Designing Enzymatically-Powered PLGA Nanobots and Exploring its Swarming Behavior and Oil Interface Intercation

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Two main objectives have been considered in this study. Firstly, the design and development of enzymatic nanobots based on organic materials, which will improve its biocompatibility and biodegradability. Secondly, the study of the swarming behavior of these new enzymatic nanobots and their interaction with oil interfaces.

Nanobots have been widely investigated as the next generation of vehicles for drug delivery. Active motion, and especially their collective behavior (swarming), have shown an enormous advantage in terms of movement in complex medias,[1] overcoming biological barriers,[2] drug delivery[3] and tumor penetration.[4] Not only that, but also *in vivo* therapeutics outcomes have been observed.[5] Nevertheless, there is a general concern about the composition and simplicity of the different designs used, which may hinder their clinical applications. There is still the need to develop a simple nanobot based on organic materials which would be more appealing for industry and clinicians. Here, we present and compare the synthesis and characterization of two new urease-nanobots designs. Both are based on an organic biocompatible and biodegradable chassis of poly(lactic-co-glycolic acid), PLGA (FDA approved material and already used in clinics).[6] For their functionalization with urease, amine groups must be incorporated in the chassis surface. As PLGA is negatively charged, two different strategies have been developed. In one case, the core is combined with Chitosan (during synthesis), a natural positive polymer used as a dietary supplement. On the other hand, polyethylenimine (PEI) is used for providing a positive layer around the PLGA core (after synthesis). Moreover, the versatility of the chassis synthesis allowed us to encapsulate with high-efficiency hydrophobic (oil in water emulsion, OW) and hydrophilic (water in oil in water emulsion, WOW) standard drugs.

Studying its collective behavior, it was demonstrated how in the presence of the fuel (urea), nanobots experiment a sudden expansion that allows them to explore and reach further areas, if compared with passive controls. In parallel, we have seen how an oil surface acts as a barrier for nanobots. However, in the presence of the fuel, their catalytic reaction provokes the mixing of the oil/aqueous interface, displacing upwards the remaining oil phase. That allows the nanobots to cross this barrier. This phenomenon could be explored for common diseases such as acne, which is characterized by overproduction and accumulation of sebum (protective skin oil).

With all, PLGA has been demonstrated to be an efficient candidate for developing enzymatic nanobots. Further studies are required to understand how these new approaches will behave in front of biological systems, *in vitro* and *in vivo*.

References

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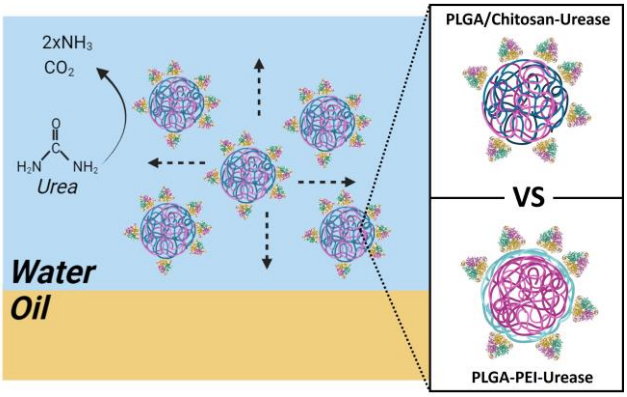

Figure 1. Graphical Abstract