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# Advances in Biomechanics: Exploring Biophysical Models in Cellular Mechanics

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**Abstract** Biomechanics and cellular mechanics provide crucial insights into how cells respond to their environment, influencing various biological processes and pathology. This study explores the evolution of biophysical models for understanding cell behavior and reviews their development from early mechanical methods to modern hybrid models. The key model types-continuous mechanics, discrete element models, and hybrid methods-were emphasized, as well as their applications in studying cell deformation, migration, and cell-cell or cell-matrix interactions. Further investigation was conducted on the experimental methods and computational techniques used to validate these models, emphasizing the integration of experimental and simulation methods. Despite progress, there are still challenges in expanding models to capture the complexity of cellular processes. The future directions include multi-scale modeling, artificial intelligence, and potential applications in personalized healthcare. Biophysical models will continue to play a key role in advancing biomechanical research and deepening understanding of cellular mechanics in health and disease.

**Keywords** Cellular mechanics; Biophysical models; Continuum mechanics; Cell deformation; Computational simulations

## 1 Introduction

Biomechanics, the study of mechanical principles applied to biological systems, has evolved significantly over the past few decades (Oomens, 2014). Initially dominated by mechanical and civil engineers, the field has expanded to include a diverse array of disciplines such as biology, biophysics, and bioengineering. Cellular mechanics, a subfield of biomechanics, focuses on understanding how cells respond to mechanical forces and how these forces influence cellular functions and behaviors (Mow, 2011). This interdisciplinary approach has led to significant advancements in our understanding of cellular processes, including cell adhesion, migration, and mechanotransduction (Zhu et al., 2000).

Biophysical models play a crucial role in elucidating the complex mechanical behaviors of cells (Rodriguez et al., 2013). These models integrate experimental data with computational simulations to provide a comprehensive understanding of cellular mechanics at multiple spatial scales, from protein polymers to whole cells (Wang et al., 2021). The development of accurate and predictive biophysical models is essential for interpreting experimental observations, designing therapeutic techniques, and developing biomimetic materials (Liebman et al., 2020). Moreover, these models help in understanding the mechanobiological processes underlying various diseases, including cancer, by linking changes in cellular mechanics to disease progression and treatment responses（Ji and Bao, 2011).

This study integrates the latest developments in the field of cellular mechanics, with a particular focus on biophysical models; Key developments and emerging trends will be highlighted, covering various aspects of cellular mechanics, including the mechanical response of cells to external forces, the role of cell adhesion, and the deformation of biomolecules. In addition, we will also discuss the challenges and future prospects faced in developing integrated, multi-scale interdisciplinary cell models. I hope these detailed studies can deepen our understanding of cellular mechanics and stimulate further research in this rapidly developing field.

## 2 Historical Perspective and Evolution of Biophysical Models

### 2.1 Early models in cellular mechanics

The study of cellular mechanics has a rich history, beginning with the fundamental recognition of cells as the basic structural and functional units of life. Early models primarily focused on understanding the mechanical properties of cells and their responses to external stimuli. These initial efforts laid the groundwork for the development of more sophisticated models. For instance, the use of micropipette aspiration, a technique that has been in use for over five decades, enabled researchers to study the mechanical properties of various cell types by applying controlled suction to a cell and observing its deformation (Nathwani et al., 2018). This technique highlighted the importance of mechanical forces in cellular behavior and provided a quantitative method to measure cellular mechanical properties (Cheng et al., 2017).

### 2.2 Key developments in biomechanical research

As the field progressed, significant advancements were made in both experimental techniques and theoretical models. The development of force spectroscopy techniques allowed for the precise measurement of mechanical forces at the single-molecule level, bridging the gap between biochemical and mechanical perspectives of cellular functions. Additionally, the advent of computational models has been instrumental in interpreting experimental data and understanding complex cellular structures. These models have facilitated the study of cell mechanics at multiple spatial levels, from protein polymers to whole cells, and have been crucial in developing diagnostic and therapeutic techniques. The interplay between mechanical properties and cellular functions has also been a focal point of research. Studies have shown that mechanical forces and deformations play a critical role in regulating cell behavior and function, influencing processes such as mechanotransduction and cell rheology. The integration of experimental and computational approaches has provided a comprehensive understanding of these processes, enabling predictive in silico studies that complement experimental observations (Jones and Chapman, 2012).

### 2.3 Transition to modern biophysical modeling

The transition to modern biophysical modeling has been marked by the development of integrated, multiscale models that capture the complexity of cellular mechanics. Recent reviews have highlighted the progress in mathematical models that describe the responses of cells to various biophysical cues, such as dynamic strain, osmotic shock, and fluid shear stress. These models have been essential in understanding the dynamic feedback mechanisms between cells and their microenvironments (Rodriguez et al., 2013). Furthermore, the field has seen significant advancements in the modeling of tissue growth and development. Theories that model the interplay between growth patterns and mechanical stress have applications in areas such as arterial mechanics, embryo morphogenesis, and tumor development. These models are categorized into continuum models and cell-based models, each offering unique insights into the mechanical behavior of growing tissues. In summary, the evolution of biophysical models in cellular mechanics has been driven by advancements in experimental techniques and computational modeling (González-Bermúdez et al., 2019). The integration of these approaches has provided a deeper understanding of the mechanical properties of cells and their responses to biophysical cues, paving the way for future research and applications in the field of biomechanics (Wang et al., 2021).

## 3 Types of Biophysical Models in Cellular Mechanics

### 3.1 Continuum mechanics models

Continuum mechanics models treat tissues and cells as continuous materials, allowing for the application of classical mechanics principles to describe their behavior under various conditions. These models are particularly useful for understanding the mechanical responses of cells and tissues to external forces and internal stresses. For instance, the deformation gradient decomposition method is a continuum approach that allows for the development of residual stress fields from incompatible growth fields, which is crucial for modeling phenomena such as arterial mechanics and bone remodeling (Jones and Chapman, 2012). Additionally, continuum-based models have been employed to study the dynamics of biomembranes, emphasizing the importance of hydrodynamic effects in membrane biophysics. These models are grounded in elasticity theory, fluid dynamics, and statistical mechanics, providing a robust framework for simulating cellular mechanics over a range of length and time scales.

### 3.2 Discrete element models

Discrete element models, on the other hand, consider tissues and cells as collections of individual elements or particles. These models are particularly adept at capturing the behavior of individual cells and their interactions. For example, agent-based models, which fall under the category of discrete element models, simulate mechanical and physiological phenomena in cells and tissues by considering individual cell behaviors and interactions. These models include lattice-based models (such as cellular automata and cellular Potts models) and off-lattice models (such as center-based and vertex models). Discrete models are valuable for understanding cell-cell interactions, cell division, and the emergence of complex spatial patterns from simple rules governing single-cell dynamics (Chaplain et al., 2018).

### 3.3 Hybrid models combining continuum and discrete approaches

Hybrid models combine the strengths of both continuum and discrete approaches to provide a more comprehensive understanding of cellular mechanics. These models are particularly useful for simulating complex biological processes that involve both large-scale tissue deformations and individual cell behaviors. For instance, a mechanistic hybrid continuum-discrete model has been developed to simulate the dynamics of epithelial cell colonies, capturing both the collective cell dynamics and individual cell behaviors such as division and shape changes (Dallon, 2000). Another example is the use of hybrid models to study wound healing and cellular aggregation, where discrete and continuum variables are interpolated to solve the models using numerical techniques3. These hybrid approaches offer a versatile framework for studying a wide range of biomechanical phenomena in cellular mechanics. By integrating continuum and discrete models, researchers can achieve a more nuanced understanding of the mechanical behavior of cells and tissues, paving the way for advancements in areas such as tissue engineering, cancer research, and developmental biology (Aland et al., 2015).

## 4 Applications of Biophysical Models in Cellular Mechanics

### 4.1 Modeling cell deformation and migration

#### 4.1.1 Deformation mechanics in different cell types

Biophysical models have significantly advanced our understanding of cell deformation across various cell types. For instance, a mechanobiochemical model has been developed to simulate 3D cell deformation and movement, incorporating the actin filament network as a viscoelastic and contractile gel. This model uses a force balancing equation to account for displacements, pressure, and concentration forces driven by actin and myosin dynamics, which are modeled by reaction-diffusion equations on a moving cell domain. The numerical simulations from this model demonstrate complex cell deformations, including cell expansion, protrusion, and contraction. Additionally, a high-resolution computational mechanics cell model has been used to study the regeneration of liver tissues, showing how cells respond to mechanical stress and migrate to close tissue lesions (Murphy and Madzvamuse, 2019).

#### 4.1.2 Migration mechanisms under various stimuli

Cell migration is influenced by a variety of mechanical and biochemical stimuli. A mechanobiochemical model has been developed to understand cell migration at the whole-cell scale, integrating cytoskeleton contraction mechanics with the signaling network of reaction-diffusion of biomolecules. This model can simulate cell polarization and shape-dependent localization of protrusion signals, recapitulating phenomena such as durotaxis (Boocock et al., 2020). Furthermore, a chemomechanical model has been used to study single cell migration during cell-to-cell interaction, considering the effects of chemoattractant concentration gradients, dynamic adhesion strength, and relative motion between cells. This model has been validated with experimental data, demonstrating that cell migration velocity can be influenced by dynamic adhesion forces (Sun et al., 2021).

#### 4.1.3 Impact of biophysical models on understanding pathologies

Biophysical models have also provided insights into pathological conditions. For example, the mechanobiology of cells interacting with their microenvironment has been studied to understand disease diagnosis and potential therapeutics. Mechanical measurements of cell deformability, migration on micro/nano-topographies, and traction in 3D matrices have highlighted the promise of these models in linking molecular and biophysical phenotypes

with disease states. Additionally, a model integrating biomechanics and biochemistry has been used to study cell migration in the context of wound healing, providing a quantitative understanding of spatiotemporal waves and their role in collective cell migration (Gou et al., 2020).

### 4.2 Understanding cell-cell and cell-matrix interactions

Biophysical models have been instrumental in elucidating the interactions between cells and their surrounding matrix. For instance, a review of various experimental approaches has summarized the techniques developed to characterize forces at the cellular and subcellular levels, emphasizing the importance of mechanical regulation in cell-matrix interactions. Moreover, a holistic model for cell motility in 3D environments has been proposed, focusing on the mechanical cues from the extracellular matrix and their impact on cell migration and invasion. This model considers the bi-directional interactions between the cell and its microenvironment, including the cytoskeleton and nucleus (Mierke, 2020).

Mierke (2020) found that electrospun fibrous gel matrix models offer significant advancements over traditional extracellular matrix models by allowing independent control of matrix properties. In contrast to the interconnected variation in traditional models-where alterations in concentration also affect pore size and elasticity—electrospun models enable more precise tunability. By using photocross-linking techniques, elasticity and porosity can be adjusted independently, leading to more customizable environments for cellular interaction. Moreover, matrix degradation can be selectively controlled by employing a mixture of degradable and non-degradable fibers, adding another layer of flexibility to the system. This innovation in matrix modeling provides a more adaptable framework for tissue engineering and biomedical applications, where independent control over matrix properties is crucial for replicating complex biological environments. These advances enhance the ability to mimic in vivo conditions more accurately, promoting better research outcomes in cellular and tissue dynamics.

### 4.3 Insights into cellular force generation

The generation of forces within cells is a critical aspect of cellular mechanics. Recent advances in biophysical models have provided insights into how cells generate and respond to mechanical forces. For example, a contraction-reaction-diffusion model has been developed to integrate biomechanics and biochemistry in cell migration, showing how cytoskeleton contraction generates distributed forces for mechanosensing and signaling (Marzban et al., 2019). Additionally, a high-resolution computational mechanics cell model has been used to study the forces exerted by cells during tissue regeneration, providing a quantitative understanding of the impact of cell-biomechanical effects on tissue organization. These models highlight the complex interplay between mechanical forces and cellular behavior, offering new perspectives on cellular force generation and its implications for health and disease (Liedekerke et al., 2019).

## 5 Experimental Validation and Computational Techniques

### 5.1 Experimental methods for model validation

Experimental methods play a crucial role in validating biophysical models in cellular mechanics. Techniques such as micropipette aspiration have been extensively used to study the mechanical properties of cells. This method allows for the precise measurement of cellular responses to mechanical stress, providing valuable data for validating computational models (Gravett et al., 2021). Additionally, advanced imaging techniques have been employed to observe the dynamics of cytoskeletal molecular motors, offering insights into their mechanical operations within cells. These experimental approaches are essential for ensuring the accuracy and reliability of computational models in cellular biomechanics (Guo et al., 2023).

### 5.2 Computational tools and simulations

Computational tools and simulations have become indispensable in the study of cellular mechanics. Molecular dynamics (MD) simulations (Sinha et al., 2023), for instance, have been widely used to investigate the structure and function of biomembranes, providing atomic-level details that are often challenging to obtain experimentally. Similarly, deep Markov state modeling has emerged as a powerful technique for analyzing the long-timescale behavior of complex systems, such as proteins, by incorporating experimental data restraints to improve model

accuracy. These computational approaches enable researchers to explore the intricate details of cellular components and their interactions, facilitating a deeper understanding of cellular mechanics.

### 5.3 Integration of experimental and computational approaches

The integration of experimental and computational approaches is pivotal for advancing our understanding of cellular mechanics. By combining experimental data with computational models, researchers can achieve a more comprehensive and accurate representation of cellular processes. For example, the integration of biophysical experiments with biomolecular simulations has led to significant advancements in understanding the function of biomolecules at an atomic level (Figure 1) (Bottaro and Lindorff-Larsen, 2018). This synergistic approach allows for the refinement of simulations based on experimental observations and vice versa, leading to more robust and predictive models. Furthermore, the use of computational biophysics to study macromolecular machines acting on genes exemplifies the power of combining structural and biophysical experiments with advanced computational methods to uncover the mechanisms underlying fundamental biological processes. This integrated approach is essential for bridging the gap between experimental observations and theoretical models, ultimately enhancing our ability to decipher the complexities of cellular mechanics. In summary, the combination of experimental methods and computational tools is crucial for validating and advancing biophysical models in cellular mechanics. The integration of these approaches provides a more holistic understanding of cellular processes, paving the way for future discoveries and innovations in the field (Mardt and Noé, 2021).

Bottaro and Lindorff-Larsen (2018) found that integrating molecular simulations with experimental data allows for a more comprehensive understanding of biomolecular processes by leveraging both forward and inverse modeling approaches. Forward modeling uses molecular simulations to predict system behaviors, which are then compared against experimental results. Meanwhile, solving inverse problems helps elucidate the underlying factors leading to observed phenomena. The combination of quantum mechanical models, molecular mechanics, and coarse-grained simulations enables the study of biomolecules at various spatial and temporal resolutions, with progressively reduced computational complexity. As these computational methods become more sophisticated, they offer insights into thermodynamics and kinetics that require fewer experimental inputs. This synergy between simulation and experimentation is particularly valuable for probing complex biological systems and understanding their dynamic behaviors on a deeper level, significantly enhancing the precision of biomolecular modeling and reducing experimental limitations.

## 6 Challenges in Modeling Cellular Mechanics

### 6.1 Complexity of cellular processes

Modeling cellular mechanics is inherently complex due to the multifaceted nature of cellular processes. Cells are composed of various components, including the cytoskeleton, cell membrane, and nucleus, each contributing to the overall mechanical behavior. The interactions between these components and their response to external stimuli add layers of complexity. For instance, the cytoskeleton's elasticity, membrane tension, and cell-substrate adhesion are crucial for cellular functions such as migration and differentiation, but these interactions are challenging to model accurately. Additionally, the dynamic nature of cellular processes, such as mechanotransduction and cell signaling, further complicates the development of comprehensive models (Stirnemann, 2022).

### 6.2 Limitations of current models

Despite significant advancements, current models of cellular mechanics face several limitations. One major challenge is the accurate representation of the heterogeneous and dynamic nature of cell membranes. While molecular dynamics simulations have provided insights into membrane organization, they often fall short in capturing the full complexity of multicomponent systems. Moreover, many models struggle to integrate the mechanical properties of subcellular components with the overall cellular mechanics, leading to incomplete or oversimplified representations. Another limitation is the difficulty in directly probing nuclear mechanics, which plays a crucial role in cellular behavior but remains challenging to measure and model (Stirnemann, 2022).

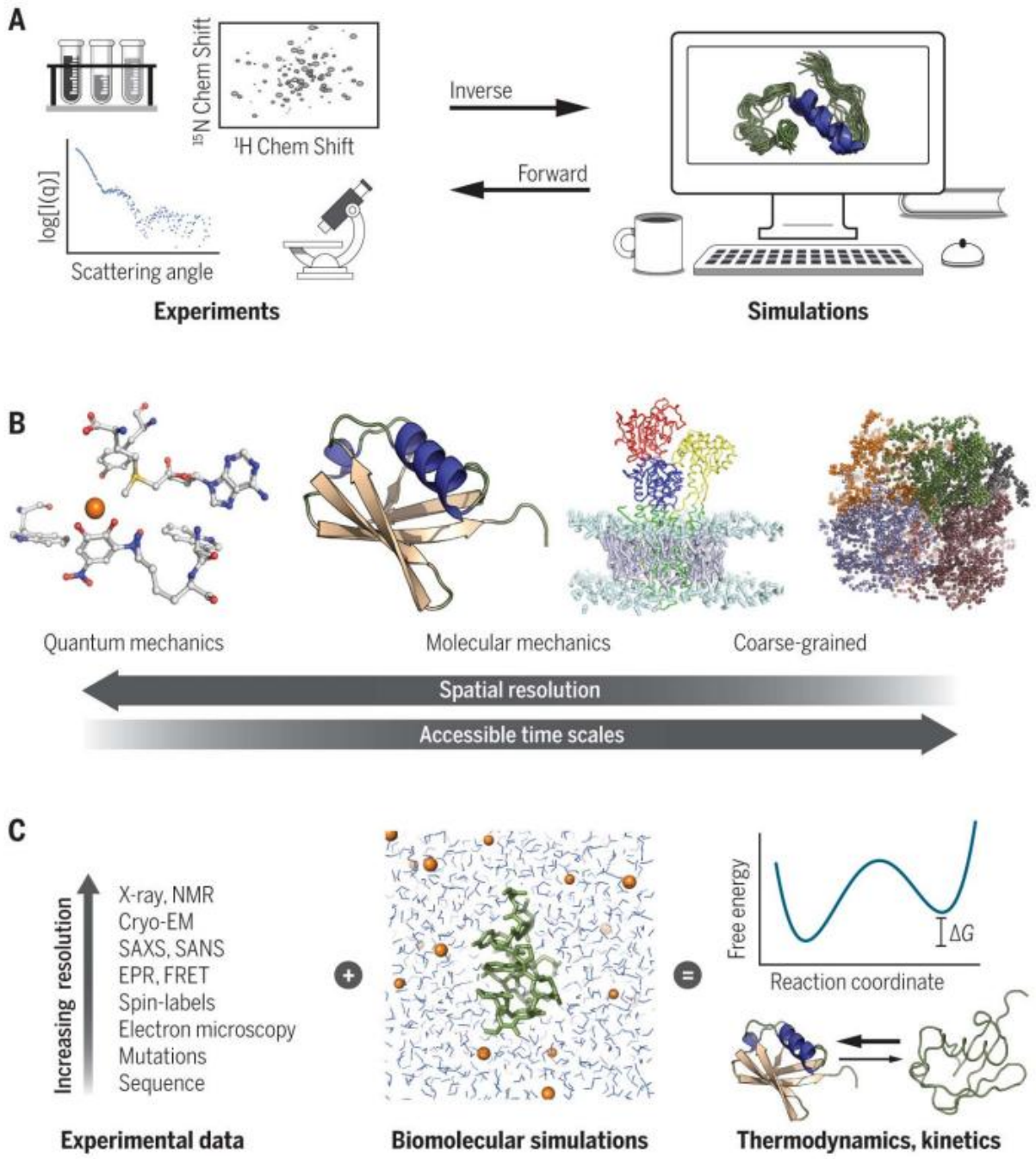


Figure 1 Simulations and experiments are complementary (Adopted from Bottaro and Lindorff-Larsen, 2018)

Image capton: (A) Solving an inverse problem aims to describe causal factors that produce a set of observations. Molecular simulations, conversely, can be used to construct a set of microscopic molecular conformations that can be compared with experimental observations through the use of a forward model. (B) Computational approaches to studying biomolecules range from detailed quantum mechanical models to atomistic molecular mechanics to coarse-grained models, where several atoms are grouped together. The decreased computational complexity granted by progressive coarse-graining makes it possible to access longer time scales and greater length scales. (C) Experimental data can be combined with physical models to provide a thermodynamic and kinetic description of a system. As the model quality improves, it becomes possible to describe more complex phenomena with less experimental data. SANS, small-angle neutron scattering; EPR, electron paramagnetic resonance; FRET, fluorescence resonance energy transfer; DG, Gibb's free energy (Adopted from Bottaro and Lindorff-Larsen, 2018)

### 6.3 Scalability and computational challenges

Scalability and computational challenges are significant hurdles in modeling cellular mechanics. High-resolution models that capture detailed biophysical interactions require substantial computational resources, making it

difficult to scale these models to larger systems or longer timescales (Marrink et al., 2019). Additionally, ensuring the physical consistency of conservation laws across composite models is a complex task that can constrain progress (Pastor-Escuredo and Álamo, 2020). The integration of novel in vivo measurements and advanced computational techniques, such as machine learning, holds promise for overcoming these challenges, but the field is still in the early stages of developing these integrated approaches (Hussan et al., 2022).

## 7 Future Directions in Biophysical Modeling

### 7.1 Advances in multiscale modeling

Multiscale modeling has emerged as a powerful tool to integrate data across different scales and uncover mechanisms that explain the emergence of function in biological systems. This approach is particularly effective in biomechanics, where it can bridge the gap between molecular biophysics and macroscopic tissue mechanics. Integrative biomechanics, which uses multiscale models to address clinical problems at the tissue and organ levels, exemplifies the potential of this approach. However, challenges remain in developing better models and acquiring the necessary data to parameterize and validate these models. The integration of machine learning with multiscale modeling offers a promising avenue to overcome these challenges by efficiently combining large datasets from different sources and levels of resolution, thereby creating robust predictive models that incorporate the underlying physics (Marrink et al., 2019).

### 7.2 Role of artificial intelligence and machine learning

Artificial intelligence (AI) and machine learning (ML) are revolutionizing the field of biophysical modeling by providing new methods to analyze and interpret large, complex datasets. Recent advances in deep learning (DL) and reinforcement learning (RL) have opened up novel opportunities for mining biological data, which were previously intractable due to their size and complexity. The combination of ML with multiscale modeling can naturally complement each other, creating robust predictive models that integrate the underlying physics to manage ill-posed problems and explore massive design spaces. This integration can provide new insights into disease mechanisms, help identify new targets and treatment strategies, and inform decision-making for the benefit of human health.

### 7.3 Potential for personalized medicine applications

Personalized medicine stands to benefit significantly from advances in biophysical modeling. Image-based predictive modeling of heart mechanics, for example, uses state-of-the-art cardiac imaging technologies, modern computational infrastructure, and advanced mathematical modeling techniques to noninvasively analyze and predict in vivo cardiac mechanics. This approach can aid in clinical diagnosis and developing personalized treatment plans by integrating in vivo measurements of cardiac structure and function using sophisticated computational methods. The potential for personalized medicine applications extends beyond cardiology, as integrative biomechanics can be applied to various clinical problems, including genomic applications and the development of improved interventional procedures and protocols. Addressing the challenges in this field will require a coordinated effort from both the clinical-imaging and modeling communities to bridge the gap between basic science and clinical translation (Mardt and Noé, 2021).

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## Conflict of Interest Disclosure

The authors affirm that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

### References

Aland S., Hatzikirou H., Lowengrub J., and Voigt A., 2015, A mechanistic collective cell model for epithelial colony growth and contact inhibition, Biophysical Journal, 109(7): 1347-1357.
https://doi.org/10.1016/j.bpj.2015.08.003

Boocock D., Hino N., Ružičková N., Hirashima T., and Hannezo É., 2020, Theory of mechanochemical patterning and optimal migration in cell monolayers, Nature Physics, 17: 267-274.
https://doi.org/10.1038/S41567-020-01037-7

Bottaro S., and Lindorff-Larsen K., 2018, Biophysical experiments and biomolecular simulations: a perfect match, Science, 361: 355-360.
https://doi.org/10.1126/science.aat4010

Chaplain M.A.J., Lorenzi T., and Macfarlane F.R., 2018, Bridging the gap between individual-based and continuum models of growing cell populations, Journal of Mathematical Biology, 80(1): 343-371.
https://doi.org/10.1007/s00285-019-01391-y

Cheng B., Lin M., Huang G., Li Y., Ji B., Genin G., Deshpande V., Lu T., and Xu F., 2017, Cellular mechanosensing of the biophysical microenvironment: a review of mathematical models of biophysical regulation of cell responses, Physics of Life Reviews, 22-23: 88-119.
https://doi.org/10.1016/j.plrev.2017.06.016

Dallon J.C., 2000, Numerical aspects of discrete and continuum hybrid models in cell biology, Applied Numerical Mathematics, 32(2): 137-159.
https://doi.org/10.1016/S0168-9274(99)00021-5

González-Bermúdez B., Guinea G., and Plaza G., 2019, Advances in micropipette aspiration: applications in cell biomechanics models and extended studies, Biophysical Journal, 116(4): 587-594.
https://doi.org/10.1016/j.bpj.2019.01.004

Gou X., Yang J.C., and Sun D., 2020, Combined single-cell manipulation and chemomechanical modeling to probe cell migration mechanism during cell-to-cell interaction, IEEE Transactions on Biomedical Engineering, 67(5): 1474-1482.
https://doi.org/10.1109/TBME.2019.2938569

Gravett M.S.C., Cocking R.C., Curd A.P., Harlen O., Leng J., Muench S.P., Peckham M., Read D.J., Rogers J., Welch R., and Harris S., 2021, Moving in the mesoscale: understanding the mechanics of cytoskeletal molecular motors by combining mesoscale simulations with imaging, Wiley Interdisciplinary Reviews: Computational Molecular Science, 12(3): e1570.
https://doi.org/10.1002/wcms.1570

Guo J.J., Bao Y.Q., Li M.R., Li S., Xi L.L., Xin P.Y., Wu L., Liu H.X., and Mu Y.G., 2023, Application of computational approaches in biomembranes: from structure to function, Wiley Interdisciplinary Reviews: Computational Molecular Science, 13(6): e1679.

Hussan J.R., Trew M.L., and Hunter P.J., 2022, Simplifying the process of going from cells to tissues using statistical mechanics, Frontiers in Physiology, 13: 837027.
https://doi.org/10.3389/fphys.2022.837027

Ji B., and Bao G., 2011, Cell and molecular biomechanics: perspectives and challenges, Acta Mechanica Solida Sinica, 24(1): 27-51.
https://doi.org/10.1016/S0894-9166(11)60008-6

Jones G., and Chapman S., 2012, Modeling growth in biological materials, SIAM Rev., 54: 52-118.
https://doi.org/10.1137/080731785

Li Y., Wong I., and Guo M., 2022, Reciprocity of cell mechanics with extracellular stimuli: emerging opportunities for translational medicine, Small, e2107305.
https://doi.org/10.1002/smll.202107305

Liebman C., McColloch A., Rabiei M., Bowling A., and Cho M., 2020, Mechanics of the cell: Interaction mechanisms and mechanobiological models, Current Topics in Membranes, 86: 143-184.
https://doi.org/10.1016/bs.ctm.2020.09.001

Liedekerke P., Neitsch J., Johann T., Warmt E., González-Valverde I., Hoehme S., Grosser S., Kaes J., and Drasdo D., 2019, A quantitative high-resolution computational mechanics cell model for growing and regenerating tissues, Biomechanics and Modeling in Mechanobiology, 19: 189-220.
https://doi.org/10.1007/s10237-019-01204-7

Mardt A., and Noé F., 2021, Progress in deep Markov state modeling: coarse graining and experimental data restraints, The Journal of Chemical Physics, 155(21): 214106.
https://doi.org/10.1063/5.0064668

Marrink S.J., Corradi V., Souza P.C.T., Ingólfsson H.I., Tieleman D., and Sansom M., 2019, Computational modeling of realistic cell membranes, Chemical Reviews, 119(9): 6184-6226.
https://doi.org/10.1021/acs.chemrev.8b00460

Marzban B., Kang J., Li N., Sun Y., and Yuan H., 2019, A contraction-reaction-diffusion model: integrating biomechanics and biochemistry in cell migration, Extreme Mechanics Letters, 32: 100566.
https://doi.org/10.1016/j.eml.2019.100566

Mierke C.T., 2020, Mechanical cues affect migration and invasion of cells from three different directions, Frontiers in Cell and Developmental Biology, 8: 583226.
https://doi.org/10.3389/fcell.2020.583226

Murphy L., and Madzvamuse A., 2019, A moving grid finite element method applied to a mechanobiochemical model for 3D cell migration, Applied Numerical Mathematics, 158: 336-359.
https://doi.org/10.1016/j.apnum.2020.08.004

Nathwani B., Shih W.M., and Wong W.P., 2018, Force spectroscopy and beyond: innovations and opportunities, Biophysical Journal, 115(12): 2279-2285.
https://doi.org/10.1016/j.bpj.2018.10.021

Oomens C., 2014, Cellular and biomolecular mechanics and mechanobiology, Computer Methods in Biomechanics and Biomedical Engineering, 17: 694-694.
https://doi.org/10.1080/10255842.2012.705081

Pastor-Escuredo D., and Álamo J.C., 2020, How computation is helping unravel the dynamics of morphogenesis, Frontiers in Physics, 8: 31.
https://doi.org/10.3389/fphy.2020.00031

Rodriguez M., McGarry P., and Sniadecki N., 2013, Review on cell mechanics: experimental and modeling approaches, Applied Mechanics Reviews, 65: 060801.
https://doi.org/10.1115/1.4025355

Sinha S., Pindi C., Ahsan M., Arantes P.R., and Palermo G., 2023, Machines on genes through the computational microscope, Journal of Chemical Theory and Computation, 19(7): 1945-1964.
https://doi.org/10.1021/acs.jctc.2c01313

Stirnemann G., 2022, Recent advances and emerging challenges in the molecular modeling of mechanobiological processes, The Journal of Physical Chemistry B, 126(7): 1365-1374.
https://doi.org/10.1021/acs.jpcb.1c10715

Sun W.X., Gao X., Lei H., Wang W., and Cao Y., 2021, Biophysical approaches for applying and measuring biological forces, Advanced Science, 9(5): 2105254.
https://doi.org/10.1002/advs.202105254

Wang C., Li S., Ademiloye A.S., and Nithiarasu P., 2021, Biomechanics of cells and subcellular components: A comprehensive review of computational models and applications, International Journal for Numerical Methods in Biomedical Engineering, 37(12): e3520.
https://doi.org/10.1002/cnm.3520

Zhu C., Bao G., and Wang N., 2000, Cell mechanics: mechanical response cell adhesion and molecular deformation, Annual Review of Biomedical Engineering, 2(1): 189-226.
https://doi.org/10.1146/ANNUREV.BIOENG.2.1.189