Lecture 4
Intro to Registration with ITK

(Bio)Medical Image Analysis - Spring 2026
16-725 (CMU RI) : BioE 2630 (Pitt)
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Based in part on Damion Shelton's slides from 2006

For more info/gory detail…

- Please see the following for exhaustive detail:
  - Chapter 3 in the ITK Software Guide Book 2
  - *Insight into Images*
  - ITK Source Tree
    - Examples/RegistrationITKv4/
    - E.g. Examples/RegistrationITKv4/ImageRegistration1.cxx
  - ITK Doxygen
    - http://www.itk.org/Doxygen53/html/group__Group-Registration.html
    - https://itk.org/Doxygen53/html/group__ITKRegistrationMethodsv4.html
    - http://www.itk.org/Doxygen53/html/group__Group-Numerics.html
  - SimpleITK:
    - http://insightsoftwareconsortium.github.io/SimpleITK-Notebooks/
      - See all the Python Registration (6x) notebooks, especially:
      - http://insightsoftwareconsortium.github.io/SimpleITK-Notebooks/Python_html/60_Registration_Introduction.html
      - https://simpleitk.org/doxygen/v2_3/html/classitk_1_1simple_1_1ImageRegistrationMethod.html

What is registration?

- The process of aligning a target image to a source image
- More generally, determining the transform that maps points in the target image to points in the source image

Transform types

- Rigid (rotate, translate)
- Affine (rigid + scale & shear)
- Deformable = non-rigid (affine + vector field)
- Many others

Registration in ITK

- ITK uses an extensible registration framework
- Various interchangeable classes exist
- Relatively easy to “twiddle” the part you’re interested in while recycling prior work

- The newer ITKv4 Registration framework is separate from the legacy framework.
  - The legacy framework follows traditional practice
  - Version 4 registration is more flexible and thus more complex
  - Use the v4 framework whenever practical

- SimpleITK also supports registration

- For “simplified” complex registration, consider using ANTS instead:
  - http://picsl.upenn.edu/software/ants/
  - http://stnava.github.io/ANTs/

New since ITKv4 (ImageRegistrationMethodv4, etc.)

- New unified, improved, and fully multi-threaded optimization and registration framework (including multi-threaded metrics)
- Dense deformation fields (including a new transform that encapsulates a dense deformation field)
- Point Set registration methods (landmark or label guided registration)
- Automatic parameter scale estimation for transforms
- Automatic step-size selection for gradient-based registration optimizers
- Composite Transforms (grouping multiple transforms into a single one)
- Symmetric registration (where the Fixed and Moving images make unbiased contributions to the registration)
- New metrics for Demons and Mutual Information
- Diffeomorphic (velocity field) deformable registration
- Additional evolutionary optimizers
- Improved B-Spline registration approach available and bug fixes to old framework
- Accurately transform and reorient covariant tensors and vectors

List taken from http://www.itk.org/Wiki/ITK_Release_4/Why_Switch_to_ITKv4 and http://www.itk.org/Wiki/ITK_Release_4/Migration_Plan/Release_Notes/ITKv4_Final_Release_Notes

ITKv4 Registration

- Uses a different framework than “traditional” ITK registration. The new framework is designated with a “v4” suffix.
- You must use a v4 metric and a v4 optimizer when doing a v4 registration!

- Take a look here:

  http://www.itk.org/Doxygen53/html/group__ITKRegistrationMethodsv4.html
  http://www.itk.org/Doxygen53/html/group__ITKMetricsv4.html
  http://www.itk.org/Doxygen53/html/group__ITKOptimizersv4.html
  ITK source code: Modules/Registration/RegistrationMethodsv4/include/
  ITK source code: Modules/Registration/Metricsv4/include/
  ITK source code: Modules/Numerics/Optimizersv4/include/
- Pay special attention to:
  - MattesMutualInformationImageToImageMetricv4
  - DemonsImageToImageMetricv4
  - QuasiNewtonOptimizerv4 (an improved gradient descent)

Typical registration terminology

- Fixed image $f(x)$ - stationary in space
- Moving image $m(x)$ - the fixed image with an unknown transform applied
- Goal: recover the transform $T(x)$ which maps points in $f(x)$ to $m(x)$

Typical registration framework

- 2 input images, fixed and moving
- Metric - determines the “fitness” of the current registration iteration
- Optimizer - adjusts the transform in an attempt to improve the metric
- Interpolator - applies transform to image and computes sub-pixel values

Typical registration flowchart

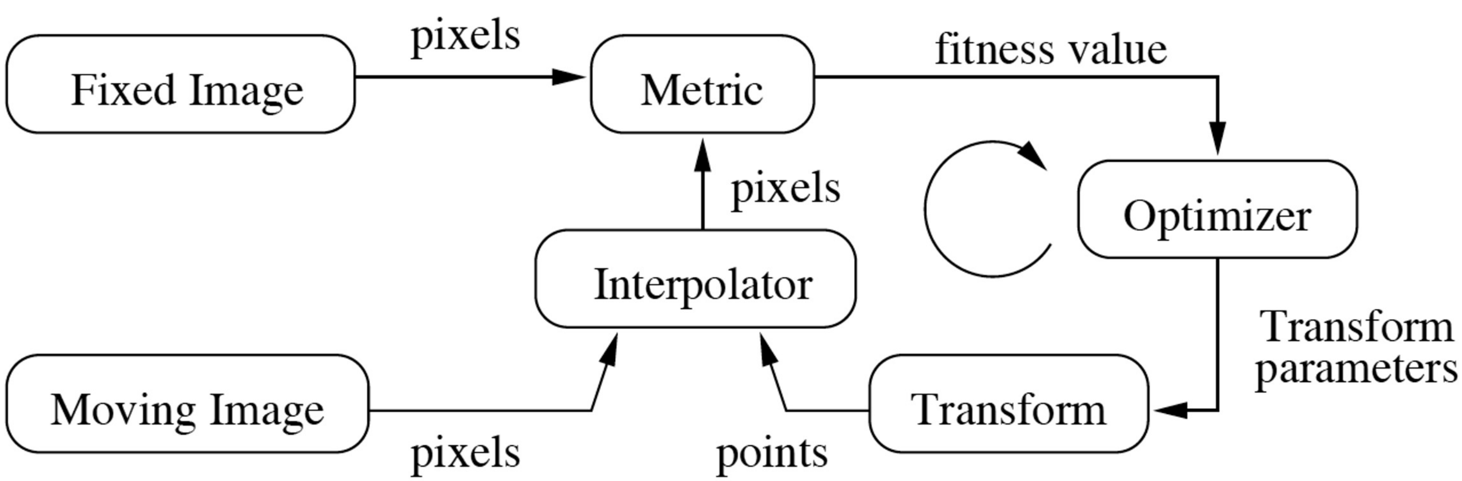


Figure 8.2 from the ITK Software Guide v 2.4, by Luis Ibáñez, et al.

ITK v4 registration flowchart

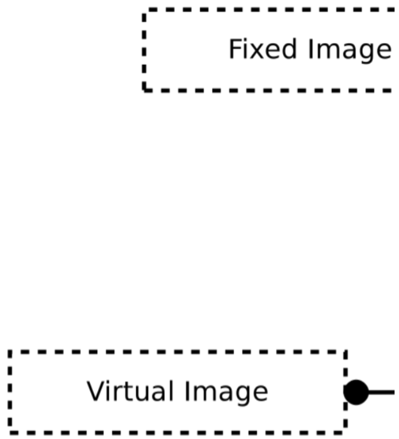


Figure 3.3 from the ITK Software Guide Book 2, Fourth Edition, by Hans J. Johnson, et al.

ITK v4: key differences

- Both input images are transformed into a common virtual domain, which determines:
  - The output resampled-image dimensions and spacing
  - The sampling grid (not necessarily a uniform grid)
  - Defaults to the fixed image domain
- Only the Moving Transform is Optimized
- Fixed Transform defaults to identity transform
  - But it could be set to the result of a previous registration, etc.

ITK v4 Virtual Domain

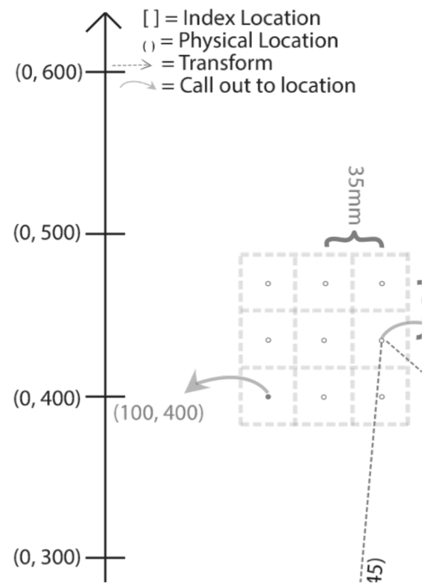


Figure 3.8 from the ITK Software Guide Book 2, Fourth Edition, by Hans J. Johnson, et al.

ITK’s “Hello world” registration example

- Uses ITK’s v4 framework, but in the “typical” traditional style
- Please see the software guide (Book 2, Section 3.2) for code specifics
- I am going to cover what each piece does, not look at code per se

ITK's "Hello World" Example: Flow Chart for Everything

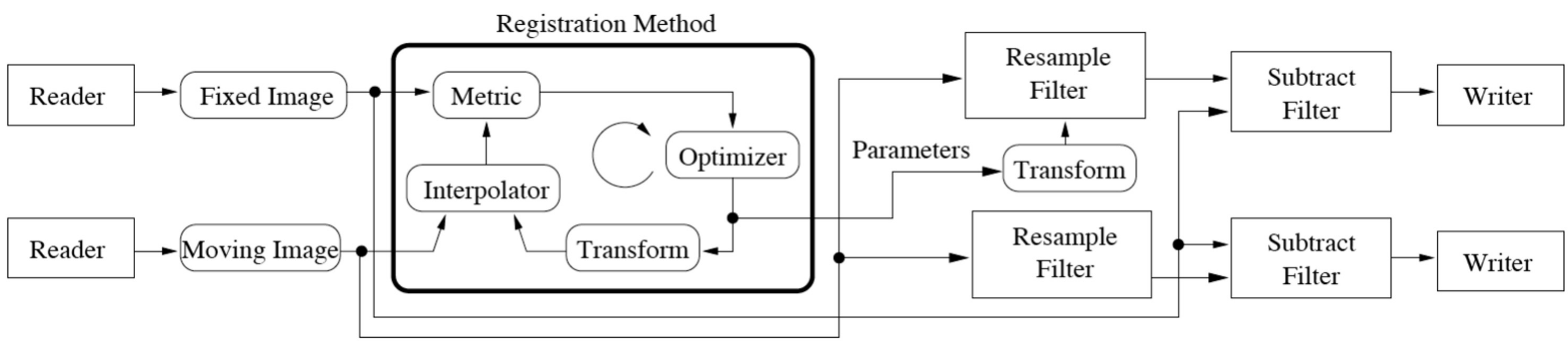


Figure 8.5 from the ITK Software Guide v 2.4, by Luis Ibáñez, et al.

Input images

- 2D floating point
- Floating point avoids loss of precision problems with integer pixel types

Transform

- TranslationTransform
- Permits *translation only* in 2D

- ITKv4 still uses the same legacy transforms
- ITKv4 also supports new *composite transforms*:
  - Two or more successive transforms…
  - Combined into a single transform object
  - Can initialize with one transform and optimize another

Metric

- MeanSquaresImageToImageMetricv4
- Sum of squared differences between 2 images on a "pixel-by-pixel" basis
  - Remember that both images are transformed to the virtual domain before doing the comparisons
- A bit naïve
- Works for 2 images that were acquired with the same imaging modality

Optimizer

- RegularStepGradientDescentOptimizerv4
- Follows the derivative of the metric
- Step size depends on rapid changes in the gradient's direction
- Step size eventually reaches a user-defined value that determines convergence

Interpolator

- LinearInterpolateImageFunction
- Fast and conceptually simple

Wrapper

- ImageRegistrationMethodv4
- Combines all of the previous classes into a master class

```
registration->SetMetric( metric );
registration->SetOptimizer( optimizer );
metric->SetFixedInterpolator( FixedInterpolator);
metric->SetMovingInterpolator( MovingInterpolator);
```

- Registration method automatically instantiates its own internal transform
  - Based on its template parameters

Other steps

- Read the input images
- Setup the virtual domain
  - Defaults to the fixed image
- Set the region of the fixed image the registration will operate on
  - Useful for ignoring bad data
- Initialize the transforms
  - Fixed transform defaults to identity
- Setup multi-level registration
  - Like image-pyramids, but better
  - Defaults to a single level
- Use a C++ try/catch block to avoid crashing on errors
- Twiddle the optimizer for best performance*

*may involve pain and suffering

Hello world input

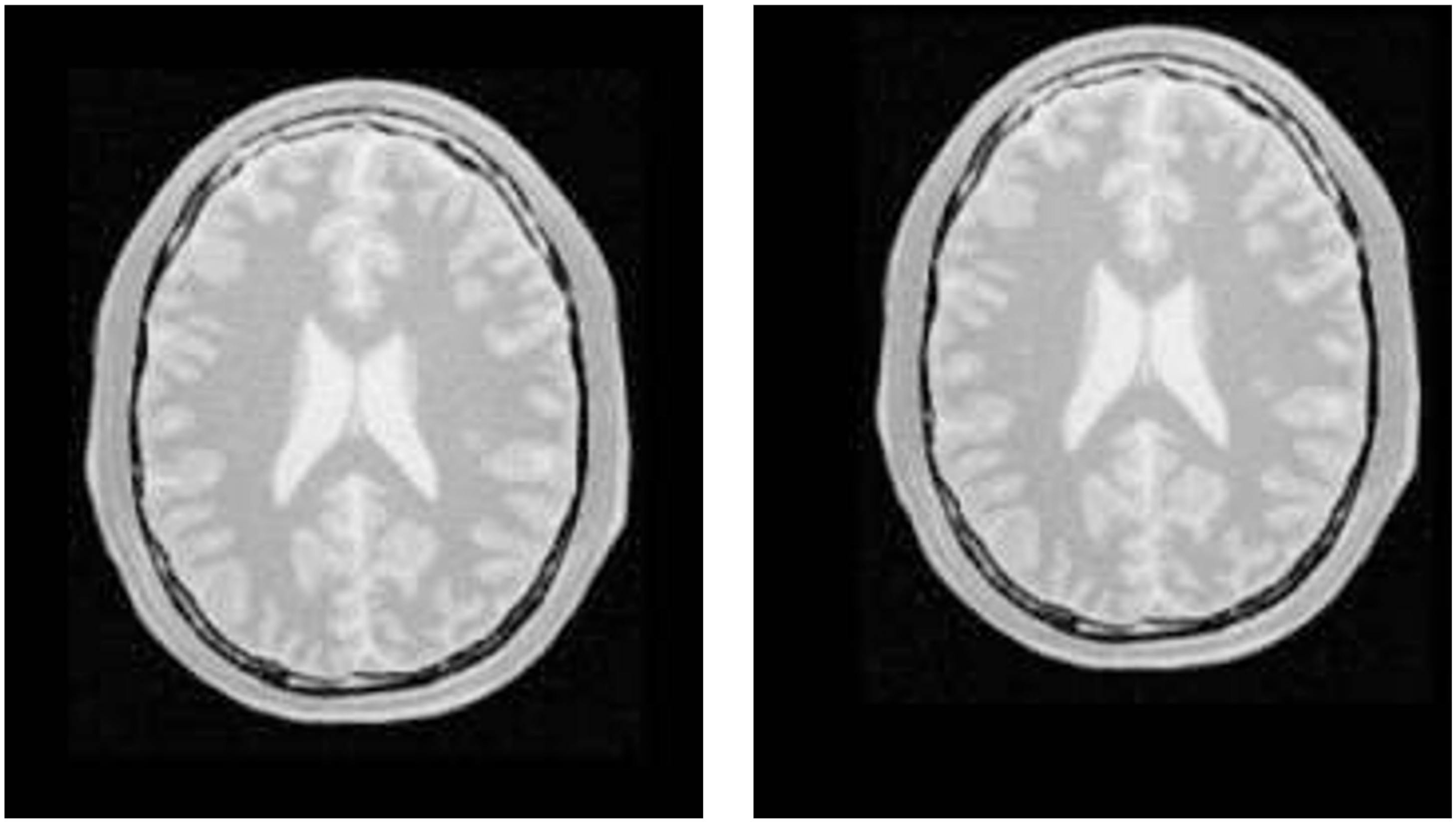


Figure 8.3 from the ITK Software Guide v 2.4, by Luis Ibáñez, et al.

X & Y translation vs. time

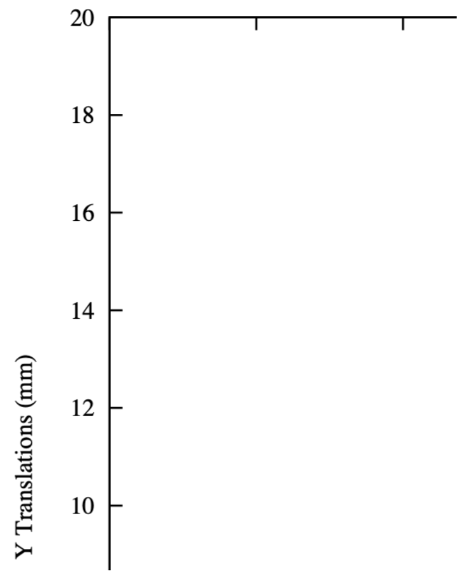


Figure 3.7 (left) from the ITK Software Guide Book 2, Fourth Edition, by Hans J. Johnson, et al.

Metric vs. time

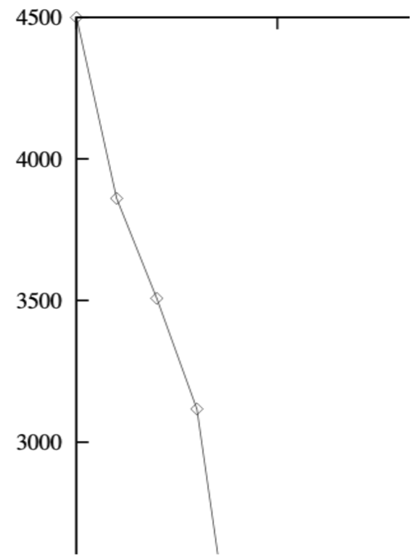


Figure 3.7 (left) from the ITK Software Guide Book 2, Fourth Edition, by Hans J. Johnson, et al.

Registration results

- After registration converges/terminates, you recover the optimized transform with:

```
registration->GetTransform()
```

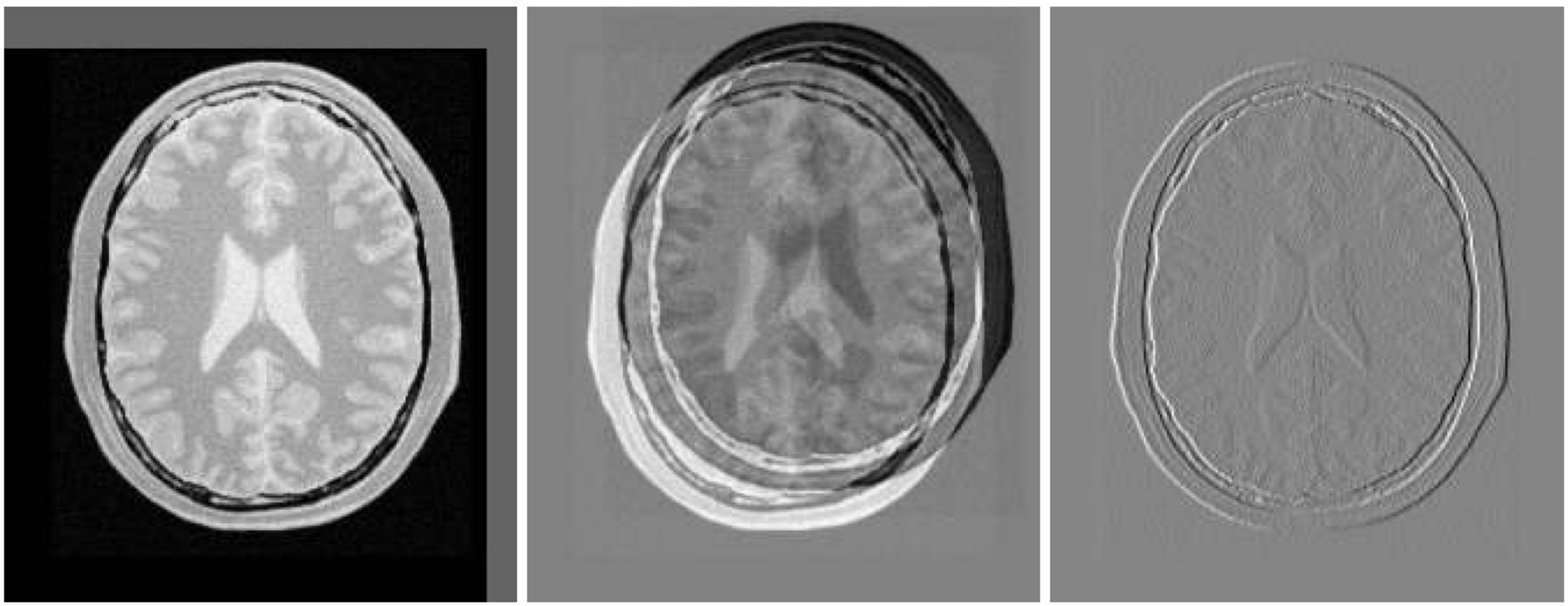
- For the Hello World example there are 2 parameters, X & Y translation
- If you used a separate initial moving transform, create a composite to get the total transform:

```
outputCompositeTransform->AddTransform(
    movingInitialTransform);
outputCompositeTransform->AddTransform(
    registration->GetModifiableTransform());
```

Double checking results

- Use ResampleImageFilter to apply the transform for the fixed and moving images
- Take the outputs, and compute their difference
- In this case, just subtract the registered images
  - Good registration results in nothing much to see

Image comparison



Registered moving image | Difference before registration | Difference after registration

Figure 8.4 from the ITK Software Guide v 2.4, by Luis Ibáñez, et al.

Keeping tabs on registration

- Registration is often time consuming
- It’s nice to know that your algorithm isn’t just spinning it’s wheels
- Use the observer (**itk::Command**) mechanism in ITK to monitor progress
  - ITK software guide, book 1: 3.2.6 and book 2: 3.4
- We’ll see this again later, when we discuss how to write your own ITK filters
  - **itk::ProgressEvent** is one example

Observer steps

- Write an observer class that will process "iteration" events
  - (Just copy some code from an example)
- Add the observer to the optimizer
  - As a generic note, observers can observe any class derived from **itk::Object**
- Start registration as usual

Things observers can do

- Print debugging info
- Update GUI
- Other small management functions
- *Should not* do anything too processor intensive

ITK v4 Registration Observer

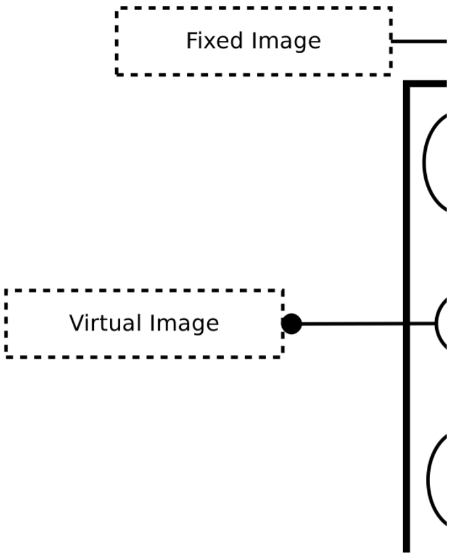


Figure 3.9 from the ITK Software Guide Book 2, Fourth Edition, by Hans J. Johnson, et al.

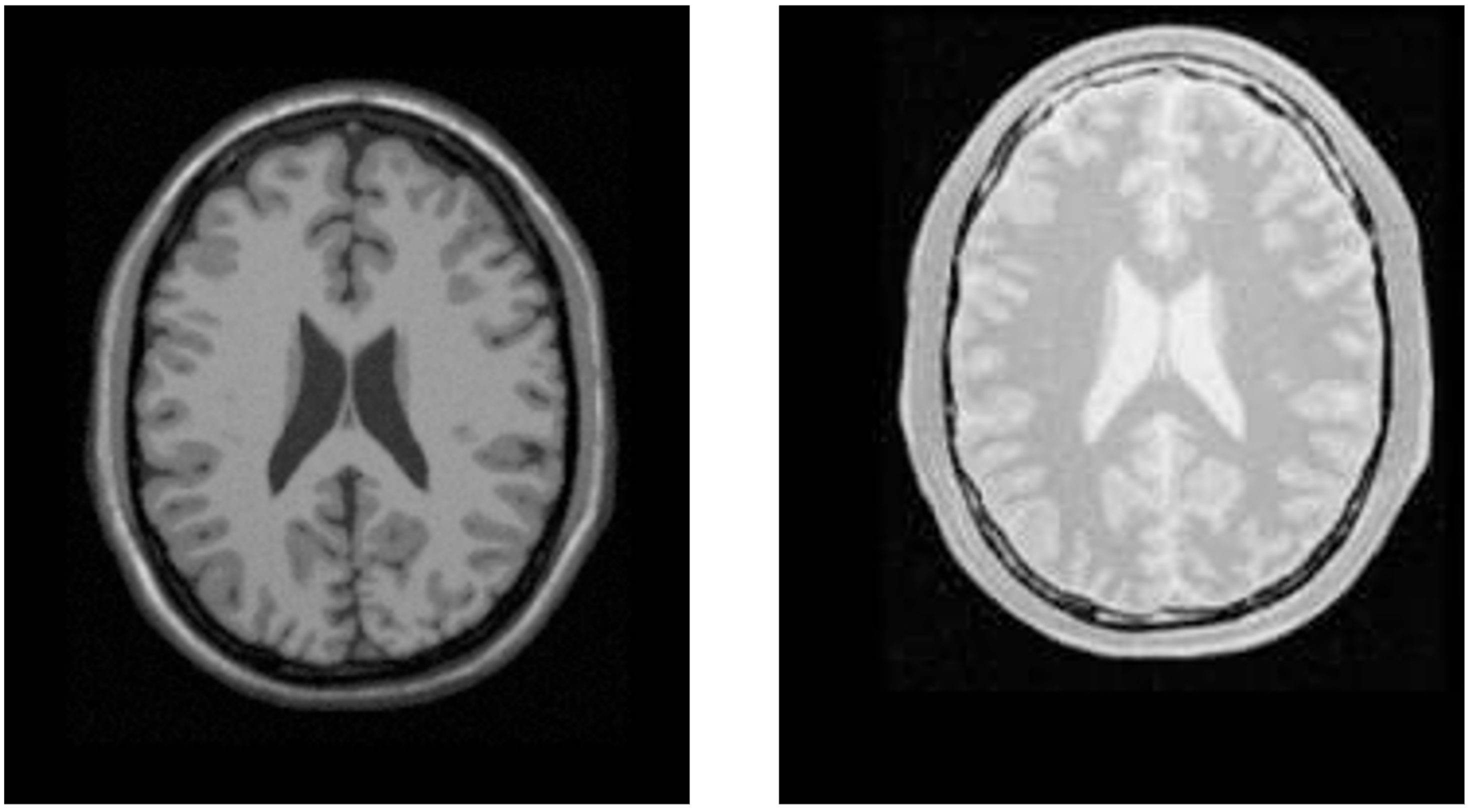
Multi-modality registration

- Remember how I said sum-of-squares difference is relatively naïve?
- Mutual information helps overcome this problem
- Section 3.5 shows how to implement a simple MI registration
  - Note that Mattes MI is usually easier to use than Viola-Wells MI

Notes about the MI example

- Significantly, largely the same piece of code as Hello World
- Mutual Information is a *metric*, so we can keep the optimizer, the interpolator, and so on
- Majority of differences are in tweaking the metric, not in rewriting code

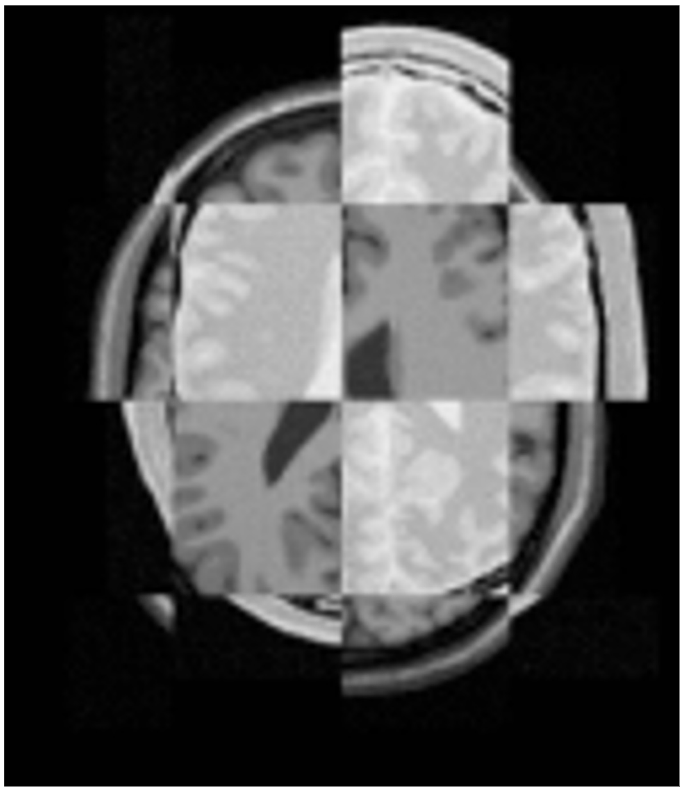
MI Inputs



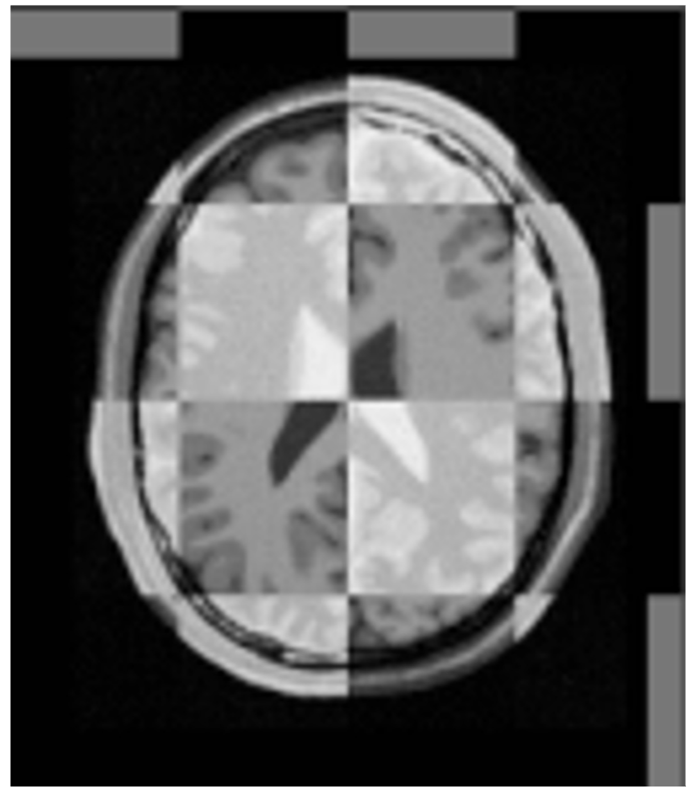
T1 MRI Proton density MRI

Figure 8.9 from the ITK Software Guide v 2.4, by Luis Ibáñez, et al.

MI Output: Image Comparison



Before



After

This is an example of a checkerboard visualization

Taken from Figure 8.10 of the ITK Software Guide v 2.4, by Luis Ibáñez, et al.

Centered transforms

- More natural (arguably) reference frame than having the origin at the corner of the image
- Big picture is not appreciably different from other rigid registrations
- But, for the moment there are implementation complexities and differences, see 3.6

An aside: “Twiddling”

- A common criticism of many/most registration techniques is their number of parameters
- A successful registration often depends on a very specific fine-tuning of the algorithm
- “Generalized” registration is an open problem

Multi-Resolution registration

- Useful to think of this as algorithmic "squinting" by using image pyramids
- Start with something simple and low-res
- Use low-res registration to seed the next higher step
- Eventually run registration at high-res
- Also called "coarse to fine"

Multi-resolution idea

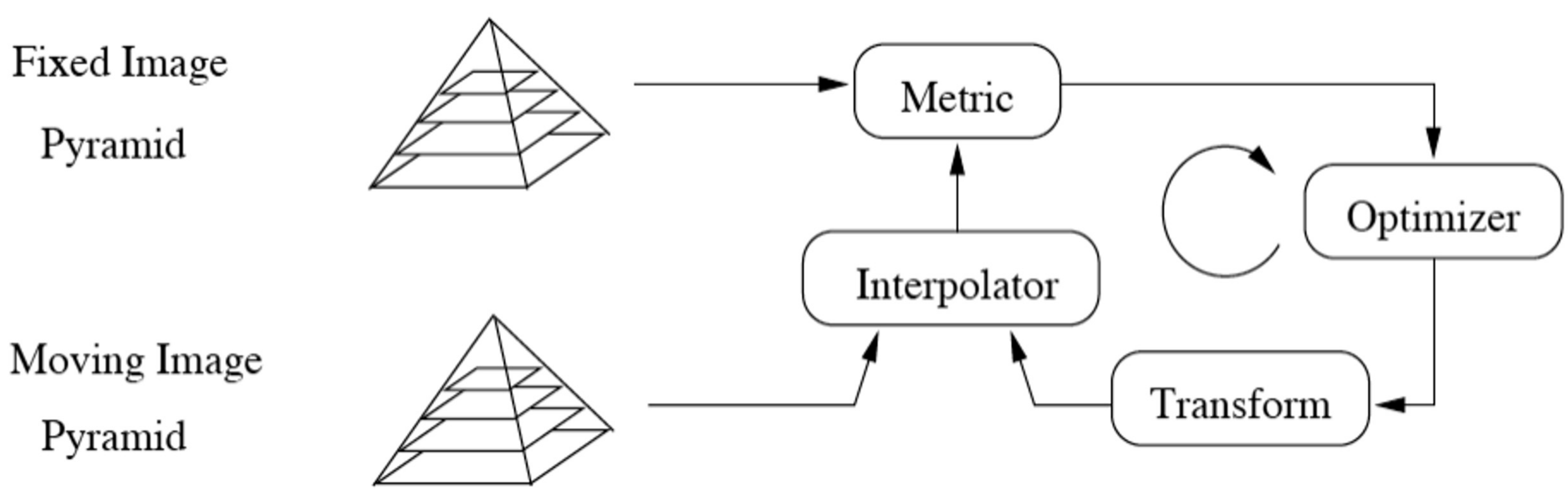


Figure 8.36 from the ITK Software Guide v 2.4, by Luis Ibáñez, et al.

Image pyramids

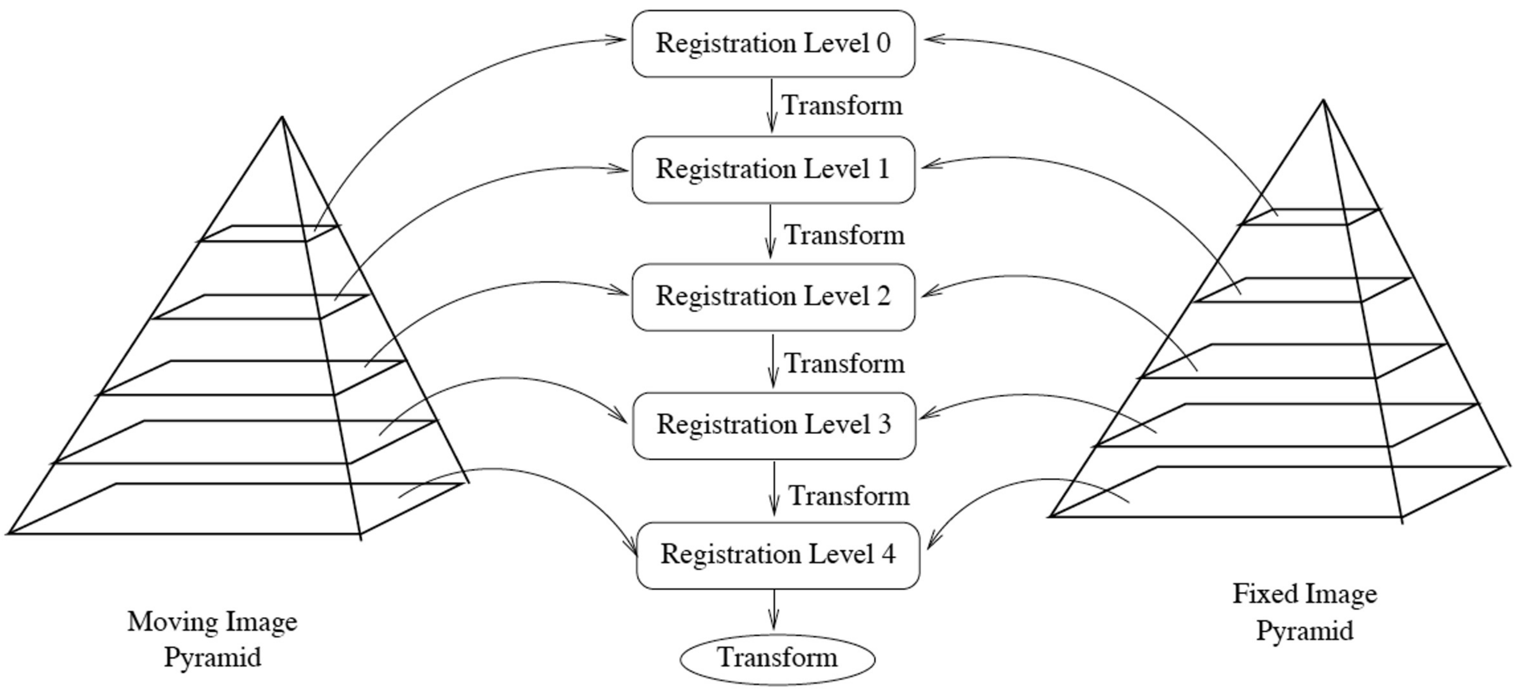


Figure 8.37 from the ITK Software Guide v 2.4, by Luis Ibáñez, et al.

Optimization

- Parameter dependency rears its ugly head
- You often/usually need to adjust optimizer parameters as you move through the pyramid
- You can do this using the Observer mechanism

Multi-resolution example

- Again, mostly the same code as Hello World
- Multi-Resolution is now built into all of ITKv4 registration, so no need for extra classes or image pyramids

Benefits of multi-resolution

- Often faster
- More tolerant of noise (from “squinting”)
- Minimizes initialization problems to a certain extent, though not perfect

Multi-resolution

- Remember, at large (high) scale only large objects are visible
- Higher scale is higher in the image pyramid
  - So higher scale has lower resolution
- Lower scale is lower in the image pyramid
  - So lower scale has higher resolution

See the software guide for…

- Detailed list of:
  - Transforms
  - Optimizers
  - Interpolation methods
- You’re encouraged to mix and match!

Deformable registration

- Three common techniques:
  - Finite element: treat small image regions as having physical properties that control deformation
  - Bsplines: deform a mapping grid
  - Demons: images are assumed to have iso-intensity contours (isophotes); image deformations occur by pushing on these contours

Model based registration

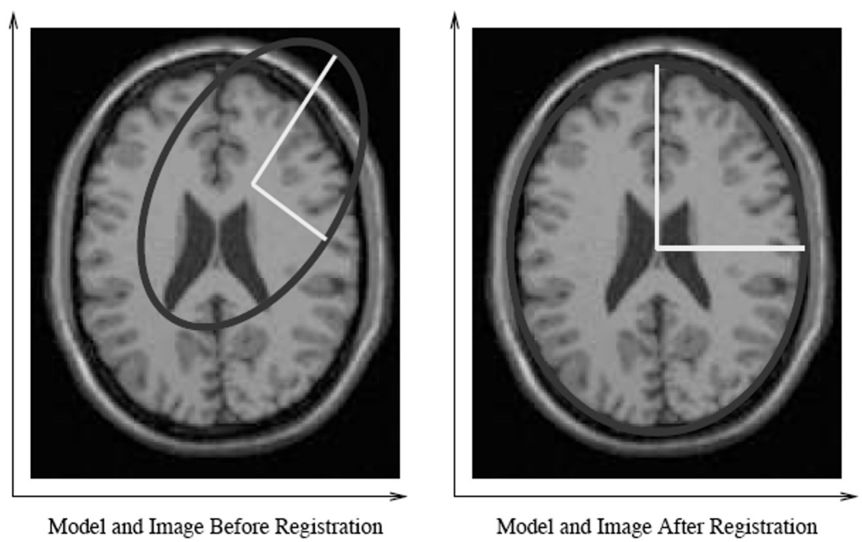
- Software guide, book 2, ch. 3, section 16.

- Build a simplified geometric model from a training set
- Identify parameters that control the characteristics of the model
- Register the model to a target image to adapt to a particular patient

Model based, cont.

- Uses the Spatial Objects framework for representing geometry
- Useful because it derives analytical data from the registration process, not just a pixel-to-pixel mapping

Model-based example



Note: This is what we want, NOT the output of an actual registration

Figure 8.60 from the ITK Software Guide v 2.4, by Luis Ibáñez, et al.

Model-based reg. schematic

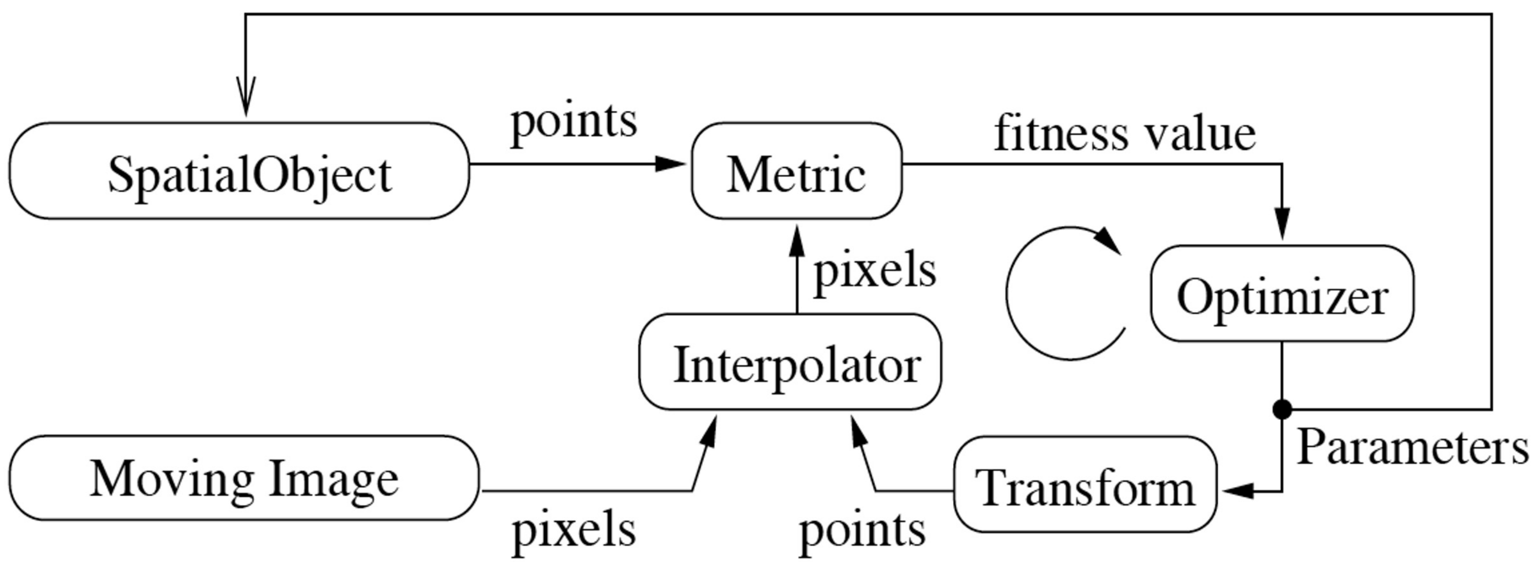


Figure 8.59 from the ITK Software Guide v 2.4, by Luis Ibáñez, et al.

Model-based registration: Warning!

- ITK does not yet directly support generic model-based registration "out of the box"
- ITKv4 does support point-set to image registration
- Otherwise, model-based reg. requires writing your own custom ITK transform, with new parameters
  - Transform's new parameters → Spatial Object parameters
  - *You* must individually map your custom transform's new parameters to the specific spatial object parameters you want to allow registration to adjust
  - This isn't too complicated if you know what you're doing
  - Search Insight Journal for examples

Speed issues

- Execution time can vary wildly
  - Optimizer (more naïve = faster)
  - Image dimensionality (fewer = faster)
  - Transform (fewer DOF = faster)
  - Interpolator (less precise = faster)

Take home messages

- Exactly what parameters do what is not always obvious, even if you are familiar with the code
- Successful registrations can be something of an art form
- Multi-resolution techniques can help
- Work within the framework!