Rapid Diagnostic Approaches for Ensuring Food Security

Training Workshop on Risk Identification and Screening Technologies of Agro-food

Shanghai Academy of Agriculture Science

Shanghai

China

13th September 2016

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New Global Research Institute

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Judged by our Peers

Institute for Global Food Security

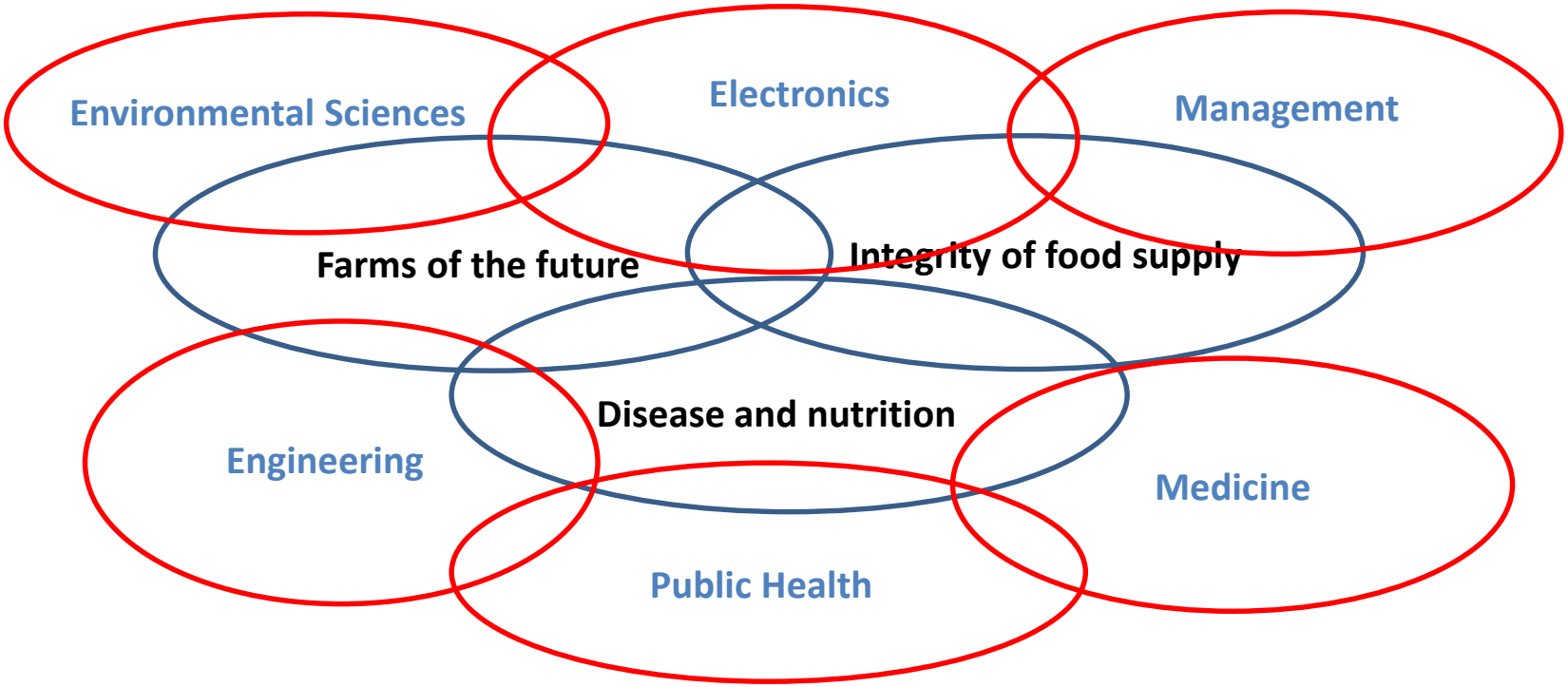
- 35 – 40 PIs
- 60 – 80 PDRAs
- 100 – 120 PhDs
- ~15 embedded support staff
- **A critical mass of 200 – 250 researchers**

REF 2014: SUBJECT RANKING ON INTENSITY

6 Agriculture, Veterinary and Food science

1	5	Queen's Belfast	33	34	98	3.26	3.20
2	=11	SRUC (joint submission with Edinburgh)	57	58	99	3.13	3.10
3	6	Reading	73	82	89	3.24	2.88
4	4	Stirling	28	32	88	3.27	2.86
5	=11	Edinburgh (joint submission with SRUC)	123	138	89	3.13	2.78
6	2	Warwick	13	16	79	3.38	2.66
7	10	Cambridge	40	49	81	3.18	2.57
8	14	Royal Veterinary College	103	126	82	3.11	2.55
9	=8	UEA	11	14	79	3.21	2.52
10	=17	Aberystwyth (joint submission with Bangor)	70	87	81	3.05	2.46

Grand Challenges



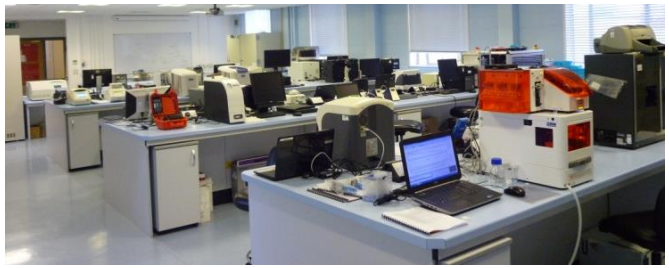
UK | EU | US | Asia | Africa

Having the credibility to link with recognised centres of excellence and thought leaders wherever they are located

State of the Art Facilities

Food Analysis (Wet chemistry LAB): Sample preparation for food, feed and environmental sample analysis

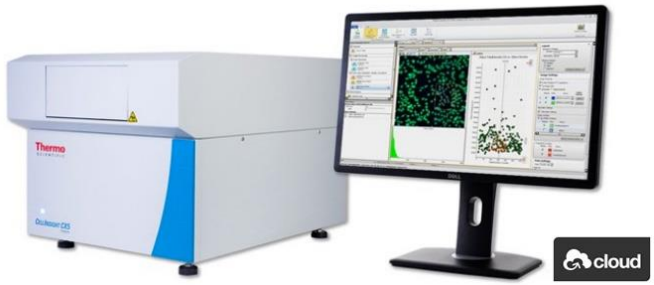
ASSET LAB: Highly innovative rapid diagnostics including biosensor (SPR, acoustic wave, microarrays, lateral flow, flow cytometry, electrochemistry) and spectroscopic (IR and RAMAN) technologies



Advanced ASSET LAB: Suites of HPLCs, UPLC coupled to mass spectrometers including QTof, Xevo-TQ, Xevo-TQS, PDA, REIMS, Isotope ratio, ICP-MS for chemical analysis

Mammalian cell culture Facility for in vitro toxicological assessments using high content screening analysis

Pathogen LABs: Category 2 and Category 3 Pathogen labs



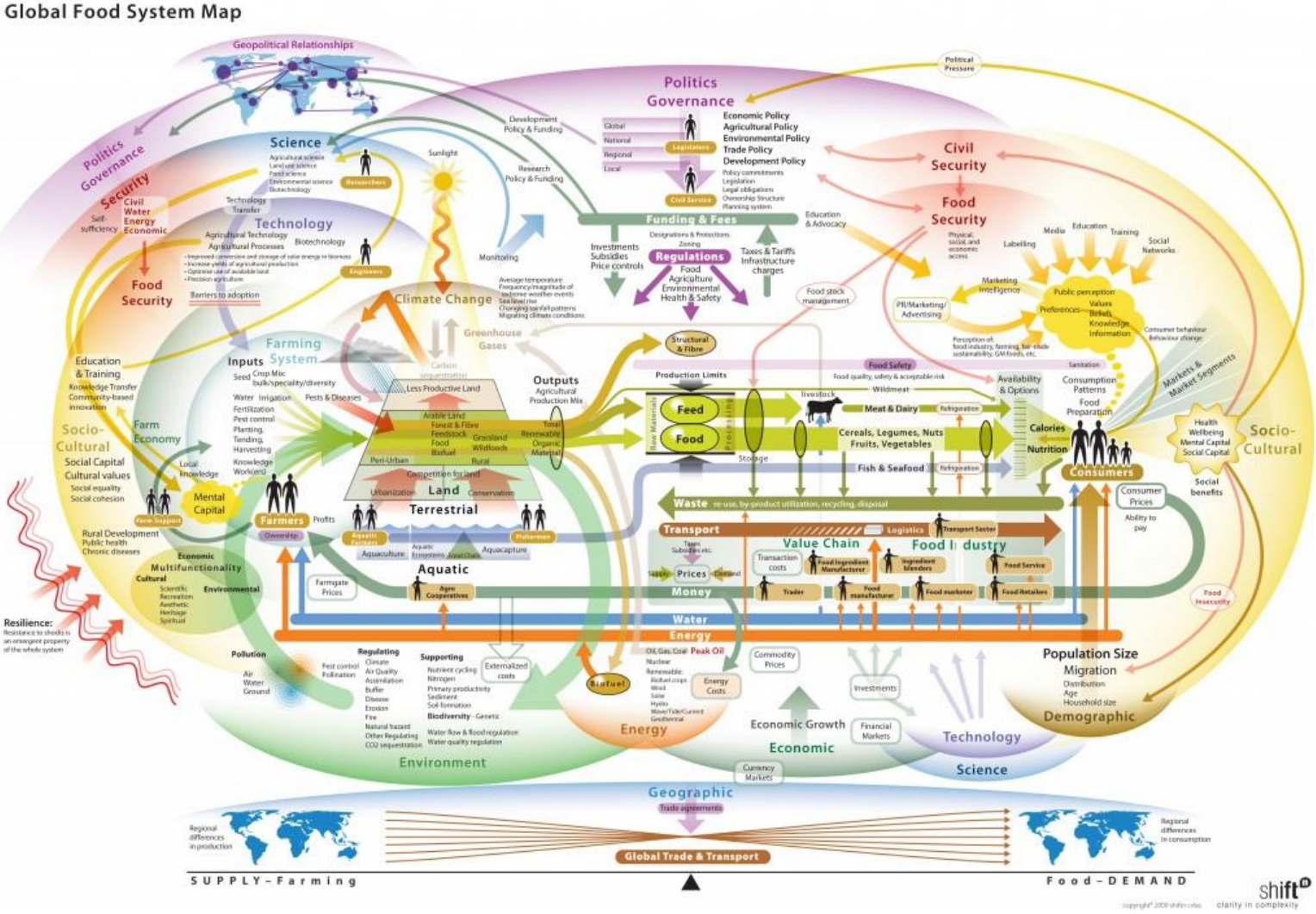
Animal facility for in vivo toxicological assessment

Institute for Global Food Security (IGFS)

The World Food Summit of 1996 defined food security as "**when all people at all times have access to sufficient, safe, nutritious food to maintain a healthy and active life".**

The driver for IGFS research is to support national and international efforts to provide **sufficient, safe, authentic and nutritious food.**

Map of Global Food System



Global Food Safety System

Global Food System is highly complex involving many factors and disciplines

- Politics and governance
- Science
- Environmental
- Technology
- Security
- Economics
- Societal

Supply versus demand

- Faster food production faster testing required for release to market

Impact of contamination at any point in the supply chain can affect all factors

Food contaminant testing is mainly only performed if legislatively required and if methods are available

Food Safety Testing

Under the current EU Food Hygiene legislation Producing safe food is the responsibility of Food Business Operators (FBOs)

The safety of food may be checked throughout the food supply chain at Hazard Analysis and Critical Control Points (HACCPs) such as

- Source of raw materials (pre and post harvest)
- Production site
- Processing sites
- End product testing

These checks may be performed as

- Routine by the larger companies through in-house testing
- Through legislated regulatory monitoring of certain products

The equipment normally employed are sophisticated instruments such as

- Mass spectrometry
- Molecular detection platforms such as PCR

Methods applied to food analysis

1. Functional Assays
   a. Animal assays
   b. Cell based
   c. Receptor based
   d. Enzyme based
   e. Fluorescence based

- Level of contaminant measured is relative to the biological effect of the sample
- May detect new toxic analogues
- Contaminant identification is not unequivocal
- Technology transfer of methods is difficult

2. Biochemical Assays
   a. ELISA
   b. Lateral flow devices
   c. Biosensor

- Binder a
- Toxicity
  cross-re
- Sample
- Screeni
  rapid re

Methods applied to food analysis

3. Spectroscopic methods
   a. Near IR
   b. Mid IR
   c. RAMAN
   d. SERS

- Fingerprinting techniques
- Non-destructive methods little to no sample prep
- Require chemometric models of known samples
- Sensitivity is questionable

4. Analytical methods
   a. HPLC
   b. LC-MS
   c. GC-MS
   d. ICP-MS

- Contaminants can only be identified and quantified for available analytical standards
- Toxicity equivalent factors must be applied
- Sample clean-up is extensive with oxidation steps being required in cases
- Data analysis is laborious
- LC-MS is unequivocal for identification

ANALYTICAL METHODS TRADITIONAL CONFIRMATORY METHODS

Criteria for a Screening Test

Food is produced on an ever-increasing scale

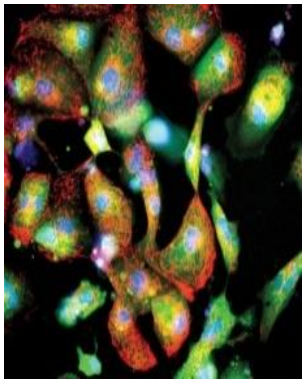
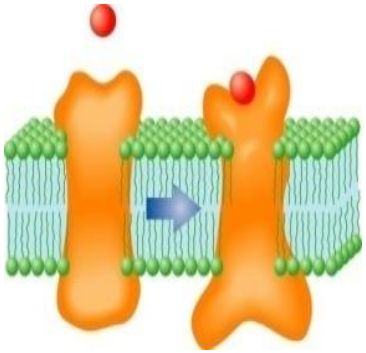
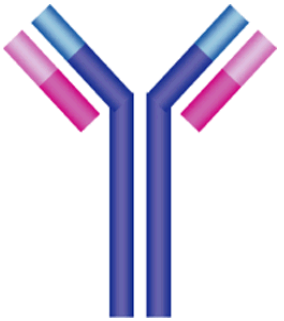
Screening interventions are designed to identify contaminants in a commodity early, thus enabling earlier intervention and management to prevent risk to human health

- **Rapid**
- **Reliable**
- **Low cost**
- **Low false positives**
- **No false negatives**
- **Safe**

2.2. SCREENING METHODS

Only those analytical techniques, for which it can be demonstrated in a documented traceable manner that they are validated and have a false compliant rate of < 5 % (ß-error) at the level of interest shall be used for screening purposes in conformity with Directive 96/23/EC. In the case of a suspected non-compliant result, this result shall be confirmed by a confirmatory method.

Screening Tests for Food Analysis

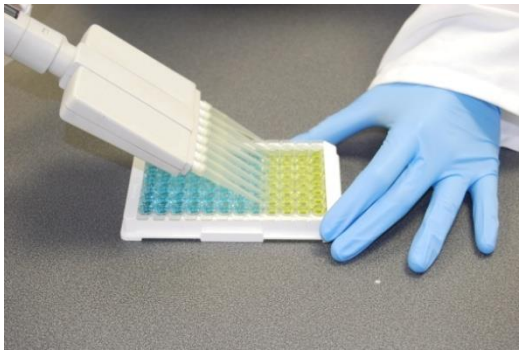
Animal Based	Cell Based	Receptor Based	Antibody Based
			
Toxins in food Botulism Marine toxins	Antibiotics residues in milk	Dioxins in feed & food	Chemical contaminants in foods

Screening tests that require special facilities for use

Immunological methods for food analysis

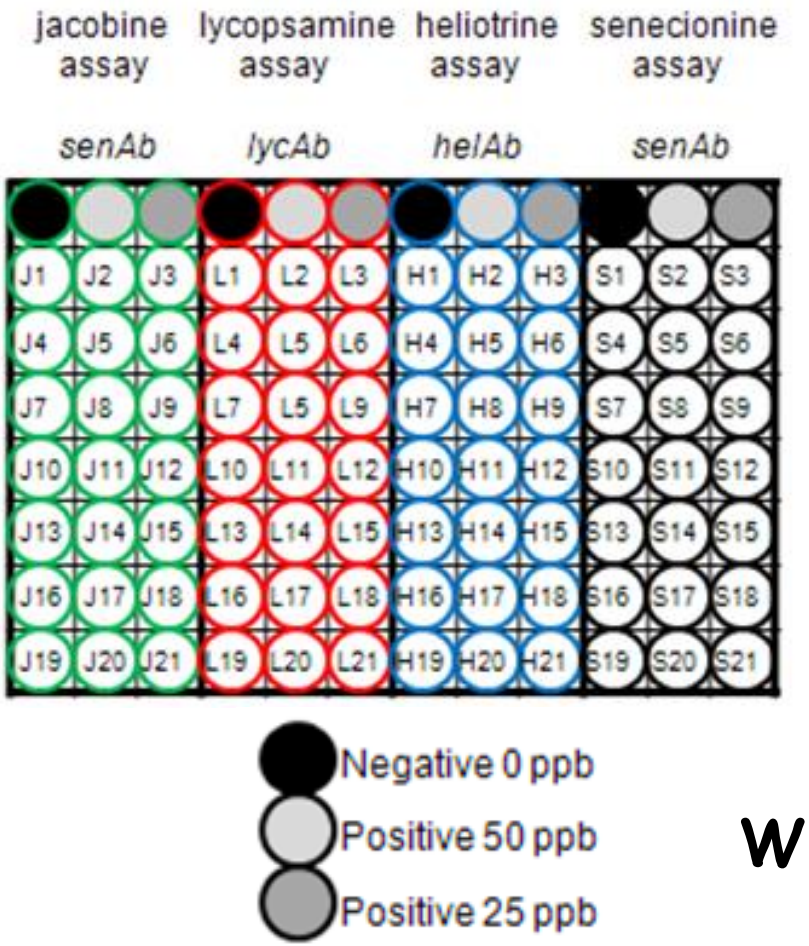
Antibodies specific for a desired antigen can be conjugated with a fluorescent label, or colour-forming enzyme & are used as a "probe" for detection.

Well known applications of this include lateral flow tests eg pregnancy tests, ELISA and immunohistochemical staining of microscope slides.



The speed, accuracy & simplicity of such tests has led to the development of rapid techniques for the diagnosis of disease, microbes & chemical contaminants in food.

Emerging Issues - Pyrrolizidine Alkaloids



1 h coating of the microtitre plate with antibodies

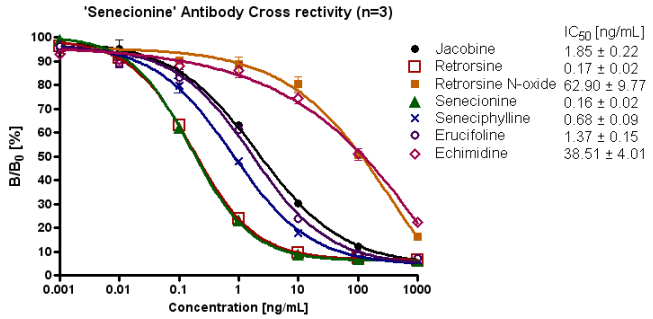
30 min incubation with samples/ standards and HRP conjugates

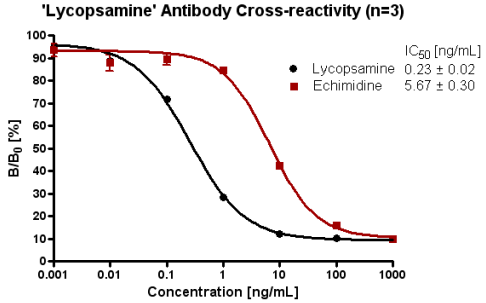
15 min colour development with TMB substrate

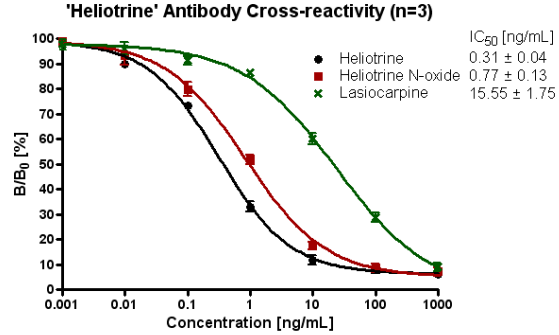
addition of the stop solution and optical density (OD) measurement at 450 nm

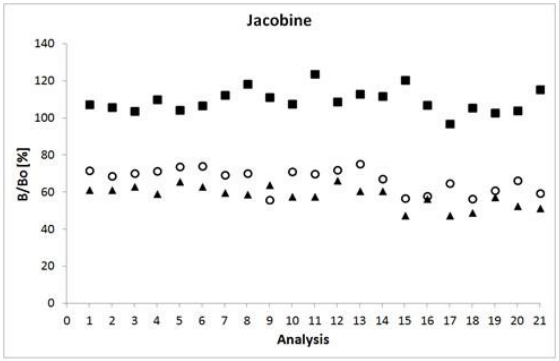
With pre-coated antibody plates
Analysis time = 45mins

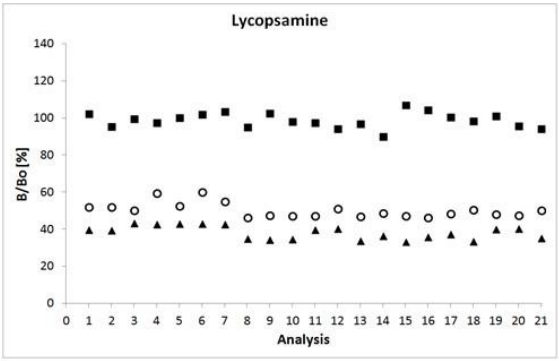
Emerging Issues - Pyrrolizidine Alkaloids

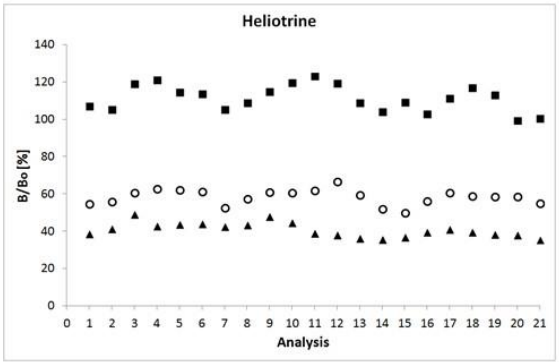












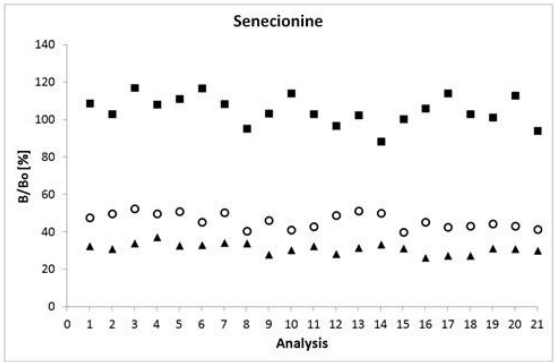
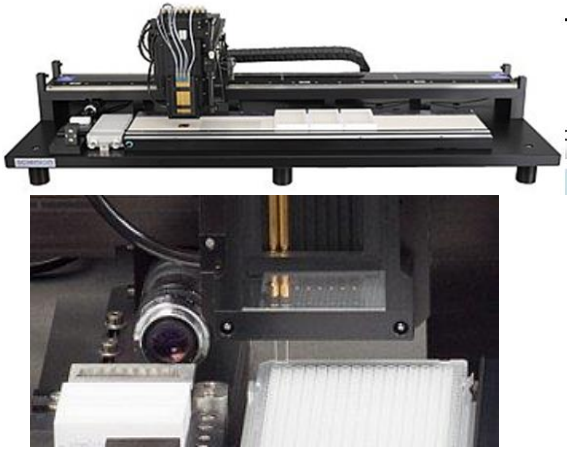
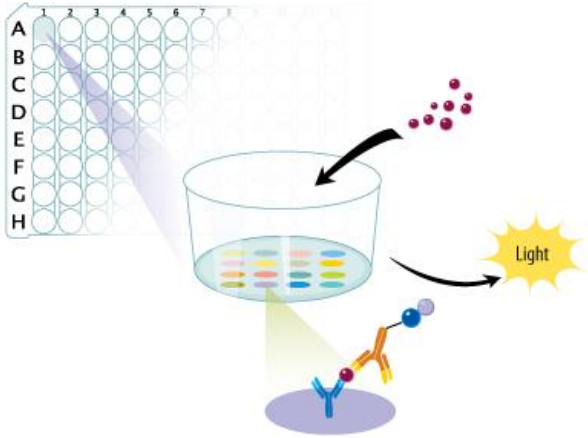
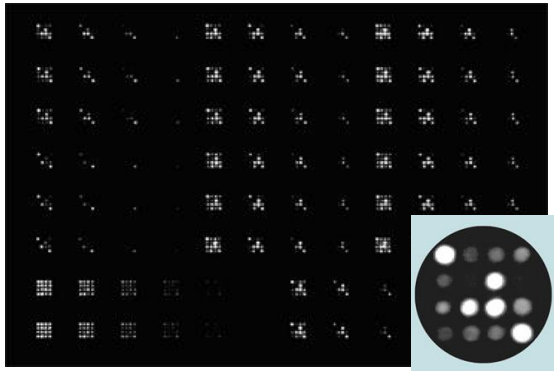


Illustration of the detection capability of the multiplex ELISA for jacobine, lycopsamine, heliotrine and senecionine in honey matrix over the three days at 3 levels 0 μg/kg (■), 25 μg/kg (O) and 50 μg/kg (▲).
Day 1: Analysis 1 to 7; Day 2: Analysis 8 to 14; Day 3: Analysis 15 to 21.

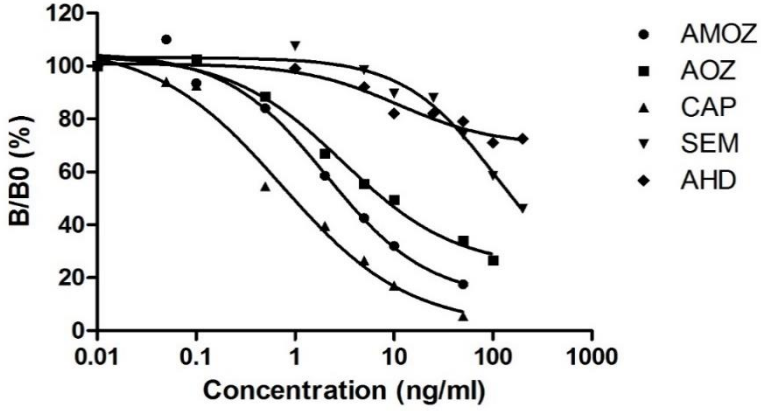
Multiplexing technology – Antibiotic Residues







Nitrofurans and chloramphenicol



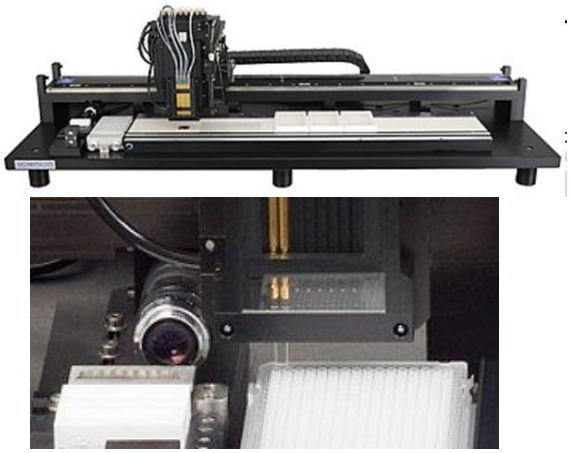
Advantages

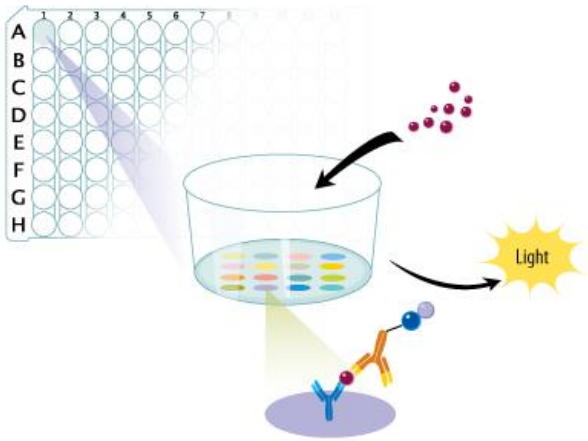
Cost-effective

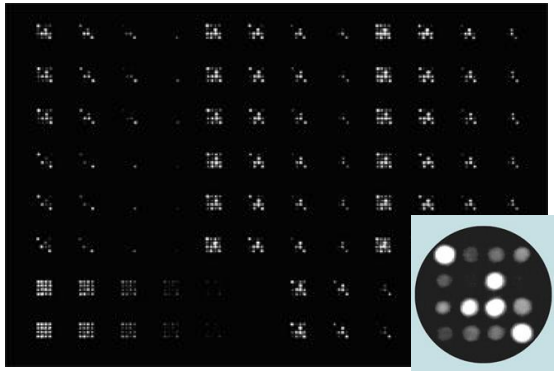
Simple to use – ELISA

Offers 5 tests in one

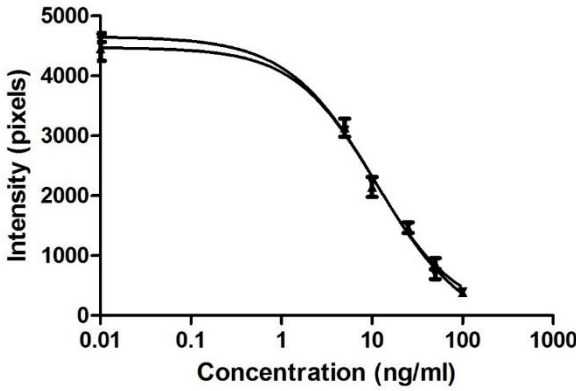
Multiplexing technology – Mycotoxins



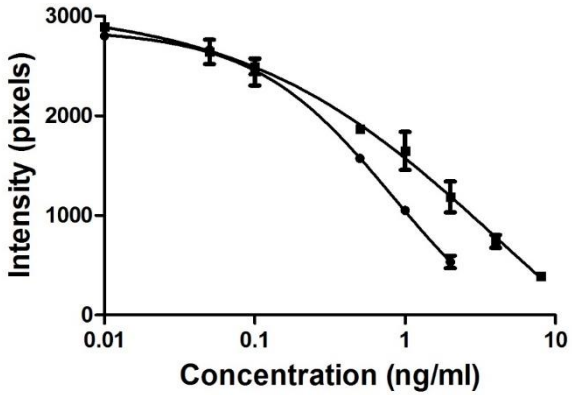




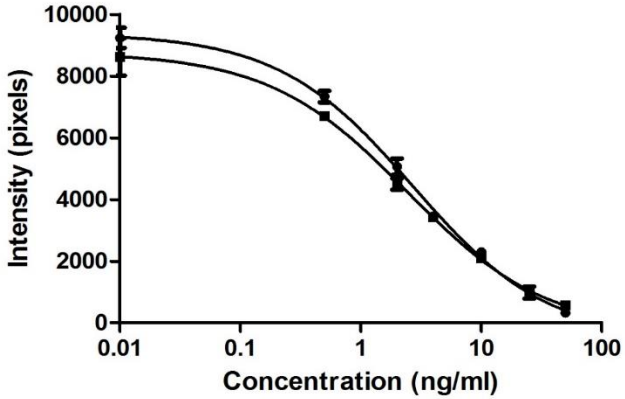
Fumonisins



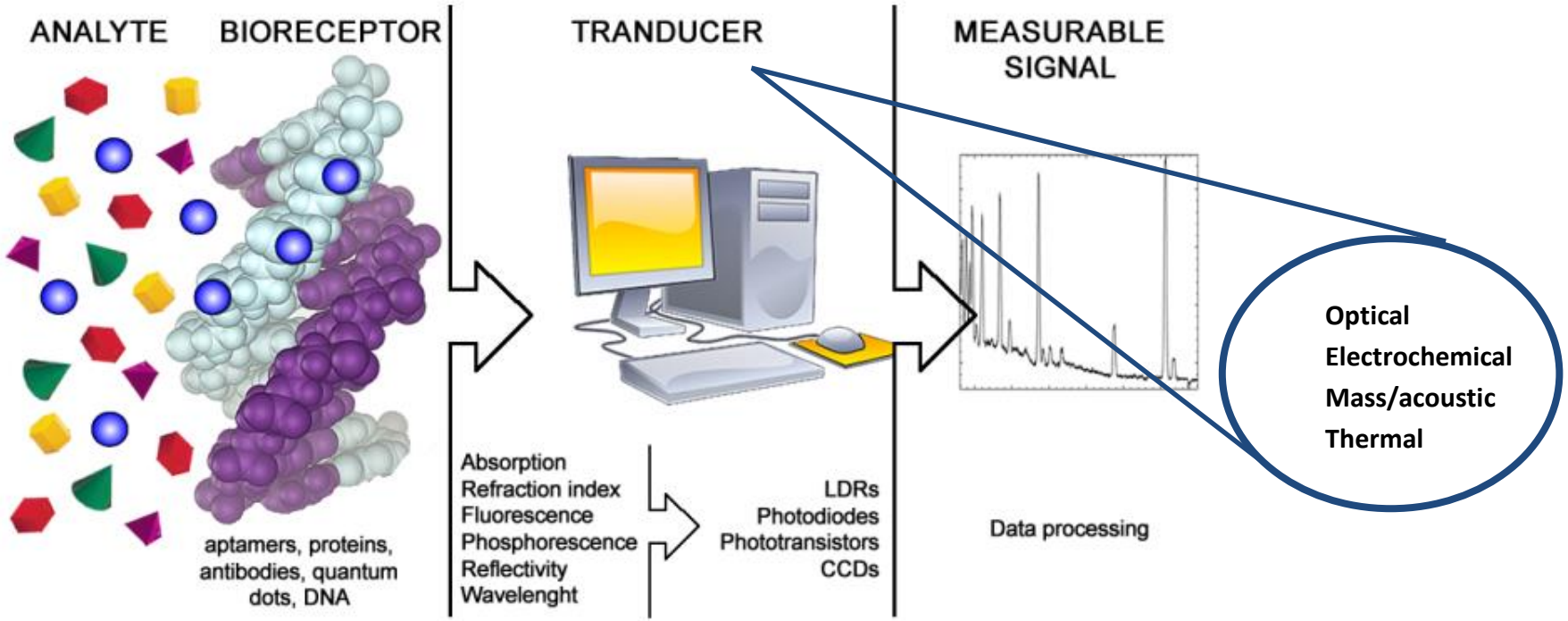
T2



Zearalenone



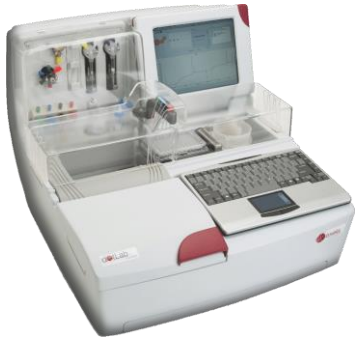
Biosensors



"A biosensor is an analytical device incorporating a biological or biologically derived sensing element either intimately associated with or integrated within a physicochemical transducer. The usual aim is to produce a digital electronic signal which is proportional to the concentration of a specific analyte or group of analytes"

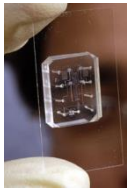
Turner, A.P.F., Karube, I. and Wilson, G.S. (1987). *Biosensors: Fundamentals and Applications. Oxford University Press, Oxford. 770p.*

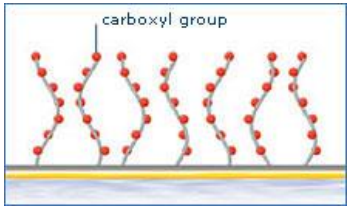
Bio to nanosensor



Bio to nanosensors

SPR Biosensor
Invented by Liedberg, Nylander, Lunström (1983)





High Tech MS analysis

Why nanosensors?

Smaller and faster
Require less power to run
Greater sensitivity
Better specificity
Cost-effective
Remote use
Simple to use

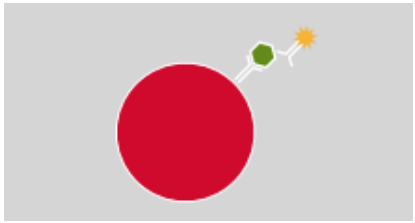
Multi mycotoxin methods

Multi pesticide methods

Untargeted analysis
Fingerprint profiling

Semi-portable multiplexing technology

Luminex Technology



Antibodies attach to fluorescent nanoparticles to detect chemicals or foodborne pathogens

Particles can have a different core that identifies a specific assay in a multiplex system

The label attached to the antibody determines the level of binding in a similar way to the ELISA.

Anal Bioanal Chem (2012) 404:1361–1373
DOI 10.1007/s00216-012-6214-1

ORIGINAL PAPER

Development of a five-plex flow cytometric immunoassay for the simultaneous detection of six coccidiostats in feed and eggs

Monique E. Bienenmann-Ploum · Anne-Catherine Huet · Katrina Campbell · Terence L. Fodey · Ursula Vincent · Willem Haasnoot · Philippe Delahaut · Christopher T. Elliott · Michel W. F. Nielen

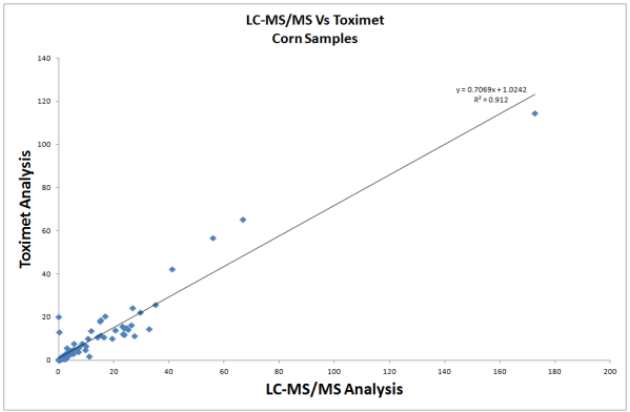
Multidetection of Paralytic, Diarrheic, and Amnesic Shellfish Toxins by an Inhibition Immunoassay Using a Microsphere-Flow Cytometry System

María Fraga †, Natalia Vilariño *†, M Carmen Louzao †, Paula Rodríguez †, Katrina Campbell ‡, Christopher T. Elliott ‡, and Luis M. Botana *†
† Departamento de Farmacología, Facultad de Veterinaria, Universidad de Santiago de Compostela, 27002 Lugo, Spain
‡ Institute for Global Food Security (IGFS), School of Biological Sciences, Queen's University Belfast, David Keir Building, Stranmillis Road, Belfast, Northern Ireland, BT9 5AG

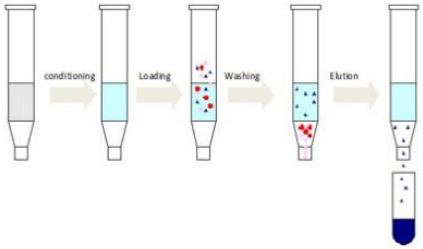
Anal. Chem., 2013, *85* (16), pp 7794-7802
DOI: 10.1021/ac401146m
Publication Date (Web): July 17, 2013

Semi-portable multiplexing technology

Toximet Technology



Good Correlation with LC-MS for aflatoxin



Mycotoxin analysis - Aflatoxins

Sensors and Actuators B: Chemical
Volume 239, February 2017, Pages 1087–1097

Evaluation of an alternative spectroscopic approach for aflatoxin analysis: Comparative analysis of food and feed samples with UPLC–MS/MS

Katrina Campbell[a], (Dr), Ana L. Ferreira Cavalcante[a], Pamela Galvin-King[a], Michalina Oplatowska-Stachowiak[a] (Dr), Catherine Brabet[b] (Dr), Isabelle Metayer[b], Didier Montet[b] (Dr.), Simon A. Haughey[a] (Dr.), Christopher T. Elliott[a] (Prof.)

Show more

On site or end product testing

Lateral Flow Technology

Lateral flow immunoassays point-of-contact tests are simple to use, provide rapid results with minimum amount of sample preparation

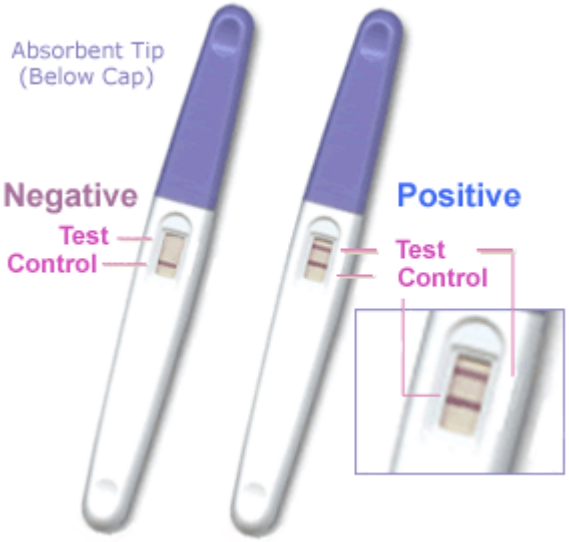
The benefits of immunochromatographic tests include:

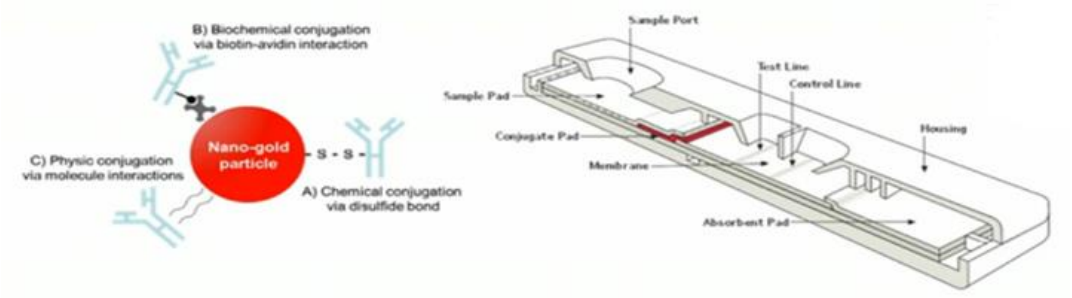
1. User-friendly format.
2. Very short time to get test result.
3. Long-term stability over a wide range of climates.
4. Relatively inexpensive to make.

These features make strip tests ideal for applications, such as
- home testing,
- rapid point of care testing
- testing in the field for various environmental and agricultural analytes.

In addition, they provide reliable testing that might not otherwise be available to developing countries.

Lateral Flow Technology





JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

J. Agric. Food Chem. **2007**, *55*, 2497–2503 **2497**

Development and Validation of a Lateral Flow Device for the Detection of Nicarbazin Contamination in Poultry Feeds

KATRINA CAMPBELL,*,† TERENCE FODEY,‡ JONATHAN FLINT,§ CHRISTOPHER DANKS,§ MARTIN DANAHER, MICHAEL O'KEEFFE, D. GLENN KENNEDY,‡ AND CHRISTOPHER ELLIOTT†

Institute of Agri-Food and Land Use, Queen's University, David Keir Building, Stranmillis Road, Belfast BT9 5AG, Agri-Food and Biosciences Institute (AFBI), Stoney Road, Belfast, BT4 3SD, Central Science Laboratory, Pocket Diagnostics, Sand Hutton, York, YO41 1LZ, United Kingdom, and Ashtown Food Research Centre, Teagasc, Ashtown, Dublin 15, Ireland

ELSEVIER

Talanta

Volume 116, 15 November 2013, Pages 663–669

Development and validation of the first high performance-lateral flow immunoassay (HP-LFIA) for the rapid screening of domoic acid from shellfish extracts

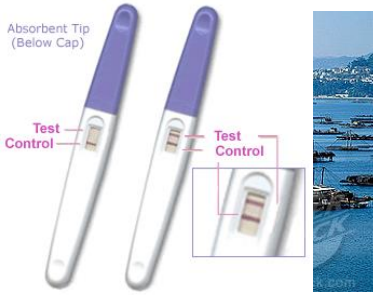
Waqass Jawaid[a, b], Julie Meneely[b], Katrina Campbell[b], Mark Hooper[a], Karrie Melville[a], Stephen Holmes[a], Jennifer Rice[c], Christopher Elliott[b]

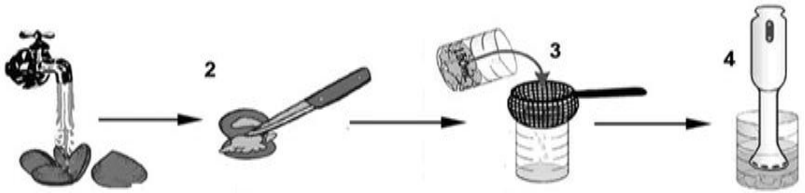
[a] Neogen Europe Limited, The Dairy School, Auchincruive, Ayr, KA6 6HW, Scotland, UK

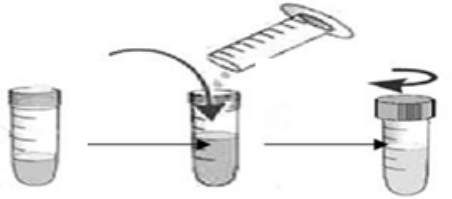
[b] Institute for Global Food Security, School of Biological Sciences, Queen's University, David Keir Building, Stranmillis Road, Belfast BT9 5AG, UK

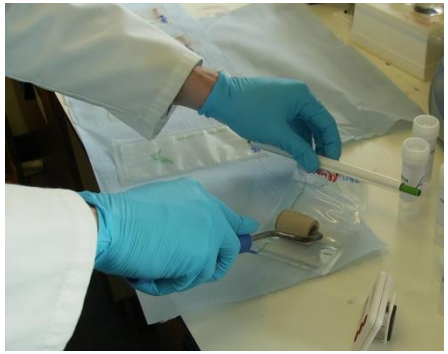
[c] Neogen Corporation, 620 Lesher Place, Lansing, MI 48912, USA

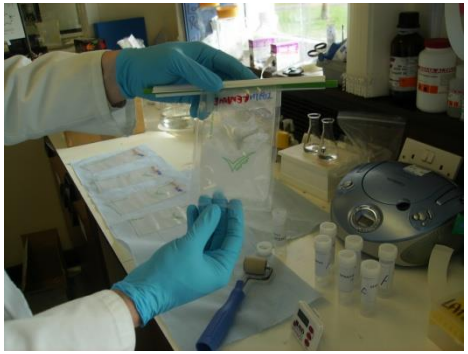
On site end product testing – ASP, DSP, PSP

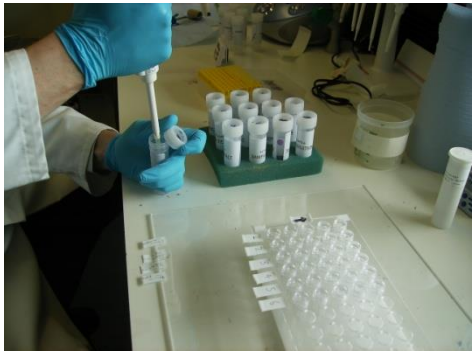


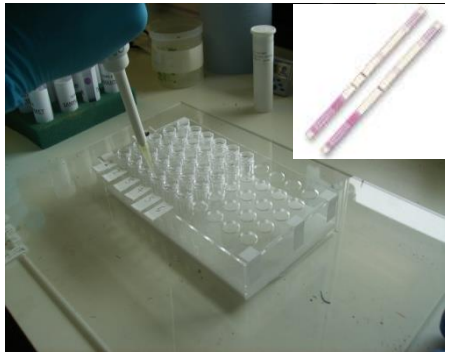


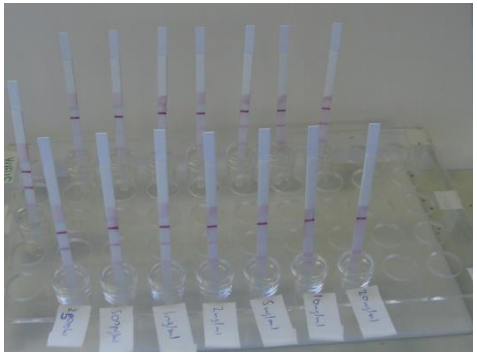


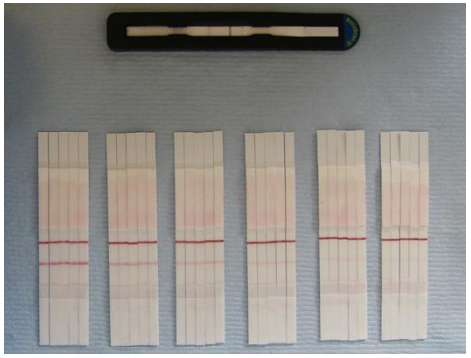












Queen's University Belfast

Institute for Global Food Security

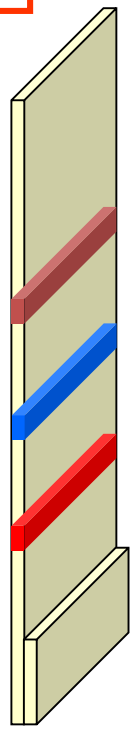
Multiplex approaches for emerging concerns

Tropane Alkaloid

atropine

CTRL

scopolamine

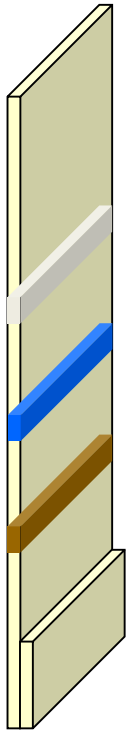


Ergot Alkaloid

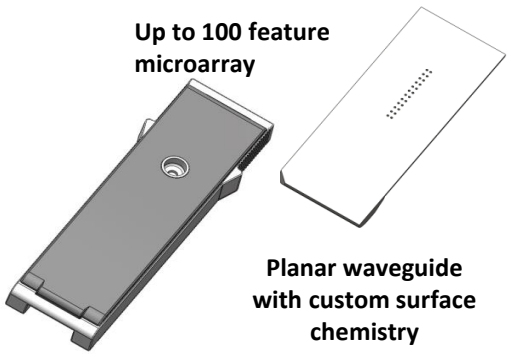
ergocristine

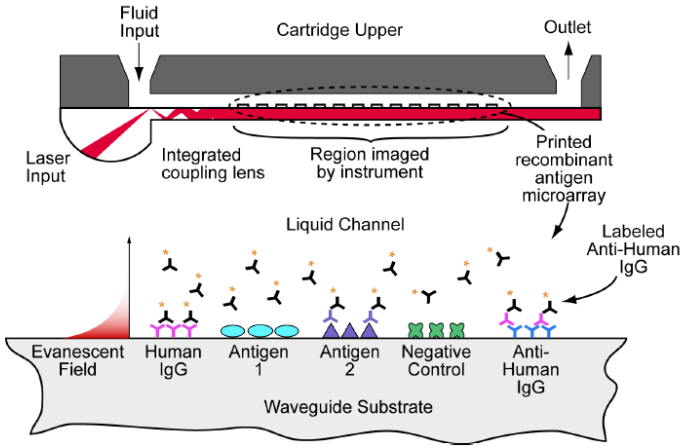
CTRL

ergotamine



Rapid Multiplex Portable Diagnostics





Scientific know how

Aim to produce a lower cost platform offering

- Low cost analysis
- Simplicity in use
- Highly specific single target analysis
- Multiplexing – multiple target analysis
- Bespoke sensitivity
- Robust – high performance
- Field deployable

Suitable for source to product testing

- **Molecular level – DNA / RNA for pathogen and speciation testing**
- **Protein Level – Allergen testing eg milk, nuts, eggs, seafood**
- **Residual level – Low molecular weight toxins / antibiotics / contaminants**

Nanotechnology in Portable Diagnostics

Printing receptors on WG chip

Assembling the WG chip into a cartridge

Applying sample and labelling reagents

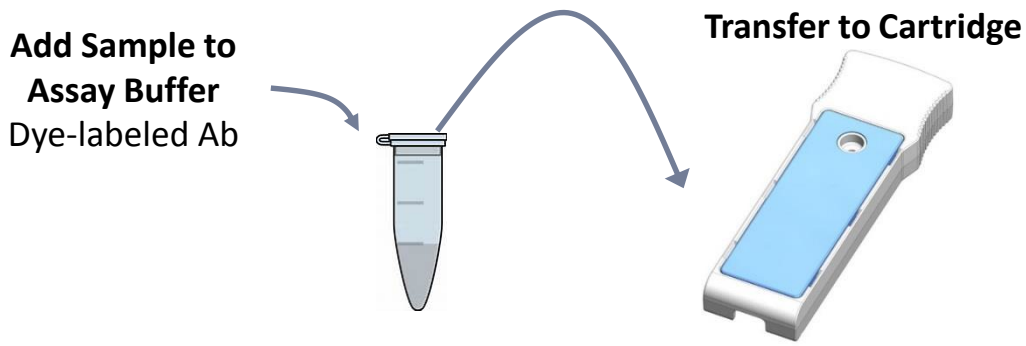
Measurement

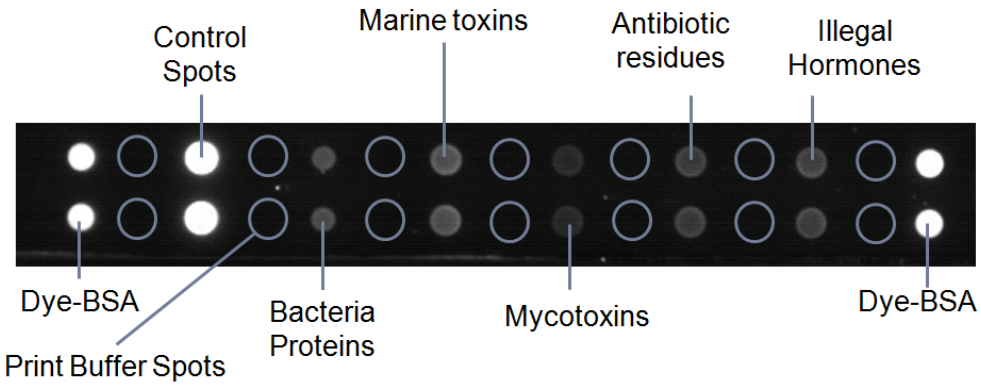
Obtaining the results

Simplicity in Use

Important to implement simple testing regimes to allow FBOs to perform testing

Offer a simple device requiring minimal sample preparation through either simple fluid application (blood, milk, juice) or dissolution of solid foods in buffering reagents

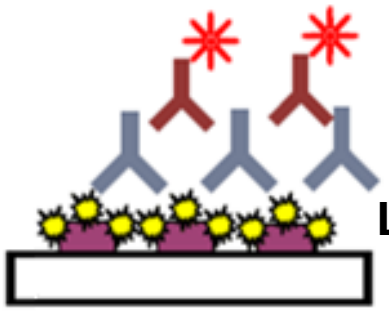




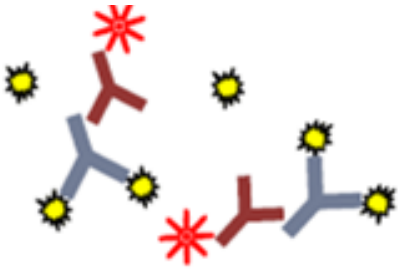
Depending on the complexity required
Qualitative – YES/NO Answer
Quantitative – Provide a concentration

Antigen Coated Competitive ELISA

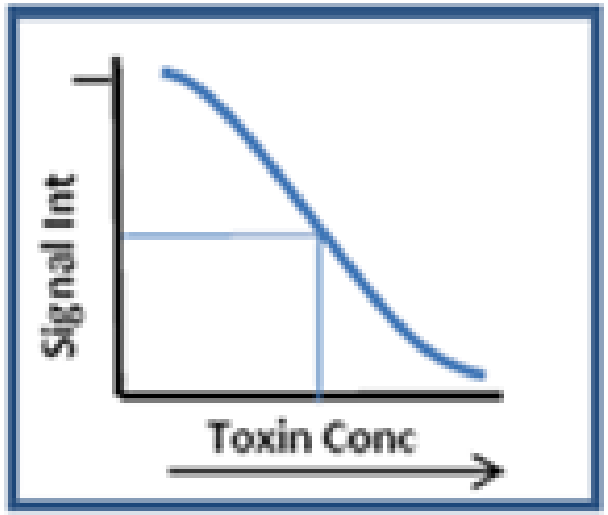
Toxin protein conjugate (TPC)



No toxin in sample
Antibody binds to TPC
Labelled antibody binds to antibody
High response

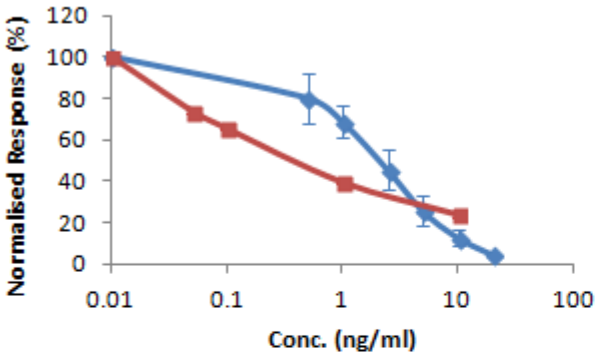


Toxin in sample
Antibody binds to toxin
Wash step removes antibody
Low response

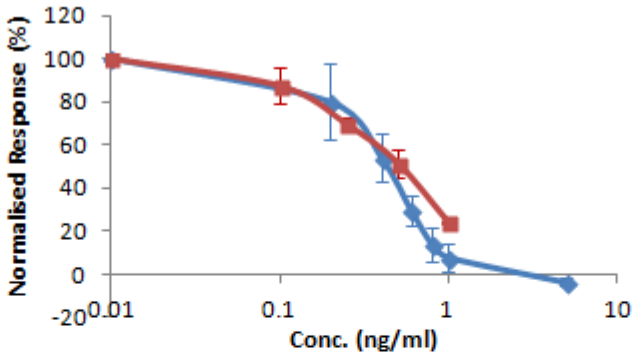


Marine and fresh water toxin assay

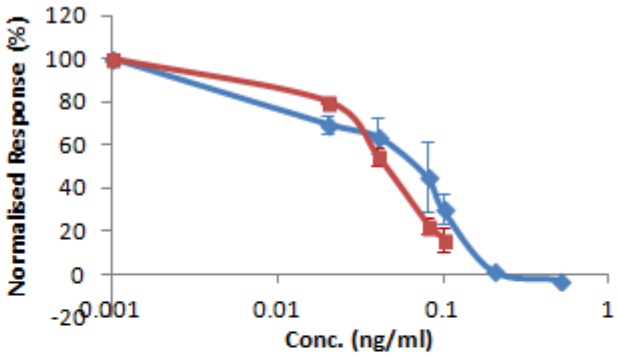
a: Domoic acid



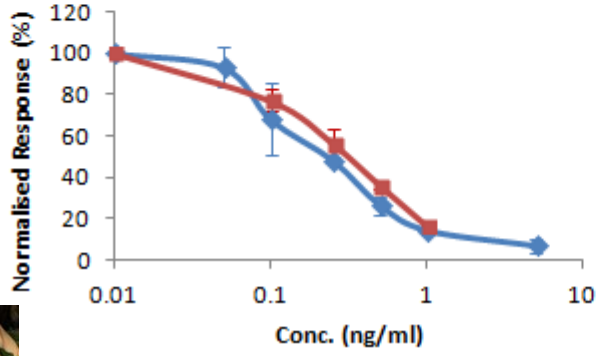
b: Okadaic acid



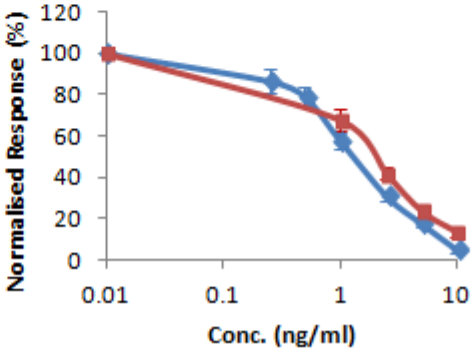
c: Saxitoxin

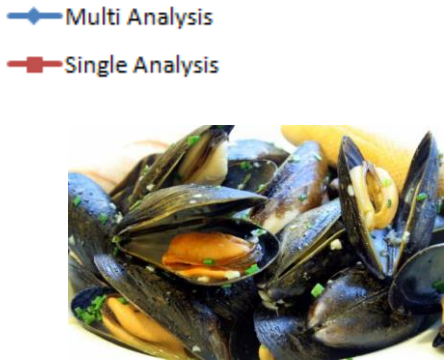


d: Cylinderspermopsin

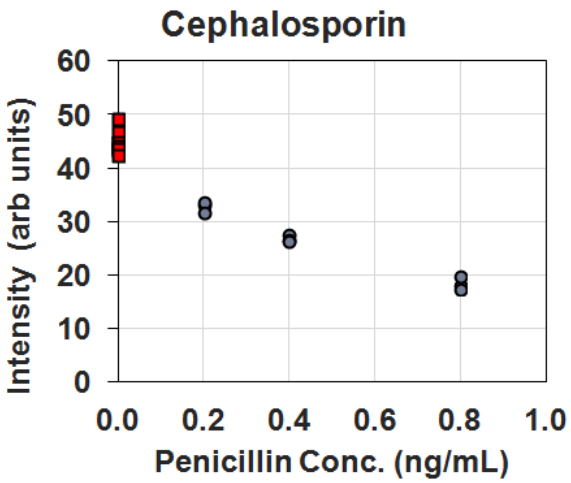


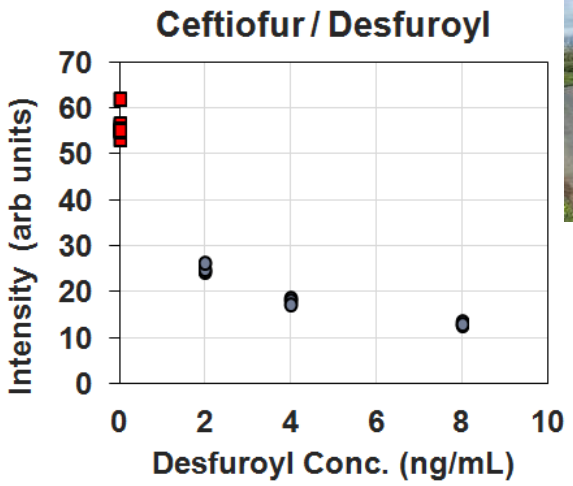
e: Microcystins

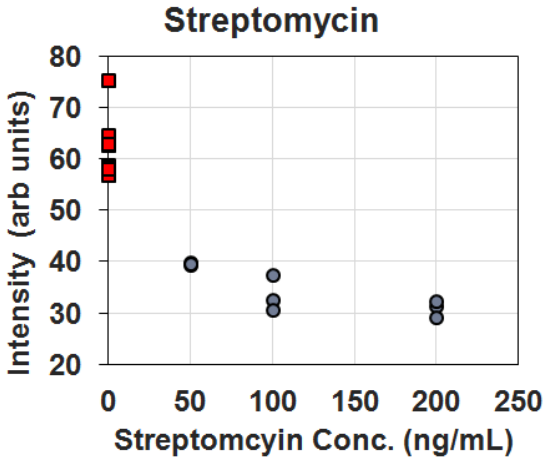


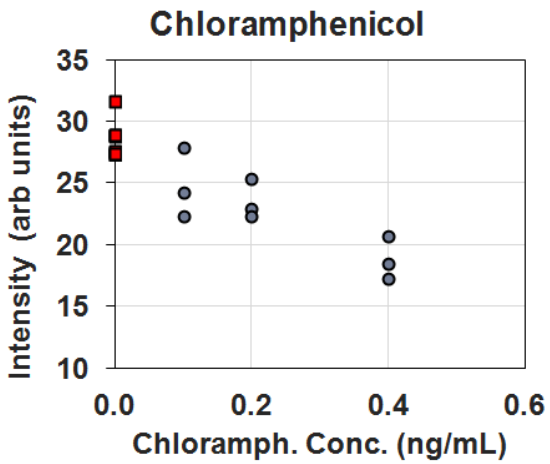


Assay for Antibiotics in milk



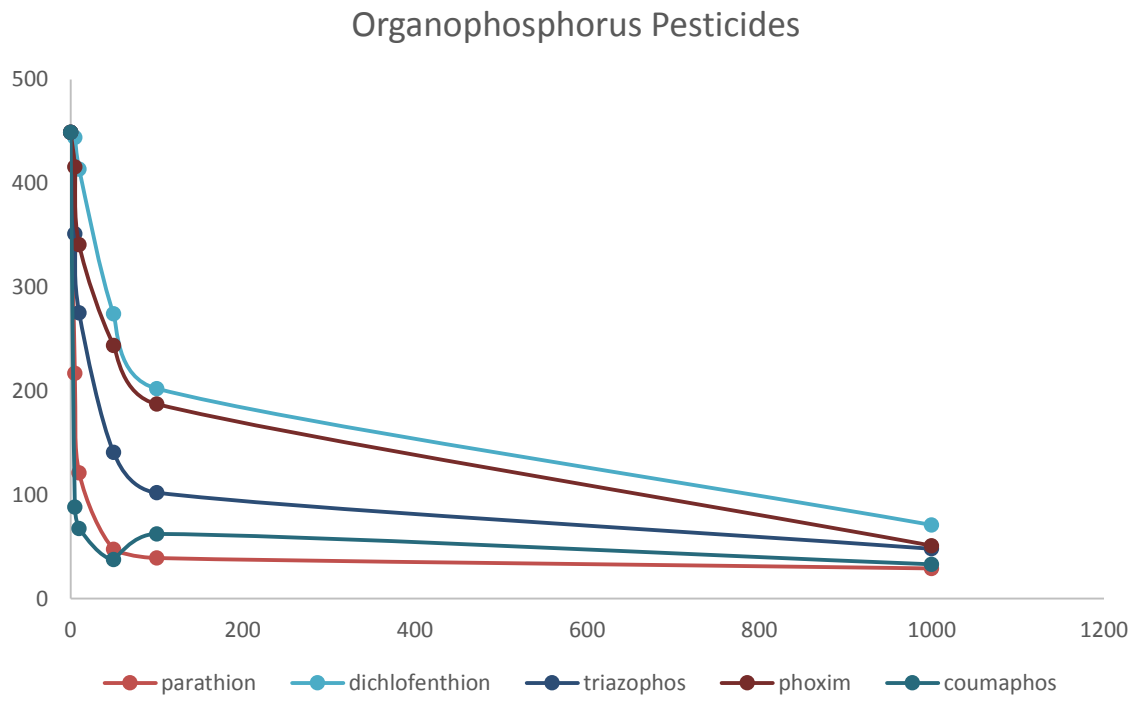






Multiplex Test for detecting antibiotics at MRL values

Organophosphous Pesticides



Spectroscopic techniques

"fingerprinting" technique giving unique spectra
Little or no sample preparation
Ideal technique for use with adulteration of food eg fats and oils
Multivariate techniques can be used to extrapolate the desired chemical information

HANDHELD RAMAN

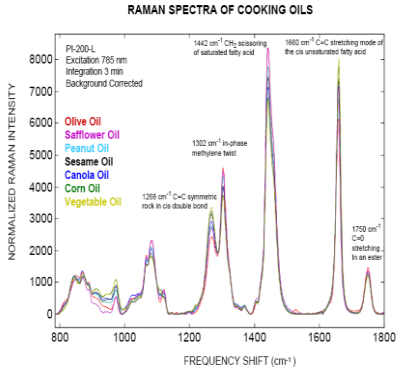


Image Detector Processor Data Answer

Summary for Rapid methods

- Speed – higher throughput
- Simplicity in use
- Minimal sample preparation
- Relatively low cost
- Multiplexing
- Portability
- Remote sensing
- Requirements of regulators or industry
- End product testing for release systems

Looking for new approaches to investigate
Known and unknown food safety concerns

Thank You for Listening

Training Workshop on Risk Identification and Screening Technologies of Agro-food

Shanghai Academy of Agriculture Science

Shanghai

China

13th September 2016

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Lecturer in Bioanalytical Systems