MPI-DS Seminar

MAX PLANCK INSTITUTE
FOR DYNAMICS AND
SELF-ORGANIZATION

Enhanced DNA repair through droplet formation and p53 oscillations

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The fundamental mechanisms that control and regulate biological organisms exhibit a surprising level of complexity. Oscillators are perhaps the simplest motifs that produce time-varying dynamics and are ubiquitous in biological systems. The tumor suppressor protein, p53, is a master regulator of DNA damage response and when the cell is exposed to multiple DNA double-strand breaks, it exhibits sustained oscillations with a well-defined period of approximately 5.5 h. However, why such oscillations emerge and in what way they might help the cell respond to external stresses is not resolved. A characteristic hallmark of the response is the formation of sub-compartments around the site of damage, known as foci. Following multiple DNA breaks, the transcription factor p53 exhibits oscillations in its nuclear concentration, but how these dynamics can affect the repair remains unknown. In this talk, I will present different ways in which the oscillations can be stimulated and how complex dynamics might stimulate groups of genes. This will lead me to the formulation of a theory for "foci" formation through droplet condensation and discover how oscillations in p53, with its specific periodicity and amplitude, optimize the repair process by preventing Ostwald ripening and distributing protein material in space and time. Based on the theory predictions, I present experimental data showing that the oscillatory dynamics of p53 enhance the repair efficiency. These results connect the dynamical signaling of p53 with the microscopic repair process and create a new paradigm for the interplay of complex dynamics and phase transitions in biology.

Wednesday, April 26th, 2023 at 11:00 am

MPI-DS, SR 0.79
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