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# MOLECULAR AND BIOPHYSICAL BASIS OF MECHANOTRANSDUCTION IN ENDOTHELIAL CELLS

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**Annotation:** This study investigates the molecular and biophysical mechanisms of mechanotransduction in endothelial cells, with a focus on how physical forces such as shear stress and cyclic stretch are converted into biochemical signals. Laboratory simulations and computer-based models were employed to demonstrate the role of mechanosensitive ion channels, cytoskeletal dynamics, and membrane-associated signaling complexes in endothelial mechanotransduction. The experiments highlighted how changes in membrane tension, ion fluxes, and cytoskeletal remodeling contribute to vascular function and homeostasis. The results provide insights into the bioelectrical and molecular foundations of endothelial responses to mechanical stimuli and underscore the importance of combining theoretical and experimental approaches in understanding vascular physiology.

**Keywords:** Mechanotransduction; Endothelial cells; Shear stress; Cytoskeleton; Ion channels; Membrane tension; Vascular biofizika; Signal transduction; Molecular dynamics; Biophysical modeling

## INTRODUCTION

Endothelial cells line the inner surface of blood vessels and are continuously exposed to mechanical forces generated by blood flow and vessel wall deformation. These cells possess specialized mechanisms to sense and transduce mechanical stimuli into biochemical and electrical signals, a process known as mechanotransduction. The ability to convert shear stress and cyclic strain into intracellular responses is fundamental for vascular homeostasis, regulation of blood pressure, and angiogenesis.

Mechanotransduction relies on a combination of molecular structures and biophysical properties, including mechanosensitive ion channels, integrins, cytoskeletal filaments, and membrane-associated signaling complexes. Shear stress induces conformational changes in ion channels and membrane proteins, leading to $Ca^{2+}$ influx, activation of kinases, and remodeling of the actin cytoskeleton. Similarly, cyclic stretch influences focal adhesion dynamics and modulates endothelial barrier function.

Understanding these processes is critical not only for vascular biology but also for developing biomedical applications, such as tissue engineering, cardiovascular disease modeling, and targeted drug delivery. In this study, laboratory simulations were conducted with students to demonstrate the interplay between mechanical forces and endothelial bioelectrical and molecular responses.

## OBJECTIVES OF THE STUDY



The main objective of this study is to examine the molecular and biophysical basis of mechanotransduction in endothelial cells. Specific aims include:

1. To analyze how shear stress and cyclic stretch affect ion channel activity and membrane potential in endothelial cells.

2. To study the role of the cytoskeleton and focal adhesions in transmitting mechanical forces into biochemical signals.

3. To simulate and visualize mechanosensitive responses using laboratory and computer-based models.

4. To integrate theoretical knowledge with practical observation to improve student understanding of vascular biofizika.

5. To demonstrate the significance of mechanotransduction for vascular physiology and pathophysiology.

## MATERIALS AND METHODS

The study was conducted at the Department of Biophysics, Tashkent State Medical University. Medical students participated in laboratory exercises and computer-based simulations. Endothelial mechanotransduction was modeled using shear flow chambers and stretchable membrane devices, complemented by virtual simulations of ion channel dynamics and cytoskeletal remodeling.

Simulations demonstrated how shear stress induces conformational changes in mechanosensitive ion channels, leading to $Ca^{2+}$ influx and downstream signaling. Cyclic stretch experiments highlighted actin filament reorganization, focal adhesion remodeling, and changes in membrane tension. Membrane potential changes were recorded using electrophysiology simulation software. Data analysis included stimulus-response relationships, correlation between force magnitude and cellular responses, and visualization of intracellular signaling pathways.

## RESULTS

Laboratory simulations and practical exercises revealed that mechanical forces applied to endothelial cells lead to significant bioelectrical and molecular responses. Shear stress induced activation of mechanosensitive ion channels, resulting in rapid $Ca^{2+}$ influx and membrane depolarization. Cytoskeletal remodeling and focal adhesion rearrangement were observed in response to cyclic stretch, illustrating the transmission of mechanical forces to intracellular signaling pathways.

Computer-based simulations allowed visualization of the interplay between ion fluxes, membrane tension, and cytoskeletal dynamics, confirming that mechanotransduction is a highly coordinated process. Students were able to correlate the magnitude and duration of applied mechanical stimuli with the intensity of intracellular responses, demonstrating the graded and adaptive nature of endothelial mechanosensing.

These results emphasize the critical role of molecular structures and physical forces in converting mechanical stimuli into biochemical signals, providing a comprehensive understanding of endothelial mechanotransduction.



## DISCUSSION

The study confirms that endothelial mechanotransduction is governed by an intricate interplay of molecular dynamics, membrane mechanics, and cytoskeletal remodeling. Shear stress and cyclic stretch trigger conformational changes in ion channels and membrane proteins, leading to $Ca^{2+}$-mediated signaling cascades that influence vascular tone and barrier function. Cytoskeletal adaptations ensure that mechanical forces are transmitted efficiently to intracellular signaling complexes, coordinating biochemical responses to external forces.

Practical exercises demonstrated that mechanical stimuli produce graded bioelectrical responses in endothelial cells, reinforcing theoretical knowledge of vascular physiology. The integration of simulations with laboratory observations allowed students to appreciate the biophysical principles underlying mechanotransduction, highlighting the relevance of this process in cardiovascular health, disease modeling, and tissue engineering.

## CONCLUSION

Mechanotransduction in endothelial cells is a highly sophisticated process that illustrates the intricate interplay between mechanical forces, molecular structures, and bioelectrical signaling within the vascular system. This study has demonstrated that mechanical stimuli such as shear stress and cyclic stretch trigger a cascade of events at both the molecular and cellular levels. Activation of mechanosensitive ion channels results in $Ca^{2+}$ influx, which serves as a key secondary messenger initiating various intracellular signaling pathways. These events are tightly coordinated with cytoskeletal remodeling and focal adhesion dynamics, ensuring that mechanical forces are efficiently transmitted from the extracellular environment to intracellular signaling networks.

The laboratory simulations conducted with students at the Department of Biophysics provided direct observation of these mechanisms, allowing learners to correlate the magnitude and direction of applied mechanical forces with the resulting membrane potential changes, ion fluxes, and cytoskeletal adaptations. Such practical exposure reinforced theoretical concepts and highlighted the importance of biophysical principles in understanding endothelial function.

Furthermore, endothelial mechanotransduction plays a pivotal role in vascular homeostasis, angiogenesis, and the development or prevention of cardiovascular pathologies such as atherosclerosis, hypertension, and vascular inflammation. Understanding the molecular and physical bases of mechanotransduction not only deepens knowledge of normal physiology but also offers potential insights for therapeutic interventions aimed at modulating endothelial responses to mechanical stress.

In conclusion, the integration of molecular dynamics, bioelectrical signaling, and cytoskeletal mechanics defines the fundamental nature of endothelial mechanotransduction. The findings of this study underscore the necessity of combining experimental simulations and theoretical approaches in medical education, allowing students and researchers to appreciate the complex processes by which endothelial cells sense and respond to mechanical forces. Future research based on these principles may contribute to the development of novel vascular therapies, tissue engineering applications, and predictive models for cardiovascular diseases, emphasizing the broader biomedical significance of endothelial mechanotransduction.



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