

# Stimuli-responsive DNA microcapsules for controlled release of loads

Wei-Ching Liao, Fujian Huang, Yang Sung Sohn,<sup>‡</sup> Marianna Riutin, Chun-Hua Lu, Alessandro Cecconello, Wolfgang J. Parak,<sup>†</sup> Rachel Nechushtai,<sup>‡</sup> and Itamar Willner\*

Institute of Chemistry, Center for Nanoscience and Nanotechnology, The Hebrew University of Jerusalem, Jerusalem 91904, Israel

<sup>†</sup>Fachbereich Physik, Philipps-Universität Marburg, Renthof 7, 35037 Marburg, Germany

<sup>‡</sup>Institute of Life Science, The Hebrew University of Jerusalem, Jerusalem 91904, Israel

The synthesis of stimuli-responsive DNA microcapsules acting as substrate carriers, and being unlocked by different triggers including biomarkers, light, and pH is described. The DNA-based microcapsules are prepared by the layer-by-layer deposition of oligonucleotides on a core template ( $\text{CaCO}_3$ ), using DNA encoded with stimuli-responsive functionalities for the dissociation of microcapsules in the presence of appropriate triggers. The preparation of biomarkers-responsive DNA microcapsules by using anti-ATP or anti-VEGF aptamer as bridging units is demonstrated. The photoresponsive microcapsules are prepared by the deposition of oligonucleotides labeled with the photocleavable o-nitrobenzyl-phosphate ester units. The pH-responsive microcapsules are constructed by embedding Hoogsteen triplex structures into DNA assembly layers. The stimuli-responsive microcapsules loaded with tetramethylrhodamine-modified dextran (TMR-D), CdSe/ZnS quantum dot (QDs), microperoxidase-11 (MP-11), or doxorubicin-modified dextran (DOX-D) are presented. The release of loads from respective microcapsules proceeds in the presence of ATP, VEGF, light irradiation, or pH changes as triggers. Preliminary cell experiments reveal the preferred permeation of the DOX-D-loaded microcapsules into MDA-MB-231 breast cancer cells as compared to normal MCF-10A epithelial breast cells. The cytotoxicity of ATP-responsive DOX-D-loaded microcapsules toward the cancer cells is attributed to the effective unlocking of the microcapsules by overexpressed ATP.

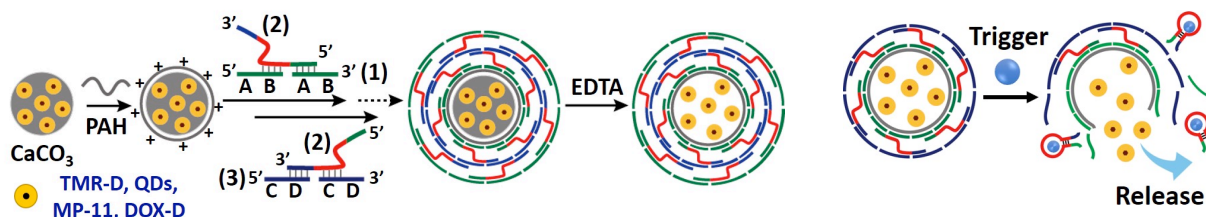


Fig. 1: Layer-by-layer deposition of oligonucleotides on PAH-coated  $\text{CaCO}_3$  template microparticles loaded with TMR-D, QDs, MP-11 or DOX-D, and the formation of DNA microcapsules by the EDTA-induced dissolution of the  $\text{CaCO}_3$  cores.

Fig. 2: Schematic trigger-driven release of the loads encapsulated in the microcapsules through the dissociation of the microcapsules.

This research was supported by the Minerva Center for Complex Biohybrid Systems. Support from the Council for Higher Education in Israel is acknowledged by W.-C.L. Parts of this work were supported by LOEWE (project SynChemBio to W.J.P.)

[1] W.-C. Liao et al., *Adv. Funct. Mater.* 2016 (in press).