GEANT4-DNA
A SIMULATION TOOLKIT

Geant4-DNA: status update

geant4-dna.org

On behalf of Geant4-DNA collaboration

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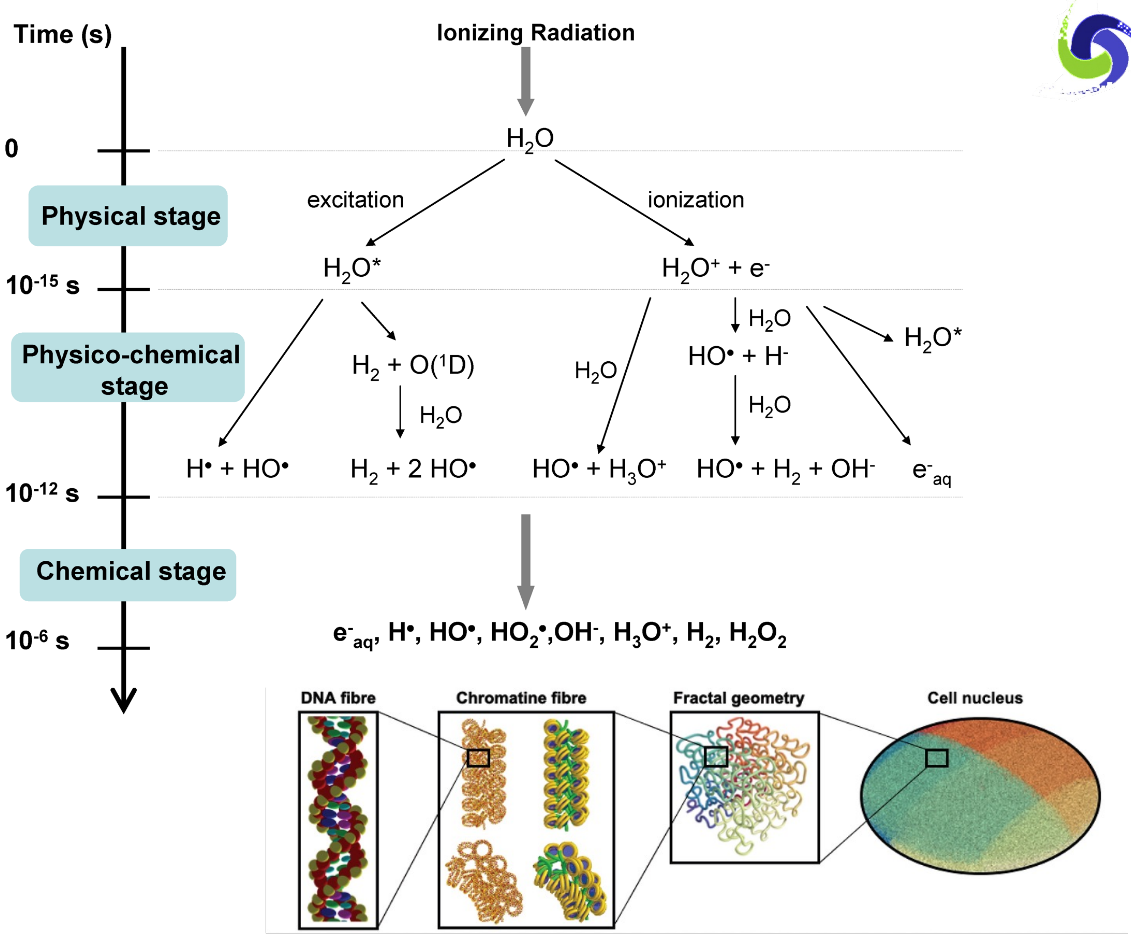
25–29 sept. 2023, Hokkaido University, 28th Geant4 Collaboration Meeting

Geant4-DNA for radiobiology



Extension of the Geant4 Monte Carlo simulation toolkit for radiobiology

- **Track structure code**: simulates each particle-matter interaction
  - **physical stage**
- Simulate the production and tracking of radiolytic species, together with their mutual interactions
- DNA-scale geometries

Physical stage

New DNA_Option4 model
developed at the Univ. of Ioannina

- ✓ Makes further improvements to the existing DNA_Opt4 model and extends it to relativistic energies
- ✓ A robust and updated model that permits electron transport in liquid water from 10 MeV down to 10 eV
- ✓ Extends G4's TS capabilities by covering more RT applications

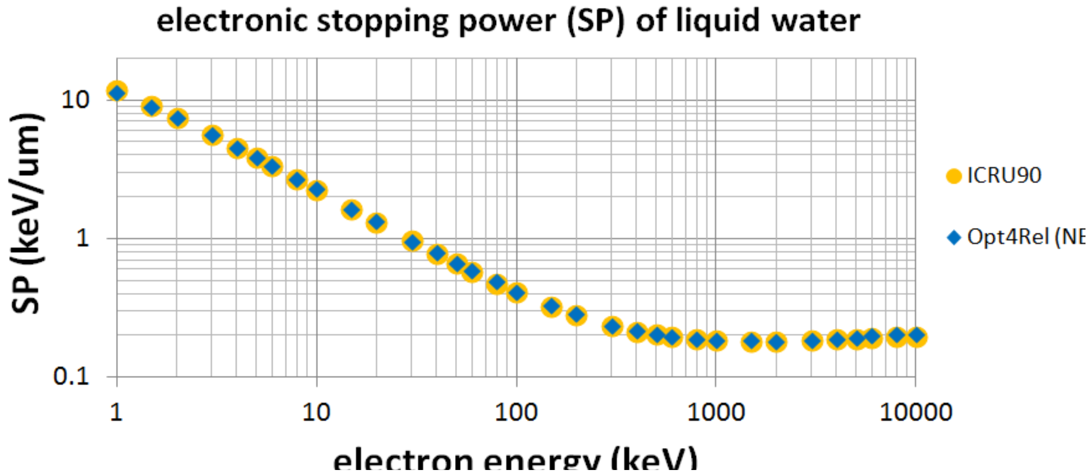
New features

i. Updated Energy-Loss-Function (ELF) using the algorithm developed at the Univ. of Ioannina
   - ✓ Improved sum-rule consistency
   - ✓ Improved parameterization of experimental data
   - ✓ Improved high-energy asymptotic trend

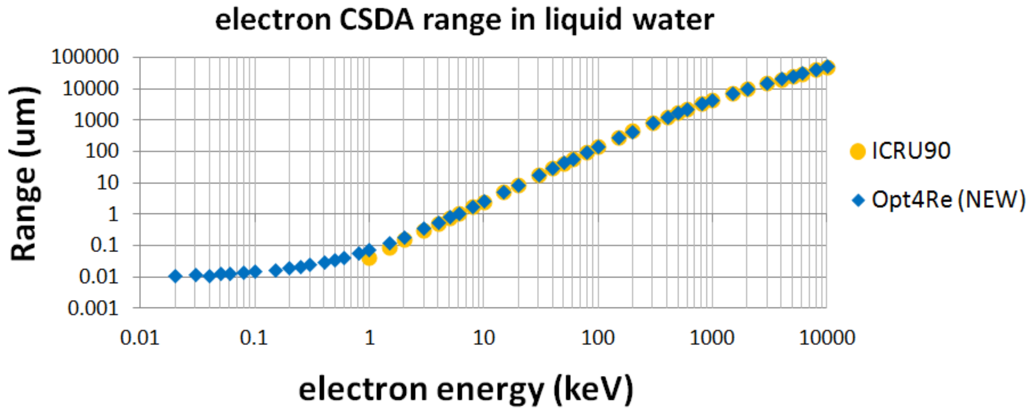
ii. More consistent implementation of low-energy Born corrections

iii. Implementation of the Fermi density correction directly to the DCS (differential cross section)

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



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



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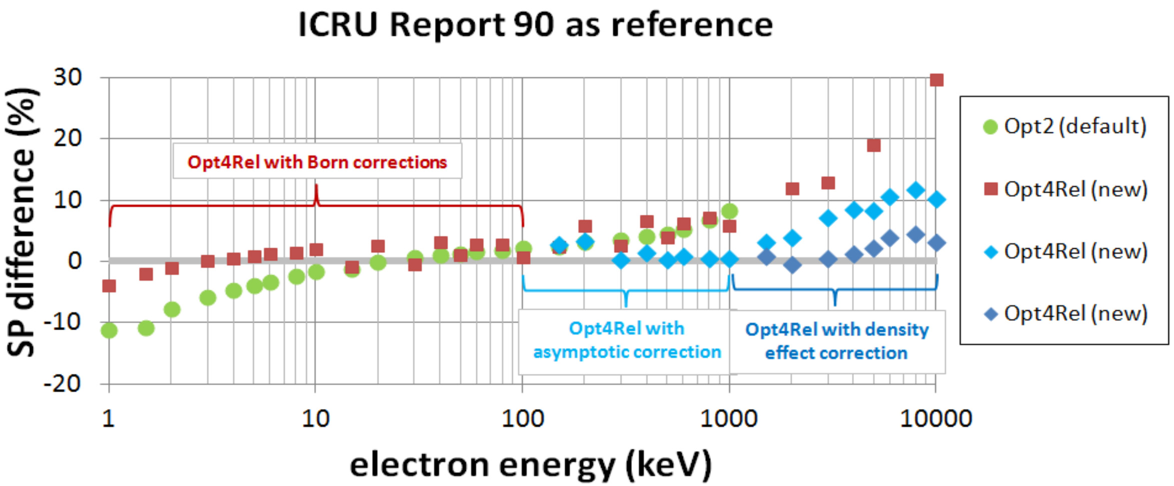
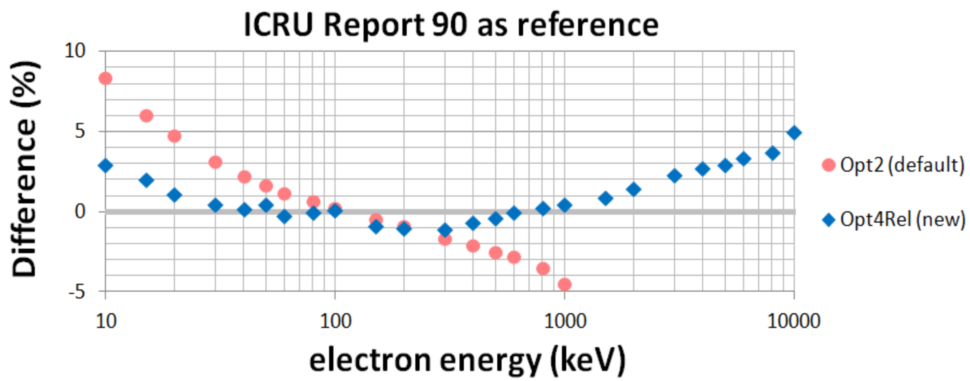


Default model (Opt2) within 10% from ICRU up to 1MeV



Default model (Opt2) within 8% from ICRU up to 1MeV

Proton up to 300 MeV

Tracking of protons from 100 MeV up to 300 MeV with Geant4-DNA developed at the Univ. of Sevilla

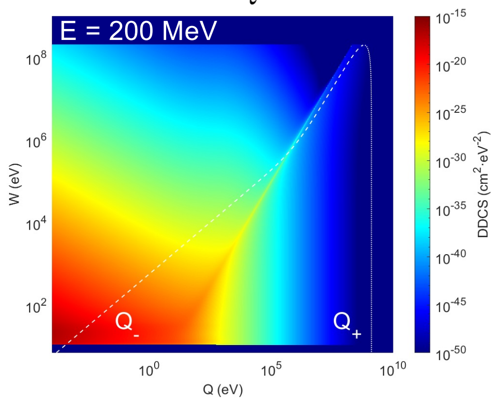
Relativistic Plane Wave Born Approximation

$$\frac{d^2\sigma}{dW\,dQ} = \frac{2\pi Z_P^2 e^4}{m_e c^2 \beta^2} \left\{ \frac{2m_e c^2}{WQ(Q+2m_e c^2)} + \frac{2m_e c^2}{[Q(Q+2m_e c^2) - W^2]^2} \left[\beta^2 - \frac{W^2}{Q(Q+2m_e c^2)} \right] \right\} \frac{df(Q,W)}{dW}$$

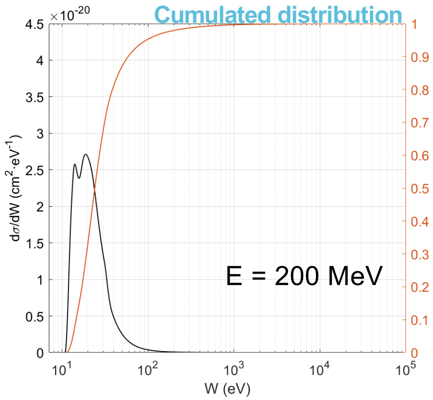
Ionization differential cross section in energy loss

Generalized oscillator strength (GOS)

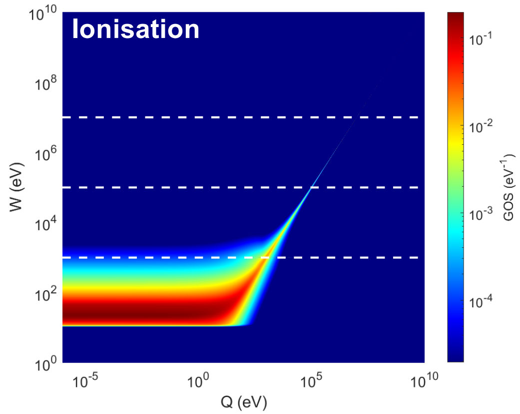
$$\frac{d^2\sigma(Q,W)}{dW\,dQ} \rightarrow \frac{d\sigma}{dW} = \int_{Q_-(W)}^{Q_+(W)} dQ \frac{d^2\sigma}{dW\,dQ}$$



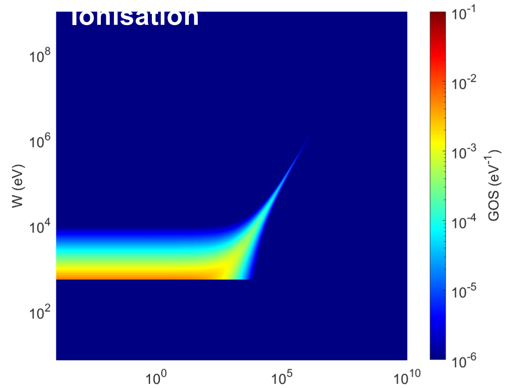
$$\sigma = \int_0^E dW \frac{d\sigma}{dW}$$



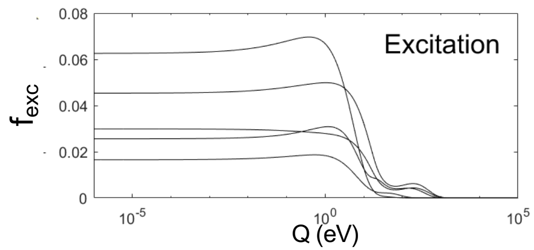
Sum of outer shells **(Drude model)**



K – Shell **(Hydrogenic GOS)**



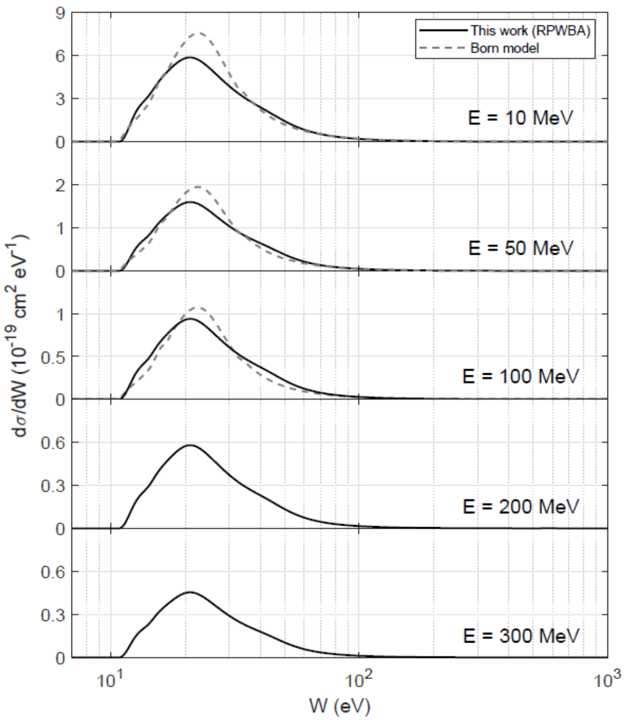
$$\frac{df_{\mathrm{exc}}(Q,W)}{dW} = f_{\mathrm{exc}}(Q)\delta(W - W_{\mathrm{exc}})$$



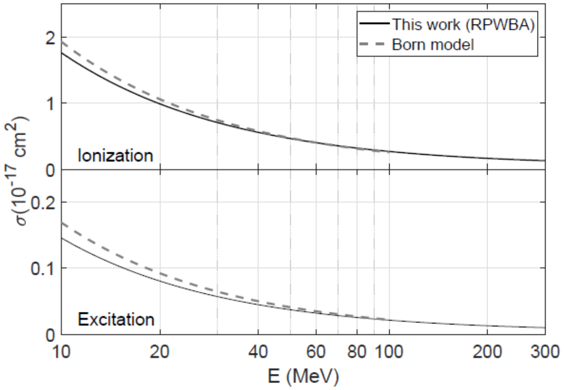
Tracking of protons from 100 MeV up to 300 MeV with Geant4-DNA under the RPWBA

Model verification

Ionization differential cross setion

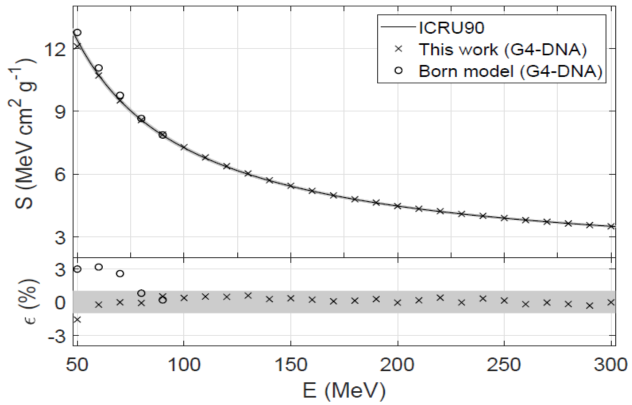


Cross section

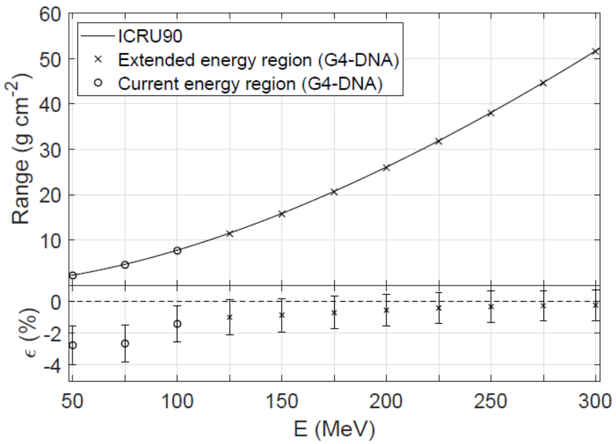


Maximum deviation w.r.t. existing Born model of 5% and 2%, ionization and excitation, respectively, for protons at 100 MeV

Implementation verification



spower example



range example

A. D. Domínguez-Muñoz et al., *Radiat. Phys. Chem* 199: 110363 (2022) (link)

Beyond liquid water

DNA materials

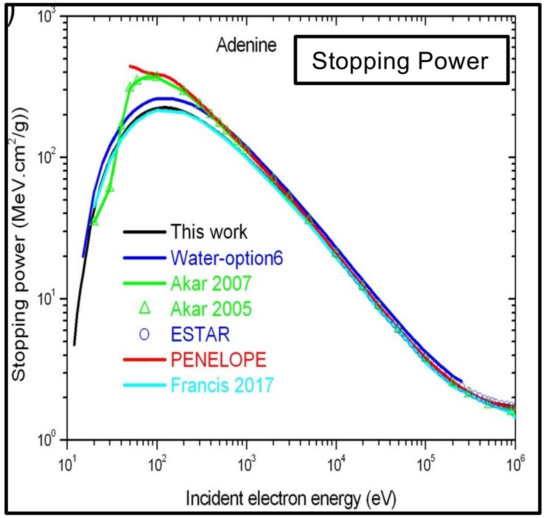
- Implementation of electron physics models in DNA bases and backbone in addition to water following the same procedure as in CPA100 code
- 3 physics model classes:

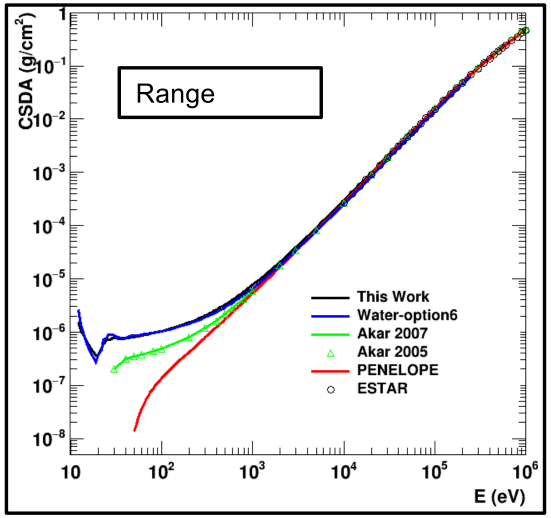
- Elastic scattering (Independent Atomic Model)
- Ionisation (Relativistic Binary Encounter Bethe Model)
- Excitation (scaled from water inelastic XS and bases ionisation XS)
- Energy range (11 eV – 1 MeV)

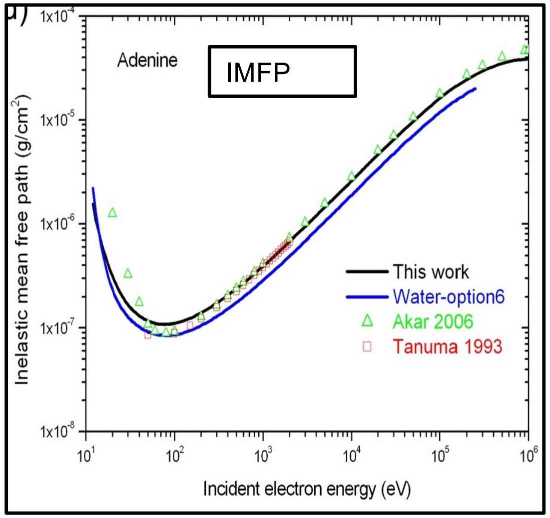
S. A. Zein *et al.*

DNA materials

S. Zein *et al. Nimb (2021) and (2023)*







- Calculations done for all 6 DNA materials (Adenine, Guanine, Thymine, Cytosine, Deoxyribose, Phosphoric acid)
- Good agreement with the literature
- Difference from liquid water is observed

Nitrogen gas cross-sections implementation

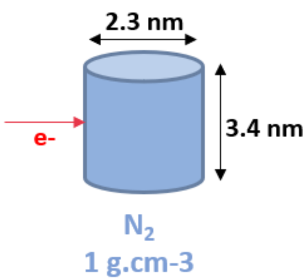
M. Pietrzak (NCBJ), H. Nettelbeck (PTB), C. Villagrasa (IRSN), Y. Perrot (IRSN)

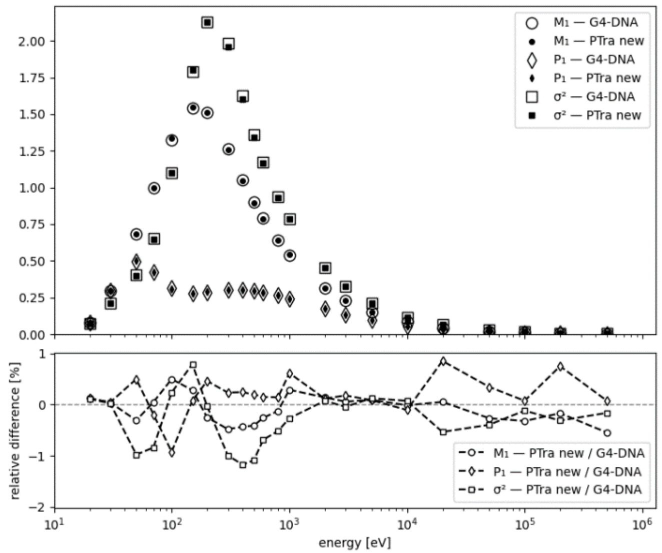
✓ Cross section data for nitrogen used in the in-house **PTB PTra** track structure code developed by Grosswendt have been implemented in Geant4-DNA

- **Electrons** ranging from 1 MeV down to the ionisation threshold (15.58 eV) for elastic scattering, electronic excitation and impact ionization including auto-ionization
- A **review of parameters and options** in Ptra and an update of PTra has been performed before the integration in Geant4-DNA
- Check of ranges and stopping powers vs NIST
- Details of the models: Pietrzak et al. Phys. Med. 102 (2022) 103-109 (link)

✓ Benchmarking the codes

- **Agreement in the comparison of the Ionization Cluster Size Distribution** (ICSD) nanodosir quantity computed with Geant4-DNA and PTra co been achieved





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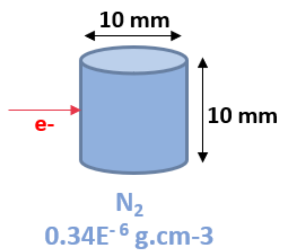
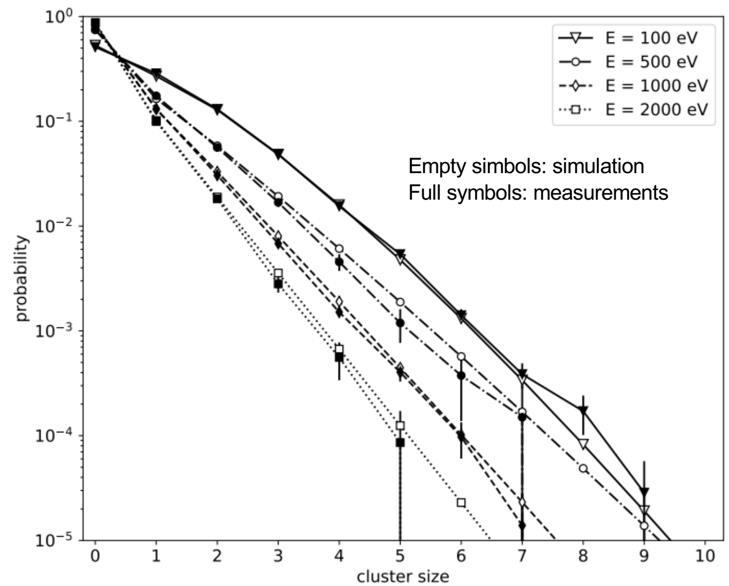
- ✓ Benchmarking the codes
  - **Agreement in the comparison of the Ionization Cluster Size Distribution** (ICSD) nanodosimetric quantity computed with Geant4-DNA and PTra code has been achieved
  - **Simulated ICSDs were also compared to** those obtained experimentally in nitrogen using the **Jet Counter nanodosimeter** at NCBJ





GEANT4-DNA

Nitrogen gas cross-sections implementation

M. Pietrzak (NCBJ), H. Nettelbeck (PTB), C. Villagrasa (IRSN), Y. Perrot (IRSN)

✓ The use of Nitrogen cross sections is illustrated in the extended/medical/dna/icsd example

- Initially, this example shows how to compute ICSD in small cylinders representing the typical dimensions of a DNA segment 10 base pairs long made of DNA material precursors
- The example has been modified to allow to choose different geometries to compute ICSD
  - Small cylindrical target (2.3 nm diameter, 3.4 nm height) made of THF
  - Cylindrical target (10 mm diameter, 10 mm height) made of low pressure nitrogen to reproduce Jet Counter experiments

✓ Work in progress:

- Extend cross sections to protons (70 keV – 10 MeV)
- Add propane cross section following the same methodology as for nitrogen
- Harmonization of Geant4-DNA implementation of models dedicated to materials other than liquid water

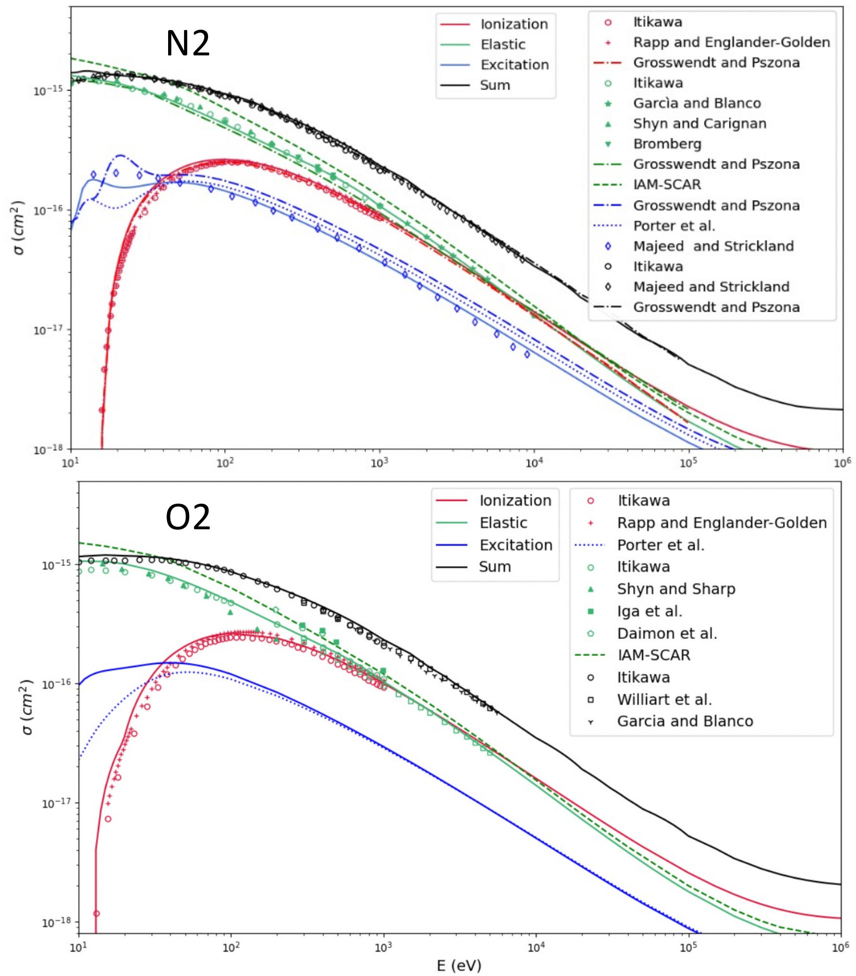
G4-DNA for atmosphere: N2 and O2 cross section models

Cosmic Ray's rule in influencing atmospheric composition remains a subject of ongoing investigation.

New G4DNA model implemented for electron impact on N2 and O2 **up to 10 MeV**:

- **Impact ionisation**: Relativistic Binary Encounter Bethe (RBEB) model
- **Elastic scattering**: Screening Corrected Additivity Rule(SCAR) model
- **Electronic excitation**: Porter's formulas with fitted cross section parameters

F. Nicolanti, et al, . Phys Med. (2023) (link)



Istituto Nazionale di Fisica Nucleare

LP2i Bordeaux

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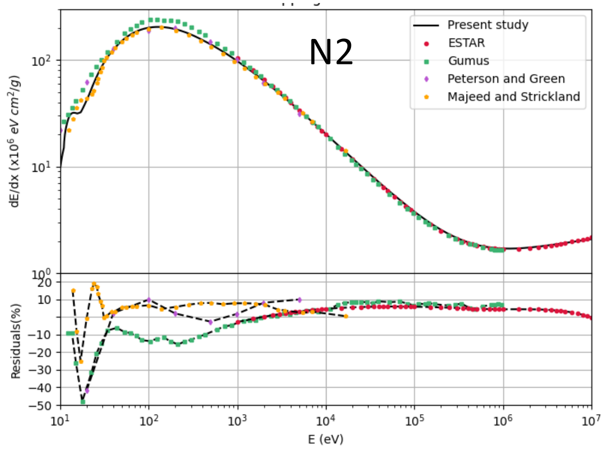
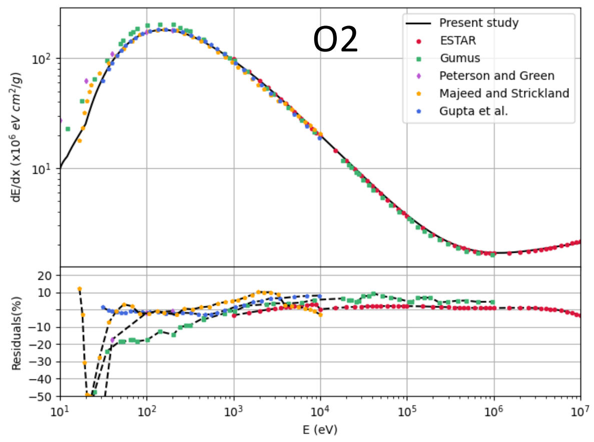
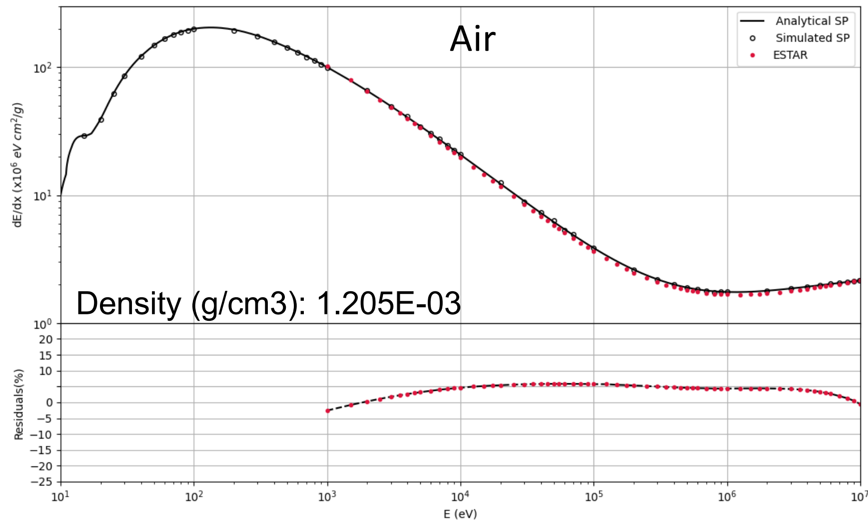
G4-DNA for atmosphere: Results

- Model classes designed to handle a mix of materials:
  - It is possible to run simulations in a simplified air material (76% N2, 24% O2)
- Agreement with **ESTAR** values:
  - **spower**: within 5.6% for N2, whitin 3.4% for O2
  - **range**: within 6% for N2, whitin 3.5% for O2
- Models and data will soon be added to Geant4
- Further work is planned to implement the physico-chemical stage







Contact: francesca.nicolanti@uniroma1.it

Chemistry stage

New « mesoscopic » approach

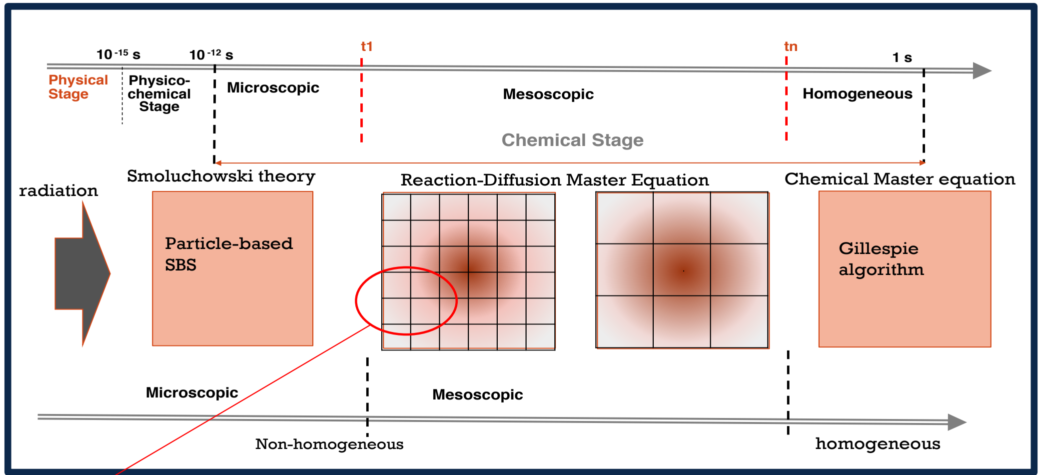
Tran et al., Int. J. Mol. Sci. (2021) 22 (link)

- Use new « mesoscopic » approach to study the production and evolution of reactive oxygen species generated under irradiation with
  different dose rate conditions, such as in FLASH RT

- Coarse-grained model: "compartment based"

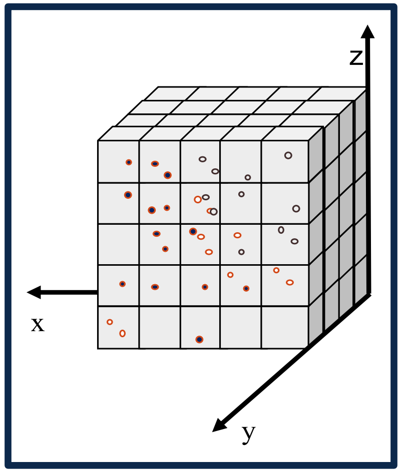
- Simulation from heterogeneous (SBS, microsecond) to homogeneous states (beyond)

- Developed in Geant4-DNA by the MAGIC Collaboration
  - CHUV, Switzerland & CNRS/LP2i, France



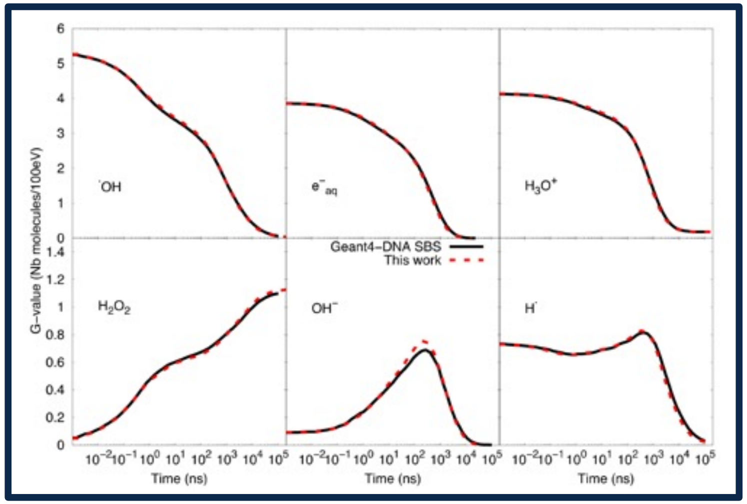
Principle of the combination of the particle-based SBS model with the compartment-based model

1. *Well mixed species in voxels*
2. *Species can react with each other in the voxels*
3. *Diffusion is modelled by jumps between adjacent voxels*



Voxelization of the simulation volume into smaller sub-volumes. Species are represented by different types of circles

Comparison of time-dependent G-values as computed with the particle-based SBS model and the SBS-RDME model (this work) from 1 ns until 100 us, for 1 MeV e-.



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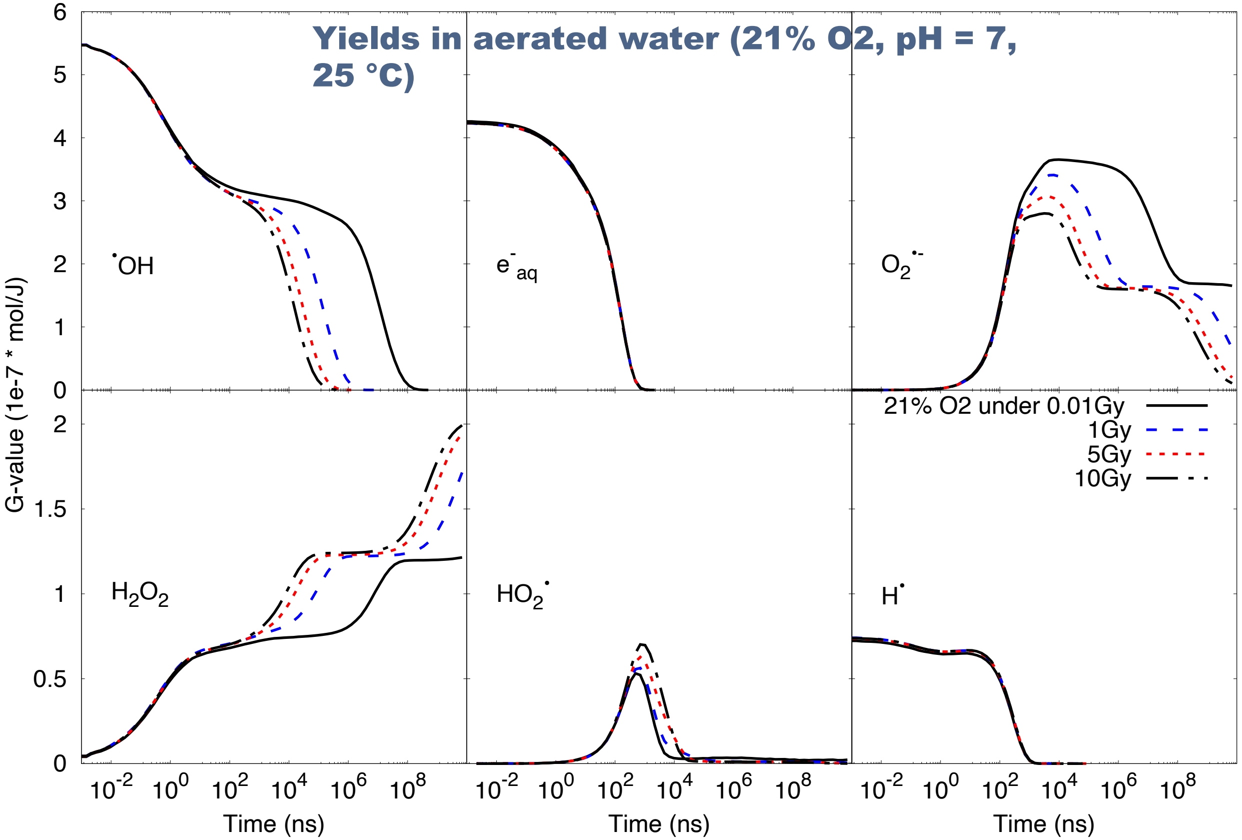
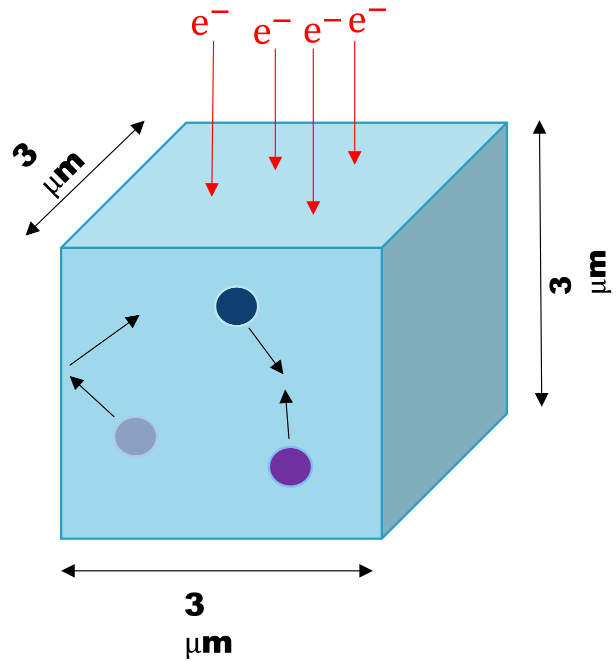
New « UHDR » example

Modelling of ultra-high dose rate (UHDR) electron beams





- Source: 1 MeV electron beam
- Simulation volume: water cube taking into account radiolytic species rebound (closed system)
- Electron irradiation until the total energy deposition reaches 1-10 Gy (UHDR) or ~ 0.01 Gy (conventional)
- Instantaneous pulse (all species are produced simultaneously)
- Extension of the chemical stage beyond the microsecond
- Study the evolution of ROS such as HO2• and O2•- produced by irradiation, pH is considered
- Currently being validated with exp. data

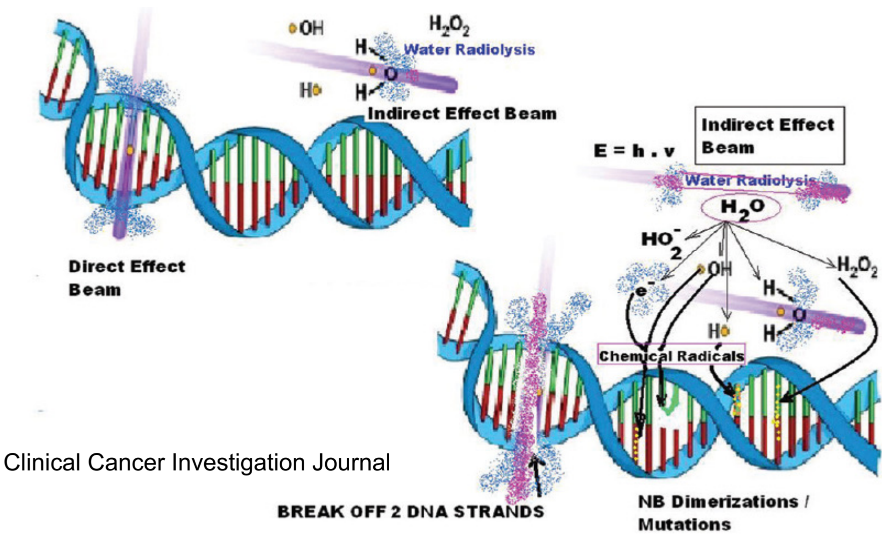
Biological geometries and applications

GEANT4-DNA

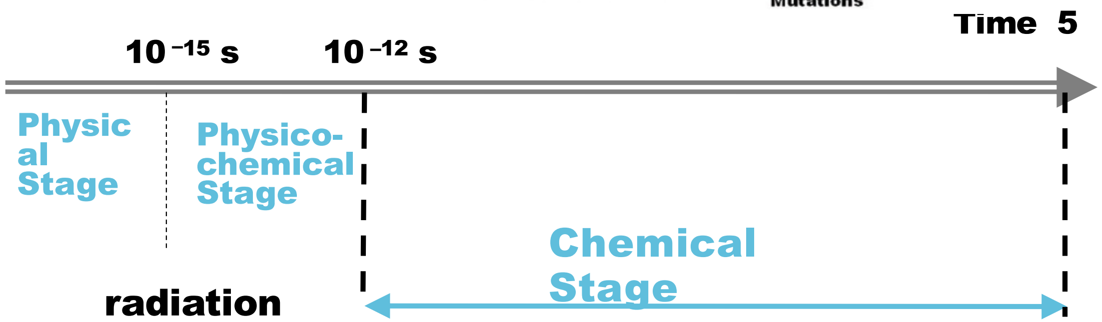
New biological geometries and applications

- **moleculardna :** simulate early DNA damage in a full DNA geometries of cell nucleus.
- **dnadamage2 :** this examples provides scoring of plasmid DNA strand breaks.
- **dsbandrepair :** a new biological geometry application from IRSN

Moleculardna: simulate early DNA damage using only Geant4 macro commands - No C++ skills needed



Clinical Cancer Investigation Journal



Simulation of physics, physico-chemistry and chemistry processes in DNA geometries.

```
/world/worldSize 10200 nm
/cell/radiusSize 3 3 3 um

/dnageom/setSmartVoxels 1
/dnageom/checkOverlaps false

/dnageom/radicalKillDistance 9 nm
/dnageom/interactionDirectRange 7 angstrom

/dnageom/placementSize 30 30 100 nm
/dnageom/fractalScaling 1 1 1 nm
/dnageom/definitionFile geometries/prisms200k_r3000.txt
/dnageom/placementVolume prism geometries/straight-216-0.txt

# Damage Model
/dnadamage/directDamageLower 17.5 eV
/dnadamage/directDamageUpper 17.5 eV

/dnadamage/indirectOHBaseChance 1.0
/dnadamage/indirectOHStrandChance 0.65
/dnadamage/inductionOHChance 0.0

/dnadamage/indirectHBaseChance 1.0
/dnadamage/indirectHStrandChance 0.65
/dnadamage/inductionHChance 0.00

/gps/particle e-
/gps/ang/type iso
/gps/energy 4.5 keV
/gps/pos/type Volume
/gps/pos/shape Sphere
/gps/pos/radius 500 nm
/gps/pos/centre 0 0 0 nm
/run/beamOn 1000
```

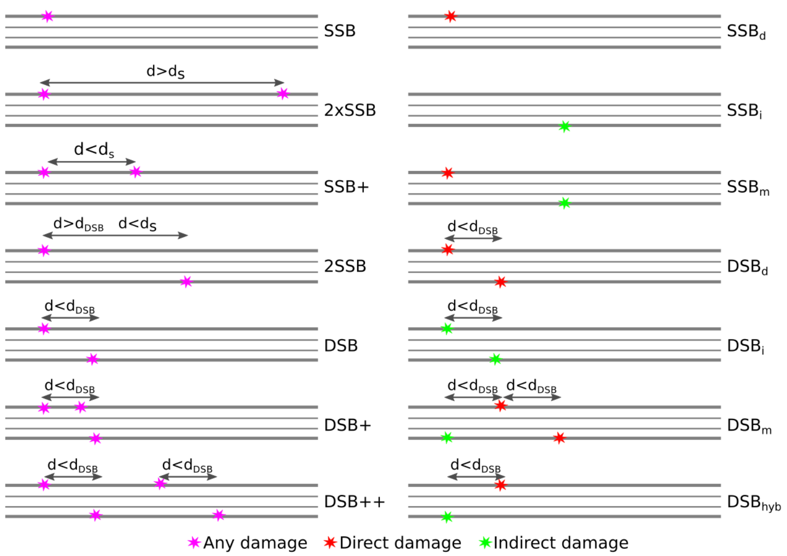
Geometry info

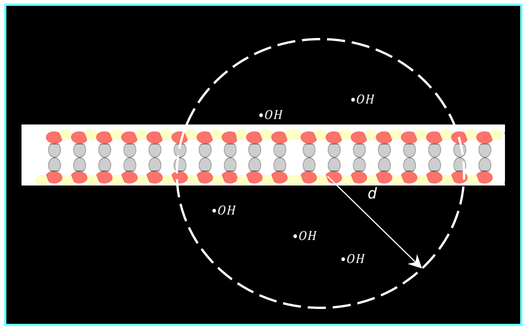
Damage model

Particle source

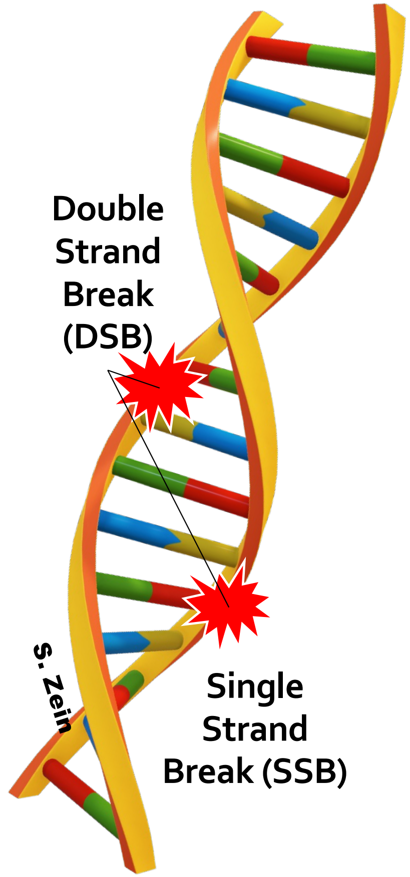
Damage model

- **Direct Damage** occurs when energy from physical processes is deposited near a DNA molecule. In molecularDNA, we associate damage either with a 'strand' molecule (sugar or phosphate placement) or a base molecule.
- **Indirect damage** is scored when a chemical reaction leads to a strand break.





- Strand breakage scheme (Nikjoo et al.1997)
- DNA segment complexity could be considered

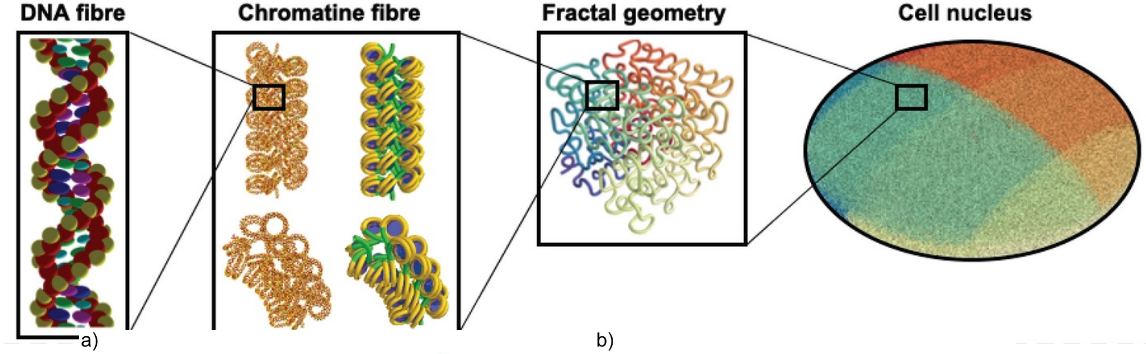


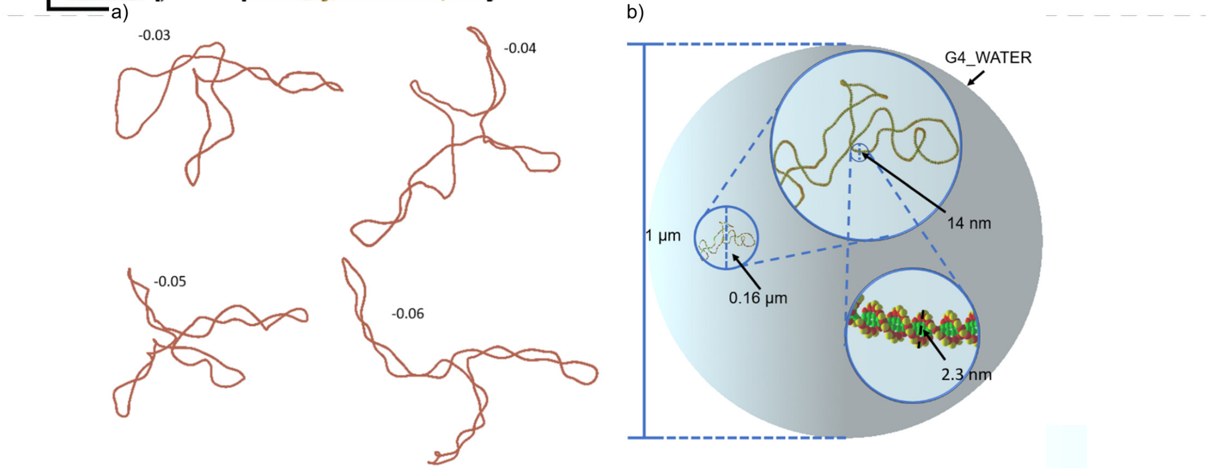
1 DSB = 2 SSB on opposite strands, less then 10 bp apart

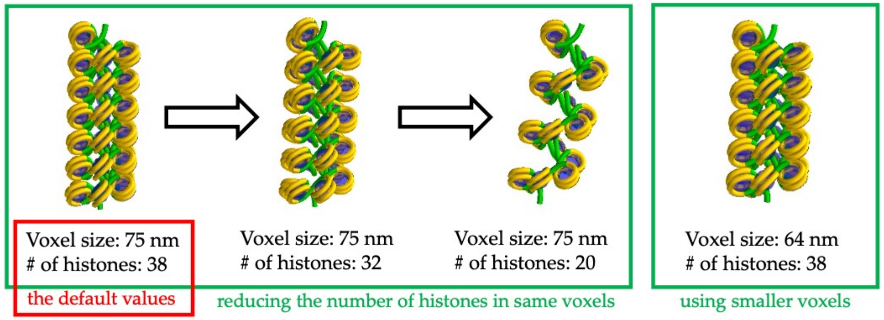
GEANT4-DNA

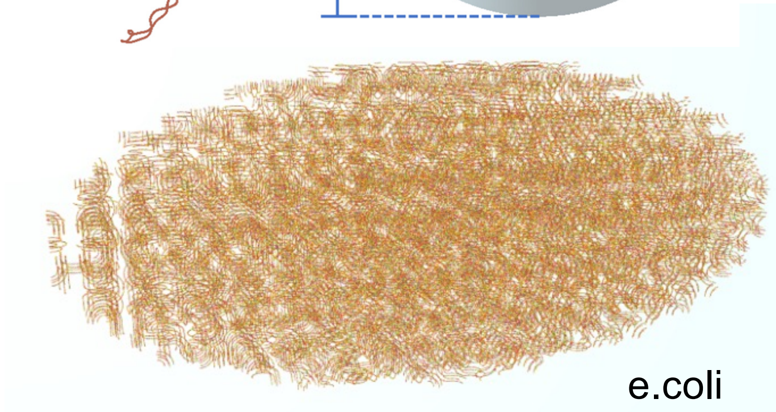
Geometry library

Human cell









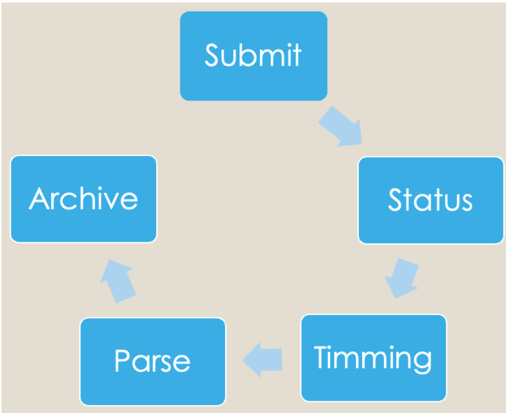
DNA-val project

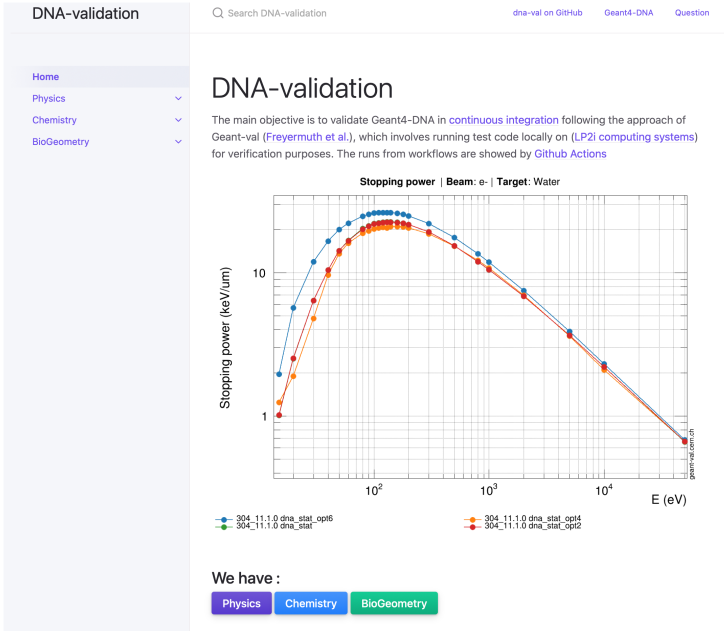
Benefit from geant-val project

GEANT4-DNA

DNA-val project

- Run code locally on (LP2i computing systems) in a workflow through Github Actions
- Tests are optimised to run for only one night then we can diagnose and prevent any bugs introduced by each MR (or each commit!!)
- The test results can be seen https://tranngochoang.github.io/dna-val/





TESTS of DNA-val

- Physics
  - TestEm12
  - icsd
  - microyz
  - range
  - spower
- Chemistry
  - chem6
    - In time
    - In LET
  - UHDR (not available)
- BioGeometry
  - moleculardna (only for simple cylinders.mac)

Limitation of DNA-val

- Need a better Front-end
- Need a big computer(s)
- Need more tests
- Percentage difference of range
- Performance test

Many technical debts

- The code needs to be renewed for new compilers (physical models and chemistry module)
- Memory optimization and computer performance
- Dependences should be reduced
- Coverity and memcheck errors
- Examples coding conventions violations
- Combination with Geant4 EM standard
- Documentation

=> Thanks Ben, Ivana, Vladimir, Gabriele,… for many advices and helps