Using single particle trajectory statistics and polymer simulations to analyze and predict changes in chromatin structure

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Biological implications of chromatin movement can be analyzed by polymer models. Here we present an analysis workflow that consists of an improved imaging regime employing high spatial and temporal resolution microscopy coupled with a statistical analysis to extract biophysical parameters from trajectories. The last step of the method is the construction of a polymer model from data to explore in simulations the chromatin condensation state and the interactions the locus experiences. Our approach allows us to differentiate between extrinsic forces from the cytoskeleton and intrinsic chromatin alterations. We have applied this to a yeast inducible double-strand break system and used the extracted parameters to predict chromatin expansion near a break. Super resolution microscopy confirms this prediction and shows that expansion depends on the INO80 nucleosome remodeler. The present method is not limited to yeast and can be used for trajectories generated from any model organism.

References

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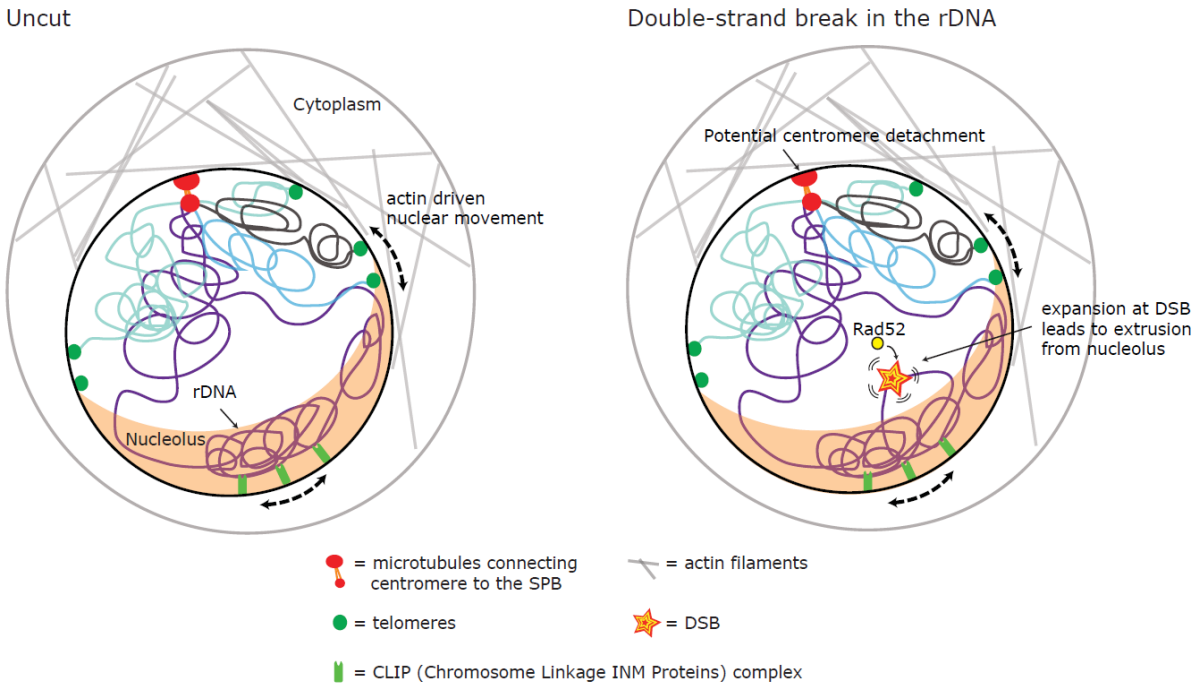

Expansion of a DSB and extrusion from the nucleolus: Yeast chromosomes are anchored to the nuclear periphery i) their centromeres attached to the spindle pole body (SPB), and ii) through the telomeres by a number of anchors including Sir proteins, SUN domain protein Mps3, Esc1 and Ku. Actin filaments can drive nuclear rotation/precession. The CLIP complex can tether the rDNA to the nuclear periphery. After a DSB is induced, local interactions at the break are reduced allowing the chromatin surrounding the break to expand. The loss of interactions allows for the break to be extruded to the periphery of the nucleolus and for the recruitment of repair factors such as Rad52.