

## Figure Captions

- 1 Comparison between the  $D_4(t)$  (here  $t_{MC}$  is the number of full MC sweeps of the chain) estimated in our Monte Carlo runs for the purely harmonic chain (scattered dots) and the theoretical prediction from the Langevin dynamics normal mode expansion (Eq. 10, continuous curve). Here  $\tau_r = 800$ .
- 2 As in fig. 1, but for a homopolymer ( $\epsilon = 0$ ) with Lennard-Jones interaction, with  $A = 3.8$  and  $R = 2$ , log-log plot. The two curves are for  $h = 1$  and for  $h = 10$ .
- 3  $D_4(t)$  for three different realizations of the quenched noise  $\eta_{i,j}$ ,  $\epsilon = 6$ .  
a) linear plot, b) log-log plot (arbitrary normalization).
- 4  $\log(D_2)$  versus  $\log(t)$  for different values of  $\epsilon$  (arbitrary normalization). The steepest line (labelled with *random*) corresponds to a system of free particles - all proposed moves accepted.
- 5 The distribution probability  $P_t(D_4)$  for four values of  $\epsilon$ . We take the same time for the 4 distributions (twice the maximum time shown in fig. 4).
- 6 The plot of time dependent probability distributions for  $\epsilon = 6$  for three different values of time. The smallest time  $t$  corresponds to the time of fig. 5.

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The fact that this exponent stays the same even if we increase the local interaction by increasing  $h$  ten times while keeping  $R$  and  $A$  fixed suggests that in the coil phase the diffusion properties in the absence of the quenched noise can be adequately described by a model of sites with a local interaction placed in an effective external field.

In the following we will mainly be interested in the dependence of the exponent  $\nu$  over  $\epsilon$ .

Let us note at first that the exponent  $\nu$  does not seem to depend on the particular realization of the quenched noise. We have not performed large scale simulations, which would be needed in order to get quantitative precise results in systems with such a dramatic critical slowing down (see ref. [5]), but we have got from our simulations quite a precise qualitative picture. We show in fig. 3  $D_4(t)$  for three different realizations of the noise, with a very similar power behavior. The non-universal coefficient of the power behavior does indeed depend on the given noise realization, but  $\nu$  does not. Of course, the energy of interaction itself does not determine  $\nu$  (as it does not determine the equilibrium shape).

In fig. 4 we show  $D_4(t)$  for different  $\epsilon$  values. For increasing  $\epsilon$  we observe a reduction of  $\nu$ : for  $\epsilon = 10$   $\nu = .52 \pm .05$

As noted in ref. [5] the correlation time shows a dramatic dependence on  $\epsilon$ : in fig. 5 we show the distribution probability  $P_t(D_4)$  for four values of  $\epsilon$ . We have selected the same time moment for the 4 distributions. The probability  $P_t(D_4)$  is obtained by averaging over several hundred initial configurations. While for  $\epsilon = 0$  the  $P(D_4)$  for times  $\simeq 10\theta$  ( where  $\theta \equiv 10^4$  updates of each chain site) is nearly stationary, for  $\epsilon = 6$  times of two orders of magnitude longer are may be just starting to be enough (see fig. 6). The new *Tempering* approach to Monte Carlo dynamics, recently proposed in ref. [13], has chances to alleviate the situation.

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where the coefficients  $c_{p,i}$  were replaced by their average values and summed over [8]. Therefore, under the above approximation, the expected relation between the exponent  $\alpha_1$  and the exponent  $\nu$  is

$$\nu = 1 - \frac{1}{\alpha} . \quad (21)$$

We have verified numerically that in the large  $\epsilon$  region the above relation is actually satisfied. This is consistent with the fact that  $\nu$  is a true universal exponent, dependent only on the energy spectrum and independent from  $\beta$ .

Our numerical result do clearly exhibit, in the large  $\epsilon$  region, the scaling relation

$$\lambda_p \sim \left(\frac{p}{N}\right)^\alpha . \quad (22)$$

for  $N$  as small as 15–30, justifying the claim we are close to the continuum limit (obviously we ignore the first six eigenvalues which are zero due to the rotational and translational symmetries).

## 4 Numerical Estimates of $\nu$

We present here our numerical determination of the dynamical critical exponent  $\nu$  we have defined before, from the *short* (but not so short) time behavior of  $D_4$ .

The four parameter which determine the Hamiltonian,  $A$ ,  $R$ ,  $h$  and  $\epsilon$  affect the behavior of  $D_4(t)$ . Let us note, at first, that the time scale  $\tau_r$  after which the power law does not hold any more

$$D_4(t) \simeq kt^\nu , \quad t \ll \tau_r \quad (23)$$

is a decreasing function of the strength of interaction, and an increasing function of the system size. Secondly, the coefficient  $k$  decreases with the strength of coupling and increases with the temperature and the system size. In fig. 1 we have shown the behavior of an harmonic chain, together with the results of the theoretical analysis.

In fig. 2 we show the time behavior of ordered systems for two different values of the parameters. Here (in the globular phase) we find a good fit with  $\nu = \frac{2}{3}$ , which coincides with the prediction of models with local interaction.

the Monte Carlo method. That means that in general condition (15) does not hold. We expect the Metropolis dynamics to reproduce the continuous dynamics only for times larger than the typical time of continuous dynamics necessary to reach the mean displacement  $\langle \delta \rangle$ . This is the time region we are interested in, and that we discriminate before analyzing the dynamical critical exponent. In this region (of times large enough not to feel the non-universal details of the dynamics, but small enough not to describe the relaxation to the asymptotic mean displacement) we will see that we can determine a critical exponent  $\nu$

$$D_4(t) \simeq t^\nu . \quad (16)$$

In the context of Langevin Dynamics we can relate the exponent  $\nu$  with the asymptotic behavior of dynamics linearized around local minima. We consider the normal modes eigenvalues of the linearized dynamics,  $\lambda_p$ . Let us assume that asymptotically (i.e. in the continuum limit of large  $N$  and small  $p$ )

$$\lambda_p = p^\alpha \quad (17)$$

and that the fluctuations of all modes are the same and not correlated. The width of the probability distribution of the  $p$ -th mode behaves as  $\frac{C}{\sqrt{\lambda_p}}$ , where  $C$  is a mode independent constant. Then we obtain

$$D_4(t) = \sum_{i,j} [\kappa_{i,j}(0) - \kappa_{i,j}(t)] , \quad (18)$$

where

$$\kappa_{i,j}(t) = c \left\{ \sum_p e^{-p^\alpha t / \tau_r} \frac{1}{p^\alpha} (c_{p,i} - c_{p,j})^2 \right\}^2 , \quad (19)$$

where the  $c_{p,i}$  are the scalar products of the  $p$ -th mode vector  $x_p$  with the position vector of the  $i$ -th site,  $r_i$ . Changing the order of the summation and converting the sum over  $p$  into an integral (in the continuum limit) we obtain

$$D_4(t) \sim \int_0^\infty dp \quad p^{-\alpha} (1 - e^{-\frac{t}{\tau_r} p^\alpha}) \sim t^{1-\frac{1}{\alpha}} , \quad (20)$$

$$\kappa_{i,j}(t) = c \left\{ \sum_p e^{-p^2 t / \tau_r} \frac{1}{p^2} \left( \cos\left(\frac{p\pi i}{N}\right) - \cos\left(\frac{p\pi j}{N}\right) \right)^2 \right\}^2, \quad (11)$$

and

$$c = 64 \times 4N \frac{b^2}{\pi^2} = 64 \times \frac{4N3k_B T}{h}; \quad (12)$$

$$\tau_r = \frac{N^2 b^2}{kT 3\pi^2} = \frac{\zeta N^2}{h\pi^2}. \quad (13)$$

$b^2 = kT/3h$  is the asymptotic equilibrium expectation value of  $d_{i,i+1}^2$ . We show the comparison of our numerical fitted data with the analytic result in fig. 1. We can see very well that the power for short times is  $\frac{1}{2}$ . Saturation starts to show up for larger times (and it is very clear for very large times, not included in the figure), also if the statistical error is already becoming, in this regime, very large.

Let us just remind again that we are using a discontinuous dynamics, the Metropolis algorithm. We know that we are getting the correct asymptotic equilibrium distribution, but for short times we do not have a simple correspondence with the corresponding Langevin dynamics. Let us discuss this point in some detail. Consider a Metropolis dynamics, where we propose a trial random increment defined by a displacement vector  $\vec{\delta}$  chosen from some probability distribution  $P(\vec{\delta})$ . The increment is accepted with probability  $P_a = \min(1, e^{\beta(H(\vec{r}) - H(\vec{r} + \vec{\delta}))})$ . Therefore the average of a single step displacement is

$$\langle \vec{r}' - \vec{r} \rangle \sim \langle \vec{\delta} \min(1, e^{\beta(H(\vec{r}) - H(\vec{r} + \vec{\delta}))}) \rangle. \quad (14)$$

For small  $\beta \vec{\delta} \cdot \vec{\nabla} H(r)$ , (corresponding to a large acceptance factor) the  $\langle \vec{r}' - \vec{r} \rangle$  be approximated as

$$-\beta \langle \vec{\delta} \Theta(\vec{\delta} \cdot \vec{\nabla} H(\vec{r})) (\vec{\delta} \cdot \vec{\nabla} H(\vec{r})) \rangle = -\frac{\beta}{6} \langle \delta^2 \rangle \vec{\nabla} H(r), \quad (15)$$

where  $\Theta$  is the step function. This is the same form one gets for a Langevin step, with a scale factor which depends on the acceptance ratio of the Metropolis procedure,  $\langle \delta^2 \rangle > \beta$ . Normally one uses the Metropolis algorithm with a trial displacement that is not small: this is indeed the big advantage of

$$D_4(t) \equiv \langle D_4(\alpha(t), \alpha(0)) \rangle , \quad (6)$$

where  $\alpha(0)$  is an equilibrium configuration.

In all our runs we have used a standard Monte Carlo dynamics.

The fluctuations of the critical exponent governing the behavior of  $D_4(t)$  from sample to sample are quite small. We average  $D_4$  over a few hundreds (100-500) of starting points for a given sample.

In order to check that we are really picking up the correct universal behavior we have studied a simple harmonic chain. Let us stress that the problem is very delicate: there is a non universal short time region (where the discreteness of the Metropolis procedure plays an important role), an asymptotic constant value for  $D_2$  (with some universal approach to  $D_4$ , and in between the (short) time region we are interested in. We have to check that we are observing, in this region, a true scaling behavior, and we can be sure of that only in the limit of large  $N$ . In order to check our results for the simple harmonic chain we have compared them to the analytic expression resulting from the normal mode expansion of the Langevin dynamics (LD).

The Langevin equation for the harmonic chain is of the form

$$\zeta \frac{dr_i}{dt} = -k (2r_i - r_{i+1} - r_{i-1}) + f_i , \quad (7)$$

where the uncorrelated random forces  $f_j$  satisfy

$$\langle f_i(t_1) f_j(t_2) \rangle = 2 \zeta k_B T \delta(t_1 - t_2) \delta_{i,j} . \quad (8)$$

$\zeta$ , a friction constant, sets here the time scale for the problem. In the continuum limit  $(2r_i - r_{i+1} - r_{i-1})$  may be replaced by  $\partial^2 r / \partial n^2$ . One can introduce normal modes in the standard way by

$$x_p = \frac{1}{N} \int_0^N dn r(n) \cos\left(\frac{p\pi n}{N}\right) \quad (9)$$

Using Wick's theorem for evaluating average of products of the coordinates  $\langle x_j x_k x_m x_n \rangle$  one can easily compute the  $D_4(t)$ , finding

$$D_4(t) = \sum_{i,j} [\kappa_{i,j}(0) - \kappa_{i,j}(t)] , \quad (10)$$

where

( $d$  is the distance between the two particles at equilibrium). For these values of the parameters the harmonic term contributes about ten percent to  $\langle E_T \rangle$  but practically does not affect the value of  $d$ .

For  $\epsilon = 0$  in the limit  $N \rightarrow \infty$  the ground state configuration is such that the chain sites lie on a face-centered cubic lattice. The lattice (which in this case coincides with the solution to the *kissing problem*, i.e. finding the maximum number of spheres of diameter  $d$  tangent to a given one) can be seen as made of centers of spheres of diameter  $d$  packed regularly with the maximum density (which in  $3d$  is 12). In this limit the harmonic energy term only determines the order in which the chain sites are placed on the lattice sites. Fukugita, Lancaster and Mitchard<sup>[6]</sup> have shown that in  $d = 2$  the lattice structure is quite clear in the  $\epsilon = 0$  case, and survives (although the evidence of ref. [6] is in this case less compelling) the transition to the disordered phase. In the  $3d$  case we find that for  $N = 30$ , in the *folded* phase, the lattice structure is lost. We clearly see the lattice structure in the  $\epsilon = 0$  case, and we see that it becomes weaker but partly survives when thermalizing the chain in the strongly disordered potential [12].

### 3 The Time Dependence of the Shape

In order to discuss the diffusion of chain configuration quantitatively, it is more convenient to introduce the following definition of distance between two configurations

$$D_4(\alpha, \beta) \equiv \frac{1}{N^2} \sum_{i,j} (d_{i,j}^{2(\alpha)} - d_{i,j}^{2(\beta)})^2, \quad (4)$$

Since

$$(d_{i,j}^{(\alpha)2} - d_{i,j}^{(\beta)2}) = (d_{i,j}^{(\alpha)} - d_{i,j}^{(\beta)})(d_{i,j}^{(\alpha)} + d_{i,j}^{(\beta)}), \quad (5)$$

where the second factor is much larger than the first, the exponent characterizing the power law short-time dependence of  $D_2$  and  $D_4$  is the same. One could also use the two definitions of the distance introduced in ref. [5], and expect to find the same critical behavior. We study the diffusion of the polymer shape by analyzing an ensemble average of  $D_4$  as a function of the time separation between the two configurations. We average over the time dynamics and over different realizations of the  $\eta_{i,j}$  couplings, and compute



fluctuations and depends on spatial extent of the chain).

Nonlinear systems with external bias are studied numerically and are expected to yield crossover between  $t^{1/2}$  and  $t^{2/3}$  power laws. It is not completely clear whether the apparent nonlocality of interaction can be treated effectively as a bias (an effective mean field due to cloud of particles) incorporated in a local nonlinear model describing nearest-neighbor interaction along the chain.

## 2 The Equilibrium Shape

We have tried to get some more informations about the equilibrium shape of the IMP heteropolymers. We have mainly used in our runs the same parameters used in IMP<sup>[5]</sup>.

Let us look at some raw number in order to try to understand what happens when we go from the homopolymer phase to the *folded* phases, where the disorder plays a crucial role. In absence of the quenched disorder ( $\epsilon = 0$ ), for  $\beta = 1$ ,  $N = 30$ ,  $a = 3.8$ ,  $r = 2$  and  $h = 1$ , the total chain energy is  $\langle E_T \rangle = -273.0 \pm .5$ , the average chain first neighbor square length  $\langle d_{i,i+1}^2 \rangle = 1.55 \pm .10$ , and the end to end chain length  $\langle d_{N,1}^2 \rangle = 6.0 \pm 1.5$ . The corresponding values for  $\epsilon = 6$  are  $\langle E_T \rangle = -635 \pm 50$ ,  $\langle d_{i,i+1}^2 \rangle = 1.7 \pm 0.5$   $\langle d_{N,1}^2 \rangle = 3.5 \pm 3.5$  (here the errors are computed by averaging over different realizations of the  $\eta_{i,j}$  couplings). These number are here only to hint an order of magnitude. Indeed in ref. [5] it has been seen that 100 millions of full chain sweeps are not at all sufficient to explore the entire phase space.

The values of  $\epsilon$  needed in IMP (for  $N = 30$ ) to go deep in the folded phase ( $\epsilon \approx 6$ ) are quite large. We have then to be quite careful in checking which terms are contributing to the ground state total energy. We find that in both the disordered and in the  $\epsilon = 0$  regimes the attractive part of the L-J energy expectation value (in which we include the part proportional to  $\epsilon$ ) is roughly equal to twice the repulsive part of the energy. This is what we find for the minimum of a L-J potential for a two-particle system, where at equilibrium

$$\frac{A}{d^6} = \frac{2R}{d^{12}} \quad (3)$$

chains whose dynamics is defined by the Hamiltonian (1). Specifically, we study the diffusion of the distance between two chain configurations defined as

$$D_2(\alpha, \beta) \equiv \frac{1}{N^2} \sum_{i,j} (d_{i,j}^{(\alpha)} - d_{i,j}^{(\beta)})^2, \quad (2)$$

where  $\alpha$  and  $\beta$  label two chain configurations at different instances of time. The time evolution of  $D_2$  tells us about the diffusion of the shape (and size) of the folded chain. We concentrate our attention on the dependence of diffusion on  $\epsilon$ , the quenched noise strength.

Analytical studies of the diffusion in the (simple) case of polymer where the interaction is local along the chain are possible in the context of normal mode decomposition of the Langevin dynamics (LD). Such simple models are known to yield a characteristic power law dependence of the mean-square displacement (squared) over time<sup>[8]</sup>,  $t^{\frac{1}{2}}$ . This power law holds in the range of times where the finite size effects are still invisible, but collective effects are already important<sup>[8]</sup>. This is an interesting regime to which we will dedicate attention in the following. Other relevant models are discussed in the context of the problem of surface aggregation (see for example [9] and [10]). For example for a nonlinear model with a local interaction in  $(1 + 1)$  dimensions the mean square displacement (squared) grows as  $t^{\frac{2}{3}}$  in the relevant regime<sup>[10, 11]</sup>.

In the case of interest (heteropolymers with long range interaction on the chain, and a L-J potential with a random quenched attractive contribution) the problem is very complex (since the Hamiltonian is disordered and non-local, and frustration can play a role). It is also important to remind that we want to study a situation where  $N$  is large but not infinite, and this finiteness can play a role. This is true both for our model (we will present here results obtained with  $N = 30$ ) and for the potential application to protein folding. In a biological application of our model the sites of our chain have to be identified with (pre-assembled) parts of the secondary structure, and  $N$  would be of order 10. The heteropolymeric chain is finite and localized (at equilibrium the distance between chain sites is finite: translational and rotational degrees of freedom do not enter in our definition of mean displacement). This implies that, after a time large enough, the mean square displacement reaches a maximum (which, roughly speaking, characterizes the amplitude of thermal

# 1 Introduction

Modeling the protein folding is one of the most relevant challenges open to Statistical Mechanics. The idea that relevant issues of the folding process can rely on the disordered nature of the amino-acid system has been put forward and investigated by many groups (see for example refs. [1] and references therein). Shakhnovic and Gutin<sup>[2]</sup> in their seminal work have been giving a first quantitative form to these ideas, implementing the mechanism of Parisi's Replica Symmetry Breaking<sup>[3]</sup>. Mezard and Parisi have applied a systematic RSB treatment to random manifolds<sup>[4]</sup>.

Iori, Marinari and Parisi in ref. [5] (IMP) have studied a very simple heteropolymer model, attempting to emphasize the difference between the static structure of spin glasses and native proteins. The model turned out to present potential important features, like the dominance of one or a small number of ground states. In ref. [6] the model is studied in  $d = 2$ , and ref. [7] studies the case of Lennard-Jones homopolymers.

The Hamiltonian of the IMP model (describing a self-interacting heteropolymer) has the form

$$H = \sum_{i,j \neq j} [hd_{i,j}^2 \delta_{i,j+1} - \frac{A}{d_{i,j}^6} + \frac{R}{d_{i,j}^4} + \frac{\sqrt{\epsilon} \eta_{i,j}}{d_{i,j}^6}] , \quad (1)$$

where  $i, j$  range from 1 to  $N$  (the number of *sites* of the polymeric chain), and  $d_{i,j}^2 \equiv (r_i - r_j)^2$ . The first term represents a harmonic force holding the adjacent sites together. This term prevents the chain from breaking into pieces. The contributions proportional to  $A$  and  $R$  (attractive and repulsive) form a conventional Lennard-Jones (L-J) potential. The last term is a quenched disorder contribution; it models a nonuniformity of the dipoles interacting by the L-J potential. The values of  $\eta_{i,j}$  are independent and uncorrelated stochastic variables (which do not vary in time). The  $\eta_{i,j}$ 's have mean value zero and variance one. The set of coefficients  $\eta_{i,j}$  can be viewed as characterizing a single native protein.

The most relevant questions concern typical realizations of the heteropolymeric chains. In the following we will mainly be interested in quantities which are averaged both on the thermal noise and on different realizations of the  $\eta_{i,j}$  couplings.

In this note we investigate the short time behavior of the heteropolymeric

# On Heteropolymer Shape Dynamics

Pawel Pliszka and Enzo Marinari<sup>(\*)</sup>

Dept. of Physics  
Syracuse University  
Syracuse, NY 13244, USA

pliszka@suhep.phy.syr.edu marinari@roma2.infn.it

(a): and Dipartimento di Fisica and Infn,  
Università di Roma *Tor Vergata*  
Viale della Ricerca Scientifica  
00173 Roma, Italy

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## Abstract

We investigate the time evolution of the heteropolymer model introduced by Iori, Marinari and Parisi to describe some of the features of protein folding mechanisms. We study how the (folded) shape of the chain evolves in time. We find that for short times the mean square distance (squared) between chain configurations evolves according to a power law,  $D \sim t^\nu$ . We discuss the influence of the quenched disorder (represented by the randomness of the coupling constants in the Lennard-Jones potential) on value of the critical exponent. We find that  $\nu$  decreases from  $\frac{2}{3}$  to  $\frac{1}{2}$  when the strength of the quenched disorder increases.

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