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Optical Resolution of Chiral Molecules by Stretching Hydrogen-Bonding Helical Polymers

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ABSTRACT: The effect of stretching polymer chains bearing helical segments induced by hydrogen-bonded chiral molecules in the mixtures of chiral molecules is theoretically studied. The end-to-end distance R of a polymer with induced helical sequences and the chiral order parameter ψ (difference in the content of left- and right-handed helices on a chain) are calculated as functions of the external tension given at the chain ends. The chiral order parameter is shown to be sensitive to chain extension and drastically enhanced by stretching. With the slightest enantiomer excess, therefore, a mixture of chiral molecules in a solution can be separated into assemblies of pure chirality by repeating the operation of stretching polymers and washing the adsorbed chiral molecules. The possibility of optical resolution of racemic solutions by stretching polymeric gels consisting of such hydrogen-bonded helical subchains is discussed.

1. Introduction

Helical ordering of polymers induced by bulky chiral side groups has been recently attracting the interest of researchers from both scientific and applicational viewpoints. One series of experiments concerns formation of helices and inversion of their helicity (or handedness) in random copolymers bearing chiral side groups with changes in the composition of S and R forms or in the temperature.[1−10] For such random copolymers, the distribution of bulky pendant groups along the polymer chain is fixed during the process of polymer synthesis, so that randomness is *frozen*, or *quenched*. The conformation change and solution properties of such random copolymers should therefore be studied as systems with *frozen randomness*. For instance, if some pendant groups of the given chirality are involved in a helix of opposite (unconfortable) handedness, they feel *frustration*, but they cannot dissociate from the chain because of the covalent bond. Besides the optical order parameter (difference between the fraction of left- and right-handed helices), the degree of frustration (the average number of chiral groups in the opposite helices) is the fundamental order parameter that characterizes such frozen systems, just as the spin glass order parameter in quenched random magnets.[11]

In contrast, helical ordering by hydrogen-bonded chiral molecules as pendant groups falls on a different category of randomness. Chiral molecules of one chirality induces helices of definite handedness when sequentially hydrogen-bonded onto the polymer chain side. The distribution of chiral molecules along the chain is random but not frozen; it can change by thermal motion or under external force. We call such randomness *annealed randomness*. In annealed randomness, chiral molecules can dissociate when they are involved in a helix of opposite handedness, so that there is in principle no frustration. Instead, one of the most fundamental properties of such hydrogen-bonded helical polymers is their sensitivity to the chirality of molecules, in particular, capability of preferential adsorption leading to the separation of mixed solutions of chiral molecules into molecules of pure chirality. The main purpose of this study is to show that such separation force, or *optical resolution* force, of the polymers is largely enhanced when they are stretched by external tensions. On the basis of a theoretical study, we propose a new simple method of resolving racemic mixtures by the deformation of gels made up of hydrogen-bonding polymers.

In a recent series of experiments,[12−16] cooperative chiral ordering induced on polymers with hydrogen-bonded chiral side groups was reported. In their experiments, cis-transoidal poly((4-carboxyphenyl)acetylene)s were observed to form helices with definite handedness along the chain in a solvent of dimethyl sulfoxide (DMSO) when hydrogen-bonded with low molecular-weight chiral molecules such as amines and amino alcohols. The handedness, or helicity, of the induced helices are decided by the chirality of adsorbed molecules. It was shown by measuring the intensity of induced circular dichroism (ICD) that the following three common rules generally hold:

(i) Nonlinear Amplification. Induction of helices is highly nonlinear; there is a sharp rise of the helical content in a very narrow concentration region of chiral molecules.

(ii) Majority Rule. Under the presence of both S and R forms of chiral molecules, the handedness of helices is predominantly decided by the type induced by the majority component.

(iii) Sergeants-and-Soldiers Rule. Under the presence of small number of chiral molecules of only one type, achiral molecules work as if they were chiral molecules of the same chirality, just like soldiers following the orders of sergeants.

In our previous paper[17] (referred to as paper I), we theoretically studied the molecular origin of such cooperative chiral ordering on the basis of standard statistical mechanics of molecular adsorption under the condition of association equilibrium. We derived the common rules described above by directly analyzing the sequence selection process when the chiral molecules are attached onto the polymer backbone, and clarified the molecular

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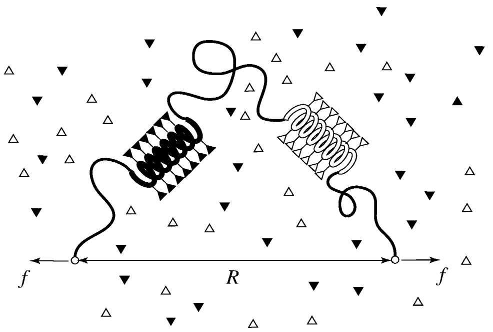

Figure 1. Single polymer chain adsorbing chiral molecules on its chain side in a solution of enantiomer mixture under the force **f** given at the ends of the chain. Molecules of the same chirality are sequentially adsorbed onto the polymer chain due to the nearest-neighbor interaction. An adsorbed sequence induces a helix of fixed handedness according to the chirality of adsorbed molecules. The end-to-end distance of the chain is given by R.

origin of cooperativity. In this paper, we study the effect of stretching such helical polymers by external forces and show that helix induction is amplified until the force exerted on the chain ends reaches a certain critical value above which helices are broken into extended chains. The sensitivity to chain stretching depends on the pitch of the induced helices. We show that under a simple condition the optical order parameter $\psi \equiv \theta^{(S)} - \theta^{(R)}$ is sufficiently enhanced, where $\theta^{(S)}$ and $\theta^{(R)}$ are the content of adsorbed molecules of the specified chirality. Separation of almost racemic mixtures into purely chiral ones is easily done by repeating the combined operation of stretching polymers and washing out the hydrogen-bonded chiral molecules, since the ratio $\theta^{(R)}/\theta^{(S)}$ is largely different from the ratio $c^{(R)}/c^{(S)}$ of the concentration in the bulk.

2. Distribution Function of the Helices on a Polymer Chain under Tension

Let us consider a single polymer chain (poly((4-carboxyphenyl)acetylene) in ref 12) made up of n monomeric units (4-carboxyphenyl acetylene), each carrying a hydrogen-bonding site (carboxylic group) in a solvent (DMSO) in the presence of chiral molecules (amines and amino alcohols). In the experiment,[12] it was found that the chiral molecules in the (S)-form induce left-handed helices on a polymer chain when attached onto it by hydrogen bonds, and those in the (R)-form induce right-handed helices, or vice versa. In this paper, we study the effect of stretching the chain by external tension. We consider a mixture of enantiomers, (S)-form and (R)-form, of the same molecular species to study their competition in adsorption. Let their molar concentrations be given by $c^{(S)}$ and $c^{(R)}$. We first find the number and length distribution of helices along the chain in adsorption equilibrium as functions of the tension **f** under a given temperature and concentrations of the chiral molecules.

Let $j_\zeta^{(\alpha)}$ be the number of helical sequences of the length ζ (in terms of the number of monomeric units) formed by the attached chiral molecules of the type $\alpha = S, R$ (see Figure 1). These sequences are randomly selected from the finite total number n of monomers, or degree of polymerization (DP), during thermal adsorption process of the chiral molecules. The external force **f** is given at the ends of the chain, and as a result, the average end-to-end vector of the chain is given by **R**. Since a chiral molecule itself has an asymmetric shape, it gains additional energy and is stabilized by taking a twisted position when it is adsorbed onto the site next to the already bonded molecule of the *same chirality*, but it cannot be adsorbed onto the nearest-neighboring site of the already bonded molecule of the *opposite chirality* because of the strong steric hindrance. We therefore, as in paper I,[17] introduce at least one nonbonded site between the helical sequences of the different handedness. Similarly, there should be at least one nonbonded site between the helical sequences of the same handedness to distinguish the two helices. The number of different ways to choose such sequences from the finite total length n is then given by

$$\omega(\{j\}) = [n - \sum\zeta(j_\zeta^{(S)} + j_\zeta^{(R)})]!/\{\prod_\zeta(j_\zeta^{(S)}!j_\zeta^{(R)}!)[n - \sum(\zeta+1)(j_\zeta^{(S)} + j_\zeta^{(R)})]!\} \quad (2.1)$$

The helix content, i.e., the total number of monomeric units in the helices of the type α relative to n is then given by

$$\theta^{(\alpha)} \equiv \sum_{\zeta=1}^{n}\zeta j_\zeta^{(\alpha)}/n, \quad \alpha = S, R \quad (2.2)$$

and the total number of helices of the type α relative to n is given by

$$\nu^{(\alpha)} \equiv \sum_{\zeta=1}^{n} j_\zeta^{(\alpha)}/n, \quad \alpha = S, R \quad (2.3)$$

We assume that the remaining nonhelical parts take the random-coil conformation because the local minima in the potential of internal rotation of the polymer are symmetrically located and separated by the energy barriers that can easily overcome by thermal activation. For simplicity, let us also assume that the helices are rigid rods and have a pitch d with p monomers in one period. The length along the rod axis per monomer is then given by $b \equiv d/p$, and the length of a helix with monomer sequence ζ is given by $b\zeta$. Let $\mathbf{e}_i$ be the unit vector specifying the direction of the ith helix along the chain, and let $\mathbf{r}_k$ be the end-to-end vector of the kth random coil part along the chain. We then have the relation

$$\mathbf{R} = \sum_k \mathbf{r}_k + b^{(S)}\sum_i \zeta_i \mathbf{e}_i^{(S)} + b^{(R)}\sum_j \zeta_j \mathbf{e}_j^{(R)} \quad (2.4)$$

for the end-to-end vector of a chain, where $b^{(\alpha)}$ with $\alpha = S, R$ is the pitch per monomer of a helix of the type α.

To find the partition function of the polymer chain associated with chiral molecules, we first describe the polymer by a chain consisting of the number n of linearly connected rigid rods of length a with isotropic orientational distribution function

$$\rho(\mathbf{l}) = \delta(l - a)/4\pi a^2 \quad (2.5)$$

Such a chain with a finite total contour length na (*random flight model*) is necessary to study the nonlinear effect of overstretching under high tension. Since we have assumed that the induced helices are rigid rods, their orientational distribution function is given by

$$\rho_\zeta^{(\alpha)}(\mathbf{l}) = \delta(l - b^{(\alpha)}\zeta)/4\pi(b^{(\alpha)}\zeta)^2 \tag{2.6}$$

under the assumption of random orientation.

By using these definitions, we find that the canonical partition function of a chain with specified $n^{(S)}$, $n^{(R)}$, and **R** is given by

$$Z_n(n^{(S)}, n^{(R)}; \mathbf{R}) = \sum_{\{j\}} \omega(\{j\}) \prod_\zeta [({\eta_\zeta}^{(S)})^{j_\zeta^{(S)}} ({\eta_\zeta}^{(R)})^{j_\zeta^{(R)}}] \times \int \cdots \int \prod_k \rho(\mathbf{l}_k)\, \mathrm{d}\mathbf{l}_k \prod_i \rho_\zeta^{(S)}(\mathbf{l}_i)\, \mathrm{d}\mathbf{l}_i \prod_j \rho_\zeta^{(R)}(\mathbf{l}_j)\, \mathrm{d}\mathbf{l}_j \tag{2.7}$$

under the condition given in eq 2.4, where ${\eta_\zeta}^{(\alpha)}$ is the statistical weight for a type α helix of the length ζ relative to the random coil, and

$$n^{(\alpha)} \equiv \sum_{\zeta=1}^{n} \zeta {j_\zeta}^{(\alpha)} \tag{2.8}$$

is the total number of adsorbed molecules of the type α.

We next move to the ensemble where the external tension **f** is the independent variable, and integrate over all end-to-end vectors and orientation of helical rods. We then find

$$Q_n(n^{(S)}, n^{(R)}; \mathbf{f}) \equiv \int \mathrm{d}\mathbf{R}\, Z_n(n^{(S)}, n^{(R)}; \mathbf{R}) e^{\beta \mathbf{f}\cdot\mathbf{R}} = \tilde{g}(\tau)^{n(1-\theta^{(S)}-\theta^{(R)})} \sum_{\{j\}} \omega(\{j\}) \prod_\zeta [({\eta_\zeta}^{(S)})^{j_\zeta^{(S)}} ({\eta_\zeta}^{(R)})^{j_\zeta^{(R)}}] \times \prod_{\zeta=1}^{n} \tilde{g}^{(S)}(\kappa^{(S)}\tau\zeta)^{j_\zeta^{(S)}} \tilde{g}^{(R)}(\kappa^{(R)}\tau\zeta)^{j_\zeta^{(R)}} \tag{2.9}$$

where the function $\tilde{g}(\tau)$ is Laplace's transform of the connection function $\rho(\mathbf{l})$:

$$\tilde{g}(\tau) \equiv \int \mathrm{d}\mathbf{l}\ \rho(\mathbf{l}) \mathrm{e}^{\beta \mathbf{f}\mathbf{l}} = \sinh(\tau)/\tau, \tag{2.10}$$

$$\tau \equiv fa/k_\mathrm{B}T \tag{2.11}$$

is the dimensionless force, and

$$\kappa^{(\alpha)} \equiv b^{(\alpha)}/a \tag{2.12}$$

for $\alpha = S, R$ is the helical pitch per monomer measured relative to the step length.

As for the random coil part, we have $\tilde{g}(\tau)$ for the freely jointed rod. It is approximately given by the Gaussian form

$$\tilde{g}(\tau) \simeq \exp(\tau^2/6) \tag{2.13}$$

for weak stretching.

To find the equilibrium distribution function, we maximize this partition function by changing $\{j\}$ under the given concentration of chiral molecules. Since the solution is a particle reservoir, we introduce the activity λ_α of the molecules of the type α as independent variables (functions of the concentration), and move to the grand partition function

$$\Xi_n(\{\lambda\}; \mathbf{f}) \equiv \sum_{n^{(S)},n^{(R)}=0}^{n} {\lambda_S}^{n^{(S)}} {\lambda_R}^{n^{(R)}} Q_n(n^{(S)}, n^{(R)}; \mathbf{f}) = \tilde{g}(\tau)^n \sum_{\{j\}} \omega(\{j\}) \prod_\zeta [({\eta_\zeta}^{(S)} {\phi_\zeta}^{(S)}(\tau) {\lambda_S}^\zeta)^{j_\zeta^{(S)}} \times ({\eta_\zeta}^{(R)} {\phi_\zeta}^{(R)}(\tau) {\lambda_R}^\zeta)^{j_\zeta^{(R)}}], \tag{2.14}$$

where the new function ϕ is defined by

$${\phi_\zeta}^{(\alpha)}(\tau) \equiv \tilde{g}(\kappa^{(\alpha)}\tau\zeta)/\tilde{g}(\tau)^\zeta \tag{2.15}$$

At this stage, we can see clearly the effect of tension on the adsorption of chiral molecules. The statistical weight η_ζ of a helix with length ζ is renormalized by two factors as

$$\eta_\zeta \rightarrow \eta_\zeta \phi_\zeta(\tau) \lambda^\zeta \tag{2.16}$$

The activity λ is proportional to the molar concentration of the chiral molecules in a dilute solution, so that the last factor gives the effect of concentration. The second factor includes the effect of orientation $\tilde{g}(\kappa\tau\zeta)$ of a rodlike helix, and entropic force $\tilde{g}(\tau)^{-\zeta}$ from the corresponding random-coil segments. In fact, by taking the logarithm of the total statistical weight of a helix, we find that its free energy is given by

$$\Delta f_\zeta(\tau)/k_\mathrm{B}T = -\ln\eta_\zeta - \ln[\sinh(\kappa\tau\zeta)/\kappa\tau\zeta] + \zeta \ln[\sinh(\tau)/\tau] + \text{const.} \tag{2.17}$$

By minimizing this free energy with respect to ζ for a given statistical weight η_ζ, we can see in a simple way that the average helix length is increased by stretching until they are finally destroyed in the limit of strong tension. The physical reason why helices are enhanced by force is that linear growth of rodlike helices gains a larger end-to-end distance than that of random coils and hence is advantageous for chain stretch under external force. More complete calculations are given in the following sections. The force laws governing the extension behavior of homopolypeptides where helices are formed by hydrogen bonds between neighboring side groups along the main chain were recently theoretically studied by Tamashiro et al.[18] and Buhot et al.[19] Although the molecular mechanism of helix formation is different, they found similar helix induction by chain extension. The rigid linearity of helical sequences is therefore more important than the details of hydrogen bonds for the conformational change under tension.

We now study the detailed mechanism of helix enhancement by finding the most probable distribution function of helices. It is found by maximizing the grand partition function Ξ by changing ${j_\zeta}^{(\alpha)}$. We then find

$${j_\zeta}^{(\alpha)}/n = (1 - \theta - \nu){\eta_\zeta}^{(\alpha)} {\phi_\zeta}^{(\alpha)}(\tau)(\lambda_\alpha t)^\zeta \tag{2.18}$$

by variational calculation. Here

$$\theta = \theta^{(S)} + \theta^{(R)} \tag{2.19}$$

is the total helix content. Similarly

$$\nu = \nu^{(S)} + \nu^{(R)} \tag{2.20}$$

is the total number of helices.

The parameter t is defined by

$$t \equiv (1 - \theta - \nu)/(1 - \theta) \tag{2.21}$$

and has the physical meaning of the probability such that an arbitralily chosen monomer belongs to the random coil part. To see this, we substitute the equilibrium distribution (eq 2.18) into the grand partition function eq 2.14 and find that it is given by

$$\Xi_n(\{\lambda\}, \tau) = [\tilde{g}(\tau)/t]^n \tag{2.22}$$

Since the probability $p(n^{(S)} = 0, n^{(R)} = 0)$ for finding a completely random coil is given by $\tilde{g}(\tau)^n/\Xi_n(\{\lambda\}, \tau)$, we find

$$p(n^{(S)} = 0, n^{(R)} = 0) = t^n \tag{2.23}$$

and hence the physical interpretation of the parameter t is apparent.

To find t as a function of the activities, we now substitute the equilibrium distribution (eq 2.18) into the definitions of $\theta^{(\alpha)}$ and $\nu^{(\alpha)}$ and find

$$\theta^{(\alpha)} = (1 - \theta)tV_1^{(\alpha)}(\tau, \lambda_\alpha t) \tag{2.24}$$

and

$$\nu^{(\alpha)} = (1 - \theta)tV_0^{(\alpha)}(\tau, \lambda_\alpha t) \tag{2.25}$$

for each handedness, where functions V_0 and V_1 are defined by

$$V_0^{(\alpha)}(\tau, x) \equiv \sum_{\zeta=1}^{n} \eta_\zeta^{(\alpha)}\phi_\zeta^{(\alpha)}(\tau)x^\zeta \tag{2.26a}$$

$$V_1^{(\alpha)}(\tau, x) \equiv \sum_{\zeta=1}^{n} \zeta\eta_\zeta^{(\alpha)}\phi_\zeta^{(\alpha)}(\tau)x^\zeta \tag{2.26b}$$

By defining eq 2.21 for t, we find that it should satisfy the condition

$$\frac{t}{1-t}\{V_0^{(S)}(\tau, \lambda_S t) + V_0^{(R)}(\tau, \lambda_R t)\} = 1 \tag{2.27}$$

This is basically the same equation found in paper I,[17] but here it is properly extended to include the effect of tension. The solution of this equation gives the probability t as a function of the temperature, the activities (and hence concentrations) of the chiral molecules, and the external force. Upon substitution of the result into the eq 2.19, together with eq 2.24, we find the total helix content θ is given by

$$1 - \theta = 1/\{1 + t[V_1^{(S)}(\tau, \lambda_S t) + V_1^{(R)}(\tau, \lambda_R t)]\} \tag{2.28}$$

The helix content and the number of helices for *each component* of chiral molecules are then calculated from eqs 2.24 and 2.25.

Let us next find the tension-elongation curve. The average end-to-end distance R can be found by the fundamental relation

$$R = \partial\{k_B T \ln \Xi_n(\{\lambda\}, \tau)\}/\partial f \tag{2.29}$$

so that we have

$$\begin{aligned} R/na &= \mathscr{L}(\tau) - (\partial t/\partial \tau)/t \\ &= (1 - \theta(\tau))\{\mathscr{L}(\tau) + t[\kappa_S W_1^{(S)}(\tau, \lambda_S t) + \\ &\qquad \kappa_R W_1^{(R)}(\tau, \lambda_R t)]\} \end{aligned} \tag{2.30}$$

where

$$\mathscr{L}(\tau) \equiv \partial \ln \tilde{g}(\tau)/\partial \tau = \coth \tau - 1/\tau \tag{2.31}$$

is Langevin's function, and functions $W_k^{(\alpha)}$ are defined by

$$W_k^{(\alpha)}(\tau, x) \equiv \sum_{\zeta=1}^{n} \zeta^k \eta_\zeta^{(\alpha)}\phi_\zeta^{(\alpha)}(\tau)\mathscr{L}(\kappa_\alpha \tau \zeta)x^\zeta \tag{2.32}$$

for $\alpha = S, R$ and $k = 0, 1, 2, ...$

3. Statistical Weight of Helices

For further calculation, we have to specify the statistical weight η_ζ. As was seen in paper I,[17] we now employ the simplest form proposed by Zimm and Bragg[20,21] (referred to as ZB) for helical polypeptides

$$\eta_\zeta = \sigma s(T)^\zeta \tag{3.1}$$

where σ comes from a boundary between a random coil part and a helical part (the *helix initiation factor* or *cooperativity factor*) and $s(T)$ comes from the hydrogen-bonding free energy between the neighboring groups to form a helix. In the present model of induced helices, they are specified as follows. Let $-\epsilon_H$ be the hydrogen-bonding energy between a monomer unit on the polymer chain and a chiral molecule adsorbed onto it, and let $-\Delta\epsilon_\alpha$ be the stabilization energy due to the interaction with the neighboring molecule of the same chirality α that is already adsorbed on the chain. We assume that repulsive interaction between the neighboring molecules of different chirality is so large due to the steric hindrance that nearest neighboring pairs of different chirality is impossible to form. Then, the statistical weight of helices of each handedness is described by the factor

$$\eta_\zeta^{(\alpha)} = \sigma_\alpha u_\alpha(T)^\zeta, \quad \alpha = S, R \tag{3.2}$$

where the factor $u_\alpha(T) \equiv \exp[(\epsilon + \Delta\epsilon_\alpha)/k_B T]$ now includes the hydrogen-bonding energy gain as well as the stabilization energy, and the helix initiation parameter is given by $\sigma_\alpha \equiv \exp(-\Delta\epsilon_\alpha/k_B T)$.

The V functions now take the form

$$V_0(\tau, \lambda t) = \sigma x v_0(\kappa\tau, x) \tag{3.3a}$$

$$V_1(\tau, \lambda t) = \sigma x v_1(\kappa\tau, x) \tag{3.3b}$$

for both S and R components, where the variable x is defined by

$$x \equiv \lambda u(T)t/\tilde{g}(\tau) \tag{3.4}$$

and new functions v are defined by

$$v_0(k, x) \equiv \sum_{\zeta=1}^{n} \tilde{g}(k\zeta)x^{\zeta-1} \tag{3.5a}$$

$$v_1(k, x) \equiv \sum_{\zeta=1}^{n} \zeta\tilde{g}(k\zeta)x^{\zeta-1} \tag{3.5b}$$

Similarly, we have

$$W_0(\tau, \lambda t) = \sigma x\, w_0(\kappa\tau, x) \tag{3.6a}$$

$$W_1(\tau, \lambda t) = \sigma x\, w_1(\kappa\tau, x) \tag{3.6b}$$

where

$$w_0(k, x) \equiv \sum_{\zeta=1}^{n} \tilde{g}(k\zeta)\mathscr{L}(k\zeta)x^{\zeta-1} \tag{3.7a}$$

$$w_1(k, x) \equiv \sum_{\zeta=1}^{n} \zeta\tilde{g}(k\zeta)\mathscr{L}(k\zeta)x^{\zeta-1} \tag{3.7b}$$

Now, the equation to determine t takes the form

$$\frac{t}{1-t}\{\sigma_S x_S v_0(\kappa_S\tau, x_S) + \sigma_R x_R v_0(\kappa_R\tau, x_R)\} = 1 \tag{3.8}$$

where

$$x_\alpha \equiv \gamma_\alpha t/\tilde{g}(\tau), \quad \alpha = S, R \tag{3.9}$$

by using the scaled concentration

$$\gamma_\alpha \equiv \lambda_\alpha u_\alpha(T) \equiv k_\alpha(T)c^{(\alpha)} \tag{3.10}$$

The activity is replaced by the concentration, and association constant $k(T) \equiv \lambda u(T)/c$ for each component is used as in paper I.[17] The association constant is proportional to the statistical weight $u_\alpha(T)$ of an adsorbed molecule and is given by $\ln k_\alpha(T) = -\Delta f_\alpha/k_BT$ in terms of the free energy change Δf_α on binding a molecule of the type α. The concentrations of chiral molecules are always accompanied by the adsorption constant and appear as a set of $\gamma = k(T)c$. In what follows we assume that these adsorption constants, and hence ϵ_H and $\Delta\epsilon$, are the same for both components since chiral molecules are chemically the same except for their stereosymmetry.

4. Chirality Order Parameter

In the experiments,[12−16] optical activity (CD intensity and specific rotation) is measured as functions of the temperature and enantiomer concentrations to detect the helical content on a chain. In paper I,[17] we theoretically calculated the *chiral order parameter* ψ defined by the difference

$$\psi \equiv \theta^{(S)} - \theta^{(R)} \tag{4.1}$$

This order parameter is proportional to the rotation angle of an incident polarized light beam, and also to the intensity of CD induced in the UV−visible region. In this study, we attempt to calculate it under tension.

From the equations obtained in the preceding section, we find

$$\psi = \frac{t[\sigma_S x_S v_1(\kappa_S\tau, x_S) - \sigma_R x_R v_1(\kappa_R\tau, x_R)]}{1 + t[\sigma_S x_S v_1(\kappa_S\tau, x_S) + \sigma_R x_R v_1(\kappa_R\tau, x_R)]} \tag{4.2}$$

where parameter t is given by the solution of eq 3.8.

5. Free End-to-End Distance

We first calculate the average square end-to-end distance $\langle R^2\rangle_0$ *in the absence of external force*. To do this, we expand the partition function $\Xi_n(\{\lambda\}, \tau)$ in powers of the dimensionless force τ. Formal expansion gives

$$\Xi_n(\{\lambda\}, \tau)/\Xi_n(\{\lambda\}, 0) = 1 + (\langle R^2\rangle_0/6a^2)\tau^2 + ... \tag{5.1}$$

so that we can find $\langle R^2\rangle_0$ from the expansion

$$t = t_0 + t_1\tau^2 + ... \tag{5.2}$$

of the parameter t, and of relation 2.22, as

$$\langle R^2\rangle_0/na^2 = 1 - 6t_1/t_0 \tag{5.3}$$

Here, t_0 is the solution of eq 3.8 under no force, $\tau = 0$. Explicit calculation of t_1 gives

$$\langle R^2\rangle_0/na^2 = 1 + (\kappa_S^2\bar{\zeta}_{\mathrm{Sw}} - 1)\theta^{(S)}(0) + (\kappa_R^2\bar{\zeta}_{\mathrm{Rw}} - 1)\theta^{(R)}(0) \tag{5.4}$$

where $\theta^{(\alpha)}(0)$ are the helix contents at $\tau = 0$, and

$$\bar{\zeta}_{\mathrm{w}} \equiv V_2(0, \lambda t_0)/V_1(0, \lambda t_0) = v_2(0, \gamma t_0)/v_1(0, \gamma t_0) \tag{5.5}$$

is the weight-average helix length on a free chain for each specified handedness.

In Figure 2a, we show the mean-square end-to-end distance $\langle R^2\rangle_0$ of a free chain (solid curves) normalized by that of Gaussian random coil na^2 in a solution of one type of chiral molecules, together with the helix content (broken lines). The total DP is fixed at $n = 300$ to compare with the experiments. The helix initiation parameter σ is varied from curve to curve. Below the concentration of the coil-to-helix transition near $\gamma = 1.0$, the end-to-end distance takes almost the random-coil value na^2. However, it first shows a small dip around the transition concentration and then sharply increases toward completion of helix formation. With many short helices around the transition point, the chain shrinks because the length of a helix $b\zeta$ is smaller than the end-to-end distance of the corresponding random coil part $a\sqrt{\zeta}$ for small ζ. Once ζ exceeds the critical value $\zeta_c = 1/\kappa^2$, the helical part becomes longer than the end-to-end distance of equivalent random coil part, leading to the increase in the total end-to-end distance. Existence of such a small minimum around the coil-to-helix transition point in helical polypeptides was first theoretically predicted by Nagai[22] and later confirmed by the viscosity measurements.[23]

In Figure 2b, we show the same figure but for a racemic mixture. The horizontal axis shows the total concentration of chiral molecules. If the helix pitch is the same for left- and right-handed helices, they equally contribute to the end-to-end distance. Hence, the chiral order parameter vanishes. (It is identical to the horizontal axis.) When there is a slight difference in the

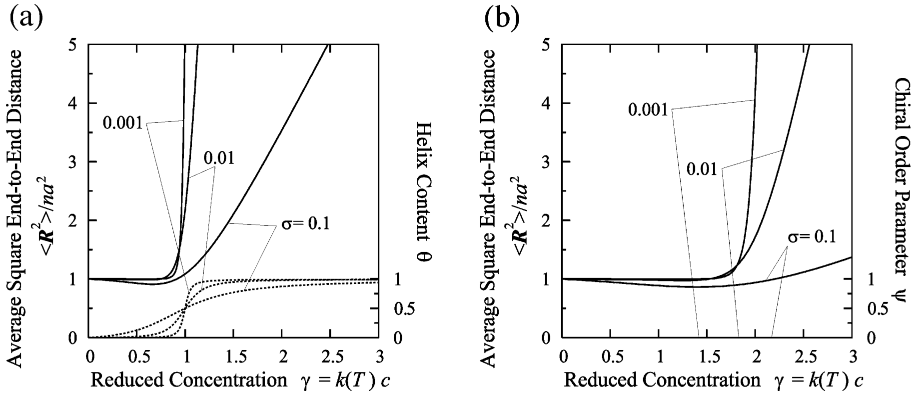

Figure 2. Mean-square end-to-end distance $\langle R^2\rangle_0/na^2$(solid lines) of helix-forming polymers under no external tension in a solution of (a) chiral molecules of one type and (b) racemic mixture of chiral molecules, plotted against the reduced concentration γ (the total molar concentration c of chiral molecules multiplied by the adsorption constant $k(T)$). DP of the polymer chain is fixed at 300. In part a, helical content θ (the number of adsorbed sites relative to the total DP n) is shown. The helix pitch κ is fixed at 0.4, while the helix initiation factor σ is changed from curve to curve. In part b, the optical order parameter $\psi = \theta^{(S)} - \theta^{(R)}$ is shown. The helix pitches are fixed at the values with a slight difference $\kappa_S = 0.401$, $\kappa_R = 0.400$.

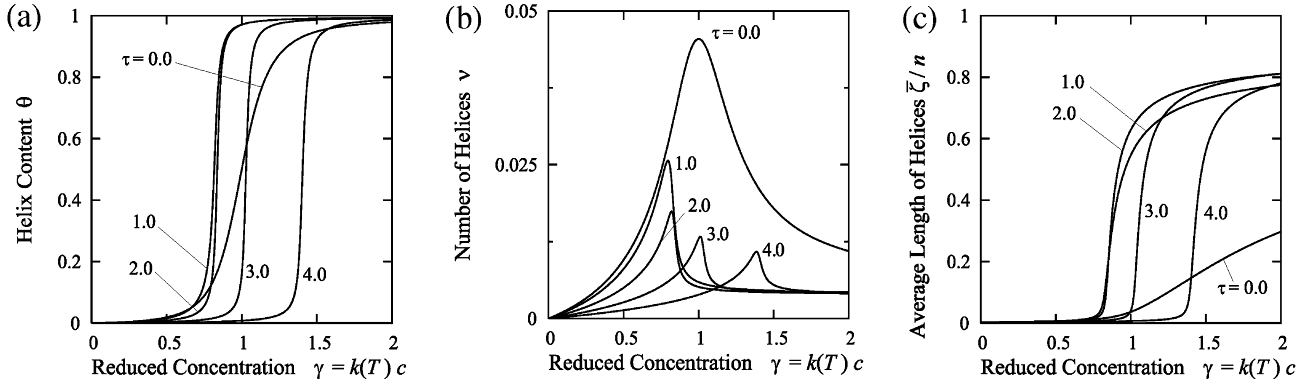

Figure 3. (a) Helix content θ plotted against the reduced concentration $\gamma \equiv k(T)c$ of the chiral molecules. The dimensionless tension $\tau \equiv fa/k_BT$ is varied from curve to curve. The DP of the chain is fixed at $n = 300$, the helix initiation factor at $\sigma = 0.01$, and the helical pitch at $\kappa = 0.4$. (b) Average number ν of helices on a polymer chain plotted against the reduced concentration of chiral molecules. (c) Average helix length $\bar{\zeta}$ in terms of the number of monomeric units plotted against the reduced concentration of chiral molecules.

pitch κ for S and R, the order parameter is canceled as shown in the figure, but as we will see in the following section, the difference in the pitch affects helix induction so strongly when the chain is stretched by tension that the optical order is enhanced enough to be observed.

6. Helix Formation under External Tension

We next study the effect of external force on the helix formation. In this section, we first study the simple case of the solutions in which chiral molecules of only one type S (or R) are dissolved. Let c be the molar concentration of the chiral molecules, and let $\gamma = k(T)c$ be their effective concentration scaled by the association constant. Equation 3.8 then reduces to

$$\frac{t}{1-t}\sigma x v_0(\kappa\tau, x) = 1 \tag{6.1}$$

where all suffices for chirality indication have been eliminated. We solve this equation for t for a given concentration γ and force τ, and substitute the results into the helix content (eq 2.24), the number of helices (eq 2.25), and the end-to-end distance (eq 2.30). Parts a–c of Figure 3 show the helix content θ, the number of helices ν, and the number-average helix length $\bar{\zeta}$ ($\equiv\theta/\nu$) plotted against the reduced concentration of chiral molecules. The dimensionless tension τ is varied from curve to curve. DP of the polymer chain is fixed at $n = 300$ to describe the polyacetylene of frequent use in the experiments.[12] With increase in the strength of tension, the critical concentration at which the helix content sharply rises first shifts to lower values as shown in part a; i.e., helix formation is enhanced. However, above certain critical values of tension, helical growth starts to be suppressed due to strong tension. As a result, the critical concentration shifts to higher values.

Such a nonmonotonic shift of the coil-to-helix transition concentration can be seen more easily from nonmonotonic shift of the peak position in the average number ν of helices as shown in part b. The average helix length $\bar{\zeta}$ also first sharply increases by tension as is seen in part c, but then it decreases with high tension. It reaches 80% of the total chain length as soon as the concentration exceeds the critical value.

Parts a and b of Figure 4 show such a tendency more clearly. In part a, solid lines show the helical content θ plotted against the external force τ. In part b, solid lines show the normalized end-to-end distance, while broken lines show that of the random flight chain, both plotted against the dimensionless external force τ. The concentration of chiral molecules is varied from curve to curve. As is seen in these figures, at a low concentration of $\gamma = 0.6$ for instance, the helical content is so low that the polymer chain is almost a complete random-coil, for which the end-to-end distance linearly increases with

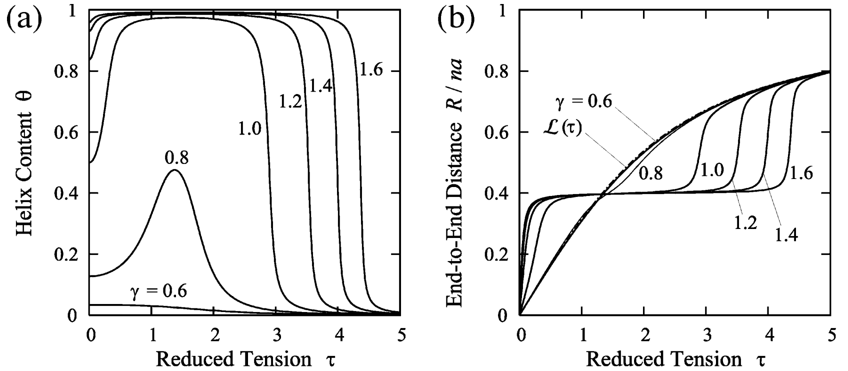

Figure 4. (a) Helical content θ, and (b) the normalized end-to-end distance R/na, plotted against the dimensionless tension $\tau \equiv fa/k_BT$. The DP of the chain is fixed at $n = 300$, the helix initiation factor at $\sigma = 0.01$, and the helical pitch at $\kappa = 0.4$, while the concentration of chiral molecules is varied from curve to curve.

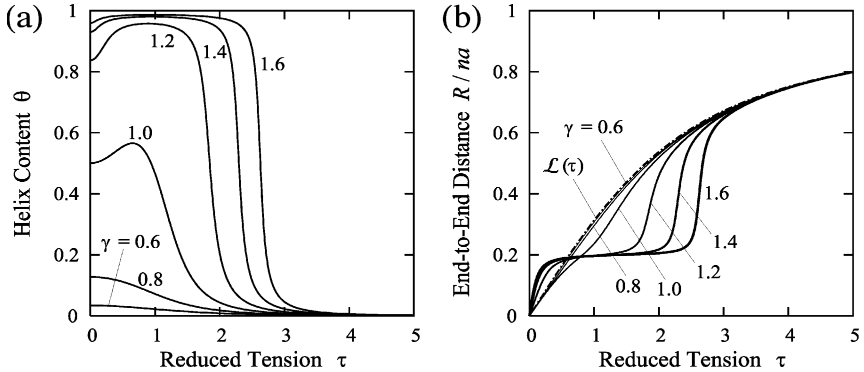

Figure 5. Same as Figure 4, but for $\kappa = 0.2$.

the tension with slope $1/3$, and then obeys the curve given by Langevin's function $\mathscr{L}(\tau)$. (Under small stretch, the random coil obeys Gaussian statistics.) For larger values of the concentration, helices are already partially formed before stretched. The mean end-to-end distance starts from 0 at vanishing tension, increases almost linearly to the critical value 0.4 (identical to helical pitch) with slopes larger than $1/3$, and then a wide flat region continues until the tension reaches certain upper critical values where helices start to be broken back to stretched coil. During the initial rise, the helices grow substantially as seen from the sharp rise in the helical content by small tension. In the plateau region, the polymer behaves almost as a rodlike molecule, lying parallel to the force direction. The tension increases with a fixed R until the helix is eventually destroyed by high tension. In the figure, the curves go back to those of stretched Langevin chains with the effect of strictly finite total length.

Parts a and b of Figure 5 show more or less the same thing, but for a smaller value of $\kappa = 0.2$. The overall behavior is quite similar to Figure 4, but helices are destroyed at smaller values of the tension, so that the plateau region is narrower.

7. Solutions Containing Both Types of Chiral Molecules

Let us now proceed to the more interesting case of enantiomer mixtures. We first introduce the total concentration $c \equiv c^{(S)} + c^{(R)}$ of enantiomers. The enantiomeric excess (referred to as ee), or chiral polarization of the media, is then defined by

$$e \equiv (c^{(S)} - c^{(R)})/(c^{(S)} + c^{(R)}) \qquad (7.1)$$

The renormalized concentration of each species can be written as

$$\gamma_S = (1 + e)\gamma/2 \quad \text{and} \quad \gamma_R = (1 - e)\gamma/2 \qquad (7.2)$$

where

$$\gamma \equiv k(T)c \qquad (7.3)$$

is for the total concentration. The equation to find the probability t now takes the form

$$\frac{\gamma t^2}{2(1-t)\tilde{g}(\tau)}\{\sigma_S(1+e)v_0(\kappa_S\tau, (1+e)\gamma t/2\tilde{g}(\tau)) + \sigma_R(1-e)v_0(\kappa_R\tau, (1-e)\gamma t/2\tilde{g}(\tau))\} = 1 \qquad (7.4)$$

The order parameter can be calculated by eq 4.2 as before.

Parts a−c of Figure 6 show (a) helix content $\theta^{(S)}$ of one component, (b) the total helix content θ, and (c) the number $\nu^{(S)}$ of helices of one component, all plotted against ee in the surrounding solution. The tension is varied from curve to curve. We can see clearly that the total amount of helices is largely amplified for both types by moderate tention $\tau \leq 3.5$.

Parts a−c of Figure 7 show (a) end-to-end distance R/na of the chain, (b) the chiral order parameter ψ, and (c) the normalized order parameter ψ/θ (solid lines) to indicate optical resolution procedure (broken lines), all plotted against ee. The tension is varied from curve to curve. As is evident from Figure 7c, under sufficiently large tension (before the breakage of helices), the order parameter is sharply enhanced as soon as ee is slightly biased (below 0.01). This means that the coverage ratio $\theta^{(S)}/\theta^{(R)}$ is largely different from that of the concentration

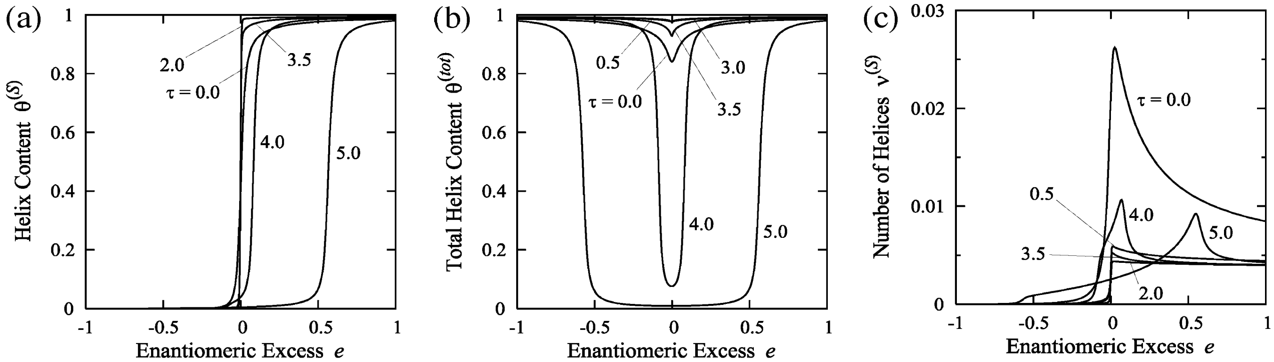

Figure 6. (a) Helix content $\theta^{(S)}$ of one component, (b) the total helix content θ, and (c) the number $\nu^{(S)}$ of helices of one component, all plotted against enantiomer excess (ee). The helical pitch is assumed to be symmetrical and fixed at $\kappa_S = \kappa_R = 0.4$. The DP of the chain is fixed at $n = 300$, the helix initiation parameter at $\sigma = 0.01$, and the total reduced concentration of chiral molecules at $\gamma = 2.6$. The tension is varied from curve to curve. The dominance of the majority component is amplified by tension.

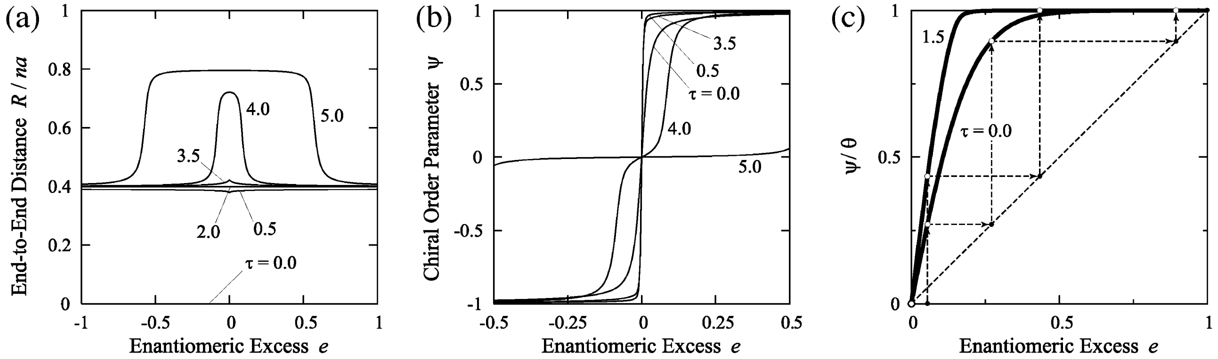

Figure 7. (a) Normalized average end-to-end distance R/na, (b) the optical order parameter ψ, and (c) the normalized order parameter (solid lines) used to indicate optical resolution procedure (broken lines), all plotted against ee. The helical pitch is symmetrically fixed at $\kappa_S = \kappa_R = 0.400$. The tension is varied from curve to curve. The DP of the chain is fixed at $n = 300$, the helix initiation factor at $\sigma = 0.01$, and the total reduced concentration of chiral molecules at $\gamma = 2.6$ in parts a and b and $\gamma = 1.4$ in part c. Finite order parameter appears as soon as ee deviates from 0, so that chiral molecules are separated by stretching the polymer chain in the presence of the concentration fluctuation.

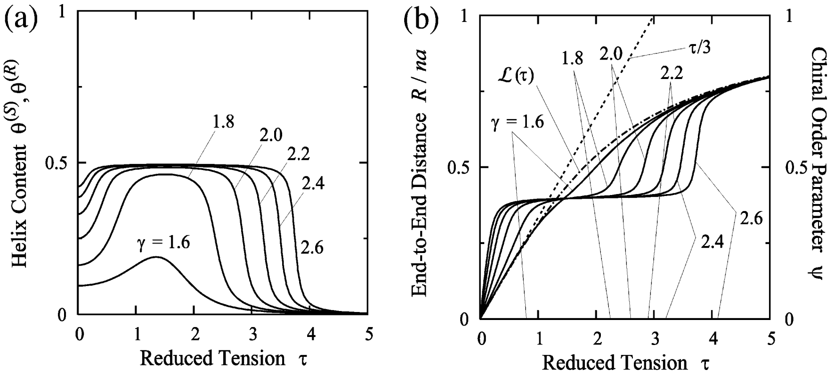

Figure 8. (a) Helix content $\theta^{(S)}$ of one component ($=\theta^{(R)}$) and (b) normalized average end-to-end distance R/na (solid lines) and optical order parameter ψ (all identical to the horizontal line) plotted against tension τ for $e = 0$. The total concentration is varied from curve to curve. The helical pitch is symmetrically fixed at $\kappa_S = \kappa_R = 0.400$. The DP of the chain is fixed at $n = 300$ and the helix initiation factor at $\sigma = 0.01$.

$c^{(S)}/c^{(R)}$ in the bulk. This indicates that chiral molecules can be separated into optically pure groups by repeating the process of adsorption of chiral molecules under tension and washing away the hydrogen-bonded molecules. The result of such repeated operation is indicated by the broken lines. If there are small concentration fluctuations (on the order of 0.01), even a racemic mixture can be separated.

Parts a and b of Figure 8 show (a) the helix content $\theta^{(S)}$ ($=\theta^{(R)}$) and (b) the end-to-end distance R/na and the chiral order parameter ψ, both plotted against the reduced tension in the case of symmetric helical pitch $\kappa_S = \kappa_R = 0.400$ for $e = 0$. The total concentration is varied from curve to curve. In Figure 8b, the optical order parameter is identical to zero by symmetry, so that optical resolution is impossible if there is no concentration fluctuation. The stress–elongation curve of Gaussian chain (broken line) and Langevin chain (broken and dot line) are drawn as reference curves.

8. Asymmetry in Helical Pitch Leading to Optical Resolution

We next examine the possibility of separating exactly racemic mixtures by stretching helical chains.

Parts a–c of Figure 9 show (a) the end-to-end distance R/na of the chain, (b) the chiral order parameter ψ, and

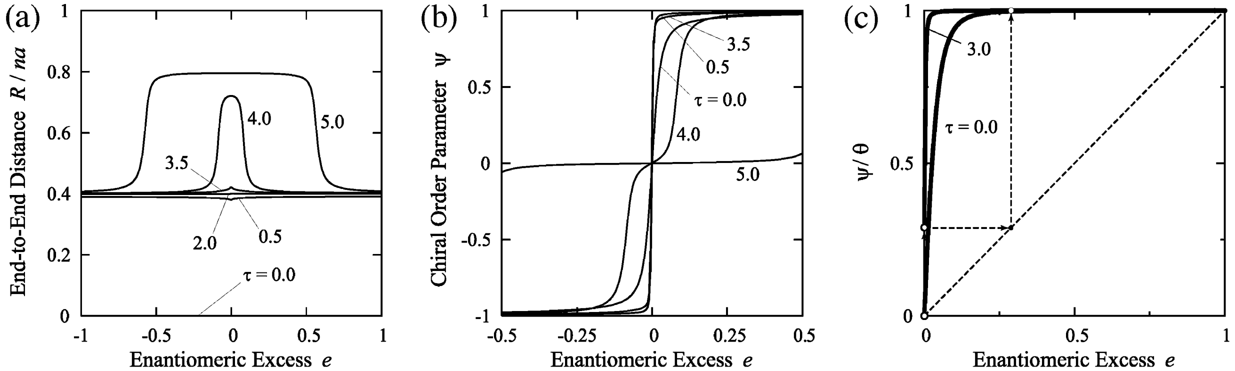

Figure 9. (a) Normalized end-to-end distance R/na, (b) the optical order parameter ψ, and (c) the normalized order parameter ψ/θ (solid lines) used to indicate optical resolution procedure (broken lines), all plotted against ee. The tension is varied from curve to curve. The helical pitch is assumed to be slightly different as $\kappa_S = 0.401$, $\kappa_R = 0.400$. The DP of the chain is fixed at $n = 300$, the helix initiation factor at $\sigma = 0.01$, and the total reduced concentration of chiral molecules at $\gamma = 2.6$ in (a),(b) and $\gamma = 2.2$ in (c). The majority rule is largely enhanced by tension. Even for exactly racemic mixture ($e = 0$), finite order parameter appears.

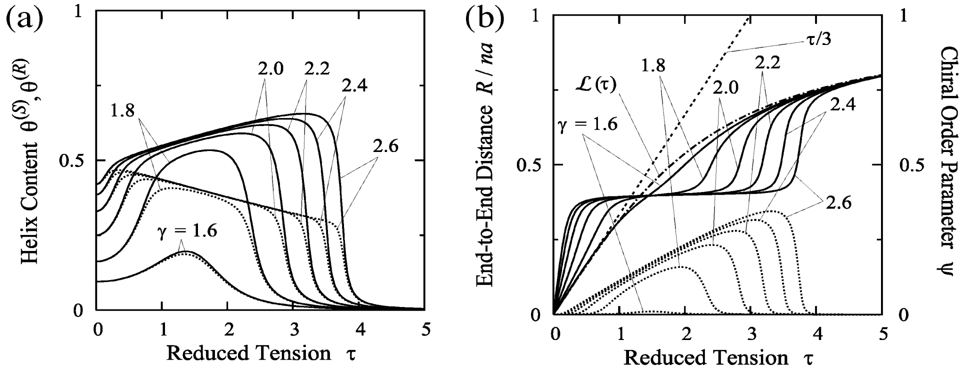

Figure 10. (a) Helical content of (S)-form (solid lines) and (R)-form (dotted lines), and (b) the normalized end-to-end distance R/na (solid lines) and the optical order parameter ψ (dotted lines) plotted against dimensionless tension. The concentration is varied from curve to curve. The DP of the chain is fixed at $n = 300$ and the helix initiation factor at $\sigma = 0.01$. The helical pitch is fixed slightly asymmetrically at $\kappa_S = 0.401$, $\kappa_R = 0.400$. It is clearly seen that about 40% of chiral molecules in the racemic mixture are separated on the polymer chain with such a small difference in the helical pitch when large tension ($\tau = 3.5$) is given to the chain.

(c) the normalized order parameter ψ/θ (solid lines) to indicate optical resolution procedure (broken lines), all plotted against ee for asymmetric helical pitch; i.e., the pitch of helices formed by (S)-form chiral molecules is slightly ($1/400 = 2.5 \times 10^{-3}$) larger than that of helices formed by (R)-form. The tension is varied from curve to curve. As is evident from Figure 9c, under sufficiently large tension (before the breakage of helices), the order parameter is sharply enhanced as soon as ee is slightly biased (below 0.01). This means that the coverage ratio $\theta^{(S)}/\theta^{(R)}$ is largely different from that of the environmental concentration $c^{(S)}/c^{(R)}$ in the bulk. In particular, the order parameter takes a finite value even for $e = 0$ if helical pitch has a slightest difference. Therefore, if there is a small difference between the pitch of right- and left-handed helices, even racemic mixtures can be separated into optically pure groups. In this calculation, for instance, the order parameter ψ reaches about 40% under $\tau = 3.5$.

Parts a and b of Figure 10 demonstrate how the order parameter emerges by tension for $e = 0$. Without tension, the coverages are equal to each other, $\theta^{(S)} = \theta^{(R)}$. When tension is given, helices with larger pitch are predominantly induced. When the total concentration is $\gamma = 2.6$, for instance, the order parameter reaches a maximum value of about 40% just before the helices are broken by strong force. One of the simplest practical methods as application of this principle is to make gels with such hydrogen-bonding polymers and uniaxially elongate them in the solutions. Gels are swollen and stretched. As a result, molecules with one type of chirality are preferentially adsorbed onto the network chains, leading to the formation of helices with predominantly one type of handedness in the gel.

9. Conclusions and Discussion

We have theoretically demonstrated that helices induced on a polymer chain by hydrogen bonds with chiral molecules are drastically enhanced by the external tension before they are broken in the limit of high tension. Thus, the slightest difference either in the concentration of the hydrogen-bonding chiral molecules or in the helical pitch between left- and right-handed helix, can lead to a largely different population ratio between the chiral molecules attached on the polymer chain. Small fluctuations in the local concentration, or in the pitch length of helices, are sufficient to produce finite optical order parameter. Hence, polymeric gels made by cross-linking such hydrogen-bonding polymers should preferentially adsorb one type of chiral molecules from racemic mixtures when they are uniaxially stretched.

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