Inferring Oocyte Cytoplasmic Material Properties from Cytoplasmic Streaming Movies Using Physics-Informed Neural Networks

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1. Introduction

Infertility affects approximately one in six adults worldwide [1], and declining fertility rates have intensified reliance on assisted reproductive technologies (ART). The success of ART cycles hinges primarily on oocyte quality, yet current assessment relies on static morphology with limited predictive power [2]. While deep learning approaches can predict blastocyst development from static oocyte images, these remain black-box methods requiring large datasets and offering little mechanistic insight.

Cytoplasmic streaming—an actin-driven intracellular flow—plays established mechanistic roles in mammalian oocytes: Arp2/3-dependent streaming maintains asymmetric spindle positioning, drives symmetry breaking, and establishes cortical polarity [3, 4]. Quantitative studies have shown that cytoplasmic movement velocity is sensitive to oocyte state, responding to aging, cryopreservation, and maturation conditions, while aberrant cortical dynamics can compromise developmental potential. However, extracting intrinsic material properties such as effective viscosity from noisy, incomplete velocity measurements constitutes an ill-posed inverse problem.

Physics-informed neural networks (PINNs) provide a principled framework for this challenge by embedding governing equations directly into the learning objective, enabling reconstruction of continuous spatiotemporal fields from sparse observations while simultaneously inferring unknown parameters [5]. This approach has proven powerful in fluid mechanics for recovering latent velocity and pressure fields from partial measurements [6]. Here we introduce a PINN-based framework to infer effective cytoplasmic viscosity directly from time-lapse microscopy of cytoplasmic streaming in mouse oocytes, and validate the inferred values against independent bead-based microrheology measurements.

2. Methods

2.1 Velocity field extraction

Time-lapse microscopy movies of mouse oocytes were processed through an optical-flow/PIV pipeline. Oocytes were segmented within a circular ROI estimated from image contrast, and frames were aligned via intensity-based registration to correct stage drift. After preprocessing (CLAHE, bilateral filtering), dense optical flow was computed between consecutive frames using multiple algorithms (Farnebäck, Dual TV-L1, DIS) to accommodate different motion regimes. Velocities were converted to physical units (μm/min) and quality metrics—including coherence, warping error, and photometric consistency—were computed to select informative time windows.

2.2 PINN formulation

We model cytoplasmic streaming as two-dimensional incompressible flow governed by:

$$\partial_t \mathbf{u} + (\mathbf{u} \cdot \nabla)\mathbf{u} = -\nabla p + \nu \nabla^2 \mathbf{u} + \mathbf{f}, \quad \nabla \cdot \mathbf{u} = 0 \qquad (1)$$

where $\mathbf{u}$ is velocity, p is pressure, ν is an effective viscosity parameter, and $\mathbf{f}$ is a prescribed forcing capturing active intracellular stresses. Incompressibility is enforced exactly via a streamfunction representation: a network $\mathcal{N}_\theta : (x, y, t) \to (\psi, p)$ predicts a streamfunction ψ with $u = \partial_y \psi$, $v = -\partial_x \psi$. Viscosity ν is learned as a trainable scalar with positivity enforced via $\nu = \nu_{\min} + \exp(\tilde{\nu})$.

The composite loss $\mathcal{L} = \mathcal{L}_{\text{data}} + \mathcal{L}_{\text{phys}} + \mathcal{L}_{\text{prior}}$ combines velocity supervision, PDE residuals computed via automatic differentiation (using a vorticity formulation to mitigate pressure gauge freedom), and weak quadratic priors on inverse parameters to prevent unphysical drift.

2.3 Hybrid training curriculum

We employ a three-stage strategy (Fig. 1): (i) *numerical pretraining* on simulated flows to learn stable representations and initialize inverse parameters; (ii) *frozen-parameter adaptation* where network weights adapt to experimental velocities while ν is held fixed; and (iii) *unfrozen refinement* where ν is released and stabilized by split physics weighting and weak priors. This design mitigates the tendency of naive inverse training to absorb experimental mismatch via abrupt viscosity changes.

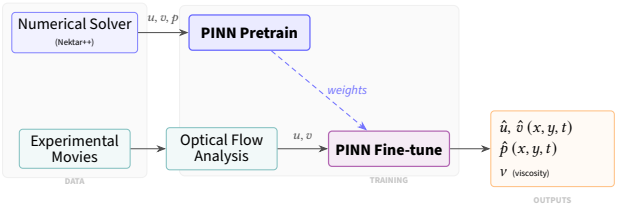

Fig. 1: Two-phase PINN inference pipeline. Numerical simulations provide full-field supervision for pretraining; pretrained weights transfer to the fine-tuning stage, which ingests experimental optical-flow velocities and jointly infers velocity, pressure, and viscosity ν.

3. Results

Numerical validation. Pretraining on simulated flows across multiple reference viscosities demonstrated stable convergence of both physics residuals and data mismatch, with inferred viscosity stabilizing rather than drifting. Noise robustness tests (Gaussian and Laplacian perturbations) showed that viscosity inference remains reliable at low-to-moderate noise levels, with increased variance and systematic bias emerging only at higher noise amplitudes.

Optical-flow characterization. Optical-flow overlays provided qualitative validation by pairing raw movie frames with quiver plots of the estimated velocity field. Across the analyzed oocyte movies, flow reconstructions showed spatially organized streaming patterns with coherent rotational components. Quality scores were consistently high across samples (median overall quality $\approx$0.65; median coherence $>$0.8), confirming that the extracted velocity fields are sufficiently reliable for downstream PINN training.

PINN-inferred viscosity agrees with experimental microrheology. Two-phase finetuning on experimental data achieved improved data fit during the frozen phase, followed by gradual viscosity evolution during the unfrozen phase. We compared the PINN-inferred viscosity against independent bead-based microrheology estimates obtained via single-particle tracking and the Stokes–Einstein relation. The two estimators yielded values in the same physical range, confirming that the PINN framework recovers physically plausible material properties from streaming movies alone, without requiring invasive bead measurements.

Sample-to-sample variation is consistently captured. Importantly, across multiple oocyte movies and replicate finetuning runs, both the inverse-PINN viscosity and the closed-form estimate captured reproducible sample-to-sample variation (Fig. 2). Oocytes with stronger streaming consistently yielded lower inferred viscosity, while those with weaker or less organized flow produced higher estimates. This ranking was preserved across different checkpoint initializations, indicating that the pipeline reliably resolves inter-sample differences in cytoplasmic material properties even when the simplified 2D flow model limits absolute quantitative accuracy. These results establish the framework as a tool for comparative, non-invasive characterization of oocyte biophysical state.

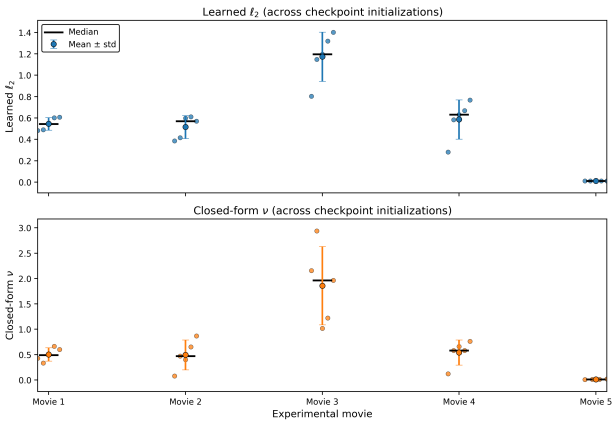

Fig. 2: Per-sample viscosity estimates across checkpoint initializations. Top: inverse-PINN learned viscosity; bottom: closed-form ν. Dots: individual replicates; bars: median. Sample-to-sample ranking is consistently preserved across initializations.

Acknowledgments

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