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Ultrasound and Sonochemistry for Radical Polymerization: Sound Synthesis

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1. Introduction

Chemical reactions typically benefit from the use of an energy source to overcome activation barriers and allow the desired reaction to proceed; heat, light, and pressure are all used extensively for such purposes. Alternatives to these common stimuli can provide benefits in particular circumstances, usually stemming from differences in how energy is transmitted or transferred to the site of activation (e.g. light penetration for photochemistry, heat transfer for thermally-activated reactions, etc.). Some examples of lesser-investigated stimuli include ultrasound, microwave radiation, mechanical force, and electrical energy (i.e. electrochemistry).[1] Each of these offers a relatively unique mechanism of activation, or energy transfer. The effects of ultrasound are often not as quantifiable as more common physical stimuli,[2] lending it an air of mystery (and sometimes confusion). However, ultrasonic waves offer the ability to generate extremely large energies that are highly localized and short-lived in almost any liquid medium that can carry the sound waves, offering an enticing degree of control over ultrasound-induced chemical reactions.[3-4]

The use of external stimuli to activate polymerization reactions has been gaining interest in recent years – especially for chain-growth polymerizations, where the ability to start and stop the polymer chain from growing offers unique opportunities to finely control chain lengths and/or molecular weight distributions.[5] Light-activated polymerizations are particularly effective in this regard, allowing advanced applications in surface-grafting and patterning to be achieved under otherwise mild reaction conditions.[6-8] Recently, sonochemical reactions have garnered attention in the field of controlled chain-growth polymerization.[9-11] "Sonochemistry" is simply the application of ultrasound-induced physical and chemical events to a chemical process.[2] It inherently contains many of the traits desired of "green chemistry", such as the use of less hazardous chemicals and solvents, reduced energy consumption, and increased product selectivity.[12] The chemical events resulting from ultrasound can be further categorized as primary sonochemistry (the gas-phase chemistry occurring inside the collapsing bubble), secondary sonochemistry (solution-phase chemistry occurring outside of the bubble), and physical sonochemistry/mechanochemistry (chemical events occurring as a result of the strong shear forces generated upon bubble collapse).[13]

In this review we aim to present the fundamental and empirical aspects of ultrasound and sonochemistry with a focus on how these can be used as a stimulus for radical polymerization. Although all radical polymerizations are considered, particular focus will be put on chain-growth polymerizations operating under pseudo-“living” conditions, including reversible addition-fragmentation chain transfer (RAFT) polymerization, atom transfer radical polymerization (ATRP), and nitroxide-mediated polymerization (NMP).

1.1 Ultrasonic frequencies

Sound frequencies are measured in Hertz (Hz), with 1 Hz equal to 1 cycle per second. The typical range of hearing for an average human is approximately 20 Hz – 20 kHz. Hearing ranges for other animals differ considerably – for example a bat may hear in the range 1 kHz – 150 kHz. However, the term “ultrasound” is derived from the human perspective, and so often refers to frequencies higher than 20 kHz (**Figure 1**). Ultrasound employed for sonochemistry has been investigated across a broad range of frequencies, from 20 kHz up to frequencies greater than 2 MHz.[14] However, sonochemical activity at high frequencies requires more power since more energy is lost to molecular motion. For this reason, chemists have traditionally employed operating frequencies in the range of 20 – 50 kHz, although frequencies in the range 100 kHz to 1 MHz have recently gained increasing interest due to both the advantages these frequencies offer when radical generation is required, as well as the production of low-cost equipment capable of generating sound waves at these frequencies with high operating powers.

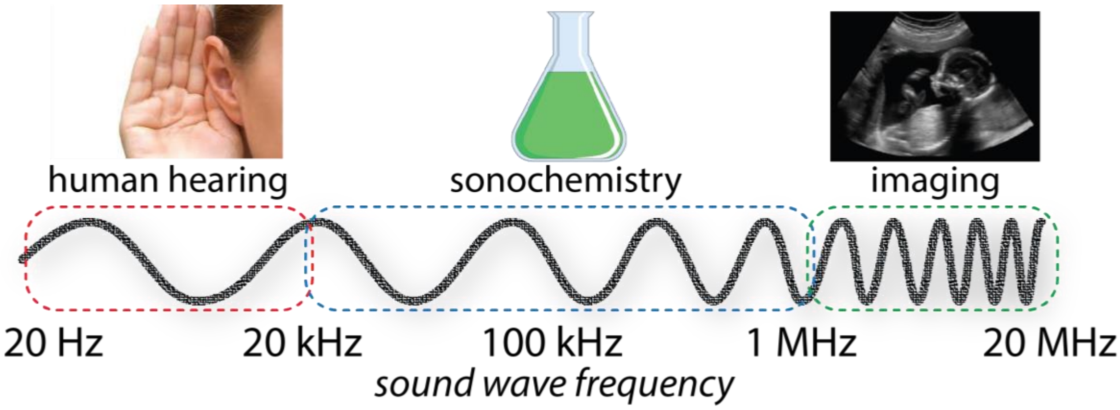


Figure 1. The sound wave frequency spectrum with selected regions of interest.

1.2 Cavitation events

Chemical activity in a liquid subjected to ultrasound is the result of the spontaneous formation, growth, and, eventually, collapse of gaseous bubbles within the liquid, a process known as “acoustic cavitation” (referred to hereafter simply as “cavitation”). The phenomena of cavitation and its effects on chemical reactivity are active and wellestablished scientific fields. For brevity, we will focus only on the more applied aspects of cavitation in this review, where the interested reader is directed to more specialised texts.[15-16]

Several key parameters affecting the effectiveness of ultrasound to promote sonochemistry are: 1) solution viscosity; 2) the applied frequency and intensity (sometimes referred to as 'power'); 3) the vapour pressure of any dissolved species; 4) the homogeneity/heterogeneity of the solution; 5) the presence of dissolved gasses (and the nature of the gas); and 6) the solution temperature (mainly through changes in the solvent/reagent vapour pressures).[14, 17] For example, the type of dissolved gas may seem innocuous, but can have a dramatic effect on the sonochemical activity of a given system.[18] To illustrate this, simulations have been performed to determine the chemical and physical nature of cavitation events in Ar- or N_2-saturated solutions.[19] The peak temperature upon bubble collapse is predicted to be significantly hotter for Ar (3922 K) compared with N_2 (2476 K), leading to a 100-fold increase in the production of radicals in Ar-saturated solutions. Interestingly, the microturbulence velocities resulting from bubble collapse in each case were similar (6.039 mm s^{-1} vs 7.066 mm s^{-1}), indicating a negligible difference in the physical effects of cavitation between the two systems.

The frequency and intensity of the applied ultrasound are typically the simplest to tune, as these can be chosen prior to the experiment and held constant or changed throughout the course of a reaction, where desired. Both parameters can have a significant effect on cavitation events and rates of sonochemical activity and/or radical formation.[16, 20] For example, it is generally well known that the rate of hydroxyl radical formation via the ultrasonication of an aqueous solution varies with the frequency of ultrasound, with lower rates of radical formation observed at low frequencies (ca. 20 kHz) and very high frequencies (>1 MHz) due to cavitation inefficiencies, and an optimal frequency of around 300 – 800 kHz often observed (**Figure 2a**).[21] Moreover, the bubble size and size distribution are significantly different at different operating frequencies (**Figure 2b**).[20] The intensity (or power) can determine whether cavitation occurs at all, with most systems having a 'threshold' intensity below which the energy supplied is not sufficient to induce cavitation. Depending on the desired outcome for a given reaction, these are key parameters that must be taken into consideration.

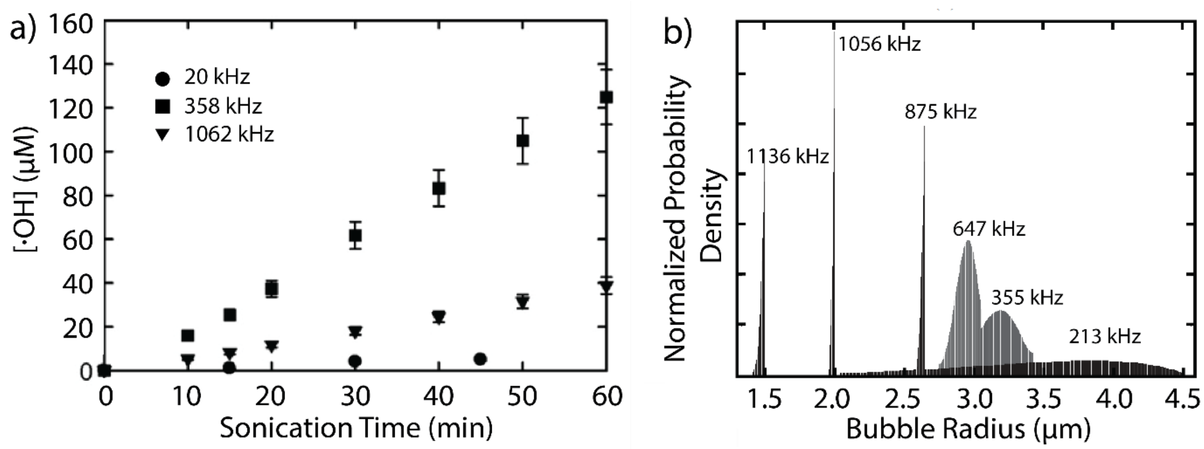


Figure 2. a) Effect of ultrasonic frequency on rate of hydroxyl radical generation from the ultrasonication of water (I = 0.90 W cm^{-2}). The rate of radical formation is significantly higher at the "optimum" frequency of 358 kHz; b) Bubble size and distribution with applied frequency. Adapted from [21] and [20].

Cavitation events can be induced by ultrasound in any liquid, provided the appropriate frequency and power are chosen.[14] This enables a potentially broad utility of sonochemistry towards a variety of organic or aqueous conditions. For example, it is commonly argued that although the cavitation threshold increases with increasing solution viscosity[22] (that is, more acoustic power is required to stimulate cavitation), provided that cavitation occurs, the effects of the bubble collapse will be much stronger, resulting in larger instantaneous temperature and pressure spikes.[2] This demonstrates that, practically, some of the above parameters may act in a compensatory fashion, making non-empirical predictions on the optimum operating conditions much more difficult.

1.2.1 Cavitation in homogeneous media

In homogeneous solutions, the effects of ultrasound are dominated by the collapse of cavitation bubbles containing solvent and/or reagent vapour, depending on the volatilities of the reaction components. Upon collapse the volatised molecules inside the bubble are subjected to such high temperatures (4500 – 5000 K)[23] and pressures (>1000 atm) that they can undergo fragmentation (or "sonolysis") into highly reactive radical species.[24] The fate of the generated radicals depends strongly on their nature, and diffusion into the bulk can occur for relatively stable radicals. Alternatively, the act of the collapsing bubble can generate such strong shear forces that reagents may be mechanically-activated towards a particular chemical reaction, or undergo mechanically-induced bond cleavage.[24] Although the rate of sonochemical radical production increases with frequency up to a maximum in the mid- to high frequency range (ca. 300 – 800 kHz) before decreasing at higher frequencies, the shear forces generated from collapsing cavitation bubbles are strongest at low frequencies, and drop off considerably as the frequency increases (**Figure 3**).[24-25] This is related to the larger bubble radius prior to collapse at lower frequencies[26] resulting in a larger void-volume that the surrounding liquid will rush to replace upon collapse.

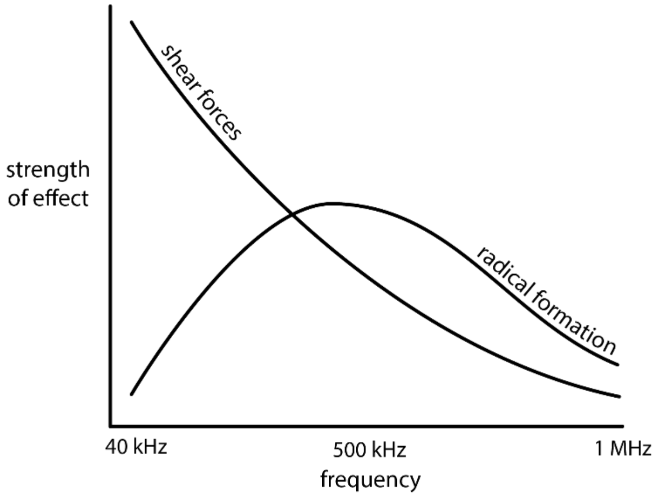


Figure 3. The two primary effects that can be utilised for sonochemical reactions are the mechanical (i.e. shear, mass transfer) forces generated from the collapsing bubble, and the reactive radicals formed from vapour molecule sonolysis. Generalised profiles for the "strength" of each of these effects at a given operating ultrasonic frequency are illustrated.

The effects of cavitation can be roughly divided into three regions within the solution:[3, 14] 1) the centre of the bubble containing vaporized molecules that may fragment under the extreme conditions during bubble collapse; 2) the interfacial region, where large temperature and pressure gradients exist, but also strong shear forces due to the rush of liquid to fill the bubble following collapse; and 3) the bulk liquid, where no direct effects of cavitation are felt, although reactions may occur with active species (radical or otherwise) that have diffused from the site of cavitation (**Figure 4**).

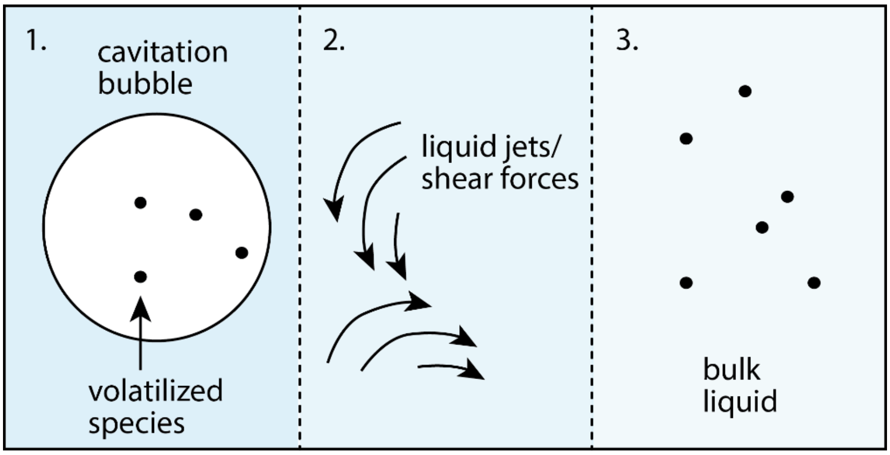


Figure 4. Different regions in a liquid undergoing ultrasound-induced cavitation: 1) the cavitation bubble containing volatilized solvent/reagent molecules; 2) the region immediately adjacent to the bubble in which strong liquid jets can generate a shear gradient upon bubble collapse; and 3) the bulk liquid in which cavitation-related physical forces are weak – reactivity in this region occurs via the diffusion of primary or secondary reactive chemical species generated in the other two regions.

1.2.2 Cavitation in heterogeneous media

Unlike for homogeneous mixtures, the presence of insoluble particles or metal surfaces can provide nucleation sites for cavitation events. This means that the chemical reactivity will be strongly localised, while the growth phase of the bubble may also be significantly affected due to features of the system such as surface roughness and surface hydrophobicity/hydrophilicity. As is well known, the effect of cavitation on an insoluble particle is often to break it up into smaller pieces. This is caused by mechanical forces acting on the particles when the bubble collapses, and is used extensively as a common tool in any chemistry laboratory to aid in the dissolution of solid materials.

1.2.3 Cavitation in biphasic systems

Another particularly useful application of cavitation-induced mechanical force is in the dispersion of a biphasic emulsion. When two immiscible liquids are mixed, the application of ultrasound can help to generated extremely fine emulsion droplets. This has found particular application in the food industry for homogenisation in the production of items such as tomato sauce or mayonnaise,[2] and will be discussed in the context of emulsion radical polymerization in a subsequent section.

1.3 Sonochemistry in synthesis

The physical effects arising from collapsing cavitation bubbles can be put to work for performing an action or transformation, allowing for the productive synthesis of many types of (in)organic compounds/materials.[15, 27] For example, in a homogeneous liquid the cavitation bubble will contain vapour from both the solvent as well as any volatile dissolved reagent. The reactive radical species formed via cavitation events can subsequently be used for radical-radical coupling[28-30], radical addition[29], and radical polymerization reactions.[31-32] Additionally, dissolved species in the immediate vicinity of the collapsing bubble subjected to strong shear forces as a result of the microjets of liquid rushing to fill the bubble can activate certain compounds or molecules to exert a mechanochemical response, with several classes of mechano-active catalysts having emerged as useful reagents for driving chemical transformations under the application of force, or mechanical energy.[1]

1.3.1 Mechanochemistry from ultrasound

The liquid microjets that occur following bubble collapse produce strong shear gradients. These forces are such that they can break covalent bonds – particularly within polymers of a certain chain length.[33] Alternatively, the mechanical force can be utilised by piezoelectric materials that respond to pressure changes. An example of this are piezoelectric catalysts such as ZnO or $BaTiO_3$, which have been shown to catalyse redox reactions under the harsh shear conditions of low frequency ultrasound.[24] This is believed to be due to a change in the shape of the catalyst material, which can generate a strain-induced voltage that alters its ability to undergo electron transfer (redox) reactions with dissolved solutes. These catalysts can be thought of as analogous to photoredox catalysts, although they are arguably much less well understood and investigated.[34] Activation of polymer-tethered chromophores or catalysts (often via polymeric coordinating ligands) can provide excellent responses to the mechanical forces generated via ultrasound, allowing for colour changes, the activation of a catalyst complex, or the release of active small molecules (e.g. acids, peroxides) that may stimulate further chemical processes.[34-35] The mechanical activation barrier in these systems is often dependent on the size of the attached polymer, and so can be readily tuned and predicted with accuracy.

1.3.2 Sonochemical formation of reactive species

For a molecule to be subjected to the extreme temperatures and pressures associated with bubble collapse it must first have entered the bubble, and therefore needs to be relatively volatile. Water presents the most well-studied liquid for sonochemical fragmentation, and can generate a wide range of radical and non-radical species including hydroxyl radicals, peroxy radicals, and hydrogen peroxide (H_2O_2).[2, 36] Any species dissolved in water may then undergo a chemical reaction with these generated reactants. Acoustic cavitation of organic solvents was not formally recognised until much later. However, the effects of ultrasound on non-aqueous solvents are identical (provided the threshold for cavitation has been reached) – i.e., the fragmentation of vapour molecules inside the bubble, and the creation of shearing forces from liquid microjets. Organo-sonochemistry remains an area with vast potential: being able to conduct controlled sonochemical reactions in organic media would significantly increase the scope of available substrates and chemistry.[13, 37-38] However, such systems also introduce significant challenges. For example, the nature of the generated radical species is expected to be much more diverse than for the sonolysis of water, while the cavitation thresholds in different media are correspondingly less well studied.

1.4 Polymers and sonochemistry

The interaction of polymer chains with physical or chemical events arising from acoustic cavitation have been studied for more than half a century,[39] yet remains a high degree of interest in field in large part due the unique aspects of both radical chemistry and mechanical force that can result from a collapsing bubble. We believe that the fields of ultrasound and polymerization are synergistically linked for two key reasons: 1) the prevalence of radical-techniques in the field of polymer chemistry as effective and versatile strategies for both chain growth and chain-end functionalization matches well with the ease and spontaneous formation of radical species under ultrasonication of a liquid; and 2) the size of polymer molecules in solution is large enough for the physical forces generated by fluid microjets surrounding collapsing cavitation bubbles to impactfully create active chemistry through mechanically-induced bond cleavage, an effect that would be extremely unlikely for smaller molecules. In fact, is well known that the shear forces generated sonochemically are often strong enough to break covalent bonds – even carbon-carbon (C-C) bonds – in the polymer backbone, thus decreasing the number-averaged molecular weight of the polymer. Conversely, given that radical polymerization is one of the most industrially useful methods of polymer synthesis, radicals generated sonochemically can be used as initiating species for polymerization when ultrasound is applied to a liquid containing dissolved monomer. Selected examples of both polymer degradation and polymer growth under the application of ultrasonic irradiation are given below.

1.4.1 Destructive reactions

Early investigators often reported a decrease in viscosity resulting from the application of ultrasound to a polymer solution. In some cases, the viscosity would return to its initial value upon standing, thus implying the breaking-up of aggregates or non-covalent (e.g. Van der Waals) interactions between molecules. However, in many cases this reduction in viscosity was found to be irreversible, indicating that a “depolymerisation” process may be occurring.[2] Polymer degradation can be easily monitored by molecular weight analysis, with a typical degradation curve of polystyrene under ultrasonication shown in **Figure 5**. This effect has been reported in a range of aqueous and organic solvents, indicating that degradation likely occurs from the mechanical effects of cavitation rather than chemical ones.[3]

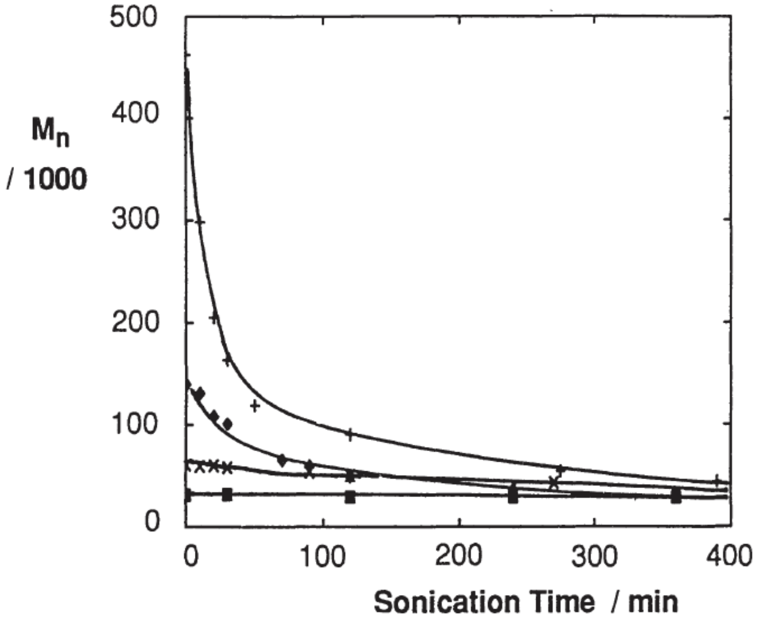


Figure 5. Degradation of polystyrene (1% polymer solution in toluene) of differing (initial) molecular weight under application of low frequency ultrasound (*f* = 20-50 kHz). Reproduced from [3].

It was recently demonstrated by Moore and co-workers that polymer chain length is much more important in determining the rate of degradation under ultrasound-induced mechanical shear than the overall molecular weight. Their investigation into the rate of mechanochemical ring-opening of a centrally-located chromophore under ultrasound revealed that when plotted as a function of chain length (i.e. “degree of polymerization” (DP)) the activation rates were identical, regardless of the polymer molecular weight (**Figure 6**).[33] Additionally, lower frequencies can degrade polymers more effectively than higher frequencies, as expected from our earlier discussion of the shear force/radical generation behaviour at differing frequencies (see Figure 3). Frequencies of 20 kHz are particularly potent degradative conditions due to the strong mechanical forces they can generate, although the irradiating intensity is also important.

Solvent interactions have been shown to have a strong influence on the ultrasonic degradation of polymers. This is thought to be due to the hydrodynamic conformation of a given polymer chain in solvents with differing solvent-polymer interactions; in solvents approaching theta conditions (so-called “good” solvents)[40] the polymer chain will be more extended than in a “poor” solvent, in which the polymer chain will be more globular or compact in nature. This affects how strongly the shear forces can act on the polymer, with more force transferred to the extended polymer chain than the compact one.

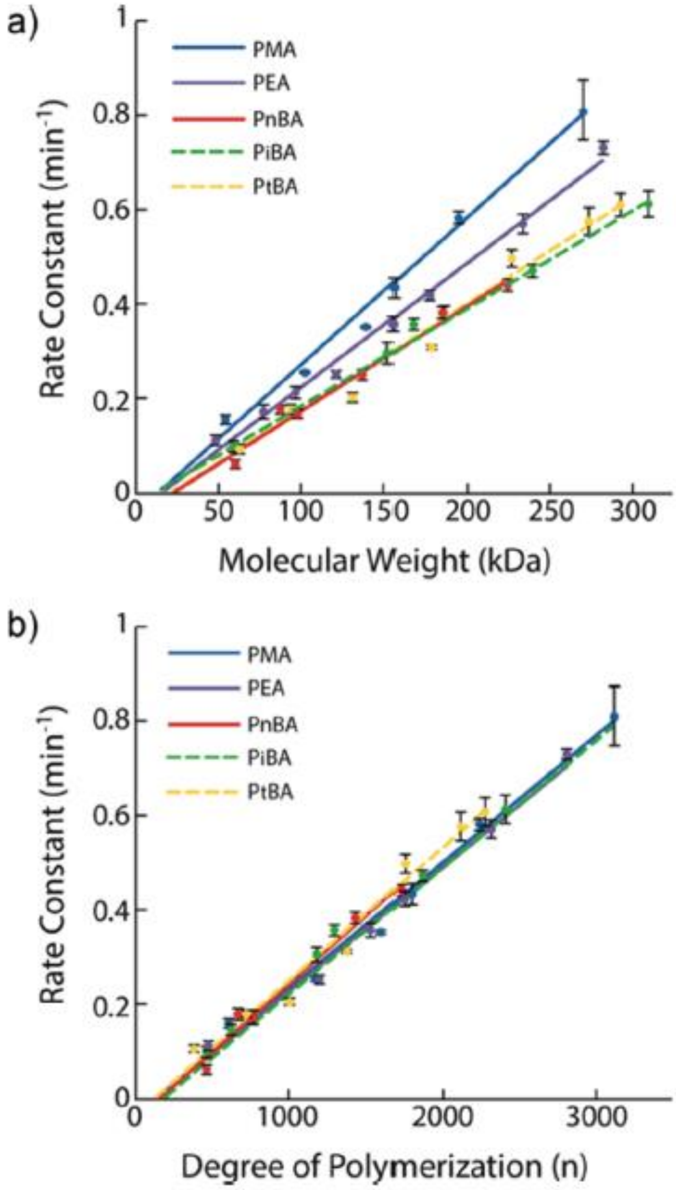


Figure 6. The mechanochemical-activation of a centrally-located chromophore under ultrasound has a rate constant that is dependent on the polymer chain length (i.e. degree of polymerization) rather than overall molecular weight. Reproduced from [33].

Another distinctive feature of polymer degradation under ultrasound-induced mechanical force is that the polymer chains typically cleave at the mid-chain position.[24] This is the result of a relatively localized strain on the extended polymer chain placing the strongest force on the covalent bonds located at the central position. This can be exploited further by embedding a weaker, “mechanically-active”, covalent bond at this position[41] – a trick made relatively trivial by the development of controlled/“living” polymerization techniques (*vide infra*).[42] Cleavage of covalent bonds under ultrasound can happen either homolytically, or heterolytically. However, homolytic bond cleavage of C-C bonds into two radical species under ultrasound is much more common, having been demonstrated by various radical trapping experiments. This offers the possibility of block copolymer formation from the combination of two macroradicals, as will be shown in the next section. One exception to this commonality is the ultrasound-induced cleavage of poly(dimethyl siloxane) (PDMA), for which no radical species could be found via trapping or electron spin resonance (ESR) spectroscopy, indicating a heterolytic cleavage mechanism.[3]

1.4.2 Constructive reactions

Much of the early research into "constructive" reactions utilising ultrasound involved the mechanically-induced homolytic chain scission of a polymer to generate a macroradical, which was demonstrated to be capable of acting as an initiator when in the presence of a monomer.[2] This can be used for the synthesis of block copolymers, "growing" from the cleaved macroradical species (**Figure 7a**). Conversely, the synthesis of block copolymers may also be achieved via the ultrasonic treatment of two differing homopolymers (in the absence of any monomer). Cleavage of both polymers yields two differing macroradicals, which can undergo radical combination to form an A-B block copolymer (**Figure 7b**). This has been investigated by Torkelson *et al.* via fluorescence-detection gel permeation chromatography (GPC) with a fluorescently-labelled block. They found that block copolymer formation can occur on the scale of 2 – 4 minutes under high intensity ultrasound.[28] This is proposed to be an excellent way to increase the compatibilization of immiscible polymer blends in a rapid and straightforward manner. Interpolymer radical coupling methods are, however, inherently inefficient due to the potential for non-block copolymer-forming side reactions, and the large amount of residual homopolymer remaining after the reaction. This limits the benefits of this technique for more advanced applications where polymers of higher chemical fidelity or purity are required.

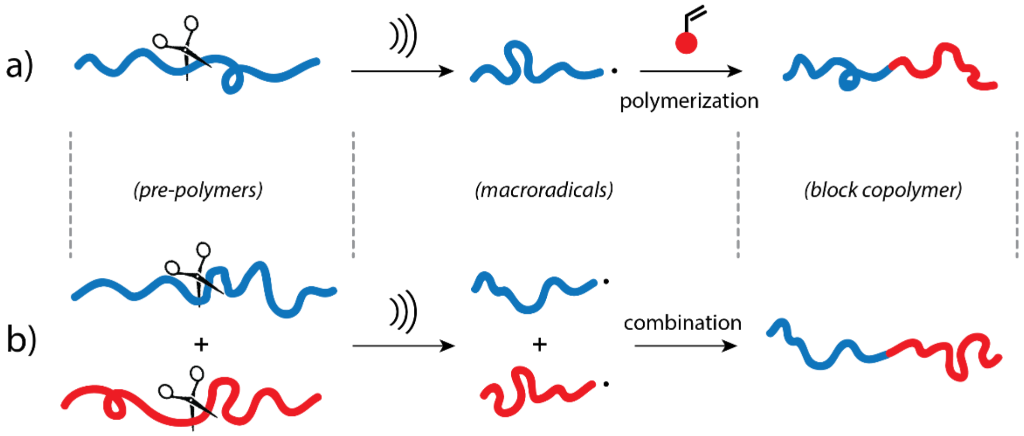


Figure 7. Block copolymer synthesis via: a) Mechanochemical degradation of a mixture of homopolymers followed by macroradical coupling; and b) Degradation of a homopolymer in the presence of a polymerizable (vinyl) compound.

The chemical effects of ultrasound can also be used in "grafting" reactions from polymeric substrates.[43] In this case, radicals formed ultrasonically can abstract protons from the dissolved polymer, forming a reactive side-chain-localised macroradical. When performed in the presence of additional monomer, this provides a site of initiation to grow a new polymer chain from the original polymer substrate. This offers a versatile and effective grafting approach, although with relatively little control over aspects such as grafting location or density.

2. Ultrasound-Mediated Radical Polymerization

Of course, direct radical initiation of monomers may also occur in the absence of any polymeric starting material. In this case, solvent-derived radicals – not macroradicals resulting from polymer chain scission – are utilised as initiators for the radical polymerization of (typically) vinyl compounds. Prior to 1972 there were very few reports of such a "direct sonochemical initiation" approach.[2] Below, some early examples of free radical polymerization using ultrasound-induced initiation are described, before introducing more recent attempts to combine ultrasound with controlled/"living" radical polymerization.

2.1 Free radical polymerization

In 1951, Lindstrom and Lamm described the potential for water-derived radicals to initiate a radical chain-growth polymerization under applied ultrasound.[39] In this pioneering work they show that the polymerization of an aqueous solution of acrylonitrile under ultrasound can proceed without the addition of any exogenous radical initiators, drawing parallels with the photolysis of water under photo- or γ-radiation as the operating mechanism. In agreement with the prior discussion of cavitation, the authors observe a "threshold ultrasonic power" below which no polymerization occurs. Moreover, they demonstrate temporal control over the polymerization, with polymerization ceasing when the source of ultrasound was switched off.[39]

An interesting use of water as the source of initiating radicals was reported by Goto et al., where instead of using it as a solvent it was added in a small amount (ca. 1 wt%) as one would a normal radical initiator.[44] This allowed for the sonochemical synthesis (f = 25 kHz) of poly(diallyl terephthalate) (a hydrophobic polymer) while maintaining homogeneity. When higher water loadings were attempted the reaction mixture became inhomogeneous and the polymer conversion was reduced. In the absence of added water polymerization was sluggish, indicating that initiation occurred primarily from water-derived radicals. The sonochemical polymerization of *N*-isopropylacrylamide (NIPAM) was performed by Ashokkumar et al., with the characteristic lower critical solution temperature (LCST) of poly(NIPAM) exploited to perform the synthesis under homogenous (20 °C) or dispersion (45 °C) conditions.[45] Both conditions resulted in efficient ultrasonic polymerization (f = 20 kHz) in the absence of a chemical initiator, with the low temperature case producing linear polymers and the high temperature (i.e. above the LCST) leading to microgels. The behaviour of microgels synthesized with and without added cross-linker above or below the LCST was investigated through a dye-release assay, as such polymer microstructures are promising candidates for controlled drug release in biomedical applications.[45]

Although water is particularly amenable to ultrasonic cavitation and early studies of ultrasound-induced radical polymerization primarily focused on the use of aqueous systems, it is now well-known that cavitation – and the resulting physical and chemical effects – can also occur in almost any organic solvent (or bulk monomer[31]), provided a sufficient power is applied to overcome the cavitation threshold.[3] Therefore, the scope for polymerization using ultrasound is very wide and not restricted to only water-soluble monomers or polymers. Indeed, when investigating the potential for ultrasonic degradation of polymers to initiate further polymerization (see section 1.4.2 above), Melville et al. observed that polymerization could occur even in the absence of the polymer 'seed'. In their experiments, bulk solutions of methyl methacrylate and styrene were found to polymerize under applied ultrasound (f = 213 kHz), while vinyl acetate showed no polymerization under these conditions. Thermal initiation was considered, but ultimately ruled out in favour of a mechanism of initiation via radicals formed during cavitation events.[46] Irradiation of bulk monomer solutions by Kruus et al. indicated that constructive polymerization occurred only with a continuous supply of Ar gas to the solution, whereas without continuous bubbling polymer degradation was observed.[47-48] This was also observed by other researchers,[49] and was thought to be due to differences in the types of cavitation events occurring under each condition, namely 'transient' cavitation and 'stable' (or sometimes referred to as repetitive transient cavitation) cavitation. Transient cavitation occurs when the bubble contains mainly the vapour of the liquid, with the cavitation formed rapidly and collapsing after only a few cycles, *which is dominated at low frequencies*. Stable cavitation occurs *at higher frequencies*, giving the bubble growth cycle a much longer lifetime and generating a more uniform distribution of bubbles throughout the liquid *due to the establishment of standing waves*.[12] This demonstrates the high sensitivity of sonochemistry on the parameters of the reaction, and the authors propose this to be a possible reason for the lack of coherence and reproducibility in some of the literature surrounding sonochemical polymer synthesis.[48]

Price and co-workers have performed extensive studies on the rates of radical formation in bulk monomer solutions under applied ultrasound, investigating parametric effects including intensity, temperature, and the presence or absence of traditional initiators.[3, 32] Their findings demonstrate that with careful consideration of the operating conditions, the rate of radical formation – and hence the rate of initiation of a radical polymerization – can be predicted and controlled with a degree of confidence. For the polymerization of bulk methyl methacrylate solutions under relatively harsh irradiating conditions (f = 22 kHz, I = 36.7 W cm^{-2}) the simultaneous growth and degradation of the polymer product was observed.[32] However, the final molecular weight of the polymer in the bulk monomer solution was higher than an analogous poly(methyl methacrylate) polymer subjected to the degradative ultrasound conditions in a non-reactive solvent (methyl butyrate), which was thought to be due to continuous monomer addition to the cleaved polymer macroradical when dissolved in the bulk monomer. The same reaction performed with 0.1 wt% azobisisobutyronitrile (AIBN) as a radical initiator gave similar observations, although the rate was faster and the maximum molecular weight was lower than the AIBN-free solution –

observations that can be explained by an increase in the radical concentration during polymerization.

The series of reactions involved in sonochemical radical polymerization can therefore be simplistically represented as:[3]

$$M\ (or\ S) + b \rightarrow 2R\cdot \#A$$

$$R\cdot +\ M \rightarrow RM\cdot \#B$$

$$RM_n\cdot +\ M \rightarrow RM_{n+1}\cdot \#C$$

$$RM_n\cdot +\ RM_n\cdot\ \rightarrow P\#D$$

$$P + b \rightarrow 2RM_n\cdot \#E$$

where: (A) interaction of the monomer (M) or solvent (S) with the cavitation bubble (b) to generate active radicals; (B) initiation; (C) propagation; (D) bimolecular termination to yield polymer, P; and (E) interaction of the polymer (P) with the bubble, leading to degradation and forming macroradicals.

Other than the “direct” formation of initiating radicals via ultrasound, it has also been applied as a supplementary source of energy to enhance radical polymerizations initiated by typical thermally-activated radical sources such as potassium persulfate, peroxides, or azo-compounds.[50] An enhancement in the radical polymerization of acrylates initiated by AIBN was even seen with the use of a standard laboratory ultrasonic cleaning bath (f = 50 kHz).[51] For these conditions, it was observed that both AIBN and ultrasound were required for polymerization to occur, with little or no polymer formed in the absence of either. The reason for the rate enhancement of systems containing traditional radical initiators is thought to be due to both an enhanced mixing effect and also the production of local “hot spots” where the initiator is rapidly degraded into its active radical form. This approach has certain similarities to the effects of microwave radiation, where there remain some questions over what the operating mechanism of rate enhancement is.[1] Other proposed reasons for the observed benefits of applying ultrasound include:[2] 1) the oxidation of impurities/inhibitors to non-interacting species; 2) ultrasonic degassing/oxygen removal; and 3) degradation of some polymer chains, leading to a higher instantaneous radical concentration. In a series of papers by Gopalan and colleagues, the activation of peroxy-mono/di-sulfate under high frequency ultrasound (f = 1 MHz, I = 0.7 mW cm^{-2}) is employed for the radical polymerization of (meth)acrylamide, and diallylamine in aqueous medium.[52-55] In the proposed mechanism, an ultrasound-induced decomposition of peroxysulfate can yield active sulfate and hydroxyl radicals, capable of reacting with vinyl monomers in solution, and hence initiating the radical polymerization pathway (**Figure 8**). It is interesting that no polymerization occurs in the absence of the peroxysulfate, indicating that these sonochemically "weak" conditions (i.e. high frequency, low intensity) do not generate sufficient cavitation of water itself to produce hydroxyl radicals via the 'solvent-derived' pathway.

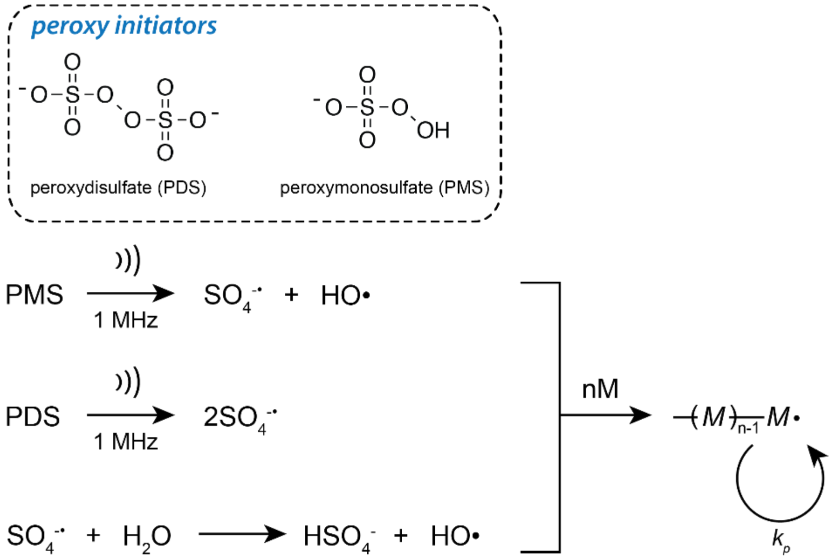


Figure 8. Mechanism of ultrasound-induced peroxysulfate decomposition and initiation pathway for radical polymerization in aqueous solution. Adapted from [52].

Interestingly, the 'constructive' and 'destructive' polymer reactions observed under ultrasound can be utilized to positive effect, as demonstrated by Kubo et al. where the formation of narrowly dispersed linear polymers was obtained by degradative reactions following radical-induced chain growth.[56] As the degradative reactions occur preferentially on higher molecular weight species in the population the overall molecular weight distribution is skewed back towards smaller chain lengths. The authors report a low final dispersity ($Đ < 1.3$) for poly(2-hydroxyethyl methacrylate) synthesized without any added chain transfer agent or other species to control the polymer molecular weight distribution. Moreover, they show that by modulating the applied ultrasonic power intensity the final number-average molecular weight (M_n) can be tuned, where a lower final M_n results when a higher power is used due to the increase in degradative events occurring under the strongly shearing conditions (**Figure 9**). In another study, Suslick et al. used the physical effects of ultrasound (f = 20 kHz) for the exfoliation of graphite into sheets of single- and few-layer graphene, while the simultaneous chemical effects were used to induce a radical polymerization of styrene (which was employed as the solvent).[57] This allowed for a one-pot synthesis of functionalized graphene, showing improved colloidal stability and re-dispersibility in a range of organic solvents due to the grafted poly(styrene) chains.

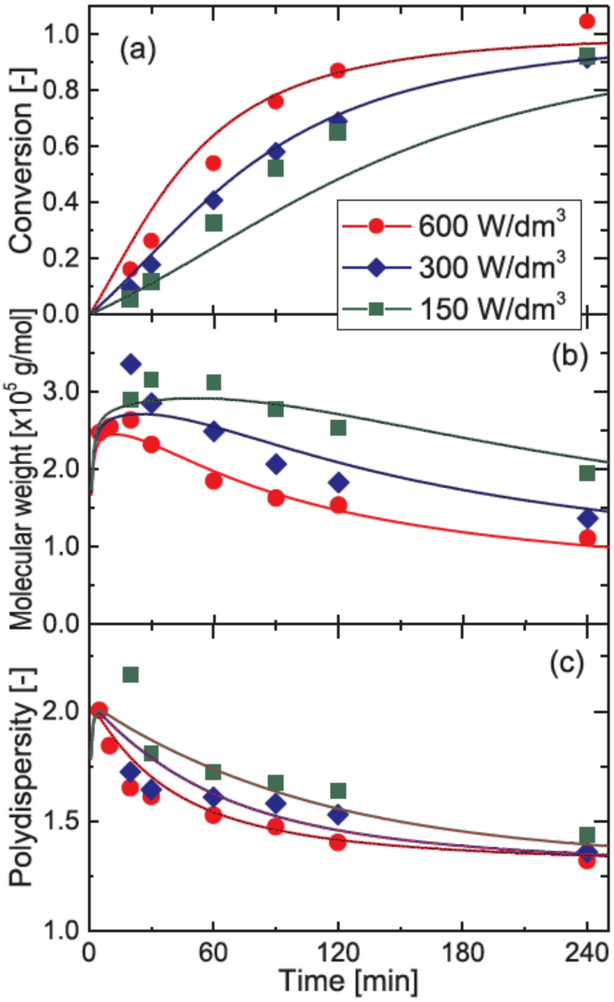


Figure 9. Simultaneous polymer synthesis and degradation under low frequency ultrasound (20 kHz) for the synthesis of low dispersity poly(2-hydroxyethyl methacrylate). Reproduced from [56].

Emulsion polymerization systems are particularly suited to benefit from ultrasound-induced synthesis,[58-60] as low frequency ultrasound is already employed regularly to generate narrowly dispersed emulsion droplets. Although dependent on ultrasonic parameters including frequency and intensity as well as chemical additive effects such as the surfactant loading concentration, the emulsification of liquid-liquid phases using ultrasound typically generates droplets in the size range between 50 – 500 nm.[19]

Sonochemical radical formation, particularly for oil-in-water emulsions, may then be used to initiate a radical polymerization inside of the emulsion droplets. This allows for the removal, or minimization, of initiators or emulsifying agents typically added to the reaction mixture. Initial studies however focused on the rate enhancement observed for conventional systems containing radical initiators when conducted with ultrasound. In 1950, Ostroski et al. reported an acceleration of a persulfate-initiated styrene emulsion polymerization when ultrasound was applied, both for low (15 kHz) and high (500 kHz) ultrasonic frequencies.[61] In other studies, under low frequency ultrasound it has often been observed that the addition of a radical initiator is essential for polymerization,[19, 62-64] indicating that the chemical effects of cavitation are minimal under these conditions. However, sonochemical polymerizations of monomer-in-water emulsions have been conducted by Biggs[65-67] and colleagues in the absence of an added initiator, resulting in the formation of uniform latex particles with conversion values dependent on the irradiating intensity. Others have investigated the (mini)emulsion polymerization of methyl methacrylate (MMA),[68-69] n-butyl acrylate (nBA),[58] n-butyl methacrylate (nBMA),[70-71] ethyl methacrylate (EMA),[72] glycidyl methacrylate (GMA),[73] 2-ethylhexyl methacrylate (EHMA),[74] and acrylonitrile (AN),[75] among others.[76] The emulsion polymerization of nBA in water was investigated by Xia et al., where it was observed that in the absence of an added surfactant (e.g. sodium dodecylsulfate (SDS)) the polymerization was extremely sluggish (2.4% conversion after 20 min vs. 91.9% conversion in the presence of SDS). This indicated that surfactant-derived radicals may play a primary role as initiating species for the emulsion polymerization.[58] This conclusion was challenged by Grieser et al., who reasoned that kinetic and nucleation arguments indicate that the contribution of surfactant-derived radicals in such oil-in-water emulsions would be unlikely under ultrasonic conditions.[68] Moreover, their data indicate that ultrasound has almost no influence on the propagation phase of the radical polymerization, only on the initiation.[68] The production of hydroxyl radicals in the systems investigated were inferred via measurement of H_2O_2 produced. Relatedly, in the study by Xia the polymerization of bulk nBA produced 28.0% conversion after 20 min, indicating that monomer-derived radicals could also be formed.[58] In almost all cases, it was reported that compared with traditional emulsion polymerizations conducted in the presence of an added initiator, higher polymer molecular weights and smaller, more narrowly dispersed latexes could be formed in shorter reaction times via ultrasonic initiation. The mechanism for a general ultrasonic emulsion polymerization is shown schematically in **Figure 10**.

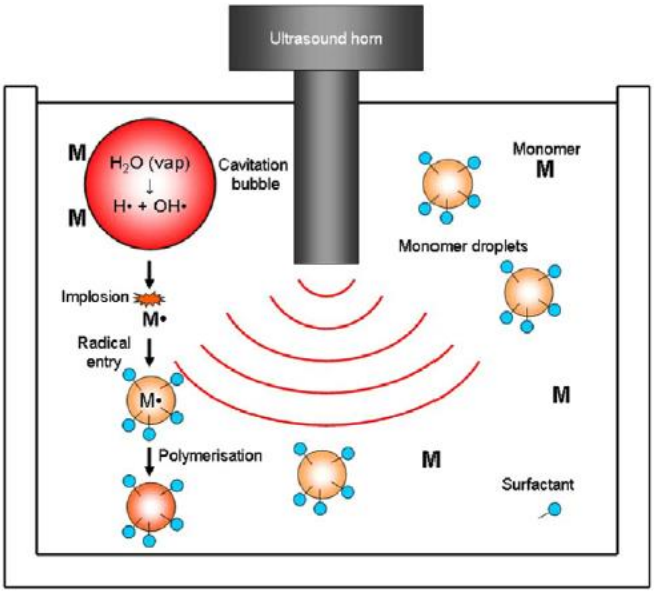


Figure 10. Proposed mechanism of radical formation and subsequent entry into emulsion droplet to initiate the polymerization under ultrasonication. Reproduced from [74].

In a study by Wang et al. it was observed that the ultrasonic emulsion polymerization of styrene could be significantly enhanced by the addition of a small amount of Fe^{2+}.[77] This is proposed to be due to the establishment of a secondary pathway towards the initiating hydroxyl radical (HO·) species: a Fenton reaction between the added Fe^{2+} and any H_2O_2 produced via the recombination of sonochemically-formed HO·. Where desired, this provides a useful pathway to “recycle” the H_2O_2 and ensure a higher efficiency of conversion from water to the radical initiating HO· species. However, excess Fe^{2+} can also quench HO· directly through non-radical-forming pathways,[78] and so there is often an optimal concentration for the enhancement effect. The same group also demonstrated that HO· recombination can be suppressed by the addition of scavengers such as aliphatic alcohols (e.g. methanol), which react with the formed HO· inside the cavitation bubble to form more stable hydroxyalkyl radicals. The more stable radical product can then diffuse from the cavitation site to react with the monomer, resulting in an increased rate of polymerization.[79]

While most of the earlier studies focused on the use of high shear, low frequency ultrasound, in 2008 Grieser et al. reported a successful microemulsion polymerization initiated via high frequency (213 kHz) ultrasound.[70] Mixtures of monomer and surfactant in water resulted in narrowly dispersed latex particles with relatively small sizes (40 – 100 nm) upon ultrasonic polymerization. Different surfactants resulted in different reaction kinetics and different sized latexes, while changes in the surfactant loading in the range 0.5 – 10.5 wt% had a negligible effect on the polymerization. The use of ionic surfactants resulted in the most rapid polymerization, with full conversion obtained within 15 min of irradiation, yielding translucent blue solutions indicative of a small and uniform particle size.[70]

In a nice example of the synergistic use of ultrasound for disaggregation of (nano)particles and radical-induced polymerization, Wang et al. utilized a low frequency ultrasound to disperse carbon nanotubes (CNTs) while simultaneously grafting a hydrophobic polymer from the CNT walls via an aqueous emulsion polymerization.[80] The initiating radicals are assumed to be sonochemically-derived, and the authors demonstrate via extraction studies that the grafted polymers show a particularly strong binding to the CNTs – indicating they are chemically grafted from the surface rather than physically adsorbed.

2.2 Controlled radical polymerization

2.2.1 Sonochemically-induced reversible addition-fragmentation chain transfer polymerization (Sono-RAFT)

An early investigation into the use of ultrasound for "living" polymerization was provided by Yan et al. in 1988.[81] Their approach entailed the synthesis of a polymeric macro-"iniferter" (*ini*tiator-trans*fer* agent-*ter*minator) – i.e., poly(styrene) with a dithiocarbamate group at one end of the polymer chain. This precursor was then subjected to low frequency ultrasonic irradiation (f = 50 kHz) in the presence of styrene monomer. Some chain-growth from the pre-polymer is indeed observed, although with low initiator efficiency. Irradiation of a non-chain-end functional poly(styrene) resulted in no chain growth – indicating that the polymerization was due to the presence of the unique iniferter moiety. The authors propose that the "mechanical forces exerted on the chains, or the high temperature at the given locality" resulting from acoustic cavitation can lead to the dissociation of the weak C-S bond of the iniferter, as per the more commonly described photo-dissociation-polymerization mechanism of such compounds.[82-83] However, given the relatively low molecular weight of the macro-iniferter (ca. 10 kDa) it is unlikely that the mechanical force generated ultrasonically would be strong enough to lead to bond dissociation – particularly at the chain end where the stretching force is minimal. Therefore, it seems more likely that either the thermal effects of cavitation are strong enough to cause dissociation, or the formation of sonochemically-derived radicals in the presence of the iniferter are what leads to the observed chain growth.

A later study into the combination of ultrasound with controlled radical polymerization was conducted by Zhu et al. in 2008.[84] In this report, a thiocarbonyl-containing chain transfer agent (or “RAFT agent”) was grafted onto the surface of silica particles, then subjected to ultrasound (f = 59 kHz) in the presence of an acrylate monomer (methyl acrylate (MA)). The reaction was conducted under strictly anhydrous conditions (dry THF), in a deoxygenated environment. The grafted polymers were shown to have properties similar to RAFT-derived polymers – i.e., relatively low dispersity, and controllable molecular weights. However, no mechanism for the polymerization step was proposed. It is arguably most likely that monomer and/or solvent-derived radicals formed from cavitation events provide the initiating radicals necessary to drive the RAFT polymerization, although it should be mentioned that cavitation at interfaces and in heterogeneous mixtures is often vastly different from the behaviour observed in homogeneous solutions.[85] Nevertheless, this work provided an interesting starting point for the combination of RAFT polymerization with ultrasound techniques.

Having developed various novel initiation strategies for radical polymerization,[86] Qiao and colleagues reported the first use of sonochemically-derived radicals for activation of an aqueous RAFT polymerization (**Figure 11**).[10] It is well accepted that hydroxyl radical generation from the sonolysis of water is significantly enhanced at higher ultrasonic frequencies (>200 kHz) than lower ones (e.g. 20-50 kHz),[87] while the shear forces generated are much lower.[14] Therefore, when conducting a sonochemically-induced RAFT polymerization using frequencies above 400 kHz the potential for polymer degradation via mechanical means is greatly diminished, allowing for the synthesis of polymers of longer chain lengths and higher molecular weights. Using a frequency of 414 kHz the sono-RAFT approach was found to allow for the controlled polymerization of a range of water-soluble (meth)acrylate and acrylamide-type monomers at ambient temperature. A range of different chain lengths were demonstrated by adjusting the molar ratio of monomer to RAFT agent, while exceptional temporal control was observed via a simple “on”/“off” experiment. This “clean” synthesis method in the absence of metal catalysts or exogenous initiators represents a promising strategy for the synthesis of well-defined water-soluble synthetic polymers.

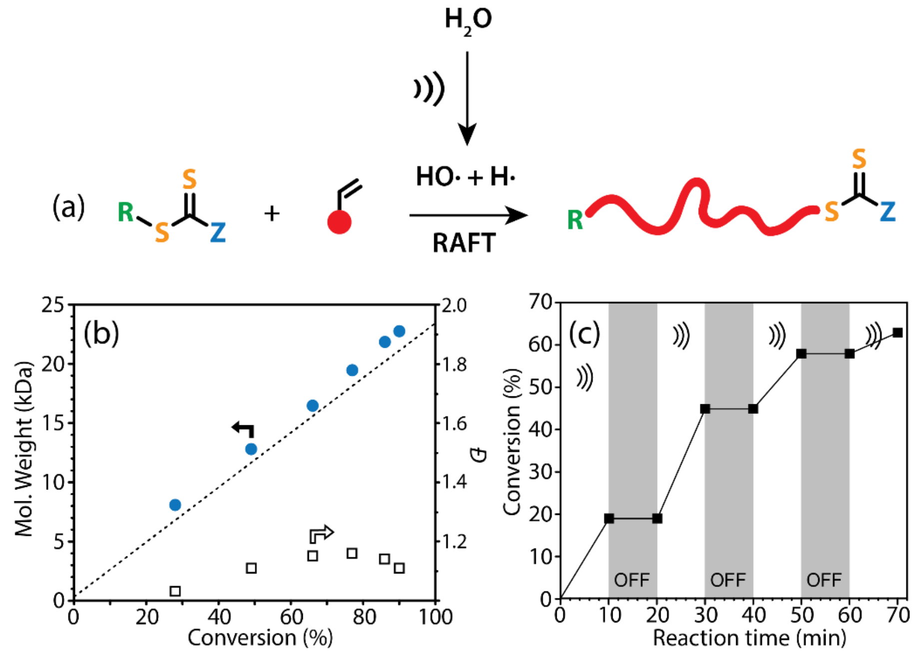


Figure 11. (a) Scheme for sonochemically-induced RAFT polymerization; (b) Molecular weight evolution characteristics with monomer conversion during sono-RAFT polymerization; and (c) Temporal control achieved via switching ultrasonic irradiation on and off. Adapted from [10].

2.2.2 Sonochemically-induced atom transfer radical polymerization (Sono-ATRP)

The combination of ultrasound with atom transfer radical polymerization (ATRP) was first reported by Yaci et al. in 2004, wherein the synthesis of block copolymers via a two-step ultrasonic degradation/radical polymerization procedure was described.[88] Macroradicals formed under the application of low frequency (f = 35 kHz) ultrasonic irradiation were capped directly with Cu(II)Cl_2, yielding halide-terminated poly(methyl methacrylate) (PMMA-Cl). The molecular weight of the pre-polymer material was observed to decrease from >500 kDa to ca. 50 kDa within 4 h of irradiation, indicating effective chain cleavage. Monomer (styrene) was added directly following the ultrasonic degradation of the pre-polymer, and the mixture placed in a heated oil bath at 110°C to activate an ATRP polymerization/chain extension (**Figure 12a**). Importantly, the active form of the copper catalyst (Cu(I)Cl) is formed *in situ* as a result of the atom-transfer of chlorine from the copper complex onto the formed macroradical, as per the “deactivation” step in a traditional ATRP.[89] However, it should be noted that the macroradicals formed from the polymer chain cleavage are non-equivalent, and although chlorine can cap both of the formed radicals, their efficiency as initiators in the subsequent ATRP reaction is markedly different. This may result in residual homopolymer chains, or broadly dispersed products following the ATRP step. In spite of this, the experimental results presented by Yagci et al. show relatively good blocking efficiency and monomodal polymer peaks via GPC analysis.[88]

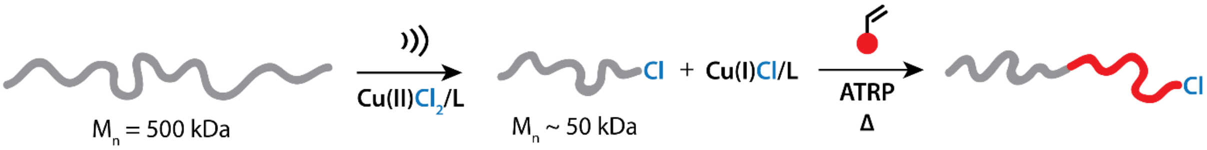
In 2016, Esser-Kahn and colleagues reported an innovative method to conduct a controlled radical polymerization using ultrasound as the polymerization stimulus.[9] They employed a piezoelectric (force responsive) catalyst that is capable – under an applied force – of facilitating an electron transfer reaction that could reduce a dissolved metal complex. Such mechanochemically-active redox catalysts can produce high electrochemical potentials (-1.23 V for the commercial barium titanate ($BaTiO_3$) nanoparticles used in this study) under applied ultrasound. Using low frequency ultrasound (20 kHz) the authors investigated the ability of the mechanoactive catalyst to reduce dissolved Cu(II) to Cu(I), which can subsequently activate an ATRP reaction at ambient temperature (**Figure 12b**). The use of this co-catalyst system in the presence of ultrasonic irradiation was found to result in the smooth polymerization of nBA, with molecular weights increasing with monomer conversion and narrow polymer dispersities observed throughout, consistent with a controlled polymerization. However, the strong shear gradients generated were found to limit the chain lengths obtainable due to potential polymer chain-breaking reactions above a critical chain length.[32-33] Indeed, the polymer molecular weights reported are relatively low (< 10 kDa), well below most threshold values where degradation begins to occur under similar ultrasonic conditions. The polymerization did not proceed significantly in the absence of $BaTiO_3$, while the use of non-piezoelectric carbon black nanoparticles instead of $BaTiO_3$ also resulted in no polymerization.[9] Expanding on this work, Matyjaszewski et al. were able to achieve temporal control for the mechano-ATRP by reducing the loading of the copper catalyst to ppm amounts (75 ppm, compared with 10 000 ppm used by Esser-Kahn et al.).[90] A variation in the observed reaction kinetics was reported for different crystal structures and particle sizes of the $BaTiO_3$ catalyst, which was thought to be due to the effect that these structural features have on its piezoelectric properties. Additionally, a PMMA-coated $BaTiO_3$ catalyst was developed to increase solubility in the reaction mixture and potentially avoid aggregation events that would lower the effectiveness of the catalyst.

The PMMA-coated $BaTiO_3$ indeed showed a modest improvement on the kinetics as compared with the native $BaTiO_3$ nanoparticles.[90] The same researchers went on to develop a zinc oxide (ZnO) catalyst that could replace $BaTiO_3$ for mechano-ATRP, further improving the characteristics of the system for the successful synthesis of a range of polymers under low frequency ultrasonic irradiation (f = 40 kHz).[91]

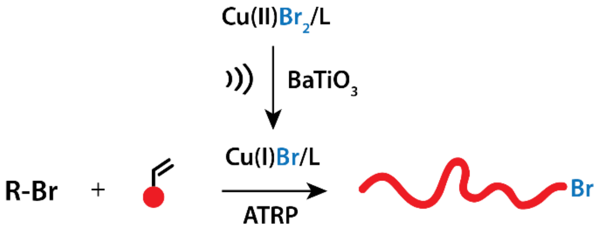
Inspired by the recent developments in sonochemical radical formation for controlled polymerization (*vide supra*), a different approach to ultrasound-induced ATRP was independently reported recently by Matyjaszewski et al.[11] and our group[92], in which the sonochemical (rather than mechanical) effects of ultrasound were utilized. Specifically, hydroxyl radicals generated via the ultrasonic irradiation of aqueous solution were used as "initiators" in a technique known as "initiators for continuous activator regeneration" (ICAR) ATRP.[89] In this case, radicals formed sonochemically are used as "reducing agents" to convert a $Cu(II)X_2/L$ (where L is a coordinating ligand and X is a halide) pre-catalyst complex into the active Cu(I)X/L form, capable of activating an ATRP reaction when in the presence of an alkyl halide initiator and a polymerizable monomer (**Figure 12c**). Throughout the reaction, any $Cu(II)X_2/L$ species that may be built-up through inevitable termination reactions can be efficiently converted back into the active catalyst form, thereby allowing for a significant reduction in the total amount of copper required for a successful reaction.[93] Matyjaszewski et al. report the successful and controlled polymerization of (meth)acrylate-type monomers including poly(ethylene glycol) methyl ether methacrylate (PEGMA) and 2-hydroxyethl acrylate (HEA), even up to relatively high molecular weights (>100 kDa). The high molecular weights were obtained in spite of the low frequency (40 kHz) – and hence strongly shearing – ultrasonic conditions, which the authors attribute to the low ultrasonic *intensity* used.[11] Temporal control over the reaction was also demonstrated, indicating the relatively rapid build-up of $Cu(II)X_2/L$ when the ultrasound is turned off such that the "deactivation" of propagating chains becomes dominant, thus halting the polymer chain growth. The synthesis of a DNA-polymer biohybrid was carried out using an alkyl halide-functionalized DNA fragment, indicating the potential for this sono-ATRP technique to be utilized for bio-conjugation reactions where aqueous conditions and ambient temperatures are often desirable.[94] Using a higher operating frequency (f = 490 kHz), Qiao et al. were able to achieve a faster polymerization rate under otherwise similar conditions.[92] This is attributed to the increased radical generation efficiency at higher ultrasonic frequencies.

However, as solution viscosities are found to detrimentally affect the sonochemical process, low operating concentrations were required in order to reach high monomer conversions. Matrix-assisted laser desorption ionization time-of-flight mass spectroscopy (MALDI-ToF MS) analysis of the resulting poly(HEA) showed remarkable chemical fidelity, with the major peak series corresponding to the alkyl halide-initiated polymer, and only a very minor peak series attributable to the hydrolysis product of the ω-terminal bromine atom.

(a) Ultrasonic degradation/ATRP chain extension



(b) Mechanically-activated ATRP (Mechano-ATRP)



(c) Sonochemically-activated ATRP (Sono-ATRP)

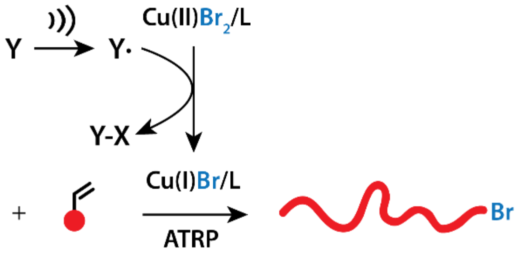


Figure 12. Different approaches to ultrasound-assisted/induced ATRP: (a) Ultrasonic degradation of high molecular weight pre-polymer in the presence of Cu(II)Cl$_2$, followed by thermally-activated ATRP chain extension; (b) Reduction of Cu(II)Br$_2$ (deactivator) to Cu(I)Br (activator) complex via mechanically-activated reducing agent BaTiO$_3$; and (c) Radical reduction of Cu(II)Br$_2$ (deactivator) complex to Cu(I)Br (activator) via sonochemically-derived radicals.

2.2.3 Sonochemically-induced nitroxide-mediated polymerization (Sono-NMP)

The ultrasonic degradation of high molecular weight polymers in the presence of various nitroxides (e.g. OH-TEMPO, TIPNO, and BIPNO) acting as radical traps in order to produce "macroinitiators" capable of undergoing subsequent controlled radical polymerization via nitroxide mediated polymerization (NMP) has been studied by Shmidt-Naake et al.[95-96] Similar to the concept developed by Yagci[88] this route relies on the mid-chain cleavage of a precursor polymer into two (non-equivalent) macroradical species. Nitroxides are a class of "stable" radical, so they can be added to the initial reaction mixture but will quickly react with carbon-centered radicals to "trap" the active species and create a dormant NMP macroinitiator (**Figure 13**). NMP can then be conducted via the thermally-induced homolytic dissociation of the nitroxide moiety to reversibly (re-)generate an active carbon radical capable of initiating the polymerization of vinyl compounds.

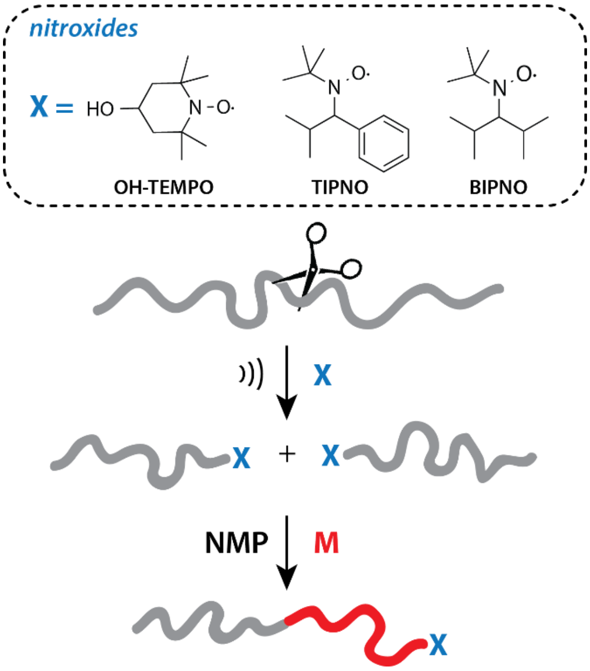


Figure 13. Ultrasonic degradation of a high molecular weight polymer in the presence of a nitroxide (acting as a radical trap) can form "macroinitiators" for subsequent polymerization via NMP.[96]

Although not directly employing sonochemistry for the controlled polymerization step, this approach shows the versatility of ultrasound in the preparation of end-functional polymers, and may allow, for example, the synthesis of block copolymers of which one (or more) blocks are not readily synthesized via NMP (or other controlled methods). This is due to the nature of mechanically-induced polymer cleavage that occurs under ultrasonic irradiation being indiscriminate towards the specific functionality/chemistry of the polymer, and solely towards the polymer size (chain length). This approach for block copolymer synthesis may, however, be limited in efficiency by the often-incomplete degradation of the polymer precursor under ultrasound.

A similar strategy had previously been employed by Huets and co-workers, wherein *in situ* polymer self-assembly for the synthesis of "hairy nanoparticles" was reported.[97] The ultrasonic degradation (20 kHz) of water-soluble polymers in the presence of hydrophobic monomers lead to the spontaneous block copolymer formation/chain extension via the generation of macroradical species. Unlike the abovementioned study, these macroradicals were not trapped by nitroxides but instead used directly as initiating species, allowing the growing polymer to self-assemble when the hydrophobic chain length reached a certain size (**Figure 14**), in a manner analogous to polymerization-induced self-assembly (PISA).[98]

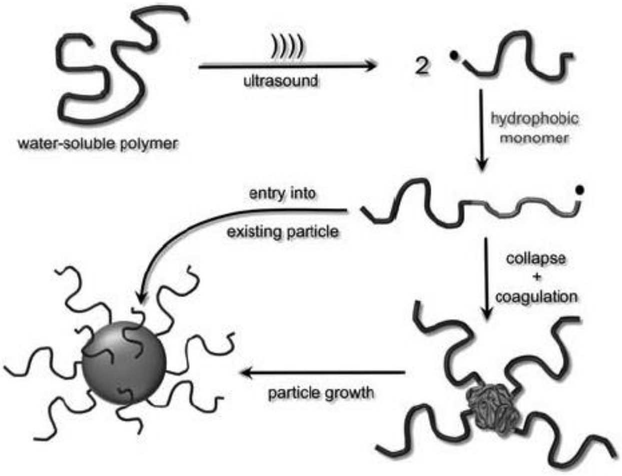


Figure 14. Proposed mechanism for the synthesis of "hairy nanoparticles" via and ultrasound-induced degradation/polymerization sequence. Reproduced from [97].

2.3 (Hydro)-Gel Formation via Ultrasound

A number of interesting reports exist on ultrasound-induced gelation in the presence of certain compounds that are deemed to be ultrasonically-activated gelators. However, as most of these act via non-radical pathways (typically changes in hydrogen bonding, isomerisation, etc.) they will not be covered in this review and so the reader is directed elsewhere for further information on such systems.[99]

For radical-induced gel formation via ultrasound very few reports were found in the literature. In 2009, Ulanski et al. described the synthesis of a range of hydrogels composed of poly(ethylene glycol) dimethacrylate (PEGDMA), poly(ethylene glycol) diacrylate (PEGDA), and vinylpyrrolidone (VP).[100] For a degassed 10% w/v PEGMA aqueous solution in the absence of any initiator or catalyst, the application of high frequency ultrasound (*f* = 622 kHz, *I* = 2.1 W cm^{-2}) led to the formation of free-standing gels within 30 – 60 s (**Figure 15**). The authors also demonstrate that a typical lab cleaning bath (*f* = 35 kHz) also led to gel formation, but at a much slower rate. The proposed mechanism consisted of the familiar sonochemical generation of hydroxyl radicals leading to the polymerization of the vinyl species, where in the presence of divinyl species cross-linking can occur. A range of different frequencies were investigated (70, 355, 622, and 1022 kHz), and the effect of monomer/cross-linker loading on the final conversion of vinyl groups studied. Furthermore, gel formation was attempted via the sonication of polymeric precursors in the absence of any monomer or cross-linker – with the goal of replicating the radiation chemistry technologies which utilize the radiolysis of water to produce hydroxyl radicals that can abstract protons from polymeric substrates and thus promote radical cross-linking reactions. The authors purposely employ high frequency ultrasound in an attempt to minimize chain-breaking reactions that may lead to weaker gels, and rely solely on the generation of hydroxyl radicals for cross-linking. Although free-standing gels are not formed in their experiment, they do observe coupling of the pre-polymer chains, indicating that under the right conditions gelation may be achievable using only sonochemically-derived hydroxyl radicals in the absence of small-molecule monomers or cross-linkers.[100]

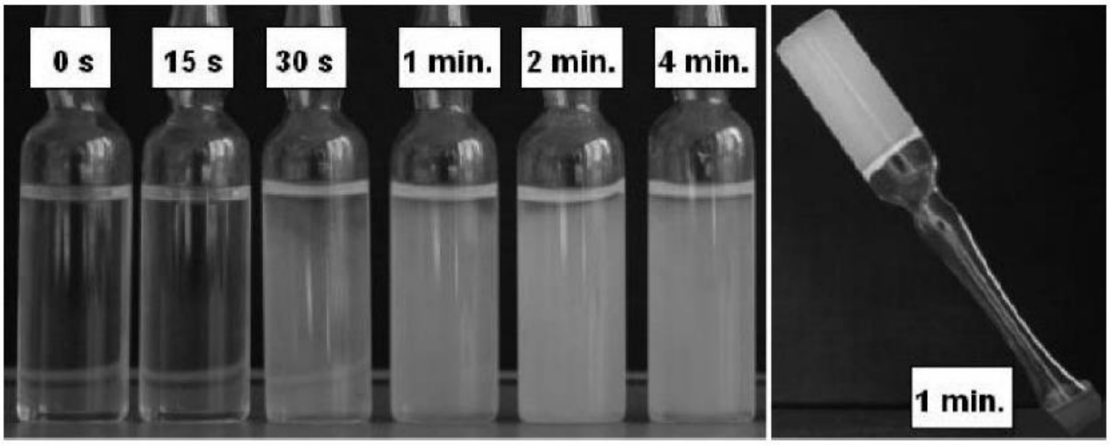


Figure 15. Gel formation via the ultrasonic irradiation of Ar-saturated PEGDA aqueous solutions (10% w/v) as a function of sonication time (*f* = 622 kHz, *I* = 2.1 W cm^{-2}). Reproduced from [100].

Shortly after the report by Ulanski et al., the group of Cass and colleagues published a study on the ultrasound-induced preparation of a range of acrylic hydrogels.[101] Although their approach was also “initiator-free”, the operating parameters are vastly different. For example, in the approach by Cass et al. highly viscous precursor solutions are used (70% w/w), and a low ultrasonic frequency is employed (f = 20 kHz, I = 56 W cm^{-2}). Moreover, it was observed that additives such as glycerol, sorbitol, or glucose were required to initiate the polymerizations, which were carried out in open vessels (i.e. not deoxygenated). The authors propose that the additives increase the viscosity of the monomer solutions, generating more violent cavitation (provided the cavitation threshold was reached) and hence a higher generation of radicals. Interestingly, a direct comparison of the gel microstructure (as observed via scanning electron microscopy (SEM)) for gels prepared via ultrasound-induced gelation and a thermal free radical initiation system demonstrate a much finer and more uniform pore structure for the ultrasound-derived gels (**Figure 16**).[101] The lack of exogenous initiators is thought to make this ultrasound-induced gel synthesis of interest for use in biomedical applications where toxicity of residual initiator is often a concern.

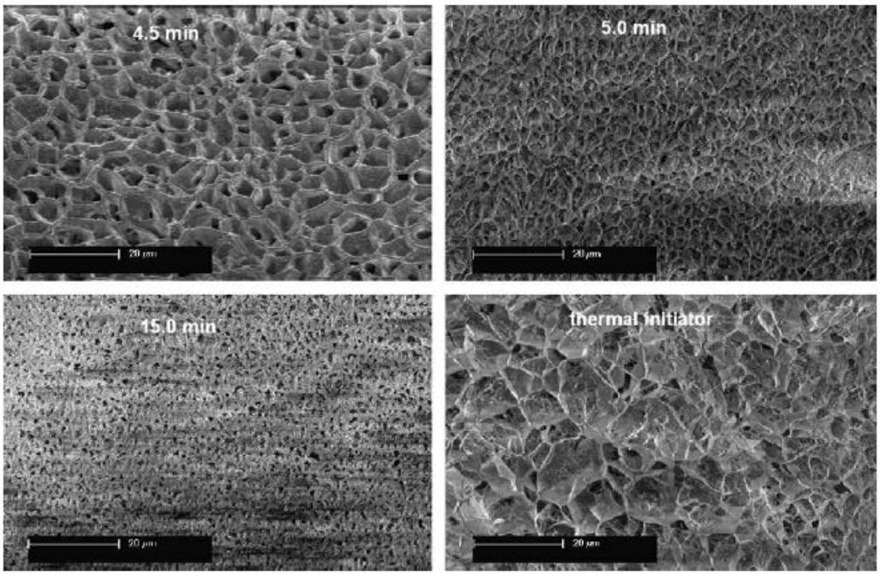


Figure 16. SEM images of dextran-based hydrogels synthesized via ultrasound-induced radical polymerization compared with a similar hydrogel synthesized via a traditional thermal free radical initiator approach. Reproduced from [101].

Although there very few examples of gel formation via ultrasound-induced radical polymerization,[100-101] this technique appears useful and versatile for the synthesis of (hydro)gel materials without the need for exogenous radical initiators. However, the formation of a cross-linked network during such a synthesis will affect cavitation events occurring under the applied ultrasonic conditions, and so consideration of how this may negatively change the radical production rate(s) should be given for each system on a case-by-case basis.

3. Perspectives

On first glance, the use of ultrasound for radical polymerization appears a perfect match, and although many successes have been reported in this field there remains a significant amount yet to be explored. A more detailed understanding of the contribution of both constructive (i.e. chain growth) and destructive (i.e. chain cleavage) reactions that may occur for certain polymer chain lengths, applied frequencies, intensities, and substrate conditions such as the solubility of the monomer/polymer species or the presence of viscosity modifiers is still required, and this will lead to the expanded practicality of ultrasound as a synthetic technique. Further development of controlled/“living” chain growth polymerization can be expected, while (hydro)gel formation remains an area that is vastly under-investigated. In particular, extending the ultrasonic frequency range out to much higher values where mechanical forces become minimized may open a plethora of new applications in a manner analogous to the expansion of the operating wavelengths for light-mediated photopolymerizations that have recently been reported in the literature.[102-105] Identification and/or design of “sonosensitizers”[106-107] and “sono-redox catalysts”[9, 24, 34] that can be activated at these higher frequencies will be of increasing importance as a means to decouple traditional sonochemical reactions based on mechanical degradation or radical formation from more specific redox or energy transfer reactions. Currently, such sono-active species are typically only used as a means of forming reactive oxygen species (ROS),[106, 108-109] although the exact mechanisms of formation are still unclear.[110] Making this pathway more generalised to include other substrates and reactions is anticipated to open up a whole new field of chemistry.[111]

Additionally, fine control of the ultrasonic waves – for example, spatially-controlled irradiation via the use of “focused” ultrasound[112-113] – may also have interesting applications for patterning and surface coating technologies. Again, many similarities will be made to the use of photochemistry, and while ultrasound cannot offer the spatial resolution of photolithography or applications such as direct laser writing,[114] it does have some associated benefits – particularly the ability for a deeper and more uniform penetration into liquids and materials. This may be well-suited to applications in the biomedical area,[115] where ultrasonic imaging and muscle therapy are already extensively utilised.

In summary, ultrasound-induced radical polymerization is a highly unique method of polymer synthesis; the particular quirks of the primary mechanism of activation, acoustic cavitation, can be intelligently utilised for effective polymerization provided a fundamental understanding of the underlying physical chemistry is known. We expect further growth in this area given the recent drive to develop polymerization techniques with a higher level of control, combined with the accessibility of reliable ultrasonic transducers capable of delivering uniform ultrasonic irradiation.

Acknowledgements

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