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CERTIFICATE

This is to certify that this project on **"Mathematical Modelling and Machine Learning for Biomathematics"** was registered under SRIVIPRA and completed under the mentorship of Dr. Mainak Mukherjee and Dr. Sudhakar Yadav during the period from 21st June to 7th October 2022.

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A Review of Machine Learning Methods for Medical Image Segmentation

Recent advances in deep learning and deep convolutional neural networks have significantly advanced the field of computer vision (CV) and image analysis and understanding. Complex tasks like classifying and segmenting medical images and locating and recognizing objects of interest have become much easier. This advance has the potential to accelerate the discovery and research of a wide range of CV-based medical applications. In this review, we emphasize the critical role of machine learning algorithms in enabling efficient and accurate segmentation in medical imaging. We focus on several key studies on the application of machine learning methods to biomedical image segmentation. We conduct a review of the machine learning literature addressing the complex visual task of medical image segmentation.

0.1 Introduction

We have seen the importance of medical imaging such as computed tomography (CT), magnetic resonance (MR), positron emission tomography (PET), mammography, ultrasound, X-ray, etc. for the early detection, diagnosis and other treatment of diseases over the last few decades [1]. Human experts such as radiologists and physicians have traditionally interpreted medical images in the clinic. Researchers and physicians have recently begun to benefit from computer-assisted interventions due to the wide variation in pathology and the potential for human expert fatigue.

Computer vision (CV) allows computers to process and analyse visual content such as 2D & 3D images and video. Image segmentation [2, 3], image registration [4], image fusion [5], image annotation [6], computer-aided diagnosis and prognosis [7, 8], lesion/landmark detection [9, 10], and microscopic imaging analysis [11, 12], are a few applications of computer vision in medicine.

Using available technologies, many researchers have proposed various automated segmentation systems. Previous systems relied on traditional techniques such as edge detection filters and mathematical methods. Then, for a long time, machine learning approaches that extract handcrafted features were the dominant technique. The main concern in developing such a system has always been designing and extracting these features, and the complexity of these approaches has been seen as a significant limitation on their use. Deep learning approaches emerged in the 2000s due to advances in hardware and began to demonstrate their considerable capabilities in image-processing tasks. The promising capabilities of deep learning approaches have propelled them to the forefront of image analysis, particularly medical image analysis.

In the realm of applying machine learning to data analysis, meaningful feature extraction or feature representation is central to the ability to get tasks done. Traditionally, useful or task-related functions have mostly been designed by human experts based on their knowledge of the target domains, making it difficult for non-experts to use machine-learning techniques for their research. Researchers have previously developed various methods for extracting low-level and high-level features from images. Vertices, edges, colour intensity, and scale-invariant features such as SIFT [13] and SURF [14]. In particular, SIFT and SURF caught the attention of the research community because they are insensitive to image scaling, rotation, pose, and lighting, all of which are major challenges in CV and medical images. These features are then used to train machine learning models to perform a specific supervised classification task. There are numerous ML algorithms [15], and the choice of an algorithm is often influenced by several factors, including the type, size, and complexity of the data and the task. Support Vector Machines (SVM) [16], Ensemble-based methods such as Random Forests (RF) [17], Artificial Neural Networks (ANN) [18] and others are common ML methods.

Deep learning [19], on the other hand, has overcome such challenges by integrating the feature engineering step into the learning step. That is, instead of manually extracting features, deep learning only needs a data set, with minor pre-processing if necessary, and then discovers informative representations in a self-taught way [20, 21]. As a result, the burden of feature engineering has shifted from the human to the computational side, allowing non-experts in machine learning to effectively use deep learning for their research and/or applications, particularly in medical image analysis. CNN (Convolutional Neural Network) [22] based methods have significantly advanced the field of CV, particularly in the areas of medical image analysis and classification [23]. These deep-learning techniques have been used since the 1980s. However, the unprecedented success of deep learning is largely due to the following factors: 1) advances in high-tech central processing units (CPUs) and graphics processing units (GPUs); 2) the availability of a vast amount of data (i.e. Big Data); and 3) the rapid exploration and development of deep learning algorithms [24–28].CNNs can capture the underlying image representation using partially connected layers and weight distribution. Many CNN architectures consist of a small number of convolution layers, followed by activation functions and pooling layers for image downsampling. The application of filters (kernels) to the input image repeatedly produces a map of activations (also known as feature maps) indicating points of interest in the input image.

In this paper, we focus on machine learning and deep learning literature, developments, and key challenges, with a focus on the computer vision tasks of medical image segmentation.

0.2 Machine Learning Methods

0.2.1 Linear Regression

Linear regression is one of the most well-known methods in statistics and machine learning with extensive theoretical research. Despite its simple framework, its concept serves as a basis for more advanced techniques. The model in linear regression is determined by linear functions whose unknown parameters are estimated from data. Simply put, linear regression is concerned with determining a linear equation that accurately represents the model. Linear regression models are often fitted by minimizing the 1-norm (e.g. 2-norm minimization is the least squares approach).

Given a dataset $\{y_i, x_{i1}, ..., x_{ip}\}_{i=1}^{n}$ of n statistical units, a linear regression model assumes that the relationship between the variable y and the p-vector of regression $\mathbf{x}$ is linear.This relationship is modeled through a disturbance term or error variable ε - an unobserved random variable that adds "noise" to the linear relationship between the dependent variable and regressors. Thus the model takes the form

$$y_i = \beta_0 + \beta_1 x_{i1} + ... + \beta_p x_{ip} + \varepsilon_i = \mathbf{x}_i^T \beta + \varepsilon_i, \quad i = 1, ..., 2 \tag{0.2.1}$$

where T denotes the transpose so that $\mathbf{x}_i^T \beta$ is the inner product between vectors $\mathbf{x}_i$ and β.

0.2.2 Random Forest

Random forests, also known as random decision forests, are an ensemble learning method for building predictive models by combining decisions from a set of base models. In order to achieve better prediction results, ensemble methods use multiple learning models. To arrive at the best possible answer in a random forest, the model creates an entire forest of random uncorrelated decision trees. These methods, known as bootstrap aggregation or bagging, are used to solve a bias-variance trade-off problem. Bias and variance can be used to explain learning errors in general. For example, if the bias is high, the test results will be inaccurate; If the variance is high, the model is only appropriate for certain datasets (e.g. overfitting or instability). Given training dataset $X = \{x_1, ..., x_n\}$ with labels $Y = \{y_1, ..., y_n\}$, bagging repeatedly and randomly samples (K times) the training dataset, and replaces the original training dataset by fitting binary trees to these samples. Let X_k and Y_k be the sampled dataset, where $k = \{1, ..., K\}$, and let T_b denote the binary tree trained with respect to X_k and Y_k. After training, predictions on the test dataset, $\bar{x}$, can be made in two ways:

- Averaging the predictions from all individual trees:

$$\bar{y} = \frac{1}{K} \sum_{K} T_b(\bar{x}) \tag{0.2.2}$$

- Taking the majority vote in the case of classification trees.

Averaging the results of individual trees reduces the learning error bias, and while a single tree's predictions are very sensitive to its training set, the mean of individual trees is not sensitive unless the trees are correlated. If trees are independent of each other, the central limit theorem would ensure that the variance is reduced. Random Forest uses an algorithm that selects a random subset of features, splitting each candidate in the process, to reduce the correlation of trees in a bagged sample [29]. Another benefit of Random Forest is that it's easy to use, with only three hyperparameters to set: the number of trees, the number of features used in a tree, and the sampling rate for bagging. In addition, the random forest results are accurate and stable; However, the internal process is a kind of black box, similar to deep learning.

0.2.3 Markov random field (MRF)

The Markov Random Field (MRF) segmentation method is another machine learning-based segmentation method. MRF is a conditional probabilistic model in which the probability of a pixel is affected by the probability of its neighbours. MRF is a stochastic process that uses the local features of the images [30, 31]. It is an effective way to connect spatial continuity as a result of prior context information. As a result, it provides valuable information for segmentation. Ibragimov and Xing [32] provides an excellent summary of the MRF: According to MRF formulation, the target image can be represented as a graph $G = \{V, E\}$, where V is the vertex set and E is the edge set. A vertex in G represents a pixel in the images and an edge between two vertices indicate that the corresponding pixels are neighbours. For each object S in the image, each vertex is assigned with label 1 when it belongs to S, and with label 0 when it does not. Then, the label of a voxel is, finally, determined by its similarity to object S(i.e., probability P_x^S) and similarity to object S of each neighbour.

0.3 Image Segmentation

The process of grouping an image into multiple coherent sub-regions based on extracted features such as colour or texture attributes and classifying each sub-region into one of the predefined classes is called image segmentation. Segmentation can also be viewed as a type of image compression, which is a crucial step in deriving knowledge from images. As a result, segmentation has extensive applications in precision medicine for the development of a computer-assisted diagnosis based on radiological images with different modalities such as magnetic resonance imaging (MRI), computed tomography (CT) or colonoscopy images.

Image segmentation is a pixel-by-pixel classification task that divides an image into areas with similar attributes. Medical image segmentation attempts to locate the region or contour of a body organ or anatomical part in images. While object detection methods often create a bounding box that defines the area of interest, segmentation methods create a pixel mask for that area. Applications include whole heart segmentation [33], lung segmentation [34], brain tumours [35], skin segmentation [36] and breast tumour segmentation [37]. Like other CV tasks, segmentation can be applied to different medical imaging modalities. The introduction of the Fully Convolutional Neural Network (FCN) led to a breakthrough in DL-based image segmentation [38]. U-Net and its extensions have also been successfully applied to a variety of segmentation tasks in medical imaging, and a detailed review is provided by Litjens et al. [39].

0.4 Datasets

Several datasets that are commonly used for segmentation and are publicly available are available. There are datasets for brain tumour segmentation (BRATS), ischemic stroke lesion segmentation (ISLES), outcome prediction in mild traumatic brain injury (mTOP), multiple sclerosis segmentation (MSSEG), neonatal brain segmentation (NeoBrainS12), magnetic resonance -Brain image segmentation available (MRBrainS). The Lung Image Database Consortium (LIDC-IDRI) image collection consists of diagnostic and screening chest CT scans with labelled, annotated lesions for lung cancer. There are public datasets on liver tumour segmentation (LiTS), 3D image reconstruction for algorithm database comparison (3Dircadb), and liver segmentation (SLIVER07). For prostate segmentation, prostate MR image segmentation (PROMISE12) and data sets for automated segmentation of prostate structures (ASPS) can be used. There is also a data set on the knee and cartilage segmentation (SKI10).

0.5 conclusion

Advances in medical image analysis and understanding over the past decade are considered unprecedented and can be measured in orders of magnitude. Complex computer vision (CV) tasks such as image classification, location and segmentation of areas of interest, and detection and tracking of objects in video streams have become relatively easy. This progress can largely be attributed to advances at the algorithm level, in particular, the development of methods based on convolutional neural networks, advances in computing power, and finally the availability of large amounts of medical images and associated data in the public domain.

This paper reviewed a few classical machine-learning methodologies, the progress of machine learning and deep learning research to accomplish the task of medical image segmentation and a few publically available medical image segmentation datasets.

Ensuring that interpretability is built into machine learning models from the ground up is an important challenge for future research. This will help build trust between physicians and patients and ensure the development of accurate, explainable DL models for immediate widespread use in the medical field. Finally, there is an urgent need for ongoing collaboration between medical and AI experts. This ensures that expert knowledge remains at the heart of the process to develop accurate, understandable and most importantly applicable CV techniques that can advance medical care worldwide and advance us.

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