Why we should use Jupyter notebook in medical image analysis

Serena Bonaretti, PhD Transparent Musculoskeletal Research <u>https://tmskr.github.io/</u>

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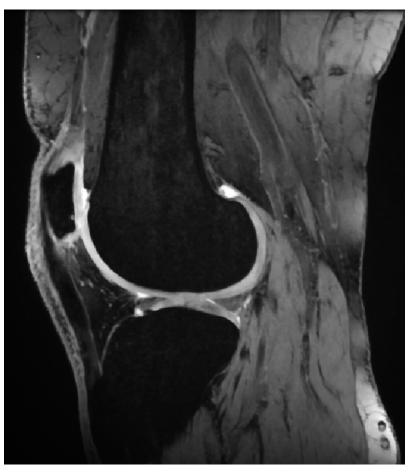
Slides at: tinyurl.com/TOR2020jupyter

Sharing my experience with Jupyter notebook in musculoskeletal imaging



I had to segment and analyze some knee images...

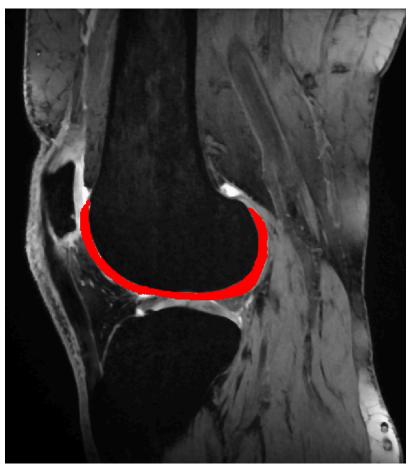
 Collaboration with scientists with limited experience in medical imaging



I had to segment and analyze some knee images...

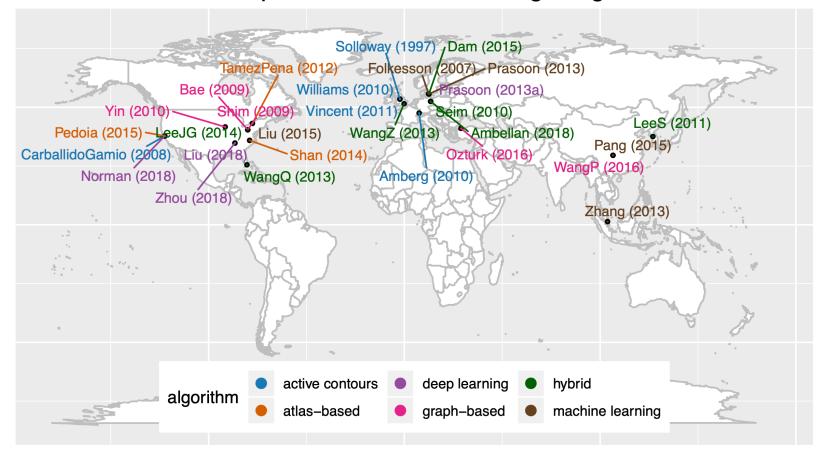
- Collaboration with scientists with limited experience in medical imaging
- They **needed code** to extract measures of OA progression
 - Femoral cartilage thickness and relaxation times

First thing: Segmentation!



I looked for existing algorithms around...

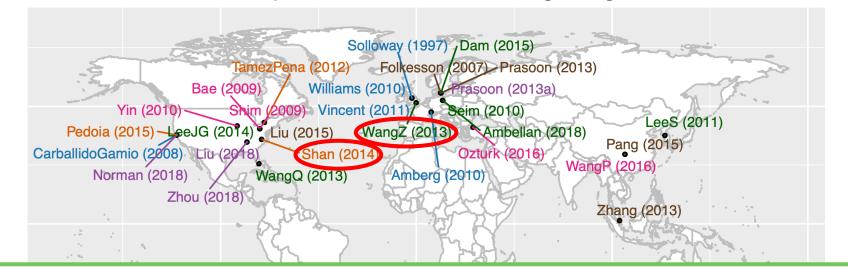
Literature map of femoral knee cartilage segmentation



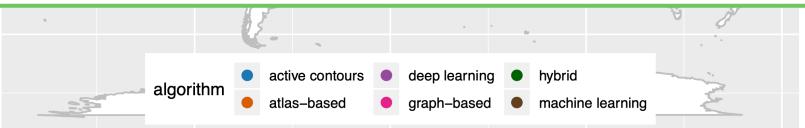
Bonaretti S, Gold GE, Beaupre GS (2020) pyKNEEr: An image analysis workflow for open and reproducible research on femoral knee cartilage. PLoS ONE 15(1): e0226501

I looked for existing algorithms around...

Literature map of femoral knee cartilage segmentation



Out of 29, only 2 implementations were open source!!!





Bonaretti S, Gold GE, Beaupre GS (2020) pyKNEEr: An image analysis workflow for open and reproducible research on femoral knee cartilage. PLoS ONE 15(1): e0226501

What to do?

- I was not interested to create another algorithm
 - There were already 29 around!
- I needed to create a *pipeline* to preprocess, segment, and analyze knee
 - Use of already existing algorithms
 - Focus on "putting the pieces together" and ease of use



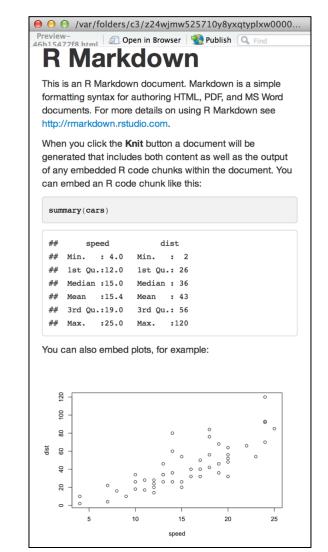
Somehow I started...

- Initially, I wanted to use Matlab
 - It was what I knew, and I already had some code
 - But it is not open source! Not everybody has a Matlab license
 - I did not want to write new closed source code (and be the 28th!)
- So I started in C++
 - I could use open libraries: ITK and elastix
 - But I had to create executables in Windows I work in MacOS!
 - Command lines are not ideal for people with limited coding experience and coding in C++ is hard for me
 - Pipeline still fragmented (e.g. code vs. visualization)



But I was still looking for a better solution...

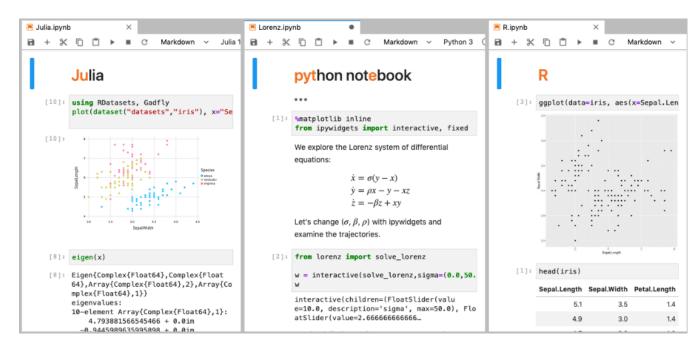
 A statistician showed me reproducible workflow using R markdown



But I was still looking for a better solution...

- A statistician showed me reproducible workflow using R markdown
- There was something similar for python, something new which was getting more and more popular...

Jupyter notebook!!!



What is Jupyter notebook?

- Web-based application integrating:
 - Narrative: text, equations, figures
 - Live code
 - Several kernels: python, C++, R, ...
 - Visualizations (graphs, 3D renderings, ...)
- Favors:
 - Reproducibility of computations
 - Sharing among researchers
 - Integration in publication
- Advantages:
 - Works for all OS
 - Runs on laptops and clusters

File Edit	View Insert Cell Kernel Help	Python 3 (
* *	12 15 ↑ ♥ ■ C Code Cell Toolbar: None	
	Exploring the Lorenz System	
	In this Notebook we explore the Lorenz system of differential equations:	
	$\dot{x} = \sigma(y - x)$	
	$\dot{y} = \rho x - y - xz$	
	$\dot{z} = -\beta z + xy$	
	This is one of the classic systems in non-linear differential equations. It exhibits a rar complex behaviors as the parameters (σ , β , ρ) are varied, including what are known solutions. The system was originally developed as a simplified mathematical model to atmospheric convection in 1963.	as chaotic
In [7]:	interact(Lorenz, N=fixed(10), angle=(0.,360.), σ =(0.0,50.0), β =(0.,5), ρ =(0.0,50.0))	
×	angle 308.2	
	max_time 12	
	σ10	
	β 2.6	
	P 28	

So where did I start?

- I had to learn:
 - Jupyter and its environment
 - python
 - python packages:
 - numpy, matplotlib, SimpleITK

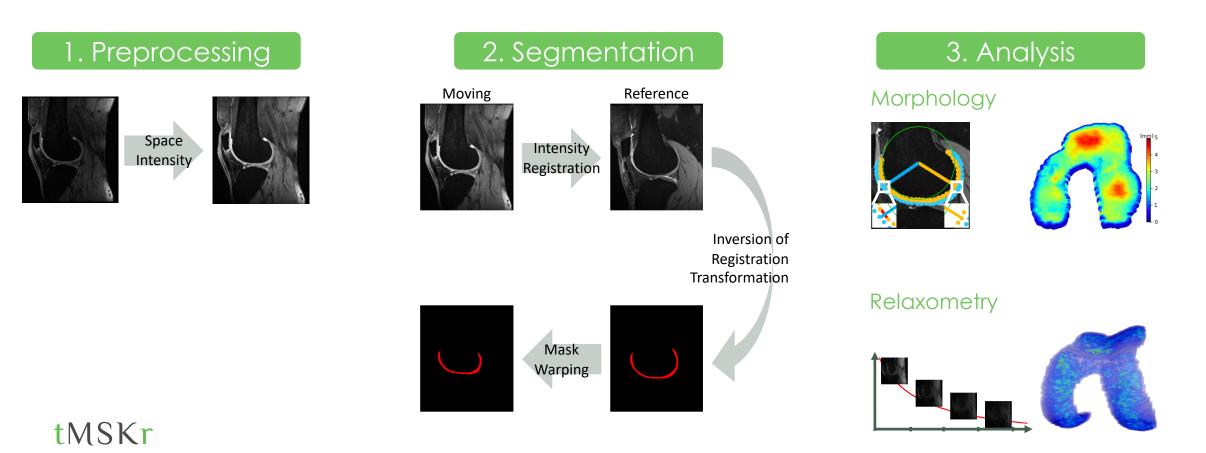
- I had to implement a workflow:
 - Image preprocessing
 - Cartilage segmentation
 - Analysis



- Online tutorials YouTube
- Blogs
- Live coding, e.g.
 - <u>https://www.learnpython.org/</u>
 - <u>https://www.w3schools.com/python/</u>
- I started by:
 - Translating the code I already had
 - Focus on language, not algorithm
 - Looking for solutions online
 - Blogs, stack overflow, etc.

And this is how created pyKNEEr!

• An image analysis workflow for **open** and **reproducible** research on femoral knee cartilage



Structure of PYKNEEr

- Each part has one (or two) Jupyter notebooks as a user-interface
 - From data upload to result visualization in one file
- "Behind" the notebooks there is the pyKNEEr python package
 - Divided in modules
 - Contains core functions
- User has just to load her/his own images and run the notebook

■ pykneer_example_2.ipynb × ■ + % □ □ ► ■ C Code ·

Relaxometry - Extended Phase Graph (EPG) modeling

Image information

Inputs:

- input_file_name contains the list of the images used to to calculate T_2 using EPG modeling - output_file_name contains average and standard deviation of the T_2 maps

input_file_name = "./image_list_relaxometry_EPG.txt"
output_file_name = "EPG_demo.csv"

Read image data

• image_data is a dictionary (or struct), where each cell corresponds to an image. For each image, information such as paths and file names are stored

image_data = io.load_image_data_EPG(input_file_name

01_DESS_01_orig -> information loaded for 1 subjects

Calculate T_2 maps

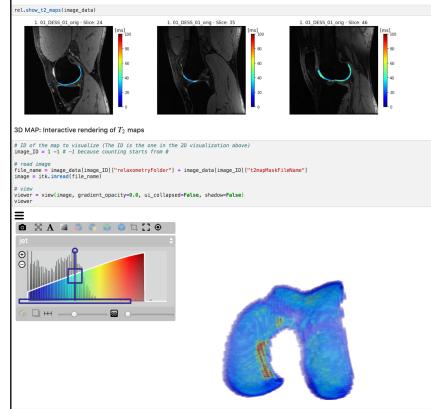
rel.calculate_t2_maps(image_data, n_of_cores)

01_DESS_01_orig -> T2 maps calculated -> The total time was 2.54 seconds (about 0 min)

Visualize T_2 maps

2D MAP: For each image, fitting maps at medial and lateral compartments and flattened map

The flattened map is an average of neighnoring voxels projected on the bone surface side of the femoral cartilage



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Link to GitHub repository

Relaxometry of Femoral Knee Cartilage

Exponential and linear fitting

Exponential fitting is computationally expensive but more accurate
 Linear fitting is faster as data are transformed to their log and then linearly interpolated. However, linear fitting is less accurate because the nonlinear logarithm transform provides larger weight to cutiliers

The fitting is computed:

pyKNEEr

 directly on the acquired images or after right registration of the following exho to the first exho voxew wise, for 6 each voxel first Echo Times (alcom tag; (0018,0081)) are the x-variable and the voxel intensities in each acquisition are the y-variable only in the margin volume to have short computation time

Image information

Inputs:

input_file_name contains the list of the images used to calculate the relexation maps method is 0 if fitting is linear, 1 if fitting is exponential registration_laips is for no registration. To frigit registration output_file_name contains average and standard deviation of the fitting maps

In []: input_file_name = "insoc_list_relaxometry_fitting_OAll_72.txt"
nethod_flag = 1 #0 = Linear, 1 = exponential
registration_lag = 1 #0 = on rigid registration, 1 = execute rigid registration
n_of_cores = 4
output_file_name = "exec_file_ligned_OAll_72.csv"

Read image data

 image_data is a dictionary (or struct), where each cell corresponds to an image. For each image, information such as paths and file names are stored

In []: image_data = io.load_image_data_fitting(input_file_name, method_flag, registration_flag)

Calculate fitting maps

Align acquisitions

Images are aligned rigidly to remove occational subject motion among acquisitions Note: This step is optional and can be skipped, given that:

When images are aligned, the fitting is calculated on interpolated values obtained with rigid registration
 When images are not aligned, the fitting is calculated on original intensities, but images might not be aligned

In []: if registration flag == 1:

rel.align_acquisitions(image_data, n_of_cores)

Compute the fitting

In []: rel.calculate_fitting_maps(image_data, n_of_cores)

Visualize fitting maps

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in []; rel.show fitting maps(image data)

3D MAP: Interactive rendering of fitting maps

(The error message "Error creating widget: could not find model" can appear when the notebook is moved to a different folder)

In []: # ID of the map to visualize (The ID is the one in the 2D visualization above)
image_ID = 1 -1 # -1 because counting starts from 0

read image file_name = image_data[image_ID]["relaxcmetryFolder"] + image_data[image_ID]["mapFileName"] image = itk.imread(file_name)

view
viewer = view(image, gradient_opacity=0.0, ui_collapsed=False, shadow=False)
viewer

GRAPH: Dots represent the average value of fitting maps per image; bars represents the standard deviation

In []: rel.show_fitting_graph(image_data)

TABLE: Average and standard deviation of fitting maps per image The table is saved as a .csv file for subsequent analyisis

In []: rel.show fitting table(image data, output file name)

References

Dependencies

[1] Bottwar, A., Wheaton A.J., Gougoutas A.J., Akellis S.V., Regatte R.R., Changurdis S.R., Roddy R., Invito, *Timssurrented of TJ disensition in the name brain at 15 Stable.* J Magn Reson Imaging, Apr;19(4):043–0204.
[2] U.X., Benjamin Ma, C., Link T.M., Castlio D.D., Blurnerikuntz G., Lozaro J., Carbalitó-Samo J., Ries M., Migurdar S. Intuor, et al. T and a discussion of a discussion at the second stable and the second stabl

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https://github.com/sbonaretti/pyKNEEr

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<> Code	Issues 0	1 Pull requests 0	Projects 0	💷 Wiki	Insights
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Branch: mas	ter • New pull	request			Create new
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code					
docs					
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Link to GitHub repository

2 Link to documentation

pyKNEEr

Relaxometry of Femoral Knee Cartilage

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in []: input_file_neme = "image_list_relaxometry_fitting_0All_72.txt"
nethod_flag = 1 #0 = Linesr,] = exponential
registration [lag = 1 # 0 = no rigid registration]
n_of_cores = 4
output_file_neme = "exo_file_aligned_0All_72.csv"

Read image data

· image data is a dictionary (or struct), where each cell corresponds to an image. For each image, information such as paths and file names are stored

n []: image data = io.load_image_data_fitting(input_file_name, method_flag, registration_flag)

Calculate fitting maps

Align acquisition

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In []: if registration flag == 1 rel.align acquisitions(image data, n of cores)

Compute the fitting

In []: rel.calculate_fitting_maps(image_data, n_of_cores)

Visualize fitting maps

n []: rel.show fitting maps(image data)

2D MAP: For each image, fitting maps at medial and lateral compartments and flattened map

```
The flattened man is an average of neighnoring voxels projected on the bone surface side of the femoral cartilage
```

3D MAP: Interactive rendering of fitting maps (The error message "Error creating widget; could not find model" can appear when the notebook is moved to a different folder

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TABLE: Average and standard deviation of fitting maps per image

The table is saved as a .csv file for subsequent analysis

In []: rel.show fitting table(image data, output file name)

References

Dependencies

[1] Borthakur A., Wheaton A.J., Gougoutas A.J., Akella S.V., Regatte R.R., Charagundia S.R., Reddy R. In vivo measurement of 7 Charles A, Masson RG, Coogous AC, Poeta V F, Heger KH, Consequence CH, Hody H, <u>In Hyperheader H, Coogous A, Coogues A,</u> and T2 mapping of articular cartilage in osteoarthritis of the knee using 3 T MRI, Osteoarthritis Cartilage. Jul;15(7):789-97. 2007

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n [:]: Nload_ext watermark %watermark -v -m -p SimpleITK,matplotlib,numpy,pandas,scipy,itkwidgets,multiprocessing

https://sbonaretti.aithub.io/pyKNEEr/

pyKNEEr	pyKNEEr
Installation	
Preprocessing	
Segmentation	
Morphology	
Relaxometry	
FAQ	MR acquisition Segmentation Cartilage thickness T ₂ map
	pyKNEEr is an image analysis workflow for open and reproducible research on femoral knee cartilage
	It is implemented in python with Jupyter notebooks

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pyKNEEr

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 method_flag = 1 #0 = Linear, 1 = exponential
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References

Dependencies

[1] Borthaizr A., Whatton A.J., Gougoutas A.J., Akolis S.V., Regatti R.R., Chanagundis S.R., Rodsy H. Is vice measurement of *TI* observation. In Ite Amazon Martin at 15 Januari, Mangi Reson Imaging, Arc119(4):043–030.
[2] U.X., Rejenrin Ma C., Link T.M., Gastilo D.D., Blumenkvintz G., Lozaro J., Carbalito-Carmo J., Reis M. (1997).

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n [:]: \$load_ext watermark %watermark -v -m -p SimpleITK,matplotlib,numpy,pandas,scipy,itkwidgets,multiprocessing

- 1. Link to GitHub repository
 2. Link to documentation
 - 3. Introduction

			- 1 Link to CitHub repository	
		<u>pyKNEEr</u>	 1. Link to GitHub repository 2. Link to documentation 	
		Relaxometry of Femoral Knee Cartilage	¹ 2. Link to documentation	
		Exponential and linear fitting		
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		acquisition are the y-variable only in the mask volume to have short computation time		001/BL
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		 image_data is a dictionary (or struct), where each cell corresponds to an image. For each image, information such as 		005/BL
	. []:	paths and file names are stored image_data = io.load_image_data_fitting(input_file_name, method_flag, registration_flag)		right
		Calculate fitting maps		006/BL
		Align acquisitions		left
		Images are aligned rigidly to remove occational subject motion among acquisitions		007/BL
		Note: This step is optional and can be skipped, given that:		left
		When images are aligned, the fitting is calculated on interpolated values obtained with rigid registration When images are not aligned, the fitting is calculated on original intensities, but images might not be aligned		008/BL
Ir	11	<pre>if registration_flag == 1: rel.align_acquisitions(image_data, n_of_cores)</pre>		left
		Compute the fitting		009/BL right
Ir		rel.calculate_fitting_maps(image_data, n_of_cores)		010/BL
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		2D MAP: For each image, fitting maps at medial and lateral compartments and flattened map The flattened map is an average of neighnoring voxels projected on the bone surface side of the femoral cartilage		011/BL
Ir		rel.show_fitting_maps(image_data)		left
		3D MAP: Interactive rendering of fitting maps		012/BL
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		# view		
		viewer = view(image, gradient_opacity=0.0, ui_collapsed= False , shadow= False) viewer		
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Ir	с. 11	rel.show_fitting_table(image_data, output_file_name)		output_file_name
		References		
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n []: input_file_name = "insoc_list_relaxonetry_fitting_OAll_72.txt" nethod_flag = 1 #0 = Linear,] = exponential registration_[lag = 1 #0 = no rigid registration, 1 = execute rigid registration n_of_cores = 4 output_file_name = "exo_fil_aligned_OAll_72.csv"

Read image data

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n []: image_data = io.load_image_data_fitting(input_file_name, method_flag, registration_flag)

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n []; rel.show fitting maps(image data)

3D MAP: Interactive rendering of fitting maps

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In [] # JD of the map to visualize (The JD is the cose is the JD visualization above) image ID = 1 # -1 # -1 because counting starts from 0 # f read image file_name = image_data[image_ID]("relaxometryFolder") + image_data[image_ID]("mapFileName") image = tki.instead(file_name)

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References

[1] Bothakur A, Whatton AJ, Gougoutas AJ, Akella SV, Regatte R.R., Charagundta S.R., Reichy R. (*in yivic measurement of T i disensitivin in the runna honit at 15 and J. Mang Resonantian and Annual Science (Science)* (2014)

Dependencies

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 watermark -v -m -p SimpleITK, matplotlib, numpy, pandas, scipy, itkwidgets, multiprocessing

1. Link to GitHub repository
 2. Link to documentation

3. Introduction

4. User inputs

5. Commands with narrative

Cartilage Thickness

Separating subcondral surface and articular surface of cartilage

To calculate cartilage thickness, first the cartilage surface is extracted from the binary mask. Then subcondral surface and articular surface are divided in two separate point clouds

morph.separate_cartilage_surfaces(image_data, n_of_cores)

Visual check

Subcondral bone surface (yellow) and articular surface (blue) are visualized as flattened point clouds. The flattening is with respect to a cylinder interpolated into the cartilage surface [2]

morph.show_cartilage_surfaces(image_data)

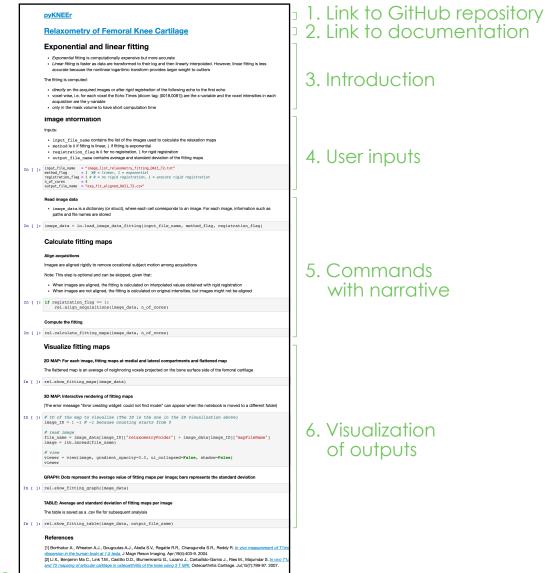
Calculating cartilage thickness

Assign the chosen algorithm

morph.algorithm(image_data, thickness_algo)

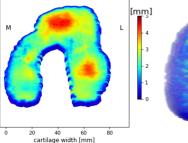
Calculate thickness

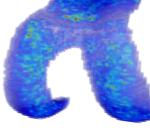
morph.calculate_thickness(image_data, n_of_cores)

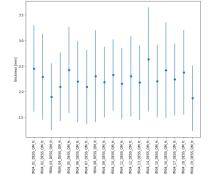


Qualitative visualizations



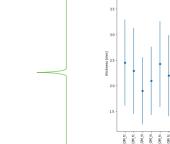




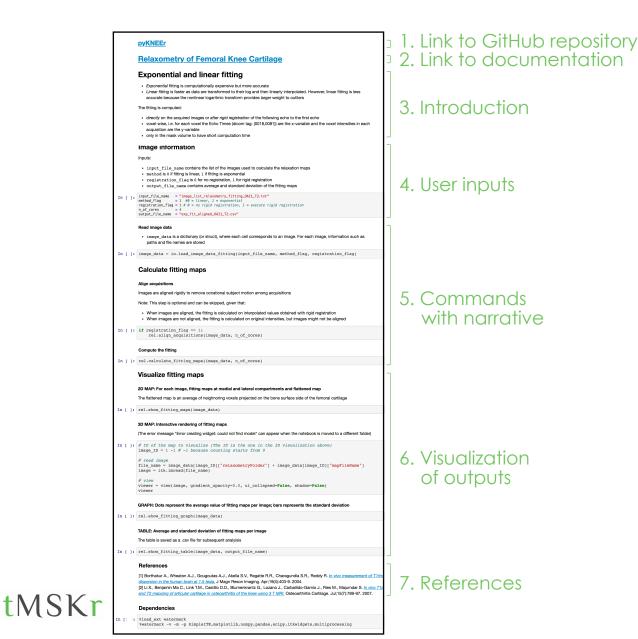


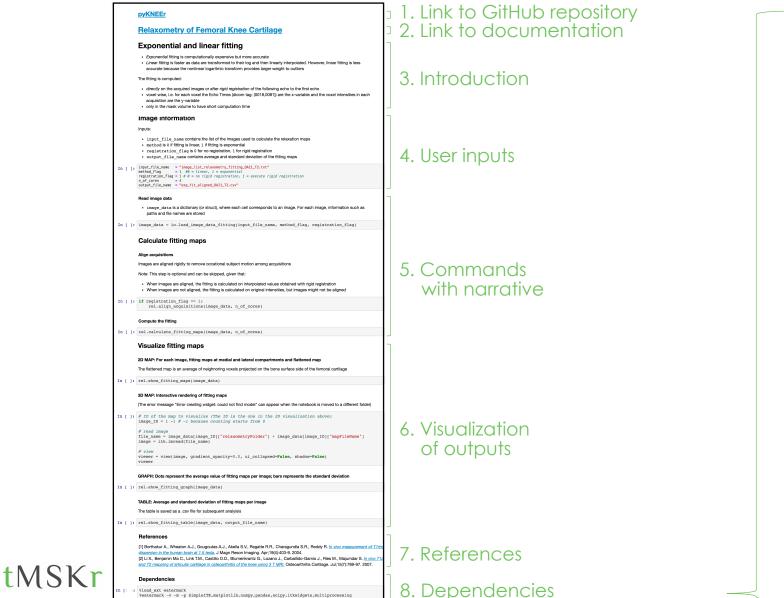
	Subjects	averageThickness	std.dev
1	YR04_01_DESS_QM_fc_thickness_1	2.45	0.84
2	YR04_02_DESS_QM_fc_thickness_1	2.29	0.84
3	YR04_03_DESS_QM_fc_thickness_1	1.90	0.65
4	YR04_04_DESS_QM_fc_thickness_1	2.09	0.67
5	YR04_05_DESS_QM_fc_thickness_1	2.42	0.84
6	YR04_06_DESS_QM_fc_thickness_1	2.20	0.79
7	YR04_07_DESS_QM_fc_thickness_1	2.09	0.72
8	YR04_08_DESS_QM_fc_thickness_1	2.30	0.90
9	YR04_09_DESS_QM_fc_thickness_1	2.19	0.69
10	YR04_10_DESS_QM_fc_thickness_1	2.32	0.70
11	YR04_11_DESS_QM_fc_thickness_1	2.16	0.69
12	YR04_12_DESS_QM_fc_thickness_1	2.30	0.79
13	YR04_13_DESS_QM_fc_thickness_1	2.18	0.73
14	YR04_14_DESS_QM_fc_thickness_1	2.63	1.02
15	YR04_16_DESS_QM_fc_thickness_1	2.21	0.71
16	YR04_16_DESS_QM_fc_thickness_1	2.42	0.93
17	YR04_17_DESS_QM_fc_thickness_1	2.24	0.70
18	YR04_18_DESS_QM_fc_thickness_1	2.38	0.82
19	YR04_19_DESS_QM_fc_thickness_1	1.87	0.64

Quantitative visualizations









: Nload_ext watermark %watermark -v -m -p SimpleITK,matplotlib,numpy,pandas,scipy,itkwidgets,multiprocessing

Dependencies

%load_ext watermark %watermark -v -m -p matplotlib,numpy,pandas,scipy

CPython 3.7.1 IPython 7.2.0

matplotlib 2.2.3 numpy 1.16.1 pandas 0.24.1 scipy 1.2.1

: Clang 4.0.1 (tags/RELEASE_401/final) compiler system : Darwin : 17.7.0 release machine : x86 64 processor : i386 CPU cores : 4 interpreter: 64bit

→ Reproducibility of computational environment

Jupyter Community | MSK

- We got a Jupyter Community Workshop grant!
 - To start building the Jupyter community in MSK imaging
 - Workshop, June 7-9, 2020 \rightarrow Online meeting June 7, 2020
- We span across the globe
 - UCSF, CU Denver, U. Calgary, UNC, ITK, U. Leuven, U. Lund, I.O. Rizzoli, U. Melbourne
- We aim to create open and reproducible workflows by
 - Combining existing code to overcome fragmentation
 - Creating new code with structured guidelines



Practical tips to create workflows with Jupyter notebook



Learn from free online material

Video tutorials



Jupyter notebook and python for scientists



Hands-on tutorials

SimpleITK notebooks

SPIE 2019 workshop

OpenMR Benelux 2020

Imperial College Course

Notebook Examples

Nipype

Deep Learning Toolkit

pyKNEEr



Open a new notebook...

- Write the narrative
- Write code
- Run cells in sequence

	Read the knee stack (dicom)
	Variable:
[4]:	<pre>image_folder = "./data/knee"</pre>
	-> Read the dicom series:
[5]:	<pre>reader = sitk.ImageSeriesReader() dicom_names = reader.GetGDCMSeriesFileNames(image_folder) # -> Task 1: Add folder name betw reader.SetFileNames(dicom_names) img = reader.Execute()</pre>
	-> Print image characteristics:
[6]:	<pre>print("Origin : " + str(img.GetOrigin())) print("Spacing: " + str(img.GetSpacing())) print("Size : " + str(img.GetSize())) # -> Task 1: Get image origin using GetSize()</pre>
	Origin : (-4.937600135803223, -57.961299896240234, 86.4000015258789) Spacing: (0.3125, 0.3125, 1.5) Size : (512, 512, 68)
	Visualize one image slice:
[7]:	<pre>slice_id = 30 slice = img[:,:,slice_id] show_image_slice (slice) # Task 1: Have a look at the function show_image_slice</pre>

Start optimizing the code...

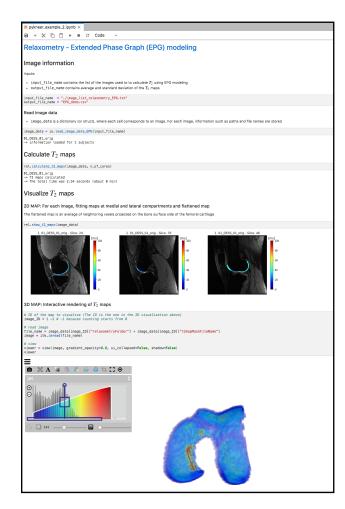
Move reusable functions to a python module

- In the notebook:
 - Import the module
 - Call the function

	<pre>calculate_volume(mask):</pre>
	Function to calculate cartilage volume It calculates the number of mask voxels and then multiply them by image spacing Input: - mask: binary mask in SimpleITK Output: - volume_mm: float
	<pre># write function here mask_gt_py = sitk.GetArrayFromImage(mask)</pre>
	<pre># get number of white voxels n_of_voxels = np.count_nonzero(mask_gt_py)</pre>
	<pre># calculate volume in voxels volume_vx = n_of_voxels</pre>
	<pre># calculate volume in mm volume_mm = volume_vx * mask.GetSpacing()[0] * mask.GetSpacing()[1] * mask.GetSpacing()</pre>
	<pre># print out volume print ("The volume is: " + "{:.2f}".format(volume_mm) + " [mm]")</pre>
	return volume_mm
	<pre>image_measurements.py</pre>
	<pre>mport image_measurement</pre>
ir	

Keep the notebook human readable

- Organize the narrative:
 - Title of the notebook
 - Divide in paragraphs with subtitles
 - Introduce code
 - Comment the results you obtain
- Organize the code:
 - Package imports
 - Functions
 - Variables
 - Workflow body
 - Dependencies



Make the notebook reproducible

- Automatically download data from a repository
- Automate data manipulation
- Define seeds to generate random numbers
- Print dependences

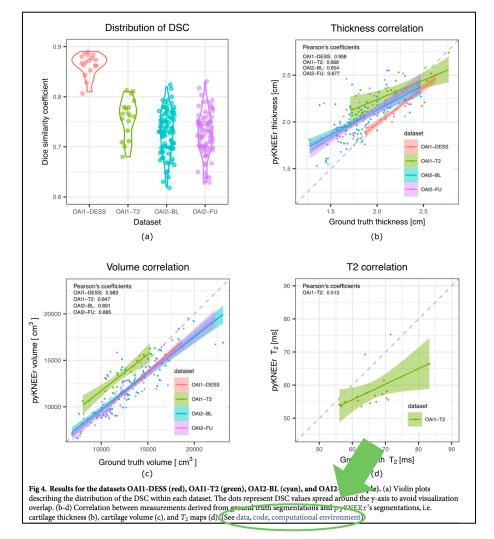
Sandve et al., (2013) Ten Simple Rules for Reproducible Computational Research, PLoS Comput Biol. 9(10): e1003285. tMSKr Rule et al. (2019) Ten simple rules for writing and sharing computational analyses in Jupyter Notebooks. Comput Biol. 15(7): e1007007. 29 See practical tutorial: <u>How to create a reproducible Jupyter notebook?</u>

Attach the notebook to the paper

Number of subjects191919888844I. Acquisition protocol Acquisition plane Number of images in series In-plane spacing [mm]DESS sagittal 2 (1 available)° 0.3646×0.3646 0.3125×0.3125 0.3646×0.3646 0.3125×0.3125 0.3646×0.3646 0.3125×0.3125 0.3646×0.3646 0.3125×0.3125 0.3125×0.3125 0	Dataset	OAI1-DESS	OA	I1-T ₂	OAI2-BL	OAI2-FU	inHous	e-DESS	inHou	ıse-CQ
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Bonaretti S, Gold GE, Beaupre GS (2020) pyKNEEr: An image analysis workflow for open and reproducible research on femoral knee cartilage. PLoS ONE 15(1): e0226501

Attach the notebook to the paper





Bonaretti S, Gold GE, Beaupre GS (2020) pyKNEEr: An image analysis workflow for open and reproducible research on femoral knee cartilage. PLoS ONE 15(1): e0226501

Share in an executable environment

	binder		
Turn a Git re	epo into a collection notebooks	ofintera	active
environment, mak	upyter notebooks? With Binder, open thosi king your code immediately reproducible b		
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tMSKr

See practical tutorial: How to share a Jupyter notebook with Binder?

So, why should we use Jupyter notebook in medical image analysis?



Because Jupyter notebooks allow us to:

- Do open and reproducible medical image analysis
- Create image analysis workflows that are complete
- Easily integrate our workflows into our papers