TOWARDS A SMART MULTI-MODAL IMAGE REGISTRATION PROCESS

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ABSTRACT

The multi-modal image registration is a complex task in the medical domain. This task requires usually several manual interventions by the user/expert of the domain to adjust the image registration parameters properly to the characteristics of the processed image data. For this aim, the user needs to extract the relevant information from the image data and their meta-information. In this paper, we propose a novel architecture for a smart fully automatic multi-modal registration process. This architecture is based on a MAPE-K loop inspired by the architecture of autonomous systems.

KEYWORDS

Image registration, multi-modal image data, MAPE-K loop, medical domain.

1. INTRODUCTION

This work is performed within Marie Sklodowska-Curie ETN MgSafe[1]. The main objective of this project is to develop and enhance imaging technologies for recently established Mg implants by quantifying their physical impact and suitability for this class of materials in future human applications.

Highly sophisticated imaging modalities such as micro Computed Tomography (μCT), Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), Ultra Sound and Photo Acoustic (USPA) and histological sections, are developed in order to deliver data on different time and length scales of the body reaction and material behaviour during Mg degradation.

The obtained multi-modal imaging data was partially combined with molecular biological/biochemical analysis. All relevant biological and chemical in vivo and ex vivo data need to be merged. The combination of these results will allow for an upscaling of the processes to-wards humans and deliver valuable data in terms of patient safety.

The project is expected to generate a vast amount of 2D and 3D data from different modalities. The aim is to combine these data and to describe their relative relation in space and time with a multi-modal image registration process. The collected data to be combined, are characterized by their heterogeneity i.e., with different modalities, color systems, dimensions and resolutions and are provided by different machines in several institutes.

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[1] https://www.mgsafe.eu/

Due to this heterogeneity, the multi-modal registration process usually needs many user's interventions to:

- Retrieve the path of the meta-files to extract relevant information.
- Collect the relevant information required to adjust the image registration parameters.
- Provide and adjust the parameters of the registration
- Pre-process the image data manually to minimize their heterogeneity e.g., applying a noise filter on an CT scan containing artifacts.

These manual interventions require an extra time and effort from the user and make the process of registration not easy to perform. In this work, we aim to develop a smart-automatic and user-friendly architecture for the management of heterogeneous image data. This architecture aims to reduce the user's intervention during the image registration process.

This paper will be organized as follows: In section 2, we present the background of our work. In section 3 is devoted we present related work dealing with automatic techniques for registration of multi-model medical images. Section 4 is devoted to detail our proposed architecture for image registration inspired by autonomous systems based on MAPE-K loop and its different steps. In section 5, at a first place, we illustrate our case study. At a second place, we apply the MAPE-K loop on this case study. In section 6, we focus on the implementation phase of the monitoring phase of the MAPE-K loop.

2. BACKGROUND

In this section, we describe the image data structure. Then, we explain the basic concepts of the image registration process in the medical domain.
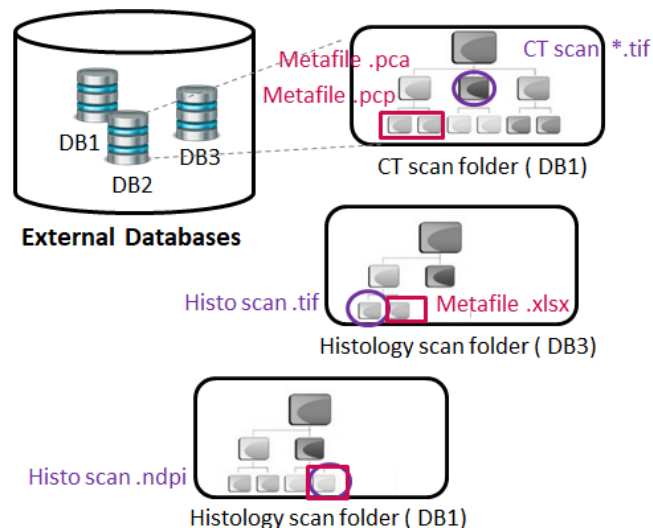
2.1. Imaging Data Description

Figure 1. Data structure heterogeneity

A specimen can be scanned in several institutes by different scanners, and an institute scans multiple specimens. Which results in a set of scans of the same specimen connected to each other according to a timeline. A scan has a specific modality (CT, MRI, US, etc.) and may have one or more meta-files describing it. Since the imaging data are stored in different external databases

belonging to several institutes, the meta-data and data structure are different from one provider institute to another. Figure 1 illustrates the data structure heterogeneity through an example of three external image databases DB1, DB2 and DB3 provided by different institutes. First, the location of meta-files and image files are different in the three databases. Moreover, the relevant information of the CT scan in DB1 should be extracted from the meta-files with ".pcp" format and the relevant information of the histology section should be extracted from the header of the ".ndpi" file which contains both the meta-data and the image. While the relevant information of the CT scan in DB3 have to be extracted from the meta-file with .xlsx format. In addition, meta-files in DB1 and DB2 provide the relevant information following different text patterns.

2.2. Image Registration Process

In a generic way, a registration process is composed mainly of three steps. The first step is the segmentation of the colored images to binary images. It's an optional step that is highly required for the histological sections modality which refers to a slice of tissue which is viewed under a microscope to give cells information.
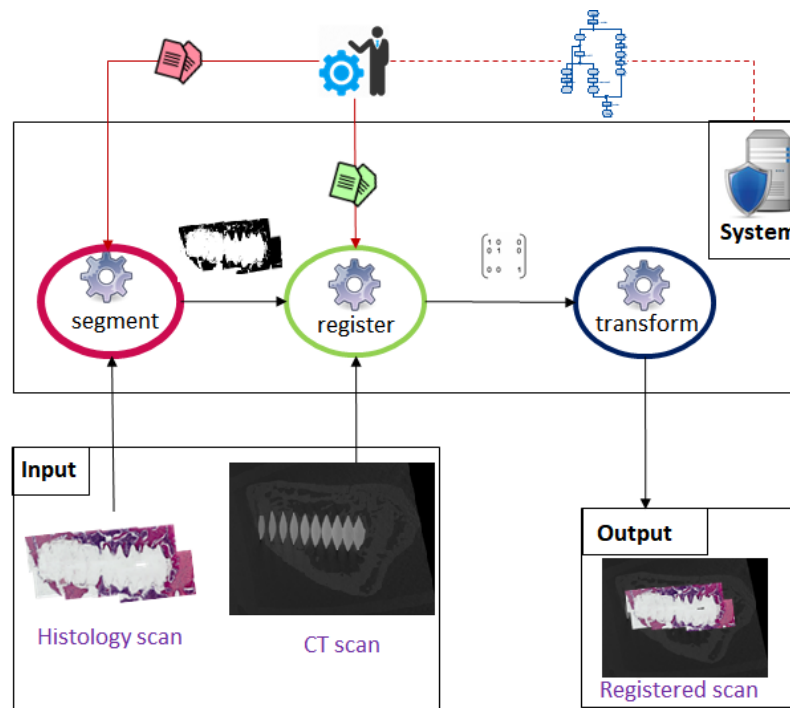

Figure 2. Image registration process

A histological section can be stained with different staining methods to highlight relevant features of the tissue e.g., "Hematoxylin and Eosin" where nuclei are stained blue, the cytoplasm are stained pink. The second step is the registration of one of the pair images inputs. And the final step is the transformation of the registered image. Figure 2 depicts the steps of an image registration process. In Figure 2, the system takes as input a 2D stained histological section and 2D section of a CT volume. First the system segments the colored histological image to a binary image. Then, it computes the transformation matrix of the binary image to match to the CT image, during the registration step. Finally, the system transforms the colored histological image according to the generated transformation matrix and gives as output a registered image.

3. RELATED WORK

In literature, there are several work dealing with 2D to 3D image registration -with the aim of combining histological sections to CT volumes-, and 3D to 3D image registration to combine CT to CT volumes over time, MRI to CT volumes and PET to CT volumes.

The work of Huanjie et al. [8] proposes an algorithm to perform the image registration of 3D bone images coming from different modalities (MR, SPECT and CT) to combine anatomical and functional information. This algorithm aims to improve the image registration accuracy based on feature-based image registration method.

Also, the research of Sabokrohiyeh et al. [6] is interested in image registration of 4D flow MRI (poor quality) to 3D cine MRI; multi 2D slices (high quality) following a sketch-based image registration method to improve registration accuracy.

With the same objective of achieving a high accuracy, the work of Liu at al. [4] suggests a weighed image registration method based on curvature feature.

In addition, the research of Albers et al. [2] is a recent work dealing with registration of 2D histological data to 3D CT volume based on an elastic image registration. This type of registration requires to be performed following 2 steps: First, retrieve the orientation of the 2D histology section to extract the appropriate section within the CT volume (manually). Then perform an automatic 2D to 2D registration. Even though the previously mentioned work are interested in performing 2D/3D to 3D image registration semi-automatically or automatically, they still limited to perform the registration image by image.

On the other hand, medical analysis relies on a big amount of imaging data. In this context, Xamflow² is a workflow-based framework proposed by Lucid. It enables to execute a workflow e.g., registration, on a vast imaging data set. This framework allows to execute static workflows which fits to process imaging data which have the same characteristics, e.g., image registration of a set CT volumes scanned overtime with the same machine.

Thus, the existing solutions are limited to process data that have the same characteristics. The current solutions are time consuming and require the user's intervention along the steps of the registration process to adjust the registration parameters properly to the given data set characteristics.

4. SMART ARCHITECTURE FOR IMAGE REGISTRATION INSPIRED FROM AUTONOMOUS SYSTEMS' ARCHITECTURE

The autonomic computing was proposed as a solution to tackle many complex tasks in several fields as industry 4.0, e-health, smart grid, and agriculture. It brings a system with self-management capabilities to dynamically adapt itself to its context.

Inspired by the autonomous systems' applications we propose to apply a MAPE-K loop [7] [1] [5] on the multi-modal image registration process. A MAPE-K loop is a conceptual architecture for autonomic applications has been suggested by IBM [3]. The aim of this architecture is to adapt autonomously the behaviour of a system according to the changes of their environments.

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² https://xamflow.lucid.ch/

The principal element of this architecture is the autonomic manager which interacts with managed entities within sensors and actuators. The autonomic manager is responsible for the phases of Monitoring, Analysis, Planning and Execution.

During the execution of the monitoring phase, the autonomic manager collects information about the context via the sensors. In the Analysis phase, it analyzes whether an adaptation of the behaviour is needed. The Planning phase consists in the selection of the most suitable reconfiguration actions which is called a plan of decision. Finally, in the Execution phase the appropriate plan of decision is selected and executed.

On the other hand, a registration process takes place as depicted in the workflow in Figure 3: The user selects two images as input e.g., a CT scan and a histology section and extracts manually the relevant information (e.g., dimensions of the image, pixel size, color system) from the meta-data of the image. Then, the user decides the different steps to be execute by the system and provides the collected relevant information in parameter: First, the system converts the data to a readable format. Second, it segments the histology-colored section and the CT images to binary images. Third, it computes the transformation matrix. And finally, it transforms the histology section and gives as output a registered image.
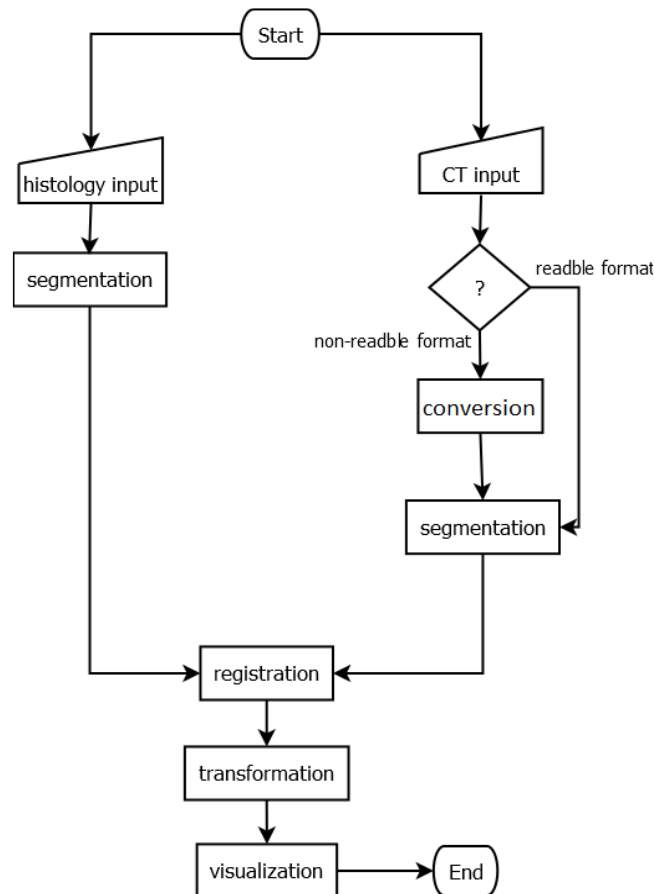

Figure 3. An example of registration workflow: histology to CT

This workflow can be automatically re-used only on another set of data containing the same characteristics, in a static way. However, due the heterogeneous nature and huge number of combinations of image data (e.g., registration CT to CT, registration CT to PET, registration MRI to USPA, etc.), more adaptability is needed to process the data automatically.

To apply the MAPE-K loop on the registration process, we define:

- − The registration workflow as the behavior of our system.
- − The image data in input as a changing context of the system, i.e., the system is required to adapt its behavior running an appropriate image registration workflow, according to the characteristics and modalities of the images in input.
- − The metadata of the images as the sensors' module providing information about the context changes.

5. CASE STUDY: MAPE-K LOOP APPLIED ON THE MULTI-MODAL REGISTRATION

In this section, we detail our case study. Figure 4 explains how the different phases of the MAPE-K loop are applied on our case study. The system is connected to the data layer composed of three databases: "Ref Database", "Knowledge base" and "Reg information database"

5.1. Ref Database

The "Ref database" is connected to the external database of the provider institute. It includes the references to the specimen folders located in the external database. It also includes information about the provider institute, modality, reference of the specimen (in order to link scans belonging to the same specimen).

5.2. Knowledge Base

The Knowledge base includes rules that describe the appropriate options that the system can run according to a specific context.

5.3. Reg Information Database

The "Reg information database" is connected to the Knowledge base. It feeds the Knowledge base with the behaviour history of the system which is the workflows executed previously. This database includes the executed workflows, the id of the rules, the selected plans of decision and the efficiency of the behaviour represented with an error function.

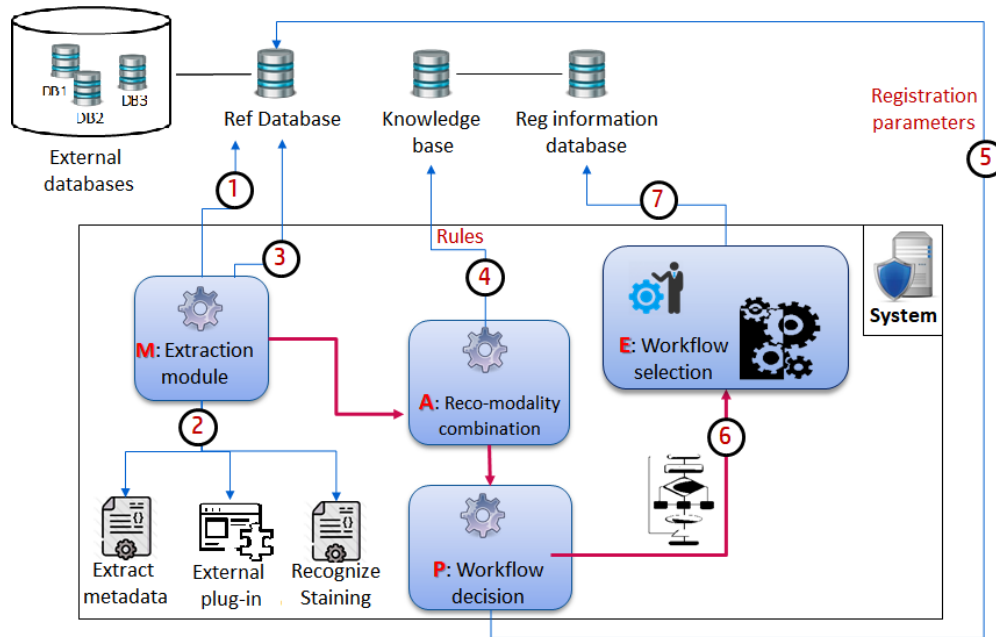## 5.4. Monitoring, Analysis, Planning and Execution

Figure 4. MAPE-K applied on image registration process

First, during the monitoring phase, the "extraction module" collects the relevant information belonging to the image data given as input. The relevant information is collected from the meta-files of the images, the header of the image files or the image files (2). The extraction module access to the external data via "Ref database" (1). After operating, it feeds "Ref database" with collected information (3). Then, in the analysis phase the "Reco modality combination" analyzes the observations provided by the previous phase, either based on the set of predefined rules or based on the historical of the behaviour of the system stored in the knowledge base (4). According to the provided analysis, in the planning phase the module "Workflow decision" decides a plan of decision suggesting a set of appropriate registration workflows to execute. The module "Workflow decision" collects the needed parameters values adequate to each suggested registration workflow from the relevant information stored in "Ref database" (5). Also, provides the description of the suggested registration workflows to "Workflow decision" module (6). Finally, in the execution phase, the "Workflow selection" module selects and executes most suitable registration workflow based on the provided plan of decision and the previous system behaviours stored in "Reg information database" (7). Then, it feeds "Reg information database" with the new system behaviour. As the Monitoring phase is critical to deal with a huge amount of data characterized by their heterogeneity, in this Paper, we highlight the Monitoring phase.

6. MONITORING PHASE: THE EXTRACTION MODULE

In the following section, we detail the implementation of the extraction module representing the monitoring phase. The required relevant information is collected from the meta-files (e.g. the pixel size and the dimensions of a CT 3D volume), from the header of the image (e.g. the dimensions of an histology image ".dicom" format), or from the image file (e.g. the staining method of an histology section).

6.1. Extraction from Meta-File

The meta-files have different location structures in the different external databases. Further, the meta-files have different text patterns depending on the type of the imaging machine. A metadata extraction module is responsible on defining the placement the appropriate meta-file containing the required relevant information.

This module, also, allows to recognize the text pattern of the meta-file. According to these two features it runs a text extraction code to extract the relevant information and store it.

6.2. Extraction from Header

Images with some format such as ".dicom" or ".ndpi" includes information in the header of the image file. Our extraction module supports ".ndpi" format. It connects to an external plugin which enables decompressing and ".ndpi" file and reading its header.

6.3. Extraction form Image File: Staining Recognition

The staining method of a histology section is an essential information required to register a histology section to any 3D grayscale volume. This information is required for the segmentation to a binary image to decide the adequate segmentation method to process. This information should be implicitly deducted from the image file.

For this aim, based on a machine learning code for colors identification, we made improvements to develop a new code for staining recognition of a histology section. Our improved code supports the four staining methods shown in Figure 5: HE, Levai Laczko, Masson's trichrome and Van Kossa.
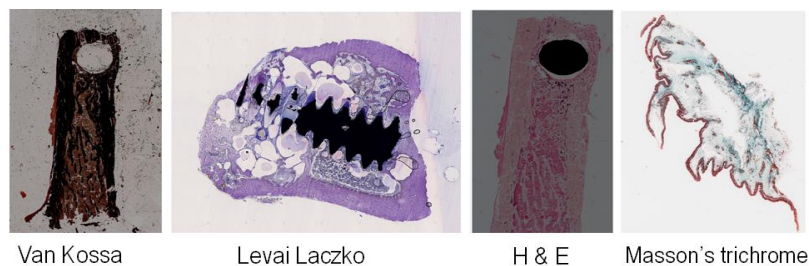

Van Kossa   Levai Laczko   H & E   Masson's trichrome

Figure 5. Examples[3] of different stained bone tissue section including an implant

Our code takes as input a histology image and gives as output the name of the used staining method. In the initial code of colors identification[4], first, the image is read. Then, the code identifies the n top existing colors based on the k-means algorithm to get colors cluster and prepares a class colors table including a set of color ranges. Then, Match the image to the appropriate class. Listing 1 shows the first and second steps of the code (respectively in line 7 and line 8).

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[3] histological sections provided by: Institute of Metallic Biomaterials, Helmholtz-Zentrum hereon GmbH, Geesthacht-Germany; Institute of Clinical Dentistry, University of Oslo, Norway; the Virtual Microscopy Database (VDM)

[4] https://github.com/kb22/Color-Identification-using-Machine-Learning

```
 1 from sklearn.cluster import KMeans
 2 import matplotlib.pyplot as plt
 3 import numpy as np
 4 import cv2
 5 from skimage.color import rgb2lab, deltaE_cie76
 6
 7 def read_image (image_path):
 8 def identify_colors (image, number_of_colors, show_chart):
 9
10 IMAGE_DIRECTORY ="..\\..\\..\\ histology_images"
11 print (IMAGE_DIRECTORY)
12 COLORS = {
13 'trichome_green_1': [50, 121, 115],
14 'trichome_green_2': [50, 200, 190],
15 'trichrome_red': [200, 30, 50],
16 'HE_pink': [240, 190 ,235],
17 'HE_purple': [200, 30, 50],
18 }
19 for file in os.listdir (IMAGE_DIRECTORY):
20 if not file.startswith ('.'):
21 images.append(get_image(os.path.join(IMAGE_DIRECTORY, file)))
22 names.append(file)
```

Listing 1. Colors threshold initialization

While, Listing 2 shows the third step our code after improvement. The histology images are stained with two or more colors. Thus, we need to match the image to a composed staining cluster instead if color cluster. For instance, we developed the method "match image by color or and" to match an image to trichrome masson goldner's staining based on a predefined rule (from line 2 to line 16). In this example the rule is: if the identified top n colors of the image contain green1 or green2 and red then the image is matched to trichrome masson goldner's cluster (line 18).

```
 1
 2 def match_image_by_color_or_and (image, color1, color2, color3,
 threshold1, threshold2, threshold3, number_of_colors ):
 3 for i in range (number_of_colors ):
 4 curr_color = rgb2lab (np.uint8 (np.asarray([[image_colors[i]]])))
 5 diff1 = deltaE_cie76 (selected_color1, curr_color)
 6 diff2 = deltaE_cie76 (selected_color2, curr_color)
 7 diff3 = deltaE_cie76 (selected_color3, curr_color)
 8 if (diff1 < threshold1):
 9 select_image1 = True
10 if (diff2 < threshold2):
11 select_image2 = True
12 if (diff3 < threshold3):
13 select_image3 = True
14 if ((select_image1 and select_image3) or (select_image2 and
select_image3)):
15 select_image = True
16 return select_image
17 plt.figure(figsize = (20 , 40))
18 show_selected_images_or_and (names,images, COLORS['trichome_green1'],
COLORS['trichome_green2'], COLORS['trichome_red'], 30 ,35 ,50 ,10)
```

Listing 2. Matching image to staining method

7. CONCLUSION

In face of the increasing amount of imaging data in the medical domain and the need of combining these data for better medical analysis, several work aim to improve image registration process in term of the registration accuracy. Other work aim to perform this process as automatically as possible on a large set of imaging data. Nevertheless, the highly heterogeneous characteristics of these data limits the proposed solutions.

Inspired by the autonomous systems, we proposed a MAPE-K loop applied on the image registration process to adapt automatically the functioning of the solution according to the changing characteristics of our data. In this paper, we detailed the monitoring phase of the MAPE-K loop as it has the most important impact on reducing the manual user intervention in the imaging registration process.

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[5] https://www.virtualmicroscopydatabase.org/

[6] https://www.hereon.de/

[7] https://www.odont.uio.no/

AUTHORS

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