



Digital Biomagnetism:

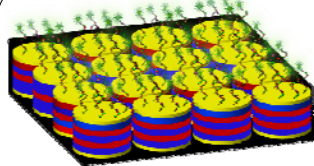
Electrodeposited Multilayer Magnetic Tags



J. Palfreyman¹, F. van Belle¹, T. Mitrelias¹, J. Cooper¹, J.A.C. Bland¹, M. Lopalco² & M. Bradley²

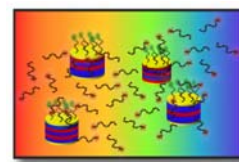
¹Cavendish Laboratory, University of Cambridge, Madingley Road, Cambridge CB3 0HE, United Kingdom

²Department of Chemistry, University of Edinburgh, Edinburgh EH9 3JJ, United Kingdom



2D microarrays – well established micro-drop printing techniques allow large library generation.

Microarrays (left) and bead-based technologies (right) have recently become standard laboratory tools for applications ranging from drug development and proteomics to SNP analysis and gene sequencing [1,2]. However both suffer from inherent difficulties, be it the optical resolution limiting microarray density [3] or the finite number of codes distinguishable on beads [4]. By exploiting the strengths of each technology combined with magnetic encoding and micro-fluidics we aim to overcome current limitations and sequence a genome a day [5].



3D bead based assays – improved reaction kinetics and washing efficiencies.

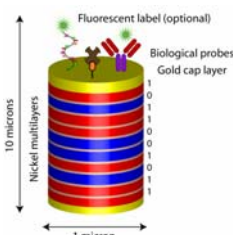
Introduction

1. Magnetic Barcodes as a biological tag

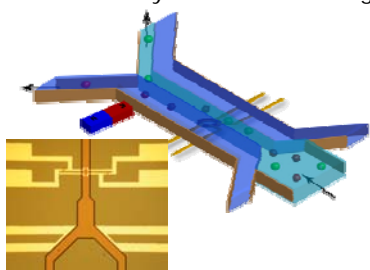
By independently aligning the spins in each magnetic layer either up or down we create a 'barcode'.

The number of possible codes doubles with every new layer.

Numerous biological molecules can be chemically attached to the tags.

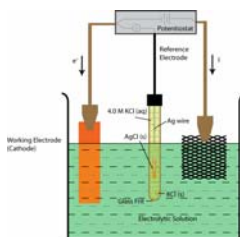
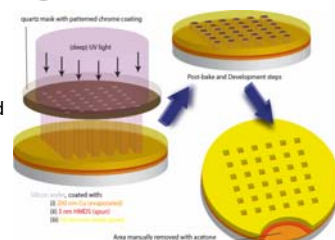


Integrated Microfluidics consisting of **focussing** (hydrodynamic & DEP), **sensing** (fluorescence & magnetic) and magnetic **sorting** (current strip lines) will allow for high-throughput screening [6].



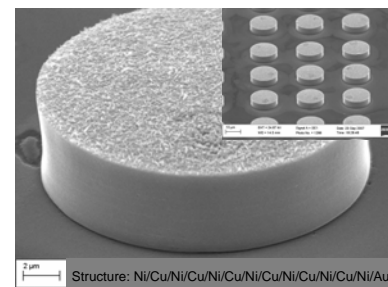
2. Micro-Pillar design and fabrication

A conductive Al/Cu release layer is evaporated onto a Silicon wafer. 15 μm diameter holes are lithographically defined in AZ9260 resist, which can be spun from 10 to 24 μm high.



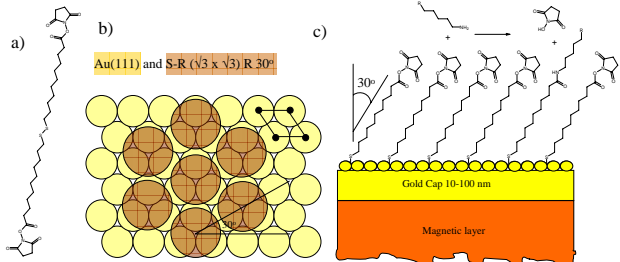
Thick Ni, Fe, Co, Cu and Au layers can be grown by simple electrodeposition. → Inexpensive and no need for UHV!

The Ni/Cu multilayers can be grown from the same bath (minimising processing steps) containing a 1:100 ratio CuSO₄:NiSO₄ in boric acid buffer, by applying potentials of -0.5V and -1.2V respectively. A separate bath is needed for the gold cap.



3. Chemistry (Self-Assembled Monolayers)

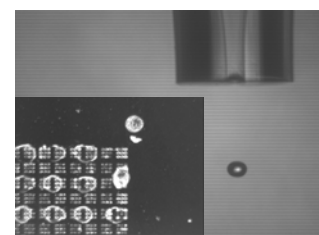
A gold cap layer allows us to chemically functionalise the tags with a disulphide based self-assembled monolayer...



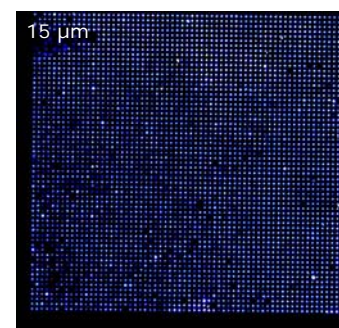
... now biological molecules (e.g. amine-modified ss-DNA probes) can be covalently bound to the S.A.M.

4. Functionalisation & Microdrop Printing

Whole chips can be functionalised with a particular bio-molecule for mass production of a particular probe/tag [7] (below), or a large library of DNA can be generated using micro-inkjet printing (right).



1600 oligos (16 replicates) is feasible on a 5 mm² chip using a 70 μm nozzle



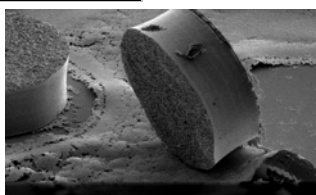
CCD-scan showing hybridisation of FITC labelled DNA on a 64 x 64 array of tags

Advances in microarray printers will determine final chip density (drop size is currently 35 μm), but we want to flow the tags using bead-based technology.

∴ the tags must be released from the substrate AFTER micro printing with ss-DNA probes ...

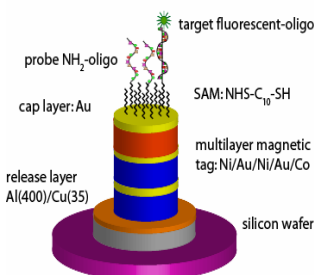
5. Chemical Release

...Mechanical release methods are very 'hit & miss' and risks damaging the tags (right).



We have developed a chemical method non-harmful to ss-DNA based on Aluminium, which is dissolved by NaOH.

The NaOH concentration should be minimised to increase biocompatibility, and by adding a thin copper layer we achieved this, plus it ...



1. prevents formation of a 'tough' Aluminium oxide layer
2. increases conductivity helping the electrodeposition
3. forms a galvanic cell with the aluminium helping to dissolve the release layer.

References and Acknowledgements

[1] M. Jayapal and A.J. Melendez, *Clinical and Experimental Pharmacology and Physiology*, **33**, 496 (2006)
 [2] D.J. Lockhart, *Nature*, **405**, 827 (2000)
 [3] D.B. Allison, X. Cui, G.P. Page, and M. Sabripour, *Nature Reviews*, **7**, 55 (2006)
 [4] K. Braeckmans, *Nature Reviews: drug discovery*, **1**, 447 (2002)
 [5] T. Mitrelias, Z. Jiang, J. Llandro and J.A.C. Bland, *Technical Proceedings of the 2006 Nanotechnology Conference*, Boston, USA, **2**, 256 (2006)
 [6] Z. Jiang, J. Llandro, T. Mitrelias and J.A.C. Bland, *J. Appl. Phys.* **99** (8), 08S105 (2006)
 [7] J. Palfreyman, F. vanBelle, W-S. Lew, T. Mitrelias, J.A.C. Bland, M. Lopalco and M. Bradley, *IEEE Trans Mag.* **43**, 2439 (2007)

The author thanks J.J. Diaz-Mochan and J.K. Cho from the University of Edinburgh for their teachings of chemistry. This work is funded by the Engineering & Physical Sciences Research Council within the Basic Technology Program.