10.10.28 Thu.

Radiopharmaceutical production using microreactor

: ^{18}**F-FDG** for PET(Positron Emission Tomography)

Sungkyunkwan University, suwon, KOREA
Accelerator and Medical Engineering Lab.

Sookyoung Jung

CONTENTS

1) Microfluidics

2) MicroReactor
   .1 What is that?
   .2 Why microreactor?

3) [^{18}F]FDG
   .1 What is that?
   .2 Why [^{18}F]FDG?

4) Chip Design

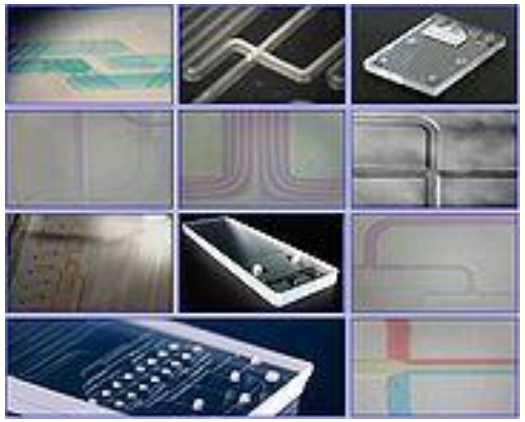
Microfluidics

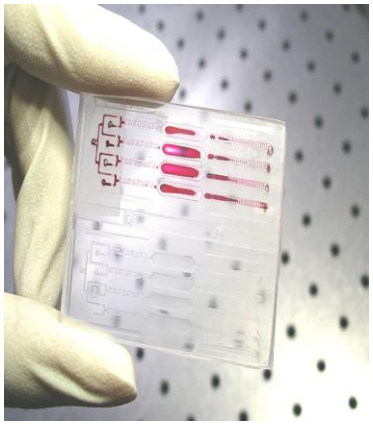
It deals with the behavior, precise control and manipulation of fluids that are geometrically constrained to a small, typically sub-millimeter, scale

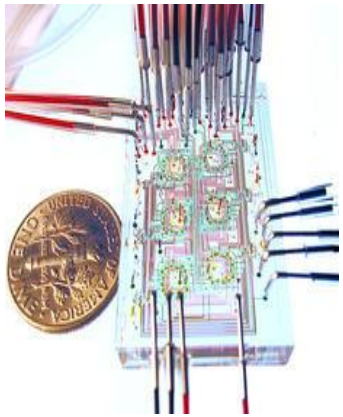
- small volumes(nl, pl, fl)
- small size
- low energy consumption
- effects of the micro domain

Multidisciplinary field intersecting

- Engineering, physics, chemistry, microtechnology, biotechnology
- DNA chips, lab-on-a-chip technology, micro-propulsion, micro-thermal technology







CONTENTS

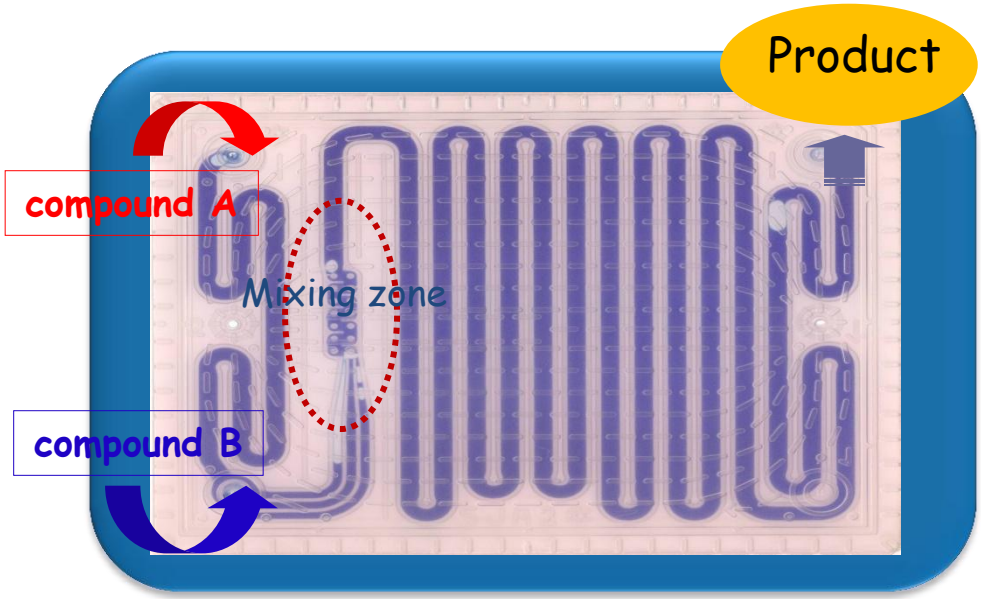
1) Microfluidics

2) MicroReactor
   .1 What is that?
   .2 Why microreactor?

3) [^{18}F]FDG
   .1 What is that?
   .2 Why [^{18}F]FDG?

4) Chip Design

.1 What is MicroReactor?



Keywords

- ✓ microcircuit
- ✓ Diffusion and eddy
- ✓ Mixture of compounds

PROCESS of reaction

- Supplying compound A,B in the microcircuit with pumps.
- Along the microcircuit, compounds are stirred through the mixing zone.
- Transferring along the circuit, reaction completed and producing the final compound.

.1 What is MicroReactor?

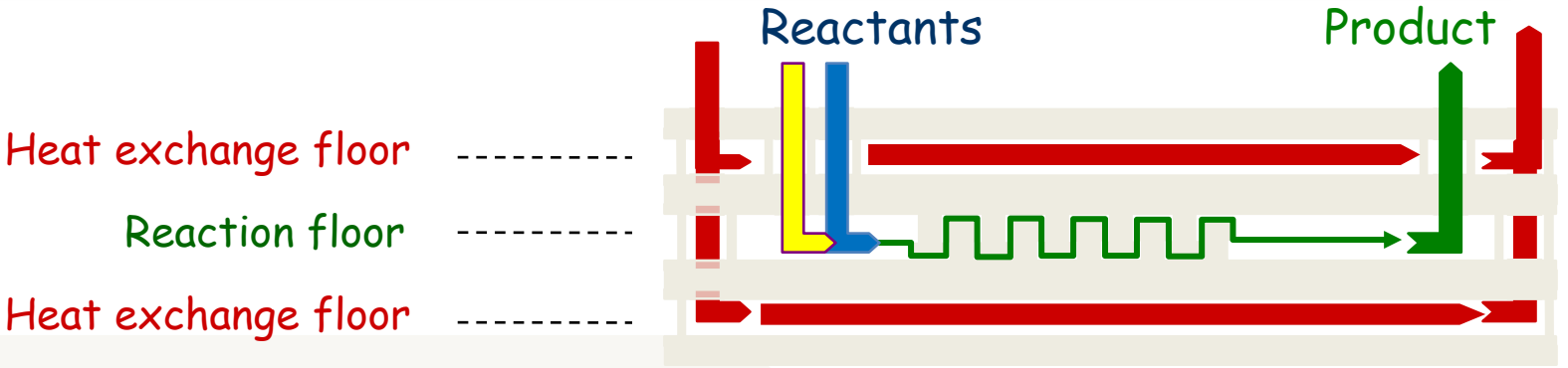
- Characteristics
  - The part of the microfluidic System
  - Inner diameter < 1 mm
  - Size(generally) : 10 –100 μm
  - Very small inherent volume

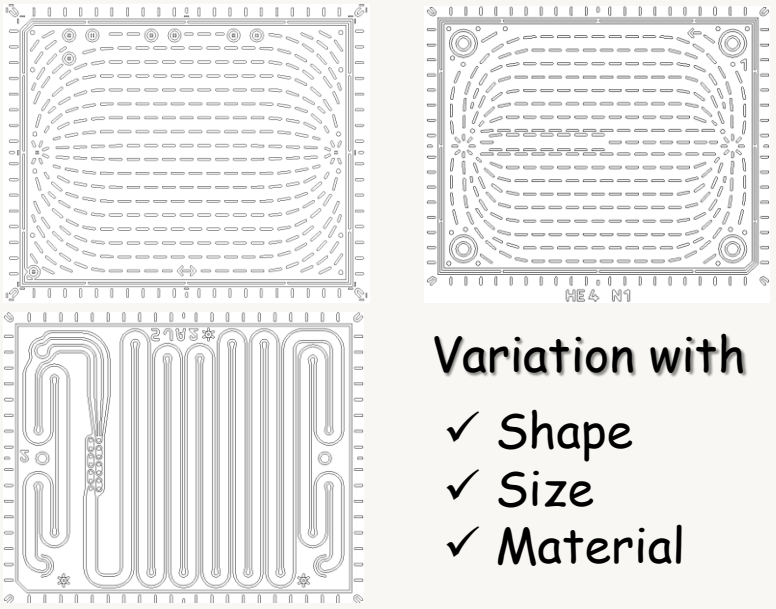
- Applications
  - Biology
  - Engineering
  - Reactors for synthetic applications

FDG Synthesis

.1 What is MicroReactor?

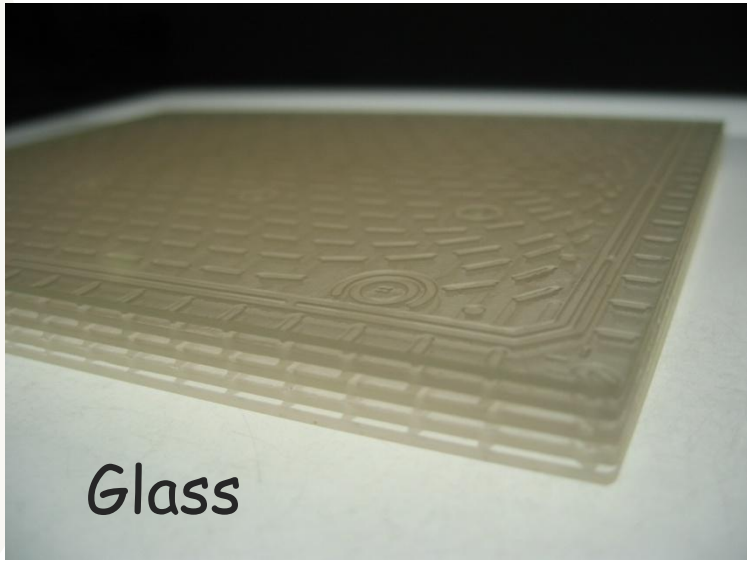
Example for construction of channel in microreactor (Glass)





Variation with

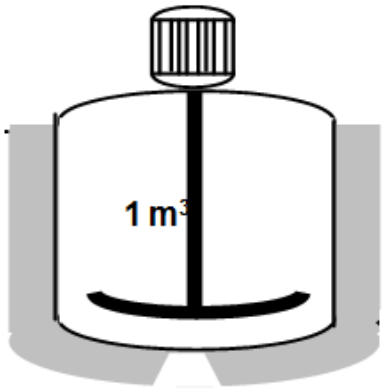
- ✓ Shape
- ✓ Size
- ✓ Material



.2 Why MicroReactor? (Advantages of microreactor)

Micro reaction technology – characteristic

Batch Reactor
(conventional)



10^6ml

MicroReactor

Feeding 100 ~ 180 ml/m
= 3.6 ~ 6.4 t / Month
*at Density 1

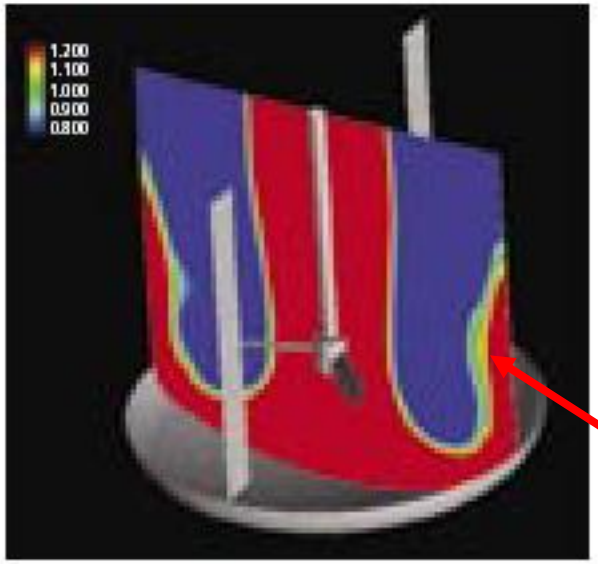
(1) 1:1 Rapid Mixture
(2) High efficiency
(3) Effective temperature control
(4) Easy multiplication
(5) Safety
(6) Little space for installation

.2 Why MicroReactor? (Advantages of microreactor)

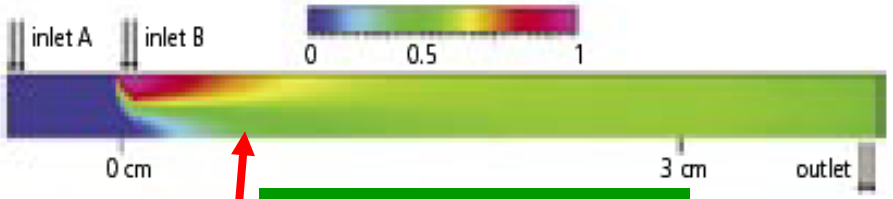
(1) Effect of 1:1 Rapid mixture

Effective Mixing (compound ratio of 1:1)

→ Increasing production by decreasing synthesis time



Batch reactor



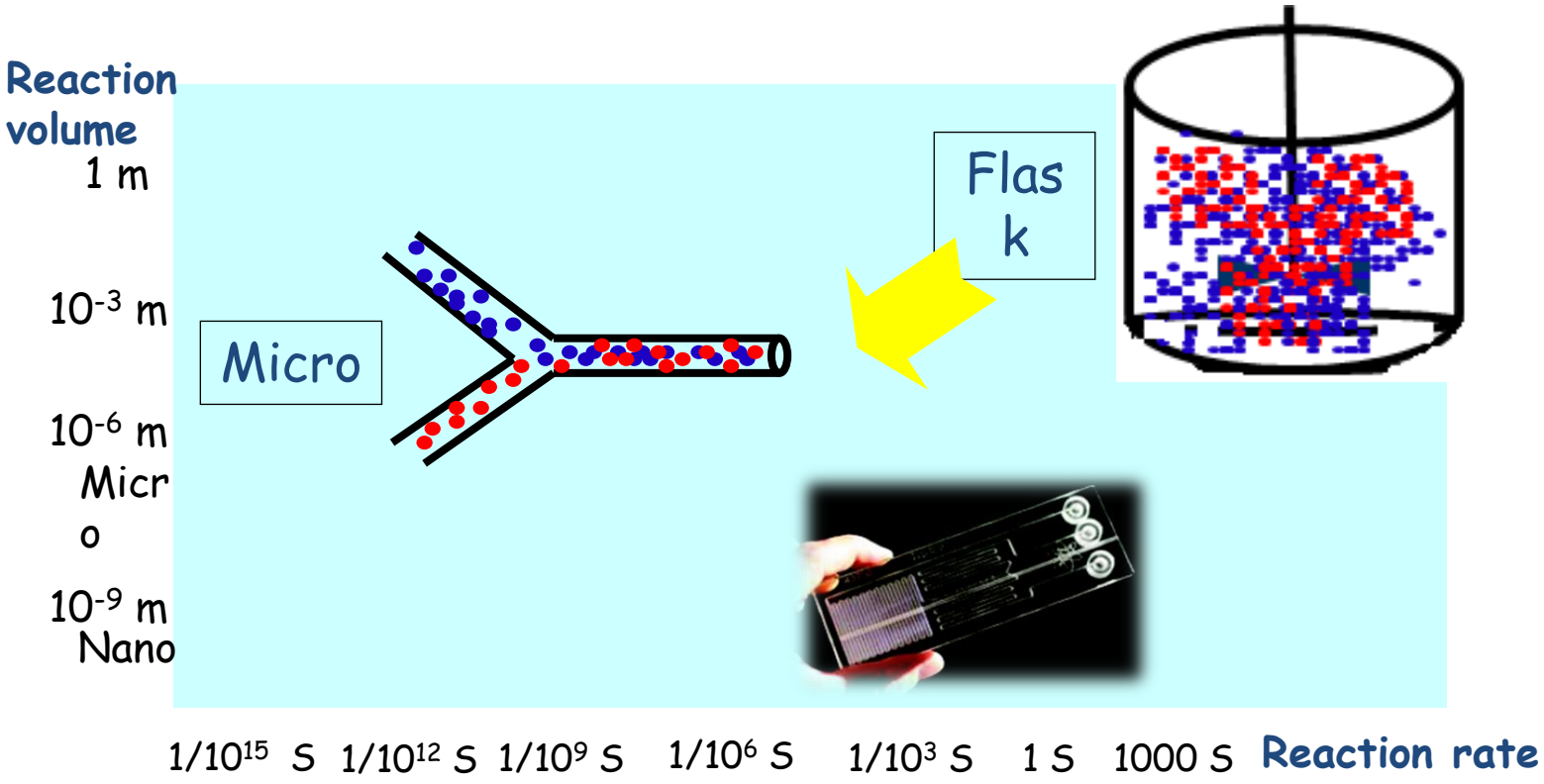
Micro reactor

Mixing efficiency

.2 Why MicroReactor? (Advantages of microreactor)

(2) Effect of mixing with high supplementary ratio

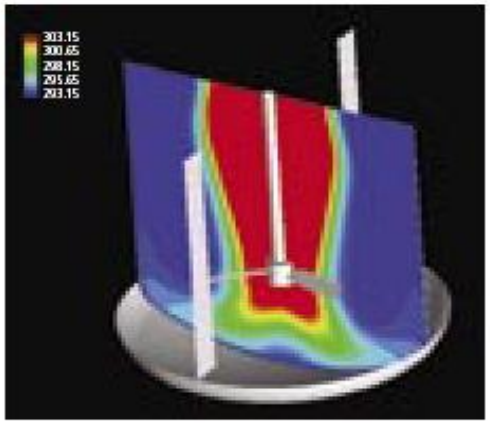
→ Effective reaction in interface using large unit surface



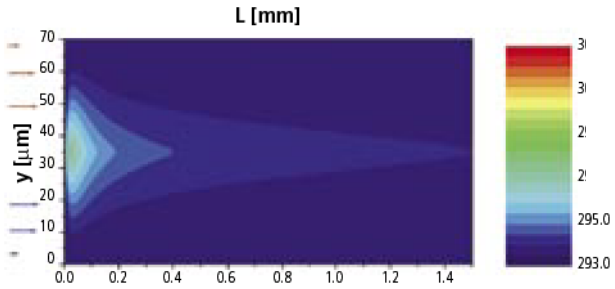
.2 Why MicroReactor? (Advantages of microreactor)

(3) Effective temperature control

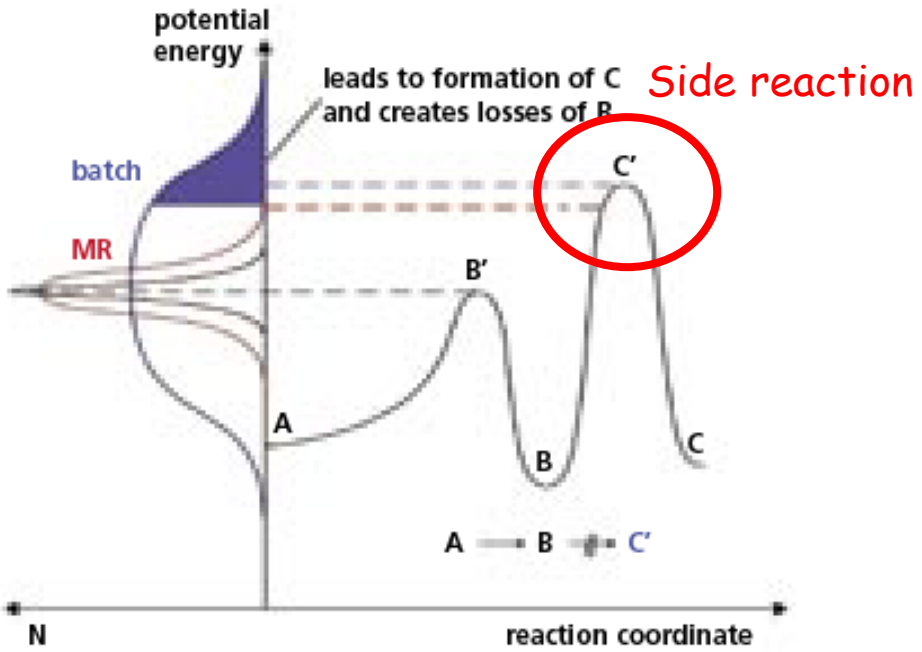
→Increasing production of final compound by suppression of side reaction



Batch reactor



Micro reactor

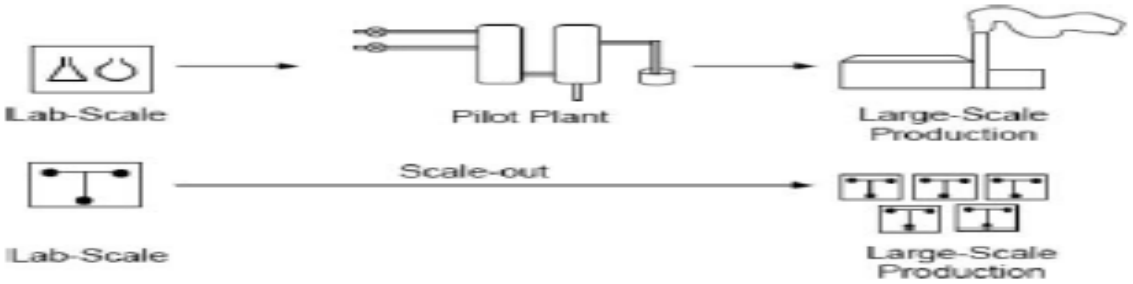


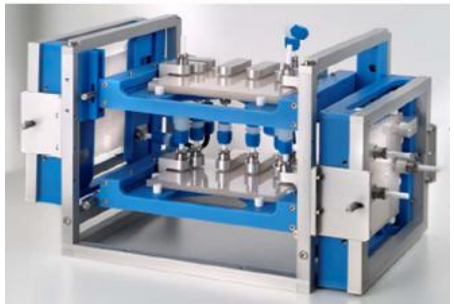
Precise controlling of temperature

.2 Why MicroReactor? (Advantages of microreactor)

(4) Easy multiplication

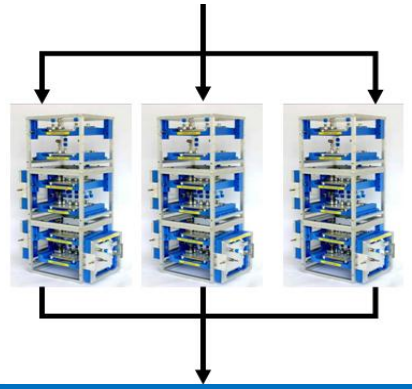
→ Possibility of immediate confront for requirement by market





Engineered reactor to fit the chemistry19

Product synthesis module to fit the process



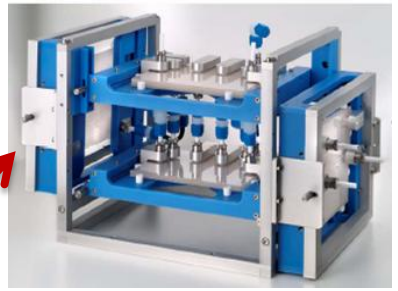
Numbering up capacity required

.2 Why MicroReactor? (Advantages of microreactor)

(5) Safety

→ Smaller damage when explosion (compared with Batch reactor)
→ Decreasing expanse for construction of safety facilities

✓Construction for safety
✓safeguard
in whole building

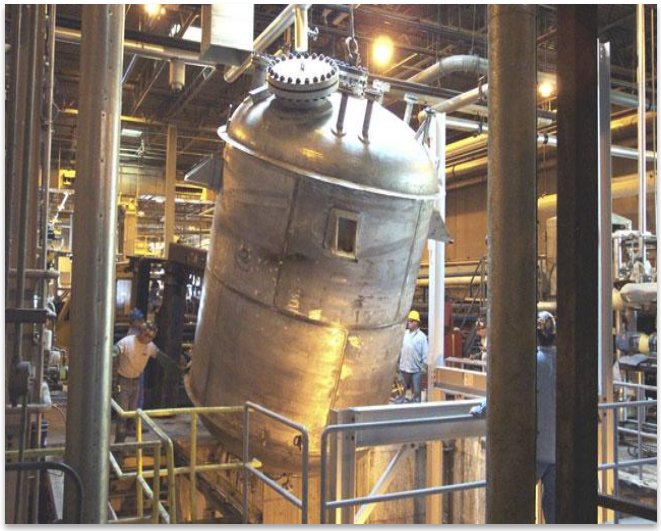


Construction for
local space

.2 Why MicroReactor? (Advantages of microreactor)

(6) Minimizing the installation space

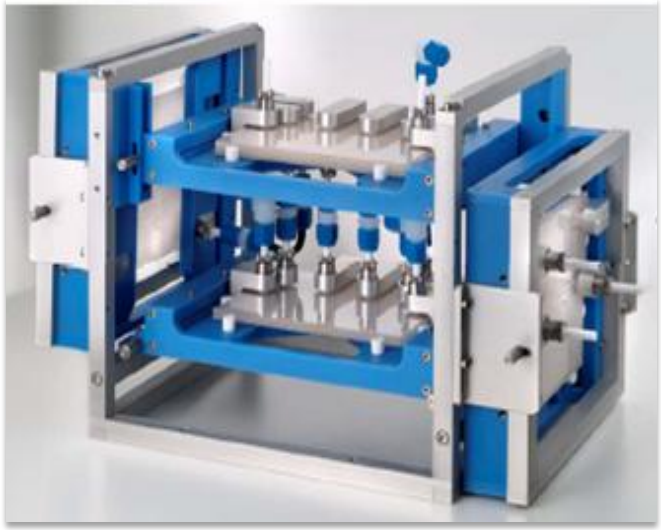
→ Decreasing expense for site



10^6ml

For the reactor of $1m^3$

- ✓ Space of $33m^2$
- ✓ Ground for plant



10 ml

- ✓ 70 X 50 X 50 cm (10Ml)
- ✓ No requirement for ground of plant

CONTENTS

1) Microfluidics

2) MicroReactor
   .1 What is that?
   .2 Why microreactor?

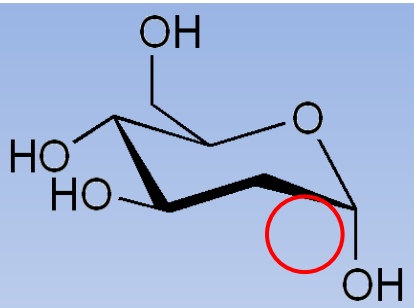
3) [^{18}F]FDG
   .1 What is that?
   .2 Why [^{18}F]FDG?

4) Chip Design

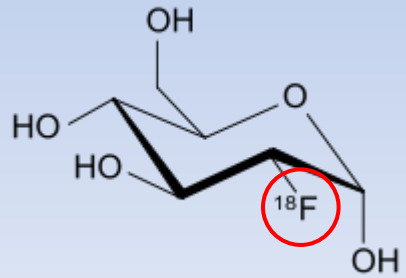
.1 [^{18}F]FDG – What is ?

^{18}F-FDG

- Fludeoxyglucose (^{18}F) of Fluorodeoxyglucose (^{18}F)
- Radiopharmaceutical used in PET for diagnoses
  (PET, Positron Emission Tomography, medical imaging modality)
- Process
  : Injection → Distribution around the body → Imaging
- Chemical characteristic
  : 2-deoxy-2-(^{18}F)fluoro-D-glucose
  (glucose analog with the positron-emitting radioactive isotope fluorine-18 substituted for the normal hydroxyl group at the 2′ position in the glucose molecule)

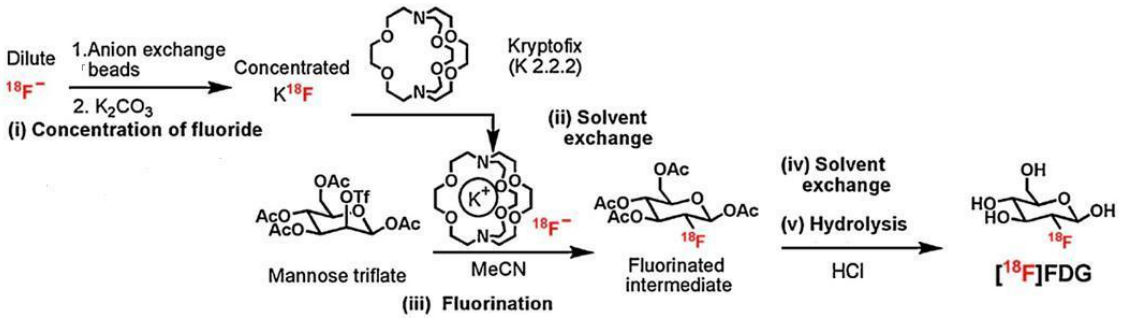


2-Deoxy-D-glucose



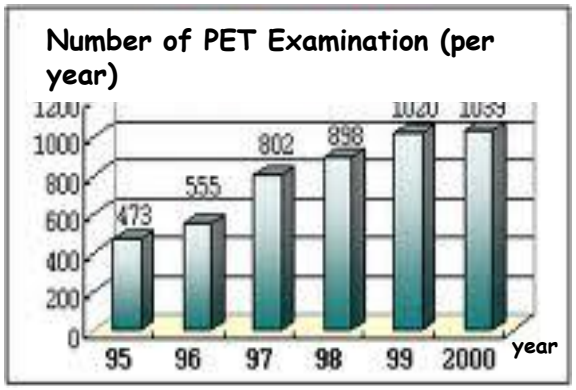
2-Deoxy-^{18}F-D-glucose

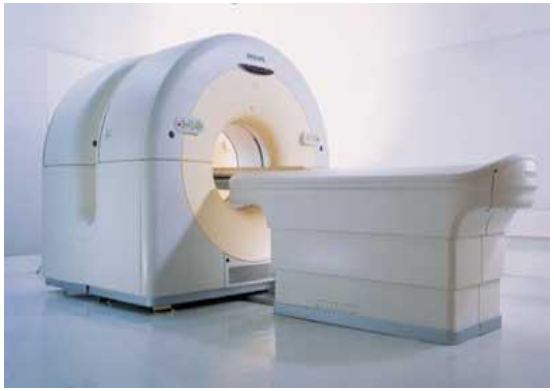
< Chemical process for ^{18}F-FDG >

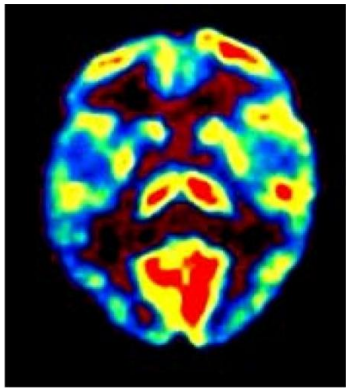


.2 [^{18}F]FDG – Why it ?

Increasing PET utilization
→ Increasing requirement of ^{18}F-FDG for PET







18F-FDG synthesis with microreactor

- Injection immediately after producing ^{18}F by cyclotron
- High degree of purity
  → Better image
- Lower expense for radiation shielding
- Guaranteeing the safety
- Decreased synthesis time with small amount of compound
  → Decreasing money and harmful by-product

CONTENTS

1) Microfluidics

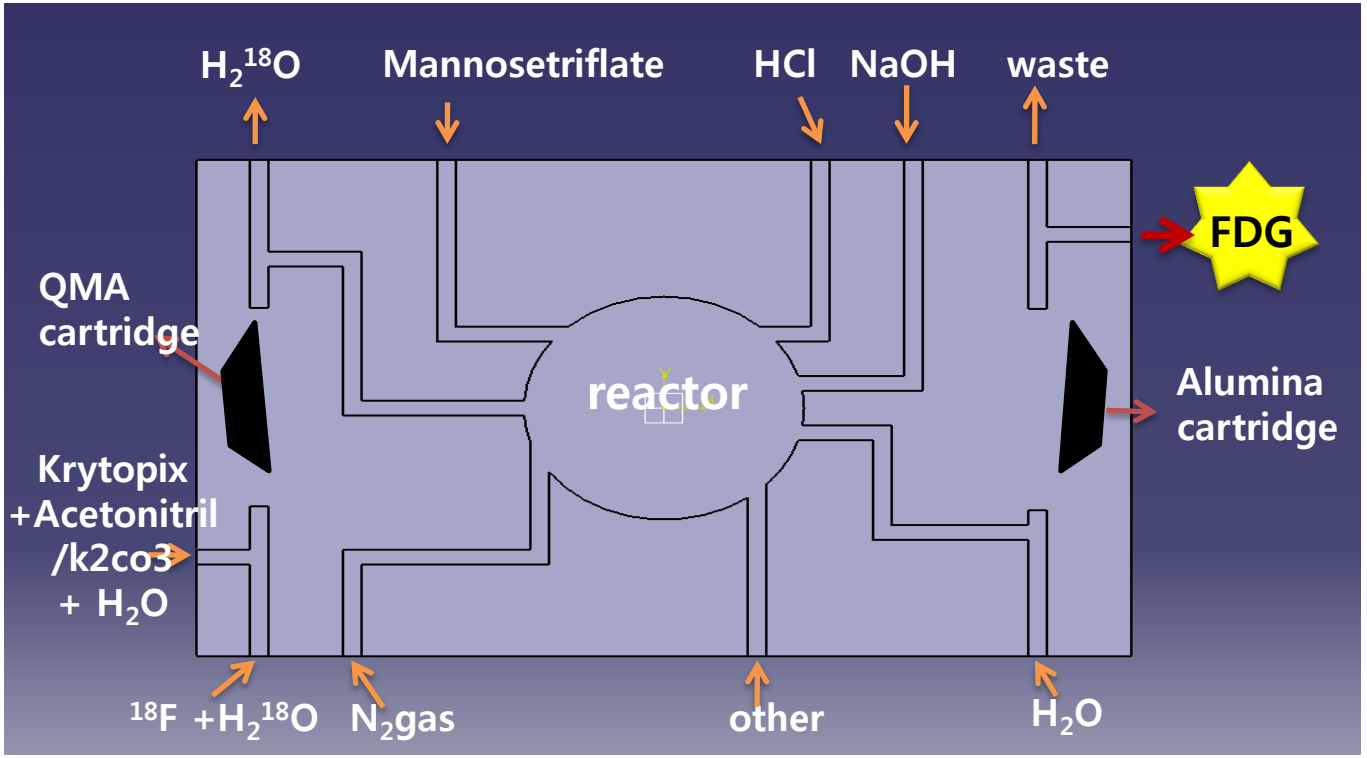
2) MicroReactor
   .1 What is that?
   .2 Why microreactor?

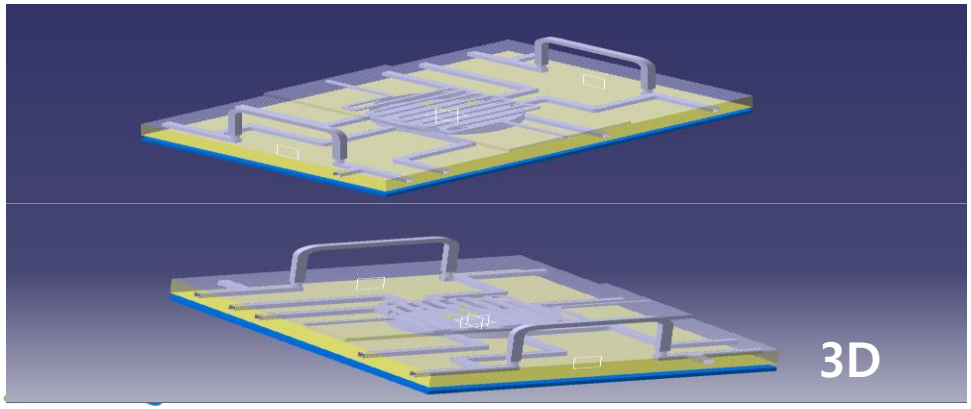
3) [^{18}F]FDG
   What is that?
   Why [^{18}F]FDG?

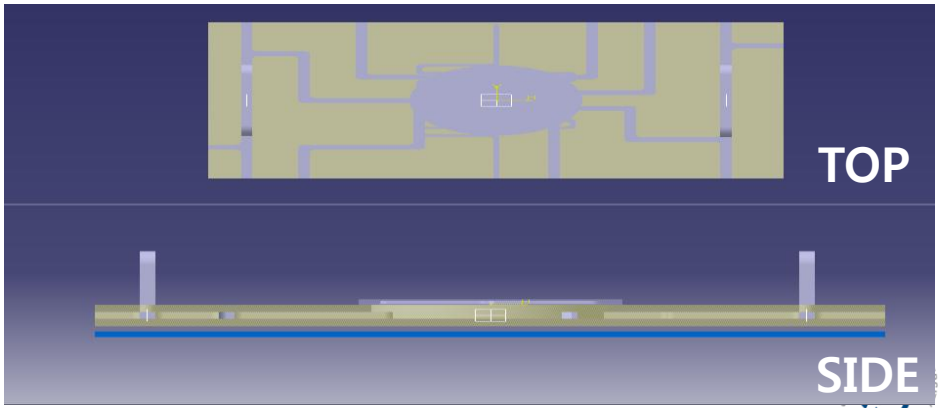
4) Chip Design

Chip Design

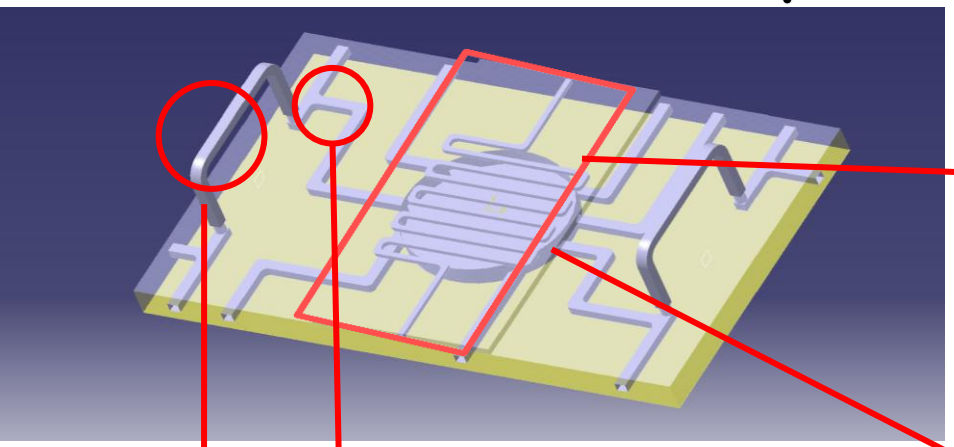
Principle of producing ^{18}F-FDG

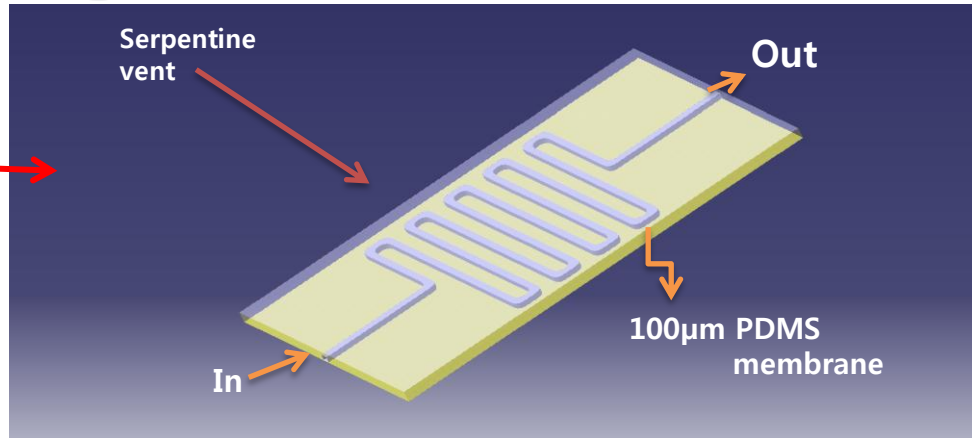


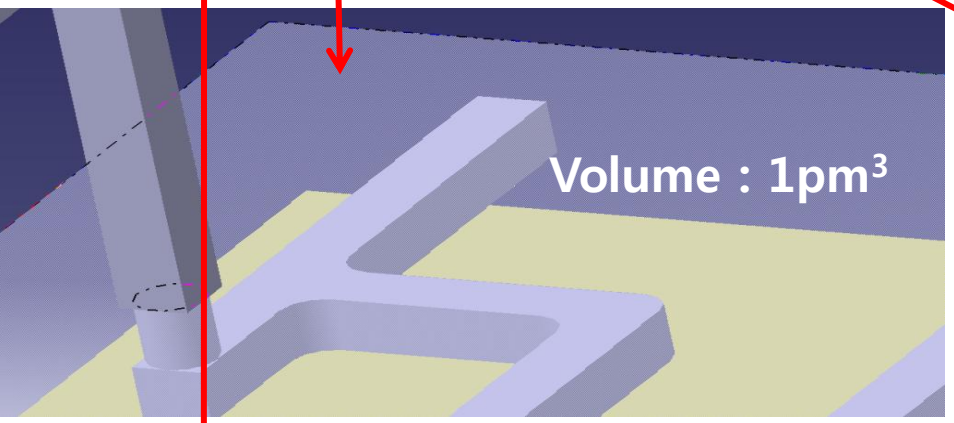


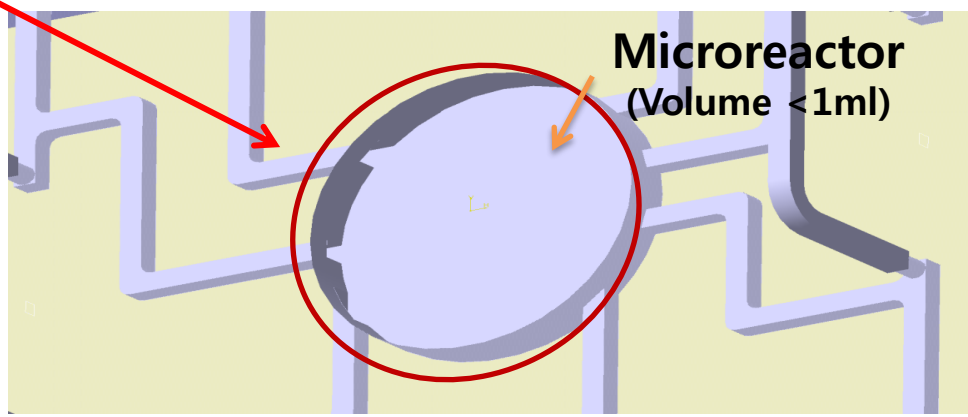


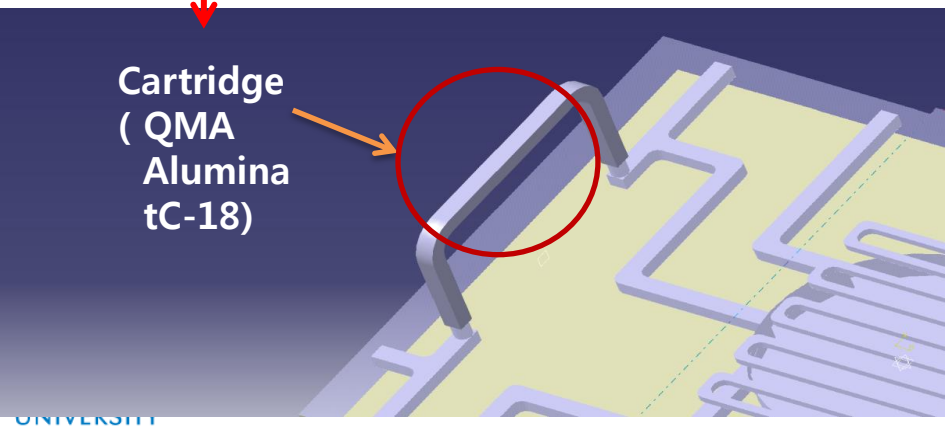
Chip Design (Detail)

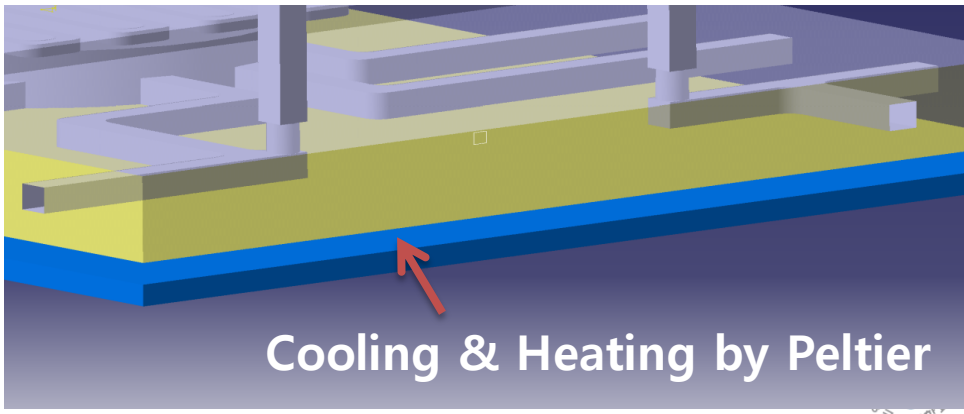






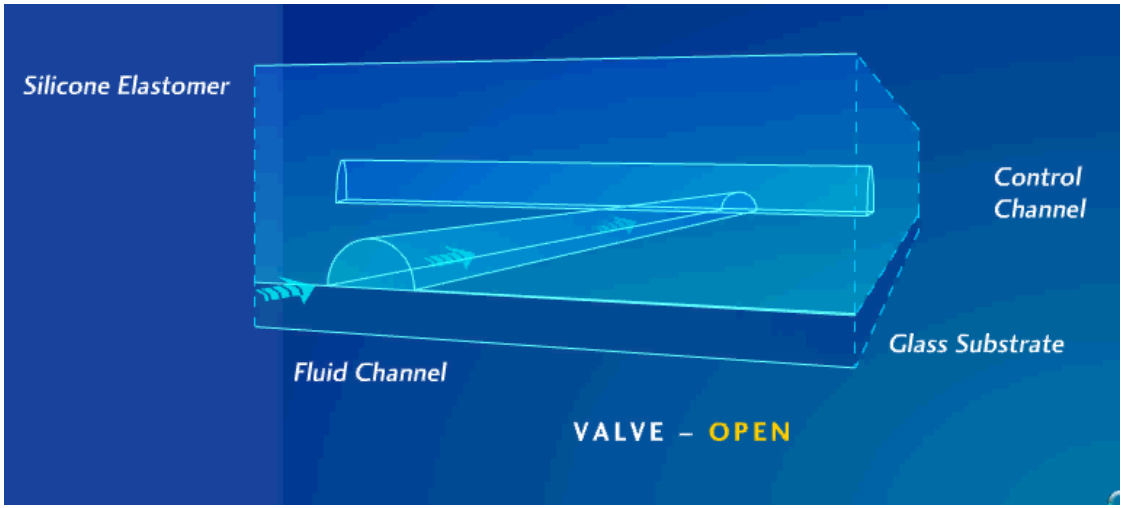




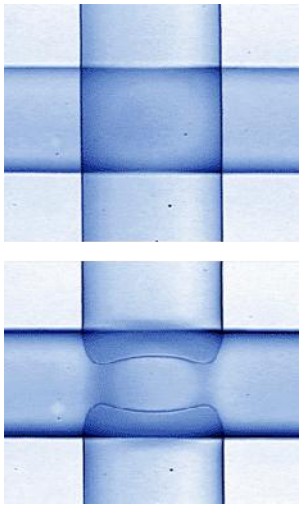


Chip Design (Controller)

Flow controller (Gas)



Top view



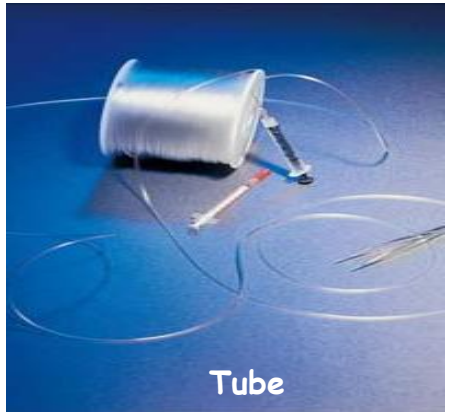
open

closed

- Pressurized gas to the channels of the upper layer → sealing the bottom layer
- Using *Labview* simulation tool
- Development of controlling software

controller

8-Channel Manifold Set

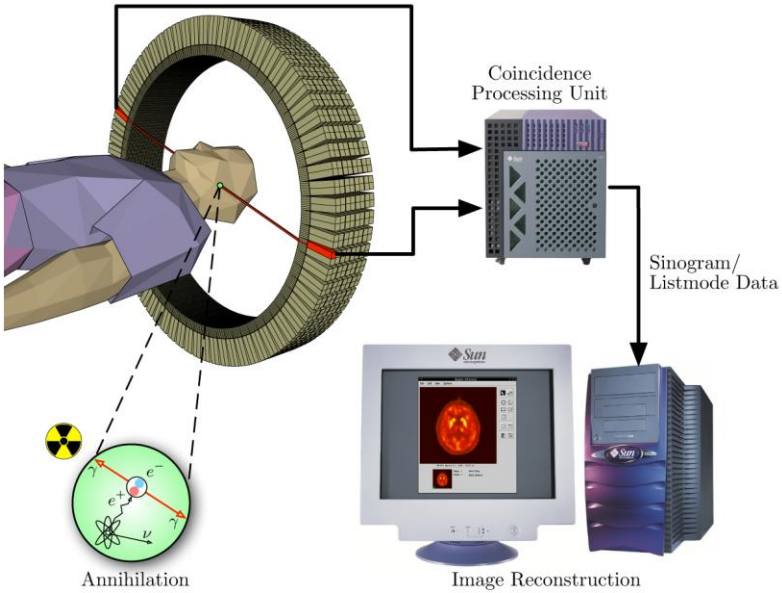


Tube

Thank you ☺

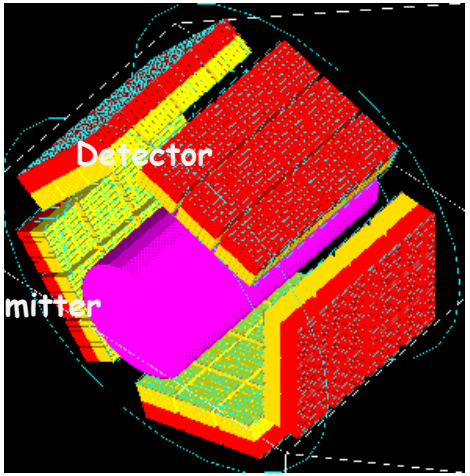
PET

- Positron Emission Tomography, PET
  : Medical imaging modality used in Nuclear Medicine
- Two 511KeV gamma in 180 degree from Annihilation
  (Radioisotopes: F-18, O-15, N-13, C-11)
- Radiopharmaceuticals : Labeled radioisotope for specific interest
- coincidence circuit measuring LOR(Line of Response)

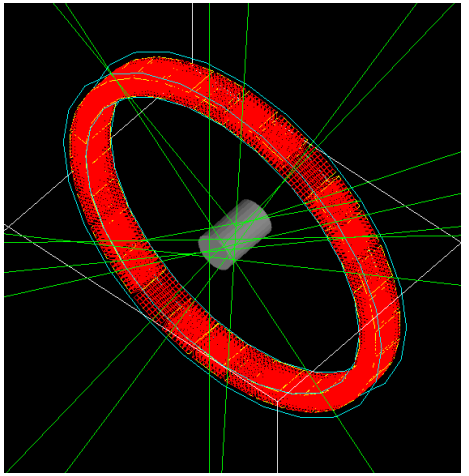


Process

Monte Carlo Simulation (GATE)



Geometry



LOR