Research Statement

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Research Vision

I build AI systems that translate complex biomedical measurements into reliable clinical and biological decisions under uncertainty. My methods — causal discovery for partially observed systems, multi-scale mechanistic simulators paired with fast neural surrogates, and probabilistic alignment of data across patients, instruments, and species — were developed in computational immunology and maternal–fetal vaccinology. The defining difficulties of those settings — high-dimensional measurements over small or heterogeneous cohorts, partial observation of the underlying biology, and the need to separate cause from correlation when intervention timing matters — recur with greater clinical urgency in perioperative and critical-care medicine, where imprecise inference at induction, decompensation, weaning, or recovery has immediate consequences. In my incoming role with MIT's Laboratory for Computational Physiology (Gemini Care Phenotype Project), I am extending the same apparatus to multi-site electronic health records and continuous physiologic data, with focus on reproducible care phenotypes for the operating room and ICU. At Stanford, I would build a faculty program that pairs mechanism-informed, uncertainty-aware AI with perioperative and critical-care physiology, supported by a second thread that brings the maternal–fetal computational modeling I lead today into the Maternal & Child Health Research Institute, the Institute for Immunity, Transplantation and Infection, and Bio-X.

A Stanford Research Program

The program I propose has a single organizing question: *how do we build AI models for perioperative and critical-care medicine whose predictions clinicians can trust because the models respect the underlying physiology and report what they do not know?* Current clinical AI systems are accurate on average and unreliable at the edges that matter most — the moments of induction, decompensation, weaning, and recovery where decisions are most consequential. The gap reflects three structural problems: opaque association in place of causal reasoning, mechanism-free black boxes that drift outside their training distribution, and miscalibrated confidence under patient and site heterogeneity.

I will address that gap through three coherent research directions: **(D1) mechanism-informed neural emulators for perioperative and critical-care decision support**, **(D2) causal phenotyping and treatment-effect estimation for perioperative recovery**, and **(D3) integrative multi-scale modeling for maternal–fetal and neonatal critical care**. Each direction builds on completed methodological work, each is sized for an independent extramural grant, and each is positioned to use the department's clinical, neural, and physiologic-monitoring infrastructure together with collaborators across Stanford Medicine, Bioengineering, the Wu Tsai Neurosciences Institute, MCHRI, ITI, and Bio-X. Figure 1 summarizes how a shared methodological core supports the three directions.

D1. Mechanism-Informed AI for Perioperative and Critical-Care Decision Support

The pharmacokinetic–pharmacodynamic models that govern anesthetic dosing, the cardiopulmonary models that govern hemodynamic management, and the ventilation models that govern critical-care support are well-developed but rarely used at the bedside. They are too slow, too parameter-sensitive,

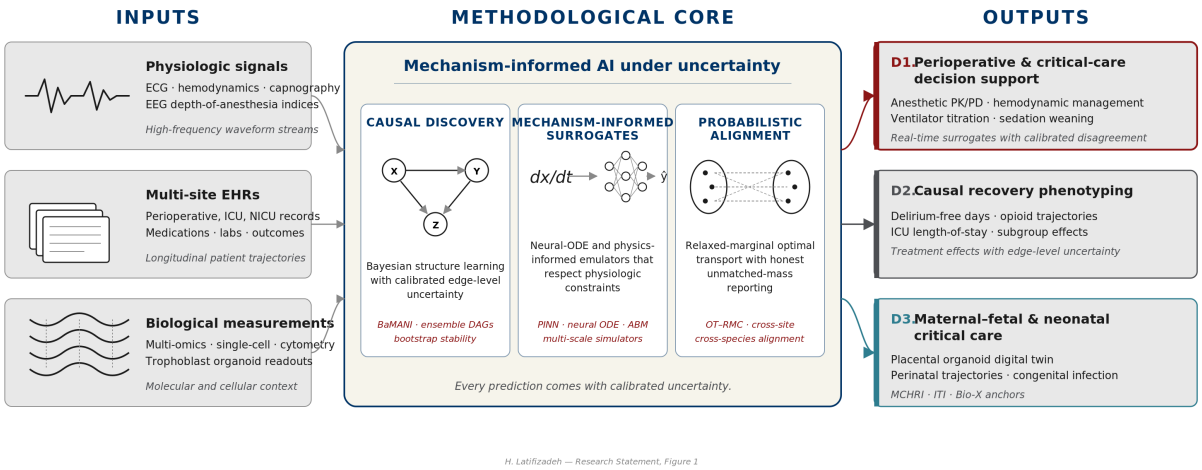

Figure 1: Proposed Stanford research program. Physiologic, EHR, and biological measurements (left) feed a shared methodological core — causal discovery, mechanism-informed neural surrogates, and probabilistic alignment under uncertainty (center) — supporting three clinical and translational outputs (right): perioperative and critical-care decision support (**D1**), causal recovery phenotyping (**D2**), and maternal–fetal critical-care modeling (**D3**).

and too brittle under patient heterogeneity to drive real-time clinical action. The result is a class of clinical decisions — intra-operative dose adjustment, hemodynamic resuscitation, ventilator titration, sedation weaning — in which mechanistic understanding exists in textbooks but is absent at the moment of action.

I will develop a class of *mechanism-informed neural emulators* that compress these mechanistic models into fast, differentiable surrogates while preserving the conservation laws and physiologic constraints that make them interpretable. The emulators will be paired with calibrated uncertainty — Gaussian-process residuals over the mechanism gap and conformal prediction over patient-level deviations — so that downstream decision-support tools express principled disagreement when learned prediction and mechanism-respecting expectation diverge. These divergences are precisely the moments in which clinicians most need a warning rather than a number.

I have built such an emulator system once, in a different clinical context. In an NIH/NIAID-funded congenital cytomegalovirus program (R01 AI173333), I lead the computational modeling that couples maternal viral and immune dynamics, a placental diffusion interface, and stochastic fetal infection [Gong et al., 2023]. The calibrated system reproduces the transmission rates observed in immunocompetent rhesus macaque dams, the elevated transmission seen under $CD4^+$ T-cell depletion, and the timing-dependent failure of late hyperimmune-globulin administration. To make this multi-scale system tractable for virtual-trial analyses under realistic sampling noise and heterogeneous infection timing, I am developing neural-ODE and physics-informed surrogates [**?**] that act as fast differentiable proxies for the underlying simulator while preserving its constraint structure (Figure 2). The same construction transfers directly to anesthetic PK/PD, intra-operative hemodynamic management, and ICU ventilator support: in each case, a slow mechanistic model is paired with a fast learned surrogate that respects its conservation laws and reports calibrated uncertainty when the patient leaves the simulator's comfort zone.

The natural next step is to ground this approach in real perioperative data. The Gemini Care Phenotype

Project I am joining at MIT centers on multimodal clinical AI built from multi-site EHRs and continuous monitoring streams, with explicit attention to how algorithms reconcile discordant evidence across heterogeneous data sources. I will use this partnership to bring the emulator design into perioperative use: intra-operative dose-adjustment support, ventilator-management exploration, and counterfactual reasoning on physiologic trajectories, with explicit subgroup auditing across demographic and clinical strata. The program is positioned for NIH NIGMS (perioperative pharmacology), NHLBI (critical-care monitoring), and NIBIB (clinical-AI methods) support in partnership with department clinical investigators.

D2. Causal Phenotyping and Treatment-Effect Estimation for Perioperative Recovery

Deep sequence models routinely conflate association with causation when applied to longitudinal clinical data, particularly under treatment-by-indication confounding. A perioperative monitoring stream tells us what happened next, not what would have happened under a different choice; protocols vary across sites and providers; recovery is heterogeneous in ways that average-effect estimators erase. The clinically useful question is rarely *what is the average effect*, but *for which patients does this intervention help, and how confident should we be?*

I will develop sequence architectures for perioperative recovery that integrate patient-specific time-varying random effects, instrument-style adjustments for confounded clinical decisions, and posterior uncertainty estimates through MCMC-based exploration over causal structures. The methodological backbone is **BaMANI** [**?**], an ensemble Bayesian causal-discovery system I led the design of: it combines constraint- and score-based structure learning with bootstrap-based stability assessment and exposes interpretable graph-level uncertainty over the inferred directed structure. The same machinery applies wherever clinicians need to separate causes from correlations in partially observed systems. I will extend it to longitudinal perioperative and critical-care data, with concrete targets including treatment effects on delirium-free days, opioid-trajectory shape, ICU length-of-stay, and identification of subgroups in which established perioperative protocols are or are not effective. The program is positioned for NIH NIGMS and AHRQ support and is designed to interface with the department's perioperative outcomes investigators and with Stanford Medicine's clinical data resources.

D3. Integrative Multi-Scale Modeling for Maternal–Fetal and Neonatal Critical Care

The congenital CMV program I lead today produces a calibrated multi-scale simulator of placental viral transmission, a parallel Vivarium-based agent-based model of placental organoid infection developed in coordination with trophoblast organoid experiments for calibration, and a forthcoming SciML emulator layer for virtual-trial analysis. The natural Stanford extension is to couple this mechanistic backbone with molecular and immunologic measurements — maternal multi-omic profiles, single-cell immune signatures, and trophoblast organoid readouts — through shared latent representations that respect the geometry imposed by the underlying differential-equation and agent-based systems. The same modeling pattern — compartmental risk transmission, spatially heterogeneous cell–virus interaction, timing-dependent intervention effects, and stochastic progression from exposure to organ-level dysfunction — extends naturally to other perinatal and neonatal critical-care problems: maternal sepsis, preeclampsia-associated organ dysfunction, fetal physiologic monitoring during labor, and NICU trajectory modeling.

The program is positioned for NICHD and NIAID support and is designed to anchor in the institutional resources Stanford uniquely offers: the **Maternal & Child Health Research Institute**, the **Institute for Immunity, Transplantation and Infection**, and **Bio-X**. It is a deliberate second thread rather

than a competitor to the perioperative direction: the methodological investments (mechanism-informed simulation, neural surrogates, calibrated uncertainty) are shared with D1, and the recovery-trajectory methodology is shared with D2.

Methodological Foundations

The directions above rest on a methodological program developed across my doctoral and postdoctoral work, supported by an NSF BridgesDH NRT Fellowship in AI and Machine Learning for Digital Health (NSF Award #2125872) and current NIH-funded postdoctoral research in the Department of Biostatistics & Bioinformatics at Duke. Four threads are mature enough to deploy.

Causal Bayesian inference. BaMANI [**?**] provides ensemble structure learning with calibrated edge-level uncertainty, applied initially to heterocellular tumor–immune networks [Klinke et al., 2022] and forming the core of D2. *Multi-scale mechanistic simulation paired with SciML emulators.* The CMV maternal–placental–fetal system and its physics-informed surrogate provide the construction described in D1 and the simulator backbone of D3. *Generative modeling with single-cell references.* I have developed pipelines that integrate single-cell and single-nucleus RNA-seq into in-silico pseudo-bulk references with generative augmentation (VAE / WGAN-GP) for cell-type estimation under platform and biological variability [White et al., 2022, Maden et al., 2023]; this capability is available for translational analyses of inflammation, immune recovery, and infection risk in perioperative and critical-care settings, and for cross-modal computational immunology. *Relaxed-marginal optimal transport.* OT–RMC [**?**] provides calibrated probabilistic alignment between data sources with honest unmatched-mass reporting; the same alignment apparatus supports cross-site phenotyping for multi-center perioperative cohorts and cross-species translation for pre-clinical immunology. Together these threads form a unified evidence base — causal discovery, mechanism-respecting prediction, and probabilistic alignment, each with explicit uncertainty.

Long-Term Vision and Collaborations

My long-term aim is a unified computational program in which causal Bayesian inference, mechanism-informed neural surrogates, and probabilistic alignment jointly support reproducible clinical reasoning across perioperative, critical-care, and maternal–fetal settings. The program is designed from the start to interface with Anesthesiology, Perioperative and Pain Medicine; with Bioengineering and the Wu Tsai Neurosciences Institute for neural and physiologic signal modeling; with MCHRI and ITI for maternal–fetal and immunologic translation; with Bio-X for cross-departmental computational collaborations; and with Stanford Medicine's clinical data infrastructure. Across the three directions, the contribution I aim to make at Stanford is mechanism-informed, uncertainty-aware AI for the moments of clinical decision in which calibrated humility matters as much as predictive accuracy.

References

Yishu Gong, Matilda Moström, Claire Otero, Sarah Valencia, Alice F. Tarantal, Amitinder Kaur, Sallie R. Permar, and Cliburn Chan. Mathematical modeling of rhesus cytomegalovirus transplacental transmission in seronegative rhesus macaques. *Viruses*, 15(10):2040, 2023. doi: 10.3390/v15102040.

D. J. Klinke, A. Fernandez, W. Deng, H. Latifizadeh, and A. C. Pirkey. Data-driven learning how oncogenic gene expression locally alters heterocellular networks. *Nature Communications*, 13(1):1986, 2022.

Sean K. Maden, Sang Ho Kwon, Louise A. Huuki-Myers, and et al. Challenges and opportunities to computationally deconvolve heterogeneous tissue with varying cell sizes using single-cell rna-sequencing datasets. *arXiv*, 2023.

BS. White, A. de Reyniès, AM. Newman, and et al. Community assessment of methods to deconvolve cellular composition from bulk gene expression. *bioRxiv*, 2022.

Figure 2: Mechanism-informed multi-scale modeling and neural-emulator design (validation domain: congenital CMV; transferable to perioperative PK/PD, hemodynamic, and ventilator modeling). Maternal ODEs and a one-dimensional placental diffusion–decay interface are coupled to stochastic fetal infection dynamics; a physics-informed / neural-ODE emulator compresses the calibrated simulator into a fast, differentiable surrogate while preserving its constraint structure, with calibrated uncertainty exposed to downstream decision-support tools (**D1**).