

Mathematics Meets Medicine: An Optimal Alignment



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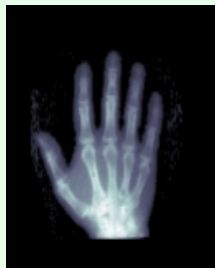


<http://www.cas.mcmaster.ca/~modersit>

Motivation

Image Registration

Given a reference image \mathcal{R} and a template image \mathcal{T} , find a **reasonable transformation** y , such that the transformed image $\mathcal{T}[y]$ is **similar** to \mathcal{R}

reference \mathcal{R} template \mathcal{T} transformed template $\mathcal{T}[y]$

Motivation

Image Registration

Given a reference image \mathcal{R} and a template image \mathcal{T} , find a **reasonable transformation** y , such that the transformed image $\mathcal{T}[y]$ is **similar** to \mathcal{R}

Questions:

- ▶ What is a **transformed** image $\mathcal{T}[y]$? \rightsquigarrow image model $\mathcal{T}[y]$
- ▶ What is **similarity** of $\mathcal{T}[y]$ and \mathcal{R} ? $\rightsquigarrow \mathcal{D}[\mathcal{T}[y], \mathcal{R}]$
- ▶ What is **reasonability** of y ? $\rightsquigarrow \mathcal{S}[y]$

Image Registration: Variational Problem

$$\mathcal{D}[\mathcal{T}[y], \mathcal{R}] + \mathcal{S}[y - y_{\text{reg}}] \xrightarrow{y} \min, \quad y_{\text{reg}}(x) = x$$

Outline

- ▶ Applications
- ▶ Variational formulation $\mathcal{D}[T[y], \mathcal{R}] + \mathcal{S}[y] \xrightarrow{y} \min$
 - ▶ image models $T[y]$
 - ▶ distance measures $\mathcal{D}[T[y], R]$
 - ▶ regularizer $\mathcal{S}[y]$
- ▶ Numerical methods
- ▶ Constrained image registration
- ▶ Conclusions

People

Bernd Fischer



Eldad Haber



Oliver Schmitt



Stefan Heldmann



Hanno Schumacher



Nils Papenberg



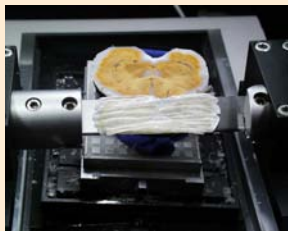
Applications



HNSP: Sectioning

with Oliver Schmitt,

Institute of Anatomy, University Rostock, Germany



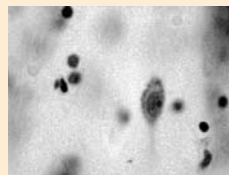
- ▶ sliced
- ▶ flattened
- ▶ stained
- ▶ mounted
- ▶ ...
- ▶ digitized



large scale digital images, up to 10.000×20.000 pixel



HNSP: Microscopy



HNSP: Deformed Images

sections 3.799 and 3.800 out of about 5.000



human



affine linear

elastic



$$|T_{\text{orig}} - R| = 100\%$$



$$|T_{\text{linear}} - R| = 72\%$$

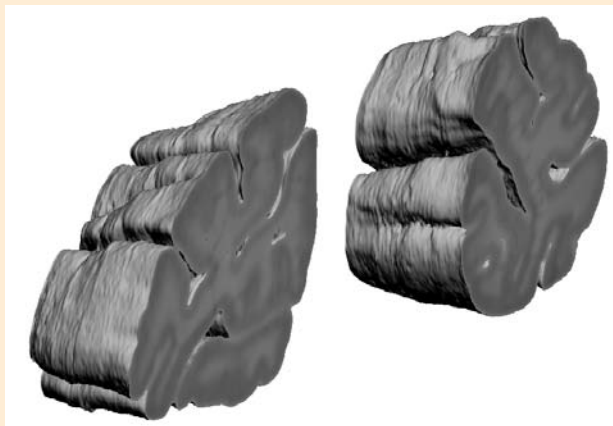


$$|T_{\text{elastic}} - R| = 50\%$$



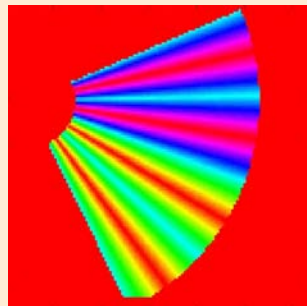
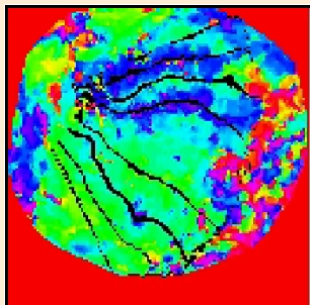
HNSP: Results

3D elastic registration of a part of the visual cortex
(two hemispheres; 100 sections á 512×512 pixel)



Neuroimaging (fMRI)

with [Brian A. Wandell](#), Department of Psychology,
Stanford Vision Science and Neuroimaging Group

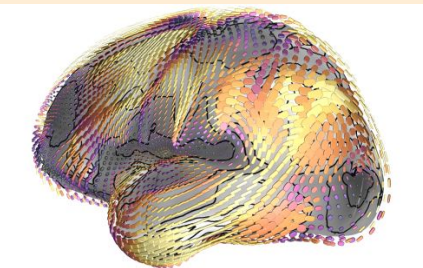


“flattened visual cortex”



DTI: Diffusion Tensor Imaging

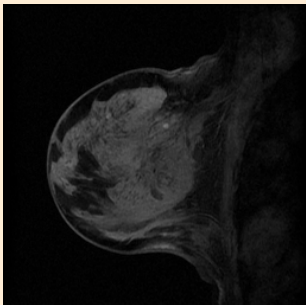
with [Brian A. Wandell](#), Department of Psychology,
Stanford Vision Science and Neuroimaging Group



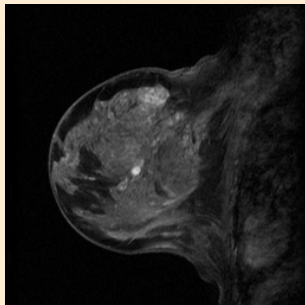
MR-mammography, biopsy (open MR)

with [Bruce L. Daniel](#),

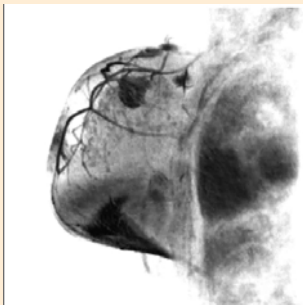
Department of Radiology, Stanford University



pre contrast



post contrast

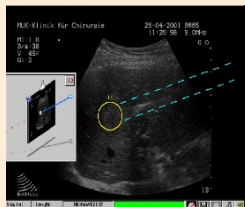
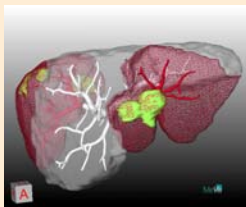


3D



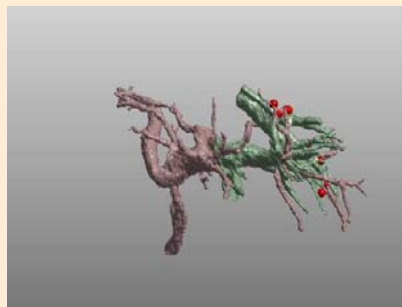
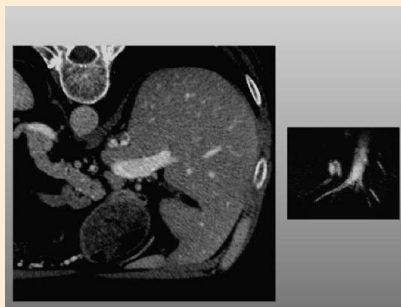
Virtual Surgery Planning

S. Bommersheim & N. Papenberg, **SAFIR**, BMBF/FUSION
Future Environment for Gentle Liver Surgery Using Image-
Guided Planning and Intra-Operative Navigation



Results for 3D US/CT

with [Oliver Mahnke](#), [SAFIR](#), University of Lübeck
& MiE GmbH, Seth, Germany



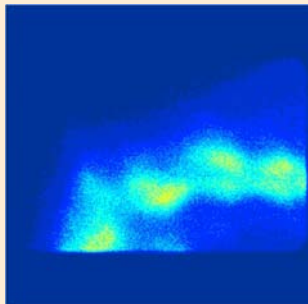
Motion Correction

from [Thomas Netsch](#),
Philips Research, Hamburg, Germany

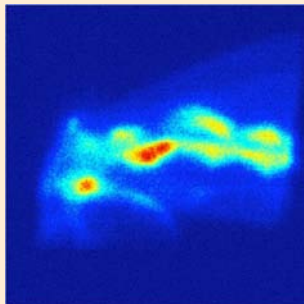


SPECT: Single Photon Emissions CT

with Oliver Mahnke, SAFIR, University of Lübeck
& MiE GmbH, Seth, Germany



image



registered



Lester



Registration in Medical Imaging

- ▶ Comparing/merging/integrating images from different
 - ▶ times, e.g., pre-/post surgery
 - ▶ devices, e.g., CT-images/MRI
 - ▶ perspectives, e.g., panorama imaging
 - ▶ objects, e.g., atlas/patient mapping
- ▶ Template matching, e.g., catheter in blood vessel
- ▶ Atlas mapping, e.g., find 2D view in 3D data
- ▶ Serial sectioning, e.g., HNSP
- ▶ ...

Registration is **not** restricted to medical applications



Classification of Registration Techniques

- ▶ feature space
 - ▶ search space
 - ▶ search strategy
 - ▶ distance measure
-
- ▶ dimensionality of images ($d = 2, 3, 4, \dots$)
 - ▶ modality (binary, gray, color, \dots)
 - ▶ mono-/multimodal images
 - ▶ acquisition (photography, FBS, CT, MRI, \dots)
 - ▶ inter/intra patient



Image Registration

Transforming Images

$$\mathcal{D}[\mathcal{T}[y], \mathcal{R}] + \alpha \mathcal{S}[y - y_{\text{reg}}] \xrightarrow{y} \min$$



Variational Approach for Image Registration

$$\mathcal{D}[\mathcal{T}[\mathbf{y}], \mathcal{R}] + \alpha \mathcal{S}[\mathbf{y} - \mathbf{y}_{\text{reg}}] \xrightarrow{\mathbf{y}} \min$$

- ▶ Continuous models \mathcal{R}, \mathcal{T} for reference and template:

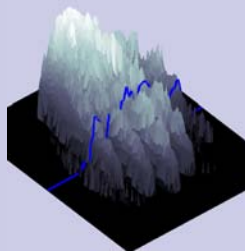
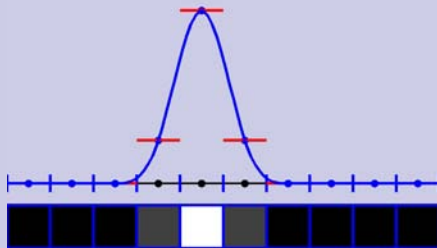
$$\text{discrete data } \mathbf{X}, \mathbf{T} \rightsquigarrow \mathcal{T}(x) = \text{interpolation}(\mathbf{X}, \mathbf{T}, x)$$

- ▶ Transformation $\mathbf{y} : \mathbb{R}^d \rightarrow \mathbb{R}^d$

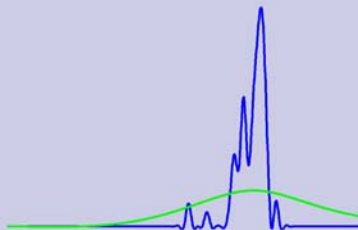
$$\mathcal{T}[\mathbf{y}](x) = \mathcal{T}(\mathbf{y}(x)) = \text{interpolation}(\mathbf{X}, \mathbf{T}, \mathbf{y}(x))$$



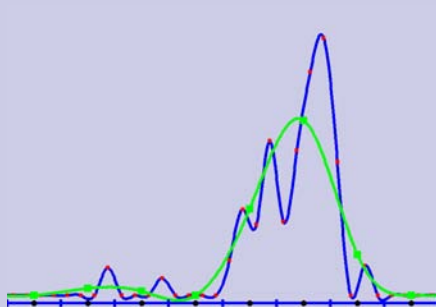
Interpolation



Multi-Scale



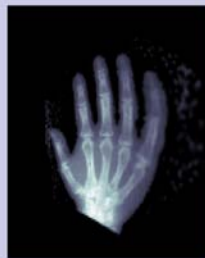
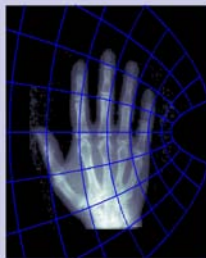
Multilevel



Transforming Images

$$\mathcal{T}[y](x) = \mathcal{T}(y(x)) = \text{interpolation}(X, T, y(x))$$

non-linear



Distance Measures

$$\mathcal{D}[\mathcal{T}[y], \mathcal{R}] + \alpha \mathcal{S}[y - y_{\text{reg}}] \xrightarrow{y} \min$$



Distance Measures

- ▶ Feature Based
(Markers / Landmarks / Moments / Localizer)

- ▶ L_2 -norm, *Sum of Squared Differences (SSD)*

$$\mathcal{D}^{\text{SSD}}[\mathcal{T}[\mathbf{y}], \mathcal{R}] = \frac{1}{2} \int_{\Omega} [\mathcal{T}(\mathbf{y}(x)) - \mathcal{R}(x)]^2 dx,$$

- ▶ correlation
- ▶ Mutual Information (multi-modal images)
- ▶ Normalized Gradient Fields
- ▶ ...

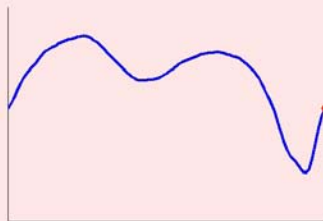


Sum of Squared Differences

 \mathcal{R}

 $\mathcal{T}[y]$

 $|\mathcal{T}[y] - \mathcal{R}|$

 SSD versus y


Mutual Information



Regularization

$$\mathcal{D}[\mathcal{T}[y], \mathcal{R}] + \alpha \mathcal{S}[y - y_{\text{reg}}] \xrightarrow{y} \min$$



Transformation y

1	2	3
4	5	6
7	8	

1	2	3
4	5	8
7	6	



- ▶ Registration is severely **ill-posed**
- ▶ **Restrictions** onto the **transformation y** needed
- ▶ **Goal:** implicit physical restrictions



Implicit versus Explicit Regularization ...

Registration is **ill-posed** \rightsquigarrow requires **regularization**

▶ Parametric Registration

- ▶ restriction to (low-dimensional) space (rigid, affine linear, spline, ...)
- ▶ regularized by properties of the space (**implicit**)
- ▶ not physical or model based

▶ Non-parametric Registration

- ▶ regularization by adding penalty or likelihood (**explicit**)
- ▶ allows for a physical model
- ▶ \rightsquigarrow **y** is no longer parameterizable



... implicit versus explicit regularization

registration is ill-posed \rightsquigarrow requires regularization

► parametric registration

parametric registration

$$\mathcal{D}[R, T; y] \stackrel{y}{=} \min \quad \text{s.t.} \quad y \in \mathcal{Q} = \{x + \sum w_j q_j, w \in \mathbb{R}^m\}$$

► non-parametric registration

non-parametric registration

$$\mathcal{D}[R, T; y] + \alpha \mathcal{S}[y - y_{\text{reg}}] \stackrel{y}{=} \min$$



References for Well-Posedness



M. Droske and M. Rumpf.

A variational approach to non-rigid morphological registration.

SIAM Appl. Math., 64(2):668–687, 2004.



B. Fischer and J. Modersitzki.

A unified approach to fast image registration and a new curvature based registration technique.

Linear Algebra and its Applications, 380:107–124, 2004.



J. Weickert and C. Schnörr.

A theoretical framework for convex regularizers in PDE-based computation of image motion.

Int. J. Computer Vision, 45(3):245–264, 2001.



...



Regularizer \mathcal{S}

$y(x) = x + u(x)$, displacement $u : \mathbb{R}^d \rightarrow \mathbb{R}^d$

- ▶ “elastic registration” $\mathcal{S}^{\text{elas}}[u] = \text{elastic potential of } u$
- ▶ “fluid registration” $\mathcal{S}^{\text{fluid}}[u] = \text{elastic potential of } \partial_t u$
- ▶ “diffusion registration” $\mathcal{S}^{\text{diff}}[u] = \frac{1}{2} \sum_{\ell=1}^d \int_{\Omega} \|\nabla u_{\ell}\|_{\mathbb{R}^2}^2 dx$
- ▶ “curvature registration” $\mathcal{S}^{\text{curv}}[u] = \frac{1}{2} \sum_{\ell=1}^d \int_{\Omega} (\Delta u_{\ell})^2 dx$
- ▶ ...



Elastic Registration

Transformation/displacement, $y(x) = x + u(x)$

$$\begin{aligned}\mathcal{S}^{\text{elas}}[u] &= \text{elastic potential of } u \\ &= \int_{\Omega} \frac{\lambda + \mu}{2} \|\nabla \cdot u\|^2 + \frac{\mu}{2} \sum_{i=1}^d \|\nabla u_i\|^2 dx\end{aligned}$$

image painted on a rubber sheet



C. Broit.

Optimal Registration of Deformed Images.

PhD thesis, University of Pennsylvania, 1981.



Bajcsy & Kovačič 1986, Christensen 1994, Bro-Nielsen 1996,
Gee et al. 1997, Fischer & M. 1999, Rumpf et al. 2002, ...



Fluid Registration

Transformation/displacement, $y(x, t) = x + u(x, t)$

$\mathcal{S}^{\text{fluid}}[u]$ = elastic potential of $\partial_t u$

image painted on honey



GE. Christensen.

Deformable Shape Models for Anatomy.

PhD thesis, Sever Institute of Technology, Washington University,
1994.



Bro-Nielsen 1996, Henn & Witsch 2002, ...



Diffusion Registration

Transformation/displacement, $y(x) = x + u(x)$

$$\begin{aligned} \mathcal{S}^{\text{diff}}[u] &= \text{oszillations of } u \\ &= \frac{1}{2} \sum_{\ell=1}^d \int_{\Omega} \|\nabla u_{\ell}\|_{\mathbb{R}^2}^2 dx \end{aligned}$$

heat equation



B. Fischer and J. Modersitzki.

Fast diffusion registration.

AMS Contemporary Mathematics, Inverse Problems, Image Analysis, and Medical Imaging, 313:117–129, 2002.



Horn & Schunck 1981, Thirion 1996, Droske, Rumpf & Schaller 2003, ...



Curvature Registration

Transformation/displacement, $y(x) = x + u(x)$

$$\begin{aligned} \mathcal{S}^{\text{curv}}[u] &= \text{oscillations of } u \\ &= \frac{1}{2} \sum_{\ell=1}^d \int_{\Omega} \|\Delta u_{\ell}\|_{\mathbb{R}^2}^2 dx \end{aligned}$$

bi-harmonic operator



B. Fischer and J. Modersitzki.

Curvature based image registration.

J. of Mathematical Imaging and Vision, 18(1):81–85, 2003.



Stefan Henn.

A multigrid method for a fourth-order diffusion equation with application to image processing.

SIAM J. Sci. Comput., 2005.



Registration of a ■

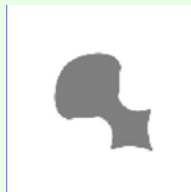
Curvature Registration

- **Goal:** do not penalize affine linear transformations
 $\mathcal{S}[Cx + b] \stackrel{!}{=} 0$ for all $C \in \mathbb{R}^{d \times d}$ and $b \in \mathbb{R}^d$
- **But:** $\mathcal{S}^{\text{diff,elas,fluid,...}}[Cx + b] \neq 0$!
- **Idea:** $\mathcal{S}^{\text{curv}}[y] = \sum_{\ell} \int_{\Omega} (\Delta y_{\ell})^2 dx \Rightarrow \mathcal{S}^{\text{curv}}[Cx + b] = 0$

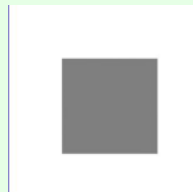
reference



“fluid”



“curvature”



Summary Regularization

- ▶ Registration is **ill-posed** \rightsquigarrow requires **regularization**
- ▶ Regularizer controls **reasonability** of transformation
- ▶ Application conform regularization
- ▶ Enabling physical models
(linear elasticity, fluid flow, . . .)
- ▶ \rightsquigarrow high dimensional optimization problems



Numerical Methods for Image Registration



Optimize \leftrightarrow Discretize

Image Registration

$$\mathcal{D}[\mathcal{T}[y], \mathcal{R}] + \alpha \mathcal{S}[y - y_{\text{reg}}] \xrightarrow{y} \min, \quad y_{\text{reg}}(x) = x$$

Numerical Approaches:

- ▶ Optimize \rightarrow Discretize
- ▶ Discretize \rightarrow Optimize
- ▶ relatively large problems:
2.000.000 – 500.000.000 unknowns



Optimize \rightarrow Discretize: ELE

Image Registration

$$\mathcal{J}[y] = \mathcal{D}[\mathcal{T}[y], \mathcal{R}] + \alpha \mathcal{S}[y - y_{\text{reg}}] \xrightarrow{y} \min, \quad y_{\text{reg}}(x) = x$$

- ▶ Euler-Lagrange eqs. (ELE) give necessary condition:
 $\mathcal{D}_y + \alpha \mathcal{S}_y = 0 \iff f[y] + \alpha \mathcal{A}y = 0$
 system of non-linear partial differential eqs. (PDE)
- ▶ outer forces f , drive registration
- ▶ inner forces $\mathcal{A}y$, tissue properties
- ▶ ELE \rightsquigarrow PDE: balance of forces



Optimize → Discretize: Summary

Continuous Euler-Lagrange equations

$$f[y] + \alpha \mathcal{A} y = 0, \quad f[y^k] + \alpha \mathcal{A} y^{k+1} = 0, \quad f[y] + \alpha \mathcal{A} y = y_t$$

- ☀ all difficulties dumped into right hand side f
- ☀ spatial discretization straightforward
- ☀ efficient solvers for linear systems
- ☀ small controllable steps (\rightsquigarrow movies)
- ☀ moderate assumptions on f and \mathcal{A} (smoothness)
- ☁ no optimization problem behind
- ☁ non-linearity only via f
- ☁ small steps
- ☀ software: <http://www.math.uni-luebeck.de/SAFIR>



Discretize \rightarrow Optimize: Summary

Discretization \rightsquigarrow finite dimensional problem: $y^h \approx y(x^h)$

$$D(y^h) + \alpha S(y^h) \xrightarrow{y^h} \min, \quad y^h \in \mathbb{R}^n, \quad h \rightarrow 0$$

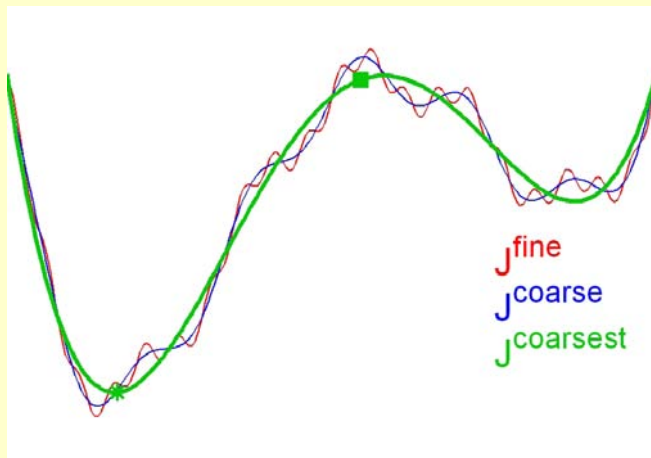
- ☀ efficient optimization schemes (Newton-type)
- ☀ linear systems of type $H \delta_y = -\text{rhs}$,

$$H = M + \alpha B^\top B, \quad M \approx D_{yy}, \quad \text{rhs} = D_y + \alpha(B^\top B)y^h$$

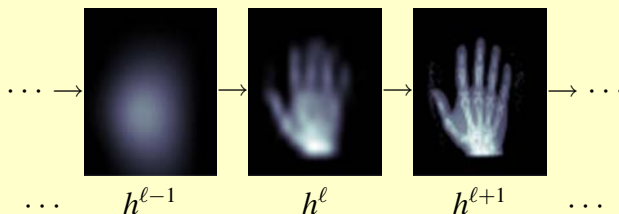
- ☀ efficient multigrid solver for linear systems
- ☀ large steps
- ☁ discretization not straightforward (multigrid)
- ☁ all parts have to be differentiable (data model)



Multilevel



Multilevel



for $\ell = 1 : \ell_{\max}$ **do**

transfer images to level ℓ

approximately solve problem for y

prolongating y to finer level \rightsquigarrow perfect starting point

end for

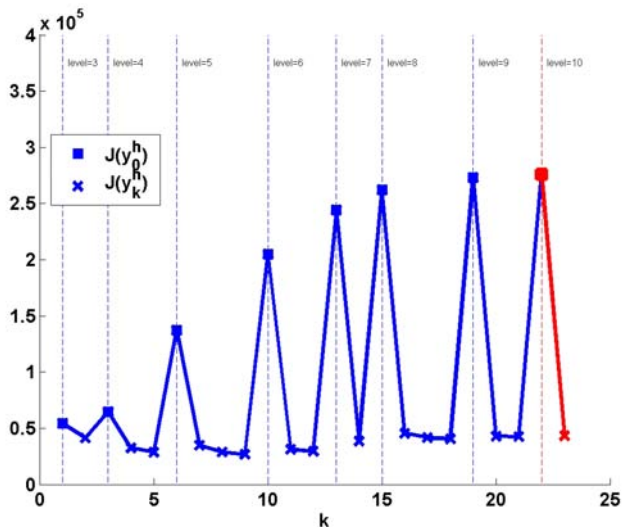


Advantages of Multilevel Strategy

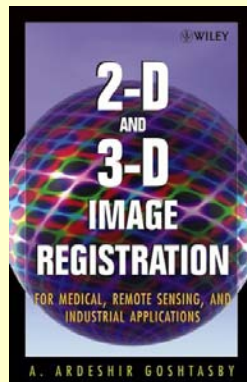
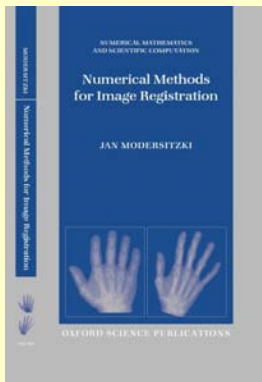
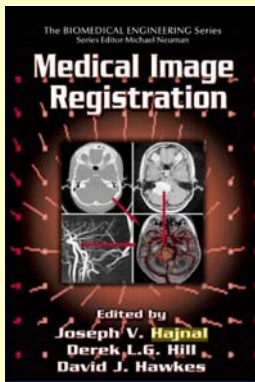
- ☀ Regularization
- ☀ Focus on essential minima
- ☀ Creates extraordinary starting value
- ☀ Reduces computation time



Example: Multilevel Iteration History



Literature



- ▶ Hajnal JV, Hill DLG, Hawkes DJ: Medical Image Registration, CRC 2001.
- ▶ Modersitzki J: Numerical Methods for Image Registration, OUP 2004.
- ▶ Goshtasby AA: 2-D and 3-D Image Registration, Wiley 2005.

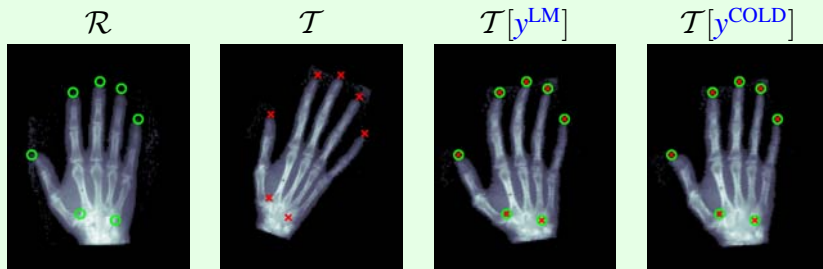


Constrained Image Registration



Example: COLD

Combining Landmarks and Distance Measures



Patent AZ 10253 784.4; Fischer & M., 2003



Adding Constraints

Constrained Image Registration

$$\mathcal{D}[\mathcal{T}[\mathbf{y}], \mathcal{R}] + \alpha \mathcal{S}[\mathbf{y} - \mathbf{y}_{\text{reg}}] + \beta \int_{\Omega} \psi(\mathcal{C}^{\text{soft}}[\mathbf{y}]) \, dx \xrightarrow{\mathbf{y}} \min$$

subject to $\mathcal{C}^{\text{hard}}[\mathbf{y}](x) = 0$ for all $x \in \Omega_{\mathcal{C}}$

Example: landmarks/volume preservation

$$\begin{aligned} \mathcal{C}_i^{\text{LM}}[\mathbf{y}] &= \|\mathbf{y}(r_i) - t_i\|, & \psi(\mathcal{C}) &= 0.5\|\mathcal{C}\|^2 \\ \mathcal{C}^{\text{VP}}[\mathbf{y}](x) &= \det(\nabla \mathbf{y}(x)), & \psi(\mathcal{C}) &= (\log \mathcal{C})^2 \end{aligned}$$

- ▶ soft constraints (penalty)
- ▶ hard constraints
- ▶ both constraints



Rigidity Constraints



Soft Rigidity Constraints

FAIR with Soft Rigidity

$$\mathcal{D}[\mathcal{T}[\mathbf{y}], \mathcal{R}] + \alpha \mathcal{S}[\mathbf{y} - \mathbf{y}_{\text{reg}}] + \beta \mathcal{C}[\mathbf{y}] \xrightarrow{\mathbf{y}} \min$$

\mathcal{C} soft constraints / penalty:

$$\mathcal{C}[\mathbf{y}] = \frac{1}{2} \underbrace{\| \mathbf{r}^{\text{linear}}(\mathbf{y}) \|^2}_{\text{linear}} + \frac{1}{2} \underbrace{\| \mathbf{r}^{\text{orth}}(\mathbf{y}) \|^2}_{\text{orthogonal}} + \frac{1}{2} \underbrace{\| \mathbf{r}^{\text{det}}(\mathbf{y}) \|^2}_{\text{orientation}}$$

$$\mathbf{r}^{\text{linear}}(\mathbf{y}) = [\partial_{1,1}\mathbf{y}_1, \dots, \partial_{d,d}\mathbf{y}_1, \partial_{1,1}\mathbf{y}_2, \dots]$$

$$\mathbf{r}^{\text{orth}}(\mathbf{y}) = \nabla \mathbf{y}^\top \nabla \mathbf{y} - I_d$$

$$\mathbf{r}^{\text{det}}(\mathbf{y}) = \det(\nabla \mathbf{y}) - 1$$

$$\mathbf{y} \text{ rigid} \iff [\mathbf{r}^{\text{linear}} = 0 \wedge \mathbf{r}^{\text{orth}} = 0 \wedge \mathbf{r}^{\text{det}} = 0]$$



The Weight \mathcal{Q}

- ▶ only locally rigid
- ▶ use weight function \mathcal{Q}
- ▶ regions to be kept rigid move with y



$$\|f\|_{\mathcal{Q}}^2 = \int_{\Omega} f(x) \mathcal{Q}(y(x))^2 dx$$



Numerical Scheme

- ▶ $Q(y^h) \approx Q(y(x^h))$
- ▶ $r(y^h) = [\text{diag}(Q(y^h)) r_1(y^h), \dots, \text{diag}(Q(y^h)) r_{\text{end}}(y^h)]$
- ▶ $C(y^h) = \frac{1}{2} r(y^h)^\top r(y^h)$
- ▶ $C_y(y^h) = \text{lengthy formula}$
- ▶ $D(y^h) + \alpha S(y^h) + \beta C(y^h) \xrightarrow{y^h} \min$
- ▶ Optimizer: Gauß-Newton type approach,

$$H \approx \nabla^2 \mathcal{D} + \alpha B^\top B + \beta r_y^\top r_y$$

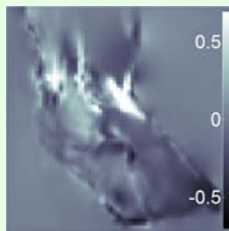
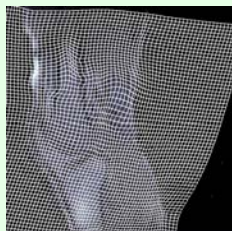


Example: Knee

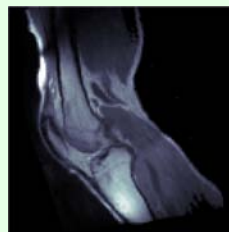
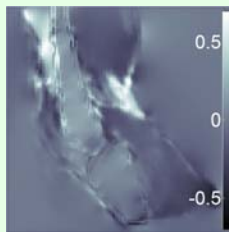
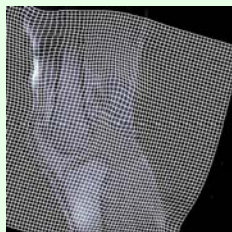
T & grid

$\det(\nabla \mathbf{y}) - 1$

$T(\mathbf{y})$



not penalized



penalized



Summary of Soft Rigidity Constraints

- ☀ Results are OK
- ☀ Implementation is straightforward
- ☁ Constraints are not fulfilled
- ☁ How to pick penalty (β, ψ) ?



Hard Rigidity Constraints

FAIR with Hard Rigidity

$$\mathcal{D}[\mathcal{T}[y], \mathcal{R}] + \alpha \mathcal{S}[y - y_{\text{reg}}] \xrightarrow{y} \min \text{ subject to } y \text{ rigid on } \mathcal{Q}$$

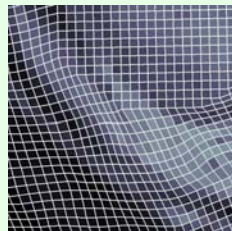
Eulerian \rightarrow Lagrangian



computations of \mathcal{D} and \mathcal{S}
involve $\det(\nabla y)$



rigidity in \mathcal{T} domain
 \leadsto “linear” constraints



$$y(x) = D_k x + t_k, \quad k = 1 : \# \text{segments}$$



Lagrangian Model of Rigidity (2D)

- rigid on segment i

$$y(x) = Q(x)w^i = \begin{pmatrix} \cos w_1^i & -\sin w_1^i \\ \sin w_1^i & \cos w_1^i \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \end{pmatrix} + \begin{pmatrix} w_2^i \\ w_3^i \end{pmatrix}$$

- $w = (w^1, \dots, w^m)$, $\mathcal{C} = (\mathcal{C}^1, \dots, \mathcal{C}^m)$, $m = \# \text{segments}$

$$\mathcal{C}^i[y, w] = y(x) - Q(x)w^i, \quad i = 1, \dots, m$$

- Lagrangian:

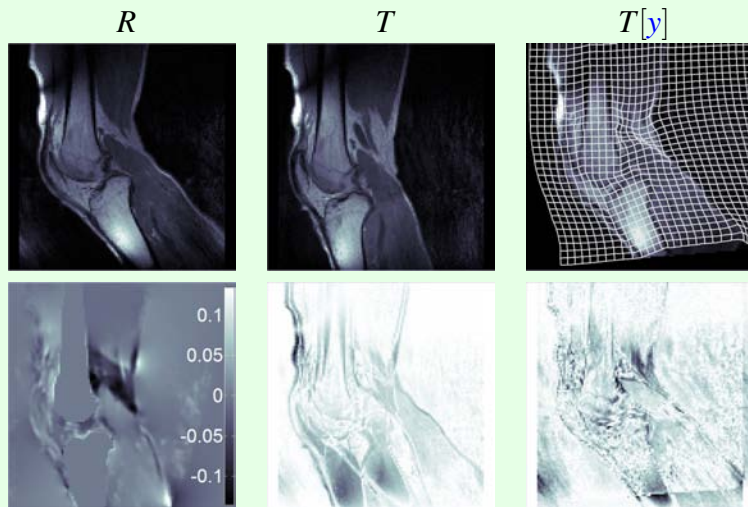
$$L(y, w, p) = \mathcal{D}[y] + \alpha \mathcal{S}[y] + p^\top \mathcal{C}[y, w]$$

- Numerical Scheme:

Sequential Quadratic Programming



Rigidity as a Hard Constraint



Summary of Hard Rigidity Constraints

- ☀ Results are OK
- ☀ Implementation is interesting
- ☀ Constraints are fulfilled
- ☀ No additional Parameters



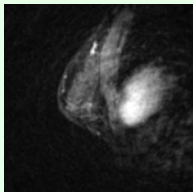
Volume Preserving Image Registration



Example: Tumor Monitoring

MRI scans of a female breast, with [Bruce L. Daniel](#)
Department of Radiology, Stanford University

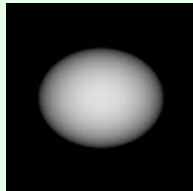
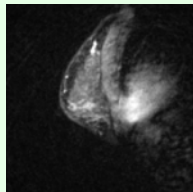
pre contrast



pre contrast



post contrast



Volume Preserving Constraints

$$\int_{\mathbf{y}(V)} dx = \int_V dx \quad \text{for all } V \subset \Omega$$

assuming \mathbf{y} to be sufficient smooth,

$$\det(\nabla \mathbf{y}) = 1 \quad \text{for all } x \in \Omega$$

Volume Preserving Constraints

$$\mathcal{C}[\mathbf{y}](x) = \det(\nabla \mathbf{y}(x)) - 1, \quad x \in \Omega_c$$



Approaches to VPIR

- Soft constraints (add a penalty)

$$\mathcal{D}[y] + \alpha \mathcal{S}[y] + \beta \int_{\Omega} \psi(\mathcal{C}[y]) \, dx = \min$$



T. Rohlfing, CR. Maurer, DA. Bluemke, and MA. Jacobs.
Volume-preserving nonrigid registration of MR breast
images using free-form deformation with an
incompressibility constraint.

IEEE TMI, 22(6):730–741, 2003.

- Hard constraints

$$\mathcal{D}[y] + \alpha \mathcal{S}[y] = \min \quad \text{s.t.} \quad \mathcal{C}[y](x) = 0 \quad \text{for all } x \in \Omega_c$$



E. Haber and J. Modersitzki.

Numerical methods for volume preserving image
registration.

Inverse Problems, 20(5):1621–1638, 2004.



Volume Preservation using Soft Constraints

$$\mathcal{D}[y] + \alpha \mathcal{S}[y] + \beta \int_{\Omega} \log^2 (\mathcal{C}^{\text{soft}}[y] + 1) dx \xrightarrow{y} \min$$

Drawbacks of Soft Constraints

- ▶ constraints are generally not fulfilled
- ▶ small soft constraints might be large on small regions (tumor!)
- ▶ additional parameters
- ▶ bad numerics for $\beta \rightarrow \infty$



Continuous Framework, Hard Constraints

VPIR

$$\mathcal{D}[y] + \alpha \mathcal{S}[y] \xrightarrow{y} \min \quad \text{s.t.} \quad \mathcal{C}[y] = 0, \quad x \in \Omega_c$$

- Distance measure \mathcal{D} with Gâteaux derivative

$$d_{y,v} \mathcal{D}[y] = \int_{\Omega} \langle f(x, y(x)), v(x) \rangle_{\mathbb{R}^d} dx$$

- Regularizer \mathcal{S} with Gâteaux derivative

$$d_{y,v} \mathcal{S}[y] = \int_{\Omega} \langle \mathcal{B}y(x), \mathcal{B}v(x) \rangle_{\mathbb{R}^d} dx$$

- Volume preserving constraints

$$\begin{aligned} \mathcal{C}[u] &= \det(\nabla y) - 1 \\ d_{y,v} \mathcal{C}[y] &= \det(\nabla y) \langle \nabla y^{-\top}, \nabla v \rangle_{\mathbb{R}^{d,d}} \end{aligned}$$



Example: Volume Preservation in 2D

$$\begin{aligned}
 \mathcal{C}[x + u(x)] &= \det(I_2 + \nabla u) - 1 \\
 &= \partial_1 u_1 + \partial_2 u_2 + \partial_1 u_1 \partial_2 u_2 - \partial_2 u_1 \partial_1 u_2 \\
 &= \nabla \cdot u + N[u]
 \end{aligned}$$

- ▶ N is nonlinear, $N[0] = 0$
- ▶ linearization

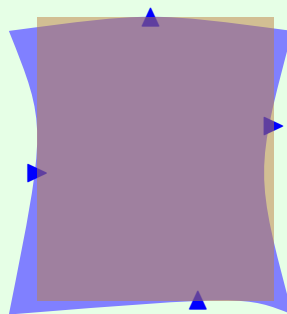
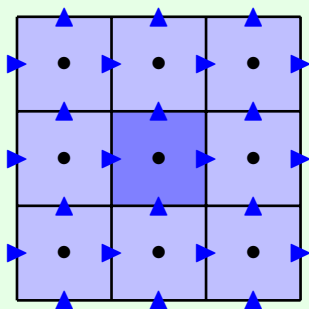
$$\mathcal{C}_y \approx \nabla \cdot \quad + [\xi(x) \cdot \partial_1 \quad \eta(x) \cdot \partial_2]$$

- ▶ \rightsquigarrow Stokes problem, needs careful discretization to keep LBB conditions or h -ellipticity



Discretizing ...

- ▶ \mathcal{T} and \mathcal{R} on cell center grid
- ▶ $y = [y_1, y_2]$ on staggered grids



- ▶ $\text{vol}(V, y) = \int_{y(V)} dx \approx \text{vol}(\text{box}), \quad c_i = \text{vol}(\text{box}_i) - h^d$
- ▶ $C(y^h) = (c_i)_{i=1}^n, \quad C_y(y^h)$ straightforward but lengthy



... and Optimize

Discrete VIPR

Find y^h such that

$$D(y^h) + \alpha S(y^h) \xrightarrow{y^h} \min \quad \text{s.t.} \quad C_i(y^h) = 0, \quad i = 1 : \# \text{voxel}$$

- ▶ SQP: Sequential Quadratic Programming
- ▶ Lagrangian with multiplier p

$$L(y^h, p) = D(y^h) + \alpha S(y^h) + p^\top C(y^h)$$

- ▶ Necessary conditions for a minimizer: $\nabla L(y^h, p) = 0$
- ▶ Gauß-Newton type method, $H = \nabla^2 D + \alpha B^\top B$

$$\begin{pmatrix} H & C_y \\ C_y^\top & 0 \end{pmatrix} \begin{pmatrix} \delta y \\ \delta p \end{pmatrix} = - \begin{pmatrix} L_y \\ L_p \end{pmatrix}$$



Details ...

- Solving the KKT system: MINRES

$$\begin{pmatrix} H & C_y \\ C_y^\top & 0 \end{pmatrix} \begin{pmatrix} \delta y \\ \delta p \end{pmatrix} = - \begin{pmatrix} L_y \\ L_p \end{pmatrix}$$

- with preconditioner

$$\begin{pmatrix} H & \\ & \hat{S} \end{pmatrix}, \quad \begin{aligned} \hat{S} &\approx C_y H^{-1} C_y^\top \\ \hat{S}^{-1} &:= C_y^\dagger H (C_y^\dagger)^\top \\ C_y^\dagger &= (C_y C_y^\top)^{-1} C_y \end{aligned}$$

- Multigrid for H and $C_y C_y^\top$



... details

- ▶ Line search for $y^h \leftarrow y^h + \gamma \delta y^h$ based on merit function

$$\text{merit}_{\text{KKT}}(y^h) := D(y^h) + \alpha S(y^h) + \theta \|C(y^h)\|_1$$

$$\theta := \|p\|_\infty + \theta_{\min}$$

$$p \text{ from } \|D_y + \alpha S_y + C_y^\top p\| \xrightarrow{p} \min$$

note,

$$(C_y C_y^\top) p = -C_y (D_y + \alpha S_y)$$

- ▶ For the projection step:

$$\text{merit}_C(y^h) := \|C(y^h)\|_2^2$$

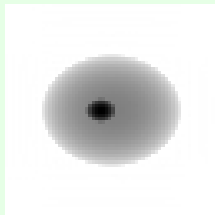
- ▶ If $\text{merit}_C(y^h) > \text{tol}$, solve for correction δy such that

$$C(y^h + \delta y) \approx C(y^h) + C_y(y^h) \delta y = 0$$

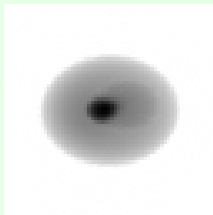


VPIR example: Blobs

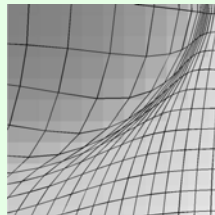
R : pre contrast



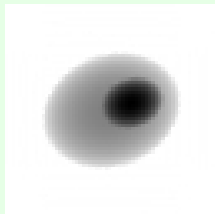
unconstrained



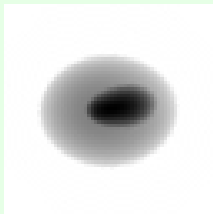
grid detail



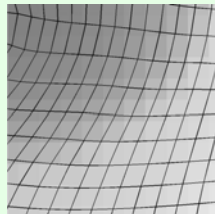
T : post contrast



VP constrained

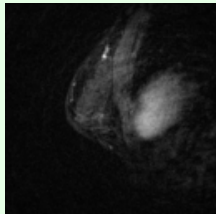


grid detail

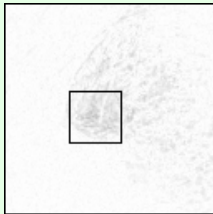


VPIR Example: Tumor Monitoring

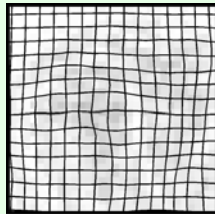
R : pre contrast



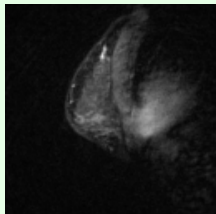
unconstrained



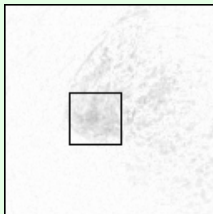
grid detail



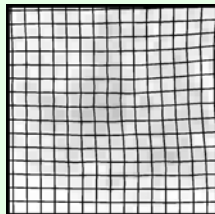
T : pre contrast



VP constrained

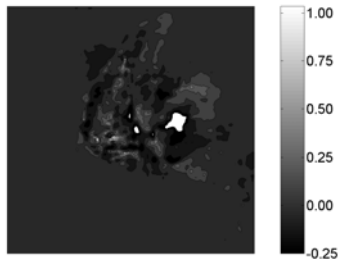


grid detail



VPIR Example: Tumor Monitoring

unconstrained



VP constrained



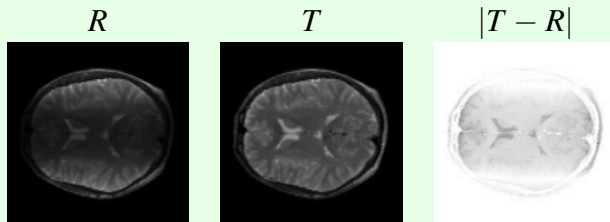
Registration and Intensity Correction



Distance Measures

- ▶ images features (moments, landmarks, markers, ...)
- ▶ sum of squared differences (SSD)
- ▶ mutual information (MI)

Problem: sophisticated distance measures enable registration, but do not correct intensities



RIC: Registration and Intensity Correction

Registration and Intensity Correction

$$\mathcal{J}[y, s] = \mathcal{D}[\mathcal{T}[y], s \mathcal{R}] + \mathcal{S}[y - y_{\text{reg}}] + \text{Hom}(s) \xrightarrow{y, s} \min$$

$$\mathcal{D}[\mathcal{T}[y], s \mathcal{R}] \stackrel{\text{e.g.}}{=} \frac{1}{2} \|\mathcal{T}[y] - s \mathcal{R}\|_{L_2}^2 = \frac{1}{2} \int \left(\mathcal{T}(y(x)) - s(x) \mathcal{R}(x) \right)^2 dx$$

intensity correction needs to be regularized
(excludes trivial solutions $s = \mathcal{T}/\mathcal{R}$, $s \equiv 1$)

choices: $\text{Hom}(s) = \int |\nabla s|^p dx, \quad |\nabla s| = \sqrt{(\partial_1 s)^2 + (\partial_2 s)^2}$

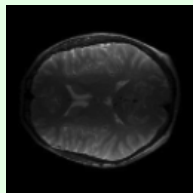
- ▶ diffusivity for $p = 2$
- ▶ total variation for $p = 1$
- ▶ Mumford-Shah penalty
- ▶ ...



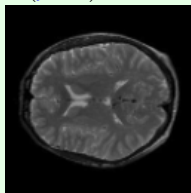
MRI inhomogeneities

Images from Samsonov, Whitaker, & Johnson, University of Utah

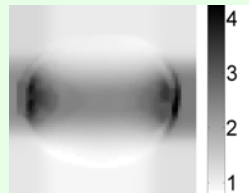
R



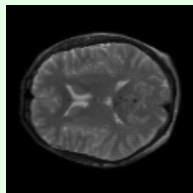
$T(y^{\text{RIC}})$



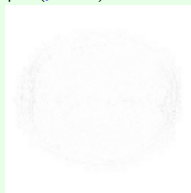
TV correction s



$s R$



$|T(y^{\text{RIC}}) - s R|$



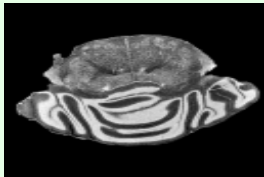
$|T(y^{\text{plain}}) - R|$



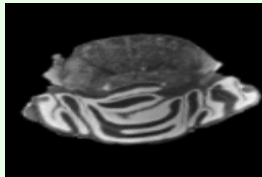
Staining Artifacts

Images from Oliver Schmitt, Anatomy, University Rostock

R



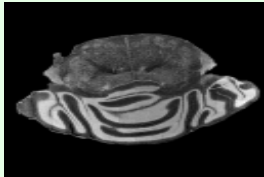
$T(y^{\text{RIC}})$



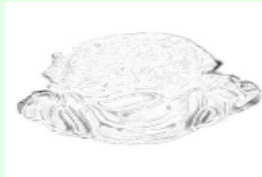
TV correction s



$s R$



$|T(y^{\text{RIC}}) - s R|$



$|T(y^{\text{plain}}) - R|$



Summary

Summary

- ▶ Introduction to image registration:
important, challenging, interdisciplinary
- ▶ General framework based on a variational approach:
 $\mathcal{D}[\mathcal{T}[y], \mathcal{R}] + \alpha \mathcal{S}[y - y_{\text{reg}}] \xrightarrow{y} \min$
- ▶ Discussion of various building blocks:
 - ▶ image model $\mathcal{T}[y]$
 - ▶ distance measures \mathcal{D}
 - ▶ regularizer \mathcal{S}
- ▶ Numerical methods:
multilevel, optimize \leftrightarrow discretize
- ▶ Constraints \mathcal{C} :
landmarks, local rigidity, intensity correction, ...

Solutions and Algorithms For Image Registration

