Yang-Lee zeros and the helix-coil transition in a continuum model of polyalanine

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Abstract

We calculate the Yang-Lee zeros for characteristic temperatures of the helix-coil transition in a continuum model of polyalanine. The distribution of these zeros differs from predictions of the Zimm-Bragg theory and supports recent claims that polyalanine exhibits a true phase transition. New estimates for critical exponents are presented and the relation of our results to the Lee-Yang theorem is discussed.

Keywords: Yang-Lee zeros, Lee-Yang theorem, Helix-coil transition, Protein folding, Generalized ensemble simulations

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1 Introduction

Recently, there has been an increased interest in the statistical physics of biological macromolecules. For instance, the conditions under which α-helices, a common structure in proteins, are formed or dissolved, have been extensively studied [1]. Traditionally, the characteristics of the observed sharp transition between random coil state and (ordered) helix, have been described in the framework of Zimm-Bragg-type theories [2]. In these theories, the molecules are approximated by a one-dimensional Ising model with the residues as “spins” taking values “helix” or “coil”, and solely local interactions. Hence, thermodynamic phase transitions are not possible in these
theories. However, in previous work [3, 4, 5] evidence was presented that polyalanine exhibits a phase transition between the ordered helical state and the disordered random-coil state when interactions between all atoms in the molecule are taken into account. Investigating the finite size scaling of various quantities such as specific heat, susceptibility and the Fisher zeros, we studied the nature of this phase transition and presented estimates for the critical exponents $\nu$, $\alpha$ and $\gamma$. Here, we continue our previous investigation by exploring the helix-coil transition in polyalanine from a different point of view. We intend to demonstrate in greater detail the differences in the critical behaviour of our model and the Zimm-Bragg theory, and we will present additional critical exponents.

Yang and Lee have established long ago [6] that the statistical theory of phase transitions can also be described by means of the distribution of the zeros of the grand partition function in the complex fugacity plane. In the case of the Ising model this description corresponds to study this model with an external magnetic field $H$ mathematically extended from real to complex values. Although complex values for the fugacity are not physical, the characteristics of the phase transition can be extracted from the distribution of the zeros. As the volume of the given (finite) system increases, the number of complex zeros grows and they will close onto the positive real fugacity axis. In the thermodynamic limit, those zeros circumscribe closed regions on this plane, thus defining thermodynamic phases which are themselves free of zeros. In Ref. [7] Lee and Yang proved the famous circle theorem, namely that in the Ising model with ferromagnetic couplings the complex zeros lie on the unit circle in the complex $y−$plane, $y = e^{-2/3H}$.

The goal of our paper is to investigate whether the helix-coil transition in biological macromolecules can also be described in the frame work of the Yang-Lee zeros. For polyalanine, the analogous of the magnetization in the Ising model is the number of helical residues $M$. Formally we can introduce a (non physical) external field $H$ as the conjugate variable to this order parameter $M$ (which plays the role of a magnetization), and study the Yang-Lee zeros. Such an investigation allows us not only to check our previous results with an independent method, it opens also the possibility to calculate new critical exponents and to point out much clearer the differences between our all-atom model of polyalanine and the Zimm-Bragg theory. If the helix-coil transition can indeed be described by the Zimm-Bragg model, then the distribution of the Yang-Lee zeros in function of the temperature should resemble that of the one dimensional Ising model. On the other hand, substantially
different distribution would demonstrate that the helix-coil transition in polyalanine is not accurately described by the Zimm-Bragg theory.

Before proceeding, we give the outline of the paper. In the next section we describe the numerical evaluation of the partition function. Our approach and numerical results are presented in the third Section, which is followed by our conclusions.

2 Methods

Our investigation of the helix-coil transition for polyalanine is based on a detailed, all-atom representation of that homopolymer. Since one can avoid the complications of electrostatic and hydrogen-bond interactions of side chains with the solvent for alanine (a nonpolar amino acid), explicit solvent molecules were neglected. The interaction between the atoms was described by a standard force field, ECEPP/2, \cite{8} (as implemented in the KONF90 program \cite{9}) and is given by:

\begin{align*}
E_{\text{tot}} &= E_C + E_{LJ} + E_{HB} + E_{\text{tor}}, \\
E_C &= \sum_{(i,j)} \frac{332 q_i q_j}{\epsilon r_{ij}}, \\
E_{LJ} &= \sum_{(i,j)} \left( A_{ij} \frac{r_{12}^{12}}{r_{ij}^6} - B_{ij} \right), \\
E_{HB} &= \sum_{(i,j)} \left( C_{ij} \frac{r_{12}^{12}}{r_{ij}^6} - D_{ij} \right), \\
E_{\text{tor}} &= \sum_{l} U_l (1 \pm \cos(n_l \chi_l)).
\end{align*}

Here, $r_{ij}$ (in Å) is the distance between the atoms $i$ and $j$, and $\chi_l$ is the $l$-th torsion angle. Note that with the electrostatic energy term $E_C$ our model contains a long range interaction neglected in the Zimm-Bragg theory \cite{4}. It was conjectured that it is this long range interaction in our model and the fact that it is not one-dimensional which allows the existence of the observed phase transition in Refs. \cite{3, 4, 5}. We remark that the 1D Ising model with long-range interactions also exhibits a phase transition at finite $T$ if the interactions decay like $1/r^\sigma$ with $1 \leq \sigma < 2$ \cite{10}.

Simulations of detailed models of biological macromolecules are notoriously difficult. This is because the various competing interactions within the polymer lead to an energy landscape characterized by a multitude of local minima. Hence, in the low-temperature region, canonical Monte Carlo or molecular dynamics simula-
thermalize within the available CPU time. Only recently, with the introduction of new and sophisticated algorithms such as multicanonical sampling \[11\] and other generalized-ensemble techniques \[12\] was it possible to alleviate this problem in protein simulations \[13\]. For polyalanine, both the failure of standard Monte Carlo techniques and the superior performance of the multicanonical algorithm are extensively documented in earlier work \[14\]. For this reason, we use again this simulation technique for our project where we considered polyalanine chains of up to \(N = 30\) monomers.

In the multicanonical algorithm \[11\] conformations with energy \(E\) are assigned a weight \(w_{\text{mu}}(E) \propto 1/n(E)\). Here, \(n(E)\) is the density of states. A simulation with this weight will lead to a uniform distribution of energy:

\[
P_{\text{mu}}(E) \propto n(E) w_{\text{mu}}(E) = \text{const} .
\] (6)

This is because the simulation generates a 1D random walk in the energy space, allowing itself to escape from any local minimum. Since a large range of energies are sampled, one can use the reweighting techniques \[15\] to calculate thermodynamic quantities over a wide range of temperatures \(T\) by

\[
< \mathcal{A} >_T = \frac{\int dx \ A(x) w^{-1}(E(x)) \ e^{-\beta E(x)}}{\int dx \ w^{-1}(E(x)) \ e^{-\beta E(x)}},
\] (7)

where \(x\) stands for configurations.

Note that unlike in the case of canonical simulations the weights are not a priori known. We needed between 40,000 sweeps \((N = 10)\) and 500,000 sweeps \((N = 30)\) for the weight factor calculations by the iterative procedure described in Refs. \[11, 16\]. All thermodynamic quantities were estimated from one production run of \(N_{\text{sw}}\) Monte Carlo sweeps starting from a random initial conformation, i.e. without introducing any bias. We chose \(N_{\text{sw}}=2\,000\,000, 2\,000\,000, 4\,000\,000, \) and \(3\,000\,000\) sweeps for \(N = 10, 15, 20, \) and \(30,\) respectively.

It follows from Eq. (8) that the multicanonical algorithm allows us to calculate estimates for the spectral density:

\[
n(E) = P_{\text{mu}}(E)w_{\text{mu}}^{-1}(E) .
\] (8)

We can therefore construct the corresponding partition function for our all-atom
At a given energy, 

$$Z(u, y) = \sum_{M=0}^{N-2} \sum_{E} n(E, M) u^E y^M,$$  

(9)

where $u = e^{-\beta}$ with $\beta$ the inverse temperature, $\beta = 1/k_B T$ and $y = e^{-H}$. We have absorbed the factor $\beta$ in the definition of the field $H$ which is the conjugate variable to our order parameter $M$. The later quantity is defined by the condition that for a helical residue the dihedral angles ($\phi, \psi$) fall in the range ($-70 \pm 20^\circ, -37 \pm 20^\circ$). Note, that for convenience we have discretized the energy in Eq. (9). In previous work we found that the partition function zeros depend only weakly on the energy bin size, and for the present study we choose energy bins of length 0.5 kcal/mol.

3 Yang-Lee Zeros of Polyalanine

In order to analyse the helix-coil transition in our all-atom model of polyalanine we first determine the (pseudo)critical temperatures. This can be done in various ways. For instance, in Ref. [4] these temperatures where calculated from the distribution of the Fisher zeros [17]. Here, we check our previous results by calculating estimates for the pseudo-critical temperatures in a different way.

Our temperature-driven transition model can be analysed by considering the coexistence of two phases: a disordered (coil) phase and an ordered (helix) phase at the critical temperature $T_c$. This behaviour can be described by the existence of an equilibrium probability distribution $P_N(M)$ for the corresponding order parameter $M$ [18, 19]. This approach leads to a definition of a finite size critical temperature by approximating the equilibrium distribution by a sum of two distributions, each one characterizing the corresponding phase. This ansatz gives origin to a two-peak like distribution separated by a minimum and has led to the finite size scaling study of the coexistence of bulk phases [20]. Following these works, we consider for our purpose the histograms of the helicity for all chain sizes $N$, which is our order parameter (and the equivalent to the magnetization in the Ising model), at different temperatures $\beta$. It is straightforward to calculate the histograms of helicity distribution at these temperatures from our multicanonical estimates of the density of states,

$$w(M) = \sum_{E} n(E, M) u^E.$$  

(10)

As expected, these histograms exhibit a clean double peak structure at what we
predominant single peak at low (high) values of the helicity. Hence, we define our critical temperatures by the condition that the reweighted histogram of the magnetization have two peaks of equal heights. As an example we show in Fig. 1 the histogram normalized to area one, for \( N = 30 \) at \( T_c = 518 \) K.

Table 1 summarizes the so obtained set of critical temperatures by this method. The quoted values and errors were obtained by reweighting independent binned data to temperatures \( T_c^i, i = 1, 2, ..., nbins \), where one obtains equal heights in the histograms for our order parameter \( M \). Our statistics were based on \( nbins = 19, 20, 16 \) and 3 for \( N = 10, 15, 20 \) and 30, respectively. for comparison we also list our previous estimates [4] which were derived from an analysis of the Fisher zeros and the position of the maximum of specific heat \( C_v \). We note, that our new results agree within the errors with our previous estimates for the pseudo-critical temperatures which demonstrates the validity of our approach.

After having demonstrated the reliability of our data we calculate now at the so obtained critical temperatures the distribution of the Yang-Lee zeros by means of Eq. (9). Our results are displayed in Fig. 2 for the case of chain lengths \( N = 30 \). In that figure we draw in addition a unit circle to point out the relative position of our zeros around it. Similar distributions are obtained for smaller systems. The presented error bars for the zeros in this figure, were estimated by considering the new partition functions at the limiting temperatures \( T_c(N) \pm \Delta T_c(N) \) where \( \Delta T_c(N) \) is the error in our pseudo-critical temperatures \( T_c(N) \). Our error bars clearly exclude the possibility that the complex zeros are distributed on the unit circle. On the other hand, the Yang-Lee zeros for the 1D Ising model (which can be calculated exactly) fall on the unit circle. This is shown in Fig. 3 for chain lengths \( N = 5, 15 \) and 30.

After having demonstrated the difference in the two models at the critical point, we extend our study to the behaviour of our polyalanine zeros as function of the temperature. In Fig. 4 we show for our smallest polyalanine chain how the zeros change with temperature \( u(\beta) \), measured in multiple of the critical value \( u_c \). Again, we draw for illustration a unit circle to call attention to the relative position of our zeros. We exhibit the smallest chain since the density of zeros increases with growing chain length making it difficult to the eyes to trace the movement of the zeros in the complex \( y \)-plane. As the temperature increases, \( u(\beta) > u_c \), we observe that the zeros move away from the unit circle and consequently the edge zero, the zero closest to the positive real \( y \)-axis, moves away from the real axis. A similar
behaviour is known for the $q$-state Potts model with $q > 2$ on finite lattices for temperatures larger than the critical one \[23\]. For $u(\beta) < u_c$, we find again that the zeros do not fall all on the unit circle. Hence, the Lee-Yang theorem does not apply for our model demonstrating again that polyalanine should not be described by Ising-type models.

Figure 4 indicates that the angle $\theta_0$, the angle at which the edge zeros deviate from the real $y$-axis, grows as the temperature is increased above $T_c$, i.e. $u(\beta) > u_c$. For larger lengths $N$, the number of zeros increases and the edge zeros move towards the real axis. Note that the movement for the edge zero seems to follow an unit arc, leading to $Re(y) = 1$ and the real value $H = 0$ in the thermodynamic limit. The movement of the edge zeros towards the real axis itself is a signal for the possibility of a true phase transition in the thermodynamic limit if the locus of zeros cut the positive real axis at finite temperature. In that case one would expect the following scaling relation for the edge zeros \[24\]:

$$\theta_0(t, N) = N^{-y_h/d}t^{y_t/d},$$

(11)

where $t = (T - T_c)/T_c$, $y_h$ is the magnetic scaling exponent and $y_t = 1/\nu$ is the thermal scaling exponent. Note, that we have introduced the scaling variable $N^{1/d}$ in place of the usual linear length $L$. This is because the number of monomers $N$ is the natural quantity to describe polyalanine chains. Since we have no theoretical indication to assume a particular integer geometrical dimension $d$ for our polypeptide, we present our results as a function of this parameter $d$.

Now, assuming that the above finite size scaling relation holds for polyalanine chains we can calculate the “magnetic” scaling exponent \[17\]

$$y_h/d = (\beta + \gamma)/d\nu$$

(12)

if we take $t = 0$, i.e. $u(\beta) = u_c$. For this reason we display in Fig. 5 the linear regression for ln ($\theta_0(N)$). The least-square fit gives us

$$y_h/d = 0.97(4),$$

(13)

with the goodness of fit $Q = 0.67$. This value for $Q$ means the fit is acceptable for the present precision data and corroborates our expectation.

If we take our estimate in Eq. (13) and the reported values for $\gamma$ and $d\nu$ from Ref. \[4\], $\gamma = 1.06(14), d\nu = 0.93(5)$, we can evaluate the exponent $\beta$ either by the
precise since it involves three parameters ($\beta = -0.16(15)$), while the second one, relying on two previous estimates, gives $\beta = -0.065(74)$. As one should expect, both estimates agree with each other within the error bars demonstrating the consistency of this study with earlier investigations [3, 4, 5]. Note also that our estimates for the critical exponent $\beta$ do not help us to answer a question we had to leave unanswered in the earlier work, namely, whether the helix-coil transition is a first order phase transition ($\beta = 0$) or a (strong) second order phase transition ($\beta \neq 0$). This is not surprising since clarifying the nature of a phase transition can be a challenging issue even for simpler systems (such as Potts models [25], to name only one example) and requires dedicated large-scale simulations. The important point here is rather that our model of polyalanine, despite its complexity, can be described in terms of a critical theory.

4 Conclusion

We have extended the Yang-Lee zeros analysis to an all-atom model of polyalanine polymers of various chain lengths. Our results were compared with the Zimm-Bragg model which is often used to describe helix-coil transitions in Biopolymers. Our analyses of the Yang-Lee zeros for both models give clear evidence for our claim that the helix-coil transition in an all-atom model of polyalanine is not adequately described by the Zimm-Bragg theory. Our results confirm earlier work where we pointed out the possibility of a thermodynamic phase transition in polyalanine which is forbidden in the Zimm-Bragg model.

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References

[1] D. Poland and H.A. Scheraga, *Theory of Helix-Coil Transitions in Biopolymers* (Academic Press, New York, 1970).
[3] U.H.E. Hansmann and Y. Okamoto, J. Chem. Phys. 110 (1999) 1267.

[4] N.A. Alves and U.H.E. Hansmann, Phys. Rev. Lett. 84 (2000) 1836.

[5] J.P. Kemp, U.H.E. Hansmann and Zh.Y. Chen, Eur. Phy. J. B 15 (2000) 371.

[6] C.N. Yang and T.D. Lee, Phys. Rev. 87 (1952) 404.

[7] T.D. Lee and C.N. Yang, Phys. Rev. 87 (1952) 410.

[8] M.J. Sippl, G. Némethy, and H.A. Scheraga, J. Phys. Chem. 88 (1984) 6231, and references therein.

[9] H. Kawai, Y. Okamoto, M. Fukugita, T. Nakazawa, and T. Kikuchi, Chem. Lett. 1991 (1991) 213; Y. Okamoto, M. Fukugita, T. Nakazawa, and H. Kawai, Protein Engineering 4 (1991) 639.

[10] F.J. Dyson, Commun. Math. Phys. 12 (1996) 91; J.F. Nagle and J.C. Bonner, J. Phys. C 3 (1970) 352; E. Bayong, H.T. Diep and V. Dotsenko, Phys. Rev. Lett. 83, (1999) 14.

[11] B.A. Berg and T. Neuhaus, Phys. Lett. B 267 (1991) 249.

[12] U.H.E. Hansmann and Y. Okamoto, in: Stauffer, D. (ed.) “Annual Reviews in Computational Physics VI” (Singapore: World Scientific), p.129 (1998).

[13] U.H.E. Hansmann and Y. Okamoto, J. Comp. Chem. 14 (1993) 1333.

[14] Y. Okamoto and U.H.E. Hansmann, J. Phys. Chem. 99 (1995) 11276.

[15] A.M. Ferrenberg and R.H. Swendsen, Phys. Rev. Lett. 61 (1988) 2635; Phys. Rev. Lett. 63 (1989) 1658(E) and references given in the erratum.

[16] U.H.E. Hansmann and Y. Okamoto, Physica A 212 (1994) 415.

[17] C. Itzykson, R.B. Pearson and J.B. Zuber, Nucl. Phys. B 220 [FS8] (1983) 415.

[18] K. Binder and D.P. Landau, Phys. Rev. B 30 (1984) 1477.

[19] M.S.S. Challa, D.P. Landau and K. Binder, Phys. Rev. B 34 (1986) 1841.

[20] J. Lee and J.M. Kosterlitz, Phys. Rev. Lett. 65 (1990) 137; Phys. Rev. B 43 (1991) 2412.
[21] S. Katsura and M. Ohminami, J. Phys. A 5 (1972) 95.

[22] Z. Glumac and K. Uzelac, J. Phys. A 27 (1994) 7709.

[23] S.-Y. Kim and R.J. Creswick, Phys. Rev. Lett. 81 (1998) 2000.

[24] R.J. Creswick and S.-Y. Kim, Phys. Rev. E 56 (1997) 2418.

[25] P. Peczak and D.P. Landau, Phys. Rev. B 39 (1989) 11932.
Table 1: Critical temperatures $T_{c}^{Hist}$ as obtained by our analysis for polyalanine chain lengths $N$. For comparison, we show also previous estimates obtained from both an analysis of Fisher zeros ($T_{c}^{Fisher}$) and the location of the peak in the specific heat ($T_{c}^{Cv}$).

| $N$ | $T_{c}^{Hist}$ | $T_{c}^{Fisher}$ | $T_{c}^{Cv}$ |
|-----|---------------|-----------------|-------------|
| 10  | 433(1)        | 442(8)          | 427(7)      |
| 15  | 496(3)        | 498(4)          | 492(5)      |
| 20  | 518(4)        | 511(5)          | 508(5)      |
| 30  | 518(3)        | 520(4)          | 518(7)      |
Figure Captions:

**Figure 1.** Histogram for the number of helical residues in conformations for chain length $N = 30$.

**Figure 2.** Distribution of complex partition function zeros in the $y-$plane with error bars, at $T_c(N = 30)$. We draw an inexistent unit circle to show how the zeros are distributed around it. The zeros do not circumscribe an unit circle as expected for the Lee-Yang theorem in Ising like systems with positive interactions.

**Figure 3.** The Yang-Lee zeros for the Ising chain with lengths $N = 5, 15$ and $30$.

**Figure 4.** The behaviour of the partition function zeros for polyalanine with chain length $N = 10$ in function of the temperature $u(\beta)$.

**Figure 5.** Linear regression for $\ln (\theta_0)$, Eq. (11), at the critical temperature.
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\[ \frac{y_h}{d} = 0.97(1) \]

\[ \ln(\theta_0) \ versus \ \ln(N) \]