[Talk 15] FDT violation and Non-Gaussian Glassy Dynamics in active systems

Daisuke Mizuno, Kyushu University

Seen as a material, the interior of biological cells is a very unique kind of active system, driven away from equilibrium by the internal energy-dissipating and force-generating machinery. We believe that there are two compounds that mostly determine the mechanics of cell interiors: cytoskeletons and glassy cytoplasm. Both are typical soft materials that highly nonlinearly respond to mechanical stresses so that cell mechanics is profoundly affected by self-generated forces. Cells can therefore smartly tune their own properties with their own activity, without remodeling their internal structures.

cytoskeletons

In much the same way that each of our bodies depends on bones for mechanical integrity and strength, each cell within our bodies is mechanically supported by a skeleton of stiff proteins, called the cytoskeleton. Furthermore, analogous to how our bones are held and moved by muscles, the cytoskeleton is activated by molecular motors, which are nanometer-sized force-generating enzymes. The interior of cells is driven far from equilibrium by such force-generating machinery. We measured the dynamics and mechanical properties of a simple three-component model system consisting of myosin II, actin filaments, and cross-linkers. In this system, we observed FDT violation due to non-thermal stresses arising from motor activity that controlled the cytoskeletal network mechanics; stiffness increased by a factor of nearly 100 and qualitatively changed the viscoelastic response of the network in an adenosine triphosphate–dependent manner. We present a quantitative theoretical model connecting the large-scale properties of this active gel to molecular force generation.

glassy cytoplasm.

Mechanics of cytoplasm is fundamental to understand cell behaviors since it governs the dynamics of core materials essential for living systems. The physical nature of cytoplasm is, however, poorly understood. Living cytoplasm is highly condensed, containing far greater amount (~ 30 % in weight fraction 7) of macromolecules (i.e. globular proteins, ribosome, etc.) that are not tethered to cytoskeletal structures. It has been found that this, collectively referred to as “macromolecular crowding”, drastically affects cell mechanics 4, 8 and therefore regulates metabolism 9. Here, we investigate, using microrheology, the mechanics of metabolism-deficient cytoplasmic models: single-component biomacromolecules (BSA) and extracts from bacterial and eukaryotic cells. Fluctuations and response of probe particles dispersed in these cytoplasmic models quantified the viscoelastic properties of surrounding

materials. The viscosities of cytoplasm extracted from totally different species were all similar and showed diverging increase at a macromolecular concentration relevant to that in living cells. Such dramatic increase of viscosity upon crowding was quantitatively consistent to the colloidal glass-forming materials close to the glass transition. While metabolically active cells maintain finite fluidity, viscosities (or fluctuation of probes) in dormant cells or in cells under slight osmotic compression were also frozen. These results point to a possibility that the cytoplasm lacking homeostatic metabolism undergoes glass transition at physiological concentration, and that the living cytoplasm is forcedly fluidized via metabolic activity.

ACKNOWLEDGEMENTS

This work is supported by a Grant-in-Aid for Scientific Research on Innovative Areas "Fluctuation & Structure" (No. 25103011) from the Ministry of Education, Culture, Sports, Science, and Technology of Japan.