Unexpected scenario of glass transition in polymer globules: an exactly enumerable model

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We introduce a lattice model of glass transition in polymer globules. This model exhibits a novel scenario of ergodicity breaking in which the disjoint regions of phase space do not arise uniformly, but as small chambers whose number increases exponentially with polymer density. Chamber sizes obey power law distribution, making phase space similar to a fractal foam. This clearly demonstrates the importance of the phase space geometry and topology in describing any glass-forming system, such as semicompact polymers during protein folding.

Although it is generally agreed that the most fundamental feature common to a large variety of different glasses is some form of ergodicity breaking, this phenomenon is still poorly understood [1]. The common scenario implies that upon lowering the temperature, increasing the pressure, or otherwise suppressing the thermal agitation, phase space is effectively divided into domains, then each of the domains is subdivided into smaller domains, and the process continues in an ultrametric (tree-like) fashion.

One problem with the theoretical understanding of glasses stems from the lack of solvable models in the field. In the present paper, we suggest and explore one such model in which ergodicity is explicitly broken. To our surprise, this model exhibits a scenario of glass transition which is dramatically different from the above mentioned classical picture. Specifically, phase space of our model appears to consist of one huge valley and a large number of very small “chambers.” When the system is further restricted, the number of small chambers grows at the expense of the single big valley, but they remain small in the sense that the distribution of domain sizes remains bimodal, with enormous gap between the big valley and small chambers. However the small chambers are themselves of different sizes, and their distribution appears to follow a power law, thus indicating fractal nature of the disjoint phase space.

The motivation for our model comes from the works on the theory of protein folding, where a toy protein is usually presented as a cubic lattice polymer with a quenched sequence of monomer species. There is a sophisticated theory [4] which predicts the equilibrium freezing transition for maximally compact heteropolymers at some temperature $T_f$. Below $T_f$, only very few of the compact conformations contribute to the partition function, although exponentially many of them contribute above the transition. It is natural to assume that $(T = T_f, \phi = \phi_{\text{max}})$ is the end point of some freezing phase transition line on the temperature $T$ vs. density $\phi$ phase diagram (see also [3]). To gain more insight into this phase diagram one may want to consider the opposite extreme of very high temperature, and varying density, $0 < \phi \leq \phi_{\text{max}}$. At high temperature all interactions are irrelevant except for the excluded volume one, and we have a homopolymer. Thus, we may expect some kind of homopolymer glass transition to occur along the $1/T = 0$ line, at a certain density $\phi_g$ (see also [3]). Although the relation of this transition to the freezing one at $\phi = \phi_{\text{max}}$ is not clear, and the question of a glass transition in the protein folding context has recently been the subject of a debate [5], we think that the glass transition in a homopolymer globule deserves attention and our goal in the present paper is to study a model of this phenomenon.

We shall operate with the $3 \times 3 \times 3$ segment of the cubic lattice, which is a standard tool in protein folding studies. In order to address the gradual change of density, we shall change (by steps of one) the length $N$ of polymer chains confined within the 27-cube. When ergodicity is in question, the rules of dynamics are to be considered as an integral part of the model. We use the conventional set of elementary moves employed in Monte Carlo simulations of polymers, including end flips, corner flips, and crankshaft moves. As soon as the model is specified, including both the set of conformations and the set of elementary moves, the conformational space should be viewed as a graph, in which nodes represent conformations, and edges represent possible moves transforming one conformation into another. The question of ergodicity is now reduced to the one of graph connectivity. If the graph of conformations contains only one connected component, the system is ergodic; every conformation can be transformed into any other conformation by a sequence of allowed elementary moves. On the other hand, if the graph of conformations consists of two or more disconnected components, ergodicity is obviously broken.

We begin with the exhaustive enumeration of all self-avoiding $N$-mers, $1 \leq N \leq 27$, that are confined within the 27-cube. As indicated in Table 1, the number of con-
formations, $\Omega_N$, is peaked at $N = 22$: at smaller $N$, each extra monomer adds to the degrees of freedom, at larger $N$ the restrictions due to the confinement become increasingly severe. Before proceeding to examine the phase space in detail, one should note that the move set has a property that if the lattice sites were colored black and white in an alternating manner, the monomers could only move between sites of the same color. This immediately results in the splitting of the phase space into two regions, but this is unrelated to the ergodicity breaking.

Table 1: Enumeration of polymer chains of length $N$ within a $3 \times 3 \times 3$ cube. “Small chambers” refer to all domains but the largest valleys. Data for $N$ from 5 through 13 (for which the numbers of conformations, $\Omega_N$, are equal, respectively, 17, 58, 193, 625, 1884, 5445, 14332, 36208, 8182) are not shown, because there are no small chambers.

| $N$ | $\phi = N/27$ | $\Omega_N$ | $\sum n_m$ | $\sum m \cdot n_m$ |
|-----|---------------|-------------|-------------|-----------------|
| 14  | 0.52          | 177018      | 0           | 0               |
| 15  | 0.56          | 337118      | 4           | 4               |
| 16  | 0.59          | 632078      | 18          | 28              |
| 17  | 0.63          | 1018452     | 54          | 112             |
| 18  | 0.67          | 1633622     | 142         | 320             |
| 19  | 0.70          | 2199836     | 742         | 1324            |
| 20  | 0.74          | 2964500     | 1742        | 3656            |
| 21  | 0.78          | 3226280     | 6385        | 14037           |
| 22  | 0.81          | 3505858     | 12722       | 31948           |
| 23  | 0.85          | 2865534     | 35507       | 108951          |
| 24  | 0.89          | 2303244     | 58728       | 199158          |
| 25  | 0.93          | 1199908     | 128271      | 673292          |
| 26  | 0.96          | 564368      | 147036      | 564368          |
| 27  | 1.00          | 103346      | 103346      | 103346          |

To understand the breaking of ergodicity, we enumerate all conformations which can be reached from each initial conformation given the move set described above. Note that while these moves are most frequently used in Monte Carlo simulations, our procedure is an exact enumeration, not a Monte Carlo simulation. The enumeration is carried out by labeling every conformation so that we not only know how large the phase space of a given initial conformation is, but also which conformations belong to the same domain. To allow for rapid searches (while checking if a conformation has already been accounted for in a domain), we store the labeled conformations in a binary tree. To construct the binary tree, note that conformations can be denoted as a sequence of directions. Thus we can denote an $N$-mer by an $(N-1)$-digit number. A conformation whose $(N-1)$-digit representation is greater (less) than another is considered to be “greater” (“less”) for the purposes of this tree. The left and right descendants of a node of the tree are “less” than and “greater” than the node, respectively. To further reduce computational time associated with searching the binary tree, we first perform this procedure on a conformation that resides in a big chamber and eliminate all of those conformations from the list of completely enumerated conformations and examine only the remaining conformations.

At $N = 14$, the system is completely ergodic, that is, all conformations are connected and form one big valley (allowing for translational symmetry). At $N = 15$, all conformations belong to the same valley except for four symmetrically unrelated conformations (see Figure 1). It can be checked directly that these four conformations are unable to convert into any other conformation. Thus ergodicity is explicitly broken, albeit by only 4 conformations. Similarly, at $N = 16$, all conformations form one huge connected valley in phase space except for 28 conformations residing in 18 small separated chambers. This set of “glassy” conformations are either obtained from the ones at the 15-mers level by appending a monomer to the head or tail, or are very similar to them. This pattern continues as we go to larger $N$. Specifically, there are two classes of domains in the phase space, one large valley (split in two because of the odd-even effect) and small chambers. The size separation between the two classes is enormous, making the distinction between valleys and chambers completely unambiguous. Enumeration data for small chambers are presented in Table 1, where $m$ is the number of conformations in one chamber, and $n_m$ is the number of chambers of the size $m$; accordingly, $mn_m$ is the number of conformations in all chambers of the size $m$. The fraction of conformations residing in small chambers grow exponentially with $N$ (see inset in the Figure 1) until at $N = 26$, the distribution of domain sizes is no longer bimodal, and there is no longer a big valley. Note that this picture of glass transition is qualitatively different from the commonly accepted one. Ergodicity is not broken uniformly. Instead, the phase space consists of one large valley containing a majority of the conformations while tiny portions of the phase space are pinched off at an exponential rate until the entire phase space consists of small chambers.

FIG. 1. Two 15-mer conformations which cannot transform into any other conformation within a $3 \times 3 \times 3$ box. The other two such conformations are obtained by relabeling the monomers in the opposite order.
Another way to look at our findings is to consider polymer entropy. It can be defined in two ways. If a chain is locked within one chamber, its entropy is given by \( \ln m \). Upon averaging over conformations, this yields \( \frac{\sum\ln m}{\Omega_N} \), where \( m \) for every conformation is the size of the chamber to which this conformation belongs. Alternatively, if there were no barriers between chambers, the entropy would be \( \ln \Omega_N \). The data for both entropies (taken per one monomer) are shown in Figure 2. Note that while the true breaking of ergodicity occurs at \( N = 15 \) (\( \phi \approx 0.55 \)), the difference between the two entropies does not become evident until \( N = 23 \) (\( \phi \approx 0.85 \)). This could explain the difficulties encountered in determining the glass transition; while there exists a true transition, the changes are too small to be measured experimentally.

The phase space in a glassy (non-ergodic) state appears to have a self-similar structure. As demonstrated by figure 3, the number of chambers, \( n_m \), has approximately a power law dependence on the number of conformations, \( n \), in each of them, \( n_m/n_1 \approx m^{-\tau} \), where power \( \tau \) remains between 2.1 and 2.2 for all \( N \) from 19 to 24 (at smaller \( N \), there are too few points to claim a power law). We found also that the number of the smallest chambers (with \( m = 1 \)) grows exponentially with \( N \) as soon as \( N \) exceeds the threshold value of 15: \( n_1 \approx e^{1.07N-14.53} \), as shown in the left inset in figure 3.

In order to understand the structure of each chamber, we can examine the distributions of overlaps between a given conformation in the chamber and all other conformations within the same chamber, where the overlap of two conformations, \( Q \), is the number of monomer bonds these two conformations have in common. We find that the distribution of \( Q \) is highly dependent upon the conformation with which the overlap is taken (see the right inset in the Figure 3). We can infer a consistent picture of the phase space chamber as having small fingers extending from the main ball-like region. Conformations which reside in these fingers have small overlaps with most other conformations which reside in the main ball. As the chamber size is increased, these fingers lengthen, so that the peak overlap decreases.

As a preliminary test of a larger system, we examined random samples of 100 conformations of \( N \)-mers for every \( N \) from 58 to 63 within a \( 4 \times 4 \times 4 \) box and found a behavior similar to that of the \( 3 \times 3 \times 3 \) system (see inset in the Figure 3).

Switching from solid results to speculations, it is tempting to view the first breaking of ergodicity at \( N = 15 \) as merely a signal of approaching to a real critical point at around \( N = 25 \). We can conjecture that for a very large system, in thermodynamic limit, there is a critical density at which the infinite phase space disintegrates into infinite set of finite disjoint domains. We can further interpret this criticality in terms of some kind of percolation in the phase space, in this case small chambers and big valley being, respectively, finite and infinite clusters. Our finding of self-similar fractal distribution of clusters, or small chambers, supports this idea qualitatively. However, on the quantitative level, the interpretation of the exponent \( \tau \approx 2.1 \) to 2.2 requires better
understanding of the underlying conformational space.

Another way to look at the conjectured phase transition would be to examine the densities higher than critical. We can consider a \((k^3 - 1)\)-mer confined in a \(k \times k \times k\) box, \(k \gg 1\), with only one empty lattice node - a vacancy. Each allowed elementary chain move can now be interpreted as the vacancy move in real space. Clearly, the vacancy can move if and only if the conformation has the properly positioned corner next to it. For a random conformation, this happens with some probability less than unity. Therefore, the probability that a vacancy can make \(r\) consecutive steps decays exponentially with \(r\). Thus, on average, vacancy can travel only some finite distance in real space \([11]\). Of course, there are some zigzag conformations allowing vacancy to move arbitrarily far, but they are exponentially rare. When translated into the language of the phase space, this immediately explains that phase space chambers are small, in the sense that their sizes remain finite and do not depend on the overall volume of the system, even in the thermodynamic limit \((k \to \infty)\). The situation becomes more complicated when several vacancies are present, since they interact. It would be interesting to look at this situation both analytically and numerically. Unfortunately, 27-cube is too small for that, while computational analysis of clusters for 64-mer is very demanding. We leave it as an unresolved challenge to understand the nature of this transition.

To conclude, we speculate on the implications of our model for the protein folding studies. Numerous works \([12]\) suggest that folding begins with a fast collapse to a semi-compact and non-specific globule state. In terms of our model it is natural to assume that such a burst collapse will bring the chain into one of the disjoint domains of its conformation space (most likely, into the big valley, if there remains one at a given semi-compact density). Speed and reliability of the further folding depends then on whether native state belongs to the same phase space domain or not. Furthermore, the observable appearance of the freezing transition may be spectacularly modified by the foam-like structure of the phase space. For instance, if denatured molten globule is restricted in one of the small chambers, and if the native conformation corresponds to a broad monomodal distribution of overlaps (see inset (b) in the Figure \(8\)), then the freezing behavior will be different from the conventional Random Energy Model behavior \([13]\).

Looking from a slightly different perspective, we can view our model as stressing the role of the underlying geometry for compact biopolymers and for other glass-forming systems. In this sense, frozen conformations in our model are somewhat similar in spirit to the so-called arching configurations in systems of hard particles such as sand. Understanding this geometry presents a significant challenge, as is convincingly proven by the example of Kepler’s conjecture on the most compact packing of hard spheres: it took over 300 years to prove \([14]\). However complicated the phase space geometry may be, it is of primary importance. If and when phase space consists of disjoint regions, or if regions are joined via narrow passes, this must be taken into account in any approach describing system in terms of a folding funnel \([15]\) or a reaction coordinate \([16]\), or considering glass as a separate thermodynamic phase \([7]\).

To summarize, we have demonstrated a novel scenario for glass transitions using a lattice model for a homopolymer. Unlike the typical picture in which the phase space is more or less evenly divided, the glass transition in our model occurs via the exponential increase of the number of small disjoint regions of phase space. As these regions comprise an extremely small fraction of the entire phase space, their initial appearance is hardly noticeable experimentally. This may contribute to the difficulty often seen in determining glass transition. While these results are highly dependent upon the restricted model which we employed and it is unclear how common this scenario is among other systems, it presents a possibility.

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