Simplified Estimation of X-Ray Induced DNA Damage from Monte Carlo Track-Structure Data

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ABSTRACT

Purpose:
To develop a fast and scalable framework to estimate the X-ray induced DNA damage while preserving the biological accuracy of detailed particle track simulations.

Methods:
We generated a database of energy-specific DNA damage events by using Monte Carlo simulations and integrating multiscale computational pipeline. The macroscale simulations modeled X-ray particle transport through a water phantom, while the microscale simulations modeled the DNA damage induced within a realistic human cell nucleus. Photon energies ranging from 60 keV to 10 MeV was simulated.

Results:
The average yield of double-strand break (DSB) was approximately 40 DSB/Gy across all energies. This is consistent with reported values for low-LET radiation. Most DSBs were classified as low-complexity (dispersed damage), with only a small fraction exhibiting highly clustered damage.

Conclusions:
The proposed framework enables rapid and biologically realistic DNA damage estimation without the need to repeat full-scale simulations (the particle transport and DNA damage) This provides a scalable approach for larger radiobiological studies.

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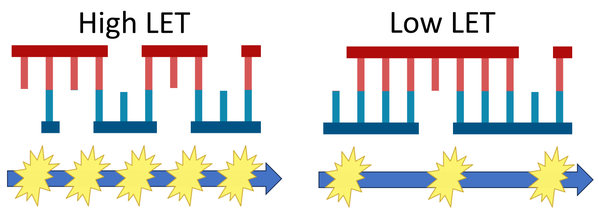
BACKGROUND

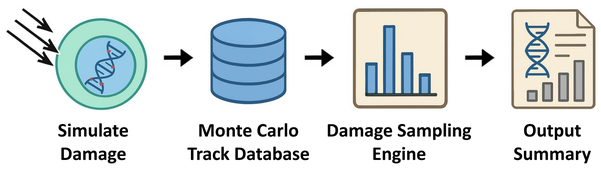
- Radiation induces biological effects primarily through DNA damage



- Geant4-DNA extends the physics models to **very low energies** and tracks the individual interactions of primary and secondary particles; TOPAS-nBio models a full 3D nucleus with **realistic DNA arrangement** and **simulates chemical species production and diffusion**
- This level of detail comes with **significant computational cost**, making it impossible for larger-scale simulations

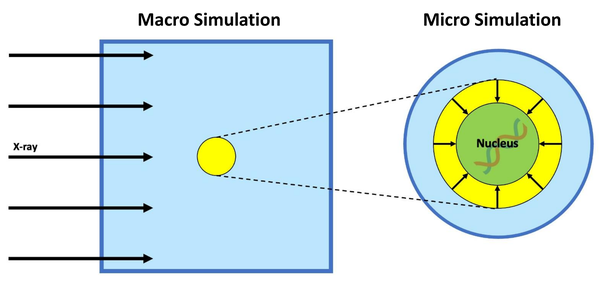
METHODOLOGY

- We proposed to develop an accelerated simulation pipeline for **estimating DNA damage** induced by X-ray irradiation, using pre-simulated Monte Carlo track data



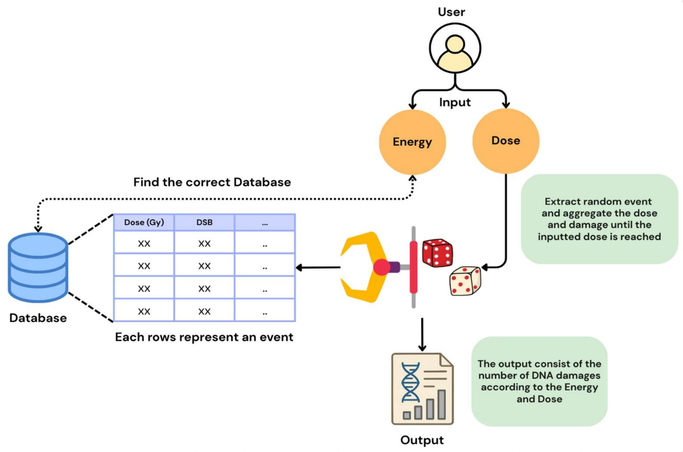
- The process involves generating energy-specific DNA damage events through Monte Carlo simulations, constructing a database, and developing a sampling engine that produces an estimation of radiation-induced DNA damage.

SIMULATION SETUP



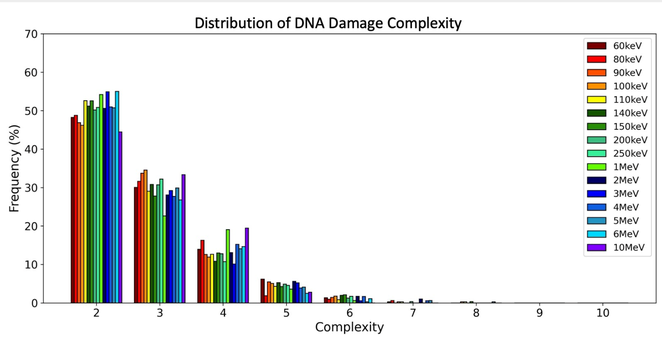
- **A multiscale simulation** approach was used to balance computational efficiency with the biological accuracy provided by track-structure simulations.
- The macroscale simulation modeled the **X-ray beam passing through a water phantom**, while the microscale simulation **modeled DNA damage within a realistic cell nucleus**.
- Phase space (represented by the yellow circle) captured the complete state of particles crossing the scoring surface in the macroscale simulation, allowing them to be **re-simulated exactly as they were** in the microscale simulation.

DNA DAMAGE ESTIMATION

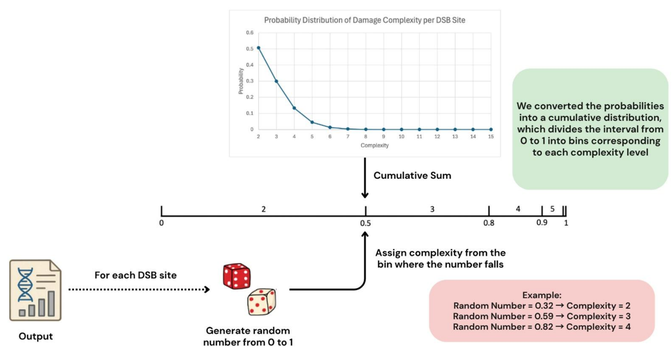


- The user specifies the **X-ray beam energy** and **the desired absorbed dose**
- Based on the input, the **corresponding energy-specific** database is automatically selected
- Radiation events are **randomly sampled and aggregated** until the target dose is reached
- The total DNA damage is estimated from the sampled events, eliminating the need for repeated track-structure simulations

DAMAGE COMPLEXITY ESTIMATION

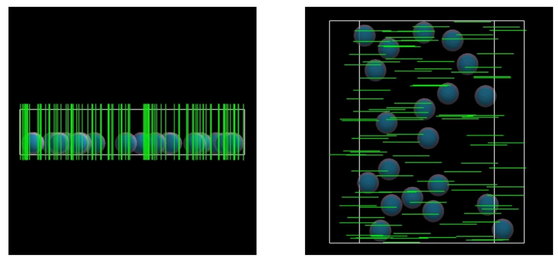


- The compiled DNA damage database was analyzed to determine the distribution of damage complexity across all photon energies, which revealed a similar pattern **dominated by low-complexity damage**
- This is expected because photons are **low-LET particles**, where the **ionization occurs sparsely along their tracks** Therefore, highly clustered damage events are relatively rare.

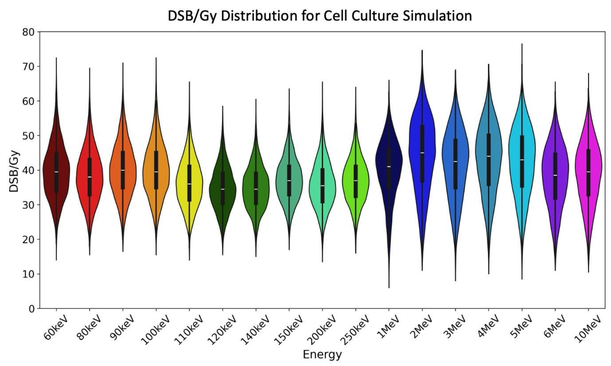


- The complexity distributions were combined to derive **an overall probability distribution representative** of low-LET photon irradiation
- For each estimated DSB site, a random number is generated and mapped to the corresponding complexity level based on the probability distribution
- The complexity of every estimated DSB site is determined without requiring additional track-structure simulations

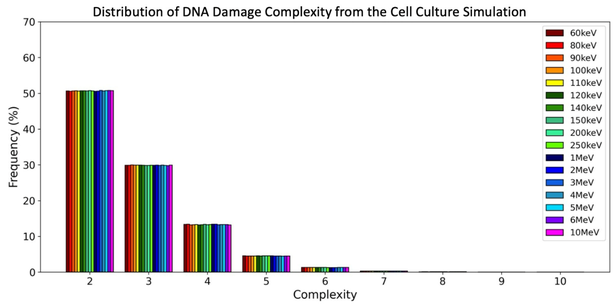
RESULTS AND DISCUSSION



- To demonstrate that the method can be scaled to larger simulations while maintaining computational efficiency, we simulated **6,000 cells** embedded in a medium and irradiated with **a homogeneous X-ray photon beam**



- The average DSB yield across all energies was **approximately 40 DSB/Gy**, consistent with the commonly reported value for low-LET irradiation.
- The outliers represent **rare but biologically plausible events** with either highly clustered or highly sparse energy deposition
- Even at the same absorbed dose, DNA damage varies because microscopic energy deposition differs from one event to another.
- This demonstrates that biological effects **depend on the spatial distribution of energy deposition**, rather than dose alone.



- The distributions across all energies appear identical, which is expected from the **Central Limit Theorem**, as the number of samples increases, fluctuations diminish, and distributions converge
- The consistency of the overall trend validates the framework and confirms the reliability of the approach

CONCLUSIONS