Groupement de recherche

MI2B Outils et méthodes nucléaires pour la lutte contre le cancer

Thème transverse Calcul

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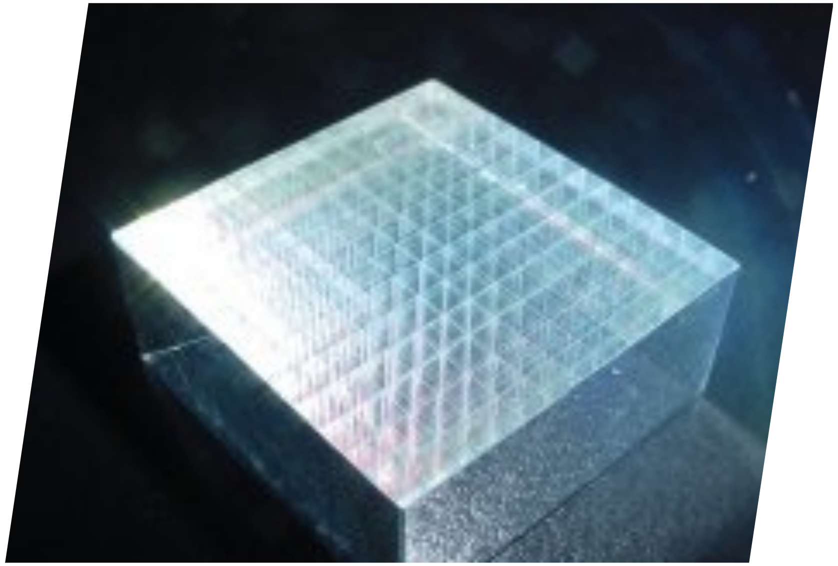
Recent developments

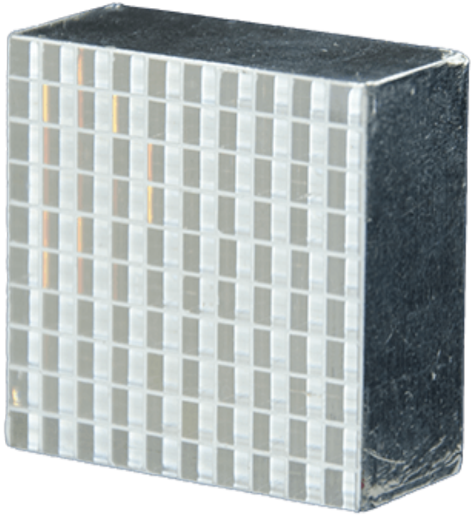
- **1°) Detector developments**
- 2°) Clinical imaging systems
- 3°) Data analysis and Python
- 4°) Complex geometry
- **5°) AI integration**
- 6°) Multiscale simulations
- 7°) Events

GATE
opengatecollaboration.org

CPPM Marseille
LPSC Grenoble
IP2I Lyon
LPC Clermont
IJCLab, Orsay
IPHC Strasbourg
CREATIS Lyon
LATIM Brest
IRCM Montpellier

UC Davis
NIRS Japon



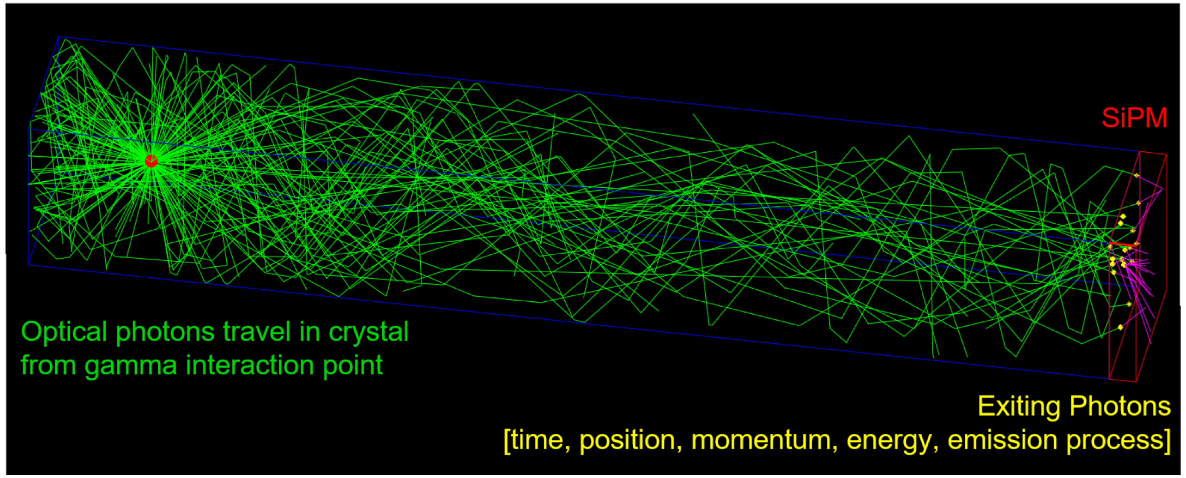


1°) Detector developments

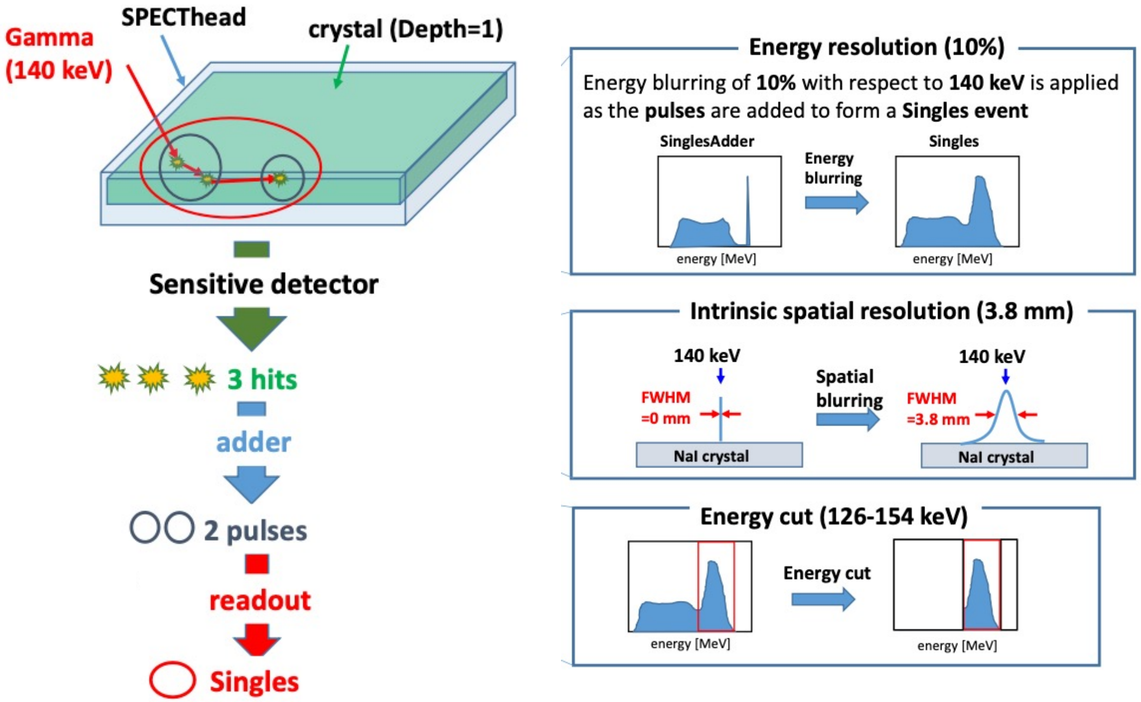
1°) Detector developments

○ 2 simulation modes

Full Monte Carlo tracking of emitted optical photons

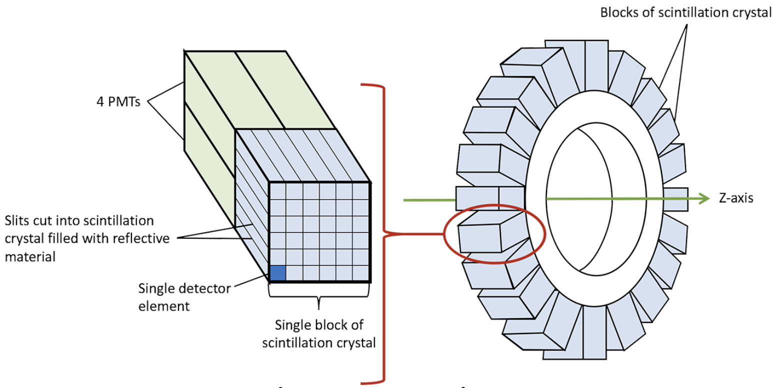


Response of the photodection components simulated by a specific module

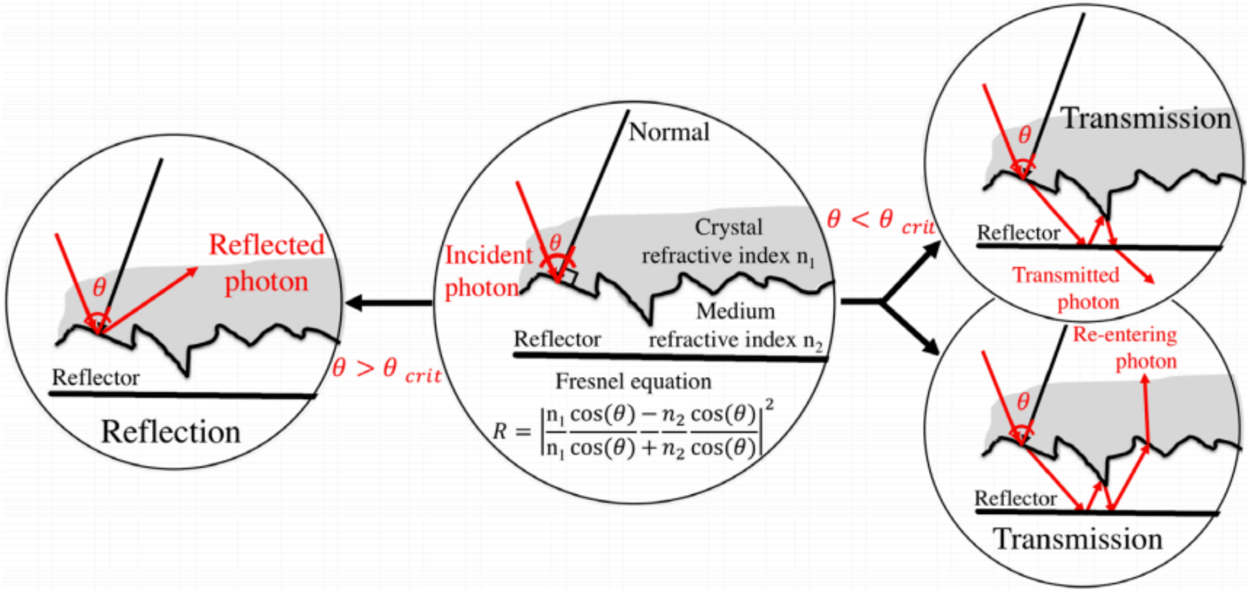


1°) Detector developments
Optical photon tracking and SiPM

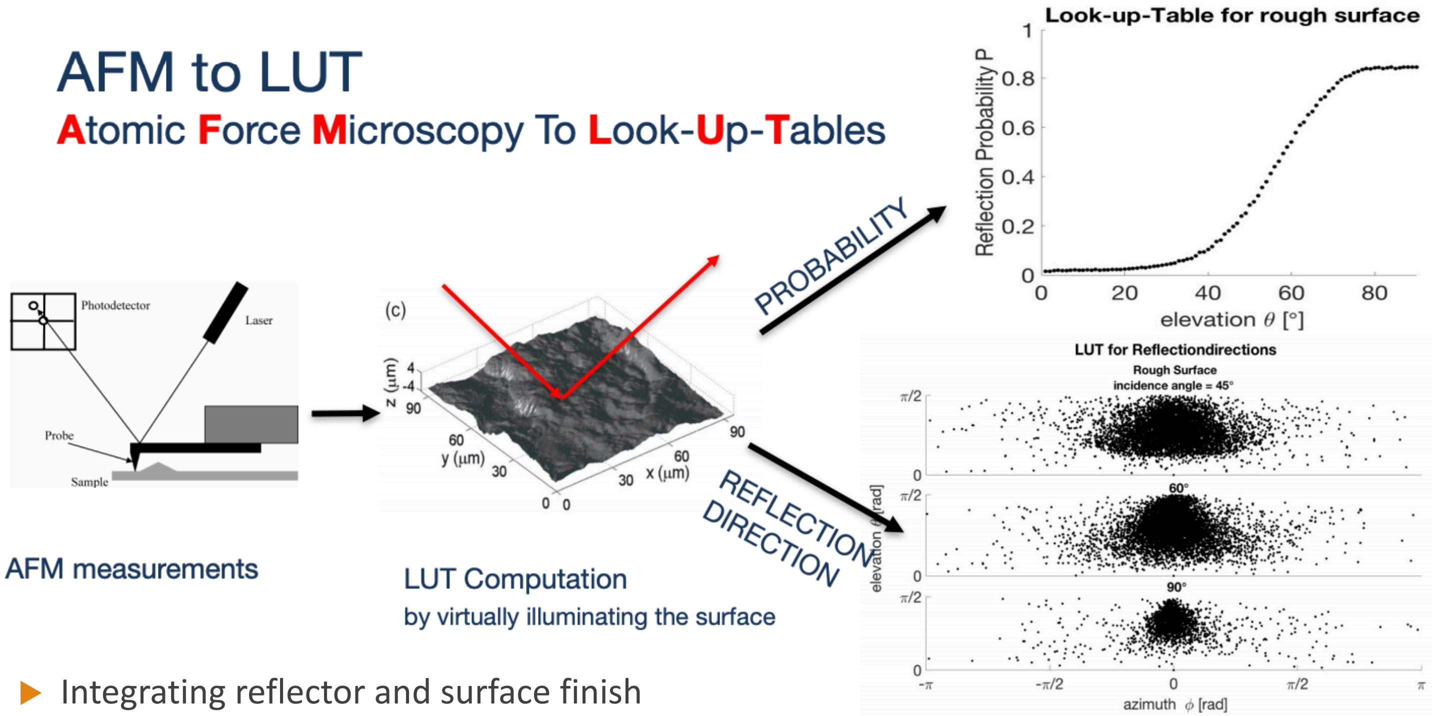
- Photons many times reflected on the surface of scintillation crystal
- Process affected by specific surface treatment and reflector materials
- Manufacturing of scintillation crystals is not a standardized process
- Optical simulations based on measured crystal surfaces

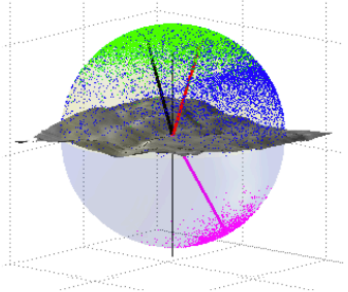


LSO and LYSO crystal layers with reflectors

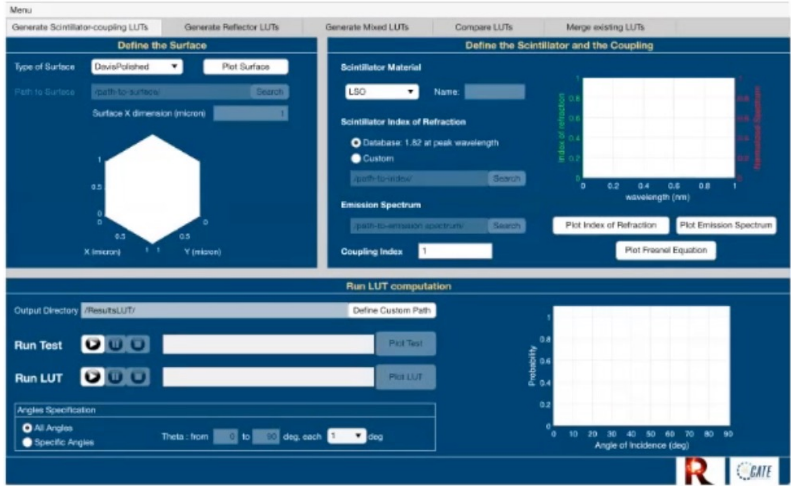


1°) Detector developments
Optical photon tracking and SiPM





Standalone user interface

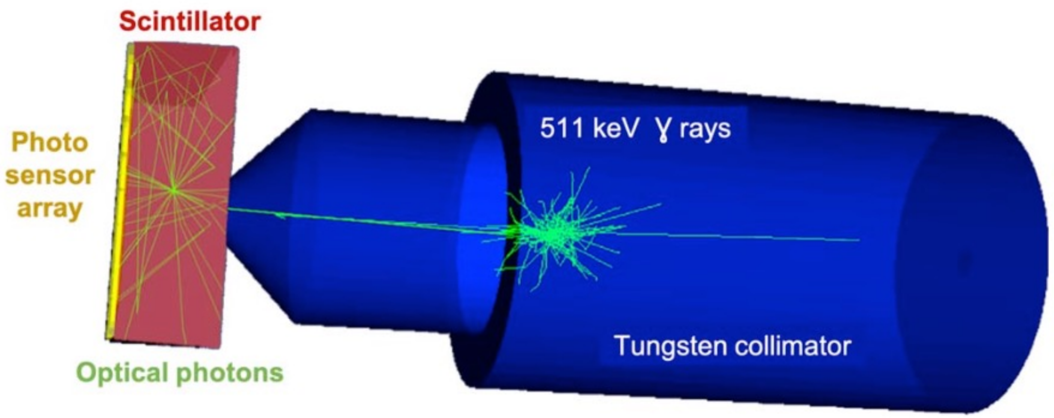


- Integrating reflector and surface finish
  - Reflectors: ESR, Teflon
  - Coupling: Air, optical grease
  - Surface finish: Polished, Rough

Trigila C, Moghe E and Roncali E 2021 Standalone application to generate custom reflectance Look-Up Table for advanced optical Monte Carlo simulation in GATE/Geant4 Med Phys.

1°) Detector developments
Optical photon tracking and SiPM

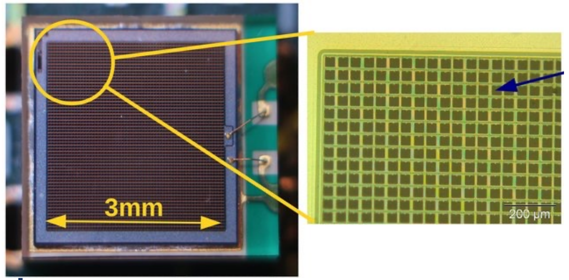
- Large monolithic scintillation detector for clinical PET systems



- gain insight into
  - physical processes difficult or impossible to measure experimentally, especially DoI.
  - influence of Compton scattered events,
  - influence of intrinsic ^{176}Lu radiation of the scintillator,
  - influence of test-equipment, e.g. collimators or housing.

1°) Detector developments
Optical photon tracking and SiPM

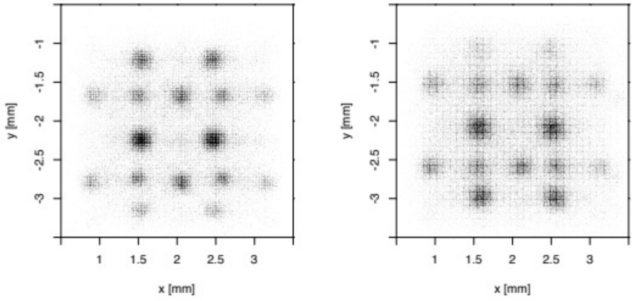
GDR Groupement de recherche
MI2B Outils et méthodes nucléaires pour la lutte contre le cancer



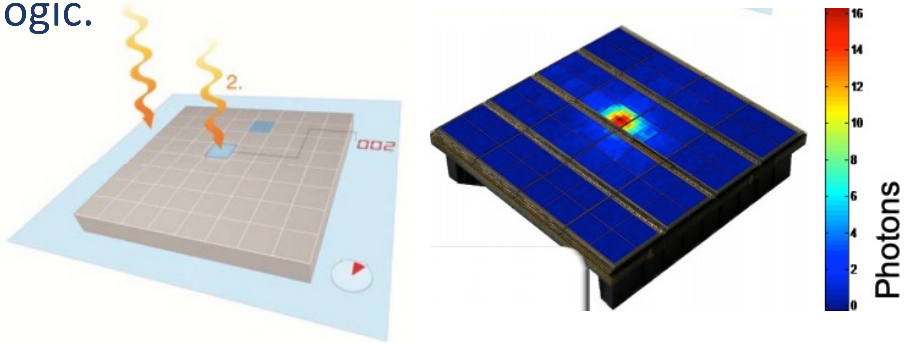
- Increasing use of SiPM in PET imaging
  - Specific digitizer modules for analog (aSiPM) and digital SiPMs (dSiPM)
    - aSiPM: takes into account aSiPM saturation and various sources of noise such as dark counts, crosstalks, afterpulses, after-crosstalks and signal white noise

Mehadji B 2020 Modélisation Monte Carlo d'une caméra Compton basée sur l'utilisation de détecteurs à scintillation sensibles à la position couplés à des SiPM PhD Thesis Aix-Marseille Université J. Instrum.

    - dSiPM: (Philips Digital Photon Counter)
      - takes into account noise sources (dark noise and optical crosstalk), the PDE of the sensor, and the specific trigger and validation logic.



(a) simulated flood histogram (b) measured flood histogram

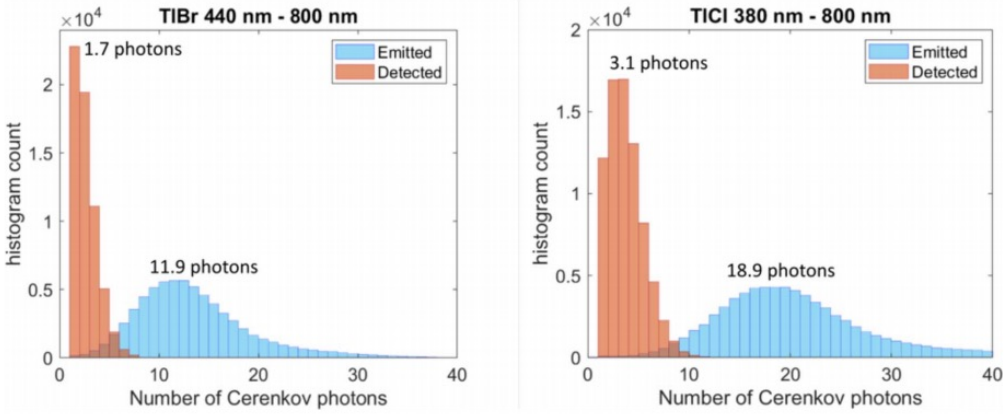


Lenz M 2020 Design and characterisation of an MRI compatible human brain PET insert by means of simulation and experimental studies
PhD Thesis Bergische Universität Wuppertal

1°) Detector developments
Cerenkov-based TOF

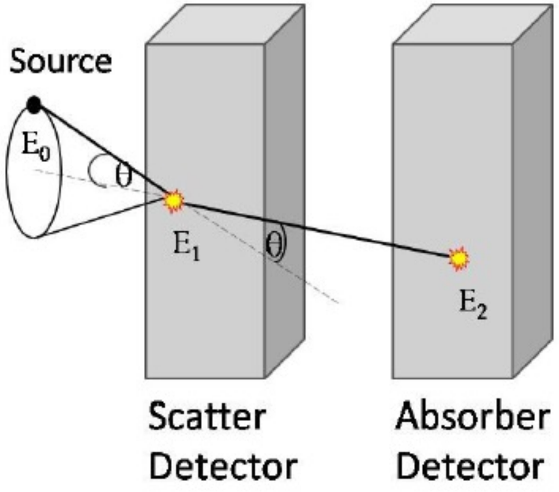
- use of ultra-fast (10 ps) Cerenkov emission for TOF PET detectors = alternative to traditional time triggering on scintillation photons
- very low number of Cerenkov photons produced by each gamma interaction in the Cerenkov radiator (around 15–20 per photoelectric interaction for BGO)
- Cerenkov production and transport in the crystal
  - direction of the initial Cerenkov photons,
  - contribution of Cerenkov photons to the detector timing resolution.

Ariño-Estrada G, Roncali E, Selfridge A R, Du J, Glodo J, Shah K S and Cherry S R 2020 Study of Čerenkov light emission in the semiconductors TlBr and TlCl for TOF-PET IEEE Trans. Rad. Plasma Med. Sci. 1



For 75000 photoelectric events

1°) Detector developments
Compton camera modules



$$\cos(\theta) = 1 - \frac{E_1 m_e c^2}{E_0(E_0 - E_1)}$$

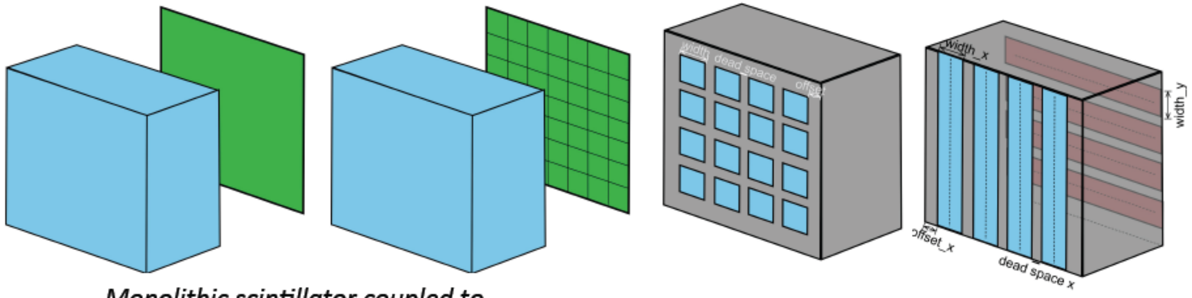
- Principle
  - Classic gamma camera:
    - inverse proportionality relationship between sensitivity and spatial resolution
    - Collimator thickness to be adjusted to the gamma energy
  - Compton Camera
    - Electronic collimation: at least 2 detectors
      - Compton scattering in the 1st detector (scatterer)
      - Photoelectric absorption in the 2nd detector (absorber)
    - Calculation of the scattering angle of the Compton interaction
      - Reconstruction of a cone with the source position located on cone surface
      - Intersection of the cones calculated for different gammas emitted from the source lead to the definition of the source position
- Challenges
  - Higher efficiency: every gamma photon reaching the camera has a probability to be scattered
  - Image resolution depends only on detectors involved
  - Wider range of gamma energies
  - Reconstruction through cone:=> 3D activity map obtained without moving the camera

1°) Detector developments
Compton camera modules

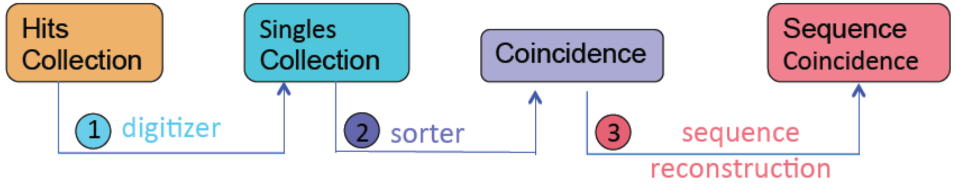
MC framework adapted to different detector geometry

- Design, optimize and predict the potentiality of the system
- Understand experimental data
- Study background rejection techniques
- Test reconstruction algorithms

CCMod: a GATE module for Compton camera imaging simulation - https://doi.org/10.1088/1361-6560/ab6529



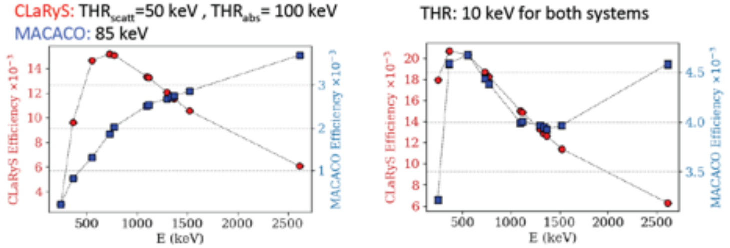
Monolithic scintillator coupled to position sensitive/insensitive detector   *Pixelated crystals*   *Strip detectors*



1. A chain of digitizer modules applied to the different detector layers to model the detector response or to recover ideal Compton kinematics
2. Time coincidence between the pulses in the different layers
3. Sequence reconstruction: order singles within a coincidence

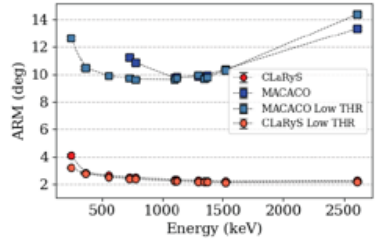
Output data available at each step
Processing steps (1,2,3) may be performed on-the-fly or offline
Same data structure as for PET/SPECT sys to be able to share developed processors

Detection efficiency normalized to the scatterer geometrical efficiency



Only 2-single-coincidences are considered

Angular Resolution measure



Energy Resolution in the scatterer
MACACO: 8.5% @ 511 keV
CLaRyS: 1.56% @ 511 keV

X-Y spatial resolution
MACACO: 2 mm sigma
CLaRyS: 0.4 mm sigma
(assuming normal distribution in the 1.4 mm strip)

2°) Clinical imaging systems

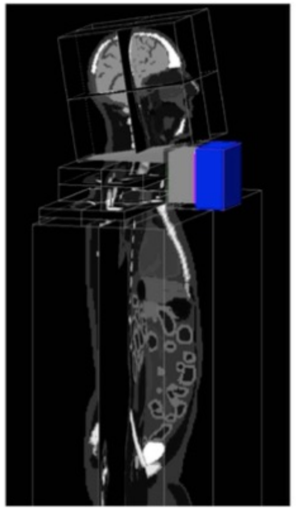
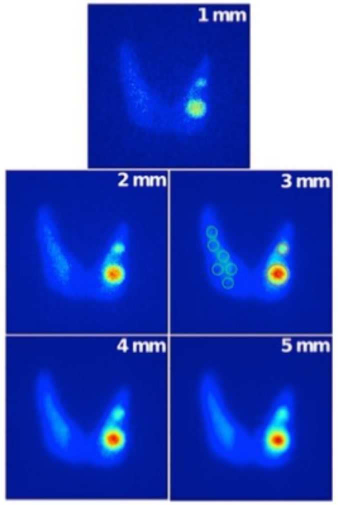
Simulated cameras for 10 years

Preclinical and clinical PET systems

2011 McIntosh *et al* (2011)	PC	Inveon, LSO, by Siemens
2011 Geramifar *et al* (2011)	C	Discovery RX, LYSO, by GE
2012 Poon *et al* (2012)	C	Biograph mCT, LSO, by Siemens
2012 Trindade *et al* (2012)	C	Gemini TF, TruFlight Select, LYSO, by Philips
2013 Lee *et al* (2013)	PC	Inveon trimodal, LSO, by Siemens
2013 Nikolopoulos *et al* (2013)	PC	Biograph DUO, LSO, by Siemens
2013 Zagni *et al* (2013)	PC	Argus, LYSO/GSO, DOI, by Sedecal
2013 Solevi *et al* (2013)	C	prototoype AX-PET, LYSO, SiPM, brain
2015 Moraes *et al* (2015)	C	Biograph mCT, LSO, by Siemens
2015 Poon *et al* (2015)	C	Biograph mCT, LSO, by Siemens
2015 Aklan *et al* (2015)	C	Biograph mMR hybrid, LSO, by Siemens
2015 Monnier *et al* (2015)	C	Biograph mMR hybrid, LSO, by Siemens
2016 Lu *et al* (2016)	PC	Inveon, LSO, by Siemens
2016 Etxebeste *et al* (2016)	PC	prototype, LYSO
2017 Sheikhzadeh *et al* (2017)	C	NeuroPET, LYSO, SiPM, brain, by PDS
2017 Li *et al* (2017)	C	Ray-Scan 64, BGO, by ARRAYS MIC
2018 Del Guerra *et al* (2018)	C	prototype TRIMAGE, LYSO
2018 Kowalski *et al* (2018)	C	prototype J-PET, plastic
2019 Abi Akl *et al* (2019)	C	prototype PET2020, LYSO
2019 Kochebina *et al* (2019)	C	prototype CaLIPSO, TMBi
2020 Emami *et al* (2020)	C	Dual ring MAMMI breast, LYSO, by Oncovision
2020 Salvadori (2020)	C	Vereos, LYSO, SiPM, Philips

Preclinical and clinical SPECT systems

2010 Mok (2010)	PC	XSPECT, multi-pinhole, ^{99m}Tc, by Gamma Medica-Ideas
2011 Robert *et al* (2011)	C	prototype, HiSens, CZT, LEHR/H13, ^{99m}Tc, ^{57}Co
2011 Boisson *et al* (2011)	PC	prototype, parallel slat, YAP:Ce, ^{99m}Tc, ^{57}Co
2015 Lee *et al* (2015b)	PC	Symbia T2, LEAP/LEHR/HE, ^{131}I, ^{99m}Tc, by Siemens
2015 Lee *et al* (2015a)	PC	Inveon, LSO, ^{123}I, ^{125}I, by Siemens
2015 Spirou *et al* (2015)	C	ECAM, NaI(Tl), ^{99m}Tc, by Siemens
2017 Georgiou *et al* (2017)	PC	γ-eye, CsI(Na), ^{99m}Tc, ^{111}In, ^{177}Lu, by Bioemtech
2017 Costa *et al* (2017)	C	Symbia T2, MEAP, ^{177}Lu, by Siemens
2018 Taherparvar and Sadremomtaz (2018)	PC	prototype, CsI(Na), ^{99m}Tc
2019 Sadremomtaz and Telikani (2019)	PC	HiReSPECT, LEHR, CsI(Na), ^{99m}Tc, by PNP

THIDOS compact mobile γ-camera for absorbed radiation dose control in IRT.

Trigila C 2019 Development of a portable gamma imaging system for absorbed radiation dose control in molecular radiotherapy PhD Thesis, Université Paris-Saclay (https://tel.archives-ouvertes.fr/tel-02475983/document)

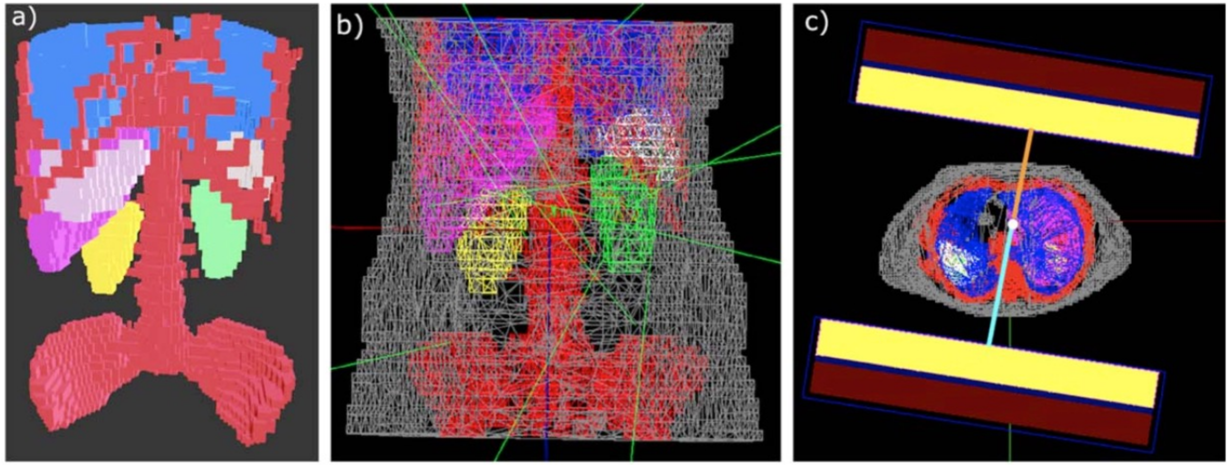
3°) Data analysis and Python

https://github.com/OpenGATE/GateTools

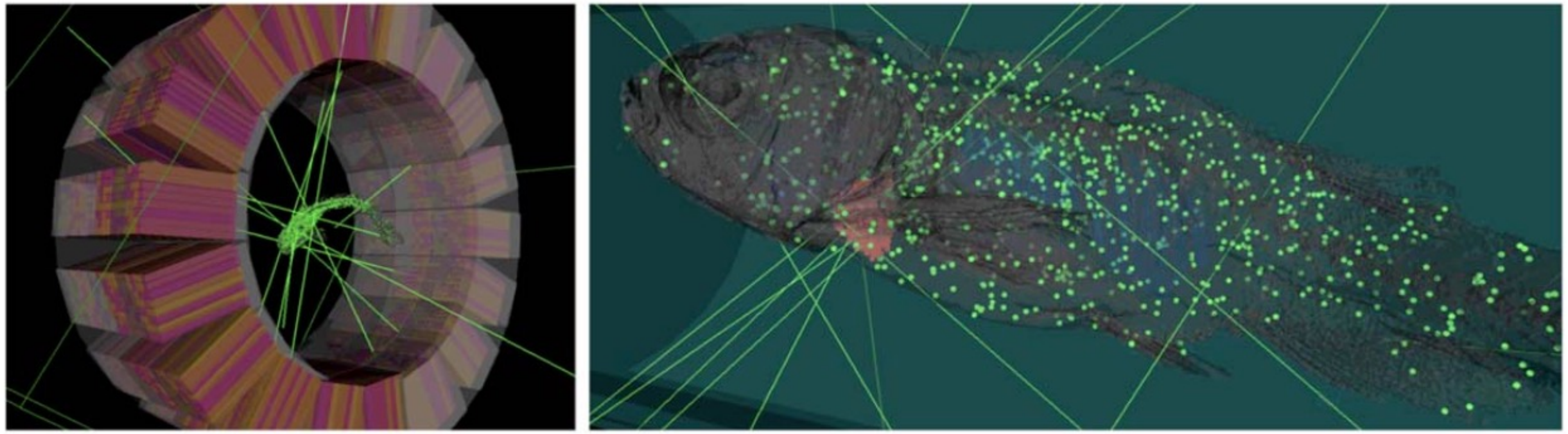
- Python: easy to learn & easy to use
  - NumPy, Matplotlib, uproot…
  - read/write data in NPY file format
- Opensource set of tools
  - convert or resize images in various file formats,
  - convert DICOM RT structures,
  - manage phase-space files
  - analyze dose map, with DVH (Dose Volume Histogram) or gamma-index for example.
- To a long term development
  - Python wrapping : pybind11

4°) Complex geometries

- Tessellated mesh geometries
  - STL files
  - Auto-contouring SPECT gamma cam motion
  - Used for attenuation and emission phantoms



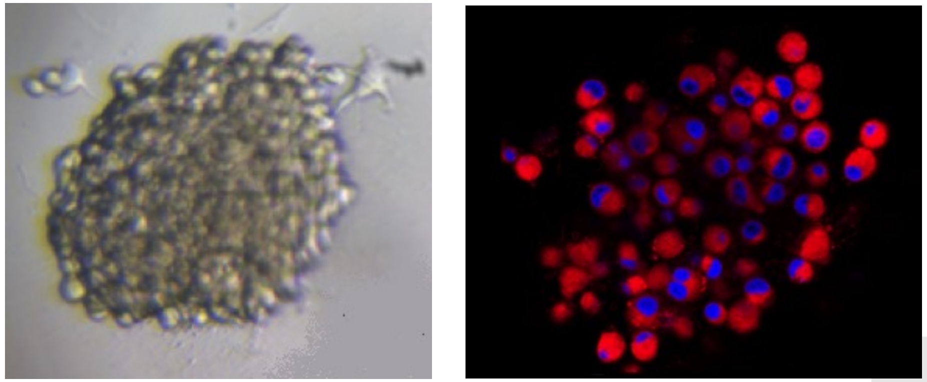
Kayal G, Chauvin M, Mora-Ramirez E, Struelens L and Bardies M 2020b Implementation of SPECT auto-contouring detector motion in GATE Monte Carlo simulation for ^{177}Lu and ^{131}I molecular radiotherapy (MRT) dosimetry Eur J Nucl Med Mol Imaging 47 1–753



Zvolský M, Schreiner N, Seeger S, Schaar M, Rakers S and Rafecas M 2019a Digital zebrafish phantom based on micro-CT data for imaging research IEEE Nuc. Sci. Symp. and Med. Imaging Conf.(NSS/MIC) 2019 1–2

4°) Complex geometries

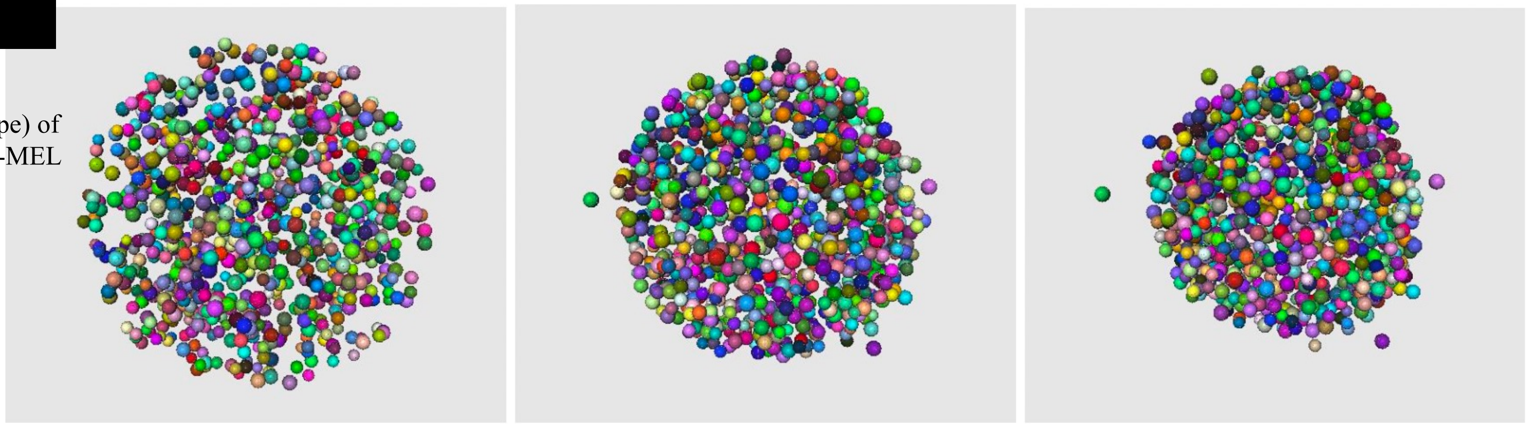
Tessellated mesh cell populations



(a) (b)

Figure 1. (a) Reverse-phased microscopy imaging of a spheroid (SK-MEL 28 type) of 550±40 µm in diameter (b) Fluorescent confocal microscopy of a spheroid (SK-MEL 28 type)

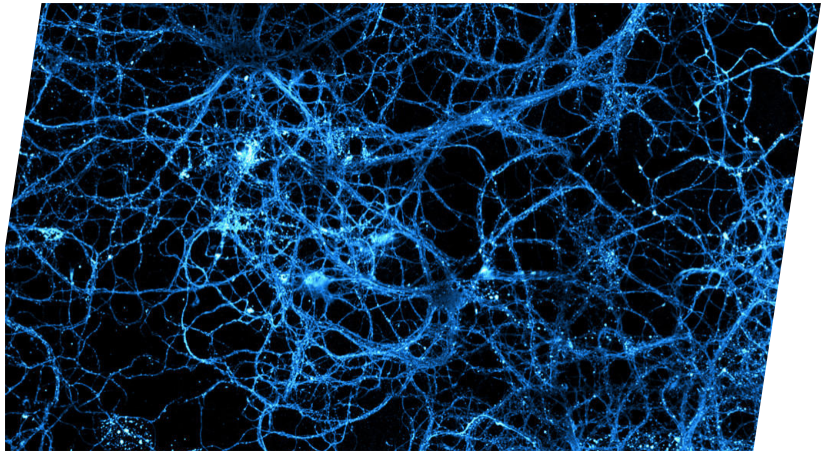
- model large three-dimensional cell populations
- independent deformable cells described with their nucleus, cytoplasm and membranes
- force law systems to manage cell-cell interactions.



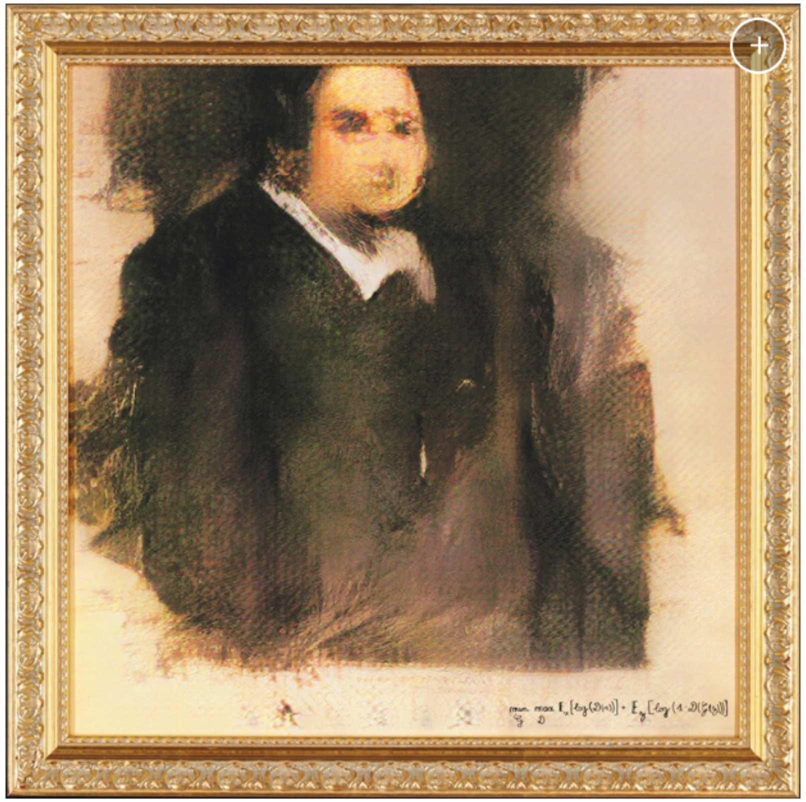
(a) (b) (c)

Figure 9. Spheroids corresponding to SK-MEL28 cell populations. (a) 962 cells generated without forces (defined as 3DCellPopulation.xml in the following studies), (b) 989 cells generated with a force rigidity=0.0007, (c) 989 cells generated with a force rigidity=0.002.

CPOP: An open source C++ cell POPulation modeler for radiation biology applications, L. Maigne, A. Delsol, G. Fois, E. Debiton, F. Degoul, H. Payno, August 02, 2021, DOI:https://doi.org/10.1016/j.ejmp.2021.07.016



Artificial Neural Networks (ANN)

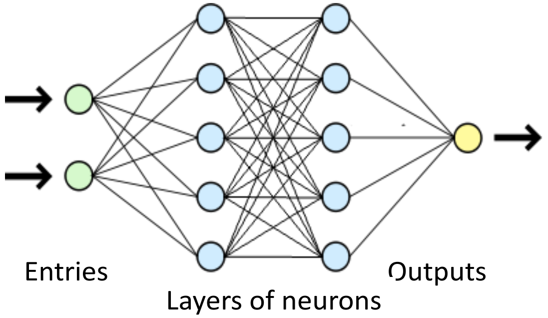


Portrait of Edmond Belamy, 2018, created by GAN (Generative Adversarial Network). Sold for $432,500 on 25 October at Christie's in New York. Image © Obvious

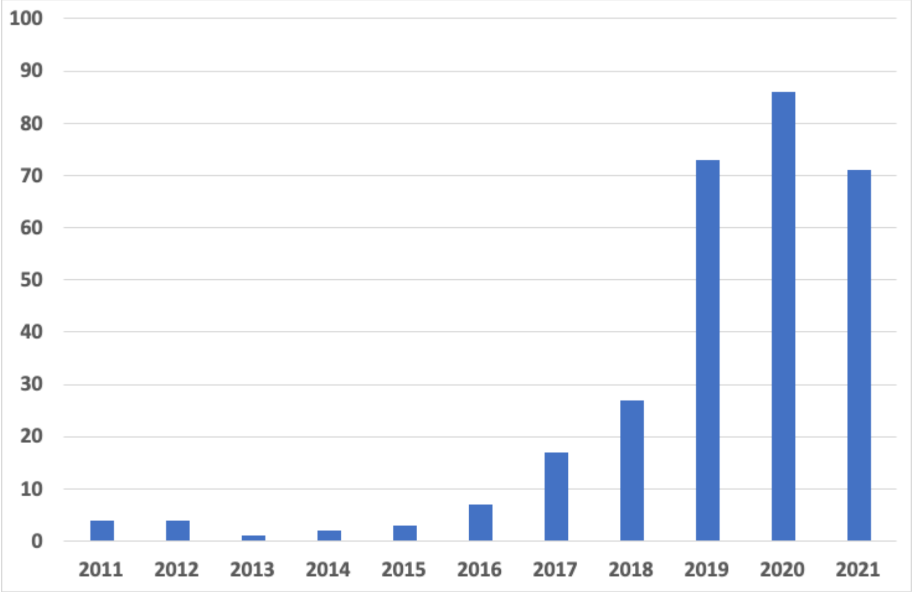
Generative Adversarial Networks (GAN)

5°) AI integration (MC)

- Monte Carlo simulations can **produce** highly accurate imaging device and patient training datasets for neural networks



Neurons: one weight per neuron
Layer: linear combination + activation function (non-linear)

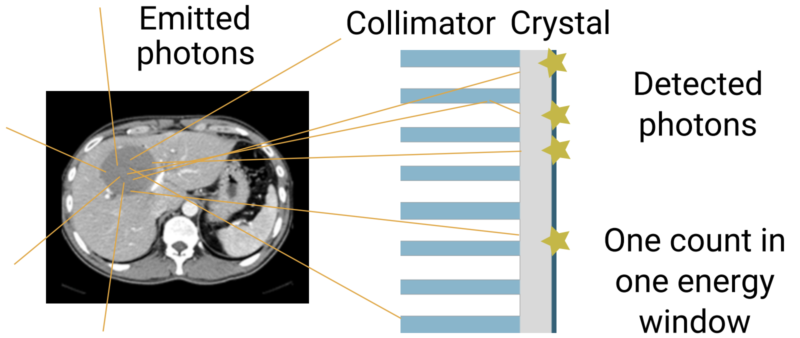


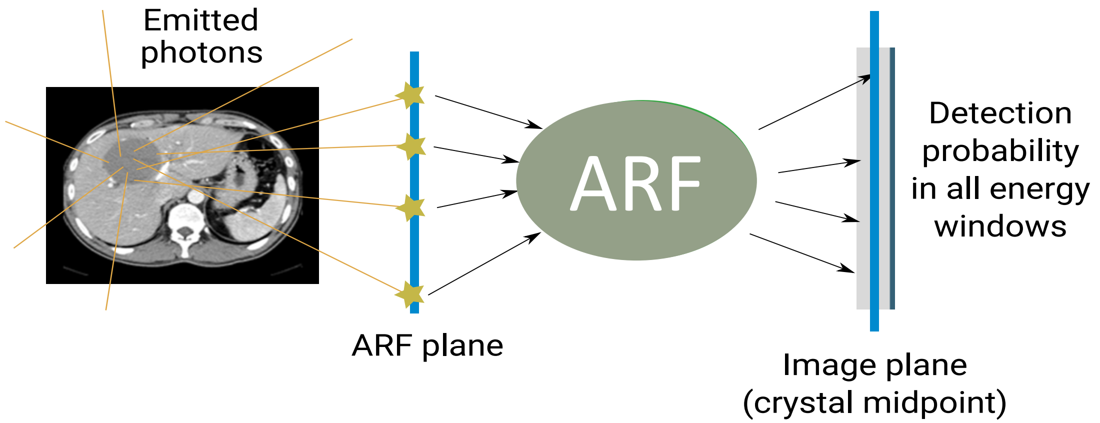
PubMed search for papers published in Medical Physics journal with neural networks as key word

- deep learning approaches can be **applied** to improve Monte Carlo simulation performance (computational efficiency)

5°) AI integration (MC)
SPECT imaging and ARF function

- Accelerate computing time for the simulation of interactions in the head of the camera
  - Only few photons are reaching the detection
- Several Variance Reduction Techniques proposed
- Angular Response Function (ARF)
  - Replace SPECT head detection with tabulated response
  - Incident particle at ARF plane use tables to get energy windows probabilities
  - Assume:
    - Spatially invariant
    - Detection depends on direction + energy
  - Speedup factor between 20 and 100
  - Computed only once

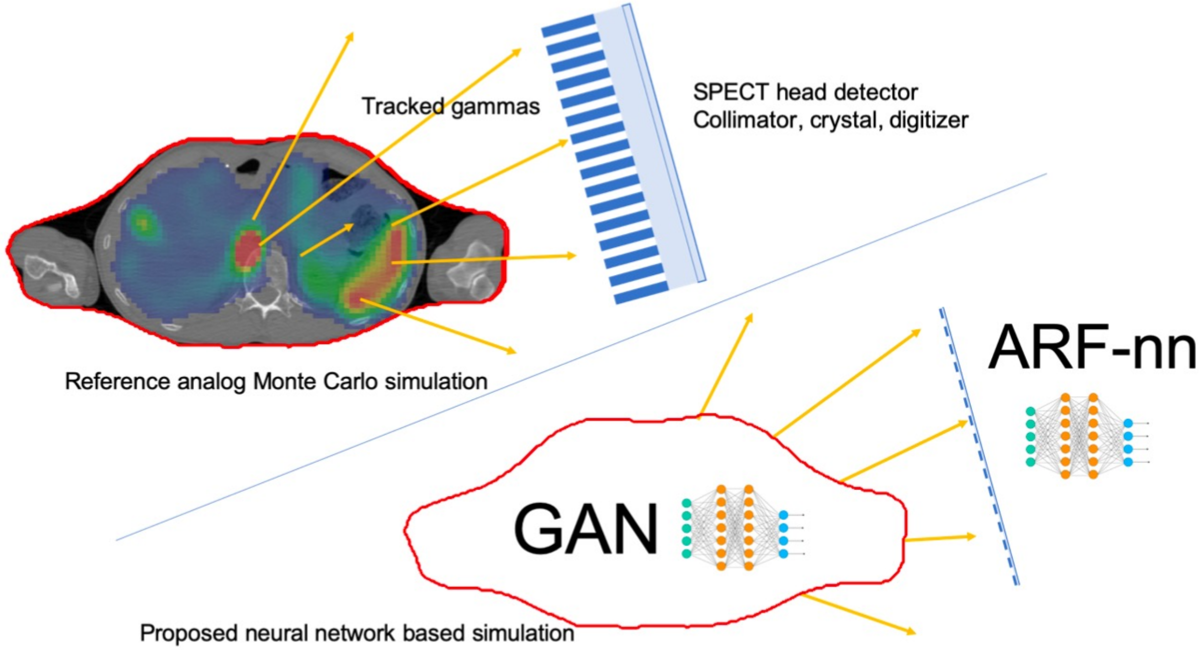




Sarrut et al. Learning SPECT detector angular response function with neural network for accelerating Monte-Carlo simulations, Phys. Med. Biol. 2018 https://doi.org/10.1088/1361-6560/aae331

5°) AI integration (MC)
SPECT imaging, GAN and ARF-nn function

(1) generate the training dataset via Monte Carlo simulation,
(2)train the GAN
(3) use the generator of the GAN as a source.
(4) a second neural network (ARF-nn), is used to model the imaging detector response and the two neural networks are combined.



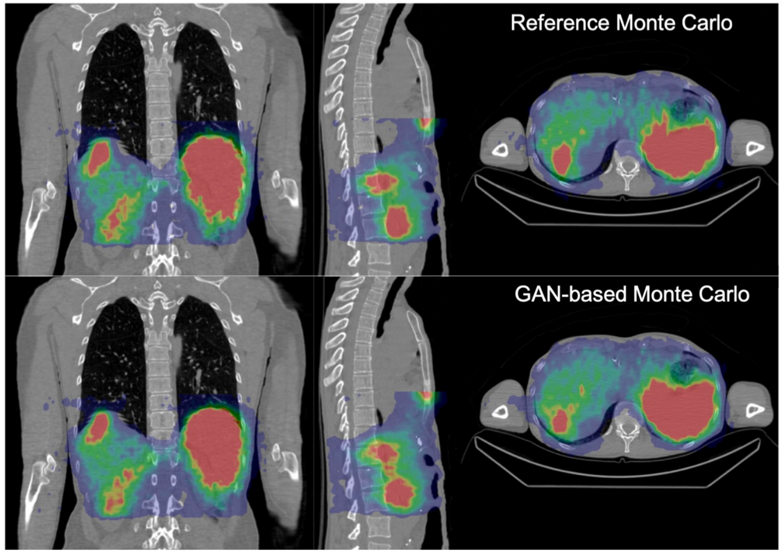


Figure 10. Reconstructed tomography SPECT overlaid on patient CT slides. Upper row: reconstruction performed with the projections obtained from the reference simulation plus ARF-nn; lower row: projections obtained via the combined GAN/ARF-nn method.

Sarrut, D., Etxebeste, A., Krah, N., Létang, J.M.
Modeling complex particles phase space with GAN for Monte Carlo SPECT simulations: a proof of concept. Phys Med Biol 66, 055014, 2021

5°) AI integration (MC)
Application to the generation of PHSP files

1 – Generate training dataset (PHSP)

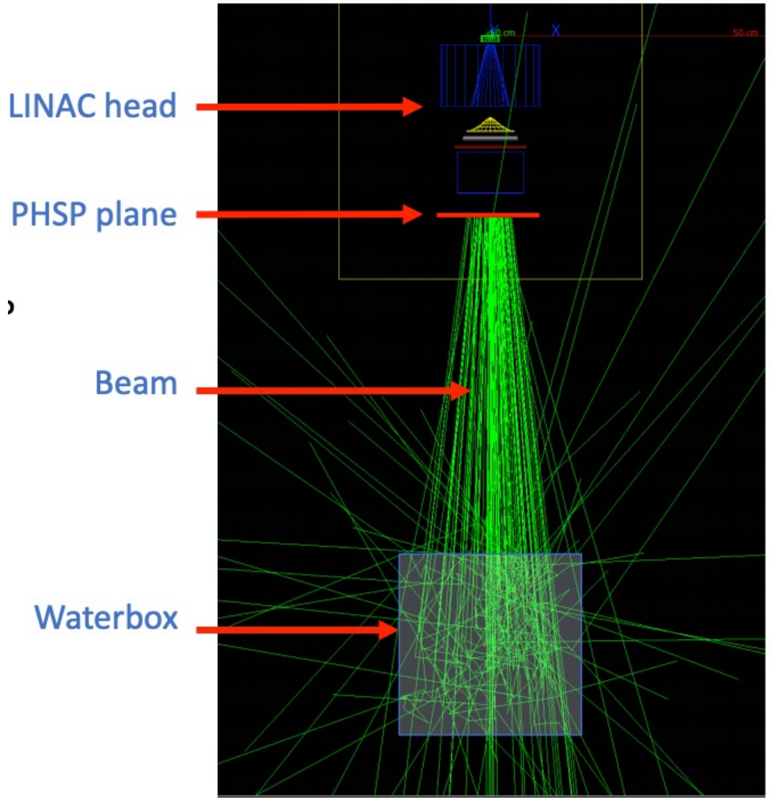
2 – Train GAN

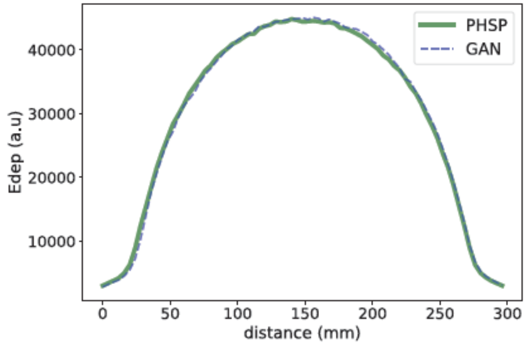
3 – Generate PHSP from GAN

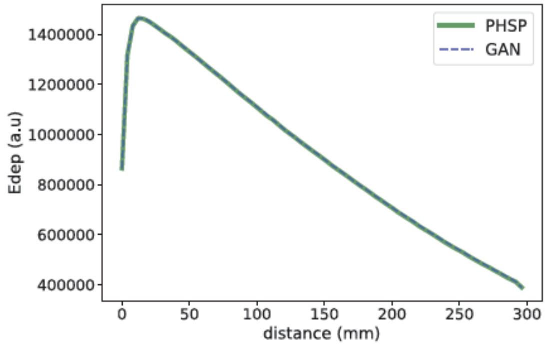
4 – Use PHSP to compute dose in waterbox

5 – Compare

PHSP	Size	Nb of particles
Elekta PRECISE 6MV	2 files of 3.9 GB	1.3×10^8 photons each file
CyberKnife IRIS 60mm	2 files of 1.6 GB	5.8×10^7 photons each file







Sarrut et al. Generative Adversarial Networks (GAN) for compact beam source modelling in Monte Carlo Simulations, Med. Phys., doi: 10.1088/1361-6560/ab3fc1

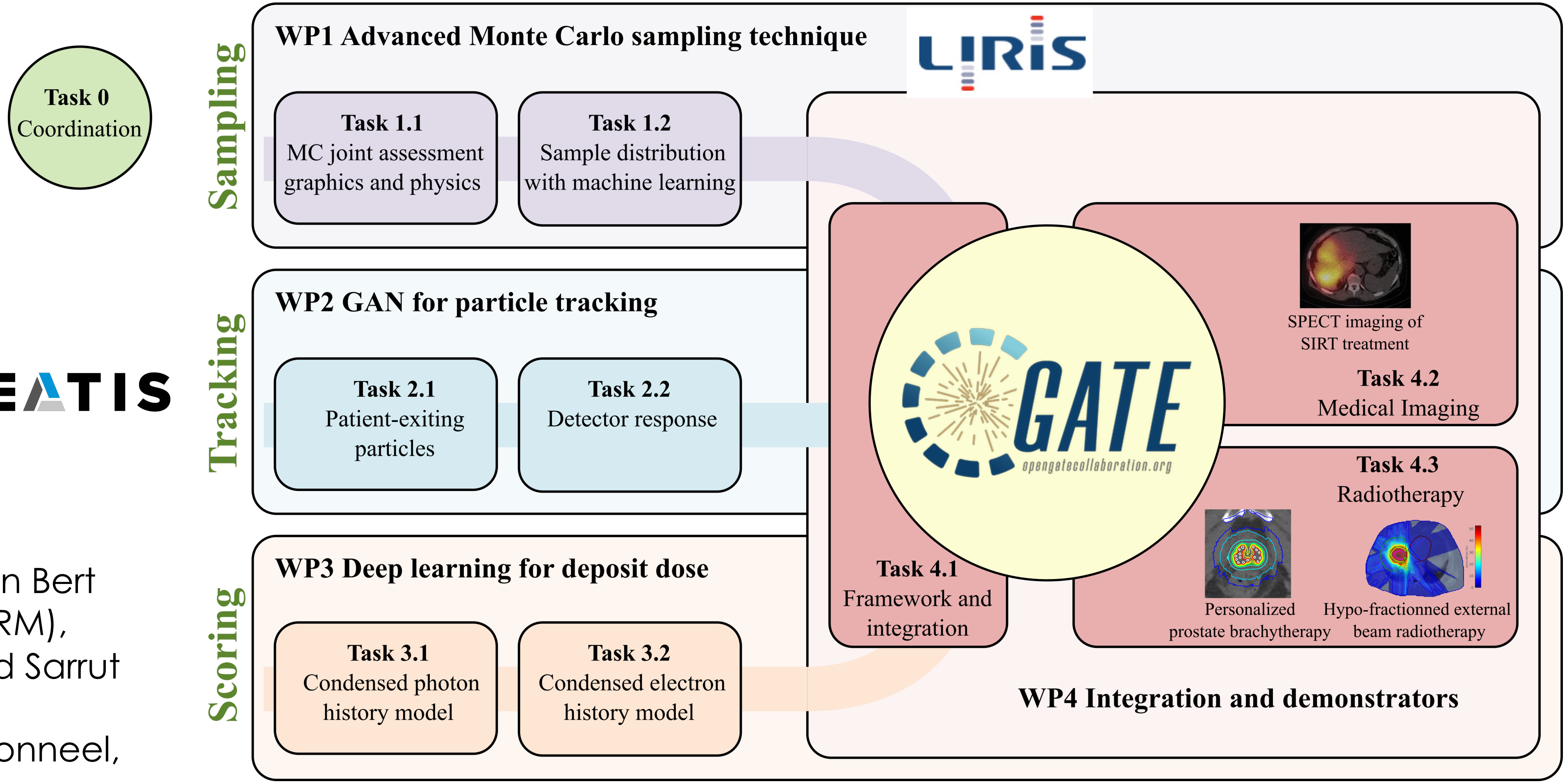
5°) AI integration (MC)
MoCaMed: Advanced Monte Carlo Methods for Medical Physics

ANR AAPG2020 – CE45

42 months

Partners

- LaTIM (INSERM), Julien Bert
- CREATIS (CNRS, INSERM), Ane Etxebeste, David Sarrut
- LIRIS (CNRS), David Coeurjolly, Nicolas Bonneel, Julie Digne, Victor Ostromoukhov



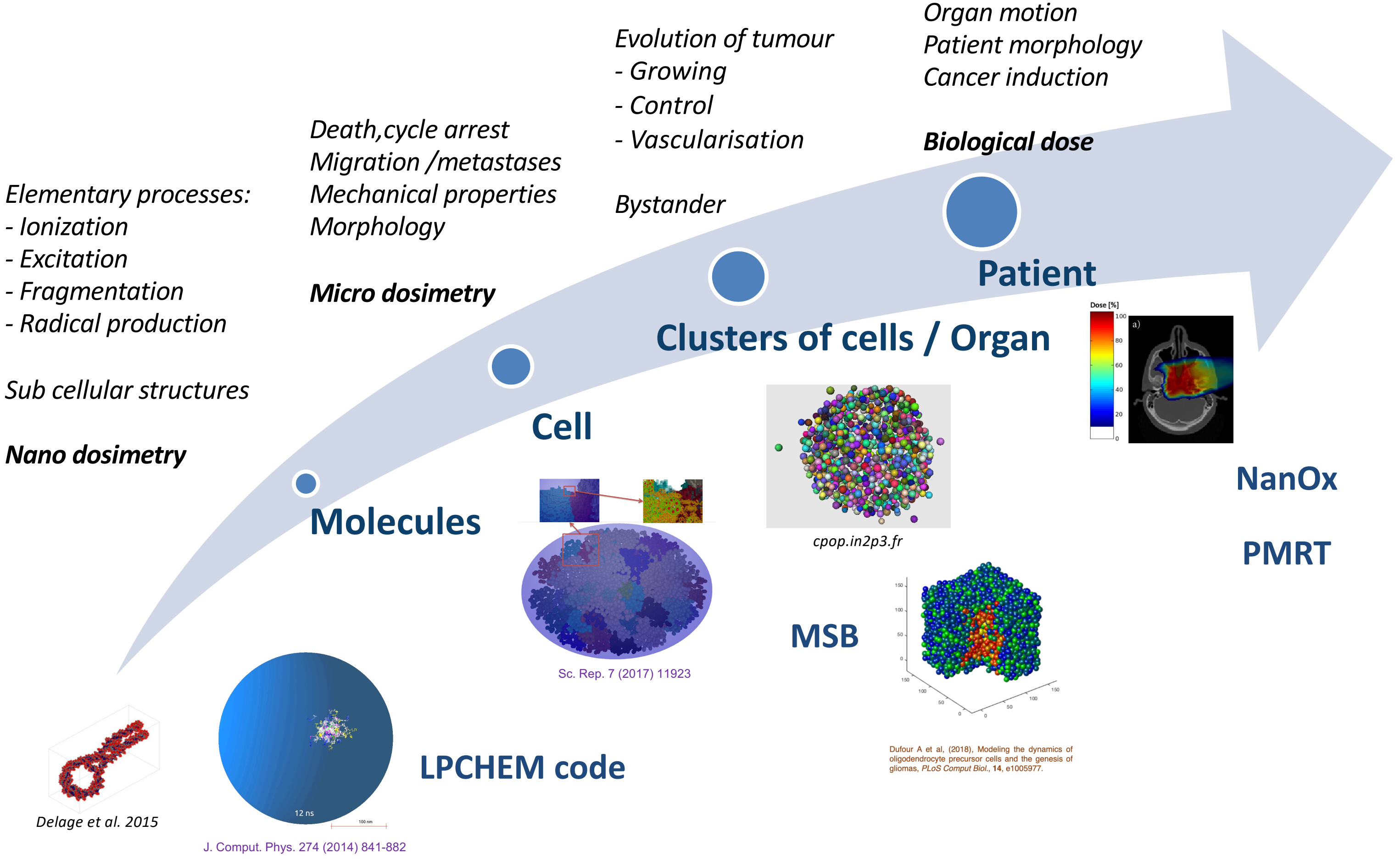
6°) Multiscale simulations

GEANT4-DNA
A SIMULATION TOOLKIT

The **unique** open source and open access simulation toolkit for micro/nano dosimetry and radiation biology

- **Long term development** fully included in Geant4 releases
- International collaboration composed of 42 collaborators
- **Coordinated by IN2P3/CNRS** since 2008
- Funded by regular support from institutions and international calls
- Fruitful involvement in international conferences & tutorials
  - Geant4 International User Conference at the Physics-Medicine-Biology frontier » series of conferences initiated by IN2P3 in 2005
  - Annual international tutorials (17)
- High rank and highly cited publications (104 since 2007)

DEVELOPMENT ACCESSIBLE TO OTHER TOOLKITS, PARTICULARLY TO GATE



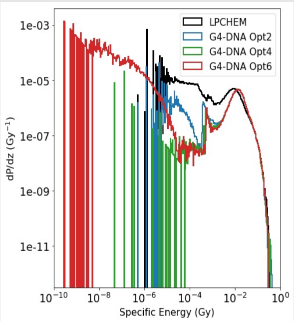
GEANT4-DNA | **Open source and open access toolkits** | GATE

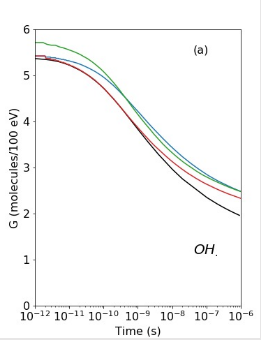
6°) Multiscale simulations

Evaluation of the biological dose in hadrontherapy

BIOPHYSICS MODELS

PRE CALCULATED DATA WITH TRACK SCTRUCTURE MC CODES

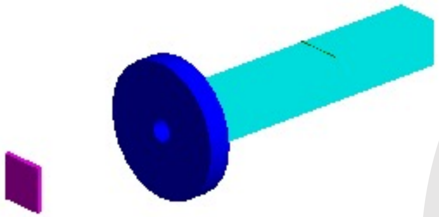


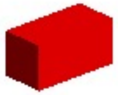


Evaluation of alpha and beta parameters for mono-energetic ion beams using data such as specific energy and water radiolysis

CLINICAL BEAM MODELING

HIMAC BEAM LINE GEOMETRY IN GATE





BIODOSE ACTOR

The biodose actor uses the biophysics models predictions to calculate the biological quantities for an SOBP in a voxelized target

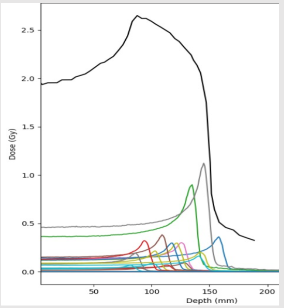
RBE

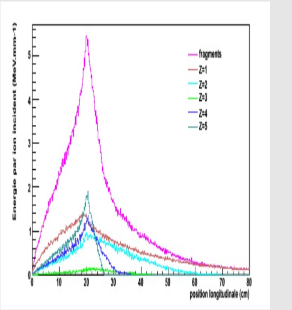
BIOLOGICAL DOSE

SURVIVAL FRACTION

SOBP

IRRADIATION FIELD WITH PRIMARY IONS AND NUCLEAR FRAGMENTS OF DIFFERENT LET





The physical dose deposition is simulated for the clinical beam line as an SOBP using PBS or passive modulation

Thèse LabEx PRIMES
Yasmine ALI (soutenance décembre 2021)

6°) Multiscale simulations
Biophysical models

MMKM

Kase et al. (2006)
Inaniwa T. et al. (2010)

BIOLOGICAL DATA

REFERENCE EXPERIMENTAL DATA

Reference α, β values, cell nucleus and radius of the sensitive volume

PHYSICAL DATA

PRECALCULATED WITH TSMC (G4DNA, LQD)

Specific energy deposited in the cell sensitive volume on a micro and nanometric scale

CHEMICAL DATA

PRECALCULATED WITH TSMC (G4DNA, LQD)

Yield of radiolytic species in the sensitive volume

NANOX

Cunha et al. (2017)
Monini et al. (2020)

6°) Multiscale simulations
Estimate cell survival

data/V79_NanOx.txt

data/CHO-K1_NanOx.txt

data/SQ20B_NanOx.txt

data/HSG_NanOx.txt

KINETIC ENERGY (MeV/n)	α	β
Hydrogen ion		
0.1	3.52	0.05
0.125	3.58	0.02
Helium ion		
0.1	1.35	0.02
0.125	1.34	0.01
Carbon ion		
0.1	0.55	0.01
0.125	0.20	0.03
Oxygen ion		
0.1	0.41	0.01
0.125	0.38	0.02

data/HSG_MMKM.txt

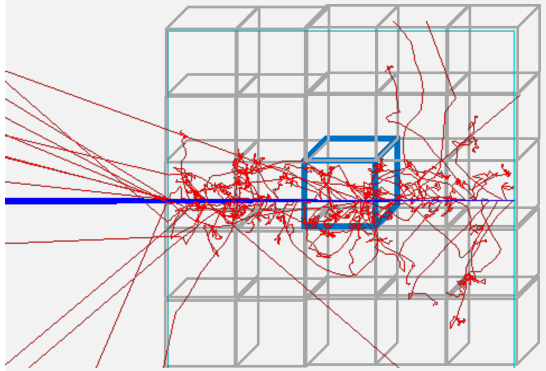
KINETIC ENERGY (MeV/n)	α	β
Hydrogen ion		
0.1	1.57	0.047
0.125	1.54	0.047
Helium ion		
0.1	1.24	0.047
0.125	1.22	0.047
Carbon ion		
0.1	0.46	0.047
0.125	0.45	0.047
Oxygen ion		
0.1	0.37	0.047
0.125	0.36	0.047

6°) Multiscale simulations
Methodology

CNRS GDR Groupement de recherche MI2B Outils et méthodes nucléaires pour la lutte contre le cancer

BEGIN OF RUN

The matrix is initialized and the target volume is voxelized.



Linear Interpolation Coefficients C++ Map

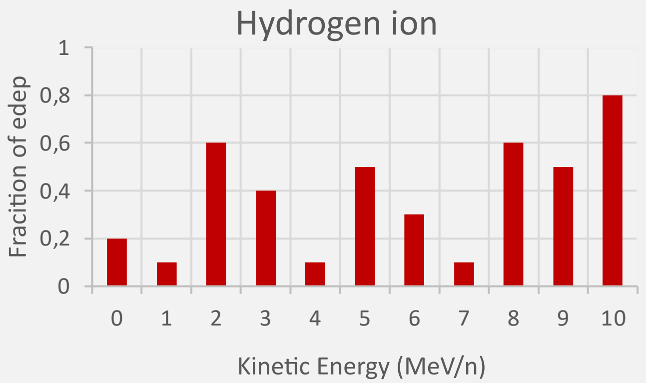
The linear interpolation coefficients are calculated after the alpha beta data table

STEPPING ACTION IN VOXEL

Voxel i

The information retrieved from each step in each voxel

Deposited Energy C++ Map



The deposited energy is retrieved to estimate the fraction of deposited energy per ion type

Alpha Beta Mix Values C ++ Map

$$\alpha_{mix} = \sum f_T \, \alpha_T \qquad \sqrt{\beta_{mix}} = \sum f_T \sqrt{\beta_T}$$

The linear interpolation coefficients are used to calculate the alpha and beta mix values

END OF RUN

Using the stored alpha and beta mix values, the following quantities are estimated per voxel :

RBE

BIOLOGICAL DOSE

SURVIVAL FRACTION

OUTPUT

The output file contains the survival fraction, biological dose and RBE per voxel

PENCIL BEAM SCANNING

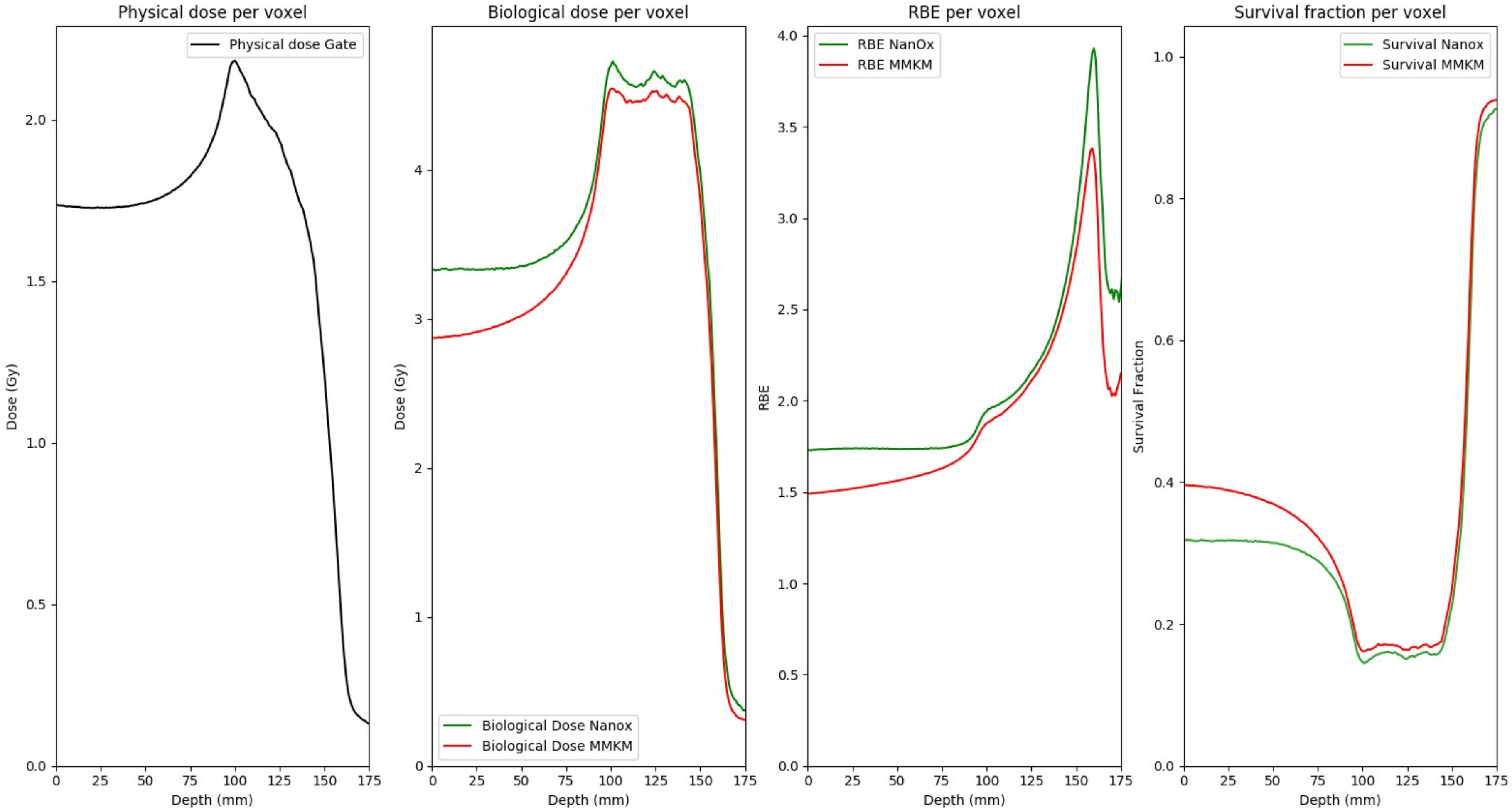
No post treatment needed

PASSIVE MODULATION

Python script to combine the output of each mono-energetic peak

6°) Multiscale simulations
Some results

HIMAC LINE
Chiba, Japan



Internship open in 2022 to continue the work in patient CT-scans

7°) Events

SAVE THE DATE

Groupement de recherche
MI2B Outils et méthodes nucléaires pour la lutte contre le cancer

GATE training for beginners 23-25 November 2021

https://cnrsformation.cnrs.fr/gate-training-on-medical-imaging-dosimetry-radiation-therapy?mc=GATE%20Training

Direction des Relations avec les Entreprises
CNRS FORMATION ENTREPRISES

Python Data Analysis for GATE simulations 8-10 March 2022

https://cnrsformation.cnrs.fr/gate-training-on-medical-imaging-dosimetry-radiation-therapy?mc=GATE%20Training

GATE trainings for master programs

- Server dedicated to training
- Initiated in France this year
- To be extended to any master program

Masters in particle & medical physics (200 students)

LABEX PRIMES UNIVERSITÉ DE LYON

IEEE NPSS NUCLEAR & PLASMA SCIENCES SOCIETY

2021 IEEE NSS MIC

GATE workshop **23rd of October 2021**
https://nssmic.ieee.org/2021/program/

Next GATE scientific meeting
18th of November 2021
Information coming soon