OTTIMIZZAZIONE DEI FLUSSI DI LAVORO PER UNA DIAGNOSI RAPIDA ED EFFICACE

F. MARCUCCILLI

RUOLO DELLA MEDICINA DI LABORATORIO?

TEST APPROPRIATO

QUELLO IN CUI IL RISULTATO FORNISCE UNA RISPOSTA AL QUESITO CLINICO E METTE IN GRADO DI PRENDERE UNA DECISIONE O INTRAPRENDERE UNA AZIONE

Evidence-based laboratory medicine: supporting decision-making
C P Price · 2000 Aug;46(8 Pt 1):1041-50.

La Medicina di Laboratorio è una componente fondamentale dei processi assistenziali e svolge un ruolo di assoluta rilevanza nella prevenzione, nella diagnosi, nel trattamento e nel follow-up di tutte le patologie (**basti considerare, in merito, che il 60-70% delle decisioni cliniche es. ricoveri, dimissioni e terapie si basano su risultati di esami di laboratorio**).

Un esame di laboratorio…***è utile solo in quanto permette di attuare un'azione sul paziente*.**

BRAIN-TO BRAIN-LOOP

Figura 6.1: Processo "Brain-to-brain loop" di George D. Lundberg.

A cura di M. Ciaccio – G. Lippi
Biochimica Clinica e Medicina di Laboratorio
EdiSES

RIMeL / IJLaM 2006; 2 (Suppl.)

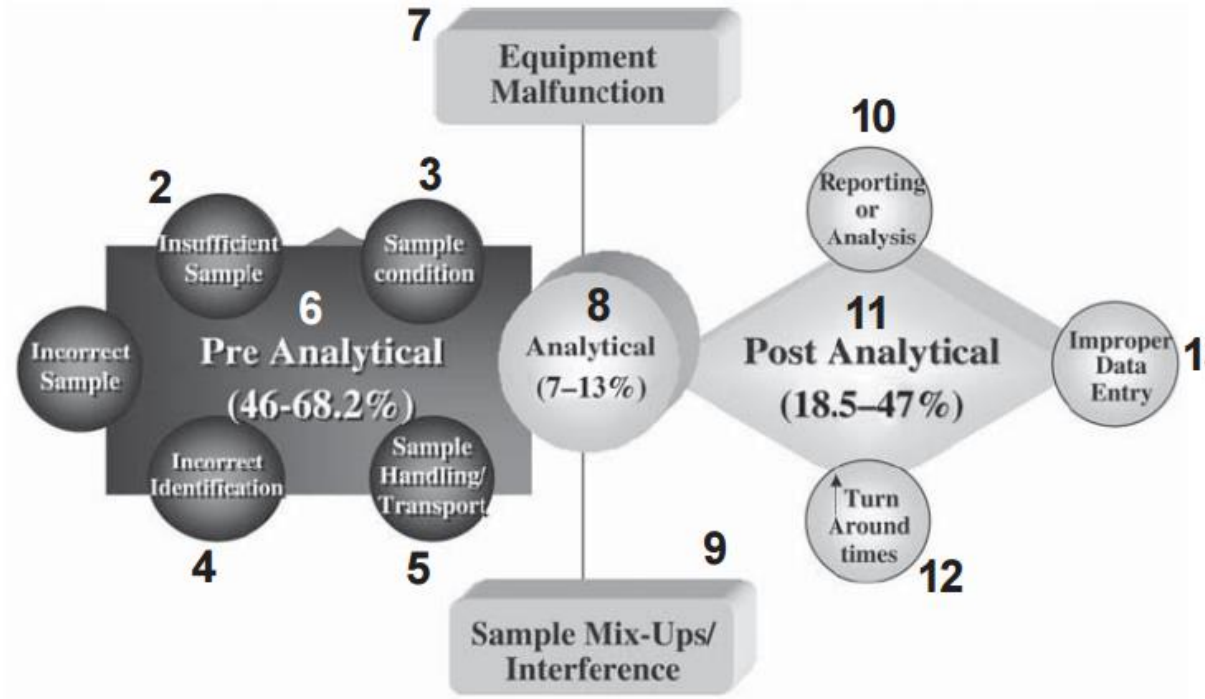

Figura 1. Tipi e percentuali di errori nelle tre fasi del processo di produzione del risultato (1. Campione non corretto; 2. Campione insufficiente; 3. Condizioni del campione; 4. Identificazione non corretta; 5. Gestione/trasporto del campione; 6. Pre-analitica (46-68.2%); 7. Malfunzionamento strumentazione; 8. Analitica (7-13%); 9. Scambio campione/Interferenza; 10. Refertazione o analisi; 11. Post-analitica (18.5-47%); 12. TAT; 13. Inserimento dati non corretti) (modificata da Rif. 3).

Conseguenze di un errore nel dato di laboratorio

Falsi negativi: - ritardo nel risolvere un problema acuto
- mancanza diagnosi

Falsi positivi: - richiamo non necessario del paziente
- aumento tempi degenza
- richiesta ulteriori esami
- inutilità della terapia
- tossicità farmaci

NCI
North Clin Istanb 2022;9(4):391–400
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Original Article Biochemistry

Direct cost analysis for 32,783 samples with preanalytical phase errors

Pinar Eker

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ABSTRACT

OBJECTIVE: Errors in the laboratory process often occur in the preanalytical phase (PA). The study aims to calculate the direct cost elements of PA errors, including material, logistics, transfer, personnel workforce, and medical waste.

METHODS: Medical laboratory PA phase errors were retrospectively reviewed using the Laboratory Information Management System. We evaluated the whole 2019 laboratory data of the 836-bed Health Sciences University Umraniye Training and Research Hospital (UTRH). We assessed the direct cost elements of PA errors, such as those related to material, logistics, transfer, human resources, and waste. We performed the procedure for both samples analyzed in the hospital and transferred to the central laboratory.

RESULTS: We analyzed 1,939,650 patient samples and 46,534,532 parameters studied in 2019 for UTRH. The rates for rejected tests and rejected samples (tube) for UTRH were noted as 0.32% and 1.7%, respectively. The total direct cost for PA errors was TRY 438,284.51 (68,918.07 euros) for 32,783 patient samples and 147,893 tests. We calculated the total cost for PA test errors detected in the hospital as TRY 390,238.06, while the total cost for PA test errors detected in the central laboratory was TRY 48,046.45. 89% of the total cost was for PA errors detected in the hospital, and 11% was for the errors detected in the central laboratory. The 2019 direct PA error cost we calculated based on our hospital's data was 0.153% of the 2019 hospital operating cost. We calculated the direct cost per rejected sample as TRY 13.37 (2.1 Euro).

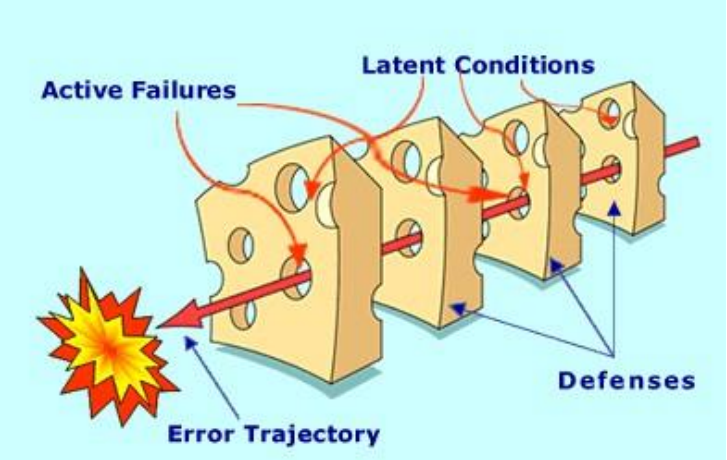
CONCLUSION: Providing reliable laboratory service with the least possible financial loss is one of the main goals in terms of laboratory medicine. In achieving this goal, the prevention of error costs is a priority. The direct cost elements for the PA phase, where laboratory errors are concentrated, can be easily identified. The amount of PA phase error direct cost will attract the attention of health policy decision-makers and field professionals and inspire further research. Therefore, we tried to determine a threshold cost regarding interventions and practices required to prevent PA phase errors.

Keywords: Direct cost; error cost analysis; medical laboratory; patient safety; preanalytical phase.

Cite this article as: *Eker P. Direct cost analysis for 32,783 samples with preanalytical phase errors. North Clin Istanb 2022;9(4):391–400.*

Il modello cosiddetto "svizzero" di Reason: gli errori attivi e latenti

La maggior parte degli incidenti in organizzazioni complesse è generato dall'interazione fra le diverse componenti del sistema: tecnologica, umana ed organizzativa. **James Reason** evidenzia le insufficienze latenti presenti nei processi sanitari. Quando si modificano più fattori che normalmente agiscono come barriere protettive ed i buchi si possono allineare si avrà il concatenarsi di condizioni che portano al verificarsi dell'Evento Avverso.



Gli **ERRORI ATTIVI** corrispondono ad errori individuali, legati alle persone quindi direttamente connessi con l'attività che si sta svolgendo nel Servizio o nel Reparto con effetti immediati e di più facile riscontro.

Gli **ERRORI LATENTI** sono il prodotto di attività diverse e sono legati ad organizzazioni (Reparto, Servizio) anche distanti tra loro. Il percorso clinico diagnostico e terapeutico del paziente, può nascondere numerose occasioni di errori. Questi errori, silenti, indicati da Reason come "patogeni" possono superare tutte le azioni di contenimento predisposte dalle varie organizzazioni e causare l'evento avverso.

Alla ricerca degli errori …

MEDICINA DI LABORATORIO

Errori latenti

- Gestione personale
- Carichi di lavoro
- Competenze
- Leadership
- Organizzazione
- Struttura
- Comunicazione
- Logistica
- Clima organizzativo

Errori attivi

- Errata accettazione
- Errata preparazione del paziente
- Errato prelievo dei campioni
- Errata conservazione/trasporto del campione
- Omessa igiene mani
- Ecc. ecc.

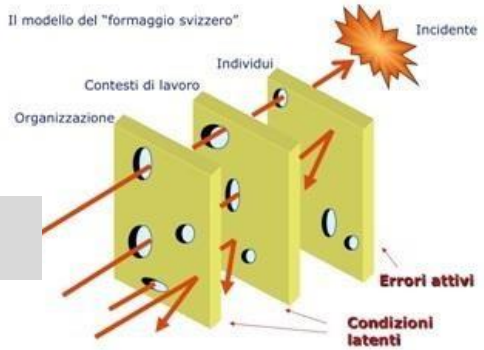
Barriere

- Procedure
- Protocolli
- Formazione
- Linee guida

HARD

- DPI
- Ambienti

Errore diagnostico

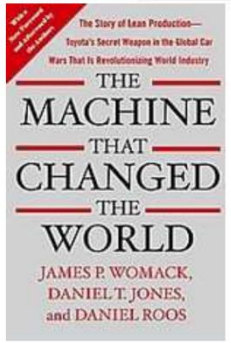


PREANALITICA

GATING-POLICY

Si definisce "gating policy" l'approccio volto a migliorare l'appropriatezza nella richiesta di esami di laboratorio, stabilendo dei criteri che debbono essere soddisfatti dal richiedente ed in mancanza dei quali la richiesta di esame non viene, di fatto, generata. I criteri da soddisfare sono, essenzialmente, di natura clinica nel senso che la richiesta di esami e subordinata all'inserimento di appropriati dati clinici o alla dimostrazione di conformità rispetto a criteri di selezione, precedentemente concordati ed esplicitati.

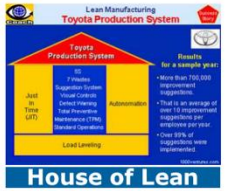
SISTEMA LEAN



Il termine "Lean" (snello) è stato reso famoso da **James Womack** nel libro "The machine that changed the world" (1990)

Prima innovazione pensata da **Henry Ford** sulla produzione in linea

Rivoluzionaria idea di ***Taiichi Ohno*** *(大野 耐; 1912-1990)*, ingegnere giapponese, considerato il padre del sistema di produzione attuato nell'azienda automobilistica Toyota:
il **Toyota Production System** (TPS), noto anche come **Lean production**



Alla base del *TPS* si trova l'idea di **'fare di più con meno'**, cioè di utilizzare le (poche) risorse disponibili nel modo più produttivo possibile con l'obiettivo di incrementare la produttività.

VANTAGGI SISTEMA LEAN

I benefici che scaturiscono dall'applicazione dei principi *Lean:*

snellimento delle attività

- conseguenti migliori risultati,
- aumento della produttività,
- maggiore qualità e sicurezza,
- minori errori e incidenti,
- ambiente di lavoro stabile con procedure chiare e standardizzate.

diagnostics

MDPI

Review

Serological Diagnosis of Flavivirus-Associated Human Infections

Didier Musso [1,2,*,†] and Philippe Desprès [3,†]

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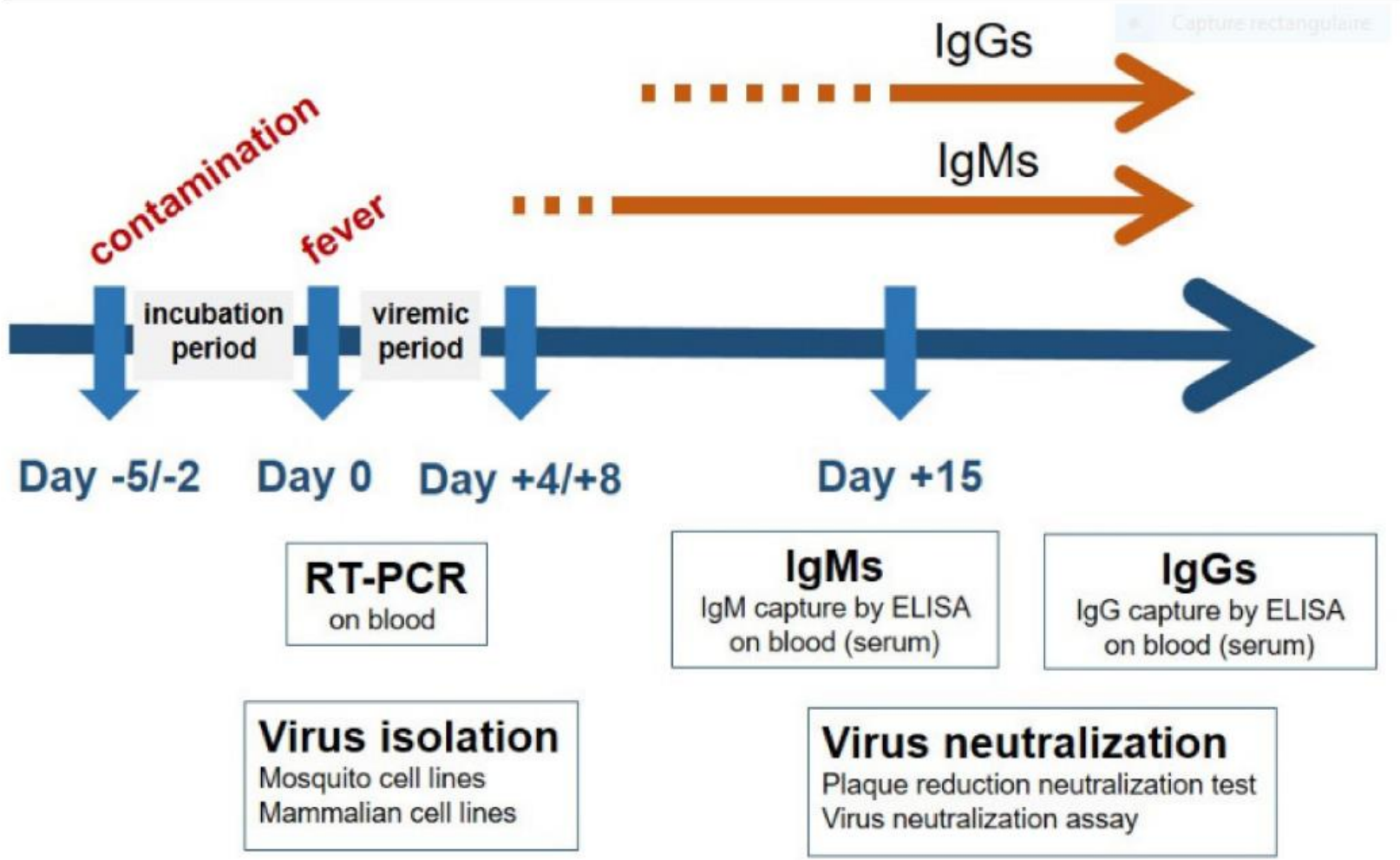

Figure 1. Flow chart of molecular and serological diagnosis tests in the course of human flavivirus infections.

DIAGNOSI ARBOVIRUS

2. Laboratory Diagnosis of Flavivirus-Associated Human Diseases

Routine diagnosis of flavivirus-associated human diseases relies on the detection of the pathogen, its nucleic acids or specific viral antigens during the acute phase of the disease followed by the capture of specific antibodies at least one week after the infection. Advantages and limitations of each method and the window of detection are detailed in Table 1 and Figure 1.

Table 1. Current laboratory techniques for the diagnosis of acute human flavivirus infections.

Methods	Advantages	Critical Evaluation
RT-PCR	• Diagnosis is performed by detection of viral nucleic acids. • Specificity and sensitivity. • Rapidity. • RT-PCR diagnosis test kits.	• Positivity often limited to the acute stage of disease (2–7 days). • Flavivirus infection can cause a weak or no viremia.
Virus isolation	• Direct pathogen detection plays a key role in diagnosing flavivirus infection	• Biosafety Laboratory considerations (BSL levels 2 to 4). • Requirement of cultured cell lines for viral growth. • Virus identification using specific detection tools. • Time consuming.

Diagnostics **2020**, *10*, 302

Table 1. *Cont.*

Methods	Advantages	Critical Evaluation
Viral antigen capture	• Diagnosis of acute dengue virus infection based on soluble NS1 capture. • Rapid diagnosis test kits.	• Only available for dengue. • False-dengue positivity has been documented.
Serology	• Diagnosis is performed by IgM and IgG capture or virus neutralization assays. • Qualitative and quantitative serologic diagnosis tests. • Licensed rapid serologic diagnosis test kits.	• Specificity and sensitivity. • Complexity of serological flavivirus diagnosis. • False interpretation of dengue diagnostic serology tests during secondary dengue infection. • Virus neutralization assays require BSL levels 2 to 4. • Serological assays performed in BSL are time consuming. • Detection of antib convalescent patie other illnesses wit

microorganisms

MDPI

Review

Latest Advances in Arbovirus Diagnostics

Jano Varghese, Imesh De Silva and Douglas S. Millar *

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Abstract: Arboviruses are a diverse family of vector-borne pathogens that include members of the *Flaviviridae*, *Togaviridae*, *Phenuviridae*, *Peribunyaviridae*, *Reoviridae*, *Asfarviridae*, *Rhabdoviridae*, *Orthomyxoviridae* and *Poxviridae* families. It is thought that new world arboviruses such as yellow fever virus emerged in the 16th century due to the slave trade from Africa to America. Severe disease-causing viruses in humans include Japanese encephalitis virus (JEV), yellow fever virus (YFV), dengue virus (DENV), West Nile virus (WNV), Zika virus (ZIKV), Crimean–Congo hemorrhagic fever virus (CCHFV), severe fever with thrombocytopenia syndrome virus (SFTSV) and Rift Valley fever virus (RVFV). Numerous methods have been developed to detect the presence of these pathogens in clinical samples, including enzyme-linked immunosorbent assays (ELISAs), lateral flow assays (LFAs) and reverse transcriptase–polymerase chain reaction (RT-PCR). Most of these assays are performed in centralized laboratories due to the need for specialized equipment, such as PCR thermal cyclers and dedicated infrastructure. More recently, molecular methods have been developed which can be performed at a constant temperature, termed isothermal amplification, negating the need for expensive thermal cycling equipment. In most cases, isothermal amplification can now be carried out in as little as 5–20 min. These methods can potentially be used as inexpensive point of care (POC) tests and in-field deployable applications, thus decentralizing the molecular diagnosis of arboviral disease. This review focuses on the latest developments in isothermal amplification technology and detection techniques that have been applied to arboviral diagnostics and highlights future applications of these new technologies.

Keywords: isothermal amplification; arboviral diagnostics; point of care; decentralized testing

Citation: Varghese, J.; De Silva, I.; Millar, D.S. Latest Advances in Arbovirus Diagnostics. *Microorganisms* **2023**, *11*, 1159. https://doi.org/10.3390/microorganisms11051159

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1. Introduction

Arboviral disease in humans can range from asymptomatic to life-threatening conditions, such as hemorrhagic fevers and encephalitis. Arboviruses are distributed worldwide [1] with some viruses showing restricted geographical distribution (Figure 1). However, as a result of environmental destruction, the travel boom, deforestation, urbanization and failure of vector control programs, arboviruses have expanded into areas not previously seen [2]. Due to the severity and global distribution of arboviral disease, it is vital to have sensitive and rapid diagnostics tests available to determine the causative agent responsible for infection and the implementation of control strategies. Traditionally, care-

Table 3. Summary table comparing the main isothermal amplification techniques to RT-PCR.

Amplification Method	Template	Temperature	Primers	Time to Result	Enzymes (RNA)	Advantages	Disadvantages
Real-time PCR	DNA/RNA	Thermal cycling	2	15–60 min	2	Established method, high sensitivity and specificity; multiplexing.	Thermal cycler required and highly trained staff.
Nucleic-Acid-Sequence-Based Amplification	RNA	41 °C	2	90–120 min	3	Isothermal, rapid.	RNA-based amplification only.
Strand Displacement Amplification	DNA/RNA	37–65 °C	4	10–60 min	3	Isothermal, rapid results NEAR method <10 min. POC compatible	Sensitivity can be lower than other methods. Thermal denaturation required for DNA.
Helicase Dependant Amplification	DNA/RNA	37–65 °C	2	30–60 min	3	Isothermal, rapid. POC compatible.	Not as sensitive as other techniques
Loop mediated AMPlification	DNA/RNA	65 °C	4–6	5–30 min	2	Isothermal, rapid, POC adaptable. Multiplex capability.	Complex primer design.
Recombinase Polymerase Amplification	DNA/RNA	37–42 °C	2	5–30 min	3	Isothermal, rapid, POC compatible.	RUO only reagents available.

INTELLIGENZA ARTIFICIALE

medicina

MDPI

Article

Computer Viewing Model for Classification of Erythrocytes Infected with *Plasmodium* spp. Applied to Malaria Diagnosis Using Optical Microscope

Eduardo Rojas [1,2], Irene Cartas-Espinel [1,3], Priscila Álvarez [1], Matías Moris [1], Manuel Salazar [1], Rodrigo Boguen [1], Pablo Letelier [1], Lucia San Martín [1,2], Valeria San Martín [1,2], Camilo Morales [4] and Neftalí Guzmán [1,*]

check for updates

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Results: The model with the best performance was VGG-19, with an AUC of 98%, **accuracy of 93%, precision of 92%**, recall of 94%, and F1 score of 93%. Conclusions: Based on the results, we propose a convolutional neural network model (VGG-19) for malaria diagnosis that can be applied in low-complexity laboratories thanks to its ease of implementation and high predictive performance.

Università di Roma Tor Vergata

PTV FONDAZIONE PTV POLICLINICO TOR VERGATA

-INTELLIGENZA ARTIFICIALE

-AUTOMAZIONE

-TECNOLOGIE FAST

frontiers | Frontiers in Cellular and Infection Microbiology

TYPE Perspective
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Laboratory automation, informatics, and artificial intelligence: current and future perspectives in clinical microbiology

Antonella Mencacci [1,2*], Giuseppe Vittorio De Socio [3], Eleonora Pirelli [1], Paola Bondi [1] and Elio Cenci [1,2]

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Clinical diagnostic laboratories produce one product—information—and for this to be valuable, the information must be clinically relevant, accurate, and timely. Although diagnostic information can clearly improve patient outcomes and decrease healthcare costs, technological challenges and laboratory workflow practices affect the timeliness and clinical value of diagnostics. This article will examine how prioritizing laboratory practices in a patient-oriented approach can be used to optimize technology advances for improved patient care.

KEYWORDS

laboratory automation, artificial intelligence, informatics, laboratory workflow, Kiestra, WASPLab

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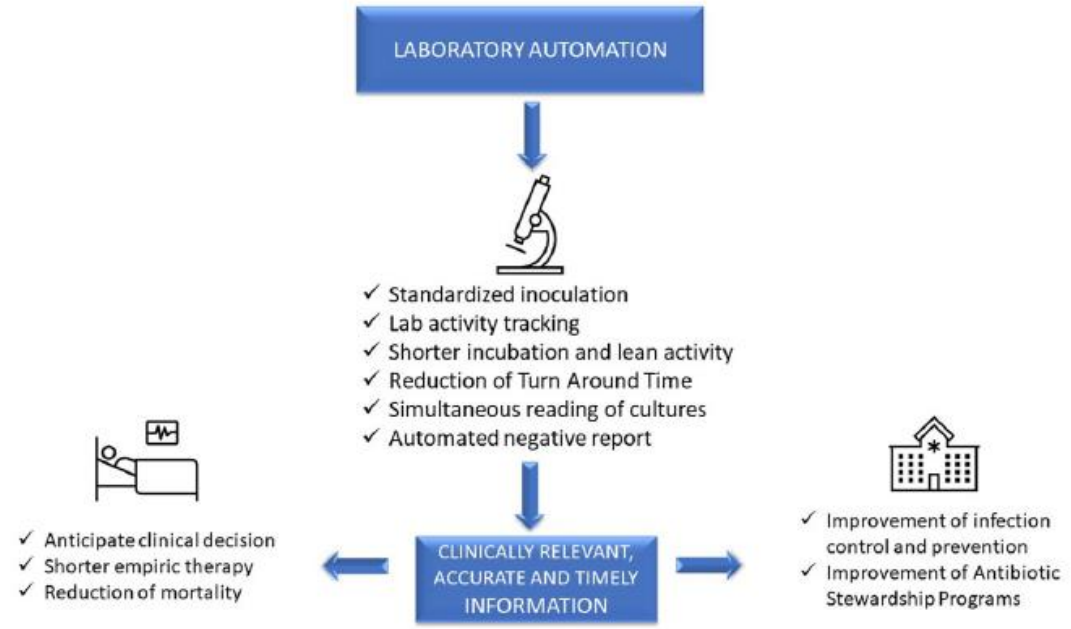
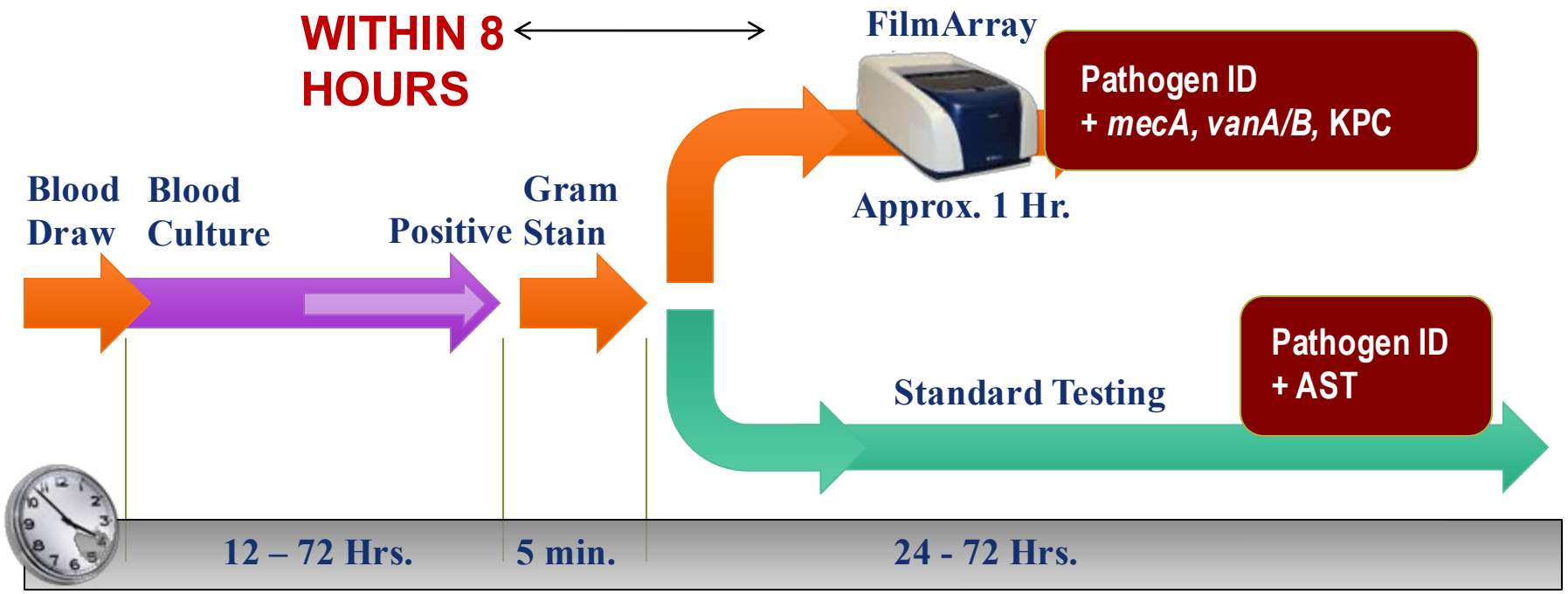


FIGURE 1

Impact of automation on laboratory, patient, and hospital management.

TECNOLOGIA FAST NELLA DIAGNOSI DELLA SEPSI

FilmArray BCID Workflow



Blood Culture Identification Panel

Gram + Bacteria:

Enterococcus
L. monocytogenes
Staphylococcus
S. aureus
Streptococcus
S. agalactiae
S. pyogenes
S. pneumoniae

Antibiotic Resistance:

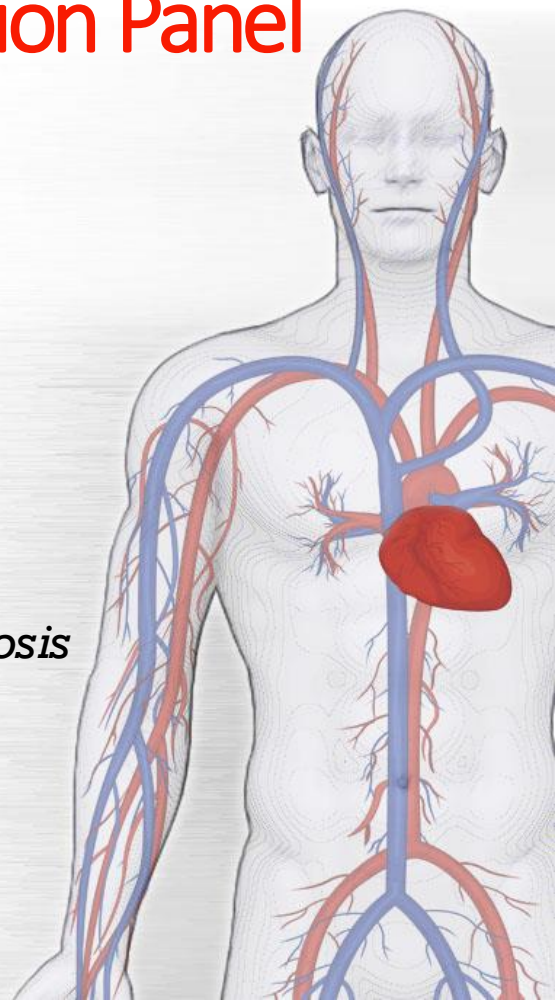
mecA
Van A/B
KPC

Gram - Bacteria:

A. baumannii
H. influenzae
N. meningitidis
P. aeruginosa
Enterobacteriaceae
Enterobacter cloacae complex
E. coli
K. oxytoca
K. pneumoniae
Proteus
S. marcescens

Yeast:

C. albicans
C. glabrata
C. krusei
C. parapsiolosis
C. tropicalis



TECNOLOGIE FAST

DIAGNOSI RAPIDA DEI MICETI

OXFORD FEMS

FEMS Microbiology Reviews, fuz015, 43, 2019, 517–547

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Advance Access Publication Date: 3 June 2019
Review article

REVIEW ARTICLE

Recent trends in molecular diagnostics of yeast infections: from PCR to NGS

Consortium OPATHY[1] and Toni Gabaldón[2,3,4,*]

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One sentence summary: The authors discuss the current status of the use of high-throughput (-omics) technologies on the diagnostics of yeast infections.

Editor: Baddrt Thomma

ABSTRACT

The incidence of opportunistic yeast infections in humans has been increasing over recent years. These infections are difficult to treat and diagnose, in part due to the large number and broad diversity of species that can underlie the infection. In addition, resistance to one or several antifungal drugs in infecting strains is increasingly being reported, severely limiting therapeutic options and showcasing the need for rapid detection of the infecting agent and its drug susceptibility profile. Current methods for species and resistance identification lack satisfactory sensitivity and specificity, and often require prior culturing of the infecting agent, which delays diagnosis. Recently developed high-throughput technologies such as next generation sequencing or proteomics are opening completely new avenues for more sensitive, accurate and fast diagnosis of yeast pathogens. These approaches are the focus of intensive research, but translation into the clinics requires overcoming important challenges. In this review, we provide an overview of existing and recently emerged approaches that can be used in the identification of yeast pathogens and their drug resistance profiles. Throughout the text we highlight the advantages and disadvantages of each methodology and discuss the most promising developments in their path from bench to bedside.

Keywords: yeast pathogens; diagnosis; *Candida*; candidemia; sequencing; proteomics

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PTV FONDAZIONE PTV POLICLINICO TOR VERGATA

TECNOLOGIE FAST

SMARTPHONE BASED POINT OF CARE

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REVIEW

ADVANCED SCIENCE Open Access
www.advancedscience.com

Virus Detection: From State-of-the-Art Laboratories to Smartphone-Based Point-of-Care Testing

Meng Xiao, Feng Tian, Xin Liu, Qiaoqiao Zhou, Jiangfei Pan, Zhaofan Luo, Mo Yang,* and Changqing Yi**

Infectious virus outbreaks pose a significant challenge to public healthcare systems. Early and accurate virus diagnosis is critical to prevent the spread of the virus, especially when no specific vaccine or effective medicine is available. In clinics, the most commonly used viral detection methods are molecular techniques that involve the measurement of nucleic acids or proteins biomarkers. However, most clinic-based methods require complex infrastructure and expensive equipment, which are not suitable for low-resource settings. Over the past years, smartphone-based point-of-care testing (POCT) has rapidly emerged as a potential alternative to laboratory-based clinical diagnosis. This review summarizes the latest development of virus detection. First, laboratory-based and POCT-based viral diagnostic techniques are compared, both of which rely on immunosensing and nucleic acid detection. Then, various smartphone-based POCT diagnostic techniques, including optical biosensors, electrochemical biosensors, and other types of biosensors are discussed. Moreover, this review covers the development of smartphone-based POCT diagnostics for various viruses including COVID-19, Ebola, influenza, Zika, HIV, et al. Finally, the prospects and challenges of smartphone-based POCT diagnostics are discussed. It is believed that this review will aid researchers better understand the current challenges and prospects for achieving the ultimate goal of containing disease-causing viruses worldwide.

1. Introduction

Emerging viruses present one of the greatest public health threats facing human populations. The outbreak of Coronavirus Disease 2019 (COVID-19) has evolved into a global crisis, which has been defined as a public health emergency of international concern by the World Health Organization (WHO). As of February 25, 2022, authorities in 206 countries and territories had reported over 431 million cases, resulting in at least 5.9 million deaths worldwide. Controlling the spread of these viruses continues to be a global challenge. China has been the most successful country in containing the epidemic and its successful experience lies in early detection for early control. Early detection of virus infection is critical for virus containment because it can effectively identify suspected individuals and cut off the transmission chains. In addition, early detection of virus infection is critical in tracing transmission chains, such as "who-infected-whom," contact tracing, and human-to-human transmission timelines, thereby assisting in interrupting the spread of virus.

Viruses are composed of nucleic acids (DNA or RNA) and an envelope protein coat. They typically require a host cell to replicate their genomes and multiply virus particles. Based on this unique characteristic, molecular diagnostic methods such as virus isolation,[1,2] enzyme-linked immunosorbent assay (ELISA),[3,4] polymerase chain reaction (PCR)[4,5] and hemagglutination/inhibition[5] assay have been developed for virus identification and/or quantitation. These traditional

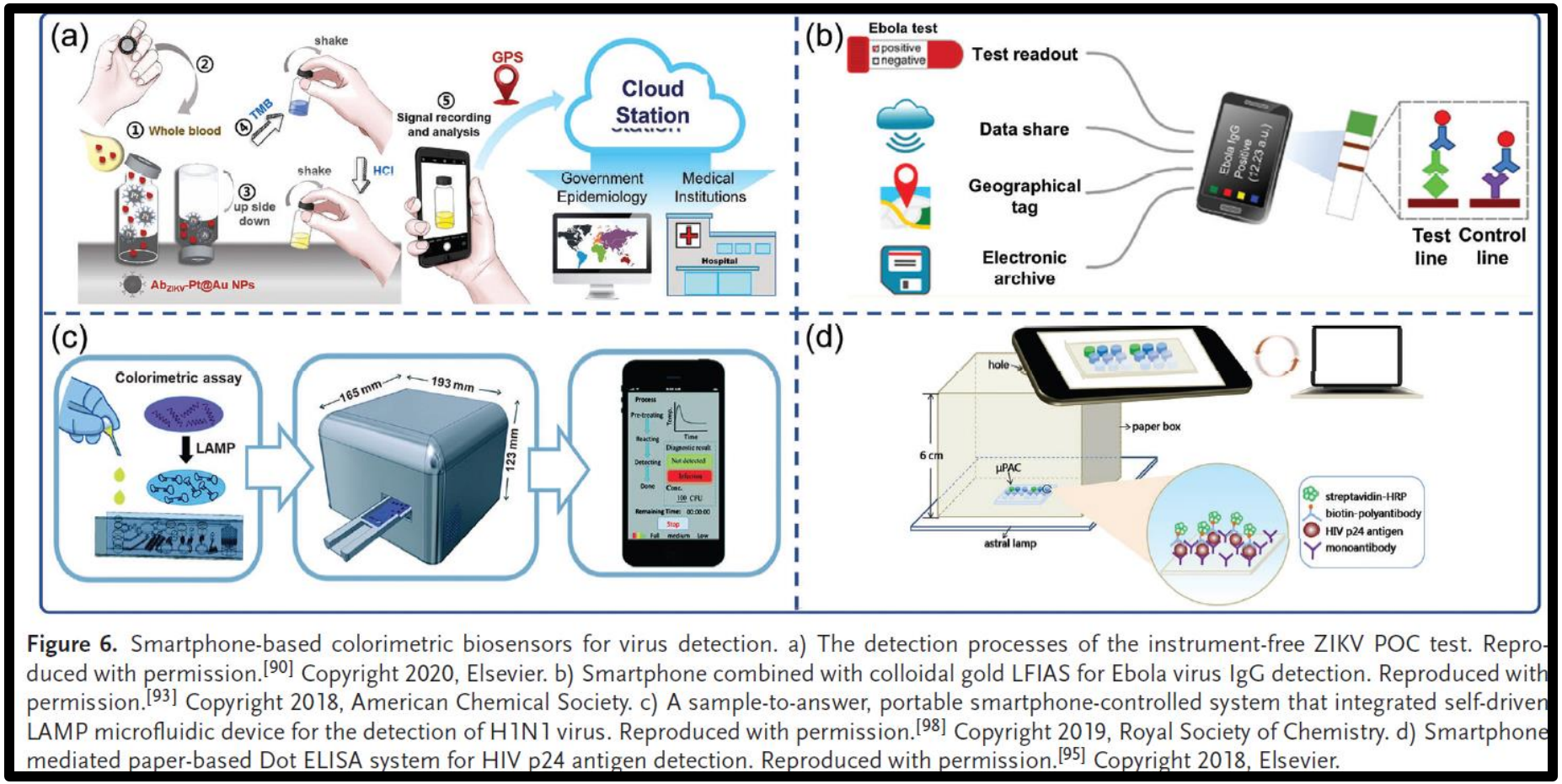


Figure 6. Smartphone-based colorimetric biosensors for virus detection. a) The detection processes of the instrument-free ZIKV POC test. Reproduced with permission.[90] Copyright 2020, Elsevier. b) Smartphone combined with colloidal gold LFIAS for Ebola virus IgG detection. Reproduced with permission.[93] Copyright 2018, American Chemical Society. c) A sample-to-answer, portable smartphone-controlled system that integrated self-driven LAMP microfluidic device for the detection of H1N1 virus. Reproduced with permission.[98] Copyright 2019, Royal Society of Chemistry. d) Smartphone mediated paper-based Dot ELISA system for HIV p24 antigen detection. Reproduced with permission.[95] Copyright 2018, Elsevier.

Table 3. Comparison of the presented methods for virus diagnosis.

Platform	Analytical sensitivity	Clinical sensitivity	Specificity	Cost	Setting	Detecting time	Advantage	Disadvantage
RT-PCR	1–10 copies μL^{-1}	High	Moderate	10–60 USD	Laboratory	1–3 h	Highly specific, sensitive, and reliable	Sampling errors (false negatives or false positives)
RT-LAMP	Lower than RT-PCR	Moderate	High	Low	Laboratory	30–60 min	Low-cost equipment without thermal alternations required	Difficult in primer design; high false-positive results; unable of quantitative analysis
CRISPR/Cas12a/Cas13	10–100 copies	Moderate	High	3–10 USD	Laboratory	15–30 min	No need for expertise and infrastructure; suitable for field testing	Unsatisfactory sensitivity and need for pre-amplification
ELISA	0.01–0.1 ng	High	High	10–20 USD per test	Laboratory	2–3 h	Highly sensitive and selective with high throughput	Tedious process and sample preparation
Immunoassay	pg. mL^{-1}–ng mL^{-1}	High	Moderate	Low	Laboratory	10–30 min	Fast response, low cost, good flexibility, and high sensitively	Susceptible to cross-reactive; weak stability
Miniaturized PCR device	1–10 copies μL^{-1}	≥96%	≥97%	20–50 USD	Commercial POCT	1–3 h	Accurate quantification, high sensitivity and throughput	High reagent cost; expensive and complex
LOAD device	High	N/A	High	Moderate	Commercial POCT	70–150 min	Large-scale parallelization, simple and independent liquid handling	Difficult in on-board reagent storage, short shelf life
Lateral flow device	pg mL^{-1}–ng mL^{-1}	≥92.2%	≥ 95%	5–10 USD	Commercial POCT	10–20 min	Rapid; easy fabrication and transport; user-friendly	Difficult in quantitative detection; limited capability of multiple detection
Smartphone-based NAATs	1–100 copies μL^{-1}	N/A	Moderate	Low	Field	30–80 min	Fast, simple, and high acceptable to users	Low accuracy; complex pre-preparation process
Smartphone-based LOC devices	Moderate	N/A	High	Low	Field	15–60 min	Easy to integration; automated result analysis; sample-to answer detection	Difficult in fabricating, packaging, and interfacing
Smartphone-based LFS reader	pg mL^{-1}–ng mL^{-1}	N/A	Moderate	Very low	Field	10–25 min	Low cost; independent on equipment; suitable for home and community testing	Highly dependent on antibody affinity and specific molecular assay; high false negatives or false positives

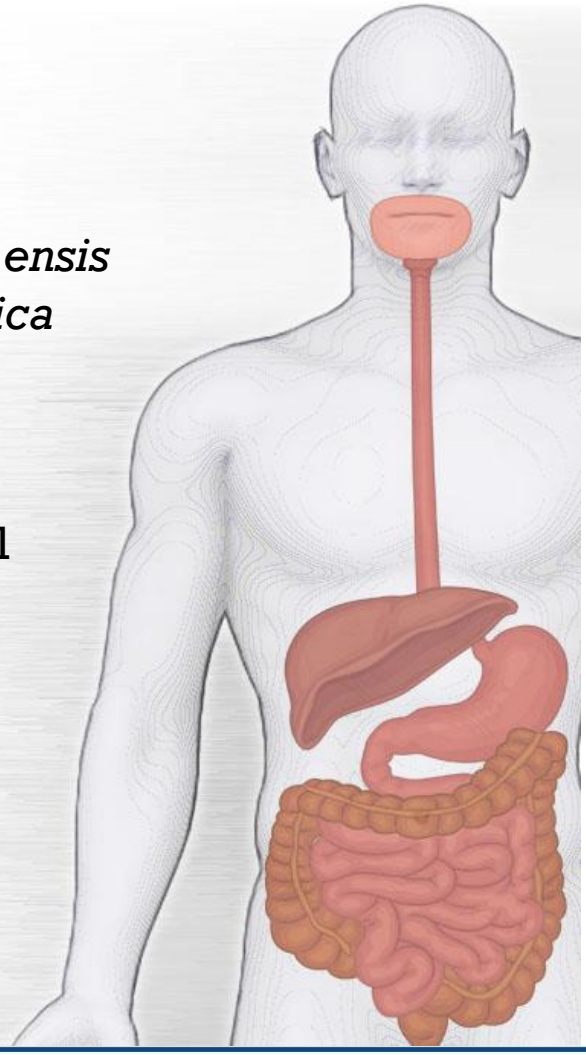
GI Panel

Bacteria:
Campylobacter
Clostridium difficile (Toxin A/B)
Plesiomonas shigelloides
Salmonella
Vibrio
Vibrio cholerae
Yersinia enterocolitica

Diarrheagenic *E. coli / Shigella*
E. coli O157
Enteroaggregative *E. coli* (EAEC)
Enteropathogenic *E. coli* (EPEC)
Enterotoxigenic *E. coli* (ETEC)
Shiga-like toxin-producing *E. coli* (STEC)
Shigella/Enteroinvasive *E. coli* (EIEC)

Protozoa:
Cryptosporidium
Cyclospora cayetanensis
Entamoeba histolytica
Giardia lamblia

Viruses:
Adenovirus F 40/41
Astrovirus
Norovirus GI/GII
Rotavirus A
Sapovirus



FUTURO METAGENOMICA

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Review

Computational Metagenomics: State of the Art

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Abstract

Computational metagenomics has revolutionized our understanding of the human microbiome, enabling the characterization of microbial diversity, the prediction of functional capabilities, and the identification of associations with human health outcomes. This review provides a concise yet comprehensive overview of state-of-the-art computational approaches in metagenomics, alongside widely used methods and tools employed in amplicon-based metagenomics. It is intended as an introductory resource for new researchers, outlining key methodologies, challenges, and future directions in the field. We discuss recent advances in bioinformatics pipelines, machine learning (ML) models, and integrative frameworks that are transforming our understanding of the microbiome's role in health and disease. By addressing current limitations and proposing innovative solutions, this review aims to outline a roadmap for future research and clinical translation in computational metagenomics.

Keywords: computational metagenomics; microbiome; *16S* sequencing; bacterial genomics; computational tools; phylogenetic colocation; machine learning (ML)

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1. Introduction

The human microbiome, a complex ecosystem of microorganisms, plays a fundamental role in host physiology and disease [1]. High-throughput sequencing technologies have provided unprecedented insights into its composition and function. However, the sheer volume and complexity of metagenomic data—characterized by high dimensionality, sparsity, and compositionality—present formidable analytical challenges that require robust computational solutions [2,3].

Microbial communities residing in and on the human body have a profound impact on host physiology, immunity, and metabolic processes [1]. The advent of next-generation sequencing (NGS) technologies, particularly whole-genome shotgun (WGS) sequencing and

OTTIMIZZAZIONE PER LA DIAGNOSI RAPIDA ED EFFICACE

- Migliorare la fase Pre-pre-analitica (Necessità di richiedere esami mirati per ridurre la possibilità di risultati anomali e tardivi)
- Pannelli Multipli
- Test reflex
- Presenza di procedure e protocolli (Algoritmi Diagnostici)
- Scelta dei test diagnostici utili alle esigenze della clinica
- Sostenibilità del personale nella gestione degli strumenti
- Disponibilità di risorse e ottimizzazione delle stesse
- Formazione del personale e cultura del life long learning
- Comunicazione efficace **e confronto continuo con i clinici**
- Partecipazione ai processi di qualità (VEQ)

GRAZIE PER L'ATTENZIONE