On the Monte Carlo simulation of neutron-induced direct and indirect DNA damage to estimate neutron relative biological effectiveness

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MOTIVATION

- We know from the neutron radiation weighting (w_R) [1] and quality (Q) [2] factors that the risk of stochastic biological effects (such as cancer) due to neutron exposure is energy dependent.
- Previous studies on simulated neutron irradiations have shown that this energy dependence correlates with the relative biological effectiveness (RBE) of neutrons for inducing clusters of DNA lesions [3, 4], particularly, clusters containing difficult-to-repair double-strand breaks (DSBs).
- However, these Monte Carlo simulation studies only modeled neutron direct action.
- Thus, a study modeling the potentially influential effects of neutron indirect action is outstanding.

OBJECTIVES

Part 1
- Extend our group's existing simulation pipeline [3] to include a validated model for indirect action.

Part 2
- Characterize the influence of indirect action on neutron-induced DNA lesions and damage clusters.
- Obtain an energy-dependent estimate of neutron RBE for inflicting DNA damage clusters via direct and indirect action.

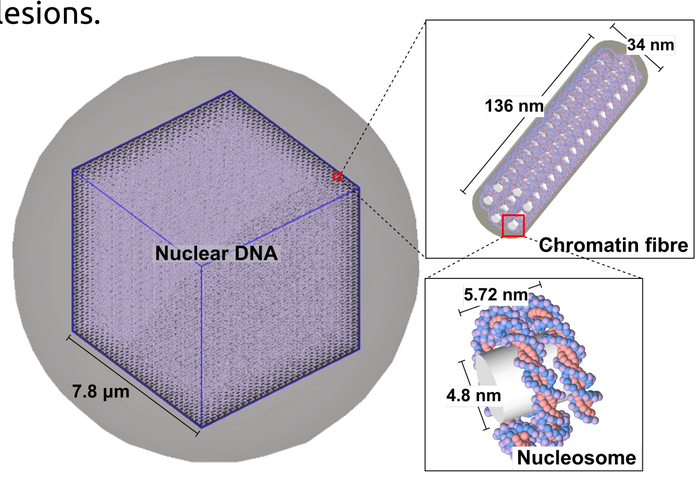
MATERIALS AND METHODS

Part 1: Indirect action modeling and validation

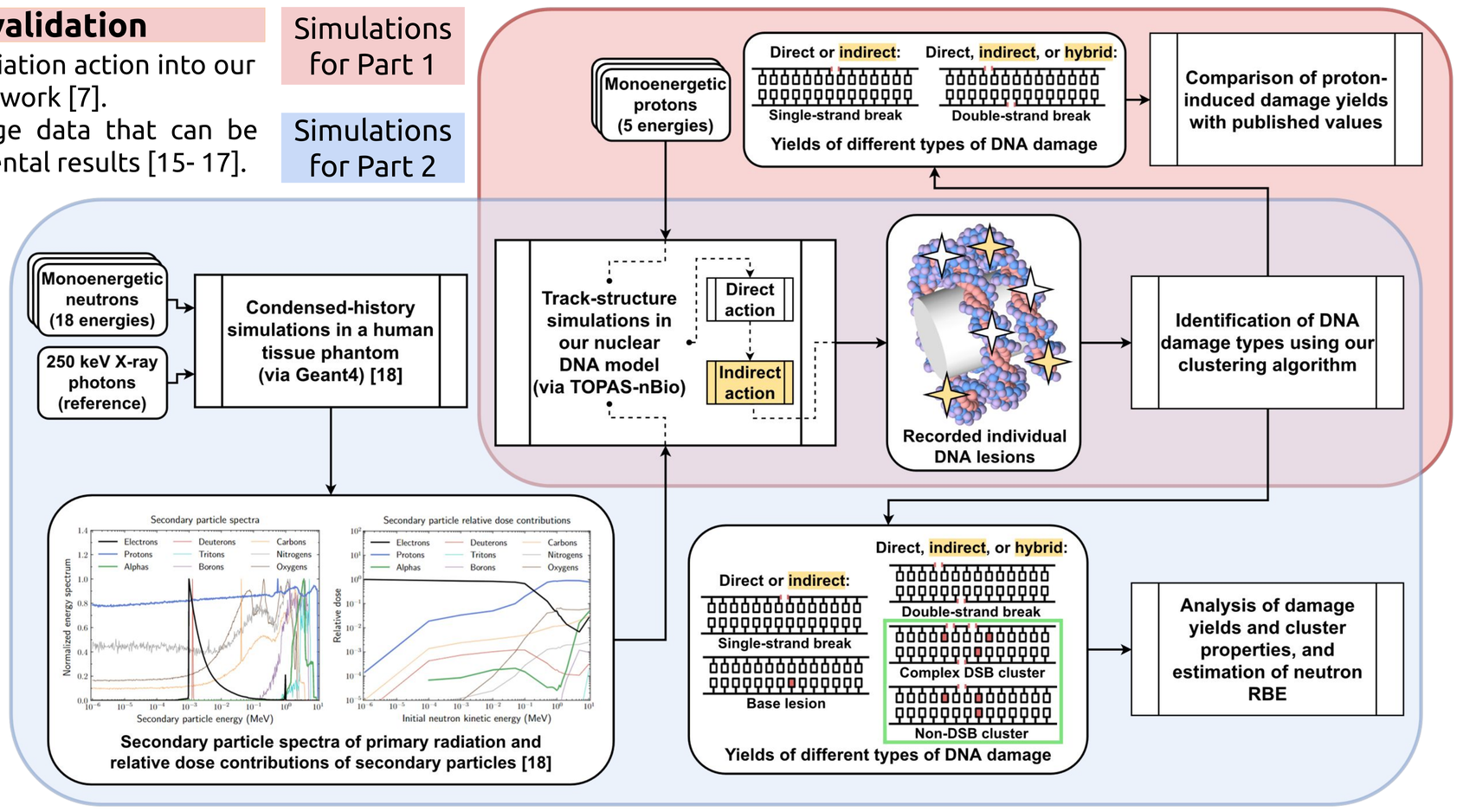
- Adapted TOPAS-nBio's [5, 6] algorithm for indirect radiation action into our simulation pipeline [3] via the TOPAS extensions framework [7].
- Simulated proton irradiations to obtain DNA damage data that can be compared with other simulation [5, 8-14] and experimental results [15- 17].

Part 2: Neutron RBE estimation

- Simulated neutron and X-ray irradiations to obtain DNA damage and cluster data for analysis.
- Compared neutron and X-ray DNA damage yields to estimate neutron RBE for inducing clusters of DNA lesions.



Our full cell model (with custom nuclear DNA [3]) integrated in our existing simulation pipeline.

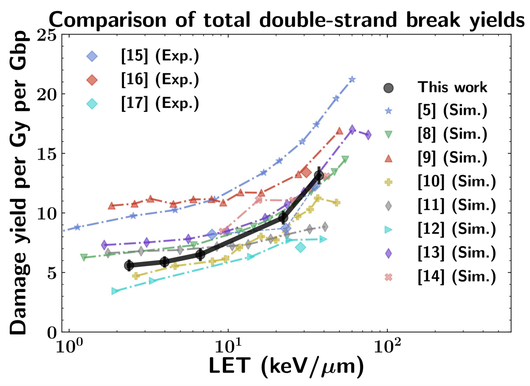


Our updated simulation pipeline. Yellow: updates related to the indirect action model. Green box: types of DNA damage clusters

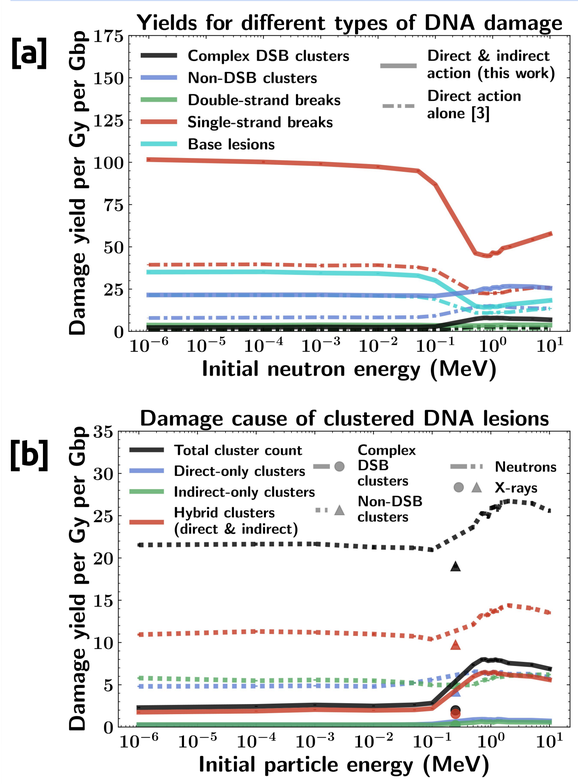
RESULTS

Part 1: Indirect action modeling and validation

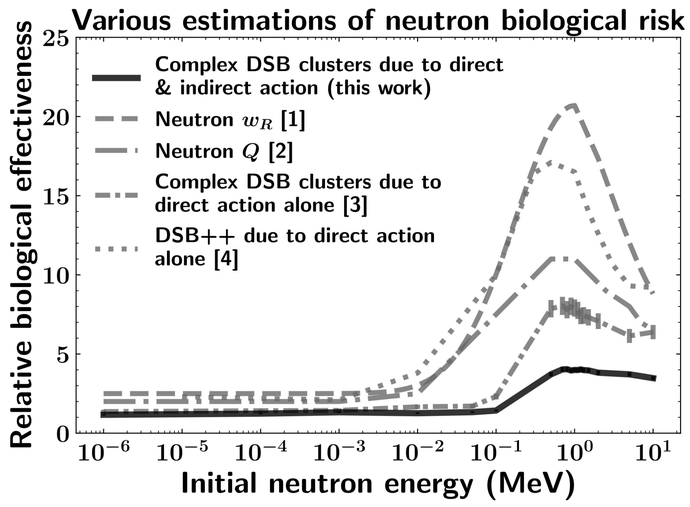
- Our SSB/DSB ratios (due to protons) are consistent with published data [5, 9, 11, 14].
- The proportion of our strand break (SB) yields due to indirect action (~68% of all SBs) agrees with experimental findings [19, 20].
- Our DSB yields are consistent with most other simulation and experimental results (shown below).
- Thus, we have an experimentally-validated model for indirect radiation action.



Part 2: Neutron RBE estimation



- Including indirect action significantly increased DNA damage yields [a], cluster length (~50%), and the number of lesions per cluster (~25%).
- Most clusters of DNA damage are hybrid in nature (contain lesions due to direct and indirect action) [b].
- Our estimated energy-dependent neutron RBE follows similar trends as radiation protection factors [1, 2] and previous estimates [3, 4], but is lower in magnitude [c].



CONCLUSIONS

- A model for indirect action that is reasonably consistent with published data [5, 8-17, 19, 20] has been integrated into our simulation pipeline.
- Indirect action has significant effects on radiation-induced DNA damage and serves to amplify the effects of direct action.
- The energy-dependent risk of neutron-induced stochastic effects is related to, but not completely explained by, the induction of DNA damage clusters.

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