Heavy Ion Therapy Research Integration

Simulation as Essential Tool in Hadron Therapy

With generous input from
F. Cerutti, F. Salvat Pujol et.al.
from FLUKA.CERN team

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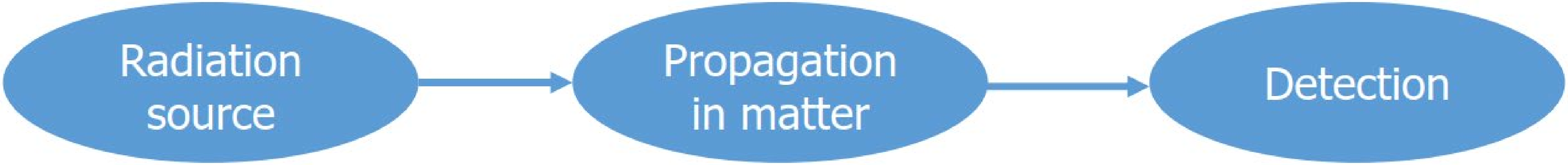
Statistical Processes in High-Energy Physics



Photons,
Leptons (e±, μ±, τ±, ν),
Hadrons (n, p, π, Σ,…),
Ions (Z,A),
Radioactive sources
Cosmic rays,
Colliding particle beams,
Synchrotron radiation,
…
“Monoenergetic”/Spectral
Energies:
- keV-PeV,
- down to thermal energies for neutrons.

Arbitrary geometry,
Various bodies,
materials, compounds.

Radiation-matter interaction,
Secondary particles,
Particle shower,
Material activation,
Magnetic and electric fields…

Measure/estimate/score:
- Energy-angle particle spectra,
- Deposited energy,
- Material damage,
- Biological effects,
- Radioactive inventories…

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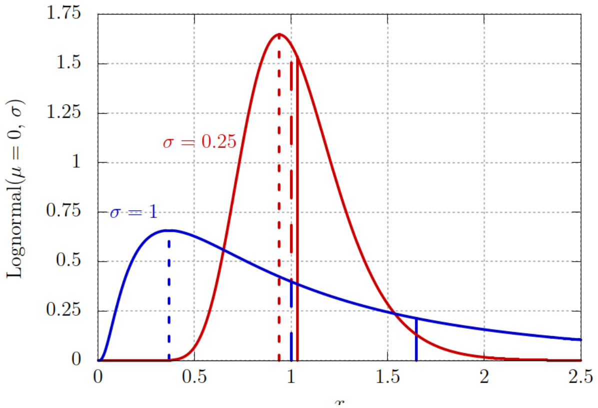
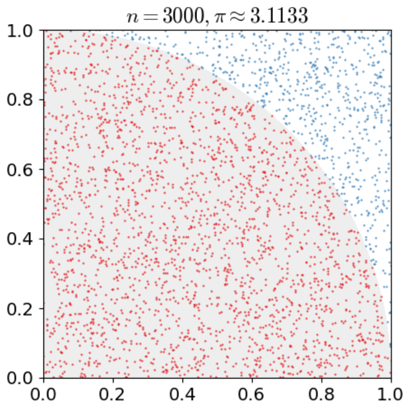
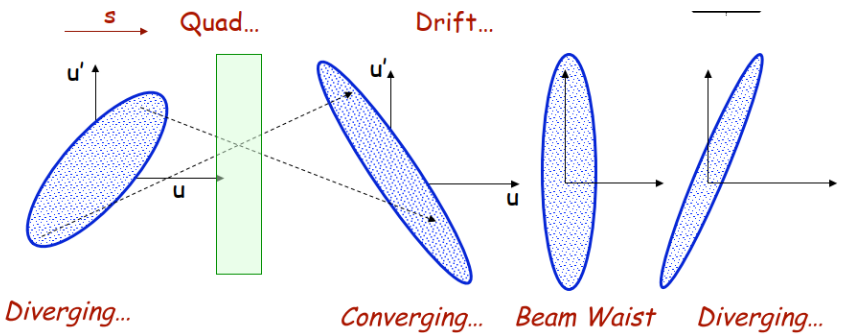
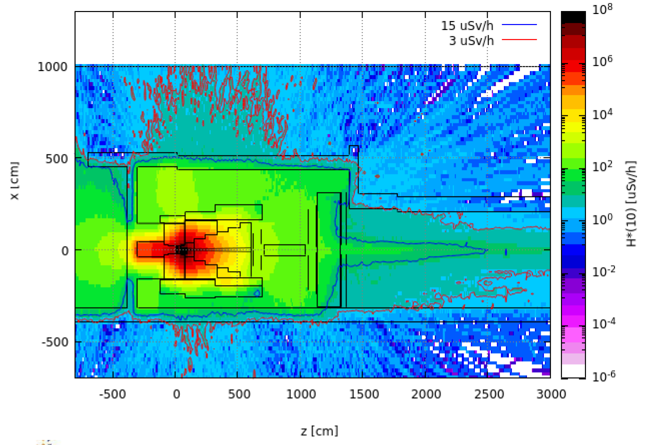
Content

- Introduction to Statistics
- Particle Transport
- Monte-Carlo Simulations
- Software Codes for Monte-Carlo Simulations









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Introduction to Statistics

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Random variables

A random variable X describes the outcome of a process whose value we cannot predict with certainty, but nevertheless we know:

- Its possible values.
- How likely each value is, governed by the probability density function (PDF), p(x).

- Properties of p(x):
  - Positive defined: p(x)>=0 for all x
  - Unit-normalized: ∫dx p(x) = 1
  - Integral gives probability: $\int_a^b$ dx p(x) = P(a<x<b)
- The expectation value $\langle X \rangle = \int_{-\infty}^{\infty} \mathrm{d}x\, x p(x)$ measures the average value of X.
- The variance σ^2 measures the square deviation from <X>.

$$\sigma^2 = \langle (X - \langle X \rangle)^2 \rangle = \ldots = \langle X \rangle^2 - \langle X^2 \rangle$$

- The standard deviation σ measures the average deviation from <X>.

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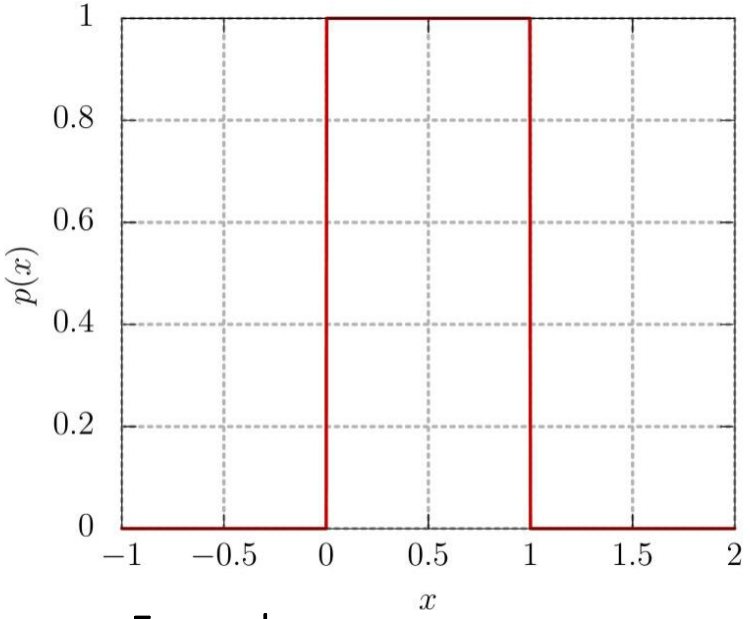
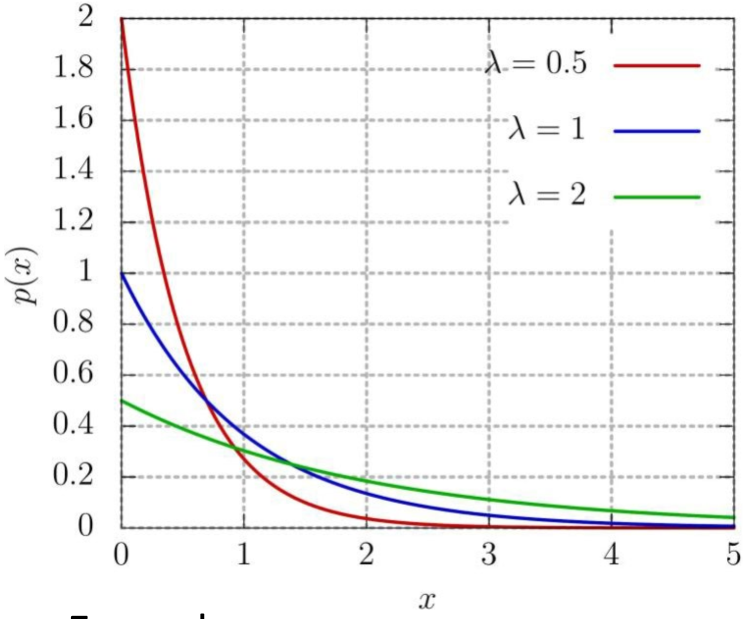
Common PDFs

Uniform



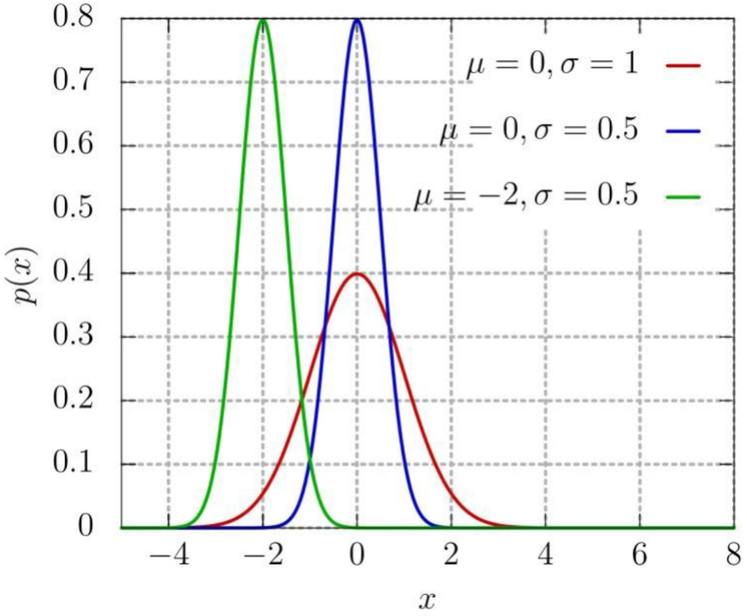
Examples:
- Required dose in tumor
- Strongly collimated beam

Exponential



Examples:
- Sizes of stars, meteorites, cities
- The time until a radioactive decays
- Distance between DNA mutations
- Number of citations per publication
- Wealth across people

Gaussian



Examples:
- Human height, weight
- Scattered beam

Quantities of statistical distributions

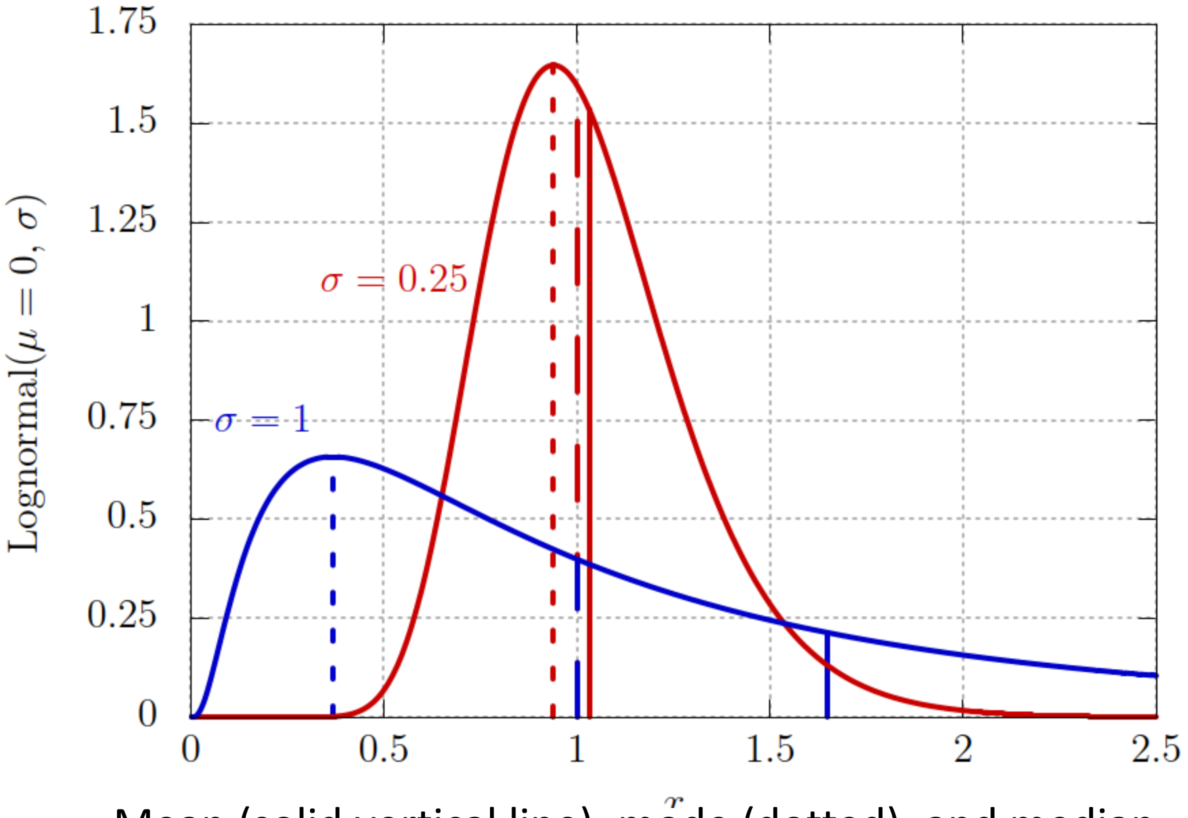
- Mean (expectation value)

$$\langle X \rangle \equiv \int_{-\infty}^{\infty} \mathrm{d}x \; x p_X(x).$$

= Sample average for N→∞

(Central Limit Theorem)

- Mode $\quad x_{\mathrm{mode}} \equiv \mathrm{argmax}\left[p_X(x)\right].$
- Median $\quad F_X(x_{\mathrm{med}}) = \int_{-\infty}^{x_{\mathrm{med}}} \mathrm{d}x \; p_X(x) = \frac{1}{2}.$
- For symmetric distributions, the mean and the median coincide.
- For symmetric and unimodal distributions, the mean, the median, and the mode coincide.



Mean (solid vertical line), mode (dotted), and median (dashed) for log-normal distributions with σ = 0.25 (red) and σ = 1 (blue)

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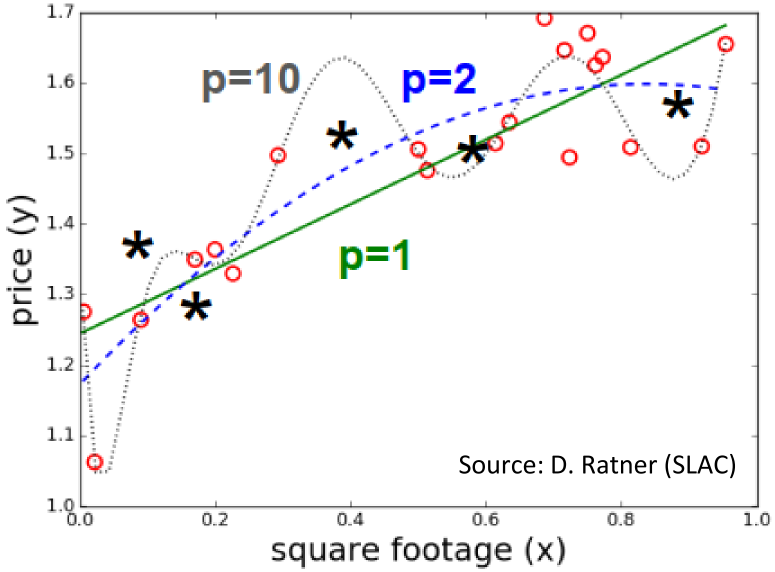
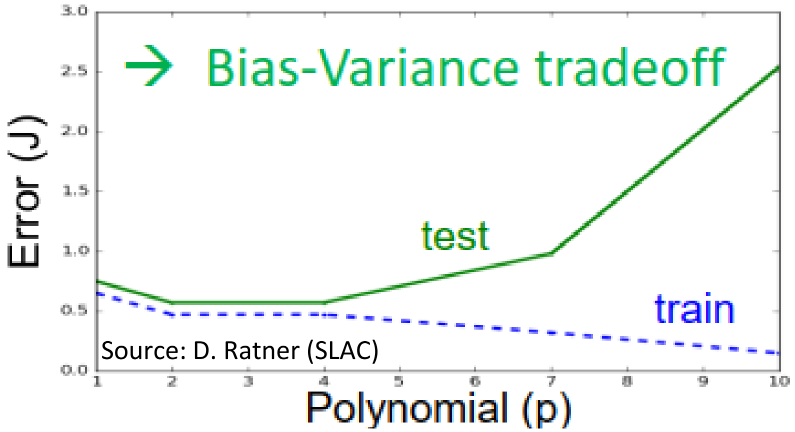
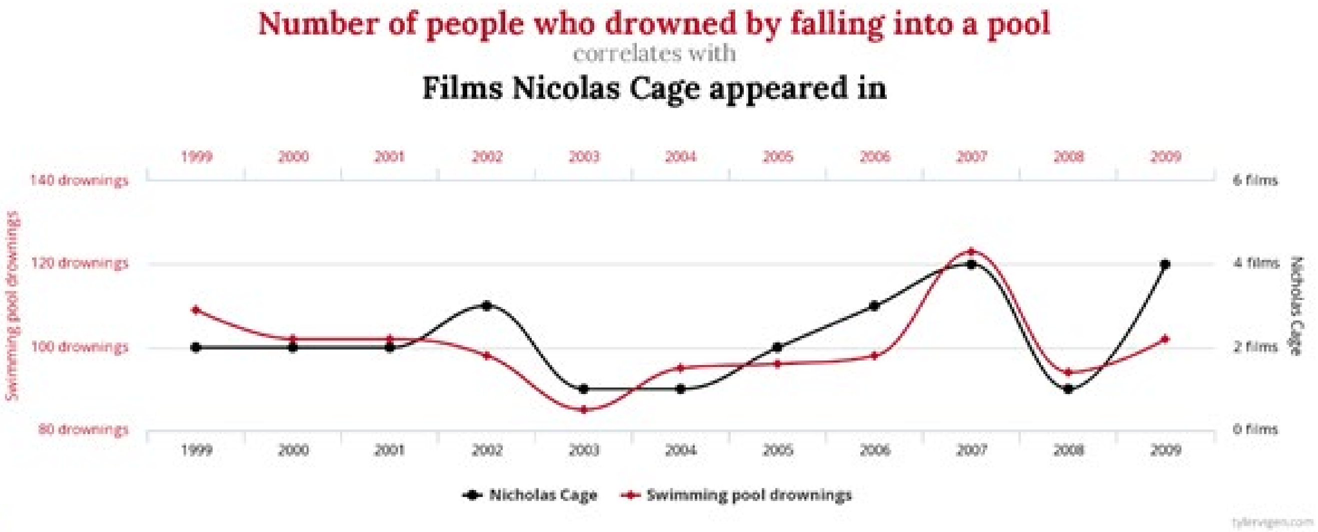
Dependency of Variables

- If the outcome of one random variable may influence the outcome of another, such random variables are called dependent
- Linear dependency is called correlation
- Correlation does not imply causality!
- Non-linear dependencies exist: How to determine a suitable model?







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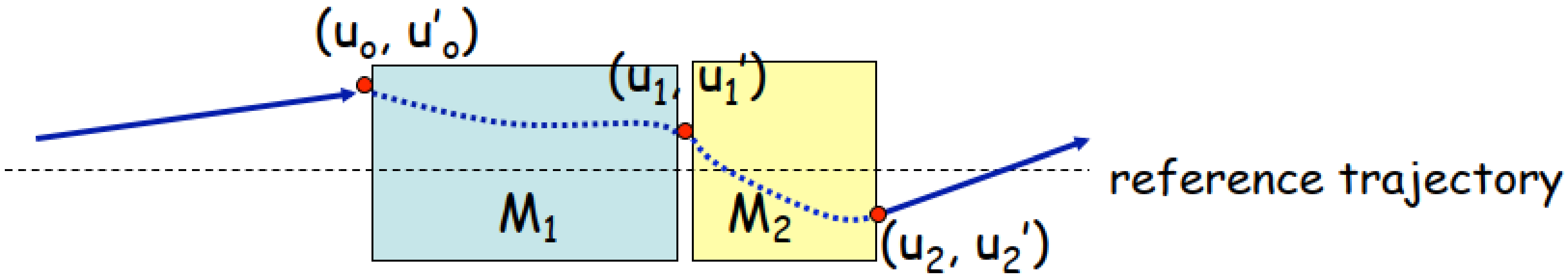
Particle Transport

Description of One Particle Propagation

- Linear algebra description by 2-D vector in one transverse plane

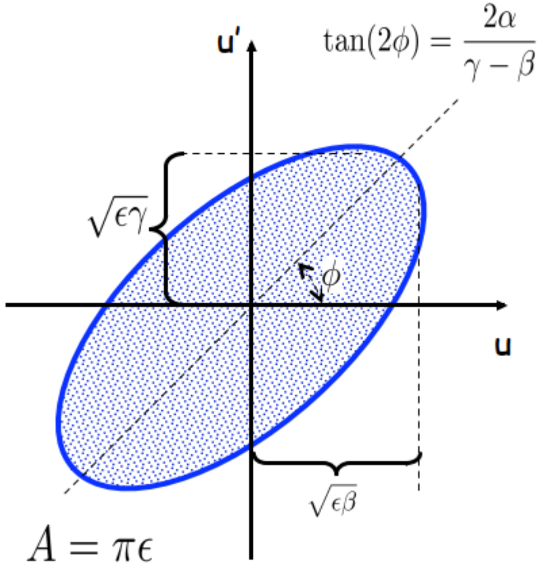


$$\begin{pmatrix} u_1 \\ u_1' \end{pmatrix} = M_1 \begin{pmatrix} u_o \\ u_0' \end{pmatrix} \text{ then, } \begin{pmatrix} u_2 \\ u_2' \end{pmatrix} = M_2 \begin{pmatrix} u_1 \\ u_1' \end{pmatrix} = M_2 \left(M_1 \begin{pmatrix} u_o \\ u_0' \end{pmatrix} \right) = M_2 M_1 \begin{pmatrix} u_o \\ u_0' \end{pmatrix}$$

- Since we live in 3 dimensions, particle can be described by a 6-dimensional vector

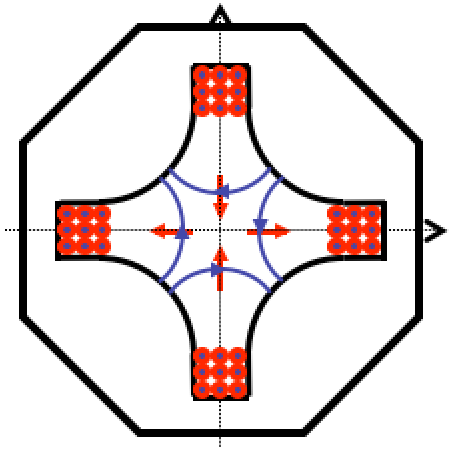
Credit: Jeff Holmes, Stuart Henderson, Yan Zhang
USPAS

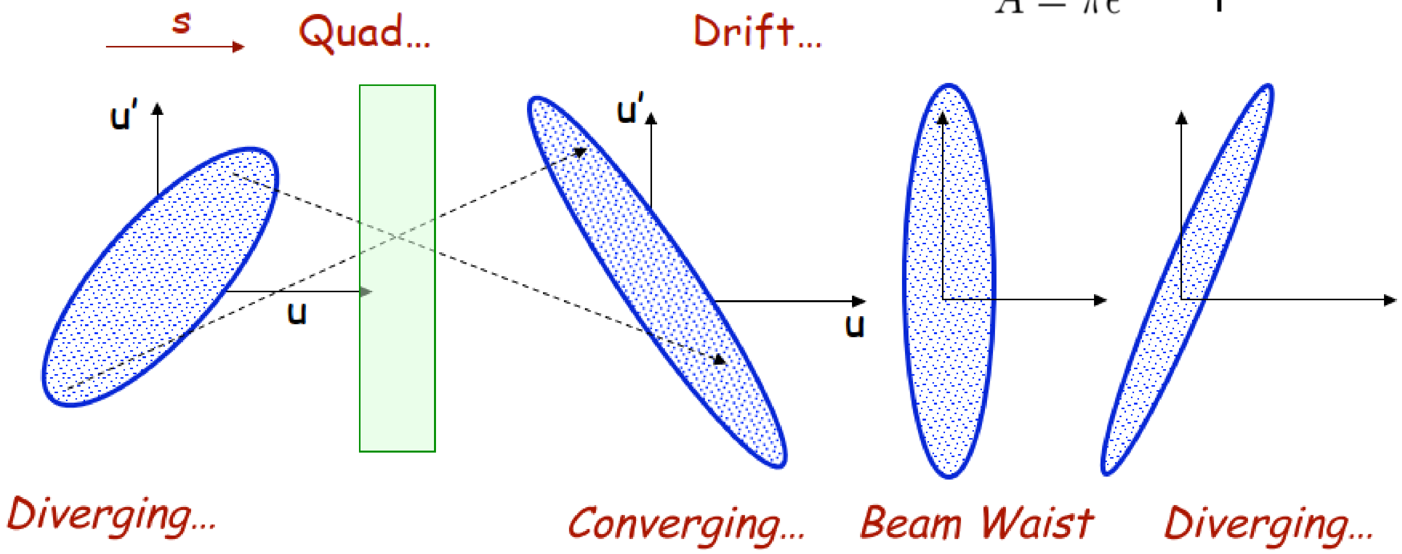
Description of Multi-Particle Beam



The beam emittance is the phase space area of the beam.

Emittance is a parameter used to gauge beam quality.





Credit: Jeff Holmes, Stuart Henderson, Yan Zhang
USPAS

Solutions to Transport Equations

- Transport equation to be solved for an arbitrary source density $n_0(\mathbf{r},E,\Omega,t)$, an arbitrary geometry, and realistic interaction cross sections.
- Solution strategies:
  - Analytical: only for restricted geometries and restricted interaction models.
  - Spectral: exploit symmetries and expand in appropriate basis functions. Only for restricted cases.
  - Numerical integration: general, but inefficient for high-dimensional integrals.
  - Monte Carlo method: general, efficient, can treat arbitrary radiation fields and geometries.
- Monte Carlo is a stochastic method, exploiting random numbers to:
  - Simulate an ensemble of particle histories governed by known interaction cross sections.
  - Track them in arbitrary geometries.
  - Accumulate contribution of each track to statistical estimator of the desired physical observables.

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Monte-Carlo Simulations

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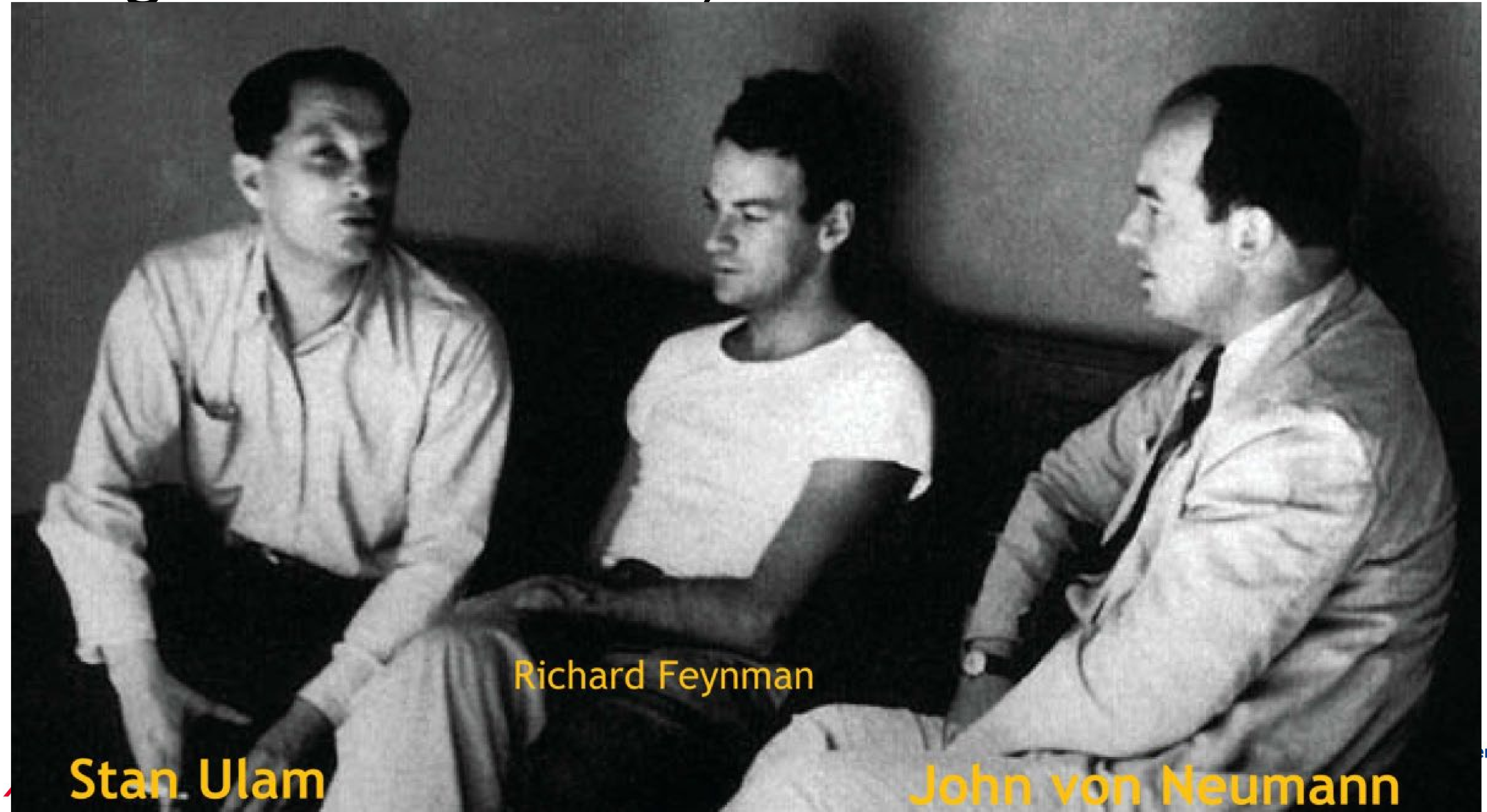
Origins – Los Alamos, 1946



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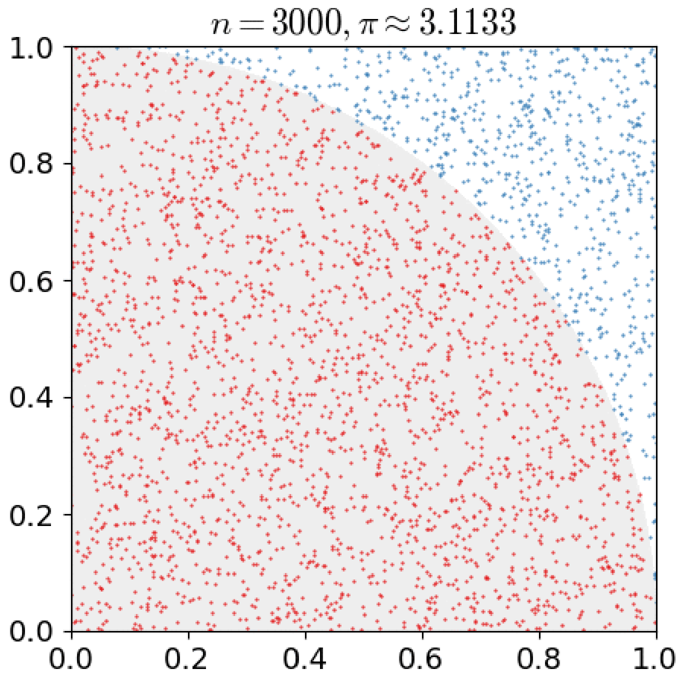
How does Monte Carlo simulation work?

1. Define a domain of possible inputs
2. Generate inputs (pseudo-)randomly from a probability distribution over the domain
3. Perform a deterministic computation on the inputs
4. Aggregate the results

- Example: Calculate the value of π



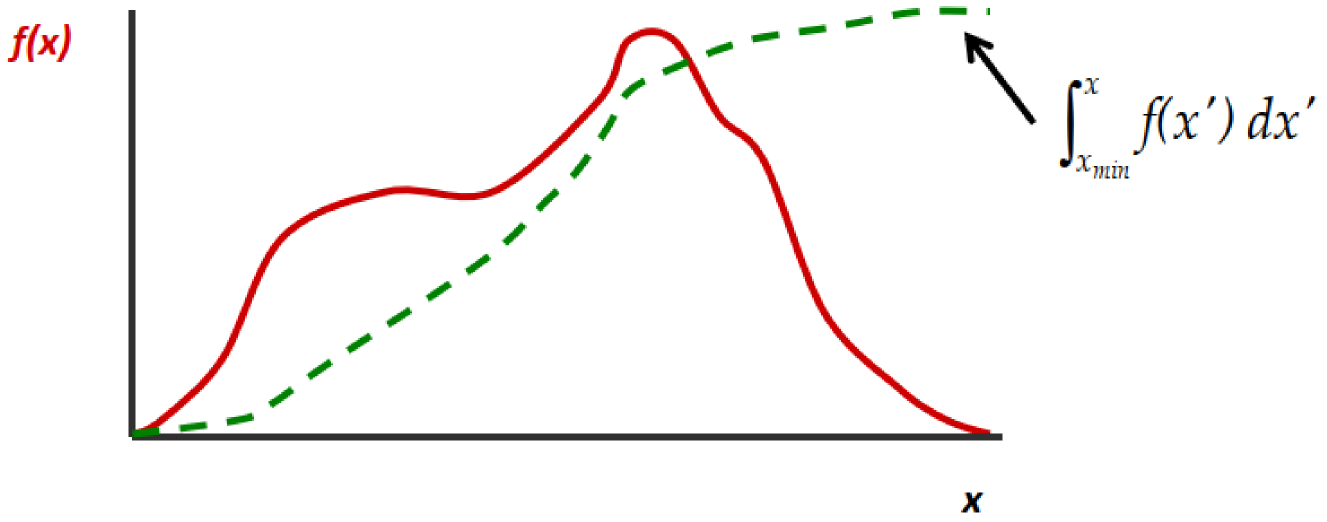
Credit: Wikipedia

Pseudo-Random Number Generators

- For reasons of reproducibility, we use pseudo-random numbers: uniformly distributed numbers between 0 and 1 obtained from a deterministic algorithm (not random!) which pass all tests of randomness.
- Needs one/several seed values, X_1, from which the sequence starts: $X_{n+1} = f(X_n, X_{n-1}, X_{n-2}, \ldots, X_1)$
- Different seed values yield different random number sequences.
- E.g.: the random number generator used in FLUKA is RM64, based on an algorithm by G. Marsaglia et al. Stat. Probabil. Lett. 66 183-187 (2004) and 8 35-39 (1990).
- Requirement:
  - **Homogeneous distribution.** The generated sequence of pseudo-random numbers must be homogeneously distributed between 0 and 1.
  - **Long period.** Generated sequence of pseudo-random numbers necessarily has a period, after which it repeats. A good PRNG will have a period long enough that it will not be exhausted in the particular application/simulation.
  - **Repeatability.** For testing and debugging purposes it is necessary to repeat a calculation with exactly the same sequence of random numbers as in the problematic run, or to (re)start it at an intermediate stage. Thus, it is convenient to use a PRNG with the ability to easily return to any of its possible states.
  - **Jump ahead.** It may be convenient to know what is the state Xi+n of the PRNG given a state Xi for an arbitrary n.
  - **Portability.** The PRNG should yield the same results (within machine accuracy) in different computer architectures and compiler versions of the employed programming language.
  - **Efficiency.** A good PRNG should yield pseudo-random numbers at a fast enough rate and consume as little memory as possible.

Sampling

- In Monte Carlo we sample: step lengths, event type, energy losses, deflections…
- Sampling: generation of random values according to a given distribution.
- Fundamental problem: we know how to sample uniformly distributed values, but how do we sample from arbitrary distributions?
- There's a whole array of sampling techniques:
  - Inverse sampling
  - Rejection sampling



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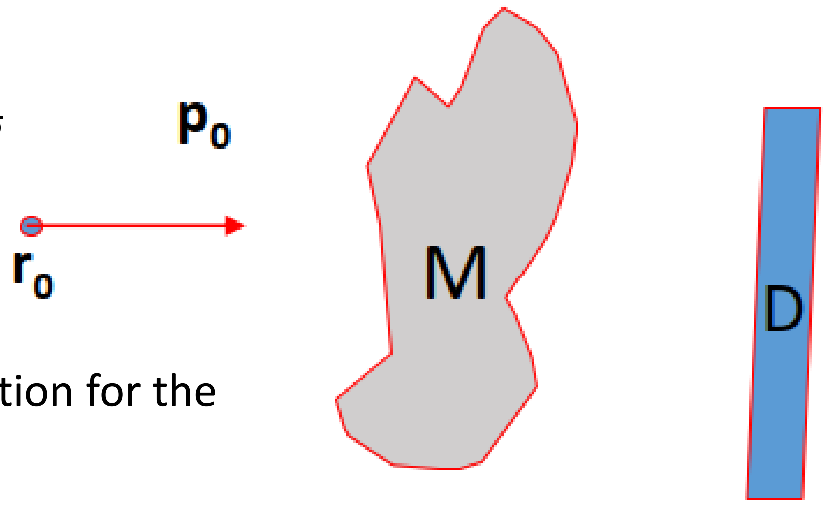
Simulation of Beam-Matter Interaction

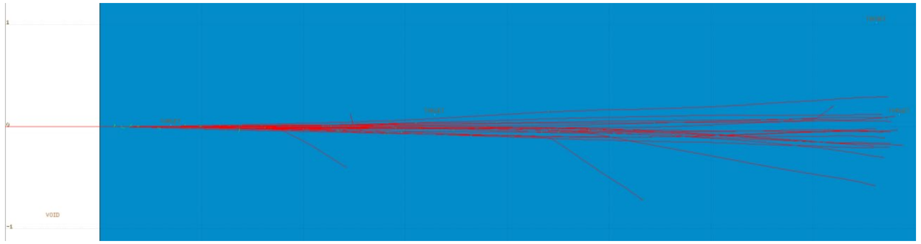
Loop over n_p primary events:

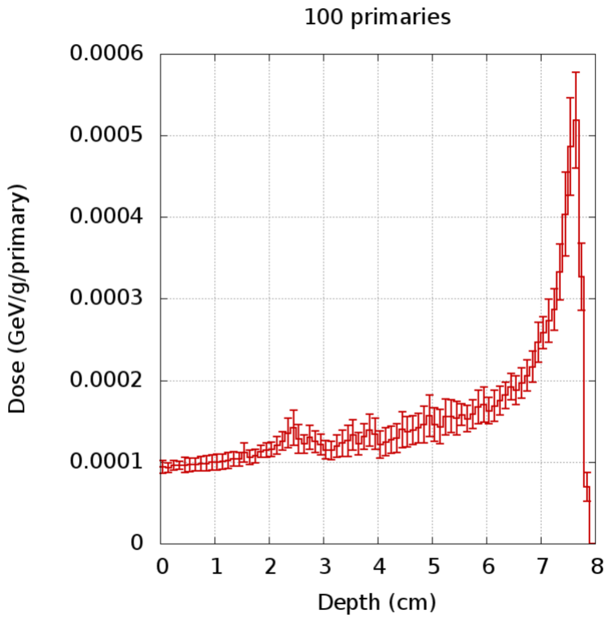
1. Initialize source particle position and momentum.
2. If particle is in vacuum, advance it to next material boundary.
3. Determine total interaction cross section at present energy and material: σ
4. Evaluate the mean free path to the next interaction: $\lambda = 1/(N\sigma)$
5. Sample step length to next interaction from $p(s) = (1/\lambda)\, e^{-s/\lambda}$
6. Decide nature of interaction: $P_i = \sigma_i / \sigma$, $i=1,2,\ldots,n$
7. Sample energy loss (and/or change of direction) from differential cross section for the selected interaction mechanism i. Update energy and direction of motion.
8. Add generated secondary particles to the stack if any.
9. Score contribution of the track/event to the desired physical observables.
10. Go to 2 unless:
    - Particle energy drops below user present threshold
    - Particle exits the geometry

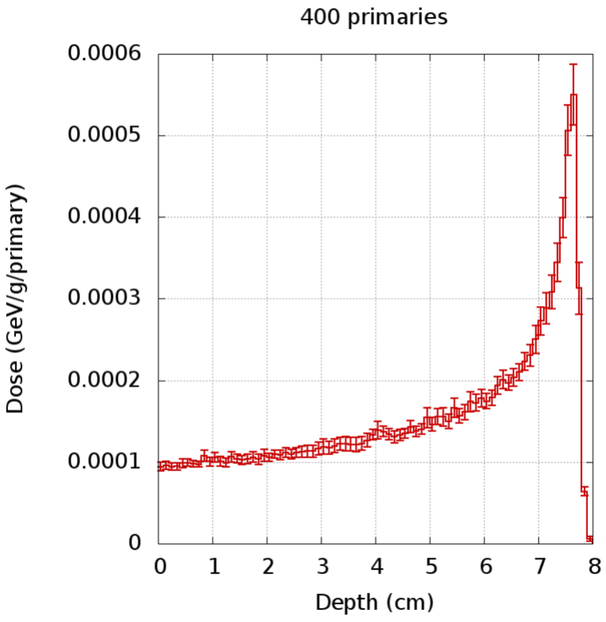


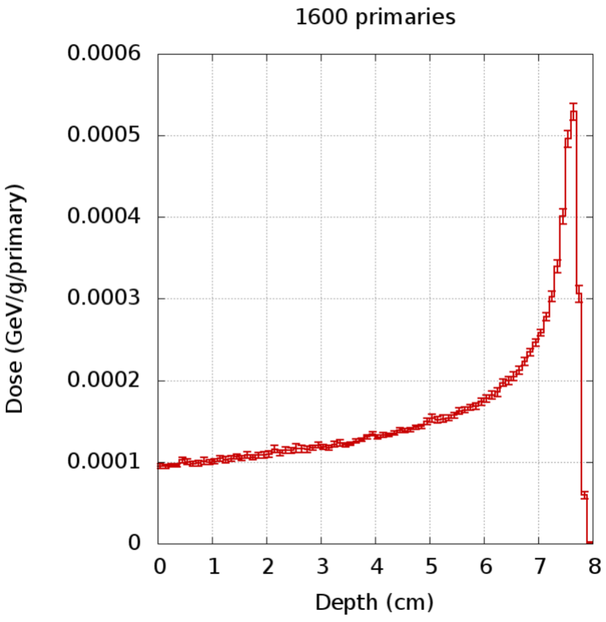
Statistical Uncertainties

- Example: 100-MeV proton beam in water



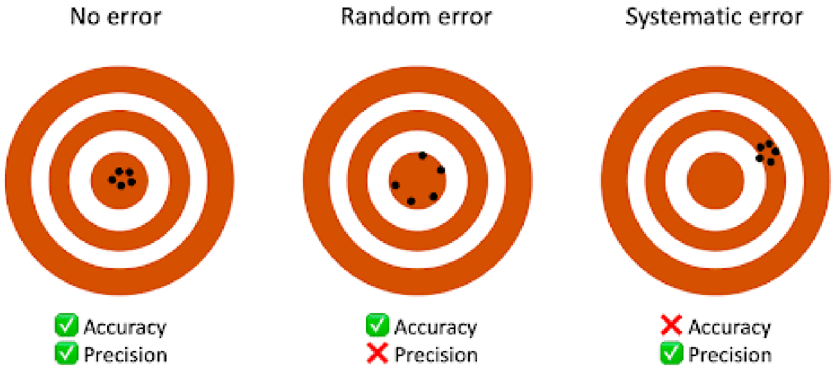






Statistical uncertainty decreases with the number of contributions N as 1/sqrt(N).

Systematic Uncertainties



- We have discussed statistical uncertainties above.
- That’s only part of the uncertainty in the results of any MC simulation. The rest are systematic uncertainties, due to:
  - Adopted physics models: different codes are based on different physics models. Some models are better than others. Some models are better in a certain energy range. Model quality is best shown by benchmarks at the microscopic level (e.g. thin targets)
  - Transport algorithm: due to imperfect algorithms, e.g., energy deposited in the middle of a step, inaccurate path length correction for multiple scattering, missing correction for cross section and dE/dx change over a step, etc. Algorithm quality is best shown by benchmarks at the macroscopic level (thick targets, complex geometries)
  - Cross-section data uncertainty: an error of 10% in the absorption cross section can lead to an error of a factor 2.8 in the effectiveness of a thick shielding wall (10 attenuation lengths). Results can never be better than allowed by available experimental data

Systematic Uncertainties

- Systematic errors due to incomplete knowledge:
  - Patient anatomy
  - Material composition not always well known. E.g. concrete/soil composition (how much water content? Can be critical)
  - Beam losses: most of the time these can only be guessed. Close interaction with engineers and designers is needed.
  - Presence of additional material, not well defined (cables, supports...)
  - Is it worth to do a very detailed simulation when some parameters are unknown or badly known?

- Systematic errors due to simplification:
  - Geometries that cannot be reproduced exactly (or would require too much effort)
  - Air contains humidity and pollutants, has a density variable with pressure

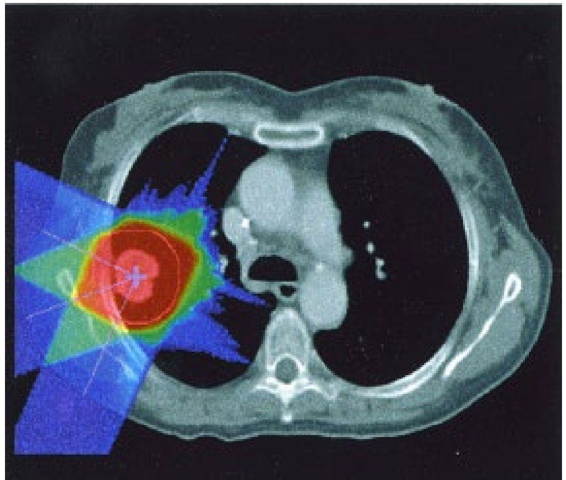


Figure Credit: Monty Python, Medaustron

Software Codes for Monte-Carlo Simulations

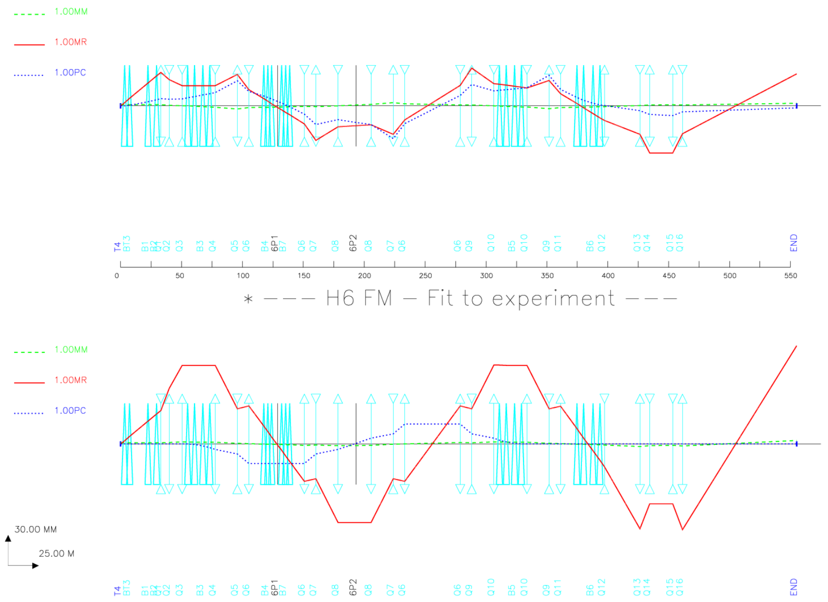
Code types and some examples

- Mathematical, no beam physics integrated
  - MatLab, Mathematica, Python with NumPy library
- Linear algebra based codes for simulating the beam propagation
  - Transport, MADX, (Win)AGILE, COSY
- Tracking codes without beam-matter interaction
  - Turtle, Track, OPAL, MADX Tracking module, MADX PTC
- Tracking codes with beam-matter interaction
  - FLUKA, MCNP, Geant4, Geant4-based codes (G4Beamline, BDSIM, TOPAS)

TRANSPORT + TURTLE

- TRANSPORT:
  - Code for beam optics calculations
  - Matrix based calculation tool
  - Written in Fortran
  - Card based input
  - Can perform matching (in first order)
- TURTLE:
  - Tracking tool written in Fortran
  - Can simulate absorption at collimators and at magnet aperture transmission and particle distributions (X, X’, Y, Y’, ε_L, $\Delta p/p$)
  - Input almost identical to TRANSPORT

```
"P42 TRANSPORT FROM T4 TO T10"
100
15.0  1.0 "MM" 0.1   ;
15.0  9.0 "KG" 0.994 ;
13.0  18.0 ;
13.0  19.0 ;
13.0  41.0  ;
1.0  1.0  0.6  1.0  0.6  0.0  0.2  447.3  ;
3.0  0.0  "T4"  ;
3.0  1.35   ;
2.0  0.000 ;  4.0  3.6  2.919  0.0  "B1" ;  2.0  0.040 ;
3.0  0.6 ;
2.0 -0.040 ;  4.0  3.6  2.919  0.0  "B1" ;  2.0  0.080 ;
3.0  8.05    ;
3.0  1.615  "TAX7" ;
3.0  0.01  ;
3.0  1.615  "TAX8" ;
3.0  0.41   ;
2.0 -0.040 ;  4.0  3.2  -6.567  0.0  "B2" ;  2.0 -0.040 ;
3.0  3.78 ;
2.0 -0.080 ;  4.0  3.2 -13.134  0.0  "B3" ;  2.0 -0.080 ;
3.0  0.39   ;
```



MADX

- Most commonly used optics software, at CERN and worldwide
- C++ style input, calculations possible
- Optimized for use with Twiss parameters (synchrotrons)
- Use of matrix multiplication formalism
- Can perform matching
- Has tracking capability (Track module, PTC)
- Can produce survey output

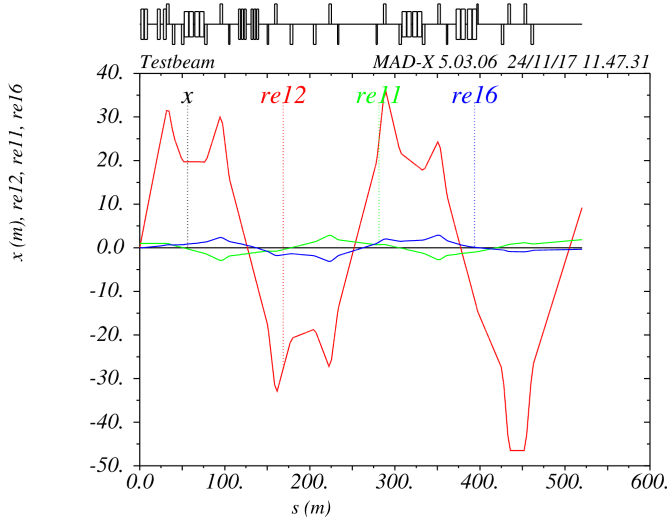
```
// define lengths of elements

l_quad1 = 3.00000;
l_quad2 = 2.99000;
l_quad3 = 1.49000;
l_quad4 = 2.94800;

l_bend1 = 3.60000 ;
l_bend2 = 3.20000 ;
l_bend3 = 5.00000 ;
l_bend4 = 2.50000 ;

// define quadrupole strengths


k1_quad1 = 43.2884 / (l_quad1*Brho);
k1_quad2 = -13.2930 / (l_quad2*Brho);
k1_quad3 = -18.5278 / (l_quad2*Brho) ;
k1_quad4 = -20.6160 / (l_quad2*Brho);
k1_quad5 = 49.3652 / (l_quad2*Brho) ;
k1_quad6 = 49.3652 / (l_quad2*Brho) ;
k1_quad6 = -34.9446 / (l_quad3*Brho);
k1_quad7 = 49.3758  / (l_quad2*Brho);
k1_quad8 = -20.6889 / (l_quad2*Brho);
k1_quad9 = 49.3653  / (l_quad2*Brho);
k1_quad10 = -20.6168 / (l_quad2*Brho);
k1_quad11 = -35.4599  / (l_quad3*Brho);
k1_quad12 =  12.5443 / (l_quad3*Brho);
k1_quad13 = -42.6260 / (l_quad2*Brho);
k1_quad14 = 34.0230 / (l_quad4*Brho) ;
k1_quad15 = 35.2822 / (l_quad4*Brho);
k1_quad16 = -41.7871 / (l_quad2*Brho);
```



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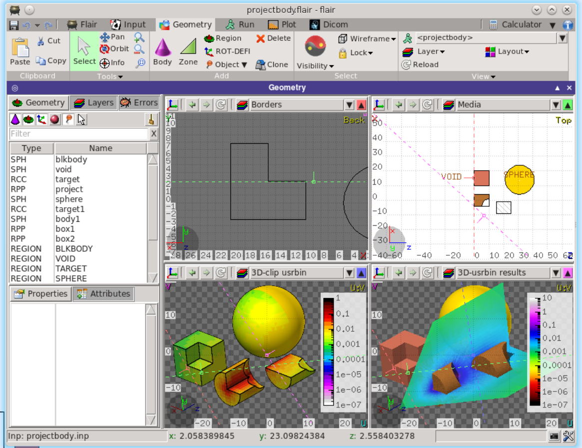
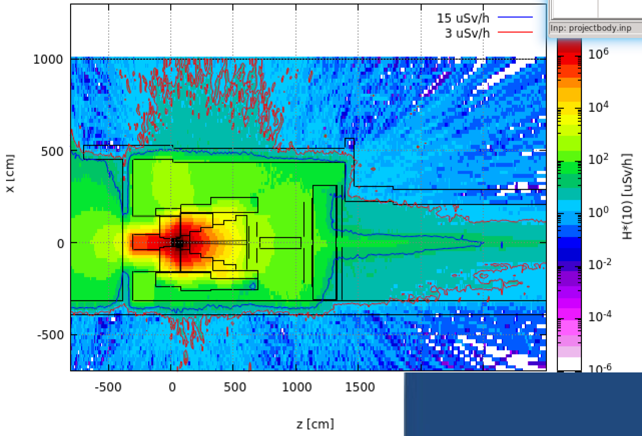
FLUKA

- Fortran based tool
- Large user community and support at CERN
  https://fluka.cern/
- Well calibrated
- Used by Radiation Protection
- Has Line Builder for beamline design
- Used for medical physics benchmarking
- GUI Flair for Hadrontherapy TPS





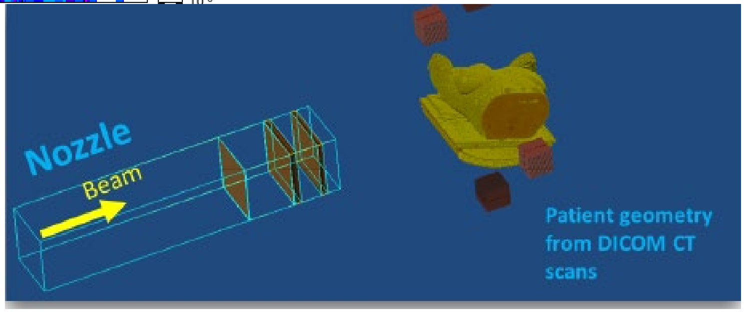


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Figure credit: C. Cuccagna (TERA Foundation)

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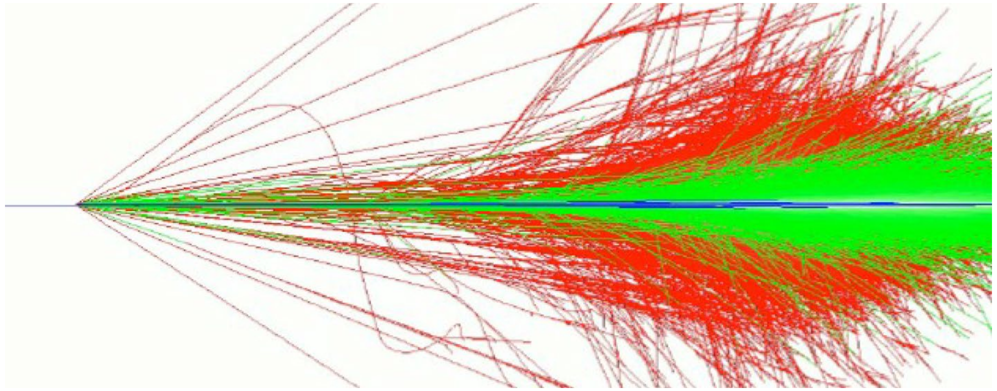
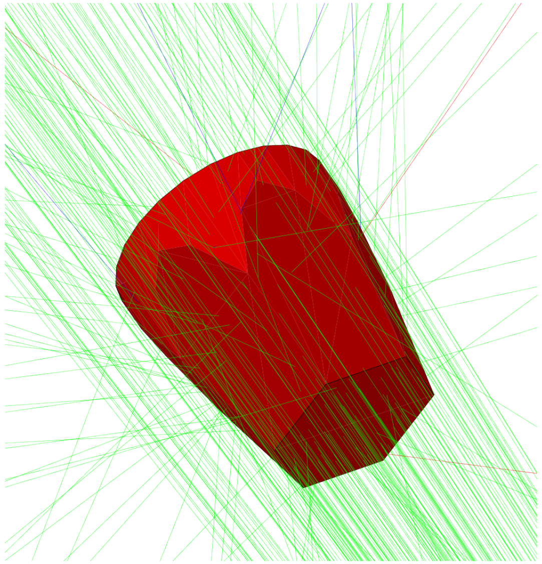
GEANT4
A SIMULATION TOOLKIT

- Developed in C++
- Open source
- Large worldwide user community
- Mostly used by groups designing detectors
- Used for medical physics benchmarking
- Serves as basis for several accelerator physics programs, such as TOPAS, G4Beamline and BDSIM





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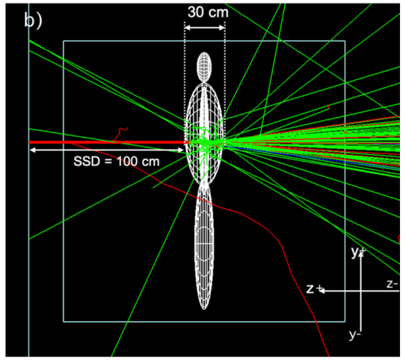
G4beamline

BDSIM Beam Delivery Simulation

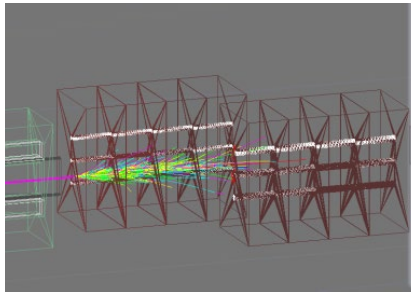
TOPAS

- TOPAS often used for simulation of beam delivery, nozzle, collimation and dose calculation in patient tissue
- All three codes use Geant4 to simulate the beam-matter interaction
- One can generate BDSIM input from MADX output
- BDSIM has been used for medical facility simulation (IBA, PSI), but not for treatment planning

TOPAS



G4Beamline



BDSIM

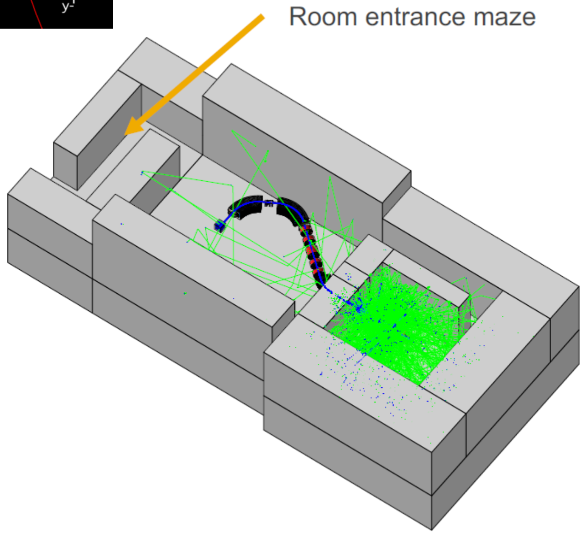


Figure credit: C. Hernalsteens (IBA), J. Bateman (Oxford), M. Dosanjh (Oxford)

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partrec

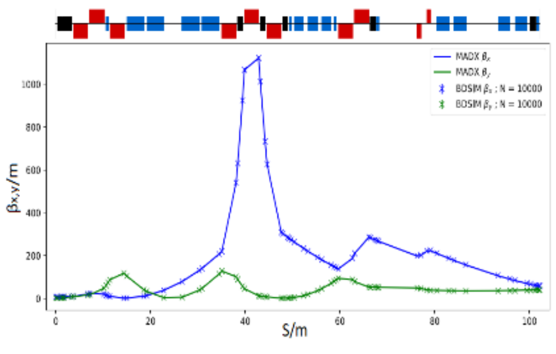
How to select the right code?

- Determine what are the primary physical effects in the simulations, and what **functionality** the code must have.
- Is there a **know-how** and a **support** team responsible for maintenance and upgrades of the new software, which you could contact?
- There is a large user **community** for the software, preferably at your lab / university
- What **interfaces** to other groups and software packages do you need?

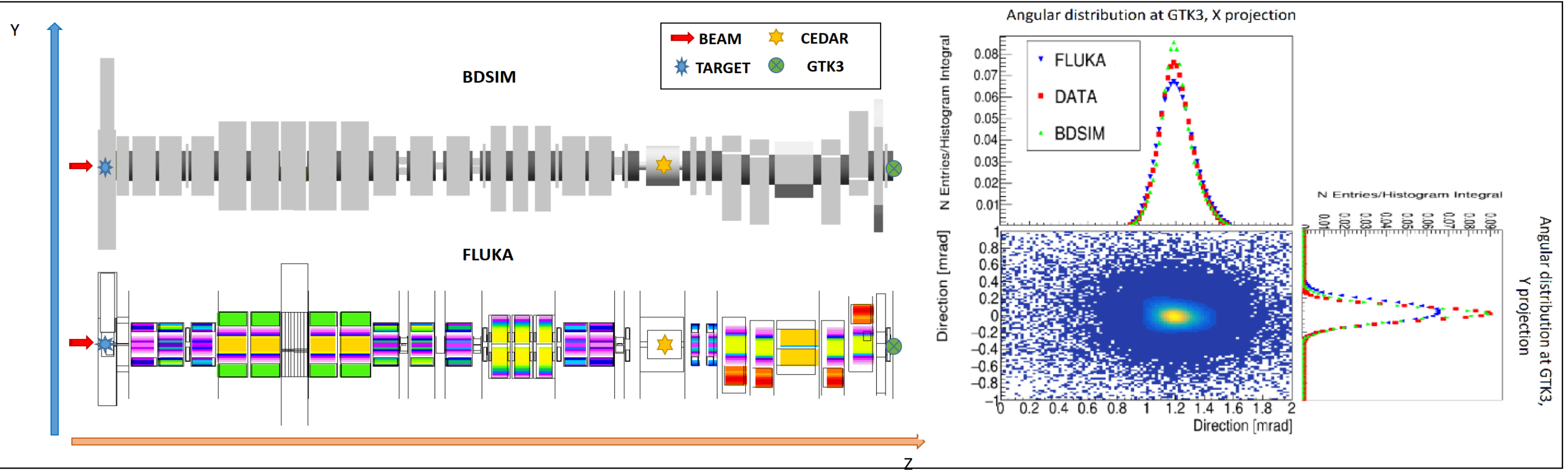
Benchmarking

- Some models can be adapted in several codes.
- Why? In order to
  - **<u>Avoid errors</u>** in implementation
  - **<u>Cross-calibrate</u>** the physics models of different codes
  - Have the same beam line model with **<u>different interfaces</u>**, e.g. to detector groups (Geant4-type) and RP (FLUKA-type)

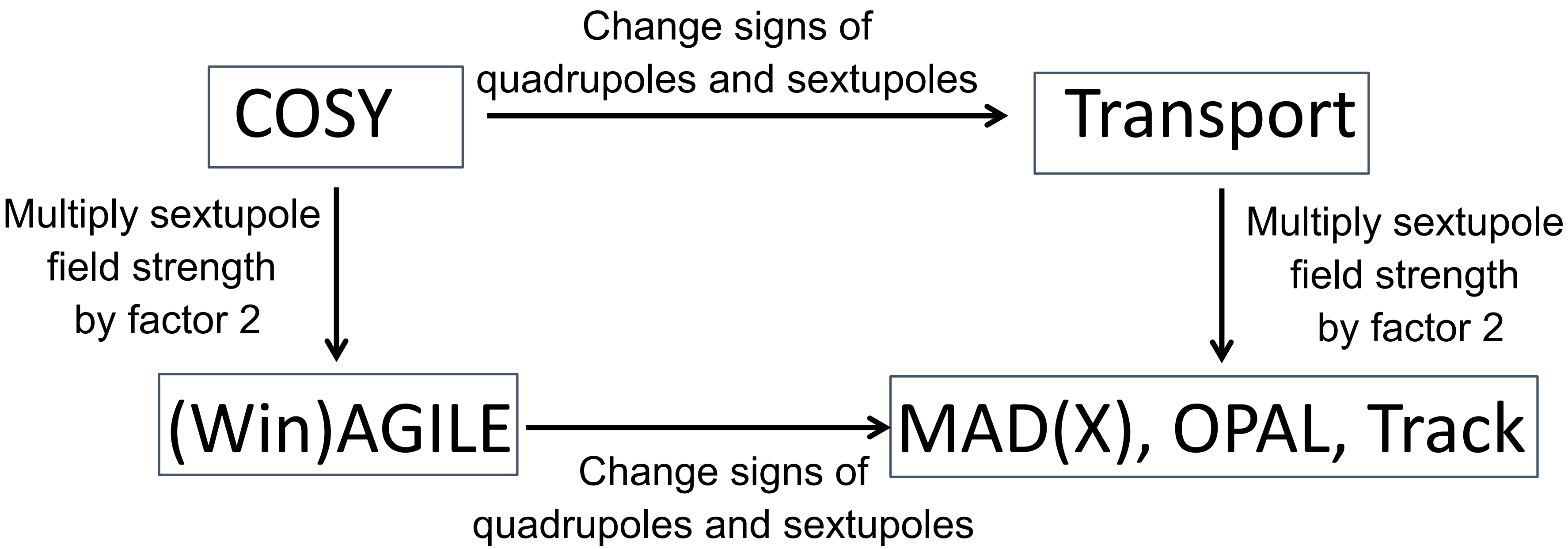
BDSIM vs MADX:

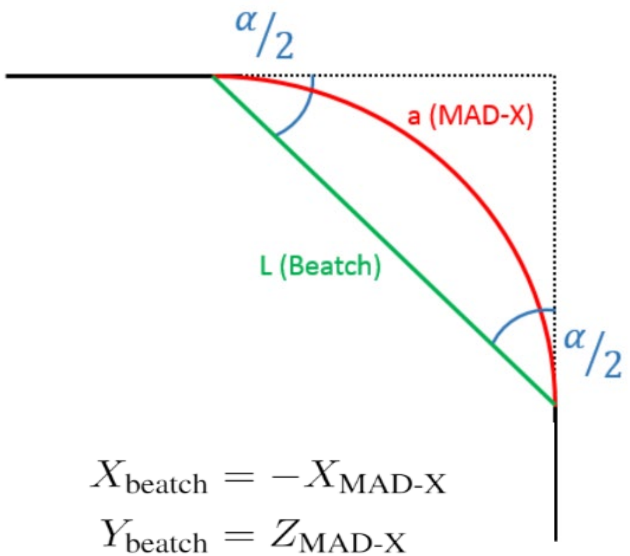


BDSIM vs FLUKA:



Beware of Conventions!





$$X_{\text{beatch}} = -X_{\text{MAD-X}}$$
$$Y_{\text{beatch}} = Z_{\text{MAD-X}}$$
$$Z_{\text{beatch}} = Y_{\text{MAD-X}}$$
$$\theta_{\text{h,beatch}} = \theta_{\text{MAD-X}} + \frac{\pi}{2}$$
$$\theta_{\text{v,beatch}} = \phi_{\text{MAD-X}}$$
$$\alpha_{\text{beatch}} = -\alpha_{\text{MAD-X}}$$
$$\psi_{\text{e,beatch}} \rightarrow -\psi_{\text{e,MAD-X}}$$

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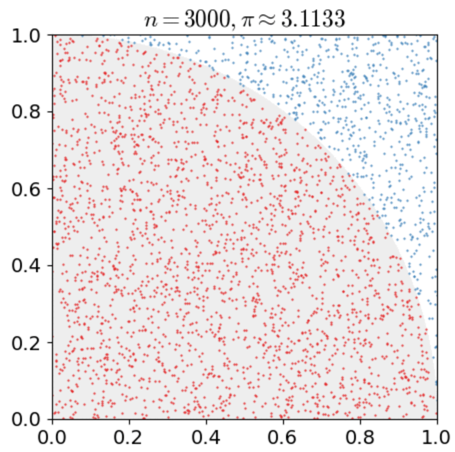
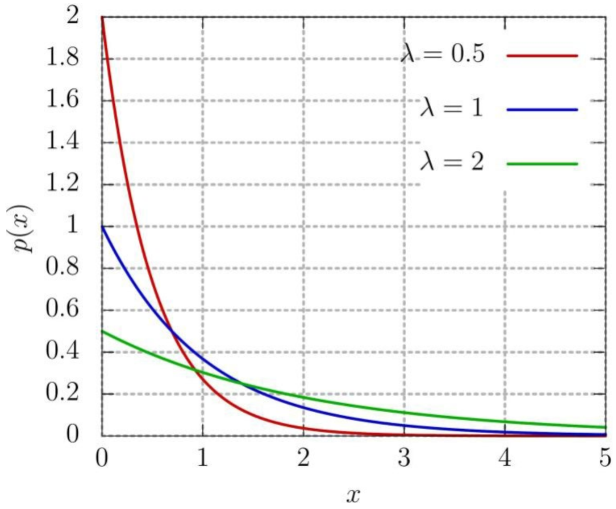
Summary

- Statistical processes determine a big share of high energy particle behaviour
- Monte-Carlo methods are an established tool to simulate those processes
- A number of codes exists to perform different types of Monte-Carlo simulations





Thank you for your attention!
Questions?

Sources:

- “Introduction to the Monte Carlo simulation of radiation transport” by F. Cerutti et.al. (CERN)
- “Probability, statistics, and data analysis” by F. Salvat Pujol (CERN)
- D. Ratner (SLAC)
- J. Holmes, S. Henderson, Y. Zhang (USPAS)