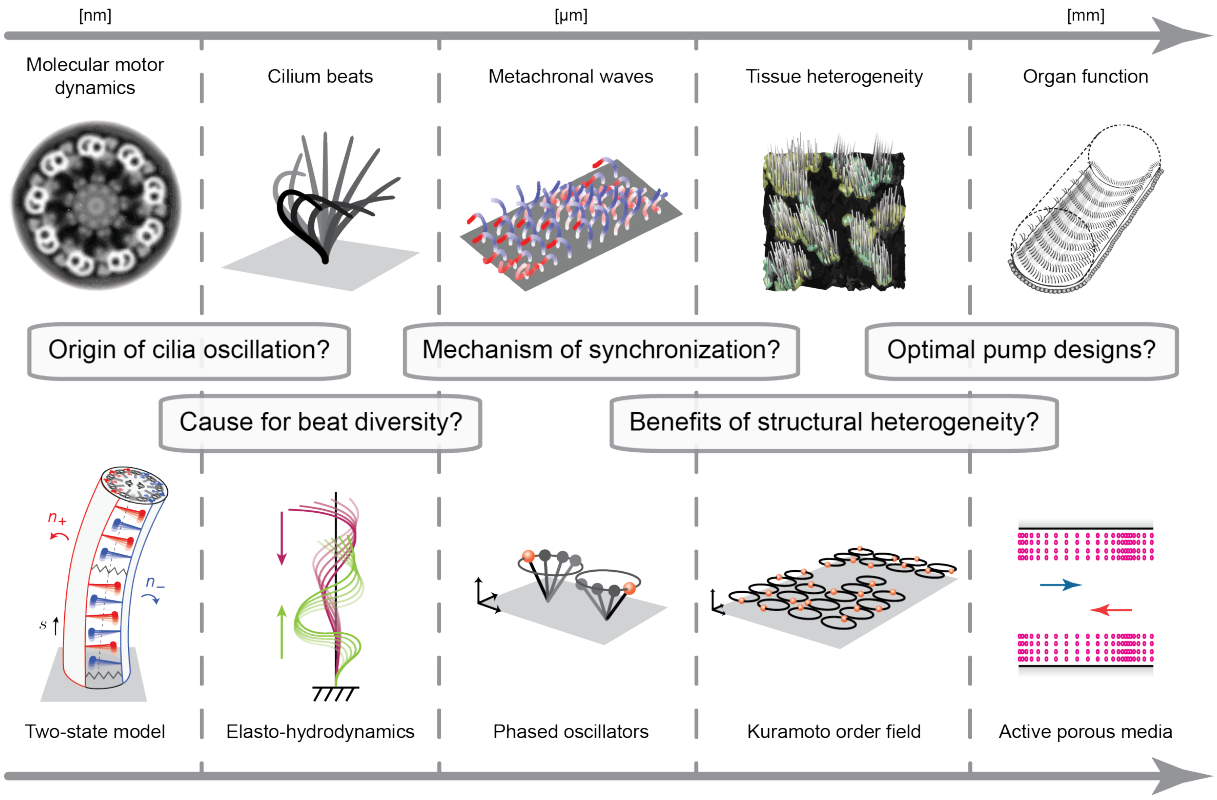
Personal Statement

Feng Ling (凌峰)

Research Objectives

My primarily research direction is on the topic of **soft matter** and **active matter**, such as microorganism locomotion and the *collective behavior* of living matter like motile cilia. I am very interested in constructing **multiscale models** to understand the origins and mechanisms of **diversity and coordination** in complex non-equilibrium phenomenon, and establish the **structure-to-function maps** for such features. My expertise is in **low Reynolds number fluid dynamics**, and **elastic microfilament** modeling, as well as **experimental measurement of viscoelasticity**. I also have experience in standard **machine learning and reinforcement learning** techniques.



Cilia as a model system for multi-scale coordination: motor proteins eventually lead to coordinated function of ciliated tissue.
https://youtu.be/QocO7-QFJtU

A. Multi-scale Modeling of Motile Cilia Motile cilia are micron-sized, hair-like protrusions on Eukaryotic cells that enable locomotion, sensing and transport of materials in the fluidic environment. Cilia motion is driven by thousands of nanoscale molecular motors (axonemal dynein complexes) exerting forces on semi-rigid microfilaments (microtubule doublets). Cilia operate in diverse contexts: individually as propellers for single-cell flagellates or animal spermatozoa; in coordinated pairs, as seen in algae like Chlamydomonas, which function analogously to mammalian appendages; or in large groups, covering surfaces in microorganisms such as Paramecium and Stentor, as well as in human epithelial tissues in brain ventricles, airways, and reproductive tracts. Understanding cilia can provide us insights into the development of chronic conditions such as chronic obstructive pulmonary disease (COPD) and asthma, potentially guiding new therapeutic approaches.
My research has focused on addressing the following specific questions in cilia mechanics across multiple scales:

1. **Nanoscale (nm):** How are motor proteins able to drive diverse oscillatory behaviors in cilia despite structural conservation? Through studies on mechanical instabilities [1–3], I have explored how nanoscopic forces produce cilia oscillations.
2. **Microscale (μm):** How does hydrodynamics influence coordination and fluid pumping in multiciliated tissues? Using a phased oscillator model, I demonstrated how hydrodynamic interactions coordinate cilia motion and impact fluid transport [4] (**PNAS**).
3. **Mesoscale (mm):** What governs the morphology of ciliated ducts across species? We model cilia as active porous media to show that functional requirements, rather than phylogeny, dictate the morphology of ciliated ducts [5] (**Nature Physics**). Currently, we are developing a fluid mechanics model that maps cilia kinematics and tissue organization to their clearance function. This model aims to provide a framework for *in vitro* experimental designs, facilitating disease phenotyping and enhancing our understanding of cilia-driven fluid transport in pathological conditions [6] (in review **Nature Communications**).

Future Objectives Building on the above, I aim to advance these specific areas:
Quantitative Modeling of Cilia Oscillation: With continual advancements in cryo-EM and related technologies, there is a strong interest in developing quantitative mechanical models of cilia oscillation grounded in the biochemical dynamics of molecular motors. This includes integrating multi-state models and examining the impact of intraflagellar transport (IFT) on dynein motor assembly.
Experimentally-Sound Model of Large-Scale Cilia Coordination: Further work is needed in computational and theoretical (continuum) modeling to understand large-scale cilia coordination, particularly with complex geometrical constraints and on curved spaces. In biological setting, cilia are often densely packed, and steric interactions between neighboring cilia – frequently overlooked in current

theories – may play a critical role in their coordination. Addressing these challenges will provide deeper insights into cilia coordination and its influence on tissue function across diverse biological contexts.

Experimental Validation of Flow Models: Our work published in **Nature Physics** [5] would benefit from further experimental validation, particularly through the application of more advanced numerical models already under development and innovative bioengineering approaches. I plan to continue my collaboration with Dr. Janna Nawroth's team at **Helmholtz Munich** to create microfluidic systems with in vitro human cells, which will provide a robust platform for validating and refining our models.

True Multi-Scale Modeling: Establishing a comprehensive multi-scale model that connects nanoscale parameters with macroscopic fluid dynamics and overall tissue function remains a primary objective. By incorporating machine learning-enabled analysis of microscopy data, this model could effectively bridge molecular-level details with tissue-level functional insights. Such an approach has the potential to advance our understanding of diseases related to primary ciliary dyskinesia (PCD) and other ciliopathies, providing a framework for both diagnosis and therapeutic exploration.

B. High-throughput Microrheology of Mucus Currently, there is a lack of high-throughput, user-friendly methods that can analyze minuscule amounts of mucus produced by large-scale *In vitro* air-liquid interface (ALI) cultures of airway epithelial tissues. To address this, we are refining a microscopy-based technique, Differential Dynamic Microscopy (DDM), to pave the way for robust, automated microrheology measurements of mucus. This approach will enable integration with other cilia kinematic metrics, supporting long-term tracking and facilitating large-scale experiments.

Objectives We are preparing our publication [7] in collaboration with biomedical teams, including Prof. Yohannes Tesfaigzi's group at Harvard Medical School, to investigate correlations between mucus viscosity development in in vitro tissues exposed to altered environmental conditions (such as cigarette smoke) and diverse genetic backgrounds. This approach aims to provide insights into mucus rheological changes related to environmental pollutants, the severity of chronic obstructive pulmonary disease (COPD), and donor characteristics such as obesity. The resulting database, combining cilia mechanics models and additional bioinformatics data, will support our understanding of impaired mucociliary clearance across different diseases and elucidate its underlying physical mechanisms.

C. Collective Motion of Multi-Agent Systems We applied model-free reinforcement learning techniques to analyze the robustness of control policies for a reduced-order model of elastic, active fish locomotion in fluid environments [8]. Additionally, we used numerical simulation and statistical mechanics tools to reveal how geometric confinement induces intermittent and multi-stable collective behaviors of fish schools [9]. My plan in this direction is to combine these approaches and, by incorporating my expertise in microscopy techniques such as DDM, extend the study to other microscopic multi-agent systems with potential experimental validations. This integrated approach promises to yield valuable insights into multicellular interactions, with specific applications to processes such as wound healing, tumor formation, and morphogenesis. On a larger scale, the theoretical findings in this area could also enhance our understanding of complex systems and embodied artificial intelligence.

Objectives Building on the simplified fish school model, I aim to analyze the spontaneous collective evasion behaviors of various fish species in predator-prey scenarios. This research will deepen theoretical exploration of **non-reciprocal interactions in active matter**. I plan to expand the use of reduced-order modeling and reinforcement learning techniques to other **microscopic phenomena**, such as active filament models resembling cilia and multicellular group migration. This objective includes collaboration in areas like cellular imaging and manipulation, as well as microfluidic biochip assays. Additionally, I aim to determine optimal conditions that enable constrained filaments to exhibit diverse self-organized coordination modes / gaits under different resistive environments.

Teaching Interests

I am deeply interested in teaching courses related to **fluid dynamics**, **statistical mechanics** and **thermodynamics**, and I am also enthusiastic about instructing foundational courses in advanced mathematics and computational methods for undergraduate students, particularly those from other disciplines. I have a strong interdisciplinary background, with extensive experience interacting across fields such as engineering, mathematics, and biology.

Previously, I served as a teaching assistant in thermodynamics and computational methods at USC, and earned the Ph.D. Teaching Award from USC's Viterbi School of Engineering. I also participated in test lectures under the guidance of Prof. Christoph Haselwandter on 'Mechanics of Morphogenesis' for graduate students in physics, with lecture materials available here https://slides.com/levincoolxyz/growth. In addition, I have actively participated in outreach programs, including SHINE USC, where I used engaging table-top experiments to demonstrate the counter-intuitive properties of viscous and non-Newtonian fluids. I have also participated in Introduce a Girl to Engineering Day (now STEM Girl Day) at UT Austin, introducing K-12 students to foundational concepts in engineering and scientific exploration.

References

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