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

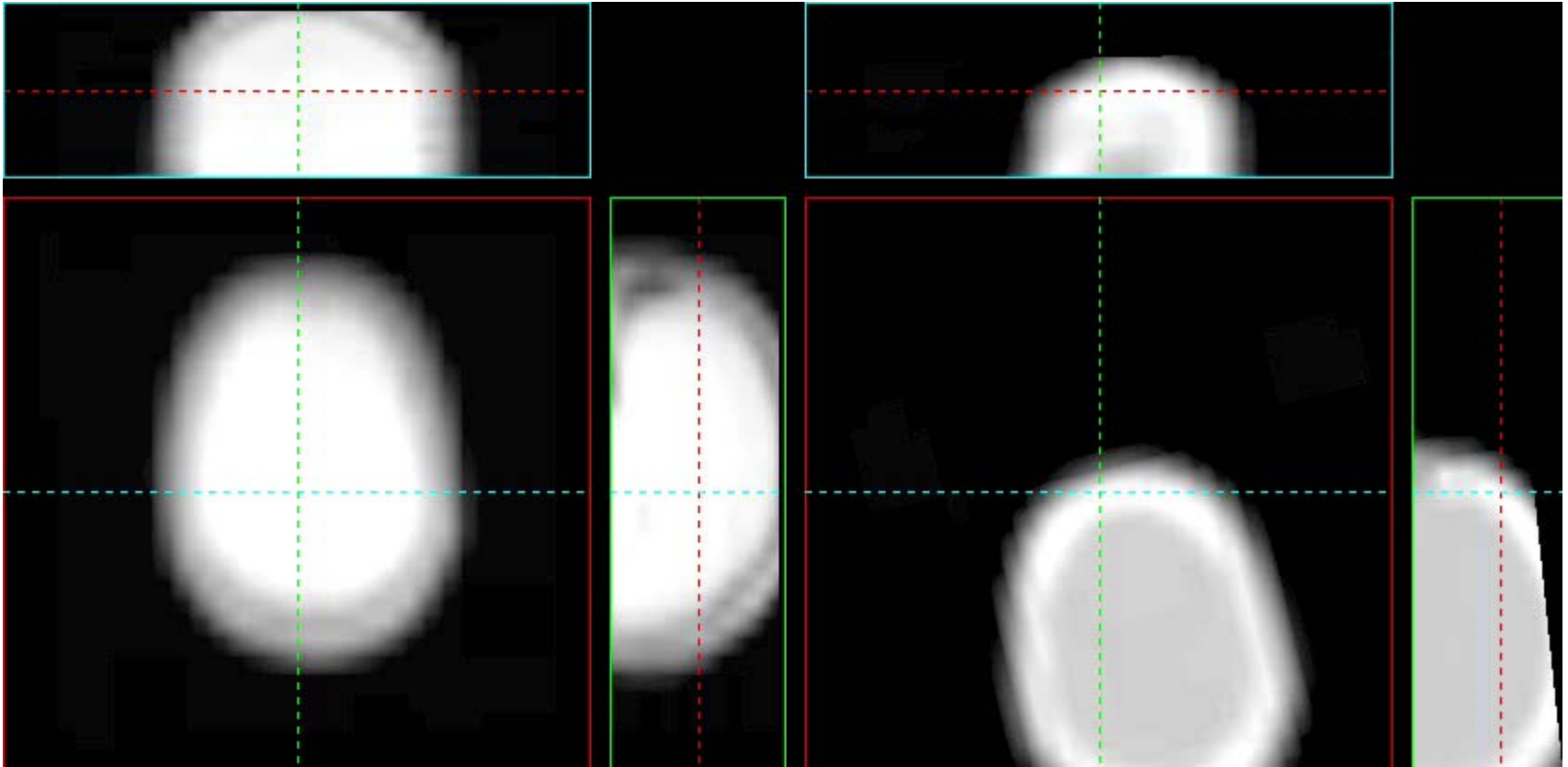
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# Medical Image Registration II

**HST 6.555**

**Lilla Zöllei and William Wells**

# CT-MR registration movie

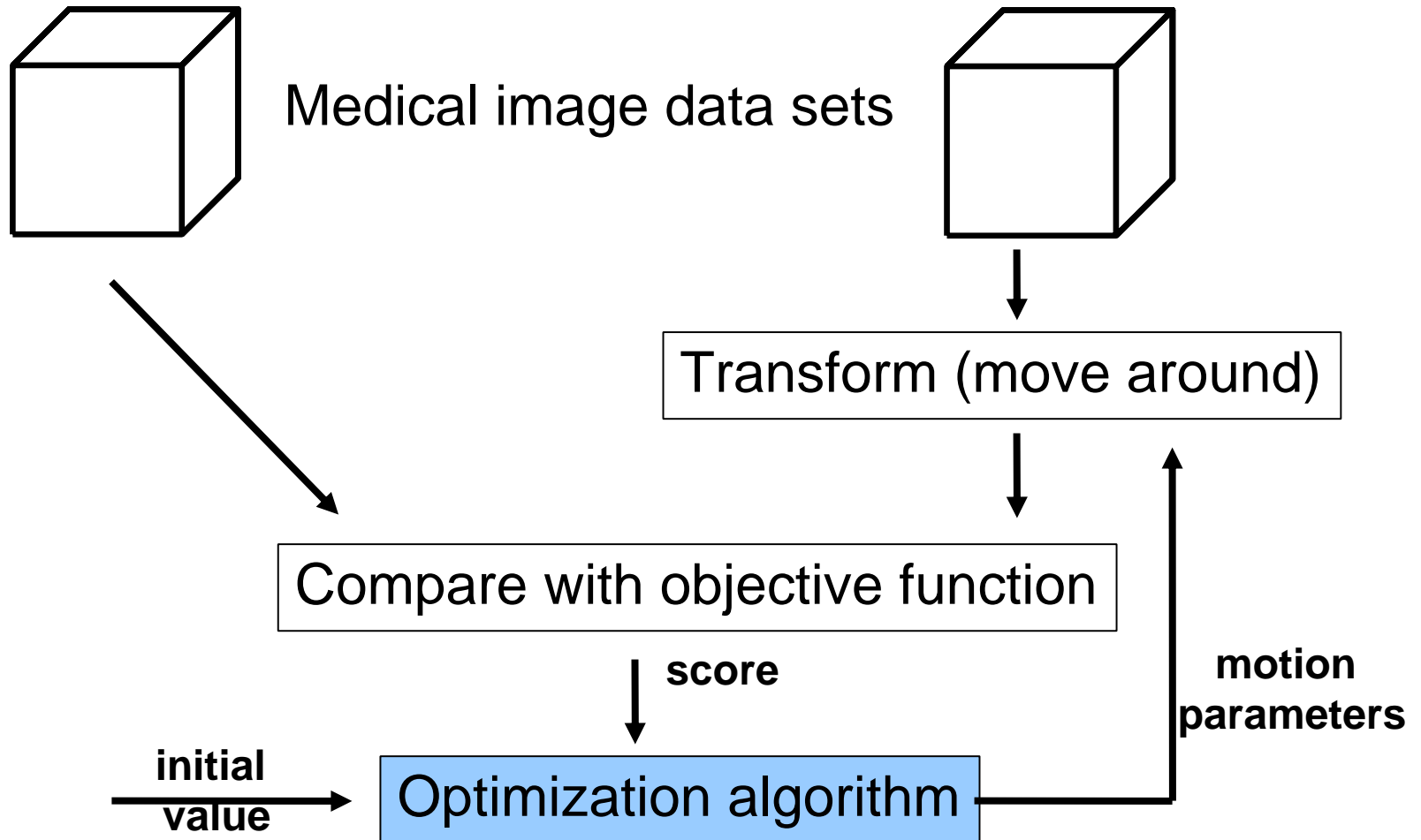


From: Wells, W. M., et al. "Multi-modal Volume Registration by Maximization of Mutual Information."  
*Medical Image Analysis* 1, no. 1 (March 1996): 35-51.  
Courtesy Elsevier, Inc., <http://www.sciencedirect.com>. Used with permission.

# Roadmap

- ✓ Data representation
- ✓ Transformation types
- ✓ Objective functions
  - ✓ Feature/surface-based
  - ✓ Intensity-based
- ➔ Optimization methods
- Current research topics

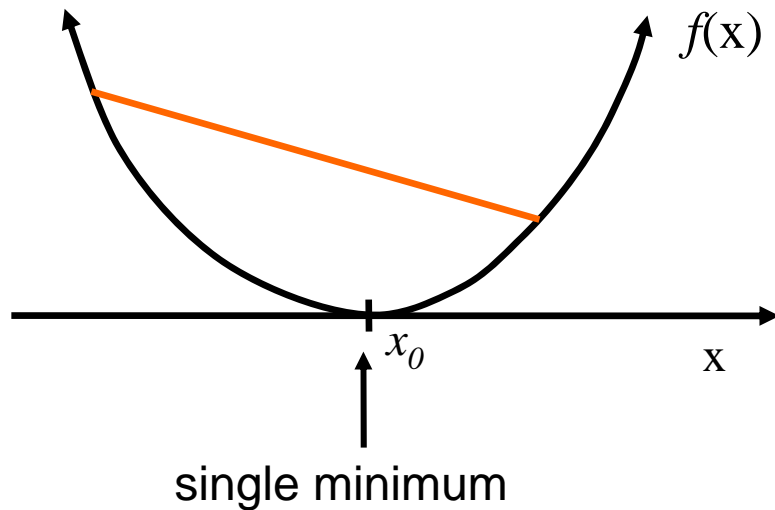
# Medical Image Registration



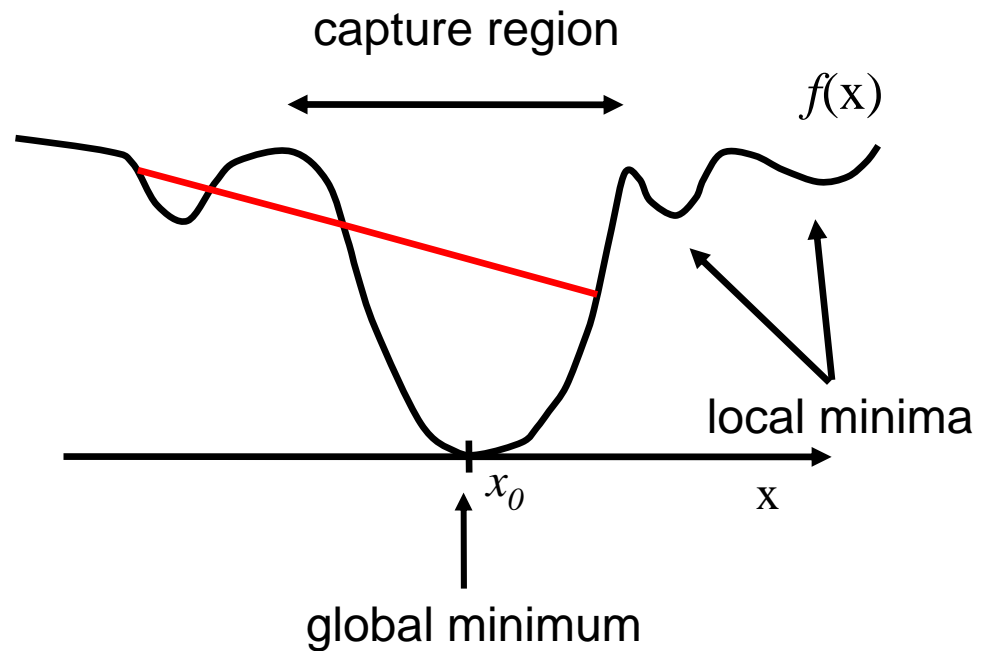
# Optimization -- terminology

- find  $x$  that minimizes  $f(x)$

convex:



non-convex:



# Optimization (for registration) (1)

- Goal: find  $\mathbf{x}$  that optimizes  $f(\mathbf{x})$ 
  - do it quickly, cheaply, in small memory; (or evaluate  $f$  as few times as possible)
- Parameter recovery: “search” for solution
  - Standard mathematical function (with T dependency) to be optimized
    - use only function evaluations
    - use gradient calculations (more guidance, but costly)
- Based upon prior information:
  - *constrained*, e.g.:  $x_1 \leq x \leq x_2$
  - *unconstrained*

# Optimization (for registration) (2)

- No guarantees about global extremum
  - Local extrema:
    - sometimes sufficient\*\*
    - find local extrema from a wide variety of starting points; choose the best
    - perturb local extremum and see whether we return
  - Ambitious algorithms:
    - simulated annealing methods
    - genetic algorithms



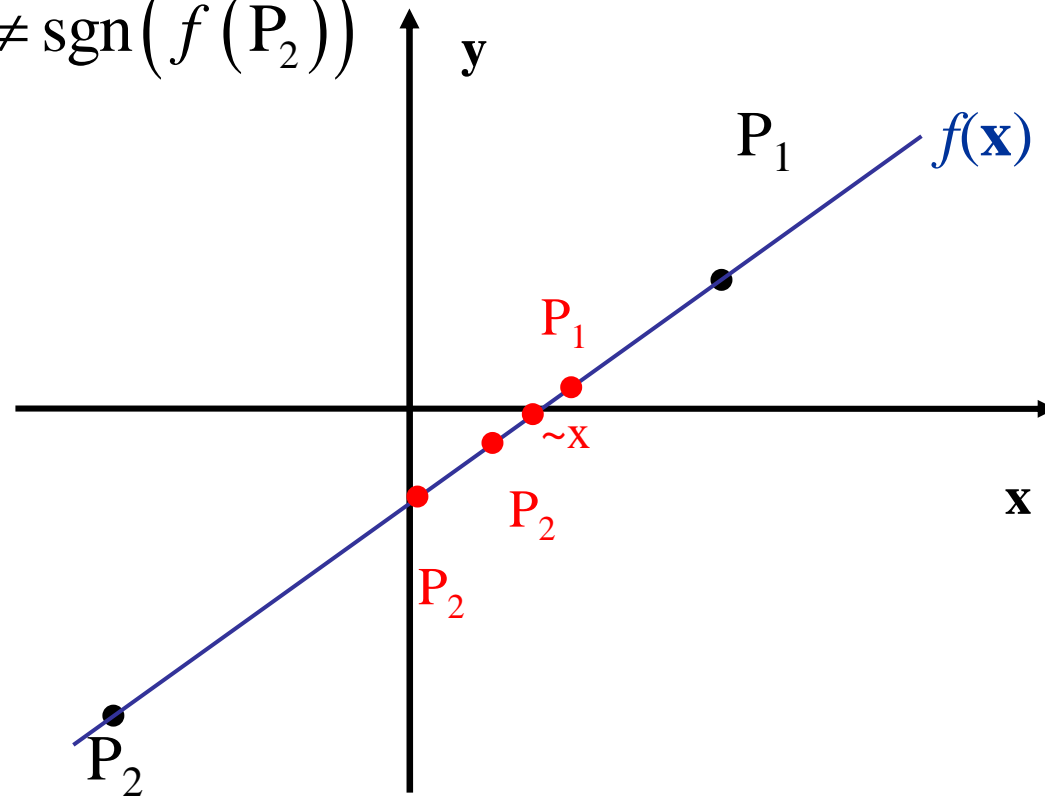
# Search Algorithms

- **1D solutions** – minimum bracketing is possible
  - Golden Section Search
  - Brent's Method
  - Steepest Descent
- **Multi-dimension** – initial guess is important!
  - Downhill Simplex (Nelder & Mead)
  - Direction Set Methods
    - Coordinate Descent
    - Powell's Method
  - Gradient Methods
    - Conjugate gradient methods

# Root finding by bisection

- Root-bracketing by two points:  $(P_1, P_2)$

$$\text{sgn}(f(P_1)) \neq \text{sgn}(f(P_2))$$



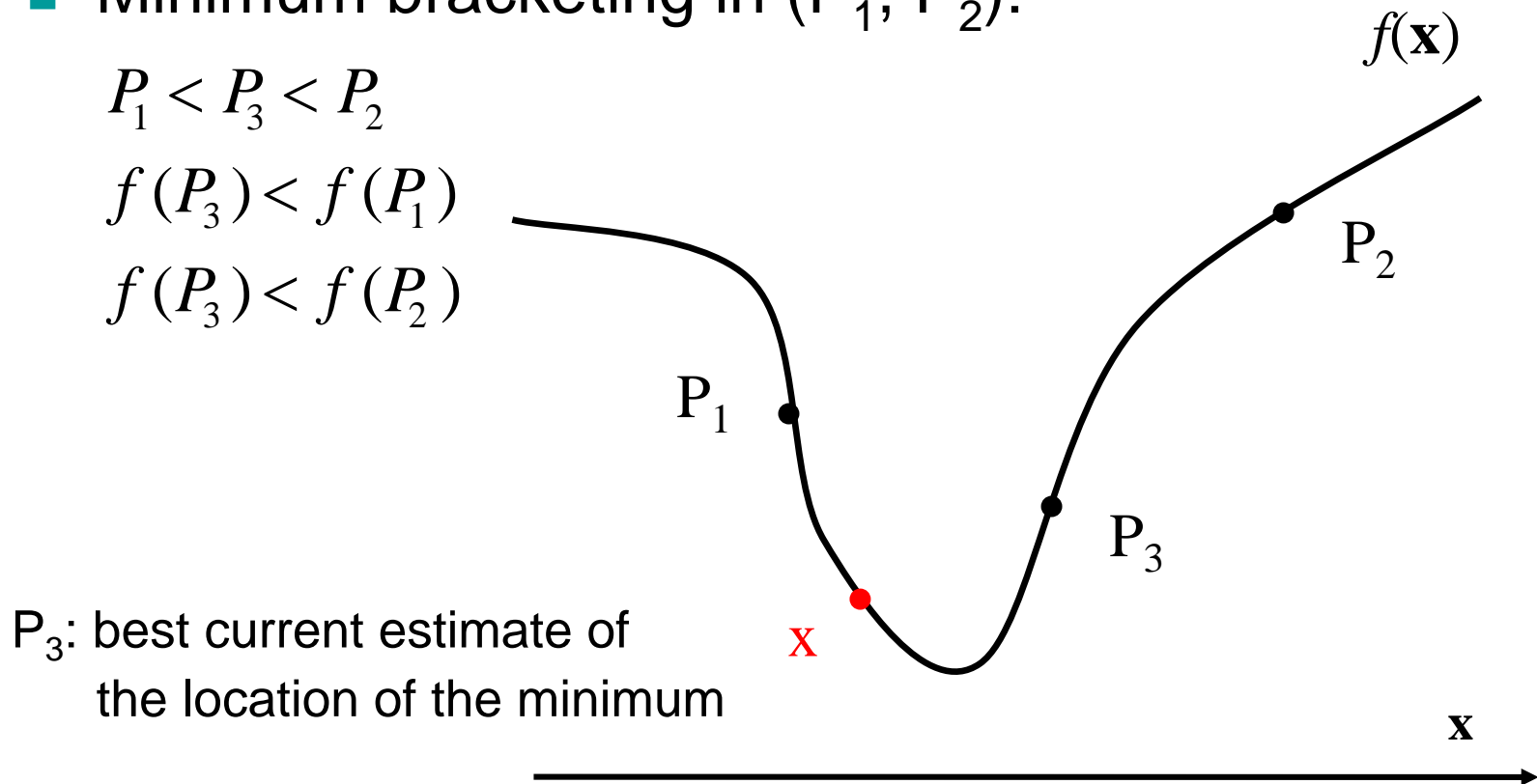
# Minimization of convex function

- Minimum bracketing in  $(P_1, P_2)$ :

$$P_1 < P_3 < P_2$$

$$f(P_3) < f(P_1)$$

$$f(P_3) < f(P_2)$$



$P_3$ : best current estimate of the location of the minimum

# Golden Section Search

## ■ Minimization strategy:

- (i) select the larger of  $\overline{P_1P_3}, \overline{P_3P_2}$   
 $\rightarrow$  assign this interval to be  $L$

- (ii) position  $x$  in  $L$  s.t.

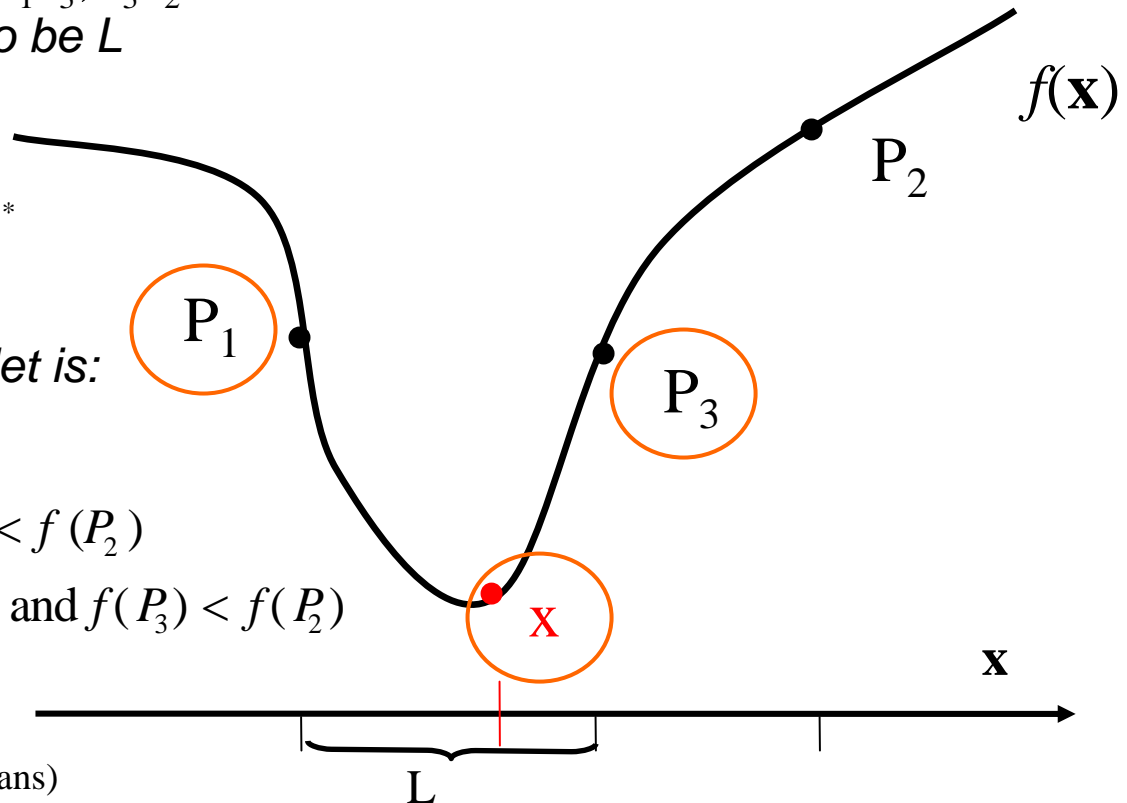
$$\frac{\|\overline{P_3x}\|}{\|L\|} = \frac{(3-\sqrt{5})}{2} \approx .38197^*$$

- (iii) new bracketing triplet is:

$(P_1, x, P_3)$  if

$$f(x) < f(P_1) \text{ and } f(x) < f(P_2)$$

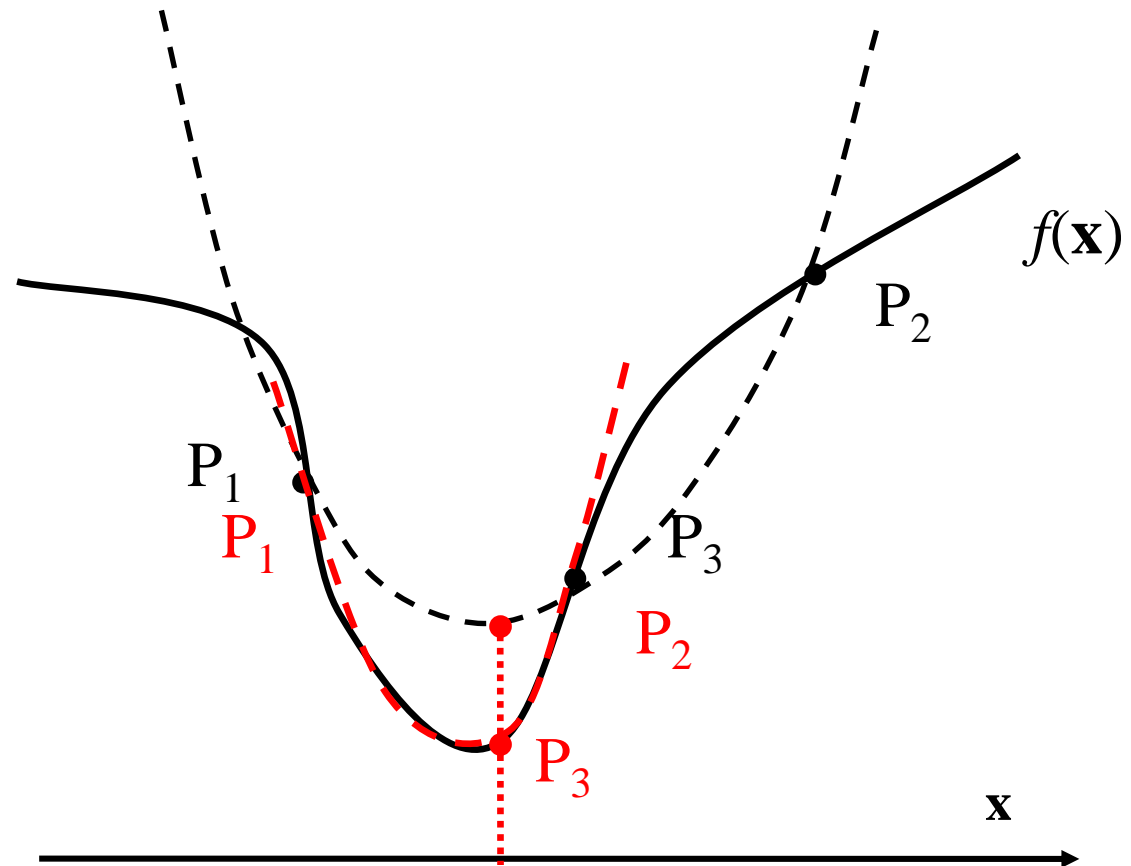
$(x, P_3, P_2)$  if  $f(P_3) < f(x)$  and  $f(P_3) < f(P_2)$



\*golden mean / golden section (Pythagoreans)

# Brent's Method

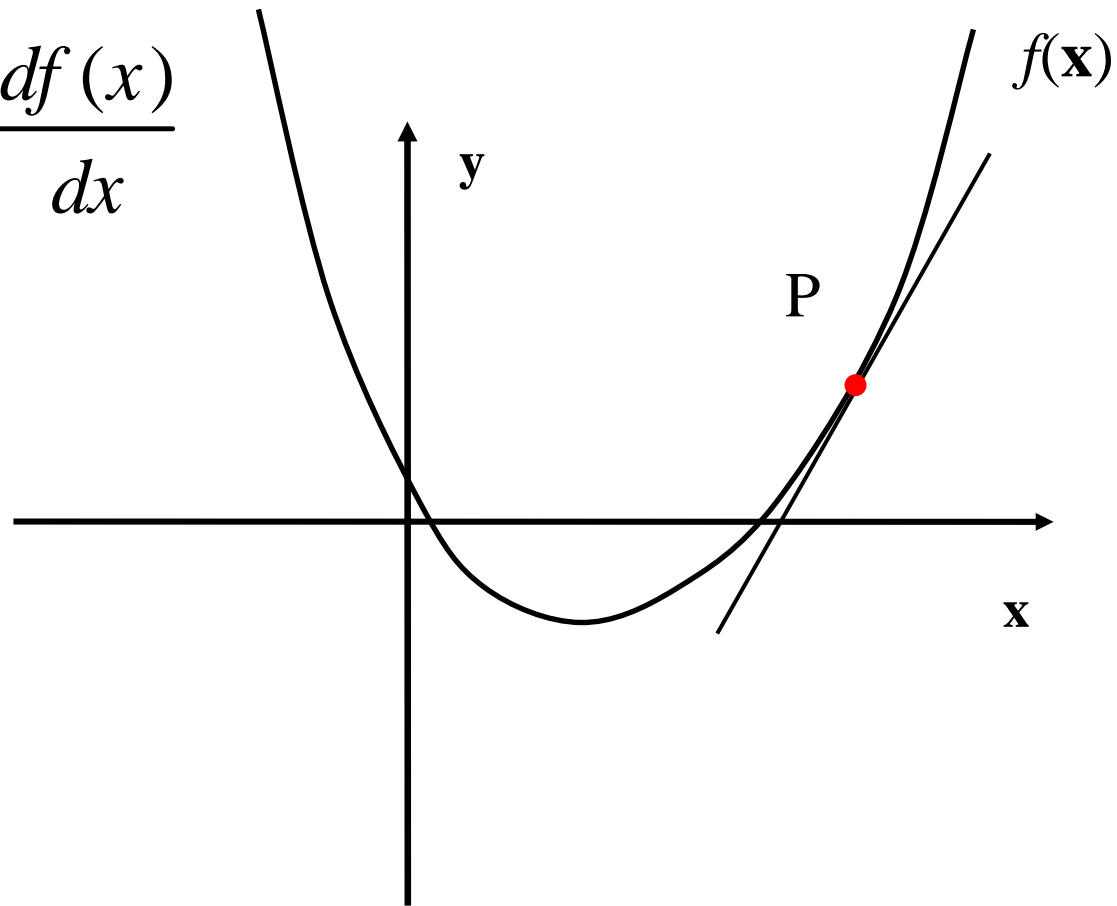
- Minimum bracketing
- Parabolic interpolation



# Gradient Descent

$$m = \text{slope} = \frac{df(x)}{dx}$$

$$P' = P + \alpha m$$



# Downhill Simplex Method (1)

- due to Nelder and Mead\*
- self-contained; no 1D line minimization
- only function evaluations, no derivatives
- not efficient in terms of number of function evaluations, but easy-to-implement
- geometrical naturalness
- useful: when  $f$  is non-smooth or when derivatives are impossible to find

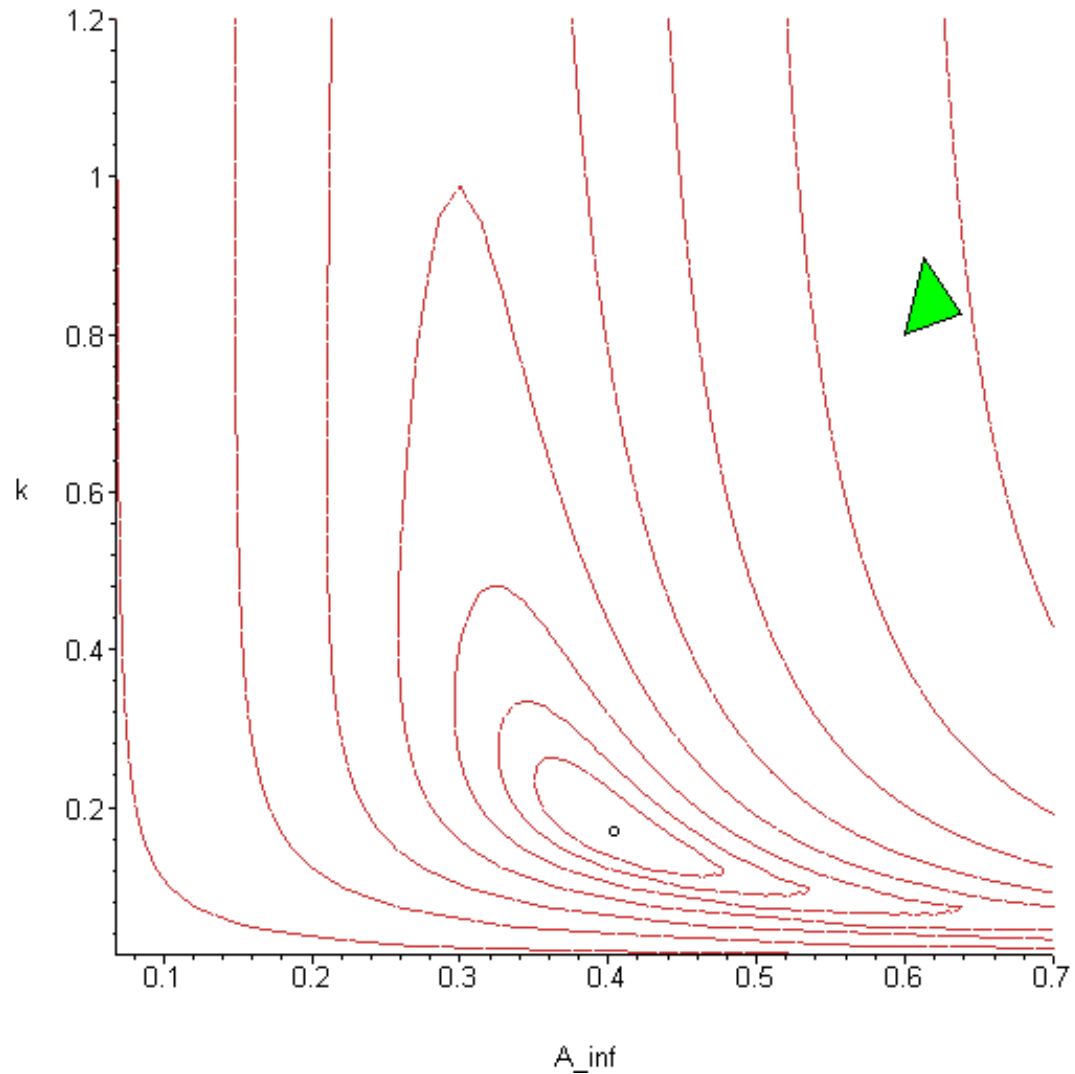
Nelder, J.A, and Mead, R. 1965, Computer Journal, vol. 7, pp. 308-13.

# Downhill Simplex Method (2)

- *simplex*: geometrical figure; in N dimensions, (N+1) points/vertices
  - e.g.: in 2D: triangle, in 3D: tetrahedron
  - non-degenerate! (encloses a finite N-dimensional volume)
- starting guess ((N+1) points)
  - $\mathbf{P}_0$  and  $\mathbf{P}_i = \mathbf{P}_0 + \lambda \mathbf{e}_i$        $\mathbf{e}_i$ : unit vectors;  
 $\lambda$ : constant, guess of characteristic length scale

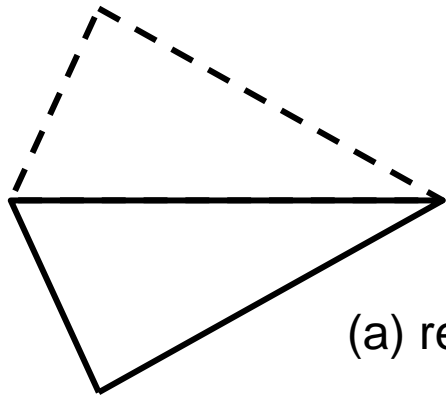
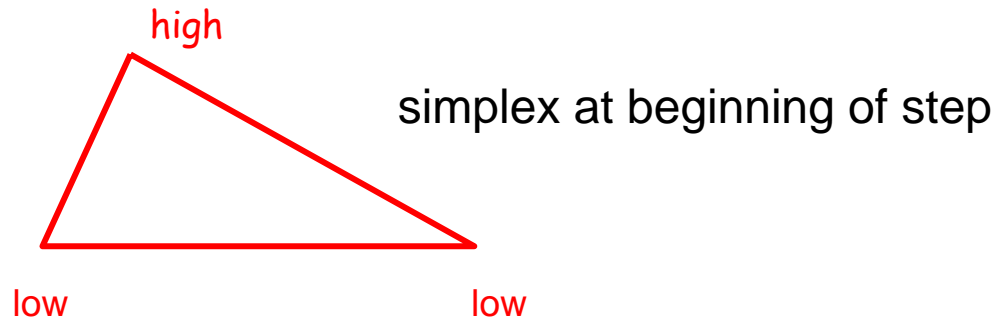


animation of progress of sequential simplex

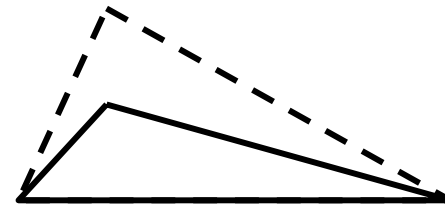


Courtesy of E. G. Romero-Blanco and J. F. Ogilvie. Used with permission.

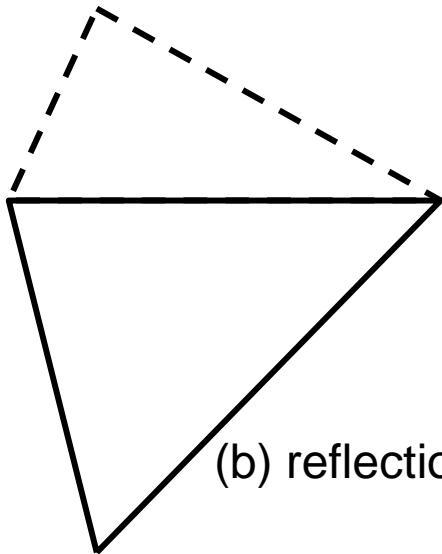
# Valid simplex steps:



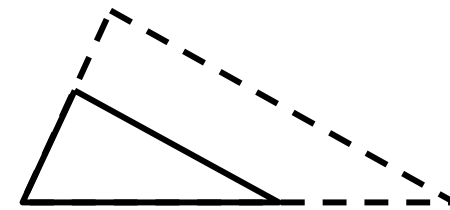
(a) reflection



(c) contraction



(b) reflection and expansion



(d) multiple contraction

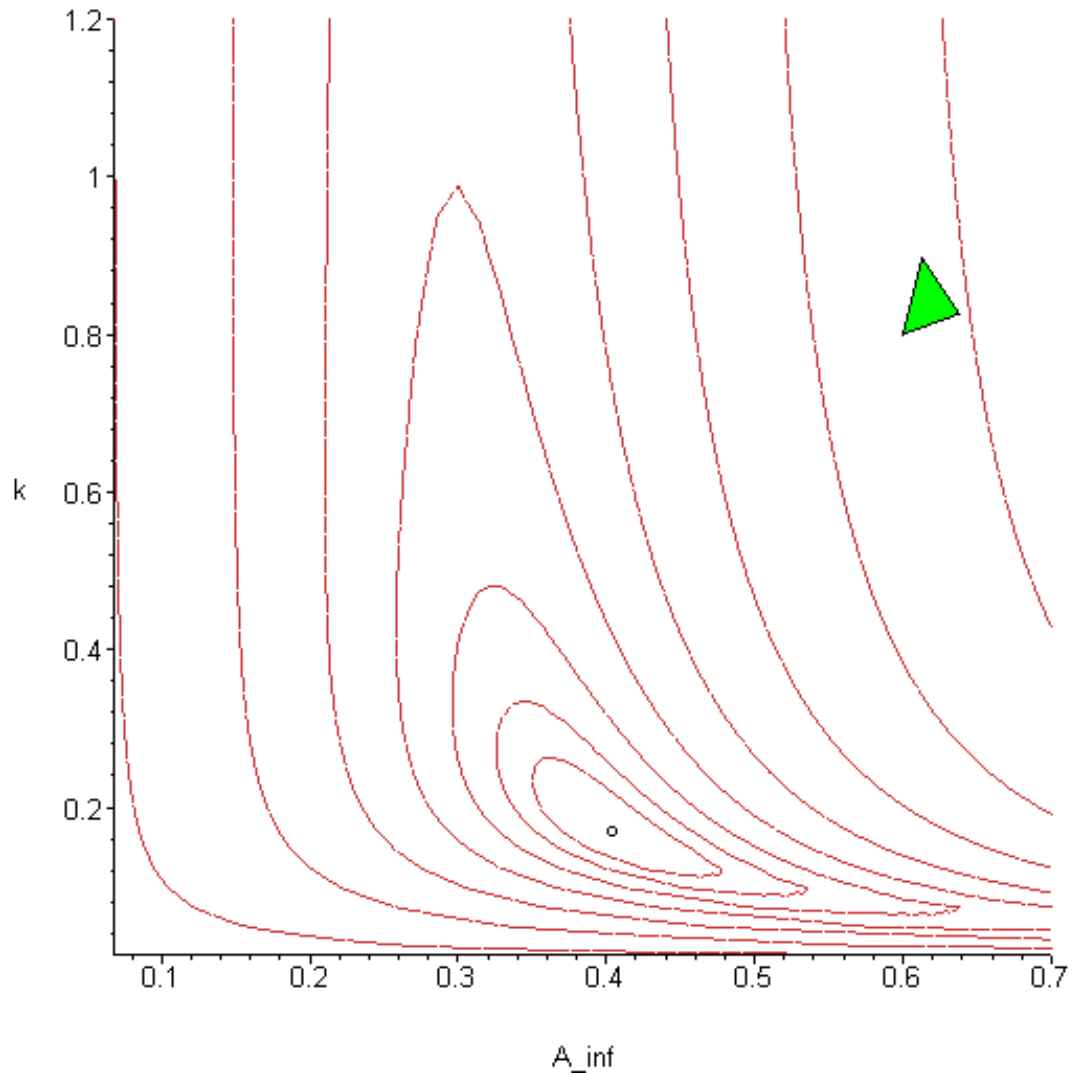
# Downhill Simplex Method (3)

- possible moves (from previous figure):
  - reflection (conserving volume of the simplex)
  - reflection and expansion
  - contraction
  - multiple contraction
- termination criterion
  - use threshold on moved vector distance
  - or threshold on function value change
- *restart* strategy
  - needed as even a single anomalous step can fool the search algorithm

# Implementation details

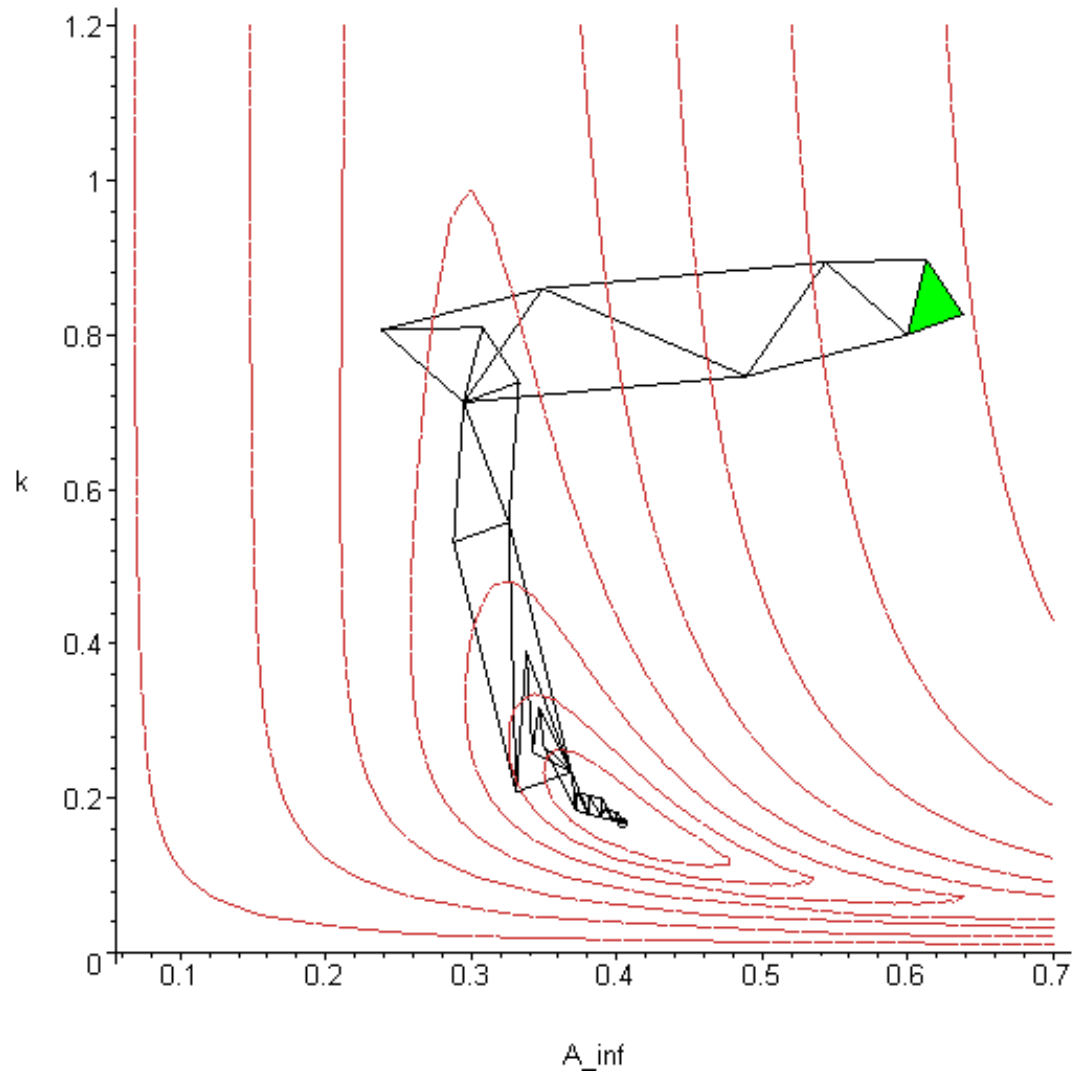
- *fminsearch* in MATLAB
    1. build initial simplex
    2. do reflections, expand if appropriate
    3. in “valley floor” contract transverse
      - ooze down valley
- 
- works well in some medical registration methods
  - has implicit *coarse-to-fine* behavior

animation of progress of sequential simplex



Courtesy of E. G. Romero-Blanco and J. F. Ogilvie. Used with permission.

### sequential simplex track

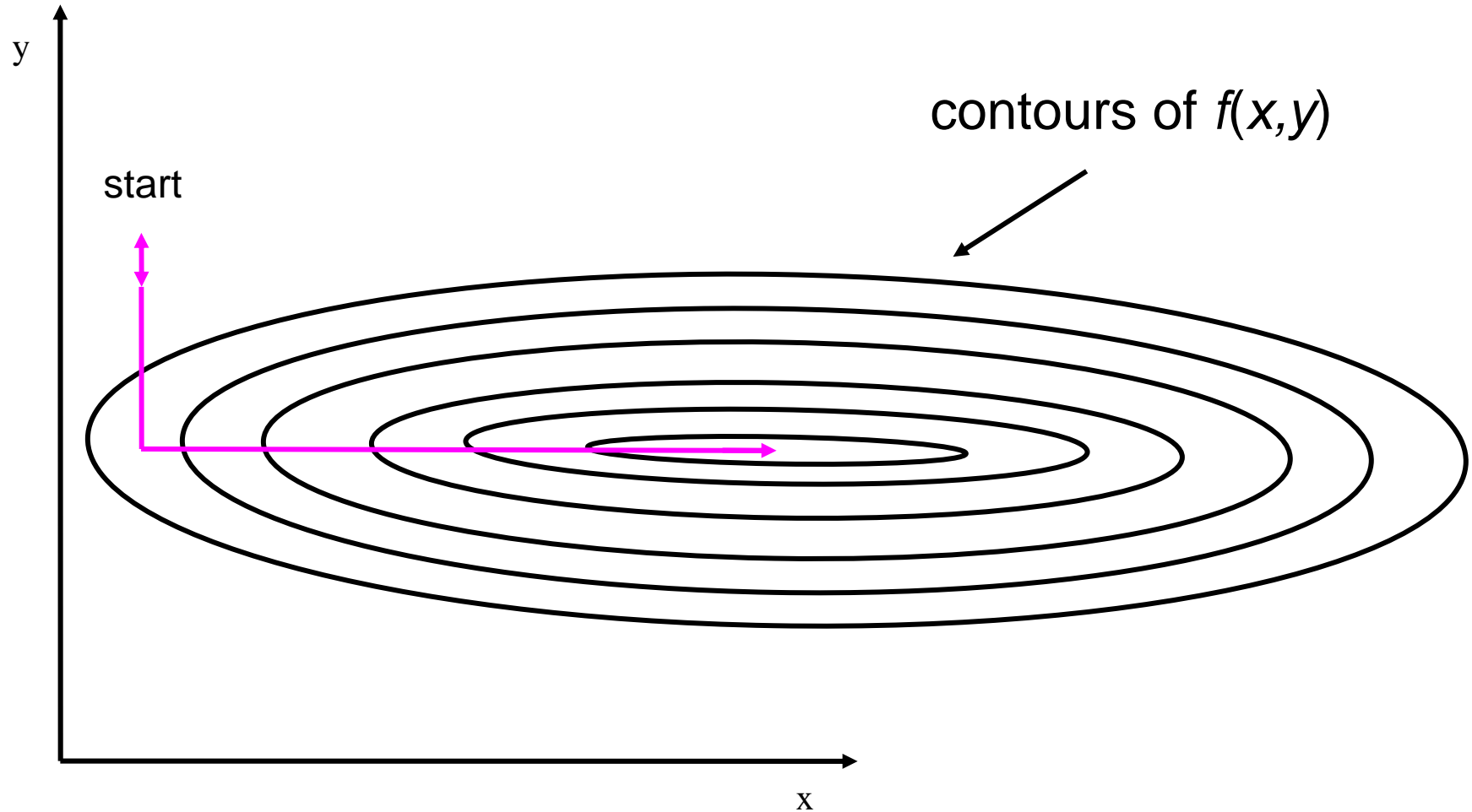


Courtesy of E. G. Romero-Blanco and J.F. Ogilvie. Used with permission.

# Direction Set Methods

- Successive line minimizations
- No explicit gradient calculation
- How to select the best set of directions to follow?
  - simple example: follow the coordinate directions
  - direction set methods: compute “good” or non-interfering (conjugate) directions

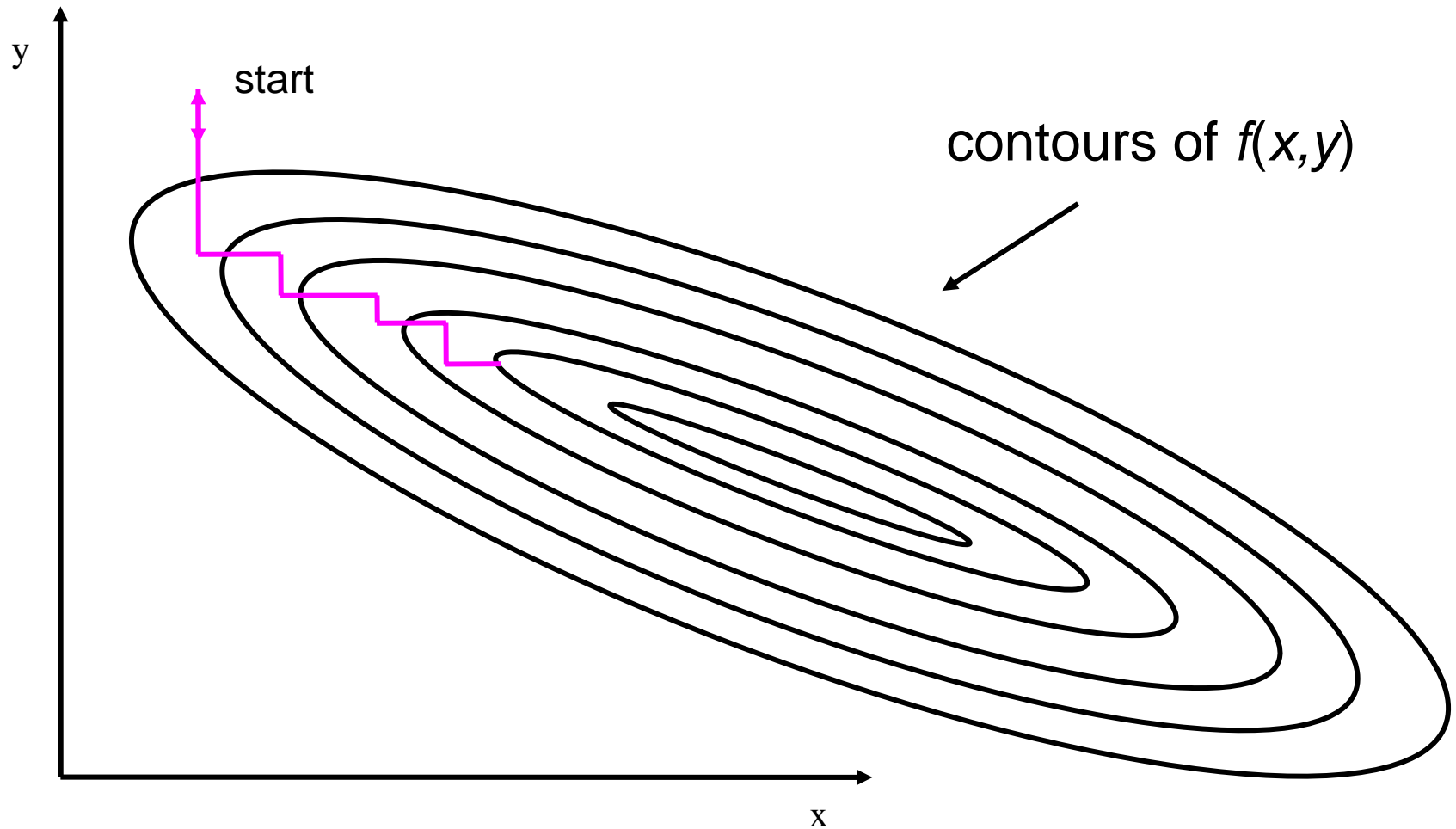
# Follow the coordinate directions



Ideal situation: only two steps are enough to locate the minimum



# Follow the coordinate directions



In general: can be very inefficient; large number of steps can be required to find the minimum.

# Conjugate Directions

- non-interfering directions: subsequent minimizations should not spoil previous optimization results
- *goal*: come up with a set of  $N$  linearly independent, mutually conjugate directions  
⇒  $N$  line minimizations will achieve the minimum of a quadratic form

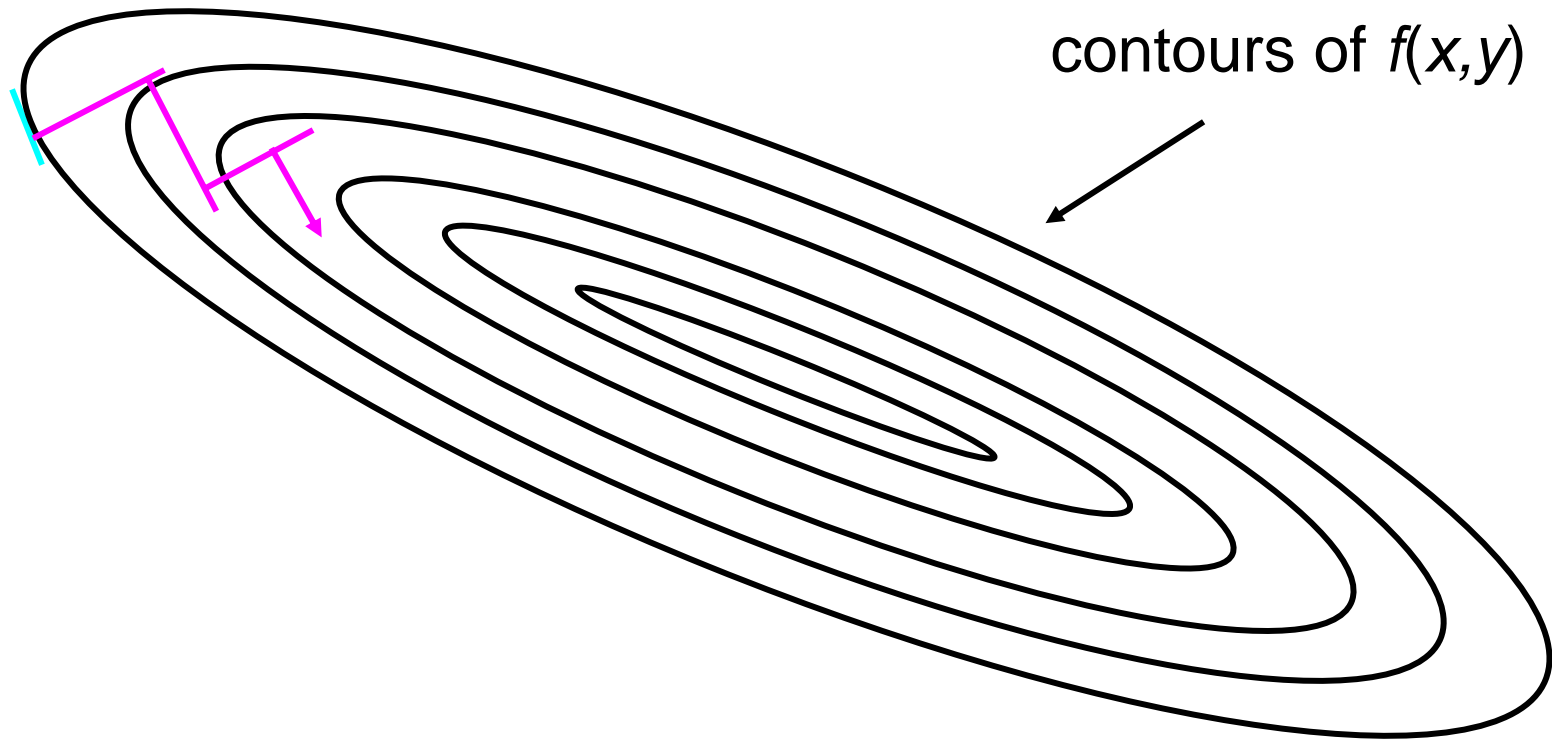
# Powell's Method

- $N(N+1)$  line minimizations to achieve the minimum
- possible problem with linear dependence after update
  - fix
    - re-initialize the set of directions to the basis vectors
    - few good directions (instead of  $N$  conjugate ones)

# Conjugate Gradient Methods

- gradient calculation is needed
- order N separate line minimizations
- computational speed improvement
  - Steepest Descent method
    - right angle turns at all times
  - Conjugate Direction methods

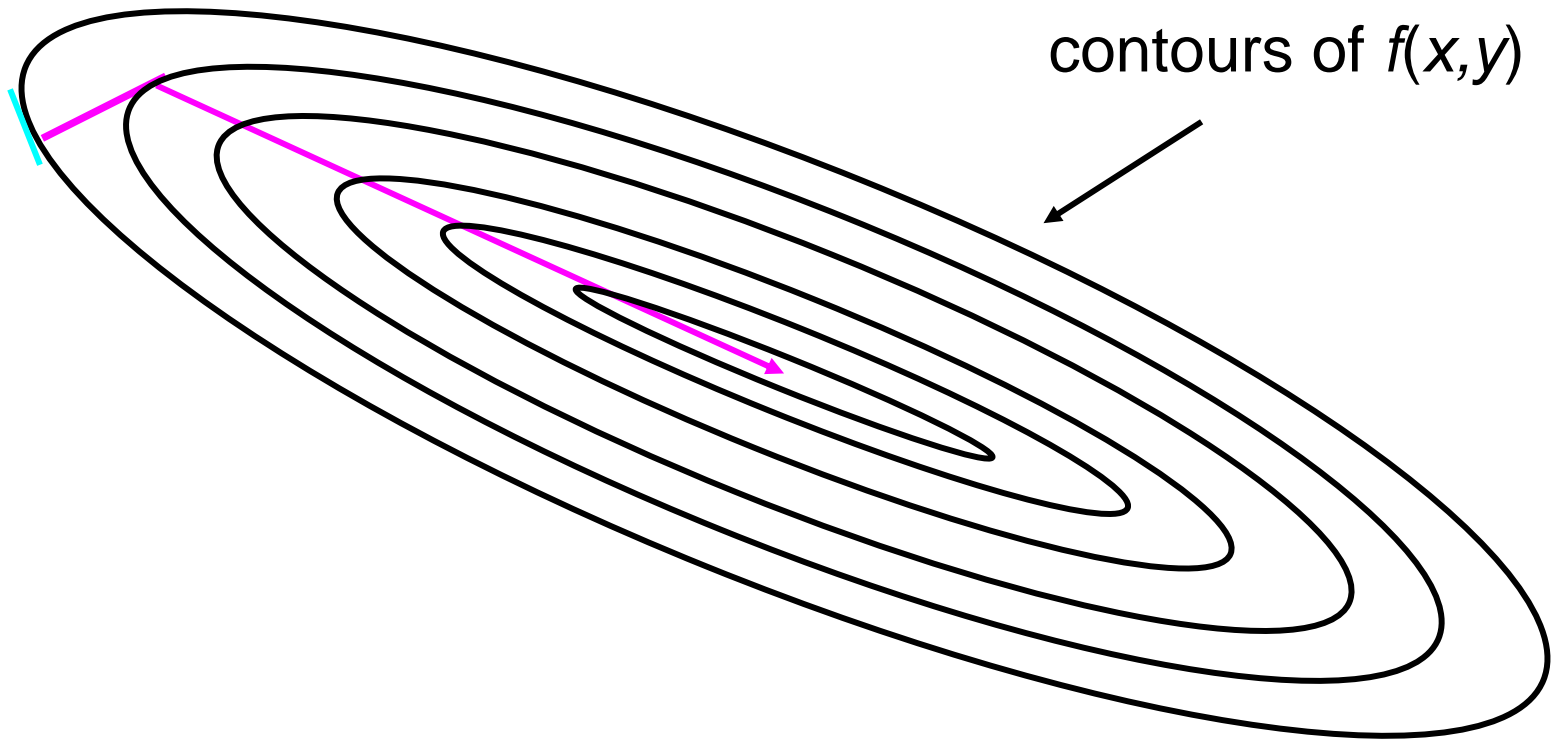
# Steepest Descent method



Steepest descent method – still a large number of steps is required to find the minimum.

See <http://www.tcm.phy.cam.ac.uk/~pdh1001/thesis/node57.html>

# Conjugate Gradients method



Conjugate gradients method - only two steps are required to find the minimum.

See <http://www.tcm.phy.cam.ac.uk/~pdh1001/thesis/node57.html>

# Simulated Annealing

- exploits an analogy between the way in which a metal cools and freezes into a minimum energy crystalline structure (the *annealing* process) and the search for a minimum in a more general system
- employs a random search accepting (with a given probability) both changes that decrease and increase the objective function
- successful at finding global optima among a large numbers of undesired local extrema

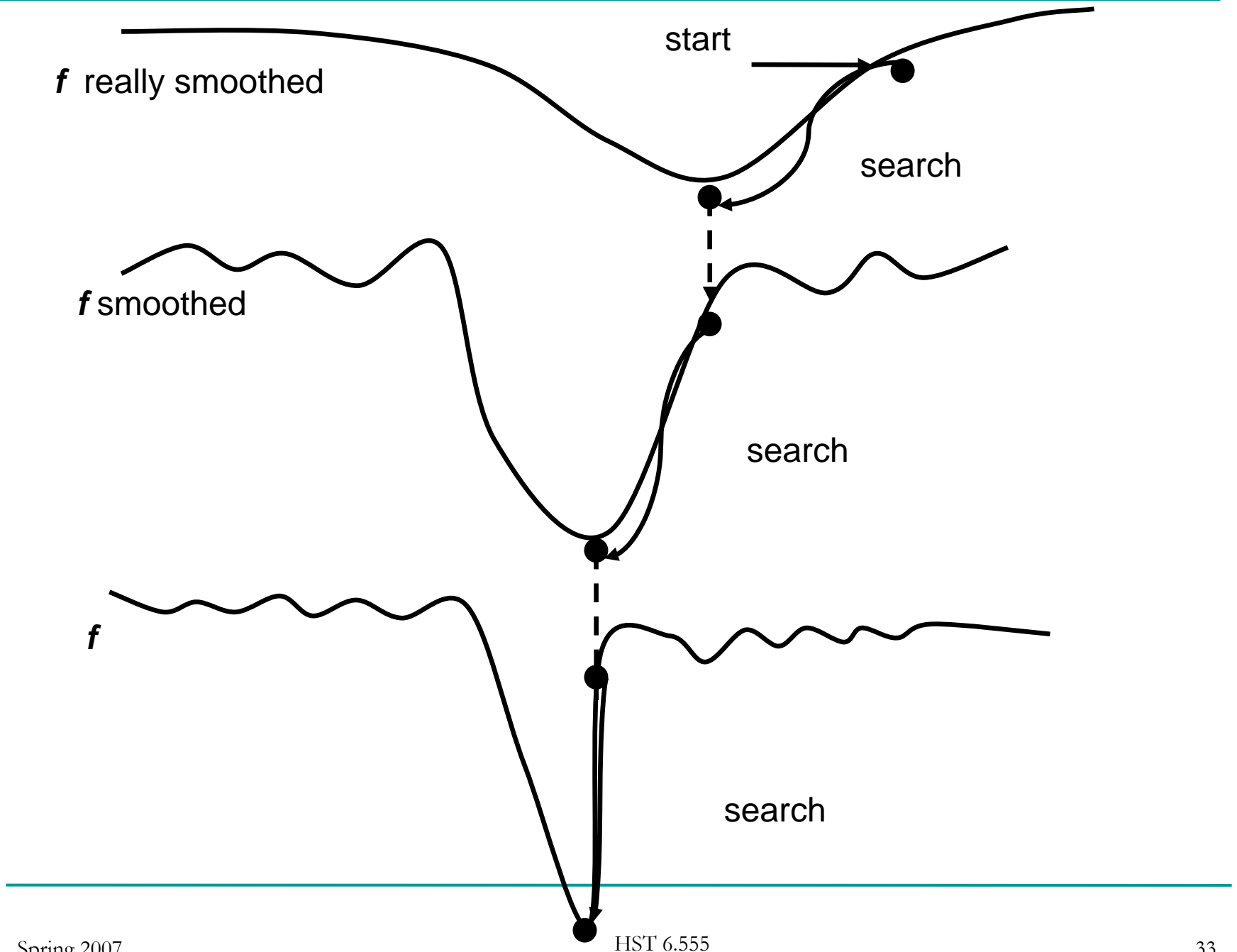
# Genetic Algorithm

- works very well on mixed (continuous *and* discrete), combinatorial problems; less susceptible to getting 'stuck' at local optima than gradient search methods
- tends to be computationally expensive
- represents solution to the problem as a *genome* (or *chromosome*); creates a population of solutions and apply genetic operators (mutation, crossover) to evolve the solutions in order to find the best one(s).
- most important aspects of using genetic algorithms are
  - (1) definition of the objective function
  - (2) definition and implementation of the genetic representation
  - (3) definition and implementation of the genetic operators
- <http://lancet.mit.edu/~mbwall/presentations/IntroToGAs/>

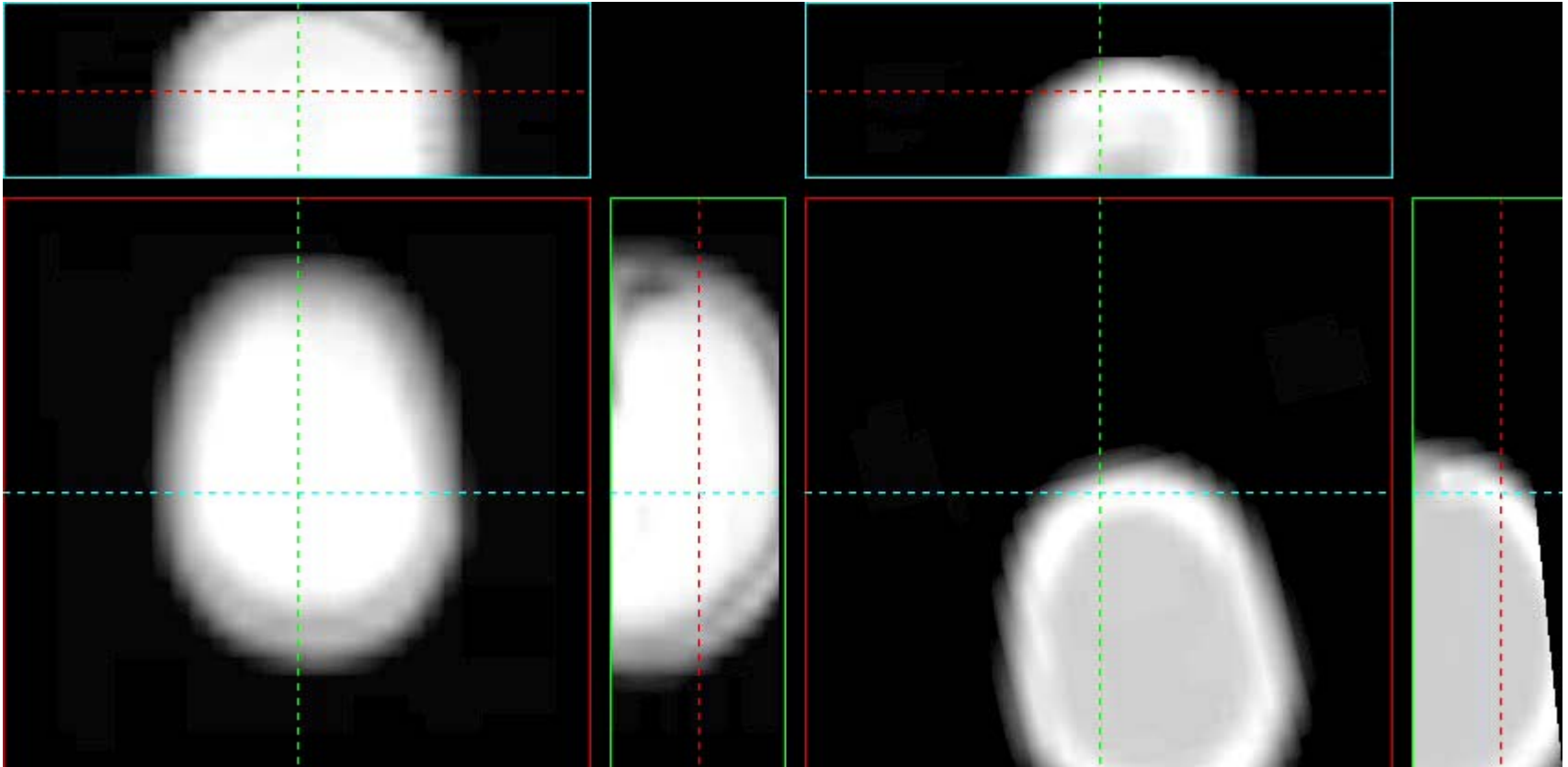


# Coarse-to-Fine Strategy

- Technique:
  - smooth objective function  $f_N$  (e.g.: blur with Gaussian)
  - optimize smoothed version (use result as start value for original objective  $f_N$ )
- Advantages:
  - avoiding local extrema
  - speed up computations



# CT-MR registration movie



From: Wells, W. M., et al. "Multi-modal Volume Registration by Maximization of Mutual Information." *Medical Image Analysis* 1, no. 1 (March 1996): 35-51.

Courtesy Elsevier, Inc., <http://www.sciencedirect.com>. Used with permission.

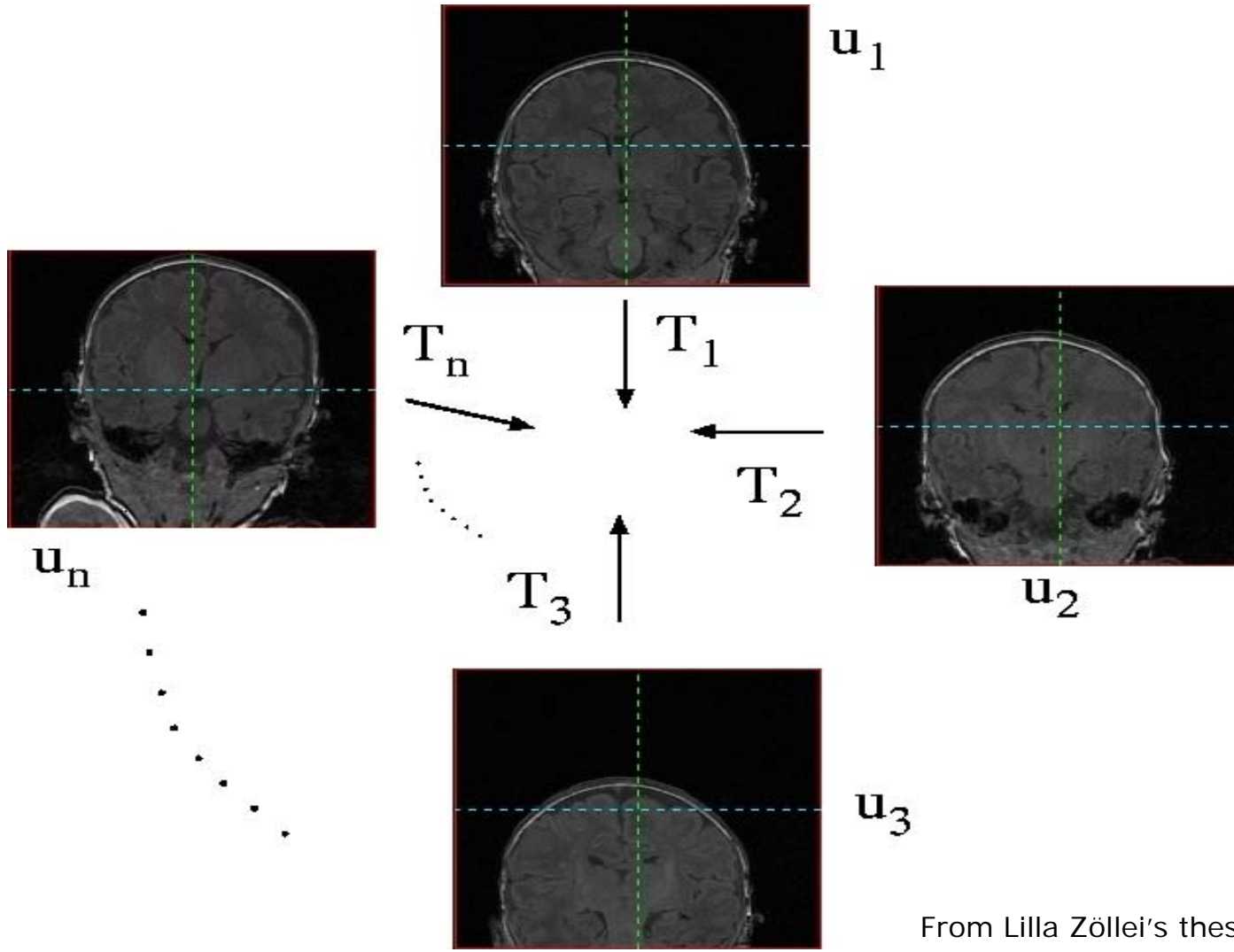
# More examples

- ***Numerical Recipes in “C”***  
***<http://www.nrbook.com/nr3/>***

# Current Research topics

- group-wise (vs. pair-wise) registration
- Diffusion Tensor (DT) MRI alignment
- surface-based (vs volumetric) alignment
  
- Open questions: tumor growth modeling, structural – functional alignment, ....
- Registration evaluation and validation

# Group-wise registration



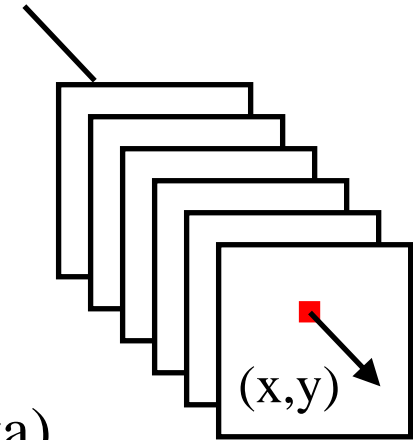
From Lilla Zöllei's thesis research.

# Group-wise registration styles

- Template-dependent
  - Fixed template
    - Arbitrary member of the population
    - Pre-defined atlas
  - Online computed template
    - Sequential pair-wise alignment to evolving “mean”
- Template-free
  - Simultaneous

# The Congealing method

- *Def.:* simultaneous alignment of each of a set of images to each other
- Applications:
  - Handwritten digit recognition (binary data)
  - Preliminary baby brain registration (binary data)
  - Bias removal from MRI images

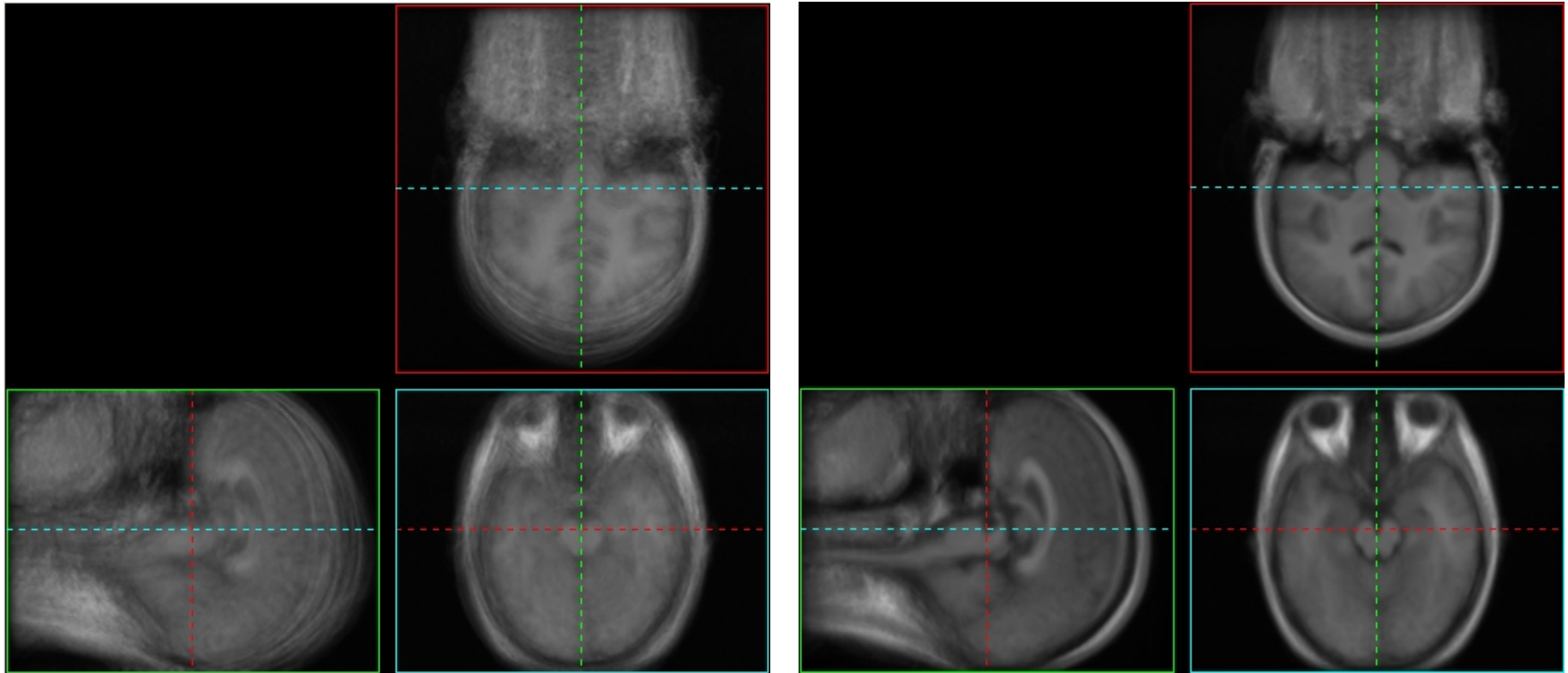




# Advantages of Congealing

- Computational advantages
- Can accommodate very large data sets
- Can accommodate multi-modal data
- Robust to noise and imaging artifacts
- No single central tendency assumption

# Adult brain data set - mean volumes



**Unaligned** input data sets

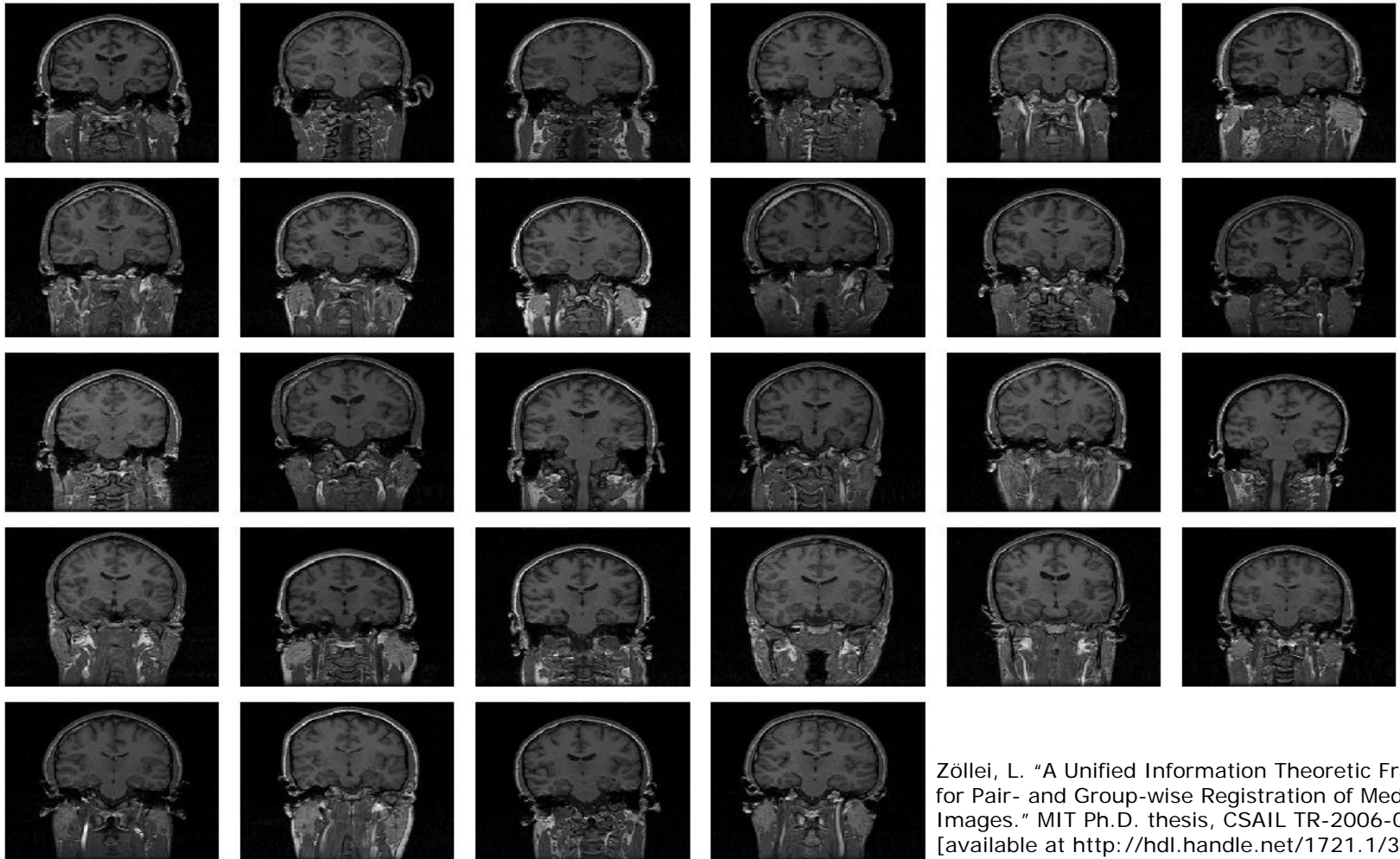
**Aligned** input data sets

Data set: 28 T1-weighted MRI; [256x256x124] with (.9375, .9375, 1.5) mm<sup>3</sup> voxels

Experiment: 2 levels; 12-param. affine; N = 2500; iter = 150; time = **1209 sec!!**

Zöllei, L. "A Unified Information Theoretic Framework for Pair- and Group-wise Registration of Medical Images."  
MIT Ph.D. thesis, CSAIL TR-2006-005 [available at <http://hdl.handle.net/1721.1/30970>].

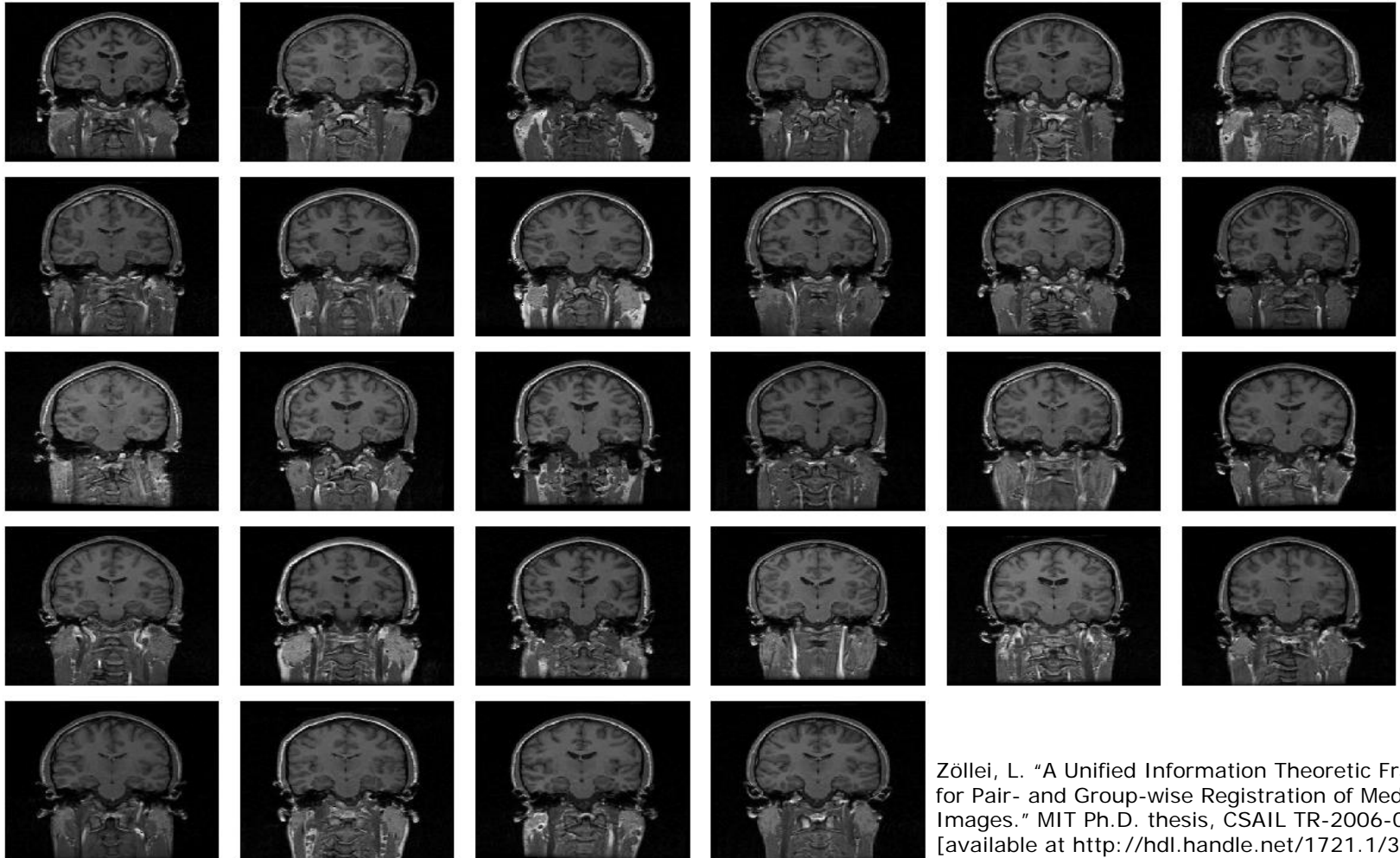
# Central coronal slices



Zöllei, L. "A Unified Information Theoretic Framework for Pair- and Group-wise Registration of Medical Images." MIT Ph.D. thesis, CSAIL TR-2006-005 [available at <http://hdl.handle.net/1721.1/30970>].

## Unaligned input

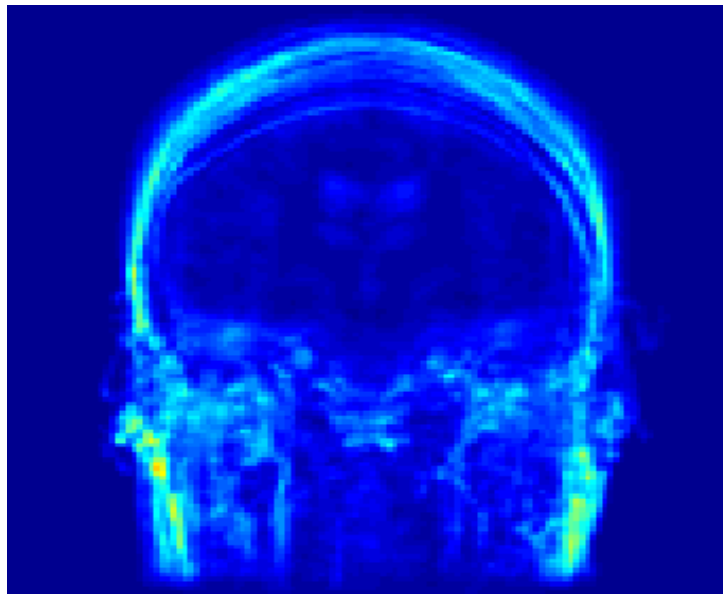
# Central coronal slices



Zöllei, L. "A Unified Information Theoretic Framework for Pair- and Group-wise Registration of Medical Images." MIT Ph.D. thesis, CSAIL TR-2006-005 [available at <http://hdl.handle.net/1721.1/30970>].

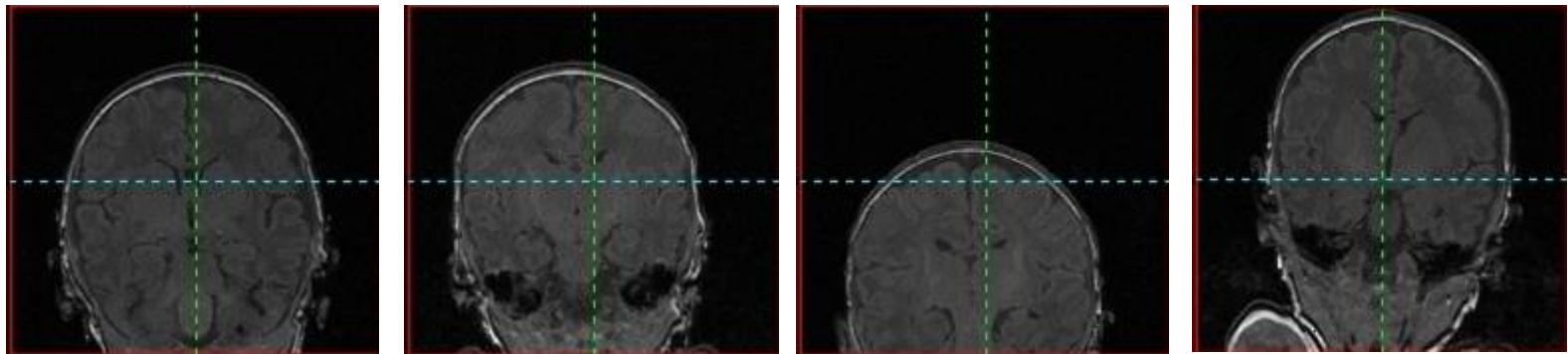
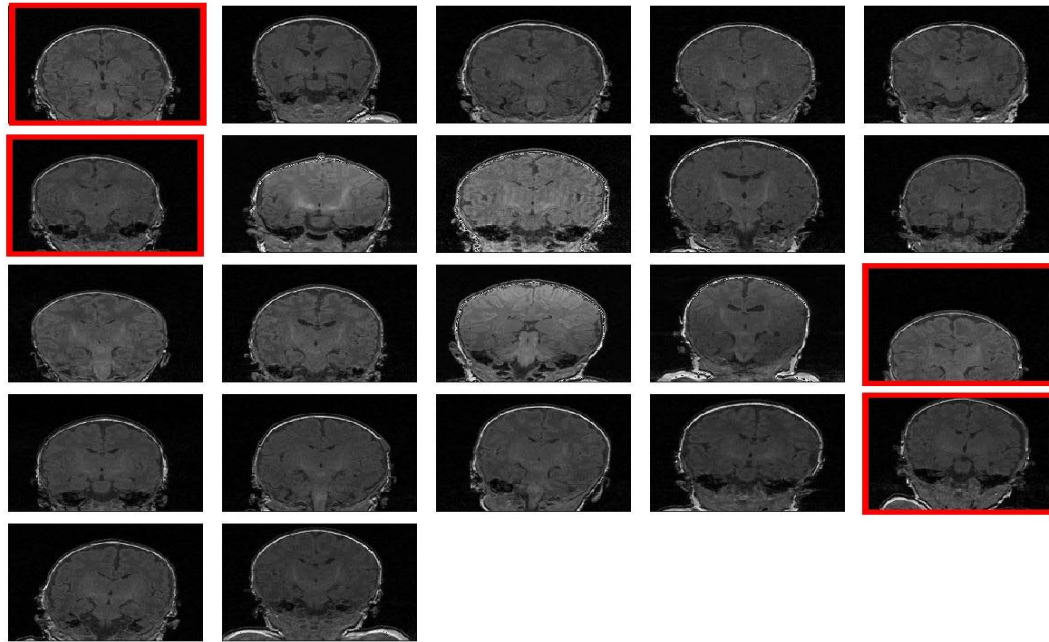
## Aligned input

# Variance volume - during registration



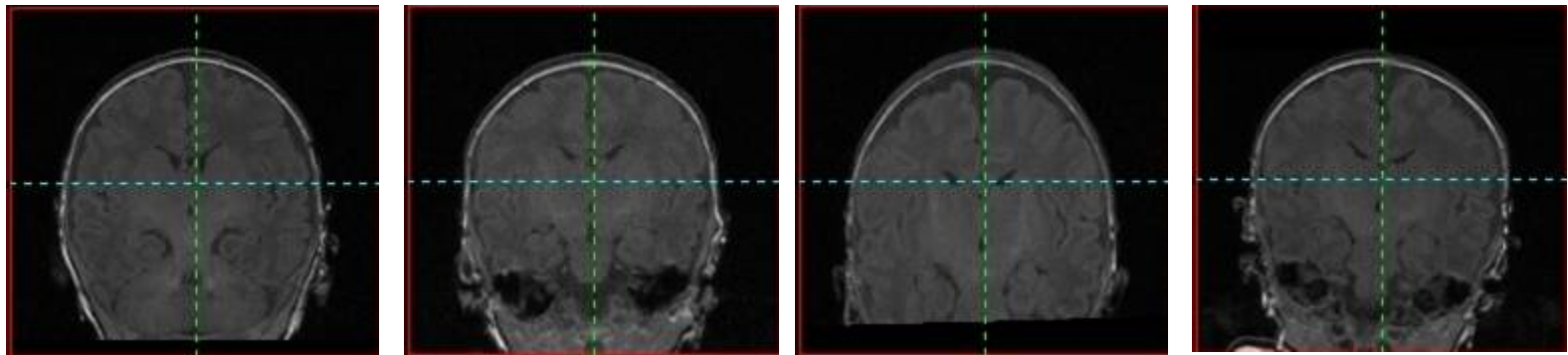
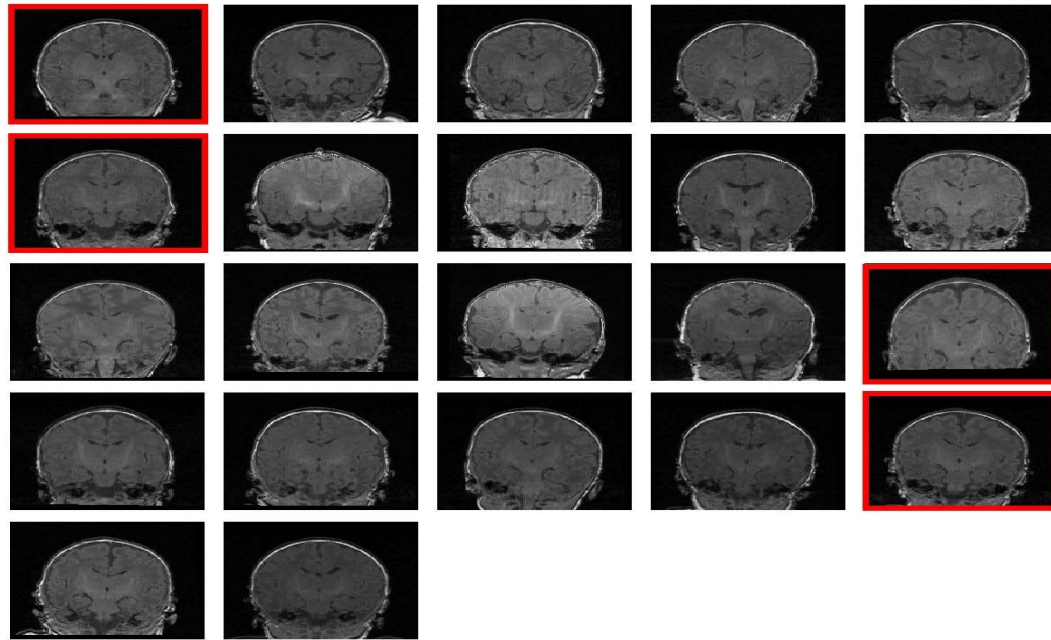


# Baby brain data set – central slices



Zöllei, L. "A Unified Information Theoretic Framework for Pair- and Group-wise Registration of Medical Images."  
MIT Ph.D. thesis, CSAIL TR-2006-005 [available at <http://hdl.handle.net/1721.1/30970>].

# Baby brain data set – central slices



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MIT Ph.D. thesis, CSAIL TR-2006-005 [available at <http://hdl.handle.net/1721.1/30970>].

Spring 2007

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Cite as: Lilla Zöllei and William Wells. Course materials for HST.582J / 6.555J / 16.456J, Biomedical Signal and Image Processing, Spring 2007. MIT OpenCourseWare (<http://ocw.mit.edu>), Massachusetts Institute of Technology. Downloaded on [DD Month YYYY].

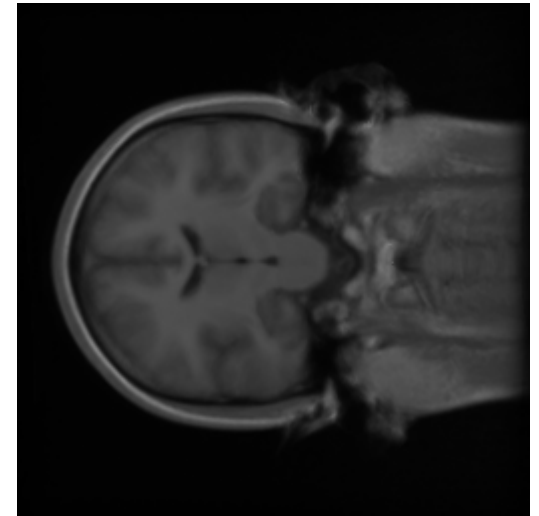
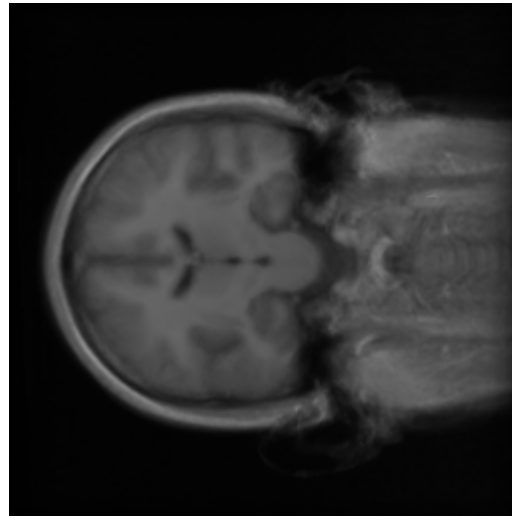
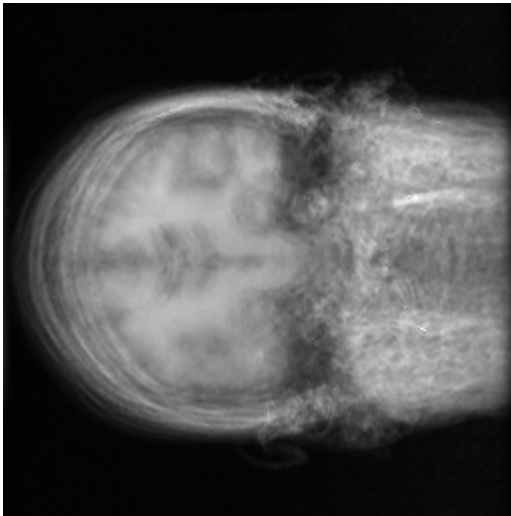
# Very large data set



Zöllei, L. "A Unified Information Theoretic Framework for Pair- and Group-wise Registration of Medical Images." MIT Ph.D. thesis, CSAIL TR-2006-005 [available at <http://hdl.handle.net/1721.1/30970>].



# Affine + B-splines Deformation



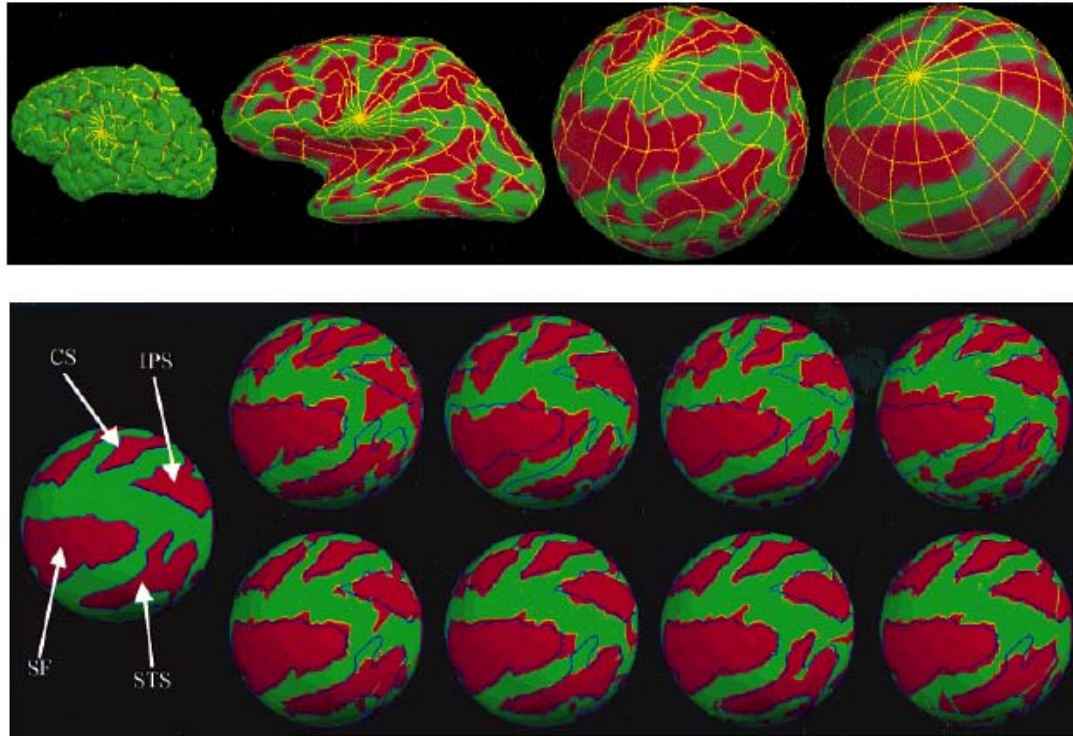
Courtesy of Serdar K Balci and Kinh Tieu. Used with permission.

# DT MRI alignment

Figure 2 from this article (sequence of eight images) removed due to copyright restrictions.

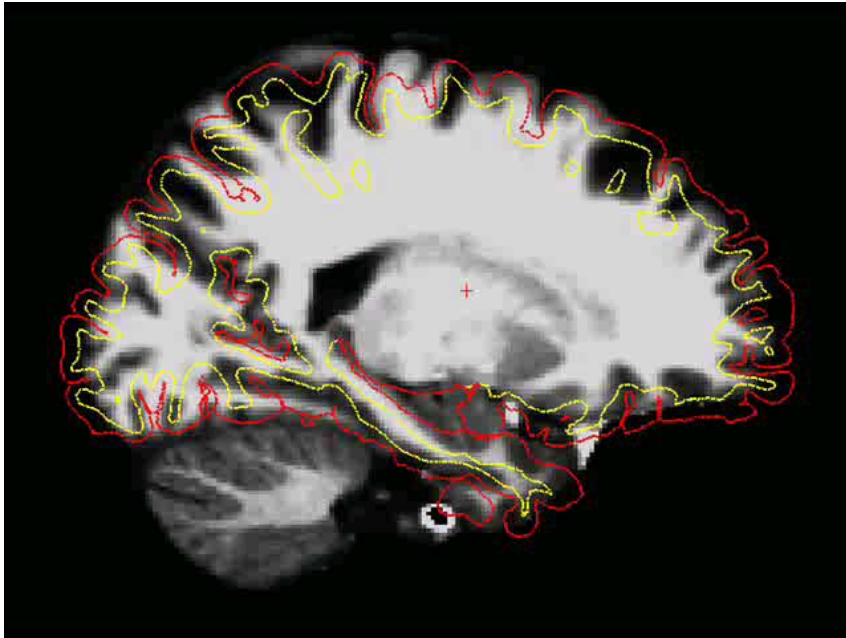
O'Donnell, L. J., et al.: *High-Dimensional White Matter Atlas Generation and Group Analysis*  
MICCAI, 243-251, 2006.

# Surface-based alignment



From: Fischl, B., et al. "High-resolution Inter-subject Averaging and a Coordinate System for the Cortical Surface." *Human Brain Mapping*, 8:272-284. Copyright © 1999. Reprinted with permission of Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.

# Combined surface-based and volumetric alignment



Images removed due to copyright restrictions.

Two brain MRI images from Fig 3 in Postelnicu, Gheorghe, Lilla Zollei, Rahul Desikan, and Bruce Fischl. "Geometry Driven Volumetric Registration." *LNCS 4584* (2007): 243–251.

Courtesy of Gheorghe Postelnicu. Used with permission.

# Further open questions:

- tumor growth modeling
- structural – functional alignment (MRI-fMRI)
- population comparison
- ....

# Registration evaluation and validation

- Retrospective Image Registration Evaluation Project (Vanderbilt University, Nashville, TN)  
<http://www.vuse.vanderbilt.edu/~image/registration/>
- Non-Rigid Image Registration Evaluation Program (NIREP); University of Iowa  
<http://www.nirep.org>

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# END