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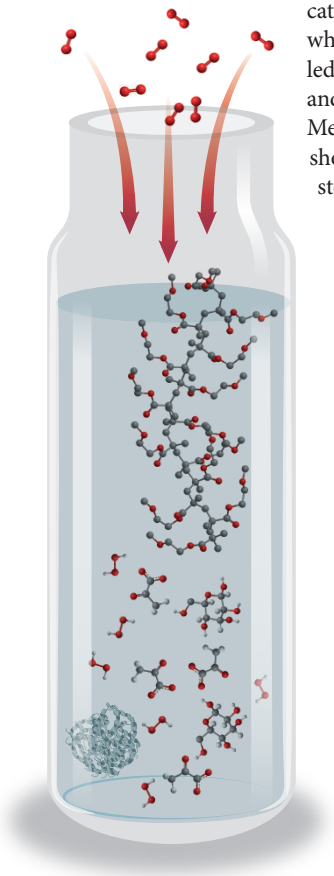
ATOM-TRANSFER RADICAL POLYMERIZATION

New method breathes life into ATRP

> The basic idea was inspired by classical respiration cycles operating in cells



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Of all the controlled polymerization methods at our disposal, atom transfer radical polymerization (ATRP) is particularly useful because it is amenable to a wide scope of monomers, initiators and catalysts. Despite this broad applicability, ATRP, like any conventional radical polymerization, has an important limitation in that the reaction mixtures are highly sensitive to atmospheric O_2. These molecules interact rapidly with propagating radicals, forming stabilized peroxy radicals that act as powerful inhibitors in the polymerizations. Moreover, ATRP is typically catalysed by Cu(I) complexes, which are sensitive to O_2. A team led by Krzysztof Matyjaszewski and Alan Russell at Carnegie Mellon University addressed this shortcoming by devising a two-step catalytic cycle to overcome O_2 inhibition of ATRP. This new and sustainable technology is described in *Angewandte Chemie International Edition*.

Controlled free-radical polymerization is simple to perform in the laboratory, in which the necessary anaerobic conditions are routinely achieved by either freeze–pump–thaw degassing cycles, bubbling inert gas through a reaction mixture or working in a glovebox. On an industrial scale, similar challenges exist and "tolerance to air may certainly attract more companies to use ATRP with ppm loadings of Cu catalysts in systems with substantial amounts of O_2 present, or even in mixtures essentially open to air" says Matyjaszewski. Indeed, his team conducted controlled polymerizations in air by taking inspiration from biology in order to minimize the concentration of dissolved O_2. They made use of phosphate-buffered saline solutions of glucose oxidase (GOx) — an enzyme that converts O_2 and glucose to D-glucono-1,5-lactone and H_2O_2 — as part of a strategy that had previously been applied to free-radical polymerizations.

Although H_2O_2 does not interfere with the growth of radical chains, it oxidizes Cu(I) to Cu(II), such that the ATRP reaction cannot be saved from O_2 using GOx alone. Moreover, through Fenton-like chemistry, the Cu(I) catalyst converts H_2O_2 into OH^- and $OH^{\cdot}$, the latter initiating the growth of new chains. These deleterious processes ruin the control for which one would use ATRP in the first place. A problem that remained for the Matyjaszewski group was how to mop up H_2O_2, and mimicking biology once more provided the answer. Here, in a reaction that is part of the Krebs cycle, they made use of pyruvate ($AcCO_2^-$) to scavenge H_2O_2 and generate the now completely benign products CO_2, H_2O and AcO^-. "The basic idea was inspired by classical respiration cycles operating in cells," notes Matyjaszewski, who accordingly dubs this methodology 'breathing ATRP'.

The effects of 'breathing ATRP' are clear: when phosphate-buffered saline solutions of oligo(ethylene oxide) methyl ether methacrylate (OEOMA), Cu(I), GOx, glucose and NaBr were stirred in vials open to the air, they did not afford polymers. Although polymerization did occur when the same mixture was left to stand in a capped vial, the product distribution was broad and centred at a molar mass much lower than that predicted for a reaction that does not suffer from O_2-induced deactivation. In each case, the solution absorbed at 870 nm, which is in line with the conversion of Cu(I) into the open-shell ion Cu(II), a reaction the team also conducted independently. Lastly, simply by adding pyruvate to trigger the second of the two 'clean-up' reactions in the 'breathing ATRP', one could convert OEOMA into polymer mixtures with a narrow molar mass distribution ($Đ = 1.17$) centred at a mass (111,000 Da) near the predicted value (95,400 Da). The conversion was almost complete in only 90 minutes.

Fittingly, the bio-inspired 'breathing ATRP' also turns out to be biocompatible, allowing for the synthesis of protein–polymer conjugates. Matyjaszewski and co-workers first decorated the surface of bovine serum albumin by converting lysine residues into amides with Br-terminated groups as ATRP initiating sites. The latter moieties initiated growth of poly(OEOMA) chains outwards from the protein to give well-defined hybrids with polymer chains of uniform length. Indeed, base hydrolysis of the amide bonds liberated chains with a low polydispersity.

Although the findings of the team certainly make ATPR more practical, the present methodology is nevertheless restricted to aqueous reaction mixtures. The team "would like to extend the systems to organic solvents but that requires decorating GOx with polymer chains to stabilize the enzyme in organic media, as already demonstrated for some other systems," says Matyjaszewski.

Johannes Kreutzer, Associate Editor, Nature Communications

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