Lu and Yb Separation

An Ion Exchange Chromatography Process Optimized by **Design of Experiments**

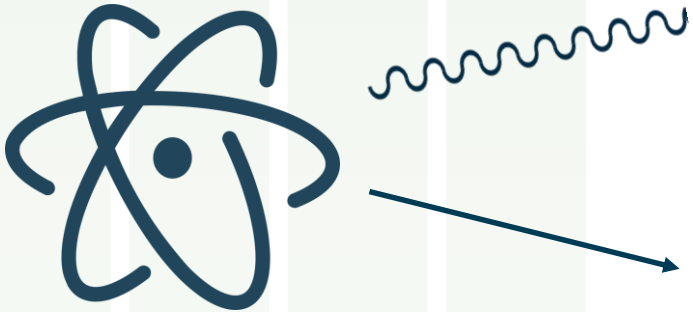
R. M. Nory, M. O. Damasceno, V. Tapetti, and E. G. Moreira

^{177}Lu

^{177}Lu: characteristics

- Lutetium is a **lanthanide**;
- Artificially produced in nuclear reactors;
- Main characteristics:

$t_{1/2}$
6,6 days



γ 113 keV (6,4%)
208 keV (11%)

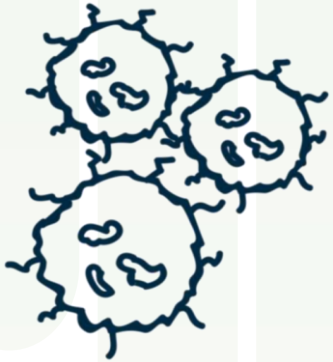
β^- 497 keV (78,6%)

^{177}Lu: theranostic agent

Personalyzed medical care

TRT – *Targeted Radionuclide Therapy*

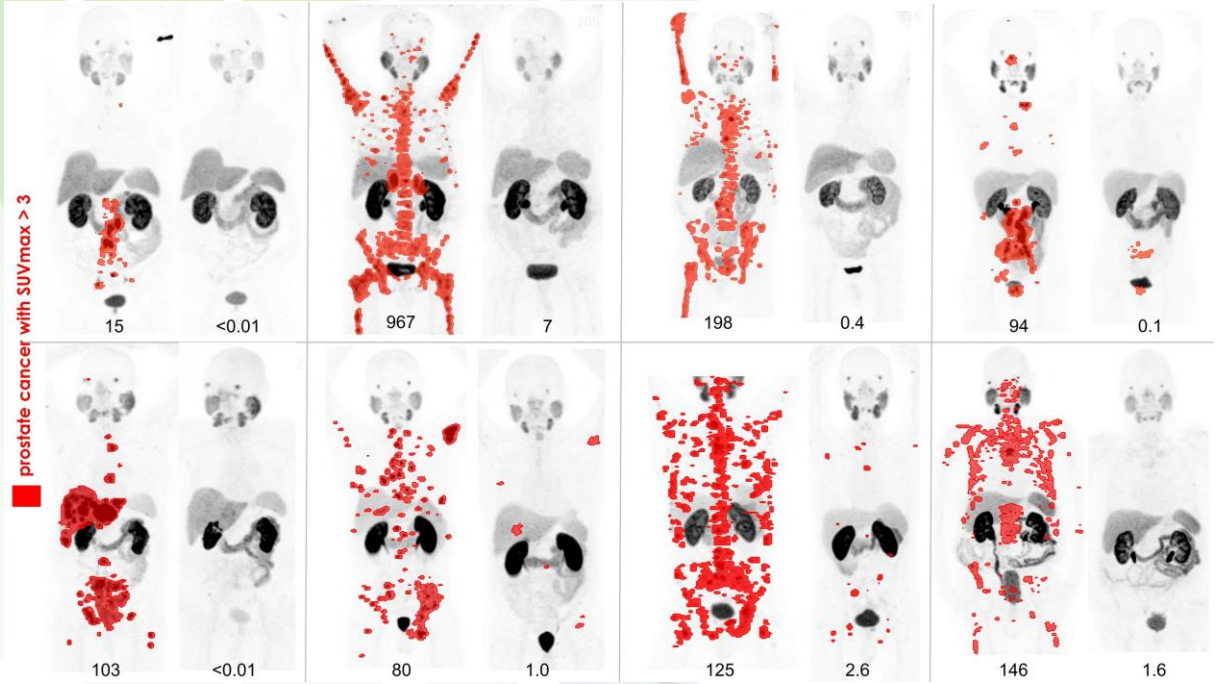
Therapy



Diagnosis

^{177}Lu: medical applications

Image of the year (2018) – SNMMI: ^{177}Lu-DOTA-PSMA



^{177}Lu in Brazil

Radiolabeling only

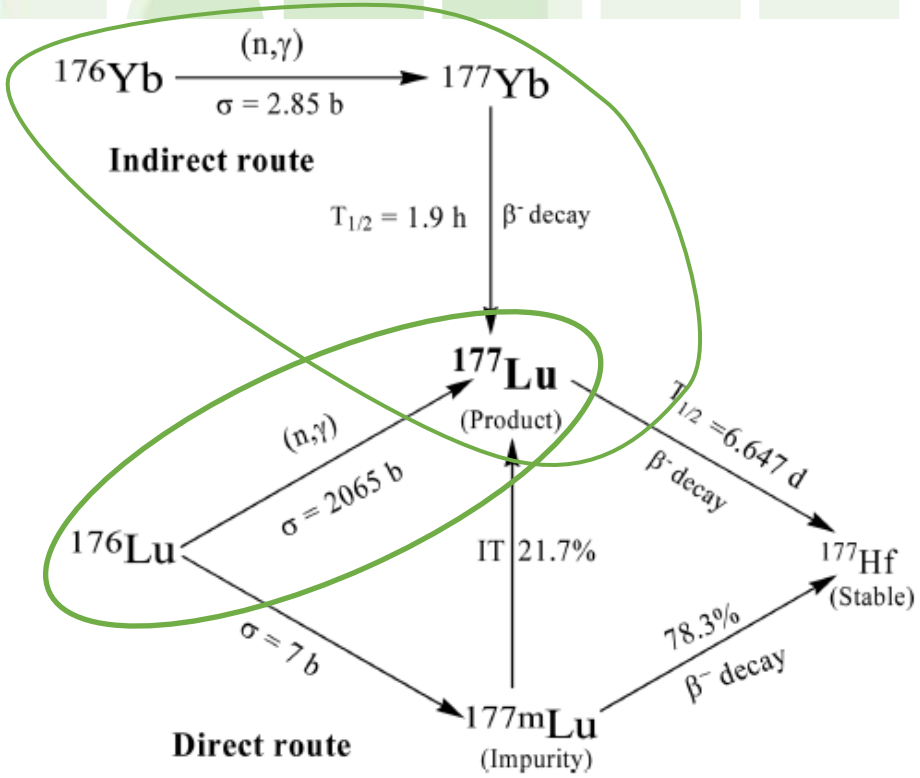
ipen

100% imported
(Russia and Israel)

High costs

Increasing demand

^{177}Lu: production routes



Indirect route

^{177}Lu NCA

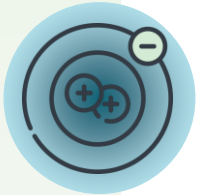
Complex radiochemical separation process

Higher specific activity

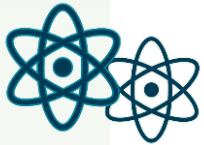
Lu and Yb Separation

Complex task...

Very similar chemical properties



Oxi-reduction



Atomic radius differences

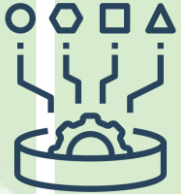
Ligand affinity

Solubility differences

Design of Experiments

Design of Experiments: Why to use it?

In this study, we have:



Multiple variables to analize

Time-consuming experimental runs

High cost imputs

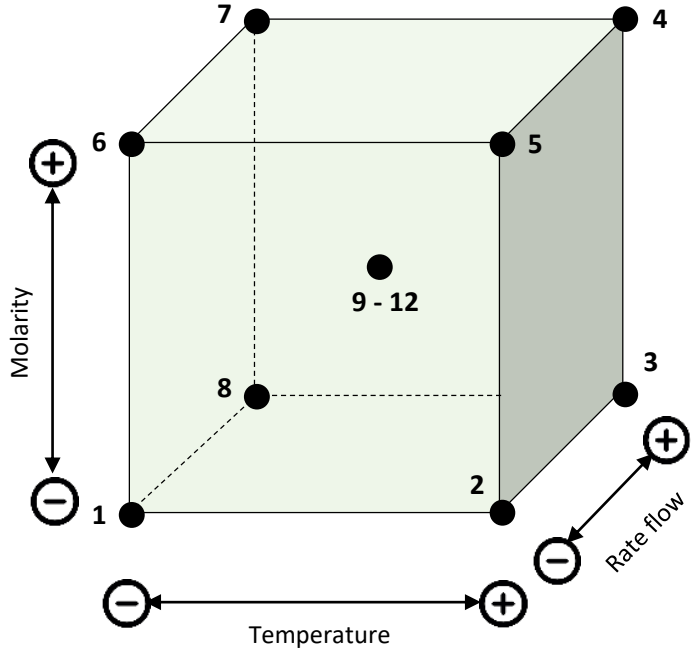
So, we need ..... OPTIMIZATION!

Design of Experiments: Why to use it?

Reduced number of experiments to find the best conditions for the separation of Lu and Yb

12 runs

(8 points + 4 central points)



Cube of experiments

DoE and Anion Exchange Chromatography

DoE and AEC: Parameters

Stationary phase: Bio-Rad® AG 1-X4 anion exchange resin (20 cm)

Mobile phase: Phosphoric acid (H_3PO_4) as eluent

Masses:
0.14 mg Lu / Yb (each) + radiotracers

Temperature
3 – 83
(°C)

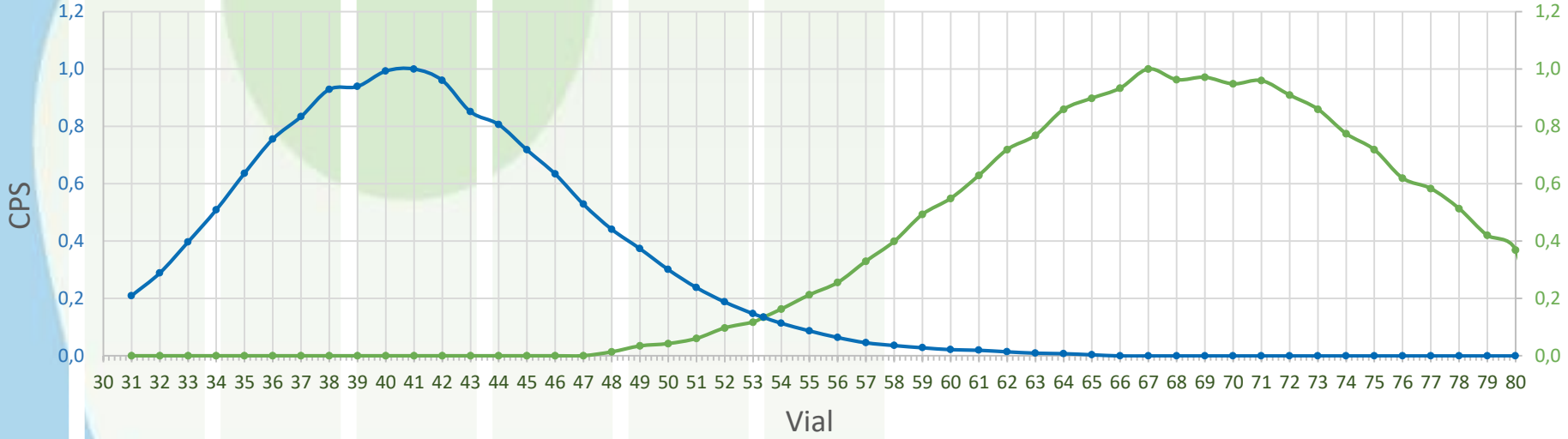
Eluent molarity
0.25 – 1.0
(mol L^{-1})

Eluent flow rate
0.6 – 3.5
(mL cm^{-2} min^{-1})

Vials:
1 mL each

Chromatograms: example

Conditions: 43 °C – 0.62 mol L^{-1} – 2.0 mL cm^{-2} min^{-1} (Central Point)



Lu presents higher affinity for the resin than Yb

Results

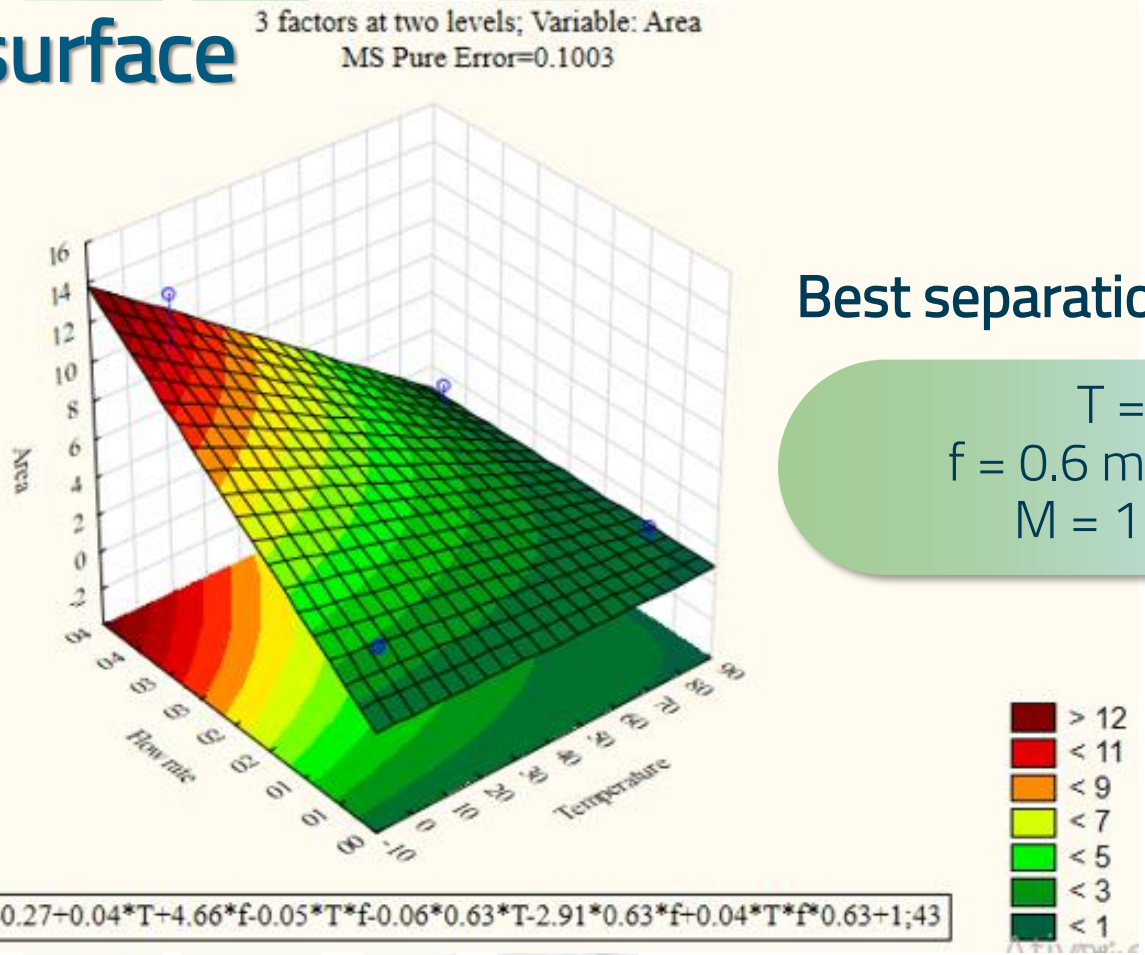
Analysis and results

Software:
Statistica

Output result:
Intersection area between peaks

Temperature and **flow rate**:
the most important variables

Fitted surface



Best separation condition:

T = 83 °C
f = 0.6 mL cm^{-2} min^{-1}
M = 1.0 mol L^{-1}

Modeled optimized equation

A=-0.27+0.04*T+4.66*f-0.05*T*f-0.06*0.63*T-2.91*0.63*f+0.04*T*f*0.63+1;43

Any questions?

Send an e-mail to

remenry@usp.br
or
emoreira@ipen.br