

Using Mesoscopic Models to Design Strong and Tough Biomimetic Polymer Networks

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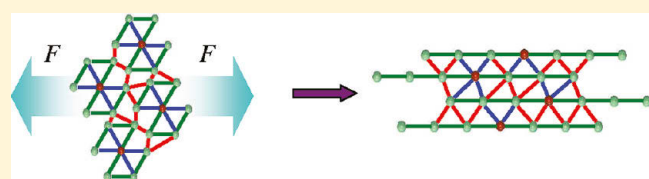
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ABSTRACT: Using computational modeling, we investigate the mechanical properties of polymeric materials composed of coiled chains, or “globules”, which encompass a folded secondary structure and are cross-linked by labile bonds to form a macroscopic network. In the presence of an applied force, the globules can unfold into linear chains and thereby dissipate energy as the network is deformed; the latter attribute can contribute to the toughness of the material. Our goal is to determine how to tailor the labile intra- and intermolecular bonds within the network to produce material exhibiting both toughness and strength. Herein, we use the lattice spring model (LSM) to simulate the globules and the cross-linked network. We also utilize our modified Hierarchical Bell model (MHBM) to simulate the rupture and reforming of N parallel bonds. By applying a tensile deformation, we demonstrate that the mechanical properties of the system are sensitive to the values of N_{in} and N_{out} , the respective values of N for the intra- and intermolecular bonds. We find that the strength of the material is mainly controlled by the value of N_{out} with the higher value of N_{out} providing a stronger material. We also find that, if N_{in} is smaller than N_{out} , the globules can unfold under the tensile load before the sample fractures and, in this manner, can increase the ductility of the sample. Our results provide effective strategies for exploiting relatively weak, labile interactions (e.g., hydrogen bonding or the thiol/disulfide exchange reaction) in both the intra- and intermolecular bonds to tailor the macroscopic performance of the materials.



INTRODUCTION

The ideal polymeric material that could satisfy the demands of a range of technological applications would be both strong and tough.^{1–3} Creating materials that integrate both these desirable mechanical properties remains a significant challenge. Polymers with a high strength or high modulus are usually stiff and, thus, lack the ductility that would contribute to the toughness of the material. On the other hand, tough materials commonly have low moduli. A strategy that might be useful in addressing this challenge is to take components that individually exhibit one of the desirable attributes and integrate these components in a manner that produces the desired collective properties. An ideal structural unit that would contribute toughness is a material that possesses a folded secondary structure, such as that found in various proteins (e.g., titin^{4,5} or fibronectin^{6,7}) or synthetic foldamers.⁸ As the coiled chains or globules were stretched, they would unfold and this unfolding would dissipate energy, which in turn would contribute to toughness. A facile unfolding, however, could diminish the strength of the material. A component that contributes to high strength is strong bonds, but the introduction of strong bonds between the sheets of the folded chain would inhibit the unfolding and thus be detrimental. If, however, one were to cross-link the globules into an extended network and

harness stronger bonds as the intermolecular or interglobular linkages, one might create a material that yields the optimal traits.

Using computational modeling, we implement the above design strategy; namely, we create a material that is composed of coiled chains that are cross-linked into an extended network. (The specific nature of the cross-links is detailed in the Methodology.) Notably, a number of experimental studies have focused on similar attempts.⁹ For example, Guan et al.^{10,11} introduced reversibly unfolding cross-linkers between polymer chains to enhance the properties of the networks. Additionally, Guan et al.^{12,13} synthesized a linear polymer that encompassed an array of globular units, which mimicked the architecture of titin. In these various systems, the intramolecular bonds (i.e., those within the folded structures) were weak, labile bonds. The intermolecular bonds, on the other hand, were taken to be covalent bonds.

An advantage of utilizing computational modeling in determining effective bonding strategies for creating these cross-linked materials is that we can readily tailor both the inter- and intramolecular interactions. Furthermore, we can determine how

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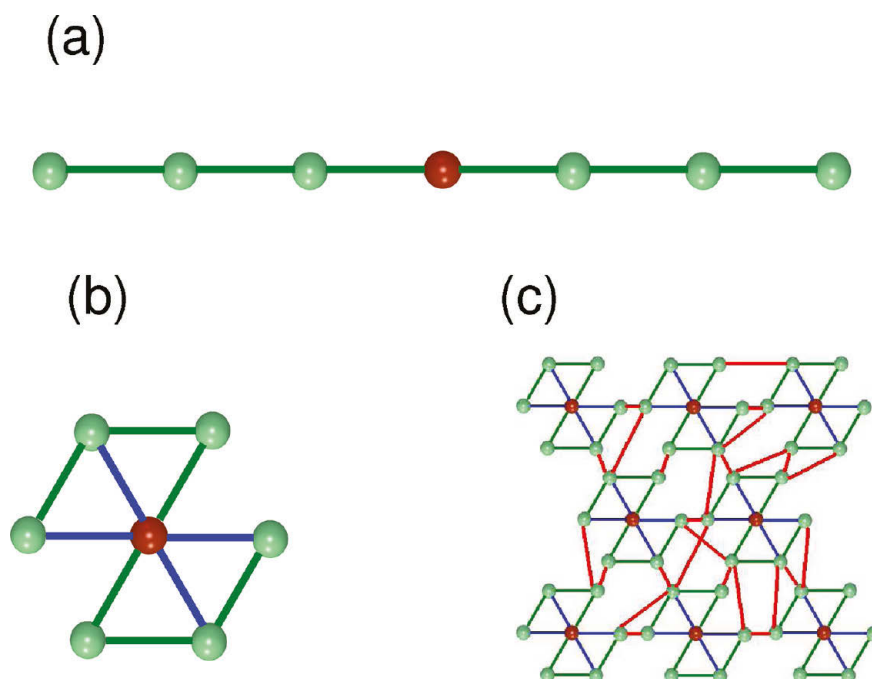


Figure 1. (a) Schematic of an elementary globular unit in the unfolded state. (b) The same globular unit in a folded conformation. The chain consists of seven nodes shown as beads and of permanent bonds shown as green lines. (c) Illustration of a cross-linked globule network. The chains are cross-linked with the inner linkages (blue lines) and the outer linkages (red lines). Each linkage can consist of a number of parallel bonds.

each of these interactions contributes to the mechanical properties and, thus, establish useful predictions concerning optimal features of the bonding interactions in the system. It is noteworthy that molecular dynamics^{14,15} and cross-linked network models¹⁶ have been used to investigate the network's mechanical behavior, as well as gelation and phase separation processes.^{17–19}

In previous computational studies of cross-linked nanogels,^{20,21} we found that labile intermolecular bonds allowed the system to undergo a reshuffling in response to mechanical deformation and thereby prevented catastrophic failure. These studies revealed the utility of harnessing weak interactions (e.g., hydrogen bonding or the thiol/disulfide exchange reaction) to cross-link the elemental units into an extended network. Thus, in these studies, we introduce weak or labile bonds between both the intra- and intermolecular associations. Mindful, however, of the hypothesis articulated in the first paragraph, we tailor the strength of these labile bonds and investigate the relative benefits of harnessing the relatively weaker or stronger bonds as the intra- or intermolecular linkages.

We take as our basic structural unit a folded chain that includes two hairpin turn and thus encompasses the simplest β sheet motif (see Figure 1). Conceptually, this simple folded structure mimics a globular protein or a single-strand foldamer ribbon,⁸ where hydrogen bonds form the intramolecular junctions between the sheets. The surface of our globular chain is decorated with ligands, which subtend reactive groups that are responsible for the formation of inter- and intramolecular linkages. As we discuss in the Methodology section, we implement our modified Hierarchical Bell model (MHBM)²¹ to model the breaking and remaking of these cross-links. In our MHBM, a cross-link can represent N parallel, reformable bonds; in this way, we model a ligand on our globules encompassing N reactive sites, and thus, the interaction between two ligands can lead to N parallel bonds. By varying N , we can alter the effective strength of the linkage; for

example, by changing $N = 1$ to $N = q$, we change the linkage from a single hydrogen bond to a cluster of q parallel hydrogen bonds. It is worth emphasizing that the bonds in our model are reformable: if a bond is broken in particular time step, it can reform at a later time. The remaking of broken bonds can readily occur with reactive functional groups and particularly if the time scale for the deformation is slower than the rate of bond formation, which is the limit we consider here.

As we show below, the performance of our cross-linked material is strongly dependent on the location of the relatively weak and strong bonds. Furthermore, we isolate a parameter range that yields a material that displays both high strength and toughness. It is important to note that our globules are all oriented in the same direction and, in particular, are oriented along the direction of the applied force. This represents an idealized scenario, but nonetheless is especially instructive since it reveals the optimal behavior that can be achieved by exploiting the unfolding of the coiled chains in response to mechanical deformation and, hence, the effective improvement of the mechanical properties of the material.

METHODOLOGY

As noted in the Introduction, we focus on the structural rearrangements within materials formed from cross-linked “globules” as the sample is subjected to mechanical deformation. The deformation can lead to the rupture and reforming of bonds both within a globule and between different globules. To capture the dynamic behavior of this system, we must adopt a sufficiently coarse-grained approach that we can model not only the individual coiled chains, but also the extensive, dynamically evolving network formed by these interacting macromolecules. To this end, we use the lattice spring model (LSM)^{20–24} to construct our network and

simulate the micromechanical behavior of the sample, as we discuss below.

In the LSM, point-like masses (nodes) are interconnected by Hookean springs, which represent bonds. Within our system, there are three types of bonds. The permanent bonds along the backbone of a macromolecule (drawn in green in Figure 1) do not break. On the other hand, both the intramolecular and intermolecular bonds are labile and, hence, can break and readily reform.

Figure 1a,b show the seven node model that represents an individual macromolecule. (All these green nodes are assumed to be chemically identical.) Within this macromolecule, the nodes interact through the potential $U(r)$, which involves both an attractive Hookean spring term and a repulsion term that mimics the excluded volume around each node

$$U(r) = \begin{cases} \frac{\kappa}{2} \left(r^2 + \frac{a}{r} \right) & r \leq r_c \\ \text{const} & r > r_c \end{cases} \quad (1)$$

Here, κ is the spring stiffness constant, r is the distance between the nodes, and a is the repulsion parameter.^{20,21} The equilibrium length of a single bond is equal to $d = (a/2)^{1/3}$, which corresponds to the minimum of $U(r)$ in eq 1. For the intramolecular links that can break and reform (blue lines in Figure 1b), the potential $U(r)$ is taken to be as a constant at $r > r_c$, so that the bonding interaction is cut off at r_c . The cutoff distance is set to $r_c = 2d \equiv (4a)^{1/3}$.

The same interaction potential is used in the case of the reversible intermolecular bonds. If a reversible bond (intra- or intermolecular) is broken, then the interaction potential between the two interacting nodes is given solely by $U(r)$ at $r < d$. For all the reversible bonds, the spring constant κ is taken to be six times weaker than that for the permanent (green) bonds. (While different values for the latter spring constants could be chosen, we note that for the large number of nodes considered here (in excess of 1000 for large samples), significant difference between the breakable and permanent spring constants can give rise to numerical instabilities.) We neglect thermal fluctuations in the nodal positions; the effect of temperature is, however, taken into account in the probabilities for the bonds to rupture and reform, as given by eqs 2 and 3 below.

We focus on the overall mechanical stability of the material and do not probe the details of the (fast) fracture process that occurs at high stresses. In particular, we take the dynamic behavior of our system to be in the overdamped limit, where we neglect the inertial terms in our equations of motion for the nodes. Thus, the velocity of a node is taken to be proportional to the net force acting on the node (where the net force is the sum of forces from neighboring nodes and from an external tensile force). The latter assumption is commonly made in studies of gel dynamics.^{25,26} Specifically, each gel node obeys the following dynamical equation: $d\mathbf{r}_i/dt = \mu \mathbf{F}_i$, where μ is the mobility and $\mathbf{F}_i$ is the force acting on node i . Here, we take μ to be a constant and, thus, neglect the dependence of the mobility on the polymer density. The force acting on the node i is defined as follows: $\mathbf{F}_i = -\partial U_{\text{tot}}/\partial \mathbf{r}_i + \mathbf{F}_i^{\text{ext}}$, where the elastic energy U_{tot} is equal to $U_{\text{tot}} = (1/2) \sum_{m,n} U(|\mathbf{r}_m - \mathbf{r}_n|)$, where the summation is made at a given bond configuration at a particular moment of time, and $m \neq n$. The force $\mathbf{F}_i^{\text{ext}}$ is the external force that is permanently applied to the nodes initially residing at the vertical edges of a rectangular

sample. We numerically integrate the equations of motion using the fourth-order Runge–Kutta algorithm.

The applied force can drive the labile bonds to rupture and reconnect. We adopt a variation of the Bell model²⁷ to describe the dynamics of this bond breaking and remaking. The Bell model serves as a useful framework for describing the relationship between bond dissociation and stress²⁷ and has been widely used to describe the reversible bonds formed in proteins,²⁸ and between biological cells and surfaces.^{29–31} In the Bell model, the rupture rate, k_r , is an exponential function of the force applied to the bond

$$k_r = k_{0r} \exp \left[\frac{r_0 F}{k_B T} \right] \quad (2)$$

The term $k_{0r} = \nu \exp[-U_0/(k_B T)]$ is the reactivity of an unstressed bond and F is the absolute value (i.e., the norm) of the force due to a bond between two nodes, which is obtained by differentiating the potential in eq 1. In the latter equation for k_{0r} , U_0 is the potential well depth at zero mechanical stress, and ν is an intrinsic frequency of an unstressed bond. In eq 2, the parameter r_0 characterizes the change in the reactivity of the bond under stress, k_B is the Boltzmann constant, and T is the temperature.

The reforming rate, k_f , for a single broken bond is calculated directly from the detailed balance principle,^{29,31} and is given by

$$\frac{k_f}{k_r} = \frac{k_{0f}}{k_{0r}} \exp \left(\frac{\Delta U(r)}{k_B T} \right) \quad (3)$$

where ΔU is the difference in the potential energies of a connected and broken bond. At small distances, $r \leq d$, the energy difference is $\Delta U(r) = 0$, whereas at $d \leq r \leq r_c$, $\Delta U(r) = U(r)$. At distances larger than r_c , the bonds are ruptured. By combining eqs 2 and 3, we obtain for $d \leq r \leq r_c$

$$k_f = k_{0f} \exp \left(\frac{r_0 F - \Delta U(r)}{k_B T} \right) \approx k_{0f} \exp \left(\frac{r_0 F - \kappa_1 (r - d)^2/2}{k_B T} \right) \quad (4)$$

where the bond potential, eq 1, is approximated by the quadratic function in the vicinity of the equilibrium bond length d and $\kappa_1 = d^2 U(r)/dr^2|_{r=d} = 3\kappa$. We use this approximated value of k_f in eq 5 below to update the state of the bonds at every time step. In particular, the probability for a connected bond to break and the probability for a broken bond to reform within a simulation time step Δt were taken to be of the following form

$$\begin{aligned} w_r &= 1 - \exp[-k_r \Delta t] \\ w_f &= 1 - \exp[-k_f \Delta t] \end{aligned} \quad (5)$$

In the Hierarchical Bell model (HBM),^{32–35} two interacting sites on a chain can be interconnected by n parallel bonds. Through the use of the HBM, we can capture the fact that a single node in our coarse-grained model can encompass $n > 1$ reactive sites and can thus contribute multiple binding interactions. Thus, the internode springs now represent bonds that lie in parallel. In this case, the total force applied to a single bond is equal to $F = F_{\text{tot}}/n$.

Although the HBM is useful for modeling such multiply interconnected segments, the previous formalism^{32–35} did not include the possibility of bond reformation. Once a bond was broken, it could not be reconnected. Though this approximation

is appropriate in situations where the material experiences very rapid deformations, it might not be valid in cases where the sample is undergoing a slower stretching or pulling. Furthermore, for chains that are decorated with labile bonds (involving, for example, hydrogen, thiol, or disulfide groups), the reformation of broken bonds can readily occur.

We recently modified the HBM²¹ to take into account the reformation of bonds that lie in parallel. We note that researchers have developed models that take into account the reformation of a single Bell bond;^{31,36–39} in our model, that would correspond to the $N = 1$ limit. What is distinctive about our modified HBM (MHBM) is that we consider reformable linkages that encompass N parallel bonds. As noted in the Introduction, through this model, we can capture the fact that the ligands on the globules can subtend multiple reactive groups, and thus, each ligand–ligand interaction can lead to multiple parallel bonds. Specifically, in our model, the state of each breakable interconnection between two nodes at a given time is characterized by the number of connected reactive bonds, n , with the maximum number being equal to N .

In our MHBM approach,²¹ the probability for a single stressed bond to break and reform is described by eqs 2–5. Given that n bonds are initially connected, the probability of rupturing m bonds within a time step Δt is equal to

$$p_r(m, n) = C_m^n w_r^m (1 - w_r)^{n-m} \quad (6)$$

where C_m^n is the binomial coefficient that accounts for the number of ways that m bonds that break can be chosen from a set of n initially connected bonds, and w_r is defined by eq 5 at an applied force equal to F . Similarly, the probability of m' bonds forming (if $n' = N - n$ bonds are initially ruptured) is equal to

$$p_f(m', n') = C_{m'}^{n'} w_f^{m'} (1 - w_f)^{n'-m'} \quad (7)$$

The rupture and formation of bonds in a given time step are considered statistically independent processes. Consequently, the total probability $W(n_1, n)$ for a link to have n_1 connected bonds at the subsequent time step is computed as a sum over all possibilities of the rupture and formation processes

$$W(n_1, n) = \sum_m p_r(n - n_1 + m, n) p_f(m, N - n) \quad (8)$$

The probabilities p_r and p_f in eq 8 are set equal to zero if the first argument is negative or is greater than the second argument; in other words, both the probability to break more bonds than were initially connected and the probability to connect more bonds than were initially ruptured are strictly equal to zero. In the simulations, we use eqs 2–8 to update the system of bonds at each time step Δt .

At the onset of the simulations, the macromolecules are folded in the manner shown in Figure 1b; these globules represent the elementary units in our model. To reiterate, an intramolecular link is formed solely between the red node and a green node of the same molecule (see Figure 1a and b). Such links are shown as blue lines in Figure 1b, where each link (blue line) can encompass multiple parallel labile bonds. The maximum number of bonds allowed in such a link is given by $N = N_{in}$. An intermolecular link can be formed between a pair of green nodes on different units (globules) and can encompass up to $N = N_{out}$ parallel labile bonds, or between a red node and a green node on different units and can then encompass up to $N = N_{in}$ parallel labile bonds. In the simulations, we vary the values of the maximum number of parallel bonds of both types in the range $1 \leq N \leq 2$.

The elementary units (globules) in a nondeformed sample were arranged in the following manner: 5 rows, with 10 units in each row, 8 rows with 12 units in each row, and 12 rows with 15 units in each row. For each of these configurations, we examined 8 independent samples. The layers were constructed with a lattice spacing of $3d$ between the centers of the units, where d is the equilibrium distance between the nodes. (The initial horizontal size of the unit is $2d$.) The vertical spacing between the layers was set equal to $1.3d$. At this step, all possible bonds within the cutoff radius were established and marked as breakable bonds with $N_{in} = N_{out} = 1$. The sample was then equilibrated for 400 units of time (at this stage, we do not allow the nodes to move). During the equilibration, the most stressed bonds were ruptured in accordance with the probability in eq 2. In the second step, we allow the nodes to move, specify the values of N_{in} and N_{out} , and equilibrate the sample for an additional 400 units of time. We then apply a tensile stress to the material.

We set the potential well depth equal to $U_0 = 20k_B T$ for breakable bonds.^{28,31} We also assign the equilibrium distance d equal to 20 nm, so that the total length of the unfolded molecule is equal to 120 nm. We set our unit of time T_0 equal to the relaxation time in a sparsely cross-linked PDMS^{40,41} (of molecular weight $\sim 5 \times 10^4$ g/mol) gel, giving a value of $T_0 \approx 10^{-5}$ s. The spring constant of a permanent bond is taken to be equal 4×10^{-4} N/m, which corresponds to a sparsely cross-linked PDMS gel^{40,41} with a shear modulus of 2.5 kPa at room temperature. The mobility of the nodes in the equation of motion was approximated as $\mu = 1/(T_0 \kappa)$. The parameter r_0 , which describes the change in the reactivity of a stressed bond, was chosen so that the maximum decrease in the energy barrier (the exponent in eq 2) as a result of the tensile load equals $2k_B T$.²⁸ The time step in the integration was chosen to be $\Delta t = 2 \times 10^{-2} T_0$.

RESULTS AND DISCUSSION

Each globule in the network acts as a unit of stored length; once a tensile load is applied, the globules unfold into linear chains. This responsive behavior provides the material with enhanced ductility and, as we show below, a distinctive mechanism for delaying the catastrophic failure of the sample. Thus, the proposed design rules could facilitate the synthesis of novel adaptive and sustainable materials. The range of parameters that can be modified to optimize the properties of such materials is relatively large. Herein, we focus on investigating the role of reformable, parallel bonds on the mechanical properties (strength and toughness) of these networks. In particular, we examine how differences in the maximum number of parallel bonds N for the intramolecular (N_{in}) and the intermolecular (N_{out}) linkages affects the response of the samples to mechanical deformation. To this end, we examine the material's behavior under a tensile deformation that is applied at a constant strain rate or at a constant stress. In both cases, we vary the values of N_{in} and N_{out} in the range $1 \leq N \leq 2$. These examples serve to illustrate the differences in the performance of the material that can be achieved by tailoring the cross-links within the system and, more specifically, controlling the location of the relatively weak ($N = 1$) and strong ($N = 2$) bonding interactions.

A. Constant Strain Rate Test on a Small Sample. We utilized the constant strain rate test to quantify the total strain in a sample until it fractures into two pieces. We initially considered small samples composed of 5 rows of units with 10 units in each row, as

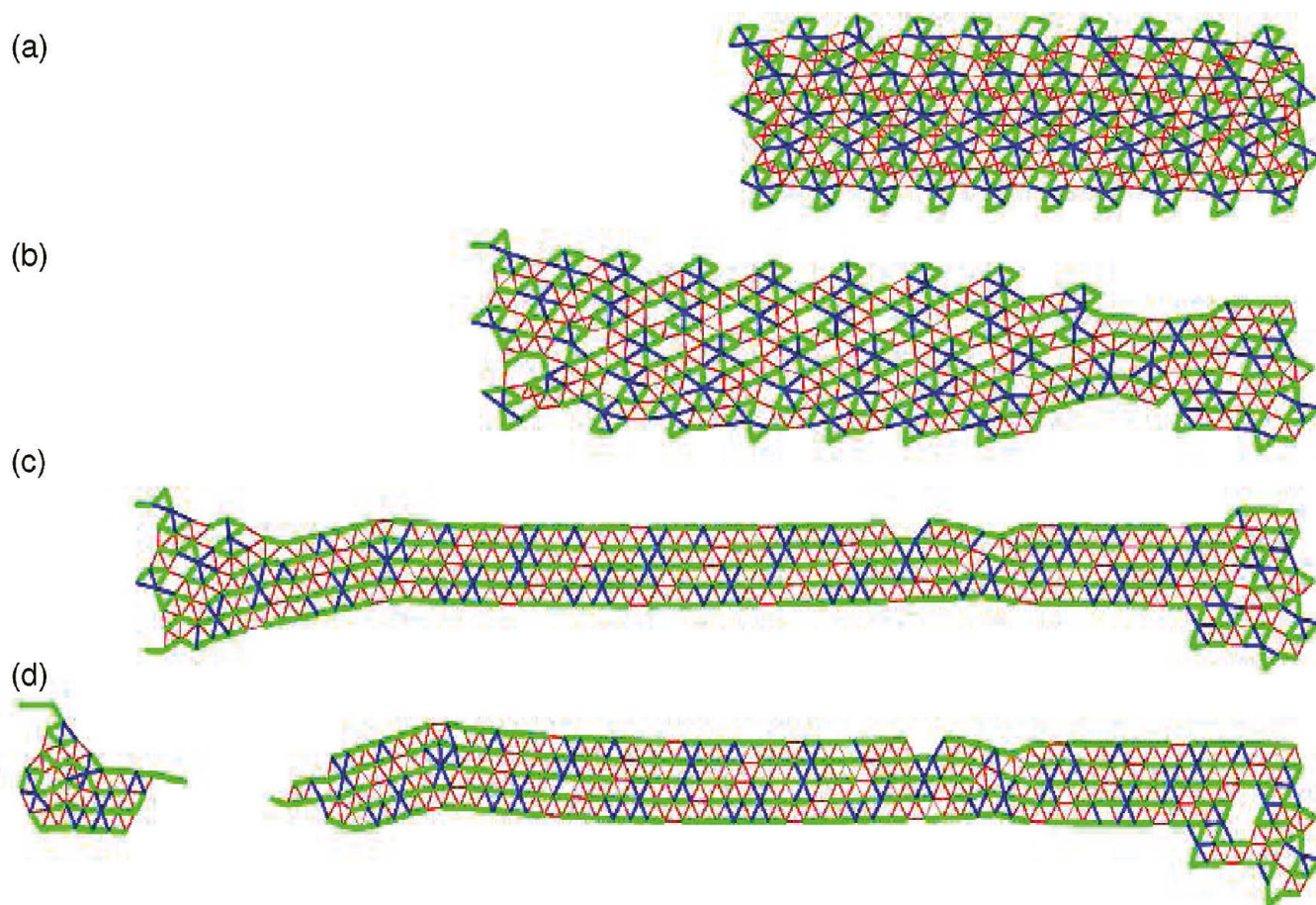


Figure 2. Snapshots of a small sample for $N_{\text{in}} = 1$ and $N_{\text{out}} = 2$ at different moments of time: (a) $t/T_0 = 4.00 \times 10^2$; (b) $t/T_0 = 2.74 \times 10^4$; (c) $t/T_0 = 8.98 \times 10^4$; (d) $t/T_0 = 1.11 \times 10^5$.

shown in Figure 2. The sample was stretched at a constant velocity and the tensile stress was computed as a function of the strain $\varepsilon = (L - L_0)/L_0$. Specifically, the rightmost nodes of the sample were held fixed in the direction of applied load, while the leftmost edges were displaced along the horizontal axis with a speed V ; the nodes are allowed to move freely in the vertical direction. The specific pulling velocity was chosen equal to $V = 1.64 \times 10^{-3} d/T_0$, which is equivalent to $V = 3.3 \times 10^{-4}$ cm/s for representative experimental parameters (see the Methodology section). We note that such constant strain rate measurements are widely used in the characterization of cross-linked polymers.^{41,42}

At the regions of high strain, where plastic deformation takes place, the true stress is higher than the calculated engineering stress due to the decrease of the sample's cross section in the course of deformation. Thus, these calculations give an estimate from below for the stability region of the material.

Figure 2 shows snapshots at various times for samples at $N_{\text{in}} = 1$ and $N_{\text{out}} = 2$. Here, a green line designates a permanent bond. A red line marks a link between two green nodes (see Figure 1) with a maximum of $N_{\text{out}} = 2$ bonds, and a blue line indicates a link between either a red node and another node (green or red) with a maximum of $N_{\text{in}} = 1$ bonds. As can be seen, the macromolecules unfold in the course of the deformation (Figure 2b). Before the sample fractures into two, the backbones of the macromolecules are essentially aligned parallel to the applied deformation (Figure 2c and d).

To characterize the unfolding process, we calculate the instantaneous radius of gyration of the globular units in the sample

$$R_g^2 = \frac{1}{N_{\text{node}}} \sum_{i=1}^{N_{\text{node}}} (|\mathbf{r}_i^m - \mathbf{r}_c^m|)^2 \quad (9)$$

Here, $N_{\text{node}} = 7$ is the number of nodes in a macromolecule, $\mathbf{r}_i$ is the radius vector of the node i , and $\mathbf{r}_c^m = (1/N_{\text{node}}) \sum_{i=1}^{N_{\text{node}}} \mathbf{r}_i^m$ is the radius vector of the geometrical center of m th unit. Note that unstressed, folded units (Figure 1b) have a radius of gyration equal to $R_g = (6/7)^{1/2} d$, while unstressed, completely unfolded (linear) macromolecules have a radius of gyration $R_g = 2d$. Figure 3 shows the evolution of the distribution of R_g in the small samples in the course of deformation. The plots in Figure 3a–d are computed for the respective samples in Figure 2a–d. Figure 3a indicates the distribution for an initial sample (Figure 2a), where all the units have a radius of gyration close to the unperturbed value of $(6/7)^{1/2} d$. As the units unfold in the course of deformation, the characteristic R_g increases (Figure 3b,c). At the moment of time when the sample breaks, most of the units have unfolded; the respective R_g values are close to the maximum value of $2d$ (Figure 3d).

Figure 4 reveals the time evolution of the mean radius of gyration; due to the unfolding of the units, $\langle R_g \rangle$ increases monotonically up to $t \approx 8 \times 10^4 T_0$, which corresponds to the

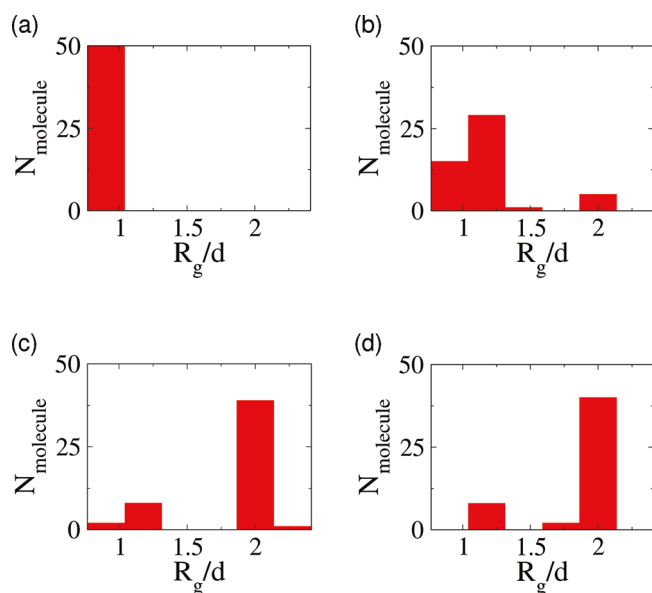


Figure 3. Distributions of the radii of gyration for globules in a small sample for $N_{in} = 1$ and $N_{out} = 2$ under constant tensile strain rate at different moments of time. The histograms (a–d) correspond to the respective frames (a–d) in Figure 2.

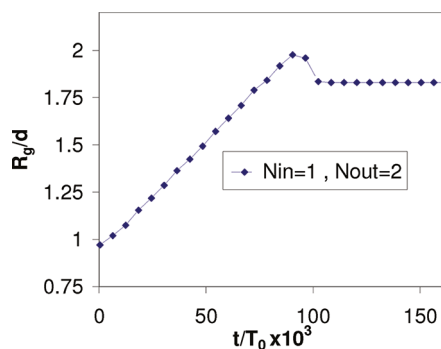


Figure 4. Time evolution of the mean radius of gyration of a small sample at $N_{in} = 1$ and $N_{out} = 2$ computed for the simulations shown in Figure 2.

initiation of the fracture process. After the sample has broken into two, the stretched macromolecules relax and the $\langle R_g \rangle$ reaches an equilibrated, constant value. (It is worth noting that the data in Figure 4 is sampled every $6000T_0$, which is longer than the relaxation time; thus, we do not resolve the fast relaxation of the sample after it breaks.)

To further characterize the material's mechanical properties and determine means of optimizing the response of the sample to the mechanical deformation, we calculate the stress–strain curves shown in Figure 5, where we altered the values of N_{in} and N_{out} in the range $1 \leq N \leq 2$. The engineering stress for the two-dimensional sample is normalized by the spring constant, κ , of the intramolecular bonds at $N_{in} = 1$. The two-dimensional stress $\sigma = F_{inst}/A_0$ was computed as a ratio of the instantaneous force F_{inst} acting on the nodes at the left edge of the sample and the initial vertical width of the sample A_0 . As is evident from Figure 5, the stress monotonically increases at small strains of $\varepsilon < 0.1$. Oscillations of the stress–strain curves at higher strains are caused by the breaking and subsequent remaking of the bonds in

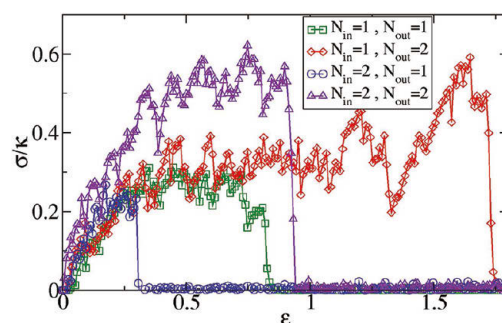


Figure 5. Stress–strain curves calculated for the small sample at $N_{in} = 1, 2$ and $N_{out} = 1, 2$. The stress σ is normalized to the bond stiffness κ .

the course of deformation. The sharp drop of the stress to zero is attributed to the catastrophic failure of the samples. We define the strain at break, ε_b , of the sample as the strain at which this drop occurs. It is evident from Figure 5 that the sample at $N_{in} = 1$ and $N_{out} = 2$ exhibits the best ductility, producing a value of $\varepsilon_b \approx 1.70$. On the other hand, the sample at $N_{in} = 2$ and $N_{out} = 1$ is the least stable and ruptures at $\varepsilon_b \approx 0.3$. Namely, an almost 6-fold increase in the ε_b for sample can be achieved by varying the location of the $N = 2$ linkages from the intramolecular to the intermolecular associations.

To more completely quantify the behavior of this material under tensile deformation, we apply the Weibull statistical analysis. For these studies, we conducted eight runs for each set of parameters (at a given N_{in} and N_{out}) and used Weibull statistics to calculate the strain at break in the small sample. In this analysis, we assume that the probability, p_b , for a sample to break at a certain strain, ε , has the following functional form

$$p_b = 1 - \exp[-(\varepsilon/\varepsilon_b)^m] \quad (10)$$

where ε_b is the mean breaking strain. To evaluate the left-hand side of eq 10, we determined the strain to break for eight samples ($N_{test} = 8$) and arranged these values in ascending order so that the sample $j = 1$ breaks first and sample $j = 8$ designates the sample that fractures last. Then, the Bernard and Bos-Levenbach approximation⁴³ was used to obtain p_b as follows

$$p_b(\varepsilon = \varepsilon_b^j) = \frac{j - 0.3}{N_{test} + 0.4} \quad (11)$$

where ε_b^j is the breaking strain for the j th sample. By fitting the function in eq 10 to our results (using a least-squares method), we calculate the fitting parameters ε_b and m . The plot in Figure 6 demonstrates the dependence of the probability for a sample to rupture, p_b , at strain to break, ε_b , for a sample at $N_{in} = 1$, $N_{out} = 2$; each blue point represents the strain to break of an independent simulation. The red curve shows the result of fitting the data to eq 10 for eight independent runs.

Table 1 summarizes the results of the Weibull analysis for the strain at break and for the radius of gyration computed for small samples at the four combinations of N_{in} and N_{out} considered here. The strain at break is highest for the samples with $N_{in} = 1$ and $N_{out} = 2$, and hence, these samples exhibit the highest ductility. The strain at break is the lowest for the samples with $N_{in} = 2$ and $N_{out} = 1$, indicating that these are the most brittle materials. As noted above, the ε_b is roughly five times greater for the ductile material than the brittle ones. These results demonstrate the significant improvements in mechanical properties that

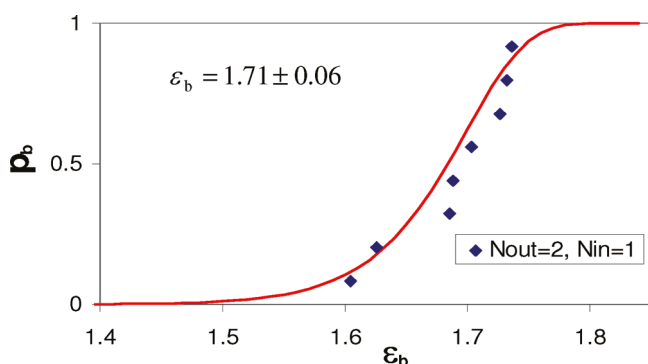


Figure 6. Probability for the small sample to break, p_b , as a function of strain at break, ε_b . Blue diamonds show the results of the simulations conducted at a constant strain rate for $N_{in} = 1$ and $N_{out} = 2$. The red line indicates a least-squares fit between our data and the Weibull probability distribution function (eq 10).

Table 1. Calculated Strain and Mean Radius of Gyration at Fracture for Small Samples at $N_{in} = 1, 2$ and $N_{out} = 1, 2$, from the Constant Strain Rate Simulations

N_{in}	N_{out}	ε_b	$R_{g,b}/d$
1	1	0.80 ± 0.13	1.249 ± 0.065
1	2	1.71 ± 0.06	1.860 ± 0.019
2	1	0.35 ± 0.05	1.019 ± 0.005
2	2	0.99 ± 0.19	1.235 ± 0.069

can be attained through small, judicious changes in the relative values of N_{in} and N_{out} .

Interestingly, the samples with $N_{in} = N_{out}$ display an intermediate ductility, with a strain to break that lies roughly midway between those obtained for $N_{in} = 2$ and $N_{out} = 1$ and for $N_{in} = 1$ and $N_{out} = 2$. It is worth noting that the strain at break for the samples with $N_{in} = N_{out} = 1$ and that for $N_{in} = N_{out} = 2$ are equal to each other within the estimated error.

To establish the extent of unfolding in each case, we used the same Weibull statistical analysis for calculating the mean radius of gyration, $R_{g,b}$, immediately after fracture of the sample (see Table 1). It is evident that the larger the strain at break, ε_b , the larger the mean radius of gyration, $R_{g,b}$. In other words, there is direct correspondence between the ductility of the material and extent to which the units unfold in the course of the tensile deformation.

B. Constant Tensile Stress Test for the Smaller Sample. To obtain another measure of the mechanical properties of the material, we applied a tensile force (along the X axis) at the edges of a small sample. (In this test, the force was applied to the edge nodes of the rightmost and leftmost units in the opposite directions.) The force was applied gradually, as shown in Figure 7, to prevent the premature failure of the sample at the edges. In Figure 7, the stress σ is normalized by σ_b^* , which is the mean stress to break for the sample at $N_{in} = N_{out} = 1$ (see further below). In the simulations, the tensile stress test was applied for a total time of $t = 1.2 \times 10^4 T_0$ and the sample was held under a constant force (or engineering stress) for a period of time $t = 8 \times 10^3 T_0$.

To calculate the stress at break for the small sample, we again use the Weibull statistical analyses (see eq 10). Now, however, the fitting parameters are the characteristic stress at which the

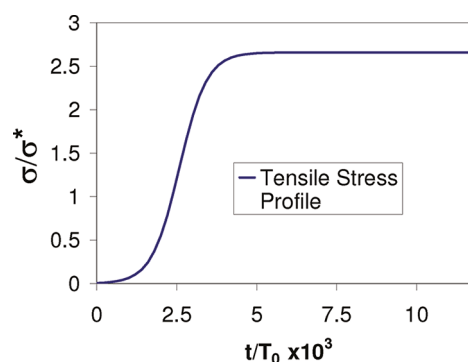


Figure 7. Time dependence of the stress applied to a small sample in constant stress tests. The stress σ is normalized to the value σ_b^* obtained for the small sample at $N_{in} = N_{out} = 1$.

Table 2. Calculated Stress at Fracture for Small Samples at $N_{in} = 1, 2$ and $N_{out} = 1, 2$, from the Constant Stress Simulations

N_{in}	N_{out}	σ_b/σ_b^*
1	1	1.00 ± 0.16
1	2	1.96 ± 0.15
2	1	1.20 ± 0.10
2	2	2.01 ± 0.17

sample fractures onto two pieces, σ_b , and the exponent m (which characterizes the brittleness of the sample). We again performed eight independent simulations for each set of parameters.

The results of the analysis are summarized in Table 2. (We normalize the stress at break to the mean value σ_b^* calculated for the sample at $N_{in} = N_{out} = 1$.) It is evident from the table that, within the estimated error, the stress at break values are equal for both materials with $N_{out} = 2$. Specifically, $\sigma_b/\sigma_b^* = 1.96 \pm 0.15$ for the samples with $N_{in} = 1$ and $\sigma_b/\sigma_b^* = 2.01 \pm 0.17$ for the samples with $N_{in} = 2$. It also follows from Table 2 that the stress at break for the samples with the larger number of external bonds, $N_{out} = 2$, is approximately two times higher than the stress at break for the samples with $N_{out} = 1$. We can conclude that the strength of this material is controlled by the value of N_{out} .

C. Constant Strain Rate Test for the Medium Size and Large Samples. Finally, we consider the cases of medium and large samples that encompass 8 rows with 12 particles in each row and 12 rows with 15 particles in each row. The results of the analysis of the two larger samples are quantitatively similar, and thus, we present the data for the largest sample. In these simulations, we apply a tensile deformation at a constant velocity ($V = 1.64 \times 10^{-3} d/T_0$) similar to the procedure described above for the small samples, and then use the Weibull statistical analysis to determine the strain at break of the material. In this section, we focus on the samples with $N_{in} = 1$, $N_{out} = 2$, because, as follows from the above discussion, these samples demonstrate the highest toughness and stability.

The graphical output of the simulations for $N_{in} = 1$ and $N_{out} = 2$ is shown in Figure 8. (Note that, since we allow the edge nodes to move freely in the vertical direction, the sample is not necessarily aligned with the direction of the applied load.) In contrast to the small sample in Figure 2, it is obvious from Figure 8 that there is a wide area around the edges of the large

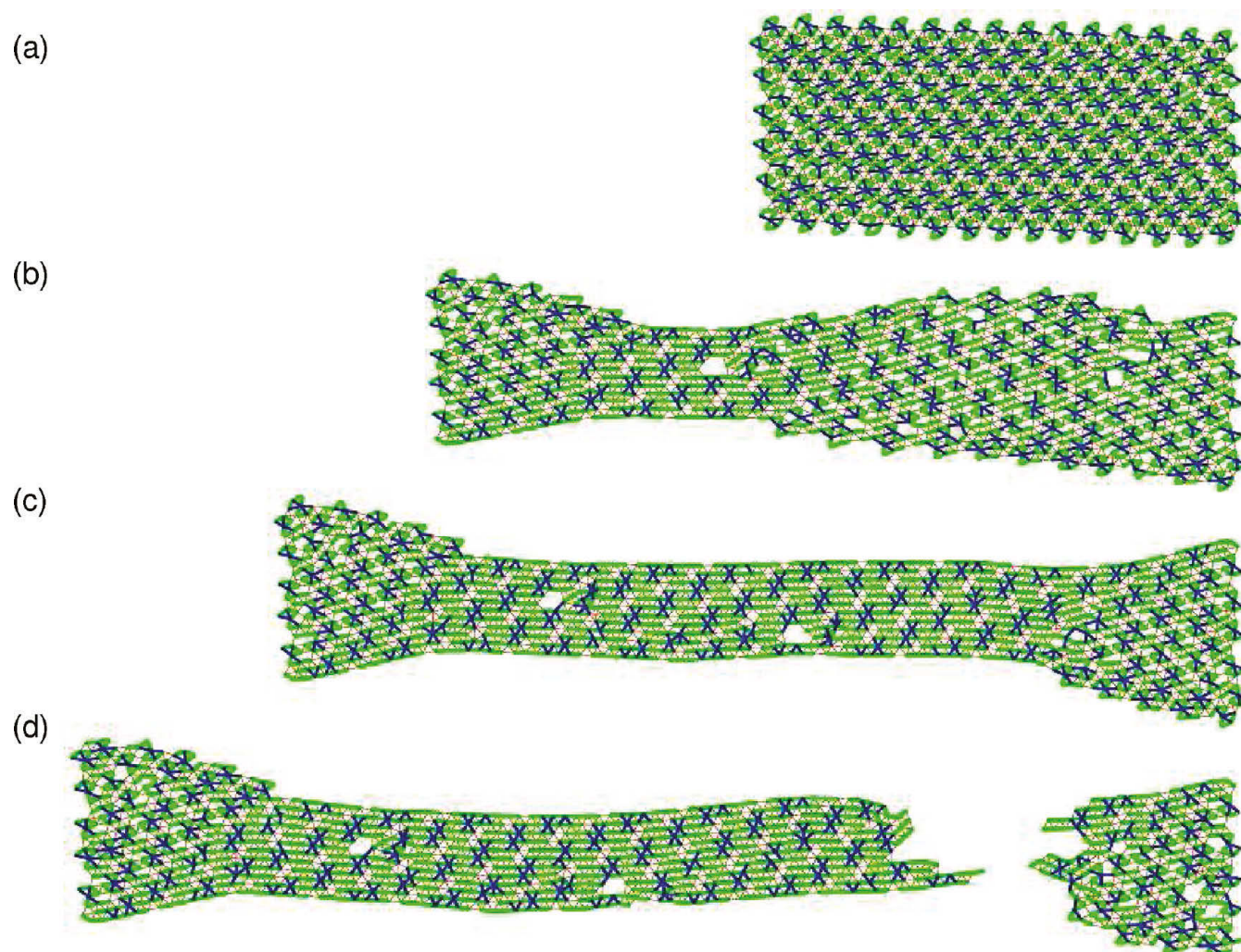


Figure 8. Snapshots of a large sample at $N_{\text{in}} = 1$ and $N_{\text{out}} = 2$ at different moments of time: (a) $t/T_0 = 4.00 \times 10^2$; (b) $t/T_0 = 4.96 \times 10^4$; (c) $t/T_0 = 7.66 \times 10^4$; (d) $t/T_0 = 9.10 \times 10^4$.

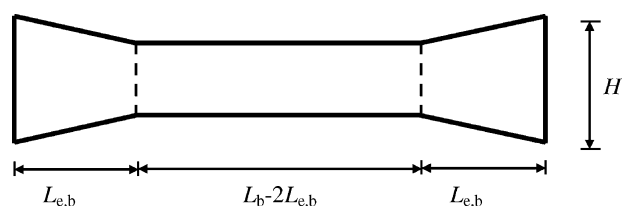


Figure 9. Schematic of shape of deformed medium or large samples at the moment before they fracture. $L_{e,b}$ is the length of part where the globules do not unfold due to edge effects; L_b and H are the total length and the width of the sample before the fracture, respectively.

sample where the units do not unfold. Evidently, these edge effects will affect the apparent strain at break calculated as $\varepsilon_b^{\text{app}} = (L_b - L_0)/L_0$ where L_b is the total length of the sample at the moment when it fractures. To properly take into account the edge effects and correctly estimate the strain at break, we use the geometric model shown in Figure 9. In this model, the material prior to fracture is represented as a dog bone shaped sample. According to the results of our simulations (Figure 8), we can estimate that the length of the edge, $L_{e,b}$, where the units do not unfold is approximately equal to the width of the sample, H .

Table 3. Strain to Break Corrected for Boundary Effects for $N_{\text{in}} = 1$ and $N_{\text{out}} = 2$

sample size	$\varepsilon_b^{\text{app}}$	ε_b
medium (8×12)	1.51 ± 0.09	1.80 ± 0.11
large (12×15)	1.27 ± 0.29	1.64 ± 0.37

According to a simple geometric analysis, the corrected value of the strain at break is determined as

$$\varepsilon_b = \frac{(\varepsilon_b^{\text{app}} + 1 - L_{e,b}/L_0)}{1 - L_{e,0}/L_0} - 1 \quad (12)$$

We use eq 12 to estimate the strain at break from the results of the Weibull statistical analyses of the numerical data for $\varepsilon_b^{\text{app}}$.

The results of this analysis for the large and medium sized samples for $N_{\text{in}} = 1$ and $N_{\text{out}} = 2$ are presented in Table 3. By comparing the data in Tables 1 and 3, we see that the results of the tensile tests for the different-sized samples are in good agreement with each other. In particular, we see that the strain at break for the large sample at $N_{\text{in}} = 1$ and $N_{\text{out}} = 2$ (Figure 8) is equal to $\varepsilon_b = 1.64 \pm 0.37$.

CONCLUSIONS

We investigated the mechanical properties of a material created by utilizing reactive bonds to cross-link individual globular modules, which encompass a secondary structure, into a macroscopic network. Aside from the permanent bonds that make up the backbone of the chains, all the links in this material are labile and a linkage can encompass a maximum of $N = 2$ parallel bonds. A distinctive feature of these computational studies is that all the labile bonds are reformable, i.e., a bond can break and remake. The latter feature models the reactive nature of labile links created, for example, through hydrogen bonding or thiol/disulfide exchange reactions. To capture the behavior of these parallel, reformable bonds, we utilized our recently developed modified Hierarchical Bell model (MHBM), which allowed us to examine the role of the labile linkages on the response of the material to a tensile deformation. Additionally, we could focus on the conformational changes of the globules as the material is stretched and the labile bonds are reshuffled.

We applied the tensile deformation at a constant force and a constant strain rate and varied the values of the maximum number of parallel bonds N for the intramolecular (N_{in}) and the intermolecular (N_{out}) linkages. The tests at constant force showed that the strength of the material is mainly controlled by the value of N_{out} , with the higher value of N_{out} providing a stronger material. The tests at constant strain rate revealed that the ductility of the material depends on the extent to which the globules can unfold and this, in turn, depends on the relative value of N_{in} . Specifically, if N_{in} is smaller than N_{out} , the globules can unfold under the tensile load before the sample fractures and, in this manner, can increase the ductility of the material. Under these conditions, one can exploit the globules as units of stored length, which can improve the toughness of the system. On the other hand, if N_{in} is larger than N_{out} , then the intramolecular bonds prevent the chains from completely unfolding and the material is more brittle than in the case with $N_{\text{in}} < N_{\text{out}}$. In other words, small variations in the location of the relatively weaker bonds can lead to significant changes in the mechanical behavior of the material.

The findings from these studies provide useful guidelines for integrating different elements to create materials with both high strength and toughness. As noted above, the units of stored length provided by the weakly bound coils can improve toughness since they provide an energy dissipating capacity as the material is deformed. The $N_{\text{out}} = 2$ cross-links between the coiled chains provide a strong backbone for the network, and since the bonds are labile, they also allow the material to undergo some reshuffling that delays the catastrophic failure of the material.²⁰ In summary, such computational studies provide an effective means of determining how best to exploit the combination of weak intramolecular interactions and stronger intermolecular interactions to tailor the macroscopic performance of the materials. In future studies, we will utilize our approach to design a new generation of biomimetic, superelastic “glues”, or fibers formed from cross-linked globules. We will then determine how these fibers can be harnessed to improve the self-healing behavior of polymer networks.

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REFERENCES

- (1) Calvert, P. *Adv. Mater.* **2009**, *21*, 743–756.
- (2) Yoshida, R. In *Nonlinear Dynamics with Polymers: Fundamentals, Methods and Applications*; Pojman, A. J., Tran-Cong-Miyata, Q., Eds.; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, 2010; Chapter 7.
- (3) Gong, J. P. *Soft Matter* **2010**, *6*, 2583–2590 and references therein.
- (4) Rief, M.; Gautel, M.; Oesterhelt, F.; Fernandez, J. M.; Gaub, H. E. *Science* **1997**, *276*, 1109–1112.
- (5) Tskhovrebova, L.; Trinick, J.; Sleep, J. A.; Simmons, R. M. *Nature* **1997**, *387*, 308–312.
- (6) Vogel, V. *Annu. Rev. Biophys. Biomol. Struct.* **2006**, *35*, 459–488.
- (7) Erickson, H. P. *J. Muscle Res. Cell Motil.* **2002**, *23*, S75–S80.
- (8) Hill, D. J.; Mio, M. J.; Prince, R. B.; Hughes, T. S.; Moore, J. S. *Chem. Rev.* **2001**, *101*, 3893–4011.
- (9) Guan, Z. *Polym. Int.* **2007**, *56*, 467–473.
- (10) Kushner, A. M.; Gabuchian, V.; Johnson, E. G.; Guan, Z. *J. Am. Chem. Soc.* **2007**, *129*, 14110–14111.
- (11) Shi, Z.-M.; Huang, J.; Zhao, X.; Guan, Z.; Li, Z.-T. *Macromolecules* **2010**, *43*, 6185–6192.
- (12) Kushner, A. M.; Vossler, J. D.; Williams, G. A.; Guan, Z. *J. Am. Chem. Soc.* **2009**, *131*, 8766–8768.
- (13) Yu, T.-B.; Bai, J. Z.; Guan, Z. *Angew. Chem., Int. Ed.* **2009**, *48*, 1097–1101.
- (14) (a) Tsige, M.; Stevens, M. J. *Macromolecules* **2004**, *37*, 630–637. (b) Tsige, M.; Lorentz, C. D.; Stevens, M. J. *Macromolecules* **2004**, *37*, 8466–8472.
- (15) Nouri, N.; Ziaei-Rad, S. *Macromolecules* **2011**, *44*, 5481–5489.
- (16) Tessier, F.; Boal, D. H.; Discher, D. E. *Phys. Rev. E* **2003**, *67*, 011903.
- (17) Peleg, O.; Kröger, M.; Rabin, Y. *Phys. Rev. E* **2009**, *79*, 040401.
- (18) Peleg, O.; Kröger, M.; Hecht, I.; Rabin, Y. *Europhys. Lett.* **2007**, *77*, 58007.
- (19) Kröger, M.; Peleg, O.; Ding, Y.; Rabin, Y. *Soft Matter* **2008**, *4*, 18–28.
- (20) Kolmakov, G. V.; Matyjaszewski, K.; Balazs, A. C. *ACS Nano* **2009**, *3*, 885–892.
- (21) Salib, I. G.; Kolmakov, G. V.; Gnegy, C. N.; Matyjaszewski, K.; Balazs, A. C. *Langmuir* **2011**, *27*, 3991–4003.
- (22) Buxton, G. A.; Balazs, A. C. *Phys. Rev. B* **2004**, *69*, 054101.
- (23) Buxton, G. A.; Care, C. M.; Cleaver, D. J. *Modelling Simul. Mater. Sci. Eng.* **2001**, *9*, 485–497.
- (24) Ladd, A. J. C.; Kinney, J. H.; Breunig, T. M. *Phys. Rev. E* **1997**, *55*, 3271–3275.
- (25) Yashin, V. V.; Balazs, A. C. *Science* **2006**, *314*, 798–801.
- (26) Kuksenok, O.; Yashin, V. V.; Balazs, A. C. *Soft Matter* **2007**, *3*, 1138–1144.
- (27) Bell, G. I. *Science* **1978**, *200*, 618–627.
- (28) Wiita, A. P.; Ainarapu, S. R. K.; Huang, H. H.; Fernandez, J. M. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 7222–7227.
- (29) Bell, G. I.; Dembo, M.; Bongrand, P. *Biophys. J.* **1984**, *45*, 1051–1064.
- (30) (a) King, M. R.; Hammer, D. A. *Proc. Natl. Acad. Sci. U.S.A.* **2001**, *98*, 14919–14924. (b) Chang, K. C.; Tees, D. F. J.; Hammer, D. A. *Proc. Natl. Acad. Sci. U.S.A.* **2000**, *97*, 11262–11267.
- (31) Bhatia, S. K.; King, M. R.; Hammer, D. A. *Biophys. J.* **2003**, *84*, 2671–2690.
- (32) Ackbarow, T.; Chen, X.; Keten, S.; Buehler, M. J. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 16410–16415.
- (33) Ackbarow, T.; Buehler, M. J. *Nanotechnology* **2009**, *20*, 075103.
- (34) Ackbarow, T.; Keten, S.; Buehler, M. J. *J. Phys.: Condens. Matter* **2009**, *21*, 035111.

- (35) Buehler, M. J.; Keten, S.; Ackbarow, T. *Prog. Mater. Sci.* **2008**, *53*, 1101–1241.
- (36) Evans, E. *Annu. Rev. Biophys. Biomol. Struct.* **2001**, *30*, 105–128.
- (37) Piper, J. W.; Swerlick, R. A.; Cheng Zhu, C. *Biophys. J.* **1998**, *74*, 492–513.
- (38) Zhu, C. *J. Biomech.* **2000**, *33*, 23–33.
- (39) Zhu, C.; Bao, G.; Wang, N. *Annu. Rev. Biomed. Eng.* **2000**, *2*, 189–226.
- (40) Takahashi, H.; Ishimuro, Y.; Watanabe, H. *J. Soc. Rheol. Jpn.* **2006**, *34*, 135–145.
- (41) Takahashi, H.; Ishimuro, Y.; Watanabe, H. *J. Soc. Rheol. Jpn.* **2007**, *35*, 191–198.
- (42) Dirama, T. E.; Varshney, V.; Anderson, K. L.; Shumaker, J. A.; Johnson, J. A. *Mech. Time-Depend. Mater.* **2008**, *12*, 205–222.
- (43) Bernard, A.; Bos-Levenbach, E. C. *Statistica* **1953**, *7*, 163–173.