



Research Proposal

Can We Smell Diabetes?

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

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1 Introduction

Diabetes management still relies on measurements that can be invasive, intermittent, or costly. Acetone in exhaled breath offers a promising optical signal, but a spectrum is not a metabolic state. The quantities of clinical interest—blood β -hydroxybutyrate (BHB), acetoacetate, acetone, and how they change over time—must be inferred from noisy, indirect observations. Cavity-enhanced systems have detected breath acetone near 1670 nm, giving us a realistic optical starting point [4]. A previous QLab project also demonstrated both the promise and practical limits of student-built breath-acetone spectroscopy [5].

We will proceed in stages, beginning with computational and engineering work in parallel. Mohan will develop the slow-fast model, classical PINN, and a small simulated quantum layer; meanwhile, Aarjav will design and build the optical system. They will exchange information early, combining quantum and classical information analyses with measured absorption cross-sections and practical source/spectrometer constraints to choose candidate wavelengths and geometry before procurement. Next, the team will pump controlled acetone vapor, generated from a liquid standard, through the cavity. These measured spectra—not synthetic observations generated by the same forward model—will provide the first external test of both classical and quantum-enhanced reconstruction. Only after this calibration gate and required review will the team consider longitudinal breath measurements from willing adult TJ faculty. Results at each stage will update the observation model and may send the design back for a different wavelength, source, coating, or path length. This feedback loop is the project’s central test; a quantum advantage and large qubit count are not assumed.

1.1 Intellectual Merit

The project brings mechanistic multiscale modeling, hybrid quantum-classical learning, quantum information geometry, and a physical optical instrument together around one inverse problem. In doing so, it explores quantum modeling and optical sensing while building methods that could eventually support noninvasive monitoring of a disease affecting hundreds of millions of people worldwide.

1.2 Broader Impact

A low-cost, noninvasive way to track ketone dynamics could eventually help flag dangerous metabolic changes earlier. One possible long-term application is monitoring for diabetic ketoacidosis, a serious complication associated with insufficient insulin and rising ketones, without skin insertion. This project is a feasibility study, not a diagnostic device; any faculty breath study will proceed only with required approval and informed consent.

2 Background and Prior Work

Ketone metabolism unfolds on two coupled time scales. A slow compartment model tracks the production, interconversion, and clearance of BHB, acetoacetate, and acetone. A fast pulmonary model then maps blood acetone to exhaled concentration through gas exchange and airway transport. After nondimensionalization, a finite-difference forward solver will generate trajectories and synthetic observations. Our inverse problem is to recover hidden ketone states and selected physiological parameters from sparse optical breath measurements.

Physics-informed neural networks (PINNs) combine observations with differential-equation residuals and initial or boundary conditions, allowing hidden states and parameters to be estimated without abandoning the governing physics [1]. Our classical framework and verified forward solvers will serve as the baseline for any quantum extension. A quantum PINN replaces or augments part of the classical model with a parameterized quantum circuit. Trahan, Loveland, and Dent found that quantum and hybrid PINNs solved several differential equations with competitive accuracy and, in some cases, fewer trainable parameters [2]. Their results motivate a controlled ketone-reconstruction test, not an assumption that the hybrid model will win.

Quantum Fisher information (QFI) quantifies how strongly a parameterized quantum state responds to an encoded parameter, and thus bounds the precision of its estimation. Variational methods can estimate or bound QFI and optimize a quantum probe without a complete analytic model of sensor dynamics [3]. Here, the QFI matrix will serve as an information-geometric diagnostic: its diagonal entries and eigenvectors can reveal informative parameter combinations, expose poorly identifiable directions, and help prioritize spectral features for testing. The optical apparatus itself is not a quantum sensor; QFI is a tool for analyzing the simulated variational model.

In a Fabry–Pérot cavity, wavelength-dependent interference changes with cavity geometry, refractive index, absorption, and analyte concentration. A 2025 study measured an acetone near-infrared methyl-overtone cross-section across 1671.5–1675 nm under pressure and humid-breath conditions [6], making the 1670s-nm band our leading candidate. We will also consult HITRAN for relevant species, wavelength coverage, units, and measurement conditions [8]. Zheng et al. demonstrate broadband cavity-enhanced sensing with a 1650-nm LED and an 8-cm high-reflectivity cavity; this is a useful engineering precedent, though not evidence that the LED’s center wavelength is sensitive to acetone [7]. Other breath-acetone work illustrates the sensitivity challenge and potential need for preconcentration [4], while QLab’s GLASS project highlights practical issues such as source power and humidity [5]. The Oxford group associated with Grant Ritchie has published related cavity-enhanced breath-acetone research, offering a valuable point of comparison and motivating our request for general setup details [4, 11].

Project Need / Research Gap. Quantum PINNs, information-based quantum optimization, and breath spectroscopy have largely been studied separately. We will bring them together to test whether a small simulated quantum layer and information-guided instrument design improve reconstruction of a physiologically meaningful, multiscale state, using measured acetone standards and a student-built interferometer. QFI will characterize sensitivity in the circuit state; classical Fisher information, calculated from the measured spectral response and noise, will separately describe what the physical instrument can identify.

3 Research Goals

All comparisons will report improvements, null results, and degradations with equal emphasis.

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: Formalize preliminary equilibrium/steady-state, positivity, and boundedness analysis; verify the nondimensionalized slow ODE and fast pulmonary PDE solvers against manufactured or high-resolution numerical solutions. Train the classical inverse PINN on

synthetic data with fixed splits and repeated seeds, then test robustness with deliberately mismatched forward generators and held-out pumped acetone-vapor measurements to avoid relying only on data generated by the same model.

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: Use PennyLane to embed selected normalized features into a small simulated circuit and return expectation values to the PINN. Compare hybrid, original PINN, and parameter-matched classical bottleneck under identical observations, losses, budgets, and repeated seeds. Compute QFI for the circuit and classical Fisher information from the predicted/observed instrument response; analyze both alongside absorption magnitude, noise, and parameter sensitivities [3, 9].

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 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: In parallel with computational work, compare a narrow-line pigtail laser diode with a broadband LED and candidate spectrometers. Prioritize 1671.5–1675 nm using published acetone cross-sections; consider 1200–1500 nm only if HITRAN/literature and measured signal-to-noise support a useful acetone feature there. Convolve wavelength-dependent cross-sections with each source’s measured or datasheet spectral profile (a Gaussian is an initial approximation, not a universal 5–10-nm linewidth). Optimize flat mirror coatings, cavity spacing, alignment, and effective path length jointly with source power and spectrometer resolution. Then use a pump to feed controlled acetone-vapor standards generated from a small acetone solution into the cavity, with blank and reference runs.

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: Iterate between absorption-weighted QFI/classical Fisher rankings and practical optics constraints; insert measured source spectrum, cavity transmission/path length, spectrometer instrument function, noise, drift, and missingness into reconstruction. Pumped acetone-vapor data are the required experimental validation gate. Only after successful calibration and required human-subject review may consenting adult TJ faculty provide longitudinal breath samples 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 work will pass through three gates, beginning with computation and engineering in parallel. Mohan will formalize the slow metabolic ODE and fast pulmonary PDE, develop the preliminary equilibrium, positivity, and boundedness analysis, nondimensionalize the system, verify its finite-difference solutions, and establish the classical inverse PINN. At the same time, Aarjav will compare components, model the Fabry–Pérot cavity, and begin a bench prototype. Their early design reviews will put model-based information priorities beside actual component and measurement constraints, so wavelength, source, and cavity choices can still change before procurement.

Our leading candidate is the 1671.5–1675 nm acetone band. The reported methyl-overtone cross-section peaks near 1672.44 nm at approximately $1.22 \times 10^{-21} \text{ cm}^2$ [6]. We will compare that study with HITRAN data for acetone and likely interferences, recording pressure, temperature, spectral resolution, and units [8]. The 1200–1500 nm telecom region could offer lower-cost components, but we will consider it only if cross-section data and instrument-weighted sensitivity identify a useful acetone feature there. Zheng et al.’s 1650-nm LED cavity is an engineering precedent for broadband source/cavity integration, not evidence that a source centered at 1650 nm covers the acetone peak [7]. We will compare a broadband LED with a narrow-line pigtail laser diode, representing each by its measured or manufacturer-specified spectrum. A Gaussian is a useful first approximation; we will not assume a generic 5–10-nm linewidth for a laser diode without checking its datasheet or measuring it. A Thorlabs 950–1700-nm spectrometer is one candidate, but its reported resolution of under 9 nm is wider than the published feature’s roughly 3.5 nm span and may blur it substantially [12]. Before purchase, we will check instrument-convolved sensitivity, throughput, detector response, and vendor pricing; a higher-resolution alternative may be necessary.

We will optimize the source wavelength, power, and spectral width alongside flat high-reflectivity mirror coatings, cavity spacing and alignment, fiber coupling, detector response, free spectral range, finesse, and effective path length. A 10-m effective path—about 40 traversals of a 25-cm cavity if that geometry is selected—is a design target to evaluate, not a promise of 10% absorbance. As a Beer–Lambert check, the reported peak cross-section predicts an optical depth of about 1.5×10^{-4} at 25°C and 5 ppm acetone, equivalent to roughly 0.015% absorption over 10 m before accounting for cavity enhancement and spectral convolution. Calibration must replace this preliminary estimate. The gap between this estimate and the 10% target makes clear that we may need a longer effective path, preconcentration, a stronger transition, or another sensitivity strategy. Path length and mirror reflectivity affect absorption contrast; spectrometer resolution determines how finely spectral structure can be distinguished. They are separate, interacting design variables rather than inverse quantities.

Synthetic data remain useful for controlled ablations, but testing only on observations generated by the same equations and discretization risks an inverse crime. We will therefore pair matched synthetic splits with stress tests using a different solver, perturbed or omitted nuisance physics, shifted parameters, realistic noise, and held-out sampling schedules. The first external check will use pumped acetone vapor from controlled liquid standards, with blanks and repeated concentrations. An approved preparation and calibration procedure will establish vapor concentration rather than inferring it from liquid concentration alone. We will first evaluate the classical model using the measured instrument response, then compare the quantum-augmented model on the same calibrated data and under the same computational budgets.

Following the quantum-PINN approach in [2], the hybrid model will replace or augment one compact classical feature layer with a shallow parameterized circuit. PennyLane supports differentiation and QFI routines for small state-vector simulations, making it suitable for this scale of study [9]. We will use only the qubits needed to encode retained features and increase circuit depth or size only when ablations justify it. Each hybrid configuration will be compared with the original PINN and a parameter-matched classical bottleneck using the same data, random seeds, optimizer budgets, and stopping rules. Primary outcomes are held-out RMSE for BHB, acetone, and their time derivatives, as well as parameter recovery, physics residual, training stability, and wall time.

For each selected circuit, Mohan will estimate QFI and compare its eigenvalues and parameter sensitivities with classical Jacobian and Fisher analyses. Wavelength selection will also account for absolute absorption cross-section and predicted absorbance, not merely a normalized information score. For source i , the model will integrate attenuated light across its spectral profile $S_i(\lambda)$ and the detector/spectrometer response $R(\lambda)$ using acetone cross-section $\sigma_A(\lambda)$. We will calculate classical Fisher information from this instrument-level signal and measured noise covariance. D-optimality offers a principled way to choose measurements under correlated noise [10]; our analysis will ground it in measured spectral covariance and absorption. Keeping the two analyses distinct avoids treating circuit QFI as if it directly measured physical-instrument identifiability. QUBO or QAOA could later help with discrete wavelength or VOC selection; continuous design would require discretization or a continuous/hybrid optimizer and is beyond the minimum project.

Aarjav will model, assemble, align, and characterize the Fabry–Pérot interferometer. After staff review of the optical path and materials, a pump will carry gas equilibrated over a small acetone-water solution—or another approved vapor standard—through the measurement cell. Reference-gas, blank, and controlled-vapor runs will measure repeatability, concentration response, free spectral range, finesse, drift, noise, response time, and limit of detection. This controlled-sample stage must be completed before any human sampling.

Measured source spectra, cavity response, spectrometer instrument function, and noise will be folded into the forward observation model and returned to Mohan’s inverse model. They may

prompt another design iteration: if an informative wavelength has inadequate source power or detector response, the team will select and reanalyze the best feasible alternative. Only after acetone-standard validation and required school or institutional human-subject review may consenting adult TJ faculty provide longitudinal breath samples under a written, non-diagnostic protocol. Results will not inform treatment decisions. QUBO/QAOA wavelength optimization and human measurements are extensions, not prerequisites for the core result.

5 Expected Results and Data Analysis

We expect the verified forward model to reproduce reference ketone and pulmonary-transport solutions to numerical tolerance. Inverse reconstruction should become less accurate as optical noise grows or sampling becomes sparse. The classical PINN will show how much of the latent metabolic trajectory can be recovered from breath acetone alone, and whether additional spectral features or longitudinal data are needed.

We do not assume a quantum advantage. The hybrid model could reduce held-out error or parameter count, or improve recovery from sparse data; it could also match the classical controls or prove slower and less reliable. We will summarize repeated-seed results with effect sizes, confidence or bootstrap intervals, and full error distributions. Comparing accuracy with wall time will separate statistical performance from computational cost. QFI eigenvalues and rankings will be tested across circuit initializations, noise assumptions, and feature encodings, then compared with classical sensitivity rankings. We will treat QFI as useful only if it yields a stable, experimentally testable priority—not simply a large value in one circuit.

We expect the apparatus to produce repeatable interference spectra before it reaches physiological acetone sensitivity. The 1671.5–1675 nm feature is our literature-based starting band [6]; the 1650-nm LED study demonstrates a broadband cavity architecture, but not acetone sensitivity at that center wavelength [7]. We will report wavelength accuracy, source spectrum, free spectral range, finesse, drift, signal-to-noise ratio, response linearity, concentration response, and limit of detection. The proposed 10-m effective path (about 40 traversals) will be evaluated against measured cross-sections and acetone standards; 10% absorbance is a target to test, not an expected result. Prior cavity breath-acetone systems show that high sensitivity may require high finesse or preconcentration [4]. If the initial source or path falls short, measurements will guide a narrower diode, more reflective coating, longer effective path, preconcentration, or another band.

The project will build evidence in stages: (1) parallel model and instrument analyses; (2) empirical response and sensitivity measurements using pumped acetone standards; and (3) reconstruction with the measured instrument response, followed—only if approved—by longitudinal faculty breath feasibility data. Cross-solver, mismatched-physics tests and external acetone-standard measurements will address the limitations of synthetic data generated by the same model. Any human measurements will assess repeatability, not diagnosis. A valid conclusion may favor the classical model, find QFI useful for design without better hybrid predictions, or show that hardware—not model choice—is the limiting factor.

6 Feasibility and Resources

The existing slow-fast model, finite-difference solvers, and preliminary inverse PINN reduce computational risk. Initial mathematical analysis has established equilibrium and steady-state behavior and is developing positivity and boundedness guarantees. These properties will help constrain valid

parameters and check numerical trajectories. Quantum experiments will use small state-vector simulations rather than large hardware runs; PennyLane supplies differentiable circuits and QFI/Fisher tools appropriate to this scale [9].

The key experimental resource is a near-infrared spectrometer. A Thorlabs instrument spanning roughly 950–1700 nm is under consideration, but its resolution and throughput near 1672–1675 nm—and a current quote—must be confirmed before purchase [12]. We will compare broad-band LEDs with pigtail laser diodes, verify their actual spectral profiles, and choose mirrors with high reflectivity across the selected band. Other needs include mounts, fibers, a pump, an approved gas cell and tubing, acetone standards, and humidity and temperature sensors. We will pursue the 1200–1500 nm telecom alternative only if sensitivity analysis supports it. Designs, calibration files, model configurations, random seeds, and raw spectra will be version-controlled.

7 Safety and Risk Considerations

We will use low-power LEDs for alignment whenever possible. Sources will be enclosed or kept at controlled beam height, and students will never look directly into LEDs, fibers, or reflected beams. Any laser will be operated under QLab procedures, with wavelength-appropriate eyewear and supervision. Mirrors, glass, electronics, and power supplies will be secured in place.

Acetone is volatile and flammable, so calibration quantities will be kept small. Staff will supervise preparation and use of any acetone-water solution or pump-fed headspace system in approved containers and ventilation, away from ignition sources, and will direct storage and disposal in accordance with safety data sheets. We will check pressure, flow, and exhaust to prevent vessel overpressure or vapor release. Breath collection will begin only after school and required participant review. Adult volunteers will give informed consent; the study will make no medical claims, store coded rather than directly identifying data, use disposable mouthpieces and one-way flow components, and allow participants to 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. 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

Training and testing on synthetic observations from the same forward model can make reconstruction look more accurate than it will be on real data (an inverse crime); a predicted path length may also overstate absorbance.

Solution: Use a different solver and perturbed/mismatched forward physics for synthetic tests, then require pump-delivered acetone-standard measurements as the first external validation. Estimate gas-phase concentration and absorbance from the selected cross-section, measured source spectrum, effective path, and blank/reference calibration. A preliminary calculation with the reported peak cross-section predicts only about 0.015% absorption for 5 ppm over 10 m before cavity enhancement, so treat the 10-m/40-traversal geometry and 10% absorbance as targets to test, not assumed results.

Challenge 7

The candidate source or spectrometer may not resolve the narrow acetone feature, and cheaper telecom-band parts may not overlap useful absorption.

Solution: Convolve cross-section data with measured source and instrument spectral profiles; obtain vendor specifications/quotes; compare a broadband LED, narrow-line pigtail diode, and candidate bands before procurement. Keep the 1670s-nm acetone band as the initial evidence-led choice and retain telecom only if data support it.

Challenge 8

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: October–November: Parallel Model and Engineering Design

Task — What will you do? Formalize equilibrium/steady-state, positivity, and boundedness analysis; validate the forward model and classical PINN; in parallel, compare sources, mirror coatings, flat-mirror cavity geometry, spectrometer options, and HITRAN/literature cross-sections.

Objective — What measurable result should this work produce? Produce verified solver metrics, cross-solver/mismatched synthetic tests, a spectral sensitivity budget, and a component decision matrix before purchase.

Goal — What larger research capability or milestone does this establish? Set an evidence-based initial wavelength, path-length target, and build configuration while maintaining model-to-optics feedback.

Milestone 2: December–January: Prototype and First Computational Rankings

Task — What will you do? Implement the small PennyLane quantum layer and matched classical control; calculate QFI and instrument-level classical Fisher information; assemble and align the cavity with selected source and coatings.

Objective — What measurable result should this work produce? Complete repeated computational trials and obtain reference/blank spectra, measured source profiles, free spectral range, finesse, and drift.

Goal — What larger research capability or milestone does this establish? Pass the initial design review and prepare the controlled acetone-standard test.

Milestone 3: February–March: Pumped Acetone-Standard Validation

Task — What will you do? Use an approved pump-fed headspace/acetone-standard arrangement to measure blanks and controlled concentrations; quantify response and noise; revise source, band, path length, or coating if the absorption budget misses target.

Objective — What measurable result should this work produce? Produce calibrated spectra, concentration-response curves, detection limits, and a documented design iteration based on measured data.

Goal — What larger research capability or milestone does this establish? Complete required empirical instrument validation before interpreting any breath data.

Milestone 4: April: Instrument-Constrained Reconstruction

Task — What will you do? Train and evaluate classical PINN then QPINN with the measured source/cavity/spectrometer response and acetone-standard data; assess repeatability and compare with mismatched synthetic tests.

Objective — What measurable result should this work produce? Compare idealized versus measured-instrument reconstruction, classical versus hybrid performance, and predicted versus measured spectral information.

Goal — What larger research capability or milestone does this establish? Close the core model-instrument feedback loop using experimental calibration data.

Milestone 5: May: Human Feasibility Extension and Final Analysis

Task — What will you do? If calibration gates and required human-subject approvals are met, collect longitudinal breath spectra from willing adult TJ faculty; otherwise complete standards-based analysis and documentation.

Objective — What measurable result should this work produce? Produce coded feasibility/repeatability results if approved, final uncertainty and sensitivity analysis, apparatus documentation, paper, and presentation.

Goal — What larger research capability or milestone does this establish? Report a reproducible conclusion about model performance, optical feasibility, and limitations without making diagnostic claims.

10 Group Responsibilities

Mohan Parthasarathy

Leads the mathematical and computational work: nondimensionalization; verification of the slow metabolic ODE and fast pulmonary PDE; finite-difference reference solutions; classical and hybrid PINNs; QFI, identifiability, uncertainty, and sensitivity analyses; and reconstruction using measured instrument response. He will translate model findings into quantitative priorities for wavelength, precision, and sampling.

Aarjav Jain

Leads the optical work: Fabry-Pérot design and simulation; comparison of broadband LEDs and pigtail laser diodes; selection of mirror coatings, cavity spacing and path length, fibers, detector, and spectrometer; fabrication, alignment, and wavelength/response calibration; pump-fed acetone-vapor tests; and characterization of resolution, finesse, drift, noise, absorbance, and detection limit. He will translate hardware measurements into a response and noise model for reconstruction.

Together, the students will define the interface between the mathematical and optical components; check QFI, classical Fisher, and absorption rankings against hardware feasibility; plan design iterations; follow safety and participant protocols; interpret findings; and write the final paper. Computation and engineering begin in parallel. Model-based priorities guide the first hardware choices, calibration updates the forward observation model, and reconstruction results may prompt another hardware revision. Pumped acetone standards are the required experimental validation stage; human participants are considered only after that gate and approval. The two workstreams thus form one feedback loop rather than separate deliverables.

Surya Raj (Engineering Pd 1)

Leads the breath-sampling and environmental-control system. He will design and fabricate the breath inlet and gas-handling assembly, an automated valve system to control sample entry, and an enclosure for breath vapor, then automate the sampling sequence. The system will introduce fresh breath consistently while limiting water vapor and residual sample that could interfere with LED or laser measurements. Coordinated valves and timing will introduce a sample, isolate the measurement chamber, and prepare it for the next run. Surya will characterize flow, humidity, and sampling consistency, and work with Aarjav to measure how the sampling system affects optical signals and instrument noise.

11 Appendix: Mathematical Model

11.1 Slow Metabolic Ketone Dynamics

The slow model follows three blood ketone bodies: $B(t)$ for β -hydroxybutyrate (BHB), $Q(t)$ for acetoacetate (AcAc), and $A(t)$ for acetone. Hepatic production occurs at rate $R_K(t)$, with fraction ρ_B entering the BHB pool and the remainder entering AcAc. BHB and AcAc interconvert at rates k_{BQ} and k_{QB} ; BHB and AcAc also undergo non-acetone clearance at rates k_B and k_Q . AcAc converts to acetone at rate k_{QA} . The resulting compartment balances are

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

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

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

Each balance is accumulation equals inflow minus outflow. In particular, AcAc gains material from ketone production and BHB conversion, and loses it through reverse conversion, clearance, and conversion to acetone. The effective removal rate $k_{A,\text{eff}}$ summarizes pulmonary and other acetone clearance on the slow time scale. Under local blood–air equilibrium, alveolar gas-phase acetone is

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

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

11.2 Qualitative Analysis

For nonnegative initial conditions, nonnegative ketone production, and positive rate constants, the nonnegative state region is forward invariant. At each boundary where a concentration is zero, its derivative is nonnegative:

$$\left. \frac{dB}{dt} \right|_{B=0} \geq 0, \quad \left. \frac{dQ}{dt} \right|_{Q=0} \geq 0, \quad \left. \frac{dA}{dt} \right|_{A=0} \geq 0. \quad (5)$$

Thus, physiologically valid initial concentrations cannot become negative under the model.

To establish boundedness, define total ketone burden as $S = B + Q + A$. Internal conversion terms cancel, leaving

$$\frac{dS}{dt} = R_K(t) - k_B B - k_Q Q - k_{A,\text{eff}}A. \quad (6)$$

If production is bounded by $R_{\max}$ and $k_{\min} = \min\{k_B, k_Q, k_{A,\text{eff}}\} > 0$, then

$$\frac{dS}{dt} \leq R_{\max} - k_{\min}S, \quad (7)$$

which implies

$$S(t) \leq S(0)e^{-k_{\min}t} + \frac{R_{\max}}{k_{\min}} \left(1 - e^{-k_{\min}t}\right). \quad (8)$$

All three concentrations therefore remain finite. Under constant ketone production, $R_K(t) = R_K^*$, the linear system has a unique nonnegative equilibrium, found by setting all three derivatives to zero. It represents the long-run balance among production, interconversion, and clearance. Positivity keeps model states physiologically meaningful; boundedness rules out artificial blow-up; and the equilibrium offers a benchmark for checking the finite-difference solver and initializing or constraining the inverse PINN. Together, these analyses help distinguish reconstruction limits caused by sparse or uninformative data from instabilities in the forward model.

11.3 Fast Pulmonary and Airway Transport

Within a single breath, let $x \in [0, L]$ denote position along an effective one-dimensional airway, from alveoli ($x = 0$) to mouth ($x = L$). Let $C(x, t_b; t)$ be gas-phase acetone at fast within-breath time t_b , with slow metabolic time t held fixed. The gas balance accounts for axial advection at air velocity u , molecular dispersion with coefficient D , and reversible airway-wall exchange:

$$\frac{\partial C}{\partial t_b} + u \frac{\partial C}{\partial x} = D \frac{\partial^2 C}{\partial x^2} - k_{aw} \left(C - \frac{C_w}{\lambda_{w:a}} \right). \quad (9)$$

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

$$\frac{\partial C_w}{\partial t_b} = k_{wa} (\lambda_{w:a} C - C_w) - k_{wb} (C_w - \lambda_{w:b} A(t)), \quad (10)$$

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

$$C(0, t_b; t) = \frac{A(t)}{\lambda_{b:a}}, \quad \frac{\partial C}{\partial x}(L, t_b; t) = 0. \quad (11)$$

The model-predicted exhaled concentration is the mouth value

$$C_{\text{exh}}(t_b; t) = C(L, t_b; t). \quad (12)$$

The slow model therefore sets the blood-acetone level entering each breath, while the fast model describes how transport and wall exchange reshape it before measurement. Once metabolic and within-breath initial conditions are specified, we solve this dimensional forward problem by finite differences.

11.4 Optical Observation Model

The interferometer does not measure B , Q , or A directly. It records wavelength-dependent intensity from the exhaled volatile-organic-compound mixture. At candidate wavelength λ_m , our first observation model is Beer-Lambert:

$$y_m(t) = -\log\left(\frac{I_m(t)}{I_{0,m}}\right) = \ell_{\text{eff},m} \sum_j \epsilon_j(\lambda_m) C_{j,\text{exh}}(t) + \eta_m(t), \quad (13)$$

Here $I_{0,m}$ is the reference intensity, ϵ_j is the absorption coefficient of compound j , $\ell_{\text{eff},m}$ is effective cavity path length, and η_m collects detector noise, drift, humidity effects, and model discrepancy. A finite-bandwidth source and spectrometer require an instrument-level model integrated over wavelength:

$$I_i(t) = \int R(\lambda) S_i(\lambda) I_0(\lambda) \exp \left[-\ell_{\text{eff}} \sum_j \sigma_j(\lambda) C_{j,\text{exh}}(t) \right] d\lambda + \eta_i(t), \quad (14)$$

Here $S_i(\lambda)$ is the measured or manufacturer-specified source profile (initially, it may be approximated as Gaussian), $R(\lambda)$ includes spectrometer throughput and wavelength-spread function, and $\sigma_j(\lambda)$ is the molecular absorption cross-section. LEDs and laser diodes emit across a spectrum, not at one exact wavelength; each source’s width must come from its datasheet or measurement rather than a generic 5–10 nm assumption. We will use the 2025 acetone study and HITRAN data, documenting pressure, temperature, and resolution [6, 8]. The integral makes clear that source width, spectrometer resolution, path length, and absorption strength jointly determine observable contrast.

The 1671.5–1675 nm acetone feature is our initial candidate band. A 10-m effective path—about 40 traversals of a 25-cm cavity—is a geometry target to test with Beer–Lambert calculations and calibration, not a prediction of 10% absorbance. At 25°C and 5 ppm, the published peak cross-section yields a preliminary estimate of about 0.015% absorption over 10 m before cavity enhancement and instrument-response effects [6]. The 10% figure must therefore remain a target, not an assumption. Path length and mirror reflectivity affect absorption contrast; spectrometer resolution determines how finely spectral structure can be distinguished. We will optimize these distinct but interacting quantities together. The initial optical model includes acetone alone, with interfering VOCs considered in later versions. Aarjav’s calibration measurements will replace idealized source bandwidth, path length, and noise assumptions with the measured Fabry–Pérot response.

11.5 Initial Classical PINN Implementation

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

$$\mathcal{N}_{\Theta}(t) = (\hat{B}(t), \hat{Q}(t), \hat{A}(t)). \quad (15)$$

Automatic differentiation supplies the time derivatives. Substituting the network outputs into the metabolic equations gives residuals f_B , f_Q , and f_A . Predicted acetone then passes through the airway solver and optical observation model, so training uses breath measurements rather than unobserved blood states. This extends PINNLab’s inverse-problem workflow, which trains a neural-network state representation against observations, governing-equation residuals, and initial conditions. The baseline objective is

$$\mathcal{L} = w_d \mathcal{L}_{\text{data}} + w_p \langle f_B^2 + f_Q^2 + f_A^2 \rangle + w_0 \mathcal{L}_{\text{IC}} + w_+ \mathcal{L}_+ + w_r \mathcal{L}_{\text{prior}}. \quad (16)$$

The five terms respectively fit optical observations, enforce the metabolic equations, anchor the initial low-ketosis state, discourage negative concentrations, and apply weak physiological priors to 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 Γ_A ; oracle and population settings provide upper-bound and pooled-data comparisons. This classical implementation is the baseline for testing the proposed quantum layer under the same observations, physics, and evaluation metrics.

Annotated Bibliography

References

- [1] 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*, vol. 378, pp. 686–707, 2019. doi:10.1016/j.jcp.2018.10.045.

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.

- [2] C. Trahan, M. Loveland, and S. Dent, “Quantum Physics-Informed Neural Networks,” *Entropy*, vol. 26, no. 8, p. 649, 2024. doi:10.3390/e26080649.

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.

- [3] J. L. Beckey, M. Cerezo, A. Sone, and P. J. Coles, “Variational Quantum Algorithm for Estimating the Quantum Fisher Information,” *Physical Review Research*, vol. 4, no. 1, p. 013083, 2022. doi:10.1103/PhysRevResearch.4.013083.

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.

- [4] T. P. J. Blaikie et al., “Portable Device for Measuring Breath Acetone Based on Sample Preconcentration and Cavity Enhanced Spectroscopy,” *Analytical Chemistry*, vol. 88, no. 22, pp. 11016–11021, 2016. doi:10.1021/acs.analchem.6b02837.

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.

- [5] A. Dixit and R. Yelisetty, “GLASS: Glucose Level Measuring via Breathe Acetone Sensing through Laser Spectroscopy,” TJHSST QLab, 2025. <https://qlab.sites.tjhsst.edu/projects/detail/93/>.

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.

- [6] J. Bounds, E. Aluaee, A. A. Kolomenskii, and H. A. Schuessler, “Acetone Absorption Cross-Section in the Near-Infrared of the Methyl Stretch Overtone and Application for Analysis of Human Breath,” *Optics*, vol. 6, no. 1, article 9, 2025. doi:10.3390/opt6010009.

What did this work do? Reports an empirical acetone near-infrared cross-section model over 1671.5–1675 nm and studies pressure and humid-breath conditions relevant to breath analysis.

Why is it relevant? Its measured band location and cross-section are essential to choosing source wavelengths, predicting absorbance, and determining whether the spectrometer can resolve the signal.

How will we use it? We will use its spectral data as a leading reference for instrument-convolved absorbance and Fisher-information calculations, then compare with our own calibrated acetone-vapor measurements.

- [7] K. Zheng et al., “Near-Infrared Broadband Cavity-Enhanced Spectroscopic Multigas Sensor Using a 1650 nm Light Emitting Diode,” *ACS Sensors*, vol. 4, no. 7, pp. 1899–1908, 2019. doi:10.1021/acssensors.9b00788.

What did this work do? Demonstrates broadband cavity-enhanced sensing using a 1650-nm LED and an 8-cm high-reflectivity cavity for methane and acetylene measurements.

Why is it relevant? It is a practical precedent for combining a broadband diode source, reflective cavity, and spectrometer, while its analytes differ from our target acetone band.

How will we use it? We will use its architecture and reported instrument sensitivity to inform prototype design, but will independently verify acetone-specific absorption and wavelength compatibility.

- [8] HITRAN Database, “HITRANonline: Absorption Cross Section Search.” <https://hitran.org/xsc/>.

What did this work do? Provides measured molecular absorption cross-section datasets with associated spectral and experimental conditions.

Why is it relevant? Acetone and interferent cross-sections help assess candidate wavelengths and the conditions under which optical predictions apply.

How will we use it? We will inspect available acetone/VOC datasets, record units and measurement conditions, and use suitable data to compare candidate wavelength regions before hardware procurement.

- [9] V. Bergholm et al., “PennyLane: Automatic Differentiation of Hybrid Quantum-Classical Computations,” arXiv:1811.04968, 2018. <https://arxiv.org/abs/1811.04968>.

What did this work do? Introduces PennyLane as a software framework for differentiable hybrid quantum-classical computations.

Why is it relevant? The project needs a simulation framework for variational circuits, gradient-based training, and small-circuit information calculations.

How will we use it? We will use PennyLane to implement the compact quantum layer and compute QFI for the circuit while keeping simulation sizes limited to the features needed.

- [10] D. Ucinski, “D-Optimal Sensor Selection in the Presence of Correlated Measurement Noise,” *Measurement*, vol. 164, article 107873, 2020. doi:10.1016/j.measurement.2020.107873.

What did this work do? Develops information-based sensor selection for parameter estimation when measurements are correlated.

Why is it relevant? Our PDE-constrained inverse problem also has limited candidate VOC and wavelength measurements and correlated instrument noise.

How will we use it? We will compare candidate wavelength subsets using sensitivities and classical Fisher information with measured covariance; a discrete D-optimal/QUBO formulation is a possible extension.

- [11] Ritchie Group, “Breath Analysis and Laser Spectroscopy Research,” University of Oxford, Department of Chemistry. <https://www.chem.ox.ac.uk/people/grant-ritchie>.

What did this work do? Provides Grant Ritchie’s University of Oxford research profile and links to the group’s optical-spectroscopy work.

Why is it relevant? Ritchie is a coauthor of published cavity-enhanced breath-acetone research that closely informs our proposed architecture.

How will we use it? We will use the published work as an experimental precedent and may request general setup guidance; no collaboration is presumed.

- [12] Thorlabs, “Compact CMOS Spectrometers.” <https://www.thorlabs.com/compact-cmos-spectrometers?tabName=Overview>.

What did this work do? Describes compact spectrometers, including a candidate near-infrared configuration spanning approximately 950–1700 nm with resolution specified by the vendor.

Why is it relevant? The candidate instrument’s range and resolution determine whether the acetone absorption feature can be measured with adequate spectral contrast.

How will we use it? We will verify current resolution, sensitivity, configuration, availability, and price with the manufacturer before purchasing; product bandwidth alone does not establish adequacy.