Preparation of Whole Slide Images for usage in Neural Networks

Master Thesis

Submitted in partial fulfillment of the requirements for the degree of

Master of Science (M.Sc.) in Applied Computer Science

at the

Berlin University of Applied Sciences (HTW)



First Supervisor: Prof. Dr. Peter Hufnagl

Second Supervisor: Diplom Informatiker Benjaming Voigt

Submitted by: Sascha Nawrot (B.Sc.)

Berlin, May 25, 2016

Preface

Hello, this is the preface

Abstract

This is the abstract.

Contents

1	Intr	oduction	3
	1.1	Motivation	3
	1.2	Research Objective	4
	1.3	About this thesis	5
2	Bac	kground	6
	2.1	Definition of terms	6
		2.1.1 Deep Zoom Image Format	6
			7
		2.1.3 Neural Network	8
	2.2	Process Chain	9
		2.2.1 Definition of Conversion Service	0
		2.2.2 Definition of Annotation Service	1
		2.2.3 Definition of Tessellation Service	2
3	Cor	version Service 1	3
	3.1	Methodology	3
			4
		3.1.2 Deepzoom.py	6
		3.1.3 VIPS	7
	3.2	Implementation	8
	3.3	Test	0
		3.3.1 Setup	0
		3.3.2 Result	1
4	Anı	notation Service 2	2
	4.1	Methodology	2
		4.1.1 DICOM	2
	4.2	Implementation	2
	4.3	Test	2
		4.3.1 Setup	2
		4.2.2. Doubt	0

5	Tess	sellation Service	23
	5.1	Methodology	23
	5.2	Implementation	23
	5.3	Test	23
		5.3.1 Setup	23
		5.3.2 Result	23
6	Con	clusion	24
	6.1	Results	24
	6.2	Conclusion	24
		Future tasks	24
Aı	pen	dices	25
\mathbf{A}	List	ing of Conversion Service Test Data	26
		Aperio (.svs)	26
		Generic Tiled tiff (.tiff)	27
		Hamamatsu (.ndpi)	27
		Hamamatsu (.vms)	27
		Leica (.scn)	28
		Mirax (.mrxs)	29
		Trestle (.tiff)	30
		Ventana (.bif)	30
Bi	bliog	craphy	31
Li	st of	Figures	33
Li	st of	Tables	34

Introduction

1.1 Motivation

The medical discipline of pathology is in a digital transformation. Instead of looking at tissue samples through the means of traditional light microscopes it now is possible to digitalize those samples. This digitalization is done with the help of a so called slide scanner. The result of such an operation is awhole slide image (WSI) [2]. The digital nature of WSIs opens the door to the realm of image processesing and analysis which yields certain benefits, such as the use of image segmentation and registration methods to support the pathologist in his/her work. A very promising area of image analysis are the so called neural networks¹, which follow a machine learning approach. Their use, especially in the area of image classification and object recognition, made big breakthroughs possible in the recent past, e.g. Karpathy and Fei-Fei [1], who created a neural network which is capable of describing an image or a scene with written text (see fig. 1.1 for some examples).

There is enormous potential in the use of neural networks in the digital pathology as well, but to transfer these algorithms and technologies, certain hindrances must be overcome. One of those hindrances is the need for proper training samples and an established ground truth². While generally there are huge amounts of WSIs, most of them won't be usable without further preparation as a training sample. One way of preparing them are annotations. These can be added to the WSIs, stored and later used for training.

Therefore the goal of this thesis is to give tools into the hands of pathologists to annotate whole slide images and save those annotations in such a way that they will be usable later in the combination with neural networks.

¹See chapter 2.1.3

² Ground truth refers to a training sample whose outcome is known and validated as true.

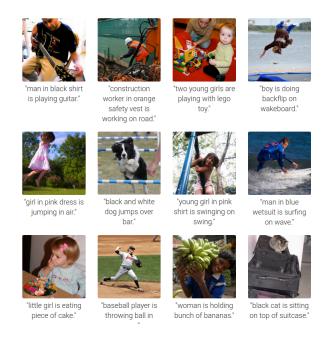


Figure 1.1: Example results of the in [1] introduced model (source: http://cs.stanford.edu/people/karpathy/deepimagesent/)

1.2 Research Objective

The objective of this thesis is the conceptualization and implementation of tools for WSIs, which allow for their annotation and a further usage in neural networks. As a requirement, the tools have to be implemented in the form of microservices³, each one with their own short documentation, including instructions for installation, usage and some examplary use cases. To achieve this goal, the implementation of 3 microservices is necessary.

The first microservice needs to be capable of converting a given set of image formats into the so called *Deep Zoom Image Format*⁴. The supported image formats are *.bif*, *.mrxs*, *.ndpi*, *.scn*, *.svs*, *.svslide*, *.tif*, *.tiff*, *.vms* and *.vmu*, in accordance with the capabilities of the Openslide framework [4].

The second microservices task is to give a tool at hand with which a pathologist will be able to annotate all those WSIs which were converted using the first microservice. Furthermore, the made annotations need to be persisted together with the highest resolution of the corresponding image.

The third microservice will be responsible for preparing the annotated WSIs for the further usage in neural networks. For that purpose the service needs to

³See chapter 2.1.2

⁴See chapter 2.1.1

be capable of dividing a single annotated whole slide image into multiple tiles, with the choice of either using the whole image or just the annotated areas.

1.3 About this thesis

Apart from the *Introduction*, there are 5 more chapters in this thesis.

Chapter 2 - Background defines some terminoligy and the general, required process chain which are all necessary to understand further chapters of this thesis. Furthermore, 3 microservices will be introduced in short.

Chapter 3 - Methodology gives an overview over the current state of research for each microservice, as well as best practices.

Chapter 4 - Implementation goes into further details about how each microservice is implemented and which software and frameworks were used for that.

Chapter 5 - Discussion will introduce a measurement for each microservice to measure its success. It will discuss the test setup as well as list the results.

Chapter 6 - Conclusion will interpret the Results from Chapter 5 and analyze them closer. Furthermore, it will give an idea of what steps are to be taken next in the future.

Background

2.1 Definition of terms

To prevent missunderstandings and confusion, the following subsections 2.1.1 - 2.1.3 will define some terminoligy which will be mandatory for the understanding of certain areas of this thesis.

2.1.1 Deep Zoom Image Format

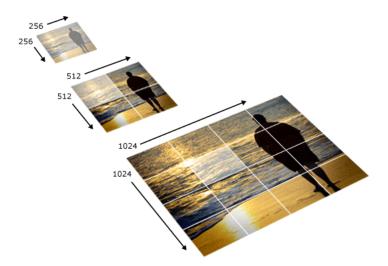


Figure 2.1: 3 consecutive levels of a dzi image (source: https://i-msdn.sec.s-msft.com/dynimg/IC141135.png)

The Deep Zoom Image Format (dzi) is an xml-based file format maintained by Microsoft to improve performance and quality in the handling of large image

files. For this purpose an image is represented in a tiled pyramid (see fig. 2.1).

As seen in fig. 2.1 there are multiple versions of a single image in different resolutions. Each resolution in the pyramid is called a *level*. At each level the image is scaled down by the factor 4 (2 in each dimension). Furthermore, the image gets tiled up into 256^2 tiles (256 in each dimension) [13].

If a viewer wants to view a certain area of the image (e.g. the highlighted tile in the last image in fig. 2.1), only the corresponding tiles need to be loaded. This saves large amounts of bandwidth and memory. The same goes for a viewer, who is zoomed out very far. In such a view the full level of detail isn't needed, so that a version from a lower level can be loaded.

A dzi file consists of two parts: a describing .xml file¹ and a folder with more subfolder. Each subfolder describes a level and as such contains all the tiles for that particular level.

2.1.2 Microservice

The concept of microservices is to separate one monolithic software construct into several smaller, modular pieces of software. According to [15], the idea of microservices is not new, but can be found in the UNIX philosophy. Three basic ideas are stated in [15]:

- A program should fulfill only one task, and it should do it well.
- Programs should be able to work together.
- Besides, the programs should use a universal interface.

As such, microservices are a modularization concept. However, they differ from other concepts, since they are independet from each other. This is a trait, other modularization concepts usually lack. As a result, changes in one microservice don't bring up the necessity of deploying the whole product again but just the one service.

Because of their inherent traits, microservices need to be their own processes in one way or another, may it be as an actual operating system process or as e.g. a docker container².

One big advantage of this modularization is that each service can be written in a different programming language, using different frameworks and tools. Furthermore, each microservice can bring along its own support services and data storages, like data bases. It is imperative for the concept of modularization, however, that each microservice has its own storage of which it is in charge of.

A disadvantage of this modularization is, that inter process communication becomes a necessity. However, there are different approaches with which microservices can communicate. [15] suggests the following:

 $^{^1 \}mbox{Frameworks}$ like OpenSeaDragon also support further formats, such as .json.

²Docker is a tool, which enables software to be wrapped up in so called "containers". Those containers are a complete, but stripped down, filesystem containing everything the software needs to run (e.g. source code, runtime environment, system tools and libraries, ...). See https://www.docker.com/what-docker

- communication via protocols like REST³
- an HTML user interfaces with links to other microservices
- data replication

It is important to define how and with which technology to communicate with, when addressing each microservices to ensure that this particular one can actually be reached with the defined method.

2.1.3 Neural Network

Artificial neural networks (NN) are a group of models inspiried by biological neural networks⁴. In a NN, regardless if artificial or biological, many neurons are interconnected with each other. The construct of interconnected neurons can be seperated into layers, of which there are three kinds:

- input layer
- hidden layer
- output layer

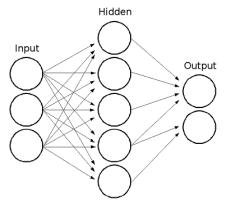


Figure 2.2: 3 layer NN (source: http://docs.opencv.org/2.4/_images/mlp.png)

Basically, the input layer, as the name suggests, is the layer where the NN gets its input data from. After that, there are a number of hidden layers⁵,

³Representational state transfer (REST) is architectural style for distributed hypermedia systems, see [7].

⁴For the remainder of this thesis, neural network will always represent the artificial one, unless explicitly stated otherwise.

 $^{^5\}mathrm{A}$ NN doesn't necessarily need to have any hidden layers. For non trivial problems however, it becomes mandatory.

which are responsible for further computation of the input values. At the end is the output layer which is responsible for communicating the results of the prior operations (compare fig. 2.2). Each single neuron has input values and an output value. Once the input reaches a certain trigger point, the cell in the neuron sends a signal as output.

A huge benefit of NN, over other software models, is their ability to learn. While certain problems are easier to solve in a sequential, algorithmic fashion (say an equation or the towers of hanoi), certain problems are so complex that new approaches are needed, while other problems can't be solved algorithmic at all. With the use of adequate training samples, a NN can train to solve a problem, not unlike a human, by learning. Since this topic alone is enough for a number of theses, the author refers to [12] for further detailed information.

2.2 Process Chain

This section and its following subsections (2.2.1 - 2.2.3) are dedicated to illustrate the process chain necessary to accomplish the research objective stated in chapter 1.2. The process chain consists of the following steps:

- (a) convert WSIs of different⁶ formats to dzi format
- (b) annotate dzi images with the annotation tool made for this purpose
- (c) persist made annotations in a file
- (d) seperate annotated images into tiles of custom size
- (e) keep correspondence between tiles of an image and its annotations

To fulfill those steps, 3 Microservices will be introduced in the following subsections. Those are:

- Conversion Service (see chap. 2.2.1)

 This service will be responsible for converting WSIs into the dzi format (a).
- Annotation Service (see chap. 2.2.2)
 This service will offer a tool to annotate an image (b) and persist made annotations (c).
- Tessellation Service (see chap. 2.2.3)
 This service will be responsible for seperating an image into tiles (d) and keep the correspondence between tiles and annotations (e).

 $^{^6\}mathrm{See}$ chap. 2.2.1 for a listing of valid input formats.

2.2.1 Definition of Conversion Service

The devices which create an WSI, so called whole slide scanners, create images in various formats, depending on the producer. The conversion service has the goal of converting those formats into the dzi format, not only for the purpose of unification, but also to add the deep zoom feature⁷ to the images (see fig. 2.3). This is of special importance, since an average WSI with 1,600 megapixels has a size of approximately 4.6 GB [6].

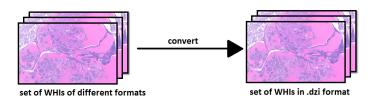


Figure 2.3: Visualization of the Conversion Service

The Conversion Service will be implemented as a python script, which upon calling takes every single WSI of a certain format inside a given folder and converts it to the dzi format. Each converted WSI will be saved in another specified folder. Valid image formats (and their corresponding producers) for conversion are:

- .bif (Ventana)
- .mrxs (Mirax)
- .ndpi (Hamamatsu)
- .scn (Leica)
- .svs (Aperio)
- .svslide (Sakura)
- .tif (Aperio, Trestle, Ventana)
- .tiff (Philips)
- .vms (Hamamatsu)
- .vmu (Hamamatsu)

 $^{^7}$ See chap. 2.1.1

2.2.2 Definition of Annotation Service

The first step to create a valid training sample for a NN is to annotate the WSIs which will later serve as that. To do so, a GUI must be deployed which enables a pathologist to make annotations to an WSI. Additionally, the Annotation Service also needs to be capable to persist made annotations (see fig. 2.4). This will happen by saving the annotations into a file which will be placed next to the image.

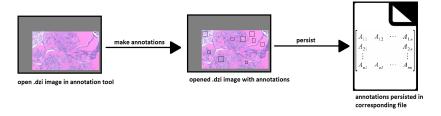


Figure 2.4: Visualization of the Annotation Service

To enable the pathologist to make annotations in the first place, a GUI needs to be offered by the service. This GUI will be developed in iterations with the help of a number of pathologists to adapt it to their wishes and grant the best possible usability. The basic concept of the first iteration will be based on the Microdraw⁸ GUI (see fig. 2.5).

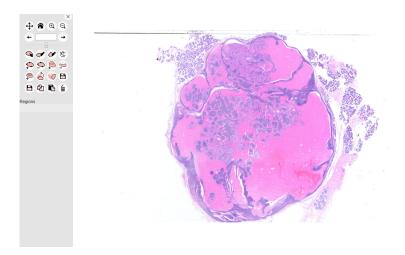


Figure 2.5: Microdraw GUI with opened WSI

 $^{^8 \}mathrm{See}$ https://github.com/r03ert0/microdraw for more information on the Microdraw project

Microdraw is a webbased annotation tool, which describes itself as

"[...] a collaborative vectorial annotation tool for ultra high resolution data, such as that produced by high-throughput histology." [14]

Therefore, the GUI of the Annotation Service, or Annotation Service Viewer (ASV), will run as a web application in a browser. Annotations will be made by selecting a shape or annotation method from the various tools in the toolbar (see the gray bar on the left in fig. 2.5). After selecting the area to be annotated, an actual description of that area can be made via keyboard input.

When the pathologist is done or wants to save the made annotations, the Annotation Service will create a file in which they will be persisted in. Only one WSI can be opened in one ASV at a time.

2.2.3 Definition of Tessellation Service

The task of the Tessellation Service is to tessellate a given WSI into multiple tiles while keeping up the correspondence between image areas and annotations (see fig. 2.6). Tessellation describes the process of seperating a geometric space (e.g. a plane) into multiple tiles of one or more shapes. No matter if the tiles are unifrom or of different shapes, there must be no gaps or overlapping areas in the resulting tiles.

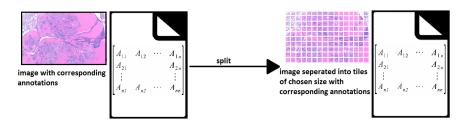


Figure 2.6: Visualization of the Tessellation Service

The tessellation of the Tessellation Service differs from the given definition in two aspects. First, all tiles will be of a unifrom shape (square). Second, the service will also offer the possibility of seperating only the annotated areas of an WSI into tiles. Therefore, the "no gaps" rule is invalid, when this option is chosen. The rule of no overlapping areas holds true in either case, however.

As mentioned before, the second task of the Tessellation Service is to ensure the correspondence between tiles and annotations of the original WSI. This means that, if the original WSI has an annotation in the area of a tile, this tile needs to have the same annotation.

Conversion Service

3.1 Methodology

The objective of the Conversion Service is to convert a given set of input WHIs into dzi files. Since a dzi is layered into a pyramid scheme, it is necessary to calculate the needed number of levels, as well as the dimensions of each level (see fig. 3.1 for an example).

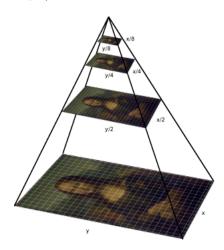


Figure 3.1: Example of a pyramid scheme in image processing (source: http://ipimage.sourceforge.net/images/pyramid.png)

Therefore, the Conversion Service must be able to open an WHI img_{input} of any of the in 2.2.1 defined formats. Based on the size of img_{input} the number of necessary levels lvl must be calculated. Once lvl has been determined, img_{input} must be resized into an appropriate scale for each lvl_i in lvl. The resized image will be called img_i , with i representing the corresponding level. In the next

step, every img_i will be tessellated into x * y tiles. Each tile will be referrenced via $t_{c,r}^i$, with r being the row and c being the column of the tile in whi_i . To complete the conversion, the Conversion Service must create a describing xml file for each converted image img_{dzi} .

3.1.1 Creating a Deep Zoom Image

To create a dzi, the Conversion Service must be capable of all the afore mentioned tasks. According to [9], there is a number of frameworks, that can achieve this task (see tab. 3.1).

Since the conversion to dzi is required, two frameworks are not usable from the start. Those are MapTiler, who creates tms¹ images and Kakadu, which creates iiif² images. Furthermore, the various desktop applications are not usable either, since the Conversion Service should operate as a microservice.

For a python script, deepzoom.py would be the natural choice, however at a second glance it can be seen that VIPS offers "[...] for a number of languages" (see tab. 3.1). One of those languages happens to be python. Therefore, deepzoom.py and VIPS will be further investigated in the following two subsections.

 $^{^1\}mathrm{Tile}$ Map Service (tms) is a tile scheme developed and maintained by the Open Source Geospatial Foundation [8]

²International Image Interoperability Framework (iiif), specified by the International Image Interoperability Framework group, is an image delivery API which responds to requests via HTTP and HTTPS [5]

option	description	image	for-
		mat	
Deep Zoom Com-	dekstop app for Windows	dzi	
poser			
Image Composite	panoramic image stitcher	dzi	
Editor	from Microsoft Research		
	for the Windows desktop		
DeepZoomTools.dll	.NET-library, comes with	dzi	
	Deep Zoom Composer		
deepzoom.py	Python	dzi	
deepzoom	Perl utility	dzi	
PHP Deep Zoom	PHP	dzi	
Tools			
Deepzoom	PHP	dzi	
DZT	an image slicing library	dzi	
	and tool written in Ruby		
MapTiler	desktop app for Windows,	tms	
	Mac, Linux		
VIPS	command line tool and li-	dzi	(via
	brary for a number of lan-	dzsave	fea-
	guages	ture)	
Sharp	Node.js, uses VIPS	dzi	
MagickSlicer	shell script (Linux/Max)	dzi	
Gmap Uploader	C++	dzi	
Tiler			
Node.js Deep Zoom	Node.js, under construc-	dzi	
Tools	tion		
OpenSeaDragon	Web app (and PERL and	dzi	
DZI Online Com-	PHP scripts)		
poser			
Zoomable	service, offers embeds; no	dzi	
	explicit API		
ZoomHub	service, under construc-	dzi	
	tion		
Kakadu	C++ library to encode or	iiif	
	decode JPEG 2000 images		
PyramidIO	Java (command line and	dzi	
	library)		

Table 3.1: Overview of conversion options for zooming image formats (source: [9])

3.1.2 Deepzoom.py

Deepzoom.py³ is a python script and part of Open Zoom⁴. It can either be called directly over a terminal or imported as a module in another python script. The conversion procedure itself is analogous for both methods.

If run in a terminal the call looks like the following:

```
$ python deepzoom.py [options] [input file]
```

The various options and their default values can be seen in tab. 3.2. If called without a designated output destination, deepzoom.py will save the converted dzi right next to the original input file.

option	description	default
-h	show help dialog	-
-d	output destination	-
-s	size of the tiles in pixels	254
-f	image format of the tiles	jpg
-O	overlap of the tiles in pixels (0 - 10)	1
-q	quality of the output image $(0.0 - 1.0)$	0.8
-r	type of resize filter	antialias

Table 3.2: Options for deepzoom.py

The resize filter is applied to interpolate the pixels of the image when changing its size for the different levels. Supported filters are:

- cubic
- biliniear
- bicubic
- nearest
- antialias

When used as module in another python script, deepzoom.py can simply be imported via the usual *import* command. To actually use deepzoom.py, a Deep Zoom Image Creator needs to be created. This class will manage the conversion process:

```
# Create Deep Zoom Image Creator
creator = deepzoom.ImageCreator(tile_size=[size],
tile_overlap=[overlap], tile_format=[format],
image_quality=[quality], resize_filter=[filter])
```

³See https://github.com/openzoom/deepzoom.py for further details

⁴See https://github.com/openzoom for further details

The options are analogous with the terminal version (compare tab. 3.2). To start the conversion process, the following call must be made within the python script:

```
# Create Deep Zoom image pyramid from source creator.create([source], [destination])
```

Upon calling, the ImageCreator opens the input image img_{input} and creates a description with all the needed information for the dzis describing xml file⁵. After that, the number of levels is calculated. For this, the bigger value of height and width of img_{input} is chosen (see eq. 3.1) and then used to determine the number of levels lvl (see eq. 3.2).

$$max_dim = max(height, width)$$
 (3.1)

$$lvl = \lceil log_2(max_dim) + 1 \rceil \tag{3.2}$$

Once lvl has been determined, img_{input} will be resized in the chosen quality (-q/image_quality) for every level i, with $i \in (0, lvl - 1)$. The new resolution will be calculated for both dimensions dim with a function scale (see eq. 3.3) analogously. Furthermore, the image will be interpolated with the specified filter (-r/resize_filter). The resized image will be called img_i .

$$scale = \lceil dim * 0.5^{lvl-i} \rceil \tag{3.3}$$

Once img_i has been created, it will be tessellated into as many tiles of the specified size (-s/tile_size) and with the specified overlap (-o/tile_overlap) as possible. Since not every image will be of the size $2^n, n \in$ in either dimension, it is highly likely that the set of tiles for the last column/row will be smaller then specified in either dimension.

Every tile will be saved as [column]_[row].[format] ([format] depending on - $f/file_format$) in a folder called according to the corresponding level i. This folder will be located inside another folder, called [filename]_files. The describing xml file will be persisted as [filename].dzi on the same level.

3.1.3 VIPS

VIPS (VASARI Image Processing System) describes itself as "[...] a free image processing system [...]" [3]. It includes a wide range of different image processing tools, such as various filters, histograms, geometric transformations and color processing algorithms. It also supports various scientific image formats, especially those needed for the Conversion Service⁶ [3].

VIPS comes in two parts: the actual library (called library) and a GUI (called nip2). library offers interfaces for C, C++, python and the command

⁵Compare chap. 2.1.1

 $^{^6}$ See chap. 2.2.1

line. The GUI will not be further discussed, since it is of no interest for the implementation of the Conversion Service.

One of the strongest traits of VIPS is its speed and little data usage compared to other imaging libraries [11]. Given the task of the Conversion Service to convert WSIs of various formats, which tend to be quite large, both of those perks are especially welcome.

VIPS superior speed and little data usage comes from a fully demand-driven image input/output system. While conventional imaging libraries queue their operations and go through them sequentially, VIPS awaits a final write command, before actually manipulating the image. All the queued operations will then be evaluated and molded into a few single operations. Thus, requiring no additional disc space for intermediates and no unnecessary disc in- and output. Furthermore, if more than one CPU is available, VIPS will automatically evaluate in parallel [10].

As mentioned before, VIPS has a command line and python interface. In either case, a function called dzsave(...) will manage the conversion from a WSI to a dzi. A call in the terminal will look like the following:

```
$ vips dzsave [input] [output] [options]
```

When called, VIPS will take the image [input], convert it into the dzi file format and then save it to [output]. The various options and their default values can be seen in tab. 3.3.

option	description	default
layout	directory layout (allowed: dz, google, zoomify)	dz
overlap	tile overlap in pixels	1
centre	center image in tile	false
depth	pyramid depth	onepixel
angle	rotate image during save	d0
container	pyramid container type	fs
properties	write a properties file to the output directory	false
strip	strip all metadata from image	false

Table 3.3: Options for VIPS

A call in python does have the same parameters and default values. It looks like this:

```
image = Vips.Image.new_from_file(input)
image.dzsave(output[, options])
```

In line 1 the image gets opened and saved into *image*. While being opened, further operations could be done. The command in line 2 writes the processed image into the specified output location.

3.2 Implementation

As stated before, the Conversion Service is implemented as a python script. The first iteration of the script used deepzoom.py for the conversion. This caused severe performance issues though. Out of all the image files in the test set⁷, only one could be converted⁸. Every other file was either too big, so the process would eventually be killed by the operating system or exit with an IOError concerning the input file from the PIL imaging library. The second iteration of the Conversion Service uses VIPS, which is faster then deepzoom.py and also capable of converting all the given test images.

The script has to be called inside a terminal in the following fashion:

```
$ python ConversionService.py [input dir] [output dir]
```

It is mandatory to specify the input and output directory in the call, so the script knows where to look for images up to conversion and where to save the resulting dzi files.

Upon calling, the main() routine will be started, which or chestrates the whole conversion process. It looks as follows:

```
def main():
    path = checkParams()
    files = os.listdir(path)

for file in files:
    print("-------")

extLen = getFileExt(file)
    if(extLen != 0):
        print("converting " + file + "...")
        convert(path, file, extLen)
        print("done!")
```

checkParams() checks if the input parameters are valid and, if so, returns the path to the specified folder or exit otherwise. Furthermore, it will create the specified output folder, if it doesn't exist already. In the next step, the specified input folder will be checked for its content. getFileExt(file) looks up the extension of each contained file and will either return the length of the files extension or 0 otherwise. Each valid file will then be converted with the convert(...) function:

```
# convert image source into .dzi format
# param path: directory of param file
# param file: file to be converted
# param extLen: length of file extension
def convert(path, file, extLen):
dzi = OUTPUT + file[:extLen] + "dzi"
im = Vips.Image.new_from_file(path + file)
im.dzsave(dzi, overlap=OVERLAP, tile_size=TILESIZE)
```

The name for the new dzi file will be created from the original file name, however, the former extension will be replaced by "dzi" (see line 6). OUTPUT

 $^{^7}$ See chap. 3.3

⁸CMU-3.svs from Aperio, see Appendix A

specifies the output directory which the file will be saved to. Next, the image file will be opened with Vips' Image class. Afterwards, dzsave(...) will be called, which handles the actual conversion into the dzi file format. OVERLAP and TILESIZE are global variables which describe the overlap of the tiles and their respective size. Their values are 0 (OVERLAP) and 256 (TILESIZE). The output will be saved to the same folder as ConversionService.py is operating from, plus "dzi/[OUTPUT]/".

3.3 Test

To test the correct functionality of the Conversion Service, test data is needed. OpenSlide offers a selection of freely distributable data⁹, which can be used for that purpose.

Since the WSIs are of enormous size, they are not delivered via the repository. Instead they need to be downloaded separately from the OpenSlide homepage. For a complete listing of the used test data see Appendix A.

3.3.1 Setup

To create a controlled environment for the test, a new directory will be created, called *CS_test*. A copy of ConversionService.py as well as a directory containing all the test WSIs (called *input*) will be placed in that directory.

Input contains the following slides:

- (1) CMU-2 (Aperio, .svs)
- (2) CMU-1 (Generic Tiled tiff, .tiff)
- (3) OS-3 (Hamamatsu, .ndpi)
- (4) CMU-2 (Hamamatsu, .vms)
- (5) Leica-2 (Leica, .scn)
- (6) Mirax2.2-3 (Mirax, .mrxs)
- (7) CMU-2 (Trestle, .tif)
- (8) OS-2 (Ventana, .bif)

Because of their structure, (4), (6) and (7) will be placed in directories titled with their file extension. Fig. 3.2 shows the content of the input folder.

⁹See OpenSlides Homepage: http://openslide.cs.cmu.edu, or directly for the test data: http://openslide.cs.cmu.edu/download/openslide-testdata/

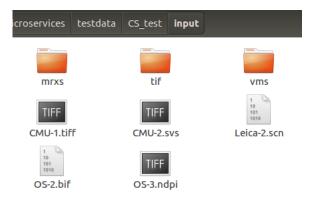


Figure 3.2: Content of input directory

This makes multiple calls of the Conversion Service necessary. The calls, in that order, are:

```
$ python ConversionService.py input/ out_1/
$ python ConversionService.py input/mrxs out_2/
$ python ConversionService.py input/tif out_3/
$ python ConversionService.py input/vms out_4/
```

3.3.2 Result

All runs of ConversionService.py were successful. Tab. 3.3 shows an overview of the results:

input	output	time (sec)
input/	CMU-1.dzi, CMU-2.dzi, Leica-2.dzi, OS-2.dzi, OS-3.dzi	1992
input/mrxs/	Mirax2.2-3.dzi	500
input/tif/	CMU-2.dzi	56
input/vms/	CMU-2-40x - 2010-01-12 13.38.58.dzi	305

Table 3.4: Results of Conversion Service Test

The vast difference in file size of the test data accounts for the different run times of the tests. While the first test converted 5 WSIs (399 sec/WSI), every other test converted a single one. The conversion of (6) was much faster, since the file was smaller in size (304.22 MB) compared to the others (1495.24 MB on average).

Annotation Service

- 4.1 Methodology
- 4.1.1 DICOM
- 4.2 Implementation
- 4.3 Test
- 4.3.1 Setup
- **4.3.2** Result

Tessellation Service

- 5.1 Methodology
- 5.2 Implementation
- 5.3 Test
- 5.3.1 Setup
- 5.3.2 Result

Conclusion

- 6.1 Results
- 6.2 Conclusion
- 6.3 Future tasks

Appendices

Appendix A

Listing of Conversion Service Test Data

The test data for the Conversion Service can be found at OpenSlides homepage, at the freely distributable test data section¹. Various slides can be found there. The following subsections (A.1 - A.8) give listings of all used WSIs, sorted by vendor and file format.

A.1 Aperio (.svs)

name	size (MB)	description
CMU-1-JP2K-33005.svs	126.42	Export of CMU-1.svs, bright-
		field, JPEG 2000, RGB
CMU-1-Small-Region.svs	1.85	Exported region from CMU-
		1.svs, brightfield, JPEG, small
		enough to have a single pyramid
		level
CMU-1.svs	169.33	Brightfield, JPEG
CMU-2.svs	372.65	Brightfield, JPEG
CMU-3.svs	242.06	Brightfield, JPEG
JP2K-33003-1.svs	60.89	Aorta tissue, brightfield, JPEG
		2000, YCbCr
JP2K-33003-2.svs	275.85	Heart tissue, brightfield, JPEG
		2000, YCbCr

 $\label{lem:cs.cmu.edu/download/openslide} Table A.1: Aperio data set (source: http://openslide.cs.cmu.edu/download/openslide-testdata/Aperio/)$

¹http://openslide.cs.cmu.edu/download/openslide-testdata/

A.2 Generic Tiled tiff (.tiff)

name	size (MB)	description
CMU-1.tiff	194.66	Conversion of CMU-1.svs to
		pyramidal tiled TIFF, brightfield

A.3 Hamamatsu (.ndpi)

name	size (MB)	description
CMU-1.ndpi	188.86	Small scan with valid JPEG
		headers, brightfield, circa 2009
CMU-2.ndpi	382.14	Brightfield, circa 2009
CMU-3.ndpi	270.1	Brightfield, circa 2009
OS-1.ndpi	1,860	H&E stain, brightfield, circa
		2012
OS-2.ndpi	931.42	Ki-67 stain, brightfield, circa
		2012
OS-3.ndpi	1,370	PTEN stain, brightfield, circa
		2012

A.4 Hamamatsu (.vms)

name	size (GB)	description
CMU-1.zip	0.62	Brightfield
CMU-2.zip	1.13	Brightfield
CMU-3.zip	0.91	Brightfield

Table A.4: Hamamatsu data set (.vms, source: http://openslide.cs.cmu.edu/download/openslide-testdata/Hamamatsu-vms/)

A.5 Leica (.scn)

name	size (GB)	description
Leica-1.scn	0.28	Brightfield, single ROI,
		2010/10/01 schema
Leica-2.scn	2.1	Mouse kidney, H&E stain,
		brightfield, multiple ROIs with
		identical resolutions, 2010/10/01
		schema
Leica-3.scn	2.79	Mouse kidney, H&E stain,
		brightfield, multiple ROIs with
		different resolutions, 2010/10/01
		schema
Leica-Fluorescence-1.scn	0.02	Fluorescence, 3 channels, single
		ROI, 2010/10/01 schema

Table A.5: Leica data set (source: http://openslide.cs.cmu.edu/download/openslidetestdata/Leica/)

A.6 Mirax (.mrxs)

name	size (GB)	description
CMU-1-Exported.zip	2.02	Export of CMU-1.mrxs
		with overlaps resolved,
		brightfield, JPEG, CUR-
		RENT_SLIDE_VERSION 2.3
CMU-1-Saved-1_16.zip	0.003	Quick save of CMU-1.mrxs
		at 1/16 resolution (multi-
		ple positions per image),
		brightfield, JPEG, CUR-
		RENT_SLIDE_VERSION 1.9
CMU-1-Saved-1_2.zip	0.14	Quick save of CMU-1.mrxs at
		1/2 resolution (multiple images
		per position), brightfield, JPEG,
		CURRENT_SLIDE_VERSION
		1.9
CMU-1.zip	0.54	Brightfield, JPEG, CUR-
		RENT_SLIDE_VERSION 1.9
CMU-2.zip	1.22	Brightfield, JPEG, CUR-
		RENT_SLIDE_VERSION 1.9
CMU-3.zip	0.65	Brightfield, JPEG, CUR-
		RENT_SLIDE_VERSION 1.9
Mirax2-Fluorescence-	0.06	Fluorescence, 3 channels, JPEG,
1.zip		CURRENT_SLIDE_VERSION 2
Mirax2-Fluorescence-	0.04	Fluorescence, 3 channels, JPEG,
2.zip		CURRENT_SLIDE_VERSION 2
Mirax2.2-1.zip	2.61	HPS stain, brightfield, JPEG,
		CURRENT_SLIDE_VERSION
		2.2
Mirax2.2-2.zip	2.38	HPS stain, brightfield, JPEG,
		CURRENT_SLIDE_VERSION
		2.2
Mirax2.2-3.zip	2.77	HPS stain, brightfield, JPEG,
		CURRENT_SLIDE_VERSION
		2.2
Mirax2.2-4-BMP.zip	0.95	Brightfield, BMP, CUR-
		RENT_SLIDE_VERSION 2.2
Mirax2.2-4-PNG.zip	1.01	Brightfield, PNG, CUR-
		RENT_SLIDE_VERSION 2.2

 $\label{lem:alpha} \begin{tabular}{ll} Table A.6: Mirax data set (source: http://openslide.cs.cmu.edu/download/openslide-testdata/Mirax/) \end{tabular}$

A.7 Trestle (.tiff)

name	size (MB)	description
CMU-1.zip	158.87	Brightfield
CMU-2.zip	304.22	Brightfield
CMU-3.zip	223.11	Brightfield

 $\label{lem:cs.cmu.edu/download/openslide.cs.cmu.edu/download/openslide-testdata/Trestle/)} Table A.7: Trestle data set (source: http://openslide.cs.cmu.edu/download/openslide-testdata/Trestle/)$

A.8 Ventana (.bif)

name	size (GB)	description
OS-1.bif	3.61	H&E stain, brightfield
OS-2.bif	2.53	Ki-67 stain, brightfield

 $\label{lem:table A.8: Trestle data set (source: http://openslide.cs.cmu.edu/download/openslide-testdata/Trestle/)} \\$

Bibliography

- [1] L. Fei-Fei A. Karpathy. Deep Visual-Semantic Alignments for Generating Image Descriptions. Department of Computer Science, Standford University, 2015. http://cs.stanford.edu/people/karpathy/cvpr2015.pdf.
- [2] T. Cornish. An introduction to digital whole slide imaging and whole slide image analysis. http://www.hopkinsmedicine.org/mcp/PHENOCORE/CoursePDFs/2013/13%2019%20Cornish%20Digital%20Path.pdf, July 2013. Accessed: 12.04.2016.
- [3] J. Cupitt. Vips. http://www.vips.ecs.soton.ac.uk/index.php?title= VIPS. Accessed: 25.05.2016.
- [4] A. Goode et al. Openslide: A vendor-neutral software foundation for digital pathology. *J pathol inform*, 4(1), September 2013. http://download.openslide.org/docs/JPatholInform_2013_4_1_27_119005.pdf.
- [5] M. Appleby et al. Iiif image api 2.0. http://iiif.io/api/image/2.0/#status-of-this-document. Accessed: 26.04.2016.
- [6] N. Farahanil et al. Whole slide imaging in pathology: advantages, limitations, and emerging perspectives. Pathology and Laboratory Medicine International, 7, June 2015. https://www.dovepress.com/whole-slide-imaging-in-pathology-advantages-limitations-and-emerging-p-peer-reviewed-fulltext-article-PLMI#ref10.
- [7] R. Fielding. Architectural Styles and the Design of Network-based Software Architectures. PhD thesis, University of Carolina, 2000. http://www.ics.uci.edu/~fielding/pubs/dissertation/top.htm.
- [8] Open Source Geospatial Foundation. Tile map service specification. http://wiki.osgeo.org/wiki/Tile_Map_Service_Specification. Accessed: 26.04.2016.
- [9] I. Gilman. Openseadragon. http://openseadragon.github.io/examples/creating-zooming-images/. Accessed: 26.04.2016.
- [10] K. Martinez J. Cupitt. Vips: an image processing system for large images. *Proc. SPIE*, 2663:19 - 28, 1996. http://eprints.soton.ac.uk/252227/ 1/vipsspie96a.pdf.

- [11] K. Martinez J. Cupitt. Vips a highly tuned image processing software architecture. In *IEEE International Conference on Image Processing*, pages 574 577, September 2005. http://eprints.soton.ac.uk/262371/.
- [12] D. Kriesel. A Brief Introduction to Neural Networks, 2007. http://www.dkriesel.com/en/science/neural_networks.
- [13] Microsoft. Deep zoom file format overview. https://msdn.microsoft.com/en-us/library/cc645077(v=vs.95).aspx. Accessed: 11.04.2016.
- [14] Roberto Toro. Microdraw. https://github.com/r03ert0/microdraw/wiki. Accessed: 18.04.2016.
- [15] E. Wolff. *Microservices Primer*. innoQ, January 2016. https://leanpub.com/microservices-primer/read.

List of Figures

1.1	Example results of the in [1] introduced model (source: http://cs.stanford.edu/people/karpathy/deepimagesent/)	4
2.1	3 consecutive levels of a dzi image (source: https://i-msdn.sec.s-	
	msft.com/dynimg/IC141135.png)	6
2.2	3 layer NN (source: http://docs.opencv.org/2.4/_images/mlp.png)	8
2.3	Visualization of the Conversion Service	10
2.4	Visualization of the Annotation Service	11
2.5	Microdraw GUI with opened WSI	11
2.6	Visualization of the Tessellation Service	12
3.1	Example of a pyramid scheme in image processing (source: http:	
	<pre>//iipimage.sourceforge.net/images/pyramid.png)</pre>	13
3.2	Content of input directory	21

List of Tables

3.1	Overview of conversion options for zooming image formats (source:
	[9])
3.2	Options for deepzoom.py
3.3	Options for VIPS
3.4	Results of Conversion Service Test
A.1	Aperio data set (source: http://openslide.cs.cmu.edu/download/openslide-
	testdata/Aperio/)
A.2	Generic Tiled tiff data set (source: http://openslide.cs.cmu.edu/download/openslide-
	testdata/Generic-TIFF/)
A.3	Hamamatsu data set (.ndpi, source: http://openslide.cs.cmu.edu/download/openslide
	testdata/Hamamatsu/)
A.4	Hamamatsu data set (.vms, source: http://openslide.cs.cmu.edu/download/openslide-
	testdata/Hamamatsu-vms/)
A.5	Leica data set (source: http://openslide.cs.cmu.edu/download/openslide-
	testdata/Leica/)
A.6	
	testdata/Mirax/)
A.7	Trestle data set (source: http://openslide.cs.cmu.edu/download/openslide-
	testdata/Trestle/)
A.8	Trestle data set (source: http://openslide.cs.cmu.edu/download/openslide-
	testdata/Trestle/)