NITMB Workshop Report

Machine Learning of Cytoskeletal Machines: Cell Migration and Mitosis

November 3–5, 2025

Workshop Overview

This workshop convened mathematical modelers, experimental biologists, and data scientists to bridge the gap between traditional bottom-up biophysical modeling and modern machine learning approaches in cytoskeletal biology. Traditional models have generated powerful mechanistic insights but often struggle to capture multiscale complexity; data-driven approaches excel at pattern recognition but frequently neglect underlying physics. The workshop explored how these disciplines can be fused to decode the dynamics of the cytoskeleton during cell division and migration, with talks organized around two interconnected themes: mitotic spindle mechanics and cell migration/morphodynamics. We had participants from universities and companies in the United States and Europe and all career stages, from graduate students to full professors. Junior participants were given a chance to present posters and short talks, and even parts of major talks.

Mitotic Spindle Assembly and Mechanics

The workshop opened with structural and mechanical analyses of the mitotic spindle. Stefanie Redemann presented cryo-electron tomography data challenging classical spindle models, revealing that approximately half of spindle microtubules form interdigitated antiparallel networks rather than connecting to poles or chromosomes. Daniel Needleman discussed integrating cryo-EM with ML-based data analysis to study mesoscale microtubule self-organization. Nigel Burroughs employed Bayesian inference on lattice light-sheet kinetochore tracking data, revealing substantial heterogeneity in kinetochore mechanics and distinct mechanical phases during prometaphase. Jacques Pécréaux applied principal component analysis and ML regression to C. elegans spindle data, finding that just three eigenvectors capture 95% of variability and that late metaphase elongation predicts anaphase length.

Several talks addressed force generation and spindle positioning. Jing Chen presented an energetic framework using effective potential energies to predict factors essential for bipolar spindle recovery, validated experimentally in tetraploid cancer cells. Meredith Betterton explored spindle-nuclear envelope coupling in closed mitosis, showing how force balance drives nuclear shape remodeling. Radhika Subramanian proposed that cargo density governs motor selection (KIF4A vs. KIF20A) for positioning the Chromosomal Passenger Complex at the midzone. At the molecular scale, Tamara Bidone demonstrated how unsupervised ML and graph neural networks can accelerate molecular dynamics simulations to access biologically relevant timescales. Viji Draviam introduced the SpinX framework integrating AI-guided segmentation with predictive modeling to reconstruct continuous 3D trajectories. Anna Nelson presented mechanistic modeling of microtubule dynamics in neurons, addressing how stable networks balance with dynamic reorganization after injury. Lightning talks by Stanley Nicholson (mitotic waves), Saptarshi Chatterjee (virtual cell modeling), and Sayandeepa Raha (nonequilibrium steady states) further enriched this theme.

Cell Migration and Morphodynamics

The second theme focused on decoding rules of cell shape and movement. Chase Broedersz demonstrated data-driven inference of stochastic equations of motion, revealing how cells exhibit intricate nonlinear dynamics adapted to confinement geometry. Margaret Gardel

discussed how the cytoskeleton processes mechanical information to control proliferation, barrier function, and cell fate. Julien Berro presented quantitative microscopy and molecular force sensor engineering to measure biophysical quantities in clathrin-mediated endocytosis.

A striking sub-theme emerged around cell morphology as an upstream regulator. Gaudenz Danuser argued that cell shape and cytoskeletal architecture regulate signaling, particularly in cancer, inverting the classical "form follows function" paradigm. Susanne Rafelski applied dynamical systems theory to morphological image features, identifying stable attractors that suggest first-order phase transitions between cell states. Kwonmoo Lee presented unsupervised learning tools designed to preserve morphodynamic heterogeneity, enabling high-resolution phenotyping of cancer cells and megakaryocytes. Ming Guo extended these concepts to multicellular systems using graph neural networks to model embryogenesis and collective migration. Madeleine Oudin reviewed computational models for predicting metastasis, emphasizing microenvironmental cues. Ben Larson described frameworks for decomposing complex single-cell behaviors into stereotyped sequences, revealing how geometry and mechanics encode function. Lightning talks by Wenzheng Shi (actin dynamics) and Binghao Chai (digital pathology foundation models) completed the program.

Emerging Themes and Future Directions

A clear synthesis emerging from the workshop is the shift toward physics-informed learning in cytoskeletal biology. Rather than treating ML as a black box for classification, researchers are increasingly using it to infer governing equations (Broedersz), accelerate physical simulations (Bidone), decode hidden mechanical states (Burroughs), and reconstruct dynamics from sparse data (Draviam). This hybrid approach addresses limitations of sparse biological data while maintaining mechanistic interpretability. The integration of structural data (Redemann) with energetic models (Chen) and dynamic tracking suggests a future where static snapshots can be rigorously connected to dynamic function through learned physical laws.

The workshop also highlighted that biological heterogeneity represents signal, not noise. Multiple talks (Lee, Rafelski, Danuser, Burroughs) demonstrated that variability in cell shape, kinetochore mechanics, and migration trajectories contains rich information about cell state and regulation. Future directions identified by participants include extending single-cell frameworks to multicellular tissues (Guo), solving the "inverse problem" of mapping morphological features back to molecular perturbations, and applying these methods to clinical problems in cancer metastasis. The consensus is that the next generation of cytoskeletal models will be data-centric, extracting minimal rules from high-dimensional datasets to build predictive theories of cell function.

The workshop was very well received, with enthusiastic feedback from junior participants who highlighted how much they learned over the three days and how much they were inspired by the talks. The main constructive criticism was: many talks were on traditional cytoskeleton modeling not involving ML, and there was not enough focus on technical issues of modeling. This has to be taken into account for future such meetings.