From molecular mechanochemistry to stress-responsive materials

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Current activity in, and future prospects for, the incorporation of mechanochemically active functional groups ("mechanophores") into polymers is reviewed. This area of research is treated in the context of two categories. The first category is the development of new chemistry in the service of material science, through the design and synthesis of mechanophores to provide stress-sensing and/or stress-responsive elements in materials. The second category is the reverse—the development of new material architectures that efficiently transmit macroscopic forces to targeted molecules in order to generate chemical reactivity that is inaccessible by other means.

Introduction

The mechanical forces typical of daily life have the potential to induce dramatic reactivity at the molecular level. The force between an infant's clenched finger and thumb, for example, is more than ten billion times that of the force between atoms in a carbon–carbon bond. Not only are macroscopic forces many orders of magnitude greater than atomic forces, they are also directional, and therefore differ from conventional forms of energy input such as heat and light. In the past four years, several studies have demonstrated that macroscopic mechanical forces can be harnessed at the molecular level, creating a new tool for the organic and materials chemist alike. Broadly, the opportunities in this area can be divided into two categories. First, there is the opportunity to develop new chemistry in the service of material science by designing and synthesizing mechanically activated functional groups ("mechanophores") and incorporating them as stress-sensing and/or stress-responsive elements in materials. The second opportunity is the complement of the first—the development of new material architectures that efficiently transmit macroscopic forces to targeted molecules and, in so doing, open up a world of chemical reactivity that is inaccessible by other means. We will refer to these as "*chem* → *mat*" and "*mat* → *chem*" mechanochemistry, respectively (Fig. 1). The field of mechanochemistry therefore touches on materials chemistry from the point of view of each of its principle progenitors with potential utility in areas ranging from stoichiometric reactivity and catalysis to stress-responsive and self-healing polymers.

We see the greatest opportunities in mechanochemistry arising from situations in which the mechanical force is directly applied to the mechanophore, so that a directional coupling between the vector of applied force and the reaction of interest is possible. The focus of this paper, then, will be on the mechanochemistry of polymers under tension, where the mechanical coupling is most obvious and, therefore, most amenable to the chemist's intuition. Other aspects of mechanochemistry, such as those involved in the milling of crystals, metals, and alloys,[1] are well known and important fields, but they will not be discussed here. A comprehensive review of mechanochemistry in polymers has been published recently by Caruso *et al.*,[2] and it is not our intent to duplicate that effort here. Rather, after a brief historical overview, we will first review some recent highlights and their potential impact, and then present our view of the primary challenges and opportunities in both the immediate and long-term future.

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Background

The effects of mechanical tension on polymers vary from simple conformational changes to bond stretching and deformation, and finally to bond cleavage at sufficiently high stresses. Respective examples include the force-induced *cis*/*trans* isomerization of proline,[3] bond deformations in polymer films under elongational tension,[4] and polymer degradation from bond scission by ultrasonication-induced shear forces.[5] Historically,[1,6] the focus of polymer mechanochemistry has been on polymer degradation *via* homolytic bond scission reactions.[7–26] Studies of flow-induced mechanochemistry[5,16,23–30] provided a firm theoretical and experimental foundation for the field. Mechanochemistry in polymers adsorbed to surfaces[31,32] or in the bulk is also known, and free radical generation due to stress-induced bond scission has been detected spectroscopically.[14,15,33,34] Mechanical forces have been implicated in not only bond scission reactions, but also bimolecular reactions such as polyamide hydrolysis[35] and polyolefin ozonolysis.[36–42] These examples of mechanochemical activation are best viewed as destructive, and only recently has the idea of productive mechanochemistry in polymers taken shape. Nonetheless, that history validates two critical foundations of the current work in the area of productive polymer mechanochemistry: (i) macroscopic forces in polymers can be enormous—large enough to induce 90 kcal mol^{-1} bond scissions and suggesting that an applied mechanical force of the correct magnitude might be able to direct almost any organic transformation of interest; (ii) mechanochemistry in polymers can be made selective, by strategically coupling the applied force to the desired reaction mechanism.

The physical basis for mechanically induced changes in reactivity was first described by Eyring and Kauzmann[24] and extended by Bell.[43] Briefly, if mechanical potential energy decreases as the chemical potential energy of the reaction increases, the activation energy is lowered by the applied stress. For example, lengthening a carbon–carbon bond during homolytic bond scission will lower the mechanical potential of the system, but only to the extent that the force is coupled to the bond-breaking process. A barrier still exists; mechanochemical activation only enhances thermochemical activation (Fig. 2). In the simplest model, the mechanically induced reduction in the activation energy, ΔE_{act}, is proportional to the magnitude of the applied force, F, and the geometry change that is aligned with the applied force during the reaction. The change in activation energy, $\Delta(\Delta E_{act})$, is therefore proportional to F through Δd, the difference in geometry of the transition state *vs.* that of the reactant projected along the vector of applied force:

$$\Delta(\Delta E_{act}) = F \cdot \Delta d \quad (1)$$

Despite its (over)simplicity, eqn (1) reveals one of the primary challenges to productive mechanochemistry: molecules, and therefore Δd, are small. Thus, mechanochemistry will tend to be relevant in materials science under conditions of high stress (for example, just prior to or immediately following stress-induced crack initiation), and mechanochemistry will only be useful in chemistry when very large forces can be coupled to the reactions of interest. As a useful frame of reference, enhancing a chemical reaction rate by a factor of 10 at 298 K is $\Delta E_{act} = RT \cdot \ln(10)$, or 9.5 pN nm, and so a Δd of 1 Å requires 95 pN of applied force.

A reasonable design strategy for mechanochemistry in polymers is provided by the following hierarchy, which we follow in the organization of this article.

I. How are macroscopic forces directed through a material architecture to particular molecules? ($F_{macro} \rightarrow f_{mol}$)

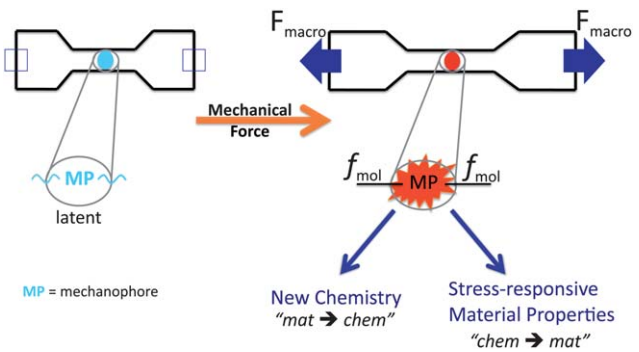

Fig. 1 Schematic representation of the transfer of a macroscopic force (F_{macro}) to molecular forces (f_{mol}) that act on an embedded mechanophore (MP), resulting in new chemistry and/or stress-responsive materials.

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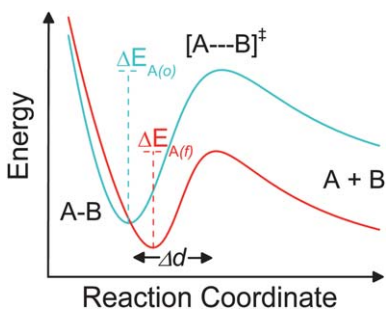

Fig. 2 Representation of the potential energy surface of a reaction in the absence of a coupled force (blue) and in the presence of a coupled force (red). The force leads to a net reduction in activation energy of $\Delta(\Delta E_{act}) = \Delta E_{A(0)} - \Delta E_{A(f)}$. Note that eqn (1) in the text assumes that the distance Δd from reactant to transition state does not change as a function of force, but that perturbations are possible.

II. How are those forces funneled through the molecular architecture to the desired atoms and bonds? (f_{mol} → single bond)

III. How does an applied force couple onto various reaction mechanisms?

As is discussed below, in some cases the answers to these questions are known, while in others the situation is quite poorly understood.

Force transmission, part I: channeling F_{macro} to f_{mol}

For both *chem* → *mat* and *mat* → *chem* objectives, the influence of mechanical force on molecular reactivity relies on the coupling of macroscopic forces (F_{macro}) to molecular forces (f_{mol}), as depicted in Fig. 1. In the case of *chem* → *mat*, the relative onset of mechanochemistry *vis-à-vis* failure is important for stress-sensing, self-toughening and self-repair. For example, under what circumstances does molecular stress response occur prior to macroscopic failure? What is the correlation between the extent and distribution of molecular responses and macroscopic changes in properties? In addition to the threshold for molecular processes, the spatial (and temporal) distribution of f_{mol} as a function of F_{macro} and material architecture is crucial for *chem* → *mat* material design, because one would desire mechanophores in regions where they are most needed. The broad concerns in the case of *mat* → *chem* objectives are similar, because of the need to maximize f_{mol} and the desire to activate a high percentage of molecules with nearly the same f_{mol}, in order to provide consistent chemical activity. The question becomes: how does one choose a material architecture to accomplish these goals?

It is well accepted that forces are not distributed homogeneously throughout a material under load. Finite elements, and related continuum models, are often used to predict or explain the distribution of forces and resulting deformation in a material under load. One illustrative example of the information extracted from these models is that the "intermediate zone" of the temporomandibular joint disc, located between the mandible and skull, experiences the most stress during clenching of the jaw.[44] Analyses of this type are useful in that one can assess, for example, the influence of the direction of force loading on the accumulation of force in different regions of the material. As is the case in the example provided, most analyses predict deformations at the macroscopic or mesoscopic level, and they do not specifically address molecular distributions of f_{mol}, although recent efforts are focused on developing atomistic finite element models that would be useful in this regard.[45] Still, the continuum models provide useful information for material design. For example, experiment and theory show that forces in composites under load are typically concentrated at the interfaces between components.[46] From the *chem* → *mat* standpoint, this demonstrates that interfaces are logical sites for failure detection, suppression, and/or repair. Similarly, for *mat* → *chem* applications, interfaces in composites provide an attractive location for the placement of mechanophores in order for them to experience the maximum f_{mol}.

The quantitative relationship between F_{macro} and f_{mol} is therefore of great interest, motivating the development of molecular probes that respond to a high stress environment by generating a spectroscopic signal that can be measured, imaged and used to quantify f_{mol} and its distribution. An important breakthrough in this regard is the demonstration by Davis *et al.* that a spiropyran derivative will change color and fluoresce in response to forces applied to both elastomeric and glassy spiropyran-embedded polymer supports.[47] Davis *et al.* used the spiropyran to map molecular force distributions in beads under compression. They found that fluorescence is concentrated in the center of the beads, consistent with the predictions of continuum mechanics models.[48] While the fluorescence patterns confirm relative stress distributions, it is important to note that they have not yet been correlated with specific values of f_{mol}.

Stress-induced material coloration has also been shown during tensile elongation of dye-containing polyethylene films.[49] This mechanochromic material was prepared by the melt-processing of polyethylene with oligo(phenylenevinylene) (oPV) luminescent dyes. During mechanical deformation, oPV aggregates within the polymer films were broken up resulting in the formation of fluorescent oPV monomers that served as reporters of localized mechanical deformation.

Other examples of mechanochroism have been observed by the use of FRET pairs[50,51] incorporated within polymeric materials. Karthikeyan and Sijbesma took advantage of poly(tetrahydrofuran) (pTHF) bis-urea elastomers that phase separate into 'soft' pTHF and 'hard' bis-urea segments.[50] A substituted coumarin FRET donor with hard bis-urea segments and naphthalimide FRET acceptor with soft pTHF substituents were prepared and mixed with native pTHF/bis-urea polymer, resulting in elastomeric films in which the FRET donor and acceptor were separated into either the hard or soft segment of the material. The elastomers were then subjected to strains of up to 500%. With increasing strain, the FRET signal was observed to decrease, suggesting that proximal donor/acceptor pairs were "pulled apart" under polymer tension. Of particular significance is that the FRET pairs probe strains on a length scale of tens of nanometres, intermediate to that of the spiropyran-functionalized acrylates and oPV blends.

The Clark group was also able to employ FRET with a protein based nanosensor to detect structural deformation in a polymer matrix (Fig. 3).[51] Whereas Karthikeyan *et al.* showed a net separation of FRET pairs with increasing material strain, Clark *et al.* showed the opposite effect. FRET pairs were encapsulated within a thermosome and covalently attached within a polyacrylamide hydrogel. During the hydrogel preparation, the internal stresses within the polymer served to separate the FRET pairs, leading to a low FRET signal in the native polymer. Upon polymer deformation and subsequent crack formation, the polymer and thermosome locally relaxed, bringing the FRET pairs closer together and generating an increased FRET signal at sites of material damage.

Another approach to molecular stress distribution mapping is to couple fluorescence directly to bond scission reactions. Cho *et al.* prepared a material in which the cycloaddition of tricinnamates resulted in the formation of stress-bearing cyclobutane cross-links.[52] Fracture in the cross-linked material necessarily involves the rupture of covalent bonds. Here, a facile pathway for bond rupture is the reversal of the cycloaddition reaction, and so the cinnamates are formed again as part of material fracture. Because the cinnamates are good fluorophores, whereas their cross-linked cyclobutane form is not, crack

propagation can be monitored by fluorescence microscopy. This system allows for the detection of the exact position of cracks in a stressed material, but only *after* the destruction event had already occurred. The latter point highlights one of the main challenges in molecular strain mapping, in that the onset of known imaging signals is almost always coincident with an irreversible change in material properties, and so the use of molecular signals as a warning of impending damage (rather than an indicator of damage that has already occurred) that triggers external corrective action prior to failure is currently quite limited.

While *in situ* methods of molecular force mapping are clearly desirable, some questions regarding force distribution can in principle be answered by analyzing a polymer sample after the material has experienced a loading environment of interest. To that end, the use of highly functionalized polymers such as *gem*-dichlorocyclopropanated (*g*DCC) polybutadiene are potentially useful.[53] The *g*DCC mechanophore ring opens to form a 2,3-dichloroalkene product. This reaction is generally very slow under ambient conditions ($t_{1/2} \approx$ years), but it is accelerated by an applied tension and is effectively irreversible. As a result, a polymer can be placed under stress and then the fraction of activated *g*DCCs can be assessed afterwards by conventional organic spectroscopic methods. Because thousands of these mechanophores can be placed on a single polymer chain, the distribution of force within an individual polymer can be assessed. For example, under large extensional shear flows it has been reported that roughly 35% of mechanophores are opened on the time scale of rupture of a single bond.[53]

While much progress has been made towards mapping stress distributions in polymers, the noted examples currently do not provide quantitative information about the magnitudes of the molecular forces within those distributions. Such mapping could assist both those interested in *chem* → *mat* and *mat* → *chem* mechanochemistry, as discussed at the conclusion of this article. Questions of interest include: how many unstressed molecules are in the regions of high stress, and how many stressed molecules are in the region of overall low stress? How far apart must mechanophores be placed to ensure that at least one is activated prior to crack initiation anywhere in a material?

Force transmission, part II: from f_{mol} to specific atoms and bonds

For a given force f_{mol} acting on a specific polymer molecule, our next consideration is how molecular architecture directs the mechanical force associated with a polymer under tension (different molecular deformation modes, *e.g.* compression,[54] generate substantially different considerations) to specific bonds. The first point to mention is that the forces generated in a polymer under tension are (to first order) restricted to the polymer main chain, and therefore the primary mechanochemical coupling is restricted to the bonds that are within the polymer main chain. This defining characteristic creates a unique form of reaction regioselectivity in *chem* → *mat* applications, in that the same functional group can be selectively activated (or not) based on its position relative to the polymer main chain.[53] It also provides an important control experiment for supporting mechanochemical, as opposed to thermal or photochemical, mechanisms of induced reactivity.[47]

It is important to recognize that the details of force "funneling" depend on the nature of the macroscopic force. For example, the tension generated by extensional shear flow induces force accumulation at the center of the polymer chain, whereas static tension distributes force evenly along the polymer. The consequences of an uneven force distribution in extensional shear are most commonly manifested in the preference for midchain

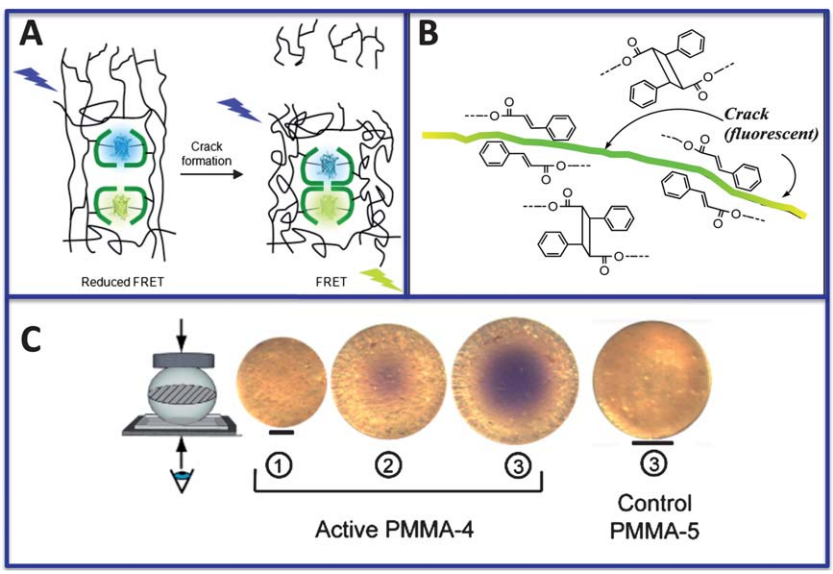

Fig. 3 Stress-mapping in polymers. (A) Plastic deformation due to crack formation and propagation allows for relaxation within the material and subsequent FRET signal increase.[51] Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission. (B) Crack propagation reforms fluorescent cinnamates through cycloaddition reversal.[52] Adapted with permission from Elsevier. (C) Compression of a glassy mechanophore cross-linked polymer demonstrating maximum tensile stress at the center of the bead as predicted by continuum mechanics model.[47] Reprinted by permission from Macmillan Publishers Ltd: Nature 2009.

scission in polymers during pulsed ultrasound. The growth and subsequent collapse of cavitation bubbles in solution create a substantial velocity gradient along the polymer backbone,[26] leading to nonequivalent force contributions at different polymer chain segments. Forces near the center of the polymer chain are sufficient to induce covalent bond rupture or trigger polymer mechanochemistry, and specific examples of ultrasound-induced mechanochemistry are discussed later in this paper. The differential force distribution is further supported by a lack of mechanophore activation when the mechanophore is placed at the end of polymer chains.[47] While the force is focused in the center of the chain, however, it extends well beyond a single bond, as evidenced for example by the previously mentioned example of *g*DCC-functionalized polybutadiene.

The rules that apply for extensional shear flow fields are not operative in the realm of static tension, generated, for example, by the forces associated with the spreading of brushlike macromolecules on a surface.[31] The even distribution of forces along these polymers results in randomly distributed carbon–carbon bond scission reactions; there is not a specific region along the main chain that is always stressed more than others.[31] This force distribution is also operable in single molecule force microscopy experiments.[55,56]

Unique molecular topologies introduce an additional method of channeling mechanical force to chemical bonds. For example, knots convert tension to a mixture of tension and constriction. As a result of the contributions from topological constriction, bond scission reactions are observed at much lower forces than from pure tension alone.[57] For example, tying a knot in an actin filament followed by stretching the filament with optical tweezers led to filament fracture in ~10 s at a pulling force of 1 pN. This combination of tension and constriction greatly reduces the forces required to break bonds considering the tensile strength of unkotted actin is ~600 pN.[57] Similar effects apply to synthetic polymers. Molecular dynamics simulations have been used to show, for example, that C–C bonds in knotted polyethylene experience much greater stress at the entrance and exit to a knot *vs.* those along unknotted segments when the polymer is placed under tension[57–60] (Fig. 4). The use of synthetic knots and related molecular topologies might therefore provide a distinct mechanical advantage for new classes of highly active mechanophores.

Force transmission, part III: the force–reactivity relationship

Once a mechanical stress has been transmitted through a material to individual polymers, and then to specific bonds within the polymer, the final consideration is how forces couple to various reaction mechanisms, or, alternatively, how the rates of reactions vary as a function of applied force. In many circumstances (although, as discussed below, certainly not all), the observed trends in mechanical activity are immediately and intuitively satisfying. For example, weak covalent bonds are often more likely to undergo force-induced homolytic bond scission than are stronger bonds. The preferential scission of weak bonds has been observed, in ultrasound-induced degradation studies, for peroxides within poly(vinylpyrrolidone)[61] and diazo linkages within poly(ethylene glycol).[5] Karthikeyan *et al.* have reported that the coordination bonds between silver and polymer-tethered *N*-heterocyclic carbene ligands are especially susceptible to sonication-induced scission, to the extent that the polymer molecular weight could be clipped to values well below 10 kDa—far smaller than the limiting molecular weights observed in conventional covalent polymers.[62]

The relationship between bond strength and mechanical stability is not absolute, however. Beyer quantified the force-dependent lifetimes of several different covalent bonds using density functional theory,[63] taking the shape of the potential energy surfaces into account in the application of eqn (1). The calculations show that, in general, homolytic bond rupture will occur first for bonds with lower bond strength, but that the relationship is not absolute, depending on the magnitude of the forces.

Another reasonable expectation is that reactions that proceed through similar geometry changes (*i.e.*, similar reactants proceeding *via* the same mechanism) should exhibit similar force dependencies (consider two reactions for which the values of Δd, eqn (1), are the same). This homology between reaction mechanism and mechanics was observed in one of the first experimental characterizations of well-defined mechanochemical reaction other than homolytic bond scission. Single-molecule force spectroscopy (SMFS) analyses of ligand exchange in Pd pincer complexes have shown that mechanical activation accelerates bimolecular substitution reactions, and that the magnitude of the acceleration is effectively identical for the force-induced dissociation of two different pyridine ligands from the same metal center.[64]

Quantifying the effects of force on reaction rates can be complicated, as demonstrated by two contrasting studies of the effect of force on the reduction rate of a disulfide bond (Fig. 5). Ainavarapu *et al.* showed that the reduction rate increased tenfold when subjecting a disulfide-containing protein to mechanical forces of 100 to 400 pN, applied to single molecules using an atomic force microscope. The authors concluded that the increase was due to a lengthening of the disulfide bond at the transition state, and that the magnitude of the effect was consistent with the expected values of Δd associated with the

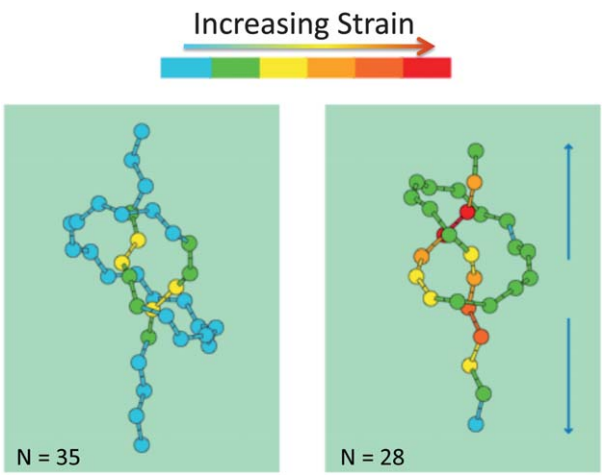

Fig. 4 Constrained classical MD simulations show that tightening a polyethylene knot leads to strain localization on bonds at the entrance and exit of the knot.[60] Adapted by permission from Macmillan Publishers Ltd: Nature 1999.

lengthening of the sulfur–sulfur bond.[55] Conversely, Kucharski *et al.* used the force associated with the internal strain of a macrocycle to show that applying a force of approximately 350 pN along the bond of interest had no measurable effect on the rate of disulfide reduction, commenting that previously observed rate enhancements were likely due to an increased accessibility of the disulfide bond to solvent soluble reductants.[65] This result contrasts significantly from a prior, related study of cyclobutene ring opening, for which a greater than 10^6 fold acceleration was observed.[66] Notably, the values of Δd for the scissile bonds are similar for the two reactions. The authors note that while the S–S bond elongates to the appropriate transition state geometry, the separation between attached methylenes does not change over the course of the reaction, due to rehybridization at sulfur under the nucleophilic attack from a free thiolate. Consistent with this interpretation, the carbon–carbon distance between outwardly rotating methylenes in cyclobutene increases more than that of the carbon atoms in the scissile bond, and it is the latter separation that matches the experimentally measured rate dependence. The nature of the experiments might also contribute to the difference in results, as recent work has shown that mechanochemical coupling in polymers might differ significantly from direct coupling of force to a small molecule.[67] The complexities associated with force coupling have been demonstrated previously in the mechanochemistry of noncovalent interactions, in particular the forced unfolding of proteins.[68–70] Together, these results emphasize the complexity of the force–reactivity relationship, and indicate that a more complete model for a description of the coupling of mechanical force in polymers to the molecular reaction coordinate is still required.

The magnitude of accessible mechanical forces, relative to interatomic forces, holds special promise for *mat* → *chem* mechanochemistry. This is certainly true in polymer sonochemistry, where mechanical forces have been used to effect rapid homolytic scission of strong (*e.g.*, carbon–carbon) covalent bonds. As such, ultrasonication has the ability to force molecules into reaction pathways that are otherwise impossible (Fig. 6). This potential of a mechanochemical approach was recently demonstrated for the ring opening of benzocyclobutene.[72] Hickenboth *et al.* showed that ultrasonication of solutions of benzocyclobutene (BCB) centered polymers accelerated the electrocyclic ring opening of the BCB. When the BCB was pulled open *via trans* attachments to the polymer, the thermally allowed conrotatory ring opening was accelerated. When the BCB was coupled to the polymer *via cis* attachments, however, the mechanical forces steered the ring opening in the symmetry-forbidden disrotatory path. For the organic chemist, this result highlights a critical aspect of mechanically initiated reactions—that a mechanical force can alter a potential energy surface such that a 'forbidden' process becomes accessible, even to the extent that it is the sole detectable reaction pathway. This type of control, realized in forcing both *cis* and *trans* benzocyclobutene to proceed through an *E,E-ortho*-quinodimethane intermediate, cannot be achieved by adjusting any chemical or physical parameter of the system. The reaction is simply biased towards the transition state which best relieves the applied stress.

Hickenboth *et al.*'s results speak more generally to the potential utility of mechanically assisted rate accelerations. Indeed, the allowed (~40 kcal mol^{-1}) and disallowed (~60 kcal mol^{-1}) BCB ring openings[72] have activation energies that are comparable to or exceed that of those processes that require high temperatures (~150 °C) and long times in order to be useful on the lab bench. Under shear-induced mechanical stretching, however, both reactions proceed in a matter of minutes at less than 10 °C. Even more interesting is that the disallowed disrotatory ring opening of *cis*-benzocyclobutene (~60 kcal mol^{-1}) proceeds as fast or slightly faster than the allowed conrotatory opening of the *trans*-adduct (~40 kcal mol^{-1}), despite the fact that thermolysis of *cis*-benzocyclobutene leads not to diene products, but to a complex mixture of degraded products. Using theoretical calculations, it has been shown that between 0.51 and 1 nN of force is enough to bring the disrotatory and conrotatory pathways to equal barrier heights[73,74] and that the barrier to conrotatory ring opening in the *trans* isomer disappears above 2 nN of applied force.[73]

The notion of a 40 kcal mol^{-1} activation barrier essentially disappearing has been taken one step further in a recent report using ultrasound to activate *gem*-difluorocyclopropane (*g*DFC)–polybutadiene copolymers.[75] The mechanochemical activation of the *g*DFCs leads to the conversion of the more stable *trans*-*g*DFC into its less stable *cis*-*g*DFC isomer. Notably, this

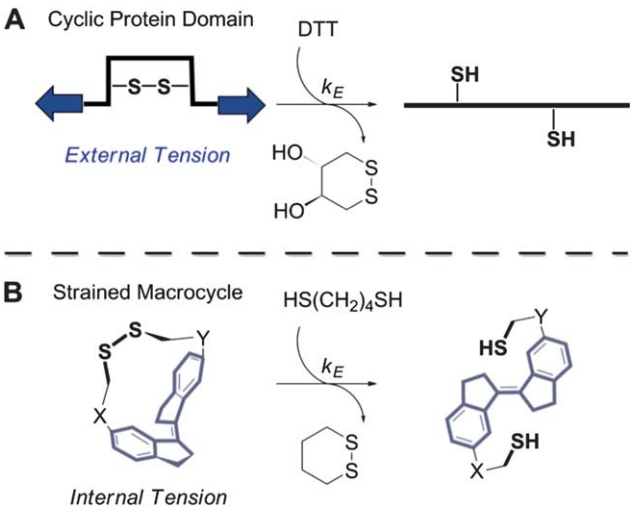

Fig. 5 The effect of force on the rate of disulfide reduction. (A) Pulling on disulfides within a biopolymer strand *via* AFM leads to an acceleration in the rate of disulfide reduction.[71] Copyright (2006) National Academy of Sciences, USA, and adapted with permission. (B) In comparison, forces applied to disulfides within strained macrocycles result in negligible changes in the rate of reduction.[65] Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Adapted with permission.

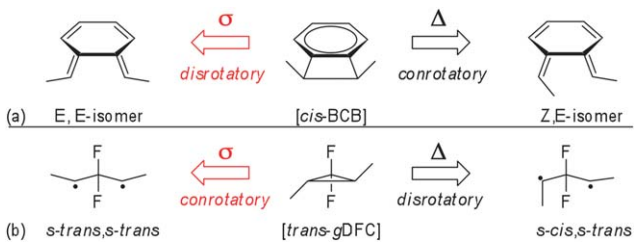

Fig. 6 Applying a mechanical force (σ) fundamentally alters the potential energy surface of ring opening reactions, providing access to thermally *forbidden* reaction products as observed in the electrocyclic ring opening of (a) *cis*-BCB and (b) *trans*-*g*DFC.

isomerization corresponds to a net contraction of the *g*DFC in response to transient extension. The results imply a mechanism in which the *g*DFC is pulled open into and held in an extended 1,3-diradical conformation that is formally a transition state in the force-free isomerization of *g*DFCs, and this picture is supported by electronic structure calculations and molecular dynamics simulations. The mechanical forces are sufficiently high that a structure that is typically the global maximum on the reaction potential energy surface is trapped as the global minimum. The net formation of the *cis*-*g*DFC isomer reflects the dynamics of the transition state once the force is removed. The diradical, which typically exists only over the course of a single vibrational motion ($<10^{-13}$ s), is trapped by the coupled tension for long enough ($>10^{-9}$ s) that it can be trapped chemically by the addition of free radical trap.

In addition to the consequences for *mat* → *chem*, the BCB and *g*DFC work have significant implications for *chem* → *mat*. The activation of BCB and the subsequent addition to the *o*-quinodimethane intermediate was demonstrated in the absence of chain scission, demonstrating that mechanically triggered bond forming reactions could occur in advance of chain scission. If similar reactivity could be used to create stress-responsive cross-linking in materials, it would represent a potential approach to redistributing load in regions of high stress. Along those lines, the formation of numerous, reactive diradicals along the main chain of *g*DFC-functionalized polymer can be thought of as a proof-of-concept for a notional "mechanoplasma", in which mechanical force triggers a large number of highly reactive radical species that might be useful in various cross-linking strategies.

Another example of mechanochemistry with *mat* → *chem* implications is the force-induced isomerization of binaphthyl atropisomers.[76] The thermal interconversion of these stereoisomers is complicated by their decomposition at the temperatures required for timely isomerization. Wiggins *et al.* have shown that mechanical forces can be employed to effect this isomerization quantitatively without any detectable damage either to the binaphthyl or the polymer tether used to transmit force. Because these molecules represent a class of important ligands in asymmetric synthesis, the ability to manipulate their conformation under otherwise benign conditions might create new methodological avenues.[77]

In addition to stoichiometric reactivity, mechanical forces have been used by Sijbesma's group to activate latent catalysts by displacing a ligand from its coordinated metal.[78] Among the catalysts whose activity has been demonstrated is a ruthenium-based metathesis catalyst.[78] The activation of a metathesis reaction holds particular significance for potential *chem* → *mat* applications, because the chemistry could be used to repair local cross-links and/or initiate ring-opening metathesis polymerization within materials in response to otherwise catastrophic levels of stress.

Future prospects

We conclude with a subjective and speculative look at the future of polymer mechanochemistry, as defined in this article. The following is perhaps less prediction than "wish list", and we openly admit that we do not necessarily see a clear and unimpeded path forward to realizing all of these goals. On the other hand, we are aware of no definitive physical limits that preclude any of them, and we admit to ongoing attempts at the realization of several within our own laboratory (Fig. 7).

1. Quantitative stress–strain mapping of molecular force distributions

What fraction of molecules experience what level of tension under various macroscopic loads? What are the relevant scales of heterogeneity (both spatial and temporal) in molecular force distributions? Understanding where stresses are greatest in a material is crucial to both angles of mechanochemistry, so that active moieties can be placed in the regions of greatest stress in order to achieve maximum activation. There is, deservedly, much current activity in this area, particularly in the development of new molecular probes. We are particularly intrigued by the possibility of: (i) probes that report a range of molecular stress/strain states, rather than on/off signals in response to a threshold value; (ii) probes that permit a quantitative, ratiometric fluorescent signal that can be used to quantify response down to the single molecule level, in order to reveal subpopulations of states within what is likely to often be a heterogeneous ensemble.

2. A "perfect" stress distribution (or as close to it as possible)

For *mat* → *chem* applications in particular, it would be highly desirable to devise material platforms within which large numbers of mechanophores can be activated simultaneously and to equal molecular forces. These platforms might also be useful in their ability to produce dramatic changes in properties in response to critical levels of stress for *chem* → *mat* applications. We propose elastomeric bimodal networks as one example of a candidate material that can tolerate high strains with theoretically even molecular force distributions.[79]

3. Molecular stress relief

Polymer material failure is often attributed at the molecular level, to regions of localized, high stress concentration. We envision mechanochemical processes that lead to a redistribution of that stress away from the polymer segments that are in danger of failing, but preserve them as active, stress-bearing segments. One potential mechanism is "stress relief", in which the critical chain segments react so that they become irreversibly longer prior to failure, creating slack in the at-risk segments and providing the opportunity for redistribution of stress to nearby segments. The stress relief strategy has proven useful in noncovalent mechanochemistry, where forced unfolding of modular domains creates toughness in biological systems such as titin and synthetic polymers inspired by titin and related biological systems.[80,81] Unlike the noncovalent systems, covalent stress relief would typically be irreversible, triggered at very large forces, and able to provide extensions in increments of angstroms. We wonder about the macroscopic consequences of such molecular processes. How much molecular slack is necessary to create a meaningful response? The *gem*-dihalocyclopropanes[53] represent one intriguing candidate for initial studies.

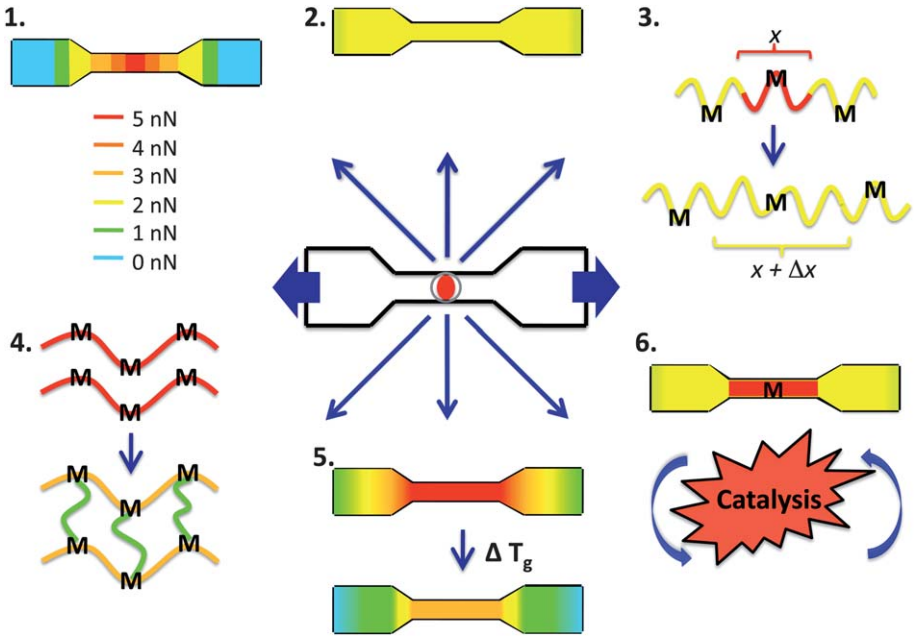

Fig. 7 A partial "wish list" for mechanochemically active polymers, *circa* summer of 2010. Numbers correspond to the list of topics provided, along with brief descriptions, in the main text.

4. Stress-induced cross-linking

Another mechanism by which critical levels of stress might be locally redistributed is through stress-induced cross-linking. For this to be possible, stress must activate a bond forming reaction that creates a new cross-link prior to, or immediately following, chain scission. Prior work on BCB-containing polymers shows that bond formation can be triggered without chain scission, but applications in materials require an affirmative answer to slightly different questions: can more bond-forming reactions than bond scission reactions be induced under conditions of chronic, destructive load? Can the bonds that form actively bear stress, or must they involve a reaction that forms an unstressed final state? The challenges involved in forming a bond that is immediately stress-bearing suggests potential synergies with the stress-relief strategy proposed previously.

5. "Mechanoplasticizers" and "mechano-antiplasticizers"

The free volume and glass transition temperature (T_g) of a polymer have important consequences for its modulus and mechanical properties. We wonder about the consequences of mechanochemical transformations in polymer structure that alter the local T_g relative to that of the bulk, and whether raising or lowering (or both, or neither) would exacerbate or ameliorate the concentration of stress that presumably triggered the mechanochemistry.

6. Fluxional mechanocatalysis

Polymers change their conformations under tension, from adopting an all-*trans* conformation along the backbone of polyethylene[82] to chair-to-boat transitions in polysaccharides.[83] We see no reason that well-defined conformational changes could not be coupled to catalysis, in a manner that complements the activation of latent catalysts reported by Piermattei *et al.*[78] Here, catalyst structure could be tuned and/or reversibly switched between multiple active states, providing a new route to catalyst optimization and potentially access to new products, if catalyst switching could be driven on the time scale of catalytic turnover.

Conclusion

Regardless of its specific future path, the recent explosion of successes in the field of polymer mechanochemistry seems certain to continue for the foreseeable future. The immediate challenges comprise the fundamental and the applied, the technical and the theoretical. We argue that the field represents an exciting opportunity for materials chemistry, lying at the confluence of chemical reactivity and polymer materials science, and through which the capabilities of chemistry and materials might provide useful approaches and solutions to important challenges in the other.

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