IRSN
INSTITUT
DE RADIOPROTECTION
ET DE SÛRETÉ NUCLÉAIRE

Enhancing nuclear safety

Track structure calculations with the Geant4-DNA toolkit and ongoing development's

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***IRSN** (Institut de Radioprotection et de Sûreté Nucléaire, France)**

MiND-IBCT Workshop, Wiener Neustadt (Austria) 07-09 May 2014.

The Geant4-DNA project : a part of Geant4

GEometry ANd Tracking

Geant4: **A set of libraries** to simulate interactions of particle with matter with MC technique.

- Objected-Oriented technology (C++)-> Extensibility,
- Allows defining flexible geometries and transport particles within
- Open source: two public releases/year
- Set of libraries not a user code

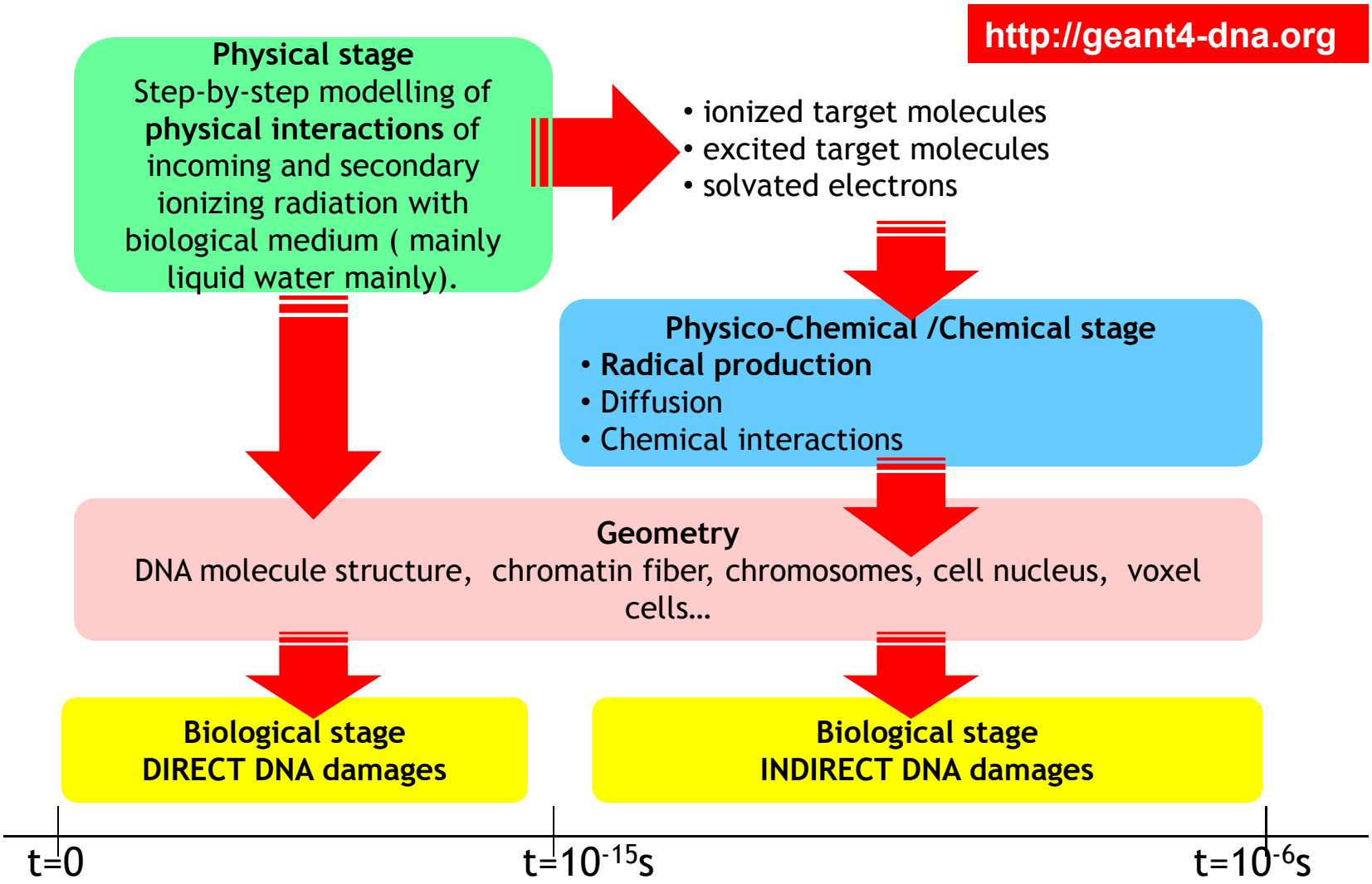
Geant4-DNA

http://geant4-dna.org

Objective : Extend the general purpose Geant4 Monte Carlo toolkit for the simulation of interactions of radiation with biological systems at the cellular and DNA level in order to predict early DNA damages

- Initiated in 2001 by **Dr. Petteri Nieminen** at ESA (European Space Agency) and aiming to provide the scientific community with an open source access easily upgraded and improved.
- First prototypes of physics models were added to Geant4 in 2007
- Currently an on-going interdisciplinary activity of the Geant4 collaboration « low energy electromagnetic physics » working group -> Coordinated par S. Incerti CNRS/IN2P3 since 2008

The Geant4-DNA project



Monte Carlo simulation of the physical stage

General characteristics

- **Electron transport** down to very low kinetic energy (electron thermalitation)
  - « Sub-excitation electrons» (< ~9 eV) can follow elastic scattering and loose energy by vibrational excitations of the target medium or attachment …

- **DISCRETE interactions**
  - All interactions are simulated in an **event by event** bases.
  - **No slow down approximation**

- **Models** can be purely analytical and/or use interpolated data
  - Ex. Computation of integral cross-sections

- They use the **same software design as all electromagnetic models** available in Geant4 ("standard" and "low energy" EM models)

- Geant4-DNA physics models are applicable to liquid water. New experimental **DNA cross sections** from PTB are being implemented (BioQuaRT project).

http://geant4-dna.org

Models used in the Geant4-DNA processes (V.10.0)

- Electrons
  - Elastic scattering
    - Screened Rutherford and Brenner-Zaider below 200 eV
    - Champion's approach (partial wave framework, 3 contributions to the interaction potential)
  - Ionisation
    - 5 levels for H_2O
    - Dielectric formalism & FBA using Heller optical data up to 1 MeV, and low energy corrections
  - Excitation
    - 5 levels for H_2O
    - Dielectric formalism & FBA using Heller optical data and semi-empirical low energy corrections
  - Vib. Excitation
    - Michaud *et al.* xs measurements in amorphous ice
    - Factor 2 to account for phase effect
  - Dissociative attachment
    - Melton *et al.* xs measurements

Photons

With EM « standard » and « low energy » processes

- Protons & H

http://geant4-dna.org

  - Excitation
    - Miller & Green speed scaling of e^- excitation at low energies and Born and Bethe theories above 500 keV
  - Ionisation
    - Rudd semi-empirical approach by Dingfelder *et al.* and Born and Bethe theories & dielectric formalism above 500 keV (relativistic + Fermi density)
  - Charge change
    - Analytical parametrizations by Dingfelder *et al.*

- He^0, He^+, He^{2+}
  - Excitation and ionisation
    - Speed and effective charge scaling from protons by Dingfelder *et al.*,
  - Charge change
    - Semi-empirical models from Dingfelder *et al.*

- C, N, O, Fe
  - Ionisation
    - Speed scaling and global effective charge by Booth and Grant

A Multiscale approach

Combination of processes for different geometric regions

Particularly useful for gamma irradiations

Gammas (Livermore or Penelope(2008) models for) :

- Photoelectric effect
- Compton scattering
- Gamma conversion
- Rayleigh scattering
- + fluorescence emission or Auger electron production

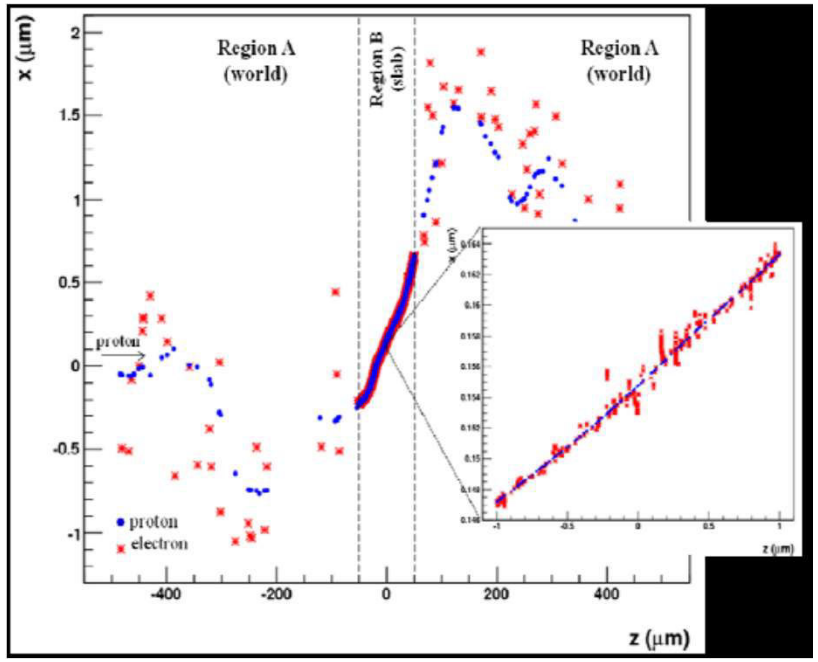
Electrons :

Outside the target volume

- Moller-Bhabha model for ionization
- Standard Bremsstrahlung model
- Standard Multiple Scattering model

Inside the target volume

- G4DNA elastic collisions (Champion Elastic Model),
- G4DNA ionization (Born Ionization model),
- G4DNA excitation (Born Excitation Model),
- electron capture T_e < 9 eV

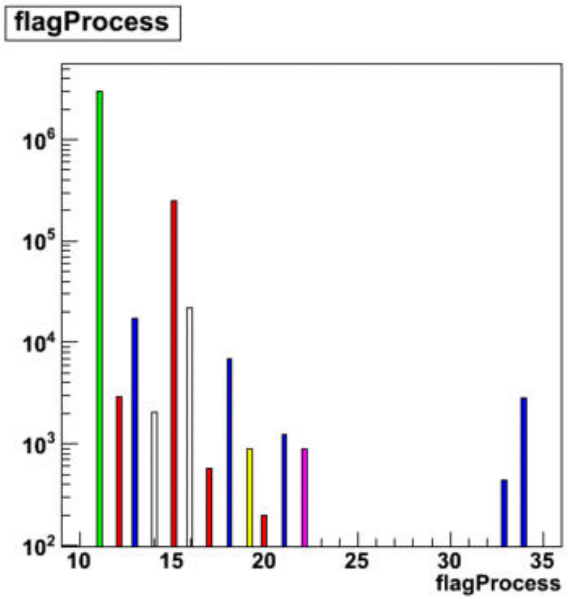


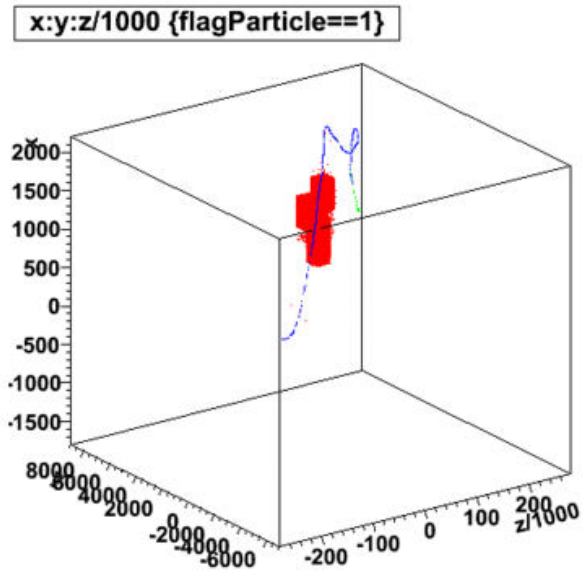
See Prog. Nucl. Sci. Tec. 2 (2011) 898-903

The microdosimetry Geant4 “advance example”

Purpose:

- Explain to users how to use Geant4 very low energy electromagnetic processes for microdosimetry
- Calculation of track structure of a He+ particle in liquid water, ROOT macro provided for data analysis





Ongoing developments in the physical stage

DNA cross-sections

➢ Geant4-DNA physics models are applicable to liquid water. New experimental **DNA cross sections from PTB** are being implemented (BioQuaRT project).

THF: tetrahydrofuran
TMP: trimethylphosphate
PY: pyrimidine
PU: purine

- THF (with TMP) is similar to the DNA backbone.
- PY and PU can represent the nucleobases.

Implementation in Geant4-DNA:

Geant4-DNA is a Geant4 “extension” with its own working logic:

- Geant4 “core” calls the process which call themselves the models.
- The data tables and associated calculations are done in the model c++ classes.

Implementation of new c++ **model classes** for **ionization, elastic, excitation and Auger models.**
New material management system.

- PhysicsList:

```
modelDNAPTBIonisation = new G4DNAPTBIonisationModel();
theDNAPTBIonisationProcess = new G4DNAIonisation("e-_G4DNAPTBIonisation");
theDNAPTBIonisationProcess->SetEmModel(modelDNAPTBIonisation);
```

Indirect effects simulation with Geant4-DNA

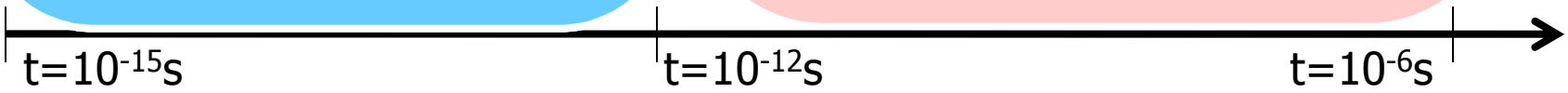
M. Karamitros PhD (23/11/2012, CENBG)

Physico-chemical stage

Chemical stage

Step By Step (SBS) model

- The probability of encounter is evaluated after each time step.



Indirect effects simulation with Geant4-DNA

M. Karamitros PhD (23/11/2012, CENBG)

Physico-chemical stage

- **Dissociation** :
  $H_2O^{*/+}$
  $\hookrightarrow$ $(H_3O^+, {}^{\circ}OH, e_{aq}, H, H_2)$
- **Thermalization** of the products down to their energy of diffusion at equilibrium.

- Ionised molecules convert into :

$$H_2O^+ + H_2O \blacktriangleright H_3O^+ + OH^{\bullet}$$

- Excited molecules relax or dissociate :

	Process	Decay channel	Fraction (%)
Ionisation (H_2O^+)			
$1b_1$, $3a_1$, $1b_2$, $2a_1$, K	Dissociative decay	$H_3O^+ + {}^{\bullet}OH$	100
Excitation (H_2O^*)			
A^1B^1	Dissociative decay	${}^{\bullet}OH + H^{\bullet}$	65
	Relaxation	$H_2O + \Delta E$	35
B^1A^1	Auto-ionisation	$H_3O^+ + {}^{\bullet}OH + e^-_{aq}$	55
	Dissociative decay	$H_2 + {}^{\bullet}O^{\bullet}$	15
	Relaxation	$H_2O + \Delta E$	30
Ryd, diff bands	Auto-ionisation	$H_3O^+ + {}^{\bullet}OH + e^-_{aq}$	50
	Relaxation	$H_2O + \Delta E$	50

Kreipl et al, Radiat Environ Biophys, 2009

$t \sim 10^{-15}$ s $\quad$ $t \sim 10^{-12}$ s

Indirect effects simulation with Geant4-DNA

M. Karamitros PhD (23/11/2012, CENBG)

Radical species and Diffusion

Species	Diffusion Coefficient D (10^{-9} m^2 s^{-1})
e^-_{aq}	4.9
•OH	2.8
H•	7.0
H_3O^+	9.0
H_2	4.8
OH^-	5.0
H_2O_2	2.3

Brownian diffusion $< R > \alpha \, D \, \Delta t$

Time(s)	Δt (ps)
Jusqu'à 10^{-11}	0.1
10^{-11}-10^{-10}	1
10^{-10}-10^{-9}	3
10^{-9}-10^{-8}	10
Après 10^{-8}	100

Chemical reactions

Reaction	Reaction rate (10^{10} M^{-1} s^{-1})
$H• + e^-_{aq} + H_2O \rightarrow OH^- + H_2$	2.65
$H• + •OH \rightarrow H_2O$	1.44
$H• + H• \rightarrow H_2$	1.20
$H_2 + •OH \rightarrow H• + H_2O$	4.17×10^{-3}
$H_2O_2 + e^-_{aq} \rightarrow OH^- + •OH$	1.41
$H_3O^+ + e^-_{aq} \rightarrow H• + H_2O$	2.11
$H_3O^+ + OH^- \rightarrow 2\ H_2O$	14.3
$•OH + e^-_{aq} \rightarrow OH^-$	2.95
$•OH + •OH \rightarrow H_2O_2$	0.44
$e^-_{aq} + e^-_{aq} + 2\ H_2O \rightarrow 2\ OH^- + H_2$	0.50

For this prototype software, the set of parameters published by the authors of the PARTRAC software was followed.

However these parameters can be modified by the user.

Kreipl et al, Radiat Environ Biophys, 2009

Indirect effects simulation with Geant4-DNA

Geant4-DNA generated track of 1 keV electron, followed up to 100 ns during chemical stage.
Using pre-release Geant4 10.1 code.

First, the physical stage of radiation action is modeled, using Geant4-DNA physics. 1 keV electron track is fully slowed down and thermalized in a 150 nm sphere of liquid water.

Yellow points correspond to interaction events in liquid water.

Next, the chemical stage simulation for first 100 ns is visualized. Individual radical species diffusing in space and reacting with each other are shown as colour trails, the color coding chemical species type.

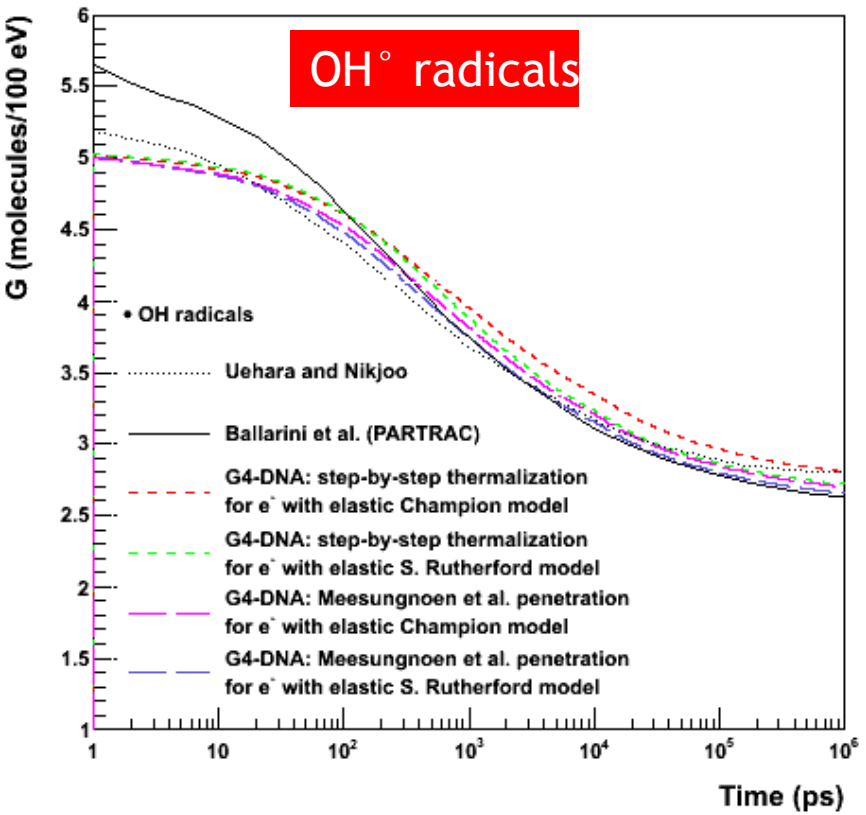
References:
Geant4 10.0, patch 01, Geant4 DNA chemistry code e964ead.
Code using the chem3 example by M. Karamitros, S. Meylan, Y. Perrot and V. Štěpán, video rendered by V. Štěpán on March 31, 2014.

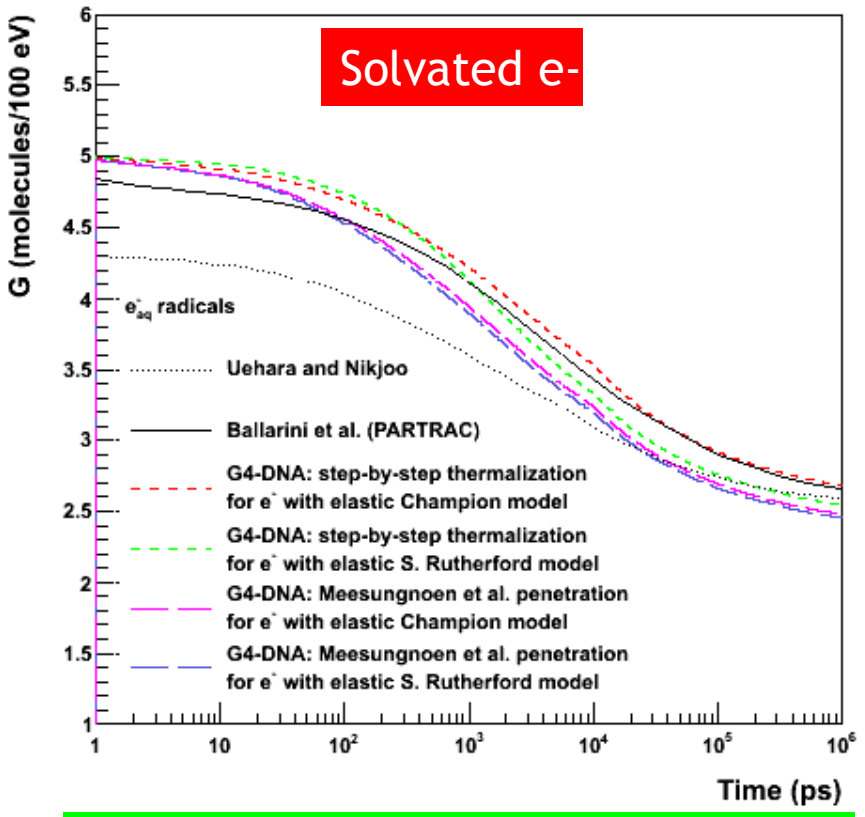
Štěpán, Václav; Karamitros, Mathieu; Meylan, Sylvain; Perrot, Yann; Incerti, Sebastien (2014): Geant4-DNA visualization: Evolution of 1 keV electron track in liquid water in space and time. fig**share**.
http://dx.doi.org/10.6084/m9.figshare.978887

Modelling Indirect effects with Geant4-DNA

Radiochemical yields versus time

M. Karamitros PhD (23/11/2012, CENBG)



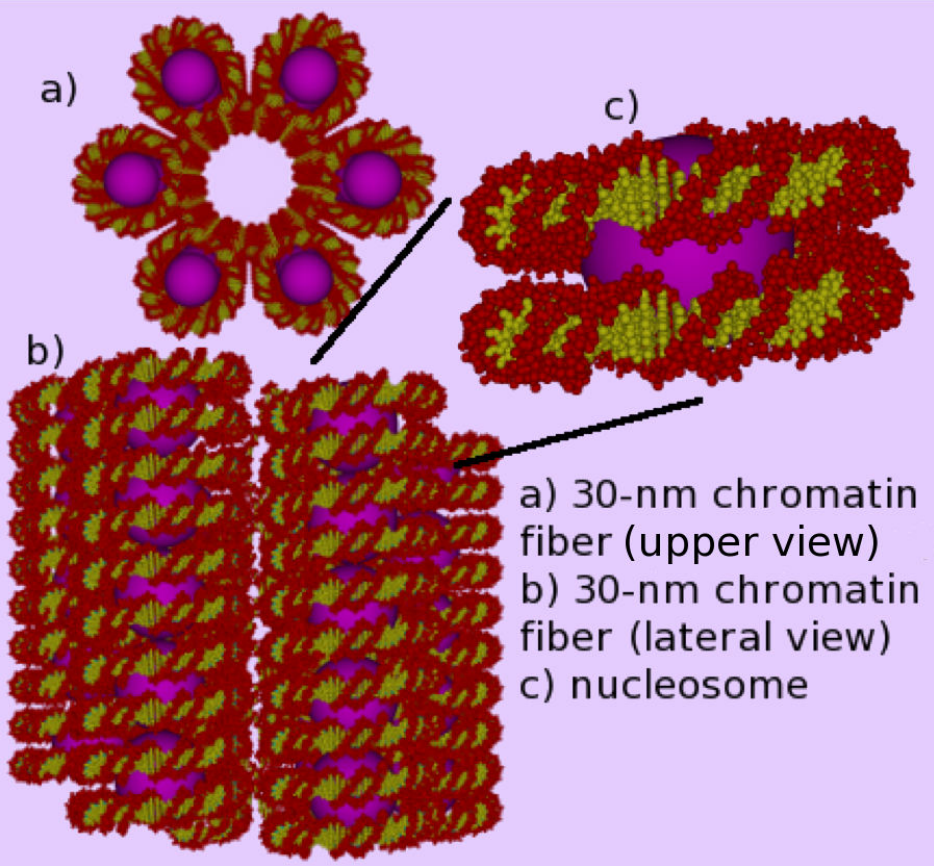


PARTRAC: Ballarini et al., REB (2000),39:179-188
Uehara et Nikjoo, J. Radiat. Res. (2006),47:69-81

- Effect of the two **alternative** electron elastic scattering models
- Results are obtained in **30 minutes** on a cluster of 80 CPUs (Physics + Chemistry)

DNA Geometrical models

B-DNA atomistic geometrical model (Bernal et al. CPC. 184 (12), 2013)



- All DNA atoms are accounted for explicitly.
- Five organization levels of the genetic material, from the nucleotide pair up to the 30-nm chromatin fiber.
- The DNA chain is continue along the whole chromatin fiber
- Constructed by geometrical optimization.
- It complies with the packing ratio of each structure.
- A subroutine to determine which is the closest atom with respect to an arbitrary point in space was developed and published.

Geometrical parameters of the nucleosome.

Parameter	Variable	Dimension[a]	Dimension[b]
Superhelix pitch	P_{nucl}	2.370	2.59
Internal radius	–	~2.860	–
Central radius	RC_{nucl}	4.045	4.19
External radius	R_{nucl}	~5.230	–
Number of bp/turn	NBP_{nucl}	77	80
Number of bp around nucleosome	–	154	147
Bottom of the nucleosome	Z^{min}_{nucl}	0	–
Top of the nucleosome	Z^{max}_{nucl} $(6R_{hel})$	7.11	–

[a] This work.
[b] Richmond and Davey [19].

DNA Geometrical models

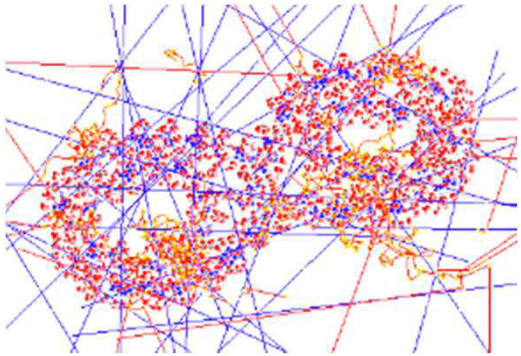
(E. Dalage, Y. Perrot, Q.T.Pham, LPC France)

- **Atomic representation of DNA based on Protein Data Bank files (PDB)**

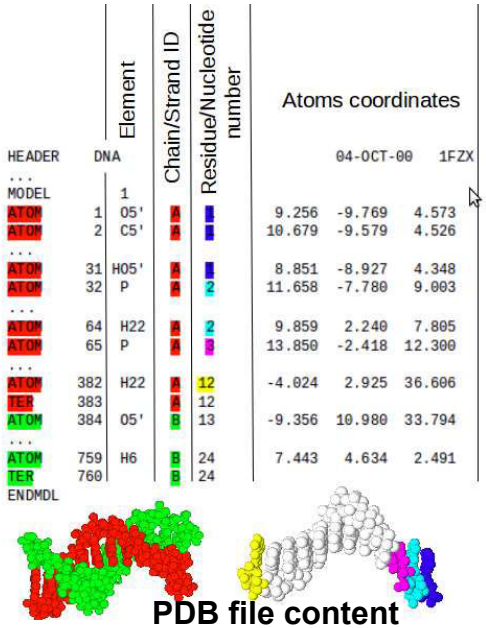
- **PDBlib: an independent C++ library**
  - Load geometry data structure into memory (no direct geometry)
  - Algorithm to find the closest atom to a 3D coordinate

- **PDB4DNA: a Geant4 User application**
  - Computation of direct damages
  - Geant4 geometry (spheres) for visualization purposes
  - To be released in december 2014

- **To be proposed:**
  - Expansion of the nucleosome geometry
  - Indirect damages
  - Adaptation to the GATE platform

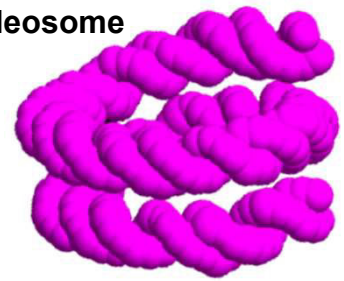


Geant4-DNA simulation of the irradiation of a dinucleosome (protons)

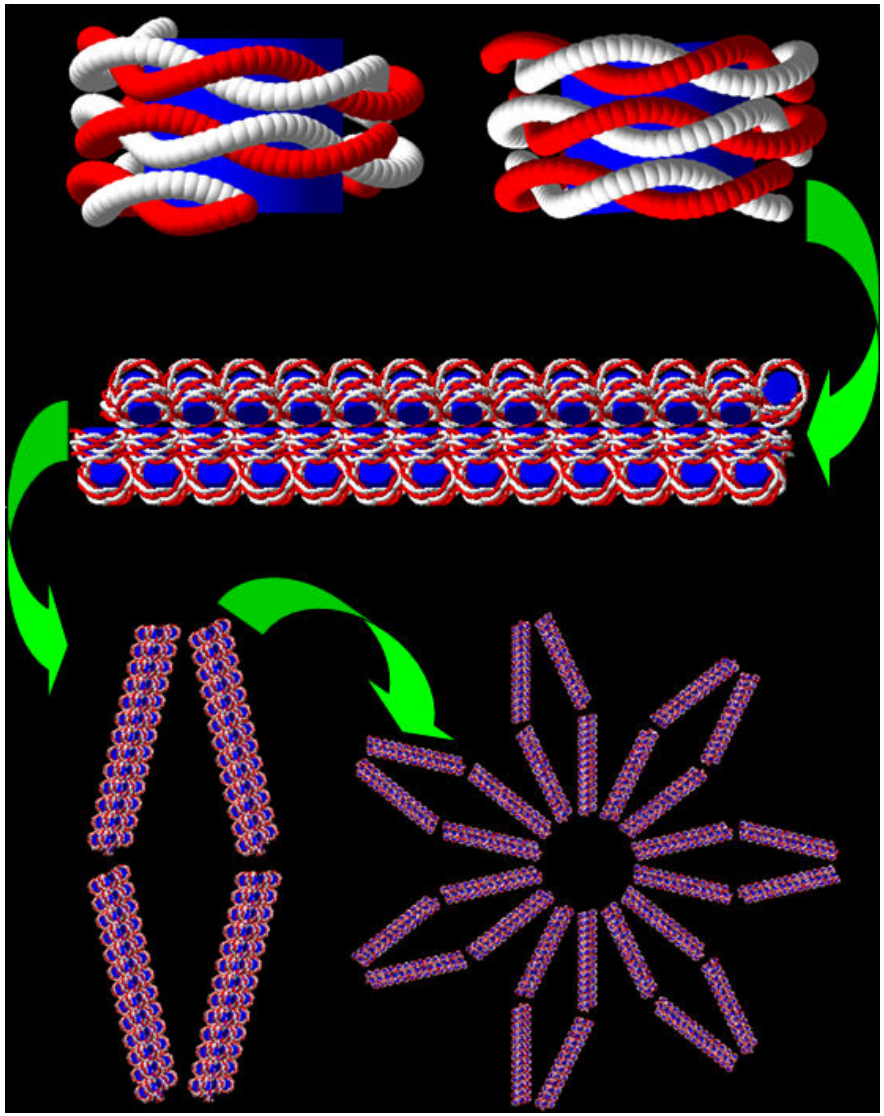


PDB file content

Nucleotides of a nucleosome



DNA Geometrical models
G4DNAGeometry (advanced examples)



M. Dos Santos PhD. Work (IRSN/ 2013)

Nucleosome

- 200 bp / nucleosome
- DNA diameter = 2.16 nm
- Histone = cylinder of 6.5 nm in diameter and 5.7 nm in height

Chromatin fiber

- 90 nucleosomes / fiber
- 7 nucleosomes / turn
- D = 31 nm
- L = 161 nm

Chromatin fiber loop

- 4 fibers / loop assembled in a diamond shape
- 7 loops to form a “flower”*

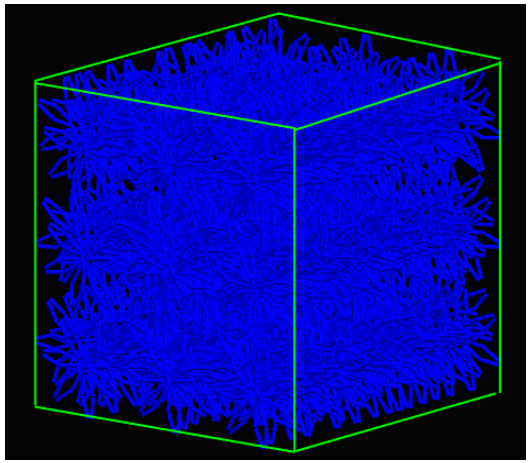
** W. Friedland & al, Simulation of DNA damage after Proton irradiation, Radiation Research 59 (2003), 401-410.*

G4DNAGeometry example (advanced examples)

M. Dos Santos PhD. Work (IRSN/2013)

Detector Construction: Containing the description of an elliptical cell nucleus with similar dimensions of fibroblast grown in a microscopic plate at confluence.

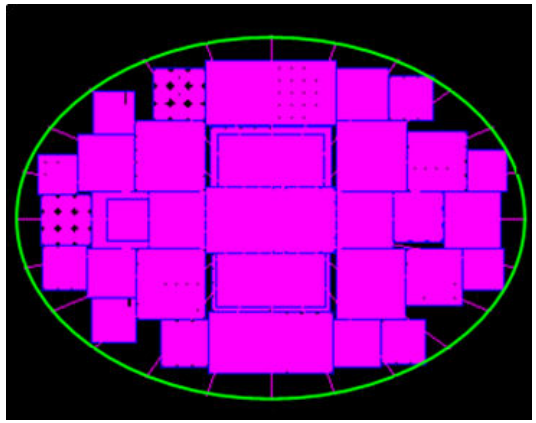
- Chromosome domain example



Per nucleus:
- 23 pairs of chromosomes
- 11875 flowers or 83125 loops
- 332 500 chromatin fibers
- 29 925 000 nucleosomes
- ~ 6 Gbp

M. Dos Santos, C. Villagrasa, I. Clairand and S. Incerti. "Influence of the DNA density on the number of clustered damages created by protons of different energies". NIM B 298 (2013) 47-54.

- « Fibroblast » cell nucleus



- Nucleus-> ellipsoid
- Dimensions: 19.7 * 14.2 * 5 μm^3
- V = 732 μm^3
- 0.42 % of DNA / nucleus

G4DNAGeometry example (advanced examples)

Use of the G4DNAGeometry example :

Based on the existing G4DNAPhysics but including the simplified DNA geometry in the DetectorContruction

Output: **A root file** containing an n-tuple with the following values only for those energy transfer points located on the backbone region :

- **Particle type** at the origin of the energy deposition
- **Process type (ionization, excitation)**
- Information on the **DNA strand** (flag 1 / 2)
- **Coordinates of the energy deposition** (x,y,z)
- **Energy deposition** amount

The example is still evolving: in next release, the **next version** of the geometry will allow **visualization, multi-threading** calculations and an **improved calculation time**.

Geant4-DNA sur Internet

Site Web de la collaboration Geant4-DNA: http://geant4-dna.org

The Geant4-DNA project

Extending the Geant4 Monte Carlo simulation toolkit for radiobiology

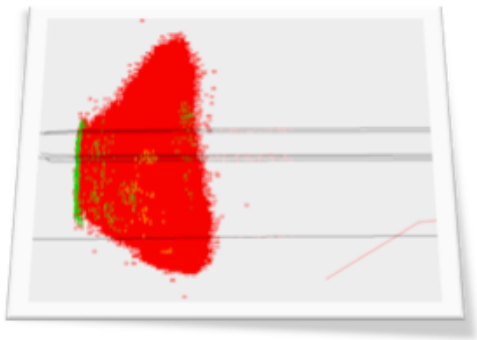
Geant4-DNA | Software | Physics | Chemistry | Examples & tutorials | Publications | Collaboration | Funding

Welcome to the Internet page of the **Geant4-DNA project**.

The Geant4 Monte Carlo simulation toolkit is being extended with processes for the **modeling of early biological damages induced by ionising radiation at the DNA scale**. Such developments are on-going in the framework of the Geant4-DNA project, originally initiated by the European Space Agency/ESTEC.

On-going developments include

- **Physics** processes in liquid water and other biological materials
- **Physico-chemistry** and **chemistry** processes for water radiolysis
- Molecular **geometries**
- Quantification of **damage** (such as single-strand, double-strand breaks, ...)



Recent posts

Check-out our new movie in the **Chemistry** section !

The last Geant4 release (10.0+P01) is available for download, see our **Software** section.

A new advanced example, dnageometry, is available, see our **Examples & tutorials** section.

PhD theses by the Geant4-DNA collaboration are listed in the **Publications** section.

Acknowledgments

- The Geant4-DNA collaboration thanks all theoreticians who are helping us for the development of this extension in the Geant4 toolkit, in particular:
  - Dr M. Dingfelder (East Carolina U., NC, US)
  - Dr D. Emfietzoglou (Ioannina U., Greece)
  - Dr B. Grosswendt (PTB, Germany)

- We also thank Dr W. Friedland (Helmholz Zentrum, Munich, Germany), developer of PARTRAC, for his guidance and constant support, since the early days of Geant4-DNA

Thank you for your attention