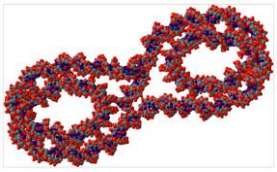

Topas-nBio: A toolkit for radiobiological simulations

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TOPAS for Monte Carlo Simulation

TOPAS wraps and extends the Geant4 Simulation Toolkit to make advanced Monte Carlo simulation of all forms of radiotherapy easier to use for medical physicists.

TOPAS was originally designed to be used for proton therapy applications. However, TOPAS is now available for use in all areas of radiation therapy research.

http://www.topasmc.org

Perl J, Shin J, Schumann J, Faddegon B, Paganetti H. TOPAS: an innovative proton Monte Carlo platform for research and clinical applications. Med Phys. 39, 6818-37 (2012).

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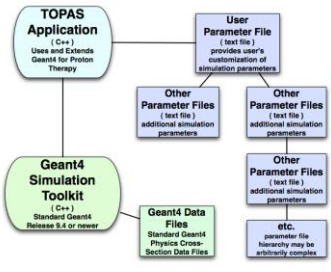

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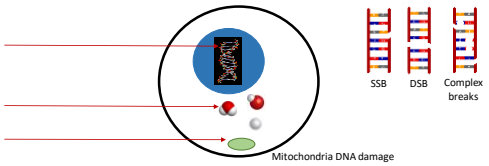
The next step

- Clinical endpoint of interest is a biological effect not the physical dose.
- Understand how radiation interacts with tissue on a cellular level.
- New advances are most likely to come from the interface of biology, chemistry and physics.

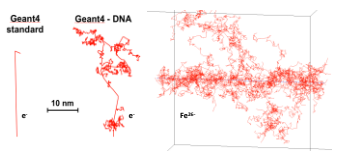
Radiation damage in cells



Physics	Chemistry	Biochemistry/Biology
10^{-18} s	10^{-12}-10^{-6} s	minutes-generations

TOPAS-nBio

- Provide MC simulation on a nanometer scale.
- Easy-to-use parameter files, users do not need advanced programming skills.
- Aimed at radiation biology researchers and physicists with interest in biology.



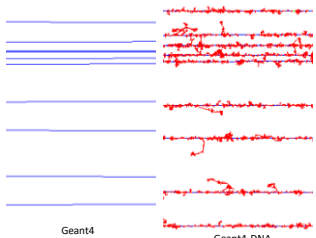
Bernal, et al. (2015), Phys. Med. 31, 861-874
Incerti et al. (2010), Med. Phys. 37,4692-4708

Geant4-DNA

- Geant4-DNA **Physics processes and models** can simulate **step-by-step interactions** of particles in **liquid water down to the eV scale**.
- Software for the simulation of water radiolysis has been released with Geant4 10.1

- **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, base oxidation…)

Bernal et. al., Phys. Med. 31 (2015) 861-874.
Incerti, et. al., Med. Phys. 37 (2010) 4692-4708.



Geant4 Standard | Geant4-DNA

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Parameter Files

```
# TOPAS-nBio example.
# A simple spherical cell with organelles modelled with EM physics.

b:Ge/QuitIfOverlapDetected="false"

d:Ge/World/HLX=1. cm
d:Ge/World/HLY=1. cm
d:Ge/World/HLZ=1. cm

s:Ge/MyCell/Type="TsSimpleCell"
s:Ge/MyCell/Parent="World"
d:Ge/MyCell/CellRadius=10. um
s:Ge/MyCell/Material="G4_WATER"
s:Ge/MyCell/Color="black"

#Nucleus
d:Ge/MyCell/Nucleus/NuclRadius=5. um
s:Ge/MyCell/Nucleus/Material="G4_WATER"
s:Ge/MyCell/Nucleus/Color="red"
s:Ge/MyCell/Nucleus/DrawingStyle="solid"

#Mitochondria
b:Ge/MyCell/Mitochondria/random="true"
i:Ge/MyCell/Mitochondria/NbOfMito=20
d:Ge/MyCell/Mitochondria/a=0.5 um
d:Ge/MyCell/Mitochondria/b=0.3 um
d:Ge/MyCell/Mitochondria/c=0.9 um
s:Ge/MyCell/Mitochondria/Material="G4_WATER"
s:Ge/MyCell/Mitochondria/Color="grass"
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s:Ge/MyCell/Mitochondria/DrawingStyle="solid"

Ph/Default/Modules = 1 "g4em-standard_opt0"
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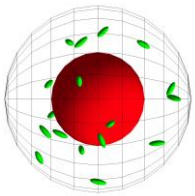

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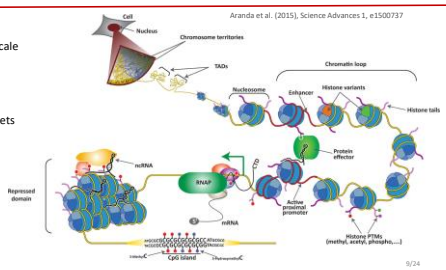
Designing Geometries

From macroscale (organelle) to nanoscale (DNA molecule).

Radiation targets:
1. DNA
2. Non-nuclear targets (mitochondria)

Aranda et al. (2015), Science Advances 1, e1500737



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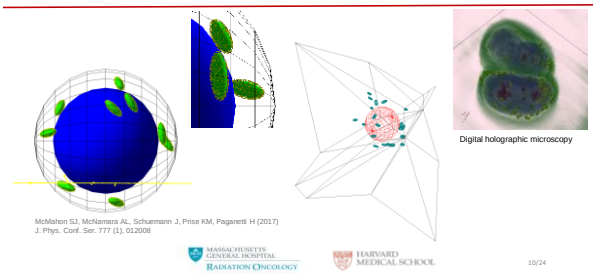
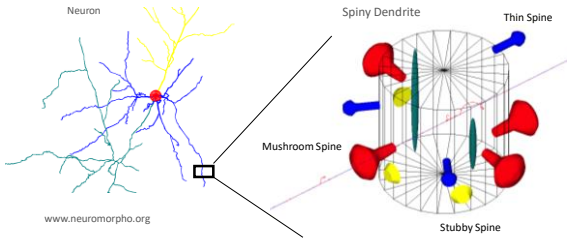
Cellular/Organelle Level

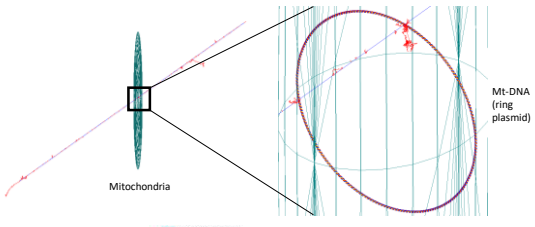


McMahon SJ, McNamara AL, Schuemann J, Prise KM, Paganetti H (2017) J. Phys. Conf. Ser. 777 (1), 012008

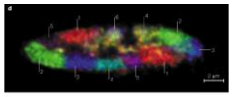
Neurons



Cellular/Organelle Level



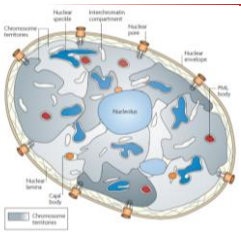
Nucleus and Chromosome Territories



Nature Reviews | Genetics

Mid-plane light optical section through a chicken fibroblast nucleus shows mutually exclusive chromosome territories (CTs) with homologous chromosomes seen in separate locations.

T. Cremer & C. Cremer, *Nature Reviews Genetics* 2, 292-301 (2001)
Lanctôt, C., Cheutin, T., Cremer, M., Cavalli, G., & Cremer, T., *Nature Reviews. Genetics*, *8*(2), 104–115 (2007).



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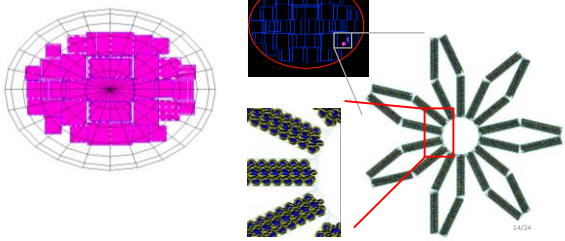
Chromatin Fibers



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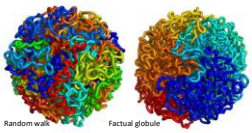
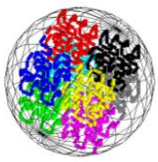
Nucleus and Chromosome Territories



Lieberman-Aiden et al. (2009) Science, 326, 289



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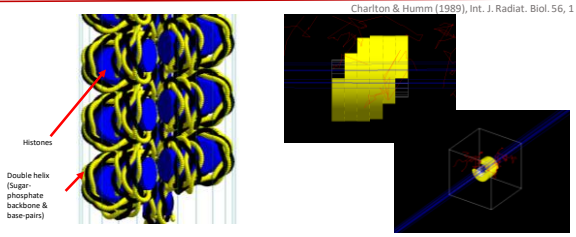
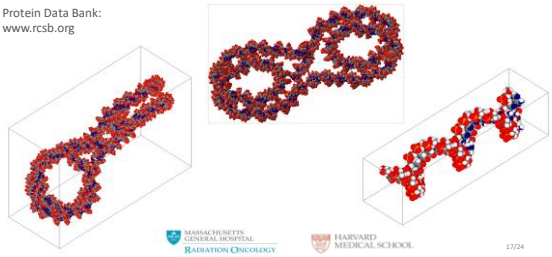
DNA

Charlton & Humm (1989), Int. J. Radiat. Biol. 56, 1

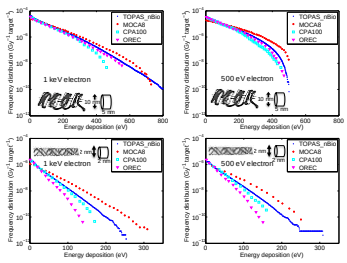


Nucleic acids and other protein molecules

Protein Data Bank:
www.rcsb.org



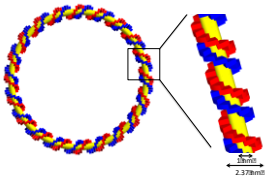
Validation studies

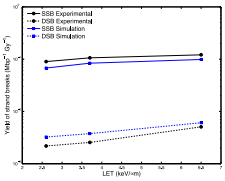


- Geant4-DNA (TOPAS-nBio), CPA100, OREC cross sections based on data for liquid water.
- MOCA8 cross sections based on data for gaseous water.
- CPA100 and Geant4-DNA use the same data for cross-sections.

McNamara et al. (2017) Phys Med, 33, 207-21

Validation studies





L. Vysn, K. P. Brabcova, V. Stepan, P. Moretto-Capelle, B. Bugler,
429 G. Legube, et al., Proton-induced direct and indirect damage of plasmid
430 DNA, Radiat Environ Bioph 54 (3) (2015) 343(352.

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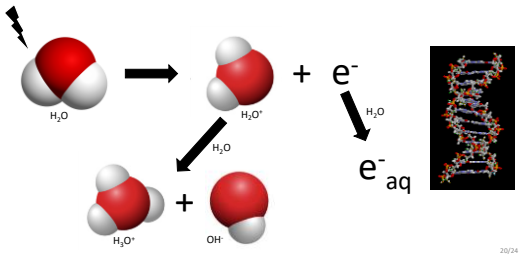
Chemistry Models



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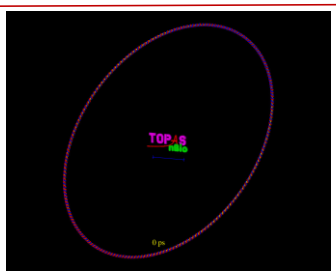
Chemistry Models

- 1 MeV proton in water.
- Plasmid DNA ring consisting of 2000 base-pairs.

Courtesy of
Jose Ramos-Mendez



Physics:
proton
electron

Chemistry:
OH
e^-_{aq}
H_3O^+
H_2O_2

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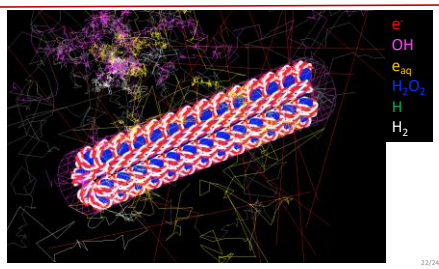
Chemistry Models

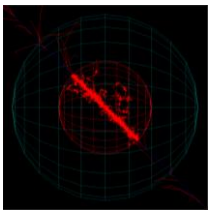
Poster: SU-I-GPD-T-650 (Jose Ramos-Mendez et al.)



Courtesy of Jose Ramos-Mendez

Summary

- TOPAS-nBio is a powerful MC tool for radiobiology simulations.
  - Users interact with the toolkit via easy-to-use parameter files.
- TOPAS-nBio provides the user with a range of biological geometries: from cell/organelle to DNA level.
- Unique tool for promoting interdisciplinary research.



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Acknowledgements

- TOPAS-nBio collaboration:
  - Jan Schuemann
  - Jose Ramos Mendez
  - Joseph Perl
  - Bruce Faddegon
  - Harald Paganetti
- TOPAS collaboration:
  - Jungwook Shin
  - David Hall

(NIH/NCI RO1 CA7300045)

http://www.topasmc.org

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