Exploiting the Mechano-Responsiveness of Polydiacetylene Nanoparticles to Track Polymeric Nanoparticle Blends During Cellular Uptake

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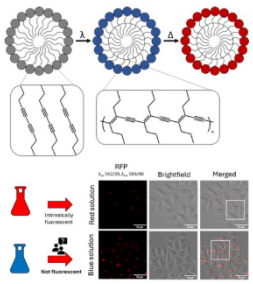
Polydiacetylene nanoparticles (PDA NPs) are conjugated polymeric NPs known for their vivid chromatic transitions in response to external stimuli (e.g. temperature, pH, and mechanical stress) [1] which can induce a red-shift and fluorescent colorimetric change, making PDAs highly valuable in sensor applications. [2] These transitions arise from conformational changes in the polymer backbone, typically composed of alternating C=C and CC bonds formed by UV-induced polymerisation (Figure TOP). PDAs exhibit a blue, non-fluorescent colour, which shifts to red and fluorescent upon structural perturbation. The mechanochromic behaviour of PDAs has been documented in solid and liquid state systems. [3] Differently, in the present work, we have observed a spontaneous blue-to-red transition in PDA NPs upon uptake into live cells in 2D culture of different cell types, breast (Figure BOTTOM) and skin cancer and fibroblast. Our preliminary controls screened temperature effects and showed no chromatic alteration under the pH conditions of cell culture media or at endosomal pH levels, suggesting instead effects on PDA backbone structure NPs during the wrapping and endocytosis processes. In this regard, it has been previously observed that soft NPs would deform during the uptake.[4] However, PDA chromatic change due to cell uptake has not been described in the literature before and represents an interesting strategy to track polymeric NPs. In fact, for therapeutic applications, it is crucial to monitor the kinetics of tissue and cellular drug uptake, organ-specific accumulation, *in vivo* biodistribution, and the intracellular fate of therapeutics. In particular, *i n vitro* experiments, polymeric NPs are commonly loaded with fluorophores. However, this approach suffers from dye leakage and separation from the nanoparticles, making it difficult to distinguish signals from intact particles versus free fluorophore, often leading to overestimation of nanoparticle uptake. [5] Polymer blending offers an alternative that can minimise unwanted drug release and reduce fluorescence.[6] To our knowledge, the transition blue-to-red (fluorescent) occurring at the interface of cell membranes of PDAs NPs alone or blended with other polymers has not yet been explored and could be used as a low-cost, non-leachable alternative to track polymeric NPs. Importantly, this chromatic response could also be harnessed in more environmentally relevant contexts, for instance to monitor the fate of polymer liquid formulations (PLFs) such as polymeric surfactants or additives following their release into natural systems. This broadens the utility of the phenomenon beyond cellular models.



TOP. Schematic of the PDA micelles (as simplest representation) formation/polymerisation under light irradiation and conformational change under external stimuli (e.g., temperature, pH and mechanical stress). BOTTOM. Uptake characteristics of red solutions of PCDA formulations in breast cells.

References:

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