

Developments in Diagnostics

Advanced Point of Care Platforms

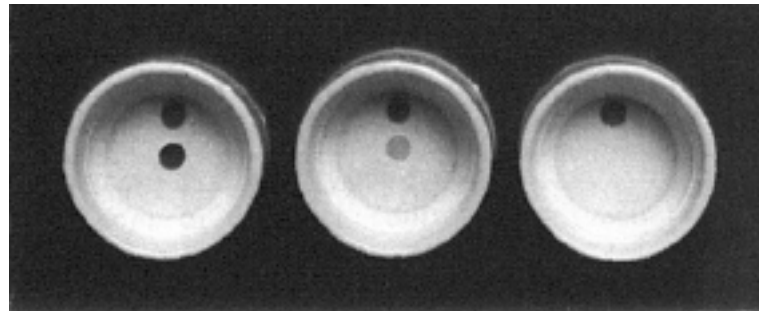
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Brief History of Lateral Flow Technology - 1980'S

A- Flow through format

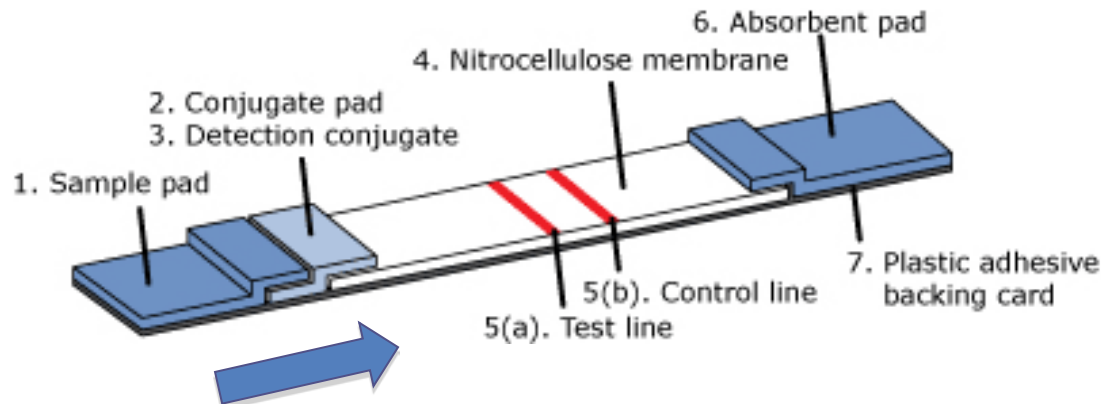
- Flow through
- Enzyme-linked Immunoassay: antibody-enzyme conjugates
- Color generated by precipitation of substrate turned over by captured enzyme conjugate
- Visual qualitative read or instrumented quantitative read (CKMB)
- Multiple manual steps and reagents
- High sensitivity



Brief History of Lateral Flow Technology 1980'S till today

B- Lateral Flow format

- Capillary flow across reactive zones, accumulation of labeled conjugate on test and control capture lines generates a measurable signal
- Sandwich immunoassay: signal proportional to analyte concentration
 - Visual read: Visible antibody-label conjugates
 - Instrumented read: fluorescent, magnetic antibody-label conjugates
- Competitive Immunoassays: signal inversely related to analyte concentration
- “One-step” test concept (Not counting sample prep)
- Variations on the configuration of test components and workflow, mainly to circumvent fundamental IP



Lateral Flow Assays Products

- Cardiac diseases markers: CKMB, Myoglobin, Troponin (Multiplex), BNP, D-Dimer, etc.
- Hormones:
 - Pregnancy, fertility, menopause (hCG, LH, FSH)
 - Thyroid function (TSH)
- Infectious diseases:
 - direct antigen detection: Strep A, Strep B, Flu A/B, RSV, mono, *C. trachomatis*, *N. gonorrhoea*, *C. difficile* and *C.diff.* toxins, *G. lamblia*, *E. histolytica*, and *Cryptosporidium*, etc.
 - antibody to infectious agents: *H. pylori*, HIV 1/2, HAV, HBV, HCV, etc.
- Autoimmune: IgE
- Cancer markers: kidney markers, PSA, FIT
- Drugs of Abuse
- Agro: Plant viruses, toxins, pesticides, hormones
- Food: Bacteria, viruses, toxins
- Bio-Defense: Bacteria, viruses, toxins



Lateral Flow Technology: Instrumentation

- Non-instrumented for yes/no and semi-quantitative applications: most tests - mainly infectious diseases and drugs of abuse, pregnancy tests, defense, agro and food applications
- Instrument-based
 - For quantitative measurements e.g.: cardiac marker platform
 - To improve the sensitivity of detection
 - OTC to remove the guesswork in interpreting results



Advantages of Lateral Flow Technology

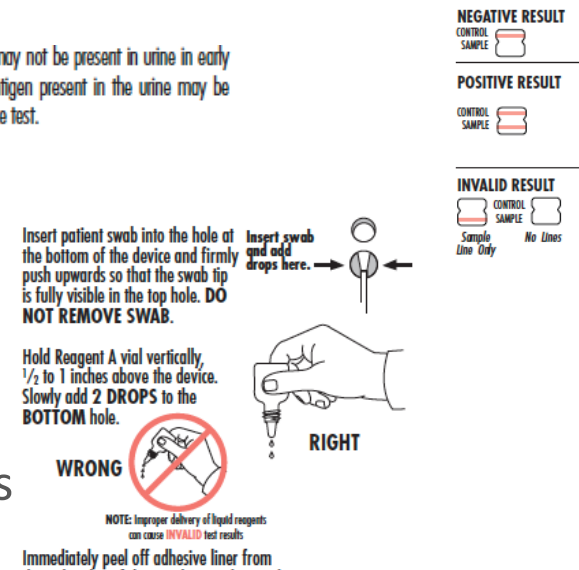
- Rapid results while the patient waits
- Broad array of tests available
- Yes/No and semi-quant tests do not require instruments
- Easy to use, minimum training required
- Well-proven technology, refined over 25+ years
- Well accepted in POC environments
- Automated, high throughput manufacturing plants
- Low cost manufacturing
- Low cost diagnostic tests



Problems & Challenges of Lateral Flow Technology

- Lack of sensitivity
 - Generates false negative results
 - Restricts potential portfolio
- Hands-on time, timing constraints
- Non-instrumented assays:
 - Subjective interpretation of visual results
 - Risk of false negative results
 - Inconsistent interpretation between users
 - Manual data entry increases risks for errors
- Variability between protocols from different manufacturers
- Instrumented assays:
 - Expensive connectivity to LIS
 - Low precision, high CVs compared to other lab instruments
- Low level of multiplexing

may cause disease, antigen may not be present in urine in early infection, and the level of antigen present in the urine may be below the detection limit of the test.



Ideal rapid test platform ?

- Sensitive
- Specific
- Quantitative, Reproducible
- Multiplex
- Broad portfolio of tests available
- Low cost manufacturing
- Low cost to end user
- Low / No risk of errors
 - Instrumented reading
 - Connected (Patient entry, result recording)
 - Built-in memory for later download (field use)
- Rugged, stable system for everyday use, multiple settings (POL, decentralized labs, field (agro, food, water), developing countries/emerging markets)



Ideal rapid test platform - Attributes

POC Platform Attribute	Minimally Acceptable	Nominal Design Goal	Stretch Goal
Accuracy (A.U.C.)	0.80	0.90	0.99
Confidence (%)	90	95	98
Limit of Detection – LOD (pg/mL)	5	1.0	0.10
Multiplex Level (#)	5	10	25
Turnaround Time – TAT (min)	60	20	5
Coefficient of Variation – CV (%)	25	10	3
Size – Volume (cm ³)	10,000	600	50
Weight (kg)	10	5	0.5
Power (W)	5	1.0	0.1
Consumable Reagents (mL/test)	1.0	0.50	0.10
Capital Cost (\$)	2,000	500	100
Consumable Cost (¢/test)	50	10	1
O & M Cost (\$/year)	50	10	0
Power Pack (# tests)	1,000	5,000	10,000
MTBM (years)	1	2	4
MTBF (years)	2	4	8

Presented by John Carrano , Carrano Consulting LLC



Axxin's Platform-based Approach

- Improve the overall performance of the platform (sensitivity, specificity, CV)
- Multiplex for small panels, multi-assay, random access platform
- Simple and robust workflow (“Operator” mode and “Supervisor” mode)
- Ease of use by any user – true “walk-away”
- Reduce the risk of error
 - Use barcode for cartridge, patient ID, operator ID
 - Record retention and transfer through connectivity (pre-built LIS, Bluetooth, WiFi)
- Affordable instrument, low-maintenance, no moving parts
- Small footprint for busy bench tops in the labs, for limited space in Minute Clinics and the like, and for portability
- Low power consumption for lab and field use (universal 12 Volt DC power supplies, internal battery or 12 Volt automotive power source)



Axxin's Platform-based Approach



Desktop POC Instrument



Portable POC Instrument

“Axxin provides diagnostic delivery systems as a complete integrated solution; Clinical Lab instrument quality at the POC”

The Problem

- Major expansion in IVD diagnostics POC tests requiring rapid testing, near patient location and higher sensitivity (eg H1N1, MRSA, HIV, Cardiac Biomarkers)
- Range of tests, knowledge, and expertise required exceed user capabilities
- Clinicians and Physician Offices want to streamline rapid diagnostic platforms, reduce errors, improve traceability, shorten time to treatment

The Solution

- Easy to learn, easy to use, cost effective, random access instrument suitable for IVD and broader POC applications. Laboratory to Field applications
- Manages existing assays in POC market and provides migration path to higher sensitivity assays
- Integrates with existing IT systems and provides additional licensing opportunities



Thank You!



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