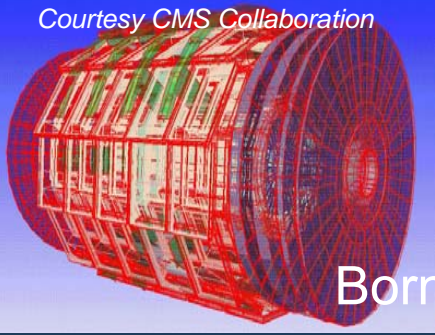# Geant4-DNA
Physics and biological models

S. Chauvie, Z. Francis, S. Guatelli, S. Incerti, B. Mascialino,
Ph. Moretto, G. Montarou, P. Nieminen, M.G. Pia

Topical Seminar on Innovative Particle and Radiation Detectors
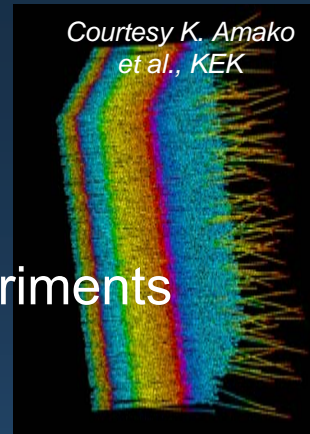
Siena, 1- 5 October 2006

Maria Grazia Pia, *INFN Genova*
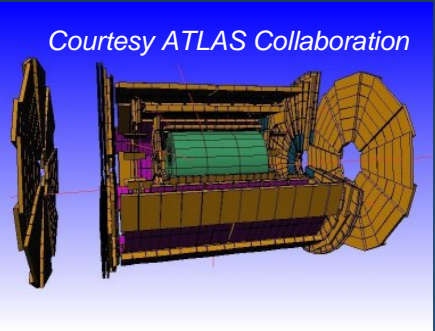
Geant 4

Courtesy CMS Collaboration

Courtesy K. Amako et al., KEK

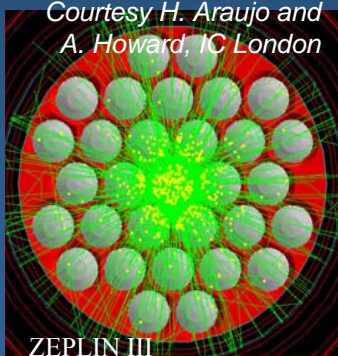**Born from the requirements of large scale HEP experiments**
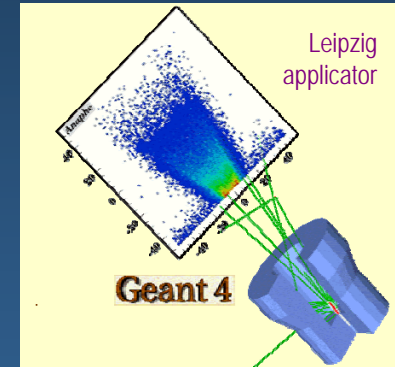

Courtesy ATLAS Collaboration

Widely used also in

- Space science and astrophysics
- Medical physics, nuclear medicine
- Radiation protection
- Accelerator physics
- Pest control, food irradiation
- Humanitarian projects, security
- etc.
- Technology transfer to industry, hospitals…

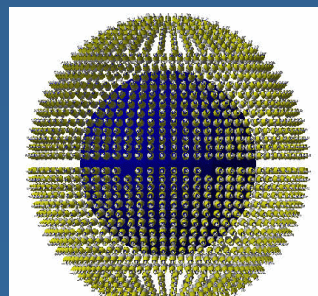*Courtesy H. Araujo and A. Howard, IC London*
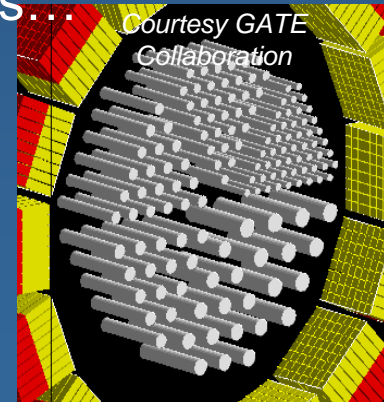ZEPLIN III

Leipzig applicator
Geant 4

Courtesy R. Nartallo et al.,ESA

Courtesy Borexino
INFN Genova

Most cited "engineering" publication in the past 2 years!

Courtesy GATE Collaboration

Geant 4

OO technology

Openness to extension and evolution

- new implementations can be added w/o changing the existing code

Robustness and ease of maintenance

- protocols and well defined dependencies minimize coupling

Strategic vision

Toolkit

A set of compatible components

- each component is **specialised** for a specific functionality
- each component can be **refined** independently to a great detail
- components can be **integrated** at any degree of complexity
- it is easy to provide (and use) **alternative** components
- the user application can be **customised** as needed

Maria Grazia Pia, *INFN Genova*
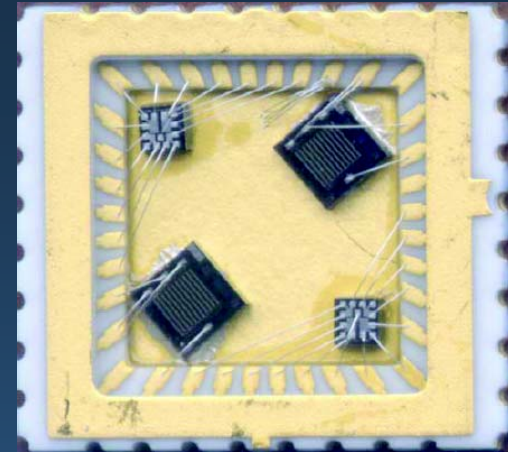
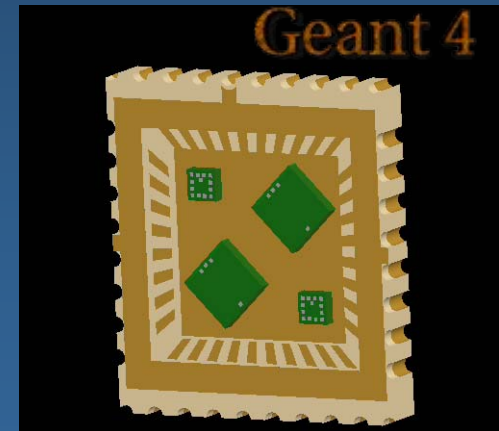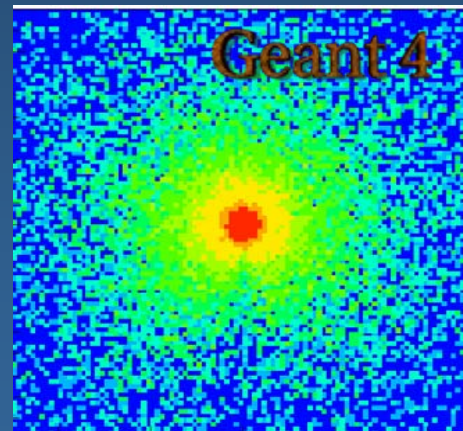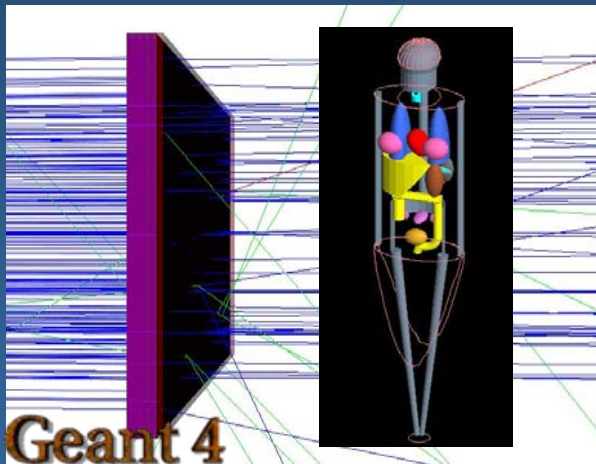# Multi-disciplinary application environment

Dosimetry

Space science

Radiotherapy

Effects on components

Wide spectrum of physics coverage, variety of physics models
Precise, quantitatively validated physics
Accurate description of geometry and materials

Maria Grazia Pia, *INFN Genova*

Precise dose calculation

Geant4 Low Energy Electromagnetic Physics package

- **Electrons and photons (250/100 eV < E < 100 GeV)**
  - Models based on the Livermore libraries (EEDL, EPDL, EADL)
  - Models à la Penelope
- **Hadrons and ions**
  - Free electron gas + Parameterisations (ICRU49, Ziegler) + Bethe-Bloch
  - Nuclear stopping power, Barkas effect, chemical formula, effective charge etc.
- **Atomic relaxation**
  - Fluorescence, Auger electron emission, PIXE

photon transmission , Pb 1 micrometer

shell effects

Ion Ionisation Losses in Aluminum

ions

$_{40}$Ar

$_{12}$C

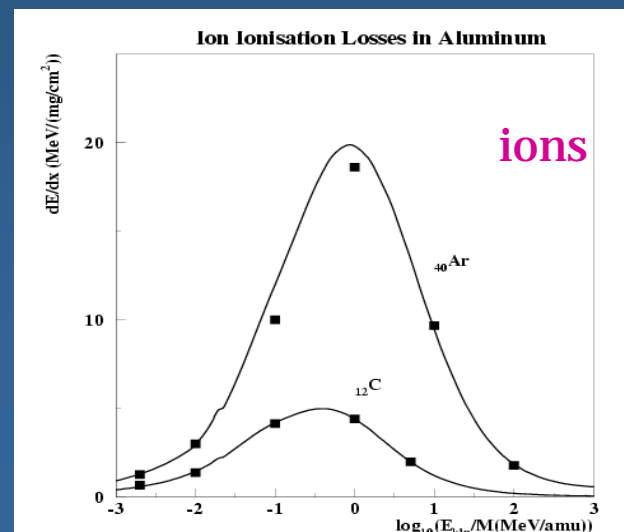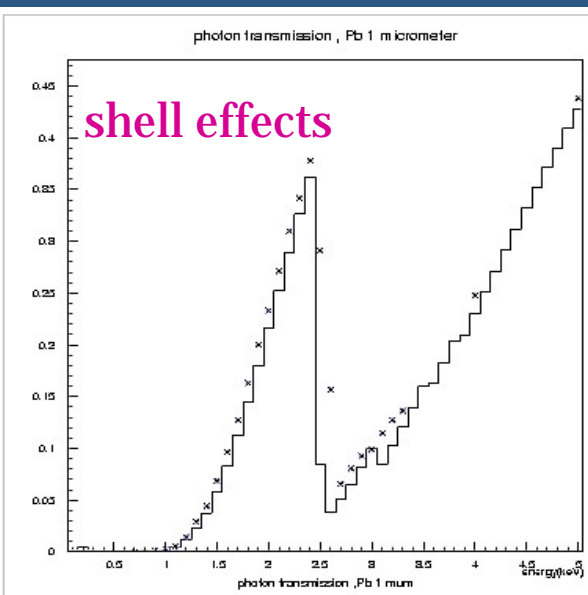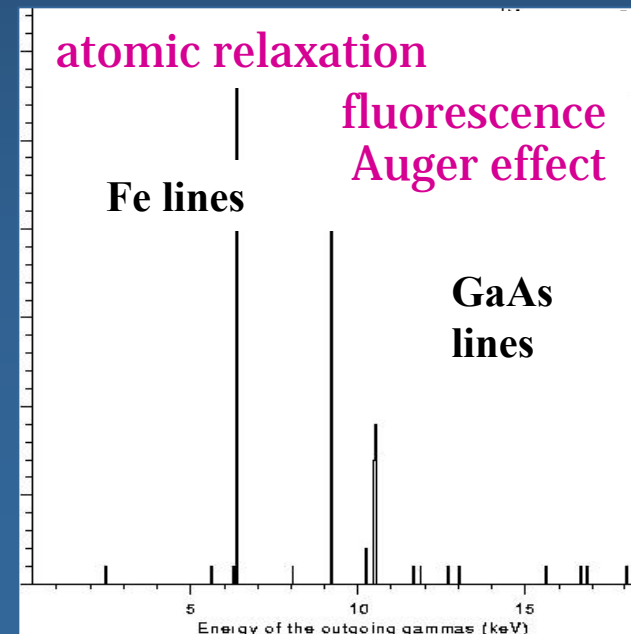Figure 9: Ion electronic stopping power in aluminum. Points - the best fit on the data from Ref.[12], solid line - GEANT+ parametetrisation. The accuracy of the data is about 5 %.

atomic relaxation

fluorescence
Auger effect

Fe lines

GaAs lines

Energy of the outgoing gammas (keV)

Maria Grazia Pia, *INFN Genova*

Biological models in Geant 4

Relevance for space:
astronaut and aircrew radiation hazards

eesa

Geant 4 DNA

INFN
Istituto Nazionale di Fisica Nucleare

- Home

- Requirements
- Documents
- Talks
- Papers
- Meetings
- Team

- Geant4
- Geant4-INFN
- Geant4 LowE Physics

- Useful links

Simulation of Interactions of Radiation with Biological Systems at the Cellular and DNA Level
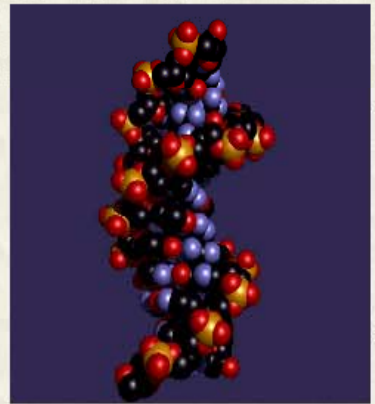
Estimating **cancer risk for human exposures to space radiation** is a challenge which involves a wide range of knowledge in physics, chemistry, biology and medicine.

Traditionally, the biological effects of radiation are analysed in top-bottom order, i.e. evaluation of the absorbed macroscopic radiation dose at a given location in the biological tissue is translated to the degree of danger it presents, and dose limits are consequently set that are considered to be acceptable.

A novel approach, based on the new-generation object-oriented **Geant4** Monte Carlo Toolkit, proceeds in a reverse order, from bottom to top, by analysing the nano-scale effects of energetic particles at the cellular and DNA molecule level.

This project is sponsored by the European Space Agency (ESA) and is pursued by a multidisciplinary European team of biologists, physicians, physicists, space scientists and software engineers.

2000/11/26 16:48
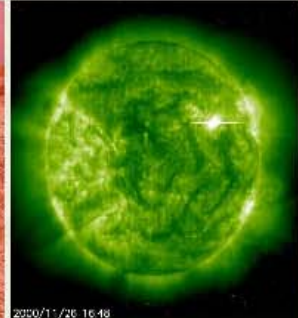
Pictures courtesy of ESA

Geant 4 for radiation biology
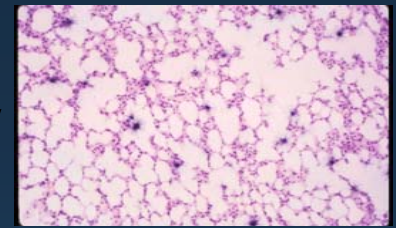
- **Several specialized Monte Carlo codes have been developed for radiobiology/microdosimetry**
  - Typically each one implementing models developed by its authors
  - Limited application scope
  - Not publicly distributed
  - Legacy software technology (FORTRAN, procedural programming)

- **Geant4-DNA**
  - Full power of a general-purpose Monte Carlo system
  - Toolkit: multiple modeling options, no overhead *(use what you need)*
  - Versatility: from controlled radiobiology setup to real-life ones
  - Open source, publicly released
  - Modern software technology
  - Rigorous software process

Maria Grazia Pia, *INFN Genova*
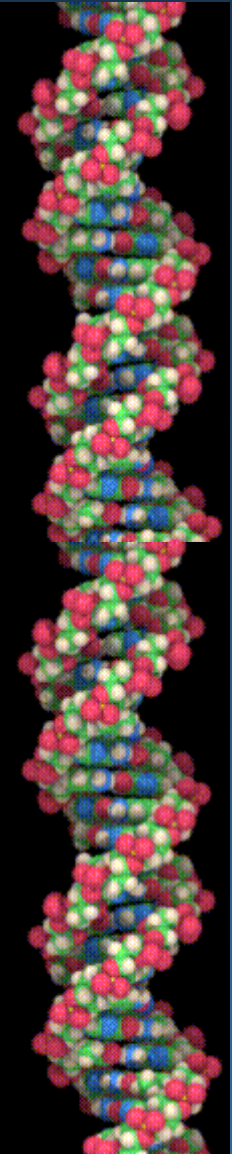
Geant 4

(advanced software technology)

- **Macroscopic level**
  - calculation of dose
  - already feasible with Geant4
  - develop useful associated tools

- **Cellular level**
  - cell modelling
  - processes for cell survival, damage etc.

- **DNA level**
  - DNA modelling
  - physics processes at the eV scale
  - bio-chemical processes
  - processes for DNA damage, repair etc.

Complexity of

software, physics and biology

addressed with an
iterative-incremental
software process

Parallel development
at all the three levels

(domain decomposition)

Low Energy Physics extensions

- **Specialised processes down to the eV scale**
  - at this scale physics processes depend on the detailed atomic/molecular structure of the medium
  - 1st cycle: processes in water

- **Releases**
  - β-version in Geant4 8.1 (June 2006)
  - Refined version in progress
  - Further extensions to follow

- **Processes for other materials to follow**
  - interest for radiation effects on components

Particle	Processes
e	Elastic scattering Excitation Ionisation
p	Excitation Charge decrease Ionisation
H	Charge increase Ionisation
He++	Excitation Charge decrease Ionisation
He+	Excitation Charge decrease Charge increase Ionisation
He	Excitation Charge increase Ionisation

Maria Grazia Pia, *INFN Genova*

Software design

Innovative design introduced in Geant4: **policy-based class design**
Flexibility of modeling + performance optimisation

G4VProcess
(from processes_management)

+ *AlongStepDoIt()*
+ *AlongStepGetPhysicalInteractionLength()*
+ *AtRestDoIt()*
+ *AtRestGetPhysicalInteractionLength()*
+ *PostStepDoIt()*
+ *PostStepGetPhysicalInteractionLength()*
+ *IsApplicable()*

Abstract interface
to tracking

G4VDiscreteProcess
(from processes_management)

GetMeanFreePath()
+ PostStepDoIt()

CrossSection
FinalState

G4DNAProcess

GetMeanFreePath()
+ IsApplicable()
+ PostStepDoIt()

Parameterised
class

Policies
- cross section calculation
- final state generation

CrossSection
FinalState
G4DNAProcess

<<bind>>
(G4MyCrossSection,G4MyFinalState)

<<typedef>>
G4DNAMyProcess

G4CrossSectionPolicy

+ ApplicableParticleType()
+ CalculateCrossSection()

G4FinalStatePolicy

+ GenerateFinalState()
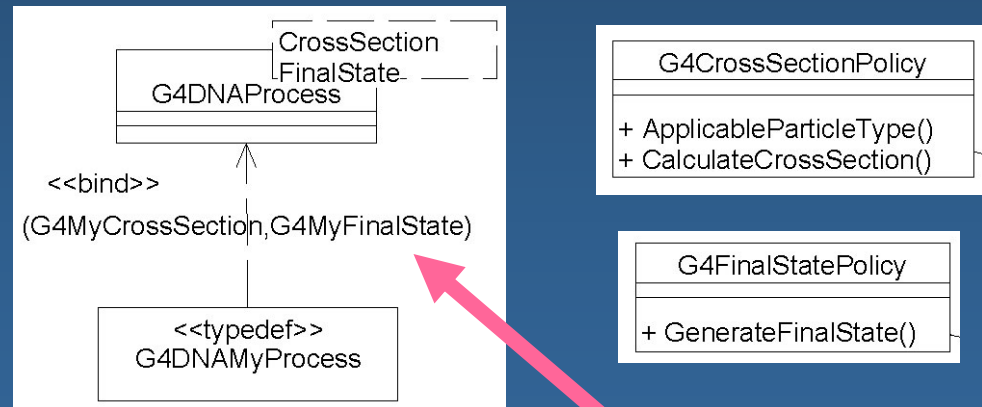
The process can be configured with
a variety of physics models by
template instantiation

Policy based design

- **Policy based classes are parameterised classes**
  - classes that use other classes as a parameter
- **Specialization of processes through template instantiation**
  - The code is bound at compile time

- **Advantages**
  - Policies are not required to inherit from a base class
  - Weaker dependency of the policy and the policy based class on the policy interface
  - In complex situations this makes a design more flexible and open to extension
  - No need of virtual methods, resulting in faster execution

- **Clean, maintainable design of a complex domain**
  - Policies are orthogonal

- **Open system**
  - Proliferation of models in the same environment

Maria Grazia Pia, *INFN Genova*

Implementation

- **First set of models implemented chosen among those available in literature**
  - Direct contacts with theorists whenever possible

- **Future extensions foreseen**
  - Made easy by the design
  - Provide a wide choice among many alternative models
  - Different modeling approaches
 - Complementary models

- **Unit testing in parallel with implementation**

D. Emfietzoglou, G. Papamichael, and M. Moscovitch, "An event-by-event computer simulation of interactions of energetic charged particles and all their secondary electrons in water", *J. Phys. D: Appl. Phys.*, vol. 33, pp. 932-944, 2000.

D. J. Brenner, and M. Zaider, "A computationally convenient parameterization of experimental angular distributions of low energy electrons elastically scattered off water vapour", *Phys. Med. Biol.*, vol. 29, no. 4, pp. 443-447, 1983.

B. Grosswendt and E. Waibel, "Transport of low energy electrons in nitrogen and air", *Nucl. Instrum. Meth.*, vol. 155, pp. 145-156, 1978.

D. Emfietzoglou, K. Karava, G. Papamichael, and M. Moscovitch, "Monte Carlo simulation of the energy loss of low-energy electrons in liquid water", *Phys. Med. Biol.*, vol. 48, pp. 2355-2371, 2003.

D. Emfietzoglou, and M. Moscovitch, "Inelastic collision characteristics of electrons in liquid water", *Nucl. Instrum. Meth. B*, vol. 193, pp. 71-78, 2002.

D. Emfietzoglou, G. Papamichael, K. Kostarelos, and M. Moscovitch, "A Monte Carlo track structure code for electrons (~10 eV-10 keV) and protons (~0.3-10 MeV) in water: partitioning of energy and collision events", *Phys. Med. Biol.*, vol. 45, pp. 3171-3194, 2000.

M. Dingfelder, M. Inokuti, and H. G. Paretzke, "Inelastic-collision cross sections of liquid water for interactions of energetic protons", *Rad. Phys. Chem.*, vol. 59, pp. 255-275, 2000.

D. Emfietzoglou, K. Karava, G. Papamichael, M. Moscovitch, "Monte-Carlo calculations of radial dose and restricted-LET for protons in water", *Radiat. Prot. Dosim.*, vol. 110, pp. 871-879, 2004.

J. H. Miller and A. E. S. Green, "Proton Energy Degradation in Water Vapor", *Rad. Res.*, vol. 54, pp. 343-363, 1973.

M. Dingfelder, H. G. Paretzke, and L. H. Toburen, "An effective charge scaling model for ionization of partially dressed helium ions with liquid water", in *Proc. of the Monte Carlo 2005*, Chattanooga, Tennessee, 2005.

B. G. Lindsay, D. R. Sieglaff, K. A. Smith, and R. F. Stebbings, "Charge transfer of 0.5-, 1.5-, and 5-keV protons with H2O: absolute differential and integral cross sections", *Phys. Rev. A*, vol. 55, no. 5, pp. 3945-3946, 1997.

K. H. Berkner, R. V. Pyle, and J. W. Stearns, "Cross sections for electron capture by 0.3 to 70 keV deuterons in H2, H2O, CO, CH4, and C8F16 gases", *Nucl. Fus.*, vol. 10, pp. 145-149, 1970.

R. Dagnac, D. Blanc, and D. Molina, "A study on the collision of hydrogen ions H1+, H2+ and H3+ with a water-vapour target", *J. Phys. B: Atom. Molec. Phys.*, vol. 3, pp.1239-1251, 1970.

L. H. Toburen, M. Y. Nakai, and R. A. Langley, "Measurement of high-energy charge transfer cross sections for incident protons and atomic hydrogen in various gases", *Phys. Rev.*, vol. 171, no. 1, pp. 114-122, 1968.

P. G. Cable, Ph. D. thesis, University of Maryland, 1967.

M. E. Rudd, T. V. Goffe, R. D. DuBois, L. H. Toburen, "Cross sections for ionisation of water vapor by 7-4000 keV protons", *Phys. Rev. A*, vol. 31, pp. 492-494, 1985.
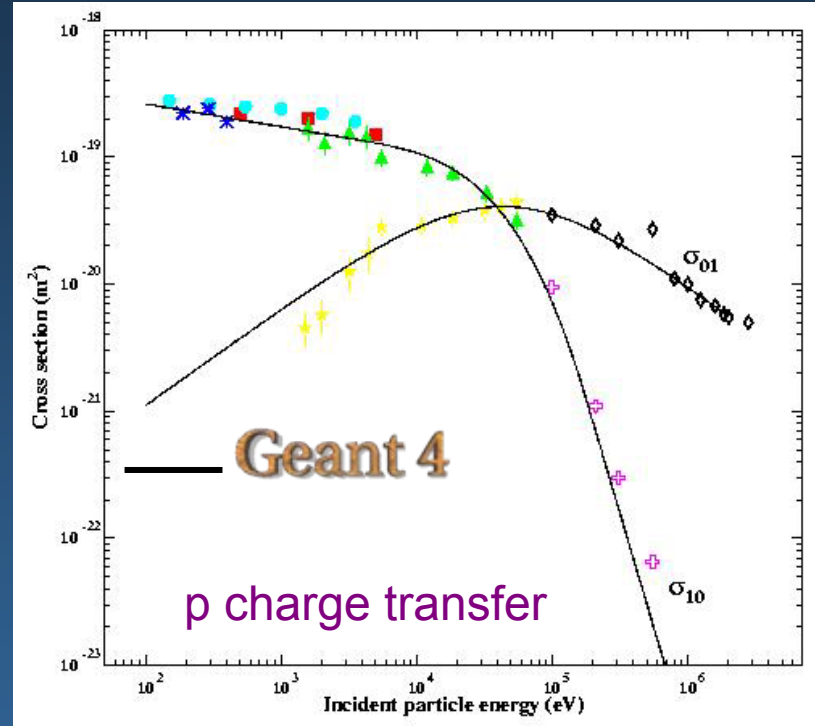
Test

Verification
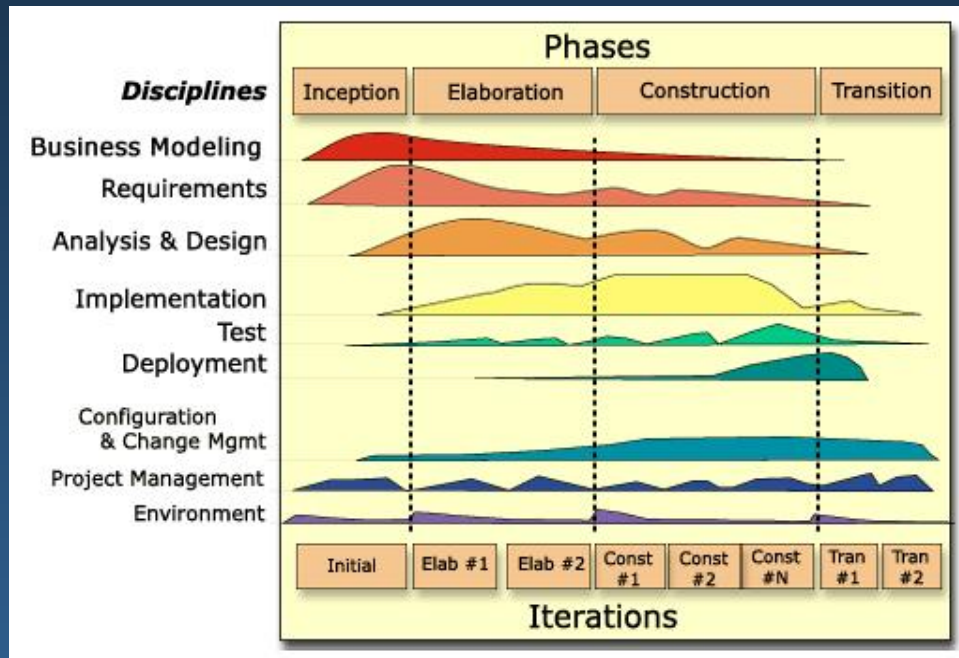### against theoretical models

e elastic scattering

theory

● Geant 4

p excitation
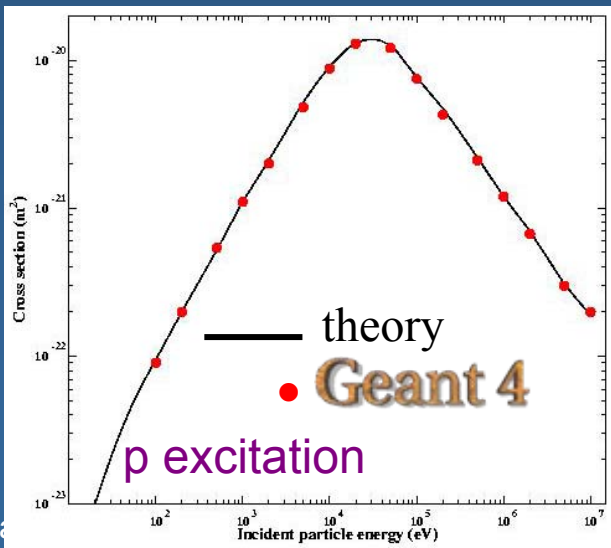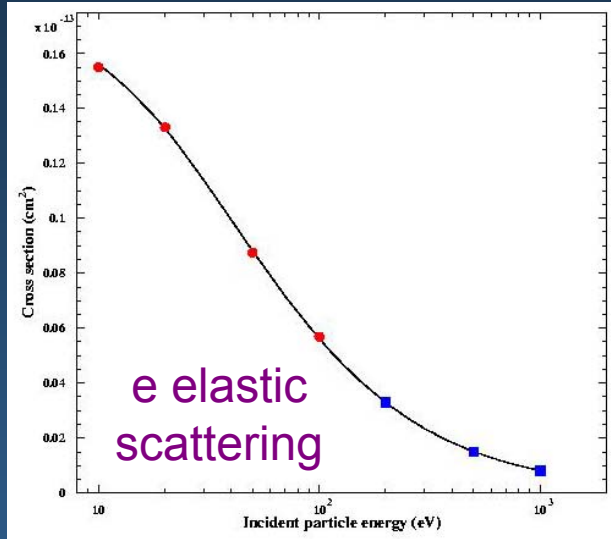
Validation
against experimental data

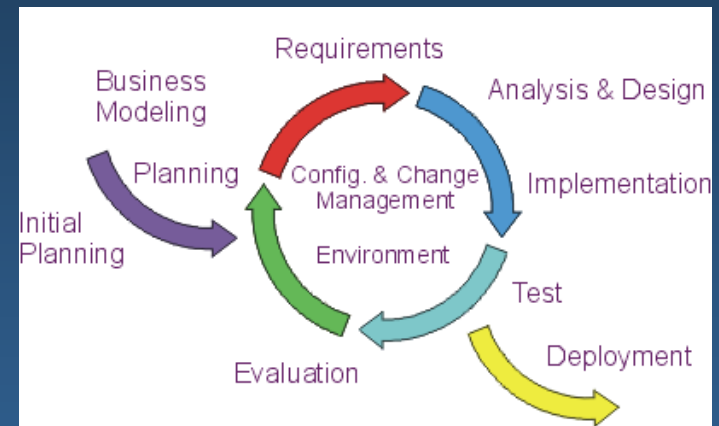Geant 4

p charge transfer

Scarce experimental data

Large scale validation project planned

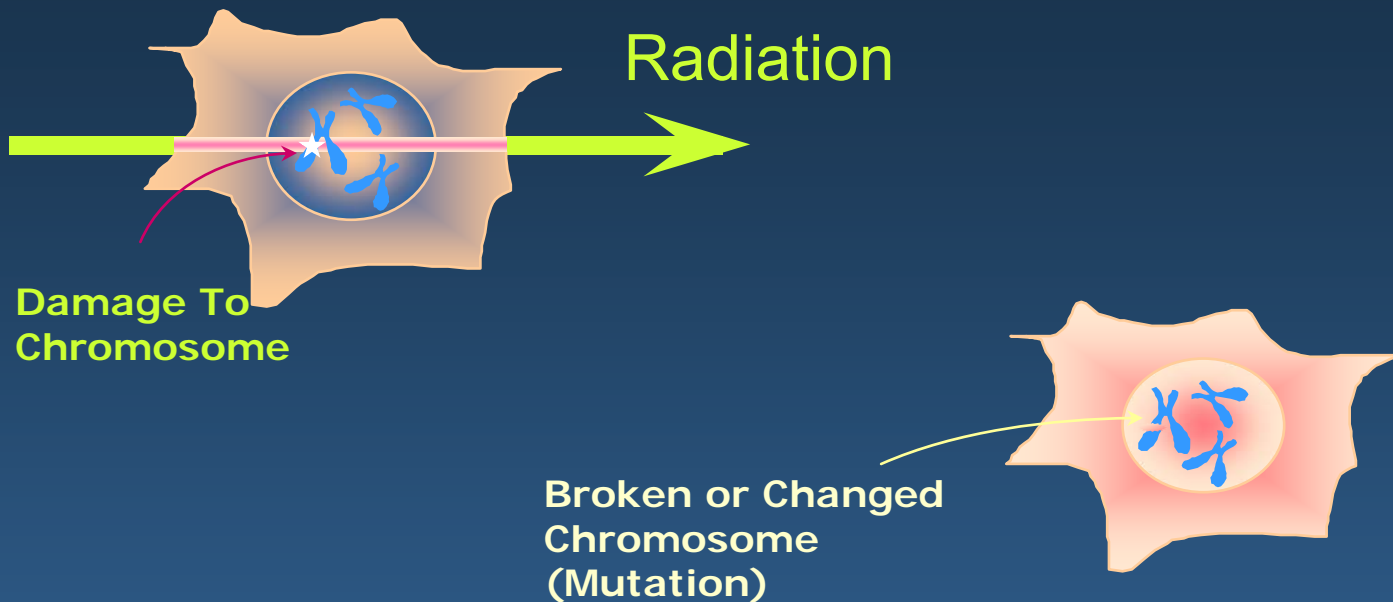Maria

…and behind everything

Unified Process

A rigorous software process
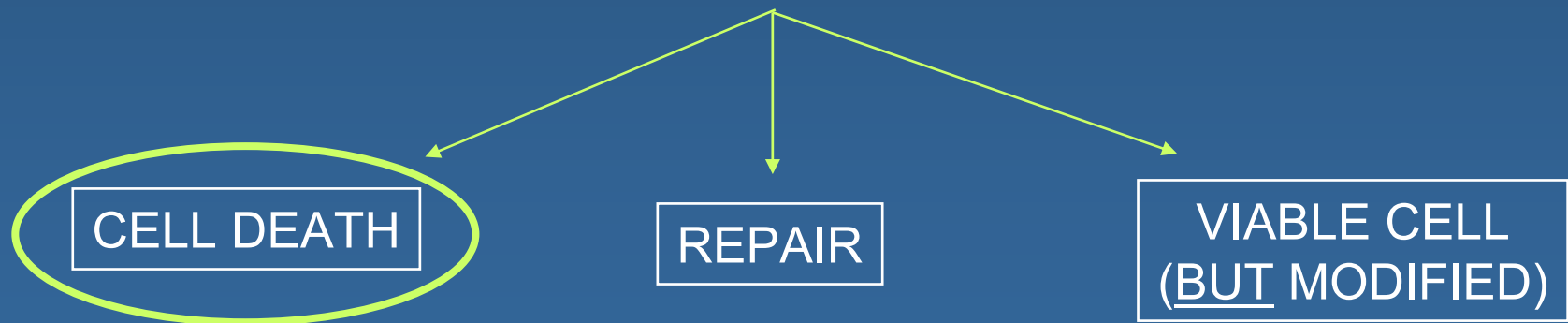
Incremental and iterative lifecycle
RUP™ as process framework, tailored to the specific project
Mapped onto ISO 15504

Theories and models for cell survival

TARGET THEORY MODELS

- Single-hit model
- Multi-target single-hit model
- Single-target multi-hit model

MOLECULAR THEORY MODELS

- Theory of radiation action
- Theory of dual radiation action
- Repair-Misrepair model
- Lethal-Potentially lethal model

Geant 4 approach: variety of models all handled through the same abstract interface

in progress

Geant 4

Requirements
Problem domain analysis

Analysis & Design
Implementation
Test

Incremental-iterative software process

Experimental validation of Geant4 simulation models

Maria Grazia Pia, *INFN Genova*

TARGET THEORY	SINGLE-HIT
TARGET THEORY	MULTI-TARGET SINGLE-HIT
MOLECULAR THEORY	RADIATION ACTION
MOLECULAR THEORY	DUAL RADIATION ACTION
MOLECULAR THEORY	REPAIR-MISREPAIR LIN REP / QUADMIS
MOLECULAR THEORY	REPAIR-MISREPAIR LIN REP / MIS
MOLECULAR THEORY	LETHAL-POTENTIALLY LETHAL
MOLECULAR THEORY	LETHAL-POTENTIALLY LETHAL – LOW DOSE
MOLECULAR THEORY	LETHAL-POTENTIALLY LETHAL – HIGH DOSE
MOLECULAR THEORY	LETHAL-POTENTIALLY LETHAL – LQ APPROX

$$S = e^{-D / D_0}$$

$$S = 1 - (1 - e^{-qD})^n$$

In progress

REVISED MODEL

$$S = e^{-q_1 D} \left[1 - (1 - e^{-q_n D})^n \right]$$

$$S = e^{-p (\alpha D + \beta D^2)}$$

$$S = S_0 \, e^{- k (\xi D + D)^2}$$

$$S = e^{-\alpha D}[1 + (\alpha D T / \varepsilon)]^\varepsilon$$

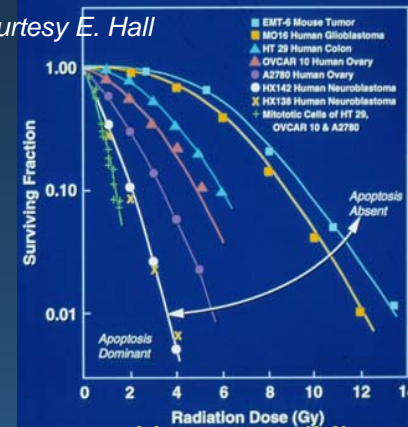$$S = e^{-\alpha D}[1 + (\alpha D / \varepsilon)]^{\varepsilon \Phi}$$

Courtesy E. Hall

Human cell lines irradiated with X-rays

$$S = \exp\left[- N_{TOT}\left[1 + \frac{N_{PL}}{\varepsilon (1 - e^{- \varepsilon B A tr})} \right]^\varepsilon \right]$$

$$S = e^{-\eta_{AC} D}$$

$$- \ln[S(t)] = (\eta_{AC} + \eta_{AB}) D - \varepsilon \ln[1 + (\eta_{AB} D/\varepsilon)(1 - e^{-\varepsilon B A \, tr})]$$

$$- \ln[S(t)] = (\eta_{AC} + \eta_{AB} e^{-\varepsilon B A tr}) D + (\eta^2_{AB}/2\varepsilon)(1 - e^{-\varepsilon B A \, tr})^2 D^2]$$
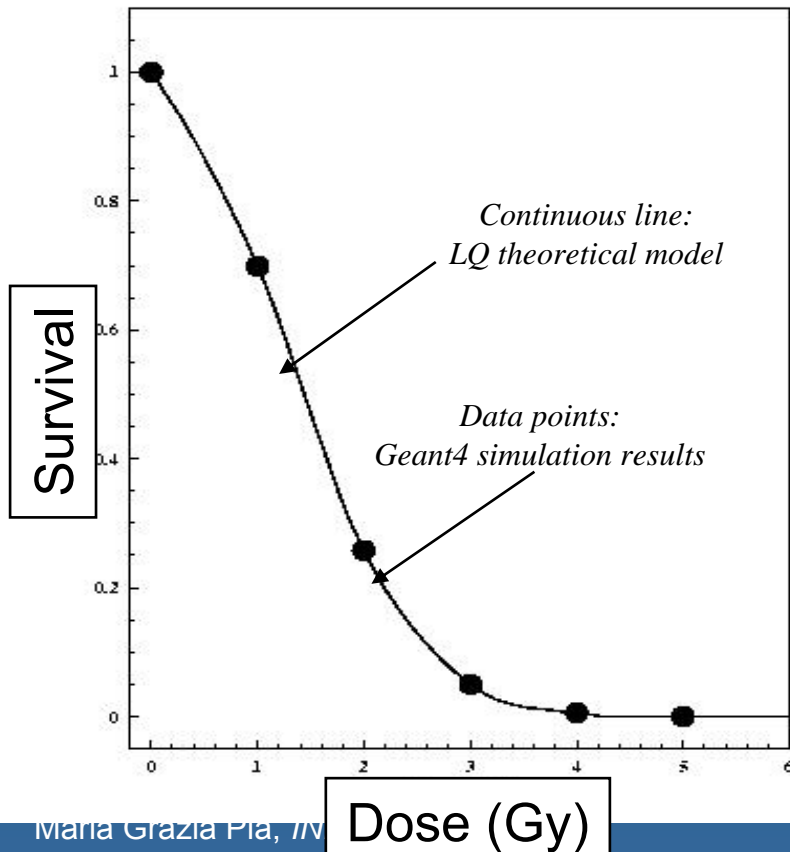
Maria Grazia Pia, *INFN Genova*

Prototype development

Design, implementation and usage of
one cell survival model in Geant4

Verification

Survival vs Dose (Gy)

Continuous line:
LQ theoretical model

Data points:
Geant4 simulation results

Monolayer

V79-379A cells

Proton beam
E= 3.66 MeV

**Linear-Quadratic
model**

$$S = e^{-\alpha D - \beta D^2}$$

$\alpha = 0.32$
$\beta = -0.039$

Folkard et al., Int. J. Rad. Biol., 1996

Maria Grazia Pia, *INFN*

Scenario for Mars (and earth…)

Geant4 simulation treatment source
+
geometry from CT image
or
anthropomorphic phantom

Dose in organs at risk

Geant4 simulation with biological processes at cellular level (cell survival, cell damage…)
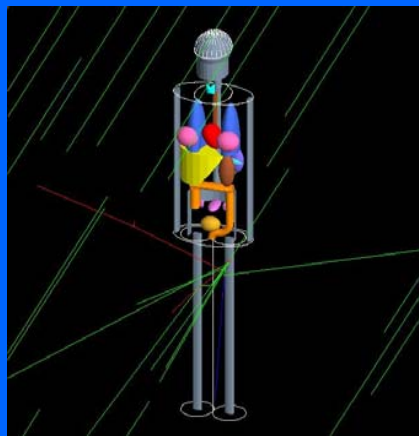
Phase space input to nano-simulation

Geant4 simulation with physics at eV scale
+
DNA processes

Oncological risk to astronauts/patients

Risk of nervous system damage

Maria Grazia Pia, *INFN Genova*

Geant 4

Powerful **geometry** and **physics** modelling in an advanced computing environment

Wide spectrum of complementary and alternative physics models

Multi-disciplinary dosimetry simulation

Precision of physics
Versatility of experimental modelling

Geant 4 DNA

Extensions for bio-molecular systems
Physics processes at the eV scale
Biological models

Multiple levels in the same simulation environment

Conventional dosimetry
Models at cellular level
Models at DNA level

Rigorous software engineering
Advanced object oriented technology
in support of physics versatility