



Research Proposal

Can We Smell Diabetes?

Quantum-Optimized Reconstruction of Ketone Dynamics from Fabry-Pérot Optical Breath Measurements

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1 Introduction

Diabetes management depends on measurements that are often invasive, intermittent, or expensive. Acetone in exhaled breath is linked to ketone metabolism and can be measured optically, but a breath spectrum is not itself a metabolic state: the clinically meaningful quantities—blood β -hydroxybutyrate (BHB), acetoacetate, acetone, and their rates of change—must be inferred from noisy, indirect observations. Prior cavity-enhanced systems have detected breath acetone near 1670 nm, establishing a realistic optical starting point [1]. Earlier QLab students also demonstrated the feasibility and practical limitations of student-built breath-acetone spectroscopy [2].

We propose a coupled computational and experimental project. Mohan will extend a verified slow-fast ketone model and classical physics-informed neural network (PINN) with a small variational quantum layer, then use quantum Fisher information (QFI) to quantify which model parameters and optical features are most identifiable. Aarjav will design and fabricate a Fabry-Pérot interferometer, select light-emitting diodes and a near-infrared spectrometer, and characterize its resolution, stability, and acetone sensitivity. QFI-guided priorities will inform wavelength and component choices; measured instrument noise and spectral response will then be returned to the inverse model. The project will test whether this feedback loop improves reconstruction accuracy and uncertainty relative to matched classical baselines, without presuming a quantum advantage or requiring a large number of qubits.

1.1 Intellectual Merit

The project connects mechanistic multiscale modeling, hybrid quantum-classical learning, quantum information geometry, and a real optical instrument in one identifiable inverse problem. Beyond investigating quantum modeling applications and optical sensing, this project could result in a practically useful tool for monitoring a disease impacting hundreds of millions of people worldwide.

1.2 Broader Impact

A low-cost, noninvasive method for tracking ketone dynamics could ultimately support earlier warning of dangerous metabolic changes. In particular, a byproduct of our research could involve a tool for predicting diabetic ketoacidosis (a dangerous complication of diabetes caused by insufficient insulin and rising ketones) without requiring skin insertion. With that said, this project serves as a feasibility study, not a diagnostic device, and any faculty breath study will proceed only with required approval and informed consent.

2 Background and Prior Work

Ketone metabolism evolves across two coupled time scales. A slow compartment model describes production, interconversion, and clearance of BHB, acetoacetate, and acetone. A fast pulmonary transport model maps blood acetone into exhaled concentration through gas exchange and airway transport. After nondimensionalization, a finite-difference forward solver will generate trajectories and synthetic observations. The inverse problem is to reconstruct latent ketone states and selected physiological parameters from sparse optical breath measurements.

Physics-Informed Neural Networks (PINNs) incorporate differential-equation residuals, initial and boundary conditions, and observations into a common training loss, allowing hidden states and parameters to be estimated while preserving mechanistic structure [3]. Our existing classical framework and verified forward solvers provide the control against which any quantum addition

must be judged. Quantum PINNs replace or augment a classical component with a parameterized quantum circuit. Trahan, Loveland, and Dent found that quantum and hybrid PINNs could solve several differential equations with competitive accuracy and, in some settings, fewer trainable parameters [4]. Those results motivate a controlled test on ketone reconstruction but do not imply that the hybrid model will be superior.

Quantum Fisher Information (QFI) measures how sensitively a parameterized quantum state changes with respect to an encoded parameter and therefore bounds achievable estimation precision. Variational methods can estimate or bound QFI and optimize a quantum probe without requiring a full analytic model of the sensor dynamics [5]. In this project, the QFI matrix will be used as an information-geometric diagnostic: its diagonal structure and eigenvectors will help rank parameter combinations and encoded spectral features, expose poorly identifiable directions, and guide which wavelength regions merit experimental attention. This does not mean that the optical apparatus itself is a quantum sensor; QFI is being used within the simulated variational model to prioritize information.

Experimentally, a Fabry–Pérot cavity produces wavelength-dependent interference whose transmission changes with cavity geometry, refractive index, absorption, and analyte concentration. Cavity-enhanced breath-acetone work near 1670 nm achieved sub-ppm-scale detection after pre-concentration [1], while the earlier QLab GLASS project showed that diode power, humidity control, and limited data are important student-laboratory constraints [2]. These precedents support an LED/interferometer/spectrometer prototype while emphasizing the need for calibration and honest limits of detection.

Project Need / Research Gap. Prior work treats quantum PINNs, information-based quantum optimization, and breath spectroscopy mostly as separate problems. We will test whether a small simulated quantum layer and QFI-guided instrument design can improve reconstruction of a physiologically meaningful, multiscale latent state governing diabetic ketoacidosis when the model is constrained by the measured capabilities of a student-built interferometer.

3 Research Goals

In all comparisons, we will equally emphasize improvements, null results, and degradations.

Goal 1— Validate the Slow–Fast Ketone Reconstruction Baseline

Question / Objective: Determine how accurately the existing mechanistic model and classical PINN reconstruct BHB, acetoacetate, acetone, and selected rates or parameters from sparse breath-acetone observations.

Approach: Verify the nondimensionalized slow ODE and fast pulmonary PDE solvers against manufactured or high-resolution numerical solutions, then generate synthetic observations across realistic sampling rates and noise levels. Train the classical inverse PINN using fixed data splits and repeated random seeds.

Measurement / Output: Forward-solver error, held-out state and parameter RMSE, physics residuals, uncertainty or sensitivity summaries, and robustness curves versus noise and sampling frequency.

Success Criterion: A reproducible baseline with verified forward error and held-out reconstruction metrics for every retained observation regime.

Goal 2— Test a Small Quantum Layer and QFI-Guided Identifiability

Question / Objective: Determine whether a shallow variational quantum layer changes reconstruction accuracy, stability, or parameter efficiency, and whether QFI identifies informative parameter and spectral directions.

Approach: Embed selected normalized time, state, and spectral features into a small simulated circuit and return measured expectation values to the PINN. Compare the hybrid model with the original PINN and a parameter-matched classical bottleneck under identical data, losses, stopping rules, and repeated seeds. Compute the QFI matrix for retained encodings and analyze its spectrum and parameter sensitivities [5].

Measurement / Output: Held-out RMSE for ketone states and slopes, parameter error, convergence and wall time, circuit size, seed-to-seed variation, and QFI-based wavelength rankings with uncertainty.

Success Criterion: Complete matched comparisons and determine whether QFI rankings are stable enough to produce testable optical design priorities; a null or negative quantum result satisfies this goal.

Goal 3— Fabricate and Characterize a Fabry–Pérot Breath-Sensing Prototype

Question / Objective: Determine the spectral resolution, stability, and acetone sensitivity achievable with an LED-driven Fabry–Pérot interferometer and an available near-infrared spectrometer.

Approach: Use simulations and QFI priorities to select candidate wavelengths, then choose compatible LEDs, mirrors/cavity spacing, fibers, detector, and spectrometer. Calibrate wavelength response and acquire repeated reference, blank, and controlled acetone-vapor measurements before any breath collection.

Measurement / Output: Transmission spectra, free spectral range and finesse, signal-to-noise ratio, drift, calibration curve, limit of detection, and measured noise model.

Success Criterion: A documented apparatus that produces repeatable spectra and an empirically estimated sensitivity and noise floor, even if physiological breath acetone lies below that floor.

Goal 4— Close the Model–Instrument Feedback Loop

Question / Objective: Determine whether information from the model improves apparatus choices and whether real apparatus characteristics improve realistic reconstruction assessment.

Approach: Use QFI and classical sensitivity rankings to prioritize wavelengths or VOCs; insert measured bandwidth, noise, drift, and missingness into synthetic training and validation; then, subject to approval, collect longitudinal breath spectra from consenting TJ faculty volunteers for a non-diagnostic feasibility test.

Measurement / Output: A traceable record of design changes, simulated and experimental reconstruction results, and comparison of predicted versus observed information content.

Success Criterion: At least one complete iteration from computational priority to optical measurement and back to a retrained or reevaluated inverse model.

4 Proposed Methods and Research Design

The computational work will begin from an existing slow metabolic ODE system for BHB, acetoacetate, and acetone and the fast pulmonary transport PDE that maps blood acetone to exhaled concentration (developed in the appendix). Mohan will nondimensionalize the coupled system, verify finite-difference forward solutions, and generate reference trajectories. Synthetic measurement schedules will span plausible noise, missingness, and temporal resolution. The classical inverse PINN will estimate latent state trajectories and selected parameters using a loss containing observation error, ODE/PDE residuals, initial and boundary conditions, and physiologically justified constraints.

A hybrid model will replace or augment one compact classical feature layer with a shallow parameterized quantum circuit following the quantum-PINN concept in [4]. Only the number of simulated qubits required to encode the retained features will be used; qubit count and depth will be increased only when justified by ablation results. Every hybrid configuration will be compared with both the original PINN and a parameter-matched classical bottleneck across common data, seeds, optimizer budgets, and stopping criteria. Primary outcomes are held-out RMSE for BHB, acetone, and their time derivatives; parameter recovery; physics residual; training stability; and wall time.

For each retained circuit, Mohan will compute or estimate the QFI matrix. Eigenvalues and parameter-wise sensitivities will be compared with classical Jacobian/Fisher or finite-difference sensitivity analyses so that a claimed QFI priority must be robust rather than circuit-specific. D-optimal design provides a principled way to choose measurements that maximize parameter identifiability; Uciński develops this approach for PDE-governed systems with correlated measurement noise [6]. As later extensions, QUBO feature selection could choose a discrete subset of wavelengths or VOCs under cost constraints, with QAOA solving the binary problem; continuous instrument variables would first require discretization or a continuous/hybrid optimizer and are not part of the minimum viable project.

Aarjav will model, assemble, align, and characterize an LED-driven Fabry–Pérot interferometer. Candidate hardware includes a Thorlabs compact near-infrared spectrometer (<https://www.thorlabs.com/compact-cmos-spectrometers?tabName=Overview>) covering approximately 950–1700 nm, subject to confirming that its resolution and sensitivity are adequate near the QFI-prioritized bands. Procurement will follow simulation and component review rather than assume the broadest spectral range is optimal. Calibration will progress from reference and blank spectra to safe controlled acetone-vapor standards, with repeated trials quantifying free spectral range, finesse, drift, noise, response time, and limit of detection.

The measured instrument response will be convolved with simulated spectra and injected into PINN training. If we are able to obtain human-participant approval, we might ask consenting adult TJ faculty to provide longitudinal breath samples under a written, non-diagnostic protocol, but no treatment decisions will be made from the results.

5 Expected Results and Data Analysis

The verified forward model is expected to reproduce reference ketone and pulmonary-transport solutions to numerical tolerance, while inverse accuracy should worsen as optical noise increases or sampling becomes sparse. The classical PINN will establish how much of the latent metabolic trajectory is identifiable from breath acetone alone and whether additional spectral features or longitudinal structure are required.

We do not assume any quantum advantage. The hybrid model may lower held-out error, reduce the number of trainable parameters, or improve recovery under sparse data; it may also be statistically indistinguishable from the classical controls or train more slowly and less reliably. Metrics will be summarized across repeated seeds using effect sizes, confidence intervals or bootstrap intervals, and full error distributions. Accuracy versus wall time will distinguish statistical performance from computational cost. QFI eigenvalues and rankings will be tested across circuit initializations, noise assumptions, and feature encodings and compared with classical sensitivity rankings. A useful QFI result is a stable, experimentally testable priority, not simply a large value from one circuit.

The optical apparatus is expected to produce repeatable interference spectra before it achieves physiological acetone sensitivity. Characterization will report wavelength accuracy, free spectral range, finesse, drift, signal-to-noise ratio, response linearity, and limit of detection. Because published near-infrared cavity systems used high-finesse cavities and, in some cases, preconcentration [1], failure to reach sub-ppm sensitivity with the initial LED system would be informative rather than fatal. It would motivate a narrower source, longer effective path, preconcentration, or a different band.

The central result will be the feedback-loop comparison: reconstruction under idealized noise versus measured instrument response, before and after QFI-guided wavelength or component selection. Longitudinal faculty data, if approved and collected, will be used only to test repeatability and feasibility; reconstructed values will not be interpreted as diagnoses. A complete project may conclude that the classical model is preferable, that QFI is useful for design even without better hybrid predictions, or that hardware limitations dominate model choice.

6 Feasibility and Resources

The classical slow-fast model, finite-difference solvers, and preliminary inverse PINN already exist (implemented on a Macbook Pro in MATLAB), reducing computational risk. Hybrid experiments will use small state-vector simulations rather than large quantum hardware runs; the number of qubits will be limited to the encoded variables needed for the scientific comparison. Python or MATLAB, an automatic-differentiation framework, a quantum-machine-learning library, and standard laboratory computers are sufficient for the minimum viable analysis, although natural extensions may require systems capable of executing more quantum-demanding tasks.

The main experimental resource is a near-infrared spectrometer. A Thorlabs unit in the approximately 950–1700 nm class is expected to cost roughly \$3,000–\$6,000, but the final model and quotation will be chosen only after wavelength, resolution, detector sensitivity, and QFI analyses. Additional needs include compatible LEDs, mirrors, mounts, fibers, a safe gas cell, reference materials, and humidity/temperature sensing. The work will proceed in stages so that simulation, cavity fabrication, and calibration remain valuable even if a purchase is delayed or human breath collection is not approved. All designs, calibration files, model configurations, seeds, and raw spectra will be version-controlled.

7 Safety and Risk Considerations

Optical alignment will use low-power LEDs whenever possible. Sources will remain enclosed or beam-height controlled, and students will not stare into LEDs, fibers, or reflected beams. Any source classified as a laser will be used only under QLab laser procedures with wavelength-appropriate eyewear and supervision. Mirrors, glass, electronics, and power supplies will be mounted securely.

It is unlikely that we will require large acetone quantities beyond breath. However, we recognize that acetone is volatile and flammable. Calibration quantities will be used only if absolutely necessary and handled in minimal quantities only in approved containers and ventilation, away from ignition sources, with staff-approved storage, disposal, and safety data sheets. Human breath collection will begin only after any required human-participant review near the end of the year, use informed consent from adult volunteers, avoid medical claims, and store coded rather than directly identifying data. Disposable mouthpieces and one-way flow components will prevent cross-contamination; volunteers may withdraw at any time.

8 Potential Pitfalls and Alternative Strategies

Challenge 1

Breath acetone may not uniquely identify BHB, acetoacetate, and patient-specific transport parameters.

Solution: Use structural and practical identifiability analyses before fitting all parameters, estimate only identifiable combinations, incorporate priors or longitudinal constraints, and report uncertainty rather than a single overconfident trajectory.

Challenge 2

The hybrid model may appear better because of parameter count, tuning, or one favorable initialization rather than the quantum layer.

Solution: Use a parameter-matched classical bottleneck, identical data and optimization budgets, repeated seeds, held-out evaluation, and preregistered primary metrics. A null or negative result will be retained.

Challenge 3

The QFI ranking may depend strongly on circuit encoding or may not correspond to real optical information.

Solution: Compare rankings across encodings and seeds and against classical sensitivity/Fisher analyses. Only stable priorities that map to accessible wavelengths and exceed the measured noise floor will guide procurement or redesign.

Challenge 4

A broad 950–1700 nm spectrometer may have insufficient resolution or sensitivity at the most informative acetone band, and LED emission may be too broad or weak.

Solution: Measure or verify resolution and throughput before purchase; consider a narrower

spectrometer, narrowband diode, filters, greater cavity finesse/path length, or preconcentration (use QFI output as a deciding factor). Retain benchtop calibration as a valid deliverable if breath-level detection is not reached.

Challenge 5

Humidity, carbon dioxide, temperature, alignment drift, or contamination may dominate the acetone signal.

Solution: Collect blanks and reference spectra, monitor temperature and humidity, standardize sampling, randomize measurement order, clean or replace exposed components, and incorporate the measured nuisance response into the inverse model.

Challenge 6

Approval or recruitment may prevent longitudinal faculty breath measurements.

Solution: Complete all primary comparisons with synthetic data and controlled standards; human data are a gated extension and will not be required to validate the apparatus or computational feedback loop.

9 Research Timeline

Milestone 1: September–October: Baseline and Optical Design

Task — What will you do? Verify the nondimensional slow-fast solver and classical inverse PINN; simulate candidate Fabry–Pérot geometries and survey LEDs, spectrometers, and spectral bands.

Objective — What measurable result should this work produce? Produce verified forward errors, baseline reconstruction metrics, a component decision matrix, and a preliminary wavelength/sensitivity requirement.

Goal — What larger research capability or milestone does this establish? Freeze the classical control and define an experimentally realistic optical design space.

Milestone 2: November–December: Hybrid Model and Bench Prototype

Task — What will you do? Implement the small quantum layer and matched classical control; compute initial QFI matrices; assemble and align the first interferometer.

Objective — What measurable result should this work produce? Complete repeated hybrid/classical trials and obtain stable reference interference spectra with measured free spectral range and drift.

Goal — What larger research capability or milestone does this establish? Generate the first computational design priorities and demonstrate an operating optical cavity.

Milestone 3: January–February: Calibration and Feedback Iteration

Task — What will you do? Calibrate with blanks and controlled acetone standards; quantify instrument noise; compare QFI and classical sensitivity rankings; revise the source, wavelength, or cavity design if justified.

Objective — What measurable result should this work produce? Produce calibration curves, detection limits, QFI robustness results, and at least one documented model-to-instrument design decision.

Goal — What larger research capability or milestone does this establish? Close the first half of the feedback loop by converting computational information priorities into a tested measurement configuration.

Milestone 4: March–April: Instrument-Constrained Reconstruction

Task — What will you do? Inject measured spectral response and noise into training and evaluation; if approved, begin longitudinal measurements from consenting adult TJ faculty.

Objective — What measurable result should this work produce? Compare idealized and instrument-constrained reconstruction error and, if available, quantify repeatability on coded breath spectra.

Goal — What larger research capability or milestone does this establish? Close the full feedback loop from model to apparatus and back to the inverse reconstruction.

Milestone 5: May: Final Analysis and Research Product

Task — What will you do? Complete statistical comparisons, uncertainty analysis, figures, apparatus documentation, paper, and presentation.

Objective — What measurable result should this work produce? Produce a reproducible package containing code/configurations, calibration data, final metrics, design decisions, and limitations.

Goal — What larger research capability or milestone does this establish? Deliver a defensible conclusion about hybrid reconstruction, QFI-guided sensing, and the feasibility of optical ketone monitoring.

10 Group Responsibilities

Mohan Parthasarathy (Pd 1)

Primary responsibility for the mathematical and computational work: nondimensionalization; verification of the slow metabolic ODE and fast pulmonary PDE models; finite-difference reference solutions; classical and hybrid PINN development; QFI, identifiability, uncertainty, and sensitivity analyses; and instrument-constrained reconstruction. Mohan will translate model results into quantitative wavelength, precision, and sampling priorities.

Aarjav Jain (Pd 3)

Primary responsibility for the optical work: Fabry–Pérot design and simulation; LED, mirror, fiber, detector, and spectrometer selection; fabrication and alignment; wavelength and response calibration; controlled acetone measurements; and characterization of resolution, finesse, drift, noise,

and limit of detection. Aarjav will translate measured hardware constraints into a response/noise model for the reconstruction.

Both students will jointly define the interface between the mathematical and physical components, review QFI and classical sensitivity rankings against hardware feasibility, plan each design iteration, maintain the safety and human-participant protocol, interpret results, and write the final paper. The project will not be treated as two parallel products: its central deliverable is a documented feedback loop in which the model guides the instrument and the instrument constrains the model.

Surya Raj (Engineering Pd 1)

Primary responsibility for the breath-sampling and environmental-control system: designing and fabricating the breath inlet and gas-handling assembly; engineering an automated opening and closing valve system to control when new breath enters the measurement chamber; developing the enclosure that holds the breath vapor; and automating the sampling process. Surya will design the system so that fresh breath can be introduced in a controlled and repeatable manner while limiting water vapor and residual breath that could interfere with LED or laser measurements. He will also coordinate the valves, sampling sequence, and measurement timing so that the system can automatically introduce a sample, isolate the measurement chamber, and prepare the system for the next measurement. Surya will characterize flow, humidity, and sampling consistency and work with Aarjav to determine how the breath-handling system affects the optical measurements and instrument noise.

Annotated Bibliography

- [1] T. P. J. Blaikie, J. Couper, G. Hancock, P. L. Hurst, R. Peverall, G. Richmond, G. A. D. Ritchie, D. Taylor, and K. Valentine, “Portable device for measuring breath acetone based on sample preconcentration and cavity enhanced spectroscopy”, *Analytical Chemistry* **88**, 11016–11021 (2016).

What did this work do? Demonstrated a compact breath-acetone system using a 7-cm high-finesse optical cavity, polymer preconcentration, and a near-infrared diode near 1670 nm, with a reported 159-ppbv detection limit on breath-bag samples.

Why is it relevant? It shows that cavity-enhanced near-infrared acetone measurement is physically plausible and identifies demanding sensitivity and preconcentration requirements.

How will we use it? We will use its wavelength and performance scale to evaluate candidate components and interpret whether our measured detection limit is adequate for breath experiments.

- [2] A. Dixit and R. Yelisetty, *GLASS: glucose level measuring via breathe acetone sensing through laser spectroscopy*, Thomas Jefferson High School for Science and Technology QLab, <https://qlab.sites.tjhsst.edu/projects/detail/93/> (visited on 09/22/2026).

What did this work do? Built a student-scale near-UV breath-acetone spectroscopy setup with a multipass gas chamber, 275-nm diode, and humidity control; preliminary results demonstrated acetone detection while exposing diode-power and data limitations.

Why is it relevant? This former QLab project is the closest local precedent for our apparatus, sample-handling constraints, and noninvasive diabetes motivation.

How will we use it? We will build on its practical lessons while using a Fabry–Pérot design, near-infrared component selection, quantitative calibration, and a mechanistic reconstruction model.

- [3] M. Raissi, P. Perdikaris, and G. E. Karniadakis, “Physics-informed neural networks: a deep learning framework for solving forward and inverse problems involving nonlinear partial differential equations”, *Journal of Computational Physics* **378**, 686–707 (2019).

What did this work do? Introduced the modern PINN framework for forward and inverse differential-equation problems by combining observations with equation, initial-condition, and boundary-condition residuals.

Why is it relevant? Our ketone problem is an inverse problem with latent states governed by coupled ODE and PDE physics.

How will we use it? We will use its physics-informed formulation as the conceptual basis for the classical baseline and for the loss surrounding the quantum layer.

- [4] C. Trahan, M. Loveland, and S. Dent, “Quantum physics-informed neural networks”, *Entropy* **26**, 649 (2024).

What did this work do? Compared quantum, hybrid quantum–classical, and classical PINNs on transient and steady differential equations and reported competitive accuracy with fewer trainable parameters in some settings.

Why is it relevant? It directly establishes the feasibility of inserting parameterized quantum circuits into a physics-informed model.

How will we use it? We will adapt the hybrid architecture to ketone reconstruction while adding parameter-matched controls, repeated seeds, and held-out physiological-state metrics.

- [5] J. L. Beckey, M. Cerezo, A. Sone, and P. J. Coles, “Variational quantum algorithm for estimating the quantum fisher information”, *Physical Review Research* **4**, 013083 (2022).

What did this work do? Developed a variational algorithm that bounds quantum Fisher information and used it to optimize parameter-estimation sensitivity without requiring an explicit analytic sensor-dynamics model.

Why is it relevant? QFI provides a principled measure of how distinguishable nearby encoded parameter values are and therefore which directions are poorly or strongly identifiable.

How will we use it? We will compute or estimate QFI for our small circuits, analyze its spectrum, and test whether stable rankings can prioritize model variables or optical bands.

- [6] D. Uciński, “D-optimal sensor selection in the presence of correlated measurement noise”, *Measurement* **164**, 107873 (2020).

What did this work do? Develops a D-optimal framework for selecting sparse measurements in PDE-governed spatiotemporal parameter-estimation problems while accounting for correlated measurement noise.

Why is it relevant? Our VOC sensing problem is likewise a PDE-constrained inverse problem in which a limited set of wavelengths and VOC measurements must identify latent metabolic states and kinetic parameters.

How will we use it? We will use D-optimality to define a classical information-based objective for selecting candidate VOCs and wavelengths from sensitivity or Fisher-information calculations. We will then formulate a discrete approximation of that design problem as a QUBO for subsequent quantum optimization.

Appendix: Classical Mathematical Model Development

Slow Metabolic Ketone Dynamics

The metabolic component tracks three ketone bodies in blood: $B(t)$ is the concentration of β -hydroxybutyrate (BHB), $Q(t)$ is the concentration of acetoacetate (AcAc), and $A(t)$ is the concentration of acetone. Let $R_K(t)$ denote the total hepatic ketone-production rate. A fraction ρ_B enters the BHB pool directly, while the remaining fraction $1 - \rho_B$ enters the AcAc pool. BHB and AcAc reversibly interconvert with rate constants k_{BQ} and k_{QB} . BHB and AcAc are also cleared

through non-acetone pathways at rates k_B and k_Q , while AcAc decarboxylates to acetone at rate k_{QA} . These assumptions give the compartment balances

$$\frac{dB}{dt} = \rho_B R_K(t) - k_{BQ}B + k_{QB}Q - k_B B, \quad (1)$$

$$\frac{dQ}{dt} = (1 - \rho_B) R_K(t) + k_{BQ}B - (k_{QB} + k_Q + k_{QA})Q, \quad (2)$$

$$\frac{dA}{dt} = k_{QA}Q - k_{A,\text{eff}}A. \quad (3)$$

Each equation follows directly from accumulation equals inflow minus outflow. For example, the AcAc pool gains material from direct ketogenesis and BHB-to-AcAc conversion, and loses material through reverse conversion, metabolic clearance, and conversion to acetone. The effective acetone-removal coefficient $k_{A,\text{eff}}$ summarizes pulmonary and other clearance on the slow metabolic time scale. If blood and alveolar gas are assumed to equilibrate locally, the corresponding gas-phase acetone concentration is

$$C_A(t) = \frac{A(t)}{\lambda_{b:a}}, \quad (4)$$

where $\lambda_{b:a}$ is the blood–air partition coefficient. The slow system therefore supplies the time-varying acetone boundary condition for the respiratory model.

Fast Pulmonary and Airway Transport

During a single breath, let $x \in [0, L]$ measure position along an effective one-dimensional airway, with $x = 0$ at the alveolar end and $x = L$ at the mouth. Let $C(x, t_b; t)$ denote gas-phase acetone during the fast within-breath time t_b , while the slow metabolic time t is treated as fixed over that breath. Conservation of acetone in a differential airway control volume includes axial advection with air velocity u , molecular dispersion with coefficient D , and reversible exchange with the airway wall:

$$\frac{\partial C}{\partial t_b} + u \frac{\partial C}{\partial x} = D \frac{\partial^2 C}{\partial x^2} - k_{aw} \left(C - \frac{C_w}{\lambda_{w:a}} \right). \quad (5)$$

Here $C_w(x, t_b; t)$ is the acetone concentration stored in the airway wall, k_{aw} is the gas-to-wall exchange rate, and $\lambda_{w:a}$ is the wall–air partition coefficient. A local wall balance accounts for uptake from the gas and exchange with blood:

$$\frac{\partial C_w}{\partial t_b} = k_{wa} (\lambda_{w:a} C - C_w) - k_{wb} (C_w - \lambda_{w:b} A(t)), \quad (6)$$

where k_{wa} and k_{wb} are exchange rates and $\lambda_{w:b}$ is the wall–blood partition coefficient. The alveolar boundary is set by the slow blood-acetone state, while a zero-gradient condition represents outflow at the mouth:

$$C(0, t_b; t) = \frac{A(t)}{\lambda_{b:a}}, \quad \frac{\partial C}{\partial x}(L, t_b; t) = 0. \quad (7)$$

The model-predicted exhaled concentration is the mouth value

$$C_{\text{exh}}(t_b; t) = C(L, t_b; t). \quad (8)$$

Thus the slow model determines the blood-acetone level entering each breath, and the fast model determines how transport and airway exchange reshape that signal before measurement. The dimensional forward problem is solved numerically by finite differences after specifying the metabolic and within-breath initial conditions.

Optical Observation Model

The interferometer does not observe B , Q , or A directly. It records wavelength-dependent intensity produced by the exhaled volatile-organic-compound mixture. For a candidate wavelength λ_m , a first observation model is the Beer–Lambert relation

$$y_m(t) = -\log\left(\frac{I_m(t)}{I_{0,m}}\right) = \ell_{\text{eff},m} \sum_j \epsilon_j(\lambda_m) C_{j,\text{exh}}(t) + \eta_m(t), \quad (9)$$

where $I_{0,m}$ is reference intensity, ϵ_j is the absorption coefficient of volatile compound j , $\ell_{\text{eff},m}$ is the effective cavity path length, and η_m collects detector noise, drift, humidity effects, and model discrepancy. The initial acetone-only implementation retains the acetone term; later versions may include interfering VOCs. Aarjav’s calibration measurements will replace idealized bandwidth, path-length, and noise assumptions with the measured Fabry–Pérot response.

Initial Classical PINN Implementation

The initial inverse model is a patient-specific classical PINN whose neural network maps slow time to normalized state estimates,

$$\mathcal{N}_\Theta(t) = (\hat{B}(t), \hat{Q}(t), \hat{A}(t)). \quad (10)$$

Automatic differentiation supplies the time derivatives of these outputs. Substitution into the three metabolic equations produces residuals f_B , f_Q , and f_A . Predicted acetone is then propagated through the airway solver and optical observation model so that the network is trained against breath measurements rather than unobserved blood states. This construction extends the inverse-problem workflow implemented in PINNLab, in which a neural-network state representation is trained jointly against observations, governing-equation residuals, and initial conditions. The original objective is

$$\mathcal{L} = w_d \mathcal{L}_{\text{data}} + w_p \langle f_B^2 + f_Q^2 + f_A^2 \rangle + w_0 \mathcal{L}_{\text{IC}} + w_+ \mathcal{L}_+ + w_r \mathcal{L}_{\text{prior}}. \quad (11)$$

The five terms respectively fit the optical observations, enforce the metabolic equations, anchor the initial low-ketosis state, penalize negative concentrations, and impose weak physiological priors on uncertain parameters. Bounded logistic transformations keep learned parameters within plausible ranges. Training uses curriculum-weighted Adam with multiple random restarts, brief refitting of the best restart, and optional L-BFGS refinement. The primary practical configuration uses prior information for the patient-specific acetone-clearance quantity $\Gamma_A = \frac{k_{A,\text{eff}}}{k_B}$; oracle and population settings serve as upper-bound and pooled-data comparisons. This classical implementation is the baseline that the proposed quantum layer must improve under identical observations, physics, and evaluation metrics.