Mechanical Model of Globular Transition in Polymers

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In complex, multicomponent systems, polymers often undergo phase transitions between distinct conformations. This paper reports a millimeter-scale granular model of coil-to-globule transitions: one "polymer" chain—a cylinders-on-a-string "pearl necklace"—and many spheres, all shaken on a horizontal surface. It is possible to describe the behavior of this granular system by using formalisms generally used in statistical physics of polymers. Two sets of experiments allowed the observation of first- and second-order coil-to-globule transitions. The model shows that the competition between long- and short-range interactions leads to a first-order transition. Well-designed granular system represents another kind of approach to the study of polymer phase transitions and might inspire future designs of polymer-like mesoscale systems.

Although a homopolymeric molecule experiencing Brownian motion in solution, and a "pearl necklace" shaken on a horizontal flat surface in an assembly of spheres, are very different systems, they exhibit surprisingly similar statistical–physical behavior. The problem we have explored is the extent to which systems topologically analogous to polymers, but with a scale of components large enough to be visible and with numbers of components small enough that all can be accounted for explicitly, exhibit complex phenomena, such as phase transitions. Such systems could provide a tool for improving intuition about molecular phase transitions, and guide the design of molecular and nanoscale systems that exhibit such transitions. Numerous theoretical and experimental studies are actively performed to understand the folding of proteins, or the coil-to-globule transition, and often involve intensive computations, or sophisticated experimental methods.[1–5] In parallel, solid–liquid granular phase transitions have been reported, and described in detail for layers on horizontally vibrating devices.[6,7] Herein, we designed a granular system to simulate a phase transition ubiquitous in homopolymers in solution: the transition from an expanded fluctuating coil state to a col-

lapsed globule state, which depends on the intermolecular interactions between the polymer and the surrounding solvent, and on intramolecular interactions between different regions of the polymer.[1,8] This transition is usually second order (continuous), but there is evidence that it could occur as a first-order (discontinuous) transition as well.[3,9]

We previously introduced mechanical agitation (MecAgit) as a method for physical simulation of the behavior of microscopic systems, by using a two-dimensional arrangement of millimeter-sized components that move under pseudorandom agitation.[10,11] Although MecAgit systems are macroscopic, out-of-equilibrium, and dissipative, and even though their motions are not completely random, we used them to mimic experimentally the folding of a short-chain RNA,[12] the statistics of conformations of worm-like chain (WLC) polymers,[10] and the development of a Boltzmann distribution.[11] Other groups have used chain models as well: Ben-Naim et al. studied topological constraints such as knots,[13] Safford et al. the effect of confinement,[14] Zou et al. glass transition in chains,[15] Blair and Kudrolli the formation of chains by shaking magnetic beads and free particles,[16] and Yuan et al. segregation in mixtures of granular chains and spherical grains.[17] The novelty of our approach is the focus on designing granular models of phase transitions in polymer physics, and the use of polymer statistical physics to describe the collapse of macroscopic cylinders-on-a-string shaken in an assembly of free spheres. We shook millimeter-sized cylinders-on-a-string (the "polymer chain") on a flat horizontal surface within a region bounded by vertical walls, in the presence of a variable number of free spheres (Figure 1a). We changed the filling ratio (FR) of free spheres, that is, the ratio between the number of spheres in the system and the number of spheres required to completely fill the available area with a single layer of spheres with compact hexagonal packing (for closed-packed packing, FR = 100 %). Unlike other horizontally shaken granular systems,[7,18] ours has a pseudorandom agitation motion, which results from a combination of an orbital shaking of the surface, and randomization by agitation of a pendulum hanging underneath, with a linear actuator.[12] This type of agitation randomizes some aspects of the motion of the chain (although the motion of the spheres is strongly correlated), such that this motion could be described to a useful approximation by a "macroscopic temperature": a parameter that has a simple experimental relationship with the frequency of the orbital shaker, f, and describes the steady-state behavior of the chain.[10,11] Our granular system is a model of polymers in solution: the cylinders-on-a-string represent a polymer molecule and the assembly of free spheres represent a thermal bath of solvent molecules. To characterize

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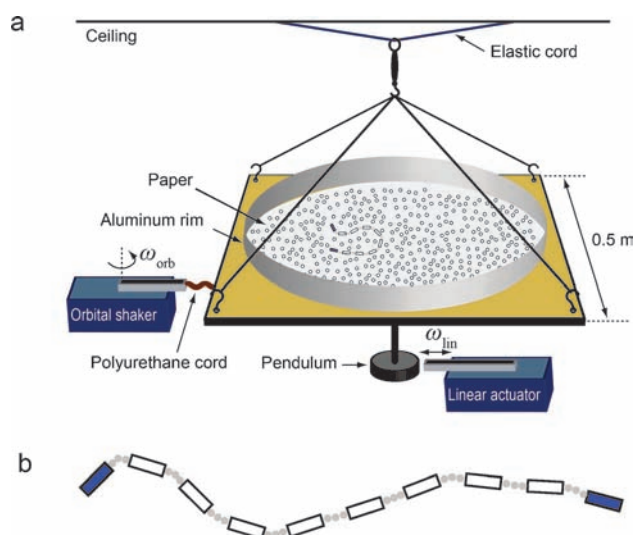
Figure 1. a) Illustration of the experimental apparatus. b) Schematic illustration of the flexible chain. To facilitate image analysis, we dyed the cylinders at the termini of the chain blue.

Figure 2. a) Time-lapse photography of the initial collapse of the chain, starting from an extended conformation. b) Time-lapse photography of the steady behavior of the chain. Scale bars: 2 cm; FR = 80%; f = 130 rpm.

the folding state of the chain, we used its radius of gyration, R_g, defined as the root-mean-square distance between the monomer units and the center of mass of the polymer.[19]

First, we studied a chain made of 10 cylinders threaded on a string and separated by small spheres that allowed the chain to bend (Figure 1 b).[12,20] The contour length of the chain was equal to 23.9 cm; in the absence of free spheres, the chain had an extended (but not completely stretched) conformation under agitation that was described by a WLC behavior with a persistence length equal to 12.2 cm.[10] Under certain experimental conditions, the chains collapsed after collisions with free spheres (Figure 2 a). In a three-cylinder chain, the collapse, as we described previously,[11] is a consequence of imbalanced rates of collision with spheres between the open and closed sides of the chain—the spheres exert a "pressure" that can close the chain, if it overcomes its intrinsic rigidity. By extrapolating this mechanism, the collapse of longer chains will occur if the "sphere pressure", which increases at larger FRs, is strong enough.[18]

The collapsed conformation was not static: the chain reached a steady state, in which it continuously stretched and shrunk, but never returned to a completely extended conformation (Figure 2 b). Once the chain reached steady state, we took multiple snapshots of the system at equally spaced time intervals to determine the more likely conformations and their probability of occurrence. The steady distribution of R_g is shown as a function of f and FR in Figure S1 in the Supporting Information. At a low FR of free spheres (FR = 40%), the chain always stayed in an extended (but not stretched) conformation: FR was sufficiently low that the spheres did not perturb the behavior the chain displayed in their absence. When we increased f, the distribution of R_g broadened and shifted continuously towards lower values—a WLC behavior that we also observed in an analogous system without spheres.[10] From FR = 50 to 70%, the mean value of the R_g distribution, denoted as
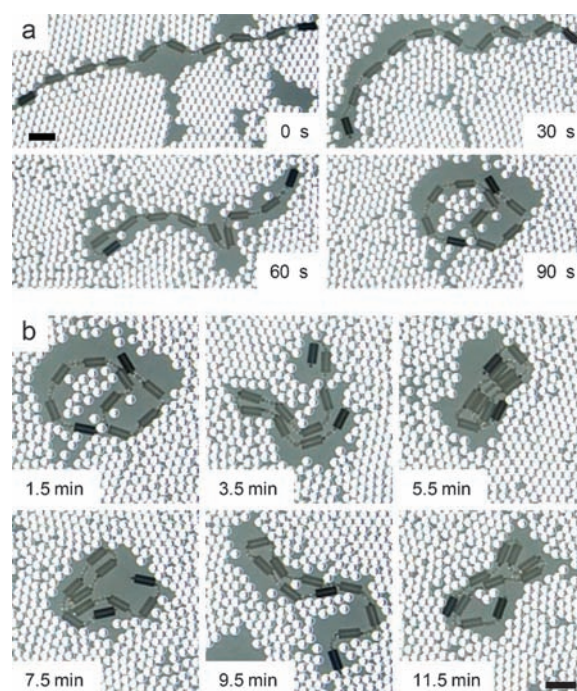
$<R_g>$, first increased with f, and then decreased, as we varied f from low to high values (Figure 3 a). Because, in our system, f plays the role of temperature, the change in the sign with which the system responded to variations in f indicates that the chain transitioned between two states with different "temperature" dependencies. In analogy with the coil and globule states of polymers, in which the radius of gyration had different temperature dependencies, we identified a coiled state that corresponded to a chain with $<R_g>$ increasing with f, and a globular state that corresponded to a chain with $<R_g>$ decreasing with f. We calculated the agitation frequency at which the transition occurred, f_0(FR), as the intersection of the linear regressions corresponding to each behavior: f_0 (FR = 50%) = 99 rpm, f_0 (FR = 60%) = 97 rpm, and f_0 (FR = 70%) = 88 rpm; f_0 is the extrapolated frequency at which $<R_g>$ is maximum. If a large fraction of free spheres was present on the dish (FR = 80%), the chain remained collapsed throughout agitation. The distribution of R_g was narrow and its average, $<R_g>$, was independent of f. This behavior corresponds to a compact globule state of a polymer molecule.[1] A similar tendency was observed for a three-cylinder-long system, which collapsed in a compact state increasing f and FR.[11]
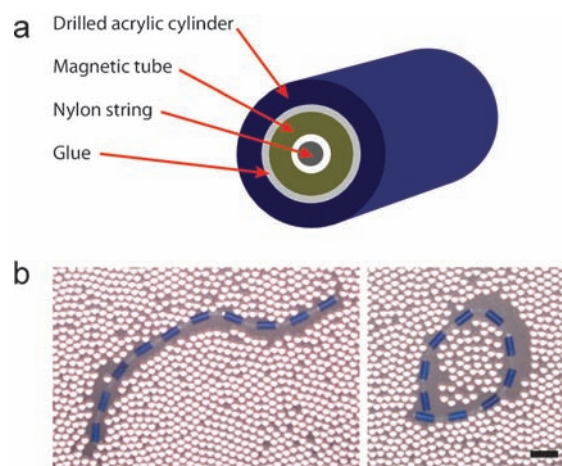
Figure 3 b provides a summary of the previous descriptions as a four-phase (WLC-type, coil, globule, and compact globule) diagram in the (f, FR) space. We performed Kolmogorov–Smirnov tests on R_g distributions on either side of the frontiers between the phases to confirm they were statistically distinct: between the WLC and the coil-globule phases (same f, FR = 40 and 50%), between the coil–globule and the compact globule phases (same f, FR = 70 and 80%), and between the coil and
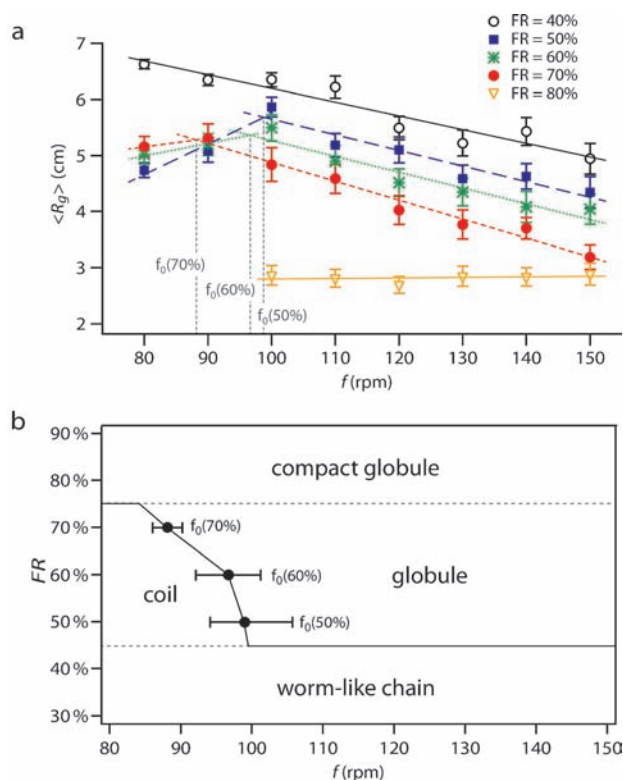
Figure 3. a) Evolution of the average radii of gyration, $<R_g>$, and their linear regressions, as a function of f for different FRs. b) Phase diagram of the experimental model system as a function of f and FR.
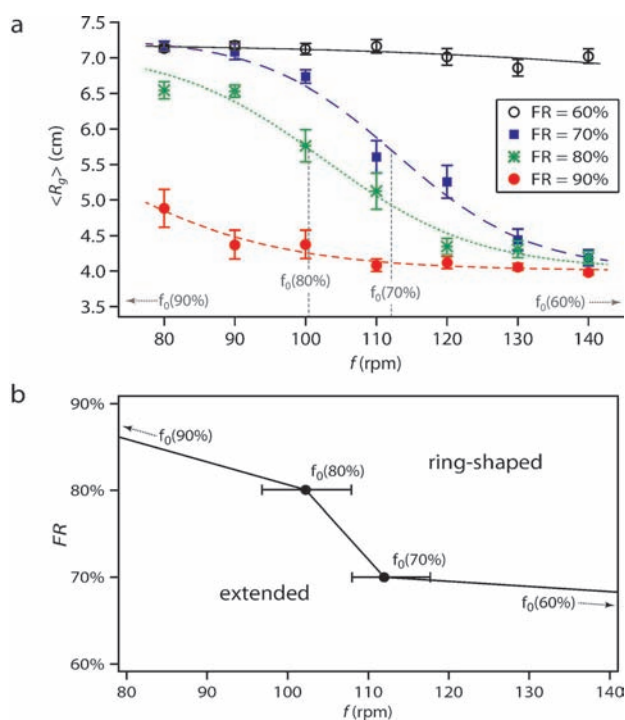

Figure 4. a) Schematic illustration of the cross section of an individual cylinder. b) Representative photographs of the two equilibrium conformations of the chain: extended (left) and ring shaped (right). Scale bar: 2 cm.

globule phases (f below and above f_0, same FR). The p values for all tests were lower than 0.03. The transitions between the phases of the diagram were thus quantitative at the scale of the experimental meshing of the (f, FR) space. In addition to its dependence on f, the unimodality of the R_g distribution for all (f, FR) conditions between FR $= 50$ and 70% is another signature of a second-order transition.[1] The coil-to-globule transition of the MecAgit model described herein is thus analogous to a coil-to-globule transition in polymers, as induced by a change in temperature. The assembly of spheres is analogous to a "poor" solvent, as observed for some polymers and proteins.[4] As f increased, the model chain exhibited the gradual compaction characteristics of second-order phase transitions of polymer chains.[5,19,21]

First-order phase transitions are encountered in some polymer systems, such as charged polymers, but experimental proof of such transitions at the molecular scale remains controversial, and their mechanistic origin is still a subject of investigation.[1,3,9] To observe such transitions in our granular system, we designed a system in which two antagonistic forces acted at different scales: we chose a thicker thread that stabilized the extended conformation of the chain and we inserted magnetic cylinders (Figure 4a) to add attractive interactions between the cylinders of the chain and favor the collapsed conformation. The length scale of the elastic interaction that is due to the stiffness of the thick thread is on the order of magnitude of the persistence length of the chain, that is, tens of centimeters, whereas the length scale of the attraction between the magnets is of a few centimeters. Under agitation, the chain had two primary conformations: one ring shaped and one extended (Figure 4b). The ring-shaped conformation was the more compact conformation; the rigidity of the thread prevented compaction below the ring size. The existence of two primary conformations was confirmed by two distinct peaks in the distributions of R_g: one centered at 4.0 cm, which corresponded to the ring-shaped conformation, and one centered at 7.2 cm, which corresponded to the extended conformation (Figure S2 in the Supporting Information). At high and low coverage of the surface by free spheres, the distributions of R_g did not depend on f: For FR ≥ 90%, the chain collapsed to the ring-shaped conformation, and for FR ≤ 60%, the chain remained in the extended conformation. For intermediate FR, we observed both distributions and the predominant conformation evolved from extended to ring shaped as f increased. For the (f, FR) conditions in which the two distributions were present, the chain opened and closed from the extended to the ring-shaped conformation randomly. The evolution of $<R_g>$ as a function of f could be fitted approximately by a sigmoid, in which f_0 was the frequency at the center of the sigmoid and depended on FR: f_0 (FR $= 60$%) $= 284$ rpm, f_0 (FR $= 70$%) $= 112$ rpm, f_0 (FR $= 80$%) $= 101$ rpm, and f_0 (FR $= 90$%) $= 64$ rpm (Figure 5a).

Figure 5b provides a summary of the previous discussions in a phase diagram; the f_0 values correspond to the frequencies of transition. At low FR, the tension of the string is predominant (high persistence length) and the magnetic attractions are negligible. As we increased FR, the "pressure" of the free spheres counteracted the tension of the string, making it more compact; in this conformation, the short-range magnetic attractions began to be significant. Both the pressure of the free sphere and the attraction of the magnetic beads favored the collapsed state. Introducing interactions at two different scales gave rise to only two observable conformations; intermediate conformations were thus not apparent in the statistical description of the system, that is, the R_g distributions. In some

Figure 5. a) Evolution of the average radii of gyration, $<R_g>$, and their sigmoidal fits, as a function of f for different FRs. b) Phase diagram of the experimental model system as a function of f and FR.

behavior analogous to that of molecular homopolymers in solution. The physical simulations reported herein go beyond a simple topological analogy, because we introduce intrachain forces and generate a type of folding transition that is uncommon in polymers and not well understood. The MecAgit approach is novel for three reasons: 1) We used a more complex system those previously reported, with the introduction of two antagonistic forces at different scales, which led to a first-order phase transition; to the best of our knowledge, this effect has never been reported before with granular models (most of them were simply vertically vibrated, leading to fundamentally different behavior). 2) The origin of a first-order phase transition is still a subject of debate in the polymer physics community. We proved, by a physical experiment, that the hypothesis of using two antagonistic forces at different scales was valid. 3) Our work demonstrates that phenomenological analogies are important and give insights into complex behavior. Although the precise mechanistic details were different between granular systems and molecules in solution,[23] we were able to validate a general principle that could determine the order of phase transitions in microscopic systems. Our ability to change the order of the folding transition by adding competing long- and short-range interactions might suggest that a similar approach would work at the molecular scale, although its success is not certain. Controlling interactions at the molecular level is a real challenge, because numerous interdependant experimental conditions are present simultaneously: temperature, nature of the monomers, length and rigidity of the polymer, nature of the solvent, concentration of the solutes, and so forth. Polymer-like mesoscale systems reported by others, however, might provide better opportunities for designing phase behavior. For example, Liu et al. demonstrated the possibility of directing the self-assembly of gold nanorods in linear conformations, just as monomers assembled to form polymers.[24] Our work, which shows that the engineering of interparticle interactions is a valid approach to control phase transitions in millimeter-scale granular systems, might thus inspire the design of future polymer-like mesoscale systems.

sets of (f, FR) conditions, for example, for (f, FR) = (110 rpm, 70%), (120 rpm, 70%), (100 rpm, 80%), and (110 rpm, 80%), the R_g distribution had two distinct peaks, corresponding to ring-shaped and extended conformations. Thus, the system was not a simple switch, for which we would have observed only one peak in the distribution. The presence of bimodal R_g distributions and the sigmoidal shape of the evolution of $<R_g>$ as a function of f are typical signatures of a first-order transition.

The collapse of the chain in our granular system is favored by the phase separation between the cylinders of the chain and the free rolling spheres. These two types of components react differently to the external conditions: they have different responses to friction and different responses to agitation (as a result of their different shapes, masses, and inertias). If a component is surrounded by homologous ones, all particles experience the same driving force and few interparticle collisions occur. If two components are different, they feel different driving forces and experience frequent collisions. The distinct mobility of different types leads to their separation, which tends to reduce the rate of collisions as much as possible.[22] Phase separation is enhanced if the density of the components is increased and if external driving forces are increased;[7] this is why the collapsed conformations of the chains were favored at high FR and high f.

Although the nature of the strongest forces acting on particles is different at the mesoscopic granular scale (friction, hard-sphere collisions, and here magnetic dipole forces) than at the microscopic scale (electrostatic and van der Waals forces), we observed that cylinders-on-a-string demonstrated statistical be-

Experimental Section

We prepared a circular mixing area with a diameter of 0.48 m by using an aluminum rim, and we covered the area inside the rim with paper to generate an area with a constant friction coefficient on which the objects would roll, but not slide, when the plate was agitated. To avoid any possible electrical charging by contact electrification within the experimental setup, we maintained a relative humidity (RH) of more than 60% by using a humidifier connected to the enclosed space above the plate.[14] In all experiments, we filled the mixing area with simple (spheres) and composite (cylinders connected by a string) polymeric objects. We varied the FR of spheres between 40 and 90% (see the definition of FR in the main text). To simulate molecular phenomena in the presence of thermal agitation, we shook the system with a combination of orbital translation (with f from 80 to 150 rpm) and randomly timed flicks to make the movement of particles aperiodic. The movement of the cylinders-on-a-string was followed by taking snapshots with a picture digital camera. For each (f, FR) condition, we took one hun-

dred pictures at regular intervals to probe all possible conformation taken by the chain. We extracted the R_g values for each picture with a custom-made program.

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