Nano-tailored biosensing interfaces for improved biomolecular interactions

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The interaction between bioreceptor and target is key during the development of sensitive, specific and robust diagnostic devices. Moreover, the performance of these devices is strongly related to the design of the biosensing interface at the nanolevel. Uncontrolled positioning of the bioreceptors on the surface of any biosensor with suboptimal inter-receptor distances and orientation will impede an optimal interaction between bioreceptor and target leading to a decreased biosensor performance[1,2].

In this work we present scaffold-based 3D DNA origami structures as a tool to nanostructure the surface of the disc-shaped microparticles in the microfluidic environment of the innovative Evalution™ platform. Starting from a 24-helix bundle[3], an antenna-like DNA origami structure was designed to precisely position thrombin-specific aptamers. An inter-receptor distance of 16.3 nm was found optimal, perfectly accommodating the aptamer-thrombin complex, covering a region of ± 7 nm diameter. Immobilization of the capturing aptamers through the assay-specific tailored origami structure enabled reproducible detection of fluorescent thrombin (CV: 4.1 %), but also revealed a 7.8-fold increased binding potential compared to directly-coupled aptamers (holding 5.3-fold more bioreceptors). In addition, optimal spacing of the bioreceptors through DNA origami resulted in an increase in the apparent reaction rate from 0.07 min^{-1} for the directly-coupled to 0.30 min^{-1} for origami-linked aptamers. Furthermore, we demonstrated that DNA origami nanostructured biosensing interfaces outperformed basic aptamer coupling with respect to limit of detection (LOD: 11 × improved) and signal-to-noise ratio (SNR: 2.5 × better) in a DNA-based sandwich bioassay.

In conclusion, our results highlight the potential for assay-specific DNA origami nano-tailored surfaces to improve biomolecular interactions at the sensing surface and hereby increasing the overall biosensor performance. The immobilization of bioreceptors using a well-designed DNA origami structure results in the formation of a less densely packed surface with reduced steric hindrance and a favored upward orientation which increases their accessibility leading to enhanced biomolecular interactions. The reported surface functionalization strategy provides a general approach that can be directly transferred for the detection of various target molecules. We believe that the obtained results will lead to better insight into the receptor-target interactions and improved sensing devices for diagnostics.

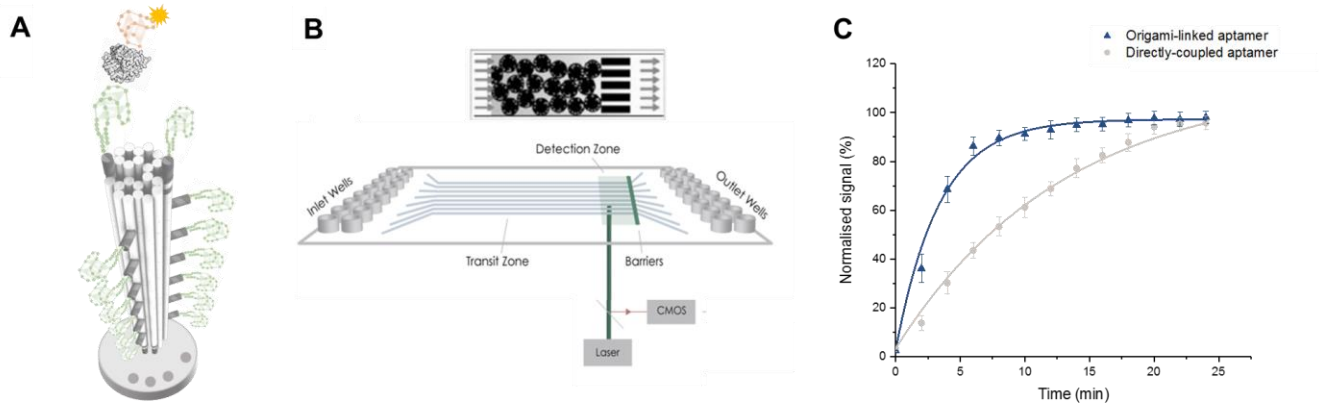

Figure 1: Schematic overview of the DNA-based microfluidic bioassay. A) Modified 3D DNA origami structure with strands for bioreceptor and biosensor surface coupling on the barcoded disks (not to scale). Thrombin is captured by an aptamer (TBA2) and detected through a fluorescent secondary aptamer (TBA1). B) Overview of the disposable microfluidic cartridge, confining the encoded microparticles, with a close-up of the detection zone. C) Reaction kinetics of thrombin (84 nM) with origami-linked and directly-coupled aptamer bioreceptors. Error bars represent one standard deviation (n = 3).

References

[1] Lin, M. *et al*. *Angew.Chemie - Int. Ed.* 2015, **54**, 2151–2155; [2] Ye, D. *et al*. *Annu. rev. anal. chem*.-2018, **11**, 171–195; [3] Daems, D. *et al. ACS Appl. Mater. Interfaces* 2018, **10**, 23539–23547.