Deutsche
Gesellschaft
für Nuklearmedizin
e.V.

SUMMER SCHOOL 2014

Translational Research in Molecular Imaging and Radionuclid Therapy

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Kinetic modelling for quantitative imaging (with PET and SPECT)

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What is it all about?

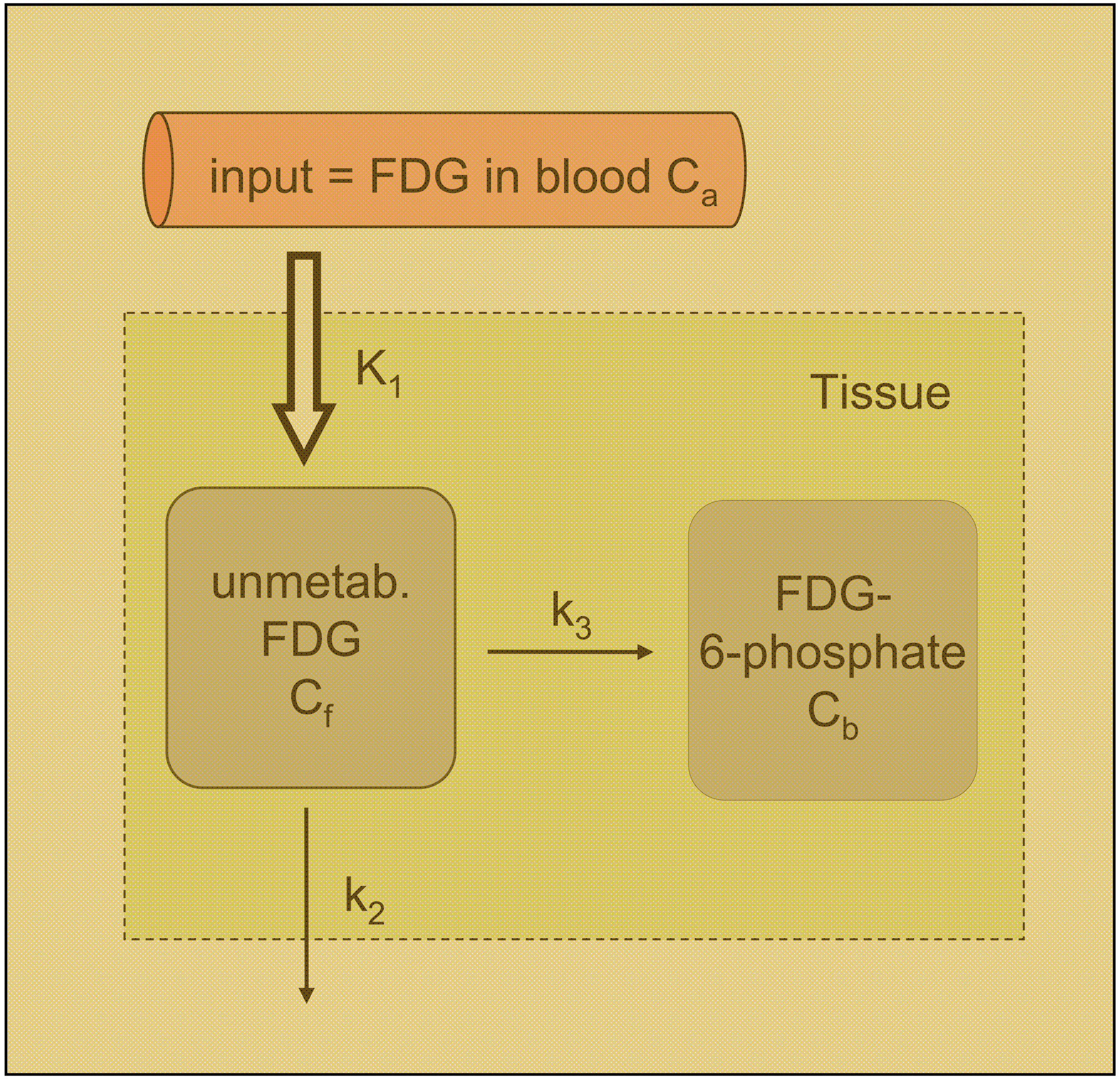
Quantification!

Level 1 („dosimetry"): tracer concentration (kBq/ml)

Level 2 („diagnostics"): physiologic parameters

- perfusion (ml blood / g tissue / min)
- metabolic rates (µmol substrate / g tissue / min)
- receptor density (fmol / mg)
- affinity of tracer for target (nM)
- …

Quantification of physiologic parameters in PET: problem



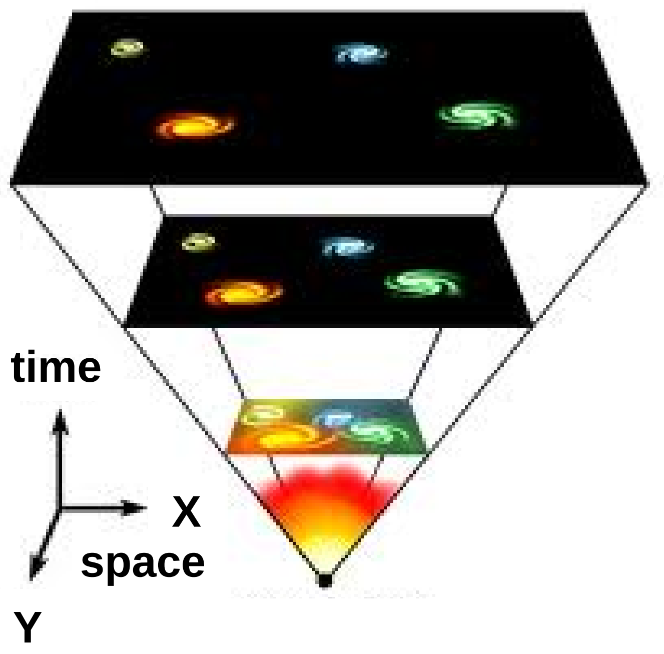
PET image volume element (voxel)

sum of signals from all compartments

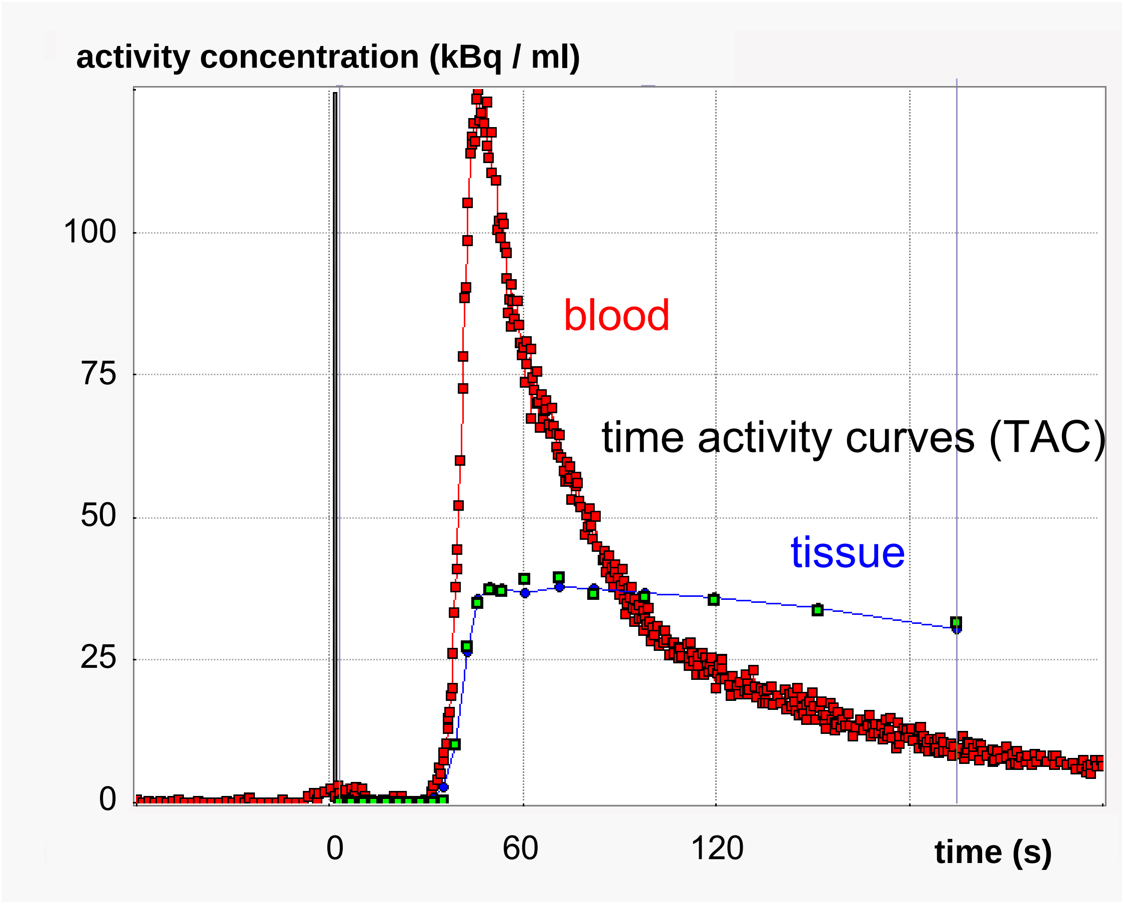
compartments defined by function, not localization

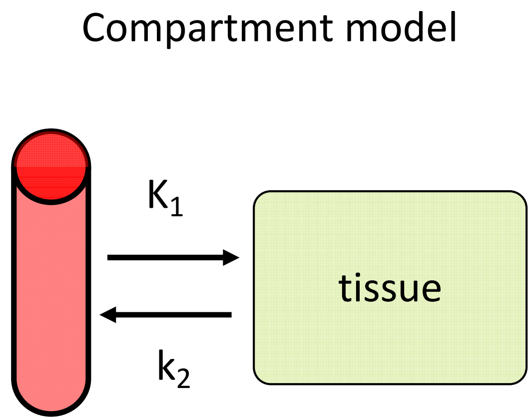
Quantification of physiologic parameters in PET: solution

functional compartments might be separated in **time** (rather than space)



Quantification of physiologic parameters: tracer **kinetic** modelling





Workflow

1a) dynamic PET / SPECT imaging

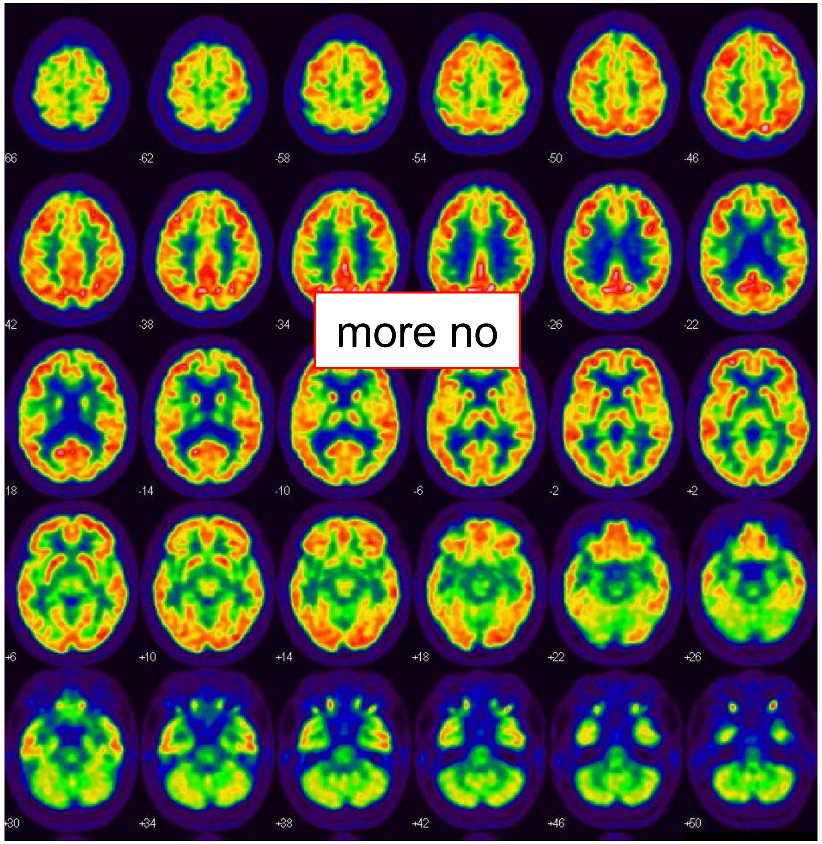
1b) blood sampling (input function)

2. fit model to measured data

(→ „modelling“)

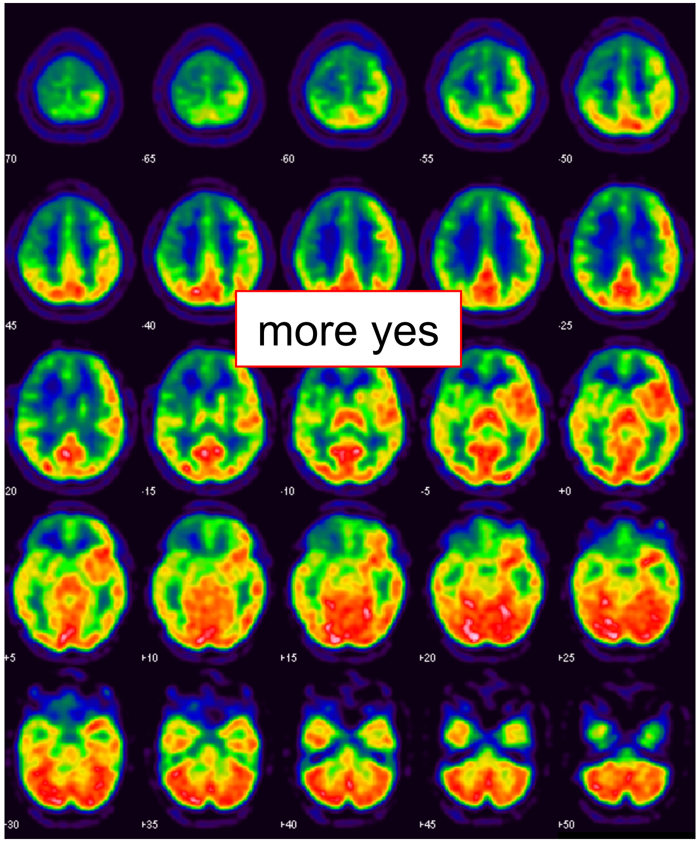
Kinetic modelling: To model or not to model?

F-18-FDG (glucose metabolism)

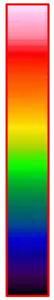


uptake
(arbitrary)

O-15-water (perfusion)

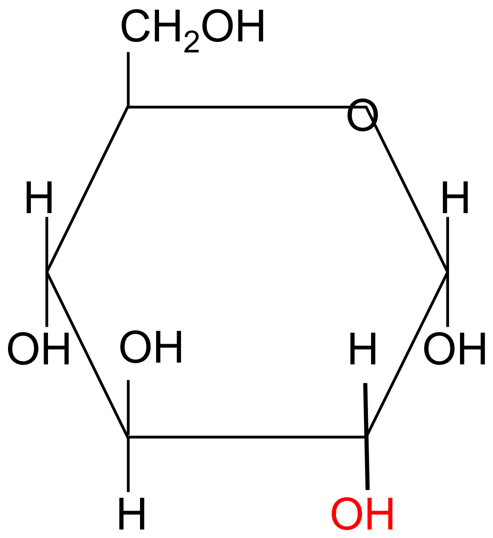


regional
cerebral
blood flow
(ml/100g/min)

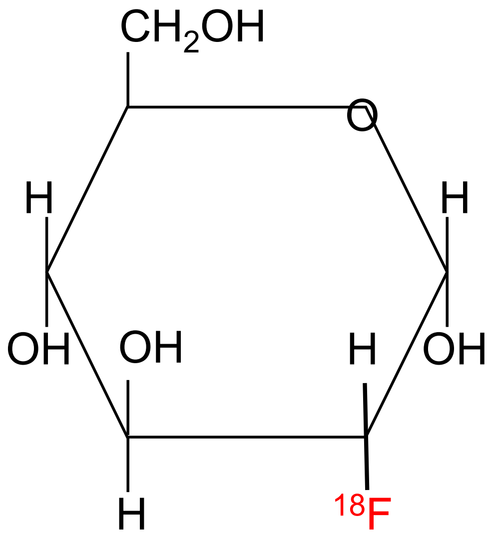


[F-18]-fluorodeoxyglucose (FDG)

target of modelling: metabolic rate of glucose MRGlc (µmol glucose / g tissue / min)



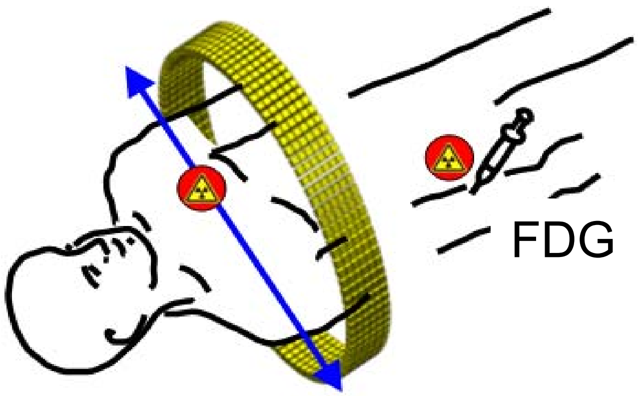
glucose



[^{18}F]-fluorodeoxyglucose (FDG)

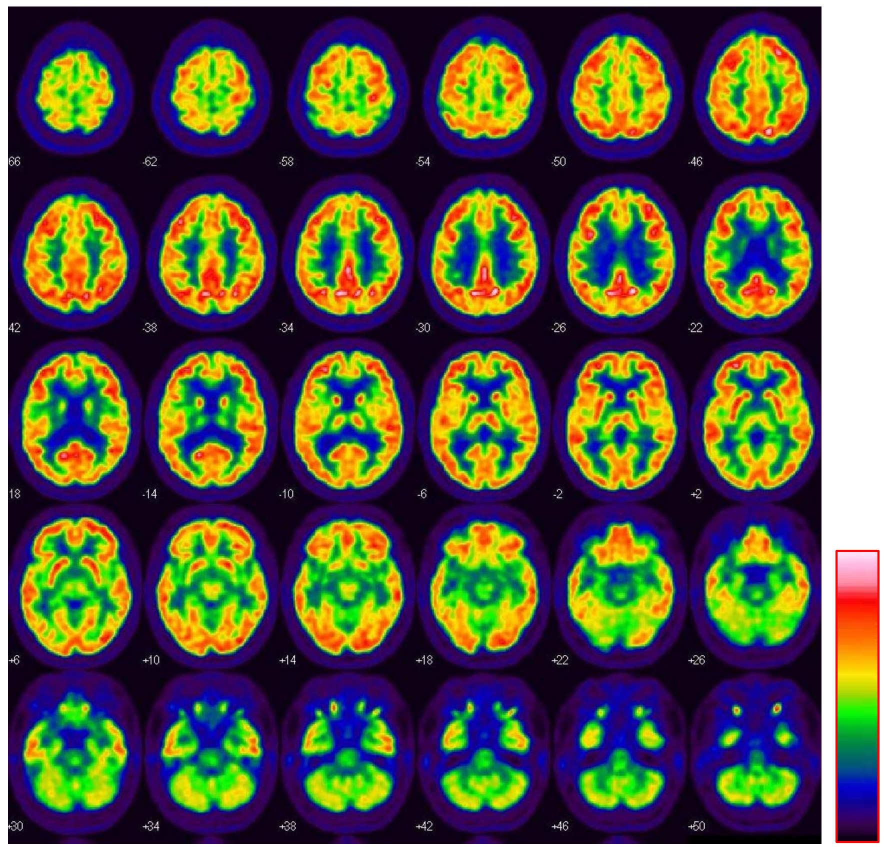
- β^+ decay (BR 100%)
- half-life 110 min

FDG-PET: conventional procedure



40 min p.i.

static uptake (retention) image



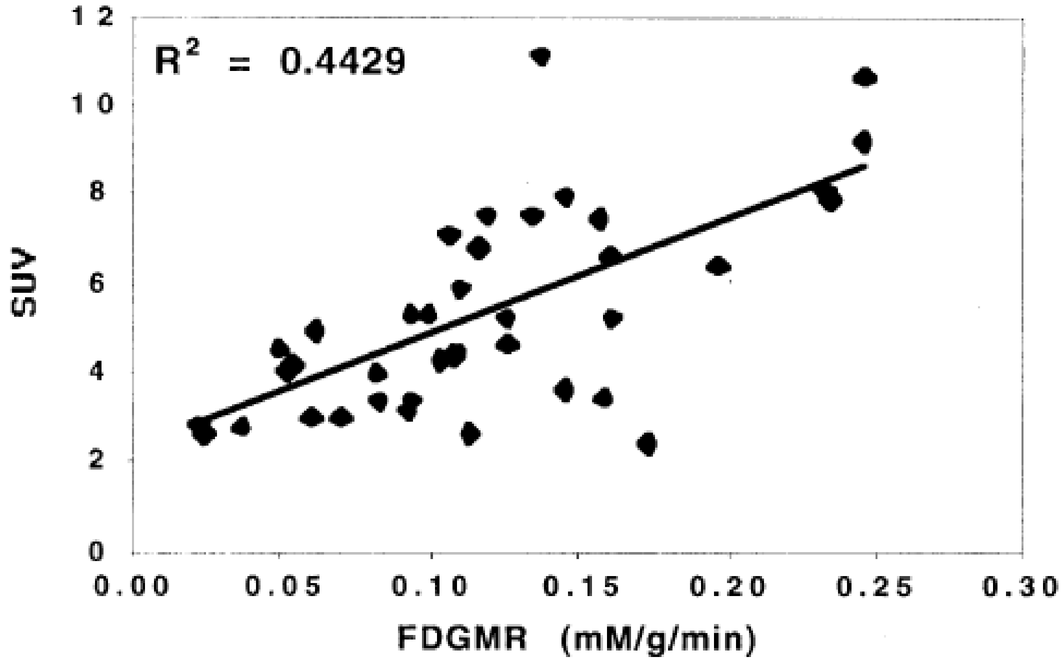
FDG retention = MRGlc?

FDG-PET: tracer kinetic modelling versus retention image

Graham M et al., Nucl Med & Biol 2000; 27: 647-55

FDG retention
(standardized uptake value, SUV)

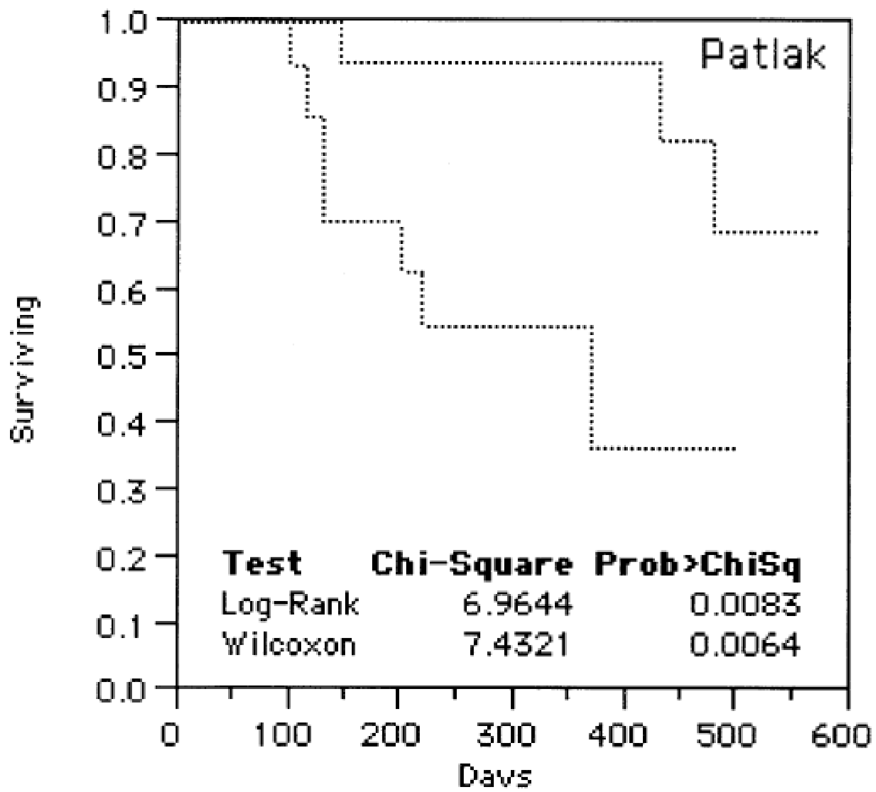
40 patients with colon cancer

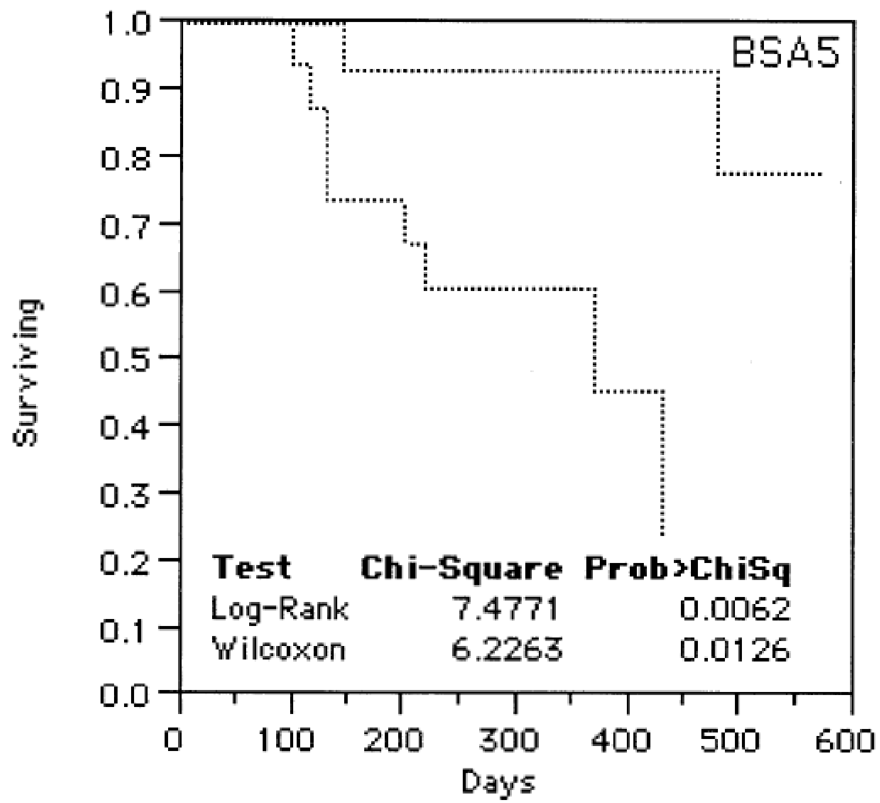


metabolic rate of glucose
(kinetic modelling)

FDG-PET: tracer kinetic modelling versus retention image

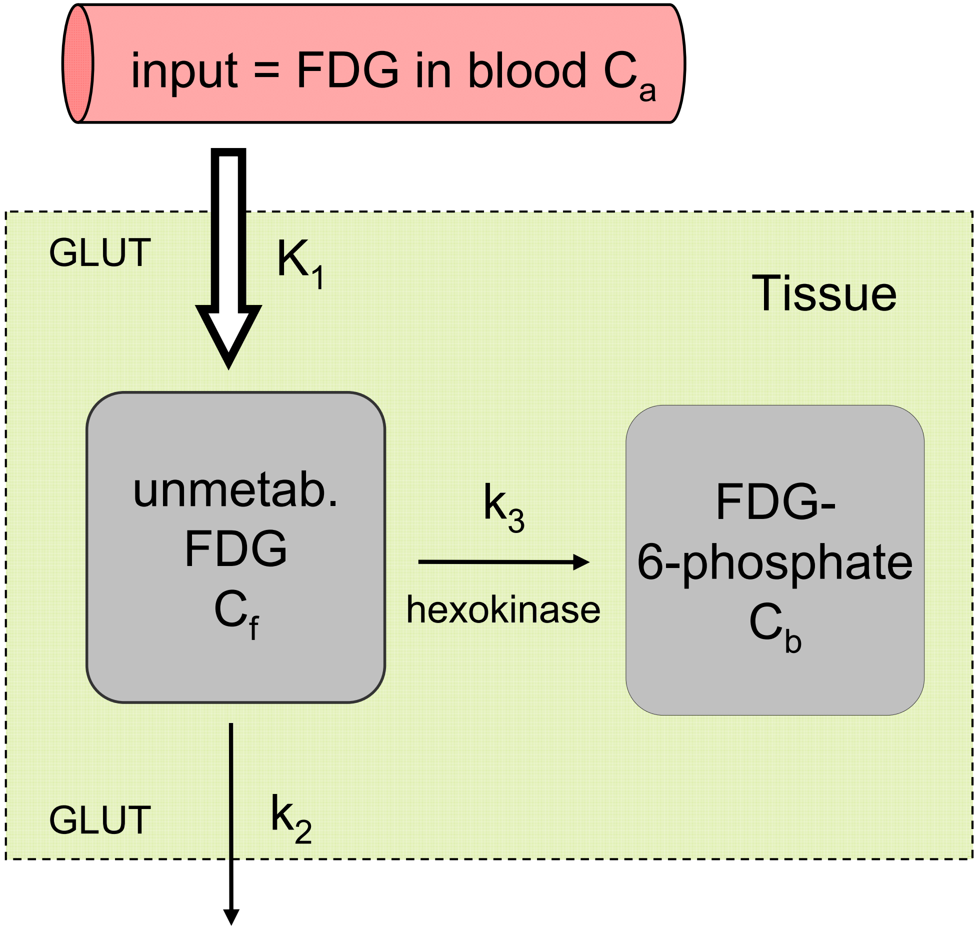
Graham M et al., Nucl Med & Biol 2000; 27: 647-55





metabolic rate of glucose (kinetic modelling) equivalent FDG retention (standardized uptake value, SUV)

FDG: pharmacokinetics



healthy subjects (brain, euglycemia)

K_1 = 0.07 ml/g/min

k_2 = 0.12 min^{-1}

k_3 = 0.04 min^{-1}

- phosphorylation is irreversible
- single pass extraction fraction is small

$K_1 = E * F$

F = perfusion (ml / 100g / min)

E = extraction = $1 – \exp(-PS/F)$
(Renkin-Crone)

PS = permeability surface area product

$E \approx 1 – (1 – PS/F) = PS/F$

$K_1 = E * F \approx PS/F * F = PS$

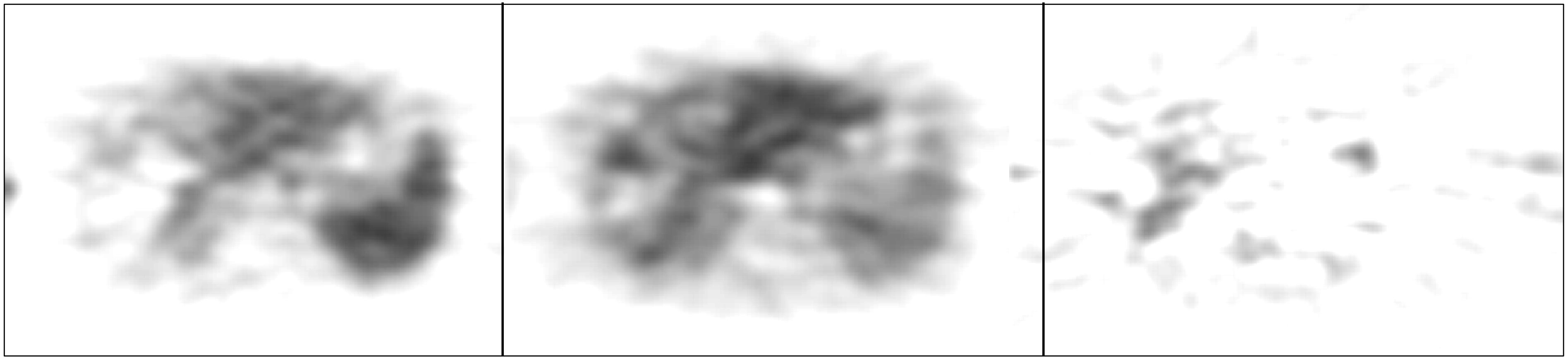
i.e., K_1 independent of perfusion

FDG retention ~ metabolic rate

FDG: cave in extreme conditions

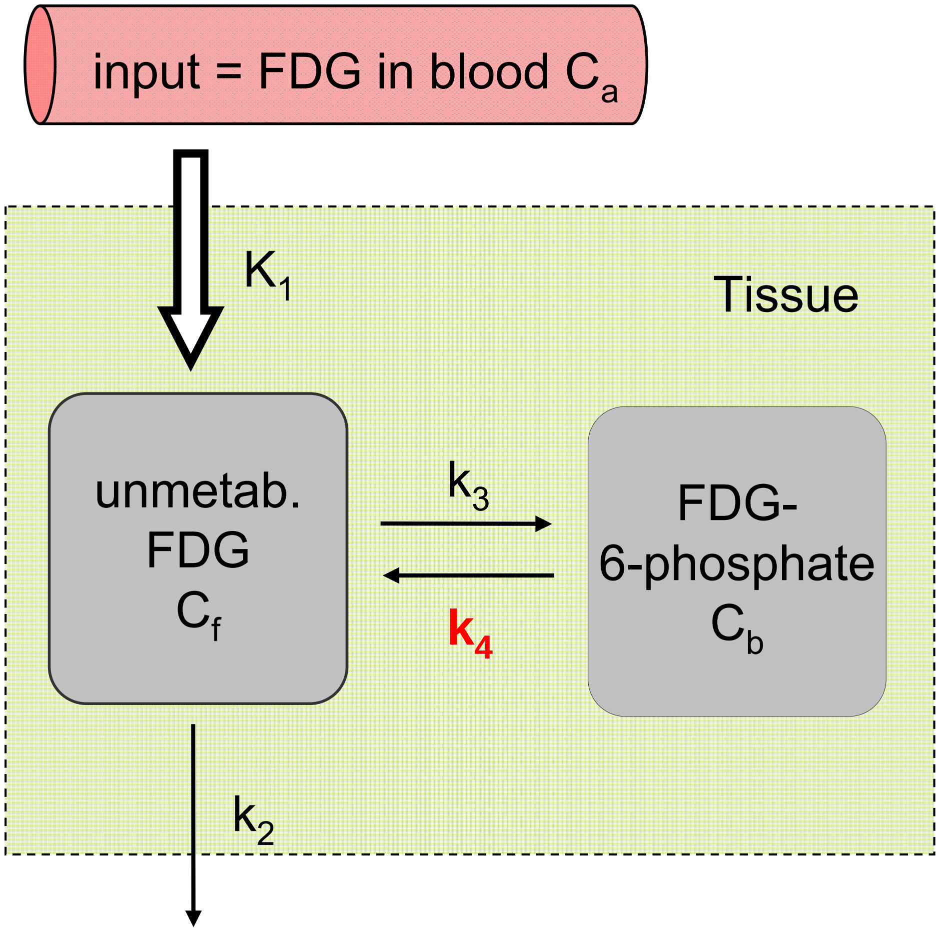
Recurrence of hepatocellular carcinoma after chemoembolisation

perfusion ($H_2{}^{15}O$) | FDG retention | glucose consumption rate



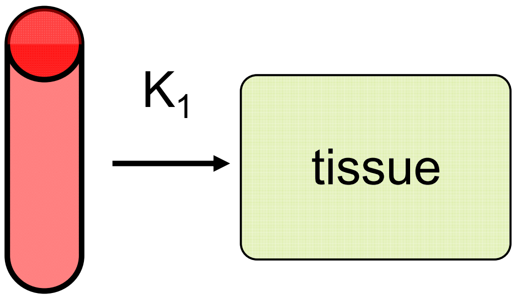
adapted from Wolfgang Burchert, Bad Oeynhausen

FDG: cave liver

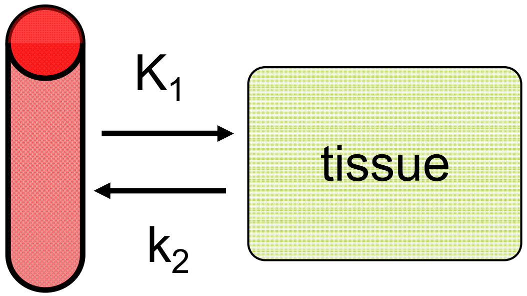


Compartment models

1-tissue compartment models



unidirectional transport



bidirectional transport

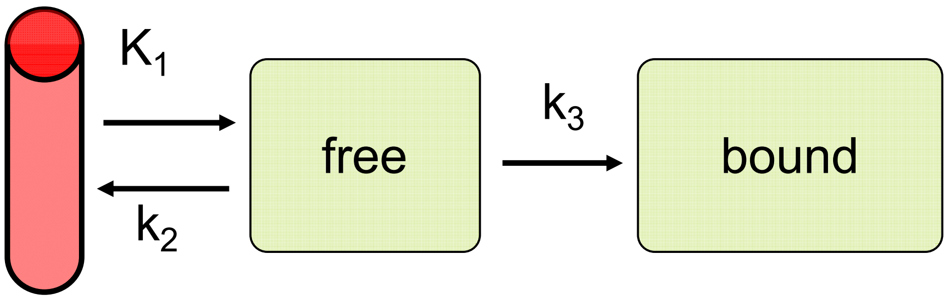
O-15-water

freely diffusible

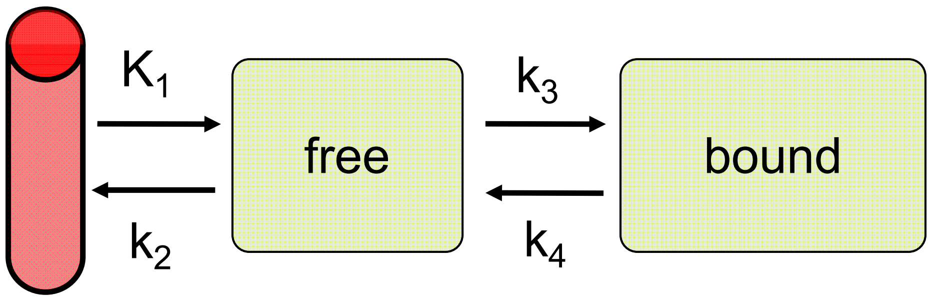
$K_1 = E * F \approx F$

F-18-FDG

2-tissue compartment models



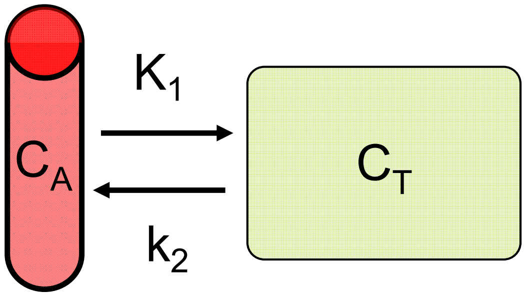
irreversible binding



reversible binding

Bidirectional transport

graphical representation



one-to-one translation

formula representation

$$\frac{dC_T}{dt} = K_1 C_A - k_2 C_T$$

$$C_T = K_1 \int_0^t e^{-k_2 (s-t)} C_A(s) ds$$

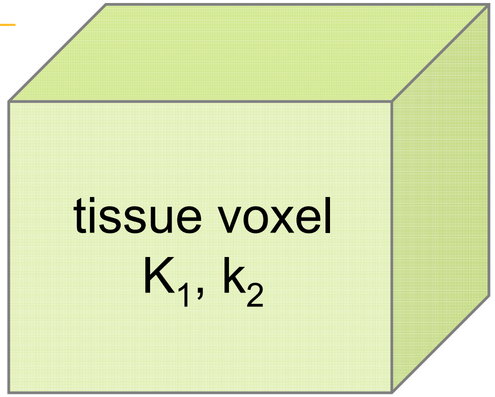
operational equation

PET signal (time activity curve)

Modeling: (linear) system

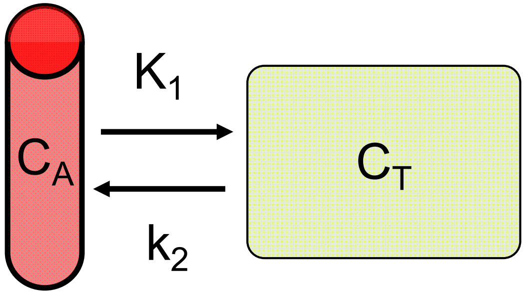
stimulus(t)

C_A = tracer in blood



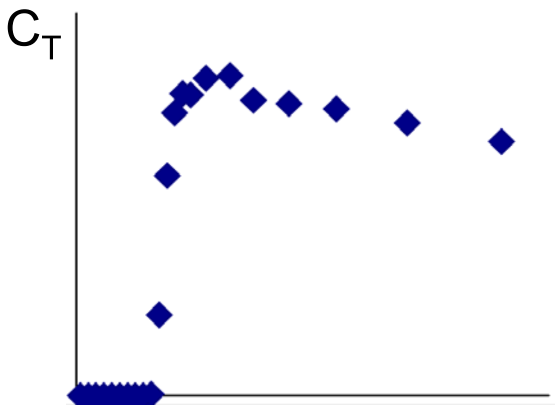
response(stimulus; K_1,k_2; t)

C_T = tracer in tissue



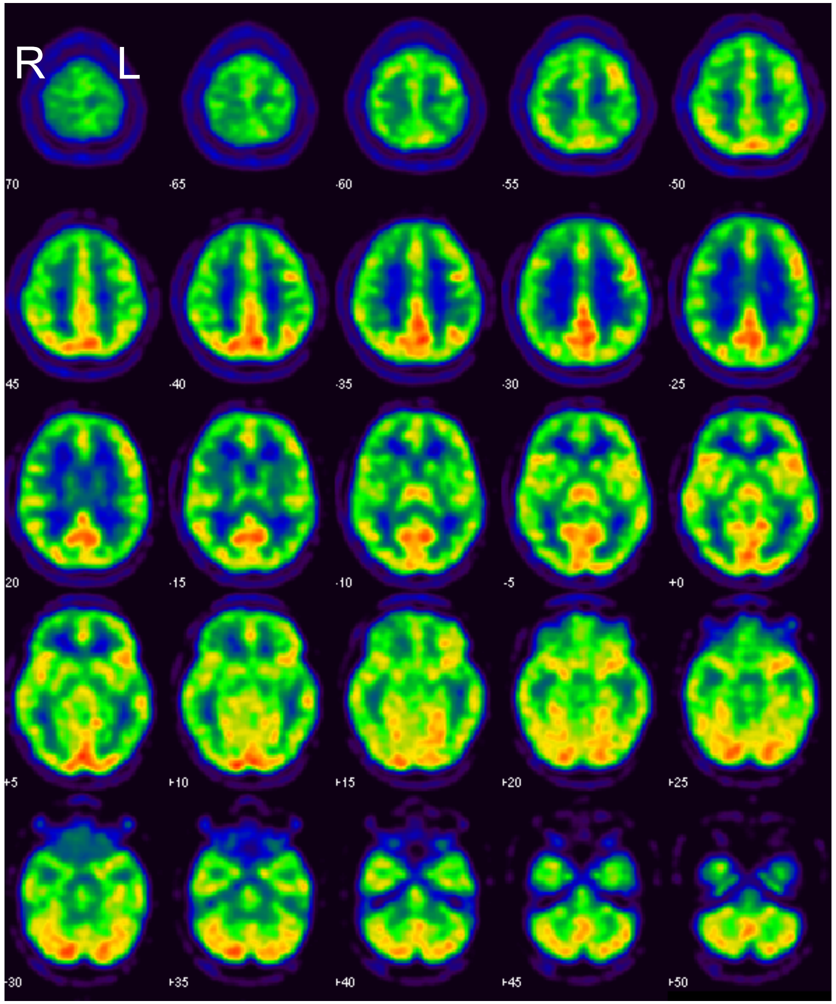
$$C_T = K_1 \int_0^t e^{-k_2(s-t)} C_A(s) ds$$

(least squares) fit

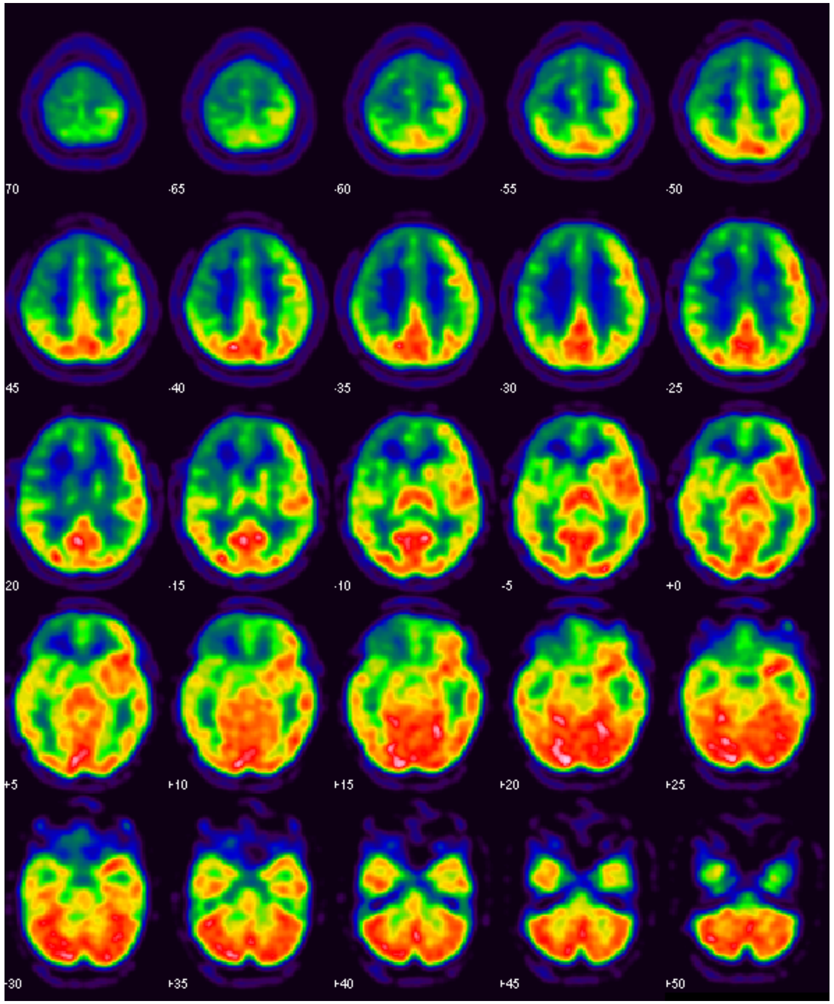


Female, 16 y, Moyamoya disease

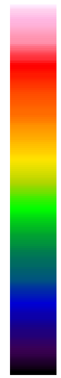
rest



maximum dilatation of blood vessels (Diamox)



rCBF
(ml/100g/min)



Female, 16 y, Moyamoya disease

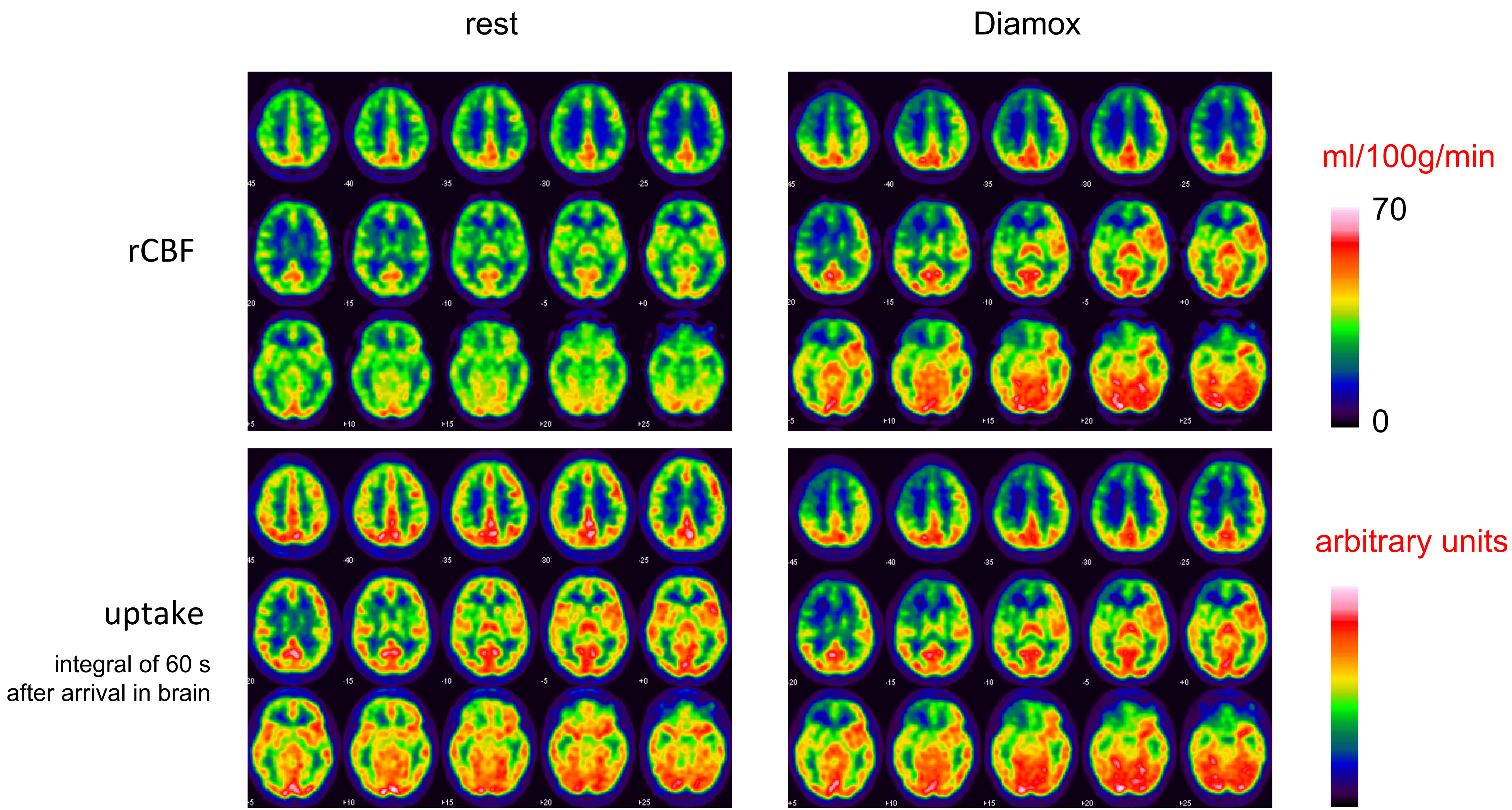
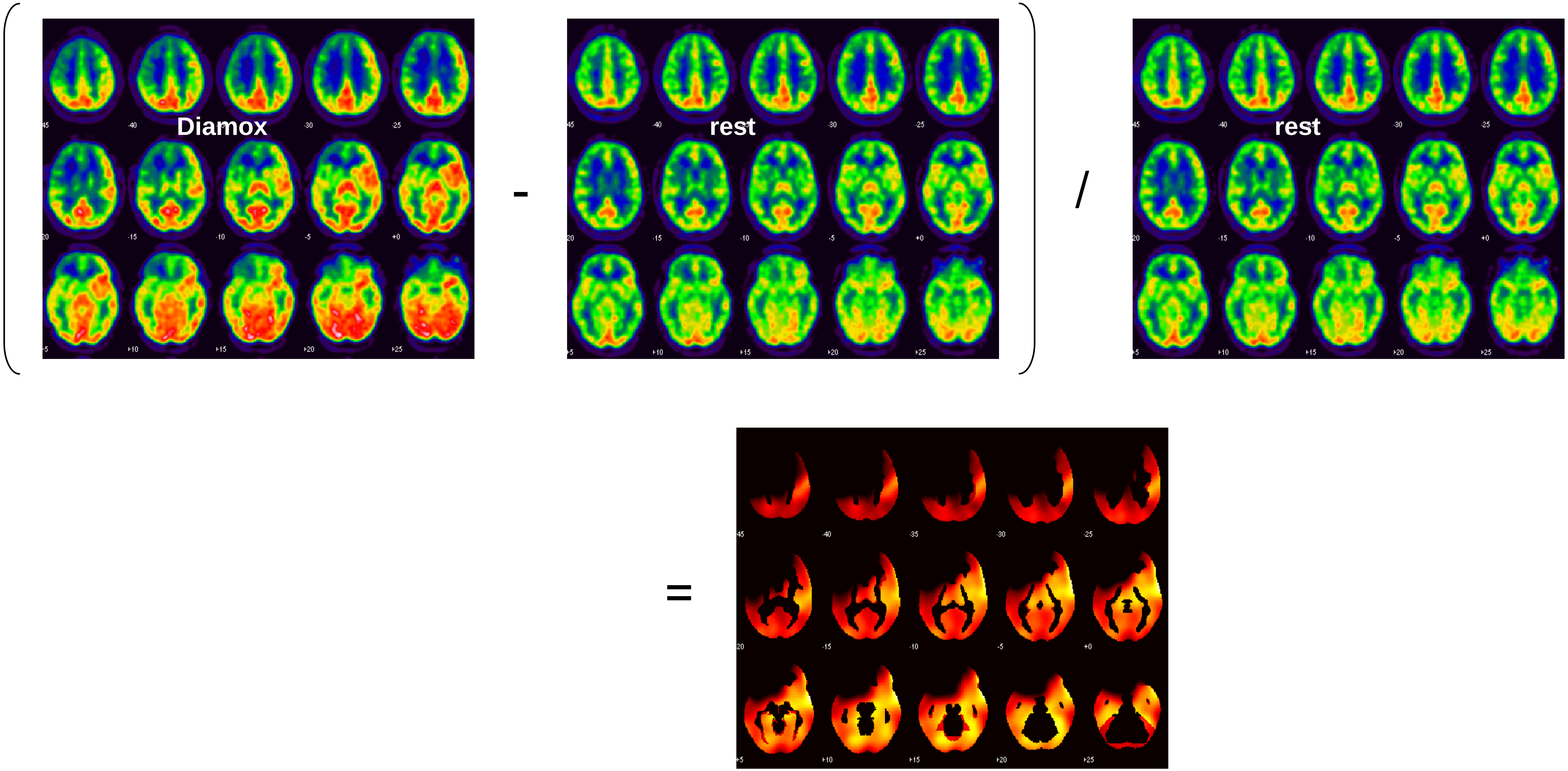
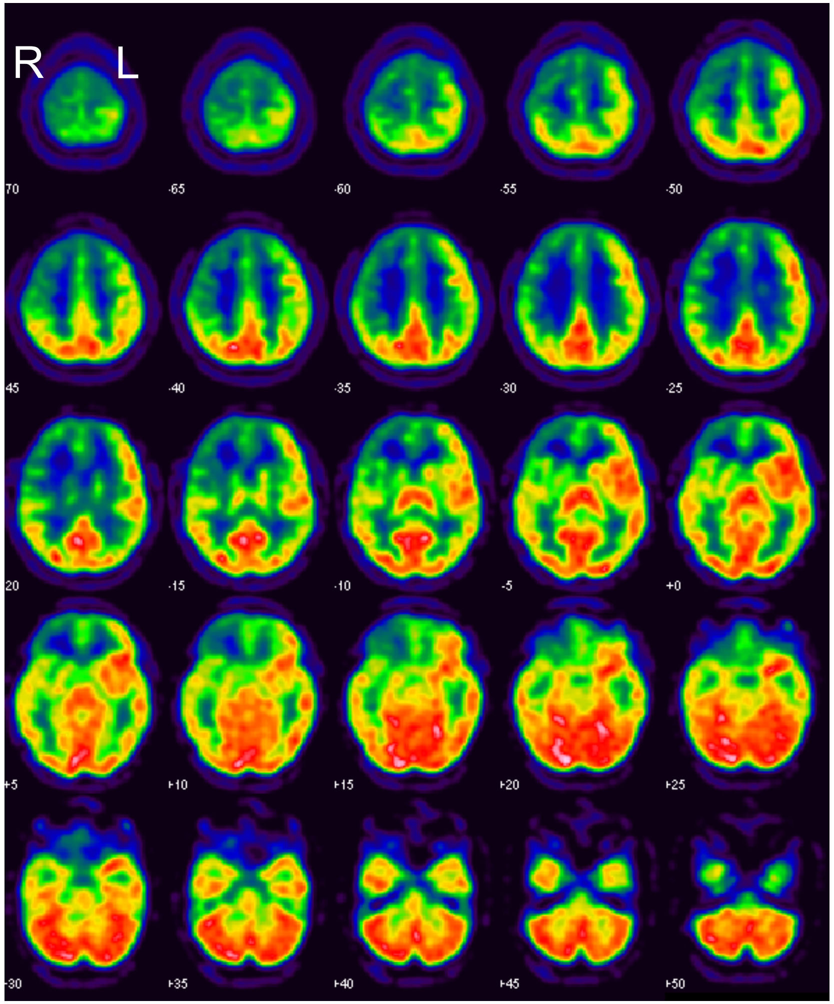


image algebra



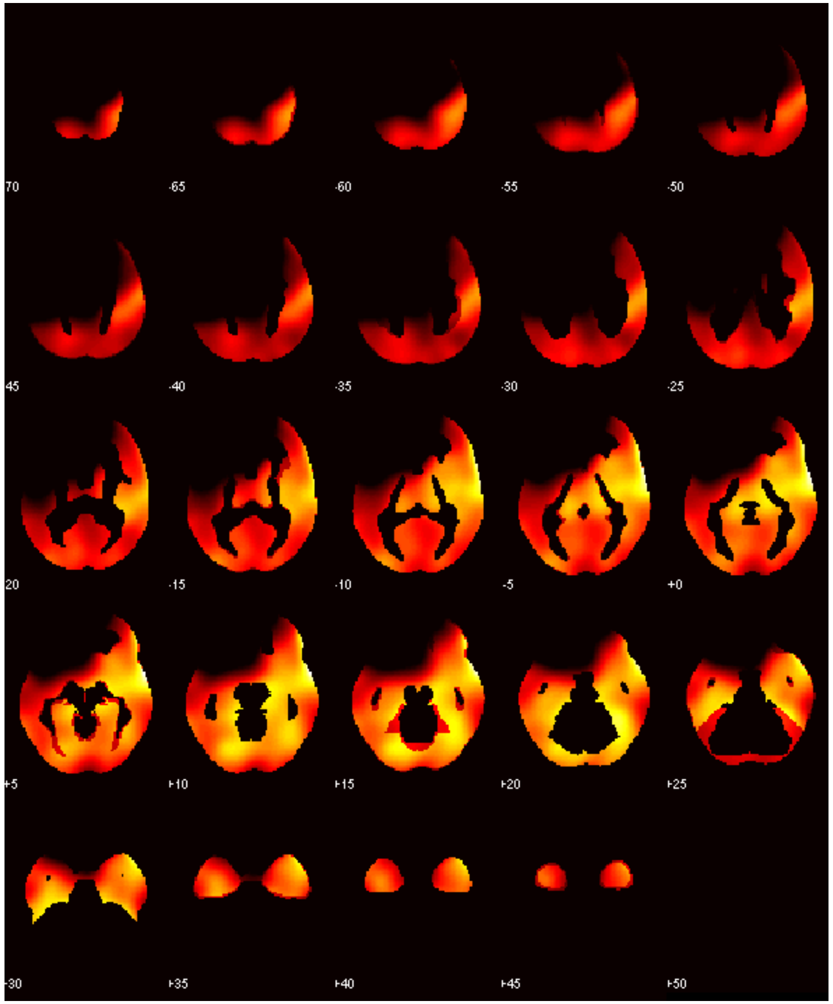
Female, 16 y, Moyamoya disease

Diamox

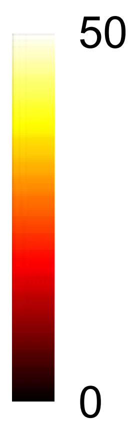


cerebrovascular reserve (%)

= 100*(Diamox-rest)/rest



CVR (%)



global effects

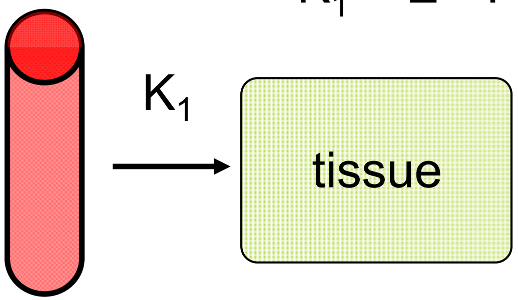
follow-up

….

perfusion SPECT with Tc-99m-HMPAO

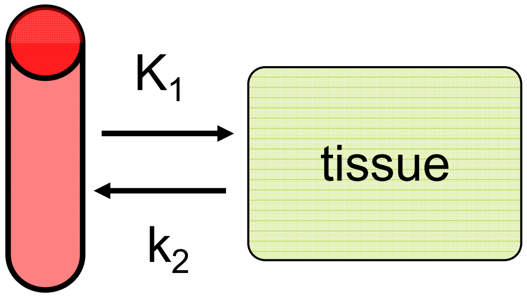
chemical microsphere

$K_1 = E * F \approx F$



unidirectional transport

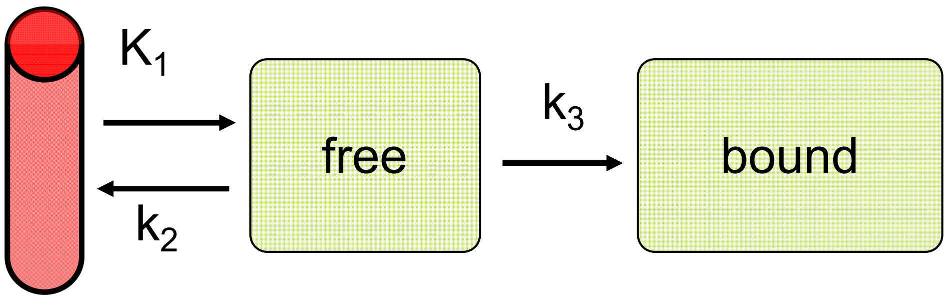
O-15-water



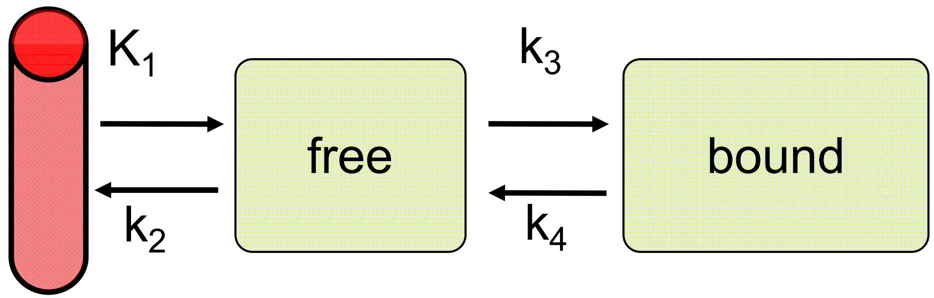
bidirectional transport

F-18-FDG

2-tissue compartment models



irreversible binding



reversible binding

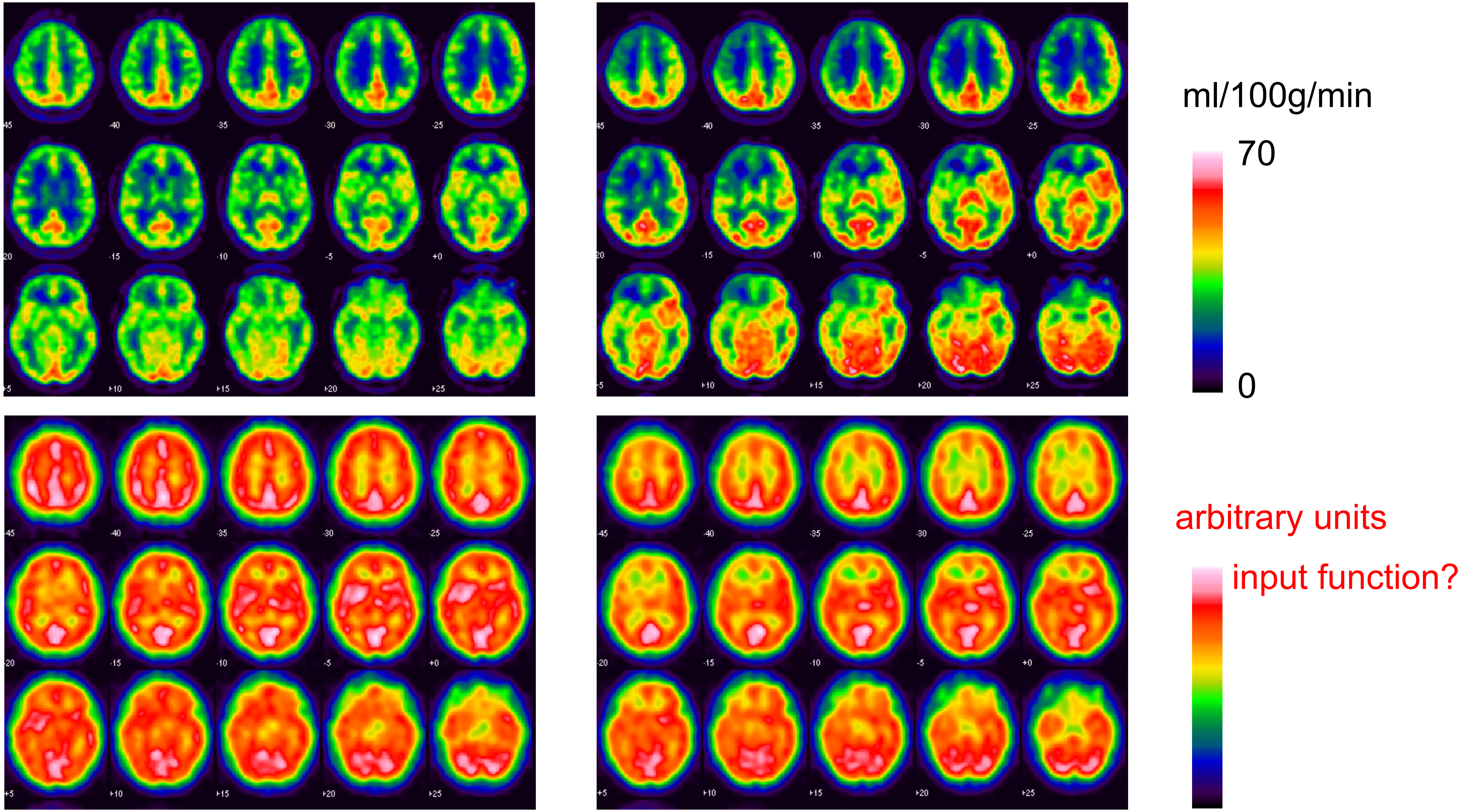
Female, 16 y, Moyamoya disease

rest

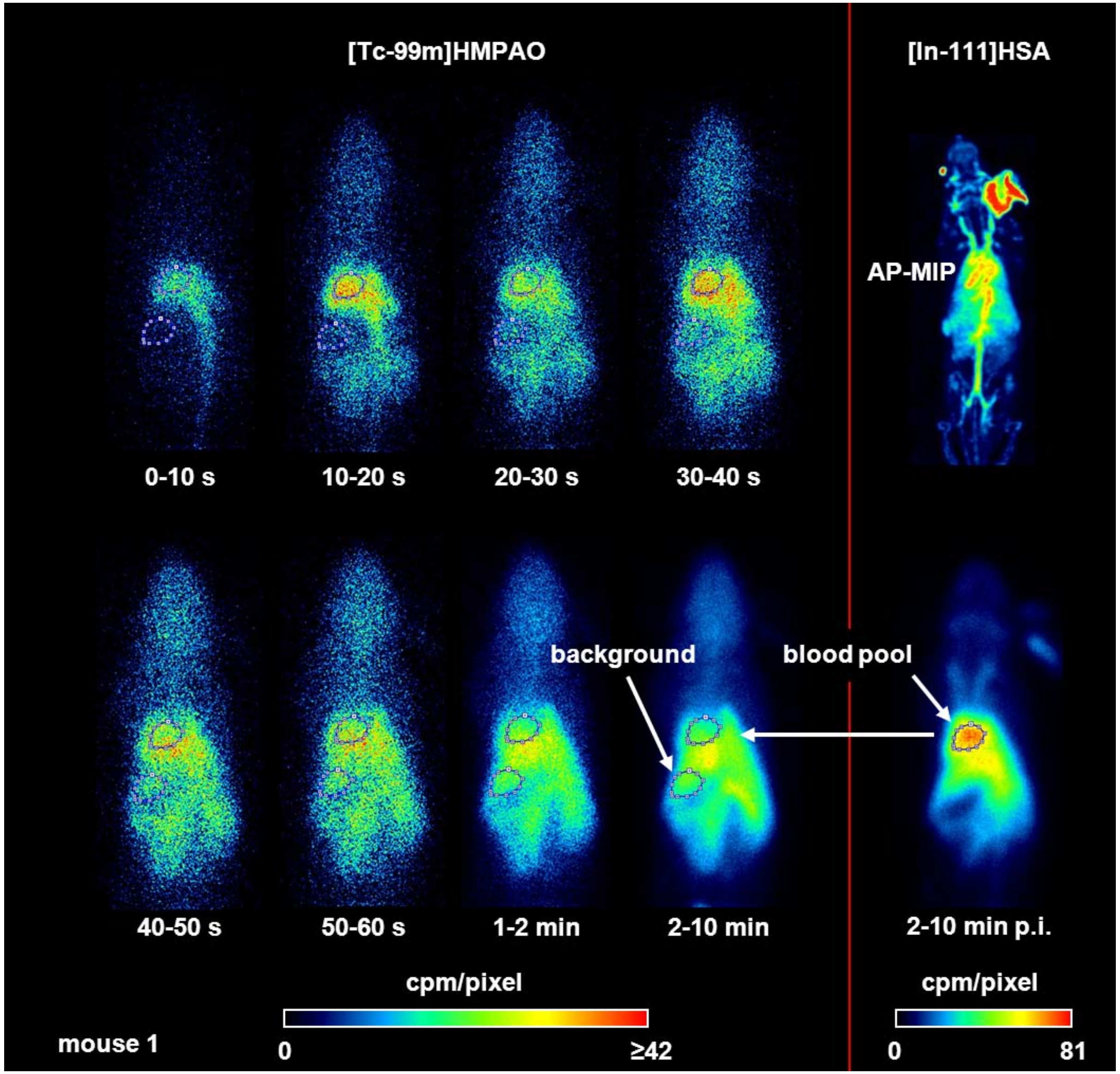
Diamox

rCBF

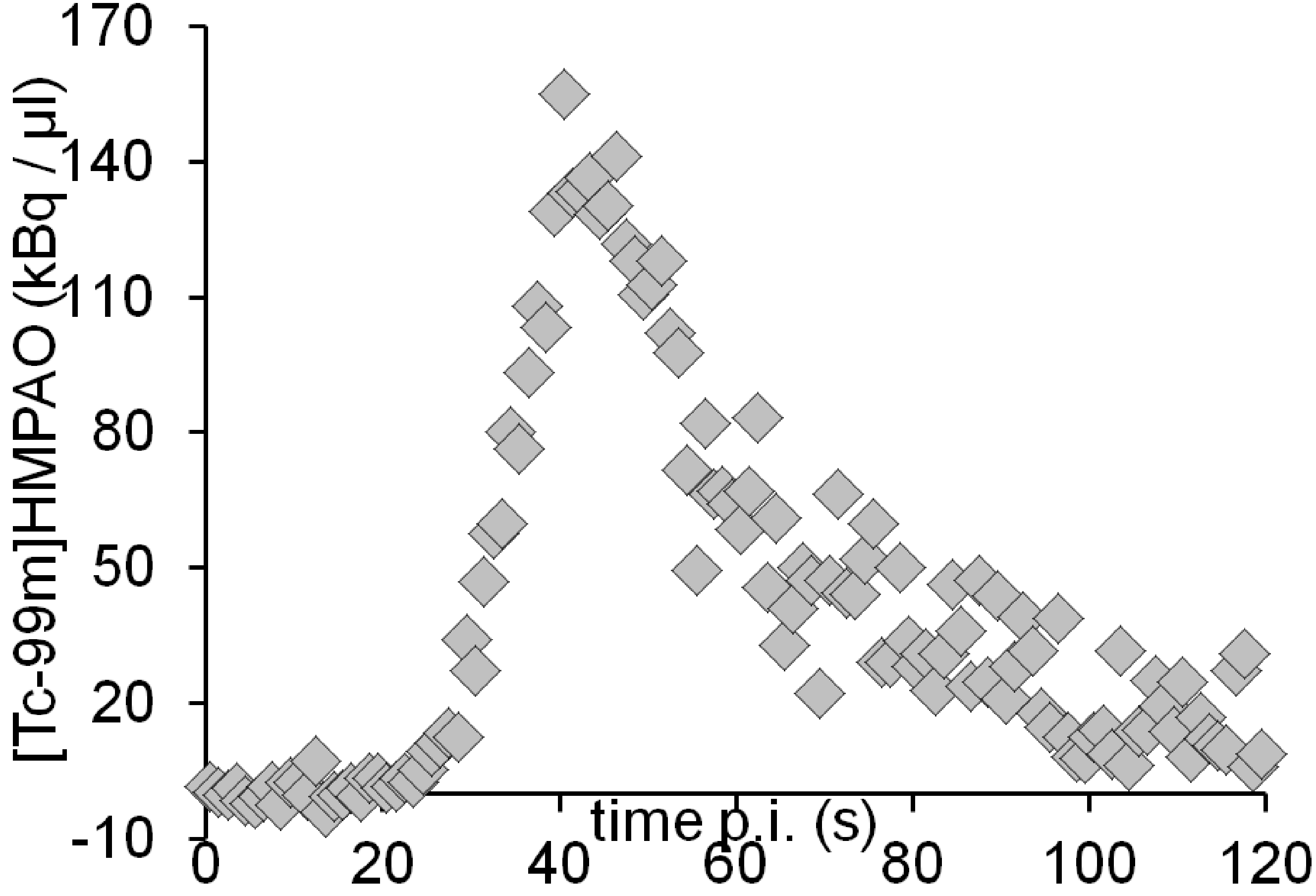
HMPAO uptake



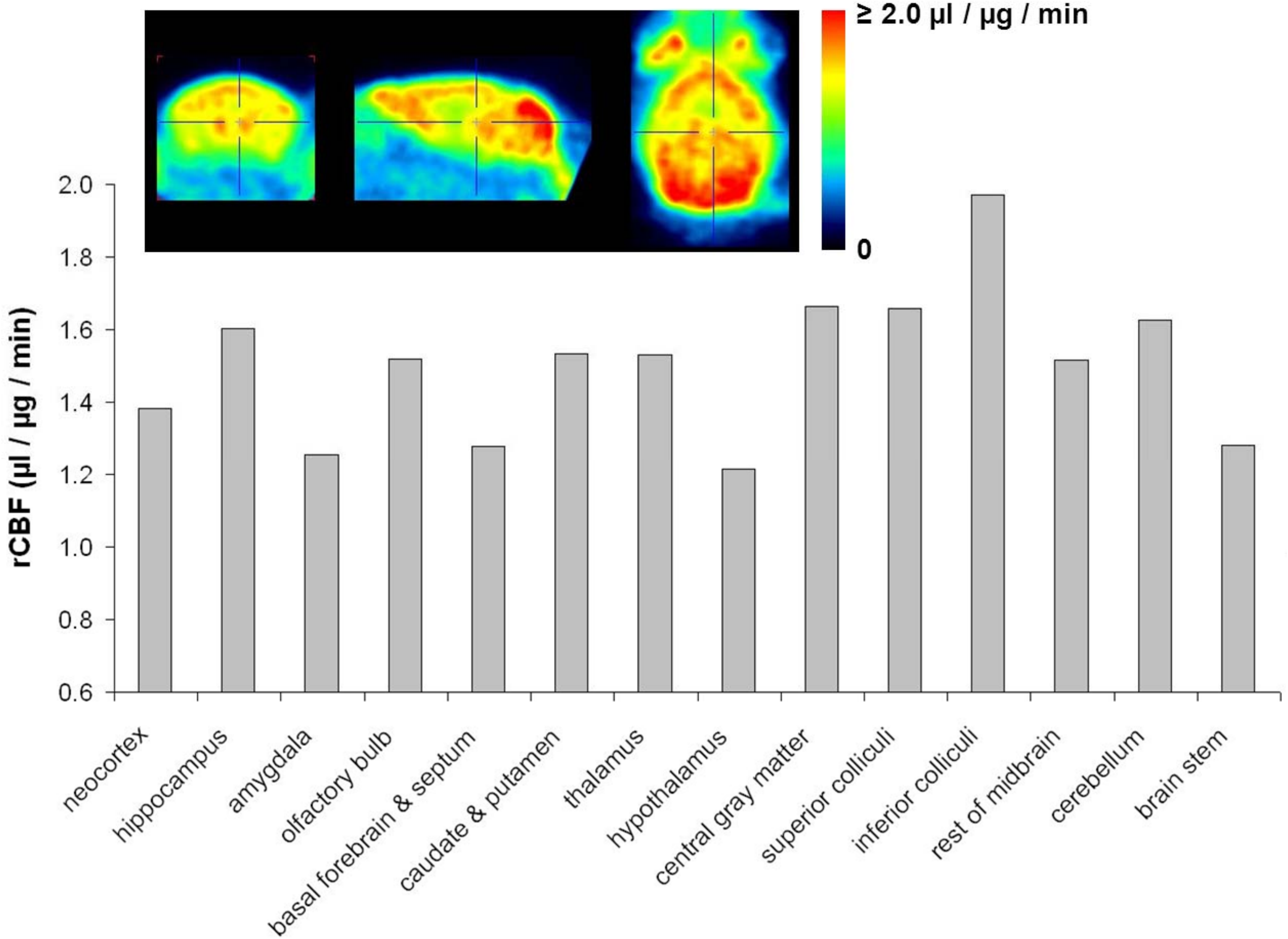
HMPAO-SPECT in mice: dynamic planar imaging



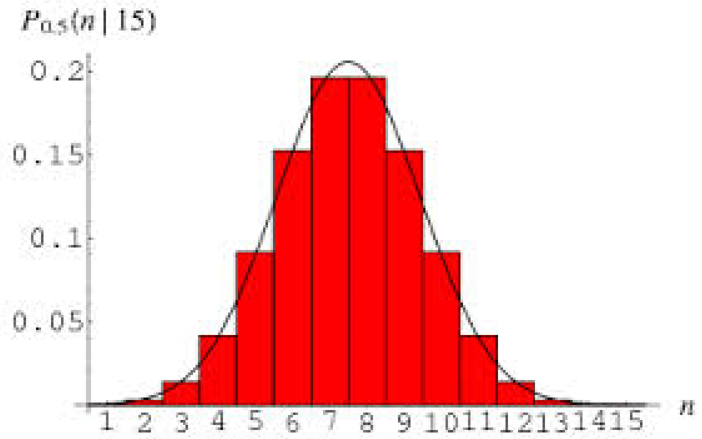
HMPAO-SPECT in mice: input function



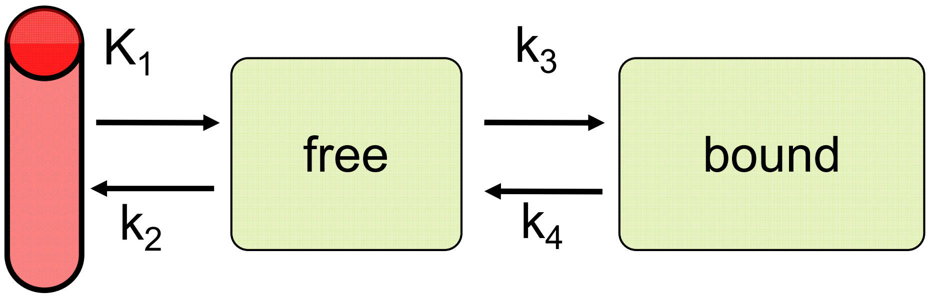
HMPAO-SPECT in mice: regional cerebral blood flow



some „technical“ issues



statistical noise

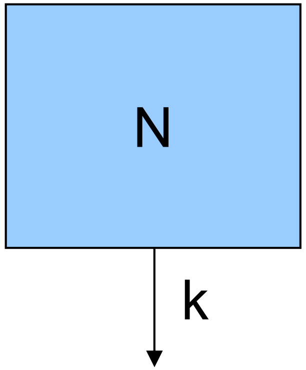


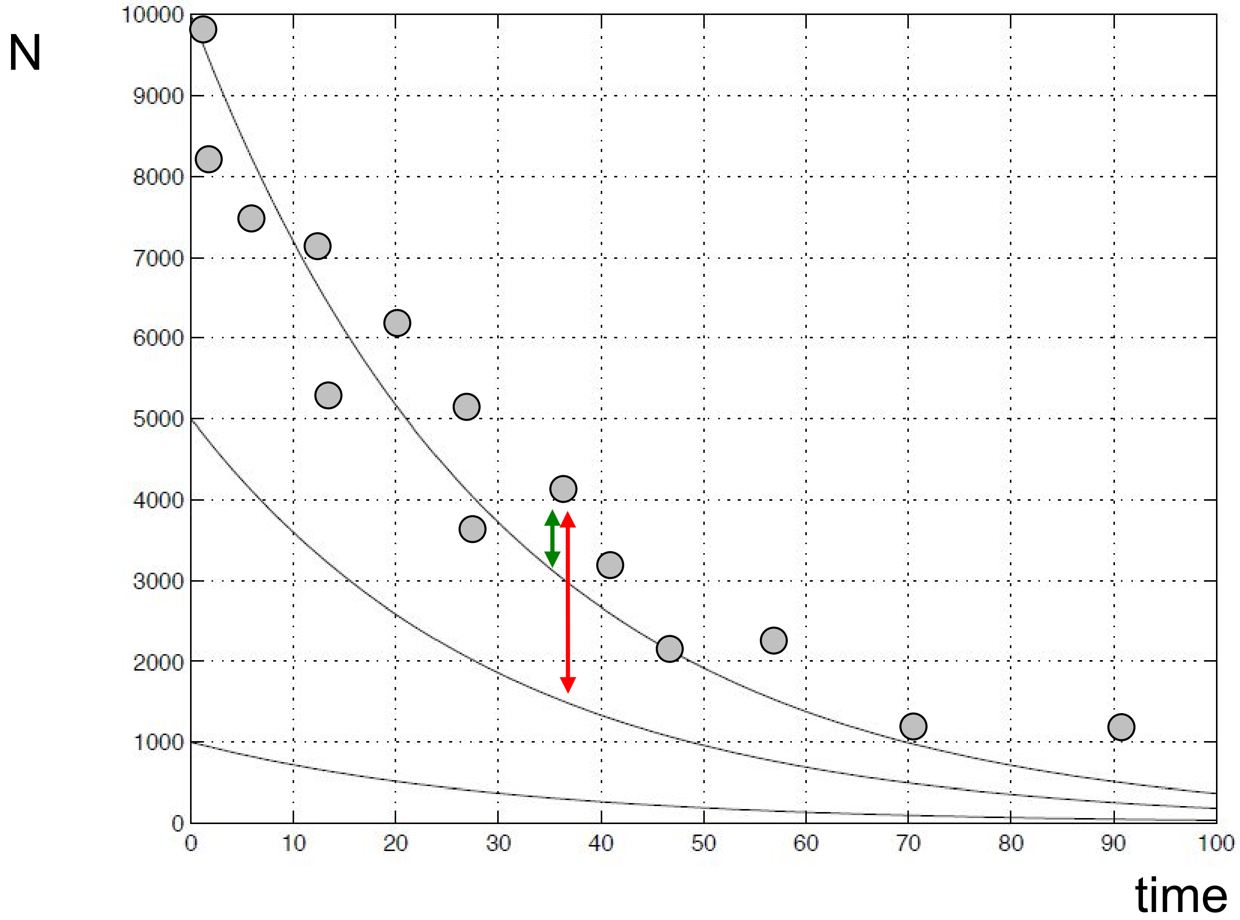
reversible binding

non-linear operational equations

How to handle statistical noise: minimize sum of squared differences

radioactive decay

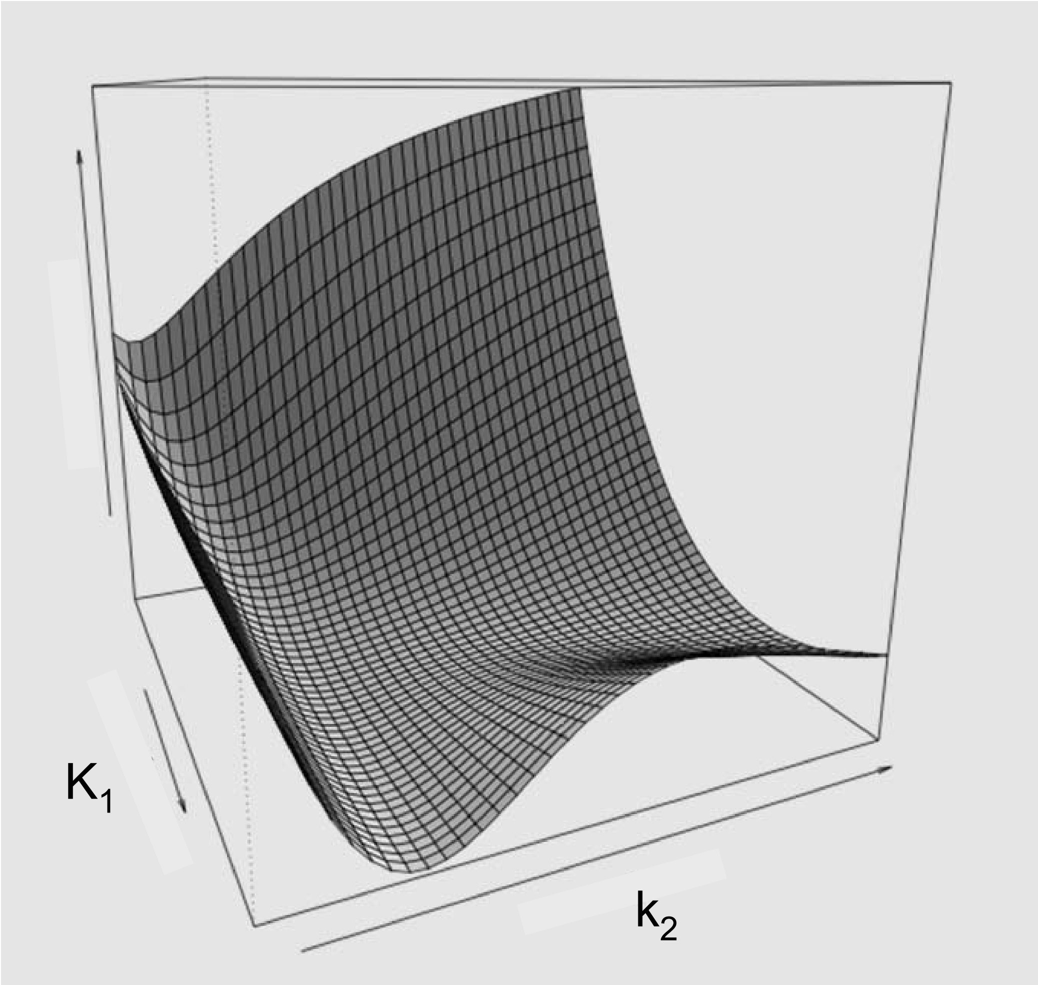




provides „best“ solution (based on some assupmtions)

Method to handle nonlinearity: no perfect general solution

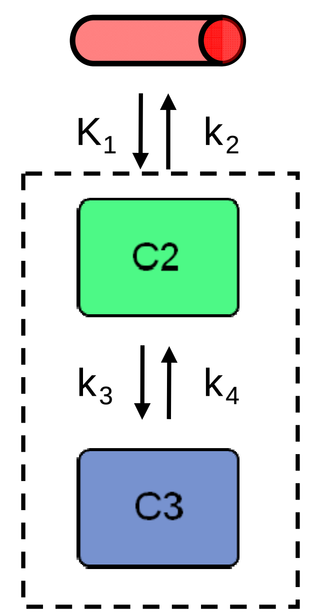
sum of squared differences

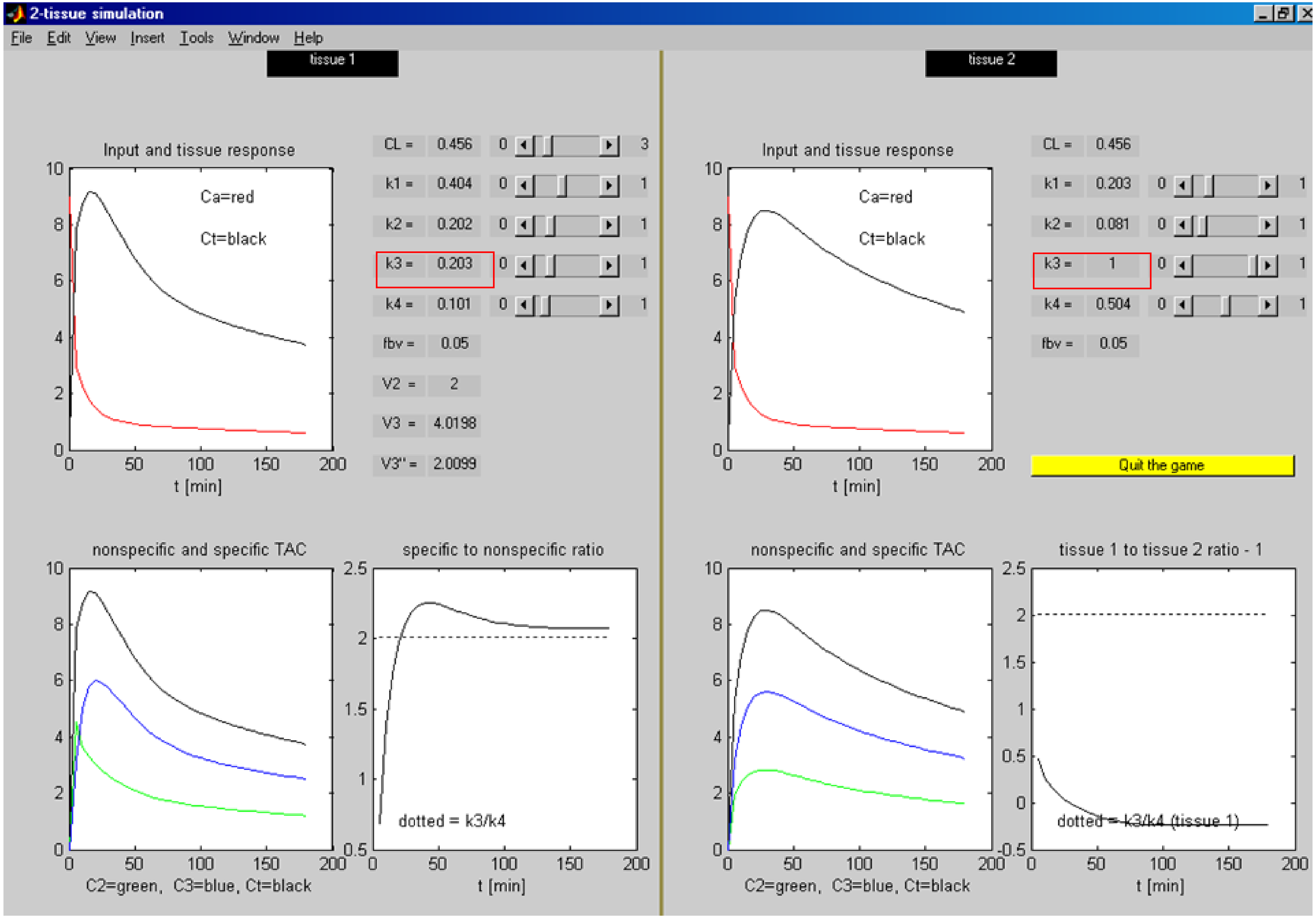


identifiability?

particularly in presence of noise

Identifiability





linearization (Gjedde-Patlak…)?

Tracer kinetic modelling: cons

- risk and burden for patient (arterial blood sampling, extended imaging duration)
- radiation exposure of staff (blood sampling)

except with
reference tissue methods

- „expensive“

  - scanner allocation > 60 min
  - staff (well counter measurements, analysis…)

- prone to errors (noise, calibration, patient motion…)

Tracer kinetic modelling: pros

• differentiation of physiologic functions (transport, metabolism…)

• *quantitative* characterization of physiologic function of interest

- intra-subject comparison (follow-up)
- inter-subject comparison (range of normal values)

• improved contrast

• improved statistical image quality

Thank you!