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Intracellular mechanics: connecting rheology and mechanotransduction

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Cell mechanics is crucial for a wide range of cell functions, including proliferation, polarity, migration and differentiation. Cells sense external physical cues and translate them into a cellular response. While force sensing occurs in the vicinity of the plasma membrane, forces can reach deep in the cell interior and to the nucleus. We review here the recent developments in the field of intracellular mechanics. We focus first on intracellular rheology, the study of the mechanical properties of the cell interior, and recapitulate the contribution of active mechanisms, the cytoskeleton and intracellular organelles to cell rheology. We then discuss how forces are transmitted inside the cell during mechanotransduction events, through direct force transmission and biochemical signaling, and how intracellular rheology and mechanotransduction are connected.

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Introduction

Cells interact physically with their environment. They can probe the mechanical properties of their substrate and apply forces onto their surroundings. Conversely, external mechanical constraints can induce cellular responses. In a process called mechanotransduction [1,2], external forces, in the form of tensile, compressive or shear stresses, are sensed by cells and transmitted to the cell interior to elicit a new cell behavior. Force transmission within the cell interior may be affected by the mechanical properties of the cytoplasm. Intracellular rheology, which focuses specifically on the mechanical properties of the cell interior, has received a growing interest in recent years [3,4]. The general view is that the cell interior behaves as a viscoelastic material and its frequency-dependent rheological moduli follow a weak power law [5]. However, whether intracellular material properties can impact on mechanotransduction and reciprocally is still unclear.

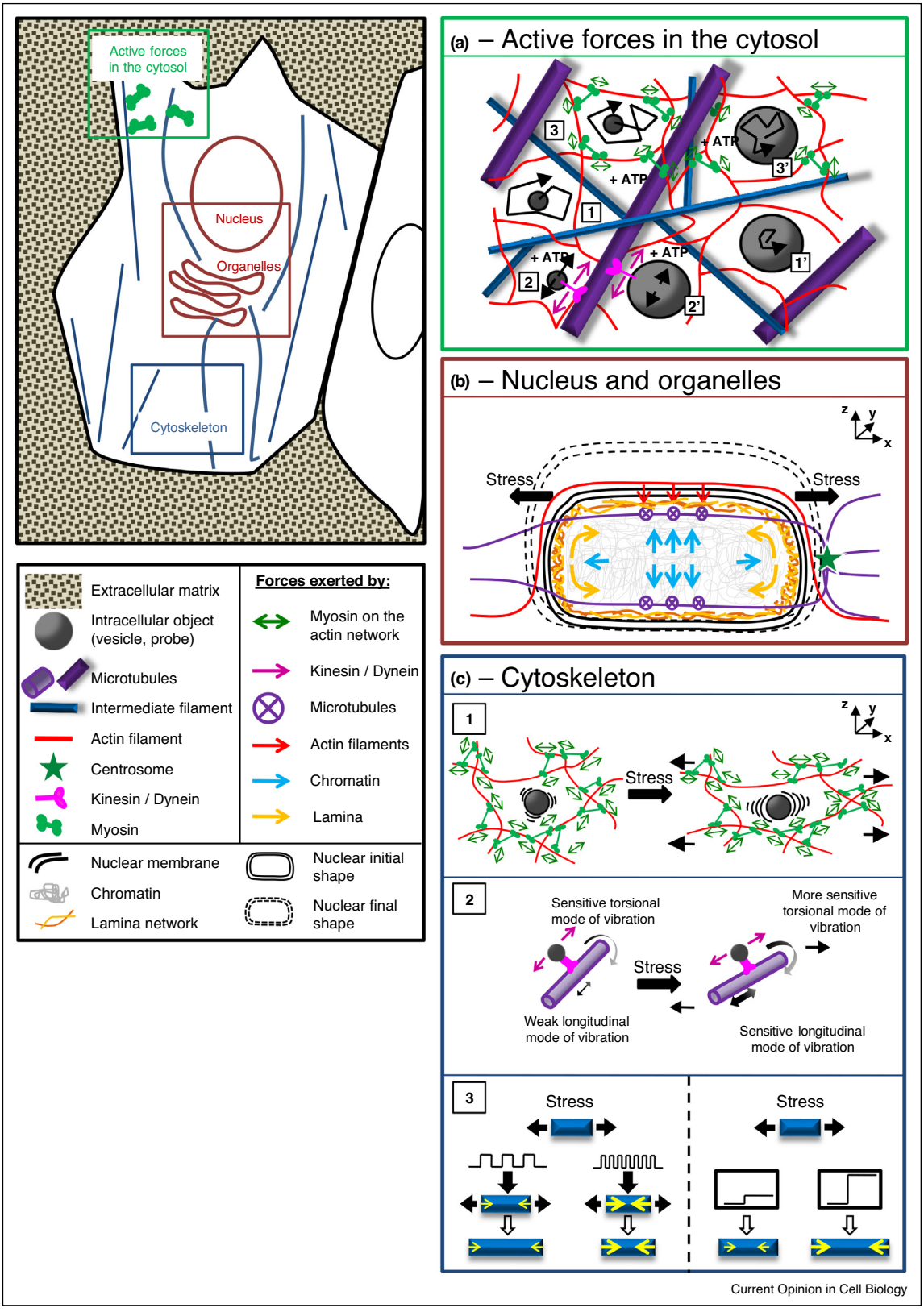
In this review, we first discuss the latest findings in intracellular rheology with an emphasis on the critical role of the spatial and temporal scales. The contribution of active out-of-equilibrium forces has recently taken center stage. We also describe how the cytoskeleton [3] and intracellular organelles participate to intracellular rheology. We then turn to mechanotransduction and how forces are transmitted from the plasma membrane to the cell interior and intracellular organelles. Here again, spatio-temporal scales appear to be crucial to determine whether forces are directly transmitted to organelles via a purely physical mechanism or whether biochemical signaling is required. Throughout this review, we chose to highlight recent studies in which quantitative mechanical measurements were performed, mostly in mammalian cells. We do not detail the latest technical developments in the field of intracellular mechanics and refer to Refs. [6–12] for recent reviews on the technical aspects.

Intracellular rheology

Mechanics of the cell cytoplasm and role of non-equilibrium active forces

Because most cellular functions are regulated by intracellular processes that take place in the cytoplasm, intracellular rheology has emerged as an essential aspect of cell mechanics. While the cytoplasm can be viewed as a viscoelastic material, its mechanical properties strongly depend on the spatio-temporal scale at which they are probed. First, the size of the probe used to measure intracellular viscoelastic moduli determine which cytoplasmic structures will dominate the measurement (Figure 1a). The cytoplasm was shown to behave as an elastic solid using 100–500 nm-size optically-trapped beads [13] or as a viscoelastic liquid using micron-size superparamagnetic wires [14]. Second, the cytoplasm is not homogeneous and its rheology depends on the position within the cell. The perinuclear region is usually stiffer than the cell periphery [15•]. This may reflect differences in cytoplasmic crowding, for instance in regions of high densities of cytoskeletal or soluble proteins. Consistently, when the cell volume decreases, intracellular stiffness increases [16•]. Third, the viscoelastic properties of the cytoplasm are strongly frequency-dependent [17••].

Figure 1



Some examples of recent advances in intracellular rheology.
(a) Active forces in the cytosol. The mechanics of the cytoplasm depends on the frequency at which it is probed and on the size of the probe.