Critical review of experimental polymer mechanochemistry and its interpretational frameworks.

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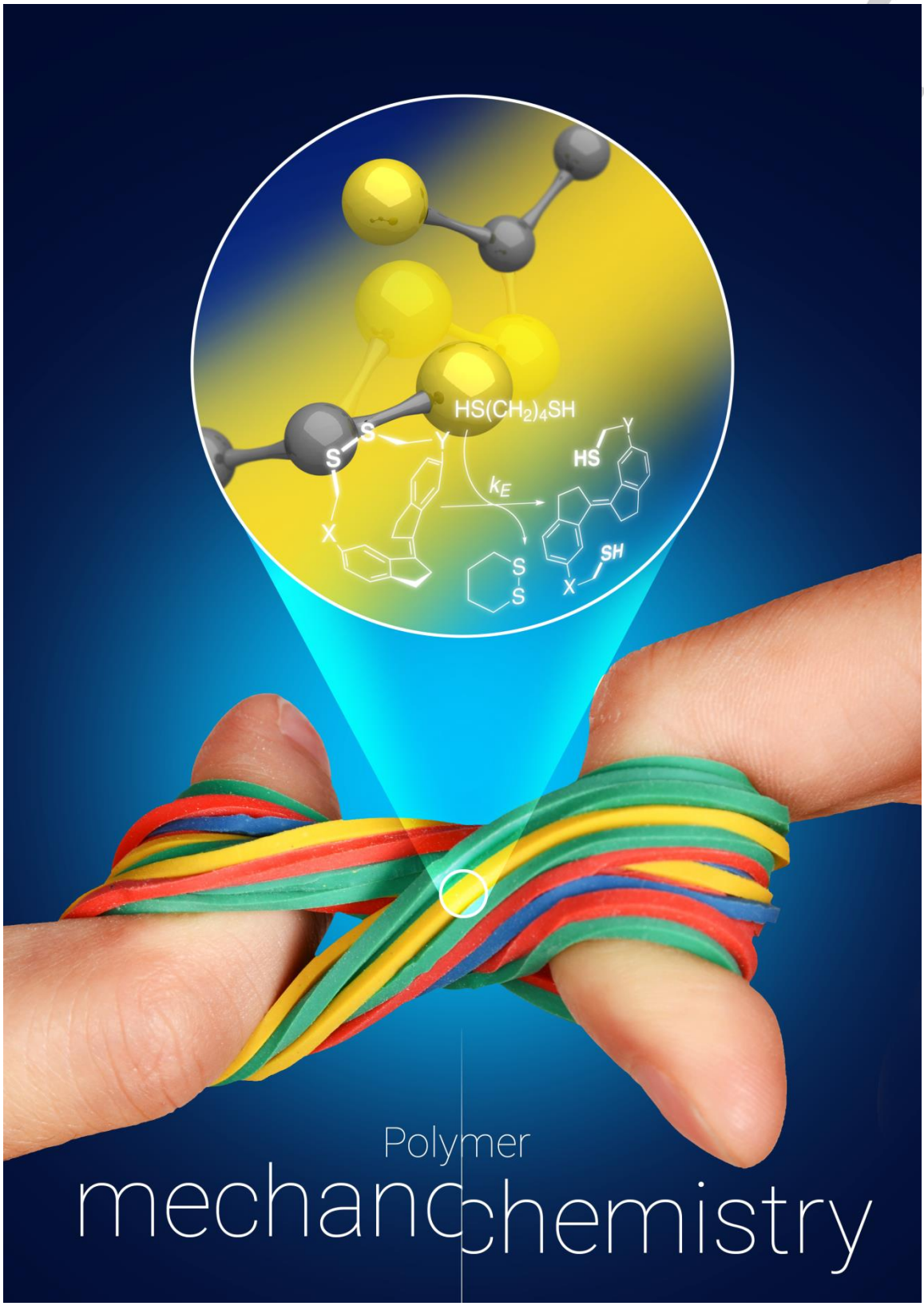

Abstract: Polymer mechanochemistry is an emerging field at the interface of chemistry, materials science, physics and engineering. It aims at understanding and exploiting unique reactivities of polymer chains confined to highly non-equilibrium stretched geometries by interactions with their surroundings. Macromolecular chains or their segments become stretched in bulk polymers under mechanical loads or when polymer solutions are sonicated or flow rapidly through abrupt contractions. Increasing amount of empirical data suggest that mechanochemical phenomena are widespread wherever polymers are used. In the past decade, empirical mechanochemistry has progressed enormously, from studying fragmentations of commodity polymers by simple backbone homolysis to demonstrations of self-strengthening and stress-reporting materials and mechanochemical cascades using purposefully designed monomers. This progress has not yet been matched by the development of conceptual frameworks within which to rationalize, systematize and generalize empirical mechanochemical observations. As a result, mechanistic and/or quantitative understanding of mechanochemical phenomena remains, with few exceptions, tentative. In this review we aim at systematizing reported macroscopic manifestations of polymer mechanochemistry, and critically assessing the interpretational framework that underlies their molecular rationalizations from a physical chemist's perspective. We propose a hierarchy of mechanochemical phenomena which may guide the development of multiscale models of mechanochemical reactivity to match the breadth and utility of the Eyring equation of chemical kinetics. We discuss the limitations of the approaches to quantifying and validating mechanochemical reactivity, with particular focus on sonicated polymer solutions, in order to identify outstanding questions that need to be solved for polymer mechanochemistry to become a rigorous, quantitative field. We conclude by proposing 7 problems whose solution may have a disproportionate impact on the development of polymer mechanochemistry.

1. Introduction

Polymer mechanochemistry aims at understanding and exploiting reactivity of macromolecular chains in highly non-equilibrium stretched geometries resulting from interactions between the chains and their surroundings. The most common means of creating such highly stretched chains (or at least parts of chains) is to mechanically load a bulk polymer, hence the "mechano" part of the name. At the macroscopic scale, such loading compresses, stretches, shears and/or twists the material. These macroscopic dimensional changes are ultimately accommodated, at least in part, by stretching of individual polymer chains. An unknown, but probably very small, fraction of the chains is stretched enough to manifest chemical reactivity that is considerably different from that observed in the same polymer in its minimum-energy geometry. For example, force of 5 nN stretching a single chain of polystyrene reduces the half-life of its backbone C-C bonds from 10^{38} years to the microsecond time scale at 300 K.

Such load-induced polymer fragmentation was discovered soon after the modern concept of the polymer emerged.[1] Because polymers are subject to mechanical loads throughout their lifecycle, from production to recycling, the technological importance of polymer mechanochemistry is probably far greater than is currently appreciated. Polymer mechanochemistry is almost certainly a key yet poorly understood determinant in the origination and growth of microcracks that contribute to catastrophic failure of polymers.[2] Mechanochemical polymer degradation probably affects the behavior of tires, desalination membranes and polymer-modified surfaces, such as the ones used in microfluidic diagnostics[3] and high-performance liquid chromatography. It's likely important in jet injections (for example in inkjet printing of organic electronic circuits), polymer melt processing, high-performance lubrication,[4] enhanced oil recovery by polymer flooding[5, 6] and turbulent drag reduction schemes.[7, 8] Importance of mechanochemical fragmentation of biopolymers during handling of their solutions has long been recognized[9] and occasionally exploited.[9, 10] The connection between tribochemistry and mechanochemistry is well appreciated.[11, 12] In most (but not all) of these examples, mechanochemical effects are deleterious, leading to, or accelerating, the loss of function.

Exploiting mechanochemical phenomena can yield new materials and processes, including very tough elastomers; materials capable of autonomously reporting their "overstressed" regions at high risk of catastrophic failure; and/or are self-reinforcing, i.e., capable of autonomously generating more than 1 new load-bearing bond per each bond lost by load-induced molecular fragmentation. Carefully designed mechanochemical reaction cascades may yield fundamentally new tools to study polymer dynamics at high temporaspatial resolutions. Exploiting the coupling between localized reactivity and macroscopic dynamics could yield practical photoactuation,[13] which is direct conversion of light into motion to power autonomous micromechanical devices and control information flow in optical computing without the intermediacy of thermal or electrostatic gradients and methods to capture waste mechanical energy. A few of these potential applications have been prototyped and demonstrated at the proof-of-concept level, but most remain speculative.

A major challenge in learning how to engineer macroscopic mechanical properties of materials at the single-monomer level, whether or not they involve chemical reactions, is the coupling of dynamic processes across multiple length and timescales.[14] In mechanochemistry, this means that dynamics at the macroscopic scale is governed by and directly controls correlated motion of atoms responsible for chemical reactions, which therefore cannot be averaged out and hence adequately "coarse-grained" into a few continuum parameters, but must be considered explicitly. In contrast, in conventional chemistry reaction rates are almost always independent of the motion of macroscopic objects. In the rare cases of a dependence (e.g., flame chemistry in the chamber of an internal combustion engine[15]) coupling between the macroscopic and molecular dynamics can be adequately described by time-dependent macroscopic parameters, such as pressure or temperature.

In chemical kinetics, the Eyring equation relates the macro-

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scopic control parameter (temperature and pressure) to the rate constant by means of free energy of activation.[16] The equation is so useful in part because every parameter in it has a clear molecular interpretation, at least in the ideal gas approximation, arising either from the kinetic theory of gases or the statistical-mechanical definitions of thermodynamic functions. As a result the rate of a chemical reaction can often be predicted, with a reasonably useful accuracy, from quantum-chemical calculations. More broadly, reaction rates and how they change with temperature and pressure can be related to, and rationalized in terms of, molecular parameters of the reacting molecules. Without the ability to do so, modern chemistry would hardly exist.

The same cannot yet be achieved in mechanochemistry. Mechanochemistry introduces another macroscopic control parameter, such as stress tensor, that we know affects the kinetics of chemical reactions in the material. Empirical expressions relating stress to reaction rates have been proposed (see section 3, Mechanochemistry of polymers in solids below), but their parameters lack any molecular interpretation, making the equations neither general nor predictive and therefore of very limited utility. One problem is the lack of a theoretically sound molecular definition of mechanical stress.[17-19] In its absence, it may be possible to develop at least semi-quantitative models of polymer mechanochemistry that would be somewhat general and predictive by defining a hierarchy of mechanochemical phenomena (Figure 1). This hierarchy would allow the existing models that perform reasonably well within individual rungs of the hierarchy (e.g., chemical kinetics, statistical-mechanical models of quasi-universal chain dynamics[20], continuum mechanics, etc.) to be applied systematically to relating the macroscopic stress tensor (or other quantifiers of mechanical load) to rates of chemical reactions. A similar multiscale approach has proven successful in diverse areas of physical[21] and biological[22] sciences, and engineering.[23]

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Roman Boulatov received his PhD from Stanford University for synthesis and studies of metalloporphyrins in context of biomimetic studies of respiratory oxygen reduction and as platforms supporting unusual chemical bonding. After a postdoc at Harvard, he joined the University of Illinois, Urbana. During the time at Illinois he developed a suite of experimental, theoretical and computational methods to explore, understand and exploit chemical reactions that occur when polymeric materials are subject to mechanical loads. He moved his research group to the University of Liverpool in September 2012. His interests include the development and application of chemical tools to study macromolecular dynamics and response of soft matter to mechanical loads.

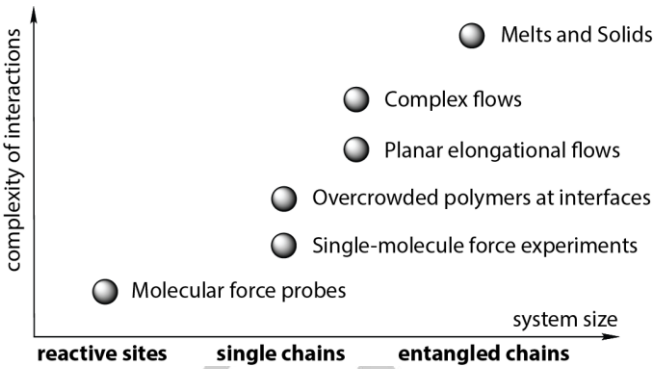

Figure 1. A plausible hierarchy of mechanochemical phenomena. Model studies of mechanochemistry using small-molecule ("molecular force probes") and overcrowded polymers at interfaces were reviewed in [24]. All other manifestations of polymer mechanochemistry are discussed below.

An example of such an approach, based on the concept of restoring force, is sketched in Figure 2. The restoring force of a strained object is the force that attempts to recover the original, unstrained shape of this object: for example, when we stretch a rubber band, the restoring force of the band is what pulls our hands closer together. First, the macroscopic control parameter(s) that govern the macroscopic response of the material to mechanical deformation are related to the distribution of single-chain forces of the constituent macromolecules (or their segments between, for example, entanglement points or chemical cross-links). It seems reasonable to assume such a relationship to be quasi universal, e.g., the same for chemically distinct polymers with comparable chain stiffness. Knowing the tensile force acting along a polymer chain (or its segment) may allow the force experienced by the constituent monomers (or more formally, the restoring forces of the relevant molecular degrees of freedom of the stretched chain[25]) to be estimated. The distribution of local restoring forces along the chain certainly depends on the chain composition[26] but it may be amenable to accurate description using simple force fields of molecular mechanics. This is already possible for the simplest examples of polymer mechanochemistry, observed in single-molecule force experiments,[26, 27] which allow direct measurements of the relationship between single-chain force and local reactivity as discussed below. Finally, the local restoring force is then used to estimate the changes in the chemical reactivity of the anisotropically strained reactive site. It appears that for most (or maybe any) highly anisotropically strained reactive site, a local molecular coordinate exist whose restoring force uniquely determines the strain-induced perturbation of the reactivity. This relationship is available from quantum-chemical calculations[11, 12] (see below) and usefully accurate estimates can even be obtained in some cases without extensive calculations.[27, 28] Experimentally it has been elucidated using purposefully designed non-polymeric models of reactive sites in stretched polymers that allow fairly straightforward quantification of the molecular strain by force (so called molecular force probes[29-35]).

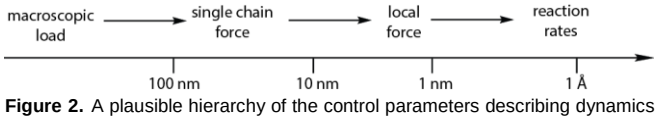

Figure 2. A plausible hierarchy of the control parameters describing dynamics at various scales determining the chemical response of polymer materials to mechanical loads. [36]

The advantage of discussing mechanochemical reactivity in terms of force-dependent reaction rates (i.e., of integrating force

into the standard formulations of chemical kinetics) is the same that favors Newtonian vs. Lagrangian formulation of classical mechanics: force offers a "kind of approximate, truncated description of the dynamics of matter [that] is easier to use and focuses on the relevant"[37] than the alternatives. Although this force-based modelling of mechanochemical kinetics introduces some conceptual difficulty (e.g., how to quantify molecular strain in terms of force), which is avoided when limiting oneself to energies, force is an intensive property. This means that it captures equally well the reactivity-perturbing effect of the distortion imposed on a small molecule by constraining one of its non-binding internuclear distances to a non-equilibrium distance in a quantum-chemical calculation or in a polymer stretched in an elongational flow, regardless of the length of the polymer or the small-molecule model.

1.1. Hierarchy of mechanochemical phenomena

Mechanochemistry aims at understanding and exploiting the changes in chemical reactivity induced by stretching polymer chains. Chains can only be stretched if they couple to their surroundings in a specific way. Details of this coupling determine how much, how fast and for how long a chain is stretched and hence the range of chemical reactions that may be observed. The complexity of the coupling also determines how amenable the resulting mechanochemical response is to detailed atomistic description and how generalizable it is.

At a minimum a stretched polymer chain must couple to its surroundings at two points to maintain its high-energy non-equilibrium geometry. Single-molecule force spectroscopy (SMFS) comes closest to realizing this conceptually simplest coupling mode. In SMFS an isolated polymer chain is connected to a surface of a positional scanner at one end and an AFM tip at the other (Figure 3)[38]. The resulting macromolecular bridge is stretched by translating these two microscopic objects away from each other. Unlike any other manifestation of polymer mechanochemistry, SMFS allows direct control of how much and how fast the chain is stretched and a reasonably accurate estimate of the force needed to achieve this strain. The output of a SMF measurement is a force/extension curve and the fact that stretching a chain induces a chemical reaction is established by the existence of specific features of such curves.

Because on the time scale of milliseconds or longer the stretched chain is in an internal mechanical equilibrium, a fairly simple relationship exists between the strain (or force) imposed on the chain termini and that of any of its constituent monomers.[25] Consequently, an adequate model of a SMF experiment is the polymer chain (or its portion) with a compressed (harmonic or overdamped) spring connecting two of its atoms. Because such a model is compatible with molecular electronic structure methods, such as DFT, force/extension curves are the only examples of polymer mechanochemistry that can be predicted semi-quantitatively by quantum-chemical calculations.[33, 39] While the technical aspects of SMFS limit the range of reactions and rate constants that are amenable to such studies and preclude the use of spectroscopic techniques to establish the product(s) of these reactions[36], it is a powerful tool to study polymer mechanochemistry in its simplest. Mechanochemistry of certain dihalocyclopropanes, cyclobutanes, spiropyrans and azobenzene observed by SMFS appears to be qualitatively similar to that induced by mechanical loading of amorphous samples and/or sonication of dilute polymer solutions. An important if rarely discussed conceptual challenge in generalizing the results of SMF experiments to practically relevant manifestations of polymer mechanochemistry is how closely, especially quantitatively, the force/extension curves measured in SMFS represent ensemble-average behavior of the same polymer. The latter controls the chemical response of bulk materials to load, which controls practical manifestations of mechanochemistry. Whereas conventional chemical measurements represent an averaged behavior of trillions of molecules, each force/extension curve results from reactions of at best ~10^2 sites[39-48] (and sometimes as few as one[38, 49-51]) and most but not all studies of single-chain mechanochemistry reported to date are based on fewer than 15 curves. With such a limited number of events, even the most basic ideas of statistical data analysis, e.g., that the force at which a mechanochemical reaction is observed to occur is distributed normally around its ensemble-average value and hence the uncertainty of the estimated values can be represented by a variance, are not obviously applicable.

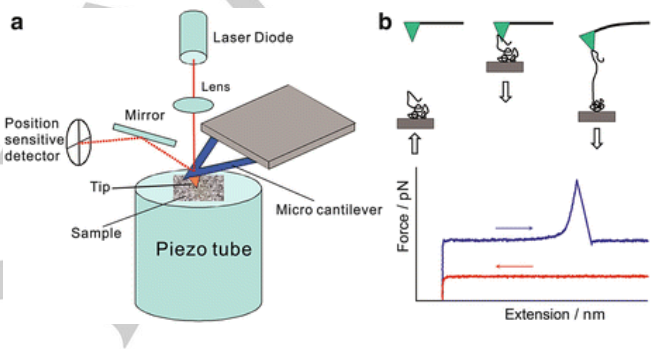

Figure 3. Basic setup of single-molecule force (SMF) spectroscopy with AFM (a) and force/extension curve obtained in a simple SMF experiment (b). In this example, when stretched to a sufficiently high force the chain simply fragments or detaches from one of the surfaces resulting in a mechanical instability as evidenced by a negative slope of the force/extension curve (b). Reprinted with permission from ref [52]. Copyright 2015 Springer International Publishing Switzerland

Isolated polymer chains in elongational solvent flows[53] constitute the next level of conceptual complexity in polymer mechanochemistry. In such flows the chain dynamics is determined by intermolecular interactions among thousands of its atoms and those of the surrounding solvent, and maintaining these interactions require constant input of energy into the system, i.e., elongational flows are dissipative.

Steady-state planar elongational flows with a stagnation point (Figure 4) are most amenable to quantitative microscopic modelling.[54] A polymer chain can be trapped at a stagnation point and kept in a stretched state for hours, under favorable conditions.[55] Chain dynamics in such flows has been extensively studied both experimentally and computationally[53] although no clearly established examples of a mechanochemical reaction in a polymer chain trapped at a stagnation point have ever been reported (early claims[56-58] are now thought to reflect mechanochemistry in turbulent flows away from the stagnation point[54, 59]). Because of the technical difficulties of generating flow rates high and stable enough to induce mechanochemistry in trapped chains, steady-state planar elongational flows have not found their application in modern polymer mechanochemistry despite being the simplest examples of polymer stretching by multi-site coupling between the chain and its surroundings.

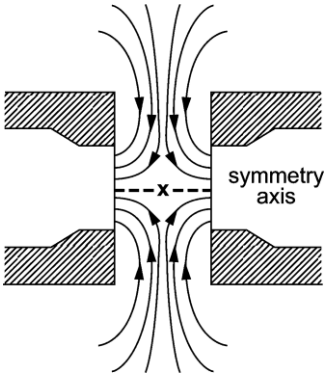

Figure 4. A schematic illustration of the flow field (arrows) in a steady-state planar elongational flow with a stagnation point (marked with x). Reprinted with permission from ref [60]. Copyright 2009 American Chemical Society. [56]

Widely-studied, technically simple but atomistically intractable realizations of polymer mechanochemistry in solvent flows are created by sonicating polymer solutions. The technique is characterized by a highly heterogeneous reaction environment where the macroscopic effects (e.g., changes in the chemical composition of the sonicated solution) result from a tiny but unknown fraction of the polymer solute subject to extreme microscopic conditions (e.g., flow strain rates) that change on the sub-μs timescales. Consequently, in contemporary mechanochemistry polymer solutions are sonicated primarily for qualitative demonstrations that a particular chemical reaction is induced by stretching a polymer containing a specific reactive site. Microscopic (much less atomistic) descriptions of mechanochemical response of sonicated polymer solutions are lacking. Given the likely extreme conditions responsible for polymer mechanochemistry during sonication, even semi-quantitative description of mechanochemical kinetics would represent a very demanding test of our understanding of chemical reactivities of molecules subject to very large anisotropic strain.

At least as conceptually intractable is polymer mechanochemistry in amorphous materials and melts. In such systems chain are stretched by complex, constantly changing chain-chain interactions that have so far proven resistant to theoretical description or atomistic computations. Consequently, molecular interpretation of load-induced chemical changes in amorphous polymers remains largely qualitative and the main focus in this area of polymer mechanochemistry has been on empirical exploration and some proof-of-concept exploitation of materials created by incorporating force-sensitive reactive sites into more inert polymer matrices.

Several examples were reported of overcrowded polymers at gas/liquid, liquid/solid and gas/solid interfaces and of surface-crafted polymer brushes undergoing spontaneous chain fragmentation or other reactions that were also observed in polymers under mechanical loads.[24] These systems are probably best viewed as models of polymer mechanochemistry because in most if not all the examples the polymers are confined to high energy reactive geometries not as a result of externally imposed load.

1.2. Experimental, computational and theoretical models of mechanochemistry

Most manifestations of mechanochemistry, particularly in technologically relevant contexts, remain intractable at the molecular level. This situation necessitates the use of model studies both to interpret and rationalize the existing phenomenology of polymer mechanochemistry and to develop, validate and refine the conceptual frameworks and quantitative descriptions of mechanochemistry. Experimental models of polymer mechanochemistry attempt to reproduce, either in non-polymeric molecules or in polymers not subject to mechanical load, the molecular strain that localized reactive sites experience in mechanically loaded macromolecules. The most important examples of non-macromolecular models are strained macrocycles based on stiff stilbene.[31, 36, 61] Overcrowded polymers stretch when placed at liquid/gas or liquid/solid interfaces, allowing reactive sites to be strained without loading the macromolecules mechanically.[24]

Although chemists have studied the effect of molecular strain on chemical reactivity for over a century, the strain responsible for mechanochemical reactivity of polymers is so different that reproducing it outside mechanically stretched chains requires new molecular architectures. The intrinsically high anisotropy of linear polymers means that localized reactive sites in stretched macromolecules are strained primarily along a single molecular axis, with several implications. First, this strain can be quantified as the strain energy gradient along this axis (i.e., restoring force of a specific molecular coordinate) instead of the traditional strain energy of physical organic chemistry. Second, the reactivity depends on what molecular axis the strain is applied to. Compared to classical strained organic molecules, models of polymer mechanochemistry are useful only if the underlying molecular architectures allow the tensile strain to be varied in sufficiently small increments over a reasonably wide range, including 0 force (i.e., strain-free reference). In contrast, most small strained molecules manifest compressive strain, lack well-defined strain-free references and do not come in series of gradually increasing strain.

The main advantage of non-polymeric models is their size, which makes them amenable to accurate quantum-chemical calculations. This not only allows the restoring forces of all internal molecular coordinates to be quantified (thus validating the assumption that the strain distribution of the reactive site mimics that in a stretch polymer and allowing direct mapping of the kinetics measured in such models to mechanochemical behavior of polymers[36]) but also explicit atomistic description of chemical kinetics to be compared with approximate, force-based one. Perhaps the main disadvantage of stiff-stilbene based models is the limited range of restoring forces that can be generated in the reactive site, which is mostly limited by the thermal stability of strained E stiff stilbene to ~1 nN. Overcrowded polymers allow localized reactive sites to be strained to much larger forces (probably up to ~2+ nN), but offer no means of quantifying these forces accurately.

Likewise, because direct quantum-chemical calculations of mechanochemical response of polymer chains remains beyond reach, computational mechanochemistry uses models of stretched polymers, typically by replacing most of the polymer, except for the reactive site, with a constraining potential[11, 12] (which is often, if not necessarily correctly, referred to as “force”). In other words, the stretched polymer is modelled by the reactive site with the pair of atoms at which it is connected to the polymer backbone constrained to a non-equilibrium value. In these models the constraining potential is a coarse-grained representation

of tens of thousands of molecular degrees of freedom of a stretched polymer. Such coarse-graining allows meaningful estimates of the reaction kinetics and mechanism in a stretched polymer because the polymer beyond the reactive site contributes to the kinetic barriers only by changes in its strain energy. Geometrical changes in the reactive site during the reaction allow the rest of the stretched polymer to partially relax, stabilizing the transition state(s) and reducing the height(s) of the kinetic barriers (in theory the strain of the rest of the polymer can also increase as a localized reaction happens, corresponding to load-inhibited reactions, but these cases have not yet been demonstrated experimentally in synthetic polymers). Fortunately, reasonable quantitation of these changes in the strain energy of the rest of the stretched polymer do not require detailed atomistic description of polymer geometries but can be approximated reasonably accurately as a product of the stretching force and the change in the length of the constrained distance between the reactant and the rate-determining transition state (so-called work).

Several implementations of this approach have appeared that are equivalent conceptually but vary technically in which parameter is under the user control: constraining force, constrained distance or the compliance of the constraining potential. The first two are the limiting cases of the third one, corresponding to the infinitely compliant and infinitely stiff constraining potential, respectively. In geometry optimizations under constant force (so-called EFEI (external force explicitly included) or EGO (enforced geometry optimization) models), molecular geometry relaxes until the restoring force of the constrained distance equals the applied force. In constrained optimizations the constrained distance remains fixed while the rest of the molecule relaxes, which typically decreases the restoring force of the constrained distance. All methods yield the same parameters and are equally appropriate for quantifying how the molecular geometry and energy changes in response to changing applied force using a series of static geometry optimizations.

Occasionally quantum-chemical models of localized reactions in stretched polymers are classified as isotensional or isometric (Figure 5), corresponding to either the constraining force or the constrained distance being constant in the reactant and kinetically significant transition states and intermediates. Isotensional models reflect the physical reality better when the molecular model is small but as the size of the model of the polymer increases, the difference between parameters (e.g., activation energies, reaction paths) computed under isotensional and isometric conditions decreases. QM molecular dynamic simulations are generally limited to very small polymer fragments and are therefore more physical when performed under isotensional conditions, as do reaction path calculations. Isometric conditions assume that the geometry and therefore the strain energy of the coarse-grained parts of the stretched polymer do not change during the reaction. This assumption is poor when the stretched polymer is modelled by just the reactive site, but when a sufficiently large part of the polymer is included, the energetic contribution of the coarse-grained parts becomes relatively insignificant (Figure 5).

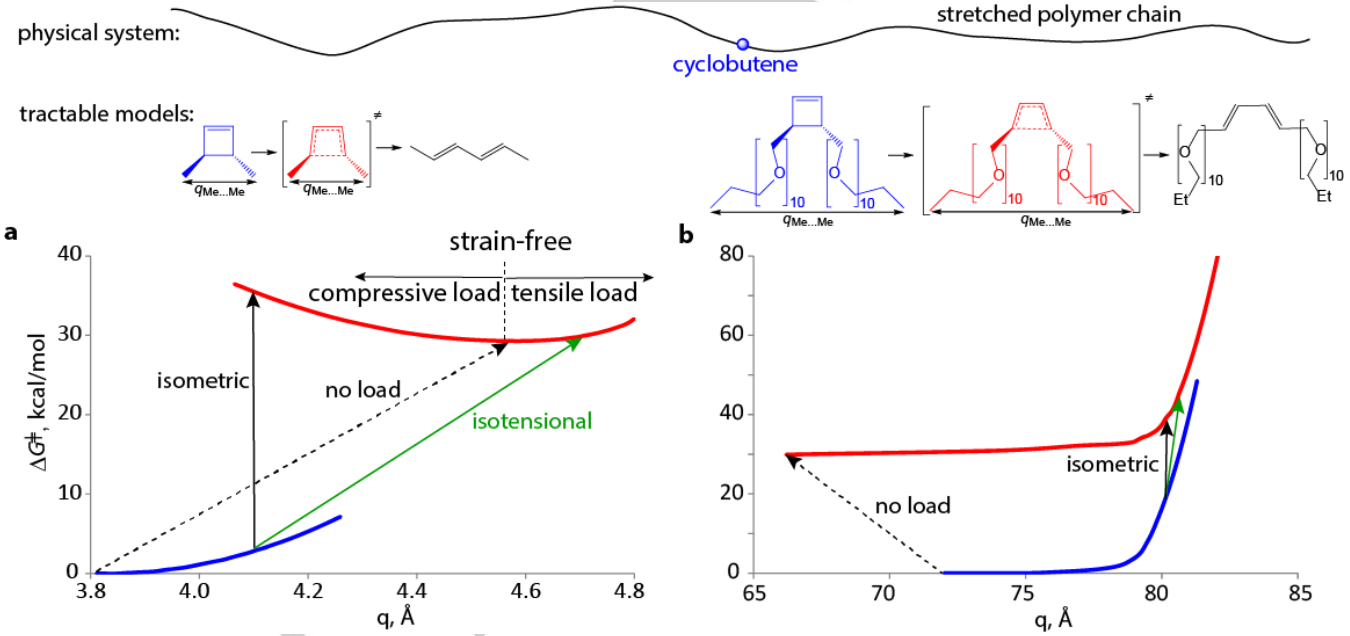

Figure 5. An illustration of the difference between isometric and isotensional models of cyclobutene isomerization in a stretched macromolecule using the minimal model of the reactive site (a) and a larger more realistic polymer fragment (b). Graphs are projections of the free energy reaction surface of cyclobutene isomerization along the internal coordinate defined by the separation of the C atoms of the methyl groups, $q_{Me...Me}$. Dashed arrows describe the transition in the absence of load and the solid arrows are transitions in the polymer stretched to 1.5 nN. In the minimal model (a) isometric and isotensional models are very different, with the isometric model corresponding to a nonphysical situation where isomerization of cyclobutene under 1.5 nN of tensile force generates the transition state with the geometry corresponding to 2.1 nN of compressive force. With the more physically realistic larger model (b) the difference between isotensional and isometric models is much smaller. The vertical displacement of the points connected by each arrow equals the activation free energy of isomerization in the strain-free and isometric regimes but does not include the changes in the strain energy of the constraining potential (so called "work potential") in the isotensional regime. With the work potential included, the activation free energy is smallest in the isotensional regime, with the isometric approximation approaching the isotensional value in the limit of large polymer fragment.

The timescales at which a small reactive site traverses an activation barrier, a long macrochain adjusts its conformation, and microscopic objects, such as an AFM tip adjust to changes in the geometry of the attached macrochain differ by orders of magnitude.[62] This means that during a mechanochemical reaction only a portion of the stretched polymer adjusts to changes in

the local geometry, with the rest of the polymer and the environment being stationary.[62] Consequently, a sufficiently large atomistic model of a polymer coupled to an infinitely stiff potential is probably the most realistic representation of mechanochemical reaction in a stretched polymer, at least in single-molecule force experiments. Sufficiently large means that at the same length of the constrained distance in the reactant and the rate-determining transition state the corresponding restoring forces are within a few percent of each other; alternatively, at the same applied force, the constrained distance in these two kinetically significant geometries is within <0.1%.

The question of the proper size of the polymer fragment containing the reactive site that has to be treated atomistically to correctly reproduce the mechanochemical reactivity has attracted much less attention that it deserves. Computed force-dependent free energies of activation using complete conformational ensembles of all kinetically significant stationary states of increasingly large fragments of macrochains clearly depend both on the length of the fragment and its composition.[27, 28, 33, 34, 63] A few single-molecule force experiments suggest that the molecular structure of the polymer beyond the immediate reactive site can affect the force at which the reaction is observed,[40] although the molecular mechanism of this effect has not been convincingly established.[26] In contrast the relationship between the restoring force of a local molecular coordinate of the reactive site (e.g., the separation of the methylene C atoms immediately adjacent to the cyclobutene ring in Figure 5b) and the changes in the activation free energies are fairly independent of the size of the polymer fragment.

Little is known about the accuracy with which quantum-chemical calculations, especially at the DFT level, can predict the kinetics, mechanisms or product distribution of localized reactions in stretched polymers. Single-molecule force spectroscopy is the only technique available to date for characterization of mechanochemical kinetics and accurate quantum-chemical predictions of measured force/extension curves of 3 mechanochemically active polymers have been reported.[33, 39] Success in predicting the product distribution of mechanochemical reactions is mixed,[40, 64] although the situation is complicated by the very small number of experimental examples and the frequent lack of sufficient details to allow meaningful comparisons between the experiment and calculations. Most reported quantum-chemical calculations of mechanochemical reactions have not been compared with experiment, and experimental benchmarking of the methods of quantum-chemical calculations of mechanochemical reactivity is probably the most important outstanding question in computational mechanochemistry.

Quantum-chemical calculations of mechanochemical reactivity, especially using complete conformational ensembles of homologous series of increasingly large polymer fragments and exhaustive search of all plausible reaction paths requires extraordinary computational resources and considerable expertise. As a result such calculations are generally beyond most research labs working in the field of polymer mechanochemistry and may be too resource-demanding to be broadly useful in initial screening of candidate reactions with specific mechanochemical profiles. This motivates continued search for simple models that allow semi-quantitative extrapolations of force-dependent activation barriers from strain-free values, which are generally much easier to obtain experimentally or computationally.

First attempts to develop a theoretical model of polymer mechanochemistry go back to Eyring, who postulated that that activation energy of a chain fragmentation in an elongational flow is proportional to the force stretching the chain.[65] This approach was applied to cell adhesion[66] and to bulk materials by replacing force with stress[70, 71] (see section 3, "Mechanochemistry of polymers in solids"). It was extended to time-varying force[67, 68] (in context of dynamic force spectroscopy) within the formalism of Kramers' formulation of reaction rates. Subsequent elaborations[69] of these ansatzs included considering different shapes of the free energy profile along the molecular coordinate defining the pulling axis (i.e., the pair of atoms at which the molecule is stretched) and attempts to extend this approach to the 2nd dimension in a way that is analogous to the classical physical organic approach of analyzing the effect of external parameters (e.g., solvent polarity) on the reaction mechanisms and structures of the transition states (sometimes called "bema-hapothle").[31, 72]

The main drawback of these empirical models is that they offer no molecular interpretation of the model parameters in a way that would enable predictions of mechanochemical reactivity from chemical structure or inform about structural changes in reacting molecules, beyond the most general qualitative statements that the rate-determining transition state is longer or shorter than the reactant along the pulling axis.[36] In their empiricism these Eyring-Bell-Evans models of mechanochemical kinetics resemble the Arrhenius equation of chemical kinetics: While they have contributed considerably to the development of phenomenological mechanochemistry, particularly in single-molecule force experiments, their potential to support the development of a general, predictive and theoretically-sound foundation of the field appears rather limited.

We and others suggested that it may be possible to move beyond the empirical relationships between force-dependent activation energies and applied force by treating the Eyring proportionality as the 1st order Taylor expansion of the activation energy of the reaction with respect to the externally imposed perturbation, i.e., applied force, *f*.[25, 36, 61] The next logical step would then be to improve the model by including the 2nd order Taylor expansion coefficient (eq. 1, where $\Delta G^{\ddagger}_{o}$ and $\Delta G^{\ddagger}_{f}$ are the activation free energies in strain-free reaction and reaction under force *f*, respectively). Eq. 1 is fairly unambiguous for elementary (single-barrier) reactions, but for multi-barrier mechanisms, the reaction activation free energy in general deviates from the relative free energy of the least-stable transition state, potentially introducing another source of uncertainty.[35] Eq. 1 assumes that the force does not change as the molecule reacts, i.e., the reaction occurs under isotensional conditions. How physical this assumption is remains to be established.

$$\Delta G^{\ddagger}_{f} - \Delta G^{\ddagger}_{o} \approx \underbrace{\left(f\frac{\partial G_{ts}}{\partial f}\bigg|_{f=0} + \frac{f^2}{2}\frac{\partial^2 G_{ts}}{\partial f^2}\bigg|_{f=0} + \cdots \right)}_{transition-state\ (ts)\ energy} - \underbrace{\left(f\frac{\partial G_{r}}{\partial f}\bigg|_{f=0} + \frac{f^2}{2}\frac{\partial^2 G_{r}}{\partial f^2}\bigg|_{f=0} + \cdots \right)}_{reactant\ (r)\ energy} \quad \text{(eq. 1)}$$

This approach is more useful than the existing empirical models only if it allows molecular definition of the parameters,

i.e., the derivatives. Assuming that *f* is the restoring force of the constrained internuclear distance allows the difference of the 1st and 2nd Taylor expansion coefficients, $\partial G_{ts}/\partial f - \partial G_r/\partial f$ and $\partial^2 G_{ts}/\partial f^2 - \partial^2 G_r/\partial f^2$, to be equated to the difference in the constrained distance and the difference of its harmonic compliances between the rate-determining transition state and the reactant, both in the absence of force. These definitions allow, at least in theory, to predict force-dependent activation energy without laborious optimizations of force-coupled molecular geometries.

In practice, however, this approach presents 2 potential complications for which no solution appears to exist. First, with the exception of single-molecule force experiments, macromolecules in mechanochemical phenomena are not stretched by constraining a single internuclear distance to a non-equilibrium value. The definition of *f* becomes more ambiguous when a stretched chains couples to its surroundings through more than 2 atoms. If such a stretched macrochain (or its fragment containing the reactive site) is in internal mechanical equilibrium, the restoring forces of molecular coordinates are related by the molecular compliance matrix.[25] Extensive quantum-chemical computations[27, 28, 30, 32, 34, 35, 63] indicate that in such a case, multiple internuclear coordinates (including coordinates localized to the reactive site) can be used in eq. 1 to yield reasonably accurate predictions of $\Delta G^{\ddagger}_{f}$ under isotensional conditions, provided that *f* is the restoring force of the selected coordinate, which may differ from the applied force (the ratio of the restoring force of a local coordinate to that of the constrained distance, which equals the applied force, is called "chemomechanical coupling coefficient"). The local coordinate approach was demonstrated to predict the critical force at which mechanochemical reactivity is observed in single-molecule force experiments.[33, 39] It seems plausible that stretched macrochains in sonicated solutions or loaded amorphous materials are also reasonably close, on average, to internal mechanical equilibrium, but this speculation remains to be tested experimentally and computationally.

The other complication is the effect of conformational ensembles. The states whose relative energies determine reaction kinetics are comprised of multiple conformers and the relative contributions of these conformers to the kinetically relevant states in general changes with force. This role of conformers explains the fact that the early hope, by us[25, 27, 28, 36, 61, 62] and others[73-75] that the 2nd order Taylor expansion may improve the accuracy of extrapolated activation energies, was not realized. Local coordinates appear to be sufficiently stiff that at applied forces <3 nN the main contributor to the force dependence of the 1st Taylor coefficient ($\partial G/\partial f$) are changes in the relative contributions of different conformers to the reactant and/or transition states.[27, 63] These contributions cannot be captured by the 2nd Taylor coefficient ($\partial^2 G/\partial f^2$) but require much more complex models.[28, 63] At the same time, the Taylor expansion fails for softer coordinates (e.g., the constrained distance) because in strain-free molecules such coordinates are so anharmonic that the 2nd Taylor (harmonic) coefficient accounts for only a small fraction of the actual force-dependent change of the corresponding $\partial G/\partial f$ values.

Attempts to extrapolate activation free energies of reactions under force from force-free values must consider the possibility that the reaction mechanism changes with force. Failure to do so can lead to qualitatively incorrect predictions as illustrated recently by an attempt to extrapolate force-dependent activation energy of dissociation of an adduct of anthracene and maleimide[74], Figure 6a. According to DFT calculations the adduct dissociates by a concerted mechanism in the absence of force. Depending on the functional, an alternative 2-step radical dissociation path may or may not exist in the absence of force. For those functionals (e.g., uMPW1K) that predict its existence, the radical path is considerably higher in energy than the concerted alternative. Even small force reverses the order of these two mechanisms, with the stepwise path becoming dominant at applied force of ~0.1 nN and the concerting mechanism disappearing altogether at 0.4 – 0.8 nN (depending on the substituents R and R' and the functional). The reason is that the concerted mechanism is destabilized by force (Figure 6b black line), whereas the stepwise analog is strongly stabilized by it (grey lines). As a result, dissociation is marginally inhibited by tensile force below ~0.1 nN but is accelerated at higher force when the stepwise mechanism dominates (grey line, Figure 6c). Not surprisingly, extrapolating the strain-free barrier of the concerted process using the Taylor expansion yields a qualitatively incorrect prediction of force inhibited dissociation kinetics (black line, Figure 6c).

1.3. Scope and objective of the review

Numerous reviews of polymer mechanochemistry have been published in the last decade, including extensive compilations of experimental[60, 76, 77] and computational[11, 12] phenomenology, outlines of plausible conceptual basis of polymer mechanochemistry[25, 36]; its possible applications[13, 78-80]; its current and probable future place in the broader field of polymer science[81-84] or chemistry,[62] approaches to modelling of mechanochemical phenomena with strained small molecules and overcrowded polymers[24], and narrower summaries of individual authors' research in the field.[84-88]. What is missing from the literature is a critical assessment of interpretative frameworks that underlie (often implicitly) molecular rationalizations of macroscopic manifestations of mechanochemistry. Being a conceptually complex but fairly new field at the interface of chemistry, physics and engineering, at present mechanochemistry lacks the intellectually rigorous foundation that guides and informs the work in more mature fields, such as synthetic polymer chemistry and physical organic chemistry.

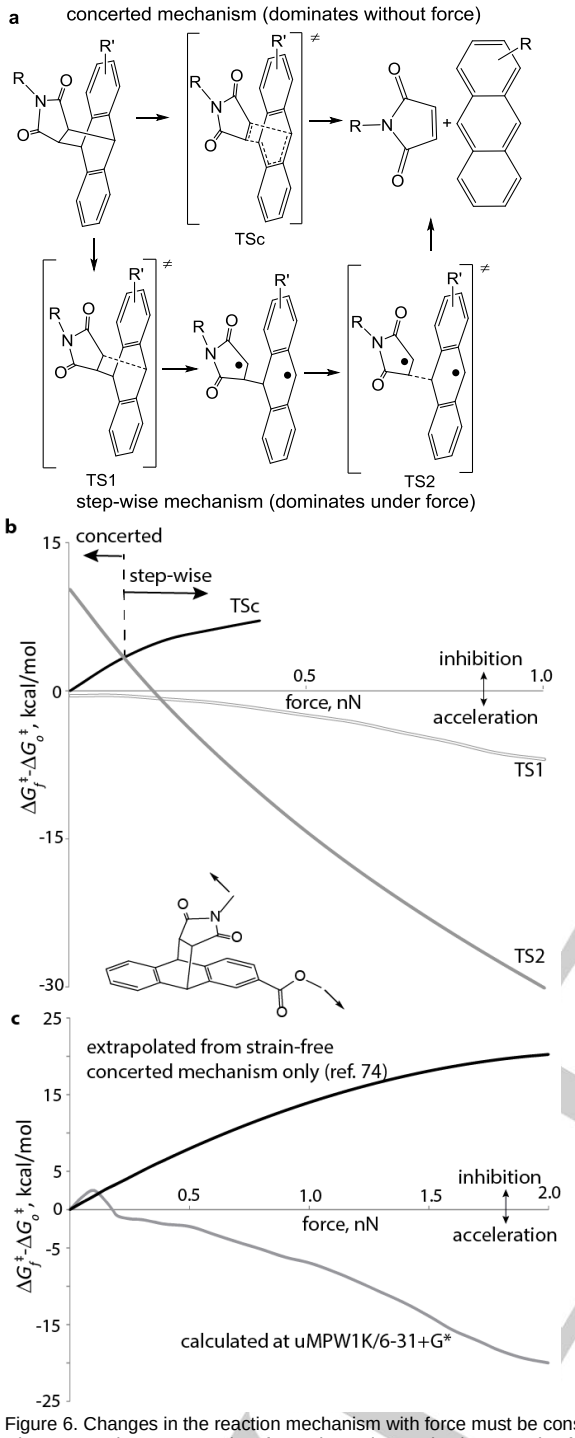

Figure 6. Changes in the reaction mechanism with force must be considered when attempting to extrapolate force-dependent activation energies from strain-free values as illustrated on the example of dissociation of anthracene/maleimide adduct. (a) the two reaction mechanisms; (b) changes in the free energies of the concerted and stepwise transition states relative to that of the reactant as a function of applied force at the uMPW1K/6-31+G(d) level of theory; (c) a comparison of the explicitly calculated dissociation barrier (grey line) with that predicted in ref. 74 using the 2nd order Taylor expansion on the concerted dissociation mechanism. The data in (b) and (c) is for the adduct derivative shown pulled along the molecular axis specified by the arrows.

The absence of such a foundation makes macroscopic manifestations of mechanochemistry especially susceptible to overinterpretation, overgeneralization and oversimplification. It also allows claims that are more expansive and/or made with greater confidence that is warranted by our currently primitive understanding of the relationship between macroscopic parameters that are amenable to control by an experimentalist and microscopic conditions that determine the bulk response. The situation is not unique to mechanochemistry[89, 90]. By systematizing and analyzing various approaches to interpretation of mechanochemical observations that appeared in the literature and explicitly summarizing the underlying assumptions and the limits of their applicability we hope to achieve two objectives. The first is to articulate research opportunities, particularly in developing new experimental and data processing protocols, whose pursuit will accelerate the evolution of the field. The second is to convince the practitioners of the importance of disclosing more of the measured data (instead of just conclusions drawn from it) to enable its re-interpretation as new models emerge. Short of this, we hope at least to prompt a more complete disclosure of the uncertainties underlying the molecular interpretations of experimental observations than appears to be the norm now. Some of the points we make below echo those of Price from 1990[91], albeit in a slightly different context, which judging by the contemporary literature in polymer mechanochemistry, have not necessarily been embraced by the community.

We hope that the review would be of value to broader research community by placing polymer mechanochemistry in a proper context. All mechanochemical phenomena are manifestations of the effect of molecular strain on chemical reactivity. Thus polymer mechanochemistry may appear superficially to be an extension of the long studied field of strained small molecules. However, molecular strain responsible for most mechanochemical phenomena in polymers is unlike anything chemists are familiar with from small molecules, both qualitatively and quantitatively. In most cases, its magnitude far exceeds that in any small strained molecule reported to date and it is far more anisotropic (i.e., reactive sites are strained primarily along a single molecular axis). These differences mean that chemical intuition based on generalizations of trends established in small strained molecules does not map particularly well to polymer mechanochemistry and can even be misleading. It seems reasonable to say that the most interesting mechanochemical phenomena would most likely appear counterintuitive to both a chemist and a polymer scientist. At the same time, whether a particular mechanochemical reaction follows the reactivity patterns of small strained molecules probably has no impact on the likelihood that it is real.

The bulk of our review focuses on sonication, because it is the most commonly used method of demonstrating and studying polymer mechanochemistry (in addition to other types of mechanochemistry[92]). Sonication experiments are as easy to do technically as they are challenging to interpret mechanistically and/or quantitatively. A more realistic and physically justified framework for systematizing, rationalizing and extrapolating results of such sonication experiments would probably do more to advance polymer mechanochemistry than any other research development we can think of. We limit our discussion of mechanochemical phenomenology to a few examples that illustrate the trends, outstanding questions or competing interpretations. The currently limited molecular understanding of mechanochemical phenomena in solution or solid means that when we can point out unresolved issues or seeming inconsistencies in the reported interpretations of observations far more often than we can offer alternative explanations.

2. Mechanochemistry of polymers in sonicated solutions

Ultrasonication of dilute solutions of polymers is an example of a mechanochemical phenomenon with complex coupling between an isolated polymer chain and its environment. High frequency sound waves passing through a liquid create cavitation (Figure 7), which is the generation, growth and violent collapse of bubbles. This collapse creates a transient solvent flow with a considerable elongational component. Because the flow velocities decrease very rapidly away from the edge of the collapsing bubble, segments of polymer chains closer to the bubble are subject to a higher flow rate (and hence a larger hydrodynamic drag) than those farther away, which stretches the chain.

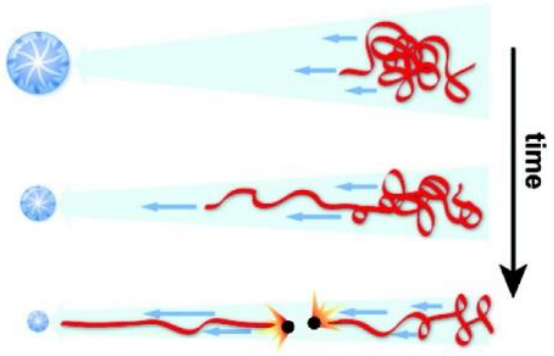

Figure 7. A cartoon representation of a polymer solute (red) in the vicinity of a collapsing cavitation bubble (not to scale). Blue arrows signify the elongational component of the solvent flow with longer arrows corresponding to faster motion. It's not known if an average chain becomes stretched from a terminus or from an internal segment or how long the stretched polymer segment is. Adapted from ref [60] with permission. Copyright 2009 American Chemical Society.

Polymer chain dynamics is complex even in planar steady-state elongational flows[53, 93] and it is further complicated in the rapidly changing flow fields generated by the collapsing bubble. At the typically used sonication frequency of 20 kHz in low viscosity solvents a cavitation bubble collapses within <10 μs and significant fluid strain rates are only generated at the latest stages of the collapse[94]. Thus during sonication a chain may evolve from a strain-free to highly stretched geometry corresponding to restoring forces in the nN range on a sub-microsecond timescale. Under these conditions, it may no longer be meaningful to discuss mechanochemical kinetics in terms of force acting on the chain, but rather loading rates (change of force with time) the chain experiences. Replacing a time independent perturbation (force) with a time-variable one (loading rate) eliminates whatever residual intuition could be employed to think about the kinetics of the mechanochemical reaction. At sufficiently high loading rates, one can no longer define the rate-determining and product–determining steps for complex reaction mechanisms and closed-form integral rate laws become unavailable for all but unimolecular reactions with the simplest dependence of the activation free energy on force. Moreover, the key postulate of the transition state theory – that vibrational energy redistributes among various molecular degrees of freedom much faster than the reaction rate[95] – may break down at the loading rates and lifetimes that are likely responsible for mechanochemical reactions in sonicated polymer solutions. Finally, all discussions of the microscopic conditions responsible for mechanochemistry are implicitly based at best on models of single-bubble sonication[96] (or more often on even-less relevant planar steady-state elongational flows[97, 98]), whereas all mechanochemical studies reported to date were performed in the multi-bubble regime. The simultaneous generation of multiple cavitation bubbles induces new phenomena, including bubble entrainment and coalescence, microstreaming and shock waves. The latter also produce elongational flows potentially capable of stretching macromolecule.[94, 99, 100] The standard practice of using short on/off cycles of sonication, designed to minimize temperature increases in the sonicated solutions, further complicates fluid dynamics.[101] Consequently, very few attempts to model chain behavior under conditions relevant to mechanochemistry in sonicated solutions have been reported.[96] Single-bubble dynamics in acoustic fields is reasonably well understood[94] and at present is probably the only starting point for developing a quantitative microscopic model of sonication-induced mechanochemistry.

Cleverly designed "mechanophores" (reactive sites which respond to tensile load by undergoing reactions more complex than simple bond homolysis) and/or mechanochemical reaction cascades[39] may allow experimental validation of such models by enabling usefully accurate quantitation of the microscopic conditions experienced by reacting macromolecules in sonication solutions. Such effort remains to be reported. To date, the focus of sonication studies has been primarily empirical with only few tentative attempts to apply the simplest microscopic models of chain dynamics at the stagnation point of steady-state planar elongational flows to rationalize bulk mechanochemical response of polymers to sonication[97, 98].

Historically, polymer solutions were sonicated to study how the rate of molar mass degradation of common synthetic (polystyrene, polyalkylacrylates) or biological (cellulose, dextran) polymers was affected by the chemical composition, degree of polymerization and side chains of the polymer, by the solvent, the presence of non-macromolecular solutes, the temperature, pressure and acoustic power flux[91]. These studies were motivated as much if not more by engineering rather than chemical interests and therefore rarely focused on molecular interpretation of the observations. A few generalizations can be made from this considerable, albeit fairly contradictory, body of empirical observations. For example, all other things being equal, shorter chains degrade slower than longer chains and a sonicated polymer chain fragments with the highest probability close to its center of mass (although claims of random fragmentations also appear in the literature[102]). Beyond this, studies of non-selective fragmentation have not yet yielded insights into the microscopic conditions responsible for mechanochemical chain scission during sonication. In the last decade, by far the most common objective of sonicating polymer solutions became demonstrations that reactions more complex than simple bond homolysis are accelerated by stretching polymer chains. Acceleration of over 20 such complex (albeit exclusively unimolecular) reactions was demonstrated convincingly in sonicated solutions of polymers.[39, 43, 96-98, 103-130] For 4 additional reactions subsequent reports raised questions about the original claims or the original publications did not provide sufficient information for us to assess independently the plausibility of their claims, which have not been followed up in subsequent literature reports.

For 6 reactions[43, 97, 98, 104, 106, 115, 119-121, 130-140] qualitatively similar results were observed in sonication and bulk amorphous

or semicrystalline materials under mechanical loads, suggesting that polymer sonication can at least qualitatively mimic the chemical response of macromolecules to mechanical loads in practically relevant (but technically harder-to-study) contexts. Conversely, we are aware of three kinetically-controlled reactions that were reported[141-143] to occur in loaded amorphous polymers, but, despite some publicity[144] that the reports garnered, the behaviour of the same polymers in sonicated solution has never been described (thermodynamically controlled mechanochemical reactions are much harder to detect in solution than in a solid due to rapid reestablishment of the equilibrium once the macrochain escapes the elongational flow). It is both technically easier to demonstrate a mechanochemical reaction in a sonicated polymer solution than in loaded solid samples and an accepted practice in contemporary mechanochemistry to substantiate claims of any new such reactions by establishing its occurrence in sonicated solutions. Consequently, we are tempted to speculate that sonicating the same polymers did not (or would not) result in productive chemistry. If this speculation is correct, the reactions would be valuable for helping quantify the vast difference in the conditions responsible for mechanochemistry in sonication and loaded bulk samples (an alternative explanation is that the chemistry observed in loaded bulk polymers occurred by mechanism other than strain-induced acceleration, such as pressure effects, a possibility noted by others[104, 145, 146]).

Several well-defined reaction cascades have been demonstrated whereby sonication-induced mechanochemical reaction produced a reactant or a catalyst for a subsequent, non-mechanochemical reaction[103, 104, 108, 130, 140, 147, 148]. Three cascades were shown to occur both in sonicated solutions and in sheared or axially compressed bulk polymers, further supporting the utility of sonicating polymer solutions as a means of mimicking the mechanochemical response of solid polymers[130, 139, 140].

2.1. Kinetic laws for polymer degradation by sonication

In chemistry, kinetic studies yield data that contains important insights into the reaction mechanism(s), allows estimations of reaction rates at different temperatures and benchmarking of quantum-chemical calculations of the reaction mechanisms and energies. None of these goals is yet achievable with any reported kinetic study of polymer degradation in sonication. The main reason is that during sonication only a tiny, but unknown, fraction of polymer solute is stretched. As a result, the measured bulk rate constants do not reflect the microscopic reaction probability as they do in conventional chemical kinetics, but rather a complex convolution of probabilities, including the probability of a chain to be trapped in the elongational flows, of the trapped chain to accumulate sufficient total (Hencky[53]) strain to be stretched, and of the stretched chain to react. Consequently, bulk rate constants have no relationship to the kinetic barriers of the underlying reactions or the range of the forces or loading rates that an average fragmented macrochain experiences (a similar problem is present in relating the rates of chemical remodeling of bulk materials under load to microscopic kinetics of underlying chemical reactions, as described below).

Furthermore, whereas conventional rate constants reflect the rate of the disappearance of the reactant, or appearance of the product(s), kinetics of polymer sonication is routinely discussed in terms of changes in the molar mass distribution (MMD) of the sample, often reduced to a single parameter, such as number- or weight- averaged molar mass (M_n and M_w, respectively). The focus on changes in M_n or M_w instead of the fractions of the reactant/product(s) is motivated by the common use of polymers too disperse and/or of analytical methods too crude to distinguish original polymer chains from those produced by polymer fragmentation and hence to measure MMDs of the reactant and the product separately. Even when such individual MMDs are available, the data is relatively rarely analyzed in terms of the rate of depletion of the initial polymer (notable exceptions are [149, 150]). Such analyses are very valuable for establishing if a single rate constant rather than a distribution of rate constants is sufficient to describe the observed reactivity and for validating the more unconventional kinetic models, as demonstrated below.

A confusing plethora of formulas describing the evolution of M_n with sonication time, t, exists in the literature. Most assume unimolecular kinetics (exceptions are some early studies) and either random or midchain scission (i.e., either every backbone bond in a stretched chain breaks with equal probability or the chain only breaks to two identical fragments). More complex distributions of fragmentation probabilities along the polymer chains were derived mathematically,[151] but the resulting formulas have not yet been applied to the analysis of experimental data. The most commonly used models for random and midchain scission yield eqs. 2-3, respectively, with a number of further (largely empirical) elaborations of eq. 3 appearing in the literature (e.g., eqs. 4-5), where m_0 is the molecular weight of the monomer, c is the concentration and M_{lim} is an empirical fitting parameter discussed below[102, 152-155]. Note that the rate constant in eq. 4 has the units of $s^{-1}M$, not s^{-1} despite the underlying assumption of unimolecularity.

$$kt = \frac{m_0}{M_n(t)} - \frac{m_0}{M_n(0)} \qquad (2)$$

$$kt = ln\left(\frac{1-\frac{M_{lim}}{M_n(0)}}{1-\frac{M_{lim}}{M_n(t)}}\right) \qquad (3)$$

$$kt\frac{M_{lim}}{cm_0} = ln\left(\frac{1-\frac{M_{lim}}{M_n(0)}}{1-\frac{M_{lim}}{M_n(t)}}\right) \qquad (4)$$

$$kt\left(\frac{M_{lim}}{m_0}\right)^2 + \frac{M_{lim}}{M_n(0)} + \frac{M_{lim}}{M_n(t)} = ln\left(\frac{1-\frac{M_{lim}}{M_n(0)}}{1-\frac{M_{lim}}{M_n(t)}}\right) \qquad (5)$$

Eq. 2 is based on two assumptions: each backbone bond has the same probability to break, and the total probability of chain fragmentation is independent of the number of backbone bonds. Because the latter is a product of the former and the number of bonds in the backbone, together these two assumptions require that as the polymer size increases, the probability that any of its backbone bond breaks during sonication decreases proportionally. In other words, the probability of any backbone bond of a sonicated chain to break is inversely proportional to the number of bonds in the chain. Since the intrinsic reactivity of a chemical bond is not affected by substituents further than a few bonds away (<1 nm), eq. 2 implicitly assumes that the force experienced by a fragmenting chain in an elongational flow decreases with chain length, the opposite to what might be

expected from steady-state elongational flows with a stagnation point[53] (the only relevant benchmark for which a fair understanding of single-chain forces exists). We are not aware of any rationalization of such a counterintuitive relationship between the polymer chain and force at fragmentation.

Although eq. 2 was derived for random chain scission, it is often used to model the supposedly site-specific fragmentation kinetics of polymers containing a single scissile mechanophore per chain[74, 105, 109, 122, 125]. "Mechanophore" is sometimes used to describe a reactive site whose chemical response to tensile strain is more complex than simple fragmentation by homolysis of a single bond (although mechanochemical reactions of all "mechanophores" reported to date are based on dissociation of one or more covalent bonds). While such polymers typically fragment both at the mechanophore and elsewhere in the backbone, the probabilities of the two paths are sufficiently different that application of eq. 2 to such kinetics appears to typically yield nonphysical results. An illustrative example is a recent report of fragmentation kinetics of poly(methyl acrylates) (PMA) probably containing a single cyclobutane derivative per chain (Figure 8),[122] which were claimed to fragment exclusively by [2+2] cycloreversion of cyclobutane. The paper presented gel-permeation chromatograms (GPCs) for sonication of one polymer sample, which allow the reported rate constant (derived by eq. 2) to be compared with the rate at which MMD of the polymer changes. For this sample, fitting $M_n(t)$ to eq. 2 yielded the rate constant of 5×10^{-6} min^{-1} (the authors erroneously reported the rate constant as the slope of the $M_n^{-1}(t)$ vs. sonication time correlation, which was ~6×10^{-5} $min^{-1}kDa^{-1}$; the number we cite is the rate constant obtained by dividing the slope by m_o, the molecular weight of methyl acrylate, as required by eq. 2). This rate constant corresponds to the half-life of ~102 days of sonication. In contrast, the reported GPCs (which reflect the underlying MMD) suggest that at least 75% of the initial polymer fragmented after only 110 min of sonication. In other words, the application of a kinetic equation derived for random chain scission to the supposedly selective fragmentation of polymer chains containing a single dissociatively labile group per chain underestimated the fragmentation kinetics by ~10^3-fold. The very large discrepancy between the kinetic model and the changes in MMD can potentially be diagnostic of site-specific vs. non-specific fragmentation, but it also means that the fitted rate constants probably lack physical significance (see below). Another difficulty in quantifying the observed fragmentation kinetics is the high dispersity of the initial polymer: the strong dependence of the fragmentation probability on the polymer size means that the reactivity of such a sample cannot be adequately described by a single rate constant. The preferential depletion of the high-molar mass fraction of the initial polymer is obvious in the reported GPCs.

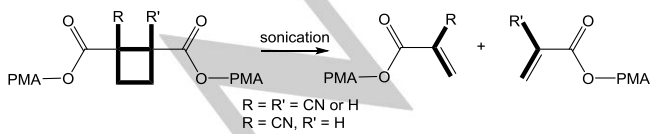

Figure 8. Sonication of PMA containing a derivative of cyclobutane (highlighted in bold) was claimed[122] to result in selective mechanochemical [2+2] cycloreversion but the fragmentation kinetics was analyzed assuming equal-probability fragmentation of every backbone bond.

Whereas eq. 2 is derived for a hypothetical randomly fragmenting polymer, eq. 3 lies at the other extreme: it assumes that above a certain critical size (M_{lim} when expressed as molar mass) chains only break in the middle, at a rate that is independent of their size while smaller chains do not fragment at all. The nonphysical nature of this assumption and hence the corresponding parameter (M_{lim}) was discussed in the past,[57] but M_{lim} obtained by fitting the experimental data to eq. 3-5 is still used to quantify the polymer susceptibility to fragmentation in sonication. A fundamental limit on the size of the chain which undergoes mechanochemistry during sonication is almost certainly exists. It is probably determined both by the properties of the polymer (its molar mass, contour length and backbone compliance), which define the longest relaxation time and hence the critical strain rate of the solvent flow below which the chain cannot be stretched by the flow, and on the maximum fluid strain rate achievable by sonication, whose dependence on experimental conditions is not understood. Yet no evidence appears to exist that this limit is related to M_{lim} in eqs. 3-5 or that M_{lim} derived by application of eqs. 3-5 to polymers of different compositions or for different sonication conditions even qualitatively reflect the variation of this fundamental limit with chemical composition or sonication conditions.

Data in ref. [97] illustrate why under certain conditions changes in M_n of a sonicated polymer can be fitted to eq. 2 even if the fragmentation probability of different backbone bonds varies considerably. The paper reports the fragmentation kinetics of a series of polymers with the backbones made of C-C, C-O and C-S bonds. Increasing the fraction of C-S and C-O bonds (i.e., increasing the n to m ratio, Figure 9) increases the apparent fragmentation rate concomitantly with producing increasingly non-linear $M_n(t)^{-1}$-$M_n(0)^{-1}$ vs. t correlations (Figure 9). The increasing non-linearity is unlikely to represent a change in the distribution of fragmentation probabilities from random scission (for which $M_n(t)^{-1}$-$M_n(0)^{-1}$ is postulated to be proportional to sonication time t) to primarily midchain scission. Instead it reflects the fact that up to modest conversions the right-hand site of eq. 3 (fragmentation only at the center of mass) is accurately approximated as $M_n(t)^{-1}$-$M_n(0)^{-1}$ (fragmentation anywhere along the chain), i.e., eqs. 2-3 are numerically indistinguishable (the slopes, however, have very different physical meaning: for a randomly fragmenting polymer the slope equals k/m_o but for the polymer fragmenting at the center, the slope is k/M_{lim} so that using eq. 2 for approximately site-specific fragmentation equation vastly underestimates the fragmentation rate constant, as illustrated by the previous example of cyclobutane containing PMAs). The more labile a selectively fragmenting polymer, the larger its molar mass reduction over the fixed sonication period, and the more its fragmentation kinetics will deviate from that of a randomly fragmenting chain as evident in Figure 9.

Confusingly, some studies quantify the fragmentation kinetics by eq. 2 and also report M_{lim} usually from a linear regression of the rate constants derived from applying eq. 2 to a series of polymers with different initial molar masses, $M_n(0)$, despite the assumption of eq. 2 that the fragmentation kinetics is independent of molar mass. This hodgepodge of incompatible assumptions sometimes yields curious results. For example, the data in Tables S1 and S3 of ref. [156] obtained from fitting $M_n(t)$ of a sonicated polymer to eq. 2 suggest that the fragmentation rate of this supposedly selectively-fragmenting polymer *decreases* with increasing polymer size, and the extrapolated limiting molar mass, M_{lim}, below which the reported polymer does fragment in

sonicated solution is larger than any polymer whose fragmentation the study reports. Although M_{lim} obtained by an extrapolation of the fitting parameter of eq. 2, and M_{lim} appearing in eqs. 3-5 are both interpreted as defining the largest polymer which does not fragment when sonicated, these two parameters reflect mutually exclusive sets of assumptions about how the chain fragments when trapped in the solvent flow. The 2 examples above illustrate that M_{lim} extrapolated from rate constants obtained by eq. 2 more likely reflects one's patience, equipment base and experimental techniques than some physically-significant parameter.

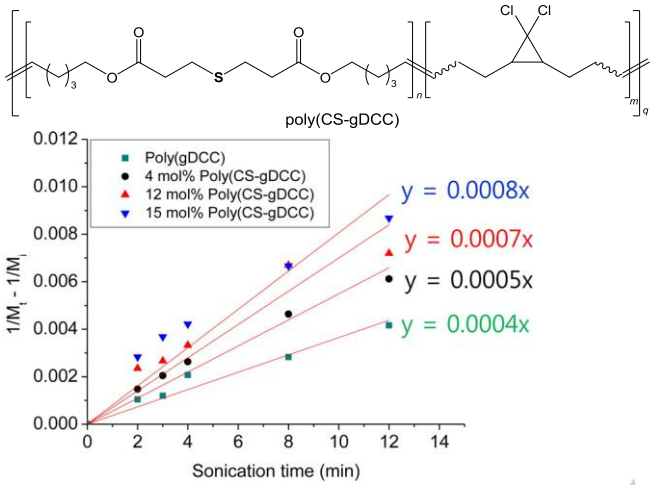

Figure 9. Kinetics of fragmentation of polymers with increasing content of C-S bonds (poly(CS-gDCC) during sonication fitted to eq. 1. Adapted from ref [97].

Given the current absence of any examples of randomly fragmenting polymers (i.e., in which every backbone bond fragments with equal probability), it is internally far more consistent (if not necessarily more insightful physically) to treat the experimental fragmentation kinetics by eq. 3, with single M_{lim} applied across any series of chemically-identical polymers of different molar masses. The current use of eq. 2 is especially problematic when slopes of $M_n^{-1}(t)$ vs. t dependences are used to differentiate between site-specific and non-selective fragmentations of different polymers.[105, 109] Contrary to the assumption implicit to this use of such slopes, their differences may reflect distinct M_{lim} values rather than different rate constants particularly in the view of previous literature reports that M_{lim} values are far more sensitive to the chemical composition of the chain than rate constants[122] making them unsuited for differentiating between site-specific and non-specific fragmentations.

Much energy has been expanded arguing whether the rate of molar mass degradation is determined by polymer's M_n, its equivalently-averaged degree of polymerization (DP), its contour length or some other quantifier of chain size[102, 106, 122, 150, 157-162]. The standard method of changing M_n without changing DP or the contour length, or of keeping M_n constant while changing both DP and the contour length is to vary the side chains. When the variation is small (e.g., 1 H atom per monomer is replaced by Br or a Me group is substituted by Et), polymers of the same DP (and hence the same contour length) fragment at the same rate. When polymers with very different side groups but otherwise identical monomers are compared (e.g., methyl vs. octadecyl acrylates), M_n appears to be a better predictor of relative susceptibility to fragmentation than DP. The significance of the observed trends is somewhat obscured by the fact that many of these studies were performed on fairly disperse polymers (Đ up to 4.7) so that the measured rates represent complex averaging over a broad range of intrinsic reactivities, which depends on the extent of the reaction and the method of quantifying M_n.

Analyses of MMD evolution during sonication attempt to establish not only the probability that a randomly selected chain would fragment (which in theory is reflected in the rate constant(s)) but also the probability that the fragmentation yields products of given fractional molar masses, i.e., the distribution of fragmentation probabilities along the chain length[163, 164]. This approach is typically considered a more sophisticated form of kinetic analysis than the time evolution of a single parameter of the distribution, e.g. $M_n(t)$. Yet, it suffers from the current lack of understanding of the microscopic conditions experienced by the mechanochemically fragmenting chain and the limited number of observables to constrain the modelling properly. The MMD of the products of primary fragmentation of a uniform (Đ = 1) polymer equals the distribution of the fragmentation probabilities along the polymer chain. For practically relevant disperse samples, multiple unique distributions of fragmentation probabilities are in general consistent with typically observed MMDs of the initial polymer and products of its fragmentation.

All published analyses assume, without justification, a Gaussian distribution of fragmentation probabilities, centered at the chain's center of mass. This choice can be rationalized by assuming that the activation energy of fragmentation decreases linearly with force, which decreases as a square of the fractional distance from the chain center of mass. Superficially, these dependences may seem plausible. The former assumption is supported by quantum-chemical calculations of activation free energies of C-C bond homolysis, which decrease linearly with force above ~5 kcal/mol, but manifest more complex dependence at smaller values. At the likely loading rates experienced by fragmenting chains during sonication, the reaction probably proceeds over barriers <5 kcal/mol. The quadratic decrease of the hydrodynamic force from the center of mass reflects the consensus for chains trapped at the stagnation point of steady-state planar elongational flows, where the solvent flow rate decreases linearly with distance from the stagnation point (uniform velocity gradients)[165]. However, this assumption is not obviously applicable to the flow fields generated by a collapsing cavitation bubble. First, the existing models of single-bubble sonication suggest that within the regions of the highest straining rates (within <5 times the radius of the bubble at rest away from the bubble edge) the flow rate varies at least as a cube of the distance[94]. Linearizing such dependence over the 0.1-0.5 μm contour length of the macrochains whose fragmentation is typically studied by sonication probably introduces large errors. Second, the parabolic distribution of force along the chain implicitly assumes that the reacting chain is (nearly) fully stretched, which is expected under the stretching conditions leading to the abrupt coil-to-stretch transition (CST). However, at the very large deformation rates caused by bubble implosion the relevance of CST is uncertain. Instead, under such conditions few-monomer long highly strained segments may exist with the rest of the chain remaining largely strain-free.[53] These effects may cancel each other, resulting in a Gaussian distribution of fragmentation probabilities, but such a distribution is at best unproven.

In practice analysis of MMDs is further complicated by the fact that the product MMD has contributions not only from the

fragmentation of the original polymer (primary fragmentation) but also from fragmentation of its fragments (secondary and subsequent fragmentations). We are aware of only a few reported attempts[149, 163, 166, 167] to accommodate sequential fragmentation in analyses of MMD evolution during sonication. Unfortunately, all these attempts relied on implausible or unsupported assumptions regarding the dependence of the kinetics of sequential fragmentation on the polymer mass and/or on mathematical processing of experimental GPCs that likely introduced considerable bias in the resulting MMDs.[149, 167] This illustrates a broader problem that fragmentation of homopolymers is unlikely to provide enough observable data to constrain the multitude of plausible microscopic conditions responsible for mechanochemistry during polymer sonication. Considerably more diverse set of kinetic information is available when stretching a polymer results in competition between multiple reaction pathways with distinct microscopic mechanochemical kinetics. This new family of polymers should probably contain one or two distinct reactive sites, which could be placed at arbitrary positions relative to the chain's center of mass to enable direct "mapping" of the mechanochemical reaction probabilities along the polymer chain. In this scheme non-selective backbone fragmentation would act as an "internal standard" to account for variations in the total fragmentation probabilities (see below). Additional mechanistically significant information should be available from directly measuring the bulk rate constants of primary, secondary and tertiary fragmentation as a function of the molar mass of the polymer, although to avoid ambiguities of mass-dependent kinetic heterogeneities of polymer ensembles, such experiments would have to be conducted on nearly uniform (Đ <1.01) samples and use high-resolution methods of quantifying MMD.

Two attempts have been reported to use polymers that undergo competing mechanochemical reactions when stretched to gain molecular insights into polymer dynamics in sonicated solutions[97, 98]. Sonication of a polymer of dichlorocyclopropane (Figure 10) reduced the average molar mass of the sample and yielded polymers with cyclopropane moieties isomerized to olefin (the analytical methods employed did not allow one to established if the fragmented polymers were enriched in cyclopropane or the product of its isomerization, i.e., if the polymer fragmentation was accompanied by cyclopropane isomerization at the level of individual chains or these two reactions occurred in separate chains).

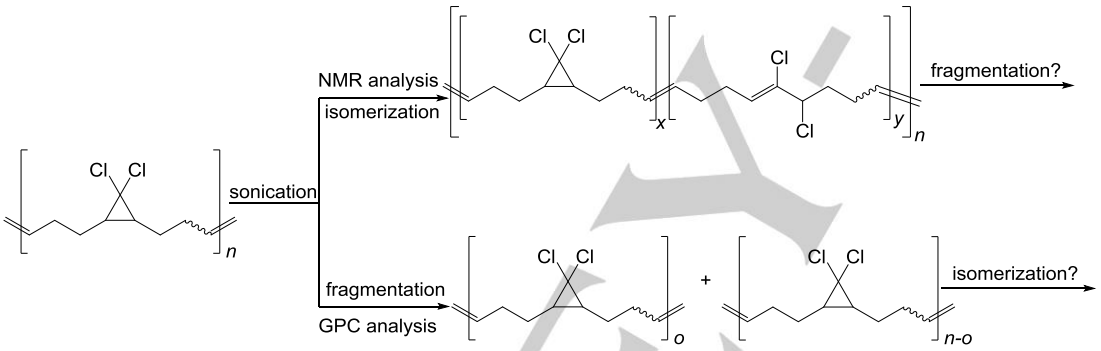

Figure 10. Sonication of a polymer of dichlorocyclopropane leads to isomerization of cyclopropane moiety and chain fragmentation, although it is not known if the two processes happen in the same or different chains.[98]

The ratio of the fraction of the isomerized cyclopropane moieties to the log of the fractional change of the average molar mass $\ln(M_n(t)/M_n(0))$ was independent of the experimental conditions (temperature, acoustic power, polymer concentration and solvent). The importance of this finding lies in demonstrating that the bulk mechanochemical *selectivity* is independent of overall bulk *reactivity* (i.e., that partitioning among competing reaction channels averaged over the sample is independent of the probability that a randomly selected chain will have reacted over a specific sonication period). It is important to be mindful that these bulk probabilities are not indicative of single-chain probabilities and the observed independence is consistent with a number of microscopic mechanisms. For example, the total bulk reaction probability may be determined by a non-chemical (i.e., non-thermally activated) process, such as the probability of the chain to be trapped in the flow field. Any trapped chain is then guaranteed to react. Alternatively, any chain that becomes stretched enough to react then undergoes a rapid sequence of further reactions without ever escaping the flow. This scenario would produce a mixture of intact chains and chains that underwent multiple fragmentations and containing primarily isomerized cyclopropanes. Modifying the experimental procedures to distinguish among these possibilities would considerably advance our understanding of microscopic conditions responsible for observed mechanochemistry.

A related work studied sonication of polymers with backbones containing a mixture of dichlorocyclopropane moieties and either S-C, benzylic C-O or N=N bonds as "weak links"[97]. The ratio of the fraction of intact cyclopropane, χ_{cp}, to the log of the fractional decrease in the number-average molar mass, $\log(M_n(t)/M_n(0))$ was independent of the sonication time but varied with the nature of the weak link. The mechanistic significance of this study is two-fold. First, it provided another example[30] that the bond dissociation energy is not the primary determinant of the probability of bond dissociation under force, thus addressing a common misconception[57] in polymer mechanochemistry. Second, it illustrates the extreme challenge of inferring chain-level behavior from bulk observations. In this case, it requires a series of assumptions whose validity has not yet been established experimentally, computationally or theoretically. The observed dependence of $\chi_{cp}/\log(M_n(t)/M_n(0))$ ratio on the composition of the chains reports on the microscopic conditions only if the fragmentation and cyclopropane isomerization kinetically compete in an average chain (as opposed to fragmentation and isomerization occurring primarily in separate chains). If this assumption is true the observed bulk reactivity is determined by a complex convolution of several parameters: (1) the difference of the activation free energies of the competing paths (cyclopropane isomerization and homolysis of various backbone bonds) as a function of the force; (2) the loading rate; (3) the

fraction of the backbone that is stretched and, (4) if only a part of the chain is stretched, the distribution of probabilities that a particular segment of the chain is stretched, its length and the rate at which the stretched segment grows. While the differences of the activation free energies are accessible with useful accuracy from quantum-chemical calculations, we are not aware of any experimental or computational methods to estimate the values of the remaining parameters. Even postulating the preferentially midchain fragmentation does not constrain the range of the force/loading rate and their distribution along the chain that are responsible for the observed chemistry. If one further assumes that the mechanochemical reactions only occur in a fully stretched chain (another assumption that lack experimental support and seems fairly unlikely[53]), only uniform distribution of force/loading rate along the chain can be eliminated. While the authors suggested that the observations may be consistent with the force experienced by the reacting chain decreasing as a square of the fractional distance from the chain's center of mass, any dependence of force on fractional distance that assumes maximum at the center of mass appears to reproduce the experimental data with only small variations of the loading rate (which is unknown even at the order-of-magnitude accuracy).

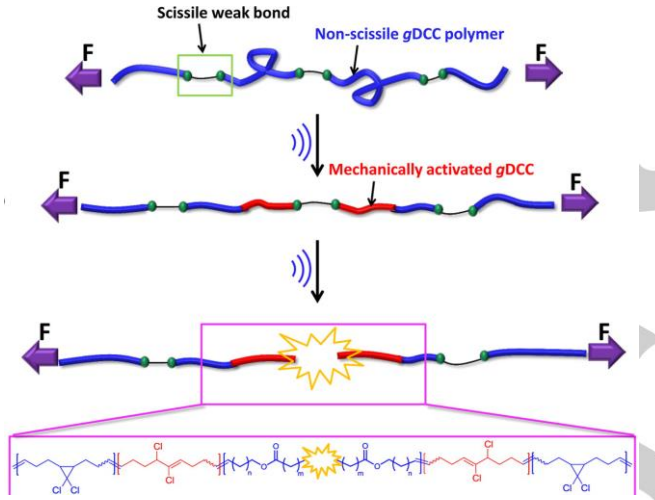

Figure 11. Sonication of polymers containing cyclopropane moieties (gDCC, blue) and weak bonds (S-C, C-O or N=N, green) in the backbone leads to isomerization of cyclopropane moieties to olefins (red) and fragmentation of the polymer . Adapted from ref [97] under Creative Commons License.

2.2. Parameters affecting polymers degradation kinetics during sonication

At least 30 reported studies have been devoted to quantifying the effects of macroscopic control parameters on the kinetics of linear polymer degradation during sonication (the literature on degradation of topologically complex polymers is very limited[76]). The fairly contradictory literature probably reflects the complexity of the problem and the limitations of both experimental design and data interpretation. For example, many studies were conducted on polymers (a) with dispersities >1.1, and thus represent implicit averaging of a wide range of reactivities in a manner that is difficult to reproduce, that depends on the model used to fit the measured changes in M_n and on the degree of molar mass degradation; and (b) at concentrations considerably above the "ultradilute" limit ($<10^{-2}[\eta]^{-1}$ where [η] is intrinsic viscosity),[168] so that the observed variations in the kinetics may reflect the contributions from changing interactions between partially stretched chains in addition to the intrinsic behavior of the chain. In several studies, the kinetics were analyzed with equations that were not consistent with the observed changes in the MMD (e.g., eq. 2 while primarily midchain scission is expected or suggestive by the shapes of GPCs), reported in quantities that are not directly comparable among or even within studies, and only rarely with statistical analysis, making assessment of statistical significance of fairly small variations typically observed in response to changes in control parameters impossible to assess. Thus the reported observations can only be generalized qualitatively: increasing acoustic power at constant reaction volume probably increases the bulk fragmentation rate, while increasing the temperature or polymer concentration decreases it.

The effect of acoustic power is traditionally ascribed to "an increase in both the size and density of the cavitation bubbles"[98] but is likely more complex. Sonications of pure liquids or non-polymer solutions suggest that increasing acoustic power (by increasing the oscillation amplitude of the horn) changes the shape of the multibubble cloud, increases its size, leads to lensing of acoustic power along the axis of the horn and period doubling (which decreases the number of collapses per unit time), with the cloud increasingly behaving as a single bubble.[94] Because of the tendency of bubbles to self-organize in complex structures, the effect of power on the density of the bubbles in such structures is not obvious but calculations suggest that the mean size of the bubble increases with increasing power up to a threshold value that depends on the solvent and solutes. For isolated non interacting bubbles, higher acoustic pressure amplitudes (which correlate directly with acoustic power) result in higher accessible velocities of the bubble wall during implosion, which translates into higher fluid strain rates. At higher powers, the interaction between the sound and shock waves with the walls of the container may also be important.[169] We are unaware of approaches or assumptions that would allow a guestimate of the contribution of each of these factors to changes the chain dynamics in the elongational flow.

The inhibiting effect of temperature on the mechanochemical kinetics in sonicated solutions is traditionally attributed to "an increase in the amount of solvent vaporization into a forming cavitation bubble"[98]. The relative importance of this contributing factor is unknown. Temperature change also correlates negatively with changes in solvent viscosity and surface tension, the pressure amplitude of shock waves[94] and the relaxation times of the chain[53], which may determine the range of strain rates that are necessary and sufficient to induce mechanochemistry. The speed of sound in the solvent (which determines the acoustic loss from the bubble) increases with temperature and temperature likely affects interactions among bubbles. The difficulty of disentangling such influences is illustrated by the lack of consensus on the origin of the temperature dependence of single-bubble sonoluminescence, despite many careful studies and understood bubble dynamics. Because sonication subjects solutions to considerable thermal fluxes (e.g., as much as 100 W in 2-5 mL of solvents with moderate heat capacities) and probably creates thermal gradients that may persist on the timescales comparable to the rates of mechanochemical transformations, the mechanochemical kinetics may reflect local temperature that considerably exceeds bulk solution temperature, and the thermal contributions may depend on parameters that are difficult to reproduce, such as the shape of the reaction vessel and the rate at which heat is removed from the sonicated solution.

Similarly, the origin of the inhibition of the rate of polymer fragmentation with increasing polymer concentration (e.g., eq. 4 above) remains unknown, being variously assigned to increases in "chain entanglement"[85], "solution viscosity that raises the cavitation threshold and to [decrease in] the solution volume available for cavitation bubbles to form"[98], and/or "the larger number of polymer chains will break up the solvent flows around the bubble and hence lessen its effect"[149], as well as the increased probability of recombination of mechanochemically generated macroradicals and the effect of concentration of conformational ensembles of chains.[57, 60, 91] The effect of "diluteness" in sonication of polymer solutions has not received nearly as much experimental and theoretical attention as in elongational rheology of polymer solutions.[53] Extrapolating from the latter field, polymer mechanochemistry in sonicated solutions should be studied by default under "ultradilute" conditions ($<10^{-2}[\eta]^{-1}$, where [η] is intrinsic viscosity; for example the maximum concentrations should be ~200 μg/mL and ~30 μg/mL for polystyrene of 0.1 MDa and 1 MDa, respectively, in THF at 25 ^{o}C), unless one establishes that the rate remains the same at higher concentrations (which might be better suited for the analytical techniques used) or is interested in the effect of polymer concentration. This would eliminate the contributions to observed kinetics of hard-to-reproduce interactions between partially stretched chains in elongational fields and the concomitant perturbations of the flow. We are aware of a single report[149] of the kinetics of polystyrene fragmentation during sonication as a function of the concentration down to ~10 μg/mL (M_p = 1 MDa, Đ < 1.05): the rate of the depletion of the initial polymer was independent of its concentration at 10 μg/mL and 20 μg/mL and decreased monotonically with concentration at ≥100 μg/mL. However, the reliability of this data is somewhat weakened by the mathematical manipulations of the gel-permeation chromatograms that likely introduced bias as discussed below.

Little experimental evidence appears to support literature claims[85] of any discernible trends in the dependence of the degradation rates during sonication on the solvent's vapor pressure or viscosity, or "gas solubility of solvent". The effect of solvent parameters, small-molecule solutes (including dissolved gasses) and the static pressure on the dynamics of cavitation bubble and some of the physical manifestation of bubble collapse, such as sonoluminescence, is fairly well understood,[94] but similarly careful and extensive experiments have not been conducted for polymer solutions. Design and interpretation of experiments aiming to understand the effect of solvent parameters on mechanochemical kinetics are further complicated by the difficulty of changing solvent viscosity without affecting its vapour pressure, surface tension and/or solvent/polymer interactions, all of which likely affect the bubble and chain dynamics. Perhaps the only statement that can be made with reasonable confidence at present is that the solvent can affect the polymer degradation rate but for typical solvents used in mechanochemistry (THF, toluene, ethyl acetate, etc.) the effect may well be within the limit of experimental reproducibility.

Several studies have been devoted to measuring the effect of the molar mass on the rate of fragmentation of chemically identical polymers.[91, 102, 122, 149, 150, 158, 159] Such molar-mass scaling potentially allows differentiation among various models of chain dynamics,[53, 57, 93] but at present the required high quality experimental data and quantitative models are lacking. As with other studies of fragmentation kinetics in sonicated solutions of polymers, the existing literature is contradictory, with most studies reporting scaling of variously defined rate constants as M^x, where x varies from 0 to >3 among different authors and M is typically either number- or weight-average molar mass. The dependent of the fragmentation rate constant on M^x is inconsistent with the existence of the M_{lim} (limiting molecular weight below which a polymer chain does not fragment), claimed in many of these studies (unless x = 0). In only one case the rate was proposed to scale as $(M-M_{lim})^x$, but the underlying kinetic data was obtained after extensive mathematical manipulation of the measured GPCs to remove what authors considered to be excessive broadening of the peaks due to significant axial dispersion[149]. The original GPCs had poorly resolved peaks of the reactant and fragmentation products, forcing the authors to assume Gaussian shape of the product peaks, thus biasing subsequent processing.

The effect of backbone chemistry on the kinetics of mechanochemical fragmentation is one area where notable progress has been made in the last 30 years. Modest but detectable selectivity of fragmentation was observed both in sonication[97, 158, 161] and other forms of transient elongational flows.[93] For example, replacing some C-C bonds in a polymer backbone with N=N or C-S bonds, which are generally thought to be more susceptible to homolysis under tensile load, increased the fragmentation rate by 2-3 fold.[97] The relatively weak mechanochemical selectivity during sonication probably accounts the failure of the early studies[91] to detect any effect of backbone chemistry on fragmentation kinetics. The low selectivity may reflect the fact that most chains that undergo mechanochemical reactions are trapped in the flow field until they break (which could be attributed to the rapid increase in the fluid straining rate and consequently the stretching force acting on the trapped chain during bubble collapse). Alternatively, it may reflect the low intrinsic selectivity of mechanochemical relaxation of highly stretched chains, which is tentatively supported by quantum-chemical calculations demonstrating that the *differences* in the activation free energies of homolysis of diverse covalent bonds (e.g., C-C bonds in polystyrene and polyethylene, C-O bonds in polyethylene oxide and C-N bonds in polyamides) decrease with applied force. The question, however, has not been studied carefully enough and the capacity of DFT-level calculations to reproduce quantitatively the kinetic barriers for homolysis of highly strain covalent bonds is unknown. In the view of the large empirical body of evidence of low mechanochemical selectivity during sonication, the recent claim[74] that the fragmentation stability of PMA containing a single moiety of anthracene/maleimide adduct was increased "over 100-fold" by simply changing the atom of the anthracene moiety to which a PMA arm was connected is quite remarkable if not improbable.

Other parameters that may affect the kinetics of mechanochemical reactions in sonicated solutions include the shape of the reactor and of the ultrasound source but we are not aware of any attempts to quantify such effects, which arguably may be quite difficult to do systematically.[170]

2.3. Demonstration of mechanochemical acceleration of complex reactions by polymer sonication

Since ~2005 the focus in sonicating polymer solutions largely

shifted from studying the fragmentation of commodity polymers in transient elongational flows to demonstrating acceleration of mechanistically diverse dissociation reactions by tensile load. The goal is accomplished by incorporating a small-molecule reactive site ("mechanophore") into a polymer backbone. Polymers containing on average one mechanophore per chain have been studied most commonly. Such polymers are synthesized by modifying the "mechanophore" to act as a dual-site polymer initiator from which a pair of "mechanochemically inert" macrochains (almost exclusively polyacrylate) is grown.[104] This strategy rarely produced polymers with dispersities below 1.1-1.2, which means that most of the chains contained the mechanophore far from the center of mass. For the typically reported number-average degree of polymerization of 500-10^3 simple calculations suggest that <15% of the chains contain the mechanophore within the central 10% of the chain; and <75% of the chains contain the mechanophore within the middle third. These estimates are broadly consistent with a single experimental attempt to quantify the location of the mechanophore in such polymers[110]. The location of the mechanophore relative to the center of mass of the chain is important because the probability of a sonicated chain to undergo a mechanochemical reaction of any type appears to be highest at the center of mass and decreases fairly quickly away from it (which may or may not reflect the distribution of force experienced by an average chain in an elongational flow). Even more problematic is the likelihood that the high-molar mass fraction of the polymers obtained by this method is enriched in chains containing 2 "mechanophores" separated by about a half of the chain length.[110] Because the probability of a chain to react mechanochemically in a sonicated solution probably increases faster than linearly with polymer size, most reported studies of such polymers were likely dominated by the high-molar mass fractions, potentially biasing the results in a manner that is difficult to quantify.

Fewer reported studies focused on multi-mechanophore polymers despite such polymers offering distinct advantages for product characterization[98, 117, 126, 171]. Most such multi-mechanophore polymers were prepared either by polycondensation or ROMP of suitably derivatized "mechanophores" and had dispersities >1.2, thus complicating quantitative interpretations of their mechanochemical kinetics observed in sonication (but not in single-molecule force experiments[39-41, 43, 46, 47, 172]). Cyclopropanation of commercial polybutadienes, which are available in very low dispersities, was reported[41] but the method has been rarely used and is of limited substrate scope.

It is now established that any macrochain would undergo non-selective backbone fragmentation during sonication irrespective of how dissociatively labile the "mechanophore" it may contain is[97, 109, 122, 173]. In other words, in a bulk sample mechanophore-centered chemistry, whether or not it results in chain dissociation, always competes with chain fragmentation elsewhere along the backbone (whether this competition occurs at the level of individual macromolecules, or selective and non-selective chemistries happen in different chains, potentially trapped in elongational flows created by different mechanisms, is not known). This means that the observation of the reduction of the average molar mass of the polymer during sonication by itself does not establish the mechanochemical dissociation of the "mechanophore", despite recurrent literature attempts[122, 156] to use it as such. A somewhat more convincing evidence of mechanophore-centered reactivity is the appearance of a spectroscopic signal attributable to the expected product. This approach was used mostly[106, 174] for mechanochromic reactions, i.e., mechanochemical reactions whose product, but not the reactant, possesses detectable absorption or emission. The problem with this approach is that the fraction of the mechanochemically reacted polymer that generated the chromophore or fluorophore is rarely quantified. An instructive example is a recent claim of "selective" mechanochemical dissociation of a Diel-Alder adduct of anthracene and maleimide based on the appearance of absorption of the anthracene chromophore (Figure 12)[74].

Comparison of the reported UV-vis spectra of the solution before and after sonication (Figure 12c), using the reported extinction coefficients of the polymer, anthracene and maleimide reveals that dissociation of the anthracene/maleimide adduct contributed <0.1% to the observed halving of the molar mass of the polymer during sonication. In other words, 99.9% of polymer fragmented without dissociation of the "mechanophore" (Figure 12a). The only reason that such a minor reaction path is detectable at all is that its product has the extinction coefficient that exceeds that of the major pathway by orders of magnitude. Other studies demonstrated much greater selectivity for chain fragmentation by dissociation of anthracene/maleimide adduct[114] and related compounds[132].

UV-vis detection was also applied to non-mechanochromic reactions by reacting a non-chromophoric product with a small-molecule chromophore and demonstrating that the resulting polymer adduct manifests the expected absorbance[128, 148, 156]. Reliable quantitative interpretation of the results requires reasonable certainty that the chromophore is incorporated in the polymer by reaction with the product of the mechanochemical reaction instead of by alternative mechanisms, including reactions mediated by sonolytically generated small-molecule radicals, or macroradicals originating from non-selective backbone fragmentation as well as reactions with sonolytically-modified "inert" parts of the polymer outside the "mechanophore" generated during sonication. The susceptibility of this method to such false positives is probably higher than is generally acknowledged in the literature, as illustrated by results in ref. [156] where considerable incorporation of the chromophore in the polymer was observed even prior to sonication. The chemistry responsible for this incorporation is not known.

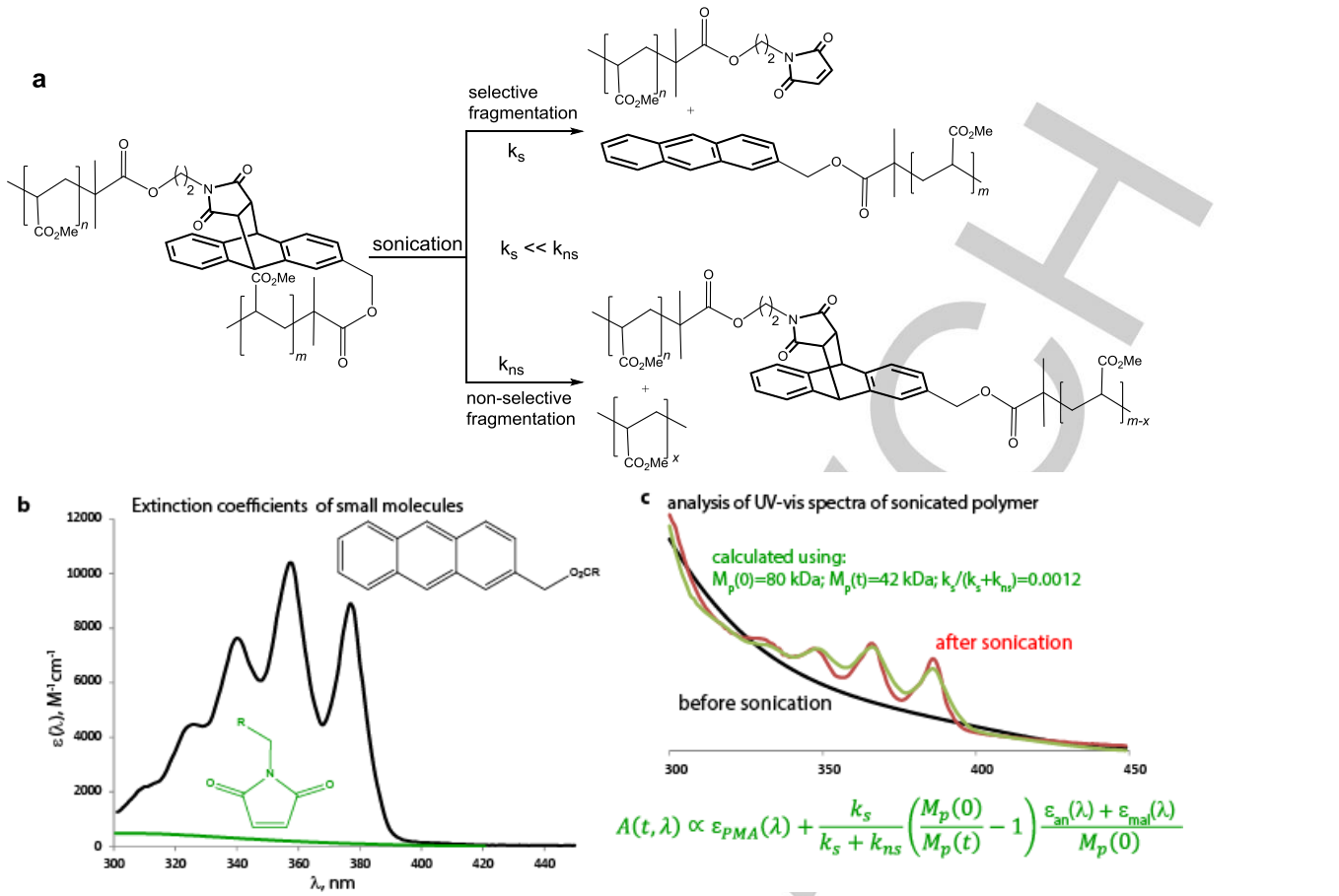

Figure 12. a) Sonication of a polymer containing a Diels-Alder adduct of anthracene and maleimide (highlighted in bold) leads primarily to non-selective backbone scission. The contribution of selective fragmentation by mechanochemical dissociation of the Diels-Alder adduct to total fragmentation rate was calculated from the known extinction coefficients of anthracene and maleimide (b) and the UV-vis spectra of the polymer before and after sonication as shown in ref. [74] using the formula (green) for the absorbance of the solution as a function of the sonication time, t, peak molar masses of the polymer prior to sonication ($M_p(0)$) and at time t, $M_p(t)$; the rate constants for polymer fragmentation by dissociation of the adduct, k_s and of any other backbone bond, k_{ns}; and the molar extinction coefficients of PMA, anthracene and maleimide, ε_{PMA}, ε_{an} and ε_{mal} ,respectively (c).

NMR analysis of polymers containing a single mechanophore per chain is rarely informative because the mechanophore signals are obscured by those of the rest of the polymer, unless the mechanophore contains a label, such as ^{13}C or CF_3. In contrast, multi-mechanophore polymers are well suited to characterization of their sonication-induced reactivity by ^{1}H- and/or ^{13}C NMR spectroscopy. Because both the intact mechanophore and its product(s) are detectable, the product distribution and the degree of conversion are quantifiable. Combined with the determination of the molar mass distribution (MMD) or at least one of its moments (i.e., M_n or M_w), the method allows accurate estimates of the selectivity for mechanophore-centered chemistry vs. chain fragmentation. The main drawback of this approach, as currently implemented, is the inability to determine the fraction of the reacted and intact mechanophores as a function of the polymer molar mass. For example, sonicating solutions of polymers of dihalocyclopropanes reduces their average molar mass while also generating 1,2-dihaloalkene isomers (Figure 10)[98]. In one study, halving of M_n of the sample was accompanied by isomerization of ~60 %mol of the cyclopropane moieties. However, since the measured fraction of the reacted cyclopropane was averaged over intact and fragmented polymer chains, one cannot conclude if cyclopropane ring opening occurs without chain fragmentation and vice versa, or backbone fragmentation always accompanies cyclopropane isomerization. Such information, together with quantum-chemical calculations of force-dependent kinetic barriers of the isomerization and fragmentation, would provide important clues to the range of microscopic conditions reacting chains experience during sonication. For example, demonstrating the presence of 1,2-dihaloakene moieties in polymers of the original molar mass or of polymer fragments containing only intact cyclopropane moieties would strongly suggest that the two reactions occur primarily in different chains, i.e., independent of each other.

Because of the lack of any direct evidence that (parts of) polymer chains are stretched in sonicated solutions, the assertion that the observed changes in the chemical composition of the solution result from stretched mechanophore-containing chains is based on failing to observe the same chemistry in control experiments. These include sonicating polymers with mechanophores at a chain terminus (or in a side chain), where it cannot be strained when the chain is stretched, or polymers with the size below which no reactions can be detected under given sonication conditions. While the control experiments established that stretching a polymer is a necessary requirement for the observed chemistry, it offers no indication of the contribution of local temperature and sonolitically generated small-molecule radicals to the observed chemistry. Because the implosion of an isolated cavitation bubble is thought to occur mostly adiabatically, the temperature of the generated elongational flows remains close to ambient. In contrast, shock waves generated by syn-

chronous implosion of a bubble cloud would likely be accompanied by significant thermal fluxes. If the observed mechanochemistry occurs primarily in flow fields generated by shock waves, the contribution of local heating cannot be excluded. This thermal effect will not be detectable in control experiments because a modest temperature raise will have a much more readily detectable effect on kinetics over activation barriers already reduced by tensile load. For example, increasing the local temperature from 300 to 350 K will accelerate a reaction with the activation free energy of 25 kcal/mol ~340-fold to the still undetectable half-life of >400 s in a control experiment. If the same barrier is reduced by force to 10 kcal/mol, the reaction is much more likely to occur at the timescale of the imploding bubble at 350 K ($t_{1/2}$ < 0.2 μs) than at 300 K ($t_{1/2}$ >2 μs). We are aware of a single attempt to quantify the thermal contribution to observed polymer mechanochemistry during sonication[175]. A systematic study would require a reactive site whose kinetic stability is insensitive to tensile load but is strongly accelerated thermally.

In contrast, sonolitically generated small-molecule species were demonstrated to affect the non-mechanochemical reactivity of intact polymers or their mechanochemically generated products.[175] Since radical traps have long been used to demonstrate and quantify the formation of macroradicals (presumably generated by homolysis of a backbone bond in a stretched chain) and the generation of biradical intermediates,[118] it seems quite likely that sonolitically produced radicals (e.g., from the solvent) would also participate in similar reactions, affecting the kinetics and/or product distribution of a diverse set of mechanochemical reactions. Such a contribution is rarely discussed, and has not been systematically studied but could probably be easily detected by NMR spectroscopy using isotopically-enriched solvents or solvents containing F atoms. This effect would be particularly significant for reactions that proceed through biradical intermediates, which definitely include isomerization of difluorocyclopropane, and dissociation of cyclobutane, oxirane and dioxetane derivatives, and may also include isomerization of other dihalocyclopropanes and of spyropyranes[106, 117, 121, 122, 126]; and reactions whose products are susceptible to radical addition, such as anthracene. Particularly interesting is the possibility that adventitious radicals may create new reaction paths by adding to highly strained C=C bonds, or transiently abstracting H atoms bound to highly strained backbones, or stabilize mechanisms that in the absence of radicals are not kinetically competitive. Understanding the effects of reaction pathways that are created or greatly stabilized only under the extreme local conditions in the vicinity of an imploding bubble (or bubble cloud) on the observed bulk chemistry in sonicated polymer solutions is one of the most overlooked aspects of the area.

2.4. Summary of polymer mechanochemistry in sonicated solution

Sonicating polymer solutions is so technically simple that it is currently the most commonly used technique to study polymer mechanochemistry. No direct evidence exists that in sonicated solutions chains (or their segments) are stretched but several mechanochemical reactions observed in single-molecule force spectroscopy and bulk loaded materials also occur in sonicated solutions, suggesting that (a fraction of) sonicated macromolecules are stretched in a manner qualitatively similar to that in other manifestations of mechanochemistry. However, there are reasons to speculate that only a subset of mechanochemical reactions can be observed in sonicated solutions, probably illustrating the differences of the timescale on which the highly stretched geometries can be maintained in SMFS, sonicated solutions and loaded bulk polymers. Despite the widespread use of sonication, even qualitative interpretation of changes in chemical compositions of sonicated polymer solutions is far more uncertain than is generally acknowledged. Empirical evidence suggests that non-selective backbone fragmentation always competes with site-specific chemistries (i.e., chemistries of reactive sites – occasionally called mechanophores – designed to undergo reactions more complex than simple bond homolysis when stretched). In some reported examples, only a tiny fraction of the reacted macrochains appears to undergo selective chemistry. While carefully designed control experiments can probably rule out purely thermal or sonolytic mechanisms, we lack any methods of quantifying the contributions of local heating, sonolytically produced small-molecule radicals and (probably) very high loading rates to the observed chemistry.

Although sonication of polymer solution is increasingly presented[85] as a quantitative tool, the physical significance of the numbers that have so far been measured on sonicated solutions of polymers is far from obvious. The literature offers very few indications that the bulk kinetics of mechanochemical reactions in such solutions can be quantified reproducibly much less at a level of detail and accuracy expected by a physical chemist. It seems justified to say that the parameters obtained by fitting experimental measurements to any of the proposed kinetic laws have far less mechanistic significance than they are typically credited with. Quantitation of bulk selectivity (e.g., non-selective chain fragmentation vs. site-specific chemistry[97, 98] or speciation of distinct mechanochemical products[64]) is probably more reproducible than absolute rate constants, but no less mysterious from the viewpoint of inferring microscopic conditions responsible for the observed chemistry. Nothing is known about these conditions at any reasonable degree of confidence. Estimates of forces or straining rates in fragmenting polymers, or their distributions along the chain length that appear in the literature are best treated as educated guesses.

While the microscopic conditions responsible for mechanochemistry in sonicated polymer solutions are very challenging both intellectually and technically to quantify, experience of other fields, including multi-bubble sonoluminescence and chain dynamics in turbulent flows suggest that they are not intractable. Progress will most likely require new polymer designs, more precise methods of quantifying molar mass distributions, and a tighter integration of measurements, quantum-chemical calculations and physical models than has been the norm so far. The paucity of literature reports of detailed physicochemical studies of the conditions experienced by mechanochemically reacting macrochains in sonicated solutions despite the recognized need for such data,[82, 83] may reflect both the scale of the problem and the fact that the field still has too many low-hanging fruit (i.e., qualitative demonstrations of new reactions in sonicated solutions) to justify investing the resources into much more challenging pursuits, however important they might be for the long-term vitality of the field or its technological impact.

3. Mechanochemistry of polymers in solids

Mechanical loads acting on bulk polymeric materials change their dimensions, which is accommodated by stretching of individual macromolecules (or their segments), eventually altering the kinetic stability of the constituent monomers. The diverse physical (entanglements) and chemical (covalent and non-covalent cross-links) interactions among individual chains in such materials lead to a complex, and only tentatively understood, distribution of forces experienced by individual chains and chain segments.[176, 177] Consequently, quantitative molecular interpretation of observed changes in the chemical composition of loaded polymer samples, much less predictions of such changes are at present impossible, although simple extrapolations of the existing body of empirical observations allow in certain cases plausible qualitative guestimates of the range of chemical reactions that may be induced in a polymer sample by loading it mechanically.

The chemical effects of loading bulk polymers have been studied for decades with the simplest examples being homolysis of covalent bonds of polymer backbones, transiently producing macroradicals detectable by EPR. The usually high reactivity of such radicals means that they react further by multiple mechanisms at rates that may or may not be sensitive to the applied load. A few examples of stress induced changes in the chemical composition of bulk polymer samples, presumably caused by reactions more complex than bond homolysis, were also reported[178, 179]. For example, stretching highly oriented polyamides films in the presence of water resulted in the growth of IR signals corresponding to the COOH groups, probably by mechanochemical hydrolysis of amides.[179] Observed rates of changes in the chemical composition of bulk samples under load and the dependence of such rates on this load are routinely discussed in terms of stress-dependent rate constants τ or activation energies U_o. These are derived from fitting the observable parameters to the Zhurkov equation[70, 71] (or its later variants), $\tau = \tau_0 \times exp\left(\frac{-(U_0-\gamma\sigma)}{RT}\right)$ where σ, R, T are the applied stress, the gas constant and the temperature, respectively; and τ_0, γ are fitting constants. Molecular interpretation of parameters τ_0 and U_o is far from straightforward because of the lack of information about the rate determining steps in the complex sequences of elementary steps, both physical and chemical, that are responsible for changes in the chemical composition of stressed bulk polymers. While it may be tempting to postulate that these changes reflect accelerations of individual elementary chemical steps (implicitly assuming that chemical reactions are rate-determining), such assumptions are neither justified nor universally applicable.

An instructive example is a series of the kinetics of oxygenation of stretched polypropylene films in the presence of O_3.[180, 181] The rate of propagation of the volume of the material containing carboxylic groups increased with strain in the elastic regime (up to 10%) but decreased at larger strains corresponding to plastic deformations of the material. While these results were later overinterpreted as indicating stress-induced inhibition of an unspecified chemical reaction[182], the authors ascribed the inhibition to the increased crystallinity of plastically deformed samples, which suppressed both the chain mobility and O_3 diffusion through the material (thus explicitly assigning the rate-determining steps to physical rather than chemical processes). Stretching a polypropylene film undoubtedly increases the probability of backbone fragmentation, thus accelerating initiation of the radical cascades responsible for oxygenation by increasing the flux of C-based radicals with very high reactivity toward O_2 and O_3[183]. The kinetics of the remaining steps, including chain propagation, branching and termination remains unknown [184]. The rates of these steps depend on chain mobility, which is reasonably well established to decrease with increased crystallinity of the polymer, which often increases under plastic deformation[185].

Little progress appears to have been made in the last 20 years towards understanding the molecular mechanisms and microscopic kinetics of chemical remodelling of commodity polymers in solid state. Instead the focus seems to have shifted to polymers incorporating purposefully designed moieties in which imposition of an axial molecular strain accelerates reactions more complex than backbone fragmentation by bond homolysis. Mechanochromic polymers have attracted most attention although some intriguing preliminary work on manipulation of bulk mechanical properties of polymers using mechanochemical reactions was reported. Examples include mechanochemical toughening of gels,[186] and polymers that are potentially self-strengthen (i.e., form more than 1 new load-bearing bond per each failed bond) thank to a sequence of reactions initiated by mechanical load.[139, 140]

3.1. Mechanochromism

Mechanochromic materials change their optical properties (e.g., absorption or emission color) under load. The existing mechanochromic polymeric materials are based either on a physical process, and occur at length scales above ~10 nm, or chemical reactions, which are typically localized within sub-nm^3 volumes. Examples of physical mechanochromism include rapture of dye-containing microcapsules, load-dependent spacing of layers of photonic crystals, phase transitions, aggregation and conformational changes[79, 187]. Chemical mechanochromism requires a reaction, such as load-dependent equilibria between aggregates and isolated molecules of certain aromatic dyes[79] or between spyropyrane and merocyanine isomers[188], or load-accelerated thermal dissociations of 1,2-dioxetane derivatives[121], which transiently creates chemiluminescence, of hexaarylbisimidazole[104], diarylbibenzofuranone[189], dianthracene[190] or dicinnamate derivatives[191] (Figure 13). Proposed or realized applications of mechanochromic materials include autonomous indicators of mechanical damage, camouflage[192], security paper and labels[193], optical storage[194] and fundamental studies of polymer adhesion, friction, crack propagation and plastic flow.

The mechanochromic response of aggregatochromic dyes and probably spiropyrans is thermodynamically controlled, i.e., its intensity is controlled by the effect of the force experienced by the dye on the equilibrium between the aggregate (or spiropyran) and monomer (or merocyanine). The mechanochromic response of the remaining molecular mechanophores is kinetically controlled, i.e., it is observed only above a threshold force at which mechanochromic reaction occurs on the timescale comparable to or shorter than that at which the local load dissipates. Research on mechanochromism of aggregatochromic dyes was recently reviewed[195].

Most reported studies of mechanochromic materials were

aimed at qualitative demonstration of mechanochromism in response to mechanical load, including axial stretching[121, 135, 136, 138, 188, 196] or axial compression[135, 188], shearing[197], bending,[190, 191] swelling,[198] electro-mechanochemical contraction[192] and shockwaves[199]. Coloration of glassy polymers containing dimers of anthracene or cinnamate (Figure 13)[190, 191] but not dioxetane[121] was reported in the immediate vicinity of a crack generated by impact. Thermal dissociation of anthracene dimers has activation barriers <27 kcal/mol and therefore may proceed even in strain-free polymer chains because local temperatures around a propagating crack in polymers may exceed 500 °C above ambient.[200] Because coloration of anthracene-dimer containing polymers was only observed around cracks and control experiments designed to rule out the contribution of local heating were not reported, claims of anthracene dimers being mechanochromic should at present be viewed as tentative.

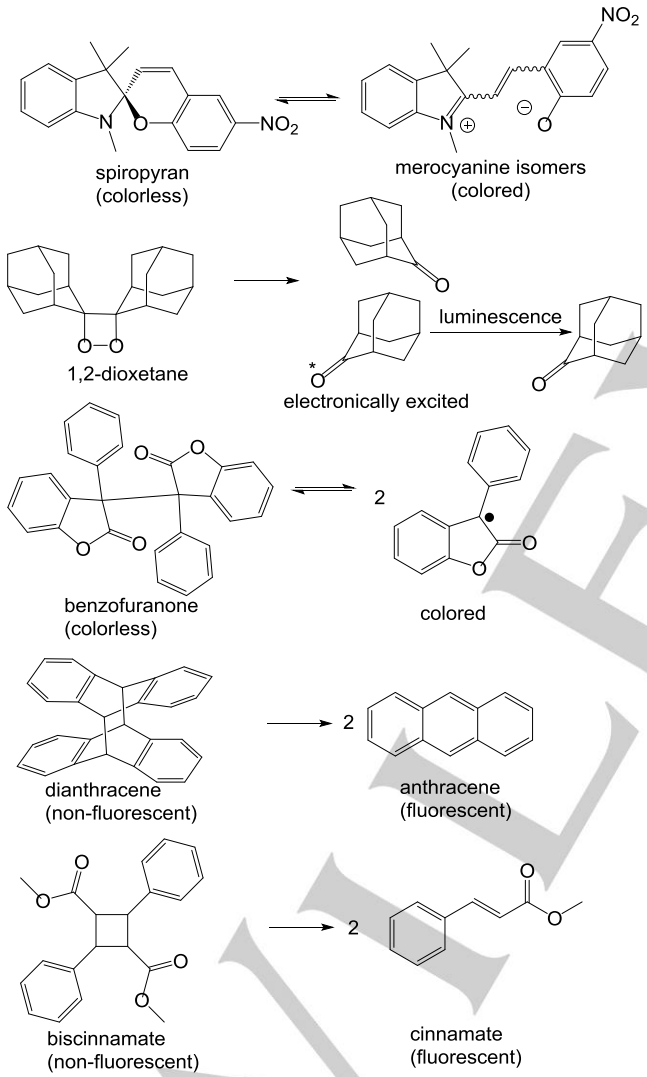

Figure 13. Mechanochromic reactions reported to occur in the solid state.

By far the most extensively studied mechanochrome is spiropyran (Figure 13), which was incorporated in the main chain and/or as a cross-link in PMA[188], PMMA[198], PDMS[143] and polyurethanes[136, 201]. In most polymers, spiropyran appears to be thermodynamically more stable than its merocyanine isomers in the absence of load, as evidenced by strain-free materials being colorless and colored materials bleaching upon removal of load. In one study, as-synthesized colorless polyurethane became blue on storage in the dark, suggesting spontaneous isomerization of spiropyran to a merocyanine isomer. Spiropyran is known to be solvatochromic,[202] i.e., solvent polarity and H-bonding capacity shift the equilibrium between spiropyran and at least one of merocyanines from endergonic (unfavorable) or exergonic (favorable). The outstanding questions are the rate of spontaneous coloration of this polyurethane in the absence of load, and whether it reflects the kinetics of spiropyran/merocyanine equilibration or of microscopic remodeling of the material with the color reporting changes in the chemical composition of the polymer matrix surrounding chromophore. The distinction is important because it determines which process the kinetic measurements performed on the colorless material characterized.

The intensity and/or rate of mechanochromism was studied as a function of the chemical composition of the polymer matrix, the method of mechanical loading, the loading rate, the position of spiropyran in the polymer network and the temperature.[135, 203, 204] In all but 2 cases,[131] colorless materials developed color when loaded, with the absorption maxima varying between studies. Insufficient data is available to ascribe these variations to differences in the peripheral substitution of the spiropyrans used, solvatochromism due to differences in the microenvironment of the chromophore, or different speciation of the merocyanine isomers. Isomerization between different merocyanines is most likely responsible the initially produced blue color evolving to purple before bleaching after load removal observed in two cases.[136, 143] In most studies, coloration was detectable only in plastically deformed samples,[136, 188, 197] with the color intensity correlating with the accumulated plastic strain in PMA elastomers[188]. The spatial distribution of fluorescence intensity of merocyanines in axially-compressed beads of glassy spiropyran-derivatized PMMA was reported to correlate with the calculated distribution of normalized traverse stress (Figure 14), but microscopic significance of this correlation is unknown[188]. Little appears to be known at present how common such correlations are because mechanochromic intensity appears to be quite sensitive to the loading rate[135] and the loading geometry. In contrast, spiropyran-derivatized PDMS was reported to undergo reversible coloration upon elastic deformation[143]. No case has been reported of the color persisting after load removal. Molecular interpretation of all these results is complicated by the lack of a detailed mechanism of thermal and photochemical interconversion between spiropyran and its various merocyanine isomers (of which there are at least 4), including respective standard and activation enthalpies and entropies and the quantum yields (or at least compositions of photostationary states) and the effect of molecular strain, temperature and environment on these parameters.

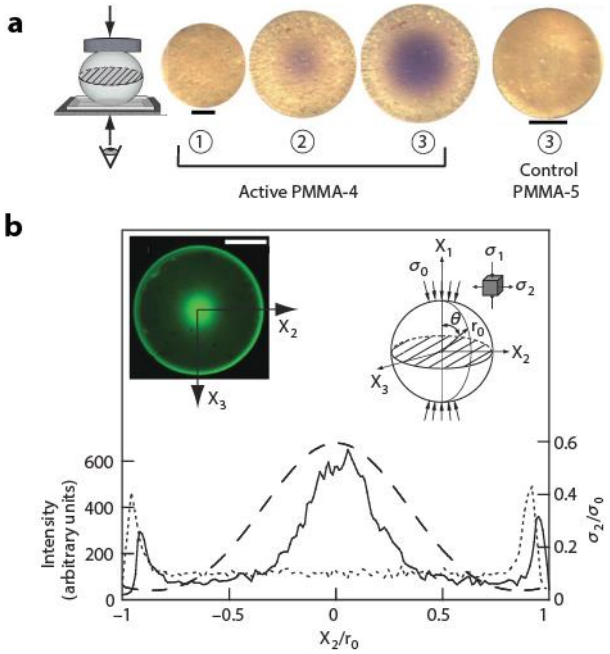

Figure 14. a) Compression of beads of glassy crosslinked spiropyran-derivatized PMMA (called "Active PMMA-4" in the figure) yields color and fluorescence with spatial distribution of intensity (solid line in b) consistent with the calculated distribution of normalized traverse stress (dashed line in b). Reprinted with permission from ref. [188]. Copyright © 2009, Rights Managed by Nature Publishing Group.

The major drawback of all spiropyrans reported to date as mechanochromes either for practical applications or for fundamental studies of chain dynamics and local stress distribution in loaded materials is the very low single-chain force at which the mechanochromic response saturates. In single-force experiments, spiropyran converts quantitatively into an isomer of merocyanine at applied force <0.3 nN.[47] In bulk spiropyran-modified polymers that were axially stretched to failure, coloration is not confined to the area around the newly formed interface (as happens with other mechanochromic compounds) but appears to be quite uniform throughout the sample[136, 143, 188] (we are not aware of literature analyses of the spatial distribution of absorption/fluorescence intensities in such samples). As a result, spiropyran cannot be used to distinguish overstressed regions of a loaded material (i.e., volumes where the material is most likely to fail), where a large fraction of chains may experience forces above 1 nN from only weakly stressed regions, where single-chain forces are <1 N, because in both cases, spiropyran will have converted to merocyanine quantitatively.

In contrast, luminogenic dissociation of dioxetane appears to be highly localized when polymers incorporating dioxetanes in backbones or as cross-links are loaded (Figure 15a)[77, 115, 121, 137]. Mechanochromism of dioxetane results from force-accelerated generation of triplet ketone, which reverts to the single state with emission of blue light. As a result, dioxetane mechanochromism is both transient and irreversible and can only be observed in real time. Unlike spiropyrans, emission intensity of dioxetane-derivatized polymers under load is localized in front of a propagating crack tip[121, 138] (Figure 15b). Light-emitting dioxetane dissociation was also demonstrates as a non-mechanochemical part of a reaction cascade induced by load.[108]

Perhaps the main limitations of dioxetane are the non-adiabatic dissociation mechanism[205] that largely precludes quantum-chemical calculations of force-dependent kinetics and the difficulty of synthetic elaborations of the dioxetane core to adjust the threshold force that triggers luminescence or the sensitivity of the rate to the applied force. Fairly low thermal stability also limits processing methods suitable for dioxetane-containing polymers.

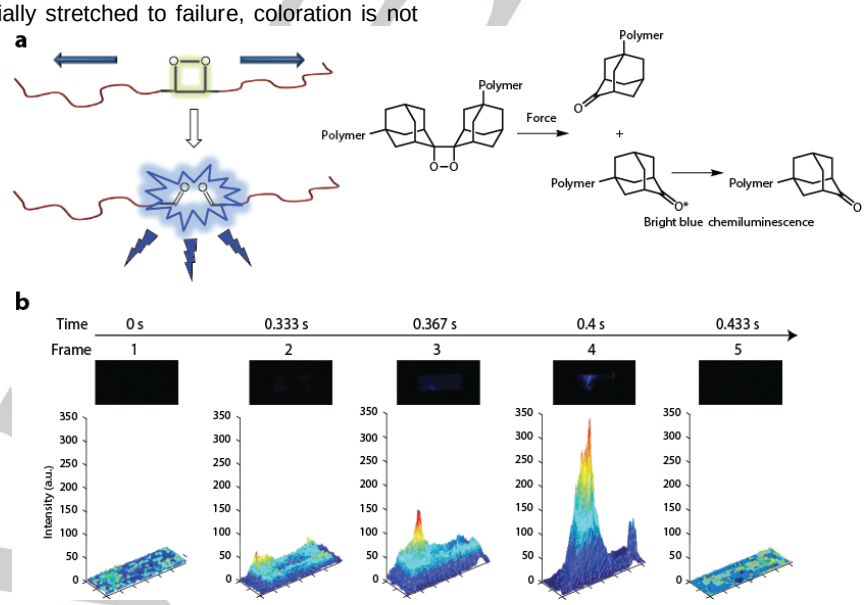

Figure 15. a) Force induced cycloreversion of 1,2-dioxetane leads to bright blue chemiluminescence; b) Time-lapsed images of a elastomeric film of linear PMA with 1,2-dioxetane incorporated near the center of the chains under uniaxial stretching and the corresponding emission intensity graphs. Reprinted with permission from ref. [121]. Copyright © 2012, Rights Managed by Nature Publishing Group.

4. Outlook: 7 challenges for polymer mechanochemists

It seems safe to speculate that the number of demonstrated mechanochemical reactions will continue to increase, with most demonstrations in sonicating polymer solutions. This effort is facilitated by the well-understood principles of designing reactive

sites whose dissociation is accelerated by stretching macromolecules containing them and the accepted protocols for demonstrating such mechanochemical acceleration. This work will be particularly impactful if it ventured beyond the reasonably established idea that stretching force accelerates dissociations of covalent bonds along the pulling axis. It also seems likely that the diversity and sophistication of mechanochemical cascades, involving sequences of mechanochemical and purely thermal reactions or multiple mechanistically and/or kinetically coupled mechanochemical reactions will grow. More excitingly, polymer mechanochemistry may be reaching the level of sophistication where complex problems of broad interdisciplinary significance are becoming addressable. Below we propose 7 such problems.

1. **New patterns of mechanochemical reactivity.** All mechanochemical reactions demonstrated to date involve dissociation of at least one covalent bond and are accelerated by stretching the macrochain. Yet theoretical considerations[61, 62] and computations[63, 73, 206, 207] suggest that the effect of tensile load on localized reactions is much more diverse, including inhibition of dissociation of loaded bonds and accelerated fragmentation of unloaded bonds that are not directly coupled to the applied force (i.e., bonds whose restoring force remains close to 0 regardless of the applied force). Although the possibility of tensile force inhibiting molecular fragmentation reactions has long been speculated (e.g., ref. [208]), such inhibition has never been demonstrated experimentally (early claims of such inhibition resulted either from misinterpretation of the original papers or are now recognized to be experimental artefacts[184]) The primary reason appears to be the fact that the existing experimental tools for studying mechanochemistry are not suitable for reactions that are inhibited by force. For example, sonication of a polymer containing an adduct whose dissociation is inhibited by force will simply result in chain fragmentation at other backbone bonds. Single-molecule force spectroscopy allows quantitative studies of force-dependent inhibition of certain dissociation reactions with favorable strain-free kinetics, but only at modest forces (<0.5 nN) and weak inhibitions (<2-fold). Other challenges include designing molecular architectures that allow reactive sites to be stretched along the necessary molecular axes and the development of quantitative protocols to measure the mechanochemical kinetics and selectivity of such reactions accurately. These challenges are worth overcoming because experimental validation of "unconventional" patterns of mechanochemical response will not only expand the diversity of reactions that could be exploited to yield new stress-responsive materials but also constitute a valuable dataset for testing the performance of theoretical models of mechanochemistry.

2. **Efficient and accurate methods of determining activation free energies of mechanistically diverse reactions as a function of applied force.** This data is essential for improving our understanding of how force affects chemical reactivity and for enabling efficient design of materials with desired mechanochemical profiles. At present the only source of such data are quantum-chemical computations. Although such calculations can be performed fairly routinely, the accuracy of the resulting activation energies and mechanisms is not obvious. Single-molecule force experiments are useful for benchmarking the computations over a fairly narrow range of forces, corresponding to half-lives on the order of 100 ms.[33, 39] Incorporation of the reactive sites into properly designed macrocycles (molecular force probes[29-35]) allows benchmarking of the computed results at forces <1 nN. Neither method is however particularly simple or has a broad substrate range. Neither can access forces needed to reduce the half-lives of most reactions to the 10 μs range, or achieve high loading rates that might be relevant at a tip of a propagating crack. Related to this problem is the lack of data to establish any trends in the performance of DFT functionals for calculations of force-dependent activation energies and mechanisms.

3. Quantitative microscopic models of mechanochemistry in sonicated solutions. Sonicating polymer solution is and will probably remain the primary method of demonstrating covalent polymer mechanochemistry. It is technically simple, has broader substrate scope than single-molecule force spectroscopy, requires relatively little material and is compatible with a full array of spectroscopic analytical techniques. At present its role in mechanochemistry is limited to qualitative demonstrations of acceleration of unimolecular reactions in stretched polymers. While several reactions were demonstrated both in sonicated polymer solutions and in bulk solids under load, so far sonication experiments do not appear to add much to simple qualitative considerations based on molecular geometry in rationalizing mechanochemical behaviour of solids or guiding the selection of monomers to yield desired solid-state mechanochemical response. Given that of all manifestations of polymer mechanochemistry, sonication is best suited for a high-throughput automated use, improving our capacity to extract quantitative molecular (or microscopic) data from sonication experiments has the potential to significantly improve the quality and quantity of experimental data needed to identify broad trends in mechanochemical reactivity as a function of molecular geometry, strain-free reactivity and potentially loading parameters.

4. The effect of polymer architecture on its mechanochemical properties. With very few exceptions, in contemporary mechanochemistry polymer chains are treated simply as inert transducers of a macroscopic mechanical load to reactive sites. Topologically complex polymers (with star, H and hyperbranched architectures) manifest chain dynamics that is often remarkably different from that of linear analogs. Such differences played a key role in fundamental studies of chain dynamics in entangled polymer liquids[209] and are increasingly exploited technologically.[103] Detailed quantitative studies of the effect of polymer topology on the mechanochemical kinetics and load-dependent mechanisms of localized reactions would likely be of considerable applied and fundamental value. For example, complex polymer topologies may allow the field to move beyond single-axis straining, which would be important for advancing our understanding of the relationship between anisotropic strains and reactivity. Although topologically complex polymers are not essential, they could be quite helpful for systematically exploring mechanochemical anisotropy of reaction kinetics, i.e., the sensitivity of force/activation energy correlations to the pulling axis. Given the much longer relaxation times of topologically complex polymers relative to their linear analogs in entangled liquids (e.g., polymer melts or solids above T_g) under load, derivatizing such polymers with "mechanophores" may yield qualitatively new patterns of mechanochemical response than has been observed to date. In other words, combining localized load-dependent chemistry with polymer topology may widen considerably the range of design parameters to be exploited in creating bulk materials with complex mechanical and mechanochemical be-

haviors.

5. The distribution of single-chain forces in bulk polymers. Mechanochemistry and specifically kinetically-controlled mechanochromic compounds offer exciting possibilities for studying the response of bulk polymeric materials at sub-μm and sub-μs scales, perhaps even at the molecular level. Single-chain forces and/or accumulated local strains in loaded materials could be quantified by monitoring the rate and/or extent of mechanochemical reactions as a function of the time the material was loaded. Realization of this potential, however, requires both accurate activation and standard free energies of reactions as functions of the local restoring and single-chain forces and reliable means of quantifying the extent of reactions in solids. The former is accessible by quantum-chemical calculations, ideally benchmarked against experimental data, including those from single-molecule force experiments and model studies. The empirical data available to date suggests that mechanochromism potentially offers a convenient method of quantifying reaction progress in loaded solids by monitoring the changes in their optical (absorption and/or emission) properties. For such measurements to yield quantitative information new mechanochromes are required with force/rate profiles that are amenable to accurate quantitation (both computationally and experimentally by single-molecule force spectroscopy) and tuneable by simple chemical modifications over a broad range, and whose mechanochemical response is persistent but reversible on energy input. No mechanochromic compound reported to date satisfies all these criteria and the chemical identity of such a "universal" mechanochrome is not yet apparent.

6. Models of polymer mechanochemistry beyond localized reactions. While it may be tempting to view polymer mechanochemistry simply as experimental system to study the effect of force on chemical reactivity, successful exploitation of mechanochemical phenomena in new materials, devices and processes may require a much broader perspective, both conceptually and methodologically. With the exception of single-molecule force spectroscopy, the single-chain force cannot be controlled even indirectly in any of the known manifestations of polymer mechanochemistry. Consequently, quantitative understand of mechanochemistry in practically relevant contexts requires means of relating macroscopic control parameters (e.g., stress tensors for solids, pressure gradients for flows and acoustic power fluxes for sonication) to single-chain forces of constituent macromolecules. One potentially productive approach is to estimate single-chain forces by studying bulk rates and product distributions of reactions with carefully established microscopic mechanochemical kinetics and mechanisms as a function of the macroscopic control parameters. Reactions that proceed by competing mechanisms with different force dependences could be particularly useful as such "internal competition" would be less sensitive to experimental parameters that are difficult to control and account for (e.g., the shape of the reaction vessel in sonication experiments). This data will have to be incorporated in multiscale, probably coarse-grained models, for example building on a recently reported attempt.[210]

7. Technological importance of polymer mechanochemistry. Increasing amount of empirical data suggests that mechanochemistry is an important determinant of mechanical properties of polymers in solution, melts and bulk materials, and mechanochemistry can limit processing methods and application niches for which the polymer is suitable. However, we are not aware of any literature reports of systematic studies of the nature, extent, mechanisms and macroscopic manifestations of mechanochemical phenomena in technologically important processes. It seems quite likely that empirical solutions have been found and implemented to suppress, or compensate for, deleterious effects of mechanochemistry in common applications of polymers (e.g., antioxidant additives in polymers subject to large cyclic mechanical loads to suppress aging) and understanding them could yield valuable insights into the mechanism of coupling between mechanical loads and chemical reactivity. While such systematic studies would probably require close cooperation with industry, in part because some processes that appear susceptible to mechanochemical effects may be based on proprietary technology, they are likely to have significant technological and potentially economic impact and therefore may be of interest to industry.

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Keywords: mechanochemistry • polymers • sonication • force • kinetics

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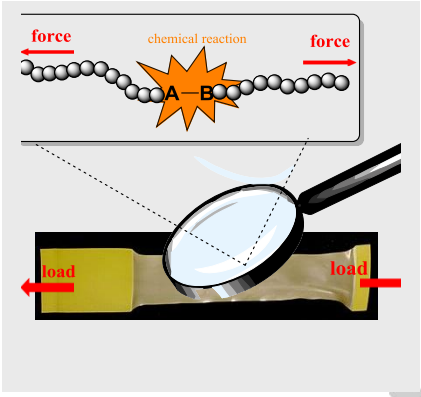
REVIEW

Polymer mechanochemistry aims to understand and exploit unique reactivities of highly stretched polymer chains. In this review we systematize reported macroscopic manifestations of mechanochemistry, and critically assess the interpretational frameworks enabling their molecular rationalizations. We discuss the limitations of these approaches to identify outstanding questions that need to be solved for mechanochemistry to become a rigorous, quantitative field.



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