Rheology and fluctuations 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. Understanding out-of-equilibrium machinery in cells or other active systems is challenging. Cellular compounds are typically soft and highly nonlinearly responding so that their mechanics is profoundly affected by self-generated forces. It is therefore essential to develop experimental and theoretical methodologies to quantify both of these (force and mechanics) in active systems. This would be possible, as long as we know, with "microrheology" operated in two different modes that observe fluctuation (passive mode) and response (active mode) of embedded probe particles.

Here we performed both active and passive microrheology simultaneously in cultured eukaryotic cells using high-bandwidth laser interferometry and optical trap technology implemented with a smooth 3-dimensional feedback of a piezo-mechanical sample stage. This technique allows us to stably track a probe particle in cells, over several hours, within the laser focus regardless of vigorous spontaneous flows and fluctuations naturally existing in active systems. Our experiments demonstrate the breaking of the fluctuation-dissipation theorem as an excessive (non-thermal) fluctuation in the low frequency domain, where the out-of-equilibrium activity should critically affect the mechanics of active polymeric materials in cells. We also developed a theoretical methodology to relate the observed non-thermal fluctuations to internal force generations and confirmed it in a reconstituted cell model, consisting of cross-linked filamentous actin driven by myosin motor proteins, that have been shown to usefully resemble nonequilibrium situations in cells. In prior studies, the second moment of the non-thermal fluctuations has been investigated following the standard procedure established for the microrehology in homogeneous continuum in equilibrium where Gaussian fluctuations are expected. Actually, however, the non-thermal fluctuations observed in active cytoskeletons was found to follow highly non-Gaussian distribution. We investigate the origin of non-Gauss and heavy-tailed probability distribution of fluctuations. Considering the action and dynamics of the force generators randomly-distributed in a homogeneous media, we provide analytical expression for the observed distribution which we call truncated Lévy. The model includes both Gauss and complete Lévy as the limiting cases of the experimentally controllable parameters and quantitatively describes the intermediate behaviors in physically attainable situations.

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.