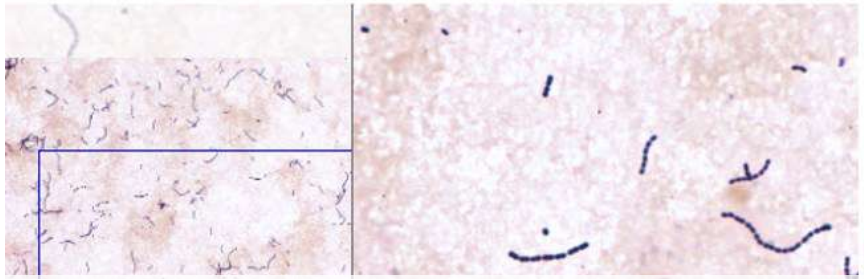
Universität Zürich[UZH]

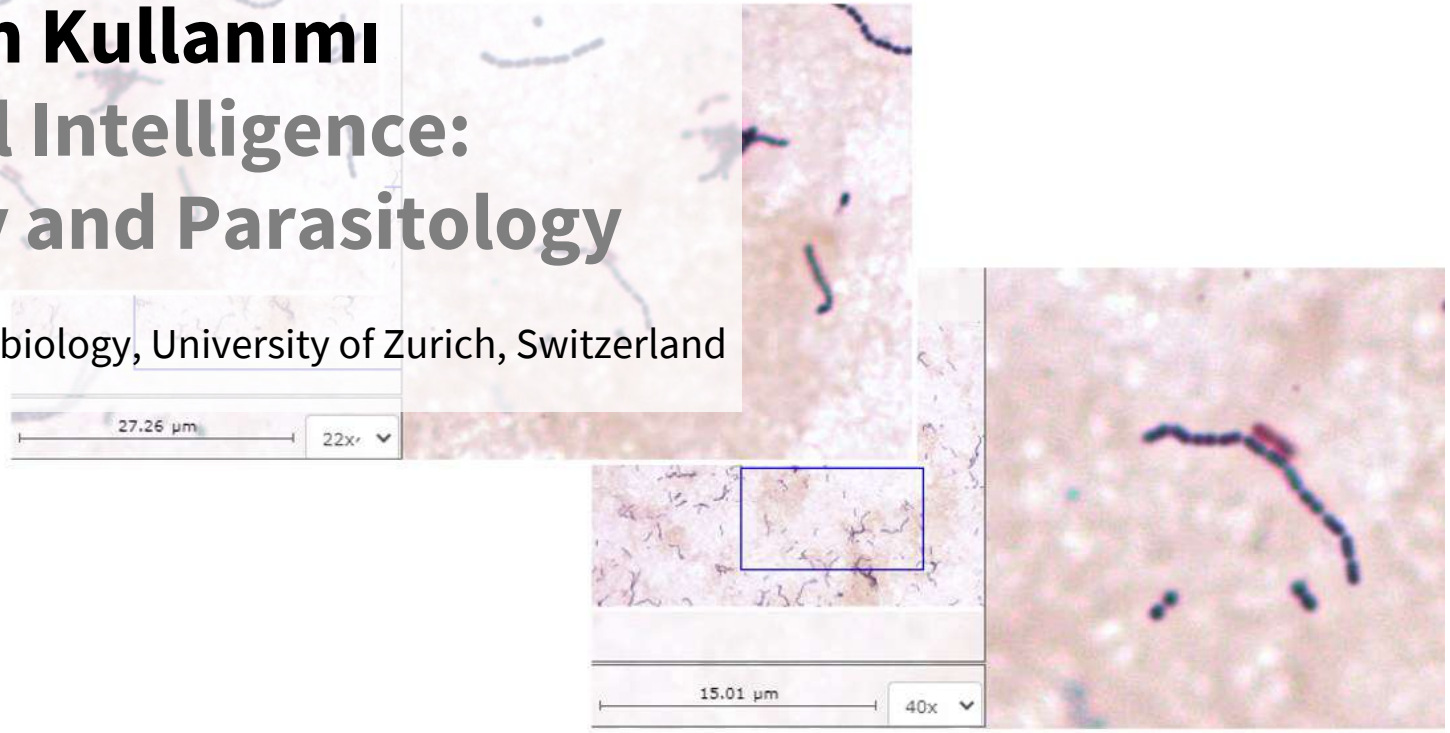
Institute of Medical Microbiology (IMM)



Mikroskoptan Yapay Zekaya: Mikrobiyoloji ve Parazitolojide Yapay Zekanın Kullanımı

From Microscope to Artificial Intelligence: The Use of AI in Microbiology and Parasitology

Dr. Oliver Nolte
Head Department Diagnostics, Institute of Medical Microbiology, University of Zurich, Switzerland



Learning objectives

Structure of my lecture and **key points/objectives** to take away from today

— **AI in diagnostics** – **applications** in labs and **interaction** with clinicians

— **AI/ML in a nutshell** – image analysis and **conceptual basis**

— **slide-scanning, digital microbiology, use cases** – limitations, benefits and supporting role of AI

  — Malaria: *Plasmodium* detection – **limitation** of automation

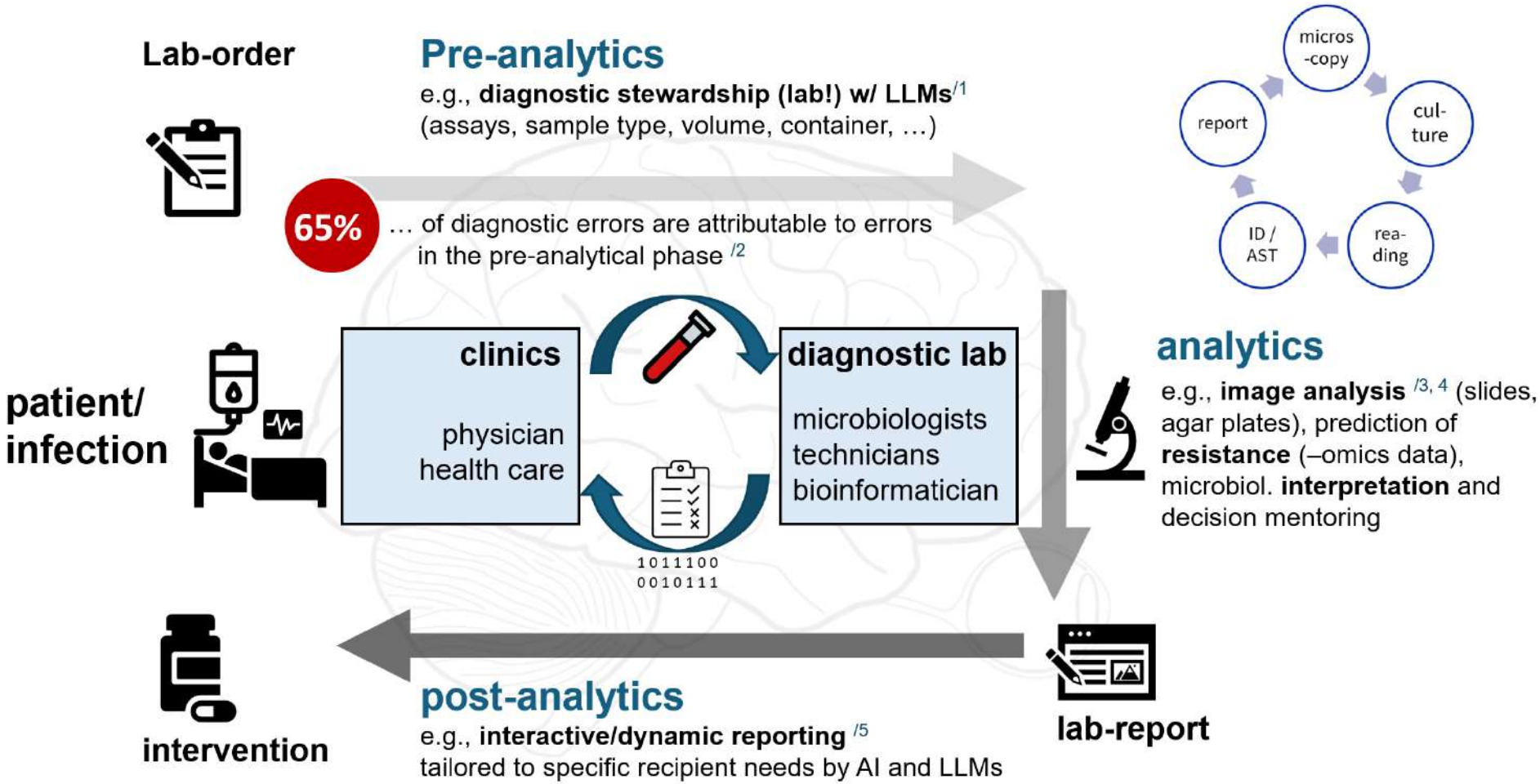
  — intestinal parasite detection – possible **benefits** and support

  — bacteriology – **implementation** concept, standardization and daily use

— **conclusion AI in microscopy** – **partner** in labs of tomorrow

The diagnostic circle – work together

Potential AI/ML support



References

/1 Bressan, M., Meijer, E., Nolte, O., … Egli, A. (2025): acc.: Poster ESCMID Global

/2 Lange, F. (2023): Clin. Chem. Lab. Med.

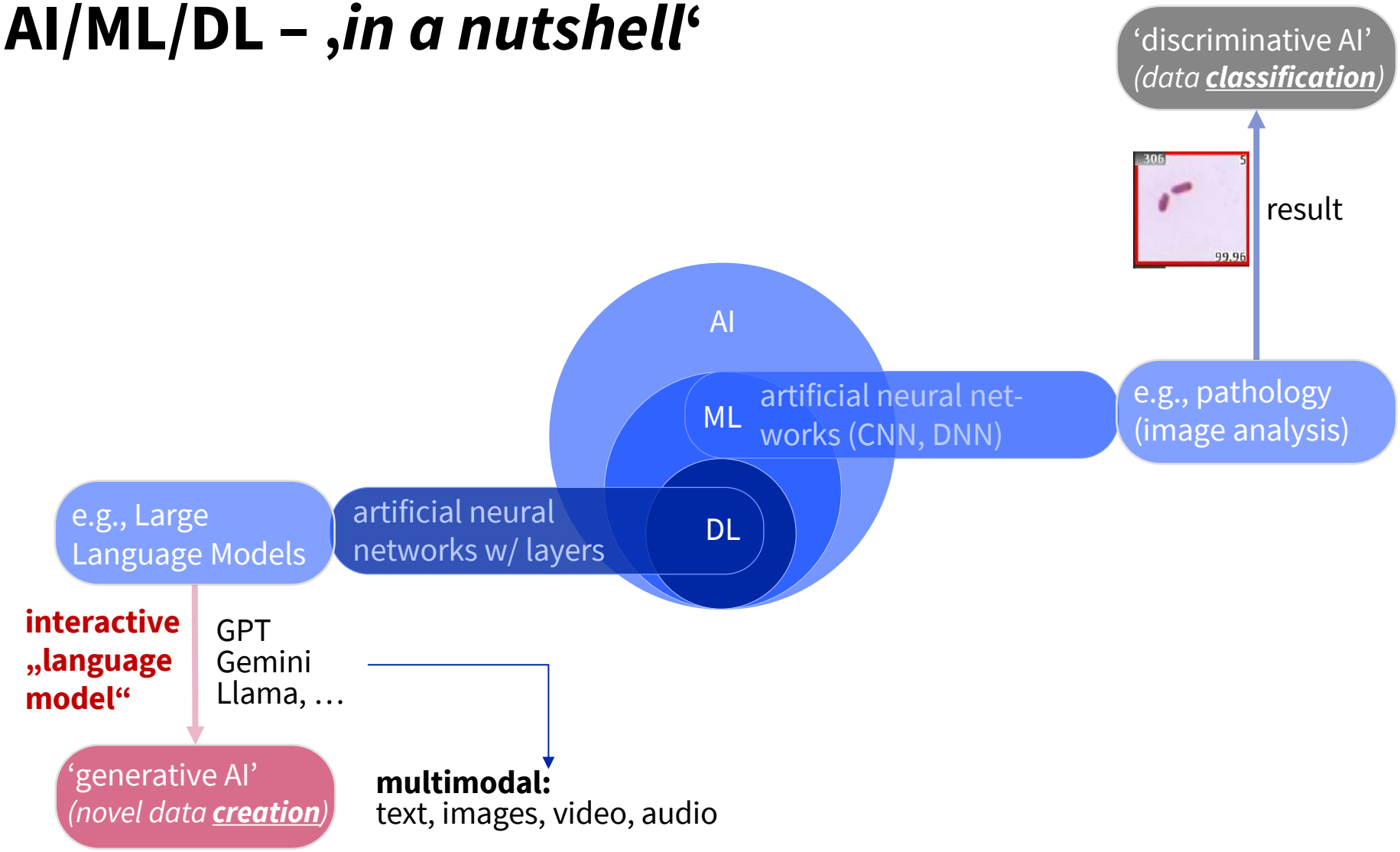
/3 Walter, C., ... & Nolte, O. (2024): J.Clin. Microbiol.

/4 Giske, C,… Nolte, O., & Egli, A. (2024): J. Clin. Microbiol.

/5 Mutschler, E... Nolte, O., Egli, A., & Seth-Smith, H. M. (2024): PeerJ, 12, e17673.

concept: Egli A., Nolte O. (2025): BIO*spektrum*

AI/ML/DL – *‚in a nutshell‘*



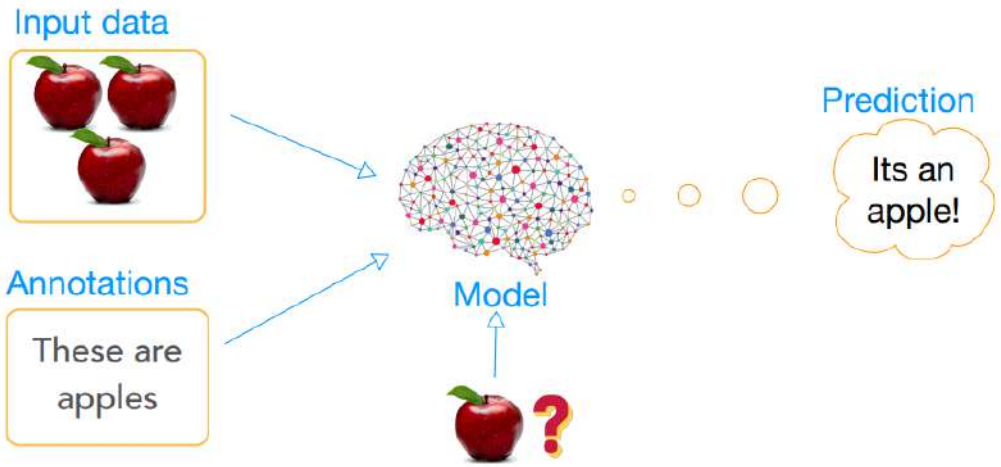
Artificial intelligence (AI):
A set of rules that allows a computer [software] to make decisions and perform tasks that would normally be done by a human brain.

Machine learning (ML):
A subset of AI algorithms that are **adaptive** and evolve over time (learning from data, predicting the future).

KAUSHAL, V., & GUPTA, R. (2022)
Technologies for Improving Healthcare
(adapted)

Types of Machine Learning (… in a nutshell)

Supervised Learning

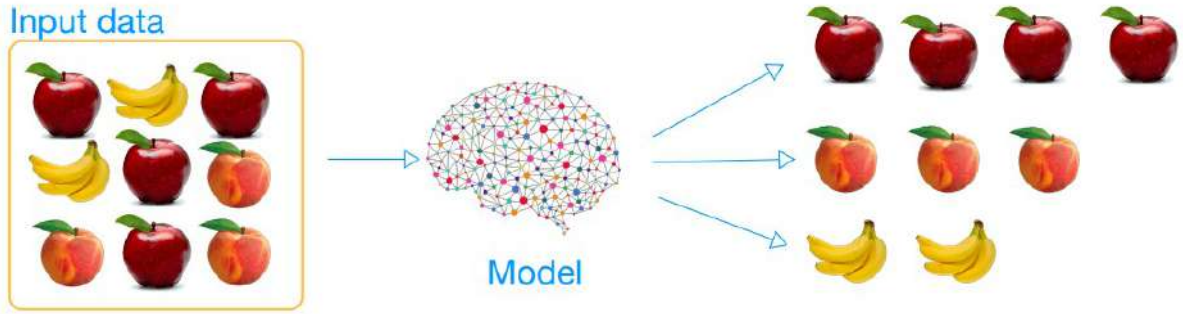


training data set w/ pre-classified data

https://devopedia.org/supervised-vs-unsupervised-learning

Types of Machine Learning (… in a nutshell)

Supervised Learning **Unsupervised Learning**



Modell searches for patterns, classifies by itself

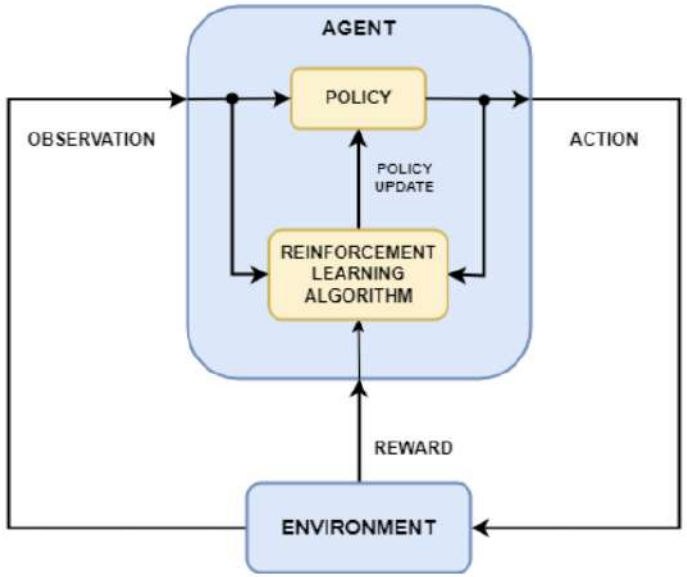
https://devopedia.org/supervised-vs-unsupervised-learning

Types of Machine Learning (… in a nutshell)

Supervised Learning

Unsupervised Learning

Reinforcement Learning
«Learning through reward»



AI «learns» independently to maximize “reward”

https://ch.mathworks.com/

Types of Machine Learning (… in a nutshell)

environment

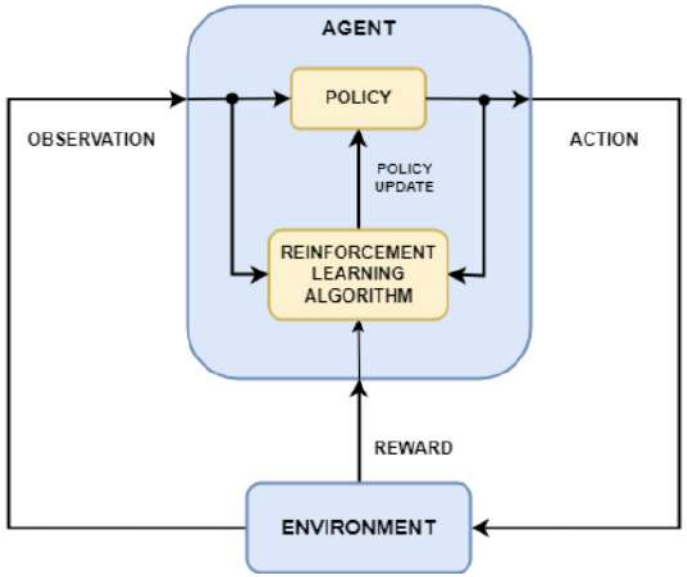
controller uses readings from cameras, accelerometers, gyroscopes, a GPS receiver, and lidar (**observations**)

steering, braking, and acceleration commands (**actions**)

vehicle computer = **agent**

policy = mapping that selects actions based on the observations from the environment

Reinforcement Learning
«Learning through reward»



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https://ch.mathworks.com/ | www.automobil-industrie.vogel.de/

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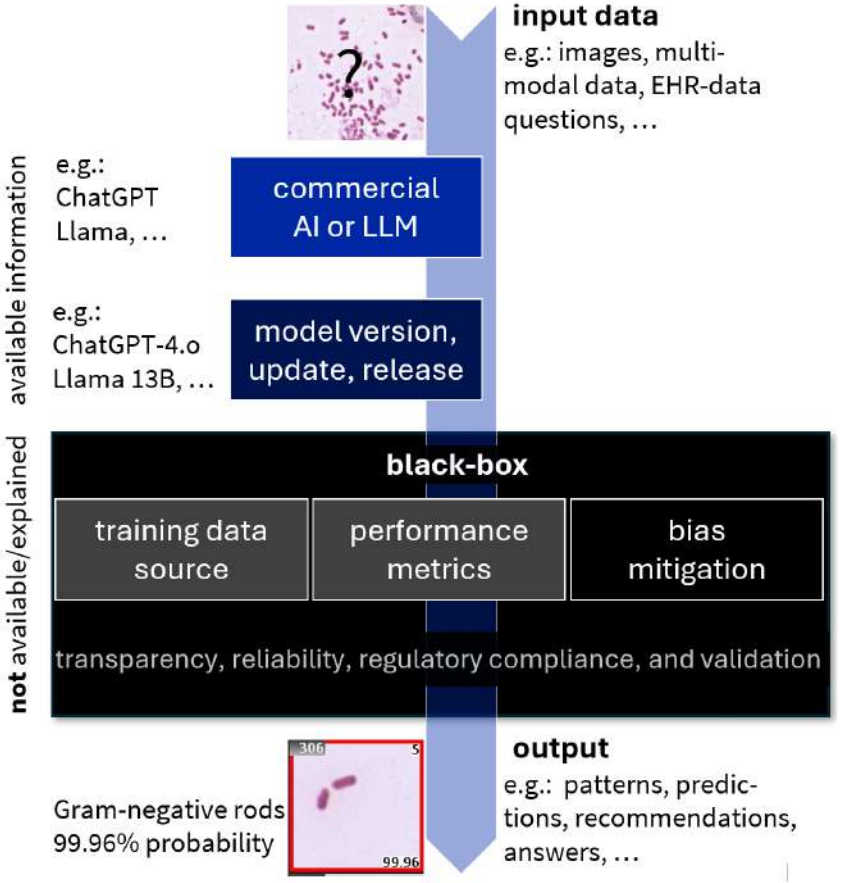
Reinforcement Learning



https://ch.mathworks.com/ | www.automobil-industrie.vogel.de/

Slide scanning and digital microbiology/pathology

Manufacturer	Product	Target area	Regular status
CellaVision (Sweden)	DM96 slide scanner	Hematology, WBC detection & diff.	FDA
		single RBC imaging and classification w/ *Plasmodium*, *Babesia* detection	Research
Metasystems (Germany)	Metafer Slide scanner/ Neon, MetaCyte SW	Gram-stained slides, auramine stain	CE-IVD
Motic Digital Pathology (China/USA) w/ Applied Spectral Imaging ASI (Germany)	EasyScan GO	Malaria (blood smear, Plasmodium detection)	Under development
Techcyte (US)		Gram-stained slides 3rd party scanners	CE-IVDD (EU), RUO (US)
West Medica (Austria)	Vision Gram	Gram-stained slides (vaginal swabs)	RUO

ChatGPT DeepResearch, verified w/ various WWW and NCBI sources

WBC white blood cells, RBC red blood cells

Malaria – microscopy as gold standard

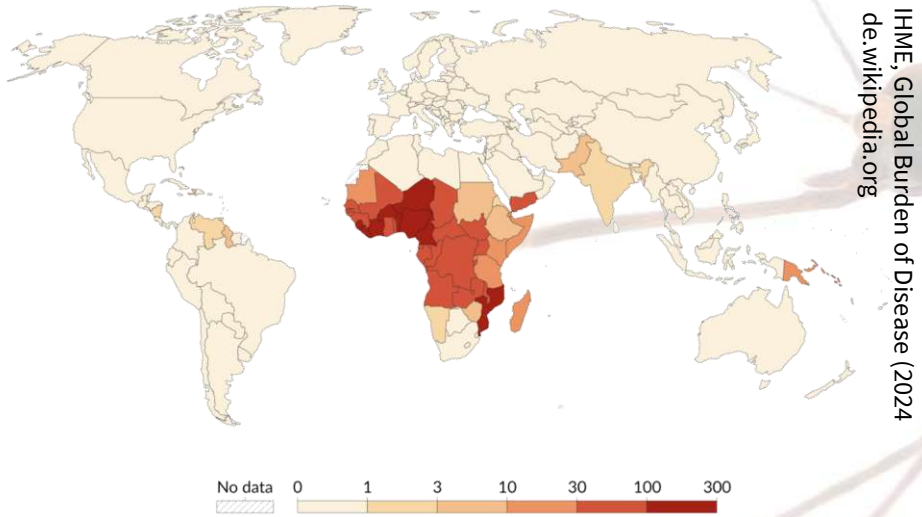
Malaria disease/mortality burden 2023 (WHO)

Disease burden: 247 Mio (228 - 267 Mio)

Malaria-related death: 619 000 (565 000 - 680 000)
(67% children <5y)

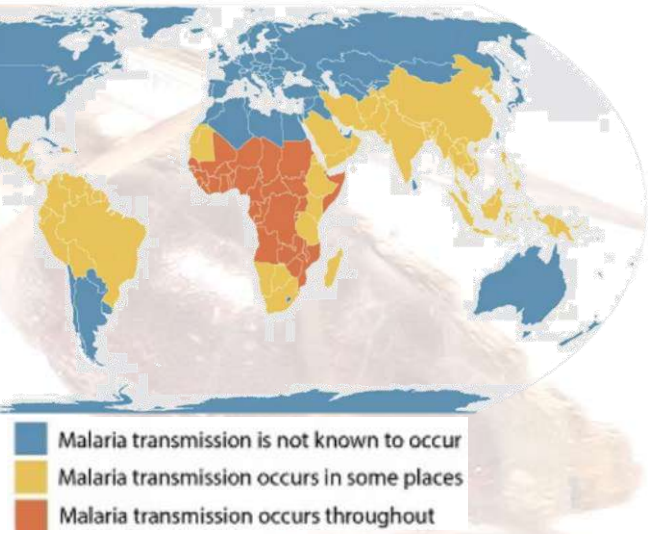
Death rate from malaria, 2021

Estimated number of deaths from malaria per 100,000 people.



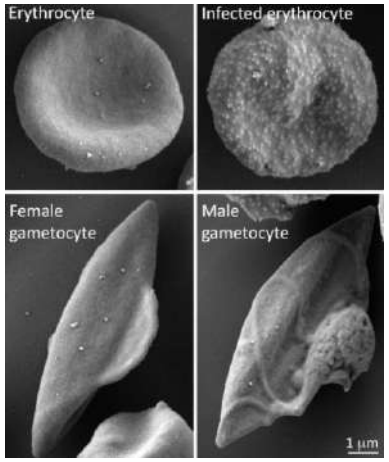
IHME, Global Burden of Disease (2024
de.wikipedia.org

Malaria endemicity

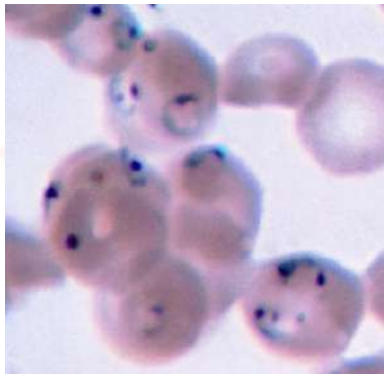


de.wikipedia.org

Plasmodium falciparum
(Maier GA et al (2019):
Trends.Parasitol **35**:6



Plasmodium falciparum
ring stages, blood smear
(animalia-life.club; modified)



Diagnostics:

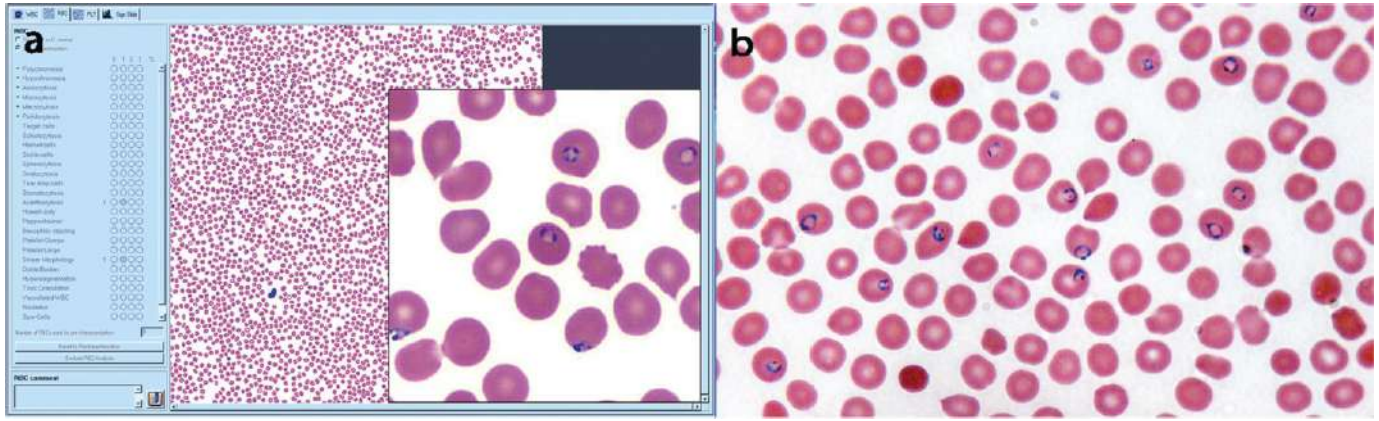
Microscopy (thick blood smear) - **gold standard**
RDTs (POC in endemic regions)
PCR (highly sensitive, high complexity and cost [at least LMIC])

background: Anopheles gambiae (en.m.wikipedia.org; modified)

Plasmodium detection by automated AI-powered microscopy

CellaVision DM96 hematology (!) analyzer, positive for *Plasmodium*

Conventional blood smear, positive for *Plasmodium*



System utilizes neural networks to locate, digitize, and pre-classify white blood cells (100x/oil) and characterize red blood cell morphology (50x/oil; not approved for intra-cellular parasites)

Malaria:
rapid and accurate dx
Plasmodium species and parasitemia **required** for **treatment** initiation

microscopy still **reference** method
Giemsa staining, ring stages of trophozoites

min **5'000 cells/300 HPF**[/1] thick smear (**two !** microscopists)
→ laborious, time consuming, depends largely on highly trained staff
→ LOD 4 parasites/µl

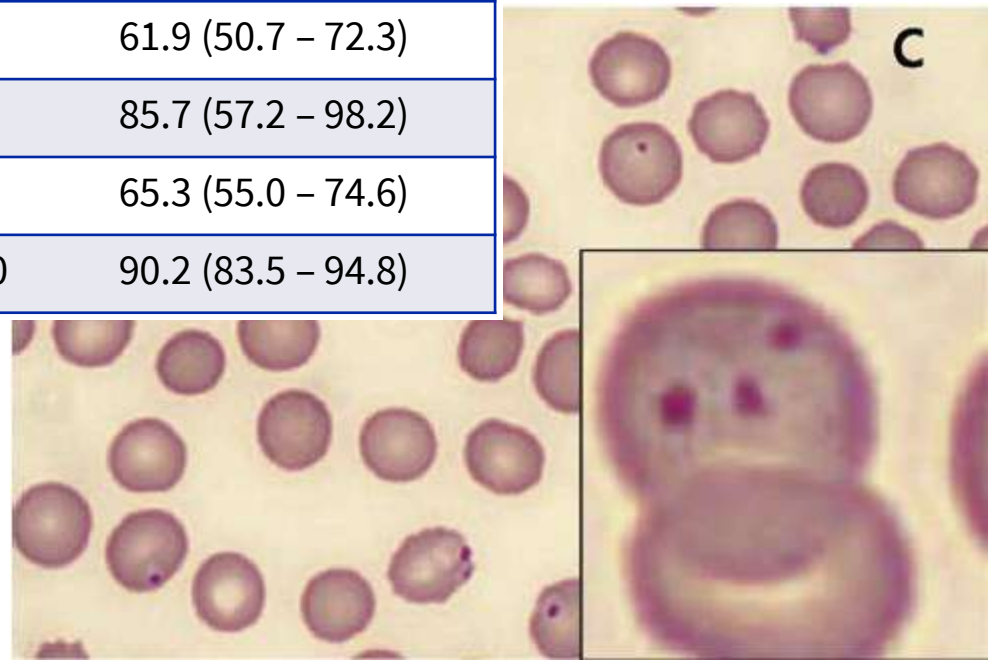
RASCA LD *et al* (2015): J.Clin.Microbiol.

[/1] HPF high power field, 100x w/ oil

Plasmodium detection by automated AI-powered microscopy

CellaVision DM96 hematology analyzer vs. microscopists

		CellaVision DM96		Conventional blood smear	
Species	**No slides**	**Autom. dtc**		**Manual dtc**	
		No pos.	Sens. (%) (95% CI)	No pos.	Sens. (%) (95% CI)
P. vivax	84 (85.7%)	19	22.6 (14.2 – 33.1)	52	61.9 (50.7 – 72.3)
P. falciparum	14 (14.3%)	4	33.3 (9.9 – 65.1)	12	85.7 (57.2 – 98.2)
total	98 (100%)	23	23.5 (15.5 – 33.1)	64	65.3 (55.0 – 74.6)
negative	122	99	81.1 (73.1 – 87.7)	110	90.2 (83.5 – 94.8)



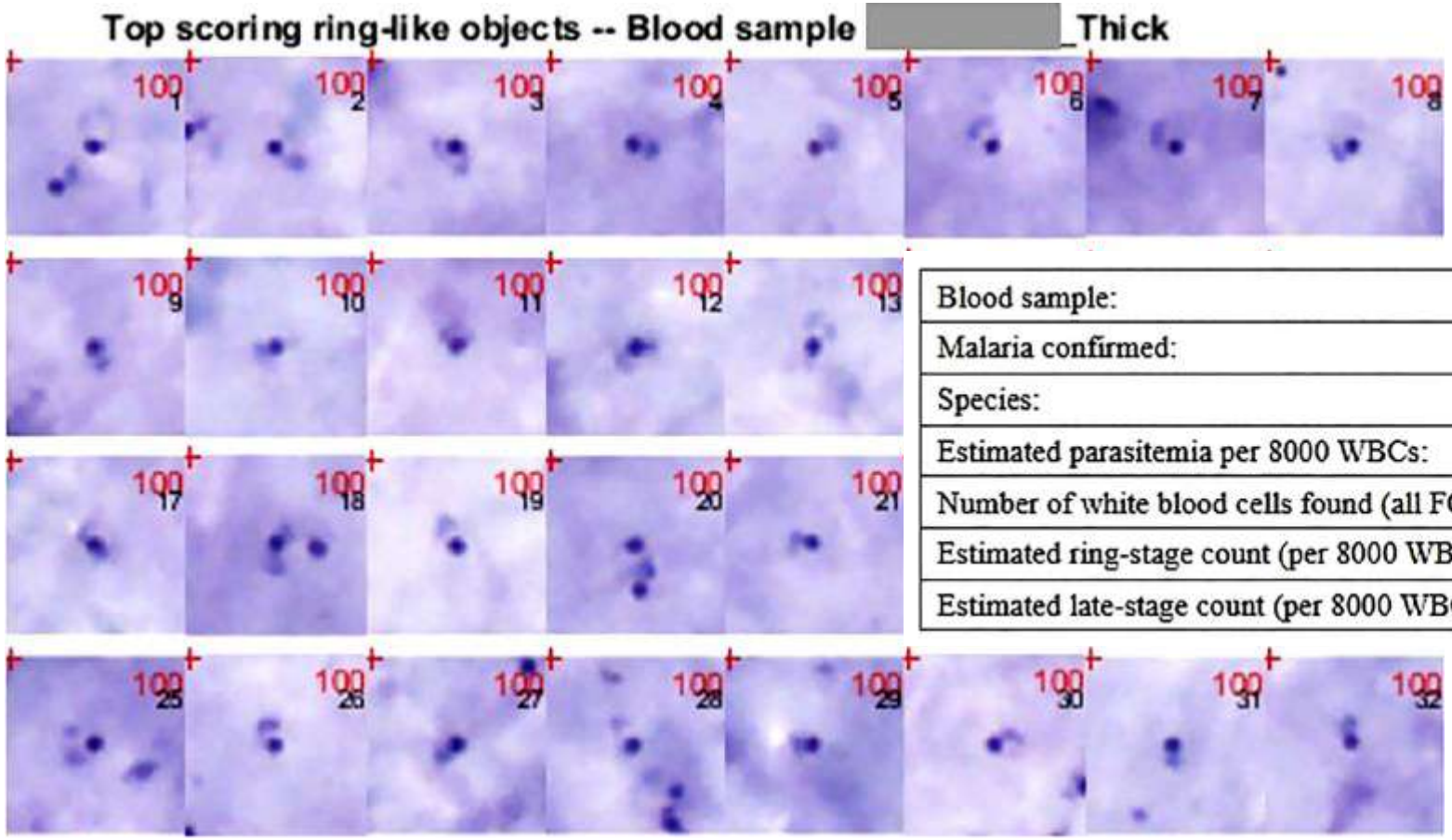
P. falciparum positive slide
visible image area of 1.17 high-power field (HPF) and 0.05 HPF

2’000 – 2’500 RBC per sample
→ threshold sensitivity appr. 1600–2000 parasites/µl
→ not sensitive enough for clinical application!

YOON J, *et al* (2019): Acta Tropica

Plasmodium detection by automated AI-powered microscopy

EasyScan GO, automated scanning microscope w/ ML software (malaria parasites in field-prep. Giemsa-stained blood films)



Blood sample:	[redacted]_Thick
Malaria confirmed:	**YES**
Species:	falciparum
Estimated parasitemia per 8000 WBCs:	54000 (range 54000 to 60000)
Number of white blood cells found (all FOV):	1117
Estimated ring-stage count (per 8000 WBCs):	54000
Estimated late-stage count (per 8000 WBCs):	<50

REES-CHANNER RR *et al* (2023): Front.Med.

Plasmodium detection by automated AI-powered microscopy

EasyScan GO, automated scanning microscope w/ ML software (malaria parasites in field-prep. Giemsa-stained blood films)

	LM vs. PCR	EasyScan GO vs. PCR	EasyScan GO vs. LM
Sens., % (95% CI) N/N_{tot}	72% (64 – 79) 111/154	69% (61 – 76) 106/154	88% (80 – 93) 99/113
Spec., % (95% CI) N/N_{tot}	100 % (99 – 100) 1046/1048	89% (87 – 91) 933/1048	89% (87 – 91) 967/1089
Likelihood ratio $^{(+)}$	377.69 (94 – 1513)	6.27 (5.12 – 7.68)	7.82 (6.53 – 9.37)
Likelihood ratio $^{(-)}$	0.28 (0.22 – 0.36)	0.35 (0.28 – 0.44)	0.14 (0.09 – 0.23)

Light microscopy (LM) as reference

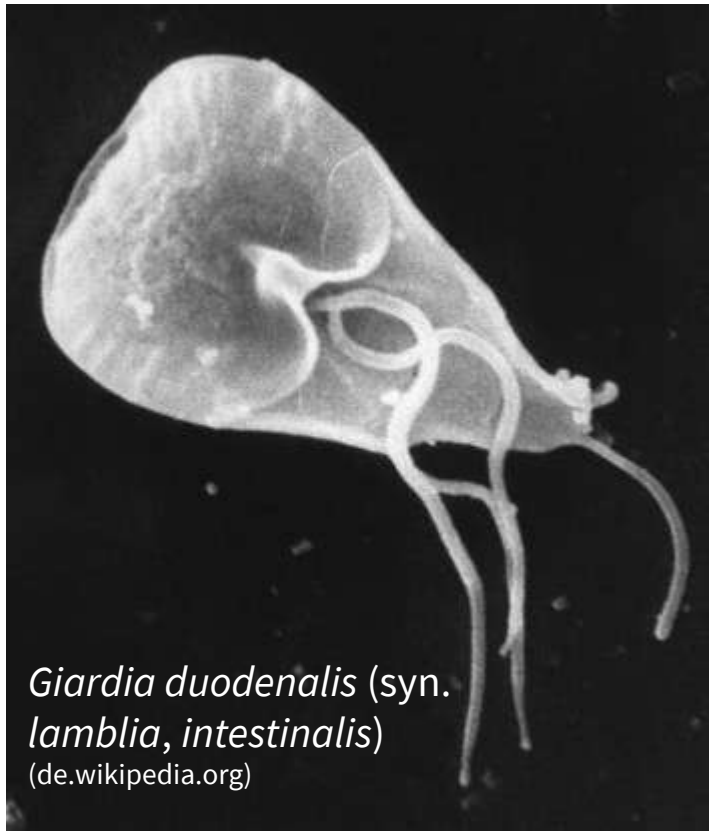
WHO: 50% samples should be within +/-25% of the true parasitemia
→ EasyScan GO: 33%
→ performance issues w/ low parasitemia, diff. of non-*falciparum* species!

REES-CHANNER RR *et al* (2023): Front.Med.

Plasmodium detection by automated AI-powered microscopy

Currently no automated scanning/detection system available to replace conventional microscopy with slide scanning and AI-enhanced *Plasmodium* detection.

Intestinal Parasitic Infections (IPI)

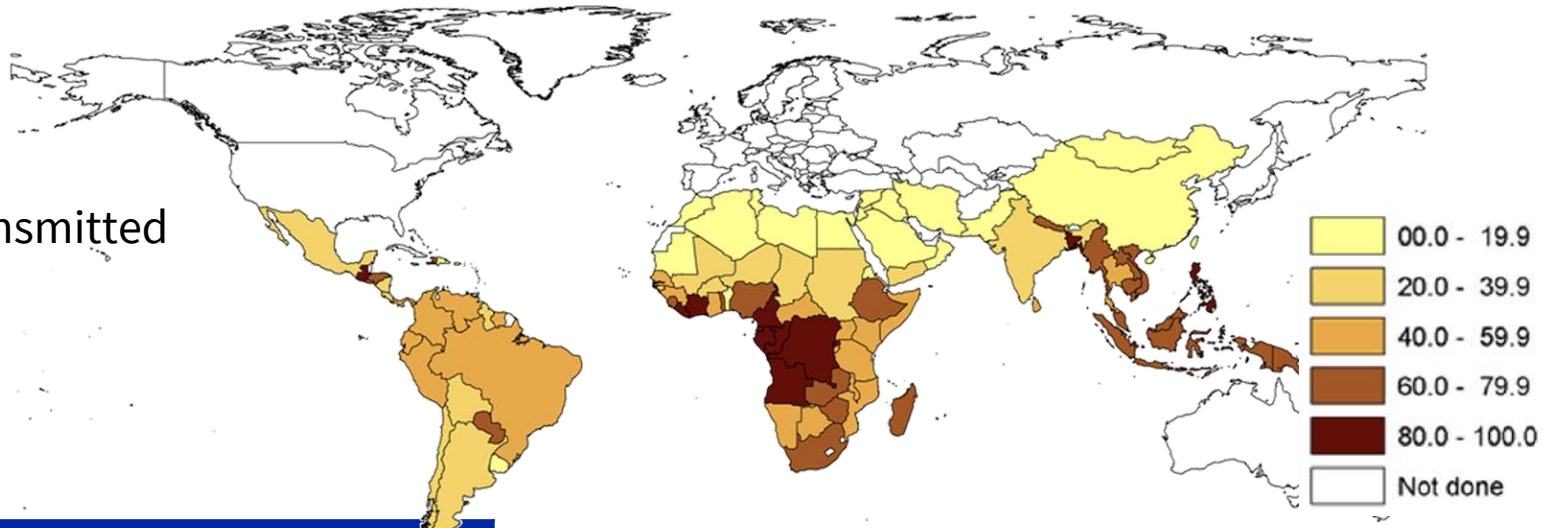


Giardia duodenalis (syn. *lamblia*, *intestinalis*)
(de.wikipedia.org)

Image analysis AI in clinical parasitology

intestinal parasitic infections (IPI)

- global burden: ~ 3,5 billion affected
- 450 mill. ill (mainly children)
- ~ ¼ human infected w/ population soil-transmitted helminth
- DALY (disability-adjusted life year):
  10 helminth infections plus toxoplasmosis
  → 8,78 mill. DALY



Prevalence of infection with any species of intestinal nematode worms (*A. lumbricoides*, *T. trichiura* and the two hookworm species *A. duodenale* and *N. americanus*), HALL A et al (2009).

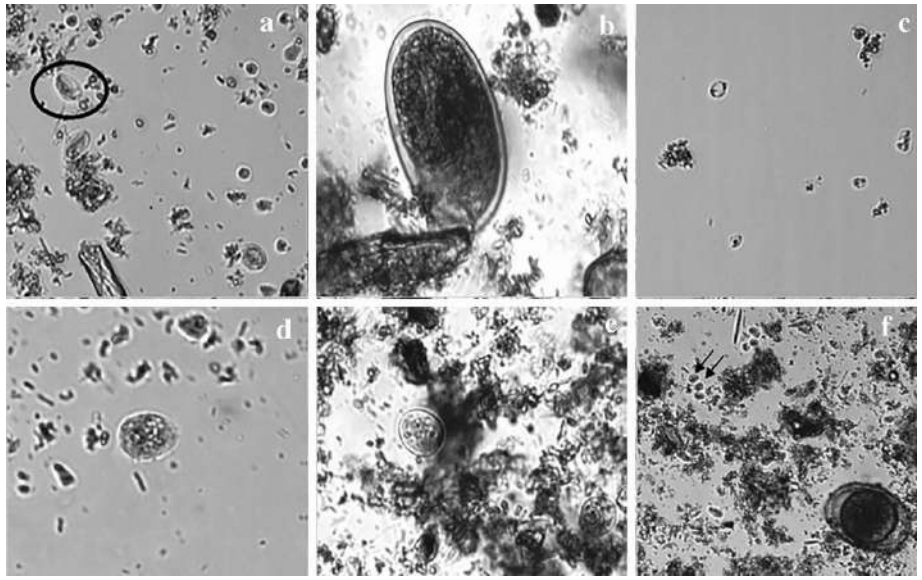
intestinal parasites	
protozoa	**helminths**
Giardia duodenalis (syn. *lamblia*, *intestinalis*)	*Enterobius vermicularis*
Cryptosporidium parvum, *C. hominis*	*Ascaris lumbricoides*
Blastocystis spp.	*Trichuris trichiura*
Cyclospora cayetanensis	*Anyclostoma duodenale*
Cystoisospora belli	*Necator americamus*
Entamoeba histolytica	AHMED M (2023)

KAMINSKY & MÄSER (2025): *Front. Parasitol.* **4**:1546195, Hall A., et al (2009): PLoS Trop.Negl.Dis. **3**:3 e402, AHMED M (2023): Gastroenterol. Res. **16**:3

Image analysis AI in clinical parasitology

ova and parasite examination (O&P) …

- detection of helminth eggs, or larvae, cysts of protozoans, trophozoites
- manual light microscopy (gold standard) (MATHISON B.A., *et al*, 2020)
- variable sensitivity (biological variation, ability of technologist, operator, lab-specific variation)
- time-consuming, resource-intensive
- lost, or at least “dying arts in microbiology”
  - technologists are more attracted by modern methods
  - decline in prevalence = loss of training



Images from SediMAX2 software. **a**. *G. lamblia* cysts (circled) **b**. Hookworm egg **c**. *B. hominis* vacuolar stage **d**. *E. hystolitica*/*dispar* cyst **e**. *E. coli* cysts **f**. Double infection: *E. nana* cysts (arrows) & *A. lumbricoides* egg.

FERNÁNDEZ-RIVAS, G *et al* (2021): *Sci Rep* **11**, 13105, MATHISON B.A., *et al* (2020): J. Clin. Microbiol. **58**:6

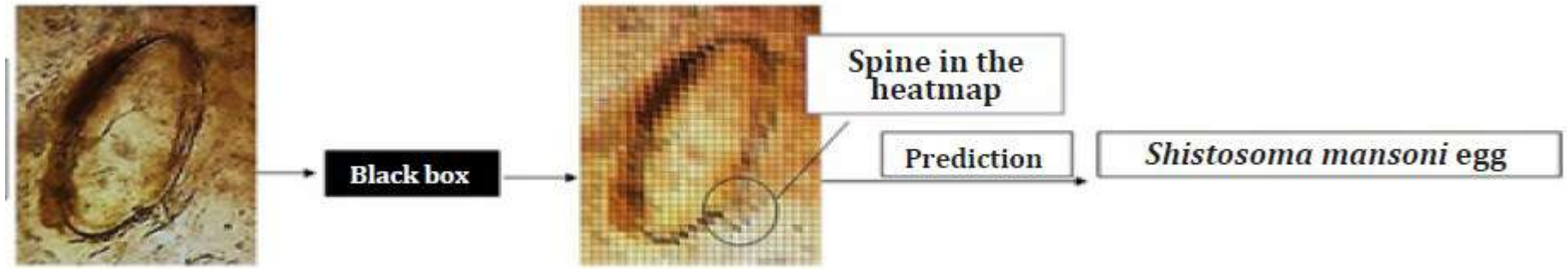
Image analysis AI in clinical parasitology

Two concepts:

Screening for **negative** slides
→ **low** prevalence settings, labelling of **positive** slides **for review**

Pre-classification of **positive** slides (w/ **presumptive identification** of parasites)
→ **high** prevalence areas

!**confirmation** by technologist/ microbiologist **required**!



EL SAFTAWY EA (2023) PUJ

Image analysis AI in clinical parasitology

commercial SediMAX2® (A. Menarini, urine sediment analyzer)

automated processing of wet mounts

- *transfer to cuvettes and dilution*
- 20 whole-field high-definition images (3 scans per sample)

sample set

- 197 stool samples (178 patients)
- 146 positive samples
  - *124 with one parasite only*
  - *24 double- or triple-infections*
- 54 negatives

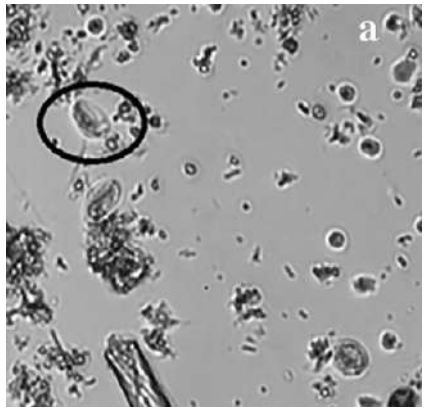
over-representation of positive samples

results

- 16/197 discrepant
- 13 false negative; 2 pos./wet mount neg.

SediMAX2® comp. to wet mount	
sensitivity	89.51%
specificity	98.15%
PPV	99.22%
NPV	77.94%

on-screen analysis, 20 – 60 images
"particle detection" by neutral network but **no** AI parasitology application
review of *positive* slides (i.e., particles) by experts
relevant **time-savings**



Example of a positive image (particles detected) w/ *Giardia duodenalis* (*G. lamblia*) cyst

FERNÁNDEZ-RIVAS, G *et al* (2021): *Sci Rep* **11**, 13105

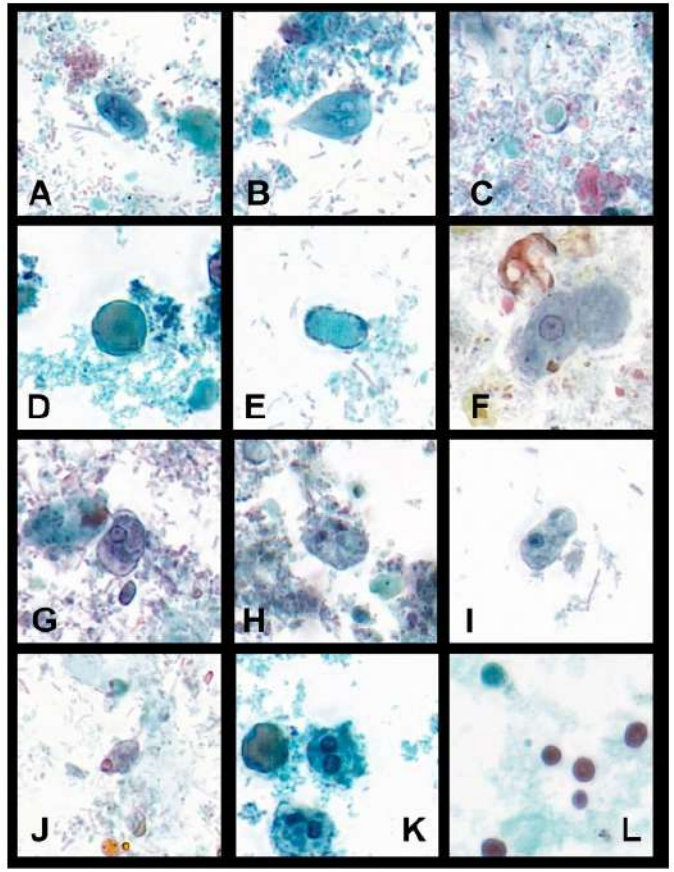
Image analysis AI in clinical parasitology

ova and parasite examination (O&P) …

- scanned trichrome-stained slides w/ coverslip
- 13.1 mm x 10.2 mm (image = scanned area)
- 108.000 x 84.400 px @82,4 magnification
- segmented to 250 x 250 px (=scenes)
- organism (parasite) usually 3% to 25% of the scene (MATHISON B.A., *et al*, 2020)
- Techcyte[/1] proprietary AI model

CNN model analysis result	O&P examination result (*n*)	
	Positive	Negative
Positive	86	2
Negative	1	104

CNN vs. O&P examination result
pos. percent agreement: 98,88% (95% CI 93,76 – 99,98)
neg. precent agreement: 98,11% (95% CI 93,35 – 99,77%)



parasite classes used
representative examples of classes as detected by Techcyte

Mathison B.A., et al (2020): J. Clin. Microbiol. **58**:6; Techcyte (https://techcyte.com/ Orem UT/USA)

Techcyte: Image analysis AI in clinical parasitology

commercial solution O&P (**RUO**, not FDA cleared)

Modified acid fast solution

- *Cryptosporidium* sp. and *Cyclospora cayetanensis* oocysts
- Yeast

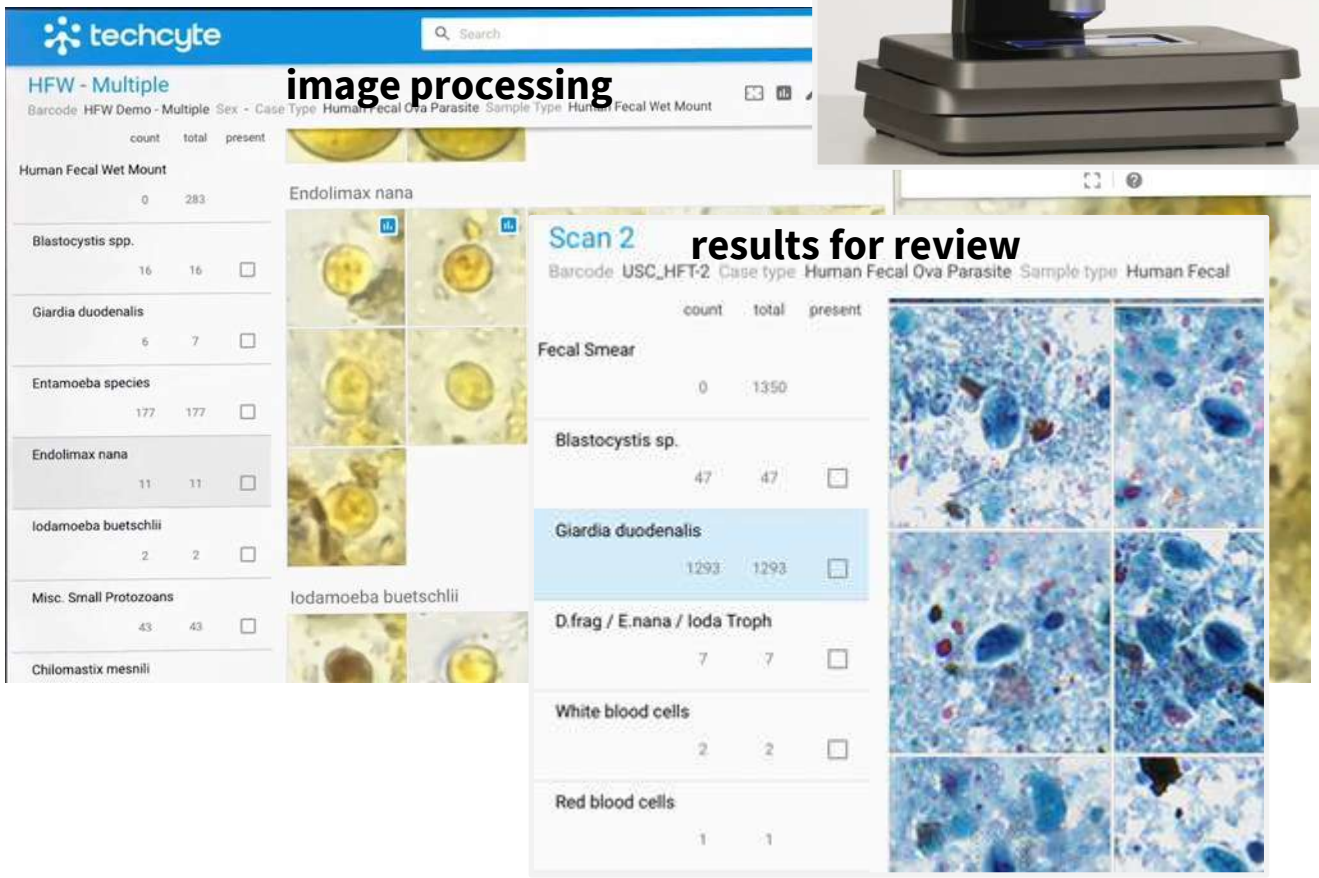
Trichrome

- parasites cysts and trophozoites
- red blood cells
- white blood cells
- yeast

wet mount

- parasites cysts and trophozoites
- helminths

Techcyte[/1] proprietary AI model



Techcyte (https://techcyte.com/ Orem UT/USA)

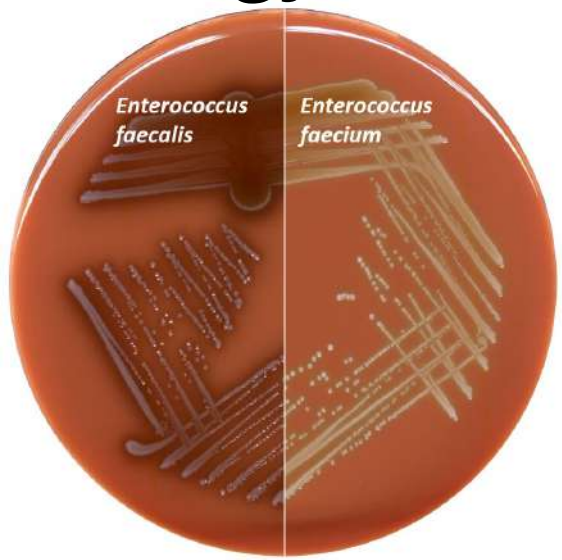
Image analysis AI in clinical parasitology

Currently no automated scanning/detection system available to replace conventional microscopy with slide scanning and AI-enhanced detection of intestinal parasites.

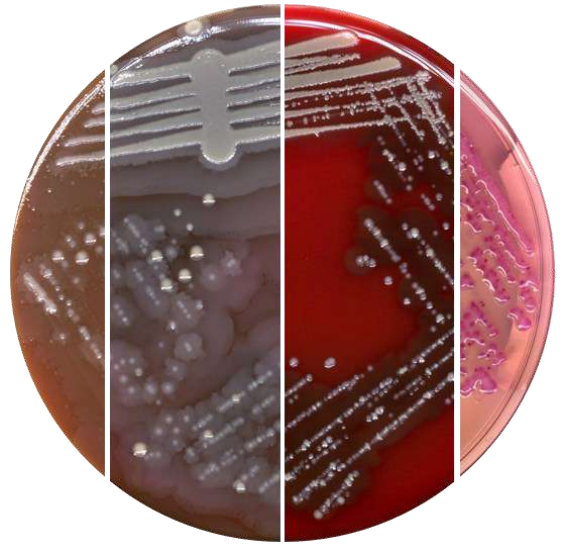
Promising solutions under development (screening for and getting rid of negatives, while positives need expert review and confirmation)

Automation and standardization in diagnostic microbiology

credits: Centre for Laboratory Medicine SG; image NOLTE



positive blood cultures, different patients and dates, 10 µl WASP® DT, 4-quadrant streaking



wound swab, four different plates, 10 µl WASP® DT, 4-quadrant streaking

Automation – Slide scanning & microscopy

ca. 1 min

step 1:

- *slide feeding* process
  - pick-up from *slide trays*
  - barcode reading
  - autom. placement microscope

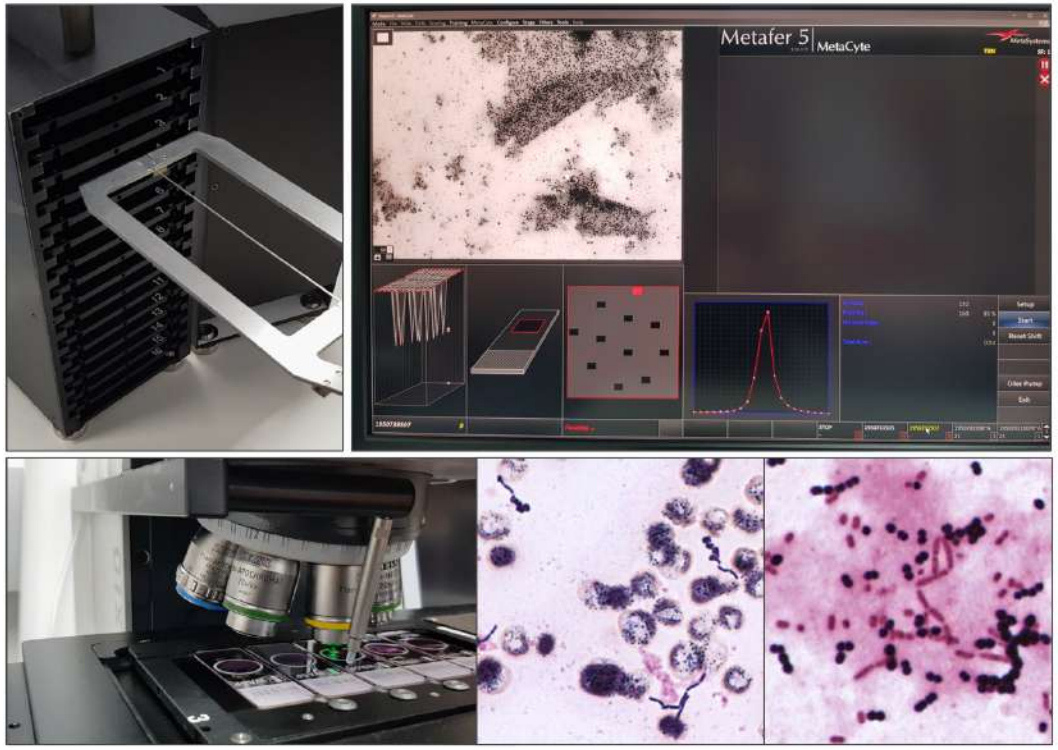
step 2:

- *pre-scan*
  - slide overview LPF (10x)

ca. 3.5 min

step 3:

- *image acquisition*
  - autom.: immersion oil
  - HPF (40x)

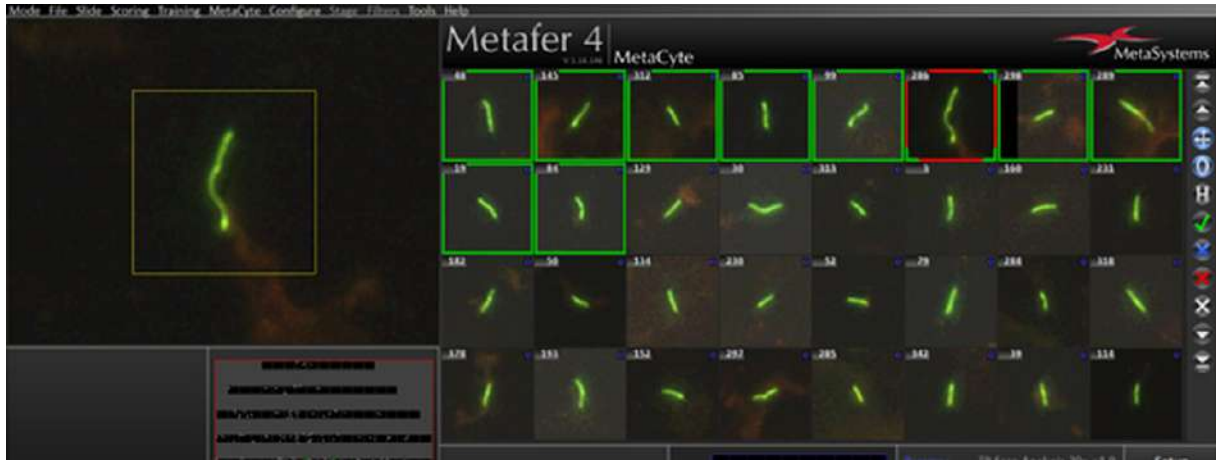


credits: Centre for Laboratory Medicine, St. Gall

AI in microscopy/auramine staining

validation study analogue screening vs. Mycobacteria*Detect*

- 928 patients, 1233 specimens (76.5% respiratory)
- 1192 slides: auramine *analogue* screening, followed by MetaCyte Mycobacteria*Detect* module (150 suspicious in both → ZN-counterstain)



Gallery-view Mycobacteria*Detect* w/ acid fast bacilli detected throughout the slide

- ground truth (positivity rate: 1.85% MGIT)
  Metafer: PPV **38.17%**, NPV **98.48%** (accuracy: 91.86%)
  significant time gain Metafer over analogue screening

BRÜLISAUER, SEIFFERT, WEISSERT, NOLTE – in preparation

WHO-recommendation
for screening auramine slides:

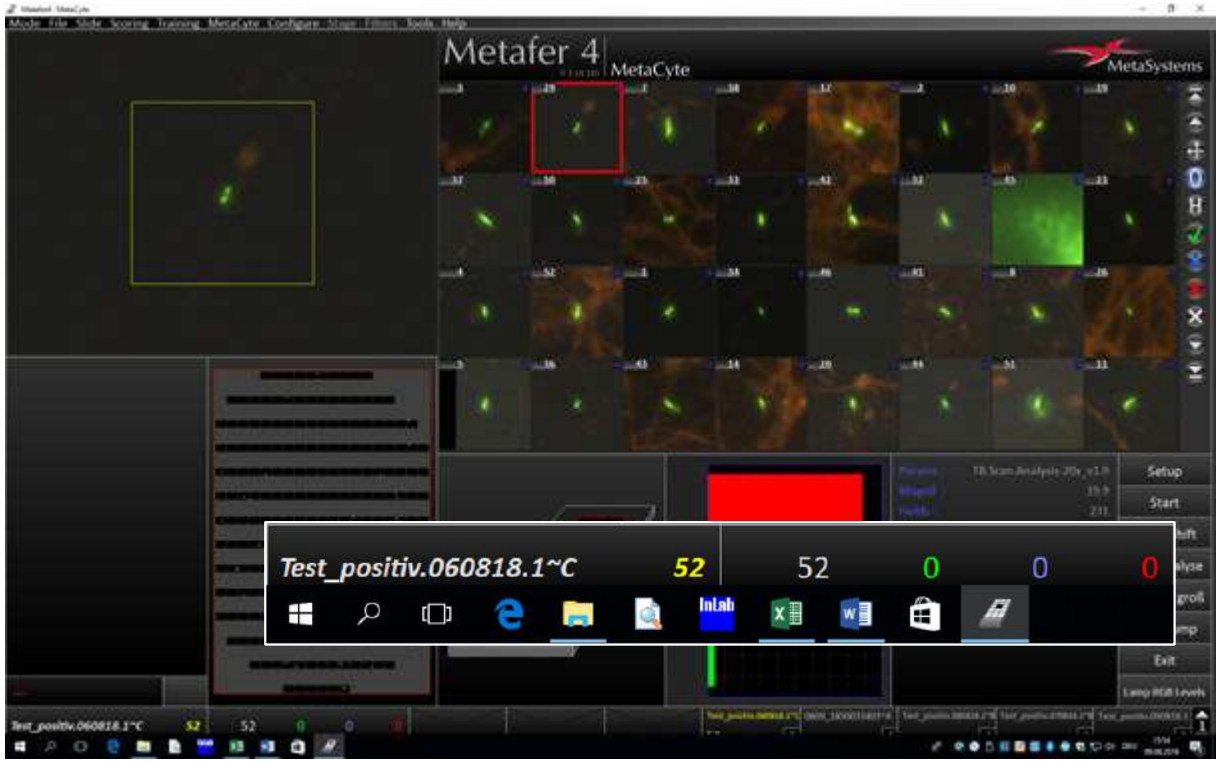
300 fields of view (40x)
~5 – 15 min per slide

auramine-positive elements need to be confirmed by counterstaining

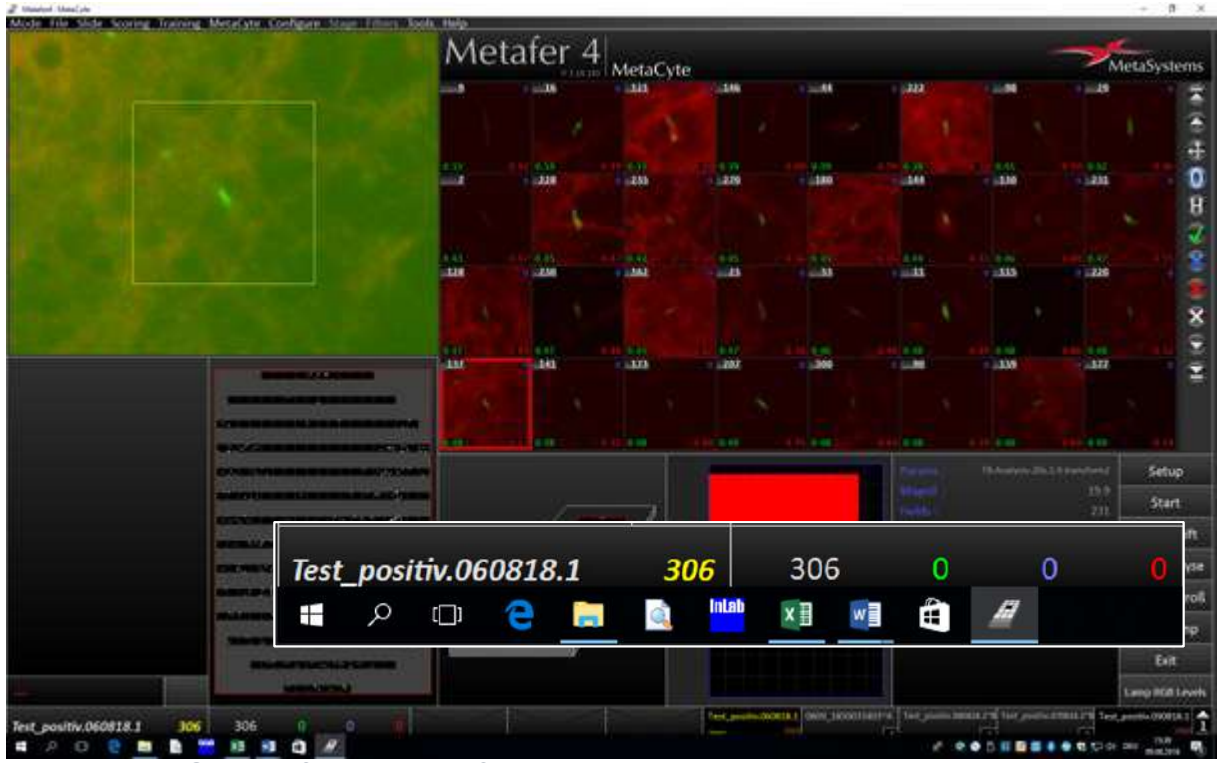
challenge:
slides w/ low mycobacterial count (i.e., 1 – 3 mycobacteria in 300 FOV)

AI in microscopy/auramine staining

Impact of different analytic classifiers in Mycobacteria*Detect*



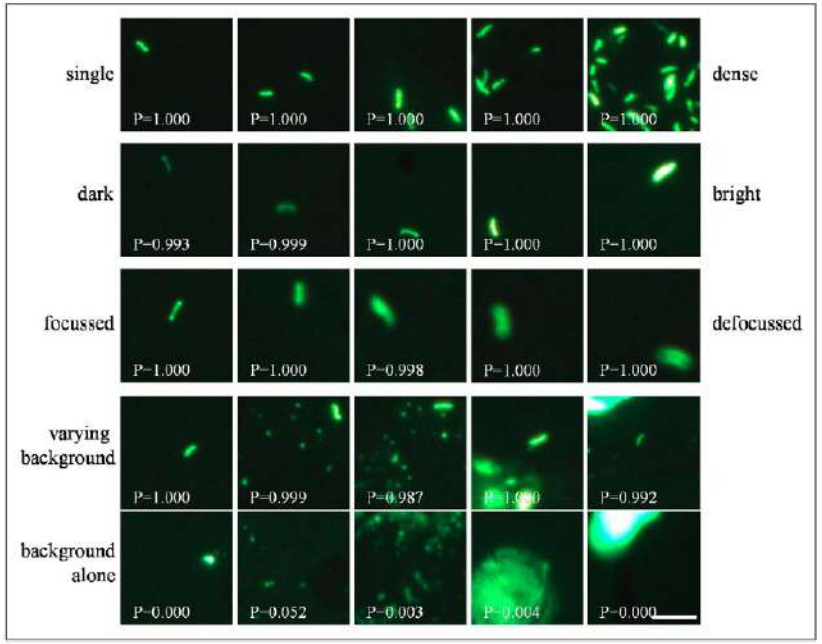
Classifier: Analysis-20x_v1.9

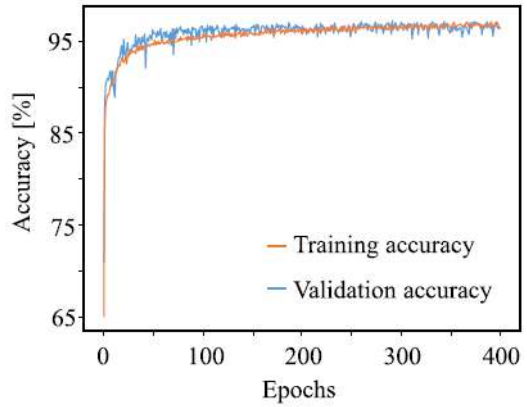


Analysis Classifier: transform2

BRÜLISAUER, SEIFFERT, WEISSERT, NOLTE – in preparation

AI in microscopy/auramine staining





HORVATH L *et al* (2020): Tuberculosis

613 auramine slides (531 for clinical validation)

culture (ground truth) vs.	sensitivity	specificity	NPV	PPV
manual microscopy	60.7%	97.5%	95.7%	72.8%
machine assisted microscopy	71.4%	93.3%	96.7%	54.3%
automated microscopy	96.4%	60.0%	99.3%	21.1%

higher sensitivity of the automated system at the cost of specificity (steep increase in false positives)

→ very high NPV!
→ **significant time gain** (10 sec. vs. rec. 5 – 15 min) per slide plus verification by expert

Do we still need GRAM-stain? Technically …

NO … - (*probably*) not for

- superficial wounds (KAFTANDZIEVA *et al*, 2012)
- burn wounds (ELSAYED *et al*, 2003)
- orthopedic samples (e.g. synovial fluid, biopsies, …)

GRAM-stain in …

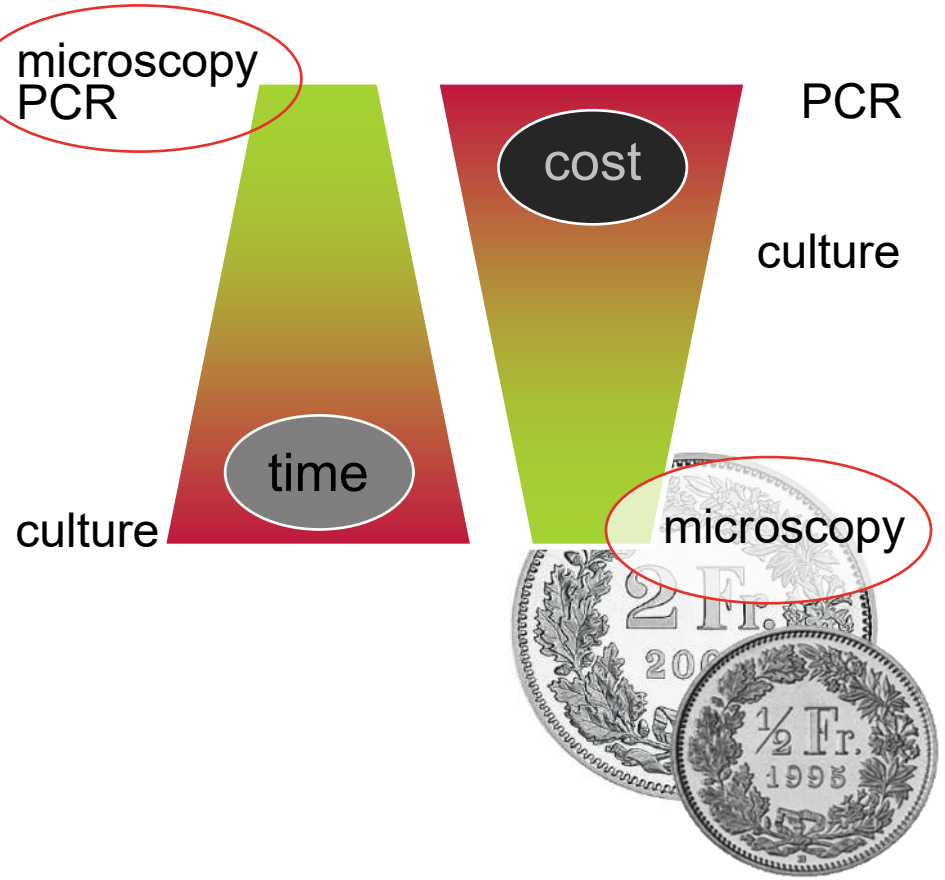
- the diagnosis of septic arthritis: 111/143 **(78%) false negative** (STIRLING *et al*, 2014)
- non-gonococcal septic/bacterial arthritis - **sensitivity ~50%** (GOLDENBERG, 1998)
- synovial fluid samples - 100/830 culture positive; GRAM **sensitivity 17%**, **specificity 99.7%** (GBEJUADE *et al*, 2019; who concluded that „… *the GRAM stain test is an unreliable investigation in diagnosing native joint infections*. “)

Do we still need GRAM-stain? Technically …

YES … because (*at least in my lab*) it's

- a comparatively **inexpensive** method (even when automated[/1])
- comparatively **fast** (< 1 hrs)
- (+/-) **standardized** and integrated in automation
- fully **digitized** and traceable
- an **indicator** of sample **quality** and guidance for downstream analytics
- a method for having a **personalized** diagnosis in short time

- and it supports **antimicrobial stewardship**



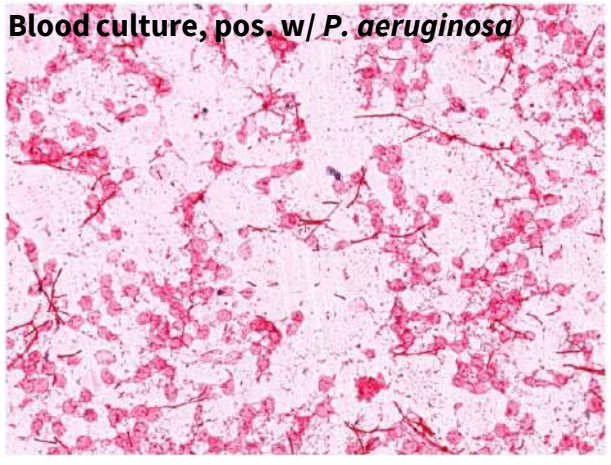
[/1] ~2.50 Fr./slide:
investment slide scanner incl. maintenance, depreciation 8 years, GRAM- and auramine scans, reagents, stainer, personnel extra;

savings in working hours not included in the calculation

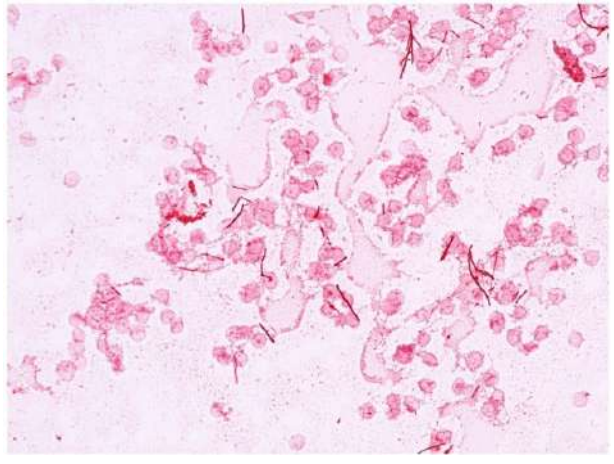
technical variation (Gram-stainers)

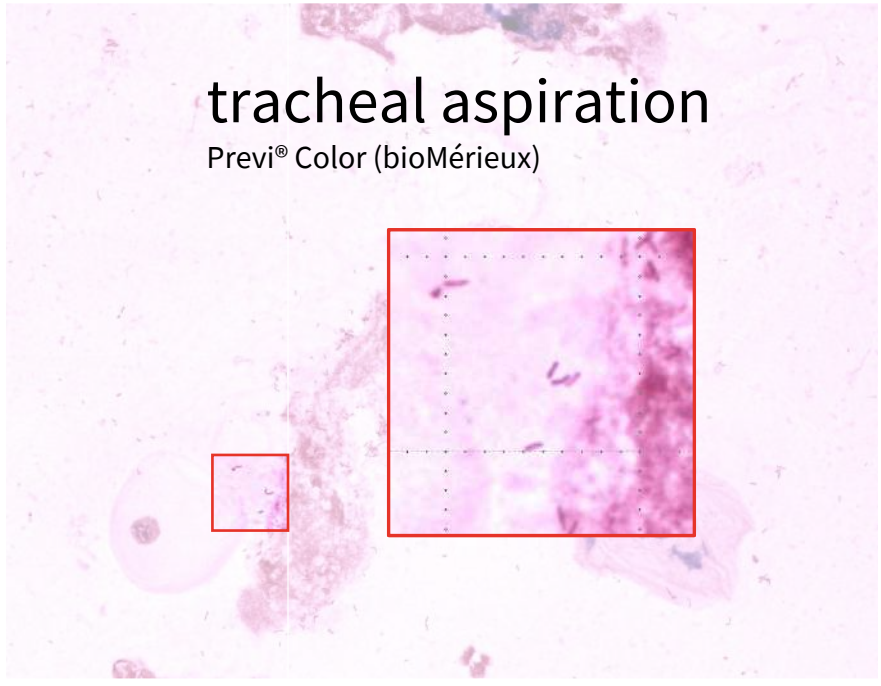
ColorAX (Axonlab)

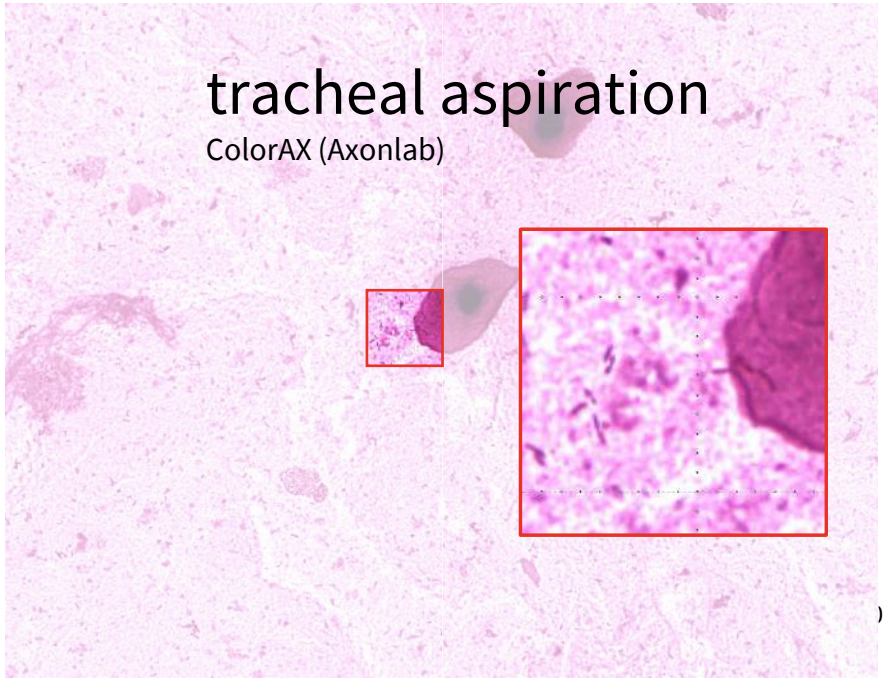
Philipp Schläpfer ZLMSG



Previ® Color (bioMérieux)





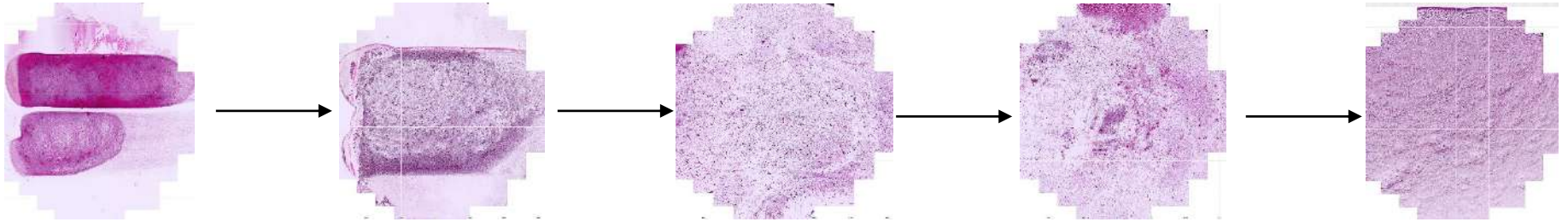


Gram-scanning technical optimization slides

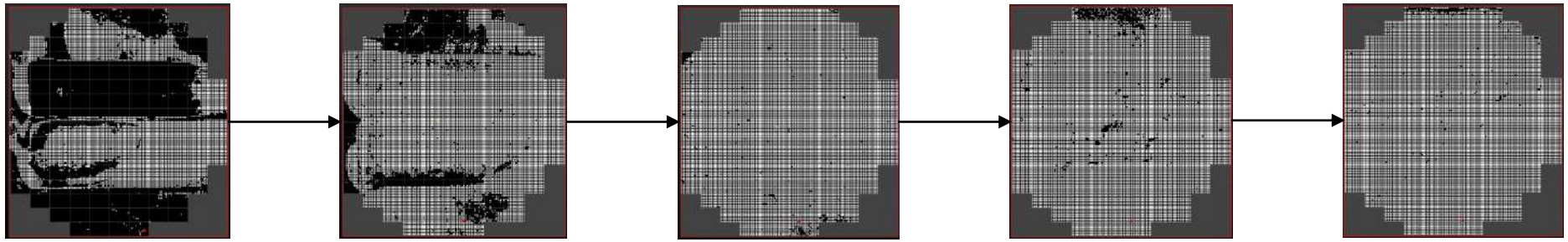
add. of NaCl and different smearing/drying techniques

manual vs. automated staining

quality of blood smear



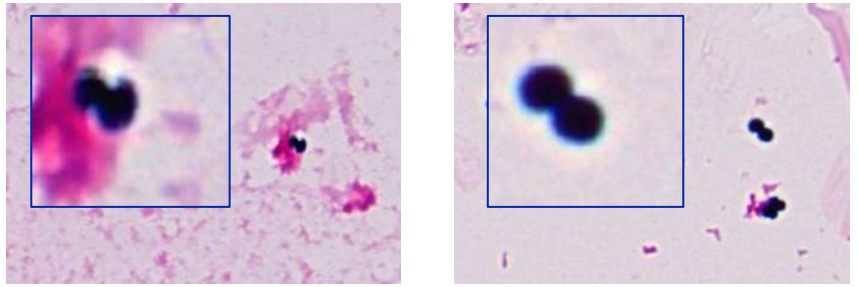
quality of slide scanning by Metafer system



vol. pos. BC

1 x 10µ | 1 x 10µl | 1 x 10µl | 3 x 1µl | 3 x 1µl

all images: low power whole slide scans w/ Metafer system



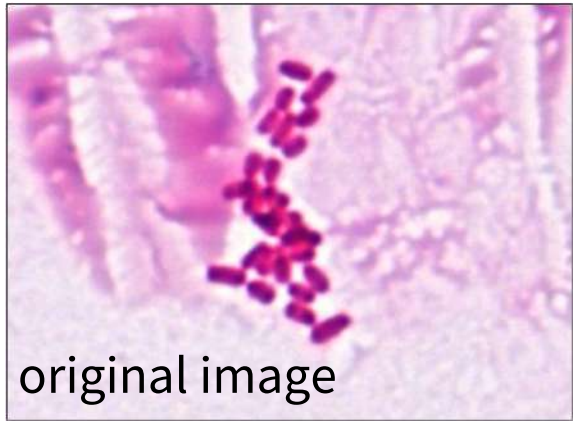
heat vs. methanol fixation

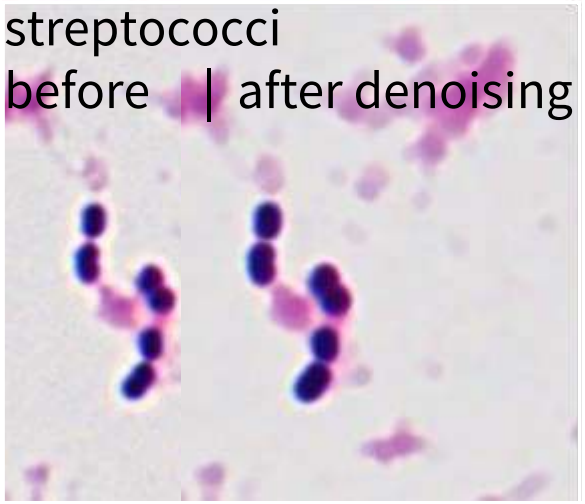
images: high power fields (63x oil), optical enlargement of detailed structures (Metafer system)

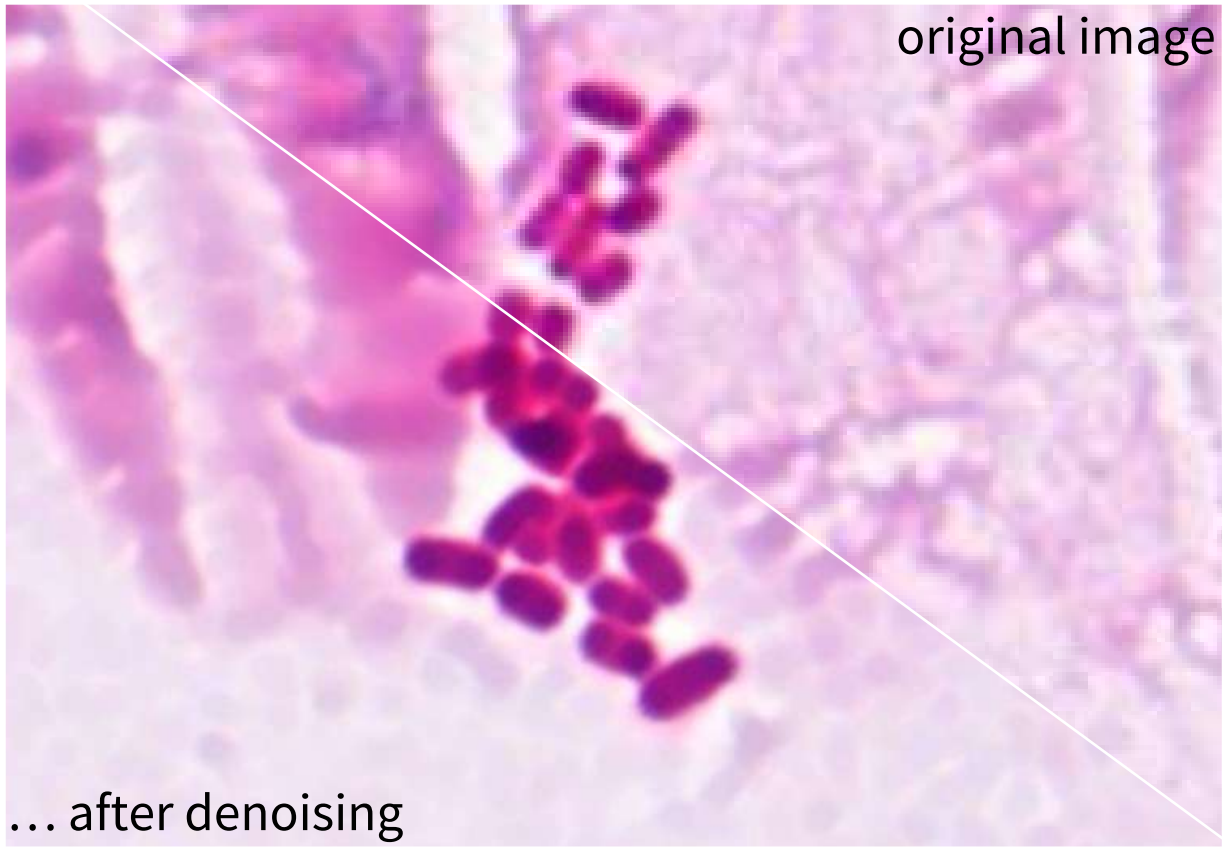
IMM, internal validation data (unpublished), Dominique HILTI

technical optimization

E.coli (Metafer, 63x, oil

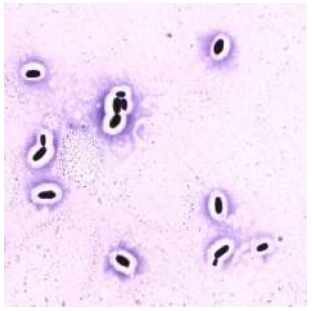




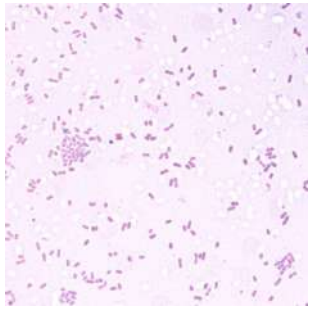


IMM, internal validation data (unpublished), Dominique HILTI
denoised images obtained from Metasystems

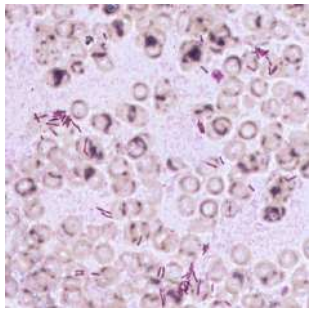
technical optimization



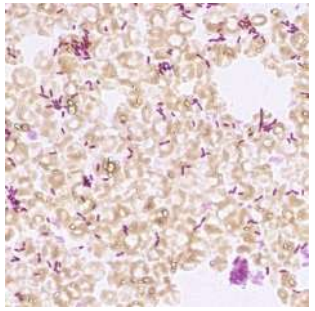
C. tropicalis



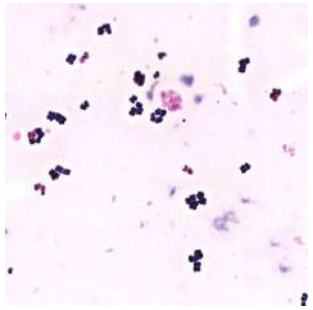
K. oxytoca



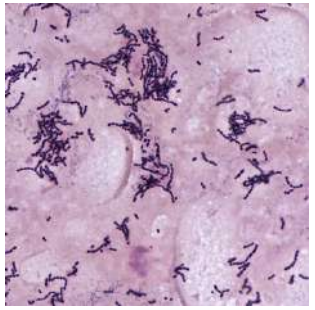
P. aeruginosa



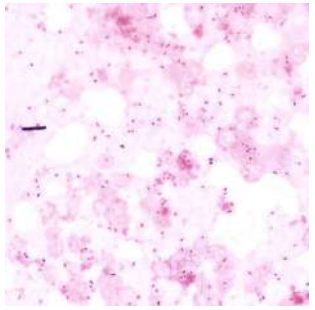
E. coli



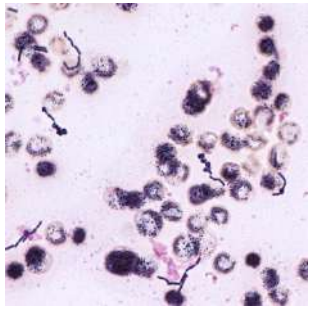
S. hominis



S. pyogenes



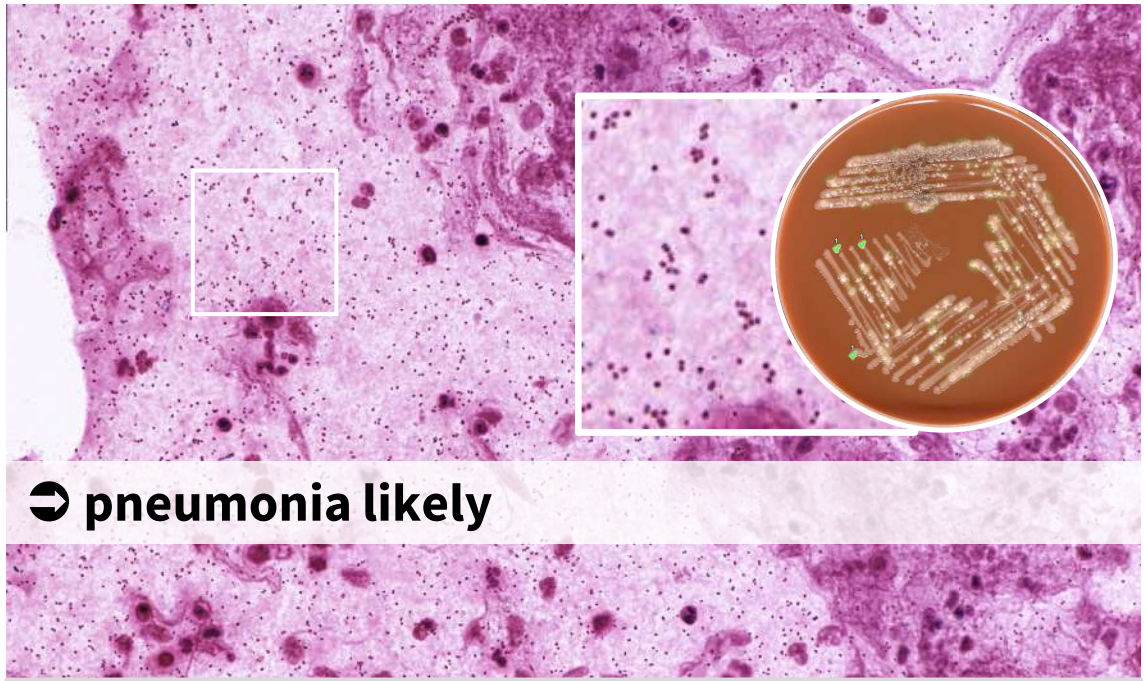
B. cereus &
S. pneumoniae



Lactobacillus
rhamnosus

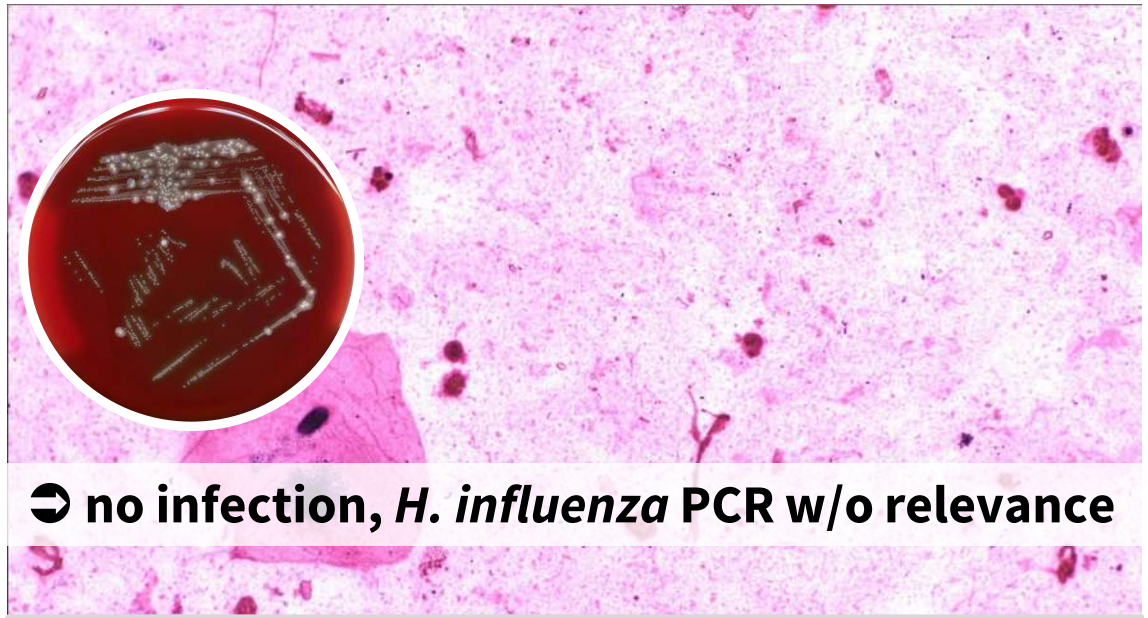
Gram-staining and culture automation

analysis of respiratory specimens



➲ **pneumonia likely**

sputum, ♂ 57y, palliative care, 40x (oil) and 100% crop, plenty *M. catarrhalis* w/ upp.airway flora

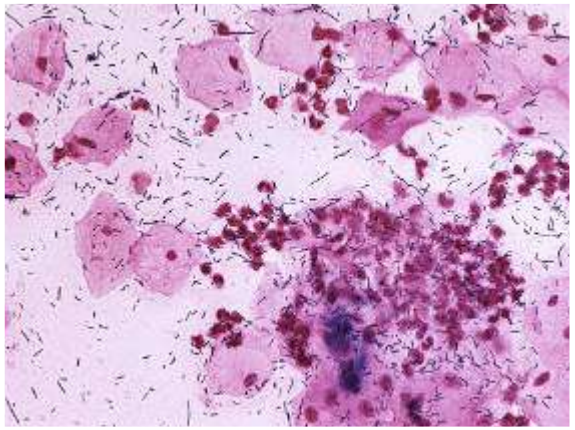


➲ **no infection, *H. influenza* PCR w/o relevance**

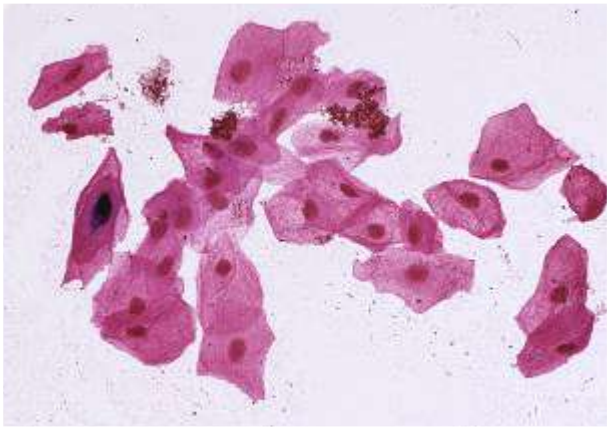
(sputum), ♀ 75y, normal ward, 40x (oil), upper airway flora; CRP elevated for 18 month multiplex-PCR: *H. influenzae* (Ct 36)

just digitization, no AI!

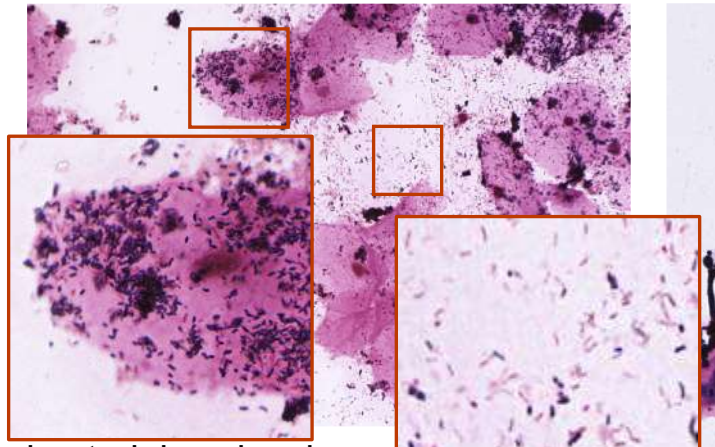
GRAM-stain – personalized result



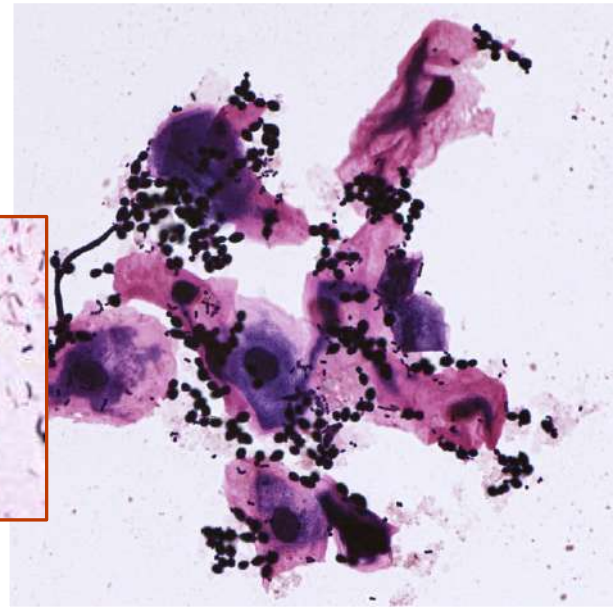
normal vaginal flora w/ plenty of *Lactobacillus*



vaginal epithelial cells w/ reduced number of lactobacilli



bacterial vaginosis (clue cells & *Mobi-lunc* negative rods)



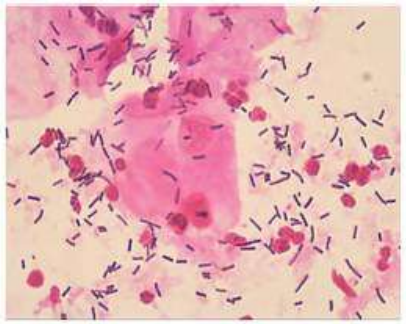
vaginal mycosis w/ plenty of *Candida* and absence of *Lacto-bacillus*

Presence/absence of *Lactobacillus*, *Gardnerella* and *Mobiluncus* (i.e. curved GRAM-variable rods) for diagnosis of bacterial vaginosis

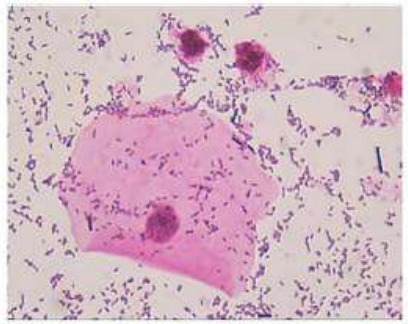
(Ref.: NUGENT RP *et al*, 1991, ISON CA *et al*, 2002, SHERRARD J *et al* 2018, KHEDKAR R & PAJAI S, 2022)

all images: single HPFs („tiles“) 40x/oil Metafer Gram-scanner, vaginal swabs, Center for Laboratory Medicine (ZLM) St. Gall/CH

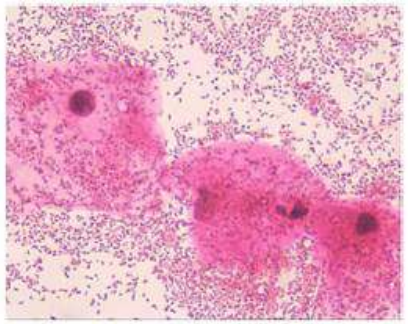
GRAM-stain – personalized result



(i) Normal Vaginal Flora (0-3)



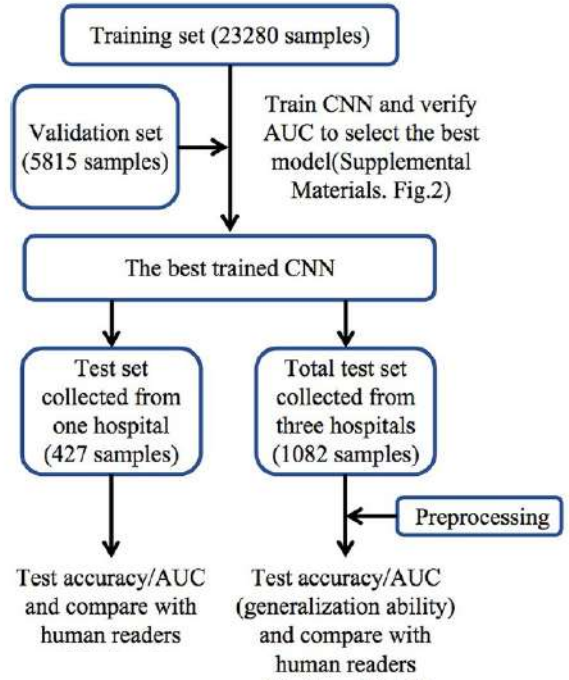
(ii) Altered Vaginal Flora (4-6)

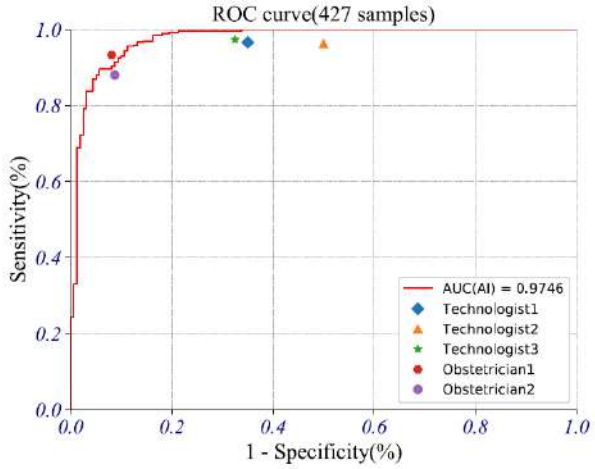


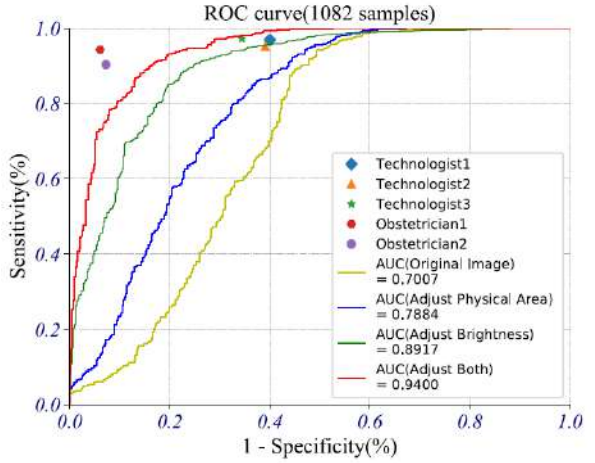
(iii) BV (7-10)

microscopic images of vaginal swabs

nugent scores (0 – 10) and clinical characterization (BV bacterial vaginosis)





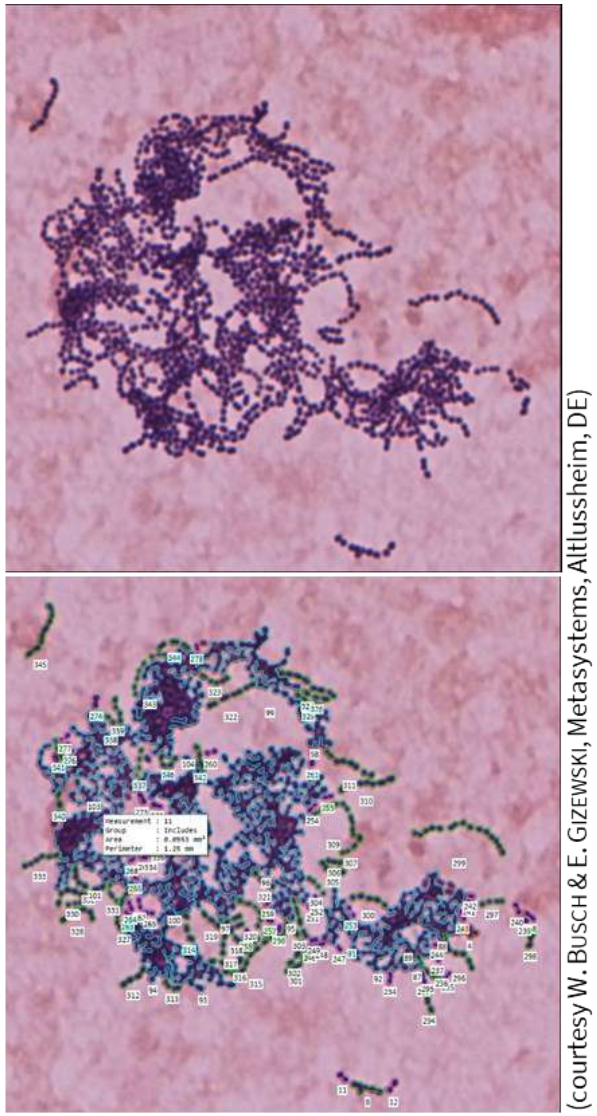


WANG Z *et al* (2021) J.Clin.Microbiol

Supervised learning – annotation of bacteria

Prospective validation study GRAM-scanning and pre-classification

- positive blood cultures, two tertiary care centers (Univ. Heidelberg, Germany, ZLM St. Gall, Switzerland)
- 1’555 monomicrobial BC, GRAM-stained
- analysis in routine and scanned w/ Metafer Gram-scanner
- CNN for pre-classification in
  - G^+ clustered cocci (GPCCL)
  - G^+ chained/paired-cocci (GPCC/GPCP)
  - G^- rods/rod-shaped (R)
  - yeast (Y)
  - polymicrobial
- review by microbiologist

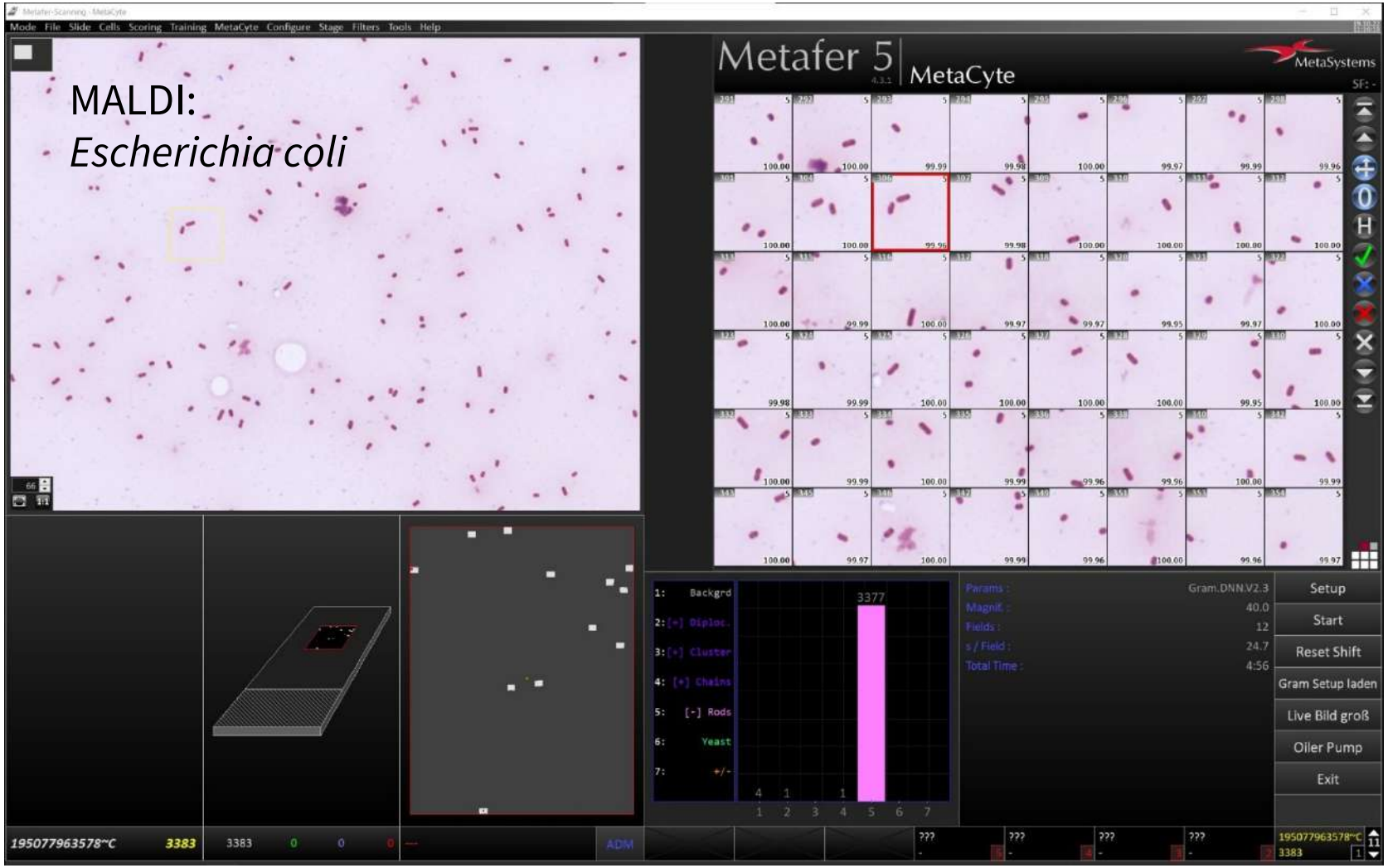


(courtesy W. BUSCH & E. GIZEWSKI, Metasystems, Altlussheim, DE)

Annotation of Streptococci in a Gram-stain

WALTER C, … & NOLTE O (2024): JCM

Blood cultures – AI-assisted pre-classification

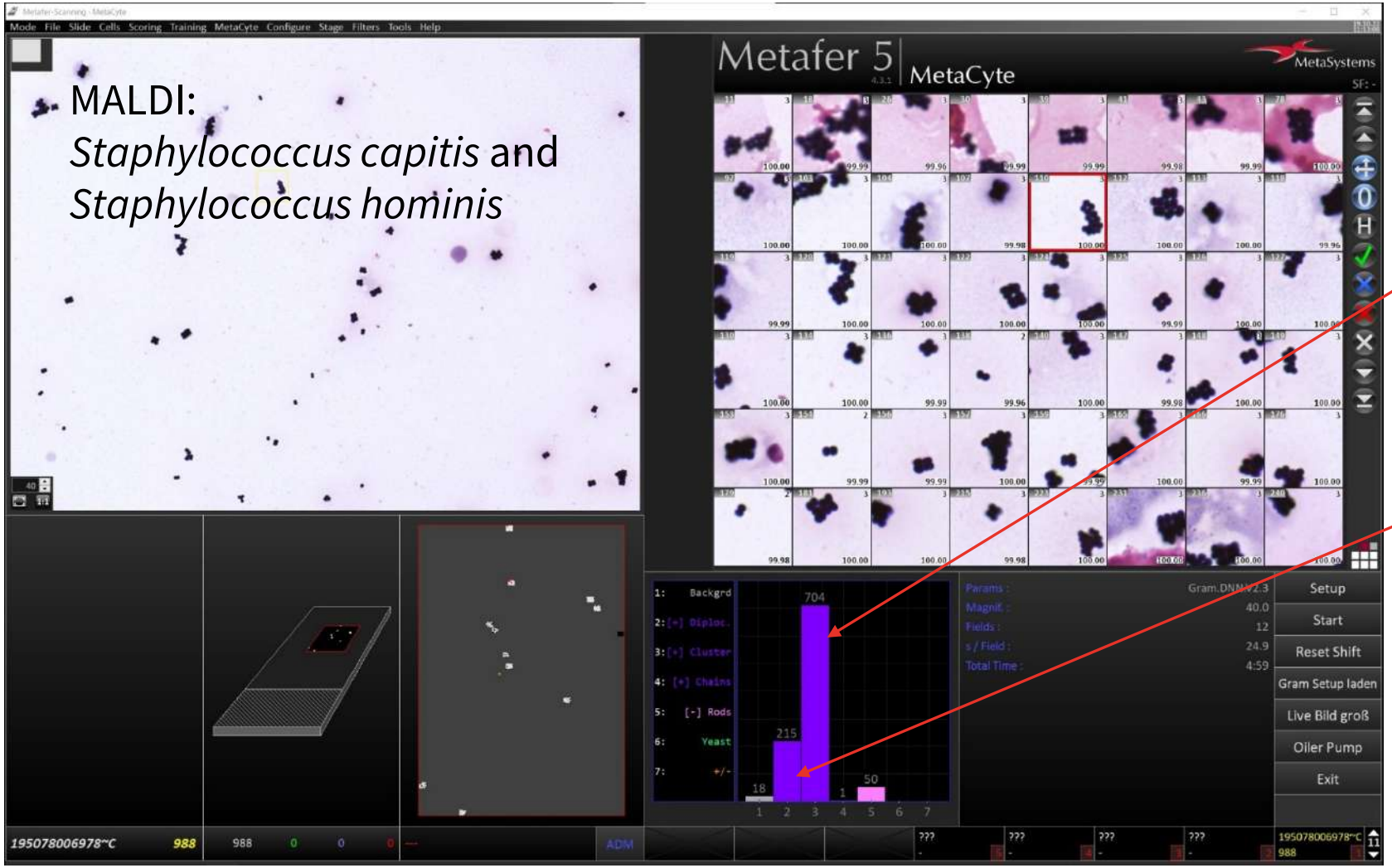


WALTER C, … & NOLTE O (2024): JCM

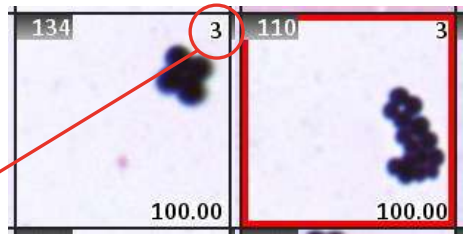
Segmentation: Single object in gallery view with probability score

Pre-classification result (quant.)

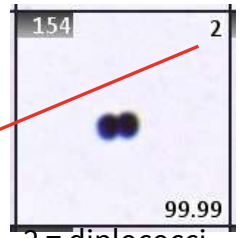
Blood cultures – AI-assisted pre-classification



Segmentation: Single object in gallery view with probability score



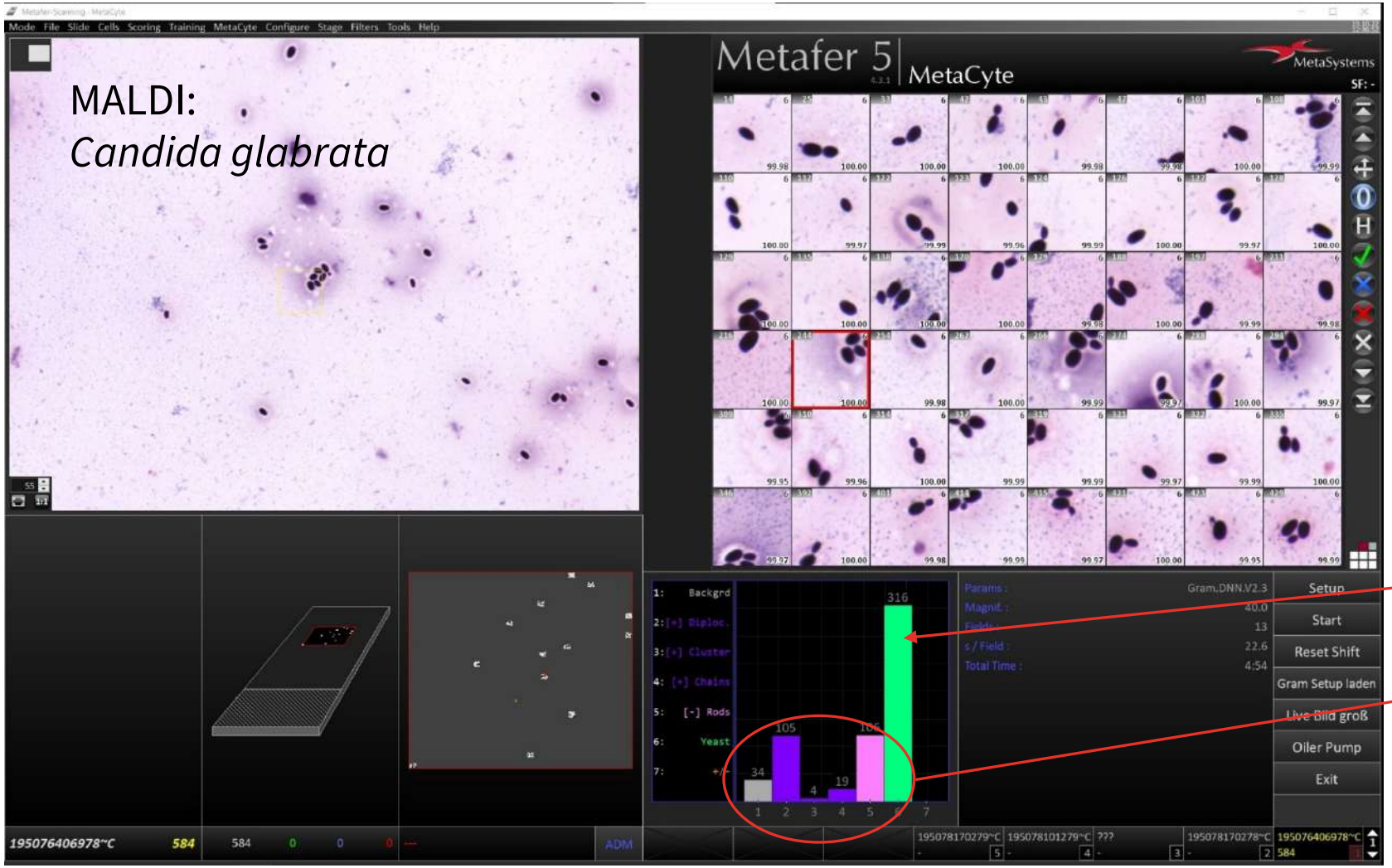
3 = clustered cocci



2 = diplococci

WALTER C, … & NOLTE O (2024): JCM

Blood cultures – AI-assisted pre-classification

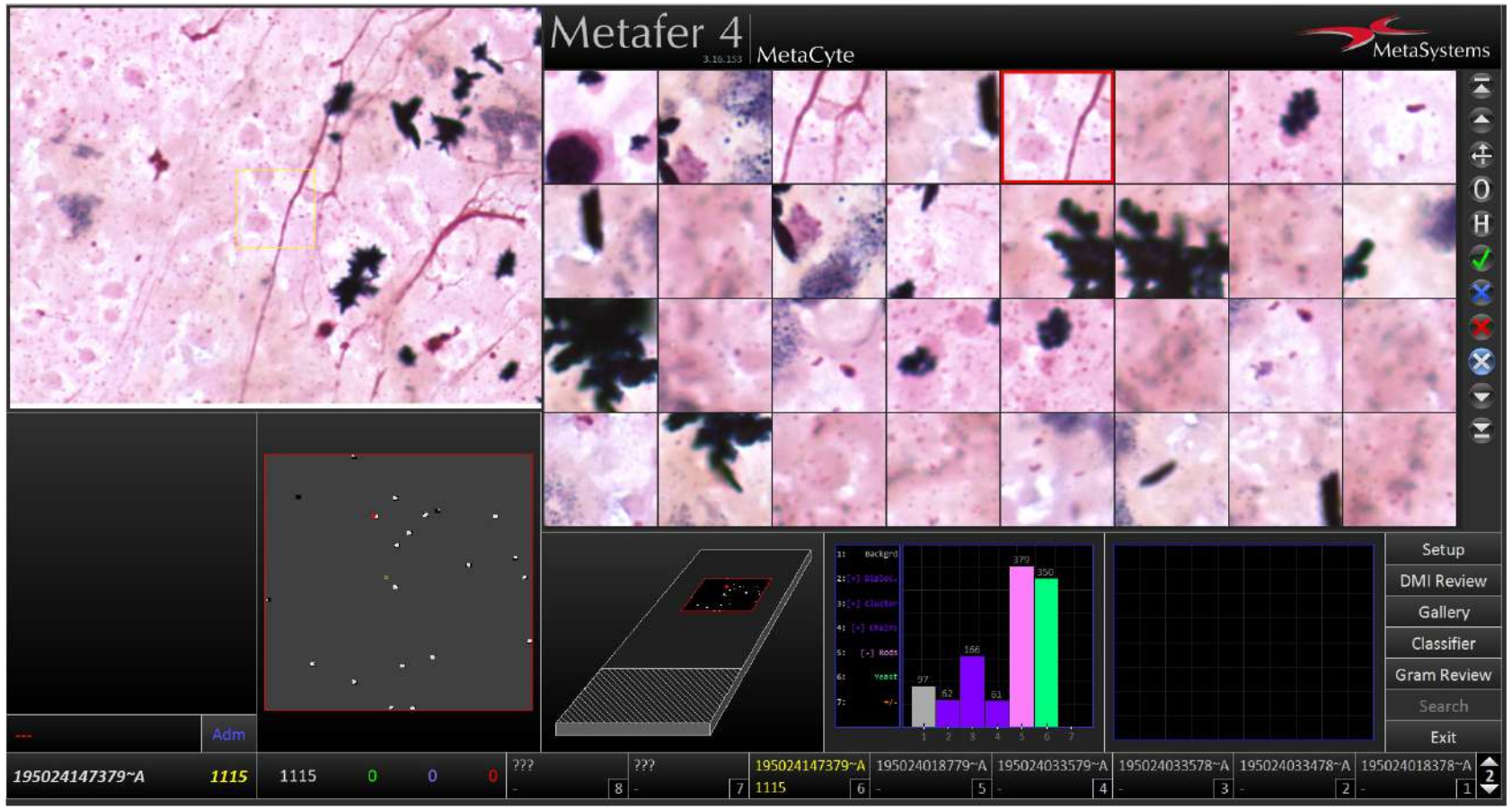


yeast elements

non-specific pre-classifications (cocci, rods – staining artefacts)

WALTER C, … & NOLTE O (2024): JCM

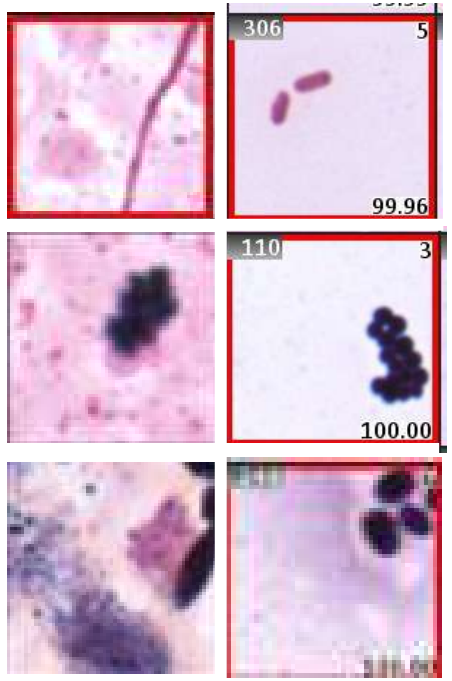
Blood cultures – AI-assisted failure in pre-classification



Staining artefacts

are wrongly pre-classified as Gram-negative rods, Gram-positive cocci and fungi

artefact | typical pattern



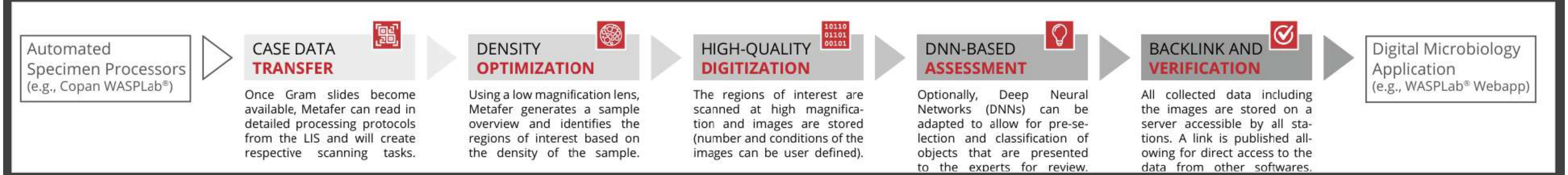
Blood cultures – AI-assisted pre-classification

TABLE 4 Comparative analysis of clinical validation results[a]

Comparison	Class	PPA (%)	95% CI	NPA (%)	95% CI
BCA-assisted interpretation to manual microscopy	GPCCL	95.8	93.8–97.1	98.0	96.8–98.6
	Negative/false positive	87.7	75.6–93.6	98.3	97.5–98.8
Manual microscopy to MALDI-TOF MS	GPCCL	99.8	99.0–100.0	99.8	99.3–99.9
	GPCP/GPCC	98.6	96.0–99.5	99.8	99.3–99.9
	RSB	99.6	98.7–99.9	99.9	99.4–100.0
	Yeasts	92.3	79.9–97.4	100.0	99.8–100.0
	Negative/false positive	100.0	94.4–100.0	99.7	99.3–99.9

[a]BCA, blood culture application; CI, confidence interval; GPCCL, Gram-positive cocci in clusters; GPCP/GPCC, Gram-positive cocci in pairs/Gram-positive cocci in chains; MALDI-TOF MS, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry; NPA, negative percent agreement; RSB, rod-shaped bacilli; PPA, positive percent agreement.

DNN-assisted pre-classification embedded in a fully automated workflow



screenshot: manufacturers website: metasystems-international.com

Walter C, … & Nolte O (2024): JCM

Do we still need GRAM-stain? Conclusion

Yes – GRAM stain in the clinical microbiology lab

- is part of a bundle of techniques to provide high **quality** results in a **timely** manner,
- is not a stand-alone diagnostic but rather **directs** or **complements** diagnostic workflow,
- can now be **automated** and standardized, overcoming lots of its previous limitations,
- is now open for **digitization**, thus **fostering the way for AI-application**,
- is **appreciated by clinicians** as a personalized result early in the diagnostic process

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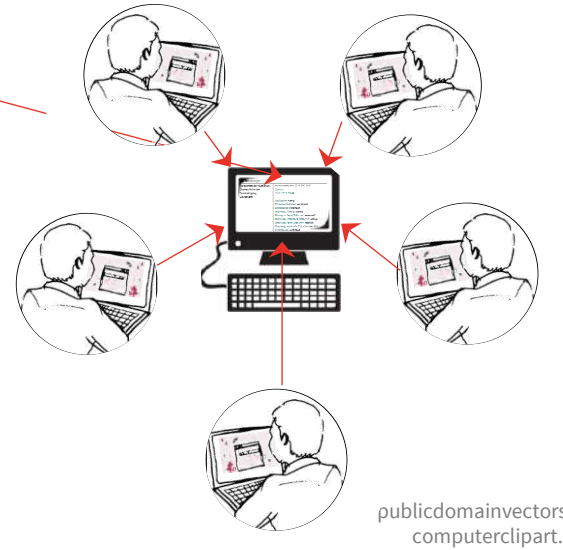
Metafer slide-scanning:

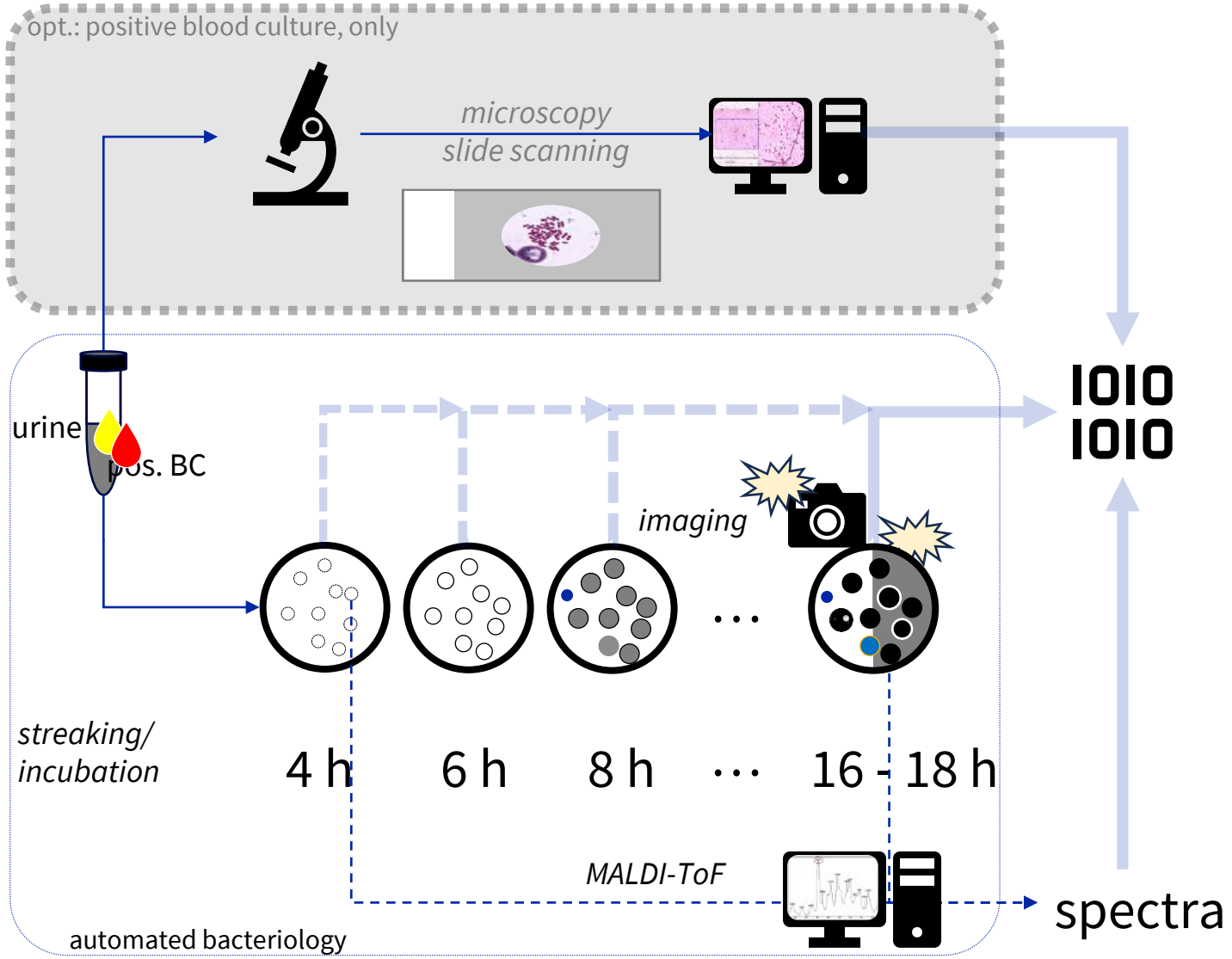
slides available on screen in Copan WebApp

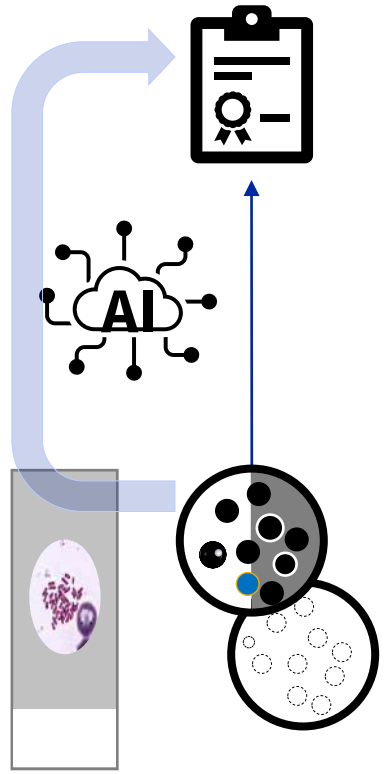
- **cross-check** w/ culture results
- **convenient**: comfortable, ergonomic working
- **quality, traceability** (QC!)
- **decentralized** working (multi-user analysis)



publicdomainvectors.org
computerclipart.com
joachim-czichos.de

different digital sources – foundation model





AI for microscopy data analysis

- at the very beginning and many hurdles
- use case *Plasmodium* and IPI detection:
  - not sufficiently sensitive enough
  - would have significant diagnostic relevance
- use case Gram-staining (e.g., positive blood cultures)
  - sensitivity/specificity comparable to conventional microscopy
  - more convenient working, centralization
  - value of microscopy in clinical microbiology subject of debate
  - closes one of the last gaps in automation!
- Step further to foundation model in lab diagnostics

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