

GEANT4-DNA

Simulation of interactions of radiation with biological systems at the cellular and DNA level

User Requirements Document

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Abstract

This document describes the User Requirements for the Geant4-DNA Project. A general description of the main capabilities and constraints is provided. Specific requirements are listed and classified.

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1. Introduction

Purpose of the document

This document collects the specific User Requirements for the Geant4-DNA Project, an object-oriented toolkit for the simulation of interactions of radiation with biological systems at the cellular and DNA level, to be integrated into the Geant4 Toolkit.

Scope of the software

The main aim of Geant4-DNA is to produce a toolkit, which allows a user to construct a simulation program for the interactions of radiation at the cellular and DNA level. The emphasis of the project is on application to studies in the space environment; applications in the medical environment are envisaged too.

The development of the baseline product is subject to the continuation of the project, following the initial phase of capture of user requirements.

Definitions, acronyms and abbreviations

DEFINITIONS

Parameterisation: a simulation that replaces the detailed particle tracking, physics and response of the detector for some particles inside some volume.

Phase 1: the phase of development of a baseline product.

Phase 2: the phase of development of a second-generation product, expanding the capabilities at the microscopic level.

Phase 3: the phase of development of a third-generation product, expanding the capabilities at the DNA level.

ACRONYMS

ESA: European Space Agency

GEANT: a toolkit for constructing a particle detector simulator (GEometry ANd Tracking)

Geant4: the current version of GEANT based on object-oriented technology

HEP: High Energy Physics

OOA, OOD, OOP: Object Oriented Analysis, Object Oriented Design, Object Oriented Programming

HZE: high Z and energy

ABBREVIATIONS

T. b. d.: The expression ‘T. b. d.’, which stands for ‘To be defined’, used to qualify the requirement stability attribute, indicates that the requirement is dependent on feedback from other phases of the software development and may be subject to change.

References

- i. <http://wwwinfo.cern.ch/asd/geant4/geant4.html>
- ii. <http://www.ge.infn.it/geant4/lowE/index.html>
- iii. <http://www.ge.infn.it/geant4/dna/index.html>
- iv. <http://wwwinfo.cern.ch/asd/lhc++/AIDA/index.html>

Overview of the document

The first chapter of this document provides introductory material, definitions and references. The second chapter provides a general overview of the software. The third chapter includes the lists of user requirements.

2. General matters

Product perspective

We envisage an object-oriented toolkit, which allows a user to construct a framework for the simulation of interactions of radiation with biological systems, which will then be tailored to a particular set-up. The resulting computer program will then be used to simulate the interactions of particles in the chosen set-up. Thanks to its object-oriented design, ensuring openness to extension and flexibility for a variety of applications, the Geant4 Toolkit can play such role, if complemented by a set of additional components specific to the simulation of biological systems.

The Geant4-DNA Project will provide additional components to the Geant4 Toolkit to deal with the simulation of radiation interactions with biological systems. The emphasis of the project is on developments relevant to studies in the space environment.

General capabilities

The framework produced from the Geant4 toolkit offers the ability to build a geometrical model and to define sensitive elements, for which particular information (*hits*) is recorded and ultimately gathered (*digitisation*). The simulated response is thus achieved by using the *hits* as input to the (user supplied) digitisation codes. Events may arise from a variety of sources, both internal and external.

The Geant4-DNA Project will contribute to this framework by providing components to handle geometry, material, particle, process and other simulation features specific to biological systems. Thanks to the complementary contribution from the Geant4-DNA Project, the resulting Geant4 Toolkit will provide to the user the capabilities listed below.

- The user shall be able to define the materials relevant for biological systems.
- The user shall be able to define physical, chemical and biochemical processes.
- The user shall be able to define the geometry of biological systems.
- The user shall be able to define the particles relevant for biological applications and their properties and to associate particles and processes.
- The user shall be able to define the events.
- The user shall be able to define the sensitivity of each geometrical element and what data is to be recorded.
- The user shall be able to start, stop, pause and abort the simulation.
- The user shall be able to specify the action at each step of the tracking.
- The user shall be informed of the results of the actions at each step of the processing.

Much of the above is a result of the toolkit approach, which allows the user to assemble the framework at compile time from chosen components, many of which can be user-supplied.

General Constraints

The components of the Geant4-DNA Project will be designed according to advanced object-oriented technologies. The user will be able to easily extend or modify their services in a suitable way for his/her specific applications.

The design and implementation of the Geant4-DNA Project should be done with the maximum use of the experience acquired from the Geant4 Toolkit, in particular from the existing space-oriented and bio-medical activities in Geant4 Working Groups.

A spiral cyclic software process, based on the Booch methodology, should be applied.

The analysis associated to the simulation should be based on new generation Object Oriented Analysis Tools systems.

User characteristics

The Geant4-DNA Project should address the three different types of typical users of the Geant4 Toolkit: the framework provider, the simulation application programmer and the end user.

The framework provider creates a simulation framework by using components in the Geant4 Toolkit and interfacing them to external packages. He/she knows the techniques of

OOAD and OOP and actively sets the software requirements, including components and interfaces.

The simulation application programmer creates a simulation program, which is specific to his/her set-up, based on the framework provided by a framework provider. He/she does not need to know the complete structure of the simulator, but may write or modify user codes.

The simulator end user runs the simulation program by controlling run time parameters such as the selection of processes and the setting of tracking conditions with the standard interface.

Operational environment

The software will be for use in a Unix environment with an ISO compliant C++ compiler, subject to the same choice of supported platforms as the Geant4 Toolkit, or to a subset of them. It will require the installation of various HEP software packages for simulation and analysis and other related utilities, all either freely distributed or available to Geant4 member institutes at reasonable terms.

Co-operation with external packages of interest for biological or space applications should occur through well-defined interfaces.

The main environment for the software documentation is meant to be the World Wide Web.

Assumptions and dependencies

This document relies on the assumption that the Geant4-DNA Project will be approved and adequately funded for the analysis, design and implementation phases.

The analysis, design and development of software for chemical and biochemical processes, as well as for geometrical components of biological systems, is subject to the availability of experts in the related fields to collaborate with software designers and developers at least at the level of consultants.

The User Requirements listed in the Geant4 URD, Version ??, corresponding to the first production version Geant4.0 (December 1998) are meant to be valid for the Geant4-DNA Project as well; they are not repeated in this document.

3. Specific Requirements

Capability Requirements

1 Physics and biological processes

- 1.1 The user shall be able to generate electromagnetic physics processes concerning interactions of electrons, photons, hadrons and ions in water.

Need: Essential

Priority: Phase 1

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

NOTE: The energy range to be considered is defined in UR I.a.

- 1.2 The user shall be able to generate electromagnetic physics processes concerning interactions of electrons, photons, hadrons and ions in tissue-equivalent gas.

Need: Essential

Priority: Phase 1

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

NOTE: this is useful for comparison with experimental data.

NOTE: The energy range to be considered is defined in UR I.a.

- 1.3 The user shall be able to generate electromagnetic physics processes concerning interactions of electrons, photons, hadrons and ions in biological tissue.

Need: Essential

Priority: Phase 1

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

NOTE: The energy range to be considered is defined in UR I.a.

- 1.4 The user shall be able to generate electromagnetic physics processes concerning interactions of electrons, photons, hadrons and ions with molecules.

Need: Essential

Priority: Phase 2

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

NOTE: The energy range to be considered is defined in UR I.a.

- 1.5 The user should be able to generate hadronic physics processes of HZE particles in water.

Need: Essential

Priority: Phase 2

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

NOTE: The energy range to be considered is defined in UR I.a.

- 1.6 The user should be able to generate hadronic physics processes of HZE particles in tissue-equivalent gas.

Need: Essential

Priority: Phase 2

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

NOTE: The energy range to be considered is defined in UR I.a.

- 1.7 The user should be able to generate hadronic physics processes of HZE particles in biological tissue.

Need: Essential

Priority: Phase 2

Stability: T. b. d.

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

NOTE: The energy range to be considered is defined in UR I.a.

1.8 The user shall be able to activate detailed chemical processes.

Need: Essential
Priority: Phase 2
Stability: T. b. d.
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

1.9 The user shall be able to activate parameterisation at the place of detailed chemical processes (corresponding to UR 1.8).

Need: Essential
Priority: Phase 1
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

1.10 The user shall be able to activate detailed biochemical processes.

Need: Essential
Priority: Phase 3
Stability: T. b. d.
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

1.11 The user shall be able to activate parameterisation at the place of detailed biochemical processes (corresponding to UR 1.10).

Need: Essential
Priority: Phase 1
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

1.12 The user should be able to verify effects of microgravity.

Need: The usefulness is subject to investigation.
Priority: Phase 3
Stability: T. b. d.
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

2 Geometry and materials

2.1 The user shall be able to describe the geometry and material composition of shielding components.

Need: Essential

Priority: Phase 1

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

NOTE: *Shielding* means any object in between the primary radiation source and the biological sample.

2.2 The user shall be able to describe an anthropomorphic phantom.

Need: Essential

Priority: Phase 2

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

2.3 The user shall be able to describe an organ at risk within an anthropomorphic phantom.

Need: Essential

Priority: Phase 2

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

2.4 The user shall be able to describe a biological tissue.

Need: Essential

Priority: Phase 1

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

2.5 The user shall be able to describe a cell.

Need: Essential
Priority: Phase 1
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

2.6 The user shall be able to describe the nucleus of a cell.

Need: Essential
Priority: Phase 1
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

2.7 The user shall be able to describe the DNA.

Need: Subject to investigation
Priority: Phase 3
Stability: T. b. d.
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

2.8 The user shall be able to describe a population of cells at any stage of their life cycle.

Need: Essential
Priority: Phase 2
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

2.9 The user shall be able to describe a typical experimental set-up for irradiation of biological samples.

Need: Essential
Priority: Phase 1
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

2.10 The user shall be able to deal with time-dependent geometries.

Need: Essential
Priority: Phase 2
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

3 General simulation

3.1 The user shall have access to a primary generator describing the space radiation environment.

Need: Essential
Priority: Phase 1
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

NOTE: This may be available either through an interface to an external generator or through a Toolkit component.

3.2 The user shall have access to the 3D information of tracks.

Need: Useful
Priority: Phase 1
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

3.3 The user shall have access to the 3D space and time information of the occurrence of processes.

Need: Useful
Priority: Phase 1
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

3.4 The user shall have access to the 3D information of deposited energy.

Need: Essential
Priority: Phase 1
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

3.5 The user shall be able to track molecules.

Need: Essential
Priority: Phase 2
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

3.6 The user shall be able to select the tracking of particles as subject to physical, chemical and biochemical processes.

Need: Essential
Priority: Phase 2-3
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

4 Particles

4.1 The user shall be able to define a molecule by its physical and chemical properties.

Need: Essential
Priority: Phase 2
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

- 4.2 The user shall be able to define the association between a molecule and processes.

Need: Essential
Priority: Phase 2
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

5 Visualisation

- 5.1 The user shall be able to visualise the geometry set-up in its entirety or in subsections or by individual components, down to the molecular level.

Need: Essential
Priority: Phase 1-2-3
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

- 5.2 The user shall be able to display the parameters of geometrical entities down to the molecular level.

Need: Essential
Priority: Phase 1-2-3
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

- 5.3 The user shall be able to visualise particle trajectories at each step of the particle tracking, including the case when particles are molecules.

Need: Essential
Priority: Phase 1-2-3
Stability: Stable
Source: Geant4-DNA Collaboration
Clarity: Clear
Verifiability: To be verified

5.4 The user shall be able to visualise detailed features of physical processes.

Need: Useful

Priority: Phase 2

Stability: T. b. d.

Source: Geant4-DNA Collaboration

Clarity: The features to be visualised should be specified

Verifiability: To be verified

5.5 The user shall be able to visualise detailed features of chemical processes.

Need: Useful

Priority: Phase 2-3

Stability: T. b. d.

Source: Geant4-DNA Collaboration

Clarity: The features to be visualised should be specified

Verifiability: To be verified

5.6 The user shall be able to visualise detailed features of biochemical processes.

Need: Useful

Priority: Phase 3

Stability: T. b. d.

Source: Geant4-DNA Collaboration

Clarity: The features to be visualised should be specified

Verifiability: To be verified

6 Data Analysis

6.1 The user shall be able to produce histograms of relevant quantities.

Need: Essential

Priority: Phase 1

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

- 6.2 The user should be able to interface external auxiliary tools or user code to evaluate macroscopic effects resulting from the simulation at the microscopic level.

Need: Essential

Priority: Phase 1

Stability: T. b. d.

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

NOTE: Macroscopic evaluations may be:

- recognition of chromosome aberrations
- measurement of DNA fragment size
- production of cell survival curve
- calculation of cell inactivation cross-section
- estimate of RBE
- calculation of cancer risk

Constraint requirements

I. Physics and biological processes

- a. The physics processes involve primary particles typical of the space radiation environment (as specified in 3.1) and related secondaries.

Need: Essential

Priority: Phase 1

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

NOTE: The energy range of primary particles to be considered is:

- $\sim 300 \text{ eV} < E < 20 \text{ MeV}$ for photons
- $\sim 10 \text{ keV} < E < 20 \text{ MeV}$ for electrons
- $\sim 100 \text{ keV} < E < 100 \text{ GeV}$ for protons
- $\sim 1 \text{ MeV/nuc} < E < 100 \text{ GeV/nuc}$ for ions

- b. The physics processes involve primary particles typical of radiotherapy applications and related secondaries.

Need: Useful

Priority: Phase 1

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

NOTE: The energy range of primary particles to be considered is:

- $\sim 10 \text{ keV} < E < 20 \text{ MeV}$ for electrons and photons
- $\sim 10 \text{ MeV} < E < 250 \text{ MeV}$ for protons
- $\sim 5 \text{ GeV} < E < 10 \text{ GeV}$ for ions

c. The electromagnetic physics processes shall be valid at the μm scale for applications at the cellular level.

Need: Essential for applications at the cellular level

Priority: Phase 1

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

d. The electromagnetic physics processes shall be valid at the nm scale for applications at the DNA level.

Need: Essential for applications at the DNA level

Priority: Phase 2

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

e. Secondaries from electromagnetic physics processes shall be generated and tracked down to the μm scale for applications at the cellular level.

Need: Essential for applications at the cellular level

Priority: Phase 1

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

f. Secondaries from electromagnetic physics processes shall be generated and tracked down to the nm scale for applications at the DNA level.

Need: Essential for applications at the DNA level

Priority: Phase 2

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

g. The chemical processes should include:

- generation of free radicals
- diffusion of free radicals
- reactions of free radicals with relevant molecules
- breaking of bonds
- oxidative processes
- repair of oxidative damage through natural and artificial scavengers
- effects of hypoxia

NOTE: they may be implemented either as detailed processes or as parameterisations.

Need: Essential

Priority: Phase 1

Stability: T. b. d.

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

h. The biochemical processes should include:

- mechanism of induction of single and double strand break in DNA
- DNA corruption
- biochemical checkpoints through cell-cycle
- identification of the occurrence of damage
- DNA repair mechanisms
- effects of genomic instability

NOTE: they may be implemented either as detailed processes or as parameterisations.

Need: Essential

Priority: Phase 1

Stability: T. b. d.

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

i. It should be possible to handle time-dependent processes.

Need: Useful

Priority: Phase 2

Stability: T. b. d.

Source: Geant4-DNA Collaboration

Clarity: To be verified

Verifiability: To be verified

II. Geometry and materials

a. Organs at risk should include:

- eyes
- reproductive organs
- central nervous system
- intestines

Need: Essential

Priority: Phase 2

Stability: T. b. d.

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

III. Other tools and interfaces

a. The Geant4-DNA Project shall be based on the Geant4 simulation framework.

Need: Essential

Priority: Phase 1

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

b. Access to external auxiliary tools should be provided through common interfaces, without any dependency on such tools.

Need: Useful

Priority: Phase 1

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

c. The user shall be able to easily plug in his/her own physics, chemical and biochemical interaction procedures via the use of object oriented technology.

Need: Essential

Priority: Phase 1

Stability: T. b. d.

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

d. A common interface should be defined for a variety of space radiation environment generators.

Need: Essential

Priority: Phase 1

Stability: T. b. d.

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

IV. Transparency

a. The user shall be able to determine easily and, when necessary, modify the data and assumptions used in the simulation of the physics, chemical and biochemical processes.

Need: Essential

Priority: Phase 1

Stability: T. b. d.

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

V. Platforms

a. The software should run on a PC under Linux OS.

Need: Essential

Priority: Phase 1

Stability: T. b. d.

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

b. Visualisation and histogram outputs should be visible from Unix and Windows platforms.

Need: Essential

Priority: Phase 1

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

VI. Version release

a. The Geant4-DNA software shall be released as part of the Geant4 Toolkit.

Need: Useful

Priority: Phase 1

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified

VII. Production of documents

a. The Geant4-DNA documentation, including design documents, algorithm descriptions, physics and biological reference guides and user guide, shall be made available together with the software release.

Need: Useful

Priority: Phase 1

Stability: Stable

Source: Geant4-DNA Collaboration

Clarity: Clear

Verifiability: To be verified