Machine Learning methods for Thin Vessel Segmentation

in Fundus Images

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This thesis is submitted in requirements of the course BITS C421T

May 2015

I would like to dedicate this thesis to my loving parents ...

Declaration

I hereby declare that except where specific reference is made to the work of others, the contents of this dissertation are original and have not been submitted in whole or in part for consideration for any other degree or qualification in this, or any other university. This dissertation is my own work and contains nothing which is the outcome of work done in collaboration with others, except as specified in the text and Acknowledgements. This dissertation contains fewer than 65,000 words including appendices, bibliography, footnotes, tables and equations and has fewer than 150 figures.

Kushal Khandelwal
May 2015

Acknowledgements

And I would like to acknowledge ...

Abstract

This is where you write your abstract ...

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Chapter 1

Introdcution

1.1 What is loren ipsum? Title with math σ

Lorem Ipsum is simply dummy text of the printing and typesetting industry (see Section 1.3). Lorem Ipsum [2] has been the industry's standard dummy text ever since the 1500s, when an unknown printer took a galley of type and scrambled it to make a type specimen book. It has survived not only five centuries, but also the leap into electronic typesetting, remaining essentially unchanged. It was popularised in the 1960s with the release of Letraset sheets containing Lorem Ipsum passages, and more recently with desktop publishing software like Aldus PageMaker including versions of Lorem Ipsum [1, 3, 4].

The most famous equation in the world: $E^2 = (m_0c^2)^2 + (pc)^2$, which is known as the **energy-mass-momentum** relation as an in-line equation.

A *LaTeX class file* is a file, which holds style information for a particular LaTeX.

$$CIF: \quad F_0^j(a) = \frac{1}{2\pi\imath} \oint_\gamma \frac{F_0^j(z)}{z-a} dz \tag{1.1}$$

1.2 Why do we use loren ipsum?

It is a long established fact that a reader will be distracted by the readable content of a page when looking at its layout. The point of using Lorem Ipsum is that it has a more-or-less normal distribution of letters, as opposed to using 'Content here, content here', making it look like readable English. Many desktop publishing packages and web page editors now use Lorem Ipsum as their default model text, and a search for 'lorem ipsum' will uncover many

web sites still in their infancy. Various versions have evolved over the years, sometimes by accident, sometimes on purpose (injected humour and the like).

1.3 Where does it come from?

Contrary to popular belief, Lorem Ipsum is not simply random text. It has roots in a piece of classical Latin literature from 45 BC, making it over 2000 years old. Richard McClintock, a Latin professor at Hampden-Sydney College in Virginia, looked up one of the more obscure Latin words, consectetur, from a Lorem Ipsum passage, and going through the cites of the word in classical literature, discovered the undoubtable source. Lorem Ipsum comes from sections 1.10.32 and 1.10.33 of "de Finibus Bonorum et Malorum" (The Extremes of Good and Evil) by Cicero, written in 45 BC. This book is a treatise on the theory of ethics, very popular during the Renaissance. The first line of Lorem Ipsum, "Lorem ipsum dolor sit amet..", comes from a line in section 1.10.32.

The standard chunk of Lorem Ipsum used since the 1500s is reproduced below for those interested. Sections 1.10.32 and 1.10.33 from “de Finibus Bonorum et Malorum" by Cicero are also reproduced in their exact original form, accompanied by English versions from the 1914 translation by H. Rackham

“Lorem ipsum dolor sit amet, consectetur adipisicing elit, sed do eiusmod tempor incididunt ut labore et dolore magna aliqua. Ut enim ad minim veniam, quis nostrud exercitation ullamco laboris nisi ut aliquip ex ea commodo consequat. Duis aute irure dolor in reprehenderit in voluptate velit esse cillum dolore eu fugiat nulla pariatur. Excepteur sint occaecat cupidatat non proident, sunt in culpa qui officia deserunt mollit anim id est laborum."

Section 1.10.32 of “de Finibus Bonorum et Malorum", written by Cicero in 45 BC: “Sed ut perspiciatis unde omnis iste natus error sit voluptatem accusantium doloremque laudantium, totam rem aperiam, eaque ipsa quae ab illo inventore veritatis et quasi architecto beatae vitae dicta sunt explicabo. Nemo enim ipsam voluptatem quia voluptas sit aspernatur aut odit aut fugit, sed quia consequuntur magni dolores eos qui ratione voluptatem sequi nesciunt. Neque porro quisquam est, qui dolorem ipsum quia dolor sit amet, consectetur, adipisci velit, sed quia non numquam eius modi tempora incidunt ut labore et dolore magnam aliquam quaerat voluptatem. Ut enim ad minima veniam, quis nostrum exercitationem ullam corporis suscipit laboriosam, nisi ut aliquid ex ea commodi consequatur? Quis autem vel eum iure reprehenderit qui in ea voluptate velit esse quam nihil molestiae consequatur, vel illum qui dolorem eum fugiat quo voluptas nulla pariatur?"

1914 translation by H. Rackham: “But I must explain to you how all this mistaken idea of denouncing pleasure and praising pain was born and I will give you a complete

account of the system, and expound the actual teachings of the great explorer of the truth, the master-builder of human happiness. No one rejects, dislikes, or avoids pleasure itself, because it is pleasure, but because those who do not know how to pursue pleasure rationally encounter consequences that are extremely painful. Nor again is there anyone who loves or pursues or desires to obtain pain of itself, because it is pain, but because occasionally circumstances occur in which toil and pain can procure him some great pleasure. To take a trivial example, which of us ever undertakes laborious physical exercise, except to obtain some advantage from it? But who has any right to find fault with a man who chooses to enjoy a pleasure that has no annoying consequences, or one who avoids a pain that produces no resultant pleasure?"

Section 1.10.33 of “de Finibus Bonorum et Malorum", written by Cicero in 45 BC: “At vero eos et accusamus et iusto odio dignissimos ducimus qui blanditiis praesentium voluptatum deleniti atque corrupti quos dolores et quas molestias excepturi sint occaecati cupiditate non provident, similique sunt in culpa qui officia deserunt mollitia animi, id est laborum et dolorum fuga. Et harum quidem rerum facilis est et expedita distinctio. Nam libero tempore, cum soluta nobis est eligendi optio cumque nihil impedit quo minus id quod maxime placeat facere possimus, omnis voluptas assumenda est, omnis dolor repellendus. Temporibus autem quibusdam et aut officiis debitis aut rerum necessitatibus saepe eveniet ut et voluptates repudiandae sint et molestiae non recusandae. Itaque earum rerum hic tenetur a sapiente delectus, ut aut reiciendis voluptatibus maiores alias consequatur aut perferendis doloribus asperiores repellat."

1914 translation by H. Rackham: “On the other hand, we denounce with righteous indignation and dislike men who are so beguiled and demoralized by the charms of pleasure of the moment, so blinded by desire, that they cannot foresee the pain and trouble that are bound to ensue; and equal blame belongs to those who fail in their duty through weakness of will, which is the same as saying through shrinking from toil and pain. These cases are perfectly simple and easy to distinguish. In a free hour, when our power of choice is untrammelled and when nothing prevents our being able to do what we like best, every pleasure is to be welcomed and every pain avoided. But in certain circumstances and owing to the claims of duty or the obligations of business it will frequently occur that pleasures have to be repudiated and annoyances accepted. The wise man therefore always holds in these matters to this principle of selection: he rejects pleasures to secure other greater pleasures, or else he endures pains to avoid worse pains."

Chapter 2

Background and Literature Review

This chapter aims to provide the basic background knowledge to understand the work of thesis. Clustering algortighm and Dictionary Learning algortihms are discusses. We further discuss the various evaluation measures.

2.1 Machine Learning

Machine learning is the study dealing with the process to learn characteristic information from data. Given some data, X , a machine learning algorithm learns a function $f(X)$ which maps the input X to an output variable y . The learnt model than can be used to make predictions on previously unseen data X'.A machine learning algorithm learns the parameters of an adpative model from a training set, typically optimizing a function. The learnt model is then used to make predictions on previously unseen new data. On the basis of presence or absence of label information in the dataset, the learning algorithms are categorized as supervised learning algorithms and unsuperverised learning algorithms respectively.

In a supervised setting , given a set of labelled data points known as the training data:

$$T = \{(x_1, y_1), ..., (x_n, y_n)\}$$

, where $x_i \in X$ and $x_i \in X$,we find a function f, which maps any point in the domain of X to its corresponding label in Y. If Y is a set of discrete values then the it is known as a classifcation problem and if Y is in a continous range then it is a problem of regression.

In an unsupervised setting, the task is to find group relations between instances of the unlabeled training dataset with a subsequent aim of categorizing or clustering the data. The algorithm finds the previous unknown structure in the data.

The data point x_i is typically represented as a vector comprising of feature values and is known as a feature vector. For example, given a dataset $X = \{x_1, x_2, ..., x_m\}$ where x_i is an image patch of size p x q,each patch can be represented as a vector of length pq of grey scale intensity values at each pixel. The entire dataset then can be represented as a matrix:

$$X = \begin{pmatrix} x_{1,1} & x_{1,2} & \cdots & x_{1,pq} \\ x_{2,1} & x_{2,2} & \cdots & x_{2,pq} \\ \vdots & \vdots & \ddots & \vdots \\ x_{m,1} & x_{m,2} & \cdots & x_{m,pq} \end{pmatrix}$$

Here each row of the matrix dentoes individual data points and $x_{i,j}$ is the gray scale intensities of patch x_i at pixel location j.

Depending on whether the data is labelled or unlabelled, the machine learning algorithms can be divided into two types namely :

1. Supervised Learning Algorithms

2. Unsupervised Learning Algorithms

2.2 Clustering

A cluster is collection of data points grouped together on basis of some common properties.The data objects or points within a cluster are similar to each other, whereas the points in different groups are disimilar.

The process of partioning the data points into smaller groups (called as clusters) with an aim to minimize the intra cluster variance and maximize the inter cluster variance, is known as clustering. The grouping of data points is based on the similarity or disimilarity of the objects as described by their properties or features.

Similarity or disimilarity between two objects can be very subjective and hence various measures are used to describe them quantitatively with distance measure being the most common.The distance measure is used to specify the distance between two objects and can be used to create a distance matrix called as similarity/disimilarity matrix. The most used distance metric is the Eucledian Distance.

The eucledian distance D between two points $p = \{x_1, x_2, ..., x_n\}$ and $q = \{y_1, y_2, ..., y_n\}$ can be defined as:

$$\begin{aligned} dist(p,q) &= \sqrt{(x_1 - y_1)^2 + (x_2 - y_2)^2 + ... + (x_n - y_n)^2} \\ &= \sqrt{\sum_{i=1}^{n} (p_i - q_i)^2} \\ &= \|\mathbf{p} - \mathbf{q}\| \end{aligned} \tag{2.1}$$

As the data labels are unknown,cluster analysis is known as an unsupervised method of data partionining.This is contast to classification where the data can be partitioned on the basis of their class labels. Thus, clustering segments the data on the basis of the properties of the objects within the dataset and finds previously unkown grouping within the data.

The distance based clustering algorithms can be divided into two types namely Partioning based and Hiearchical methods.

We look into these different types of Clustering methods.

2.2.1 K-Means Clustering

In this section we look into the K-Means clustering algorithm. We assume that the number of clusters 'K' is given and we use it to initiate our clustering algorirthm.

We are give a dataset D with n objects. Each n object in the dataset is described by a feature vector of length m. The feature vector can be anything which can represent the datapoint. For examples, for an image the feature vector can be grayscale values at every pixel. The aim of the clustering algorithm is to partition the the dataset D[m x n] into 'K' clusters while optimizing an objective function. The clusters are formed so as to the objects within the same cluster are similar and disimilar to objects in other clusters.

K-Means is a centroid based partioning method I.e the centroid of the cluster is the representative data point for the cluster. The centorid of the cluster is defined by the mean of all the data points within the cluster.

Give a dataset D with n objects in the Eucledian space, the aim is to partition the dataset into k cluster C1,C2...Ck susch that Ci subset of D and Ci Cj is nil. That is each point withing the dataset is exclusive to one cluster. Each of the clusters Ci is represented by its centroid ci. Each cluster is consists of p points and the distance between the point p and the cluster representative ci is defined as dist(p,ci). If the data points are in m dimensional , then the distance is defined as [eucledian distance]

The clustering algorithm optimizes the inter cluster variation, this is the Sum of Squared Error(SSE) between the data points in the cluster and the centroid. The SSE is defined as

Error =
Algorithm
Algorithm

2.3 Dictionary Learning

2.3.1 Sparse Coding

2.4 Preprocessing Methods

2.4.1 Normalization

2.4.2 CLAHE

2.5 Evaluation

Chapter 3

Framework

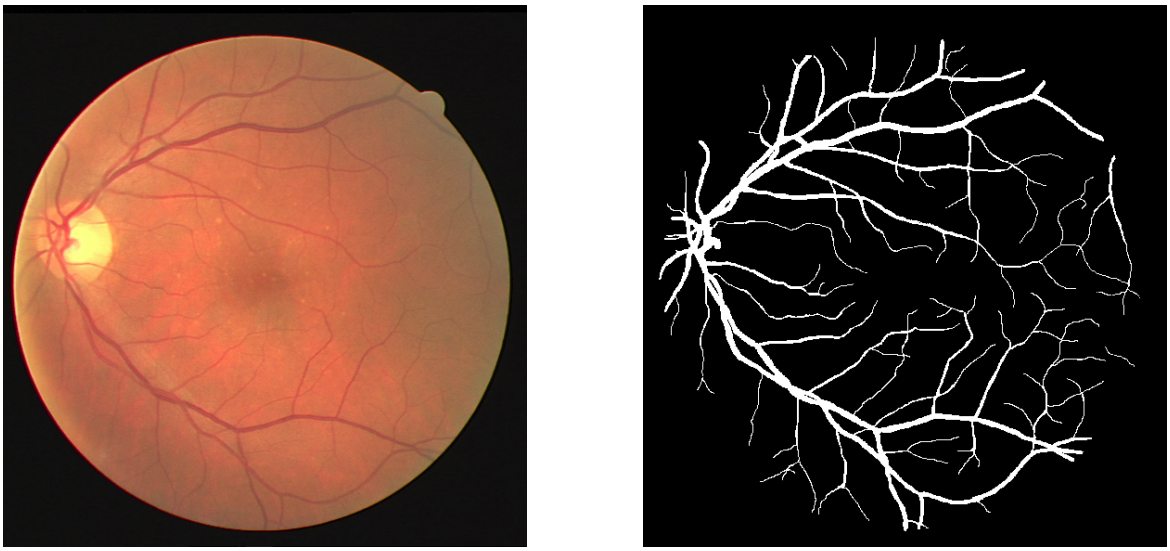
The chapter aims to present the basic framework for our vessel segmentation algorithm. The chapter is divided into 4 parts. In the first part we discuss the basic framework of our algorithm. Part 2 and Part3 talk about the various preprocessing methods and how the methods was applied to our problem.

3.1 Vessel segmentation Framework

The image segmentation framework takes as its input a list of fundus images, $I = (I^{(1)}, I^{(2)}....., I^{(n)})$ and their correspoding ground truth segmentation maps $S = (S^{(1)}, S^{(2)}....., S^{(n)})$. The fundus images I^n can be grayscale or RGB color images. For each n, S^n ,the binary segmentation map is of the same size as of I^n. For a given fundus image, I^n, let $I^n(x,y)$ denote the pixel value at position (x,y) and $S^n(x,y)$ denotes the corresponding pixel in the segmentation map S^n. The pixels in segmentation map take either a value of 1 or 0 denoting the presenece or absence of vessel respectively.

For clarity and simplicity, the fundus images will be referred as I and the corresponding segmentation image as S. Fig 3.1 shows an example of fundust image on the left and the correspoding segmentation image on the right.

In this thesis we aim to develop methods that use the training data I and S to learn a predictor that segments the vessels in new unseen fundus images.The proposed problem is solved in a patch based framework, in which we decompose each image into smaller images (called as patches) centered around each pixel of the original image. Thus a given fundus



(a) Fundus Image (b) Segmented Vessels

Fig. 3.1 Fundus Image and its segmentation

image I and segmentation map S can be represented in terms of their patches as

$$I = \{P^I_{x,y}\} \tag{3.1}$$

$$S = \{P^S_{x,y}\} \tag{3.2}$$

where $P^I_{x,y}$ and $P^S_{x,y}$ represent a w x w patch centered at pixel (x,y) of I and S respectively.

The training set I & S is composed of such small patches and a classifier is trained which learns a set of patches

3.1.1 Preprocessing

In our task we have explored some of the preprocessing steps including Patch Normalization, Contrast streteching, Local contrast nomralization.

All the input patches are normalizaed by subtracting the mean and standard deviation per patch. In addition to this we also test with normalizing the entire image before patch generation.

In some of the experiments, we improve the image contrast by utilizing Contrast Limited Adaptive Histogram Equalization (CLAHE) as explained in section.

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Rotations To provide for rotational invariance and learn better representatives, rotated patches are also included in our learning phase. Each of the training images are additionaly rotated at angles of 30,60,90 and patches are calculated.

3.2 Datasets

For testing the performance of our algorithm , we train and test our system on the following publically available datasets. In this section we describe the characteristics of these datsets

3.2.1 DRIVE

The Digital Retinal Images for Vessel Extraction (DRIVE) dataset consists of 40 color retinal images randomly selected from diabetic retinopathy screening program for 400 diabetic patients.Each of these images in dataset are JPEG compressed and have a dimensions of 768 x 584 pixels captured at a resolution on bits per pixel. The images are captures with a 45degree field of view (FOV). Of the 40 images in the datset, 7 show sign of diabetic retinopathy , while the remaining 33 do not consist of any pathology. Each image is provided with a corresponding mask delineating the FOV.

The dataset is divided is provided with divisions in terms of training and testing set, with each set consisting of 20 images. Each of the 40 images have been manually segmented by human observers trained by an experienced optamologist. For the training set, single ground truth segmentation of the vessels is provided. The test set is provided with two ground truth segmentations, of which the first one is used as gold standard and the other is used to compare the performance with an independent human observer.

3.2.2 STARE

The STARE dataset consists of 20 images with blood vessel segmentations, out of which 10 show signs of pathology. The images have been capture with a FOV of 35degrees at 8 bit per pixel resolution, with dimesnsions of each image as 605 x 700 pixels. The dataset consists of segmentation provided by two human observers. In our experiements, we consider the segmentations provided by the first observer as ground truth.

Table 3.1 Even better looking table using booktabs

Dental measurement	Species I		Species II	
	mean	SD	mean	SD
I1MD	6.23	0.91	5.2	0.7
I1LL	7.48	0.56	8.7	0.71
I2MD	3.99	0.63	4.22	0.54
I2LL	6.81	0.02	6.66	0.01
CMD	13.47	0.09	10.55	0.05
CBL	11.88	0.05	13.11	0.04

For the experiements, the dataset is randomly divided into training and test sets each consisting of 10images.

3.2.3 HRF

he High Resolution Fundus (HRF) image databse consists of 45 images of which 15 images come from healthy patients , 15 from patients with diabetic retinopathy and 15 of glacumatous patients.

The images were captured with a FOV of 60degrees, at a high resolution of 24bits per pixel. The size of each image is 3504 x 2336 pixels and stored with JPEG compression.

Each image is provided a manual segmentation of vessesl as segmented by three independent human observers trained by experienced optahmologists.The dataset also provides a corresponging mask image of each image delineating the FOV.

3.2.4 ARIA

The ARIA dataset consists of three groups of images. One of the group consists of 92 images with age-related macular degeneration, the other with 59 images from diabetic patients and the last group with 61 images from a control group. The images are captures with a 50degree FOV, stored in uncompressed TIFF format, with a resolution of 8bits oer pixel. Each image has dimensions of 768 x 576 pixels.

The dataset provides with blood vessel segmentation images as manually segmented by experts and a corresponding mask delinating the FOV region.

References

[1] Abramovich, Y. A., Aliprantis, C. D., and Burkinshaw, O. (1995). Another characterization of the invariant subspace problem. *Operator Theory in Function Spaces and Banach Lattices.* The A.C. Zaanen Anniversary Volume*, Operator Theory: Advances and Applications*, 75:15–31. Birkhäuser Verlag.

[2] Aupetit, B. (1991). *A Primer on Spectral Theory*. Springer-Verlag, New York.

[3] Conway, J. B. (1990). *A Course in Functional Analysis*. Springer-Verlag, New York, second edition.

[4] Ljubič, J. I. and Macaev, V. I. (1965). On operators with a separable spectrum. *Amer. Math. Soc. Transl. (2)*, 47:89–129.

Appendix A

How to install LaTeX

Windows OS

TeXLive package - full version

1. Download the TeXLive ISO (2.2GB) from
   https://www.tug.org/texlive/
2. Download WinCDEmu (if you don't have a virtual drive) from
   http://wincdemu.sysprogs.org/download/
3. To install Windows CD Emulator follow the instructions at
   http://wincdemu.sysprogs.org/tutorials/install/
4. Right click the iso and mount it using the WinCDEmu as shown in
   http://wincdemu.sysprogs.org/tutorials/mount/
5. Open your virtual drive and run setup.pl

or

Basic MikTeX - TeX distribution

1. Download Basic-MiKTeX(32bit or 64bit) from
   http://miktex.org/download
2. Run the installer
3. To add a new package go to Start » All Programs » MikTex » Maintenance (Admin)
   and choose Package Manager

4. Select or search for packages to install

TexStudio - TeX editor

1. Download TexStudio from
   http://texstudio.sourceforge.net/#downloads

2. Run the installer

Mac OS X

MacTeX - TeX distribution

1. Download the file from
   https://www.tug.org/mactex/

2. Extract and double click to run the installer. It does the entire configuration, sit back and relax.

TexStudio - TeX editor

1. Download TexStudio from
   http://texstudio.sourceforge.net/#downloads

2. Extract and Start

Unix/Linux

TeXLive - TeX distribution

Getting the distribution:

1. TexLive can be downloaded from
   http://www.tug.org/texlive/acquire-netinstall.html.

2. TexLive is provided by most operating system you can use (rpm,apt-get or yum) to get TexLive distributions

Installation

1. Mount the ISO file in the mnt directory

   ```
   mount -t iso9660 -o ro,loop,noauto /your/texlive####.iso /mnt
   ```

2. Install wget on your OS (use rpm, apt-get or yum install)

3. Run the installer script install-tl.

   ```
   cd /your/download/directory
   ./install-tl
   ```

4. Enter command 'i' for installation

5. Post-Installation configuration:
   http://www.tug.org/texlive/doc/texlive-en/texlive-en.html#x1-320003.4.1

6. Set the path for the directory of TexLive binaries in your .bashrc file

For 32bit OS

For Bourne-compatible shells such as bash, and using Intel x86 GNU/Linux and a default directory setup as an example, the file to edit might be

```
edit $~/.bashrc file and add following lines
PATH=/usr/local/texlive/2011/bin/i386-linux:$PATH;
export PATH
MANPATH=/usr/local/texlive/2011/texmf/doc/man:$MANPATH;
export MANPATH
INFOPATH=/usr/local/texlive/2011/texmf/doc/info:$INFOPATH;
export INFOPATH
```

For 64bit OS

```
edit $~/.bashrc file and add following lines
PATH=/usr/local/texlive/2011/bin/x86_64-linux:$PATH;
export PATH
MANPATH=/usr/local/texlive/2011/texmf/doc/man:$MANPATH;
export MANPATH
```

```
INFOPATH=/usr/local/texlive/2011/texmf/doc/info:$INFOPATH;
export INFOPATH
```

Fedora/RedHat/CentOS:

```
sudo yum install texlive
sudo yum install psutils
```

SUSE:

```
sudo zypper install texlive
```

Debian/Ubuntu:

```
sudo apt-get install texlive texlive-latex-extra
sudo apt-get install psutils
```

Appendix B

Installing the CUED class file

LaTeX.cls files can be accessed system-wide when they are placed in the <texmf>/tex/latex directory, where <texmf> is the root directory of the user's TeXinstallation. On systems that have a local texmf tree (<texmflocal>), which may be named "texmf-local" or "localtexmf", it may be advisable to install packages in <texmflocal>, rather than <texmf> as the contents of the former, unlike that of the latter, are preserved after the LaTeXsystem is reinstalled and/or upgraded.

It is recommended that the user create a subdirectory <texmf>/tex/latex/CUED for all CUED related LaTeXclass and package files. On some LaTeXsystems, the directory look-up tables will need to be refreshed after making additions or deletions to the system files. For TeXLive systems this is accomplished via executing "texhash" as root. MIKTeXusers can run "initexmf -u" to accomplish the same thing.

Users not willing or able to install the files system-wide can install them in their personal directories, but will then have to provide the path (full or relative) in addition to the filename when referring to them in LaTeX.