Physica A 393 (2014) 86–95

Contents lists available at ScienceDirect

Physica A

journal homepage: www.elsevier.com/locate/physa

Quinary lattice model of secondary structures of polymers

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HIGHLIGHTS

- A new model of lattice polymers with non-local interaction is introduced.
- The formation of lattice models of secondary structures is described.
- All native conformations for sufficiently short (less than 39) lattice polymers are described.

ARTICLE INFO

Article history:
Received 5 May 2013
Received in revised form 4 September 2013
Available online 13 September 2013

Keywords:
Proteins
Lattice polymers
Secondary structures

ABSTRACT

In the standard approach to lattice proteins models based on nearest neighbor interaction are used. In this kind of model it is difficult to explain the existence of secondary structures—special preferred conformations of protein chains.

In the present paper a new lattice model of proteins is proposed which is based on non-local cooperative interactions. In this model the energy of a conformation of a polymer is equal to the sum of energies of conformations of fragments of the polymer chain of length five.

It is shown that this quinary lattice model is able to describe at a qualitative level secondary structures of proteins: for this model all conformations with minimal energy are combinations of lattice models of alpha-helix and beta-strand. Moreover for lattice polymers of length not longer that 38 monomers we can describe all conformations with minimal energy.

1. Introduction

Lattice models of polymers (in particular proteins) have been extensively discussed in the literature, cf. Ref. [1]. For a review of the physics of proteins see Ref. [2].

The standard lattice models of polymers (in particular the HP model [3,4]) describe nearest neighbor interaction of monomers (see the discussion in the next section). Conformations with low energy in the standard model have the form of compact globules. In proteins native conformations are usually combinations of secondary structures—special preferred regular conformations, in particular alpha-helices and beta-sheets. The aim of the present paper is to introduce a lattice polymer model (quinary lattice model) where energy minima will be combinations of lattice secondary structures (models of alpha-helices and beta-strands).

The energy of a polymer in this model will be equal to the sum over conformations of fragments of a polymer of length five. Therefore instead of consideration of explicit interactions between amino acids in a protein we consider cooperative interaction in a polymer chain. We fix a set of conformations of fragments of polymer chains and construct low energy conformations of polymers as combinations of conformations of fragments from the mentioned set.

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0378-4371/$ – see front matter
http://dx.doi.org/10.1016/j.physa.2013.09.020

The crucial point of our lattice model is that for two conformations of fragments of a polymer it is not always possible to construct a larger fragment which will contain both shorter fragments. This implies a set of selection rules for conformations of neighboring short fragments of a polymer. Therefore the number of possible conformations with low energy of lattice polymers in the introduced model will be small in comparison with standard models of lattice polymers with contact interaction where all compact globules will have sufficiently low energy. Actually in this paper all possible conformations with minimal energy for sufficiently short (with length less that 39) lattice polymers are enumerated.

Let us stress that we do not pretend that the proposed model gives a realistic approximation of conformations of real proteins. This model is a mathematical toy model which describes the effect of creation of secondary structures in lattice polymers by non-local cooperative interaction.

Let us compare the approach of the present paper and some of the known results in lattice (and some off-lattice) models of proteins.

In Refs. [5,6] the design of sequences of polymers which fold to given conformations was discussed. Reviews of recent results in this direction can be found in Refs. [7,8].

In Ref. [9] the model of HP (hydrophobic-polar) copolymers was considered. Primary structures of the so called protein-like copolymers (with globules which have hydrophobic core and polar shell) were investigated; long-range correlations in the primary structures were found.

In Ref. [10] the lattice HP-model of polymers was studied. Compact structures of 27-mers (which lie in $3 \times 3 \times 3$ cubes) were enumerated and the number of sequences which minimize the energy in the given compact conformation was computed for each of the mentioned structures. It was discussed that the highly designable structures (corresponding to large numbers of sequences) exhibit certain geometrical regularities which are reminiscent of the secondary structures in natural proteins.

For other lattice and off lattice polymer models see Refs. [11–14].

In the abovementioned paper lattice secondary structures were discussed in the framework of long-range order and low entropy. In particular, helix like conformations in these models are combinations or right and left handed helix patterns. In the present paper we show that a special cooperative interaction can explain not only long range order but also the formation of very particular conformations; in particular, the helix conformations in our approach are right-handed only.

In Ref. [15] proteins were considered as combinations of short fragments (in particular 5-tuples) of amino acids; in Ref. [16] the statistics of conformations of fragments of proteins was discussed.

In the work [17], see also Refs. [18–21], it was proposed to consider a small data bank of (off-lattice) protein fragments that can be used as elementary building blocks to reconstruct virtually all native protein structures. It was found that oligomers of short length (usually between 5 and 20) found in a coarse grained representation of native structures of proteins do not vary continuously but gather in a few clusters. These clusters can be represented by structural fragments, or oligons, which can be considered as centers of these clusters. Let us note that the characteristic length of an oligon in Ref. [18] is five or six amino acid residues, and in the present paper we use fragments of a lattice polymer of length five.

The structure of the present paper is as follows.

In Section 2 we introduce the quinary lattice model of a polymer and show that the lattice models of alpha-helix and beta-strand are the energy minima for the introduced model.

In Section 3 we describe the minima of energy of the proposed model and show that these conformations can be considered as combinations of lattice alpha-helices and beta-strands.

In Section 4 we consider the heteropolymer version of the introduced model and show that in this case we can describe polymers which possess a native tertiary structure—a conformation which minimizes the energy and is uniquely defined by the sequence of the polymer. The obtained tertiary structure is a combination of secondary structures described in Sections 2 and 3.

In Section 5 we discuss the model of the energy of a lattice polymer which is a combination of the quinary lattice model and the standard model of the nearest (in the lattice) neighbor interaction of amino acids.

In Section 6 we give a conclusion for our results.

2. The quinary lattice model

The standard model of the energy of lattice polymers has the following form, see Ref. [1]. One considers a linear lattice polymer (a finite sequence of monomers connected by edges of length one); the monomers are situated at vertices of the cubic lattice $\mathbb{Z}^3$. A conformation of a polymer of length N is a sequence of neighboring vertices without self-intersections in the cubic lattice $\mathbb{Z}^3$, i.e. the injective map

$$\Gamma : \{1, \dots, N\} \to \mathbb{Z}^3, \tag{1}$$

where neighboring natural numbers map to neighboring (i.e. distance one) vertices of the lattice $\mathbb{Z}^3$. In the following we will denote by Γ also the image of this map.

The energy of the conformation Γ in the standard model is proportional to the following sum:

$$E_2(\Gamma) = -\sum_{1 \le i < j \le N} \delta(d(\Gamma(i), \Gamma(j))), \tag{2}$$