Oxygen Tolerant RAFT Polymerisation: Application in the Design of Anti-Microbial Polymers

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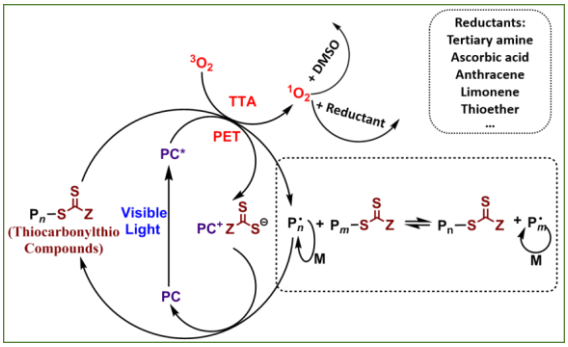
The presence of oxygen during controlled/living radical polymerisation (CLRP) can be detrimental owing to its rapid quenching of carbon-centred radicals. As a result, CLRPs are typically performed after the removal of dissolved and atmospheric oxygen by nitrogen sparging or freeze-pump-thaw cycling. This requires specialist equipment and sealed reaction vessels, which can limit the scalability of CLRP particularly when considering high throughput polymer synthesis at low reaction volumes. Furthermore, improving the tolerance to oxygen in CLRP can significantly improve or expand the scope of polymer applications in surface modification, biomolecule functionalisation and (micro)flow chemistry by removing the need for deoxygenation processes.[1] Furthermore, the development of such process can fast track the synthesis of polymer libraries.



As a result, in recent years, there has been renewed interest in performing CLRP without the need to first apply physical deoxygenation techniques. Our team has focused on the development of photopolymerisation technique named photoinduced electron/energy transfer – reversible addition fragmentation chain transfer (PET-RAFT) polymerisation, which can convert oxygen into inactive species. The PET-RAFT process uses photoredox catalysts, including organo-dyes and metal based photoredox catalysts, and in the presence of a suitable reducing agent, polymerisations can be conducted in the presence of oxygen (or air) at microlitre volumes (> 10 µL) and at low concentration.[2] These polymerisations proceed under mild conditions at room temperature in water or organic solvents, with excellent polymerisation control achievable even at molecular weights approaching 100 000 g/mol. These RAFT polymerisations are compatible with a range of monomer families and can be performed in microtiter well plates[3] and even in discrete droplets.[4] Using this platform, we demonstrate that the ability to perform multiple parallel polymerisations can greatly aid in the synthetic optimisation of polymeric architectures such as star polymers and self-assembled nanoparticles (spherical-, worm-micelles and vesicles).[5] We have demonstrated the effectiveness of this fast throughput strategy via the rapid preparation of a library of anti-microbial polymers and test their antimicrobial activities against different gram-negative bacteria.[6] Using this process, we have been able to rapidly prepare library of anti-microbial polymers and test their antimicrobial activities against different gram-negative bacteria. Interestingly, the anti-microbial activities can be affected by the monomer placement in the polymer chain as well as by the monomer structure and polymer composition. To improve anti-microbial activity, Nitric oxide donor molecules were conjugated to the polymer structure. Nitric oxide donors can release NO gas under specific conditions, which promotes the dispersion of bacterial biofilm. By combining NO and anti-microbial polymers, we can see synergetic anti-microbial activities against a range of different bacteria.

References:

1. Corrigan, N., Almasri, A., Taillades, W., Xu, J. & Boyer, C. Controlling Molecular Weight Distributions through Photoinduced Flow Polymerization. *Macromolecules* **50**, 8438-8448 (2017).
2. Xu, J., Jung, K., Atme, A., Shanmugam, S. & Boyer, C. A robust and versatile photoinduced living polymerization of conjugated and unconjugated monomers and its oxygen tolerance. *J. Am. Chem. Soc.* **136**, 5508-5519 (2014).
3. Gormley, A.J., *et al.* An Oxygen-Tolerant PET-RAFT Polymerization for Screening Structure–Activity Relationships. *Angewandte Chemie - International Edition* **57**, 1557-1562 (2018).
4. Yeow, J., Chapman, R., Xu, J. & Boyer, C. Oxygen tolerant photopolymerization for ultralow volumes. *Polymer Chemistry* **8**, 5012-5022 (2017).
5. Shanmugam, S., Xu, J. & Boyer, C. Photoinduced Oxygen Reduction for Dark Polymerization. *Macromolecules* **50**, 1832-1846 (2017).
6. Judzewitsch, P.R., Nguyen, T.-K., Shanmugam, S., Wong, E.H.H. & Boyer, C.A.J.M. Towards Sequence-Controlled Antimicrobial Polymers: Effect of Polymer Block Order on Antimicrobial Activity.

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Biography: Prof Cyrille Boyer received his Ph.D. from the University of Montpellier II. After working with Dupont Performance Elastomers, Cyrille moved to UNSW in the centre for advanced macromolecular design. He was awarded the SCOPUS Young Researcher of the year Award in 2012, one of the six 2015 Prime Minister's Science Prizes (Malcolm McIntosh Prize for Physical Scientist of the year), the 2016 LeFevre Memorial Prize and nominated as one of the inaugural Knowledge Nation 100 selected by the Knowledge Society, guided by Australia's Chief Scientist, Professor Ian Chubb and senior commentators from The Australian newspaper. Cyrille's research has also been recognized by several international awards, including 2016 ACS Biomacromolecules/Macromolecules Award, 2016 Journal of Polymer Science Innovation Award, 2018 Polymer International-IUPAC award and 2018 Polymer Chemistry Lectureship. Cyrille has co-authored over 235 articles, which have gathered over 13 000 citations. He has been ranked as Highly CIted Researcher by Clarivante in 2018.
Cyrille is the co-director of Australian Centre for Nanomedicine and member of Centre for Advanced Macromolecular Design. The Australian Centre for Nanomedicine regroups 10 academics, 20 post-docs and research associates and 80 PhD students.