universität ulm

Physikalisches Kolloquium — Physics Colloquium

Einladung — **Invitation**

Monday, 09 November 2026

Lecture Hall O25/H2, at 16:15
Coffee and cookies will be served in front of the lecture hall from 16:00

Imaging, Quantifying and Mapping Chromatin Remodeler Dynamics in Live Human Cell Nucleus, One Molecule at a Time

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SWI/SNF chromatin remodelers are a key subfamily of multi-subunit complexes that regulate genome access via nucleosome translocation/ejection. Despite their prevalent implications in cancers, their intranuclear dynamics *in vivo* and how misregulation of such dynamics could underpin cancers remain poorly understood. Using single-molecule tracking (SMT), we systematically quantified the live-cell diffusion and chromatin-binding dynamics of the fully assembled human SWI/SNF remodeler complexes. Leveraging a novel super-resolved mapping strategy termed STAR, we further revealed heterogeneous, nanoscale remodeler binding “hotspots” across the nucleoplasm, pointing to a model where successive binding events preferentially clustered within the “hotspots” lead to sustained productive remodeling, which gets variably disrupted in remodeler mutants implicated in cancers across tumor types. To further elucidate the underlying driving force for such heterogeneous intranuclear organization, we showed that BRG1, the core ATPase/translocase subunit common to all major subtypes of the SWI/SNF subfamily, undergoes phase separation both *in vitro* and in live cell nucleus, mediated by its IDR-rich C-terminus ($BRG1_C$). Intranuclear condensates of $BRG1_C$ are highly dynamic, with their formation, localization and liquid-like properties governed primarily by patterned charge blocks in its sequence. Importantly, $BRG1_C$ condensates selectively partition into the fibrillar center phase of the nucleolus, modulated by rRNA transcription. Correlative single-molecule tracking and condensates mapping further reveals that nucleolar condensation constrains $BRG1_C$ mobility, while spatiotemporally enriching its chromatin-binding to more efficiently engage rDNA for remodeling and facilitate rRNA transcription. Collectively, these findings unveil a multi-modal, condensation-mediated landscape for organizing remodeler dynamics in space and time, and provide unique, mutant-specific signatures that establish the biophysical basis for aberrant remodeler–chromatin interactions underpinning cancer-associated remodeler mutations.

Host: Prof. Dr. Christof Gebhardt, Institute of Experimental Physics

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