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Abstract

Preface

Bla bæa

Contents

Chapter 1

Background

This chapter encompasses background knowledge that optimizes the understanding of essential topics in this project, such as patellofemoral pain and deep learning. Regarding patellofemoral pain it is relevant to get knowledge about the anatomy of the knee as well as pain and pain measurements if a deeper understanding of the syndrome is considered necessary. Furthermore, the chapter is essential for getting a basic understanding of some properties in the neural network models used in this project.

1.1 Anatomy of the Knee

The knee is the largest synovial joint in the body and consists of a hinge and a gliding joint. The hinge joint is placed between the lateral and medial femoral condyles and the lateral and medial tibial condyles. The gliding joint is formed between the patella and femur. The structure of the knee is illustrated in figure 1.1.[1]

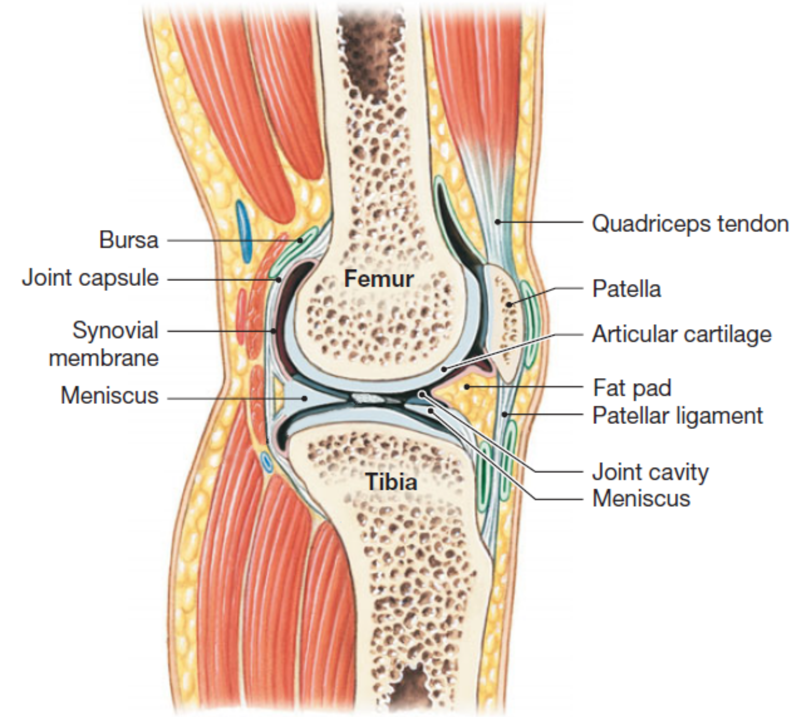

Figure 1.1: *The figure illustrates the anatomy of the knee. Edited from [1].*

It is shown in figure 1.1 that the patella is a sesamoid bone. At birth the patella consists of cartilaginous and ossifies when the child's extremities gets stronger, which typically proceeds between age two or three and the beginning of puberty.

The patella is surrounded by the tendon of the quadriceps femoris. Quadriceps femoris is the muscles which controls the extending of the knee. The quadriceps tendon is combined to the surface anterior and superior of patella. Tibia is combined to the anterior and inferior surface of the patella by the patellar ligament. The bones, tibia and femur, are covered by articular cartilage with the purpose of protecting the bones from friction. The articular cartilage on the two bones are separated from one another by synovial membranes that contains synovial fluid, that further reduce the friction. The primary functions of the synovial fluid is to lubricate, distribution of nutrient and absorption of shock.[1]

The fat pads and menisci are placed between the articular cartilages. The fat pads' function is to protect the cartilage and fill out space as result of the joint cavity changes. The menisci stabilize the knee and acts like pads, that conform shape when femur moves. In addition to fat pads and menisci the bursa acts as friction minimization between patella and tissues.[1]

There are three separate articulations in the knee joint. The first is between the patella and the patellar surface of the femur and the rest are between the femoral and tibial condyles. Additionally, the knee consist of seven major ligaments that stabilize the knee joint, which is shown in figure 1.2.[1]

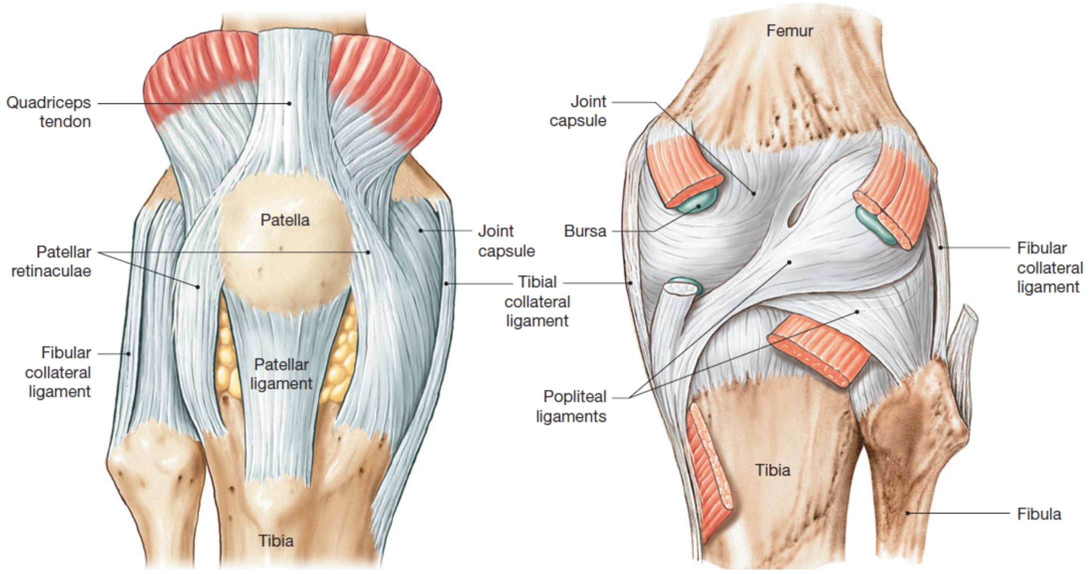

Figure 1.2: *The figure illustrates the anatomy of the knee with focus on the ligaments. Edited from [1].*

The ligaments patellar retinaculae and patellar ligament support the anterior surface of the knee. When the knee is fully extended, the tibial and fibular collateral ligament are responsible for stabilizing the joint. Between femur and the two lower bones in the leg, tibia and fibula, is the location of the two popliteal ligaments, which stabilize the posterior surface of the joint. In addition to the visible ligaments in figure 1.2 there are the anterior cruciate ligament (ACI) and posterior cruciate ligament (PCL) in the joint capsule. The two ligaments cross each other and are connected to the tibial and femoral condyles. They reduce the movement, anterior and posterior.[1]

As previously mentioned the gliding joint is formed between the patella and femur, so that during knee movement patella is gliding up and down at the femoral condyle. A condition associated with incorrect movement of the patella, is patellofemoral pain syndrome (PFPS), that occurs when the patella moves outside of its ordinary track, which for instance can be movement in lateral direction.[1]

1.2 Pain

The International Association for the Study of Pain (IASP) has defined pain as being "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" [2, 3].
Humans are aware of the surroundings and threats to their bodies because of the pain. The pain indicates that there might be a risk for permanent damage on the body, which refrain humans from danger and therefore increases the chances of survival.
Pain can be either nociceptive or neuropathic. Nociceptive pain is associated with tissue damage. This type of pain is related to the nociceptors, which are receptors with a high threshold that when stimulated gives the perception of pain in tissues [4]. Neuropathic pain occurs central from the nervous system. This pain can be caused by illness or physical damage.

Furthermore, pain can be divided into three categories: acute pain (less than three months), persistent or chronic pain and cancer pain.[5] Additionally, the sense of pain can be divided into some qualities, which is shown in figure 1.3.

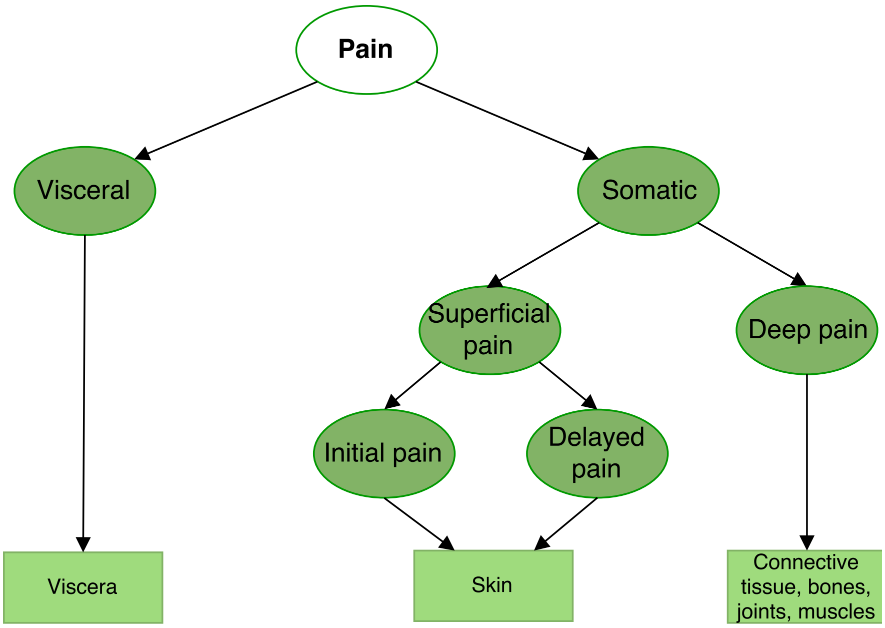

Figure 1.3: *Model of pain qualities. Ovals with green background represent qualities of pain. The rectangles show where the pain occured. Edited from [4].*

Pain can be divided into two qualities; visceral and somatic pain. Visceral pain is associated with e.g. gallstone pain and appendicitis. This pain can be characterised as a dull or diffuse feeling. Somatic pain is subdivided into superficial pain and deep pain. If the pain derives from the skin it is superficial pain, which furthermore is divided into initial pain and delayed pain. The initial pain is the first pain that is received, and this pain is characterised as sharp and localizable. The delayed pain, also known as the second pain, is sensed as a dull or burning pain that occur after a half to one second. This pain is more difficult to localise than

the initial pain and lasts longer.[3, 4] The other somatic pain is deep pain, which is associated with pain from the muscles, bones, joints and connective tissue. This pain is described as a dull pain and it radiates into the surrounding tissue, which makes the exact pain area hard to point out.[3, 4]
Since the aetiology of PFPS still remains unclear [6], it is hard to place this type of pain in addition to nociceptive and neuropathic pain. But PFPS can be classified as deep pain and acute or chronic pain. Since the PFPS is often longer than six month it is described as a chronic deep pain.

1.3 Pain measurement

There are many ways of measuring pain, but none of them are valid or reliable in terms of objectively quantifying a subjects experienced pain [7]. There is both subjective and objective methods to measure and identify pain. The subjective method is used to collect knowledge of the subjects pain intensity, behavior and how it is experienced. Whereas the objective methods are used to identify the pain and find some physical damage that causes the pain.

1.3.1 Subjective pain measurement

Pain is experienced and perceived subjectively [2, 7] and is dependent on personality and character [4], which is why it is important to measure the pain from the subject's perspective. One of the subjective methods used to measure knee pain is Knee injury and Osteoarthritis Outcome Score (KOOS), which is a questionnaire about symptoms, stiffness, pain, function daily living, function, sports and recreational activities and quality of life. When the subjects fill the scheme a score between zero and one hundred is achieved. A score at zero represents extreme knee problems, whereas a score at one hundred represents no knee problems.[8] The questionnaire can be seen in Appendix A.1.

1.3.2 Objective pain measurement

A objective pain measurement is often used when a subject experiences knee pain where a clinical examination of the knee can occur. This examination involves i.a. provocative tests, such as anterior and posterior drawer test, Lachman's test and pivot test that examines the integrity of the ACL and PCL. Furthermore is McMurray test which test for meniscal tear.[9] Illustrations of the tests are shown in figure 1.4.

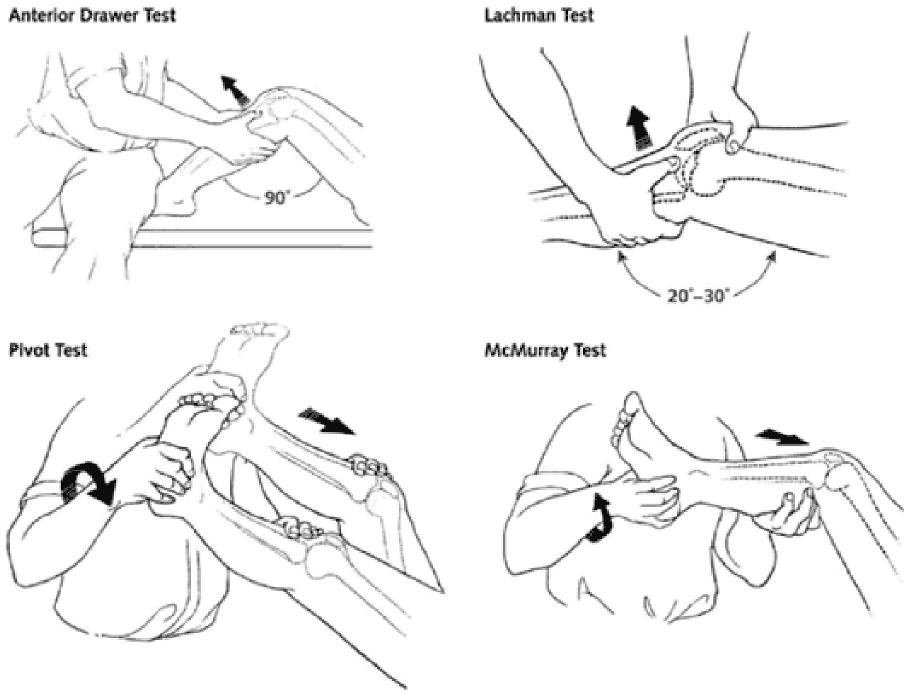

Figure 1.4: *Clinical examination with provocative tests; Anterior Drawer Test, Lachman Test, Pivot Test and McMurray Test.[9]*

In addition to clinical tests is there some paraclinical tests such as X-ray and MRI, but PFPS does not show any structural changes in the knee [10] which makes it difficult for healthcare personnel to treat the subjects. A method that makes it possible for subjects to describe their pain is pain mapping, which is described in the following section.

1.3.3 Pain mapping

Pain mapping is a technique, that Harold Palmer introduced in 1949 [11], which is used to transfer a patient's perceived pain into an objective graph or map by drawing the pain area. Pain drawings can be made by the patients who draw their pain areas on a display on which a body outline is shown, or it can be made by observers who observe the patients and then draw from the signs the patients are showing. An example of a body outline is shown at figure 1.5. Sometimes a questionnaire is added to the pain drawings to get a more detailed overview of the pain.[12]

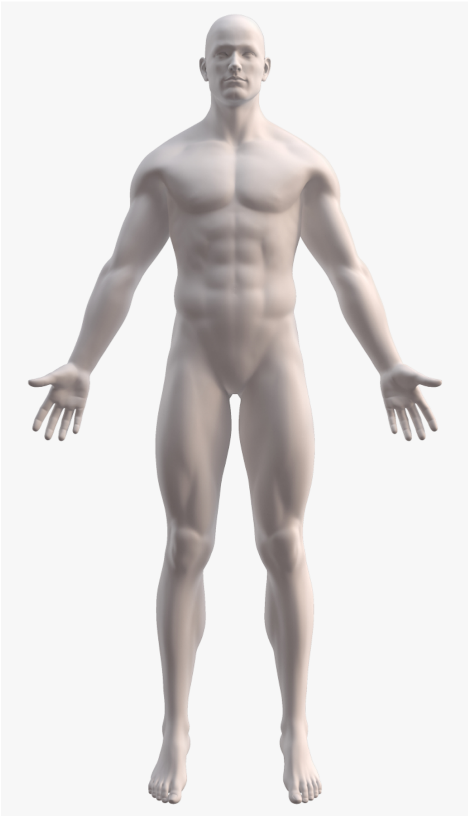

Figure 1.5: *The figure illustrates an anterior body outline for pain drawing. The figure is a screenshot from the application Navigate Pain.*

Pain mapping are commonly used in clinical practice [12], and can be useful for patients when they try to describe their pain. Pain maps may also be helpful in diagnosing patients and follow-ups during or after treatment to get an indicator of the patient's response to the treatment.[13] According to Schott there are some issues with the graphical representations of pain, some of which are problems with drawing a three-dimensional feeling of pain on a two-dimensional surface, and distinguishing between internal and external perceived pain on a map.[12]

1.4 Knee regions

Patients with PFPS often describe the knee pain as a diffuse pain, and when looking at pain drawing samples from multiple patients it is also evident that there is a high variability in the distribution of pain patterns across different areas of the knee. To distinguish between different pain areas, the knee can be divided into various regions as seen in figure 1.6, where atlases of the left and right anterior knees are illustrated. The atlases has been provided by Shellie Boudreau.

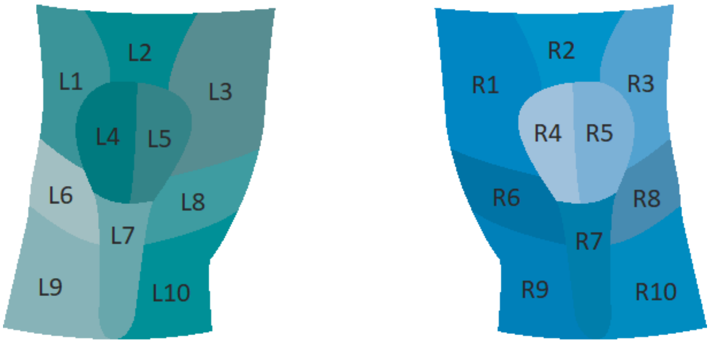

Figure 1.6: *The figure illustrates atlases of the left and right knees, where each knee is split into ten regions.*

1.5 Machine learning

Machine learning describes the use of algorithms to make a system able to identify different data types, like images or text, for transcription of speech into text, matching news items, posts or selection of relevant results of search [14]. Machine learning is a method that uses inductive inference in order to identify rules in a dataset from given input and output [15]. If the computer learns this feature, it can be used to make intelligent decisions and predict specific outcomes.[15] It is a field that has seen a lot of progress over the past decades, partially because developers recognize the ease in training a system only using examples of the desired in- and output behavior. This is simply easier than trying to manually write a piece of code that anticipate different scenarios from different input types.[16]

1.5.1 Deep Learning

Deep learning is a branch of machine learning. The main difference between the use of machine learning and deep learning, is that machine learning is not suitable for handling raw data form. Instead a machine learning system often needs a feature extractor, that will generate a feature vector from the data that can be used as an input for the machine learning system. Deep learning is based on different techniques that makes it able to handle that data in its raw form, mainly because of its structure.[14, 17] Because of this the system will automatically detect the necessary representations needed for classification and detection. Neural network is a structure of deep learning which consists of different layers, that can be divided into a input-layer and an output-layer, with one or more hidden layers in between [17]. The key aspect of these layers is that the features are not defined by programmers, but they are found and learned from raw data using a general–purpose learning procedure.[14] An example of the structure can be seen in figure 1.7.

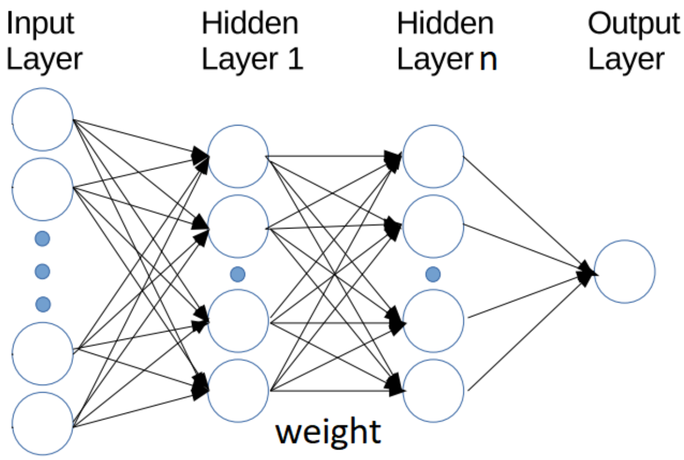

Figure 1.7: *Example of the neural network with possible layers[18].*

The different layers consist of a series of nodes, where each node is connected by weights to one or several other nodes from a different layer. In the input-layer the nodes are fed with the data that the system is given. The second layer will then receive the output from the previous layer, and this process continues through the layers until the output-layer is reached.[17] An example of how the hidden layers affect an image can be explained as follows: Firstly, the system detects minor changes like edges. Secondly, the edges are compared and put together to make up different kind of shapes. In the third hidden layer, it will be further combined to make up an object that can be identified.[14]

Learning scenarios

There are three main learning scenarios: supervised, unsupervised and semi-supervised learnings.

Supervised learning is the most common way of training in machine learning [14]. When using this method the system is trained with labeled data, where the generated output can be compared with an expected output, and thereby see how accurate the system is. The weights are interconnection between two layers and they work as a set of coefficients, defining an image feature.[19] By adjusting weights in the neural network it is possible to fit the model better to the training data, and thereby increase its accuracy and reduce error [14]. Supervised learning is mostly associated with classification, regression, and ranking problems [20]. Differently from supervised learning the input in unsupervised learning is received with unlabeled data and the predictions. Then the system organizes the data by searching for common characteristics [20]. An example of an unsupervised learning algorithm is clustering, where the unlabeled dataset goes through a classification, and split into different classes.[21] In semi-supervised learning the learner is receiving both labeled, unlabeled data and then it searches for common characteristics in data. It is used mainly when the labeled data is hardly collected and unlabeled data is easily reachable.[20]

1.5.2 Convolutional Neural Networks

Convolutional neural networks (CNNs) perform highly in several tasks, including digit recognition, image classification and face recognition. The key aspect of CNNs is to automatically learn a complex model by extracting visual features from the pixel-level content. CNNs are feed–forward models that map input data with a set of suitable outputs. Accuracy and performance rely on large training datasets and training procedure based on back-propagation with optimization algorithm such as gradient descent which is used for finding minimum value of the function.[18]

Back-propagation

Back–propagation is a popular learning algorithm in CNN. It is valuable because of the simplicity and computationally efficient [22]. The basic idea behind it is to minimize the overall output error as much as possible during the learning stage. This algorithm process is divided in two main stages: forward and backward. In the first process (forward), the back-propagation architecture is described as the inputs and weights multiplication of each node (separate input) summed with additional coefficients called biases.[19]

In the backward process, weights will be updated to minimize the error between input and output layers. This process will be applied until optimal weights with minimum error is reached.[19]

Chapter 2

Aim of the project

Patellofemoral pain is a musculoskeletal condition that is presented as pain behind or around patella. Generally, pain is defined as an unpleasant sensory experience associated with potential or actual tissue damage, and it can be divided into different categories of pain depending on duration and location of the pain. Subjects with PFPS often describe the knee pain as being diffuse and hard to locate. PFPS is often classified as a chronic pain when the duration of the condition is longer than six months. Despite the feeling of pain in the knee, there is often no structural changes in the knee and therefore no definitive clinical test that can be used to diagnose PFPS. The diagnosis of PFPS is then often based on the perceived pain in the knee when doing pain provoking exercises. There are different methods for measuring pain, but since pain and pain intensity are very subjective and hence perceived differently, there are few reliable methods for objectively measuring pain. A method used to transfer a subject's perceived pain into a relative objective illustration of the pain area is pain mapping, where subjects draw their pain areas on a body outline of the knee.

The aim of this project is to test whether or not it is possible to classify variables associated to subjects with PFPS through the use of deep neural network, and a limited dataset. Furthermore different types of classifications will be tested to see how the variables affect the performance of the network. The choice of using a deep neural network solution is based on the fact that pain is subjective, from which it is assumed that there is no linear relation between the subjects. Furthermore it is not in the scope of this project to find the dominating features used for classification, to where the neural network is chosen since it's able to discover these features itself. Thereby is the aim of this project again only to see if a classification can be made and optimised. Classifications will be based on the gender, and how the subject perceive PFP expressed through pain maps. The morphology of the pain maps are considered to be a possible contributor for correct classification. To test this, the pain maps will be represented in different ways: pain morphology, pain regions and a combination of these. According to Boudreau and et.al. Kamavuako there is a correlation between the duration of PFPS above and below five years and the pain areas. SOMETHING ABOUT WHY WE WANT TO USE PAIN INTENSITY? SHELLIE WE NEED YOUR HELP!!

2.0.3 Hypothesis

From the previous section the following hypothesis is given.
It is hypothesized that different data representations of pain maps will affect the performance accuracy of a neural network, as well as the classification between either duration or pain intensity.

Chapter 3

Materials

This chapter creates an understanding of the given data and the different programs respectvely the program where pain maps are created and the program for development of the neural networks.

3.1 Data

Data used in this project were collected beforehand. The data consists of pain maps which were drawn by subjects with PFP through the use of an application Navigate Pain in a clinical setting. The data contained information regarding the subjects in terms of i.a. age, gender, height and weight. For each individual subject information related to the PFPS was also collected, regarding the duration of PFP and which knee was the most prominent for pain. The number of samples available during this study was collected from ??? subjects with PFP. An example of a pain drawing can be seen in figure 3.1.

Figure 3.1: *Pain drawings of the lower extremities. The red markings indicate the area of pain perceived by the individual subject. In this case the PFP is bilateral (on both knees).*

3.1.1 Navigate Pain

Navigate Pain is an application that is used to visualise the location, shape and spatial distribution of pain from patient to healthcare personnel. The application permits subjects to draw their pain into a body outline with different colors and line thickness. Navigate Pain is developed by Algance Solutions within Aalborg University in Denmark.[24] Figure 3.2 illustrate the process using the application.

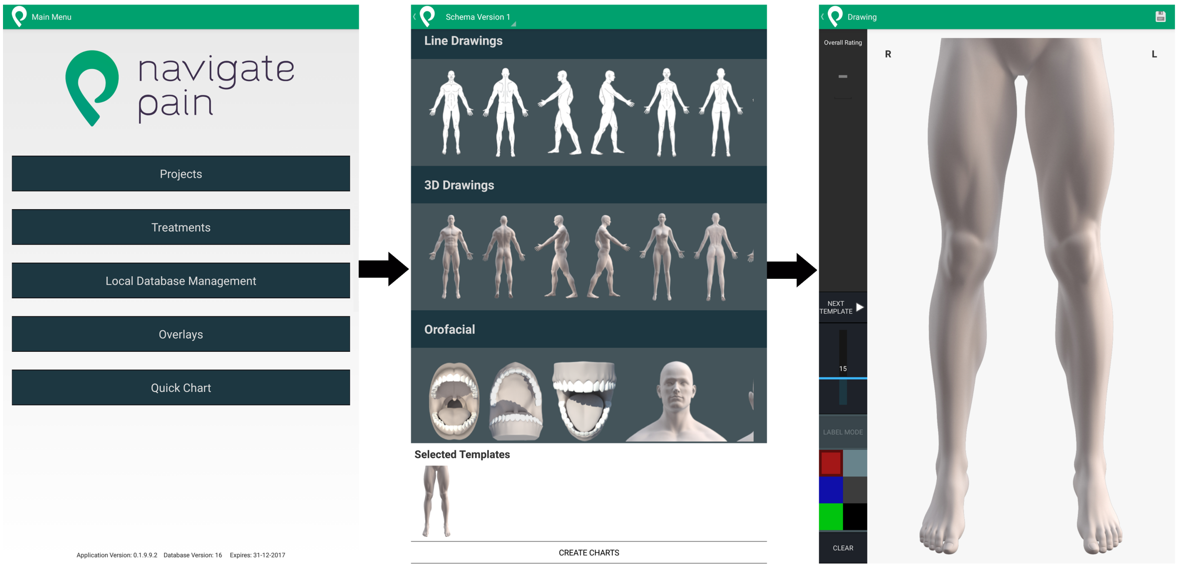

Figure 3.2: *The figure illustrates the process for making a pain map with Navigate Pain. There is three screenshots of the application.*

The left screen in figure 3.2 is the main screen. By clicking on "Project" a folder with subjects is created. From each subject information like name, age, height is saved. Before the subject can draw their pain areas, the body outline has to be chosen, which illustrates the screen in the middle. The body outlines is divided into five categories: Line Drawings, 3D Drawings, Orofacial, Special Zooms and Knee Pain. In the bottom the seleceted templates is shown. When clicking on "CREATE CHARTS" the right screen is shown. Here it is possible to draw the pain areas with different colors and line thickness, which can be seen in the left side of the screen. Afterwards the pain map can be saved.

3.2 Programs

In this project it is chosen to use Python v3.6.3 for development of the neural network. Python is an object-oriented and general-purpose programming and scripting language. Python is among other things used for programming websites, mobile applications, desktop GUI's, but also used for machine learning programming. When developing a machine learning application, there are different libraries that can be used, where some of the most popular is the Theano and the TensorFlow libraries.[25]

In this project the TensorFlow v1.3.0 library has been used. TensorFlow is an open source library for development of machine learning applications, that has been released by Google [25].

maybe something about keras... if we are gonna use it. Keras is a high-level neural network library, that runs on top of either TensorFlow or Theano. Keras is a simplified version of the two libraries, which makes it easier to program in Python, but still allows for building complex models.[25]

Chapter 4

Data Processing

** REMEMBER TEXT! **

4.1 Pre-processing

The data is pre-processed in MatLab where the pain maps are imported. To easier analyse the data afterwards all the images are converted into vectors and then inserted into a single matrix. The pain maps are represented in three different data representations and therefore the pain maps are processed in three different ways before compiling all image-vectors in a matrix. The three data representations are a matrix consisting of the pain morphology, a matrix with only the knee regions that are covered in pain, and lastly a matrix consisting of both the pain morphology and the affected knee regions. To get additional information about the subjects and the associated pain maps, another input, gender, is added to the three matrices. This is done by including an extra vector containing genders after the last column in each matrix. Furthermore, the three data representations have to be tested in neural network models with two different output parameters; duration of PFPS and pain intensity. The output parameters are, like gender information, added as vectors to the matrices so that the neural network models can analyse the pain information, gender and either duration or pain intensity. Only one output parameter is added to each matrix, which results in six different matrices.

4.1.1 Morphology

The first representation of data is a binary matrix of the original pain maps. Firstly, the image of the original pain map is gray-scaled to get a one-dimensional matrix instead of a three-dimensional RGB-matrix. This matrix is then converted into a matrix consisting of zeroes and ones, where the pain pixels are symbolized with ones. Afterwards the matrix is resized, since the given data has different sizes. Furthermore the matrix is cropped to sort out unnecessary data like the areas inferior and superior to the knee. An image consisting of a binary matrix is shown as figure 4.1.

Figure 4.1: Image consisting of a binary matrix where white color represents the pain pixels.

4.1.2 Regions

The second representation of the data is a matrix consisting of vectors with 20 values which indicate pain in relation to knee regions. The knee regions shown in figure 1.6 are converted into a matrix consisting of 20 values, which represent each knee regions. This matrix is superimposed to the binary image of the pain map, which results in a matrix with pain represented in each knee region. In figure 4.2 is there two illustrations of regions with different values (figure 4.2(a)) and the pain in the specific regions (figure 4.2(b)).

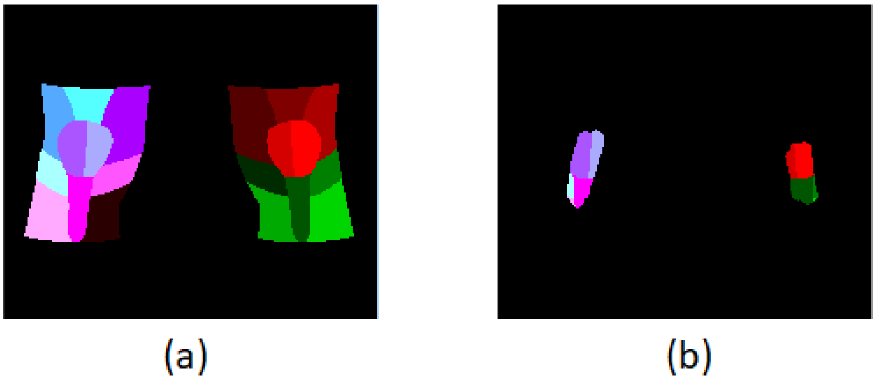

Figure 4.2: (a) Knee regions and (b) pain in the specific regions.

After superimposing the two matrices, knee regions and pain, the number of pixels in each active knee region is found. This number is compared to the total number of pixels that are in each knee region, so knee regions with less than 15 % pain are excluded. WHY 15%. As an result is a vector with 20 values created.

4.1.3 Superimposed morphology and regions

The third representation of the data is a matrix consisting of subject's pain divided into the knee regions. In this representation the superimposed matrix from the second data representation is used. Since the data representation should reflect the morphology of the pain and divide the pain into the different knee regions is one-hot encoding used. One-hot encoding is a way to separate categorical data into binary data [**?**]. This means that the 20 values for each knee region do not have a correlation. After one-hot encoding the superimposed matrix consists of 20 layers where each layer represents a knee region.

Chapter 5

Results

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Appendix A

Appendix

A.1 Appendix I