Solvable Models of Random Hetero-Polymers at Finite Density: I. Statics

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We introduce $\infty$-dimensional versions of three common models of random hetero-polymers, in which both the polymer density and the density of the polymer-solvent mixture are finite. These solvable models give valuable insight into the problems related to the (quenched) average over the randomness in statistical- mechanical models of proteins, without having to deal with the hard geometrical constraints occurring in finite dimensional models. Our exact solution, which is specific to the $\infty$-dimensional case, is compared to the results obtained by a saddle-point analysis and by the grand ensemble approach, both of which can also be applied to models of finite dimension. We find, somewhat surprisingly, that the saddle-point analysis can lead to qualitatively incorrect results.

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I. INTRODUCTION

The study of random hetero-polymers is regarded as a natural first step towards a better understanding of the physics of proteins [1]. The latter are believed to be special realisations of random hetero-polymers which have been selected by nature; before tackling these atypical (selected) cases, one first investigates the properties of typical hetero-polymers. Several models of such systems have been proposed and studied (for an overview see e.g. [2][3]). Most involve a coarse-grained description of the polymer chain, where each monomer (which may consist of many atoms) is represented as a single bead, and effective two-body interactions between monomers and/or solvent molecules. Since proteins are hetero-polymers of fixed composition, one is mostly interested in the case of quenched disorder. Yet, studying the case of annealed disorder can also be relevant, since it may describe a situation in which the monomers are able to change their chemical properties (e.g. by undergoing chemical reactions or by exchanging charge), and secondly (at a technical level) since one can approximate the quenched result by a series of annealed averages following the scheme of Morita [4].

The principal objective of this paper is to clarify the problems that occur when following a saddle point (SP) approach in dealing with the (quenched) randomness in those coarse grained models of random hetero-polymers which take into account the incompressibility of the solvent-monomer system. Although the behaviour of random hetero-polymers in finite dimensions will obviously differ from those in high dimensions (due to the crucial role in the former of the chain constraint), we find that the study of infinite dimensional models provides valuable insight into the appropriateness of some of the approximations and assumptions that are usually being made, as it disentangles the problems induced by the disorder from those generated by the configurational entropy. It is beyond the scope of this work to discuss the numerous variational approaches that have been introduced, often in combination with a saddle-point treatment. Neither do we want to go into details about possible replica symmetry breaking (RSB) that may occur in some models. Although the dominance of the entropy in our present models does not permit real phase transitions at finite temperatures, we do observe phase coexistence and, especially in the case of annealed disorder, (re-entrant) cross-over between swollen and compact phases, which may indicate real (re-entrant) phase transitions in the corresponding finite dimensional models.

This paper is organised as follows. In section II we introduce our models, and illustrate connections with related models such as those describing matching problems and poly-dispersity. In sections III and IV we derive the (exact) solution for the case of discrete disorder, and for arbitrary disorder distributions (in terms of mesoscopic variables), respectively. In section V we study the same models with a (naïve) mean field approach, and point out the latter’s weaknesses. In section VI we follow the grand ensemble approach of [4], where the quenched average is approximated by a series of annealed averages. Although hard to implement for real quenched disorder, this scheme may quite accurately describe polymers with so-called permuted disorder, where the monomers are allowed to migrate along the chain. Finally, in section VII, we discuss our results and present an outlook on future work.

II. MODEL DEFINITIONS

We consider large chains of random hetero-polymers. The position of each monomer $i = 1, \ldots, N$ along a chain is given by a vector $\vec{r}_i$. A function $g(\vec{r})$ will incorporate all the constraints on the possible configurations of the chain, such as self-avoidance, bond length, lattice con-

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Each monomer to carry a set of labels with bond-disorder. Alternatively we could choose for \( i, j \) independently for each pair \((i, j)\) with \( i < j \), we have a model with bond-disorder. Alternatively we could choose for each monomer to carry a set of labels \( \lambda_i \in \mathbb{R} \), specifying its electro-chemical properties, and define the interaction energies as fixed functions of the labels of the monomers involved, i.e. \( \lambda_{ij} = \lambda(\lambda_i, \lambda_j) \), which would lead to a model with site disorder.

Since (1) cannot be calculated for all possible disorder realizations, and since the free energy is a self-averaging quantity (i.e. the average value is the typical value), one is interested in its average over the disorder, the so-called quenched free energy \( F_q = \langle F \rangle_{\{\lambda_{ij}\}} \). In order to investigate the influence of disorder in the interactions between the different monomers, without having to make additional approximations to deal with the configurational entropy, we consider the following simplified \( \infty \)-dimensional model:

- There are \( N \) monomers labeled \( i = 1, \ldots, N \), and \( R \) sites labeled \( r = 1, \ldots, R \).
- Every site is a neighboring site to every other site, and thus the chain constraint of the polymer is always trivially satisfied.
- Each site can contain up to \( n_c \) monomers. This accounts for the incompressibility of the polymer-solvent system, and restricts the global density according to \( N/R \leq n_c \), with equality corresponding to the situation where all sites are completely filled with monomers.
- Those positions at a given site which are not occupied by monomers, are occupied by solvent molecules.
- Only those particles interact which find themselves in the same site.

The problem of calculating the free energy has now been reduced to a relatively simple combinatorial one. The number of monomers at site \( r \) is denoted by \( n_r \). Hence, in terms of the notation of (1), \( g(\{r\}) = 1 \) for all configurations with \( n_r \leq n_c \) for all \( r \), and 0 otherwise:

\[
g(\{r\}) = \prod_{r=1}^{R} \left(1 - \sum_{k>n_c} \delta_{k,n_r(\{r\})}\right)
\]  

Note that we must always satisfy the following relations

\[
n_r \equiv \sum_i \delta_{r,r_i}, \quad \sum_r n_r = N, \quad N \leq \sum_i n_{r_i} \leq n_c N.
\]

The problem is symmetric under arbitrary permutations of the sites. We now order these such that the first \( C_{n_c}N \) sites contain \( n_c \) monomers, the next \( C_{n_c-1}N \) contain \( n_c-1 \) monomers, etc. (see FIG. 1). The last \( C_0N \) sites contain no monomers. We define the total fraction of monomers that find themselves at a site which is occupied by \( l \) monomers as \( f_l \equiv lC_l \), \( l = 1, \ldots, n_c \). Thus

\[
\sum_{l=0}^{n_c} lC_l = \sum_{l=1}^{n_c} f_l = 1, \quad \sum_{l=0}^{n_c} C_l = \alpha.
\]

A monomer at a site occupied with \( n_c \) monomers is said to be in the (maximally) compact state, a monomer at a site where there are no other monomers is said to be in a swollen state, and monomers which find themselves at sites with an intermediate number of monomers are in a semi-compact state. The macroscopic state of the polymer is characterised by the numbers \( \{C_l, l = 0, \ldots, n_c\} \) (which are proportional to the fractions of sites with a given monomer occupation number). The overall compactness of the polymer can be measured by a single parameter \( D \), with \( D = 0 \) describing a maximally swollen configuration and \( D = 1 \) describing a maximally compact one:

\[
D = \frac{(1 - \alpha + C_0)}{(1-1/n_c)}
\]

FIG. 1. Illustration of the \( \infty \)-dimensional model, for \( n_c = 3 \), with some of the allowed moves indicated with arrows. The upper configuration is one where the sites are not yet ordered; the lower configuration is obtained upon ordering the sites according to monomer occupation numbers.
By varying $\alpha$, the total monomer density and the fraction of monomers in (semi-)compact states at high temperatures can be made arbitrarily small. The state where all monomers are found at the same finite density $n_c$ is the high-dimensional version of the compact globular phase for random hetero-polymers, which is often considered in the literature. Note that it is not appropriate to view the present models as coarse-grained high-dimensional limits of lattice models, although the short range nature of the interactions is mimicked by representing small elementary volumes by sites and taking only (delta) interactions within this volume, ignoring the interactions between these elementary volumes. For a true high-dimensional limit, the number of sites in an elementary volume would increase exponentially with the dimension, while here it is kept finite. Hence, it is rather a geometry-free version of the finite dimensional continuum models that have been considered.

We can now calculate typical quantities for boxes containing $l$ monomers, provided we add the entropic contribution $S_{\text{ord}}$ to the free energy which reflects our ordering of sites, given by the logarithm of the associated combinatorial factor:

$$\log \left( \frac{(R)!}{\prod_{l=0}^{n_c}(C_l N)!} \right) \approx N \left[ \alpha \log(\alpha) - \sum_{l=0}^{n_c} C_l \log(C_l) \right],$$

(7)

(using Stirling’s formula). As a consequence of the fractions $\{C_l\}$ being a finite number of intensive macroscopic observables, we will be able to solve our models by minimizing the free energy with respect to the $\{C_l\}$ (or, equivalently, the $\{f_l\}$). Alternatively, we can separate the total entropy $S$ into two contributions: the entropy $S_k$ of grouping the $N$ monomers,

$$\log \left( \prod_{l=1}^{n_c}(C_l N)! \right) = \log\left( \frac{N!}{\prod_{l=1}^{n_c}(C_l N)!} \right) \approx N(1 - \sum_{l=1}^{n_c} C_l \log(N)) + \log(N) - N \left[1 - \sum_{l=1}^{n_c} C_l \log(l! C_l)\right],$$

(8)

and, secondly, the residual entropy $S_p$ describing the remaining freedom in positioning the monomers at the $\alpha N$ sites:

$$\log \left( \frac{(\alpha N)!}{(C_0 N)!} \right) = (\alpha - C_0) N \log(N) + N[\alpha \log(\alpha) - C_0 \log(C_0) - (\alpha - C_0)].$$

(9)

Hence, the total entropy $S$ is given by

$$S_k + S_p = N \log(N) - N + N[\alpha \log(\alpha) - \sum_{l=0}^{n_c} C_l \log(l!)]$$

(10)

Since $S_k$ contains a term proportional to $N \log(N)$, the entropy will always dominate the free energy, except at properly rescaled (very low) temperatures. This was already recognized by Vannimenus et al. [3] for so-called matching problems. In what follows we will systematically omit all contributions to the entropy which are independent of the configuration; the entropy may consequently become negative at low temperatures, and non-monotonicity of the free energy need no longer indicate a phase transition in the system.

Our model can be interpreted as a hetero-polymer on a simplex in $\alpha N - 1$ dimensions. It differs, though, from the infinite dimensional random Potts model, firstly through the fact that the (quenched) randomness is not in the background (i.e., in the sites or in interactions coupling sites (in fact there are no couplings between different sites), but in the (mobile) monomers, and secondly since only a finite number of monomers are allowed to be at the same site. For the latter reason, and because the energy per site depends on the (number of) particles present at that site, it also differs from the back-gammon model of Ritort [6]. However, it shares the property that the entropy is not extensive. Our model can be seen as similar to those describing matching problems (with here monomers as the objects to be ‘matched’). Note that in standard matching problems either the density is fixed (typically at $n_c = 2$) [3, 4], or properly scaled chemical potentials are introduced [3], both with the objective to keep the non-extensive (permutational) part of the entropy constant. In contrast, in the present model the latter is achieved by limiting the number of available sites to $\alpha N$. Although the interesting behaviour of matching problems (such as freezing) only occurs at properly rescaled (extremely low) temperatures, and a lower bound on the interaction distribution is needed to have a finite ground-state energy, we have not investigated this temperature regime in the present paper, but in analogy with those papers on random hetero-polymer models whose assumptions and methods we wish to investigate, we have considered continuous disorder distributions of a Gaussian form. Finally, one can also view our model as one describing the coexistence of a large number (or, equivalently) a poly-disperse mixture (see e.g. [10] and references therein).

What remains to fully specify our models is to make explicit choices for the pair-interactions between monomers. In the present paper we consider the three most commonly used interaction types:

- In the random hydrophobic/hydrophilic model (RHM) [11–14] a label $\lambda_i$ is assigned to each monomer (with $\lambda_i > 0$ for hydrophilic and $\lambda_i < 0$ for hydrophobic monomers), and

$$\lambda_{ij} = \lambda_i + \lambda_j \ (\lambda_i \ i.i.d. r.v.):$$

(11)

$$\mathcal{H}(\{r\}) = \frac{1}{2} \sum_{i \neq j}^{N} \lambda_i + \lambda_j \delta_{r_i, r_j} = \sum_{i}^{N} \lambda_i n_{r_i} + \text{const}$$

Note that this is only the configuration depen-
dent term of the full interaction energy. Each contact of a monomer \(i\) with a solvent molecule contributes \(-\lambda_i\) to the energy (hence the name hydrophilicity). The full Hamiltonian is thus given by \(H = -\sum_i \sum_s \lambda_s \delta_{r_i,r_s} = -\sum_i \lambda_i (n_c - n_r)\) with the index \(s\) running over the solvent molecules.

- The random charge model (RCM) \cite{[3][4]} (or ‘random sequence’ model) describes inter-monomer Coulomb-like interactions. Again each monomer carries a label \(\lambda_i\) (its ‘charge’). The contribution to the energy is proportional to the product of the charges of monomers in contact, such that equally signed charges either repel \((\epsilon = 1)\) or attract \((\epsilon = -1)\) each other:

\[
\lambda_{ij} = \epsilon \lambda_i \lambda_j \quad (\lambda_i \text{ i.i.d.r.v.)} : \quad (12)
\]

\[
\mathcal{H}(|\vec{r}|) = \frac{\epsilon}{2} \sum_{i \neq j} \lambda_i \lambda_j \delta_{r_i,r_j} = \frac{\epsilon}{2} \sum_r \lambda_r^2 + \text{const}
\]

where \(\lambda_r \equiv \sum_i \lambda_i \delta_{r_i,r}\) is the total charge in box \(r\), and \(\epsilon = \pm 1\). Solvent molecules are assumed to be neutral.

- In the random interaction model (RIM) \cite{[5][6]} (or ‘random bond’ model) the \(\frac{1}{2}N(N-1)\) interactions \(\lambda_{ij}\) between the pairs of monomers are themselves taken to be independent identically distributed random variables (i.i.d.r.v.), drawn from a probability distribution \(P(\lambda)\), which may either be discrete or continuous:

\[
\lambda_{ij} \text{ i.i.d.r.v.} \quad (\lambda_{ij} \equiv \lambda_{ij}) : \quad (13)
\]

\[
\mathcal{H}(|\vec{r}|) = \frac{1}{2} \sum_{i \neq j} \sum_{s=1}^N \lambda_{ij} \delta_{r_i,r_j} .
\]

III. DISCRETE DISORDER: EXACT SOLUTIONS

In this section we deal with the case where the interactions take discrete values, i.e. where the \(\lambda_i\) (for RHM and RCM) or the \(\lambda_{ij}\) (for RIM) have probability distributions of the form

\[
P(\lambda) = \sum_{\sigma=1}^{N_\sigma} p_\sigma (\lambda - \lambda_\sigma) , \quad (14)
\]

with finite \(N_\sigma\). We define ‘local states’ as the monomer configurations that can occur at a given site (for site-disordered models these local states are fully characterised by the number of monomers of a given type present). Note that for finite \(n_c\) and finite \(N_\sigma\) the number \(N_{ls}\) of possible local states is also finite. Furthermore, due to the nature of the Hamiltonian \(\mathcal{H}\), the total energy is just the sum of the local energies in at the \(\alpha N\) sites. We define the concentration \(c_{ls}\) of a local state \(s_l\) as the number of times it occurs among the \(\alpha N\) sites \((s_l = 1, \ldots, N_{ls})\) divided by \(N\), and the number of monomers occupying a site in local state \(s_l\) by \(n_{ls}\). We then always have to satisfy the normalisation requirements

\[
\sum_{s_l} c_{s_l} = \alpha \quad \text{and} \quad \sum_{s_l} n_{ls} c_{s_l} = 1 . \quad (15)
\]

A. RHM & RCM

For the (site-disordered) RHM and RCM models, one can define the local state at a given site by a set of numbers \(\{n_\sigma\} (\sigma = 1, \ldots, N_\sigma)\), where each \(n_\sigma\) specifies the number of monomers present of type \(\sigma\). This expression is to be minimized with respect to the parameters, under the constraints \(15,16\). This procedure, even for \(N \to \infty\), grows considerably with the number of monomer species \(N_\sigma\) and with \(n_c\), we have restricted ourselves to the case \(n_c = 3\) and \(n_r = 2\) (bimodal disorder: \(\lambda_i = \pm 1\)). This case turns out to already exhibit all the essential features of our models. The results of determining the order parameters \(\{c_{(m^\sigma)}\} \) by minimization of \(\mathcal{F}_{sl}\) are compared with numerical simulations in FIG. 2 and FIG. 3 for the RHM and the RCM respectively.
We clearly observe the tendencies one expects. In the RHM model the low temperature local configurations are ones where either a site is fully filled with hydrophobic monomers (which thereby avoid contact with solvent molecules), or contains a single hydrophilic monomer (which then maximises the contacts with solvent). For the RCM we see that at low temperatures for $\epsilon = 1$ (equal charges repel) the system favors states where opposite charges pair, whereas for $\epsilon = -1$ (equal charges attract) the preferred states are the ones where equally charged monomers maximally group together. In all cases the agreement between theory and experiment is excellent.

B. RIM

In order to solve the Random Interaction Model (RIM) we have to follow a slightly different strategy. Firstly, because the local state at a site $r$ is now defined by the number $n_r$ of monomers situated at $r$, in combination with the $n_r \times n_r$ traceless interaction matrix $M_r$ of the interaction energies between pairs of these monomers. The number of independent matrix elements of $M_r$ is $n_r(n_r-1)/2$, each can take all of the $N_\sigma$ different values, giving rise to $N_\sigma^{n_r(n_r-1)/2}$ different possible local matrices. Since we can freely permute the monomers at a given site, many of these matrices give rise to the same local state, and it is sufficient to select a prototype for each of the non-equivalent classes. Given a local interaction matrix $M$, we can divide the monomers into $N_t$ classes of size $m^t, \ t = 1, ..., N_t$, such that $M$ is invariant under all permutations within the same class, and not so for any permutation of two monomers from different classes. Secondly, because only a negligible fraction of the labels $\lambda_{ij}$ are actually visible in the interactions, we cannot impose the equivalent of the condition in (14), but instead we use the fact that the ensemble probability that a label $\lambda$ occurs, is given by $P(\lambda)$. Note that this equivalent to assuming that the annealed approximation of the quenched average is valid; in appendix B we will prove the validity of this assumption at finite temperatures. The state-dependent part of the free energy is now asymptotically given by

$$\mathcal{F}_{\text{sd}} = (E - TS)/N = \sum_{(n,M)} c_{(n,M)} \left[ E(n,M) + \frac{1}{\beta} \log \left( \frac{\prod_s m_s^{1/2} c_{(n,M)}}{\prod_s (p_{s\sigma})^{m_{s\sigma}}} \right) \right] \quad (N \to \infty),$$

where $m_{s\sigma}^r$ is the number of times the interaction $\sigma$ occurs one entry above the diagonal in the matrix $M$, and the model is exactly solved at finite temperatures.
of possible labels $N_{ls}$. Therefore, we have again restricted ourselves to the simple case $n_c = 3$ (for which the $(n, M)$ are fully determined by the numbers $m_{ij}^M$, whence $c(m_{ij}^M)$, $N_s = 2$ with $N_b = 8$; the result of comparing the predictions of the theory with numerical simulations is shown in FIG. 4.

IV. CONTINUOUS DISORDER: EXACT SOLUTIONS

In the general case of arbitrary and possibly continuous disorder distributions, we introduce densities $c(l, \vec{\lambda}_l)$ of boxes with a specified number $l$ of monomers and given labels $\vec{\lambda}_l$ (representing local attributes such as hydrophilicities, charges or sub-matrices of interactions, depending on the model at hand). Since the For $N \to \infty$ we assume the fraction of sites with $l$ monomers and $\vec{\lambda}_l \in [\Lambda_l, \Lambda_l + \Delta \Lambda_l]$ to be given by $c(l, \vec{\lambda}_l)\Delta \lambda_l$, where $c(l, \vec{\lambda}_l)$ depends continuously on $\vec{\lambda}_l$ and is self-averaging. For these assumptions to be true the dimension of $\vec{\lambda}_l$ must be small compared to $N$. The $c(l, \vec{\lambda}_l)$ are so-called mesoscopic variables. Note that our approach is similar to that of the sublattice magnetisations as introduced for spin models in [21], and applies for as long as the number of possible labels $\vec{\lambda}_l$ is sufficiently small to guarantee that the number of members in each class of monomers with prescribed labels is infinite, and that the fluctuations in the $c(l, \vec{\lambda}_l)$ will not contribute to the free energy.

A. RHM & RCM

For the RHM and the RCM, the solution involves only minor adaptations/generalisation of the one obtained for discrete disorder. The asymptotic state-dependent contribution to the free energy can formally be written as a functional over the above densities, where $\vec{\lambda}_l \equiv \{\lambda_{lk}, k = 1, ..., l\}$ are the labels of the $l$ monomers present at a given site:

$$F_{sd} = \sum_{i=0}^{n_c} \int d\vec{\lambda}_l \ c(l, \vec{\lambda}_l) \left[ E(l, \vec{\lambda}_l) + \frac{1}{\beta} \log(1 - c(l, \vec{\lambda}_l)) \right], \quad (N \to \infty) \quad (20)$$

where $d\vec{\lambda}_l \equiv (\prod_{k=1}^l d\lambda_{ik})$ and where $E(l, \vec{\lambda}_l)$ is the contribution to the system’s total energy from a site with $l$ monomers characterised by label vector $\vec{\lambda}_l$. The term $-c(l, \vec{\lambda}_l) \log(1 - c(l, \vec{\lambda}_l))$ in the entropy reflects the fact that the $c(l, \vec{\lambda}_l)$ are invariant under permutations of the $\lambda_{ik}, \ k = 1, ..., l$. In the case of there being a non-vanishing probability for the monomers to be identical, i.e. when the probability distribution of the labels contains delta peaks (as for discrete disorder) we have to add to the entropy the term $-c(l, \vec{\lambda}_l) \log(\prod_{k=1}^l \delta_{\lambda_{ik}})$, where $\lambda$ runs over the different values which the components of $\vec{\lambda}_l$ take, and where $n_\lambda \equiv \sum_{k=1}^l \delta_{\lambda_{ik}} \lambda$. The equilibrium values of the concentrations $c(l, \vec{\lambda}_l)$ are to be determined via minimization of $[21]$, subject to the constraints

$$1 = \sum_{l=1}^{n_c} \ l \ C_l, \quad \alpha = \sum_{l=0}^{n_c} C_l, \quad (21)$$

$$P(\lambda) = \sum_{l=1}^{n_c} \int d\vec{\lambda}_l \ c(l, \vec{\lambda}_l) \left( \sum_{k=1}^l \delta(\lambda_{ik} - \lambda) \right).$$

where $C_l \equiv \int d\vec{\lambda}_l c(l, \vec{\lambda}_l)$. Note that the first constraint of [21] need not be imposed separately, since it follows upon integrating the third constraint over $\lambda$. Upon introducing corresponding Lagrange multipliers $\{B, \mathcal{P}(\lambda)\}$ to enforce the constraints, we obtain our order parameter equations. Variation with respect to the $c(l, \vec{\lambda}_l)$ yields

$$c(l, \vec{\lambda}_l) = \frac{1}{l !} \exp \left(-[1 + \beta(E(l, \vec{\lambda}_l) + B + \sum_{k=1}^l \mathcal{P}(\lambda_{ik}))] \right). \quad (22)$$

To simplify notation we define $\phi(\lambda) \equiv \exp(-\beta \mathcal{P}(\lambda))$ and $\tilde{B} \equiv \exp(-(1 + \beta B))$:

$$c(l, \vec{\lambda}_l) = \frac{\tilde{B}}{l !} \left( \prod_{k=1}^l \phi(\lambda_{ik}) \right) \exp(-\beta E(l, \vec{\lambda}_l)) \quad (23)$$
Next we have determine \( \hat{B} \) and \( \phi(\lambda) \) by enforcing the constraints (21), which leads us to the following non-linear integral equation for \( \phi(\lambda) \)

\[
\alpha \phi \left( \sum_{i=1}^{n_c} \int \prod_{k=1}^{l} (d\lambda_{ik} \phi(\lambda_{ik})) \delta(\lambda - \lambda_1) \exp(-\beta E(l, \tilde{x}_i)) \right) \\
\times \left( \sum_{i=0}^{n_c} \int \prod_{k=1}^{l} (d\lambda_{ik} \phi(\lambda_{ik})) \exp(-\beta E(l, \tilde{x}_i)) \right)^{-1} = P(\lambda),
\] (24)

We now work out our results for the RHM and RCM models separately:

- In the case of the RHM, \( E(l, \tilde{x}_i) = \sum_{k=1}^{l} E_1(l, \lambda_{ik}) \), such that (24) reduces to

\[
\alpha \phi \left( \sum_{i=1}^{n_c} \exp(-\beta E_1(l, \tilde{x}_i)) \frac{G(\beta, l)^{(l-1)}}{(l-1)!} \right) \\
\times \left( \sum_{i=0}^{n_c} G(\beta, l)^{(l-1)} \right)^{-1} = P(\lambda),
\] (25)

where \( G(\beta, l) \equiv \int d\lambda_{ik} \phi(\lambda_{ik}) \exp(-\beta E_1(l, \lambda_{ik})) \). This reduces to a discrete set of equations upon inserting the trial solution \( \phi(\lambda) = P(\lambda)[\sum_{i=1}^{n_c} d_i \exp(-\beta E_1(l, \lambda_{ik}))]^{-1} \). The \( d_i \) are to be solved numerically from

\[
d_i = \frac{\alpha G(\beta, l)^{(l-1)}}{(l-1)!} \left( \sum_{i=0}^{n_c} \frac{G(\beta, l)^{(l-1)}}{l!} \right)^{-1}.
\] (26)

The results of these calculations are compared with numerical simulations in FIG. 5 for Gaussian distributed hydrophilicities/hydrophobicities.

• In the case of the RCM, \( E(l, \tilde{x}_i) = \frac{\varepsilon}{2} (\sum_{k=1}^{l} \lambda_{ik})^2 \) and using a Hubbard-Stratonovich transformation, we obtain

\[
\alpha \phi \left( \int Dz \exp(\sqrt{\varepsilon} \lambda z) \sum_{i=1}^{n_c} K(\beta, z)^{(l-1)} (l-1)! \right) \\
\times \left( \int Dz \sum_{l=0}^{n_c} K(\beta, z)^{(l)} \right)^{-1} = P(\lambda),
\] (27)

in which \( Dz \equiv dz \exp(-z^2/2\sqrt{2\pi}) \) and \( K(\beta, z) \equiv \int d\lambda \phi(\lambda) \exp(-\varepsilon \beta \lambda z) \). We are not able to solve (27) for general \( P(\lambda) \) and/or variable monomer density. However, for fixed monomer density, i.e.

\( c(l, \tilde{x}_i) \equiv \delta_{l,n_c} \left( \prod_{k=1}^{l} \phi(\lambda_{ik}) \right) \exp(-\beta E_1(l, \tilde{x}_i)) \), in combination with the choice \( P(\lambda) = \sqrt{2\pi} \exp(-v(\lambda-\lambda_0)/2) \), we obtain

\[
\phi(\lambda) = \frac{\sqrt{a^{(n_c-1)/n_c}}}{2\pi} a \left( v - n_c \varepsilon \beta + \sqrt{(v - n_c \varepsilon \beta)^2 + 4v(n_c - 1)\varepsilon \beta} \right),
\] (28)

The results of solving these equations are compared with numerical simulations in FIG. 5 for Gaussian distributed hydrophilicities/hydrophobicities.

![FIG. 5. Order parameters C1 as functions of temperature, for the Random Hydropobic/Hydrophilic Model (RHM), with n_c = 3, \alpha = 1, and P(\lambda) = N(0, 1). Full lines: theory. Dots: numerical simulations (N = 3000).](image-url)
where the remaining equations numerically are compared with constraints in (21). The results of solving and distribution classes \( N \equiv \{ sd \}, \alpha = 1 \) (equal charges repel). Lower graphs: \( \varepsilon = -1 \) (equal charges attract). Left graphs: theoretical predictions. Right graphs: numerical simulations \( (N = 3000) \).

**B. RIM**

In the case of the RIM, we can divide the monomers in classes \( \{ l, \tilde{X}_l \} \) where \( l \) is the number of monomers and \( \tilde{X}_l \equiv \{ \lambda_k, i_m, k < m = 1, ..., l \} \). As in the discrete case, we cannot impose the equivalent of the \( P(\lambda) \) condition in (21), but at finite temperatures the annealed approximation is exact (see appendix B), and the ensemble probability that the label vector \( \tilde{X}_l \) occurs, is given by 

\[
\prod_{l < k} P(\lambda_{ik}) \quad \text{Hence, the state-dependent part of free energy per monomer is}
\]

\[
\mathcal{F}_{\text{sd}} = \sum_{l=0}^{n_c} d\tilde{X}_l \; c(l, \tilde{X}_l) \left[ E(l, \tilde{X}_l) + \frac{1}{\beta} \log \left( \prod_{l < k} P(\lambda_{lk}) \right) \right]. \tag{29}
\]

where \( c(l, \tilde{X}_l) \) is the density of states. The equilibrium distribution \( c^*(l, \tilde{X}_l) \) is determined by minimization of (29), yielding

\[
c(l, \tilde{X}_l) = \left( \prod_{i<k=1}^l P(\lambda_{ik}) \right) \frac{\mathcal{N}^lB}{l!} \exp(-\beta E(l, \tilde{X}_l)) \tag{30}
\]

where \( \mathcal{N} \) and \( B \) have to be chosen such that the first two constraints in (21) are satisfied. The results of solving the remaining equations numerically are compared with the results of carrying out numerical simulations in FIG. 2.

**V. CONTINUOUS DISORDER: NAIVE MEAN FIELD SOLUTION**

We now compare the solutions of our models, as obtained directly in the previous section, to the result of following the standard procedure: which is to calculate the typical quenched free energy via the replica method:

\[
\langle -\beta F \rangle = \lim_{n \to 0} \frac{\langle Z^n \rangle - 1}{n}, \quad Z^n = \text{Tr} \exp(-\beta \mathcal{H}), \tag{31}
\]

where \( Z^n \) is the \( n \)-replicated partition sum and \( \text{Tr}(\{\tau_r^+\}) \) denotes the trace over all configurations of the replicas with the constraint that each box contains at most \( n_c \) monomers. We now perform the average over the disorder, and, in analogy with the continuum models considered in the literature, we enforce the conditions

\[
n^a_r \equiv \sum_i \delta_{r,r_i} \quad \text{and} \quad q^{ab}_{rr'} \equiv \sum_i \delta_{r,r_i} \delta_{r', r_i^b} \quad \text{by introducing the conjugate variables} \quad \hat{n}^a_r, \quad \hat{q}^{ab}_{rr'}.
\]

This yields the following expression for the replicated partition sum:

\[
\langle Z^n \rangle = \sum_{\{\hat{n}^a_r\}} \sum_{\{\hat{q}^{ab}_{rr'}\}} \left( i \sum_{r,a} \hat{n}^a_r n^{a+}_{r} \right. \quad \left. + i \sum_{r,r',a,b} \hat{q}^{ab}_{rr'} q^{ab}_{rr'} + g_1(n^a_r, q^{ab}_{rr'}) + g_2(\hat{n}^a_r, \hat{q}^{ab}_{rr'}) \right). \tag{32}
\]

where \( g_2 \) is given by

\[
\sum_l \log \left( \frac{\mathcal{N}_{l=1}^l \exp(-i \sum_a n^a_r - i \sum_{a < b} q^{ab}_{rr'})}{\mathcal{N}_{l=1}^l} \right). \tag{33}
\]

and \( g_1 \) is given by

\[
\begin{cases}
-\beta \lambda_0 \left( \sum_{ar} n^a_r - n N n_c \right) + \frac{\beta^2 \lambda^2}{2} \sum_{ar,br} n^a_r n^b_r M_{ar,br} n^b_r & \text{for the RHM} \\
-\frac{\varepsilon \beta \lambda^2}{2} \sum_{ar,br} n^a_r R^{-1}_{ar,br} n^b_r - \frac{1}{2} \log(\det(R_{ar,br})) & \text{for the RCM} \\
-\frac{\beta \lambda_n}{2} \left( \sum_{ar} n^a_r - n N \right) + \frac{\beta^2 \lambda^2}{4} \sum_{ar,br} (M_{ar,br})^2 & \text{for the RIM}
\end{cases} \tag{34}
\]
where
\[ M_{ar,br'} = n_r^a \delta_{r,r'} \delta_{a,b} + q_{rr'}^{ab} (1 - \delta_{a,b}) \ , \]
\[ R_{ar,br'} = (1 + \varepsilon \beta^2 n_r^a) \delta_{r,r'} \delta_{a,b} + \frac{\varepsilon \beta^2}{2} q_{rr'}^{ab} (1 - \delta_{a,b}) \ . \]

The MF treatment up to equation (34) is perfectly valid. At this stage, however, it is important to note that the \( q^a \in \{0,1,...,n_a\} \) and \( q^{ab}_{rr'} \in \{0,1,...,n_a n_b\} \) are discrete microscopic variables, rather than self-averaging order parameters (compare to e.g. spin-glass theory [2]). Of these at finite density, there are \( \mathcal{O}(N) \) and \( \mathcal{O}(N^2) \) respectively, while in the finite dimensional analogon, the volume occupied by the polymer is \( \mathcal{O}(N) \). Note, furthermore, that for any \( n_c \simeq \mathcal{O}(N^\nu) \) with \( \nu < 1 \) (in our case \( \nu = 0 \)), even in the most compact configuration the vast majority of the \( q^{ab}_{rr'} \) will have to be zero. In appendix B, we will show that at finite \( T \) the non-zero \( q^{ab}_{rr'} \)’s will be 1. Having a finite fraction of the non-zero \( q^{ab}_{rr'} \)'s \( > 1 \), leads to a decrease in the entropy of order \( N \log(N) \), while the energetic gain is at most extensive (this is specific to our \( \nu \)-dimensional model). Hence, the integrals over the \( \hat{n}^a_r \) and \( \hat{q}^{ab}_{rr'} \) cannot be treated as SP integrals (there is no large parameter \( N \)). Nevertheless, since the integrals cannot be performed explicitly, one could consider SP integration as a first approximation. We here find that a SP treatment of the \( \hat{n}^a_r \) leads to at least qualitatively correct results, which may explain the relative success of MF models for homo-polymers [23]. In many studies the \( n^a_r \) are kept constant anyway, as one focuses on the properties of the compact phase, eliminating the SP-problem altogether. We will show, however, that a (naive) saddle-point treatment of the \( q^{ab}_{rr'} \) may lead to qualitatively incorrect results. Several variational approaches have been proposed to deal with this problem [13-20]. The quality of a variational approach depends on the quality of the trial function(s), and there is always the risk that the true physical behaviour is not included. To develop a self-consistent MF theory for random hetero-polymers, it may be necessary to find a good set of “true” order parameters. It may well be that the origin of some of the incongruences between the results obtained by analytical methods for continuum models and those found numerically for lattice models [14,17], lay in the application of the saddle-point method for strongly fluctuating quantities such as the \( q^{ab}_{rr'} \) and \( \hat{q}^{ab}_{rr'} \).

\[ A. \text{Mean Field solution of the RHM} \]

In this model, one can completely avoid the \( q^{ab}_{rr'} \) (and hence the \( \hat{q}^{ab}_{rr'} \)), by using the equality
\[ \sum_{rr'} n_r^a q^{ab}_{rr'} n_{r'}^b = \sum_{r} n_r^a n_{r'}^b \ . \] (36)

Due to the fact that the \( q^{ab}_{rr'} \) appear linearly in \( g_l \) [34], the introduction of the \( \hat{q}^{ab}_{rr'} \) and the solution of the SP equations, replaces the \( q^{ab}_{rr'} \) by their average value. As they are summed over, one obtains the same (exact) result as by using (34) directly. Since only one-replica-index parameters remain, no replica symmetry breaking (RSB) will occur. After some rewriting, using the Hubbard-Stratonovich transformation, replica symmetry (RS), and keeping only leading terms in \( n \), we obtain for \( g_l^2 \)
\[ nN \int Dz \log \left( \text{Tr}_{r'=1}^N \exp \left( -i \hat{n}_r - \frac{\beta^2 \lambda^2}{2} n_r^2 + \beta \lambda n_r \right) \right) . \] (37)

Similarly, the SP equations with respect to the \( \hat{n}_r^a \), can be written
\[ n_r = N \int Dz \frac{\exp(-i \hat{n}_r - \frac{\beta^2 \lambda^2}{2} n_r^2 + \beta \lambda n_r)}{\text{Tr}_{r'=1}^N \exp(-i \hat{n}_r - \frac{\beta^2 \lambda^2}{2} n_r^2 + \beta \lambda n_r)} \ , \] (38)

which have to interpreted as equations for the \( \hat{n}_r^a \). As explained before, for any finite \( n_c \), the most general solution for the \( n_r \) can be written down in terms of a finite number of parameters \( C_l \). With the definitions
\[ \Delta_k \equiv \frac{\sum_l (n_r)^k}{N} = \sum_{l=1}^{n_c} C_l l^k = \sum_{l=1}^{n_c} l^k \delta^{k-1} , \ \forall k \in \mathbb{N} \ , \]
\[ h(z,l) = -i \hat{n}_l - \frac{\beta^2 \lambda^2}{2} l^2 + \beta \lambda \beta l \]
\[ N(z) \equiv \sum_{l=0}^{n_c} C_l \exp(h(z,l)) \ , \]

and adding the entropic correction [4], we obtain the following expression for the state-dependent part of the free energy per particle in the SP approximation
\[ F_{sd} = -\lambda_0 (n_c - \Delta_2) - \frac{\beta^2 \lambda^2}{2} \Delta_3 + \frac{1}{\beta} \left(i \sum_{l=1}^{n_c} l C_l \hat{n}_l + \right)
+ \int Dz \log(N(z)) - \sum_{l=0}^{n_c} C_l \log(C_l) \ , \] (40)

With the constraint \( \Delta_1 = 1 \), the equations (38) reduce to \( n_c + 1 \) non-equivalent equations for the \( \hat{n}_l \) and \( n_c - 1 \) equations for the \( C_l \) \( (l = 2,...,n_c) \):
\[ l = \int Dz \exp(h(z,l))/N(z) \ , \] (41)
\[ \lambda_0 (l-1) - \frac{\beta^2 \lambda^2}{2} (l^2 - 1) + \frac{1}{\beta} \left(i (\hat{n}_l - \hat{n}_l) + \frac{1}{l} \log(C_l) - \right)
- \log(C_l) + \frac{(l-1)}{l} \log(C_0) = 0 \ . \] (42)

From [11], one sees that for all temperatures \( -i \hat{n}_0 = -\infty \), and that only differences between the \( \hat{n}_l \) are important. Thus, the \( \hat{n}_l \) are defined up to a constant, which
drops out of the final expression for the free energy. At any temperature, the free energy \[ \frac{1}{\beta} \sum_{i=2}^{n_c} C_i \log \left( \frac{l_i}{l} \right) \] to the free energy \[ \int A \] (and make the corresponding correction in \[ \int A \]), to obtain even quantitatively excellent results.

To show that we obtain the correct low temperature behaviour, we solve equations \[ \int A \] (with the correction) in the limit \( \beta \rightarrow \infty \) analytically. It can be shown that in that limit the \( C_i \) for intermediate values \( 1 < l < n_i \), vanish. Hence, we immediately start with this simple ansatz: \( C_i N \) boxes contain \( n_c \) monomers, \( C_1 N = (1 - n_c C_n) N \) boxes contain 1 monomer, and \( C_0 N = (\alpha - (1 + (n_c - 1) C_n)) N \) boxes contain no monomers. We call this phase separation, because the monomers are either in the maximally compact or in the swollen phase. In the limit \( \beta \rightarrow \infty \) only the leading exponential survives, such that

\[
i \hat{n}_c = -\frac{1}{2} \beta^2 \lambda^2 n_c^2 + \beta \lambda A n_c + C,
i \hat{n}_1 = -\frac{1}{2} \beta^2 \lambda^2 + \beta \lambda A + C.
\]

where \( A \) is defined via

\[
f_{n_c} = n_c C_{n_c} = \int_A \frac{dz}{\sqrt{2}} = \frac{1}{2} \text{erfc}(\frac{A}{\sqrt{2}}),
\]

Inserting all this into \[ \int A \], we obtain for the ground state energy

\[
E_0(A^*) = -(n_c - 1) \left( \lambda_0 (1 - f_{n_c}^*) + \lambda \frac{\exp(-A^2/2)}{\sqrt{2\pi}} \right)
\]

\[
= -(n_c - 1) \int_0^\infty dA \lambda P(A)
\]

where \( A^* \) is the value that maximizes \[ \int A \], i.e.

\[
A^* = \frac{\lambda_0}{\lambda}, \quad f_{n_c}^* = \frac{1}{2} \text{erfc}(\frac{\lambda_0}{\sqrt{2\lambda}}).
\]

This result makes perfect sense: given \( \lambda_0 \) and \( \lambda \), the fraction of monomers that are negative, i.e. hydrophobic, is exactly \( f_{n_c}^* \). For energetic reasons, these monomers want to be in the maximally compact state \( (n_r = n_c) \), while the others are hydrophilic and want to be maximally swollen \( (n_r = 1) \). Note that the free energy can become arbitrarily negative for \( n_c \rightarrow \infty \). At high temperature we know the exact solution, and at low temperature the energetic term dominates and is calculated exactly by SP integration, because \( \beta \) acts as the large parameter. Numerical analysis shows that also at intermediate temperatures the obtained curves are indistinguishable from the exact solution (FIG. 3).

We conclude that the RHM is probably the only model in which the SP method leads to qualitatively correct results. This could be anticipated by the observation that using \[ \int A \], the \( q_{n_r}^0 \) could have been avoided altogether.

### B. Mean Field Solution of the RCM

Before turning to the technical analysis of the model, we anticipate what to expect for the low temperature behaviour.

- First, we consider the case \( \varepsilon = +1 \), such that equal charges repel each other. When the average charge is 0 \( (\lambda_0 = 0) \), we expect the monomers to group together into boxes such that the total charge in each box goes to zero, because the energy is exactly the sum of the squares of the local charges \( \lambda_r \). When \( \lambda_0 \neq 0 \) (take \( \lambda_0 > 0 \) without loss of generality), however, there is a total charge \( N\lambda_0 \), a total negative charge \( N\lambda_n \), and we define \( A \) by

\[
\int_A^\infty dA \lambda P(A) \lambda_0 (A - A) = -\lambda_n.
\]

The ground state energy per monomer \( E_0 \) is then limited from below by

\[
E_0 \geq \int_0^A dA \lambda P(\lambda) \lambda_1^2 + A^2 \int_A^\infty dA \lambda P(\lambda).
\]

In this case the most positive charges are compensated by negative ones to become \( A \), until all negative charges are used up (with a finite number of charges in each box, it is not guaranteed that this can indeed be done). The remaining (excess) positive charges will stay alone in a box. A closer look at the expression for \( g_1 \) (34) shows that it is well defined at all temperatures for \( \varepsilon = +1 \) (equal charges repel).

- For the case \( \varepsilon = -1 \), we expect the monomers to group together in order to maximize \( |\lambda_r| \) for all the occupied boxes, and the ground state energy per monomer is hence limited by

\[
E_0 \geq - \int_{-\infty}^\infty dA \lambda P(A) (n_r \lambda_1)^2.
\]

A closer look at the expression for \( g_1 \) (34) reveals that there is a critical \( \beta_c \) (dependent on \( n_c, \lambda^2 \), but independent of \( n \)) for any finite \( n \), such that for
starting from the Hamiltonian, we obtain
\[ E_0 = 0 \] (56)
for the ground state energy. Because of (13), this result can obviously not be correct for \( \lambda_0 \neq 0 \).

C. Mean Field Solution of the RIM

Following a similar procedure for the RIM, it is not possible to decouple the “saddle-point” equations with respect to the \( q^a_{rr'} \) for the different replica’s, because the \( q^a_{rr'} \) are not the product of single replica quantities as was the case for the RHM and RCM. Therefore, extra approximations, such as variational approaches, are needed. Nevertheless, one can see that in a SP treatment, the \( q^a_{rr'} \) will again be replaced by their average values. From (34) one easily sees that the \( q^a_{rr'} \) dependent term is \( O(N) \) when \( q^a_{rr'} \in \{0,1,..,n_r\} \), but becomes \( O(1) \) when we replace them by an averaged value. In appendix B, we show that at any finite temperature the dominant contribution comes from the entries \( q^a_{rr'} = 1 \). This alternatively explains why the \( q \) dependent part of (13) for the RIM will be a constant and the quenched average reduces to the annealed one at finite \( T \). Furthermore, we introduce a set of true order parameters which can be treated using the SP method. We show that a finite fraction of \( q^a_{rr'} > 1 \) implies a reduction of the entropy of order \( O(N \log(N)) \), while the energetic gain is at most extensive. Only at reduced temperatures \( T' = T/\sqrt{\log(N)} \), the system starts deviating from the annealed behaviour, because the energetic part of the free energy can compete with the over-extensive part of the entropy. We only signal the onset of this phenomenon. A detailed study of the low temperature behaviour is beyond the scope of this present paper, and has been done for the very similar matching problems \([5,8,9]\). Hence, due to the invariance of the model for permutations of the monomers (which is definitely not true for finite dimensional models!), it turns out that the simple annealed average is equivalent to the quenched one (at finite temperatures). We will return to this issue in the next section on annealed averages.

Nevertheless, even at finite temperatures deviations from the annealed behaviour are observed in the simulations (see FIG. 6). These are finite size effects, because limitations in computer memory do not allow system sizes large enough to make \( 1/\sqrt{\log(N)} \) effects negligible.

VI. CONTINUOUS DISORDER: GRAND ENSEMBLE APPROACH

An alternative approximation scheme is the Grand Ensemble Approach. It consists in approximating the quenched average by a series of constrained annealed averages, and is originally due to Morita \([4]\). For a review and detailed description, we refer to \([24]\). Since the chain constraint is negligible in our simple model, we expect good results upon fixing only the moments of the overall probability distribution of the randomness. In finite dimensional models, however, this does not prevent the random variables to choose their most favorable
position along the chain. Therefore, one may have to enforce conditions on the correlations along the chain, in order to obtain a good approximation for the quenched free energy \[14\]. Apart from being an approximation for the quenched case, the (constrained) annealed average also describes a different physical situation where the monomers are allowed to change their properties on the same time scale as their configuration.

Using the same notation as in the previous section, we find that the equations for the \( \hat{h}_i \) are temperature independent, and the same as in the quenched case at infinite temperature. Therefore, we can correct them exactly to yield the entropic term
\[
\chi \equiv \sum_{l=0}^{n_c} C_l \log(l! C_l). \quad (57)
\]

**A. Annealed Averages for the RHM**

First, we calculate the average of the partition sum directly
\[
\exp(-\beta N \mathcal{F}_{a_0}) \equiv \langle \mathcal{Z} \rangle, \quad (58)
\]
which yields the annealed free energy
\[
\mathcal{F}_{a_0} = -\lambda_0(n_c - \Delta_2) - \frac{1}{2} \beta \lambda^2 (\Delta_3 - 2n_c \Delta_2 + n_c^2) + \frac{\chi}{\beta}. \quad (59)
\]

At intermediate temperatures, the SP equations for the \( f_l, l = 2, ..., n_c \) have to be solved numerically. In the low temperature limit however, they can be solved analytically with the phase separation ansatz \( f_1 = 1 - f_{n_c} \), to yield for the ground state energy
\[
E^{a_0}_0 = -\lambda_0(n_c - 1) + \frac{1}{2} \beta \lambda^2 (n_c - 1)^2 (f_{n_c} - f_{n_c}^2). \quad (63)
\]

The minimum is at \( f_{n_c}^* = \frac{1}{2} \), such that half of the monomers will be hydrophobic and in a completely filled

\[\mathcal{F}_{a_1} = -\lambda_0(n_c - \Delta_2) - \frac{1}{2} \beta \lambda^2 (\Delta_3 - \Delta_2^2) + \frac{\chi}{\beta}. \quad (62)\]

At intermediate temperatures, the SP equations for the \( f_l, l = 2, ..., n_c \) have to be solved numerically. In the low temperature limit however, they can be solved analytically with the phase separation ansatz \( f_1 = 1 - f_{n_c} \), to yield for the ground state energy

\[E^{a_0}_0 = -\lambda_0(n_c - 1) + \frac{1}{2} \beta \lambda^2 (n_c - 1)^2 (f_{n_c} - f_{n_c}^2). \quad (63)\]

The minimum is at \( f_{n_c}^* = \frac{1}{2} \), such that half of the monomers will be hydrophobic and in a completely filled.
box, while the other half will be hydrophilic and alone in their box. In FIG. 8, we observe cross-over to phase separation at low temperatures, indicating a real phase transition in models with an extensive entropy \[^{[14]}\].

Thirdly, we impose the constraints that both the average and the variance of the \( \lambda_i \) must be equal to the quenched ones.

\[
\exp(-\beta N \mathcal{F}_{a_2}) \equiv \exp \left( \frac{2}{\beta} \left( \sum_i (\lambda_i - \lambda_0) \delta \sum_i (\lambda_i - \lambda_0)^2 - \lambda^2 \right) \right).
\]

To impose these constraints, we introduce the conjugates \( \dot{M} \) and \( \dot{S} \). Their SP values are \( \dot{M} = \frac{\lambda \dot{S}}{\lambda_0 c} + \beta (\Delta_2 - n_c) \), and \( \dot{S} = \frac{1}{2} (-1 + \sqrt{1 + 4 \lambda^2 \beta^2 (\Delta_3 - \Delta_2^2)}) \). The free energy is then given by

\[
\mathcal{F}_{a_2} = -\lambda_0 (n_c - \Delta_2) + \frac{\log(1 + \dot{S})}{2\beta} + \frac{\dot{S}}{2\beta} \frac{\beta \lambda^2}{2(1 + \dot{S})} (\Delta_3 - \Delta_2^2) + \chi.
\]

At intermediate temperatures, the SP equations for the \( f_1, f_2, \ldots, f_{n_c} \) have to be solved numerically. In the low temperature limit, however, they can be solved analytically with the phase separation ansatz \( f_1 = 1 - f_{n_c} \) to yield for the ground state energy

\[
E_{a_2} = \lambda_0 (n_c - \Delta_2) - \lambda \sqrt{\Delta_3 - \Delta_2^2}.
\]

The minimum occurs for

\[
f_c^* = \frac{1}{2} \left( 1 - \frac{\lambda_0}{\sqrt{\lambda^2 + \lambda_0^2}} \right),
\]

which is already very close to the quenched result \[^{[17]}\]. In FIG. 8, c we observe that the cross-over type of behaviour in the case of very negative \( \lambda_0 \) has vanished as it should for the quenched case. In FIG. 8, we compare approximation \[^{[25]}\] with quenched numerical simulations.

B. Annealed Averages for the RCM

In order to describe both the cases \( \varepsilon = \pm 1 \) at all temperatures, we have limited ourselves to the case where both the average and the variance of the disorder are constrained. Introducing the conjugate variables \( \dot{M} \) and \( \dot{S} \) respectively, we obtain the following expression for the free energy

\[
\mathcal{F}_{a_2} = -\frac{1}{2} \left( \dot{S} - \log(1 + \dot{S}) + \frac{\lambda^2 \dot{M}^2}{(1 + \dot{S})^2} \sum_{i=0}^{n_c} C_i \log(1 + \frac{\varepsilon \beta \lambda^2 l_i}{(1 + \dot{S})^2}) \right) + \chi.
\]

This approximation is compared with the results of quenched numerical simulations in FIG. 10, a, b. One observes that this leads to at least qualitatively correct results.

FIG. 9. The order parameters \( C_l \) as a function of temperature, for the Random Hydrophilic/hydrophobic Model (RHM) with \( n_c = 3, \alpha = 1, \lambda = 0 \) resp., and \( P(\lambda) \sim N(0,1) \). Full lines: annealed theory with fixed mean and variance. Dots: numerical (quenched) simulations \( (N = 3000) \). The results are qualitatively correct.

FIG. 10. a, b The order parameters \( C_l \) as a function of temperature, for the Random Charge Model (RCM) with \( n_c = 3, \alpha = 1, \varepsilon = \pm 1 \) resp., and \( P(\lambda) \sim N(0,1) \). Full lines: annealed theory with fixed mean and variance. Dots: (quenched) numerical simulations \( (N = 3000) \). The results are qualitatively correct.
**C. Annealed Averages for the RIM**

Due to the fact that there are \( N(N-1)/2 \) disorder parameters \( \lambda_{ij} \), fixing any overall moment of their probability distribution does not have any effect. One can e.g. check that the leading order of the SP values of \( \hat{\lambda} \) is correct. For the random interaction model additional assumptions are found to be even qualitatively incorrect for the random interaction model certainly needs further investigation. It can be viewed as a generalisation of the existing results for matching problems, and may be qualitatively different due to the non-bounded nature of the grand state energy. Although absent at finite densities, phase transitions may occur when the density is allowed to become arbitrarily high.

Finally, the study of the dynamics of this model both at finite and at high density is currently in progress and will be published elsewhere.

I am grateful to A.C.C. Coolen and R. Kühn for valuable suggestions.

VII. CONCLUSIONS

We have studied a simple model for random heteropolymers in \( \infty \)-dimensions, the finite dimensional analogues of which had been studied using various approaches [11]-[20]. The simplicity and transparency of the model has allowed us to formulate an exact solution in terms of true order parameters for discrete disorder, and in terms of self-averaging mesoscopic variables for continuous disorder. Although the behaviour of finite dimensional models will obviously be very different, due to the crucial role in the latter of the chain constraint, our model gives valuable insight into the problems inherent in the saddle point approximation for the parameters that occur naturally in a mean field (replica) treatment. Whereas qualitatively correct for the random hydrophilic-hydrophobic model, the results for the random charge model are found to be even qualitatively incorrect. For the random interaction model additional assumptions are needed, but in our \( \infty \)-dimensional model at finite temperatures, the simple annealed average is found to coincide with the quenched result. Variational approaches have been successful in capturing certain aspects of the behaviour of random hetero-polymers, but it may well be that the origin of some of the incongruences between the results obtained by analytical methods for continuum models and those found numerically for lattice models [14,15], lay in the undue application of the saddle point approximation for strongly fluctuating quantities. It is not our goal to diminish previous work which has led to many valuable insights, but to draw the reader’s attention to the inherent risks of the saddle point approximation in random hetero-polymers.

The Grand Ensemble Approach [16,21] is a different powerful tool to describe the case of permuted disorder, but it is technically very hard to impose independence of the disorder along the sequence. Hence, a good detailed description of the quenched case based on the Grand Ensemble Approach is as yet still out of reach in finite dimensional models [13].

We have established links between our model, and the Backgammon model [16], models for polydispersity [10], and matching problems [5,7–9]. The latter in particular suggests that in order to develop a self-consistent mean field theory for random hetero-polymers, it may be necessary to find a good set of “true” order parameters (see appendix B).

The protein folding problem can be viewed as a geometrically constrained matching problem for the monomers. Hence, new insights may be gained using the techniques developed for the matching problem [16,21], imposing some weak (geometrical) constraints that can be treated analytically. The low temperature phase for the random interaction model certainly needs further investigation. It can be viewed as a generalisation of the existing results for matching problems, and may be qualitatively different due to the non-bounded nature of the ground state energy. Although absent at finite densities, phase transitions may occur when the density is allowed to become arbitrarily high.

Finally, the study of the dynamics of this model both at finite and at high density is currently in progress and will be published elsewhere.

I am grateful to A.C.C. Coolen and R. Kühn for valuable suggestions.

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APPENDIX A: CORRECTIONS TO THE SADDLE-POINT

The first correction to the SP for the free energy is easily calculated, and given by

\[ -\frac{1}{2} \log \det (H^*) \simeq \frac{1}{2\beta} \sum_{l=2}^{n_n} C_l \log (l), \tag{A1} \]

where \( H^* \) is the Hessian of \( -\beta F_q \) with respect to the \( \hat{n}_r \) taken in the SP (\ref{eq:SP}). As we will see now, this correction is not enough to obtain the correct entropy at high temperature.

In the limit \( \beta \to 0 \) equations (\ref{eq:SP}) simplify to \(-i\hat{n}_t \simeq \log (l)\), and the entropy is given by

\[ \sum_{l=1}^{n_n} f_l \log (l) - \sum_{l=0}^{n_n} C_l \log (C_l) = - \sum_{l=0}^{n_n} C_l \log (\frac{C_l}{l}) , \tag{A2} \]

which is not correct! From a simple box counting argument one can show that the non-constant part of the entropy in the high temperature limit is given by

\[ - \sum_{l=0}^{n_n} C_l \log (C_l) - \sum_{l=2}^{n_n} C_l \log (l!) = - \sum_{l=0}^{n_n} C_l \log (l!) C_l. \tag{A3} \]

The first term comes from the permutation of the boxes, while the second one comes from the permutations of monomers within the same box. To obtain result (\ref{eq:SP}) analytically, one should in principle perform all the integrations over the \( \hat{n}_r \), exactly, or equivalently, consider the whole expansion around the SP. This is an unfeasible task, since at all temperatures all orders in the expansion around the SP contribute to the same order in \( N \). Instead, at all temperatures, we add the high temperature correction

\[ \frac{1}{\beta} \sum_{l=2}^{n_n} C_l \log (\frac{l}{l}) \tag{A4} \]

to the free energy (\ref{eq:SP}) (and the corresponding correction to (\ref{eq:SP})). In this way, we are at least ensured to obtain the exact result in the high temperature limit.

APPENDIX B: VALIDITY OF THE ANNEALED APPROXIMATION FOR THE RIM.

For simplicity and for comparison with the so-called matching problem (\ref{eq:SP}), we take \( n_c = 2, \alpha = \frac{1}{n_c} = \frac{1}{2} \).

We introduce the following order parameters

\[ d_{a_1,..,a_k} = \frac{2}{N} \sum_{i<j}^{N} \left( \prod_{p=1}^{k} \delta_{s_{i,p} s_{j,p}} \right), \tag{B1} \]

\[ 1 \leq a_1 < .. < a_k \leq n, \quad k = 2,..,n, \]

which have the clear physical meaning of being the fraction of monomers that are coupled to the same partner in all replicas \( a_1,..,a_k \). The quenched free energy per particle (see (\ref{eq:SP})) can then be rewritten as

\[ \mathcal{F}_q = \frac{\partial}{\partial n} \left[ \frac{\lambda_0}{2} \left( \sum_{a=1}^{n_n} \Delta_a^2 - n \right) - \frac{3\beta^2}{4} \left( \sum_{a=1}^{n_n} \Delta_a^2 + 2 \sum_{a=b=1}^{n} \left( 1 + d_{ab} \right) \right) - \frac{1}{\beta N} \sum_{m=1}^{n} \mathcal{S}_m \right] \bigg|_{n=0} , \tag{B2} \]

where \( \Delta_a^2 = n_c \) (for \( \alpha = \frac{1}{n_c} \)). \( \mathcal{S}_m \) is the entropy of replica \( m \) given the configuration of replicas \( 1,..,m-1 \) and given the mutual overlaps \( d_{a_1,..,a_k} = d_k, \forall k = 1,..,n, \forall a_1 < .. < a_k \). The particles of the \( m \)-th replica can be divided into the following non-equivalent groups:

\[ \left( \begin{array}{c} m-1 \\ k-1 \end{array} \right) \quad \text{groups of size :} \]

\[ N s_{m,k} = N \left[ \prod_{l=0}^{m-k} \{ (-1)^l \left( \begin{array}{c} m-k \\ l \end{array} \right) \} \right] k = 1,..,m, \tag{B3} \]

where \( d_1 = 1 \) and \( \sum_{k=1}^{m} \left( \begin{array}{c} m-1 \\ k-1 \end{array} \right) s_{m,k} = 1 \). Note that \( k \) indicates the number of replicas (including replica \( m \)) in which the couples are equal. Hence, the couples in the groups with \( k > 1 \) are fixed, because they are equal to at least one couple in replicas \( 1,..,m-1 \). The remaining monomers in \( s_{m,1} \) are still free to form couples with the only restriction that they are not equal to any of the
where we have used the equalities

\[ \text{Rescaling the temperature } \beta \text{ as there are constrained from the fact that all group sizes } s \leq 1 \text{ under the assumption that freeze, i.e. can be found. Eventually, the system will completely } \]

\[ d \text{ energy per particle to leading order } \]

This expression has to be maximized with respect to the existing couples in replicas \( 1, \ldots, m - 1 \). Hence, the entropy of replica \( m \) is composed of both the possible divisions in groups, and the possible couplings in the last group of size \( Ns_{m,1} \). The total number of ways in which \( R \gg 1 \) particles can be coupled is denoted by \( I_R \), while \( I_R^0 \) is the number of ways in which \( R \) particles can be coupled such that none of the couples is equal to any of the couples the other replicas. The number of already existing couples in the other replicas is \( cR^2 \) with \( 1 \leq c \leq (m-1) \). Thus,

\[ I_R = \frac{R!}{(2!)^{R/2}(R/2)!}, \quad S_R \approx R/2(\log(R) - 1), \quad (B4) \]

\[ I_R \leq I_R^0 \leq I_R - \frac{cR^2}{4}I_{R-2}, \quad S_R^0 \approx S_R - O(\log(R)). \]

Using (B3)-(B4), the entropy \( S_m \) of replica \( m \) is given by

\[ S_m \approx \frac{N}{2} \left[ \sum_{k=2}^{m} \left( \frac{m}{k} - 1 \right) s_{m,k} \log(s_{m,k}) + s_{m,1}(\log(N) - 1) \right] , \quad (B5) \]

under the assumption that \( s_{m,1} = O(1) \). The total contribution of \( n \) replicas to the entropy \( S = \sum_{m=1}^{n} S_m \) to leading order in \( N \) is now given by

\[ S \approx \frac{N}{2} \log(N) \sum_{m=1}^{n} s_{m,1} = \frac{nN}{2} \log(N) \left[ 1 + \sum_{k=2}^{\infty} \frac{d_k}{k} \right] , \quad (B6) \]

where we have used the equalities

\[ \sum_{m=0}^{p} \binom{m}{k} = \left( \frac{p + 1}{k + 1} \right), \quad \lim_{n \to 0} \binom{n}{k} \approx \frac{n(-1)^{k-1}}{k} . \quad (B7) \]

Rescaling the temperature \( \beta = \beta' \sqrt{\log(N)} \), yields the following state-dependent part of the quenched free energy per particle to leading order

\[ \mathcal{F}_n \approx \frac{\sqrt{\log(N)}}{2} \left[ \frac{\beta' \lambda^2}{2}d_2 - \frac{1}{\beta'} \sum_{k=2}^{\infty} \frac{d_k}{k} \right] . \quad (B8) \]

This expression has to be maximized with respect to the \( d_k \) with \( k \) even, while it has to be minimized with respect to the \( d_k \) with \( k \) odd. The \( d_k \) cannot be freely extremised as there are constrained from the fact that all group sizes \( s_{m,k} \) are positive: e.g. \( 0 \leq d_2 \leq 1, \max(0, 2d_2 - 1) \leq d_3 \leq d_2 \), etc.

For \( \beta' < \frac{1}{2} \) the entropy dominates and the annealed approximation (i.e. \( d_k = 0, \forall k > 1 \)) is exact. For \( \beta' \geq \frac{1}{2} \) the energy starts competing and solutions with \( d_k > 0 \) can be found. Eventually, the system will completely freeze, i.e. \( d_k \approx 1, \forall k \), but then expressions (B3)-(B8) are no longer valid, since the \( s_{m,k} \) are no longer of order \( O(1) \).

Although our reasoning remains qualitatively valid for \( n_c > 2 \) and \( \alpha > \frac{1}{n_c} \), the details become extremely complicated as the necessary set of order parameters will be given by

\[ C_I = \frac{1}{N} \sum_{k=1}^{N} \delta_{i,n_r} \lambda_{i} , \quad l = 0, \ldots, n_c \quad (B9) \]

\[ d_{a_1, \ldots, a_k} = \frac{t!}{N} \sum_{i_1 < \ldots < i_t} \left( \prod_{p=1}^{k} \prod_{l=1}^{t} \delta_{i_1, i_1} \right) , \quad (B10) \]

1 \leq a_1 < \ldots < a_k \leq n , \quad k = 2, \ldots, n_c \quad \text{, t = 2,} ... n_c \]