

A Handheld Immunosensing Device Based on Low-cost Self-contained Microchips and Ferromagnetic Actuation

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Figure 1. BioFiniti® reader and cartridge

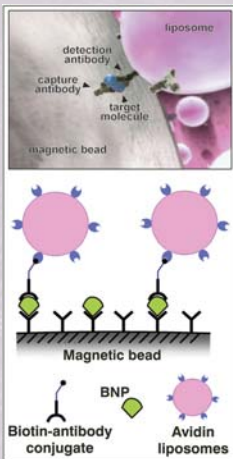


Figure 2. Reagent scheme

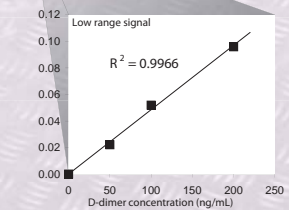
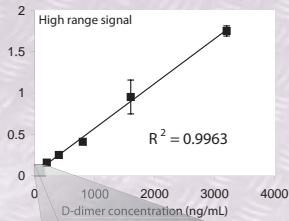


Figure 4. D-dimer results

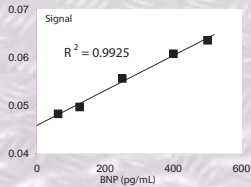


Figure 5. BNP assay response

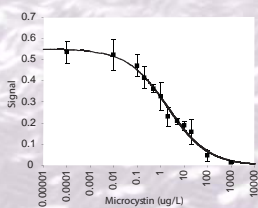


Figure 6. Microcystin competition curve

INTRODUCTION

Point-Of-Care (POC) analyses are currently performed using lateral-flow devices (LFD), compact analyzers such as Roche's Cardiac® or Biosite's Triage®, or Abbott's handheld iStat®. LFDs are low-cost but frequently suffer from poor quantification. Other POC devices provide better quantitation but require stable, controlled, bench-top environments. Achieving high performance detection in simple, rugged devices has remained a technical challenge. Existing technologies cannot deliver high performance in patient-side settings outside of controlled environments.

METHOD

A handheld biosensor has been developed. It is capable of sensitive quantification of small organics, large proteins and pathogens. The BioFiniti® system comprises a fully autonomous, hand-held electronic device that controls and reads disposable cartridges (Fig 1), with key features as summarized in Table 1.

Table 1. Summary of BioFiniti® features

Reader	Cartridges
<ul style="list-style-type: none"> • Self-contained • Battery or 12V DC power • Cartridge heating • Rugged (can be shaken during use) • Zero fluidic interconnects • Fully programmable for complex sequences • Variable pumping rates to $\pm 100\mu\text{L}/\text{min}$, independent of viscosity • Ethernet, USB & Bluetooth interfaces 	<ul style="list-style-type: none"> • Metering • 2 positive displacement ferrofluidic [1] pumps • 'Closed loop' [2] configuration • Stop, mixing and directing 'valve' functions • Reagent storage • Calibration • Immuno Magnetic Separation • Washing • Electrochemical detection • Waste storage • Injection molded • Zero moving parts

The BioFiniti® sensor was evaluated on D-dimer (fibrin degradation product for diagnosis of thrombotic conditions), b-type natriuretic peptide (ventricular protein indicative of heart failure) and microcystin (algal peptidic hepato-toxin posing health risks via ingestion or contact) assays, all using tosylactivated 2.8 μm magnetic beads (Invitrogen). Formats are summarized in Table 2.

Table 2. Summary of BioFiniti® assay formats

Target	D-dimer	BNP	Microcystin
Format	Sandwich	Sandwich	Competition
Incubation time	2 minutes	5 minutes	5 minutes
Total duration	15 minutes	18 minutes	15 minutes

RESULTS

Figure 4 shows D-dimer detection results for high and low quantification ranges. The BioFiniti® device displays excellent linearity and good reproducibility in both ranges, detecting to sub-50ng/mL concentrations.

Figure 5 shows the linear response of the BioFiniti® handheld sensor to sub-100p molar levels of BNP.

Figure 6 shows sub-30 min Microcystin detection in water samples with an IC50 value of approximately 1 $\mu\text{g}/\text{L}$.

Method in brief:

- Sample mixed off-cartridge with magnetic beads and marker-loaded liposomes, both conjugated to biological receptors (Fig 2)
- Unmetered mixture placed on cartridge
- Sample is automatically metered
- Flows onto capture magnet (Fig 3a)
- Buffer wash and matrix substitution (Fig 3b)
- Electro-active marker lysed from liposomes (Fig 3c, 3d)
- Amperometric analysis (Fig 3d) of amplified signal [3].

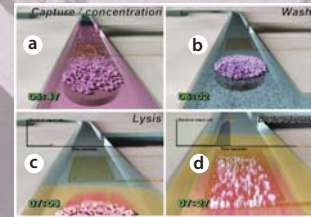
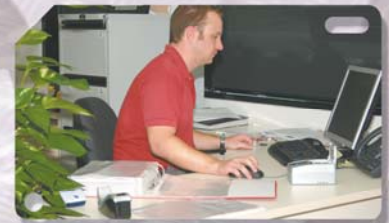


Figure 3. Assay process

CONCLUSIONS

The BioFiniti® device provides a commercial alternative for POC quantification of low concentration targets in difficult matrices by integrating complex microfluidic features and electronic sensing elements into a low-cost injection-molded microchip. Its versatility is demonstrated across a range of targets in a range of matrices. Fully programmable assay control facilitates rapid development of new assays, or conversion of existing immunoaffinity tests.

The BioFiniti® device is rugged and capable of use in harsh environments, offering many new opportunities for Mobile Point-of-Care™ testing.



REFERENCES

- [1] Hatch, A., Kamholtz, A. E., Holman, G., Yager, P., Bohringer, K. "A ferrofluidic magnetic micropump", Journal of Microelectromechanical Systems, 10(2), 215-221, 2001.
- [2] PCT/AU2005/001341.
- [3] Kwakye, Sylvia D. "A micro-total analysis system based on nucleic acid sequence recognition", MSc Thesis, Cornell University, May 2002.

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