Simulation of radiation-induced DNA damage with the code RITRACKS

Ianik PLANTE[1], Hera CANAJ[2], Andrew SCORTEA[2], Ariana CLERKIN[2], Justin RENDLEMAN[2], Devany WEST[2], Jason WEEKS[3], Viviana RISCA[2]

[1]KBR, Houston, TX 77058, USA; [2]Laboratory of Genome Architecture and Dynamics, The Rockefeller University, New York, NY; [3]NASA JSC, Houston, TX 77058

Radiation-induced DNA damage, especially double-strand breaks (DSBs), have important biological consequences [1]. The human DNA is packaged into chromatin, which can take on locus-dependent and cell type-dependent spatial conformations that correspond to epigenetic states. Epigenetic differences can affect radiation-induced DNA break patterns, potentially creating distinct DNA repair, and signaling outcomes across the genome in different cells [2].

The stochastic track structure simulation code RITRACKS (Relativistic Ion Tracks) was used to model radiation-induced DNA damage to isolated nucleosomes by ions and photons [3]. In this work, more complex atomic-scale DNA structures were generated based on information provided by the code meso-WLCsim [4,5], which takes the mechanical properties of DNA into account. We simulated the fragment length distributions (FLD) of irradiated DNA structures and obtained results representative of those obtained with Radiation-Induced Correlated Cleavage with sequencing (RICC-Seq) experiments [6].

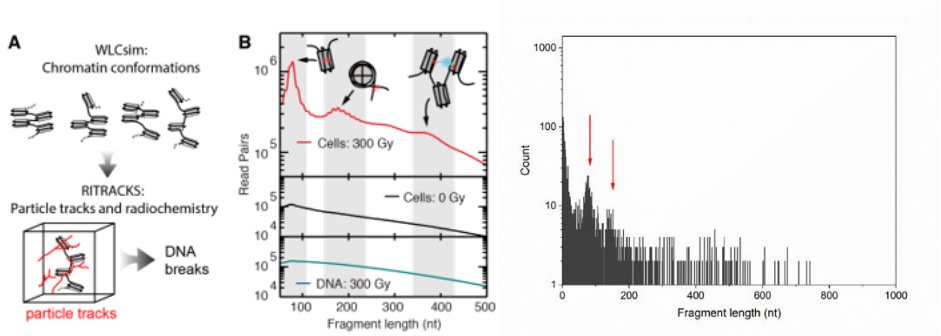


Figure 1. (A) Strategy to combine Monte Carlo sampling of chromatin conformation ensembles followed by prediction of DNA damage for sampled conformations. (B) RICC-seq FLD for irradiated cells (red), unirradiated cells (black) and irradiated naked DNA (cyan). (C) FLD calculated by RITRACKS for a 5-nucleosome extended DNA structure irradiated with 10-MeV protons, showing the first and second peaks at 78 and 150 base pairs, corresponding to 1 and 2 DNA wraps around a nucleosome.

The recent updates in the code RITRACKS allow the calculation of several quantities such as the DNA damage yield and the FLD. This approach can be used to model epigenetic state-specific chromatin structure parameters to leverage the epigenetic state data available for many human cell types to infer relative DNA damage sensitivity among genomic loci.

[1] Ward J.F. *Int. J. Radiat. Biol.* 66, 427-432 (1994); [2] Rydberg B. et al, *Acta Oncol* 40,682-685 (2001); [3] Plante I. et al. *BioTech* 13, 17 (2024); [4] MacPherson Q. et al. *PNAS* 115, 12739-12744 (2018); [5] Clerkin A.B. et al., *bioRxiv*, doi: https://doi.org/10.1101/2024.07.28.605011 (2024); [6] Risca V.I. et al. *Nature* 541, 237-241 (2017).