HST.582J / 6.555J / 16.456J Biomedical Signal and Image Processing
Spring 2007

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Laboratory Project 4
Registration of Medical Images

DUE: 5/4/07

1 Introduction

The registration or fusion of medical images is used in many applications ranging from image-guided surgery to neuroscience. A common approach to this problem uses an *objective function* to measure the agreement of two data sets as one is transformed with respect to the other. This lab will investigate the behavior of several objective functions on various 2D images in a rigid-motion scenario (translation and rotation only), by way of *probing* the objective functions. The project will culminate in an experiment concerning the automated registration of MRI and CT (optionally PET) in 2D. The medical images used in this lab were part of the Vanderbilt "Retrospective Image Registration Evaluation Project", National Institutes of Health, Project Number 8R01EB002124-03, Principal Investigator, J. Michael Fitzpatrick, Vanderbilt University, Nashville, TN. You can learn more about this project at this website: http://www.vuse.vanderbilt.edu/ image/registration/

2 Probing Experiments

The basic idea of a probing experiment is to characterize the utility of objective functions by plotting their scores as a pre-defined set of transformations are applied to one of a pair of images. A probing experiment takes place on a parameter space defined by the range of transformation components used in the objective function evaluations. The more thoroughly we explore that parameter space, the more accurately we can predict the behavior of the objective function in a registration scenario.

2.1 Evaluation

Useful probing experiments provide information about the following characteristics of the objective functions on a specified pair of images:

- *existence of extremum*

  Does an extremum exist in the right region?

- *bias in extremum*

  Is the extremum located in the right place in the parameter space?

- *capture region*

  What is the extent of the *capture region* about the extremum, that is, how large is the region of the parameter space surrounding the extremum that is *down-hill or up-hill* to the extremum? A more formal definition: the *capture region* is the set of points in the parameter space such that when initialized to a point in this set an optimization procedure will dynamically evolve to a particular attractor/extremum.

- *quality of extremum*

  Does the extremum appear to be local or global? How well does an extremum distinguish itself from other extrema. That is, how big is the capture region around the extremum. If it is global, how much better is it than the other extrema. Could the difference just be due to noise?

2.2 Design

In designing probing experiments, we need to choose the points in the space of the transformation parameters to be sampled for evaluation of the objective function. Using a large number of samples can provide rich information about an objective function, but for some objective functions, such probing experiments will be computationally prohibitive.

Issues to keep in mind while designing the experiments include:

- Are the samples spaced densely enough so that local extrema are unlikely to be missed, and the location of the extremum can be evaluated?
- *Separate* probing along the various axes will require fewer evaluations than *complete* sampling as x y and angle co-vary, but will be less informative.
- Is the parameter space sufficiently covered to evaluate the capture region?

3 Specific Instructions

The goal of this lab is to learn about designing and evaluating experiments to probe objective functions and then to use appropriate objective functions for registering 2D MRI and CT (and optionally PET) data.

3.1 Supplied Data and Code

All data for this lab are located in the **/mit/6.555/data/reg** directory.* All code segments and functions related to Lab 3 can be found in **/mit/6.555/matlab/reg**. Please make a local copy of this code to use for your lab.

3.2 Getting Started...

In this first part of the lab project you will use a collection of objective functions to become familiar with probing experiments.

1. Load and display the the images that we will use in this lab. Use the supplied **load_reg_data.m** function in order to read in the data sets. There are two main data sets. The first dataset is a collection of three alien robot brain scans, **scan1**, **scan2**, and **scan3**. The second dataset is a collection of MRI, CT, and PET scans. **mri**, **ct**, and **pet** are MRI, CT and PET scans taken of a single subject's brain. **mri2** is an MRI of a different subject. **load_reg_data.m** will also load a few constants that will be used later in the lab (ROI_ALIEN_BRAIN and ROI_MRI).

Question 1 *Include appropriately labeled images for both data sets in your lab report. The function* **display_image.m** *may be helpful to assist you in the display.*

2. Write code for the **sse** (summed squared error/intensity) and **sav** (summed absolute value) objective functions covered in lecture. You may copy the templates from **sse.m** and **sav.m** and then modify them in your directory. Include a copy of these functions in the appendix of your lab report.

In the following experiments, you will use four objective functions (the two you just wrote and two others provided) to illustrate different aspects of the image registration problem. The two objective functions provided are joint entropy and cross correlation coefficient. These functions are located in **joint_entropy.m** and **xcorr_coeff.m**.

* For OCW users: these data and code files are supplied in the supporting ZIP archive.

3.3 Probing Experiments

The main idea in the probing part of the lab is to design and carry out experiments that will characterize the utility of four different objective functions. For this lab we will only consider rigid transformations restricted to translation and rotation. This gives us a 3D parameter space: Δ_x,Δ_y, and θ.

A simple probing experiment template script for analyzing the registration of an image pair is provided in **probing_experiment.m**. This code evaluates the **sse**, **sav**, **joint_entropy** and **xcorr_coeff** objective functions on the region of the parameter space. The script calls **probe.m** which takes two images (one to be fixed and one to move), a region of interest (ROI), a set of objective functions and a range for Δ_x, Δ_y and θ. For each parameter setting **probe** transforms the image to be moved and then evaluates each objective function on the fixed image and transformed image within the specified ROI. Set **ploton = 1** to display the transformations as **probe** runs. The function **probe** returns a cell array of probing surfaces; **surfaces{k}(yi,xi,ti)** will give you the result of the k^{th} objective function at the yi^{th}, xi^{th} and ti^{th} setting of Δ_y, Δ_x and θ respectively.

The region of interest (ROI) is specified by a vector $[min_x\ max_x\ min_y\ max_y]$ or you can use the **specify_roi** function to graphically select an ROI within an image. Specifying an ROI is a simple way to avoid boundary conditions where there is missing data. For example, if you simply translate an image by N pixels vertically down it will leave N pixels at the top that are undefined (here they are filled in as 0 by default). We do not want these undefined pixels to factor in when considering whether or not the images are registered. Using an ROI is a simple way to avoid this issue. In addition, an ROI can be used when you wish to focus on registering a particular structure or region of the image.

3.3.1 Probing Alien Brain Scans

In this section we perform some simple probing experiments to align the alien robot brain scans (**scan1**, **scan2** and **scan3**). While these are highly intelligent aliens their brains look very simplistic in our top secret alien brain scanner. These simple structures will help us characterize the utility of the four different objective functions and some of the potential challenges in image registration.

3. Execute code for a probing experiment to align **scan1** with itself using **translation only** ($\Theta = 0$) for all the objective functions. Set the region of interest to ROI_ALIEN_BRAIN. Look at the resulting scores/probing surface, and consider how to interpret these results.

Question 2 *In your lab report, include plots of the four 2D probing surfaces that you obtained running this experiment on the* **scan1** - **scan1** *image pair. What is the optimal transformation in this case?*

Question 3 *Compare the four probing surfaces, and describe each one in terms of the characteristics listed in Section 2.1. The functions* **capture_region**, **local_extrema**, **global_extrema** *may be helpful. Which objective function would be preferable for use with an automated registration algorithm? How do the comparisons between objective functions change if you sample the parameter space more coarsely?*

scan2 is a second scan of the same alien brain, but this time some of the data has been lost due to occlusion. We can think of this vertical black stripe as some form of an alien brain tumor or perhaps someone left a metal bar in the scanner that occluded part of the brain.

Question 4 *Based on your knowledge of the objective functions, predict (prior to running the experiments) which one will provide the most useful probing surface to describe the alignment between the* **scan1** - **scan2** *image pair. Justify your answer.*

4. The **scan1** and the **scan2** images are misregistered. Perform probing experiments and estimate the transformation parameters that best align the two ($\hat{T}_{1-2}$). Again, only consider translation (set $\theta = 0$) and try all four objective functions. Let **scan1** be the fixed image.

Question 5 *What is the best transformation estimate* $\hat{T}_{1-2} = [\Delta_x, \Delta_y, 0]$ *for each objective function? Do they all agree? If not, describe the differences in terms of the characteristics listed in Section 2.1 and the form of the objective functions. Which objective functions, if any, are correct? Which ones, if any fail? Why? Provide a plot/image of the best alignment you found (you can use* **image_transform** *to apply the best transformation and* **display_alignment** *to display the result).*

scan3 is a third scan of the same alien brain using a different imaging technology.

Question 6 *Based on your knowledge of the objective functions, predict (prior to running the experiments) which one will provide the most useful probing surface to describe the alignment between the* **scan1** - **scan3** *image pair. Justify your answer.*

5. The **scan3** and the **scan1** images are misregistered. Perform probing experiments and estimate the transformation parameters that best align the two ($\hat{T}_{1-3}$). Again only consider translation (set $\theta = 0$) and try all four objective functions. Let **scan1** be the fixed image.

Question 7 *How do the probing surfaces for the* **scan1** - **scan3** *experiments differ from those in the original* **scan1** - **scan1** *experiments? Characterize the new probing surfaces. Which objective function performs best for the* **scan1** - **scan3** *image pair? Why? (Include graphical results in your report to support your arguments.)*

3.3.2 Unimodal MR Probing Registration

In this section (and from now on) we will work on registering images/scans of human brains using the knowledge we gained from those simple alien brain experiments. **mri** and **mri2** are MR images taken of two different subjects. We wish to register these two MR images to help study the small tumor in the brain of subject 2 (**mri2**).

6. Perform probing experiments and estimate the transformation (translation and rotation) parameters that best align the two ($\hat{T}_{mr-mr2}$). Set the ROI to be ROI_MRI and make **mri** be the fixed image. Use your experience from Section 3.3.1 to guide the design of your probing experiments. Start by running lower dimensional (2D) probing experiments in order to get a good estimate of the intervals that you need to search. The lower dimensional probing experiments will allow you to roughly characterize the objective function behavior and estimate sufficient probing intervals for all three degrees of freedom in the transformation.

7. After exploring the results of your 2D probing experiments, perform a 3D probing experiment and inspect the probing surface to determine the 3D transformation required to register the images. Use the **volumeslicer** tool to help visualize the 3D surfaces. Verify that the images are correctly registered when you apply $\hat{T}_{mr-mr2}$.

Question 8 *(3 Parts)*
(1) What is your transformation estimate $\hat{T}_{mr-mr2} = [\Delta_x, \Delta_y, \theta]$*? (Include graphics of the probing plots and images of the registered input pair in your report)*
(2) Which objective function did you use to determine this result? Justify your answer.
(3) Be sure to include the design of your probing experiment: Did you run lower dimensional probing functions? What kind? What was the interval on which you probed the objective functions? What were the probing step sizes that you used?
(4) Is the resulting alignment the best possible registration? What, if anything, could you change to find (or allow for) a better registration?

8. Next specify a more focused ROI. That is, pick an interesting structure in the **mri** image and set your ROI to only include that small area. (Do not make it any smaller than 20x20). Rerun step 6. and 7. with this smaller ROI.

Question 9 *In your lab report, include a plot showing your chosen ROI and the resulting probing surfaces. How did choosing a more focused ROI change the probing surfaces? Again, discuss how the characteristics listed in Section 2.1 are effected by this change. Are there any particular regions in the* **mri** *image that would be difficult to align to using a small ROI? Any regions that would be easy?*

3.3.3 Multimodal Probing Experiments

The next experiments concern the registration of MRI and CT, a classic problem of multi-modality fusion. The **mri** and the **ct** images are misregistered. Both of these images were obtained from the same subject. Once more, your task is to perform probing experiments and find an estimate of the transformation that would best align the two ($\hat{T}_{mr-ct}$).

9. Design probing experiments in order to estimate $\hat{T}_{mr-ct}$. Set the ROI back to ROI_MRI and use **mri** as the fixed image. Think carefully about your choice of objective function. Again, start by running lower dimensional probing experiments first and visualize your results.

Question 10 *What is your transformation estimate* $\hat{T}_{mr-ct}$*? Which objective function did you use to get this result? Justify your choice. (Include graphics of the probing plots and images of the registered input pair in your report). Be sure to include the design of your probing experiment: Did you run lower dimensional probing functions? What kind? What was the interval on which you probed the objective functions? What were the probing step sizes that you used?*

10. (OPTIONAL) If you have extra time. Design a probing experiment to find an estimate of the transformation ($\hat{T}_{mr-pet}$) that would best align the MR image **mri** and and the PET scan **pet**.

Question 11 *(OPTIONAL) What is your transformation estimate* $\hat{T}_{mr-pet}$*? Which objective function did you use to get this result? Justify your choice. (Include graphics of the probing plots and images of the registered input pair in your report).*

3.3.4 Coarse-to-Fine Probing Experiments

The final probing experiment concerns using the *scale space* or *coarse-to-fine* approach to combat possible local extrema. One strategy for avoiding such phenomena in an automated search is to blur the images and downsample. The hope is that searches in the blurred images will converge to the *correct* extremum, at the expense of accuracy. Once a solution is obtained from the blurred and downsampled images, it might be used as the starting value for a search using the original images.

11. Create a blurred and downsampled version of **mri** and **mri2**. You can apply a Gaussian filter to the original images using **fspecial** and **imfilter** and then manually downsample. Alternatively you can look into using **imresize**. It is up to you to choose the amount of blur and how much to downsample.

12. Using the blurred images, repeat the probing experiments for the **mri** - **mri2** image pair.

Question 12 *Include the code for your blurring operation in the appendix of your lab report. Include the blurred and downsampled images in your lab report. Does the* coarse-to-fine *approach appear to be promising? What transformation parameters ($\hat{T}_{mrblur}$) best align the blurred images? How does this compare to the result of high-resolution (unblurred) probing experiments using in step 5?*

3.4 Automated Search

The following experiment concerns the implementation and testing of an automated registration method for the multimodal registration. Choose to align **ct** and **mri** or **pet** and **mri**. (Optionally, if you have time you can do both).

13. Use **fminsearch6555**, a modification of Matlab's implementation of the downhill simplex optimization method, to search for an extremum of the objective function of your choice applied to the registration of the **mri** and **ct** (or **pet**) images using rigid-body transformations. Set **mri** to be the fixed image.

You will need to write a wrapper function around the objective function in order to use it with the optimization code. Try different starting points to explore the capture range. **fminsearch6555** has an extra parameter that lets you control how the simplex is initialized. Use the following form:

```
opt = optimset('Display','iter');
T = fminsearch6555(@wrapperFunction,initial_T,initial_delta_T,opt)
```

where **inital_T** is the starting transformation and **initial_delta_T** is the small offset used to create the initial simplex. Try **initial_delta_T = [5 5 pi/16]** which indicates a starting simplex at **initial_T** with a spreed of 5 pixels in Δ_x, 5 pixels in Δ_y and $\pi/16$ radians in Θ. Matlab's **fminsearch** is equivlant to using **initial_delta_T = 1.05*initial_T**.

Question 13 *Describe your observations on the behavior of the optimization algorithm. Report on your choice of objective function, the final parameter values, and the number of iterations and function evaluations used. What was the most extreme starting position from which the images could be correctly aligned? You may find it useful to add print/plot statements or other diagnostics to your wrapper code to help in interpreting and presenting the behavior of the algorithm.*

Question 14 *How do your transformation estimates from the probing experiments compare to the result obtained by the automatic search?*

14. (OPTIONAL) Implement a coarse-to-fine approach that uses this automated search method. Register **ct** (or **pet**) with **mri** using this approach.

Question 15 *(OPTIONAL) How well did your automatic coarse-to-fine work? Provide a plot of the resulting alignment/registration. Supply your code for automatic coarse-to-fine in the appendix of your lab report.*

4 Overall Feedback

Question 16 *What did you find most challenging about this lab exercise?*

Question 17 *What is the most important thing that you learned from this lab exercise? (Suggested length: one sentence)*

Question 18 *What did you like/dislike the most about this lab exercise? Suggested length: one sentence)*

In the appendix of your report, please be sure to include the Matlab code for the functions sse and sav, as well as the code for the blurring operation.