

Histone Sliding Model With Chromatin de-Compaction

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Assume a simplistic geometrical chromatin arrangement in which the chromatin is compacted in a zigzag manner before UVC initiation. The compacted chromatin will be stretched in an angle θ_1 , such that the rightmost damage point s , initially above L_0 , can be projected onto L_0 after stretching.

We further assume that by crowding of repair proteins in the damage zone no conformational changes are occurring, but the point s is translated to L_1 . Protein crowding does not alter compaction of the chromatin, but is responsible for some percentage of histone and DNA loss from the ROI. We assume further that the sub-mechanism of sliding (plus pushing) is responsible for conformational changes along the chromatin. In the simplistic geometrical description of chromatin compaction, we therefore assume that the expansion caused by sliding changes the conformation such that the chromatin de-compact into a more straight configuration in such a way that θ_1 changes to $\theta_2 < \theta_1$, for which the point s is translated from L_1 to L_2 (See figure 1).

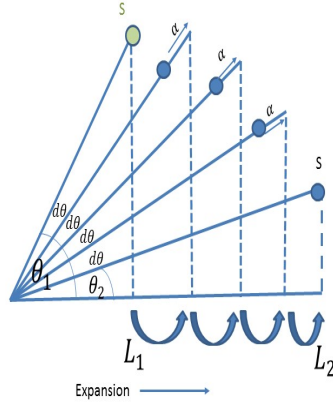


Figure 1:

With this model, the aerial distance that the point s has to move in order to translate from L_1 to L_2 is given by

$$\frac{L_2}{\cos(\theta_2)} - \frac{L_1}{\cos(\theta_1)}$$

The DNA and histone loss from a ROI of radius L_2 can therefore be described using the following equations

$$d = \frac{L_2 - L_0}{L_2} \quad (1)$$

$$h = \frac{L_2 - L_0}{L_2} + \frac{\alpha \cos(\theta_1) \left(\frac{L_2}{\cos(\theta_2)} - \frac{L_1}{\cos(\theta_1)} \right)}{L_2} \quad (2)$$

The expansion factor

The ratio $R = \frac{L_2}{L_0}$ is the expansion ratio. From the equation for d we get

$$R = \frac{1}{1 - d} \quad (3)$$

However, the function above is unbounded for d values close to 1. Since we cannot lose all DNA from the ROI, several values of d are not feasible, and so we need to determine upper and lower boundaries for R . From the equation for h , we can extract L_1

$$L_1 = L_2 \left(\frac{1 - h}{\alpha} + \frac{\cos(\theta_1)}{\cos(\theta_2)} \right) - \frac{L_0}{\alpha} = L_2 \left(\frac{1 - h}{\alpha} + \gamma(\theta) \right) - \frac{L_0}{\alpha} \quad (4)$$

with γ - the chromatin relaxation factor.

Since $L_1 > L_0$ we can set a lower boundary for the expansion factor $R = \frac{L_2}{L_0}$

$$L_2 \left(\frac{1 - h}{\alpha} + \gamma \right) - \frac{L_0}{\alpha} > L_0 \Rightarrow \frac{L_2}{L_0} = R \geq \frac{1 + \alpha}{1 - h + \alpha\gamma}$$

And from $L_1 < L_2$, we can find the upper bound of R

$$R \leq \frac{1}{1 - h + \alpha(\gamma - 1)}$$

In general

$$\frac{1 + \alpha}{1 - h + \alpha\gamma} \leq R \leq \frac{1}{1 - h - \alpha(1 - \gamma)} \quad (5)$$

The contribution of sliding to the expansion

If only measure h and d are available, we can give an estimate of the sliding contribution to the overall expansion based on the values and γ . For this end, we calculate several auxiliary functions

$$\begin{aligned}\frac{h}{d} &= 1 + \frac{\alpha(\gamma L_2 - L_1)}{L_2 - L_1} \\ \frac{h-d}{\alpha d} - \frac{\gamma}{d} &= -\frac{L_1}{L_2 - L_0}\end{aligned}$$

We can notice that

$$\frac{h}{d} + \alpha(\gamma - 1) \left(\frac{h-d}{\alpha d} - \frac{\gamma}{d} \right) = 1 + \alpha\gamma \frac{L_2 - L_1}{L_2 - L_0}$$

Substituting the auxiliary function in the expression above, we get an expression for the sliding contribution

$$\frac{L_2 - L_1}{L_2 - L_0} = \frac{h}{d\alpha} - \frac{\gamma - 1}{d} - \frac{1}{\alpha\gamma} \quad (6)$$

We can therefore limit the valid values for γ for a given h and d using the fact that $0 \leq \frac{L_2 - L_1}{L_2 - L_0} \leq 1$. After substitution, the inequalities in γ are given by the quadratic equations

$$\gamma^2 - \gamma \left(1 + \frac{h}{\alpha} \right) + \frac{d}{\alpha} \leq 0 \quad (7)$$

$$\gamma^2 - \gamma \left(1 - d + \frac{h}{\alpha} \right) + \frac{d}{\alpha} \geq 0 \quad (8)$$

The two condition must be met simultaneously. Finding the roots of the polynomials above, then gives us the boundaries of the valid γ range.

Using this result we can perform three calculations in the following order

1. For any values $0 \leq h \leq 1$ and any value $d \leq h$, calculate the valid range for the chromatin relaxation factor γ by finding the roots of the two polynomials in 7;
2. Calculate the relative sliding contribution as a function of the valid γ range according to 6;

3. Calculate the minimal and maximal expansion factor, R , in the valid range of γ according to 5.

Examples of the relative sliding contribution for $d = 0.23$ and $0.3 \leq h \leq 0.45$ are given in Figure 2

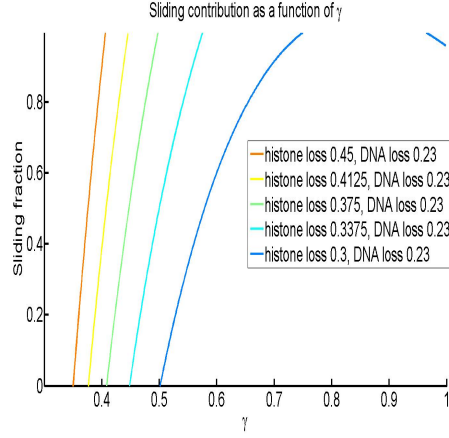


Figure 2: