Overview of the Geant4-DNA Project

Geant4-DNA

geant4-dna.org

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Geant4-DNA tutorial
INFN-LNS, Catania, Italy
9-10/10/2025

**Geant4 version 11.3
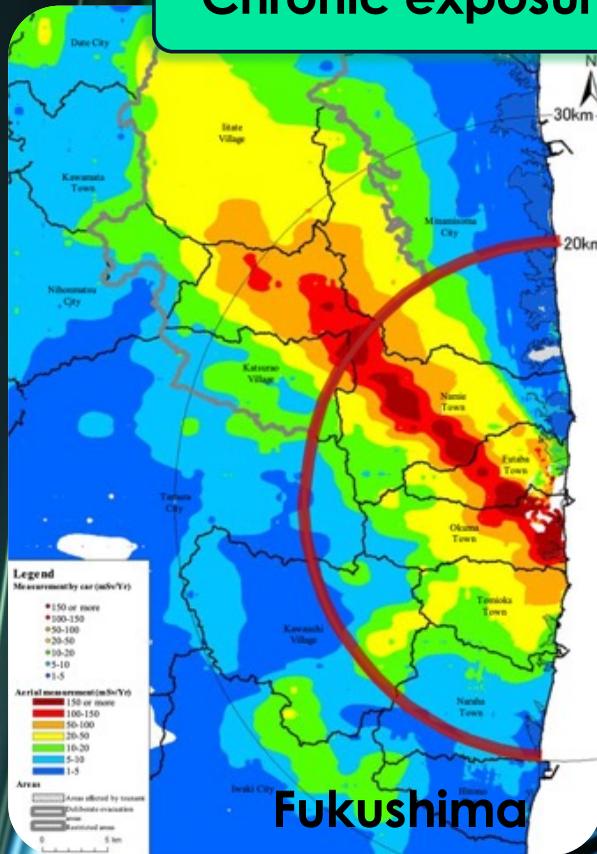Released in December 2024**

Contents of this talk

➢ Context of the Geant4-DNA project
➢ Physical stage
➢ Physico-chemical & chemical stage
➢ Geometrical models
➢ DNA damage and biological models
➢ More…

GEANT4-DNA

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➢ More…

GEANT4-DNA

Modeling biological effects of ionising radiation remains a major scientific challenge
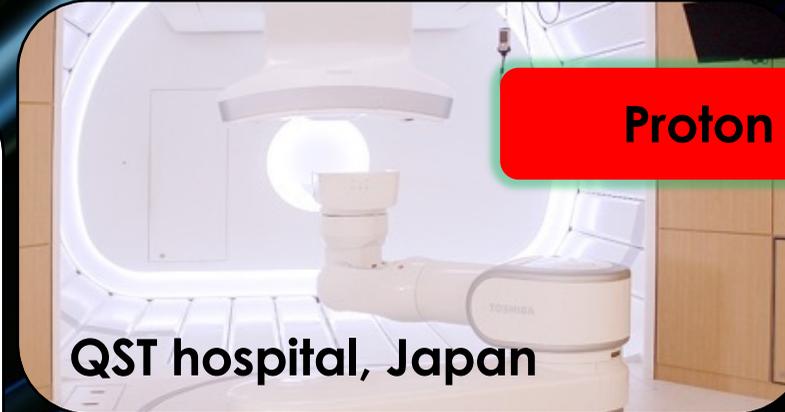
Chronic exposure

Diagnosis

Proton & ion-therapy

CT

QST hospital, Japan

Moon

Space missions

Fukushima

IAEA

Space exploration

Mars

ESA & NASA

ISS

Radiation effects scales

stockgiu/Freepik
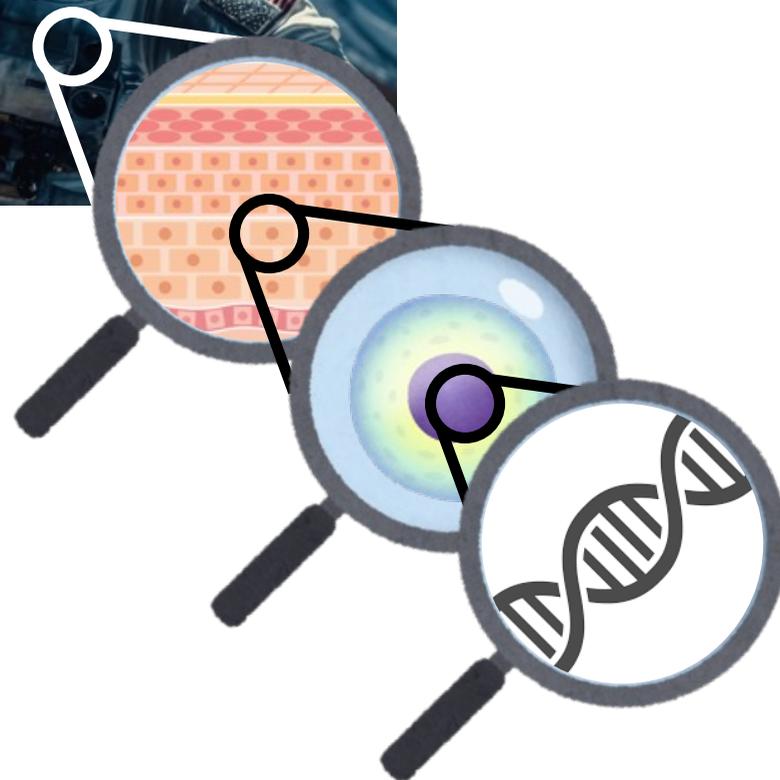
Human body: **~ 1cm - 100 cm**

Radiation sickness (organ-level effects)

Tissue: **~ 1 mm - 10 mm**

Radiation injury
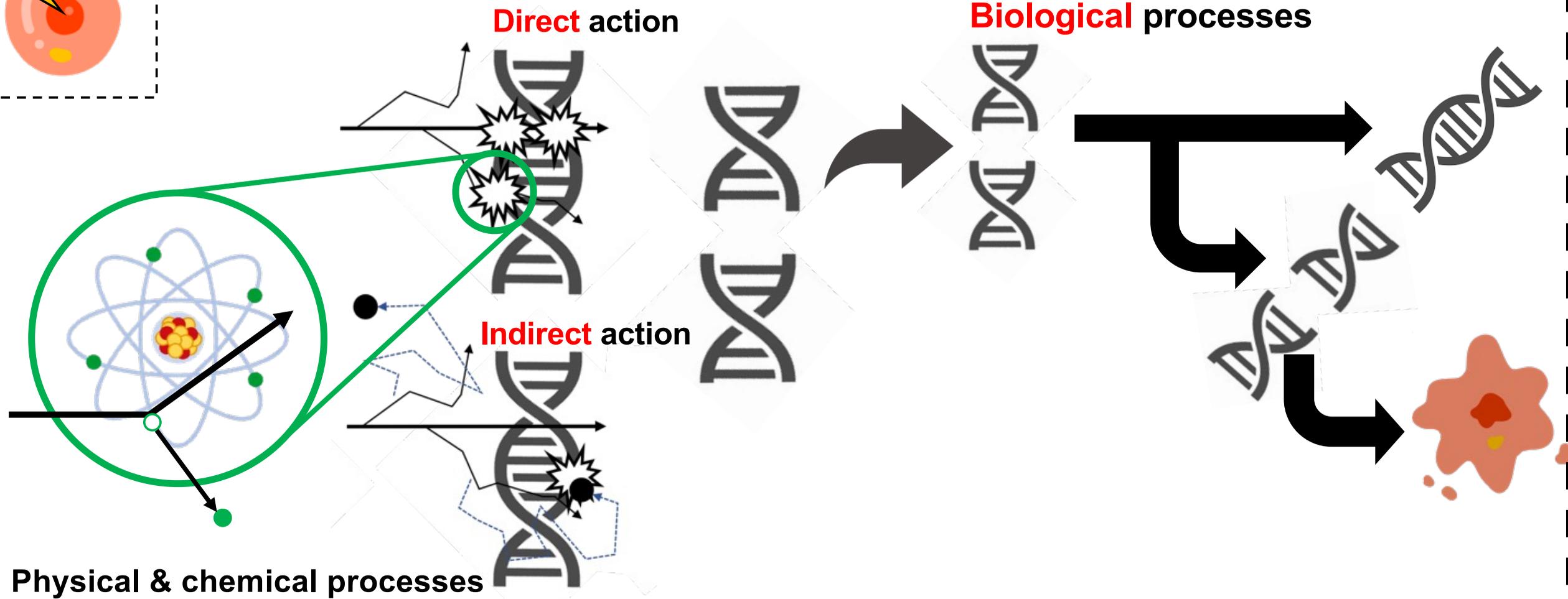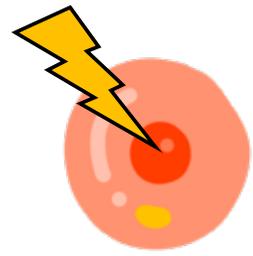
Cell: **~ 1 μm - 10 μm**

Cell death

DNA: **~ 1 nm - 10 nm**

DNA damage, mutation, …

Geant4-DNA main target

Radiobiological processes after irradiation


Direct action

Biological processes

Indirect action

Physical & chemical processes

The Monte Carlo approach

- Many **Monte Carlo codes** are already available today in radiobiology for the simulation of track structures at the molecular scale in biological medium

    - E.g. **PARTRAC**, **MC4***, **KURBUC**, **RETRACKS/RITRACKS**, **NOREC**, …

    - Include **physics & physico-chemistry** processes, detailed **geometrical** descriptions of biological targets down to the DNA size, **DNA and chromosome damage** simulation and even **repair** mechanisms (PARTRAC)…

- Usually designed for very specific applications

- Not always easily accessible

    - Is it possible to access the source code?

    - Are they adapted to recent OSs?

    - Are they extendable by the user?

Open-source track structure **MC codes**
for radiobiological simulations is in high demand

What is Geant4?
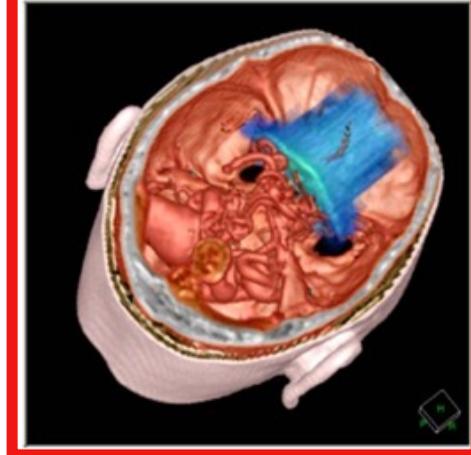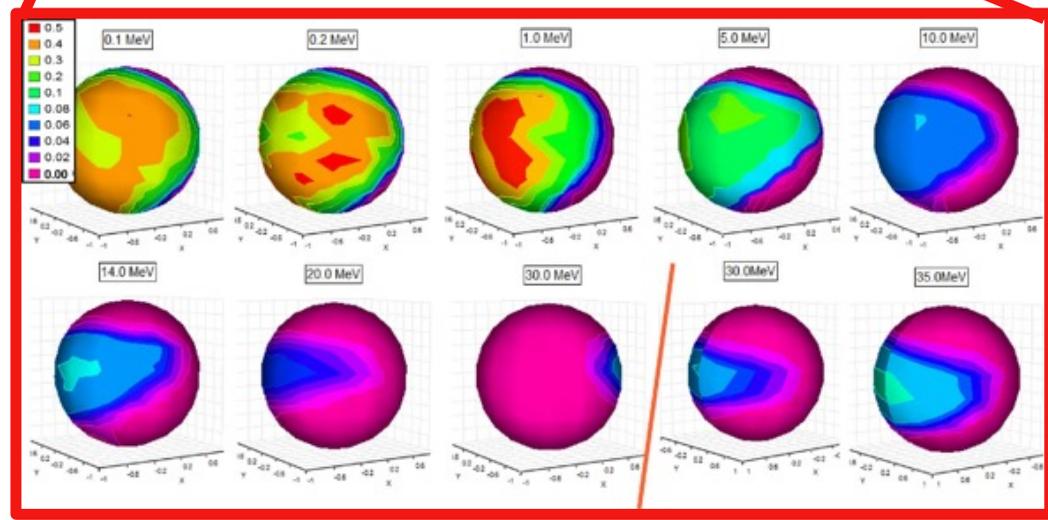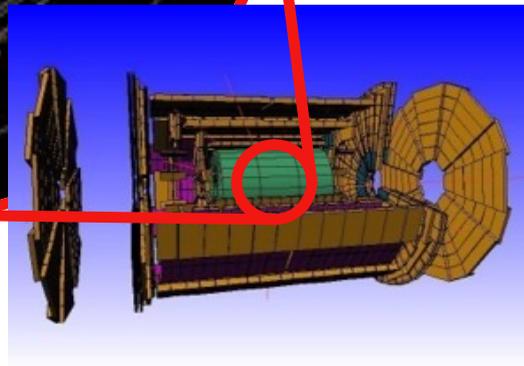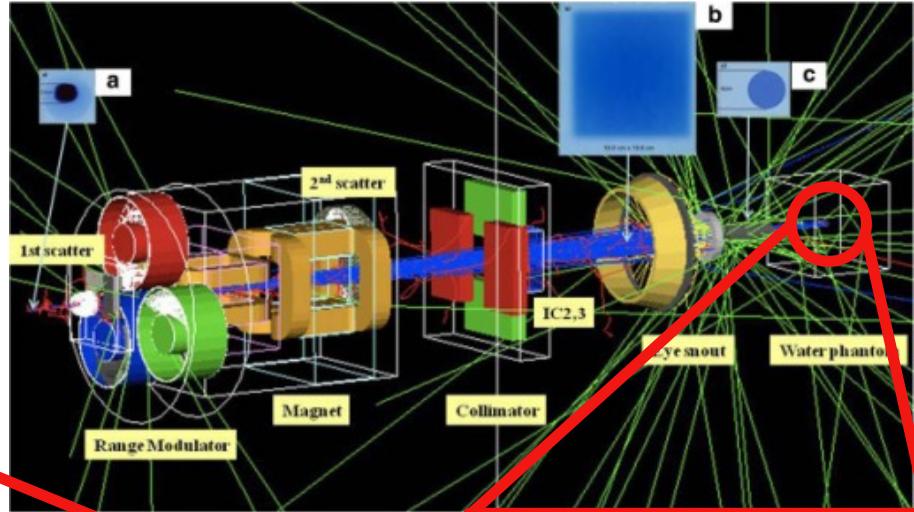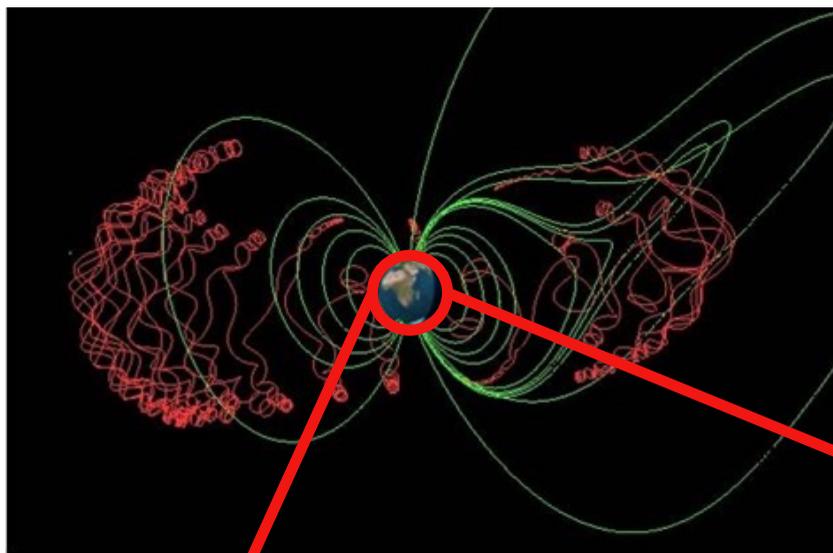
What is Geant4-DNA?
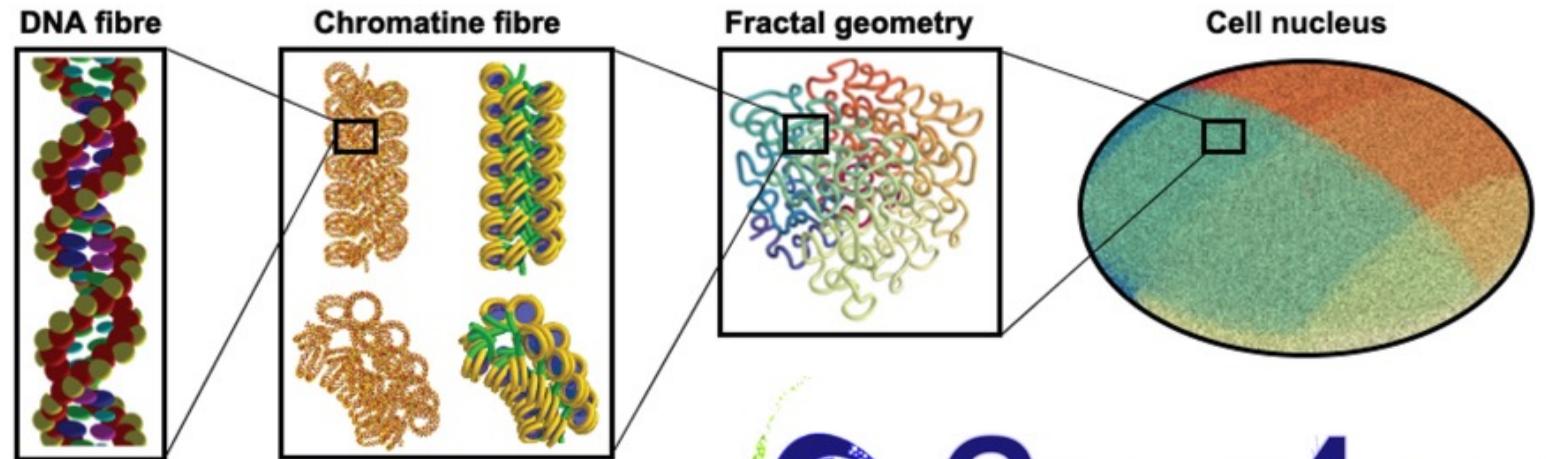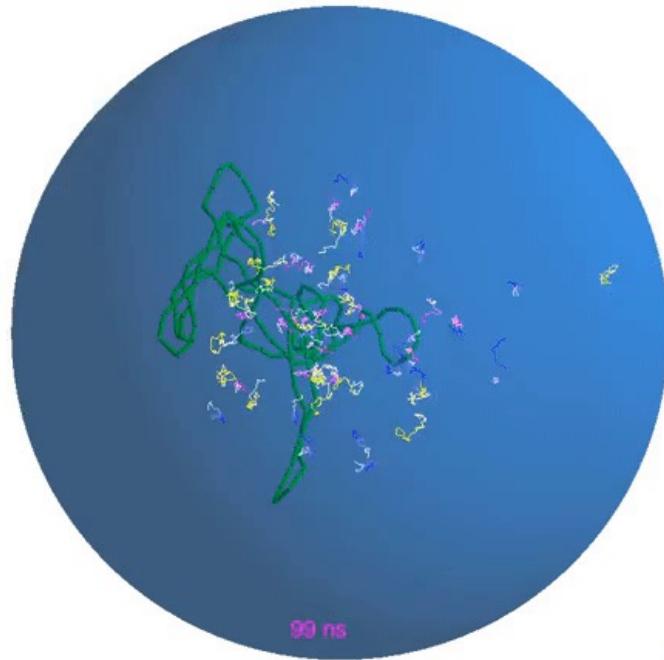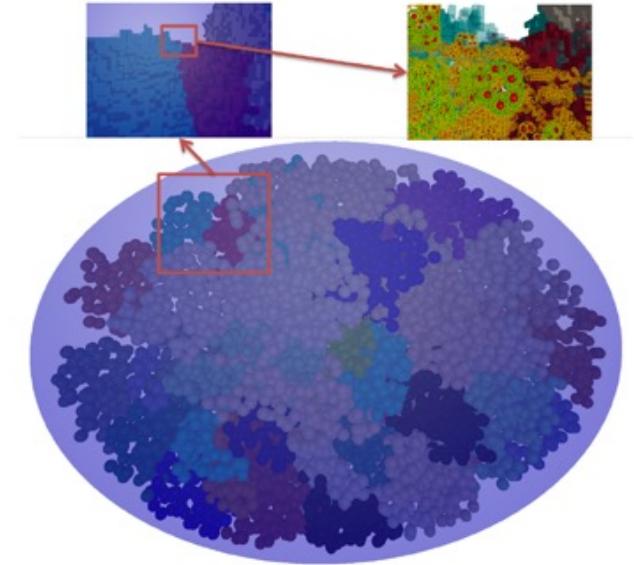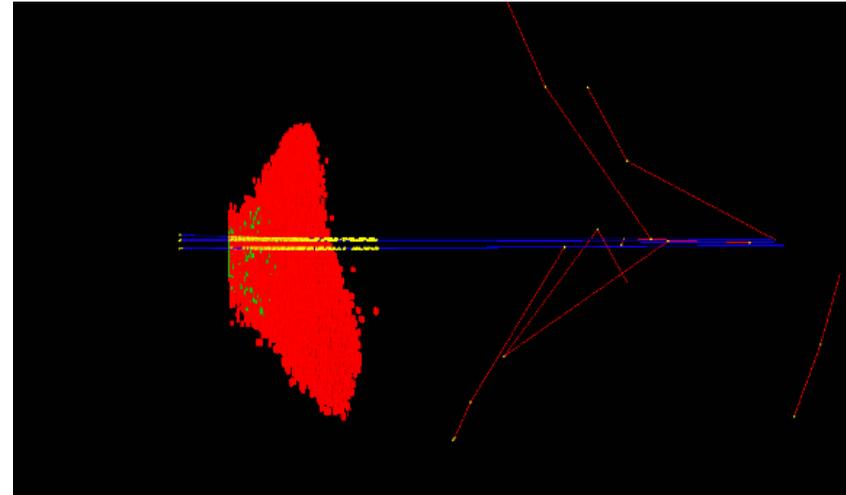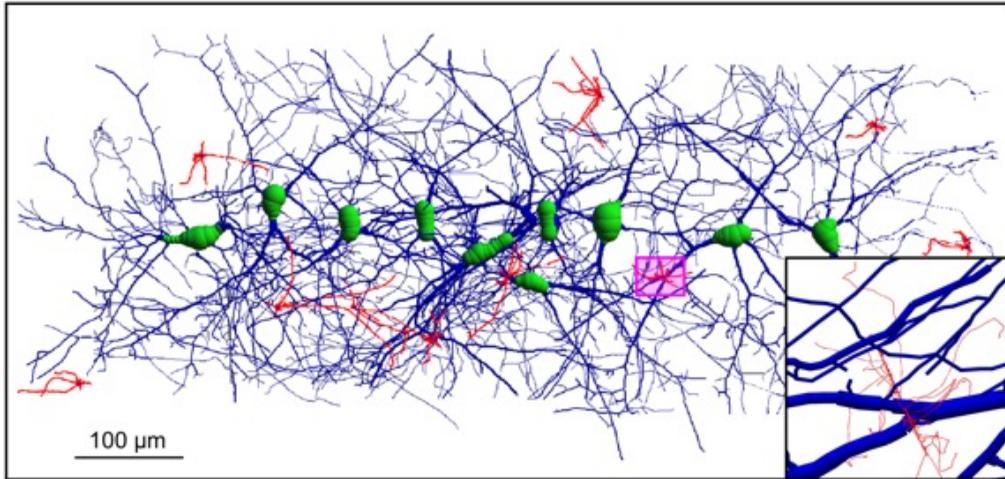
Why Geant4-DNA?
- Requirements for radiobiological simulations -

Damage distribution by X-ray

Damage distribution by ion

Ionizing Radiation

Low-LET
(X-rays, γ-rays)

High-LET
(protons, FLASH, carbon ions, BNCT)

Single DSB

Complex DSB

DNA Repair

Delayed DNA Repair or misrepair
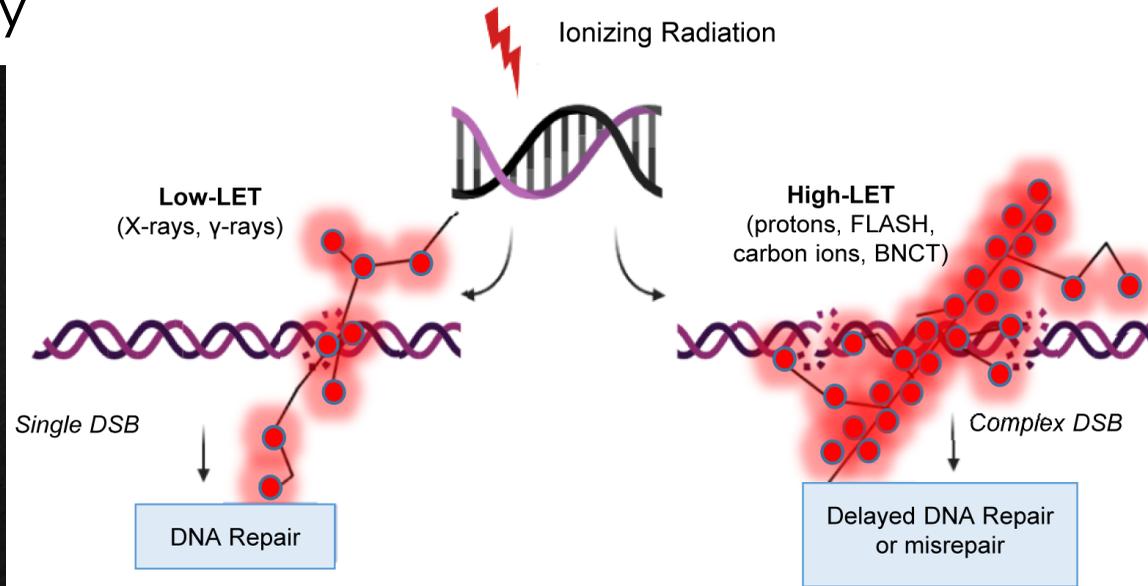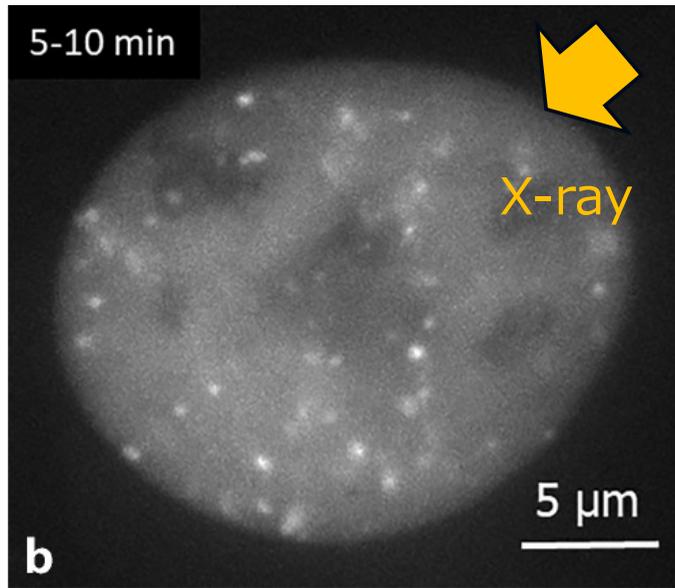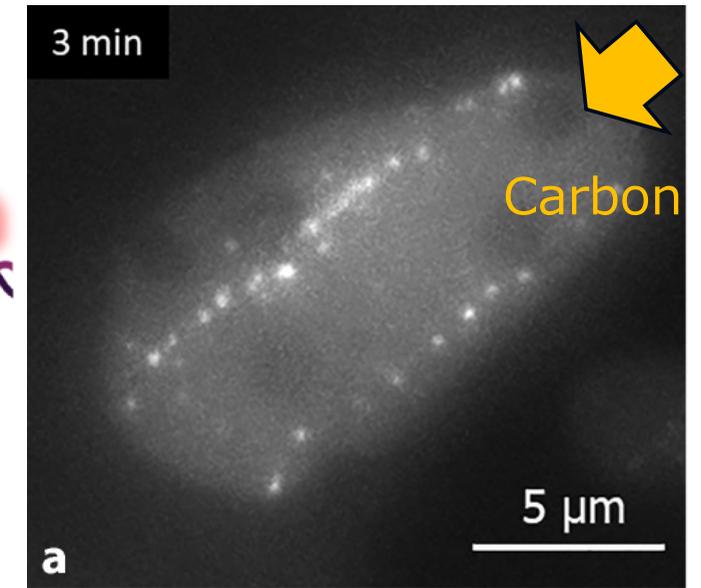
LET: Linear Energy Transfer (~ dE/dx)

Low LET: Simple DNA damage
→ Easy to repair

High LET: Complex DNA damage
→ Difficult to repair

High spatial resolution simulation (Geant4-DNA) allows
deep investigation of DNA damage and biological response.

Why Geant4-DNA?
- Requirements for radiobiological simulations -
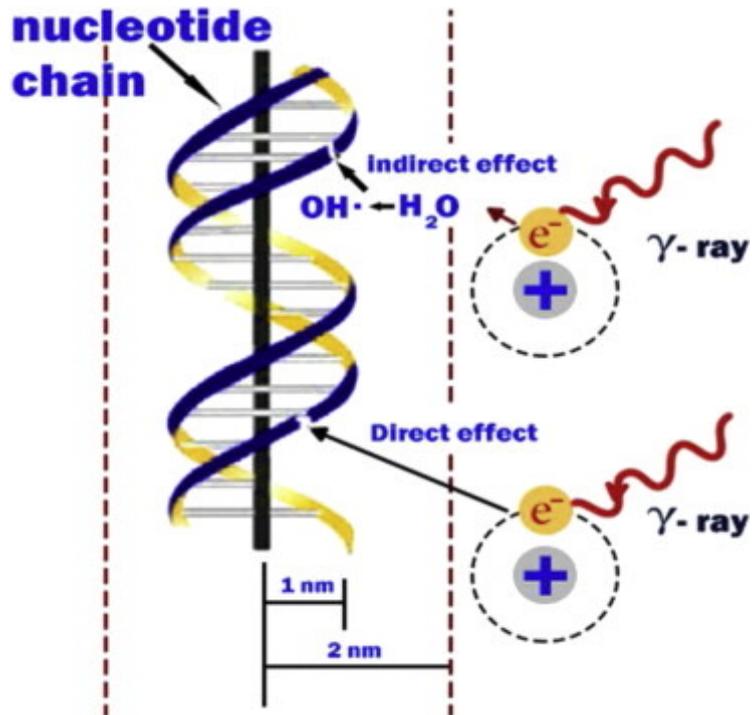
☐ Direct action: Damage by physical process
☐ Indirect action: Damage by chemical process
(reaction with chemical molecules created via water radiolysis)

➤ **Physical Process**
— Interaction with water molecule
— Interaction with bio-components

➤ **Chemical Process (with time evolution)**
— Radiolysis Production
— Diffusion of molecule
— Interaction with molecule/bio-components

Physical processes influence radiolysis yields and subsequent chemical interactions.
Integrated implementation is necessary.

Chemical domain
Spur
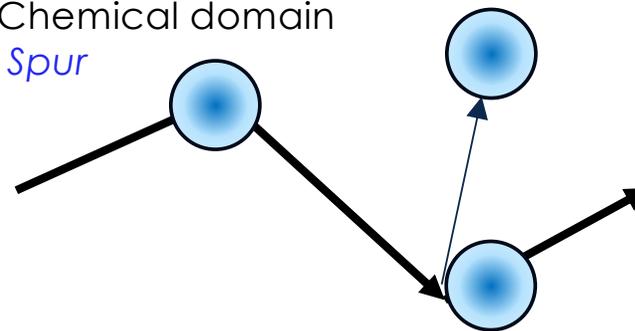
Low-LET (slow chemical reaction)   High-LET (fast chemical reaction)
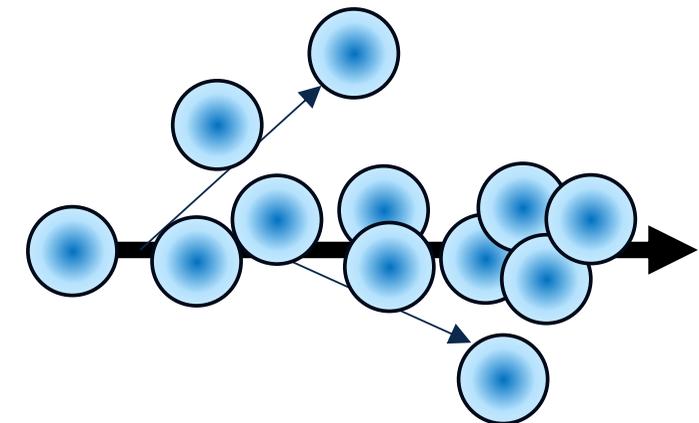
Ref: J Rad. Res. App. Sci. (2015) 8, 247-254

Why Geant4-DNA?
- Requirements for radiobiological simulations -

1. **High spatial resolution (few µm, nm), low energy limit, reliable physics for sub-keV energies**

   Geant4:

   Fast / Low spatial resolution, $E_{limit} \sim 250$ eV

   Geant4-DNA:

   Slow / High spatial resolution, $E_{limit} \sim 10$ eV

2. **Interface to water radiolysis**

   Geant4:

   No interface

   Geant4-DNA:

   Production/Diffusion of chemical molecules
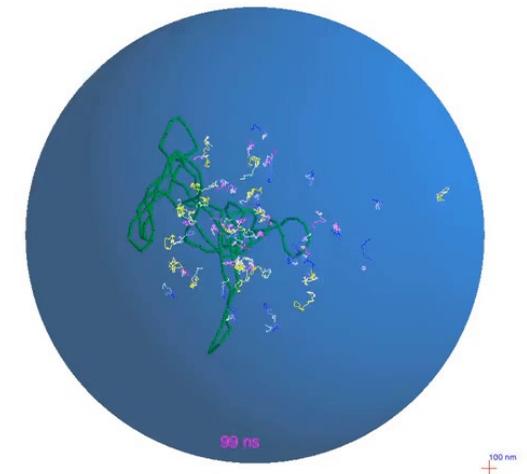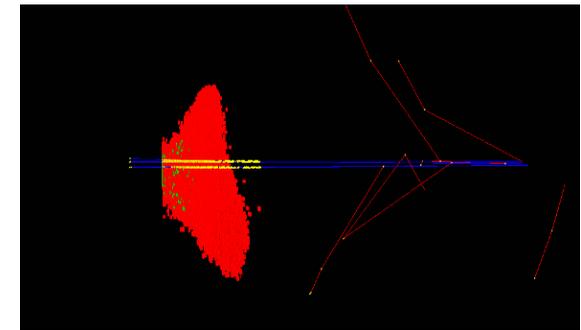
Requirement for physics: ① **High spatial resolution**

Trajectory in real world

Track-Structure approach
- All physical interactions are simulated individually in a sequential manner
- Example: **Geant4-DNA**, PARTRAC, RITRACKS, NOREC, KURBUC, PHITS-TS…
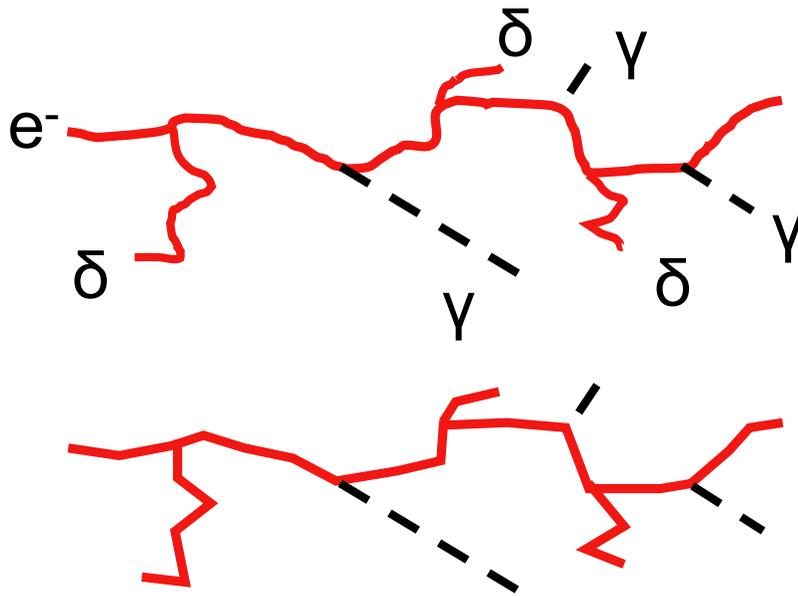
High accuracy/Slow computing
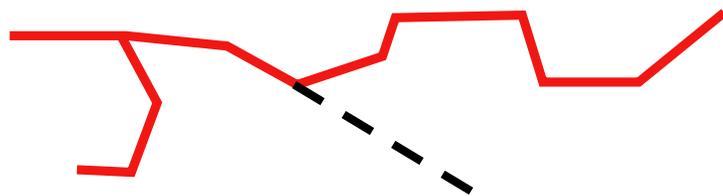
Low accuracy /**Fast computing**

Condensed-History approach
- Several discrete physical interactions are "condensed" into a single transport step
- Multiple-scattering approximation
- Example: **Geant4**, PHITS, EGS, FLUKA, PENELOPE, MCNP…

Ref.: Nucl. Instrum. and Meth. B 273, 95-97 (2012), Prog. Nucl. Sci. Tec. 2, 898-903 (2011)
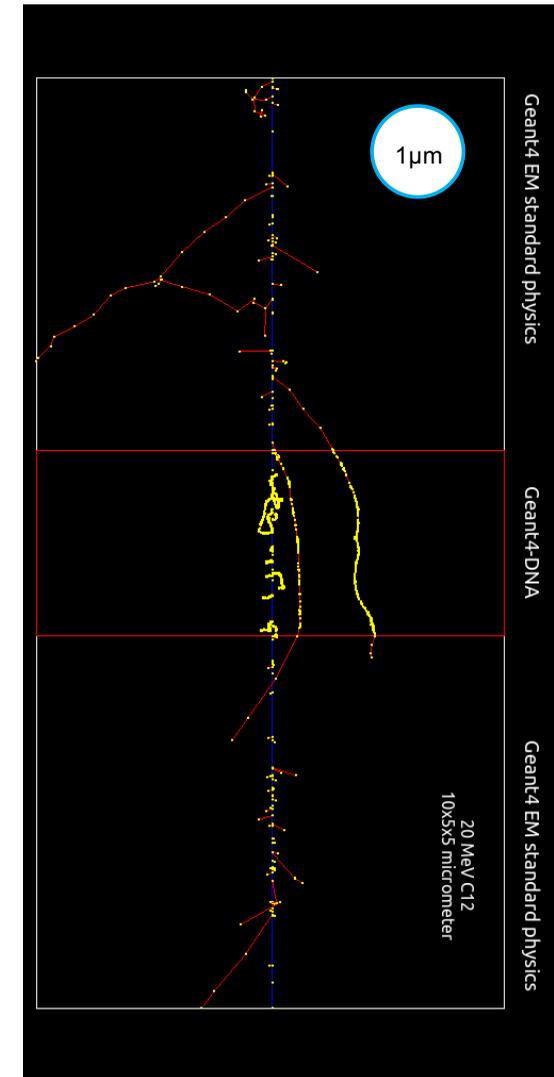
Requirement: ② Water radiolysis

Time (sec)

Physical processes

10^{-15}

Physico-chemical processes

10^{-12}

Chemical processes

10^{-6}

H_2O — Ionisation

Excitation

H_2O^* H_2O^+ e^-

H_2O H_2O

$H\bullet + \bullet OH$ $\bullet OH + H_3O^+$ e^-_{aq}

H_2 $\bullet OH$ H_2O_2 H_3O^+ OH^- $H\bullet$ e^-_{aq}

H_2 H_2O_2 O_2 H_2O

Reaction with Solute

(Y. Muroya, 2017)

e^-_{aq} H_3O^+ $H\bullet$ $\bullet OH$ H_2O_2

Water molecule decomposition

Spur creation

Diffusion (spur break-up)

Random distribution
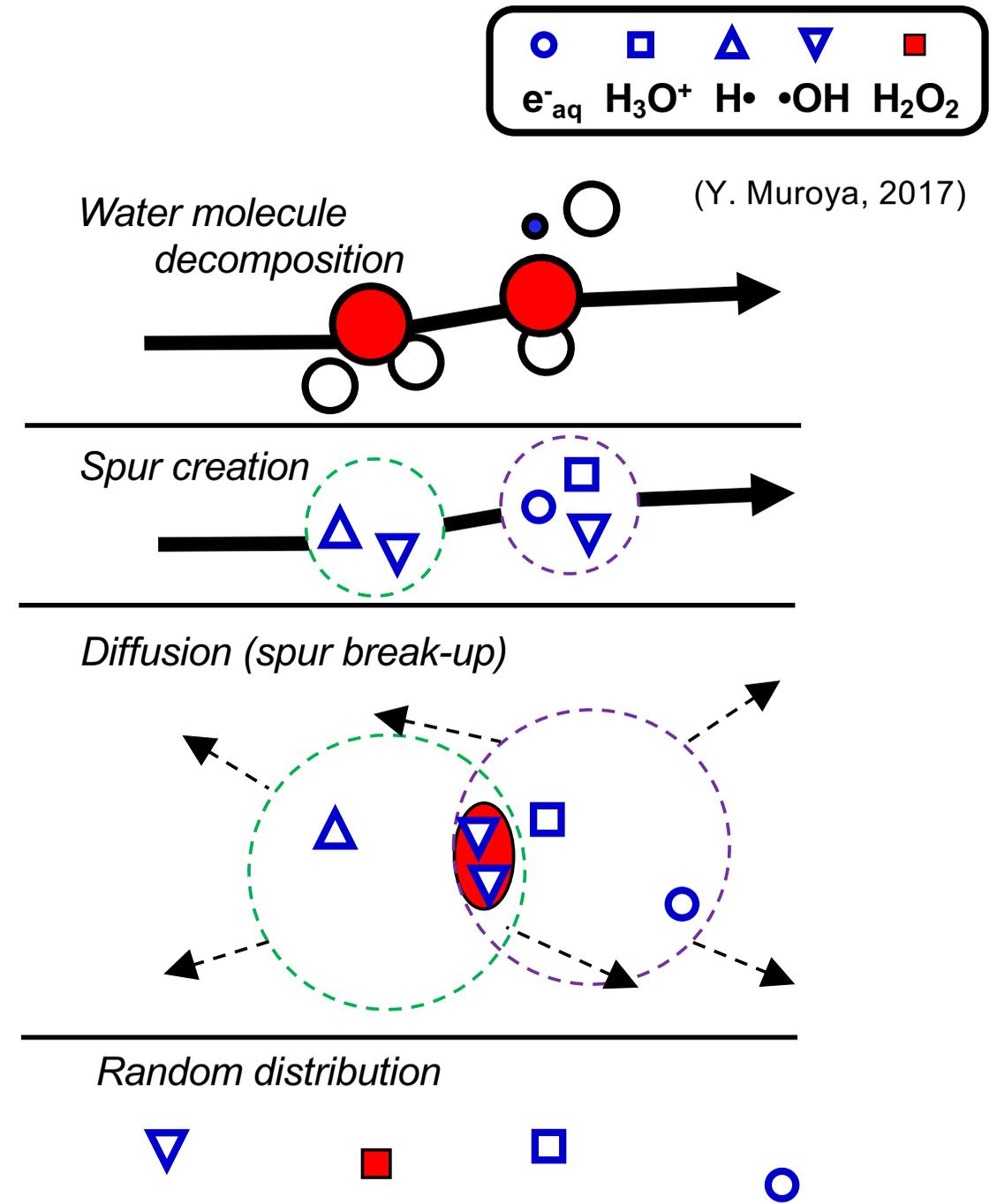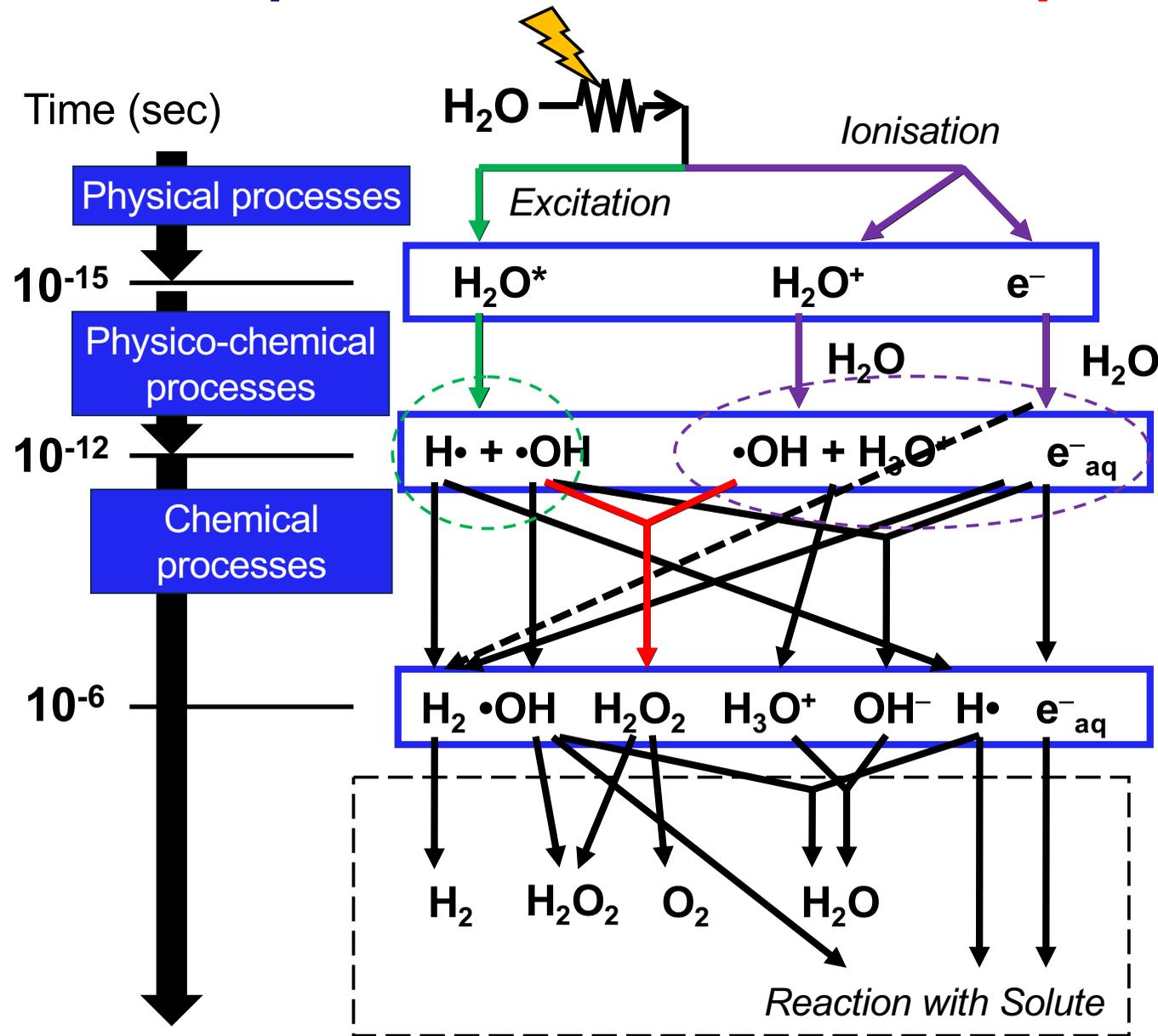
Geant4-DNA history

2001

Initiated by the **European Space Agency/ESTEC**

2007

First prototypes of **physics models** for liquid water added to Geant4 **9.1**

2008

Re-engineered to be coherent with Geant4 EM physics in Geant4 **9.3**

2014

Chemistry stage extension ready for end users in Geant4 **10.1**

2014

First extended examples applicable to **"DNA-scale" geometries** released in Geant4 **10.4**

2019 - 2023

Development of fully integrated radiobiological applications
Integration of Phys. + Chem. + Geometry in **10.5**
Integration with biological prediction models in **11.1**

2024-2025

Extension of Physics (energy, materials)
New approaches in chemistry

dnaphysics
microdosimetry
pdb4dna
wholeNuclearDNA

dnadamage1 in 10.5 (2019)
dnadamage2 in 11.1 (2022)
moleculardna in 11.1 (2022)
dsbandrepair in 11.2 (2023)

UHDR in 11.3 (2024)

GEANT4-DNA

Conceptual design of the Geant4-DNA approach

Simulation Block

Prediction Block

Direct action
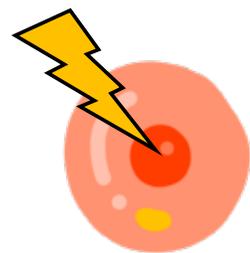
Biological processes

Indirect action

Score:
Damage yields
Damage type

Output:
Protein accumulation
DNA rejoining
Cell survival

Physical & chemical processes

The Geant4-DNA approach

MC Simulation Block

Physical stage
step-by-step modelling of physical interactions of incoming & secondary ionising radiation with biological medium (liquid water)

- Excited water molecules
- Ionised water molecules
- Solvated electrons

Physico-chemical/chemical stage
- Radical species production
- Diffusion
- Mutual chemical interactions

Geometrical models
DNA strands, chromatin fibres, chromosomes, whole cell nucleus, cells...
for the prediction of damage resulting from direct and indirect hits

DIRECT DNA damage

INDIRECT DNA damage

Prediction Block

Biological repair

Prediction of biological parameter yields using semi-empirical biological repair model from nDSB and complex DSB fraction.

- Protein/enzyme kinetics
- DNA rejoining
- Cell survival

$t=0$ $t=10^{-15}s$ $t=10^{-9} \sim 10^{-6}$ s

GEANT4-DNA

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The Geant4-DNA approach

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t=0   t=10^{-15}s   t=10^{-9}~10^{-6} s

Geant4-DNA physics for liquid water

- **Geant4-DNA processes and models allows the transport in liquid water**
  - Electrons: ionisation, excitation, elastic scattering, vibrational excitation, electron attachment
  - Protons, H (0,+): ionisation, excitation, elastic, charge increase/decrease processes
  - Alpha, He (0,+,2+): ionisation, excitation, elastic, charge increase/decrease processes
  - Generic ions: ionisation

- **Geant4-DNA Physics constructors for simulations in liquid water**
  - **G4EmDNAPhysics_option2** (since version 9.1): accelerated default constructor, simulating electron interactions (elastic, inelastic, dissociative attachment, vibrational excitation) **up to 1 MeV**, as well as other particle interactions
  - **G4EmDNAPhysics_option4** (since version 10.2): contains electron elastic and inelastic models, **up to 10 keV**; extended up to 10 MeV (to be released)
  - **G4EmDNAPhysics_option6** (since version 10.4): contains CPA100 electron elastic and inelastic models, **up to 256 keV**

NOTE
- Protons can be tracked up to 300 MeV
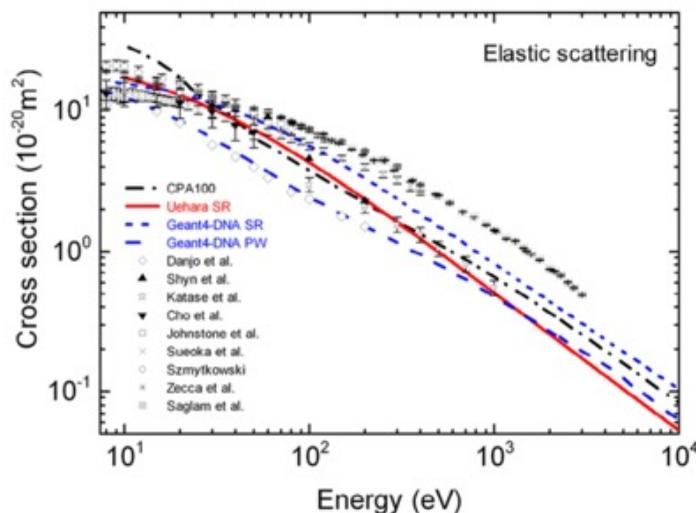- Option4 and option6 can go up to 1 MeV (beyond the default limits, Born models are used)

Multi-scale combination of physics processes

- Geant4-DNA is mainly dedicated to **(very) low energy charged particles**
  - Is it possible to simulate neutral particles such as photons?
  - Can we include the physics processes for high-energy particles?

- Any Geant4-DNA process can be combined with other Geant4 process such as:
  - Geant4 **photon** processes: photoelectric effect, Compton scattering, Rayleigh scattering, pair production
    - Livermore (EPDL97) included by default
  - Geant4 **alternative EM** processes for charged particles
    - E.g. bremsstrahlung
  - Geant4 **atomic de-excitation** (fluorescence + Auger emission, including cascades)
    - EADL97
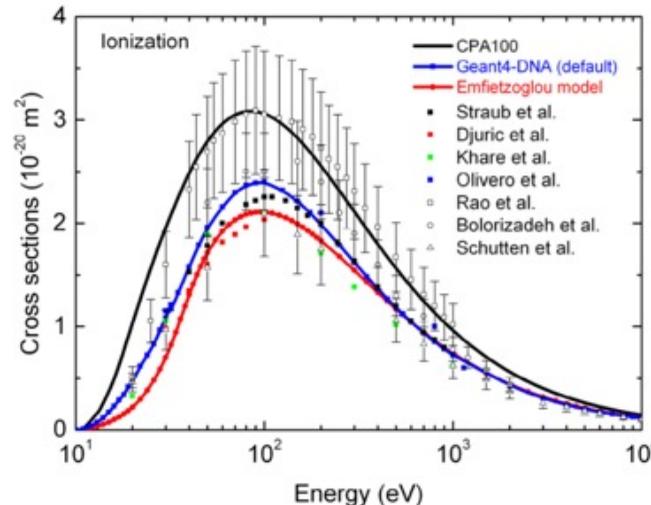   - Bearden
  - …and also Geant4 **hadronic physics**

E.g. of validation and verification of Physics : total cross sections
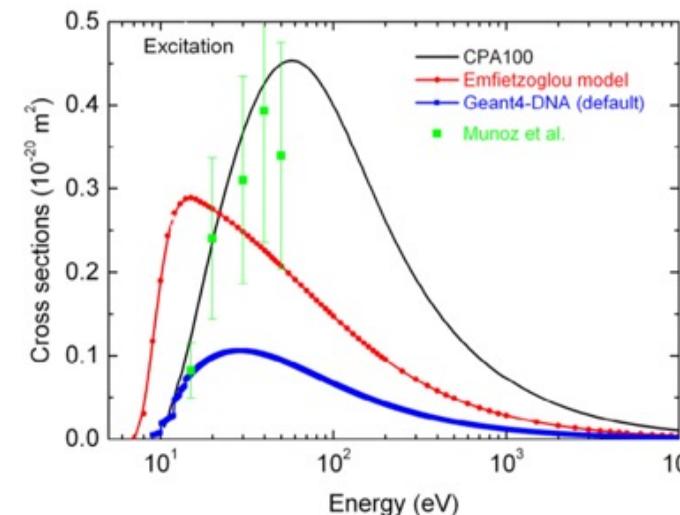
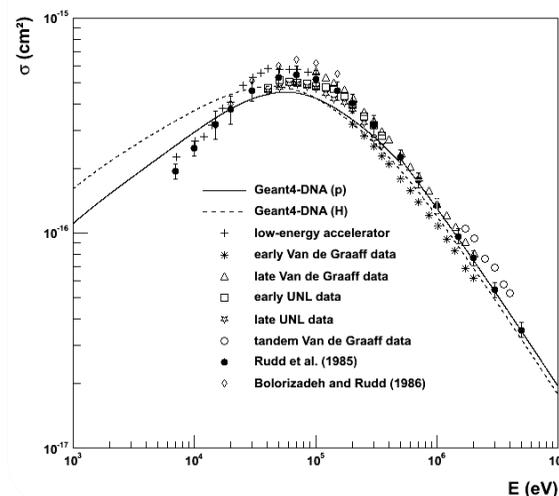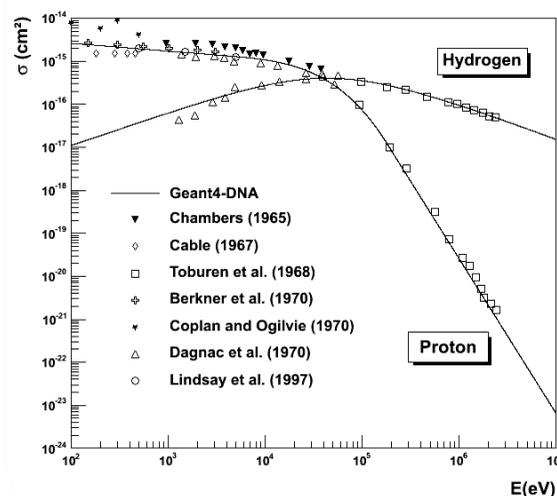**Electron CS:** **Elastic** **Ionisation** **Electronic excitation**

Proton CS: **Ionisation** **Charge exchange** **Helium CS:** **Ionisation** **Charge exchange**
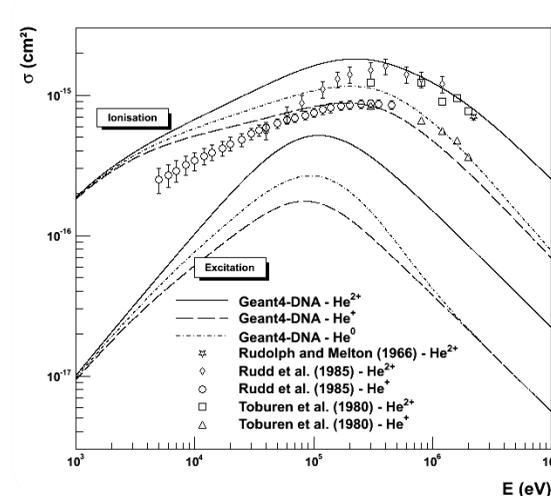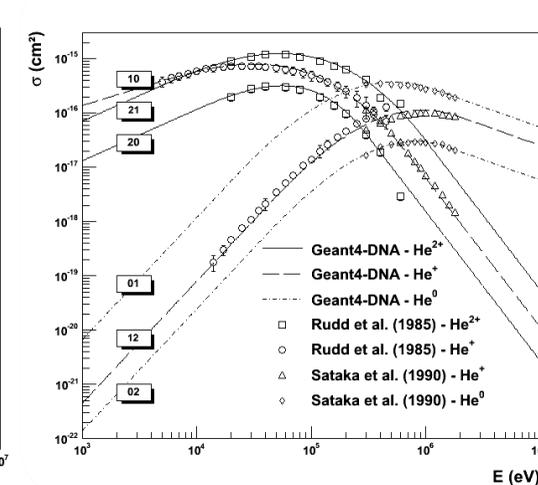
Geant4-DNA
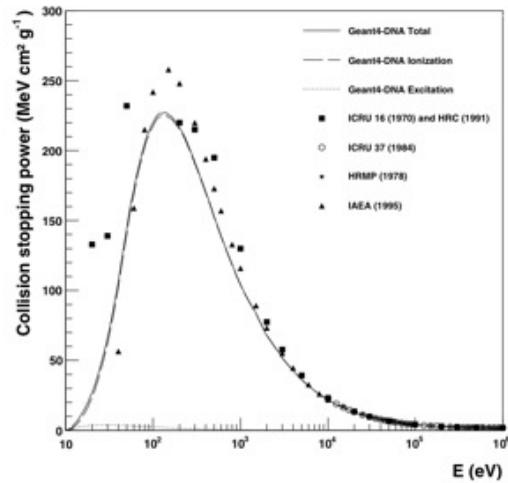
E.g. of validation and verification of Physics: range and stopping power

Stopping power:
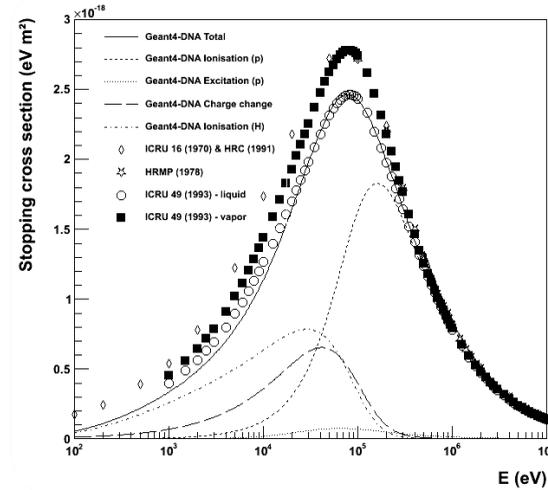
Electron	Proton	Helium

Range:

Electron	Proton	Helium

Ref.: Med. Phys. 37, 4692-4708 (2010), Nucl. Instrum. Meth. B 343, 132-137 (2015), Med. Phys. 45, e722-e739 (2018)

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The Geant4-DNA approach

Physical stage
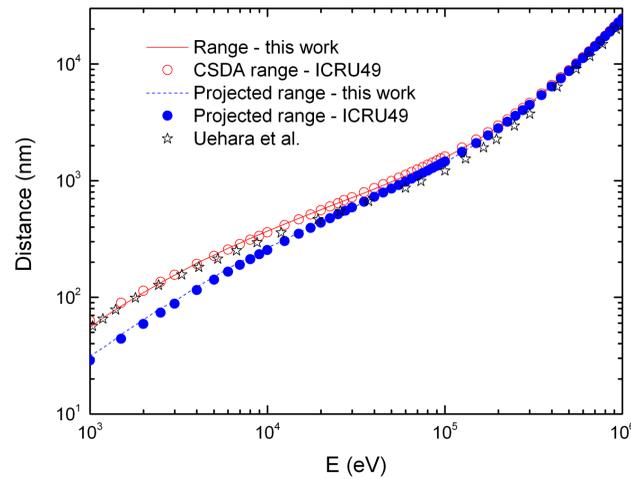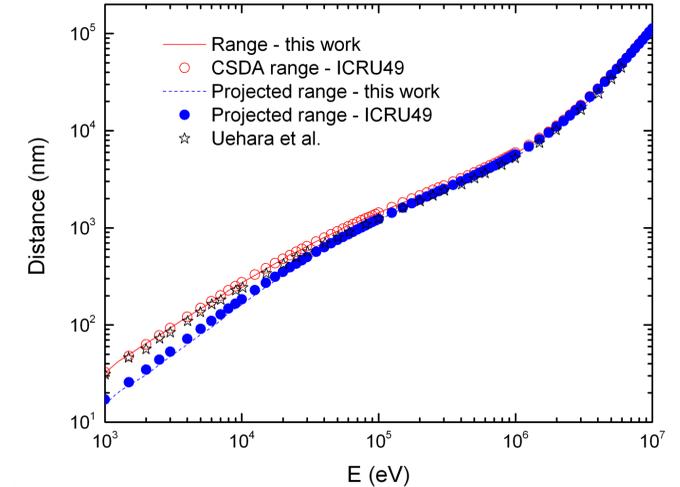step-by-step modelling of physical interactions of incoming & secondary ionising radiation with biological medium (liquid water)

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t=0   t=10^{-15}s   t=10^{-9}~10^{-6} s

GEANT4-DNA

Geant4-DNA chemistry models

- **Geant4-DNA chemistry allows the water radiolysis simulation:**
  - **Production of molecules**: e.g, place decomposed molecules at 1 ps
  - **Diffusion**: Geant4-DNA offers 3 types of diffusion algorithm
    - **Step-by-Step (SBS)**: Fixed time step molecular transport method.
    - **Independent Reaction Time (IRT)**: Calculates the reaction times between all possible pairs. Reactions occur one by one, starting with the pair with the shortest reaction time.
      - **IRT-sync**: IRT-sync stores all molecular positions **at each time step**, as the SBS approach.
    - **Mesoscopic**: A compartment-based representation that describes the evolution of species through their concentrations in different compartments.
  - **Reaction**: Geant4-DNA handles reactions between molecules.

- **Geant4-DNA chemistry constructors:**
  - `G4EmDNAChemistry`: First constructor implemented with parameter values from Karamitros et al.
    – from PARTRAC
  - `G4EmDNAChemistry_option1`: Implements a revisited set of chemistry parameters from Shin et al.
    – from TRACs + Burns et al. (1981) + Rowe et al. (1988)
  - `G4EmDNAChemistry_option2`: Includes chemistry parameters for reactions with DNA components
    – from Buxton et al. (1988)
  - `G4EmDNAChemistry_option3`: Implements the IRT approach from Ramos-Mendez et al. (2020)
    – from RITRACKS & Elliot et al. (1994)

Ref.: Med. Phys. 51 5873–5889 (2024)
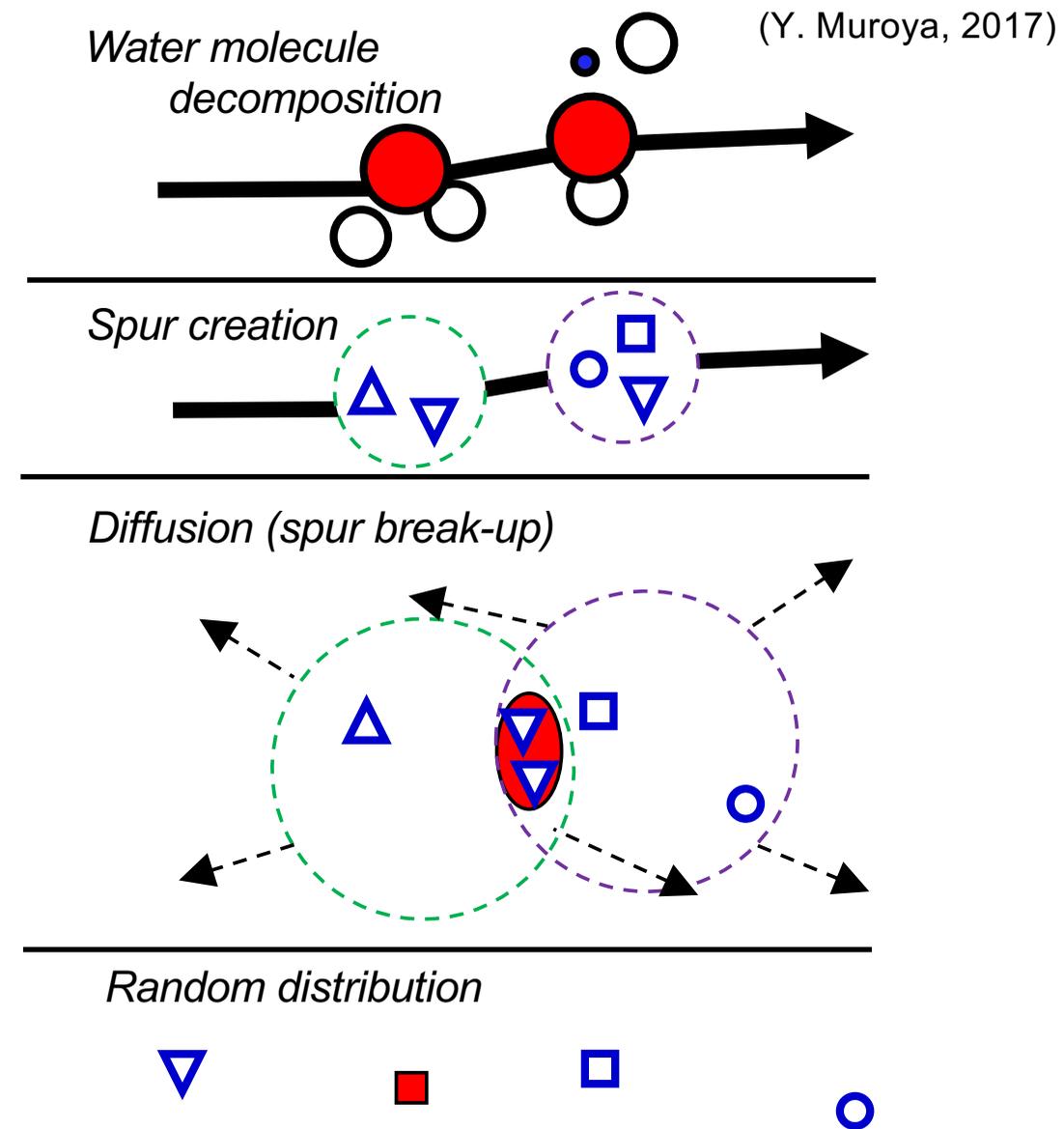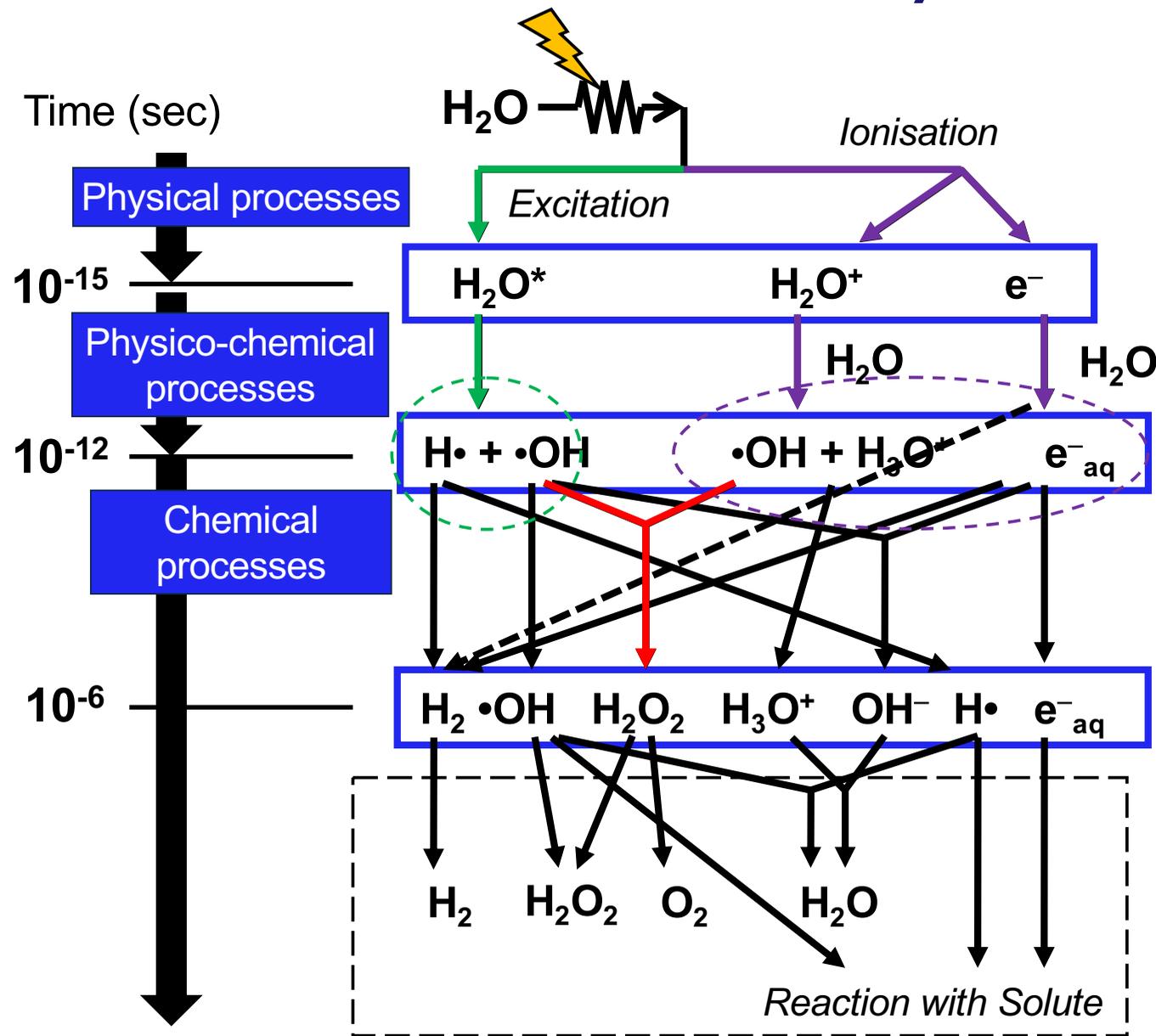
Geant4-DNA chemistry extended examples

- The « **chem1** » **extended/medical/dna** example illustrates how to **activate** the simulation of water radiolysis (step-by-step method).

- The « **chem2** » **extended/medical/dna** example illustrates how to **set minimum time step** limits on water radiolysis (step-by-step method).

- The « **chem3** » **extended/medical/dna** example illustrates how to **implement user actions** in the chemistry module (step-by-step method).

- The « **chem4** » **extended/medical/dna** example illustrates how to **compute radiochemical yields ("G") versus time**, including a dedicated ROOT graphical interface (step-by-step method).

- The « **chem5** » **extended/medical/dna** example illustrates how to **compute radiochemical yields ("G") versus time**, using alternative physics and chemistry lists (step-by-step method).

- The « **chem6** » **extended/medical/dna** example illustrates how to **compute radiochemical yields ("G") versus time and LET** using IRT method.

- The « **scavenger** » **extended/medical/dna** example illustrates how to **simulate scavenging using an easy-to-use interface** and the IRT method.

- The « **UHDR** » **extended/medical/dna** example illustrates how to activate the **chemistry mesoscopic model in combination with the step-by-step model** and allows to simulate chemical reactions beyond 1 μs post-irradiation.
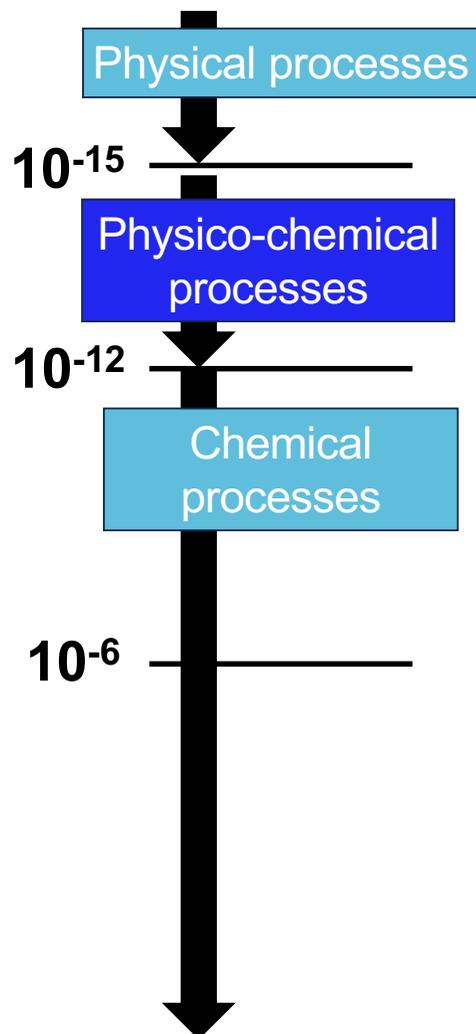
Towards FLASH simulations…

You remember, chemistry interface needed

(Y. Muroya, 2017)

Legend: e^-_{aq} (○), H_3O^+ (□), $H\bullet$ (△), $\bullet OH$ (▽), H_2O_2 (■)

Time (sec)

Physical processes

10^{-15}

Physico-chemical processes

10^{-12}

Chemical processes

10^{-6}

H_2O — Ionisation — Excitation

H_2O^* H_2O^+ e^-

H_2O H_2O

$H\bullet + \bullet OH$ $\bullet OH + H_3O^+$ e^-_{aq}

H_2 $\bullet OH$ H_2O_2 H_3O^+ OH^- $H\bullet$ e^-_{aq}

H_2 H_2O_2 O_2 H_2O

Reaction with Solute

Water molecule decomposition

Spur creation

Diffusion (spur break-up)

Random distribution

Chemistry / Physico-chemical stage: Molecule production

Time (sec)

Physical processes

10^{-15}

Physico-chemical processes

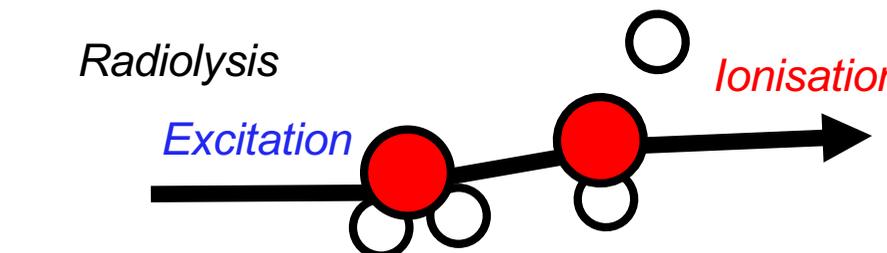10^{-12}

Chemical processes
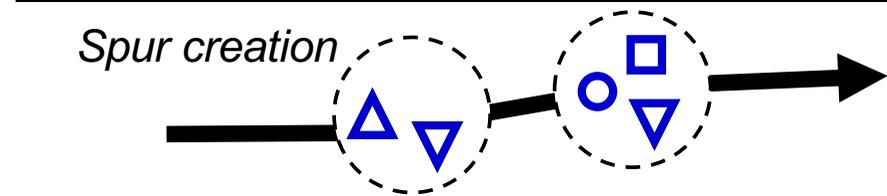
10^{-6}

Radiolysis

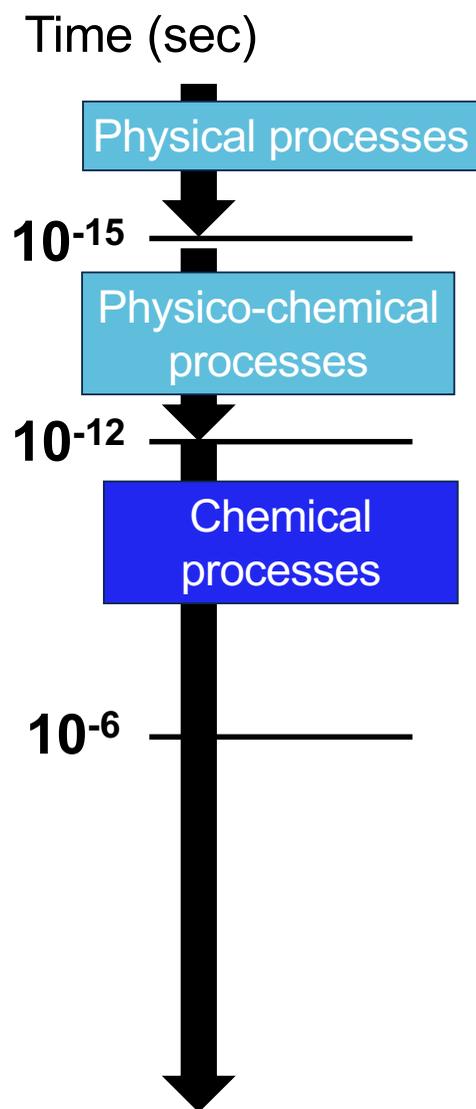*Excitation*   *Ionisation*

Spur creation

- Geant4-DNA starts from **altered water molecules** which underwent changes in their electronic configuration from physical processes occuring during the **physical stage**.

- Dissociation of water molecules by ionising radiation **during physico-chemical stage, creating molecules** in « spur ».

Electronic state	Dissociation channels	Fraction (%)
All single ionisation states	$H_3O^+ + \bullet OH$	100
Excitation state A1B1: $(1b1) \rightarrow (4a1/3s)$	$\bullet OH + H\bullet$	65
	$H_2O + \Delta E$	35
Excitation state B1A1: $(3a1) \rightarrow (4a1/3s)$	$H_3O^+ + \bullet OH + e^-_{aq}$	55
	$\bullet OH + \bullet OH + H_2$	15
	$H_2O + \Delta E$	30
Excitation state: Rydberg, diffusion bands	$H_3O^+ + \bullet OH + e^-_{aq}$	50
	$H_2O + \Delta E$	50
Dissociative attachment	$\bullet OH + OH^- + H_2$	100

Ref: J. Comput. Phys. 274, 841-882 (2014)

Chemistry / Chemical stage: Diffusion of molecules

Time (sec)

Physical processes

10^{-15}

Physico-chemical processes

10^{-12}

Chemical processes

10^{-6}

- After the physico-chemical stage, molecules **diffuse, breaking-up spurs**.

- Finally, the molecules are distributed **homogeneously**, after 1 μs from irradiation.

- Geant4-DNA uses a table to control the diffusion speed. The user can change these values.

Diffusion (spur break-up)

Random distribution
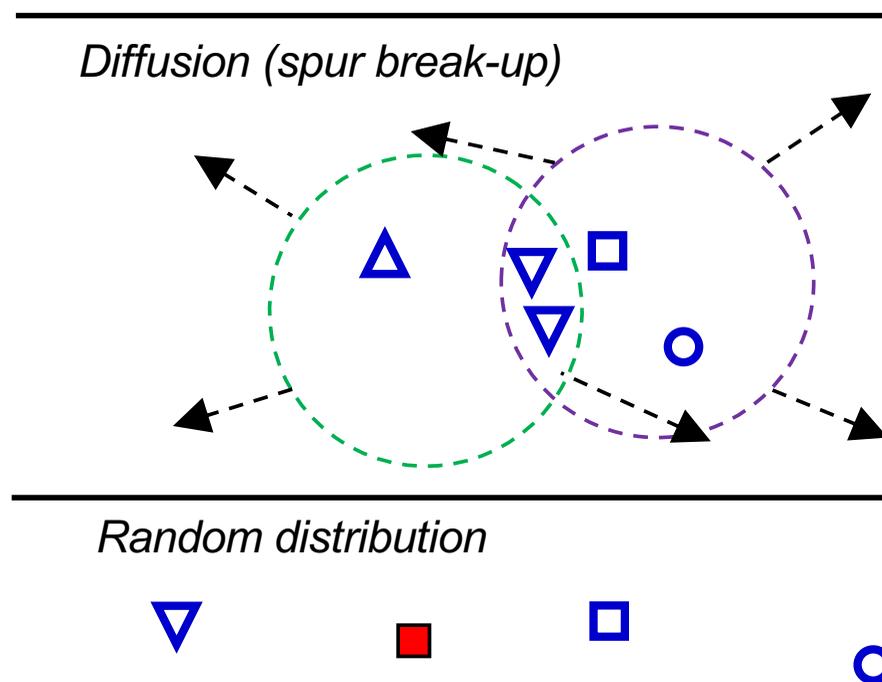
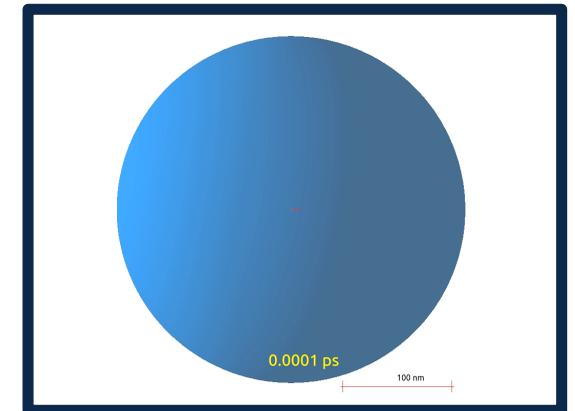| Species	Diffusion coefficient D $(10^{-9}\,m^2\,s^{-1})$
H_3O^+	9.0
$H\bullet$	7.0
OH^-	5.0
e^-_{aq}	4.9
H_2	5.0
$\bullet OH$	2.8
H_2O_2	1.4
H_2O	2.0

Ref: J. Comput. Phys. 274, 841-882 (2014)

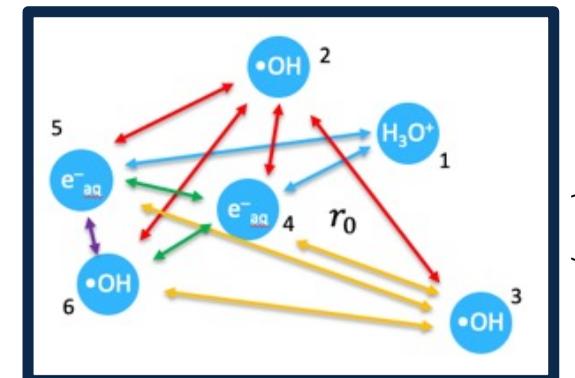# Chemistry / Chemical stage: Diffusion of molecules

■ SBS (Step-By-Step)

- **Brownian transport** of molecules using the Smoluchowski model

- Chemical species are represented by point objects which diffuse in the liquid medium (continuum). Chemical reactions are « **controlled by diffusion** »: two reactants interact when their separation is smaller than the reaction radius, which is calculated from the rate constant of the reaction.

- *8 species, 9 chemical reactions*

0.0001 ps

100 nm

+: Tracking of species
-: Very slow & memory cons.

■ IRT (Independent Reaction Time)

- From the 1980's by Clifford, Green et al., **widely used today**.

- Iterative process where the approximation of « **independent pairs** » is assumed: calculates the reaction times between all possible pairs of reactive species, as if they were isolated. Then, reactions occur one by one, starting with the pairs having the **shortest reaction times**.

- No longer necessary to diffuse the chemical species and to calculate the possible reactions between the species at each time step.

- *15 species, 72 chemical reactions (totally & partially diff. controlled)*

- A « **synchronous** » alternative hybrid version (« IRT-sync ») which gives all spatio-temporal info. on radicals required for combination with geometries
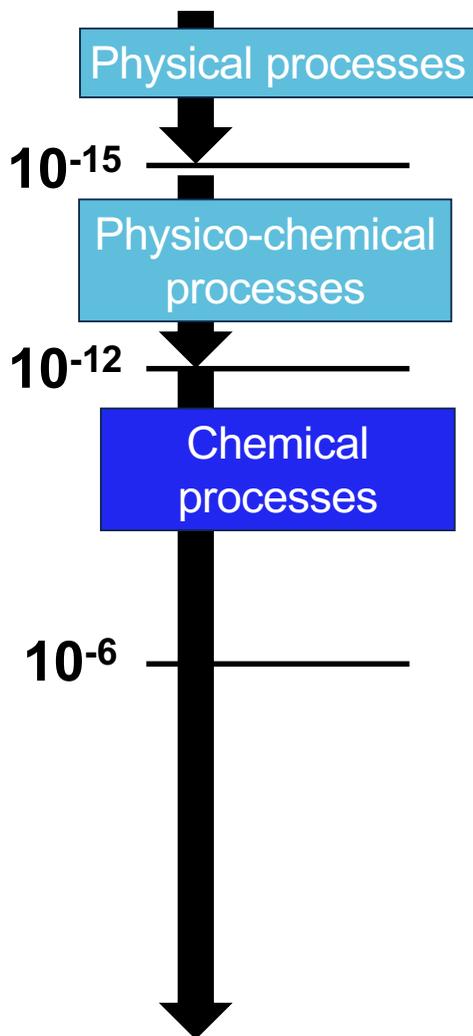

Clifford et al. (1986)

+: Very fast
-: Tracking of species

Chemistry / Chemical stage: Reactions

Time (sec)

Physical processes

10^{-15}

Physico-chemical processes

10^{-12}

Chemical processes

10^{-6}

- During the chemical stage, a molecule can encounter and react with another molecule, creating a new molecule.

- Geant4-DNA uses a table to manage the reaction probabilities, e.g. as listed.

$H\bullet + \bullet OH$ $\bullet OH + H_3O^+$ e^-_{aq}

$+H_2O$

H_2 $\bullet OH$ H_2O_2 H_3O^+ $\bullet OH^-$ $H\bullet$ e^-_{aq}
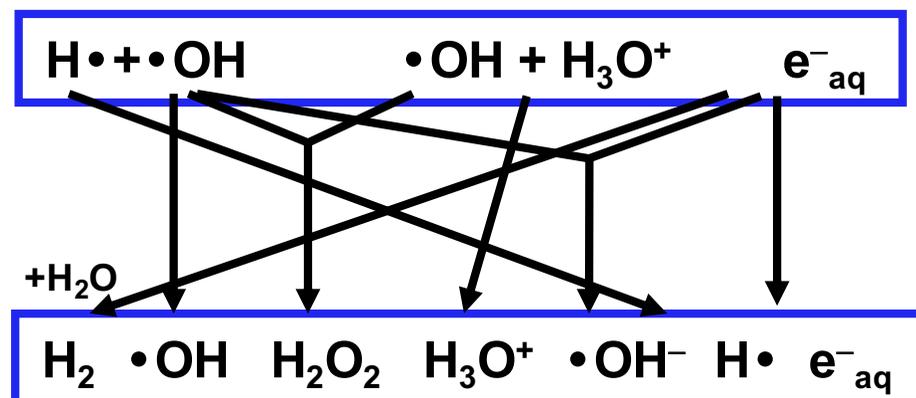
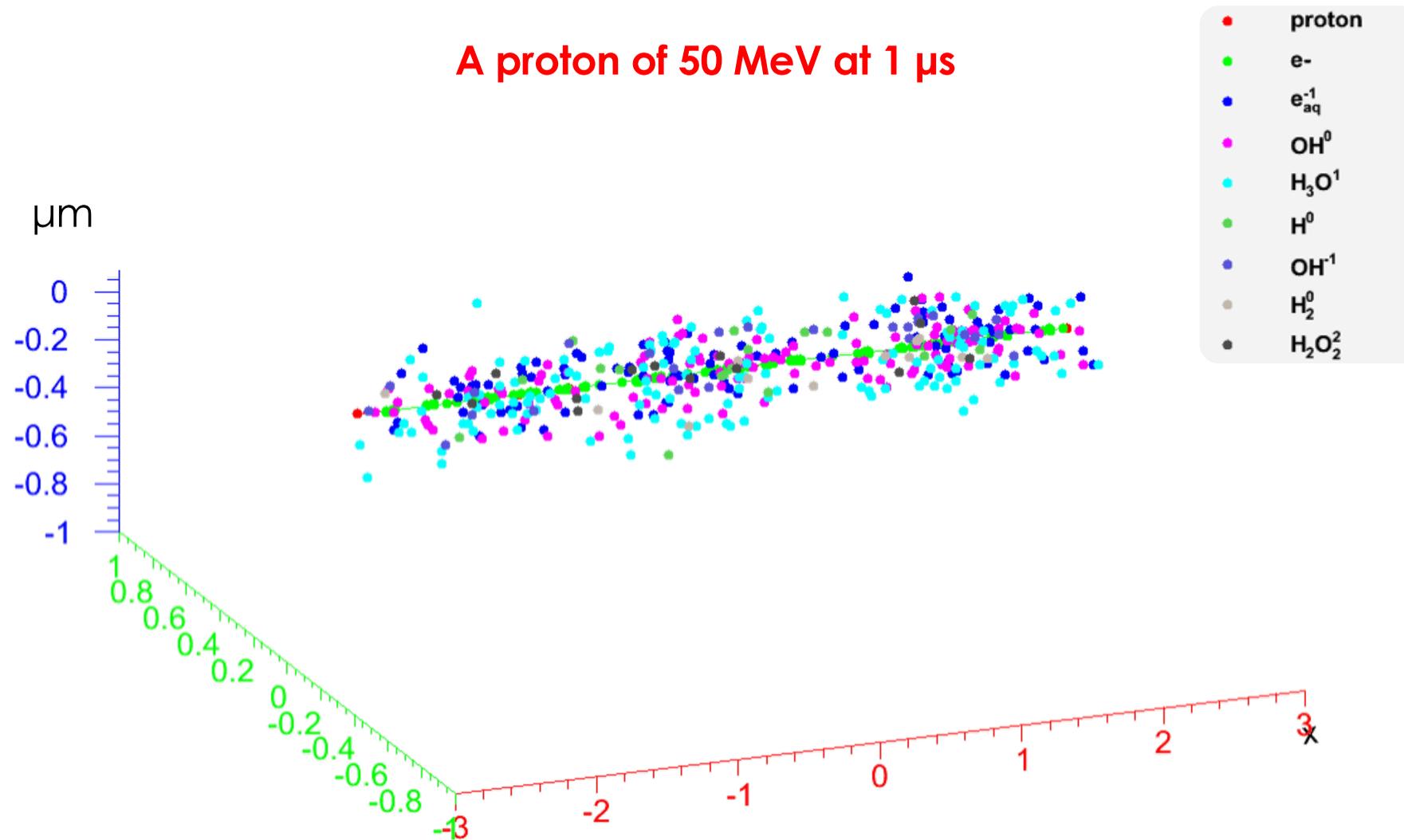| Reaction	Reaction rate $(10^7 \text{ m}^3 \text{ mol}^{-1} \text{ s}^{-1})$
$H_3O^+ + OH^- \rightarrow 2\,H_2O$	14.3
$\bullet OH + e^-_{aq} \rightarrow OH^-$	2.95
$H\bullet + e^-_{aq} + H_2O \rightarrow OH^- + H_2$	2.65
$H_3O^+ + e^-_{aq} \rightarrow H\bullet + H_2O$	2.11
$H\bullet + \bullet OH \rightarrow H_2O$	1.44
$H_2O_2 + e^-_{aq} \rightarrow OH^- + \bullet OH$	1.41
$H\bullet + H\bullet \rightarrow H_2$	1.20
$e^-_{aq} + e^-_{aq} + 2\,H_2O \rightarrow 2\,OH^- + H_2$	0.50
$\bullet OH + \bullet OH \rightarrow H_2O_2$	0.44

Ref: J. Comput. Phys. 274, 841-882 (2014)

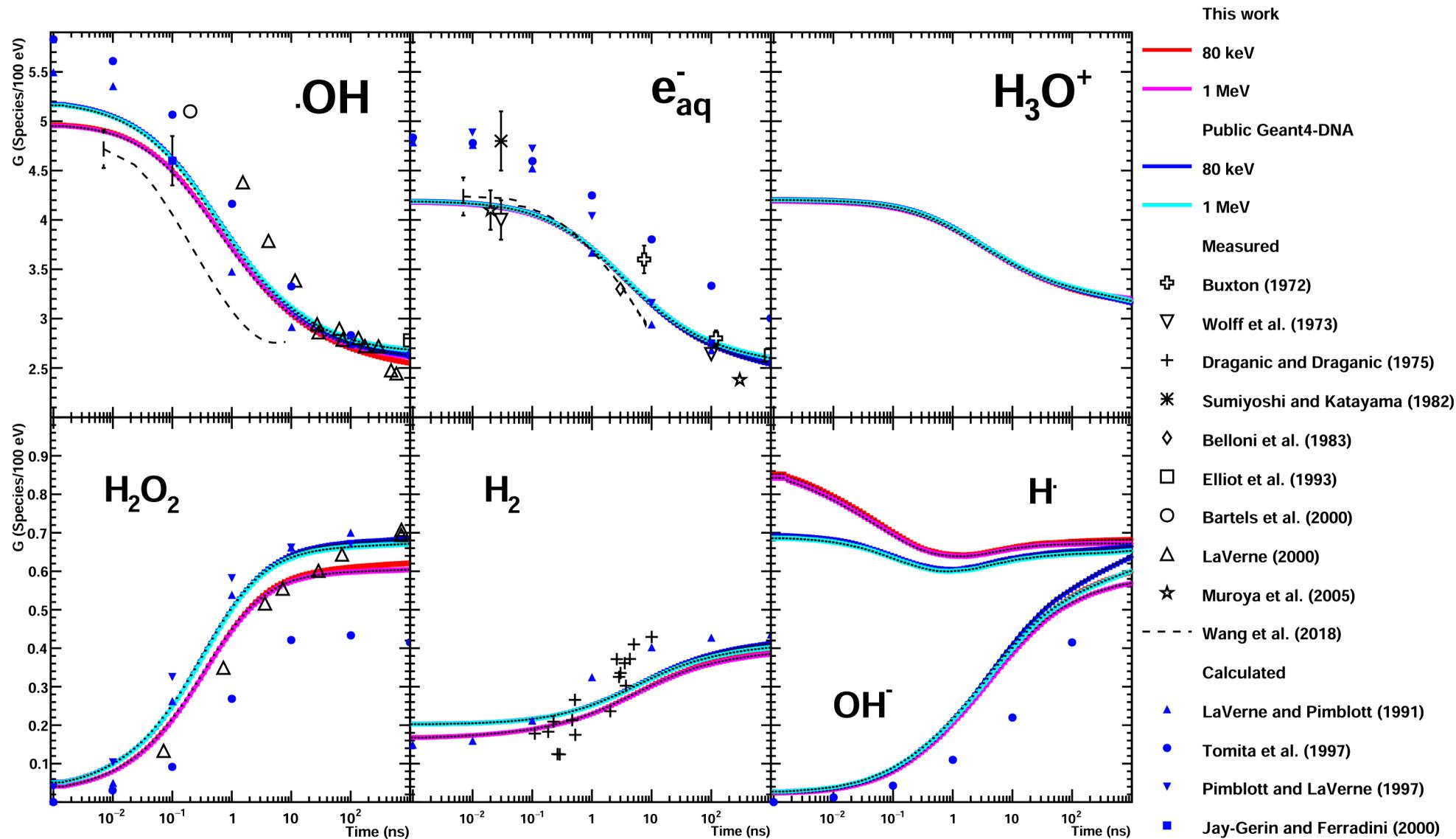# Distribution of chemical molecules using Geant4-DNA

A proton of 50 MeV at 1 ps
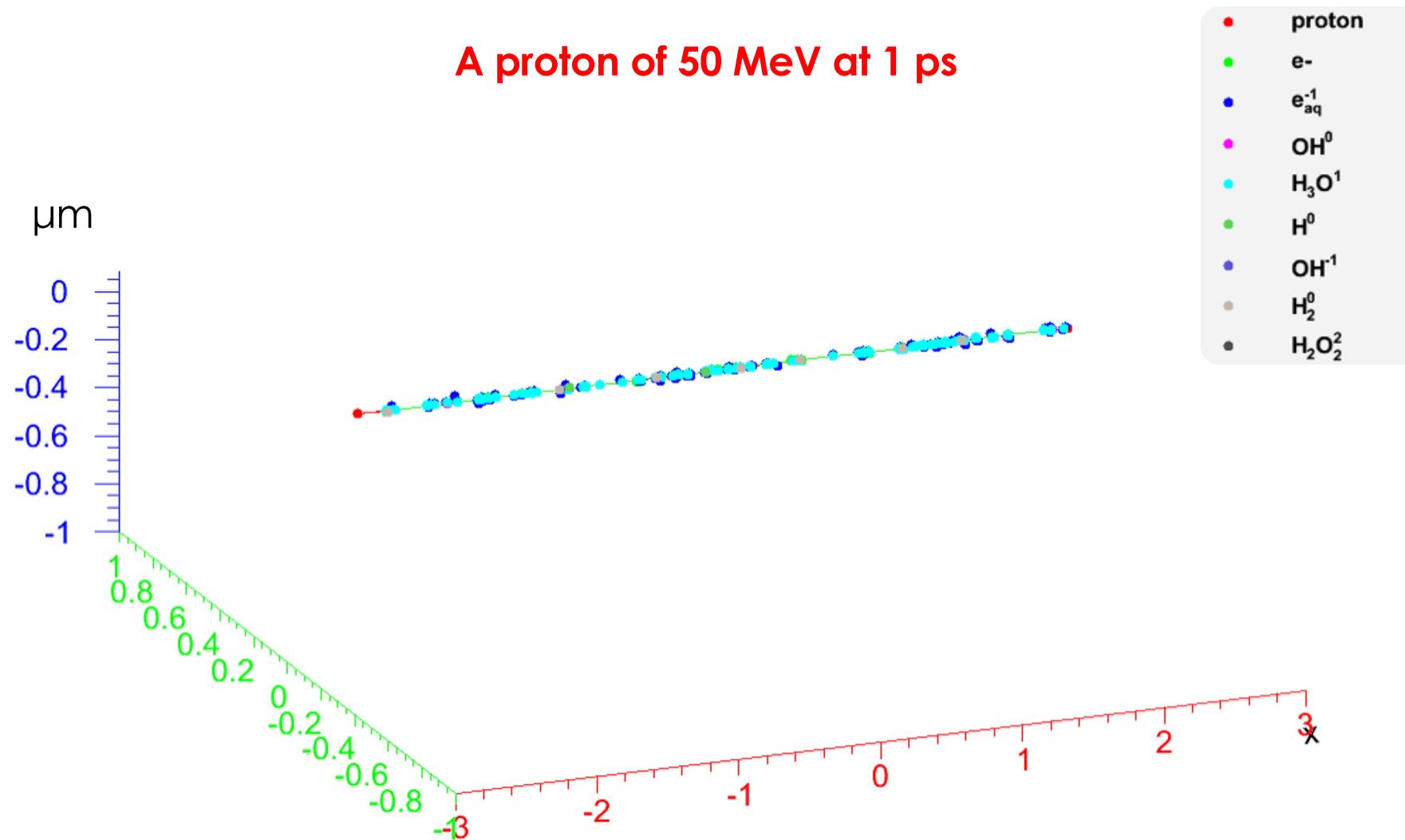
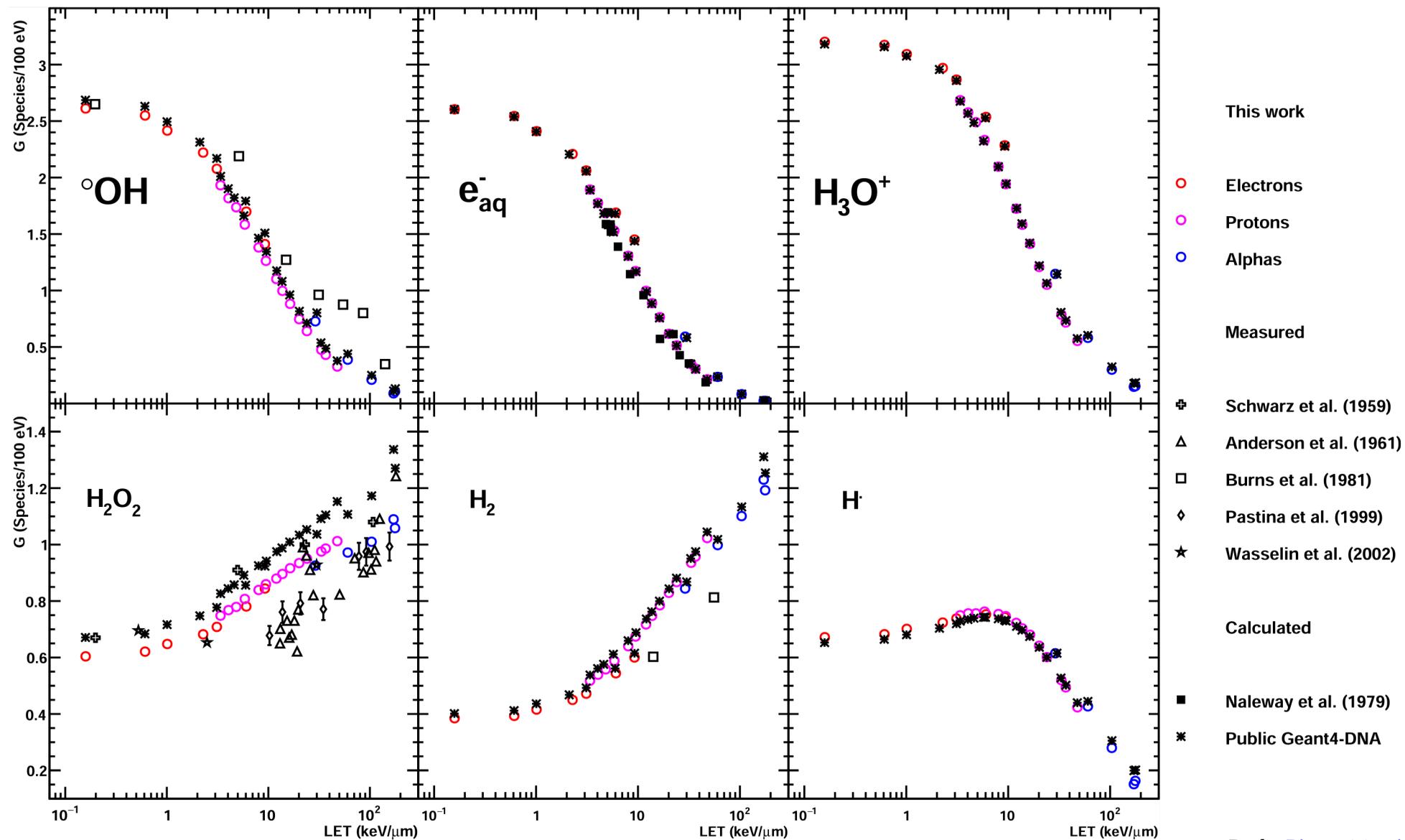# Distribution of chemical molecules using Geant4-DNA

A proton of 50 MeV at 1 µs

Validation and verification of chemistry: G-value vs time
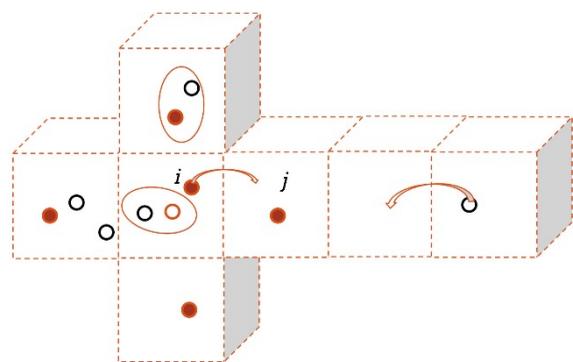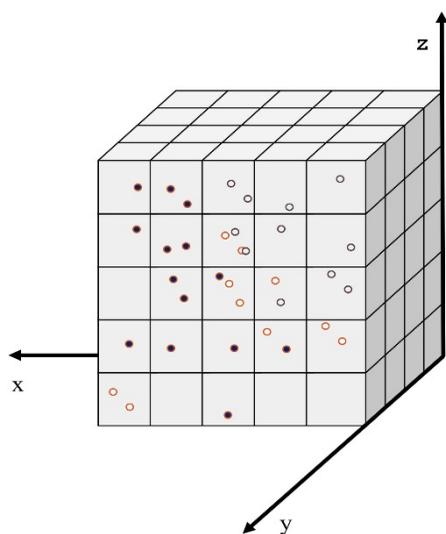

Ref.: Phys. Med. 88, 86-90 (2021)

Ref.: Phys. Med. 88, 86-90 (2021)

The "mesoscopic" model

Compartment-based model

- For SBS, IRT model, computation time remains the main drawback when simulations deal with a **large number of species** or **long-time scales**.
- An alternative approach has recently been implemented in Geant4-DNA using the **compartment-based** representation

Using Brownian dynamics and Smoluchowski theory

Using Reaction-Diffusion Master Equation (RDME)

✓ Homogeneous
✓ Species react with each other in the same voxel
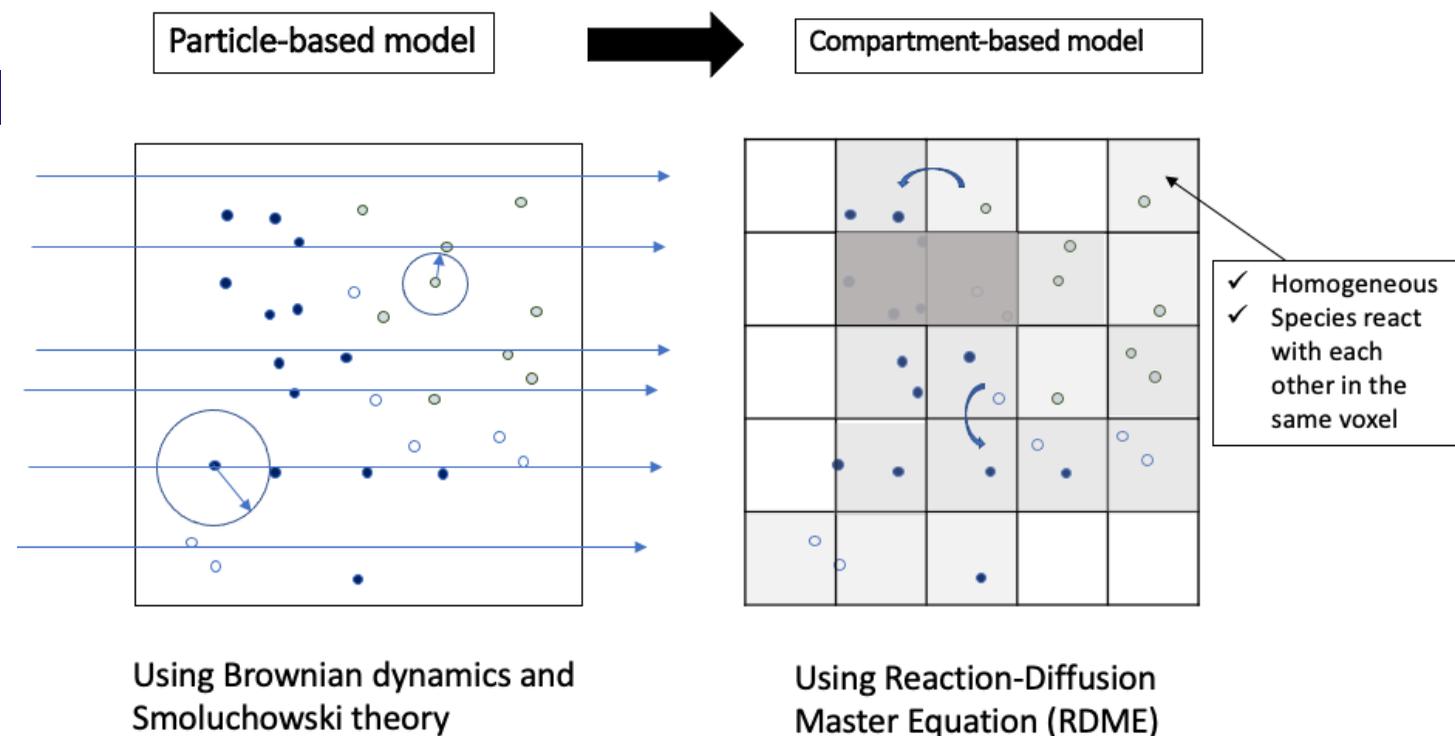
- Well-mixed species in voxels
- Species can react with each other in the voxels
- Diffusion is modelled by jumps between adjacent voxels

Promising approach for ultra-high dosre rate radiolysis simulations...

See more details in Chemistry talk

GEANT4-DNA

Contents of this talk

➢ Context of the Geant4-DNA project
➢ Physical stage
➢ Physico-chemical & chemical stage
➢ Geometrical models
➢ DNA damage and biological models
➢ More…

GEANT4-DNA

The Geant4-DNA approach

Physical stage
step-by-step modelling of physical interactions of incoming & secondary ionising radiation with biological medium (liquid water)

- Excited water molecules
- Ionised water molecules
- Solvated electrons

Physico-chemical/chemical stage
- Radical species production
- Diffusion
- Mutual chemical interactions

Biological repair

Prediction of biological parameter yields using semi-empirical biological repair model from nDSB and complex DSB fraction.

Geometrical models
DNA strands, chromatin fibres, chromosomes, whole cell nucleus, cells...
for the prediction of damage resulting from direct and indirect hits

- Protein/enzyme kinetics
- DNA rejoining
- Cell survival

DIRECT DNA damage

INDIRECT DNA damage

t=0   t=10^{-15}s   t=10^{-9}~10^{-6} s

Geant4-DNA geometry models (in examples)
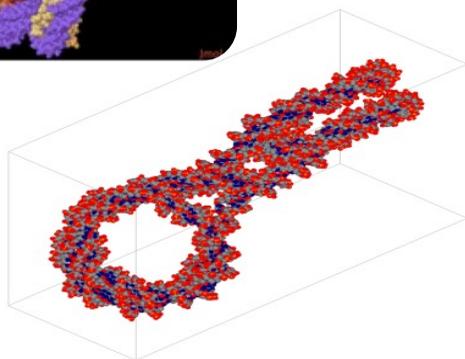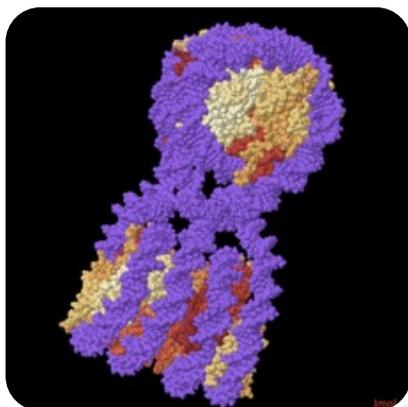
10^{-10} 10^{-9} 10^{-6} [m]

- **Atomic** scale
  - `pdb4dna`

- **Molecular** scale
  - `wholeNuclearDNA`
  - `dnadamage1,2`
  - `dsbandrepair`
  - `molecularDNA`

- **Cellular** scale or larger
  - `microbeam`
  - `neuron`
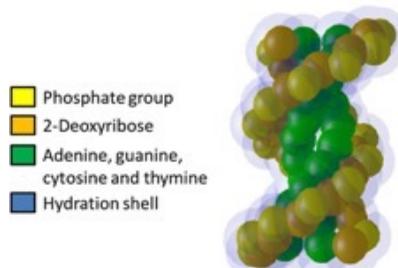
Phosphate group
2-Deoxyribose
Adenine, guanine, cytosine and thymine
Hydration shell
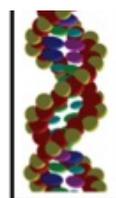
20 nucleotides

ine fibre
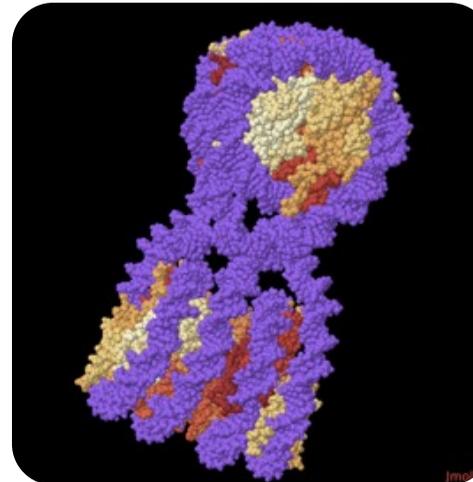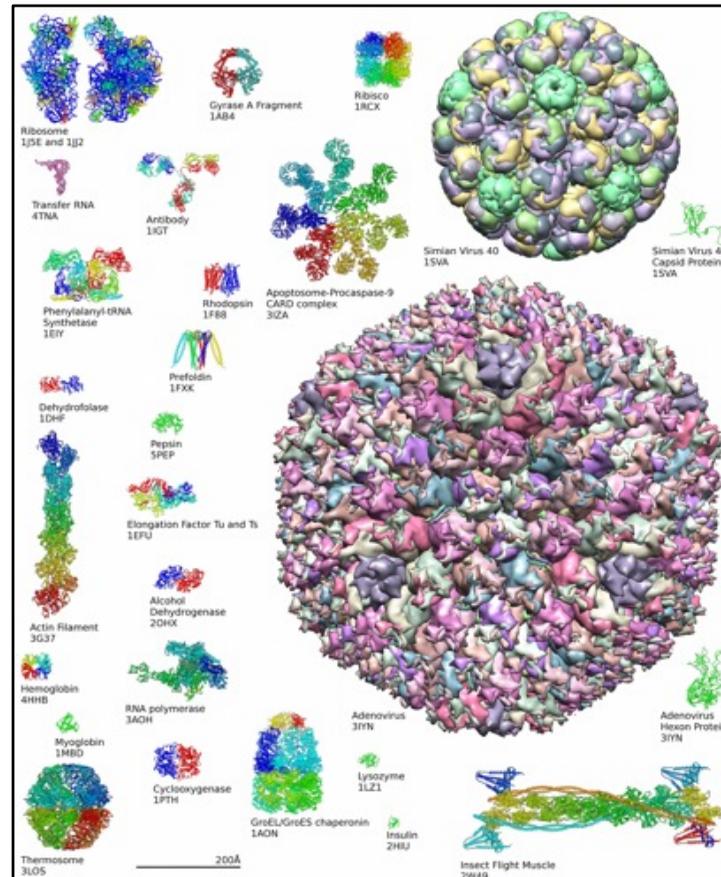
Fractal geometry

Cell nucleus

100 µm

GEANT4-DNA
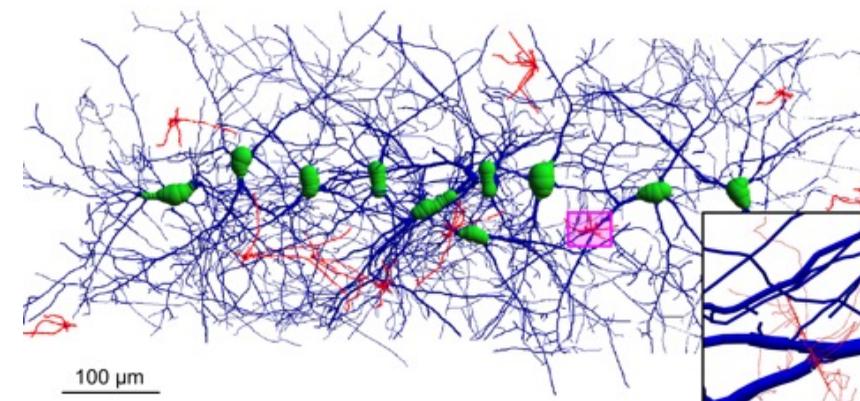
Geometry: **Atomic** scale pdb4dna example

- **Protein Data Bank (PDB)**
  http://www.rcsb.org/pdb/
  - 3D structure of molecules
  - Proteins
  - Nucleic acids

Ref.: Comput. Phys. Commun. 192, 282-288 (2015)

E.g.: 1ZBB.pdb
— Tetranucleosome
— 2 nucloosomes: 347 pairs of bases
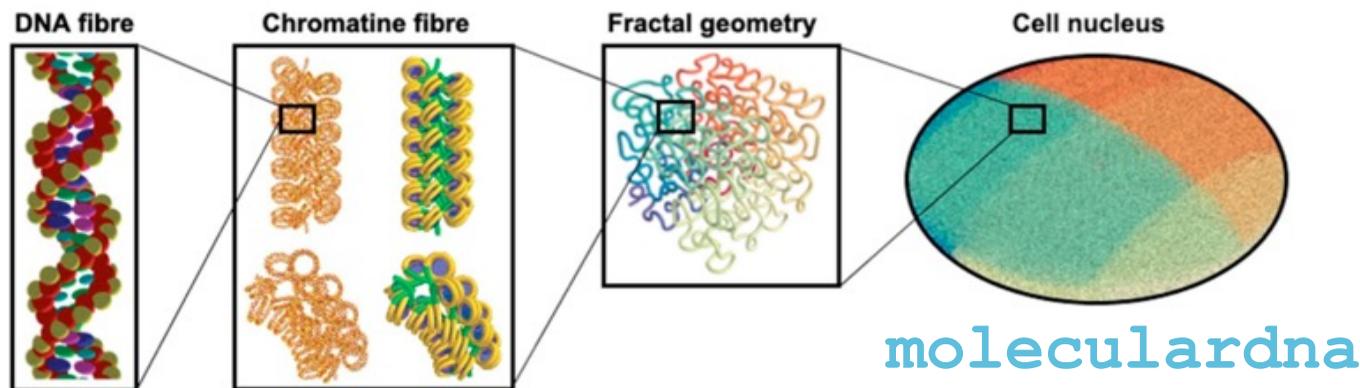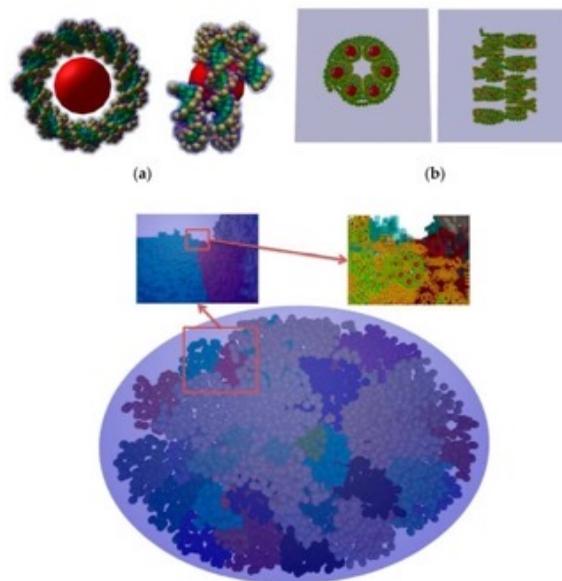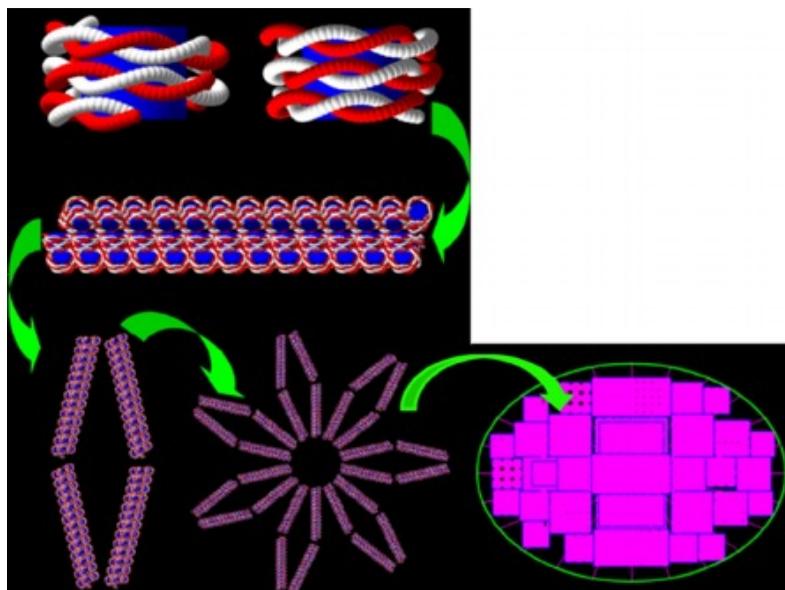— $(9,5 \times 15,0 \times 25,1 \text{ nm}^3)$

```
HEADER    STRUCTURAL PROTEIN/DNA              08-APR-05  1ZBB
TITLE     STRUCTURE OF THE 4_601_167 TETRANUCLEOSOME
...
ATOM      1 O5' DA I  1    70.094 16.969 123.433 0.50238.00    O
ATOM      2 C5' DA I  1    70.682 18.216 123.054 0.50238.00    C
ATOM      3 C4' DA I  1    69.655 19.289 122.776 0.50238.00    C
...
TER   14223     DT J 347
...
HELIX    1  1 GLY A  44  SER A  57 1                     14
HELIX    2  2 ARG A  63  ASP A  77 1                     15
...
SHEET    1  A 2 ARG A  83  PHE A  84 0
SHEET    2  A 2 THR B  80  VAL B  81 1 O  VAL B  81  N  ARG A  83
```

See implementation in
geant4/examples/extended/medical/dna/pdb4dna

See http://geant4-dna.org → Examples

Geometry: Molecular scale

wholeNuclearDNA

moleculardna

DNA fibre — Chromatine fibre — Fractal geometry — Cell nucleus

- Geant4-DNA offers **5 examples** of cell nucleus models, which consist of molecular-based DNA geometry models
  - wholeNuclearDNA*
  - dnadamage1,2
  - dsbandrepair
  - moleculardna

- These examples offer the possibility of simulating the **water radiolysis*** as well as the **energy deposition** of ionizing radiation at a nanometric scale within a geometrical representation of the **whole DNA molecule contained in a cell nucleus**.

See http://geant4-dna.org → Examples

Geometry: **Cellular** scale or Larger

neuron

100 μm
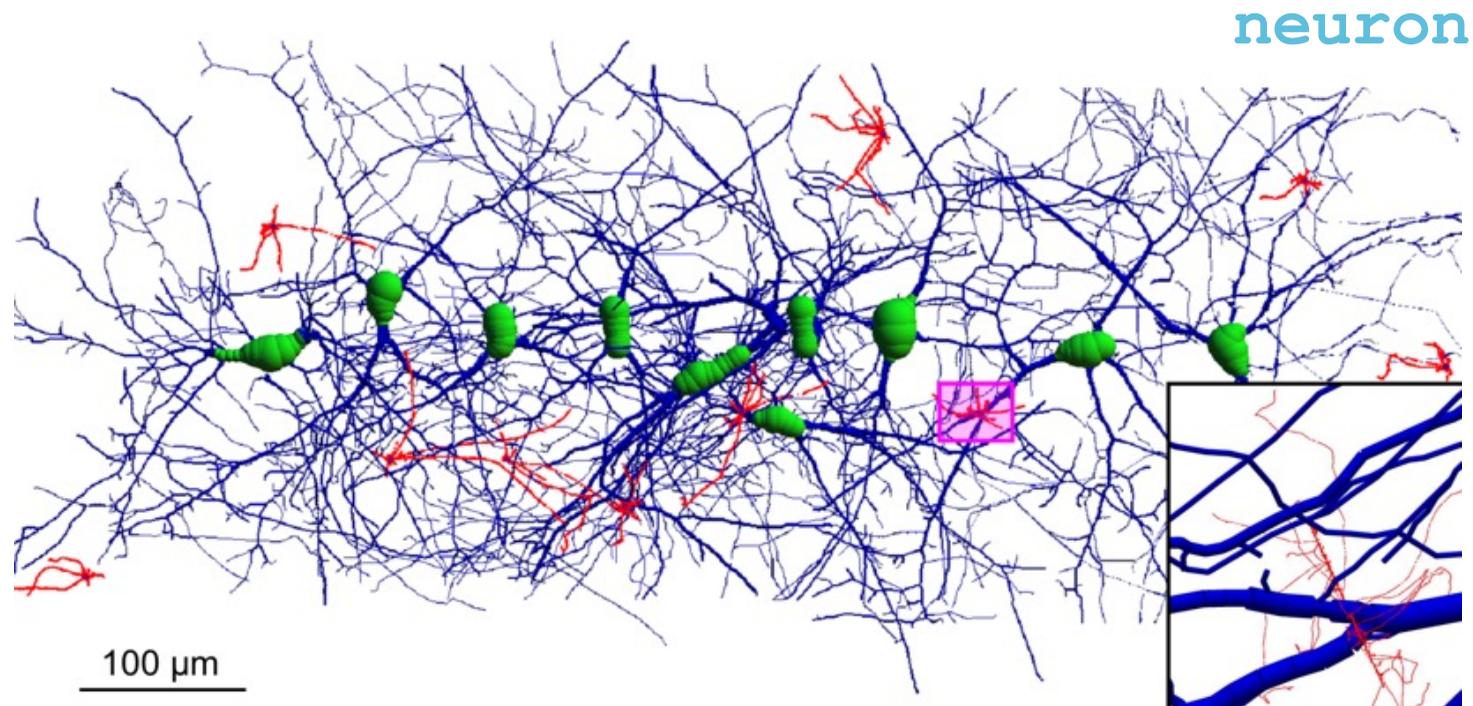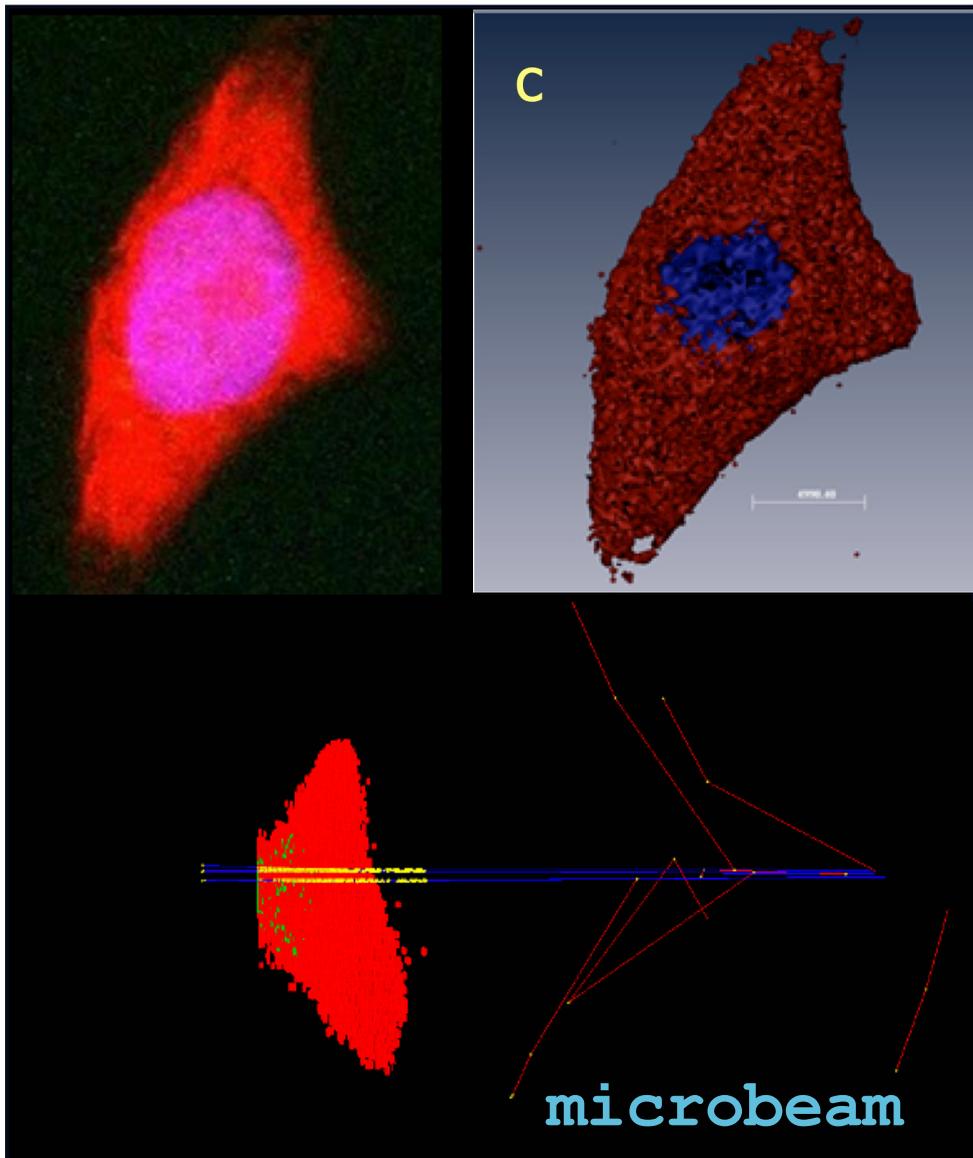
microbeam

- Geant4-DNA also offers 2 examples that provide realistic geometry of a cell and neurons:
  - `microbeam`
  - `neuron`

See http://geant4-dna.org → Examples

Contents of this talk

➢ Context of the Geant4-DNA project
➢ Physical stage
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➢ Geometrical models
➢ DNA damage and biological models
➢ More…

GEANT4-DNA

The Geant4-DNA approach

DNA damage and biological models

- Geant4-DNA follows a **standard** DNA damage calculation approach:
  - **Direct** action: **Structural damage to DNA molecules induced by excitation/ionisation processes**
    - Score local energy deposition in a nanoscopic domain: nanodosimetric approach
    - Two damage probability models are commonly used:
      - Threshold model (KURBUC model)
      - Proportional model (PARTRAC model)
  - **Indirect** action: **Structural damage to DNA molecules induced by a chemical process**, typically interaction with reactive oxygen species
    - A constant probability model can be used (the probability should be adjusted)

- **DNA damage classification**:
  - The complexity of the DNA damage structure affects the subsequent biological repair process and its endpoint. In particular, two strand breaks within a short distance (leading to physical disconnection of the DNA fiber), so-called **Double Strand Break (DSB)**, induce crucial radiobiological effects such as cell death.
  - Thus, the classification of DNA damage is one of the most important issues in evaluating the radiobiological effects.
  - So far, two classification models are proposed: Nikjoo's model and the Standard DNA Damage (SDD) model.

Damage classification: Nikjoo's classification

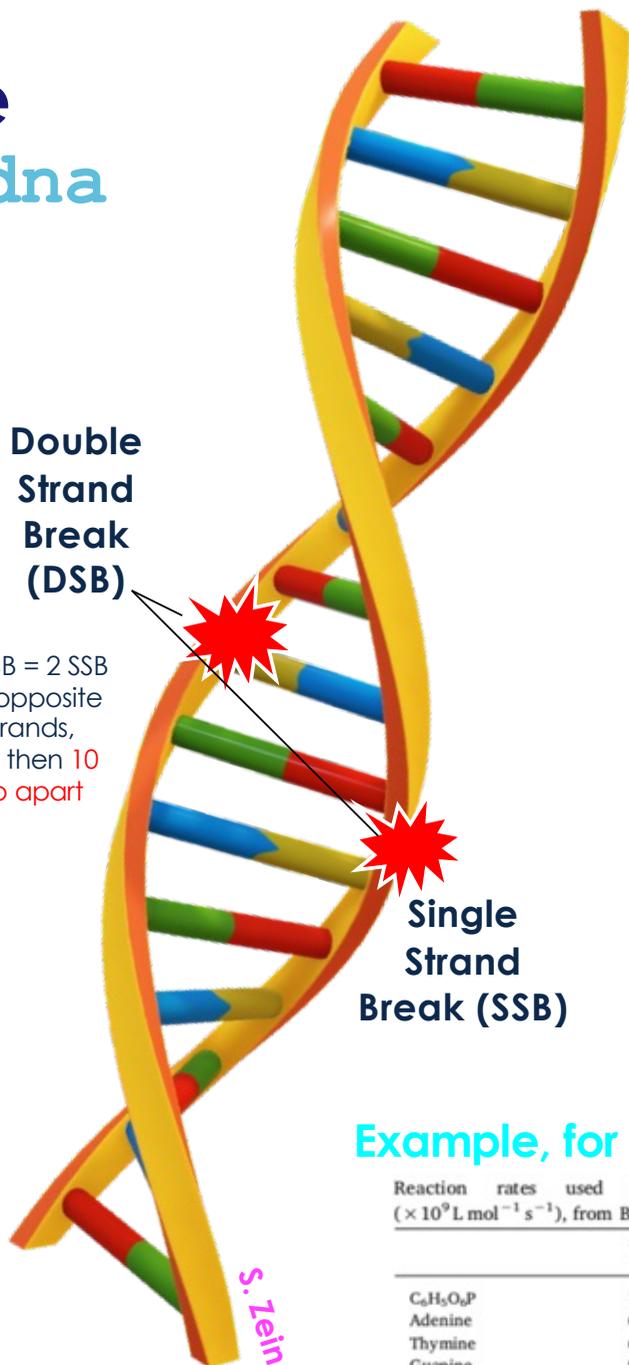# Damage classification: SDD classification

Ref.: Radiat. Res. 191(1), 76-92 (2019)

48
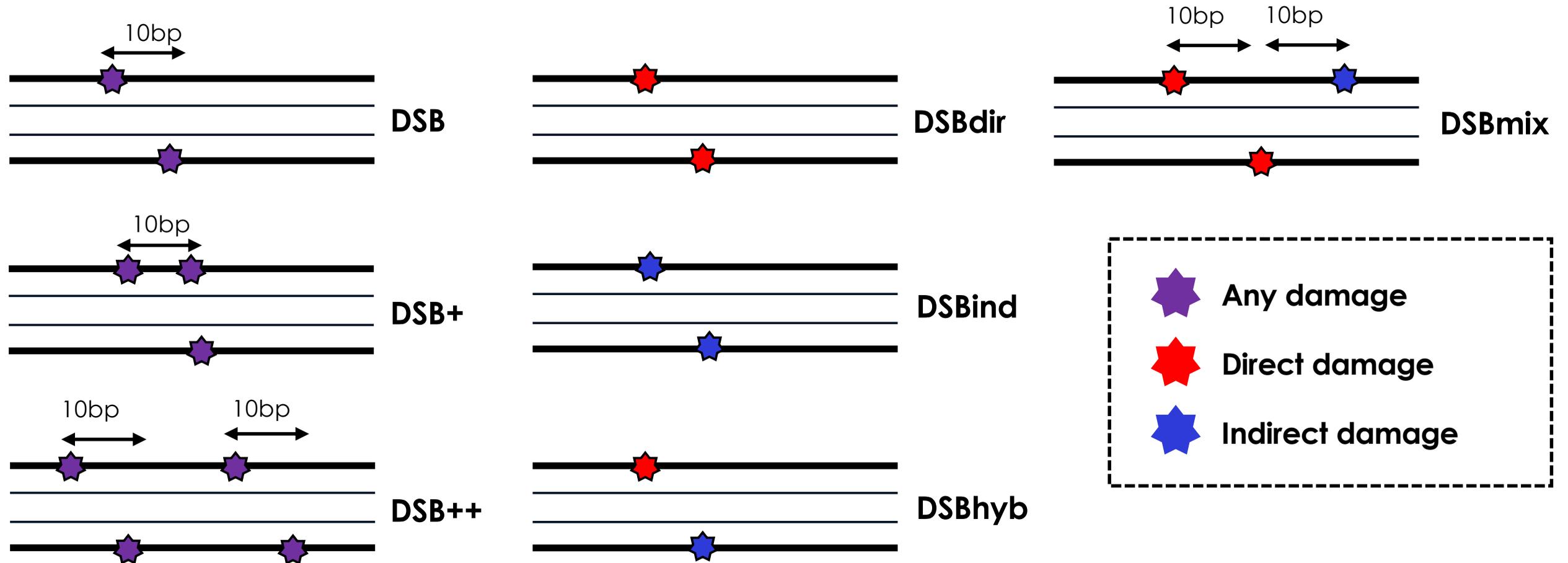
Important: parameter choice – e.g. `moleculardna`

CAUTION TRIPPING HAZARD

Physics

DIRECT damage induction

1. **Choice of G4DNA physics constructor**

2. **Volume for energy deposition scoring in DNA backbone (S or P molecule)**

3. **Probability of Single Strand Break induction in DNA backbone**
   - Threshold, linear…

NON-DIRECT damage induction

1. **Choice of G4DNA chemistry constructor**
   - Including reactions with DNA components

2. **Probability of non-direct SSB induction**
   - •OH on DNA backbone : e.g. 40.5 %

3. **Distance from DNA to kill radicals (mimic scavenging in cells)**

4. **Histones considered as full scavengers (in cells)**

5. **Radiolysis maximum time steps**

6. **Chemical stage end time**

Double Strand Break (DSB)

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

Single Strand Break (SSB)

S. Zein

Example, for item 2:

Energy assigned to closest molecule in radius r of deposit

E.g. 2 A° for ~1 hydration layer
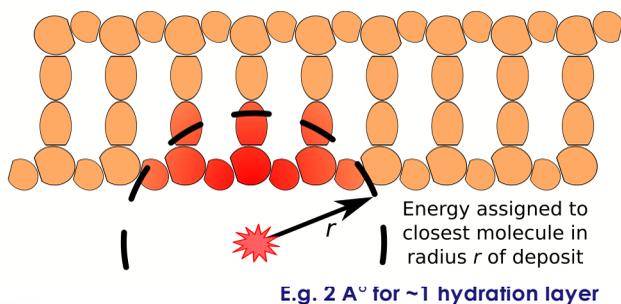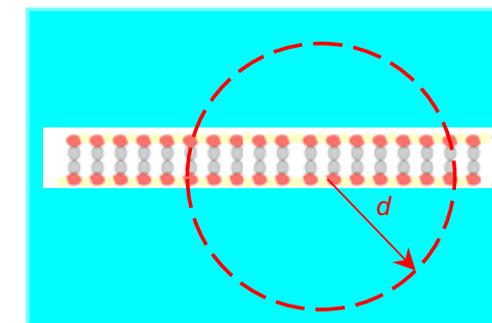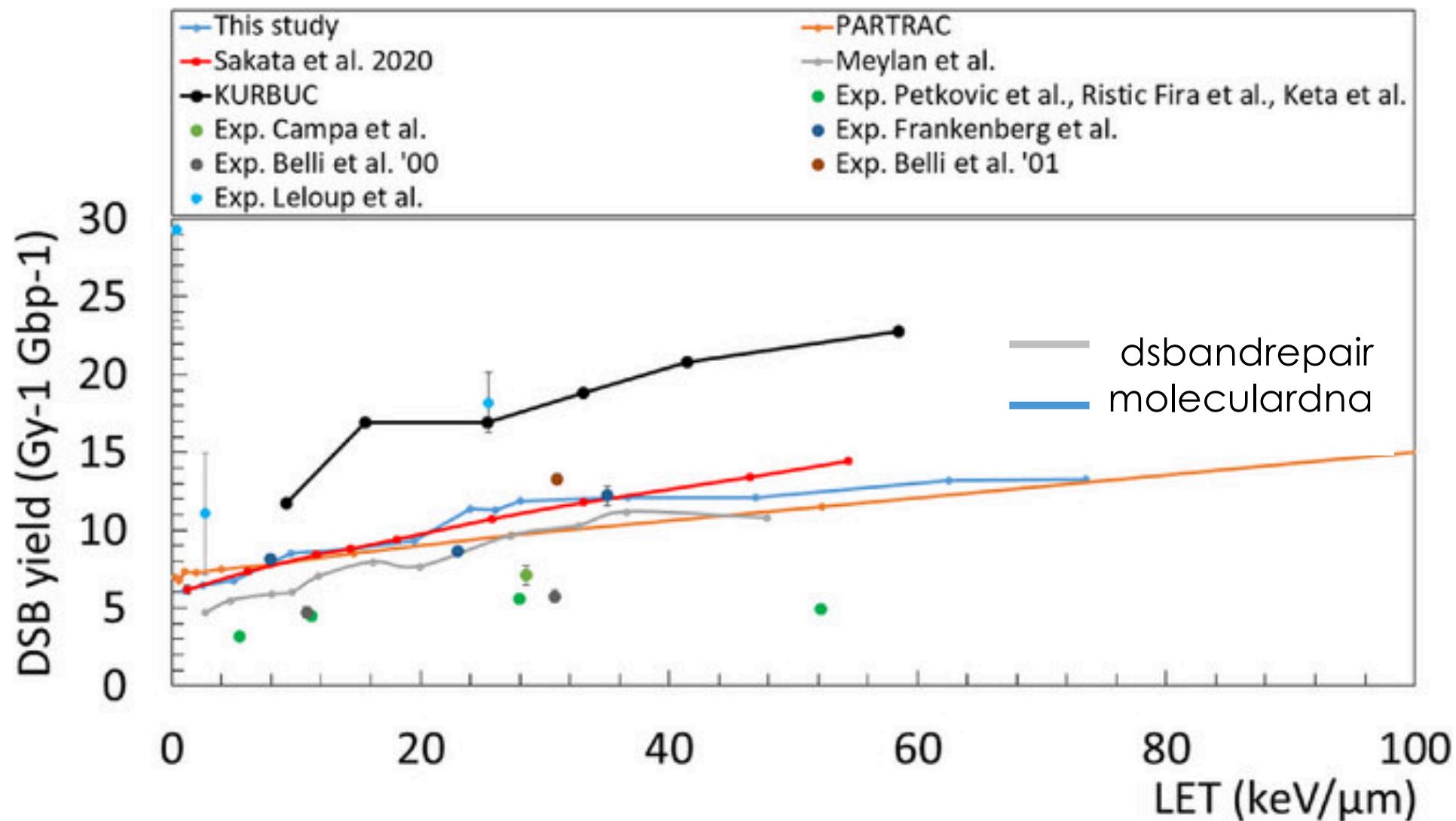
Example, for item 1:

Reaction rates used between radicals and DNA components ($\times 10^9$ L mol^{-1} s^{-1}), from Buxton et al. [65].

	˙OH	H˙	e_{aq}^-
$C_5H_5O_6P$	1.8	0.029	0.01
Adenine	6.1	0.10	9.0
Thymine	6.4	0.57	18.0
Guanine	9.2	–	14.0
Cytosine	6.1	0.092	13.0

Example, for item 3:

d

GEANT4-DNA

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Validation and verification: Damage yield from protons

Ref.: Prec. Radiat. Oncol. 7, 4-14 (2023)

Validation and verification: Fragment yield
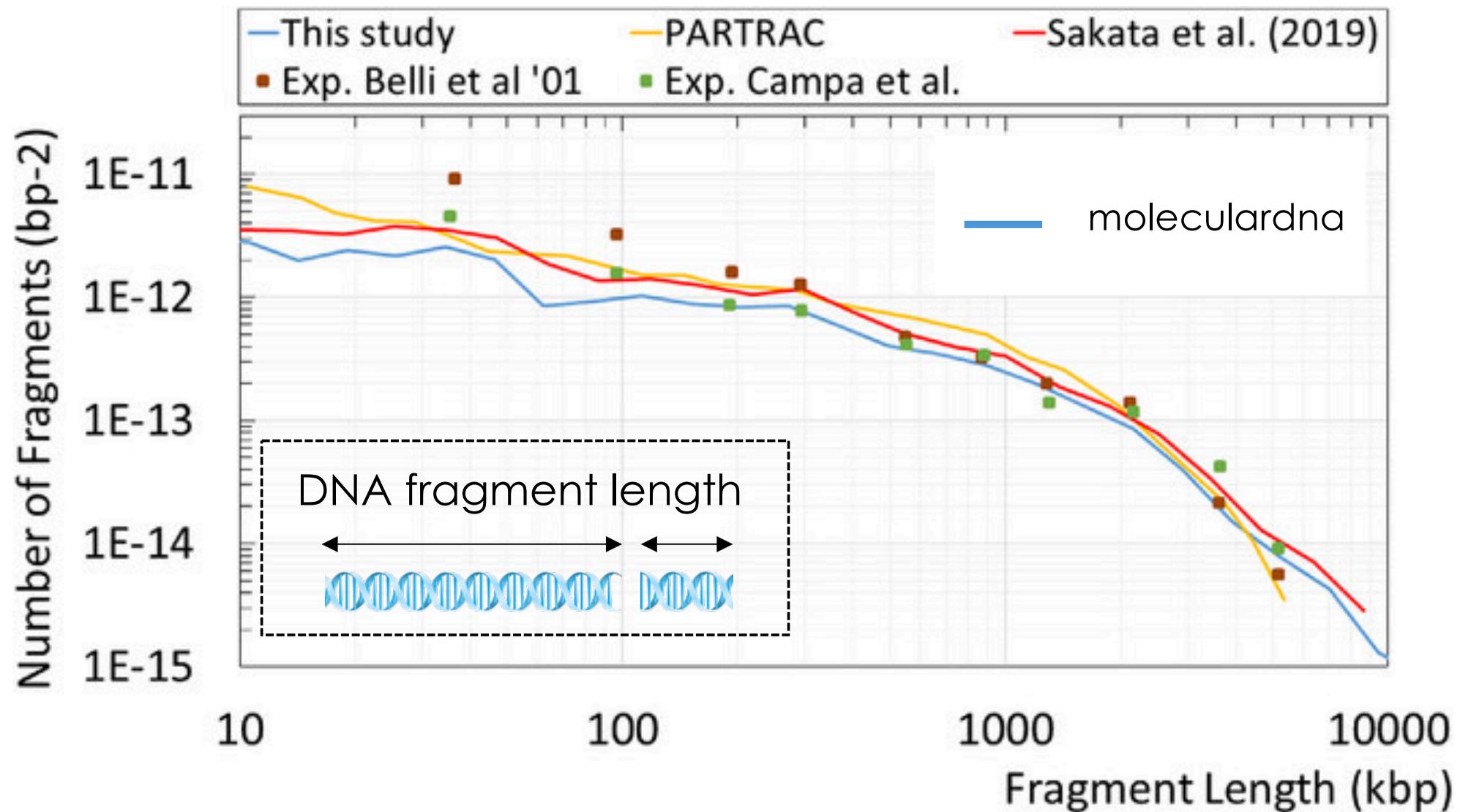
Validation and Verification: Indirect damage fraction

Geant4-DNA
Exp. Xray (Hirayama)
Exp. C (Hirayama)
Exp. Fe (Hirayama)
Exp. C (Ito)
Exp. Si (Ito)
Exp. Fe (Ito)

moleculardna
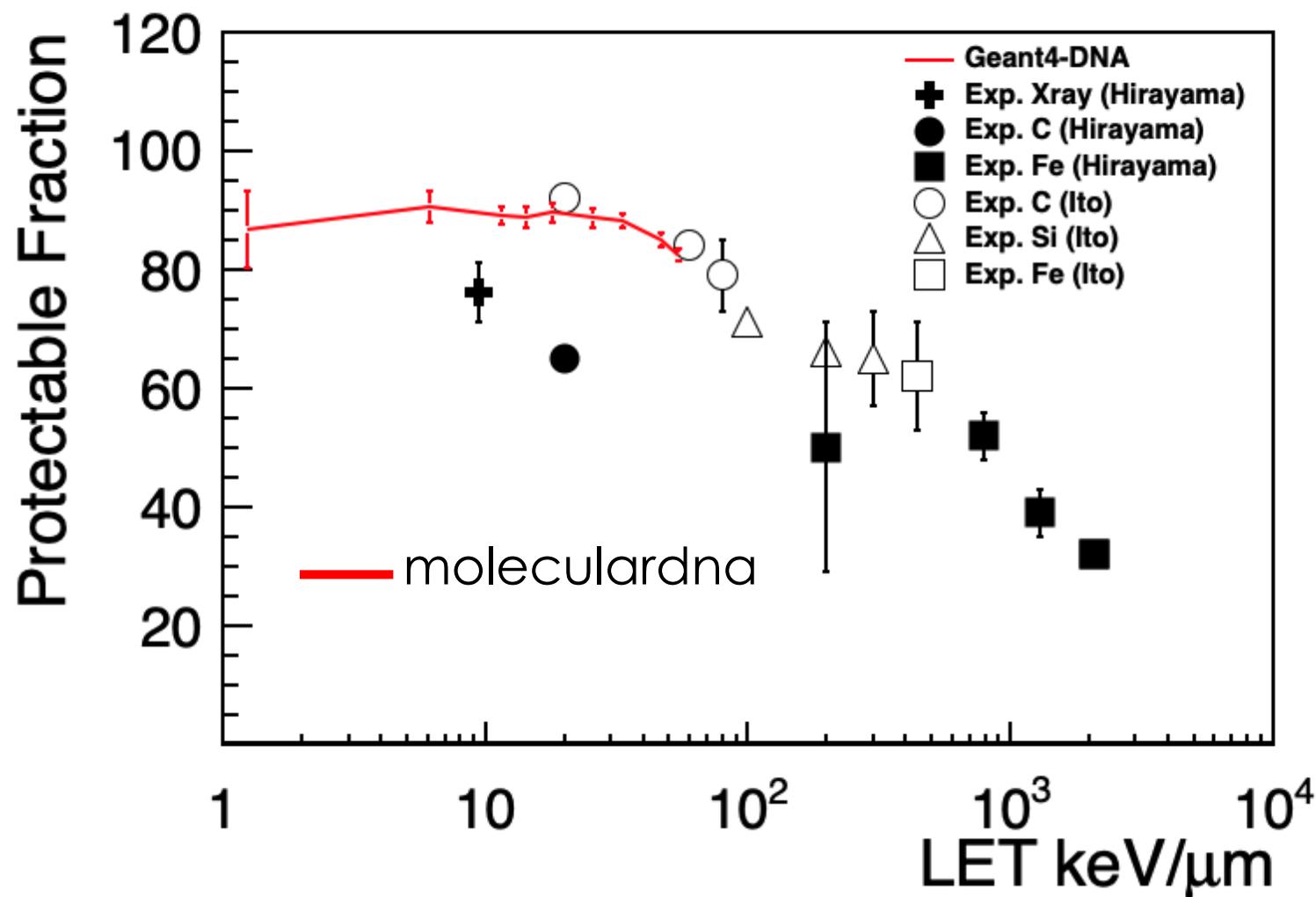
Protectable fraction
(damage type based)

$$\frac{N_{DSB_{ind}} + N_{DSB_{hyb}}}{N_{DSB_{dir}} + N_{DSB_{mix}} + N_{DSB_{ind}} + N_{DSB_{hyb}}}$$

DSBdir

DSBmix

DSBind

DSBhyb

10bp   10bp

Direct damage
Indirect damage

The Geant4-DNA approach

Physical stage
step-by-step modelling of physical interactions of incoming & secondary ionising radiation with biological medium (liquid water)

- Excited water molecules
- Ionised water molecules
- Solvated electrons

Physico-chemical/chemical stage
- Radical species production
- Diffusion
- Mutual chemical interactions

Geometrical models
DNA strands, chromatin fibres, chromosomes, whole cell nucleus, cells… for the prediction of damage resulting from direct and indirect hits

DIRECT DNA damage

INDIRECT DNA damage

Prediction Block

Biological repair

Prediction of biological parameter yields using semi-empirical biological repair model from nDSB and complex DSB fraction.

- Protein/enzyme kinetics
- DNA rejoining
- Cell survival

$t=0$

$t=10^{-15}s$

$t=10^{-9} \sim 10^{-6}\ s$

DNA damage and biological models

- Prediction models are able to **link DNA damage to biological endpoints**:

  - **Belov model**: Prediction model of **protein/enzyme accumulation yield** from the number of DSBs and **irreparable fraction**. In Geant4-DNA applications, the irreparable fraction is assumed to be the fraction of complex DSBs w.r.t the total number of DSBs.

  - **Two-Lesion kinetic (TLK)** model: The TLK model model links the number of simple-/complex-DSBs and **cell survival**, considering the rejoining of DSBs and lethality of the residual DNA damage.

  - **Local Effect Model (LEM)-IV**: The LEM-IV calculates **cell survival** from a number of lethal damage that considers the induction of DSBs and their spatial distribution and fast-/slow-rejoining of DSBs.

- Geant4-DNA examples offer such biological prediction models:

  - `wholeNuclearDNA`: No biological prediction model provided (Physics only)

  - `dsbandrepair`: Belov model, TLK model and LEM-IV model

  - `moleculardna`: Belov model, TLK model

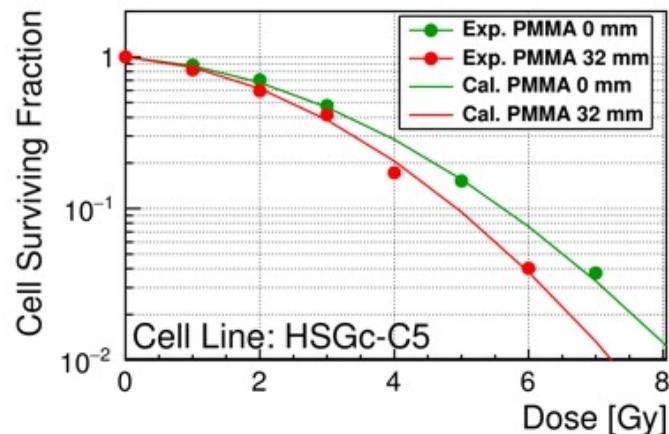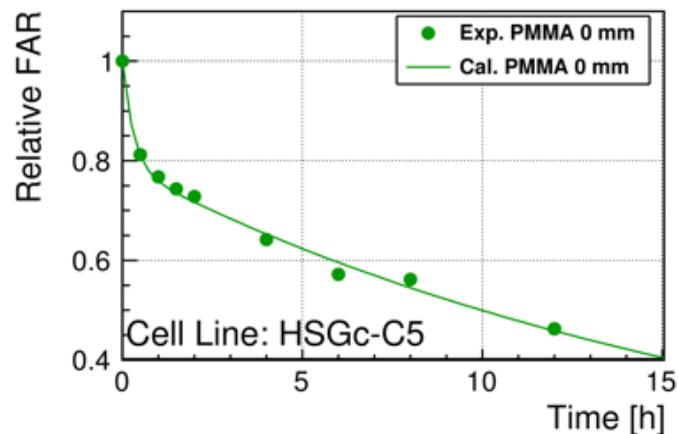# Validation and verification: time evolution of **foci yields**
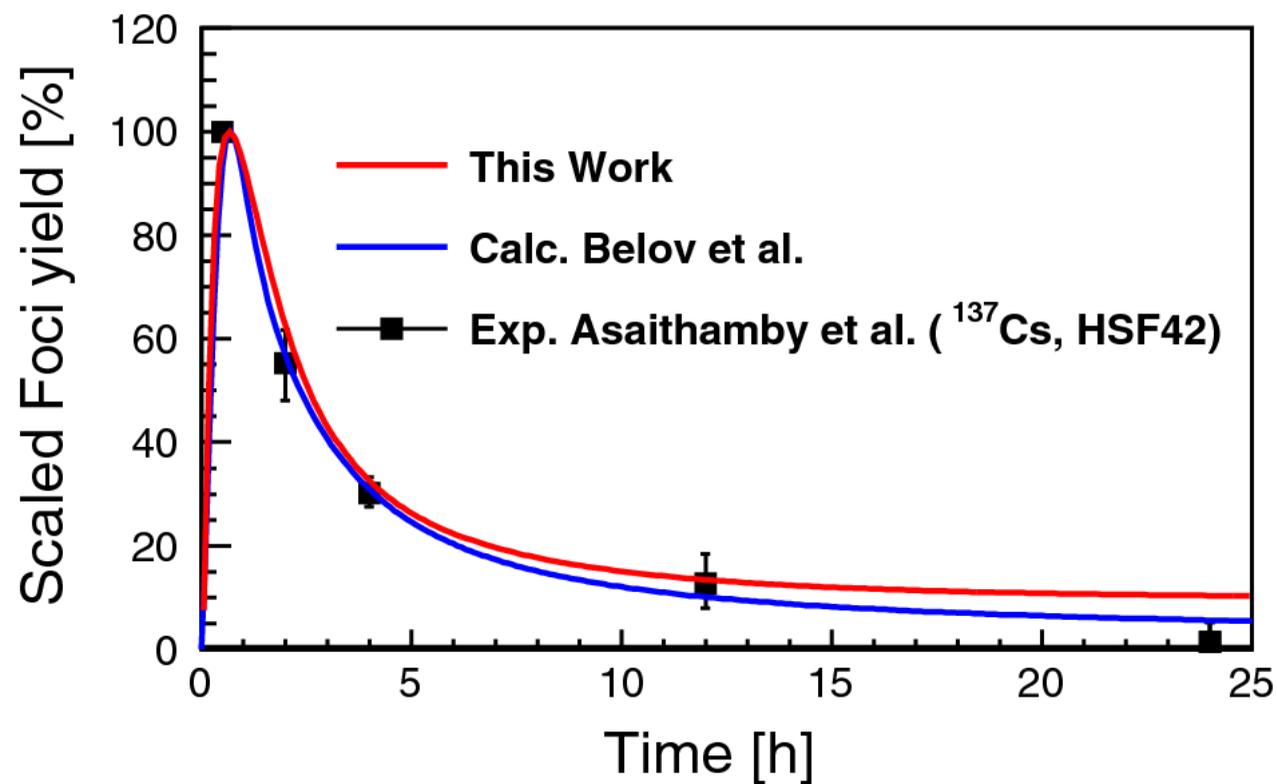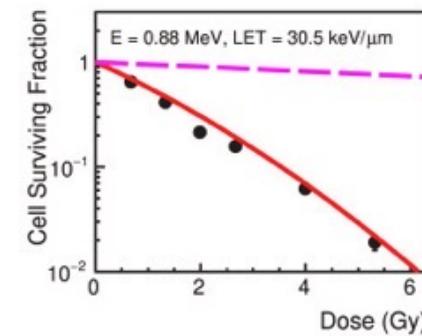

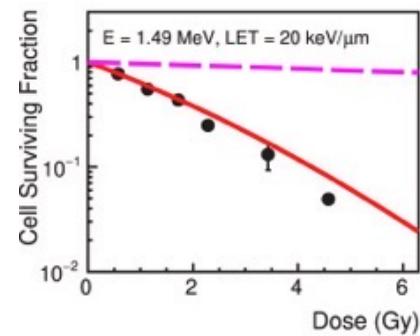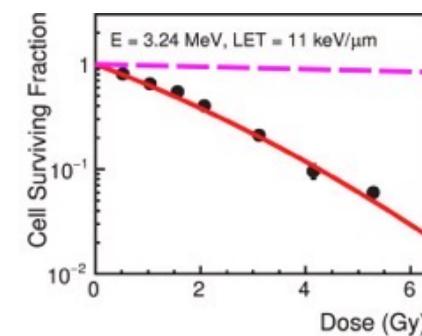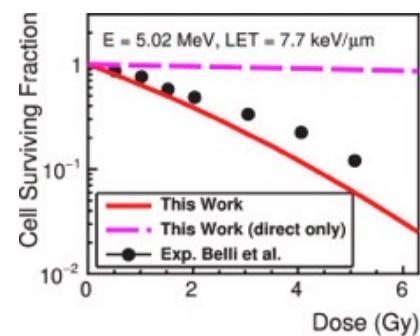**moleculardna**: for gamma-ray (^{137}Cs)
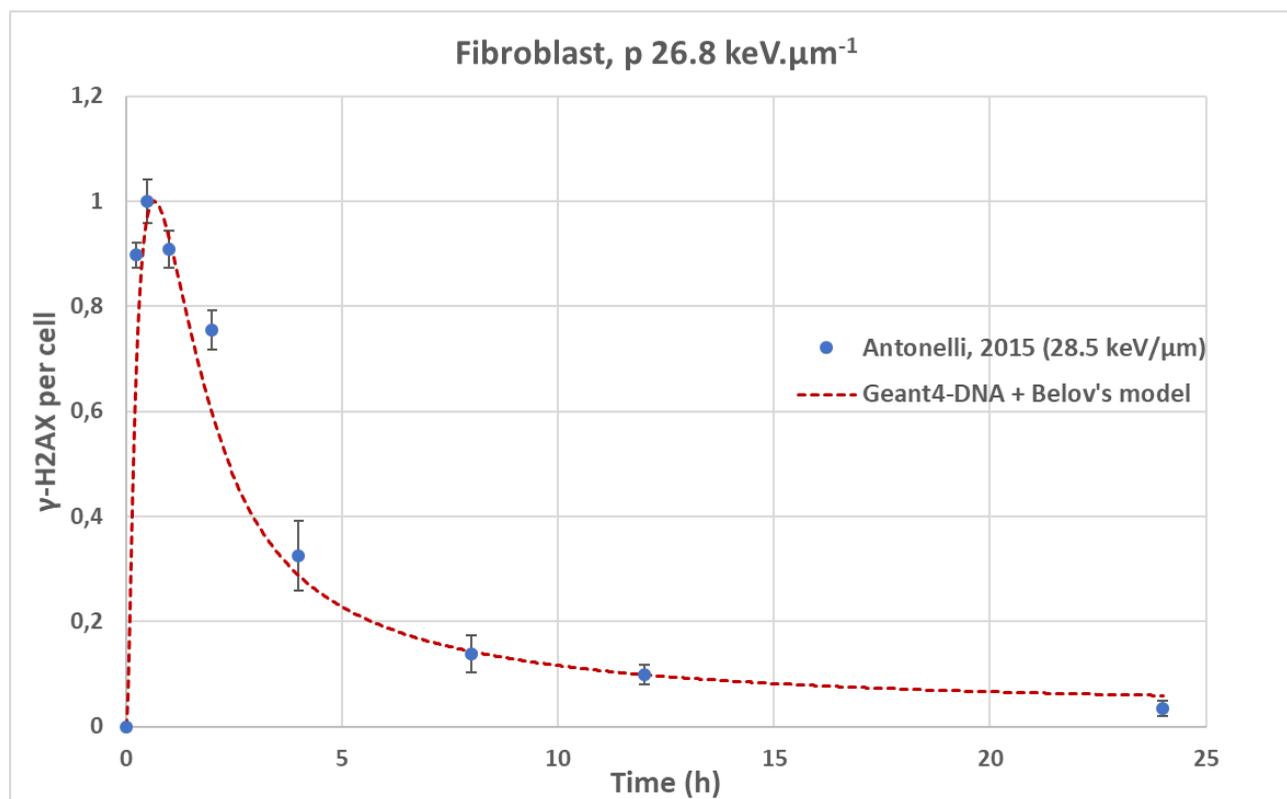
dsbandrepair: for proton
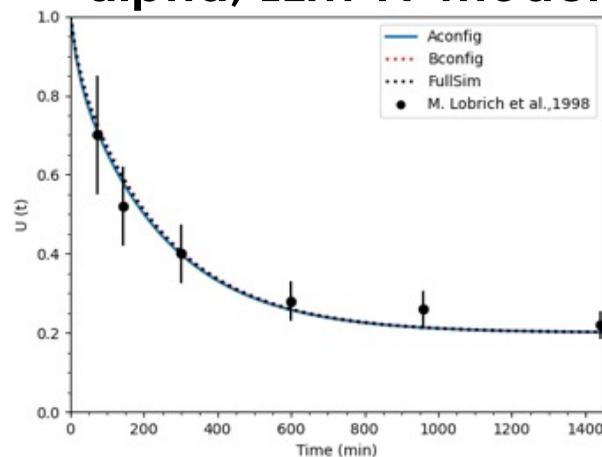
GEANT4-DNA

Validation and verification: DNA rejoining & cell survival

`moleculardna`: proton, TLK model, HSGc-G5 cell
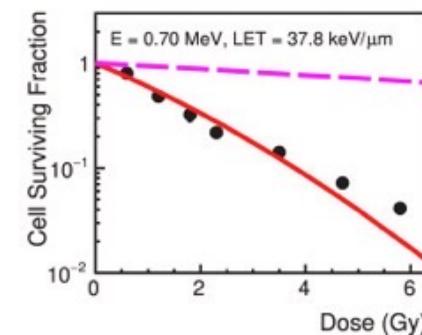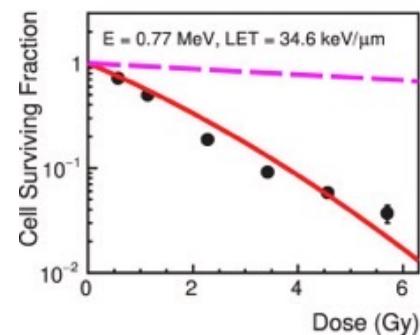
`moleculardna`: proton, TLK model, V79 cell

`dsbandrepair`: alpha, LEM-IV model

`dsbandrepair`: alpha, TLK model
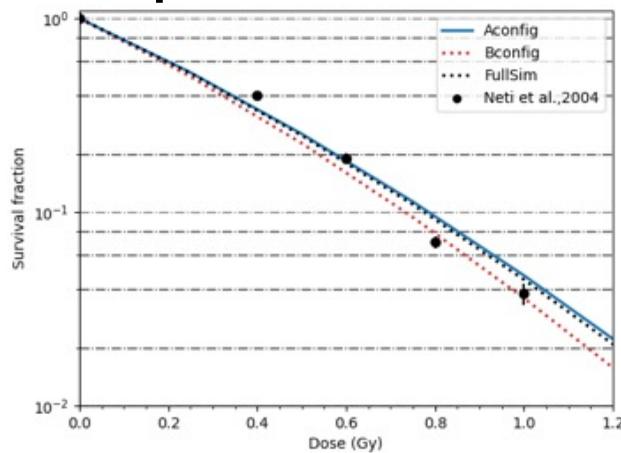
Ref.: Cancers 13, 6046 (2021), Phys. Med. 105, 102508 (2023), Phys. Med. 124 (2024) 103422

GEANT4-DNA

Contents of this talk

- ➢ Context of the Geant4-DNA project
- ➢ Physical stage
- ➢ Physico-chemical & chemical stage
- ➢ Geometrical models
- ➢ DNA damage and biological models
- ➢ More…

Geant4-DNA

Geant4-DNA examples available in Geant4

	Example code name	Purpose	Location
Track structure physics	dnaphysics	• Usage of Geant4-DNA Physics processes • Automatic combination of Standard EM with Geant4-DNA Physics processes • variable density	$G4INSTALL/examples/extended/medical/dna
	microdosimetry	"Hand" combination of Standard EM or Low Energy EM processes with Geant4-DNA Physics processes	$G4INSTALL/examples/extended/medical/dna
	range	Range simulation	$G4INSTALL/examples/extended/medical/dna
	spower	Calculation of stopping power	$G4INSTALL/examples/extended/medical/dna
	mfp	Mean Free Path	$G4INSTALL/examples/extended/medical/dna
	wvalue	W values	$G4INSTALL/examples/extended/medical/dna
	svalue	S values	$G4INSTALL/examples/extended/medical/dna
	microyz	Microdosimetry spectra (y, z)	$G4INSTALL/examples/extended/medical/dna
	microprox	Microdosimetry proximity functions	$G4INSTALL/examples/extended/medical/dna
	slowing	Electron slowing down spectra	$G4INSTALL/examples/extended/medical/dna
	clustering	Clustering code	$G4INSTALL/examples/extended/medical/dna
	icsd	Usage of alternative bio-materials	$G4INSTALL/examples/extended/medical/dna
	splitting	Acceleration of processes	$G4INSTALL/examples/extended/medical/dna
	AuNP	Gold NP	$G4INSTALL/examples/extended/medical/dna
	jetcounter	ICSD in a Jet Counter nanodosimeter	$G4INSTALL/examples/extended/medical/dna
Radiolysis chemistry	chem1, chem2, chem3, chem4, chem5, chem6	Usage of Geant4-DNA chemistry (SBS & IRT)	$G4INSTALL/examples/extended/medical/dna
	scavenger	UI for IRT & scavengers	$G4INSTALL/examples/extended/medical/dna
	UHDR	Mesoscopic chemistry	$G4INSTALL/examples/extended/medical/dna
Geometries & damage	wholeNuclearDNA	Cell nucleus (physics only)	$G4INSTALL/examples/extended/medical/dna
	pdb4dna	Interface to PDB database	$G4INSTALL/examples/extended/medical/dna
	neuron	3D neural network	$G4INSTALL/examples/extended/medical/dna
	dnadamage1	DNA damage induction in a chromatin fiber	$G4INSTALL/examples/extended/medical/dna
	dnadamage2	DNA damage induction in plasmids	$G4INSTALL/examples/extended/medical/dna
	dsbandrepair	DNA damage induction in various biological models	$G4INSTALL/examples/advanced/dna
	moleculardna	DNA damage induction in various biological models	$G4INSTALL/examples/advanced/dna
	microbeam	3D cellular phantom	$G4INSTALL/examples/advanced
TS & CH physics	TestEm5	Atomic deexcitation tagging	$G4INSTALL/examples/extended
	TestEm12	DPK	$G4INSTALL/examples/extended
	TestEm14	Extraction of cross sections	$G4INSTALL/examples/extended

Where to find more information ?

https://geant4-dna.org/

Our publications are also announced on X

@geant4_dna

Geant4 Virtual Machine

Examples, publications

Documentation

Contact us

An international collaboration

62 collaborators in 2025

- · **Radiation physics**
- · **Radiation chemistry**
- · **Radiobiology**
- · **Computing**

Map labels:

- G4AI
- ESA
- UCSF
- MGH
- Sevilla U.
- INFN/LNS
- Sahara
- CERN
- NPI
- Belgrade U.
- Ioannina U.
- Patras U. & BIOEMTECH
- St.Joseph U.
- JINR
- Warsaw U.
- Tomsk U.
- Mongolia U.
- SNU
- NCC
- KEK
- AIST
- UNICAMP
- ANSTO
- Wollongong U.
- Melbourne

Thank you for your attention!

Backup

Monte Carlo methods in particle & molecule transport

"Monte Carlo simulation is a model used to predict the probability of various events when the potential for random variable is present"

We can use the MC method to simulate particle transport (such as particle hits, scattering, etc).
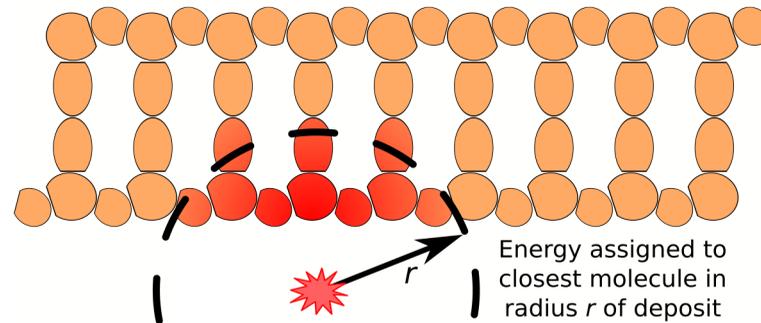
Hit!   Pass

1 2 3 4 5 6   −π   +π

1 2 3 4 5 6

©DESIGNALIKIE

GEANT4-DNA
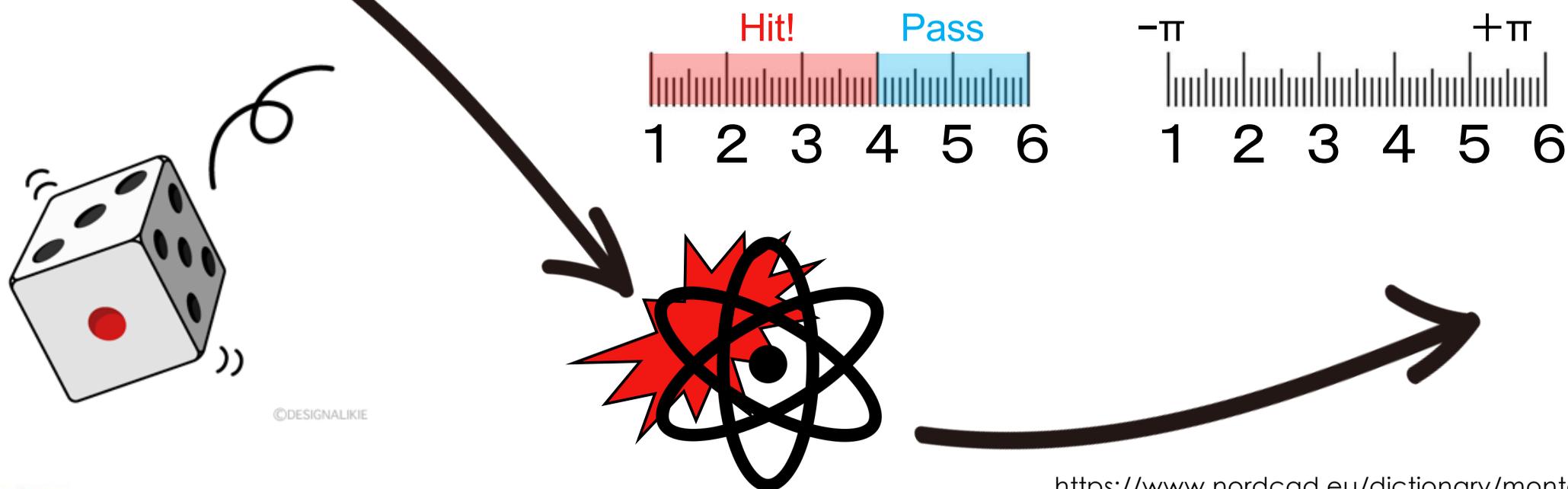
How can we score DNA damage?
- DNA damage model – (e.g. `moleculardna`)

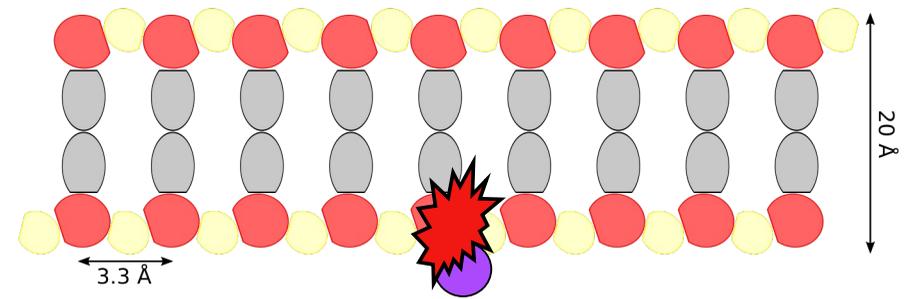**Direct** action model

R_{direct} (R of nucleotides: 2.3~2.6 Å)

E_{dep} assigned to closest strand molecule

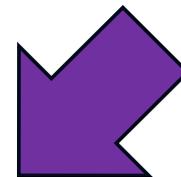Energy assigned to closest molecule in radius r of deposit

KURBUC model
PARTRAC model

17.5eV
5eV   37.5eV

Indirect action model

20 Å
3.3 Å

$$DNA + \cdot OH \rightarrow SSB$$

P_{OH}: possible range (measured) $40 - 80\%$
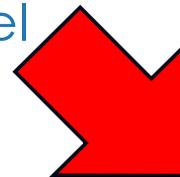
Each single damage is regarded as a <u>strand break</u>.

Extensions of Geant4-DNA

- **GATE**
(http://www.opengatecollaboration.org/)
    - GATE is a particle transport simulation toolkit based on Geant4 and dedicated to numerical simulations in medical imaging and radiotherapy. GATE can perform Geant4-DNA physics and chemistry simulations, directly in the platform which proposes a Python interface.

- **TOPAS-nBio**
(https://github.com/topas-nbio/TOPAS-nBio)
    - TOPAS-nBio is based on Geant4-DNA. The goal is to provide user friendly interface, making Monte Carlo simulations easy-to-use with focus on radiation biology at sub-cellular scales.

- **MPEXS-DNA**
(https://wiki.kek.jp/display/mpexs/MPEXS+Project)
    - MPEXS-DNA is a newly developed MC code based on Geant4-DNA physics/chemistry models that offer high computing performance by using a GPU.