# Physics Models for Biological Effects of Radiation and Shielding

## ESA AO6041 project overview

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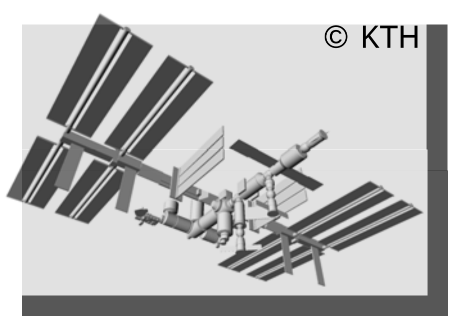
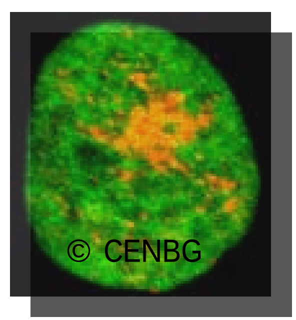
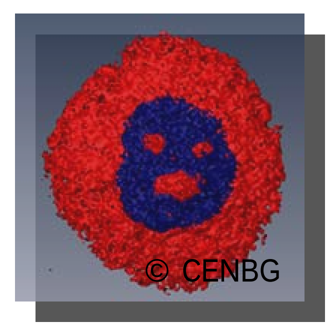
Bengt Lund-Jensen, KTH, Stockholm

**on behalf of the ESA-AO6041 team**




**15th Workshop on Radiation Monitoring for the International Space Station**
**Frascatti, 7-9 September 2010**

# Content of this talk

- Context of ESA AO6041
- Overview of main activity, including
  - Requirements & review of materials and methods
  - Geant4 ion Physics
  - ISS radiation environment
  - Geant4-DNA
  - Search for traces of life
- The ESA AO6041 team
- To learn more

# Context of ESA AO6041

- Funded by ESA for the 2010-2013 period

- Extend Geant4 Physics & capabilities for the
  - modelling of biological effects of ionising radiation at the sub-cellular scale
    - In the context of the Geant4-DNA project
  - modelling of shielding for astronauts in manned space missions
    - Validation & extension of Geant4 ion physics models

- Including a modelling of the radiation environment aboard the International Space Station
  - Application : development of biochips for search of traces of life, including a mission aboard the ISS

- and a global verification & validation of the delivered software

# The Geant4 toolkit : GEometry ANd Tracking

Geant4

Geant4 : a set of libraries to simulate interactions of particles with matter

- Initiated by CERN in 1994 for HEP (LHC), successor of Geant3 (20 years)
- R&D RD44, 1994-1998, 1st release in December 1998
- Now developed by an international collaboration (~100 members)
- Object-Oriented technology (C++)
- Libraries, not a user code
- Constantly updated, entirely open source and free
- Two public releases / year

http://geant4.org

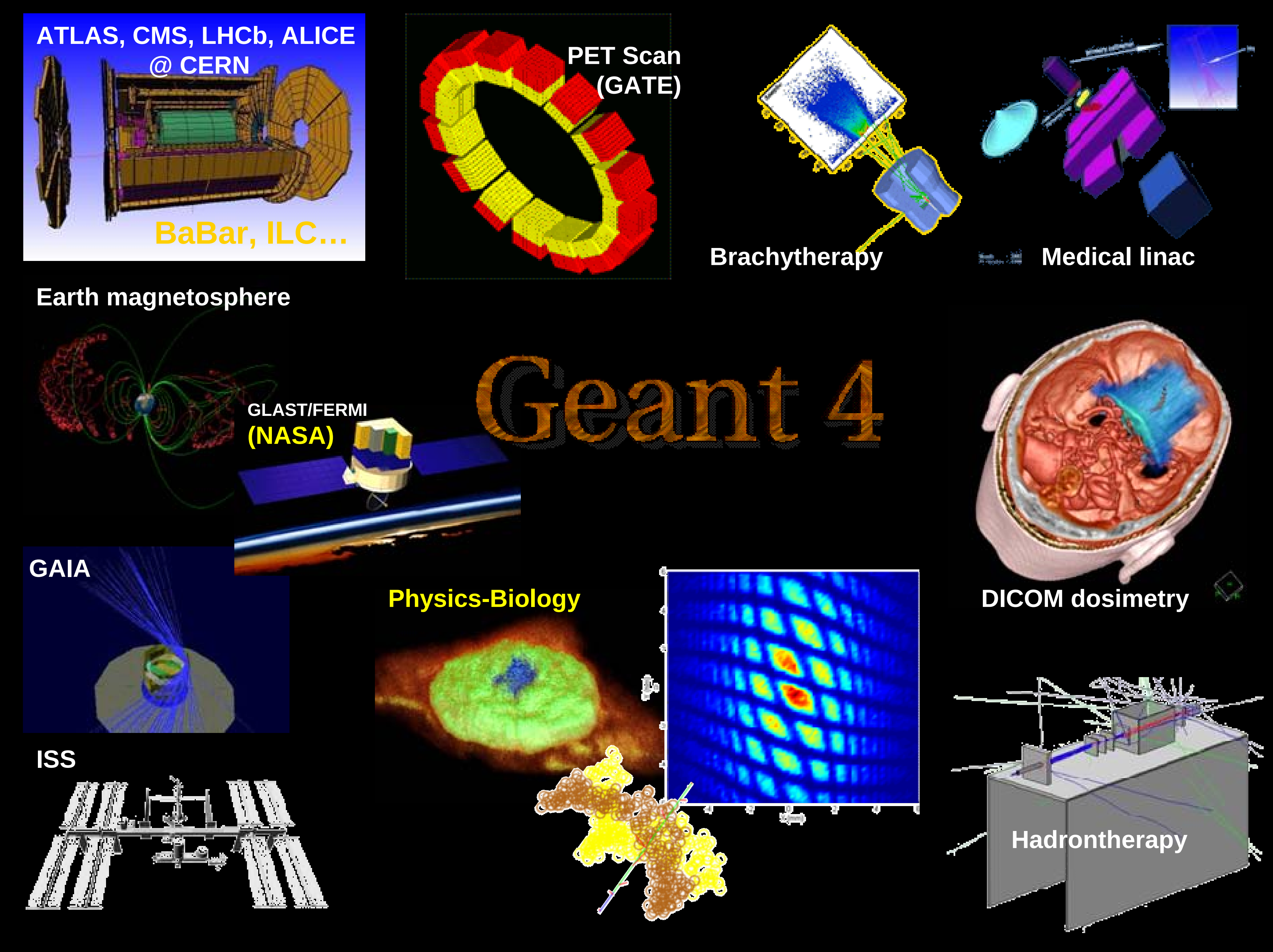
Geant4 : simulation of a particle physics experiment

- Define a flexible geometry
- Model interaction processes (electromagnetic, hadronic)
- Generate initial particles and follow them within the geometry
- Save physics quantities and analyze them

Capabilities

- Visualization
- Interactivity
- Extensibility

Kobe, Oct. 2008


ATLAS, CMS, LHCb, ALICE
@ CERN
BaBar, ILC...
PET Scan
(GATE)
Brachytherapy
Medical linac
Earth magnetosphere
GLAST/FERMI
(NASA)
Geant 4
DICOM dosimetry
GAIA
Physics-Biology
ISS
Hadrontherapy

# 1) Collecting requirements and review of materials & methods

Coordinated & courtesy of I. Gudowska in collaboration wih B. Mascialino
Stockholm U., Sweden

# Requirements and review of radiation transport simulation software relevant to space radiological effects

- Establish the requirements for radiation transport codes, models and methods, including particle charge and energy ranges, materials, geometry implementations and radiobiological analytical approaches (microscopic and macroscopic).

- Review Monte Carlo radiation transport codes, analytical tools and other methods already available.

- For these codes, in particular evaluate:
  - Geometry modelling capabilities
  - Particle species and energy ranges of hadronic and electromagnetic physics models, in particular for heavy ions in the range **300MeV/n – 100GeV/n**
  - Existing model validation against experimental data
  - Computational requirements
  - Existing use cases of space applications.

# Radiological dose analysis methodologies

- Review existing space radiation dose analyses methods and practices, with a view of future European capabilities in the domain, including
  - investigation of geometry modelling
  - observed radiation fluxes and doses within the ISS “storm shelter”
- benefiting from already existing ISS practices
- considering future missions outside of the Earth’s magnetosphere (eg. Mars)

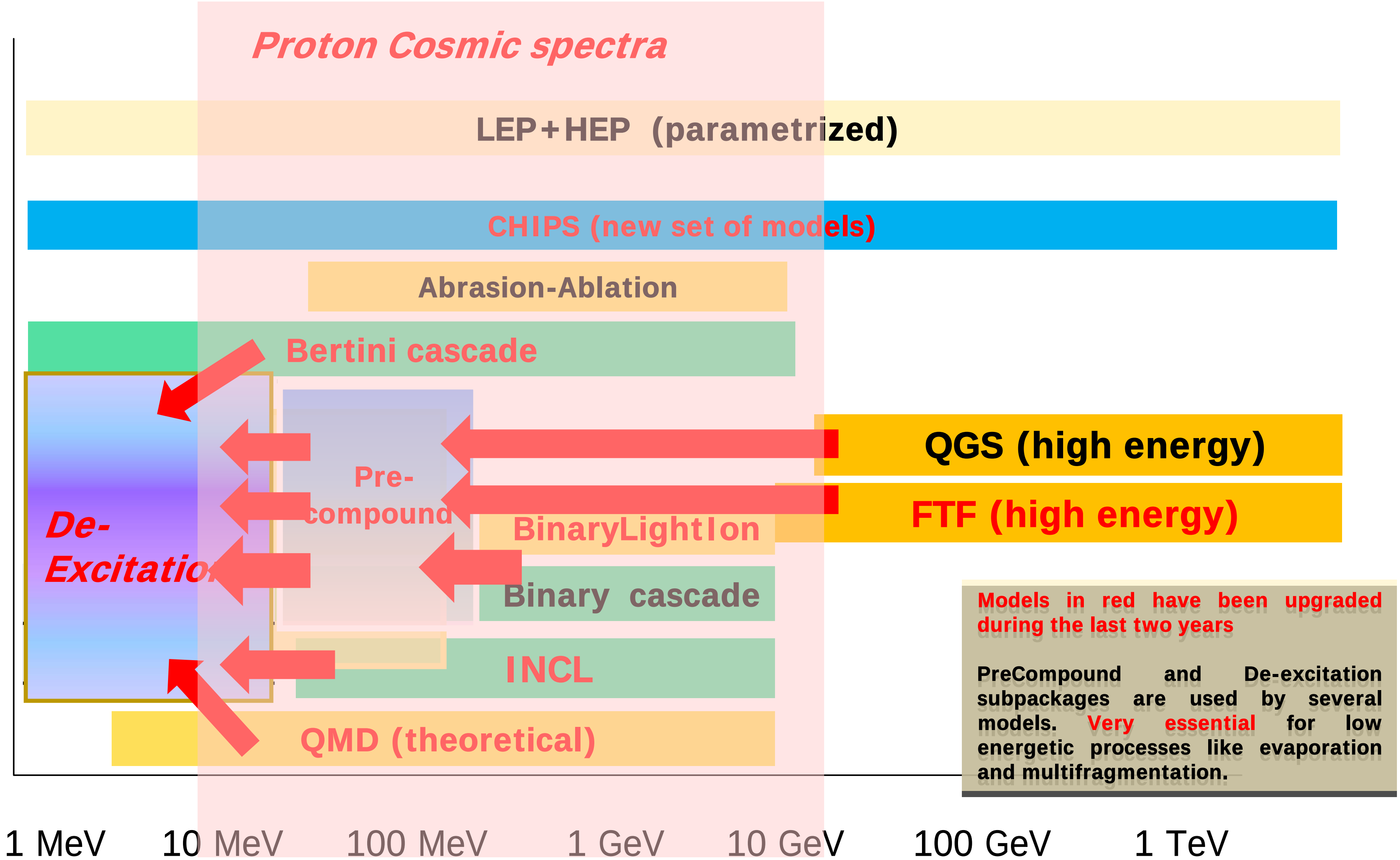
# 2) Geant4 ion Physics

Coordinated & courtesy of A. Ivantchenko
CNRS/IN2P3/Bordeaux U., France

# Review of Geant4 models and validation with exp. data

- The development of Geant4 Physics models require intensive validation
- Testing suites have been created for thin and thick target validation of Geant4 models (BIC, BERT, CHIPS, ...) versus experimental data
  - Thin targets: EXFOR database on NRD (IAEA), HARP experiment
  - Thick targets: EXFOR
  - Hadronic test suite focused on Space Exploration
- New data and exercise tests on regular basis after each upgrade of hadronic models;
- Several upgrades of Geant4 pre-compound and de-excitation models for Geant4 9.4 BETA (V. Ivanchenko, J.M. Quesada)
- Ion-ion interactions will be extended
  - Low energy fragmentation models below 10 GeV/A
  - High energy up to 100 GeV/A

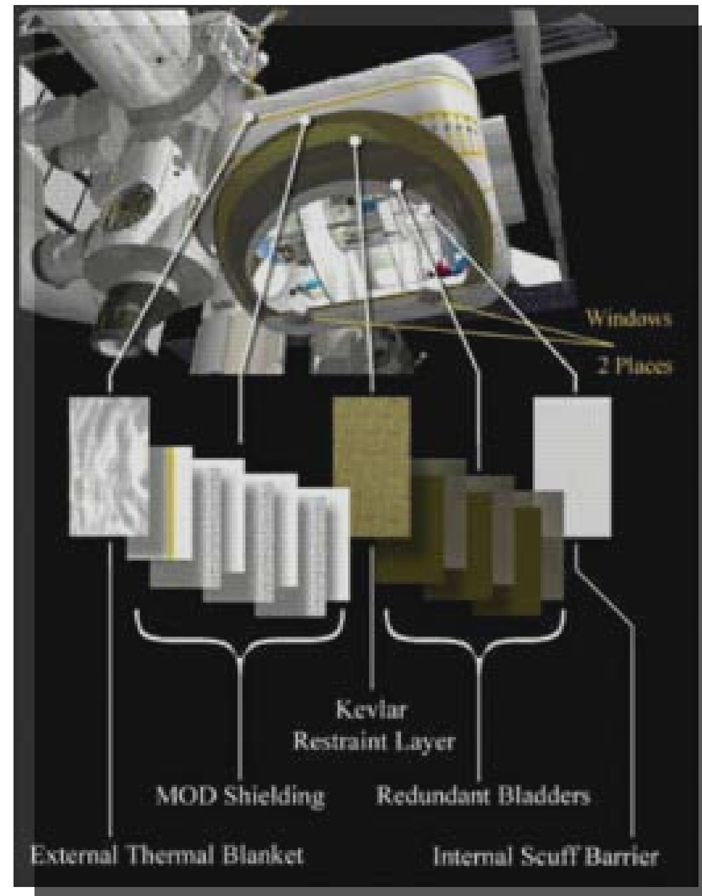
# Geant4 models studied in this work




A. Ribon, *et al.*, Status of Geant4 Hadronic Physics, CERN-LCGAPP-2010-01 (2010)

# Extension of material database

- Several materials will be added to the Geant4 database for space applications, including in particular:
  - Solid materials
    - Spacecraft environment, ISS materials...: Kevlar, Neoprene, Dacron, Brass, High Grade Steel
  - Human body materials
    - DNA bases
  - Addition of specific data on stopping powers and other parameters



# 3) The ISS radiation environement

Coordinated & courtesy of B. Lund-Jensen
KTH, Stockholm, Sweden

# The DESIRE project

- Dose Estimation by Simulation of the ISS Radiation Environment
- Coordinated by B. Lund-Jensen *et al.*, KTH, Sweden.
- The project ended in July 2007.
- Two reference publications from DESIRE
  - Influence of geometry model approximations on Geant4 simulation results of the Columbus/ISS radiation environment, T. Ersmark et al., **Radiation Measurements, 42, (2007)**
  - Geant4 Monte Carlo simulations of the belt proton radiation environment on-board the International Space Station/Columbus, T. Ersmark et al., **IEEE Trans. Nucl. Sci. 54 (2007)**

# The DESIRE project: outcome

- Geant4 works well for this type of study
  - Physics models perform well in most cases
  - Computational time for full-scale simulations acceptable
  - ~100 CPU-days for proton results with statistical errors <1.6%

- ISS geometry models have been developed as Geant4 GDML-files

- The simulated trapped proton dose rates are comparable with experimental data

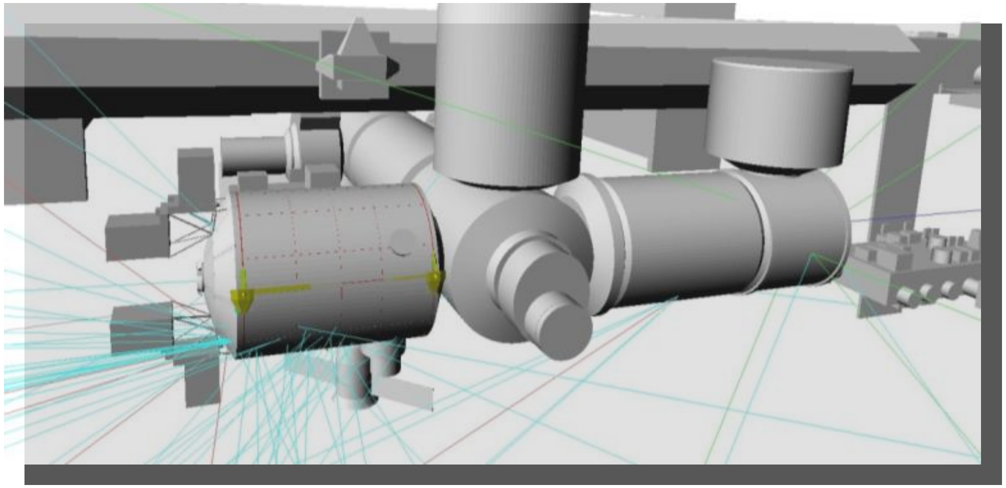
- The GCR dose equivalent rates are about a factor 3 below experimental data
  - 10 GeV/N high-energy limit of Geant4 hadronic ion-nuclei interaction models
  - Problems with existing models for ions >C

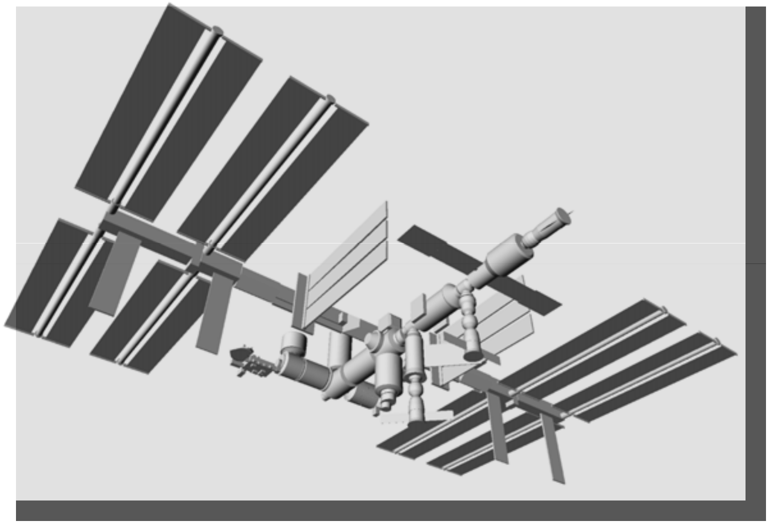
- GCRs contribute a major fraction to the dose equivalent rate on-board ISS
  - For GCR protons >40% is due to the energy range >10 GeV

- Implementation of hadronic ion-nuclei interaction models for such energies in Geant4 are a pre-requisite for detailed studies of the GCR-induced ISS radiation environment

# International Space Station radiation environment modelling

- ISS/Columbus model
  - Adaptation of DESIRE to Geant4.9.3
  - Upgrade of final configuration
  - Upgrade of "Storm Shelter"





# International Space Station radiation environment modelling

- Assessment of ISS radiation data
  - Have access to some Altea & Alteino data
  - Detailed investigation of available data

- Comparison of Geant4 and PHITS models and experimental data
  - PHITS2 available in Japan (May 2010). Will investigate availability.
  - Comparisons between Alteino silicon telescope data and Geant4

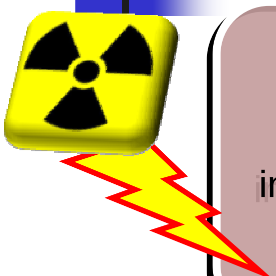
# 4) Geant4-DNA

Coordinated by S. Incerti in collaboration with A. Mantero
CNRS/IN2P3/Bordeaux U., France
INFN Genova, Italy

# The Geant4-DNA project : Geant4 for nanodosimetry

- History : initiated in 2001 by Dr Petteri Nieminen at ESA/ESTEC
- Objective : adapt the general purpose Geant4 Monte Carlo toolkit for the simulation of interactions of radiation with biological systems at the cellular and DNA level
  - domain of « nanodosimetry »
  - Prediction of early DNA damages (~1 microsecond after irradiation)
  - applications : human space exploration missions, radiobiology, radiotherapy…
- Phase 1 started in 2001
  - Delivered work package reports and a user requirement document
- Phase 2 ongoing since 2004
  - First Physics models were added to Geant4 in late 2007 for the discrete modelling of light particle interactions down to the eV scale
  - An on-going interdiciplinary activity of the Geant4 low energy electromagnetic Physics working group, in coolaboration with theoreticians: C. Champion, M. Dingfelder, D. Emfietzoglou, W. Friedland
  - Coordinated by CNRS/IN2P3/CENBG since 2008

# How can Geant4-DNA model radiation biology ?



**Physics 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-chemistry / chemistry stage**
- **Radical** species production
- Diffusion
- Mutual interactions

**Geometry stage**
DNA strands, chromatine fibers, chromosomes, whole cell nucleus, individual cells…
for the prediction of damages resulting from direct and indirect hits

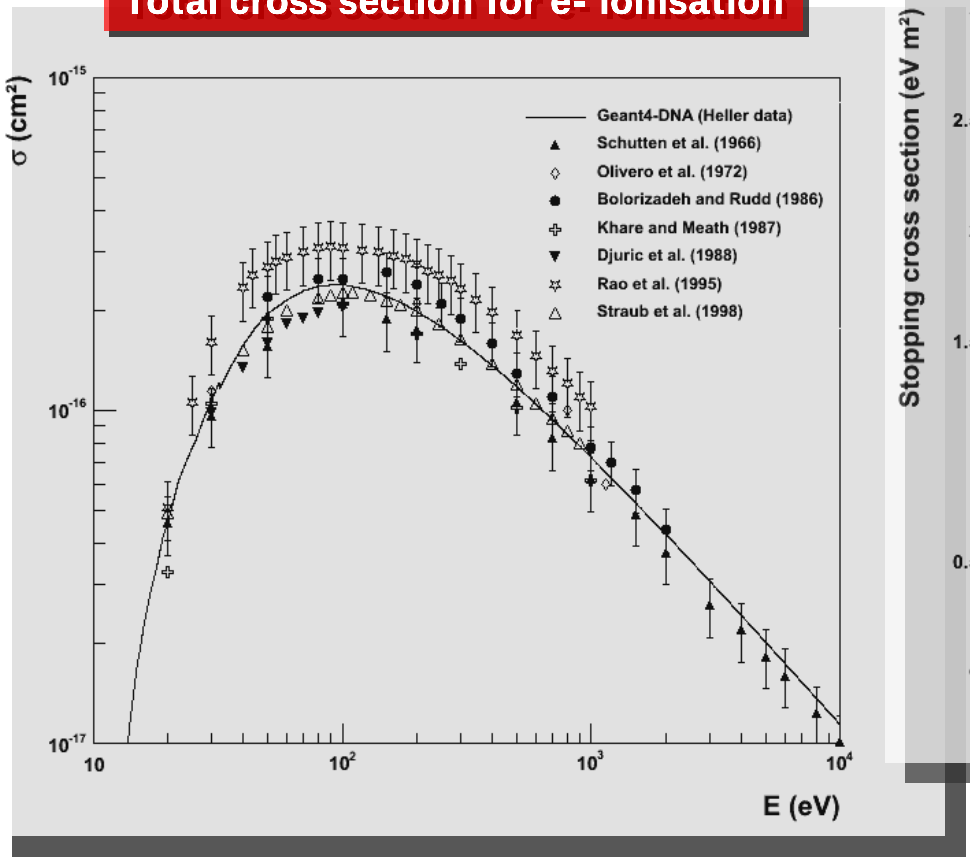
**Biology stage**
**DIRECT** DNA damages

**Biology stage**
**INDIRECT** DNA damages (~70%)

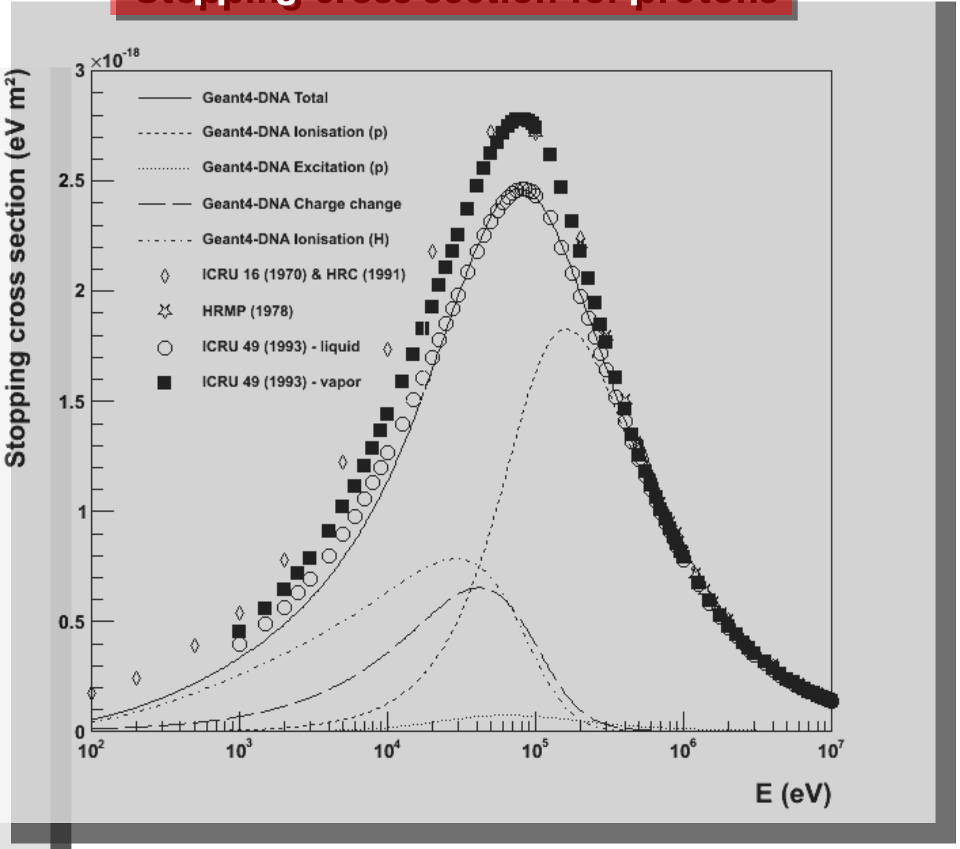
$t=0$ $t=10^{-15}$s $t=10^{-6}$s

# Geant4-DNA Physics validation examples in liq. water

**Total cross section for e- ionisation**

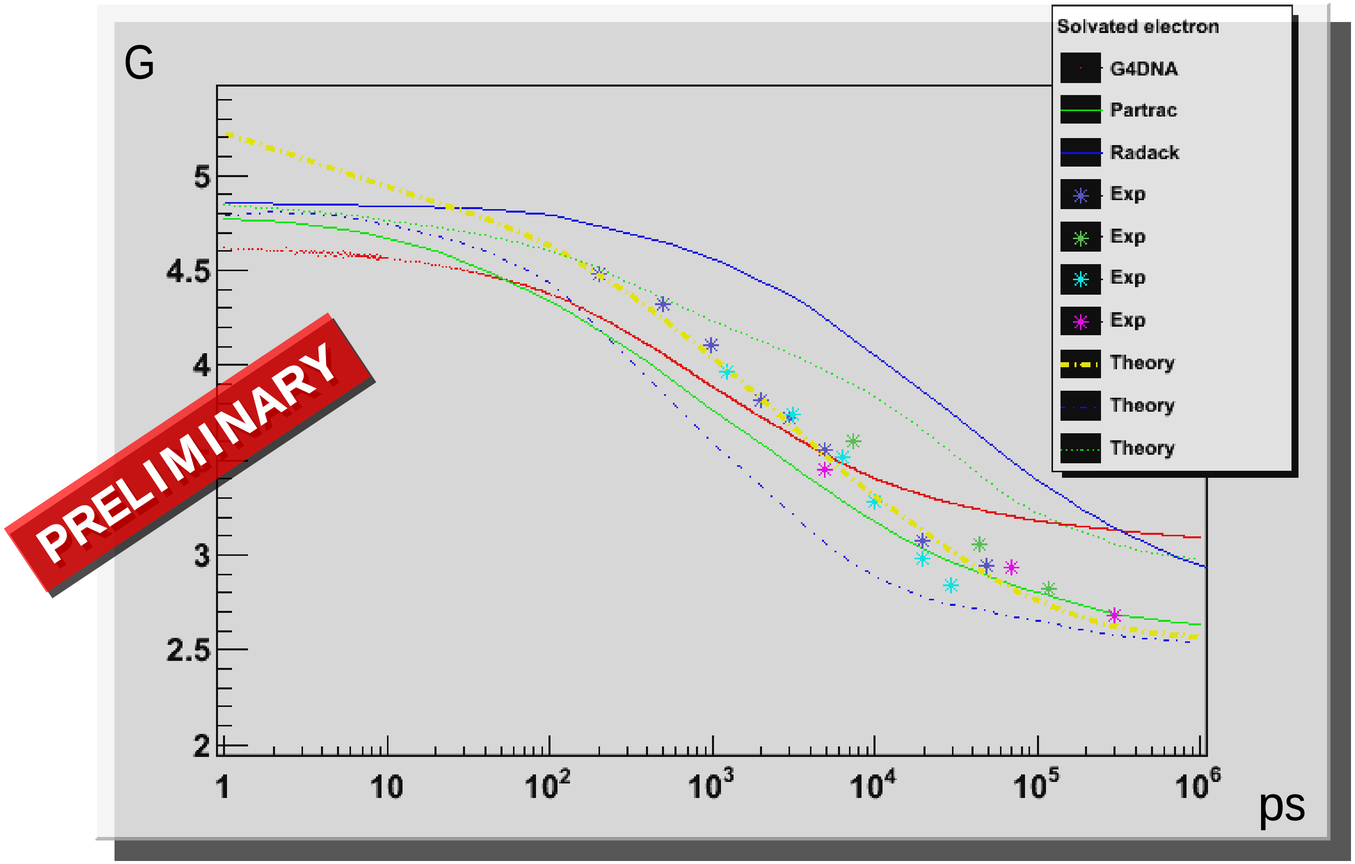



**Stopping cross section for protons**



# Chemistry : first results

- Radiolytic yield G for hydrated electrons (e_aq/100 eV) vs time, up to 1 µs (early biological damages)



# Geant4-DNA on-going developments

See G4 9.4 December 2010

- Physics : add complementary/additional theoretical models
  - other incident particles (C, O, ...)
  - other target materials (DNA, ...)
  - down to the sub-eV range
  - allowing the simulation of direct DNA damages (~30%)

- Physico-chemical and chemistry for the production of radical species
  - needed for the simulation of water radiolysis & indirect DNA damages (~70%)
  - a challenge in Geant4

- Cellular and sub-cellular geometries : model realistic geometries down to the DNA scale following two approaches
  - atomistic approach
  - voxellized approach from confocal microscopy

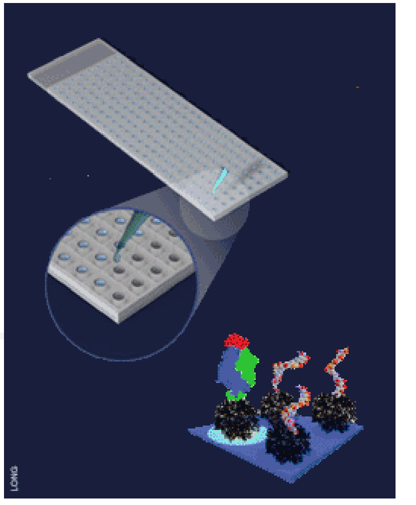
- Biological damage prediction -SSBs, DSBs- and comparison to experimental measurements:
  - For water radiolysis validation : LRad, CEA, Saclay, France
  - Through cellular irradiation : microbeam irradiation facility at CENBG

- Comparison to other Monte Carlo codes

# 5) Biochips

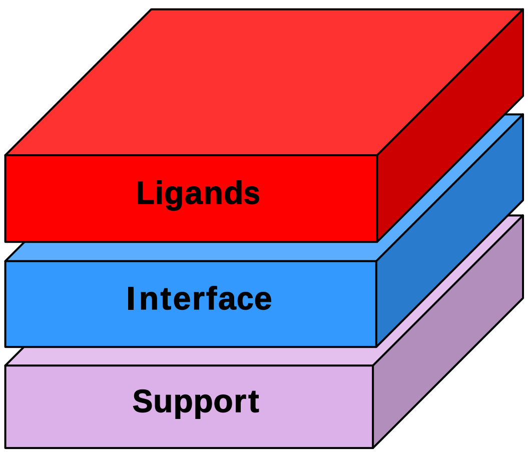
Courtesy of A. Le Postollec *et al.*
BioMas-ARCOR team

# Biochips



- Solar system
  - Search for past/present traces of life
  - Study the degree of chemical evolution
- Should be able to detect organic compounds with variety of structure, properties, molecular weight
- Investigate feasability for space missions

# Multi-disciplinary activity




**Make the good choice !!**

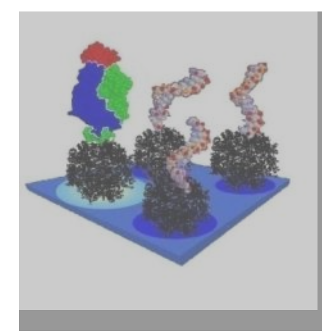
**• Space criteria**

- Lifetime
- Thermal resistance
- Vacuum resistance
- Vibration resistance
- Radiation resistance
- Degasing

**• Analysis criteria**

- Surface state
- Geometry
- Optical properties
- Resistance to solvants
- Diversity of targets
- Ultra sensibility

**Optimized prototype**

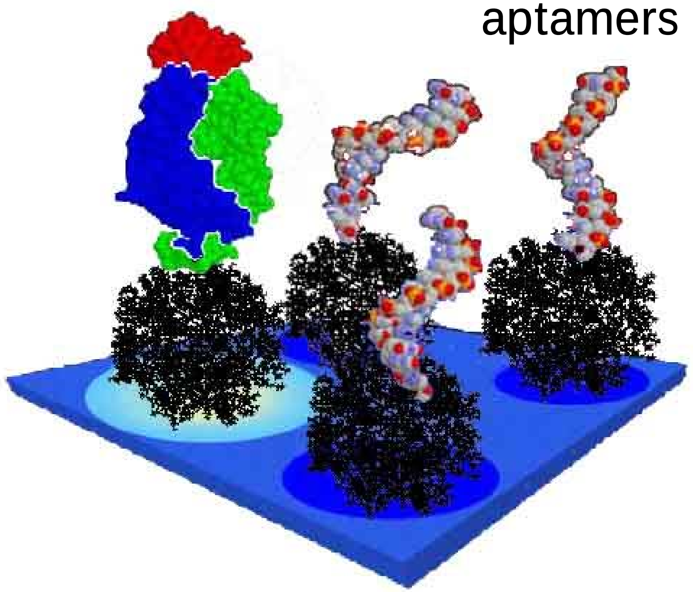


# Biochip & ionising radiation

Whole antibodies or fragments

Oligonucleotides (DNA, RNA) aptamers

➡ **Resistance to space constraints ?**



- We propose to use antibodies and aptamers as ligands
- They are stable between -80°C and 50°C several months
- but antibodies are sensitive to thermal cycles (freezing/de-freezing)
- DNA is sensitive to ionising radiation

➡ **Few / no data on lyophilized ligand stability under ionising radiation (BiOMAS-ARCoR)**

# Challenge

- Radiation is a key factor to study the biochip resistance to space environment

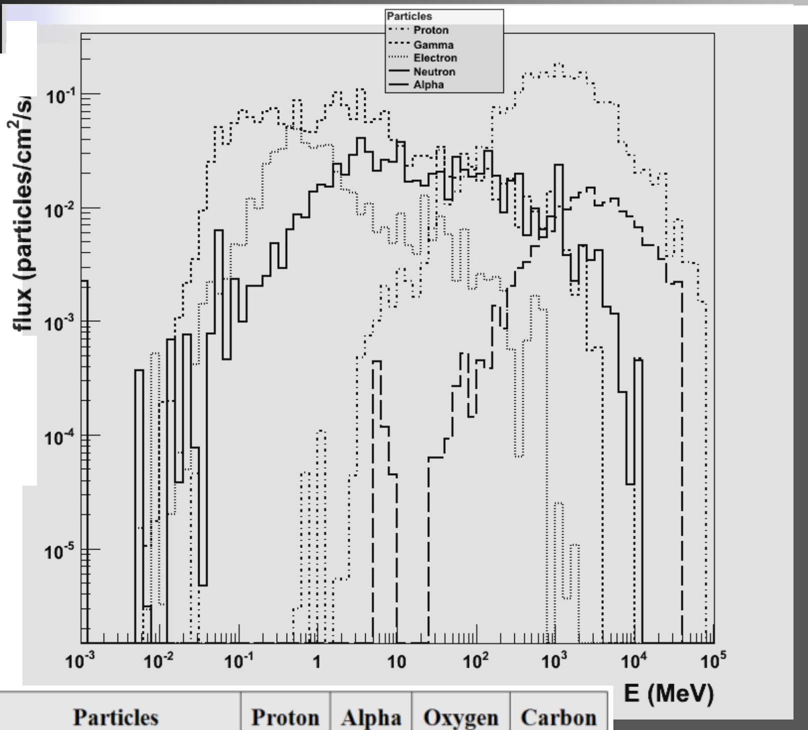
- Ligands (antibodies and aptamers in our case) behavior under cosmic particles fluxes must be studied
  - There is a lack of data

- Use of 3 complementary approaches to determine ligands behavior under space radiations
  - Geant4 simulations
  - Laboratory experiments
  - A real space mission aboard the ISS

# 1) Geant4 GRAS & Planetocosmics

## Transit towards Mars (6 mo)

GCR Maximum + 1 max solar event

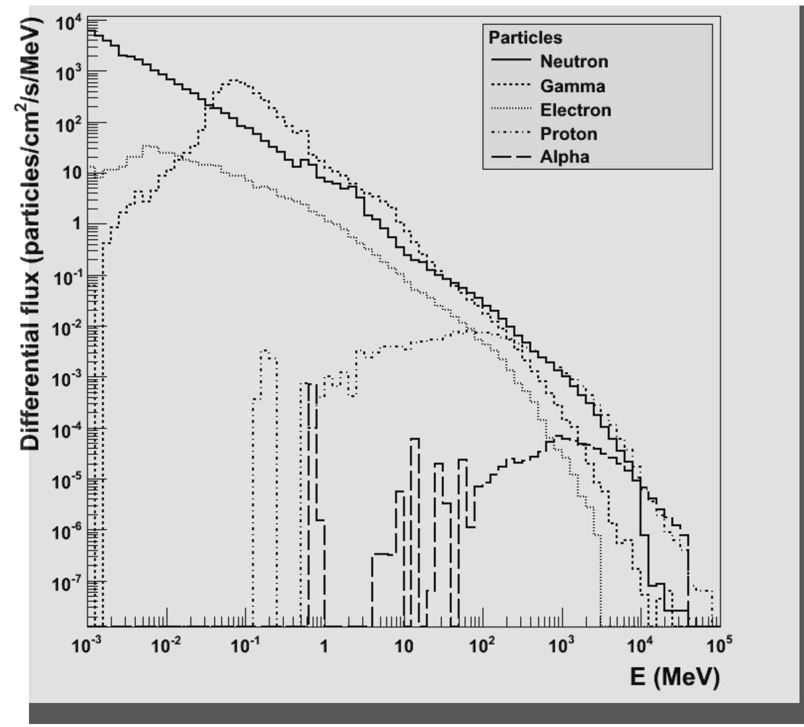



| Particles | Proton | Alpha | Oxygen | Carbon |
|---|---|---|---|---|
| Dose (mGy) | 25.1 | 11.2 | 4.3 | 2.2 |
| Statistical error (mGy) | 1.28 | 0.37 | 0.13 | 0.06 |

GCR dose : **43 mGy**
Solar dose: **1.8 Gy**
**Protons dominant species**

## Mission on Mars (1 mo)

Interaction des particules cosmiques avec le sol

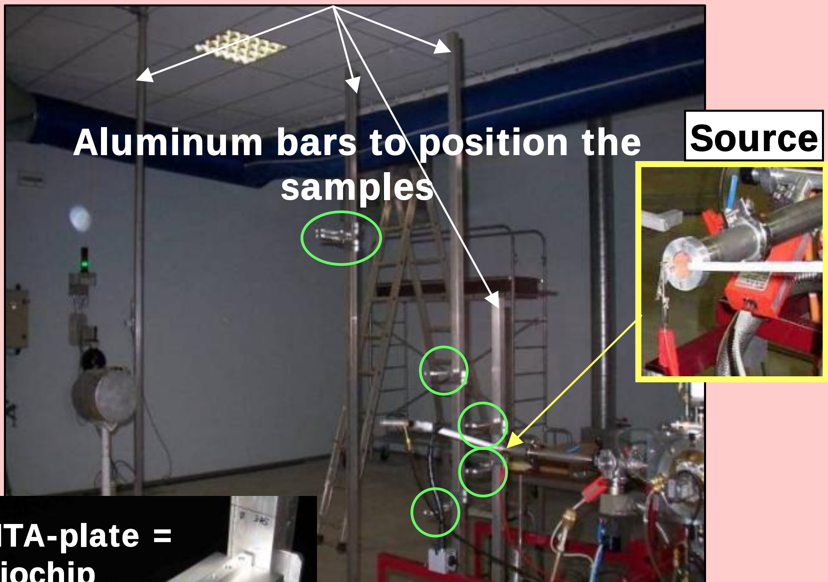


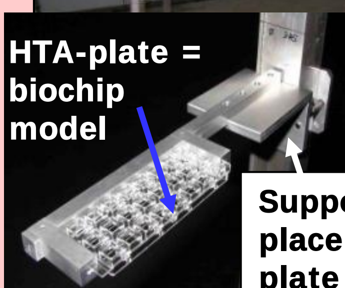

Dose: **27 mGy**
**Neutrons dominant**
**(@ 1.5 m above ground)**

Le Postollec et. al. Astrobiology (2009)

# 2) Irradiation experiments: neutrons

## AIFIRA/CENBG/Bordeaux, France

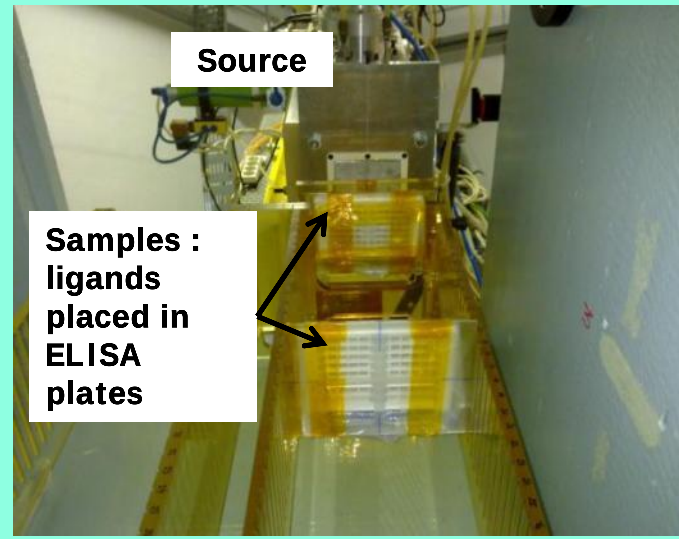



Samples placed at different distances from the source to test 4 different fluences.

Neutrons of 0.6 and 6 MeV tested.
No degradation of antibodies (freeze-dried or in solution).

## Louvain la Neuve, Belgium



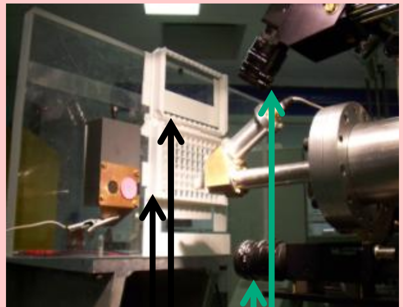

2 samples supports placed at 2 different distances from the source to test 2 different fluences at the same time.

Neutrons spectrum dominated by a peak in the region of 23 MeV (mean value = 16.56 MeV).
No degradation of freeze dried antibodies and aptamers.

Le Postollec et al. 2009. Astrobiology, 9, 637-645

# Irradiation experiments: protons

## AIFIRA/CENBG/Bordeaux, France

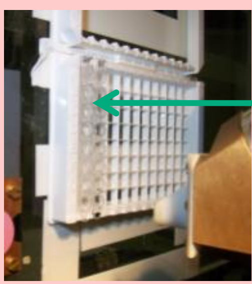


Mobile support

Beam line : protons extracted in air

Cameras

Samples holders



8-wells strips containing the freeze-dried ligands

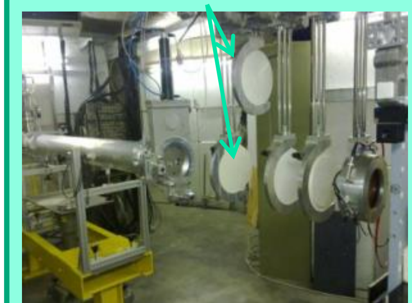
2 MeV protons tested.

No degradation of antibodies and aptamers.

## Louvain la Neuve, Belgium

Samples position

Filters to control particles energy



Laser pointing to center the samples

25 MeV and 50 MeV protons tested.

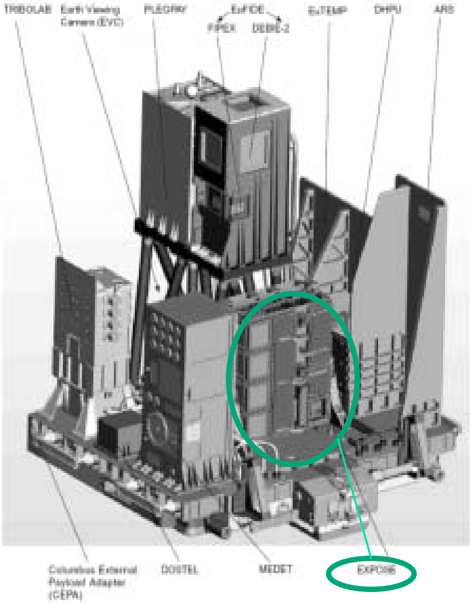
No degradation of aptamers.

Some degradation of antibodies irradiated by 25MeV protons
⇒ interpretation still under study.

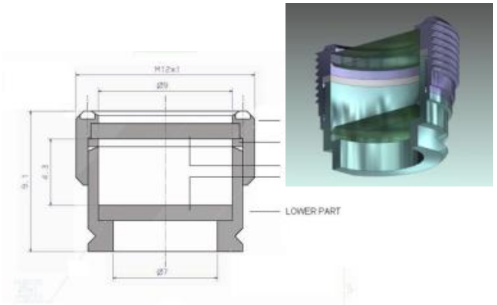
Baqué et al. 2010a. Submitted to PSS.
Baqué et al. 2010b. Submitted to Astrobiology.

# 3) ISS experiment

- Experiment selected by ESA in the frame of the PSS project.
- Experiment on the EXPOSE facility




- Flight scheduled in December 2011
- 15 to 18 months of exposition
- Samples placed onto closed stainless cells.



# ISS experiment

- Objective: study antibody and aptamer resistance to cosmic radiation in space

- Advantages
  - ISS: intermediary step between laboratory and interplanetary irradiations
  - Study of ligands resistance under real space irradiation conditions
  - Combination of several factors of a real space mission: spacecraft launch, vacuum, thermal cycles, radiations, long time storage, etc.
  - Opportunity to collect validation data for Geant4 simulations and laboratory experiments

# Simulation and data needs

- A precise Geant4-based modeling of ISS radiation environment
  - Physics requirements:
    - protons and ions up to Z=26
    - Energy up to > 10 GeV/A
  - for several solar conditions
  - taking into account trapped protons anisotropy
  - using the most recent ISS geometry model available
  - using the GRAS tool to calculate fluences and doses

- Dosimetry data collected from the past and ongoing experiments on ISS (outside ISS and in specific locations near EXPOSE facility), in order:
  - To perform simulations with accurate **input data** (especially particles spectra at ISS altitude)
  - To **validate Geant4** simulations results on specific locations (taking into account shielding, geometry,...)

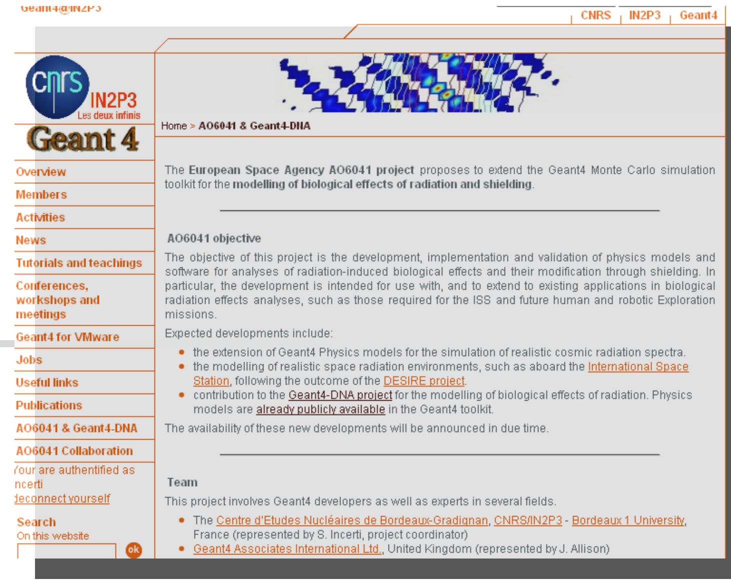
# The AO6041 team

# Partners & collaborators

- G4AI Ltd, UK
  - J. Allison, V. Grichine (ESA), A. Ivanchenko (ESA - WP2)
- IN2P3, France
  - M. Karamitros (PhD) , B. Rabier, S. Incerti, H. Seznec, H. Tran (PhD)
- INFN, Italy
  - G. Cuttone (WP5), A. Mantero (ESA - WP4)
- IRSN, France
  - Z. Francis, C. Villagrasa, M. Dos Santos (future PhD)
- KTH, Sweden
  - B. Lund-Jensen (WP3), PhD (ESA)
- Metz U., France
  - C. Champion, V. Ivanchenko
- Stockholm U., Sweden
  - I. Gudowska (WP1), B. Mascialino (ESA)
- BioMas-Arcor team, France
  - M. Bacqué, G. Coussot, M. Dobrijévic, S. Incerti, A. Le Postollec, O. Trambouze
- Geant4 collaboration
  - J.M.Quesada, D.Wright, P.Truscott…

# Where to get more information ?

# Where to get more information ?




- Project web site
  - http://geant4.in2p3.fr

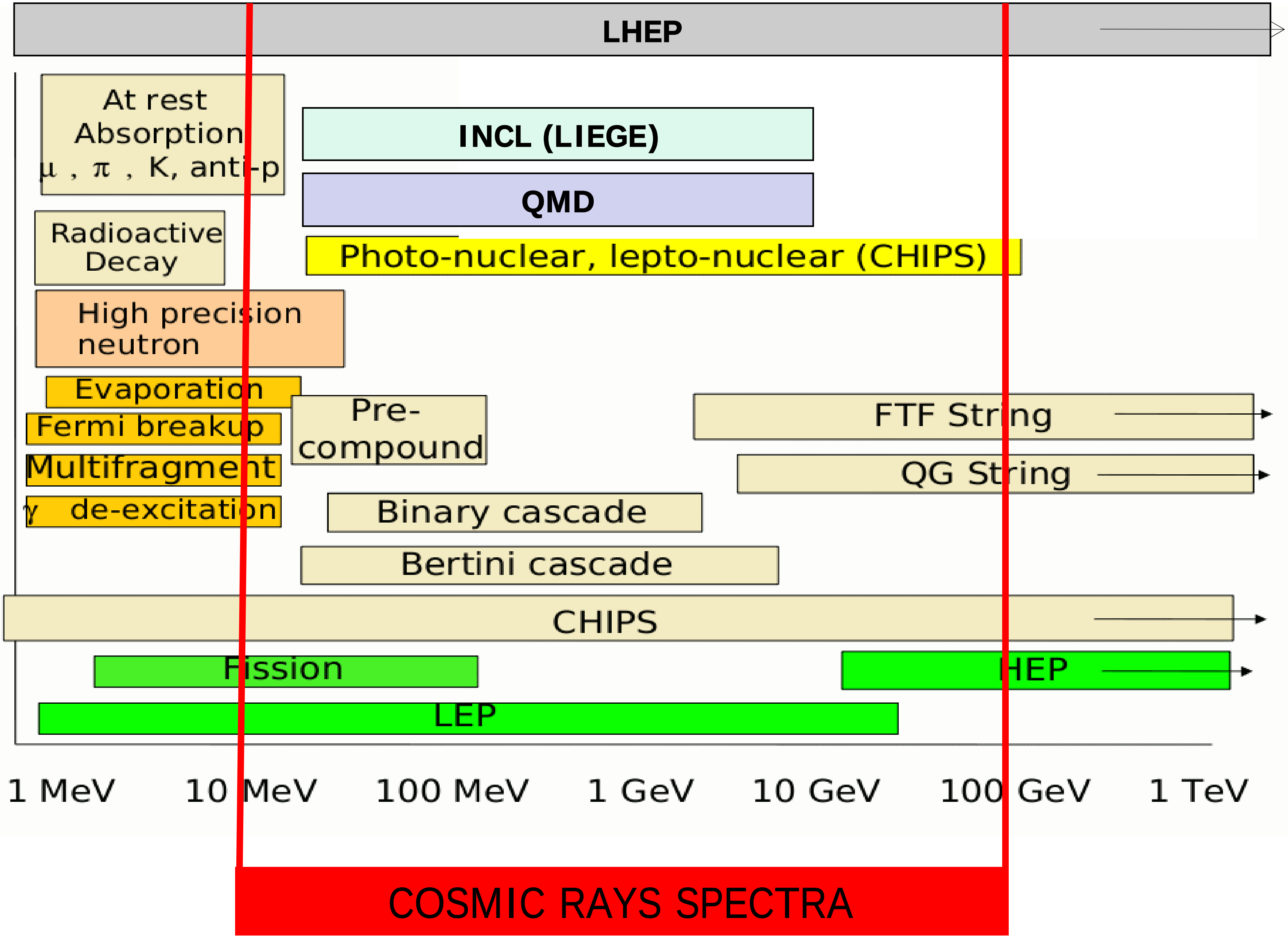
- Conferences, workshops
  - Geant4 Space User's Workshops 2011, 2012...
  - COSPAR conferences 2010, ...
  - ISS community workshops

- Some recent publications
  - Comparison of GEANT4 very low energy cross section models with experimental data in water,
    S. Incerti et al. ***Med.Phys.*** **37, 4692-4708, (2010)**
  - The Geant4-DNA project,
    S. Incerti et al., ***Int. J. Model. Simul. Sci. Comput.*****, 1(2), 157-178 (2010)**
  - Monte-Carlo Simulation of the radiation environment encountered by a biochip during a mission to Mars,
    A. Le Postollec et al., **Astrobiology 9 (3) (2009) 311-323**

# Thank you for your attention

# Backup

# Geant4 models (not all shown)



# Ion-Ion models in Geant4

- Binary-Light-Ion
  - An extension of the Binary cascade
  - E < 10GeV
  - Ion with A < 16
  - *In development, should be tested more*
- Wilson Abrasion and Ablation model
  - Simplified macroscopic model
  - 70 MeV <E <10 GeV
  - Valid for all nuclei
  - Is not precise, shold be tested
- Electromagnetic dissociation model
  - implementation of the NASA model
  - 100 MeV <E <500 GeV
  - Valid for all nuclei;
  - Some probability table of fragments production (Z,A)
  - Uses Geant4 de-excitation model to handle excited fragments and projectile residual
  - *Testing should be established*
- DPMJET (P.Truscott, Qinetiq)
  - Space cosmic rays oriented model, developed and used in the Qinetiq project
  - 5 GeV< E < 10000 TeV
  - *Testing should be established*
- QMD (T.Koi, SLAC)
  - Based on old PHITS-JQMD code
  - E <10 GeV
  - Valid for all nuclei
  - Uses Geant4 Pre-Compound and Evaporation models
  - Valid for all nuclei, very good results are shown by Tasumi Koi on previous workshops

# Physics stage :
# Physics models available in Geant4-DNA

- Applicable to liquid water, the main component of biological matter

- Can reach the very low energy domain (sub-eV limit)
  - Including vibrational excitation of water molecules
  - Compatible with molecular description of interactions

- Purely discrete
  - Simulate all elementary interactions on an event-by-event basis
  - No condensed history approximation

- Models can be purely analytical and/or use interpolated data tables
  - eg. cross sections

- Since December 2009, they use the same software design as all electromagnetic models available in Geant4 (standard EM and low energy EM)

- In 2010, extensive validation of Physics models : comparison to experimental data & international recommendations (stopping powers)

- More to come in December 2010 release…

# Chemistry stage

- A challenge in Geant4...
  - Particle/matter interactions only
- Molecular species classes already implemented in Geant4
- Dominant chemical reactions are taken into account as well as chemical diffusion
- Time is cut in short very slices up to 1 µs, following the PARTRAC approach (Friedland *et al.*)
- First results will be presented at MC2010 conference, November 2010, Tokyo, Japan
- Software will be made public end of 2011

| Species | $D$ ($\times 10^{-9}$ m$^2$ s$^{-1}$) |
|---|---|
| $e^-_{aq}$ | 4.9 |
| $^{\bullet}OH$ | 2.8 |
| $H^{\bullet}$ | 7.0 |
| $H_3O^+$ | 9.0 |
| $H_2$ | 4.8 |
| $OH^-$ | 5.0 |
| $H_2O_2$ | 2.3 |

| Reaction | $k$ (M$^{-1}$s$^{-1}$) |
|---|---|
| $e^-_{aq} + e^-_{aq} + 2H_2O \longrightarrow H_2 + 2OH^-$ | $0.50 \times 10^{10}$ |
| $e^-_{aq} + {}^{\bullet}OH \longrightarrow OH^-$ | $2.95 \times 10^{10}$ |
| $e^-_{aq} + H^{\bullet} + H_2O \longrightarrow H_2 + OH^-$ | $2.65 \times 10^{10}$ |
| $e^-_{aq} + H_3O^+ \longrightarrow H^{\bullet} + H_2O$ | $2.11 \times 10^{10}$ |
| $e^-_{aq} + H_2O_2 \longrightarrow OH^- + {}^{\bullet}OH$ | $1.41 \times 10^{10}$ |
| ${}^{\bullet}OH + {}^{\bullet}OH \longrightarrow H_2O_2$ | $0.44 \times 10^{10}$ |
| ${}^{\bullet}OH + H^{\bullet} \longrightarrow H_2O$ | $1.44 \times 10^{10}$ |
| $H^{\bullet} + H^{\bullet} \longrightarrow H_2$ | $1.20 \times 10^{10}$ |
| $H_3O^+ + OH^- \longrightarrow 2H_2O$ | $1.43 \times 10^{11}$ |

| Time interval (s) | $\Delta t$ (ps) |
|---|---|
| Until $1.0 \times 10^{-11}$ | 0.1 |
| $1.0 \times 10^{-11}$–$1.0 \times 10^{-10}$ | 1 |
| $1.0 \times 10^{-10}$–$1.0 \times 10^{-9}$ | 3 |
| $1.0 \times 10^{-9}$–$1.0 \times 10^{-8}$ | 10 |
| Above $1.0 \times 10^{-8}$ | 100 |

# Recent Upgrades of Geant4 Pre-Compound and De-excitation models

- Now successfully used by other Geant4 models
  - FTF, QGS, Binary cascade, QMD, etc.

- For Geant4 9.3p01 (December 2009) improvement of:
  - Light ion production
  - Fission of excited residual fragments
  - Isotope production

- For Geant4 9.4beta (June 2010) new developments:
  - FermiBreakUp model for light ion fragments (A < 17)
  - G.E.M. evaporation samples 68 decay channels
  - Photon Evaporation module
  - Multi-Fragmentation model (off by default)

# Development of new Geant4 models & methods for ions

- Elastic interactions
  - Coulomb scattering combined with nuclear scattering
  - Develop elastic cross sections in connection with interface between Coulomb and strong forces
  - Provide NIEL computation
- Ion-ion interactions
  - Low energy fragmentation models below 10 GeV/A
  - High energy up to 100 GeV/A
- Biasing methods
  - For primary flux of ions
  - For neutron transport