Molecular self-assembly by HCR for signal enhancement in nucleic acids biosensors

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Some of the possible perspective advantages of the uptake of nucleic acids biosensor technology are already within reach, still, the sometimes limited sensitivity can seriously inhibit the application of biosensor-based methods when these could be useful towards detection of nucleic acids variants present only at a very low concentration. In a research lab, this objective is achieved using complex but sensitive amplification techniques, such as PCR, or the deployment of sophisticated and sensitive instruments, this goal might prove a prohibitive task for point-of-need biosensors.
We have adapted and attempted at using the hybridization chain reaction (HCR)[1] towards enhancing the signal due to the specific recognition and binding of soluble nucleic acids to a surface-bound probe. The enhancement strategy consists in a triggered supramolecular polymerization of DNA sequences or nanostructures at the location of specific nucleic acids recognition. We have showed that the method can be used towards the detection of an arbitrary DNA target through proper design of the sequences of the components[2]. Preliminary experimental evidence shows a significant enhancement of the signal, which could prove useful in some applications. We also proved that HCR can have single-nucleotide sensitivity for the detection and signal enhancement.
We have recently worked at the extension of the application of HCR towards the detection of circulating miRNA targets, biomarkers of considerable interest for diagnostics. We have showed that HCR reagents can be designed to distinguish between closely-related miRNA targets, as it would be needed in diagnostics. Modifications of the HCR design can yield hyperbranched or target-recycling assembly and thus significantly increase the detection signal. We have preliminary results on branched a HCR design that could be compatible with surface-bound biosensors implementation (electrochemical, fluorescence, luminescence, SPR).
The successful implementation of signal-enhancement strategies based on self-assembly could lead not only to signal amplification, but also to the increase of the specificity of the detection and to the widening of the detectable concentration range of the analytes. All these are especially valuable towards miRNA profiling. We propose that HCR could be a good candidate for achieving these goals for the detection of circ-miRNA on biosensors platforms.

[1] R. M. Dirks, N. A. Pierce, Proc. Natl. Acad. Sci. U.S.A. 101, 15275 (2004).
[2] F. M. Spiga et al. Biosensors and Bioelectronics 54, 102–108 (2014).