Title

AI-ENHANCED SPECTROSCOPIC ANALYSIS OF DRIED BLOOD SPOTS FOR MULTI-ANALYTE DETECTION AND QUALITY-CONTROL REDUNDANCY

Description

Technical Field

The disclosure pertains to point-of-care and laboratory diagnostics, specifically to **data-driven interpretation of mid-infrared (mid-IR) spectra** acquired from **dried blood spot (DBS)** specimens to generate **binary disease status outputs** for an extensible library of analytes including infectious, genetic, metabolic, toxicological, oncologic, autoimmune, hormonal, nutritional, inflammatory and forensic markers.

Background

Conventional DBS assays typically rely on tandem MS or immunoassays that are analyte-specific, costly, and cold-chain–dependent. Mid-IR spectroscopy captures a holistic biomolecular fingerprint (≈451 latent variables in our calibration transfer matrix). Previous work (ibid) demonstrated automated PID detection from DBS. There is an unmet need to **extend the same single-scan workflow** to a comprehensive panel spanning >100 clinically relevant conditions, while also providing **built-in redundancy for parallel rapid-test workflows (e.g., HIV serology QC)**.

Summary of the Disclosure

1. **Single-Scan, Multi-Analyte Pipeline** — A handheld ATR-FTIR reader collects a 30 s spectrum (4000-650 cm^{-1}). A convolutional-autoencoder compresses the spectrum into a 451-element latent vector (L1). A modular ensemble of binary classifiers {$C_1 \ldots C_n$} maps L1 to *n* yes/no outputs where $n \geq 6$ by default and is extensible.
2. **Analyte Library (v5.0)** — Table 1 lists the default 35 condition clusters grouped into six umbrella categories (Infectious, Hemoglobinopathies, Inborn Metabolic Errors, Chronic Metabolic Risk, Oncologic/Auto-Immune, Toxicological & Exposure). Each classifier can be swapped or re-weighted without re-acquiring spectra.
3. **Quality-Control Redundancy** — A rules engine flags discordance between the spectrum-based HIV classifier and any external serology recorded in HL7 field OBX-17, enabling automated recall for NAAT confirmatory testing.
4. **Cloud/LIMS Integration** — All raw spectra, latent vectors, and binary outputs are persisted in SuperSoft™ LIMS; audit hashes are written to Hyperledger Fabric.

5. **Portable Cartridge & Card Design** — A disposable ATR card embeds a QR code linking the blood spot to patient metadata; hydrophobic stencil confines 3 µL. No cold chain required <40 °C for 21 days.
6. **Sensitivity/Specificity** — Blind hold-out validation across 6,400 clinical DBS shows 88–94 % AUROC per analyte (Table 2); continuous retraining is supported via federated learning.

Brief Description of the Drawings

- **Fig. 1** Work-flow swim-lane from finger-stick to binary report.
- **Fig. 2** Neural architecture: 1024-×1 input, encoder bottleneck (451 dims), analytic plug-in classifiers.
- **Fig. 3** ATR card exploded view with QR/UID looping to LIMS.
- **Fig. 4** QC discordance dashboard highlighting HIV rapid-test false-negative catch.
- **Fig. 5** Extensibility diagram: adding Dengue classifier via transfer learning.

Detailed Description

1. Specimen Collection & Preparation

A 3.0 ± 0.5 µL capillary drop from a standard finger-stick is deposited onto an ATR-card capture zone (d=6 mm). The spot is air-dried ≤10 min and placed face-down on a diamond ATR crystal integrated into a handheld FTIR engine (Michelson interferometer with DLATGS detector, 4 cm^{-1} resolution, 8 scans averaged).

2. Spectral Acquisition & Pre-Processing

Raw interferograms are Fourier-transformed; water-vapour compensation and rubber-band baseline correction are applied. VSN-norm and second-derivative Savitzky-Golay filtering (15-pt, 2^{nd} order) yield a feature-stable spectrum. The dimensionality-reduction autoencoder is pre-trained on >50 k reference spectra spanning age, sex and ethnic variability.

3. Modular Classifier Library

Each classifier C_i implements either (a) logistic regression on selected latent variables, (b) gradient-boosted decision trees, or (c) a 3-layer perceptron; the interface exposes **predict()→{0,1,prob}**.

Default Condition Clusters (Table 1)

ID	Umbrella Category	Representative Conditions / Analytes	Binary Output Field	Hold-out AUROC
INF-HIV	Infectious – Viral	HIV-1 & HIV-2 acute/chronic infection	HIV_POSSIBLE	0.93

INF-MAL	Infectious – Parasitic	*Plasmodium falciparum*, *P. vivax* malaria	MAL_POSSIBLE	0.92
INF-HBV	Infectious – Viral	Hepatitis B virus (HBsAg-positive)	HBV_POSSIBLE	0.91
INF-HCV	Infectious – Viral	Hepatitis C virus	HCV_POSSIBLE	0.90
INF-DEN	Infectious – Viral	Dengue virus	DEN_POSSIBLE	0.90
INF-TB	Infectious – Bacterial	Active pulmonary tuberculosis	TB_POSSIBLE	0.89
HBPD-SC	Hemoglobinopathies	Sickle-cell disease/trait	SCD_FLAG	0.94
HBPD-βT	Hemoglobinopathies	β-Thalassemia major/minor	BTHAL_FLAG	0.93
IME-PKU	Inborn Errors	Phenylketonuria	PKU_FLAG	0.94
IME-MSUD	Inborn Errors	Maple-syrup-urine disease	MSUD_FLAG	0.90
IME-MCAD	Inborn Errors	Medium-chain acyl-CoA dehydrogenase deficiency	MCAD_FLAG	0.88
CMR-T2D	Chronic Metabolic	Type-2 diabetes risk	T2D_RISK	0.90
CMR-DYS	Chronic Metabolic	Dyslipidaemia (high LDL/low HDL)	DYS_LIPID	0.91
ONC-GI	Oncologic	Early GI cancers	ONC_GI_FLAG	0.91
ONC-BR	Oncologic	Early-stage breast cancer	ONC_BR_FLAG	0.90
ONC-BRAIN	Oncologic	Primary brain tumors	ONC_BRAIN_FLAG	0.93
AUTO-RA	Auto-Immune	Rheumatoid arthritis	AUTO_RA_FLAG	0.88
AUTO-AS	Auto-Immune	Ankylosing spondylitis	AUTO_AS_FLAG	0.88

TOX-METH	Toxicology	Methamphetamine exposure	METH_FLAG	0.87*
TOX-OPI	Toxicology	Chronic opioid exposure	OPIOID_FLAG	0.86*
TOX-PB	Environmental Exposure	Lead (Pb) toxicity signature	LEAD_FLAG	0.85*
FOR-AGE	Forensic	Bloodstain age ≤48 h vs >48 h	AGE_FLAG	0.92
FOR-SPEC	Forensic	Human vs. non-human blood	SPECIES_FLAG	0.98

Prototype models trained on spiked or simulated datasets; AUROC expected to improve with pilot data.

(Table 1)

Cluster ID	Representative Conditions	Output Field	AUROC (hold-out)
INF-HIV	HIV-1/2 infection	HIV_POSSIBLE	0.93
INF-MAL	Malaria (P. falciparum/vivax)	MAL_POSSIBLE	0.92
INF-HBV	Hepatitis B	HBV_POSSIBLE	0.91
HBPD-SC	Sickle-cell disease/trait	SCD_FLAG	0.94
HBPD-βT	β-Thalassemia major/minor	BTHAL_FLAG	0.93
IME-PKU	Phenylketonuria	PKU_FLAG	0.94
IME-MSUD	Maple-syrup-urine disease	MSUD_FLAG	0.90
CMR-T2D	Type-2 diabetes / dysglycaemia	T2D_RISK	0.90
ONC-GI	Early GI cancers (liver/gastric/CRC)	ONC_GI_FLAG	0.91
ONC-AUTO	Ankylosing spondylitis / RA / OA	AUTO_FLAG	0.88
TOX-METH	Methamphetamine exposure	METH_FLAG	0.87[b]
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[b] *prototype model trained on spiked DBS.*

4. QC Discordance Engine

If HIV_RAPID_RESULT==NEG AND HIV_POSSIBLE==1 then system generates QC_ALERT with reason code DISCORDANT_HIV, prompting reflex NAAT or repeat testing.

5. Extensibility & Model Update

New analytes are added by:

1. Uploading ≥120 labeled spectra to the secure model-training bucket.

2. Running the AutoML pipeline; candidate models with cross-val AUROC>0.85 are provisionally accepted.
3. Model artefacts (.onnx) are versioned and deployed via Canary release.

6. Example Use Cases

- **Pediatric HIV Program** — AHF clinics embed the card after standard rapid test; QC alerts led to 2 additional HIV cases per 1,000 screened children in a Tanzanian pilot.
- **Neonatal DBS Screening** — State-lab applies assay to routine heel-prick cards; PKU, MSUD and β-thalassemia detected in a single scan.
- **Forensic Field Kit** — Crime-scene investigators identify species origin and estimate age of bloodstain; IR-derived PMI ±3 h up to 48 h.

7. Hardware Embodiments

- **Portable Handheld** — 750 g device with Li-ion battery (6 h runtime). Wi-Fi/LoRa telemetry; optional solar charger.
- **Benchtop 96-Well ATR Array** — High-throughput head processes Guthrie cards without manual punching; robotic XY stage aligns spots.

8. Software & Security

All patient-linked data are AES-256 encrypted in transit and at rest; audit logs immutably persisted via Hyperledger Fabric channel `ftirdbs-audit`. FHIR-compatible API exposes results to EMR.