PET-BIDS Tool Demonstrations and Tutorials

Quantification

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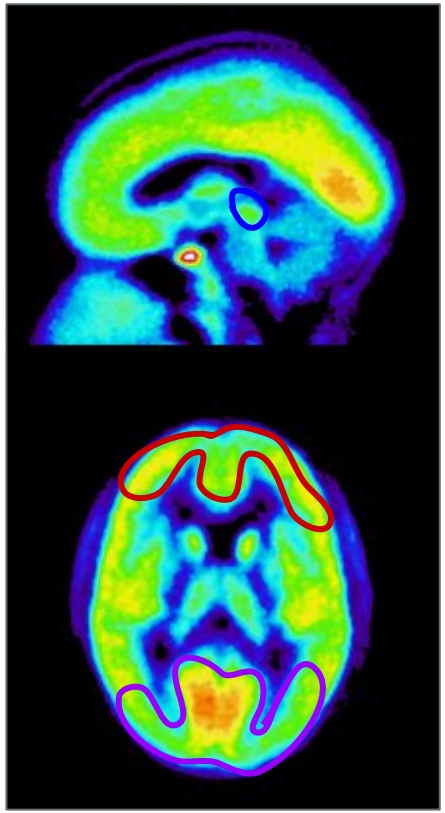
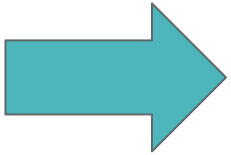
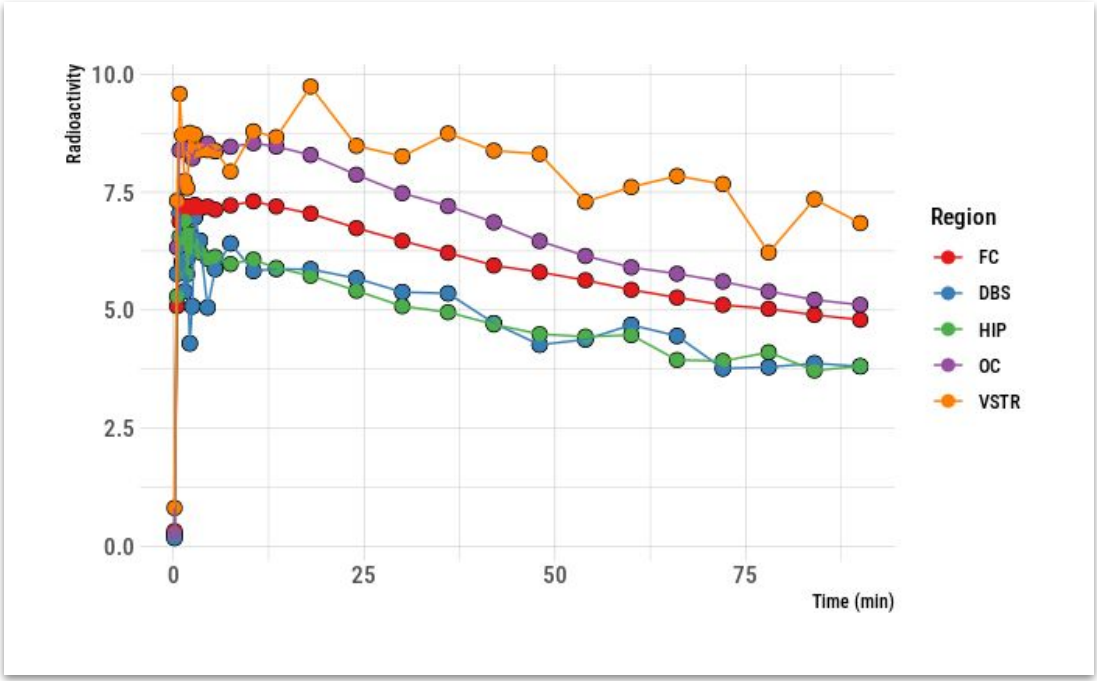
Image analysis & Preprocessing







Quantification

Considerations

Study design

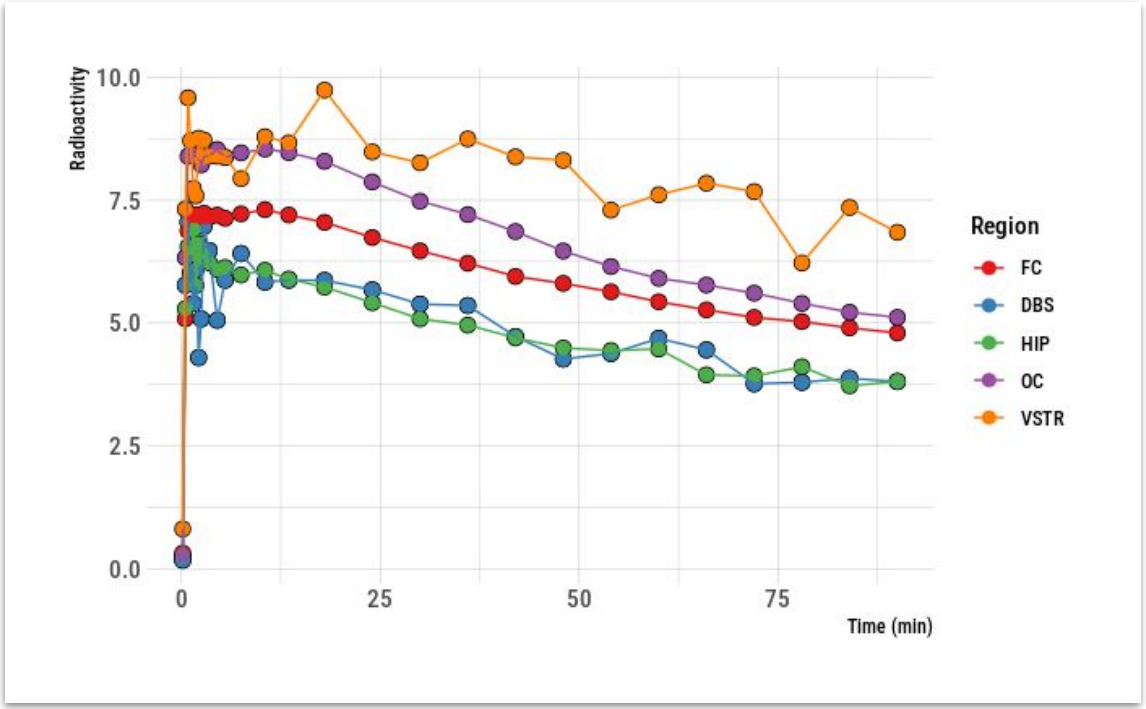
- Data and quantification strategy
  - Research question
  - Biological considerations
  - Radiotracer properties

bloodstream

- Blood
  - Combining blood data
  - Modelling blood data

kinfitr

- Pharmacokinetic modelling
  - Blood-TAC delay
  - Noise structure (i.e. weights)
  - Model selection
  - Linearised models: t* choice



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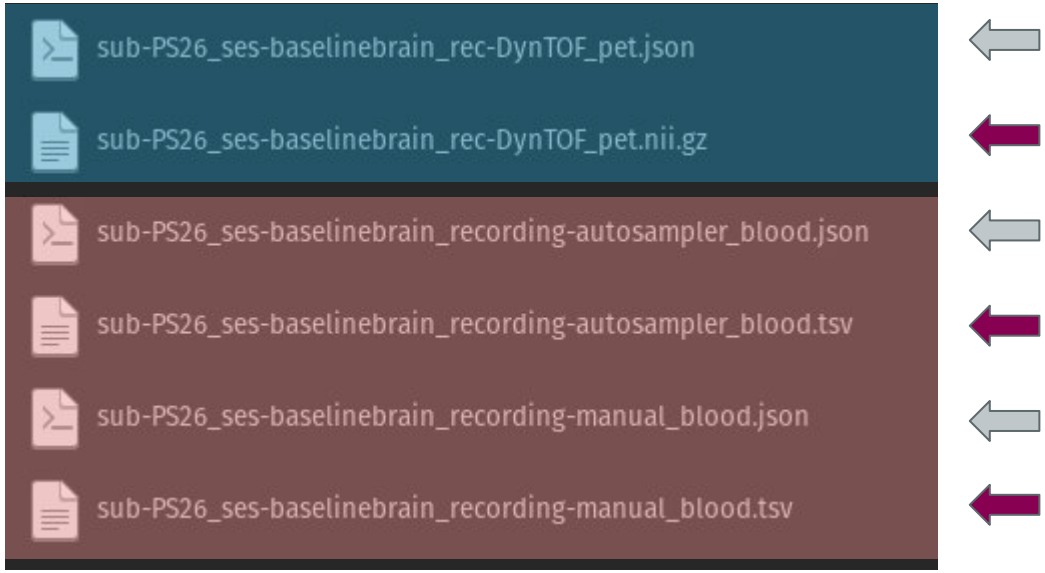
Blood processing using ***bloodstream***

BIDS Blood Data



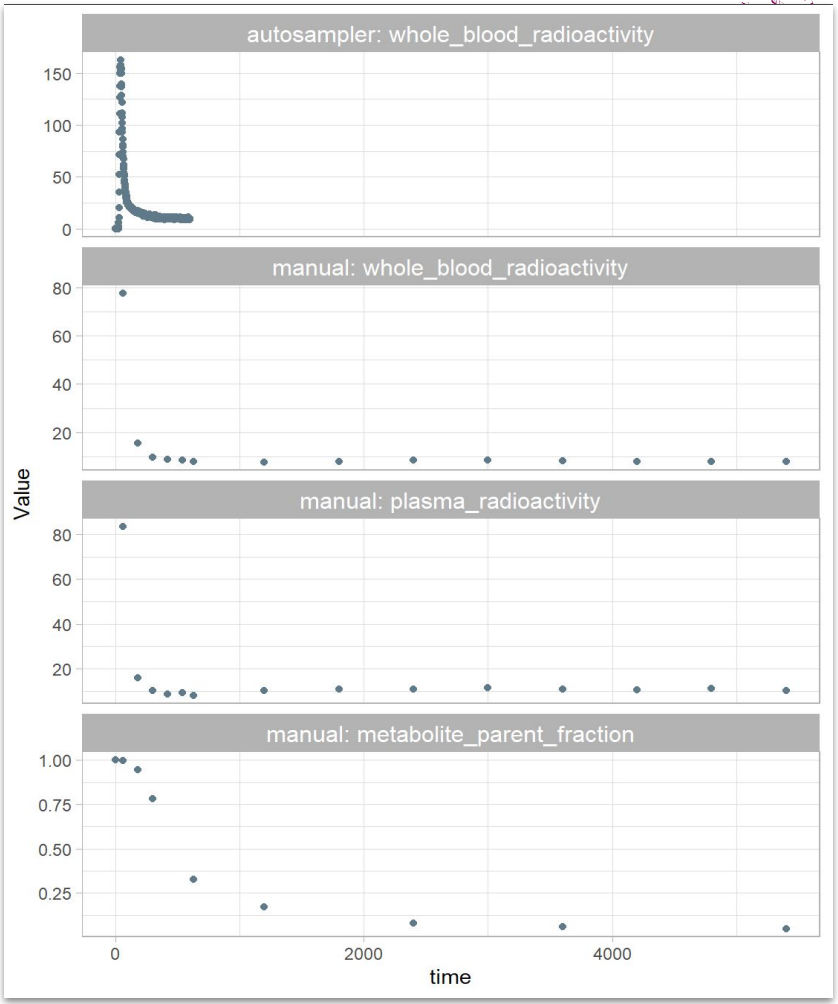
BIDS Blood Data

Autosampler

Manual

Manual

Manual



Blood Processing: The Problem

What we want:

- **Frequency**: High temporal granularity
- **Specificity**: Measurements of what we want
- **Accuracy**: Little to no measurement error

In reality

- We *can* measure with high frequency, but not what we really want
- We *can* measure what we want - but with low frequency
- Errors originate from all of the multiple sources

BIDS Blood Data

Autosampler

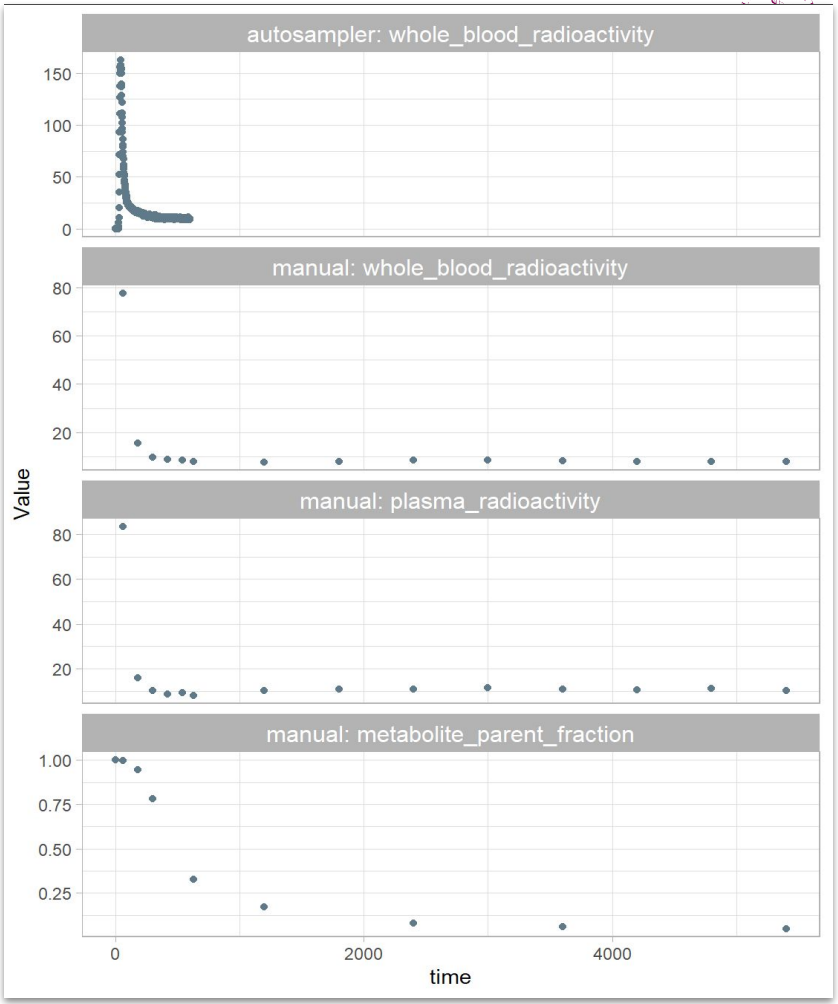
Manual

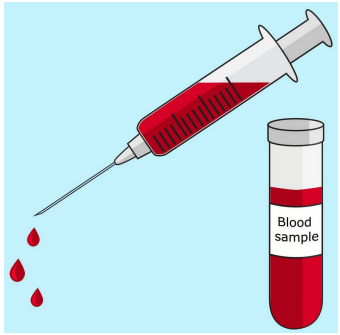
Manual

Manual

Goals

1. Combine
2. Improve



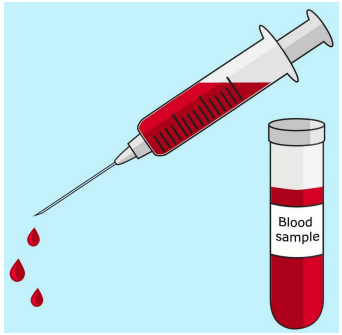


Manual sampling

Autosampler

Whole blood radioactivity

Gamma counter

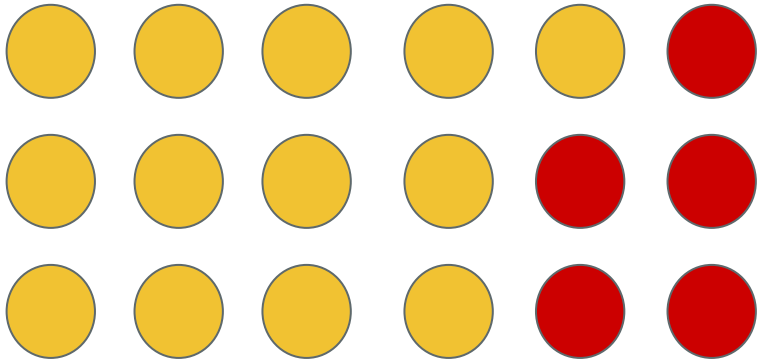


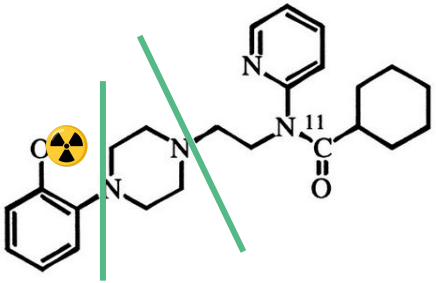
Manual sampling

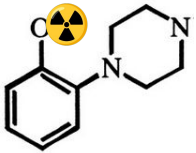
Plasma radioactivity

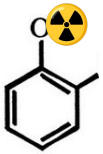
Bound to blood cells

Gamma counter

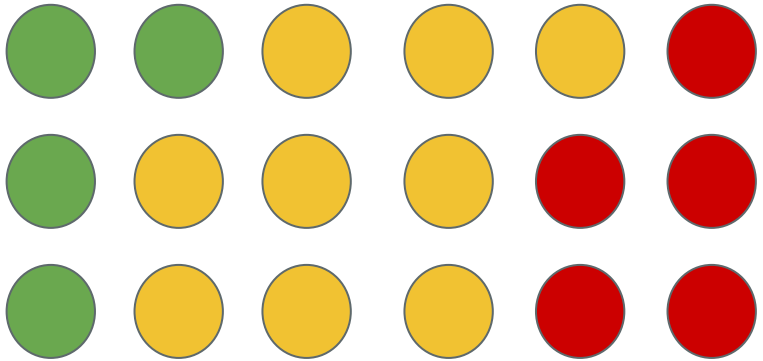


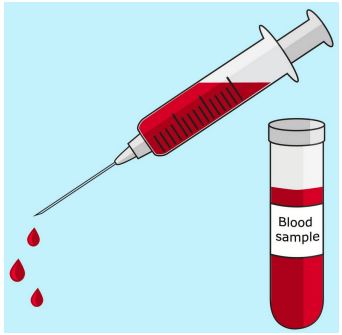


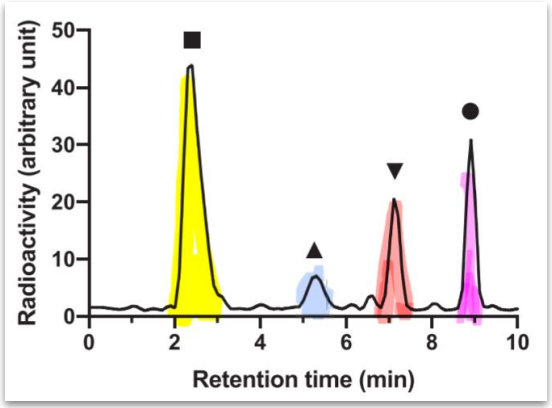




Plasma parent	Plasma metabolites	Bound to blood cells



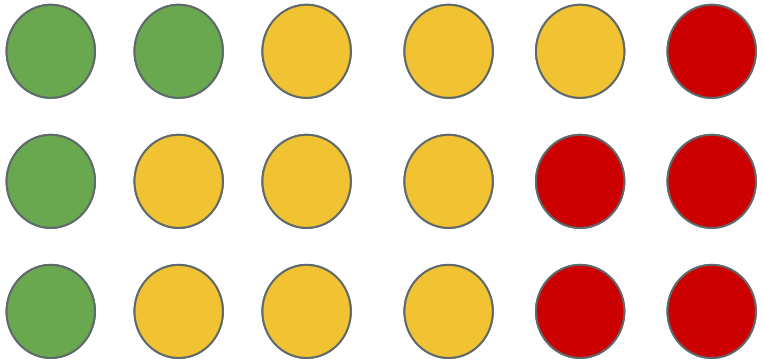




Manual sampling

Plasma parent	Plasma metabolites	Bound to blood cells

HPLC



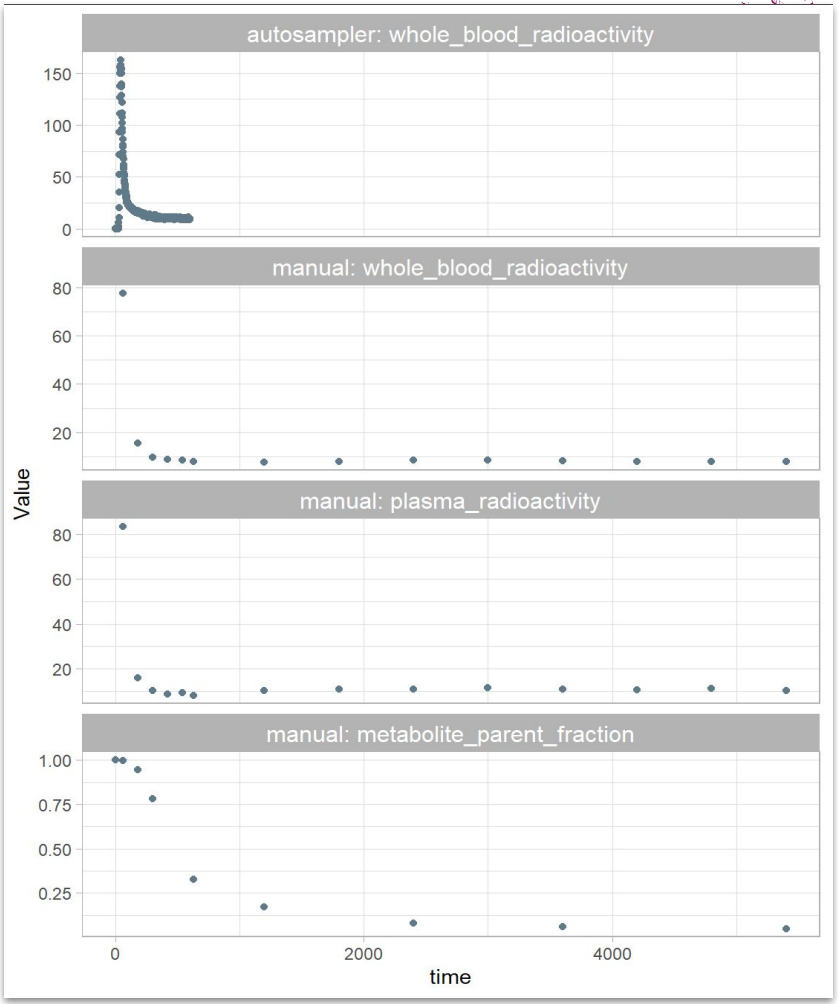
BIDS Blood Data

Autosampler

Manual

Manual

Manual



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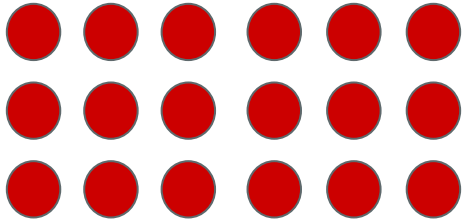

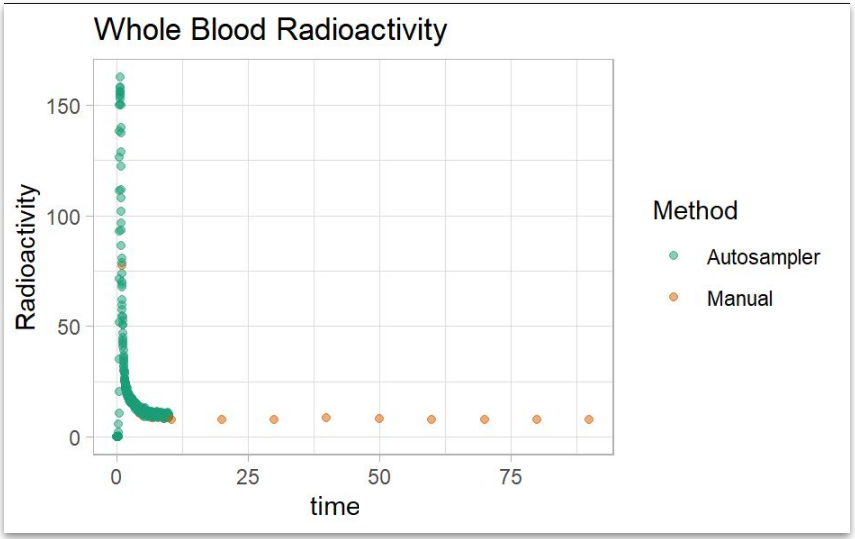

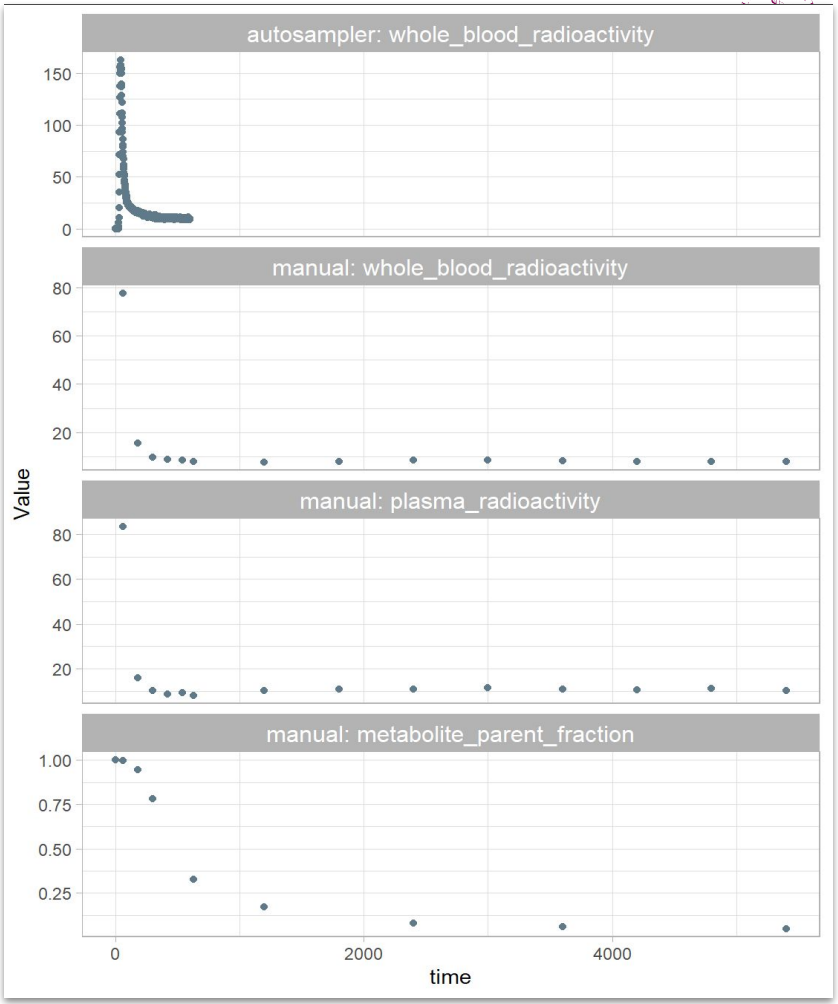

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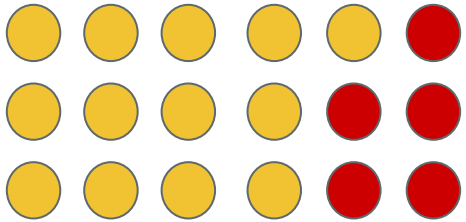

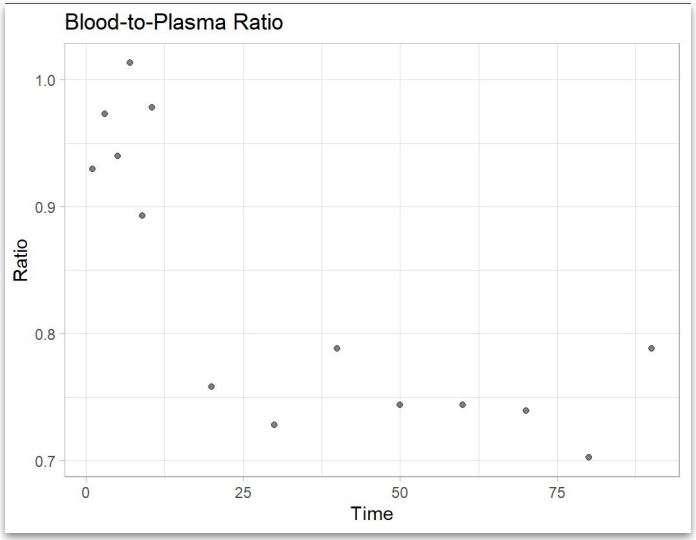

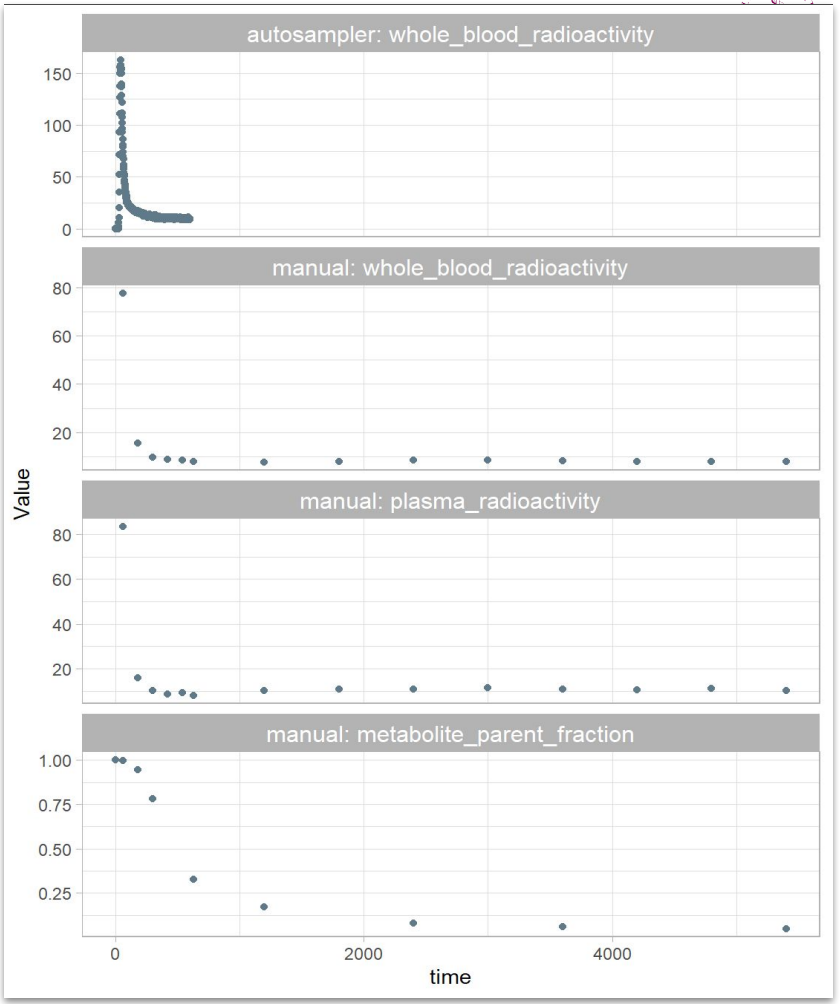

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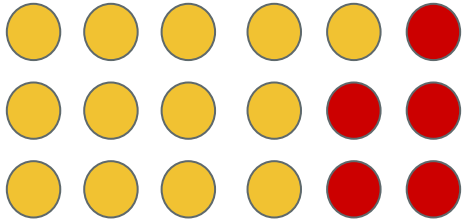

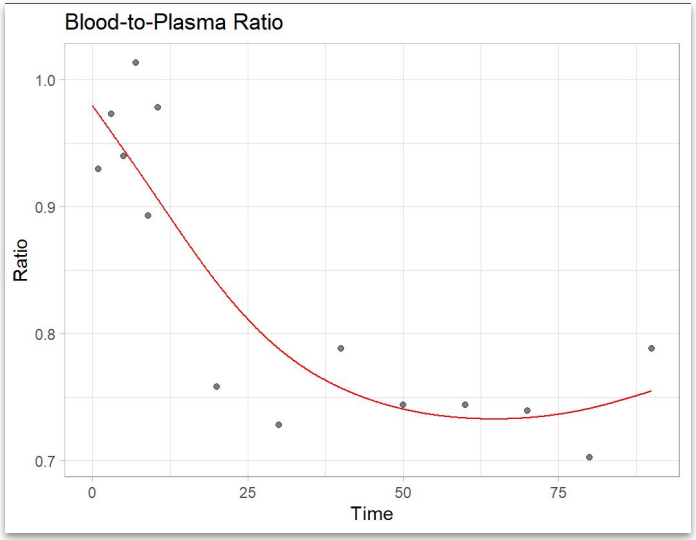

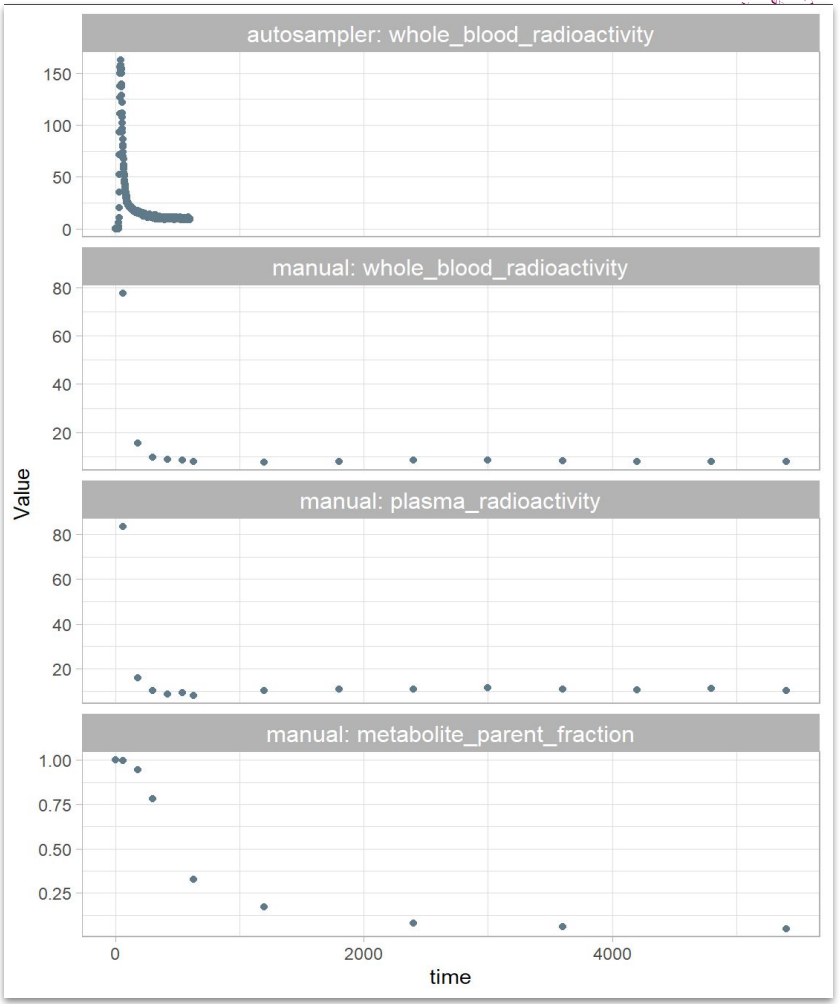

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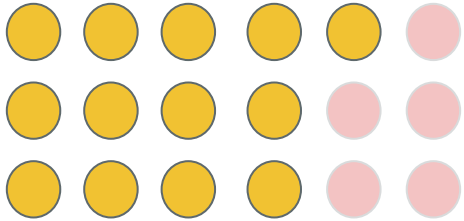

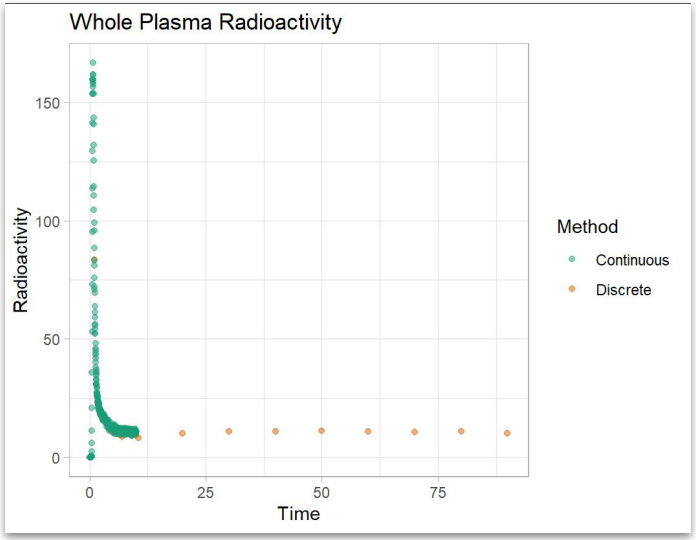

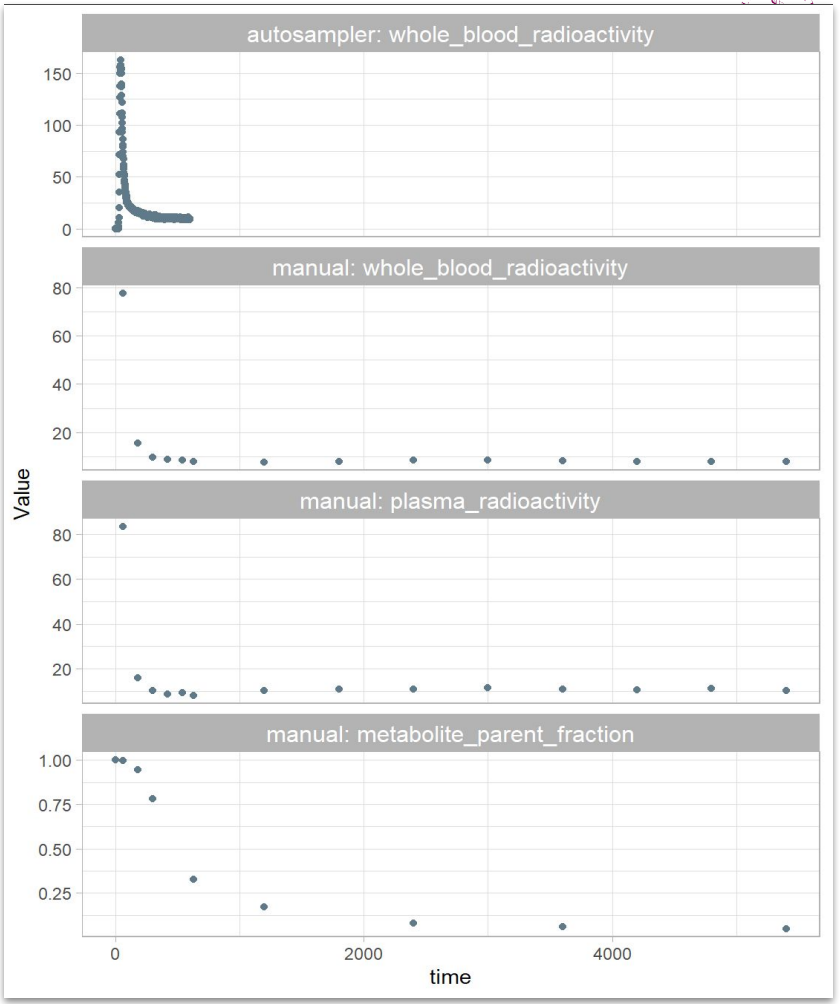

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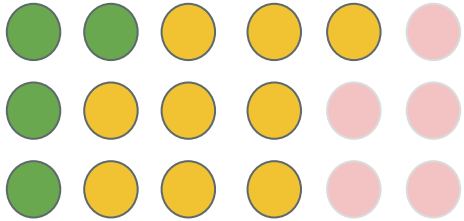

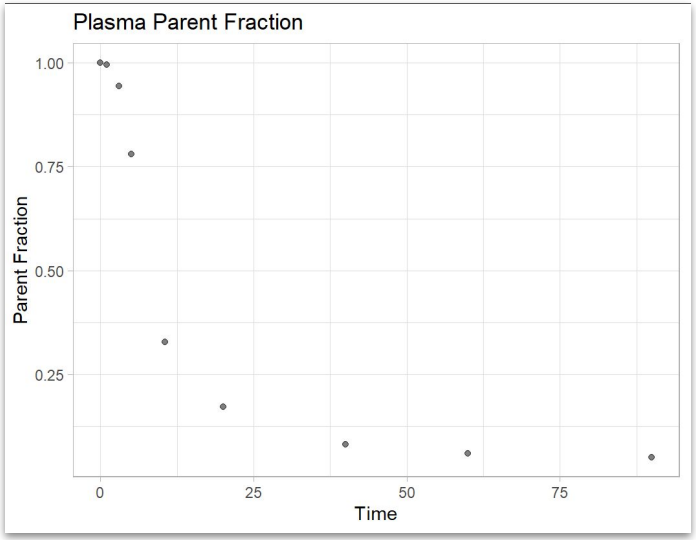

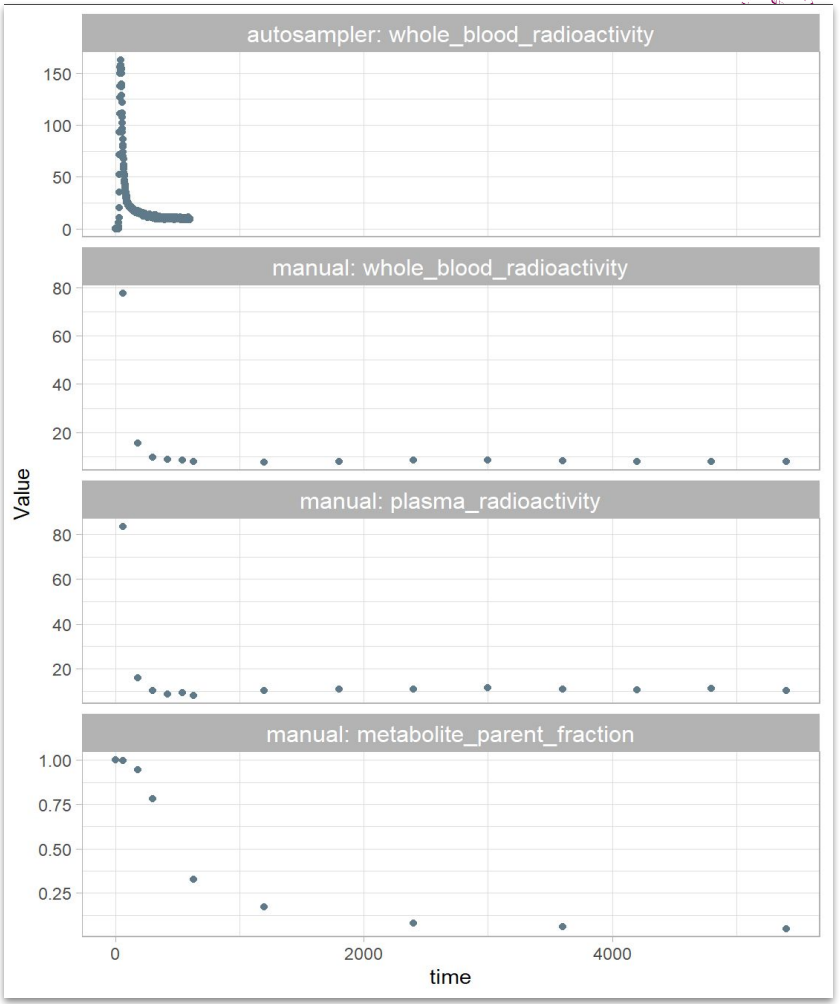

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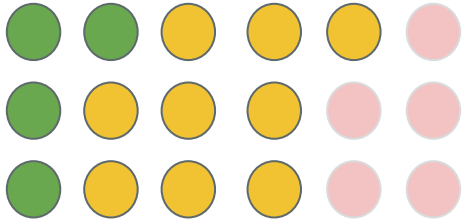

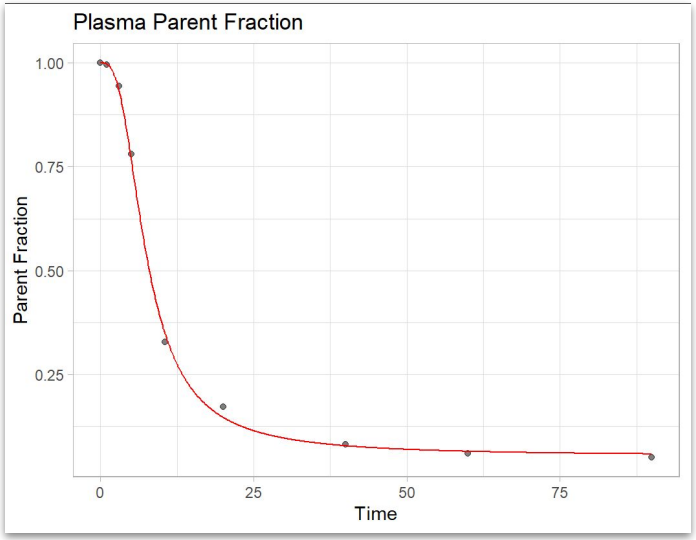

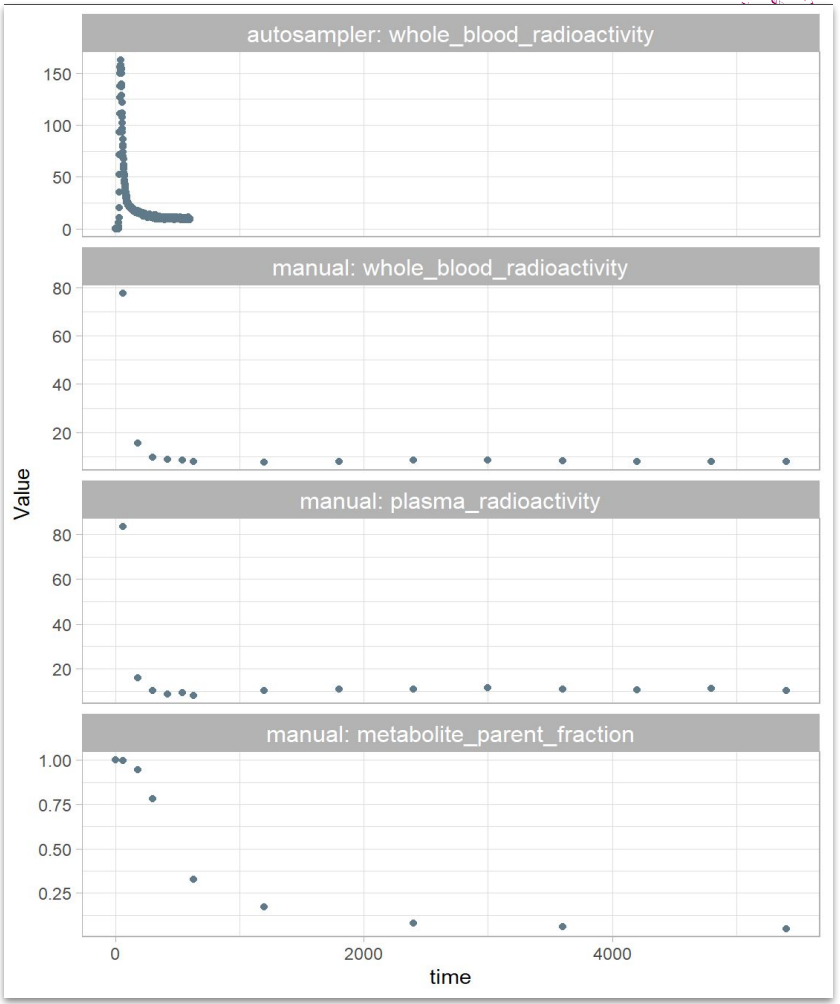

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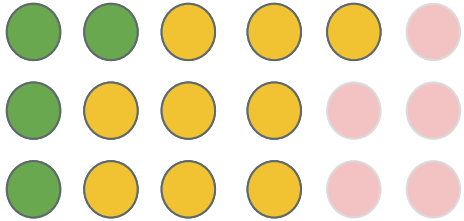

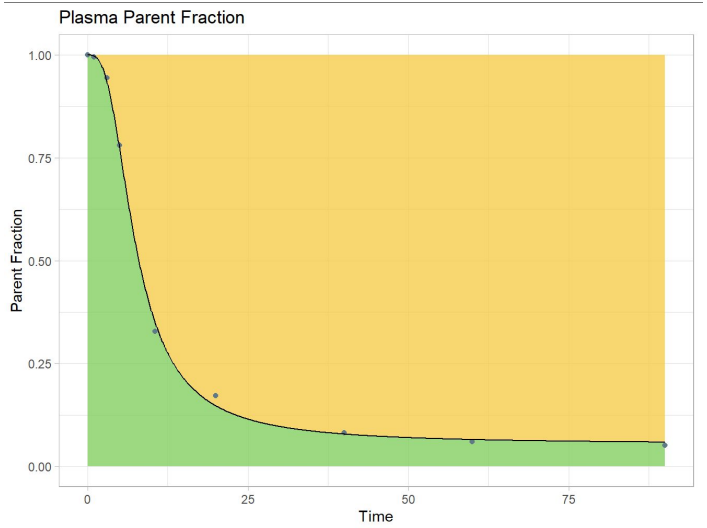

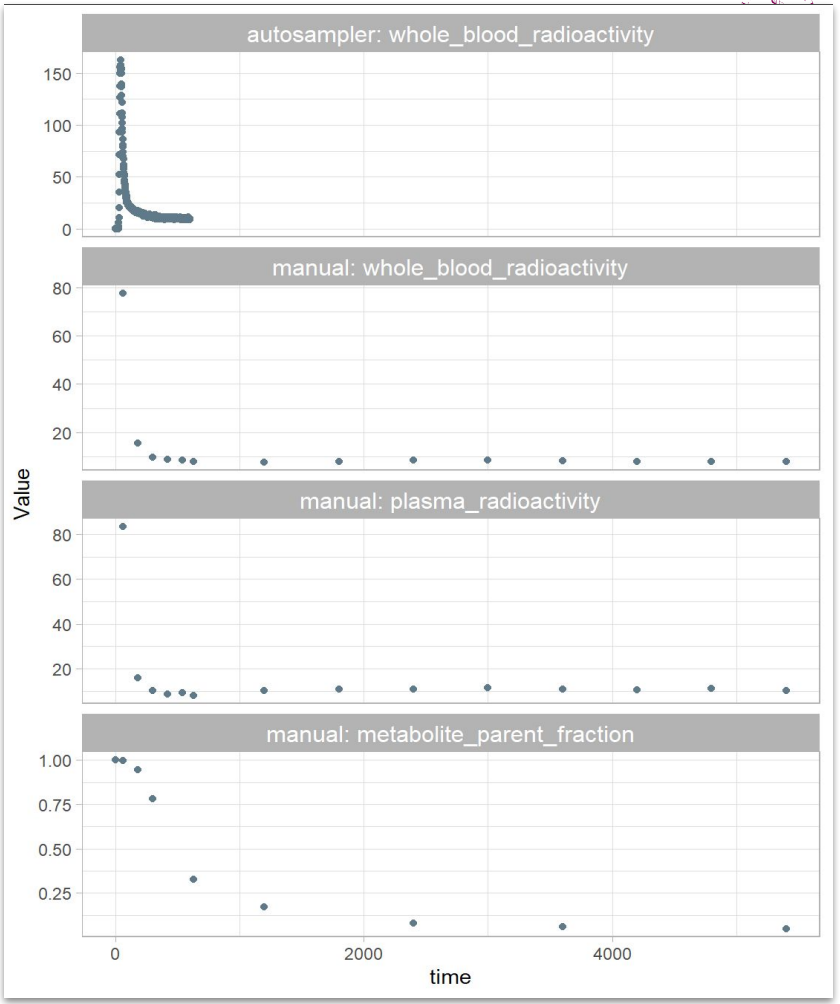

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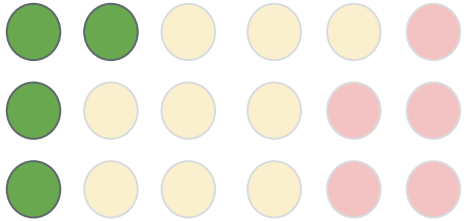

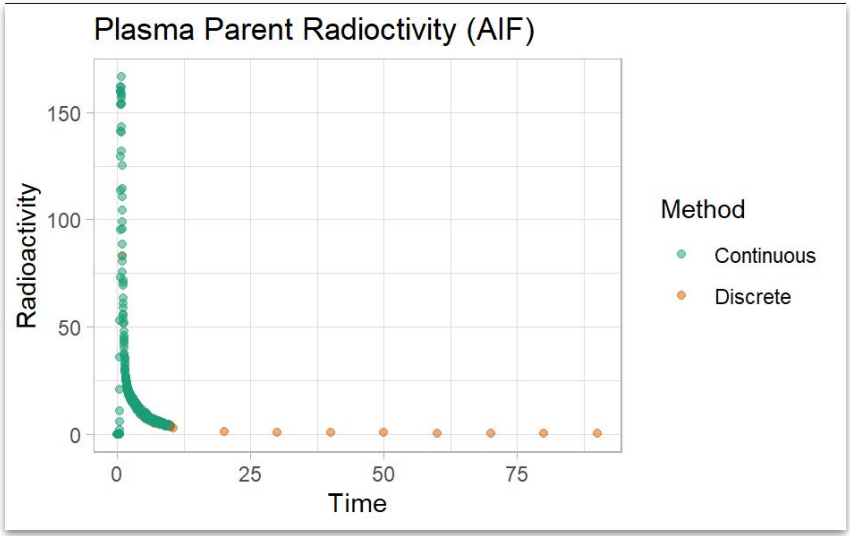

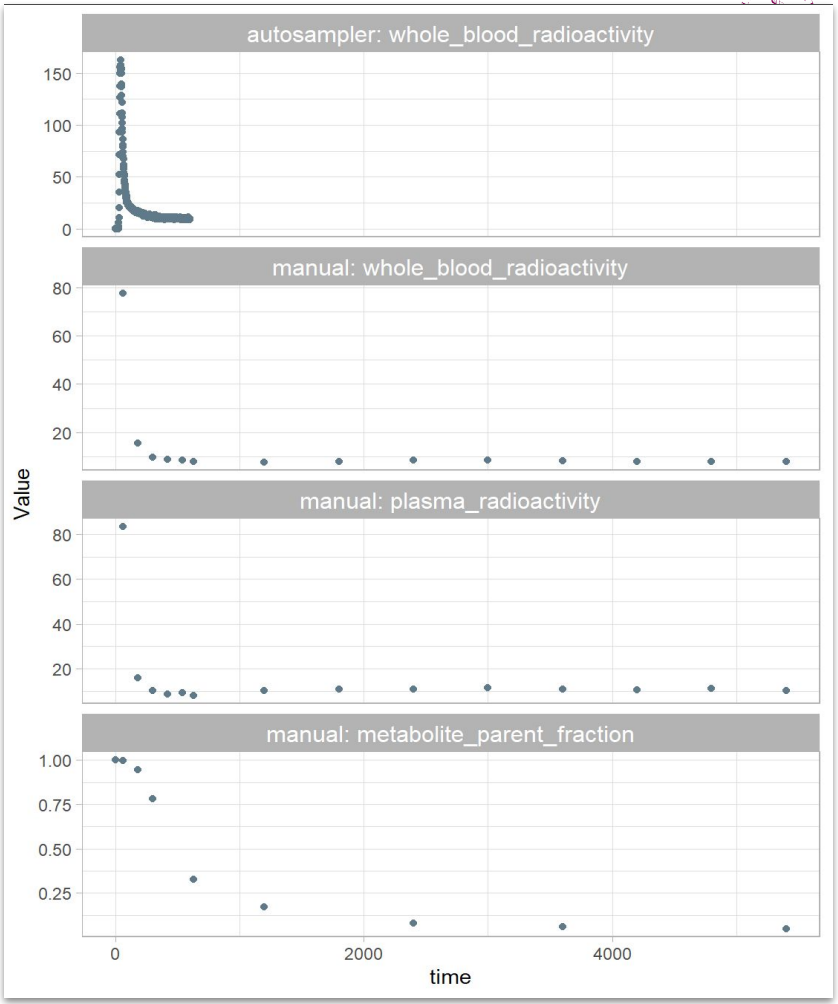

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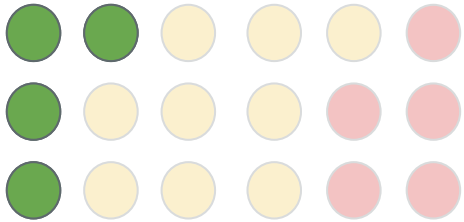
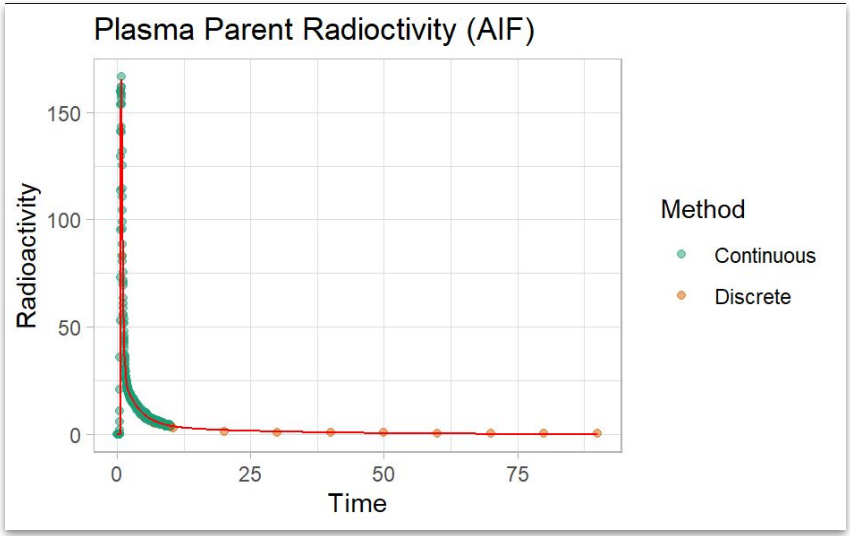
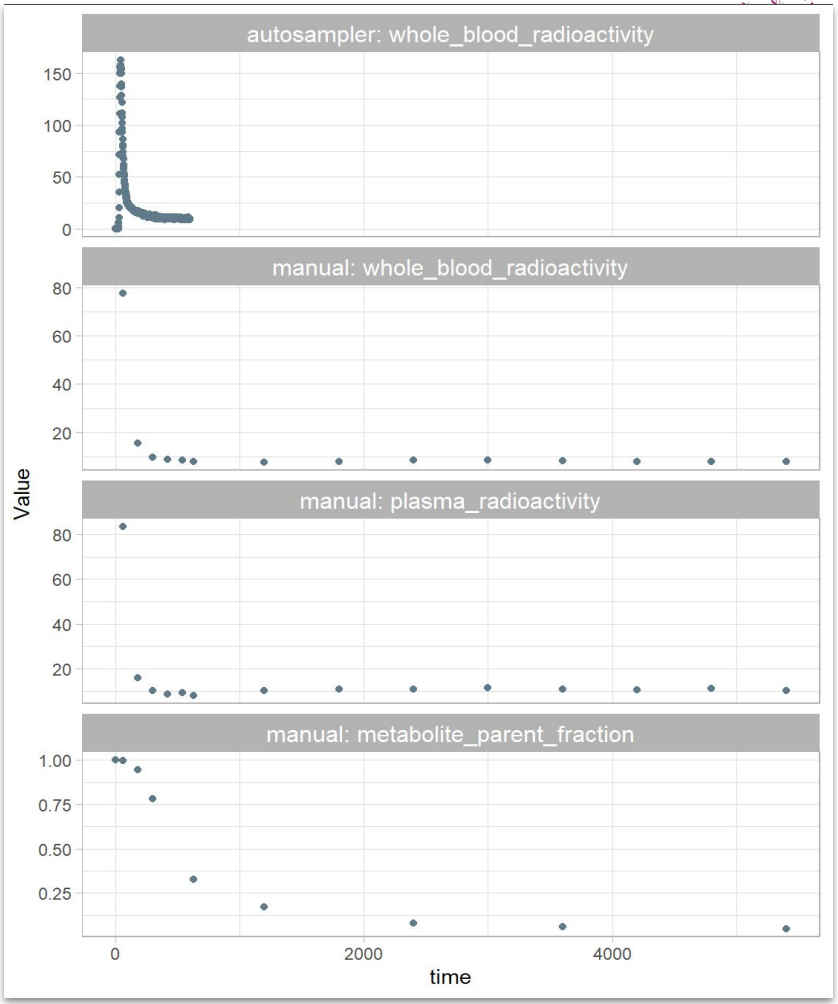






Basic strategy

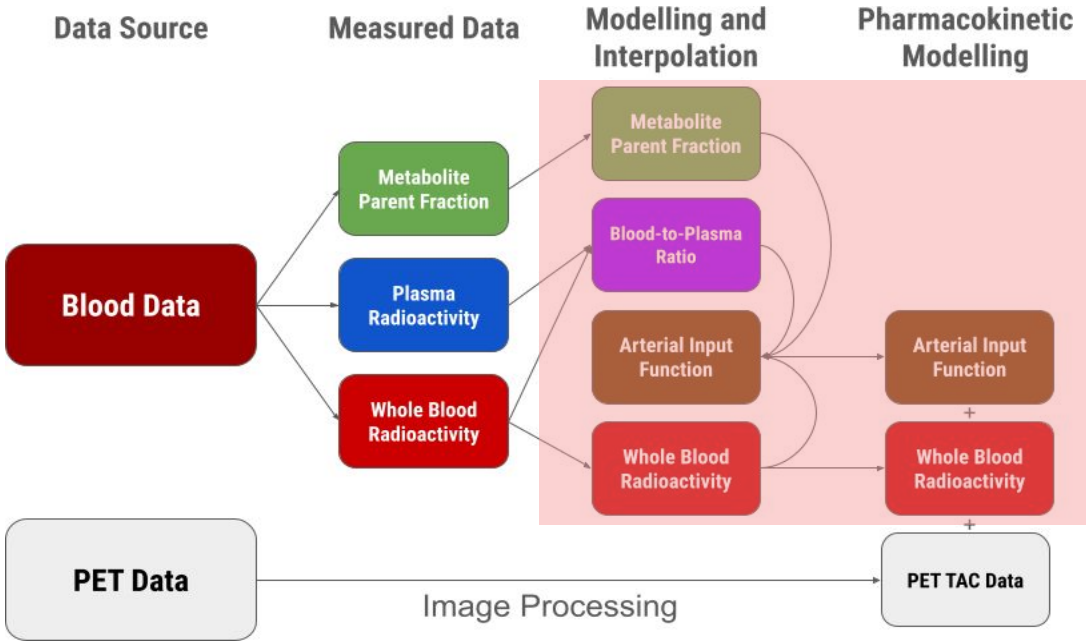
Linear interpolation of all curves followed by combination

More advanced strategy

Model some or all of the functions to reduce measurement error

(Subjective) order of importance:

1. *Parent Fraction*
2. *Blood-to-plasma ratio*
3. *Arterial Input Function*
4. *(Whole blood)*



bloodstream

Usage (docker)

```
docker run --user $(id -u):$(id -g) -v /path/to/bids_data/:/data/
mathesong/bloodstream:latest
```

→ simple linear interpolation of all curves

```
docker run --user $(id -u):$(id -g) -v /path/to/bids_data/:/data/
mathesong/bloodstream:latest config_file.json
```

→ modelling of one or more of the curves

Usage (R)

```
remotes::install_github(“mathesong/bloodstream”)
```

→ installation

```
bloodstream(“/path/to/bids_data/”)
```

→ simple linear interpolation of all curves

```
bloodstream(“/path/to/bids_data/”, “config_file.json”)
```

→ modelling of one or more of the curves

Create a customised bloodstream config file

Data Subset

Use these options to apply this config to a subset of the data. Values should be separated by semi-colons. All measurements fulfilling all the conditions will be included. Leave options blank for no subsetting is desired, i.e. leaving sub blank implies that all subjects should be included.

sub

ses

rec

task

run

TracerName

Modelling Choices

Select the modelling approach for each of the blood curves which should be fitted to the data. The default approach for each is simply to apply linear interpolation to the observed data. As a rule of thumb, modelling the parent fraction and the blood-to-plasma ratio are usually a good idea. Modelling the AIF and the whole blood are mostly best left for specific applications. For debugging, I recommend using simple interpolation and inspecting the plots and QC output.

Parent Fraction | Blood-to-Plasma Ratio | Arterial Input Function | Whole Blood | Download

Parent Fraction Model Selection

There are many options available for modelling the parent fraction. For most tracers, a good default option is the `Fit Individually: Choose the best-fitting model` option, which will choose the model which fits best on average, and applies that model to all of the data. Hierarchical models (more to come) are best left for experienced users.

Parent fraction model

Interpolation

- Fit Individually: Choose the best-fitting model
- Fit Individually: Hill
- Fit Individually: Exponential
- Fit Individually: Power
- Fit Individually: Sigmoid
- Fit Individually: Inverse Gamma
- Fit Individually: Gamma

to (min)

Inf

GAM dimension of the basis (k)

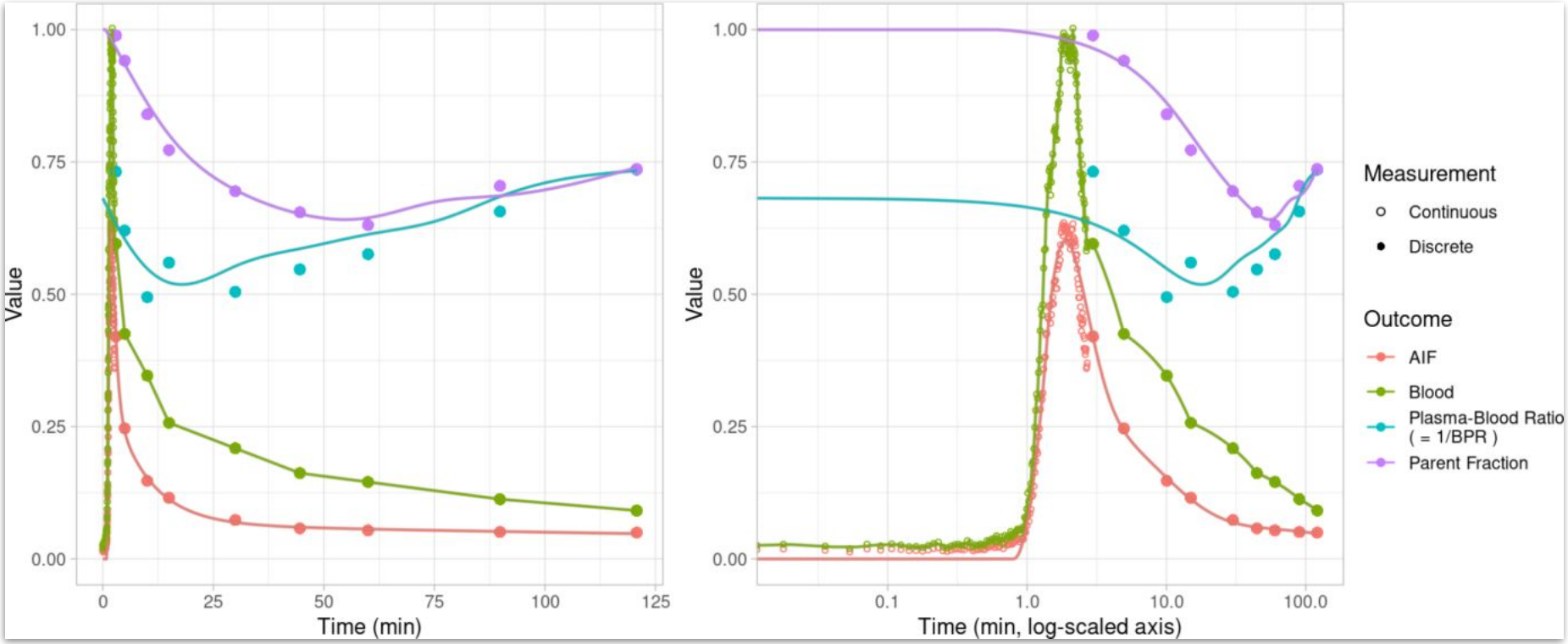
6

This value must sometimes be reduced when there are too few data points, or increased for extra wiggliness.

bloodstream

Produces

- an html file to inspect all the fits
- Interpolated outputs



bloodstream

https://github.com/mathesong/bloodstream

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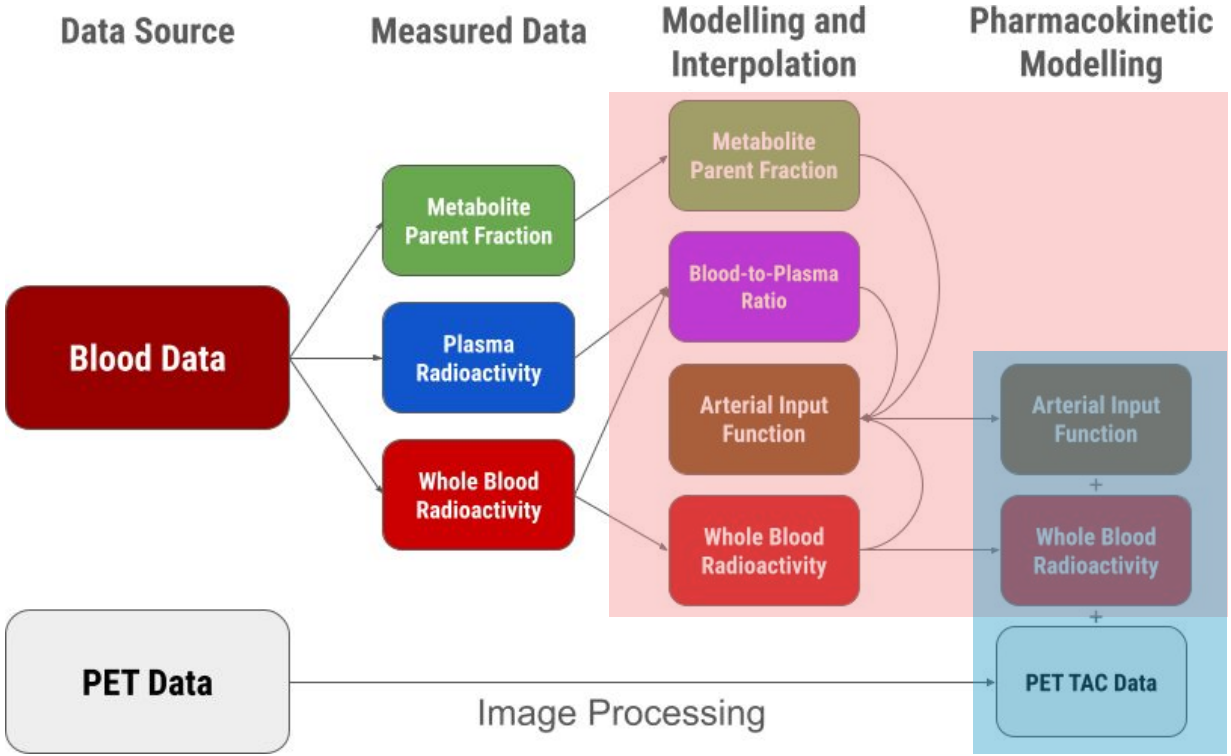
Kinetic Modelling using *kinfitr*

Kinetic modelling



bloodstream

kinfitr

PK Parameters

BP_{ND}
BP_{P}
V_{T}
R_{1}
K_{1}
etc...

Kinetic modelling using *kinfitr*

Kinfitr is an R package which contains

- Blood processing methods
  - (bloodstream wraps around these functions)
- Invasive and non-invasive kinetic models
  - ~20 different models
- Weighting schemes
  - For accommodating changing noise the TAC
- Blood-to-TAC delay fitting methods
  - For aligning blood and brain data in time
- t* selection helpers
  - For using linearised kinetic models
- Miscellaneous
  - Diagnostics: Fit plots, residual plots, ease of model comparison
  - Convenience: Unit conversion, decay correction and un-correction
  - BIDS: PET-BIDS parsing functionality

Full tutorials at granvillematheson.com

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Pharmacokinetic Modelling of PET Data in R using kinfitr. Part 1: Theory.

A brief theoretical background.

a.k.a. Let me tell you why you this is cool

Posted by Granville Matheson Friday, February 21, 2020

Pharmacokinetic Modelling of PET Data in R using kinfitr. Part 2: Basics and Iteration

Basic usage and how best to iterate.

a.k.a. Let's take this baby for a test-drive

Posted by Granville Matheson Friday, February 21, 2020

Pharmacokinetic Modelling of PET Data in R using kinfitr. Part 3: Finding tstar

How to interpret the tstar finder outputs.

a.k.a. Admire my busy graphs

Posted by Granville Matheson Friday, February 21, 2020

Pharmacokinetic Modelling of PET Data in R using kinfitr. Part 4: Blood Processing

Storage and Modelling.

a.k.a. Model all the things

Posted by Granville Matheson Friday, February 21, 2020

kinfitr : The BIDS App!

- Needs to be able to automatically parse
  - PET-BIDS data (e.g. blood data)
  - PET-BIDS derivative data (i.e. output from other pipelines)
    - Processed blood data from e.g. *bloodstream*
    - Processed TAC data from e.g. *petprep*

- Needs to allow users to define complex chains of commands and allow checking at intermediate steps
- Want to allow users to experiment with optimal model configurations like graphical user interface (GUI) tools

Still in active development, but I've released an early version, and working on expanding functionality!

kinfitr : The BIDS App!

Two parts / interfaces

1. Region definition

index	name
2	Left-Cerebral-White-Matter
7	Left-Cerebellum-White-Matter
8	Left-Cerebellum-Cortex
10	Left-Thalamus
11	Left-Caudate
12	Left-Putamen
13	Left-Pallidum
16	Brain-Stem
17	Left-Hippocampus
18	Left-Amygdala
24	CSF
26	Left-Accumbens-area
28	Left-VentralDC
31	Left-choroid-plexus
41	Right-Cerebral-White-Matter
46	Right-Cerebellum-White-Matter
47	Right-Cerebellum-Cortex
49	Right-Thalamus
50	Right-Caudate
51	Right-Putamen
52	Right-Pallidum
53	Right-Hippocampus
54	Right-Amygdala
58	Right-Accumbens-area
60	Right-VentralDC
63	Right-choroid-plexus
130	AirCavity
165	Skull
172	Vermis
174	Pons
257	CSF-ExtraCerebral
258	Head-ExtraCerebral
1001	ctx-lh-bankssts
1002	ctx-lh-caudalanteriorcingulate
1003	ctx-lh-caudalmiddlefrontal
1005	ctx-lh-cuneus
1006	ctx-lh-entorhinal
1007	ctx-lh-fusiform
1008	ctx-lh-inferiorparietal
1009	ctx-lh-inferiortemporal
1010	ctx-lh-isthmuscingulate
1011	ctx-lh-lateraloccipital
1012	ctx-lh-lateralorbitofrontal
1013	ctx-lh-lingual
1014	ctx-lh-medialorbitofrontal
1015	ctx-lh-middletemporal
1016	ctx-lh-parahippocampal
1017	ctx-lh-paracentral
1018	ctx-lh-parsopercularis
1019	ctx-lh-parsorbitalis
1020	ctx-lh-parstriangularis
1021	ctx-lh-pericalcarine
1022	ctx-lh-postcentral
1023	ctx-lh-posteriorcingulate
1024	ctx-lh-precentral
1025	ctx-lh-precuneus

Caudate

Putamen

Cingulate

This is considered common to all “analyses” of the data

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kinfitr : The BIDS App!

Two parts / interfaces

1. Region definition
2. Modelling

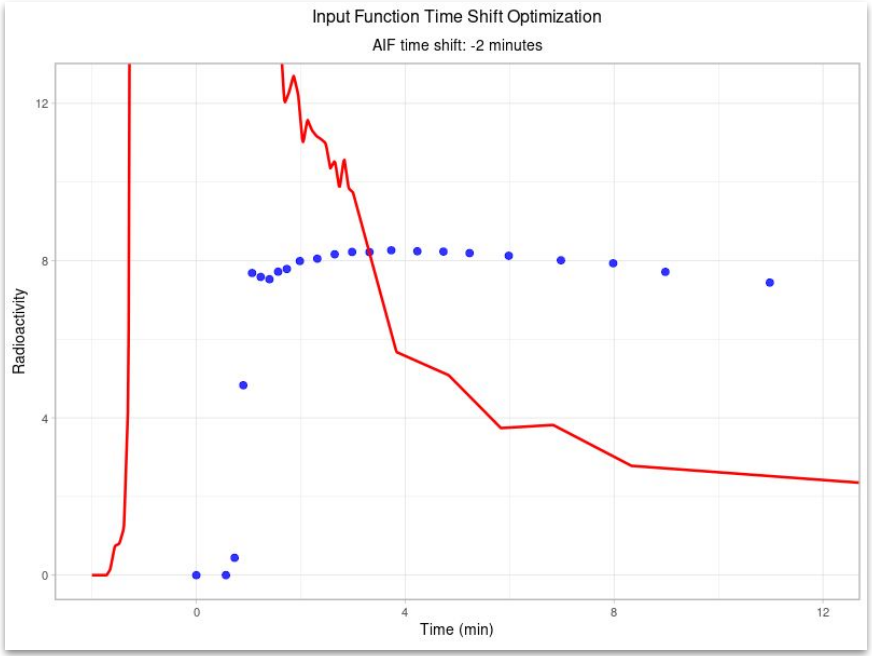
- Separated into analyses, e.g.
  - Region subsets
  - Session subsets
  - Restricted to first 60 minutes
- Each analysis allows up to 3 models with parameter inheritance
- Each analysis consists of several parts, which can be executed individually, and each of which produces its own report
- A sandbox feature will allow experimenting with model configuration to assess appropriateness

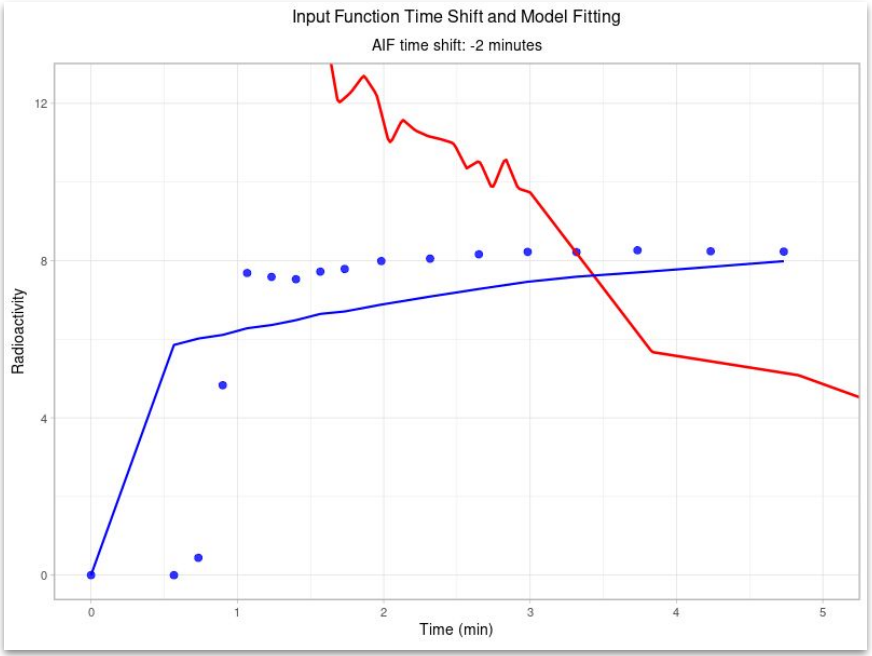
To the demo…

```
https://github.com/mathesong/kinfitr_app
```

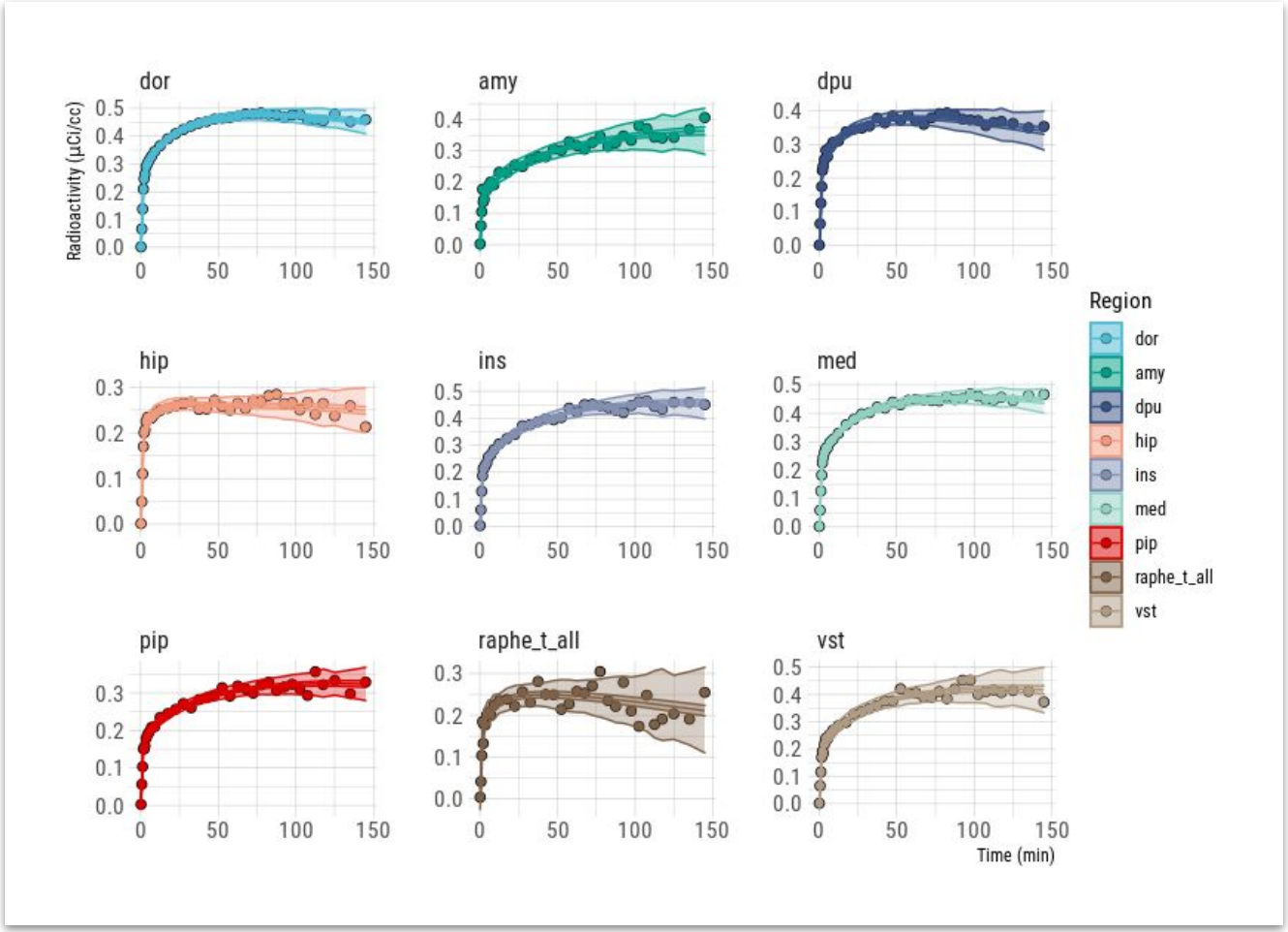
(usage instructions in the README)

Delay correction





Weights


dor
amy
dpu
hip
ins
med
pip
raphe_t_all
vst
Radioactivity (µCi/cc)
Time (min)
Region
dor
amy
dpu
hip
ins
med
pip
raphe_t_all
vst