http://geant4-dna.org

The Geant4-DNA project

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CNRS / IN2P3 / LPC Clermont & CENBG

Bordeaux, France

representing the efforts of the Geant4-DNA Collaboration

Belgrade, Serbia – October 28, 2016

Thank you to the organizers !

- Pablo Cirrone, INFN-LNS (Italy)
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- Ivan Petrovic, VINS-UB (Serbia)
- Aleksandra Ristic-Fira, VINS-UB (Serbia)
- Francesco Romano, INFN-LNS (Italy)

Schedule of Geant4-DNA tutorial

- First part (Sebastien)
  - Geant4-DNA overview talk
  - Hands-ons: dnaphysics, svalue, TestEm12, microbeam
- Second part (Nathanael)
  - Geometry talk
  - Hands-on: pdb4dna
  - Chemistry talk
  - Hands-ons: chem1 (, chem3)

Contents of this talk

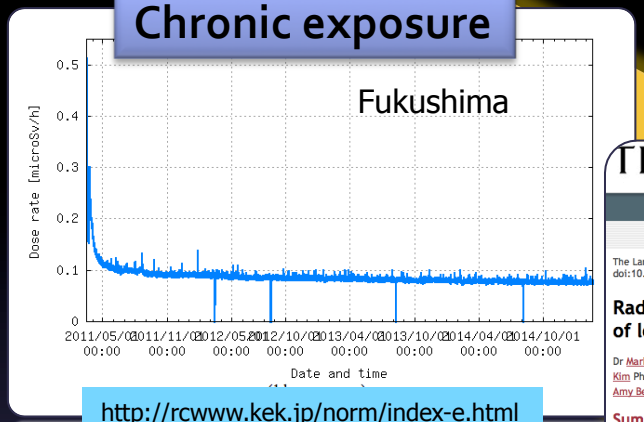
1. Context of the Geant4-DNA project
2. Physical stage
3. Physico-chemical & chemical stages
4. Geometrical models of biological targets
5. Where to find more information ?

See Geant4-DNA reference …(link)

1) CONTEXT

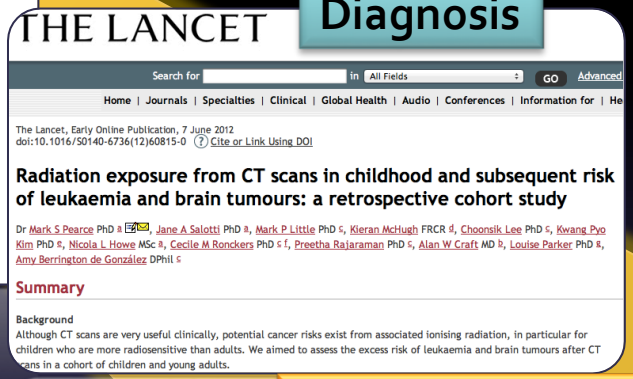
Modelling biological effects of ionising radiation remains a major scientific challenge

Chronic exposure



http://rcwww.kek.jp/norm/index-e.html

Diagnosis



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The Lancet, Early Online Publication, 7 June 2012
doi:10.1016/S0140-6736(12)60815-0 Cite or Link Using DOI

Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study

Dr Mark S Pearce PhD a, Jane A Salotti PhD a, Mark P Little PhD c, Kieran McHugh FRCR d, Choonsik Lee PhD c, Kwang Pyo Kim PhD e, Nicola L Howe MSc a, Cecile M Ronckers PhD c f, Preetha Rajaraman PhD c, Alan W Craft MD b, Louise Parker PhD a, Amy Berrington de González DPhil c

Summary

Background

Although CT scans are very useful clinically, potential cancer risks exist from associated ionising radiation, in particular for children who are more radiosensitive than adults. We aimed to assess the excess risk of leukaemia and brain tumours after CT scans in a cohort of children and young adults.

Space missions

Space exploration

Proton & hadrontherapy

« A MAJOR CHALLENGE LIES IN PROVIDING A SOUND MECHANISTIC UNDERSTANDING OF LOW-DOSE RADIATION CARCINOGENESIS »

L. MULLENDERS *ET AL.*

ASSESSING CANCER RISKS OF LOW-DOSE RADIATION

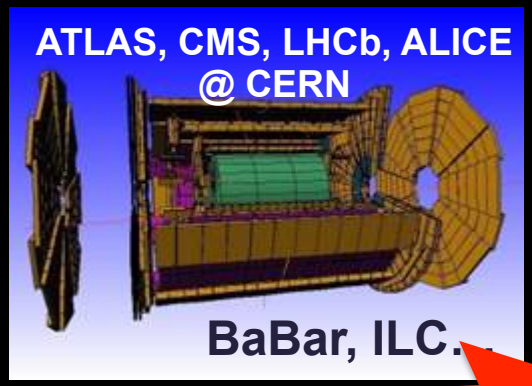
NATURE REVIEWS CANCER (2009)

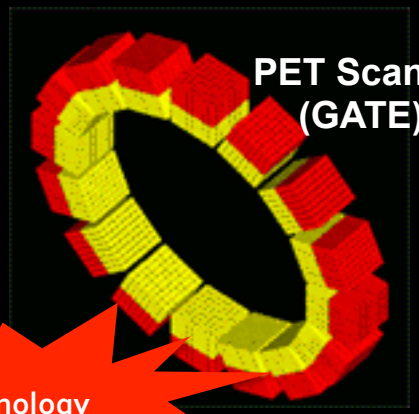
The Monte Carlo approach

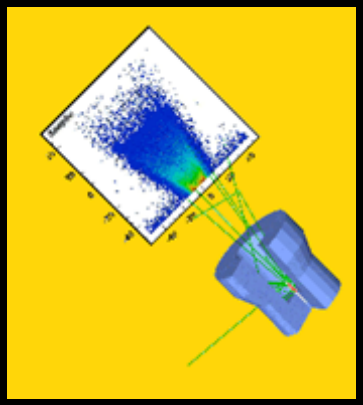
- Can « reproduce » with accuracy the stochastic nature of particle-matter interactions
- Many Monte Carlo codes are already available today in radiobiology for the simulation of track structures at the molecular scale in biological medium
  - E.g. PARTRAC, MC4*, KURBUC, RETRACKS/RITRACKS, NOREC, …
  - 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 ?

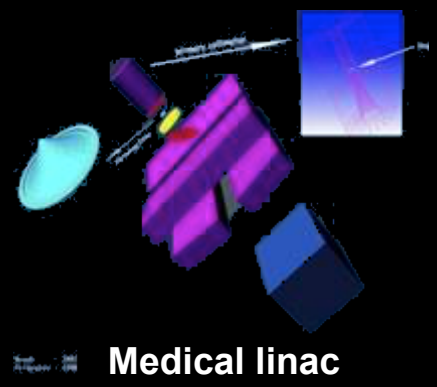
« To expand accessibility and avoid 'reinventing the wheel', track structure codes should be made available to all users via the internet from a central data bank»

H. Nikjoo, IJRB 73, 355 (1998)

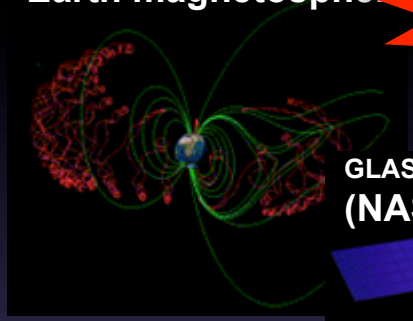


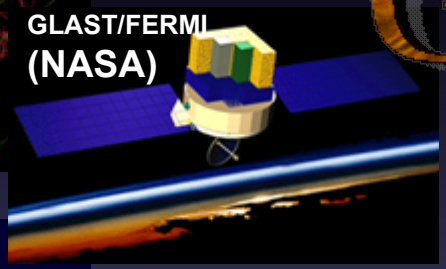






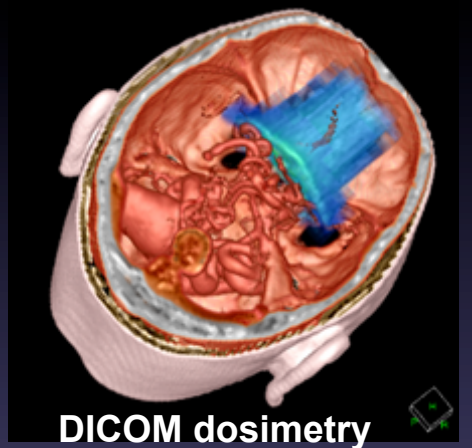
Technology transfer

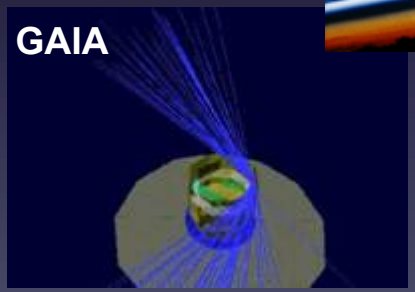


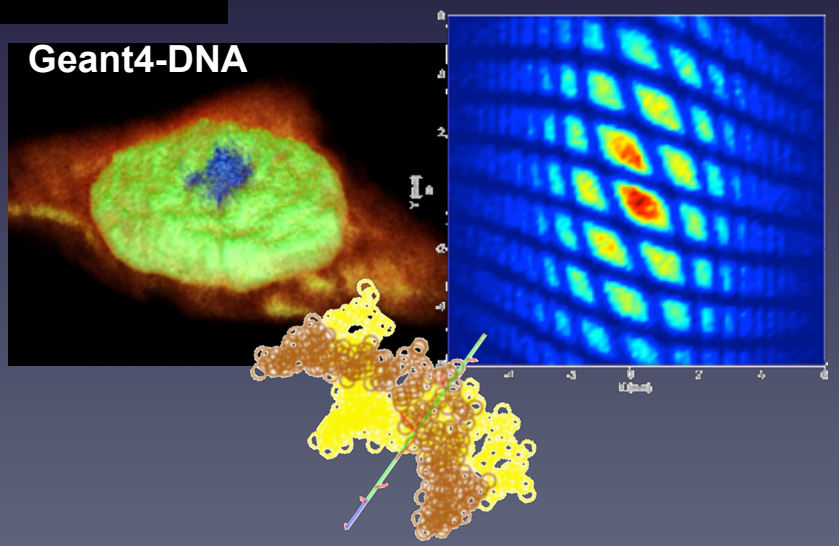


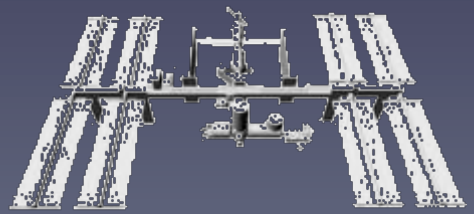
Geant 4

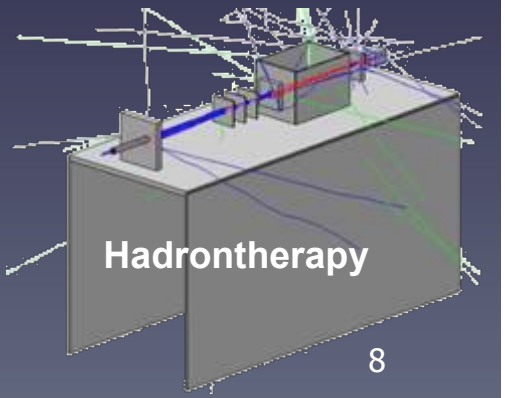
http://geant4.org











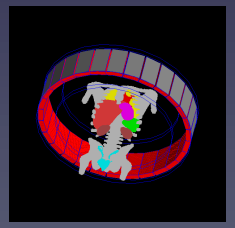
Geant4 for radiobiology

- Can we try to extend Geant4 to model biological effects of radiation ?
- Limitations prevent its usage for the modelling of biological effects of ionising radiation at the sub-cellular & DNA scale
  - Condensed-history approach
    - No step-by-step transport on small distances, a key requirement for micro/nano-dosimetry
  - Low-energy limit applicability of EM physics models is limited
    - « Livermore » Low Energy EM models can technically go down to 10 eV but accuracy limited < 250 eV
    - 100 eV for « Penelope 2008 » Low Energy EM models
  - No description of target molecular properties
    - Liquid water, DNA nucleotides, other
  - Only physical particle-matter interactions
    - At the cellular level, physical interactions are NOT the dominant processes for DNA damage at low LET…

Int. J. Model. Simul. Sci. Comput. 1 (2010) 157 (link)

The Geant4-DNA project

- The code is fully included in Geant4
- It is an independent sub-category of the electromagnetic physics category of Geant4: $G4INSTALL/source/processes/electromagnetic/dna
- An interdisciplinary activity of the Geant4 « low energy electromagnetic physics » working group
- Both are coordinated by CNRS/IN2P3 since 2008
- Integration in Geant4 enables the use of Geant4-DNA physics from inside GATE (2014) and TOPAS (2015)



http://www.opengatecollaboration.org

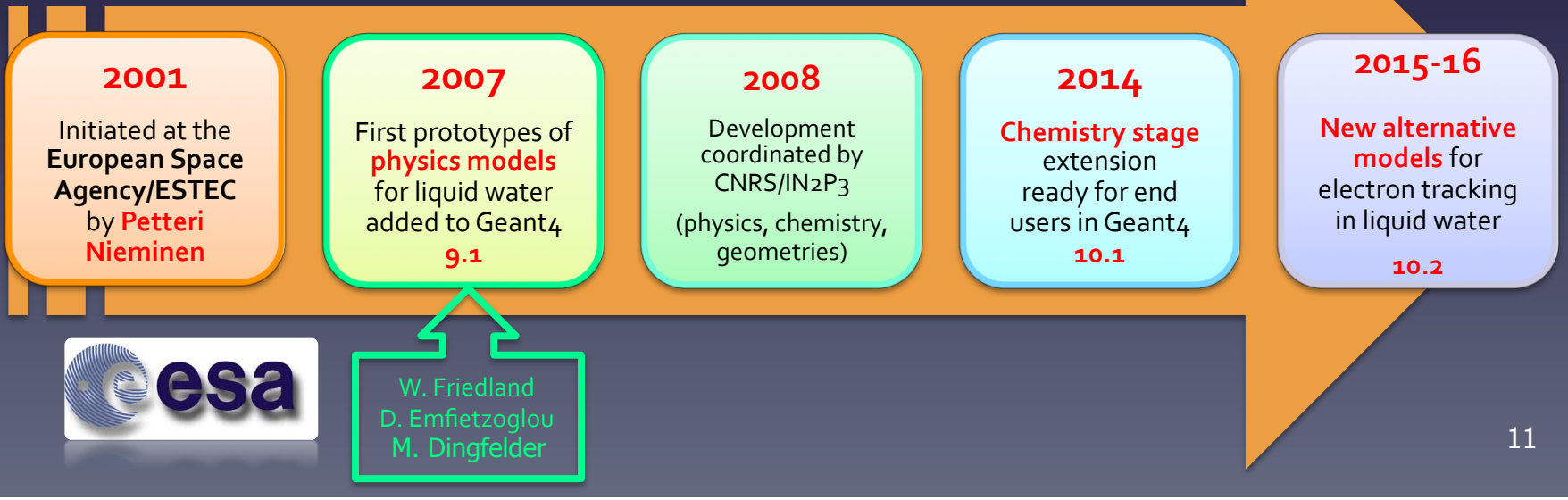
http://www.topasmc.org

Status of Geant4-DNA

Main 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 and late DNA damage in the context of manned space exploration missions (« bottom-up » approach).

Designed to be developed and delivered in a FREE software spirit under Geant4 license, easy to upgrade and improve.



How can Geant4-DNA model early DNA damage ?

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

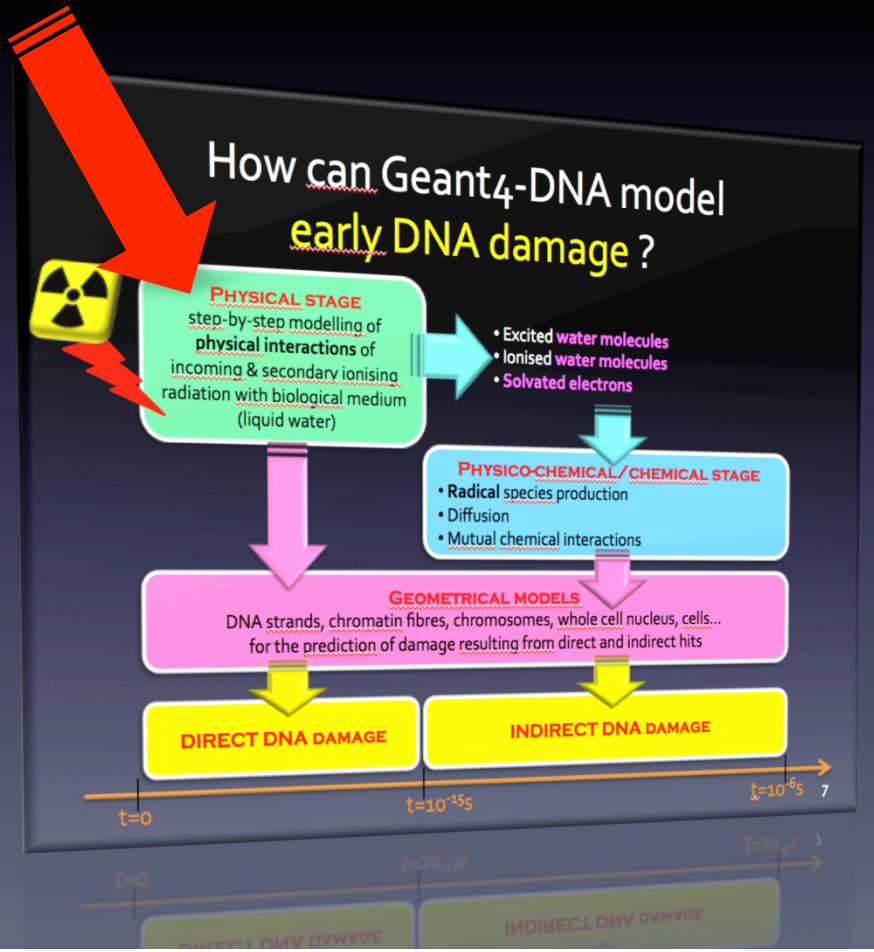
DIRECT DNA DAMAGE

INDIRECT DNA DAMAGE

REPAIR

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

2) PHYSICAL STAGE



Overview of physics models for liquid water

G4 10.2+P02
June 2016

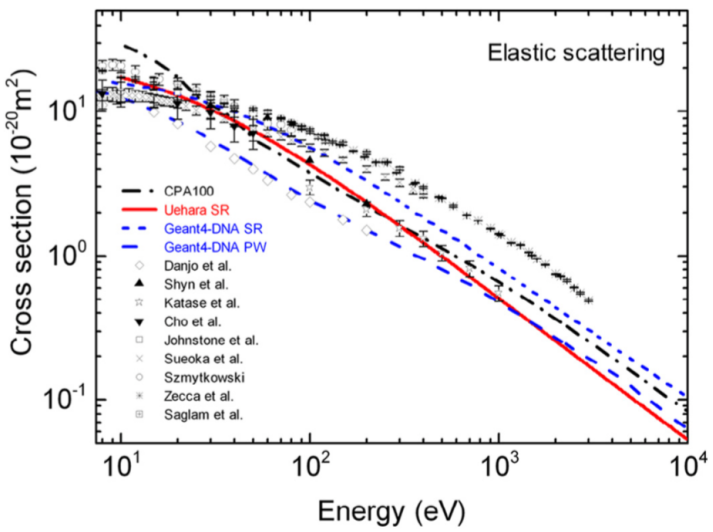
- **Electrons**
  - **Elastic scattering**
    - Screened Rutherford and Brenner-Zaider below 200 eV
    - Updated alternative version by Uehara
    - Partial wave framework model by Champion et al.,
      3 contributions to the interaction potential
  - **Ionisation**
    - 5 levels for H_2O
    - Dielectric formalism & FBA using Heller optical data up to 1 MeV, and low energy corrections, derived from the work of Emfietzoglou et al.
    - Improved alternative version by Emfietzoglou and Kyriakou
  - **Excitation (*)**
    - 5 levels for H_2O
    - Dielectric formalism & FBA using Heller optical data and semi-empirical low energy corrections, , derived from the work of Emfietzoglou et al.
    - Improved alternative version by Emfietzoglou and Kyriakou
  - **Vibrational excitation (*)**
    - Michaud *et al.* xs measurements in amorphous ice
    - Factor 2 to account for phase effect
  - **Dissociative attachment (*)**
    - Melton xs measurements

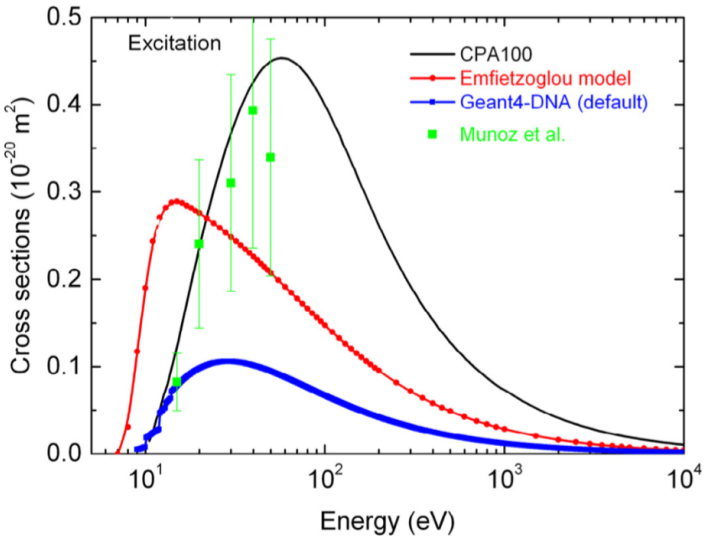
Med. Phys. 37 (2010) 4692 (link)
Appl. Radiat. Isot. 69 (2011) 220 (link)
Med. Phys. 42 (2015) 3870 (link)
Phys. Med. 31 (2015) 861 (link)
Nucl. Instrum. and Meth. B 343 (2015) 132 (link)

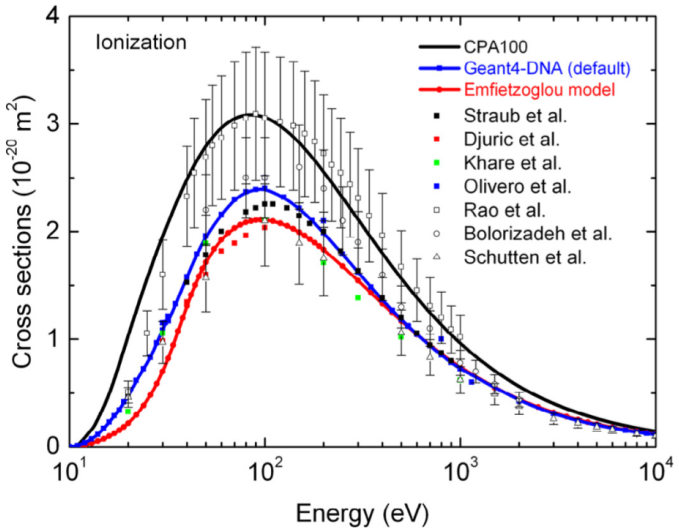
(*) only available in Geant4-DNA

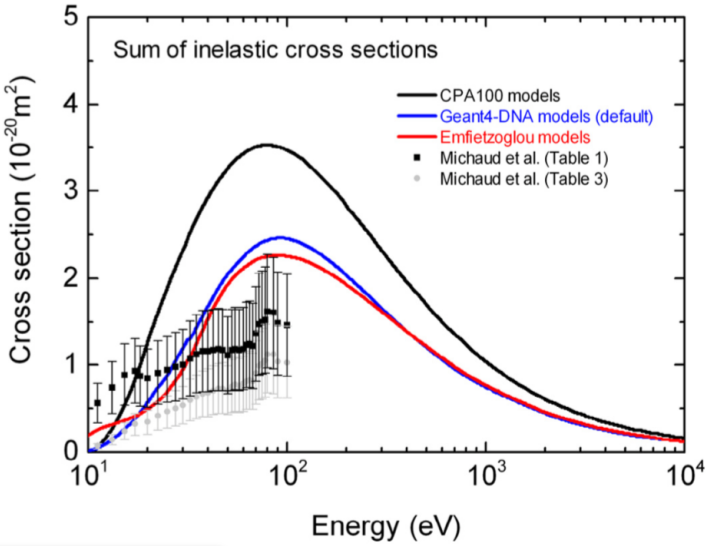
- **Protons & H**
  - **Excitation (*)**
    - Miller & Green speed scaling of e^- excitation at low energies and Born and Bethe theories above 500 keV, from Dingfelder *et al.*
  - **Ionisation**
    - Rudd semi-empirical approach by Dingfelder *et al.* and Born and Bethe theories & dielectric formalism above 500 keV (relativistic + Fermi density)
  - **Charge change (*)**
    - Analytical parametrizations by Dingfelder *et al.*
  - **Nuclear scattering**
    - Classical approach by Everhart *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.*
  - **Nuclear scattering**
    - Classical approach by Everhart *et al.*
- **Li, Be, B, C, N, O, Si, Fe**
  - **Ionisation**
    - Speed scaling and global effective charge by Booth and Grant
- **Photons**
  - from EM « standard » and « low energy »
    - Default: « Livermore » (EPDL97)

Cross section models for electrons









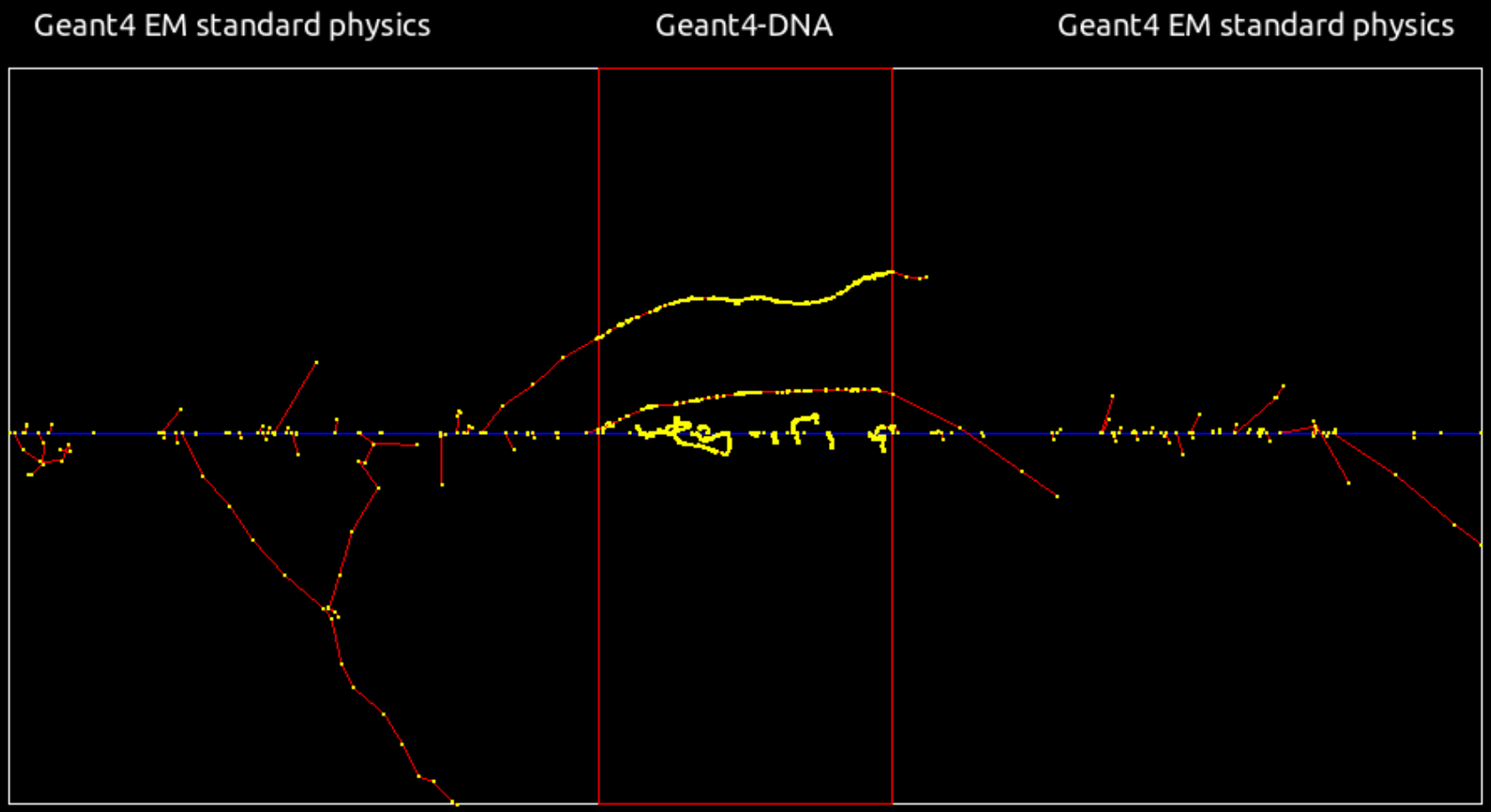
Phys. Med. 31 (2015) 861 (link)

Multiscale combination of EM processes

Thanks to a unified software design, users can **easily combine Geant4-DNA processes and models** with existing Geant4 physics such as:

- Geant4 **photon** processes and models
  - Photoelectric effect, Compton sc., Rayleigh sc., pair production
  - Livermore (EPDL97) included by default
- Geant4 alternative **electromagnetic processes and models for charged particles**
  - Ionisation, bremsstrahlung, etc…
  - Electrons, positrons, ions, etc…
- Geant4 **atomic deexcitation** (fluorescence + Auger emission, **including cascades**)
  - EADL97, Bearden
- …and also Geant4 **hadronic physics**

Mixed physics lists in geometrical regions: the « microdosimetry » extended example



/gps/particle ion
/gps/ion 6 12 6
/gps/energy 240 MeV

Courtesy of V. Stepan (CENBG)

Nucl. Instrum. and Meth. B 273 (2012) 95 (link)
Prog. Nucl. Sci. Tec. 2 (2011) 898 (link)

Geant4-DNA Physics constructors

6 constructors are available (4 new as BETA)

Constructor name	Content
G4EmDNAPhysics	Default models
G4EmDNAPhysics_option1 (beta)	Same as G4EmDNAPhysics but uses New multiple scattering model G4LowEWentzelVIModel
G4EmDNAPhysics_option2	Same as G4EmDNAPhysics but faster (usage of CDCS for ionisation processes)
G4EmDNAPhysics_option3 (beta)	Same as G4EmDNAPhysics but includes nuclear scattering for protons and alphas
G4EmDNAPhysics_option4 (beta)	New electron ionisation and excitation models by Ioannina team
G4EmDNAPhysics_option5 (beta)	Same but faster (usage of CDCS)

All are located in

$G4INSTALL/source/physics_lists/constructors/electromagnetic

Phys. Med. 31 (2015) 861 (link)

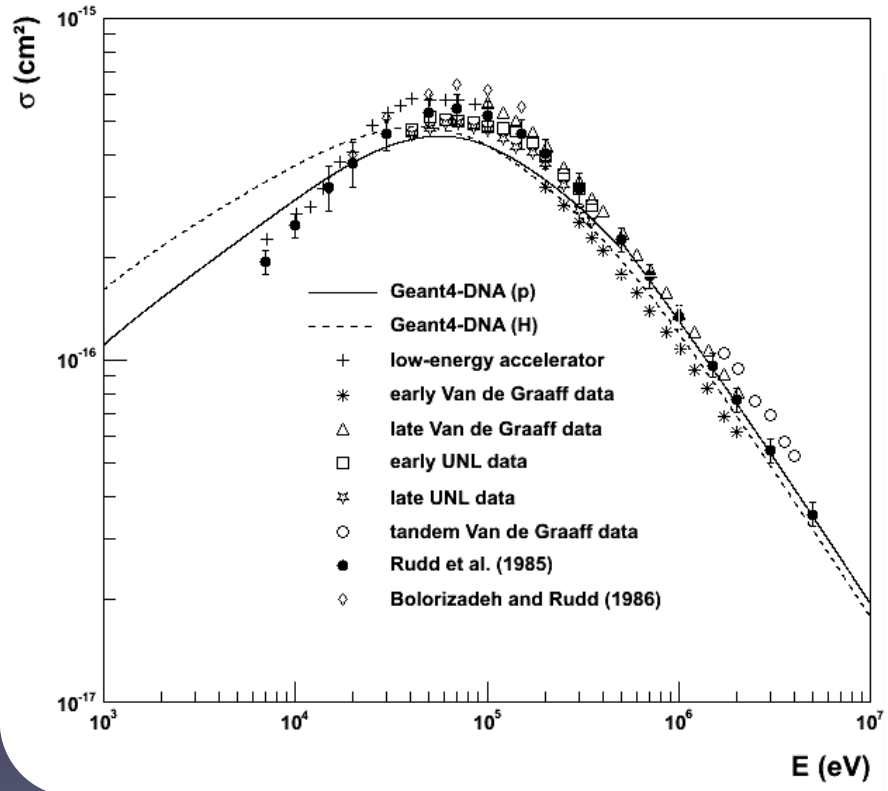
Overview of verification activities

Quantity	Incident particle	References
Cross sections	electron, proton, alpha particle	Med. Phys. 37, 4692 (2010)
Dose Point Kernels	electron	Appl. Radiat. Isot. 83, 137 (2014)
Frequency of energy deposition	electron, proton, alpha particle	Nuclear Inst. and Methods in Physics Research B 306, 158 (2013)
Ionization cluster size	electron	Eur. Phys. J. D 60, 85 (2010)
Lineal energy	proton	Appl. Radiat. Isot. 69, 220 (2011)
Mean energy deposition	proton	Appl. Radiat. Isot. 69, 220 (2011)
Radial doses	proton, alpha particle, ions	Nuclear Inst. and Methods in Physics Research B 333, 92 (2014) Phys. Med. Biol. 59, 3657 (2014)
Range	electron, proton, alpha particle	Nuclear Inst. and Methods in Physics Research B 269, 2307 (2011)
S-values	electron	Nuclear Inst. and Methods in Physics Research B 319, 87 (2014) Med. Phys. 42, 3870 (2015)
Slowing down spectrum	electron	Phys. Med. Biol. 57, 1087 (2012)
Stopping power or stopping cross section	electron, proton, alpha particle, C, O, Si, Fe	Med. Phys. 37, 4692 (2010) Phys. Med. Biol. 57, 209 (2011) Nuclear Inst. and Methods in Physics Research B 269, 2307 (2011)
W-value	electron	Phys. Med. Biol. 57, 1087 (2012) Med. Phys. 42, 3870 (2015)

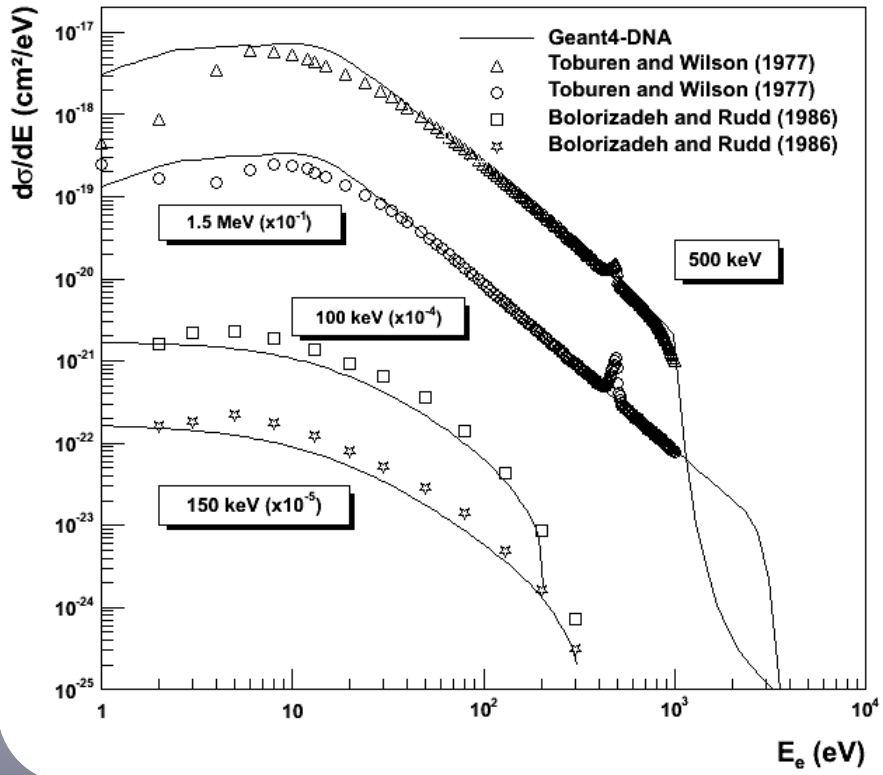
Verification

Proton & Hydrogen ionisation

Total XS



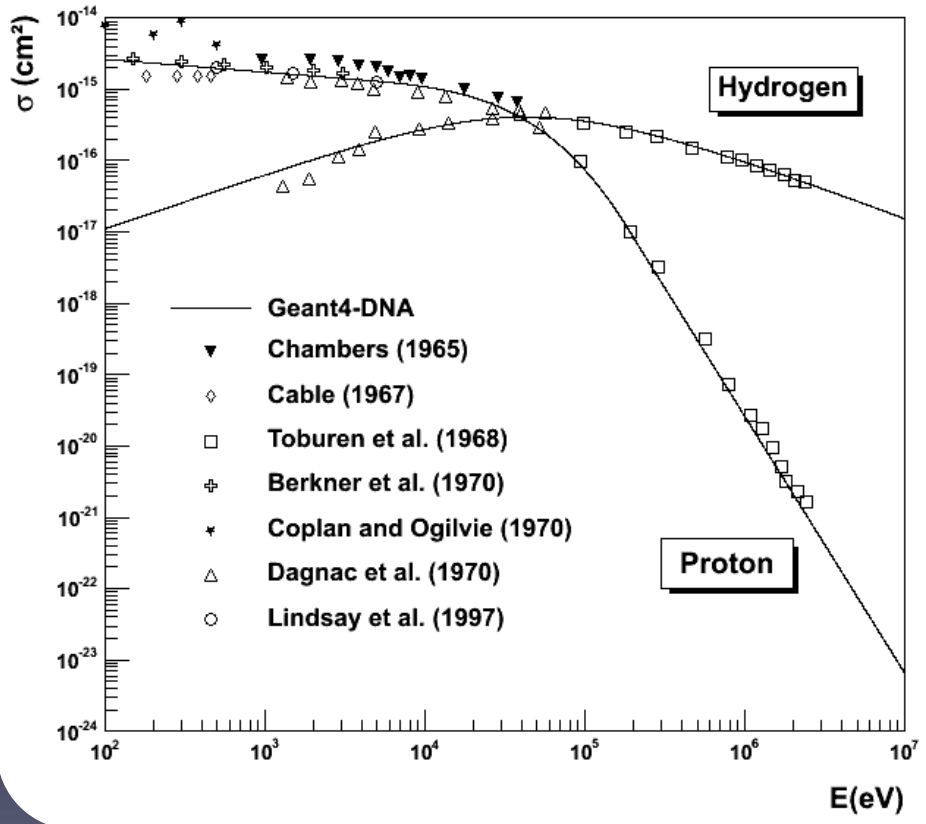
Differential XS



Verification

Proton and Hydrogen charge exchange

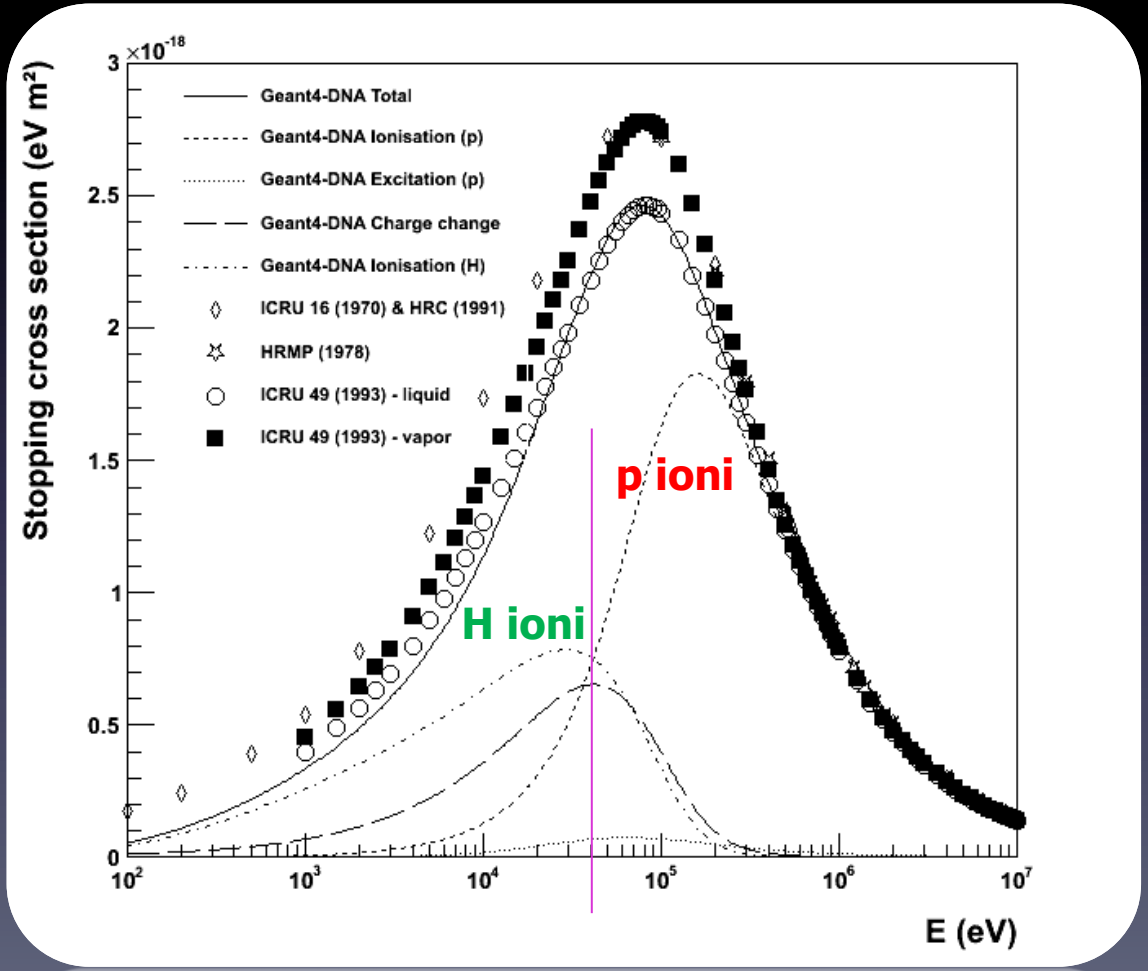
Total XS



Verification

Proton stopping cross section in liquid water

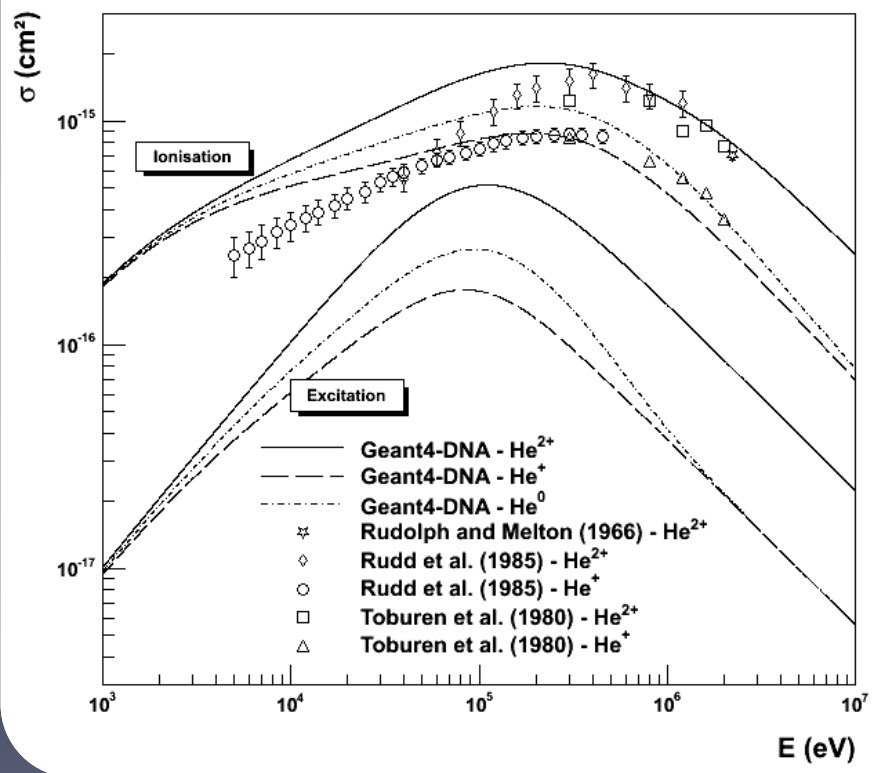
- Contributions of **ionisation** (p, H), **excitation** (p) and **charge change**
- Comparison to recommendations (ICRU, HRMP) for **liquid** and **vapour** water



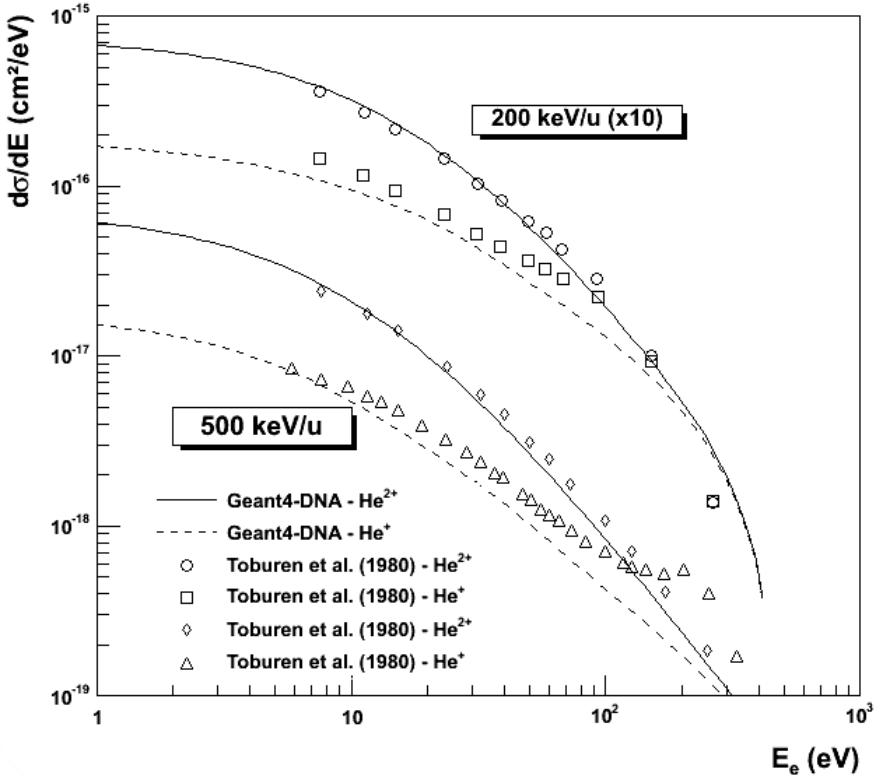
Verification

Helium ionisation

Total XS



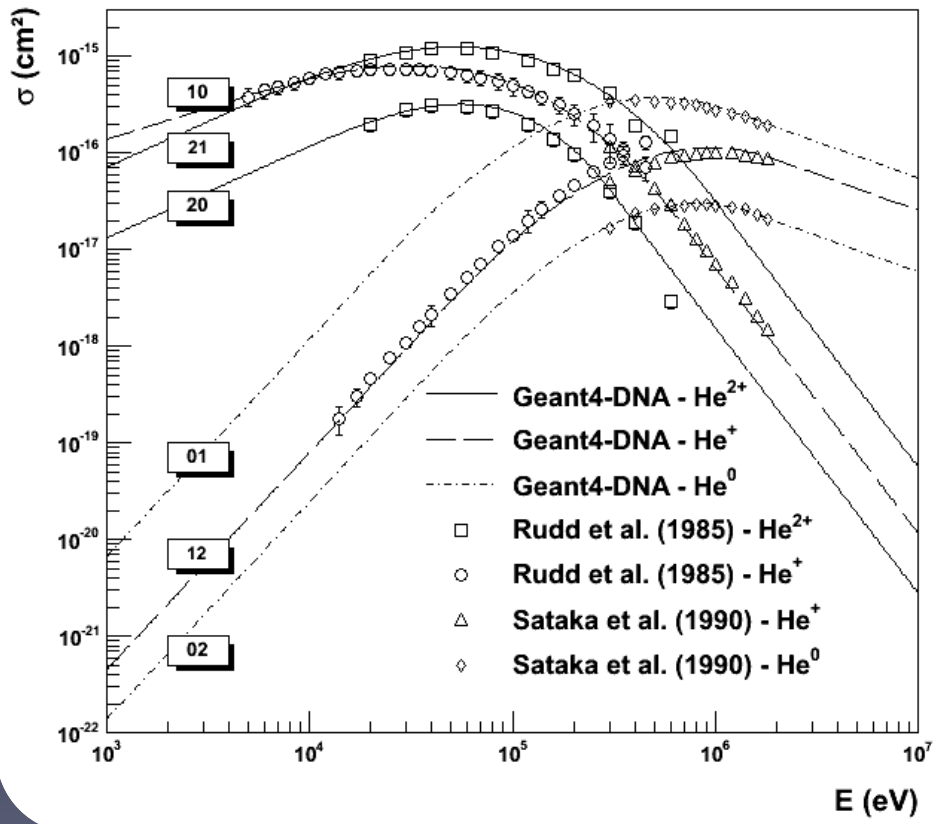
Differential XS



Verification

Helium charge exchange

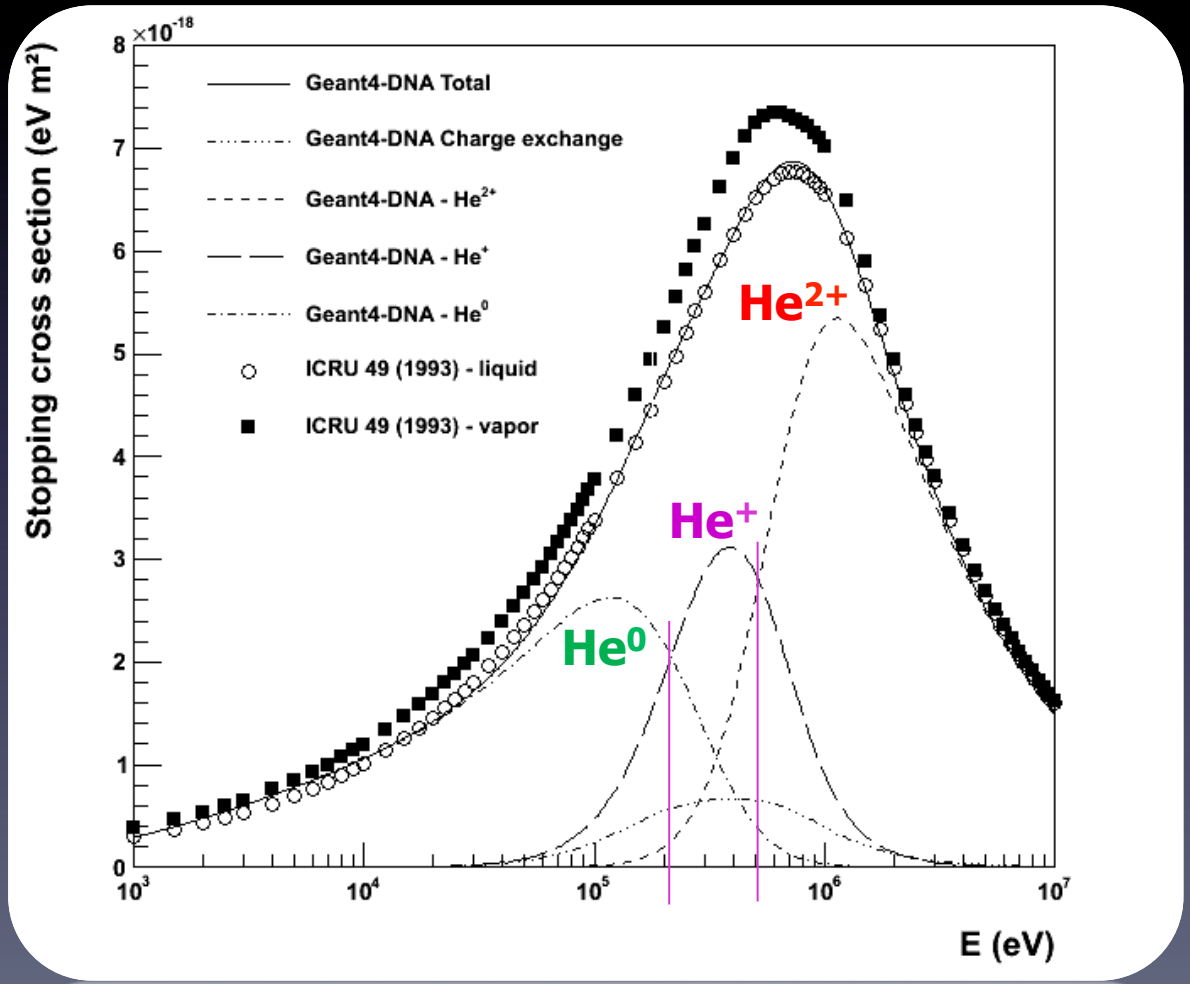
Total XS



Verification

Helium stopping cross section

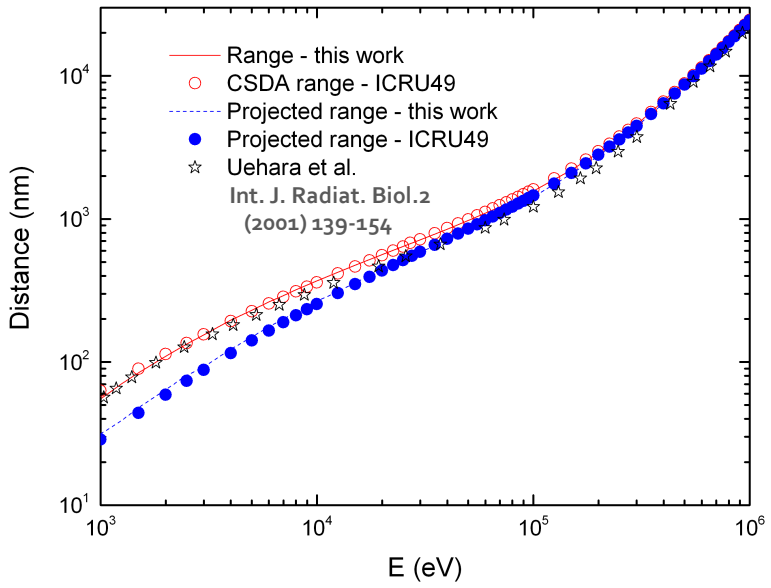
- Contributions of **3 charged states** of Helium
- Comparison to recommendations (ICRU) for **liquid** and **vapour** water



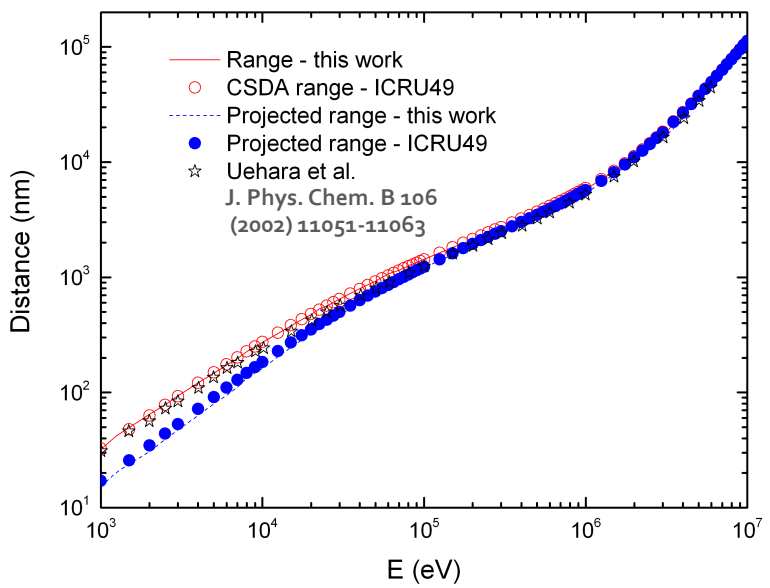
Verification

Range and projected range

Protons



Alphas

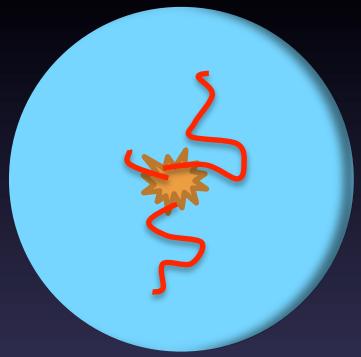


All Geant4-DNA processes are taken into account: excitation, ionization, charge-exchange and elastic scattering down to the tracking cut-off energy values

Verification

Dose Point Kernel simulations

- Accurate test of electron transport in small scale geometries
- We compared Geant4-DNA electron Dose Point Kernels (DPK) in liquid water with several MC codes
  - CPA100
  - EGSnrc
  - FLUKA 2011.2.15
  - MCNPX 2.7.0
  - PENELOPE 2006



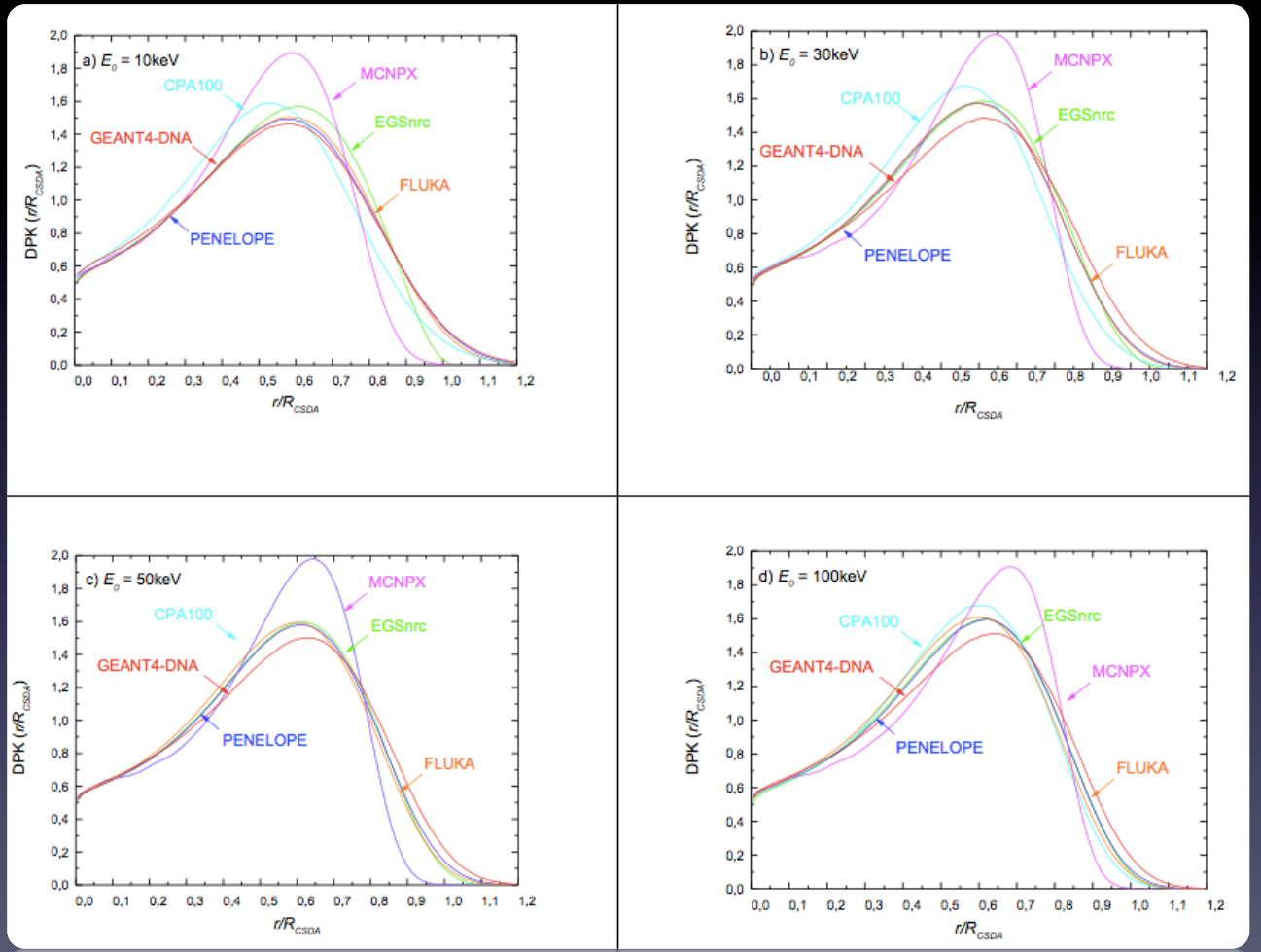
- 4 electron energies : 10 keV, 30 keV, 50 keV and 100 keV and 120 bins (r/r_{CSDA})
- Geant4-DNA partial wave elastic scattering model
- Kolmogorov-Smirnov test used to compare Geant4-DNA with the other Monte Carlo codes

Verification

DPK simulations in liquid water

- Geant4-DNA is compatible with EGSnrc, PENELOPE and FLUKA
- But not compatible with CPA100 (30 keV and 50 keV) and with MCNPX* (all energies)

*
- v2.7.0
- F8 tally
- EFAC=0.917
- transport cutoff of 1 keV
- ITS option
- ESTEP = 10 or 100



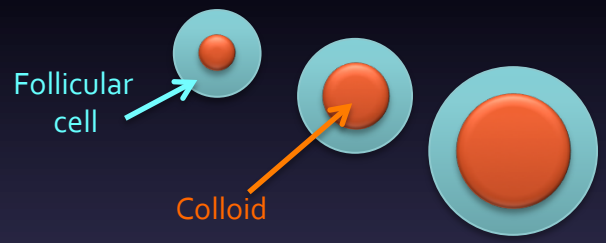
The geometrical granularity used in this study might be too large to get accurate DPK profiles using MCNPX

Appl. Radiat. Isot. 83 (2014) 137 (link)

Verification

S-values simulations in liquid water

- Alternative accurate test of electron transport in small scale geometries
- We compared Geant4-DNA electron S-values in liquid water with several MC codes
  - CPA100
  - EGSnrc
  - EPOTRAN/CELLDOSE
  - MC4V
  - MCNP
  - PENELOPE



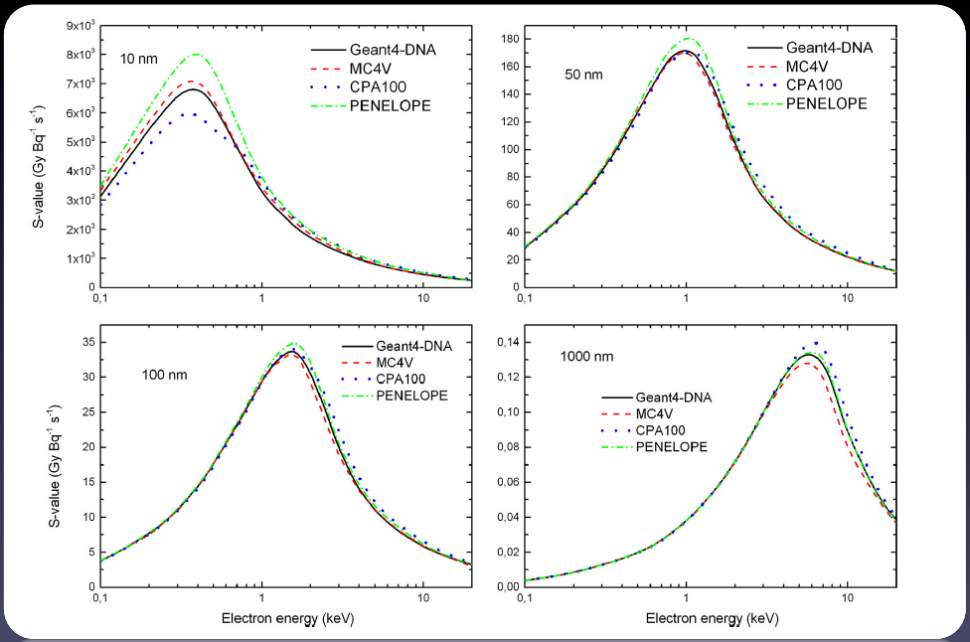
$$\overline{D}(r_T \leftarrow r_S) = \tilde{A}_{r_S} S(r_T \leftarrow r_S),$$

- Electron energies
  - monoenergetic case in a sphere of liquid water
  - 5 iodine isotopes: 131, 132, 133, 134, 135 in context of thyroid targeted immunotherapy
    - Two concentric spheres of liquid water separated by 10 microns :
      inner sphere with varying radius (colloid) and outer sphere with 10 micron thickness (follicular cell)

Verification

S-values simulations in liquid water

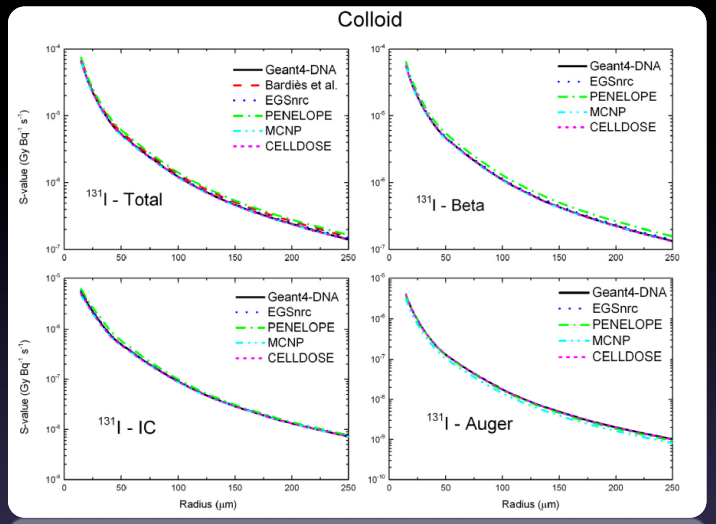
Monoenergetic electrons

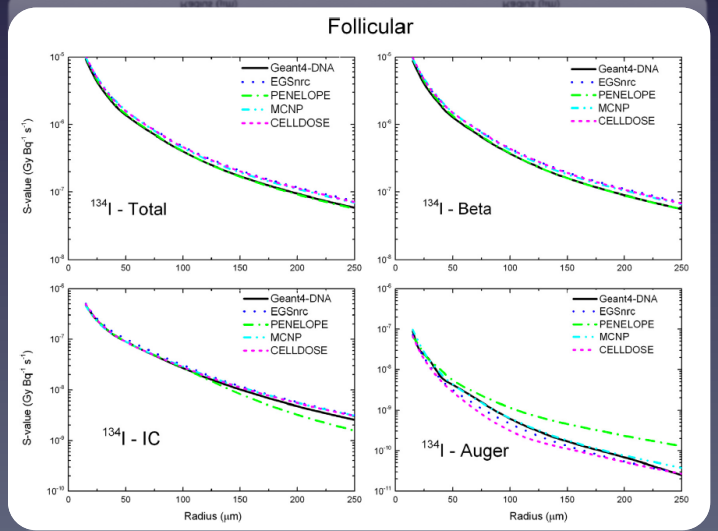


Best agreement with MC4V

Iodine : colloid and follicular

Best agreement with CELLDOSE



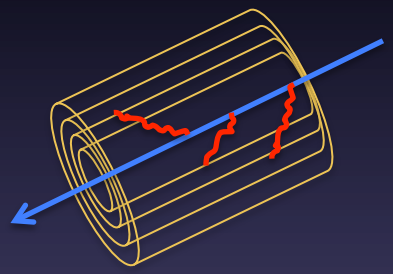


See Nucl. Instrum. and Meth. B 319 (2014) 87-94 (link)

Verification

Radial doses

- Investigation of Geant4-DNA performance for radial dose distribution around ion tracks
  - Protons, alphas, C, O, Fe
  - MeV–GeV range
- Comparison to published data
  - Analytical calculations
  - Monte Carlo simulations
  - Experimental data in tissue equivalent gas

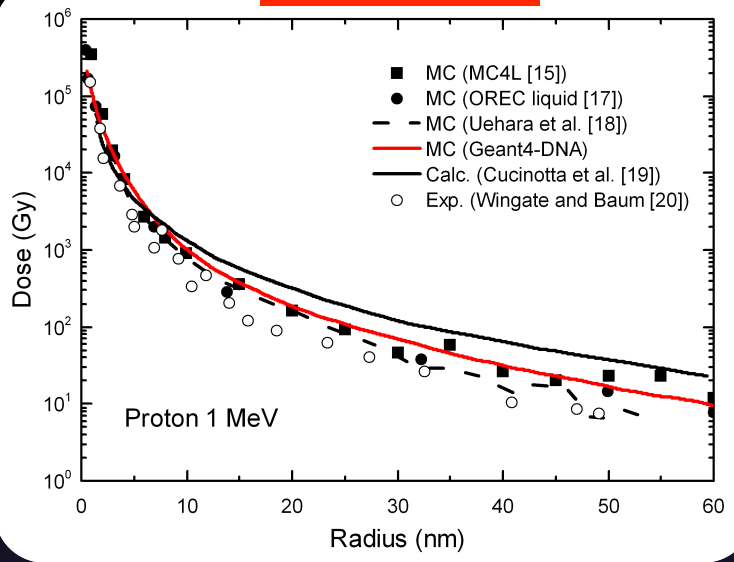


Verification

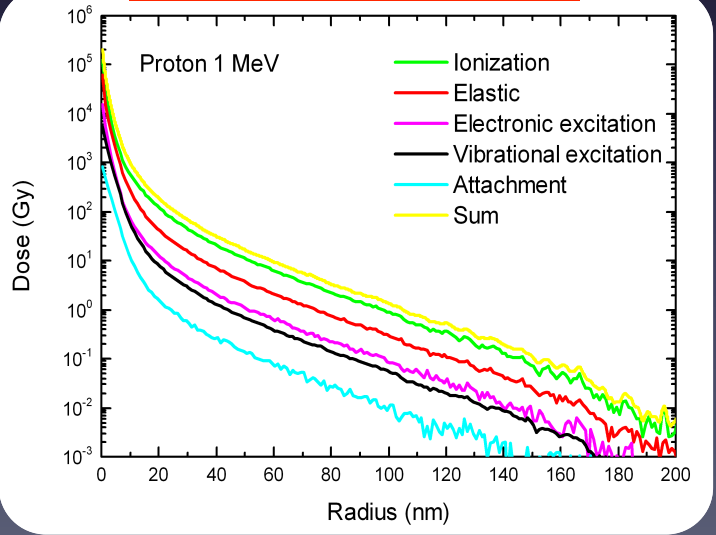
Radial doses

- General good agreement of dose profiles with a variety of literature data
- Selection of results for 1 MeV protons
  - Dose profile
  - Geometrically restricted LET
  - Individual process contribution to absorbed dose

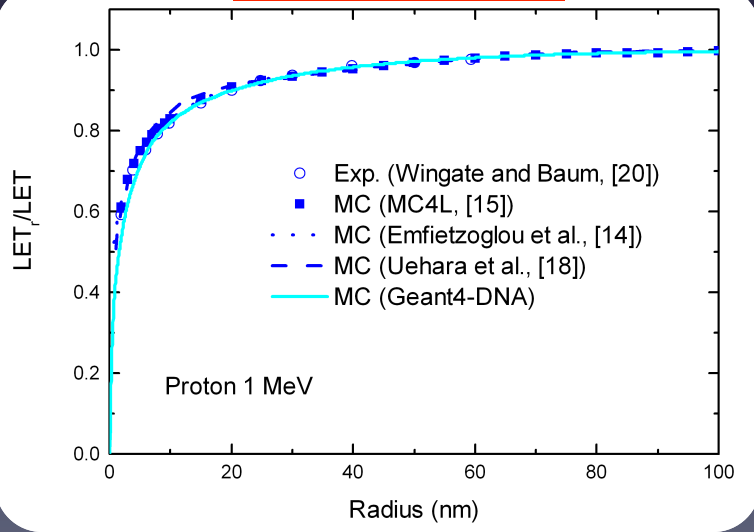
Dose profile



Process contribution



Restricted LET



Nucl. Instrum. and Meth. B 333 (2014) 92 (link)

S. Okada, K. Murakami, T. Sasaki et al., KEK, Japan

Porting Geant4-DNA to GPU

Electrons, protons and doubly charged heliums (He++) with specific kinetic energy were shot into a voxelized water phantom

Achieved up to 70 speedup compared to single CPU (Intel Xeon E5-2643V2) for electron and gamma simulation using NVIDIA Tesla K20 GPU

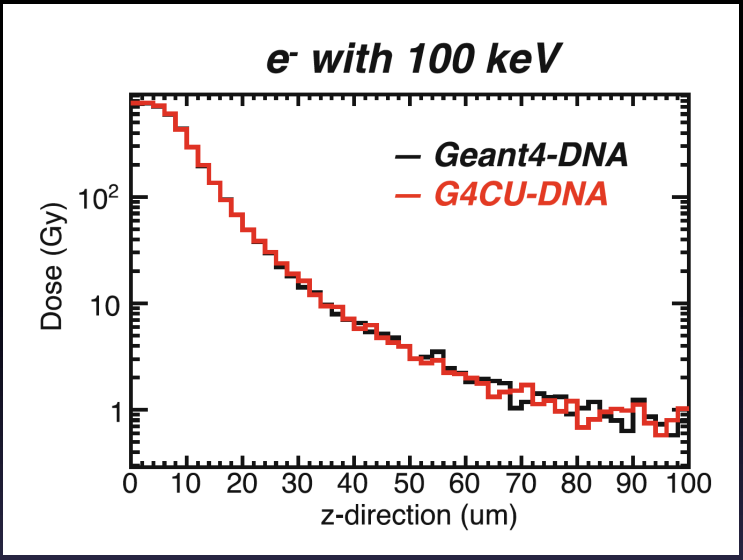
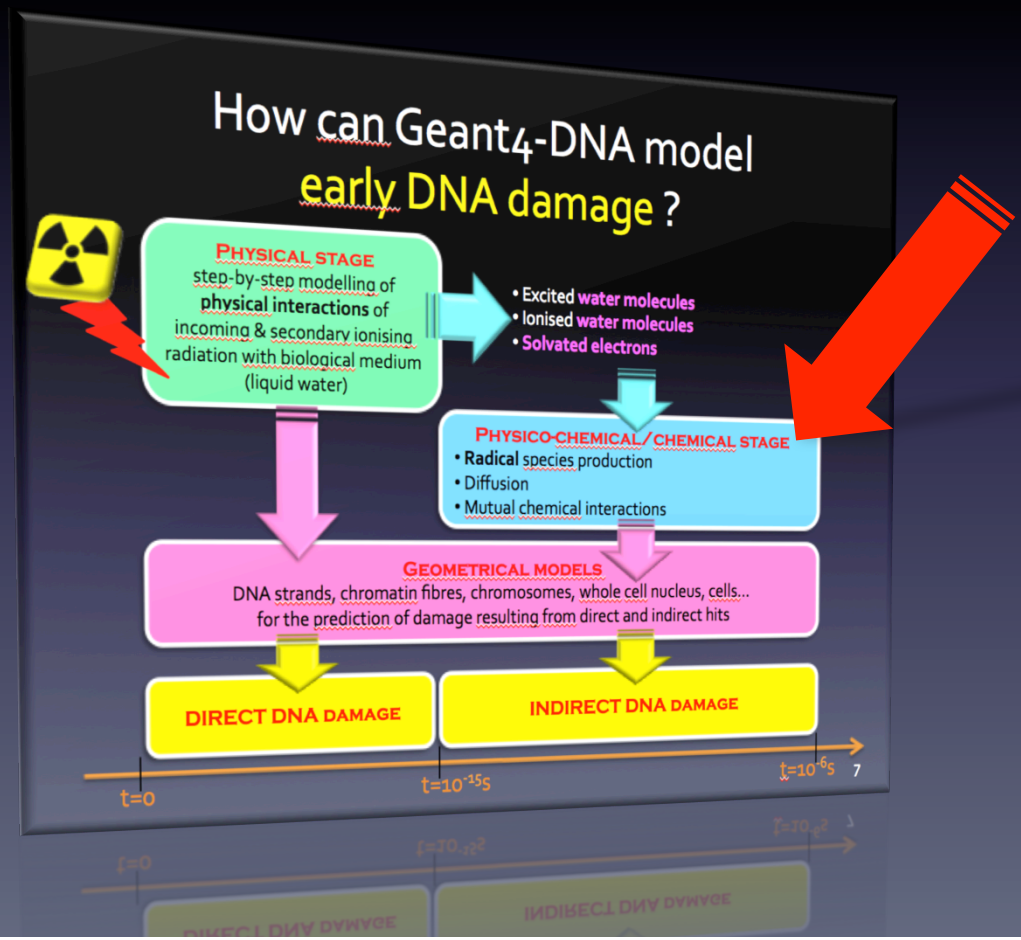


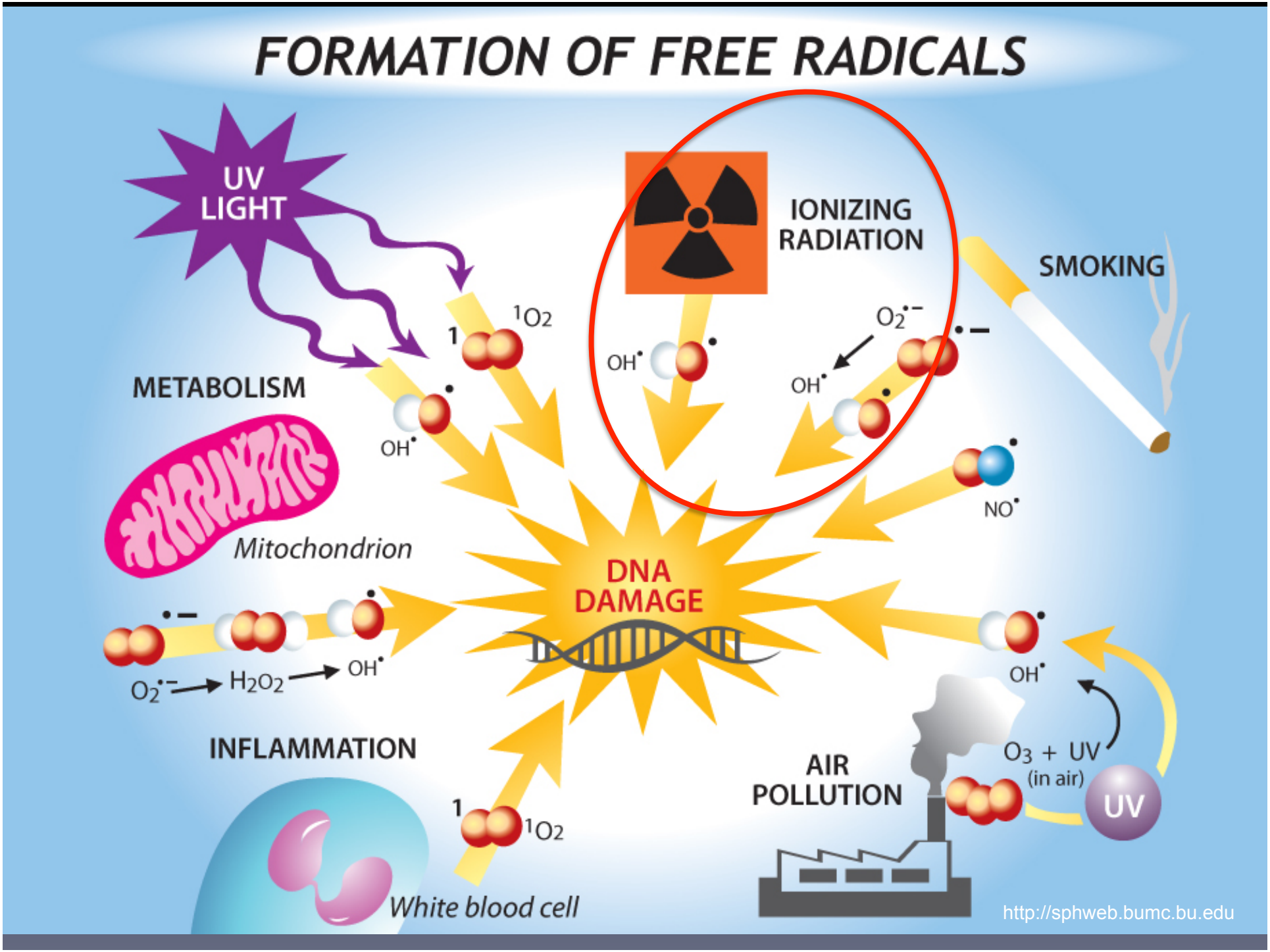
Table 4 Comparisons of computation time between GPU and CPU simulations

Incident particle	Initial energy	Geant4-DNA (CPU) (sec/particle)	G4CU-DNA (GPU) (sec/particle)	Speedup factor (=G4/G4CU)
e^-	100 keV	7.64×10^{-1}	1.05×10^{-2}	**72.9**
p	1 MeV	11.8	6.10×10^{-1}	**19.4**
He^{++}	1 MeV	12.3	6.63×10^{-1}	**18.6**

Innovation in Medicine and Healthcare 2015
Volume 45 of the series Smart Innovation, Systems and Technologies (2015) 323 (link)

3) PHYSICO-CHEMICAL & CHEMICAL STAGE




FORMATION OF FREE RADICALS
UV LIGHT
IONIZING RADIATION
SMOKING
METABOLISM
Mitochondrion
DNA DAMAGE
INFLAMMATION
White blood cell
AIR POLLUTION
O3 + UV (in air)
UV
NO•
OH•
H2O2
http://sphweb.bumc.bu.edu

Hirayama *et al*, 2009

Contribution of indirect effects

Survival vs Dose with different DMSO concentrations

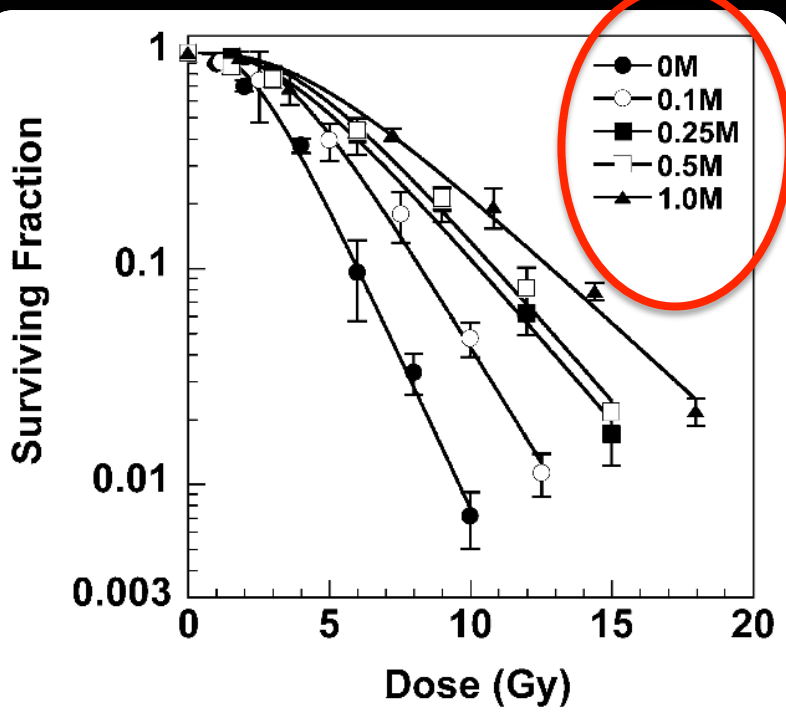


FIG. 1. X-ray survival of V79 cells in the presence of DMSO. Error bars represent the standard deviations (n = 2–3). These curves were fitted by the single-hit multitarget equation as described in the Materials and Methods.

Contribution of indirect effects VS LET

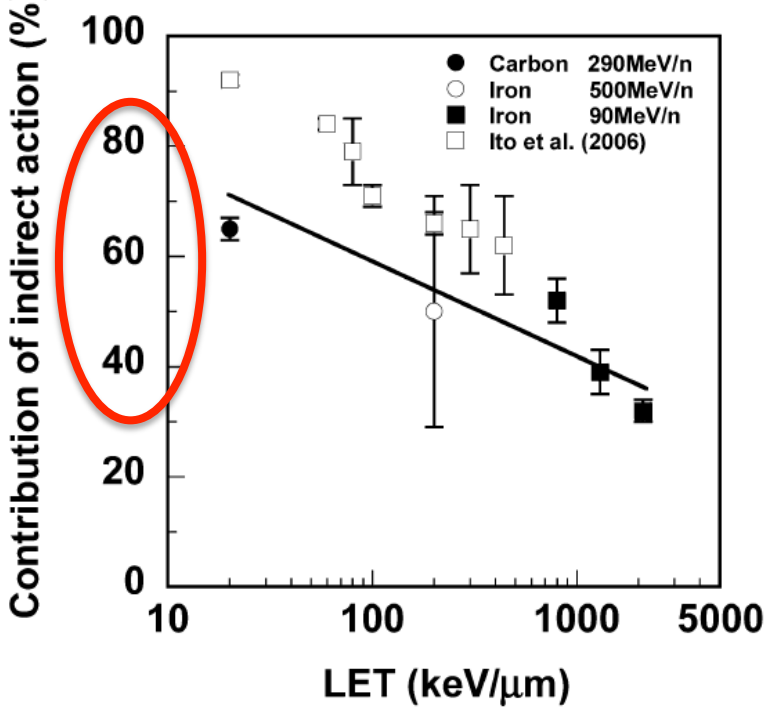


FIG. 4. LET dependence of the contribution of indirect action in cell killing. The error bars are standard errors for a protectable fraction calculated from a regression line. Data from Ito *et al.* for HL-60 cells (*6*) are plotted in the figure.

Challenge

extend Geant4 for the modeling of radiation chemistry

Geant4

- Simulations with Geant4 are HEP oriented
  - Sequential handling of tracks
  - Simulation based on geometrical space, where interaction length is the main quantity of interest
    - No time synchronization
- No individual molecules
- No Brownian motion

Key requirements for Geant4-DNA RC

1. A generic system for handling interactions between tracks
2. Molecular species as tracks and targets
3. Brownian motion
4. Chemical reactions

J. Comput. Phys. 274 (2014) 841 (link)

PhD thesis of M. Karamitros

Modelling water radiolysis

- **Water radiolysis** = dissociation of water molecules by ionising radiation
  - Creation of oxydative species
  - They can interact chemically with one another or with the « biological medium » (« non-direct effects ») and interfere with the normal functioning of cells

- **Stage 1 : Physico-chemistry stage**

  we start from altered water molecules which underwent changes in their electronic configuration from physical processes occuring during the « Physical stage »
  - Electronic excitation, ionisation
  - The electronic rearrangement may lead to their dissociation
    - We use branching ratios and positioning of dissociation products, which can be modified by the user

Modelling water radiolysis

- **Stage 2 : Chemistry stage**

  the dissociative products can recombine to form new chemical species

  – A new stepping algorithm was developed to handle this recombination and more generally manage collisions between tracks

    - Requires the synchronization of tracks during simulation
    - All tracks are transported simultaneously during dynamic or fixed « time steps »

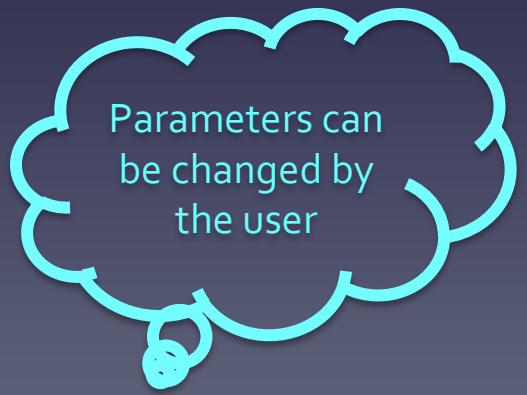
  – A table of chemical reactions and their reaction rates must be provided

- All parameters are provided through a « Chemistry list » as Geant4 users would do with a « Physics list »

  – G4EmDNAChemistry

- Note that the chemistry can be started as a standalone application

  – Input user defined « physics » phase space



$t=10^{-15}s$ $t=10^{-12}s$

Physico-chemical stage

- During this stage, water molecules
  - Dissociate if ionized
  - Relax or dissociate if excited

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

- Products thermalize down to their energy of diffusion at equilibrium

$t=10^{-15}s$ $t=10^{-12}s$ $t=10^{-6}s$

Chemical stage

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

InConstructMolecule()

We followed the set of parameters published by the authors of the PARTRAC software (Kreipl et al., REB 2009). However, these parameters can be modified by the user.

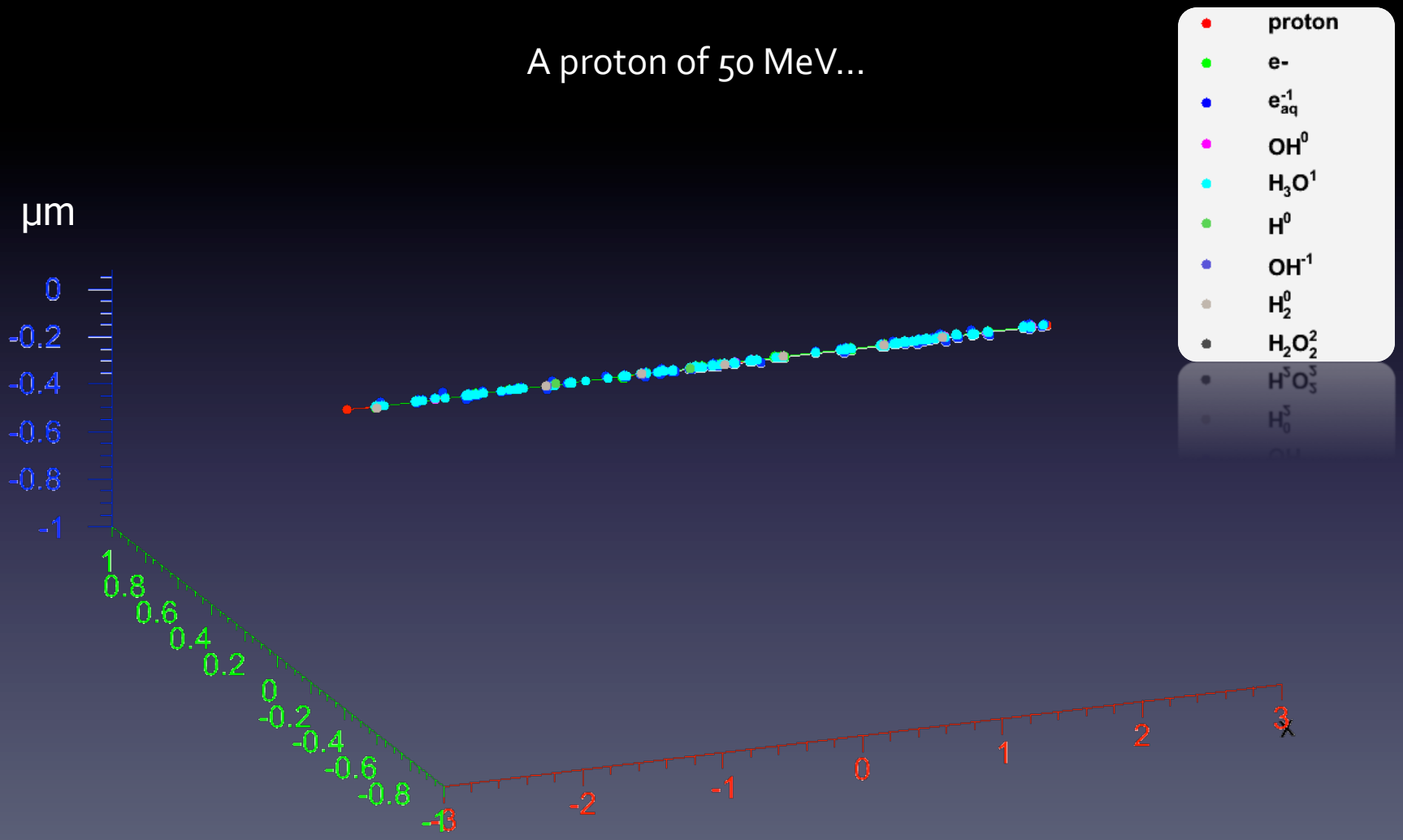
Reaction	Reaction rate (10^7 m^3 mol^{-1} s^{-1})
$H_3O^+ + OH^- \rightarrow 2\ H_2O$	14.3
$\bullet OH + e^-_{aq} \rightarrow OH^-$	2.95
$H\bullet + e^-_{aq} + H_2O \rightarrow OH^- + H_2$	2.65
$H_3O^+ + e^-_{aq} \rightarrow H\bullet + H_2O$	2.11
$H\bullet + \bullet OH \rightarrow H_2O$	1.44
$H_2O_2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

InConstructReactionTable()

Kreipl *et al*, 2009

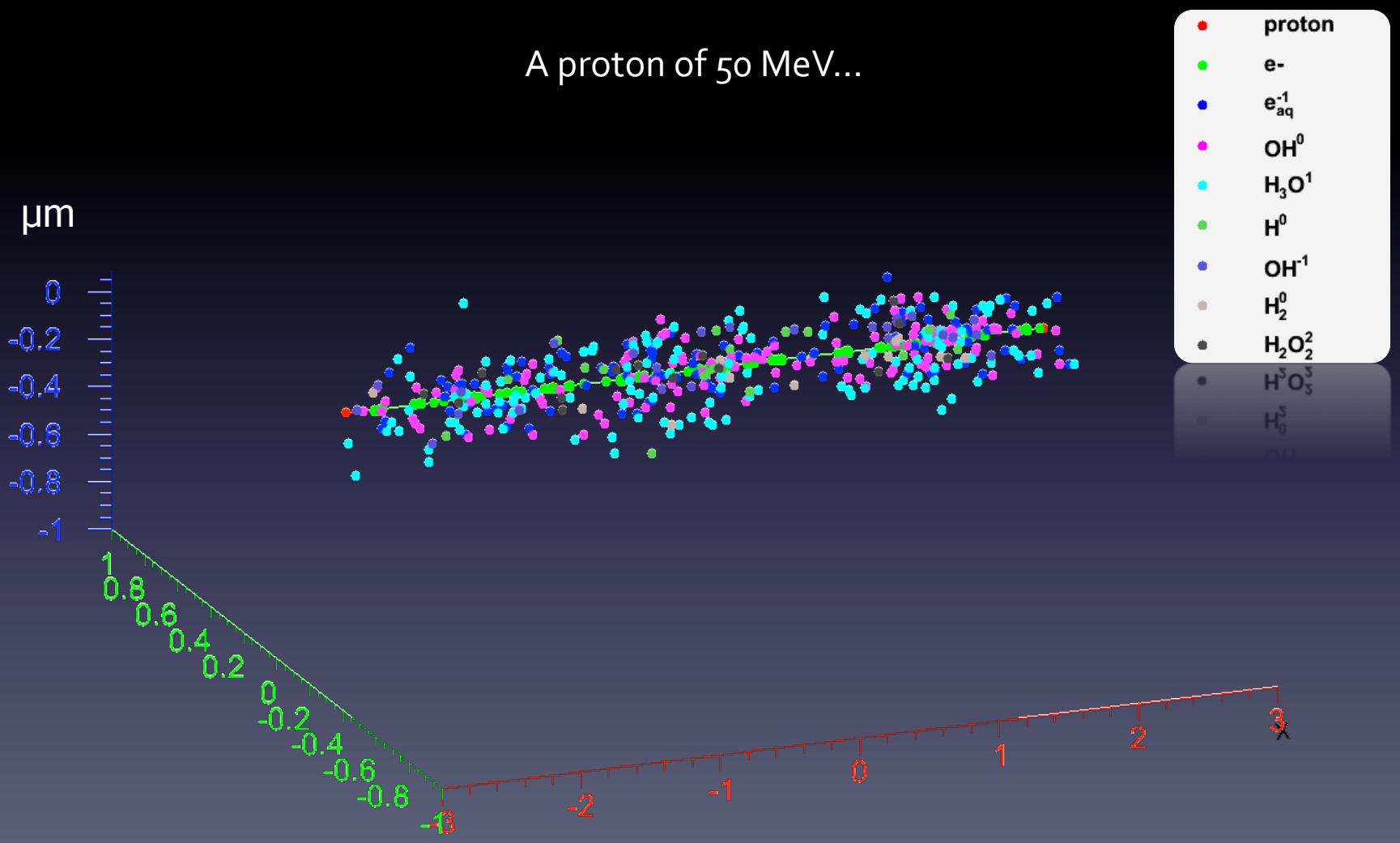
Situation at 1 picosecond

A proton of 50 MeV...



Situation at 1 microsecond

A proton of 50 MeV...



Definition of radiochemical yield *G*

Number of molecules of a given species

for 100 eV of deposited energy

Time-dependent radiochemical yield

$$G(t) = \frac{N(t)}{E_{dep}}$$

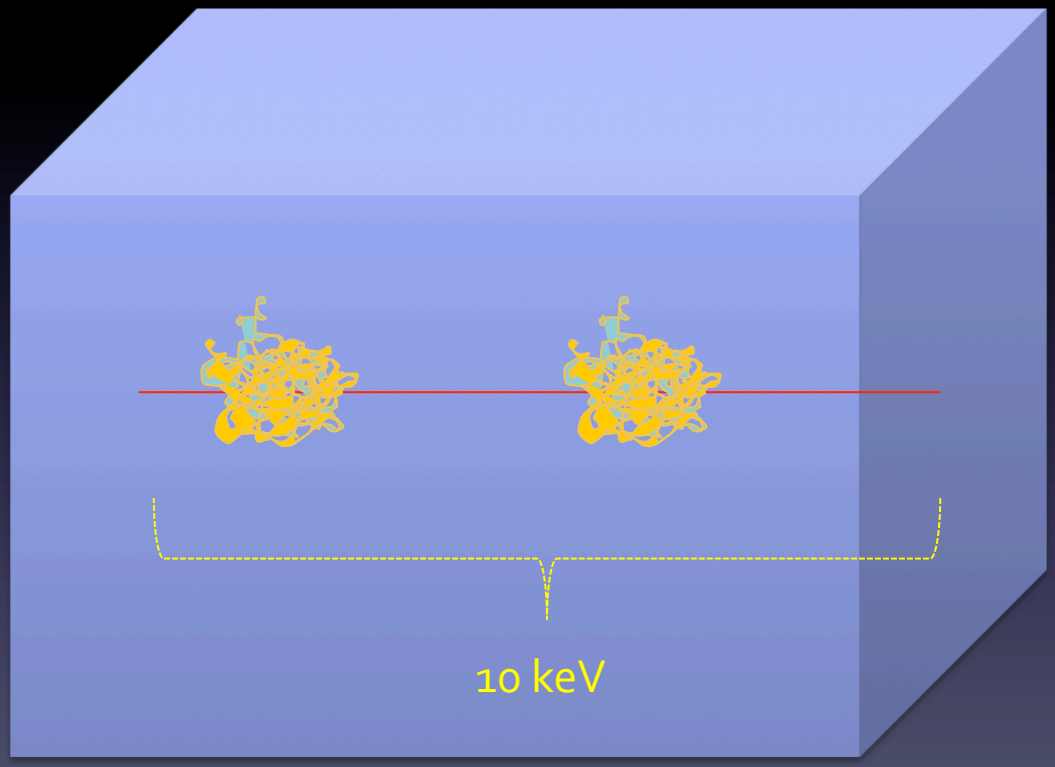
Number of molecules at time *t*

Deposited energy scaling to 100 eV

An observable quantity commonly used to evaluate chemistry modeling accuracy…

SIMULATION SETUP #1

- 1 MeV electrons in infinite liquid water volume
- Only the first 10 keV deposit energy are taken into account for the chemistry

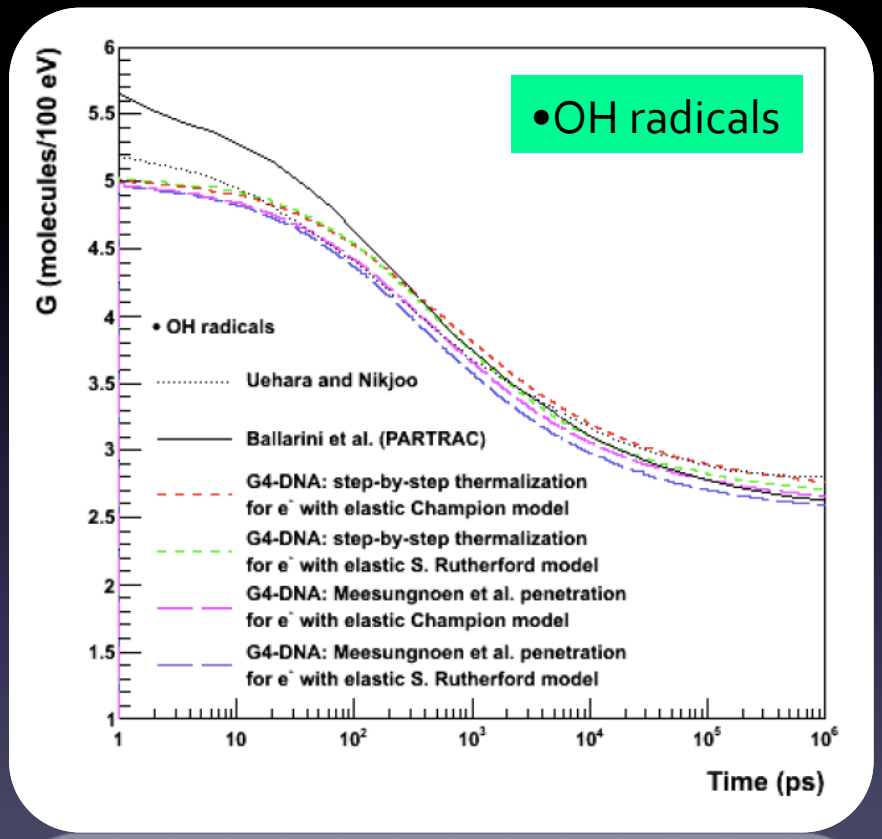


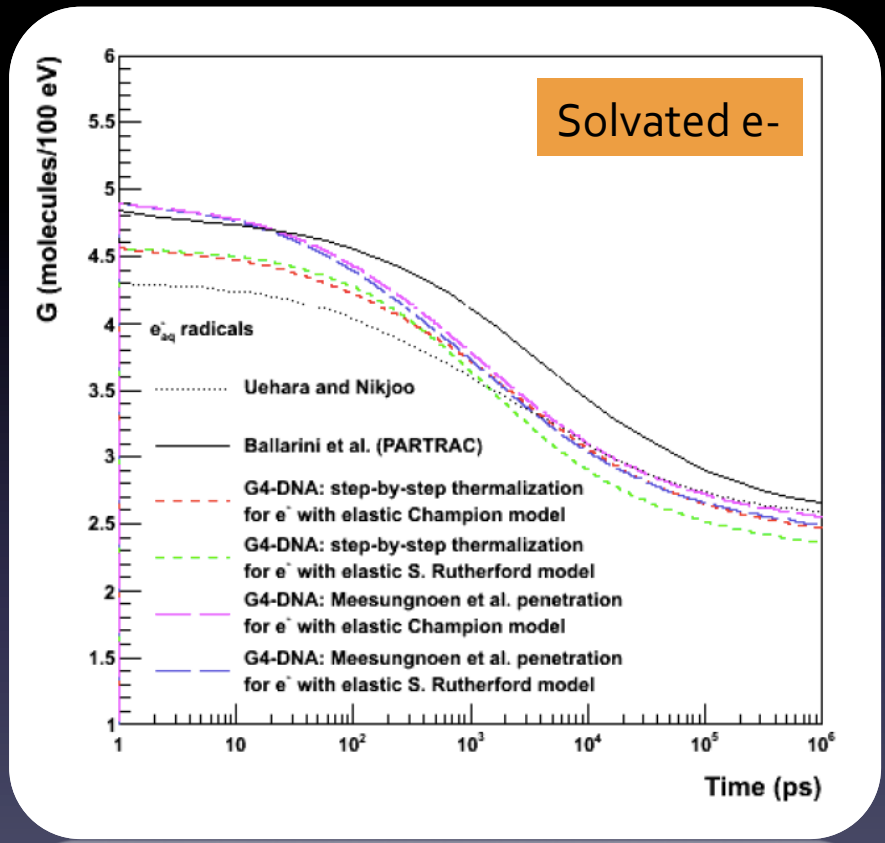
Electron

Secondaries

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

Radiochemical yields VS time





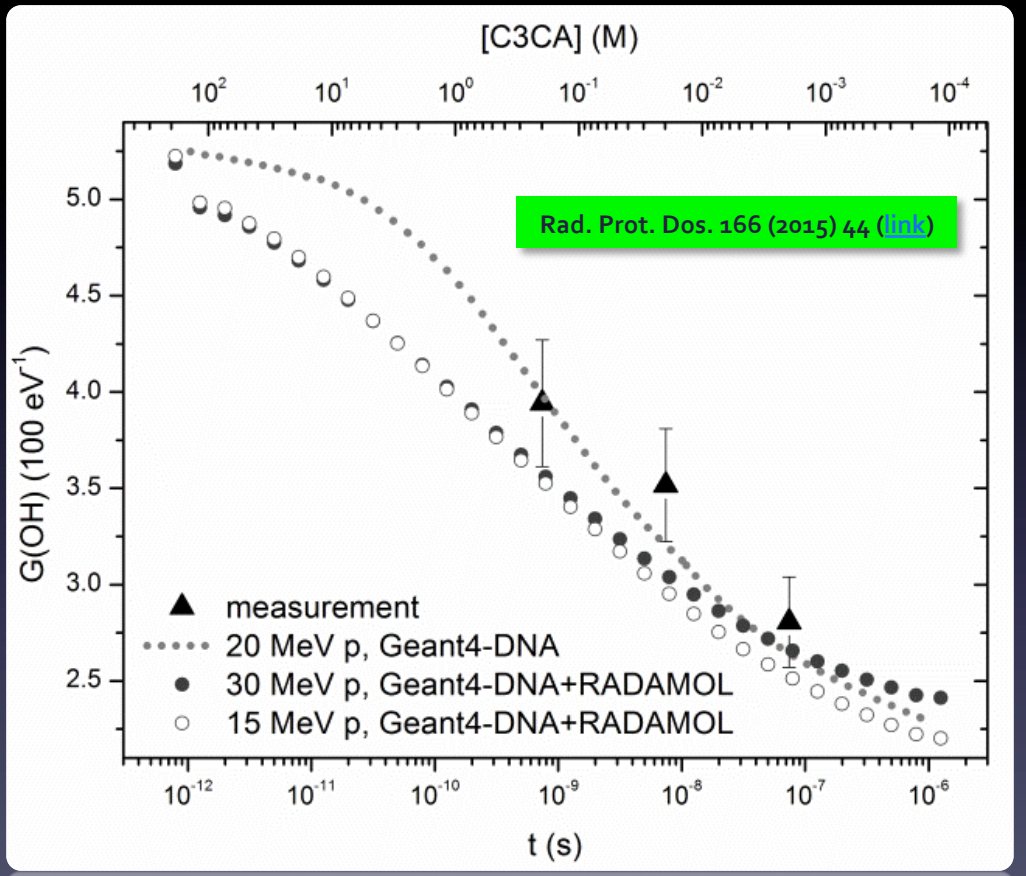
- Effect of the two **alternative** electron elastic scattering models of Geant4-DNA
- Results are obtained in **30 minutes** on a cluster of 80 CPUs (Physics + Chemistry)

Prog. Nucl. Sci. Tec. 2 (2011) 503 (link)

Radiochemical yields VS time

First direct validation

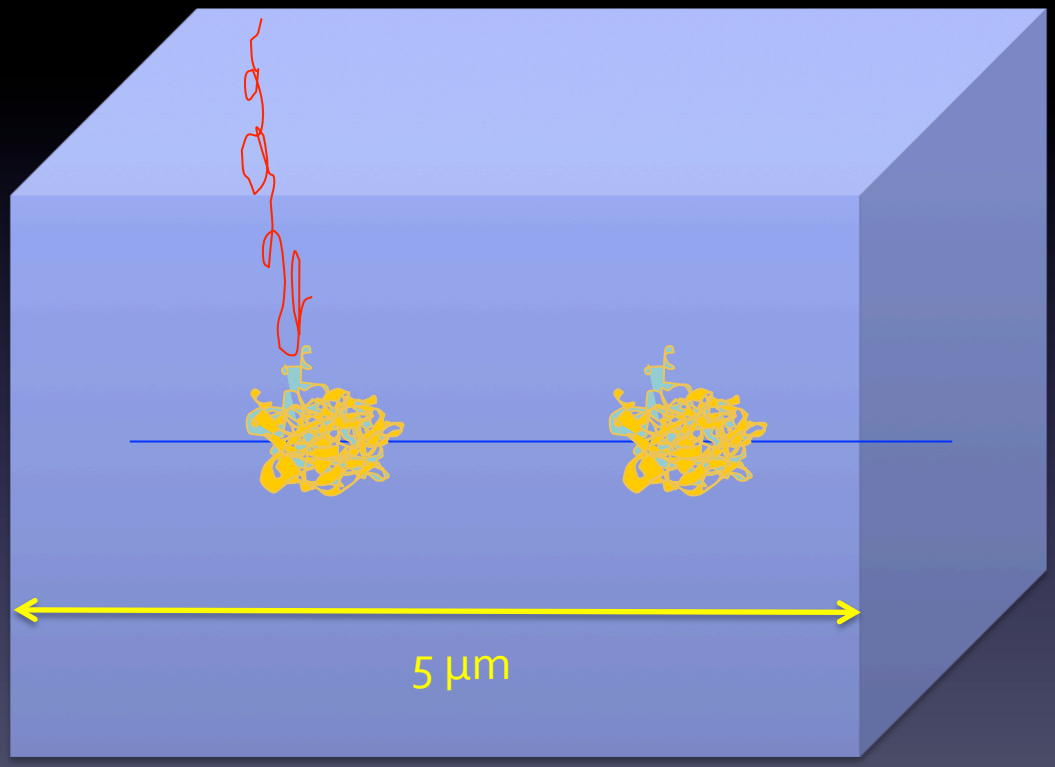
- We compared measured G values of OH radicals in liquid water to Monte Carlo simulations
- Experiment
  - 30 MeV proton beam at NPI in Prague
  - Target is coumarin-3-carboxylic acid scavenger (C3CA), 3 concentrations (2, 20, 200 mM). C3CA forms fluorescent product with OH, 7-hydroxycoumarin-3-carboxylic acid (7-OH-C3CA) The inverse of the reaction rate k [C3CA] corresponds to the time scale of the reaction.
- Simulations
  - Geant4-DNA physics + RADAMOL for radiolysis (15 & 30 MeV) developed at NPI (M. Davidkova et al.)
  - Geant4-DNA physics + radiolysis (20 MeV)
  - Same geometry as in previous setup : we selected three energies in order to to cover the energy decrease of protons in the sample



« Calculated OH radical yields in time are in acceptable agreement with the experimental data, notably when utilising Geant4-DNA chemistry simulation capabilities »

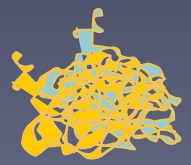
SIMULATED SETUP #2

- Protons in 5 µm finite cube of liquid water
- When a particle leaves the cube, it is taken out from the simulation



Proton

Electron

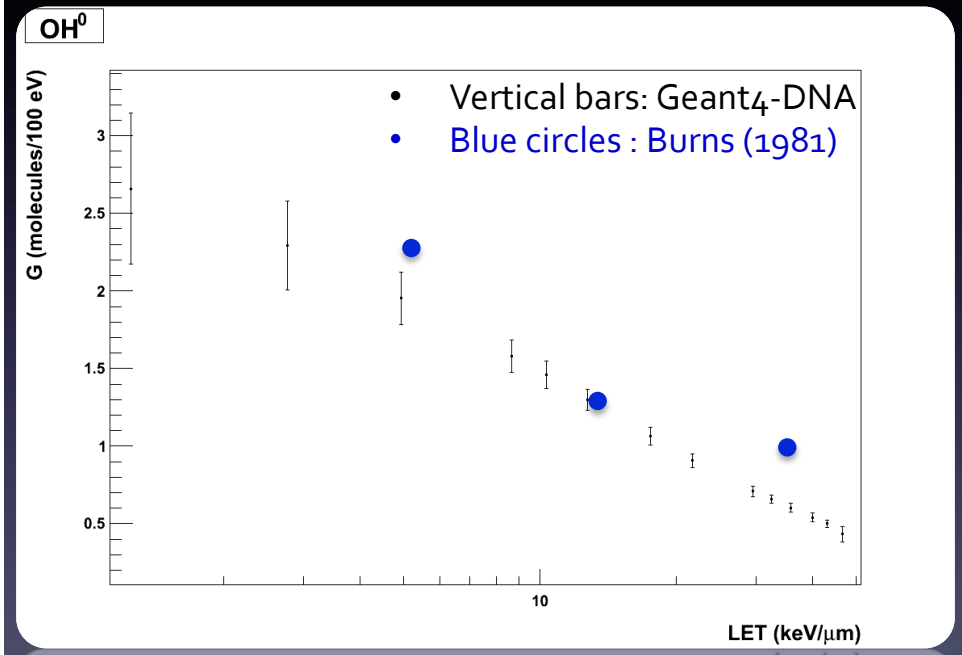


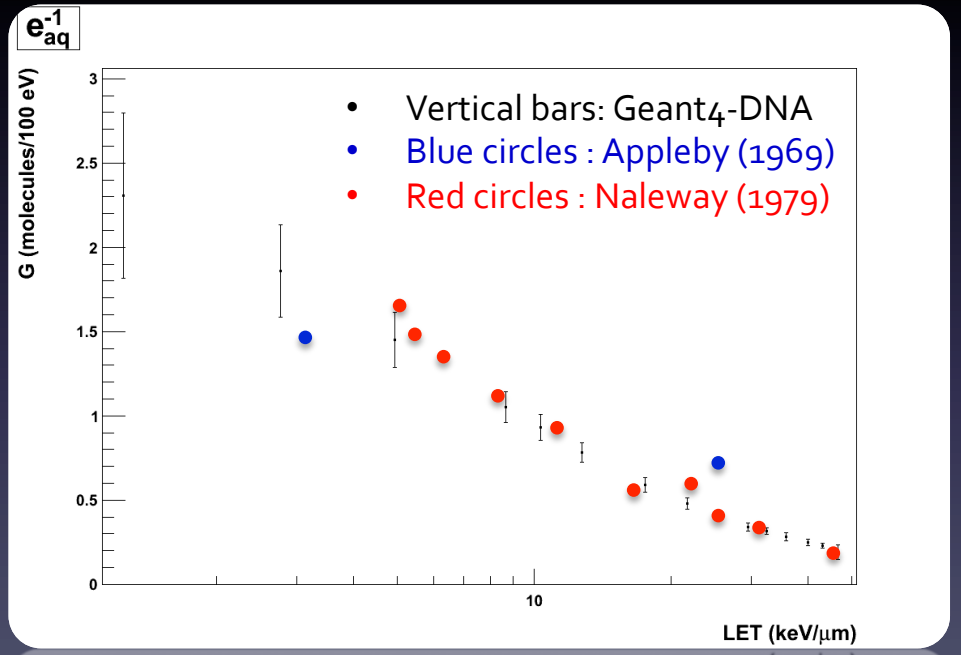
Secondaries

Radiochemical yields VS LET

•OH radicals

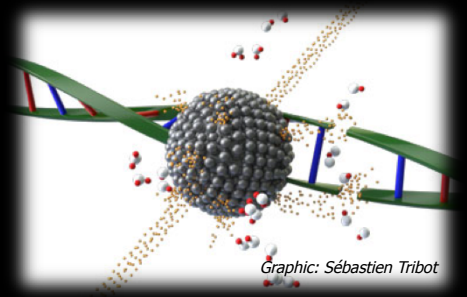
Solvated e-





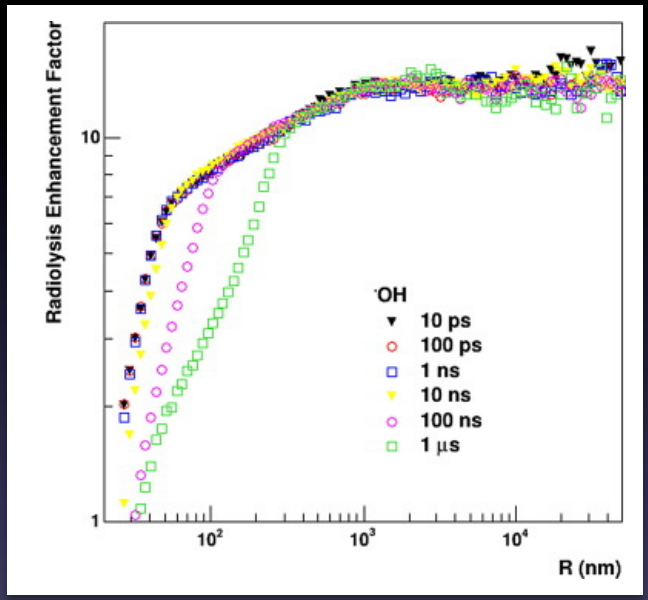
J. Comput. Phys. 274 (2014) 841 (link)

Investigation of radiotherapy boost effects using high-Z nanoparticles



- Hot topic: high-Z NP internalized in cells could boost energy deposition and increase the efficacy of radiotherapy

- Well established for photon beams (photoelectric effect), not so clear for proton beams…

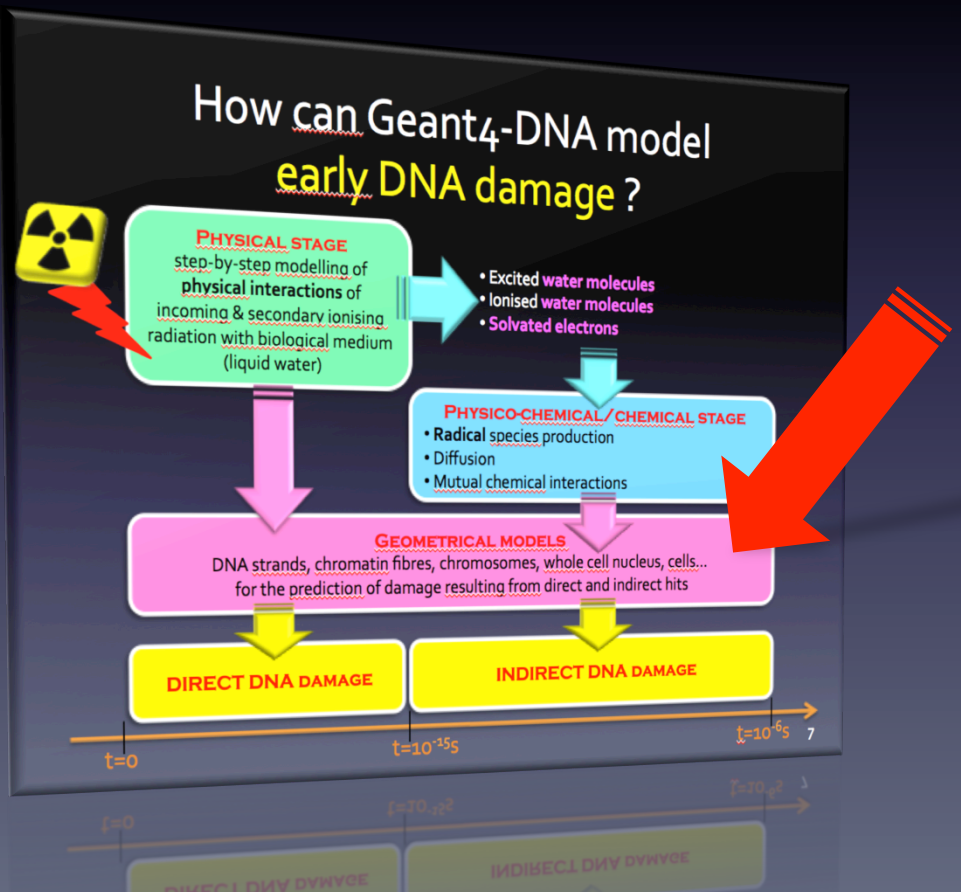


- Still a challenge to perform mechanistic simulations
  - We initiated a specific Geant4-DNA activity on the subject in 2015
  - Simulation of physics + physico-chemistry + chemistry around NP
  - Eg. Radiolysis Enhancement Factor as a function of distance from GNP compared to WNP

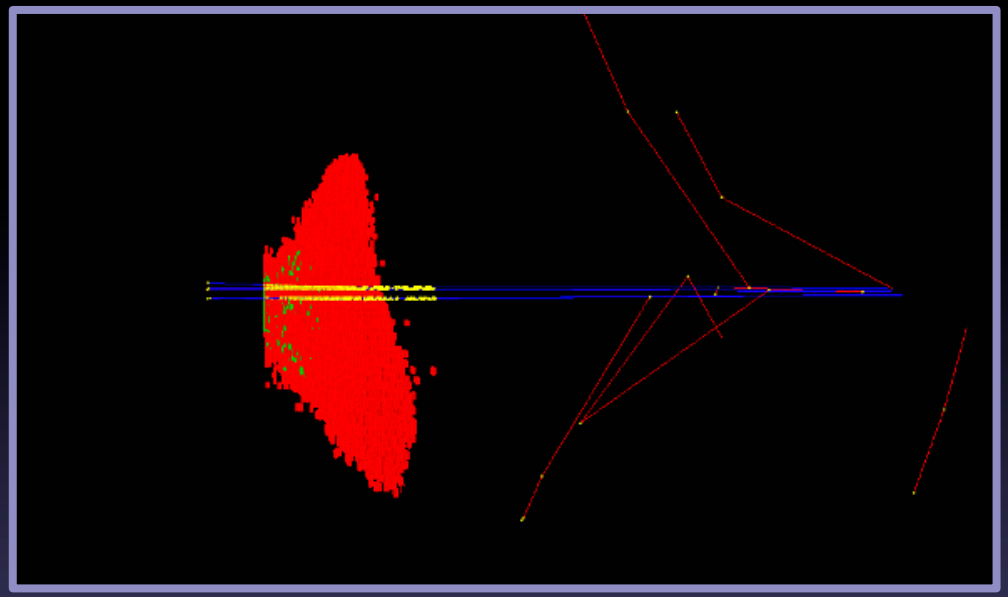
Nucl. Instrum. Meth. B 373 (2016) 126 (link)

See Nathanael's talk on chemistry….

4) GEOMETRICAL MODELS



« microbeam » advanced example

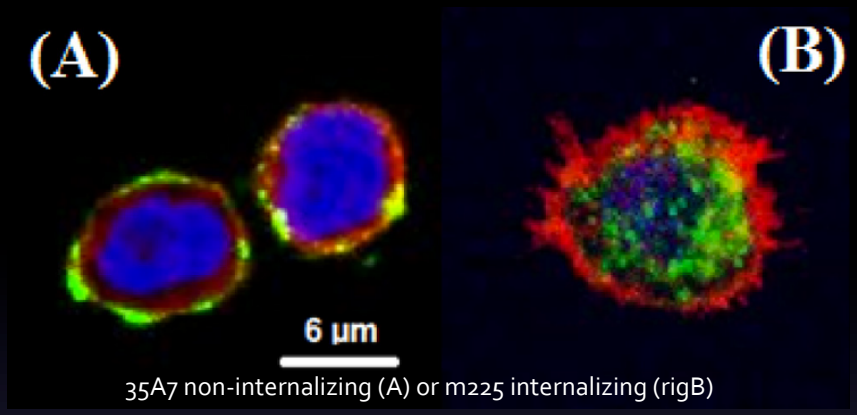


- Simulation of single HaCat cell targeted irradiation using a focused alpha particle microbeam @ CENBG, Bordeaux, France
- Implements a realistic 3D cellular phantom constructed from confocal imaging and ion beam elemental chemical analysis
  - Nucleus, nucleoli, cytoplasm
  - About 5×10^4 voxels, each of size $360 \times 360 \times 160$ nm^3
- By default, uses Geant4 « low energy » Livermore-based electromagnetic physics
- Can extract energy deposition per voxel

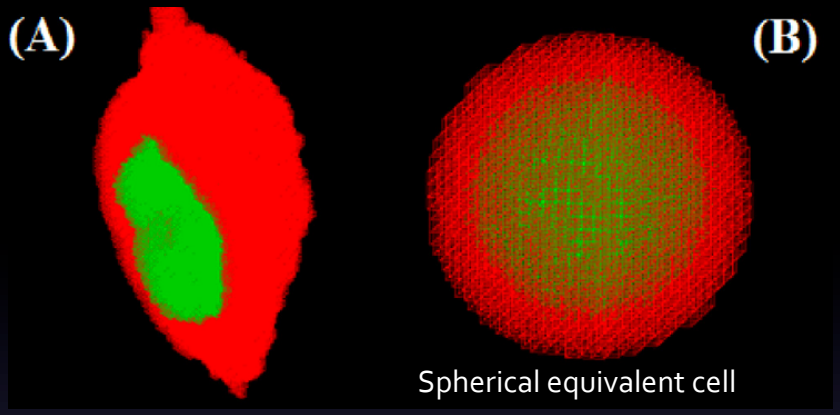
Rad. Prot. Dos. 133 (2009) 2 (link)

Cellular dosimetry

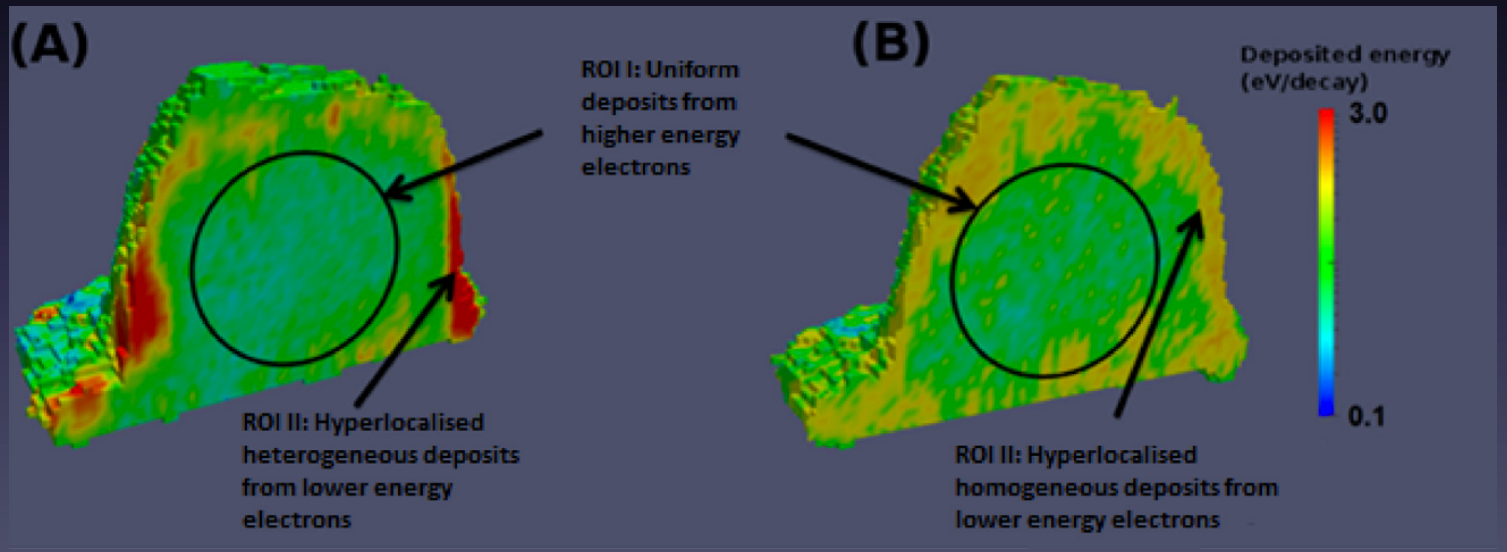
Nucl. Instrum. and Meth. B 366 (2016) 227 (link)



35A7 non-internalizing (A) or m225 internalizing (rigB)

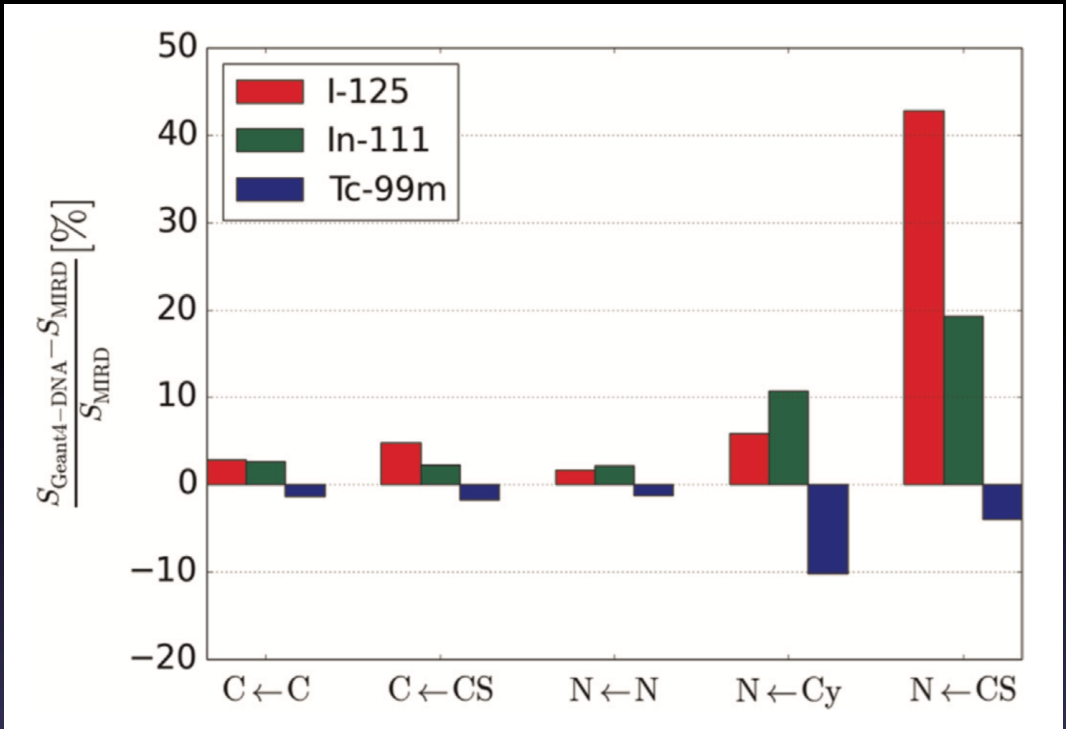


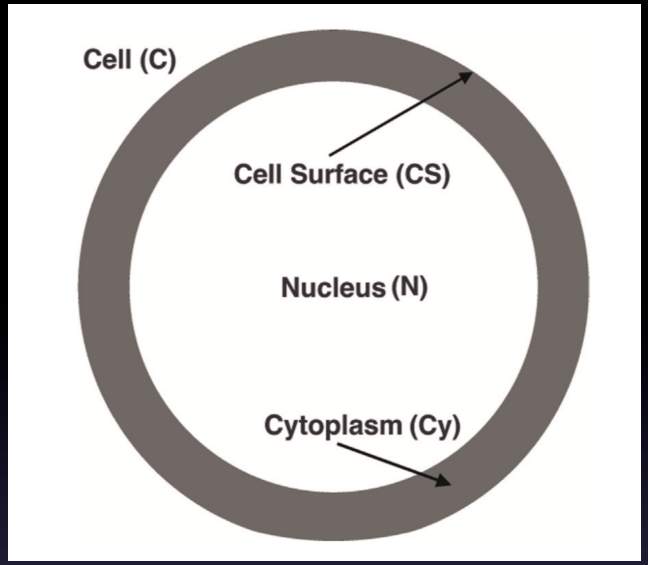
Spherical equivalent cell



- Vulvar squamous carcinoma A-431 cells treated with non-internalizing and internalizing antibodies labelled with Auger emitter I-125
- Geant4: Livermore based + Coulomb scattering + « microbeam » adv. example (« cellular phantom »)
- Simulation of the distribution of energy deposition in the cell model for non-uniform (A – from fluorescence signal) and uniform (B) emission probabilities from I-125 electrons with 35A7 non-internalizing antibodies (logarithmic colour scale).

S-values





$$\overline{D}(r_T \leftarrow r_S) = \tilde{A}_{r_S} S(r_T \leftarrow r_S),$$

- New benchmark of Geant4-DNA models against Committee on Medical Internal Radiation Dose (MIRD) data for S-values for several radionuclides
- Also investigated cellular morphology dependence
- Based on the « svalue » extended example

Appl. Radiat. Isot. 104 (2015) 113 (link)

See Nathanael's talk on geometries….

5) Where to find more information ?

Geant4-DNA website

A unique web site for 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

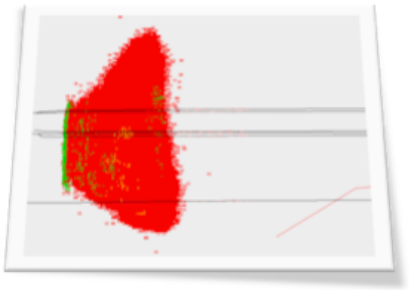
9 PhD theses

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.

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Geant4-DNA examples included in Geant4

Example code name	Purpose	Location
dnaphysics	• Usage of Geant4-DNA Physics processes • variable density	$G4INSTALL/examples/extended/medical/dna
microdosimetry	Combination of Standard EM or Low Energy EM processes with Geant4-DNA Physics processes	$G4INSTALL/examples/extended/medical/dna
range	Range simulation with Geant4-DNA	$G4INSTALL/examples/extended/medical/dna
svalue	Usage of Geant4-DNA Physics processes in spheres	$G4INSTALL/examples/extended/medical/dna
wvalue	Calculation of W values	$G4INSTALL/examples/extended/medical/dna
clustering	Clustering code	$G4INSTALL/examples/extended/medical/dna
chem1, chem2, chem3	Usage of Geant4-DNA chemistry	$G4INSTALL/examples/extended/medical/dna
wholeNuclearDNA	Cell nucleus	$G4INSTALL/examples/extended/medical/dna
pdb4dna	Interface to PDB database	$G4INSTALL/examples/extended/medical/dna
microbeam	3D cellular phantom	$G4INSTALL/examples/advanced
TestEm12	DPK	$G4INSTALL/examples/extended
TestEm14	Extraction of cross sections	$G4INSTALL/examples/extended

Geant4 Virtual Machine

http://geant4.in2p3.fr

A virtual Linux PC with Geant4 and tools fully installed

Windows™
Mac™
Linux™

Full free access

Twitter @Geant4VM

Perspectives

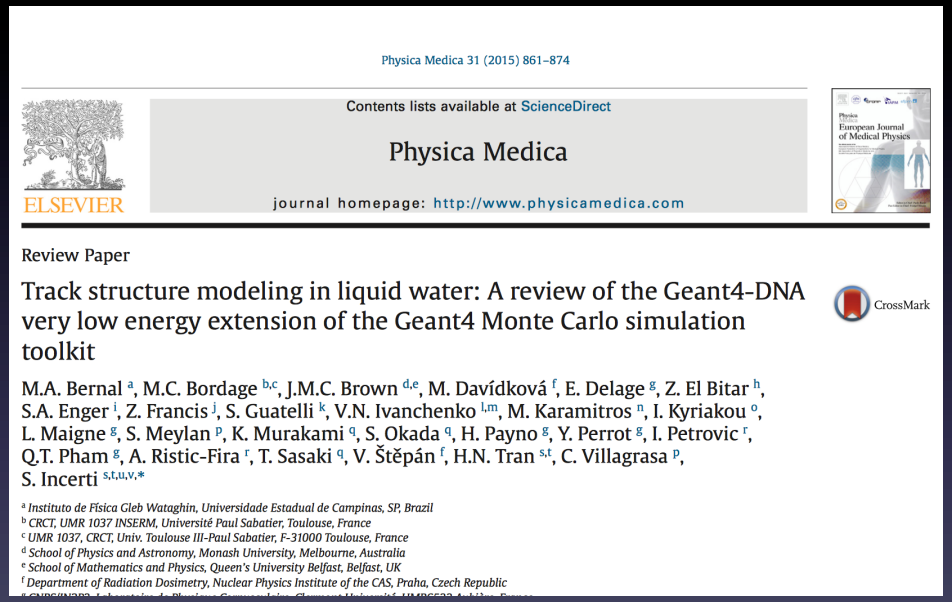
- **PHYSICS**
  - Inclusion of alternative cross section models for electrons and ions
    - Liquid water + DNA-like materials + gas materials for nanodosimeters + metals
- **PHYSICO-CHEMISTRY/CHEMISTRY**
  - « chem4 » for G yields
  - Alternative approaches for the simulation of radiolysis
  - Combination of geometry & chemistry : two approaches
    - Granular approach
    - Composite material & voxellized approach
  - Addition of scavenger species and reactions
- **BIOLOGY**
  - Multi-scale geometrical models of biological targets, including « deformable » geometries
  - Prediction of direct and non-direct DNA simple & complex damages in plasmids and realistic cells
  - Time evolution of damage: repair processes
- **COMPUTING ACCELERATION: GPU FOR CHEMISTRY**
- **VERIFICATION (WITH OTHER CODES) AND VALIDATION (WITH EXPERIMENTAL DATA)**

All these developments take time – once published, they are delivered publicly in Geant4

Most recent publications

Physica Medica 31 (2015) 861 (link)

Overview of technical developments



Physica Medica 31 (2015) 861–874

Contents lists available at ScienceDirect

Physica Medica

journal homepage: http://www.physicamedica.com

Review Paper

Track structure modeling in liquid water: A review of the Geant4-DNA very low energy extension of the Geant4 Monte Carlo simulation toolkit

M.A. Bernal [a], M.C. Bordage [b,c], J.M.C. Brown [d,e], M. Davídková [f], E. Delage [g], Z. El Bitar [h], S.A. Enger [i], Z. Francis [j], S. Guatelli [k], V.N. Ivanchenko [l,m], M. Karamitros [n], I. Kyriakou [o], L. Maigne [g], S. Meylan [p], K. Murakami [q], S. Okada [q], H. Payno [g], Y. Perrot [g], I. Petrovic [r], Q.T. Pham [g], A. Ristic-Fira [r], T. Sasaki [q], V. Štěpán [f], H.N. Tran [s,t], C. Villagrasa [p], S. Incerti [s,t,u,v,*]

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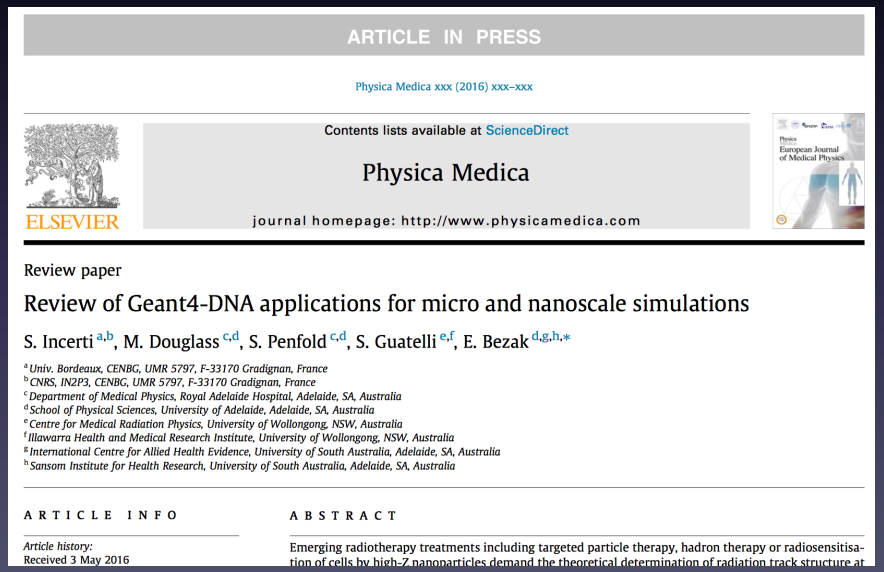
Physica Medica (2016) in press (link)

Review of Geant4-DNA applications



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Physica Medica xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Physica Medica

journal homepage: http://www.physicamedica.com

Review paper

Review of Geant4-DNA applications for micro and nanoscale simulations

S. Incerti [a,b], M. Douglass [c,d], S. Penfold [c,d], S. Guatelli [e,f], E. Bezak [d,g,h,*]

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ABSTRACT

Emerging radiotherapy treatments including targeted particle therapy, hadron therapy or radiosensitisation of cells by high-Z nanoparticles demand the theoretical determination of radiation track structure at

http://geant4-dna.org

Thank you for your attention
…and a special thank you to

Theory & MC experts

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2015 Collaboration Meeting

http://geant4-dna.org