PET-BIDS Derivatives & PET-Specific Considerations for Data Curation

Nordic PET-BIDS Onboarding and ezBIDS Workshop
28-29 August 2025

UNIVERSITY OF COPENHAGEN
FACULTY OF SCIENCE

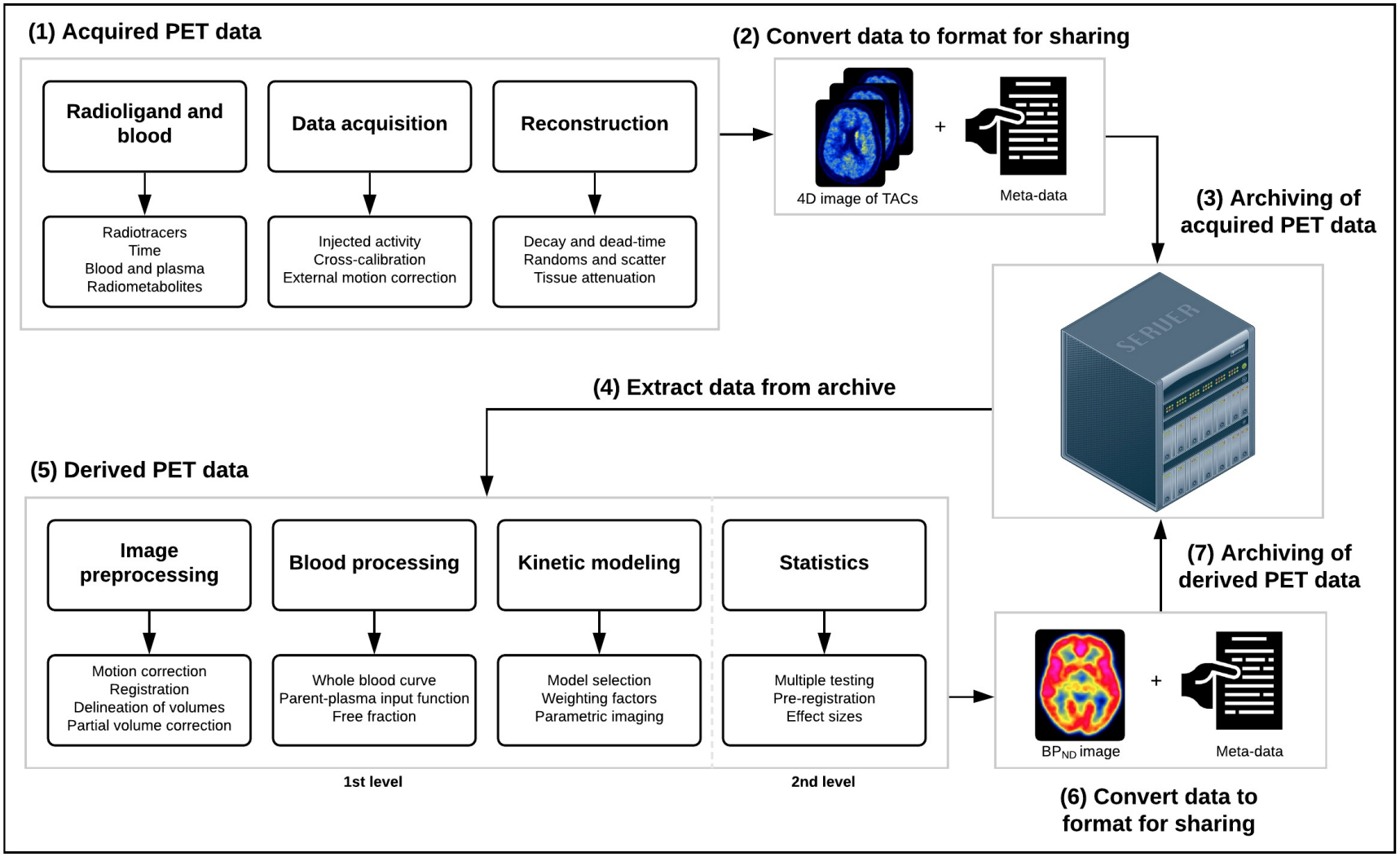
Neurobiology Research Unit
Rigshospitalet
Copenhagen University Hospital

NIH National Institute of Mental Health

Stanford | Center for Reproducible Neuroscience

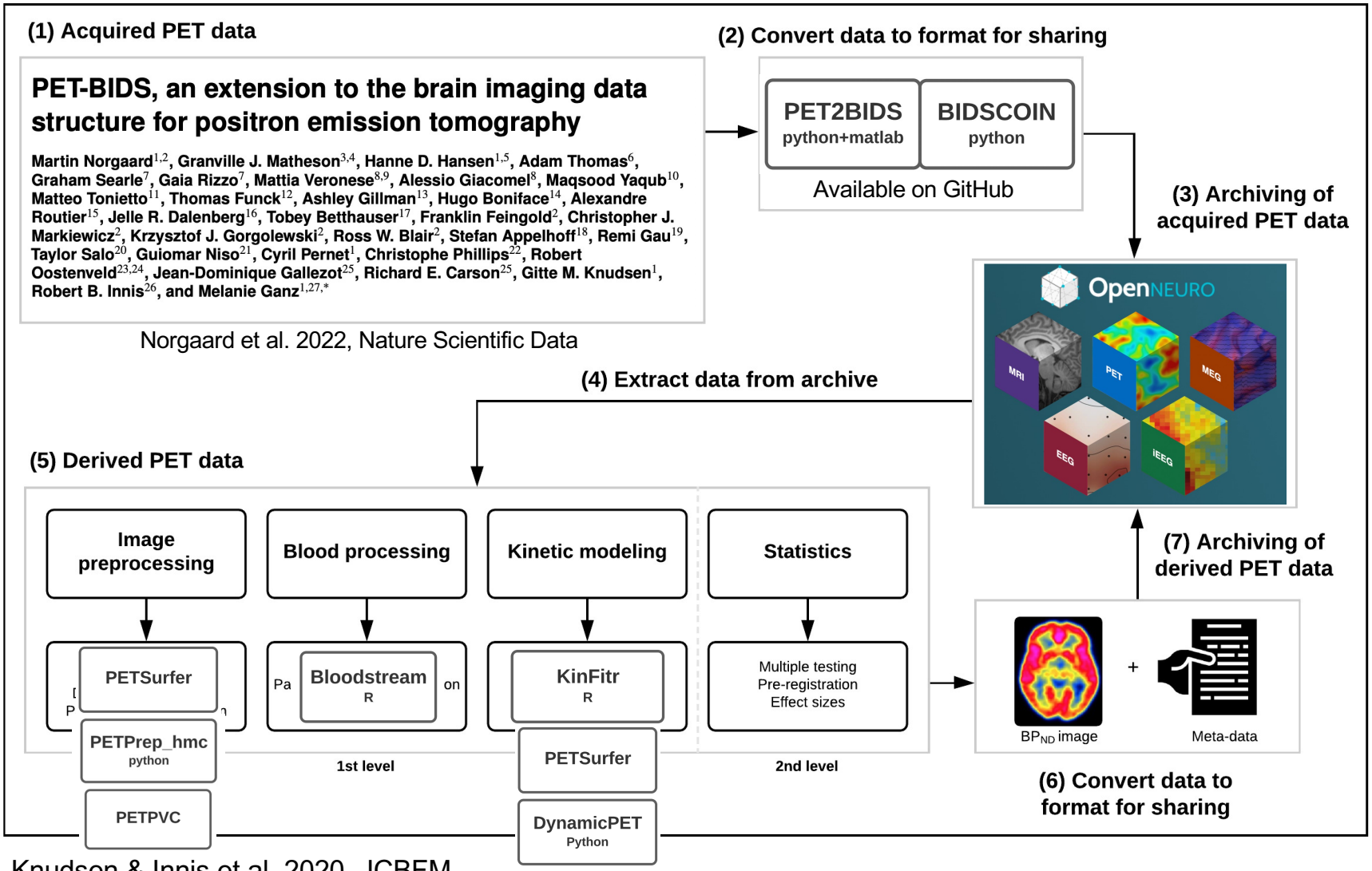
Stanford University

Guidelines for the format and content of PET data



Knudsen & Innis et al. 2020, JCBFM

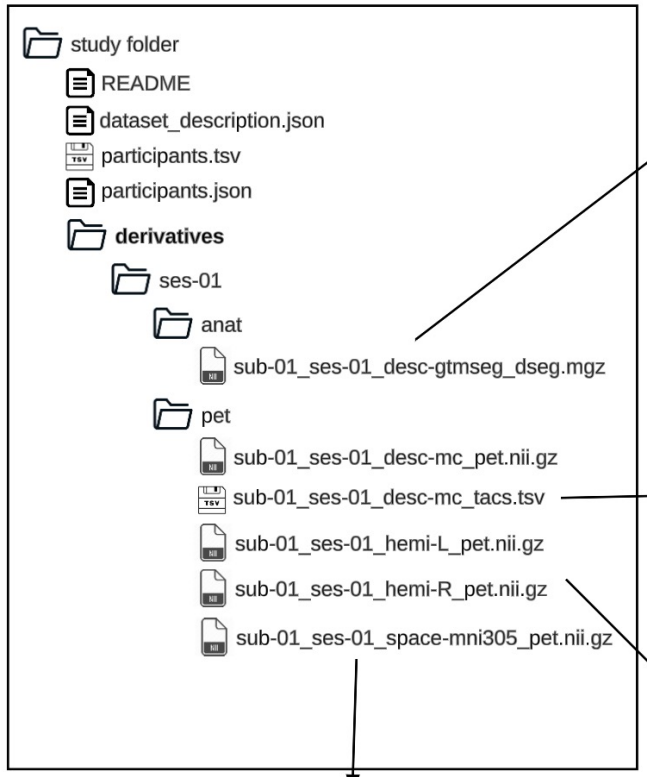
Guidelines for the format and content of PET data

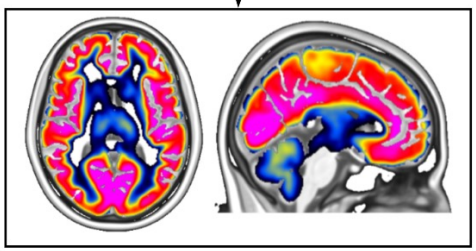


Knudsen & Innis et al. 2020, JCBFM

PET-BIDS Derivatives

Processed PET data



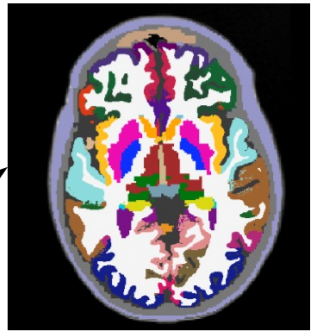


neuroreceptor maps

Kinetic model library

MRTM, MRTM2, $Logan_{ref}$, SRTM, SRTM2, Logan, FRTM, ESRTM, ESRTM2, Patlak

volumes of interest



Start [s]	End [s]	Hippocampus [Bq/mL]	Brainstem [Bq/mL]
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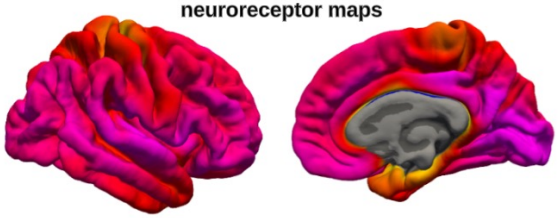
TACs

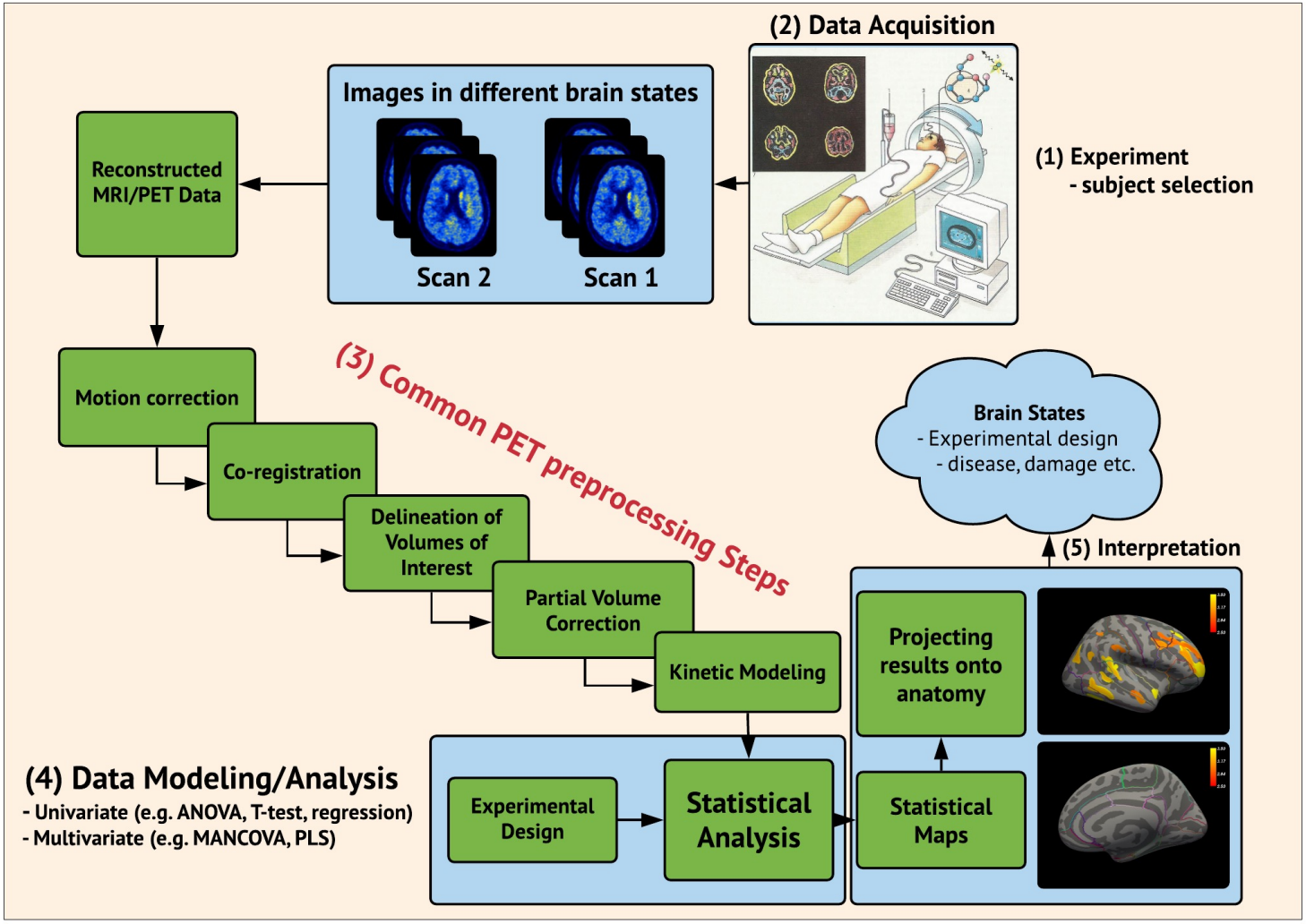
neuroreceptor maps



PET-BIDS Derivatives specification (BEP23):
https://docs.google.com/document/d/1yzsd1J9GT-aA0DWhdlgNr5LCu6_gvbjLyfvYq2FuxlY/edit#heading=h.mqkmyp254xh6

Common PET workflow

Norgaard et al. 2019, Neuroimage 199, 466-479.



Kinetic evaluation and test–retest reproducibility of [^{11}C]UCB-J, a novel radioligand for positron emission tomography imaging of synaptic vesicle glycoprotein 2A in humans

Journal of Cerebral Blood Flow & Metabolism
2018, Vol. 38(11) 2041–2052
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Sjoerd J Finnema[1], Nabeel B Nabulsi[1], Joël Mercier[2], Shu-fei Lin[1], Ming-Kai Chen[1], David Matuskey[1], Jean-Dominique Gallezot[1], Shannan Henry[1], Jonas Hannestad[2], Yiyun Huang[1] and Richard E Carson[1,3]

Image registration and definition of regions of interest

An average PET image (mean of the frames corresponding to 0–10 min) was aligned to each subject's MR image via a rigid registration with mutual information. The individual MR image was normalized to Montreal Neurological Institute space using an affine linear plus nonlinear registration (BioImage Suite 2.5), to extract regions-of-interest (ROIs) from the automated anatomic labeling (AAL) template.[28,29] Regional time–activity curves were obtained by applying the template ROIs to PET space using the inverse of the two image-transformations (i.e. PET-to-MRI and MR-to-template). The following AAL regions were included: amygdala, anterior cingulate cortex, caudate nucleus, cerebellum, frontal cortex, globus pallidus, hippocampus, insular cortex, occipital cortex, parietal cortex, posterior cingulate cortex, putamen, temporal cortex and thalamus. The ROI for the centrum semiovale was based on the AAL region but was eroded by two voxels on all borders to minimize partial volume effects.

Software
MC: ?
Reg: BioImage Suite
Regions: AAL
KinMod: in-house (IH)

%SE less than 25%. Parametric images for the 1T model were created with a basis function method with k_2 limited to the range (0.01–1.0 min^{-1}) and with no post-smoothing. All modeling was performed with in-house programs written within IDL 8.0 (ITT Visual Information Solutions, Boulder, CO, USA).

Kinetics and 28-day test–retest repeatability and reproducibility of [^{11}C]UCB-J PET brain imaging

Journal of Cerebral Blood Flow & Metabolism
0(0) 1–13
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DOI: 10.1177/0271678X20964248
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Hayel Tuncel[1], Ronald Boellaard[1], Emma M Coomans[1], Erik FJ de Vries[2], Andor WJM Glaudemans[2], Paula Kopschina Feltes[2], David V García[2], Sander CJ Verfaillie[1], Emma E Wolters[1,3], Steven P Sweeney[4], J Michael Ryan[4], Magnus Ivarsson[4], Berkley A Lynch[4], Patrick Schober[5], Philip Scheltens[3], Robert C Schuit[1], Albert D Windhorst[1], Peter P De Deyn[6,7], Bart NM van Berckel[1] and Sandeep SV Golla[1]

Data analysis

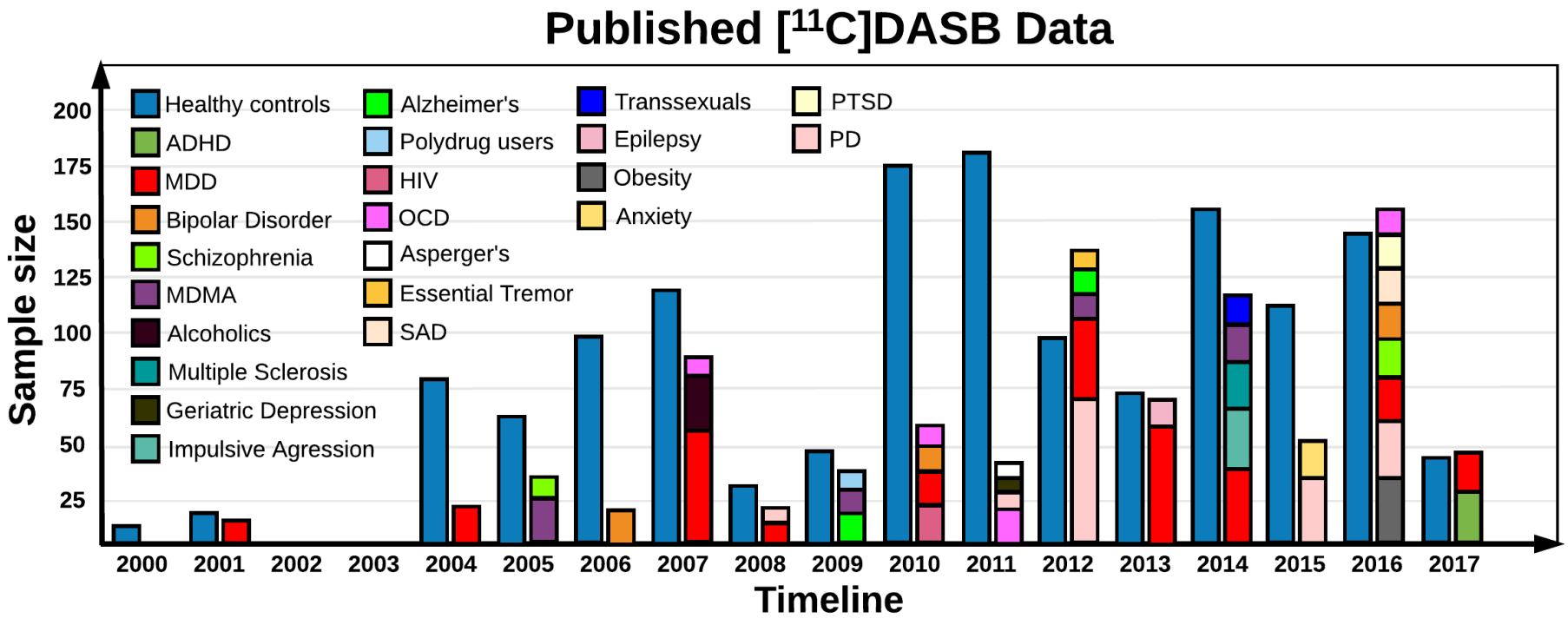
Structural 3D T1-weighted MRI images were co-registered to the PET images using Vinci v 2.56 software. The Hammers template,[23] which is incorporated in PVElab,[24] was used to delineate regions of interest (ROIs) on the co-registered MR scan and superimposed onto the dynamic PET scan to obtain regional time-activity curves (TACs). Online arterial blood TACs were calibrated and corrected for plasma to whole blood ratios, radiolabeled metabolites and delay, using the information from manual blood samples. Eventually, individual metabolite-corrected plasma input functions were generated. Various compartmental models[25] were used to fit the regional TACs: single tissue reversible (1T2k) and two-tissue irreversible (2T3k) and reversible (2T4k) compartmental models, with and without blood volume (V_B) as additional fit parameter. To determine the optimal pharmacokinetic model for in vivo kinetics of [^{11}C]UCB-J, the Akaike information criterion (AIC)[26] was used. Furthermore, the SRTM[27] was assessed by

Software
MC: no MC
Reg: Vinci
Regions: PVElab / IH
KinMod: in-house

comparing SRTM-derived binding potential (BP_{ND}) with plasma input derived distribution volume ratio (DVR). The white-matter centrum semi-ovale (SO) was manually defined using an in-house built tool and was considered as a reference region. Mean SO VOI size was 5.4 ± 2.5 cc for HCs and 4.0 ± 2.6 cc for AD patients. SUVr using three time intervals (40–60, 50–60 for both groups; and 70–90 min only for HCs) were also evaluated. SUVr values obtained from these time intervals were compared with corresponding plasma input derived DVR values.

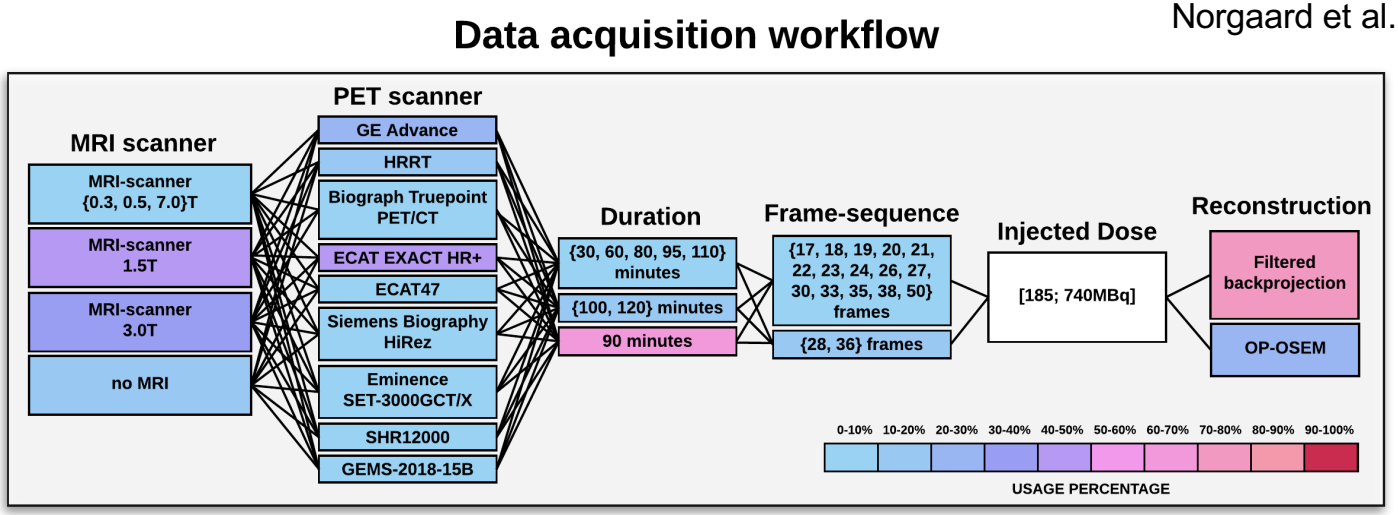
Capturing the story of [^{11}C]DASB

Norgaard et al. 2018, JCBFM

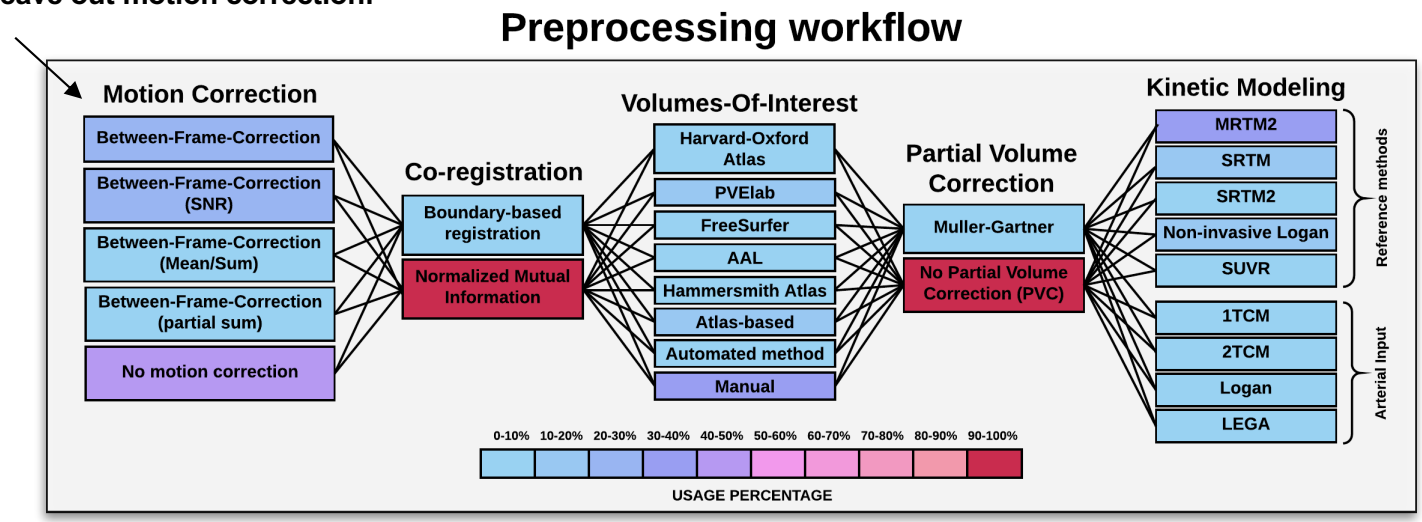


Acquisition and preprocessing choices for PET

Norgaard et al. 2018, JCBFM



40% of studies leave out motion correction!



<u>Combinations in total?</u>
<u>21.150.720 different workflows!</u>

Stanford University

The NRM grand challenge 2018

Veronese et al. 2021, JCBFM

JCBFM

Original Article

Journal of Cerebral Blood Flow & Metabolism
0(0) 1–19
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DOI: 10.1177/0271678X211015101
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Reproducibility of findings in modern PET neuroimaging: insight from the NRM2018 grand challenge

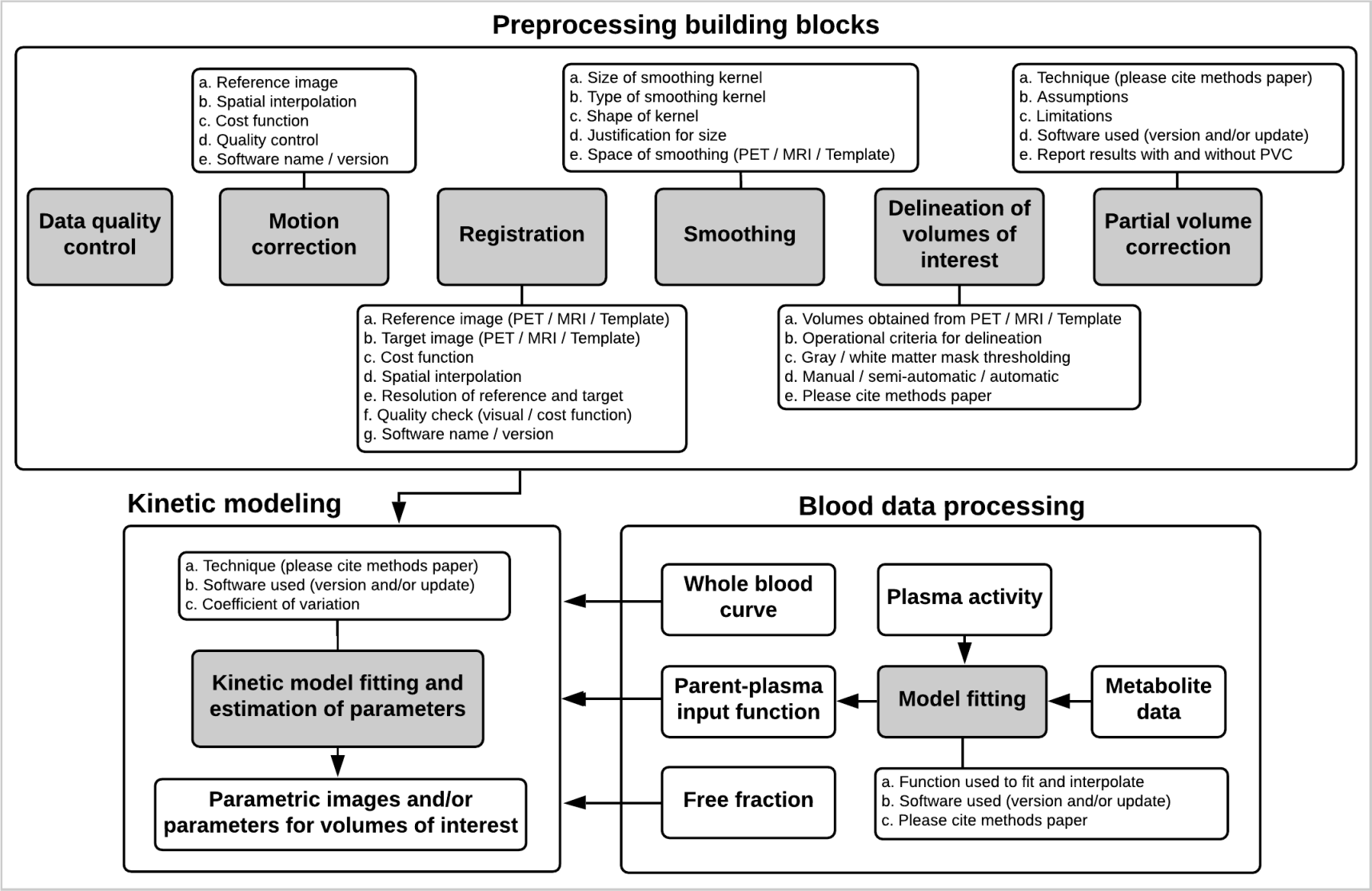
Mattia Veronese[1,*], Gaia Rizzo[2,*], Martin Belzunce[3], Julia Schubert[1], Graham Searle[2], Alex Whittington[2], Ayla Mansur[2,4], Joel Dunn[3,5], Andrew Reader[3] and Roger N Gunn[2,4]; and the Grand Challenge Participants[#]

Abstract

The reproducibility of findings is a compelling methodological problem that the neuroimaging community is facing these days. The lack of standardized pipelines for image processing, quantification and statistics plays a major role in the variability and interpretation of results, even when the same data are analysed. This problem is well-known in MRI studies, where the indisputable value of the method has been complicated by a number of studies that produce discrepant results. However, any research domain with complex data and flexible analytical procedures can experience a similar lack of reproducibility. In this paper we investigate this issue for brain PET imaging. During the 2018 NeuroReceptor Mapping conference, the brain PET community was challenged with a computational contest involving a simulated neurotransmitter release experiment. Fourteen international teams analysed the same imaging dataset, for which the ground-truth was known. Despite a plurality of methods, the solutions were consistent across participants, although not identical. These results should create awareness that the increased sharing of PET data alone will only be one component of enhancing confidence in neuroimaging results and that it will be important to complement this with full details of the analysis pipelines and procedures that have been used to quantify data.

Making the PET workflow transparent

Knudsen et al. 2020, JCBFM



Software for PET analysis pipelines

SOFTWARE	Motion correction	Registration	Smoothing	Delineation of Volumes of Interest	Partial Volume Correction (PVC)	Pharmacokinetic Modeling	**Open source**
AIR	x	x					x
FreeSurfer	x	x	x	x	x	x	x
FSL	x	x	x	x			x
SPM*	x	x	X	x			
PMOD	x	x	x	x	x	x	
MIAKAT*	x	x	x	x	x	x	
PVElab*		x		x	x		
APPIAN		x		x	x	x	x
Kinfitr						x	x
PETPVC					x		x

*Runs via MATLAB, and is therefore not open source.

Statistics from Nørgaard et al. 2019 (review of 105 published DASB papers):
AIR (N=7), FreeSurfer (N=2), FSL (N=3), SPM (N=60), PMOD (N=34), MIAKAT (N=0), PVElab (N=15), APPIAN (N=0), Kinfitr (N=0), PETPVC (N=0).

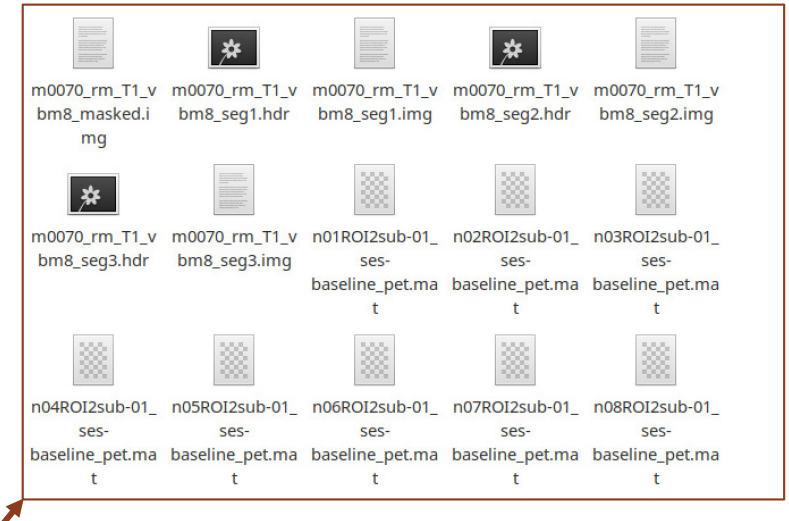
➔ SPM gets used 57% of the time and PMOD about 32% of the time for preprocessing. Kinetic modelling itself is then afterwards often done with PMOD or in-house software (stats there less clear).

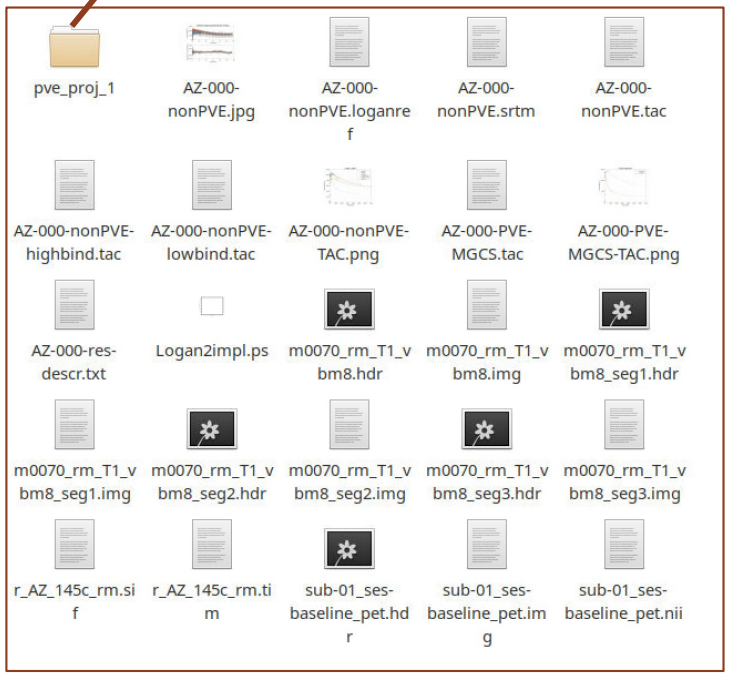
But why are we using specific tools over other tools?

- Domain knowledge - often we use the tools we are familiar with
- Availability – ”everything I need is available in MATLAB”
- Code language – e.g. python vs. Matlab
- Resources – operating systems (windows vs. Linux)
- Infrastructure - local computers vs. servers
- Easy - there is a ”cost” involved in switching practices

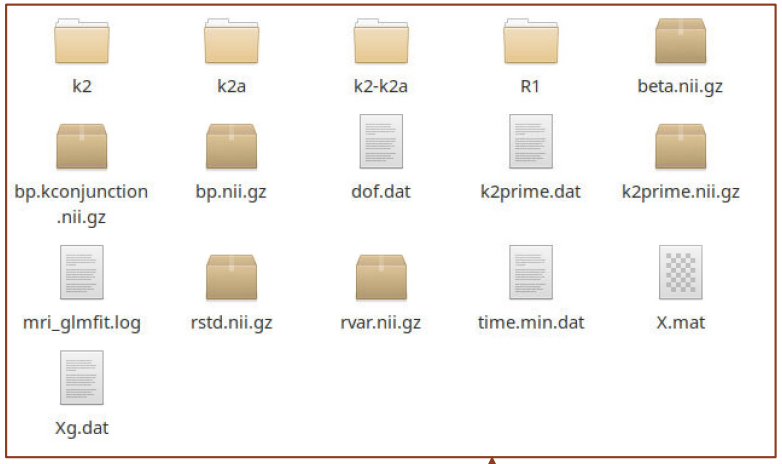
Problem?

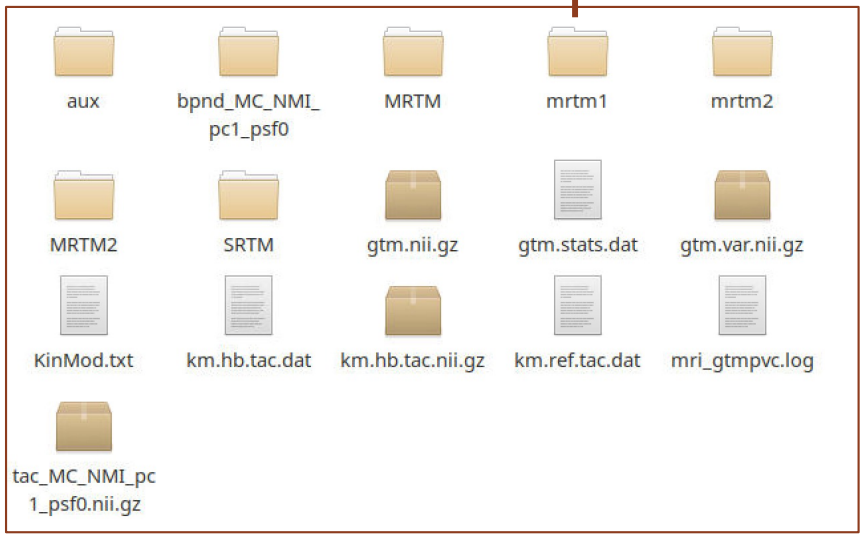
PVElab





PETsurfer





PET-BIDS

Norgaard et al. 2022, Scientific Data

```
{
    "BIDSVersion": "1.6.0",
    "Licence": "CCO license",
    "Name": "[11C]AZ10419369 PET dataset",
    "Authors": "NRU, Copenhagen",
    "Acknowledgements": "Hansen et al. 2020
    Visual stimuli induce serotonin release...,
    Hum Brain Mapp. 2020; 41: 4753– 4763.
    https://doi.org/10.1002/hbm.25156",
    "Funding": "Lundbeck Foundation",
    "DatasetDOI: ""
}
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{
    "Modality": "MR",
    "MagneticFieldStrength": 3,
    "Manufacturer": "Siemens",
    "ManufacturersModelName": "Trio",
    "EchoTime": 0.00304,
    "RepetitionTime": 1.55,
    "InversionTime": 0.8,
    "FlipAngle": 9,
    "NonLinearGradientCorrection": true
    ....
}
```

```
{
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    "ManufacturersModelName": "High-Resolution
    Research Tomograph (HRRT, CTI/Siemens)",
    "BodyPart": "Brain",
    "Units": "Bq/mL",
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    "TracerRadionuclide": "C11",
    "InjectedRadioactivity": 640,
    "InjectedRadioactivityUnits": "MBq",
    ....
}
```

- study folder
  - README
  - dataset_description.json
  - participants.tsv
  - participants.json
  - sub-01
    - ses-01
      - anat
        - sub-01_ses-01_T1w.json
        - sub-01_ses-01_T1w.nii.gz
      - pet
        - sub-01_ses-01_pet.json
        - sub-01_ses-01_pet.nii.gz
        - sub-01_ses-01_recording-manual_blood.json
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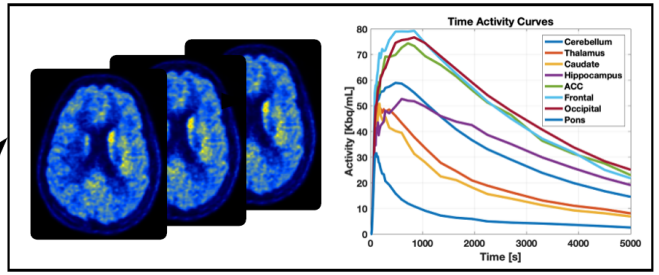
1 2 3 4 5 6

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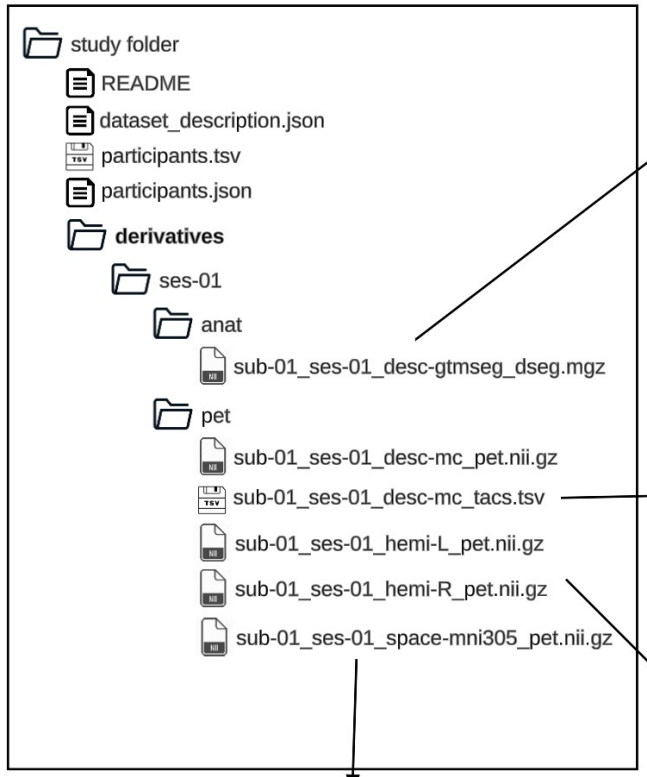
    "time": {
        "Description": "Time in relation to time zero
        defined by the _pet.json",
        "Units": "s"
    },
    ....
}
```

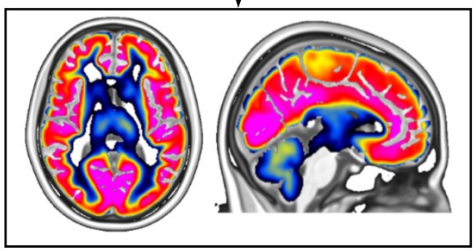
time	plasma_radioactivity	whole_blood_radioactivity	metabolite_parent_fraction	metabolite_polar_fraction
0	0	0	1	0
145	43.31	33.79	0.5749	0.1336
292	48.96	37.42	0.3149	0.2746
602	39.84	32.05	0.1469	0.3548
1248	37.38	31.52	0.073	0.444

https://bids-specification.readthedocs.io/en/bep-009/04-modality-specific-files/09-positron-emission-tomography.html

PET-BIDS Derivatives

Processed PET data





neuroreceptor maps

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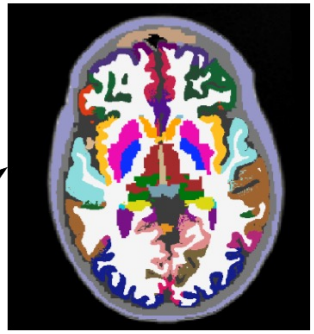

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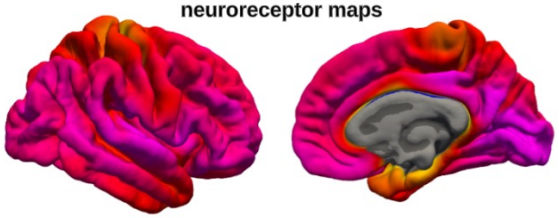

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https://docs.google.com/document/d/1yzsd1J9GT-aA0DWhdlgNr5LCu6_gvbjLyfvYq2FuxlY/edit#heading=h.mqkmyp254xh6

PET-BIDS Derivatives

Template:

```
<pipeline_name>/
    sub-<participant_label>/
        <datatype>/
            <source_entities>[] _<suffix>.<ext>
```

https://bids-specification.readthedocs.io/en/bep-009/05-derivatives/02-common-data-types.html

PET-BIDS Derivatives

Template:

petprep/
    sub-01/
        pet/
            sub-01_[] _pet.nii.gz
            sub-01_[]_pet.json

Common file level metadata fields

Each derivative data file SHOULD be described by a JSON file provided as a sidecar or higher up in the hierarchy of the derived dataset (according to the Inheritance Principle) unless a particular derivative includes REQUIRED metadata fields, in which case a JSON file is also REQUIRED. Each derivative type defines their own set of fields, but all of them share the following (non-required) ones:

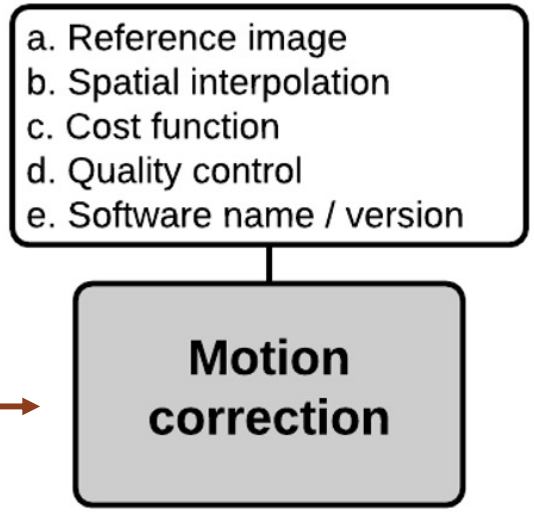
Key name	Requirement level	Data type	Description
Description	RECOMMENDED	string	Free-form natural language description of the nature of the file.
Sources	OPTIONAL	array of strings	A list of files with the paths specified relative to dataset root; these files were directly used in the creation of this derivative data file. For example, if a derivative A is used in the creation of another derivative B, which is in turn used to generate C in a chain of A->B->C, C should only list B in `Sources`, and B should only list A in `Sources`. However, in case both X and Y are directly used in the creation of Z, then Z should list X and Y in `Sources`, regardless of whether X was used to generate Y.
RawSources	OPTIONAL	array of strings	A list of paths relative to dataset root pointing to the BIDS-Raw file(s) that were used in the creation of this derivative.

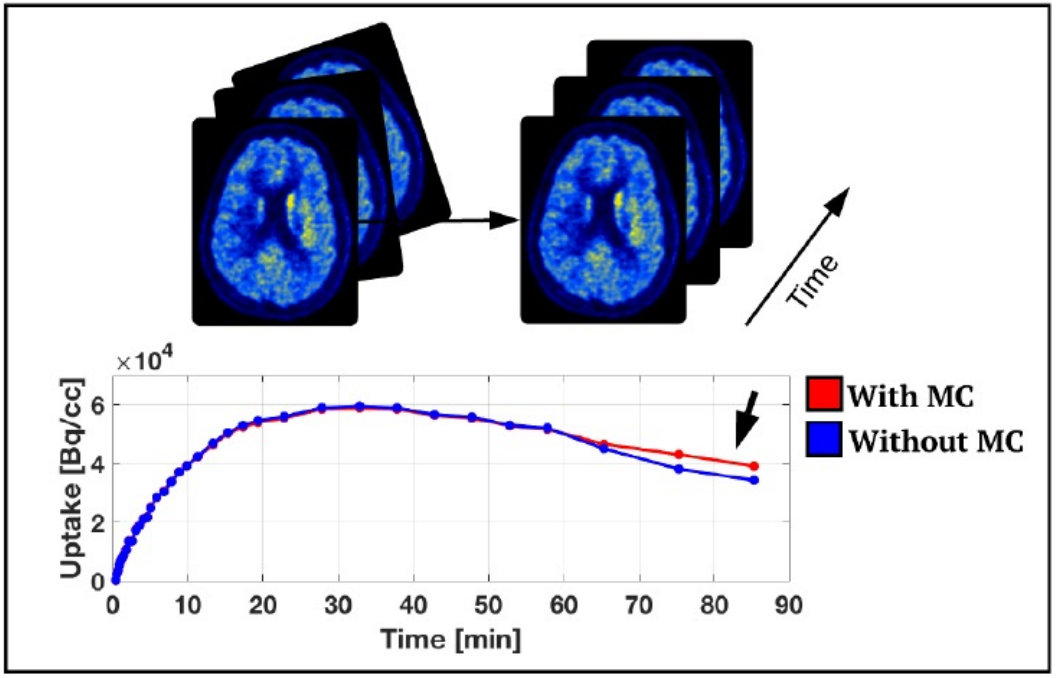
https://bids-specification.readthedocs.io/en/bep-009/05-derivatives/02-common-data-types.html

PET-BIDS Derivatives

Template:

petprep/
    sub-01/
        pet/
            sub-01_desc-mc_pet.nii.gz
            sub-01_desc-mc_pet.json





PET-BIDS Derivatives

Template:

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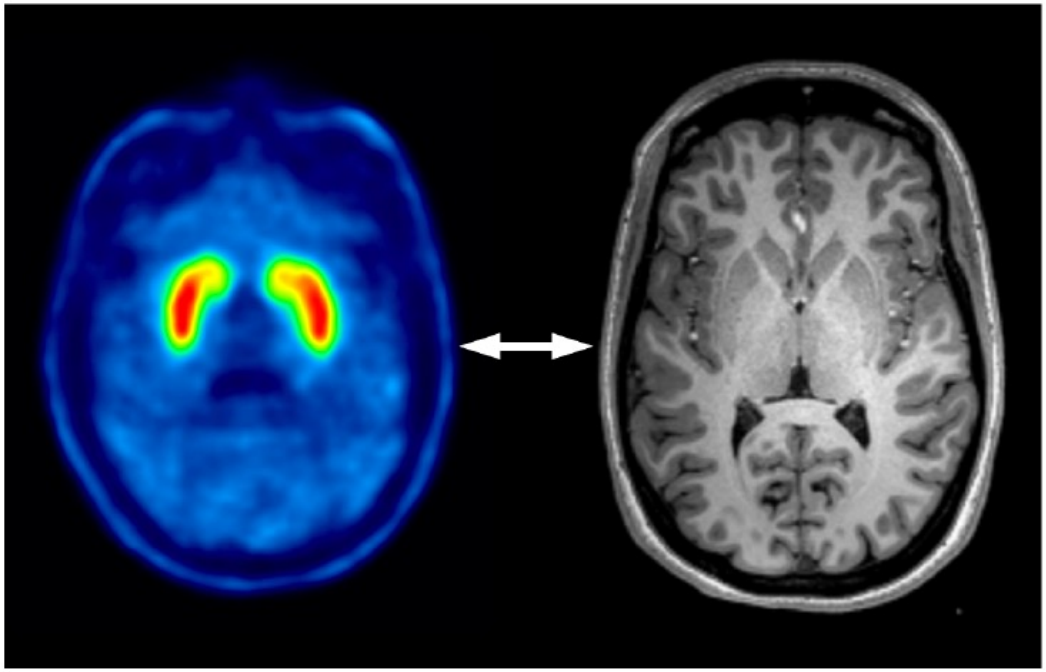


Registration

a. Reference image (PET / MRI / Template)
b. Target image (PET / MRI / Template)
c. Cost function
d. Spatial interpolation
e. Resolution of reference and target
f. Quality check (visual / cost function)
g. Software name / version

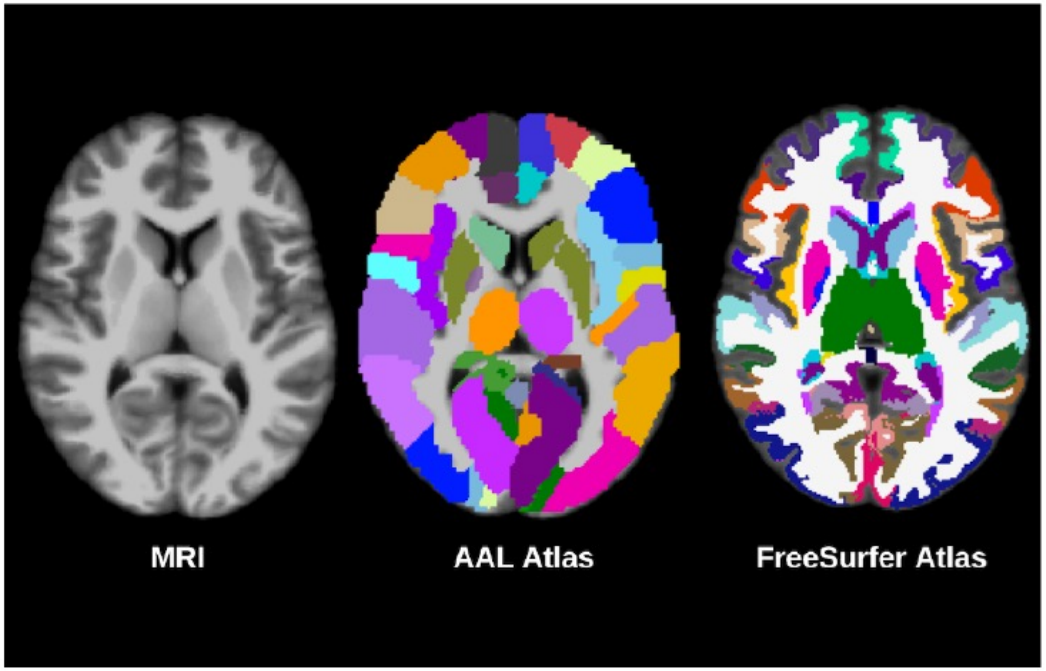
PET-BIDS Derivatives

The following metadata fields apply to all segmentation files:

Key name	Requirement level	Data type	Description
Manual	OPTIONAL	boolean	Indicates if the segmentation was performed manually or via an automated process.
Atlas	OPTIONAL	string	Which atlas (if any) was used to derive the segmentation.
Resolution	REQUIRED if `res` is present	string or object mapping labels to strings	Specifies the interpretation of the resolution keyword.

Template:

petprep/
    sub-01/
        pet/
            sub-01_space-T1w_seg-gtm_dseg.nii.gz
            sub-01_space-T1w_seg-gtm_dseg.json



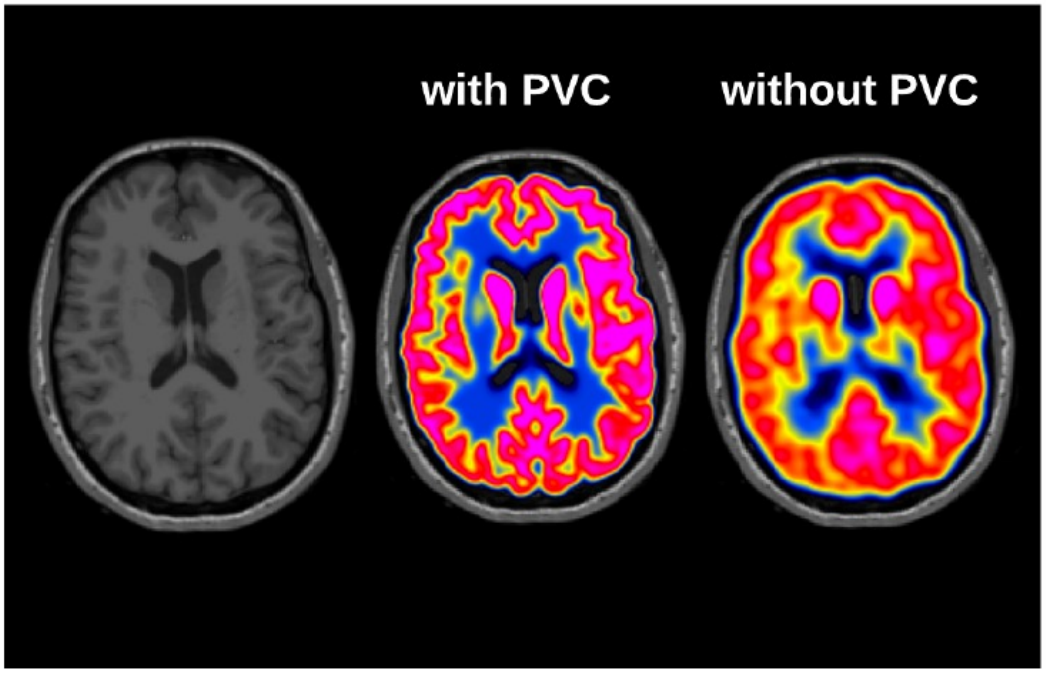
Delineation of volumes of interest

a. Volumes obtained from PET / MRI / Template
b. Operational criteria for delineation
c. Gray / white matter mask thresholding
d. Manual / semi-automatic / automatic
e. Please cite methods paper

PET-BIDS Derivatives

Template:

petprep/
    sub-01/
        pet/
            sub-01_space-orig_pvc-MG_seg-gtm_desc-mc_pet.nii.gz
            sub-01_space-orig_pvc-MG_seg-gtm_desc-mc_pet.json



a. Technique (please cite methods paper)
b. Assumptions
c. Limitations
d. Software used (version and/or update)
e. Report results with and without PVC

Partial volume correction

PET-BIDS Derivatives

Template:

petprep/
    sub-01/
        pet/
            sub-01_space-orig_pvc-MG_km-MRTM2_bpnd.tsv
            sub-01_space-orig_pvc-MG_km-MRTM2_bpnd.json

Journal of Cerebral Blood Flow & Metabolism (2007), 1–7
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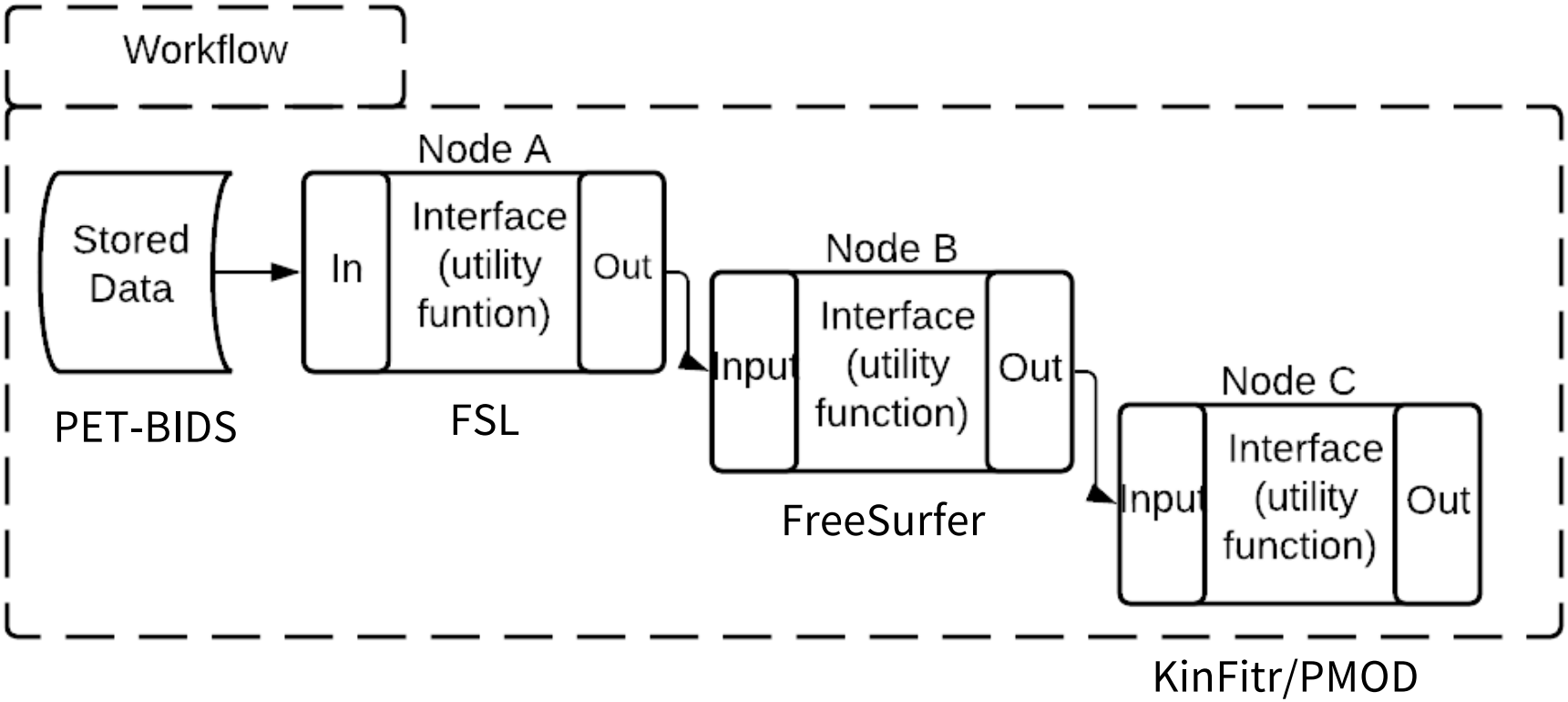
www.jcbfm.com

Review Article

Consensus nomenclature for *in vivo* imaging of reversibly binding radioligands

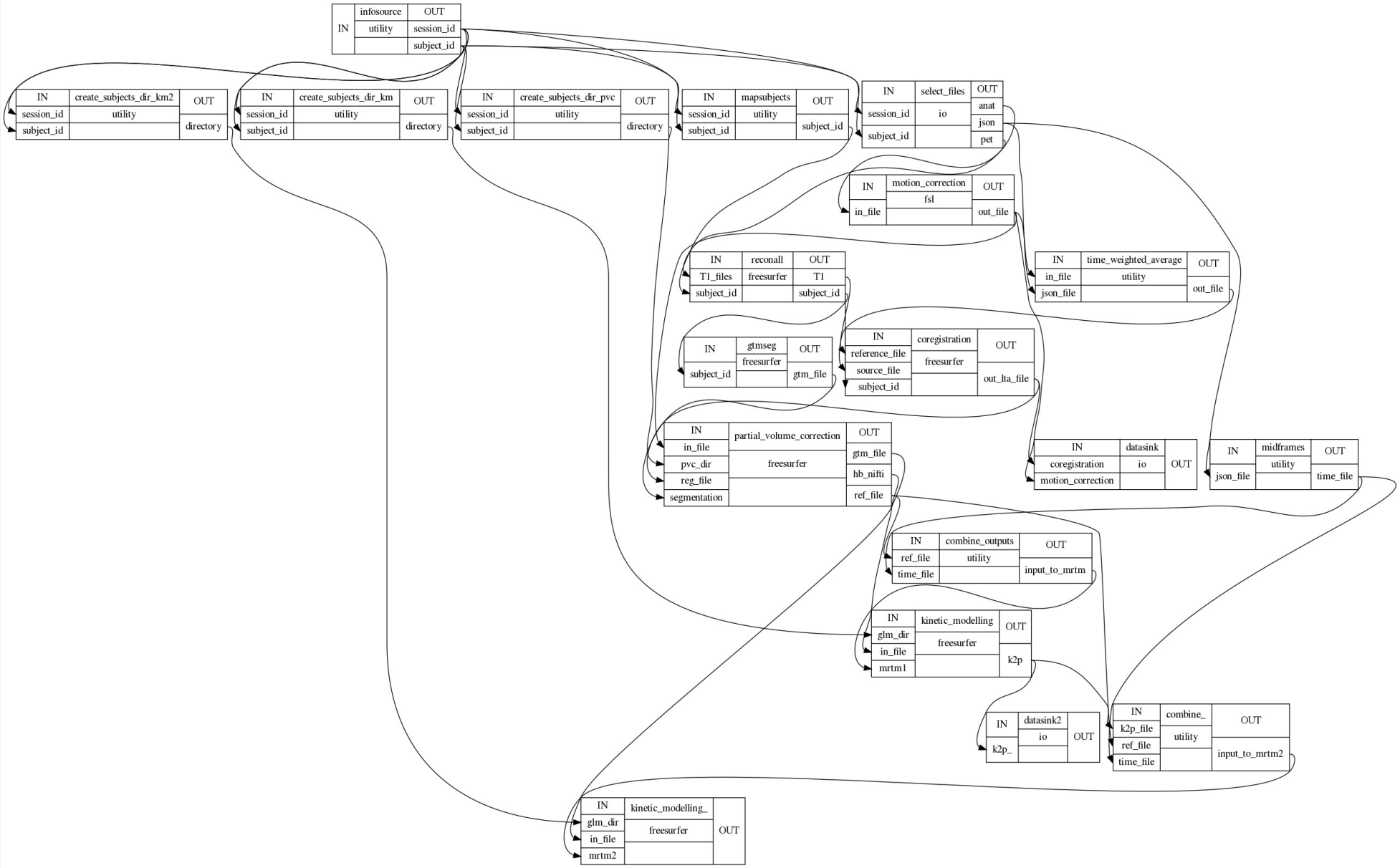
Robert B Innis[1], Vincent J Cunningham[2], Jacques Delforge[3], Masahiro Fujita[1], Albert Gjedde[4], Roger N Gunn[5], James Holden[6], Sylvain Houle[7], Sung-Cheng Huang[8], Masanori Ichise[9], Hidehiro Iida[10], Hiroshi Ito[11], Yuichi Kimura[12], Robert A Koeppe[13], Gitte M Knudsen[14], Juhani Knuuti[15], Adriaan A Lammertsma[16], Marc Laruelle[2], Jean Logan[17], Ralph Paul Maguire[18], Mark A Mintun[19], Evan D Morris[20], Ramin Parsey[9], Julie C Price[21], Mark Slifstein[9], Vesna Sossi[22], Tetsuya Suhara[11], John R Votaw[23], Dean F Wong[24] and Richard E Carson[25]

Components of the PET analysis pipeline



Courtesy by Avneet Kaur, CS MSc student

Overview of input-output relations providing full transparency



Summary

- We need to join forces to define how derived PET data should be stored/structured and what metadata should be present
- We are currently building all the necessary components to provide fully transparent and reproducible PET analysis pipelines to everyone
- Will make it easier to understand PET analysis pipelines and what has been done to the data
- Everyone are encouraged to join the efforts

  https://shorturl.at/2kk2G (BEP23)

Acknowledgements

+ many others

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