

**Statistical Thermodynamics of DNA Denaturation
processes**

Course: Statistical Thermodynamics

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Spring quarter 2012

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1 Nomenclature

F	Free Energy	[J]
x	Coordinate	[m]
y	Coordinate	[m]
ϵ	Energy	[J]
k	Spring constant	[N/m]
k_b	Boltzmann's constant	[J/K]
T	Temperature	[K]
h_n	Distance between adjacent base planes	[m]
L	Distance between adjacent bases	
h	Planck's constant	[J s]
S	Entropie	[J/K]
K	Spring constant	[N/m]

2 Introduction

Since the Deoxyribonucleic acid (DNA) was decoded there have been several investigations in order to fully understand its properties. Therefore the application of statistical mechanics to DNA-molecules, in order to describe their behavior regarding the denaturation transition, has become a popular way to theoretically describe the transition mechanisms. These mechanisms are of high importance for the transcription processes. The denaturation can be induced by a rise of temperature over a certain critical temperature as well as by external forces or torques. This paper will shortly describe the structure of DNA and give an overview of two different mathematical attempts to describe its partition function. Therefore the used assumptions as well as approximations and associated problems are explained briefly. Subsequently the achieved results regarding the denaturation process will be described and, if available, compared to experimentally obtained results.

3 Structure of DNA

DNA consists of two entangled polymers, which create a double helix. These polymers are built of monomers; the nucleotides. They are compounded of two elements: phosphate groups and sugar rings building the sugar phosphate backbones. The bases, which can be adenine, guanine, cytosine or thymine, connect both sugar phosphate backbones. These bases exist in pairs and have, depending on the base pair combination, hydrogen bonds that are of high importance to understand the denaturation process. Therefore modeling these bonds is very important to provide a good model of the DNA-molecule that can be examined analytically. Figure 1 shows the double helix structure of DNA. [1]

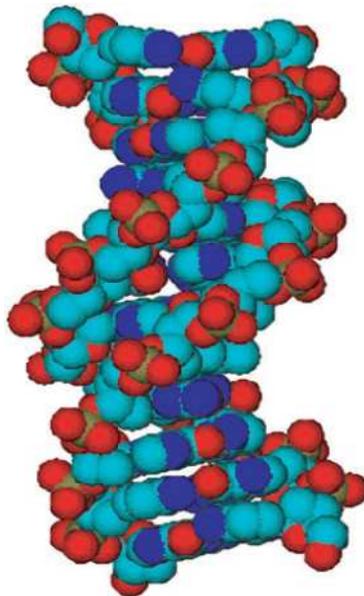


Figure 1: Double helix structure of DNA [1]

4 Theoretical Statistical Mechanics of DNA Molecules

In order to apply statistical physics to DNA molecules you need to build a model that can be described analytically. To determine values of the Entropy or the Free Energy it is necessary to calculate the partition function, which is generally defined as:

$$Z = \sum_i g_i e^{-\frac{\varepsilon_i}{kT}}$$

The different involved energies ε_i are often summarized by the Hamiltonian operator.

$$H = \sum_i \varepsilon_i$$

The first model shown here was developed by Peyrard et. al [2]. Their main aim was to avoid the need of a continuum approximation when calculating the partition function for the hydrogen bonds, by using a transfer integral technique. In addition nonlinear effects were included in the model.

The used model uses two degrees of freedom for each base pair whose hydrogen bonds were modeled by a Morse potential. It describes two chains that are connected by the Morse potential i.e. hydrogen bonds. Overall the considered kinds of energy in the Hamiltonian were kinetic energy, potential energy as well as the mentioned Morse potential (last term, second sum) leading to the following Hamiltonian:

$$H = \left(\sum_n \frac{m\dot{x}^2}{2} + \frac{1}{2}K(x_n - x_{n-1})^2 \right) + \left(\sum_n \frac{m\dot{y}^2}{2} + \frac{1}{2}K(y - y_{n-1})^2 + D \left(e^{(-a\sqrt{2} y_{n-1})^2} \right) \right)$$

This leads to the following formula for Z:

$$Z = \int_{-\infty}^{\infty} \prod_{n=1}^N e^{-\beta H} d\dot{x}_n d\dot{y}_n dx_n dy_n$$

In this model the masses of all bases were assumed to be the same. Additionally the motions in x and y direction were considered to be independent from each other. The solution for Z regarding the momentum parts is easy to handle and results in the familiar solution for N particles. In contrast to the momentum parts, the calculation of the integral over y used a

transfer integral technique in order to avoid a continuum approximation¹. This leads to an equation formally the same as the Schrödinger equation. With the result for the partition function it is now possible to calculate thermodynamic properties like the free Energy F. However, an important quantity to describe the denaturation is the mean stretching $\langle y \rangle$ of the hydrogen bonds that can generally be calculated with:

$$\langle y_m \rangle = \frac{1}{Z_y} \int \prod_{i=1}^N y_m e^{-\beta f(y_n, y_{n-1})} dy_n$$

The results obtained by the used model are extremely sensitive to parameters used to characterize the particular energies (k for potential Energy, D for the Morse potential). With the correct set of parameters the model gives a good value for the denaturation temperature, but so far there is no explanation how the denaturation works. In order to provide this, the authors used Newton's law of motion in y-direction, which leads to nonlinear differential equations that are connected to Z by y. Thereby the authors were now in position to derive an equation for $\langle y^2 \rangle$ using the partition function as well as the nonlinear differential equation (Figure. 2). One can see the stretching rising spontaneously with rising temperature. Depending on the used "spring constant" k the transition process happens within a various range of temperature.

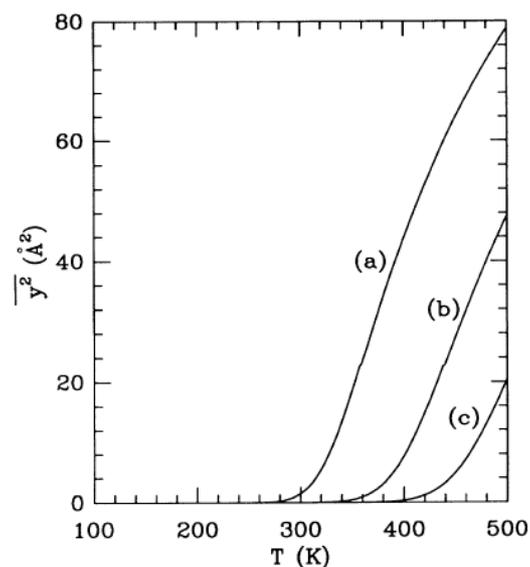


Figure 2: $\langle y^2 \rangle$ over T for three different values of k (Rising from a to c) [2]

¹ For a detailed evaluation of the integral technique and the therefor needed eigenfunctions and eigenvalues see [2]

According to the authors the issues with this model are especially neglected inhomogeneities concerning masses of different bases. Potential improvement of the model could be achieved by adding additional degrees of freedom since the present model shows a low sensitivity regarding vibrational behavior of DNA. Overall, the authors concluded that the data obtained with this model indicates that the denaturation behavior is caused by energy-localization analogously found in self-focusing plasmas.

In a paper published in 2004 by Peyard et al [1] additional extensions to model the DNA behavior were used to obtain more precise results. The used Hamiltonian Operator was similar to the one used before i.e the modeling of the respected forces was basically the same. However, the model here only used one degree of freedom and in addition to the first model there is an additional potential energy involved that is supposed to describe interactions between adjacent bases. Figure 3 shows the structure of the dynamic model.

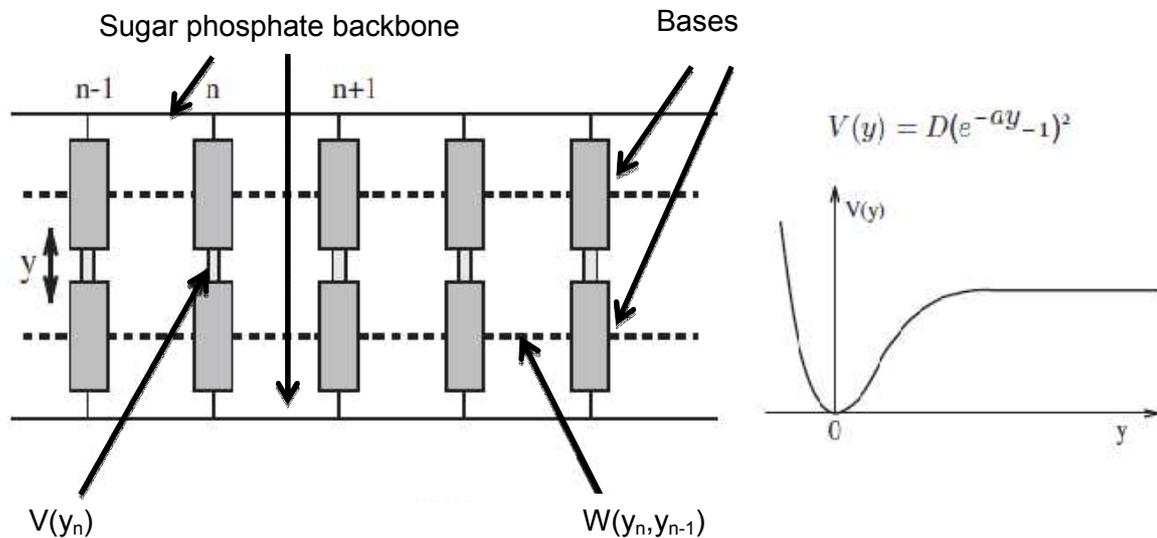


Figure 3: Structure of the DNA model (left), Morse potential between bases (right)

$V(y_n)$ is the Morse potential used to describe the behaviour of the hydrogen bonds and $W(y_n, y_{n-1})$ is potential modelled to describe interactions of adjacent bases.

Using the Hamiltonian a numerical simulation was able to outline the denaturation process in a thermal bath for 256 base pairs. However, this process (i.e. the rise of temperature) had to be finished in a few nanoseconds which lead to a non-equilibrium situation for the molecule. Despite that the obtained results were in good agreement to observations, the basic process of denaturation can be described well.

Still, so far there is again no exact model that describes the mechanisms of denaturation in detail. In order to improve the model concerning this aim the approach was to include non-linear mechanics with the equation of motion leading to a system of coupled differential equations. These equations² lead to a nonlinear Schrödinger equation with which an approximate solution of $Y_n(t)$ can be calculated. Since, the model so far does not contain any variance in respect to T in order to consider thermal fluctuations statistical mechanics had to be taken into account. Furthermore, the obtained analytical results by nonlinear dynamics do not exist in reality because of the thermal fluctuations. Therefore the partition function was calculated with the same transfer integral technique as before. With this partition function the authors were in position to calculate the denaturation temperature. The model with the “new” potential energy W was compared with two different equations for W in order to describe the stacking interaction between adjacent bases.

$$W_1 = \frac{1}{2}K(y_n - y_{n-1})^2$$

$$W_2 = \frac{1}{2}K(1 + \rho e^{-\alpha(y_n + y_{n-1})} (y_n - y_{n-1})^2)$$

The theoretical results achieved with both of these versions of the model are shown in Figure 4. This diagram shows the fraction of bound base pairs over the normalized temperature. The lines marked with triangles are achieved by using W_1 and the other by using W_2 . For the

² These equations cannot be solved exactly so the authors used a substitution technique. For more details see [1]

first model one can see a smooth transition of the bound base pairs. For the new model the transition happens very sudden which fits experimental observed behaviour better. Additionally you can see a jump in entropy, which is caused by the transition/denaturation of the DNA.

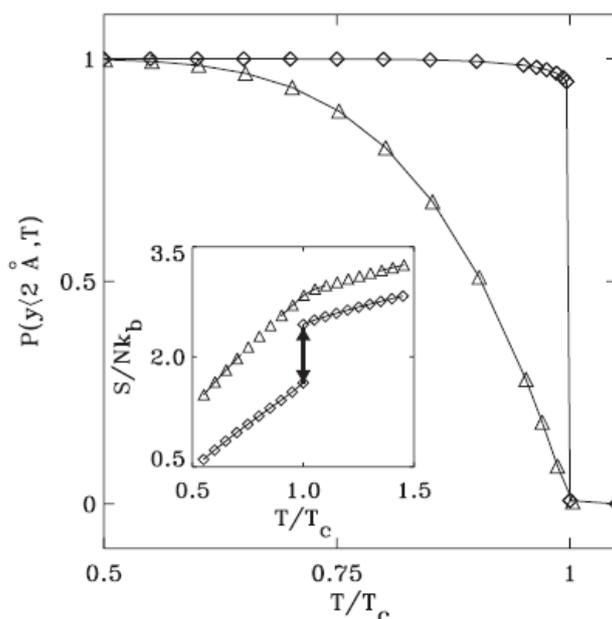


Figure 4: Fraction of bound base pairs over T/T_c , Inset: Normalized entropy over T/T_c [1]

Since the authors noticed that the equation of motion has a “domain wall solution”³ another approach to the denaturation with the free energy calculation could describe the process. The contributions to the free energy caused by the domain wall are separated in a part F_{Wall} and $F_{\text{Fluctuations}}$. The first one is easy to calculate so here we will focus on the second term. Its origin is the vibrational modes around the wall. The partition function for this can be calculated and is⁴:

$$Z = \prod_q \frac{1}{1 - e^{-\frac{\beta \hbar \omega(q)}{2\pi}}} \cong \prod_q \frac{2\pi}{\beta \hbar \omega(q)}$$

³ This separates open and closed regions of base bonds

⁴ $\omega = 2^{1/2} q$, where where $q_i = i\pi/p$ and p is the number of particles

Using an integral calculation for the log over all products of q leads to a function for $F_{\text{Fluctuations}}$ that shows the following properties⁵:

- By increasing x_0 (gives the position), which tends to close the open bases, and small T the DNA can reduce its free energy for
- For large T the free energy can be reduced by decreasing x_0

With this result it is also possible to calculate the denaturation temperature. The result with this method is exactly the same as with the statistical mechanics mentioned above.

In addition to the above-mentioned thermal induced mechanisms of DNA denaturation, denaturation of DNA can be raised due to torque-induced strains. In order to investigate the transition behaviour Cocco et al. [3] generated a model that took the supercoiled nature of DNA into account since the structure of it has a tremendous impact on its mechanical behaviour. The model created for this is pictured in figure 5 in which the distance between adjacent bases is kept constant (L).

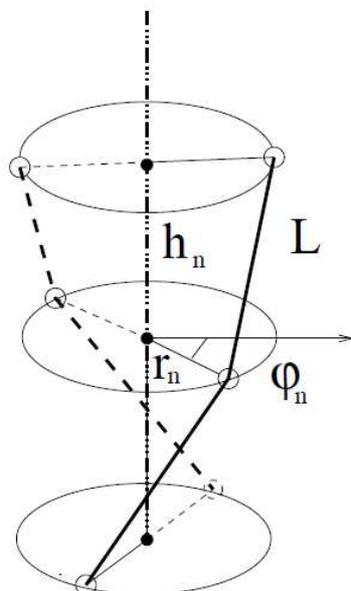


Figure 5: General structure of the model created by Cocco et al. [3]

The modelling of the particular potentials in the molecule were similar to those used by Peyrard et al. The features of them are⁶:

⁵ Compare [1] page 24 and 25

- Short range morse potential between bases
- Shear force induced by sliding motions modelled by a stacking potential
- Elastic Energy to describe the vibrations of bases as a function of their coordinates (radius r_n and angle φ_n)

The data achieved with this particular model showed that additional stresses induced by a torque indeed have an impact on the denaturation behaviour, especially the temperature the denaturation starts. The achieved results with this model were in good agreement with experimental observed values. For instance, the calculated Gibbs free energy is 0,022 eV compared to 0,025 eV observed in experiments. The authors found out that especially the “direction” of the additional torque is important. Torques, which undertwist the molecule, result in a lower temperature of denaturation since the stretching of the hydrogen bonds is higher in this case.

⁶ For detailed parameters of the particular potentials see [3]

5 Conclusion

This paper summarized three different theoretical models of DNA. The used models were able to predict the denaturation behaviour of DNA well. It showed that the modelling of the hydrogen bonds is a very important part achieving good results. The often-used Morse potential achieves good results here. Another important point in order to provide a good model is the potential influence of adjacent bases. Thus an additional potential that models this behaviour W (see above) is needed to provide a “first order like” jump of open base pairs like similarly observed in experiments. Another important point in order to provide a good model for the investigated properties is the scale of the model. For instance, models at the atomic scale is couldn't take adjacent neighbours into account. As shown the influence of adjacent bases on each other has a huge impact on the denaturation behaviour. Especially near the critical denaturation temperature the additional consideration of such influences can improve the model profoundly. All models shown here assume homogenous masses of the bases which is a needed assumption in order to keep the model as simple as possible. If one wants to consider a variance of base pairs, numerical simulations are needed to determine the particular properties.

6 References

- [1] Michel Peyrard, "Nonlinear dynamics and statistical physics of DNA", 2004
- [2] M. Peyrard, "Statistical Mechanics of a Nonlinear Model for DNA Denaturation", 1989
- [3] Simona Cocco et al. "Statistical Mechanics of Torque Induced Denaturation of DNA", 1999