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Chromosome Territories Reposition During DNA Damage-Repair Response
Ishita S. Mehta, Mugdha Kulshreshtha, Sandeep Chakraborty, Ullas Kolthur-Seetharam, Basuthkar J. Rao.
Department of Biological Sciences, Tata Institute of Fundamental Research, Mumbai, Maharashtra, India, 400005.
Local higher order chromatin structure, dynamics and composition of the DNA are known to determine DSB frequencies and efficiency of repair. However, the effect of DNA damage response, *vis-a-vis* spatial organisation of chromosome territories is still unexplored. Our report investigates the effect of DNA damage on spatial organization of chromosome territories (CTs) within interphase nuclei of human cells. We show that DNA damage, in a dose dependent manner, induces a large-scale spatial (nuclear interior to periphery and vice versa) repositioning of CTs that are relatively gene dense. Further, we have found that CT repositioning is contingent upon DSB recognition and damage sensing. Importantly, our results suggest that this is a reversible process where following repair, CTs re-occupy positions similar to that in undamaged control cells. Thus, our report, for the first time highlights DNA damage dependent spatial reorganization of chromosomes, which might be an integral aspect of cellular damage response.

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Structure and Mechanical Properties of the Bacterial Chromosome in E.Coli
Nastaran Hadizadeh[1], Calin C. Guet[2], Reid C. Johnson[3], John F. Marko[4].
[1]Physics and Astronomy, Northwestern University, Evanston, IL, USA, [2]Institute of Science and Technology Austria, Klosterneuburg, Austria, [3]Department of Biological Chemistry, University of California, Los Angeles, Los Angeles, CA, USA, [4]Physics and Astronomy, Molecular Biosciences, Northwestern University, Evanston, IL, USA.
Our knowledge of the scheme by which the bacterial chromosome is physically organized is at best incomplete. Through in vivo visualization using an inducible GFP fusion to the nucleoid-associated protein Fis, to non-specifically decorate the entire chromosome, we have been able to observe the global chromosome structure in live cells, where the dynamics of structure could be followed in real time. Quantitative analyses of the nucleoid and sub-nucleoid structures have indicated that the chromosome is a self-adherent, folded object with defined and long-lived folding patterns, including an overall coiled shape, in which nucleoid-associated proteins play a major role. In addition to the in vivo studies, we have developed an assay to carry out mechanical experiments on nucleoids removed from cells, using magnetic tweezers technique. We use this assay to study the effects of the major nucleoid-associated proteins mutations on the chromosome by probing changes in the mechanical properties, in order to get a better understanding of the roles played by major chromosome-folding proteins in organizing the physical state of the chromosome.

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Nucleoid Reorganization by the Stress Response Protein Dps
Elio A. Abbondanzieri, Natalia Vtyurina, Anne Meyer.
TU Delft, Delft, Netherlands.
All living cells must organize their DNA into dynamic three-dimensional architectures that are compatible with essential cellular processes such as transcription, translation, and DNA repair. While this organization fundamentally affects such broad phenomena as antibiotic resistance, cell division, and the aggressiveness of cancer cells, DNA organization remains poorly understood due to the complexity of the many protein-DNA interactions involved. Recently it has been shown that DNA is able to condense into a crystalline lattice in bacterial cells exposed to stressful conditions. The single protein responsible for creating these DNA 'biocrystals' is Dps (DNA-binding protein from starved cells). When present at sufficiently high concentrations, Dps drives the condensation of DNA into a biocrystal both in vitro and in vivo. Here we investigate the energetics and kinetics that determine biocrystal formation. We have developed a novel single molecule assay to probe the physical interactions between fluorescently tagged Dps and DNA. Long DNA molecules were immobilized on a surface to study their spatial distribution during Dps-DNA biocrystal formation using total internal reflection fluorescence microscopy (TIRF) and epifluorescence microscopy. In addition, due to strong inter-particle interactions between Dps, the protein can form a two-dimensional crystal even in the absence of DNA. This two-dimensional crystal may represent an intermediate on the pathway to biocrystal formation. We have measured key features of this structure from atomic force microscopy (AFM) studies of Dps and DNA. From these data, we present a model for biocrystal formation.

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Brownian Dynamics Simulations of a Self-Avoiding Chain Model of a Chromosome in a Spherical Confinement
Young-Gui Yoon[1,2], Changbong Hyeon[2].
[1]Chung-Ang University, Seoul, Republic of Korea, [2]Korea Institute for Advanced Study, Seoul, Republic of Korea.
Advances in experimental techniques such as 3C and high-C technologies reveal structural information on chromosomes in detail. Computation of dynamical properties of simple models can be used to shed light on chromosome dynamics inside nuclei of different size. We performed Brownian dynamics simulations of a self-avoiding chain model in a spherical confinement with varying sizes. The simulation results indicate that the model system exhibits significant dynamical heterogeneity below a critical volume fraction of the confinement. The biological implication of the results is discussed in the light of chromosome dynamics.

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Coarse-Grained Simulations of Nucleoid Structure
Tyler M. Earnest[1], Zaida Luthey-Schulten[2].
[1]Department of Physics, University of Illinois at Urbana-Champaign, Urbana, IL, USA, [2]Department of Chemistry, University of Illinois at Urbana-Champaign, Urbana, IL, USA.
A coarse-grained computational model of dsDNA is developed to investigate the folding and compaction of the Caulobacter crescentus nucleoid. Using a custom GPU accelerated Brownian dynamics code, we simulate the full 4.0 million base pair genome using a discrete wormlike-chain/bead model. With 10 base pairs represented by each bead, we are able to reach millisecond timescales. We simulate the packing of the nucleoid into the bacterial cell by placing a small ring of beads at the cell pole and periodically adding beads to the ring until the genome size has been reached. This packing process is extended by adding nucleoid associated proteins (NAPs) which can cross-link distal regions of the chromosome. The NAPs diffuse freely in the cell and when bound to the nucleoid can diffuse in one dimension and unbind depending on the binding affinity to that locus. With the binding affinities of these proteins to the bead depending on the bead locus, we can use information from chromosome capture experiments to build in more biological realism into our simulation and study the effect of NAP cross-linking on the nucleoid structure.

Membrane Dynamics I

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Shape Pairing of Cholesterol with Oxidized Phospholipid Species in Lipid Bilayers
Bastien Loubet[1], Piotr Jurkiewicz[2], Agnieszka Olzynska[2], Martin Hof[2], **Himanshu Khandelia**[1].
[1]University of Southern Denmark, Odense, Denmark, [2]J. Heyrovský Institute of Physical Chemistry of ASCR, Prague, Czech Republic.
We show that (1) cholesterol protects bilayers from disruption caused by lipid oxidation by sequestering conical shaped oxidized lipid species (PZPC) away from phospholipid, because cholesterol and the oxidized lipid have complimentary shapes and (2) mixtures of cholesterol and oxidized lipids can self-assemble into bilayers much like lysolipid-cholesterol mixtures. The evidence for bilayer protection comes from MD simulations and DLS measurements. Bilayers containing high amounts of PZPC become porous, unless cholesterol is also present. The protective effect of cholesterol from oxidized lipids has been observed previously using EPR and electron microscopy imaging of vesicles. The evidence for the pairing of cholesterol and PZPC comes from the 2-D density plots and different thickness regimes from simulations. The density plots show that these two molecules co-localize in bilayers. Cholesterol-PZPC rich regions are thinner than phospholipid-rich regions in the same bilayer. We further demonstrate the affinity of PZPC and cholesterol in self-assembly simulations, where we show that cholesterol-oxidized lipid mixtures can form bilayers without phospholipids at specific concentrations, reminiscent of lysolipid-cholesterol mixtures. The additivity of the packing parameters of cholesterol and PZPC explains their cohabitation in a planar bilayer.