Practical Aspects of Radionuclide Production

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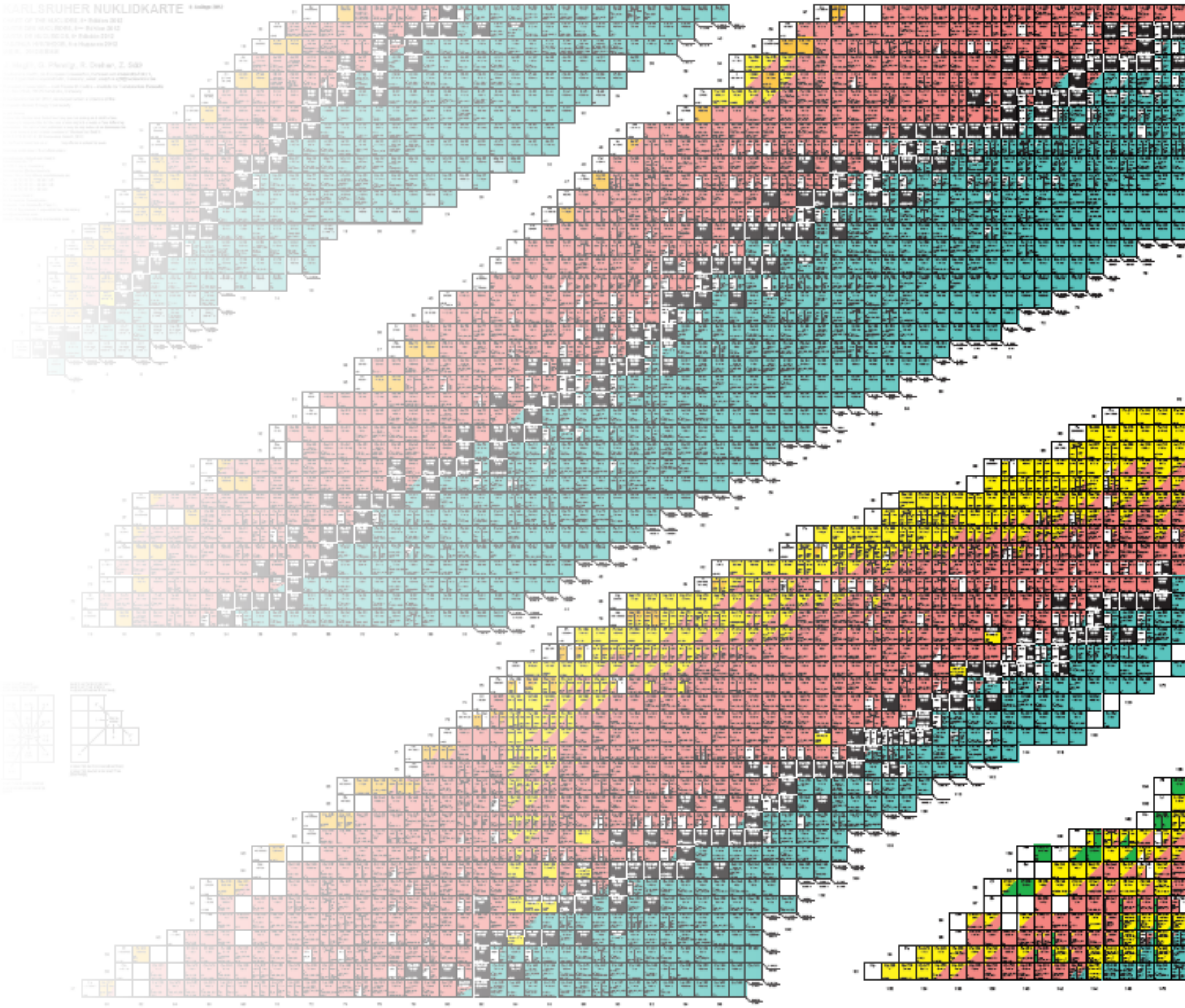
Isotopes

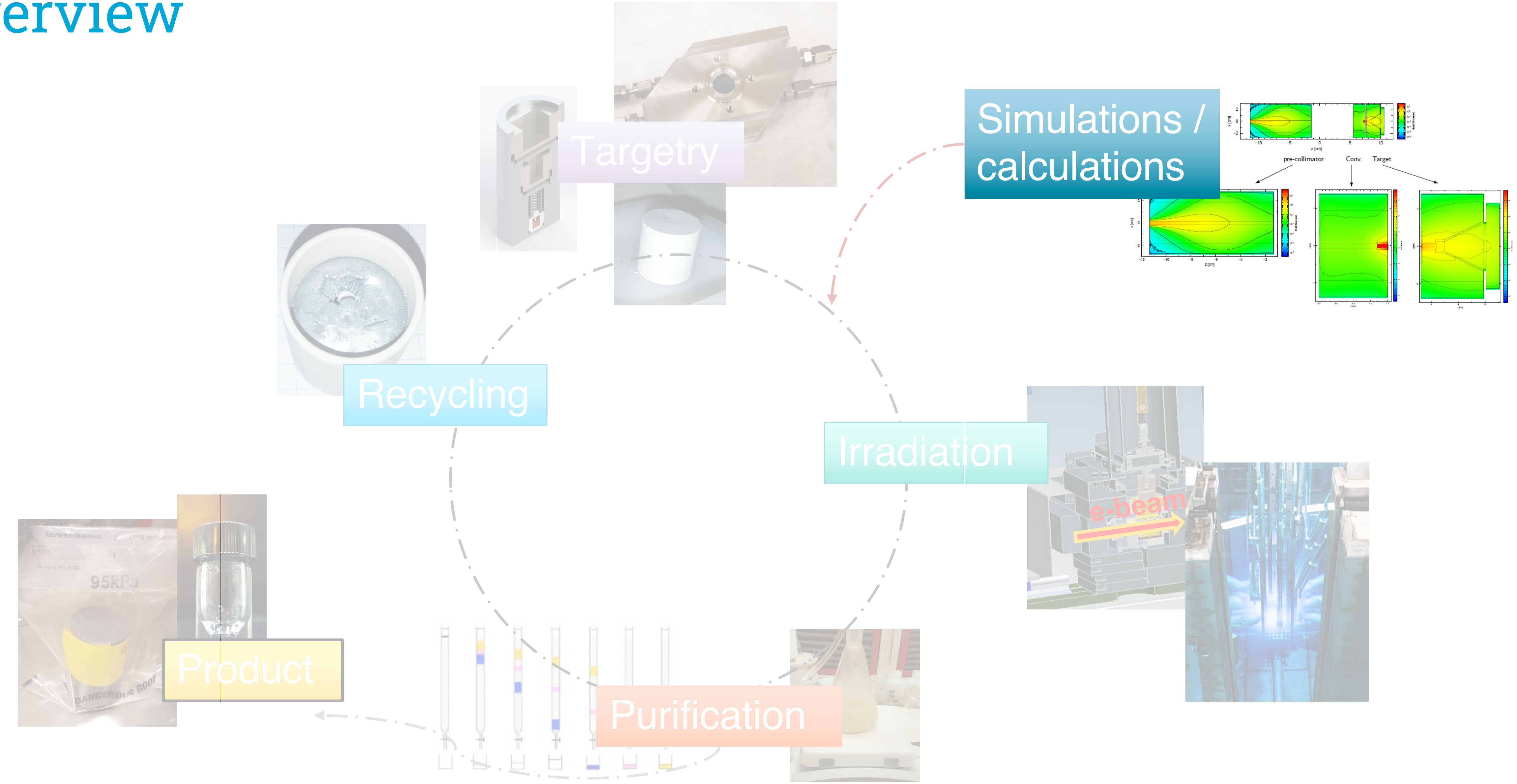
> 3000 isotopes

applications today:

- nuclear medicine
- drug metabolism studies
- study of essential elements
- sterilization of food / medical instruments

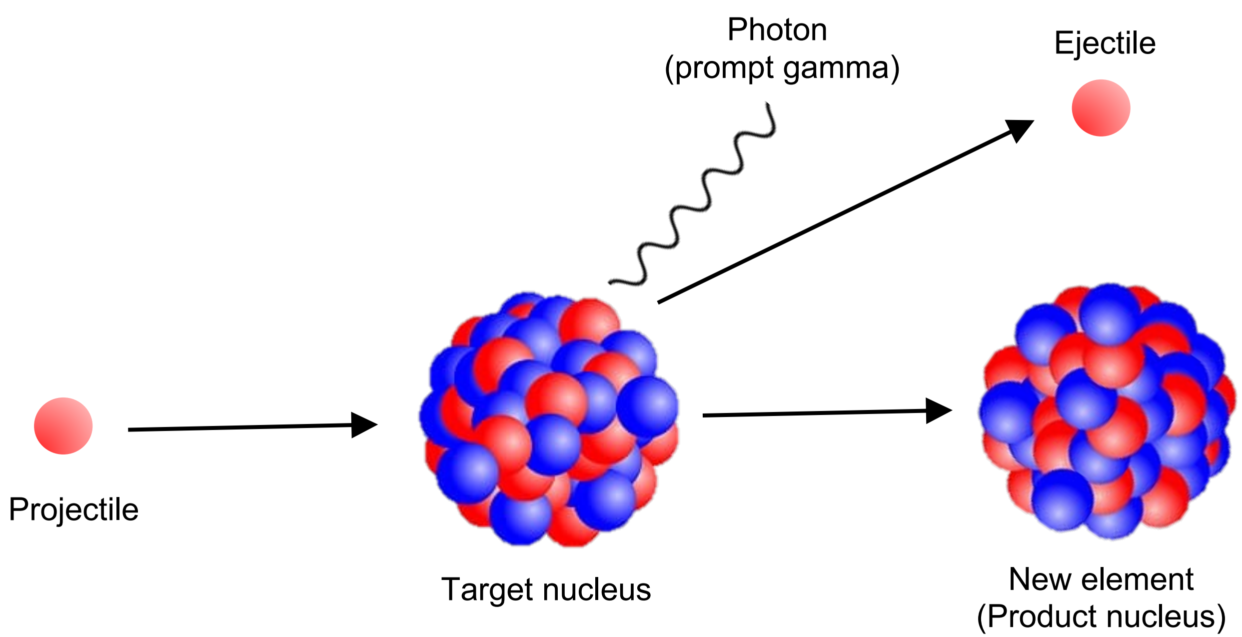


Overview


Targetry
Simulations / calculations
pre-collimator
Conv.
Target
Recycling
Irradiation
e-beam
Product
95kPa
Purification

Nuclear reactions

Nomenclature:

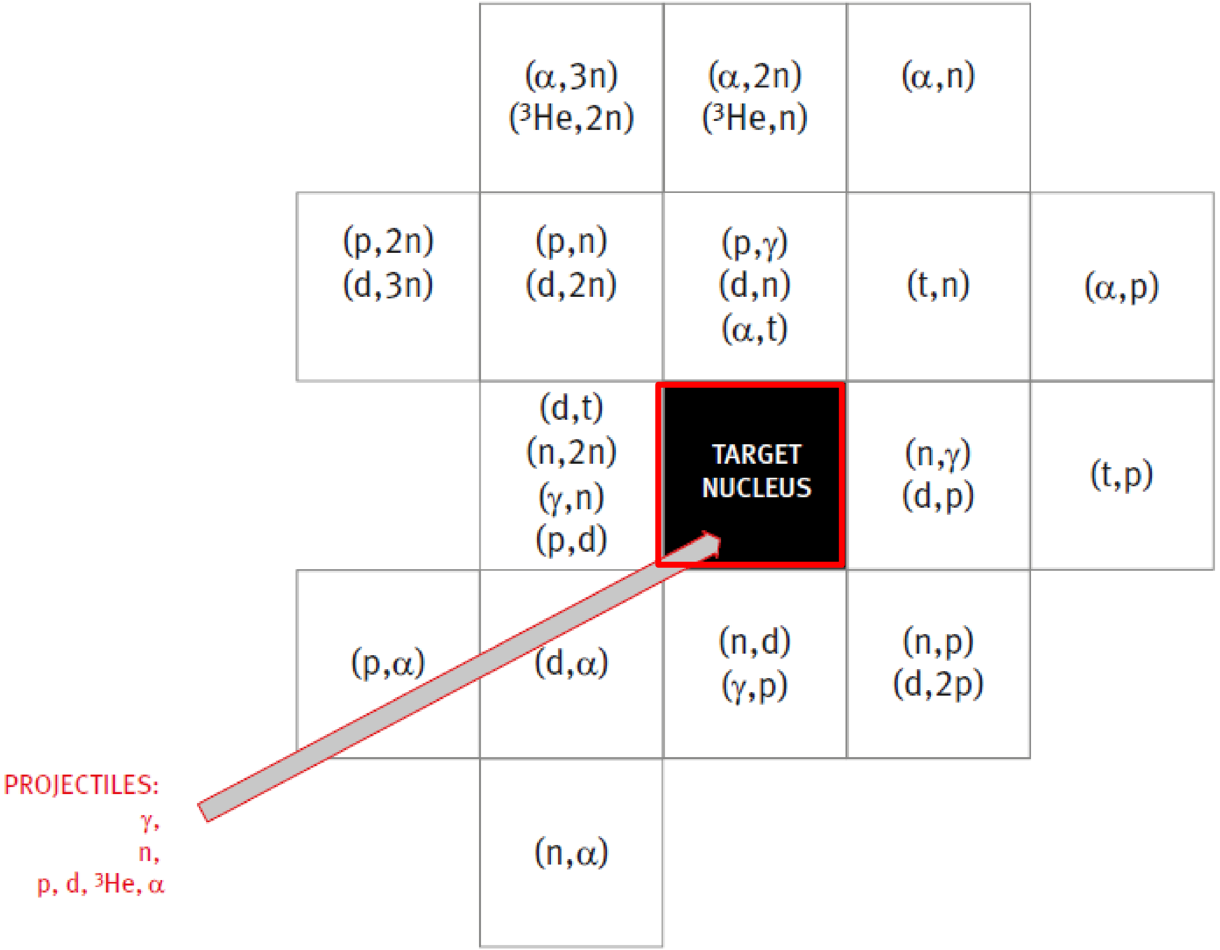


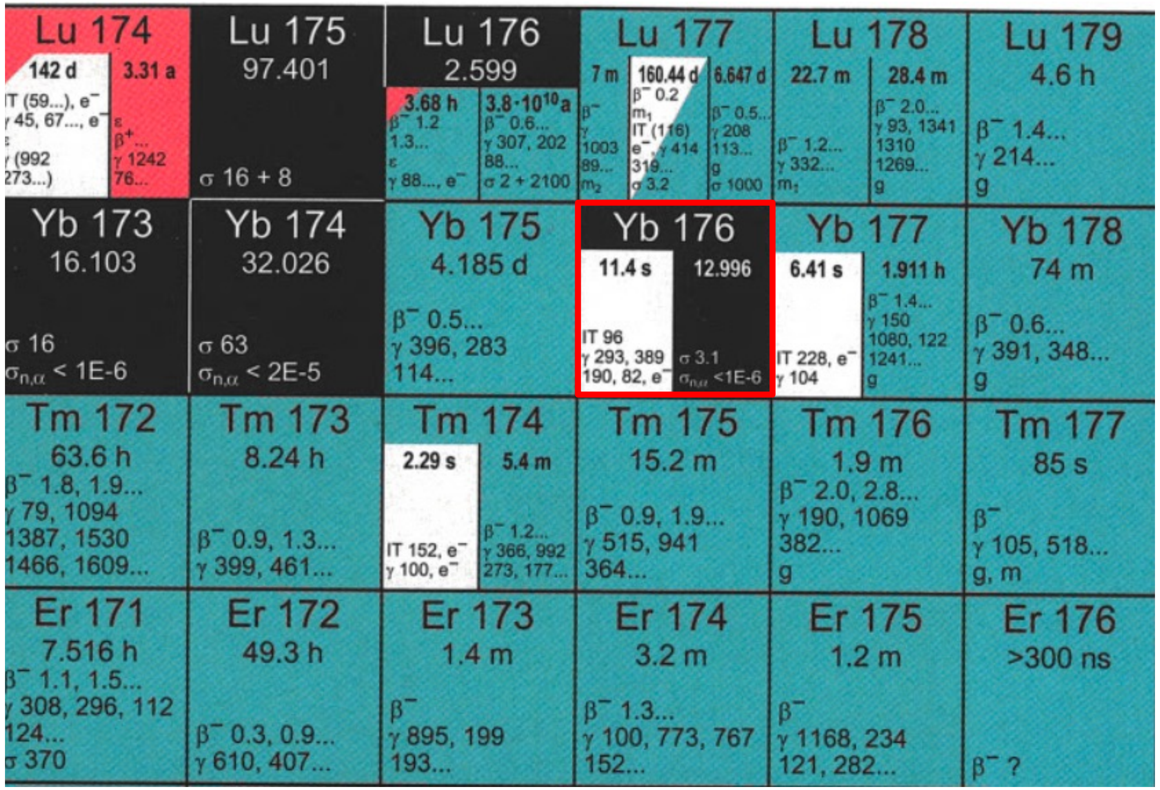
Projectile: a, Target: A, Product: B, Ejectile: b

$$a + A \rightarrow B + b$$

$$A(a,b)B$$

Possible production reactions





How much can be produced?

The produced activity (A_B) after irradiation depends on:

- **Flux (ϕ)** – Number of particles used for irradiation
- Number of **target atoms (N_A)**
- **Cross section (σ)** – Reaction probability

$$A_B \sim \varphi \cdot N_A \cdot \sigma$$

Always given as activity [Bq = decays per second]

Alternative unit: Curie [1 Ci = 3.7 x 10^{10} Bq]

Flux (φ)

$$A_B \sim \varphi \cdot N_A \cdot \sigma$$

Reactors: [neutrons·cm^{-2}·s^{-1}]

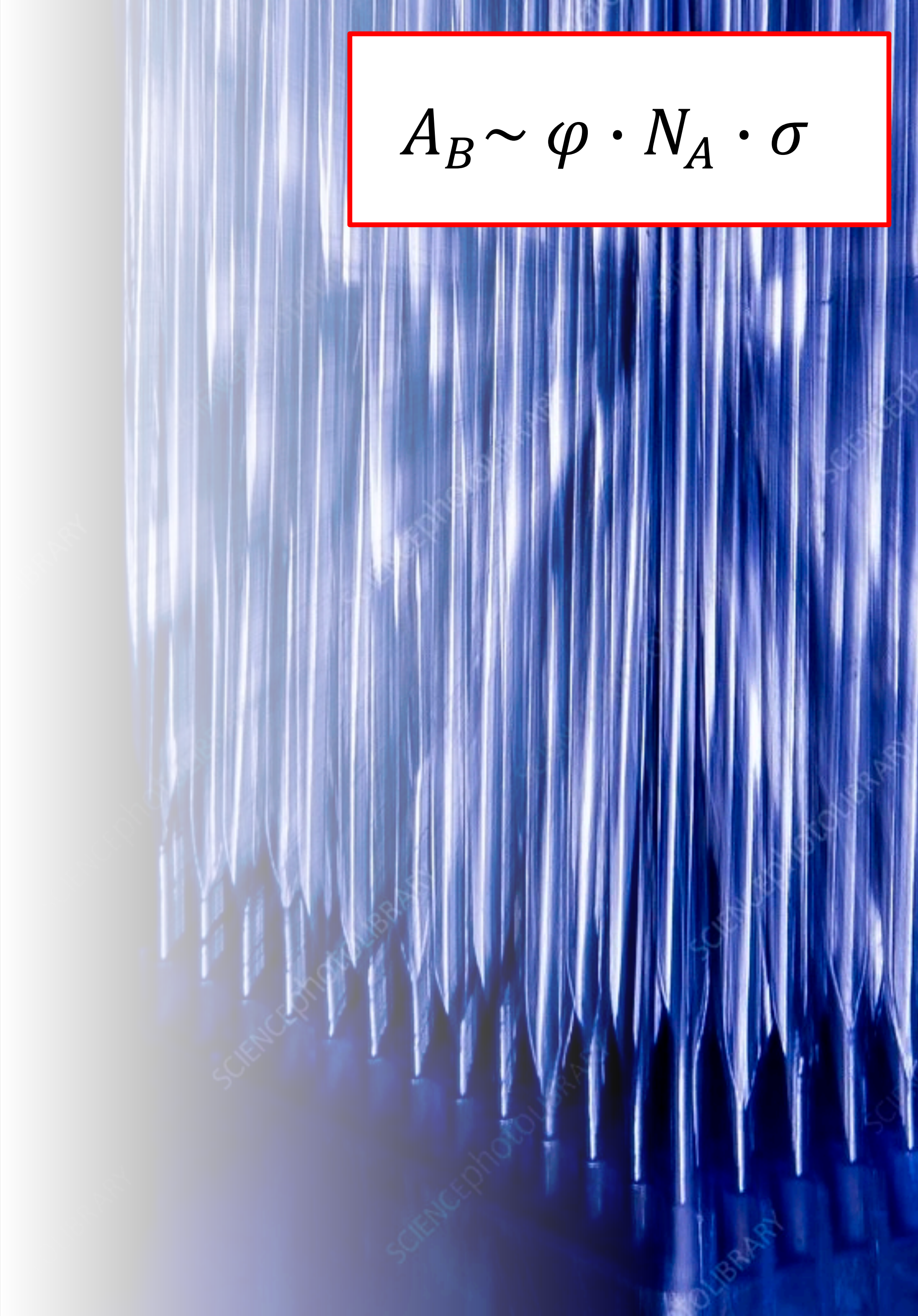
Thermal neutron flux:

- Research reactor: 10^{10} to 10^{13} n·cm^{-2}·s^{-1}
- Production reactor: 10^{14} to 10^{15} n·cm^{-2}·s^{-1}

Accelerators: [μA]

Proton flux in a medical cyclotron 20 μA – 300 μA

- 20 μA = 1.25·10^{14} protons/s
- $\mathrm{A(Ampere)} = \frac{\mathrm{C\ (Coulomb)}}{\mathrm{s\ (second)}}$; $1.6 \cdot 10^{-19}\,\mathrm{C/proton}$



Number of target atoms (N_t)

$$A_B \sim \varphi \cdot N_A \cdot \sigma$$

Mass of target

Isotopic abundance

Avogadro's constant

$$N_t = \frac{mh}{M} N_{Av}$$

Number of target atoms

Molar mass

Difference between reactors and accelerators:

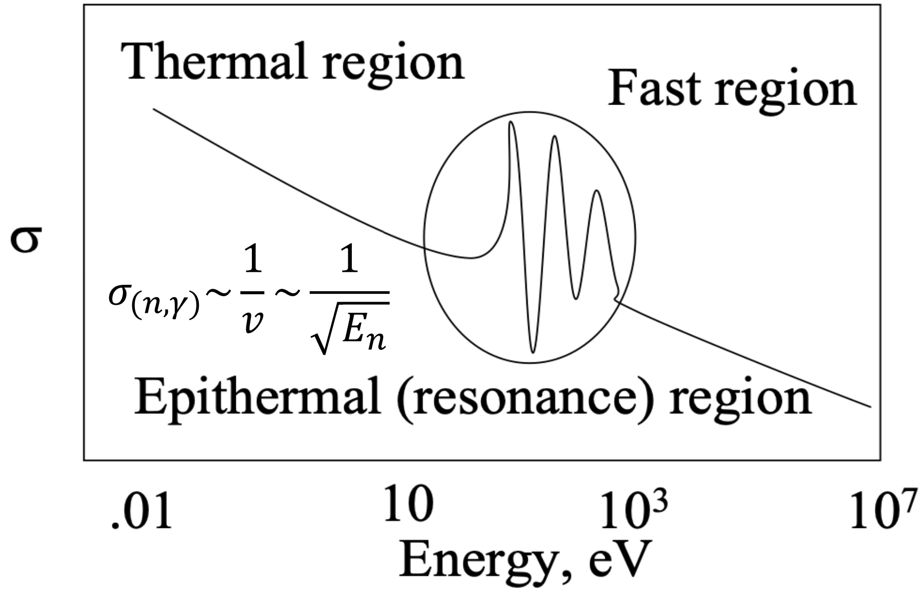
Reactor	Accelerator
Immersion of small target in sea of neutrons	Beam is generally smaller than target
• Φ = neutrons/cm²s • N_t = total number of atoms in target $N_t = \frac{mh}{M} N_{Av}$	• Φ = particles/s • N_t = atoms/area; i.e. [atoms/cm²] N_t = nr of atoms in irradiated volume $N_t = \frac{\rho \cdot V \cdot h}{M} \cdot N_{Av}$ per irradiated area $A = \pi \left(\frac{d}{2}\right)^2$

Cross section (σ)

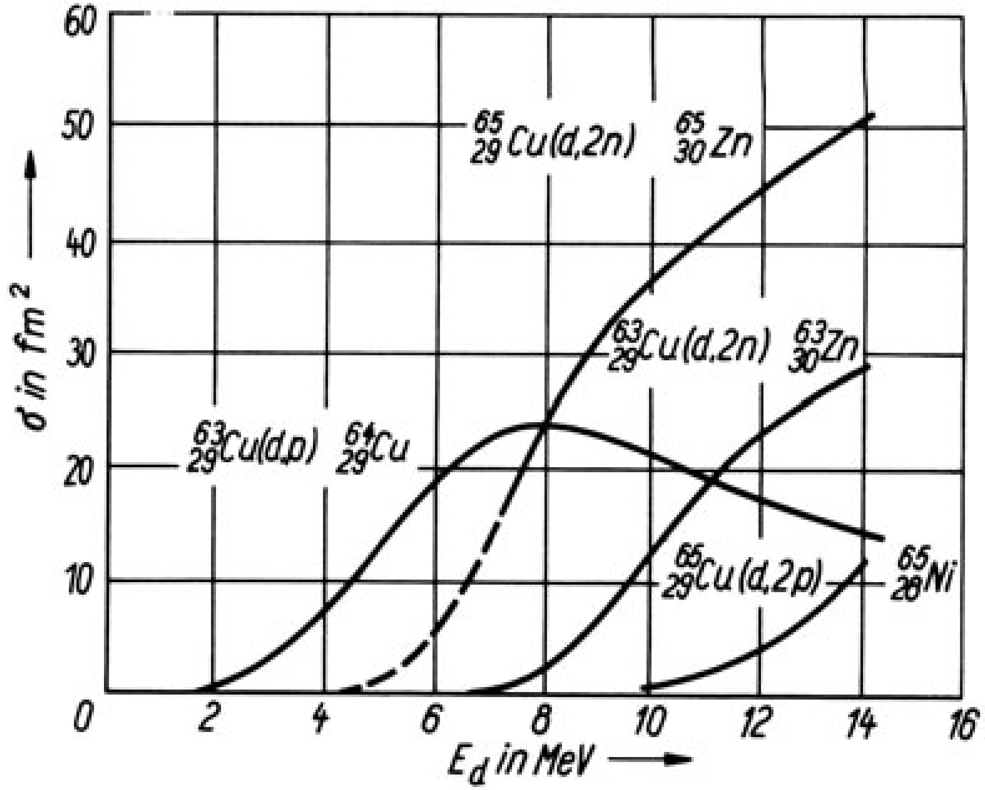
$$A_B \sim \varphi \cdot N_A \cdot \sigma$$

- Cross section: Reaction probability (σ)
- Unit: 1 barn = 100 fm^2 = 10^{-28} m^2 = 10^{-24} cm^2

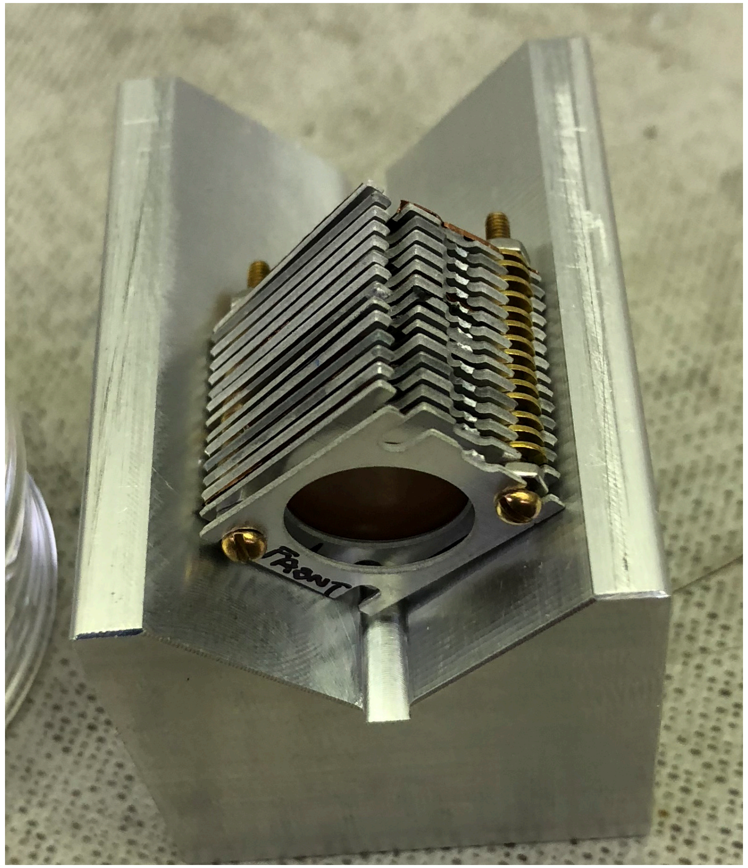
Cross section of neutron capture:



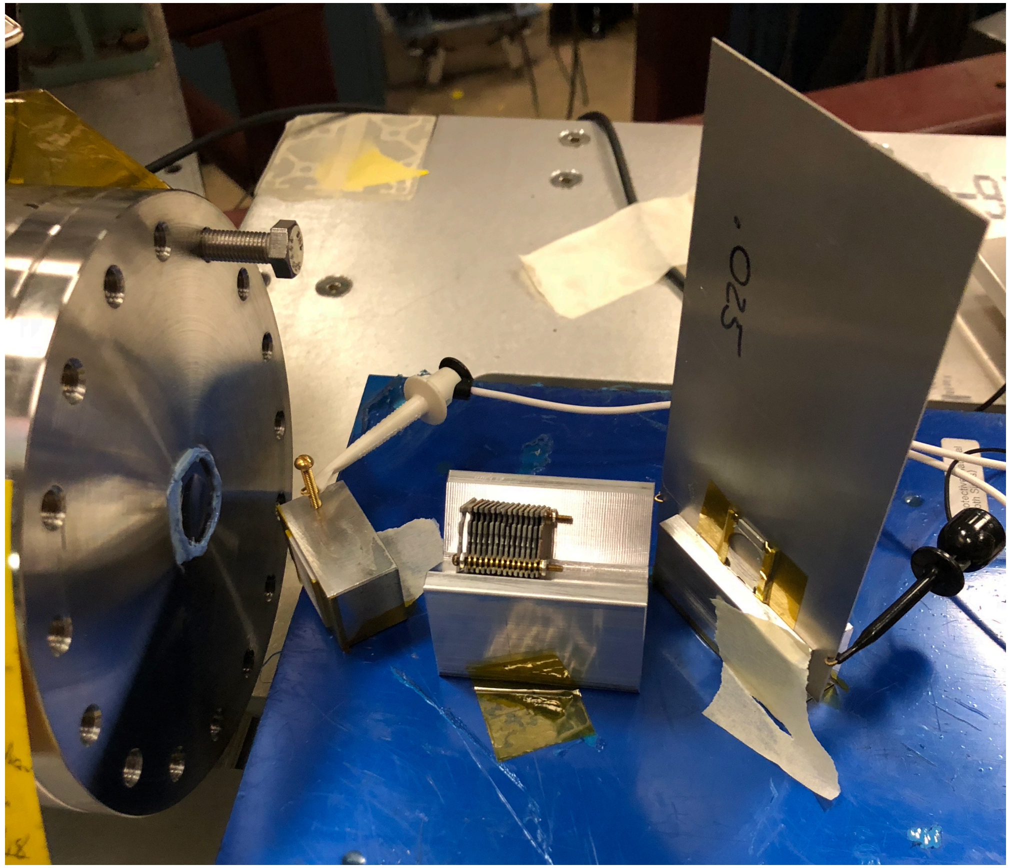
Cross section of charged particles:



Cross section determination – an experiment

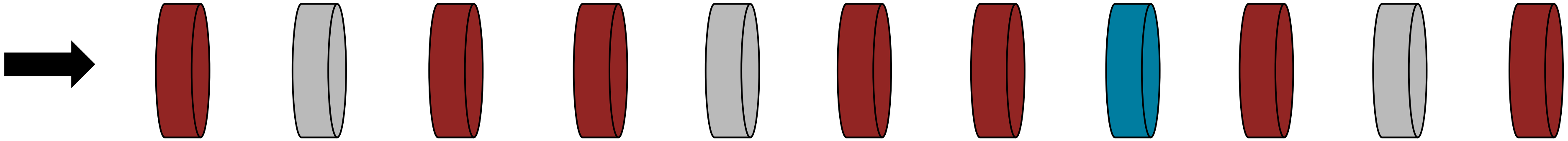


Target Stack for Cross Section Measurements



Irradiation Setup

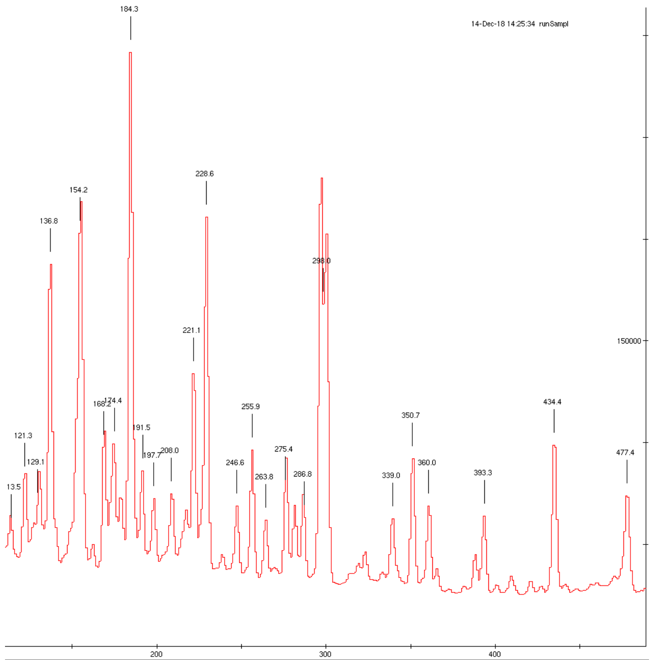
Cross section determination – an experiment



Foil	1	2	3	4	5	6	7	8	9	10	11
Metal	Cu	Ir	Cu	Cu	Ir	Cu	Cu	Re	Cu	Ir	Cu
E_α	36.35	**36.06**	36.00	35.50	**35.00**	34.95	34.60	**34.10**	34.05	**33.55**	33.50

Calculated cross section (mb) for given incoming alpha energy

Alpha Energy	^{192}Au	^{193}Au	^{194}Au
36.06	10.3	247.1	9.3
35.00	12.3	223.3	13.3
33.55	8.1	222.5	10.1
32.40	48.7	229.7	94.5



Yields of nuclear reactions

Decay of product has to be taken into account:

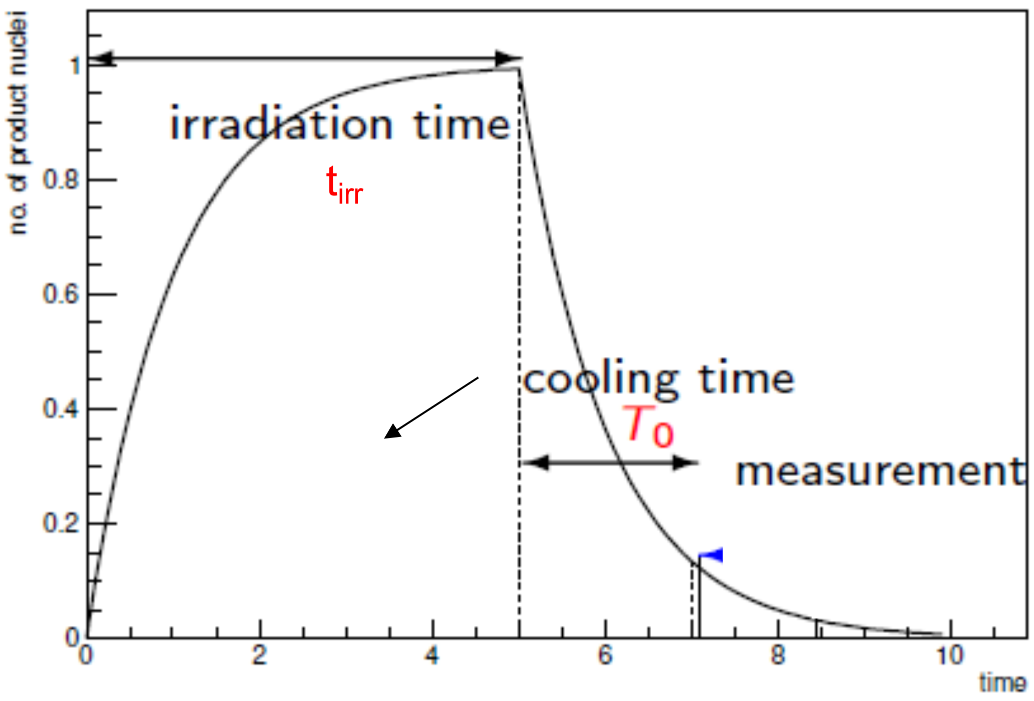
$$\left(\frac{dN_B}{dt}\right)_{Production} = \varphi\sigma N_A \qquad \left(\frac{dN_B}{dt}\right)_{Decay} = -\lambda N_B$$

$$\left(\frac{dN_B}{dt}\right)_{Total} = \varphi\sigma N_A - \lambda N_B \quad \Rightarrow \quad N_B = \frac{\varphi\sigma N_A}{\lambda}\left(1 - e^{-\lambda t_{irr}}\right)$$

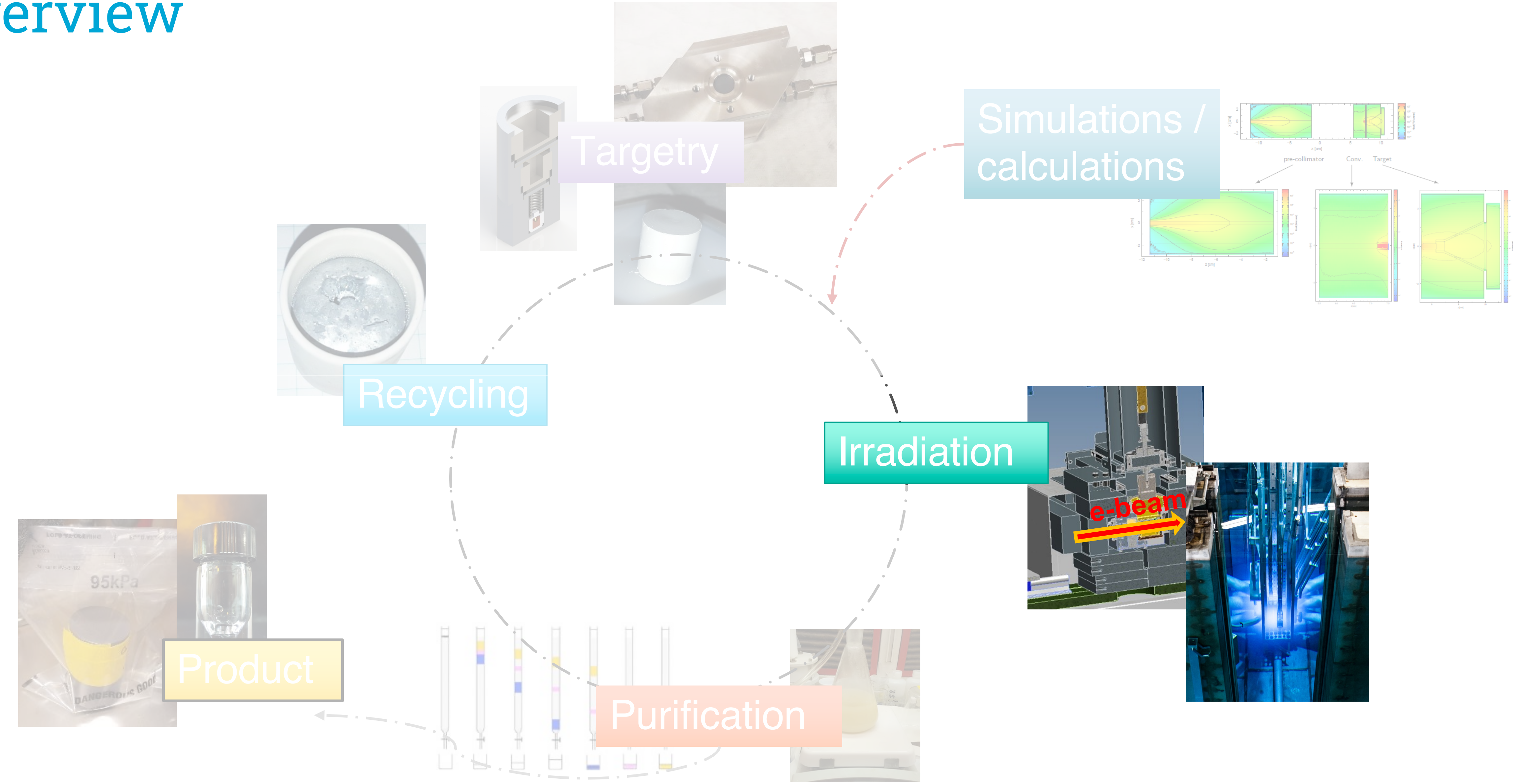
- Activity at end of irradiation:

$$A_B = \lambda N_B = \varphi\sigma N_A\left(1 - e^{-\lambda t_{irr}}\right)$$

- Take cooling time into account by multiplying A with $e^{-\lambda T_0}$



Overview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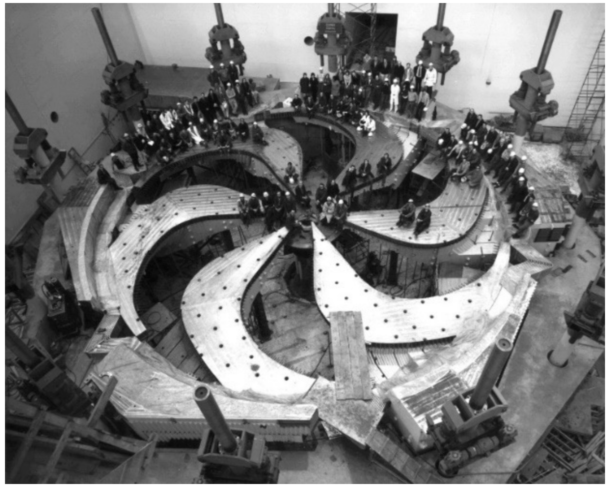
Production facilities

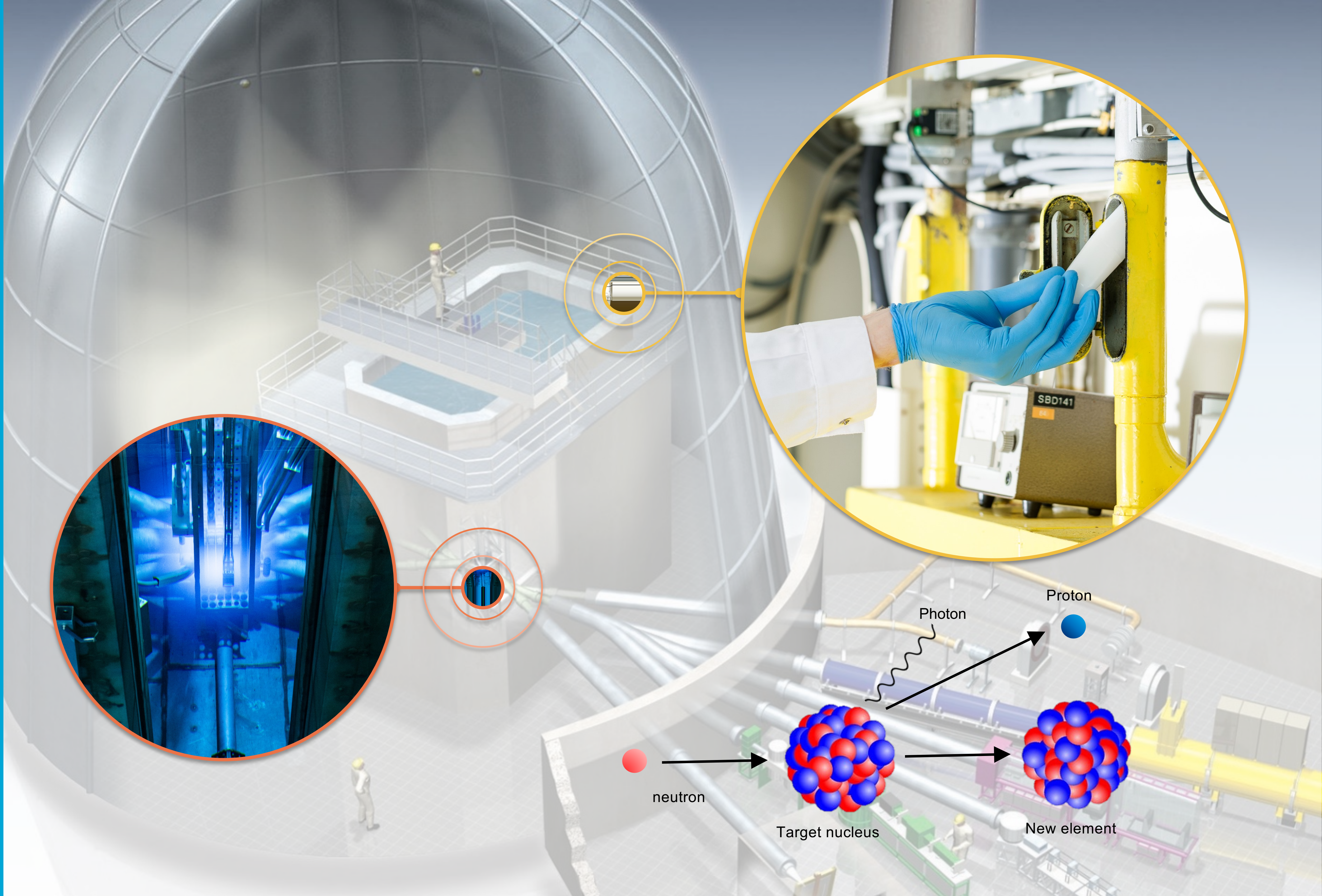
- Nuclear reactors
- Accelerators
  - Cyclotrons
  - Linear accelerators



Hoger onderwijs reactor (HOR)

- 2.3 MW pool-type research reactor
- Neutrons available for research:
  - Radio isotopes (α,β,γ)
  - Neutrons as probes
  - Positrons

- OYSTER-program finally finished: cold source installed in our nuclear reactor!



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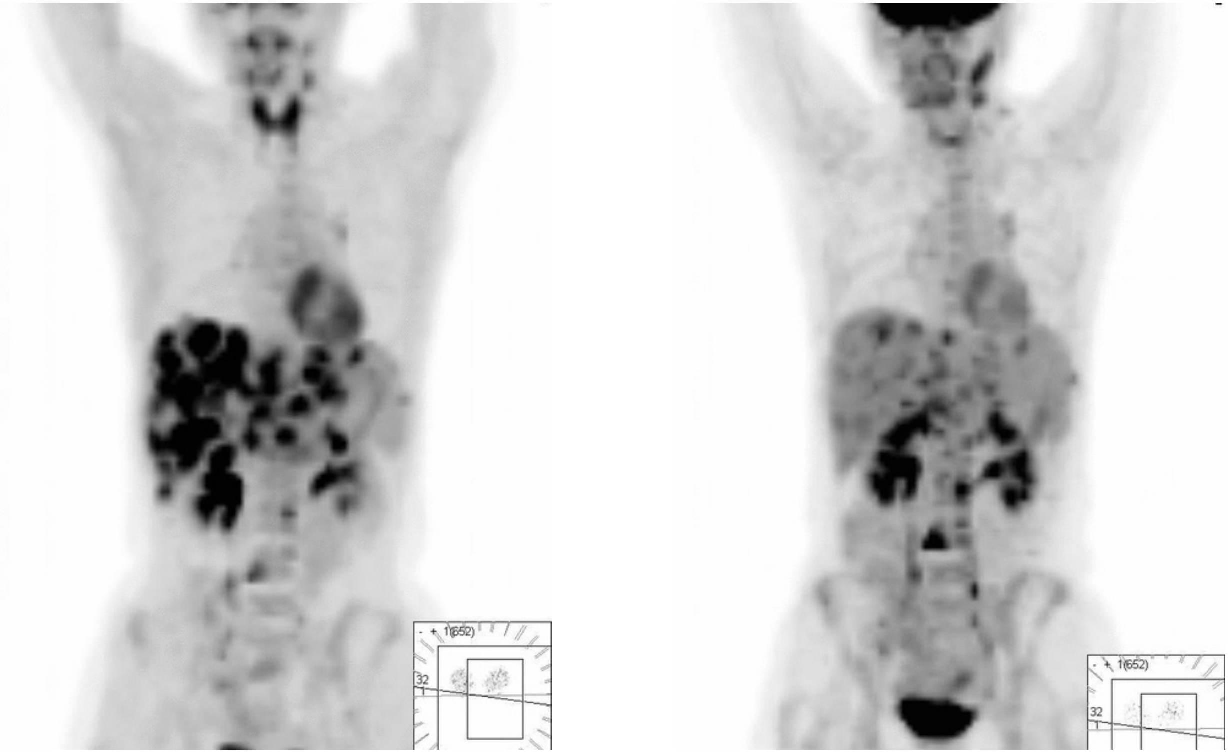
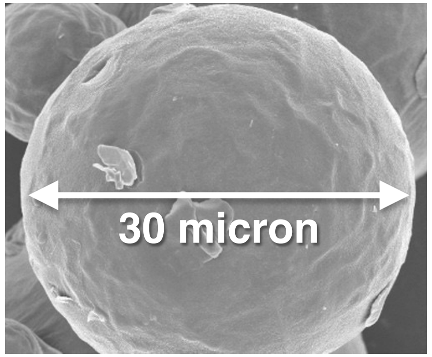
Research example: holmium microspheres



^{99m}Tc in a tumor-seeking compound as tracer

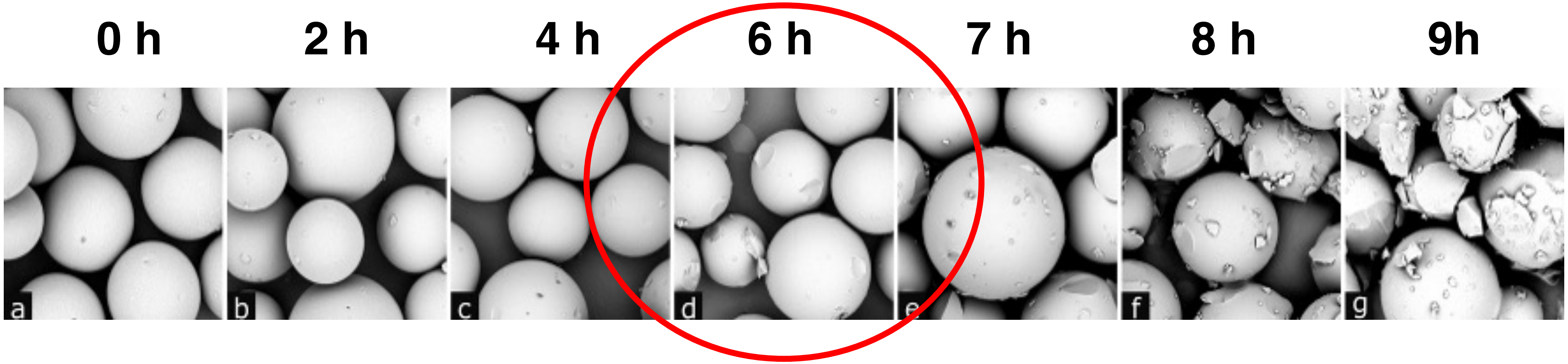
^{166}Ho-containing microspheres



Irradiation times

Microsphere get damaged around 6 hours which limits the specific activity that can be obtained.

We need more activity → longer irradiation times

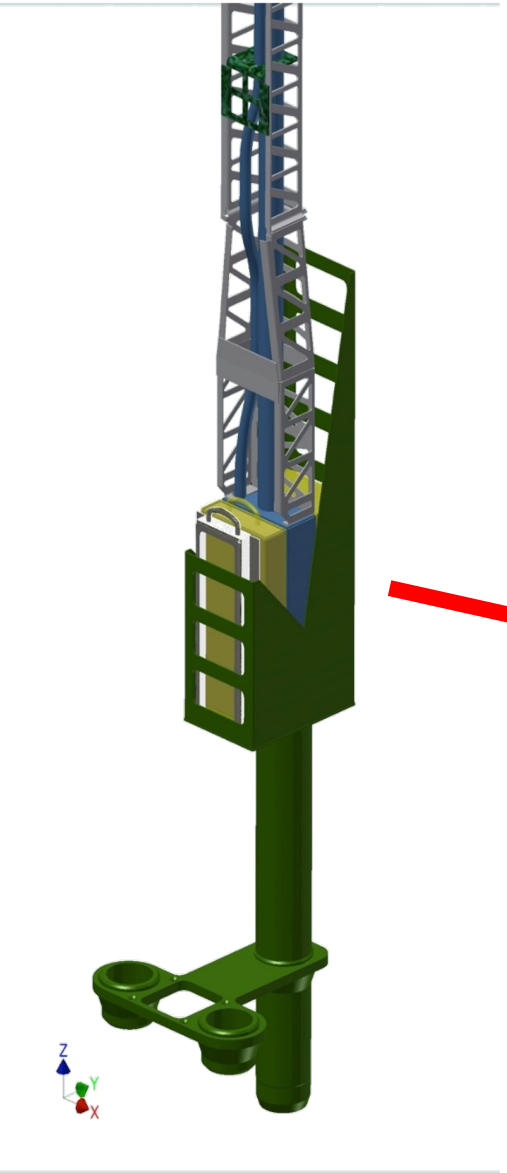


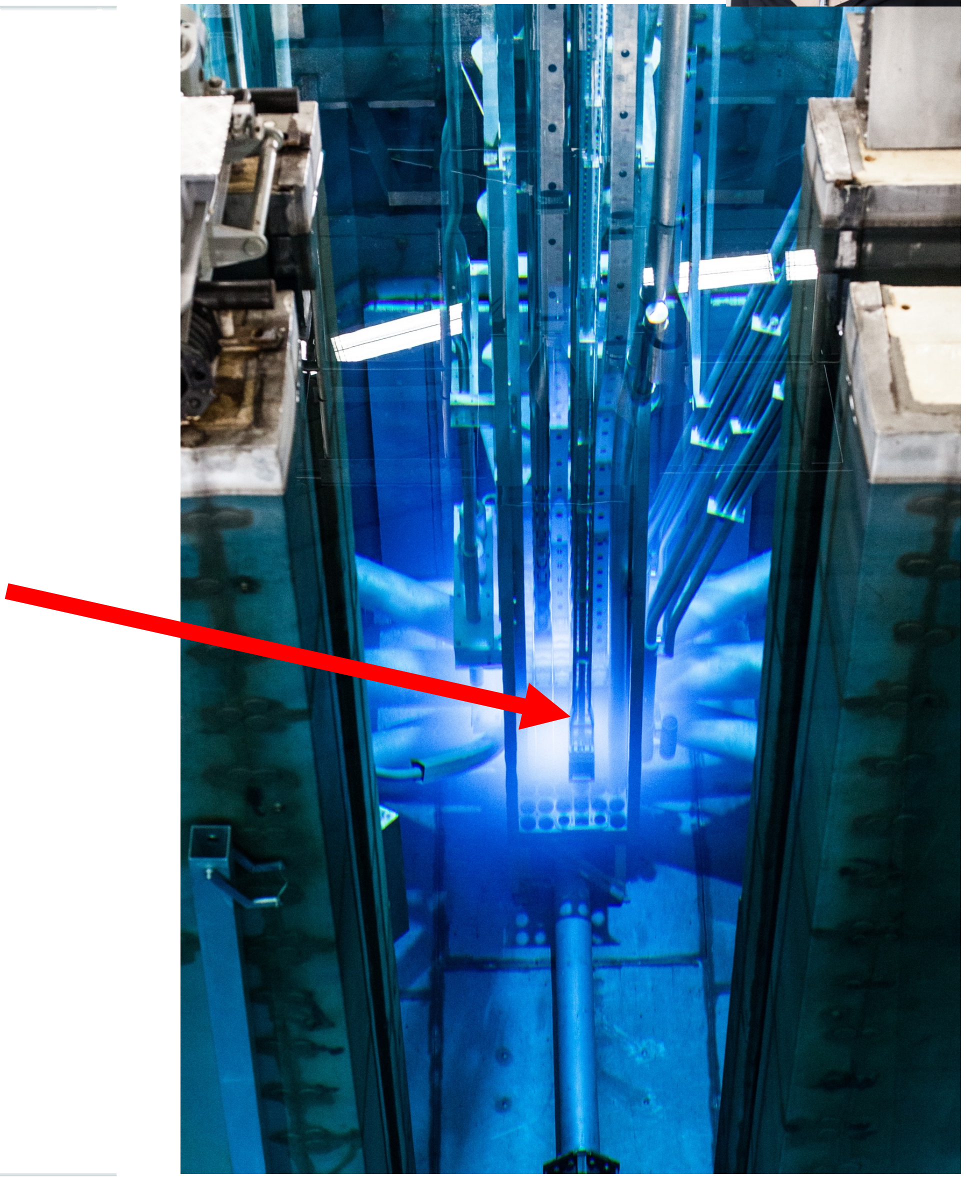
Irradiation facility

Exchangeable shielding blocks

→ optimization
(neutron/gamma-ray flux)

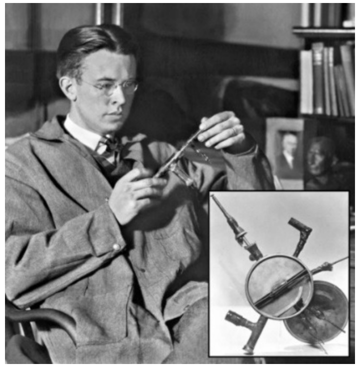
→ insertion of blocks
composed of other materials,
e.g., for neutron filtering.



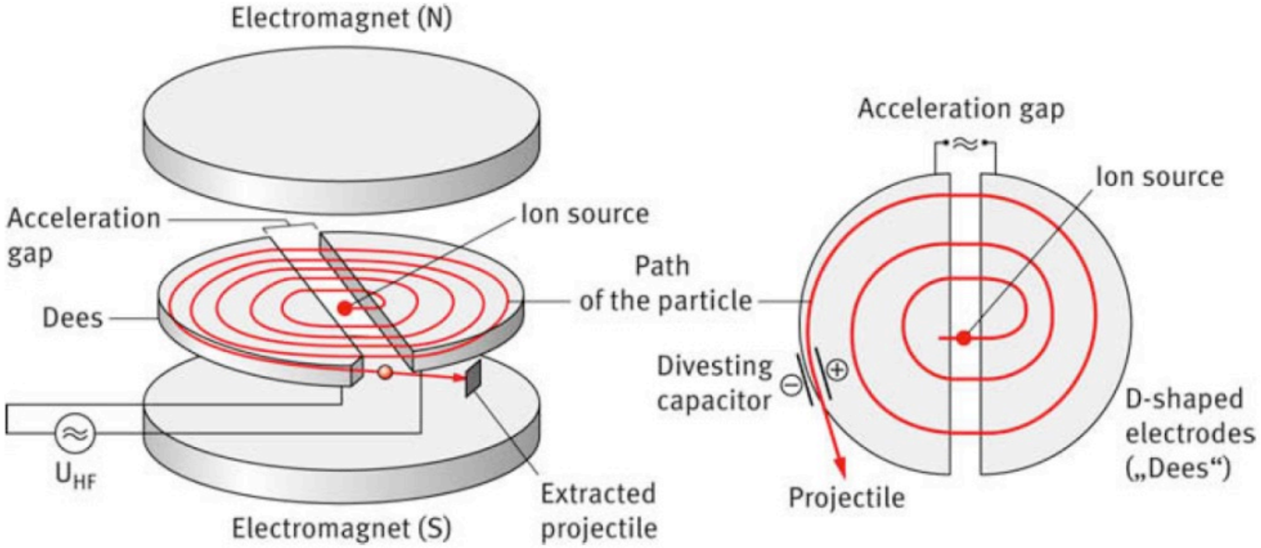


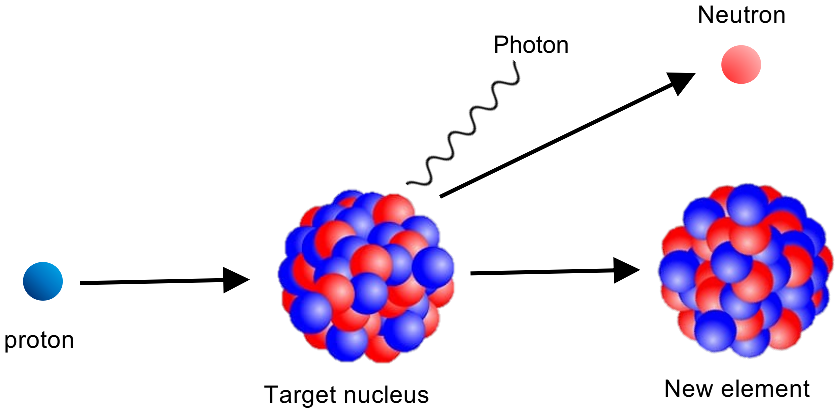
Cyclotron

- Accelerating ions are moved along a spiral trajectory by a static magnetic field.
- The increased kinetic energy of the ion results in an increased radius of its path.
- Finally, the ions are extracted.



1930 E.O. Lawrence & M.S. Livingston – 80 keV cyclotron

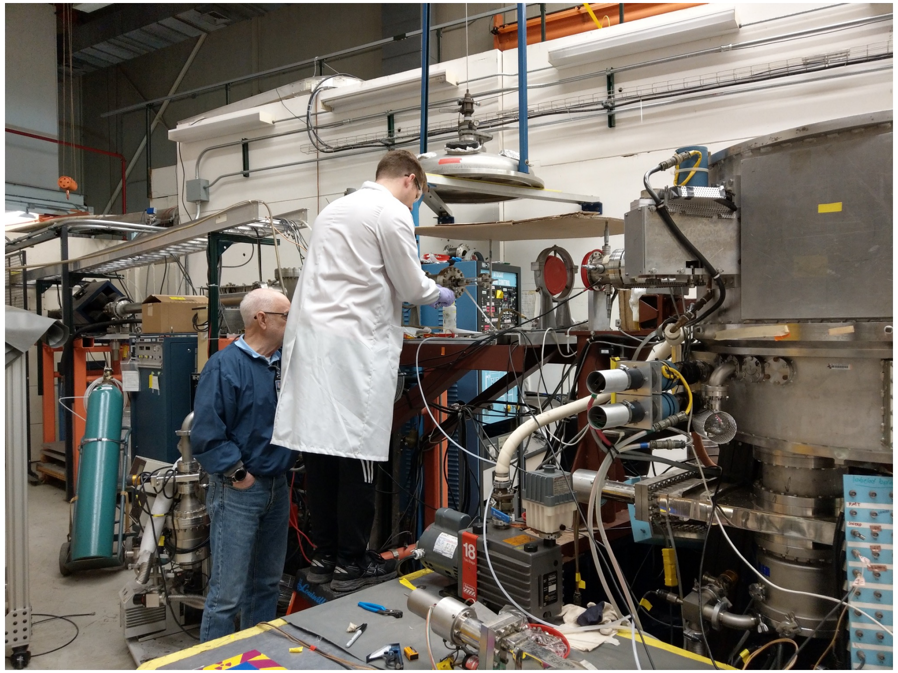


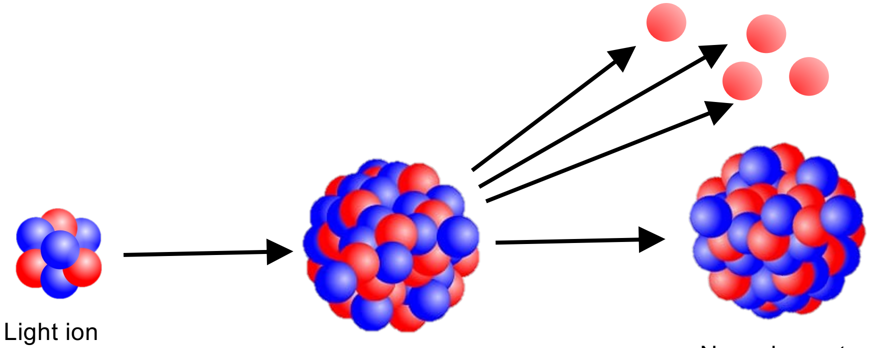


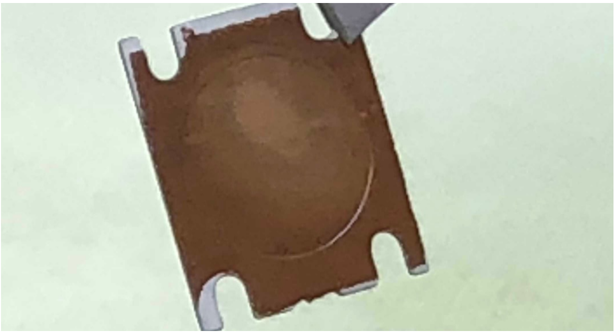
Linear accelerators

Superconducting ion linac

- Can accelerate a variety of light and heavy ions (protons, ^{3}He, ^{4}He, ^{6}Li, ^{7}Li, …) for ion-induced isotope production





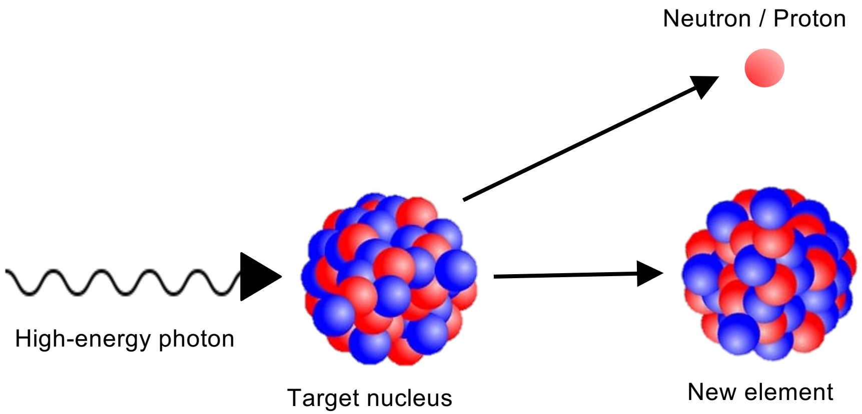


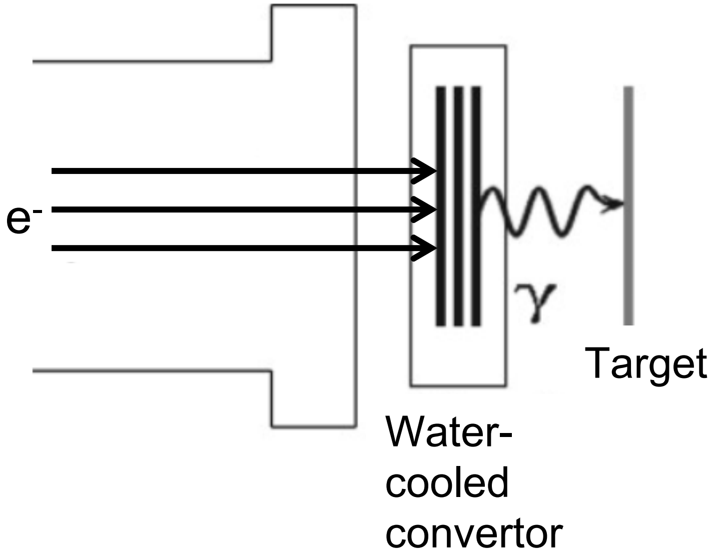
Foil after irradiation

Linear accelerators

Electron linac

- Tungsten target converts electrons to photons
- Used for mainly photonuclear reactions: (γ,n) and (γ,p)





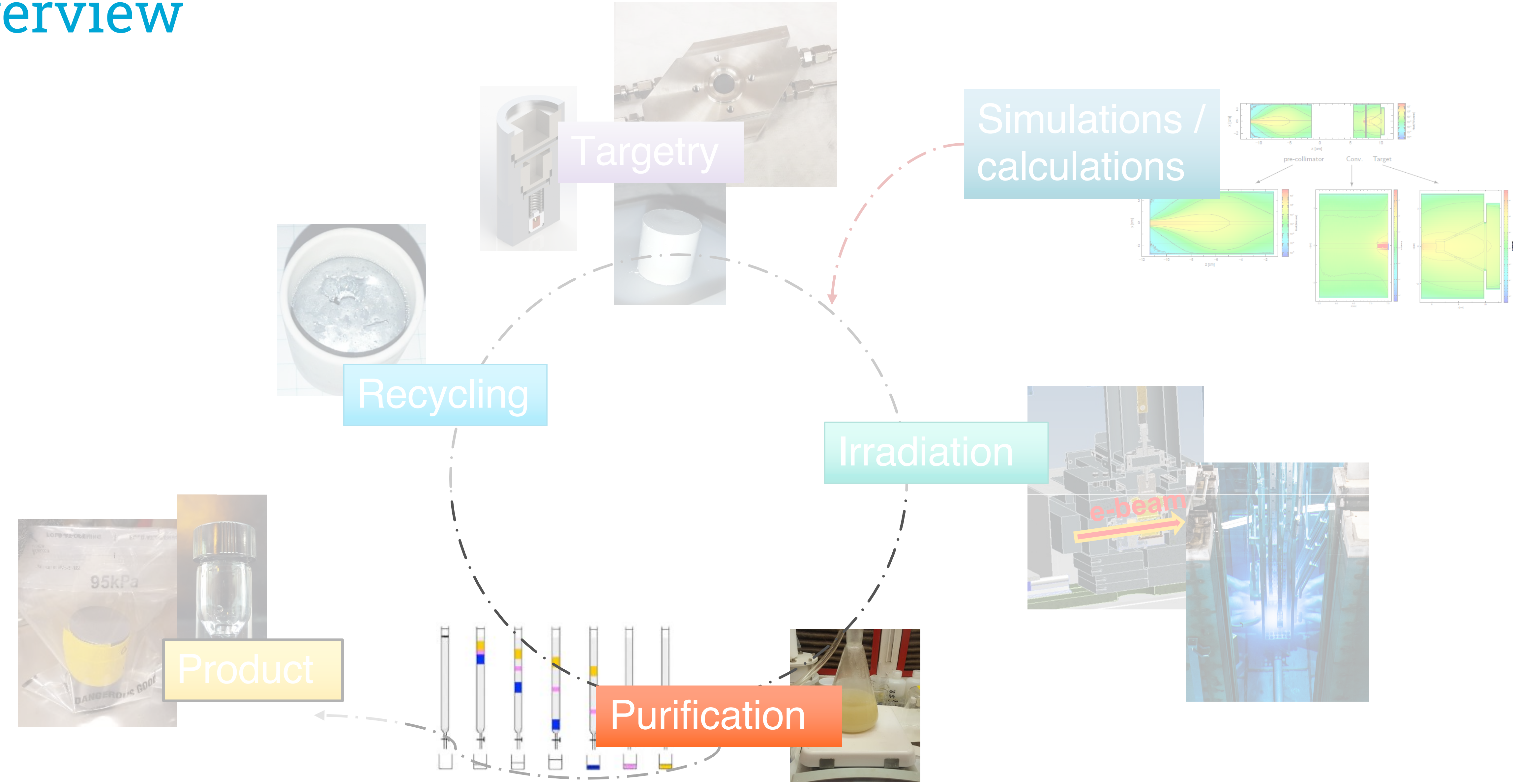
https://www.anl.gov/sites/www/files/2018-10/Radioisotope%20Research_Oct2018.pdf

Advantages and disadvantages

Reactor	Cyclotron	Linac

• **Neutron-rich isotopes**
• Neutron capture reactions & fission
• Advantages
  • Large volume for irradiation
  • Simultaneous irradiation of several samples
  • Possibility to produce a wide variety of radioisotopes
• Disadvantages
  • Availability
  • Nuclear Waste
	• **Proton-rich isotopes**
	• Reactions using charged particles
	• Advantages
	  • Locally available (at least small accelerators)
	  • No big waste problem
	  • Many reaction options
	• Disadvantages
	  • Only one irradiation at a time (sometimes 2 if dual beam is possible)
	  • Small irradiation volume
		• **Proton-rich isotopes**
		• Reactions using photons and charged particles
		• Advantages
		  • No big waste problem
		  • Many reaction options
		• Disadvantages
		  • Only one irradiation at a time (sometimes 2 if dual beam is possible)
		  • Small irradiation volume

Overview



Targetry
Simulations / calculations
Recycling
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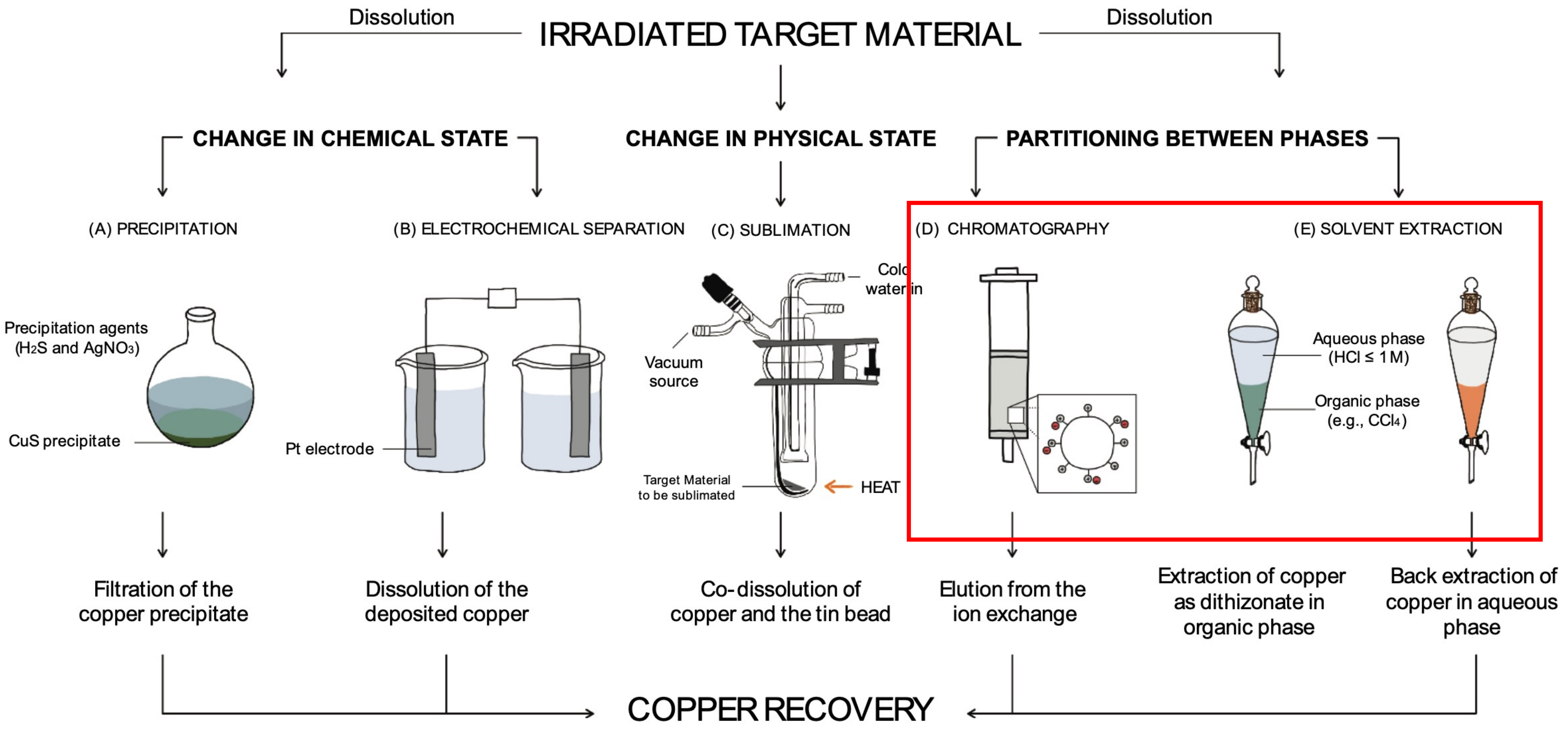
95kPa
Purification

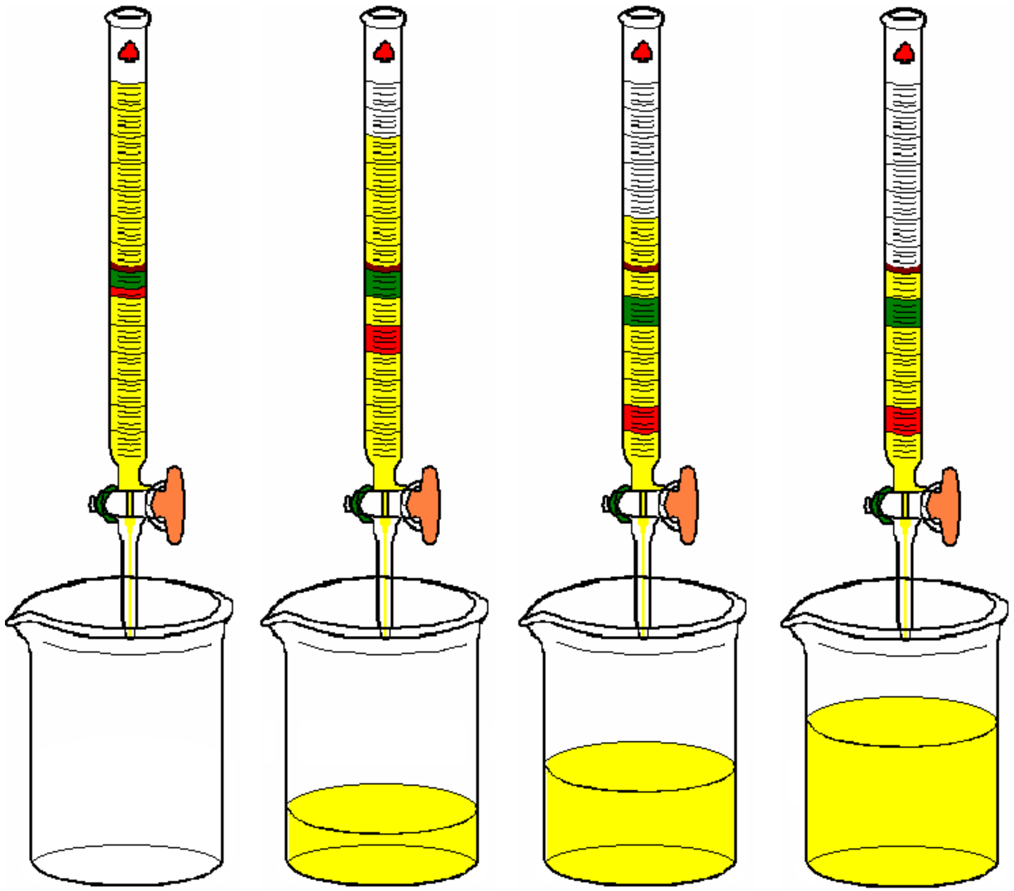
Separation / purification options



https://doi.org/10.1080/15422119.2023.2270469

Chromatography

- Stationary phase held in narrow tube through which the mobile phase is forced under pressure or gravity
- Types:
  - Liquid chromatography (LC, HPLC, IEC, GPC)
  - Gas chromatography (GLC, GSC)

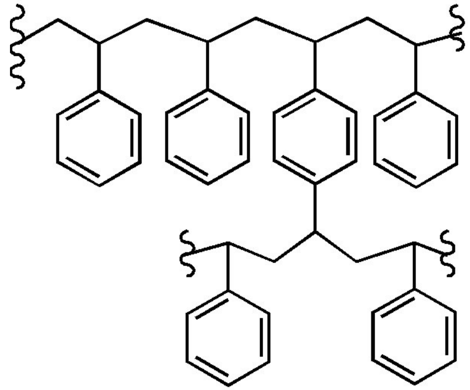


Ion exchange chromatography

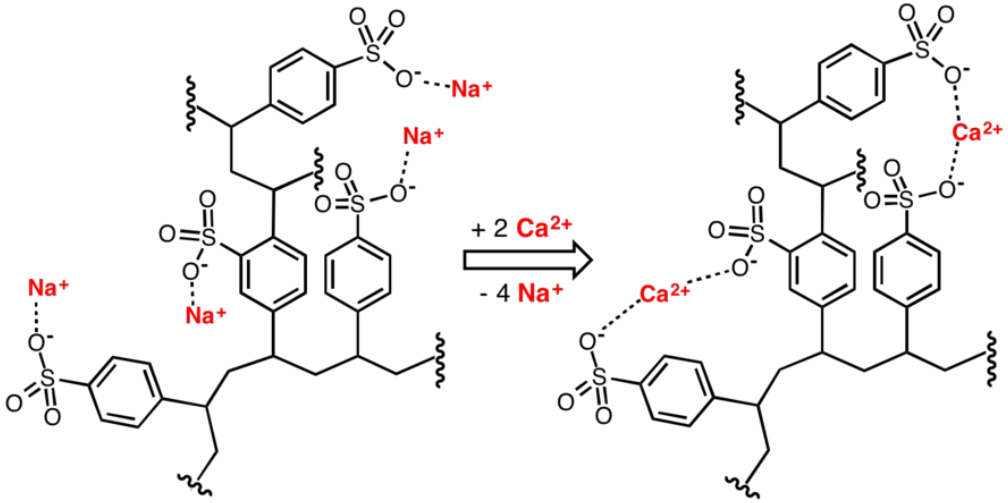
Ion exchangers consist of

- a **resin**, e.g. a cross-linked polystyrene matrix
- **functional groups** that can exchange ions,

  e.g. sulfonic acid

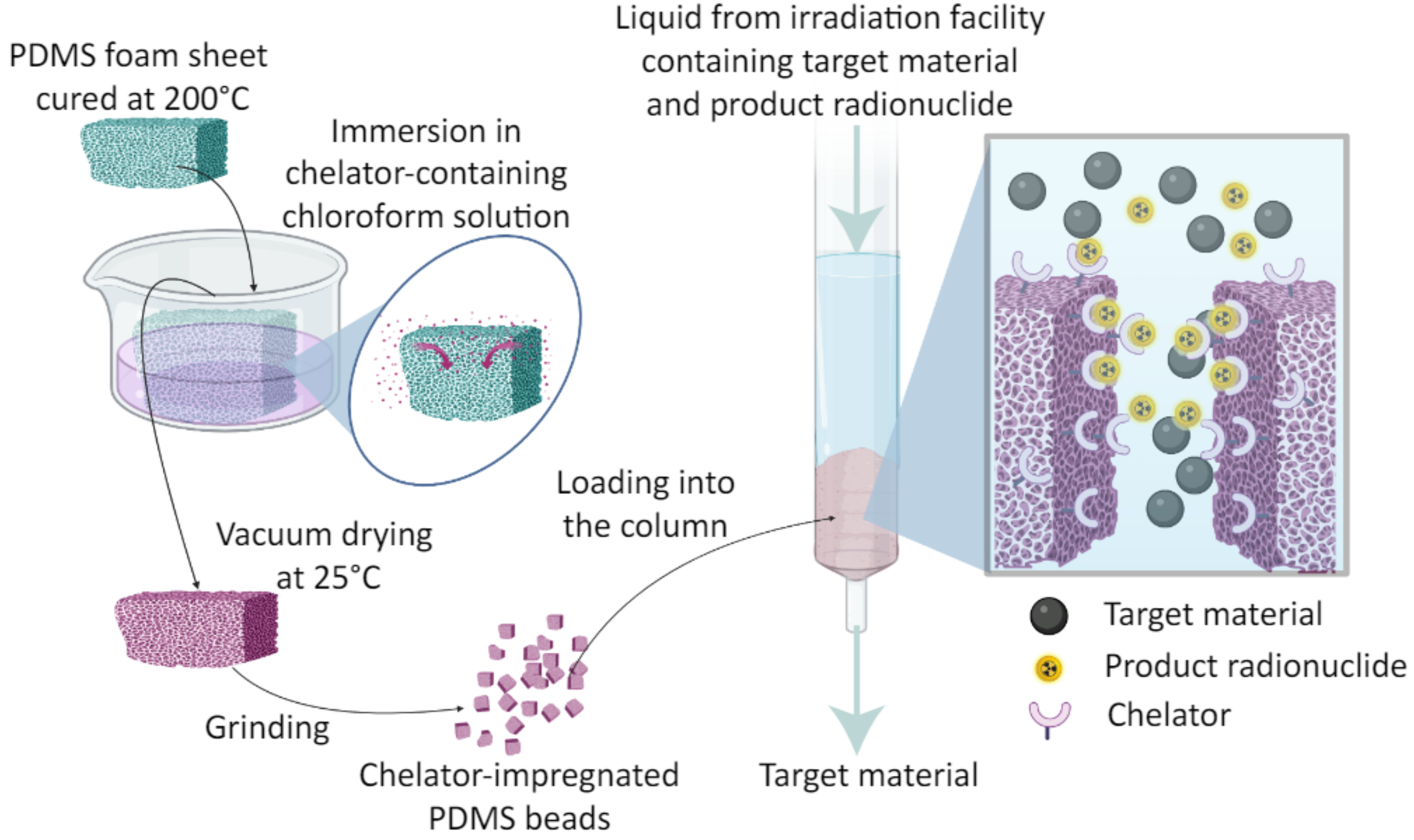


$$\mathrm{R} - SO_3^- H^+ + M^+ X^-$$
$$\rightleftharpoons R - SO_3^- M^+ + H^+ X^-$$

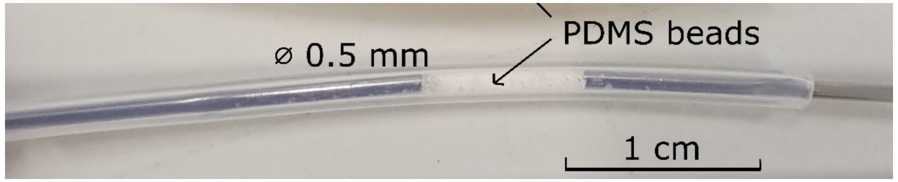


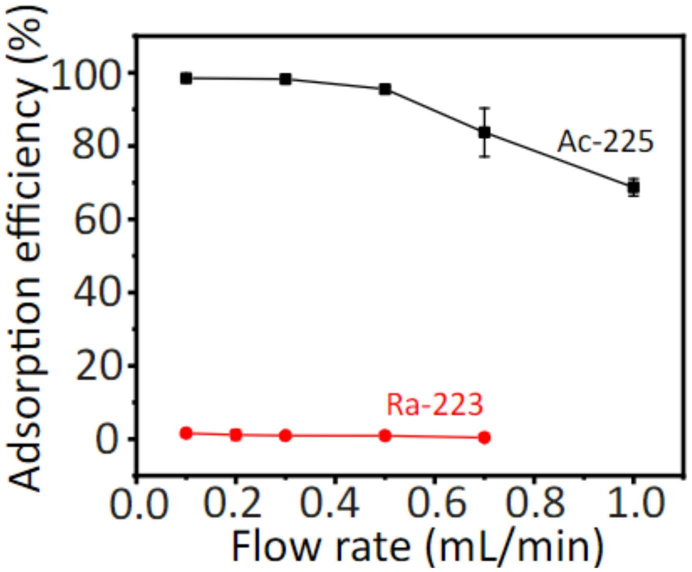
Exchange of Na^+ ions for Ca^{2+} ions

Chelator resins



5 mg impregnated PDMS beads in tube





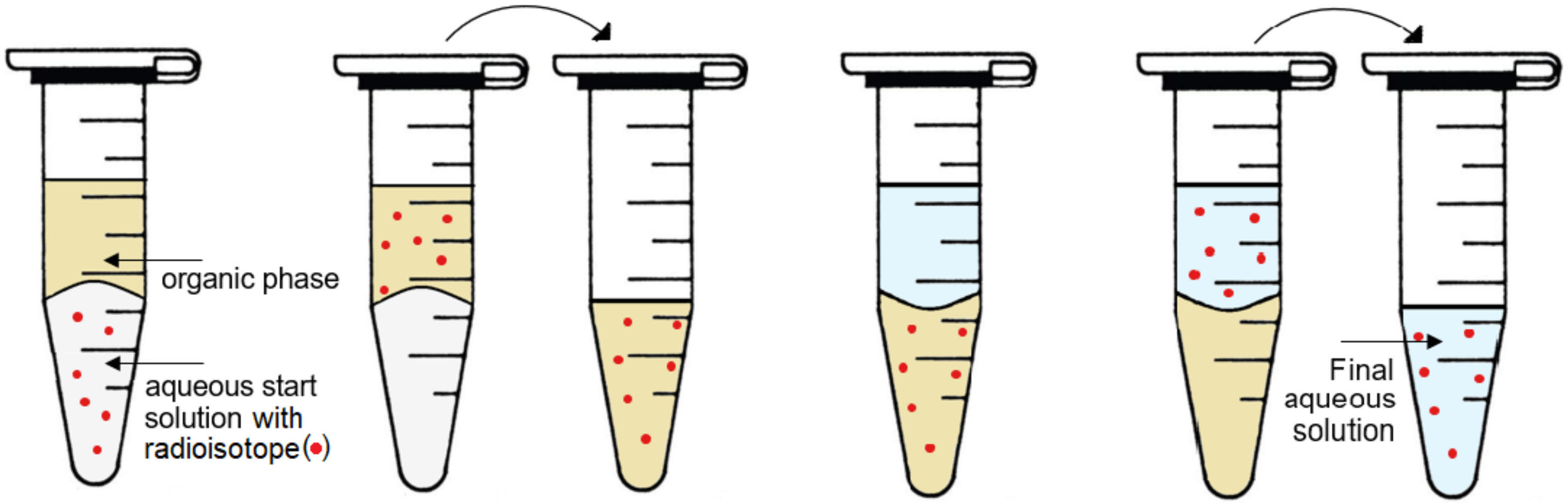
Patent 2037212: *Method for preparing silicon elastomer beads loaded with chelating agents and their use for the separation of radionuclides*

Solvent extraction

Transferring a substance from any matrix to the appropriate liquid phase

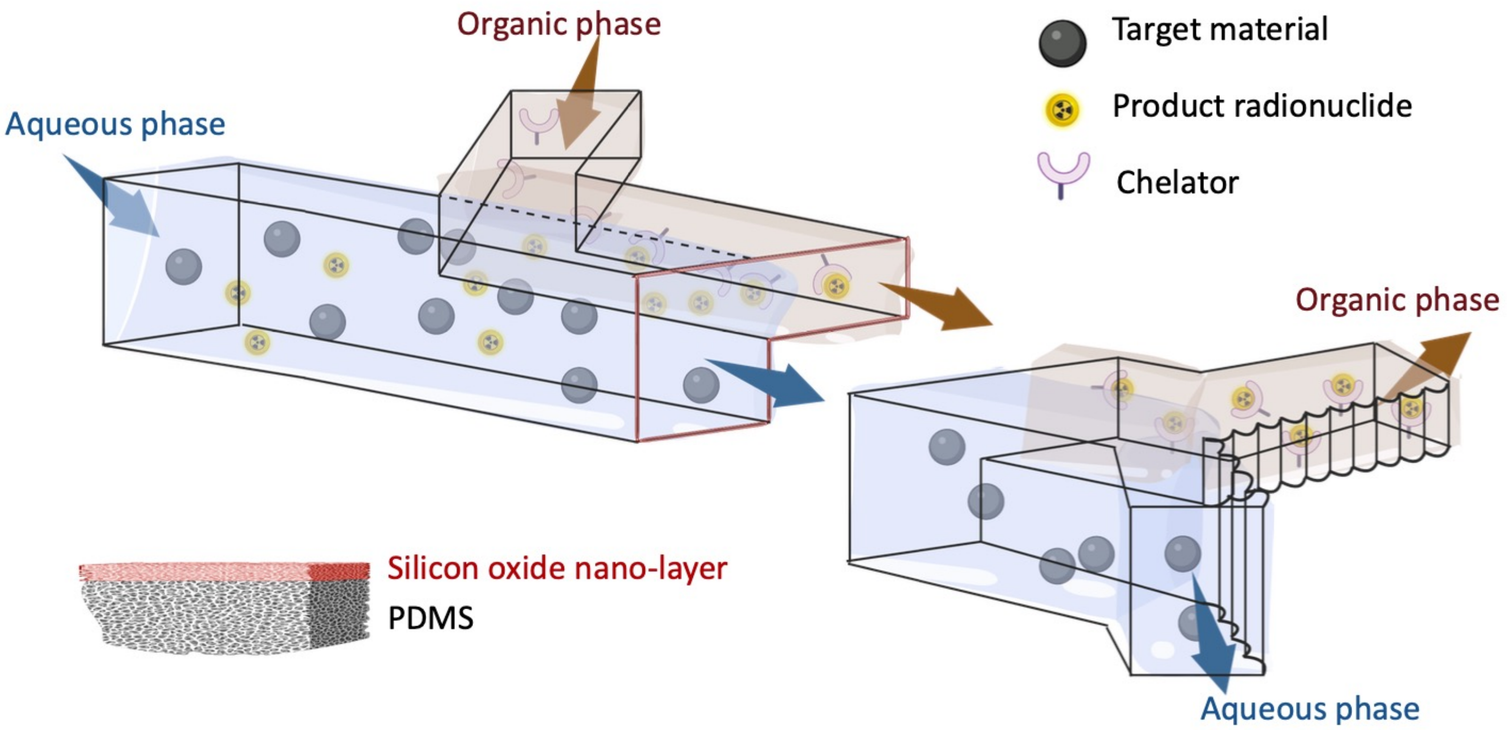
Also called **liquid-liquid extraction**

- extraction of a solute from one liquid phase to another immiscible phase



Microfluidic radionuclide separation

- Radionuclide purification consists of **long, multistep processes**.
- We developed a **microfluidic chip**, based on liquid-liquid extraction, to **speed up** the purification step.
  - Zn/^{68}Ga,
  - Zn/^{64}Cu,
  - Ba/^{140}La
  - Ra/^{225}Ac



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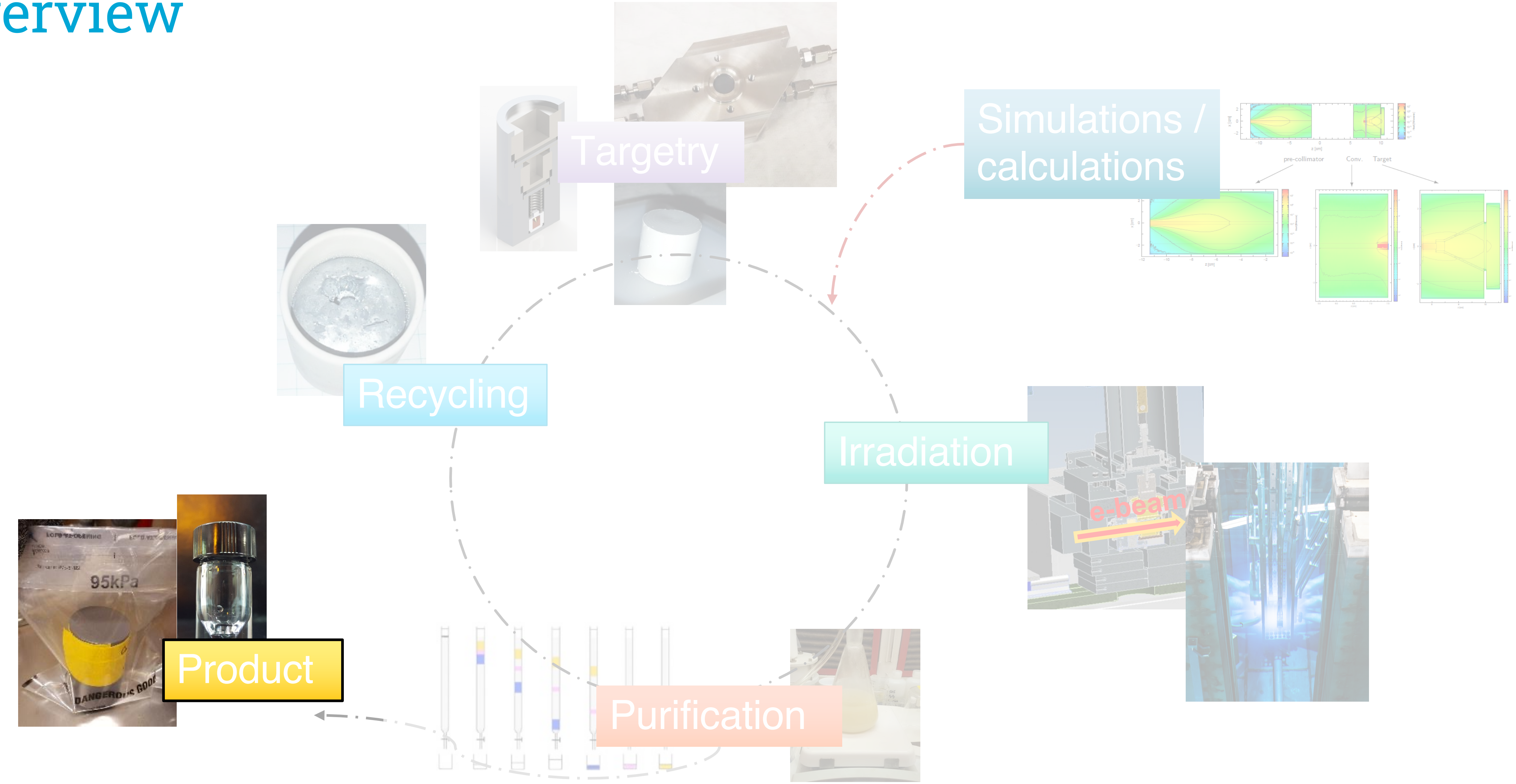
Overview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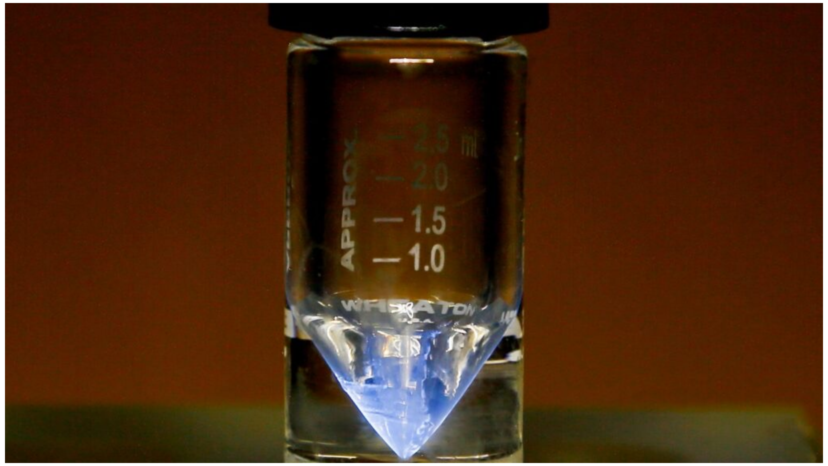
Product quality

- How much can be produced?
- Specific activity
- Radioisotopic purity
- Radionuclidic purity
- Other factors:
  - Availability of production facility
  - Waste production
  - Purification processes
  - Transport
  - Price of production



Specific activity (SA)

*For a given radionuclide the **activity** divided by the **mass** of the sum of **all radioactive and stable isotopes** isotopic with the element involved*

with as unit either Bq/g, Bq/mol or Ci/g, Ci/mol.

$$\mathrm{SA} = \frac{\mathrm{A(t)}}{\mathrm{m}}$$

Specific activity – a matter of definitions 😵‍💫

$$SA = \frac{A(t)}{m}$$

Radionuclide production:

Specific activity	m = mass of same element
Effective specific activity	m = mass chemically similar elements
Radiopharmacy:	m = mass of chemical compound
Radiological health physics:	m = total mass or volume of solution

➢ Low specific activity affects the application of radioisotopes.

Radioisotopic purity

Production of several radioactive isotopes of the **same element**

Possible solutions:

1. Use of enriched isotopes
2. Separation (very difficult)

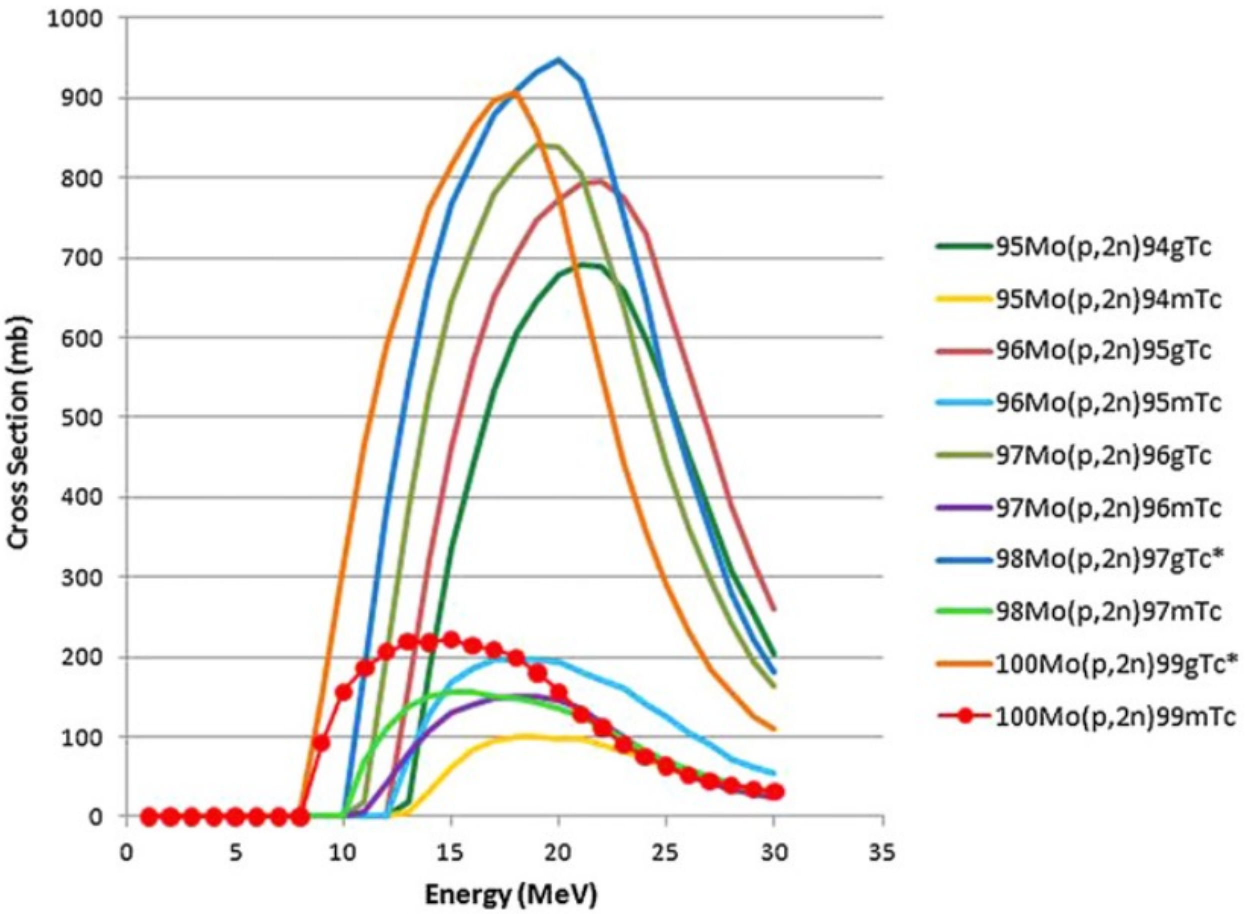


Image taken from: Phys. Med. Biol. 56 (2011) 5469–5484

Radionuclidic purity

- Production of several radioactive isotopes of **different elements** is possible
- Either separation or waiting time until undesired isotopes are decayed

Example: Proton irradiation of $^{nat}Zn(NO_3)_2$

Parent	Daughter	Halflife (min)	Cross-section (mb)
Zn-68	Ga-68	67.71	153.00
Zn-67	Ga-68	67.71	0.02
Zn-70	Ga-70	21.14	3.42
Zn-67	Ga-67	4694.4	20.30
Zn-66	Ga-67	4694.4	0.11
Zn-66	Ga-66	569.4	145.00
Zn-64	Ga-65	15.2	0.18
Zn-64	Ga-64	2.63	66.30
Zn-70	Zn-69	56.4	0.00
Zn-70	Zn-69m	825.6	0.00
Zn-66	Zn-65	351259.2	0.01
Zn-64	Zn-63	38.47	0.00
Zn-70	Cu-67	3709.8	0.21
Zn-70	Cu-66	5.12	0.00
Zn-68	Cu-64	762	0.00
Zn-67	Cu-64	762	5.25
Zn-64	Cu-61	199.8	47.80
N-14	C-11	20.33	11.00
O-18	F-18	109.77	150.00
O-16	N-13	9.965	35.00

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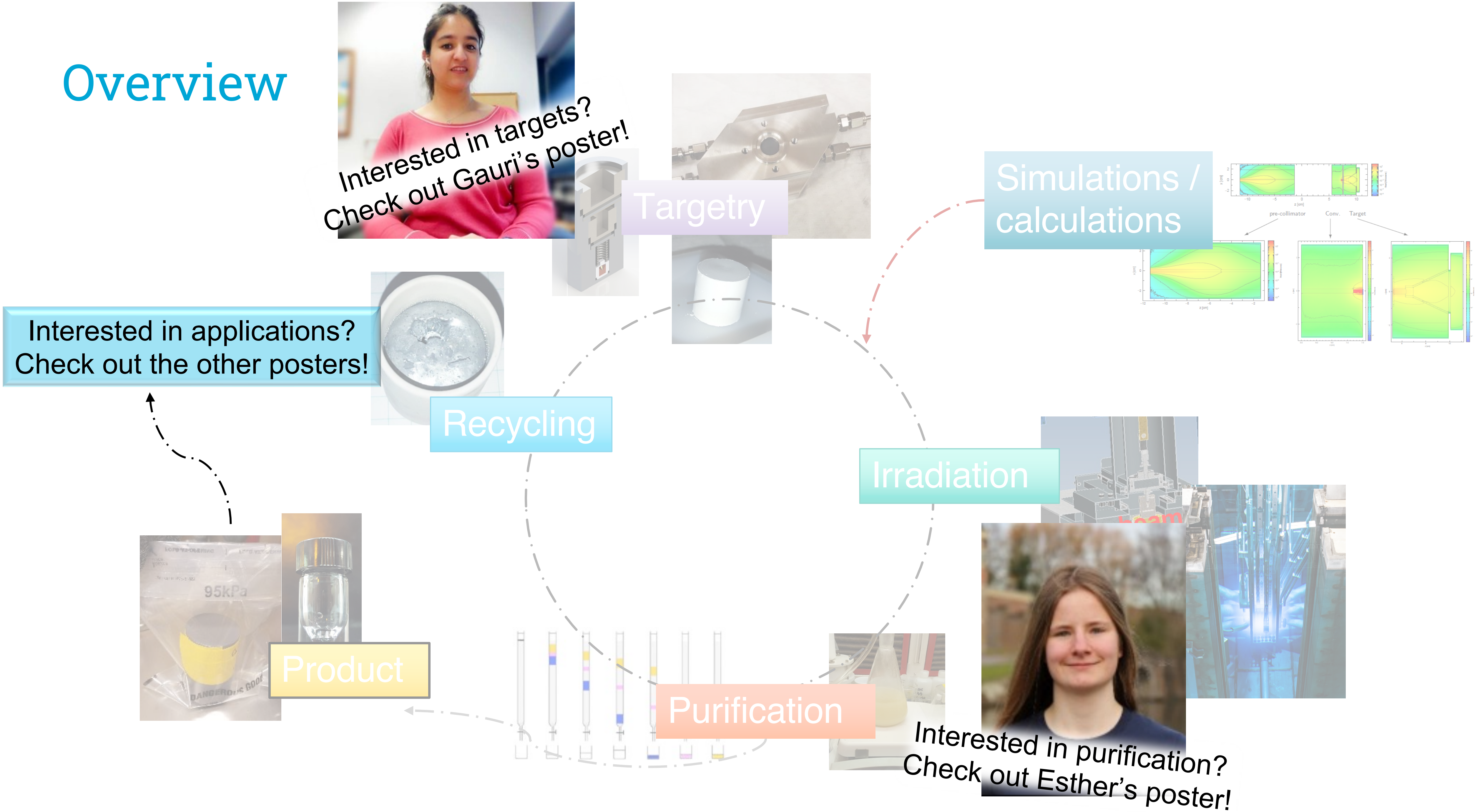
Interested in targets?
Check out Gauri's poster!
Targetry
Simulations / calculations
pre-collimator
Conv.
Target
Interested in applications?
Check out the other posters!
Recycling
Irradiation
Product
95kPa
Purification
Interested in purification?
Check out Esther's poster!

Registered for the reactor tour?

Follow me to the RID, and don't forget your **ID** document!

Thank you!

Robin de Kruijff