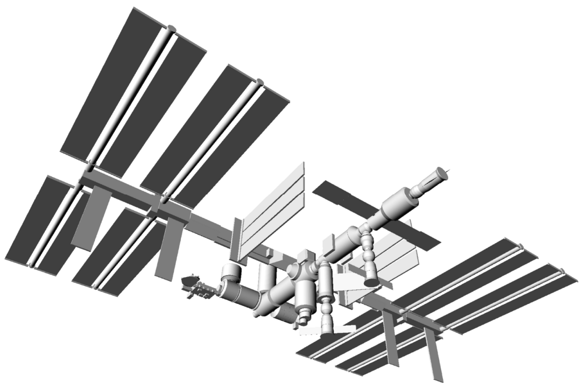
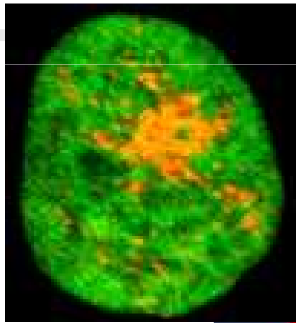
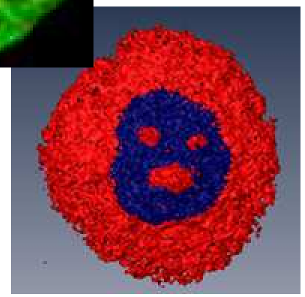
Physics Models for Biological Effects of Radiation and Shielding

ESA AO6041 project overview



Sébastien Incerti
CNRS/IN2P3/Bordeaux U., France





On behalf of the AO6041 team

7th Geant4 Space Users' Workshop
Seattle, WA, USA, 18-20 August 2010

Content of this talk

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

Context of ESA AO6041

- 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

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

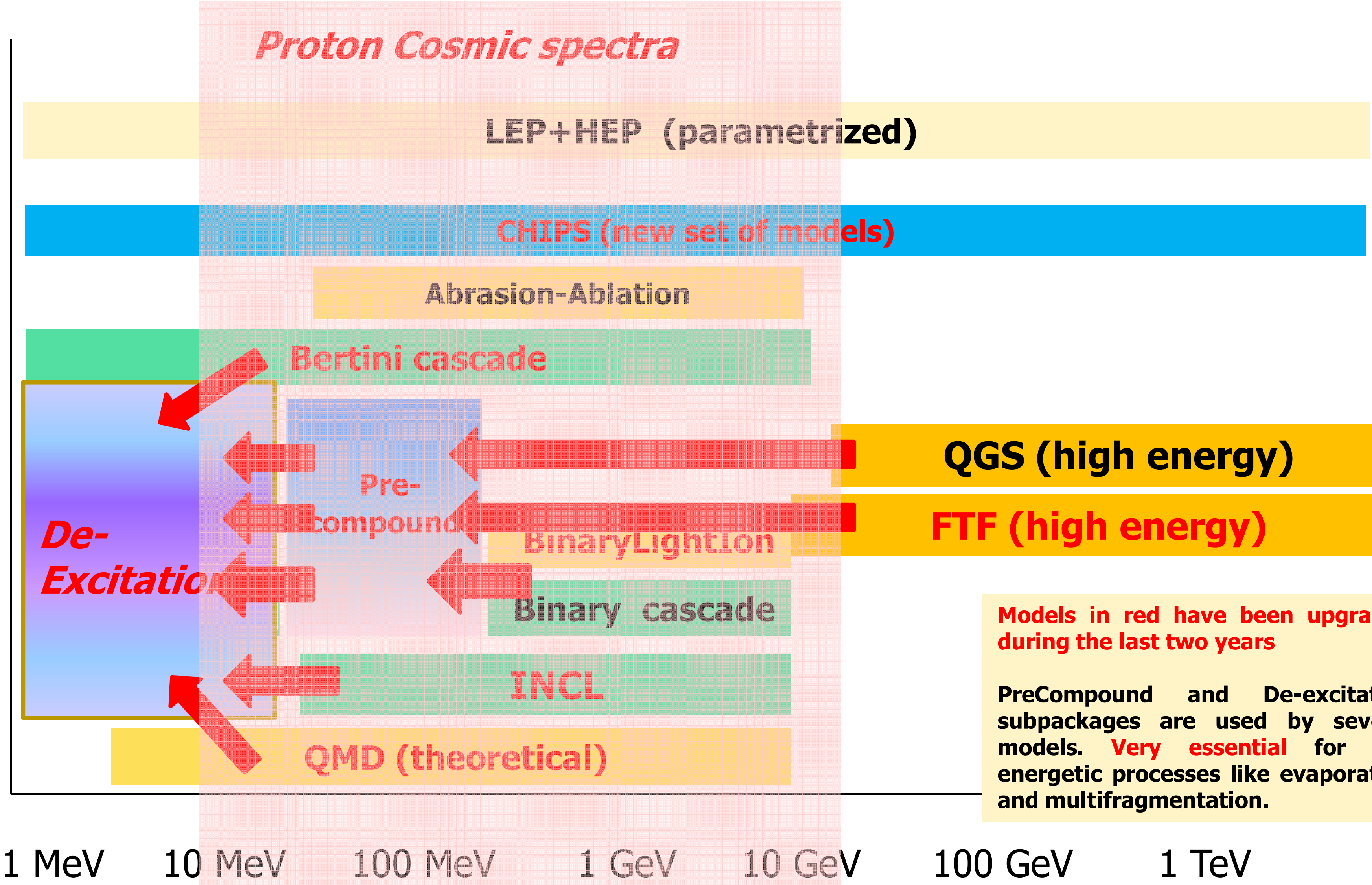
- The development of Geant4 Physics models require intensive validation

- 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 9.4 BETA (V. Ivanchenko, J.M. Quesada)

Geant4 models studied in this work

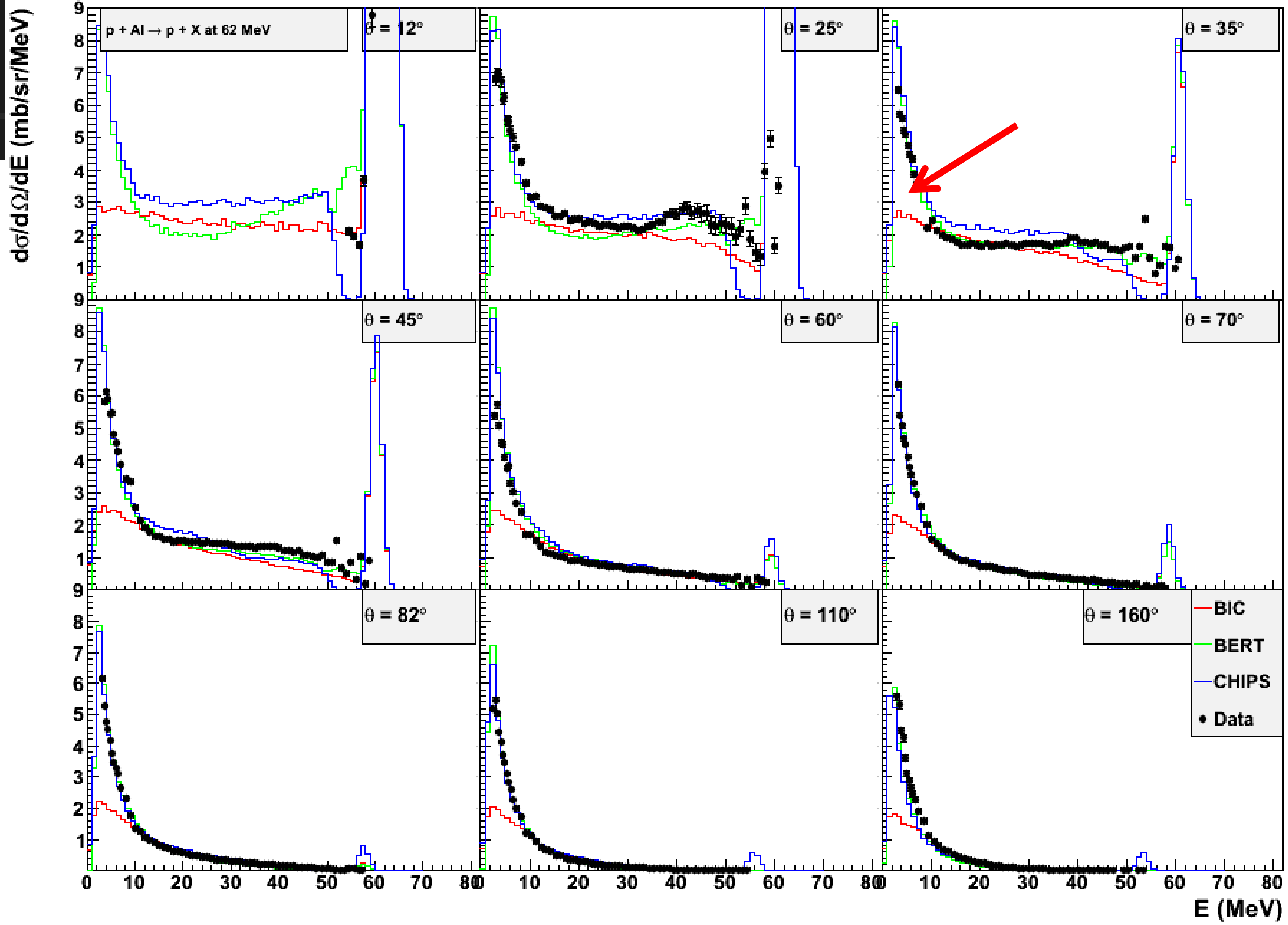


Models in red have been upgraded during the last two years

PreCompound and De-excitation subpackages are used by several models. Very essential for low energetic processes like evaporation and multifragmentation.

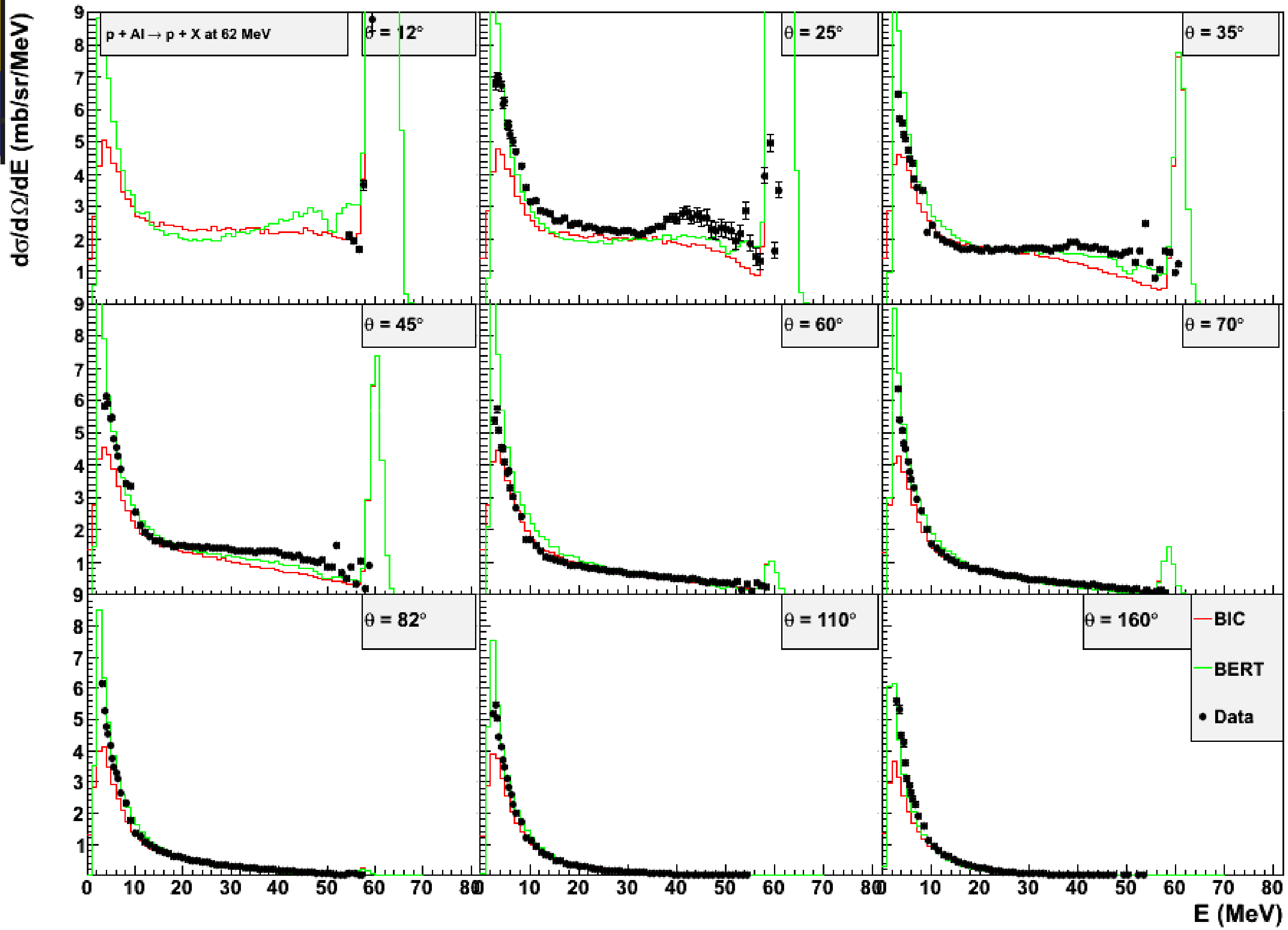
A. Ribon, et.al., Status of Geant4 Hadronic Physics, CERN-LCGAPP-2010-01 (2010)

Al (p,xp) 61.5 MeV, patch01, Bug



Underestimation of amount of evaporation protons in BIC cascade model

Al (p,xp) 61.5 MeV, ref03c - Bug fixed



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

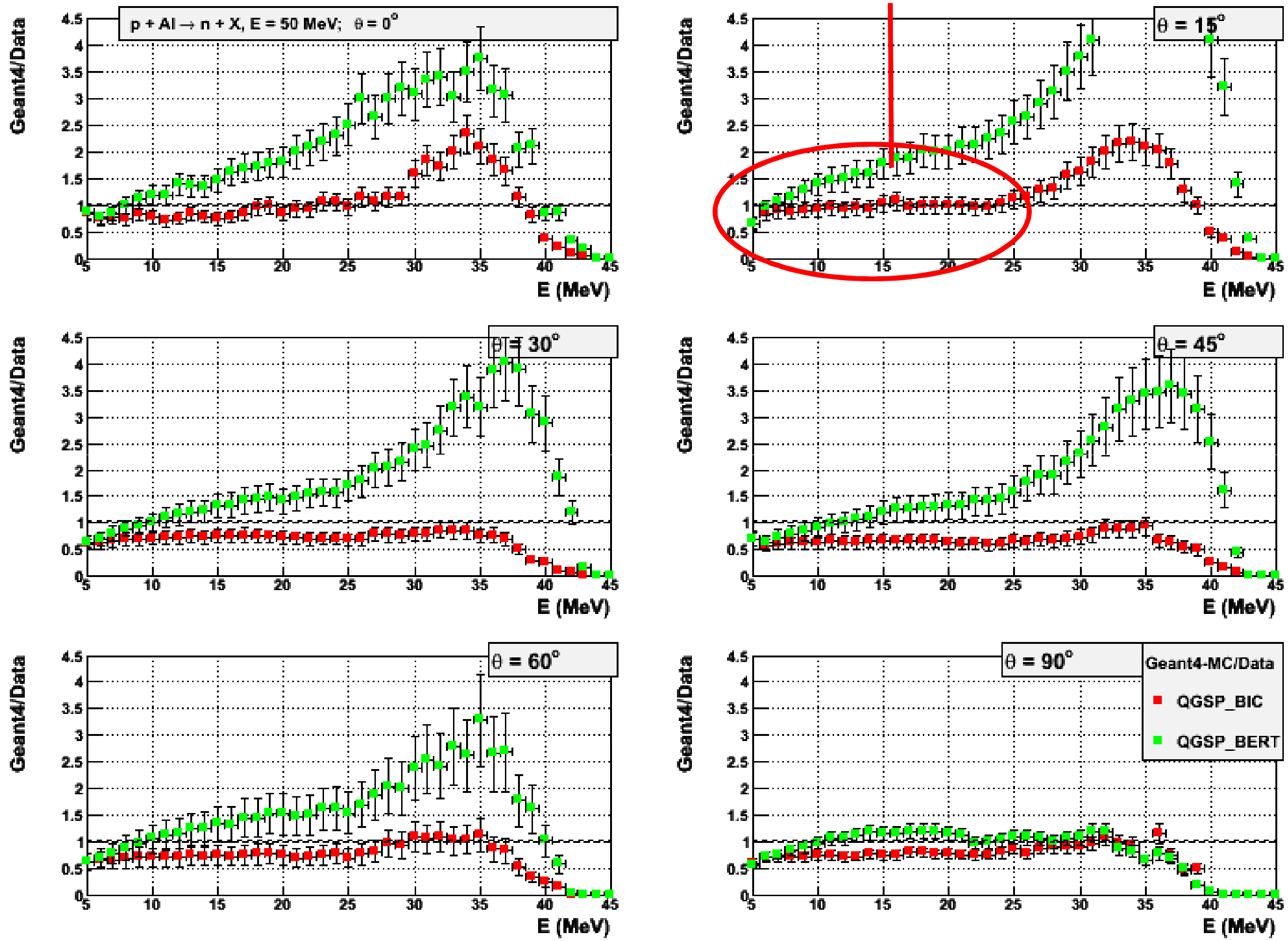
- Now successfully used by other Geant4 models
  - FTF, QGS, Binary cascade, QMD, etc.

- 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)

TTNY, Al(p,n) 50MeV, g4 9.3.p01

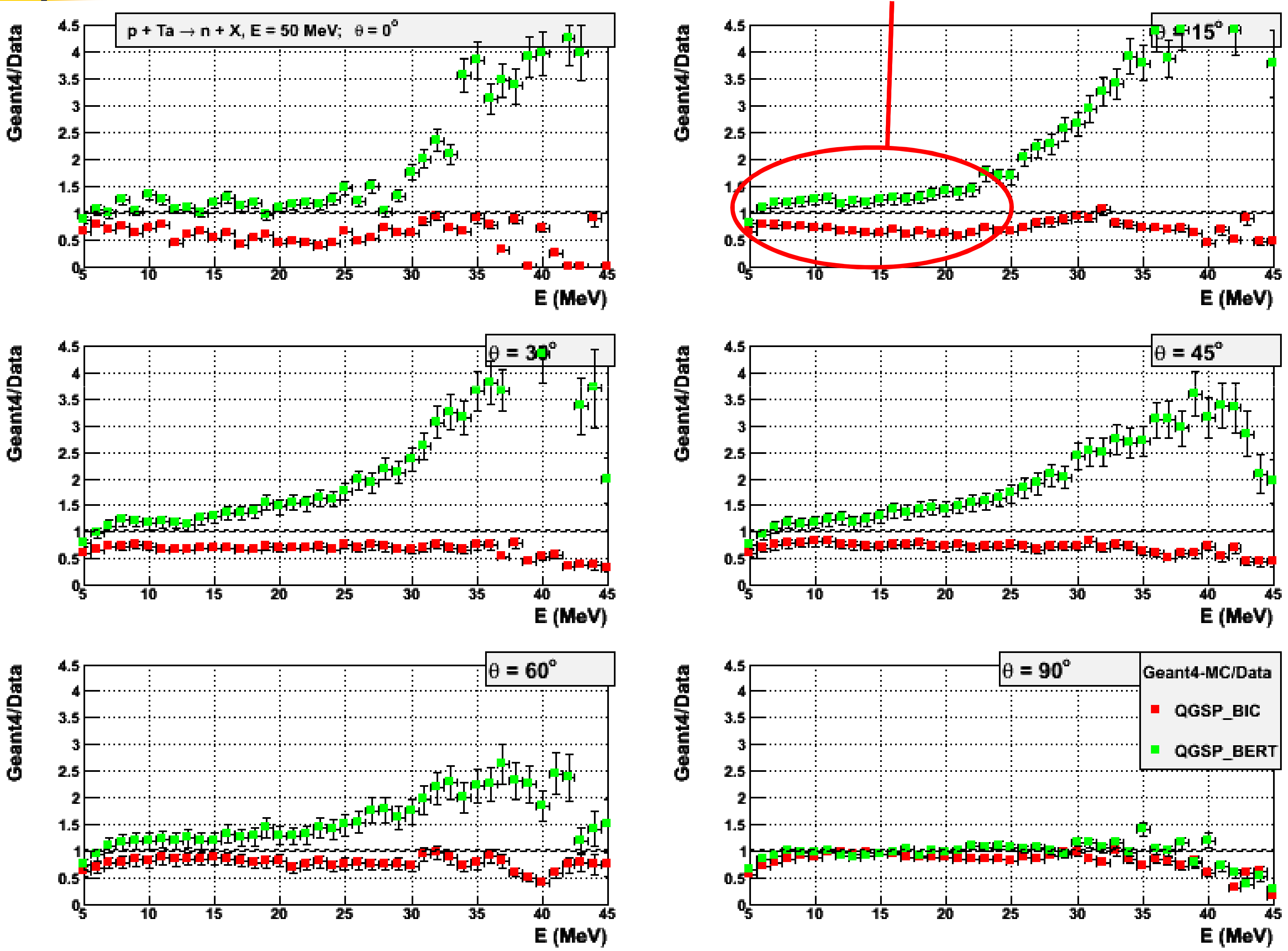
90% of events [0,25] MeV



Results for Al(p,xn): comparison of Geant4/exp. data, [5,45] MeV. QGSP_BIC has highest precision. QGSP_BERT has problems at forward angles, it is more precise at large angles 60° and 90°.

TTNY, Ta(p,n) 50MeV, g4 9.3.p01

90% of events [0,25] MeV



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

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…
  - Human body materials
  - 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, P. Carlson, E. Daly, C. Fuglesang, I. Gudowska, B. Lund-Jensen, P. Nieminen, M. Pearce, G. Santin,
    Radiation Measurements, 42, (2007)
  - **Geant4 Monte Carlo simulations of the belt proton radiation environment on-board the International Space Station/Columbus**,
    Tore Ersmark, Per Carlson, Eamonn Daly, Christer Fuglesang, Irena Gudowska, Bengt Lund-Jensen, Petteri Nieminen, Mark Pearce, and Giovanni Santin,
    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

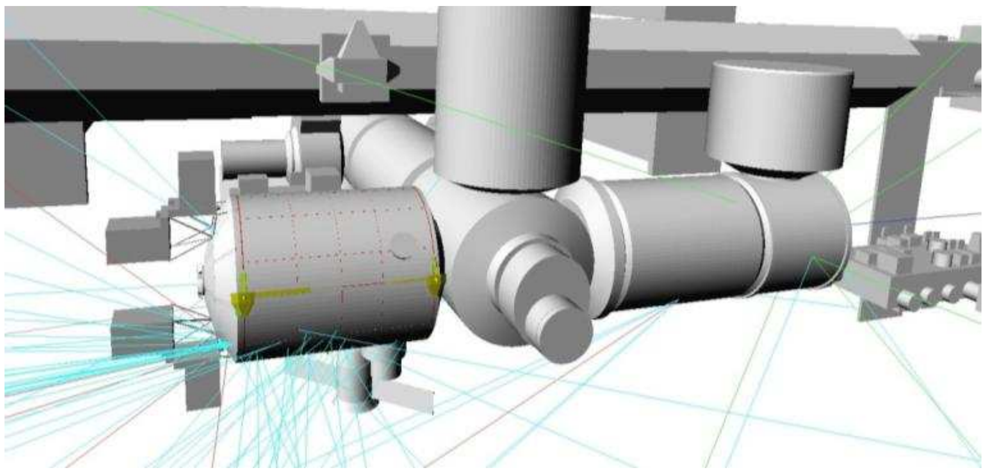
➡ GCRs contribute a major fraction to the dose equivalent rate on-board ISS

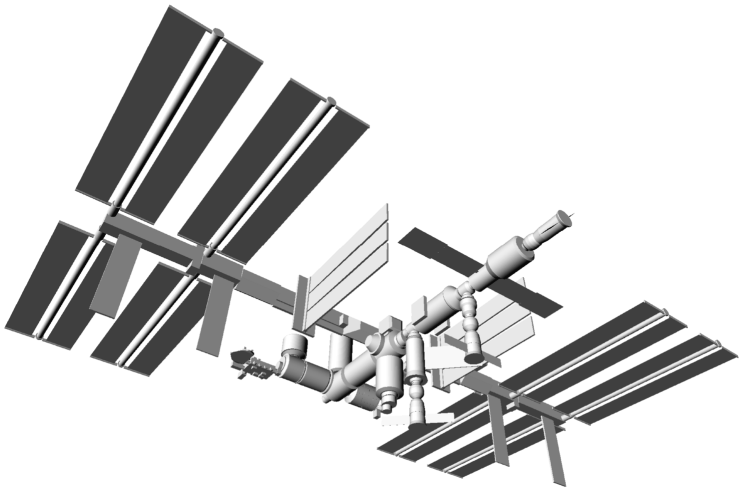
- For GCR protons >40% is due to the energy range >10 GeV

➡ 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

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

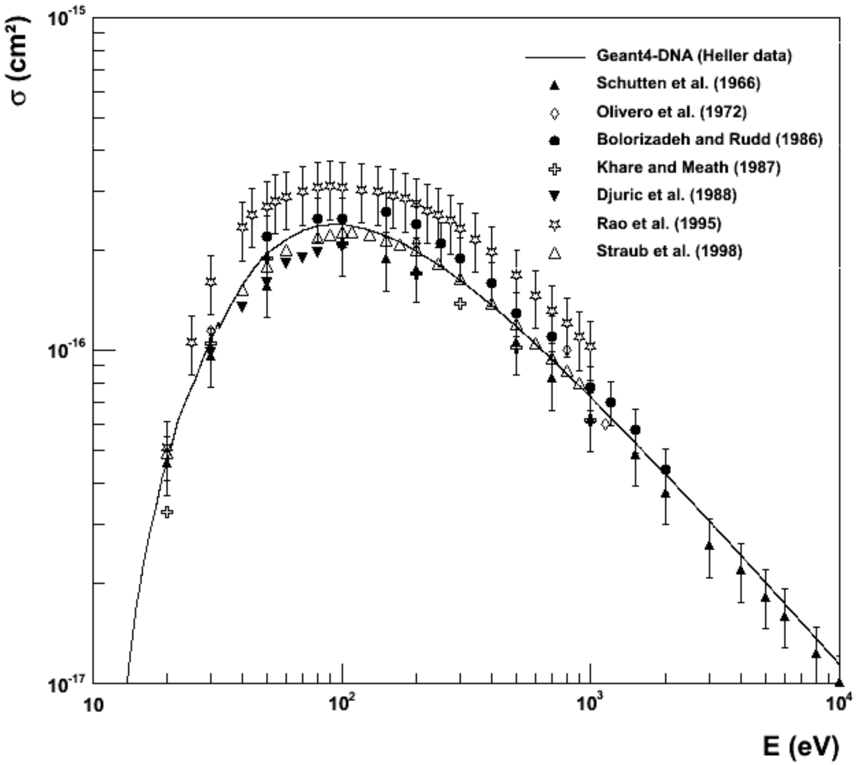
- Since December 2009, they use the same software design as all electromagnetic models available in Geant4 (standard EM and low energy EM)

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

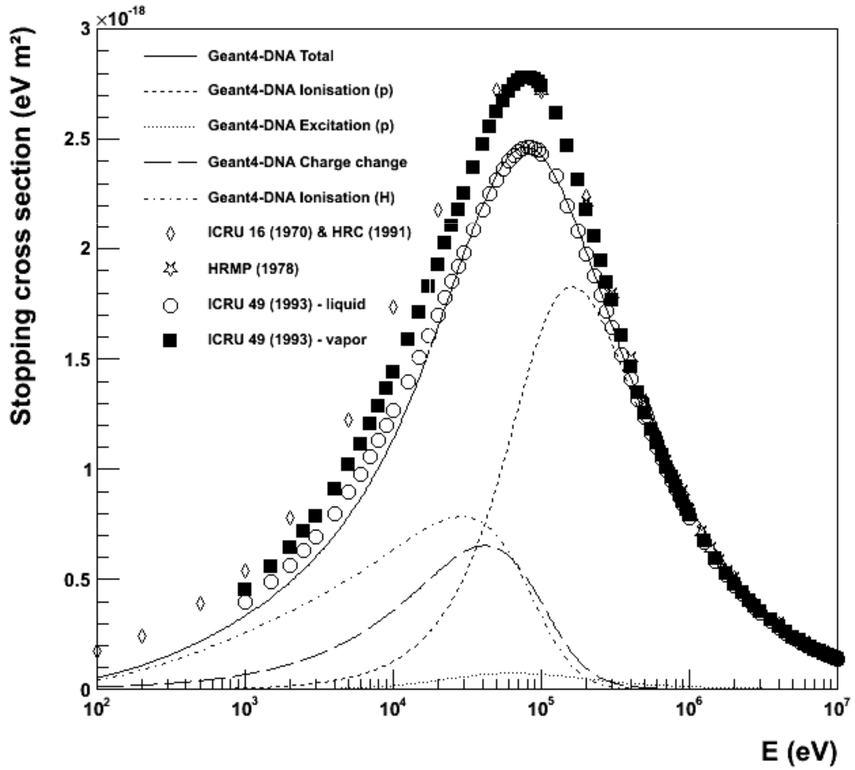
- More to come in December 2010 release…

Geant4-DNA Physics validation examples

Total cross section for e- ionisation



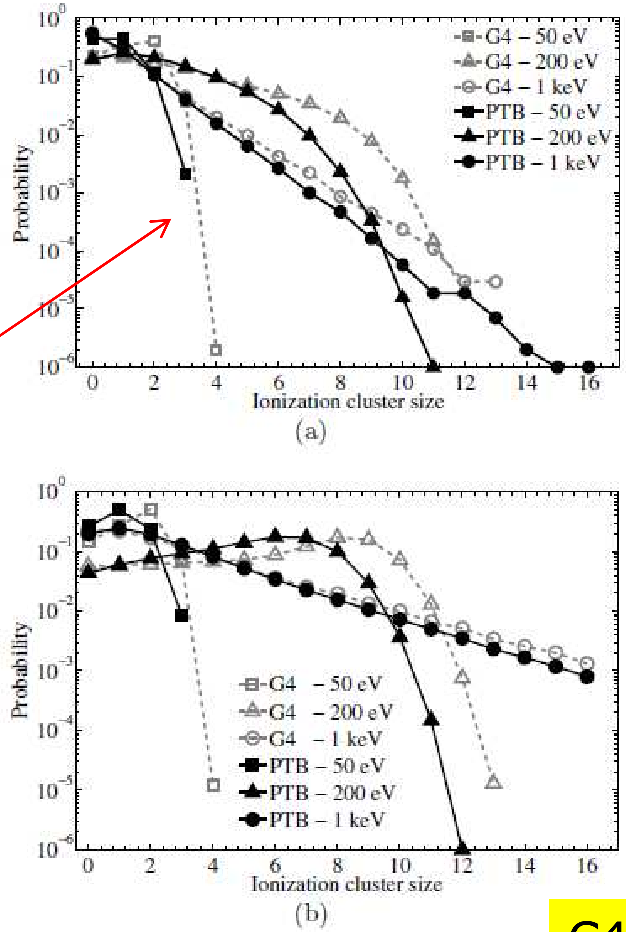
Stopping cross section for protons

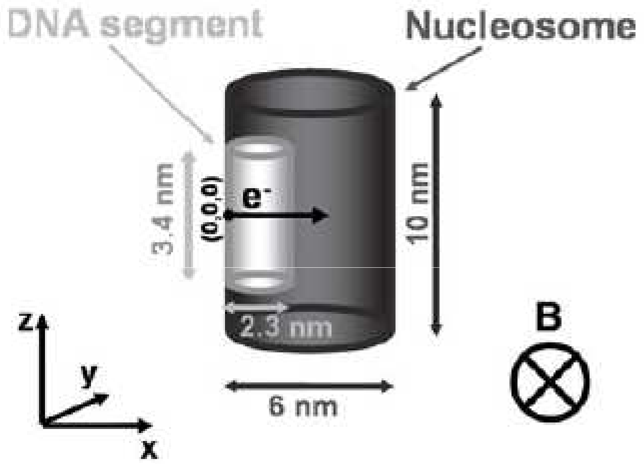


Geant4-DNA verification: ionization cluster sizes

DNA segment

nucleosome





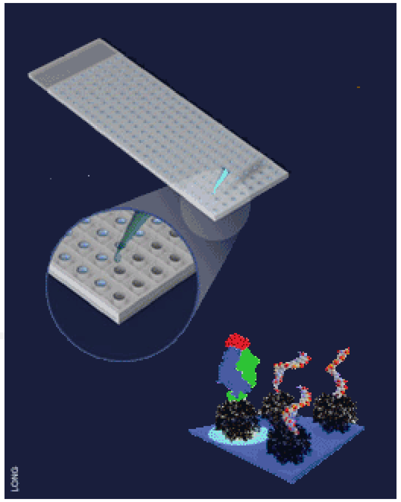
A collaboration between Geant4 developers and Geant4 users

M. Bug et al., Eur. Phys. J. D (2010)

G49.2+P01

5) Biochips

Biochips

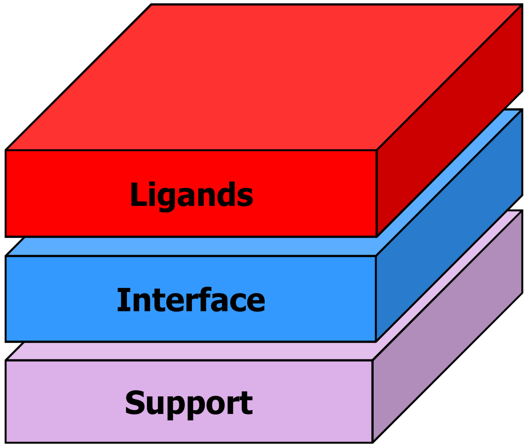


- Solar system
  - Search for past/present traces of life
  - Study the degree of chemical evolution

- 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 !!

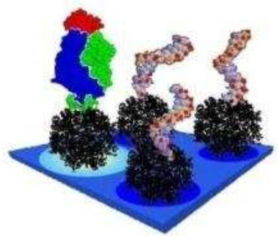
• Space criteria

- 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

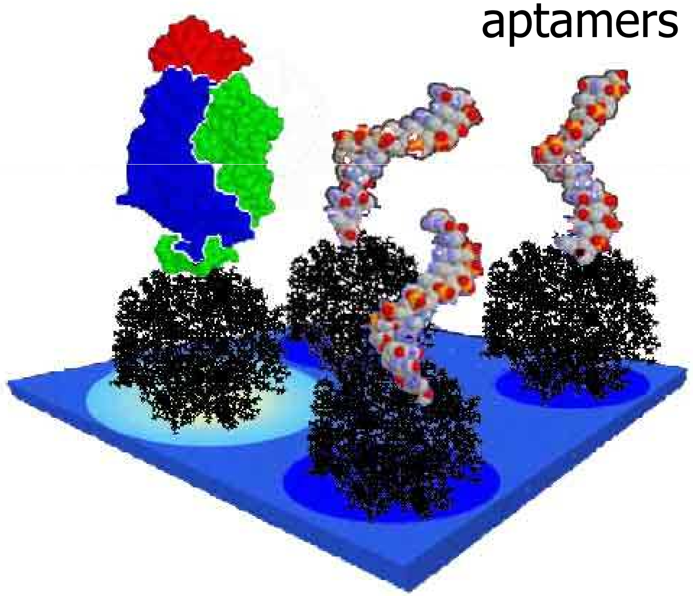
Optimized prototype



Biochip & ionising radiation

Whole antibodies or fragments

Oligonucleotides (DNA, RNA) aptamers



➡ **Resistance to space constraints ?**

- Antibodies and aptamers 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 (in liquid)

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

Challenge

- Radiation : key factor to study the biochip resistance to space environment

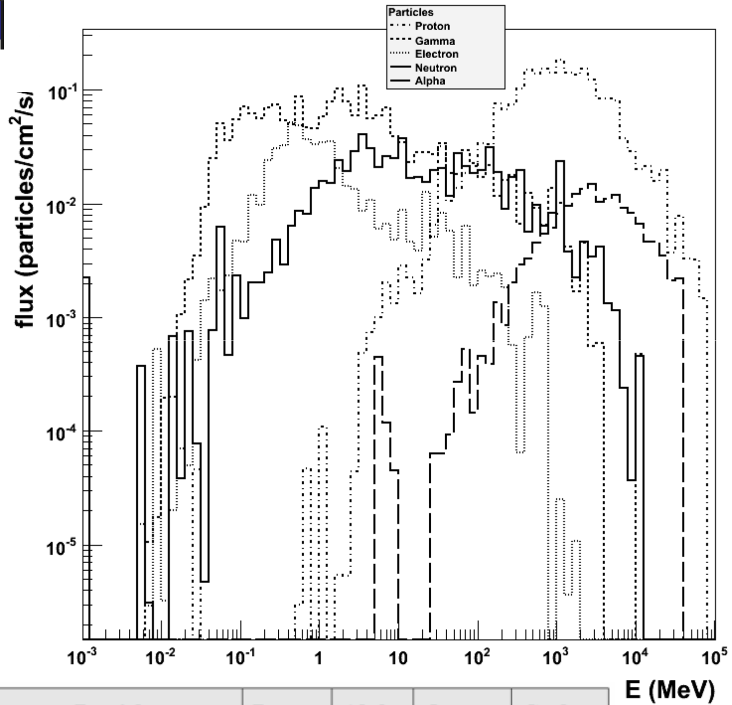
- Ligands (antibodies and aptamers in our case) behavior under cosmic particles fluxes must be studied
  - There is a lack of data

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

GRAS & Planetocosmics

Transit towards Mars (6 mo)

GCR Maximum + 1 max solar event

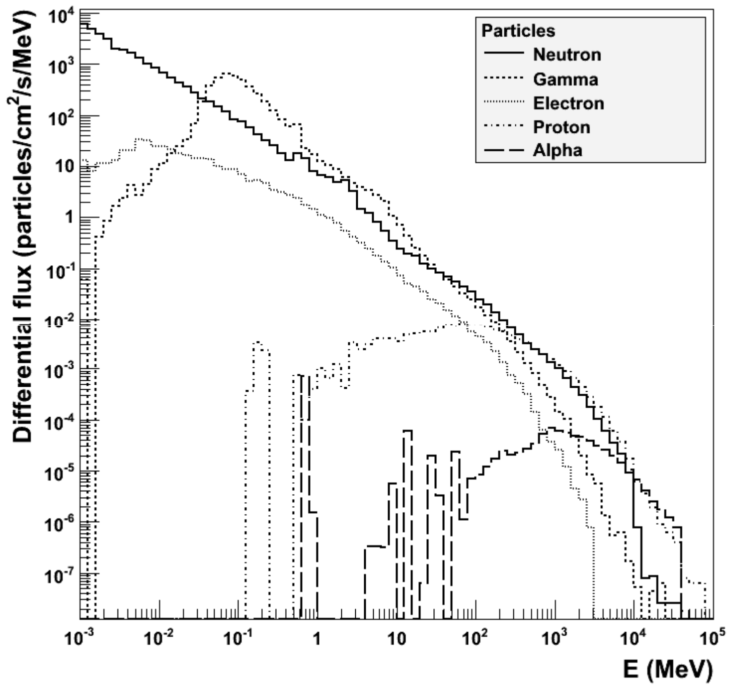


Particles	Proton	Alpha	Oxygen	Carbon
Dose (mGy)	25.1	11.2	4.3	2.2
Statistical error (mGy)	1.28	0.37	0.13	0.06

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

Mission on Mars (1 mo)

Interaction des particules cosmiques avec le sol

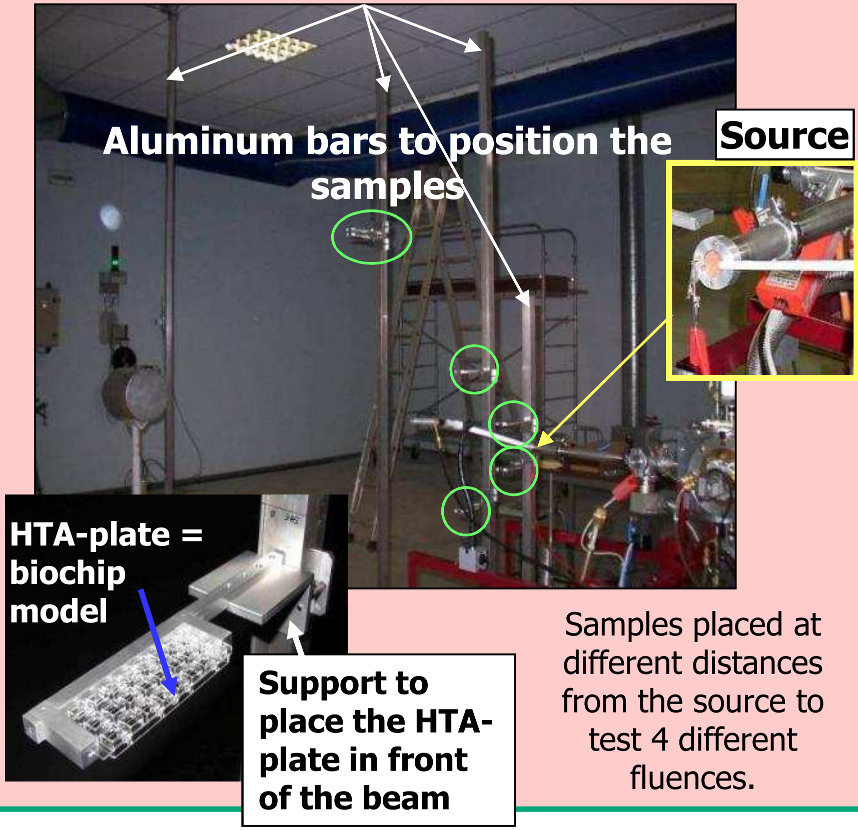


Dose: **27 mGy**
Neutrons dominant
(@ 1.5 m above ground)

Le Postollec et. al. Astrobiology (2009)

Irradiation experiments: neutrons

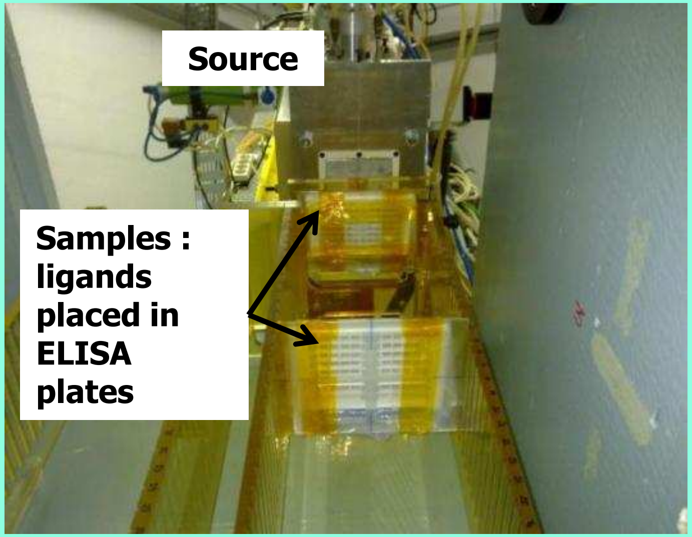
AIFIRA/CENBG/Bordeaux, France



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



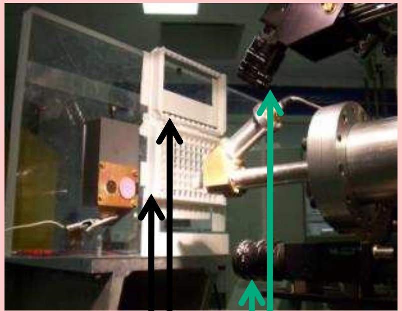
2 samples supports placed at 2 different distances from the source to test 2 different fluences at the same time.

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

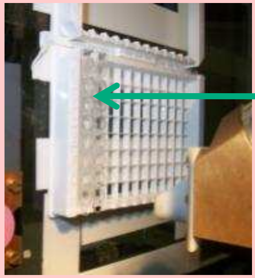


Mobile support

Beam line : protons extracted in air

Cameras

Samples holders



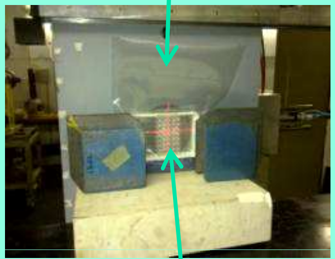
8-wells strips containing the freeze-dried ligands

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.

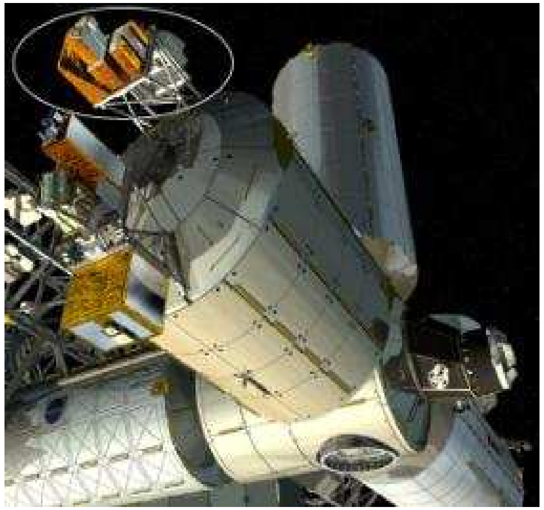
Some degradation of antibodies irradiated by 25MeV protons

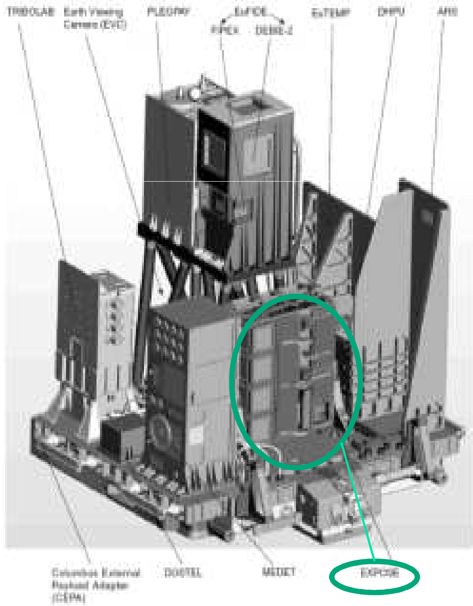
⇒ interpretation still under study.

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

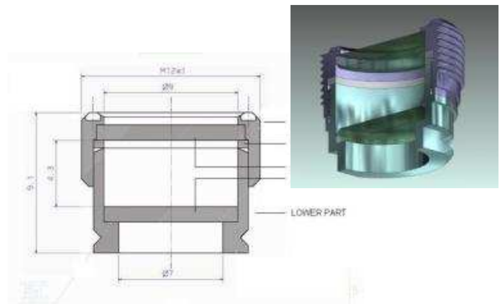
ISS experiment

- 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 a space environment

- 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…

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
    - WRMISS 2010
- Some recent publications
  - The Geant4-DNA project,
    S. Incerti et al., International Journal of Modeling, Simulation, and Scientific Computing 1(2) (2010) 157-178
  - 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