

Hetero-coated magnetic microcarriers for point-of-care diagnostics

C. Ciorra Eusey^{*1}, D.M. Love¹, J. Llandro¹, J.J. Palfreyman¹, C.H. W. Barnes¹, Liz Muir², Geoff Cook², and Roger Keynes²

¹Cavendish Laboratory, Madingley Road, Cambridge University, Cambridge, CB3 0HE, UK2

²Department of Physiology, Development and Neuroscience, University of Cambridge, CB2 3DY, UK

*Corresponding author: Email: cc650@cam.ac.uk

Abstract Summary: We report on the latest advances in the development of our magnetic encoded microcarriers [1,2] comprised of a polymer backbone, magnetic elements and surface functionalisation with biomolecules for medical diagnostic applications.

Introduction:

Thin magnetic strips ('bits') are encapsulated in a biocompatible polymer backbone to form 'tags'. The tags can be used to generate a large library of magnetically labelled bio-chemical analytes. Since the magnetic encoding can be applied post fabrication, all microcarriers are nominally identical, which makes them a cost effective micro-tagging strategy [3]. The number of unique codes doubles with every extra bit added, which also makes magnetic encoding extremely scalable. For instance a 7-bit tag offers $2^7=128$ codes, but a 32-bit tag would offer over 4 billion unique codes. Applications range from DNA/protein analysis for genotyping and point-of-care diagnostics to drug development and combinatorial chemistry.

We will be focussing on some novel aspects of surface chemistry and the effects of various linker molecules on binding efficiency [4]. Since then we have introduced a thin nanostructured gold interface on to one side of the microcarriers to provide a second functional coating. With this, we can now pursue two different chemical routes (carbodiimide chemistry and thiol-containing self-assembled monolayers) to add particular probe molecules to each side. While one probe remains specific to the analyte of interest, the other acts as a hybridisation control to interrogate the assay's binding conditions.

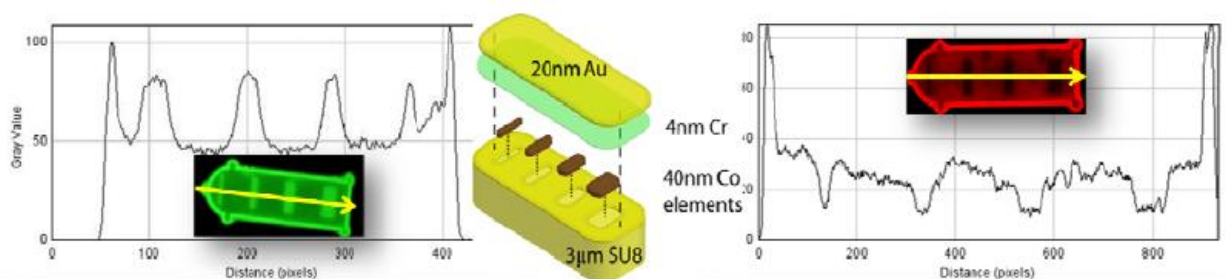


Figure: Exploded schematic of a hetero-functional magnetic microcarrier (centre) and line-intensity profiles showing microcarriers dual-labelled with fluorescein and TAMRA. The peaks and troughs are indicative of whether the fluorescence is on the top or bottom side respectively.

The complimentary target (pre-labelled with TAMRA) is added to the sample serum as a positive control. This eliminates the possibility of seeing no fluorescence and not being confident of whether the analyte was absent (true negative) or whether the binding conditions were insufficient (false negative). The target strand can be labelled with a different colour, e.g. with PicoGreen in an additional step, so that now a positive result causes the microcarrier to fluoresce red on one side and green on the other. As can be seen from the figure, there is a clear signature (peaks vs. troughs) in the intensity profile corresponding to the microcarrier's orientation.

The microcarriers are read in-flow through a 50µm wide channel, which includes a TMR sensor able to detect the stray field (magnetic signature) of the passing microcarrier [5]. Thus, by combining the fluorescence data and the TMR data it is possible to conduct a multiplexed assay very quickly and cost-effectively on a small footprint device.

Acknowledgements

This work was supported by the EPSRC within the nano Doctoral Training Centre.

References

- [1] T. Mitrelias, T. Trypiniotis, C.H.W. Barnes et al., JAP 105, 07B301 (2009)
- [2] J.J. Palfreyman, C.H.W. Barnes et al., IEEE Transactions on Magnetics 49, 285-295 (2013).
- [3] B. Hong, T.J. Hayward, C.H.W. Barnes et al., JAP 105, 034701 (2009)
- [4] J.J. Palfreyman, P. Beldon, C.H.W. Barnes et al., AIP Conf. Proc 1311, 184-191 (2010)
- [5] K.N. Vyas, J.J. Palfreyman, C.H.W. Barnes et al., Lab-on-a-chip (2012)