Helical structures from an isotropic homopolymer model

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Abstract

We present Monte Carlo simulation results for square-well homopolymers at a series of bond lengths. Although the model contains only isotropic pairwise interactions, under appropriate conditions this system shows spontaneous chiral symmetry breaking, where the chain exists in either a left- or a right-handed helical structure. We investigate how this behavior depends upon the ratio between bond length and monomer radius.

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Naturally occurring polymers, such as proteins (polypeptides) and nucleic acids (polynucleotides), are capable of adopting very specific single-chain conformations under certain conditions. It is believed that this structural specificity plays a crucial role in the biological function of a given molecule. Consequently, the essential mechanism of how the overall structure of a polymer arises from the basic interactions between its constituent monomers is of great fundamental interest. A recurring motif in many diverse biopolymers is the helix. This structure has also been observed in synthetic polymers — for example, meta-phenylacetylene oligomers [1], and the isotactic form of poly(methyl methacrylate) [2] in various solvents. The occurrence of helical structures in polymers with substantially different monomer chemistries suggests an underlying generic behavior, which has prompted significant efforts to produce “minimal” models that naturally display helical structures [3, 4, 5, 6]. An underlying assumption in the vast majority of these models is stated explicitly by Kemp and Chen [7]: “an isotropic potential interaction is not sufficient to produce helical ground states.” In this letter, we present simulation results for a polymer model using only pairwise isotropic monomer interactions. We explicitly demonstrate that this model breaks chiral symmetry at low temperatures and show evidence that it forms stable helices.

The general theoretical perspective [8, 9] has been to view helix formation as a discrete process. Each polymer element (monomer) can only take on one of two states, “helical” or “coil” (non-helical), and a free energy is assigned to each of these states. This approach has been fairly successful in describing the helix-coil transition in polymer systems. One shortcoming of this approach, however, is that it presupposes the existence of a particular helix, and, as a consequence, it is difficult to determine the conditions under which a helical conformation can naturally arise.

Another line of research has been to apply molecular simulations techniques to examine the structural behavior of minimal polymer models, which has lead to interesting results. Zhou and coworkers discovered [10, 11] a freezing transition for linear homopolymers composed of tangent-hard spheres that interact with each other through an attractive square-well potential. During this discontinuous transition, the collapsed “molten” globule state freezes into a highly symmetric crystalline-like state. While this transition does result in structural specificity, the observed ordered state does not resemble any of the structural motifs seen in biopolymers. Noguchi and Yoshikawa [12] extended the model of Zhou and coworkers by adding a bond bending potential, which introduced stiffness to the polymer model. Upon increasing the stiffness of the chain, toroidal and rod-like phases were observed — analogous to structures exhibited by isolated DNA
chains [13, 14]. However, they did not observe the formation of helices in their simulation studies. Kemp and Chen [4, 7] have developed a simple homopolymer model that displays a helix-coil transition; however, the monomer-monomer interactions in this model are asymmetric.

For thick strings confined within a fixed geometry (e.g., inside a cube), a helix can be the optimal packing configuration [15]. These “close-packed” configurations may play a role in determining the structure of linear chains in a similar manner as the close-packed structures for hard spheres play for the solid phase of spherically symmetric molecules. Structures other than the helix were shown to optimize the packing under appropriate conditions; the nature of the optimal structure depends on such parameters as the thickness and length of the string, as well as the geometry of the confinement.

Although anisotropic, attractive interactions between monomers can induce a chain to form a helix, we will demonstrate that the delicate interplay between purely isotropic, attractive interactions and packing (due to excluded volume interactions) of monomer segments can also induce a helix. A homopolymer chain in poor solvent conditions will tend to collapse into a compact conformation in order to maximize self-interactions. Beyond a critical packing fraction, optimal configurations tend to maximize the entropy available to a system. Therefore, for situations where the helix is the optimal configuration for a string, we expect a transition to a helical structure for a sufficiently string-like polymer model.

We consider polymers consisting of \( N \) linearly bonded hard spheres of diameter \( \sigma \). The distance between bonded spheres are restricted to lie between \( 0.9l \) and \( 1.1l \), where \( l \) is the bond length, which is not necessarily equal to \( \sigma \). Spheres that are not directly bonded interact via a square-well potential \( u(r) \), given by:

\[
u(r) = \begin{cases} 
\infty & \text{for } r < \sigma \\
-\epsilon & \text{for } \sigma < r < \lambda \sigma \\
0 & \text{for } \lambda \sigma < r 
\end{cases}
\] (1)

where \( r \) is the distance between the centers of the spheres, \( \lambda \sigma \) is the width of the attractive square-well (\( \lambda = 1.5 \) in this work), and \( \epsilon \) is the magnitude of the interaction, which sets the energy scale of the model. For \( l = \sigma \), this model is precisely the same as that studied by Zhou and coworkers [10, 11].

We have carried out Monte Carlo simulations to study the behavior of unconfined, isolated polymers with \( N = 20 \) (20-mers) and values of \( \sigma/l \) between 1.0 and 1.9. Parallel tempering [16]
was employed, with 16 replica systems at temperatures between $k_B T/\epsilon = 0.2$ and $k_B T/\epsilon = 7.0$ (where $k_B$ is the Boltzmann constant), placed such that the ratio between successive temperatures was constant \[17\]. Within each replica system, the configuration of the polymer was modified using a combination of pivot moves \[18\], kink-jump moves \[19\], and continuum configurational bias regrowth moves \[20\]. Bond length fluctuations were implemented by performing standard particle displacement moves \[21\] on individual monomer spheres. After 400 attempted moves in each box, replica exchange moves were attempted. Samples were taken every 80 attempted swap moves. The simulation consisted of a total of $8 \times 10^5$ attempted swap moves. Smooth interpolation of data between the replica temperatures has been performed using multiple histogram reweighting \[22\].

The structure of the polymer conformations has been characterized using the local torsion $\tau_i$ and curvature $\kappa_i$ \[23\] around the bond vector joining monomers index $i$ and $i + 1$ ($i \in [1, N]$). Curvature is defined so that is always positive; the sign of the torsion around a bond indicates whether it has a left- or right-handed “twist”. These quantities are calculated using a central difference scheme \[24\]; as such, $\tau_i$ is defined on $i \in [3, N - 2]$, and $\kappa_i$ on $i \in [2, N - 1]$. It is a necessary and sufficient condition for a perfect helical structure to have $\tau_i / \kappa_i$ independent of \[25\], taking the value $p/2\pi r_h$, where $p$ is the pitch of the helix and $r_h$ is the radius. This quantity will be quoted as an average along the polymer for a given conformation, denoted $\gamma$, and given by:

$$\gamma = \frac{\sum_{i=3}^{N-2} (\tau_i / \kappa_i)}{(N - 4)}$$

This conformation average should not be confused with the usual thermal (ensemble) average. As an indicator of “helicity”, we also measure the conformational root variance for this average, $s_\gamma$. This quantity should take consistently low values for a helical phase, since the ratio $\tau_i / \kappa_i$ will be constant for a perfect helical configuration.

The variation of the isochoric heat capacity $C_v$ with temperature $T$ for a typical 20-mer chain ($\sigma/l = 1.6$) is shown in Fig. 1(a). Cooling from high temperature, the heat capacity rises through a broad peak or shoulder as the radius of gyration (not shown) undergoes a large, though gradual, decrease. This is the “$\Theta$-point” transition from extended coil to disordered globule, where the repulsive excluded volume interactions between the monomers are balanced by the attractive interactions. This transition is analogous to the vapor-liquid transition in bulk fluids. A snapshot configuration from the globule phase is shown in Fig. 2(a).
Figure 1: (a) Variation with temperature of the isochoric heat capacity $C_v/k_B$ and mean conformational root variance, $\langle s_\gamma \rangle$ for a homopolymer composed of 20 monomers, $\sigma/l = 1.6$; jackknife estimated error is never more than 2% of the values shown. (inset) Mean end-to-end distance $\langle r_e \rangle$ for the same system; jackknife estimated error is never more than 2% of the values shown. Dotted drop lines indicate the temperatures of maxima in $C_v$. (b) Probability density histograms $P(\gamma)$ for the ratio of configuration average torsion and curvature for the same system, temperatures as in legend.

Upon further cooling, the heat capacity passes through another peak at $k_B T/\epsilon = 0.58$. We attribute this peak to the adoption of a compact, ordered structure by the polymer and denote this temperature $T_f$. Snapshot configurations taken from the simulations below this temperature appear to be helical in character. An example is given in Fig. 2(b). Since snapshot configurations are not a reliable indicator of structure, we have characterized the observed structures using the conformational mean torsion-curvature ratio $\gamma$, and its conformational root variance $s_\gamma$.

Probability density plots $P(\gamma)$ for this system are shown in Fig. 1(b). At high temperature, these have an approximately Gaussian form, centered on zero. As the system is cooled below $T_\theta$, $P(\gamma)$ gradually becomes double peaked, with the two peaks symmetrically placed around zero and separated by a shallow trough. The free energy barrier between states with $\gamma > 0$ (right-handed) and $\gamma < 0$ (left-handed) is relatively low, and the polymers can freely exchange between them. There is no clear thermodynamic indicator of the temperature below which this characteristic
Figure 2: Snapshot homopolymer configurations (a) 20-mer with $\sigma/l = 1.6$ and $k_BT/\epsilon = 0.75$ (globule phase), (b) 20-mer with $\sigma/l = 1.6$ and $k_BT/\epsilon = 0.48$ (helix 1 phase), (c) 20-mer with $\sigma/l = 1.6$ and $k_BT/\epsilon = 0.2$, (helix 2 phase) and (d) 32-mer with $\sigma/l = 1.9$ and $k_BT/\epsilon = 0.2$.

Below $T_f$, the character of $P(\gamma)$ changes once again. As the temperature passes below $T_f$, the two symmetrically placed peaks become separated by a region of very low probability. This marks the breaking of chiral symmetry, with the system adopting either a counterclockwise ($\gamma < 0$) or a clockwise ($\gamma > 0$) helix. These two states are separated by a large free energy barrier, and, consequently, the polymers are not expected to exchange between the counterclockwise and clockwise helix conformations. It should be noted that sampling of both peaks occurs mainly because of the use of parallel tempering in the simulations. That the two peaks are sampled with approximately equal weight is evidence that the simulations are ergodic and well equilibrated.

Passing down in temperature through $T_f$, a sigmoidal decrease in $\langle s_\gamma \rangle$ to a low, approximately temperature-independent value is also observed, showing that the $\tau/\kappa$ values for individual bonds are becoming strongly correlated, indicating a transition to a helical state.

It can be seen from Fig. 1(a) that there is a further low-temperature peak in $C_v$ at $k_BT/\epsilon = 0.3$. Upon cooling across this temperature, $P(\gamma)$ remains double peaked and shows a sudden shift inward, toward zero. Snapshot configurations remain helical, with an example shown in Fig. 2(c). The inset to Fig. 1(a) shows that the mean end-to-end difference for the polymer decreases upon cooling across this temperature. This tallies with the observed decrease in $\gamma$, indicating a decrease in pitch and/or increase in radius for a helical configuration.

The general, qualitative behavior shown in Fig. 1 is also observed for polymers with $\sigma/l = 1.475$ to $\sigma/l = 1.65$. For values $\sigma/l \geq 1.7$, the behavior is as described above, but with only a single low-temperature peak observed in the isochoric heat capacity. For values $\sigma/l < 1.475$, chiral symmetry breaking is not observed; the observed histograms for $P(\gamma)$ remain unimodal and centered on zero across the studied temperature range. These observations are summarized in the
Figure 3: Schematic phase diagram. Points represent observed isochoric heat capacity peaks; the statistical uncertainty in the positions is smaller than symbol size. Lines serve only as guides to the eye; see text for discussion. Text indicates the structure observed in that region.

We have shown that stiffness of the polymer induced by the bulkiness of the monomers plays an important role in the development of structure at low temperatures. For values of $\sigma/l \geq 1.475$, the equilibrium low temperature structure appears to be helical (see Fig. 3); further evidence for this is provided by the consistently low values for the quantity $\langle s_\gamma \rangle$ under these conditions, indicating an approximately constant value for $\tau_i/\kappa_i$ across individual conformations. The torsional symmetry breaking associated with helix structure formation must be associated with a thermodynamic phase transition for an infinite system; no attempt is made to establish the order of this transition, as the small size of the system studied would make any such attribution unreliable. We have identified these transitions by the associated increase in energy fluctuations (maxima in heat capacity). Across the temperature range studied, no ordered low temperature structures are observed for $\sigma/l < 1.475$. For $\sigma/l = 1$, the globule should freeze into an ordered crystalline phase [10, 11] at sufficiently low temperature. For other values of $\sigma/l$, however, the low temperature structure is still unclear.

For values $1.475 \leq \sigma/l \leq 1.66$, the helix-globule transition line is reentrant. With increasing $\sigma/l$, the helix initially gains, then rapidly loses stability with respect to the globule. At low temperature, there is a line of heat capacity maxima which coincides with a sudden drop in the torsion-curvature ratio and decrease in mean end-to-end distance for the observed helices. We interpret it as indicating a transition to a less extended helical structure at low temperature, since $\tau/\kappa$.
gives the pitch-radius ratio for a helix. This line of maxima appears to join with the helix-globule
transition line for $\sigma/l \geq 1.675$. No further heat capacity maxima or discontinuities in torsion are
observed between this line and the lowest temperature studied. Since the high temperature helix is
not observed for $\sigma/l \geq 1.675$, and there must exist a transition line between a symmetry breaking
and a non-symmetry breaking state, we can therefore infer the existence of a helix-helix-globule
triple point in the range $1.66 \leq \sigma/l \leq 1.675$. The less extended helical structure is the low-
temperature equilibrium configuration observed for all $\sigma/l \geq 1.475$, and appears to increase in
stability monotonically with $\sigma/l$. Extrapolation of the helix-globule transition line and the helix-
helix transition line to low temperatures for $\sigma/l < 1.475$ suggests that a further, low temperature
helix-helix-globule triple point may exist.

The precise reasons for the occurrence of two helical structures separated by an apparent transi-
tion line, and for the sudden decrease in stability of the high temperature helix are, as yet, unclear.
Results using an anisotropic model [4, 7], constructed to yield a specific helix, suggest a two-step
mechanism for helix formation, where the initial globule-helix transition results in a structure with
disordered end segments, followed by a transition to a fully-helical structure. Another speculative
possibility is that allowed helical states are discretized due to a preference for monomers to sit
at interstitial sites in neighbouring layers of the helix, leading to a succession of helical phases
separated by transitions rather than a continuum of possible torsion values. Further study will be
necessary to understand these behaviors.

Another factor playing an important role is the overall length of the polymer. We have studied
the square-well chain model for different lengths $N$, and preliminary results suggest that, though
the system breaks chiral symmetry at low temperature for all chain lengths studied, helices are
only stable inside a window of values for $N$. An example low-temperature snapshot configuration
for a longer polymer is shown in Fig. 2(d); a detailed examination of the influence of chain length
on structure will be the subject of a further communication.

In summary, we have demonstrated spontaneous chiral symmetry breaking using a model which
is achiral (no dependence upon bond torsions) and isotropic (no dependence upon bond angles).
This spontaneous symmetry breaking reflects the formation of helical structures at low tempera-
ture, providing support for the notion of helices as “optimal configurations” for string-like objects
[15], which as such do not need to be “engineered in” to a model or molecule through specific
directional interactions. We do not seek to suggest that directional interactions do not play an
important role in the formation and stabilisation of helical structure; however, the purely steric
effect which we have demonstrated may also play a crucial role which we have not yet been aware of. The observed phase behavior for the model is rich, including an apparent helix-helix transition, with a reentrant helix-globule coexistence curve for one helix leading to a helix-globule-helix triple point, and offers many possibilities for further investigation.

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