In the name of GOD

Point Of Care Testing (POCT) in health care

Supervisor: Dr. Ismaeil Haririan

Seyedeh Azin Mirmotahari

PhD candidate in pharmaceutical biomaterials

Introduction

- We are increasingly seeing **traditional examinations** of a patient's body fluids, excreta and tissues carried out generally in the controlled and regulated environment of a recognized medical laboratory being phased out.

- Advances in technology have resulted in compact, easy-to-use **in vitro diagnostic (IVD)** medical devices that make it possible for some examinations to be carried out at, or close to, the location of the patient.

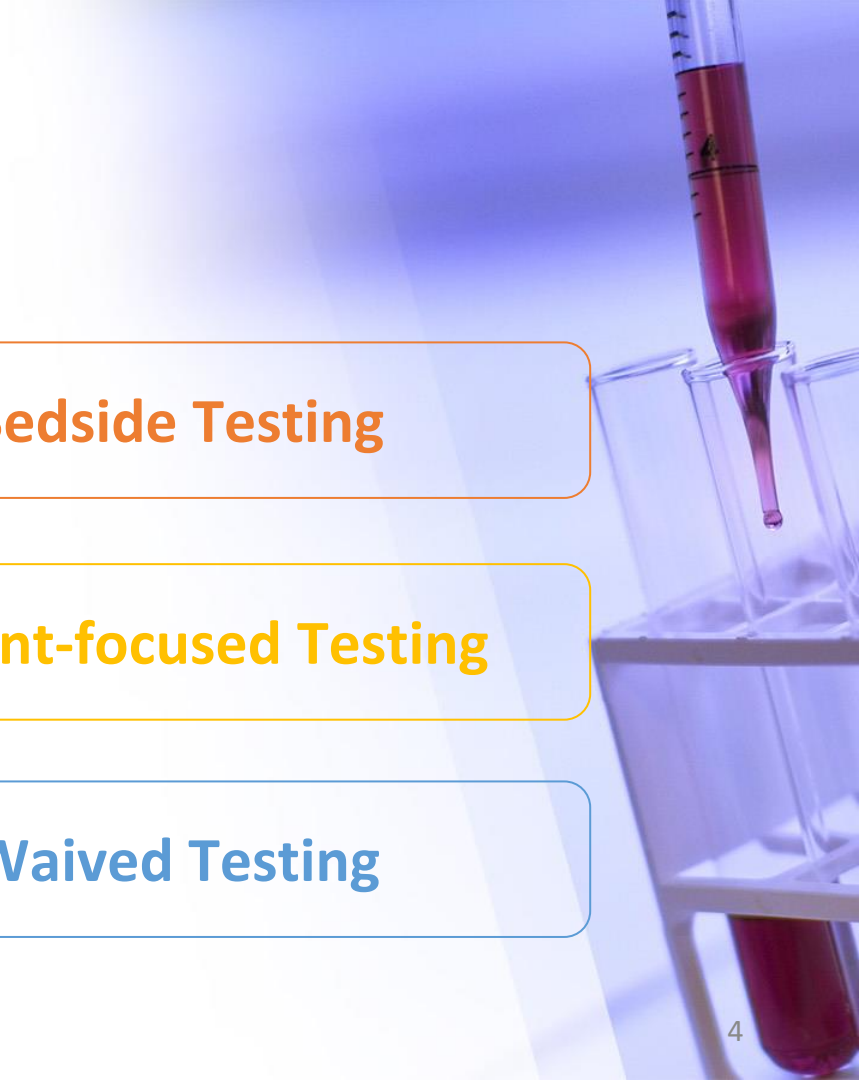
What is Point of care testing (POCT)?

- "…testing that is performed **near** or **at the site** of the patient with the result leading to possible change in the care of the patient."
- "… any analytical test performed for a patient by a healthcare professional **outside the conventional laboratory**."

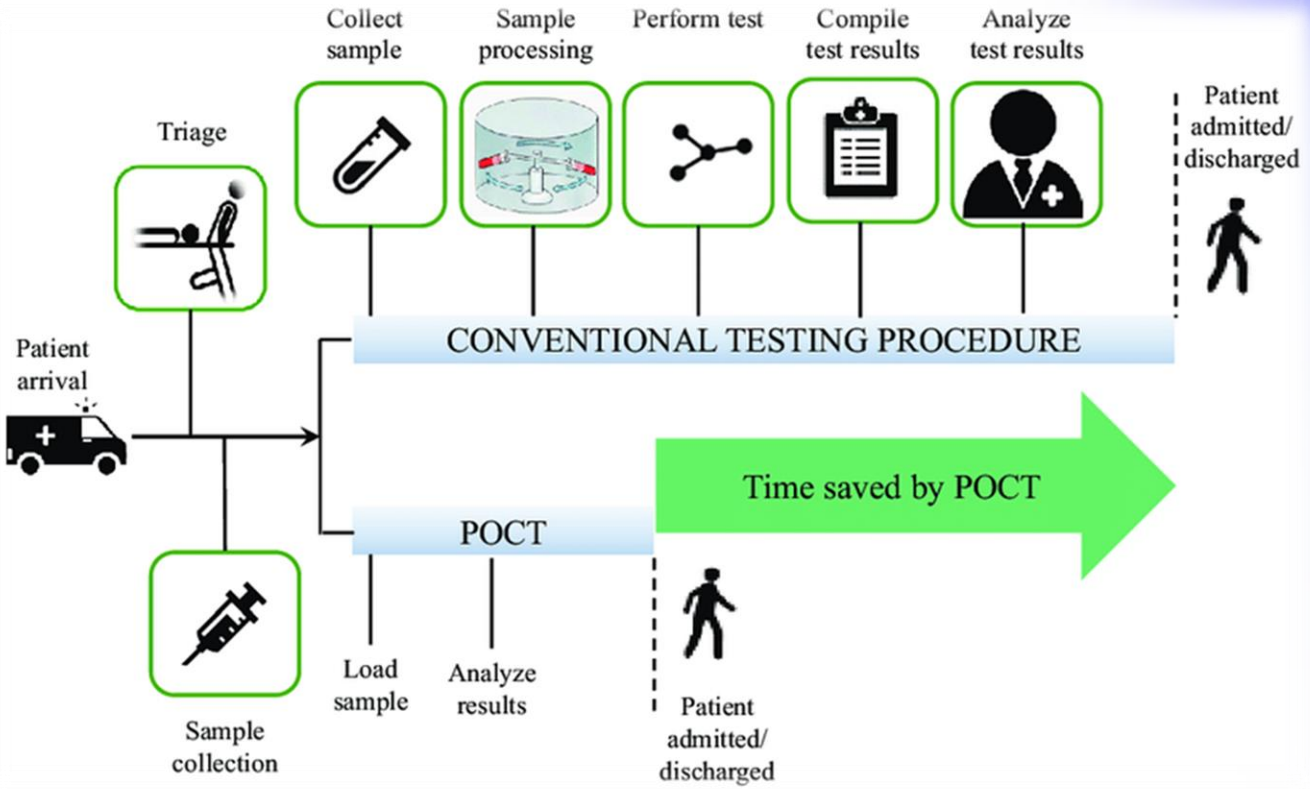
- **Note:** POCT is not a replacement for conventional laboratory testing but rather a supplement to it. POC test results which are used for diagnosis or critical patient management decisions, or which give unexpected results should be confirmed by hospital laboratories to ensure accurate diagnosis and to facilitate correct patient management decisions.

Synonyms of POCT

- Near Patient Testing
- Bedside Testing
- Decentralized Testing
- Patient-focused Testing
- Extra laboratory testing
- Waived Testing



Difference between Conventional Testing & POCT



POCT properties

- Transportable
- Disposable
- Portable
- Handheld
- Rapid
- Benchtop

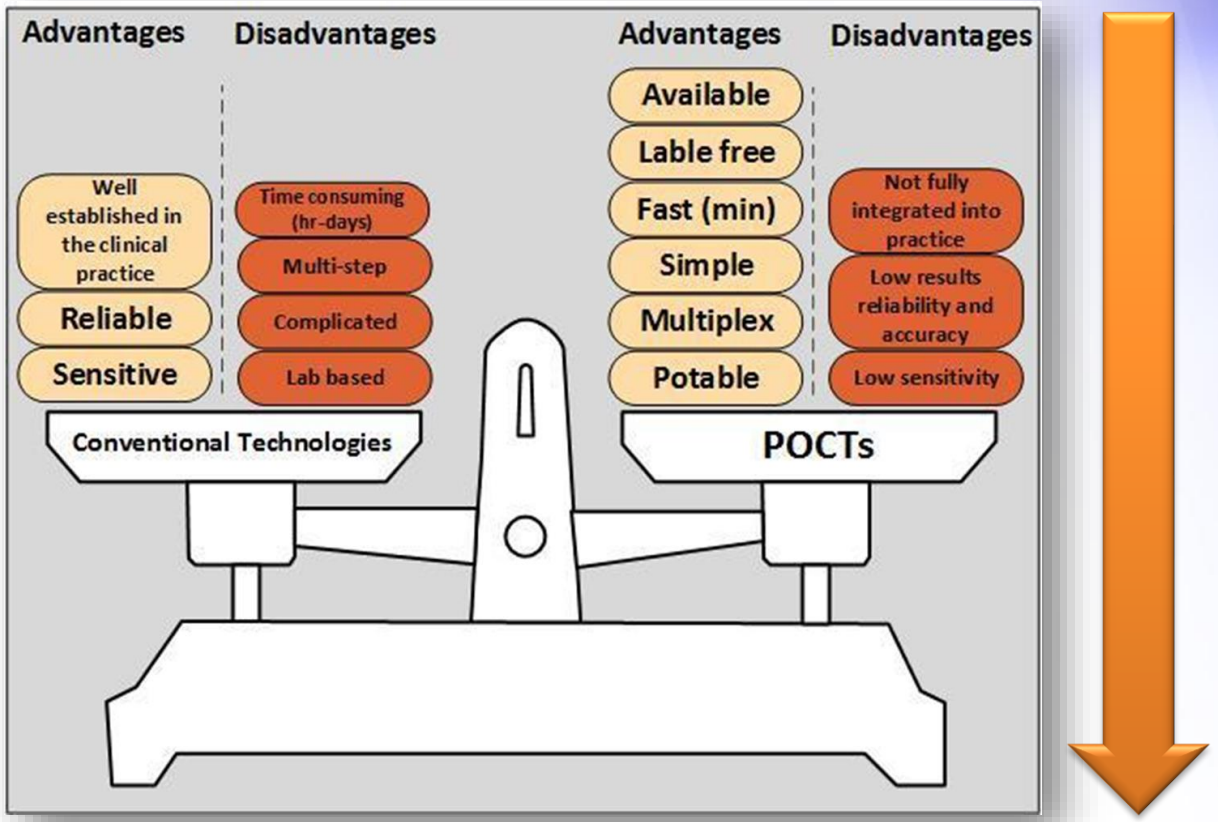
ADVANTAGES

- Identify critical diagnosis/screen quickly
- Evidence available on site
- Simple steps procedure
- Smaller sample volume – less waste
- Cost saving- (not always!)
- Improved outcome & patient education
- Remote testing at a variety of locations

DISADVANTAGES

- Lower accuracy and precision
- Less skilled personnel to perform tests
- Lack of data systems
- Difficulty in assuring quality
- Difficulty in managing testing
- Lack of comparability- need standardization

Conventional tests or POCT?



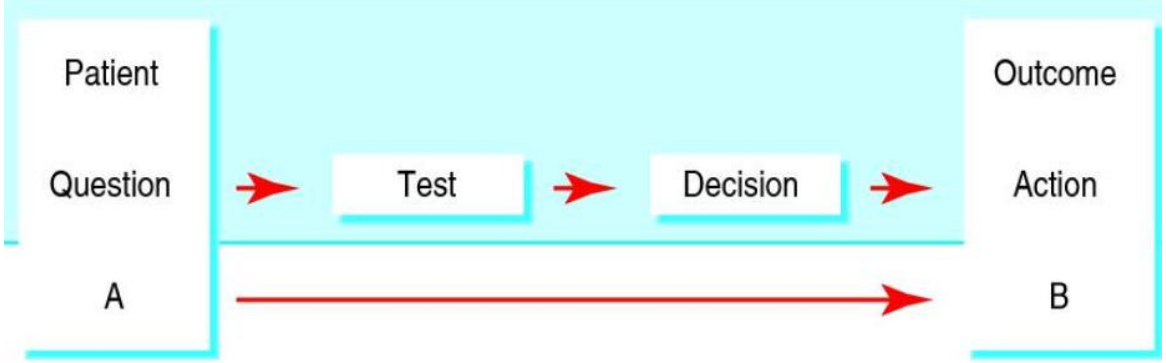
Some examples of improved clinical outcomes from using point of care testing

Outcome	Example
Faster decision making	Chest pain, drug overdose
Starting treatment earlier	Drug overdose
Improved adherence to treatment	Diabetes
Reduced incidence of complications	Diabetes
Quicker optimisation of treatment	Anticoagulation
Reduced reoperation or readmission rate	Parathyroidectomy
Patient satisfaction	Fewer journeys, ownership of disease

Some examples of economic outcomes from use of point of care testing

- Reduced number of clinic visits
- Reduced length of hospital stay
- Earlier discharge from hospital
- Fewer unnecessary hospital admissions
- Better optimised drug treatment

- Less inappropriate use of drugs
- Reduced use of blood products
- Reduced use of staff, equipment, and estate
- Improved quality of life



Widely used ASSURED criteria for rapid tests by WHO

- A = Affordable
- S = Sensitive
- S = Specific
- U = User friendly - simple to perform
- R = Robust and Rapid (results available in less than 30 minutes)
- E = Equipment free
- D = Deliverable to those who need the test

Guidelines

IFBLS' Guidelines regarding Point of Care Testing (POCT)

IFBLS
International Federation of Biomedical Laboratory Science

Web site: http://www.ijbls.org/

Where POCT is used?

- **Within hospitals:** in emergency units, in acute departments, e.g. anaesthesia and intensive care units, other hospital departments and outpatients' departments.

- **Outside hospitals:** in institutions, in nursing and care units, in community treatment centres, at clinics in primary health care, in physician's offices and in patients' homes.

- As part of the ambulance services or other mobile facilities.

- Patients' self-testing.

Certification and accreditation of point of care testing

Use of POCT must be accredited or certified if this is required by national laws and regulations.

All POCT should comply with the requirements of the International Organization for Standardization (ISO).

ISO International Organization for Standardization

- ✓ ISO 22870 Point-of-care testing (POCT) – Requirements for quality and competence.
- ✓ ISO 15189 Medical laboratories – Particular requirements for quality and competence.
- ✓ ISO 15190 Medical laboratories – Requirements for safety.

Policy statement and primary principles for point of care testing in Health Care

Biomedical laboratory scientists are responsible for:

- The evaluation and selection of methods and equipment to be used in point of care testing.
- The content of user guidelines (standard operating procedures) and practical training for users.
- Training and guidance to ensure that methods are carried out and equipment is used in accordance with approved protocols and to secure patients safety.
- Designing and conforming to internal and external quality control protocols.
- Organizing quality systems for all measures surrounding the POCT analysis.
- Protocol for reporting analytical results from POCT analysis.

Consider these elements before introducing point of care testing

Decision criteria for or against POCT

- Medical aspects
- Clinical benefits
- Turnaround Time (TAT)
- Sample volume
- Analytical quality

Economical aspects

- Fixed costs
- Variable costs
- Personnel costs
- Cost-effectiveness

Organizational aspects

- Personnel
- Storage and safety
- Training
- Management and leadership

Quality assurance

- Adequate sensitivity / specificity
- Internal quality control
- External quality control
- Documentation

Quality assurance of point of care testing

The chronological link between test results, quality control results and instrument status must be retained. Any users of POCT must comply with any relevant standards that may be required under national and international regulations.

- **Internal quality control (IQC)**

  A system for validating the results before they are issued.

- **External quality assessment (EQA)**

  A system for validating the results after they are issued

Descriptions of procedures and equipment

For each point of care method, there shall be a procedural description, in respect of how the testing shall be performed, possible sources of errors and reporting protocols for the measurement result. The method description should include:

- Clinical indication
- Patient preparation, sampling technique and sample material
- Handling of samples
- Measuring principle
- Apparatus and additional equipment
- Reagents, storage and shelf-life
- Internal and external controls
- How to carry out analysis
- Reference range/therapeutic range
- Sources of error and deviation management
- Recording, reporting and interpreting results
- Contact persons at the laboratory

Documentation

- **Documentation of measurement result**

✓ patient’s medical chart

- **Documentation of quality assurance work**

✓ The documentation shall include the name of the person performing the measurement, the time, deviations and procedures followed when the controls are out of range

Devices Available Today

- Blood gases and electrolytes analyzers
- Coagulation
- Blood Chemistries, ex. Glucose, cholesterol, uric acid
- Drug abuse
- Pregnancy screening
- Cardiac markers
- Hemoglobin and Hematocrit

Point-of-Care Drug of Abuse Testing in the Opioid Epidemic

OPIOID POINT-OF-CARE TESTING

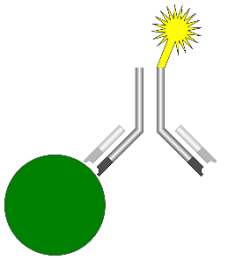
- Opioids are a class of drugs that can produce analgesic, depressant, and euphoric effects on the central nervous system.
- Currently, the United States is experiencing a national opioid epidemic.
- In 2017, 67.8% of drug overdose deaths involved opioids, a 90% increase from 2013.
- Drug testing is an essential tool to counter the opioid epidemic by providing critical information about opioid use.
- Several biological specimens can be used for opioid testing, including urine, saliva, sweat, blood, hair, and breath.
- **Point-of-care (POC)** drug of abuse testing is a useful tool to combat the intensified opioid epidemic.

2 major types of drug tests

- **Screening testing (presumptive testing)**

✓ Qualitative technique

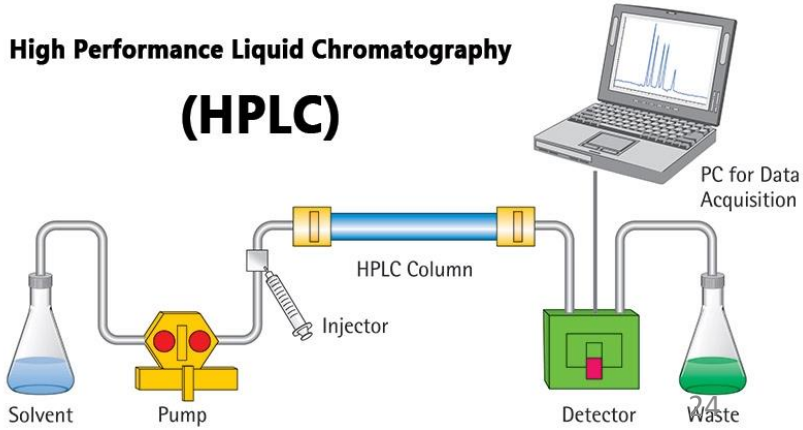
✓ Most commonly used method: immunoassay



- **Confirmatory drug testing (definitive testing)**

✓ Quantitative technique

✓ Methods: highly specific and sensitive analytical methodology such as gas chromatography–mass spectrometry (MS) and liquid chromatography (LC)–tandem MS (MS/MS)



Advantages of POC tests of opioid

- Compared with cumbersome laboratory instruments, POC devices have many advantages in meeting the challenges of the opioid epidemic:

1) POC tests are able to detect opioids and/or metabolites rapidly within minutes and enable immediate treatment decisions.
2) POC tests are relatively inexpensive (approximately $1–10; costs vary with respect to methodology, device needs, and the number of tests in a cartridge)
3) POC tests are simple to perform in a practitioner’s office or at home.

Challenges

Compared with gold standard tests, although opioid POC screening has many advantages, it faces several challenges, including

1) lower analytical sensitivity and higher detection thresholds, which can lead to false-negative results;

2) lower specificity and difficulty in distinguishing the parent opioid and its active metabolites ;

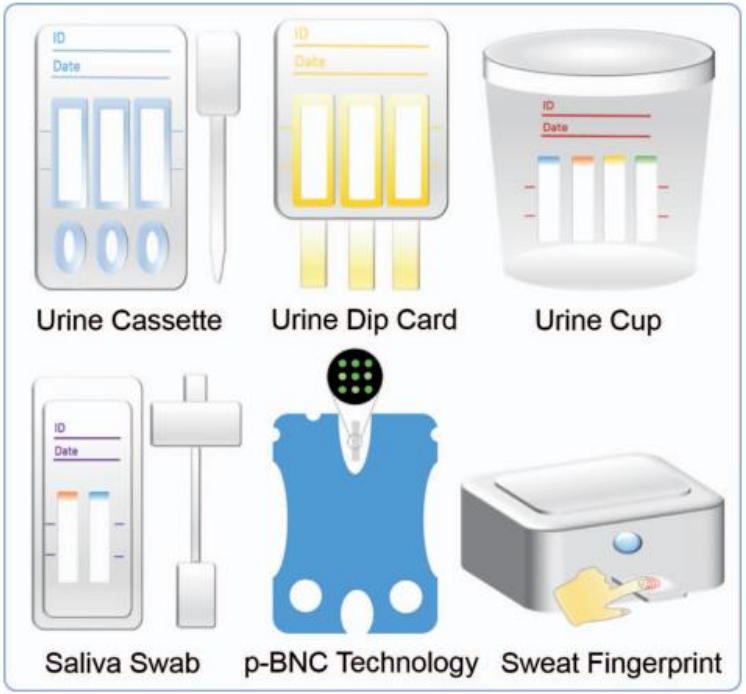
3) cross-reactivity with other substances, which can lead to false-positive results. Analytical sensitivity is usually better for MS-based methods, and POC devices are less sensitive.

Commercially Available Point-of-Care Devices for Drug of Abuse Testing Involving Opioids

Company	Product	Technology	No. of Drugs
Alfa Scientific Designs, Inc	Instant-view Multi-Drug Urine Tests	LFA	6
	Instant-view Push Button Multi-Drug of Abuse Urine Cup		14
	Single Drug Urine Test (eg, fentanyl, amphetamine, cocaine)		1
Craig Medical Distribution, Inc	RapidCheck 12 Panel Test Card	LFA	12
	QuickScreen PRO 5 DSC		5
	SalivaConfirm 11 + Alco		12
Abbott	Alere iCup Drug Screen	LFA	13
	Alere iScreen Dip Card		5
	Alere Triage Drugs of Abuse Plus TCA Panel		8
	SoToxa Mobile Test System (for forensic use only)	NA	6
DrugTestsInBulk.Com	Multi-Drug USA Made Drug Test	LFA	12
	Generic Panel Dip Card Drug Test		12
	Urine Drug Test (Pipette)		10
	Prescreen Plus Cups		13
	T-Cup All In One Drug Test		14
	Integrated E-Z Split Key Cup		6
	Clear Scan Drug Test Cup		13
	SwabScreen Oral Drug Test		10
	Oral Cube Drug Test		12
	Oralert Saliva Drug Test		6
	InstaCube Saliva Drug Test		12
CareHealth America	DrugCheck Dip Drug Test	LFA	14
	DrugCheck NxStep Cup		15

Formats of commercially available point-of-care drug of abuse testing devices involving opioids

- Most commercially available POC devices: based on **lateral flow assay (LFA)** technology
- These LFA-based devices include urine cassettes, urine dipsticks, combination urine collection/test cups, and saliva swabs
- Two novel platforms are based on fingerprint and programmable bio-nano-chip technology, using a microfluidic cartridge for loading sweat or urine samples.



RESEARCH PROGRESS OF OPIOID POC TESTING

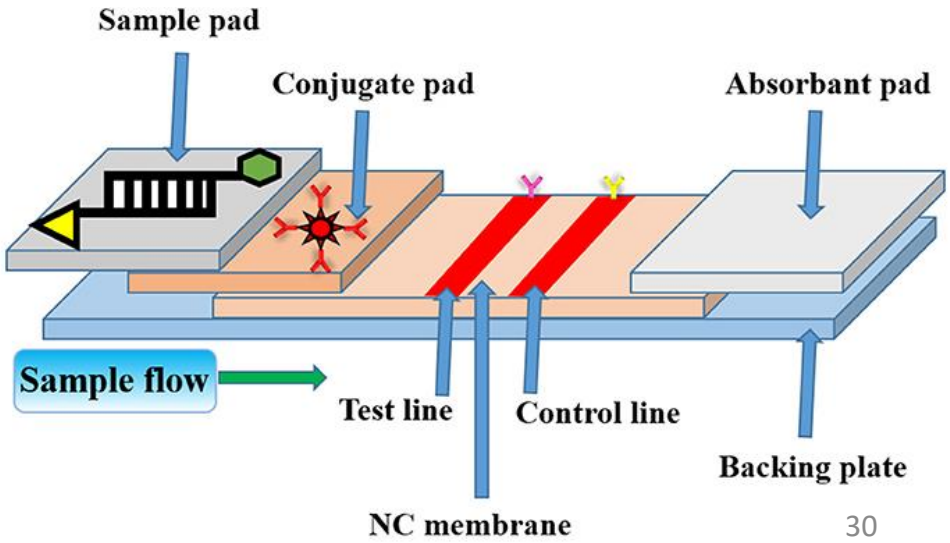
Various novel opioid POC testing technologies have been reported including:

- LFA strips
- Microfluidics
- optical biosensor
- miniaturized enzyme-linked immunosorbent assay (ELISA)/MS

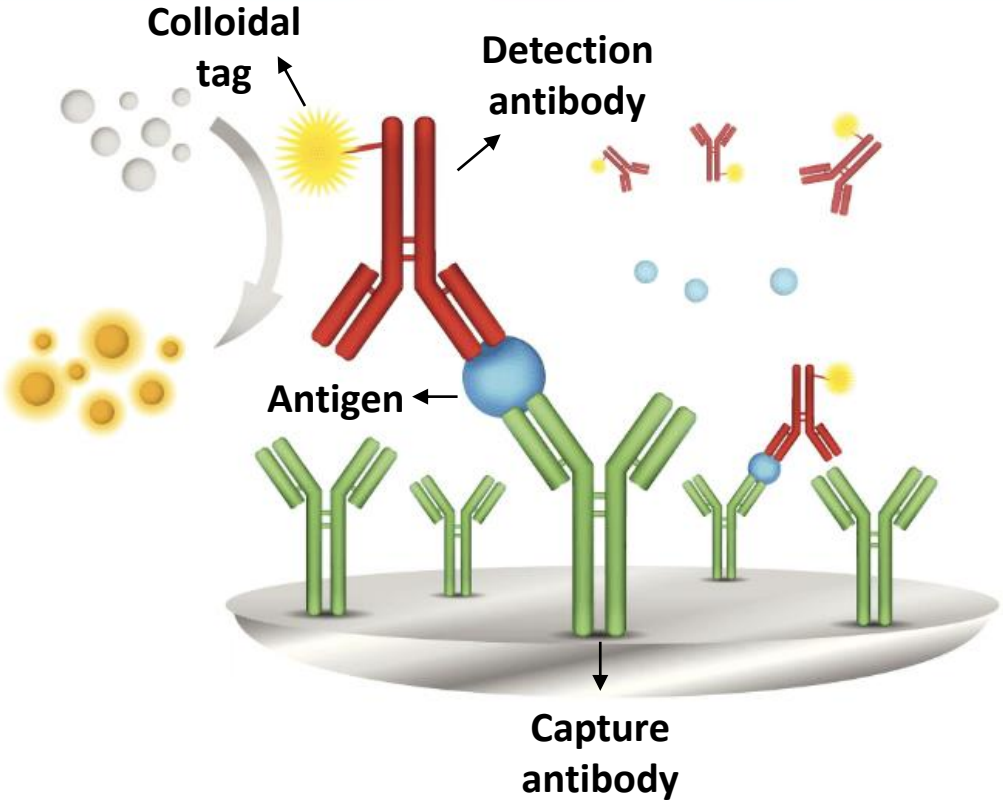
LFA Platforms

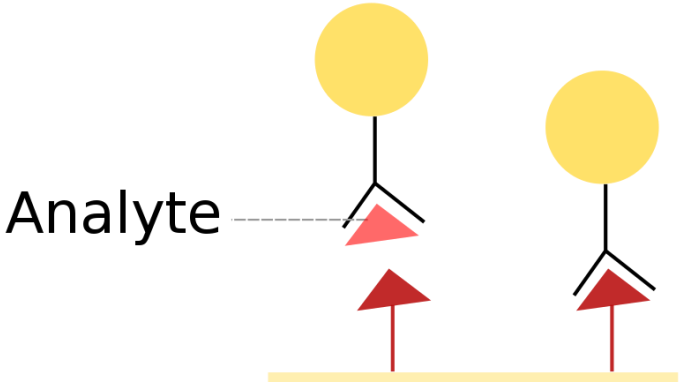
- LFTs operate on the same principles of **affinity chromatography** as the enzyme-linked immunosorbent assays (ELISA). In essence, these tests run the liquid sample along the surface of a pad with reactive molecules that show a visual positive or negative result.

- To achieve quantitative colorimetric readout of LFA strips, various optical strip readers (eg, smartphone, scanner) and image-processing algorithms are designed to measure the intensities of test/control lines.
- LFTs can operate as either **competitive** or **sandwich** assays:

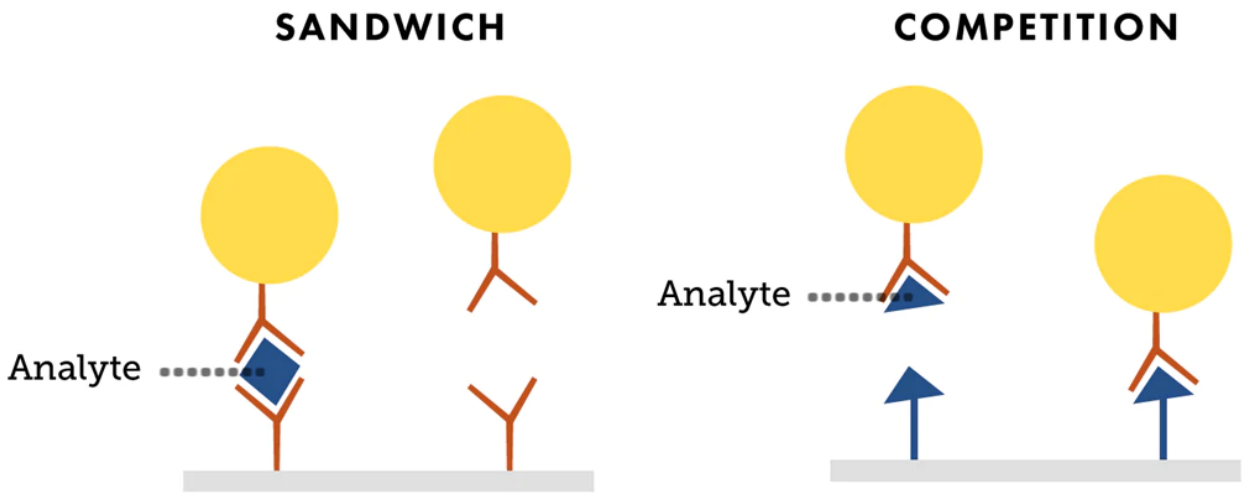


Sandwich & Competitive assays:





So…



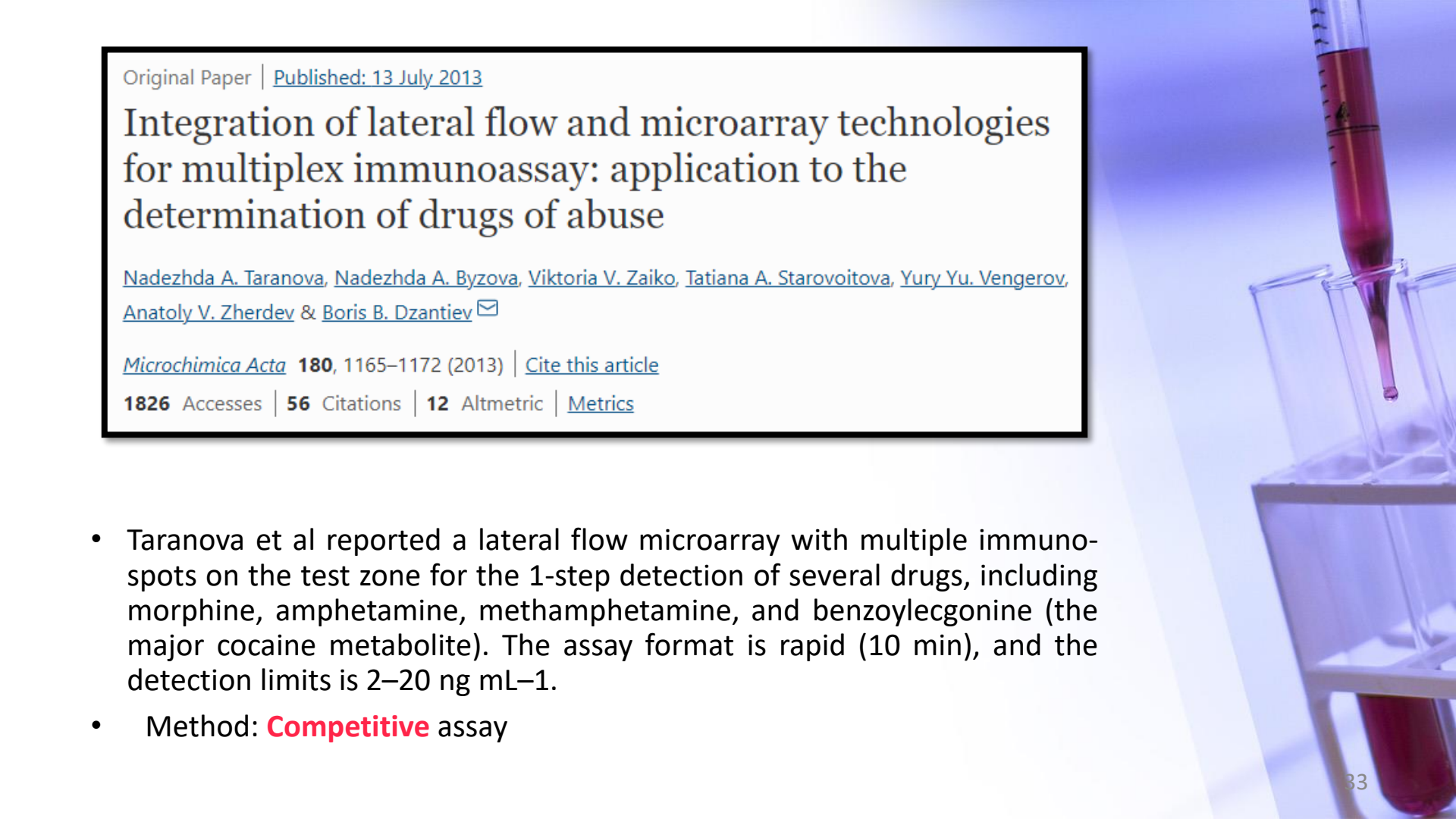
Analyte present?	✓	✗	✓	✗
Signal readout?	✓	✗	✗	✓

Original Paper | Published: 13 July 2013

Integration of lateral flow and microarray technologies for multiplex immunoassay: application to the determination of drugs of abuse

Nadezhda A. Taranova, Nadezhda A. Byzova, Viktoria V. Zaiko, Tatiana A. Starovoitova, Yury Yu. Vengerov, Anatoly V. Zherdev & Boris B. Dzantiev

Microchimica Acta **180**, 1165–1172 (2013) | Cite this article



- Taranova et al reported a lateral flow microarray with multiple immuno-spots on the test zone for the 1-step detection of several drugs, including morphine, amphetamine, methamphetamine, and benzoylecgonine (the major cocaine metabolite). The assay format is rapid (10 min), and the detection limits is 2–20 ng mL–1.
- Method: **Competitive** assay

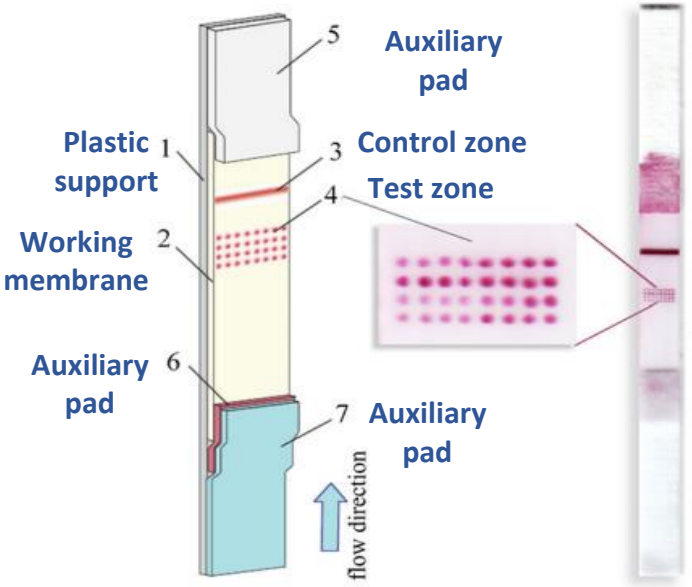
Steps

1) Preparation of colloidal gold particles (with 30 nm average diameter).
2) Conjugation of anti-hapten antibodies with colloidal gold.
3) Fabrication of lateral flow microarray test strip.

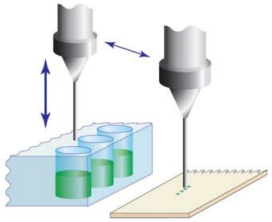
Mixture of conjugates were spotted onto a glass fiber membrane

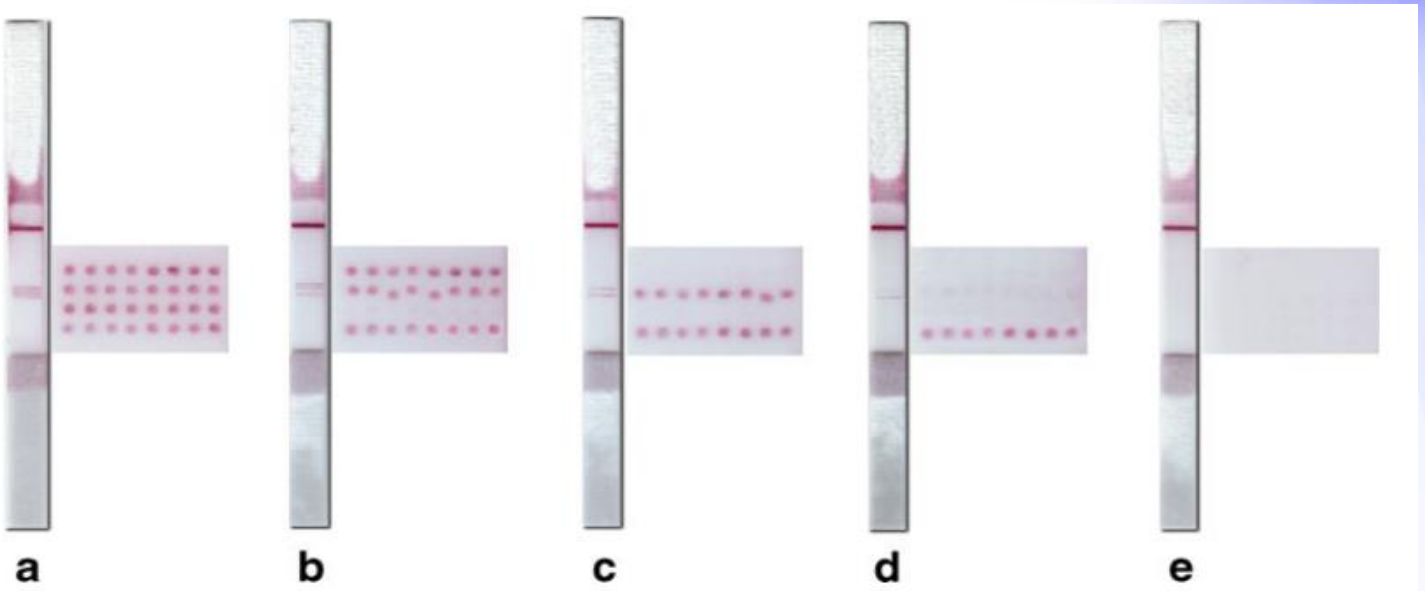
The control zone of test strips was formed by dispensing goat anti-mouse immunoglobulin antibodies onto a working membrane.

The test zone was formed on each test strip using conjugates of haptens (drugs of abuse or their metabolites) and BSA in two concentrations for each conjugate. Microarrays were spotted by touching the membrane with a steel pin.



Spotting of reactants onto the membrane surface using a pin





without analytes

amphetamine

amphetamine, benzoylecgonine

amphetamine, benzoylecgonine, methamphetamine

amphetamine, benzoylecgonine, Methamphetamine, morphine

Open Access Article

Automated Low-Cost Smartphone-Based Lateral Flow Saliva Test Reader for Drugs-of-Abuse Detection

by Adrian Carrio [1,*], Carlos Sampedro [1], Jose Luis Sanchez-Lopez [1], Miguel Pimienta [2] and Pascual Campoy [1]

[1] Computer Vision Group, Centre for Automation and Robotics (UPM-CSIC), Calle José Gutiérrez Abascal 2, Madrid 28006, Spain

[2] Aplitest Health Solutions, Paseo de la Castellana 164, Madrid 28046, Spain

[*] Author to whom correspondence should be addressed.

Academic Editor: Gonzalo Pajares Martinsanz

Sensors **2015**, *15*(11), 29569-29593; https://doi.org/10.3390/s151129569

Received: 31 August 2015 / Revised: 10 November 2015 / Accepted: 16 November 2015 / Published: 24 November 2015

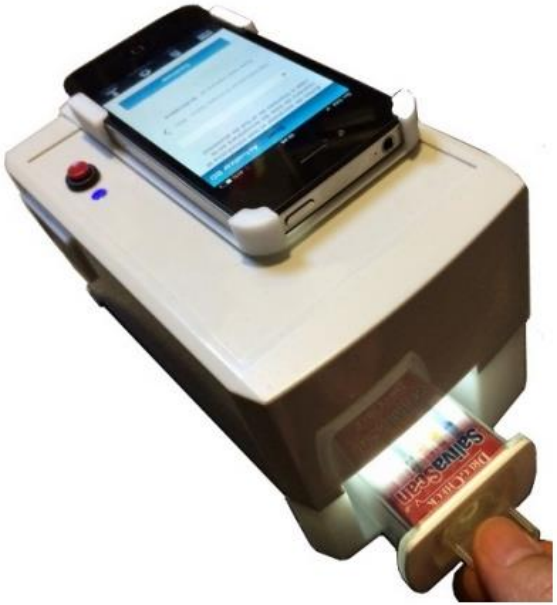
(This article belongs to the Special Issue State-of-the-Art Sensors Technology in Spain 2015)

- Carrio et al developed an automated smartphone-based strip reader for drug of abuse LFA tests.
  Obtaining a result is usually subject to visual interpretation of colored areas on the test by a human operator, introducing subjectivity and the possibility of errors in the extraction of the results. While automated test readers providing a result-consistent solution are widely available, they usually lack portability.

Automated smartphone-based strip reader

Light box with embedded electronic lighting system, which minimizes the relative movement between the smartphone and the test and the effects of external illumination changes.

- Test images captured with the smartphone camera are processed in the device using computer vision and machine learning techniques to perform automatic extraction of the results. A deep validation of the system has been carried out showing the high accuracy of the system.



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RESEARCH ARTICLE | MATERIALS SCIENCE

Skiving stacked sheets of paper into test paper for rapid and multiplexed assay

MINGZHU YANG, WEI ZHANG, JUNCHUAN YANG, BINFENG HU, [...] XINGYU JIANG +4 authors Authors Info & Affiliations

SCIENCE ADVANCES • 1 Dec 2017 • Vol 3, Issue 12 • DOI: 10.1126/sciadv.aao4862

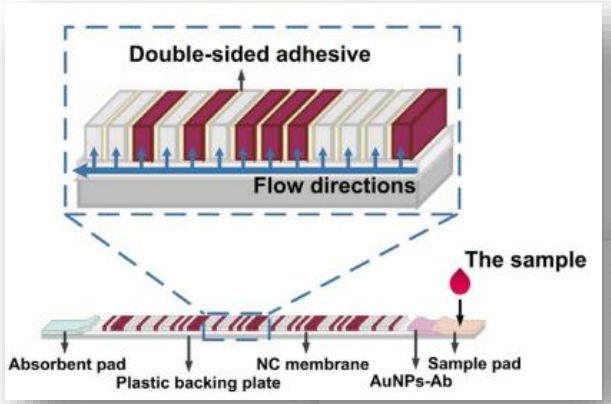
1,456 1

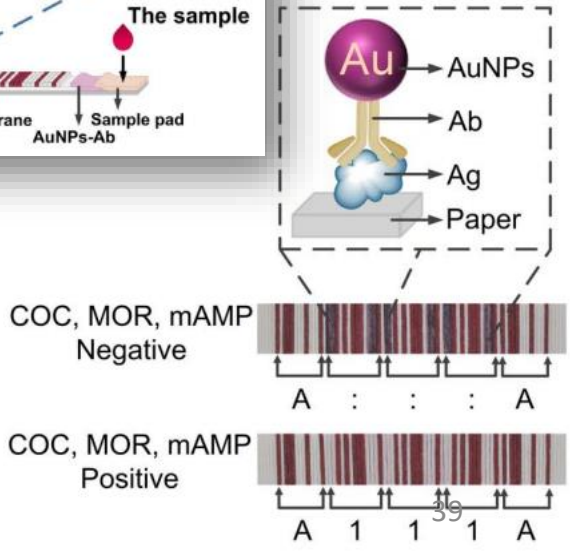
- Yang et al developed a stacked paper-based assay for the simultaneous detection of multiple drugs, which combined the LFA method with a bar code technology . Hence, its qualitative results can be read out conveniently by a bar code scanner.
- Method: **Competitive** assay

Paper-based barcode assay system (PBAS)

- simultaneous detection of multiplex targets in a single-step within 10 min.
- gold nanoparticles (AuNPs): generate colorimetric signals
- Detection by barcode scanner: is more objective and accurate

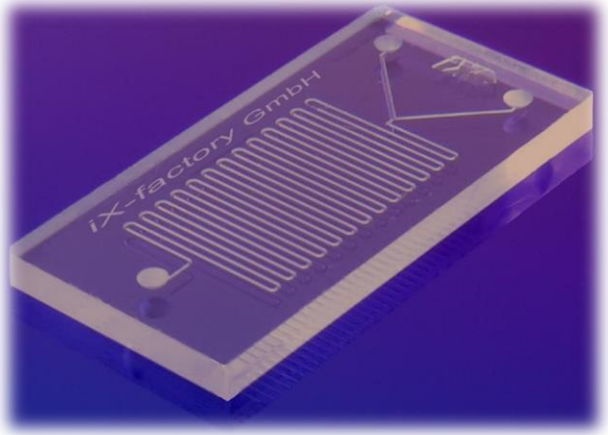
- when the samples are positive: “A111A”
- When the samples are negative: “A:::A”





Microfluidics

- A microfluidic chip is a set of micro-channels etched or molded into a material (glass, silicon or polymer).
- This network of micro-channels trapped into the microfluidic chip is connected to the outside by inputs and outputs pierced through the chip, as an interface between the macro- and micro-world.



- A microfluidic system is a small portable system that can complete sample pretreatment, separation, dilution, mixing, chemical reaction, detection, and product extraction. Moreover, the process of analysis can be completely automated, eliminating human interference, preventing pollution, and allowing for efficient repeating of experiments.

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Indirect Competitive Assays on DVD for Direct Multiplex Detection of Drugs of Abuse in Oral Fluids

Lingling Zhang[†‡], Xiaochun Li[‡], Yunchao Li[*†], Xiaoli Shi[†], and Hua-Zhong Yu[*‡§]

View Author Information

Cite this: *Anal. Chem.* 2015, 87, 3, 1896−1902
Publication Date: December 23, 2014
https://doi.org/10.1021/ac5040715

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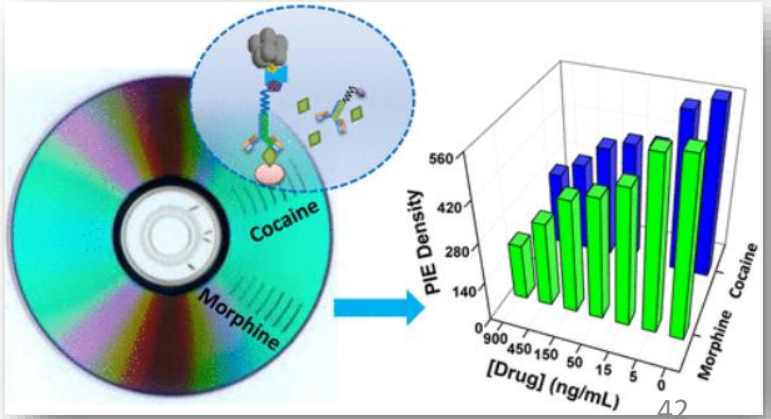
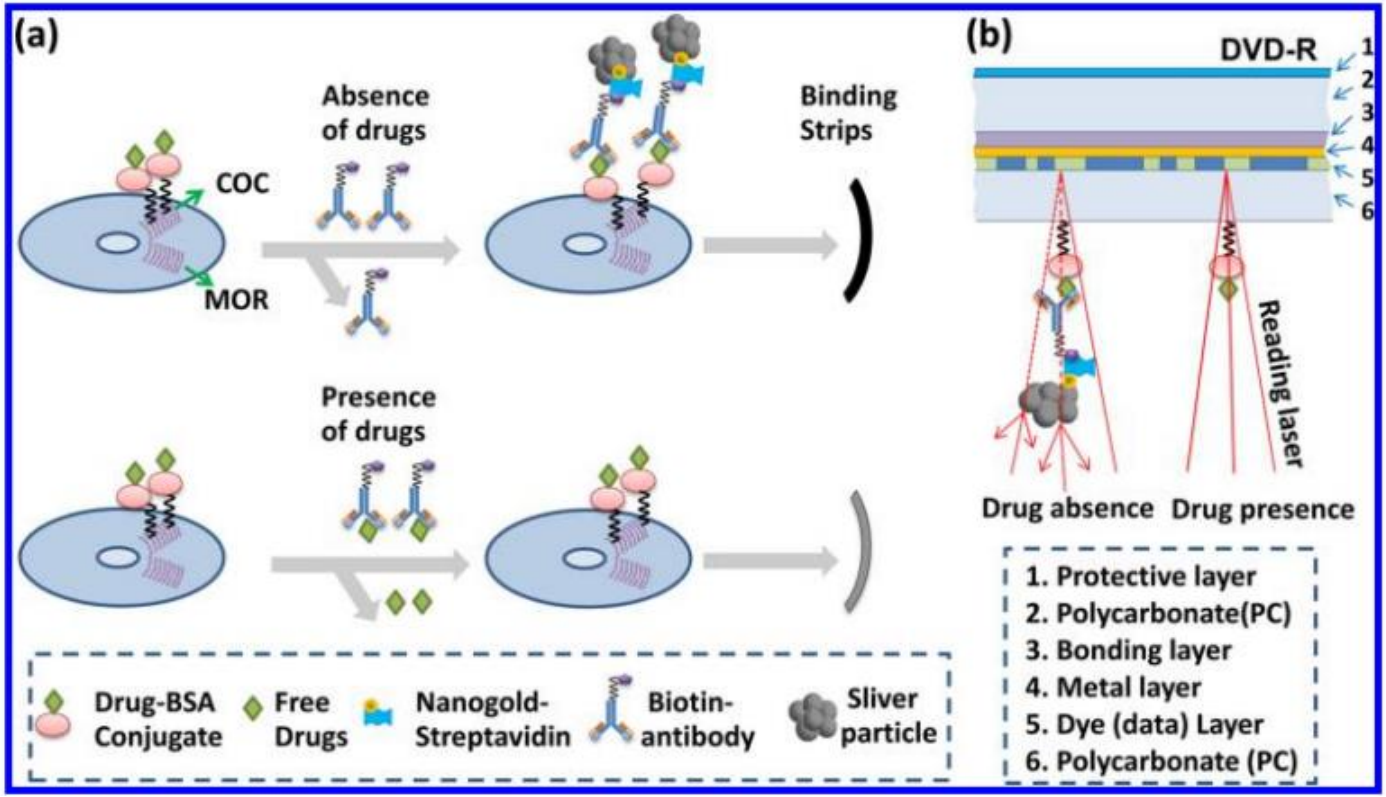
- Zhang et al reported a DVD-based microfluidic platform for the quantitative and multiplexed detection of drugs of abuse in saliva, obtaining digital signal readout with a conventional optical DVD drive.
- Method: **Competitive** assay

DVD-based microfluidic platform

- DVD technology-based immunoassay platform
- Quantitative detection of drugs of abuse (morphine and cocaine) in oral and blood fluids individually or simultaneously
- Detection limit : 1.0 ppb for morphine
  5.0 ppb for cocaine



Competitive Assay Design and Digital Reading Protocol



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Fast, Sensitive, and Quantitative Point-of-Care Platform for the Assessment of Drugs of Abuse in Urine, Serum, and Whole Blood

Ying Li[†‡], Uvaraj Uddayasankar[§], Bangshun He[⊥†‡], Ping Wang[*§∥], and Lidong Qin[*†‡]

View Author Information

Cite this: *Anal. Chem.* 2017, 89, 16, 8273−8281
Publication Date: July 12, 2017
https://doi.org/10.1021/acs.analchem.7b01288

Article Views 1991 | Altmetric - | Citations 25

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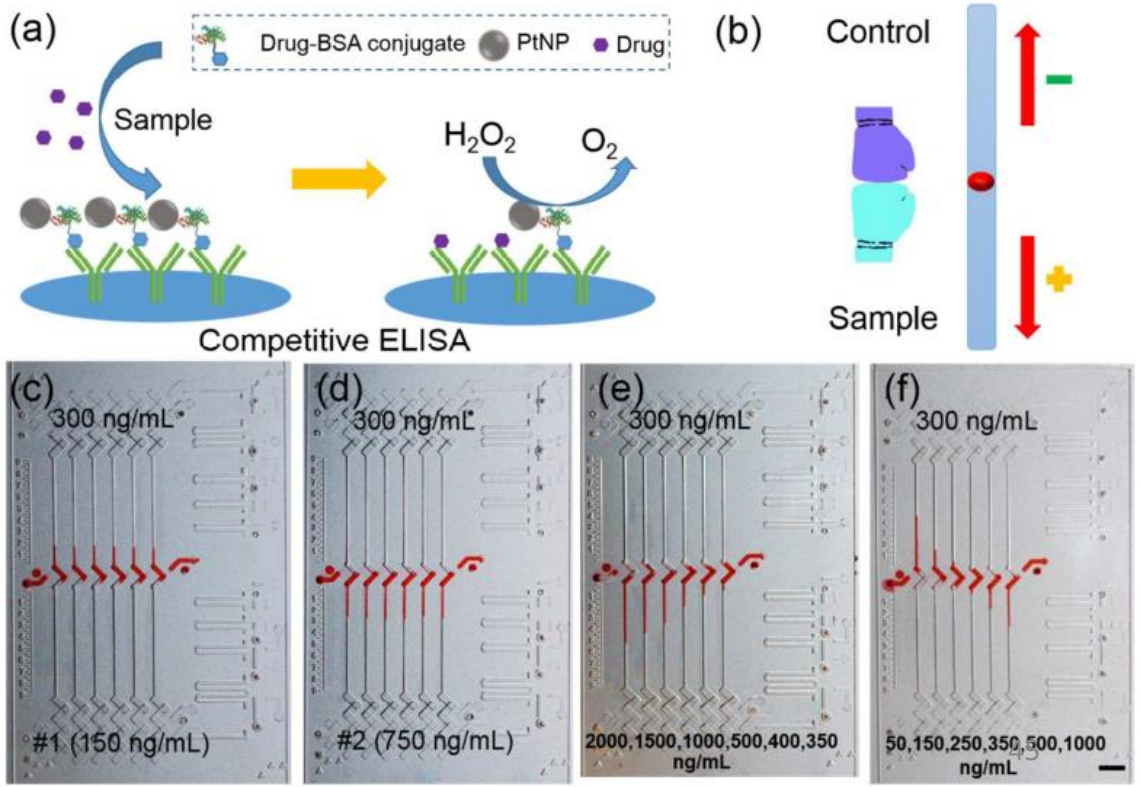
- Li et al developed an integrated competitive volumetric bar-chart chip (CV-Chip) to detect multiple drug targets (eg, cocaine, opiates) in urine, serum, and whole blood
- Method: **Competitive** assay

Volumetric-bar-chart Chip (CV-Chip)

- Sample: finger-prick blood
- The CV-Chip platform displayed visual positive or negative bar-chart results based on the direct competition of gas generated by the sample and the internal control.
- negative samples generate more gas than the control and produce an upward ink bar; conversely, positive samples produce a downward inks bar.

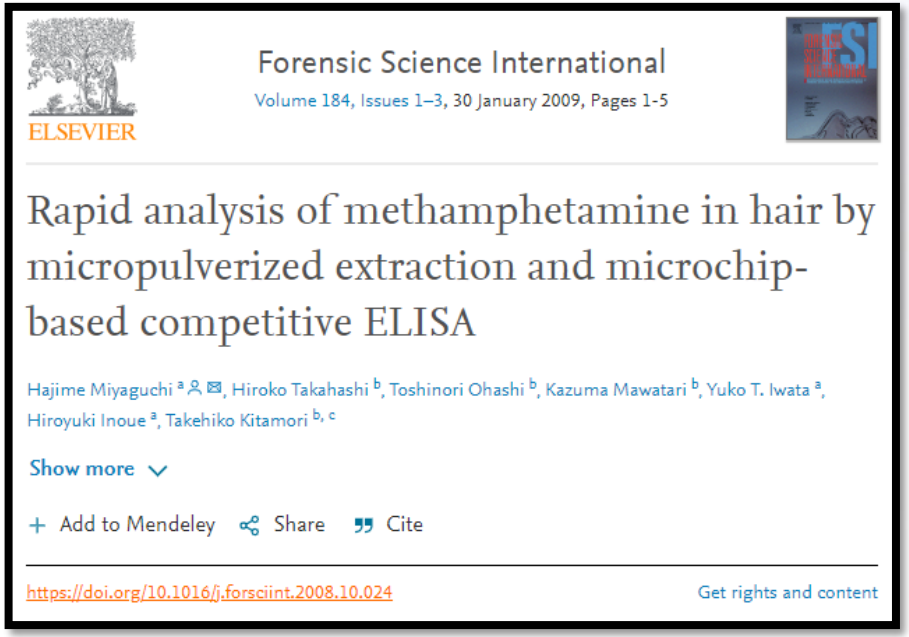


Miniaturized ELISA/MS

- The traditional ELISAs or gold standard MS analyzers have also been miniaturized so that they could be used at POC to detect drugs rapidly. Integration of sample preparation, microfluidic, and control/detection instrumentation components into a miniature system remains a huge challenge for POC diagnostics.

Miniaturized MS testing

Fast and Miniaturized ELISA testing



Forensic Science International

Volume 184, Issues 1–3, 30 January 2009, Pages 1-5

ELSEVIER

Rapid analysis of methamphetamine in hair by micropulverized extraction and microchip-based competitive ELISA

Hajime Miyaguchi [a], Hiroko Takahashi [b], Toshinori Ohashi [b], Kazuma Mawatari [b], Yuko T. Iwata [a], Hiroyuki Inoue [a], Takehiko Kitamori [b, c]

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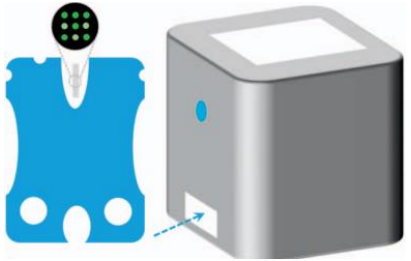
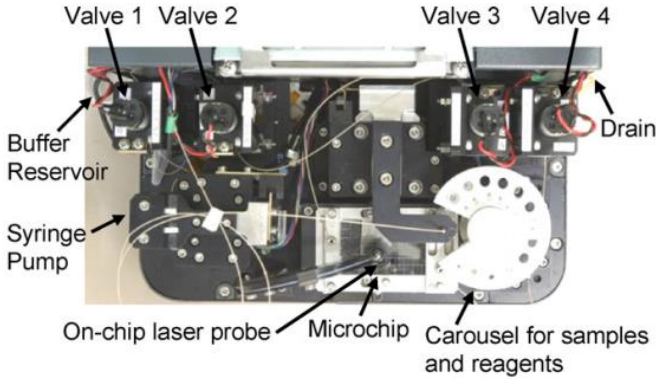
- Miyaguchi et al reported a portable microchip-based ELISA system for quantitative detection of drug in hair. Sample preparation (micropulverized extraction) and quantitation of microchip-based ELISA can be accomplished in less than 30 minutes. The programmable bio-nano-chip analyzer along with customized disposable cartridges had the proven multiplexed and sensitive detection capacity of 12 drugs in oral fluid.

microchip-based ELISA system (microELISA)

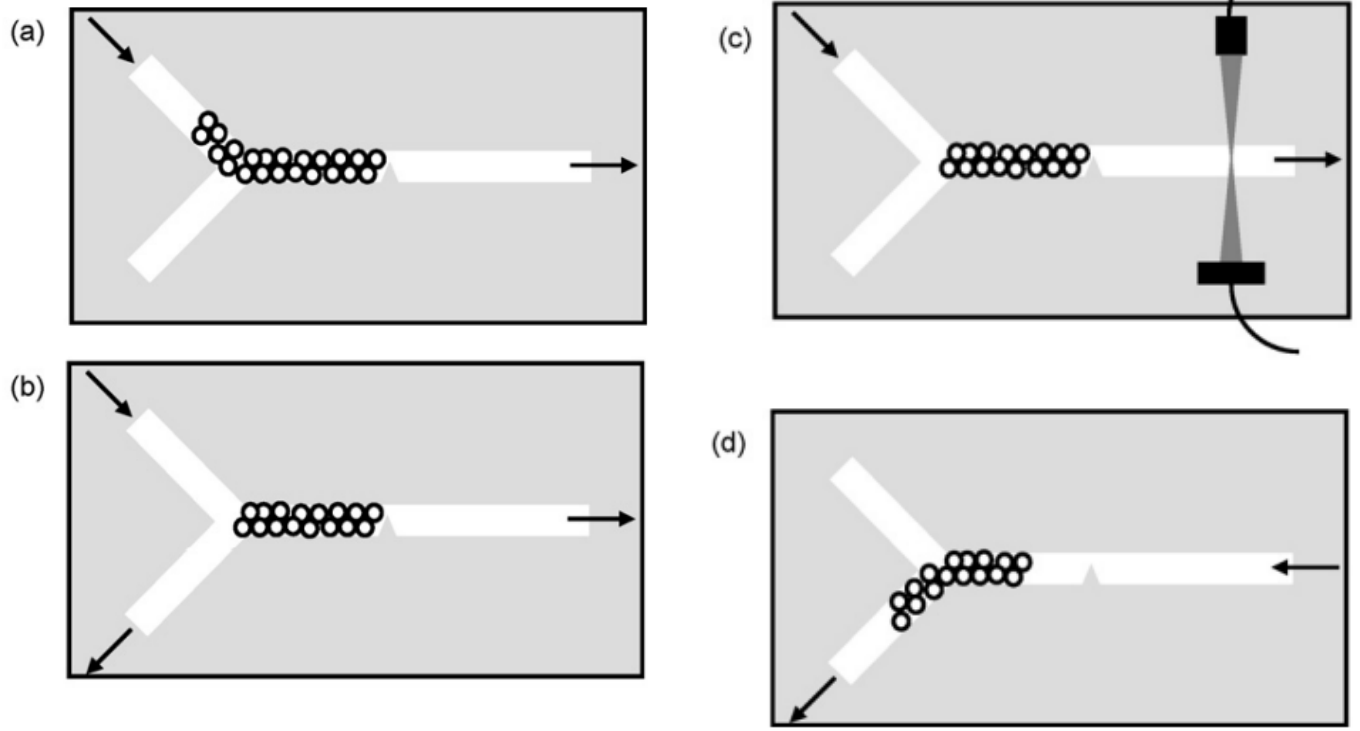
- An antibody and a peroxidase-linked methamphetamine, both are commercially available, were used for the competitive ELISA assay.
- Method validation: LC/MS/MS
- Time: less than 30 min
- contamination-free environments
- without the need for an expensive cleanroom, a fume hood, a helium or nitrogen gas supply, a high-current power supply and a vacuum source.

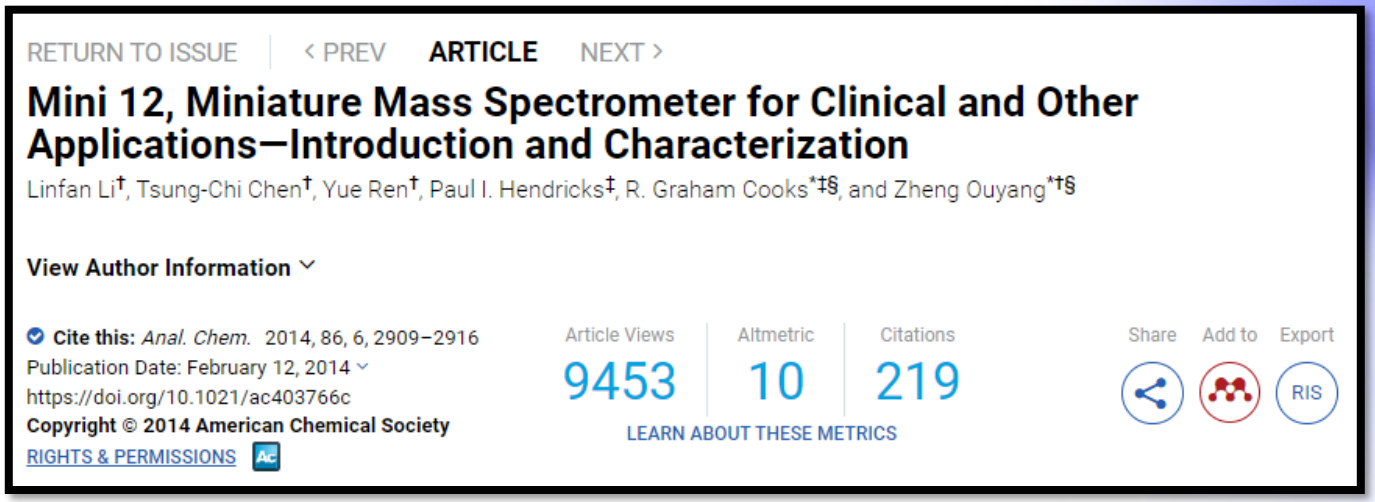




A top view of the microELISA apparatus

Automatic microchip operation for the competitive ELISA





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Mini 12, Miniature Mass Spectrometer for Clinical and Other Applications—Introduction and Characterization

Linfan Li[†], Tsung-Chi Chen[†], Yue Ren[†], Paul I. Hendricks[‡], R. Graham Cooks[*‡§], and Zheng Ouyang[*†§]

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Cite this: *Anal. Chem.* 2014, 86, 6, 2909−2916
Publication Date: February 12, 2014
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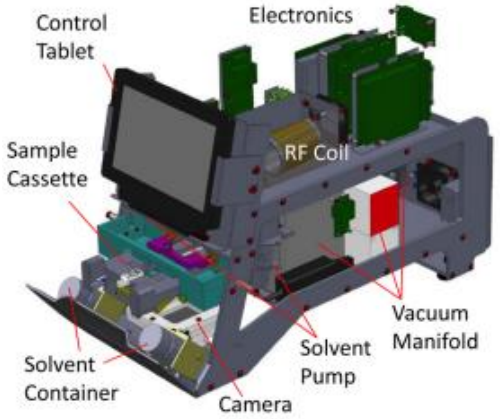
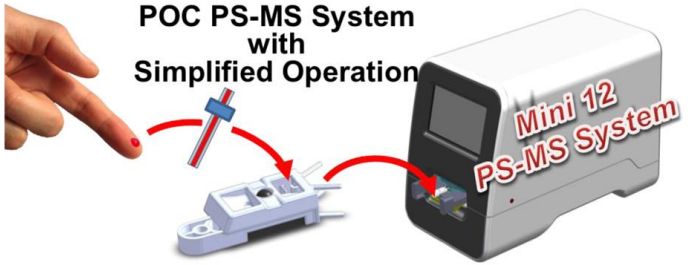
- Ouyang's group developed a benchtop miniature MS/MS system (25 kg, $19.6 \times 22.1 \times 16.5$ in [$49.8 \times 56.1 \times 41.9$ cm]) with digital microfluidics and ambient ionization source capabilities.

A benchtop miniature MS/MS system

- Multiple drugs could be quantified from 4 dried urine samples in less than 15 minutes. The limits of quantitation for cocaine, benzoylecgonine, and codeine were 51, 21, and 39 ng/mL, respectively.

- Limits of quantitation (LOQ) of 7.5 ng/mL





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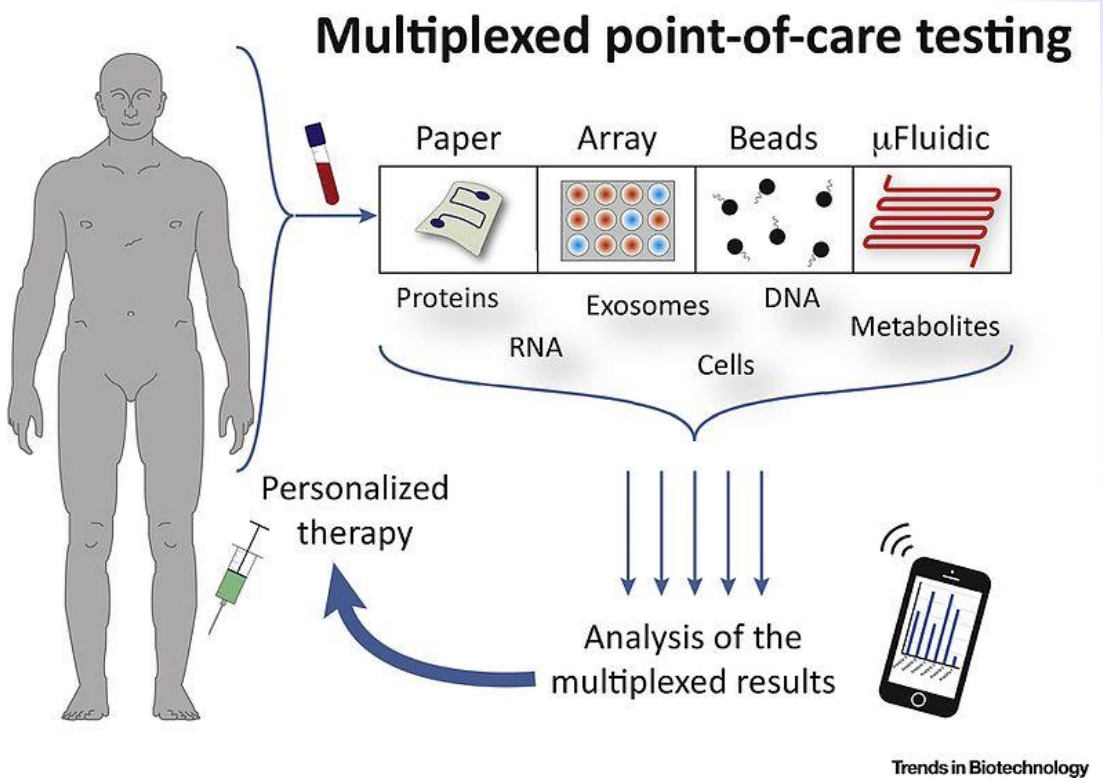
Multiplexed point-of-care testing
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Exosomes
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RNA
Cells
Personalized therapy
Analysis of the multiplexed results
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Thank you