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EDITORIAL
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Editorial: Membrane and Cytoskeleton Mechanics

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Editorial on the Research Topic

Membrane and Cytoskeleton Mechanics

As two main structural components of a cell, the lipid bilayer membrane [1] and cytoskeleton [2] are responsible for stabilizing the cell shape as well as playing key roles in different cellular functions. For example, important processes like cell migration [3–6], division [7, 8], and embryo development [9, 10] are all driven by internal forces generated within the cytoskeleton. In addition, various mechano-sensitive proteins in the membrane allow cells to probe their microenvironment and perform functions such as mechano-transduction [11, 12] and volume regulation [13, 14]. For these reasons, extensive efforts have been devoted in the past few decades to elucidating key factors dictating the mechanical response of the lipid membrane and cytoskeleton [15–18] as well as connecting them to the capability of cells to perform biological duties or the progression of diseases such as cancer [19] and malaria [20]. This research topic intends to present a collection of substantial advances made in this field recently.

The paper by Burgos-Bravo et al. shows that proteoglycan receptor Syndecan-4 can form a ternary complex with $\alpha_V\beta_3$ integrin and the neuronal protein Thy-1, increase the lifetime of Thy-1 – $\alpha_V\beta_3$ integrin binding, modulate their mechano-transduction function, and eventually result in faster neurite retraction and suppressed neurite outgrowth under pro-inflammatory conditions.

The paper by Ricketts et al. focuses on how ionic conditions influence the rearrangement of networks of actin and microtubules. Specifically, the authors show that the bulk contraction of both actin and actin-microtubule networks increases when Mg^{2+} concentrations varies from 2 to 20 mM. Interestingly, actin networks begin to contract at lower Mg^{2+} concentrations and shorter times than actin-microtubule networks. These results shed light on how varying environmental conditions can dynamically tune the morphology of the cytoskeleton without the help of motor proteins.

The paper by Bashirzadeh et al. discusses how the properties of actin crosslinkers and surrounding confinement geometry regulate the formation of actin bundles and bundle networks. Specifically, depending on the size of giant unilamellar vesicles (GUVs) encapsulating actin and concentration of fascin, a short crosslinker, straight F-actin bundles, or crosslinked bundle networks can be formed. In addition, the authors also show that the presence of a long crosslinker, α-actinin, impacts fascin-induced GUV shape changes and significantly impairs the formation of filopodia-like protrusions.

The paper by Dasanna et al. presents how the contrast/ratio of viscosities between RBC cytosol and blood plasma affects the shape and dynamics of RBCs via mesoscopic hydrodynamics simulations. Interestingly, it is found that distinct RBC shapes, including tumbling cells, parachutes, and tank-treading slippers, can all appear depending on the values of viscosity contrast, flow rate, and tube diameter. Furthermore, the authors demonstrate that the tumbling-to-slipper transition, as well as the size of the parachute region, is strongly affected by viscosity contrast.

The paper by Galluzzi et al. discusses the influence of photothermal effects of fluorescent dyes on the mechanical response and stability of membranes. Specifically, the authors show a 30 min laser

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irradiation, with intensity similar to that in a typical confocal scanning microscopy experiment, is enough to trigger a ~40% decrease in the breakthrough force of the stained phospholipid bilayer membrane along with a ~30% reduction in its apparent elastic modulus, highlighting the importance of considering such effect when using, for example, atomic force-fluorescence correlative microscopy to investigate the deformability and permeability of cell membranes.

The paper by Schmidt and Kierfeld proposes a chemomechanical model of microtubule dynamics on the dimmer level. By taking into account the attachment/detachment and hydrolysis of tubulin dimers, the deformation of protofilaments, and the rupture/formation of lateral bonds between them, the authors show the model is computationally efficient to capture repeated catastrophes and rescues at realistic tubulin concentrations and hydrolysis rates, as well as gain insight into microscopic structural features triggering these events.

The paper by Chen et al. discusses the organization of F-actin and viscoelasticity distribution in migrating cells in response to pH changes in the microenvironment. In particular, by using multifrequency atomic force microscopy (AFM) with amplitude modulation-frequency modulation (AM–FM), the authors show that, unlike the randomly distributed F-actin and the homogeneous viscoelasticity at the normal pH level, living Huh-7 cancer cells with the reduced pH level of 6.5 exhibits highly oriented and organized F-actin along the lamellipodium direction coupled with a spatial gradient both in elasticity and viscosity of the cell.

The paper by Castaneda et al. reviews recent progress on understanding how different environmental factors contribute to actin bundle assembly, organization, and mechanics. Specifically, the effects of macromolecular crowding, cation interactions, and actin-crosslinking proteins on F-actin bundling, higher-ordered structure formation, and mechanical response of the resulting network are discussed in detail.

The paper by Leong et al. presents coarse-grained molecular dynamics models of spike proteins in SARS-CoV-2 coronavirus and angiotensin-converting enzyme 2 (ACE2) receptor proteins to study the endocytosis of the virus under physiologically relevant spatial and temporal scales. The coarse-grained molecular simulations show that, during their interaction with the ACE2 receptors, the spike proteins adopt bent configurations because of their unique flexibility, which facilitates their attachment to the host cell membrane, compared with rigid spikes.

The paper by Mierke reviews the current understanding of the bidirectional mechanical interplay between cells and their microenvironment. Specifically, it points out how, on the one hand, the intracellular cytoskeletal architecture and, on the other hand, the matrix architecture contribute to cellular stiffness or contractility and thereby determines the emergence of a distinct migration mode of cells. In addition, it also discusses whether universal hallmarks of the migratory phenotype can be defined.

The paper by Strychalski presents a 3D dynamic computational model for describing cell blebbing where membrane locally detaches from the actin cortex, resulting in a pressure-driven flow of the cytosol and membrane expansion. In particular, bleb expansion dynamics under different initiation mechanisms are analyzed. Furthermore, the author also discusses the influence of treating the cytoplasm as a viscous fluid or as a poroelastic material on blebs' shape and growing speed.

AUTHOR CONTRIBUTIONS

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