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highly dynamic substrate engagement is very important during protein synthesis, allowing TF to accommodate the permanently changing composition of binding sites in the nascent polypeptide that grows by up to 20 amino acid residues per second.

Saio *et al.*'s study provides a milestone in understanding how TF performs its dynamic and multifaceted functions in the cell. The work will pave the way for further exciting advances in understanding the plasticity of this and other ATP-independent chaperones. However, several important questions remain to be answered about the activity of the TF chaperone. For example, Saio *et al.* investigated purified TF, which was not in complex with the ribosome, and it thus remains to be shown whether the binding sites of ribosome-

tethered TF are similar. Three binding sites are located in the central body and one in the head domain, but no binding site is found in the amino-terminal tail that tethers TF to the ribosome (see the figure). TF undergoes some structural changes upon binding to ribosomes (11) and may thus expose other or additional binding sites.

Another open question is how the dynamic association of one or perhaps more TF molecules with nascent polypeptides is coordinated with the activity of other chaperones that bind to nascent proteins in later stages of protein synthesis (3). And finally, TF that is not bound to ribosomes can form dimers that can encapsulate small native-like proteins using primarily polar contacts. This TF activity may promote the assembly of substrates

into large complexes (12). Further analyses are required to understand how TF can switch between hydrophobic and hydrophilic binding modes for substrates.

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MATERIALS SCIENCE

An Internal Cure for Damaged Polymers

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Design strategies for structural polymers and polymer matrix composites that opt for damage management in lieu of damage prevention may greatly improve materials longevity and reduce repair costs. Nature has evolved many elegant examples of self-healing. Bone continuously remodels via the resorption and replacement of damaged tissue, latex “gasket” excretion in plants self-seals wounds (1), and dynamic, sacrificial metalloprotein complexes form the adhesive of the mussel byssus (2). Scientists have drawn inspiration from nature to develop self-healing strategies in structural polymeric systems. On page 620 of this issue, White *et al.* (3) show how to heal a large volumetric loss in a synthetic polymer autonomously. Their innovative approach enables restoration of mechanical integrity to a damage volume that is roughly 100 times the largest defect previously healed in this manner (4).

White *et al.* developed a vascular repair system that can fill and polymerize a defect 10 mm in diameter and 3 mm thick. This defect is “full thickness”—it creates an opening that extends through the sample. Complex and rapid gelation chemistry had to be developed that could plug the hole quickly

and prevent bleed-out of the healing agent. Fluids containing healing agents in microchannels wet the surface of the defect, mix, and rapidly and completely fill the defect with gel (see the figure, panel A) as long as surface tension and cohesive and adhesive forces dominate over gravity flow. Polymerization progresses over time scales that are long compared to the gelation time scale. The lost volume is replaced by new structural polymer that forms a viable interface with the matrix polymer and restores mechanical integrity (see the figure, panel B). White *et al.* did not restore the original polymer composition, so, like scar tissue, the repair is functional but not completely regenerative. Nevertheless, the elastic modulus, strength, and impact resistance of the repair site are all restored to structural polymer values; specifically, 62% of native epoxy impact energy is achieved upon self-healing.

Earlier approaches to damage management in polymer design used external stimuli (thermal, electrical, and others) to trigger a healing response [see, for example (5, 6)]. Wudl and co-workers used Diels-Alder-based polymer networks with reversible covalent bonds to mend cracks and fractures upon thermal activation (6) in a strategy replicating the sacrificial bonds of byssus threads. Multiple healing cycles were achieved with mechanical performance res-

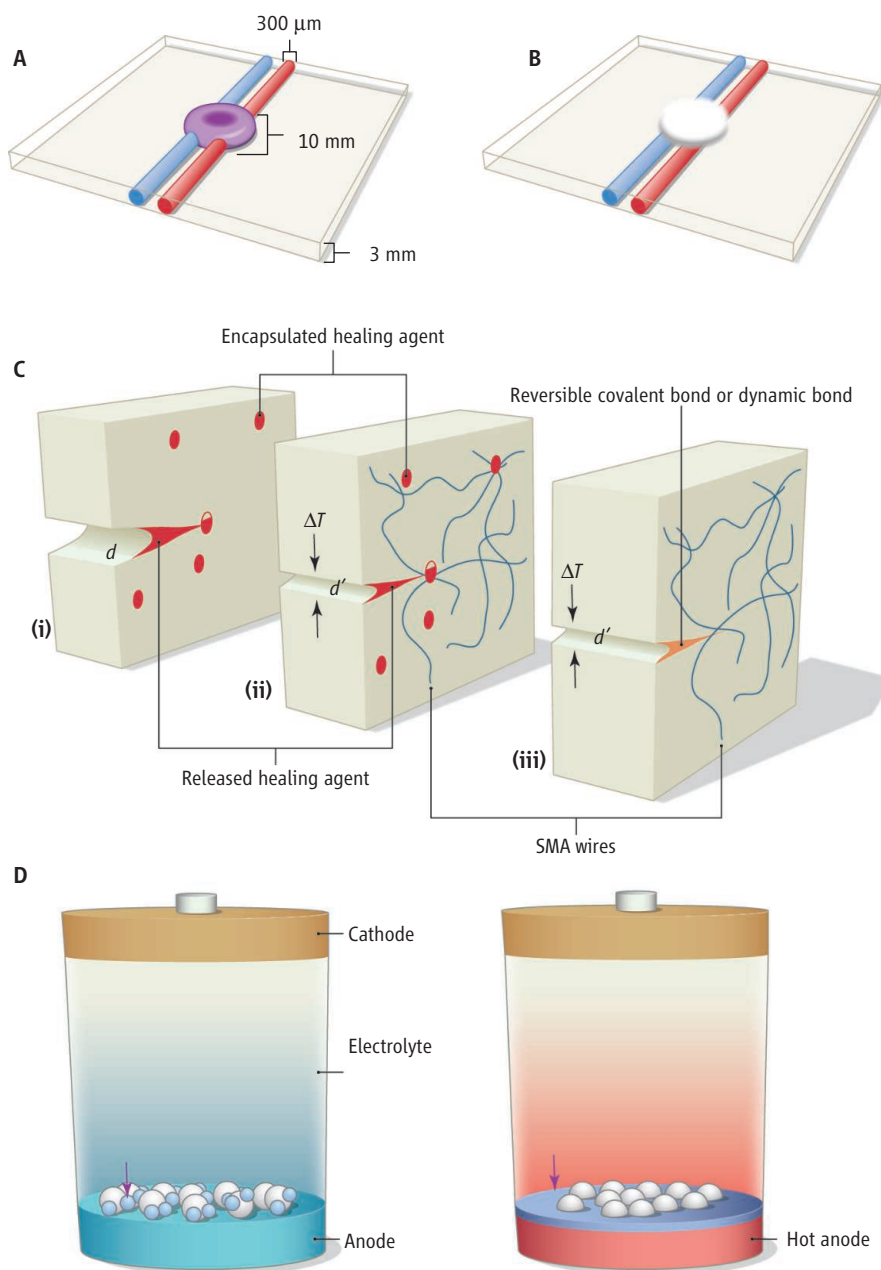
A vascular system of microchannels delivers polymer-forming reagents that seal and repair large damaged regions.

torations of up to 60%. Subsequent research moved this approach from stimuli-responsive to autonomous healing by designing dynamic noncovalent bonding or reversible covalent bonding at room temperature (7, 8). Reversible interactions allow repeated healing cycles but are limited to defects in which the surfaces are in intimate contact (4).

The work of White *et al.* highlights self-healing strategies that transport mass—a healing agent in liquid form—to local defects. Capsular strategies embed reparative materials within compartments dispersed throughout a polymer matrix that rupture at a proximal damage site. Vascular strategies embed the healing agent within channels or reinforcing fibers (9) to be released when damage occurs. Refillable microvascular networks for storage and transport of healing agent have also been developed (10). Vascular systems offer multiple healing cycles through the perfusion of fresh healing agent fluids to a damage site until channels are ultimately segmented by multiple damage events.

Recent strategies to improve healing efficiency combine one or more self-healing approaches with stimuli-responsive polymers. For example, Kirkby *et al.* incorporated shape-memory alloy (SMA) wires into the matrix of a polymer that also contained a capsular self-healing system (11)

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Autonomous strategies in polymer systems. In the approach of White *et al.*, (A) healing agents in two independent chambers mix and fill a large, through-thickness defect to seal the hole quickly and (B) polymerization of the healing agents restores structural integrity. (C) Combining healing strategies can improve healing efficiency. Adding temperature change-triggered (ΔT) shape-memory alloy (SMA) wires to capsular (ii) or (iii) intrinsic self-healing strategies improves contact of the defect surfaces (d') compared to the self-healing strategy alone (d) in (i). (D) Multifunctional autonomous polymer microspheres (purple arrow, left) function as part of the shutdown separator in a battery during normal operation but melt (purple arrow, right) if the battery begins to overheat to seal the anode and shut down operation.

further ionic conduction (15) (see the figure, panel D).

Although these recent advances are exciting, the long-term performance of autonomously healed polymers has largely remained unexamined. Repaired performance efficiencies typically measured are short-term mechanical properties under ambient conditions, so the effects of cyclic loading, aging, and various hostile environmental conditions on the healing efficiency and the integrity of repaired defects are not known. In most self-healing approaches, the repaired sites are not the same composition as the native polymer, so testing of the materials under more realistic conditions, both pre- and post repair, is needed. Methods are also needed to assess and monitor the potential healing ability after multiple repair events. Here again, elegant examples that have evolved in nature can inspire solutions for the next generation of structural polymer designs.

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(see the figure, panel C). Tee *et al.* combined supramolecular reversible bonds with conductive nanoparticles to develop an electronic sensor skin that demonstrated rapid restoration of mechanical and electrical properties (12).

Although numerous efforts are being made to tackle healing of ever-increasing defect sizes, there is an appreciation for the detrimental effects of microscale cracks on the structural integrity of polymer composites. The development of smaller capsular and vascular systems (13) can potentially eliminate fracture in these materials by preventing small, noncritical cracks from propagating to critical sizes.

Damage management can compromise performance if a substantial fraction of the polymer mass is engaged only in repair rather than the primary structural functions. One solution is to incorporate multifunctionality into the healing components. An example is solid-state microvascular channels that structurally reinforce the polymer matrix and melt upon application of a temperature rise to repair a defect (14). The multifunctional approach has recently been demonstrated in a nonstructural polymer application in which the shutdown separator in a battery is comprised of polymer microspheres that melt before a catastrophic temperature rise and prohibit

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