Istituto Nazionale di Fisica Nucleare
LABORATORI NAZIONALI DI LEGNARO

Laboratori Nazionali di Legnaro – INFN

Validation of a biophysical model for the radiobiology of TRT

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Motivation of the model

How to assess the efficacy of a Targeted Radionuclide Therapy (TRT)

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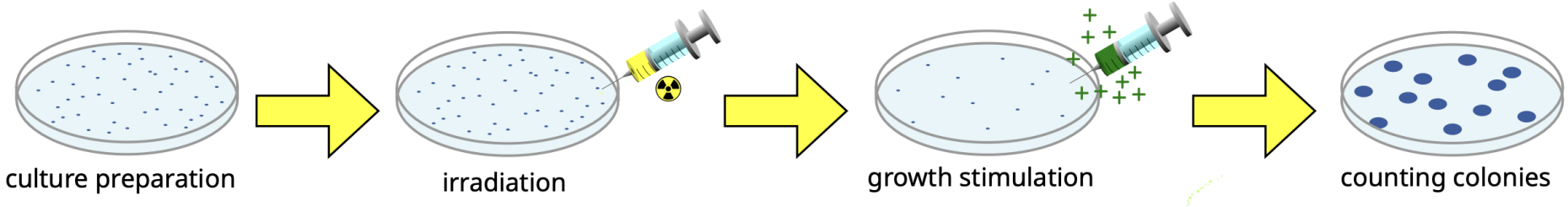
Cell survival trial



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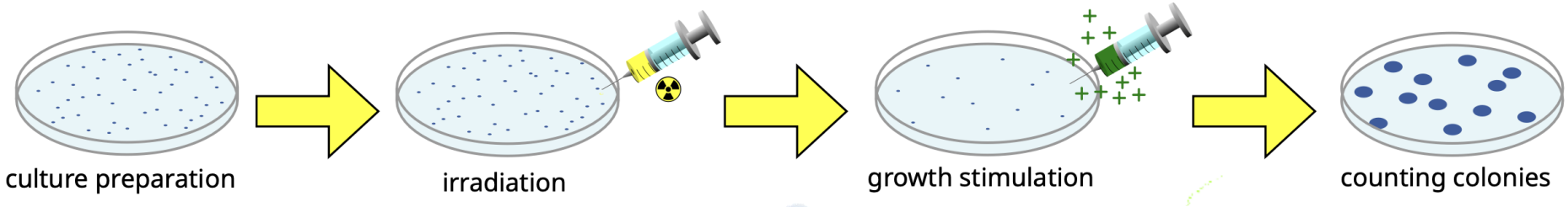

How the molecular kinetics and the number of cells affect the radiation delivery to cells

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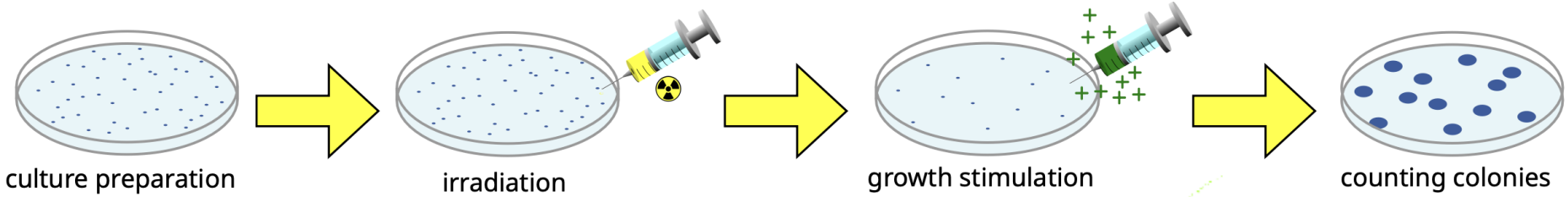
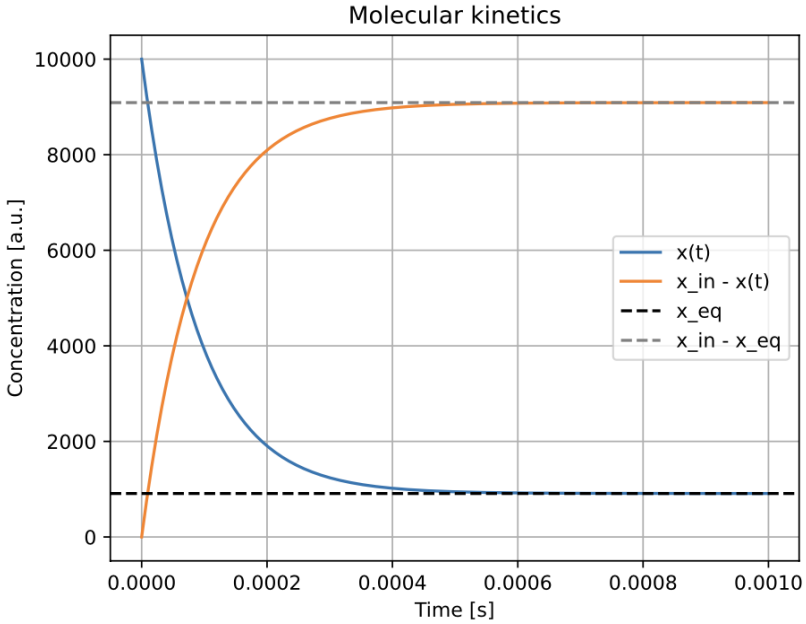


How the molecular kinetics and the number of cells affect the radiation delivery to cells

Develop a mathematical model

Assumptions

Molecular kinetics act at a lower timescale than the processes affecting the cell population and can be assumed in equilibrium for a fixed number of cells.



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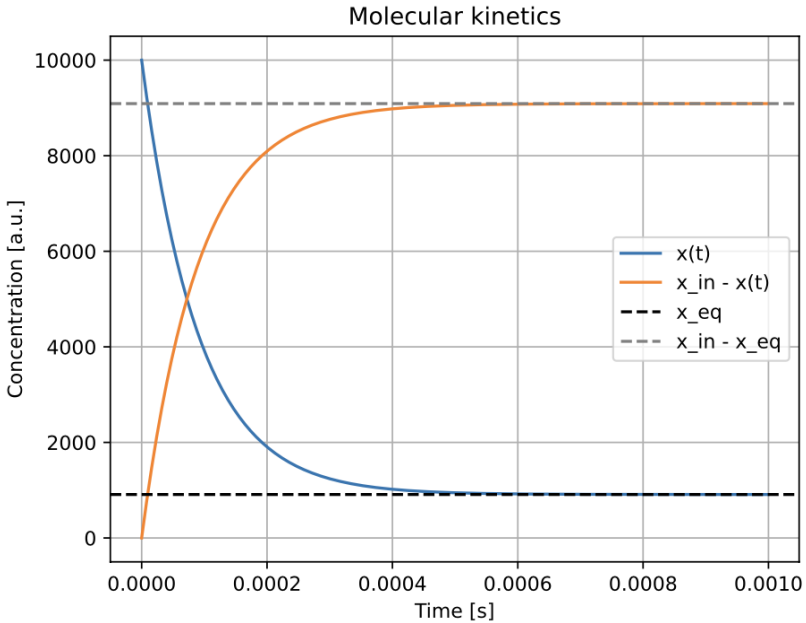
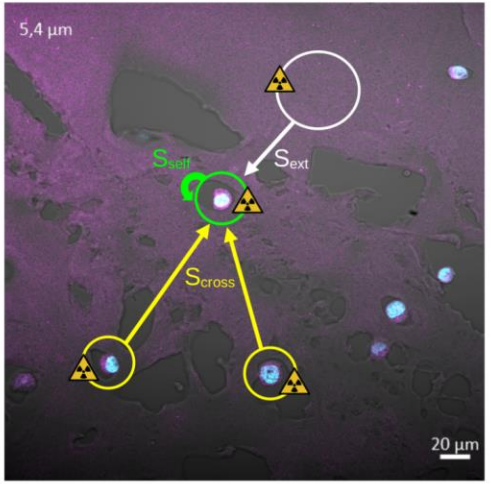
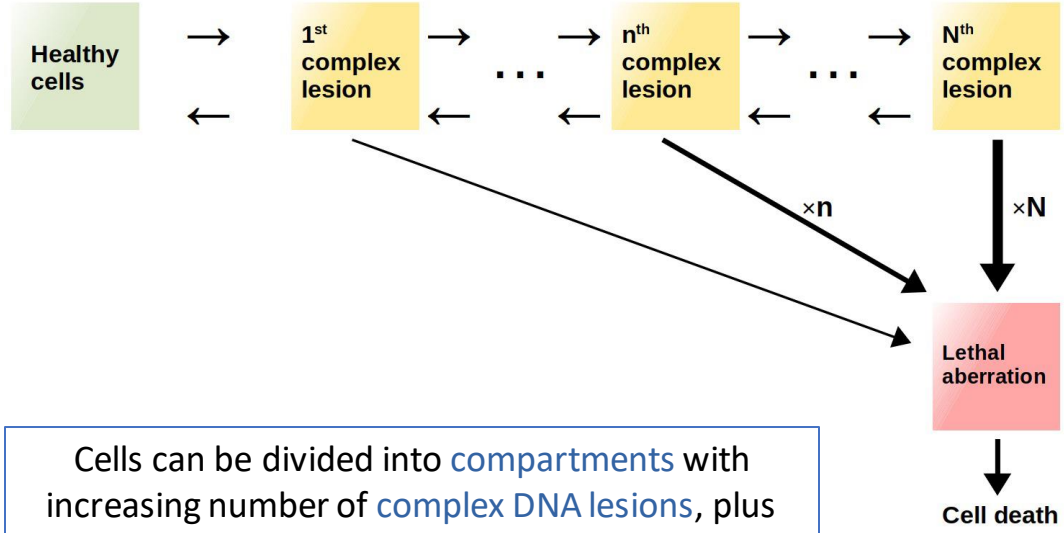




DNA damage will have 3 components:

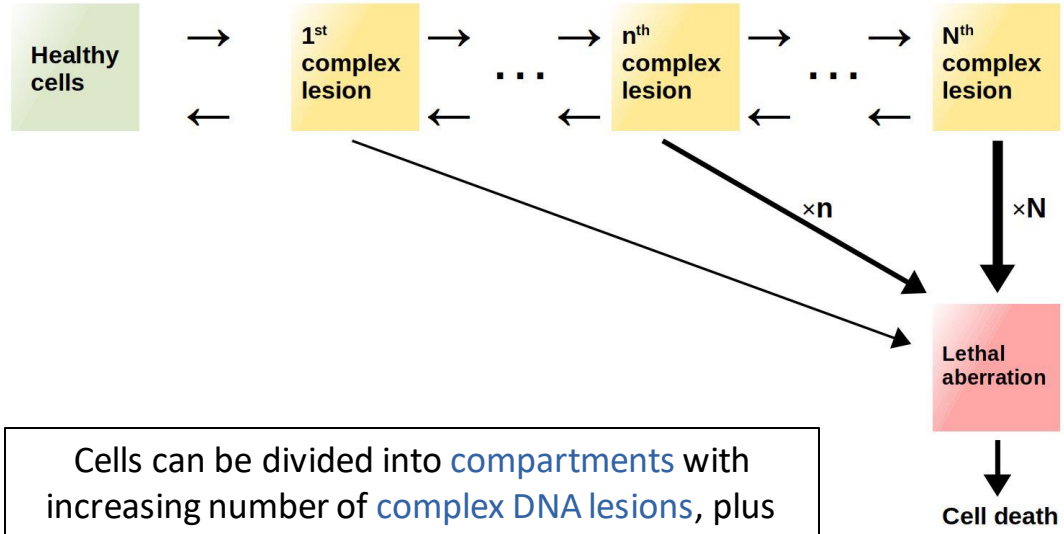
- self-absorbed
- crossfire
- culture medium

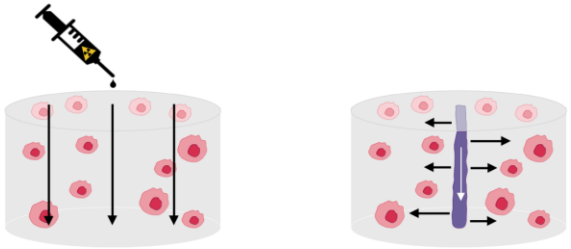
Assumptions



Cells can be divided into compartments with increasing number of complex DNA lesions, plus another one for cells with lethal aberrations. Undamaged cells can reproduce.

Assumptions

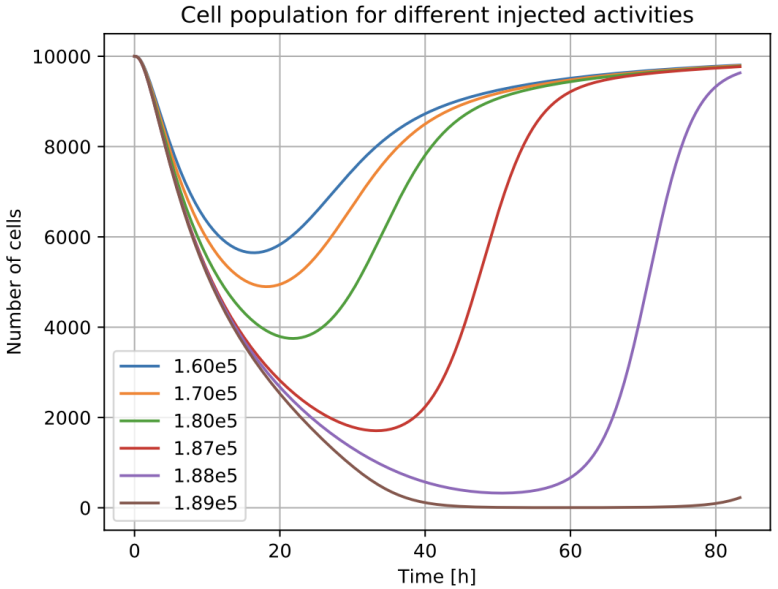




Cells can be divided into compartments with increasing number of complex DNA lesions, plus another one for cells with lethal aberrations. Undamaged cells can reproduce.

Non-uniform activity distributions can be modelled with the addition of a spatial variable depending on scaffold geometry and injection mode.

Validation of the model



Reference: ^{125}I-labelled drugs were used on SK-OV-3 and A-431 cancer cell lines.

The model was applied considering the parameters given in the article, then varying the missing ones (complex lesions per unit dose and misrepair probability, δ and k_a) in order to get the best agreement between model outcomes and data.

From the model, the minimum number of cells reached by the curve is taken as the surviving fraction and compared with the experimental value.

J. P. Pouget et Al., 'Cell membrane is a more sensitive target than cytoplasm to dense ionization produced by auger electrons'. Radiat Res. 2008 Aug;170(2):192-200.

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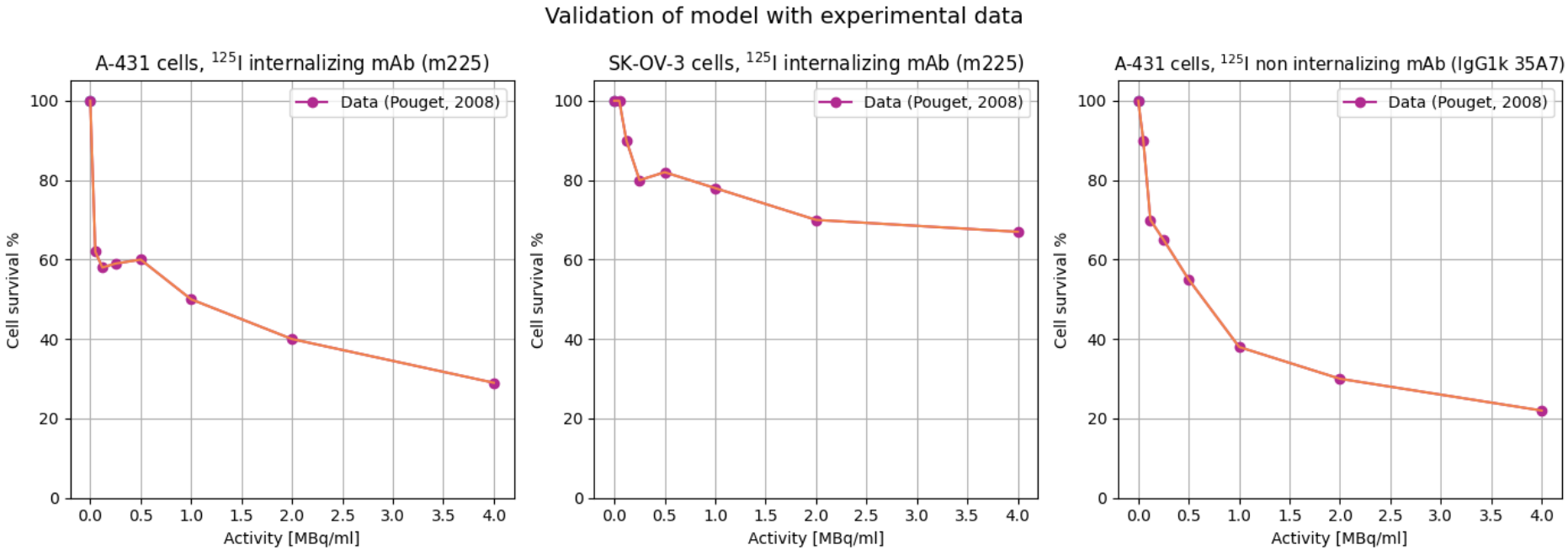

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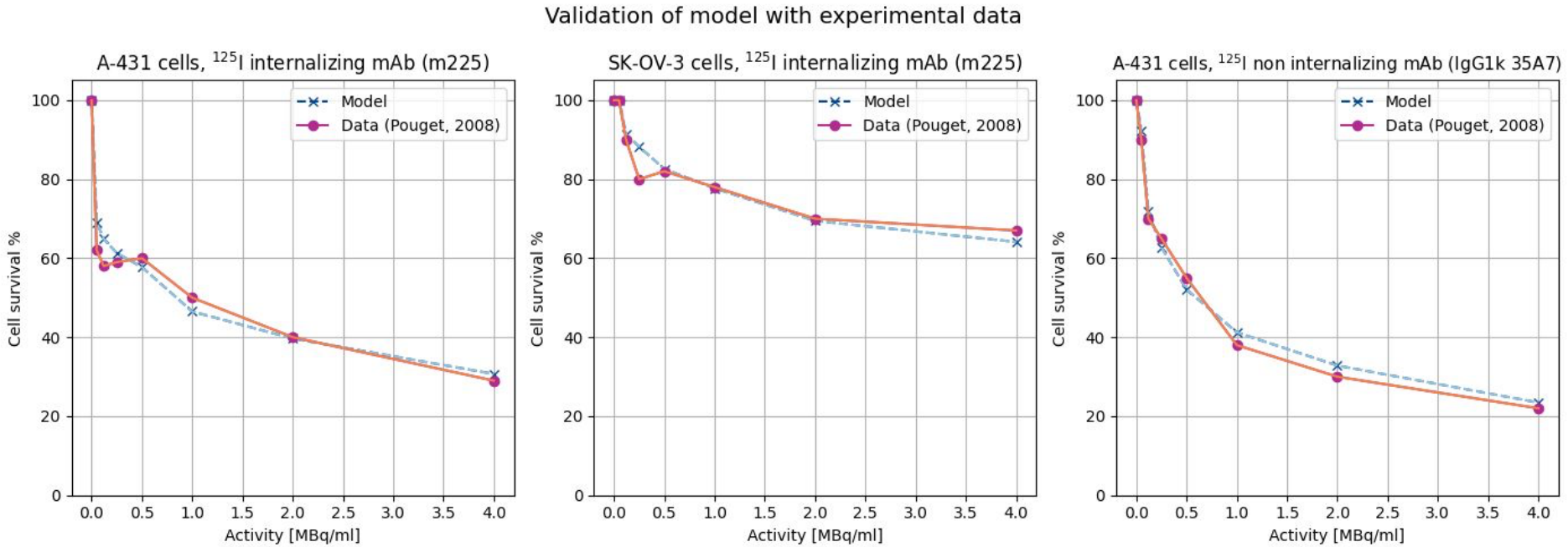


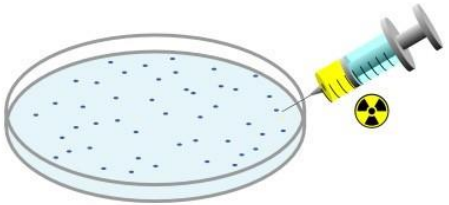
The experimental results are reproduced quite well with δ=0.006 1/Gy and k_a=0.01. Different values of k_a do not reproduce the experimental slope.

Updates on future work

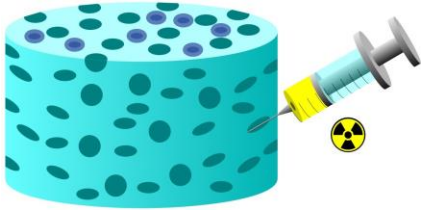
Cell survival studies

Study the cell survival in the ADMIRAL scheduled experiments

2D cultures

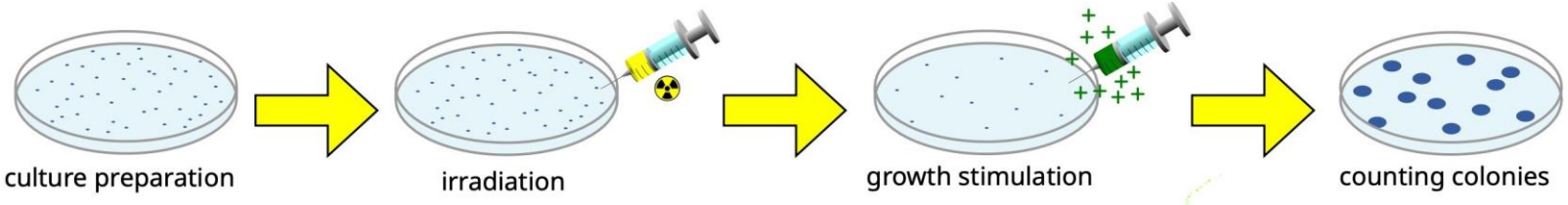


3D scaffolds



Clonogenic assay

2D geometry



3D geometry

Need to develop an apposite protocol

The plan of action for 3D studies

Use a DLP printer to produce 3D scaffolds with cells inside

Work on 2 sides in parallel

Cold station (Trento)

Studies on cells without radioactive materials

Hot station (Pavia)

Studies on cells with ^{111}Ag

Thanks for the attention