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Non-rigid Registration

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Outline

- Non-rigid registration: The basic formulation
 - Exercise: Parametric registration in Scalismo

• Advanced Priors

- Likelihood functions
 - Exercise: ASMs in Scalismo

• Optimization



Why is it important?

- Do automatic measurements
- Compare shapes
 - Statistics
 - Build statistical models
- Transfer labels and annotations
 - Atlas based segmentation



Maybe the most important problem in computer vision and medical image analysis

Registration as analysis by synthesis



Probabilistic formulation $\theta^* = \arg \max_{\theta} p(\theta | I_T, I_R) = \arg \max_{\theta} p(\theta) p(I_T | \theta, I_R)$

Mapping $\varphi[\theta^*]$ is trade-off that

- how well does the mapping explain the target image (likelihood function)
- matches the prior assumptions (prior distribution)

$$\theta^* = \arg\max_{\theta} p(\theta | I_T, I_R) = \arg\max_{\theta} p(I_T | \theta, I_R)$$



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Probabilistic formulation

$$\varphi^* = \arg \max_{\varphi} p(\varphi | I_T, I_R) = \arg \max_{\varphi} p(\varphi) p(I_T | \varphi, I_R)$$

Main questions:

- How do we represent the mapping?
- How do we define the prior?
- What is the likelihood function?
- How can we solve the optimization problem?

Representation of the mapping φ





Representation of the mapping φ





Representation of the mapping arphi



Assumption: Images are rigidly aligned

• Mapping can be represented as a displacement vector field:

$$\varphi(x) = x + u(x)$$
$$u : \Omega \to \mathbb{R}^d$$

Representation of the mapping arphi



Assumption: Images are rigidly aligned

• Mapping can be represented as a displacement vector field:

 $\begin{aligned} \varphi(x) &= x + u(x) \\ u &: \Omega \to \mathbb{R}^d \end{aligned}$

Observation:

Knowledge of u and I_R allows us to synthesize target image I_T

Registration as analysis by synthesis





Define the Gaussian process $u \sim GP(\mu, k)$ with mean function $\mu: \Omega \to \mathbb{R}^2$ and covariance function $k: \Omega \times \Omega \to \mathbb{R}^{2 \times 2}$.

Example prior: Smooth 2D deformations



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Example prior: Smooth 2D deformations



 $s_1 = s_2$ small, $\sigma_1 = \sigma_2$ large

Example prior: Smooth 2D deformations



Example prior: Smooth 2D deformations



 $s_1 = s_2$ large, $\sigma_1 = \sigma_2$ large

Parametric representation of Gaussian process

Represent $GP(\mu, k)$ using only the first r components of its KL-Expansion $u = \mu + \sum_{i=1}^{r} \alpha_i \sqrt{\lambda_i} \phi_i, \quad \alpha_i \sim N(0, 1)$

- We have a finite, parametric representation of the process.
- We know the pdf for a deformation *u*

$$p(u[\alpha]) = p(\alpha) = \prod_{i=1}^{r} \frac{1}{\sqrt{2\pi}} \exp(-\alpha_i^2/2) = \frac{1}{Z} \exp(-\frac{1}{2} \|\alpha\|^2)$$

Registration as analysis by synthesis



Likelihood function: Image registration

Images are similar when the intensities match

Assumptions:

• Corresponding points have the same image intensity (up to i.i.d. noise)



 $p(I_T(\varphi[\theta](x))|I_R,\theta,x) \sim N(I_R(x),\sigma^2)$

Likelihood function: Image registration

Images are similar when the intensities match

Assumptions:

• Corresponding points have the same image intensity (up to i.i.d. noise)



Registration as analysis by synthesis



Registration problem

$$\theta^* = \arg \max_{\theta} p(\varphi[\theta]) p(I_T | \varphi[\theta], I_R)$$

= $\arg \max_{\theta} \frac{1}{Z_1} \exp\left(-\frac{1}{2} \|\theta\|^2\right) \frac{1}{Z_2} \prod_{x} \exp\left(-\frac{\left(I_T(\varphi[\theta](x)) - I_R(x)\right)\right)^2}{\sigma^2}\right)$

• Parametric problem, since:

$$\varphi[\theta](x) = x + \mu(x) + \sum_{i=1}^{r} \theta_i \sqrt{\lambda_i} \phi_i(x)$$

• Can be optimized using gradient descent

$$\arg \max_{\theta} \frac{1}{Z_{1}} \exp\left(-\frac{1}{2} \|\theta\|^{2}\right) \frac{1}{Z_{2}} \prod_{x} \exp\left(-\frac{\left(I_{T}\left(\varphi[\theta](x)\right) - I_{R}(x)\right)\right)^{2}}{\sigma^{2}}\right)$$

$$\arg \max_{\theta} \ln \frac{1}{Z_{1}} \exp\left(-\frac{1}{2} \|\theta\|^{2}\right) + \ln \frac{1}{Z_{2}} \prod_{x} \exp\left(-\frac{\left(I_{T}\left(\varphi[\theta](x)\right) - I_{R}(x)\right)\right)^{2}}{\sigma^{2}}\right)$$

$$= \arg \max_{\theta} \ln \frac{1}{Z_{1}} - \frac{1}{2} \|\theta\|^{2} + \ln \frac{1}{Z_{2}} - \sum_{x \in \Omega} \frac{\left(I_{T}\left(\varphi[\theta](x)\right) - I_{R}(x)\right)\right)^{2}}{\sigma^{2}}$$

$$= \arg \min_{\theta} \sum_{x \in \Omega} \frac{\left(I_{T}\left(\varphi[\theta](x)\right) - I_{R}(x)\right)\right)^{2}}{\sigma^{2}} + \frac{\lambda}{2} \|\theta\|^{2}$$
Image metric

Probabilistic formulation $\theta^* = \arg \min_{\theta} - \ln(p(I_T | I_R, \varphi[\theta])) - \ln p(\varphi[\theta])$

Variational formulation

$$\theta^* = \arg\min_{\theta} D[I_T, I_R, \varphi[\theta]] + \lambda R[\varphi[\theta]]$$

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Exercise: Registration in Scalismo



Type into the codepane:

goto("http://shapemodelling.cs.unibas.ch/exercises/Exercise14.html")

Scalismo 0.16: Check examples in https://github.com/unibas-gravis/pmm2018

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A selection of Gaussian process priors

Why are priors interesting?

 $\theta^* = \arg \max_{\theta} p(\varphi[\theta]) p(I_T | I_R, \varphi[\theta])$



Why are priors interesting?

 $\theta^* = \arg \max_{\theta} p(\varphi[\theta]) p(I_T | I_R, \varphi[\theta])$



Models of smooth deformations

- Typical assumption:
 - Deformation field is smooth
- GP approach
 - Choose smooth kernel functions $k(x, x') = s \exp(-\frac{\|x - x'\|^2}{\sigma^2})$
- Regularization operators
 - Penalize large derivatives

$$\mathcal{R}[u] = ||Ru||^2 = \sum_{i=0}^n \alpha_i ||D_iu||^2$$



Connection between regularizer and kernel

Discrete setting: Finite difference operators

Regularizer: $\mathcal{R}[\hat{u}] = \|\widehat{D}\hat{u}\|^2$



Steinke, Florian, and Bernhard Schölkopf. "Kernels, regularization and differential equations." *Pattern Recognition* 41.11 (2008): 3271-3286.

Connection between regularizer and kernel

$$p(\hat{u}) = \exp(-\frac{1}{2}\mathcal{R}[\hat{u}]) = \exp(-\frac{1}{2}\|\widehat{D}\hat{u}\|^{2})$$
$$\widehat{D}^{T}\widehat{D} = K^{-1}$$
$$= \exp(-\frac{1}{2}(\widehat{D}\hat{u})^{T}(\widehat{D}\hat{u}) = \exp(-\frac{1}{2}\hat{u}^{T}\widehat{D}^{T}\widehat{D}\hat{u})$$

- D specifies the "inverse" covariance matrix
- Can compute K from:

 $\widehat{D}^T \widehat{D} K = I$

Green's functions and covariance functions

$$\mathcal{R}[u] = ||Ru||^2 = \sum_{i=0}^n \alpha_i ||D_iu||^2$$

Corresponding covariance function for GP is the Greens function G:

$$R^*RG(x,y) = \delta(x-y)$$

• We can define Gaussian processes, which mimic typical regularization operators.

T. Poggio and F. Girosi; Networks for Approximation and Learning, Proceedings of the IEEE, 1990
Example: Gaussian kernel

$$k(x, x') = \exp(-\frac{\|x - x'\|^2}{\sigma^2})$$

$$\mathcal{R}[u] = \|Ru\|^2 = \sum_{i=0}^{\infty} \frac{\sigma^{2i}}{i! \, 2^i} \|D_i u\|^2$$

- Non-zero functions are penalized
 - pushes functions to zero away from data

Yuille, A. and Grzywacz M. A mathematical analysis of the motion coherence theory. International Journal of Computer vision

Example: Exponential kernel (1D case)

$$k(x, x') = \frac{1}{2\alpha} \exp(-\alpha ||x - x'||)$$

$$\mathcal{R}[u] = \|Ru\|^2 = \alpha^2 u + \|D_1 u\|^2$$

Rasmussen, Carl Edward, and Christopher KI Williams. *Gaussian processes for machine learning*. Vol. 1. Cambridge: MIT press, 2006.

Matérn class of kernels

$$k(x,x') = s \frac{2^{1-\nu}}{\Gamma(\nu)} \left(2\sqrt{2\nu} \frac{\|x-x'\|}{\rho} \right)^{\nu} K_{\nu}(\sqrt{2\nu} \frac{\|x-x'\|}{\rho})$$

- Γ is the Γ function, k_{ν} the modified Bessel function and ν , ρ are parameters
- Process $u \sim GP(0, k)$ is v 1 times m.s. differentiable
- Special cases:

•
$$\nu = \frac{1}{2}$$
: $k(x, x') = s \exp(-\frac{\|x - x'\|}{\rho})$
• $\nu = \frac{3}{2}$: $k(x, x') = s(1 + \frac{\sqrt{3}\|x - x'\|}{\rho}) \exp(-\frac{\sqrt{3}\|x - x'\|}{\rho})$

• $\nu \rightarrow \infty$ Gaussian kernel

Thin-plate splines

- Minimizes the bending energy of a metal sheet $R[u] = \|(\nabla^T \nabla u)\|^2$
- Corresponding covariance function

$$k(x, x') = \frac{1}{12} (2\|x - x'\|^3 - 3R(\|x - x'\|^2 + R^3))$$

where $R = \max_{x, x' \in \Omega} \|x - x'\|$

Rohr, Karl, et al. "Landmark-based elastic registration using approximating thin-plate splines." *IEEE Transactions on medical imaging* 20.6 (2001): 526-534.

Williams, Oliver and Fitzgibbon Andrew, "Gaussian process implicit surfaces"

B-Splines

• We can build a covariance function from B-Spline basis functions β (*s* is a scaling constant)

$$k(x,y) = \sum_{k \in \mathbb{Z}^d} \beta(sx - k)\beta(sy - k)$$

• Corresponding deformation model often called "free form deformations"

- Rueckert, Daniel, et al. "Nonrigid registration using free-form deformations: application to breast MR images." *IEEE transactions on medical imaging* 18.8 (1999): 712-721.
- Klein, Stefan, et al. "Elastix: a toolbox for intensity-based medical image registration." *IEEE transactions on medical imaging* 29.1 (2010): 196-205.

Many standard models for registration can be formulated using Gaussian processes

- Yields probabilistic interpretation
- We can sample and visualize deformation fields
- Can use them as building blocks for more complicated priors

Constructing s.p.d. kernels



1.
$$k(x, x') = f(x) f(x')^T, f: X \to \mathbb{R}^d$$

2. $k(x, x') = \alpha k_1(x, x'), \alpha \in \mathbb{R}_+$ (scaling)
3. $k(x, x') = B^T k_1(x, x')B, B \in \mathbb{R}^{r \times d}$ (lifting)
4. $k(x, x') = k_1(x, x') + k_2(x, x')$ (or relationship)
5. $k(x, x') = k_1(x, x') \cdot k_2(x, x')$ (and relationship)

Multi-scale kernels

Add kernels that act on different scales:

$$k(x,x') = \sum_{i=0}^{n} \sum_{k \in \mathbb{Z}^d} \beta (2^{-i}x - k) \beta (2^{-i}x' - k)$$

• Wavelet like multiscale representation

Opfer, Roland. "Multiscale kernels." *Advances in computational mathematics* 25.4 (2006): 357-380.



Anisotropic priors

Scale deformations differently in each direction

$$k(x,x') = R^T \begin{pmatrix} \sqrt{s_1} & 0\\ 0 & \sqrt{s_2} \end{pmatrix} k(x,x') \begin{pmatrix} \sqrt{s_1} & 0\\ 0 & \sqrt{s_2} \end{pmatrix} R$$

- R is a rotation matrix
- k is scalar valued
- s_1 , s_2 scaling factors

Anisotropic priors



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Spatially-varying priors

Use different models for different regions

 $k(x, x') = \chi(x)\chi(x')k_1(x, x') + (1 - \chi(x))(1 - \chi(x'))k_2(x, x')$

 $\chi(x) = \begin{cases} 1 & \text{if } x \in \text{thumb region} \\ 0 & \text{otherwise} \end{cases}$



Freiman, Moti, Stephan D. Voss, and Simon K. Warfield. "Demons registration with local affine adaptive regularization: application to registration of abdominal structures." *Biomedical Imaging: From Nano to Macro, 2011 IEEE International Symposium on*. IEEE, 2011.

Spatially-varying priors



Statistical deformation models

Estimate mean and covariance function from data:



Example 5: Statistical deformation models



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A selection of likelihood functions

Landmark likelihood

For one landmark pair (l_R, l_T) :

 $p(l_T|\theta, l_R) = N(\varphi[\theta](l_R), I_{2x2}\sigma^2)$

For many landmarks $L = ((l_R^1, l_T^1), \dots, (l_R^n, l_T^n))$

$$p(l_1^T, \dots, l_n^T | \theta, l_R^1, \dots, l_R^n)$$
$$= \prod_i N(\varphi[\theta](l_R), I_{2x2}\sigma^2)$$



Landmark likelihood: Some remarks

- Classical problem in registration
- Needs either many landmark points or good structure of prior to achieve good results



Rohr, Karl, et al. "Landmark-based elastic registration using approximating thin-plate splines." *IEEE Transactions on medical imaging* 20.6 (2001): 526-534.

Landmark registration using GP Regression



Given:

- Gaussian process: $u \sim GP(\mu, k)$
- Observations: $\{(l_i^R, \tilde{u}_i), i = 1, ..., n\}$

Assume:

$$\tilde{u}_i = u(l_i) + \epsilon$$
 with $\epsilon \sim N(0, \sigma^2 I_{2\times 2})$.

Goal:

• Find posterior distribution

$$u \mid l_1^R$$
, ..., l_n^R , \tilde{u}_1 , ..., \tilde{u}_n

Gaussian process regression



The posterior $u \mid l_1^R, \dots, l_n^R, \tilde{u}_1, \dots, n$ is a Gaussian process $GP(\mu_p, k_p)$ Its parameters are known analytically.

 $\mu_p(x) = \mu(x) + K(x, Y)(K(Y, Y) + \sigma^2 I_{2n \times 2n})^{-1}(\tilde{u} - \mu(Y))$ $k_p(x, x') = k(x, x') - K(x, Y)(K(Y, Y) + \sigma^2 I_{2n \times 2n})^{-1}K(Y, x')$

Landmark registration using GP Regression





Hybrid registration

- Combine landmark registration with intensity:
 - 1. Use Gaussian process regression to obtain posterior from $GP(\mu, k)$ from landmarks
 - 2. Use $GP(\mu_p, k_p)$ as new prior model for registration
- Simple solution to otherwise difficult problem

Wörz, Stefan, and Karl Rohr. "Hybrid spline-based elastic image registration using analytic solutions of the navier equation." *Bildverarbeitung für die Medizin 2007*. Springer Berlin Heidelberg, 2007. 151-155.

Lu, Huanxiang, Philippe C. Cattin, and Mauricio Reyes. "A hybrid multimodal non-rigid registration of MR images based on diffeomorphic demons." *Engineering in Medicine and Biology Society (EMBC), 2010 Annual International Conference of the IEEE*. IEEE, 2010.

Likelihood function: Image registration

Images are similar when the intensities match

Assumptions:

• Corresponding points have the same image intensity (up to i.i.d. noise)



 $p(I_T(\varphi[\theta](x))|I_R,\theta,x) \sim N(I_R(x),\sigma^2)$

Likelihood function: Image registration

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Assumptions:

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Image vs. Landmark registration

- Landmark registration is easy
 - All components are Gaussian
 - Closed form solution using Gaussian process regression
- Image registration is hard
 - Image destroys Gaussian assumption
 - Likelihood function is not Gaussian
 - Problem with many local minima

What about surface registration?



Reference (surface): Γ_R

Target (surface): Γ_T

A trick: Implicit definition of a surface

- Any surface Γ can be represented as the zero level set of a level set function Φ

 $\Gamma = \{x \mid \Phi(x) = 0\}$

• Popular choice is the signed distance function defined as

$$D_{\Gamma}(x) = \|CP_{\Gamma}(x) - x\|$$

with
$$CP_{\Gamma}(x) = \arg\min_{x' \in \Gamma} \|x - x'\|$$



Likelihood function: Surface registration

- We define the distance functions and use image to image likelihoods $p(D_T(\varphi[\theta](x))|\theta, D_R, x) \sim N(D_R\varphi[\theta](x), \sigma^2)$
- Most likely solution will map points on the zero level-sets to each other
 - Noise parameter σ^2 has geometric interpretation (variance of distance between the mapped points)



Likelihood function: Active shape models

Shape is well matched if environment around profile points is likeli under trained model.



• ASMs model each profile $\rho(x_i)$ as a normal distribution $p(\rho(x_i)) = N(\mu_i, \Sigma_i)$ Extract

Extracts profile (feature) from image

- Single profile point x_i : $p(\rho(\varphi[\theta](x_i))|\theta, x_i) = N(\mu_i, \Sigma_i)$
- Image likelihood:

 $p(\rho(\varphi[\theta](x))|\theta, \Gamma_R) = \prod_i N(\mu_i, \Sigma_i)$

Exercise: Active Shape Models in Scalismo



Type into the codepane:

goto("http://shapemodelling.cs.unibas.ch/exercises/Exercise16.html")

Scalismo 0.16: Check examples in https://github.com/unibas-gravis/pmm2018

Summary: Modelling

- GPs provide probabilistic interpretation to classic registration models
 - Can visualize assumptions
 - New ways to combine priors to individual applications.
- Modelling of prior is separate from likelihood
 - Any GP model can be combined with any likelihood function
- Flexible framework to tailor model and algorithm to needs of applications
 - No increase in complexity
- Modelling and model fitting are separated
 - Gradient based methods are important, but not the only method

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Optimization

The optimization problem

$$\theta^* = \arg \max_{\theta} p(\varphi[\theta]) p(I_T | I_R \circ \varphi[\theta])$$

- The final problem is a difficult optimization problem
- Possibly many local minima

- Non-linearity due to image term
 - Not possible to avoid it
- Flexible models makes things worse



Local minima

- Rigid Transformation
 - Minima due to structure of object

Possible approach: Multi-resolution

- Non-rigid Transformation
 - Minima appear/dissappear when shape changes

Possible approach: Multi-scale models, regularization



Multi resolution

Idea: Solve optimzation problem for a sequence of smoothed out objects.



Implementation

- Smooth the input shapes
- For images, achieved by Gaussian blurring



Initial registration

Almost no local minima No-details





Final registration Many local minima All-details
Multi-scale / Regularization

Idea: Solve optimization problem for a sequence of increasingly detailed deformations





Initial registration

Only large, smooth deformations Large regularization value Final registration

Allow detailed deformations Almost no regularization

Doing the registration

Strategies:

- Gradient-based registration
 - Compute gradient and use local optimization methods
 - Quasi-Newton schemes , SGD, ...
- Gradient free registration
 - Use global optimization method directly on cost function
 - Examples: Simulated annealing, Particle Swarm, ...
- ICP-based methods
 - Assume correspondence and solve in each iteration analytic problem
 - Examples: Non-rigid ICP, Active Shape models, CPD

Model-fitting using Markov Chain Monte Carlo

