From thermally activated to viscosity controlled fracture of biopolymer hydrogels

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We report on rate-dependent fracture energy measurements over three decades of steady crack velocities in alginate and gelatin hydrogels. We evidence that, irrespective of gel thermo-reversibility, thermally activated “unzipping” of the non-covalent cross-link zones results in slow crack propagation, prevailing against the toughening effect of viscous solvent drag during chain pull-out, which becomes efficient above a few mm.s$^{-1}$. We extend a previous model [Baumberger et al. Nature Materials, 5, 552 (2006)] to account for both mechanisms, and estimate the microscopic unzipping rates.

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A variety of biopolymers (e.g. proteins and polysaccharides) can self-assemble into physically cross-linked networks in aqueous solutions. The resulting hydrogels are usually bio-compatible and show mechanical properties that mimic those of extracellular matrices. They are therefore good candidates as scaffolds for in vivo tissue regeneration, e.g. cartilage [1]. Such applications require sufficient mechanical strength to withstand manipulations associated with implantation and in vivo existence [2]. Surprisingly, understanding the physical mechanisms at work during the ultimate behavior (yield and failure) of non-covalently cross-linked hydrogels is still in its infancy. In this context, Baumberger et al. [3] have identified a basic dissipative process in the slow fracture of gelatin which they accounted for in a minimal model: gelatin gels belong to a wider class of biopolymer networks with extended cross-link zones, e.g. H-bond stabilized multiple helices, distributed along the chains and acting as mechanical fuses which may unzip or unreel under tension [4], forcing overall polymer pull-out without chain scission, at the cost of the viscous dissipation due to the solvent drag on the whole chain. This highly efficient mechanism makes these nominally weak gels amazingly resistant to crack propagation even at moderate velocities of 1 mm.s$^{-1}$ and above. In contrast, under quasi-static loading physical gels generally creep under stress [5] and ultimately break after a strongly stress-dependent, random delay [6]. Though this low rate behaviour, especially in thermoreversible networks, undoubtly pinpoints the role of thermal activation, it remains unclear whether the rate-limiting process in fracture of such intrinsically disordered materials is the nucleation of unstable cracks [6] or their subsequent growth [7]. Generally speaking, unraveling nucleation and growth effects is a subtle task [8] and, when feasible experimentally, studying low velocities, steady state crack propagation provides more straightforward insight into the fracture mechanisms. Dealing with gelatin gels, however, reliable measurement of both small crack-tip velocities and the associated energy release rates is hindered by two intrinsic limitations: (i) Thermal activation promotes crosslink rearrangements in the bulk as well, hence stress relaxation which competes with crack propagation to release elastic energy; (ii) Strong pinning of the crack front by network inhomogeneities may result in front instabilities [9] which makes tip position and fracture area measurements ambiguous [10]. As reported in this letter we circumvent these drawbacks by using alginate gels in which cross-linking is ensured by ionic bridges along extended zones between polyelectrolyte chains, with binding energies intermediate between H-bond and covalent ones. Though non-thermoresversible, these gels can be termed physical since interchain bounds remain weaker than backbone ones. Taking advantage of their negligible creep under small stresses [11] and of the absence of crack-front instability down to velocities in the 10 μm.s$^{-1}$ range, we clearly evidence that at low enough rates, crack propagation in these gels is thermally activated; moreover, after checking that they also exhibit a viscosity controlled regime, we extend a previous model [3] to account for thermally activated, stress-aided cross-link deziping. The outcome is an estimate of the debonding rate which lends further support to the prevailing picture of “egg-box” bonding zones in alginate [12].

Alginates are polysaccharides composed of sequences of two sugar residues, referred to as G and M [13]. According to the “egg-box” model [12], gelation occurs via interchain chelation of divalent ions (eggs), here Ca$^{2+}$, at specific sites (boxes) formed by the assembly of two subsequences made of several contiguous G-units (Fig. 1). The length of a binding GG pair is $a = 0.9$ nm.

Sodium alginate was purchased from Kalys (France). From supplier’s specifications (average molecular weight 216 kDa and 55% “M” residues) the average contour length is $\Lambda = 550$ nm. We use different alginate concentrations $c$ between 0.5 and 2.5 g for 100 ml of solvent (deionized water, otherwise specified) and a constant ratio of $10^{-3}$ mol of Ca$^{2+}$ for 1 g of alginate known to minimize gel shrinking (syneresis). Homogeneous gel samples are obtained [14] by in situ progressive release of Ca$^{2+}$ ions from insoluble CaCO$_3$ particles subsequent to the addition of a slowly hydrolyzing acid (“GDL” from
Sigma) quickly mixed with the pregel solution before casting it in a mold. The samples — 30 cm long slabs, 1 cm thick and 3 cm wide, attached to parallel grips — are stretched along their widths. Details of the set-up have been given previously [3]. All experiments are performed at $T = 295$ K. Cracks are initiated by notching in the mid-plane. When micron-sized CaCO$_3$ particles (from Sigma) are used, gelling is slow and homogeneous. However, at low $c$, particle sedimentation occurs leading to a toughness gradient as revealed by a tilted crack front. With nanoparticles of average size 90 nm (American Elements, CA), no sedimentation occurs but gelation is much faster and, at high $c$, yields inhomogeneous samples as revealed by a non-planar, tortuous crack front. We have therefore used a mixture of nano- and micro-particles, in such proportions as to yield straight crack fronts perpendicular to the slab faces and propagating along its mid-plane, a very stringent requirement.

Steady crack velocities $V$ are measured by video tracking of the crack tip. In our fixed grip configuration, the energy release rate $G$ is imposed. We compute it, neglecting edge effects, from the total stored elastic energy as determined from the force vs. stretching ratio loading curve measured on an unnotched sample. The small strain shear modulus $\mu = 1.5$ kPa for $c = 1.5\%$ varies approximately as $c^2$ in the studied range.

Figure 2 displays $G(V)$ curves for alginate gels with different $c$. They share with gelatin ones the principal features we associate with a visco-plastic fracture mechanism via scissionless chain pull-out [3]: a quasi-linear strong growth at high $V$, extrapolating at $V = 0$ to a non-zero threshold value of order a few J.m$^{-2}$, with a slope increasing linearly with the solvent viscosity $\eta$. This latter property is confirmed in a control experiment: using a glycerol/water mixture we induce a 2.5-fold increase of $\eta$, resulting in a clear toughening with respect to a pure water-based gel. When plotted vs. $\eta V$, however, both $G$ curves collapse over the whole $V$-range (Fig. 2).

Beyond these remarkable similarities (irrespective of the thermoreversibility of the gels), $G(V)$ curves for alginate specifically exhibit a systematic round-off at lower velocities, which implies no clear threshold for crack propagation. This is reasonably ascribable to thermally activated unzipping. Since with these systems $T$ cannot be varied widely enough to build a significant Arrhenius plot, we must rely on modeling to test this hypothesis. This leads us to extend our previous model [3] to account for thermal activation. In this description, the complex network features are lumped into a few parameters, namely the average chain contour length $\Lambda$, the areal density $\Sigma_0$ of chains crossing the fracture plane, the size $a$ of a binding unit and the activation barrier $U$. The fracture energy is then computed according to the Dugdale-Barenblatt theory [15] assuming a uniform stress $\sigma_{\text{tip}}$ over a small-scale cohesive zone at the crack tip. The fracture criterion corresponds to the overall pull-out of chains, stretched taut, i.e. to a maximum opening $\Lambda$ of the tip in the cohesive zone (Fig. 1b). The fracture energy is thus simply:

$$G = \sigma_{\text{tip}} \Lambda$$  \hspace{1cm} (1)

Note that $G \gtrsim 1$ J.m$^{-2}$ entails $\sigma_{\text{tip}} \gtrsim 2$ MPa $\gg \mu$. This justifies that the chains are almost fully stretched in the crack tip vicinity. Accordingly, if $\nu$ is the frequency at which units are released, neglecting re-bonding rate, the pull-out velocity reads: $\vartheta = a \nu$.

There is little hope to compute the very shape of the cohesive pre-crack due to the strongly non-linear, anisotropic elastic field which prevails ahead of the tip, where stresses reach values of order $\sigma_{\text{tip}} \gg \mu$ [10]. Instead we assume a wedge-shaped tip, which provides a simple kinetic relationship:

$$\vartheta = a \nu = \alpha V$$  \hspace{1cm} (2)

where the fitting parameter $\alpha$ should consistently be $\gg 1$ to account for crack blunting [10].

Closure of the problem requires relating $\sigma_{\text{tip}}$ to $\vartheta$ hence to $\nu$. The chain tension decreases along the polymer away
from the crack edge due to a viscous drag of order $\eta \dot{\theta}$ per unit of contour length. Let us make a crude estimate of the tension $f_Y$ under which reeds yield as:

$$f_Y \simeq \frac{\sigma_{\text{tip}} - p}{\Sigma_0} - \eta \Lambda \dot{\theta}$$  \hspace{1cm} (3)

The stress $p$ stems from the capillary pressure jump which tends to suck-in the chain when it is pulled-out dry. It is zero when the crack tip opening is wetted by a drop of solvent [3] but is $p = \epsilon_H \Sigma_0 / a$ for a dry tip, with $\epsilon_H$ the free energy of solvation per residue of length $a$ (the work done by the capillary force against drawing a residue into the gap).

Following Kramers [17], the bond breaking rate in the biased binding potential is given by:

$$\nu = \nu_0 \exp[-(U - f_Y a)/k_B T]$$  \hspace{1cm} (4)

where $\nu_0$ is the frequency of attempt to escape over the binding barrier.

Eqs. (1)–(4) yield:

$$\mathcal{G} = \Delta \mathcal{G}_H + \mathcal{G}_0 \left[1 + \frac{k_B T}{U} \ln(V/V^*) + \gamma \eta V \right]$$  \hspace{1cm} (5)

with

$$\mathcal{G}_0 = \frac{U \Sigma_0}{a}, \quad \Delta \mathcal{G}_H = \frac{\epsilon_H \Lambda \Sigma_0}{a}, \quad V^* = \frac{a \nu_0}{\alpha}, \quad \gamma = \frac{a \Lambda \alpha}{U}$$  \hspace{1cm} (6)

As seen on Fig. 2, the functional form of $\mathcal{G}(V)$ in eq. (5) provides an excellent overall fit of experimental data for gels of composition $c$ ranging from 0.5 % to 2.5 %. In order to put this analysis on a more quantitative footing, we note that the expression of eq. (5) features three independent fitting parameters only. Disregarding multiplicative constants of order unity in eq. (6), and setting $\Lambda$ and $a$ to their nominal average values, there remain four parameters actually unknown: $U$, $\alpha$, $V^*$ and $\mathcal{G}_0$. $\Delta \mathcal{G}_H$ is determined through an independent experiment where the crack tip is wetted by a drop of the solvent; for gelatin gels [8], this results in a shifted $\mathcal{G}(V)$ curve. For alginate gels, we have observed no significant effect of wetting the tip with water (with NaCl added to equilibrate the Na$^+$ concentration with that of the bulk sodium alginate one). We conclude that the polyelectrolyte alginate chains are pull-out in a hydrated state, hence $\Delta \mathcal{G}_H \simeq 0$.

The relatively simple eggbox structure of interchain binding in alginate prompts us to choose the activation barrier height $U$ as an input for data fitting with eq. (5). To do so, we compute the electrostatic energy of a Ca$^{2+}$ ion assuming it is involved in purely ionic bonds with its nearest neighbours O atoms in the GG<>GG cage (Fig. 4). With an average Ca–O distance $r = 2.3 \AA$ [12], this entails $U/k_B T = 4 \epsilon_B / r = 12$ at 295 K in water where the Bjerrum length $l_B$ is 7\AA. We now restrict our analysis to a $c = 1.5$ % gel for which we have got the most extensive data set although the same qualitative conclusions can be drawn from the other concentrations. The corresponding fit is shown on Fig. 4. The Griffith, or “$T = 0$ K” energy threshold is $\mathcal{G}_0 \simeq 4.6$ J.m$^{-2}$. A mere extrapolation to $V = 0$ of the apparent linear regime over the experimental velocity window underestimates this value. Strictly speaking, the purely viscous regime is only reached asymptotically for $V \to V^*$. Here, $V^* \simeq 0.6$ m.s$^{-1}$, out of experimental range. One can however check on eq. (6) that the correction to the slope of $\mathcal{G}(V)$ due to the activated term is negligible for $V$ larger than 1 mm.s$^{-1}$, i.e. that the asymptotic slope can be safely estimated from the low velocity ($V < V^*$) data set. The value $\alpha \simeq 8$ obtained from this slope is indicative of a strongly blunted tip.

Although the fitting value for $V^*$ is strongly sensitive to approximations in the trial value for $U$, we claim that the order of magnitude of the attempt frequency $\nu_0 \simeq 5.5 \times 10^9$ s$^{-1}$ yields deep insight into the unzipping dynamics. As discussed by Evans [18], in liquids, the thermal impulses that drive unbinding events are damped by viscous coupling to the environment. Accordingly, the opening of a GG<>GG molecular cage is expected to induce hydrodynamic flow over a size of order $a$ hence a damping rate scaling as $k_B T / \eta a^3 = 5.4 \times 10^8$ s$^{-1}$ in water at 295 K. This is precisely the order of magnitude of $\nu_0$, lending strong support to a simple unzipping scenario where calcium ions would be released one by one.
as might be schematically expected from the egg box picture of the cross-links. This is, to our best knowledge, the first time a dynamical argument is given in favor of the egg-box architecture.

On approaching $V^*$, the activation barrier smooths out and the escape rate is no longer given by eq. (11) since advection-driven, deterministic debonding events becomes increasingly prevalent. In the opposite range, as $V \to 0$, re-binding events must become relevant and lead to a regime ruled by the slow creep of the cross-links themselves, with $f_Y$ going linearly to zero $[5]$. Consequently, eq. (4) becomes unphysical for $f_Y \to 0$ i.e. for $V \lesssim V_{\text{min}} = V^* \exp(-U/k_BT)$. For alginate gels, we estimate $V_{\text{min}} \simeq 4 \mu \text{m.s}^{-1}$, well below the lower bound of our velocity set. This legitimates a posteriori using eq. (5) over the whole experimental window, which fulfills the requirement $V_{\text{min}} \ll V \ll V^*$.

The previous discussion is based on generic features of zipper-like cross-linked gels. It can be therefore expected that thermally activated, stress-aided dezing will be all the more efficient in thermoreversible gels. This prompts us to reassess, at least qualitatively, the case of gelatin. As already mentioned, this requires taking special care. First of all, using a $c = 10 \%$ gelatin/water gel, the crack front instability $[9]$ is pushed down below $V_c = 20 \mu \text{m.s}^{-1}$. Moreover, we set-up a procedure to correct the fracture energy for stress relaxation. For this purpose, we record the crack velocity vs. time in response to various crack openings. A twin sample, kept unnotched, is submitted to the very same stretching sequence while recording the loading force. The stored elastic energy is computed assuming that stress relaxation in such weak, transient networks occurs via debonding of cross-links which eventually rebind at a more favourable place, therefore resulting in a drift of the reference state, hence in a mere shift of the non-linear stress-strain curve $[19]$. As shown on fig. 3, this tedious procedure ultimately reveals a clear logarithmic behaviour over at least two decades, essentially below $1 \text{mm.s}^{-1}$, which was therefore overlooked in previous studies $[3]$.

According to the present model, breaking one-by-one H-bonds ($U \simeq 0.1 \text{ eV}$) between peptidic residues distant of $a = 0.3 \text{ nm}$ would result in a logarithmic shift of the fracture energy of water-based gels strictly between $V^* = 4 \text{ m.s}^{-1}$ and $V_{\text{min}} = V^* \exp(-U/k_BT) = 8 \text{ cm.s}^{-1}$ where we use the conservative value $\alpha = 10$ for the blunting parameter $[2]$. Both the span of this velocity bracket and its absolute location are clearly incompatible with the experimental observation. We are therefore led to propose that the basic thermal event involves the cooperative debonding of $n$ several subsequent H-bonds along a cross-link zone. This we attribute to the strong topological constraint imposed by the triple-helix structure of the cross-links $[20]$, the unzipping of which requires also large-scale unwinding. This cooperative mechanism cannot be discriminated from a one-by-one unzipping as long as one probes (through $G_0$) the yield tension $f_Y$ which reads $nU/na = U/a$. However, the characteristic unbinding rates are dramatically affected by the effective barrier energy ($\sim nU$) and by the bulkiness of the activated unit ($\sim na$). On this respect, a cooperativity level of $n \approx 3$ would make gelatin gels looking similar to alginate ones, everything equal otherwise.

This analysis confirms the importance of thermally activated rate processes in soft matter fracture physics $[3, 21]$. Our claim that the “subcritical” fracture behaviour is sensitive to distinctive topological features of zipper-like cross-linked networks opens the way to a more extensive experimental study, taking advantage of the wealth of network architecture offered by biopolymer hydrogels.

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