# PMOD Artificial Intelligence Framework (PAI)

# USER MANUAL Version 4.3

PMOD is a software FOR RESEARCH USE ONLY (RUO) and must not be used for diagnosis or treatment of patients.



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# 1 PAI Introduction

Computer algorithms based on Artificial Intelligence (AI) have become a success story and are now part of daily life. Machine Learning (ML) is a subset of AI in which humans provide the input data and expected results, and the computer determines "rules" with which it can process the data to approach the expected results. These "rules" may be considered as representations of the data. Deep Learning (DL) is considered a further subset of ML, in which there are successive layers of representations. ML methods have resulted in solutions ranging from facial recognition to web-based language translation. They have also been applied in many domains of biomedical research. However, the setup and use of ML toolkits is a task requiring a lot of methodological insight as well as specialized IT expertise.

The aim of PAI is to drastically lower the entry barrier to the ML methodology for researchers analyzing biomedical images. PAI is designed as a framework, allowing users to develop their own tailored ML-based image segmentation solution while working entirely within the familiar PMOD environment.

# 1.1 PAI Purpose

Segmentation of pathology or of organs/regions that do not conform to common templates can be a tedious, time-consuming and subjective procedure. The use of machine learning to automatically perform such a segmentation has the potential to save large amounts of time and improve reproducibility.

In the example shown below, regions of necrotic, gadolinium-enhancing and penumbra of a brain tumor are shown in color on a gray-scale anatomical T1-weighted MR image. Contrast from four MR series (T1-weighted, T2-weighted, T2-FLAIR, gadolinium-enhanced T1-weighted) were used to define these regions. For the top row, created by an expert reviewer using manual segmentation, this process takes many minutes or even hours. In the bottom row, the broadly similar segmentation result was generated by a trained convolutional neural network and took seconds.



However, training a convolutional neural network to perform such a segmentation task requires a substantial amount of data, time and effort.

PMOD's PAI framework aims to make training and deploying ML-based segmentation more accessible to non-expert users. PMOD's well-tested tools for image processing and traditional

segmentation provide an excellent base to prepare the training data needed for supervised machine learning.

In addition to AI-based segmentation, PAI also supports classification tasks. An example of classification in imaging is the assignment of a label "amyloid positive" or "amyloid negative" to amyloid PET images for tracers such as <sup>11</sup>C-PiB. PMOD's database functionality provides the base to organise data into classes for training of a neural network. The trained neural network then returns a probability of a new image belonging to a given class.

# **1.2 PAI Overview**

The structure of the PAI framework is illustrated below.



The actual ML platform used by PAI is the well-known <u>TensorFlow</u> solution. The neural network structure and the training method are correspondingly developed as Python scripts suitable for TensorFlow and constitute the ML model. The data for supervised learning are prepared in PAI, communication with TensorFlow is implemented via the R console in PMOD.

#### Learning Set

The Learning Set in PAI consists of references to the training data (i.e. Links to the input series in a PMOD database) and a specification of the preprocessing steps required to bring the data into a format suitable for machine learning. The training data itself consists of data samples. Each data sample consists of an input (one or several images) and its expected segmentation or classification result (one or several segments, in the format of label maps that can be associated with the input images, or label for a given class).

#### Training

Training is performed in TensorFlow using a Learning Set and an ML model. There are different mechanisms available, which will be explained below. Basically, training can be performed locally on your local machine, or delegated to a more powerful infrastructure such as Cloud-Computing.

#### **Training Result**

The result of training is a "trained model" - a set of **Weights** for the layers in the neural network, and a **Manifest** file containing information about the training process. These results are added to the **Learning Set**, making it ready for use in **Prediction** (i.e. automated segmentation or classification). As new training data become available, it can be added to the Learning Set and incremental training performed to improve prediction. An export functionality allows transfer of the result to other PMOD installations for prediction (sometimes known as Deployment).

#### Prediction

Prediction applies the trained model to a new set of input image data, resulting in a segmentation or classification result. Segmentation results may then be converted to VOIs and used for quantification.



#### Implementation in PMOD tools

PAI functionality is available in PBAS, PSEG and PCARDM. If PAI has been licensed, a **+** AI indication appears next to View, **PSEG** and PCARDM in the main PMOD ToolBox:

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	Kinetic
	PXMod
	⊻iew + Al
6	Fusion
	Segment + Al
	3 <u>D</u>
	Cardiac PET
	Cardiac <u>M</u> R + Al
4	Flow
<u></u>	Alzheimer
	Neuro
	Roden <u>t</u> Brain
	Configuration
	× Quit

In View, shortcuts to AI Segmentation and Classification become available on the View tab, and Machine Learning is available as an option in the Segmentation interface:



Learning Sets for AI projects are prepared via the Edit Learning Set option in the main View tool menu:

## **PAI Introduction**



#### In PSEG the Segment tab becomes Segment + AI



and the menu button as well:

🔺 Segment + Al » 🔹 🖓 🛐 🏧 🔺

In PCARDM the Machine Learning Segmentation option becomes available for either MRI\_Myocardium\_2D (mouse) or MRI\_Human\_Myocardium model:



# **1.3** Architectures included in Distribution

Two version of a neural network architecture for segmentation tasks, and an architecture for classification, are provided with PAI. These architectures have already been trained with appropriate data as part of our Case Studies. The architectures are available in the Pmod4.3/resources/pai folder, labeled by type.

### 1.3.1 Support Vector Machine (SVM)

The SVM architecture for classification in PAI uses an interface to the Python library scikit-learn.

Support vector machines are supervised learning models used for classification and regression.

SVM is particularly suited to image reduction strategies such as using the average voxel value in a set of VOIs (e.g. brain atlas VOIs for brain PET data - see Amyloid PET classification case study). Linear, RBF, Sigmoid and Poly kernels are available according to the scikit-learn library (see Learning Set Preparation). Our testing of the architecture in PAI has used 2 classes.

The output of a trained SVM classification model is a probability that an input to prediction belongs to one of the classes included in training.

An example of the SVM architecture in practice is provided in our Amyloid PET classification case study. Data to test the Amyloid PET SVM classification model is available in our Demo database.

#### 1.3.2 uNET

<u>uNET</u> is a convolutional neural network developed for image segmentation (Ronneberger et al., 2015).

A modified uNET was used by Isensee et al. (2018) in the MICCAI Brain Tumor Segmentation Challenge (BraTS). The BraTS data and this modified uNET were used for our first case study and the Multichannel Segmentation architecture for segmentation in PAI. The modified uNET structure is illustrated here:



Additional case studies were made using this architecture: • Rat brain dopaminergic PET segmentation

- Human brain MRI deep nuclei segmentation (IXI)
- Human cardiac MRI segmentation for function analysis

This architecture is available as Multichannel Segmentation in the <u>Create Learning Set</u><sup>145</sup> dialog.

The loss function used for this architecture is Dice Coefficient.

A classical uNET architecture is also available for segmentation projects. It is available as uNET Segmentation in the Create Learning Set dialog. Its structure for 2D input data is illustrated here:



This architecture is used for mouse cardiac MRI segmentation in the PCARDM tool, and it has additionally been used for the following case study:

• mouse femur/tibia trabecular segmentation

The loss function used for this architecture is **Binary Cross Entropy**.

For 3D training data its structure is illustrated here:



#### References:

Isensee et al. (2018), Brain Tumor Segmentation and Radiomics Survival Prediction: Contribution to the BRATS 2017 Challenge, https://arxiv.org/abs/1802.10508

Ronneberger et al. (2015), U-Net: Convolutional Networks for Biomedical Image Segmentation, https://arxiv.org/abs/1505.04597?

# 2 Installation of PAI Infrastructure

PAI requires the following elements (note specific versions are necessary):

- PMOD version 4.3 with PAI licensed (please use the latest build available in our download area)
- Local installation of R version 4.1.1 with the required packages. Please refer to the *PMOD Base Functionality User Guide* for details about the integration of R with PMOD.
- Configuration of the PMOD R Console to use a local R installation
- Local installation of Python (version 3.8 is required)
- Installation of TensorFlow (version 2.4.1) and Scikit-Learn via Python

Please follow the installation instructions applicable for your operating system.

# 2.1 Windows

Windows 10 or Windows Server 2019 are required as the operating system.

#### 2.1.1 Python and TensorFlow Installation

The additional packages required for PAI on Windows should be installed from their respective websites.

Please follow these steps:

- 1. Install Microsoft Visual Studio 2015, 2017, 2019 Runtime (i.e VC\_redist.x86.exe). https://support.microsoft.com/en-us/help/2977003/the-latest-supported-visual-c-downloads
- Check whether you have a compatible GPU. TensorFlow only supports NVIDIA GPUs in combination with NVIDIA's CUDA Toolkit. Tables of compatible GPUs are available on <u>https://developer.nvidia.com/cuda-gpus</u>
- 3. If your GPU is compatible, install NVIDIA drivers, Toolkit and models for TensorFlow 2.4:
  - a. Drivers 11.0: <u>https://www.nvidia.com/download/index.aspx?lang=en-us</u>
  - b. CUDA Toolkit 11.0: <u>https://developer.nvidia.com/cuda-toolkit-archive</u>
  - c. cuDNN 8.0.4 for CUDA 11.0: https://developer.nvidia.com/rdp/cudnn-download
- 4. Install Python 3.8 64-bit (select "Add Python to PATH", enable pip option and long paths). <u>https://www.python.org/downloads/windows/</u>
- 5. Upgrade pip by entering in a command terminal: python -m pip install --upgrade pip
- 6. Install TensorFlow by entering in a command terminal: python -m pip install --upgrade tensorflow
- 7. Check that tensorflow appears in the list of installed packages: python -m pip list
- 8. Test TensorFlow by entering in a command terminal: python -c "import tensorflow as tf;print(\"Num GPUs Available: \", len(tf.config.experimental.list\_physical\_devices('GPU')))" This test returns the number of compatible GPUs available for PAI. Zero is an acceptable result if you do not have a CUDA-compatible NVIDIA GPU.
- 9. Install scikit-learn by entering in a command terminal: python -m pip install -U scikit-learn
- 10.Test scikit-learn by entering in a command terminal: python -c "import sklearn; print(sklearn\_version\_)"

Note: GPU support for Windows (point 3. above) was tested for TensorFlow 2.4.

#### 2.1.2 R Installation

Please download and install R version 4.1.1 for Windows from https://cran.r-project.org/

There is no need to manually install additional R packages. PMOD will automatically download and install the necessary packages when the PMOD R Console is started for the first time. If no R functionality besides PAI is used in a particular PMOD installation, the installation can be restricted to a minimal package set as described in <u>Minimal R Configuration</u><sup>D</sup><sup>17</sup> below.

Note: in case of problems during R installation it may be necessary to set the R Home path for your specific system, and/or switch off automatic CRAN selection. Both are described in the <u>next</u> section  $^{D14}$ .

#### 2.1.2.1 Default R Configuration

Following R installation, start PMOD and open the **Configuration** facility from the main ToolBox.

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	R Statistics Console R Home C	? × Clear packages ④ (登) R Configuration tes /Program Files/R/R-4.1.1/bin/x64/	it
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	R Statistics Console R Home C Python Use C	Clear packages      miniput R Configuration tes /Program Files/R/R-4.1.1/bin/x64/ Required packages from repository on start. Install to Comprehensive R Archive Network (CRAN) location: Europe	et
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On the Users/Settings **STATISTICS** tab ensure that the checkbox R Statistics Console is checked and verify that the path to the local R installation is correct. Select **Install to Pmod folder** to avoid permission problems when installing the R packages.

Restart PMOD and wait for the **R** icon on the main ToolBox to become active.



Then click on the **R** icon to open the **PMOD Console**. The required packages are downloaded and installed, followed by an execution test and printing of the R version information:



The settings button indicated above opens the dialog window below.

R console settings				2
Additional packages > (To load on start)	tseries			
Tools location	Layout:	ক্রি <b>।িিশ</b> R diagnostics		4 1
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Max columns in table Max lines in printout	Report printout: 9 1000			
	Ok	Cancel		

Note that in case of problems connecting to Python when using PAI, the Path to Python can be configured in the **Configuration** facility from the main ToolBox:

PMOD Configuration and User Settings			2
	@ FTP Nodes D On Start		
User1 User1 I I Edit user name  Ad User settings are sa SETTINGS PXMOD Models PKIN Models REPORT DATABASES FTP Nodes APP Hottest Pixels Analysis Number of pixels Peak VOI volume 1.0	Id new user    Kernove user  KeAD / WRITE Formats  LOADING TOOLS  COL  KEARANCE  STATISTICS  PRESETS  Hypoxia Index threshold  (Absolute va  [ccm]	OR TABLES MODULES	](0-1)
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R Home C/Pro	gram Files/R/R-4.1.1/bin/x64/		Θ
Python			
Com	Required packages from repository on start. Install to prehensive R Archive Network (CRAN) location: Europe	o Pmod folder 🔍 d   D	
▶ 0 I I ?	Qk	<u>C</u> ancel	

Next open the Package Manager. All packages should have status OK.

	Type	Status	Installed version	CRAN version	
psych	CRAN	OK	2.1.9	2.1.9	
e1071	CRAN	OK	1.7.9	1.7-9	_
UsingR	CRAN	OK	2.0.6	2.0-6	
lawstat	CRAN	OK	3.4	3.4	
tseries	CRAN	OK	0.10.48	0.10-48	
np	CRAN	OK	0.60.11	0.60-11	
openair	CRAN	OK	2.8.4	2.8-5	
foreign	CRAN	OK	0.8.81	0.8-81	
Hmisc	CRAN	OK	4.6.0	4.6-0	
car	CRAN	OK	3.0.11	3.0-11	
phia	CRAN	OK	0.2.1	0.2-1	
compare	CRAN	OK	0.2.6	0.2-6	
reshape	CRAN	OK	0.8.8	0.8.8	
sfsmisc	CRAN	OK	1.1.12	1.1-12	
Cairo	CRAN	OK	1.5.12.2	1.5-12.2	
pROC	CRAN	OK	1.18.0	1.18.0	
survival	CRAN	OK	3.2.11	3.2-13	
glmnet	CRAN	OK	4.1.2	4.1-2	
stringr	CRAN	OK	1.4.0	1.4.0	
mcr	CRAN	OK	1.2.2	1.2.2	
session	CRAN	OK	1.0.3	1.0.3	
reticulate	CRAN	OK	1.22	1.22	
keras	CRAN	OK	2.6.1	2.6.1	
jsonlite	CRAN	OK	1.7.2	1.7.2	
lubridate	CRAN	OK	1.8.0	1.8.0	
sfsmisc	CRAN	OK	1.1.12	1.1-12	
RNifti	CRAN	OK	1.3.1	1.3.1	
memuse	CRAN	OK	4.1.0	4.2-1	
pm.base	Local	OK	4.301.4		
pm.ai	Local	OK	4.301.27	-	-

Note: If package installation fails, please check the R Home path in the Main Configuration, turn off automatic CRAN selection, and if problems continue, please check your firewall settings or contact your IT service.

#### 2.1.2.2 Minimal R Configuration

For instances of PMOD that will only be used for PAI it is possible to install a reduced set of R packages. To achieve this, perform the following configuration and installation procedure.

Following R installation, start PMOD and open the **Configuration** facility from the main ToolBox.

On the **STATISTICS** tab ensure that the checkbox R Statistics Console is checked and and verify that the path to the local R installation is correct. Select **Don't install**.

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L Fyu	Required packages from repository on start. Don't	install 🗸 🖌
	Use Comprehensive R Archive Network (CRAN) location: Europ	e v () b

Restart PMOD and wait for the  ${\bf R}$  icon on the main ToolBox to become active.

Then click on the **R** icon to open the **PMOD Console**. The internal packages **pm.base** and **pm.ai** were installed automatically whereas the remaining packages are skipped and **not loaded** messages listed:

			Outpu	t							×
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Packa	ige la	wsta	at not lo	aded	L.						
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The **Settings** button indicated above opens the dialog window below.

Additional packages > (To load on start)	tseries			
	Ter Package manager	rffr IN R diagnostics		
	Layout			
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Task tabs location	LEFT	~	4	Þ
	Workspace:			
Initial Workspace Data		4	2	0
	Save workspace on exit to the selected R Da	ta file		
Initial script	NONE	~	4	Þ
	Use initial script after each workspace is loa	ded		
	Editing:			
	Text output			
Font	Fixed	*	4	•
Max columns in table Max lines in printout	Report printout: 9 1000			
	Qk	Cancel	_	_

Open the **Package Manager**. Most packages will have **Requires installation** in the **Status** column

Joon	I IVDe	Status	Installed version	CRAN version
KCDD	CRAN	Requires inst.	incluie a foreient	1.0.7
toBy	CRAN	Requires inst		4611
osvch	CRAN	Requires inst		2.1.9
e1071	CRAN	Requires inst		1.7-9
JsingR	CRAN	Requires inst		2.0-6
awstat	CRAN	Requires inst		3.4
series	CRAN	Requires inst		0.10-48
qr	CRAN	Requires inst		0.60-11
openair	CRAN	Requires inst		2.8-4
oreign	CRAN	OK	0.8.81	0.8-81
Hmisc	CRAN	Requires inst		4.6-0
car	CRAN	Requires inst		3.0-11
ohia	CRAN	Requires inst		0.2-1
compare	CRAN	Requires inst		0.2-6
eshape	CRAN	Requires inst		0.8.8
sfsmisc	CRAN	Requires inst		1.1-12
Cairo	CRAN	Requires inst		1.5-12.2
ROC	CRAN	Requires inst		1.18.0
survival	CRAN	OK	3.2.11	3.2-13
glmnet	CRAN	Requires inst		4.1-2
stringr	CRAN	Requires inst		1.4.0
mcr	CRAN	Requires inst		1.2.2
session	CRAN	Requires inst		1.0.3
eticulate	CRAN	Requires inst		1.22
(eras	CRAN	Requires inst		2.6.1
sonlite	CRAN	Requires inst		1.7.2
ubridate	CRAN	Requires inst		1.8.0
sfsmisc	CRAN	Requires inst		1.1-12
RNifti	CRAN	Requires inst		1.3.1
memuse	CRAN	Requires inst		4.1-0
om.base	Local	OK	4.301.4	
om.ai	Local	OK	4.301.27	-

To install only the packages necessary for PAI, please select **Install PAI only** and then **Yes** 

Package	Type	Status	Installed version	CRAN version
RCDD	CRAN	Requires inst.		1.0.7
doBy	CRAN	Requires inst		4.6.11
osych	CRAN	Requires inst		2.1.9
e1071	CRAN	Requires inst		1.7-9
JsingR	CRAN	Requires inst		2.0-6
awstat	CRAN	Requires inst		3.4
series	CRAN	Requires inst		0.10-48
qr	CRAN	Requires inst		0.60-11
openair	CRAN	Requires inst		2.8-4
oreign	CRAN	OK	0.8.81	0.8-81
Hmisc	CRAN	Requires inst		4.6-0
car	CRAN	Requires inst		3.0-11
sfsr Cair pRC surv gIm strir	The follo	wing packages wil stringr session reticulate keras	l be installed:	2
sfsr Cair pRC sun strir mmor ses retic sor lubr sfsr RNi mer pm.	The follo This ope Do you v	wing packages will stringr session reticulate keras joonlite lubridate sfsmisc RNifti memuse pm.ai eration is time cons want to continue?	I be installed: uming and can't be sto	2
sfsr Cair pRC surv glm strir mor ses ses ses sor retic (?) (ubr sfsr RNi mer pm. pm.	The follo This ope Do you v	wing packages will stringr session reticulate keras joonlite lubridate sfsmisc RNifti memuse pm.ai eration is time cons want to continue?	uming and can't be sto	pped.

Following installation the **Status** entries will be updated:

Rcpp JoBy bsych	CRAN	OK	Installed version	CRANVEISION
ioBy osych	CRAN		107	107
osych		Doquiros inst	1.0.7	1.0.7
Jayun	CRAN	Requires inst.		2.10
1071	CRAN	OK	170	17.0
leinaP	CRAN	Requires inst	1.7.5	20.6
awstat	CRAN	Requires inst.		3.4
corioc	CRAN	Requires inst.		0.10-48
n	CRAN	Requires inst.		0.60-11
nenair	CRAN	Requires inst		2.8-4
oreign	CRAN	OK	0.8.81	0.8-81
Imisc	CRAN	Requires inst	0.0.01	4.6-0
ar	CRAN	Requires inst		3.0-11
hia	CRAN	Requires inst		0.2-1
compare	CRAN	Requires inst		0.2-6
eshane	CRAN	Requires inst		0.8.8
sfsmisc	CRAN	OK	1112	1.1-12
Cairo	CRAN	Requires inst		15-122
ROC	CRAN	Requires inst		1 18 0
survival	CRAN	OK	3211	32-13
Imnet	CRAN	Requires inst		4 1-2
stringr	CRAN	OK	14.0	140
ncr	CRAN	Requires inst		122
ession	CRAN	OK	1.0.3	1.0.3
eticulate	CRAN	OK	1.22	1.22
eras	CRAN	OK	2.6.1	2.6.1
sonlite	CRAN	OK	1.7.2	1.7.2
ubridate	CRAN	OK	1.8.0	1.8.0
fsmisc	CRAN	OK	1.1.12	1.1-12
RNifti	CRAN	OK	1.3.1	1.3.1
nemuse	CRAN	OK	4.1.0	4.1-0
om.base	Local	OK	4.301.4	-
im ai	Local	OK	4.301.27	-

Closing the window with  $\ensuremath{\text{Ok}}$  completes the installation.

Note: When prediction is launched at a later time point, the R Console will report the packages that were not installed, but the **Execution test** will still pass as illustrated below.



#### 2.1.3 Selection of Python installation

Multiple installations and versions of Python may cause the PAI infrastructure test to fail.

In this situation you should define the path to Python 3.8 in the **Configuration** facility from the main ToolBox:

LIOCOG			
User1 VSERS	T Editusernam	me <b>* Add new user ×</b> Remove user ettings are saved when switching the user.	
SETTINGS	PXMOD Models PKIN	N Models READ / WRITE Formats LOADING TOOLS COLOR TABLES MODULES	
REPORT	DATABASES FTP Nod	des APPEARANCE STATISTICS PRESETS	
Hottest	Pixels Analysis Number of p Peak VOI vol SUV Scan Date / R Statistics Con	pixels 5 Hypoxia Index threshold 0.0 (Absolute value) Probability threshold 0.5 plume 1.0 [ccm] Time ● Series ○ Acquisition ○ Scan VOI Classification mode:  ♥ ♥ Save Patient Info in VOIs (required by DB restoring from file system) msole ? × Clear packages ● rem IVM R Configuration test Home C/Program Files/R/R-4.1.1/bin/x64/	(0-1)
	D Py	ython	
	_	Required packages from repository on start: Don't install  Comprehensive R Archive Network (CRAN) location: Europe	4   Þ 4   Þ

Restart PMOD after setting the path to Python 3.8.

# 2.2 MacOS

MacOS Big Sur or Catalina are recommended. Older MacOS may not support the PAI infrastructure.

Note: the XQuartz package is required for plotting in the R console (to support X11 libraries). The XQuartz project is officially supported by Apple: <u>https://www.xquartz.org/</u>

#### 2.2.1 Python and TensorFlow Installation

Although MacOS provides Python libraries by default we recommend installing the newest available Python version 3.8 from the website <u>https://www.python.org/downloads/mac-osx/</u>

1. Install TensorFlow using the Terminal command:

python3 -m pip3 install -u tensorflow==2.4.1

2. Check that tensorflow appears in the list of installed packages:

python3 -m pip list

3. Test TensorFlow using the command:

```
python3 -c "import tensorflow as tf;print(\"Num GPUs Available: \",
len(tf.config.experimental.list_physical_devices('GPU')))"
```

This test returns the number of compatible GPUs available for PAI (zero is an acceptable result if you do not have a compatible NVIDIA GPU).

- 4. Install scikit-learn by entering in Terminal: python3 -m pip3 install -U scikit-learn
- 5. Test scikit-learn by entering in Terminal: python3 -c "import sklearn; print(sklearn. version )"

#### 2.2.2 R Installation

Please download and install R version 4.1.1 for MacOS from https://cran.r-project.org/

There is no need to manually install additional R packages. PMOD will automatically download and install the necessary packages when the PMOD R Console is started for the first time. If no R functionality besides PAI is used in a particular PMOD installation, the installation can be restricted to a minimal package set as described in <u>Minimal R Configuration</u><sup>D</sup><sup>17</sup> below.

Note: in case of problems during R installation it may be necessary to set the R Home path for your specific system, and/or switch off automatic CRAN selection. Both are described in the <u>next</u> section  $\mathbb{D}^{26}$ .

#### 2.2.2.1 Default R Configuration

Following R installation, start PMOD and open the **Configuration** facility from the main ToolBox.

On the **STATISTICS** tab ensure that the checkbox R Statistics Console is checked.Select **Install** to **Pmod folder** to avoid permission problems when installing the R packages. We recommend selecting **Use Comprehensive R Archive Network (CRAN) location**. In rare cases the connection to CRAN may be unsuccessful. In this case, unselect **Use Comprehensive R Archive Network (CRAN) location**, then select the CRAN location from the native R dialog that appears when R Console is started. This situation has been encountered on MacOS Catalina.

🛡 User1 🔻	DICOM DAT	TABASE @ FTP Nodes On Start  * Add new user  Remove user
🗹 Login enabl	led [+] 🥂 Usersetting	gs are saved when switching the user.
SETTINGS	PXMOD Models PKIN Mo	Iodels READ / WRITE Formats LOADING TOOLS COLOR TABLES MODULES
REPORT	DATABASES FTP Nodes	APPEARANCE STATISTICS PRESETS
Hottest	Pixels Analysis Number of pixel Peak VOI volum SUV Scan Date / Tim	els 5 Hypoxia Index threshold 0.0 (Absolute value) Probability threshold 0.5 (0-1) ne 1.0 [ccm] ne Series O Acquisition O Scan VOI Classification mode:
		✓ Save Patient Info in VOIs (required by DB restoring from file system)
	R Statistics Console	✓ Save Patient Info in VOIs (required by DB restoring from file system)         Ie       ? × Clear packages ● months in the system
	R Statistics Console R Hom	Save Patient Info in VOIs (required by DB restoring from file system)  P × Clear packages  Chibrary/Frameworks/R framework/Resources/  Configuration test
	R Statistics Console R Hom	Save Patient Info in VOIs (required by DB restoring from file system)      Clear packages     Immuno Info in VOIs (required by DB restoring from file system)      /Library/Frameworks/R framework/Resources/     Immuno Info in Info in VOIs (required by DB restoring from file system)
	R Statistics Console R Hom	Save Patient Info in VOIs (required by DB restoring from file system)      Clear packages     The Configuration test      /Library/Frameworks/R.framework/Resources/      Required packages from repository on start Install to Pmod folder
	R Statistics Console R Hom Pythor	Save Patient Info in VOIs (required by DB restoring from file system) In ? × Clear packages  Image: Clear packages (Image: Configuration test
	R Statistics Console R Hom Pythor V	✓ Save Patient Info in VOIs (required by DB restoring from file system)     Information Vois (required by DB restoring from file system)     Information Vois (required by DB restoring from file system)     Information Vois (required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring from file system)     Information Vois (Required by DB restoring for the file system)     Information Vois (Required by DB restoring for the file system)     Information Vois (Required by DB restoring for the file system)     Information Vois (Required by DB restoring for the file system)     Information Vois (Required by DB restoring for the file system)     Information Vois (Required by DB restoring for the file system)     Information Vois (Required by DB restoring for the file system)<

Restart PMOD and wait for the R icon on the main ToolBox to become active.



Then click on the **R** icon to open the **PMOD Console**. The required packages are downloaded and installed, followed by an execution test and printing of the R version information:

MR . Relaxometry	<ul> <li>General</li> </ul>	ANOVA	₹ ?	×   🛄 🝷
	Output			B ×
0.00000	R version 4.1.1 (2021-0 Copyright (C) 2021 The	08-10) "Kick Things e R Foundation for St	s" atistical Computing	
	Platform:			
	R is free software and You are welcome to re Type 'license()' or 'licen	comes with ABSOLU distribute it under cer nce()' for distribution (	ITELY NO WARRANTY tain conditions. details.	r.
	R is a collaborative pro	ject with many contri	butors.	
	Type 'contributors()' for 'citation()' on how to cite	more information an e R or R packages in	id i publications.	
	Type 'demo()' for some	demos 'heln/\' for o	n line beln or	
	'help.start()' for an HTM	L browser interface t	to help.	
and a second	Type 'q()' to quit R.			
	Loading default setting	js Loaded.		
	Execution test Passe	ed.		

The Settings button indicated above opens the dialog window below.

<b>派</b> R console settings			>
Additional packages > (To load on start)	tseries		
	रिक्ते Package manaç	er क्रिफ्रिम्भि F	R diagnostics
Tools location	TOP		▼ 4   Þ
Task tabs location	LEFT		▼
Initial Workspace Data	Workspace:	selected R Data file	4   F @
Initial script	NONE		- 4 4
	Use initial script after each wo Editing: Parentheses autocomplete Text output	rkspace is loaded	
Font	Fixed		▼ 4 >
Max columns in table Max lines in printout	Report printout: 9 1000		
	<u>O</u> k	Cancel	

Open the Package Manager. All packages should have status OK.

Package	Type	Status	Installed version	CRAN version	
psych	CRAN	OK	2.1.9	2.1.9	
e1071	CRAN	OK	1.7.9	1.7-9	-
UsingR	CRAN	OK	2.0.6	2.0-6	
lawstat	CRAN	OK	3.4	3.4	
tseries	CRAN	OK	0.10.48	0.10-48	
np	CRAN	OK	0.60.11	0.60-11	
openair	CRAN	OK	2.8.4	2.8-5	
foreign	CRAN	OK	0.8.81	0.8-81	
Hmisc	CRAN	OK	4.6.0	4.6-0	
car	CRAN	OK	3.0.11	3.0-11	
phia	CRAN	OK	0.2.1	0.2-1	
compare	CRAN	OK	0.2.6	0.2-6	
reshape	CRAN	OK	0.8.8	0.8.8	
sfsmisc	CRAN	OK	1.1.12	1.1-12	
Cairo	CRAN	OK	1.5.12.2	1.5-12.2	
pROC	CRAN	OK	1.18.0	1.18.0	
survival	CRAN	OK	3.2.11	3.2-13	
glmnet	CRAN	OK	4.1.2	4.1-2	
stringr	CRAN	OK	1.4.0	1.4.0	
mcr	CRAN	OK	1.2.2	1.2.2	
session	CRAN	OK	1.0.3	1.0.3	
reticulate	CRAN	OK	1.22	1.22	
keras	CRAN	OK	2.6.1	2.6.1	
jsonlite	CRAN	OK	1.7.2	1.7.2	
lubridate	CRAN	OK	1.8.0	1.8.0	
sfsmisc	CRAN	OK	1.1.12	1.1-12	
RNifti	CRAN	OK	1.3.1	1.3.1	
memuse	CRAN	OK	4.1.0	4.2-1	
pm.base	Local	OK	4.301.4	1	
pm.ai	Local	OK	4.301.27	-	

Note: If package installation fails, please check the R Home path in the Main Configuration, turn off automatic CRAN selection, and if problems continue, please check your firewall settings or contact your IT service.

#### 2.2.2.2 Minimal R Configuration

For instances of PMOD that will only be used for PAI it is possible to install a reduced set of R packages. To achieve this, perform the following configuration and installation procedure.

Following R installation, start PMOD and open the **Configuration** facility from the main ToolBox.

On the **STATISTICS** tab ensure that the checkbox R Statistics Console is checked and verify that the path to the local R installation is correct. Select **Don't install**.We recommend selecting **Use Comprehensive R Archive Network (CRAN) location**. In rare cases the connection to CRAN may be unsuccessful. In this case, unselect **Use Comprehensive R Archive Network (CRAN) location**, then select the CRAN location from the native R dialog that appears when R Console is started.

Login enab	led [+] (+) U	ser settings are s	saved when switt	ching the user	uve user				
SETTINGS	PXMOD Models	PKIN Models	READ / WRIT	E Formats	LOADING TOOL	S COLOR TAB	LES MODULE:	S	
REPORT	DATABASES F1	TP Nodes AP	PEARANCE	STATISTICS	PRESETS				
	Peak SUV Scan	VOI volume 1.0 Date / Time () S VOI () S cs Console ?	[ccm] Series O Acquis Classification m Save Patient Info i × Clear packa	ition O Scan ode: 🚺 👻 In VOIs (requir uges 💿 👩	ed by DB restorin	g from file system) guration test			
		R Home /Lib	rary/Framework	s/R.framewor	k/Resources/				۳
		Python Use Con	Required pa	ackages from i rchive Networi	repository on start k (CRAN) location	Don't install		▼   4   <b>b</b> ∀   4   5	

Restart PMOD and wait for the R icon on the main ToolBox to become active.

Then click on the **R** icon to open the **PMOD Console**. The internal packages **pm.base** and **pm.ai** were installed automatically whereas the remaining packages are skipped and **not loaded** messages listed:

Output
Output is free software and com iu are welcome to redist pe 'license()' or 'licence() is a collaborative project pe 'contributors()' for mo tation()' on how to cite R pe 'demo()' for some de alp.start()' for an HTML bi- pe 'q()' to quit R. ading default settings ackage Rcpp not loaded. ackage doBy not loaded. ackage doBy not loaded. ackage usnigR not loaded. ackage beries not loaded. ackage penair not loaded. ackage compare not loaded. ackage compare not loaded. ackage compare not loaded. ackage phia not loaded. ackage compare not loaded. ackage compare not loaded. ackage sfsmisc not loaded. ackage compare not loaded. ackage compare not loaded. ackage sfsmisc not loaded. ackage compare not loaded. ackage pROC not loaded. ackage pROC not loaded.

The **Settings** button indicated above opens the dialog window below.

Additional packages > (To load on start)	tseries			
	Package manager	TET POI R diagnostics		
	Layout		1	
Tools location	TOP	-	4	Þ
Task tabs location	LEFT	~	4	•
	Workspace:			
Initial Workspace Data		4	2	0
	Save workspace on exit to the selected R Data file			
Initial script	NONE	~	4	
	Use initial script after each workspace is loaded			
	Editing:			
	Parentheses autocomplete			
Font	Fixed	-		l F
	Report printout:			
Max columns in table	9			
Max lines in printout	1000			
	Ot	Cancel	_	_

# Open the Package Manager. Most packages will have Requires installation in the Status column

	Type	Status	Installed version	CRAN version
Ксрр	CRAN	Requires inst		1.0.7
doBy	CRAN	Requires inst.		4.6.11
osych	CRAN	Requires inst.		2.1.9
e1071	CRAN	Requires inst		1.7-9
JsingR	CRAN	Requires inst.		2.0-6
awstat	CRAN	Requires inst		3.4
series	CRAN	Requires inst		0.10-48
np	CRAN	Requires inst		0.60-11
penair	CRAN	Requires inst.		2.8-4
oreign	CRAN	OK	0.8.81	0.8-81
Imisc	CRAN	Requires inst		4.6-0
ar	CRAN	Requires inst		3.0-11
ohia	CRAN	Requires inst		0.2-1
compare	CRAN	Requires inst.		0.2-6
eshape	CRAN	Requires inst		0.8.8
sfsmisc	CRAN	Requires inst		1.1-12
Cairo	CRAN	Requires inst		1.5-12.2
ROC	CRAN	Requires inst		1.18.0
urvival	CRAN	OK	3.2.11	3.2-13
Imnet	CRAN	Requires inst		4.1-2
stringr	CRAN	Requires inst		1.4.0
ncr	CRAN	Requires inst		1.2.2
ession	CRAN	Requires inst		1.0.3
eticulate	CRAN	Requires inst		1.22
eras	CRAN	Requires inst		2.6.1
sonlite	CRAN	Requires inst		1.7.2
ubridate	CRAN	Requires inst.		1.8.0
sfsmisc	CRAN	Requires inst		1.1-12
RNifti	CRAN	Requires inst.		1.3.1
nemuse	CRAN	Requires inst		4.1-0
om.base	Local	OK	4.301.4	-
om.ai	Local	OK	4.301.27	2

To install only the packages necessary for PAI, please select **Install PAI only** and then **Install/Update** 

Package	Туре	Status	Installed version	CRAN version
Rcpp	CRAN	Requires inst		1.0.7
loBy	CRAN	Requires inst		4.6.11
psych	CRAN	Requires inst		2.1.9
e1071	CRAN	Requires inst		1.7-9
UsingR	CRAN	Requires inst		2.0-6
lawstat	CRAN	Requires inst		3.4
series	CRAN	Requires inst		0.10-48
np	CRAN	Requires inst		0.60-11
openair	CRAN	Requires inst		2.8-4
oreign	CRAN	OK	0.8.81	0.8-81
Hmisc	CRAN	Requires inst		4.6-0
car	CRAN	Requires inst		3.0-11
pRC sun gim mcr ses ses sor ubr sfsr RNi mer pom. pom.	This ope Do you v	stringr session reticulate keras jsonlite lubridate sfsmisc RNifti memuse pm.ai rration is time cons vant to continue?	uming and can't be sto	pped.
		✓ <u>Y</u> es	× <u>N</u> o	
		Install a	II packages Install F	PAI only 🛓 Install
		Install a	II packages Install F	Al only 📕 Install
	<u>O</u> k	Install a	II packages Install F	PAI only Install

Following installation the Status entries will be updated:

Package	Type	Status	Installed version	CRAN version
Rcpp	CRAN	OK	1.0.7	1.0.7
doBy	CRAN	Requires inst		4.6.11
psych	CRAN	Requires inst		2.1.9
e1071	CRAN	OK	1.7.9	1.7-9
UsingR	CRAN	Requires inst		2.0-6
lawstat	CRAN	Requires inst		3.4
tseries	CRAN	Requires inst		0.10-48
np	CRAN	Requires inst		0.60-11
openair	CRAN	Requires inst		2.8-4
foreign	CRAN	OK	0.8.81	0.8-81
Hmisc	CRAN	Requires inst		4.6-0
car	CRAN	Requires inst		3.0-11
phia	CRAN	Requires inst		0.2-1
compare	CRAN	Requires inst		0.2-6
reshape	CRAN	Requires inst		0.8.8
sfsmisc	CRAN	OK	1.1.12	1.1-12
Cairo	CRAN	Requires inst		1.5-12.2
pROC	CRAN	Requires inst		1.18.0
survival	CRAN	OK	3.2.11	3.2-13
gImnet	CRAN	Requires inst		4.1-2
stringr	CRAN	OK	1.4.0	1.4.0
mcr	CRAN	Requires inst		1.2.2
session	CRAN	OK	1.0.3	1.0.3
reticulate	CRAN	OK	1.22	1.22
keras	CRAN	OK	2.6.1	2.6.1
sonlite	CRAN	OK	1.7.2	1.7.2
lubridate	CRAN	OK	1.8.0	1.8.0
sfsmisc	CRAN	OK	1.1.12	1.1-12
RNifti	CRAN	OK	1.3.1	1.3.1
memuse	CRAN	OK	4.1.0	4.1-0
pm.base	Local	OK	4.301.4	-
om ai	Local	OK	4.301.27	-

Closing the window with **Ok** completes the installation.

Note: When prediction is launched at a later time point, the R Console will report the packages that were not installed, but the **Execution test** will still pass as illustrated below.



#### 2.2.3 Selection of Python installation

Multiple installations and versions of Python may cause the PAI infrastructure test to fail.

In this situation you should define the path to Python 3.8 in the **Configuration** facility from the main ToolBox:

USERS	DICOM		E @ FTP1	Nodes 🖸 C	n Start				
🗢 User1 🔻	▲   ▶ T Edit u	iser name 🛛 🏶	<u>A</u> dd new user	▼ × <u>R</u> em	ove user				
Login enabl	led [+] <u> </u>	User settings are	saved when sw	itching the user					
SETTINGS PXMOD Models PKIN Models			IS READ / WRITE Formats LOADING TOOLS COLOR TABLES MODULES						5
REPORT	DATABASES	FTP Nodes A	PPEARANCE	STATISTICS	PRESETS				
Hottest	Pixels Analysis Nun Pea SUV Scar	nber of pixels 5 k VOI volume 1.0 n Date / Time VO vo r tics Console ?	Hypo [ccm] Series O Acqu I Classification Save Patient Inf × Clear pac	xia Index thresh iisition O Scan mode: 🔽 👻 o in VOIs (requir kages 💿 👩	old 0.0 (Ab ed by DB restoring f	psolute valu from file sy tration test	e) Probab stem)	ility threshold	0.5 (0-1)
		R Home /Li	brary/Framewo	rks/R.framewor	k/Resources/				
		Python							
			Required	packages from r	epository on start	Don't inst	all		
		C	omprehensive R	t Archive Networ	(CRAN) location:	Europe			w 4   b
. La l	. ?			OF	t			Ca	ncel

Restart PMOD after setting the path to Python 3.8.

# 2.3 Linux Platforms

Note: in case of problems during R installation it may be necessary to set the R Home path for your specific system, and/or switch off automatic CRAN selection. Both are described in the <u>next</u> section  $^{\square 36}$ .

### 2.3.1 R Installation

PAI requires R version 4.1.1. Please perform the following installation steps (Ubuntu 18.04):

#### Install R:

```
sudo apt-key adv --keyserver keyserver.ubuntu.com --recv-keys
E298A3A825C0D65DFD57CBB651716619E084DAB9
sudo add-apt-repository 'deb https://cloud.r-
project.org/bin/linux/ubuntu bionic-cran40/' sudo apt update
sudo apt install r-recommended
```

#### Install the required libraries:

```
sudo apt install libcurl4-openssl-dev
```
```
sudo apt install libcairo2-dev
sudo apt install xorg-dev
sudo apt install libssl-dev
sudo add-apt-repository ppa:c2d4u.team/c2d4u4.0+
sudo apt-get update
sudo apt-get install r-cran-lme4
sudo apt-get install r-cran-snow
sudo apt-get install r-cran-vgam
```

### Start R at the command line as administrator ("sudo R") and install the required packages:

```
install.packages("doBy")
install.packages("psych")
install.packages("e1071")
install.packages("UsingR")
install.packages("lawstat")
install.packages("tseries")
install.packages("np")
install.packages("openair")
install.packages("foreign")
install.packages("Hmisc")
install.packages("car")
install.packages("phia")
install.packages("compare")
install.packages("reshape")
install.packages("sfsmisc")
install.packages("Cairo")
install.packages("pROC")
install.packages("survival")
install.packages("glmnet")
install.packages("mcr")
install.packages("stringr")
```

```
install.packages("reticulate")
install.packages("jsonlite")
install.packages("session")
install.packages("keras")
install.packages("memuse")
```

### Main Configuration in PMOD User Interface

Following R and package installation, launch PMOD and check that R Statistics Console is activated in the Main Configuration, on the USERS, STATISTICS tab:

ETTINGS PXMOD Models EPORT DATABASES FT	PKIN Models READ	/ WRITE Formats	LOADING TOOLS CO PRESETS	DLOR TABLES MO	DULES			
EPORT DATABASES FT	Nodes APPEARANC		PRESETS	OLOR IMBLES   MO	DOLES			
			The affect of					
Hottest Pixels Analysis	Number of pixels 5 Peak VOI volume 1. Scan Date / Time 0 VO	Hypo 0 [ccm] Series Acquis Classification mo	ia Index threshold tion O Scan de: 🔽 👻	0.0 (Abs	olute value) Pr	obability threshold	0.5	(0-1)
S R	itatistics Console	Save Patient Info  Clear pa	n Võis (required by E ickages 🛞	)B restoring from I	file system) guration test			
	Dathan							
		Required pack	ages from repository	y on start: Install	to Pmod folder			
	🕑 Use Co	mprehensive R An	hive Network (CRAN)	location: Europ	e		* 4 F	

Note: If package installation fails, please check the R Home path in the Main Configuration, turn off automatic CRAN selection, and if problems continue, please check your firewall settings or contact your IT service.

# 2.3.2 Python and TensorFlow Installation

Python version 3.8 is required. Install Python, TensorFlow and Scikit-Learn as follows:

sudo apt update sudo apt upgrade
sudo apt install build-essential
sudo apt install python3

sudo apt install python3-pip
pip3 install --upgrade pip
pip3 install tensorflow
pip3 install -U scikit-learn

Note: TensorFlow can alternatively be installed in Python's virtual environment. scikit-learn can be tested using the command: python3 -c "import sklearn; print(sklearn.\_\_version\_\_)"

# *3 Preparation of Training Data and Neural Network*

# **3.1** Data Preparation

### Image Import

The use of a database is a prerequisite for developing an ML model in PAI. Please refer to the *PMOD Basic Functionality User Guide* for instructions how to create and use databases. In the example below a database called **BraTS** was created and the data from the MICCAI BraTS Challenge imported.

### Image Association

A training sample consists of one or several image series, and either the segmentation reference result or class for classification from which the neural network should learn. All of these images need to be associated in the database so that when a single image is referenced all related images are identified.

To associate the images, select a subject in the **Subjects** list and then all series to be associated in the **Series** list. From the option menu indicated below select **Associate Images**, which brings up a dialog window confirming association of the selected series.



To identify which image series is the reference segment map, select it in the list, then the **TAG** column, and in the menu that appears

Set series TAGGING	NONE	
		M NONE
		D PET
		CT
		SEGMENT

select the **SEGMENT** entry. If more than one input image is required for the segmentation, it is important that they always appear in the same order in the association list. Please use the arrow buttons to the right of the list for shifting the position of a selected element.

Existing associations can be checked by selecting one of the image series and activating the button indicated below:

Subject Name	Study Da	te Time	Study Description	A Pro	ject	Series Descriptio	on Modification		Last Use		Mod	i	T
BraTS20_Training.	2020.07	.13 20:51:5	T1	1.T1			2020-11-0	4 14	2021-0	3-1	MR		
raTS20_Training.	2020.07	.13 20:51:5	T1CE	2.T1C	E		2020-11-0	4 14	2021-0	3-1	MR		
raTS20_Training.	2020.07	.13 20:51:5	FLAIR	3.FLAII	R		2020-11-0	4 14	2021-0	3-1	MR.		
raTS20_Training.	2020.07	.13 20:51:5	T2	4.T2			2020-11-0	4 14	2021-0	3-1	MR		
raTS20_Training.	2020.07	.13 20:51:5	SEG	5.SEG	MENTS		2020-11-0	4 14	2021-0	3-1	SEG		
			н										
🐥 A <u>d</u> d		🐣 Add All		I🕶 Edit	8 Delete	具 Associate Images	▼ ₩ ⊅	<b>Q</b> H	a .	т	•	۲	[
elected for loadi					Associa	ted serie(s):		ITAC			100		
	Type N	ame	LT1CE			0810	2 TICE/PraTE 205	NONE			_		
	IMAGE B	aTS20_Training_001	FLAIR			<4/53/0/	3 FLAIR /BraTS 20>	NONE					
	IMAGE B	raTS20 Training 001	1 T2 1			<4/100/0	)/4.T2/BraTS 20>	NONE					
	IMAGE B	aTS20 Training 001	SEG			<4/83/0/	5.SEGMENTS/BraTS	. SEGM	ENT				
	VOI V	OI ( BraTS20_Trainin	g_001)2020-11-04			<4/4/107	/*/BraTS_20>	CROP	PING_BO	Х			
									(		_		
	the statements	e association					Set series T/	AGGING	NONE		*	4.1	9
	× kemov												

Note that VOIs may also be used as Reference without a Segment. In this case the **TAGGING** for the Reference VOIs must be set to **NONE**.

### Adding a Descriptive Variable or Class for Training (Project Description)

For segmentation projects we strongly recommend adding a descriptive label to the series used for training by defining the **Project** using **Assign to Project | Group**. This description will be used to check that new data used for Prediction has the same content as that used for Training.

If a difference in the Project description (or number of studies) in Training/Prediction is detected, warning messages based on the following structure will be returned:

• • •	Message
I	Segmentation cancelled: Images in the input sample (associated series) have different description, than images used to generate weights. Please verify the following database fields for the input images: Field 'Project': Image 1: found: 1., expected: 1.t1 Image 2: found: 2., expected: 2.t1ce
	X <u>C</u> lose

For classification projects the **Group** label is required as assignment of the Class that the sample belongs to. For example, see the Amyloid PET classification Case Study: samples are in either "AD" or "YC" class (Alzheimer's disease or Young Control) and the model is trained to Predict (with probability) which of these classes a new sample belongs.

### **Data Cropping**

Another part of the data preparation consists of reducing the data volume to the relevant portion. In the brain segmentation example the image should be restricted to the brain. This process can be included in the training set definition by creating a VOI that will serve as the cropping box and associating it with the input data using the same tools as image association. The VOI must be given the Tag **CROPPING BOX** in the **Associated Series** dialog.



To achieve this, open the input image, create a suitable VOI such as a box, position it properly and save it to the database. Then select the input image in the **Series** list on the DB Load page, followed by **Associate VOI** from the same menu where the images were associated.

		🗆 Assign to Project   Group
😣 Delete	봤 Associate VOI	Associate Images     Associate VOI     Associate Mask (SEGMENT)
		Associate Whole blood     Associate Plasma     Associate Parent fraction

In the dialog window which opens select the saved VOI and activate Set Selected.

Asso	ciated serie(s):		2
Туре	Name	DBID	TAG
IMAGE	PAI1   T1CE   original contrast-enhanced T1 skull-stripped	<1221/1769/0/2.T1CE/Demo>	NONE
IMAGE	PAI1   FLAIR   original T2-FLAIR skull-stripped	<1221/1768/0/3.FLAIR/Demo>	NONE
IMAGE	PAI1   T2   original T2-weighted skull-stripped	<1221/1767/0/4.T2/Demo>	NONE
VOI	Tight-cropping-box ( PAI1 ) 2020-10-24	<1/5/33/1.T1/PAI_4_DEMO>	CROPPING BOX
× Ren	nove association	Set series TAGO	

Note that VOIs may also be used as Reference without a Segment. In this case the **TAGGING** for the Reference VOIs must be set to **NONE**.

### **Automatic Association Creation**

The neural network training process requires the preparation of a large number of samples. To make this process easier a mechanism for the automatic association of the images is available. It uses either the **Incoming Folder** method or batch assignment of Project using database queries. A folder that is regularly checked for data to be imported into the database is defined in the **DICOM** 

**Server** configuration. It takes into account information prepared in a csv file that must also be located in the incoming folder. The structure of such a csv file is illustrated below:

	A	E .	с	D	G	н	1	1	K
1	FILENAME	PTID	NAME	AGE	PROTOCOL	DIAGNOSIS	PROJECT	MODALITY	STUDYDES
2	BraTS20 Training 001 flair.nii.gz	BraTS20 Training 001	BraTS20 Training 001	60	protocol	FLAIR	3.FLAIR	MR	FLAIR
3	BraTS20 Training 001 seg.nii.gz	BraTS20 Training 001	BraTS20 Training 001	60	protocol	SEG	5.SEG [SEGMENT]	SEG	SEG
4	BraTS20 Training 001 t1.nii.gz	BraTS20 Training 001	BraTS20 Training 001	60	protocol	T1	1.T1	MR	T1
5	BraTS20 Training 001 t1ce.nii.gz	BraTS20 Training 001	BraTS20 Training 001	60	protocol	T1CE	2.T1CE	MR	T1CE
6	BraTS20 Training 001 t2.nii.gz	BraTS20 Training 001	BraTS20 Training 001	60	protocol	T2	4.T2	MR	T2
7	BraTS20 Training 002 flair.nii.gz	BraTS20 Training 002	BraTS20 Training 002	52	protocol	FLAIR	3.FLAIR	MR	FLAIR
8	BraTS20 Training 002 seg.nii.gz	BraTS20 Training 002	BraTS20 Training 002	52	protocol	SEG	5.SEG [SEGMENT]	SEG	SEG
9	BraTS20 Training 002 t1.nii.gz	BraTS20 Training 002	BraTS20 Training 002	52	protocol	T1	1.T1	MR	T1
10	BraTS20 Training 002 t1ce.nii.gz	BraTS20 Training 002	BraTS20 Training 002	52	protocol	T1CE	2.T1CE	MR	T1CE
11	BraTS20 Training 002 t2.nii.gz	BraTS20 Training 002	BraTS20 Training 002	52	protocol	T2	4.T2	MR	T2
12	BraTS20 Training 003 flair.nii.gz	BraTS20_Training_003	BraTS20 Training 003	54	protocol	FLAIR	3.FLAIR	MR	FLAIR
13	BraTS20_Training_003_seg.nii.gz	BraTS20_Training_003	BraTS20_Training_003	54	protocol	SEG	5.SEG [SEGMENT]	SEG	SEG
14	BraTS20_Training_003_t1.nii.gz	BraTS20_Training_003	BraTS20_Training_003	54	protocol	T1	1.T1	MR	T1
15	BraTS20_Training_003_t1ce.nii.gz	BraTS20_Training_003	BraTS20_Training_003	54	protocol	T1CE	2.T1CE	MR	T1CE
16	BraTS20_Training_003_t2.nii.gz	BraTS20_Training_003	BraTS20_Training_003	54	protocol	T2	4.T2	MR	T2
17	BraTS20_Training_004_flair.nii.gz	BraTS20_Training_004	BraTS20_Training_004	39	protocol	FLAIR	3.FLAIR	MR	FLAIR
18	BraTS20_Training_004_seg.nii.gz	BraTS20_Training_004	BraTS20_Training_004	39	protocol	SEG	5.SEG [SEGMENT]	SEG	SEG
19	BraTS20_Training_004_t1.nii.gz	BraTS20_Training_004	BraTS20_Training_004	39	protocol	T1	1.T1	MR	T1
20	BraTS20_Training_004_t1ce.nii.gz	BraTS20_Training_004	BraTS20_Training_004	39	protocol	T1CE	2.T1CE	MR	T1CE
21	BraTS20_Training_004_t2.nii.gz	BraTS20_Training_004	BraTS20_Training_004	39	protocol	T2	4.T2	MR	T2
22	BraTS20_Training_005_flair.nii.gz	BraTS20_Training_005	BraTS20_Training_005	68	protocol	FLAIR	3.FLAIR	MR	FLAIR
23	BraTS20_Training_005_seg.nii.gz	BraTS20_Training_005	BraTS20_Training_005	68	protocol	SEG	5.SEG [SEGMENT]	SEG	SEG
24	BraTS20_Training_005_t1.nii.gz	BraTS20_Training_005	BraTS20_Training_005	68	protocol	T1	1.T1	MR	T1
25	BraTS20_Training_005_t1ce.nii.ga	BraTS20_Training_005	BraTS20_Training_005	68	protocol	T1CE	2.T1CE	MR	T1CE
26	BraTS20_Training_005_t2.nii.gz	BraTS20_Training_005	BraTS20_Training_005	68	protocol	T2	4.T2	MR	T2
27	BraTS20_Training_006_flair.nii.gz	BraTS20_Training_006	BraTS20_Training_006	67	protocol	FLAIR	3.FLAIR	MR	FLAIR
28	BraTS20_Training_006_seg.nii.gz	BraTS20_Training_006	BraTS20_Training_006	67	protocol	SEG	5.SEG [SEGMENT]	SEG	SEG
29	BraTS20_Training_006_t1.nii.gz	BraTS20_Training_006	BraTS20_Training_006	67	protocol	T1	1.T1	MR	T1
30	BraTS20_Training_006_t1ce.nii.gz	BraTS20_Training_006	BraTS20_Training_006	67	protocol	T1CE	2.T1CE	MR	T1CE

The label defined in the **Project** column is assigned to the imported image series. Once imported, **Associate Images Automatically** can be used to generate the associations. Note that in the example, four images in each sample are used as input for the segmentation according to the requirements for the MICCAI BraTS Challenge. To establish a consistent order, numbers are used in the labels.

		Subje	dID.		71	Iodification Date	Sex			Date of	Birth		
BraTS20_Training_001		BraTS	20_Training_0	01	202	🖫 Associate Images Automatica	lly ×						
						Projects					/		
🐥 Add to "S	Selected for loading"			1×	Edit Sub	1.T1 2.T1CE			4 Associate	e Images Au	omatically	• 30 M	irge 😅 spi
						3.T2		-					
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Subject Name 5 BraTS20_Training_0 2 BraTS20_Training_0 2	Study Date Tin 020.07.27 13: 020.07.27 13:	Study. 57	BraTS20_T. BraTS20_T.	Modification 2020-07-27 13 2020-07-27 13	Last Us 2020-07 2020-07	At least 2 projects should be sele	cted.	240 240	Urgan	1514	Pmod	User1 User1	3.T2 2.T1CE
Subject Name 5 BraTS20_Training_02 BraTS20_Training_02 BraTS20_Training_02	Study Date Tin 020.07.27 13: 020.07.27 13: 020.07.27 13:	Study 57 T2 56 T1CE 54 T1	BraTS20_T BraTS20_T BraTS20_T BraTS20_T	Modification 2020-07-27 13 2020-07-27 13 2020-07-27 13	Last Us 2020-07 2020-07 2020-07	At least 2 projects should be sele Association will be created in the	cted. order of projects	240 240 240	Organ	SN	Pmod Pmod Pmod	User1 User1 User1	3.T2 2.T1CE 1.T1
Subject Name 5 BraTS20_Training_0 2 BraTS20_Training_0 2 BraTS20_Training_0 2 BraTS20_Training_0 2	Study Date         Tin           020.07.27         13:           020.07.27         13:           020.07.27         13:           020.07.27         13:           020.07.27         13:	Study 57	BraTS20_T BraTS20_T BraTS20_T BraTS20_T BraTS20_T	Modification 2020-07-27 13 2020-07-27 13 2020-07-27 13 2020-07-27 13	Last Us 2020-07 2020-07 2020-07 2020-07	At least 2 projects should be sele. Association will be created in the Process can be time consuming.	cted. order of projects	240 240 240 240	Urgan	SN	Pmod Pmod Pmod Pmod	User1 User1 User1 User1 User1	3.T2 2.T1CE 1.T1 5.SEG[SEG

Automatic association may also be used for data already in a database, when advanced database query can be used to easily batch label series. For example, when each subject in the database has only a single image series and single segment series, all image series can be given the Project "input" and all segments the Project "[SEGMENT]". These two Projects are then selected in the Associate Images Automatically dialog.

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ndfemur b6-16 n	netaphysis 0461	mdfemur	b6-16 metaphysis 2	2021-04-24 13:40:19.476							-
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# 3.2 Control Mechanism

# **Data Consistency**

A prerequisite of training a neural network is that all samples are consistent. For example, the MICCAI BraTS example described in the <u>Multichannel MRI Segmentation</u><sup>D80</sup> (brain tumor) Case Study expects four input MR images, each from a particular type of MR sequence, and reference segments identifying three tissue types for segmentation. Adding a sample with only two input MR images, or reference segments with five labels provokes a failure. Likewise, prediction using the trained neural network will fail with data of a different structure.

In a classification project, all samples must have a Class assigned or a warning that unassigned samples are present will be returned and the samples excluded from training. At least two classes must be selected for training. During prediction the use of input data with different dimensionality to the data used for training will return a warning, as will missing VOIs used as part of data reduction in the SVM architecture (see <u>Amyloid PET classification</u><sup>D94</sup> Case Study).

### **Manifest File**

To ensure consistency, PAI uses a manifest file (JSON format) to store information about the training process and history. The consistency check includes the number and type of datasets included, their descriptions, as well as the pre-processing procedures. The manifest file is based on the first valid sample ("leading sample") when the first training occurs. The manifest file is additionally associated with the weights file resulting from training of a model. If a mismatch between manifest and weights is detected when importing/retrieving these files in the Edit Learning Set dialog, a warning will be returned when additional training, or prediction, is attempted.

### **Data Checks**

The following checks are included;

• Proper loading of the associated images – checking whether all associated images are properly loaded.

- Number of dimensions the number of dimensions of the input images must be consistent with the number of dimensions of the images used for the original training. It must also be consistent with the number of dimensions supported by the chosen model. Dimensions = 2D/3D/4D data, while the matrix size or number of frames may vary between samples and should be standardized using the Box and Pixel Size preparation steps.
- Number of associated images the number of associated input images must be the same as the number of images associated in the samples used for the original training.
- Segmentation: "Project" field, serving as image description the description of the associated input images stored in the "Project" database field must be the same as in the images used for the original training
- Classification: "Group" field, class assignment the classes detected are reported before training is started and warnings are returned for samples missing a class, or if less than two classes are detected, or if the selected samples do not contain all classes detected in the learning set
- Modalities the modalities of the associated input images must be the same as for the images used for the original training.

If one of the above requirements is not met, PAI will do the following according to the workflow in use:

- · Prediction: Cancel processing and inform the user
- Re-training: Skip the sample and print the information in the log

### **Model Configuration Check**

The final control checks the settings in the user interface. Every time the user starts a training or saves the learning set, the content of the selected manifest file will be compared to the current settings in the user interface. This avoids accidental use of training parameters that differ from previous training sessions. The user is prompted to copy either all or only critical settings between manifest and learning set.

### **Control Overview**

The data and model consistency checks are performed in the background during the workflows. Issues will be automatically detected and the user guided to correct them.

# 3.3 Learning Sets

In PAI, a **Learning Set** organizes all of the necessary data and parameters for training, including the data samples, the data preparation parameters and the neural network settings.

Note that any necessary <u>data preparation</u>  $D^{40}$  should be done before creating or extending a **Leaning Set**.

### Learning Set Creation

To create a Learning Set or start a training run, select Edit Learning Set (Training) from the View + AI menu:

<b>\$</b>	Select Format and Load Image Data 🕨
	Save Image Data
×	Close All
閘	Aggregate VOI Statistics
2	Batch pipeline
Dig	Create DICOMDIR
	DICOM Query/Retrieve
E	Edit Learning Set (Training)
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۰.	Settings •
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A dialog window appears that lists the existing learning sets in the upper section. It allows new learning sets to be created and existing learning sets to be extended in the lower section.

Create Learning Se	rt																	
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BraTS20_Training	2020 07 13	20.51.57	11			2020-11-04 14:2	2021-10-18 0	MR	1	155	240	240			BI A			
BraTS20_Training	2020.07.13	20:56:38	11			2020-11-04 14:2	2021-10-18 0	MR	- 1	155	240	240			Br			
Bra1920_Training	2020 07 13	21:06:49				2020-11-04 14:2	2021-10-180	MPC		100	240	240			EI C			
Bratiszu_Training	2020.07.13	21.10.04	74			2020-11-04 14 2	2021-10-18 0	NPC NPC		100	240	240			00			
BraTE20 Training	2020.07.13	21-10-35	74			2020-11-04 14.2	2021-10-180	MP		100	240	240			De			
BraTS20 Training	2020 07 13	21.10.00	TI			2020-11-04 14.2	2021-10-18 0	MP		100	240	240			Dr			
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A text description can be appended to the Learning Set using the Description navigation button:

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Note that the description may include HTML formatting.

Existing Models can also be imported using the **Import** Learning Set button. A database containing the same samples as used for training, with same database and sample naming, is required. The

Learning Set may be imported to another database if desired. The corresponding weights and manifest files will also be imported and the Model available via the database for Prediction. This mechanism can be used to import models that were trained on different machines (or cloud computing).

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### Learning Set Content

The next step is to add training samples. First select the learning set in the **1. Learning Set** list, then select **Add Samples** at the bottom of **2. Samples**.

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A dialog window appears for selection of the input images. The flat database view

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Clear after loading	▲ ● <sup>4</sup> ⊞

and advanced filtering options are useful to list the only the image series which are first in the **Associated** list. Select all appropriate series from the filtered list and **Set Selected**. The dialog window is closed and the samples added are listed in **2. Samples**. For a quick quality control, the fusion of the sample image and the corresponding reference segment can be shown in the **Validate Sample** area by activating the **Preview** box:



The Define Test Set Samples option is used as part of model evaluation after successful training. A number of samples may be excluded from training and "held back" for model evaluation. These samples can be selected in 2. Samples and marked as Test samples using the Define Test Set Samples button. Following training, an automated model evaluation process can be started using these samples using the Evaluate Model button. Prediction will be run in R Console and each predicted segment compared to the reference associated with the sample. An average loss value for the test set samples will be returned.

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### **Architecture Selection & Settings**

In 3. Training parameters, architecture to be used and the training settings are configured.

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BraTS20_Training	2020.07.13	21:08:25 T1	2020-11-04 14:2 2021-10-18 0 MR 1 155 240	240
BraTS20_Training	2020.07.13	21:04:45 T1	2020-11-04 14:2 2021-10-18 0 MR 1 155 240	240
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The AI task (Segmentation or Classification) is selected on the left, followed by the neural network **Architecture**.

The neural network architecture is selected from the drop-down menu **Architecture**. The list corresponds to the the content of the PMOD installation */resources/pai* folder, where the neural network configurations are stored in sub-directories. See <u>Architectures included in Distribution</u><sup>D10</sup>

Note that the architectures provided by PMOD are designed to be retrainable. For example, the Multichannel Segmentation architecture was initially tested for the 4 input series, 3 segment output MICCAI BraTS example case, and was successfully reapplied for the Rat Brain Dopaminergic PET example case. This retraining is described as a Case Study later in this documentation.

The checkbox **Use GPU** allows you to choose between training using the CPU or available/compatible GPU. Note that the Classification architecture SVM can only use CPU.

The training parameters for **SEGMENTATION** are:

• **Batch Size**: This parameter defines the number of samples that are processed before the internal model parameters are updated.

- Number of Epochs: Defines the number of times that the learning algorithms processes the entire training data sets. The length of the vector of loss values recorded in the Manifest corresponds to the number of epochs. Hence multiple epochs are required to observe an evolution of the loss value through training. During training a plot of the loss value (y-axis) by epoch (x-axis) is displayed, allowing the user to gauge the progress of training (and stop training if a plateau in loss value is observed).
- Learning Rate: Defines the rate of change of the Weights. (For a Learning Set that has been used for training the final learning rate reported in the Manifest is shown)

The training parameters for **CLASSIFICATION** vary by SVM **kernel** selected (see <u>scikit-learn</u> for additional details):

- Linear: Max. iterations, Cost factor
- RBF: Max. iterations, Cost factor, Gamma (Auto, Scale, User defined)
- Sigmoid: Max. iterations, Cost factor, Gamma, Coefficient
- Poly: Max. iterations, Cost factor, Gamma, Coefficient, Degree

Kernel: Linear	▼ ( ) E	Max. iterations 32 Cost factor 1.0	*
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Average Fram	es 🔽 Ima	ge reduction: VOI statistics 🔻 4 🕨 Averaged 🗢	▲ ► Select VOIs (1,2,3:7,9)

### **Data Preparation**

al S20 Training	2020 07 13	21-116-20				-11-04 14-2	2021-10-18.0	MP	1	1 4 4 4	240	240
TS20 Training	2020.07.13	21-16-04	T1		202	0-11-04 14:2	2021-10-18 0	MR	1	155	240	240
TS20 Training	2020 07 13	21:02:35	T1		202	0-11-04 14:2	2021-10-18 0	MR	1	155	240	240
aTS20 Training	2020 07 13	21 18 06	T1		202	0-11-04 14:2	2021-10-18 0	MR	1	155	240	240
aTS20 Training	2020.07.13	21:05:42	T1		202	0-11-04 14:2	2021-10-18 0	MR	1	155	240	240
aTS20 Training	2020.07.13	21:07:52	T1		202	0-11-04 14:2	2021-10-18 0	MR	1	155	240	240
aTS20 Training	2020.07.13	21:15:23	T1		202	0-11-04 14:2	2021-10-18 0	MR	1	155	240	240
raTS20 Training	2020.07.13	20:56:58	T1		202	0-11-04 14:2	2021-10-18 0	MR	1	155	240	240
aTS20 Training	2020.07.13	21:15:04	T1		202	0-11-04 14:2	2021-10-18 0	MR	1	155	240	240
aTS20_Training	2020.07.13	21:08:25	T1		202	0-11-04 14:2	2021-10-18 0	MR	1	155	240	240
aTS20 Training	2020.07.13	21:04:45	T1		202	0-11-04 14:2	2021-10-18 0	MR	1	155	240	240
aTS20_Training	2020.07.13	21:06:31	T1		202	0-11-04 14:2	2021-10-18 0	MR	1	155	240	240
raTS20_Training	2020.07.13	21:09:50	T1		202	0-11-04 14:2	2021-10-18 0	MR	1	155	240	240
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The available data preparation steps are:

- Anonymize Samples: Anonymizes all images selected for training or workspace export (this is particularly relevant for training on cloud-computing infrastructure).
- Resize: input samples may not all have the same image matrix size, pixel size or field-of-view. Standardization is beneficial to training the neural network. This can be achieved through a combination of cropping and interpolation. Crop to VOI: Enables cropping to the associated VOI

as described in <u>Data Preparation</u><sup>140</sup>. Alternatively a fixed **Box** and **Voxel** size can be used, defining the **New matrix**. The icon retrieves the current box and voxel size from the sample selected in **2.** Samples to make a comparison between the **New matrix** and **Current matrix** easier. Useful tips can be displayed by clicking the **?** help icon.

- Gaussian Smoothing: Input image smoothing to reduce noise.
- Scale Values to: Normalization of the pixel value range by scaling according to a method selected.
- Average Frames: Reduce the dimensions of the input data by averaging the available frames.
- Gaussian Smoothing: Input image smoothing to reduce noise.
- For **Classification** additional options for **Image Reduction** are available. The tool tips provide additional information about the methods available:
- Average: average of available slices in z direction, creating a 2D image from 3D input
- MIP: calculates the maximum intensity projection in z direction, creating a 2D image
- VOI Statistics: reduces the sample to a vector by calculating a chosen statistic in associated VOI(s). A subset of the VOIs available in an associated VOI file can be defined using the Select VOIs checkbox. The VOIs to be selected can either be defined by manually entering the VOI numbers to be used or by checking the desired VOIs in the interface provided by From VOIs.

Preprocessing parameters	5. Target settings 6.	Weights & Manifest			
Anonymize samples	Box 50.0 50.0	50.0 [mm] Voxel 2.0	2.0 2.0	[mm] New matrix: 79 x 91 x 59 [mm] Current matrix: 79 x 91 x 59	

The effect of the selected Preprocessing parameters can be examined by generating a Preview of the sample after preprocessing using the Preview button:



Note that as an alternative to such pre-processing steps, the input images could be (manually) preprocessed in other PMOD tools. In this case the user must ensure that identical operations are applied to the input images before prediction.

Data preparation helps to reduces the amount of unnecessary information in the sample and standardize images which were not acquired using the same protocol.



image after preprocessing in PMOD

### **Definition of Target Settings**

The target settings, defined on 5. Target Settings, that are required depend on whether a segmentation or classification task has been defined. For segmentation tasks a list of the integer labeled segments or VOI numbers to be used must be provided if more than one segment is present in the reference. The reference segment image may contain more segments than actually required. The option Select mask values allows the integer value of the required segments to be specified by entering the label values of the target segments, separated by a "comma". The From VOI interface may be used where VOIs are available instead of or as well as segments.



For classification tasks the classes defined in the samples are reported. If the list of classes is incorrect the Project label per sample should be edited using the database interface.



#### Saving of Training Result

Two files result from a neural network training, **Weights** and **Manifest**. The **Weights** file contains the weighting given to each layer in the network. The **Manifest** file contains details of the **Learning Set** and the training process such as the samples used for training, samples used for validation (every fifth sample), number of epochs used, batch size, volume size, and the segments in the output.

The file locations are defined on the **5. Weights & Manifest** panel, and the files will be logically attached to the current learning set.

4. Preprocessing parameters 5. Target settings 6. Weigh	s & Manifest		
Weights file PMODSW-763-05 <717/1617/25177P/Centiloid>	1		Import
Manifest file PMODSW-763-05 <718/1618/25178/*/Centiloid>		• × 🕬	🖬 Import 🎕 Preview
Send email	py to FTP server. NODE_1	> PMOD@localhost (F	

In case of Additive Training, these defined files provide the starting point for further training of the neural network with new samples. If differences between the previous training described in the manifest and the current settings are detected, a warning appears and a shortcut to unify the settings is provided:

• • •	Consisten	icy check results
Consistency cf There are differ Warning(s): >> Cropping for dire for dire or dire for dire for dire for dire for dire	Box Size inconsistent: ction X (Learning Set: ' ction Y (Learning Set: ' ction Z (Learning Set: ' ction Z (Learning Set: ' ction X (Learning Set: ' ction Y (Learning Set: ' ction Z (Learning Set: '	ng Set settings and the attached manifest file. '22.0', Manifest: '24.8'). '20.0', Manifest: '24.8'). '30.0', Manifest: '38.2'). '0.8', Manifest: '0.3882'). '0.8', Manifest: '0.796').
	g set controls ac	conting to the mannest
	<u>O</u> k	<u>C</u> ancel
	Consisten	ncy check results
Consistency ch All inconsistenci	neck: es cleared.	
	§ Set controls ac           Qk	ccording to the Manifest <u>C</u> ancel

Before starting training we recommend saving the learning set in its current state using **7**. **Save** Learning Set. Save As may be used when editing an existing learning set (e.g. changing preprocessing parameters) and wishing to save it as a new copy in the database.

The **Send email** option is provided in case of training on cloud computing infrastructure. When training has been completed an email will be sent to the address provided (we suggest testing this functionality with a limited training run to ensure that your institutional firewall settings allow receipt of the email). The weights resulting from training (on cloud computing) may also be copied to an FTP server according to the settings provided.

**Export as Model** is used to save the required information to use a trained neural network for <u>Prediction</u><sup>D64</sup> in the PMOD installation *resources/pai* folder. The resulting model in the architecture/weights folder can be copied to other PMOD installations. Trained models can also be used for Prediction in the same PMOD installation without **Export as Model**, and will be available as Learning Sets in the database.

# 4 Training of Neural Network

Training of the neural network can be performed in three different ways represented by the three buttons at the bottom of the dialog window:

Train Network 🛛 🖶 Export R Workspace 🛛 👼 Train Network with Workspace

- The Train Network button directly starts the configured training locally. Depending on the checkbox Use GPU, either your CPU or GPU will be used. Note that only the samples explicitly selected (left-click, ctrl+click, shift+click) in the 2. Samples list will be used for the training, according to the settings in 3. Training Parameters and 4. Preprocessing parameters. As a result, the weights and manifest files will be updated.
- 2. Using Export R workspace <sup>b</sup><sup>62</sup>, the configured preprocessing operations are applied to the selected data and the resulting images are exported together with the training configuration in the form of a compact R workspace. The workspace can then be transferred to a more powerful processing environment for the actual training. This can either be another PMOD installation on a more powerful machine or in the cloud.
- 3. The **Train Network with Workspace** button opens a dialog window in order to load a previously exported R workspace and starts the training locally.

The process is described in detail below.

### Deployment

After completion of the training, the resulting **Weights** and **Manifest** files are combined with the Learning Set definition (\*.aiset file) to form the trained model. The trained model can be used in the same PMOD installation used for training by selecting the Learning Set from the database where AI functionality is available in View and Segment tools. The trained model can also be transferred to other PMOD installations for prediction. This is most easily achieved by using Export as Model and copying the resulting files from the PMOD installation folder *resources/pai/architecture/weights* (e.g. *C:\Pmod4.3\resources\pai\unet\_002\weights\IXI\_Parcellation\*) to another PMOD installation. The paths listed below in the \*.aiset file must be manually generalized:

- MODEL\_PY\_FILE
- MANIFEST\_FILE
- WEIGHTS\_FILE

The path in the initial \*.aiset file will be specific to the machine used for model training and should be adapted. E.g.:

- MANIFEST\_FILE=C:
  - \Pmod4.3\resources\pai\unet\_002\weights\IXI\_Parcellation\IXI\_Parcellation.json
- becomes:

• MANIFEST\_FILE=.\resources\pai\unet\_002\weights\IXI\_Parcellation\IXI\_Parcellation.json It is also possible to export the Learning Set from the database **Create Learning Set** dialog. This Learning Set can be **Imported** into a database in another PMOD installation.

### Recommendations

On typical personal computers local training is only recommended for tests with a limited amount of data. Performance may be acceptable with data that has a small matrix size (e.g. 50 x 50 x 50 for cropped PET data) and low number of input series for multichannel segmentation (e.g. 1 or 2). The total time required for training cannot be estimated. While training is running you will see a significant load on CPU/GPU and a plot of loss value by epoch in PMOD's R Console. Even for powerful workstations, training with hundreds of samples may take many hours. Training on a cloud computing infrastructure with virtual machines accessing several GPUs is likely to be more time- and cost-efficient.

It is advisable to always perform a small "infrastructure check" training before launching training with your full data set and many epochs. This can be performed using the minimum requirement for input samples (2 samples), a batch size of 1 and a low number of epochs (1 is acceptable, but 2 or 3 will reveal changes in the loss value in the Manifest). If the input data has a high matrix size (e.g. 200 x 200 x 200) and/or there are multiple input series in the sample, the data volume could

be reduced by using a larger pixel size for this training test (e.g.  $2 \times 2 \times 2 \times 2$  mm instead of planned 1 x 1 x 1 mm).

# **Training Progress and Output**

For data prepared on your local system, training is started by selecting the desired samples in the **Learning Set** and clicking **Train Network**:

Subject Name	Study Date	Time	Study Description	Series Description	Modification	Last Use	Mod	nt	nz.	nx	ny	Organ	SN
remur_b6-16	2021.04.23	22:56:35	mdfemur_b6-16_meta_	moremur_b6-16_metap	2021-04-23 22:5	2021-04-27 1.	PT	1	1	608	504	a constant	10000
femur_b6-16	2021.04.23	22:56:36	mdfemur_b6-16_meta.	md emur_b6-16_metap.	2021-04-23 22:5	2021-04-27 1.	PT	1	1	608	504		
femur_b6-16	2021.04.23	22:56:36	mdfemur_b6-16_meta	md emur_b6-16_metap.	2021-04-23 22:5	2021-04-27 1	PT	1	1	608	504		
femur_b6-16	2021.04.23	22:56:37	mdfemur_b6-16_meta_	md'emur_b6-16_metap.	2021-04-23 22:5	2021-04-27 1.	PT	1	1	608	504		
femur_b6-16	2021.04.23	22:56:37	mdfemur_b6-16_meta.	md emur_b6-16_metap.	2021-04-23 22:5	2021-04-27 1.	. PT	1	1	608	504		
femur_b6-16	2021.04.23	22:56:37	mdfemur_b6-16_meta.	md emur_b6-16_metap.	2021-04-23 22:5	2021-04-27 1.	. PT	1	1	608	504		
emur_b6-16	2021.04.23	22.56.38	mdfemur_b6-16_meta_	md'emur_b6-16_metap.	2021-04-23 22 5	2021-04-27 1.	PT	1	1	608	504		
femur_b6-16	2021.04.23	22:56:38	mdfemur_b6-16_meta_	md emur_b6-16_metap.	2021-04-23 22:5	2021-04-27 1.	. PT	1	1	608	504		
femur_b6-16	2021.04.23	22:56:38	mdfemur_b6-16_meta_	md emur_b6-16_metap	2021-04-23 22:5	2021-04-27 1.	. PT	1	1	608	504		
femur_b6-16	2021.04.23	22:56:39	mdfemur_b6-16_meta_	md'emur_b6-16_metap	2021-04-23 22.5	2021-04-27 1	PT	1	1	608	504		
emur_b6-16	2021.04.23	22.56:39	mdfemur_b6-16_meta_	md emur_b6-16_metap.	2021-04-23 22:5	2021-04-27 1.	PT	1	1	608	504		
lemur b6-16	2021.04.23	22:56:39	mdfemur b6-16 meta.	md emur_b6-16_metap.	. 2021-04-23 22:5	2021-04-27 1	. PT	1	1	608	504		
femur_b6-16	2021.04.23	22:56:40	mdfemur_b6-16_meta.	mdfemur_b6-16_metap.	2021-04-23 22:5	2021-04-27 1	PT	1	1	608	504		
lemur b6-16	2021.04.23	22:56:40	mdfemur b6-16 meta.	mdfemur b6-16 metao.	2021-04-23 22:5	2021-04-27 1.	. PT	1	1	608	504		
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Preprocessing p	arameters 5	. Target settin	ngs 6. Weights & Man	ifest									
Anonymize san	nples	Box 17	2.0 1.0 Imm	Ward 0.055	5 10 Im	vml New	makir 64	v 64 v					

The **RConsole** opens and the Execution test and PAI diagnostics test are performed. If the tests are passed the selected samples (all input series and associated Segments) are loaded:

**π.pmod** 

Output	Ba 🗙
Type 'q()' to quit R.	-
Loading default settings Loaded.	
Package doBy not loaded.	
Package psych not loaded.	
Package UsingR not loaded.	
Package lawstat not loaded.	
Package tseries not loaded.	
Package np not loaded.	
Package openair not loaded.	
Package Hmisc not loaded.	
Package car not loaded.	
Package phia not loaded.	
Package compare not loaded.	
Package reshape not loaded.	
Package Cairo not loaded.	
Package pROC not loaded.	
Package gimnet not loaded.	
Package mcr not loaded.	
Package tseries not loaded.	
Execution test Passed.	=
Pmod PAI diagnostics test [1] 3.8	
Passed.	
Loading image data: 1/1 inputImages_1_1 Loaded.	
Loading image data: 1/1 maskImages_1_1 Loaded.	
Loading image data: 1/1 inputImages_2_1 Loaded.	
Loading image data: 1/1 maskImages_2_1 Loaded.	
Loading image data: 1/1 inputImages_3_1 Loaded.	
Loading image data: 1/1 maskImages_3_1 Loaded.	
Loading image data: 1/1 inputImages_4_1 Loaded.	
Loading image data: 1/1 maskImages_4_1 Loaded.	
-	
Rlog	🗈 🗙

During training the loss value is plotted with each epoch. Note that the loss value depends on the architecture selected and large changes on the y-axis are possible. In the example shown the loss value is 1 - Dice Coefficient for training of the Multichannel Segmentation architecture with <u>rat brain</u> <u>dopaminergic PET<sup>D</sup></u><sup>76</sup> data as described in our Case Study. At the start of training the loss value is 1, and successful training results in a reduction of the loss value towards zero:



Once training is complete a dialog appears to save the **Weights**. They can be saved to the database or file system (the same database as the **Learning Set** is recommended):

inter name Learning_we	cular_ML1	V Data	The second se			million (2) (2)	Second and the second	100
inter name Learning_we		i outo	Base/ *.h5 ]		× Clear	Filter 🥸 R	etresh Query	9
	eights run9				×	tac	h to <mark>Subjec</mark> t	(Serie
Subject Name *			Didh Data:		r			
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Component name	Subject name	Subject id	Series descr.	Modify time	LastUse	File size	Sex	Birt
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weights.57-0.206-05.115	-TALLEARINING W	ALLEARINING		2021-04-27 10.2	2021-04-27 1	100		
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	paces a dante m	A LEMANNED		2021042110.0	202104271	1000		
Learning weights	~[AI LEARNING SE	AI LEARNING		2021-04-27 16:0	2021-04-27 1	4819320		
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Learning_weights weights.50-0.000125.h5 weights.50-0.000125.h5	~[AI LEARNING SE ~[AI LEARNING W ~[AI LEARNING W	AI LEARNING AI LEARNING AI LEARNING		2021-04-27 16:0 2021-04-27 12:5 2021-04-27 12:4	2021-04-27 1 2021-04-27 1 2021-04-27 1	4819320 156 156		

Training may also be stopped by the user. This is useful when training appears to be unsuccessful with no improvement in the loss value or when training has been particularly successful and a plateau in loss value has been achieved with many epochs remaining:



A confirmation dialog in the R Console confirms that learning was completed and the components saved. The R Console can be closed:



The Weights and Manifest are now attached to the Learning Set:

Weights file	docu-test-1 <10	18/1818/4618/*/RAT_D	OPA_ML2>				
Manifest file	docu-test-1 <10	19/1819/4619/*/RAT_D	OPA_ML2>				
Sender	nail		Conv	to ETP server NOD	. A	-	
Senden	nan		_ Copy	to FIP Server, NODI		- 4 P G	2 × F

Details of the training are recorded in the Manifest. It can be reviewed using the **Preview** function on **6. Weights & Manifest**:

Create Learning S	📆 Manifest JSON File Preview				×		
1. Learning Set [1]:	{ "TrainingSessions": [				<b>A</b>		
	(						
Component name	"Info": {					0	
Docu-3	"SoftwareConfig" /	39.					
	"PMODVersion": "4 301"						
	"PythonVersion": "3.8.6"						
	"TFVersion": "2.4.0".						
	"RVersion": "4.1.1"						
	1.						
Create Learning	"HardwareConfig": {						
	"ComputingUnit": "CPU",					nonononono	222202020
2. Samples	"RAMgb": 23.9709						
	}						-
Subject Name	3.					nx	ny
104DTBZ^ROI1	"LearningParameters": {					0 59	49
104DTBZ^ROI2	"Cropping": true,					0 59	49
106DTBZ^ROI1	"BoxSize". [					0 59	49
106DTBZ*ROI2	26.0,					0 59	45
107MP*ROI2	28.0					0 59	41
108MP*ROI1	38.0					0 59	45
100MP/R012	"Pivel Size" [					0 59	43
110MPAROI1	12					0 59	43
TTOM ROTT	12					0 35	
	12						
Add samples	1						
- Territoria	"VOICropping": false,						
3 Training parame	"Model": "Multichannel Segmentati	on",				5	
5. Training parame	"NormalizationType": 4,						
SEGMENTATION	"AverageFrames": false,						
	"ReduceDimensions": false,						
Batch size 4	"ReduceDimensionType": "Average	e",					
	"ReductionVOIsStatistic": "Average	d",					
4. Preprocessing	"Reduction VOIsSelection" false,						
	Baichoize 4,				•		
	X Clar			R Conv to Clinboard			
Weights file d	X 200					E.	_
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Train Networ	k 📑 Export R Workspace	Train Network with Workspace	Evaluate Model	0	7. Save Lear	ning Set	Save
					12 N. 1		

# **Additive Training**

The best results are achieved by training in a single session with the maximum amount of data available. However, in a situation where the initial number of samples is limited and new samples will become available on a regular basis it is possible to try additive training. For example, where 50 samples are available at the start of a project and 10 new samples will be preprocessed every two weeks.

Additive training is achieved by adding the new samples to your existing Learning Set, selecting a subset of the total Learning Set (a combination of existing samples and new samples is recommended, e.g. select the 10 new samples and 10 existing samples), then launching **Train Network** based on the existing **Weights** and **Manifest** (identified on **5. Weights & Manifest**).

Weights file	docu-test-1 <1018/18	18/4618/*/RAT_DOP	\_ML2>			
Manifest file	docu-test-1 <1019/18	19/4619/*/RAT_DOP	_ML2>			
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If differences between the previous training described in the manifest and the current settings are detected, a warning appears and a shortcut to unify the settings is provided:

• •	Con	sistency check	k results
Consistence	check:		
There are di	fferences between	Learning Set set	ttings and the attached manifest file.
Warning(s):			
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for o	direction Y (Learnin	g Set: '20.0', Ma	anifest: '24.8').
for	lirection Z (Learnin	g Set: '30.0', Ma	anifest: '38.2').
>> Voxel for o	spacing inconsister direction X (Learnin	it: g Set: '0.8'. Man	nifest: '0.3882').
for o	lirection Y (Learning	g Set: '0.8', Man	nifest: '0.3882').
for o	firection Z (Learning	g Set: '0.8', Man	iifest: '0.796').
	§ Set cont	trols according to	o the Manifest
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## **Evaluation of the Model**

Once the model has been trained, a subset of samples in 2. Samples can be designated as Test Set samples and used as an additional evaluation of the model. Samples can be labeled as Test Set prior to training so that they are excluded for this use in evaluation.

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Component name	Subject name	Subj	ect id Series de	scr. 💌 Modify time	LastUse (	Jser Arch	P	roject	Group					
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The performance of the model on the Test Set can be calculated using Evaluate Model:

-	ubject Name	Study Date	Time	Study Description	Series Description	Modification	LastUs
	04DTBZ*ROI2	2017.03.07	09:17:49	EARLY_DTBZ	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10
D -	06DTBZ*ROI1	2017.03.08	09:10:29	EARLY_DTBZ	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10
	06DTBZ*ROI2	2017.03.08	09:10:29	EARLY_DTBZ	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10
	07MP^ROI2	2017.03.10	09:19:03	EARLY_MP	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10
	08MP^ROI1	2017.03.10	09:22:00	EARLY_MP	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10
	08MP^ROI2	2017.03.10	09:22:00	EARLY_MP	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10
1001	IPAROI2	2017.03.10	15:18:32	EARLY_MP	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10
110N	MPAROI1	2017.03.10	15:20:05	EARLY_MP	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10
1101	/IPAROI2	2017.03.10	15:20:05	EARLY_MP	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10
(							
. Tra SEG	aining paramete MENTATION	ers ▼ 4   ► Archi Number of epoch	itecture: Mull	tichannel Segmentation	▼ 4   ▶ ? □ Use	GPU	
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Prediction will be run in R Console and each predicted segment compared to the reference associated with the sample. An average loss value for the test set samples will be returned.

Confirma	ition	;
	Model evaluation finished succe Evaluation result: 0.10405	sfully.
?	Cost function used: Dice Description: value between 0 an	id 1, 0 - means the best result.
	Do you want to close Rconsole?	,
	✓ <u>Y</u> es	× No

# 4.1 Exporting an R workspace

### **Sample Selection**

When exporting an R workspace for external training the selection in the **2**. **Samples** list is relevant. Only the selected samples will be exported and used for the training. An error message will be shown if only a single sample is selected during the export.

Subject Name	Study Date	Time	Study Description	Series Description	Modification	LastUse
112DTBZ^ROI1	2017.03.16	13:15:30	EARLY_DTBZ	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10-1
112DTBZ^ROI2	2017.03.16	13:15:30	EARLY_DTBZ	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10-1
121RACAROI2	2017.03.28	14:56:37	EARLY_RAC	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10-1
122RAC^ROI1	2017.03.28	15:00:35	EARLY_RAC	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10-1
122RAC^ROI2	2017.03.28	15:00:35	EARLY_RAC	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10-1
123RACAROI2	2017.04.21	09:03:24	EARLY_RAC	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10-1
124RAC^ROI2	2017.04.21	09:08:05	EARLY_RAC	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10-1
125RACAROI1	2017.04.21	09:11:50	EARLY_RAC	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10-1
125RACAROI2	2017.04.21	09:11:50	EARLY_RAC	[CROP][Avg Frm (T)]	2021-01-31 15:5	2021-10-1
•				I		
A. Training parametric SEGMENTATION     Batch size 4     A. Preprocessing p	ers • 4   F Archit Number of epoch: arameters 5.	tecture: Mult s 60 Le Target settir	tichannel Segmentation arming rate 0.005 4 ngs 6. Weights & M	▼ 4   ▶ ? □ Use Manifest Learning Rate 1.0 anifest	GPU JE-4	
A. Training parameter     SEGMENTATION     Batch size 4     Preprocessing p     Anonymize sar     Resize Cr     Gaussian Smc	ers	ecture: Mult s 60 Le Target settin	tichannel Segmentation arming rate 0.005 4 ngs 6. Weights & M o you want to start Works	A I P ? Use Manifest Learning Rate 1.  anifest space export with [9] sampl X No	GPU )E-4 796 [m [m] b of samp	m] l m] Cui

Note that the **Anonymize samples** option is useful when exporting an R workspace, ensuring that no subject information will be transferred to another workstation or cloud-computing infrastructure:

Anonymize samples											
Resize Crop to VOI	?	Box	24.8	24.8	38.2	[mm]	Voxel	0.3882	0.3882	0.796	[mm
	<u>+</u>	-		-	-	[mm]	-	-	- 1	-	[mm
Gaussian Smoothing	.0 8.0	8.0	(mi	m] 🗹	Scale Val	lues to: Z	-Score		-	4   ⊨ of s	sample

### **R Workspace Export**

The **EXPORT** button opens the PMOD R Console, executes the preparations including data preprocessing, and opens a dialog window for saving the workspace. Typically **Save to File System** will be used to make it easily available for transfer to a different training environment:

Data MR. Relaxometry ? General ANXA ? ?   Commands [ <ch+enter> &gt; execute Vorkspace   Commands [<ch+enter> &gt; execute block, <ch+b> &gt; execute block, <ch+upidown <="" td="">   Commands [<ch+enter> &gt; execute block, <ch+b> &gt; execute block, <ch+upidown <="" td="">   Commands [<ch+enter> &gt; execute block, <ch+b> &gt; execute block, <ch+upidown <="" td="">   Commands [<ch+enter> &gt; execute block, <ch+b> &gt; execute block, <ch+upidown <="" td="">   Commands [<ch+enter> &gt; execute block, <ch+b> &gt; execute block, <ch+upidown <="" td="">   Commands Commands Commands Components    Subject ID  Output    Bith Date:   Subject ID    Component name   Components    Components    Components    Components    Components       V      V      Select all X       Data Base            V                                                                                                               <th>Rconsole</th><th>cute 🗐 Block 🗹 Auto-clear 😕 🗌</th><th></th><th>2</th><th>3</th></ch+upidown></ch+b></ch+enter></ch+upidown></ch+b></ch+enter></ch+upidown></ch+b></ch+enter></ch+upidown></ch+b></ch+enter></ch+upidown></ch+b></ch+enter></ch+enter>	Rconsole	cute 🗐 Block 🗹 Auto-clear 😕 🗌		2	3
Image: Seve as R WORKSPACE       X       mage: S(i) <- paste(masking:1,sep=');         DATABASE       Image: S(i) <- paste(masking:1,sep=');       mage: S(i) <- paste(masking:1,sep=');         Enter name       example: R-workspace       X       Notabase/ * RData ]       X         Subject Name       Birth Date:       Image: S(i) <- paste(masking:1,sep=');       mage: S(i) <- paste(masking:1,sep=');         Subject ID       Modification:       Image: S(i) <- paste(masking:1,sep=');       Ntsample: 1:         Component name       Image: S(i) <- paste(masking:1,sep=');       Ntsample: 1:         Component name       Image: S(i) <- paste(masking:1,sep=');       Ntsample: 1:         Components       Image: S(i) <- paste(masking:1,sep=');       Ntsample: 1:         Vision:       Image: S(i) <- paste(masking:1,sep=');       Ntsample: 1:         Subject ID       Modification:       Image: 1:       Image: 1:         Components       Image: 1:       Image: 1:       Image: 1:         Vision:       Image: 1:       Image: 1:       Image: 1:         Vision: <td< th=""><th>Data = Matrix = Measure = Workspace</th><th></th><th>plication MR Relaxometry • 7</th><th>General ANOVA T 7 X T T</th><th></th></td<>	Data = Matrix = Measure = Workspace		plication MR Relaxometry • 7	General ANOVA T 7 X T T	
Enter name example R-workspace	R Save as R WORKSPACE DATABASE D Prinod マイ	[ DataBase/*RData ]	× Clear Filter & Refresh Query 9	× mages5)(i) <- paste('maskimg'.i.sep=''); ● mages6);	-
✓ Seject all X ◎ Delete @ PE Export Regame     ✓ Seject all X ◎ Delete @ PE Export Regame	Enter name example R-workspace Subject Name  Subject ID Component name Current Series Components	Birth Date: : : Modification: : : Last Use: : :	X Attach to Subject (Serier	<ul> <li>mages5(ji) &lt;- paste('maskimg',i.sep=');</li> <li>st(sample1=maskimages1,sample2=maskimages2,sample2;</li> <li>j;</li> <li>k;</li> <li>k;</li></ul>	
hasimages.masimages.vray),	✓ Selectall × 🔕 Delete 🗐♦∰ Export	Regame	🕞 Save to File System	); E); Y ← pm.ai.convertImageToArray(inputImages); i ← pm.ai.convertImageToArray(maskImages); tay ← pm.ai.convertIMaskToChannels(maskImagesArray, cov[] i.getImagesID(inputImages); haskImages,maskImagesArray);	

# Training with an R Workspace

When an exported R Workspace from one PMOD installation is used for training in another installation using **Train Network with Workspace**, the **Architecture** settings may still be adjusted. Weights and Manifest files may also be selected/imported to start Additive Learning.

Train Network with Workspace				>
Architecture: Multichannel Segmentation Batch size 1 Number of epochs 1	Use GPU Learning rate 1.0E-5			Set from loaded Workspace
Weights file				🖬 Import 🖬 Import 🎕 Preview
Send email	Copy to FTP server. NODE_1	•   +   + @ >		
	QK		Cancel	

Following loading of the R Workspace, training proceeds as described  $\underline{above}^{D 55}$ .

# 5 Use of Trained Neural Network for Prediction

Trained networks can be used in **View** and **Segment (PSEG)** tools for the segmentation or classification of input images with the same characteristics as the training images. Please apply the same <u>preparations</u><sup>D40</sup> including associations and cropping VOI definition as for the training samples.

## Al-based segmentation in View tool

A shortcut to the **Segmentation** interface with **MACHINE LEARNING** segmentation method is available on the **View** tab for the data currently loaded. Alternatively the **Segmentation** tool may be opened from the **Image Processing Tools** (for segment generation) or **VOI Tools** (for direct VOI generation without segment) and **MACHINE LEARNING** selected from the list of segmentation methods on the left:



25 Segmentation	×
Image: Constraint of the state of the s	VINC
Ovr      MACHINE LEARNING     MACHINE LEARNING	Settings Histogram  Additional results:  Create VOI Template / Mask Create VOI Template / Mask All calculations are repeated after the tool dialog is accepted

Following the selection of the **MACHINE LEARNING** segmentation method the trained model should be selected from the **Select Model** list. Trained models available in resources/pai are shown with naming according to the weights folder and architecture used.

Additionally, self-trained models saved in the database can be selected using the AI Learning Set browser:

Select DB element	nts: AI LEARNING SET							×
DATABASE	Trabecular_ML1	▼ 4 Þ [ Data	Base/ *.aiSet ]		× Cle	ar Filte	r 🕴 Refrest	Query 🤗 🕤
Subject Name Subject ID Component na	* * Current Series	Birth Date: Modification: Last Use:			4 4		▼ Prj *	<ul> <li>•</li> <li>•</li> <li>•</li> </ul>
Component name LearningSet1	e Subject name ~[AI LEARNING SE	Subject id AI LEARNING	Series descr.	<b>▼</b> N 202	lodify tim 1-04-27 1	e 1 2:0 2	Last Use 2021-04-27 1	File size 4449
✓ Seject all X	Delete 😂 🏘 🖬	Export Renam	ie				😐 Set fro	m File System
					[	<u>C</u> ance	I	

Further information about the trained model selected is available in the model help:



Note that the available text shown is controlled by the user for self-trained models during creation of the Learning Set (and architecture Python files if applicable).

The dimensions of input data to a model for prediction must match the dimensions used for training of the model. The **Split Slices** and **Split Frames** options appear below **Select Model** when the dimensions of the input data for prediction are greater than those used for training. Split Frames reduces 4D data to a series of 3D images to be segmented sequentially. Likewise Split Slices reduces 3D data to a series of 2D images. Following prediction for each split image the segment is rebuilt and Segments/VOIs returned according to the dimensions of the input data. In case Split Frames/Slices are not correctly selected for use of a model, and error will be returned that the dimensions of the input data do not match the data used for training.

### **Al-based segmentation in Pipeline Processing**

The **MACHINE LEARNING** segmentation method is also available in the **Segmentation** image processing tool within **Pipeline Processing**. This makes batch processing with AI-based segmentation available.

& Batch Pipeline	
	0 🕅
List of Input studies List of Pipelines	
Database INPUT format settings      Ino loading operations (Applied to all input images)	EATCH PIPELINE
PAIS   ex vivo CT   section of femur - low res <301/301/0/IPAI_4_DEMO>	Segmentation × •
PA/6   ex vivo CT   section of femur - full res <301/302/0//PAI_4_DEMO>	Segmentation 7 4 5 9 ? Pretty
💣 Set files 🔹 Add files 🗙 Remove 🔺 属 Save 😂 Load 🔺 ave images and Non-image Results as:	Use VO(s) Use VOLUME OF INTEREST associated in Database by "Associate" function Use VO(s) No VOLUME OF INTEREST selected MACHINE LEARNING  V() P
No operation      Replace selected      Replace by algorithm (Anonymization)	Split slices Split frames
(NO SAVING ADDITIONAL OPERATION)	Max number of clusters     Minimal cluster size [pid]
Images and Non-image Results O Only Images O Only Non-image Results	
Output Format  Database ▲ 4   Cutput Format Database ▲ 4   P  Cutput Format  Database ▲ 4   P  Cutput Format  Cutput Format  Cutput Format  Cutput Format  Database ▲ 4   P  Cutput Format  Database ▲ 4   P  Cutput Format  Cutput Format  Database ▲ 4   P  Cutput Format  Database  Database ▲ 4   P  Cutput Format  Database  Data	La_ Cpit Frames = + _ K X Save _ Save Processing 😅 Load Process
Start Processing	0 1_d_1 × 0

As for interactive segmentation, the model to be used must be selected from the list. Note that **Split Slices** and **Split Frames** must be selected appropriately for the model and input data selected.

Note that the options to Use VOIs, control Max number of clusters or Minimal cluster size, and Separate Segments in Frames, are not applicable when MACHINE LEARNING is used.

# Al-based classification in View tool

A shortcut to AI-based classification is available on the View tab for the data currently loaded.

MIP	Merge series ↓ 417Z Split Slices ↓ 127 Slice Alignment ↓ Save: ■ DICOM ▲ □ All	•
8	E Classification	?
	Crop:         Size [mm]:         I           420.0         4         ▶         320.0         4         ▶         750.0         4         ▶           Interpolate         2.0         2.0         [mm]         [mm]	
Protocol / 🖉 Report 🗹 Synchronize Iayout / 2 🔺 💌 🝙 🍸 🛓 🚺	▶ <u>V</u> OIs	

The model to be used must be selected from the menu.



Self-trained models may be selected using the AI Learning Set browser.

Additional information about the model is available using the PAI Model Help button.

📆 PAI Model help		×
Model name: AmyloidPET-SVM		
PMOD version: 4.301		
Last training date: 2021-09-22 15:25:56		
Description: Model trained on linear kernel to classi	fy human brain amyloid PET images as eithe	r AD (Alzheimerâ⊡⊐s disease) or YC (Young Control).
Disclaimer: This model was developed by PMOD Te Training was performed using a specific homogene data acquired with different parameters or source ha risk and we strongly recommend careful testing on y	chnologies as a working example for demon ous data set and there is no guarantee that th ardware. Use of the model for projects involvir your data and/or additive training using your o	stration of the PAI functionality. ne model will perform well for ng quantification is at your own wn data.
Input sample description:		
Matrix size: 80 x 80 x 1 x 1		
Voxel spacing: 2.0 x 2.0 x 2.0		
Associated images:		
[image 1] modality: PT		
Results:		
Predicted classes: AD, YC		
Architecture used: Classification SVM		
Support vector machine architecture intented for class	sification tasks.	
•		
× Close	Clipboard	🖨 Print

Display of the R Console during classification is optional and is toggled using the **Show R console** checkbox.

The result of classification is shown in tabulated form below the Classification shortcut.



See the Case Study for <u>Human Amyloid PET Classification</u><sup>194</sup> for further information.

### Al-based segmentation in Segment tool

### Image Loading

PSEG does not support the loading of multiple input image series. This is not necessary for Albased segmentation. In case of a segmentation requiring multiple input images, use the reference for the association list (e.g. T1 MR for the <u>BraTS Tumor Segmentation</u><sup> $\Box$  80</sup> case study).

Subject N	lame	Study Date	Time	Study Description	Series Description	Modification	LastUse	Mod	nt	nz
raTS20_	Training	2020.07.13	20:51:57	T1	j.	2020-11-04 14:2	2021-10-18 1	MR	1	15
raTS20_	Training	2020.07.13	20:51:58	T1CE		2020-11-04 14:2	2021-10-18 1	MR	1	1
raTS20_	Training	2020.07.13	20:51:59	FLAIR		2020-11-04 14:2	2021-10-18 1	MR	1	1
raTS20_	Training	2020.07.13	20:51:57	SEG		2020-11-04 14:2	2021-10-18 1	SEG	1	1
raTS20	Training	2020 07 12	20:51:59	TO		2020 11 04 14-2	2021 10 19 1	ND	1	4
S Asso	ciated serie	e(s):	20.51.00	12		2020-11-04 14.2	2021-10-10 1	MIX		
Type	ciated serie	e(s):	20.01.00	12		DB ID	2021-10-10 1	TAG		
Type IMAGE	Name BraTS20	e(s):	T1CE	12		DB ID <4/26/0/*/BraTS_20>	2021-10-10 1	TAG		1
Type IMAGE IMAGE	Name BraTS20 BraTS20	e(s): Training_001	T1CE   FLAIR	12		DB ID <4/26/0/*/BraTS_20> <4/53/0/*/BraTS_20>	2021-10-10 1	TAG		
Type IMAGE IMAGE IMAGE	Name BraTS20 BraTS20 BraTS20	e(s): Training_001  Training_001  Training_001	T1CE   FLAIR   T2	12		DB ID <4/26/0/*/BraTS_20> <4/53/0/*/BraTS_20>	> > >>	TAG NONE NONE NONE		
Type IMAGE IMAGE IMAGE IMAGE IMAGE	Name BraTS20 BraTS20 BraTS20 BraTS20 BraTS20	e(s): Training_001  Training_001  Training_001  Training_001	T1CE   FLAIR   T2   SEG			DB ID <4/26/0/*/BraTS_20> <4/53/0/*/BraTS_20> <4/100/0/*/BraTS_20> <4/83/0/*/BraTS_20>	> > > >	TAG NONE NONE NONE SEGMEN	T	

Cropping or interpolation in the lower right are generally not required for the AI-based segmentation workflow. This will be done by the model depending on the preprocessing parameters used in the Learning Set. Cropping may be used when the image field-of-view is clearly larger than the scope of the model. For example, an MR image of the human head including neck may be cropped to brain only for the IXI Parcellation model (human brain MR deep nuclei segmentation)<sup>[h]91</sup>, see Case Study). **Masking** is not required for AI-based segmentation. We recommend using the shortcut AI Segmentation to skip to the next step in the workflow:



## **Model Selection**

On the MASK page set the segmentation method is set to MACHINE LEARNING.



Choose the appropriate model for the segmentation task using the menu Select Model.

		MACHINE LEARNING				•	٩	•
	BRATS	Tumor Detection	-	•	?	]		
	Sho	w R console it slices		IRI My Trabec BRATS XI Pari IRI Hu Rat Bra	vocar cular S Tur cella umar ain D	diun ML nor E tion h Myc	n 2D Dete ocari mine	ction dium ergic Pl
• • ?	•	▶ <u>s</u>	egmenta	ation				

Self-trained models may be selected using the AI Learning Set browser. Note that a description of the model can be retrieved using the **PAI Model Help** button:

, PAI Model help		
Model name: BRATS Tumor Detection		
PMOD version: 4 201		
Last training date: 10.09.2020		
Description: Model trained for multichann Expects 1. T1w, 2. Gd-enhanced T1w, 3. F	el (4) skull-stripped 3D MR input and output o "LAIR, 4. T2w.	of segments for three tumor tissue classes
Disclaimer: This model was developed by Training was performed using a specific h data acquired with different parameters or risk and we strongly recommend careful t	y PMOD Technologies as a working example nomogeneous data set and there is no guara source hardware. Use of the model for proje esting on your data and/or additive training us	for demonstration of the PAI functionality. Intee that the model will perform well for ects involving quantification is at your own sing your own data.
Input sample description:		
Matrix size: 128 x 128 x 128 x 1		
Voxel spacing: 1.2 x 1.41 x 1.15		
Associated images:		
[image 1] modality: MR, label: "1.T1"		
[image 2] modality: MR, label: "2.T1CE"		
[image 3] modality: MR, label: "3.FLAIR"		
[Image 4] modality: MR, Iabel: 4.12		
Results:		
Number of predicted segments: 3		
Final training loss value: 0.2103		
Final validation loss value: 0.3531		
Architecture used: Multichannel Segmen	tation	
A modified U-net architecture applicable fr	or 3D image data, intended for image segme	ntation.
The number of input channels is automati	ically adjusted to the images (associated) pe	r sample, the number of
predicted segments in the output depend	s on the Target Settings defined in the Create	Learning Set interface.
N. Olean	Ro. Olinhoard	/R point

Note that the available text shown is controlled by the user for self-trained models during creation of the Learning Set (and architecture Python files if applicable).

Displaying the R Console during prediction is optional, according to the checkbox selection **Show R Console**.

The dimensions of input data to a model for prediction must match the dimensions used for training of the model. The **Split Slices** and **Split Frames** options appear below **Select Model** when the dimensions of the input data for prediction are greater than those used for training. Split Frames reduces 4D data to a series of 3D images to be segmented sequentially. Likewise Split Slices reduces 3D data to a series of 2D images. Following prediction for each split image the segment is rebuilt and Segments/VOIs returned according to the dimensions of the input data. In case Split Frames/Slices are not correctly selected for use of a model, and error will be returned that the dimensions of the input data do not match the data used for training.

Trabecular ML	~	•	?
Show R console			
Split slices			

### Segmentation

Use the **Segmentation** workflow button to start prediction. The input data is transferred to the R Console and processed using the selected model. If **Show R console** was enabled, the resulting label maps are displayed on the image tab of the R Console:



The segmentation result is overlaid on the input series on the **SEGMENTS** page (once the R Console has been closed).



The segments are automatically converted into numbered VOIs. The interactive VOI labeling function is still available by right-clicking a segment in the image. This opens a dialog window which allows a VOI name to be selected from a list, or simply entered. Note that the VOI name from list functionality is also available via VOI Properties.

The segments label map itself can be saved using the save button in the taskbar to the right.

Please refer to the PSEG User Guide for details of the general segmentation functionality.

At the end of processing the protocol can be saved using **Save Protocol**. Using Load Protocol the workflow can be retrieved and re-executed. Additionally, the input series can be changed and the protocol used for analysis of the next sample. Protocols also provide access to batch processing.

### **Batch Processing**


A saved protocol is required to start batch processing. This saved protocol provides the settings that will be used for the workflow across all samples. A set of saved protocols can be loaded using **Set Files**, or more commonly a single protocol describing the desired workflow can be cloned for all input samples using **Clone Protocols**.

IL PSEG Batch Processing: Define List of Protocol Files	×
test-for-docu-1 ( BraTS20_Training_001 ) 2021-10-19 <4/4/2124/1.T1/BraTS_20>	
★ Set file(s)     ★ Remove     ▲     Image: Save     Image: Description	a
Results: 🖉 Save Segments 🗹 Save VOIs 🗹 Save Statistics	
Run Close after: O Start  End	X <u>C</u> lose

**Clone Protocols** opens a dialog window in which a list of input samples should be provided using **Set Files**. In the case of AI segmentation tasks that require multiple input series, the reference for the association list should be selected. PMOD will automatically retrieve the other associated series for processing. The flat view for the database and advanced database queries can be useful to select all input series for batch processing efficiently.

Select Serie(s)					2.414
BraTS_20			• 4   F   0 /	NI DBs 🐐 New SC	Clear Filter 😌 Refresh Query 🤗
Subject (Na escription (Stud)	ame , ID) * y, Series T1 0 T # × ALL •	•  •   Study D	Birth Dat	▼ 	
Series (20) 📀					Preview of selected series
ubject DBID	A Subject Name	Subject ID Study Date	Time Study Description	Series Descri	
4	BraTS20 Training 001	BraTS20_Train 2020.07.13	20:51:57 T1		
1	BraTS20_Training_002	BraTS20_Train 2020.07.13	20:56:38 T1		
	BraTS20_Training_003	BraTS20_Train. 2020.07.13	21:06:49 T1		
3	BraTS20_Training_004	BraTS20_Train 2020.07.13	21:16:04 T1		
3	BraTS20_Training_005	BraTS20_Train 2020.07.13	21:02:35 T1	-	
)	BraTS20_Training_006	BraTS20_Train 2020.07.13	21:18:06 T1		
	BraTS20_Training_007	BraTS20_Train 2020.07.13	21:05:42 T1		
	BraTS20_Training_008	BraTS20_Train 2020.07.13	21:07:52 T1		
5	BraTS20_Training_009	BraTS20_Train 2020.07.13	21:15:23 T1		Regio AX4 1
7	BraTS20_Training_010	BraTS20_Train 2020.07.13	20:56:58 T1		
2	BraTS20_Training_011	BraTS20_Train 2020.07.13	21:15:04 T1		()④ () ()
4	BraTS20_Training_012	BraTS20_Train 2020.07.13	21:08:25 T1	-	
	DesTOOD Tesisies 040	DT000 T-+i= 0000 07.43	04-04-47 TA		
-ij- Add	🐥 🗛 All 🕬	E. O Del. 🛛 🕮 Assign to Project	t Group • 사   : @ :   여 •	T • 4 1	
lected for load	ling Components Administratio	n			TEL 0.0 1.0 1.0
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				- <b>L</b> *	
					◯ Slice ● Volume ◯ All
		× Remove × Ren	move all 🗹 Clear after loading		

Confirmation				>
	Do you want to create and save test-for-docu-1 (BraTS20_	Segmentation (PSEG) protocol Training_001 ) 2021-10-19 <4	Is based on the selected one ? I/4/2124/1.T1/BraTS_20>	
BraTS20_Training_001   T1	<4/4/0/1.T1/BraTS_20>			<b>^</b>
BraTS20_Training_002   T1	<8/56/0/1.T1/BraTS_20>			
BraTS20_Training_003   T1	<3/22/0/*/BraTS_20>			
BraTS20_Training_004   T1	<18/45/0/1.T1/BraTS_20>			
BraTS20_Training_005   T1	<19/43/0/1.T1/BraTS_20>			
BraTS20_Training_006   T1	<20/95/0/1.T1/BraTS_20>			
BraTS20_Training_007   T1	<1/46/0/1.T1/BraTS_20>			=
BraTS20_Training_008   T1	<9/80/0/1.T1/BraTS_20>			
BraTS20_Training_009   T1	<16/39/0/1.T1/BraTS_20>			
BraTS20_Training_010   T1	<17/71/0/1.T1/BraTS_20>			
BraTS20_Training_011   T1	<2/76/0/1.T1/BraTS_20>			
BraTS20_Training_012   T1	<14/89/0/1.T1/BraTS_20>			
BraTS20_Training_013   T1	<5/32/0/1.T1/BraTS_20>			
BraTS20_Training_014   T1	<11/18/0/1.T1/BraTS_20>			
BraTS20_Training_015   T1	<10/64/0/1.T1/BraTS_20>			
BraTS20 Training 016   T1	<12/14/0/1.T1/BraTS 20>			•
😭 Set fil	es	1 Add files	× Remove 🔺 🖬 Sav	e 💕 Load 🔺
	✓ <u>Y</u> es		× <u>N</u> o	

配,PSEG Batch Mode							>
BraTS20_Training_001 T1  <4/4/0/1.T1/BraTS_20> <4/4/2125/*/	/BraTS_20>						
BraTS20_Training_002   T1   <8/56/0/1.T1/BraTS_20> <8/56/2126	6/*/BraTS_20>						
BraTS20_Training_003   T1   <3/22/0/*/BraTS_20> <3/22/2127/*/E	BraTS_20>						
BraTS20_Training_004   T1   <18/45/0/1.T1/BraTS_20> <18/45/2	128/*/BraTS_20>						
BraTS20_Training_005   T1   <19/43/0/1.T1/BraTS_20> <19/43/2	129/*/BraTS_20>						
BraTS20_Training_006   T1   <20/95/0/1.T1/BraTS_20> <20/95/2	130/*/BraTS_20>						
BraTS20_Training_007   T1   <1/46/0/1.T1/BraTS_20> <1/46/213	1/*/BraTS_20>						
BraTS20_Training_008   T1   <9/80/0/1.T1/BraTS_20> <9/80/2132	2/*/BraTS_20>						
BraTS20_Training_009   T1   <16/39/0/1.T1/BraTS_20> <16/39/2	133/*/BraTS_20>						
BraTS20_Training_010   T1   <17/71/0/1.T1/BraTS_20> <17/71/2*	134/*/BraTS_20>						
BraTS20_Training_011   T1   <2/76/0/1.T1/BraTS_20> <2/76/2135	5/*/BraTS_20>						
BraTS20_Training_012   T1   <14/89/0/1.T1/BraTS_20> <14/89/2*	136/*/BraTS_20>						
BraTS20_Training_013   T1   <5/32/0/1.T1/BraTS_20> <5/32/2137	7/*/BraTS_20>						
BraTS20_Training_014   T1   <11/18/0/1.T1/BraTS_20> <11/18/2	138/*/BraTS_20>						
BraTS20_Training_015   T1   <10/64/0/1.T1/BraTS_20> <12/64/2	139/*/BraTS_20>						
BraTS20_Training_016   T1   <12/14/0/1.T1/BraTS_20> <12 14/2*	140/*/BraTS_20>						
BraTS20_Training_017   T1   <7/85/0/1.T1/BraTS_20> <7/85/14	1/*/BraTS_20>						
BraTS20_Training_018   T1   <13/19/0/1.T1/BraTS_20> <13/192	142/*/BraTS_20>						
BraTS20 Training 019   T1   <6/9/0/1.T1/BraTS 20> <6/9/2143	BraTS 20>						-
1 Set file(s)	Add file(s)	× Remove	▲	Save	💕 Load	▲	- <b>T</b>
Results: 🗹 Save Segments 🗹 Save VOIs 🗹 Save Statistics	Clone protocols	Aggregate Statistics					
	-						
Run Close after: O Start O End				0	[_of_]		× <u>Close</u>

Once the desired list of protocols has been loaded or generated through cloning, batch processing can be launched using the **Run** button. Results will be saved in the same location as the input data - we strongly recommend using the database.

# 6 Case Studies - Application of PAI

PAI and the several neural network architectures included in the resources have been tested using a range of case studies. These are described here.

# 6.1 Rat Brain Dopaminergic PET

The **Multichannel Segmentation** architecture is designed to be used in new applications. It was initially tested for the 4 input series, 3 segment output MICCAI BraTS example case, and was successfully reapplied for segmentation of striatum and cerebellum in rat brain dopaminergic PET. The process of preparing the data to reapply the architecture, the training, and the evaluation of the outcome is described in this case study.

Example data to test the Rat Brain Dopaminergic PET model is available in our Demo database (Subject PAI5). The data used for the entire case study was kindly provided by Prof. Kristina Herfert at the Werner Siemens Imaging Center at the University of Tuebingen in Germany.

To try the model for yourself we recommend use of the Segment tool (PSEG). Select the **early average** series as Input series. The **late average** series will be detected automatically according to the Association mechanism. The model selection must be Rat Brain Dopaminergic PET (Multichannel Segmentation). The model was trained with 3D data so no Split Slices/Frames is available or required. The resulting VOIs can be saved and used to extract TACs from the **Inveon dynamic PET** series (e.g. standalone analysis in View, or multimodal analysis combined with **t2\_tse3d anatomical reference** MR in Fusion). Note that the PET data has already been coregistered to the MR including reslicing. The data used in this case study was all from Siemens Inveon PET and for tracers labeled with C-11 - the performance of the model may vary for data from different hardware and/or with different tracers.

#### 6.1.1 Sample Preparation

PET imaging of the dopaminergic system results in images with high tracer uptake in the basal ganglia:



Fully quantitative analysis of PET with tracers for targets in the dopaminergic system typically uses time-activity curves from the striatum (in small animals; caudate and putamen in humans) and cerebellum (reference regions devoid of dopaminergic neurons/synapses). Dynamic PET studies typically cover a time range from 0-60 minutes after intravenous tracer injection.

In both small animals and humans, brain VOI atlases and tracer-specific templates such as those available in PMOD have long been used to achieve reproducible analysis and facilitate batch processing. The application of VOI atlases and templates used depend on the availability of anatomical imaging series to complement the PET data. In small animal dopaminergic PET studies it is common to have only the dynamic PET data. Matching to a PET template normally requires averaging in a time range that reveals specific binding and reduces image noise. Due to the limited tracer distribution researchers sometimes struggle to achieve a satisfactory result.

PMOD's **Rodent Brain analysis tool (PNROD)** provides a streamlined workflow for such analysis and with careful creation of a template image and selection of the averaging range works well for batch processing of rodent brain PET data. It was used to process 382 rat brain dynamic PET image series. The data comprised PET at a range of ages and with the tracers [<sup>11</sup>C]-raclopride, [<sup>11</sup>C]-methylphenidate and [<sup>11</sup>C]-DTBZ. A template image specific to this study data was created from a subset of the data using standard functionality in **View** and **Fusion** tools.

The traditional analysis workflow for this data is summarized below:



The dynamic PET data was averaged. This average was normalized to the template, allowing atlas VOIs for striatal regions and cerebellum to be created in the original PET image space. These VOIs were used to extract time-activity curves that were used for kinetic modeling. The Simplified Reference Tissue Model was used to calculate BP<sub>nd</sub>.

PMOD's AI framework (PAI) offers an alternative approach to segmentation of such data. 382 input samples represents a reasonable number for training of an ML model, and the VOIs generated by PNROD represent gold-standard method reference segments.

The **Multichannel Segmentation** architecture presented a potential advantage over the traditional workflow in that multiple averages can be provided as input. The average used for PNROD processing was selected to provide a specific-binding signal in the striatum but also some remaining blood pool signal to represent a more general brain outline. The cerebellum is not well defined in this average. Therefore an early average image created from the first 5 minutes after tracer injection and a late average of 30-60 minutes after tracer injection were generated using **Pipeline Processing** and organized in a **Database**:



The VOI results from PNROD were converted into reference Segments using the Mask By VOI Number functionality available in the View tool and added to the Database.

The LATE and SEGMENT images were **Associated** with the EARLY image for each subject in the **Database**. The **Project** labels 1.Early and 2.Late were assigned to the EARLY and LATE images.

The **Database** was used to create a **Learning Set** for training with the **Multichannel Segmentation** architecture.

#### 6.1.2 Training and Validation

The Learning Set was exported as an R workspace  $\mathbb{D}^{62}$  and transferred to cloud computing infrastructure for training. PMOD can be installed on the virtual machine provided by the cloud computing provider and training launched using the R workspace.

The parameters used were:

- AWS p2.8xlarge, 8 GPU K80, memory 64 GB
- 382 samples (288 training, 72 validation, 22 testing)
- batch size 24
- Learning rate 0.005
- epochs 300

Training took 268 minutes at 0.07 seconds/sample. The loss values for training and validation were extracted from the **Manifest** and plotted:



The plot illustrates how the loss value reduces with each epoch until a plateau is reached.

The Learning Set, Weights and Manifest were exported from the virtual machine and used to create a new model folder Rat Brain Dopaminergic PET in the weights subfolder of the Multichannel Segmentation folder in the PMOD installation /resources/pai folder. After this Deployment it was possible to test the model performance of comparable rat brain [<sup>11</sup>C]-methylphenidate data for which an anatomical MR image was available.

The resulting VOIs are shown below on the EARLY, LATE and anatomical reference MR images:



Time-activity curves were extracted from 8 dynamic PET series (4 RAC, 4 MP) using both sets of VOIs (AI-based, PNROD reference) and BPnd calculated using the SRTM model. The mean +/-SD BPnd using the AI-based VOIs was 1.29 +/- 0.67 and for PNROD VOIs 1.39 +/- 0.79.

Example data to test the Rat Brain Dopaminergic PET model is available in our Demo database (Subject PAI5). The data used for the entire case study was kindly provided by Prof. Kristina Herfert at the Werner Siemens Imaging Center at the University of Tuebingen in Germany.

To try the model for yourself we recommend use of the Segment tool (PSEG). Select the **early average** series as Input series. The **late average** series will be detected automatically according to the Association mechanism. The model selection must be Rat Brain Dopaminergic PET (Multichannel Segmentation). The model was trained with 3D data so no Split Slices/Frames is available or required. The resulting VOIs can be saved and used to extract TACs from the **Inveon dynamic PET** series (e.g. standalone analysis in View, or multimodal analysis combined with **t2\_tse3d anatomical reference** MR in Fusion). Note that the PET data has already been coregistered to the MR including reslicing. The data used in this case study was all from Siemens Inveon PET and for tracers labeled with C-11 - the performance of the model may vary for data from different hardware and/or with different tracers.

# 6.2 Brain Tumor Segmentation - MICCAI Challenge

PAI is provided with a neural network architecture designed for multichannel segmentation. This architecture expects one or more 3D input series and generates segmentation results with one or more segments/VOIs.

The initial application of this architecture was for a case called **Tumor Detection**. A trained model **BRATS Tumor Detection (Multichannel Segmentation**) is available in the **View** and **Segmentation** tools when PAI is licensed. It is based on the MICCAI Brain Tumor Segmentation (BraTS) Challenge: <u>http://braintumorsegmentation.org</u>. BraTS utilizes multi-institutional pre-operative MRI scans and focuses on the segmentation of intrinsically heterogeneous (in appearance, shape, and histology) brain glioma tumors.



Training and testing of the **Tumor Detection** model in PAI was performed using the data from the <u>2020 BraTS Challenge</u> containing 369 samples. Each sample consists of four MR images (native T1, post-Gd-contrast T1-weighted, T2 FLAIR, T2-weighted) and one image containing three reference segments as label numbers.

The **Multichannel Segmentation** architecture is a modified version of the convolutional neural network U-Net:



The output of the **Tumor Detection** model is a label image with three segments (label 1: nonenhancing tumor; label 2: peritumoral edema; label 4: Gd-enhancing tumor).



Example data to test the BRATS Tumor Segmentation model is available in our Demo database (Subject PAI1). This example is one of the subjects available in the data for the <u>2020 BraTS</u> <u>Challenge</u>.

To try the model for yourself we recommend use of the Segment tool (PSEG). Select the **T1** series as Input series. The **T1CE**, **FLAIR & T2** series will be detected automatically according to the Association mechanism. The model selection must be BRATS tumor segmentation (Multichannel Segmentation). The model was trained with 3D data so no Split Slices/Frames is available or required. The data used in this case study was all from the BraTS Challenge and is skull-stripped 3D MR - the performance of the model may vary for data from different hardware and/or with different contrast/sequences/pre-processing.

#### **BraTS Reference:**

Bakas, Spyridon & Reyes Jan. (2019). Identifying the Best Machine Learning Algorithms for Brain Tumor Segmentation, Progression Assessment, and Overall Survival Prediction in the BRATS Challenge. <u>https://arxiv.org/pdf/1811.02629.pdf</u>

#### 6.2.1 Sample Preparation

Each sample from BraTS Challenge data consists of four MR images (native T1, post-Gd-contrast T1-weighted, T2 FLAIR, T2-weighted) and one image containing three reference segments as label numbers. These series were imported into a database and the five series per subject were associated. The reference segment series was labeled as SEGMENT in the Association interface.

As the data was already cropped and coregistered, no additional preprocessing was applied.



# 6.2.2 Training and Validation

A new Learning Set was prepared, containing the 369 available samples, configured for a segmentation task and using the Multichannel Segmentation architecture.

An R Workspace containing all samples was exported and used for training on commercial cloud computing infrastructure. Training was performed with the settings:

- AWS p3.8xlarge, 4 V100 GPU, 244 GB memory
- 369 samples (295 training, 74 validation)
- · Crop to associated VOI
- 500 epochs
- batch size of 4
- Learning rate 0.0005

The final training set loss value was 0.2103 (1 - Dice coefficent) and the validation set loss value was 0.3531. Training took 810 minutes.

The weights and manifest resulting from the training were retrieved and used to add the training model to the /resources/pai folder for deployment on local installations.

An example of the results on one subject are illustrated below:



Example data to test the BRATS Tumor Segmentation model is available in our Demo database (Subject PAI1). This example is one of the subjects available in the data for the <u>2020 BraTS</u> <u>Challenge</u>.

To try the model for yourself we recommend use of the Segment tool (PSEG). Select the **T1** series as Input series. The **T1CE**, **FLAIR & T2** series will be detected automatically according to the Association mechanism. The model selection must be BRATS tumor segmentation (Multichannel Segmentation). The model was trained with 3D data so no Split Slices/Frames is available or required. The data used in this case study was all from the BraTS Challenge and is skull-stripped 3D MR - the performance of the model may vary for data from different hardware and/or with different contrast/sequences/pre-processing.

# 6.3 Mouse Bone Trabecular Segmentation

A common application in bone research is analysis of bone remodeling in the trabecular of distal femur and proximal tibia in mice. MicroCT imaging of ex vivo femur and tibia is used to generate 3D datasets with pixel size in the range of 5 um. Analysis of trabecular bone is then performed in the metaphysis and requires an initial segmentation separating trabecular bone from cortical bone and the growth plate. Simple cropping of the 3D dataset is usually sufficient to avoid the growth plate and to define the division between metaphysis and diaphysis. Some researchers additionally distinguish between primary and secondary spongiosa.

Definition of the trabecular region to be analysed, including as much material as possible but without including cortical bone, can be laborious and even automated solutions need tedious clean up. Al-based segmentation could offer a rapid alternative and provide the starting "tissue volume" for further trabecular analysis.

We used two distal femur and eight proximal tibia microCT datasets to train a uNet architecture using two approaches. In a strategy to increase the amount of data available for training, we treated each 2D axial slice of the femur/tibia as a separate sample. One femur and all eight tibia datasets were provided with reference segments created in the Bruker microCT software CTan.



Example data to test the Mouse bone trabecular model is available in our Demo database (Subject PAI6). The data used for the case study was kindly provided by Dr. Phil Salmon from Bruker microCT.

To try the rapid model for yourself we recommend use of the Segment tool (PSEG) or segmentation interface in View. Either the low res or full res series may be used for testing. The low res series has been downsampled but includes more slices in the 3D volume. The model selection must be Trabecular ML (uNET Segmentation). The model was trained with 2D data so Split Slices is required. No further cropping of the demo data is required. The data used in this case study was from Bruker microCT - the performance of the model may vary for data from different hardware and/or with different reconstruction/pre-processing.

# 6.3.1 Sample Preparation

In the first approach - rapid model - a subset of 70 slices from two femurs were imported into a database along with their reference segments. The microCT and segment series were associated using automatic association. A learning set was prepared with all samples and segmentation using

uNET segmentation architecture. 60 samples were assigned for training - to be split into 48 training and 12 validation - and 10 samples were labeled as Test samples for evaluation of the model.

In the second approach - detailed model - all slices from the one femur with full reference segments and seven of the eight tibia were imported into a database along with their reference segments. The microCT and segment series were associated using automatic association. In total 3509 2D samples were available for training. A learning set was prepared with all samples and segmentation using uNET segmentation architecture. 3509 samples were assigned for training - to be split into 2486 training and 622 validation - and 401 were labeled as Test samples for evaluation of the model.

# 6.3.2 Training and Validation

#### **Rapid Model**

The original resolution of the samples was 5.5 and 2.8 um and for training all were resampled to 50 um. No additional cropping was applied and the image values were normalized using the z-score method. Training was performed as follows:

notebook computer with 8 core 2.3 GHz Intel i7 and 32 GB RAM using only CPU

- 70 samples (48 training, 12 validation, 10 testing)
- batch size 12
- learning rate 0.0005
- 300 epochs

Training took 151 seconds. The training loss value was 0.0368 and the validation set loss value was 0.0388. Testing was performed on the 10 additional samples using the Evaluate Model functionality with a loss value of 0.1037.

The model was tested on the second femur dataset with reduced pixel size of 0.0112 mm, and on the eighth tibia dataset with native 0.005 mm pixel size. Both datasets were loaded as 3D volumes and prediction was run with the Split Slices option. The trabecular region was correctly segmented in < 20 seconds on a notebook similar to that used for training.



Due to training with resampling to 50 um the resulting segments displayed clear staircase artefacts. There was some overlap with cortical bone. A segment smoothing approach was investigated to remove the staircase artefacts. The segment was transferred from the Segment tool to View and smoothed with a Gaussian filter at  $0.05 \times 0.05 \times 0.05$  mm FWHM. Automatic isocontouring at 50% (Max-min) threshold was used to create a new VOI.



Smoothing visually improved the VOI but some overlap with cortical bone remained. On tibia segmentation also took < 20 seconds on the notebook tested. Similar staircase artefacts and some overlap with cortical bone were present.



#### **Detailed Model**

The original resolution of the samples used was 5 and 5.5 um and for training all samples were resampled to 10 um. No additional cropping was applied and the image values were normalized using the z-score method. Training was performed as follows:

- AWS p2.8xlarge, 96 GB GPU, 488 GB RAM
- 3509 samples (2486 training, 622 validation, 401 testing)
- batch size 60
- learning rate 0.0005
- 10 epochs

Training took 600 seconds. The training loss value was 0.0546 and the validation set loss value was 0.0545. Testing was performed on all slices of the eighth tibia dataset using the Evaluate Model functionality with a loss value of 0.0580.

The trained model was tested on the same femur and tibia datasets as the rapid model. Both datasets were loaded as 3D volumes and prediction was run with the Split Slices option. Prediction on the tibia in native pixel size took approximately 90 seconds on the notebook tested. The contour

closely followed the endosteum (inner tibial surface) with some artefacts present close to the growth plate. On femur several artefacts were present that resulted in inner holes in the trabecular VOI. Manual editing was used to close the holes and allow morphometric analysis.

#### Morphometric analysis

The segments generated by both models and smoothed versions of the rapid model segments were used for further trabecular bone analysis. A single threshold of 2000 Hounsfield units (HU) was used to segment trabecular bone voxels within the model segments. The parameters BV/TV (bone / tissue volume), trabecular thickness, trabecular number, trabecular separation, and fractal dimension were calculated using the volume and surface area statistics according to the plate model.

		BV/TV	<u>Tb.Th</u> (um)	Tb.N (mm <sup>-1</sup> )	Tb.Sp (um)	Fractal Dimension
Femur	Rapid	0.188	32.2	5.85	138.8	2.54
	Smoothed result	0.185	33.9	5.46	149.2	2.54
	Detailed*	0.125	25.6	4.89	179.0	2.43
	Reference	0.191	31.8	6.02	134.4	2.53
Tibia	Rapid	0.088	15.4	5.75	158.5	2.35
	Smoothed result	0.088	17.6	5.01	181.8	2.39
	Detailed	0.100	20.3	4.92	182.8	2.44
	Reference	0.101	20.4	4.94	181.9	2.44

Morphological analysis revealed that the rapid model yielded comparable results to the reference segments for the femur tested, but resulted in marked deviation from the reference segments for the tibia tested. Smoothing of the segments generated by the rapid model did not universally improve the result. The detailed model resulted in near replication of the reference results for tibia, but did not produce good results for the femur. We believe that this was likely a result of overtraining the model towards tibia (seven tibia vs. one femur in training set).

Use of either model for study-level trabecular analysis appears feasible. Erosion of the tissue volume segment resulting from PAI by several voxels in 2D mode would likely be beneficial to further ensure that cortical bone is excluded.

Note that only the rapid model is included for testing in the PMOD distribution.

Example data to test the Mouse bone trabecular model is available in our Demo database (Subject PAI6). The data used for the case study was kindly provided by Dr. Phil Salmon from Bruker microCT.

To try the rapid model for yourself we recommend use of the Segment tool (PSEG) or segmentation interface in View. Either the low res or full res series may be used for testing. The low res series has been downsampled but includes more slices in the 3D volume. The model selection must be Trabecular ML (uNET Segmentation). The model was trained with 2D data so Split Slices is required. No further cropping of the demo data is required. The data used in this case study was from Bruker microCT - the performance of the model may vary for data from different hardware and/or with different reconstruction/pre-processing.

# 6.4 Mouse & Human Cardiac MR Cine Left Ventricle Segmentation

Cardiac MR cine acquisitions are widely used to assess left ventricular function, using the evolution of left ventricle volume over the cardiac cycle to calculate parameters such as systolic/diastolic volume, ejection fraction and cardiac output (if frame timing is provided corresponding to the actual duration of the cardiac cycle).



Manual delineation of the left ventricle is subjective and can be time consuming in case of many cine frames and/or multislice acquisitions. Automatic methods may be limited in success due to variable acquisition parameters, image contrast and noise, as well as artefacts due to swirling blood in the ventricle.

We hypothesised that AI-based segmentation could provide a useful alternative to these methods.

Example data to test the MRI Myocardium 2D and MRI Human Myocardium models is available in our Demo database (Subjects PAI2 and PAI3). The data used for the case study was provided by Bruker colleagues and in a private collaboration.

To try the models for yourself we recommend use of the **Cardiac MR Modeling tool (PCARDM)** FUNCTION workflow. See the specific documentation for PCARDM. The model selection is determined by the species selection in PCARDM. The models were trained with 2D data so Split Slices and Split Frames are required. The recommended **Heart Box** for example PAI2 is 10 x 10 mm, and for PAI3 100 x 100 mm. The data used in these cases was for a limited range of MR sequences - the performance of the model may vary for data from different hardware and/or with different contrast/pre-processing.

# 6.4.1 Sample Preparation

#### Mouse data

Mouse bright-blood cardiac cine data was collected from internal sources and contained conventional prospectively-gated as well as Bruker IntraGate and IntraGate UTE (ultrashort echo time) time. The mixture of source data resulted in a range of pixel size, number of cardiac cycle frames, as well as blood contrast/artefacts. All series were split by frames and slices to be treated as individual 2D data. Each series was rotated such that the right ventricle was displayed on the left of screen and cropped using a 10 x 10 mm box. Reference segments for myocardial epi- and endo- contours were created manually using the paintbrush VOI tools and masking functionality. Images and reference segments were associated in a database.

#### Human data

Human bright-blood cardiac cine data was shared in a private collaboration. 10 subjects were available.

The subjects had between 11-14 slice coverage of the myocardium and 25 frames of the cardiac cycle. These were split by frames/slices to be treated as individual 2D data. Reference segments

for myocardial epi- and endo- contours were manually drawn using VOI tools and images associated with reference segments in a database.

### 6.4.2 Training and Validation

#### Mouse data

All samples were added to a learning set and the uNET segmentation architecture selected.

Prediction was tested on several additional examples. Preprocessing to rotate new data such that the right ventricle is on left of screen was required for successful prediction. Dark artefacts in the blood can lead to segmentation artefacts that require manual correction before cardiac function can be accurately assessed.

#### Human data

All samples were added to a learning set and the Multichannel Segmentation architecture selected. Training was performed as follows:

- notebook Intel i7 8 x 2.3 GHz
- 32 GB memory
- no additional cropping
- 3225 samples (2580 training, 645 validation)
- 106 epochs (aborted)
- batch size 50
- learning rate 0.005

Training took 63 minutes.

Prediction could only be tested on data that was already used in training. Acceptable segmentation results and function analysis was achieved, but the model may be overtrained for this data. The example below shows a result in PCARDM using the MACHINE LEARNING segmentation option that utilises the model trained in this case study.



Example data to test the MRI Myocardium 2D and MRI Human Myocardium models is available in our Demo database (Subjects PAI2 and PAI3). The data used for the case study was provided by Bruker colleagues and in a private collaboration.

To try the models for yourself we recommend use of the **Cardiac MR Modeling tool (PCARDM)** FUNCTION workflow. See the specific documentation for PCARDM. The model selection is determined by the species selection in PCARDM. The models were trained with 2D data so Split Slices and Split Frames are required. The recommended **Heart Box** for example PAI2 is 10 x 10 mm, and for PAI3 100 x 100 mm. The data used in these cases was for a limited range of MR sequences - the performance of the model may vary for data from different hardware and/or with different contrast/pre-processing.

# 6.5 Human Deep Nuclei Segmentation

Accurate segmentation of sub-cortical brain regions (the deep nuclei - caudate, putamen, ventral striatum, thalamus, hippocampus, amygdala) from high resolution MR data such as 3D T1-weighted sequences (e.g. Siemens MPRAGE, GE FSPGR) is a requirement in the study of diseases such as Parkinson's using imaging. The segmented VOIs may be used for volumetric analysis of MRI data in the input image space or also for PET/SPECT quantification. Traditional methods of achieving this through spatial normalization to brain templates can fail or be inaccurate in some cases, particularly when there is pronounced brain atrophy. PMOD's PNEURO Parcellation workflow is specifically designed to provide increased accuracy for deep nuclei segmentation but requires additional processing time compared to template-based normalization and can still struggle in cases with severe atrophy.



We hypothesized that AI-based segmentation could be used as an alternative for cases with severe atrophy or where traditional methods struggled.

To test this hypothesis we used data from the IXI database of 3D T1-weighted MR:

https://brain-development.org/ixi-dataset/

Example data to test the IXI Parcellation model is available in our Demo database (Subject PAI4). The data used for the case study was extracted from the IXI dataset: <u>https://brain-development.org/ixi-dataset/</u>

To try the model for yourself we recommend use of the **Segment tool (PSEG)**. The PAI4 example has the required orientation and any new data used for testing should match this. Cropping is not strictly required but is recommended to reduce the field-of-view to the brain. The model selection is **IXI Parcellation (Multichannel Segmentation)**. The model was trained with 3D data so Split Slices/Frames is not available/required. The data used in these cases was all T1-weighted 3D MR - the performance of the model may vary for data from different hardware and/or with different contrast/pre-processing.

# 6.5.1 Sample Preparation

298 3D T1-weighted series from the IXI database were imported into a PMOD database for generation of reference segments using the PNEURO Parcellation workflow in batch processing mode.

The VOIs for bilateral caudate, putamen, ventral striatum, thalamus, hippocampus, amygdala, were reviewed by an experienced reviewer and any with substantial deviations were rejected for use in AI model training. Rejected samples were kept for later use as test samples.

# 6.5.2 Training and Validation

A Learning Set was created and the Multichannel Segmentation architecture selected. Training was performed as follows:

- AWS p2.8xlarge, 8 K80 GPU, 64 GB memory
- No cropping
- 200 samples (160 training, 40 validation)
- 200 epochs (aborted)
- batch size 16
- learning rate 0.005

Training took 17.5 hours.

Prediction was tested on samples excluded from training due to failed segmentation in PNEURO. The trained model was less sensitive to atrophy and large variations in ventricular anatomy than PNEURO and yielded acceptable deep nuclei VOIs. The example below illustrates the problems that can be encountered in PNEURO due to severe atrophy and successful result generated by the trained model:



A small artefact can be noted anterior to the right caudate. This could be cleaned up using the manual VOI tools and may be removed following further training of the model with additional samples.

The model only returns VOIs in the original input image space, while in successful cases PNEURO allows spatial transformation between input and atlas space.

Example data to test the IXI Parcellation model is available in our Demo database (Subject PAI4). The data used for the case study was extracted from the IXI dataset: <u>https://brain-development.org/ixi-dataset/</u>

To try the model for yourself we recommend use of the **Segment tool (PSEG)**. The PAI4 example has the required orientation and any new data used for testing should match this. Cropping is not strictly required but is recommended to reduce the field-of-view to the brain. The model selection is **IXI Parcellation (Multichannel Segmentation)**. The model was trained with 3D data so Split Slices/Frames is not available/required. The data used in these cases was all T1-weighted 3D MR - the performance of the model may vary for data from different hardware and/or with different contrast/pre-processing.

# 6.6 Human Amyloid PET Classification

Many studies have been performed using amyloid PET in the search for a biomarker predicting progression to ALzheimer's/dementia, and several databases of imaging data for amyloid PET tracers are available online (often along with anatomical MR and FDG PET). Visually, there are pronounced differences between the distribution of the amyloid PET tracer 11C-PiB in subjects without significant amyloid accumulation in cortical regions and in subjects with large accumulation. In subjects without significant accumulation, tracer uptake is clear in white matter with very low signal in grey matter/cortical regions. In subjects with significant amyloid accumulation the tracer is more uniformly distributed throughout the brain with grey matter uptake approaching/equalling white matter. Note that healthy subjects may still have amyloid accumulation and amyloid accumulation is not clear in all cases of Alzheimer's that undergo imaging.

We used an online database of 11C-PiB PET to illustrate the functionality of our AI classification using the SVM architecture:

http://www.gaain.org/centiloid-project (Standard PiB data)

This database contains amyloid PET data for subjects with Alzheimer's disease (AD) and amyloid accumulation, and comparative data from young controls (YC) with low/negligible amyloid accumulation.



Example data to test the Amyloid PET SVM model is available in our Demo database (Subject PAI7). The data used for the case study was downloaded from the GAAIN project website: <u>http://www.gaain.org/centiloid-project</u>

To try the model for yourself the workflow in the **View** tool is required. If new data is tested, cropping should be applied to reduce the field-of-view to the brain. The model selected should be AmyloidPET-SVM (Classification SVM). The data used in these cases was all cropped 3D PET for late average 11C-PiB from unknown PET hardware - the performance of the model may vary for data from different hardware and/or with different tracers/reconstruction/pre-processing.

# 6.6.1 Sample Preparation

The 79 available datasets (45 AD, 34 YC) were imported into a database. Manual cropping was performed to more precisely limit the field-of-view to the brain. No other preprocessing was applied. The resulting image series varied in matrix size (x 67-175, y 79-227, z 35-104). AD were assigned the Group label "AD" and YC the Group label "YC" to define the classes to be trained and later predicted.

# 6.6.2 Training and Validation

A Learning Set was created and the Classification SVM architecture selected. The linear kernel was used with a maximum 32 iterations and Cost factor = 1.0.

Training was performed as follows:

- Windows workstation Intel i7-2600K 3.4GHz (no GPU use possible for SVM)
- 24 GB RAM
- 79 samples (45 class = AD, 34 class = YC)
- The samples were Resized to Box size 160 x 160 x 160 mm and Voxel size 2.0 x 2.0 x 2.0 mm, resulting in a new standardized image matrix of 80 x 80 x 80 for all samples.
- The image values were normalized using the z-score method



• Image reduction was applied using MIP (maximum intensity projection)

Training took less than 5 minutes.

Randomly selected AD and YC samples were selected from the same dataset to test Prediction. The 3D input data is loaded and the MIP is calculated as part of classification. High probabilities for the expected class were returned.



Example data to test the Amyloid PET SVM model is available in our Demo database (Subject PAI7). The data used for the case study was downloaded from the GAAIN project website: http://www.gaain.org/centiloid-project

To try the model for yourself the workflow in the **View** tool is required. If new data is tested, cropping should be applied to reduce the field-of-view to the brain. The model selected should be AmyloidPET-SVM (Classification SVM). The data used in these cases was all cropped 3D PET for

*late average 11C-PiB from unknown PET hardware - the performance of the model may vary for data from different hardware and/or with different tracers/reconstruction/pre-processing.* 

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