, and ℓ_p is the persistence length of the polymer. According to the Jacobson-Stockmayer theory of loop formation [3], the probability of forming a loop of contour length L is proportional to

$$P_{loop}(L; \ell_p) \propto \left(\frac{\ell_p}{L}\right)^{3/2} - \frac{5}{4}\left(\frac{\ell_p}{L}\right)^{5/2} - \frac{79}{160}\left(\frac{\ell_p}{L}\right)^{7/2} \quad (\text{Eqn 1})$$

Figure 1 shows P_{loop} as functions of L/ℓ_p and Eqn 1, which is essentially the second equation of Ringrose *et al.* [4], and is valid for both long and short polymer chains. The optimal length of loop formation increases with the persistence length. One can find the optimal ring length r^* from Eqn 1 by differentiation $dP_{loop}/dL = 0$: $r^* = 2.537\ell_p$.

This model deals with a polymer with free ends. In the present application, however, the two ends of a section of chromatin in the middle of the genome are not free. Hence, we have the formation of 'a loop within a loop' (Figure 2a) with a probability of $P_{loop}(L, \ell_p)P_{loop}(L_T - L, \ell_p)$, where L_T is the total contour length of the section of chromatin. That is:

$$\left\{ \left(\frac{\ell_p}{L}\right)^{3/2} - \frac{5}{4}\left(\frac{\ell_p}{L}\right)^{5/2} - \frac{79}{160}\left(\frac{\ell_p}{L}\right)^{7/2} \right\} \left\{ \left(\frac{\ell_p}{L_T - L}\right)^{3/2} - \frac{5}{4}\left(\frac{\ell_p}{L_T - L}\right)^{5/2} - \frac{79}{160}\left(\frac{\ell_p}{L_T - L}\right)^{7/2} \right\}$$

(Eqn 2). Figure 2b shows several curves for different persistence lengths.

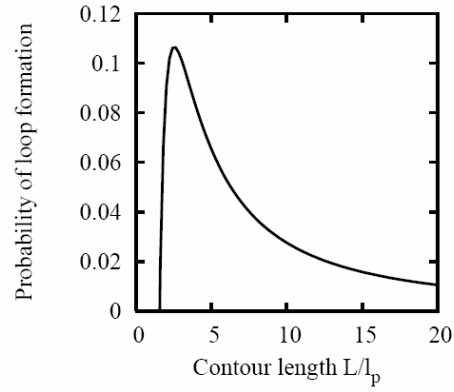


Figure 1. Probability distribution for the loop formation (Eqn 1) with contour length L , measured in terms of the persistence length l_p . When the flexibility is constant, the probability of loop formation is determined by the distance between two points.

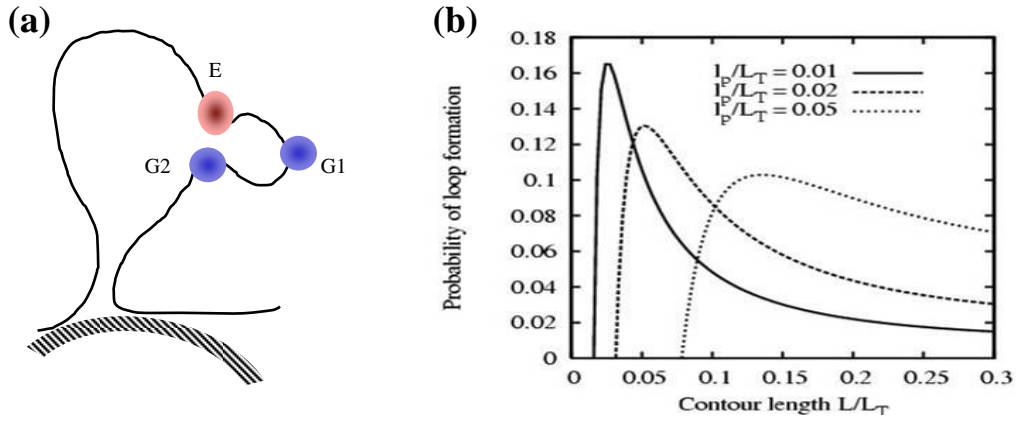


Figure 2. Formation of a loop within a loop. **(a)** A schematic diagram of loop formation within a section of chromatin anchoring at a nuclear substructure. An enhancer (E) is required to activate the cognate genes G1 and G2 (round). **(b)** Probability distributions for the loop formation (Eqn 2) within a section of chromatin with several different values for the persistence length. The x -axis is expressed in terms of the ratio of l_p/L_T . When L_T is constant, the curves show the probability of loop formation between different distances at a given flexibility.

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References

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