Recent developments in Geant4-DNA

geant4-dna.org

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Geant4 2024 Collaboration Meeting
Catania, Italy

Geant4-DNA in 2024: overview

Osaka U. 2024

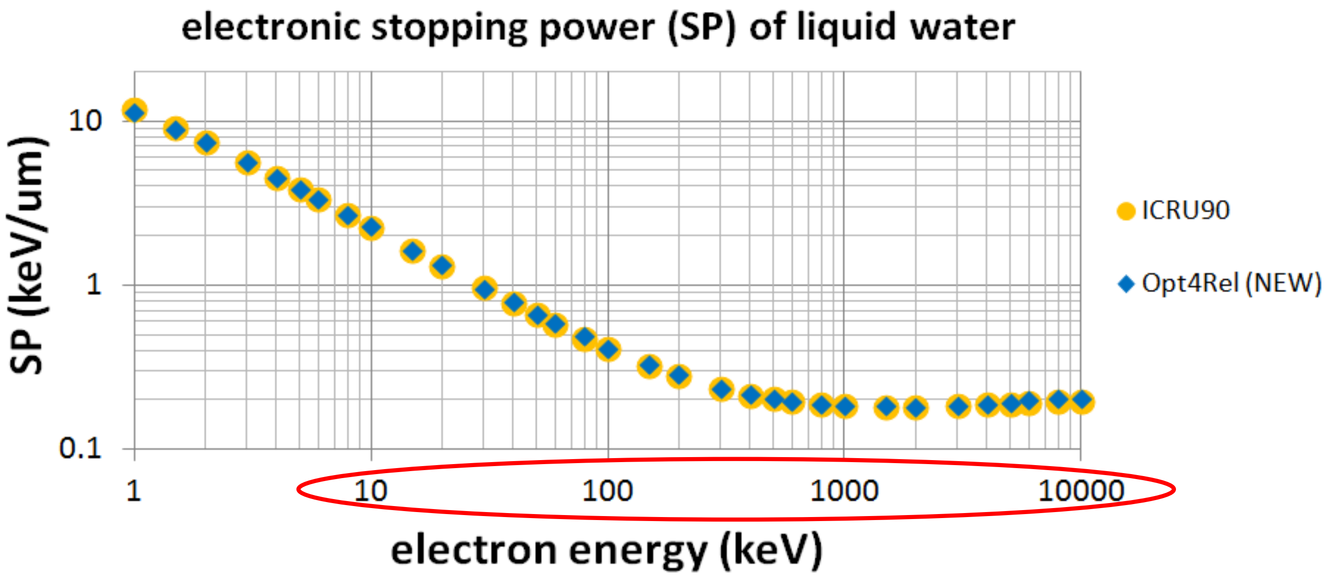
- **Physics (« very low energy » EM Physics)**
  - Update of electron inelastic models for liquid water up to 10 MeV (« dna_option4 » - up to 10 keV) by I. Kyriakou et al. (Ioannina U. team) – paper ready for submission
  - New electron discrete cross section models for O2, N2, CO2 : electronic excitation, ionisation, elastic by F. Nicolanti et al. (Roma U. team) – recently published and not yet released (https://doi.org/10.1016/j.ejmp.2023.102661) - ***towards atmospheric physico-chemistry applications***
  - New Lithium discrete cross section models for liquid water : excitation ionisation, charge gain / loss by J. Ramos-Mendez et al. (USCF team) – recently published and not yet released (https://doi.org/10.1088/1361-6560/ad5f72) - paves the way to other (selected) ions

- **Chemistry**
  - Complete review of Geant4/Geant4-DNA chemistry features (covering the 2012-2024 period) by H. Tran et al. published in Med. Phys. 51 (2024) 5873–5889 (https://doi.org/10.1002/mp.17256)
  - **Prototype software** for the simulation of water radiolysis under multi-pulse irradiation by A. Le et al. - https://arxiv.org/abs/2409.11993

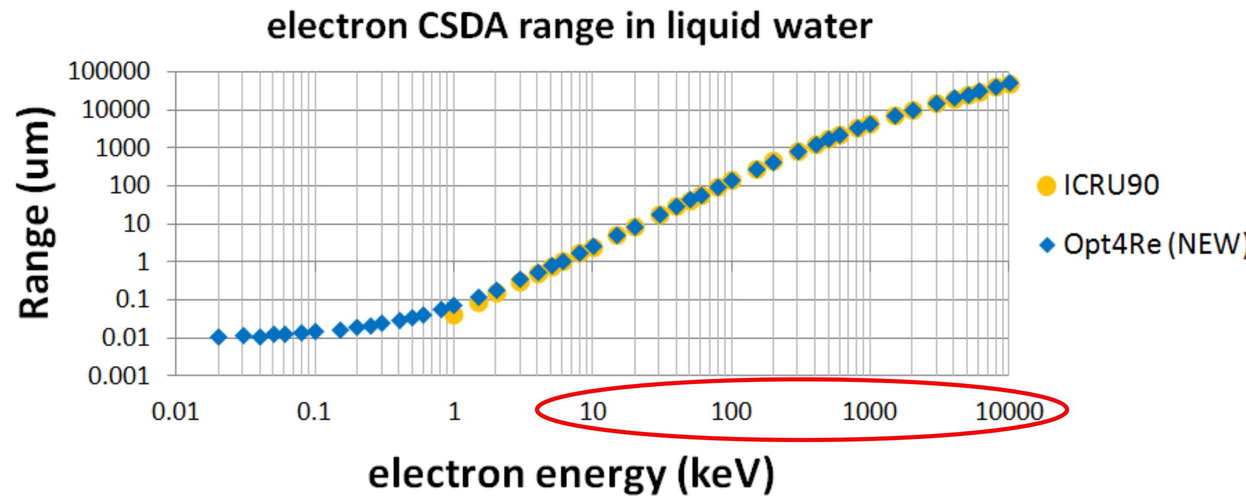
- **Other news**
  - In 2024, reactivated international tutorials « post-COVID » : CNAO, Osaka U., Accra, Bucharest
  - Collaboration Meeting in Osaka U. (thanks again Dousatsu & Takashi !)

Physics: updated (discrete) electron physics (« dna_option4 »)

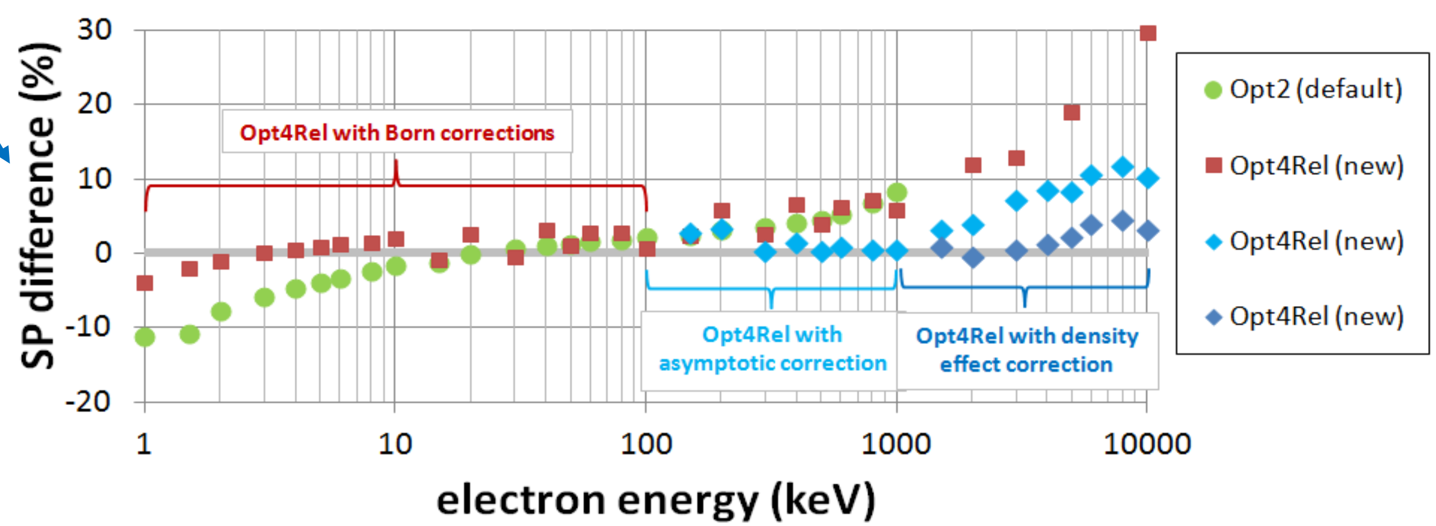
Courtesy of Ioanna Kyriakou et al.
(with ESA / BioRad3 suppport)



New model (Opt4Rel) within 5% from ICRU up to 10MeV



New model (Opt4Rel) within 5% from ICRU up to 10MeV



corrections are applied/not applied only within the energy range in which they have an effect larger/smaller than 1% to the electronic stopping power

Default model (Opt2) within 10% from ICRU up to 1MeV

GEANT4-DNA

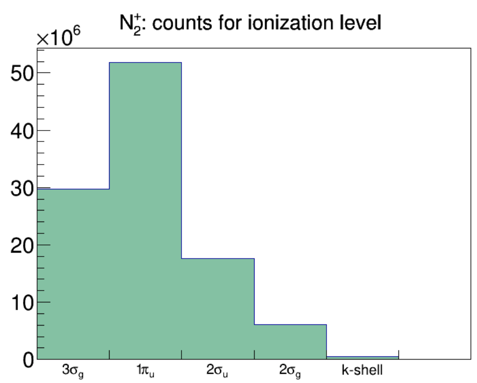
Courtesy of Franceca Nicolati, Carlo Mancini et al. (Roma U.)

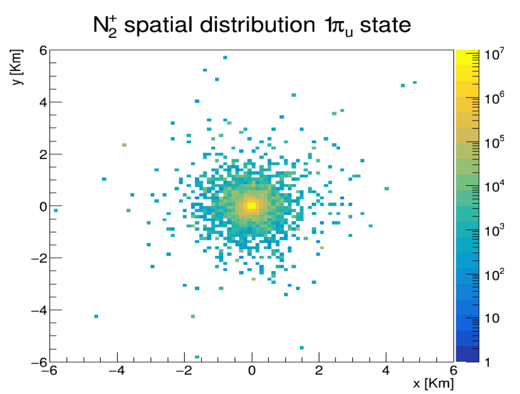
Physics: Geant4-DNA for atmospheric simulations

- Cross sections for electrons impact on N_2, O_2, CO_2 molecules have been implemented in Geant4-DNA (energy range: 10 eV – 10 MeV)
- 3 physics model classes:
  - **Elastic** scattering (Independent Atomic Model with Screening Coefficients)
  - **Ionisation** (Relativistic Binary Encounter Bethe Model)
  - **Excitation** (Porter's formula with fitted parameters)

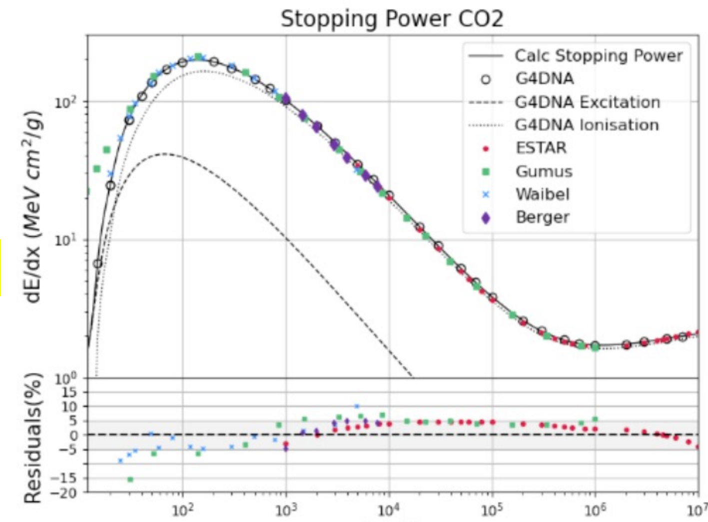
See talk of Francesca Nicolanti, Wed. 16:54

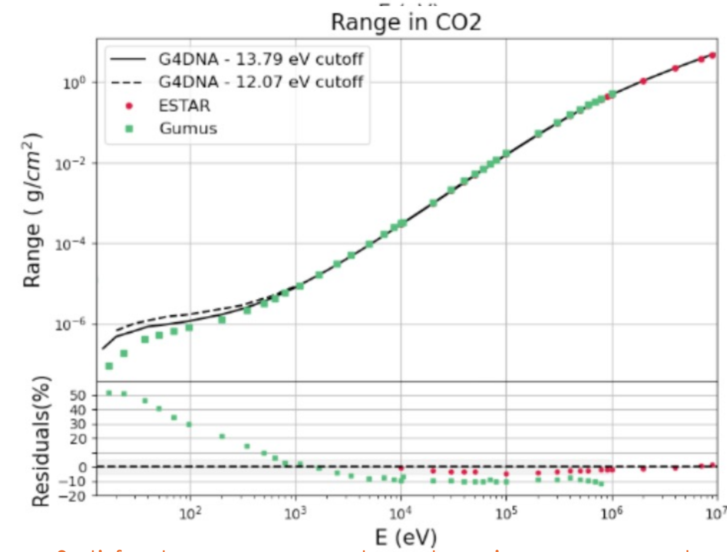
- Ranges and stopping powers verified vs NIST
- A Geant4-DNA simulation in a **thin atmospheric layer** to simulate ionization by secondary cosmic electrons has been written and is ready to run
- **Physico-chemistry dissociation process** has been included through the dissociation branching ratios for N_2 and O_2 (subsequent verification is still needed)





Work in progress:
Extend cross sections to positrons
(10 eV – 10 MeV)





Satisfactory agreement on stopping power and ranges for incident energies exceeding 200 eV

Model details: F. Nicolanti, et al, Phys Med. 2023 Sep 11;114:102661 (link)
Model implementations: F. Nicolanti, et al, Accepted by Phys Med. (2024)

Courtesy of Jose Ramos-Mendez and J. Naoki D-Kondo (UCSF)

Physics: lithium Ions Cross-Sections for Geant4-DNA (1)

- Context of **BNCT therapy**: $^{10}B(n,\alpha)^{7}Li$
  - New classes are required in Geant4-DNA for using new XS for **ionization, excitation and charge exchange** processes.
  - New particles are needed for the different states of Li. **A particle template might help** to create these new states.
- Data was obtained for all the charge states of lithium ions
  - **Ionization and excitation** were obtained by weighting the Li^{3+} cross-sections by effective charge factors[1]
  - **Charge exchange** was obtained using the Classical Trajectory Monte Carlo Method (CTMC) [2]

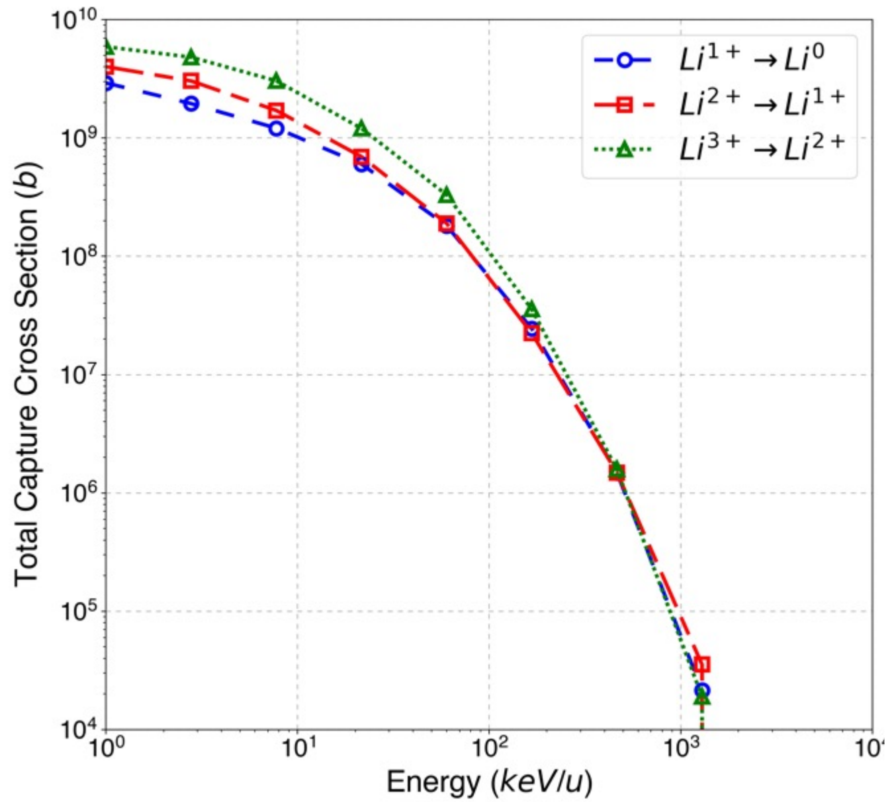
Cross-Section	Based on	Energy Ranges	Applicable to
Ionization	G4DNARuddIonizationExtended	700 eV – 7 GeV	Li^{3+}, Li^{2+}, Li^{1+}, Li^{0}
Excitation	G4DNAMillerGreenExcitationModel	70 eV – 3.5 MeV	Li^{3+}, Li^{2+}, Li^{1+}, Li^{0}
	G4DNABornExcitationModel	3.5 MeV – 700 MeV	Li^{3+}, Li^{2+}, Li^{1+}, Li^{0}
Charge Increase	CTMC	7 keV – 70 MeV	Li^{2+}, Li^{1+}, Li^{0}
Charge Decrease	CTMC	7 keV – 70 MeV	Li^{3+}, Li^{2+}, Li^{1+}

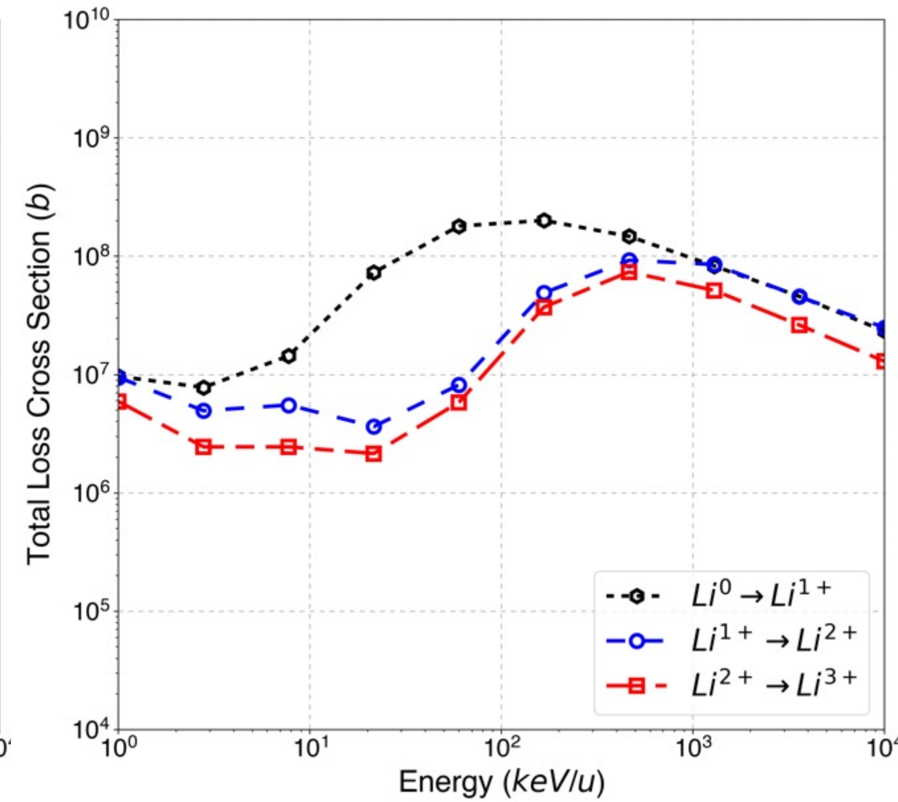
[1]R.H. Garvey, C. H. J. and A. E. S. G. (1975). Independent-particle-model potentials for atoms and ions with 36 < Z <= 54 and a modified Thomas-Fermi atomic energy formula*. *Physical Review A*, *12*(4), 1144–1152, https://doi.org/10.1080/00431672.1975.9931783

[2]Olson, R. E., & Salop, A. (1977). Charge-transfer and impact-ionization cross sections for fully and partially stripped positive ions colliding with atomic hydrogen. *Physical Review A*, *16*(2), 531–541, https://doi.org/10.1103/PhysRevA.16.531

Physics: Li charge exchange cross-sections (2)

- **Charge exchange cross-sections** for Li ions were calculated using the CTMC method.
- The cross-sections were calculated **from 7 keV/u – 7 MeV/u.**
- A C++ application was developed to calculate the new data, and it **can be used for calculating further cross-sections for other ions** (e.g. Carbon).
- Currently, work is ongoing for the implementation of these data in Geant4.

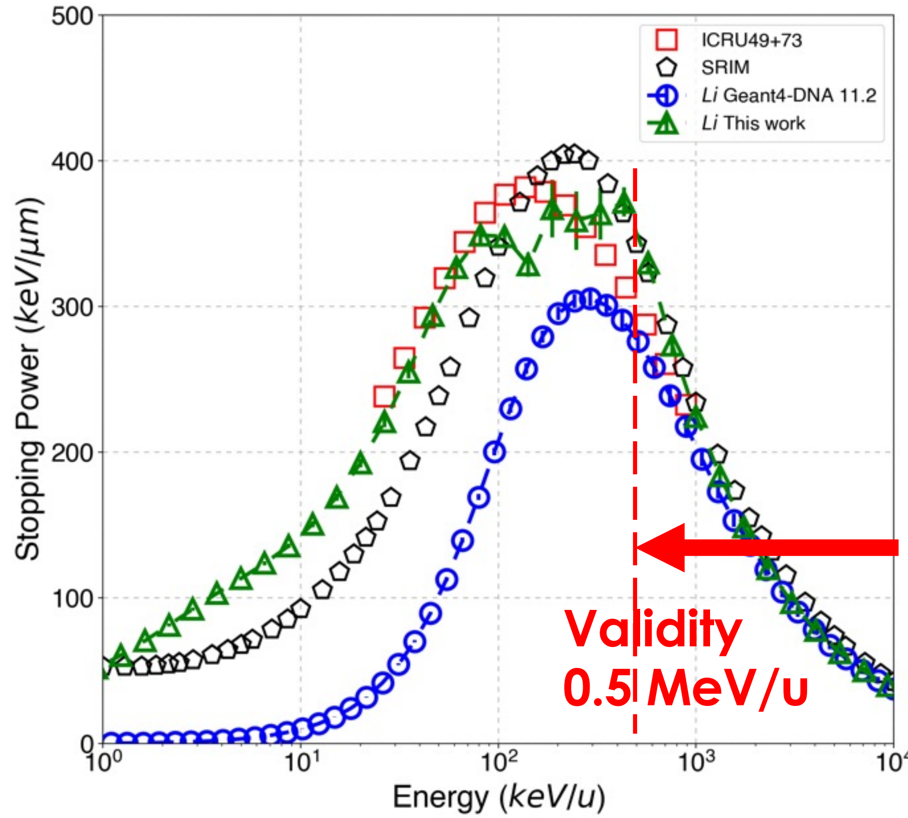


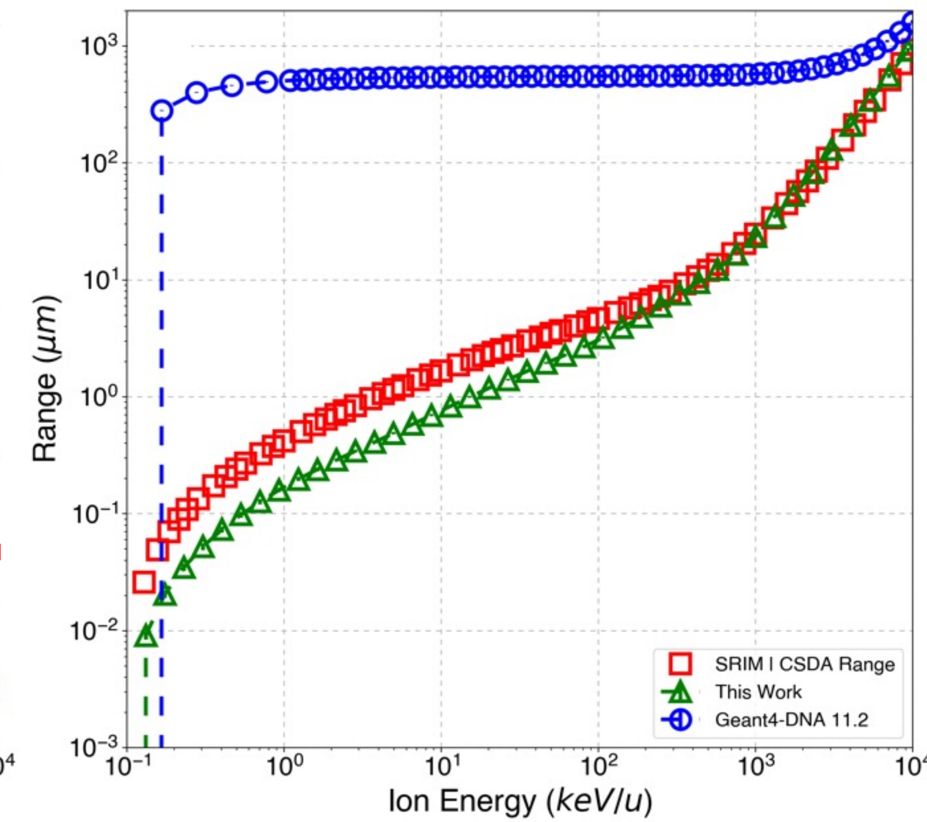


N. D-Kondo et al., (2024) https://doi.org/10.1088/1361-6560/ad5f72

Physics: Li: physical differences with existing data (3)

- Differences between the existing Geant4-DNA cross-sections are evident for
  - Stopping power and CSDA range.
- In the figure, data from ICRU3 and SRIM4 are also shown.
- More information is available in reference [5]





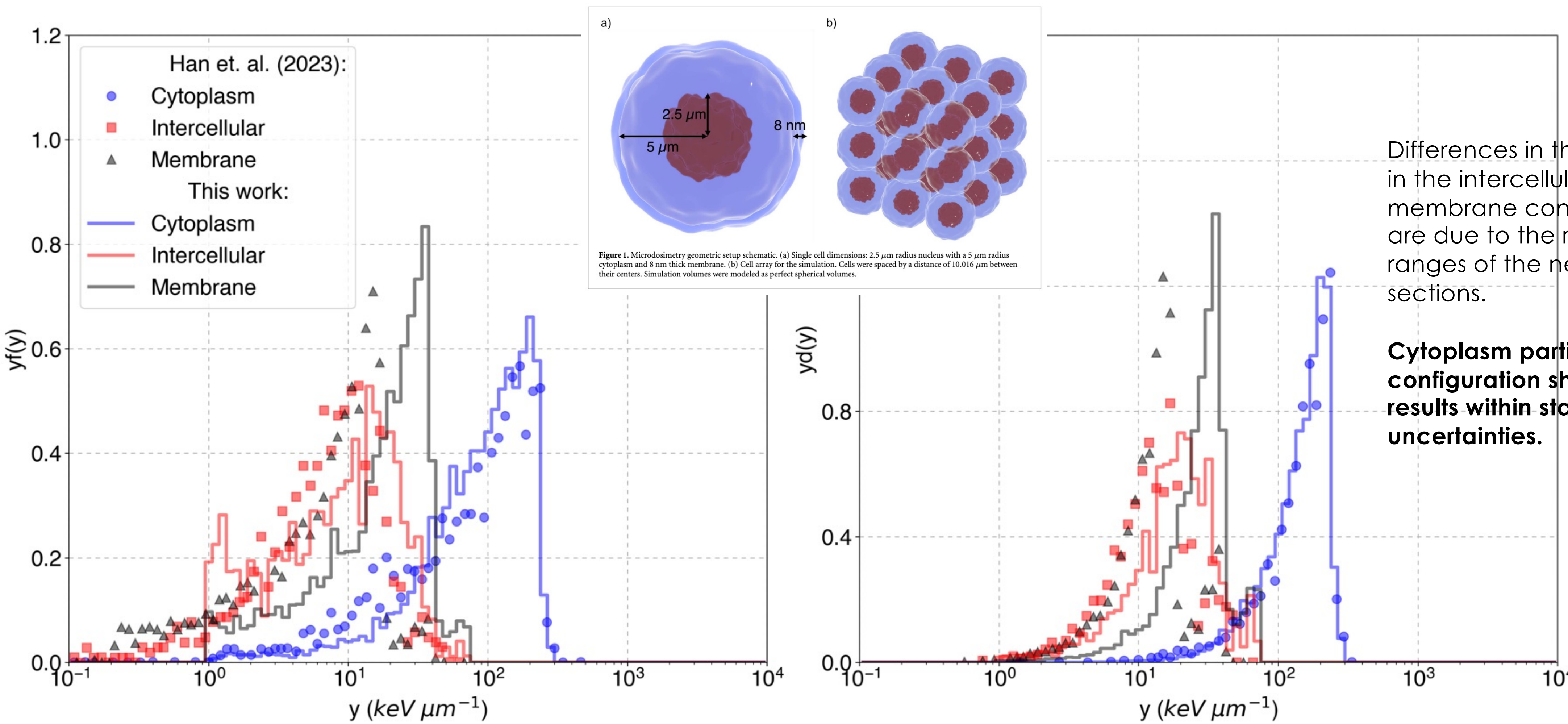
[3]International Commission on Radiation Units and Measurements 1993 *Stopping Powers and Ranges for Protons and Alpha Particles* (International Commission on Radiation Units and Measurements)

[4]Ziegler J F and Biersack J P 2010 *Stopping and Range of Ions in Matter: SRIM* (available at: www.srim.org/)

[5]D-Kondo N, Ortiz R, Faddegon B, Incerti S, Tran HN, Francis Z, Moreno Barbosa E, Schuemann J, Ramos-Méndez J. Lithium inelastic cross-sections and their impact on micro and nano dosimetry of boron neutron capture. Phys Med Biol. 2024 Jul 15;69(14), https://doi.org/10.1088/1361-6560/ad5f72

Physics: Li: impact in accuracy (4)

- **Low impact for microdosimetry** applications that used the Barkas scaling method



Differences in the lower end in the intercellular and cell membrane configurations are due to the reduced ranges of the new cross-sections.

Cytoplasm particle emission configuration shows similar results within statistical uncertainties.

Lineal energy spectra of Li for frequency-weighted lineal energy (yf (y)) and dose-weighted lineal frequency (yd(y)).

Physics: Li: impact in accuracy (5)

- **Significant impact on nanodosimetry** applications.
- In the figure, a nanodosimetric parameter from ionization cluster size distributions is shown:

$$F_5 = \sum_{v=5}^{v_{max}} f(v)$$

where $f(v)$ is the ionization cluster size distribution computed in cylindrical targets (10 bp-length).

- A side note: F_5 is directly correlated with clonogenic aerobic **cell's survival** [6].

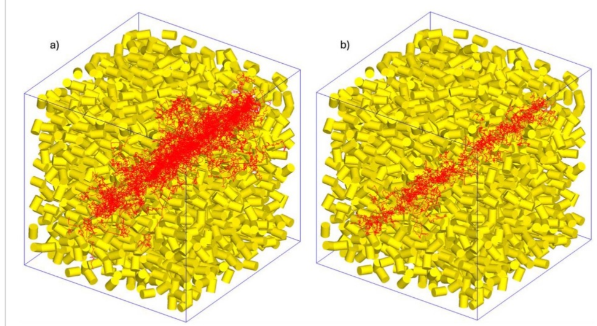
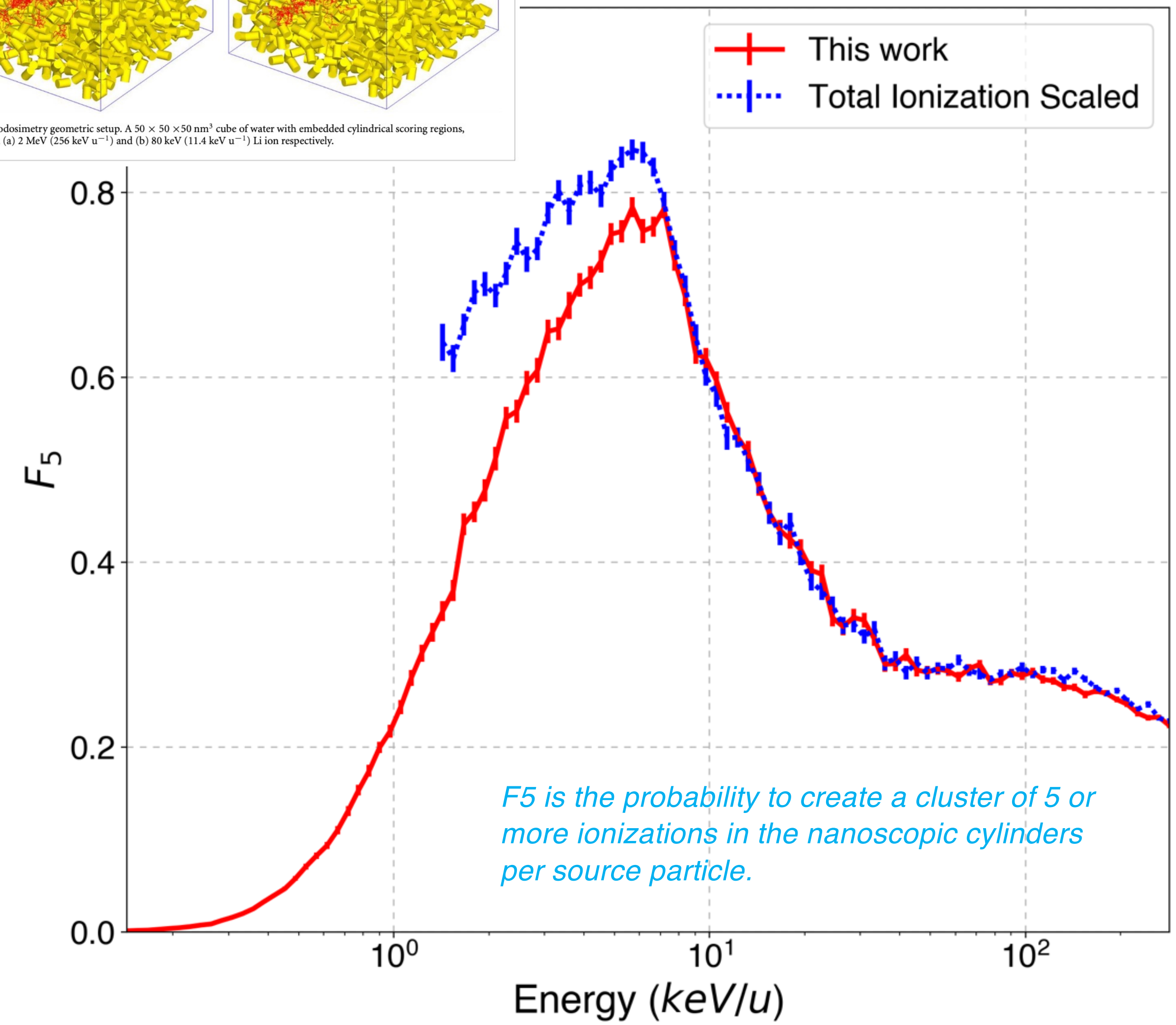


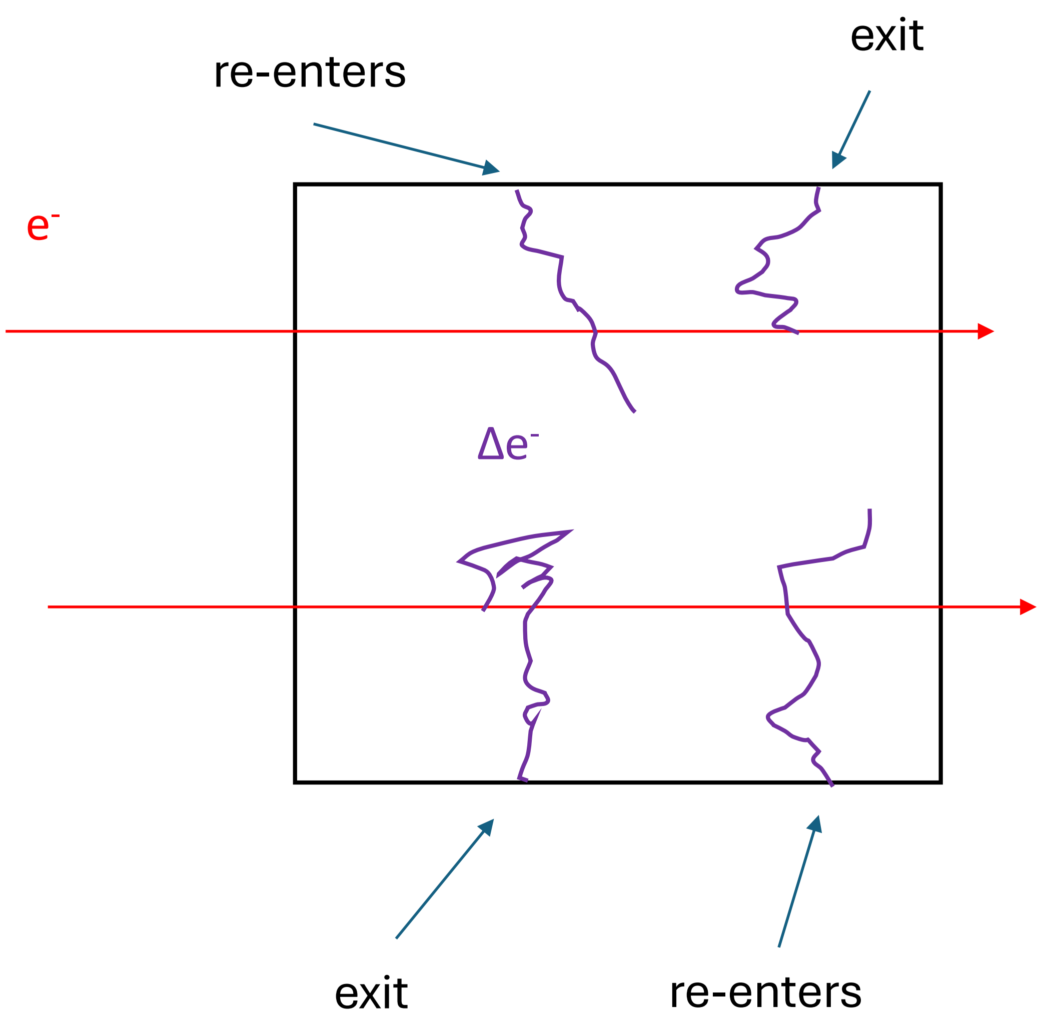
Figure 2. Nanodosimetry geometric setup. A $50 \times 50 \times 50$ nm^3 cube of water with embedded cylindrical scoring regions, irradiated by a (a) 2 MeV (256 keV u^{-1}) and (b) 80 keV (11.4 keV u^{-1}) Li ion respectively.



[6] Faddegon B, Blakely EA, Burigo L, Censor Y, Dokic I, Domínguez Kondo N, Ortiz R, Ramos Méndez J, Rucinski A, Schubert K, Wahl N, Schulte R. Ionization detail parameters and cluster dose: a mathematical model for selection of nanodosimetric quantities for use in treatment planning in charged particle radiotherapy. Phys Med Biol. 2023 Aug 14;68(17) - doi: 10.1088/1361-6560/acea16. PMID: 37489619; PMCID: PMC10565507.

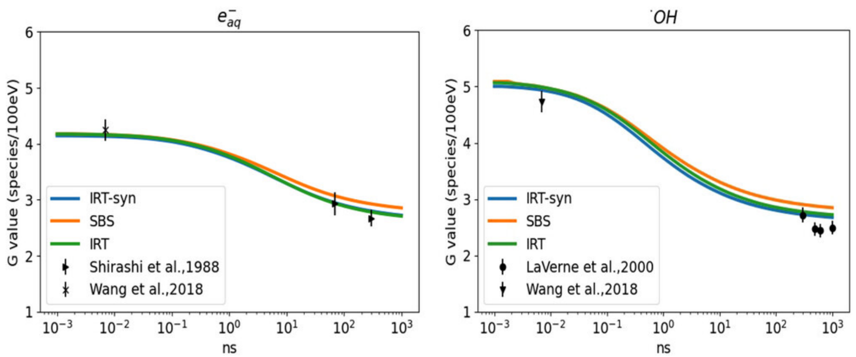
Physics: implemented periodic boundary conditions « PBC »

- **Periodic boundary conditions** (PBC) are boundary conditions that approximate an infinite volume using a small unit cell
  - Can be used to simulate the behavior of secondary electrons during the physical stage
  - Mimics the behavior in a macroscopic volume without requiring a large computational resource.
- Thanks to **Amentum Pty Ltd** (Iwan Cornelius) for granting permission to redistribute the original open-source version of PBC in Geant4
  - https://github.com/amentumspace/g4pbc
  - Shown in the "UHDR" example

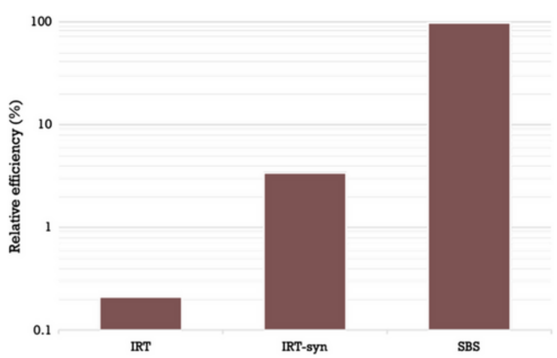


Chemistry: full review (2012-2024)

- Special Report in free access
  - Med. Phys. 51 (2024) 5873–5889 (https://doi.org/10.1002/mp.17256)
- Detailed review of
  - 4 alternative approaches
    - **Step-by-step** : tracking but slow
    - **Independent Reaction Time** : fast but no tracking
    - **Independent Reaction Time « synchronized »** : hybrid
    - **Mesoscopic** : beyond the us…
  - **Extended examples** for the simulation of water radiolysis : **chem***, **scavenger**, **UHDR**



G-values of e^-_{aq} and $^{\cdot}OH$ as a function of time for the IRT, IRT-syn, and SBS models, considering 9 chemical reactions for 1 MeV



Relative computation times for IRT, IRT-syn, and SBS.

Received: 19 January 2024 | Revised: 17 May 2024 | Accepted: 25 May 2024
DOI: 10.1002/mp.17256

SPECIAL REPORT

MEDICAL PHYSICS

Review of chemical models and applications in Geant4-DNA: Report from the ESA BioRad III Project

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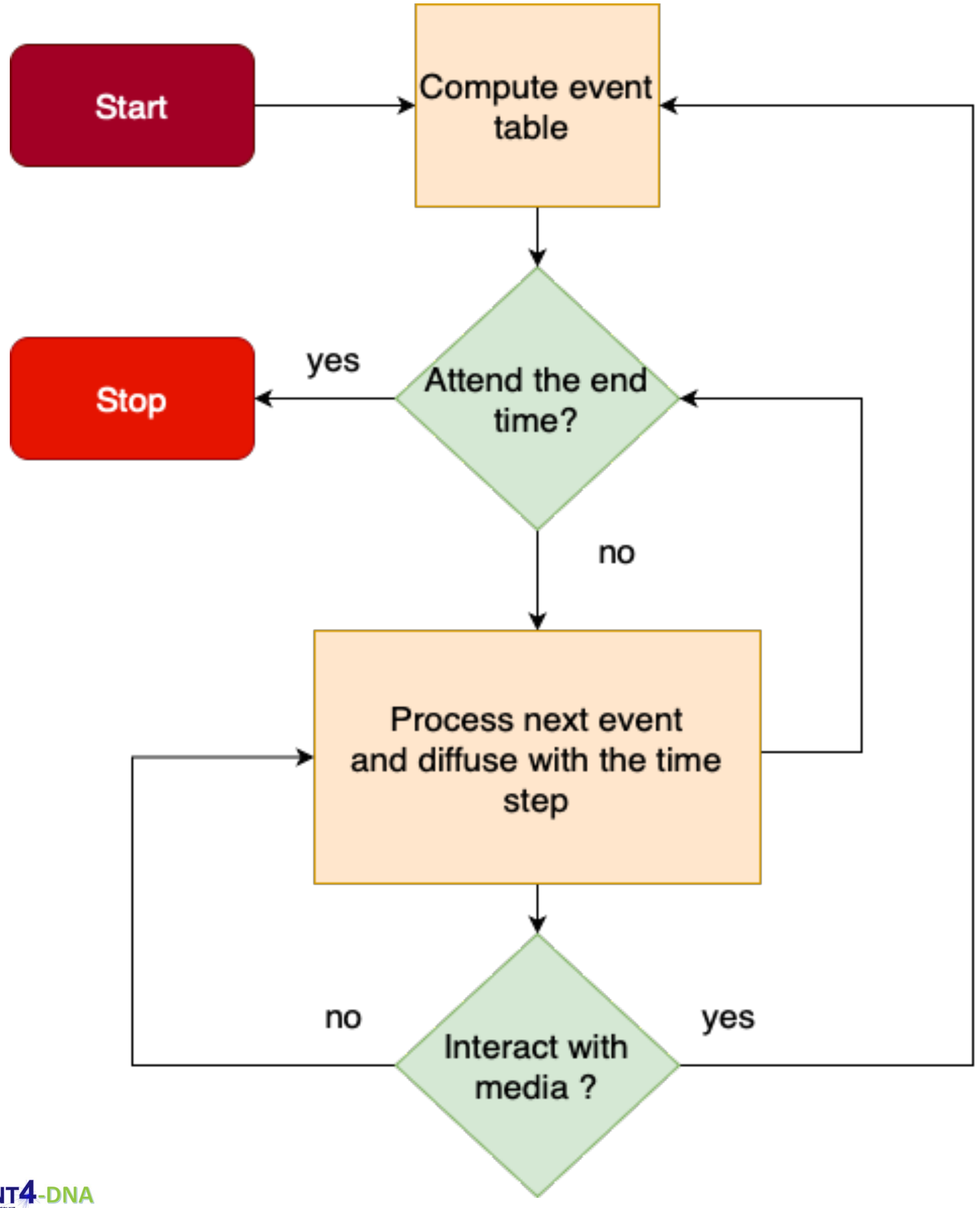
Abstract
A chemistry module has been implemented in Geant4-DNA since Geant4 version 10.1 to simulate the radiolysis of water after irradiation. It has been used in a number of applications, including the calculation of G-values and early DNA damage, allowing the comparison with experimental data. Since the first version, numerous modifications have been made to the module to improve the computational efficiency and extend the simulation to homogeneous kinetics in bulk solution. With these new developments, new applications have been proposed and released as Geant4 examples, showing how to use chemical processes and models. This work reviews the models implemented and application developments for modeling water radiolysis in Geant4-DNA as reported in the ESA BioRad III Project.

KEYWORDS
Geant4-DNA, radiation chemistry, water radiolysis

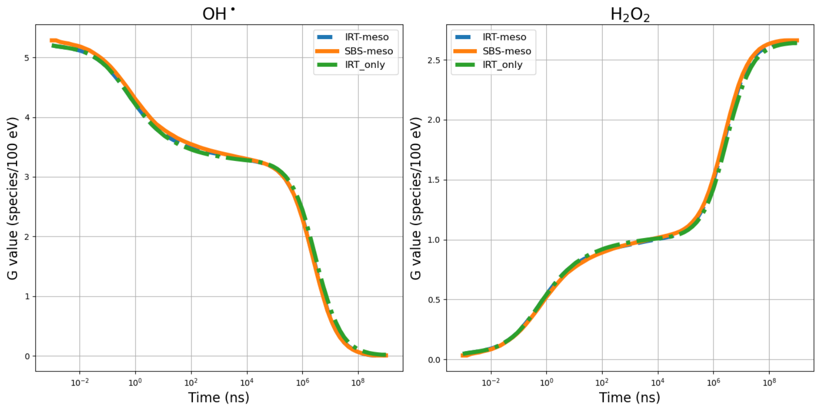
Med Phys. 2024;51:5873–5889. wileyonlinelibrary.com/journal/mp

5873

Chemistry: updated « synchronized independent reaction time » approach

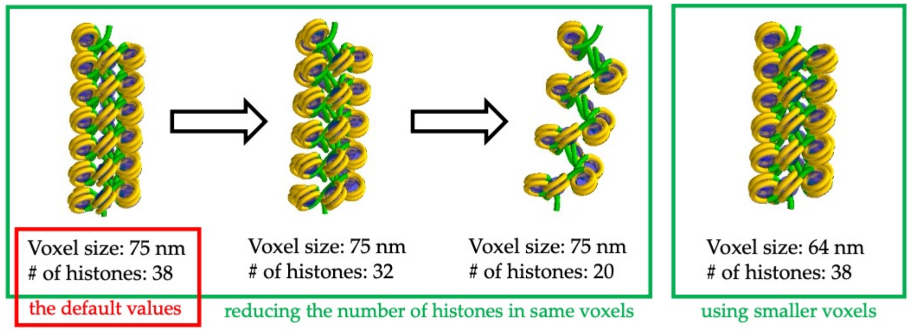


- Important **update of IRT "synchronized"**
  - The computation of chemical reaction table is only performed for the so-called "**dependent" events** (i/o all events)
    - reactions with oxygen of the medium,
    - chemical species bouncing on the volume border,
    - new primary chemical species originating from different irradiation pulse
      - Cf. talk by Serena Fattori
- These improvements are **essential for handling a large number of species** efficiently (e.g. high LET) and for performing simulations over **long time scales**
  - IRT model can now reproduce SBS+meso and IRT+meso, up to 1 s
  - About one order of magnitude faster

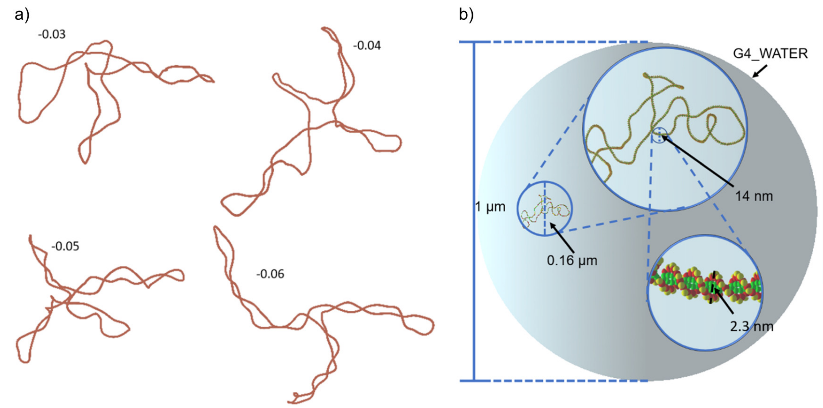


1 MeV incident electrons in a cubic volume of liquid water (3.2 um side)

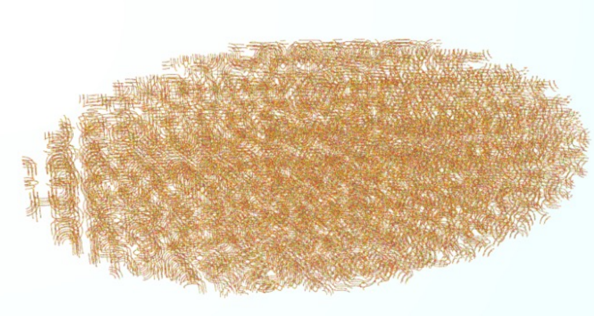
Geometries: library



Plasmids



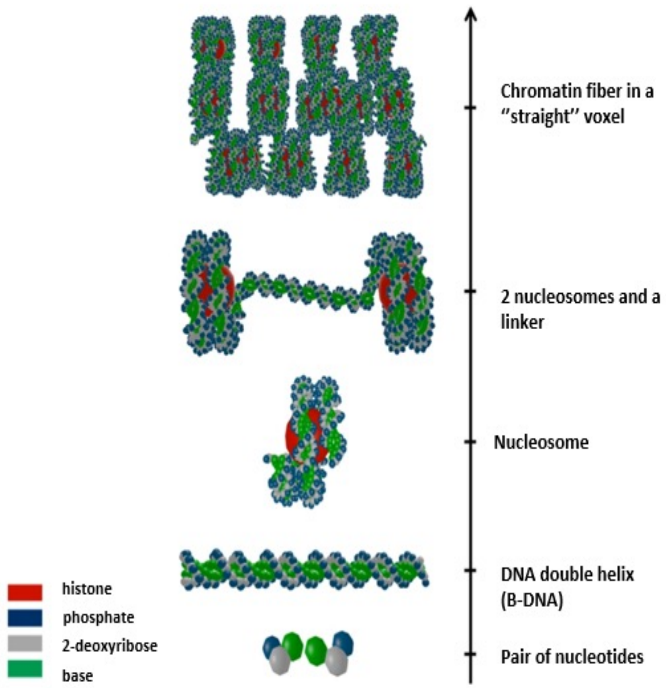
E. coli bacterium

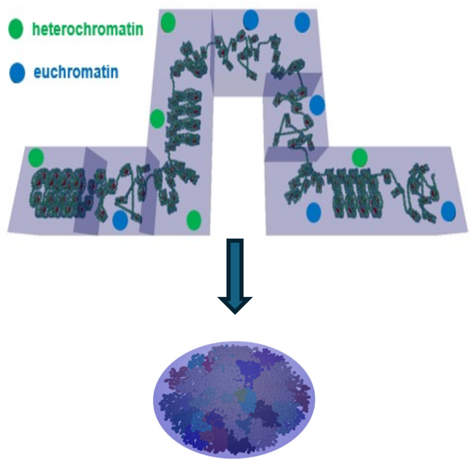


Made available in the "moleculardna" and "dsbandrepair" examples

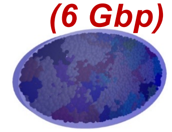
See talk of Konstantinos Chatzipapas @ TF

Voxels of chromatin



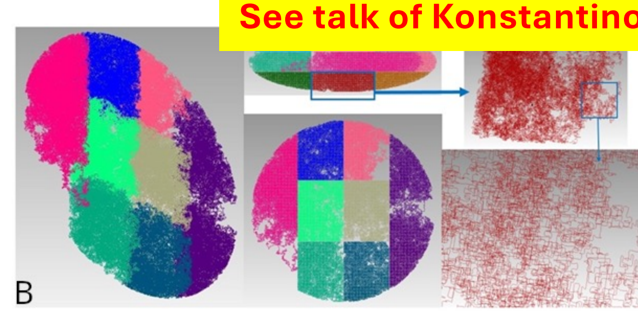


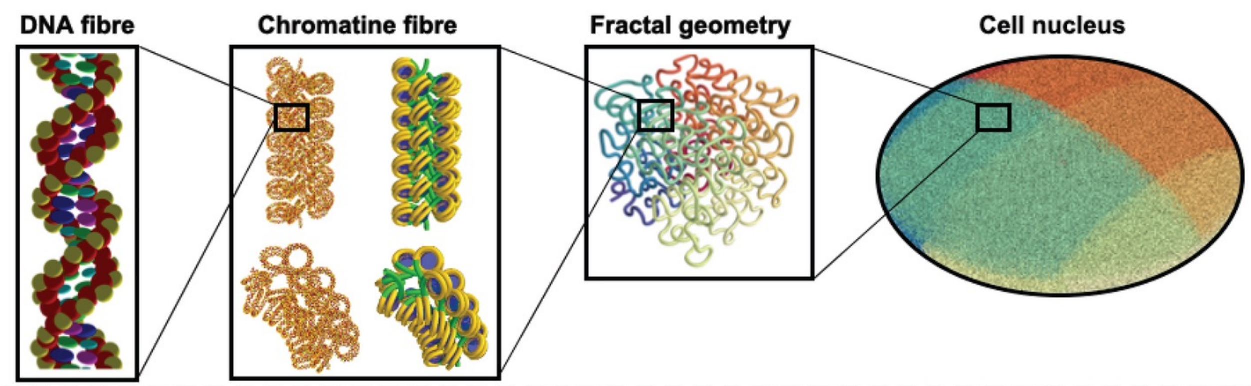
Human fibroblast (6 Gbp)



Human endothelium (6 Gbp)

Cell nuclei





Simulation chain: the « moleculardna » ext. example

http://moleculardna.org

A Geant4-DNA integral chain (physics, chemistry, geometry, DNA damage, repair & cell survival)

https://www.efomp.org/index.php?r=news/view&id=338

Physica Medica
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Announcement: Galileo Galilei Award

The *Galileo Galilei Award in Medical Physics* is given every year to the best paper published in this journal in the previous year.

In 2022, the prize has been awarded to Fabio Di Martino et al., "A new solution for UHDP and UHDR (Flash) measurements: theory and conceptual design of ALLS chamber", Phys. Med. 2022;102:9-18.

Physica Medica - the European Journal of Medical Physics, is happy to announce that the paper "*Prediction of DNA rejoining kinetics and cell survival after proton irradiation for V79 cells using Geant4-DNA*" by Dousatsu Sakata, Ryoichi Hirayama, Wook-Geun Shin, Mauro Belli, Maria A. Tabocchini, Robert D. Stewart, Oleg Belov, Mario A. Bernal, Marie-Claude Bordage, Jeremy M. C. Brown, Milos Dordevic, Dimitris Emfietzoglou, Ziad Francis, Susanna Guatelli, Taku Inaniwa, Vladimir Ivanchenko, Mathieu Karamitros, Ioanna Kyriakou, Nathanael Lampe, Zhuxin Li, Sylvain Meylan, Claire Michelet, Petteri Nieminen, Yann Perrot, Ivan Petrovic, Jose Ramos-Mendez, Aleksandra Ristic-Fira, Giovanni Santin, Jan Schuemann, Hoang N. Tran, Carmen Villagrasa, Sebastien Incerti, published in Physica Medica, Volume 105, January 2023: 102508, DOI: https://doi.org/10.1016/j.ejmp.2022.11.012, has been elected the best paper published in the journal in the year 2023.

The paper presents the intricate relation between radiobiological modelling and simulation of the physical processes of radiation interaction with cells in order to provide a better understanding on the mechanisms behind radiation cell killing and damage repair. More specifically, the paper introduces an extension of the Geant4-DNA radio-biological application by adding a feature aiming at predicting the repair of the DNA damages and their kinetics as well as the survival fraction of cells at some time after irradiation. The value of the work resides on the fact that it opens up to further basic as well as applied research with applications in radiation therapy and radiation protection, in addition to providing better understanding of the processes behind the clinical manifestations of radiation induced cell damage and cell kill leading to the eradication of the clonogenic cells in the tumoral lesions as well as to the unwanted effects in the healthy tissues.

The selection of the best paper has been performed on the basis of citations and downloads together with the assessment by the Editors, Associate Editors and members of the Editorial Board.

We congratulate the authors for this paper, as the winners of the Gali

Prof. Iuliana Toma-Dasu
Physica Medica
Editor-in-Chief

https://doi.org/10.1016/j.ejmp.2022.11.012

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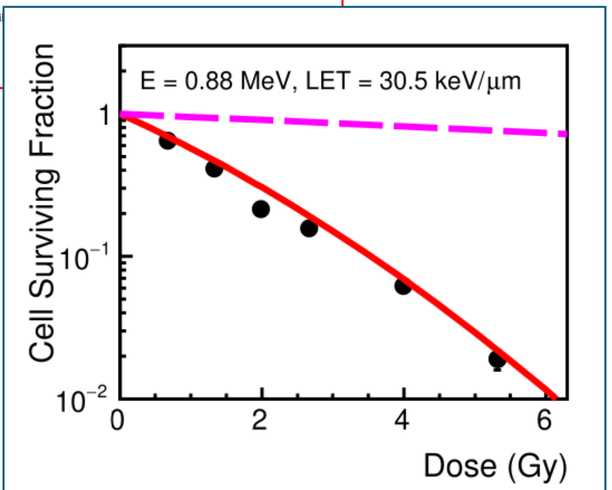
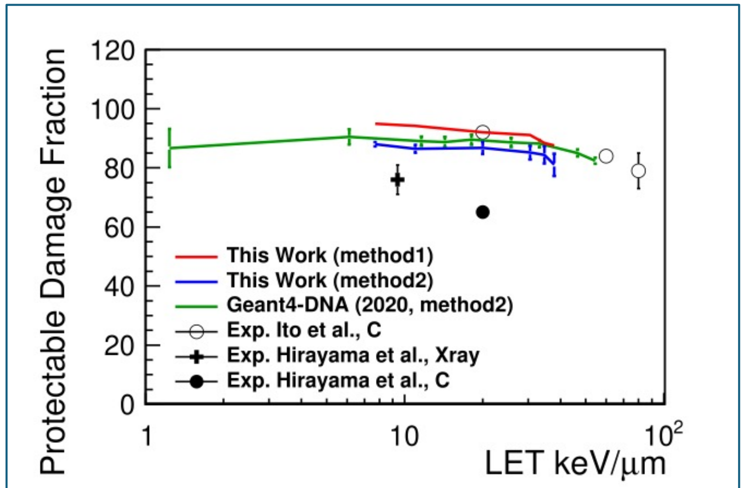
Original paper

Prediction of DNA rejoining kinetics and cell survival after proton irradiation for V79 cells using Geant4-DNA

Dousatsu Sakata[1,2,*], Ryoichi Hirayama[3], Wook-Geun Shin[4], Mauro Belli[5,a], Maria A. Tabocchini[6,a], Robert D. Stewart[7], Oleg Belov[8,9], Mario A. Bernal[10], Marie-Claude Bordage[11,12], Jeremy M.C. Brown[13,14,15], Milos Dordevic[16], Dimitris Emfietzoglou[17], Ziad Francis[18], Susanna Guatelli[14], Taku Inaniwa[1], Vladimir Ivanchenko[19,20], Mathieu Karamitros[21], Ioanna Kyriakou[17], Nathanael Lampe[22], Zhuxin Li[23], Sylvain Meylan[24], Claire Michelet[23], Petteri Nieminen[25], Yann Perrot[26], Ivan Petrovic[16], Jose Ramos-Mendez[27], Aleksandra Ristic-Fira[16], Giovanni Santin[25], Jan Schuemann[28], Hoang N. Tran[23], Carmen Villagrasa[26], Sebastien Incerti[23]





moleculardNA | Search molecularDNA | molecularDNA on GitHub | The Geant4-DNA Project

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- Building geometries

molecularDNA

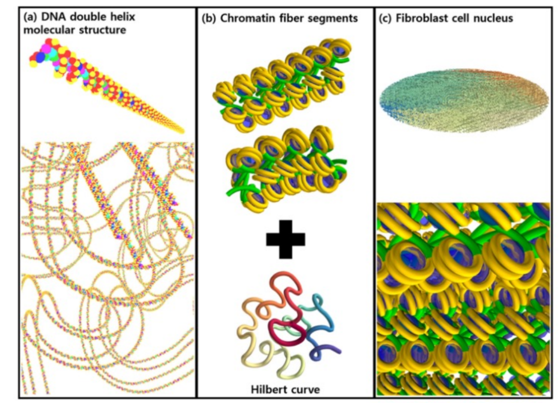
Radiation-induced DNA damage simulations in Geant4

molecularDNA is a Geant4-DNA example built to allow easy simulation of radiation-induced DNA damage with *flexible geometries* and well defined *damage parameters*.

Get started right away in *geant4/examples/extended/medical/dna/moleculardna* with a *library of pre-existing geometries*, or dive into the documentation.

A **tutorial** demonstrating molecularDNA is also available at this link.

Important : This version of molecularDNA (Geant4 11.3 BETA) is proposed as a **beta** version and may still contain bugs, thank you for your understanding. Please contact us for further detail. This example is for demonstration purpose and acts as an introductory tool to help users create their own applications; therefore users are advised to adapt the simulation parameters in their applications accordingly.



human cell example

Get started from example | See publications | Available geometries

Want to know more about how it all works? You'll want to visit our Overview page.

– Updated on Aug. 4, 2024

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Geant4-DNA : What's next?

- **Physics**
  - Delivery of recently-published models: e- in O2 & N2 & CO2, Li in water, e- in gold (version 2)
    - See talk of Francesca Nicolanti
  - Delivery of extended e- inelastic models for liquid water up to 10 MeV (dna_option4, Ioannina U. team) from ESA « BioRad III» project
    - New « dna_option4 » physics constructor (including upgrade of elastic model)
  - New discrete cross section models for C ions (UCSF + CNRS + IRSN + VI teams)
    - Coll. with Gabriele Parisi (Pavia U.) for the implementation and further calculation of XS (inelastic, CC) for carbon ions.
- **Chemistry**
  - Inclusion of prototype of software for the simulation of water radiolysis under multi-pulse irradiation in « UHDR » example – see talks of Serena Fattori & Fateme Farokhi
  - Continue verification & validation (e.g. Flash conditions)
- **Geometries**
  - Add more multi-scale geometries – see talk of Konstantinos Chatzipapas
- **Other**
  - Cleanup of examples on-going, including coding guidelines
  - Improvement of documentation
  - 2025 Geant4-DNA tutorial(s)
  - next collaborator meeting in … Catania (2025)

Thank you for your attention