Information Processing for Medical Imaging
MPHY0025 – 2020/2021

Registration exercises 3
MATLAB version

You have been provided with some utility functions for use in these exercises (some of these are the same as for the previous exercises, but there are also some new ones):

dispImage.m

resampImageWithDefField.m

calcMSD.m

calcJacobian.m

dispDefField.m

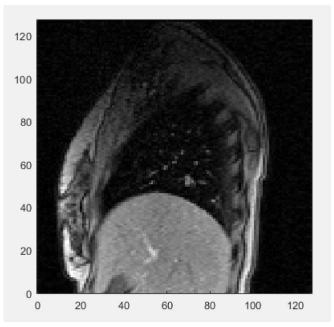
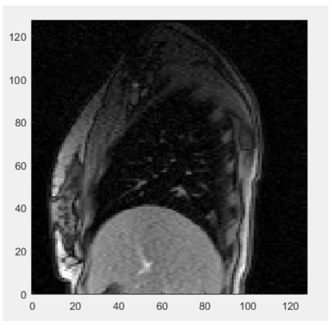
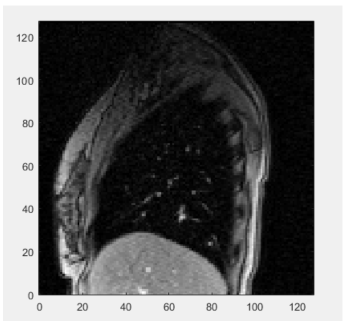
as well as a function that implements the Demons registration algorithm:

demonsReg.m

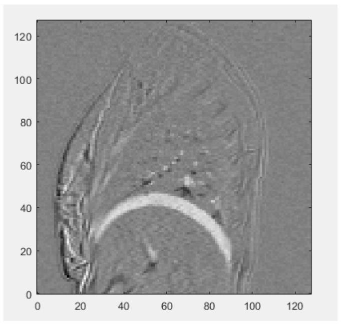
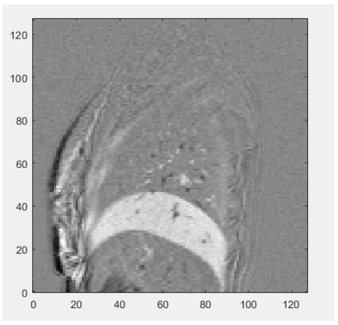
You have not been provided with a template script for these exercises since you will mostly be running the registration with different input parameters and then examining and trying to understand the results, and this is easier done from the command window than by running scripts.

You should look at the code for the utility functions and make sure you understand what they do and how they work. You should also look at the code for the *demonsReg* function and check you can follow what it is doing. You should be able to understand what each section of code is doing, even if you don't fully understand every line. If there are any parts you do not understand ask me or one of the PGTAs to explain in the lab session.

You have also been provided with three images for use in these exercises: *cine_MR_1.png*, *cine_MR_2.png*, and *cine_MR_3.png*. These images contain a 2D sagittal MR slice showing the lung, liver, and surrounding anatomy, at different points in time during free-breathing. Image 1 is at end-exhalation, image 2 at the end-inhalation for a normal breath, and image 3 at end-inhalation for a deep breath. Load in and display the three images. Don't forget to convert the images to doubles and reorientate them as in the previous exercises. The images are shown on the following page.

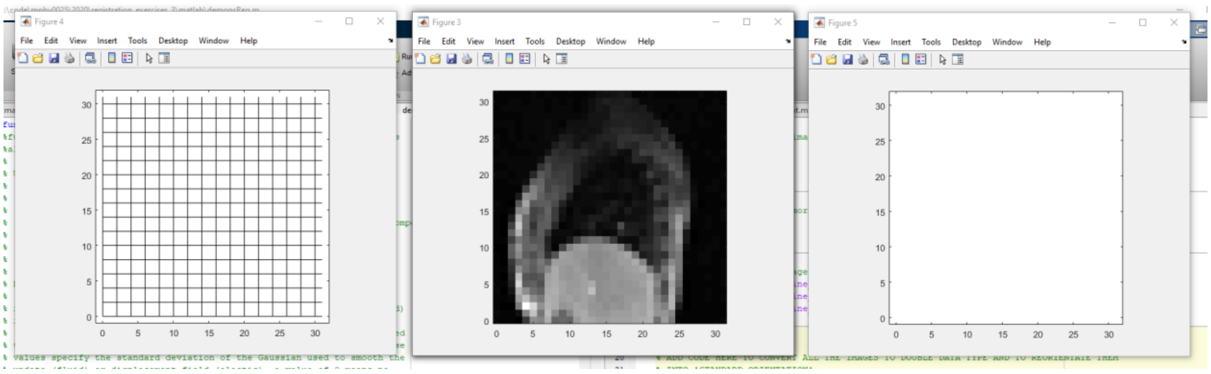
Compare the images to each other and observe the motion that occurs between the images. Difference images (one image minus another, e.g. as shown below) are a good way seeing where there are differences between the images, but it can be difficult to tell how things have moved between the images from the difference image.

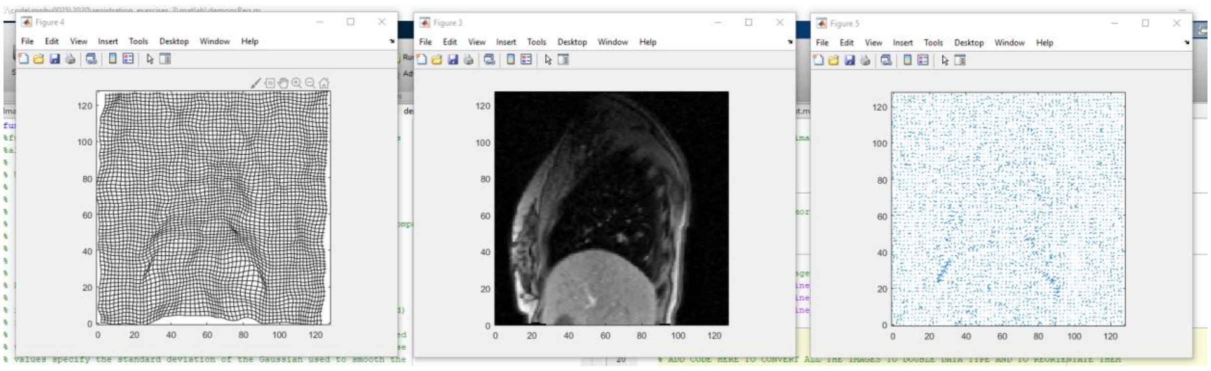
I find it easier to appreciate how things have moved/changed between images if you 'flip' between the images. The is easily achieved by displaying the images in separate figures and leaving the figure in their default position, so one is behind the other. You can then switch between the figures (e.g. by typing `figure(n)` into the command window, where n is the number of the figure you want to move to the front) and see how they differ from each other. Pay particular attention to motion that you think could be challenging for the demons algorithm to recover, such as very large motion and deformation, or sliding motion that can occur between the lung/liver and surrounding anatomy.

If you look at the comments at the start of the *demonsReg* function (which are also displayed as the help info for the function) you will see that there are two required input parameters, the source and target images for the registration. There are also a number of optional input parameters, which have default values assigned to them that will be used if an alternative value is not specified. We will explore the effects of these parameters as we go through these exercises. The outputs of the function are the final warped image and the corresponding deformation field.

Start by running a registration with cine_MR_1 as the source image and cine_MR_2 as the target image and using default values for all the other parameters. When you run the function, you will notice that 5 figures appear on the screen, initially all on top of each other. Figure 1 and 2 show the source and target images, which will remain unchanged during the registration. Figure 3 shows that transformed source image, figure 4 shows the current deformation field, and figure 5 shows the update to the deformation field for the current iteration. By default, the deformation field is displayed as a deformed grid whereas the update is displayed as a vector field. Figures 3, 4, and 5 will update during the registration. Once the figures are displayed the function will pause to allow you to rearrange the figures as desired. You can do this however you like, but I recommend moving figures 4 and 5 so that figure 3, 4, and 5 are all visible, but leaving figures 1, 2, and 3 on top of each other, as shown below. This will enable you to monitor progress during the registration and easily compare the registration result with the target and source images once the registration is finished.



While the registration is running you will notice that figures 3, 4, and 5 are updated, and that text is outputted to the command window stating the current resolution level, iteration number, and value of the Mean Squared Difference (MSD) between the target image and the current warped image. At the end of the registration figures 3, 4, and 5 should look like this:



If you look at the text output you will see that the final MSD value is 81.83 (rounded to 2 decimal places – more are shown in the command window), and that 107 iterations were performed at the final (3rd) resolution level. If you scroll up in the command window you will see that 29 iterations were also performed at the 2nd resolution level, and 14 iterations at the 1st level. If you look at the MSD value you will notice it decrease as the registration progresses, as would be expected, but that it increases between resolution levels. Do you know why it does this? Hint – it's not just because there are more pixels in the higher resolution images, as using the mean rather than sum of squared differences should account for different numbers of pixels in the images.

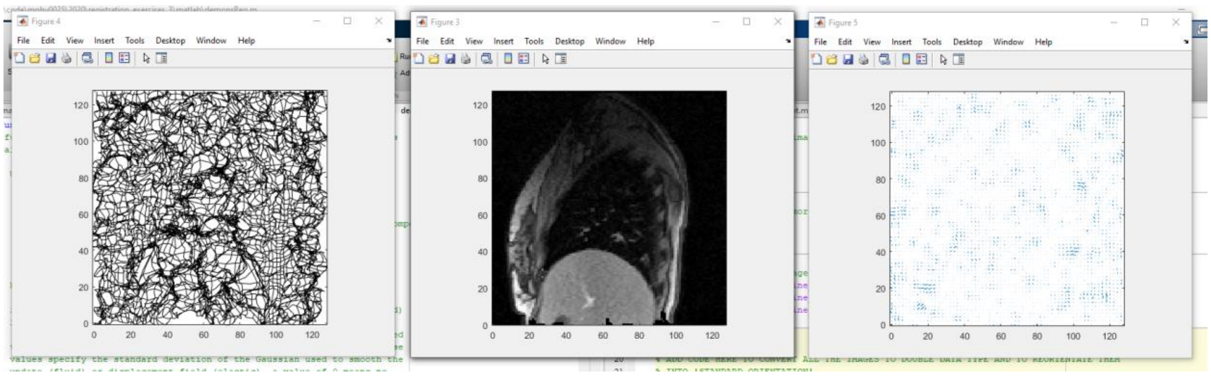
Compare the final warped image with the target and source images. How well do you think the registration did at aligning the images? Which parts of the images are well aligned, and which parts are less well aligned?

If you look at the deformation field you will see that it corresponds to the deformation that would be applied to the warped image to get back to the source image (rather than the deformation that would be applied to the source image to get to the warped image). Make sure you understand why this is the case (hint – pull-interpolation).

You can specify the values of the optional input parameters using name-value pairs, e.g.

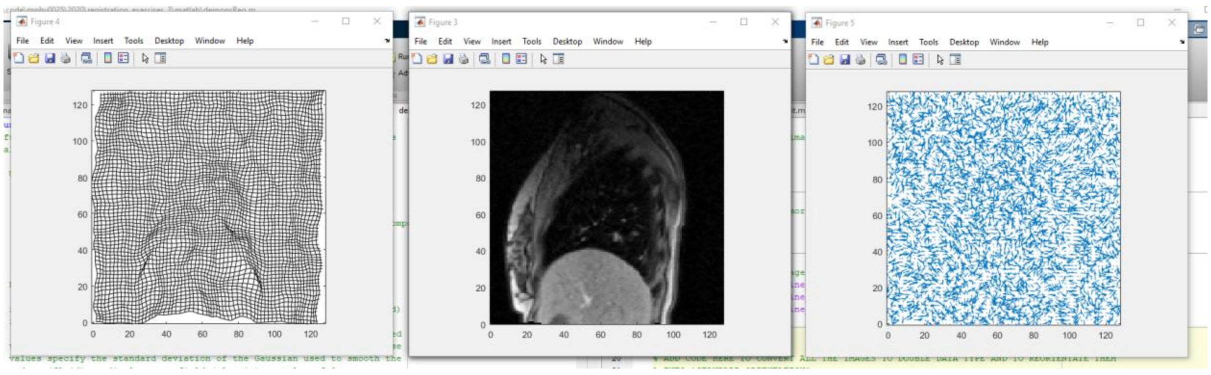
```
demonsReg(cine_MR_1, cine_MR_2, 'sigma_elastic', 0);
```

will run the registration with *sigma_elastic* set to 0, i.e. with no elastic like regularisation applied. Try running this registration. At the end figures 3-5 should appear like:



You will see that the final warped image looks very similar to the target image, and the MSD agrees with this with a value of just 18.71 (compare to 81.83 for the default parameters). However, you can see that the final deformation field is very 'crumpled' and does not look very physically plausible. Therefore, for most applications this would not be considered a good registration result. The reason that the result is like this is that without any elastic-like regularisation applied to the deformation field it is free to 'evolve' in any way that better aligns the intensities, even if this results in implausible transformations, and highlights the need for using suitable regularisation.

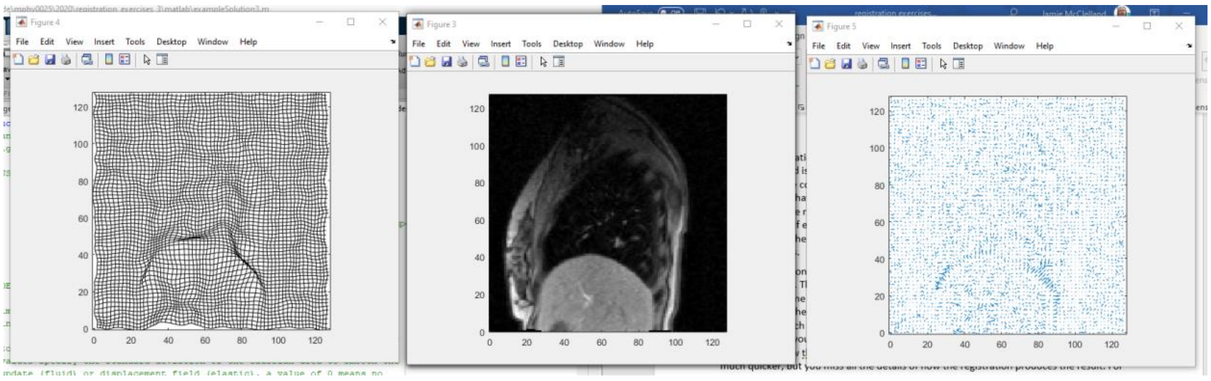
Now rerun the registration with *sigma_elastic* at its default value again but this time setting *sigma_fluid* to 0. At the end figures 3-5 should look like:



You will now see that the updates (shown in figure 5) are much larger and noisier as no regularisation is being applied to them, but the deformation field is still relatively smooth as it does have regularisation applied. If you compare the result from this registration to the result obtained with the default parameters (remember, you can store the outputs of the function so that you can directly compare the results from different registrations) you will see that the results are quite similar, but some of the structures appear better aligned by the latest registration. This is also reflected in the lower MSD value (71.71). However, the deformation field is also less smooth, and perhaps less physically plausible. Which of the results should be considered 'best' will depend on exactly what the application is. But it should be clear that the elastic-like regularisation usually has a larger effect on the result than the fluid-like regularisation does. Now try running several more registrations with different levels of elastic-like and fluid-like regularisation to get a good feel for how the combination of these parameters affects the results, and which ranges of values produce good/bad results.

Note – you can control how often the images update by setting the value of the *disp_freq* input parameter. The registrations themselves run relatively quickly, but updating the images takes some time. This makes the registrations run considerably slower but allows you to see how the deformation field and warped image change during the course of the registration, which can be very useful for understanding why the registration produces the result it does. If you set *disp_freq* to 0 then the images will only update at the start of each level and to show the final result. If you do this you will notice that the registration runs much quicker, but you miss all the details of how the registration produces the result. For most of these exercises I recommend keeping the *disp_freq* value relatively low, e.g. at the default value of 5 or less, so that you can see how the deformation field and warped image change as the registration is progressing.

You should have noticed that the registration is using a multi-resolution approach, with 3 resolution levels by default. You can specify the number of resolution levels to use with the *num_lev* input parameter. Try running a registration with *num_lev* set to 1, i.e. so that only a single resolution level is used, and the multi-resolution approach is not applied. At the end figure 3-5 should look like:



Do you think using a multi-resolution approach helps? Why?

Now try running the registration with 6 resolution levels (if you use 7 levels the 1st level only contains 4 pixels and spends several iterations not really doing anything before moving on to the next level, and if you try and use more than 7 levels you will get an error as there are not enough pixels to down-sample the images that many times). You will notice that the final MSD = 88.68 is worse than when using the default 3 resolution levels (MSD = 81.83). However, if you compare the results of both registrations to the target image you will see that the registration with 6 levels appears to align the structures within the lung and the diaphragm better than the result with 3 levels, but the structures outside the lung, e.g. the ribs, are not aligned as well. Again, which results should be considered best will depend on the exact application.

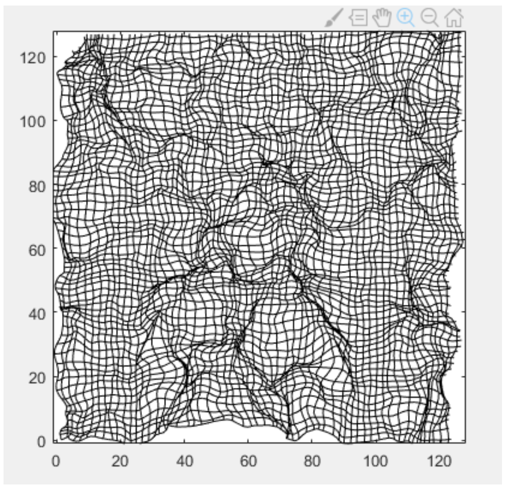
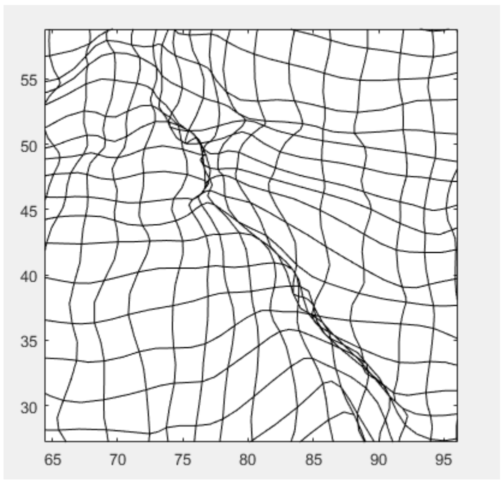
Now experiment with varying the values for the regularisation parameters as well as the number of resolution levels, and see how the results are affected.

When investigating the effects of the regularisation parameters you should have noticed that some parameters will result in warped images that look very similar to the target image, but the deformation fields do not look very plausible. In particular, sometimes the deformation field will appear to fold over itself, indicating that folding has occurred, which is often undesirable when performing registrations.

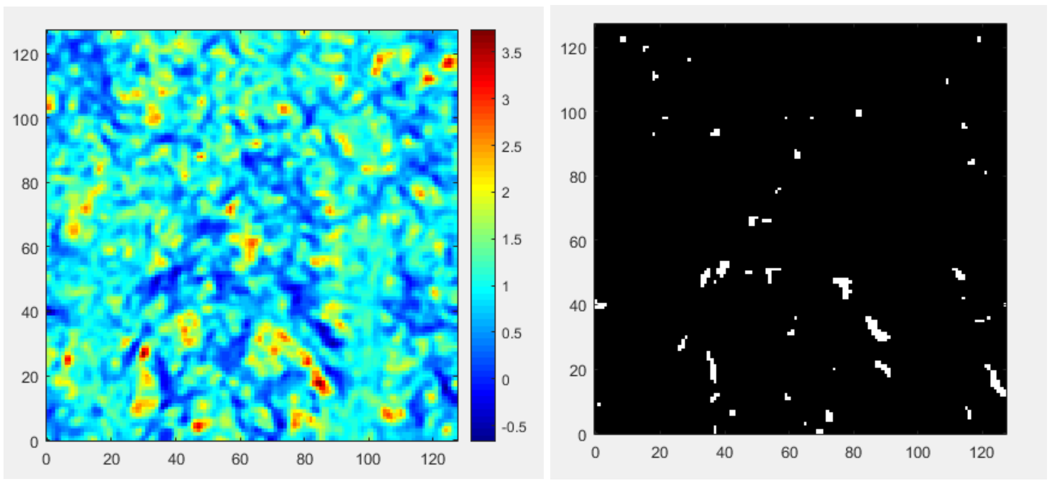
For example, if you perform a registration with the following parameters:

sigma_elastic = 0.5, *sigma_fluid* = 1, *num_lev* = 3

the result is the deformation field shown below, and as can be seen in the zoomed-in image on the right, the grid has folded over itself in some regions.

You have been provided with a function, *calcJacobian*, to calculate the Jacobian determinant (and optionally the full Jacobian matrix) at each pixel in the deformation field, and return a map (image) of the Jacobian determinants. Have a look at this function and make sure you understand how it works.
If you use this function to create an image of the Jacobian determinants for the deformation field above, and then display it (e.g. using the *dispImage* function so that the image is orientated correctly) you will notice that the image is very 'patchy', and does not show smooth expansions/contractions as would be expected during breathing. This may be easier to appreciate using a different colormap, e.g. *jet*, as shown in the image on the next page. Furthermore, if you add a colourbar you will see that it contains some very large values (>3.5, indicating the tissue at those pixels has more than tripled in size) as well as negative values, indicating that folding has occurred. You can also directly visualise the pixels where folding has occurred by creating a binary image of the pixels that have a Jacobian determinant <=0, as shown on the next page.



If you compare the location of the pixels with folding in the binary image to the deformation field you will notice that they do not align with where you can see folding occurring in the grid. This is because the grid shows the deformation in the source image space whereas the binary image corresponds to the pixels in the warped image space.

With the *demonsReg* function it is possible to compose the updates rather than add them, so that the deformation field will always represent a diffeomorphic transformation (as the updates are themselves always diffeomorphic), and hence will not contain any folding. If you look at lines 241-263 of the *demonsReg* function and you will see that the composition of two deformation fields can be implemented by treating each component of the current deformation field as an image, and resampling it with (a deformation field derived from) the update to the transformation. To see why, we can write the equation for resampling an image as:

$$I_{resamp}(\vec{x}) = I_{orig}\big(T(\vec{x})\big)$$

i.e. the intensity in I_{resamp} at $\vec{x}$ is the intensity in I_{orig} at $T(\vec{x})$ ($\vec{x}$ transformed by T). As $T(\vec{x})$ will typically not be the centre of a pixel in I_{orig}, the intensities in I_{orig} must be interpolated to calculate $I_{resamp}(\vec{x})$.

The equation for composing the update, T_{up}, with the current transformation, T_t, is:

$$T_{t+1}(x) = T_t\left(T_{up}(x)\right)$$

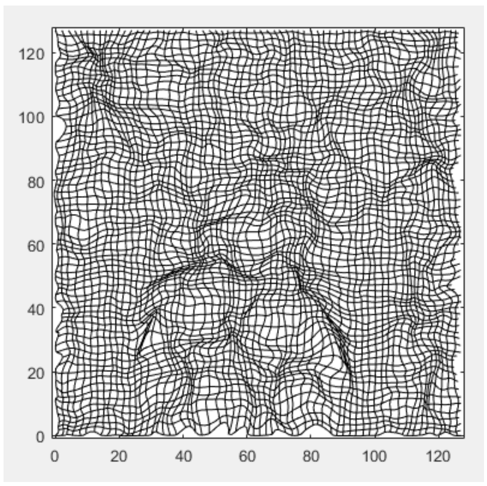
i.e. to calculate the composed transformation, T_{t+1}, we first apply the update and then the current transformation (make sure you understand why they are applied in this order – remember order matter for composition!).

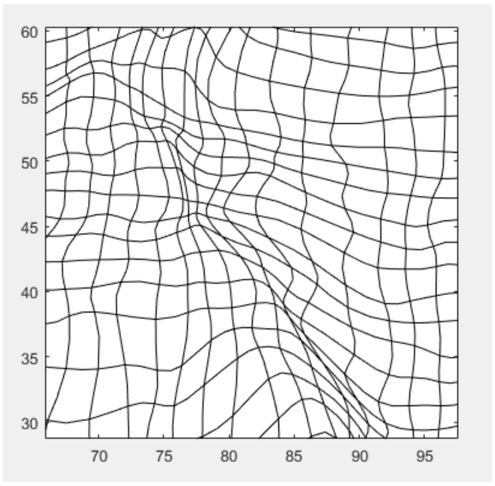
You can see that the equation for composing the transformation is the same as the equation for resampling the image, with the current transformation, T_t, replacing the image, I_{orig}, and T_{up} used as the transformation to resample the image/transformation.

Now perform a registration using the same parameters as above but use composition rather than addition to update the transformation. I.e. use the following parameters:

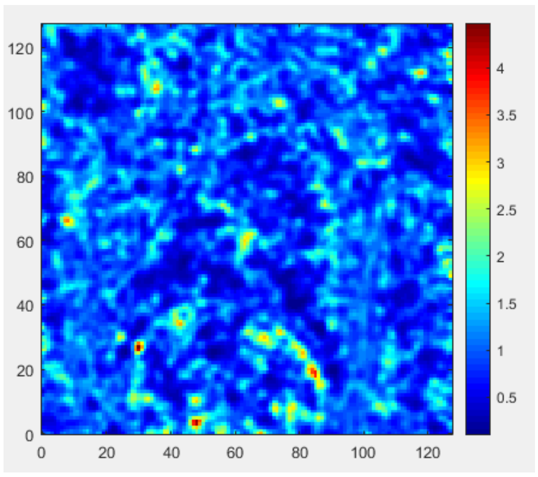
sigma_elastic = 0.5, *sigma_fluid* = 1, *num_lev* = 3, *use_composition* = true

You will notice that the deformation field no longer contains any folding:





but the Jacobian determinant map is still very patchy:



(note – a different intensity scale is used compared to the Jacobian determinant image on the previous page to show there is a different range of values)

This indicates that the deformation is still not very physically plausible. And if you look at the warped image you will see that it is not as similar to the target image as when addition was used for updating the transformation. This is reflected in the MSD value, which is 61.47 for composition and 56.77 for addition. But there is no folding when using composition and there is folding when using addition.

So which registration do you think is best?

As you will have seen, there are a number of other optional parameters that can be set. The parameters *disp_spacing*, *scale_update_for_display*, *disp_method_df*, and *disp_method_up* all effect how the deformation field and update are displayed but have no effect on the actual registration itself. The comments/help should explain how these parameters work, but if anything is unclear ask myself or one of the PGTAs in the lab session.

The *max_it* parameter sets the maximum number of iterations to be performed. The default value is 1000, but you should have noticed that usually the registration stops well before reaching this number of iterations. This is because the registration checks for an improvement in the MSD at each iteration, and if there has not been an improvement it will move on to the next resolution level or finish if it is already on the last level. This behaviour can be disabled by setting the *check_MSD* parameter to false. In this case the registration will run for the full *max_it* number of iterations at each level.

Try running a registration with the default parameters and *check_MSD* set to false. I suggest also setting *disp_freq* to 50 so that the registration does not take too long to run. By looking at the MSD values output to the command window you will notice that some iterations now cause (small) increases to the MSD. You will also notice that the registration reaches a stage at each level where the result starts to 'oscillate', with a few iterations making minor increases to the MSD and then a few making minor decreases to the MSD, and barely any noticeable changes to the warped image or deformation field. The final MSD value is lower than when *check_MSD* was set to true (74.66 compared to 81.83), but at the expense of running many more iterations. We can get a result that is very almost as good (MSD = 74.70) by setting *max_it* to 500 and only running half as many iterations, but the problem is it is difficult to know how many iterations will be required before the results start to 'oscillate' as this will depend on both the images being registered and the other parameters.

The last parameter that can be set is *use_target_grad*. This is false by default, and setting it to true will cause the registration to use the spatial gradient of the target image when calculating the demons forces rather than the spatial gradient of the source image, i.e. it will use the original demons forces rather than the common demons forces. If you run a registration with the default parameters and *use_target_grad* set to true and compare it to the results when *use_target_grad* is false, you will see there are differences in the results. However, each result aligns some regions/structures better than the other, and neither of the results are clearly the best overall (the final MSC is lower when *use_target_grad* is false, but this is not always true when different parameters are used).

Now try registering *cine_MR_1.png* to *cine_MR_3.png*, which is a more challenging registration due to the deep breath taken when *cine_MR_3.png* was acquired.

Experiment with different parameters – can you find some that give a good result?

Try swapping the source and target image over. Do you think you get better results with *cine_MR_3.png* as the source or target image (or are they equally bad for both!)?

There is a friendly competition to see who can get the best registration results between *cine_MR_1.png* and *cine_MR_3.png*. If you think you manage to achieve a good registration then email me with the parameters you used and a brief explanation (1-2 sentences) of why you think the result is good, e.g. what has it aligned well and what has it failed to align well, is the deformation field physically plausible. Please send me your results by the end Friday 12th Feb (the day after the last registration lab session) and I will announce the winner the following week. You are welcome to work in small groups on this if you prefer, and submit a result on behalf of the group.