

Engineered DNA nanostructures for photoacoustics bioimaging

Silvia Hernández-Ainsa,^{1,2}

James Joseph,^{3,4} Kevin N. Baumann,³

Alexandra C. Fux,³ Philipp Koehler,³ Judith Weber,³

Sarah E. Bohndiek^{3,4}

¹Instituto de Nanociencia de Aragón (INA), University of Zaragoza, Campus Río Ebro, Edificio I+D, 50018 Zaragoza, Spain

²ARAID Foundation, Government of Aragón, Zaragoza 50018, Spain

³Department of Physics, University of Cambridge, 19 JJ Thomson Avenue, CB3 0HE, Cambridge, UK

⁴Cancer Research UK Cambridge Institute, University of Cambridge, Robinson Way, CB2 0RE, Cambridge, UK

silviamh83@unizar.es

DNA nanotechnology is a unique assembly tool to engineer structures with accurate control in the location of any introduced functionality.[1]

In this regard, fluorophores can be arranged at controlled distances into DNA nanostructures to investigate molecular processes that occur on the nanometer scale based on the Förster resonance energy transfer (FRET) mechanism.[2] However, the use of this fluorescent pairs in biological samples is limited to shallow imaging depths due to the light scattering. Photoacoustic tomography (PAT)- a recently emerged high resolution modality for *in vivo* imaging that that combines optical excitation with ultrasound detection- represents an interesting approach to study such processes at centimeter depths.[3]

In this respect, we have shown the possibility to produce controlled distance dependent photoacoustics (PA) signal using several DNA helices containing Near Infrared (NIR) fluorophore-quencher pairs located over a range of different controlled distances (Figure 1). Indeed, we have demonstrated their potential use to reveal deep FRET processes within tissue mimicking phantoms.[4]

We have also proved that PA signal of NIR fluorophores can be enhanced by precise positioning into DNA nanostructures.[4] This property together with their biocompatibility make DNA nanostructures very promising as contrast agents nanocarriers (NCs) for cancer imaging using PAT. Namely, some of our investigated DNA NCs bearing NIR fluorophores present superior PA signal generation capabilities and tumor accumulation when compared to the free fluorophore.

Finally, we have shown that DNA nanostructures can be tailored to act as nanoprobe for photoacoustics pH imaging using a ratiometric approach (Figure 2). Interestingly, these nanoprobe work in a pH range relevant for tumour microenvironment.[5]

These reported achievements evidence the multiple applications that DNA nanotechnology can offer to PA bioimaging.

References

- [1] F. Zhang, J. Nangreave, Y. Liu and H. Yan, *J. Am. Chem. Soc.* 2014, 136, 11198
- [2] I. H. Stein, V. Schüller, P. Böhm, P. Tinnefeld, T. Liedl, *Chem. Phys. Chem.* 2011, 12, 689
- [3] L. V. Wang, S. Hu, *Science* 2012, 335, 1458
- [4] J. Joseph, K. N. Baumann, P. Koehler, T. J. Zuehlsdorff, D. Cole, J. Weber, S. E. Bohndiek, S. Hernández-Ainsa, *Nanoscale* 2017, 9, 16193
- [5] K. N. Baumann, A. Fux, J. Joseph, S. E. Bohndiek, S. Hernández-Ainsa, *Chem. Commun.* 2018, 58, 10176

Figures

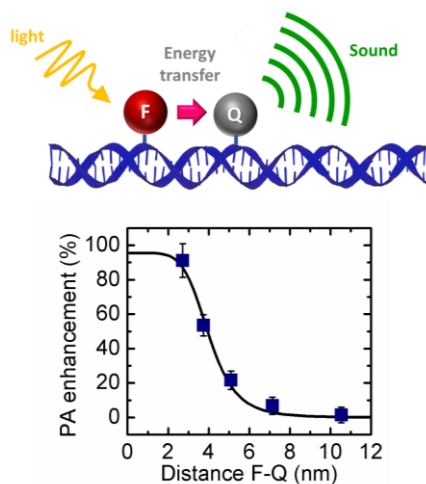


Figure 1. Scheme and graph showing the enhancement of PA signal as the distance between fluorophore and quencher attached to a DNA helix is reduced.

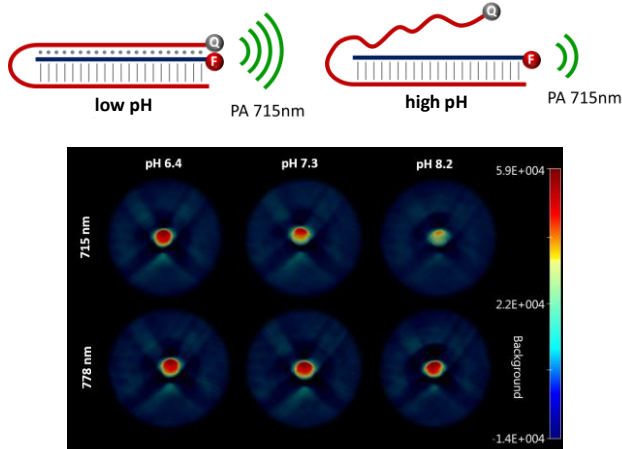


Figure 2. Scheme of the pH responsive DNA-based nanoprobe and images of samples held in phantoms showing the PA signal dependence with pH.